[Contribution from the Department of Chemistry, Emory University]

THE ACYLATION OF OLEFINS. I. THE ACETYLATION OF CYCLOHEXENE[1]

E. EARL ROYALS and C. M. HENDRY[2,3]

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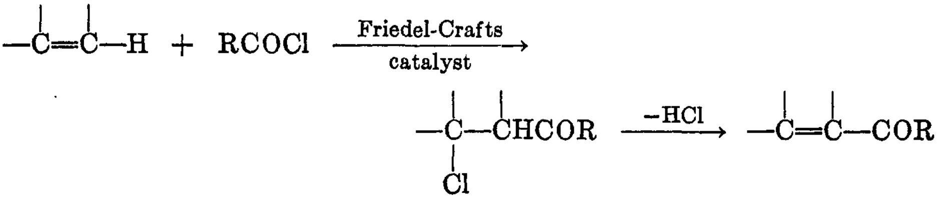
The acylation of olefins with acyl halides under the influence of Friedel-Crafts type catalysts is a general reaction (1).



$$-\overset{|}{C}=\overset{|}{C}-H + RCOCl \xrightarrow[\text{catalyst}]{\text{Friedel-Crafts}} -\underset{Cl}{\overset{|}{\underset{|}{C}}}-\overset{|}{C}HCOR \xrightarrow{-HCl} -\overset{|}{C}=\overset{|}{C}-COR$$

I II

Depending upon the catalyst used, the temperature, and other experimental conditions, the product isolated from the acylation reaction may be the chloroketone, I, the unsaturated ketone, II, or a mixture of the two. Standard practice in application of this reaction to the preparation of α,β-unsaturated ketones is to effect (or complete) the dehydrohalogenation of the crude reaction product by heating with dimethylaniline (2), sodium carbonate (3), aluminum chloride (4), or other dehydrohalogenating agent. Aluminum chloride and stannic chloride have been most frequently used as catalysts for the acylation of olefins with acyl halides. Despite the apparent generality of the olefin acylation reaction under the influence of Friedel-Crafts type catalysts, presently published information does not permit its classification as a standard synthetic procedure. There is little agreement in the published literature as to the best experimental conditions for application of the reaction to a given olefin, nor as to the results to be expected from application of a given procedure. The reaction has other drawbacks which will be discussed later in the present paper. A general investigation of the acylation of olefins has been undertaken in this laboratory with the object of developing simple, dependable procedures for the conversion of for the conversion of olefins to pure α,β-unsaturated ketones. In the present paper, we wish to report the results of our study of the acetylation of cyclohexene to 1-acetylcyclohexene.

Acetylation of cyclohexene with acetyl chloride. Darzens (2), in 1910, added

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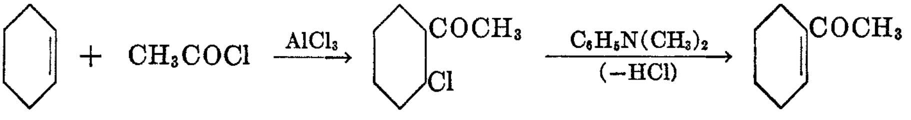
aluminum chloride to a solution of acetyl chloride and cyclohexene in carbon disulfide at 0°, and obtained a saturated chloroketone, III, which on treatment with dimethylaniline eliminated hydrogen chloride with formation of 1-acetylcyclohexene, IV.



III IV

The yield of the unsaturated ketone was reported as 42%. Wieland and Bettag (4) reported that at a lower reaction temperature, −18°, the chloroketone, III, is the principal product of the reaction. The latter workers converted the chloroketone into 1-acetylcyclohexene in 60% yield[4] by warming with a small amount of aluminum chloride in carbon disulfide solution. More recent workers have followed the general directions of Darzens and of Wieland and Bettag for acylation of cyclohexene. Thus, Christ and Fuson (3) report the formation of 1-acetylcyclohexene in 62% yield by addition of acetyl chloride to cyclohexene essentially according to the procedure of Wieland and Bettag followed by distillation of the crude chloroketone from sodium carbonate to effect dehydrohalogenation. Nightingale, Milberger, and Tomisek (5) have applied the Wieland and Bettag procedure to the synthesis of several 1-acylcyclohexenes. These workers reported that they were unable to effect complete dehydrohalogenation of the intermediate chloroketones by distillation from sodium carbonate, but that heating for two hours with dimethylaniline at 180° did give chlorine-free products. Colonge and his associates (6, 7) have reported that cyclohexene, as well as other olefins, may be acylated in excellent yields by the use of acid chlorides in the presence of very small amounts of stannic chloride. The use of catalytic amounts of the catalyst is in distinct contrast to the customary (8) employment of somewhat more than one molecular proportion of catalyst in the usual Friedel-Crafts acylation of aromatics with acyl halides.

We have investigated the acetylation of cyclohexene with acetyl chloride using aluminum chloride, zinc chloride, and stannic chloride as catalysts under a variety of experimental conditions. Stannic chloride was easier to handle and gave the smoothest reactions of any of the three catalysts used. We have been unable to reproduce the high yields of 1-acetycyclohexene reported by Christ and Fuson; an attempt to duplicate exactly their described procedure (3) gave only a 37.9% yield. We were also unable to confirm the report of Colonge and associates (6, 7) that catalytic amounts of stannic chloride may be used to effect acylation of alkenes; the use of small ratios of stannic chloride to cyclohexene gave low yields of 1-acetylcyclohexene roughly proportional to the amount of catalyst used. Despite the failure of the reaction to proceed satis-

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[4] The yield reported by Wieland and Bettag apparently refers to the dehydrohalogenation step only; this dehydrohalogenation was run on a very small scale. Examination of the figures reported by Wieland and Bettag shows that the over-all yield of 1-acetylcyclohexene from cyclohexene was not greater than 40–50%, perhaps closer to the lower figure.

factorily to completion in the presence of really catalytic amounts of stannic chloride, it was found that a full molecular proportion of stannic chloride is unnecessary. Our best results were obtained using 0.25–1.0 moles of stannic chloride per mole of acetyl chloride with a reaction period of one hour at 0–20° (36.3–40.2% yields).

Chlorocyclohexane was found to be an important by-product from all acetylations of cyclohexene with acetyl chloride; with zinc chloride as catalyst, this by-product accounted for as much as 30% of the cyclohexene reacted. The chlorocyclohexane probably results from addition of hydrogen chloride, eliminated during the reaction from the chloroketone, III, to unreacted cyclohexene. This side reaction has been previously mentioned (7, 9, 10) in the literature, but no indication has been given of its relative importance. It is known (11) that the addition of hydrogen halides to olefins is catalyzed by Friedel-Crafts catalysts.

In agreement with the observation of Nightingale and co-workers (5), we found that the 1-acetylcyclohexene resulting from acetylation of cyclohexene with acetyl chloride and dehydrohalogenation of the crude reaction product with sodium carbonate, even after careful fractionation, contained considerable chlorine. We were also unable to effect complete dehydrohalogenation of the products of acetylation with acetyl chloride by heating with dimethylaniline at 180° for three hours. Indeed, none of our samples of 1-acetylcyclohexene prepared by acetylation of cyclohexene with acetyl chloride followed by dehydrohalogenation with dimethylaniline were completely halogen-free. Parr bomb halogen determinations on several of the products consistently showed the presence of about 4% chlorine even after repeated treatments with dimethylaniline and careful fractionation. It was also noted that most samples of 1-acetylcyclohexene prepared by acetyl chloride acetylation darkened very considerably on standing. Variations in refractive index during fractional distillation also indicated a low order of purity.

Acetylation of cyclohexene with acetic anhydride. Because of the shortcomings indicated above for the acetylation of cyclohexene with acetyl chloride, the use of acetic anhydride as acetylating agent was investigated. Anhydrides have been successfully used (12, 13) in aromatic Friedel-Crafts acylations; such acylations require the use of two or more moles of the Friedel-Crafts catalyst per mole of the anhydride. Only fragmentary reports appear in the literature (14, 15, 16) regarding the use of acid anhydrides as acylating agents for olefins.

Although Experiments 1, 2, and 3 (Table I) gave no better yields of 1-acetylcyclohexene that did acylations using acetyl chloride as acetylating agent, the use of acetic anhydride offers several distinct advantages: (a) The reaction conditions are more easily reproducible, and the experimental procedure is simpler; (b) 1-Acetylcyclohexene is produced directly, thus eliminating the troublesome dehydrohalogenation step; (c) The 1-acetylcyclohexene produced is purer, as is indicated by the constancy of refractive index of successive fractions during distillation, failure of samples to darken on standing, and complete absence of chlorine (sodium fusion tests).

Variations in the procedure for acetylation of cyclohexene. In the experiments thus far described, the acetylation procedure was that used by previous investigators (2–5), namely, the addition of the catalyst portionwise to a mixture of cyclohexene and the acetylating agent. Several variations of this customary procedure were investigated in the present work. Because of the advantages of acetic anhydride over acetyl chloride as acetylating agent enumerated above, major emphasis was placed on variations in the procedure for acetylation with acetic anhydride.

The most advantageous variation in experimental procedure found was that of dropwise addition of acetic anhydride to a mixture of cyclohexene and stannic chloride (Experiments 4, 5, and 6, Table I) during a short reaction period at about room temperature. Under these conditions, 1-acetylcyclohexene was obtained in 54% yield. This product did not darken on standing, and was shown to be chlorine-free, despite the fact that considerable chlorocyclohexane (18% based on cyclohexene) was formed as a by-product in this reaction. Since the samples of 1-acetylcyclohexene prepared by acetylation with acetyl chloride invariably contained chlorine, this evidence appears to indicate that the acid chloride is not an intermediate in olefin acylation with anhydrides, as has frequently been suggested (1, 13) for aromatic Friedel-Crafts acylations with acid anhydrides. It seems more probable that the anhydride is the actual acetylating agent, and that the acylation reaction and the side-reaction of chlorocyclohexane formation proceed by some such mechanism as the following:

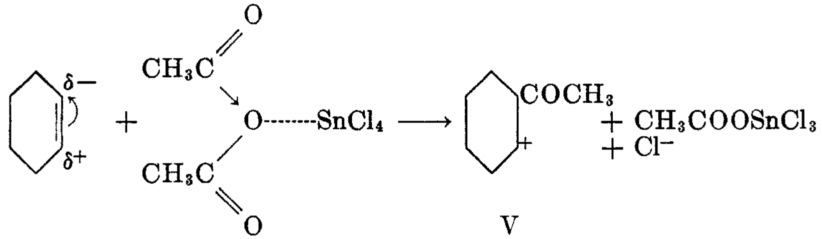
TABLE I

ACETYLATION OF CYCLOHEXENE WITH ACETIC ANHYDRIDE

RUN NO.	MOLES OF C_6H_{12}	MOLES OF Ac_2O	CATALYST USED	MOLES OF CATALYST	REACTION PERIOD IN HOURS	REACTION TEMP., °C.	YIELD OF 1-ACETYLCYCLOHEXENE, %
1[a]	1.0	1.0	$AlCl_3$	2.0	4	0 -5	28.2
2	1.05	2.5	$ZnCl_2$	2.0	4	45–55	40.3
3	1.42	1.0	$SnCl_4$	1.0	2	0 -30	40.3
4	1.0	0.75[b]	$ZnCl_2$	1.0	2.25	30–50	40.0
5	1.50	1.0[b]	$SnCl_4$	1.0	0.75	25–35	54.0[c]
6	1.50	1.0[b]	$SnCl_4$	1.25	2	0 -10	50.0[d]

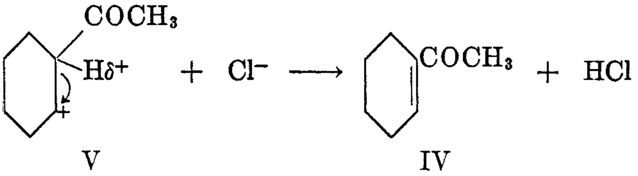
[a] In this reaction, 200 cc. of carbon disulfide was used as solvent. [b] The acetic anhydride was added gradually to the mixture of cyclohexene and catalyst. [c] This reaction also produced 32 g. of chlorocyclohexane. [d] This reaction also produced 37 g. of chlorocyclohexane

(A)

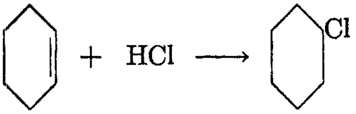


V

(B)

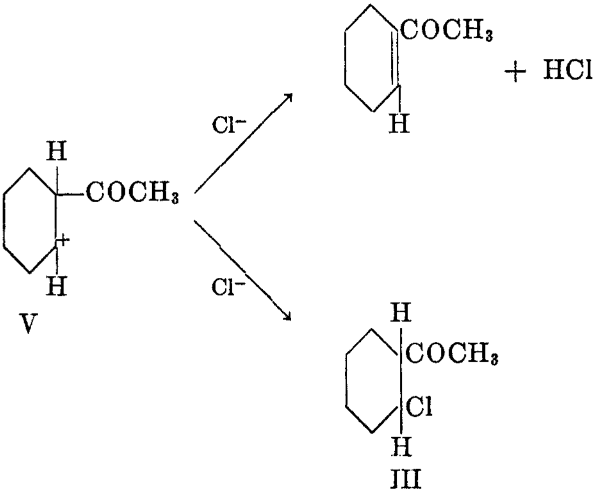


(C)



This mechanism is analogous to that usually suggested (17) for the corresponding reaction of cyclohexene with acetyl chloride. The formation of both 1-acetylcyclohexene and 1-acetyl-2-chlorocyclohexane from the acetyl chloride reaction may be rationalized on the basis of a competition between elimination of a proton from the intermediate carbonium ion, V, and combination of this carbonium ion with chloride ion:

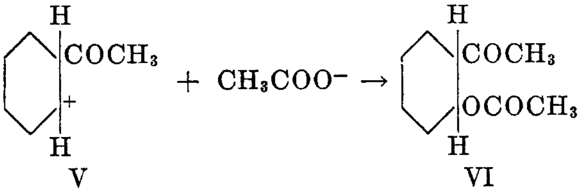
(D)



The question might, then, be raised as to why the same intermediate, V, postulated for the acetic anhydride reaction does not also combine with chloride ion to give chloroketone and the same over-all result as though the reaction had been effected with acetyl chloride. The difference probably lies in the fact that acetate ion, actual or potential, is present in the acetic anhydride reaction mixture, and if intermediate V combines with any anion, it is with the more powerfully nucleophilic acetate ion rather than chloride ion:

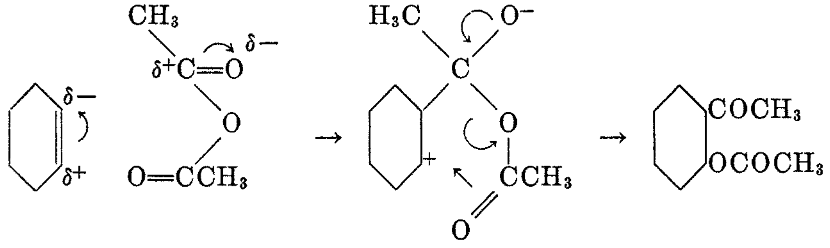
(E) $CH_3COOSnCl_3 + Cl^- \rightleftarrows CH_3COO^- + SnCl_4$

(F)



If 1-acetyl-2-acetoxycyclohexene, VI, is an intermediate in the acetic anhydride reaction, and we have no experimental evidence that it is, the postulation of a cyclic intermediate for its formation rather than the sum of equations (A) and (F) is attractive (Equation G). 1-Acetyl-2-acetoxycyclohexane, if formed in the acetic anhydride reaction, would certainly be expected to decompose during the workup procedure or during distillation to 1-acetylcyclohexene and acetic acid.

(G)



VI

Observations on possible side reactions during the acetylation of cyclohexene. Those reactions which led to low yields of 1-acetylcyclohexene gave either incomplete reaction, with recovery of considerable unreacted cyclohexene, or formation of resinous products. Several experiments were carried out in an effort to determine the source of the resinous by-products. It was observed that neither zinc chloride nor stannic chloride was effective in polymerizing cyclohexene at temperatures below 90°. Aluminum chloride effected some polymerization of cyclohexene at 45–50°. It thus appears highly unlikely that the resinous by-products arise from self-polymerization of cyclohexene. The possibility that the resins are produced by polymerization of the product, 1-acetylcyclohexene, was next investigated. 1-Acetylcyclohexene was recovered unchanged after heating with zinc chloride at temperatures below 80°; stannic chloride, however, effected considerable resinification of 1-acetylcyclohexene at temperatures as low as 25°. The presence or absence of cyclohexene had no effect on the polymerization of 1-acetylcyclohexene by zinc chloride or stannic chloride. In the presence of acetic anhydride, however, both zinc chloride and stannic chloride readily effected resinification at moderate temperatures. It would appear, then, that the resinous by-products which occur in the acetylation of cyclohexene with acetic anhydride arise from self-polymerization of 1-acetylcyclohexene and/or further reaction of 1-acetylcyclohexene with acetic anhydride. Hence, the presence of an excess of both stannic chloride and acetic anhydride during the acetylation of cyclohexene is not conducive to high yields. This probably explains the beneficial effect of the experimental procedure of adding the anhydride dropwise to a mixture of cyclohexene and stannic chloride; the excess of stannic chloride always present leads to rapid reaction, but excess anhydride is at no time present.

Other catalysts and reaction variables. Hartough and his associates (18, 19, 20) have reported excellent yields from acetylation of certain heterocyclic compounds with acetic anhydride using as catalysts small amounts of phosphoric acid, iodine, or phosphorus pentoxide. Application of these procedures to the reaction of acetic anhydride with cyclohexene was unsuccessful; at low temperatures, little reaction occurred, while at higher temperatures there was extensive resinification.

Although a few of our experiments utilized a solvent, we have made no general investigation of solvent effects.

EXPERIMENTAL PART

Preparation of 1-acetylcyclohexene using acetic anhydride. The experiment here described represents our best procedure for the preparation of 1-acetylcyclohexene. A mixture of 123 g. (1.5 moles) of cyclohexene and 260.5 g. (1.0 mole) of stannic chloride was placed in a 1-liter, three-necked flask equipped with a dropping-funnel, a reflux condenser, a thermometer extending into the reaction mixture, and a modified Hershberg stirrer (21). All openings were protected by calcium chloride-tubes. The flask was immersed in an ice-bath, and 102 g. (1.0 mole) of acetic anhydride (99–100%) was added dropwise during 30 minutes; the temperature of the reaction mixture varied from 25–35° during the addition. Stirring in the ice-bath was continued for 15 minutes. The reaction mixture was then poured onto 300–400 g. of cracked ice. The resulting mixture was extracted with ether; the ether extract was washed with sodium bicarbonate solution, then with water, and dried over calcium chloride. The ether was stripped off, and the residue fractionally-distilled through an 18-inch helix-packed column under reduced pressure. After a fore-run from which chlorocyclohexane was isolated (see below), there was obtained 67 g. (54%, based on acetic anhydride) of 1-acetylcyclohexene, b.p. 65–69°/5 mm. (202.5°/atms.) n_D^{25} 1.4883, d_4^{30} 0.9641. Reported (22) values: b.p., 201–202°, n_D^{20} 1.4881, d_4^{20} 0.9655. The product gave a semicarbazone, m.p. 220°; reported (22), m.p. 221°. The oxime was prepared and found to melt at 58–59° on crystallization from aqueous alcohol. Darzens (2) reported an oxime, m.p. 99°, from 1-acetylcyclohexene. More recently, Bergs, Wittfeld, and Wildt have reported (23) an oxime, m.p. 60–61°.

Anal. of oxime. Calc'd for $C_8H_{13}NO$: N, 10.07. Found (Kjeldahl): N, 9.91.

General procedure for the acetylation of cyclohexene with acetyl chloride. The chosen quantities of cyclohexene and acetyl chloride were placed in the apparatus just described. The reaction vessel was cooled in an ice or Dry Ice-acetone bath depending upon the temperature desired, and the catalyst was added portionwise with stirring. On completion of the reaction, the reaction mixture was poured onto a mixture of ice and hydrochloric acid, and the resulting mixture was extracted with ether. The ether extracts were washed with sodium bicarbonate solution, then with water, and dried over calcium chloride. The ether and unreacted cyclohexene were distilled off, and the residue was heated with an excess of dimethylaniline for three hours at 180°. This mixture was cooled, washed with dilute hydrochloric acid, taken up in ether, and dried over calcium chloride. The product was then isolated by fractional-distillation through an 18-inch, helix-packed column. Samples of 1-acetylcyclohexene prepared by this general procedure showed the following properties: b.p., 65–69°/5 mm., n_D^{25} 1.4921–1.4950, chlorine content (Paar bomb), $4.0 \pm 0.1\%$. The samples darkened considerably on standing.

Characterization of by-products. Chlorocyclohexane was isolated from the fore-runs in most of our acetylation experiments. This material showed the following properties: b.p., 142° (uncorr.), n_D^{25} 1.4597, d_4^{30} 0.9880. Reported (24) values: b.p., 142°, d_4^{20} 1.000, n_D^{20} 1.46264.

Anal. Calc'd for $C_6H_{11}Cl$:Cl, 29.8. Found (Parr bomb): Cl, 29.8.

Very small amounts of cyclohexyl acetate were isolated from several acetylations using acetic anhydride. Only one experiment (in which cyclohexene was added to a mixture of acetic anhydride and stannic chloride) afforded a large amount of this by-product. The cyclohexyl acetate isolated from this experiment showed the following properties: b.p.

174–175° (uncorr.), n_D^{28} 1.4379. Alkaline hydrolysis gave cyclohexanol, b.p. 158–160°; phenylurethan, m.p. 81–82°; reported (25) m.p. 82°.

SUMMARY

A study has been made of factors affecting the yield of 1-acetylcyclohexene from the acetylation of cyclohexene with acetyl chloride and with acetic anhydride in the presence of various Friedel-Crafts type catalysts. The best procedure found involves the portion-wise addition of acetic anhydride to a mixture of cyclohexene and stannic chloride during a reaction period of about one-half to one hour at 25–35°. This procedure affords 1-acetylcyclohexene in 54% yield. The product of this reaction is much purer than that resulting from acetylation of cyclohexene with acetyl chloride, and the experimental procedure is considerably simpler. The mechanism of the reaction and the nature of side reactions are briefly discussed.

Emory University, Georgia.

REFERENCES

(1) See Thomas, *Anhydrous Aluminum Chloride in Organic Chemistry*, Reinhold Publishing Corporation, New York, N. Y., 1941, pp. 752 ff. for leading references.
(2) Darzens, *Compt. rend.*, **150**, 707 (1910); Darzens and Rost, *Compt., rend.*, **151**, 758 (1910).
(3) Christ and Fuson, *J. Am. Chem. Soc.*, **59**, 893 (1937).
(4) Wieland and Bettag, *Ber.*, **55**, 2246 (1922).
(5) Nightingale, Milberger, and Tomisek, *J. Org. Chem.*, **13**, 357 (1948).
(6) Colonge and Mostafavi, *Bull. soc. chim.*, **6**, 335 (1939).
(7) Colonge and Duroux, *Bull. soc. chim.*, **7**, 459 (1940).
(8) Reference (1), p. 205.
(9) Krapavin, *Bull. Soc., Imp. Nat. Moscow*, 1 (1908) [*Chem. Abst.*, **5**, 128 (1911)].
(10) McMahon, Roper, Untemohlen, Hasel, Harris, and Brant, *J. Am. Chem. Soc.*, **70**, 2971 (1948).
(11) Reference (1), pp. 770 ff.
(12) Noller and Adams, *J. Am. Chem. Soc.*, **46**, 1889 (1924).
(13) Groggins and Nagel, *Ind. Eng. Chem.*, **26**, 1313 (1934).
(14) Byrnes, U. S. Patent 2,355,703 [*Chem. Abst.*, **39**, 87 (1945)].
(15) Doumani and Cumes, U. S. Patent 2,411,823 [*Chem. Abst.*, **41**, 1234 (1947)].
(16) Petrov and Kaplan, *Izvest. Akad. Nauk. S. S. S. R., Otdel Khim. Nauk*, 295 (1947) [*Chem. Abst.*, **43**, 1718 (1949)].
(17) Dilthey, *Ber.*, **71**, 1350 (1938).
(18) Hartough and Kosak, *J. Am. Chem. Soc.*, **68**, 2639 (1946).
(19) Hartough and Kosak, *J. Am. Chem. Soc.*, **69**, 1012 (1947).
(20) Hartough and Conley, *J. Am. Chem. Soc.*, **69**, 3093 (1947).
(21) Hershberg, *Ind. Eng. Chem. Anal. Ed.*, **8**, 313 (1936).
(22) Heilbron, *Dictionary of Organic Compounds*, Oxford University Press, New York, N. Y., 1943, Vol. I, p. 10.
(23) Bergs, Wittfeld, and Wildt, *Ber.*, **67**, 238 (1934).
(24) Reference (22), Vol. I, p. 458.
(25) Huntress and Mulliken, *Identification of Organic Compounds, Order I*, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 461.