SYNTHESIS OF (±)-OXETANOCIN AND RELATED COMPOUNDS

by

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requirements for the degree of Doctor of Philosophy

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To My Parents,

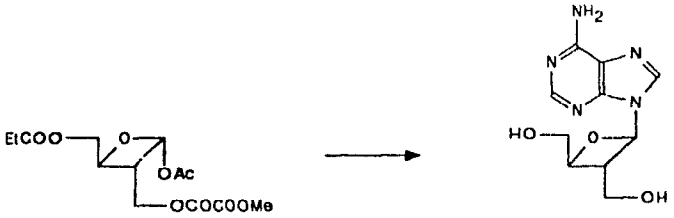
Josef and Anna Hambalek

To My Loving Wife and Colleague,

Kristina

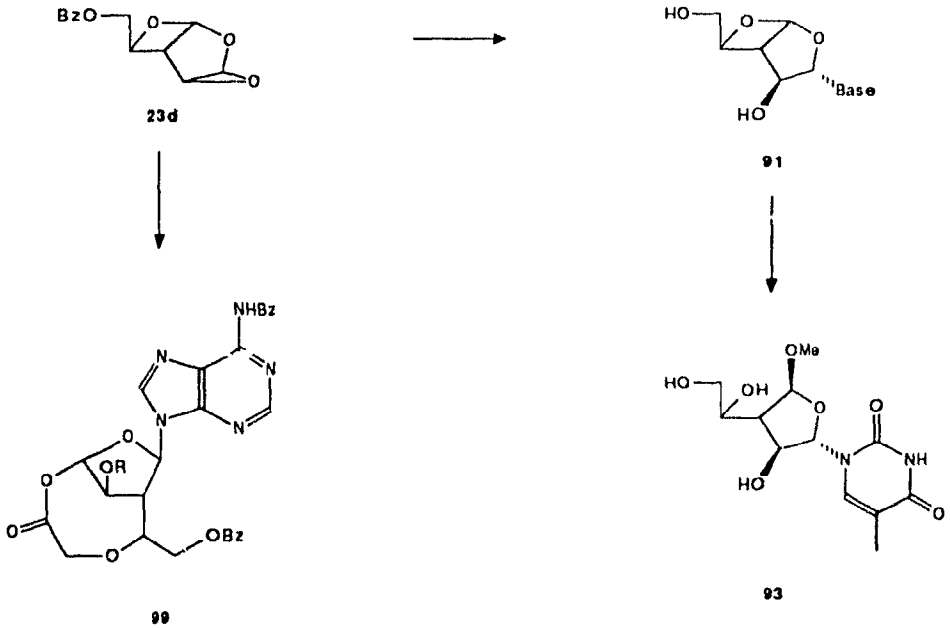
ABSTRACT

Photo-adducts of aldehydes and furan were transformed to substituted monocyclic oxetanes, using a modification of the Fraser-Reid-Mootoo glycosidation procedure, and the chemistry of these oxetanes was studied. The photo-adduct of 2-methylfuran and propionyloxyacetaldehyde was transformed in a one-pot reaction to oxetane **75a**, which gave oxetanocin and its epimer as described. The coupling of various oxetanes of the type **75** to nitrogenous bases was also investigated.



75a (±) oxetanocin

During the course of this work, it was found that epoxides of the type **23** could be transformed into bicyclic nucleosides **91** and furanosides **93**. Bicyclic nucleosides **99** were also prepared, again using a modified Fraser-Reid-Mootoo coupling procedure.



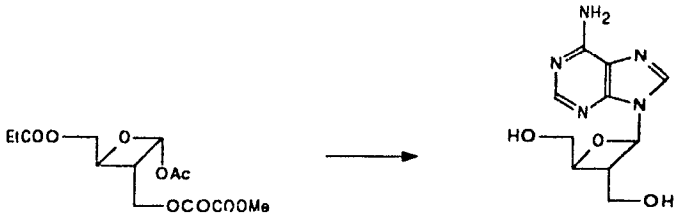
23d **91** **99** **93**

An investigation into the resolution of photo-adducts of aldehydes and furans was initiated.

RESUME

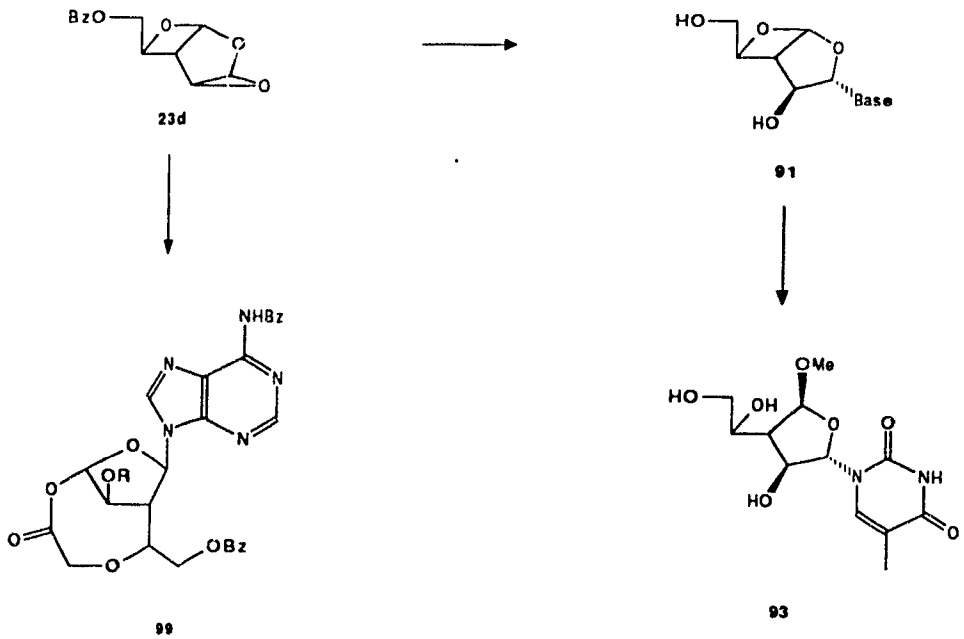
Des adduits résultant de la cycloaddition photochimiques du furane sur des aldéhydes ont été convertis en oxetanes monocycliques substitués en utilisants une modification du procédé de glycosidation Fraser-Reid—Mootoo. La chimie de ces oxetanes résultant a été également étudiée.

L'adduit dérivé de la photo-condensation du methyl-2 furane et du propionyloxyacetaldehyde a été transformé par trois réactions *in situ* en l'oxetane **75a** dont le couplage avec l'adénine a donné lieu á la formation de l'oxetanocin et de l'épimère correspondant. Une études plus générale sur la couplage des oxétanes du types **75** avec des bases puriques a été également entreprisé.



75a (±)-oxetanocin

Il a été trouvé dans le cadre de ce travail que des époxides du type **23** pourient été convertis en nucléosides bicycliques tel que **91** et du furanosides tel que **93**. Les nucléosides bicycliques **99** ont également préparés par une modification de la méthode de couplage Fraser-Reid—Mootoo.



23d **91**

99 **93**

Des travoux en vue de parvenir a la séparation des diastéréomèrs des adduits résultant de la photocondensation des aldéhydes et des furanes ont été entamés.

ACKNOWLEDGEMENTS

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GLOSSARY OF ABBREVIATIONS

Ac	acetyl
Ade	adenine
AIDS	acquired immunodeficiency syndrome
APT	attached proton test
B	base
Bn	benzyl
Bu	butyl (C_4H_9)
Bz	benzoyl
calcd	calculated
CI	chemical ionization
coll	*sym*-collidine
COSY	correlation spectroscopy
Cyt	cytosine
ddA	2',3'-dideoxyadenosine
DEAD	diethyl azodicarboxylate
DIBAL-H	di-*iso*-butylaluminum hydride
DMAP	4-dimethylaminopyridine
DMF	dimethylformamide
DMS	dimethyl sulfide
DNA	2'-deoxyribonucleic acid
E^+	electrophile
EC_{50}	effective concentration for 50% inhibition
ED_{50}	effective dose for 50% inhibition
EI	electron impact
EBV	Epstein-Barr virus
Et	ethyl (C_2H_5)
ee	enantiomeric excess
equiv.	equivalent(s)
FAB	fast atom bombardment
g	gram(s)
GC	gas chromatography
h	hour(s)
HBV	hepatitis B virus
HCMV	human cytomegalovirus

HETCOR	heteronuclear correlation
HIV	human immunodeficiency virus
HMDS	1,1,1,3,3,3-hexamethyldisilazane
HRMS	high-resolution mass spectrometry (spectrum)
HSV	herpes simplex virus
Hz	Hertz
i-	*iso-*
IC_{50}	inhibitory concentration which inhibits 50%
ID_{50}	inhibitory dose which inhibits 50%
IDCP	iodonium di-*sym*-collidine perchlorate
imid	imidazole
IR	infra-red
λ	wavelength
L	liter(s)
LRMS	low-resolution mass spectrometry (spectrum)
M	mega
M	molar(ity)
m	milli
μ	micro
MCPBA	*meta*-chloroperbenzoic acid
MCMV	murine cytomegalovirus
Me	methyl (CH_3)
MEM	methoxyethoxymethyl
MIC	minimum inhibitory concentration
min	minute(s)
MMPP	magnesium monoperoxyphthalate
mol	mole(s)
MOM	methoxymethyl
m.p.	melting point
N	normal(ity)
NBS	N-bromosuccinimide
NCS	N-chlorosuccinimide
NIS	N-iodosuccinimide
Nu	nucleophile
ppm	parts per million
Pr	propyl (C_3H_7)

Ph	phenyl
PPL	porcine pancreatic lipase
py	pyridine
R_f	distance travelled by compound, divided by that travelled by solvent front
res	resolving power (in HRMS)
RNA	ribonucleic acid
RT	room temperature
$T_{1/2}$	half-life
t- or tert-	*tertiary-*
TBAF	tetrabutylammonium fluoride
TBDMSi	*tert*-butyldimethylsilyl
TBDPhSi	*tert*-butyldiphenylsilyl
TEA	triethylamine
Tf	trifluoromethanesulfonyl-
TFA	trifluoroacetic acid
THF	tetrahydrofuran
Thy	thymine
tlc	thin layer chromatography
TMSi	trimethylsilyl
TMS	tetramethylsilane
UV	ultraviolet
v	volume
VZV	varicella-zoster virus
w	weight

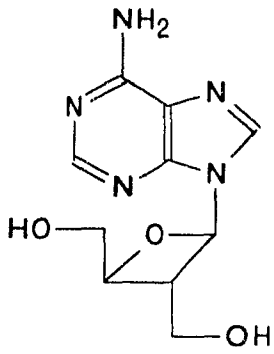
TABLE OF CONTENTS

5. APPENDICES.

1. INTRODUCTION & LITERATURE REVIEW.

1.1 Isolation and Characterization.

In 1986, an article[1] was published describing oxetanocin, a structurally novel nucleoside isolated from the culture filtrate of *Bacillus megaterium* NK 84-0218, which has been shown to possess antibacterial, antiviral and antitumor activity. Oxetanocin was isolated in yields of approximately 12 mg/L of culture filtrate and is only obtained in pure form after lengthy and tedious chromatographic separations.



Structure of oxetanocin

Oxetanocin is the first natural product which is an oxetanosyl-N-glycoside[1] and the name "oxetanoside" has been proposed by Niitsuma[2], for the glycoside possessing an oxetane ring . The structure of oxetanocin was assigned after extensive analysis of its IR, UV, ^{13}C-NMR, ^{1}H-NMR and field desorption mass spectra as well as elemental analysis. Its structure was confirmed by X-ray crystallographic studies[3].

Oxetanocin exhibited cytotoxicity against Vero cells (132.6 µg/well, 50% inhibition of cell growth)[1]. It also inhibited the growth of HeLa cells in vitro (IC_{50} 47 µg/mL)[1] and showed activity against both herpes simplex virus-I (IC_{50} 4.8 µg/mL)[4] and herpes simplex virus II (IC_{50} 10 µg/mL)[1,4,5]. Oxetanocin showed anti hepatitis B virus activity (ID_{50} 9.1 µg/mL)[6] and anti human cytomegalovirus activity (IC_{50} 13 µg/mL)[4]. However, oxetanocin did not exhibit any activity against vesicular stomatitis

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1 Shimada, N.; Hasegawa, S , Harada, T.; Tomisawa, T , Fujii, A , Takita, T , *J Antibiot* , **39**, 1623 (1986)
2 Niitsuma, S ; Ichikawa, Y , Kato, K , Takita, T , *Tetrahedron Lett* , **28**, 3967 (1987)
3 Nakamura, H.; Hasegawa, S , Shimada, N , Fujii, A ; Takita, T., Iitaka, Y , *J Antibiot.*, **39**, 1626 (1986)
4 Nishiyama, Y , Yamamoto, N , Takahashi, K., Shimada, N , *Antimicrob Agents Chemother* , **32**, 1053 (1988)
5 Shimada, N , Hasegawa, S.; Saito, S.; Nishikiori, T.; Fujii, A ; Takita, T , *J. Antibiot* , **40**, 1788 (1987)
6 Nagahata, T.; Ueda, K.; Tsurimoto, T , Chisaka, O.; Matsubara, K , *J Antibiot* , **42**, 644 (1989)

virus (RNA virus) at 100 μg/well[1]. Oxetanocin also showed strong antibacterial activity against *Staphylococcus aureus* 209P (MIC < 0.1 μg/mL), *Bacillus subtilis* PCI 219 (MIC < 0.1 μg/mL), *Bacillus polymyxa* IAM 1210 (MIC < 0.1 μg/mL) and *Bacillus megaterium* ATCC 14945 MIC = 1.56 μg/mL) Adenine and adenosine were strongly antagonistic against oxetanocin in terms of its antibacterial activity. Inosine and guanosine demonstrated only a weak antagonistic effect[1]. However, the most impressive feature of oxetanocin is its activity against the human immunodeficiency virus[7,8,9]. Moreover, it is active at very low concentrations (0.5-1.5 μg/mL) and intravenous injections of oxetanocin to mice (200 mg/kg) did not show any signs of toxicity[1]. When allopurinol and mycophenolic acid were added to oxetanocin, additive anti-HIV effects were produced[8].

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[7] Hoshino, H.; Shimizu, N.; Shimada, N.; Takita, T.; Takeuchi, T., *J. Antibiot.*, **40**, 1077 (1987).
[8] Seki, J.; Shimada, N.; Takahashi, K.; Takita, T.; Takeuchi, T.; Hoshino, H., *Antimicrob. Agents Chemother.*, **33**, 773 (1989)
[9] Wilson, F. X.; Fleet, G. W. J.; Vogt, K.; Wang, Y.; Witty, D. R.; Choi, S.; Storer, R.; Myers, P. L.; Wallis, C. J., *Tetrahedron Lett.*, **31**, 6931 (1990).

1.2 Mode of Action Against Human Immunodefiency Virus.

The tremendous interest in oxetanocin over the last few years is largely due to its ability to inhibit the HIV virus. The human immunodeficency virus belongs to a class of viruses that are known as retroviruses. Replication of the HIV virus is a complicated affair involving many steps. This is shown in Figure 1[10].

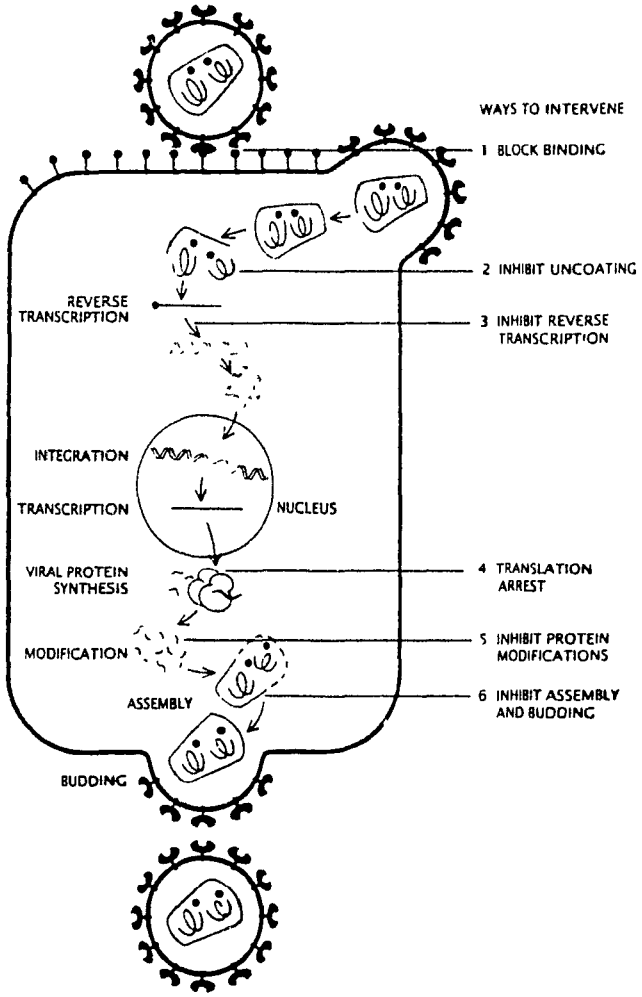

Figure 1. Life Cycle of the Human Immunodeficiency Virus. The first step involves binding of the glycoprotein on the viral envelope to the receptors on the surface of the cell. After the HIV virus has bound to the cell, it fuses with the cell membrane and releases its contents into the cytoplasm. Next, viral RNA and reverse transcriptase escape from their inner protein coat. The reverse transcriptase then binds to the viral RNA and begins synthesizing a complementary viral DNA strand. Reverse transcriptase then proceeds to make a second DNA copy of the first DNA strand. This double stranded DNA is now incorporated into the cellular DNA and is transcribed with the host cell DNA. The transcribed RNA is translated into viral proteins. The viral proteins thus produced undergo modifications to allow them to assemble into virus particles which then escape the cell by budding out of its surface.

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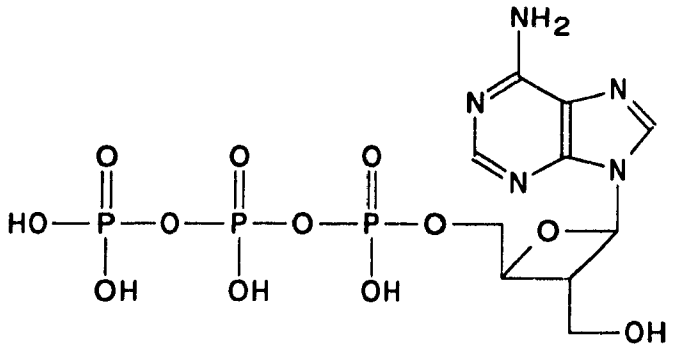
[10] From AIDS THERAPIES by Yarchoan, R.; Mitsuya, H.; Broder, S , *Scientific American*, **259**, 112 (1988).

Interference with any of the six steps shown in Figure 1. would destroy the virus' ability to replicate itself. Oxetanocin possesses anti-HIV activity due to its ability to inhibit the synthesis of viral DNA by the inhibition of HIV reverse transcriptase[11]. The causative agent of this inhibition is oxetanocin triphosphate[12], formed through cellular phosphorylation mechanisms. A great deal of effort is currently underway to determine the mechanism of inhibition of reverse transcriptase so as to make logical structural changes to known anti-HIV compounds that would enhance their effectiveness.



Oxetanocin Triphosphate

11 Seki, J.; Takeuchi, T.; Shimada, N.; Takahashi, K.; Takita, T.; Hoshino, H., *5th International Conference on Aids*, Montréal, June 4-9; M.C.P. 121, p. 562.

12 Saito, S.; Hasegawa, S.; Kitagawa, M.; Shimada, N.; Takahashi, K.; Seki, J.; Hoshino, H.; Nishiyama, Y.; Matsubara, K.; Nagahata, T., *Eur. Pat. Appl.*, EP 392,403 (1990).

1.3 Syntheses of Oxetanocin.

Shortly after we initiated our project, the first total synthesis of oxetanocin was published in 1987 by Niitsuma[13]. The synthesis, which used a glucose derivative as its starting point, produced oxetanocin in only 0.008% overall yield. The key step involved cyclization of an epoxy allylic ether to an oxetane. Unfortunately, this step proceeded in only 5% yield.

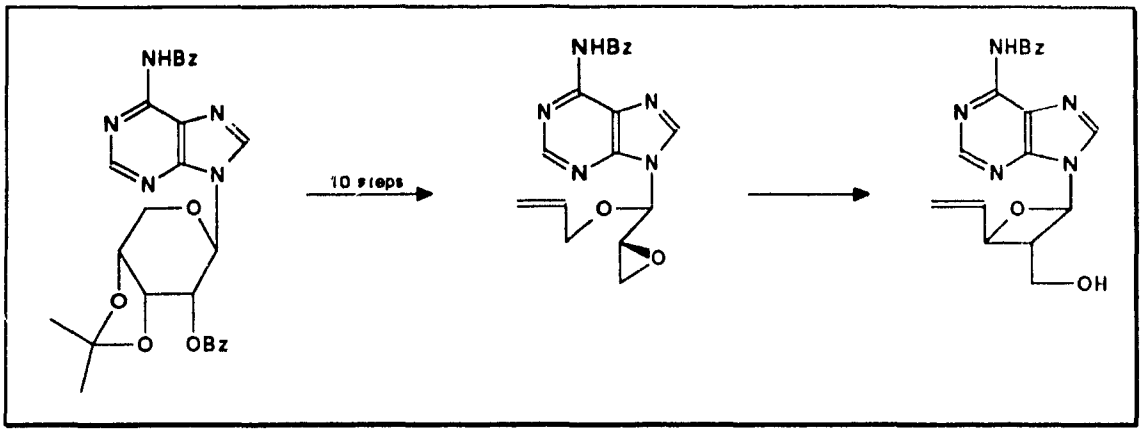


Figure 2. The Niitsuma synthesis of oxetanocin.

Approximately one year later, another equally low yield synthesis was published[14,15]. This synthesis used cis-2-buten-1,4-diol as its starting point. The starting material was transformed to mesylate **I**, which was then converted to oxetane **II**. Coupling of oxetane **II** with the nitrogenous base yielded protected oxetanocin and epioxetanocin in a 3:1 ratio. Separation of the two isomers was very tedious due to the fact that they had to be converted to their tetrabenzoate derivatives before separation was possible.

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13 Niitsuma, S.; Ichikawa, Y.; Kato, K.; Takita, T., *Tetrahedron Lett.*, **28**, 4713 (1987).
14 Nishiyama, S.; Yamamura, S.; Kato, K.; Takita, T., *Tetrahedron Lett.*, **29**, 4739 (1988).
15 Nishiyama, S.; Yamamura, S.; Kato, K.; Takita, T., *Tetrahedron Lett.*, **29**, 4743 (1988).

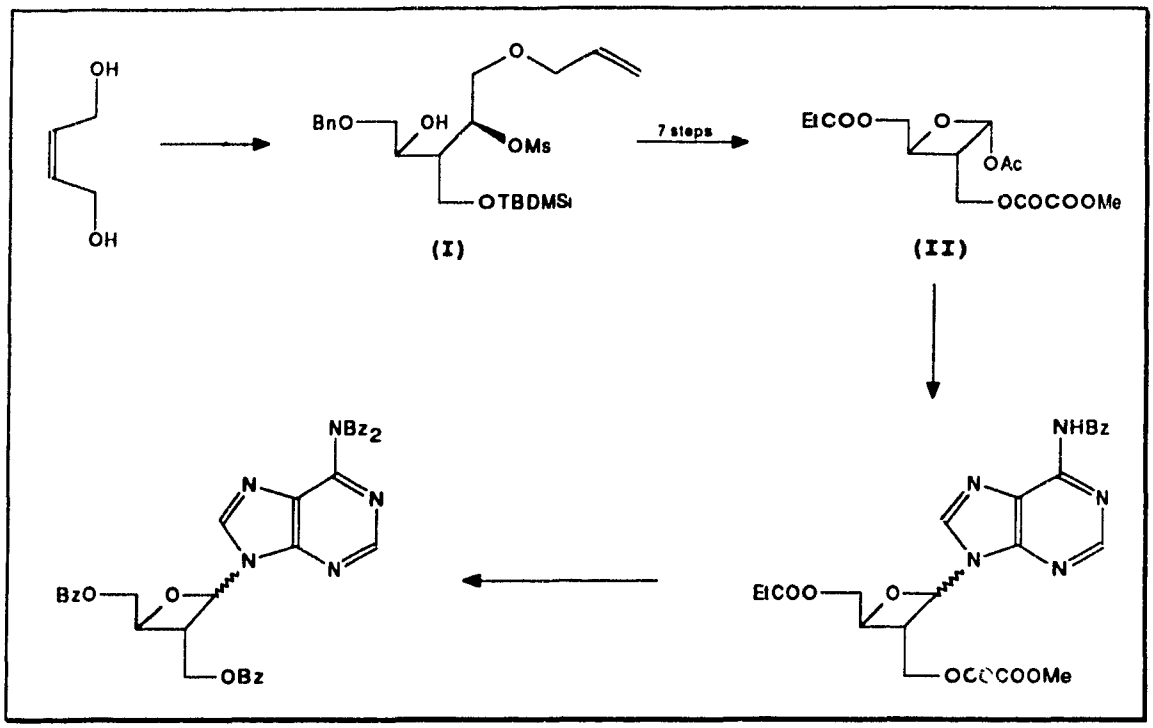


Figure 3. The Yamamura synthesis of oxetanocin.

A few weeks later, Norbeck[16] reported a 12 step synthesis of oxetanocin starting from adenosine. The synthesis proceeded in 5% overall yield. The key step involved a Wolff rearrangement of diazoketone **III**. Application of this methodology to the preparation of pyrimidine analogues of oxetanocin has not been reported in the literature.

[16] Norbeck, D. W.; Kramer, J. B., *J. Am. Chem. Soc.*, **110**, 7217 (1988).

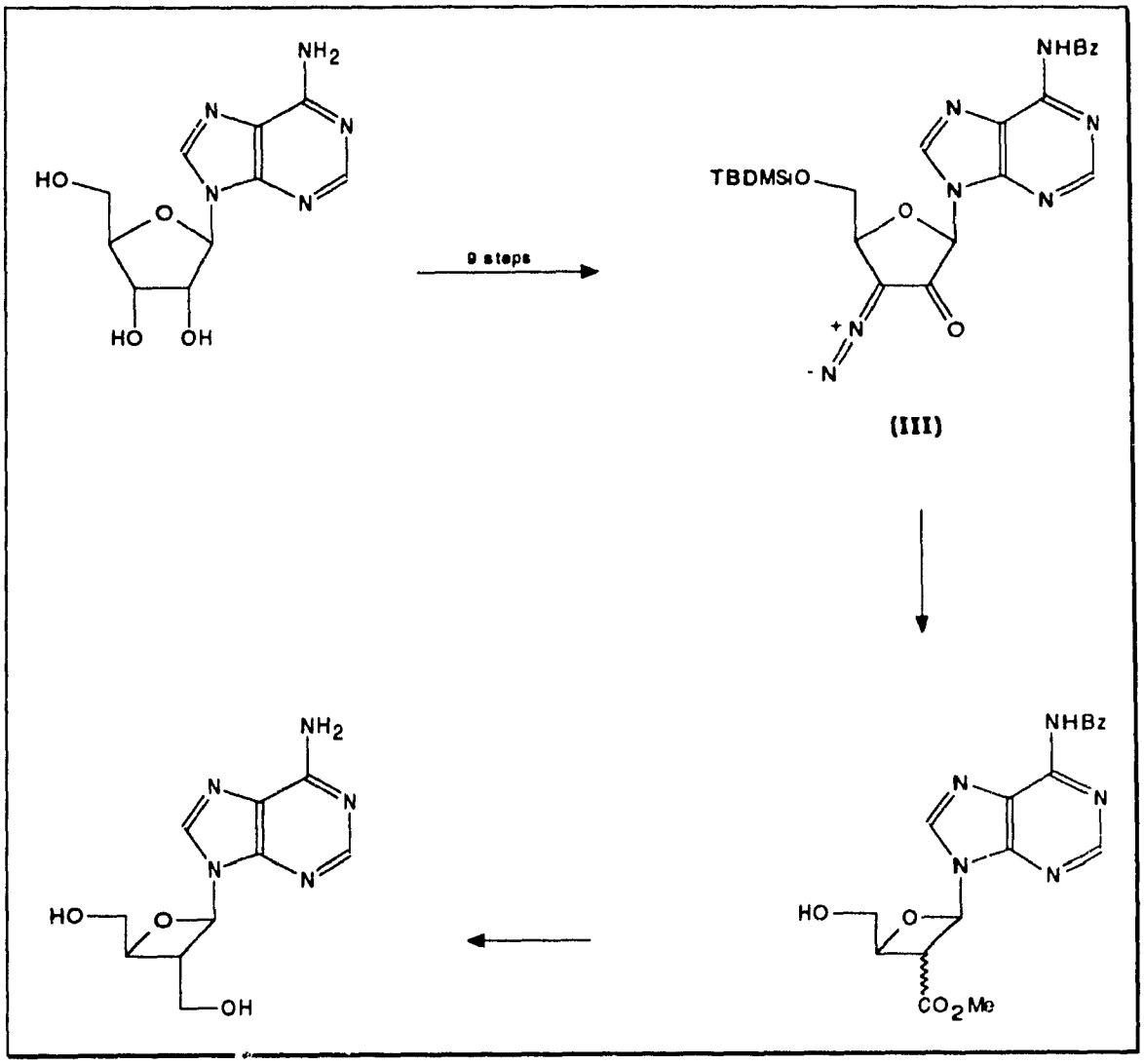


Figure 4. The Norbeck synthesis of oxetanocin.

The latest synthesis of oxetanocin was published in 1990 by Fleet[9]. Diacetone glucose was transformed to lactone **IV** in 5 steps. Ring contraction of lactone **IV** gave oxetane ester **V**. This oxetane ester was then transformed to chlorooxetane **VI**. The coupling of **VI** with adenine gave an epimeric mixture (α:β 3:2) of protected oxetanocins which were separated chromatographically. This synthesis also failed to provide oxetanocin in an anomerically pure form without resorting to tedious chromatographic separations.

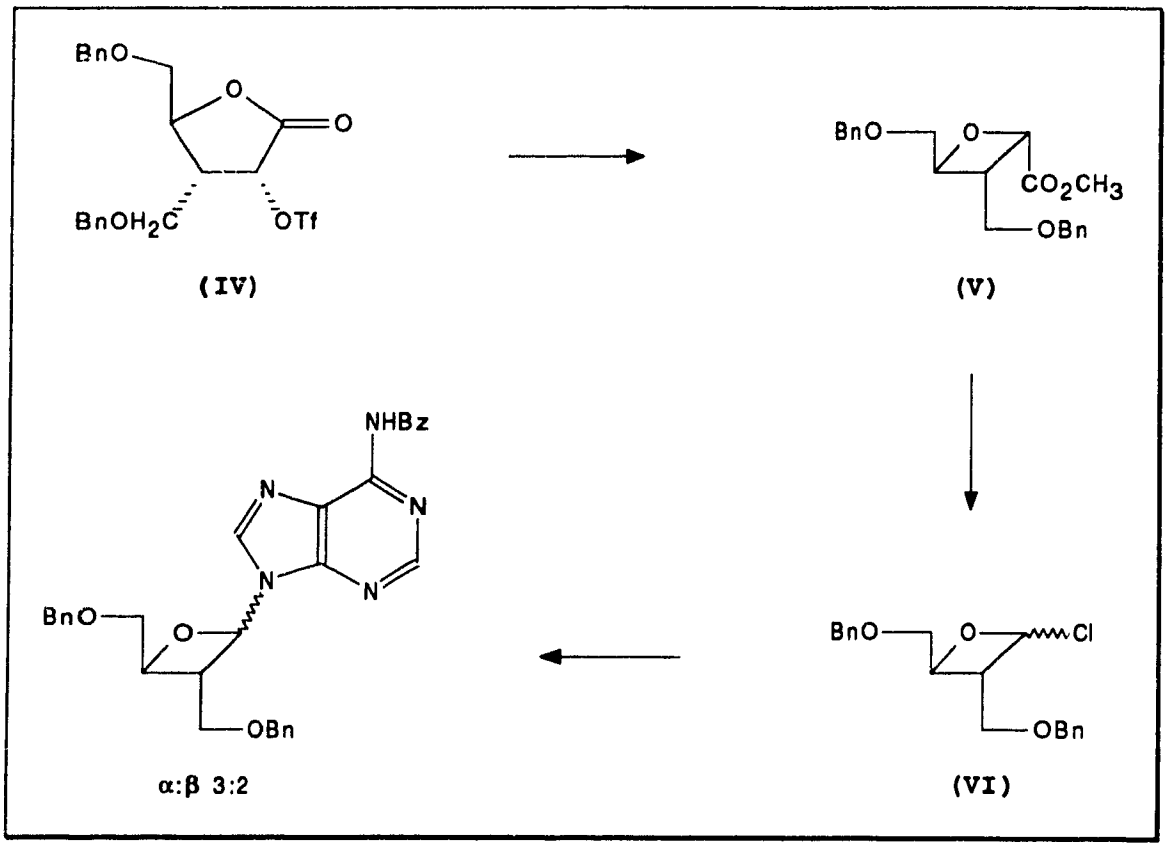
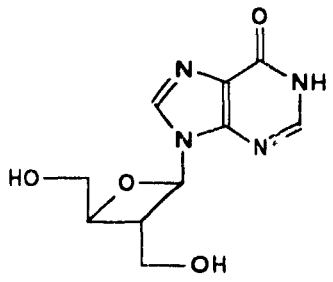


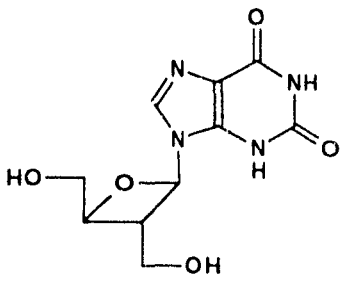
Figure 5. The Fleet synthesis of oxetanocin.

1.4 Syntheses of Oxetanocin Derivatives.

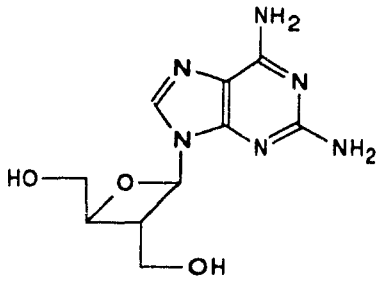
Although most nucleoside antibiotics contain a β-D-ribofuranose connected to a heterocyclic ring, the fact that oxetanocin exhibits biological activity (antibacterial, antitumor and antiviral) has fueled interest in modifying this novel nucleoside in the hope of increasing its biological activity. The first derivatives, shown in Figure 6, were synthesized from oxetanocin and involved modification of the nitrogenous base[5], usually by appropriate enzymatic reactions.



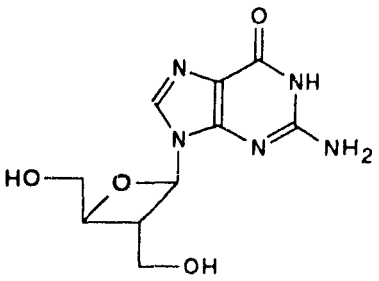
OXT-H



OXT-X



2-amino-OXT-A



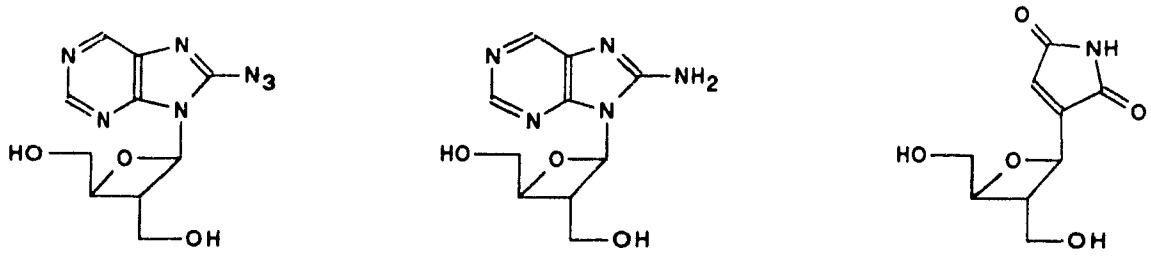
OXT-G

Figure 6. Modified Bases.

None of these derivatives exhibited antibacterial activities except for 2-amino-OXT-A, which demonstrated activity against *Bacillus cereus* IAM 1072 (MIC: 3.13 μg/mL) and *Staphylococcus aureus* 209 p (MIC: 3.13 μg/mL). OXT-G and 2-amino-OXT-A exhibited activity against herpes simplex virus type-II at 9.71 μg/well (50% inhibition of cytopathic effect)[17] and 17.68 μg/well (50% inhibition of cytopathic effect), respectively. The other derivatives were inactive against this virus[5]. In testing for activity against the hepatitis B virus, only OXT-G (ID_{50} 0.72 μg/mL) and 2-amino-OXT-A (ID_{50} 0.32

[17] Nishiyama, Y.; Yamamoto, N.; Yamada, Y.; Fujioka, H ; Shimada, N , Takahashi K , *J. Antibiot* , **42**, 1308 (1989).

μg/mL) showed antiviral activity[6]. The antiviral effects of OXT-G and 2-amino-OXT-A were 12 to 27 times as strong as that of ara-A, and they were less cytotoxic. Although the mechanism of inhibition of HBV DNA synthesis is not known, it is thought they affect HBV related reverse transcriptase[18]. OXT-G has also been found to be active against Varicella-zoster virus (ED_{50} 1-2 μg/mL)[19]. OXT-G, 2-amino-OXT-A and OXT-H exhibited activity against human cytomegalovirus (IC_{50} 1.0 μg/mL, 2.1 μg/mL and 18 μg/mL, respectively). OXT-X did not show any activity at concentrations up to 50 μg/mL[4]. OXT-G was found to have a very low acute toxicity (600 mg/kg). It has been shown that the triphosphate form of OXT-G (analogous to the triphosphate form of OXT-A shown in section 1.2) inhibits viral replication by impairing viral DNA polymerase[4,20,21]. OXT-H, 2-amino-OXT-A and OXT-G also exhibited activity against human imunodeficiency virus (EC_{50} 2.2 μg/mL, 4.7 μg/mL and 7.3 μg/mL, respectively). OXT-X did not show any activity at concentrations up to 100 μg/mL[8]. Allopurinol and mycophenolic acid potentiated the anti-HIV activity of OXT-H. OXT-H also showed the most promise for therapeutic use since its selectivity index was the highest of all of the above mentioned derivatives including OXT-A.



(VII) (VIII) (IX)

Figure 7. Modified Bases.

A few months later, 2 more derivatives involving modification of the nitrogenous base were synthesized[22]. No biological data were given for compound VII. Compound VIII exhibited activity against the human cytomegalovirus (IC_{50} 0.67 μg/mL) and the hepatitus B virus. In 1991, showdomycin analogue IX[23] was synthesized by chemists at Nippon Kayaku Co.. No information on biological activity was given.

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18 Summers, J.; Mason, W. S , *Cell*, **29**, 403 (1982).

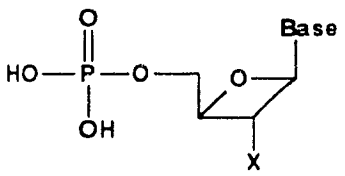
19 Shimada, N., Takahashi, K.; Masanobu, A.; Takashi, S , *Eurt Pat. Appl.*, EP 430,108 (1991).

20 Yamamoto, N.; Yamada, Y.; Daikoku, T.; Nishiyama, Y.; Tsutsui, Y.; Shimada, N.; Takahashi, K., *J Antibiot*, **43**, 1573 (1990)

21 Daikoku, T., Yamamoto, N.; Saito, S.; Kitagawa, M ; Shimada, N.; Nishiyama, Y., *Biochem. Biophys. Res. Commun* , **176**, 805 (1991).

22 Kurabayashi, K ; Saito, H,; Katsutoshi, T ; Kenichi, M ; Nishiyama, Y.; Takemitsu, N., *Jpn. Kokai Tokkyo Koho* JP 02,124,898 (1990).

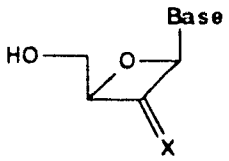
23 Watanabe, T.; Nishiyama, S ; Yamamura, S.; Kato, K.; Nagai, M.; Takita, T., *Tetrahedron Lett.*, **32**, 2399 (1991).



X = H, OH, CH_2OH

(X)

Base = Adenine, Guanine

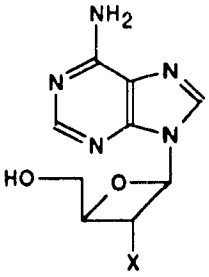


X = CH_2, O

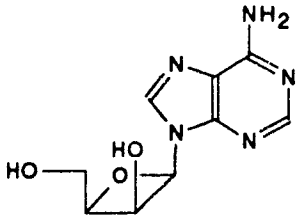
(XI)

Figure 8. Oxetane Modifications.

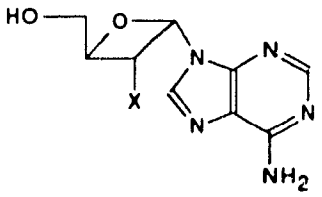
In 1989, phosphoric acid esters of the type **X** were prepared[12]. All of these compounds exhibited activity against cytomegalovirus, hepatitis B virus, herpes simplex virus-I, human immunodeficiency virus and Varicella-zoster virus. Oxetanocin derivatives of the type **XI** were also synthesized[24], but no biological data is available.



(XII) X=H
(XIII) X=OH
(XIV) $X=N_3$
(XV) X=F



(XVI)



(XVII) X=OH
(XVIII) $X=CH_2OH$

Figure 9. Oxetane Modifications.

There have also been many oxetanocin derivatives synthesized which involved modification of the oxetane ring. In 1990, oxetanocin derivatives **XIII**, **XVI** and **XVII** were synthesized[25,26]. Compound **XIII** was found to exhibit anti-HIV activity (IC_{50} 5.5 μg/mL)[27] as did compound **XVI** (IC_{50} 0.54 μg/mL). α-Noroxetanocin **XVII** did not possess any antiviral activity at concentrations up to 100 μg/mL. Saito and coworkers[27] also synthesized oxetanocin derivatives **XII**, **XIII** and **XVI** Compound

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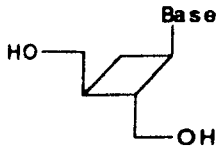
[24] Saito, S.; Hasegawa, S.; Takahashi, K.; Shimada, N.; Seki, J , Hoshino, H , Nishiyama, Y., Matsubara, K., *Eur. Pat. Appl* , EP 334,250 (1989).

[25] Wilson, F. X.; Fleet, G. W. J.; Witty, D. R ; Vogt, K.; Wang, Y.; Storer, R., Myers, P. L , Wallis, C J., *Tetrahedron: Asymmetry*, **1**, 525 (1990).

[26] Wang, Y.; Fleet, G. W. J.; Storer, R.; Myers, P. L.; Wallis, C. J ; Doherty, O ; Watkin, D. J., Vogt, K.; Witty, D. R.; Wilson, F. X.; Peach, J. M., *Tetrahedron: Asymmetry*, **1**, 527 (1990).

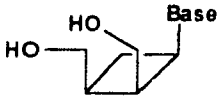
[27] Kitagawa, M.; Hasegawa, S.; Saito, S.; Shimada, N., Takita, T.; *Tetrahedron Lett* , **32**, 3531 (1991).

XII was found to possess anti-HIV activity at concentrations of 0.25 μg/mL. Azido derivative **XIV** and fluoro derivative **XV** were synthesized by Fleet[28]. Compound **XIV** was found to be active against the HIV virus (I_{50} 6 μg/mL) whereas the azido derivative **XV** showed no significant anti-viral activity at concentrations up to 100 μg/mL. Epioxetanocin **XVIII** has been synthesized by several groups[9,14,15,29]. Unfortunately, it did not possess any anti-viral activity.



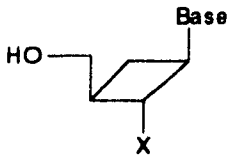
Base = Adenine, Guanine
Uracil, Thymine

(XIX)

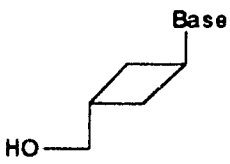


Base = Adenine
Uracil, Thymine

(XX)

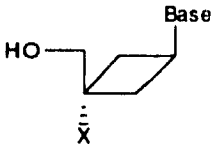


(XXI)	Base=Adenine,	X=H
(XXII)	Base=Adenine,	X=OH
(XXIII)	Base=Guanine,	X=H
(XXIV)	Base=Guanine,	X=OH

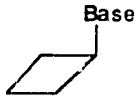


Base = Adenine, Guanine

(XXV)



(XXVI)	Base=Adenine,	X=CH_2OH
(XXVII)	Base=Adenine,	X=OH
(XXVIII)	Base=Guanine,	X=CH_2OH
(XXIX)	Base=Guanine,	X=OH



Base = Adenine, Guanine

(XXX)

Figure 10. Carbocyclic Analogues.

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[28] Wang, Y.; Fleet, G. W. J.; Wilson, F. X.; Storer, R.; Myers, P. L.; Wallis, C. J.; Doherty, O.; Watkin, D. J.; Vogt, K ; Witty, D. R.; Peach, J. M., *Tetrahedron Lett.*, **32**, 1675 (1991).
[29] Hambalek, R.; Just, G., *Tetrahedron Lett.*, **31**, 5445 (1990).

In addition to all of the derivatives shown above which involved either modified bases and/or modified oxetanes, a series of carbocyclic analogues has also been synthesized over the last few years. The first derivatives made simply replaced the oxetane ring with a cyclobutane ring[30,31,32,33,34,35,36] Adenosine and guanosine derivatives of the type **XIX** exhibited activity against HSV-I, HSV-II, HCMV, HBV, MCMV, VZV and HIV at concentrations between 0.024 μg/mL and 12.0 μg/ml The guanosine analogue of **XIX** was also active against EBV (ID_{50} 0.01 μg/mL) Neither derivative proved to be acutely toxic to mice No biological data is available for the thymidine and uridine analogues of **XIX**.

Several isomers of **XIX** have also been synthesized Derivatives of the type **XX** were recently reported by Katagiri and coworkers[35]. No information is available on their biological activity Analogues **XXI** and **XXIII** were also prepared[32,36] . The adenosine analogue **XXI** displayed no detectable activity against HSV-I, HSV-II, HCMV However, it was active against HIV at concentrations between 10 and 50 μg/mL. The guanosine derivative **XXIII** exhibited activity against all of the above listed viruses at concentrations of 8.0, 2.0, 2.6 and 10 μg/mL, respectively Derivatives **XXII** and **XXIV** were synthesized by Nishiyama and co-workers[32] Both displayed strong activity against HSV-I, HSV-II and HCMV (EC_{50} 0.12-4.2 μg/mL). Adenosine analogues of the type XXV were found to be inactive against HSV-I and HIV[36]. The guanosine derivative has not yet been evaluated.

Derivatives **XXVI** and **XXVIII** were found to be inactive against HSV-I and HIV[36]. Earlier this year, Legraverend[37] reported the synthesis of **XXVII** and **XXIX**. Both of these derivatives were reported to be inactive against the human immunodefiency virus. The adenosine analogue of the type **XXX** exhibited no activity against HSV-I and HIV[36]. No information is available concerning the biological activity of the guanosine analogue

Cyclopropane analogues of the type **XXXI** and **XXXII** were recently synthesized by Katagiri and Kaneko[38]. Neither type of derivative exhibited any activity against herpes simplex viruses I and II. However, compounds of the type **XXXII** were active against bovine leukemia virus at 5-50 μg/mL.

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30 Honjo, M.; Maruyama, T.; Sato, Y., Horii, T , *Chem Pharm. Bull*, **37**, 1413 (1989)

31 Ichikawa, Y , Narita, A , Shiozawa, A , Hayashi, Y ; Narasaka, K , *J Chem Soc., Chem Commun*, 1919 (1989).

32 Nishiyama, Y.; Yamamoto, N , Yamada, Y , Daikoku, T , Ichikawa, Y ; Takahashi, K , *J Antibiot*, **42**, 1854 (1989).

33 Slusarchyk, W. A , Young, M G., Bisacchi, G S ; Hockstein, D R , Zahler, R , *Tetrahedron Lett*, **30**, 6453 (1989).

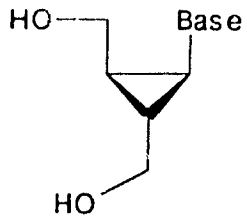
34 Norbeck, D W.; Kern, E ; Hayashi, S ; Rosenbrook, W , Sham, H , Herrin, T , Plattner, J J ; Erickson, J.; Clement, J.; Swanson, R ; Shipkowitz, N.; Hardy, D ; Marsh, K , Arnett, G , Shannon, W , Broder, S ; Mitsuya, H , *J Med. Chem* , **33**, 1285 (1990)

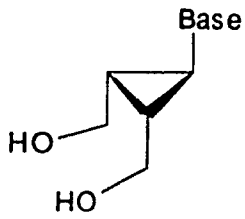
35 Katagiri, N ; Sato, H ; Kaneko, C , *Chem Pharm. Bull*, **38**, 288 (1990)

36 Maruyama, T ; Sato, Y.; Horii, T ; Shiota, H , Nitta, K , Shirasaka, T , Mitsuya, H , Honjo, M , *Chem Pharm. Bull.*, **38**, 2719 (1990).

37 Boumchita, H.; Legraverend, M , Guilhem, J ; Bisagni, E , *Heterocycles*, **32**, 867 (1991)

38 Katagiri, N.; Sato, H ; Kaneko, C.; *Chem Pharm. Bull*, **38**, 3184 (1990)

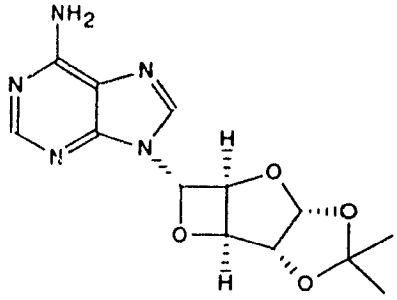


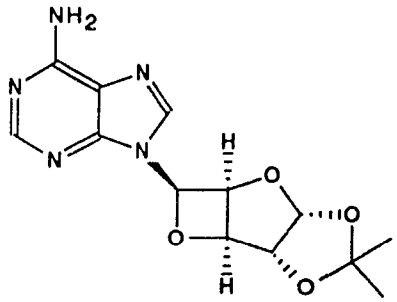


(XXXI) Base = Adenine, Thymine **(XXXII)**

Figure 11. Cyclopropane Analogues.

Tricyclic derivatives **XXXIII** and **XXXIV** were synthesized in early 1988 by Fleet[39] as part of his research involving oxetanocin. No information is available on either compound regarding its biological activity.





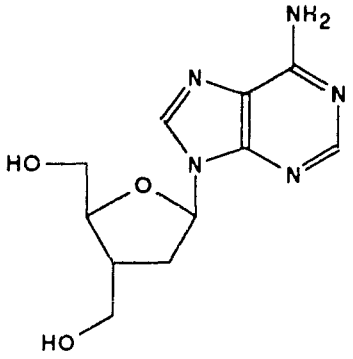
(XXXIII) **(XXXIV)**

Figure 12. Tricyclic Analogues.

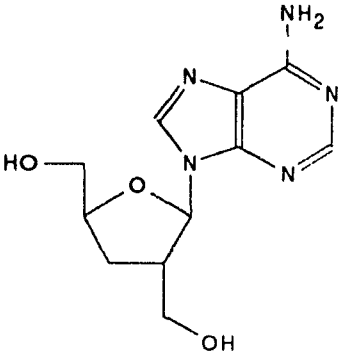
39 Fleet, G. W J.; Son, J. C.; Vogt, K.; Peach, J M ; Hamor, T. A., *Tetrahedron Lett.*, **29**, 1451 (1988).

1.5 Structure-Activity Relationship versus HIV.

Due to the difficulties involved in the synthesis of oxetanocin and oxetanocin derivatives, Marquez[40] undertook an investigation into the necessity of the oxetane or cyclobutane ring for antiviral activity. Since the tetrahydrofuran ring is known to be an excellent template for reverse transcriptase as demonstrated by the anti-HIV activity of various 2',3'-dideoxynucleosides[41], they decided to synthesize hydroxymethyl-substituted 2',3'-dideoxyadenosines **XXXV** and **XXXVI**.



(XXXV)



(XXXVI)

Figure 13.

In the modelling studies carried out, 2',3'-dideoxyadenosine (ddA) was asssumed to have the appropriate geometry and was used as a reference template. Oxetanocin and ddA were shown to have a large common sub-structure with essentially the same geometry and hence can be largely superimposed as shown in Figure 14. Since ddA possesses superior biological activity with respect to oxetanocin, it suggests the the 2' hydroxymethyl side chain in oxetanocin may hinder its ability to fit into the binding sites used by ddA.

When 2'-hydroxymethyl ddA and 3'-hydroxymethyl ddA were modelled, it was found that the 3'-hydroxymethyl isomer closely resembles oxetanocin and does indeed possess anti-HIV activity. On the other hand, the 2'-hydroxymethyl isomer does not closely resemble oxetanocin since its 2'-hydroxymethyl group is in a very different location. Also, the 2'-hydroxymethyl isomer does not exhibit any anti-HIV activity. This seems to suggest that the cleft between the 2 ring systems must be empty for binding to the active site to take place.

---

[40] Tseng, C. K-H.; Marquez, V. E ; Milne, G. W. A.; Wysocki, R. J.; Mitsuya, H ; Shirasaki, T ; Driscoll, J. S., *J. Med. Chem.*, **34**, 343 (1991).

[41] (a) Mitsuya, H ; Broder, S , *Proc. Natl Acad. Sci U.S.A.*, **83**, 1911 (1986). (b) Yarchoan, R ; Mitsuya, H.; Thomas, R. V.; Pluda, J. M.; Johns, D G.; Broder, S., *Science*, 245, 412 (1989).

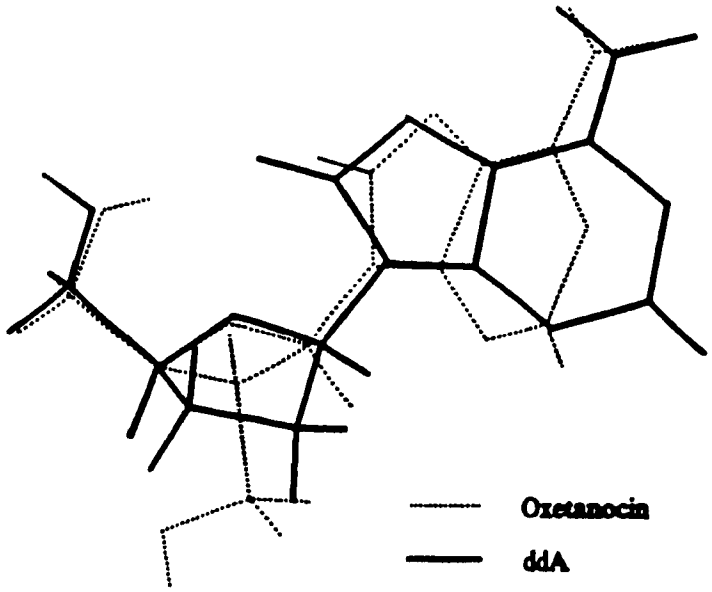


Figure 14. Modelling of Oxetanocin and ddA

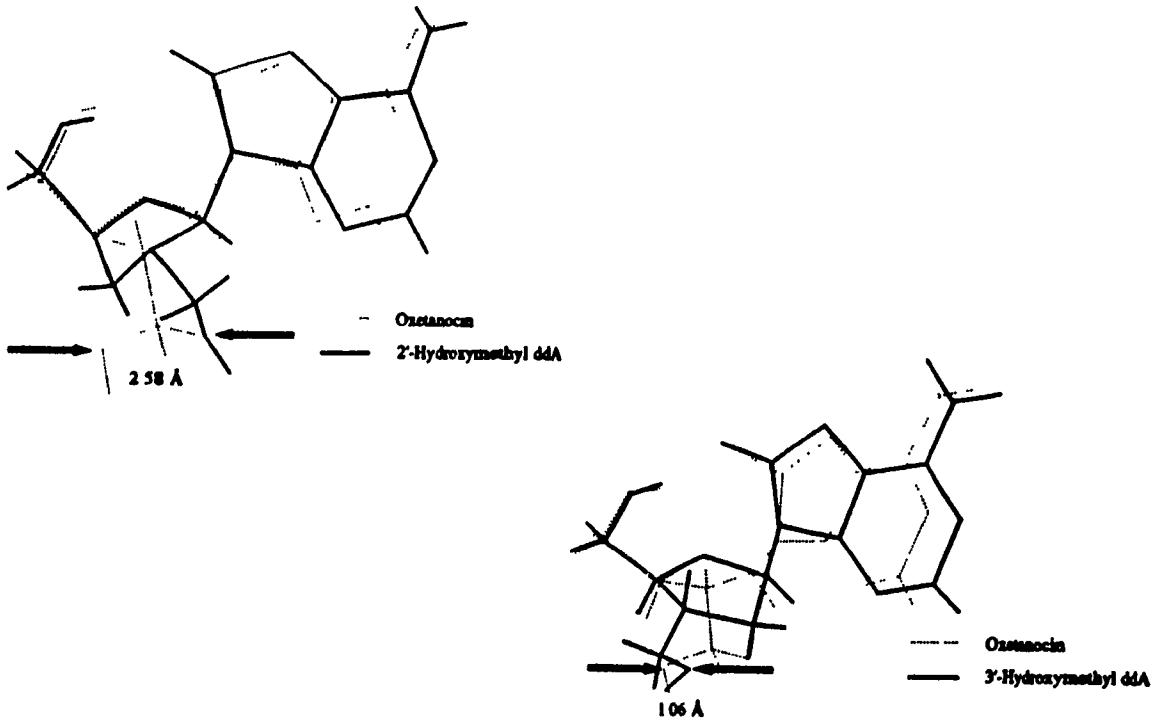


Figure 15. Modelling of Oxetanocin and Isomeric Hydroxymethyl ddA Analogues[40].

These results seem to indicate that the tetrahydrofuran ring is equivalent to the oxetane ring. It also indicates that the type and position of the side chains may be more important for anti-HIV activity than ring size.

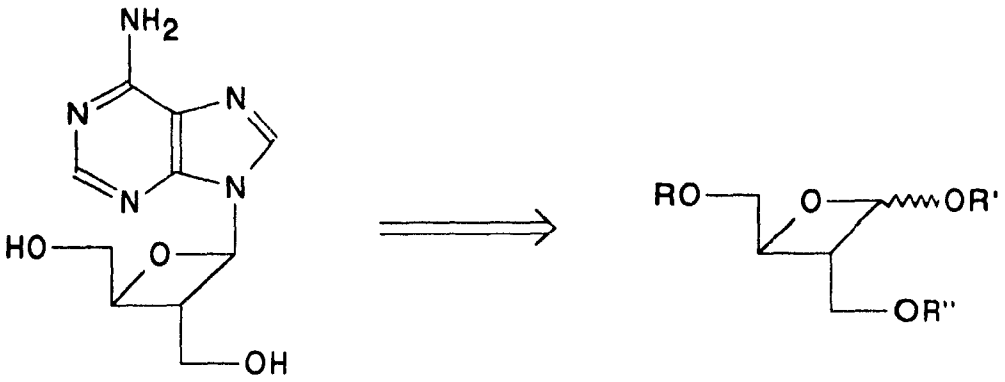
2. RESULTS & DISCUSSION.

2.1 Synthetic Strategy.

The structural features of the novel nucleoside oxetanocin 1β offer a challenging synthetic project. The unprecedented oxetanosyl-N-glycoside presents new challenges in the synthesis of nucleosides and carbohydrates as many of the principles used in furanoside syntheses are not applicable to oxetanoside synthesis. We wanted to design a scheme that was not restricted to the synthesis of oxetanocin only, but one that would enable us to efficiently synthesize derivatives of oxetanocin as it was felt by us at the time of the initiation of the project that derivatives would also be biologically active. This was borne out later in the numerous papers on oxetanocin derivatives.

It was decided from the beginning that our strategy would be based on the coupling of a suitably functionalized oxetanose moiety to the base. This approach would enable us to incorporate pyrimidine as well as purine bases. The difficulty in the coupling reaction was the control of the stereochemistry at the anomeric position. It was hoped that a coupling methodology for oxetanoses could be developed analogous to the ones that have been developed for furanose sugars Disconnection of the glycosidic bond is shown in Scheme R1.

Scheme R1



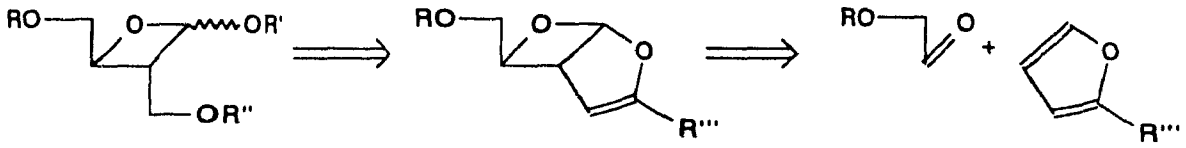
1β, oxetanocin

The sugar moiety can be derived from the well known photocycloaddition of aldehydes and furans[42,43,44]. These photo-adducts incorporate many of the stereochemical features that characterize

[42] Toki, S.; Shima, K.; Sakurai, H., *Bull. Chem. Soc. Jpn.*, **38**, 760 (1965).
[43] Shima, K.; Sakurai, H., *Ibid.*, **39**, 1806 (1966).
[44] Schreiber, S. L.; *Science*, **227**, 857 (1985) and references cited therein.

oxetanocin and offer flexibility in altering the 2' and/or 3' substituents with relative ease. It was clear that the choice of protecting and/or participating groups would have to be carefully considered since these would ultimately determine the stereochemistry of the coupling reaction. Control of the stereochemistry about the anomeric position was deemed to be critical since separation of mixtures of anomers is often very tedious and impractical as was shown by Yamamura's[14,15] and Fleet's[9] syntheses of oxetanocin. These photo-adducts also offer the benefit of being available from relatively inexpensive starting materials. One drawback of using these photo-adducts as starting materials was that they have never been obtained in enantiomerically pure form and that ultimately a methodology would have to be devised to separate the enantiomers or synthesize them in high enantiomeric excess (*ee*). The retrosynthesis of the functionalized oxetane is shown in Scheme R2.

Scheme R2



Another possible approach involved coupling of the nitrogenous base directly to a suitably functionalized/modified photo-adduct. The difficulty in this approach was that the oxetane ring has a greater tendency to open up (especially under acidic conditons) than the furan ring. Any conversion of photo-adducts to oxetanocin, or a precursor thereof, must circumvent this ring opening. It was felt that this could be accomplished by modifying the furan part of the photo-adduct in such a way as to destabilize it so that it would open in preference to the oxetane part.

2.2 Initial Attempt.

2.2a Synthesis of (3).

The photo-adduct **2a** was prepared from benzaldehyde and furan via a slight modification of the previously described [2+2] Patterno-Buchi photo-cycloaddition[41] in large quantities and in consistently good yields, typically 50%. This material served as the model for our initial investigations. Ozonolysis of **2a** in methylene chloride at -78°C, followed by dimethyl sulfide reduction provided formate **3** in virtually quantitative yield and with a purity >95%. Attempts to improve the purity by flash chromatography resulted in decompostion of **3**[45]. Nevertheless, we decided to proceed with this material as obtained and it was hoped that the anomeric formyl group would behave similar to acetate groups in coupling reactions and that the only remaining task would be to transform the aldehyde group into a suitable participating group.

Attempts to reduce the aldehyde function to the alcohol with $NaBH_4$ in methanol or ethanol at various temperatures resulted in decomposition of the starting material. Reaction with sodium cyanoborohydride in methanol also resulted in decomposition. At this point it was felt that an aprotic solvent was needed since the oxetane ring was probably being destroyed in a base catalyzed hydrolysis of the formate. Therefore, we attempted to carry out the reduction with $LiBH_4$, DIBAL-H or $Zn(BH_4)_2$ in tetrahydrofuran or ether. These approaches were also not successful. An even milder approach involved treating a methylene chloride solution of **3** with $NaBH_4$ on alumina or silica gel. This too did not give the desired alcohol. Since we were not able to reduce the aldehyde, it was decided to form the methyl acetal with cerium trichloride, methanol and trimethyl orthoformate according to the methodology described by Luche[46]. However, instead of the desired product, only the tetramethoxy olefin **4** was isolated in 43% yield.

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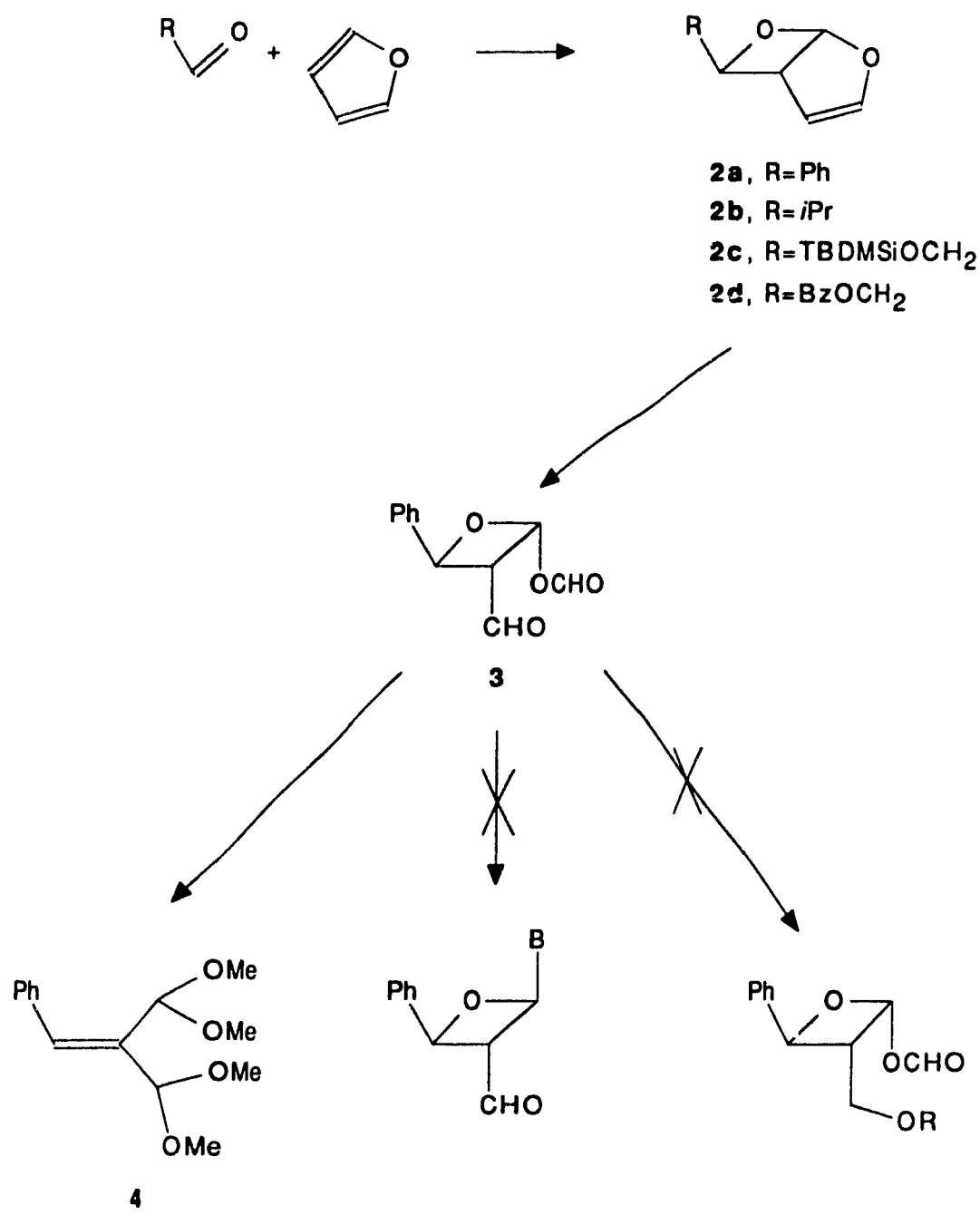
[45] Formate **3** had a shelf-life of only 1-2 weeks at -10°C before significant decomposition occurred.

[46] Luche, J.; Gemal, A., *J. Org. Chem.*, **44**, 4187 (1979).

Scheme 1


R
O
+
O
R
O
O
2a, R=Ph
2b, R=iPr
2c, R=TBDMSiOCH2
2d, R=BzOCH2
Ph
O
OCHO
CHO
3
Ph
OMe
OMe
OMe
OMe
4
Ph
O
B
CHO
Ph
O
OCHO
OR

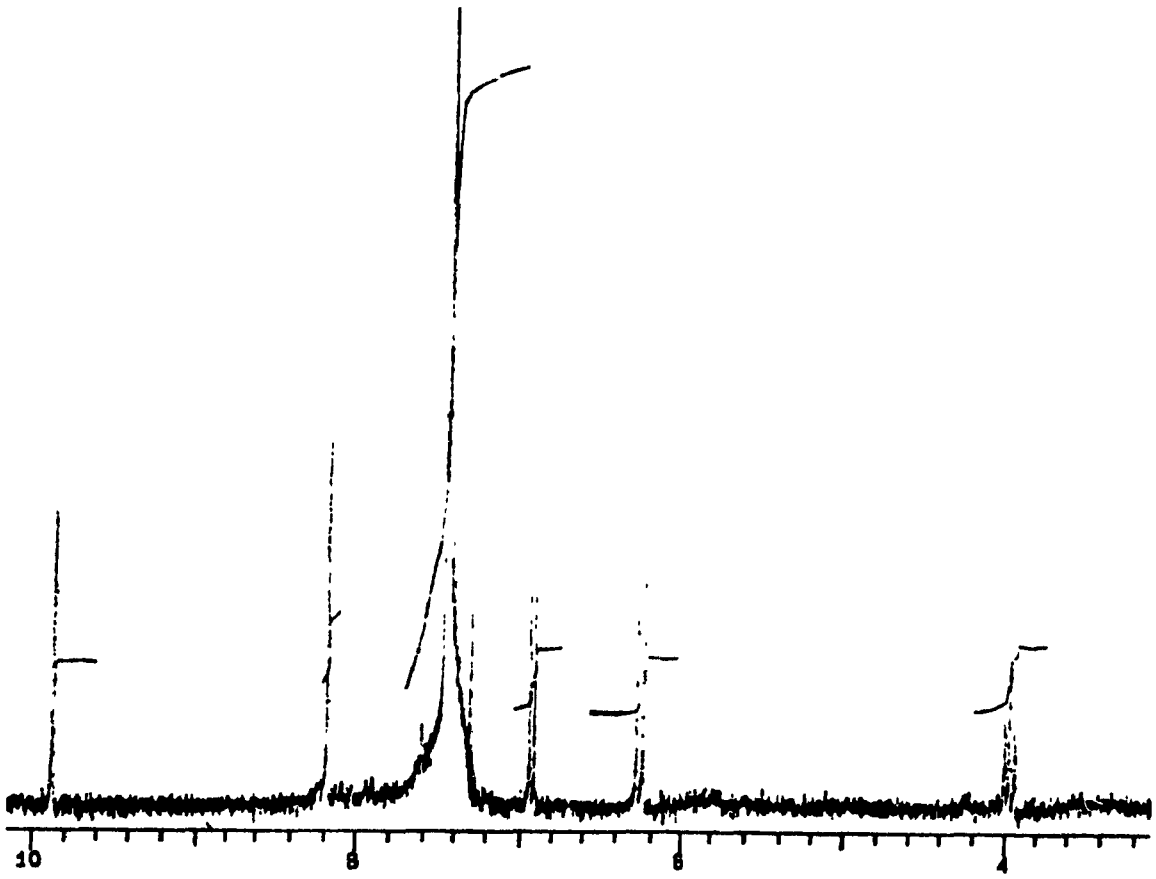


Figure 16. The 200 MHz ^{1}H-NMR spectrum of formate **3** in $CDCl_3$.

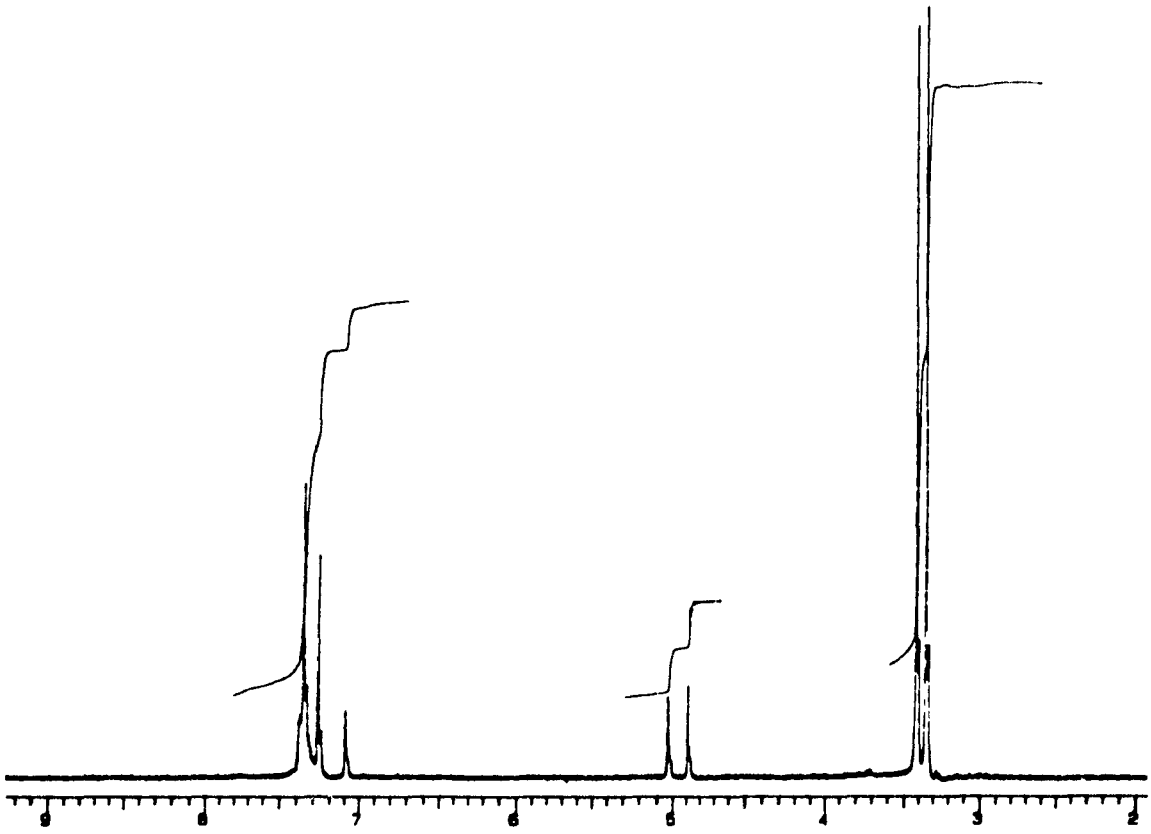
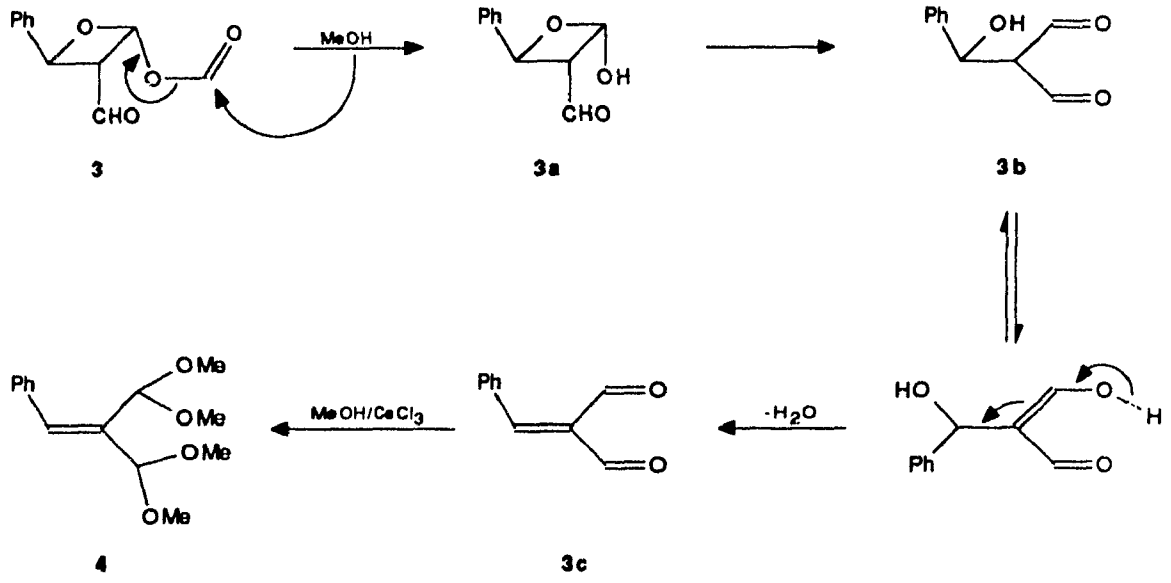


Figure 17. The 200 MHz ^{1}H-NMR spectrum of tetramethoxy-olefin **4** in $CDCl_3$.

2.2b Mechanism of Formatiom of (4).

Compound **4** is presumably formed by a hydrolysis of the formyl group to give the intermediate **3a** which tautaumerizes readily to the open chain alcohol **3b**. Dehydration of **3b**, to give the dialdehyde **3c** is not unexpected in view of the instability of β-hydroxy aldehydes. Finally, acetalization of **3c** gives the end product.

Scheme 2



2.2c Attempted Coupling of (3) to Nitrogenous Bases.

Since all efforts to transform the aldehyde function of **3** to a suitably protected group failed, we then decided to proceed with the coupling to the nitrogenous base. Our original approach was based on the classical Vorbrüggen methodology[47,48,49] and was to involve a purine base (adenine) and a pyrimidine base (cytosine) just in case the different classes of bases behaved differently. N^6-benzoyladenine was synthesized by a described method[50] and then reacted with chlorotrimethylsilane to yield the *bis*-silylated base[51] as a clear yellow glass after bulb to bulb distillation. A stock solution of this material in 1,2-dichloroethane was used for all investigations and was found to be stable for extended

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47 Vorbrüggen, H.; Krolikiewicz, K., *Agnew. Chem. internat. Edit.*, **14**, 421 (1975).
48 Vorbrüggen, H.; Höfle, G., *Chem. Ber.*, **114**, 1234 (1981).
49 Vorbrüggen, H.; Krolikiewicz, K.; Bennua, B., *Chem. Ber.*, **114**, 1257 (1981).
50 Prokop, J.; Murray, D. H., *J. Pharm. Sci.*, **54**, 359 (1965).
51 Nishimura, T.; Iwai, I., *Chem. Pharm. Bull.*, **12**, 352 (1964).

periods of time if moisture was rigorously excluded. *Bis*-silylated cytosine was obtained from the unprotected pyrimidine by a known method[50] and gave a white powder.

The coupling of oxetane 3 and *bis*-(trimethylsilyl)-N^6-benzoyladenine catalyzed by trimethylsilyl triflate, trimethylsilyl acetate or tin tetrachloride under various conditions afforded complex mixtures which contained no coupled products or otherwise identifiable compounds. Similar results were obtained when *bis*-(trimethylsilyl)-cytosine was employed as the nitrogenous base. Therefore, this approach was abandoned and other coupling methods were investigated. Reaction of 3 with *bis*-(trimethylsilyl)-N^6-benzoyladenine in acetonitrile under phase transfer conditions using dibenzo-18-crown-6 and potassium iodide under various conditions[52] gave complex mixtures which contained no coupled products. Attempts to couple oxetane 3 with the sodium salt of adenine in DMF under various conditions[53] also resulted in decomposition of the oxetane. Coupling of 3 with chloromercuri-6-benzamidopurine in 1,2-dichloroethane catalyzed by various Lewis acids under several different conditions also resulted in only decomposition of 3. Our findings regarding the instability of oxetanosyl-formates were corroborated by the Yamamura group at Nippon Kayaku Co.[14]. Due to the difficulty in coupling oxetane 3 with nitrogenous bases, it was decided that we had to develop a different sugar component, one that was considerably more stable than 3.

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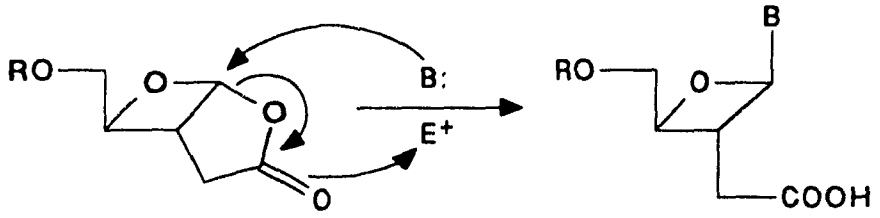
[52] Azymah, M.; Chavis, C.; Lucas, M.; Imbach, J. L., *Tetrahedron Lett.*, **30**, 6165 (1989).

[53] Carraway, K. L.; Huang, P. C.; Scott, T. G., *Synthetic Procedures in Nucleic Acid Chemistry*, 3 (1966).

2.3 Lactone Approach.

Our next attempt involved the synthesis of lactone **5**. We felt that the lactone moiety could be activated by a Lewis acid (E^+), thereby making the anomeric center susceptible to β-attack by the nitrogenous base (B:) resulting in opening of the 5-membered ring. The resulting nucleoside (an oxetanocin derivative) could then be transformed into oxetanocin simply by shortening the 2' side chain by one methylene unit.

Scheme 3

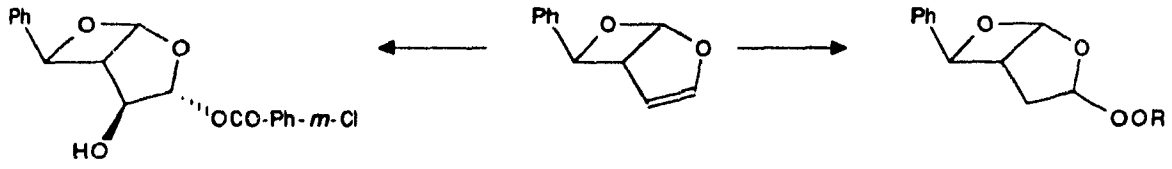


5

2.3a Synthesis of Lactone (5a).

Our initial approach was to try to convert photo-adduct **2a** to the desired lactone **5a**. Although Schreiber had recently described the oxidation of photo-adducts **2** with *m*-chloroperbenzoic acid to give compounds of the type **6**[54], we hoped that it would be possible to add a peroxide across the double bond of **2a** and then transform the resulting compound **7** to the desired lactone. Unfortunately, all attempts to add *t*-butylhydroperoxide across the double bond of **2a** failed and this approach was abandoned.

Scheme 4

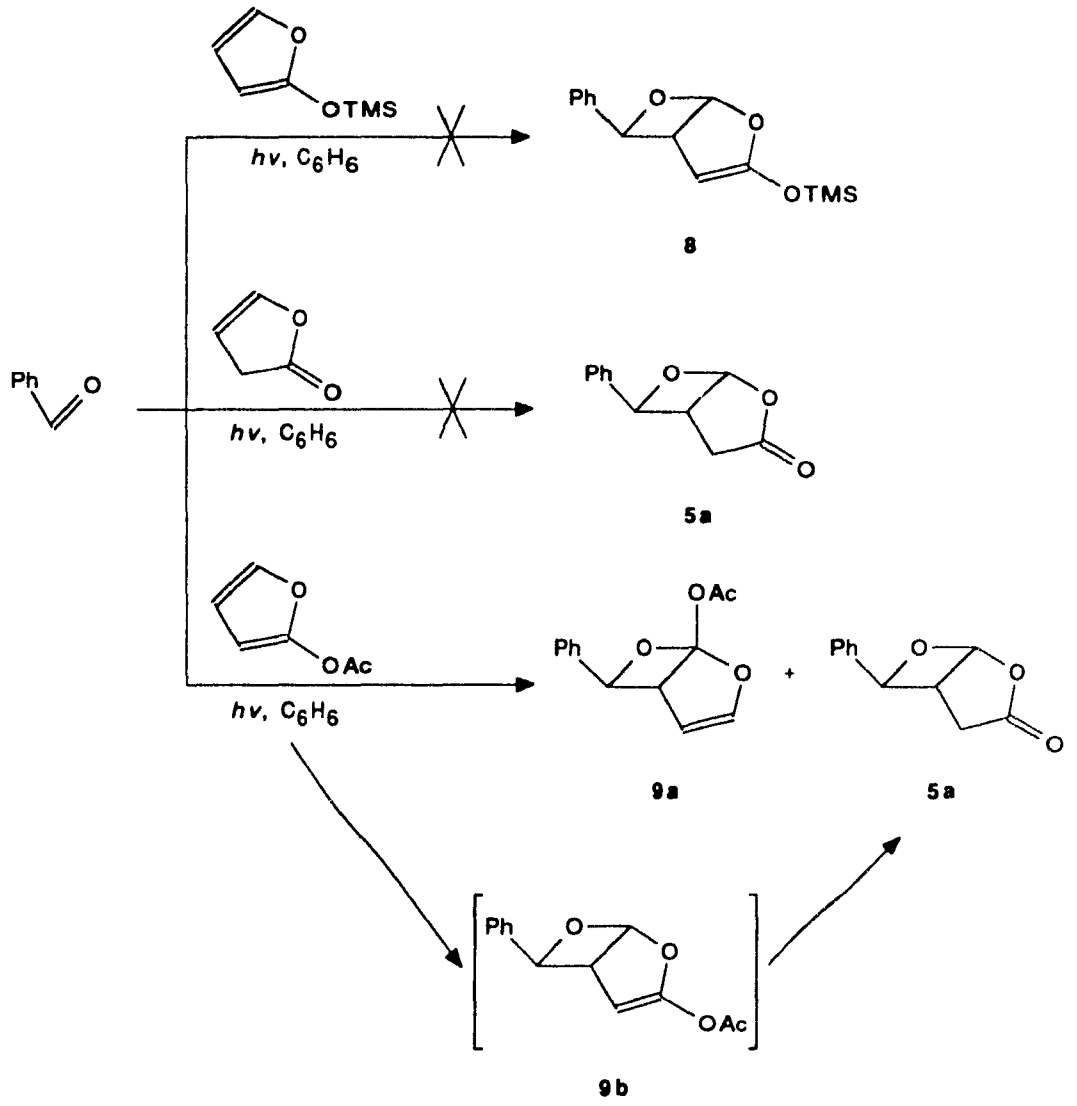


6 **2a** **7**

[54] Schreiber, S. L.; Hoveyda, A. H.; Wu, H. J., *J. Am. Chem. Soc.*, **105**, 660 (1983).

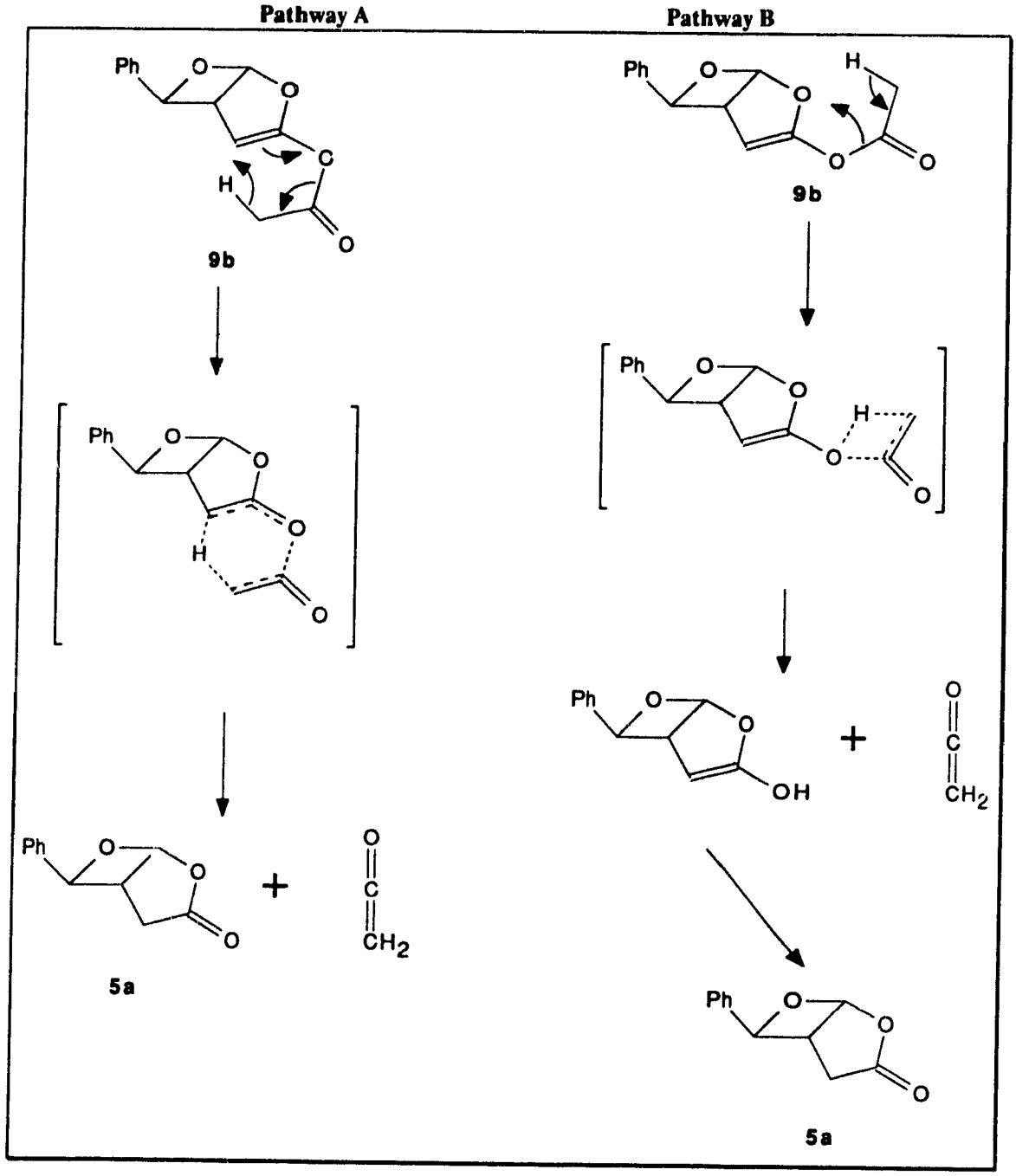
Irradiation of benzaldehyde and 2-*O*-trimethylsilyl-furan in benzene under various conditions resulted only in recovered starting material and there was no evidence of the desired photo-product **8** or lactone **5a**. Attempts to react benzaldehyde and 2-furanone in benzene photolytically also failed However, photolysis of benzaldehyde with 2-acetoxyfuran in benzene gave lactone **5a** and acetate **9a** in 14% and 5% yield (unoptimized), respectively.

Scheme 5



The lactone is presumably formed from vinyl acetate **9b**. Possible pathways for this rearrangement are shown in Scheme 6. No mechanistic studies were carried out to determine by which pathway the reaction proceeds.

Scheme 6



2.3b Attempted Coupling of Lactone (5) to Nitrogenous Bases.

With the lactone **5a** in hand, we proceeded with the coupling to the base. Reaction of 5a and *bis*-(trimethylsilyl)-N^6-benzoyladenine in 1,2-dichloroethane catalyzed by various Lewis acids resulted in no reaction taking place if mild conditions were used. On the other hand, if more forcing conditions (eg. reflux, excess catalyst) were employed, the lactone started to decompose slowly. Attempts to couple lactone **5a** with *bis*-(trimethylsilyl)-N^6-benzoyladenine in acetonitrile under phase transfer conditions using dibenzo-18-crown-6 and potassium iodide also did not yield any coupled products Similar results were obtained when *bis*-(trimethylsilyl)-cytosine was used as the base. Since we were unable to convert lactone **5a** into oxetanocin like material, a new approach had to be devised.

2.4 New Strategy.

After careful consideration, two new strategies were developed. The first one was inspired by the work of Fraser-Reid and Mootoo, who transformed 1-pentenyl glycosides to disaccharides by means of iodonium di-*sym*-collidine perchlorate (IDCP) and the appropriate sugars[55,56,57,58]. It was hoped that by functionalizing photo-adducts of the type **2** with appropriate alkenes that it would be possible to selectively open the 5-membered ring of these photo-adducts according to Pathway B to yield monocyclic oxetanes **12** which could then be coupled to nitrogenous bases to yield oxetanocin derivatives. One possible competing reaction would be the opening of the intermediate **11a** according to Pathway C to yield a bicyclic compound of the type **13a**. We felt that it was not likely that the intermediate would react this way since the approach of the nucleophile is extremely hindered by the substituent on the 4-position (especially pronounced if a bulky group is at C-4) and that the resulting compound would be more strained than compounds of type **12** (predicted by molecular modelling). The other possible side reaction would involve opening of the oxetane ring according to Pathway A to yield a bicyclic compound of type **13**. We felt this pathway was only likely in the case where the intermediate iodonium ion **11** was in close proximity to the oxetane oxygen.

The second approach centered around the investigation of the Paterno-Buchi photocycloaddition reaction in order to determine if it is possible to obtain chemoselectivity in the addition of unsymmetrically substituted furans to aldehydes. This would enable us to replace the very unstable anomeric formate group with something more stable, like an acetate (commonly employed in base coupling reactions) or benzoate group.

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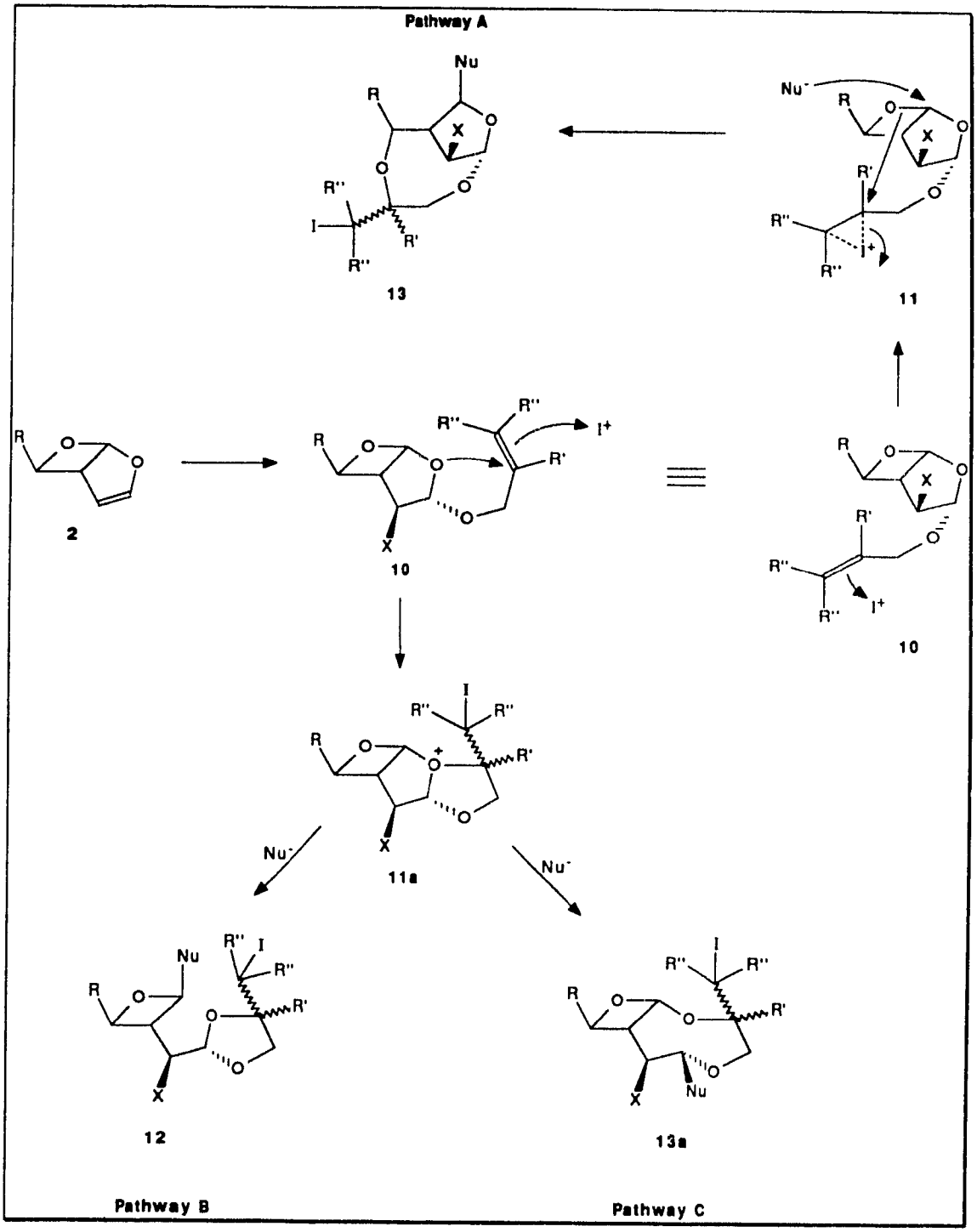
[55] Mootoo, D. R.; Date, V.; Fraser-Reid, B., *J. Am. Chem. Soc.*, **110**, 2662 (1988).
[56] Fraser-Reid, B.; Konradsson, P.; Mootoo, D. R.; Udodong, U., *J. Chem. Soc., Chem Commun.*, 823 (1988).
[57] Konradsson, P.; Mootoo, D. R.; McDevitt, R. E.; Fraser-Reid, B., *Ibid.*, 270 (1990).
[58] Lopez, J. C.; Fraser-Reid, B., *Ibid.*, 159 (1991).

Scheme 7


Pathway A
Nu
R
X
O
R''
I
R'
13
Nu⁻
11
2
10
10
11a
Nu⁻
Nu⁻
12
13a
Pathway B
Pathway C

2.5 The Fraser-Reid Approach to Monocyclic Oxetanes.

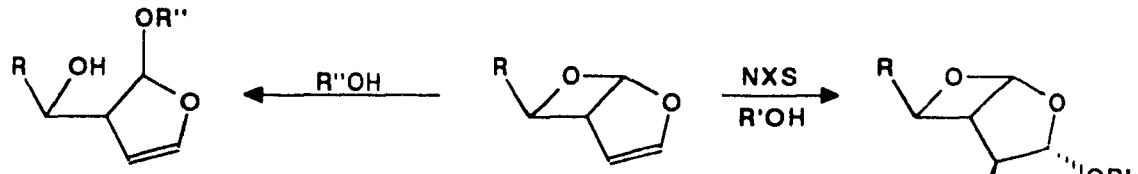
2.5a Synthesis of (9).

Our first task was to construct a photo-adduct of the type **10**. Due to the extreme difficulty that we experienced in our initial attempts to epoxidize the double bond in **2** (discussed in section 2.5d), we decided to carry out our initial studies on model compounds where the hydroxy function would be replaced by a hydrogen or halogen atom in order to see if the method was a viable one and so as not to waste time should this approach fail. We also believed that the halogen could be converted to a hydroxy group if epoxidation proved to be unachievable.

Reaction of **2a** with hot methanol gave alcohol **14** in 31% yield. The latter is derived from an acid-catalyzed opening of the oxetane ring. Treatment of photo-adducts **2a** and **2b** with allyl or methallyl alcohol and catalytic amounts of acetic acid gave the corresponding allyl (**15**: 30%) and methallyl (**16a**: 10%, **16b**: 11%) acetals. The structural assignment of **14**, and therefore of **15**, **16a** and **16b**, was based on a HETCOR carbon-hydrogen correlation, which unambiguously ruled out the bicyclic structure of type **10**.

The functionalizing of the bicyclic system **2** proceeded in a more satisfactory manner when a 0.2 M solution of photo-adducts **2a** or **2b** in the appropriate alcohol was treated with one equivalent of N-bromo or N-iodosuccinimide at room temperature for 1.5 - 2 h, giving bromo or iodo acetals **10** in variable, but frequently high yields. The results are summarized in Table 1.

Compounds of the type **10** were formed by, first, an exo coordination of the halonium ion to the double bond followed by an S_N2 type displacement from the endo face. The *trans* stereochemistry along the C3-C4 bond was confirmed by ^1H and COSY NMR, which showed no coupling between H3 and H4 since the two protons had a dihedral angle of approximately 90°. Had they been *cis*, a coupling would have occurred due to their dihedral angle being approximately 0°. The ^{13}C, APT and HETCOR NMR's also confirmed that we had obtained the desired bicyclic compounds **10**. The high purity of selected examples was established by elemental analysis.



14, R=Ph, R''=CH_3
15, R=Ph, R''=$CH_2CH=CH_2$
16a, R=Ph, R''=$CH_2C(CH_3)=CH_2$
16b, R=*i*Pr, R''=$CH_2C(CH_3)=CH_2$

2a, R=Ph
2b, R=*i*Pr

10

Table 1

ENTRY	R	R'	X	TIME	YIELD
10a	Ph	$CH_2CH=CH_2$	Br	1.5 h	22%
10b	Ph	$CH_2C(CH_3)=CH_2$	Br	1.5 h	17%
10c	Ph	$CH_2CH=C(CH_3)_2$	Br	2.0 h	76%
10d	Ph	$CH_2C(CH_3)=CH_2$	I	2.0 h	100%
10e	$(CH_3)_2CH$	$CH_2CH=CH_2$	Br	2.0 h	70%
10f	$(CH_3)_2CH$	$CH_2C(CH_3)=CH_2$	Br	2.0 h	9%
10g	$(CH_3)_2CH$	$CH_2CH=C(CH_3)_2$	Br	2.0 h	75%
10h	$(CH_3)_2CH$	$CH_2C(CH_3)=CH_2$	I	2.0 h	84%

The reaction, however, is far from general. All attempts to synthesize chloro derivatives using NCS and various alcohols (allyl, methallyl, dimethallyl, 4-pentenyl, cinnamyl) failed. It was also not possible to synthesize any iodo derivatives using the above mentioned alcohols except for methallyl alcohol. Using NBS, only the reactions with cinnamyl alcohol and 4-penten-1-ol failed. When 4-penten-1-ol was used as the alcohol, reaction with NBS or NIS resulted in intramolecular cyclization giving 2-bromomethyl or 2-iodomethyl tetrahydrofurans. It occurred more rapidly than reaction with the double bond of the photo-adducts. Surprisingly, the iodo derivatives **10d** and **10h** had life times exceeding 1 year at -10°C, whereas the bromo compounds were considerably less stable with life times of one to fifteen weeks.

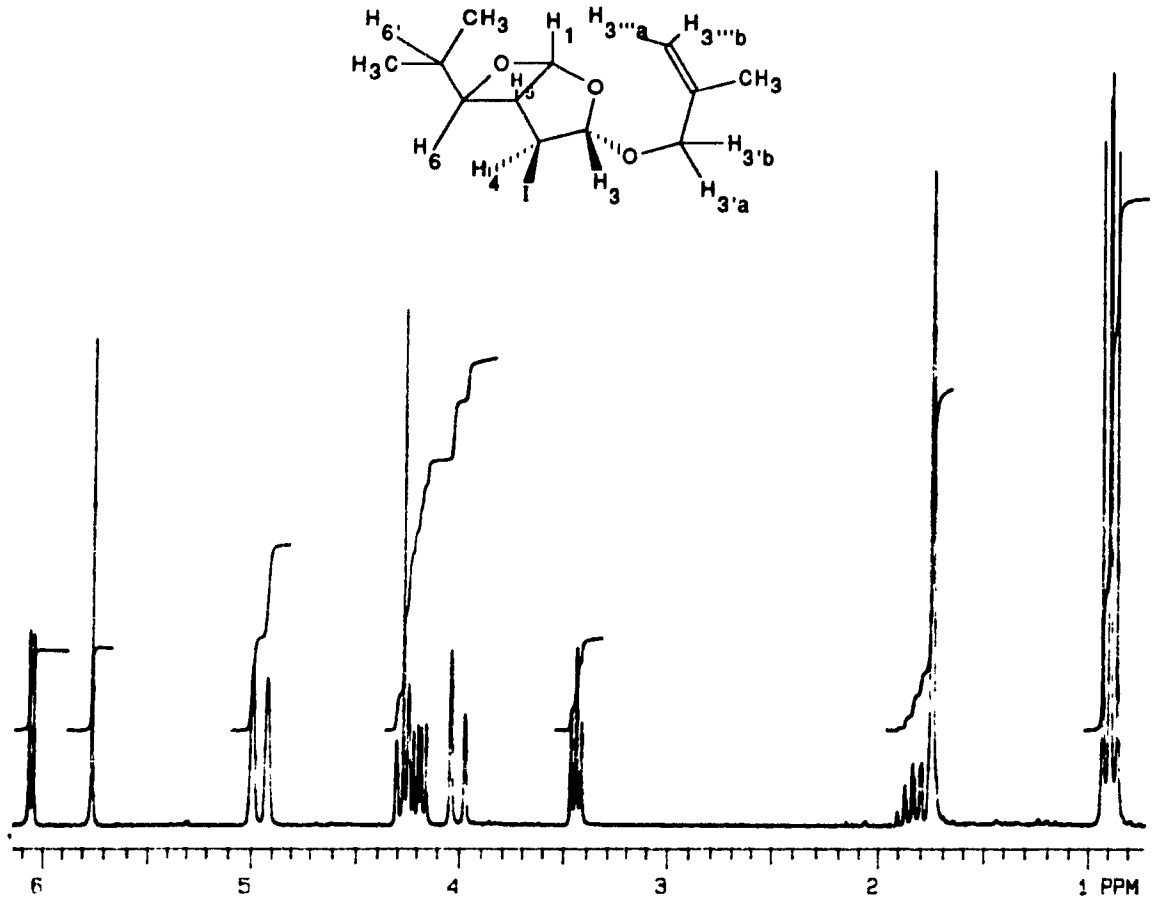


Figure 18. The 200 MHz ^{1}H-NMR spectrum of **10h** in $CDCl_3$.

2.5b Synthesis of Monocyclic Oxetanes (model studies).

Preliminary work was carried out on acetals **10b - 10f** and **10h** so that it could be determined which ones would give the best results. Using the protocol established by Fraser-Reid and Mootoo, bromoacetals **10b**, **10c**, **10e** and **10f** were treated with iodonium di-*sym*-collidine perchlorate (IDCP)[59] and methanol (5 equiv.) in benzene and gave **17b**, **17c**, **17e** and **17f** in 27 - 70% yield as a mixture of inseparable and relatively unstable diastereomers. Reaction of iodoacetals **10d** and **10h** with IDCP and methanol (5 equiv.) in benzene gave **17d** and **17h** in 67% and 30% yield, respectively. After observation of the compounds for several weeks, it became clear to us that the iodo derivatives were more stable than the corresponding bromo derivatives. We also noticed that the 2-methallyl derivatives were considerably more stable than either the 3,3-dimethallyl or allyl derivatives. These results indicated that future work should be carried out with the iodo methallyl derivatives.

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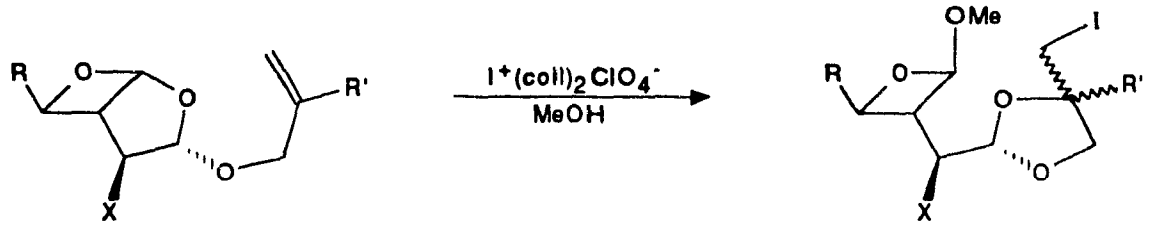
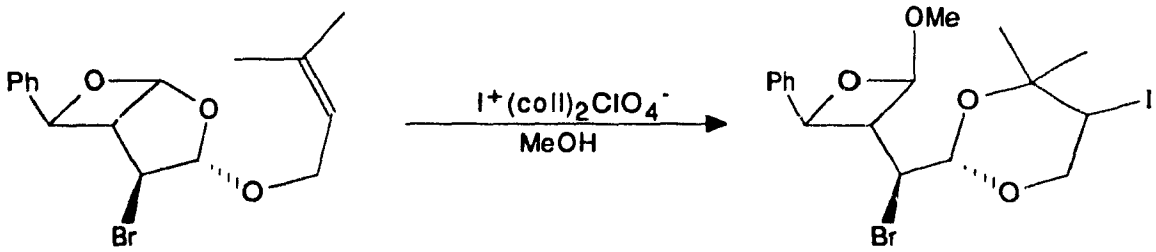
[59] Lemieux, R. U.; Morgan, A R., *Can. J. Chem.*, **43**, 2190 (1965).

Scheme 8



10b, X=Br, R=Ph, R'=CH_3
10d, X=I, R=Ph, R'=CH_3
10e, X=Br, R=*i*Pr, R'=H
10f, X=Br, R=*i*Pr, R'=CH_3
10h, X=I, R=*i*Pr, R'=CH_3

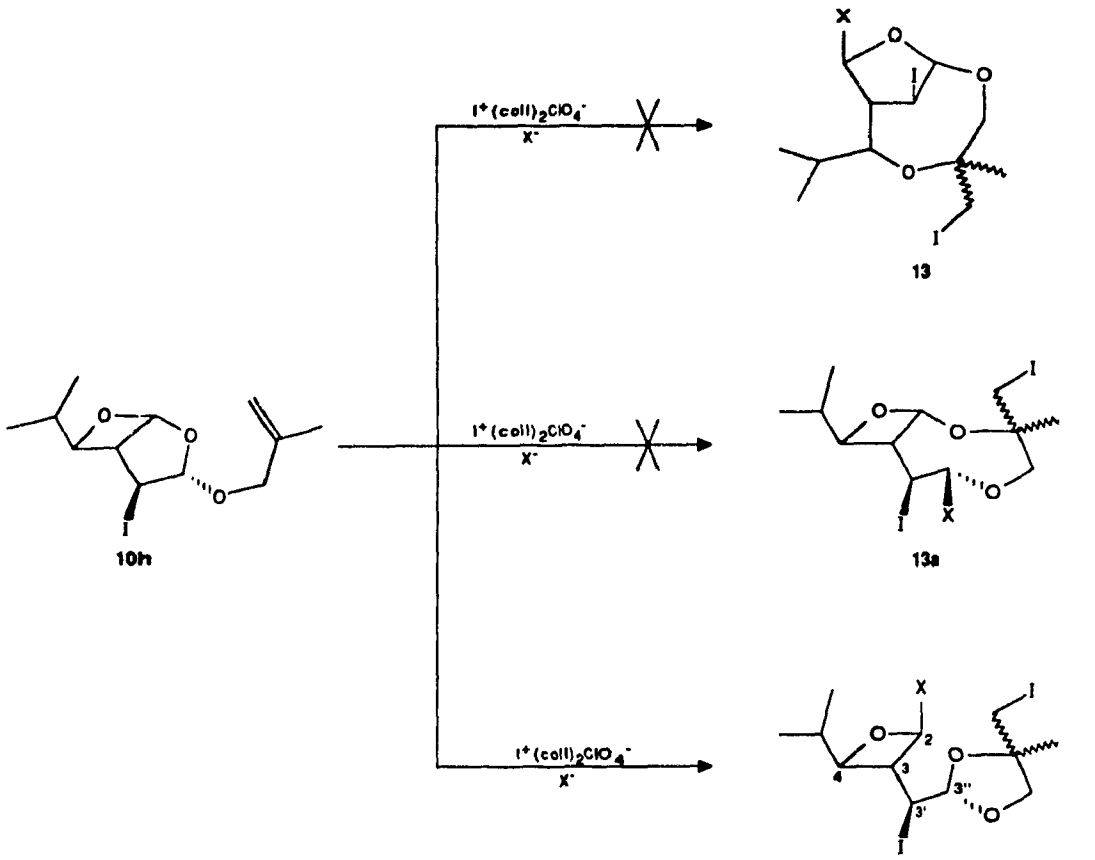
17b, X=Br, R=Ph, R'=CH_3
17d, X=I, R=Ph, R'=CH_3
17e, X=Br, R=*i*Pr, R'=H
17f, X=Br, R=*i*Pr, R'=CH_3
17h, X=I, R=*i*Pr, R'=CH_3



10c **17c**

We next explored the reaction of various nucleophiles with **10h**. Reaction of the iodo-methallyl acetal **10h** with IDCP and a variety of alcohols and carboxylic acids gave, after 4 h, **18a** - **18f** in variable yields. The results are summarized in Scheme 9 (* yields are based on recovered starting material). As can be seen, acetate **18f** could be obtained in respectable yield. All compounds **18** were isolated as mixtures of inseparable diastereomers All of these compounds decomposed slowly at -10 °C and had to be repurified after 1 - 2 weeks if required for further work. Unfortunately, the range of nucleophiles that can be employed in this reaction is not unrestricted. Attempts to carry out the reaction using bulky nucleophiles such as *t*-butanol, diacetone glucose, methyl-2,3-isopropylidene-D-ribofuranose, stigmastanol and β-cholestanol failed and only starting material was recovered. This is probably due to their sheer size which prevents them from coordinating with the electropositive centers in the intermediate. We also tried to couple nitrogenous bases [*bis*-(trimethylsilyl)-N^6-benzoyladenine and *bis*-(trimethylsilyl)-cytosine] to **10h**. Unfortunately, no reaction occurred and only starting material was recovered even if forcing conditions were used.

Scheme 9



Detailed analysis of the ^{1}H and ^{13}C-NMR spectra of these monocyclic oxetanes proves that bicyclic compounds of the types **13** and **13a** were not formed. Since two diastereomers are formed in the reaction, one would expect the ^{1}H and ^{13}C-NMR of the bicyclic compound to be quite different for the two diastereomers due to the fact that the system is relatively rigid and thus, the CH_2I and CH_3 groups would be in significantly different environments. On the other hand, the monocyclic oxetanes would not exhibit any significant differences in chemical shifts between the two diastereomers since the diastereomeric center of the molecule is reasonably removed from the oxetane part of the molecule. Also, since there is free rotation about the carbon-carbon bond which connects the dioxolane moiety to the rest of the molecule, it is not possible for the two diastereomers to be "locked" in a fixed

configuration (which would exhibit markedly different chemical shifts for the two isomers). This is exactly what we observe in the ^{1}H and ^{13}C-NMR. Also, if one examines the ^{1}H and COSY NMR's of **18e** and **18f**, we can see that of the two "anomeric" protons, the one further downfield (H2) is coupled to the one at ~ 3.5 ppm (H3) whereas the other "anomeric" proton (H3") is not coupled to any other protons This indicates that the monocyclic structure is correct since protons at anomeric positions which have ester substituents are always more deshielded than acetals due to the deshielding effects of the carbonyl group.

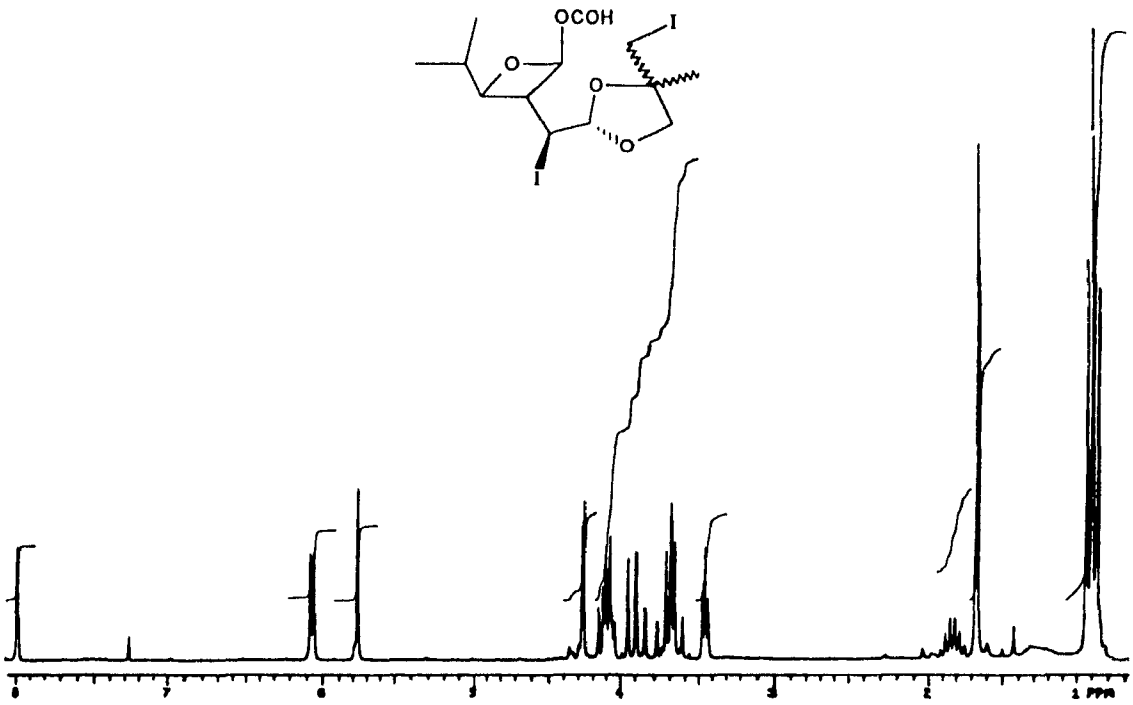
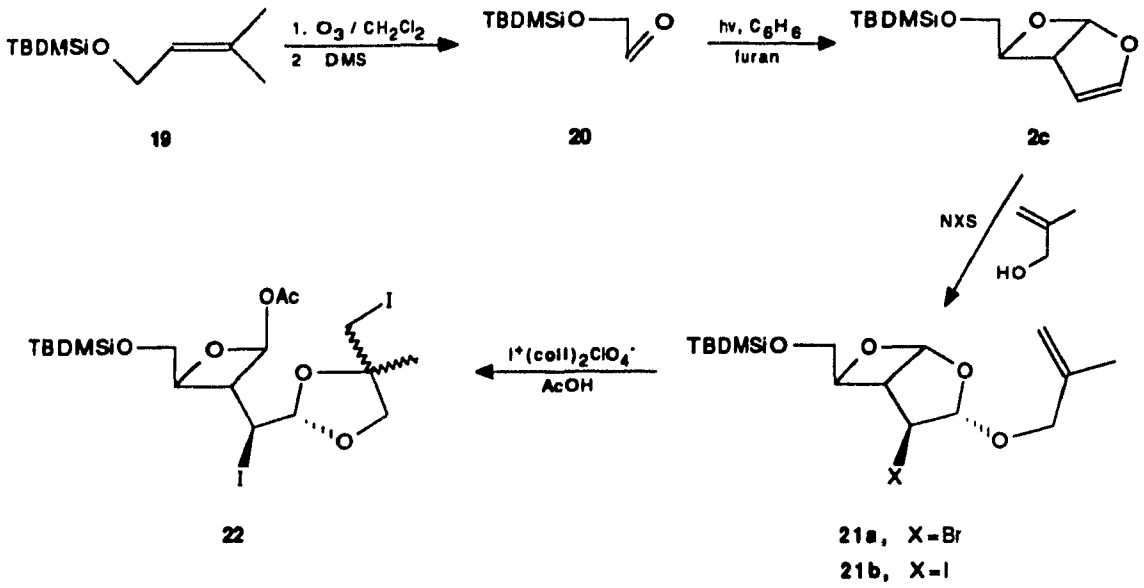


Figure 19. The 200 MHz 1H-NMR of oxetane **18e** in $CDCl_3$.

2.5c Synthesis of (20).

Having proven that the bicyclic system **2** can be opened in the desired manner using a modification of the Fraser-Reid--Mootoo methodology, we decided to prepare an intermediate which was more closely related to oxetanocin. Since we would have to protect what would eventually become the 4' hydroxy group, it was decided to use the *t*-butyldimethylsilyl protecting group since it is reasonably stable to acid (a requirement for Vorbruggen type couplings), survives ozonolysis and would not interfere with the halonium reagents used in opening of the photo-adduct.

Scheme 10



Dimethallyl alcohol was quantitatively converted to the *t*-butyldimethylsilyl ether **19** by standard means (TBDMSiCl / imidazole / DMF)[60]. Ozonolysis in methylene chloride at -78°C, followed by reduction with dimethylsulphide, gave aldehyde **20** in 95% yield. Irradiation of **20** with furan in benzene provided photo-adduct **2c** in 34% yield. Treatment of a 0.2 M solution of **2c** in methallyl alcohol with 1 equivalent of N-bromo or N-iodosuccinimide gave the corresponding bromo (**21a**) and iodo (**21b**) acetals in 34 and 27% yield, respectively. Finally, treatment of **21b** with IDCP and acetic acid gave the monocyclic oxetane **22** in 47% yield.

Since oxetanes similar to **22** had been converted to oxetanocin by reaction with *bis*-(trimethylsilyl)-N^6-benzoyladenine and tin tetrachloride, we used these reaction conditions and variations thereof to try to convert **22** to an oxetanocin like molecule. However, decomposition occurred before coupling. The instability is probably linked to the presence of the two halogens in **22**. Therefore, it was decided that the halogen on C3' would have to be replaced by a hydroxy group and this could be accomplished by either replacing the halogen in compounds **10** or by functionalizing the epoxide of **2** with methallyl alcohol.

Reaction of **10h** with excess potassium hydroxide in refluxing tetrahydrofuran / water did not result in replacement of the iodine by a hydroxy group. When silver carbonate in dioxane / water was used, no reaction occurred unless forcing conditions were used. Then, decomposition of the starting material resulted. Since we were unsuccessful in our efforts to replace the iodide with a hydroxy group, it was decided to proceed via the epoxide of **2**.

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[60] Corey, E. J.; Venkateswarlu, A., *J. Am. Chem. Soc.*, **94**, 6190 (1972).

2.5d Epoxidation of Photo-adducts (2), model studies.

Since it was known that MCPBA could not be used for the epoxidation of photo-adducts, other methods had to be explored. Reaction of **2a** with peracetic acid[61] in methylene chloride / acetic acid resulted in decomposition of the starting material. Similar results were obtained when magnesium monoperoxyphthalate (MMPP)[62] was used. At this point we felt that decomposition was occurring because the epoxide was unstable and hence could not be isolated. Therefore, we added methallyl alcohol to the reaction mixtures hoping to open the epoxide, to give the methallyl acetal, before it decomposed. This approach was not successful. When methanol / water solutions of photo-adducts **2a** and **2b** were treated with sodium percarbonate[63], no reaction occurred even when forcing conditions were used. Use of 2-butanone peroxide as the epoxidizing agent also did not yield the desired epoxides and only starting material was recovered. However, when a methylene chloride solution of **2a** was submitted to the actions of dimethyl dioxirane in acetone[64,65,66], epoxide **23a** was obtained in almost quantitative yield as a 9:1 mixture of exo and endo isomers, which were unstable to and therefore unseparable by chromatography. Unfortunately, reaction of **2b** with dimethyl dioxirane in acetone / methylene chloride did not give the desired product and no starting material was recovered. Nevertheless, we decided to proceed with our model studies using epoxide **23a**.

Since we were interested in establishing the optimum conditions for opening up the epoxide with methallyl alcohol, it was necessary to determine under what conditions the epoxide would survive and react in the desired manner. It was discovered that by dissolving **23a** in dry methanol and stirring for 16 hours causes the epoxide to open giving acetal **24a** in 61% yield. Although **24a** can be isolated and characterized without much difficulty, its lifetime is only 1 - 2 weeks at -10°C. Acetylation by standard methods (Ac_2O, py, DMAP) gave acetate **25a** in 56% yield. It was necessary to protect the free alcohol so as to increase the stability of the molecule. Reaction of **23a** with 5 equivalents of acetic acid in methylene chloride gave, after 18 h, **24b** in 56% yield. Acetylation proceeded in 93% yield to give diacetate **25b**. This result proved that the epoxide could tolerate controlled acidic conditions. Now that we had an idea of how to functionalize the epoxide, we proceeded to synthesize the methallyl acetal of **23a**. Reaction of **23a** with 5 equivalents of methallyl alcohol in methylene chloride gave **24c** in 63% yield. Protection of the free hydroxy group as an acetate (**25c**) proceeded in 71% yield.

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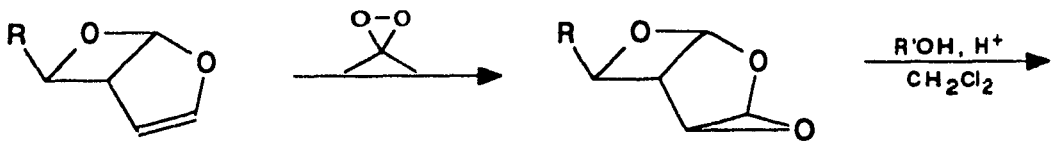
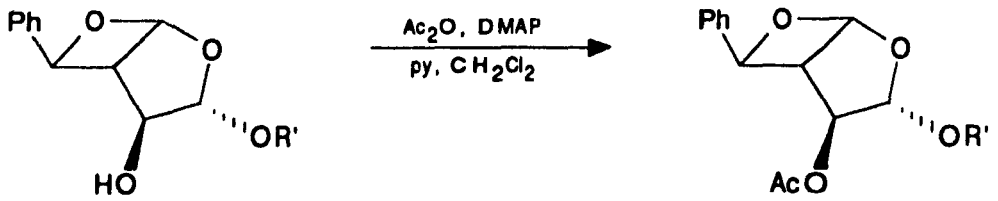
61 Reif, D. J.; House, H O., *Org Syn., Coll Vol.*, **4**, 860 (1963)
62 Brougham, P.; Cooper, M S ; Cummerson, D. A ; Heaney, H.; Thompson, N., *Synthesis*, 1015 (1987).
63 Ando, T.; Cork, D. G.; Kimura, T., *Chemistry Letters*, 665 (1986).
64 Murray, R. W.; Jeyaraman, R , *J. Org. Chem* , **50**, 2847 (1985).
65 Baertschi, S. W.; Raney, K. D.; Stone, M P.; Harris, T. M., *J. Am. Chem. Soc.*, **110**, 7929 (1988).
66 Adam, W.; Curci, R.; Edwards, J. O , *Acc. Chem. Res.*, **22**, 205 (1989).

Scheme 11



2a, R=Ph
2b, R=*i*Pr
2c, R=TBDMSiOCH$_2$

23a, R=Ph
23b, R=*i*Pr



24a, R'=CH$_3$
24b, R'=Ac
24c, R'=CH$_2$C(CH$_3$)=CH$_2$

25a, R'=CH$_3$
25b, R'=Ac
25c, R'=CH$_2$C(CH$_3$)=CH$_2$

Being satisfied with the results from our model studies, work proceeded on epoxidizing photo-adduct **2c**. Unfortunately, the conditions which were employed for **2a** proved to be unsatisfactory for **2c**. It was thought that the epoxide of **2c** was very unstable and that it could not be isolated. Therefore, we reacted **2c** with dimethyl dioxirane in acetone / methylene chloride containing 1 equivalent of methallyl alcohol hoping to open the epoxide *in situ* before it decomposed. This approach was not successful. It also did not succeed when tried with photo-adduct **2a**, but surprisingly, when **2b** was employed, epoxide **23b** was isolated in 53% yield. No explanation for why methallyl alcohol is necessary to facilitate epoxidation of **2b** can be given.

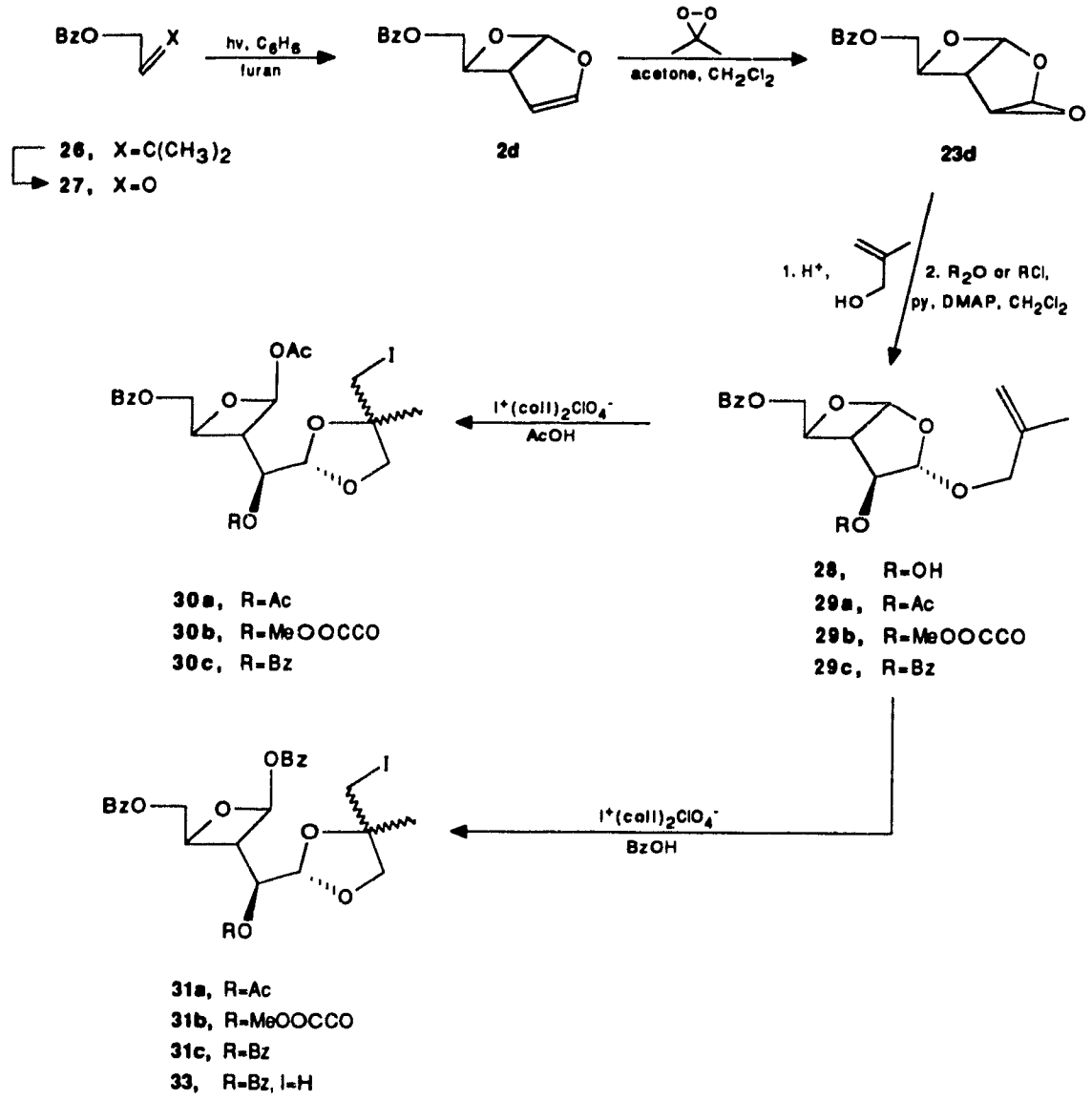
Since we were unable to epoxidize **2c**, a new photo-adduct would have to be designed. The *t*-butyldimethylsilyl group would now have to be replaced by another protecting group because we felt that the TBMDSi group was the source of instability in the epoxide of **2c**. After careful consideration, the benzoyl ester was chosen since it is stable to oxidizing agents, acidic conditons used in Vorbruggen coupling reactions, and can be removed under relatively mild conditions.

Dimethallyl alcohol was transformed in quantitative yield to its benzoate ester **26** by standard methods (BzCl, py, DMAP). Ozonolysis, followed by reduction with dimethyl sulfide, gave aldehyde **27**, which upon irradiation with furan, provided photo-adduct **2d** in 30% yield. Epoxidation with dimethyl

dioxirane in acetone / methylene chloride proceeded smoothly to give epoxide **23d** in virtually quantitative yield as a 9:1 mixture of exo and endo isomers which, as expected, were unstable to column chromatography. Treatment of **23d** with 10 equivalents of methallyl alcohol in methylene chloride gave hydroxy acetal **28**, which was transformed to acetate, methyl oxalate and benzoate **29a-c** by standard procedures in 75, 64 and 78% overall yield respectively, from epoxide **23d**. Treatment of **29a, b** and **c** with IDCP and acetic acid (5 equiv.) gave **30a, b** and **c**, whereas the use of benzoic acid as the nucleophile gave **31a, b** and **c**. All of these were obtained in moderate yield. Benzoates **31a, b** and **c** had a shelf life of 3 - 5 weeks at -10°C, whereas the acetates **30a, b** and **c** started decomposing after a few days. The NMR data of **30** and **31** were similar to those of the iodo derivatives **18e, 18f** and **22**, and confirmed that we had obtained the desired monocyclic oxetanes.

Since we felt that the presence of an iodine in our sugars was a contributing factor to their relative instabilities, we also investigated the reaction of **29a-c** with bromonium di-*sym*-collidine perchlorate[18] and acetic acid, hoping that perhaps the bromides would be more stable than the corresponding iodides. Although tlc indicated that a reaction took place, the products were so unstable that they could not be isolated even in crude form. Hence it was not possible to ascertain whether or not the desired product had formed.

Scheme 12

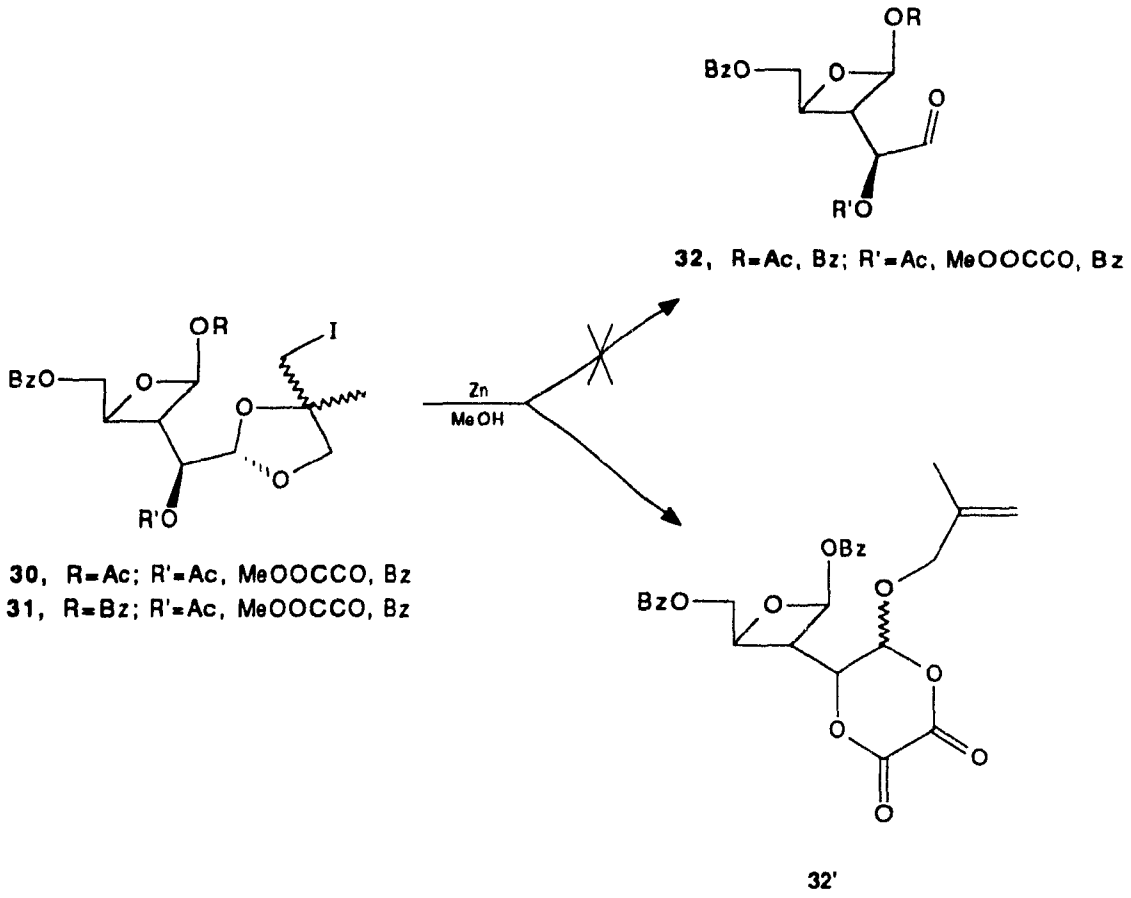


Unfortunately, both **30** and **31** decomposed during attempts to couple with persilylated bases, using Lewis acid catalysis. In order to improve the stability of oxetanes **30** and **31**, we attempted to remove the dioxolane moiety reductively by means of zinc in methanol[67]. When the reaction was carried out on oxetanes **30a-c**, **31a** and **31c**, tlc indicated formation of a new product which could have possibly been the desired aldehyde **32**. However, the product decomposed almost immediately after it was formed and thus could not be isolated. Only oxetane **31b** gave an isolatable, albeit highly unstable ($T_{1/2}$ ~ 2h at

67 Corey, E. J.; Ruden, R. A., *J. Org. Chem.*, **38**, 834 (1973).

-10°C), reduction product **32'** whose structure was tentatively assigned based only on ^{1}H-NMR. The spectrum clearly indicated the presence of the monocyclic oxetane ring as well as a methallyl side chain.

Scheme 13

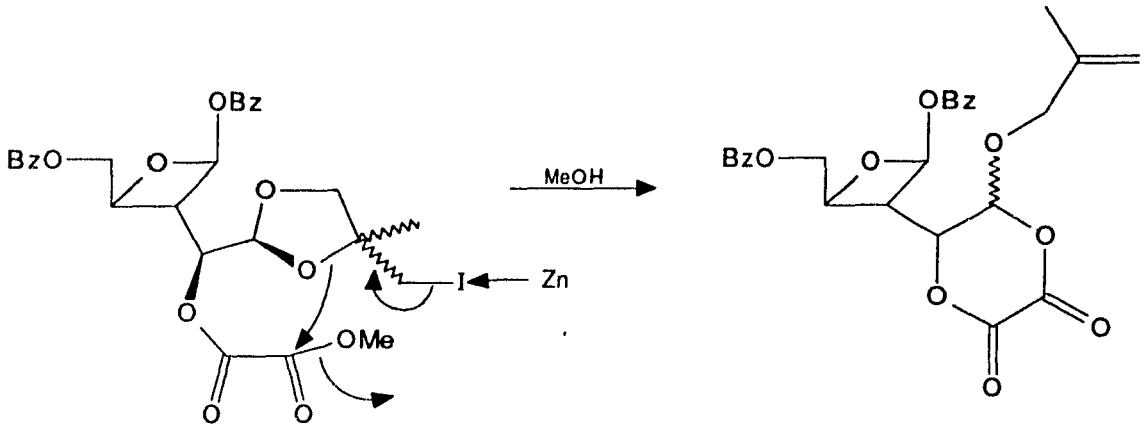


The mechanism for the formation of oxetane **32'** is shown in Scheme 14. After examination of this scheme, it is quite obvious why the reaction can only proceed through this pathway when a methyl oxalyl protecting group is used. Clearly, this pathway is preferred to the one that would lead to the formation of aldehydes **32**.

Tributyltin hydride mediated deiodination of oxetane **31** only gave the desired product **33** (I = H, 50% yield) in the case of **31c**. It is stable at -10°C for extended periods of time but could not be converted to oxetanocin like material because of decomposition under mildly Lewis acid conditions. From comparison with anomeric benzoates of type **31c** not containing the dioxolane ring (prepared in section 2.6b), we conclude that the dimethyl-dioxolane ring is the source of instability in these types of compounds since the dimethyl-dioxolane moiety is rapidly converted to an aldehyde under acidic

conditions. These aldehydes, as seen from our attempts to convert oxetanes **30** and **31** to aldehydes **32**, are extremely unstable and decompose almost immediately after formation..

Scheme 14



31b **32**

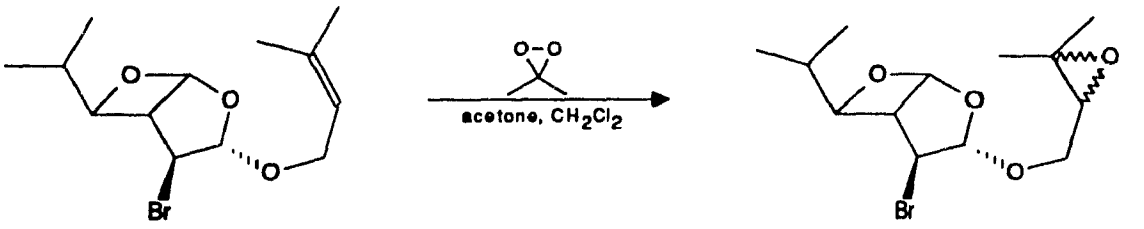
2.5e Methallyl Epoxide Approach.

At the same time as we were investigating IDCP initiated monocyclic oxetane formation, we also investigated the epoxidation of allyl type adducts. It was hoped that nitrogenous bases could be added to these epoxides in a manner analogous to the one that we developed for synthesis of monocyclic oxetanes. Again using model compounds, we subjected acetal **10g** to the actions of dimethyl dioxirane in acetone / methylene chloride and discovered that bromo epoxide **34a** was obtained in 66% yield. Similarly, epoxidation of acetal **21a** gave epoxide **34b** in 90% yield. However, acetals **10h** and **21b** did not afford their corresponding epoxides since the starting material was decomposed by the actions of dimethyl dioxirane. We believe that **10h** and **21b** decomposed (solution turned black) because the iodine was oxidized by dimethyl dioxirane.

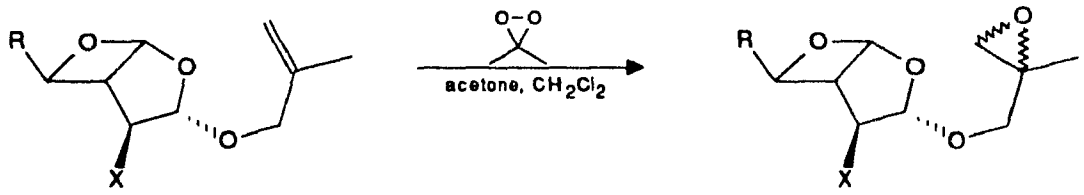
With **34b** in hand, we proceeded with the coupling to the nitrogenous base. Reaction of **34b** and *bis*-(trimethylsilyl)-N^6-benzoyladenine in 1,2-dichloroethane catalyzed by various Lewis acids resulted in decomposition of the starting material with no evidence of any coupled products of the type **35a** being formed. Similar results were obtained when *bis*-(trimethylsilyl)-cytosine was used as the base. Believing that perhaps the bromine in epoxide **34b** was the cause for its instability, epoxide **34c** was prepared by a procedure similar to that used for the preparation of **34b** in 87% yield. It was hoped that this epoxide (**34c**) would be more suitable for coupling reactions due to its increased stability. Unfortunately, we were

unable to achieve any coupling to nitrogenous bases using conditions similar to those used for **34b** and this approach was abandoned.

Scheme 15



10g **34a**

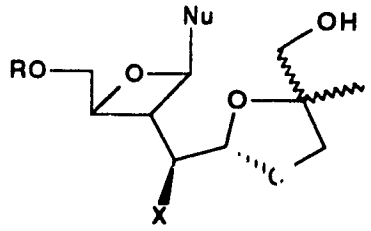


10h, R=*i*Pr, X=I
21a, R=TBDMSiOCH$_2$, X=Br
21b, R=TBDMSiOCH$_2$, X=I
29a, R=BzOCH$_2$, X=AcO

34b, R=TBDMSiOCH$_2$, X=Br
34c, R=BzOCH$_2$, X=AcO

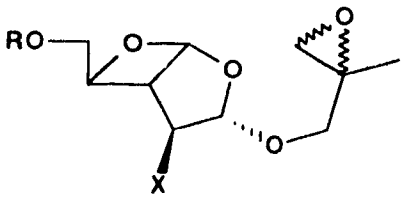
Since we had experienced difficulty in coupling nitrogenous bases directly to functionalized photo-adducts previously, it was decided to attempt to open the bicyclic compound **34c** with a thiol to yield a compound of type **35b**. This compound could then be coupled to the base via a mercury catalyst. It was thought that these types of coupling conditions are milder than the Lewis acid catalyzed methods. Reaction of **34c** with thiophenol in ether catalyzed by zinc chloride gave alcohol **36** as a mixture of inseparable diastereomers in 64% yield. The product is derived from a zinc chloride catalyzed opening of the oxetane ring and is extremely unstable. Attempts to further characterize **36** by forming an acetate failed. Also, the synthesis of **36** is very difficult and requires very dry conditions (despite the best precautions, only 1 out of 3 attempts gave **36**). All other attempts to synthesize compounds of the type **35b** failed and this approach was not pursued any further.

Scheme 16



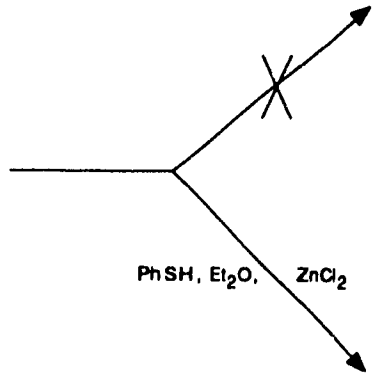
35a, R=TBDMSi, Bz; X=Br, AcO
Nu=Adenine, Cytosine

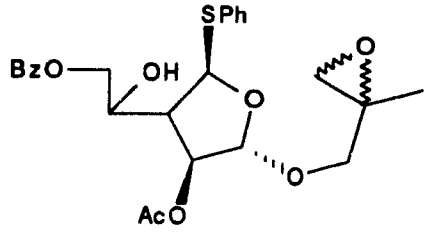
35b, R=Bz, X=AcO, Nu=SPh



34b, R=TBDMSi, X=Br

34c, R=Bz, X=AcO





36

2.6 Unsymmetrically Substituted Photo-adducts as Precursors for Oxetanocin.

2.6a Model Studies.

One of the major limitations of the Paterno-Buchi photocycloaddition reaction is the lack of regioselectivity in the addition of aldehydes to unsymmetrically substituted furans. For example, the photochemical reaction between benzaldehyde and 2-methylfuran provides a 1:1.3 mixture of photo-adducts resulting from the exo addition of the aldehyde to the less- and more-substituted double bond of furan, respectively[42]. Separation by chromatographic means is not possible, and therefore it was not possible to convert the appropriate photo-adduct to a suitably protected oxetane due to the fact that the undesired isomer decomposes during the reaction and gives a complex mixture from which it was impossible to isolate the desired sugar.

Since we were interested in synthesizing oxetane sugars directly from photo-adducts by the method developed for the synthesis of 3, an investigation of the reaction of aldehydes with various mono-substituted furans was initiated. It was hoped that a pattern would emerge regarding the effect of electron donating or withdrawing substituents on the furan ring. Another objective of this study was to provide a stock of vinyl substituted photo-adducts which could be used in the synthesis of oxetanocin. We also wanted to see if the use of non alkyl substitutents would make separation by chromatographic means feasible. Benzaldehyde was chosen as the carbonyl component due to the fact that it gives relatively stable photo-adducts, its NMR spectrum is simple and does not appear in the same region as the photo-adduct signals and it is readily available in very pure form[68]. The substituted furans chosen were ones that were readily available and contained side chains which could be modified as necessary in our synthesis of oxetanocin.

Irradiation of a benzene solution of benzaldehyde and furfural did not give any photo-products and only starting material was recovered. Similar results were obtained when 2-acetylfuran or 2-methoxyfuran were used as the furan components. However, when furfuryl alcohol **37** was used as the furan component, photo-adducts **37a** and **37b** were obtained as a 4:7 mixture of regioisomers. Purification by flash chromatography gave the vinyl substituted isomer **37a** exclusively, in 20% yield. It was possible to isolate **37a** uncontaminated by **37b** since the latter is destroyed on the column. This selective destruction is possible since silica gel is slightly acidic and catalyzes the opening of the oxetane ring in the case of the acetal substituted isomer **37b** due to the very favourable formation of a tertiary oxo-carbonium ion. The silica gel, however, is not acidic enough to catalyze oxetane ring opening in the vinyl substituted isomer.

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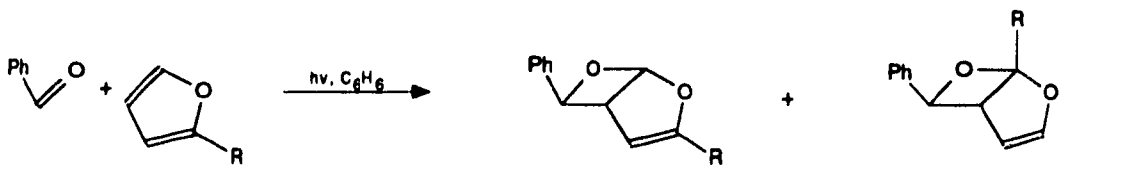
[68] In retrospect, other aldehydes should have also been investigated (especially benzoyloxyacetaldehyde) since this would have given us a better understanding of the relative stabilities of the photo-adducts under the conditions of flash chromatography.

Encouraged by this result, we then formed 2-(2-hydroxyethyl)-furan **38** in 99% yield by the reaction of furfural with methyl magnesiun bromide in ether. Irradiation of benzaldehyde with **38** in benzene gave photo-adducts **38a** and **38b** as a 3:5 mixture of regioisomers. It was possible to isolate isomer **38a** in 26% yield by flash chromatography without contamination of the other isomer **38b**. Acetalization of furfural with cerium trichloride, methanol and trimethyl orthoformate gave, in 69% yield, dimethyl acetal **39**, which was irradiated with benzaldehyde in benzene to give photo-adducts **39a** and **39b** in 46% yield as a 2:3 mixture of inseparable regioisomers.

Scheme 17



37, R=CH_2OH **37a**, R=CH_2OH **37b**, R=CH_2OH

38, R=$CH(OH)CH_3$ **38a**, R=$CH(OH)CH_3$ **38b**, R=$CH(OH)CH_3$

39, R=$CH(OMe)_2$ **39a**, R=$CH(OMe)_2$ **39b**, R=$CH(OMe)_2$

It is not possible to draw any conclusions from this study since its scope was simply not broad enough. However, we did learn that it was possible to obtain unsymmetrically substituted photo-adducts in a pure form by way of flash chromatography. The isolation of the desired isomer depended solely on the difference of the stabilities of the two regioisomers.

2.6b Synthesis of Benzoate (42) and *p*-Nitrobenzoate (43).

Since anomeric benzoates **31** were more stable than the corresponding acetates **30**, we next proceeded to synthesize **42** (Scheme 18). It was felt that these sugars would be significantly more stable than **31** since they did not contain a dioxolane moiety.

We initially decided to synthesize photo-adduct **41a** via [2+2] photocycloaddition of 2-phenylfuran and aldehyde **27**. Although we did not expect any regioselectivity in this reaction, it was hoped that the two regio-isomers could be separated by chromatography. Unfortunately, irradiation of 2-phenylfuran, prepared by a described method[69], and aldehyde **27** did not give any photo-products and only starting material was recovered. However, when using tributyl-(2 furyl)-stannane, prepared by a known procedure[70], as the furan component as described by Schreiber[71], photo-adduct **40** was obtained

[69] Bohlmann, F.; Stöhr, F.; Staffeldt, J., *Chem. Ber.*, 111, 3146 (1978).
[70] Pinhey, J. T.; Roche, E. G., *J. Chem. Soc. Perkin Trans. I*, 2415 (1988).

in 15% yield after flash chromatography without contamination of the other isomer. In order to prevent acid catalyzed decomposition of the photo-products, the reaction mixtures were buffered with anhydrous potassium carbonate. It was not possible to isolate the other regio-isomer[72] due to its instability on silica gel, even when basified with 2% triethylamine. Arylation of **40** using bromobenzene and tetrakis(triphenylphosphine)palladium(0) in refluxing tetrahydrofuran[73] proceeded in 80% yield to give **41a**. We found that the best results were obtained when the catalyst was added in small portions over the course of the reaction. This is presumably due to the fact that the catalyst becomes poisoned by the tin, which is liberated during the course of the reaction. When the reaction was carried out using iodobenzene instead of bromobenzene, the yield increased to 85%. Ozonolysis of **41a** in methylene chloride at -78°C, followed by reduction with dimethyl sulfide and reduction of the aldehyde function with sodium borohydride on alumina gel gave, after acylation, stable triacyloxy oxetane **42a** in 33% yield (unoptimized).

With anomeric benzoate **42a** in hand, we proceeded with the coupling to the base. Unfortunately, reaction of **42a** and *bis*-trimethylsilyl-N^6-benzoyladenine in 1,2-dichloroethane catalyzed by various Lewis acids resulted in no reaction taking place even if forcing conditions (reflux, 48 h, excess catalyst) were used. Since benzoate **42a** was too unreactive, we decided to substitute the benzoyl group with a *p*-nitrobenzoyl group in the hope that while at the same time being stable enough to withstand Lewis acid conditions, it would also be a better leaving group, thus allowing coupling with the nitrogenous base to proceed. Hence, **42b** was synthesized in 25% yield by a procedure similar to that used for **42a**. However, this sugar also proved to be too stable and attempts at coupling to the base proved to be unsuccessful.

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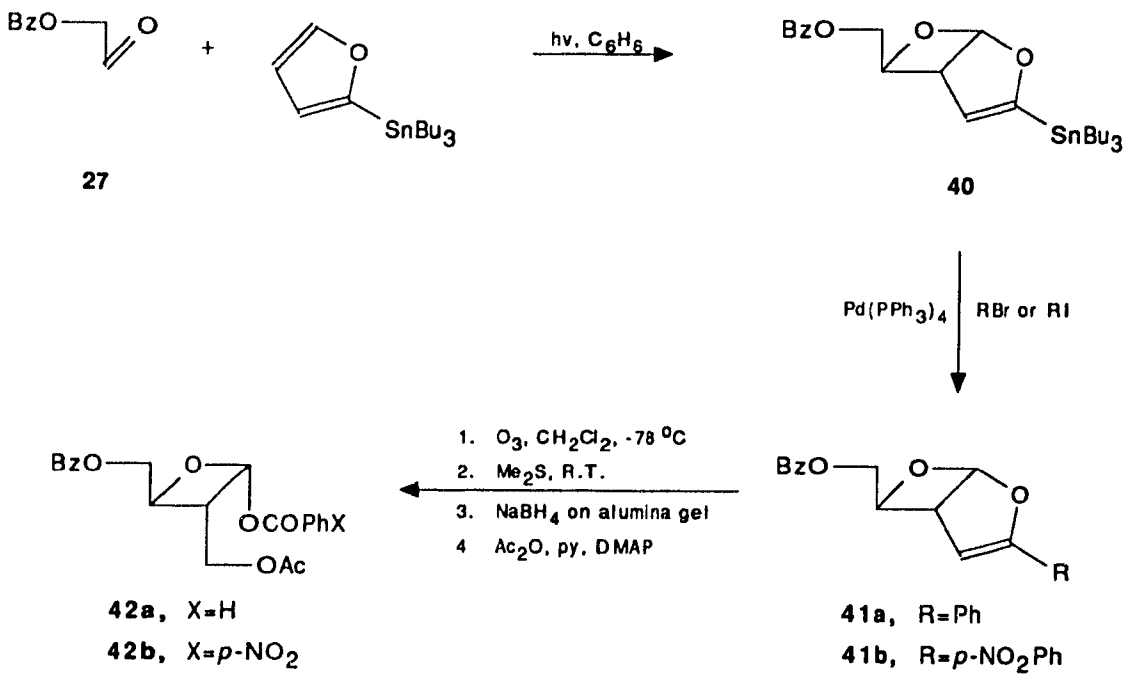
71 Schreiber, S. L.; Desmaele, D.; Porco, J. A. Jr., *Tetrahedron Lett.*, **29**, 6689 (1988).
72 The isomer with the Sn bonded to the acetal carbon was obtained in a 1.20 ratio with respect to the vinyl tributyl tin isomer as determined by integration of 200 MHz proton NMR signals.
73 McKean, D. R.; Parrinello, G.; Renaldo, A. F.; Stille, J K., *J Org. Chem.*, **52**, 422 (1987).

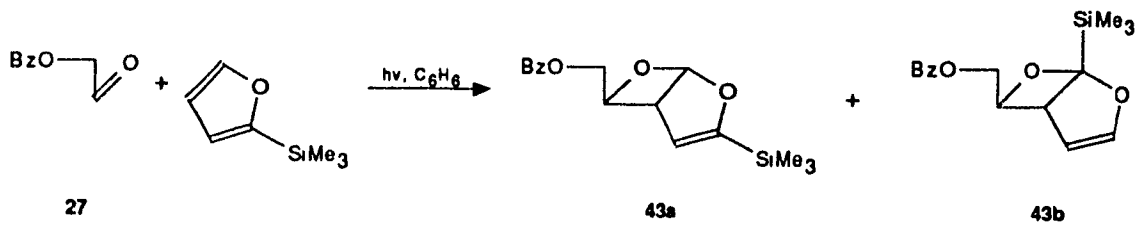
Scheme 18



2.6c Synthesis of Acetates (47).

We next investigated the photoaddition of 2-trimethylsilylfuran with aldehyde **27**. It was thought that the reaction could yield the desired vinyl silane either by chromatographic separation or by achieving high chemoselectivity as we observed earlier when we carried out a photochemical reaction with tributyl-(2-furyl)-stannane. The resultant vinyl silane **43a** could then be converted into an oxetane by the method described in Section 2.6b. Unfortunately, irradiation of 2-trimethylsilylfuran with aldehyde **27** gave photo-adducts **43a** and **43b** in 19% yield (unoptimized) as a 7:4 mixture of 2 inseparable isomers.

Scheme 19



Since we were unable to separate **43a** and **43b**, we next investigated the photoaddition of 2-methylfuran with benzoyloxyacetaldehyde. It was hoped that we could obtain the desired photo-adduct **44a** either by chromatographic separation (as observed on several occasions in our model studies; section 2.6a) or even better, by achieving regioselectivity in the photoreaction. Irradiation of a benzene solution of 2-methylfuran and **27** gave regioisomers **44a** and **44b** in a ratio of 11:8, which could be isolated by flash chromatography (ethyl acetate / petroleum ether / triethylamine). In the absence of triethylamine, **44b** decomposed and the desired photo-adduct **44a** was isolated in 30% yield. In a one-pot reaction, **44a** was transformed to **47a-c** by the following sequence: A methylene chloride solution of **44a** was ozonized at -78°C, and the ozonide reduced with dimethyl sulfide to give aldehyde **45**. Addition of sodium borohydride on alumina gel, followed by filtration gave alcohol **46**. Acylation of the alcohol function (**47a**: Ac_2O, pyridine, DMAP; **47b**: BzCl, NEt_3, DMAP; **47c**: MeOOCCOCl, NEt_3, DMAP) gave **47a**, **47b** and **47c** in 30% - 55% yield. This result was in sharp contrast to the decomposition that occurred when the corresponding furan derived photo-adduct **2d** had been submitted to the same reaction conditions. Clearly, the anomeric acetates are much more stable than the corresponding anomeric formates. It was possible to isolate and characterize the intermediate aldehyde **45** and alcohol **46**, although neither is very stable and thus cannot be stored for extended periods of time without appreciable decomposition occurring.

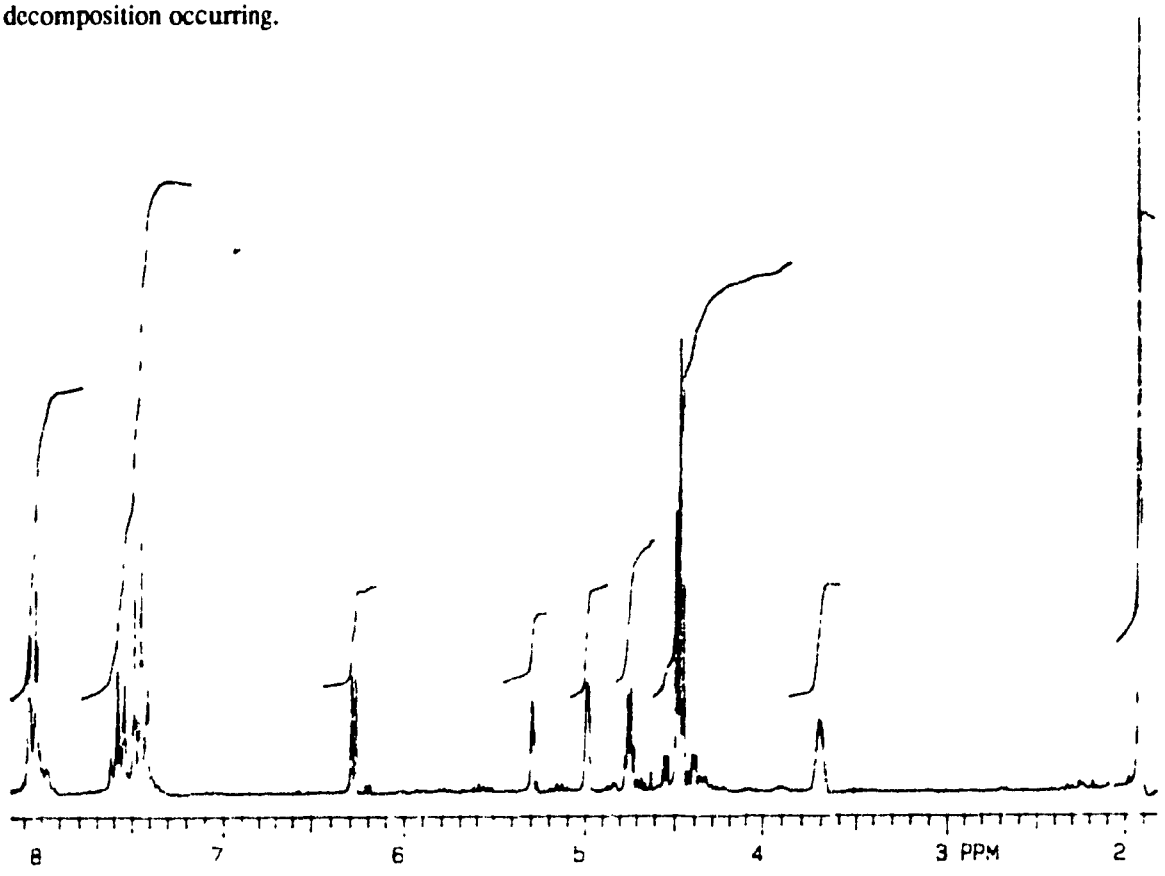
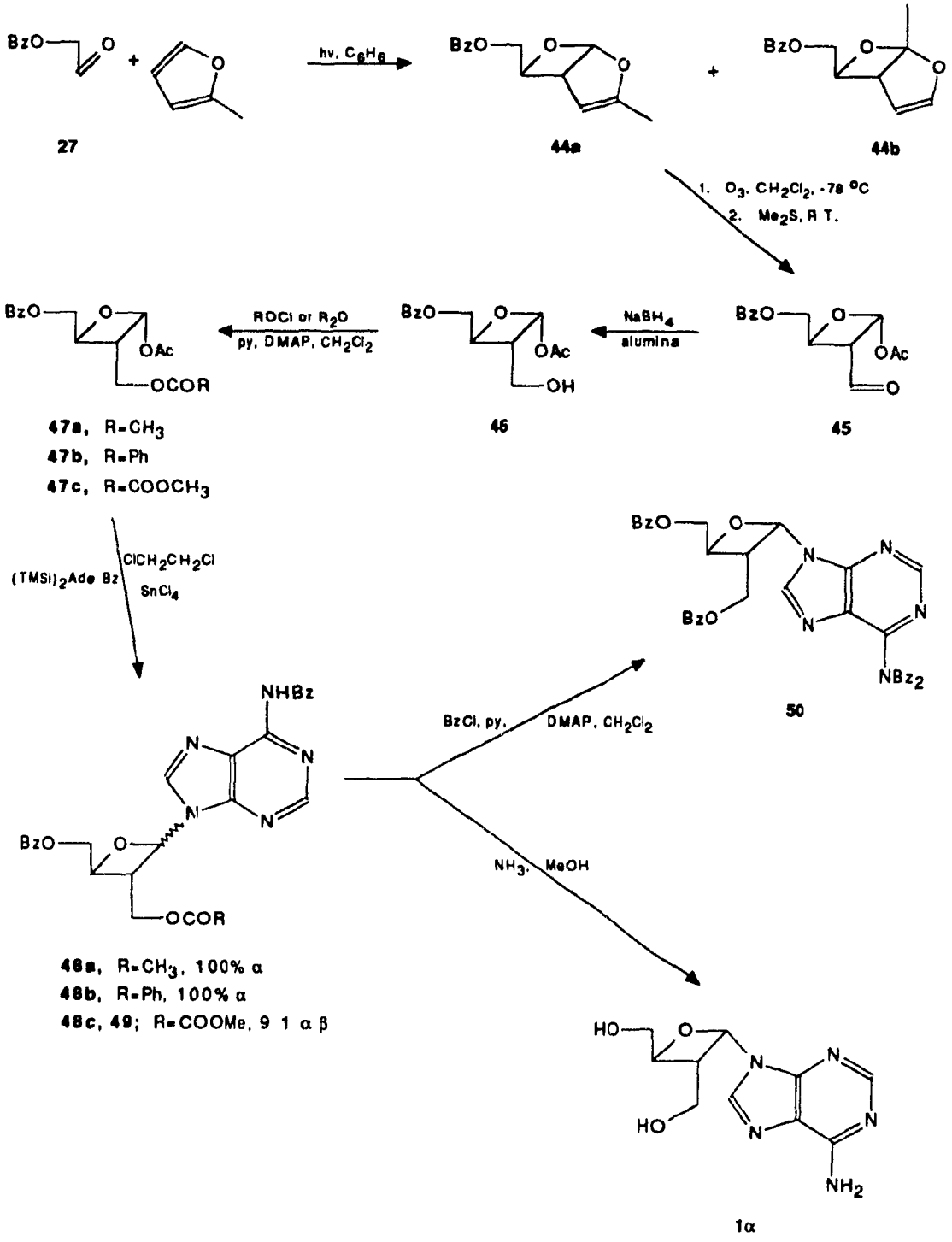


Figure 20. The 200 MHz ^{1}H-NMR of photo-adduct **44a** in CD_2Cl_2.

Scheme 20


hv, C6H6
27
44a
44b
1. O3, CH2Cl2, -78 °C
2. Me2S, R T.
45
NaBH4
alumina
46
ROCl or R2O
py, DMAP, CH2Cl2
47a, R=CH3
47b, R=Ph
47c, R=COOCH3
(TMSI)2Ade Bz
ClCH2CH2Cl
SnCl4
48a, R=CH3, 100% α
48b, R=Ph, 100% α
48c, 49; R=COOMe, 9 1 α β
BzCl, py, DMAP, CH2Cl2
50
NH3, MeOH
1α

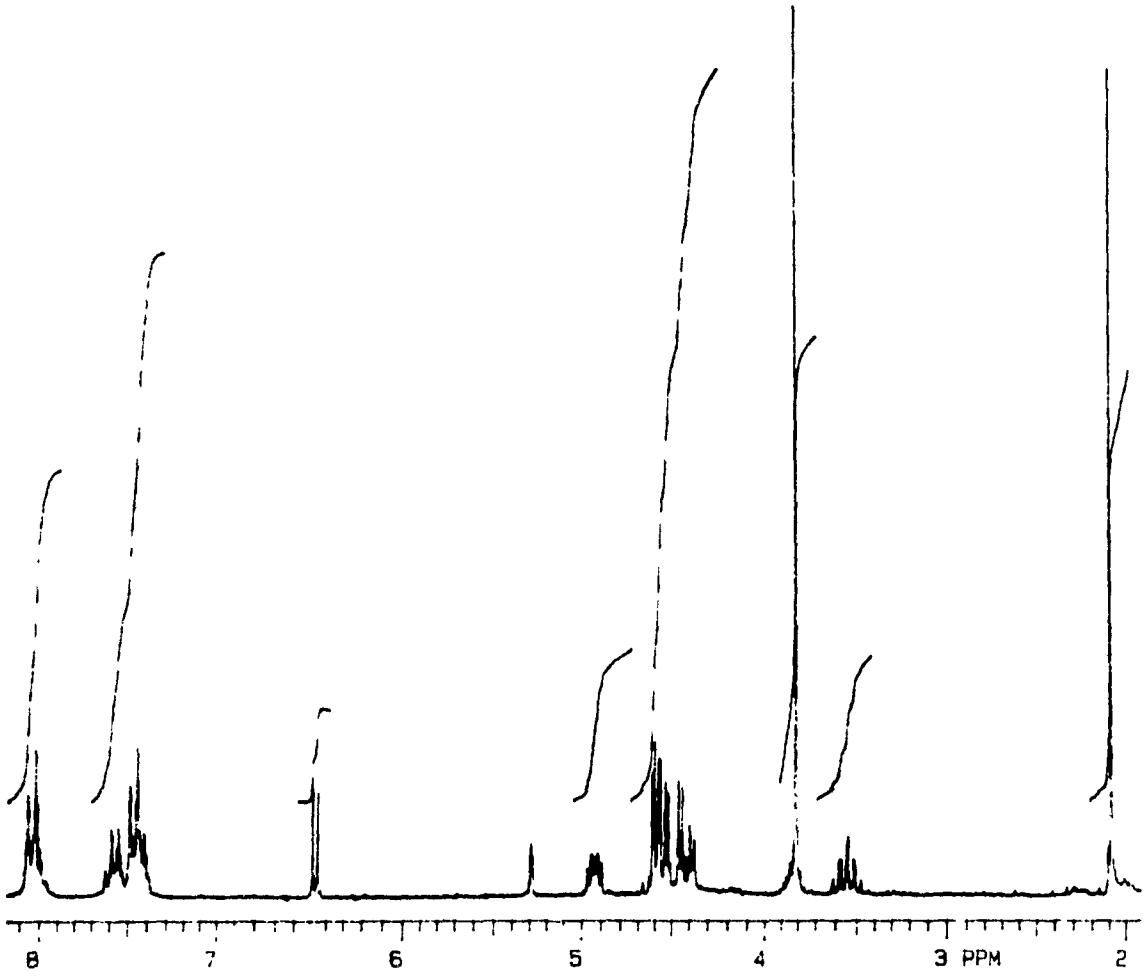


Figure 21. The 200 MHz ^{1}H-NMR of oxetane **47c** in CD_2Cl_2.

As described by Yamamura[15], reaction of **47b** with *bis*-(trimethylsilyl)-N^6-benzoyladenine and tin tetrachloride in 1,2-dichloroethane, gave protected epioxetanocin **48b** as the only isolated product in 70% yield[74]. Similar results were obtained when acetate **47a** was used as the carbohydrate component. Applying the Vorbruggen coupling to methyl oxalate **47c** gave **49** and **48c** as a 9:1 mixture of α and β anomers in 70% yield.

Since we were interested in studying the biological properties of epioxetanocin, **48b** was debenzoylated (MeOH / NH_3) to give **1α** in 71% yield, after recrystallization from methanol. However, when epioxetanocin was evaluated as an anti-viral agent against HIV *in vitro*, it showed no anti-viral effects at concentrations up to 100 μg/mL. These results were corroborated by Fleet[9].

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[74] Since we wanted to compare our product to the one obtained by Nishiyama, **48b** was benzoylated (BzCl, NEt_3, DMAP) to give N,N-dibenzoylepioxetanocin dibenzoate **50** in 89% yield. It was completely identical with the one described by Yamamura in every respect, except for the fact that our product was racemic.

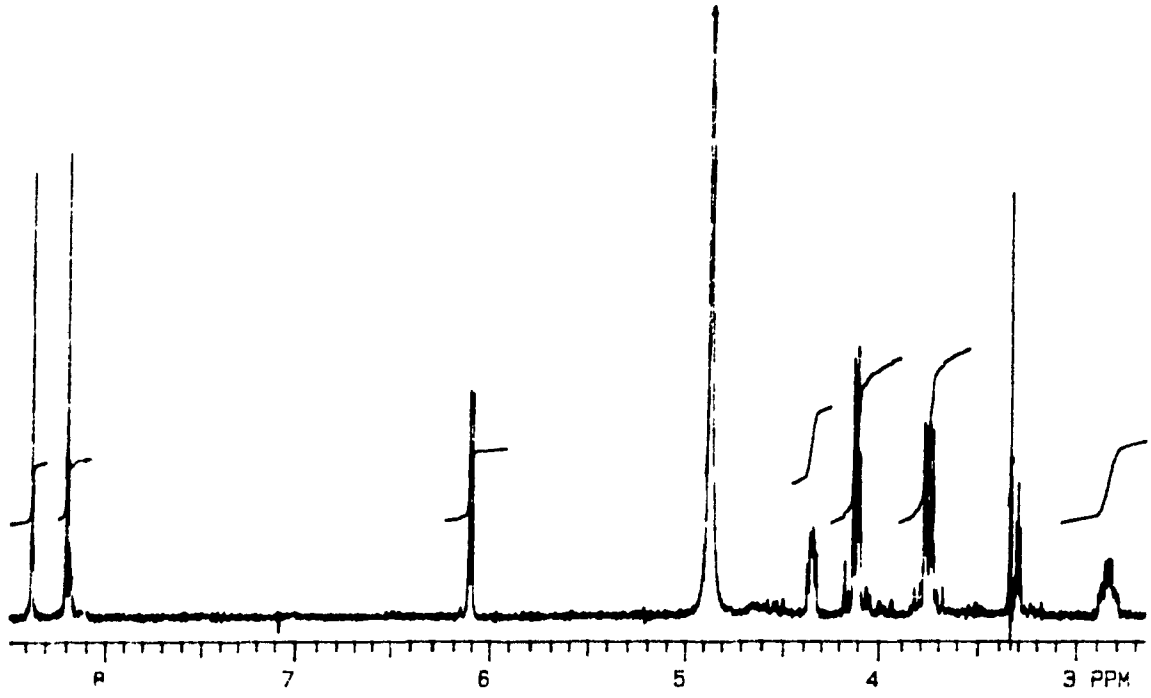
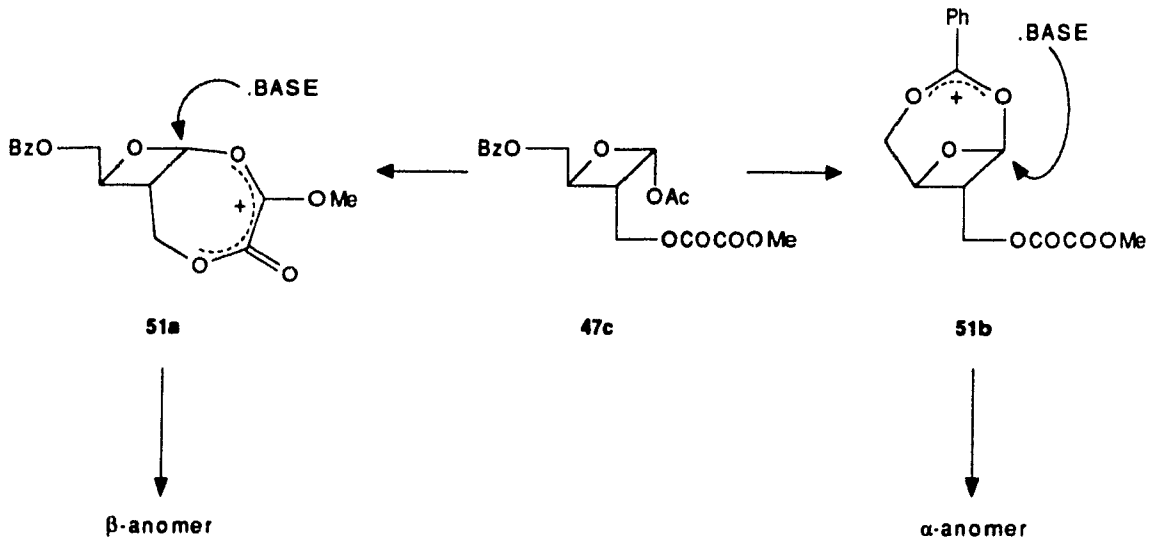


Figure 22. The 200 MHz ^{1}H-NMR of epioxetanocin 1α in CD_3OD.

2.6d Synthesis of Silyl Oxetanes (54) and (56).

We now turned our attention to obtaining oxetanocin in anomerically pure form. Since the α-anomer is formed via a favourable seven-membered intermediate **51b**, as shown below, we wanted to design an oxetanose in which it was not possible to form this intermediate (or at least limit its ability to do so), and thus obtain only the β-anomer. After careful consideration, we decided to protect the hydroxy group in the photo-adduct as a *t*-butyldimethylsilyl ether.

Scheme 21

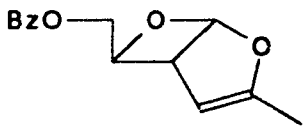


Unfortunately, irradiation of a benzene solution of 2-methylfuran and *t*-butyldimethylsilyloxyacetaldehyde did not give the desired photo-adduct. Hence, we had to obtain **53** in an indirect manner. Hydrolysis of photo-adduct **44a** with sodium hydroxide in methanol / water resulted in decomposition of the starting material. Similar results were obtained when the hydrolysis was tried using sodium methoxide in methanol. However, when **44a** was subjected to the action of lithium aluminum hydride in ether, alcohol **52** was obtained in 60% yield after flash chromatography. Silylation (TBDMSiCl / imidazole / DMF) of **52** gave photo-adduct **53** in 27% yield. In a one-pot reaction, **53** was transformed to diacetate **54** in 19% yield by a procedure similar to that used for syntheses of compounds **47**. Reaction of **54** with *bis*-(trimethylsilyl)-N^6-benzoyladenine catalyzed by tin tetrachloride gave a complex mixture which did not contain the desired product. However, two coupled products were isolated. Their structures could not be determined with any degree of certainty since purification by chromatographic methods was not possible, although we suspect that the oxetane underwent ring expansion before coupling. We felt that replacing the TBDMSi group with the more stable *t*-butyldiphenylsilyl group would circumvent this problem.

Reaction of **52** with *t*-butyldiphenylsilyl chloride[75] and imidazole in N,N-dimethylformamide gave **55** in 62% yield. Photo-adduct **55** was transformed to oxetanes **56a-c** in 18% yield by the same procedure that was used for the synthesis of oxetane **54**. All attempts to couple oxetanes **56** with *bis*-(trimethylsilyl)-N^6-benzoyladenine under Lewis acid catalysis gave very complex mixtures. No materials were isolated which contained benzoyladenine connected to an oxetane ring. The coupled products that were isolated in very low yields could not be identified with any degree of certainty due to difficulty of separation and instability of the compounds, but, as in the case with oxetane **54**, we suspect that ring expansion was taking place before coupling.

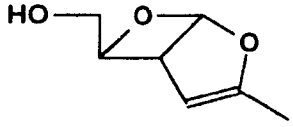
[75] Hanessian, S; Lavallée, P., *Can. J. Chem.*, **53**, 2975 (1975).

Scheme 22



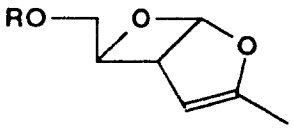
44a

$LiAlH_4$ | Et_2O

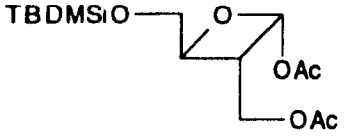


52

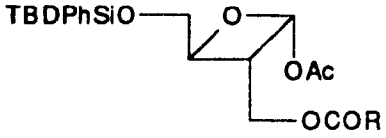
imidazole | RCl, DMF



53, R=TBDMSi
55, R=TBDPhSi



54



56a, $R=CH_3$
56b, R=Ph
56c, $R=COOCH_3$

2.6e Attempted Synthesis of Oxetanes with 4'-Non-Participating Groups.

Due to the difficulties encountered with the silyl protecting groups, we decided to use a benzyl group. It was hoped that this group would be robust enough to withstand Lewis acid catalysis and would not participate in the coupling reaction so as not to favour the α-anomer. Dimethallyl alcohol was quantitatively converted to the benzyl ether **57** by standard means (Bu_4NI / NaH / BnBr / THF). Ozonolysis in methylene chloride saturated with nitrogen at -78°C, followed by reduction with dimethyl sulfide, gave aldehyde **58** in 95% yield. Irradiation of **58** with 2-methylfuran in benzene did not give photo-adducts **59**, but surprisingly, photo-adducts **60a** and **60b** were isolated in 27% yield as a mixture of regioisomers in a ratio of 3:4.

Scheme 23

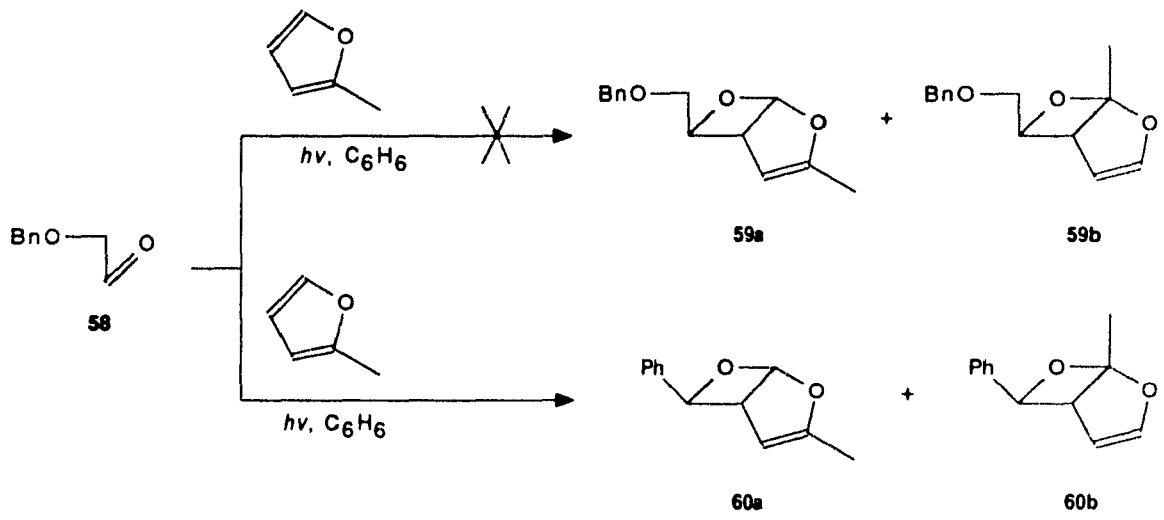


Photo-adducts **60a** and **60b** are formed by the photoreaction of benzaldehyde and 2-methylfuran. The benzaldehyde is formed by a Norrish Type II rearrangement[76] as shown below in Scheme 23. Although these types of rearrangements are not uncommon, it was surprising that rearrangement of the aldehyde took place so rapidly so as to exclude formation of the desired photo-adducts **59** entirely[77].

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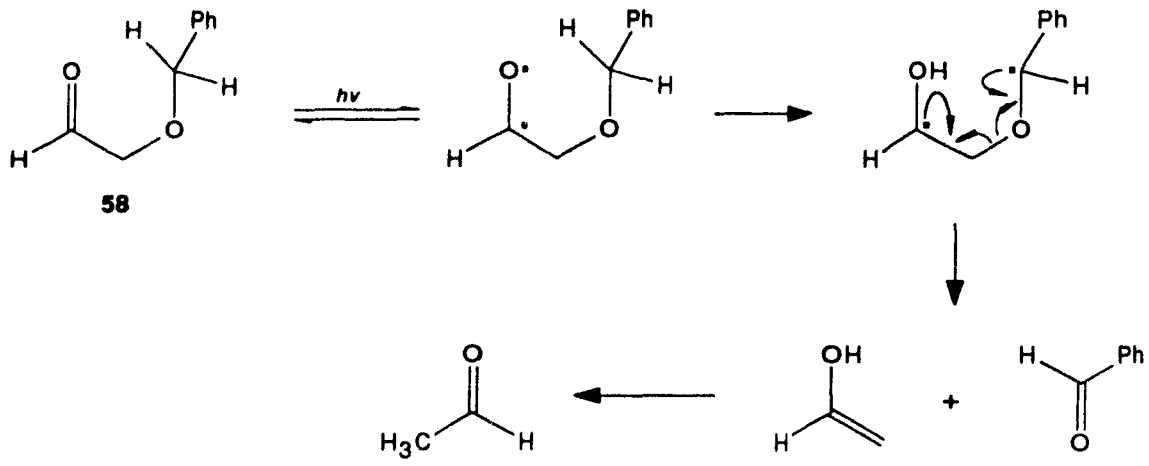
76 Norrish, R. G. W., *Trans. Farraday Soc.*, **33**, 1521 (1939).

77 No photoreaction takes place between 2-methylfuran and acetaldehyde due to the volatility of the aldehyde.

Scheme 24



Since we were unable to obtain **59a** by photochemical means, we attempted to synthesize it by an indirect route. Benzylation of photo-adduct alcohol **52** by standard methods did not give the desired product and only decomposition of starting material occurred. Unfortunately, when a milder method (BnOH / DEAD / PPh_3 / THF) was employed, the desired product was also not obtained. We attribute failure to the instability of alcohol **52**.

Being unable to synthesize **59a**, we decided to substitute the benzyl group with the *p*-anisyl protecting group[78]. Unfortunately, all attempts to form the *p*-anisyl ether of alcohol **52** failed. Hence, we attempted to form **65** via the photochemical route. Dimethallyl alcohol was protected as its *p*-anisyl ether **61** by standard methods (*p*-MeO-C_6H_4-OH / DEAD / PPh_3 / THF) in 97% yield. However, we were unable to generate the aldehyde **62** in pure form by ozonolysis due to oxidation of the phenyl ring, and since purification by distillation or flash chromatography was not possible, a new approach had to be found. Protection of glycerol acetonide as its *p*-anisyl ether **63** proceeded in 88% yield. Reaction of **63** with acetic acid and water gave diol **64** in 77% yield. Cleavage of the diol with sodium *meta*-periodate in water / methanol gave the desired aldehyde **62** in quantitative yield. Unfortunately, irradiation of a benzene solution of aldehyde **62** and 2-methylfuran did not give any photoproducts and only starting material was recovered. Hence, this approach was abandoned.

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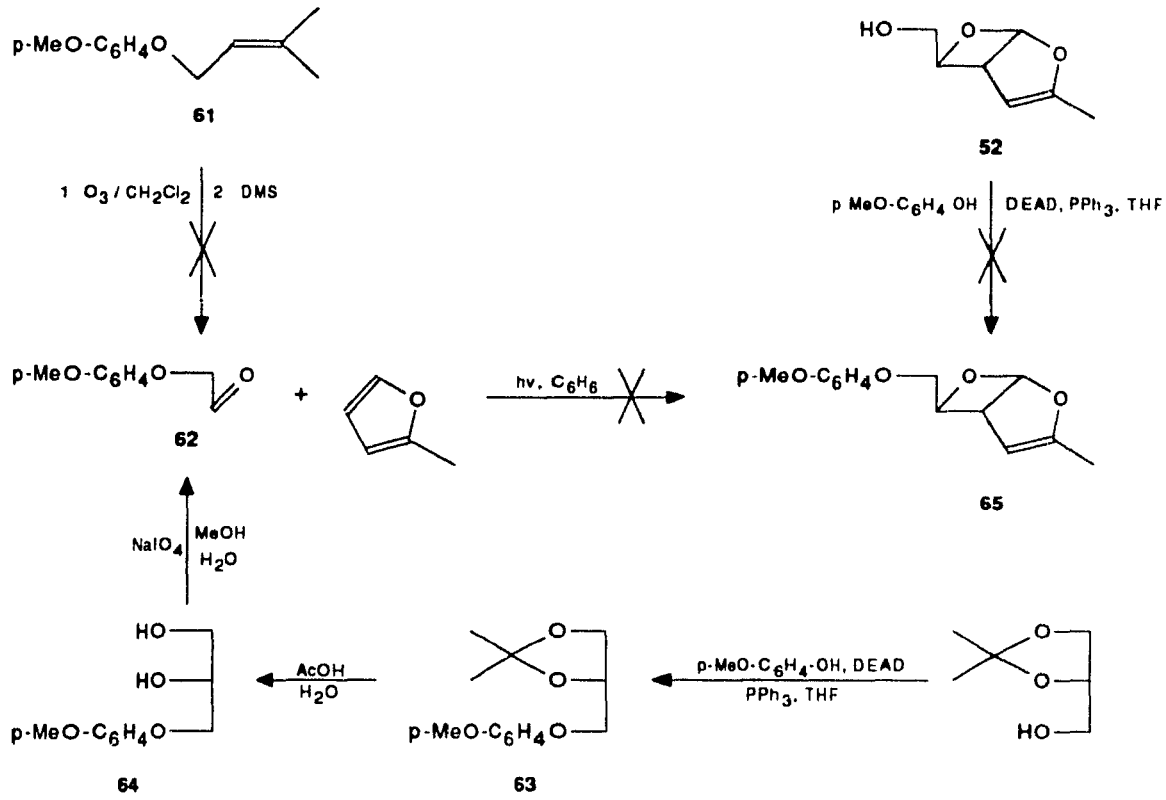
[78] Fukuyama, T.; Laird, A. A.; Hotchkiss, L. M., *Tetrahedron Lett.*, **26**, 6291 (1985).

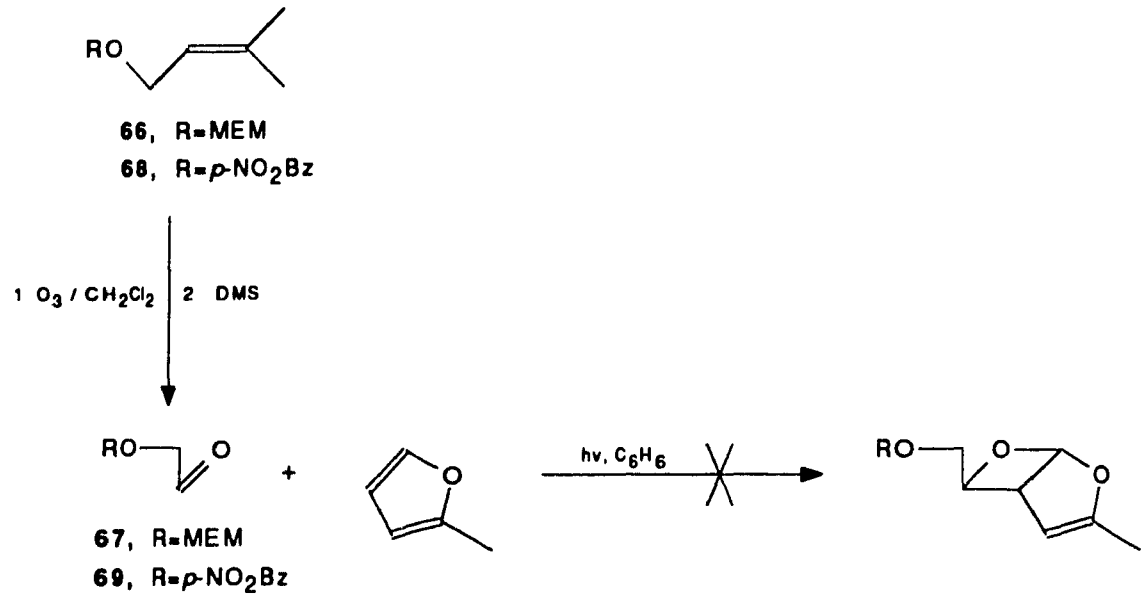
Scheme 25



We then attempted to synthesize a photo-adduct with a methoxyethoxymethyl (MEM) protecting group. However, all attempts to protect the alcohol function of **52** as a MEM ether failed. Therefore, the photochemical route to the MEM photo-adduct was investigated. Dimethallyl alcohol was transformed to its MEM ether **66** by standard methods[79] (NaH / MEM-Cl / THF) in 83% yield. Ozonolysis in methylene chloride (saturated with nitrogen) at -78°C, followed by reduction with dimethyl sulfide, gave aldehyde **67** in only 27% yield. It was very difficult to obtain pure aldehyde due to its inherent instability Irradiation of **67** with 2-methylfuran in benzene did not give the desired photo-adduct and only decomposed starting materials were recovered. It is not surprising that the reaction failed considering the instability of the aldehyde We also attempted to synthesize a photo-adduct with a *p*-nitrobenzoyl protecting group via the photochemical route. Unfortunately, irradiation of a benzene solution of *p*-nitrobenzoyloxyacetaldehyde **69**, obtained from ozonolysis of the *p*-nitrobenzoate ester of dimethallyl alcohol **68**, and 2-methylfuran did not give any photo-products, and only starting material was recovered

[79] Corey, E. J.; Gras, J. L.; Ulrich, P., *Tetrahedron Lett.*, 809 (1976).

Scheme 26



2.6f Synthesis of Oxetanes (75).

Since we were unable to synthesize a photo-adduct with a robust non-participating group on what would become the 4' position in the oxetane, we then decided to substitute the benzoyl protecting group with a propionyl group since Yamamura[15] had reasonable success with this protecting group[80]. Irradiation of a benzene solution of propionyloxyacetaldehyde **71**, obtained by ozonolysis of 1-*O*-propionyl-3-methyl-2-buten-1-ol **70**, with 2-methylfuran gave, after column chromatography, **72a** in 23% yield[81]. Ozonolysis of **72a**, followed by dimethyl sulfide gave aldehyde **73** in 92% yield. Reduction with sodium borohydride on alumina gave alcohol **74** in 68% yield. This alcohol could now be protected in many different ways in order to determine which participating group would give the best yield of oxetanocin. We hoped that we could achieve a practical anomeric control of the coupling reaction since separation of anomers by chromatographic means requires conversion to their tetrabenzoate derivatives before chromatographic separation is possible (see section 2.6c). This results in a lengthy synthesis with a low overall yield.

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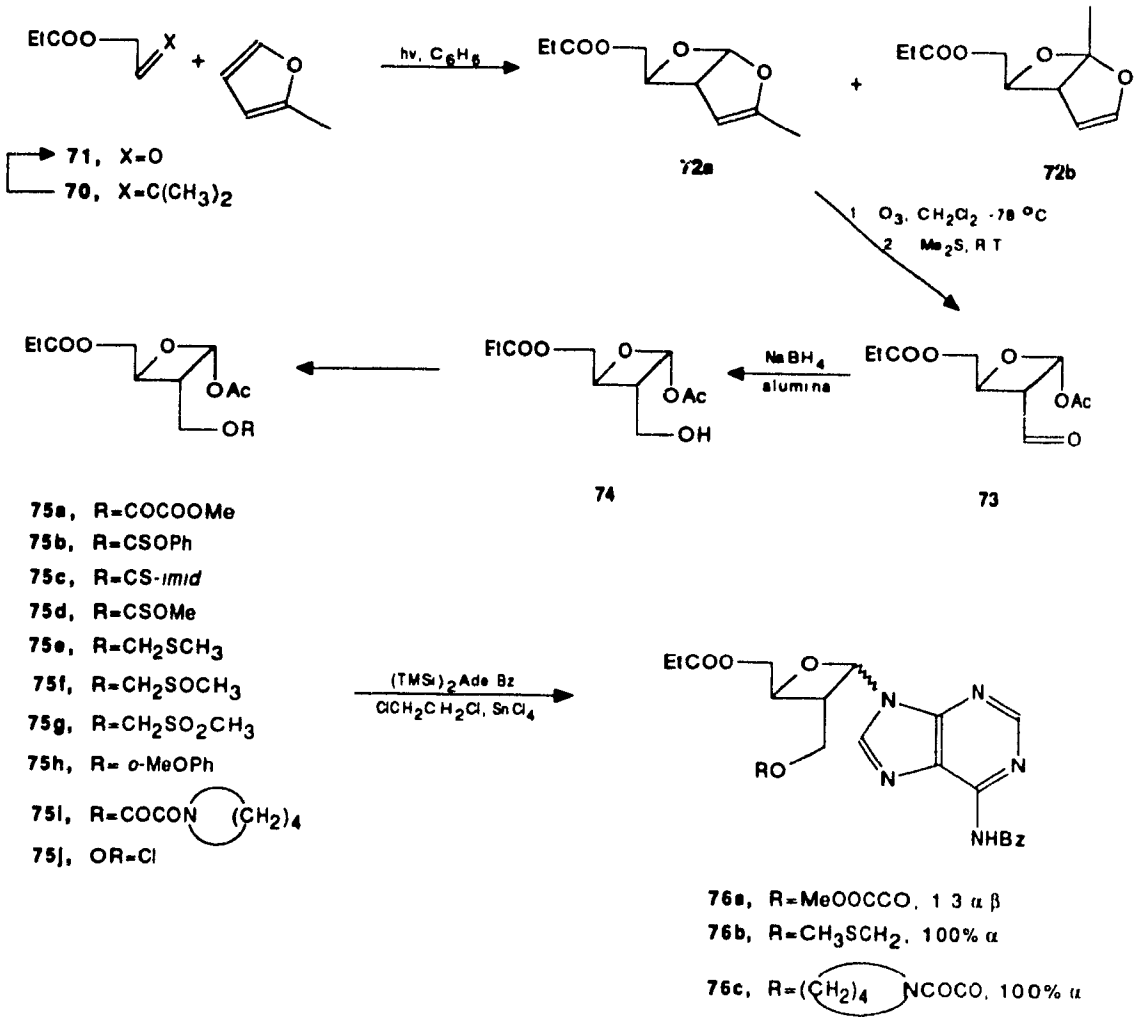
[80] We had considered using an acetate protecting group. However, due to our earlier difficulties with this group (see section 2.7b), we opted for the more stable propionyl protecting group. We also felt that there would be practically no difference in reactivity between the two groups, except for increased stability with the propionyl, since they are very similar in nature.

[81] The irradiation of aldehyde **71** and 2-methylfuran gave adducts **72a** and **72b** in a ratio of 16:11 in 33% combined yield. The less stable isomer could be isolated as a mixture of the two isomers simply by basifying the chromatography solvent with 0.5% triethylamine. Lowering the triethylamine content to 0.1% effectively destroys the minor isomer without significant destruction of the more stable (and desired) isomer.

Scheme 27



Esterification of hydroxy compound **74** with methyl oxalyl chloride gave **75a** in 45% yield. Coupling of **75a** with *bis*-(trimethylsilyl)-N^6-benzoyladenine in 1,2-chloroethane catalyzed by tin tetrachloride proceeded as described by Yamamura[15] and gave protected oxetanocin and epioxetanocin as a 3:1 mixture of inseparable anomers. Use of trimethylsilyl triflate as the Lewis acid catalyst resulted in decomposition of **75a**. Although this was an improvement over previous schemes, the β:α ratio was still not large enough (we were aiming for at least 10:1) for a practical synthesis of oxetanocin[82]. Therefore, other participating groups were investigated. It was hoped that these changes would strongly favour participation of the 3' group over the 4' group, thus reducing the amount of α-anomer formed.

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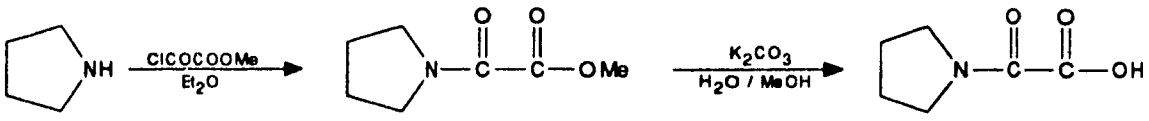
82 It is not possible to separate the two anomers chromatographically without first forming their tetrabenzoate derivatives.

We first investigated the use of thiocarbonyl participating groups since the C=S bond length is greater than the C=O bond length, thus aiding formation of the intermediate that leads to β attack. Compounds **75b** and **c** were formed from acylation of the alcohol function of **74** (**75b**: PhOCSCl, py, DMAP; **75c**: $(imid)_2CS$, pyridine). Compound **75d** was obtained from **75c** in 35% yield simply by stirring the latter in methanol at R.T.. Unfortunately, all of these new oxetanes failed to couple with *bis*-(trimethylsilyl)-N^6-benzoyladenine under Lewis acid catalysis. This was probably due to the relative instability of all of these sugars, which lead to decomposition before coupling with the base could occur.

We next investigated the use of the thio-MOM (and derivatives thereof) protecting group. Alcohol **74** was converted to its thio-MOM ether **75e** in 20% yield by the method of Pojer[83]. Upon reaction with *bis*-(trimethylsilyl)-N^6-benzoyladenine and tin tetrachloride in 1,2-dichloroethane, only the α-anomer **76b** was formed in 72% yield The use of trimethylsilyl triflate also resulted in formation of the α-anomer, but in a much lower yield. Having gone completely in the wrong direction, **75e** was converted to sulfoxide **75f** and sulfone **75g** by oxidation with sodium *m*-periodate in methanol / water in 76 and 72% yield, respectively[84,85]. These sugars however, were too stable and did not couple with *bis*-(trimethylsilyl)-N^6-benzoyladenine. When forcing conditions were used, slow decomposition of the sugars occurred.

Due to the lack of success with thio participating groups, we decided to synthesize **75h** via a Mitsunobu coupling of guaicol and alcohol **74**. This proceeded smoothly in 33% yield. Unfortunately, all attempts to obtain any products containing adenine attached to an oxetane ring failed. Since we felt that we needed a participating group that possessed stronger electron donating characteristics than the methyl oxalyl group, it was decided to synthesize an oxamide protected oxetane.

Scheme 28



77 **78**

Hence, methyl oxalyl chloride was reacted with pyrrolidine in ether to give **77** in 95% yield. Hydrolysis of **77** with potassium hydroxide in water / methanol resulted in recovery of only pyrrolidine hydrochloride[86]. Evidently, a dihydrolysis had occurred and thus, milder conditions would have to be

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83 Pojer, P. M ; Angyal, S. J , *Tetrahedron Lett.*, **17**, 3067 (1976).
84 Ichikawa, Y.; Kubota, H., Fujita, K.; Okauchi, T.; Narasaka, K., *Bull. Chem. Soc. Jpn.*, **62**, 845 (1989).
85 Okauchi, T.; Kubota, H.; Narasaka, K., *Chem. Lett.*, 801 (1989).
86 When pyrolidine hydrochloride was accidently reacted with **74** under Mitsonobu conditions, **75j** (OR=Cl) was formed in 48% yield.

employed. When the hydrolysis was attempted with potassium carbonate in methanol / water, only acid **78** was isolated, in virtually quantitative yield. A Mitsonobu coupling of **78** and alcohol **74** gave oxetane **75i** in 26% yield. Surprisingly, reaction of **75i** with *bis*-(trimethylsilyl)-N^6-benzoyladenine and tin tetrachloride in 1,2-dichloroethane gave only the α-anomer which decomposed when subjected to flash chromatography. The structure of **76c** was confirmed by deblocking (Na / MeOH) to obtain epioxetanocin **1α**.

2.6g Synthesis of Oxetane (84).

Due to our lack of success in converting **75** to oxetanocin, we investigated the possibility of synthesizing oxetanes with a halogen at the 2-position. It was thought that acetates **75** could be converted to chlorides by methods analogous to those developed for furanoses and hexoses. This approach, however, was not pursued since Fleet et *al*[9] published a synthesis of oxetanocin using these types of chloro-oxetanes at the time when we were developing our strategy. We were fortunate that this work was brought to light at this time since Fleet was not able to convert his chloro-oxetanes to oxetanocin exclusively. It was obtained as a 1:1 mixture of α and β, which had to be separated chromatographically.

We were now convinced that no matter what participating group we put on the 3'-position of the oxetanes **75**, we would always obtain some α-anomer in the coupling reaction as long as we had a group on the 4'-position that could form a seven-membered ring intermediate. To circumvent the formation of this intermediate, we decided to synthesize photo-adduct **81**. The new protecting group on the 4-position can only form a six-membered ring intermediate, thereby hindering α-anomer formation and thus favoring the formation of the intermediate which leads to the β-anomer. Originally, isopropyl glyoxalate **80** was obtained from the ozonolysis of di-*iso*-propyl fumarate **79**[87]. However, we found that it was simpler to prepare aldehyde **80** via a periodic acid cleavage of commercially available di-*iso*-propyl *l*-tartrate[88]. Irradiation of a benzene solution of isopropyl glyoxalate **80** and 2-methylfuran gave, after flash chromatography, photo-adduct **81** in 17% yield[89]. Adduct **81** was then transformed to oxetane **84** by the previously described method in 40% yield. However, all efforts to couple **84** with *bis*-(trimethylsilyl)-N^6-benzoyladenine under Lewis acid catalysis failed. If mild conditions were employed, no reaction would take place. Using more vigorous conditions simply resulted in decomposition of the starting material.

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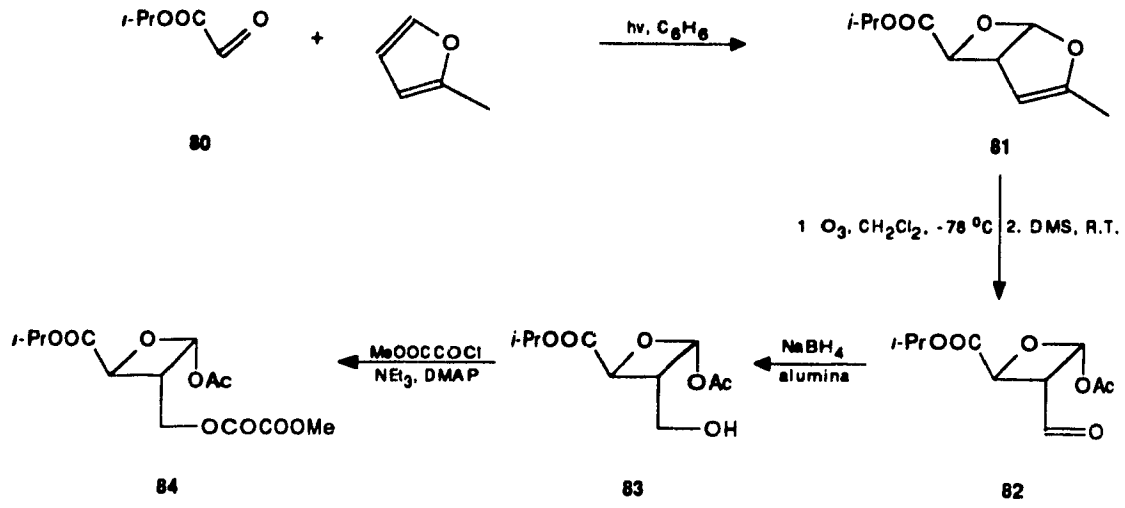
[87] Di-*iso*-propyl fumarate **79** was obtained from fumaric acid by esterification with *iso*-propyl alcohol.

[88] Kelly, T. R.; Schmidt, T. E.; Haggerty, J. G., *Synthesis*, 544 (1972)

[89] The isomer with the methyl group bonded to the acetal carbon was obtained in less than a 1:20 ratio with respect to the vinyl substituted isomer as determined by integration of 200 MHz proton NMR signals.

Scheme 29


i-PrOOC
O
+
O
hv, C6H6
i-PrOOC
O
O
80
81
1 O3, CH2Cl2, -78 °C 2. DMS, R.T.
i-PrOOC
O
OAc
OCOCOOMe
MeOOCCOCl
NEt3, DMAP
i-PrOOC
O
OAc
OH
NaBH4
alumina
i-PrOOC
O
OAc
O
84
83
82

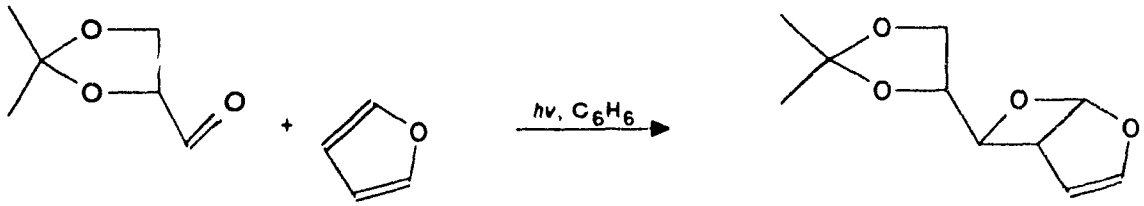
2.7 Synthesis of Enantiomerically Enriched Photo-Adducts and Oxetanes.

2.7a The "Chiral Aldehyde" Approach; Synthesis of (85).

In parallel to our synthesis of racemic oxetanocin and derivatives thereof, we also pursued a program of synthesizing chiral intermediates that could be used in our oxetanocin synthesis. Since separation of Mosher acid derivatives is often impractical for larger scale syntheses due to its cost and the necessity of tedious chromatographic separations, we investigated approaches that would eliminate at least one of these obstacles. We also decided that chromatographic separation of the two enantiomers would only be acceptable if it occurred early on in the synthesis. This would enable us to carry out further research with the "wrong" enantiomer so that the undesired enantiomer could be put to some use.

Our first approach involved the [2+2] photoaddition of a chiral aldehyde to a furan. Although Schreiber has recently shown that the furan-carbonyl photocycloaddition proceeds without diastereoface selectivity in relation to the chiral aldehyde, he did demonstrate that photo-products of the reaction of R-glyceraldehyde acetal and 3,4-dimethylfuran can be separated chromatographically[44]. Therefore we decided to synthesize photo-adduct **85** from R-glyceraldehyde acetal and furan, since it was felt that this bicyclic compound would be a good starting point for our synthesis of oxetanocin. The substituent on the C-6 position could be easily transformed into an alcohol by removal of the acetonide followed by sodium periodate / sodium borohydride cleavage to the alcohol, which could then be protected by a suitable group. Irradiation of a benzene solution of furan and R-glyceraldehyde acetal[90] gave photo-adduct **85** in 25% yield as a 1.1 mixture of diastereomers. Unfortunately, separation by flash chromatography proved to be impossible and this approach was abandoned.

Scheme 30



85

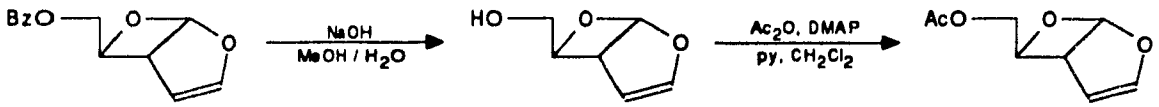
90 Baer, E.; Fischer, H. O. L., *Helv. Chim. Acta*, **22**, 463 (1939).

2.7b Enzymic Resolution of Photo-Adducts (2d) and (87).

Over the past decade, the use of enzymes in synthetic organic chemistry has increased dramatically. Enzyme-catalyzed syntheses are among the best methods for the preparation of enantiomerically pure compounds and in the last few years, methods have even been developed for using enzymes in organic solvents[91]. We felt that our photo-adduct **2d** would be a suitable candidate for enzymatic resolution since selective hydrolysis of the ester would enable us to chromatographically separate the alcohol and unreacted ester. It did not matter which enantiomer was hydrolyzed since the alcohol could be reconverted to its ester quite easily. However, we did have some concern using **2d** since practically all enzyme hydrolysis are carried out on acetates. Therefore, it was decided to synthesize photo-adduct **87**.

Ozonolysis of allyl acetate, followed by reduction with dimethyl sulfide, gave acetoxyacetaldehyde **86** in 38% yield. Irradiation of **86** with furan provided photo-adduct **87**. Unfortunately, the reaction proceeded in very low yield and a great deal of decomposition took place during the reaction which made this an impractical route to **87**. Hence, an alternate route to adduct **87** had to be found. Hydrolysis of photo-adduct **2d** with sodium hydroxide in methanol / water gave alcohol **88** in 79% yield. Acetylation of the alcohol by standard methods (Ac_2O, py, DMAP) gave **87** in 72% yield.

Scheme 31



2d **88** **87**

With acetate **87** in hand, we were now ready to proceed with our enzymatic resolution. We decided to carry out our hydrolysis with porcine pancreatic lipase (PPL) since its use in these types of reactions is well documented[92,93] and has been shown to give high *ee*'s. It was hoped that the enzyme would only hydrolyze one enantiomer and thus, the hydrolysis experiment was designed to stop when 50% conversion was obtained. Unfortunately, hydrolysis of **87** with PPL resulted in total decomposition of the starting material. We felt that this decomposition was due to the inherent instability of photo-adduct **87** and not because the enzyme was unsuitable for the reaction. Hence, it was decided to carry out

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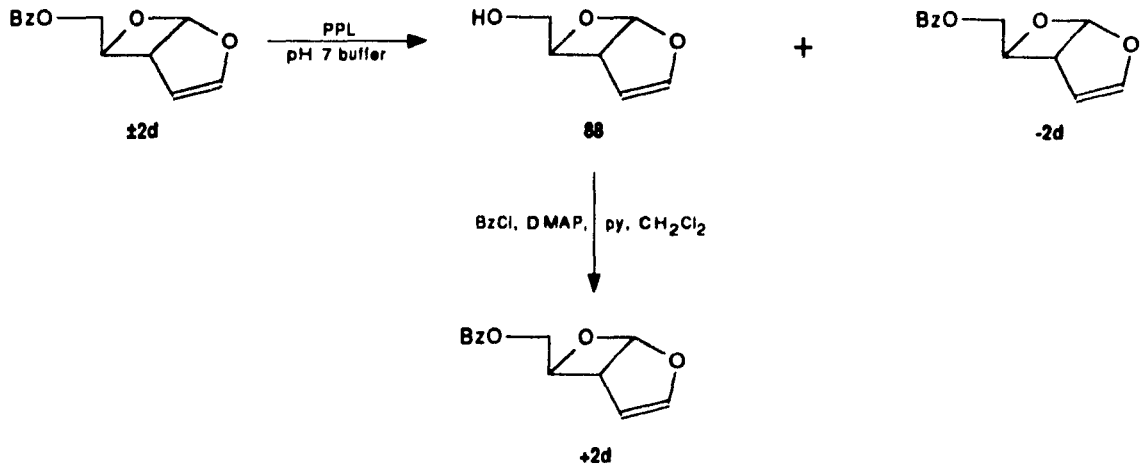
[91] Klibanov, A. M., *Acc. Chem. Res.*, **23**, 114 (1990) and references therein.
[92] Kasel, W.; Hultin, P. G.; Jones, J. B., *J. Chem. Soc., Chem. Commun.*, 1563 (1985).
[93] Hemmerle, H.; Gais, H. J., *Tetrahedron Lett.*, **28**, 3471 (1987).

the hydrolysis with photo-adduct **2d**. Using the same conditions as for acetate **87**, we managed to isolate both unreacted photo-adduct **-2d** (46% yield) and alcohol **88** (42% yield), after flash chromatography. Benzoylation of **88** via standard methods gave **+2d** in 45% yield. We then measured the rotations of both the benzoyl photo-adducts **2d** obtained from the enzyme hydrolysis and found that they were opposite {**-2d:** $[\alpha]^{20}_D$ = -15.5° (c = 3.21, CH_2Cl_2) vs **+2d:** $[\alpha]^{20}_D$ = +18.8° (c = 1.25, CH_2Cl_2)}. These numbers proved that we were indeed getting enantiomeric enrichment.

Scheme 32



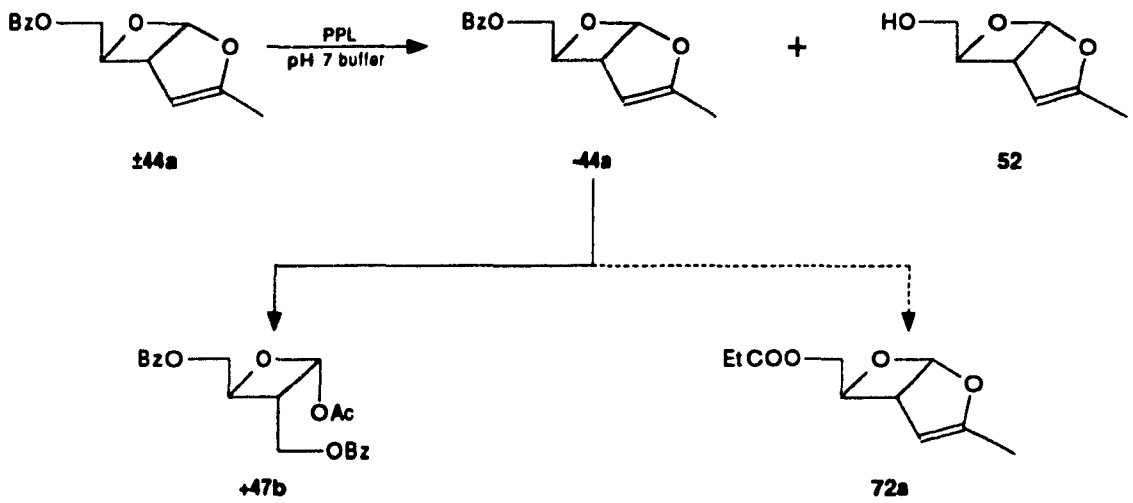
We did not attempt to establish the enantiomeric purity of resolved **2d** by Mosher ester or by the use of ^{1}H-NMR shift reagents since this project was not the main thrust of our research anymore and we were now concentrating on the use of photo-adducts **44a** and **72a** in our approach to the synthesis of oxetanocin.

2.7c Enzymic Resolution of Photo-Adducts (44a) and (72a).

As we had recently completed a total synthesis of (±)-oxetanocin[29] starting from photo-adduct **72a**, we were now interested in synthesizing optically pure oxetanocin. Using the precedent that we established in resolving photo-adduct **2d**, we decided to hydrolyze photo-adduct **72a** with PPL. Unfortunately, no identifiable products could be isolated from the reaction mixture and the chart measuring the progress of the reaction indicated that there was no selectivity for one enantiomer. Since we had earlier converted photo-adduct **44a** to photo-adduct **72a**, we decided to hydrolyze **44a** and convert the resultant alcohol or unreacted benzoate to enantiomerically pure **72a**. Using the same conditions as for photo-adduct **72a**, we managed to obtain both unreacted **44a** and alcohol **52** (as indicated on tlc). Not surprisingly, we were unable to isolate the alcohol due to its instability. However,

unreacted photo-adduct **44a** was isolated by flash chromatography in 36% yield. We then measured the rotation of recovered **44a** {$[\alpha]^{20}_D$ = -7.5° (c = 2.22, CH_2Cl_2)} and found that we were obtaining enantiomeric enrichment. Conversion of **-44a** to oxetane **47b** proceeded smoothly as described in section 2.6c. The rotation of **47b** was determined to be {$[\alpha]^{20}_D$ = +6.4° (c = 2.51, CH_2Cl_2)}. Enantiomerically pure **47b** that is the precursor[14] for epioxetanocin has $[\alpha]^{20}_D$ = +41.8°. This meant that our oxetane **+47b** had an *ee* of 15.3%.

Scheme 33



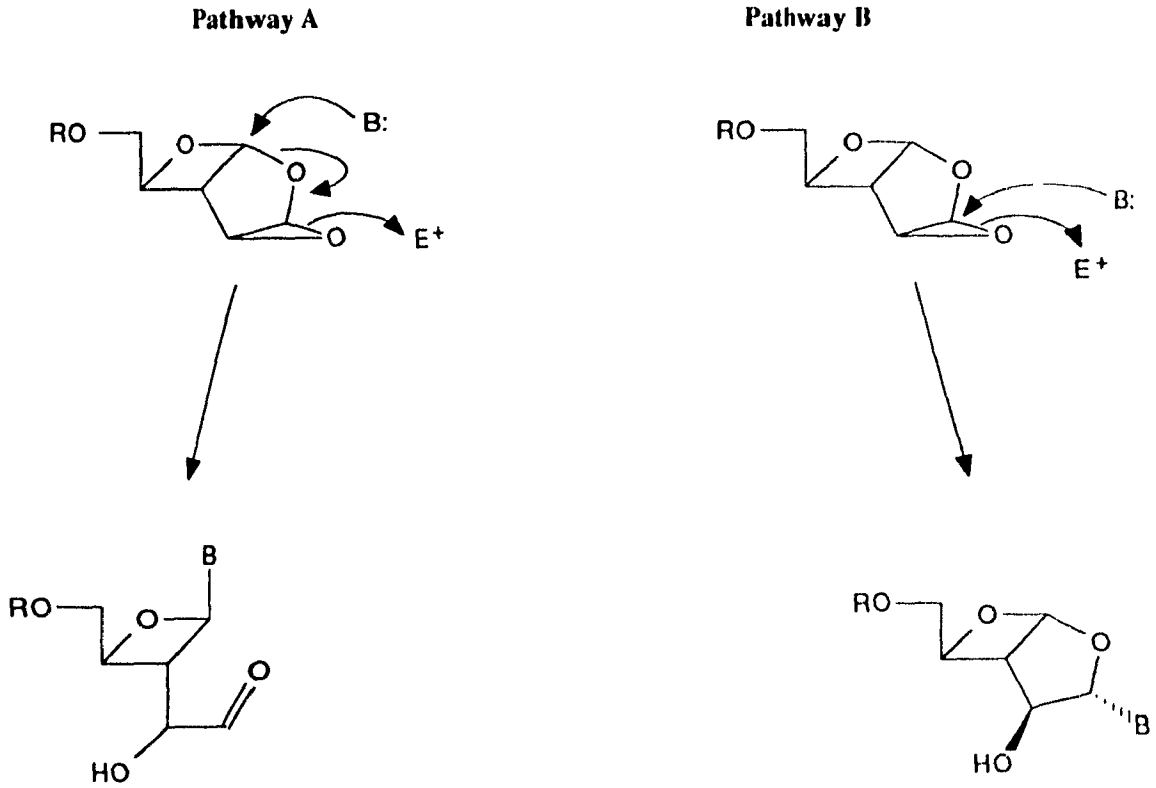
2.7d Future Considerations.

We established that racemic photo-adduct **2d** could be resolved into its two enantiomers quite easily and may only require investigation of other enzymes to determine which ones give the highest *ee*. On the other hand, resolution of photo-adducts **44a** and **72a** may require redesigning the hydrolysis experiment so as to eliminate the aqueous conditions which seem to cause decomposition of the photo-adduct alcohol **52**. Other enzymes should also be investigated since PPL did not give a very high *ee*.

2.8 Synthesis of Bicyclic Nucleosides and Derivatives.

During the course of our investigations of suitably functionalized photo-adducts for coupling to nitrogenous bases, epoxides of the type **23** were synthesized, as previously described in section 2.5d. It was hoped that these epoxides would couple to the nitrogenous bases in the manner depicted in **Pathway A** of Scheme 34 to yield an oxetanocin like nucleoside. We also realized that there were two other competing routes possible. One would involve a Lewis acid catalyzed opening of the epoxide followed by attack of the nitrogenous base to yield bicyclic nucleosides (**Pathway B**), which could then be transformed into furanose nucleosides via the use of well established methods. The other possibility would simply be the Lewis acid catalyzed opening of the oxetane ring followed by addition of the base to give furanose nucleosides.

Scheme 34



2.8a Synthesis of Bicyclic Nucleosides (89a) and (89b).

Our initial efforts were carried out with model compounds **23a** and **23b**. Reaction of these epoxides with persilylated bases and Lewis acids (tin tetrachloride, trimethylsilyl acetate, trimethylsilyl trifluoromethanesulfonate) under various conditions gave very complex mixtures. No materials were isolated which contained nitrogenous bases connected to a sugar component. Similar results were obtained when epoxide **23d** was used. However, it was found that by using zinc chloride as the Lewis acid catalyst in a variation of the procedure described by Danishefsky[94], nucleosides **89a** and **89b** were obtained in 67 and 66% yield[95], respectively as shown in Scheme 35. It is interesting to note that the free hydroxyl group becomes silylated *in situ*, presumably by chlorotrimethylsilane generated by reaction of the silylated base with zinc chloride, and survives the work-up even when the reaction mixture is washed with 5% aqueous hydrochloric acid.

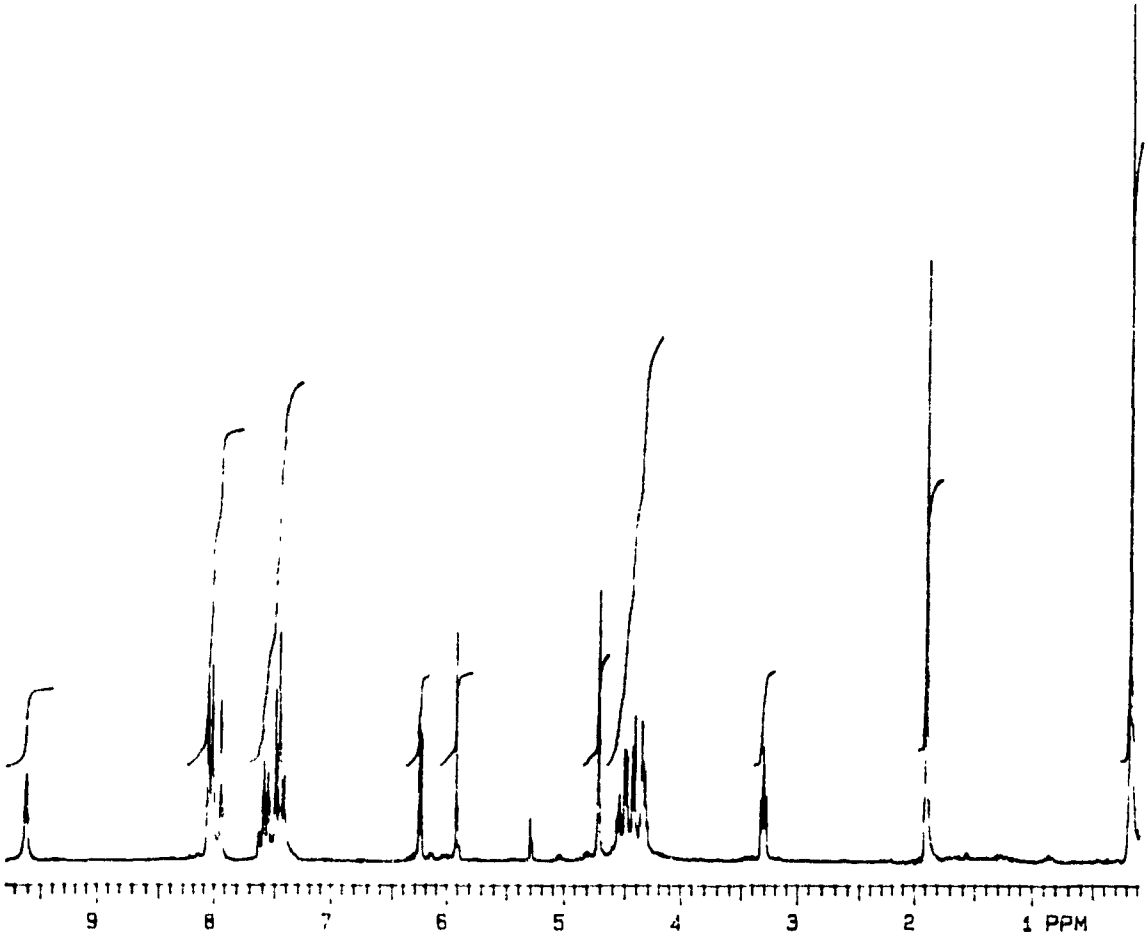


Figure 23. The 200 MHz ^{1}H-NMR of nucleoside **89a** in CD_2Cl_2.

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94 Chow, K., Danishefsky, S., *J. Org. Chem.*, **55**, 4211 (1990).

95 Upon flash chromatography over silica gel with methylene chloride / methanol, epoxide **23d** which had not coupled to the base was opened up by the methanol to give **24a'** (Ph=BzOCH$_2$) in 22% yield.

The configuration of nucleoside **89a**, and thus of **89b**, about H3' and H4' was confirmed by ^{1}H-NMR spectroscopy (Figure 23), which clearly showed couplings of ~ 0 Hz for $J_{H3',H4'}$. This indicates that the nitrogenous base and protected hydroxyl function are *trans* to one another with a torsional angle of ~ 90°. Had the two substituents been *cis*, a coupling between H3' and H4' would have been observed. The bicyclic structure was confirmed by a HETCOR carbon-hydrogen correlation (see Appendix IV) which showed that the ^{13}C signal at 110.45 ppm was coupled to the proton at 6.28 ppm, and the ^{13}C signal at 99.02 ppm was coupled to the proton at 5.94 ppm. This indicates that the nitrogenous base is connected to C3' since O-C-O carbons are always more deshielded than O-C-N carbons.

We also investigated this reaction with purine bases. However, attempts to carry out the coupling reaction with *bis*-(trimethylsilyl)-N^6-benzoyladenine and zinc chloride proved to be unsuccessful whether the silylated base was generated *in situ* using HMDS and chlorotrimethylsilane[18] or a stock solution of the silylated base in 1,2-dichloroethane was used. Further investigation of purine couplings to **23d** have not been carried out at this time.

Desilylation (Bu_4NF / THF) of nucleosides **89a** and **89b** proceeded smoothly giving excellent yields (95 and 93%, respectively) of the desilylated nucleosides **90a** and **90b**. Fully deprotected **90b** was obtained by aminolysis (NH_3 / MeOH), followed by recrystallization from methanol, in 58% yield. Nucleoside **91a** was obtained in a similar manner[96] in 65% yield, except that it was purified by flash chromatography prior to recrystallization from methanol. The X-ray crystallographic structure of **91a** (Figure 24) confirmed our NMR analyses, clearly showing the nitrogenous base *trans* to the adjacent hydroxy group. Details of the X-ray crystallographic study of nucleoside **91a** are shown in Appendix III.

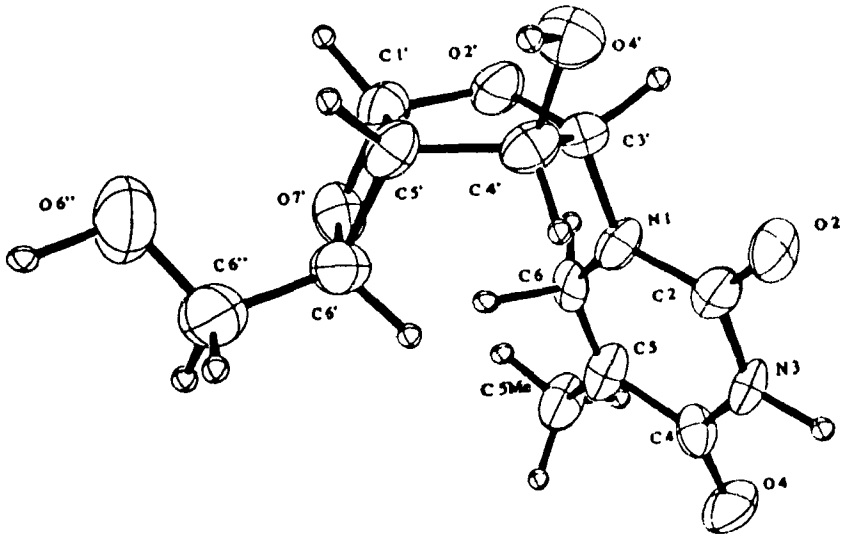
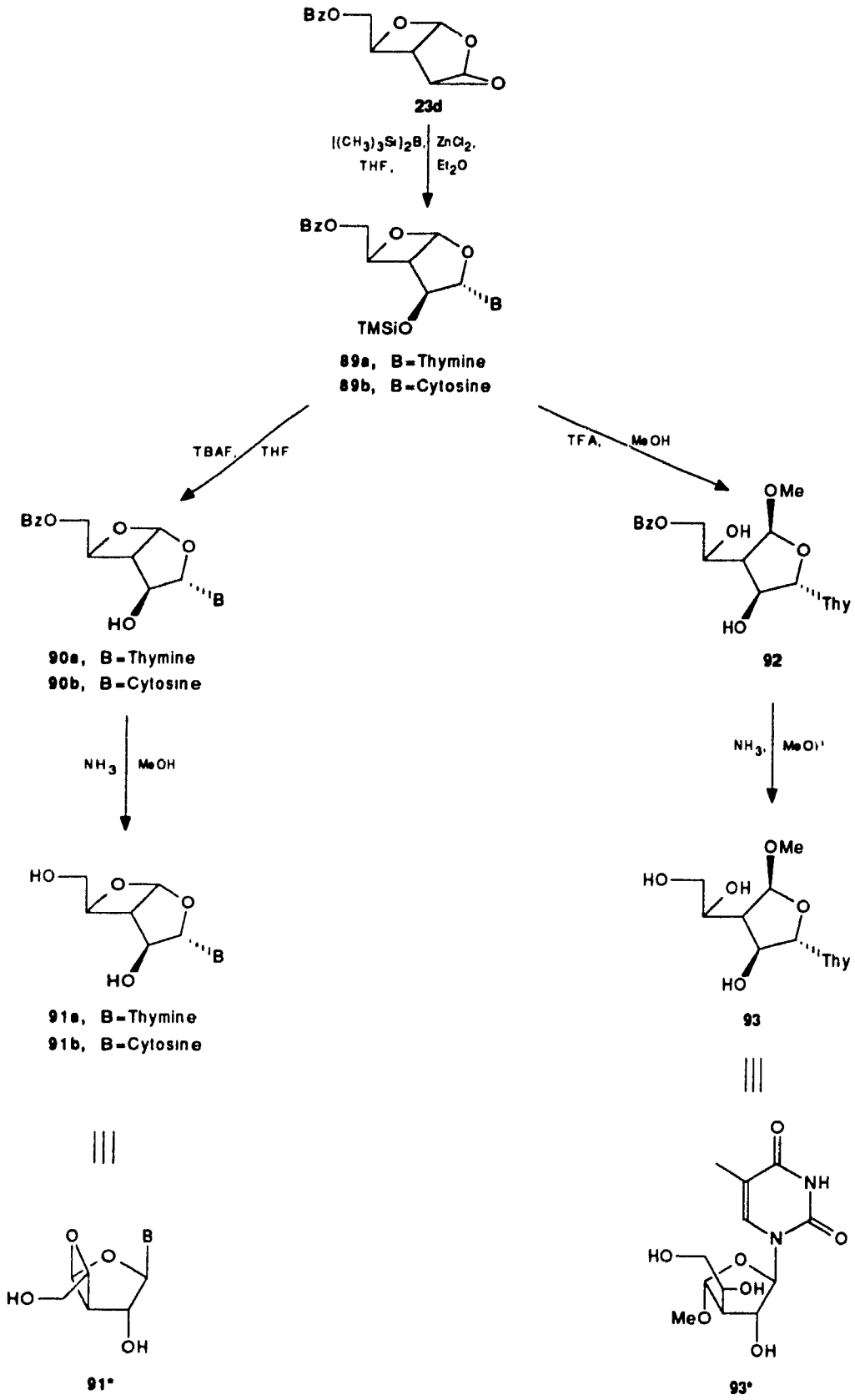


Figure 24. The X-ray crystallographic structure of nucleoside **91a**.

[96] Nucleosides **91*** are enantiomers of nucleosides **91**.

Scheme 35

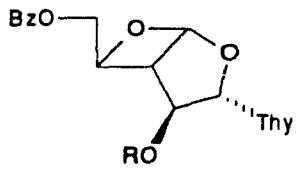

BzO
O
O
O
23d
[(CH3)3Si]2B, THF, ZnCl2, Et2O
TMSiO
B
89a, B=Thymine
89b, B=Cytosine
TBAF, THF
TFA, MeOH
HO
90a, B=Thymine
90b, B=Cytosine
OMe
OH
Thy
92
NH3, MeOH
91a, B=Thymine
91b, B=Cytosine
93
NH
N
Me
91*
93*

2.8b Synthesis of Furanoside (93).

We also felt that these novel bicyclic nucleosides could be transformed into interesting furanosides simply by opening the oxetane ring, and this is known to proceed stereospecifically in many cases. Reaction of **89a** with trifluoroacetic acid in methanol gave the ring opened nucleoside **92** in 89% yield. Debenzoylation in methanolic ammonia, followed by flash chromatography and recrystallization from acetone / hexanes gave the deprotected furanoside **93** in 86% yield[97]. All efforts to obtain crystals large enough for X-ray diffraction studies proved to be unsuccessful. Work on the synthesis of other derivatives of **93** may be undertaken in the future pending the outcome of biological evaluation currently underway.

2.8c Attempted Resolution of Enantiomers of Bicyclic Nucleoside (90a).

Since we were interested in eventually developing a method for the synthesis of enantiomerically pure **91**, a project involving the chiral derivatization of **90** was initiated. First, **90a** was acetylated by standard methods to give **94a** in 90% yield. This derivative was made so that we could have a simple model for the purpose of setting GC and HPLC condtions. Since our group is currently involved in developing a practical synthesis of enantiomerically pure α-methylvaleric acid, we decided to make the valerate ester of **90a**. Esterification proceeded smoothly giving **94b** in 95% yield Unfortunately, the 2 diastereomers were unseparable by TLC, GC and HPLC. Also, the ^{1}H-NMR exhibited no difference for the two diastereomers. We then decided to synthesize the Mosher ester derivative[98] (**94c**) of **90a**. It was obtained in 82% yield via standard methods. Again, we unable to separate the 2 diastereomers by chromatographic means. However, the ^{1}H-NMR indicated that the diastereomers existed in an approximately 1:1 ratio. Being unable to separate the isomers by derivatization, other methods (mainly enzymatic) of resolution will be investigated in the future if biological evaluation is promising.



94a, R=Ac
94b, R=$CH_3CH_2CH_2CH(CH_3)CO$
94c, R=$C_6H_5C(OCH_3)(CF_3)CO$

---

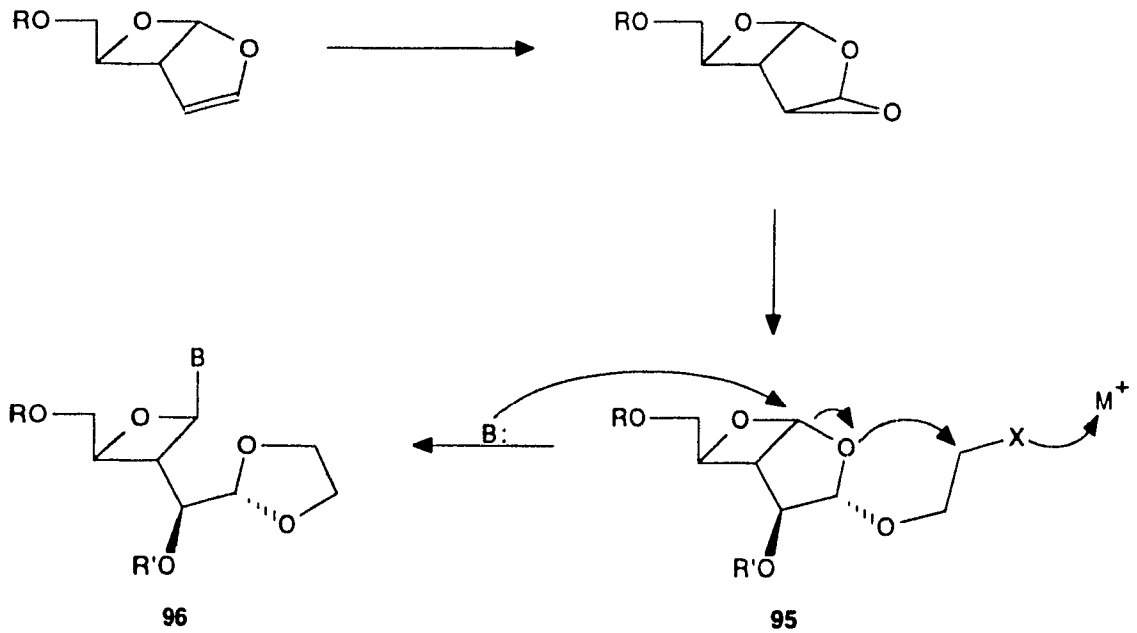
[97] Furanoside **93*** is the enantiomer of furanoside **93**.
[98] Dale, J. A.; Dull, D. L.; Mosher, H. S., *J. Org. Chem.*, **34**, 2543 (1969).

2.9 Direct Coupling of a Nitrogenous Base to a Modified Photo-adduct (via a Modified Fraser-Reid–Mootoo Approach).

2.9a Strategy.

Since all of our efforts to obtain anomerically pure oxetanocin did not succeed, a new strategy based on our modified Fraser-Reid-Mootoo method was designed. We felt that this approach would give us oxetanocin in anomerically pure form since attack from the α face is extremely hindered and attack at the C-3 position of the photo-adduct is extremely unlikely due to steric factors especially when considering that much smaller nucleophiles did not attack via this pathway (see section 2.5b). This approach had been tried earlier and had failed due to the incompatibility of IDCP with the nitrogenous bases. To circumvent this problem we decided to synthesize modified photo-adducts of the type **95** which contain halogens. It was thought that we could then couple persilylated bases to adducts of type **95** in the presence of silver salts to afford protected oxetanocin derivatives **96** as shown in Scheme 36. Nucleoside **96** could then be transformed to oxetanocin by deprotection of the aldehyde, followed by cleavage of the hydroxy aldehyde function with sodium periodate / sodium borohydride to afford the desired alcohol. Fully deprotected oxetanocin could then be obtained by removal of the 4' protecting group.

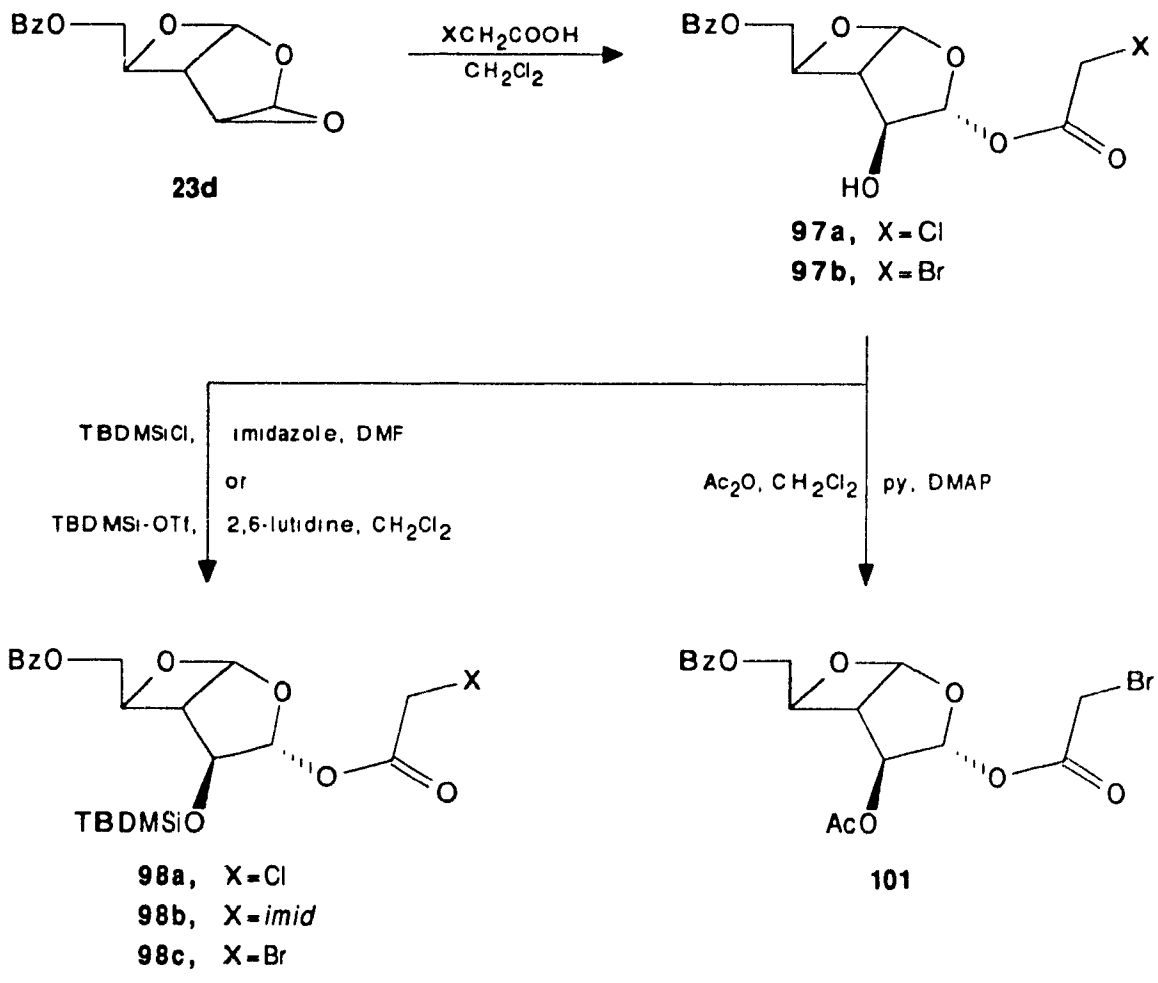
Scheme 36



2.9b Synthesis of Bicyclic Nucleosides (99).

Our first task was to construct a modified photo-adduct of the type **95**. Unfortunately, all attempts to open epoxide **23d** with 2-haloethanol were unsuccessful. However, when **23d** was treated with bromo or chloroacetic acid in methylene chloride, acetals **97a** and **97b** were obtained in 55 and 45% yield, respectively. Acetal **97a** was transformed to its *t*-butyldimethylsilyl ether **98a** in 41% yield by standard means (TBDMSiCl / imidazole / DMF). However, when the same conditions were used to silylate **97b**, adduct **98b** was obtained in 36% yield. When silylation was carried out using 2,6-lutidine / TBDMSi-OTf in methylene chloride[99], **98c** was obtained in 58% yield.

Scheme 37



23d

97a, X = Cl
97b, X = Br

98a, X = Cl
98b, X = *imid*
98c, X = Br

101

---

[99] Corey, E. J.; Cho, H ; Rücker, C.; Hua, D. H., *Tetrahedron Lett*, **22**, 3455 (1981).

We were now ready to couple the nitrogenous base to our modified photo-adducts **98**. Silver triflate was chosen as the metal salt that would trigger the reaction due to the high affinity of silver ion for halogens and because the triflate anion is an extremely poor nucleophile that would not interfere with the coupling reaction. Unfortunately, reaction of **98a** with *bis*-(trimethylsilyl)-N^6-benzoyladenine and silver triflate gave a very complex mixture. No materials were isolated which contained N^6-benzoyladenine connected to a sugar moiety. However, when **98c** was reacted with *bis*-(trimethylsilyl)-N^6-benzoyladenine and silver triflate under similar conditions, a product **99a** containing N^6-benzoyladenine connected to a sugar moiety was obtained. Its ^{1}H and ^{13}C-NMR was not consistent with nucleosides of the type **100**. Also, the instability of this compound made it difficult to work with since it decomposed shortly after purification. Therefore, we decided to deblock nucleoside **99a** not really knowing the exact structure of it. All attempts to remove silyl or benzoyl protecting groups failed[100].

Being unable to work with nucleoside **99a**, it was decided to replace the TBDMSi protecting group with an acetate group since we felt that the TBDMSi group was the cause of the instability. Acetal **97b** was acetylated by standard means to afford **101** in 95% yield. Coupling of **101** to *bis*-(trimethylsilyl)-N^6-benzoyladenine in the presence of silver triflate again afforded a nucleoside **99b** whose NMR data was not consistent with nucleosides of the type **100**. This compound was more stable than the TBDMSi derivative and it was possible to carry out extensive analysis by NMR. Unfortunately, it was not possible to obtain a mass spectrum of either nucleoside **99a** or **99b**.

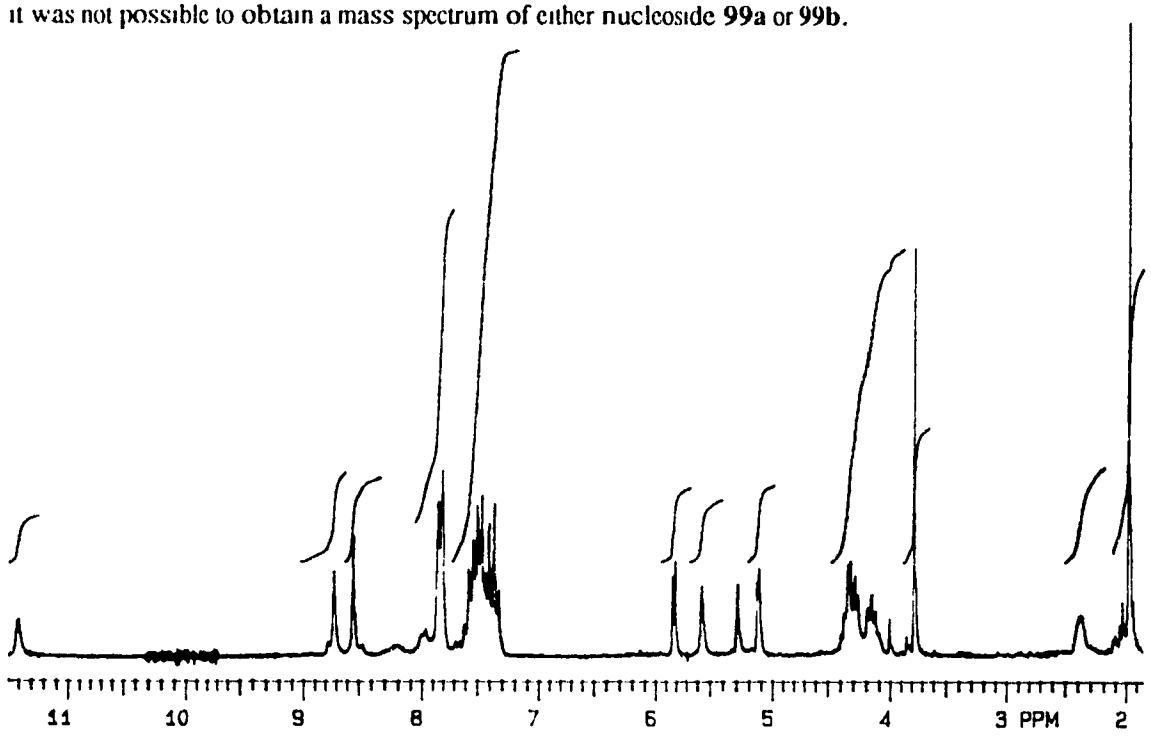
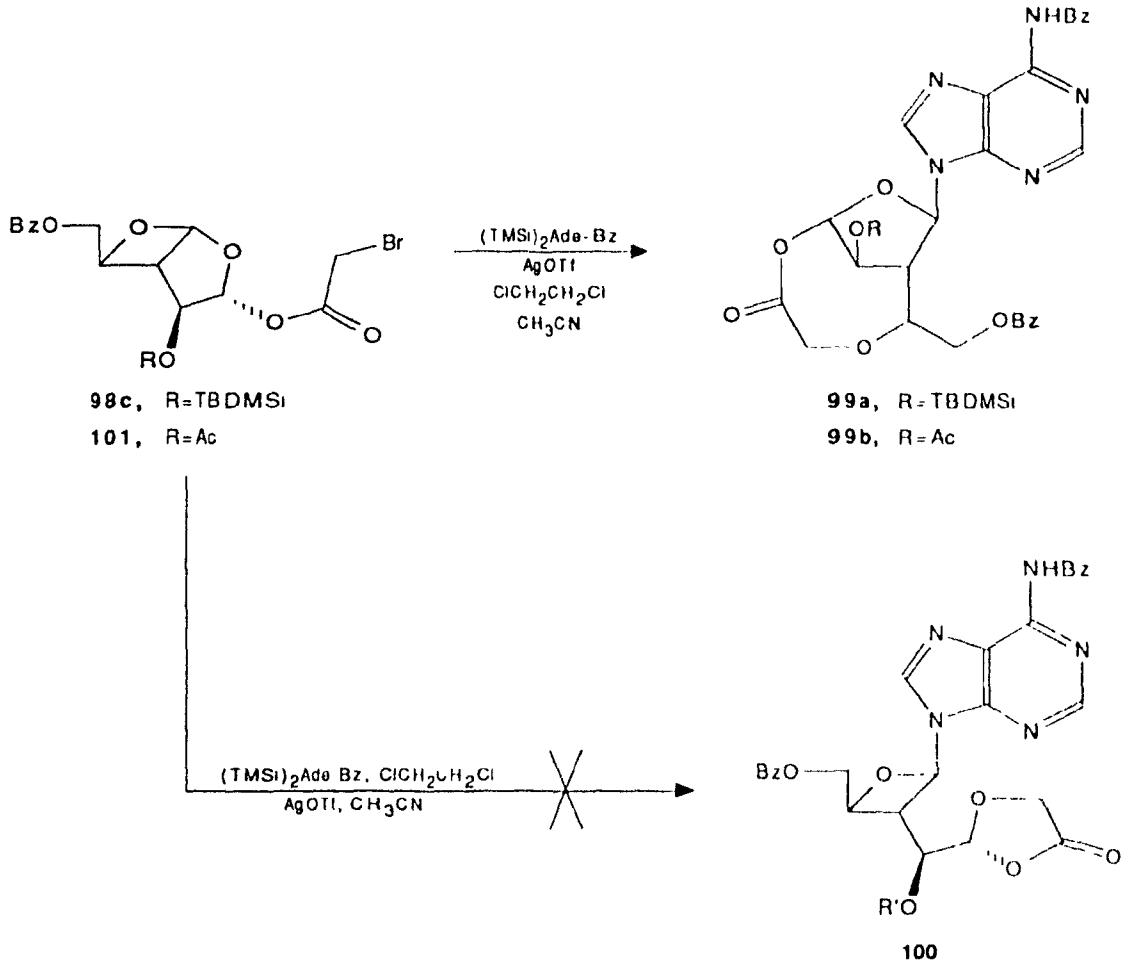


Figure 25. The 200MHz ^{1}H-NMR of nucleoside **99b** in CD_2Cl_2.

[100] Had we known the structure of nucleoside **99a** at this point, we would have obviously not attempted to hydrolyze the benzoyl group since this would open the bicyclic lactone.

Scheme 38



98c, R=TBDMSi
101, R=Ac

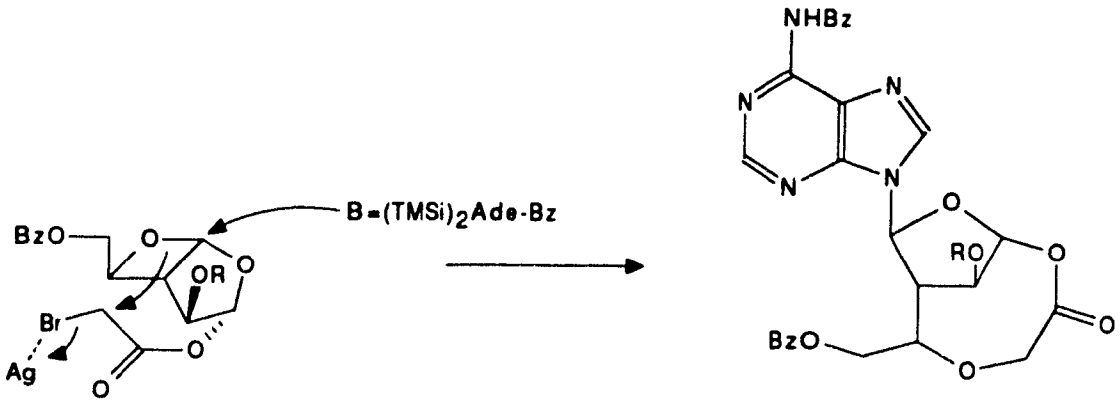
99a, R=TBDMSi
99b, R=Ac

100

Despite not being able to obtain a mass spectrum of **99b**, we were able to assign the structure of **99b**, and thus of **99a**, with a high degree of confidence based on our extensive NMR experiments. The mechanism for the formation of nucleosides **99** is shown in Scheme 39[101]. The only possible explanation as to why the reaction proceeds via this pathway, considering that we had earlier opened acetals of type **10, 21** and **29** in the desired manner to yield monocyclic oxetanes (see sections 2.5b - 2.5d), is that the oxetane oxygen is in closer proximity to the acetyl bromide side chain than the furan oxygen.

[101] Nucleoside **99'** is the enantiomer of nucleoside **99**.

Scheme 39

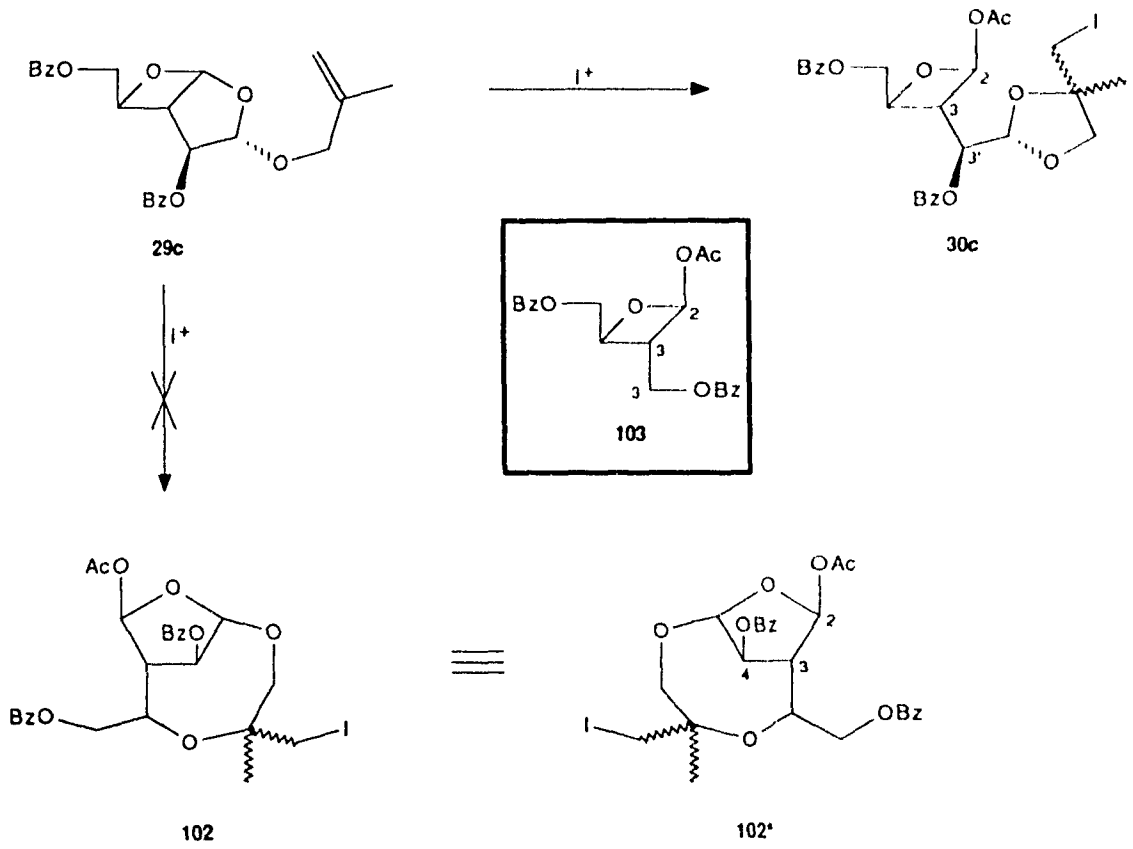


98c, R=TBDMSi
101, R=Ac

99a*, R=TBDMSi
99b*, R=Ac

Due to this unexpected result, we reexamined our structural assignment of oxetanes **17**, **18**, **22**, **30** and **31**. If we analyze the NMR data of compound **30c** (a representative sample), we see that the main distinction between oxetane **30c** and furan **102*** in the ^{1}H-NMR is the chemical shift and coupling pattern of H3. If **102*** had been formed, we should see a "ddd" at ~ 2.5 ppm like was observed in nucleosides **99**. Instead, the ^{1}H-NMR shows a triplet at 3.51 ppm. The chemical shift is very close to what Yamamura[14] reports for oxetane **103**. Also, if we examine the ^{1}H-NMR's of a variety of monocyclic oxetanes, we see that H3 is not affected very much by the substituents on C3' due to the fact that the substituent on C3 is not rigidly attached and can "swing" away to a more stable conformer. If structures of type **102*** had been formed, varying the substituents on C4 would affect the chemical shift of H3 since these substituents would be part of the ring and could not orient out of the way.

Scheme 40

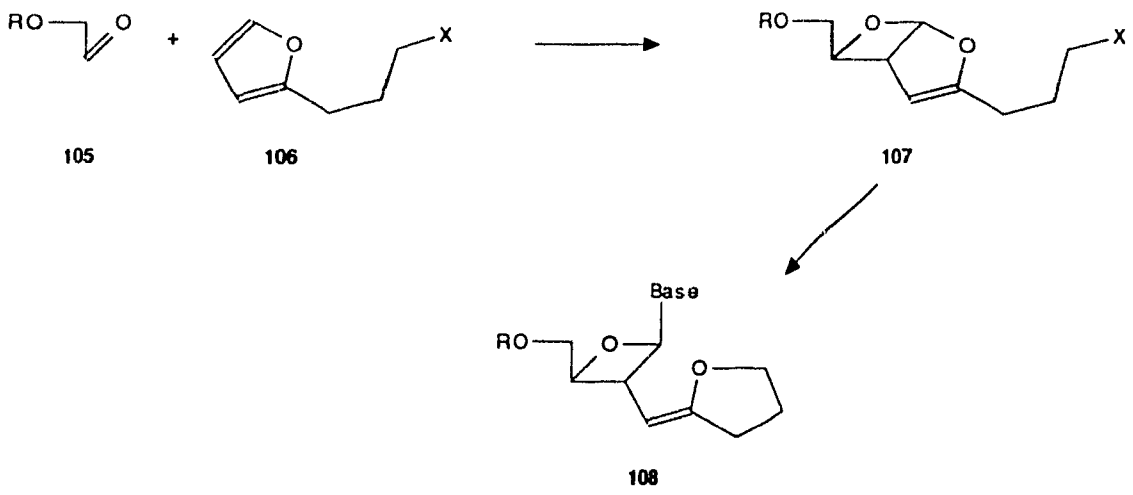


It may be possible to synthesize deprotected nucleosides of the type **99** simply by starting from an epoxide which has a protecting group that can be removed under neutral conditions and protecting the free alcohol in acetals of type **97** with a group that can also be removed under mild conditions. A problem may arise with the use of purine bases since these are normally benzoylated prior to *bis*-silylation and the benzoyl group may be difficult to remove without again destroying the bicyclic lactone as was the case when we attempted to deblock **99a**. However, no such problems should arise with the use of pyrimidine bases and this may be an interesting approach to obtain deprotected nucleosides of the type **99**.

2.10 Future Outlook.

Due to the unexpected reaction of adducts **98c** and **101** with *bis*-(trimethylsilyl)-N^6-benzoyladenine, a new adduct would have to be designed in which the halide containing side chain could not reach over to the oxetane oxygen. It has not yet been possible to synthesize an endo epoxide of type **23d**, which would be required to obtain an *exo* opening of the epoxide, and thus yield an adduct which would have the halide containing side chain closer to the furan oxygen. Therefore, we felt that perhaps an adduct of the type **107** would be suitable and allow the reaction to proceed in the desired manner to give nucleoside **108** since the halide containing side chain is locked in a position that puts it in close proximity to the furan oxygen. Adducts of the type **107** could be synthesized via a [2+2] photocycloaddition of aldehyde **105** and furan **106** as shown in Scheme 41 or by building the side chain on to a suitable photo-adduct.

Scheme 41



Although oxetanocin has generated a great deal of interest in oxetane containing nucleosides over the past few years, interest in it and derivatives thereof is slowly waning due to findings that the oxetane ring is not the sole structural feature which is responsible for activity and due to the fact that no one has yet developed a cost efficient synthesis.

3. CONTRIBUTIONS TO KNOWLEDGE

1. A number of trisubsittuted monocyclic oxetanes were prepared from photo-adducts of aldehydes and furan using a modification of the Fraser-Reid–Mootoo glycosidation procedure The chemistry of these oxetanes was also investigated.

2. Racemic oxetanocin and epioxetanocin were synthesized from photo-adducts of propionyloxyacetaldehyde and 2-methylfuran. The coupling of oxetanes, containing various participating groups, with nitrogenous bases was investigated

3. Bicyclic nucleosides containing photo-adducts of aldehydes and furan were synthesized Furanose derivatives of these nucleosides were also prepared.

4. EXPERIMENTAL

4.1 General Methods.

Melting points (m.p.) were determined on a Gallenkamp block and are uncorrected. Gas chromatographic analyses were performed on a Hewlett-Packard 5890 GC equipped with a fused silica capillary column (25m x 0.2 mm), a flame ionization detector and a HP 3392A integrator. UV spectra were obtained on a Hewlett-Packard 8451 diode array spectrophotometer. Infrared spectra were recorded on an Analect AQS-18 spectrometer in the indicated solvent. Optical rotations were measured on a Jasco DIP-140 digital polarimeter in the indicated solvent and concentration in a 1 dm cell. Low-resolution chemical ionization mass spectra were obtained on an HP-5980A quadrapole mass spectrometer in the direct-inlet mode. Low-resolution electron impact mass spectra were obtained on a DuPont 21-492B mass spectrometer in the direct-inlet mode. High-resolution chemical ionization and FAB mass spectra (low-resolution and high-resolution) were obtained on a VG ZAB-2F-HS sector mass spectrometer in the direct-inlet mode. The measurements were carried out at a resolving power (res) of 10000, unless otherwise indicated. Elemental analyses were performed by Guelph Chemical Laboratories Ltd. (Guelph, Ontario, Canada). All compounds were shown to be homogeneous by t.l.c. and high-field NMR, and to have a purity of >95%.

^{1}H-NMR spectra were obtained on either a Varian XL-200 or Varian XL-300 spectrometer at 200 MHz and 300 MHz respectively and the peak assignments were made, in some cases, with the aid of homonuclear decoupling and/or COSY experiments. Chemical shifts are given in the scale of parts per million (ppm). The residual proton signals of chloroform, DMSO, methanol and methylene chloride (assigned values of δ 7.24, 2.49, 3.30 and 5.32 ppm, respectively) were used as reference in these solvents. The multiplicities are recorded using the following abbreviations: **s**, singlet, **d**, doublet; **dd**, doublet of doublets, **ddd**, doublet of doublet of doublets; **dddd**, doublet of doublet of doublet of doublets; **t**, triplet; **q**, quartet, **h**[7], heptet; **m**, multiplet, **br**, broad; **ex**, exchangeable. ^{13}C-NMR spectra were obtained on a Varian XL-300 spectrometer at 75.4 MHz and the peak assignments were made, in some cases, with the aid of APT and/or HETCOR experiments. The ^{13}C signals of $CDCl_3$, DMSO-d_6, CD_3OD, CD_2Cl_2 and C_6D_6 (assigned values of δ 77.00, 39.50, 49.00, 53.80 and 128.00 ppm, respectively) were used as reference in these solvents. Entries with an asterisk are interchangeable. Selected 2-D experiments are shown in Appendix IV.

Tetrahydrofuran and ether were distilled from sodium benzophenone ketyl. Methylene chloride and 1,2-dichloroethane were distilled from P_2O_5. Benzene, hexanes, petroleum ether and toluene were dried over sodium wire. Methanol was distilled from magnesium. Pyridine, acetonitrile, di-*sym*-collidine and triethylamine were distilled from calcium hydride. *N,N*-Dimethylformamide was dried by shaking with KOH followed by distillation from BaO. Thin-layer chromatography (tlc) was performed on silica

gel (Kieselgel 60 F_{254}) aluminum-backed plates (0.2 mm thickness) and visualized by UV and/or dipping into a solution of 2.5 g ammonium molybdate and 1 g ceric sulfate in 10 mL sulphuric acid / 90 mL water, followed by heating. Kieselgel 60 (Merck 230-400 mesh) silica gel was used for column chromatography[102].

Photochemical reactions were carried out in 350 mL or 2 L reaction vessels using a 450 W medium pressure Hg arc lamp equipped with a VYCOR filter. Oxetanes **42**, **47**, **54**, **56**, **75** and **84** can be prepared in one-pot from their respective photo-adducts However, in some cases, an improved yield can be realized if a partial work-up is done at the alcohol stage. The nomenclature of photo-adducts **2a-d**, **37a**, **38a**, **39a**, **39b**, **40**, **41**, **43**, **44**, **52**, **53**, **55**, **72**, **81**, **85**, **87** and **88**, and any compounds derived from these adducts, refers to the enantiomer shown.

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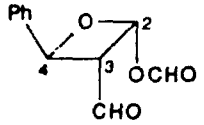
[102] Still, W. C.; Kahn, M.; Mitra, A., *J Org. Chem.*, **43**, 2923 (1978).

4.2 Experimentals for Section 2.2.

2α-O-Formyloxy-3α-C-formyl-4β-phenyl oxetane (3).

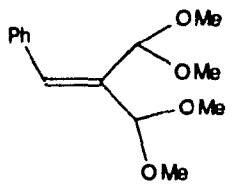
Ozone was bubbled through a solution of the photo-adduct **2a** (1.025 g, 5.89 mmol) in dry methylene chloride (250 mL) at -78°C until the solution turned blue (1 h). Dimethyl sulfide (2.16 mL, 5 equiv.) was added to the reaction mixture under nitrogen and it was allowed to warm to ambient temperature gradually overnight. The solution was washed with water (2 x 150 mL), brine (150 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to yield aldehyde **3** (1.201 g, 99% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.93 (ddd, 1H, H3), 6.22 (d, 1H, H4), 6.88 (d, 1H, H2), 7.26 - 7.39 (m, 5H, phenyl), 8.14 (s, 1H, OCHO), 9.84 (d, 1H, CHO); J_{H2-H3} = 6.2 Hz, J_{H3-CHO} = 1.0 Hz, J_{H3-H4} = 6 5 Hz, IR (CH_2Cl_2): 1730 cm^{-1} [CHO], 1743 cm^{-1} [OCHO]}.



3

Tetramethoxy-olefin (4).

To a stirred solution of aldehyde **3** (206 mg, 1.00 mmol) in dry methanol (2.5 mL) under nitrogen at room temperature was added cerium (III) chloride heptahydrate (373 mg, 1.00 mmol) and trimethyl orthoformate (0.80 mL, 7.00 mmol). After stirring for 43 h, another 0.80 mL of trimethyl orthoformate was added. After stirring for another 2 h, the reaction mixture was poured into saturated aqueous sodium bicarbonate (50 mL), extracted with ether (3 x 50 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* yielding a yellow syrup which was chromatographed over silica gel (hexanes / ether, 2 1 v/v), affording tetramethoxy-olefin **4** as a light yellow oil (108 mg, 43% yield) {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.34, 3.35, 3.41, 3.42 (4s, 12H, MeO), 4.89, 5.03 (2s, 2H, **CH**$(OMe)_2$), 7.09 (s, 1H, **CH**-Ph), 7.32 - 7.39 (m, 5H, phenyl); LRMS (CI-NH_3): m/e 221 ([MH^+ - MeOH], 100%)}.

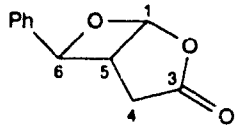


4

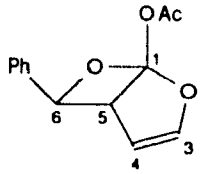
4.3 Experimentals for Section 2.3.

6β-Phenyl-2,7-dioxa-bicyclo-[3,2,0]-hepta-3-none (5a) and 1-β-acetoxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (9a).

A mixture of 2-acetoxyfuran (5.90 g, 46.8 mmol) and benzaldehyde (4.90 g, 46.2 mmol) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C and saturated with helium. The solution was then irradiated for 6 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate, 4.1 v/v) gave **5a** (1.241 g, 14% yield) and **9a** (550 mg, 5% yield) as yellow oils. **5a**: {^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.80 (A of ABX, 1H, $H4_a$), 2.96 (B of ABX, 1H, $H4_b$), 3.51 (dddd, 1H, H5), 5.42 (d, 1H, H6), 6.37 (d, 1H, H1), 7.35 - 7.44 (m, 5H, phenyl); $J_{H1\text{-}H5}$ = 4.8 Hz, $J_{H4\text{-}H4a}$ = 1.3 Hz, $J_{H4\text{-}H4b}$ = 10.0 Hz, $J_{H4a\ H4b}$ = -18.8 Hz, $J_{H5\text{-}H6}$ = 4.4 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 32.64 [C4], 42.77 [C5], 86.79 [C6], 104.75 [C1], 125.24, 128.38, 139.17 [aromatic CH], 128.23 [aromatic C], 175.96 [CO], IR (CH_2Cl_2) 1794 cm^{-1}}. **9a**: {^{1}H-NMR (200 MHz, $CDCl_3$)· δ 2.17 (s, 3H, CH_3), 3.86 (t, 1H, H5), 5.41 (d, 1H, H6), 5.51 (t, 1H, H4), 6.66 (d, 1H, H3), 7.30 - 7.45 (m, 5H, phenyl); $J_{H3\text{-}H4}$ = 3.4 Hz, $J_{H4\text{-}H5}$ = 3.1 Hz, $J_{H5\ H6}$ = 3.5 Hz; IR (CH_2Cl_2): 1767 cm^{-1}; LRMS (CI-NH_3): m/e 250 ([M + NH_4^+], 25.8%), 233 ([MH^+], 14.2%)}.



5a



9a

4.4 Experimentals for Section 2.5.

General Procedure for the Reaction of N-Halosuccinimide and Alcohols with Photo-adducts.

To a solution of **2** in dry alcohol (0.05 M - 0.20 M) at room temperature under nitrogen was added N-bromo (NBS) or N-iodo (NIS) succinimide (1 equiv.). The reaction mixture was stirred at room temperature until complete comsumption of the starting material (1 - 3 h). The remaining alcohol was removed *in vacuo* and the residue was purified by flash chromatography (petroleum ether / ethyl acetate, 10.1 - 4:1, v/v).

3α-Allyloxy-4β-bromo-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10a).

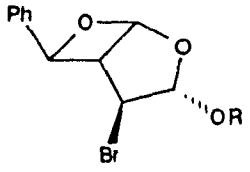
Photo-adduct **2a** (98 mg, 0.56 mmol) and NBS (99 mg, 0.56 mmol) in allyl alcohol (5 mL) gave the title compound (38 mg, 22% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.59 (t, 1H, H5), 4.32 (ddt, br, 2H, H3'$_a$, H3'$_b$), 4.50 (s, 1H, H4), 5.31 (dddd, br, 2H, H3'''$_a$, H3'''$_b$), 5.57 (d, 1H, H6), 5.74 (d, 1H, H3), 5.96 (m, 1H, H3''), 6.33 (d, 1H, H1), 7.31 - 7.41 (m, 5H, phenyl), J_{H1-H5} = 4.1 Hz, $J_{H3-H3'_a}$ = -0.3 Hz, J_{5-6} = 4.8 Hz}

3α-Methallyloxy-4β-bromo-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10b).

Photo-adduct **2a** (435 mg, 2.50 mmol) and NBS (445 mg, 2.50 mmol) in 2-methyl-2-propen-1-ol (25 mL) gave the title compound (108 mg, 17% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.80 (s, 3H, Me), 3.59 (t, 1H, H5), 4.23 (dd, br, 2H, H3'$_a$, H3'$_b$), 4.51 (s, 1H, H4), 4.96, 5.05 (2s, br, 2H, H3'''$_a$, H3'''$_b$), 5.57 (d, 1H, H6), 5.72 (d, 1H, H3), 6.33 (d, 1H, H1), 7.30 - 7.41 (m, 5H, phenyl), J_{H1-H5} = 4.1 Hz, $J_{H3-H3'_a}$ = -0.5 Hz, $J_{H3'a-H3'b}$ = -12.4 Hz, J_{H5-H6} = 4.8 Hz; LRMS (CI-NH_3): m/e 344, 342 ([M + NH_4^+], 5.7%, 4.3%), 272, 270 ([MH^+ - H_2C=C(CH_3)CH_2OH], 15.2%, 11.9%)}.

3α-Dimethallyloxy-4β-bromo-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10c).

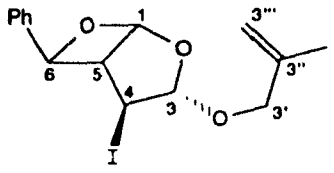
Photo-adduct **2a** (87 mg, 0.50 mmol) and NBS (89 mg, 0.50 mmol) in 3-methyl-2-buten-1-ol (5 mL) gave the title compound (129 mg, 76% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.73, 1.78 (2s, br, 6H, Me), 3.57 (t, 1H, H5), 4.31 (ddd, br, 2H, H3'$_a$, H3'$_b$), 4.48 (s, 1H, H4), 5.40 (m, 1H, H3''), 5.57 (d, 1H, H6), 5.73 (s, 1H, H3), 6.33 (d, 1H, H1), 7.30 - 7.40 (m, 5H, phenyl), J_{H1-H5} = 4.1 Hz, J_{H5-H6} = 4.7 Hz; LRMS (CI-NH_3): m/e 341, 339 ([MH^+], 5.8%, 6.2%)}.



10a, R = CH_2CH=CH_2
10b, R = $CH_2C(CH_3)$=CH_2
10c, R = CH_2CH=$C(CH_3)_2$

3α-Methallyloxy-4β-iodo-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10d).

Photo-adduct **2a** (87 mg, 0.50 mmol) and NIS (113 mg, 0.50 mmol) in 2-methyl-2-propen-1-ol (5 mL) gave the title compound (186 mg, 100% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.75 (s, 3H, Me), 3.69 (t, 1H, H5), 4.21 (dd, br, 2H, $H3'_a$, $H3'_b$), 4.49 (s, 1H, H4), 4.95, 5.04 (2s, br, 2H, $H3'''_a$, $H3'''_b$), 5.56 (d, 1H, H6), 5.84 (d, 1H, H3), 6.34 (d, 1H, H1), 7.30 - 7.43 (m, 5H, phenyl), J_{H1-H5} = 4.0 Hz, $J_{H3-H3'a}$ = -0.6 Hz, $J_{H3'a-H3'b}$ = -12.2 Hz, J_{H5-H6} = 4.8 Hz; LRMS (CI-NH_3)· m/e 373 ([MH^+], 0.2%), 301 ([MH^+ - $H_2C{=}C(CH_3)CH_2OH$], 4.2%)}.



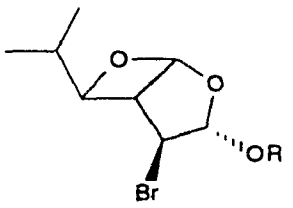
10d

3α-Allyloxy-4β-bromo-6β-*i*-propyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10e).

Photo-adduct **2b** (140 mg, 1.00 mmol) and NBS (178 mg, 1.00 mmol) in allyl alcohol (5 mL) gave the title compound (194 mg, 70% yield) as a colourless oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.86 (d, 3H, **Me**CHMe'), 0.89 (d, 3H, MeCH**Me'**), 1.82 (m, 1H, H6'), 3.32 (t, 1H, H5), 4.17 (dd, 1H, H6), 4.23 (m, br, 2H, $H3'_a$, $H3'_b$), 4.25 (s, 1H, H4), 5.25 (dddd, br, 2H, $H3'''_a$, $H3'''_b$), 5.63 (d, 1H, H3), 5.87 (m, 1H, H3''), 6.02 (d, 1H, H1), J_{H1-H5} = 4.1 Hz, $J_{H3-H3'a}$ = -0.6 Hz, J_{H5-H6} = 5.0 Hz, $J_{H6-H6'}$ = 8.2 Hz, $J_{H6'-Me}$ = 7.4 Hz, $J_{H6'-Me'}$ = 6.8 Hz}.

3α-Methallyloxy-4β-bromo-6β-*i*-propyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10f).

Photo-adduct **2b** (140 mg, 1.00 mmol) and NBS (178 mg, 1.00 mmol) in 2-methyl-2-propen-1-ol (5 mL) gave the title compound (27 mg, 9% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.87 (d, 3H, **Me**CHMe'), 0.91 (d, 3H, MeCH**Me'**), 1.75 (s, 3H, Me), 1.79 (m, 1H, H6'), 3.34 (t, 1H, H5), 4.15 (dd, br, 2H, $H3'_a$, $H3'_b$), 4.20 (dd, 1H, H6), 4.28 (s, 1H, H4), 4.93, 5.00 (2s, br, 2H, $H3'''_a$, $H3'''_b$), 5.63 (d, 1H, H3), 6.05 (d, 1H, H1), J_{H1-H5} = 3.8 Hz, $J_{H3-H3'a}$ = -0.3 Hz, $J_{H3'a-H3'b}$ = -12.4 Hz, J_{H5-H6} = 4.4 Hz, $J_{H6-H6'}$ = 8.0 Hz, $J_{H6'-Me}$ = 6.9 Hz, $J_{H6'-Me'}$ = 6.9 Hz}.



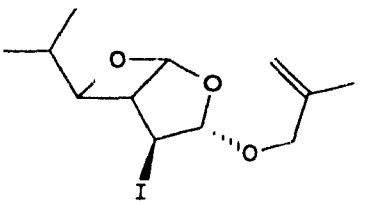
10e, R = $CH_2CH{=}CH_2$
10f, R = $CH_2C(CH_3){=}CH_2$
10g, R = $CH_2CH{=}C(CH_3)_2$

3α-Dimethallyloxy-4β-bromo-6β-*i*-propyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10g).

Photo-adduct **2b** (140 mg, 1.00 mmol) and NBS (178 mg, 1.00 mmol) in 3-methyl-2-buten-1-ol (5 mL) gave the title compound (228 mg, 75% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.87 (d, 3H, **MeCHMe'**), 0.91 (d, 3H, MeCH**Me'**), 1.69, 1.75 (2s, br, 6H, Me_2C), 1.85 (m, 1H, H6'), 3.32 (t, 1H, H5), 4.19 (dd, 1H, H6), 4.21 (ddd, br, 2H, $H3'_a$, $H3'_b$), 4.24 (s, 1H, H4), 5.35 (m, 1H, H3"), 5.63 (s, 1H, H3), 6.04 (d, 1H, H1), J_{H1-H5} = 4.2 Hz, $J_{H3-H3'a}$ = -0.6 Hz, $J_{H3'a-H3'b}$ = -11.1 Hz, $J_{H3'a-H3"}$ = 4.8 Hz, $J_{H3'b-H3"}$ = 7.4 Hz, J_{H5-H6} = 4.5 Hz, $J_{H6-H6'}$ = 8.0 Hz, $J_{H6'-Me}$ = 6.7 Hz, $J_{H6'-Me'}$ = 6.7 Hz}.

3α-Methallyloxy-4β-iodo-6β-*i*-propyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (10h).

Photo-adduct **2b** (1.68 g, 12.0 mmol) and NIS (2.71 g, 12.0 mmol) in 2-methyl-2-propen-1-ol (120 mL) gave the title compound (3.84 g, 84% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.86 (d, 3H, **MeCHMe'**), 0.89 (d, 3H, MeCH**Me'**), 1.74 (s, 3H, Me), 1.81 (m, 1H, H6'), 3.44 (t, 1H, H5), 4.13 (dd, br, 2H, $H3'_a$, $H3'_b$), 4.17 (dd, 1H, H6), 4.26 (s, 1H, H4), 4.92, 4.99 (2s, br, 2H, $H3"_a$, $H3"_b$), 5.74 (d, 1H, H3), 6.05 (d, 1H, H1); J_{H1-H5} = 4.0 Hz, $J_{H3-H3'a}$ = -0.5 Hz, $J_{H3'a-H3'b}$ = -12.4 Hz, J_{H5-H6} = 4.8 Hz, $J_{H6-H6'}$ = 8.0 Hz, $J_{H6'-Me}$ = 7.3 Hz, $J_{H6'-Me'}$ = 7.3 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 16.23, 16.97 [$\mathbf{Me_2}$CH], 19.49 [$OCH_2C(\mathbf{CH_3})=CH_2$], 24.03 [C4], 33.59 [C6'], 54.91 [C5], 71.63 [$O\mathbf{CH_2}C(CH_3)=CH_2$], 89.12 [C6], 107.92 [C1], 112.77 [$OCH_2C(CH_3)=\mathbf{CH_2}$], 113.91 [C3], 141.20 [$OCH_2\mathbf{C}(CH_3)=CH_2$]; LRMS (CI-$NH_3$): m/e 356 ([M + NH_4^+], 4.1%), 339 ([MH^+], 12.2%), 267 ([MH^+ - $H_2C=C(CH_3)CH_2OH$], 29.8%); HRMS (CI-NH_3): m/e calcd. for $C_{12}H_{20}O_3I$ [MH^+], 339.0458; found 339.0457}. Anal. calcd. for $C_{12}H_{19}O_3I$: C, 42.62; H, 5.66; I, 37.52. Found. C, 42.71; H, 5.70; I, 37.60.



10h

4,5-Dihydro-4α-(α-hydroxybenzyl)-5β-methoxyfuran (14).

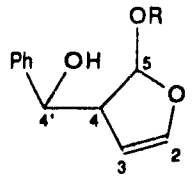
A solution of **2a** (489 mg, 2.81 mmol) in anhydrous methanol (50 mL) was refluxed under an atmosphere of nitrogen for 2 h. The solvent was removed under reduced pressure to give a white residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1, v/v) gave the title compound (180 mg, 31% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.08 (d, ex, 1H, OH), 3.05 (dddd, 1H, H4), 3.42 (s, 3H, MeO), 4.44 (dd, 1H, H4'), 4.59 (t, 1H, H3), 5.42 (d, 1H, H5), 6.39 (dd, 1H, H2), 7.32 - 7.36 (m, 5H, phenyl), J_{H2-H3} = 2.8 Hz, J_{H2-H4} = -2.0 Hz, J_{H3-H4} = 2.8 Hz, $J_{H4-H4'}$ = 8.1 Hz, J_{H4-H5} = 2.2 Hz, $J_{H4'-OH}$ = 3.0 Hz; LRMS (EI, 70 eV): m/e 206 ([M^+], 1.1%}.

4,5-Dihydro-4α-(α-hydroxybenzyl)-5β-allyloxyfuran (15).

A solution of **2a** (2.00 g, 11.5 mmol) in dry allyl alcohol (200 mL) under nitrogen at room temperature containing acetic acid (13 μL, 0.12 mmol) was refluxed for 2 days. The solution was evaporated to dryness and the residue was dissolved in EtOAc (500 mL), washed with saturated aqueous sodium bicarbonate (400 mL), brine (400 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a thick yellow residue. Flash chromatography of the residual syrup (petroleum ether / ethyl acetate, 4:1, v/v) gave the title compound (791 mg, 30% yield) as a light yellow oil and recovered starting material (552 mg). [^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.25 (d, ex, 1H, OH), 3.08 (dddd, 1H, H4), 4.13 (dddt, 2H, $H5'_a$, $H5'_b$), 4.43 (dd, 1H, H4'), 4.60 (t, 1H, H3), 5.18 (dddd, br, 2H, $H5''_a$, $H5'''_b$), 5.53 (d, 1H, H5), 5.83 (m, 1H, H5''), 6.37 (dd, 1H, H2), 7.27 - 7.39 (m, 5H, phenyl), J_{H2-H3} = 2.8 Hz, J_{H2-H4} = -1.9 Hz, J_{H3-H4} = 2.8 Hz, $J_{H4-H4'}$ = 8.0 Hz, J_{H4-H5} = 2.1 Hz, $J_{H4'-OH}$ = 2.9 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 57.21 [C4], 69.20 [$OCH_2CH=CH_2$], 74.63 [C4'], 100.81 [C3], 106.71 [C5], 117.07 [$OCH_2CH=CH_2$], 126.68, 128.11, 128..73 [aromatic CH], 134.51 [$OCH_2CH=CH_2$], 142.59 [aromatic C], 145.87 [C2]; LRMS (CI-NH_3): m/e 255 ([M + NH_4^+], 1.0%), 233 ([MH^+], 3.6%)].

4,5-Dihydro-4α-(α-hydroxybenzyl)-5β-methallyloxyfuran (16a).

The title compound was prepared in 10% yield by a procedure similar to that used for the preparation of **15**. [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.59 (s, br, 3H, Me), 1.97 (d, ex, 1H, OH), 3.11 (dddd, 1H, H4), 4.03 (dd, br, 2H, $H5'_a$, $H5'_b$), 4.51 (dd, 1H, H4'), 4.66 (t, 1H, H3), 4.86, 4.88 (2s, br, 2H, $H5'''_a$, $H5'''_b$), 5.49 (d, 1H, H5), 6.42 (dd, 1H, H2), 7.27 - 7.36 (m, 5H, phenyl), J_{H2-H3} = 2.7 Hz, J_{H2-H4} = -1.8 Hz, J_{H3-H4} = 2.8 Hz, $J_{H4-H4'}$ = 7.4 Hz, J_{H4-H5} = 2.1 Hz, $J_{H4'-OH}$ = 2.6 Hz, $J_{H5'a-H5'b}$ = -12.6 Hz; LRMS (CI-NH_3): m/e 264 ([M + NH_4^+], 1.9%), 247 ([MH^+], 5.5%); HRMS (CI-NH_3): m/e calcd. for $C_{15}H_{19}O_3$ [MH^+], 247.1333; found, 247.1334].

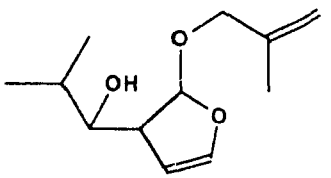


14, R = CH_3
15, R = $CH_2CH=CH_2$
16a, R = $CH_2C(CH_3)=CH_2$

4,5-Dihydro-4α-(4'-hydroxy-4''-methylpropyl)-5β-methallyloxyfuran (16b).

The title compound was prepared in 11% yield by a procedure similar to that used for the preparation of **15**. [^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.95 (d, 6H, Me_2CH), 1.50 (s, br, ex, 1H, OH), 1.73 (s, br, 3H, Me), 1.76 (m, 1H, Me_2CH), 2.91 (dddd, 1H, H4), 3.19 (ddd, 1H, H4'), 4.08 (dd, br, 2H, $H5'_a$, $H5'_b$), 4.85 (t, 1H, H3), 4.89, 4.98 (2s, br, 2H, $H5'''_a$, $H5'''_b$), 5.47 (d, 1H, H5), 6.41 (dd, 1H, H2), J_{H2-H3} =

2.7 Hz, J_{H2-H4} = -1.8 Hz, J_{H3-H4} = 2.8 Hz, $J_{H4-H4'}$ = 8.0 Hz, J_{H4-H5} = 2.4 Hz, $J_{H4'-CHMe}$ = 6.5 Hz, $J_{CHMe-Me}$ = 6.7 Hz; LRMS (CI-NH_3): m/e 230 ([M + NH_4^+], 12.4%), 213 ([MH^+], 39.2%), 141 ([MH^+ - $H_2C{=}C(CH_3)CH_2OH$], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{15}H_{19}O_3$ [MH^+ - $H_2C{=}C(CH_3)CH_2OH$], 213.1490; found, 213.1490].



16b

General Procedure for I^+(*sym*-collidine)$_2ClO_4^-$ Mediated Opening of Acetals 10, 21 and 29.

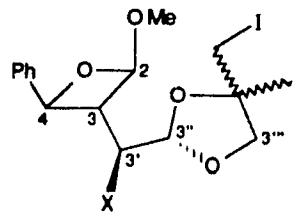
To a solution of the adduct in dry benzene (~0.03 M) under nitrogen at room temperature was added the nucleophile (5 equiv.). After stirring for 10 min., I^+(*sym*-collidine)$_2ClO_4^-$ (1.5 equiv.) was added in small portions over a 20 minute period and the solution allowed to stir until completion of the reaction (1 - 18 h). The excess I^+(*sym*-collidine)$_2ClO_4^-$ was precipitated by the addition of ether (amount equal to total solvent used) and the reaction mixture was filtered through a bed of dry Celite. The filter cake was washed with more diethyl ether and the combined filtrates were washed with saturated aqueous sodium thiosulfate, 5% hydrochloric acid, saturated aqueous sodium bicarbonate, water, dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a syrup. Flash chromatography of the residual syrup (petroleum ether / ethyl acetate, 10:1 - 2:1, v/v) gave the unsubstituted monocyclic oxetane.

Oxetane (17b).

Acetal **10b** (72 mg, 0.22 mmol) and methanol (45µL, 1.10 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (107 mg, 100% yield) as a colourless oil. **17b-minor:** [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.35 (s, 3H, Me), 3.27 (s, 3H, MeO), 3.36 (s, br, 2H, CHHI, CHHI), 3.59 (t, 1H, H3), 3.83 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.51 (s, 1H, H3'), 5.50 (d, 1H, H4), 5.72 (s, 1H, H3''), 6.32 (d, 1H, H2), 7.31 - 7.39 (m, 5H, phenyl), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.8 Hz, $J_{H3'''a-H3'''b}$ = -10.2 Hz, $J_{CHHI-CHHI}$ ~ 0 Hz]. **17b-major:** [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.37 (s, 3H, Me), 3.27 (s, 3H, MeO), 3.39 (dd, 2H, CHHI, CHHI), 3.59 (t, 1H, H3), 3.83 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.51 (s, 1H, H3'), 5.49 (d, 1H, H4), 5.72 (s, 1H, H3''), 6.32 (d, 1H, H2), 7.31 - 7.39 (m, 5H, phenyl), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.9 Hz, $J_{H3'''a-H3'''b}$ = -9.8 Hz, $J_{CHHI-CHHI}$ = -10.4 Hz].

Oxetane (17d).

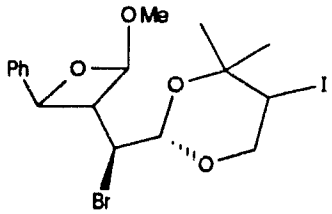
Acetal **10d** (74 mg, 0.20 mmol) and methanol (41μL, 1.10 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (71 mg, 67% yield) as a light yellow oil. **17d-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.35 (s, 3H, Me), 3.27 (s, 3H, MeO), 3.36 (s, br, 2H, **CH**HI, CH**H**I), 3.68 (t, 1H, H3), 3.82 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.49 (s, 1H, H3'), 5.48 (d, 1H, H4), 5.84 (s, 1H, H3"), 6.33 (d, 1H, H2), 7.33 - 7.39 (m, 5H, phenyl), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.6 Hz, $J_{H3'''a\text{-}H3'''b}$ = -10.2 Hz, $J_{CHHI\text{-}CHHI}$ ~ 0 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 12.14 [$\mathbf{CH_2}$I], 20.07 [$\mathbf{CH_3}$], 22.75 [C3'], 50.22 [C3], 59.86 [MeO], 71.05 [C3'''], 74.32 [$\mathbf{CCH_2}$I], 84.91 [C4], 108.45 [C2], 114.93 [C3"], 125.40, 128.44, 128.74 [aromatic **CH**], 140.56 [aromatic C]}. **17d-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.37 (s, 3H, Me), 3.27 (s, 3H, MeO), 3.39 (dd, 2H, CHHI, CHHI), 3.68 (t, 1H, H3), 3.79 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.49 (s, 1H, H3'), 5.46 (d, 1H, H4), 5.84 (s, 1H, H3"), 6.33 (d, 1H, H2), 7.33 - 7.39 (m, 5H, phenyl), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.8 Hz, $J_{H3'''a\text{-}H3'''b}$ = -9.9 Hz, $J_{CHHI\text{-}CHHI}$ = -10.1 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$}: δ 12.60 [$\mathbf{CH_2}$I], 20.21 [$\mathbf{CH_3}$], 22.71 [C3'], 49.97 [C3], 59.87 [MeO], 70.76 [C3'''], 74.30 [$\mathbf{CCH_2}$I], 84.94 [C4], 108.47 [C2], 114.93 [C3'], 125.40, 128.44, 128.74 [aromatic **CH**], 140.54 [aromatic C]}.



17b, X=Br
17d, X=I

Oxetane (17c).

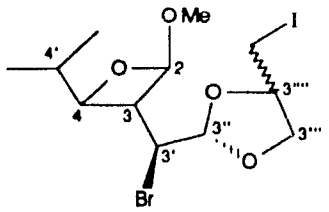
Acetal **10c** (68 mg, 0.20 mmol) and methanol (41μL, 1.00 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 45:55), (70 mg, 70% yield) as a light yellow oil. **17c-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.37 (s, 6H, CH_3), 3.23 (s, 3H, MeO), 3.59 (dd, 1H, H3), 3.93 (d, 1H, CHI), 4.23 - 4.51 (m, 2H, $H3'''_a$, $H3'''_b$), 4.54 (s, 1H, H3'), 5.67 (d, 1H, H4), 5.77 (s, 1H, H3"), 6.32 (d, 1H, H2), 7.34 - 7.41 (m, 5H, phenyl), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 5.0 Hz, $J_{H3'''a\text{-}CHI}$ = 11.4 Hz}. **17c-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.37 (s, 6H, CH_3), 3.13 (s, 3H, MeO), 3.59 (dd, 1H, H3), 3.92 (d, 1H, CHI), 4.23 - 4.51 (m, 2H, $H3'''_a$, $H3'''_b$), 4.52 (s, 1H, H3'), 5.75 (d, 1H, H4), 5.75 (s, 1H, H3"), 6.32 (d, 1H, H2), 7.34 - 7.41 (m, 5H, phenyl), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 5.1 Hz, $J_{H3'''b\text{-}CHI}$ = 11.9 Hz}.



17c

Oxetane (17e).

Acetal **10e** (56 mg, 0.20 mmol) and methanol (41μL, 1.10 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 45:55), (24 mg, 24% yield) as a light yellow oil. **17e-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.87 (d, 3H, MeCHMe'), 0.91 (d, 3H, MeCHMe'), 1.84 (m, 1H, H4'), 3.24 - 3.39 (m, 3H, H3, CHHI, CHHI), 3.43 (s, 3H, MeO), 3.66 (m, 1H, H3''''), 3.84 - 4.18 (m, 3H, $H3'''_a$, $H3'''_b$, H4), 4.27 (d, 1H, H3'), 5.65 (d, 1H, H3''), 6.03 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3'\text{-}H3''}$ = 2.7 Hz, $J_{CH\text{-}Me}$ = 6.8 Hz, $J_{CH\text{-}Me'}$ = 6.6 Hz}. **17e-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.87 (d, 3H, MeCHMe'), 0.91 (d, 3H, MeCHMe'), 1.84 (m, 1H, H4'), 3.24 - 3.39 (m, 3H, H3, CHHI, CHHI), 3.42 (s, 3H, MeO), 3.66 (m, 1H, H3''''), 3.84 - 4.18 (m, 3H, $H3'''_a$, $H3'''_b$, H4), 4.25 (s, 1H, H3'), 5.64 (s, 1H, H3''), 6.04 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3'\text{-}H3''}$ ~ 0 Hz, $J_{CH\text{-}Me}$ = 6.8 Hz, $J_{CH\text{-}Me'}$ = 6.6 Hz}.



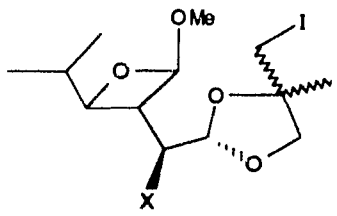
17e

Oxetane (17f).

Acetal **10f** (27 mg, 0.09 mmol) and methanol (19 μL, 0.46 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (13 mg, 32% yield) as a colourless oil. **17f-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.87 (d, 3H, MeCHMe'), 0.91 (d, 3H, MeCHMe'), 1.30 (s, 3H, Me), 1.85 (m, 1H, H4'), 3.25 (s, 3H, MeO), 3.32 (s, br, 2H, CHHI, CHHI), 3.44 (t, 1H, H3), 3.75 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.11 (dd, 1H, H4), 4.28 (s, 1H, H3'), 5.63 (s, 1H, H3''), 6.04 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\ H4}$ = 4.7 Hz, $J_{H3'''a\text{-}H3'''b}$ = -10.3 Hz, $J_{CHHI\text{-}CHHI}$ ~ 0 Hz, $J_{H4\text{-}H4'}$ = 8.0 Hz, $J_{H4'\text{-}Me}$ = 6.8 Hz, $J_{H4\text{-}Me'}$ = 6.6 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 12.21 [$\mathbf{CH_2}$I], 16.32, 16.98 [$\mathbf{Me_2}$CH], 20.18 [$\mathbf{CH_3}$], 33.63 [C4'], 49.28 [C3'], 50.22 [C3], 52.88 [MeO], 70.58 [C3''''], 74.33 [CCH_2I], 87.30 [C4], 107.82 [C2], 112.93 [C3'']}. **17f-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.87 (d, 3H, MeCHMe'), 0.91 (d, 3H, MeCHMe'), 1.32 (s, 3H, Me), 1.85 (m, 1H, H4'), 3.25 (s, 3H, MeO), 3.32 (dd, 2H, CHHI, CHHI), 3.44 (t, 1H, H3), 3.73 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.11 (dd, 1H, H4), 4.28 (s, 1H, H3'), 5.63 (s, 1H, H3''), 6.04 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.7 Hz, $J_{H3'''a\text{-}H3'''b}$ = -9.8 Hz, $J_{CHHI\text{-}CHHI}$ = -10.0 Hz, $J_{H4\ H4'}$ = 8.0 Hz, $J_{H4'\text{-}Me}$ = 6.8 Hz, $J_{H4'\text{-}Me'}$ = 6.6 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 12.60 [$\mathbf{CH_2}$I], 16.32, 16.98 [$\mathbf{Me_2}$CH], 20.30 [$\mathbf{CH_3}$], 33.63 [C4'], 49.25 [C3'], 49.99 [C3], 52.88 [MeO], 70.36 [C3''''], 74.31 [CCH_2I], 87.33 [C4], 107.78 [C2], 112.91 [C3'']}.

Oxetane (17h).

Acetal **10h** (34 mg, 0.10 mmol) and methanol (20 μL, 0.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (15 mg, 30% yield) as a clear oil and recovered starting material (5 mg). **17h-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.86 (d, 3H, **Me**CHMe'), 0.89 (d, 3H, MeCH**Me'**), 1.30 (s, 3H, Me), 1.83 (m, 1H, H4'), 3.25 (s, 3H, MeO), 3.32 (s, br, 2H, **CH**HI, CH**H**I), 3.43 (t, 1H, H3), 3.74 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.11 (dd, 1H, H4), 4.27 (s, 1H, H3'), 5.75 (s, 1H, H3"), 6.05 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.6 Hz, $J_{H3'''a\text{-}H3'''b}$ = -10.1 Hz, $J_{CHHI\text{-}CHHI}$ ~ 0 Hz, $J_{H4\text{-}H4'}$ = 7.9 Hz, $J_{H4'\text{-}Me}$ = 7.2 Hz, $J_{H4'\text{-}Me'}$ = 6.7 Hz}. **17h-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.86 (d, 3H, MeCHMe'), 0.89 (d, 3H, MeCHMe'), 1.32 (s, 3H, Me), 1.83 (m, 1H, H4'), 3.25 (s, 3H, MeO), 3.32 (dd, 2H, **CH**HI, CH**H**I), 3.43 (t, 1H, H3), 3.69 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.11 (dd, 1H, H4), 4.27 (s, 1H, H3'), 5.75 (s, 1H, H3"), 6.05 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.6 Hz, $J_{H3'''a\text{-}H3'''b}$ = -10.1 Hz, $J_{CHHI\text{-}CHHI}$ = -9.9 Hz, $J_{H4\text{-}H4'}$ = 7.9 Hz, $J_{H4'\text{-}Me}$ = 7.2 Hz, $J_{H4'\text{-}Me'}$ = 6.7 Hz}.



17f, X=Br
17h, X=I

Oxetane (18a).

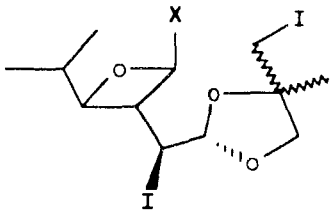
Acetal **10h** (34 mg, 0.10 mmol) and ethanol (29 μL, 0.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (12 mg, 24% yield) as a clear oil and recovered starting material (26 mg). {LRMS (CI-NH_3): m/e 528 ([M + NH_4^+], 53.3%), 511 ([MH^+], 21.8%)}. **18a-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.86 (d, 3H, **Me**CHMe'), 0.89 (d, 3H, **Me**CHMe'), 1.16 (t, 3H, $OCH_2\mathbf{CH_3}$), 1.30 (s, 3H, Me), 1.81 (m, 1H, H4'), 3.33 (s, br, 2H, **CH**HI, CH**H**I), 3.42 (t, 1H, H3), 3.42 (q, 2H, $\mathbf{OCH_2}CH_3$), 3.73 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.09 (dd, 1H, H4), 4.26 (s, 1H, H3'), 5.75 (s, 1H, H3"), 6.04 (d, 1H, H2), $J_{CH_2\text{-}CH_3}$ = 6.9 Hz, $J_{H2\text{-}H3}$ = 4.2 Hz, $J_{H3\text{-}H4}$ = 4.7 Hz, $J_{H3'''a\text{-}H3'''b}$ = -10.0 Hz, $J_{CHHI\text{-}CHHI}$ ~ 0 Hz, $J_{H4\ H4'}$ = 7.8 Hz, $J_{H4'\text{-}Me}$ = 6.8 Hz, $J_{H4'\text{-}Me'}$ = 7.2 Hz}. **18a-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.86 (d, 3H, **Me**CHMe'), 0.89 (d, 3H, **Me**CHMe'), 1.17 (t, 3H, $OCH_2\mathbf{CH_3}$), 1.32 (s, 3H, Me), 1.80 (m, 1H, H4'), 3.35 (dd, 2H, **CH**HI, CH**H**I), 3.42 (t, 1H, H3), 3.42 (q, 2H, $\mathbf{OCH_2}CH_3$), 3.70 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.09 (dd, 1H, H4), 4.26 (s, 1H, H3'), 5.75 (s, 1H, H3"), 6.04 (d, 1H, H2), $J_{CH_2\text{-}CH_3}$ = 7.0 Hz, $J_{H2\text{-}H3}$ = 4.2 Hz, $J_{H3\text{-}H4}$ = 4.7 Hz, $J_{H3'''a\ H3'''b}$ = -9.8 Hz, $J_{CHHI\text{-}CHHI}$ = -10.8 Hz, $J_{H4\text{-}H4'}$ = 7.8 Hz, $J_{H4'\text{-}Me}$ = 6.8 Hz, $J_{H4'\text{-}Me'}$ = 7.2 Hz}.

Oxetane (18b).

Acetal **10h** (68 mg, 0.20 mmol) and *i*-propanol (77 µL, 1.00 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (29 mg, 27% yield) as a light yellow oil and recovered starting material (37 mg). **18b-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.85 (d, 3H, **Me**CHMe'), 0.89 (d, 3H, CH**Me'**), 1.17 (d, 6H, Me_2CH, anomeric), 1.33 (s, 3H, Me), 1.77 (m, 1H, H4'), 3.34 (s, br, 2H, **CH**HI, CH**H**I), 3.42 (t, 1H, H3), 3.68 (dd, 2H, $H3'''_a$, $H3'''_b$), 3.77 (m, 1H, H2'), 4.08 (dd, 1H, H4), 4.25 (s, 1H, H3'), 5.75 (s, 1H, H3''), 6.04 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.2 Hz, $J_{H3\text{-}H4}$ = 4.4 Hz, $J_{H3'''a\text{-}H3'''b}$ = -10.2 Hz, $J_{CHHI\text{-}CHHI}$ ~ 0 Hz, $J_{H4\text{-}H4'}$ = 5.0 Hz, $J_{H4'\text{-}Me}$ = 7.0 Hz, $J_{H4'\text{-}Me'}$ = 6.7 Hz, $J_{H2'\text{-}Me}$ = 5.7 Hz}. **18b-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.85 (d, 3H, **Me**CHMe'), 0.89 (d, 3H, MeCH**Me'**), 1.12 (d, 6H, Me_2CH, anomeric), 1.34 (s, 3H, Me), 1.76 (m, 1H, H4'), 3.30 (dd, 2H, **CH**HI, CH**H**I), 3.42 (t, 1H, H3), 3.69 (dd, 2H, $H3'''_a$, $H3'''_b$), 3.77 (m, 1H, H4'), 4.08 (dd, 1H, H4), 4.25 (s, 1H, H3'), 5.75 (s, 1H, H3''), 6.04 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.2 Hz, $J_{H3\text{-}H4}$ = 4.4 Hz, $J_{H3'''a\text{-}H3'''b}$ = -9.8 Hz, $J_{CHHI\text{-}CHHI}$ = -10.2 Hz, $J_{H4\text{-}H4'}$ = 5.0 Hz, $J_{H4\,a\text{-}Me}$ = 7.0 Hz, $J_{H4'a\text{-}Me'}$ = 6.7 Hz, $J_{H2'\text{-}Me}$ = 5.7 Hz}

Oxetane (18c).

Acetal **10h** (68 mg, 0.20 mmol) and cyclohexanol (104 µL, 1.00 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (12 mg, 11% yield) as a clear oil and recovered starting material (60 mg). **18c-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.88 (d, 6H, **Me**CHMe'), 0.91 (d, 6H, MeCH**Me'**), 1.20 - 1.94 (m, 10H, $C_6H_{11}O$), 1.26 (s, 3H, Me), 1.81 (m, 1H, H4'), 2.28 (m, 1H, $C_6H_{11}O$), 3.21 (dd, 2H, **CH**HI, CH**H**I), 3.46 (t, 1H, H3), 3.90 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.04 (dd, 1H, H4), 4.31 (s, 1H, H3'), 5.77 (s, 1H, H3''), 6.08 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.3 Hz, $J_{H3'''a\text{-}H3'''b}$ = -10.3 Hz, $J_{CHHI\text{-}CHHI}$ = -9.7 Hz, $J_{H4\text{-}H4'}$ = 6.8 Hz, $J_{H4'\text{-}Me}$ = 6.6 Hz, $J_{H4'\text{-}Me'}$ = 5.7 Hz}. **18c-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.88 (d, 6H, **Me**CHMe'), 0.91 (d, 6H, MeCH**Me'**), 1.20 - 1.94 (m, 10H, $C_6H_{11}O$), 1.23 (s, 3H, Me), 1.81 (m, 1H, H4'), 2.28 (m, 1H, $C_6H_{11}O$), 3.21 (dd, 2H, CHHI, CHHI), 3.46 (t, 1H, H3), 3.90 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.04 (dd, 1H, H4), 4.31 (s, 1H, H3'), 5.77 (s, 1H, H3''), 6.08 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.3 Hz, $J_{H3'''a\text{-}H3'''b}$ = -10.3 Hz, $J_{CHHI\text{-}CHHI}$ = -9.7 Hz, $J_{H4\text{-}H4'}$ = 6.8 Hz, $J_{H4\text{-}Me}$ = 6.6 Hz, $J_{H4'\text{-}Me'}$ = 5.7 Hz}.



18a, X=EtO
18b, X=Me_2CHO
18c, X=$C_6H_{11}O$
18d, X=$PhCH_2O$
18e, X=HCOO
18f, X=AcO

Oxetane (18d).

Acetal **10h** (68 mg, 0.20 mmol) and benzyl alcohol (105 μL, 1.00 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 3:7), (40 mg, 35% yield) as a light yellow oil and recovered starting material (44 mg). **18d-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.83 (d, 3H, MeCHMe'), 0.87 (d, 3H, MeCHMe'), 1.40 (s, 3H, Me), 1.77 (m, 1H, H4'), 3.43 (t, 1H, H3), 3.44 (s, br, 2H, CHHI, CHHI), 3.84 (dd, 2H, H3'''$_a$, H3'''$_b$), 4.10 (dd, 1H, H4), 4.25 (s, 1H, H3'), 4.49 (s, 2H, OCH_2Ph), 5.74 (s, 1H, H3''), 6.05 (d, 1H, H2), 7.26 - 7.36 (m, 5H, phenyl), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.4 Hz, $J_{H3'''a-H3'''b}$ = -10.4 Hz, $J_{CHHI-CHHI}$ ~ 0 Hz, $J_{H4-H4'}$ = 5.7 Hz, $J_{H4'-Me}$ = 9.0 Hz, $J_{H4'-Me'}$ = 6.7 Hz}. **18d-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.84 (d, 3H, MeCHMe'), 0.85 (d, 3H, MeCHMe'), 1.43 (s, 3H, Me), 1.77 (m, 1H, H4'), 3.43 (t, 1H, H3), 3.45 (dd, 2H, CHHI, CHHI), 3.81 (dd, 2H, H3'''$_a$, H3'''$_b$), 4.10 (dd, 1H, H4), 4.25 (s, 1H, H3'), 4.50 (s, 2H, OCH_2Ph), 5.74 (s, 1H, H3''), 6.05 (d, 1H, H2), 7.26 - 7.36 (m, 5H, phenyl), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.4 Hz, $J_{H3'''a-H3'''b}$ = -9.8 Hz, $J_{CHHI-CHHI}$ = -9.7 Hz, $J_{H4-H4'}$ = 5.7 Hz, $J_{H4'-Me}$ = 1.7 Hz, $J_{H4'-Me'}$ = 5.1 Hz}.

Oxetane (18e)

Acetal **10h** (34 mg, 0.10 mmol) and formic acid (19 μL, 0.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (13 mg, 25% yield) as a colourless oil and recovered starting material (12 mg). {IR (CH_2Cl_2): 1729 cm^{-1}; LRMS (CI-NH_3): m/e 528 ([M + NH_4^+], 14.2%); HRMS (CI-NH_3): m/e calcd. for $C_{13}H_{24}NO_5I_2$ [M + NH_4^+], 527.9744; found, 527.9744}. **18e-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$). δ 0.86 (d, 3H, MeCHMe'), 0.89 (d, 3H, MeCHMe'), 1.63 (s, 3H, Me), 1.81 (m, 1H, H4'), 3.43 (t, 1H, H3), 3.67 (s, br, 2H, CHHI, CHHI), 3.96 (dd, 2H, H3'''$_a$, H3'''$_b$), 4.07 (dd, 1H, H4), 4.25 (s, 1H, H3'), 5.74 (s, 1H, H3''), 6.04 (d, 1H, H2), 7.96 (s, 1H, OCOH), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.4 Hz, $J_{H3'''a-H3'''b}$ = -10.3 Hz, $J_{CHHI-CHHI}$ ~ 0 Hz, $J_{H4-H4'}$ = 8.2 Hz, $J_{H4'-Me}$ = 7.0 Hz, $J_{H4'-Me'}$ = 7.0 Hz}. **18e-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.86 (d, 3H, MeCHMe'), 0.89 (d, 3H, MeCHMe'), 1.64 (s, 3H, Me), 1.80 (m, 1H, H4'), 3.43 (t, 1H, H3), 3.67 (dd, 2H, CHHI, CHHI), 3.99 (dd, 2H, H3'''$_a$, H3'''$_b$), 4.07 (dd, 1H, H4), 4.24 (s, 1H, H3'), 5.74 (s, 1H, H3''), 6.04 (d, 1H, H2), 7.96 (s, 1H, OCOH), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.4 Hz, $J_{H3'''a-H3'''b}$ = -10.5 Hz, $J_{CHHI-CHHI}$ = -10.7 Hz, $J_{H4-H4'}$ = 8.2 Hz, $J_{H4'-Me}$ = 7.0 Hz, $J_{H4'-Me'}$ = 7.0 Hz}.

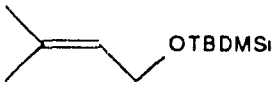
Oxetane (18f).

Acetal **10h** (505 mg, 1.50 mmol) and acetic acid (435 μL, 7.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (566 mg, 72% yield) as a clear oil and recovered starting material (88 mg). {IR ($CDCl_3$): 1734 cm^{-1}}. **18f-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.83 (d, 3H, MeCHMe'), 0.86 (d, 3H, MeCHMe'), 1.55 (s, 3H, Me), 1.73 (m, 1H, H4'), 1.99 (s, 3H, Ac), 3.40 (t, 1H, H3), 3.66 (s, br, 2H, CHHI, CHHI), 3.90 (dd, 2H, H3'''$_a$, H3'''$_b$), 4.03 (dd, 1H, H4), 4.20 (s, 1H, H3'), 5.71 (s, 1H, H3''), 6.01 (d, 1H, H2), J_{H2-H3} = 3.9 Hz, J_{H3-H4} = 4.4 Hz, $J_{H3'''a-H3'''b}$ = -9.5 Hz, $J_{CHHI-CHHI}$ ~ 0

Hz, $J_{H4\text{-}H4'}$ = 7.9 Hz, $J_{H4'\text{-}Me}$ = 7.0 Hz, $J_{H4'\text{-}Me'}$ = 6.9 Hz}. **18f-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.83 (d, 3H, MeCHMe'), 0.86 (d, 3H, MeCHMe'), 1.57 (s, 3H, Me), 1.73 (m, 1H, H4'), 1.99 (s, 3H, Ac), 3.40 (t, 1H, H3), 3.66 (s, br, 2H, CHHI, CHHI), 3.90 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.03 (dd, 1H, H4), 4.20 (s, 1H, H3'), 5.71 (s, 1H, H3''), 6.01 (d, 1H, H2), $J_{H2\text{-}H3}$ = 3.9 Hz, $J_{H3\text{-}H4}$ = 4.4 Hz, $J_{H3'''a\text{-}H3'''b}$ = -9.8 Hz, $J_{CHHI\text{-}CHHI}$ ~ 0 Hz, $J_{H4\text{-}H4'}$ = 7.9 Hz, $J_{H4'\text{-}Me}$ = 7.0 Hz, $J_{H4'\text{-}Me'}$ = 7.0 Hz}.

1-*O*-*t*-Butyldimethylsilyloxy-3-methyl-2-butene (19).

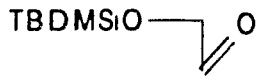
To a solution of 3-methyl-2-buten-1-ol (5.17 g, 60.0 mmol) in dry *N,N*-dimethylformamide (100 mL) under nitrogen at room temperature was added imidazole (10.20 g, 0.15 mol) and *t*-butyldimethylsilyl chloride (10.85 g, 72.0 mmol) and it was allowed to stir until all of the starting material was consumed (20 h). The reaction mixture was diluted with ethyl acetate (600 mL), washed with water (3 x 1 L), dried ($MgSO_4$), filtered and the sovent removed *in vacuo* to yield a yellow oil. Distillation of the crude product (196 °C, 760 mm Hg) gave the title compound (11.88 g, 99% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.05 (s, 6H, *t*-BuSi**Me**$_2$), 0.88 (s, 9H, *t*-Bu), 1.61 (d, 3H, CH_3), 1.69 (d, 3H, CH_3'), 4.15 (d, 2H, CH_2), 5.26 (m, 1H, CH), $J_{CH\text{-}Me}$ = -0.1 Hz, $J_{CH\text{-}Me'}$ = -1.1 Hz, $J_{CH\text{-}CH_2}$ = 6.7 Hz}.



19

2-*t*-Butyldimethylsilyloxyacetaldehyde (20).

Ozone was bubbled through a solution of **19** (11.88 g, 59.4 mmol) in dry methylene chloride (1500 mL) at -78°C until the solution turned blue (12 h). Dimethyl sulfide (21.9 mL, 5 equiv.) was added to the reaction mixture under an atmosphere of nitrogen and it was allowed to warm to ambient temperature gradually overnight. The solution was washed with water (2 x 1 L), brine (1 L), dried (Na_2SO_4), filtered and the solvent removed in vacuo to yield the aldehyde **20** (9.84 g, 95% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.10 (s, 6H, *t*-BuSi**Me**$_2$), 0.92 (s, 9H, ***t*-Bu**Si**Me**$_2$), 4.20 (d, 2H, CH_2), 9.69 (t, 1H, CHO), $J_{CH_2\text{-}CHO}$ = 0.7 Hz}.

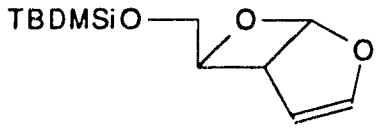


20

6β-*t*-Butyldimethylsilyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (2c).

A mixture of furan (15.6 mL, 0.214 mol) and **20** (9.32 g, 53.6 mmol) in dry benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C and saturated with argon. The solution was

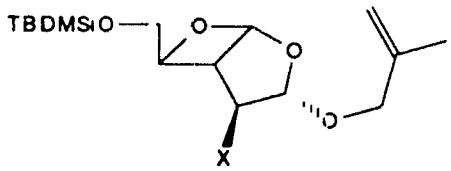
then irradiated for 6 h. Evaporation of the solvent under reduced pressure gave a yellow syrup which was chromatographed over silica gel (petroleum ether / diethyl ether, 4:1 v/v) to give the title compound (4.41 g, 34% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.08 (s, 6H, *t*-BuSi**Me**$_2$), 0.91 (s, 9H, ***t*-Bu**Si**Me**$_2$), 3.65 (dddd, 1H, H5), 3.73 (A of ABX, 1H, H6'$_a$), 3.79 (B of ABX, 1H, H6'$_b$), 4.56 (dddd, 1H, H6), 5.31 (dd, 1H, H4), 6.26 (ddd, 1H, H1), 6.60 (ddd, 1H, H3), J_{H1-H3} = -0.8 Hz, J_{H1-H5} = 4.2 Hz, J_{H1-H6} = -0.8 Hz, J_{H3-H4} = 2.9 Hz, J_{H3-H5} = -1.2 Hz, J_{H4-H5} = 2.9 Hz, $J_{H5\ H6}$ = 2.9 Hz, $J_{H6-H6'a}$ = 2.8 Hz, $J_{H6-H6'b}$ = 3.1 Hz, $J_{H6'a-H6'b}$ = -11.8 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 18.26 [$(CH_3)_3CSiMe_2$], 25.66 [*t*-BuSi**Me**$_2$], 25.83 [$(\mathbf{CH_3})_3CSiMe_2$], 45.91 [C5], 64.73 [C6'], 91.47 [C6], 104.01 [C4], 107.89 [C1], 147.98 [C3]; LRMS (CI-NH_3): m/e 225 ([MH$^+$ - H_2O], 22.2%); HRMS (CI-NH_3): m/e calcd. for $C_{12}H_{21}O_2Si$ [MH$^+$ - H_2O], 225.1310; found, 225.1310}.



2c

3α-Methallyloxy-4β-bromo-6β-*t*-butyldimethylsilyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (21a).

Photo-adduct **2c** (121 mg, 0.50 mmol) and NBS (89 g, 0.50 mmol) in 2-methyl-2-propen-1-ol (5 mL) gave the title compound (66 mg, 34% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.06, 0.08 (2s, 6H, *t*-BuSi**Me**$_2$), 0.90 (s, 9H, *t*-BuSi**Me**$_2$), 1.74 (s, 3H, Me), 3.67 (t, 1H, H5), 3.69 (A of ABX, 1H, H6'$_a$), 3 74 (B of ABX, 1H, H6'$_b$), 4.13 (dd, br, 2H, H3'$_a$, H3'$_b$), 4.32 (s, 1H, H4), 4.54 (ddd, 1H, H6), 4.90, 4.98 (2s, br, 2H, H3'''$_a$, H3'''$_b$), 5.63 (d, 1H, H3), 6.02 (d, 1H, H1), J_{H1-H5} = 4.0 Hz, $J_{H3-H3'a}$ = -0.3 Hz, $J_{H3'a-H3'b}$ = -12.7 Hz, J_{H5-H6} = 4.6 Hz, $J_{H6-H6'a}$ = 1.9 Hz, $J_{H6-H6'b}$ = 3.7 Hz, $J_{H6a-H6'b}$ = -11.9 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$). δ 18.25 [Me_3CSiMe_2], 19.52 [$OCH_2C(\mathbf{CH_3})=CH_2$], 25.70 [$Me_3CSi\mathbf{Me}_2$], 29.45 [$\mathbf{Me}_3CSiMe_2$], 49.25 [C4], 50.84 [C5], 64.03 [*t*-BuSi$Me_2O\mathbf{CH}_2$], 71.56 [$O\mathbf{CH}_2C(CH_3)=CH_2$], 82.11 [C6], 107.95 [C1], 111 60 [$OCH_2C(CH_3)=\mathbf{CH}_2$], 112.63 [C3], 141.01 [$OCH_2\mathbf{C}(CH_3)=CH_2$]; LRMS (CI-$NH_3$): m/e 323, 321 ([MH$^+$ - $H_2C=C(CH_3)CH_2OH$], 24.5%, 30.9%)}.



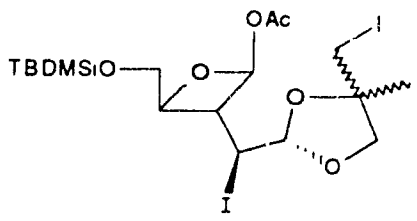
21a, X=Br
21b, X=I

3α-Methallyloxy-4β-iodo-6β-*t*-butyldimethylsilyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (21b).

Photo-adduct **2c** (968 mg, 4.00 mmol) and NIS (900 mg, 4.00 mmol) in 2-methyl-2-propen-1-ol (60 mL) gave the title compound (482 mg, 27% yield) as a clear oil {^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.06, 0.07 (2s, 6H, *t*-BuSi**Me$_2$**), 0.89 (s, 9H, *t*-BuSi**Me$_2$**), 1.73 (s, 3H, Me), 3.68 (A of ABX, 1H, H6'$_a$), 3.71 (B of ABX, 1H, H6'$_b$), 3.76 (t, 1H, H5), 4.12 (dd, br, 2H, H3'$_a$, H3'$_b$), 4.30 (s, 1H, H4), 4.52 (ddd, 1H, H6), 4.89, 4.98 (2s, br, 2H, H3'''$_a$, H3'''$_b$), 5.75 (d, 1H, H3), 6.03 (d, 1H, H1), $J_{H1\ H5}$ = 4.1 Hz, $J_{H3\ H3'a}$ = -0.5 Hz, $J_{H3'a\text{-}H3'b}$ = -12.7 Hz, $J_{H5\text{-}H6}$ = 4.4 Hz, $J_{H6\text{-}H6'a}$ = 3.0 Hz, $J_{H6\text{-}H6'b}$ = 3.5 Hz, $J_{H6a\ H6b}$ = -11.8 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$) δ 18.28 [Me_3CSiMe_2], 19.56 [$OCH_2C(\mathbf{CH_3})=CH_2$], 23.73 [C4], 23.73 [$Me_3CSi\mathbf{Me_2}$], 25.83 [$\mathbf{Me_3}CSiMe_2$], 52.79 [C5], 64.15 [*t*-BuSiMe$_2$O**CH$_2$**], 71.60 [$\mathbf{OCH_2}C(CH_3)=CH_2O$, 83.94 [C6], 108.30 [C1], 112.65 [$OCH_2C(CH_3)\mathbf{CH_2}$], 113.98 [C3], 141.21 [$OCH_2C(CH_3)=CH_2$]; LRMS (CI-$NH_3$): m/e 441 ([MH$^+$], 4.4%), 369 ([MH$^+$ - $H_2C=C(CH_3)CH_2OH$], 100%); HRMS (CI-NH_3) m/e calcd for $C_{12}H_{22}O_3ISi$ [MH$^+$ - $H_2C=C(CH_3)CH_2OH$], 369.0383, found 369.0383}. Anal calcd. for $C_{16}H_{29}O_4I$ C, 43.64; H, 6.64; Si, 6.38, I, 28.82 Found C, 44.12; H, 6.95, Si, 6.23; 28.32.

Oxetane (22).

Acetal **21b** (220 mg, 0.50 mmol) and acetic acid (150 µL, 1.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (147 mg, 47% yield) as a light yellow oil and recovered starting material (101 mg) IR ($CDCl_3$) 1735 cm^{-1}, LRMS (CI-NH_3): m/e 644 ([M + NH_4^+], 100%), 627 ([MH$^+$], 3.8%); HRMS (CI-NH_3) m/e calcd for $C_{18}H_{33}O_6I_2Si$ [MH$^+$], 627.0135, found, 627.0135}. **22-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.06 (s, 6H, *t*-BuSi**Me$_2$**), 0.90 (s, 9H, ***t*-Bu**SiMe$_2$), 1.57 (s, 3H, Me), 2.01 (s, 3H, Ac), 3.70 (s, br, 2H, **CH**HI, CH**H**I), 3.73 (d, 2H, H4'$_a$, H4'$_b$), 3.73 (t, 1H, H3), 3.94 (dd, 2H, H3'''$_a$, H3'''$_b$), 4.28 (s, 1H, H3'), 4.41 (dt, 1H, H4), 5.75 (s, 1H, H3''), 6.03 (d, 1H, H2), $J_{H2\ H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.3 Hz, $J_{H3\ a\text{-}H3\ b}$ = -10.0 Hz, $J_{CHH\text{I-}CHH\text{I}}$ ~ 0 Hz, $J_{H4\ H4'a H4'b}$ = 6.0 Hz} **22-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.07 (s, 6H, *t*-BuSi**Me$_2$**), 0.90 (s, 9H, ***t*-Bu**SiMe$_2$), 1.59 (s, 3H, Me), 2.02 (s, 3H, Ac), 3.69 (dd, 2H, **CH**HI, CH**H**I), 3.73 (d, 2H, H4'$_a$, H4'$_b$), 3.73 (t, 1H, H3), 3.93 (dd, 2H, H3'''$_a$, H3'''$_b$), 4.29 (s, 1H, H3'), 4.41 (dt, 1H, H4), 5.75 (s, 1H, H3''), 6.03 (d, 1H, H2), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.3 Hz, $J_{H3'''a\text{-}H3'''b}$ = -9.7 Hz, $J_{CHH\text{I-}CHH\text{I}}$ = -2.5 Hz, $J_{H4\ H4'a H4'b}$ = 6.0 Hz}



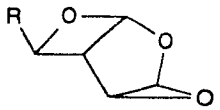
22

Epoxide (23a) of 6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene.

To a solution of **2a** (77 mg, 0.44 mmol) in dry methylene chloride (5 mL) under nitrogen at room temperature was added a 0.1 M solution of dimethyldioxirane in acetone (4.6 mL, 1.05 equiv.) and it was allowed to stir until the reaction was complete (30 min). The solution was evaporated under reduced pressure to afford the epoxide (mixture of 2 inseparable diastereomers, 9:1, exo:endo), (85 mg, 100% yield) as a light yellow oil. {LRMS (CI-NH_3): m/e 208 ([M + NH_4^+], 100%), 191 ([MH^+], 84.8%), HRMS (CI-NH_3) m/e calcd for $C_{11}H_{11}O_3$ [MH^+], 191.0710; found, 191.0708}. **23a-endo:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.27 (ddd, 1H, H5), 3.84 (dd, 1H, H4), 5.63 (d, 1H, H3), 5.64 (d, 1H, H6), 6.41 (d, 1H, H1), 7.26 - 7.47 (m, 5H, Ph), J_{H1-H5} = 3.8 Hz, J_{H3-H4} = 1.8 Hz, J_{H4-H5} = 4.2 Hz, J_{H5-H6} = 3.8 Hz}. **23a-exo:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.42 (t, 1H, H5), 3.93 (d, 1H, H4), 5.47 (d, 1H, H6), 5.48 (d, 1H, H3), 5.85 (d, 1H, H1), 7.26 - 7.47 (m, 5H, Ph), J_{H1-H5} = 3.8 Hz, J_{H3-H4} = 1.8 Hz, J_{H4-H5} = 4.0 Hz}.

Epoxide (23b) of 6β-*i*-propyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene.

To a stirred solution of **2b** (42 mg, 0.30 mmol) in dry methylene chloride (5 mL) under nitrogen at room temperature was added 2-methyl-2-propen-1-ol (25μL, 0.30 mL) and a 0.1 M solution of dimethyldioxirane in acetone (3.0 mL, 1.0 equiv.) and it was allowed to stir until the reaction was complete (1 h). The solution was evaporated under reduced pressure to yield the *exo*-epoxide exclusively (25 mg, 53% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.89 (d, 3H, MeCHMe'), 0.93 (d, 3H, MeCHMe'), 1.93 (m, 1H, H6'), 3.25 (t, 1H, H5), 3.69 (d, 1H, H4), 4.11 (dd, 1H, H6), 5.37 (d, 1H, H3), 5.59 (d, 1H, H1), J_{H1-H5} = 3.9 Hz, J_{H3-H4} = 1.6 Hz, J_{H4-H5} = 4.1 Hz, $J_{H6-H6'}$ = 7.6 Hz, $J_{H6'-Me}$ = 6.7 Hz, $J_{H6'-Me}$ = 6.7 Hz; LRMS (CI-NH_3): m/e 174 ([M + NH_4^+], 100%), 157 ([MH^+], 95.8%); HRMS (CI-NH_3): m/e calcd for $C_8H_{13}O_3$ [MH^+], 157.0859; found, 157.0864}.



23a, R=Ph
23b, R=*i*-Pr

3α-Methoxy-4β-hydroxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (24a).

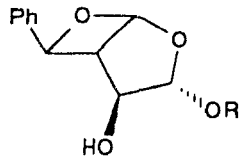
Epoxide **23a** (34 mg, 0.18 mmol) in dry methanol (5 mL) under an atmosphere of nitrogen at room temperature was stirred for 16 h. The solvent was removed *in vacuo* to give the title compound (25 mg, 63% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.97 (d, ex, 1H, OH), 3.17 (dd, 1H, H5), 3.54 (s, 3H, MeO), 4.47 (d, 1H, H4), 5.30 (s, 1H, H3), 5.45 (d, 1H, H6), 6.24 (d, 1H, H1), 7.27 - 7.39 (m, 5H, phenyl), J_{H1-H5} = 4.1 Hz, J_{H4-OH} = 3.4 Hz, J_{H5-H6} = 4.8 Hz}.

3α-Acetoxy-4β-hydroxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (24b).

To a solution of **23a** (41 mg, 0.22 mmol) in dry methylene chloride (5 mL) under an atmosphere of nitrogen at room temperature was added acetic acid (62 μL, 1.10 mmol) and it was allowed to stir for 18 h. The reaction was diluted with methylene chloride (25 mL), washed with saturated aqueous sodium bicarbonate (30 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to yield a yellow residue. Purification by flash chromatography (petroleum ether / diethyl ether, 4:1 v/v) affording **24b** (30 mg, 56% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.17 (s, 3H, Ac), 3.30 (dd, 1H, H5), 4.21 (s, br, 1H, OH), 4.58 (s, 1H, H4), 5.42 (d, 1H, H6), 6.28 (d, 1H, H1), 6.49 (s, 1H, H3), 7.32 - 7.41 (m, 5H, phenyl), $J_{H1\text{-}H5}$ = 4.1 Hz, $J_{H5\text{-}H6}$ = 4.8 Hz}.

3α-Methallyloxy-4β-hydroxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (24c).

To a stirred solution of **23a** (40 mg, 0.21 mmol) in dry methylene chloride (5 mL) under an atmosphere of nitrogen at room temperature was added 2-methyl-2-propen-1-ol (90 μL, 1.05 mmol). After 1 h, the reaction mixture was evaporated to dryness and the residue was chromatographed over silica gel (petroleum ether / diethyl ether, 2:1 v/v) to yield the title compound (35 mg, 63% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.78 (s, 3H, Me), 3.18 (dd, 1H, H5), 4.02 (d, ex, 1H, OH), 4.20 (dd, br, 2H, $H3'_a$, $H3'_b$), 4.53 (d, 1H, H4), 4.93, 5.04 (2s, br, 2H, $H3'''_a$, $H3'''_b$), 5.42 (d, 1H, H3), 5.51 (d, 1H, H6), 6.34 (d, 1H, H1), 7.20 - 7.39 (m, 5H, phenyl), $J_{H1\text{-}H5}$ = 4.1 Hz, $J_{H3\ H3'a}$ = -0.5 Hz, $J_{H3'a\ H3'b}$ = -11.9 Hz, $J_{H4\text{-}OH}$ = 4.5 Hz, $J_{H5\text{-}H6}$ = 4.8 Hz}.



24a, R = CH_3
24b, R = Ac
24c, R = $CH_2C(CH_3)=CH_2$

3α-Methoxy-4β-acetoxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (25a).

Alcohol **24a** (25 mg, 0.11 mmol) was dissolved in dry methylene chloride (5 mL) containing dry pyridine (28 μL, 0.34 mmol) and *N,N*-dimethylaminopyridine (2 mg, 0.01 mmol). Acetic anhydride (16 μL, 0.17 mmol) was then added dropwise, and the reaction was stirred at room temperature under an atmosphere of nitrogen. After 16 h, the reaction was diluted with methylene chloride (25 mL), washed with 5% hydrochloric acid (30 mL), saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a light yellow residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) gave the title compound (16 mg, 55% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.02 (s, 3H, Ac), 3.25 (dd, 1H, H5),

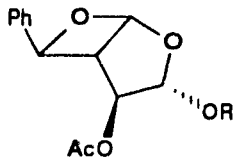
3.57 (s, br, 3H, MeO), 5.33 (s, 1H, H4), 5.35 (d, 1H, H3), 5.54 (d, 1H, H6), 6.23 (d, 1H, H1), 7.28 - 7.42 (m, 5H, phenyl), J_{H1-H5} = 4.1 Hz, $J_{H3-OCHH_2}$ = -0.8 Hz, J_{H5-H6} = 4.8 Hz; LRMS (CI-NH_3): m/e 282 ([M + NH_4^+], 0.5%), 265 ([MH^+], 5.7%), 233 ([MH^+ - MeOH, 73.3%); HRMS (CI-NH_3): m/e calcd. for $C_{14}H_{17}O_5$ [MH^+], 265.1075; found, 265.1075}.

3α-Acetoxy-4β-acetoxy-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (25b).

Alcohol **24b** was acetylated in 58% yield by a procedure similar to that used for the preparation of **25a**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.04 (s, 3H, Ac), 2.19 (s, 3H, Ac, anomeric), 3.32 (t, 1H, H5), 5.45 (s, 1H, H4), 5.53 (d, 1H, H6), 6.26 (d, 1H, H1), 6.56 (s, 1H, H3), 7.34 - 7.42 (m, 5H, phenyl), J_{H1-H5} = 4.1 Hz, J_{H5-H6} = 4.8 Hz; LRMS (CI-NH_3): m/e 293 ([MH^+], 2.0%), 275 ([MH^+ - H_2O], 6.3%), 233 ([MH^+ - AcOH], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{15}H_{17}O_6$ [MH^+], 293.1025; found, 293.1025}.

3α-Methallyloxy-4β-acetoxy-6β-phenyl-2,7-dioxa-bicyclo-heptane (25c).

Alcohol **24c** was acetylated in 71% yield by a procedure similar to that used for the preparation of **25a**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.79 (s, 3H, Me), 2.02 (s, 3H, Ac), 3.26 (dd, 1H, H5), 4.22 (dd, br, 2H, $H3'_a$, $H3'_b$), 4.94, 5.06 (2s, br, 2H, $H3'''_a$, $H3'''_b$), 5.38 (s, 1H, H4), 5.45 (d, 1H, H3), 5.58 (d, 1H, H6), 6.23 (d, 1H, H1), 7.32 - 7.40 (m, 5H, phenyl), J_{H1-H5} = 4.1 Hz, $J_{H3-H3'a}$ = -0.5 Hz, $J_{H3'a-H3'b}$ = -12.2 Hz, J_{H5-H6} = 4.8 Hz; LRMS (CI-NH_3): m/e 305 ([MH^+], 0.5%), 233 ([MH^+ - $H_2C{=}C(CH_3)CH_2OH$], 44.9%); HRMS (CI-NH_3): m/e calcd. for $C_{13}H_{13}O_4$ [MH^+ - $H_2C{=}C(CH_3)CH_2OH$], 233.0813; found, 233.0813}.



25a, R = CH_3
25b, R = Ac
25c, R = $CH_2C(CH_3){=}CH_2$

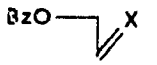
1-O-Benzoyloxy-3-methyl-2-butene (26).

A solution of 3-methyl-2-buten-1-ol (5.17 g, 60.0 mmol) in dry methylene chloride (500 mL) under nitrogen at ambient temperaure containing *N,N*-dimethylaminopyridine (733 mg, 6.00 mmol), pyridine (14.6 mL, 180 mmol) and benzoyl chloride (10.4 mL, 90 mmol) was stirred for 18 h. The solution was washed with 5% hydrochloric acid (450 mL), saturated aqueous sodium bicarbonate (450 mL), brine (450 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a yellow oil. Distillation of the crude product (101-102°C, 1.4 mm Hg) gave the title compound contaminated by an impurity which codistilled. Chromatography over silica gel (petroleum ether / ethyl

acetate, 10:1 v/v) afforded pure **26** in quantitative yield (11.39 g) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.76 (d, 3H, CH_3), 1.77 (d, 3H, CH_3'), 4.78 (d, 1H, CHH), 4.82 (d, 1H, CHH), 5.45 (m, 1H, CH), 7.36 - 7.71 (m, 3H, Ph), 8.00 - 8.06 (m, 2H, Ph), $J_{CH\text{-}Me}$ = -1.0 Hz, $J_{CH\text{-}Me'}$ = -1.0 Hz, $J_{CHH\text{-}CH}$ = 7.1 Hz, $J_{CHH\text{-}CH}$ = 7.1 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 25.55 [CH_3], 25.56 [CH_3'], 61.47 [CH_2], 118.58 [CH], 127.95, 130.27, 132.42 [aromatic CH], 129.27 [aromatic C], 138.57 [$(CH_3)_2C$], 166.16 [CO]; IR ($CDCl_3$): 1714 cm^{-1}}.

2-Benzoyloxyacetaldehyde (27).

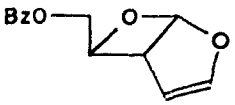
2-Benzoyloxyacetaldehyde was obtained from olefin **26** as described for the preparation of aldehyde **20**. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) gave the title compound (95% yield) as a viscous light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 4.88 (d, 2H, CH_2), 7.41 - 7.64 (m, 3H, Ph), 8.03 - 8.12 (m, 2H, Ph), 9.71 (t, 1H, CHO), $J_{CH_2\text{-}CHO}$ = 0.6 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 68.94 [CH_2], 128.47, 129.84, 133.55 [aromatic CH], 128.78 [aromatic C], 165.89 [Ph-CO], 195.83 [CHO]; IR ($CDCl_3$): 1728 cm^{-1}, 1759 cm^{-1}, 2717 cm^{-1}, 2825 cm^{-1}}.



26, X=$C(CH_3)_2$
27, X=O

6β-Benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (2d).

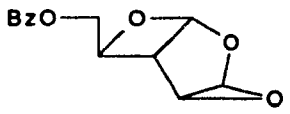
A mixture of furan (17.5 mL, 240.6 mmol) and **27** (10.11 g, 61.6 mmol) in dry benzene (320 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C and saturated with argon. The solution was then irradiated for 8 h. Evaporation under reduced pressure gave a yellow syrup which was chromatographed over silica gel (petroleum ether / ethyl acetate, 9:1 v/v) to give the title compound (4..31 g, 30% yield) as a light yellow oil, and unreacted aldehyde (5.74 g). {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.75 (dddd, 1H, H5), 4.55 (d, 2H, $H6'_a$, $H6'_b$), 4.85 (m, 1H, H6), 5.37 (dd, 1H, H4), 6.39 (ddd, 1H, H1), 6.64 (ddd, 1H, H3), 7.28 - 7.58 (m, 3H, Ph), 8.05 - 8.10 (m, 2H, Ph), $J_{H1\text{-}H3}$ = -0.9 Hz, $J_{H1\text{-}H5}$ = 4.2 Hz, $J_{H1\text{-}H6}$ = -0.8 Hz, $J_{H3\text{-}H4}$ = 2.8 Hz, $J_{H3\text{-}H5}$ = -1.3 Hz, $J_{H4\text{-}H5}$ = 2.9 Hz, $J_{H5\text{-}H6}$ = 3.5 Hz, $J_{H6\text{-}H6'a}$ = 3.5 Hz, $J_{H6\text{-}H6'b}$ = 3.5 Hz, $J_{H6'a\text{-}H6'b}$ ~ 0 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 46 61 [C5], 65.95 [C6'], 88.40 [C6], 103.65 [C4], 107.85 [C1], 128.46, 129.61, 133.27 [aromatic CH], 128.50 [aromatic C], 148.39 [C3], 166.20 [CO]; LRMS (CI-NH_3): m/e 250 ([M + NH_4^+], 6.5%), 215 ([MH^+ - H_2O], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{13}H_{11}O_3$ [MH^+ - H_2O], 205.0709; found, 205.0708}. Anal. calcd. for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 66.87; H, 5.60.



2d

Epoxide (23d) of 6β-Benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene.

Epoxide **23d** (mixture of 2 inseparable diastereomers, 9:1 exo / endo) was obtained in quantitative yield from **2d** by a procedure similar to that used for **23a**. {LRMS (CI-NH_3): m/e 266 ([M + NH_4^+], 25.8%), 249 ([MH^+], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{13}H_{13}O_5$ [MH^+], 249.0762; found, 249.0762}. **23d-endo:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.38 (dddd, 1H, H5), 3.78 (dd, 1H, H4) 4.47 (A of ABX, 1H, H6'$_a$), 4.57 (B of ABX, 1H, H6'$_b$), 4.88 (ddd, 1H, H6), 5.63 (dd, 1H, H3), 6.22 (d, 1H, H1), 7.29 - 7.61 (m, 3H, Ph), 8.00 - 8.05 (m, 2H, Ph), J_{H1-H5} = 4.2 Hz, J_{H3-H4} = 1.5 Hz, J_{H4-H5} = 3.6 Hz, J_{H5-H6} = 4.0 Hz, $J_{H6-H6'a}$ = 4.0 Hz, $J_{H6-H6'b}$ = 3.0 Hz, $J_{H6'a-H6'b}$ = -12.5 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 42.23 [C5], 55.11 [C4], 65.25 [C6'], 76.43 [C6], 88.33 [C3], 112.76 [C1], 128.32, 129.53, 133.14 [aromatic CH], 129.29 [aromatic C], 166.05 [CO]}. **23d-exo:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.58 (t, 1H, H5), 3.83 (dd, 1H, H4) 4.46 (A of ABX, 1H, H6'$_a$), 4.56 (B of ABX, 1H, H6'$_b$), 4.77 (ddd, 1H, H6), 5.41 (dd, 1H, H3), 5.74 (d, 1H, H1), 7.29 - 7.61 (m, 3H, Ph), 8.00 - 8.05 (m, 2H, Ph), J_{H1-H5} = 3.6 Hz, J_{H3-H4} = 1.4 Hz, J_{H5-H6} = 3.8 Hz, $J_{H6-H6'a}$ = 4.0 Hz, $J_{H6-H6'b}$ = 3.1 Hz, $J_{H6'a-H6'b}$ = -12.6 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 43.57 [C5], 56.68 [C4], 65.21 [C6'], 75.62 [C6], 82.55 [C3], 107.82 [C1], 128.48, 129.79, 133.38 [aromatic CH], 129.57 [aromatic C], 166.05 [CO]}.



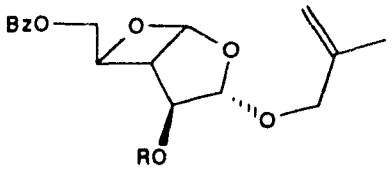
23d

3α-Methallyloxy-4β-hydroxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (28).

To a solution of epoxide **23d** (313 mg, 1.26 mmol) in dry methylene chloride (50 mL) under nitrogen at room temperature was added 2-methyl-2-propen-1-ol (1.10 mL, 12.60 mmol) and the reaction mixture was allowed to stir for 6 h. Evaporation to dryness gave **28** (359 mg, 89% yield) as a light yellow oil which was used without further purification. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.72 (s, 3H, Me), 2.88 (s, br, ex, 1H, OH), 3.30 (t, 1H, H5), 4.11 (dd, br, 2H, H3'$_a$, H3'$_b$), 4.38 (s, br, 1H, H4), 4.44 (A of ABX, 1H, H6'$_a$), 4.53 (B of ABX, 1H, H6'$_b$), 4.83 (ddd, 1H, H6), 4.89, 4.89 (2s, br, 2H, H3'''$_a$, H3'''$_b$), 5.36 (d, 1H, H3), 6.06 (d, 1H, H1), 7.30 - 7.60 (m, 3H, phenyl), 8.00 - 8.07 (m, 2H, phenyl), J_{H1-H5} = 4.0 Hz, $J_{H3-H3'a}$ = -0.2 Hz, $J_{H3'a-H3'b}$ = -12.5 Hz, J_{H5-H6} = 4.4 Hz, $J_{H6-H6'a}$ = 4.3 Hz, $J_{H6-H6'b}$ = 3.2 Hz, $J_{H6'a-H6'b}$ = -12.4 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 19.49 [$OCH_2C(CH_3)=CH_2$], 49.95 [C5], 65.84 [C6'], 71.33 [$OCH_2C(CH_3)=CH_2$], 76.45 [C4], 76.45 [C6], 107.84 [C1], 111.76 [C3], 112.52 [$OCH_2C(CH_3)=CH_2$], 128.40, 129.59, 133.26 [aromatic CH], 129.46 [aromatic C], 141.20 [$OCH_2C(CH_3)=CH_2$], 166.42 [CO]}.

3α-Methallyloxy-4β-acetoxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (29a).

Alcohol **28** was acetylated in 84% yield by a procedure similar to that used for the preparation of **25a**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.72 (s, 3H, Me), 2.04 (s, 3H, Ac), 3.37 (t, 1H, H5), 4.17 (dd, br, 2H, $H3'_a$, $H3'_b$), 4.46 (A of ABX, 1H, $H6'_a$), 4.56 (B of ABX, 1H, $H6'_b$), 4.88 (ddd, 1H, H6), 4.91, 5.03 (2s, br, 2H, $H3'''_a$, $H3'''_b$), 5.25 (s, 1H, H4), 5.41 (d, 1H, H3), 6.08 (d, 1H, H1), 7.40 - 7.59 (m, 3H, phenyl), 8 05 - 8.10 (m, 2H, phenyl), J_{H1-H5} = 4.1 Hz, $J_{H3-H3'a}$ = -0.8 Hz, $J_{H3'a-H3'b}$ = -12.5 Hz, J_{H5-H6} = 4.6 Hz, $J_{H6-H6'a}$ = 4.1 Hz, $J_{H6-H6'b}$ = 3.4 Hz, $J_{H6'a-H6'b}$ = -12.4 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 19 45 [$OCH_2C(\mathbf{CH_3})=CH_2$], 20.74 [$\mathbf{CH_3}CO$], 47.51 [C5], 65.56 [C6'], 71.49 [$\mathbf{OCH_2}C(CH_3)=CH_2$], 76.24 [C6], 77.90 [C4], 107.61 [C1], 109.10 [C3], 112.94 [$OCH_2C(CH_3)=\mathbf{CH_2}$], 128.39, 129.64, 133.18 [aromatic CH], 129.64 [aromatic C], 140.94 [$OCH_2\mathbf{C}(CH_3)=CH_2$], 166.42 [PhCO], 169.71 [CH_3CO]; LRMS (Cl-NH_3): m/e 363 ([MH^+], 1.4%), 291 ([MH^+ - $H_2C=C(CH_3)CH_2OH$], 17.2%)}. Anal. calcd. for $C_{19}H_{22}O_7$: C, 62.97; H, 612. Found: C, 62.66; H, 6.22}.



28, R=OH
29a, R=Ac
29b, R=MeOOCCO
29c, R=Bz

3α-Methallyloxy-4β-methyloxalyloxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (29b).

To a solution of alcohol **28** (1.290 g, 4.03 mmol) in dry methylene chloride (350 mL) under nitrogen at 0°C was added *N,N*-dimethylaminopyridine (49 mg, 0.40 mmol), pyridine (978 μL, 12.10 mmol) and methyl oxalyl chloride (556 μL, 6.05 mmol). The solution was gradually warmed to ambient temperature (over 1 h) and allowed to stir for 18 h. It was washed with 5% hydrochloric acid (500 mL), saturated aqueous sodium bicarbonate (500 mL), brine (500 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a yellow syrup. Flash chromatography of the residue (petroleum ether / ethyl acetate, 2:1 v/v) gave the title compound (1.18 g, 72% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.76 (s, 3H, Me), 3.51 (dd, 1H, H5), 3.87 (s, 3H, MeO), 4 18 (dd, br, 2H, $H3'_a$, $H3'_b$), 4.46 (A of ABX, 1H, $H6'_a$), 4.58 (B of ABX, 1H, $H6'_b$), 4.89 (ddd, 1H, H6), 4.94, 5.02 (2s, br, 2H, $H3'''_a$, $H3'''_b$), 5.38 (s, 1H, H4), 5.50 (d, 1H, H3), 6.11 (d, 1H, H1), 7.40 - 7.58 (m, 3H, phenyl), 8.04 - 8.09 (m, 2H, phenyl), J_{H1-H5} = 4.0 Hz, $J_{H3-H3'a}$ = -1.0 Hz, $J_{H3'a-H3'b}$ = -12.6 Hz, J_{H5-H6} = 4.4 Hz, $J_{H6-H6'a}$ = 3.8 Hz, $J_{H6-H6'b}$ = 3.5 Hz, $J_{H6'a-H6'b}$ = -12.4 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2)· δ 19.59 [$OCH_2C(CH_3)=CH_2$], 47.58 [C5], 54.10 [MeO], 65.53 [C6'], 72.00 [$OCH_2C(CH_3)=CH_2$], 76.53 [C6], 80.59 [C4], 108.04 [C1], 109.05 [C3], 113.04 [$OCH_2C(CH_3)=\mathbf{CH_2}$], 128.84, 129.94, 134.02

[aromatic **CH**], 130.36 [aromatic **C**], 141.48 [$OCH_2C(CH_3)=CH_2$], 156.75, 166.38, 166.44 [**CO**]; IR (CH_2Cl_2): 1722 cm^{-1}, 1751 cm^{-1}, 1775 cm^{-1}; LRMS (CI-NH_3): m/e 424 ([M + NH_4^+], 100%)].

3α-Methallyloxy-4β-benzoyloxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (29c).

Alcohol **28** was benzoylated in 88% yield by a procedure similar to that used for the preparation of **26**. [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.79 (s, 3H, Me), 3.54 (t, 1H, H5), 4.22 (dd, br, 2H, $H3'_a$, $H3'_b$), 4.49 (A of ABX, 1H, $H6'_a$), 4.61 (B of ABX, 1H, $H6'_b$), 4.96 (ddd, 1H, H6), 4.96, 5.06 (2s, br, 2H, $H3'''_a$, $H3'''_b$), 5.51 (s, 1H, H4), 5.58 (d, 1H, H3), 6.16 (d, 1H, H1), 7.35 - 7.60 (m, 6H, phenyl), 7.96 - 8.12 (m, 4H, phenyl), J_{H1-H5} = 4.0 Hz, $J_{H3-H3'a}$ = -0.8 Hz, $J_{H3'a-H3'b}$ = -12.8 Hz, J_{H5-H6} = 4.5 Hz, $J_{H6-H6'a}$ = 4.1 Hz, $J_{H6-H6'b}$ = 3.3 Hz, $J_{H6'a-H6'b}$ = -12.4 Hz; LRMS (CI-NH_3): m/e 425 ([MH^+], 7.9%), 353 ([MH^+ - $H_2C=C(CH_3)CH_2OH$], 10.2%)].

Oxetane (30a).

Reaction of **29a** (298 mg, 0.82 mmol) and acetic acid (269 μL, 4.12 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (113 mg, 25% yield) as a light yellow oil and recovered starting material (70 mg). **30a-minor:** [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.61 (s, 3H, Me), 2.02 (s, 3H, Ac) 2.04 (s, 3H, Ac, anomeric), 3.37 (t, 1H, H3), 3.70 (s, br, 2H, CHHI, CHHI), 3.98 (dd, br, 2H, $H3'''_a$, $H3'''_b$), 4.47 (A of ABX, 1H, $H4'_a$), 4.55 (B of ABX, 1H, $H4'_b$), 4.77 (ddd, 1H, H4), 5.27 (s, 1H, H3'), 5.40 (d, 1H, H3''), 6.08 (d, 1H, H1), 7.40 - 7.61 (m, 3H, phenyl), 8.03 - 8.07 (m, 2H, phenyl), J_{H2-H3} = 4.0 Hz, J_{H3-H4} = 4.4 Hz, $J_{H3''-H3'''a}$ = -0.9 Hz, $J_{H3'''a-H3'''b}$ = -9.9 Hz, $J_{CHHI-CHHI}$ ~ 0 Hz, $J_{H4-H4'a}$ = 4.3 Hz, $J_{H4-H4'b}$ = 3.4 Hz, $J_{H4'a-H4'b}$ = -12.4 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 11.10 [CH_2I], 20.78 [CH_3], 21.09, 21.98 [CH_3CO], 47.39 [C3], 65.60 [C4'], 70.92 [C3'''], 76.15 [C4], 77.81 [C3'], 79.62 [CCH_2I], 107.99 [C2], 109.62 [C3''], 128.47, 129.68, 133.28 [aromatic CH], 129.61 [aromatic C], 166.15 [PhCO], 169.72, 170.32 [CH_3CO]]. **30a-major:** [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.61 (s, 3H, Me), 2.01 (s, 3H, Ac) 2.03 (s, 3H, Ac, anomeric), 3.35 (t, 1H, H3), 3.73 (dd, 2H, CHHI, CHHI), 3.97 (dd, br, 2H, $H3'''_a$, $H3'''_b$), 4.47 (A of ABX, 1H, $H4'_a$), 4.55 (B of ABX, 1H, $H4'_b$), 4.77 (ddd, 1H, H4), 5.23 (s, 1H, H3'), 5.41 (d, 1H, H3''), 6.07 (d, 1H, H1), 7.40 - 7.61 (m, 3H, phenyl), 8.03 - 8.07 (m, 2H, phenyl), J_{H2-H3} = 3.6 Hz, J_{H3-H4} = 4.7 Hz, $J_{H3''-H3'''a}$ = -0.8 Hz, $J_{H3'''a-H3'''b}$ = -9.5 Hz, $J_{CHHI-CHHI}$ = -10.5 Hz, $J_{H4-H4'a}$ = 4.3 Hz, $J_{H4-H4'b}$ = 3.4 Hz, $J_{H4'a-H4'b}$ = -12.4 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 11.67 [CH_2I], 20.78 [CH_3], 20.78, 21.45 [CH_3CO], 47.56 [C3], 65.42 [C4'], 70.40 [C3'''], 76.25 [C4], 77.72 [C3'], 79.58 [CCH_2I], 107.71 [C2], 110.21 [C3''], 128.47, 129.68, 133.28 [aromatic CH], 129.61 [aromatic C], 166.15 [PhCO], 169.61, 170.06 [CH_3CO]].

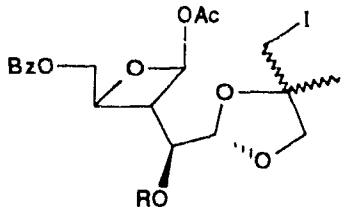
Oxetane (30b).

Reaction of **29b** (32 mg, 0.08 mmol) and acetic acid (25 μL, 0.40 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (7 mg, 15% yield). [IR (CH_2Cl_2): 1717 cm^{-1},

1722 cm^{-1}, 1751 cm^{-1}, 1774 cm^{-1}}. **30b-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.62 (s, 3H, Me), 2.02 (s, 3H, Ac), 3.52 (t, 1H, H3), 3.78 (dd, 2H, CHHI, CHHI), 3.89 (s, 3H, MeO), 4.00 (dd, br, 2H, $H3'''_a$, $H3'''_b$), 4.47 (A of ABX, 1H, $H4'_a$), 4.59 (B of ABX, 1H, $H4'_b$), 4.80 (ddd, 1H, H4), 5.39 (s, 1H, H3'), 5.54 (d, 1H, H3'), 6.10 (d, 1H, H1), 7.42 - 7.62 (m, 3H, phenyl), 8.03 - 8.09 (m, 2H, phenyl), J_{H2-H3} = 3.9 Hz, J_{H3-H4} = 4.3 Hz, $J_{H3''-H3'''a}$ = -0.9 Hz, $J_{H3'''a-H3'''b}$ = -10.1 Hz, $J_{CHHI-CHHI}$ = -9.7 Hz, $J_{H4\ H4'a}$ = 4.1 Hz, $J_{H4-H4'b}$ = 3.6 Hz, $J_{H4'a-H4'b}$ = -12.5 Hz}. **30b-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.56 (s, 3H, Me), 2.02 (s, 3H, Ac), 3.52 (t, 1H, H3), 3.79 (dd, 2H, CHHI, CHHI), 3.89 (s, 3H, MeO), 4.00 (dd, br, 2H, $H3'''_a$, $H3'''_b$), 4.47 (A of ABX, 1H, $H4'_a$), 4.59 (B of ABX, 1H, $H4'_b$), 4.80 (ddd, 1H, H4), 5.38 (s, 1H, H3'), 5.52 (d, 1H, H3''), 6.12 (d, 1H, H1), 7.42 - 7.62 (m, 3H, phenyl), 8.03 - 8.09 (m, 2H, phenyl), J_{H2-H3} = 3.7 Hz, J_{H3-H4} = 4.3 Hz, $J_{H3''-H3'''a}$ = -0.9 Hz, $J_{H3'''a-H3'''b}$ = -10.1 Hz, $J_{CHHI-CHHI}$ = -10.3 Hz, $J_{H4-H4'a}$ = 4.1 Hz, $J_{H4-H4'b}$ = 3.6 Hz, $J_{H4'a-H4'b}$ = -12.5 Hz}.

Oxetane (30c).

Reaction of **29c** (45 mg, 0.11 mmol) and acetic acid (32 μL, 0.53 mmol) gave the title compound (mixture of 2 diastereomers, 4:6), (24 mg, 37% yield) as a light yellow oil and recovered starting material (11 mg). **30c-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.54 (s, 3H, Me), 2.03 (s, 3H, Ac), 3.51 (t, 1H, H3), 3.74 (s, br, 2H, CHHI, CHHI), 4.02 (dd, br. 2H, $H3'''_a$, $H3'''_b$), 4.49 (A of ABX, 1H, $H4'_a$), 4.61 (B of ABX, 1H, $H4'_b$), 4.87 (ddd, 1H, H4), 5.51 (s, 1H, H3'), 5.57 (d, 1H, H3''), 6.15 (d, 1H, H1), 7.38 - 7.61 (m, 6H, phenyl), 7.96 - 8.10 (m, 4H, phenyl), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.3 Hz, $J_{H3''-H3'''a}$ = -1.3 Hz, $J_{H3'''a-H3'''b}$ = -10.1 Hz, $J_{CHHI-CHHI}$ ~ 0 Hz, $J_{H4-H4'a}$ = 4.1 Hz, $J_{H4-H4'b}$ = 3.4 Hz, $J_{H4'a-H4'b}$ = -12.5 Hz}. **30c-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.64 (s, 3H, Me), 2.03 (s, 3H, Ac), 3.51 (t, 1H, H3), 3.76 (dd, 2H, CHHI, CHHI), 4.03 (dd, br, 2H, $H3'''_a$, $H3'''_b$), 4.47 (A of ABX, 1H, $H4'_a$), 4.59 (B of ABX, 1H, $H4'_b$), 4.87 (ddd, 1H, H4), 5.50 (s, 1H, H3'), 5.58 (d, 1H, H3''), 6.14 (d, 1H, H1), 7.38 - 7.61 (m, 6H, phenyl), 7.96 - 8.10 (m, 4H, phenyl), J_{H2-H3} = 4.0 Hz, J_{H3-H4} = 4.3 Hz, $J_{H3''-H3'''a}$ = -1.0 Hz, $J_{H3'''a-H3'''b}$ = -9.8 Hz, $J_{CHHI-CHHI}$ = -10.5 Hz, $J_{H4-H4'a}$ = 4.1 Hz, $J_{H4-H4'b}$ = 3.4 Hz, $J_{H4'a-H4'b}$ = -12.5 Hz}.



30a, R=Ac
30b, R=MeOOCCO
30c, R=Bz

Oxetane (31a).

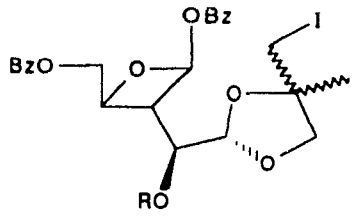
Acetal **29a** (36 mg, 0.10 mmol) and benzoic acid (61 mg, 0.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 3:7), (40 mg, 66% yield) as a light yellow oil and recovered staring material (7 mg). **31a-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.76 (s, 3H, Me), 2.01 (s, 3H, Ac), 3.37 (t, 1H, H3), 3.84 (dd, 2H, CHHI, CHHI), 4.16 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.43 (A of ABX, 1H, $H4'_a$), 4.55 (B of ABX, 1H, $H4'_b$), 4.73 (ddd, 1H, H4), 5.23 (s, 1H, H3'), 5.46 (s, 1H, H3''), 6.08 (d, 1H, H1), 7.37 - 7.57 (m, 6H, phenyl), 7.98 - 8.12 (m, 4H, phenyl), $J_{H2\text{-}H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.1 Hz, $J_{H3'''a\text{-}H3'''b}$ = -9.9 Hz, $J_{CHHI\text{-}CHHI}$ = -10.9 Hz, $J_{H4\text{-}H4'a}$ = 3.7 Hz, $J_{H4\text{-}H4'b}$ = 3.9 Hz, $J_{H4'a\text{-}H4'b}$ = -12.5 Hz}. **31a-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.77 (s, 3H, Me), 2.03 (s, 3H, Ac), 3.35 (t, 1H, H3), 3.86 (dd, 2H, CHHI, CHHI), 4.17 (dd, 2H, $H3'''_a$, $H3'''_b$), 4.43 (A of ABX, 1H, $H4'_a$), 4.55 (B of ABX, 1H, $H4'_b$), 4.73 (ddd, 1H, H4), 5.23 (s, 1H, H3'), 5.46 (s, 1H, H3''), 6.08 (d, 1H, H1), 7.37 - 7.57 (m, 6H, phenyl), 7.98 - 8.12 (m, 4H, phenyl), $J_{H2\ H3}$ = 4.1 Hz, $J_{H3\text{-}H4}$ = 4.3 Hz, $J_{H3'''a\text{-}H3'''b}$ = -9.8 Hz, $J_{CHHI\text{-}CHHI}$ = -10.6 Hz, $J_{H4\text{-}H4'a}$ = 3.7 Hz, $J_{H4\text{-}H4'b}$ = 3.9 Hz, $J_{H4'a\text{-}H4'b}$ = -12.5 Hz}.

Oxetane (31b).

Acetal **29b** (609 mg, 1.50 mmol) and benzoic acid (920 mg, 7.50 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 3:7), (578 mg, 59% yield) as a light yellow oil and recovered starting material (56 mg). {IR (CH_2Cl_2): 1717 cm^{-1}, 1722 cm^{-1}, 1751 cm^{-1}, 1774 cm^{-1}}. **31b-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.77 (s, 3H, Me), 3.52 (t, 1H, H3), 3.70 (m, 2H, CHHI, CHHI), 3.88 (s, 3H, MeO), 4.18 (dd, br, 2H, $H3'''_a$, $H3'''_b$), 4.42 (A of ABX, 1H, $H4'_a$), 4.52 (B of ABX, 1H, $H4'_b$), 4.74 (ddd, 1H, H4), 5.39 (s, 1H, H3'), 5.50 (d, 1H, H3''), 6.11 (d, 1H, H1), 7.37 - 7.58 (m, 6H, phenyl), 7.98 - 8.11 (m, 4H, phenyl), $J_{H2\text{-}H3}$ = 4.0 Hz, $J_{H3\text{-}H4}$ = 3.8 Hz, $J_{H3''\text{-}H3'''a}$ = -0.9 Hz, $J_{H3'''a\text{-}H3'''b}$ = -10.1 Hz, $J_{H4\text{-}H4'a}$ = 0.9 Hz, $J_{H4\text{-}H4'b}$ = 3.8 Hz, $J_{H4'a\text{-}H4'b}$ = -12.4 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 11.68 [$\mathbf{CH_2}$I], 21.62 [$\mathbf{CH_3}$], 47.49 [C3], 54.10 [**MeO**], 65.48 [**C6'**], 71.34 [C3'''], 76.53 [C4], 80.41 [C3'], 80.53 [$\mathbf{CCH_2}$I], 108.18 [C2], 109.89 [C3''], 128.79, 128.84, 129.94, 130.36, 133.63, 134.02 [aromatic **CH**], 129.72, 130.13 [aromatic **C**], 156.75, 166.38, 166.44, 171.14 [**CO**]}. **31b-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.78 (s, 3H, Me), 3.48 (t, 1H, H3), 3.86 (m, 2H, CHHI, CHHI), 3.88 (s, 3H, MeO), 4.19 (dd, br, 2H, $H3'''_a$, $H3'''_b$), 4.42 (A of ABX, 1H, $H4'_a$), 4.52 (B of ABX, 1H, $H4'_b$), 4.74 (ddd, 1H, H4), 5.37 (s, 1H, H3'), 5.57 (d, 1H, H3''), 6.11 (d, 1H, H1), 7.37 - 7.58 (m, 6H, phenyl), 7.98 - 8.11 (m, 4H, phenyl), $J_{H2\text{-}H3}$ = 3.7 Hz, $J_{H3\text{-}H4}$ = 3.9 Hz, $J_{H3''\text{-}H3'''a}$ = -0.9 Hz, $J_{H3'''a\text{-}H3'''b}$ = -9.8 Hz, $J_{H4\text{-}H4'a}$ = 0.9 Hz, $J_{H4\text{-}H4'b}$ = 3.8 Hz, $J_{H4'a\text{-}H4'b}$ = -12.4 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 12.10 [$\mathbf{CH_2}$I], 21.78 [$\mathbf{CH_3}$], 47.58 [C3], 54.10 [**MeO**], 65.76 [C6'], 71.07 [C3'''], 76.53 [**C4**], 80.29 [C3'], 80.53 [$\mathbf{CCH_2}$I], 108.04 [C2], 109.94 [C3''], 128.79, 128.84, 129.94, 130.36, 133.63, 134.02 [aromatic **CH**], 129.72, 130.13 [aromatic **C**], 156.75, 166.38, 166.44, 171.14 [**CO**]}.

Oxetane (31c).

Acetal **29c** (45 mg, 0.11 mmol) and benzoic acid (65 mg, 0.53 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 4:6), (32 mg, 45% yield) as a yellow oil and recovered starting material (8 mg). **31c-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.81 (s, 3H, Me), 3.50 (t, 1H, H3), 3.87 (dd, 2H, CHHI, CHHI), 4.22 (dd, 2H, H3'''$_a$, H3'''$_b$), 4.46 (A of ABX, 1H, H4'$_a$), 4.53 (B of ABX, 1H, H4'$_b$), 4.82 (ddd, 1H, H4), 5.50 (s, 1H, H3'), 5.61 (s, 1H, H3''), 6.14 (d, 1H, H1), 7.37 - 7.64 (m, 9H, phenyl), 7.93 - 8.13 (m, 6H, phenyl), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.4 Hz, $J_{H3'''a-H3'''b}$ = -9.7 Hz, $J_{CHHI-CHHI}$ = -10.5 Hz, $J_{H4-H4'a}$ = 3.7 Hz, $J_{H4-H4'b}$ = 4.0 Hz, $J_{H4'a-H4'b}$ = -12.3 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 11.94 [$\mathbf{CH_2}$I], 21.68 [$\mathbf{CH_3}$], 47.85 [C3], 65.74 [C6'], 71.00 [C3'''], 76.81 [C4], 78.71 [C3'], 80.65 [CCH_2I], 108.30 [C2], 110.73 [C3''], 128.70, 128.74, 128.83, 129.96, 130.10, 130.36, 133.58, 133.90, 133.97 [aromatic **CH**], 128.84, 129.17, 130.39 [aromatic C], 165.67, 166.77, 171.20 [CO]}. **31c-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.80 (s, 3H, Me), 3.50 (t, 1H, H3), 3.89 (dd, 2H, CHHI, CHHI), 4.22 (dd, 2H, H3'''$_a$, H3'''$_b$), 4.46 (A of ABX, 1H, H4'$_a$), 4.53 (B of ABX, 1H, H4'$_b$), 4.82 (ddd, 1H, H4), 5.49 (s, 1H, H3'), 5.64 (s, 1H, H3''), 6.14 (d, 1H, H1), 7.37 - 7.64 (m, 9H, phenyl), 7.93 - 8.13 (m, 6H, phenyl), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.4 Hz, $J_{H3'''a-H3'''b}$ = -9.8 Hz, $J_{CHHI-CHHI}$ = -10.5 Hz, $J_{H4-H4'a}$ = 3.7 Hz, $J_{H4-H4'b}$ = 4.0 Hz, $J_{H4'a-H4'b}$ = -12.3 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 12.34 [$\mathbf{CH_2}$I], 21.82 [$\mathbf{CH_3}$], 47.89 [C3], 65.80 [C6'], 71.30 [C3'''], 76.81 [C4], 78.71 [C3'], 80.55 [CCH_2I], 108.34 [C2], 110.73 [C3''], 128.70, 128.74, 128.83, 129.96, 130.10, 130.36, 133.58, 133.90, 133.97 [aromatic **CH**], 128.84, 129.17, 130.39 [aromatic C], 165.56, 166.45, 171.20 [CO]}.



31a, R=Ac
31b, R=MeOOCCO
31c, R=Bz
33, R=Bz, I=H

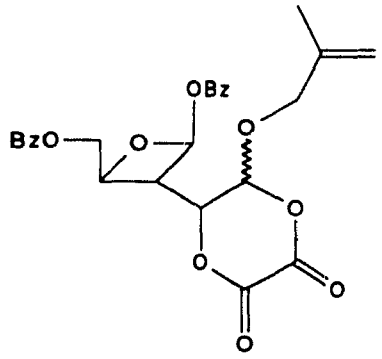
Oxetane (33).

To a solution of **31c** (67 mg, 0.10 mmol) in 7 mL of dry benzene under an atmosphere of nitrogen at room temperature was added pyridine (24 μL, 0.30 mmol) and Bu_3SnH (54 μL, 0.20 mmol). After refluxing for 15 h, tlc indicated complete disappearance of starting material. The solution was evaporated under reduced pressure and the residue purified by flash chromatography (petroleum ether / ethyl acetate, 2:1 v/v) to afford the deiodinated compound (27 mg, 50% yield) as a clear oil {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.65, 1.66 (2s, 6H, Me), 3.56 (t, 1H, H3), 4.03 (dd, br, 2H, H3'''$_a$, H3'''$_b$), 4.36 (A of ABX, 1H, H4'$_a$), 4.42 (B of ABX, 1H, H4'$_b$), 4.86 (ddd, 1H, H4), 5.51 (s, 1H, H3'), 5.64 (d, 1H, H3''),

6.13 (d, 1H, H1), 7.34 - 7.64 (m, 9H, phenyl), 7.93 - 8.12 (m, 6H, phenyl), J_{H2-H3} = 3.8 Hz, J_{H3-H4} = 4.6 Hz, $J_{H3'''a-H3'''b}$ = -9.8 Hz, $J_{H4-H4'a}$ = 3.6 Hz, $J_{H4-H4'b}$ = 3.4 Hz, $J_{H4'a-H4'b}$ = -12.5 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 23.47, 23.53 [$\mathbf{CH_3}$], 47.62 [C3], 65.36 [C6'], 73.44 [C3'''], 76.30 [C4], 78.34 [C3'], 81.27 [$C(CH_3)_2$], 107.73 [C2], 110.26 [C3'], 128.21, 128.33, 128.46, 129.48, 129.70, 129.74, 132.59, 133.23, 133.55 [aromatic CH], 129.74, 130.02, 131.57 [aromatic C], 165.35, 165.63, 166.19 [CO]; LRMS (DCI-NH_3): m/e 547 ([MH^+], 0.9%), 425 ([MH^+ - PhCOOH], 26.3%); HRMS (DCI-NH_3): m/e calcd. for $C_{24}H_{25}O_7$ [MH^+ - PhCOOH], 425.1600; found, 425.1600}.

Oxetane (32').

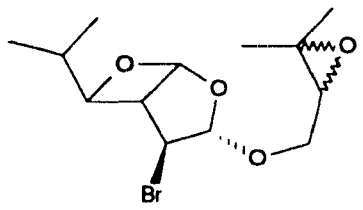
A solution of **31b** (33 mg, 0.05 mmol) and activated zinc dust (50 mg, 0.76 mmol) in dry methanol (2 mL) was stirred for 3 h under an atmosphere of nitrogen at room temperature. The zinc was removed by filtration and the filtrate evaporated to dryness *in vacuo* to give a clear syrup. The residue was dissolved in ether (30 mL), washed with saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to give the title compound (mixture of 2 inseparable diastereomers, 3:7), (16 mg, 65% yield) as an extremely unstable clear oil. {IR (CH_2Cl_2): 1717 cm^{-1}, 1722 cm^{-1}}. **32b-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.75 (s, 3H, CH_3), 3.31 (t, 1H, H3), 3.99 (dd, 2H, $\mathbf{OCH_2}C(CH_3)=CH_2$), 4.45 (A of ABX, 1H, H4'$_a$), 4.46 (s, 1H, H3'), 4.54 (B of ABX, 1H, H4'$_b$), 4.81 (ddd, 1H, H4), 4.91, 5.00 (2s, br, 2H, $OCH_2C(CH_3)=\mathbf{CH_2}$), 5.42 (s, 1H, H3''), 6.09 (d, 1H, H1), 7.24 - 7.57 (m, 6H, phenyl), 7.98 - 8.08 (m, 4H, phenyl), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.4 Hz, $J_{OCHH-OCHH}$ = -13.2 Hz, $J_{H4-H4'a}$ = 4.4Hz, $J_{H4-H4'b}$ = 3.4 Hz, $J_{H4'a-H4'b}$ = -12.1 Hz}. **32-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.75 (s, 3H, CH_3), 3.31 (t, 1H, H3), 4.14 (dd, 2H, $\mathbf{OCH_2}C(CH_3)=CH_2$), 4.42 (s, 1H, H3'), 4.45 (A of ABX, 1H, H4'$_a$), 4.54 (B of ABX, 1H, H4'$_b$), 4.81 (ddd, 1H, H4), 4.91, 5.00 (2s, br, 2H, $OCH_2C(CH_3)=\mathbf{CH_2}$), 5.39 (s, 1H, H3''), 6.09 (d, 1H, H1), 7.24 - 7.57 (m, 6H, phenyl), 7.98 - 8.08 (m, 4H, phenyl), J_{H2-H3} = 4.1 Hz, J_{H3-H4} = 4.4 Hz, $J_{OCHH-OCHH}$ = -12.5 Hz, $J_{H4-H4'a}$ = 4.4Hz, $J_{H4-H4'b}$ = 3.4 Hz, $J_{H4'a-H4'b}$ = -12.1 Hz}.



32'

Epoxide (34a) of 3α-dimethallyloxy-4β-bromo-6β-*i*-propyl-2,7-dioxa-bicyclo-[3,2,0]-heptane.

Epoxide **34a** (mixture of 2 inseparable diastereomers, 2:3) was obtained in 66% yield after flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) from acetal **10g** by a procedure similar to that used for **23a**. {LRMS (CI-NH_3)· m/e 340, 338 ([M + NH_4^+], 4.3%, 4.0%), 323, 321 ([MH^+], 1.0%, 1.7%), 221, 219 ([MH^+ - $(H_3C)_2C(O)CHCH_2OH$], 28.0%, 29.3%); HRMS (CI-NH_3). m/e calcd for $C_{13}H_{25}NO_4{}^{79}Br$ [M + NH_4^+], 338.0967; found, 338.0968}. **34a-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$)· δ 0.88 (d, 3H, **MeCHMe'**), 0.91 (d, 3H, MeCH**Me'**), 1.29, 1.32 (2s, 6H, **Me_2C**), 1.83 (m, 1H, H6'), 3.02 (dd, 1H, H3"), 3.33 (dd, 1H, H5), 3.83 (ddd, 2H, $H3'_a$, $H3'_b$), 4.18 (dd, 1H, H6), 4.26 (s, 1H, H4), 5.64 (s, 1H, H3), 6.04 (d, 1H, H1), J_{H1-H5} = 4.1 Hz, $J_{H3'a-H3'b}$ = -11.7 Hz, $J_{H3'a-H3"}$ = 5.6 Hz, $J_{H3'b-H3"}$ = 5.8 Hz, J_{H5-H6} = 4.5 Hz, $J_{H6-H6'a}$ = 4.9 Hz, $J_{H6'-Me}$ = 7.0 Hz, $J_{H6'-Me'}$ = 6.7 Hz}. **34a-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.88 (d, 3H, **MeCHMe'**), 0.91 (d, 3H, MeCH**Me'**), 1.28, 1.32 (2s, 6H, **Me_2C**), 1.84 (m, 1H, H6'), 3.02 (dd, 1H, H3"), 3.33 (dd, 1H, H5), 3.82 (ddd, 2H, $H3'_a$, $H3'_b$), 4.18 (dd, 1H, H6), 4.29 (s, 1H, H4), 5.66 (s, 1H, H3), 6.04 (d, 1H, H1), J_{H1-H5} = 4.1 Hz, $J_{H3'a-H3'b}$ = -11.1 Hz, $J_{H3'a-H3"}$ = 4.1 Hz, $J_{H3'b-H3"}$ = 7.0 Hz, J_{H5-H6} = 4.5 Hz, $J_{H6-H6'a}$ = 4.9 Hz, $J_{H6'-Me}$ = 6.8 Hz}.



34a

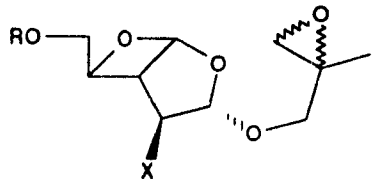
Epoxide (34b) of 3α-methallyloxy-4β-bromo-6β-*t*-butyldimethylsilyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane.

Epoxide **34b** (mixture of 2 inseparable diastereomers, 2:3) was obtained in 90% yield after flash chromatography (petroleum ether / ether, 4:1 v/v) from acetal **21a** by a procedure similar to that used for the preparation of **23a**. {LRMS (CI-NH_3). m/e 323, 321 ([MH^+ - $H_2C(O)C(CH_3)CH_2OH$], 10.6%, 9.9%)}. **34b-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.07, 0.08 (2s, 6H, *t*-BuSi**Me_2**), 0.90 (s, 9H, *t*-BuSi**Me_2**), 1.38 (s, 3H, CH_3), 2.67 (dd, 2H, $H3'''_a$, $H3'''_b$), 3.66 (dd, br, 2H, $H3'_a$, $H3'_b$), 3.66 (dd, 1H, H5), 3.73 (A of ABX, 1H, $H6'_a$), 3.73 (B of ABX, 1H, $H6'_b$), 4.36 (s, 1H, H4), 4.54 (ddd, 1H, H6), 5.65 (d, 1H, H3), 6.02 (d, 1H, H1), J_{H1-H5} = 4.0 Hz, $J_{H3-H3'a}$ = -0.6 Hz, $J_{H3'a-H3'b}$ = -11.0 Hz, $J_{H3'''a-H3'''b}$ = -4.8 Hz, J_{H5-H6} = 4.3 Hz, $J_{H6-H6'a}$ = 3.3 Hz, $J_{H6-H6'b}$ = 3.2 Hz, $J_{H6'a-H6'b}$ = -11.7 Hz}. **34b-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.07, 0.08 (2s, 6H, *t*-BuSi**Me_2**), 0.90 (s, 9H, *t*-BuSi**Me_2**), 1.35 (s, 3H, CH_3), 2.72 (dd, 2H, $H3'''_a$, $H3'''_b$), 3.66 (dd, 1H, H5), 3.72 (A of ABX, 1H, $H6'_a$), 3.72 (B of ABX, 1H, $H6'_b$), 3.81 (dd, br, 2H, $H3'_a$, $H3'_b$), 4.31 (s, 1H, H4), 4.48 (ddd, 1H, H6), 5.63 (d, 1H, H3), 6.02 (d, 1H, H1),

$J_{H1\ H5}$ = 4.0 Hz, $J_{H3\text{-}H3'a}$ = -0.5 Hz, $J_{H3'a\text{-}H3'b}$ = -10.9 Hz, $J_{H3'''a\text{-}H3'''b}$ = -5.0 Hz, $J_{H5\text{-}H6}$ = 4.3 Hz, $J_{H6\text{-}H6'a}$ = 3.5 Hz, $J_{H6\text{-}H6'b}$ = 3.1 Hz, $J_{H6'a\text{-}H6'b}$ = -11.9 Hz}.

Epoxide (34c) of 3α-methallyloxy-4β-acetoxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane.

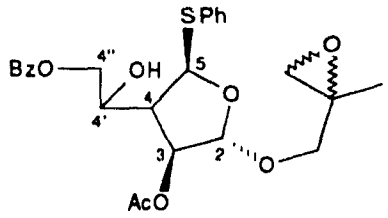
Epoxide **34c** (mixture of 2 inseparable diastereomers, 45:55) was obtained in 87% yield after flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) from acetal **29a** by a procedure similar to that used for the preparation of **23a**. {LRMS (CI-NH_3): m/e 396 ([M + NH_4^+], 57.1%), 379 ([MH^+], 28.8%), 291 ([MH^+ - $H_2C(O)C(CH_3)CH_2OH$], 81.0%); Anal. calcd. for $C_{19}H_{22}O_8$: C, 60.31; H, 5.86; found: C, 59.95; H, 5.47}. **34c-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.40 (s, 3H, CH_3), 2.03 (s, 3H, Ac), 2.67 (dd, 2H, H3'''$_a$, H3'''$_b$), 3.36 (dd, 1H, H5), 3.70 (dd, br, 2H, H3'$_a$, H3'$_b$), 4.45 (A of ABX, 1H, H6'$_a$), 4.56 (B of ABX, 1H, H6'$_b$), 4.82 (ddd, 1H, H6), 5.27 (s, 1H, H4), 5.46 (d, 1H, H3), 6.06 (d, 1H, H1), 7.39 - 7.61 (m, 3H, phenyl), 8.03 - 8.08 (m, 2H, phenyl), $J_{H1\text{-}H5}$ = 4.1 Hz, $J_{H3\text{-}H3'a}$ = -0.9 Hz, $J_{H3'a\text{-}H3'b}$ = -11.1 Hz, $J_{H3'''a\text{-}H3'''b}$ = -4.6 Hz, $J_{H5\text{-}H6}$ = 4.0 Hz, $J_{H6\text{-}H6'a}$ = 4.1 Hz, $J_{H6\text{-}H6'b}$ = 3.4 Hz, $J_{H6'a\text{-}H6'b}$ = -12.4 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 18.25 [$OCH_2C(\mathbf{CH_3})(O)CH_2$], 20.73 [$\mathbf{CH_3}CO$], 47.50 [C5], 51.58 [$OCH_2C(CH_3)(O)\mathbf{CH_2}$], 55.61 [$OCH_2C(CH_3)(O)CH_2$], 65.49 [C6'], 71.81 [$\mathbf{OCH_2}C(CH_3)(O)CH_2$], 76.23 [C6], 77.74 [C4], 107.71 [C1], 109.83 [C3], 128.40, 129.62, 133.21 [aromatic **CH**], 129.57 [aromatic C], 166.10 [Ph**CO**], 169.66 [CH_3CO]}. **34c-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.37 (s, 3H, CH_3), 2.02 (s, 3H, Ac), 2.73 (dd, 2H, H3'''$_a$, H3'''$_b$), 3.36 (dd, 1H, H5), 3.79 (dd, br, 2H, H3'$_a$, H3'$_b$), 4.45 (A of ABX, 1H, H6'$_a$), 4.55 (B of ABX, 1H, H6'$_b$), 4.82 (ddd, 1H, H6), 5.23 (s, 1H, H4), 5.42 (d, 1H, H3), 6 06 (d, 1H, H1), 7.39 - 7.61 (m, 3H, phenyl), 8.03 - 8.08 (m, 2H, phenyl), $J_{H1\text{-}H5}$ = 4.1 Hz, $J_{H3\text{-}H3'a}$ = -0.9 Hz, $J_{H3'a\text{-}H3'b}$ = -11.2 Hz, $J_{H3'''a\text{-}H3'b}$ = -4.9 Hz, $J_{H5\text{-}H6}$ = 4.0 Hz, $J_{H6\text{-}H6'a}$ = 4.1 Hz, $J_{H6\text{-}H6'b}$ = 3.4 Hz, $J_{H6'a\text{-}H6'b}$ = -12.5 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 18.53 [$OCH_2C(CH_3)(O)CH_2$], 20.73 [$\mathbf{CH_3}CO$], 47.50 [C5], 51.58 [$OCH_2C(CH_3)(O)\mathbf{CH_2}$], 55.41 [$OCH_2C(CH_3)(O)CH_2$], 65.49 [C6'], 70.09 [$\mathbf{OCH_2}C(CH_3)(O)CH_2$], 76.23 [C6], 77.74 [C4], 107.71 [C1], 109.83 [C3], 128.40, 129.62, 133.21 [aromatic **CH**], 129.57 [aromatic C], 166.10 [Ph**CO**], 169.66 [CH_3CO]}.



34b, R=TBDMSi, X=Br
34c, R=Bz, X=AcO

Thiogylcoside (36).

To an ice cooled solution of epoxide **34c** (38 mg, 0.10 mmol) and thiophenol (103 µL, 1.00 mmol) in dry ether (5 mL) under nitrogen was added a 1.0 M solution of zinc chloride in ether (1.00 mL). After stirring for 30 min, the solution was warmed to room temperature, diluted with ether (20 mL), washed with saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na_2SO_4), filtered and the solvent removed in vacuo yielding a yellow residue which was chromatographed over silica gel (petroleum ether / ethyl acetate, 2:1 v/v), affording **36** (mixture of 2 inseparable diastereomers, 45:55) as a light yellow oil (31 mg, 64% yield). **36-minor:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.40 (s, 3H, CH_3), 2.02 (s, 3H, Ac), 2.49 (s, br,ex, 1H, OH), 2.73 (dd, 2H, $H2'''_a$, $H2'''_b$), 3.21 (m, 1H, H4), 3.70 (dd, 2H, $H2'_a$, $H2'_b$), 4.43 - 4.53 (m, 3H, H4', $H4''_a$, $H4''_b$), 5.05 (s, 1H, H3), 5.27 (d, 1H, H2), 5.72 (d, 1H, H5), 7.22 - 7.62 (m, 3H, phenyl), 8.05 - 8.12 (m, 2H, phenyl), $J_{H4\text{-}H5}$ = 6.1 Hz, $J_{H2'a\ H2'b}$ = -11.2 Hz, $J_{H2'''a\ H2'''b}$ = -4.4 Hz}. **36-major:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.30 (s, 3H, CH_3), 2.02 (s, 3H, Ac), 2.49 (s, br,ex, 1H, OH), 2.75 (dd, 2H, $H2'''_a$, $H2'''_b$), 3.21 (m, 1H, H4), 3.71 (dd, 2H, $H2'_a$, $H2'_b$), 4.43 - 4.53 (m, 3H, H4', $H4''_a$, $H4''_b$), 5.06 (s, 1H, H3), 5.24 (d, 1H, H2), 5.72 (d, 1H, H5), 7.22 - 7.62 (m, 3H, phenyl), 8.05 - 8.12 (m, 2H, phenyl), $J_{H4\text{-}H5}$ = 6.1 Hz, $J_{H2'a\text{-}H2'b}$ = -11.3 Hz, $J_{H2'''a\text{-}H2''b}$ = -4.4 Hz}.

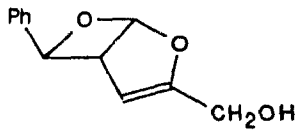


36

4.5 Experimentals for Section 2.6.

3-Hydroxymethyl-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (37a).

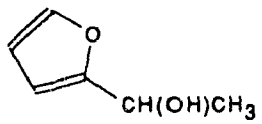
A mixture of furfuryl alcohol (38.14 g, 388.7 mmol) and benzaldehyde (10.00 g, 94.2 mmol) in benzene (300 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with helium. The solution was then irradiated for 6 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (ether / hexanes, 3:1 v/v) gave exclusively **37a** (3.845 g, 20% yield) as a light yellow oil and recovered starting material (15.02 g furfuryl alcohol, 4.05 g benzaldehyde). [^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.06 (t, ex, 1H, OH), 3.68 (ddd, 1H, H5), 4.34 (d, 2H, CH_2), 5.39 (d, 1H, H4), 5.57 (d, 1H, H6), 6.55 (d, 1H, H1), 7.31 - 7.42 (m, 5H, Ph); J_{H1-H5} = 4.4 Hz, J_{CH_2-OH} = 6.2 Hz, J_{H4-H5} = 2.8 Hz, J_{H5-H6} = 3.2 Hz; LRMS (CI-NH_3). m/e 222 ([M + NH_4^+], 28.2%), 205 ([MH^+], 100%), 187 ([MH^+ - H_2O], 32.9%); HRMS (CI-NH_3): m/e calcd. for $C_{12}H_{11}O_2$ [MH^+ - H_2O], 187.0758; found, 187.0758].



37a

2-(2'-Hydroxyethyl)-furan (38).

To a stirred ice-cooled solution of furfural (2.00 g, 20.8 mmol) in anhydrous ether (100 mL) under an atmosphere of nitrogen was added a 1.0M solution of methylmagnesium bromide in butyl ether (20.8 mL, 20.8 mmol) over a period of 30 min and the mixture allowed to gradually warm to ambient temperature. After 1.5 h, the reaction mixture was poured into ice cold 5% hydrochloric acid (30 mL) and the organic phase was washed with brine (100 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to afford pure racemic **38** (2.31 g, 99% yield) as a colourless oil [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.53 (d, 3H, Me), 1.90 (d, ex, 1H, OH), 4.87 (dq, 1H, CH), 6.21, 6.31 (2m, 2H, H3, H4), 7.36 (m, 1H, H5), $J_{CH\,OH}$ = 5.0 Hz, J_{CH-Me} = 6.6 Hz].

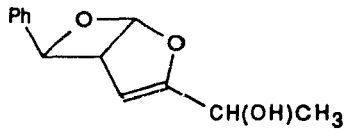


38

3-(3'-Hydroxyethyl)-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (38a).

A mixture of **38** (528 mg, 4.71 mmol) and benzaldehyde (500 mg, 4.71 mmol) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with helium. The solution was then irradiated for 5 h. The solvent was removed *in vacuo* to yield a yellow syrup.

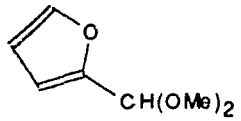
Chromatography over silica gel (ether / hexanes, 3:1 v/v) afforded **38a** exclusively (mixture of 2 inseparable diastereomers, 1:1), (292 mg, 28% yield) as a light yellow oil and recovered starting material (102 mg **38**, 100 mg benzaldehyde). {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.46, 1.47 (2d, 3H, Me), 2.03 (d, ex, 1H, OH), 3.65 (ddd, 1H, H5), 4.50, 4.52 (2dq, 1H, H3'), 5.31, 5.33 (2d, 1H, H4), 5.54 (d, 1H, H6), 6.53 (d, 1H, H1), 7.25 - 7.50 (m, 5H, Ph); J_{H1-H5} = 4.4 Hz, $J_{H3'-OH}$ = 5.0 Hz, $J_{H3'-Me}$ = 6.6 Hz, $J_{H4\ H5}$ = 2.3 Hz, J_{H5-H6} = 3.0 Hz}.



38a

2-Furaldehyde dimethyl acetal (39).

A solution of furfural (9.61 g, 100.0 mmol) in methanol (210 mL) containing $CeCl_3\ 7H_2O$ (37.25 g, 100.0 mmol) and trimethylorthoformate (87.5 mL, 800 mmol) was allowed to stir for 25 min at room temperature. The reaction mixture was poured into saturated aqueous sodium bicarbonate (1 L) and extracted with ether (4 x 500 mL). The extracts were washed with brine (2 L), dried (Na_2SO_4), filtered and the solvent removed in vacuo to afford pure **39** (9.81 g, 69% yield) as a colourless oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.34 (s, 6H, MeO), 5.43 (s, 1H, **CH**Me_2), 6.36, 6.41 (2m, 2H, H3, H4), 7.39 (m, 1H, H5)}.

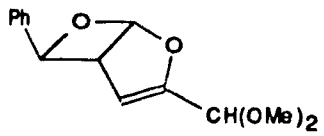


39

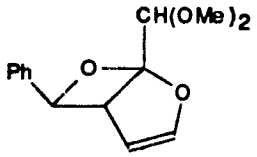
3-Dimethoxymethyl-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (39a) and
1-Dimethoxymethyl-6β-phenyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (39b).

A mixture of 2-furaldehyde dimethyl acetal **39** (2.84 g, 20.0 mmol) and benzaldehyde (2.00 g, 18.8 mmol) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with helium. The solution was then irradiated for 7 h. The solvent was removed *in vacuo* to yield a yellow residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 6.1 v/v) gave **39a** and **39b** (mixture of 2 inseparable regioisomers, 3.5), (2.132 g, 46% yield) as a light yellow oil and recovered starting material (1.39 g 2-furaldehyde dimethyl acetal, 869 mg benzaldehyde) **39a:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.45 (s, 6H, MeO), 3.70 (ddd, 1H, H5), 5.09 (t, 1H, H4), 5.58 (d, 1H, H6), 5.58 (d, 1H, H3'), 6.56 (dd, 1H, H1), 7.29 - 7.68 (m, 5H, Ph); J_{H1-H5} = 4.4 Hz, J_{H1-H6} = -0.8 Hz, $J_{H3'-H4}$ = -1.1 Hz, J_{H4-H5} = 1.1 Hz, J_{H5-H6} = 2.9 Hz; LRMS (CI-NH_3): m/e 231 ([MH^+ - H_2O], 0.5%)}. **39b:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.40 (s, 6H, MeO), 3.79 (ddd, 1H, H5), 4.48 (s, 1H, H1'), 5.41 (t, 1H, H4),

5.58 (d, 1H, H6), 6.73 (dd, 1H, H3), 7.29 - 7.68 (m, 5H, Ph); J_{H3-H4} = 3.0 Hz, J_{H3-H5} = -0.9 Hz, J_{H4-H5} = 2.9 Hz, J_{H5-H6} = 3.8 Hz; LRMS (CI-NH_3): m/e 231 ([MH^+ - H_2O], 0.5%)}.



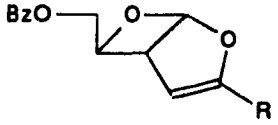
39a



39b

3-Tri-*n*-butylstannyl-6-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (40).

A mixture of tributyl-(2-furyl)-stannane (6.43 g, 18.0 mmol), aldehyde **27** (1.64 g, 10.0 mmol) and anhydrous potassium carbonate (3 g) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with helium. The solution was then irradiated for 8 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (petroleum ether / triethylamine, 1:0.02 v/v) gave **40** (782 mg, 15% yield) as a clear oil and recovered starting material (5.86 g tributyl-(2-furyl)-stannane, 390 mg aldehyde **27**). {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 0.90 (t, 9H, $SnCH_2CH_2CH_2\mathbf{CH_3}$), 1.04 (t, 6H, $Sn\mathbf{CH_2}CH_2CH_2CH_3$), 1.33 (tq, 6H, $SnCH_2CH_2\mathbf{CH_2}CH_3$), 1.60 (tt, 6H, $SnCH_2\mathbf{CH_2}CH_2CH_3$), 3.70 (ddd, 1H, H5), 4.49 (A of ABX, 1H, $H6'_a$), 4.52 (B of ABX, 1H, $H6'_b$), 4.70 (dddd, 1H, H6), 5.47 (d, 1H, H4), 6.36 (dd, 1H, H1), 7.43 -7.64 (m, 3H, Ph), 8.06 - 8.11 (m, 2H, Ph), J_{H1-H6} = -0.7 Hz, J_{H1-H5} = 4.3 Hz, J_{H4-H5} = 2.8 Hz, J_{H5-H6} = 2.2 Hz, $J_{H6-H6'a}$ = 4.3 Hz, $J_{H6-H6'b}$ = 2.9 Hz, $J_{H6'a-H6'b}$ = -12.3 Hz, $J_{SnCH_2-CH_2}$ = 7.9 Hz, $J_{CH_2-CH_2}$ = 7.2 Hz, $J_{CH_3-CH_2}$ = 7.1 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 10.14 [$Sn\mathbf{CH_2}(CH_2)_2CH_3$], 13.87 [$Sn(CH_2)_3\mathbf{CH_3}$], 27.59 [$Sn(CH_2)_2\mathbf{CH_2}CH_3$], 29.31 [$SnCH_2\mathbf{CH_2}CH_2CH_3$], 48.00 [C5], 66.84 [C6'], 88.39 [C6], 109.01 [C1], 115.91 [C4], 128.89, 129.98, 133.55 [aromatic CH], 130.42 [aromaticC], 166.53 [CO], 167.29 [C3]; LRMS (Cl-NH_3): m/e 523 ([MH^+], 2.8%), 505 ([MH^+ - H_2O], 100%); HRMS (Cl-NH_3): m/e calcd. for $C_{25}H_{37}O_3{}^{120}Sn$ [MH^+ -H_2O], 505.1765; found, 505.1764}.



40, R=$SnBu_3$
41a, R=Ph
41b, R=*p*-NO_2Ph

3-Phenyl-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (41a).

To a stirred solution of **40a** (1.042 g, 2.00 mmol) in dry tetrahydrofuran (140 ml) was added iodobenzene (448 µL, 4.00 mmol) and tetrakis(triphenylphosphine)palladium(0) (347 mg, 0.30 mmol; 35 mg added originally, the rest was added in 6 portions during the course of the reaction). The reaction

mixture was refluxed under an atmosphere of nitrogen until tlc indicated complete disappearance of starting material (36 h). The mixture was allowed to cool to room temperature, and pyridine (800 µL) was added followed by 1.2 N pyridinium fluoride solution (1.7 mL). The resulting mixture was stirred for 18 h. Evaporation of the solvent in vacuo gave a black residue which was dissolved in diethyl ether (250 mL). The resulting solution was washed with 5% hydrochloric acid (200 mL), saturated aqueous sodium bicarbonate (200 mL), brine (200 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to give a brown residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 5:1 v/v) gave the title compound (524 mg, 85% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.94 (ddd, 1H, H5), 4.58 (d, 2H, H6'$_a$, H6'$_b$), 4.90 (ddt, 1H, H6), 5.71 (d, 1H, H4), 6.52 (dd, 1H, H1), 7.26 - 7.67 (m, 8H, Ph), 8.07 - 8.13 (m, 2H, Ph), J_{H1-H5} = 4.3 Hz, J_{H1-H6} = -0.7 Hz, J_{H4-H5} = 3.1 Hz, J_{H5-H6} = 2.8 Hz, $J_{H6-H6'aH6'b}$ = 3.3 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 48.55 [C5], 66.44 [C6'], 88.57 [C6], 98.58 [C4], 108.36 [C1], 125.75, 128.79, 128.90, 129.46, 129.94, 133.61 [aromatic CH], 130.26, 130.46 [aromatic C], 158.86 [C3], 166.50 [CO]; LRMS (CI-NH_3): m/e 326 ([M + NH_4^+], 1.9%), 309 ([MH^+], 16.3%), 291 ([MH^+ - H_2O], 33.8%); HRMS (CI-NH_3): m/e calcd. for $C_{19}H_{16}O_4$ [MH^+], 309.1128; found, 309.1127}.

3-*p*-Nitrophenyl-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (41b).

1-Bromo-4-nitrobenzene and photo-adduct **40a** gave **41b** in 91% yield by a procedure similar to the one used for the preparation of **41a**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 4.04 (ddd, 1H, H5), 4.56 (A of ABX, 1H, H6'$_a$), 4.61 (B of ABX, 1H, H6'$_b$), 4.93 (dddd, 1H, H6), 6.02 (d, 1H, H4), 6.55 (dd, 1H, H1), 7.25 -7.67 (m, 3H, Ph), 7.83, 8.24 (AB q, 4H, $C_6H_4NO_2$), 8.09 - 8.14 (m, 2H, Ph), J_{H1-H6} = -0.9 Hz, J_{H1-H5} = 4.3 Hz, J_{H4-H5} = 3.3 Hz, J_{H5-H6} = 2.7 Hz, $J_{H6-H6'a}$ = 3.9 Hz, $J_{H6-H6'b}$ = 3.1 Hz, $J_{H6'a-H6'b}$ = -12.8 Hz; LRMS (CI-NH_3): m/e 371 ([M + NH_4^+], 0.6%), ([MH^+], 1.8%), 336 ([MH^+ -H_2O], 42.1%); HRMS (CI-NH_3): m/e calcd. for $C_{19}H_{14}NO_5$ [MH^+ - H_2O], 336.0877; found, 336.0871}.

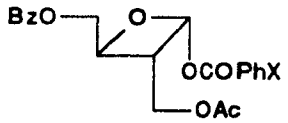
Oxetane (42a).

Ozone was bubbled through a solution of **41a** (25 mg, 0.08 mmol) in dry methylene chloride (10 mL) at -78°C until the solution turned blue (5 min). Dimethyl sulfide (60 µL, 0.80 mmol) was added to the reaction mixture under nitrogen and it was allowed to warm to ambient temperature gradually overnight. Next, sodium borohydride on alumina gel (10%), (62 mg, 0.16 mmol) was added and stirring was continued until tlc indicated reduction of the aldehyde was complete (3 h). Pyridine (20 µL, 0.24 mmol), *N,N*-dimethylaminopyridine (2 mg, 0.01 mmol) and acetic anhydride (12 µL, 0.12 mmol) were added and the reaction was allowed to stir for 16 h. The reaction mixture was diluted with methylene chloride (20 mL), washed with 5% hydrochloric acid (30 mL), saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a yellow residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 3:1 v/v) gave the

title compound (10 mg, 33% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.97 (s, 3H, CH_3), 3.58 (dddd, 1H, H3), 4.50 (A of ABX, 1H, H3'$_a$), 4.50 (A of ABX, 1H, H4'$_a$), 4.54 (B of ABX, 1H, H3'$_b$), 4.62 (B of ABX, 1H, H4'$_b$), 5.03 (ddd, 1H, H4), 6.72 (d, 1H, H2), 7.45 - 7.70 (m, 6H, Ph), 8.05 - 8.12 (m, 4H, Ph); $J_{H2\text{-}H3}$ = 5.9 Hz, $J_{H3\text{-}3'a}$ = 4.1 Hz, $J_{H3\text{-}H3'b}$ = 3.9 Hz, $J_{H3'a\text{-}H3'b}$ = -0.2 Hz, $J_{H3\text{-}H4}$ = 6.3 Hz, $J_{H4\text{-}4'a}$ = 4.5 Hz, $J_{H4\text{-}H4'b}$ = 3.3 Hz, $J_{H4'a\text{-}H4'b}$ = -12.6 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 20.48 [CH_3CO], 40.22 [C3], 60.64 [C3'], 65.42 [C4'], 80.15 [C4], 96.88 [C2], 128.53, 128.59, 129.61, 129.75, 133.29, 133.68 [aromatic CH], 128.72, 129.32 [aromatic C], 164.88, 166.05 [CO], 170.62 [CH_3CO]; LRMS (CI-NH_3): m/e 402 ([M + NH_4^+], 17.5%), 263 ([MH^+ - BzOH], 21.8%); HRMS (CI-NH_3): m/e calcd. for $C_{21}H_{24}NO_7$ [M + NH_4^+], 402.1553; found, 402.1552}.

Oxetane (42b).

Oxetane **42b** was obtained from **41b** in 25% yield by a procedure similar to that used for the preparation of **42a**. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.98 (s, 3H, CH_3), 3.60 (dddd, 1H, H3), 4.48 (A of ABX, 1H, H3'$_a$), 4.54 (A of ABX, 1H, H4'$_a$), 4.56 (B of ABX, 1H, H3'$_b$), 4.64 (B of ABX, 1H, H4'$_b$), 5.07 (ddd, 1H, H4), 6.75 (d, 1H, H2), 7.43 - 7.67 (m, 3H, Ph), 7.98 - 8.13 (m, 2H, Ph), 8.27, 8.32 (AB q, 4H, *p*-NO_2Bz); J_{AB} = 8.8 Hz, $J_{H2\text{-}H3}$ = 5.8 Hz, $J_{H3\text{-}3'a}$ = 4.3 Hz, $J_{H3\text{-}H3'b}$ = 1.3 Hz, $J_{H3'a\text{-}H3'b}$ = -12.9 Hz, $J_{H3\ H4}$ = 5.9 Hz, $J_{H4\text{-}4'a}$ = 4.7 Hz, $J_{H4\text{-}H4'b}$ = 3.0 Hz, $J_{H4'a\text{-}H4'b}$ = -12.8 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 20.80 [CH_3CO], 40.61 [C3], 60.67 [C3'], 65.57 [C4'], 80.75 [C4], 96.87 [C2], 124.07, 128.91, 131.33, 133.71, 134.77 [aromatic CH], 129.98, 135.07, 151.33 [aromatic C], 166.35, 168.90 [CO], 170.72 [CH_3CO]; LRMS (CI-NH_3): m/e 447 ([M + NH_4^+], 100%), 430 ([MH^+], 1.8%), 263 ([MH^+ - *p*-NO_2BzOH], 3.1%); HRMS (CI-NH_3): m/e calcd. for $C_{21}H_{23}N_2O_9$ [M + NH_4^+], 447.1403; found, 447.1403}.

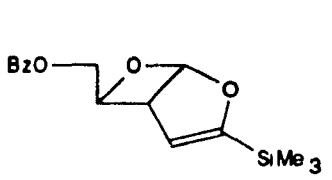


42a, X=H
42b, X=*p*-NO_2

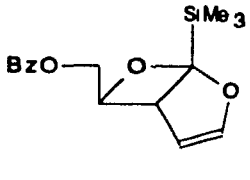
3-Trimethylsilyl-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (43a) and 1-Trimethylsilyl-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (43b).

A mixture of 2-trimethylsilylfuran (2.53 g, 18.0 mmol), aldehyde **27** (1.64 g, 10.0 mmol) and anhydrous potassium carbonate (3 g) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with helium. The solution was then irradiated for 8 h. The solvent was removed *in vacuo* to afford a yellow syrup. Chromatography over silica gel (petroleum ether / ethyl acetate / triethylamine, 42:7:1 v/v/v) gave photo-adducts **43a** and **43b** (mixture of 2 inseparable regioisomers, 7:4), (577 mg, 19% yield) as a light yellow oil and recovered starting material (152 mg

aldehyde 27). **43a:** {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 0.21 (s, 9H, $SiMe_3$), 3.74 (ddd, 1H, H5), 4.48 (A of ABX, 1H, H6'$_a$), 4.54 (B of ABX, 1H, H6'$_b$), 4.74 (ddd, 1H, H6), 5.59 (d, 1H, H4), 6.38 (dd, 1H, H1), 7.41 - 7.66 (m, 3H, Ph), 8.00 - 8.12 (m, 2H, Ph); J_{H1-H5} = 4.2 Hz, J_{H1-H6} = -0.8 Hz, J_{H4-H5} = 2.9 Hz, J_{H5-H6} = 3.0 Hz, $J_{H6-H6'a}$ = 5.4 Hz, $J_{H6-H6'b}$ = 2.8 Hz, $J_{H6'a-H6'b}$ = -11.4 Hz}. **43b:** {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 0.16 (s, 9H, $SiMe_3$), 3.54 (ddd, 1H, H5), 4.48 (A of ABX, 1H, H6'$_a$), 4.54 (B of ABX, 1H, H6'$_b$), 4.99 (ddd, 1H, H6), 5.30 (t, 1H, H4), 6.69 (dd, 1H, H3), 7.41 - 7.66 (m, 3H, Ph), 8.00 - 8.12 (m, 2H, Ph); J_{H3-H4} = 2.9 Hz, J_{H3-H5} = -1.2 Hz, J_{H4-H5} = 2.9 Hz, J_{H5-H6} = 3.0 Hz, $J_{H6-H6'a}$ = 1.5 Hz, $J_{H6-H6'b}$ = 0.7 Hz, $J_{H6'a-H6'b}$ = -13.6 Hz}.



43a

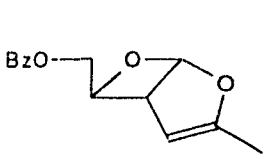


43b

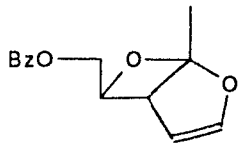
3-Methyl-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (44a) and 1β-Methyl-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (44b).

A mixture of 2-methylfuran (17.3 mL, 192 mmol) and aldehyde 27 (15.74 g, 96 mmol) in benzene (1800 mL) was placed in a 2 L photo-reaction vessel, cooled to 8°C, and saturated with argon. The solution was then irradiated for 7 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate / triethylamine, 10:1:0.01 v/v/v) gave **44a and 44b** (mixture of 2 inseparable regioisomers, 11:8), (11.10 g, 47% yield) as a light yellow oil and recovered starting material (5.62 g aldehyde 27). In the absence of triethylamine, **44b** decomposed on the column and photo-adduct **44a** was isolated (6.38 g, 27% yield) as a light yellow oil along with recovered starting material (5.62 g aldehyde **27**). **44a:** {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.94 (dd, 3H, Me), 3.73 (dddd, 1H, H5), 4.47 (A of ABX, 1H, H6'$_a$), 4.52 (B of ABX, 1H, H6'$_b$), 4.77 (dddd, 1H, H6), 5.01 (dd, 1H, H4), 6.31 (dd, 1H, H1), 7.44 - 7.66 (m, 3H, Ph), 7.99 - 8.11 (m, 2H, Ph); J_{H1-H5} = 4.4 Hz, J_{H1-H6} = -0.9 Hz, J_{H4-Me} = -1.4 Hz, $J_{H4\ H5}$ = 2.8 Hz, J_{H5-Me} = 1.4 Hz, J_{H5-H6} = 2.2 Hz, $J_{H6-H6'a}$ = 4.4 Hz, $J_{H6-H6'b}$ = 2.9 Hz, $J_{H6'a-H6'b}$ = -12.5 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 13.91 [Me], 48.12 [C5], 66.48 [C6'], 88.76 [C6], 98.91 [C4], 108.51 [C1], 128.33, 129.88, 133.52 [aromatic CH], 130.27 [aromatic C], 158.45 [C3], 166.44 [CO]; LRMS (CI-NH_3): m/e 264 ([M + NH_4^+], 1.7%), 247 ([MH^+], 0.8 %), 229 ([MH^+ - H_2O], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{14}H_{13}O_3$ [MH^+ - H_2O], 229.0865; found, 229.0864}. Anal. calcd. for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.09; H, 5.67. **44b:** {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.69 (s, 3H, Me), 3.52 (ddd, 1H, H5), 4.47 (A of ABX, 1H, H6'$_a$), 4.52 (B of ABX, 1H, H6'$_b$), 4.72 (ddd, 1H, H6), 5.31 (t, 1H, H4), 6.58 (dd, 1H, H3), 7.41 - 7.66 (m, 3H, Ph), 7.98 - 8.11 (m, 2H, Ph), J_{H3-H4} = 3.0 Hz, J_{H3-H5} = -1.0 Hz, J_{H4-H5} = 3.0 Hz, J_{H5-H6} = 2.9 Hz, J_{H6-}

$_{H6'a}$ = 4.2 Hz, $J_{H6\text{-}H6'b}$ = 2.9 Hz, $J_{H6'a\text{-}H6'b}$ = -12.6 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 23.46 [Me], 48.53 [C5], 66.31 [C6'], 85.88 [C6], 104.29 [C4], 116.22 [C1], 128.75, 130.01, 133.41 [aromatic CH], 130.23 [aromatic C], 148.43 [C3], 166.44 [CO]; LRMS (CI-NH_3): m/e 264 ([M + NH_4^+], 1.7%), 247 ([MH^+], 0.8%), 229 ([MH^+ - H_2O], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{14}H_{13}O_3$ [MH^+ - H_2O], 229.0865; found, 229.0864].



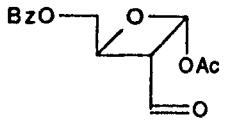
44a



44b

2α-Acetoxy-3α-C-formyl-4β-benzoyloxymethyl oxetane (45).

Ozone was bubbled through a solution of the photo-adduct **44a** (73 mg, 0.30 mmol) in dry methylene chloride (45 mL) at -78°C until the solution turned blue (15 min). Dimethyl sulfide (218 μL, 10 equiv.) was added to the reaction mixture under nitrogen and it was allowed to warm to ambient temperature gradually overnight. The reaction mixture was diluted with methylene chloride (25 mL), washed with water (2 x 25 mL), brine (25 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to yield aldehyde **45** (78 mg, 94% yield) as a light yellow oil. [^{1}H-NMR (200 MHz, CD_2Cl_2): δ 2.06 (s, 3H, Ac), 4.02 (dt, 1H, H3), 4.29 (A of ABX, 1H, $H4'_a$), 4.39 (B of ABX, 1H, $H4'_b$), 5.41 (ddd, 1H, H4), 6.58 (d, 1H, H2), 7.25 - 7.67 (m, 3H, Ph), 7.91 - 8.11 (m, 2H, Ph), 9.76 (d, 1H, CHO), $J_{H2\text{-}H3}$ = 6.4 Hz, $J_{H3\text{-}CHO}$ = 1.0 Hz, $J_{H3\text{-}H4}$ = 6.1 Hz, $J_{H4\text{-}H4'a}$ = 3.8 Hz, $J_{H4\text{-}H4'b}$ = 3.1 Hz, $J_{H4'a\text{-}H4'b}$ = -12.9 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 20.75 [CH_3CO], 50.61 [C3], 64.72 [C4'], 75.95 [C4], 95.66 [C2], 128.48, 129.61, 133.40 [aromatic CH], 129.24 [aromatic C], 166.01 [PhCO], 169.29 [CH_3CO], 194.98 [CHO]; LRMS (CI-NH_3): m/e 296 ([M + NH_4^+], 100%), 279 ([MH^+], 3.9%), 219 ([MH^+ - AcOH], 3.3%); HRMS (CI-NH_3): m/e calcd. for $C_{14}H_{18}NO_6$ [M + NH_4^+], 296.1135; found, 296.1134].

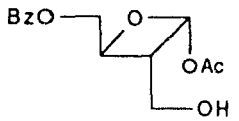


45

2α-Acetoxy-3α-hydroxymethyl-4β-benzoyloxymethyl oxetane (46).

To a stirred solution of aldehyde **45** (78mg, 0.28 mmol) in methylene chloride (45 mL) at 0°C under an atmosphere of nitrogen was added sodium borohydride on alumina gel (10%), (225 mg, 0.61 mmol) and the mixture warmed to ambient temperature gradually over 1 h. After 5 h, reduction of the aldehyde was complete. The reaction mixture was filtered through a bed of dry Celite and the filtrate was washed with 5% hydrochloric acid (40 mL), saturated aqueous sodium bicarbonate (40 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to yield the title compound (55 mg, 70% yield) as a

light yellow oil. For purposes of characterization, a small sample of alcohol **46** was chromatographed over silica gel (petroleum ether / ethyl acetate, 1:1 v/v). {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 0.88 (s, br, ex, 1H, OH), 2.13 (s, 3H, Ac), 3.32 (dddd, 1H, H3), 3.88 (A of ABX, 1H, $H3'_a$), 3.94 (B of ABX, 1H, $H3'_b$), 4.46 (A of ABX, 1H, $H4'_a$), 4.57 (B of ABX, 1H, $H4'_b$), 4.96 (ddd, 1H, H4), 6.48 (d, 1H, H2), 7.42 - 7.65 (m, 3H, Ph), 8.02 - 8.11 (m, 2H, Ph), J_{H2-H3} = 5.9 Hz, $J_{H3-H3'a}$ = 5.6 Hz, $J_{H3-H3'b}$ = 7.2 Hz, $J_{H3'a-H3'b}$ = -11.7 Hz, J_{H3-H4} = 6.1 Hz, $J_{H4-H4'a}$ = 4.6 Hz, $J_{H4-H4'b}$ = 3.0 Hz, $J_{H4'a-H4'b}$ = -12.6 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 21.28 [$\mathbf{CH_3}$CO], 43.11 [C3], 59.33 [C3'], 66.03 [C4'], 79.50 [C4], 97.75 [C2], 128.69, 129.93, 133.60 [aromatic CH], 130.13 [aromatic C], 166.49 [Ph**CO**], 169.98 [CH_3**CO**], LRMS (CI-NH_3): m/e 298 ([M + NH_4^+], 100%), 211 ([MH^+ - AcOH], 60.6%); HRMS (CI-NH_3): m/e calcd for $C_{14}H_{20}NO_6$ [M + NH_4^+], 298.1289; found, 298.1290}.



46

Oxetane (47a).

Oxetane **47a** was obtained from photo-adduct **44a** in 54% yield by a procedure similar to that used for the preparation of **42a**. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.99 (s, 3H, Ac), 2.11 (s, 3H, anomeric Ac), 3.45 (ddt, 1H, H3), 4.38 (d, 2H, $H3'_a$, $H3'_b$), 4.45 (A of ABX, 1H, $H4'_a$), 4.57 (B of ABX, 1H, $H4'_b$), 4.93 (ddd, 1H, H4), 6.47 (d, 1H, H2), 7.44 - 7.66 (m, 3H, Ph), 7.98 - 8.12 (m, 2H, Ph), J_{H2-H3} = 5.9 Hz, $J_{H3-H3'aH3'b}$ = 7.1 Hz, J_{H3-H4} = 6.1 Hz, $J_{H4-H4'a}$ = 4.5 Hz, $J_{H4-H4'b}$ = 3.3 Hz, $J_{H4'a\ H4'b}$ = -12.6 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 20.86, 21.17 [$\mathbf{CH_3}$], 40.28 [C3], 60.91 [C3'], 65.77 [C4'], 80.45 [C4], 96.48 [C2], 128.87, 129.94, 133.63 [aromatic CH], 130.10 [aromatic C], 166.37 [PhCO], 169.80, 170.94 [CH_3CO]; LRMS (CI-NH_3): m/e 340 ([M + NH_4^+], 100%), 323 ([MH^+], 0.5%), 263 ([MH^+ - AcOH], 34.4%); HRMS (CI-NH_3): m/e calcd. for $C_{16}H_{22}NO_8$ [M + NH_4^+], 340.1397; found, 340.1396}.

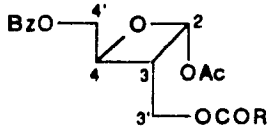
Oxetane (47b).

To a solution of alcohol **46** (28 mg, 0.10 mmol) in dry methylene chloride (15 mL) under nitrogen at 0°C was added N,N-dimethylaminopyridine (1 mg, 0.01 mmol), pyridine (24 μL, 0.30 mmol) and benzoyl chloride (17 μL, 0.15 mmol). The solution was gradually warmed to room temperature (1 h) and allowed to stir for 16 h. It was then diluted with methylene chloride (15 mL), washed with 5% hydrochloric acid (30 mL), saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na_2SO_4), filtered and the solvent removed in vacuo to yield a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate, 2:1 v/v) afforded the title compound (18 mg, 47% yield from photo-adduct **44a**) as a colourless oil. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 2.10 (s, 3H, Ac), 3.61 (dddd, 1H, H3), 4.52 (A of ABX, 1H, $H4'_a$), 4.64 (B of ABX, 1H, $H4'_b$), 4.65 (A of ABX, 1H, $H3'_a$), 4.70

(B of ABX, 1H, $H3'_b$), 5.05 (ddd, 1H, H4), 6.58 (d, 1H, H2), 7.34 - 7.76 (m, 6H, Ph), 7.90 - 8.11 (m, 4H, Ph), J_{H2-H3} = 6.0 Hz, $J_{H3-H3'a}$ = 6.8 Hz, $J_{H3-H3'b}$ = 7.7 Hz, $J_{H3'a-H3'b}$ = -11.5 Hz, J_{H3-H4} = 6.2 Hz, $J_{H4-H4'a}$ = 4.4 Hz, $J_{H4-H4'b}$ = 3.2 Hz, $J_{H4'a-H4'b}$ = -12.6 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 21.18 [CH_3], 40.49 [C3], 61.44 [C3'], 65.85 [C4'], 80.31 [C4], 96.58 [C2], 128.84, 128.90, 129.91, 130.42, 133.59, 134.14 [aromatic CH], 129.27, 129.86 [aromatic C], 166.47, 169.84, 170.98 [CO]; LRMS (CI-NH_3): m/e 402 ([M + NH_4^+], 100%), 385 ([MH^+], 0.7%), 325 ([MH^+ - AcOH], 34.4%); HRMS (CI-NH_3): m/e calcd. for $C_{21}H_{21}O_7$ [MH^+], 385.1286; found, 385.1287}.

Oxetane (47c).

To a solution of alcohol **46** (56 mg, 0.20 mmol) in dry methylene chloride (30 mL) under nitrogen at 0°C was added N,N-dimethylaminopyridine (2 mg, 0.02 mmol), triethylamine (140 µL, 1.00 mmol) and methyl oxalyl chloride (37 µL, 0.40 mmol). The solution was gradually warmed to room temperature (1 h) and allowed to stir for 16 h. It was then diluted with methylene chloride (20 mL), washed with 5% hydrochloric acid (40 mL), saturated aqueous sodium bicarbonate (40 mL), brine (40 mL), dried (Na_2SO_4), filtered and the solvent removed in vacuo to yield a yellow syrup Purification by flash chromatography (petroleum ether / ethyl acetate, 2:1 v/v) afforded the title compound (39 mg, 53% yield from photo-adduct **44a**) as a colourless oil. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 2.12 (s, 3H, Ac), 3.58 (dddd, 1H, H3), 3.85 (s, 3H, MeO), 4.46 (A of ABX, 1H, $H4'_a$), 4.59 (B of ABX, 1H, $H4'_b$), 4.59 (A of ABX, 1H, $H3'_a$), 4.63 (B of ABX, 1H, $H3'_b$), 4.96 (ddd, 1H, H4), 6.50 (d, 1H, H2), 7.44 - 7.66 (m, 3H, Ph), 8.02 - 8.10 (m, 2H, Ph), J_{H2-H3} = 6.0 Hz, $J_{H3-H3'a}$ = 7.1 Hz, $J_{H3-H3'b}$ = 7.2 Hz, $J_{H3'a-H3'b}$ = -11.5 Hz, J_{H3-H4} = 5.8 Hz, $J_{H4-H4'a}$ = 4.2 Hz, $J_{H4-H4'b}$ = 3.3 Hz, $J_{H4'a-H4'b}$ = -12.7 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 21.14 [CH_3CO], 39.95 [C3], 63.16 [C3'], 65.57 [C4'], 79.92 [C4], 96.07 [C2], 128.90, 129.98, 133.68 [aromatic CH], 129.88 [aromatic C], 157.69, 158.05 [OCOCOOMe], 166.38 [PhCO], 169.70 [CH_3CO]; LRMS (CI-NH_3): m/e 384 ([M + NH_4^+], 100%), 307 ([MH^+ - AcOH], 41.6%); HRMS (CI-NH_3): m/e calcd. for $C_{17}H_{22}NO_9$ [M + NH_4^+], 384.1293; found, 384.1294}.



47a, R=CH_3

47b, R=Ph

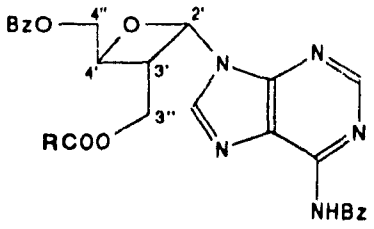
47c, R=$COOCH_3$

Nucleoside (48a).

To a solution of oxetane **47a** (13 mg, 0.04 mmol) in dry 1,2-dichloroethane (0.5 mL) under an atmosphere of nitrogen at room temperature was added a stock solution of *bis*-(trimethylsilyl)-N^6-adenine in 1,2-dichloroethane (0.339 M solution, 250 μL, 0.085 mmol) and tin tetrachloride (7.1 μL, 0.06 mmol). After stirring for 1 h, the reaction mixture was diluted with methylene chloride (25 mL), washed with saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* yielding a white residue. Purification by flash chromatography (methylene chloride / methanol, 100:3 v/v) afforded nucleoside **48a** (14 mg, 70% yield) as a white foam. [^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.05 (s, 3H, Ac), 3.47 (dddd, 1H, H2'), 4.42 (m, 4H, H2"$_a$, H2"$_b$, H3"$_a$, H3"$_b$), 5.47 (ddd, 1H, H3'), 6.26 (d, 1H, H1'), 7.32 - 7.56 (m, 6H, Ph), 7.79 - 7.84 (m, 1H, Ph), 7.92 - 8.00 (m, 3H, Ph), 8.26 (s, 1H, H8), 8.64 (s, 1H, H2), 9.39 (s, br, ex, 1H, NH), $J_{H1'-H2'}$ = 3.3 Hz, $J_{H2'-H3'}$ = 2.2 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 20.95 [$\mathbf{C}H_3CO$], 51.39 [C2'], 62.28 [C2"], 74.13 [C3"], 76.23 [C3'], 87.80 [C1'], 123.98 [C5], 128.12, 128.98, 129.23, 129.85, 133.08, 133.96 [aromatic **CH**], 130.03 [aromatic C-$COOCH_2$], 135.76 [aromatic C-CON], 141.36 [C8], 149.87 [C4], 151.96 [C6], 152.86 [C2], 164.76, 166.16 [PhCO], 170.90 [$CH_3\mathbf{C}O$]; UV (methanol), λ_{max} 234 nm and 282 nm].

Nucleoside (48b).

Nucleoside **48b** was obtained in 68% yield from oxetane **47b** by a procedure similar to that used for the preparation of nucleoside **48a**. [^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.64 (dddd, 1H, H2'), 4.48 (A of ABX, 1H, H3'$_a$), 4.53 (B of ABX, 1H, H3'$_b$), 4.66 (A of ABX, 1H, H2'$_a$), 4.76 (B of ABX, 1H, H2'$_b$), 5.60 (ddd, 1H, H3'), 6.44 (d, 1H, H1'), 7.37 - 7.72 (m, 9H, Ph), 7.84 - 7.88 (m, 1H, Ph), 7.98 - 8.14 (m, 5H, Ph), 8.31 (s, 1H, H8), 8.64 (s, 1H, H2), 9.07 (s, br, ex, 1H, NH), $J_{H1'-H2'}$ = 3.2 Hz, $J_{H2'-H2"_a}$ = 7.0 Hz, $J_{H2'-H2"_b}$ = 5.6 Hz, $J_{H2"_a-H2"_b}$ = -11.6 Hz, $J_{H2'-H3'}$ = 1.6 Hz, $J_{H3'-H3"_a}$ = 2.5 Hz, $J_{H3'-H3"_b}$ = 5.0 Hz, $J_{H3"_a-H3"_b}$ = -10.8 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 51.52 [C2'], 62.95 [C2"], 74.16 [C3"], 76.23 [C3'], 89.80 [C1'], 124.02 [C5], 128.21, 128.83, 128.94, 129.09, 129.83, 129.93, 132.96, 133.71, 133.93 [aromatic **CH**], 129.42, 129.76 [aromatic C-$COOCH_2$], 134.30 [aromatic C-CON], 141.36 [C8], 149.97 [C4], 151.86 [C6], 152.58 [C2], 165.19, 166.11, 166.39 [**CO**]; LRMS (FAB-glycerol): m/e 564 ([MH^+], 12.1%); HRMS (FAB-glycerol): m/e calcd. for $C_{31}H_{26}N_5O_6$ [MH^+], 564.1884; found, 564.1883].

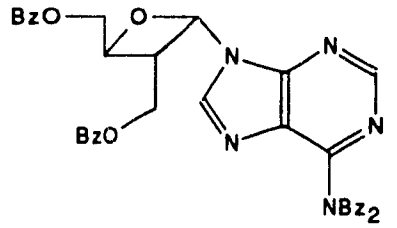


48a, R=CH_3

48b, R=Ph

***N,N*-Benzoylepioxetanocin-dibenzoate (50).**

A solution of nucleoside **48b** (36 mg, 0.064 mmol) in dry methylene chloride (1 mL) under nitrogen at ambient temperaure containing *N,N*-dimethylaminopyridine (8 mg, 0.064 mmol), pyridine (52 μL, 0.64 mmol) and benzoyl chloride (37 μL, 0.32 mmol) was stirred for 18 h. The solution was diluted with methylene chloride (25 mL), washed with 5% hydrochloric acid (25 mL), saturated aqueous sodium bicarbonate (25 mL), brine (25 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a yellow oil. Chromatography over silica gel (methylene chloride / methanol, 50:1 v/v) afforded pure **50** (38 mg, 89% yield) as a white foam. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.64 (dddd, 1H, H2'), 4.48 (A of ABX, 1H, H3"$_a$), 4.54 (B of ABX, 1H, H3"$_b$), 4.66 (A of ABX, 1H, H2"$_a$), 4.76 (B of ABX, 1H, H2"$_b$), 5.62 (ddd, 1H, H3'), 6.44 (d, 1H, H1'), 7.25 - 7.65 (m, 12H, Ph), 7.78 - 7.91 (m, 5H, Ph), 7.95 - 8.07 (m, 3H, Ph), 8.36 (s, 1H, H8), 8.49 (s, 1H, H2), $J_{H1'-H2'}$ = 3.0 Hz, $J_{H2'-H2"a}$ = 7.2 Hz, $J_{H2'-H2"b}$ = 5.6 Hz, $J_{H2"a-H2"b}$ = -11.5 Hz, $J_{H2'-H3'}$ = 2.7 Hz, $J_{H3'-H3"a}$ = 2.8 Hz, $J_{H3'-H3"b}$ = 5.7 Hz, $J_{H3"a-H3"b}$ = -10.9 Hz; ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ 49.22 [C2'], 62.74 [C2"], 72.76 [C3"], 75.79 [C3'], 87.17 [C1'], 125.56 [C5], 128.85, 128.90, 129.07, 129.10, 129.65, 129.81, 129.88, 129.97, 133.29, 133.39, 133.72, 133.77 [aromatic CH], 129.36, 129.76 [aromatic C-$COOCH_2$], 134.00, 134.32 [aromatic C-CON], 145.77 [C8], 151.27 [C4], 152.15 [C6], 152.74 [C2], 165.90, 166.23 [PhCOO], 172.47, 177.77 [OCNCO]; LRMS (FAB-glycerol): m/e 564 ([MH^+], 12.1%); HRMS (FAB-glycerol): m/e calcd. for $C_{31}H_{26}N_5O_6$ [MH^+], 564.1884; found, 564.1883}.



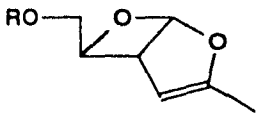
Epioxetanocin (1α).

To a solution of nucleoside **48a** (28 mg, 0.056 mmol) in anhydrous methanol (1 mL) under an atmosphere of nitrogen at room temperature was added sodium (8 mg, 0.348 mmol) and the mixture allowed to stir for 16 h. Amberlite weakly acidic resin was added until the pH was adjusted to 7 and the reaction mixture was filtered. The solvent was then removed *in vacuo* and the residue was crystallized from methanol to afford pure epioxetanocin (10 mg, 71% yield) as white needles (m.p. 117-118°C). Nucleosides **48b** and **79b** were deblocked in a similar manner. {^{1}H-NMR (200 MHz, CD_3OD): δ 2.84 (dddd, 1H, H2'), 3.73 (A of ABX, 1H, H2"$_a$), 3.77 (B of ABX, 1H, H2"$_b$), 4.08 (A of ABX, 1H, H3"$_a$), 4.12 (B of ABX, 1H, H3"$_b$), 4.35 (ddd, 1H, H3'), 6.10 (d, 1H, H1'), 8.20 (s, 1H, H8), 8.37 (s, 1H, H2), $J_{H1'-H2'}$ = 3.4 Hz, $J_{H2'-H2"a}$ = 6.9 Hz, $J_{H2'-H2"b}$ = 6.2 Hz, $J_{H2"a-H2"b}$ = -11.1 Hz, $J_{H2'-H3'}$ = 2.3 Hz, $J_{H3'-H3'a}$ = 3.0 Hz, $J_{H3'-H3'b}$ = 4.6 Hz, $J_{H3"a-H3"b}$ = -9.6 Hz; ^{13}C-NMR (75.4 MHz, CD_3OD): δ 57.44 [C2'], 61.90 [C2"], 74.25 [C3"], 77.13 [C3'], 88.58 [C1'], 129.33 [C5], 130.64 [C4], 133.61 [C6], 141.95 [C8], 153.60

[C2]; LRMS (FAB-glycerol): m/e 252 ([MH^+], 4.4%); HRMS (FAB-glycerol): m/e calcd. for $C_{10}H_{14}N_5O_3$ [MH^+], 252.1095; found, 252.1096;).

3-Methyl-6β-hydroxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (52).

To a stirred solution of photo-adduct **44a** (1.024 g, 4.16 mmol) in dry diethyl ether (80 mL) under nitrogen at 0°C was added lithium aluminum hydride (240 mg, 6.24 mmol) and it was allowed to warm to ambient temperature. After 30 min, water (240 μL), 15% aqueous sodium hydroxide solution (240 μL) and water (720 μL) were added to destroy excess hydride. The reaction mixture was filtered through a bed of dry Celite and the filter cake washed with ether (80 mL). Evaporation of the filtrate *in vacuo* gave a colourless syrup which was chromatographed over silica gel (petroleum ether / ethyl acetate, 1:1 v/v) to afford the title compound (349 mg, 59% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.94 (dd, 3H, Me), 2.27 (s, br, ex, 1H, OH), 3.64 (dddd, 1H, H5), 3.69 (A of ABX, 1H, H6'$_a$), 3.77 (B of ABX, 1H, H6'$_b$), 4.60 (dddd, 1H, H6), 4.93 (dd, 1H, H4), 6.25 (dd, 1H, H1); J_{H1-H5} = 4.4 Hz, J_{H1-H6} = -0.8 Hz, J_{H4-Me} = -1.3 Hz, J_{H4-H5} = 2.8 Hz, J_{H5-Me} = 1.4 Hz, J_{H5-H6} = 2.5 Hz, $J_{H6-H6'a}$ = 3.7 Hz, $J_{H6-H6'b}$ = 2.9 Hz, $J_{H6'a-H6'b}$ = -12.7 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 13.87 [Me], 47.31 [C5], 64.75 [C6'], 92.35 [C6], 99.16 [C4], 108.56 [C1], 158.08 [C3]; LRMS (CI-NH_3): m/e 160 ([M + NH_4^+], 3.5%l), 143 ([MH^+], 100%), 125 ([MH^+ - H_2O], 47.4%); HRMS (CI-NH_3): m/e calcd. for $C_7H_{11}O_3$ [MH^+], 143.0708; found, 143.0708}.



52, R=H
53, R=TBDMSi
55, R=TBDPhSi

3-Methyl-6β-*t*-butyldimethylsilyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (53).

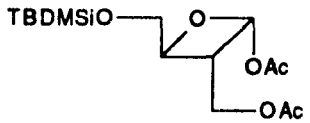
Photo-adduct alcohol **52** was silylated by a procedure similar to that used for the preparation of **19**. Purification by flash chromatography (petroleum ether / ether, 10:1 v/v) gave the title compound in 27% yield as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.07, 0.09 (2s, 6H, *t*-BuSiMe_2), 0.91 (s, 9H, *t*-BuSiMe_2), 1.92 (t, 3H, Me), 3.61 (dddd, 1H, H5), 3.72 (A of ABX, 1H, H6'$_a$), 3.78 (B of ABX, 1H, H6'$_b$), 4.50 (dddd, 1H, H6), 4.91 (dd, 1H, H4), 6.21 (dd, 1H, H1), J_{H1-H5} = 4.4 Hz, J_{H1-H6} = -0.9 Hz, J_{H4-Me} = -1.4 Hz, J_{H4-H5} = 2.7 Hz, J_{H5-Me} = 1.4 Hz, J_{H5-H6} = 3.1 Hz, $J_{H6-H6'a}$ = 3.0 Hz, $J_{H6-H6'b}$ = 3.3 Hz, $J_{H6'a-H6'b}$ = -11.7 Hz; LRMS (CI-NH_3): m/e 274 ([M + NH_4^+], 0.5%), 257 ([MH^+], 7.7%), 239 ([MH^+ - H_2O], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{13}H_{23}O_2Si$ [MH^+ - H_2O], 239.1468, found, 239.1467}.

3-Methyl-6β-*t*-butyldiphenylsilyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (55).

To a solution of photo-adduct alcohol **52** (78 mg, 0.55 mmol) in dry *N,N*-dimethylformamide (2 mL) under nitrogen at room temperature was added imidazole (79 mg, 1.10 mmol) and *t*-butyldiphenylsilyl chloride (150 μL, 0.58 mmol) and it was allowed to stir until all of the starting material was consumed (18 h). The solvent was removed *in vacuo* and the residue was chromatographed over silica gel (petroleum ether / ethyl acetate, 20:1 v/v) to afford the title compound (129 mg, 62% yield) as a clear oil. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.11 (s, 9H, *t*-BuSiPh$_2$), 1.95 (t, 3H, Me), 3.75 (dddd, 1H, H5), 3.82 (A of ABX, 1H, H6'$_a$), 3.86 (B of ABX, 1H, H6'$_b$), 4.54 (dddd, 1H, H6), 4.98 (dd, 1H, H4), 6.32 (dd, 1H, H1), 7.37 - 7.52 (m, 6H, Ph), 7.66 - 7.79 (m, 4H, Ph); J_{H1-H5} = 4.4 Hz, J_{H1-H6} = -0.9 Hz, J_{H4-Me} = -1.4 Hz, J_{H4-H5} = 2.7 Hz, J_{H5-Me} = 1.4 Hz, J_{H5-H6} = 3.0 Hz, $J_{H6-H6'a}$ = 3.0 Hz, $J_{H6-H6'b}$ = 3.0 Hz, $J_{H6'a-H6'b}$ = -11.7 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 14.04 [Me], 19.55 [$(CH_3)_3CSiMe_2$], 27.02 [$(CH_3)_3CSiMe_2$], 47.64 [C5], 66.13 [C6'], 91.72 [C6], 99.25 [C4], 108.66 [C1], 128.13, 128.28, 130.13, 130.17, 135.91, 136.02 [aromatic CH], 133.69, 133.80 [aromatic C-Si], 158.10 [C3]; LRMS (CI-NH_3): m/e 398 ([M + NH_4^+], 2.7%), 381 ([MH^+], 100%), 363 ([MH^+ - H_2O], 6.7%); HRMS (CI-NH_3): m/e calcd. for $C_{23}H_{29}O_3Si$ [MH^+], 381.1886; found, 381.1885}.

Oxetane (54).

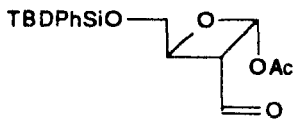
Oxetane **54** was obtained from adduct **53** in 19% yield by a procedure similar to that used for the preparation of oxetane **42a**. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 0.09, 0.10 (2s, 6H, *t*-BuSiMe$_2$), 0.93 (s, 9H, *t*-BuSiMe$_2$), 2.01 (s, 3H, Ac), 2.09 (s, 3H, anomeric Ac), 3.38 (dddd, 1H, H3), 3.71 (A of ABX, 1H, H4'$_a$), 3.81 (B of ABX, 1H, H4'$_b$), 4.31 (A of ABX, 1H, H3'$_a$), 4.36 (B of ABX, 1H, H3'$_b$), 4.58 (ddd, 1H, H4), 6.37 (d, 1H, H2), J_{H2-H3} = 5.9 Hz, $J_{H3-H3'a}$ = 7.3 Hz, $J_{H3-H3'b}$ = 7.7 Hz, J_{H3-H4} = 5.6 Hz, $J_{H3'a-H3'b}$ = -11.4 Hz, $J_{H4-H4'a}$ = 3.5 Hz, $J_{H4-H4'b}$ = 2.9 Hz, $J_{H4'a-H4'b}$ = -12.1 Hz; LRMS (CI-NH_3): m/e 350 ([M + NH_4^+], 10.2%), 333 ([MH^+], 1.5%); 273 ([MH^+ - AcOH], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{13}H_{25}O_4Si$ [MH^+ - AcOH], 273.1522; found, 273.1522}.



54

Aldehyde (56).

Adduct **55** was transformed to aldehyde **56** in 93% yield by a procedure similar to that used for the preparation of aldehyde **45**. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.10 (s, 9H, *t*-Bu), 2.10 (s, 3H, Ac) 4.14 (dt, 1H, H3), 4.52 (A of ABX, 1H, H4'$_a$), 4.63 (B of ABX, 1H, H4'$_b$), 5.16 (ddd, 1H, H4), 6.63 (d, 1H, H2), 7.36 - 7.51 (m, 6H, Ph), 7.64 - 7.85 (m, 4H, Ph), 9.82 (d, 1H, CHO), $J_{H2\text{-}H3}$ = 6.2 Hz, $J_{H3\text{-}CHO}$ = 1.4 Hz, $J_{H3\text{-}H4}$ = 6.1 Hz, $J_{H4\text{-}H4'a}$ = 7.0 Hz, $J_{H4\text{-}H4'b}$ = 7.7 Hz, $J_{H4'a\text{-}H4'b}$ = -11.5 Hz}.



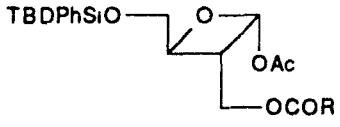
56

Oxetane (56a).

Oxetane **56a** was obtained from adduct **55** in 18% yield by a procedure similar to that used for the preparation of oxetane **42a**. {^{1}H-NMR (200 MHz, CD_2Cl_2)· δ 1.09 (s, 9H, ***t*-BuSiPh$_2$**), 1.99 (s, 3H, Ac), 2.10 (s, 3H, anomeric Ac), 3.51 (dddd, 1H, H3), 3.76 (A of ABX, 1H, H4'$_a$), 3.87 (B of ABX, 1H, H4'$_b$), 4.31 (A of ABX, 1H, H3'$_a$), 4.36 (B of ABX, 1H, H3'$_b$), 4.64 (ddd, 1H, H4), 6.46 (d, 1H, H2), 7.31 - 7.49 (m, 6H, Ph), 7.62 - 7.74 (m, 4H, Ph), $J_{H2\text{-}H3}$ = 5.8 Hz, $J_{H3\text{-}H3'a}$ = 7.3 Hz, $J_{H3\ H3'b}$ = 7.6 Hz, $J_{H3'a\ H3'b}$ = -11.4 Hz, $J_{H3\text{-}H4}$ = 6.2 Hz, $J_{H4\text{-}H4'a}$ = 3.5 Hz, $J_{H4\text{-}H4'b}$ = 2.9 Hz, $J_{H4'a\text{-}H4'b}$ = -12.0 Hz; LRMS (CI-NH_3): m/e 474 ([M + NH_4^+], 100%); HRMS (CI-NH_3)· m/e calcd. for $C_{25}H_{36}NO_6Si$ [M + NH_4^+], 474.2310; found, 474.2311}.

Oxetane (56b).

Oxetane **56b** was obtained from adduct **55** in 18% yield by a procedure similar to that used for the transformation of photo-adduct **44a** to oxetane **47b**. {^{1}H-NMR (200 MHz, CD_2Cl_2)· δ 1.08 (s, 9H, ***t*-BuSiPh$_2$**), 2.08 (s, 3H, Ac), 3.67 (ddt, 1H, H3), 3.80 (A of ABX, 1H, H4'$_a$), 3.91 (B of ABX, 1H, H4'$_b$), 4.60 (d, 2H, H3'$_a$, H3'$_b$), 4.76 (ddd, 1H, H4), 6.54 (d, 1H, H2), 7.33 - 7.60 (m, 9H, Ph), 7.66 - 7.74 (m, 4H, Ph), 7.95 - 8.06 (m, 2H, Ph), $J_{H2\text{-}H3}$ = 5.9 Hz, $J_{H3\text{-}H3'aH3'b}$ = 7.2 Hz, $J_{H3'a\ H3'b}$ ~ 0 Hz, $J_{H3\ H4}$ = 6.0 Hz, $J_{H4\text{-}H4'a}$ = 3.4 Hz, $J_{H4\text{-}H4'b}$ = 2.8 Hz, $J_{H4'a\text{-}H4'b}$ = -12.1 Hz; LRMS (CI-NH_3): m/e 536 ([M + NH_4^+], 74.9%), 459 ([MH^+ - AcOH], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{30}H_{38}NO_6Si$ [M + NH_4^+], 536.2469; found, 536.2468}.



56a, R=CH_3

56b, R=Ph

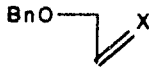
56c, R=$COOCH_3$

Oxetane (56c).

Oxetane **56c** was obtained from adduct **55** in 18% yield by a procedure similar to that used for the transformation of photo-adduct **44a** to oxetane **47c**. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.08 (s, 9H, *t*-**Bu**SiPh$_2$), 2.11 (s, 3H, Ac), 3.86 (s, 3H, MeO), 6.49 (d, 1H, H2), 7.35 - 7.73 (m, 10H, Ph), J_{H2-H3} = 5.8 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 19.50 [SiC(**C**H$_3$)$_3$], 21.19 [**C**H$_3$CO], 26.95 [SiC(**C**H$_3$)$_3$], 38.91 [C3], 52.95 [**C**H$_3$O], 63.42 [C3'], 65.03 [C4'], 82.26 [C4], 96.19 [C2], 128.05, 128.14, 130.19, 130.34, 135.93, 136.03 [aromatic **C**H], 133.48, 133.53 [aromatic C-Si], 157.12, 158.16 [OCOCOOMe], 169.76 [CH$_3$**C**O]; LRMS (CI-NH$_3$): m/e 518 ([M + NH$_4^+$], 40.5%); HRMS (CI-NH$_3$): m/e calcd. for $C_{26}H_{36}NO_8Si$ [M + NH$_4^+$], 518 2212; found, 518.2210}.

1-*O*-Benzyloxy-3-methyl-2-butene (57).

Sodium hydride (60% oil dispersion, 3.60 g, 90.0 mmol) was added to an ice-cooled solution of 3-methyl-2-buten-1-ol (5.17 g, 60.0 mmol) and tetra-*n*-butylammonium iodide (2.22 g, 6.0 mmol) in dry tetrahydrofuran (500 mL) under an atmosphere of nitrogen. After complete evolution of hydrogen (1 h), benzyl bromide (12.30 g, 72.0 mmol) was added dropwise and stirring was continued for 20 h. Florisil (10 g) was added and the reaction mixture was stirred for another 30 min. Removal of the solvent *in vacuo* gave a residue which was washed with pentane (5 x 200 mL). Evaporation of the washings gave a yellow oil which was chromatographed over silica gel (petroleum ether / ethyl acetate, 10.1 v/v) to afford the title compound (10.46 g, 99% yield) as a colourless oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.64 (s, br, 3H, CH$_3$), 1.75 (s, br, 3H, CH$_3$'), 3.99 (d, 2H, CH$_2$), 4.49 (s, 2H, **C**H$_2$Ph), 5.40 (t, br, 1H, CH), 7.26 - 7.37 (m, 5H, Ph), J_{CH_2-CH} = 6.7 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 25.67 [**C**H$_3$], 66.44 [CH**C**H$_2$O], 71.90 [**C**H$_2$Ph], 121.02 [**C**H], 127.36, 127.66, 128.19 [aromatic **C**H], 136.97 [aromatic **C**], 138.47 [Me$_2$**C**]}.



57, X=C(CH$_3$)$_2$
58, X=O

2-Benzyloxyacetaldehyde (58).

Ozone and nitrogen were bubbled through a solution of **57** (17.60 g, 100.0 mmol) in dry methylene chloride (1600 mL) at -78°C until the solution turned blue (4.5 h). Dimethyl sulfide (73.4 mL, 1.0 mol) was added to the reaction mixture under an atmosphere of nitrogen and it was allowed to warm to ambient temperature gradually overnight. The solution was washed with water (2 x 1 L), brine (1 L), dried (Na$_2$SO$_4$), filtered and the solvent removed in vacuo to yield aldehyde **58** (14.25 g, 95% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 4.00 (d, 2H, **C**H$_2$CHO), 4.51 (s, 2H, **C**H$_2$Ph), 7.25 - 7.29 (m, 5H, Ph), 9.58 (t, 1H, CHO), J_{CH_2-CHO} = 0.8 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 73.40

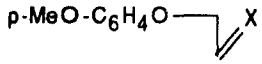
[CH_2CHO], 75.08 [CH_2Ph], 127.84, 127.99, 128.40 [aromatic CH], 136.70 [aromatic C], 200.20 [CHO]].

1-O-*p*-Anisyloxy-3-methyl-2-butene (61).

To a stirred solution of 3-methyl-2-buten-1-ol (8.61 g, 100.0 mmol) and *p*-methoxyphenol (37.24 g, 300.0 mmol) in dry tetrahydrofuran (300 mL) under nitrogen at ambient temperaure was added triphenylphosphine (34.10 g, 130.0 mmol) and diethyl azodicarboxylate (22.64 g, 130.0 mmol). The mixture was then refluxed for 2 h. Evaporation of the solvent *in vacuo* gave a white solid which was chromatographed over silica gel (petroleum ether / ethyl acetate, 100:1) to afford **61** (18.70 g, 97% yield) as a clear oil. [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.71 (d, 3H, CH_3), 1.77 (d, 3H, CH_3'), 3.75 (s, 3H, MeO), 4.43 (d, 2H, CH_2), 5.47 (m, 1H, CH), 6.81, 6.83 (AB quartet, 4H, Ph), $J_{CH\text{-}Me}$ = -0.3 Hz, $J_{CH\ Me'}$ = -1.2 Hz, $J_{CH_2\text{-}CH}$ = 6.8 Hz, J_{AB} = 9.6 Hz].

2-*p*-Anisyloxyacetaldehyde (62).

To a stirred solution of diol **64** (4.16 g, 20.0 mmol) in methanol (100 mL) and water (100 mL) at ambient temperature was added sodium *m*-periodate (4.28 g, 20.0 mmol). After 30 min, the sodium iodate precipitate was filtered off and the methanol was evaporated *in vacuo*. The remaining solution was then extracted with methylene chloride (3 x 250 mL), washed with brine (250 mL), dried (Na_2SO_4), filtered and the solvent again removed *in vacuo* to afford aldehyde **62** (3.22 g, 97% yield) as a clear oil [^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.75 (s, 3H, MeO), 4.51 (d, 2H, CH_2), 6.81, 6.84 (AB quartet, 4H, Ph), 9.83 (t, 1H, CHO), $J_{CH_2\text{-}CHO}$ = 1.1 Hz, J_{AB} = 1.9 Hz; LRMS (CI-NH_3): m/e 184 ([M + NH_4^+], 100%)].

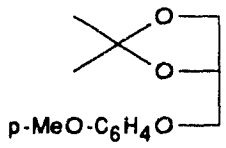


61, X=$C(CH_3)_2$

62, X=O

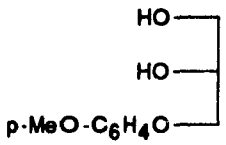
Glycerol-1-O-*p*-anisyl-2,3-O-acetonide(63).

Compound **63** was obtained in 88% yield from solketal by a procedure similar to that used for the preparation of **61**. [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.38, 1.44 (2s, 6H, CMe_2), 3.74 (s, 3H, MeO), 3.87 (A of ABX, 1H, $H1_a$)*, 3.87 (A of ABX, 1H, $H3_a$)*, 4.00 (B of ABX, 1H, $H1_b$)*, 4.14 (B of ABX, 1H, $H3_b$)*, 4.44 (dddd, 1H, H2), 6.82, 6.83 (AB q, 4H, Ph), $J_{H1a\text{-}H2}$ = 5.9 Hz, $J_{H1b\text{-}H2}$ = 5.4 Hz, $J_{H1a\text{-}H1b}$ = -9.2 Hz, J_{AB} = 1.2 Hz, $J_{H2\text{-}H3a}$ = 5.9 Hz, $J_{H2\text{-}H3b}$ = 6.4 Hz, $J_{H3a\text{-}H3b}$ = -8.6 Hz].



1-O-*p*-anisyloxyglycerol (64).

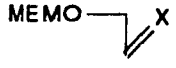
A solution of **63** (26.61 g, 107.3 mmol) in acetic acid (240 mL) and water (60 mL) was stirred at ambient temperature for 17 h. Evaporation of the solvent *in vacuo* gave a white solid which was dissolved in methylene chloride (1 L), washed with saturated aqueous sodium bicarbonate (3 x 800 mL), brine (800 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to give a white residue. Purification by flash chromatography (ethyl acetate / petroleum ether, 2:1 v/v) afforded the title compound (18.75 g, 84% yield) as a white solid (m.p. 74.5-75.5°C). {^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.41 (t, ex, 1H, OH on C3), 2.91 (d, ex, 1H, OH on C2), 3.74 (s, 3H, MeO), 3.74 (dddd, 2H, $H3_a$, $H3_b$), 4.05 (m, 1H, H2), 3.95 (m, 2H, $H1_a$, $H1_b$), 6.81, 6.82 (AB q, 4H, Ph), J_{OH-H2} = 4.5 Hz, $J_{OH-H3aH3b}$ = 6.0 Hz, J_{AB} = 0.6 Hz}.



64

1-O-Methoxyethoxymethyloxy-3-methyl-2-butene (66).

Sodium hydride (60% oil dispersion, 7.20 g, 180.0 mmol) was added to an ice-cooled solution of 3-methyl-2-buten-1-ol (12.92 g, 150.0 mmol) in dry tetrahydrofuran (500 mL) under an atmosphere of nitrogen. After complete evolution of hydrogen (1 h), 2-methoxyethoxymethyl chloride (22.42 g, 180.0 mmol) was added dropwise and allowed to stir for 16 h at room temperature. The reaction mixture was then cooled to 0°C and excess hydride was destroyed by careful addition of 0.1% hydrochloric acid. Removal of the solvent *in vacuo* gave a residue which was dissolved in methylene chloride (1 L), washed with saturated aqueous sodium bicarbonate (800 mL), brine (800 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a yellow oil. Distillation of the crude product (69-71°C, 0.5 mm Hg) gave the title compound (21.59 g, 83% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.65 (s, br, 3H, CH_3), 1.72 (d, 3H, CH_3'), 3.37 (s, 3H, MeO), 3.54 (m, 2H, OCH_2), 3.68 (m, 2H, OCH_2), 4.04 (d, 2H, OCH_2CH), 4.69 (s, 2H, OCH_2O), 5.30 (m, 1H, CH), J_{Me-CH} ~ 0 Hz, $J_{Me'-CH}$ = -1.0 Hz, J_{CH_2-CH} = 7.1 Hz}.



66, R=$C(CH_3)_2$

67, R=O

2-Methoxyethoxymethyloxyacetaldehyde (67).

Aldehyde **67** was obtained in 27% yield from olefin **66** by a procedure similar to that described for the preparation of aldehyde **58**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.37 (s, 3H, MeO), 3.54 (m, 2H,

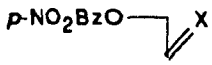
OCH_2), 3.72 (m, 2H, OCH_2), 4.19 (d, 2H, CH_2CHO), 4.82 (s, 2H, OCH_2O), 9.70 (t, 1H, CHO), $J_{CH_2\text{-}CHO}$ = 0.9 Hz; IR ($CHCl_3$): 1738 cm^{-1}}.

1-O-*p*-Nitrobenzoyloxy-3-methyl-2-butene (68).

A solution of 3-methyl-2-buten-1-ol (8.61 g, 100.0 mmol) in dry methylene chloride (125 mL) under nitrogen at ambient temperaure containing *N,N*-dimethylaminopyridine (1.22 g, 10.0 mmol), pyridine (24.3 mL, 300 mmol) and *p*-nitrobenzoyl chloride (22.27 g, 120.0 mmol) was stirred for 18 h. The solution was diluted with methylene chloride (1 L), washed with 5% hydrochloric acid (450 mL), saturated aqueous sodium bicarbonate (450 mL), brine (450 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a yellow solid which was chromatographed over silica gel (hexanes / ethyl acetate, 97:3 v/v) to afford **68** as a light yellow solid (21.60 g, 92% yield, m.p. 61.5-63.5°C). {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.76 (d, 3H, CH_3), 1.78 (d, 3H, CH_3'), 4.84 (d, 1H, CH_2), 5.45 (m, 1H, CH), 8.19, 8.25 (AB q, 4H, Ph), $J_{CH\text{-}Me}$ = -1.2 Hz, $J_{CH\text{-}Me'}$ = -1.0 Hz, $J_{CH_2\text{-}CH}$ = 7.3 Hz, J_{AB} = 9.2 Hz}.

2-*p*-Nitrobenzoyloxyacetaldehyde (69).

2-*p*-Nitrobenzoyloxyacetaldehyde was obtained from **68** as described for the preparation of aldehyde **20**. Purification by flash chromatography (petroleum ether / ethyl acetate, 2:1 v/v) gave the title compound (95% yield) as a viscous light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 4.98 (s, 2H, CH_2), 8.26, 8.31 (AB q, 4H, Ph), 9.71 (s, 1H, CHO), J_{AB} = 9.2 Hz}



68, R=$C(CH_3)_2$
69, R=O

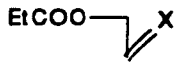
1-O-Propionyloxy-3-methyl-2-butene (70).

A solution of 3-methyl-2-buten-1-ol (86.13 g, 1.00 mol) in dry methylene chloride (1500 mL) under nitrogen at ambient temperaure containing *N,N*-dimethylaminopyridine (12.22 g, 100.0 mmol), pyridine (283.1 mL, 3.5 mol) and propionyl chloride (130.3 mL, 1.5 mol) was stirred for 18 h. The solution was washed with 5% hydrochloric acid (1500 mL), saturated aqueous sodium bicarbonate (1500 mL), brine (1500 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a yellow oil. Distillation of the crude product (57-58°C, 0.7 mm Hg) gave the title compound in virtually quantitative yield (141.49 g) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.12 (t, 3H, CH_3CH_2), 1.69 (d, 3H, CH_3), 1.74 (d, 3H, CH_3'), 2.30 (q, 2H, CH_3CH_2), 4.55 (d, 2H, CH_2CH), 5.32 (m, 1H, CH), $J_{CH\text{-}Me}$ = -1.3 Hz, $J_{CH\text{-}Me'}$ = -1.1 Hz, $J_{CH\text{-}CH_2}$ = 7.3 Hz, $J_{CH_3\text{-}CH_2}$ = 7.6 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ

8.68 [CH_3CH_2], 25.27 [Me_2C], 27.14 [CH_3CH_2], 60.74 [OCH_2CH], 118.59 [**CH**], 138.15 [$(CH_3)_2C$], 173.82 [CO]}.

Propionyloxyacetaldehyde (71).

Propionyloxyacetaldehyde was obtained from **70** as described for the preparation of aldehyde **20**. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) gave the title compound (85% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.18 (t, 3H, CH_3), 2.46 (q, 2H, CH_3CH_2), 4.65 (s, 2H, CH_2CHO), 9.59 (s, 1H, CHO), $J_{CH_3\text{-}CH_2}$ = 7.6 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 8.55 [CH_3CH_2], 26.60 [CH_3CH_2], 68.25 [OCH_2], 173.43 [EtCO], 195.71 [CHO]}.

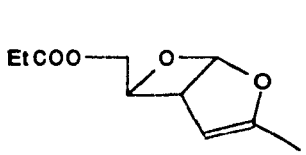


70, X=$C(CH_3)_2$
71, X=O

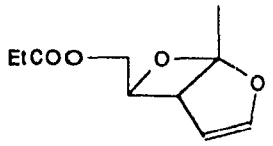
3-Methyl-6β-propionyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (72a) and 1β-Methyl-6β-propionyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (72b).

A mixture of 2-methylfuran (17.3 mL, 192 mmol) and aldehyde **71** (11.14 g, 96 mmol) in benzene (1800 mL) was placed in a 2 L photo-reaction vessel, cooled to 8°C, and saturated with argon. The solution was then irradiated for 8 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate / triethylamine, 10:1:0.01 v/v/v) gave **72a** and **72b** (mixture of 2 inseparable regioisomers, 16:11), (6.36 g, 33% yield) as a light yellow oil and recovered starting material (4.64 g aldehyde **71**). In the absence of triethylamine, **72b** decomposed on the column and photo-adduct **72a** was isolated (4.37 g, 23% yield) as a light yellow oil along with recovered starting material (4.64 g aldehyde **71**). **72a:** {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.15 (t, 3H, CH_3CH_2), 1.92 (dd, 3H, CH_3), 2.40 (q, 2H, CH_3CH_2), 3.59 (dddd, 1H, H5), 4.22 (A of ABX, 1H, H6'$_a$), 4.26 (B of ABX, 1H, H6'$_b$), 4.63 (dddd, 1H, H6), 4.97 (dd, 1H, H4), 6.22 (dd, 1H, H1), $J_{H1\text{-}H5}$ = 4.4 Hz, $J_{H1\text{-}H6}$ = -0.8 Hz, $J_{H4\text{-}Me}$ = -1.4 Hz, $J_{H4\text{-}H5}$ = 2.7 Hz, $J_{H5\text{-}Me}$ = 1.4 Hz, $J_{H5\text{-}H6}$ = 2.8 Hz, $J_{H6\text{-}H6'a}$ = 4.4 Hz, $J_{H6\text{-}H6'b}$ = 3.2 Hz, $J_{H6'a\text{-}H6'b}$ = -12.4 Hz, $J_{CH_3\text{-}CH_2}$ = 7.5 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 9.11 [CH_3CH_2], 13.70 [Me], 27.57 [CH_3CH_2], 47.89 [C5], 65.80 [C6'], 88.57 [C6], 98.81 [C4], 108.34 [C1], 158.23 [C3], 174.04 [CO]; LRMS (CI-NH_3): m/e 199 ([MH^+], 0.5%), 181 ([$MH^+ - H_2O$], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{10}H_{13}O_3$ [$MH^+ - H_2O$], 181.0865; found, 181.0864}. **72b:** {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.15 (t, 3H, CH_3CH_2), 1.71 (s, 3H, CH_3), 2.39 (q, 2H, CH_3CH_2), 3.37 (ddd, 1H, H5), 4.26 (d, 2H, H6'$_a$, H6'$_b$), 4.59 (dt, 1H, H6), 5.23 (t, 1H, H4), 6.54 (dd, 1H, H3), $J_{H3\text{-}H4}$ = 3.0 Hz, $J_{H3\text{-}H5}$ = -1.0 Hz, $J_{H4\text{-}H5}$ = 2.9 Hz, $J_{H5\text{-}H6}$ = 4.3 Hz, $J_{H6\text{-}H6'aH6'b}$ = 4.1 Hz, $J_{H6'a\text{-}H6'b}$ ~ 0 Hz, $J_{CH_3\text{-}CH_2}$ = 7.6 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 9.18 [CH_3CH_2], 23.12 [Me], 27.61 [CH_3CH_2], 48.39 [C5], 65.67 [C6'], 85.73 [C6], 104.25 [C4], 116.08 [C1], 148.37 [C3], 174.20 [CO]; LRMS (CI-NH_3): m/e 199

([MH^+], 0.5%), 181 ([MH^+ - H_2O], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{10}H_{13}O_3$ [MH^+ - H_2O], 181.0865; found, 181.0864}.



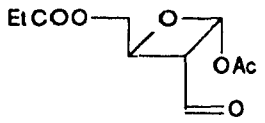
72a



72b

2α-Acetoxy-3α-O-formyl-4β-propionyloxymethyl oxetane (73).

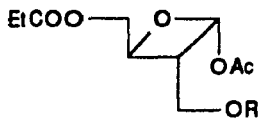
Photo-adduct **72a** was transformed to aldehyde **73** in 92% yield by a procedure similar to that used for the preparation of aldehyde **45**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.12 (t, 3H, $\mathbf{CH_3}CH_2$), 2.08 (s, 3H, Ac), 2.37 (q, 2H, $CH_3\mathbf{CH_2}$), 3.93 (dt, 1H, H3), 4.15 (A of ABX, 1H, H4'$_a$), 4.37 (B of ABX, 1H, H4'$_b$), 5.30 (ddd, 1H, H4), 6.55 (d, 1H, H2), 9.73 (d, 1H, CHO), $J_{H2\text{-}H3}$ = 6.4 Hz, $J_{H3\text{-}CHO}$ = 1.0 Hz, $J_{H3\text{-}H4}$ = 6.1 Hz, $J_{H4\text{-}H4'a}$ = 3.8 Hz, $J_{H4\text{-}H4'b}$ = 3.1 Hz, $J_{H4'a\text{-}H4'b}$ = -12.9 Hz, $J_{CH_3\text{-}CH_2}$ = 7.5 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$). δ 8.94 [$\mathbf{CH_3}CH_2$], 20.75 [$\mathbf{CH_3}CO$], 27.28 [$CH_3\mathbf{CH_2}$], 50.50 [C3], 64.19 [C4'], 75.76 [C4], 95.59 [C2], 169.30 [CH_3CO], 173.94 [EtCO], 195.09 [CHO]; LRMS (CI-NH_3). m/e 248 ([M + NH_4^+], 100%), 171 ([MH^+ - AcOH], 59.2%); HRMS (CI-NH_3): m/e calcd. for $C_{10}H_{18}NO_6$ [M + NH_4^+], 248.1133; found, 248.1134}.



73

2α-Acetoxy-3α-hydroxymethyl-4β-propionyloxymethyl oxetane (74).

Aldehyde **73** was reduced to alcohol **74** in 68% yield by a procedure similar to that used for the preparation of alcohol **46**. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 0.88 (s, br, ex, 1H, OH), 1.14 (t, 3H, $\mathbf{CH_3}CH_2$), 2.13 (s, 3H, Ac), 2.40 (q, 2H, $CH_3\mathbf{CH_2}$), 3.19 (dddd, 1H, H3), 3.83 (A of ABX, 1H, H3'$_a$), 3.90 (B of ABX, 1H, H3'$_b$), 4.20 (A of ABX, 1H, H4'$_a$), 4.33 (B of ABX, 1H, H4'$_b$), 4.82 (ddd, 1H, H4), 6.41 (d, 1H, H2), $J_{H2\text{-}H3}$ = 6.0 Hz, $J_{H3\text{-}H3'a}$ = 5.7 Hz, $J_{H3\text{-}H3'b}$ = 5.6 Hz, $J_{H3'a\text{-}H3'b}$ = -11.8 Hz, $J_{H3\text{-}H4}$ = 6.2 Hz, $J_{H4\text{-}H4'a}$ = 4.8 Hz, $J_{H4\text{-}H4'b}$ = 3.0 Hz, $J_{H4'a\text{-}H4'b}$ = -12.6 Hz, $J_{CH_3\text{-}CH_2}$ = 7.5 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 8.94 [$\mathbf{CH_3}CH_2$], 20.98 [$\mathbf{CH_3}CO$], 27.31 [$CH_3\mathbf{CH_2}$], 40.78 [C3], 58.79 [C3'], 65.10 [C4'], 79.34 [C4], 97.23 [C2], 169.62 [CH_3CO], 174.14 [EtCO]; LRMS (CI-NH_3): m/e 250 ([M + NH_4^+], 100%), 233 ([MH^+], 1.5%), 173 ([MH^+ - AcOH], 49.5%); HRMS (CI-NH_3): m/e calcd. for $C_{10}H_{20}NO_6$ [M + NH_4^+], 250.1291; found, 250.1290}.



74, R=H
75a, R=COCOOMe
75b, R=CSOPh
75c, R=CS-*imid*
75d, R=CSOMe
75e, R=CH_2SCH_3
75f, R=CH_2SOCH_3
75g, R=$CH_2SO_2CH_3$
75h, R=*o*-MeOPh
75i, R=COCON$(CH_2)_4$
75j, OR=Cl

Oxetane (75a).

Oxetane **75a** was obtained from photo-adduct **72a** in 41% yield by a procedure similar to that used for the transformation of photo-adduct **44a** to oxetane **47c**. [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.15 (t, 3H, $\mathbf{CH_3}CH_2$), 2.11 (s, 3H, Ac), 2.39 (q, 2H, $CH_3\mathbf{CH_2}$), 3.44 (dddd, 1H, H3), 3.89 (s, 3H, MeO), 4.19 (A of ABX, 1H, H4'$_a$), 4.34 (B of ABX, 1H, H4'$_b$), 4.55 (A of ABX, 1H, H3'$_a$), 4.60 (B of ABX, 1H, H3'$_b$), 4.82 (ddd, 1H, H4), 6.46 (d, 1H, H2), $J_{H2\text{-}H3}$ = 5.9 Hz, $J_{H3\text{-}H3'a}$ = 7.3 Hz, $J_{H3\text{-}H3'b}$ = 7.2 Hz, $J_{H3'a\text{-}H3'b}$ = -11.6 Hz, $J_{H3\text{-}H4}$ = 6.2 Hz, $J_{H4\text{-}H4'a}$ = 4.3 Hz, $J_{H4\text{-}H4'b}$ = 3.3 Hz, $J_{H4'a\text{-}H4'b}$ = -12.7 Hz, $J_{CH_3\text{-}CH_2}$ = 7.5 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 9.05 [$\mathbf{CH_3}CH_2$], 20.92 [$\mathbf{CH_3}CO$], 27.48 [$CH_3\mathbf{CH_2}$], 39.67 [C3], 53.75 [MeO], 63.00 [C3'], 64.86 [C4'], 79.62 [C4], 95.96 [C2], 157.56, 158.00 [OCOCOOMe], 169.58 [$CH_3\mathbf{CO}$], 174.09 [EtCO]; LRMS (CI-NH_3): m/e 336 ([M + NH_4^+], 56.8%), 259 ([MH^+ - AcOH], 25.8%); HRMS (CI-NH_3): m/e calcd. for $C_{13}H_{22}NO_9$ [M + NH_4^+], 336.1296; found, 336.1294].

Oxetane (75b).

To a solution of alcohol **74** (70 mg, 0.30 mmol) in dry methylene chloride (5 mL) under an atmosphere of nitrogen at 0°C was added N,N-dimethylaminopyridine (7 mg, 0.06 mmol), pyridine (170 μL, 2.10 mmol) and phenyl chlorothioformate (124 μL, 0.60 mmol). The solution was gradually warmed to room temperature (over 1 h) and allowed to stir for 16 h. The reaction mixture was then diluted with methylene chloride (20 mL), washed with 5% hydrochloric acid (25 mL), saturated aqueous sodium bicarbonate (25 mL), brine (25 mL), dried (Na_2SO_4), filtered and the solvent removed in vacuo to yield a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate, 4:1 v/v) afforded the title compound (24 mg, 35% yield) as a light yellow oil. [^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.16 (t, 3H, $\mathbf{CH_3}CH_2$), 2.14 (s, 3H, Ac), 2.43 (q, 2H, $CH_3\mathbf{CH_2}$), 3.59 (dddd, 1H, H3), 4.22 (A of ABX, 1H, H4'$_a$),

4.37 (B of ABX, 1H, $H4'_b$), 4.80 (A of ABX, 1H, $H3'_a$), 4.85 (ddd, 1H, H4), 4.88 (B of ABX, 1H, $H3'_b$), 6.47 (d, 1H, H2), 7.08 - 7.14 (m, 2H, Ph), 7.27 - 7.49 (m, 3H, Ph), $J_{H2\text{-}H3}$ = 5.9 Hz, $J_{H3\text{-}H3'a}$ = 7.1 Hz, $J_{H3\text{-}H3'b}$ = 7.5 Hz, $J_{H3'a\text{-}H3'b}$ = -11.3 Hz, $J_{H3\text{-}H4}$ = 6.7 Hz, $J_{H4\text{-}H4'a}$ = 4.5 Hz, $J_{H4\text{-}H4'b}$ = 3.2 Hz, $J_{H4'a\text{-}H4'b}$ = -12.6 Hz, $J_{CH_3\text{-}CH_2}$ = 7.5 Hz; LRMS (CI-NH_3): m/e 386 ([M + NH_4^+], 13.3%), 369 ([MH^+], 4.9%), 259 ([MH^+ - AcOH], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{17}H_{21}O_7S$ [MH^+], 369.1007; found, 369.1008].

Oxetane (75c).

A solution of alcohol **74** (70 mg, 0.30) mmol and *N,N'*-thiocarbonyldiimidazole (80 mg, 0.45 mmol) in dry methylene chloride (5 mL) was refluxed under an atmosphere of nitrogen for 2 h. Evaporation of the solvent *in vacuo* gave a yellow residue which was chromatographed over silica gel (petroleum ether / ethyl acetate, 1:1 v/v) to afford the title compound (69 mg, 67% yield) as a light yellow oil. [^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.14 (t, 3H, CH_3CH_2), 2.09 (s, 3H, Ac), 2.40 (q, 2H, CH_3CH_2), 3.60 (dddd, 1H, H3), 4.25 (A of ABX, 1H, $H4'_a$), 4.36 (B of ABX, 1H, $H4'_b$), 4.87 (ddd, 1H, H4), 4.92 (A of ABX, 1H, $H3'_a$), 4.98 (B of ABX, 1H, $H3'_b$), 6.49 (d, 1H, H2), 7.02, 7.63 (2d, 2H, N-CH=CH-N), 8.31 (s, 1H, N-CH=N), $J_{H2\text{-}H3}$ = 5.9 Hz, $J_{H3\text{-}H3'a}$ = 6.6 Hz, $J_{H3\text{-}H3'b}$ = 7.5 Hz, $J_{H3'a\text{-}H3'b}$ = -11.5 Hz, $J_{N\text{-}CH=CH\text{-}N}$ = 1.3 Hz, $J_{H3\text{-}H4}$ = 5.7 Hz, $J_{H4\text{-}H4'a}$ = 4.3 Hz, $J_{H4\text{-}H4'b}$ = 3.3 Hz, $J_{H4'a\text{-}H4'b}$ = -12.7 Hz, $J_{CH_3\text{-}CH_2}$ = 7.6 Hz; LRMS (CI-NH_3): m/e 343 ([MH^+], 38.8%), 292 ([MH^+ - AcOH], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{14}H_{19}N_2O_6S$ [MH^+], 343.0965; found, 343.0963].

Oxetane (75d).

Oxetane **75d** (38 mg, 0.11 mol) was dissolved in anhydrous methanol (10 mL) and allowed to stir for 24 h under an atmosphere of nitrogen at room temperature. Evaporation of the solvent *in vacuo* gave a yellow residue which was chromatographed over silica gel (petroleum ether / ethyl acetate, 2:1 v/v) to afford the title compound (23 mg, 68% yield) as a clear oil. [^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.14 (t, 3H, CH_3CH_2), 2.11 (s, 3H, Ac), 2.40 (q, 2H, CH_3CH_2), 3.50 (dddd, 1H, H3), 4.04 (s, 3H, MeO), 4.19 (A of ABX, 1H, $H4'_a$), 4.34 (B of ABX, 1H, $H4'_b$), 4.70 (A of ABX, 1H, $H3'_a$), 4.78 (B of ABX, 1H, $H3'_b$), 4.81 (ddd, 1H, H4), 6.43 (d, 1H, H2), $J_{H2\text{-}H3}$ = 5.9 Hz, $J_{H3\text{-}H3'a}$ = 7.2 Hz, $J_{H3\text{-}H3'b}$ = 7.4 Hz, $J_{H3'a\text{-}H3'b}$ = -11.3 Hz, $J_{H3\text{-}H4}$ = 6.1 Hz, $J_{H4\text{-}H4'a}$ = 4.5 Hz, $J_{H4\text{-}H4'b}$ = 3.3 Hz, $J_{H4'a\text{-}H4'b}$ = -12.6 Hz, $J_{CH_3\text{-}CH_2}$ = 7.5 Hz; LRMS (CI-NH_3): m/e 324 ([M + NH_4^+], 42.3%), 307 ([MH^+], 10.3%), 247 ([MH^+ - AcOH], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{12}H_{19}O_7S$ [MH^+], 307.0852; found, 307.0851]

Oxetane (75e).

To a stirred solution of alcohol **74** (696 mg, 3.00 mmol) in dimethyl sulfoxide (9.8 mL) under an atmosphere of nitrogen at room temperature was added acetic acid (2.0 mL) and acetic anhydride (6.4

mL). After stirring for 24 h, the reaction mixture was poured in 10% aqueous sodium carbonate (500 mL) and extracted with methylene chloride (3 x 350 ml). The combined extracts were washed with water (1 L), brine (1 L), dried (Na_2SO_4), filtered and the solvent evaporated *in vacuo* to afford a yellow residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 3:1 v/v) gave the title compound (280 mg, 32% yield) as a clear oil. [^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.14 (t, 3H, CH_3CH_2), 2.10 (s, 3H, Ac), 2.12 (s, 3H, CH_3S), 2.39 (q, 2H, CH_3CH_2), 3.28 (dddd, 1H, H3), 3.77 (A of ABX, 1H, H3'$_a$), 3.85 (B of ABX, 1H, H3'$_b$), 4.16 (A of ABX, 1H, H4'$_a$), 4.32 (B of ABX, 1H, H3'$_b$), 4.62 (s, 2H, OCH_2S), 4.72 (ddd, 1H, H4), 6.39 (d, 1H, H2), J_{H2-H3} = 5.9 Hz, $J_{H3-H3'a}$ = 7.6 Hz, $J_{H3-H3'b}$ = 7.3 Hz, $J_{H3'a-H3'b}$ = -9.7 Hz, J_{H3-H4} = 6.2 Hz, $J_{H4-H4'a}$ = 4.8 Hz, $J_{H4-H4'b}$ = 2.9 Hz, $J_{H4'a-H4'b}$ = -12.6 Hz, $J_{CH_3-CH_2}$ = 7.5 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 9.18 [CH_3CH_2], 14.02 [CH_3S], 21.15 [CH_3CO], 27.66 [CH_3CH_2], 40.66 [C3], 64.65 [C3'], 65.38 [C4'], 75.92 [OCH_2S], 80.46 [C4], 96.69 [C2], 169.78 [CH_3CO], 174.23 [EtCO]; LRMS (CI-NH_3): m/e 310 ([M + NH_4^+], 100%), 293 ([MH^+], 9.3%), 233 ([MH^+ - AcOH], 26.0%); HRMS (CI-NH_3): m/e calcd. for $C_{12}H_{21}O_6S$ [MH^+], 293.1057; found, 293.1058].

Oxetane (75f).

To a solution of oxetane **75e** (64 mg, 0.22 mmol) in methanol (0.5 mL) was added a solution of sodium periodate (51 mg, 0.23 mmol) in water (0.5 mL), and it was stirred for 18 h at room temperature. After filtration of the inorganic precipitates, the filtrate was diluted with methylene chloride (50 mL) and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure yielded a light yellow oil which was chromatographed over silica gel (ethyl acetate / hexanes / methanol, 5:3:1 v/v/v) to afford **75f** (mixture of 2 inseparable diastereomers, 1:1), (52 mg, 77% yield) as a clear oil. [^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.12 (t, 3H, CH_3CH_2), 2.09 (s, 3H, Ac), 2.36 (q, 2H, CH_3CH_2), 2.52 (s, 3H, CH_3SO), 3.31 (m, 1H, H3), 3.97 - 4.50 (m, 6H, H3'$_a$, H3'$_b$, OCH_2SO, H4'$_a$, H4'$_b$), 4.73 (m, 1H, H4), 6.39, 6.40 (2d, 1H, H2), J_{H2-H3} = 5.9 Hz, J_{H3-H4} = 6.2 Hz, $J_{CH_3-CH_2}$ = 7.6 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 8.97 [CH_3CH_2], 20.96 [CH_3CO], 27.33 [CH_3CH_2], 34.67, 34.77 [CH_3SO], 40.37 [C3], 64.87, 64.92 [C3'], 70.14, 70.17 [C4'], 79.56, 79.60 [C4], 87.68, 87.82 [OCH_2SO], 95.97, 96.03 [C2], 169.35, 169.38 [CH_3CO], 174.03 [EtCO]; LRMS (CI-NH_3): m/e 326 ([M + NH_4^+], 31.0%), 309 ([MH^+], 29.9%), 249 ([MH^+ - AcOH], 100%); HRMS (CI-NH_3): m/e calcd. for $C_{12}H_{21}O_7S$ [MH^+], 309.1009; found, 309.1008].

Oxetane (75g).

To a solution of oxetane **75e** (58 mg, 0.20 mmol) in methanol (0.5 mL) was added a solution of sodium periodate (94 mg, 0.44 mmol) in water (0.5 mL), and it was stirred for 18 h at room temperature. After filtration of the inorganic precipitates, the filtrate was diluted with methylene chloride (50 mL) and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure yielded a light yellow oil which was chromatographed over silica gel (hexanes / ethyl acetate, 1:1 v/v) to afford **75g** (60 mg, 93% yield) as a

clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.15 (t, 3H, $\mathbf{CH_3}CH_2$), 2.09 (s, 3H, Ac), 2.39 (q, 2H, $CH_3\mathbf{CH_2}$), 2.88 (s, 3H, CH_3SO_2), 3.32 (dddd, 1H, H3), 4.13 (A of ABX, 1H, H4'$_a$), 4.20 (A of ABX, 1H, H3'$_a$), 4.23 (B of ABX, 1H, H3'$_b$), 4.34 (B of ABX, 1H, H4'$_b$), 4.45 (s, 2H, OCH_2S), 4.76 (ddd, 1H, H4), 6.44 (d, 1H, H2), $J_{H2\text{-}H3}$ = 5.9 Hz, $J_{H3\text{-}H3'a}$ = 4.6 Hz, $J_{H3\text{-}H3'b}$ = 4.3 Hz, $J_{H3'a\text{-}H3'b}$ = -8.5 Hz, $J_{H13\text{-}H4}$ = 6.0 Hz, $J_{H4\text{-}H4'a}$ = 7.2 Hz, $J_{H4\text{-}H4'b}$ = 3.0 Hz, $J_{H4'a\text{-}H4'b}$ = -12.6 Hz, $J_{CH_3\text{-}CH_2}$ = 7.5 Hz; LRMS (CI-NH_3): m/e 342 ([M + NH_4^+], 100%), 325 ([MH^+], 0.6%); HRMS (CI-NH_3): m/e calcd. for $C_{12}H_{24}NO_8S$ [M + NH_4^+], 342.1222; found, 342.1222}.

Oxetane (75h).

To a stirred solution of alcohol **74** (116 mg, 0.50 mmol) and guaiacol (186 mg, 1.50 mmol) in dry tetrahydrofuran (2.5 mL) under nitrogen at ambient temperaure was added triphenylphosphine (170 mg, 0.65 mmol) and diethyl azodicarboxylate (108 μL, 0.65 mmol). The mixture was then refluxed for 3 h. Evaporation of the solvent *in vacuo* gave a white solid which was chromatographed over silica gel (petroleum ether / ethyl acetate, 100:1) to afford **75h** (90 mg, 53% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.14 (t, 3H, $\mathbf{CH_3}CH_2$), 2.06 (s, 3H, Ac), 2.39 (q, 2H, $CH_3\mathbf{CH_2}$), 3.56 (dddd, 1H, H3), 3.81 (s, 3H, MeO), 4.21 (A of ABX, 1H, H4'$_a$), 4.27 (A of ABX, 1H, H3'$_a$), 4.33 (B of ABX, 1H, H3'$_b$), 4.38 (B of ABX, 1H, H4'$_b$), 4.86 (ddd, 1H, H4), 6.51 (d, 1H, H2), 6.85 - 7.01 (m, 4H, Ph), $J_{H2\text{-}H3}$ = 5.9 Hz, $J_{H3\text{-}H3'a}$ = 8.5 Hz, $J_{H3\text{-}H3'b}$ = 2.0 Hz, $J_{H3'a\text{-}H3'b}$ = -9.9 Hz, $J_{H3\text{-}H4}$ = 6.2 Hz, $J_{H4\ H4'a}$ = 4.8 Hz, $J_{H4\ H4'b}$ = 2.7 Hz, $J_{H4'a\text{-}H4'b}$ = -12.6 Hz, $J_{CH_3\text{-}CH_2}$ = 7.6 Hz; LRMS (CI-NH_3): m/e 356 ([M + NH_4^+], 100%), 339 ([MH^+], 0.5%), 279 ([MH^+ - AcOH], 3.8%); HRMS (CI-NH_3): m/e calcd. for $C_{17}H_{23}O_7$ [MH^+], 339.1444; found, 339.1443}.

Oxetane (75i).

To a stirred solution of alcohol **74** (70 mg, 0.30 mmol) and acid **78** (43 mg, 0.30 mmol) in dry methylene chloride (2 mL) under an atmosphere of nitrogen at ambient temperaure was added *N,N*-dimethylaminopyridine (37 mg, 0.30 mmol) and *N,N'*-dicyclohexylcarbodiimide (74 mg, 0.36 mmol). After 18 h, the solvent was removed *in vacuo* to yield a yellow residue which was chromatographed over silica gel (petroleum ether / ethyl acetate, 1:1) affording **75i** (28 mg, 26% yield) as a white solid. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.14 (t, 3H, $\mathbf{CH_3}CH_2$), 1.92 (m, 4H, $\mathbf{CH_2}CH_2N$), 2.12 (s, 3H, Ac), 2.38 (q, 2H, $CH_3\mathbf{CH_2}$), 3.44 (dddd, 1H, H3), 3.49 (t, 2H, $CH_2\mathbf{CH_2}N$), 3.58 (t, 2H, $CH_2\mathbf{CH_2}$'N), 4.18 (A of ABX, 1H, H4'$_a$), 4.34 (B of ABX, 1H, H4'$_b$), 4.50 (A of ABX, 1H, H3'$_a$), 4.58 (B of ABX, 1H, H3'$_b$), 4.82 (ddd, 1H, H4), 6.45 (d, 1H, H2), $J_{H2\text{-}H3}$ = 5.9 Hz, $J_{H3\text{-}H3'a}$ = 7.6 Hz, $J_{H3\text{-}H3'b}$ = 7.3 Hz, $J_{H13'a\text{-}H3'b}$ = -11.6 Hz, $J_{NCH_2\text{-}CH_2}$ = 6.5 Hz, $J_{NCH_2'\text{-}CH_2}$ = 6.8 Hz, $J_{CH_2\text{-}CH_2}$ = 5.4 Hz, $J_{H3\text{-}H4}$ = 6.0 Hz, $J_{H4\ H4'a}$ = 4.5 Hz, $J_{H4\ H4'b}$ = 3.2 Hz, $J_{H4'a\text{-}H4'b}$ = -12.7 Hz, $J_{CH_3\text{-}CH_2}$ = 7.6 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 9.12 [$\mathbf{CH_3}CH_2$], 21.08 [$\mathbf{CH_3}CO$], 24.18, 26.22 [$\mathbf{CH_2}CH_2N$], 27.56 [$CH_3\mathbf{CH_2}$], 39.72 [C3], 46.26, 4757 [$CH_2\mathbf{CH_2}N$],

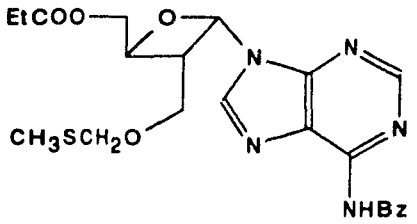
62.05 [C3'], 64.91 [C4'], 79.83 [C4], 96.01 [C2], 158.24, 162.47 [OCOCON], 169.66 [CH_3CO], 174.17 [EtCO]; LRMS (CI-NH_3): m/e 375 ([M + NH_4^+], 25.4%), 358 ([MH^+], 100%), 298 ([MH^+ - AcOH], 90.7%); HRMS (CI-NH_3): m/e calcd. for $C_{16}H_{24}NO_8$ [MH^+], 358.1502; found, 358.1501}.

Oxetane (75j).

To a stirred solution of alcohol **74** (70 mg, 0.30 mmol) and pyrrolidine hydrochloride (43 mg, 0.40 mmol) in dry tetrahydrofuran (10 mL) under an atmosphere of nitrogen at ambient temperaure was added triphenylphosphine (79 mg, 0.30 mmol) and diethyl azodicarboxylate (47 μL, 0.30 mmol). After 3 days, the solvent was removed *in vacuo* to give a white solid which was chromatographed over silica gel (petroleum ether / ethyl acetate, 4:1) affording **75j** (36 mg, 48% yield) as a clear oil. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.15 (t, 3H, CH_3CH_2), 2.13 (s, 3H, Ac), 2.39 (q, 2H, CH_3CH_2), 3.38 (ddd, 1H, H3), 3.75 (s, 1H, H3'$_a$), 3.79 (d, 1H, H3'$_b$), 4.19 (A of ABX, 1H, H4'$_a$), 4.37 (B of ABX, 1H, H4'$_b$), 4.76 (ddd, 1H, H4), 6.43 (d, 1H, H2), $J_{H2\text{-}H3}$ = 5.8 Hz, $J_{H3\text{-}H3'b}$ = 2.4 Hz, $J_{H3\text{-}H4}$ = 5.9 Hz, $J_{H4\text{-}H4'a}$ = 4.5 Hz, $J_{H4\text{-}H4'b}$ = 3.0 Hz, $J_{H4'a\text{-}H4'b}$ = -12.7 Hz, $J_{CH_3\text{-}CH_2}$ = 7.5 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 9.20 [CH_3CH_2], 21.14 [CH_3CO], 27.70 [CH_3CH_2], 40.75 [C3'], 43.05 [C3], 65.10 [C4'], 81.39 [C4], 96.16 [C2], 169.69 [CH_3CO], 174.23 [EtCO]; LRMS (CI-NH_3): m/e 270, 268 ([M + NH_4^+], 38.9%, 100%); HRMS (CI-NH_3): m/e calcd. for $C_{10}H_{19}NO_5Cl$ [M + NH_4^+], 268.0952; found, 268.0951}.

Nucleoside (76b).

Nucleoside **76b** was obtained in 65% yield fron oxetane **75e** by a procedure similar to that used for the preparation of nucleoside **48a**. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.12 (t, 3H, CH_3CH_2), 2.19 (s, 3H, CH_3S), 2.33 (q, 2H, CH_3CH_2), 3.13 (ddt, 1H, H2'), 3.86 (d, 2H, H2"$_a$, H2"$_b$), 4.26 (A of ABX, 1H, H3"$_a$), 4.34 (B of ABX, 1H, H3"$_b$), 4.63 (ddd, 1H, H3'), 4.72 (s, 2H, OCH_2S), 6.33 (d, 1H, H1'), 7.50 - 7.67 (m, 3H, Ph), 7.99 - 8.03 (m, 2H, Ph), 8.31 (s, 1H, H8), 8.73 (s, 1H, H2), 8.67 (s, br, ex, 1H, NH), $J_{H1'\text{-}H2'}$ = 3.6 Hz, $J_{H2'\text{-}H2"aH2"b}$ = 5.6 Hz, $J_{H2'\text{-}H3'}$ = 1.9 Hz, $J_{H3'\text{-}H3"a}$ = 2.1 Hz, $J_{H3'\text{-}H3"b}$ = 4.9 Hz, $J_{H3"a\text{-}H3"b}$ = -10.6 Hz, $J_{CH_3\text{-}CH_2}$ = 7.6 Hz}.

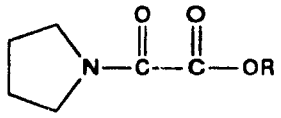


76b

Methyl Oxalyl Pyrrolidinamide (77).

Pyrrolidine (3.56 g, 50.2 mmol) was dissolved in dry ether (250 mL). Methyl oxalyl chloride (2.30 mL, 25.1 mmol) was then added dropwise, and the reaction was stirred at room temperature under

an atmosphere of nitrogen. After 2 h, the reaction was washed with 5% hydrochloric acid (200 mL), saturated aqueous sodium bicarbonate (200 mL), brine (200 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a light yellow residue. Purification by flash chromatography (ethyl acetate) gave the title compound (3.75 g, 95% yield) as a white solid. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.90 (m, 4H, $\mathbf{CH_2CH_2N}$), 3.51 (t, 2H, CH_2N), 3.61 (t, 2H, $CH_2'N$), 3.83 (s, 3H, MeO); $J_{CH_2\text{-}CH_2N}$ = 6.5 Hz, $J_{CH_2\text{-}CH_2'N}$ = 6.7 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 23.56, 25.69 [$\mathbf{CH_2CH_2N}$], 45.88, 47.19 [$\mathbf{CH_2N}$], 52.32 [**MeO**], 157.96, 162.27 [**CO**]; LRMS (EI): m/e 157 ([M^+], 48.9%), 98 ([$M^{+\cdot}$ - COOMe], 100%); IR (CH_2Cl_2): 1651 cm^{-1} [**NCO**], 1741 cm^{-1} [COOMe]}.



77, R=CH_3

78, R=H

Pyrrolidine Oxamic acid (78).

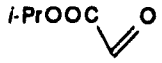
To a stirred solution of **77** (419 mg, 2.67 mmol) in methanol (100 mL) and water (50 mL) at room temperature was added potassium carbonate (738 mg, 5.34 mmol). After 1 h, the solution was adjusted to pH 2.5 with 5% hydrochloric acid and evaporated to dryness. The residue was dissolved in methylene chloride (100 mL), washed with water (100 mL), brine (100 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to yield essentially pure **78** (362 mg, 95% yield) as a white solid. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.94 (m, 4H, $\mathbf{CH_2CH_2N}$), 3.56 (t, 2H, CH_2N), 3.94 (t, 2H, $CH_2'N$), 6.70 (s, br, ex, 1H, OH), $J_{CH_2\text{-}CH_2N}$ = 6.6 Hz, $J_{CH_2\text{-}CH_2'N}$ = 6.6 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 23.94, 26.81 [$\mathbf{CH_2CH_2N}$], 48.52, 49.47 [$\mathbf{CH_2N}$], 157.32, 159.89 [**CO**]; LRMS (CI-NH_3)· m/e 161 ([M + NH_4^+], 38.5%), 144 ([MH^+], 52.4%); IR (CH_2Cl_2): 1654 cm^{-1} [**NCO**], 1783 cm^{-1} [COOMe]}.

Diisopropyl Fumarate (79)

Fumaric acid (29.02 g, 250.0 mmol) was dissolved in dry *i*-propyl alcohol (600 mL). Chlorotrimethylsilane (140 mL, 1.1 mol) was then added dropwise, and the reaction was stirred at room temperature under an atmosphere of nitrogen for 3 days. Evaporation to dryness gave a thick residue which was chromatographed over silica gel (petroleum ether / ethyl acetate, 10:1 v/v) to afford the title compound (48.03 g, 96% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.26 (d, 6H, $\mathbf{Me_2CH}$), 5.08 (h^7, 1H, $\mathbf{Me_2CH}$), 6.78 (s, 1H, =**H**CO), $J_{CH\text{-}Me}$ = 6.3 Hz}.

***i*-Propyl Glyoxylate (80).**

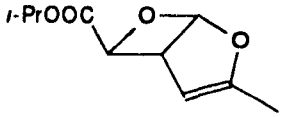
To a stirred solution of diisopropyl L-tartrate (23.43 g, 100.0 mmol) in dry ether (500 mL) cooled to 5°C was added periodic acid (22.79 g, 100.0 mmol) in portions over 1h under an atmosphere of nitrogen. The milky reaction mixture was stirred for 1 h until the solution became clear and a white solid separated. The solid was filtered off and the filtrate was dried with sodium sulfate. Evaporation of the solvent *in vacuo* afforded the title compound (11.02 g, 95% yield) as a clear oil. The ^{1}H-NMR spectrum indicated that the aldehyde exists largely in a polymeric form and only a small amount of free aldehyde was present.



80

3-Methyl-6β-*i*-propyloxyformyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (81).

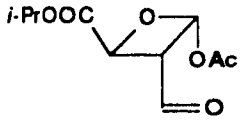
A mixture of 2-methylfuran (7.4 mL, 82 mmol) and *i*-propyl glyoxylate (2.38 g, 20.5 mmol) in benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C, and saturated with argon. The solution was then irradiated for 25 h. The solvent was removed under reduced pressure to give a yellow syrup. Purification by flash chromatography (hexanes / ethyl acetate, 10:1 v/v) gave **81** (700 mg, 17% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.28 (d, 6H, $\mathbf{Me_2}$CH), 1.94 (dd, 3H, Me), 3.69 (dddd, 1H, H5), 4.80 (d, 1H, H6), 5.01 (dd, 1H, H4), 5.11 (h^7, 1H, $\mathbf{Me_2CH}$), 6.41 (d, 1H, H1); $J_{H1\text{-}H5}$ = 4.3 Hz, $J_{H4\text{-}Me}$ = -1.3 Hz, $J_{H4\text{-}H5}$ = 2.6 Hz, $J_{H5\text{-}Me}$ = 1.4 Hz, $J_{H5\text{-}H6}$ = 3.1 Hz, $J_{CH\text{-}Me_2}$ = 6.3 Hz; ^{13}C-NMR (50.3 MHz, $CDCl_3$): δ 13.56 [**Me**], 21.46, 21.64 [$\mathbf{Me_2}$CH], 50.35 [C5], 69.10 [$\mathbf{Me_2CH}$], 86.59 [C6], 98.30 [C4], 109.03 [C1], 159.24 [C3], 170.73 [CO]; LRMS (CI-NH_3): m/e 216 ([M + NH_4^+], 16.7%), 199 ([MH^+], 35.3%), 181 ([MH^+ - H_2O], 80.4%); HRMS (CI-NH_3): m/e calcd. for $C_{10}H_{15}O_4$ [MH^+], 199.0971; found, 199.0970}. Anal. calcd. for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.84; H, 6.86.



81

2α-Acetoxy-3α-formyl-4β-*i*-propyloxyformyl oxetane (82).

Photo-adduct **81** was transformed to aldehyde **82** in 90% yield by a procedure similar to that used for the preparation of aldehyde **45**. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.26 (d, 3H, $\mathbf{CH_3}$CH), 1.28 (d, 3H, $\mathbf{CH_3}$'CH), 2.09 (s, 3H, Ac), 4.07 (ddd, 1H, H3), 5.09 (m, 1H, $\mathbf{Me_2CH}$), 5.38 (d, 1H, H4), 6.66 (d, 1H, H2), 9.75 (d, 1H, CHO), $J_{H2\text{-}H3}$ = 6.4 Hz, $J_{H3\text{-}CHO}$ = 1.2 Hz, $J_{H3\text{-}H4}$ = 6.2 Hz, $J_{CH\text{-}Me}$ = 6.2 Hz, $J_{CH\text{-}Me'}$ = 6.0 Hz; LRMS (CI-NH_3): m/e 248 ([M + NH_4^+], 100%), 231 ([MH^+], 0.2%), 171 ([MH^+ - AcOH], 0.6%); HRMS (CI-NH_3): m/e calcd. for $C_{10}H_{15}O_6$ [MH^+], 231.0868; found, 231.0868}.



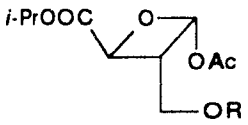
82

2α-Acetoxy-3α-hydroxymethyl-4β-*i*-propyloxyformyl oxetane (83).

Aldehyde **82** was reduced to alcohol **83** in 62% yield by a procedure similar to that used for the preparation of alcohol **46**. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 0.89 (s, br, ex, 1H, OH), 1.25 (d, 3H, CH_3CH), 1.28 (d, 3H, $CH_3'CH$), 2.13 (s, 3H, Ac), 3.27 (m, 1H, H3), 3.89 (m, 2H, $H3'_a$, $H3'_b$), 4.90 (d, 1H, H4), 5.08 (m, 1H, Me_2CH), 6.52 (d, 1H, H2), J_{H2-H3} = 5.2 Hz, J_{H3-H4} = 6.3 Hz, J_{CH-Me} = 6.3 Hz, $J_{CH-Me'}$ = 6.2 Hz; LRMS (CI-NH_3): m/e 250 ([M + NH_4^+], 70.8%), 233 ([MH^+], 8.8%), 173 ([MH^+ - AcOH], 3.4%); HRMS (CI-NH_3): m/e calcd. for $C_{10}H_{17}O_6$ [MH^+], 233.1026; found, 231.1025}.

Oxetane (84).

Oxetane **84** was obtained from photo-adduct **81** in 39% yield by a procedure similar to that used for the transformation of photo-adduct **44a** to oxetane **47c**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.25 (d, 3H, CH_3CH), 1.26 (d, 3H, $CH_3'CH$), 2.12 (s, 3H, Ac), 3.60 (ddt, 1H, H3), 3.89 (s, 3H, MeO), 4.63 (d, 2H, $H3'_a$, $H3'_b$), 4.93 (d, 1H, H4), 5.11 (m, 1H, Me_2CH), 6.58 (d, 1H, H2), J_{H2-H3} = 5.9 Hz, $J_{H3-H3'aH3'b}$ = 7.2 Hz, $J_{H3'a-H3'b}$ ~ 0 Hz, J_{H3-H4} = 6.4 Hz, J_{CH-Me} = 6.7 Hz, $J_{CH-Me'}$ = 6.2 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 21.06 [CH_3CO], 21.73 [$(CH_3)_2CH$], 42.20 [C3], 53.94 [CH_3O], 62.72 [C3'], 69.95 [$(CH_3)_2CH$], 77.37 [C4], 96.50 [C2], 157.54, 157.99 [OCOCOOMe], 169.40, 169.63 [CO]; LRMS (CI-NH_3): m/e 336 ([M + NH_4^+], 100%), 319 ([MH^+], 1.3%); HRMS (CI-NH_3): m/e calcd. for $C_{13}H_{19}O_9$ [MH^+], 319.1030; found, 319.1029}.

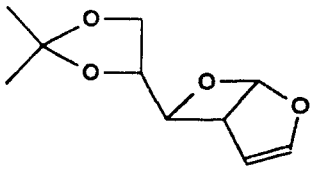


83, R=H
84, R=COCOOMe

4.6 Experimentals for Section 2.7.

Photo-adduct (85).

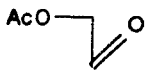
A mixture of furan (3.0 mL, 41.2 mmol) and R-glyceraldehyde acetonide (1.090 g, 8.38 mmol) in dry benzene (330 mL) was placed in a 350 mL photo-reaction vessel, cooled to 8°C and saturated with helium. The solution was then irradiated for 8 h. Evaporation under reduced pressure gave a yellow syrup which was chromatographed over silica gel (petroleum ether / ethyl acetate, 9:1 v/v) to afford the title compound (mixture of 2 inseparable diastereomers, 1:1), (415 mg, 25% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.36, 1.40, 1.44, 1.47 (4s, 6H, CMe_2), 3.62 - 4.46 (m, 4H, H6, H6', H6"$_a$, H6"$_b$), 3.68 (m, 1H, H5), 5.32, 5.33 (2t, 1H, H4), 6.28 (m, 1H, H1), 6.61 (m, 1H, H3), J_{H3-H4} = 2.9 Hz, J_{H4-H5} = 2.9 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 25.11, 26.02, 26.21, 26.62 [CMe_2], 46.68 [C5], 64.49, 65.84 [C6'], 76.95, 77.35 [C6"], 88.56, 90.49 [C6], 103.71, 103.87 [C4], 108.36, 108.65 [C1], 109.76, 109.84 [CMe_2], 148.54 [C3]}.



85

2-Acetoxyacetaldehyde (86).

2-Acetoxyacetaldehyde was obtained from allyl acetate in 38% yield by a procedure similar to that used for the preparation of aldehyde **20**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.05 (s, 3H, Ac), 4.55 (d, 2H, CH_2), 9.47 (t, 1H, CHO), J_{CH_2-CHO} = 0.3 Hz; IR ($CDCl_3$): 1746 cm^{-1}, 1762 cm^{-1}, 2713 cm^{-1}, 2817 cm^{-1}}.



86

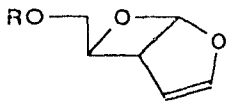
6β-Hydroxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (88).

To a stirred solution of photo-adduct **2d** (928 mg, 4.00 mmol) in methanol (100 mL) at room temperature was added aqueous sodium hydroxide (15% w/v, 10.7 mL, 40.1 mmol). After 30 min, the solution was neutralized with 0.1% hydrochloric acid, concentrated *in vacuo*, extracted with ether (5 x 100 mL). The ether extracts were dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a yellow oil. Purification by flash chromatography(petroleum ether / ethyl acetate, 1:1 v/v) afforded the title compound (403 mg, 79% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.24 (s, br, ex, 1H, OH), 3.68 (dddd, 1H, H5), 3.73 (A of ABX, 1H, H6'$_a$), 3.82 (B of ABX, 1H, H6'$_b$), 4.64 (ddd, 1H, H6), 5.37 (t, 1H, H4), 6.30 (d, 1H, H1), 6.62 (dd, 1H, H3), J_{H1-H5} = 4.3 Hz, J_{H3-H4} = 2.9

Hz, $J_{H3\text{-}H5}$ = -1.1 Hz, $J_{H4\text{-}H5}$ = 2.9 Hz, $J_{H5\text{-}H6}$ = 3.0 Hz, $J_{H6\text{-}H6'a}$ = 3.4 Hz, $J_{H6\text{-}H6'b}$ = 2.8 Hz, $J_{H6'a\text{-}H6'b}$ = 12.8 Hz; LRMS (CI-NH_3): m/e 146 ([M + NH_4^+], 31.4%), 129 ([MH^+], 100%), 111 ([MH^+ - H_2O], 70.9%); HRMS (CI-NH_3): m/e calcd. for $C_6H_9O_3$ [MH^+], 129.0552; found, 129.0551}

6β-Acetoxymethyl-2,7-dioxa-bicyclo-[3,2,0]-hept-3-ene (87).

Alcohol **88** was acetylated in 72% yield by a procedure similar to that used for the preparation of **25a**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.07 (s, 3H, Ac), 3.58 (dddd, 1H, H5), 4.19 (A of ABX, 1H, $H6'_a$), 4.24 (B of ABX, 1H, $H6'_b$), 4.63 (dddd, 1H, H6), 5.33 (t, 1H, H4), 6.24 (dd, 1H, H1), 6.59 (dd, 1H, H3), $J_{H1\text{-}H5}$ = 4.3 Hz, $J_{H1\text{-}H6}$ = -0.8 Hz, $J_{H3\text{-}H4}$ = 2.9 Hz, $J_{H3\text{-}H5}$ = -1.2 Hz, $J_{H4\text{-}H5}$ = 2.9 Hz, $J_{H5\,H6}$ = 3.2 Hz, $J_{H6\text{-}H6'a}$ = 4.7 Hz, $J_{H6\text{-}H6'b}$ = 3.5 Hz, $J_{H6'a\text{-}H6'b}$ = -12.3 Hz; LRMS (CI-NH_3): m/e 188 ([M + NH_4^+], 24.0%), 171 ([MH^+], 1.1%), 153 ([MH^+ - H_2O], 100%); HRMS (CI-NH_3): m/e calcd. for $C_8H_{11}O_4$ [MH^+], 171.0656; found, 171.0657}.



87, R=Ac
88, R=H

Enzyme-Catalyzed Hydrolysis of (2d).

Porcine pancreatic lipase (215 mg) was added to a stirred suspension of **2d** (232 mg, 1.00 mmol) in phosphate buffer (10.0 mL, 10 mM, pH 7.00). Aliquots of a 0.1 N NaOH solution were added as required to maintain the pH of the mixture between 6.95 and 7.05. After 4.5 h, a total of of 5.00 mL of base solution had been added (50% conversion). The reaction mixture was extracted with ether (6 x 50 mL), and the combined extracts were washed with saturated aqueous sodium bicarbonate (200 mL) and brine (200 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent removed in vacuo to give a yellow syrup which was chromatographed over silica gel (petroleum ether / ethyl acetate, 4:1 v/v, then 1:1 v/v) to afford the starting ester (46% yield) and alcohol (42% yield). Benzoylation of alcohol **88** via standard methods yielded benzoate **+2d** in 45% yield. **-2d:** {$[\alpha]^{20}_D$ = -15.5° (c = 3.21, CH_2Cl_2)}. **+2d:** {$[\alpha]^{20}_D$ = +18.8° (c = 1.25, CH_2Cl_2), respectively}.

Enzyme-Catalyzed Hydrolysis of (44a).

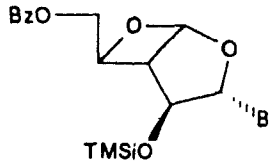
Porcine pancreatic lipase (100 mg) was added to a stirred suspension of **44a** (123 mg, 0.50 mmol) in phosphate buffer (10.0 mL, 10 mM, pH 7.00). Aliquots of a 0.1 N NaOH solution were added as required to maintain the pH of the mixture between 6.95 and 7.05. After 4.5 h, a total of of 2.50 mL of base solution had been added (50% conversion). The reaction mixture was extracted with ether (5 x 30 mL), and the combined extracts were washed with saturated aqueous sodium bicarbonate (100 mL)

brine (100 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to give a yellow syrup which was a mixture of unreacted ester **-44a** and very small amounts of alcohol **52** (as indicated by ^{1}H-NMR). Purification by flash chromatography (petroleum ether / ethyl acetate, 6:1 v/v) afforded only the starting ester (36% yield). The enantiomerically enriched photo-adduct **-44a** was transformed to oxetane **+47b** by the method described earlier. **+47b:** {$[\alpha]^{20}_D$ = -7.5° (c = 2.22, $CHCl_3$)}.

4.7 Experimentals for Section 2.8.

3'α-Thyminyl-4'β-O-trimethylsilyl-6'β-benzoyloxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (89a)

To a stirred solution of epoxide **23d** (263 mg, 1.06 mmol) in dry tetrahydrofuran (5 mL) at room temperature under an atmosphere of nitrogen was added *bis*-(trimethylsilyl)-thymine (860 mg, 3.18 mmol) and zinc chloride (1.0M solution in ether, 1.06 mL, 1.06 mmol). After 18 h, the reaction mixture was poured into cold saturated aqueous sodium bicarbonate (50 mL), extracted with methylene chloride (5 x 50 mL) and washed with brine (5 x 50 mL). The combined organic phases were then dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield a clear syrup which was chromatographed over silica gel (methylene chloride / methanol, 100:1 v/v) affording nucleoside **89a** (312 mg, 66% yield) as a white foam. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 0.18 (s, 9H, Me_3Si), 1.92 (d, 3H, CH_3 at C5), 3.34 (t, 1H, H5'), 4.35 (ddd, 1H, H6'), 4.41 (A of ABX, 1H, H6"$_a$), 4.52 (B of ABX, 1H, H6"$_b$), 4.74 (s, 1H, H4'), 5.94 (s, 1H, H3'), 6.28 (d, 1H, H1'), 7.43 - 7.65 (m, 3H, Ph), 7.95 (d, 1H, H6), 8.02 - 8.08 (m, 2H, Ph), 9.69 (s, br, ex, 1H, NH), $J_{H1'-H5'}$ = 4.1 Hz, $J_{H5'-H6'}$ = 4.4 Hz, $J_{H6'-H6"a}$ = 3.4 Hz, $J_{H6'-H6"b}$ = 3.4 Hz, $J_{H6"a-H6"b}$ = -11.8 Hz, J_{H6-Me} = -1.1 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$). δ -0.12 [$(\mathbf{CH_3})_3$Si], 12.52 [$\mathbf{CH_3}$ at C5], 50.97 [C5'], 65.15 [C6"], 76.76 [C6'], 78.11 [C4'], 99.02 [C3'], 109.47 [C5], 110.45 [C1'], 128.39, 129.52 and 133.32 [aromatic CH], 129.17 [aromatic C], 135.68 [C6], 151.00 [C2], 164.55 [C4], 165.96 [CO]; LRMS (CI-NH_3): m/e 464 ([M + NH_4^+], 28.6%), 447 ([MH^+], 100%), 357 ([MH^+ - Me_3SiOH], 78.9%); HRMS (CI-NH_3): m/e calcd. for $C_{12}H_{27}N_2O_7Si$ [MH^+], 447.1589; found, 447.1587}.



89a, B=Thymine
89b, B=Cytosine

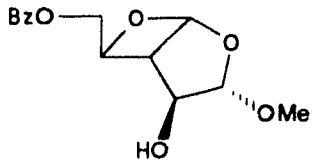
3'α-Cytosinyl-4'β-O-trimethylsilyl-6'β-benzoyloxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (89b).

Epoxide **23d** and *bis*-(trimethylsilyl)-cytosine afforded nucleoside **89b** in 58% yield by a procedure similar to the one used for the preparation of nucleoside **89a**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.16 (s, 9H, Me_3Si), 3.25 (t, 1H, H5'), 4.23 (ddd, 1H, H6'), 4.38 (A of ABX, 1H, H6"$_a$), 4.51 (B of ABX, 1H, H6"$_b$), 4.74 (s, 1H, H4'), 5.78 (d, 1H, H5), 5.95 (s, 1H, H3'), 6.24 (d, 1H, H1'), 7.35 (s, br, ex, 2H, NH_2), 7.39 - 7.61 (m, 3H, Ph), 8.00 - 8.06 (m, 2H, Ph), 8.11 (d, 1H, H6), $J_{H1'-H5'}$ = 4.3 Hz, $J_{H5'-H6'}$ = 4.0 Hz, $J_{H6'-H6"a}$ = 3.8 Hz, $J_{H6'-H6"b}$ = 3.9 Hz, $J_{H6"a-H6"b}$ = -12.4 Hz, J_{H5-H6} = 7.6 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 0.07 [$(\mathbf{CH_3})_3$Si], 51.08 [C5'], 65.24 [C6"], 76.74 [C6'], 77.76 [C4'], 93.85 [C5], 99.85 [C3'],

110.56 [C1'], 128.48, 129.64 and 133.39 [aromatic **CH**], 129.31 [aromatic **C**], 141.16 [C6], 156.32 [C2], 165.90 [C4], 166.07 [PhCO]; LRMS (CI-NH_3): m/e 432 ([MH^+], 25.3%)}.

3α-Methoxy-4β-hydroxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (24a').

Acetal **24a'** was formed when epoxide **23d** was subjected to flash chromatography using methylene chloride / methanol as eluent. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.95 (d, ex, 1H, OH), 3.29 (t, 1H, H5), 3.48 (s, 3H, MeO), 4.37 (d, 1H, H4), 4.42 (A of ABX, 1H, $H6'_a$), 4.52 (B of ABX, 1H, $H6'_b$), 4.73 (ddd, 1H, H6), 5.25 (s, 1H, H3), 6.06 (d, 1H, H1), 7.44 - 7.65 (m, 3H, phenyl), 8.04 - 8.09 (m, 2H, phenyl), J_{H1-H5} = 4.1 Hz, J_{H4-OH} = 5.0 Hz, J_{H5-H6} = 4.3 Hz, $J_{H6-H6'a}$ = 4.3 Hz, $J_{H6-H6'b}$ = 3.1 Hz, $J_{H6'a-H6'b}$ = -12.4 Hz; LRMS (CI-NH_3): m/e 281 ([MH^+], 10.9%), 249 ([MH^+ - MeOH], 98.1%)}.



24a'

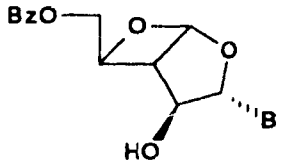
3'α-Thyminyl-4'β-hydroxy-6'β-benzoyloxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (90a).

To a stirred solution of nucleoside **89a** (322 mg, 0.722 mmol) in dry tetrahydrofuran (20 mL) at room temperature under an atmosphere of nitrogen was added tetra-*n*-butylammonium fluoride (1.0M solution in tetrahydrofuran, 1.08 mL, 1.08 mmol). After 1 h, the solvent was removed *in vacuo* to yield a white solid which was chromatographed over silica gel (methylene chloride / methanol, 20:1 v/v) affording nucleoside **90a** as a white solid (246 mg, 91% yield). {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.91 (d, 3H, CH_3 at C5), 3.29 (t, 1H, H5'), 3.48 (s, br, ex, 1H, OH), 4.33 (ddd, 1H, H6'), 4.46 (A of ABX, 1H, $H6''_a$), 4.57 (B of ABX, 1H, $H6''_b$), 5.92 (s, 1H, H3'), 6.27 (d, 1H, H1'), 7.41 - 7.63 (m, 3H, Ph), 7.92 (d, 1H, H6), 8.02 - 8.14 (m, 2H, Ph), 10.20 (s, br, ex, 1H, NH), $J_{H1'-H5'}$ = 4.1 Hz, $J_{H5'-H6'}$ = 4.2 Hz, $J_{H6'-H6''a}$ = 4.1 Hz, $J_{H6'-H6''b}$ = 3.8 Hz, $J_{H6''a-H6''b}$ = -12.3 Hz, $J_{1.o-Me}$ = -1.1 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 12.64 [CH_3 at C5], 49.61 [C5'], 65.08 [C6''], 77.53 [C6'], 78.89 [C4'], 100.02 [C3'], 110.50 [C5], 110.97 [C1'], 128.56, 129.72, 133.48 [aromatic **CH**], 129.35 [aromatic **C**], 135.71 [C6], 151.48 [C2], 164.55 [C4], 166.12 [PhCO]; LRMS (CI-NH_3): m/e 392 ([M + NH_4^+], 8.4%), 375 ([MH^+], 100%), 357 ([MH^+ - H_2O], 49.1%); HRMS (CI-NH_3): m/e calcd. for $C_{18}H_{19}N_2O_7$ [MH^+], 375.1192; found, 375.1192}.

3'α-Cytosinyl-4'β-hydroxy-6'β-benzoyloxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (90b).

Nucleoside **90b** was obtained in 96% yield as a white foam by a procedure identical to the one described for the preparation of nucleoside **90a**. {^{1}H-NMR (200 MHz, CD_3OD): δ 3.41 (t, 1H, H5'), 4.34 (A of ABX, 1H, $H6''_a$), 4.39 (ddd, 1H, H6'), 4.44 (B of ABX, 1H, $H6''_b$), 4.65 (s, 1H, H4'), 5.88 (d, 1H, H5), 6.00 (s, 1H, H3'), 6.26 (d, 1H, H1'), 7.47 - 7.68 (m, 3H, Ph), 8.04 - 8.10 (m, 2H, Ph), 8.24 (d, 1H,

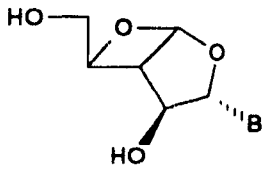
H6), $J_{H1'-H5'}$ = 4.4 Hz, $J_{H5'-H6'}$ = 4.9 Hz, $J_{H6'-H6''a}$ = 4.1 Hz, $J_{H6'-H6''b}$ = 2.8 Hz, $J_{H6''a-H6''b}$ = -12.5 Hz, J_{H5-H6} = 7.5 Hz; LRMS (CI - NH_3): m/e 377 ([M + NH_4^+], 1.3%), 360 ([MH^+], 100%), 249 ([MH^+ - cytosine], 20.2%); HRMS (CI - NH_3): m/e calcd. for $C_{17}H_{18}N_3O_6$ [MH^+], 360.1196; found, 360.1195).



90a, B=Thymine
90b, B=Cytosine

3'α-Thyminyl-4'β-hydroxy-6'β-hydroxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (91a).

An ice-cold solution of nucleoside **90a** (381 mg, 1.02 mmol) in anhydrous methanol (20 mL) was saturated with ammonia gas and allowed to warm to room temperature. After 20 h, the reaction was heated to boiling for 0.5 h, allowed to cool and the solvent removed under reduced pressure to yield a white solid which was washed repeatedly with ether. Recrystallization from methanol yielded bone white crystals of nucleoside **91a** (226 mg, 82% yield, m.p. 194-196°C). (^{1}H-NMR (200 MHz, CD_3OD): δ 1.86 (d, 3H, CH_3 at C5), 3.28 (t, 1H, H5'), 3.63 (A of ABX, 1H, H6"$_a$), 3.69 (B of ABX, 1H, H6"$_b$), 4.14 (ddd, 1H, H6'), 4.59 (s, 1H, H4'), 5.97 (s, 1H, H3'), 6.17 (d, 1H, H1'), 8.05 (d, 1H, H6), $J_{H1'-H5'}$ = 4.2 Hz, $J_{H5'-H6'}$ = 4.4 Hz, $J_{H6'-H6''a}$ = 3.8 Hz, $J_{H6'-H6''b}$ = 3.2 Hz, $J_{H6''a-H6''b}$ = -12.6 Hz, J_{H6-Me} = -1.2 Hz; ^{13}C-NMR (75.4 MHz, CD_3OD): δ 13.57 [CH_3 at C5], 51.42 [C5'], 65.22 [C6"], 80.06 [C6'], 82.63 [C4'], 101.48 [C3'], 110.92 [C5], 112.86 [C1'], 138.38 [C6], 153.42 [C2], 167.46 [C4]; LRMS (CI-NH_3)· m/e 271 ([MH^+], 100%), 253 ([MH^+ - H_2O], 7.7%); HRMS (CI-NH_3): m/e calcd. for $C_{11}H_{15}N_2O_6$ [MH^+], 271.0931; found, 271.0930). Anal. calcd. for $C_{11}H_{14}N_2O_6$: C, 48.89; H, 5.22; N, 10.37, found: C, 48.52; H, 5.49; N, 10.46.



91a, B=Thymine
91b, B=Cytosine

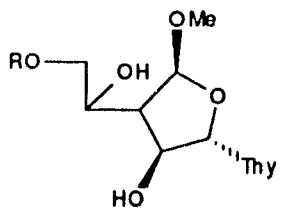
3'α-Cytosinyl-4'β-hydroxy-6'β-hydroxymethyl-2',7'-dioxa·bicyclo-[3,2,0]-heptane (91b).

Nucleoside **91b** was obtained in 77% yield as a white powder by a procedure identical to the one described for the preparation of nucleoside **91a**. (^{1}H-NMR (200 MHz, CD_3OD): δ 3.24 (t, 1H, H5'), 3.62 (A of ABX, 1H, H6"$_a$), 3.67 (B of ABX, 1H, H6"$_b$), 3.98 (ddd, 1H, H6'), 4.52 (s, 1H, H4'), 5.83 (d, 1H, H5), 5.94 (s, 1H, H3'), 6.13 (d, 1H, H1'), 8.21 (d, 1H, H6), $J_{H1'-H5'}$ = 4.1 Hz, $J_{H5'-H6'}$ = 4.6 Hz, $J_{H6'-H6''a}$ = 4.1 Hz, $J_{H6'-H6''b}$ = 3.2 Hz, $J_{H6''a-H6''b}$ = -12.6 Hz, $J_{H5\ H6}$ = 7.5 Hz; ^{13}C-NMR (75.4 MHz, CD_3OD): δ

50.41 [C5'], 64.41 [C6"], 79.05 [C4'], 81.73 [C6'], 95.07 [C5], 101.41 [C3'], 112.10 [C1'], 142.17 [C6], 158.76 [C2], 167.99 [C4]; LRMS (FAB - glycerol): m/e 278 ([M + Na^+], 23.2%), 256 ([MH^+], 35.4%); HRMS (FAB - glycerol): m/e calcd. for $C_{10}H_{14}N_3O_5$ [MH^+], 256.0933; found, 256.0933}.

Nucleoside (92).

To a stirred solution of nucleoside **89a** (322 mg, 0.72 mmol) in anhydrous methanol (22 mL) under an atmosphere of nitrogen at room temperature was added trifluoroacetic acid (63 mL, 0.72 mmol). After 30 min, the solution was evaporated to dryness. The residue was redissolved in methylene chloride (100 mL), washed with saturated aqueous sodium bicarbonate (100 mL), brine (100 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to yield the title compound in quantitative (493 mg) yield as a white foam. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 1.82 (d, 3H, CH_3 at C5), 2.45 (ddd, 1H, H3'), 3.42 (s, 3H, MeO), 4.31 - 4.45 (m, 5H, H2', H3", H3'"$_a$, H3'"$_b$, OH), 5.33 (d, ex, 1H, OH), 5.34 (d, 1H, H4'), 5.94 (d, 1H, H1'), 7.34 - 7.62 (m, 3H, Ph), 7.49 (d, 1H, H6), 8.03 - 8.08 (m, 2H, Ph), 10.39 (s, br, ex, 1H, NH), $J_{H1'-H2'}$ = 5.2 Hz, $J_{H3'-H4'}$ = 4.5 Hz, $J_{OH-H2' \text{ or } H3"}$ = 0.8 Hz, J_{H6-Me} = -0.8 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 12.36 [CH_3 at C5], 54.26 [C3'], 56.26 [CH_3O], 67.71 [C3'"], 67.86 [C3"], 77.28 [C2'], 90.90 [C1'], 105.40 [C4'], 109.96 [C5], 128.41, 129.76, 133.26 [aromatic CH], 129.66 [aromatic C], 136.64 [C6], 151.87 [C2], 164.32 [C4], 166.84 [PhCO]; LRMS (CI-NH_3): m/e 424 ([M + NH_4^+], 2.6%), 407 ([MH^+], 22.2%), 375 ([MH^+ - MeOH], 100%), 281 ([MH^+ - thymine], 12.3%); HRMS (CI-NH_3): m/e calcd. for $C_{19}H_{23}N_2O_8$ [MH^+], 407.1455; found, 407.1454}.



92, R=Bz
93, R=H

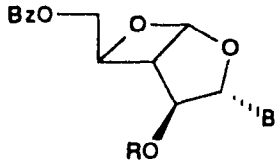
Nucleoside (93).

Nucleoside **93** was obtained in 86% yield as a white powder by a procedure identical to the one described for the preparation of nucleoside **91a**. {^{1}H-NMR (200 MHz, CD_3OD): δ 1.85 (d, 3H, CH_3 at C5), 2.19 (ddd, 1H, H3'), 3.39 (s, 3H, MeO), 3.51 (A of ABX, 1H, H3'"$_a$), 3.56 (B of ABX, 1H, H3'"$_b$), 3.85 (ddd, 1H, H3"), 4.16 (t, 1H, H2'), 5.10 (d, 1H, H4'), 6.01 (d, 1H, H1'), 7.52 (d, 1H, H6), $J_{H1'-H2'}$ = 7.2 Hz, $J_{H2'-H3'}$ = 8.2 Hz, $J_{H3'-H3"}$ = 4.4 Hz, $J_{H3"-H3'"a}$ = 7.4 Hz, $J_{H3"-H3'"b}$ = 4.4 Hz, $J_{H3'"a-H3'"b}$ = -10.9 Hz, $J_{H3'-H4'}$ = 4.2 Hz, J_{H6-Me} = -1.3 Hz; ^{13}C-NMR (75.4 MHz, CD_3OD): δ 12.36 [CH_3 at C5], 55.29 [C3'], 56.14 [CH_3O], 65.93 [C3'"], 71.24 [C3"], 75.91 [C2'], 88.63 [C1'], 105.18 [C4'], 112.18 [C5], 137.82 [C6], 152.77 [C2], 166.11 [C4]; LRMS (CI-NH_3): m/e 303 ([MH^+], 39.1%), 271 ([MH^+ - MeOH],

100%); HRMS (CI-NH_3): m/e calcd. for $C_{12}H_{19}N_2O_7$ [MH^+], 303.1191; found, 303.1192]. Anal. calcd. for $C_{12}H_{18}N_2O_7 \cdot H_2O$: C, 45.00; H, 6.29; N, 8.75; found: C, 44.83; H, 6.19; N, 8.67.

3'α-Thyminyl-4'β-acetoxy-6'β-benzoyloxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (94a).

Nucleoside **90a** was acetylated in 90% yield by a procedure similar to that used for the preparation of **25a**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.92 (d, 3H, CH_3 at C5), 2.10 (s, 3H, Ac), 3.40 (t, 1H, H5'), 4.47 (A of ABX, 1H, $H6''_a$), 4.55 (ddd, 1H, H6'), 4.64 (B of ABX, 1H, $H6''_b$), 5.55 (s, 1H, H4'), 6.22 (s, 1H, H3'), 6.23 (d, 1H, H1'), 7.41 - 7.62 (m, 3H, Ph), 7.83 (d, 1H, H6), 8.02 - 8.07 (m, 2H, Ph), 9.18 (s, br, ex, 1H, NH), $J_{H1'-H5'}$ = 4.1 Hz, $J_{H5'-H6'}$ = 3.5 Hz, $J_{H6'-H6''a}$ = 3.1 Hz, $J_{H6'-H6''b}$ = 3.0 Hz, $J_{H6''a-H6''b}$ = -11.9 Hz, J_{H6-Me} = -1.1 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 12.80 [CH_3 at C5], 20.88 [CH_3CO], 49.00 [C5'], 64.78 [C6''], 77.39 [C6'], 79.71 [C4'], 95.73 [C3'], 109 69 [C1'], 110.55 [C5], 128.48, 129.60, 133.38 [aromatic CH], 129.23 [aromatic C], 134.95 [C6], 150.39 [C2], 163.68 [C4], 165.83 [PhCO], 169.32 [CH_3CO]}.



94a, R=Ac
94b, R=$CH_3CH_2CH_2CH(CH_3)CO$
94c, R=$PhC(OCH_3)(CF_3)CO$

3'α-Thyminyl-4'β-(α-methylvaleryloxy)-6'β-benzoyloxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (94b).

To a stirred solution of nucleoside **90a** (37 mg, 0.10 mmol) and 2-methylvaleric acid (125 μL, 1.00 mmol) in dry acetonitrile (5 mL) at room temperature under an atmosphere of nitrogen was added *N,N*-dimethylaminopyridine (24 mg, 0.20 mmol) and 1,3-dicyclohexylcarbodiimide (206 mg, 1.00 mmol). After 18 h, acetic acid (13 μL) and methanol (66 μL) were added and stirring was continued for 30 min. The reaction mixture was poured into saturated aqueous sodium bicarbonate (50 mL) and extracted with methylene chloride (3 x 50 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to afford a white solid. Purification by flash chromatography (methylene chloride / methanol, 30:1 v/v) gave the title compound (mixture of 2 inseparable diastereomers, 1:1), (45 mg, 95% yield) as a white solid. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.87, 0.88 (2t, 3H, CH_3CH_2), 1.13, 1.15 (2d, 3H, CH_3CH), 1.18 - 1.81 (m, 4H, CH_2CH_2), 1.92 (s, br, 3H, CH_3 at C5), 2.47 (m, 1H, CHCO), 3.33, 3.34 (2t, 1H, H5'), 4.47 (A of ABX, 1H, $H6''_a$), 4.55 (m, 1H, H6'), 4.64 (B of ABX, 1H, $H6''_b$), 5.52, 5.54 (2s, 1H, H4'), 6.22 (s, 1H, H3'), 6.23 (d, 1H, H1'), 7.41 - 7.86 (m, 3H, Ph), 7.83 (s, br, 1H, H6), 8.02

- 8.08 (m, 2H, Ph), 8.81, 8.86 (2s, br, ex, 1H, NH), $J_{H1'-H5'}$ = 4.1 Hz, J_{CH-Me} = 6.9 Hz, 7.0 Hz, $J_{CH_3-CH_2}$ = 7.0 Hz, 7.1 Hz, $J_{H5'-H6'}$ = 4.2 Hz, 4.4 Hz, $J_{H6'-H6''_a}$ = 2.9 Hz, $J_{H6'-H6''_b}$ = 3.0 Hz, $J_{H6''_a-H6''_b}$ = -11.9 Hz}.

3'α-Thyminyl-4'β-(α-methoxy-α-(trifluoromethyl)-phenylacetoxy)-6'β-benzoyloxymethyl-2',7'-dioxa-bicyclo-[3,2,0]-heptane (94c).

Nucleoside **90a** (37 mg, 0.10 mmol) and 2-methoxy-2-(trifluoromethyl)-phenylacetic acid (234 mg, 1.00 mmol) gave the title compound (mixture of 2 inseparable diastereomers, 1:1), (48 mg, 82% yield) as a white solid by a procedure analogous to the one used for the preparation of **94b**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.86 (s, br, 3H, CH_3 at C5), 3.31 (t, 1H, H5'), 3.76 (s, 3H, MeO), 4.21 - 4.86 (m, 3H, H6', $H6''_a$, $H6''_b$), 4.70, 4.74 (2s, 1H, H4'), 5.91, 6.02 (2s, 1H, H3'), 6.26 (d, 1H, H1'), 7.29 - 7.68 (m, 8H, Ph), 7.93 (s, br, 1H, H6), 8.02 - 8.06 (m, 2H, Ph), 9.25 (s, br, ex, 1H, NH), $J_{H1'-H5'}$ = 3.9 Hz, $J_{H5'-H6'}$ = 4.1 Hz}.

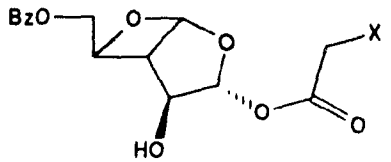
4.8 Experimentals for Section 2.9.

3α-Chloroacetoxy-4β-hydroxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (97a).

To a solution of epoxide **23d** (50 mg, 0.20 mmol) in dry methylene chloride (5 mL) under nitrogen at room temperature was added chloroacetic acid (19 mg, 0.20 mmol) and the reaction mixture was allowed to stir for 16 h. The solution was diluted with methylene chloride (25 mL), washed with saturated aqueous sodium bicarbonate (25 mL), brine (25 mL), dried (Na_2SO_4), filtered and the solvent removed in vacuo to yield a yellow syrup. Chromatography over silica gel (petroleum ether / ethyl acetate, 1:1 v/v) afforded **97a** (31 mg, 45% yield) as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.67 (s, br, ex, 1H, OH), 3.40 (dt, 1H, H5), 4.13 (s, 2H, CH_2Cl), 4.49 (A of ABX, 1H, H6'$_a$), 4 53 (s, 1H, H4), 4.58 (B of ABX, 1H, H6'$_b$), 4.75 (ddd, 1H, H6), 6.15 (d, 1H, H1), 6.50 (d, 1H, H3), 7.40 - 7.63 (m, 3H, Ph), 8.03 - 8.08 (m, 2H, Ph); $J_{H1\text{-}H5}$ = 4.0 Hz, $J_{H3\text{-}H5}$ = -1.0 Hz, $J_{H5\text{-}H6}$ = 4.3 Hz, $J_{H6\text{-}H6'a}$ = 4.2 Hz, $J_{H6\text{-}H6'b}$ = 3.2 Hz, $J_{H6'a\text{-}H6'b}$ = -12.5 Hz}.

3α-Bromoacetoxy-4β-hydroxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (97b).

Epoxide **23d** (42 mg, 0.17 mmol) and bromoacetic acid (24 mg, 0.17 mmol) gave the title compound (36 mg, 55% yield) as a light yellow oil by a procedure similar to the one used for the preparation of **97a**. {^{1}H-NMR (300 MHz, $CDCl_3$): δ 3.19 (d, ex, 1H, OH), 3.39 (t, 1H, H5), 3.89 (s, 1H, CHHBr), 3.90 (s, 1H, CHHBr), 4.47 (A of ABX, 1H, H6'$_a$), 4.57 (B of ABX, 1H, H6'$_b$), 4.58 (d, 1H, H4), 4.77 (ddd, 1H, H6), 6.13 (d, 1H, H1), 6.46 (s, 1H, H3), 7.37 - 7.59 (m, 3H, Ph), 7.99 - 8.05 (m, 2H, Ph); $J_{H1\text{-}H5}$ = 4.0 Hz, $J_{H4\text{-}OH}$ = 4.3 Hz, $J_{H5\text{-}H6}$ = 4.4 Hz, $J_{H6\text{-}H6'a}$ = 4.3 Hz, $J_{H6\text{-}H6'b}$ = 3.2 Hz, $J_{H6'a\ H6'b}$ = -12.5 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 25.79 [$\mathbf{CH_2Br}$], 49.37 [C5], 65.54 [C6'], 76.31 [C4], 76.72 [C6], 106.77 [C3], 109.04 [C1], 128.52, 129.65, 133.45 [aromatic **CH**], 129.32 [aromatic C], 166.22, 166.38 [CO]; LRMS (CI-NH_3): m/e 406, 404 ([M + NH_4^+], 34.6%, 34.9%), 389, 387 ([MH^+], 4 6%, 3.3%), 249 ([MH^+ - $BrCH_2COOH$], 37.9%); HRMS (CI-NH_3)· m/e calcd. for $C_{15}H_{19}NO_7{}^{79}Br$ [M + NH_4^+], 404.0346; found, 404.0344}.



97a, X=Cl
97b, X=Br

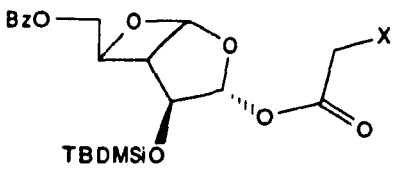
3α-Chloroacetoxy-4β-*t*-butyldimethylsilyloxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (98a).

Alcohol **97a** was silylated by a procedure similar to that used for the preparation of **19**. Purification by flash chromatography (hexanes / ethyl acetate, 9:1 v/v) gave the title compound in 41%

yield as a clear oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.07, 0.09 (2s, 6H, *t*-$BuSiMe_2$), 0.84 (s, 9H, *t*-$BuSiMe_2$), 3.23 (dt, 1H, H5), 4.13 (s, 2H, CH_2Cl), 4.41 (s, 1H, H4), 4.49 (A of ABX, 1H, H6'$_a$), 4.56 (B of ABX, 1H, H6'$_b$), 4.72 (ddd, 1H, H6), 6.14 (d, 1H, H1), 6.40 (d, 1H, H3), 7.41 - 7.62 (m, 3H, Ph), 8.03 - 8.09 (m, 2H, Ph); J_{H1-H5} = 4.1 Hz, J_{H3-H5} = -0.9 Hz, J_{H5-H6} = 4.4 Hz, $J_{H6-H6'a}$ = 4.9 Hz, $J_{H6-H6'b}$ = 3.8 Hz, $J_{H6'a-H6'b}$ = -12.2 Hz}.

3α-N^1-Imidazoylacetoxy-4β-*t*-butyldimethylsilyloxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (98b).

To a solution of alcohol **97b** (39 mg, 0.10 mmol) in dry *N,N*-dimethylformamide (0.5 mL) under nitrogen at room temperature was added imidazole (21 mg, 0.30 mol) and *t*-butyldimethylsilyl chloride (23 mg, 0.15 mmol) and it was allowed to stir until all of the starting material was consumed (72 h). The reaction mixture was diluted with ethyl acetate (30 mL), washed with water (3 x 25 mL), brine (25 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to yield a yellow syrup. Purification by flash chromatography (petroleum ether / ethyl acetate, 1:1 v/v) afforded the title compound (17 mg, 36% yield) as a light yellow oil. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 0.04, 0.06 (2s, 6H, *t*-$BuSiMe_2$), 0.83 (s, 9H, *t*-$BuSiMe_2$), 3.18 (t, 1H, H5), 4.30 (s, 1H, H4), 4.34 (ddd, 1H, H6), 4.44 (A of ABX, 1H, H6'$_a$), 4.52 (B of ABX, 1H, H6'$_b$), 4.79 (s, 2H, CH_2), 6.12 (d, 1H, H1), 6.39 (s, 1H, H3), 6.98, 7.07 (2d, 2H, N-CH=CH-N), 7.41 - 7.63 (m, 3H, Ph), 7.45 (s, 1H, N-CH=N), 8.04 - 8.09 (m, 2H, Ph); J_{H1-H5} = 4.0 Hz, J_{H5-H6} = 4.3 Hz, $J_{H6-H6'a}$ = 4.1 Hz, $J_{H6-H6'b}$ = 4.1 Hz, $J_{H6'a-H6'b}$ = -12.2 Hz, $J_{NCH-NCH}$ = 0.7 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 17.95 [$(CH_3)_3CSiMe_2$], 25.55 [*t*-$BuSiMe_2$], 25.55 [$(CH_3)_3CSiMe_2$], 48.27 [CH_2], 50.51 [C5], 65.71 [C6'], 76.25 [C6], 77.31 [C4], 106.66 [C3], 109.11 [C1], 120.23 [N-CH=CH-N], 128.54, 129.69, 133.43 [aromatic CH], 129.47 [aromatic C], 133.62 [N-CH=N], 166.02, 166.22 [CO]; LRMS (CI-NH_3): m/e 489 ([MH^+], 100%), 363 ([MH^+ - (*imid*-CH_2COOH)], 20.8%)}.



98a, X=Cl
98b, X=*imid*
98c, X=Br

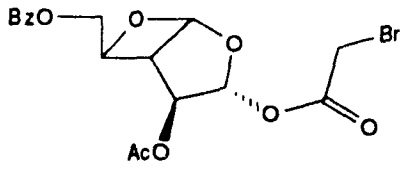
3α-Bromoacetoxy-4β-*t*-butyldimethylsilyloxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (98c).

To an ice-cooled solution of alcohol **97b** (39 mg, 0.10 mmol) in dry methylene chloride (250 μL) under an atmosphere of nitrogen was added 2,6-lutidine (35 μL, 0.30 mol) and *t*-butyldimethylsilyl trifluoromethanesulfonate (46 μL, 0.20 mmol) and the reaction allowed to stir until all of the starting

material was consumed (2 h). The reaction mixture was diluted with methylene chloride (30 mL), washed with cold 5% aqueous sodium carbonate (25 mL), brine (25 mL), dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to yield a clear residue. Purification by flash chromatography (petroleum ether / ethyl acetate, 3:1 v/v) afforded the title compound (29 mg, 58% yield) as a colourless oil. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 0.11, 0.12 (2s, 6H, *t*-BuSiMe$_2$), 0.88 (s, 9H, *t*-BuSiMe$_2$), 3.29 (dt, 1H, H5), 3.95 (s, 2H, CH_2Br), 4.46 (s, 1H, H4), 4.48 (A of ABX, 1H, H6'$_a$), 4.57 (B of ABX, 1H, H6'$_b$), 4.77 (ddd, 1H, H6), 6.14 (d, 1H, H1), 6.53 (d, 1H, H3), 7.44 - 7.66 (m, 3H, Ph), 8.05 - 8.10 (m, 2H, Ph); $J_{H1\text{-}H5}$ = 4.1 Hz, $J_{H3\text{-}H5}$ = -0.7 Hz, $J_{H5\text{-}H6}$ = 4.5 Hz, $J_{H6\text{-}H6'a}$ = 4.5 Hz, $J_{H6\text{-}H6'b}$ = 3.9 Hz, $J_{H6'a\ H6'b}$ = -12.3 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 18.22 [$(CH_3)_3CSiMe_2$], 25.73 [*t*-BuSiMe$_2$], 25.73 [$(CH_3)_3CSiMe_2$], 26.49 [CH_2Br], 50.90 [C5], 66.18 [C6'], 76.74 [C6], 77.69 [C4], 107.57 [C3], 109.61 [C1], 128.87, 129.92, 133.65 [aromatic CH], 130.07 [aromatic C], 166.19, 166.41 [CO]; LRMS (CI-NH_3): m/e 520, 518 ([M + NH_4^+], 8.7%, 5.7%), 503, 501 ([MH^+], 1.3%, 1.0%), HRMS (CI-NH_3): m/e calcd. for $C_{21}H_{30}O_7Si^{79}Br$ [MH^+], 501.0941; found, 501.0944}.

3α-Bromoacetoxy-4β-acetoxy-6β-benzoyloxymethyl-2,7-dioxa-bicyclo-[3,2,0]-heptane (101).

Alcohol **97b** was acetylated in 95% yield by a procedure similar to that used for **25a**. {^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.07 (s, 3H, CH_3), 3.45 (t, 1H, H5), 3.91 (s, 2H, CH_2Br), 4.51 (A of ABX, 1H, H6'$_a$), 4.60 (B of ABX, 1H, H6'$_b$), 4.86 (ddd, 1H, H6), 5.36 (s, 1H, H4), 6.14 (d, 1H, H1), 6.53 (s, 1H, H3), 7.41 - 7.62 (m, 3H, Ph), 8.04 - 8.09 (m, 2H, Ph); $J_{H1\text{-}H5}$ = 4.1 Hz, $J_{H5\text{-}H6}$ = 4.3 Hz, $J_{H6\ H6'a}$ = 4.0 Hz, $J_{H6\text{-}H6'b}$ = 3.3 Hz, $J_{H6'a\text{-}H6'b}$ = -12.5 Hz; ^{13}C-NMR (75.4 MHz, CD_2Cl_2): δ 20.84 [CH_3], 26.27 [CH_2Br], 47.69 [C5], 65.61 [C6'], 76.82 [C6], 77.57 [C4], 104.20 [C3], 109.07 [C1], 128.86, 129.90, 133.65 [aromatic CH], 130.01 [aromatic C], 166.22, 166.38 [CO], 169.89 [CH_3CO]; LRMS (CI-NH_3): m/e 431, 429 ([MH^+], 15.1%, 20.8%), 291 ([MH^+ - $BrCH_2COOH$], 100%); HRMS (CI-NH_3): m/e calcd for $C_{17}H_{18}O_8{}^{79}Br$ [MH^+], 429.0186; found, 429.0185}.



101

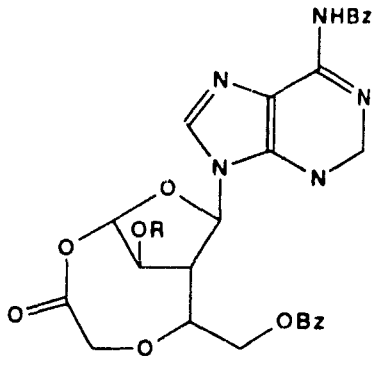
Bicyclic Furanoside (99a).

To a solution of **98c** (50 mg, 0.10 mmol) in dry acetonitrile (500 µL) under an atmosphere of nitrogen at room temperature was added a stock solution of *bis*-(trimethylsilyl)-N^6-adenine in 1,2-dichloroethane (0.339 M solution, 324 µL, 0.11 mmol) and silver triflate (26 mg, 0.10 mmol). After stirring for 1 h, the reaction mixture was diluted with methylene chloride (25 mL), washed with saturated aqueous sodium bicarbonate (30 mL), brine (30 mL), dried (Na_2SO_4), filtered and the solvent removed *in*

vacuo yielding a yellow residue. Purification by flash chromatography (methylene chloride / methanol, 100:3 v/v) afforded nucleoside **99a** (40 mg, 61% yield) as an unstable light yellow oil. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 0.04, 0.07 (2s, 6H, *t*-BuSi**Me**$_2$), 0.75 (s, 9H, *t*-**Bu**Si**Me**$_2$), 2.29 (ddd, 1H, H2'), 3.80 (s, 2H, OCH_2CO), 4.22 (m, 4H, H2", H2"'$_a$, H2"'$_b$, H3'), 5.61 (s, 1H, H4'), 5.79 (d, 1H, H1'), 7.39 - 7.59 (m, 6H, Ph), 7.84 - 7.92 (m, 4H, Ph), 8.57 (s, 1H, H8), 8.80 (s, 1H, H2), 11.44 (s, br, ex, 1H, NH), $J_{H1'-H2'}$ = 5.2 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 17.99 [**Me**$_3$CSi**Me**$_2$], 25.32[*t*-**Bu**Si**Me**$_2$], 25.54 [**Me**$_3$CSi**Me**$_2$], 26.15 [O**C**H$_2$CO], 58.30 [C2'], 67.19 [C2'"], 68.29 [C2"], 78.08 [C3'], 91.08 [C1'], 104.13 [C4'], 113.76 [C5], 128.56, 128.87, 129.75, 129.86, 132.69, 133.77 [aromatic **C**H], 129.53 [aromatic C-$COOCH_2$], 135.19 [aromatic C-CON], 146.38 [C8], 147.10 [C4], 154.04 [C2], 154.30 [C6], 165.99, 166.35, 167.07 [CO]}.

Bicyclic Furanoside (99b).

Acetal **101** (43 mg, 0.10 mmol) and a stock solution of *bis*-(trimethylsilyl)-N^6-adenine in 1,2-dichloroethane (0.339 M solution, 324 μL, 0.11 mmol) gave the title compound (41 mg, 70% yield) as an unstable white foam by a procedure analogous to the one used for the preparation of nucleoside 99a. {^{1}H-NMR (200 MHz, CD_2Cl_2): δ 2.01 (s, 3H, Ac), 2.39 (ddd, 1H, H2'), 3.81 (s, 2H, OCH_2CO), 4.17 (A of ABX, 1H, H2"'$_a$), 4.33 (B of ABX, 1H, H2"'$_b$), 4.37 (ddd, 1H, H2"), 5.16 (d, 1H, H3'), 5.60 (s, 1H, H4'), 5.86 (d, 1H, H1'), 7.44 - 7.88 (m, 6H, Ph), 7.94 - 8.04 (m, 4H, Ph), 8.58 (s, 1H, H8), 8.76 (s, 1H, H2), 11.43 (s, br, ex, 1H, NH), $J_{H1'-H2'}$ = 4.6 Hz, $J_{H2'-H3'}$ = 3.3 Hz; ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 20.78 [CH_3CO], 25.30 [O**C**H$_2$CO], 55.80 [C2'], 66.76 [C2'"], 68.03 [C2"], 78.59 [C3'], 90.68 [C1'], 100.93 [C4'], 113.10 [C5], 128.52, 128.61, 129.33, 129.59, 132.68, 133.47 [aromatic **C**H], 129.00 [aromatic C-$COOCH_2$], 134.29 [aromatic C-CON], 145.92 [C8], 146.42 [C4], 154.27 [C2], 154.53 [C6], 165.13, 166.13, 166.80 [CO], 169.99 [CH_3CO]}.

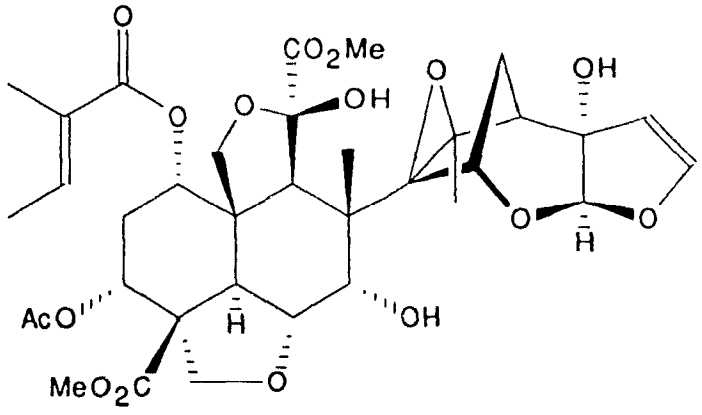


99a, R=TBDMSi
99b, R=Ac

5. APPENDICES.

APPENDIX I. Antifeedant Testing of Photo-Adducts.

Protecting our food supply from predatory insect attack in an ecologically responsible manner has led to increased interest in behavior altering chemicals from natural sources. The Indian neem tree, *Azadirachta Indica* A. Juss (Meliaceae)[103] has provided a large quantity of materials, of which one component, azadirachtin has received a great deal of attention[104]. Azadirachtin possesses extremely potent biological activity as a growth regulatory and antifeedant agent[105].



Azadirachtin

This has led to a geat deal of research into the understanding of the structure activity relationships and to synthesize simpler compounds which exhibit similar biological activity[104]. Recently, it was reported that antifeedancy can be demonstrated using relatively simple hydroxytricyclic hydrofuran derivatives of the type **109**[106]. In studies carried out by Ley, it was shown that salannin and derivatives thereof are poor antifeedants, thus indicating that the left hand side of azadirachtin is not responsible for its biological activity[104].

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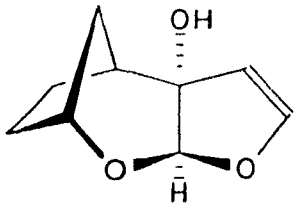
103 Morgan, E. D.; Butterworth, J. H., *J. Chem. Soc , Chem. Commun.*, 23 (1968)

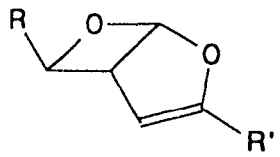
104 Ley, S.V.; Anderson, J. C.; Blaney, W. M.; Jones, P. S.; Lidert, Z; Morgan, E. D , Robinson, N. G ; Santafianos, D.; Simmonds, M. S. J ; Toogood, P. L., *Tetrahedron Lett.*, 5175 (1989) and references cited therein.

105 Yamasaki, R B.; Klocke, J. A., *J. Agric Food. Chem.*, **35**, 467 (1987)

106 Ley, S. V.; Santafianos, D.; Blaney, W M , Simmonds, M S J , *Tetrahedron Lett* , **28**, 221 (1987)



109



Due to the similarities between **109** and photo-adducts of aldehydes and furans, Dr. T. H. Chan thought that our photo-adducts might possess biological activity as antifeedants against spruce budworm. The bioassay[107] conducted involved feeding laboratory-colony spruce budworm larvae an artificial diet[108] containing 0.2% (wet weight) of test compounds. The assay showed the development of larvae reared from second instar on test diets was only significantly retarded by compounds **40** and **41a**. The results are shown in Table 2.

Table 2

Compound #	Compound	Mean Instar[a]
	Control	5.30
2c	R = $TBDMSiOCH_2$, R' = H	5.22
2d	R = $BzOCH_2$, R' = H	5.18
40	R = $BzOCH_2$, R' = $SnBu_3$	2.00
41a	R = $BzOCH_2$, R' = Ph	2.94
44a	R = $BzOCH_2$, R' = CH_3	5.18
72a	R = $EtCOCH_2$, R' = CH_3	5.22
81	R = *i*PrOOC, R' = CH_3	NA

[a]Maximum = 6.00 (all larvae 6th instars)

Since reduction in development rate could be caused by factors other than feeding, compounds **40** and **41a** are currently being evaluated by an assay that will provide a true reflection of the amount of food ingested by sixth instar larvae. Also, both of these compounds are being evaluated at lower concentrations so as to determine the limits of their effectiveness.

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[107] Bioassays were carried out by A. W. Thomas at Canadian Forestry Service Maritimes, Fredericton, N.B., Canada E3B 5P7.

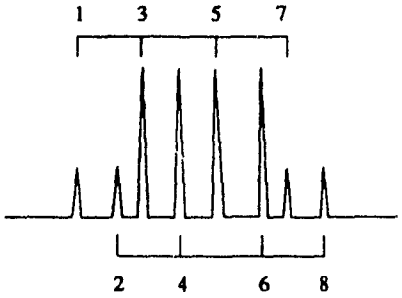
[108] McMorran, A., *Can. Entomol*, **97**, 58 (1965).

APPENDIX II. Analysis of ABX systems in ^{1}H-NMR spectra.

Thr chemical shifts and coupling constants of second order AB portions of ABX systems were calculated by the method shown below[109].

The ABX spectrum is divided into two AB systems.

AB #1



AB #2

$J_{A,B} = (8 - 6) = (7 - 5) = (4 - 2) = (3 - 1)$

AB #1

$\vartheta_1 = (1 + 3 + 5 + 7) / 4$

$(\Delta\vartheta_1) / 2 = [(1 - 7)(3 - 5)]^{1/2} / 2$

$\Delta 1^+ = \vartheta_1 + (\Delta\vartheta_1) / 2$

$\Delta 1^- = \vartheta_1 - (\Delta\vartheta_1) / 2$

$\vartheta_A = (\Delta 1^+ + \Delta 2^+) / 2$

$J_{AX} = \Delta 1^+ - \Delta 2^+$

or

$\vartheta_A = (\Delta 1^+ + \Delta 2^-) / 2$

$J_{AX} = \Delta 1^+ - \Delta 2^-$

AB #2

$\vartheta_2 = (2 + 4 + 6 + 8) / 4$

$(\Delta\vartheta_2) / 2 = [(2 - 8)(4 - 6)]^{1/2} / 2$

$\Delta 2^+ = \vartheta_2 + (\Delta\vartheta_2) / 2$

$\Delta 2^- = \vartheta_2 - (\Delta\vartheta_2) / 2$

$\vartheta_B = (\Delta 1^- + \Delta 2^-) / 2$

$J_{BX} = \Delta 1^- - \Delta 2^-$

or

$\vartheta_B = (\Delta 1^- + \Delta 2^+) / 2$

$J_{BX} = \Delta 1^- - \Delta 2^+$

Two possible sets of values are generated, but one gives unrealistic coupling constants.

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[109] Becker, E. D., (ed.), *High Resolution NMR - Theory and Chemical Applications*, Academic Press, Inc , London, (1980), chap. 7.

APPENDIX III. X-Ray Structure Determination of Nucleoside (91a).

An X-Ray study was carried out on nucleoside **91a**. The diffraction measurement was made on a Rigaku diffractometer and the data obtained is shown in the tables below.

Table XR-1

Crystal data and course of structure determination

Compound name	Nucleoside **91a**
Chemical Formula	$C_{11}H_{14}N_2O_6$
Formula weight	270.24
Crystal	
Habit	rectangular prism
X-ray specimen size (mm)	0.10 x 0.20 x 0.25
Radiation	Graphite monochromated CuKα
Crystal system	Triclinic
Space group	P-1
Lattice Constants	
a (Å)	10.0636(17)
b (Å)	10.4054(20)
c (Å)	11.9771(15)
α (°)	96.552(15)
β (°)	108.031(11)
χ (°)	90.498(14)
V (Å^3)	1182.5(3)
No. of formula in a cell	4
F (000)	567.90
Calculated density (gcm^{-3})	1.518
μ for CuKα (mm^{-1})	1.02
λ (Å)	1.54056
2θ max (°)	110.0
h, k, l ranges	-10 10, 0 11, -12 12
No. of reflections measured	3182
No. of unique reflections	2975

No. of reflections with $I_{net} > 2.5\sigma(I_{net})$	1975
For significant reflections	RF = 0.084, R_w = 0.054, G_of = 3.31
For all reflections	RF = 0.143, R_w = 0.056
Maximum shift / σ ratio	0.061
Deepest hole in D-map (e / Å^3)	-0.580
Highest peak in D-map (e / Å^3)	0.380
Secondary extinction coefficient	0.019(5)
Merging R	1.2%
Drop of standard intensities (avg.)	0.2%
Method of structure determination	Solved by direct methods using SHELXS[110]
Method of structure refinement	Refined using NRCVAX system programs[111]

Cell dimensions were obtained from 21 reflections with 2θ angle in the range 15.00° - 25.00°. The intensity data were collected using the θ/2θ scan mode.

$$RF = \Sigma (F_o - F_c) / \Sigma (F_o)$$

$$R_w = (\Sigma [w (F_o - F_c)^2 / \Sigma (wF_o^2)])^{1/2}$$

$$G_oF = (\Sigma [w (F_o - F_c)^2 / \Sigma (\#\text{ of reflections} - \#\text{ of parameters})])^{1/2}$$

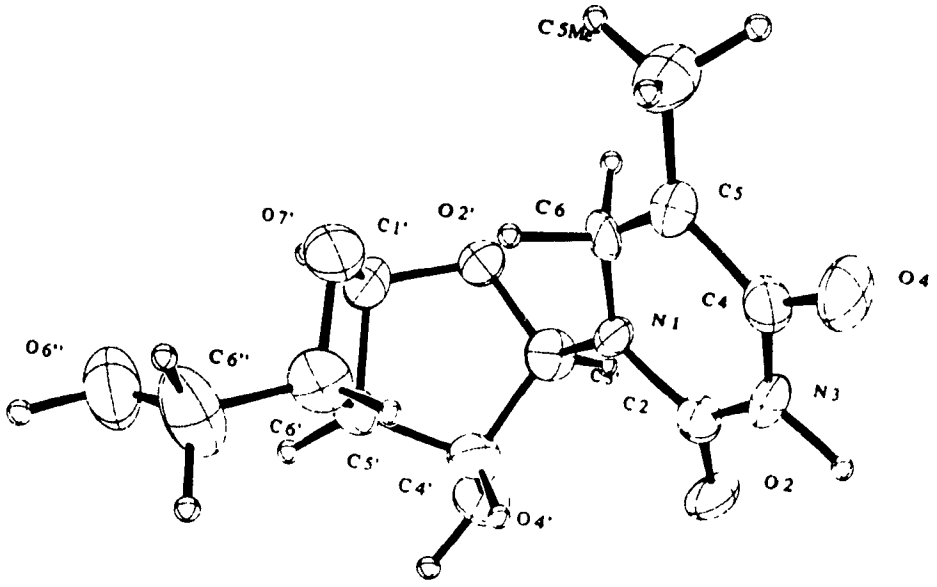


Figure XR-1. X-ray crystallographic structure of nucleoside **91a**.

[110] Sheldrick, G. M. in *Crystallographic Computing 3*; Sheldrick, G. M , Kruger, M , Doddard, R , Eds , Oxford University Press: Oxford, England, 1985; pp 175 - 189.

[111] Gabe, E. J.; Lepage, Y.; Charland, J P.; Lee, F L ; White, P. S., *J. Appl. Cryst.*, **22**, 384 (1989).

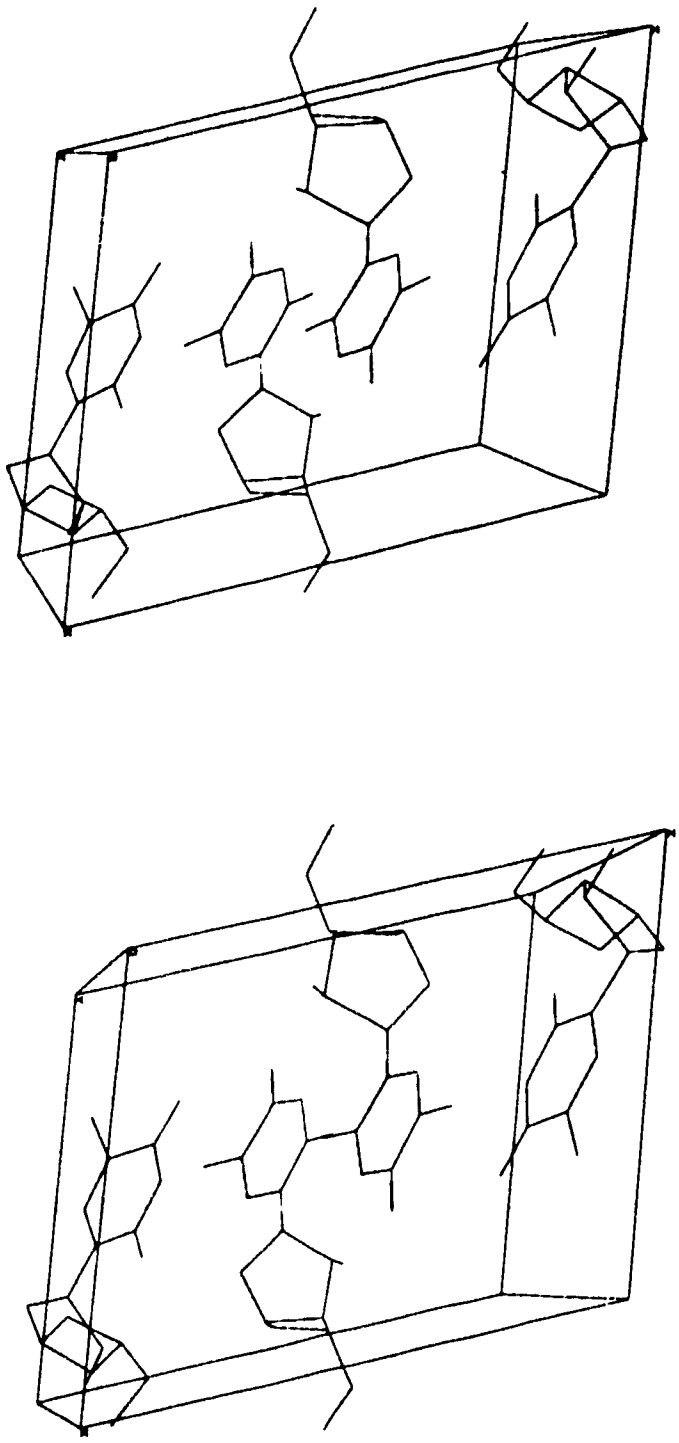


Figure XR-2. Unit cell of nucleoside **91a**.

Table XR-2

Atomic Parameters X, Y, Z and B_{eq}. E. S. Ds. refer to the last digit printed.

Atom	X	Y	Z	B_{eq}
O-2	0.2995(5)	0.8956(5)	0.7867(4)	3.5 (3)
O-4	0.6723(6)	1.1338(5)	0.7676(5)	4.1 (3)
O-2'	0.2566(5)	1.1484(5)	1.0577(4)	2.9 (3)
O-4'	0.0176(5)	0.9666(5)	0.8876(4)	3.8 (3)
O-7'	0.2146(5)	1.3524(5)	0.9833(5)	3.8 (3)
O-6"	-0.0601(6)	1.4532(6)	0.8801(5)	5.9 (4)
N-1	0.3627(6)	1.0859(5)	0.9081(5)	2.4 (3)
N-3	0.4848(6)	1.0174(5)	0.7788(5)	2.8 (3)
C-2	0.3760(8)	0.9925(7)	0.8205(6)	2.8 (4)
C-4	0.5806(8)	1.1208(7)	0.8137(6)	2.9 (4)
C-5	0.5682(8)	1.2118(7)	0.9122(6)	3.1 (4)
C-5-Me	0.6757(9)	1.3203(7)	0.9681(7)	4.1 (5)
C-6	0.4587(8)	1.1905(7)	0.9524(6)	2.8 (4)
C-3'	0.2487(8)	1.0572(7)	0.9584(6)	2.8 (4)
C-4'	0.1033(8)	1.0667(7)	0.8702(6)	3.0 (4)
C-5'	0.0574(7)	1.2000(7)	0.9026(6)	2.9 (4)
C-1'	0.1606(8)	1.2477(7)	1.0257(6)	3.1 (4)
C-6'	0.1201(8)	1.3150(8)	0.8614(7)	3.7 (4)
C-6"	0.0296(10)	1.4222(9)	0.8144(8)	5.6 (6)
O-2A	-0.5015(5)	0.8567(5)	0.5729(4)	3.4 (3)
O-4A	-0.7071(6)	0.4809(5)	0.3563(5)	5.7 (4)
O-2A'	-0.2178(5)	0.8636(5)	0.3961(4)	2.8 (3)
O-4A'	-0.1710(6)	1.0119(6)	0.6482(5)	5.9 (3)
O-7A'	-0.0747(5)	0.6836(4)	0.4420(4)	2.80 (25)
O-6A"	0.2075(5)	0.7237(5)	0.5876(4)	3.2 (3)
N-1A	-0.3970(6)	0.7544(5)	0.4457(5)	2.1 (3)
N-3A	-0.6019(6)	0.6682(6)	0.4621(5)	3 0 (3)
C-2A	-0.5007(7)	0.7655(7)	0.4993(6)	2.7 (4)
C-4A	-0.6101(8)	0.5598(7)	0 3808(7)	3 3 (4)
C-5A	-0.4987(8)	0.5532(7)	0 3287(6)	2.8 (4)
C-5-Me-A	-0 4954(9)	0.4410(8)	0.2392(7)	4.3 (5)
C-6A	-0.4004(8)	0.6484(7)	0.3624(6)	2.7 (4)
C-3A'	-0.2973(7)	0.8697(7)	0.4757(6)	2 5 (4)
C-4A'	-0.1918(8)	0 8784(7)	0.6012(6)	3.0 (4)
C-5A'	-0.0559(7)	0.8321(7)	0.5838(6)	2.6 (4)
C-1A'	-0 0820(8)	0.8220(6)	0 4505(6)	2.5 (4)
C-6A'	-0.0342(8)	0.6867(7)	0.5702(6)	2.7 (4)
C-6A"	0.1124(8)	0.6484(7)	0.6217(6)	2.9 (4)

B_{eq} is the mean of the principal axes of the thermal ellipsoid.

Table XR-3

Calculated Hydrogen Atom Parameters.

Atom	X	Y	Z	B_{iso}
H-O-4'	-0.0.86	0.971	0.826	4.5
H-O-6"	-0.124	1.530	0.842	6.8
H-N3	0.496	0.946	0.710	3.6
H5-Me_a	0.777	1.280	1.001	5.0
H5-Me_b	0.679	1.379	0.900	5.0
H5-Me_c	0.651	1.378	1.039	5.0
H6	0.501	1.186	1.047	3.4
H3'	0.259	0.960	0.983	3.7
H4'	0.109	1.058	0.781	3.7
H5'	-0.052	1.206	0.894	3.6
H1'	0.108	1.278	1.090	3.9
H6'	0.178	1.278	0.803	4.6
H6"$_a$	-0.030	1.392	0.723	6.8
H6"$_b$	0.094	1.506	0.815	6.8
H-O-4'A	0.097	1.019	0.736	5.7
H-O-6"A	0.263	0.803	0.652	4.0
H-N3A	-0.675	0.679	0.512	3.8
H5-Me_aA	-0.491	0.351	0.277	4.9
H5-Me_bA	-0.589	0.436	0.164	4.9
H5-Me_cA	-0.407	0.449	0.207	4.9
H6A	-0.301	0.604	0.395	3.4
H3'A	-0.355	0.957	0.471	3.4
H4'A	-0.227	0.818	0.655	3.7
H5'A	0.036	0.891	0.637	3.4
H1'A	0.000	0.870	0.427	3.3
H6'A	-0.108	0.634	0.599	3.6
H6"$_a$A	0.119	0.547	0.592	3.7
H6"$_b$A	0.138	0.660	0.717	3.7

Hydrogen atom positions calculated assuming C/N-H distance of 1.08 Å.
B_{iso} is derived from U_{iso} of the bonded atom plus 0.01.

Table XR-4

Bond Distances in Angstroms

Bond	Bond Distance		Bond	Bond Distance
O(2) - C(2)	1.215(9)		O(2A) - C(2A)	1.220(8)
O(4) - C(4)	1.226(9)		O(4A) - C(4A)	1.210(9)
O(2') - C(3')	1.415(8)		O(2A') - C(3A')	1.418(8)
O(2') - C(1')	1.424(9)		O(2A') - C(1A')	1.416(9)
O(4') - C(4')	1.420(9)		O(4A') - C(4A')	1.426(9)
O(7') - C(1')	1.423(9)		O(7A') - C(1A')	1.436(8)
O(7') - C(6')	1.480(9)		O(7A') - C(6A')	1.457(8)
O(6") - C(6")	1.386(11)		O(6A") - C(6A")	1.414(9)
N(1) - C(2)	1.385(9)		N(1A) - C(2A)	1 383(9)
N(1) - C(6)	1.390(9)		N(1A) - C(6A)	1.392(8)
N(1) - C(3')	1.493(9)		N(1A) - C(3A')	1.494(9)
N(3) - C(2)	1.370(10)		N(3A) - C(2A)	1.364(9)
N(3) - C(4)	1.375(9)		N(3A) - C(4A)	1.388(9)
C(4) - C(5)	1.463(10)		C(4A) - C(5A)	1.440(11)
C(5) - C(5Me)	1.500(11)		C(5A) - C(5MeA)	1.500(10)
C(5) - C(6)	1.358(11)		C(5A) - C(6A)	1.330(11)
C(3') - C(4')	1.529(10)		C(3A') - C(4A')	1.540(10)
C(4') - C(5')	1.513(10)		C(4A') - C(5A')	1.520(10)
C(5') - C(1')	1.540(10)		C(5A') - C(1A')	1.524(10)
C(5') - C(6')	1.545(11)		C(5A') - C(6A')	1.528(10)
C(6') - C(6")	1.494(11)		C(6A') - C(6A")	1.490(10)

Table XR-5

Bond Angles in Degrees

Bond	Bond Angle		Bond	Bond Angle
C(3') - O(2') - C(1')	111.0(5)		C(3A') - O(2A') - C(1A')	110.5(5)
C(1') - O(7') - C(6')	91.8(5)		C(1A') - O(7A') - C(6A')	91.7(5)
C(2) -N(1) - C(6)	121.1(6)		C(2A) - N(1A) - C(6A)	120.0(6)
C(2) - N(1) - C(3')	114.9(6)		C(2A) - N(1A) - C(3A')	114.1(5)
C(6) - N(1) - C(3')	123.6(5)		C(6A) - N(1A) - C(3A')	125.6(6)
C(2) - N(3) - C(4)	128.4(6)		C(2A) - N(3A) - C(4A)	127.8(6)
O(2) - C(2) - N(1)	122.2(7)		O(2A) - C(2A) - N(1A)	122.1(6)
O(2) - C(2) - N(3)	123.5(6)		O(2A) - C(2A) - N(3A)	123.1(6)
N(1) - C(2) - N(3)	114.3(6)		N(1A) - C(2A) - N(3A)	114.8(6)
O(4) - C(4) - N(3)	122.3(6)		O(4A) - C(4A) - N(3A)	120.4(7)
O(4) - C(4) - C(5)	122.4(7)		O(4A) - C(4A) - C(5A)	124.8(7)
N(3) - C(4) - C(5)	115.2(6)		N(3A) - C(4A) - C(5A)	114.7(6)
C(4) - C(5) - C(5Me)	120.8(7)		C(4A) - C(5A) - C(5MeA)	120.1(7)
C(4) - C(5) - C(6)	117.0(7)		C(4A) - C(5A) - C(6A)	118.3(6)
C(5Me) - C(5) - C(6)	122.2(6)		C(5MeA) - C(5A) - C(6A)	121.7(7)
N(1) - C(6) - C(5)	123.8(6)		N(1A) - C(6A) - C(5A)	124.4(7)
O(2') - C(3') - N(1)	110.3(5)		O(2A') - C(3A') - N(1A)	109.7(5)
O(2') - C(3') - C(4')	106.1(6)		O(2A') - C(3A') - C(4A')	106.6(6)
N(1) - C(3') - C(4')	112.3(6)		N(1A) - C(3A') - C(4A')	113.3(6)
O(4') - C(4') - C(3')	106.3(6)		O(4A') - C(4A') - C(3A')	107.3(6)
O(4') - C(4') - C(5')	112.3(6)		O(4A') - C(4A') - C(5A')	108.2(6)
C(3') - C(4') - C(5')	105.3(6)		C(3A') - C(4A') - C(5A')	105.2(5)
C(4') - C(5') - C(1')	104.9(6)		C(4A') - C(5A') - C(1A')	104.8(6)
C(4') - C(5') - C(6')	116.8(6)		C(4A') - C(5A') - C(6A')	118.8(6)
C(1') - C(5') - C(6')	85.0(5)		C(1A') - C(5A') - C(6A')	85.7(5)
O(2') - C(1') - O(7')	113.9(6)		O(2A') - C(1A') - O(7A')	113.3(5)
O(2') - C(1') - C(5')	107.2(5)		O(2A') - C(1A') - C(5A')	108.8(5)
O(7') - C(1') - C(5')	92.8(5)		O(7A') - C(1A') - C(5A')	91.5(5)
O(7') - C(6') - C(5')	90.4(5)		O(7A') - C(6A') - C(5A')	90.6(5)
O(7') - C(6') - C(6'')	112.3(6)		O(7A') - C(6A') - C(6A'')	112.3(6)
C(5') - C(6') - C(6'')	119.9(7)		C(5A') - C(6A') - C(6A'')	115.4(6)
O(6'') - C(6'') - C(6')	110.9(7)		O(6A'') - C(6A'') - C(6A')	111.5(6)

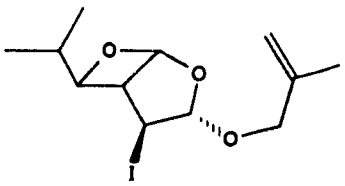
Table XR-6

Torsion Angles in Degrees

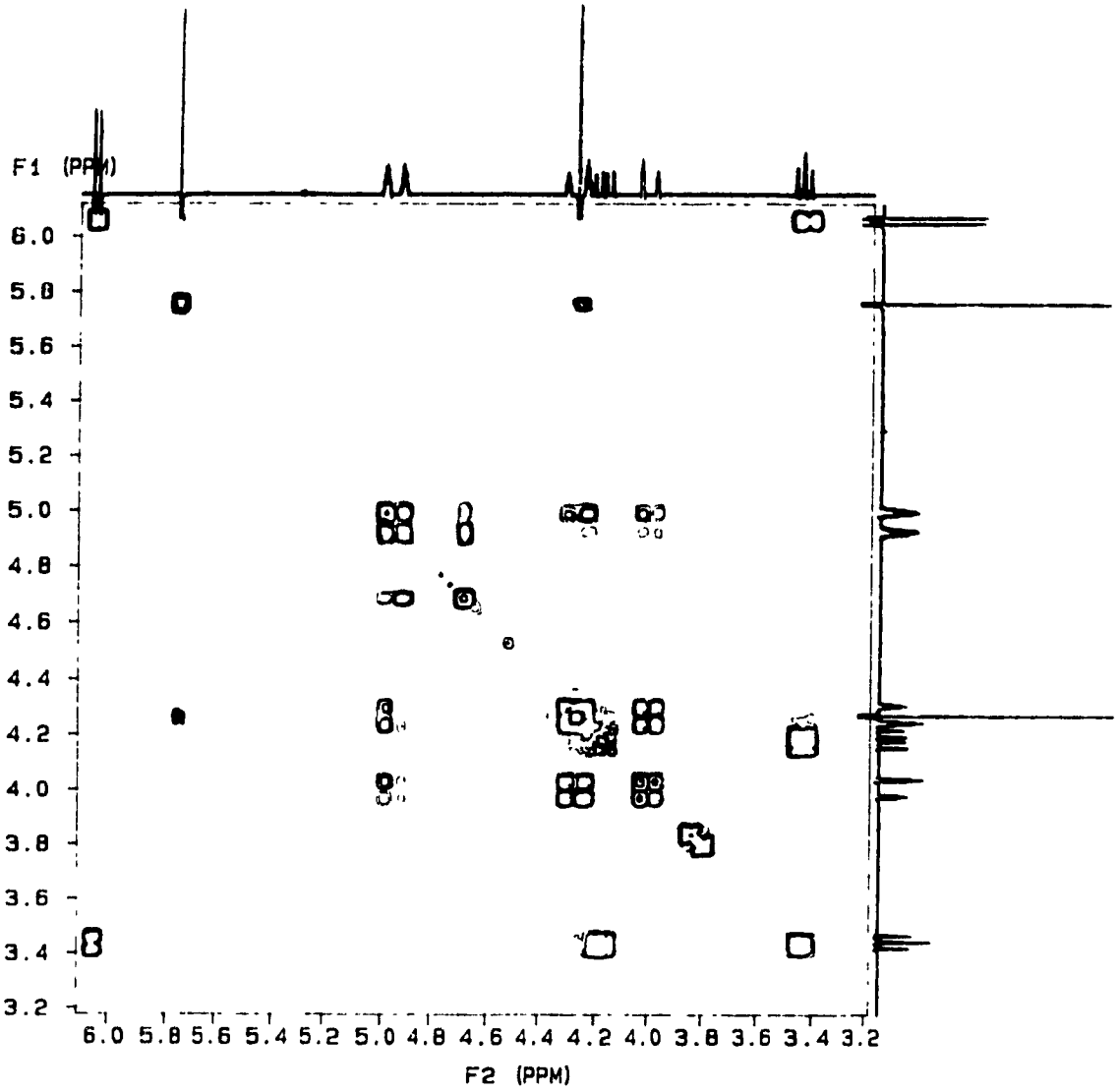
Bond	Torsion Angle	Bond	Torsion Angle
C1' - O2' - C3' - N1	98.4(5)	C1' - O2' - C3' - C4'	-23.4(4)
C3' - O2' - C1' - O7'	-86.6(5)	C3' - O2' - C1' - C5'	14.5(4)
C6' - O7' - C1' - O2'	110.1(6)	C6' - O7' - C1' - C5'	-0.2(4)
C1' - O7' - C6' - C5'	0.2(3)	C1' - O7' - C6' - C6"	123.0(7)
C6 - N1 - C2 - O2	174.5(8)	C6 - N1 - C2 - N3	-3.6(3)
C3' - N1 - C2 - O2	0.8(3)	C3' - N1 - C2 - N3	-177.3(7)
C2 - N1 - C6 - C5	2.1(4)	C3' - N1 - C6 - C5	175.2(7)
C2 - N1 - C3' - O2'	171.7(7)	C2 - N1 - C3' - C4'	-70.2(5)
C6 - N1 - C3' - O2'	-1.8(3)	C6 - N1 - C3' - C4'	116.3(6)
C4 - N3 - C2 - O2	-177.3(8)	C4 - N3 - C2 - N1	0.7(3)
C2 - N3 - C4 - O4	-178.4(8)	C2 - N3 - C4 - C5	3.4(4)
O4 - C4 - C5 - C5Me	-5.1(3)	O4 - C4 - C5 - C6	177.1(9)
N3 - C4 - C5 - C5Me	173.0(8)	N3 - C4 - C5 - C6	-4 8(3)
C4 - C5 - C6 - N1	2.3(3)	C5Me - C5 - C6 - N1	-175.4(8)
O2' - C3' - C4' - O4'	-96.7(6)	O2' - C3' - C4' - C5'	22.6(3)
N1 - C3' - C4' - O4'	142.8(7)	N1 - C3' - C4' - C5'	-97.9(6)
O4' - C4' - C5' - C1'	101.5(6)	O4' - C4' - C5' - C6'	-166.6(7)
C3' - C4' - C5' - C1'	-13.8(3)	C3' - C4' - C5' - C6'	78.1(5)
C4' - C5' - C1' - O2'	0.5(3)	C4' - C5' - C1' - O7'	116.6(7)
C6' - C5' - C1' - O2'	-115.9(7)	C6' - C5' - C1' - O7'	0.2(3)
C4' - C5' - C6' - O7'	-104.4(6)	C4' - C5' - C6' - C6"	139.3(8)
C1' - C5' - C6' - O7'	-0.2(3)	C1' - C5' - C6' - C6"	-116.4(7)
O7' - C6' - C6" - O6"	-63.9(5)	C5' - C6' - C6" - O6"	40.3(4)
C1A' - O2A' - C3A' - N1A	-102.4(5)	C1A' - O2A' - C3A' - C4A'	20.7(4)
C3A' - O2A' - C1A' - O7A'	85.6(5)	C3A' - O2A' - C1A' - C5A'	-14.6(3)
C6A' - O7A' - C1A' - O2A'	-117.1(6)	C6A' - O7A' - C1A' - C5A'	-5.8(3)
C1A' - O7A' - C6A' - C5A'	5.8(3)	C1A' - O7A' - C6A' - C6A"	-112.1(6)
C6A - N1A - C2A - O2A	179.8(7)	C6A - N1A - C2A - N3A	-1.1(3)
C3A' - N1A - C2A - O2A	-6.4(3)	C3A' - N1A - C2A - N3A	172 6(7)
C2A - N1A - C6A - C5A	0.0(4)	C3A' - N1A - C6A - C5A	-173 0(7)
C2A - N1A - C3A' - O2A'	-165.8(7)	C2A - N1A - C3A' - C4A'	75.1(5)
C6A - N1A - C3A' - O2A'	7.6(3)	C6A - N1A - C3A' - C4A'	-111.5(6)
C4A - N3A - C2A - O2A	-179.0(8)	C4A - N3A - C2A - N1A	2.0(3)
C2A - N3A - C4A - O4A	-179.9(8)	C2A - N3A - C4A - C5A	-1.5(4)
O4A - C4A - C5A - C5MeA	-1.5(4)	O4A - C4A - C5A - C6A	178.6(9)
N3A - C4A - C5A - C5MeA	-179.9(8)	N3A - C4A - C5A - C6A	0.2(3)
C 4A C 5A C 6A N 1A	0.4(3)	C5MeA - C5A - C6A - N1A	-179.5(8)
O2A' - C3A' - C4A' - O4A'	96.7(6)	O2A' - C3A' - C4A' - C5A'	-18.4(3)
N1A - C3A' - C4A' - O4A'	-142.4(7)	N1A - C3A' - C4A' - C5A'	102.5(6)
O4A' - C4A' - C5A' - C1A'	-104.9(6)	O4A' - C4A' - C5A' - C6A'	161.9(7)
C3A' - C4A' - C5A' - C1A'	9.6(3)	C3A' - C4A' - C5A' - C 6A'	-83.6(5)
C4A' - C5A' - C1A' - O2A'	2.2(3)	C4A' - C5A' - C1A' - O7A'	-113 1(6)
C6A' - C5A' - C1A' - O2A'	120.8(6)	C6A' - C5A' - C1A' - O 7A'	5.6(3)
C4A' - C5A' - C6A' - O7A'	99.0(6)	C4A' - C5A' - C6A' - C6A"	-145.8(7)
C1A' - C5A' - C6A' - O7A'	-5.5(3)	C1A' - C5A' - C6A' - C6A"	109.7(6)
O7A' - C6A' - C6A" - O6A"	54.2(4)	C5A' - C6A' - C6A" - O6A"	-47.8(4)

APPENDIX IV. 2-D NMR Spectra.

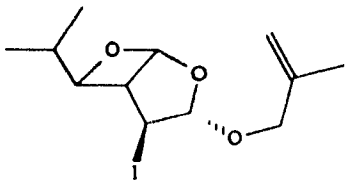
1. The 200 MHz COSY spectrum of acetal **10h**.



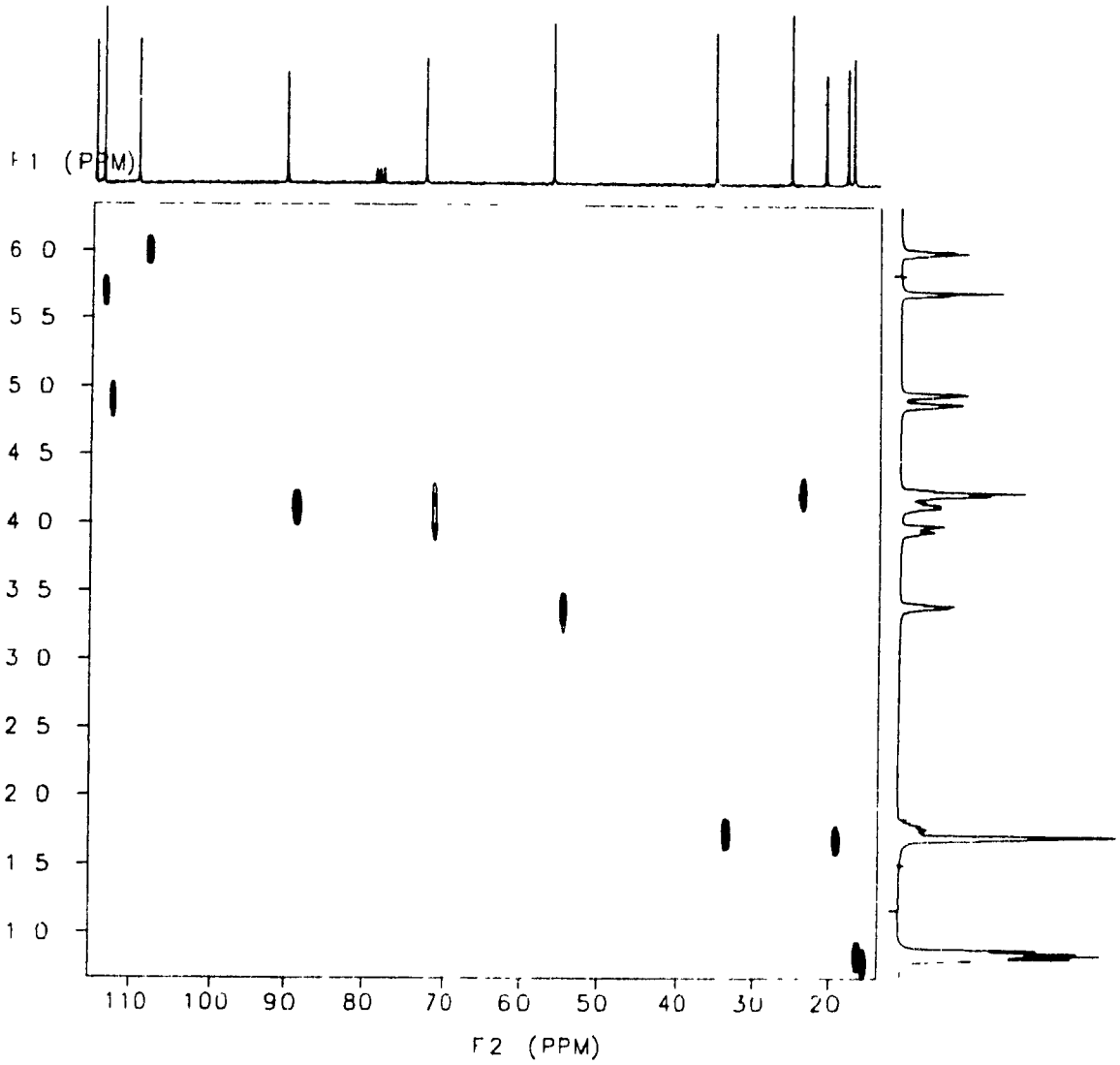
10h



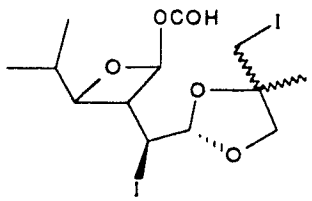
2. The 300 MHz HETCOR spectrum of acetal **10h**.



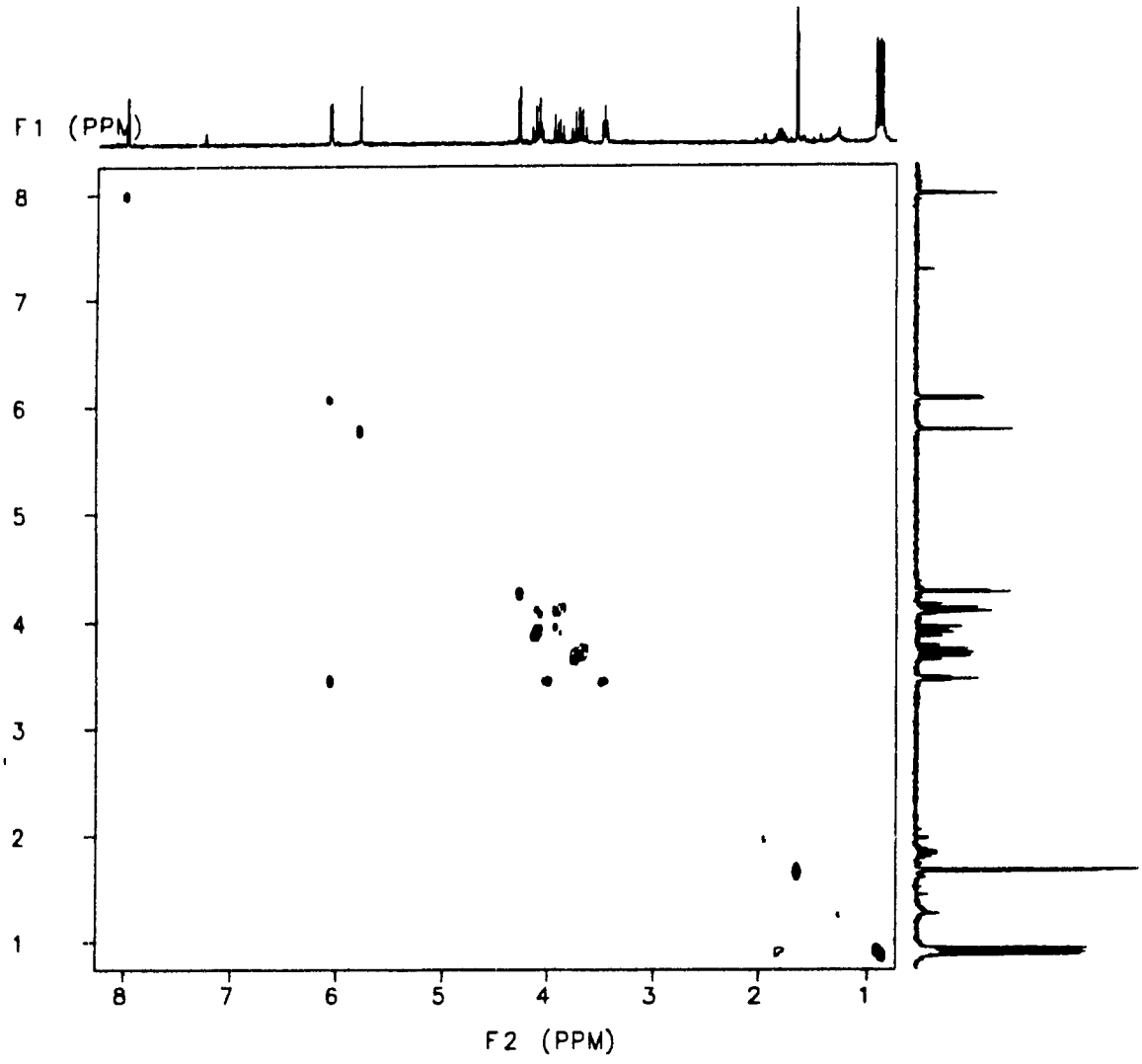
10h



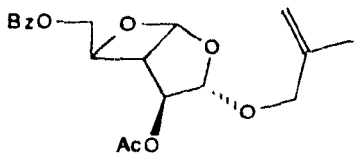
3. The 300 MHz COSY spectrum of oxetane **18e**.



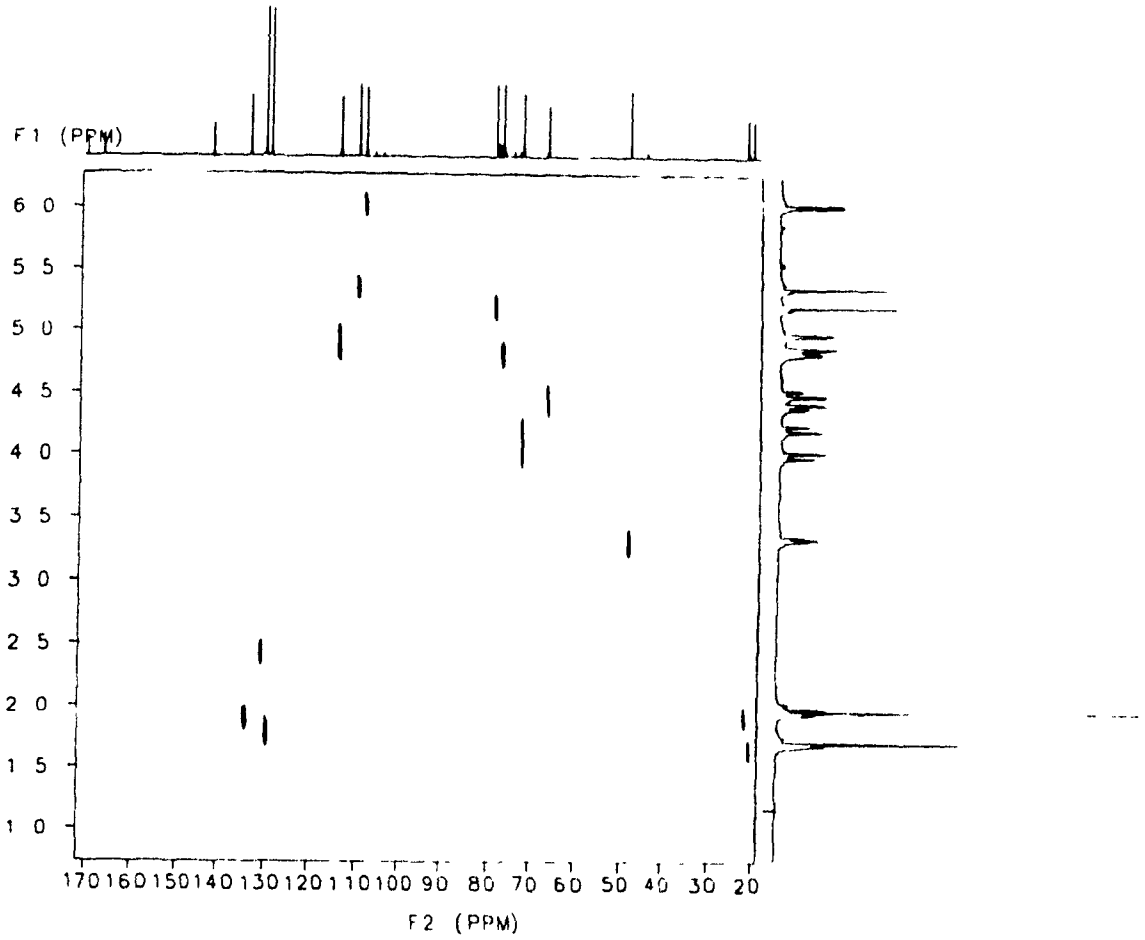
18e



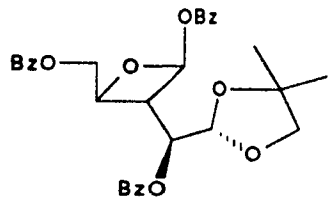
4. The 300 MHz HETCOR spectrum of acetal **29a**.



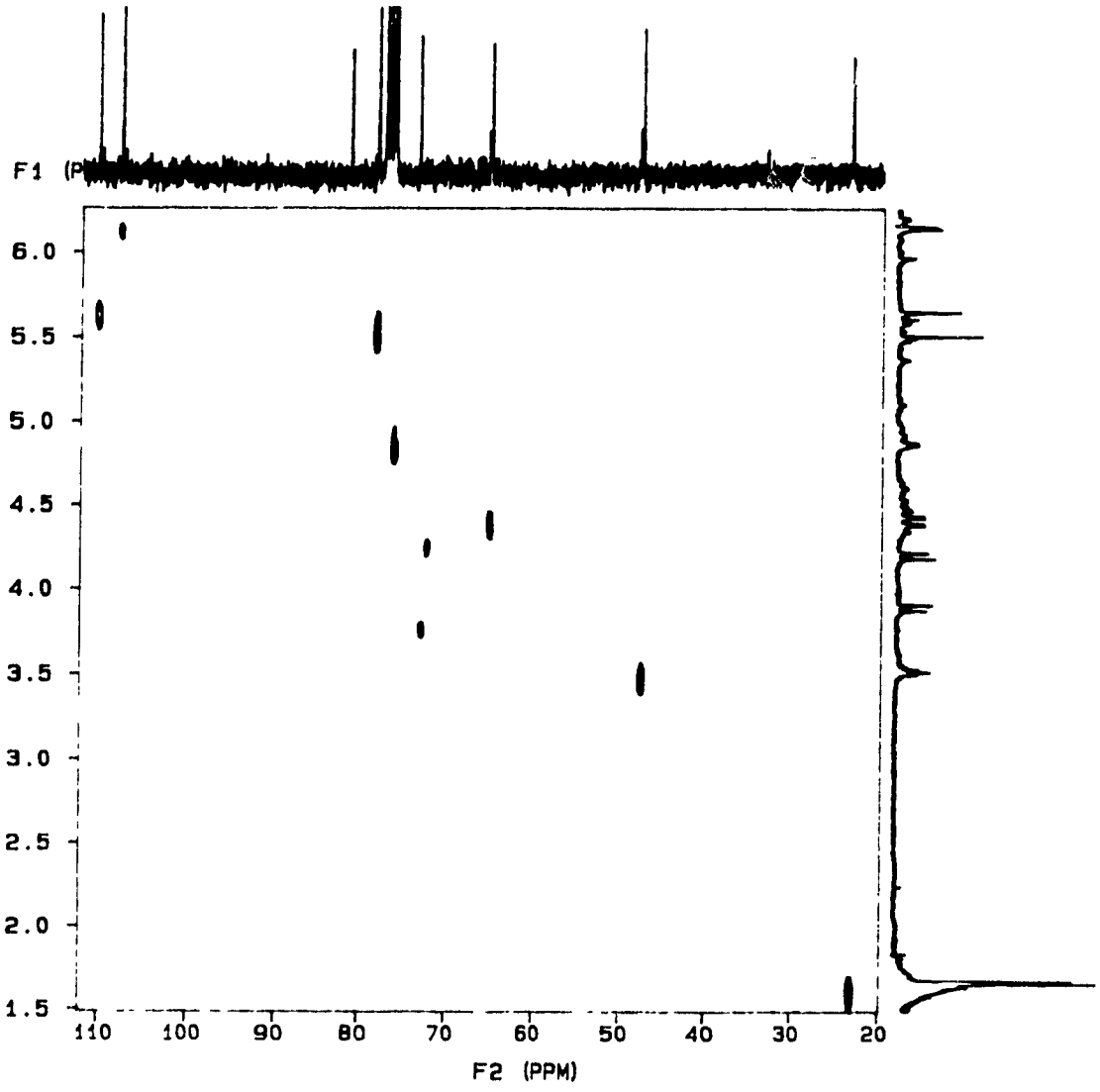
29a



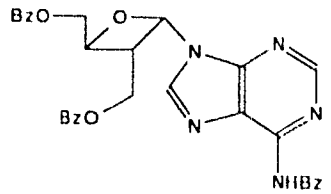
5. The 300 MHz HETCOR spectrum of oxetane **33**.



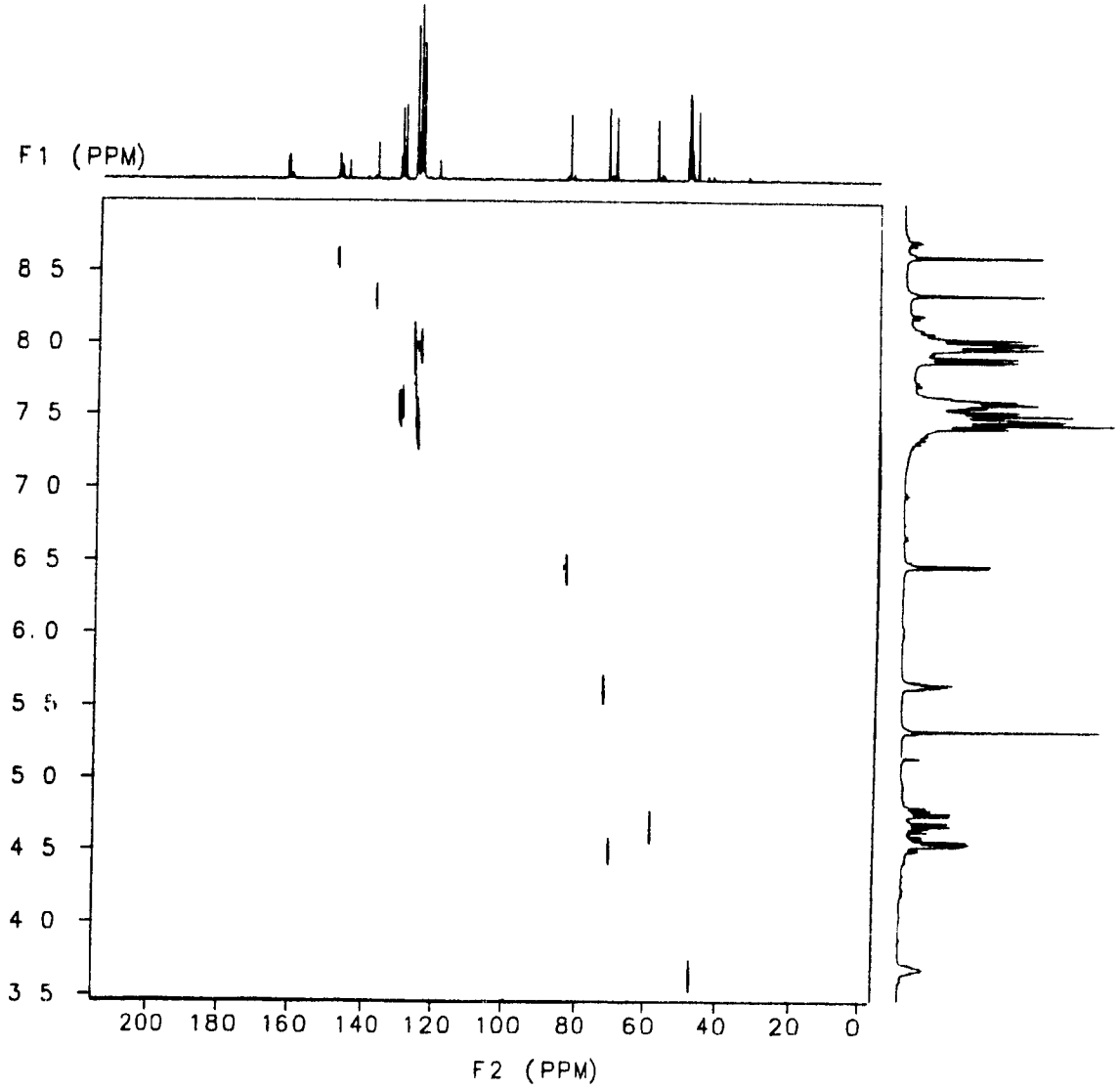
33



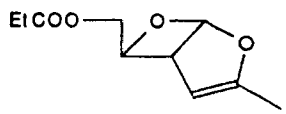
6. The 300 MHz HETCOR spectrum of tribenzoate **48b**.



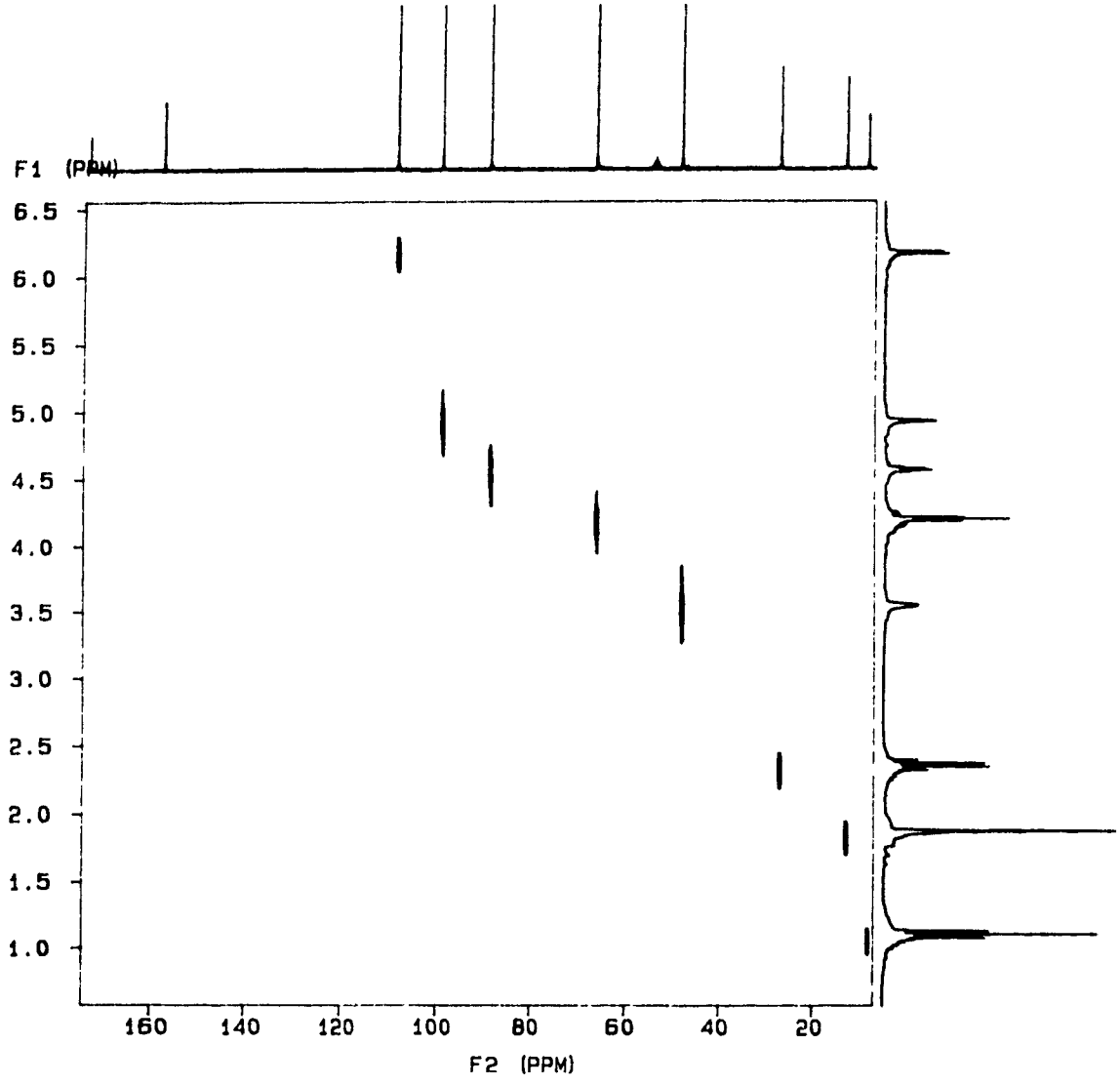
48b



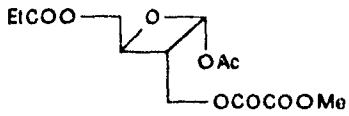
7. The 300 MHz HETCOR spectrum of photo-adduct **72a**.



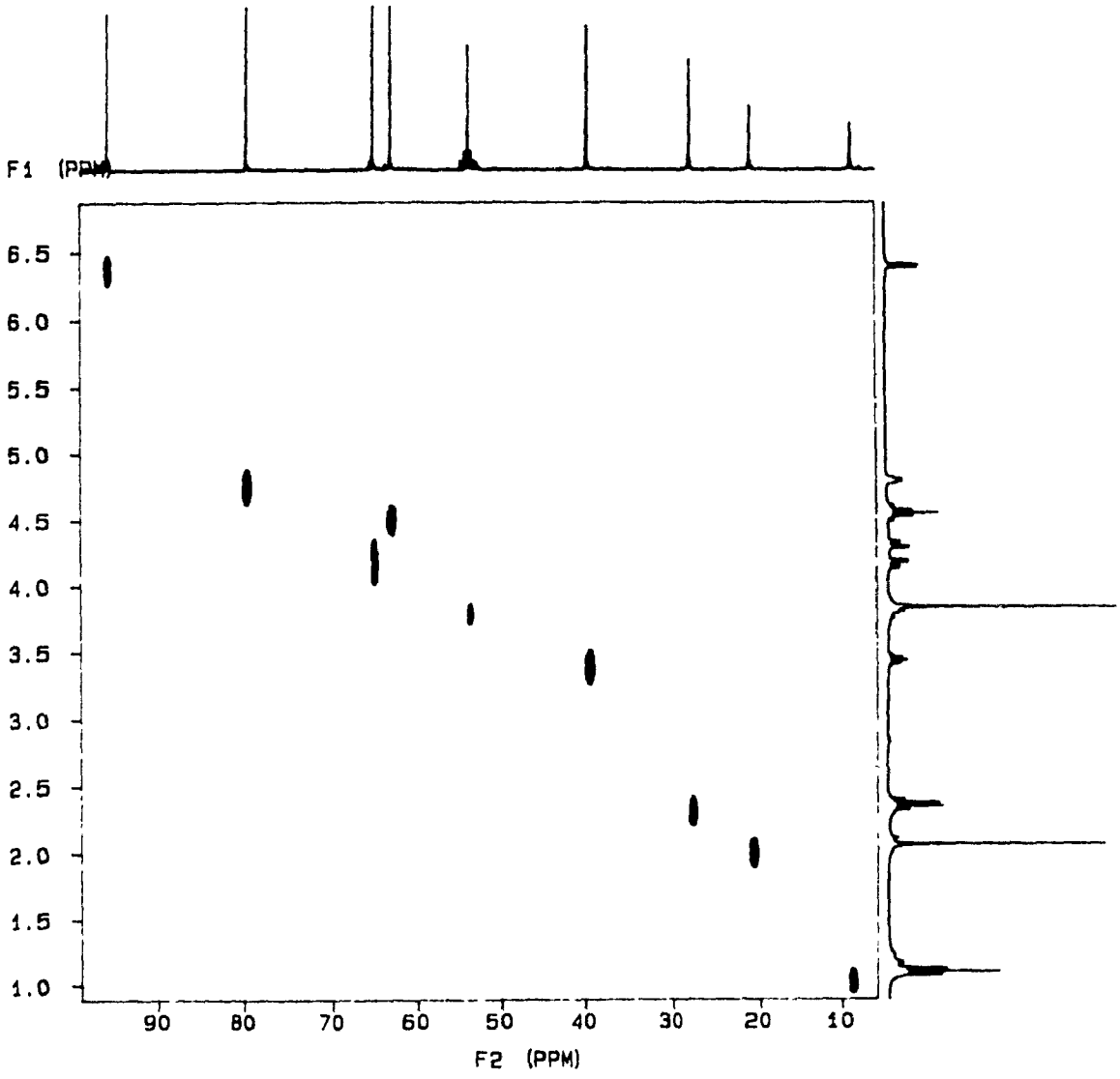
72a



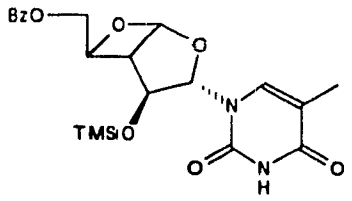
8. The 300 MHz HETCOR spectrum of oxetane **75a**.



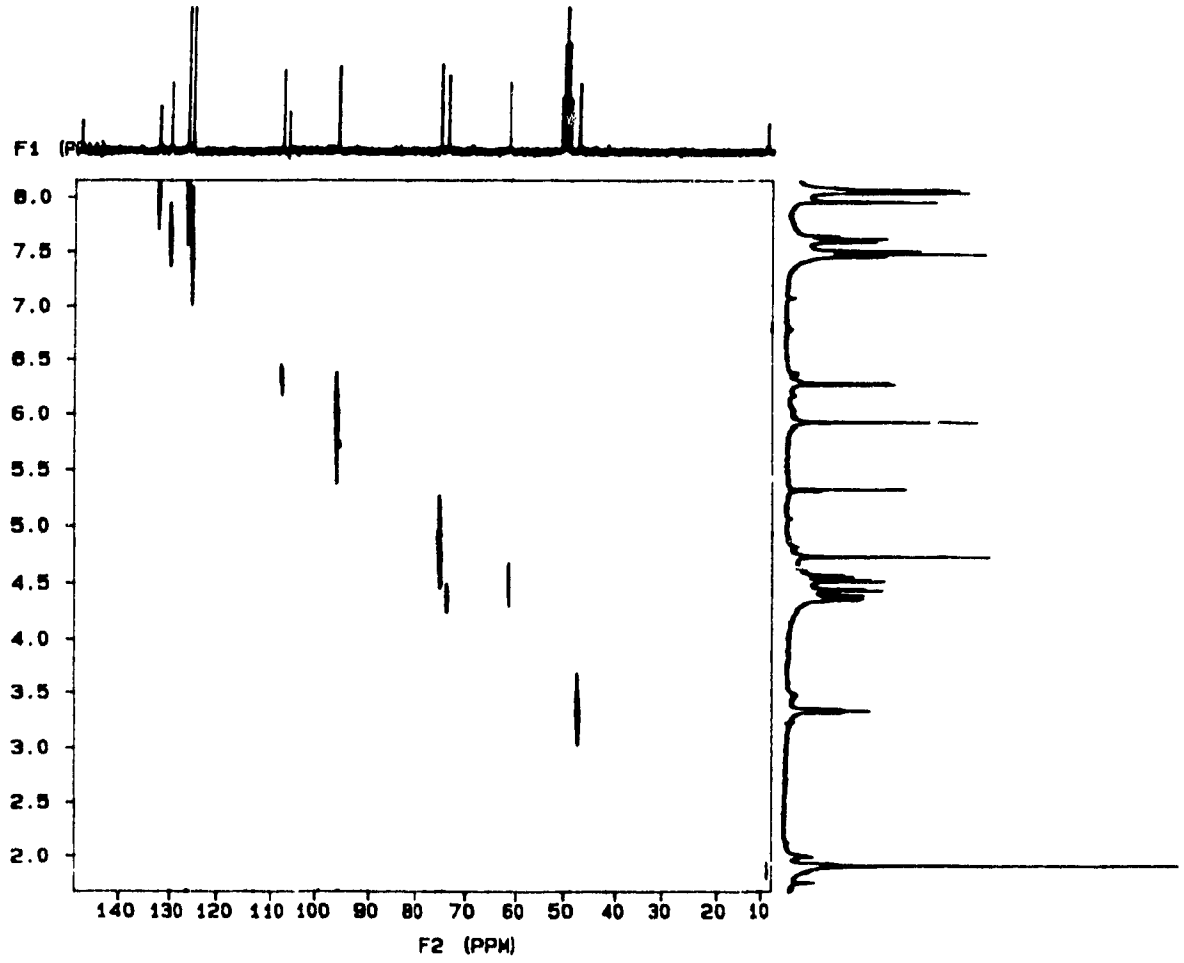
75a



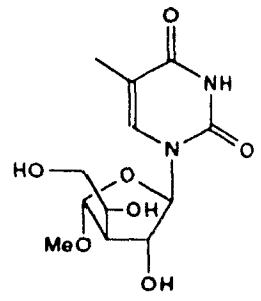
9. The 300 MHz HETCOR spectrum of bicyclic nucleoside **89a**.



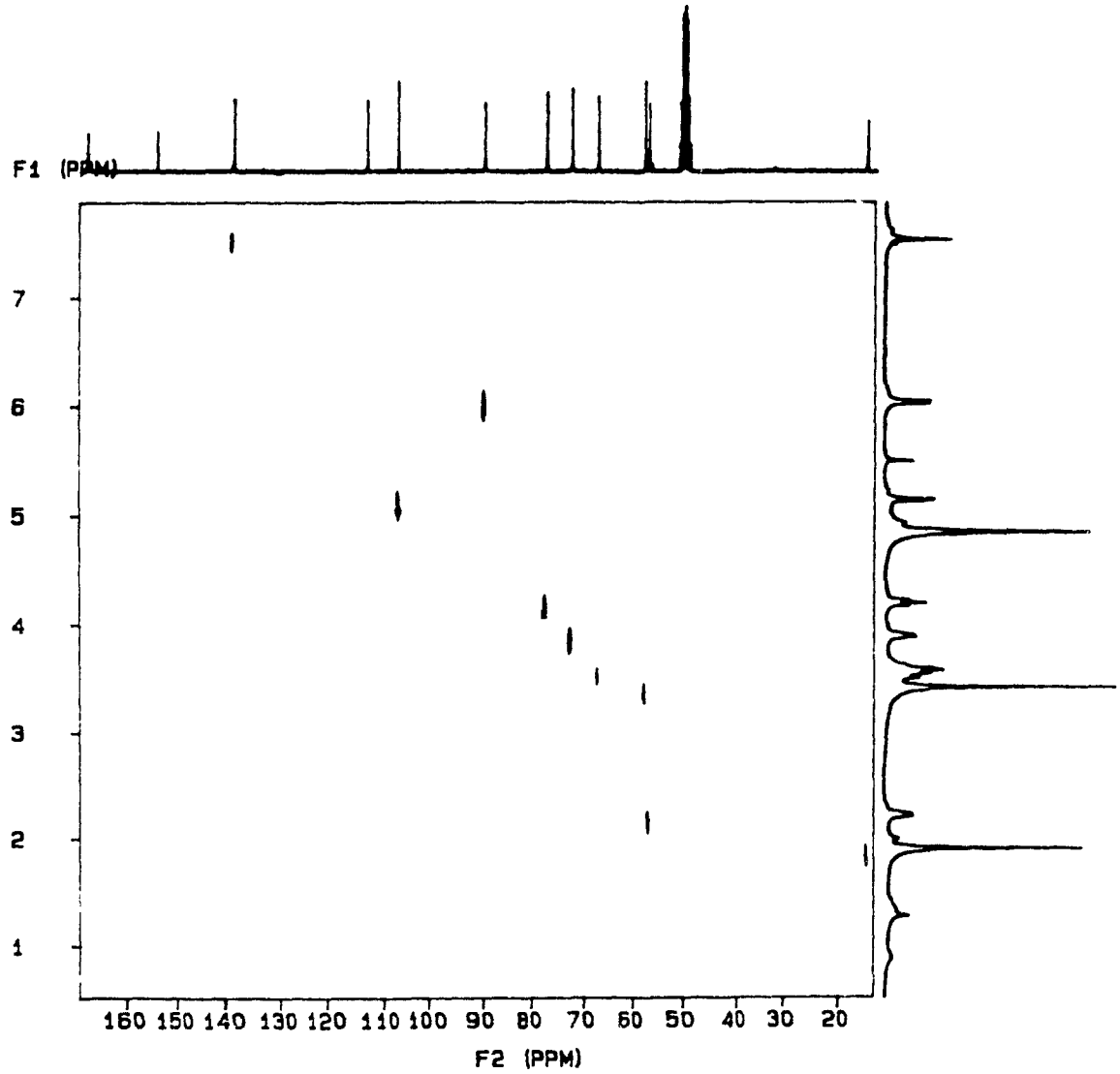
89a



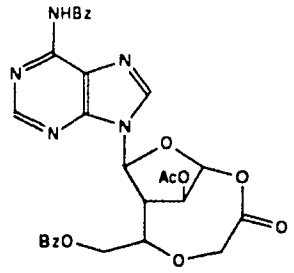
10. The 300 MHz HETCOR spectrum of nucleoside **93***.



93*



11. The 300 MHz HETCOR spectrum of bicyclic nucleoside **99b**.



99b