

TETRACHLOROPHTHALIMIDE
AS A REAGENT

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TETRACHLOROPHTHALIMIDE
AS A REAGENT IN QUALITATIVE ORGANIC ANALYSIS.

A Thesis

by

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Table of Contents.

Historical Introduction.

Physico-chemical methods.	1
Quaternary ammonium compounds	1
Solid Esters.	1
Substituted phthalimides.	1
Alkylmercuric halides	2
Anilides.	2
α -Naphthalides.	2
p-Toluides.	3
p-Bromobenzenesulphon-p-anisides.	3
3-Nitrophthalimides	5

Outline of the Work.

Limits of the method.	7
Anomalous results	8
Preparation of the analytical reagent	9

Experimental.

Preparation of tetrachlorophthalimide	11
Preparation of potassium tetrachlorophthalimide . .	12
Preparation of sodium tetrachlorophthalimide	
a. Dioxane method	13
b. Liquid ammonia method.	14
Preparation of derivatives.	15
Table of derivatives.	17
Summary.	18
Bibliography	19

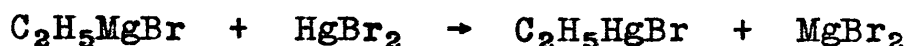
Historical Introduction.

The qualitative identification of organic halogen compounds has always been a matter of difficulty. For many years the only method was dependent upon the physical constants of the compound, such as melting and boiling point, refractive index, and density, in combination with a quantitative estimation of the halogen. There were, however, a number of reactions that gave solid derivatives having characteristics which made them more or less suitable as a means of identification. The most valuable of these have been (a) the formation of quaternary ammonium compounds with readily accessible tertiary amines such as dimethylaniline and pyridine, (b) the preparation of solid esters with the salt of a selected acid, (c) the preparation of substituted phthalimides. None of these, however, has been systematically investigated with regard to their suitability for halogen compounds in general.

The last decade has seen an awakening interest in qualitative organic analysis and the work of a large number of investigators has resulted in the establishing of satisfactory methods for identifying members of most classes of compounds. The following new methods for the identification of alkyl halides have been described.

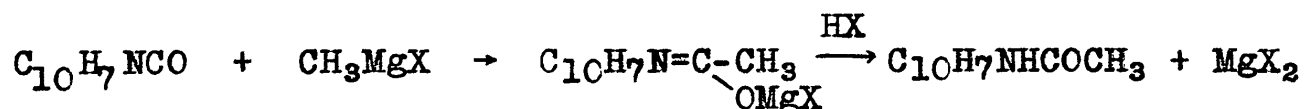
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Marvel, Gauerke and Hill (1) noticed that aliphatic Grignard reagents formed alkyl mercuric halides by interaction with the corresponding mercuric halides -



These substances are solids having sharp melting points and the yields are good, accordingly they are useful substances for identification. The bromides are purified with ease; the iodides with some difficulty. Alkyl chlorides cannot be differentiated by this method since they do not give Grignard reagents easily. Hill (2) has extended this method so as to include certain alkyl and aryl bromides and iodides which react in an analogous manner.

Gilman and Furry (3) have considered the relative merits of phenyl isocyanate and α -naphthyl isocyanate for the formation of solid derivatives, (substituted amides), with organomagnesium halides and conclude that the latter is superior because the products obtained by its use are less soluble, more easily crystallized, and of higher melting point.

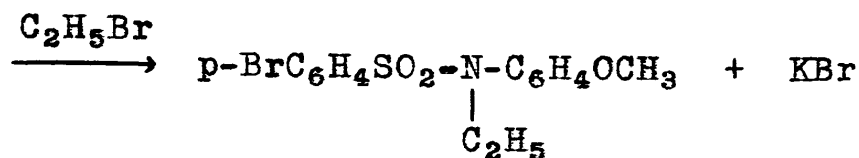


The authors suggested the use of this reaction for the identification of alkyl and aryl halides.

Schwartz and Johnson (4) agreed with Gilman and Furry that α -naphthyl isocyanate has an advantage over the phenyl compound in that the resulting amides could be purified more easily but they noticed that the anilides could be made equally useful if an excess of the isocyanate was avoided. They drew attention to another matter of importance, that more information is available in the literature concerning the phenyl derivatives.

Since the publication of the research covered in this thesis in the Journal of the American Chemical Society (5), two papers have appeared treating with the identification of alkyl halides, Underwood and Gale (6) prepared a number of p-toluides and α -naphthalides from a series of Grignard reagents. This is the same reaction as was first used by Gilman and Furry. They found that p-toluides satisfactorily distinguished between iso- and sec-butyl chlorides and, in their opinion, these might well replace the anilides. Derivatives for amyl chlorides might be anilides or p-toluides according to the individual case; α -naphthalides were unsatisfactory because of the apparent difficulty in their purification.

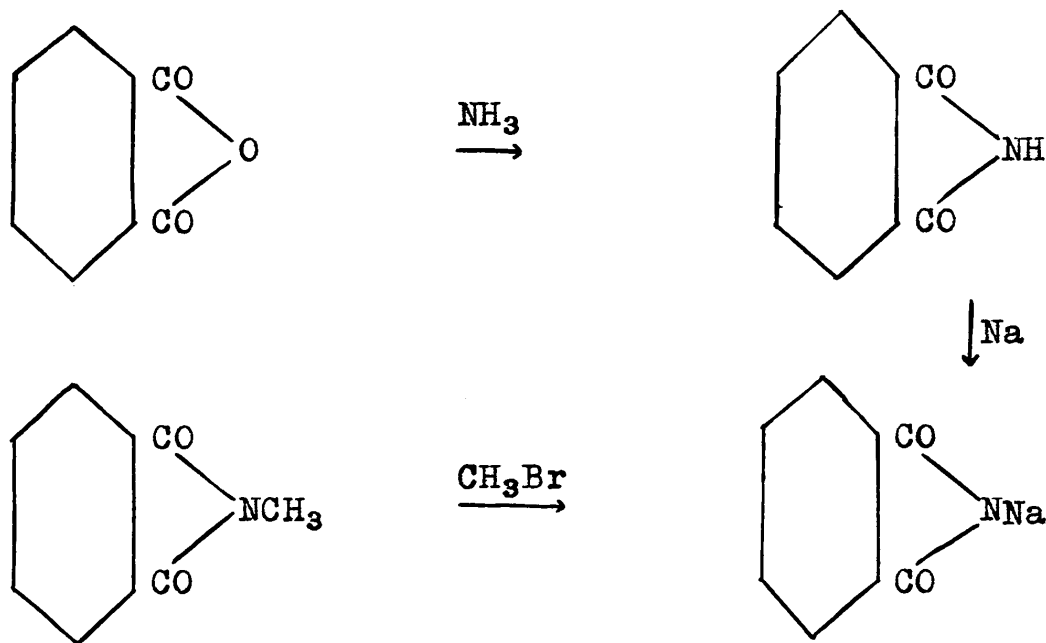
Gillespie (7) has recommended the preparation of N-substituted p-bromobenzenesulphon-p-anisides by refluxing the alkyl halides with alcoholic potash solution for one hour.



The melting points of the simple alkyl derivatives studied were nearly all below 100° C. However, the starting material was easily purified, the time of reaction was short, and the derivatives appear to be purified with ease.

All the above methods except the last involve the preparation of a Grignard reagent as an intermediate and are limited therefore to the identification of alkyl halides as a class; of the latter the following types do not react in a suitable manner - simple alkyl chlorides, tertiary alkyl halides, and aralkyl iodides.

The Gabriel phthalimide reaction has no known limits (8), and has been widely used in synthetic chemistry. The steps in the reaction are given below in generalized form.



However it has never been applied systematically to qualitative organic analysis. Indeed, it has certain characteristics which would apparently make it unsuitable for that purpose,-thus the reaction of the alkali salt and the halide usually requires a sealed tube and prolonged heating.

Sah and Ma (9) have suggested the use of 3-nitrophthalimide, since the compounds so obtained have, in their opinion, satisfactory melting points for use as derivatives and in addition the procedure did not involve the use of a sealed tube.

Outline of the Work.

Tetrachlorophthalimide was chosen for study in the present research because (a) by analogy it would appear that its N-substituted derivatives should have melting points even more satisfactory, (i.e. higher), than those of its 3-nitro homologue, (b) the tetrachlorophthalimides should be less soluble than the phthalimides, hence the yields would be better, (c) the method might be extended to include halogen compounds other than simple alkyl halides, and (d) the starting material is much cheaper than that from which the 3-nitro reagent is prepared.

Table I shows how well the theoretical predictions concerning melting points, mentioned above, have been fulfilled.

Table I.

N-substituted Phthalimides.

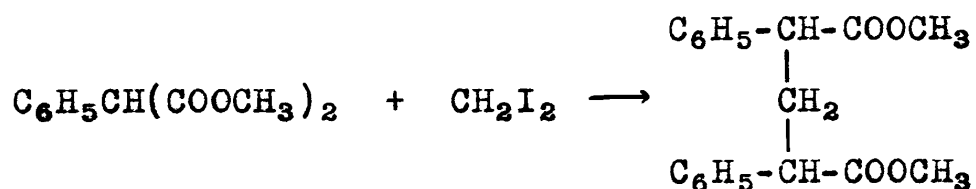
Substituent	Melting Points, °C.	
	3-nitro derivative	Tetrachloro derivative
-CH ₃	112-3	210-11
-C ₂ H ₅	105-6	192-3
-n-C ₄ H ₉	84-5	153-4
-n-C ₅ H ₁₁	71-2	145-6
-i-C ₅ H ₁₁	93-4	170-1
-CH ₂ COOC ₂ H ₅	79-80	180-1

We have found, as Sah and Ma did with the 3-nitro compounds, that the tetrachlorophthalimides are satisfactory derivatives for the identification of alkyl halides and straight chain halogen esters. In addition the method has now been extended to include the high-melting chloroformates, the halohydrins, the halo ketones, and the halo ethers.

In certain instances our method has the disadvantage that it necessitates the use of a sealed tube. Thus it can be taken as a rule that a sealed tube will be required with all halogen compounds having boiling points below 140° C. Examples of such substances are the low-boiling alkyl halides. This, however, is not a serious defect since these particular substances can be conveniently identified by other methods.

It was found that the reagent did not react with such chlorine compounds as were investigated. It did not react with the α -bromo derivatives of ethyl isobutyrate and isovalerate, nor with ethyl β -chloropropionate. There does not appear to be any satisfactory explanation for this unexpected lack of reactivity. Indeed, Hale and Britton (10) obtained a 70% yield of an imide by refluxing potassium phthalimide and isoamyl β -chloropropionate for an hour. With the low-boiling chloroformates no reaction occurred at the boiling point even on prolonged refluxing and when attempts were made to force the reaction by means of a sealed tube, explosions invariably resulted.

The following anomalous results are worthy of notice. Under the standardized conditions of procedure γ -chlorobutyrophenone yielded benzoylcyclopropane, the reagent acting to remove the elements of hydrogen chloride and close a ring. This is in accord with the research carried out by Dr. Raymond Boyer in this laboratory (11), in which it was shown that any alkaline reagent brought about the same result. Ethyl bromomalonate lost one carboethoxy group and gave a derivative identical with that from ethyl chloroacetate. This is a result comparable with the findings of Souther (12) who condensed methyl phenylmalonate with diiodomethane and prepared methyl α,γ -diphenylglutarate,



and of Carothers (13), who found that bromophenyldicarbomethoxymethane on treatment with sodium methylate gave a methyl ether of methyl mandelate by loss of methyl carbonate.



Bromotricarbomethoxymethane on reaction with the imide lost

all three of its carbomethoxy groups and gave the N-methyl imide. It is interesting to compare this with the work of Carothers (13) who has noticed that this compound reacts with sodium methylate as an aromatic halide and is extremely inactive. Epichlorohydrin and β -bromostyrene gave intractable gums.

β -Chloropropiophenone reacted normally, as would be expected from the work of Hale and Britton (10) who prepared β -aminopropiophenone by means of the Gabriel phthalimide reaction.

There are several satisfactory methods for the preparation of the analytical reagent. In our opinion the best results were obtained by carrying out the reaction in two steps, (a) the preparation of tetrachlorophthalimide and (b) the preparation of the potassium salt..

The first reaction is accomplished by heating together in the dry state equimolecular portions of tetrachlorophthalic anhydride and ammonium carbonate. The preparation of phthalimide has been extensively studied by Chao-sun Tsing (15). He has investigated various methods and found that there was little to choose between them. Noyes and Porter (14) recommended aqueous ammonia, or ammonium carbonate.

Reaction (b) is carried out by dissolving the imide in commercial dioxane and adding the appropriate amount of

potassium hydroxide in methyl alcohol.

Before it was determined that the potassium salt was more suitable than the sodium salt and, therefore, the preferable preparative reagent, the sodium salt was used in reaction with the halogen compounds. It was synthesized by two methods, (a) by interaction of the imide with metallic sodium in purified dioxane, and (b) from tetrachlorophthalic anhydride in one step by the addition of metallic sodium to a solution in liquid ammonia. The disadvantages of the first method are that it is a surface reaction and, therefore, sluggish, and a preliminary purification of the dioxane must be carried out by refluxing over sodium. The disadvantage of the second - other than the use of sodium - is that an uncommon type of apparatus is required, and the liquid ammonia must be permitted to evaporate and is wasted.

As for the minimum amount of halogen compound which can be used to prepare a derivative, it has been determined that for compounds boiling above 170° C., 1.5 g. will be required, for all others 5 g.

E x p e r i m e n t a l.Preparation of Tetrachlorophthalimide.

Thirty grams of technical tetrachlorophthalic anhydride (★) and 11 g. of ammonium carbonate were intimately mixed by grinding in a mortar. This mixture was carefully heated in a 400 cc. Pyrex beaker covered by a perforated watch-glass, or a cardboard through which passed a stirring-rod. As the heating proceeded a little water vapour was given off, then the mass became plastic, even melting in a few parts; the lumps were broken up as much as possible. After fifteen minutes of heating, the mass had become crystalline throughout, some imide had sublimed and the color had changed from fawn to a greyish-yellow. The crude product weighed 29 g., (yield 97%).

After cooling, the mass was broken up and dissolved in 150 cc. of boiling nitrobenzene, the insoluble material allowed to settle, the supernatant solution decanted and allowed to cool. The crystalline material which separated was washed with a little nitrobenzene and then with ether to free it from occluded solvent. The product so prepared was

(★) This substance was donated by the National Aniline and Chemical Co. The gift is gratefully acknowledged.

greyish-yellow in colour and weighed 27 g., (yield 91%).

Anal. Calcd. for $C_8H_2O_2NCl_4$: N, 4.9; Cl, 49.8. Found: N, 5.1, 5.1; Cl, 49.7.

The material insoluble in nitrobenzene weighed approximately 1 g. About 1 g. of material, mostly imide, was retained in the nitrobenzene, but it was not lost for the same portion of solvent could be used with the next preparation.

The phthalimide could be purified, but less conveniently, by sublimation; the product formed brilliant yellow needles, m.p. $338^\circ C$.

Preparation of Alkali Metal Salts.

a. Potassium Tetrachlorophthalimide - A solution of 1.6 g. of potassium hydroxide in 20 cc. of dry methyl alcohol was added to a saturated solution of the imide in boiling dioxane, (8 g. in 200 cc.); a voluminous precipitate immediately formed. The mixture was cooled, and the potassium salt, filtered by suction, was dried in a vacuum desiccator; the dry product was a slightly yellow amorphous powder. Although it contained variable amounts of inorganic base, it was found to be satisfactory for the preparation of derivatives and was not further purified.

Lot	Analysis: K
I	18.5%
II	13.8
III	9.1
IV	11.3
Calculated	12.1

A series of studies were carried out with the idea of determining in what state the excess base was present, and so explaining the discordant analytical results. These studies involved various methods of drying, such as the use of the Abderhalden drier, and of washing, particularly with methyl alcohol. The results, however, were not conclusive and are omitted.

The method just described is superior to those given below for the sodium salt in several respects - 1. the hydroxide can be used instead of the less convenient metal and 2. the dioxane does not need to be extensively purified. In addition it should be noted that the potassium salt is more reactive than the sodium.

b. Sodium Tetrachlorophthalimide.

1. Dioxane method - Four grams of the imide were dissolved in 100 cc. of boiling dioxane (previously dried by refluxing over sodium) to form a saturated solution, 0.33 g. of metallic sodium added, and the mixture refluxed for half

an hour with stirring. An insoluble material immediately separated. The products of several runs had the following characteristics:

Run	Analysis: Na	Weight, air dried.
I	8.0%	4.8 g.
II	7.5	4.7
III	7.8	9.2 (double size) (★)
Calculated	7.4	

(★) reacted in 100 cc. of dioxane as before.

2. Liquid ammonia method - Eight-tenths of a gram of sodium was dissolved in 200 cc. of liquid ammonia contained in a Dewar flask and 10 g. of tetrachlorophthalic anhydride were added slowly in small portions over a period of 10 minutes. After stirring for half an hour the ammonia was allowed to evaporate and the residue (11 g.) used without further purification in reaction with the halogen compounds. Necessarily under the circumstances this method is unacceptable, since the ammonia is not recovered.

Anal. Calcd. for $C_8O_2NCl_4Na$: Na, 7.5. Found: Na, 7.4.

The following experiment was considered to be sufficient proof that the potassium imide is more reactive than the sodium; accordingly it was used as the general preparative reagent. Two grams of the sodium salt were heated with 10 cc. of n-heptyl bromide for 10 hrs. in an

oil bath at 200°C. The melting point of the crude product was 148° C. The weight of the analytical sample (m.p. 152° C.) after three crystallizations from methyl alcohol was 0.5 g. (yield 20%). One and a half grams of the potassium salt were heated as before with 3 cc. of n-heptyl bromide. The weight of the crude product (m.p. 150° C.) was 0.85 g., and the weight after two crystallizations from chloroform (poured into methyl alcohol) was 0.65 g. (m.p. 151° C., yield 30%).

Preparation of Derivatives.

Two methods were standardized for the preparation of derivatives; in (a) which is used for halogen compounds boiling above 140° C., the reaction was carried out in a flask under reflux, in (b) for compounds boiling below 140° C., the reaction was completed in a sealed tube.

(a) A mixture of 5 g. of the halide (or 5 cc., if a liquid) and 2 g. of the potassium salt, contained in a small flask under a reflux condenser bearing a calcium chloride tube, was heated in an oil-bath at 200° C. for 10 hours. The product was extracted with three 5 cc. portions of boiling chloroform, filtered, and the filtrate evaporated to dryness. As crystallizing solvents (after decolorizing with charcoal if necessary) alcohol, acetone, dioxane or chloroform were found to be suitable, as indicated in Table II.

(b) By using the same quantities of materials, the mixture was heated in a sealed tube for 6 hours. The product was then purified by the same procedure as under (a).

The N-substituted tetrachlorophthalimides prepared in this research are given in Table II, together with their melting points, crystal form and analyses.

Table II.

N-Substituted Tetrachlorophthalimides.

Substituent.	M.p. °C.	Formula	Crystal Form	Chlorine %	
				Calcd.	Found
CH ₃	210-211	C ₉ H ₃ O ₂ NC1 ₄	Needles ^d	47.5	47.3
C ₂ H ₅	192-193	C ₁₀ H ₅ O ₂ NC1 ₄	Plates ^d	45.4	
n-C ₄ H ₉	153-154	C ₁₂ H ₉ O ₂ NC1 ₄	Plates ^b	41.6	41.6
n-C ₅ H ₁₁	145-146	C ₁₃ H ₁₁ O ₂ NC1 ₄	Needles ^d	40.0	40.3
i-C ₅ H ₁₁	170-171	C ₁₃ H ₁₁ O ₂ NC1 ₄	Leaflets ^b	40.0	40.2
n-C ₆ H ₁₃	150-151	C ₁₄ H ₁₃ O ₂ NC1 ₄	Leaflets ^b	38.5	38.8
n-C ₇ H ₁₅	145-146	C ₁₅ H ₁₅ O ₂ NC1 ₄	Leaflets ^b	37.1	36.8
n-C ₁₆ H ₃₃	129-130	C ₂₄ H ₃₃ O ₂ NC1 ₄	Leaflets ^d	27.9	27.7
-COOC ₄ H ₉ -n	151-152	C ₁₃ H ₉ O ₄ NC1 ₄	Leaflets ^a	37.0	36.6
-CH ₂ COOC ₂ H ₅	180-181	C ₁₂ H ₇ O ₄ NC1 ₄	Needles ^d	38.3	38.2
-CH ₂ COOC ₄ H ₉ -n	116-117	C ₁₄ H ₁₁ O ₄ NC1 ₄	Needles ^d	35.6	35.9
-CH(CH ₃)COOCH ₃	165-166	C ₁₂ H ₇ O ₄ NC1 ₄	Plates ^b	38.3	38.2
-CH(CH ₃)COOC ₂ H ₅	159-160	C ₁₃ H ₉ O ₄ NC1 ₄	Rods ^e	36.9	36.6
-CH(C ₂ H ₅)COOC ₂ H ₅	116-117	C ₁₄ H ₁₁ O ₄ NC1 ₄	Rods ^e	35.6	35.4
-CH(n-C ₃ H ₇)COOC ₂ H ₅	113-114	C ₁₅ H ₁₃ O ₄ NC1 ₄	Plates ^a	34.4	34.4
-CH(n-C ₄ H ₉)COOC ₂ H ₅	122-123	C ₁₆ H ₁₅ O ₄ NC1 ₄	Plates ^a	33.3	33.6
-CH ₂ CH ₂ OCOCH ₃	168-169	C ₁₂ H ₇ O ₄ NC1 ₄	Plates ^d	38.3	38.1
-CH ₂ CH ₂ OH	208-209	C ₁₀ H ₅ O ₃ NC1 ₄	Prisms ^c	43.2	43.0
-CH ₂ CH ₂ OC ₆ H ₅	155-156	C ₁₆ H ₉ O ₃ NC1 ₄	Rods ^c	35.1	35.0
-CH ₂ CH ₂ CH ₂ OH	165-166	C ₁₁ H ₇ O ₃ NC1 ₄	Prisms ^c	41.4	41.1
-CH ₂ CH ₂ CH ₂ Br	164-165	C ₁₁ H ₆ O ₂ NC1 ₄ Br	Prisms ^e	54.7	54.4 ^f 54.7 ^g
-CH ₂ CH ₂ CH ₂ CN	194-195	C ₁₂ H ₆ O ₂ N ₂ Cl ₄	Leaflets ^c	40.4	40.8
-CH ₂ COC ₆ H ₅	258-259	C ₁₆ H ₇ O ₃ NC1 ₄	Plates ^d	35.2	35.3
-CH ₂ CH ₂ COC ₆ H ₅	205-206	C ₁₇ H ₉ O ₃ NC1 ₄	Leaflets ^d	34.1	33.7

^aFrom methyl alcohol. ^bFrom ethyl alcohol. ^cFrom acetone. ^dFrom chloroform, poured into two volumes of methyl alcohol. ^eFrom dioxane, poured into two volumes of methyl alcohol, and water added. ^fDerivative prepared from trimethylene dibromide. ^gSame, from chlorobromide.

The method of chlorine analysis was that of Willard and Thompson (16) modified so that potassium dichromate replaced ammonium persulphate as oxidizing agent.

S u m m a r y.

1. Potassium tetrachlorophthalimide is a suitable reagent to use for the identification of many classes of halogen compounds. It reacts readily with the alkyl halides, the straight-chain α -halogen esters, the high boiling chloroformates, the halohydrins, halo ketones and halo ethers which have been studied.

With the halogen compounds that boil below 140° C., a sealed tube is required for the reaction.

2. Potassium tetrachlorophthalimide is superior to the sodium salt for this purpose.

3. The analytical reagent does not react satisfactorily with α -bromo derivatives of ethyl iso-butyrate and iso-valerate, with the low boiling chloroformates, with ethyl β -chloropropionate, with epichlorhydrin, and bromostyrene.

4. The following compounds give anomalous results: γ -chlorobutyrophenone, ethyl bromomalonate, and bromotricarbo-methoxymethane.

5. The analytical reagent is best prepared in two steps (a) the preparation of tetrachlorophthalimide from the anhydride and ammonium carbonate, and (b) the preparation of the potassium salt from the imide and potassium hydroxide.

6. Derivatives of tetrachlorophthalimide are of higher melting point than those of 3-nitrophthalimide.

B i b l i o g r a p h y.

1. Marvel, Gauerke and Hill, J. Am. Chem. Soc., 47, 3009 (1925).
2. Hill, J. Am. Chem. Soc., 50, 167 (1928).
3. Gilman and Furry, J. Am. Chem. Soc., 50, 1214 (1928).
4. Schwartz and Johnson, J. Am. Chem. Soc., 53, 1063 (1931).
5. Allen and Nicholls, J. Am. Chem. Soc., 56, 1409 (1934).
6. Underwood and Gale, J. Am. Chem. Soc., 56, 2117 (1934).
7. Gillespie, J. Am. Chem. Soc., 56, 2740 (1934).
8. Gabriel, Ber., 20, 2224 (1887); 21, 2671 (1888); 38, 633 (1905); 41, 244 (1908).
9. Sah and Ma, Ber., 65, 1630 (1932).
10. Hale and Britton, J. Am. Chem. Soc., 41, 841 (1919).
11. Allen and Boyer, Can. J. Research, 9, 159 (1933).
12. Souther, J. Am. Chem. Soc., 46, 1301 (1924).
13. Carothers, J. Am. Chem. Soc., 48, 3192 (1926).
14. "Organic Syntheses", John Wiley & Sons, New York. Coll. Vol. I, p. 446.
15. Tsing, Science Quart. Natl. Univ. Pekin., 4, 191 (1934). C. Abs., 28, 6133 (1934).
16. Willard and Thompson, J. Am. Chem. Soc., 52, 493 (1930).

