[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF MICHIGAN]

o-PHENYLENEDIACETIMIDE AND OTHER COMPOUNDS RELATED TO 3,1*H*-BENZAZEPINE

J. O. HALFORD AND BERNARD WEISSMANN

Received July 14, 1952

o-Phenylenediacetamide has been cyclized pyrolytically to *o*-phenylenediacetimide. The yield at 295° was 57% on a 190-mg. scale and 53% on a 2-g. scale, while less satisfactory yields were obtained at higher or lower temperatures. About 10% of the diamide was recovered. Attempts to improve the yield by conducting the reaction under dilution in boiling phenyl ether (ammonia evolution 87%, imide recovered 12%) and in boiling phenol (ammonia evolution slow) were not successful.

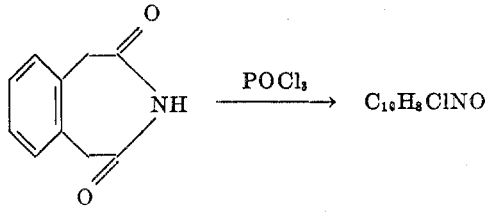
This apparent contradiction of the dilution principle has a fairly satisfactory explanation. If it is assumed that only amide linkages are formed and that the system is approaching equilibrium, there should be in a single phase a distribution of cyclic polymers whose mean molecular weight would decrease with increasing temperature or with dilution. The distribution, because of these two factors, should be about the same in the pyrolysis (higher temperature) and in the phenyl ether experiment (dilution). The pyrolytic reaction produces the better result because the product, along with a smaller quantity of the diamide, sublimes out of the sphere of reaction. It is possible, but less probable, that the solvent decreases the efficiency of the cyclization by interfering with some favorable orientation which occurs in the melt because of hydrogen bond formation. The occurrence of an optimum temperature for the pyrolysis probably means that side reactions become important as the temperature is increased.

Since *o*-phenylenediacetimide bears a relation to 3,1*H*-benzazepine analogous to that of succinimide to pyrrole, it is of interest to consider the possibility of fixing the double bonds of the tautomeric dienolic structure in position by appropriate substitution of the hydroxyl groups. The feasibility of this proposal, particularly at higher temperatures, may well depend upon the relative stability of 3,1*H*-benzazepine and the isomeric methylisoquinolines, which will be determined primarily by the resonance energies, corrected for ring strain. A rough estimate of the strain energy, 5 to 10 kcal. per mole, indicates that it is small relative to the probable resonance effect. For 3,1*H*-benzazepine it is possible to write two neutral formulations related through simple Kekulé resonance, plus twelve polar forms in which negative charge is acquired at all of the carbon atoms at the expense of the nitrogen. This combination might lead to greater stability than the isomeric methylisoquinolines, but will probably not do so because the same factors which prevent the aromatization of cycloöctatetraene may also strongly affect the azepine structure. An alternative estimate, starting with the observation that *o*-phenylenediacetimide does not show enolic properties, likewise fails to indicate the relative stability clearly.

It is therefore an open question whether the 3,1*H*-benzazepine structure can

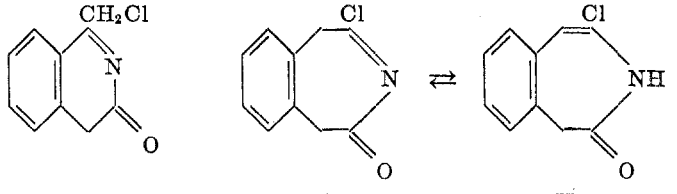
be formed at higher temperatures, since, if the isoquinoline type is more stable, production of the azepine arrangement in competition with isomerization may require a rapid low temperature reaction.

In this connection, the result of subjecting the imide to the action of phosphorus oxychloride under conditions suggested by Gabriel's (1) conversion of homophthalimide to 1,3-dichloroisoquinoline is somewhat informative. At 160°, the temperature of the Gabriel reaction, only a tarry mixture was obtained from *o*-phenylenediacetimide. Below 120°, however, a fairly smooth reaction occurred with the replacement of one hydroxyl group by chlorine.



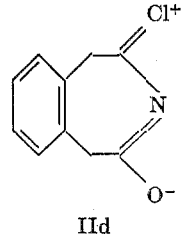
I II

Compound II can be recrystallized without change from methyl or isopropyl alcohol, but the chlorine is precipitated immediately by sodium iodide in acetone at room temperature. This leads to the consideration of two formulas, IIa and IIbc.



IIa IIb IIc

IIa is improbable because it might not react rapidly enough with sodium iodide and would be expected to react further with phosphorus oxychloride. Likewise, IIc would not react with sodium iodide and might react further with phosphorus oxychloride. This leaves IIb, which, by analogy with compounds like pseudosaccharin chloride and the simple imido chlorides might be expected to suffer replacement of the chlorine in an alcohol solution. This objection is not necessarily valid, however, since models suggest the possibility of stabilization of IIb by resonance with IId,



IId

which could decrease the susceptibility of the chlorine to nucleophilic displacement. Therefore IIb appears to be the most acceptable structure.

The structure of the imide is clear from its step-wise reduction by lithium aluminum hydride, first to the corresponding lactam and subsequently to 2,3,4,5-tetrahydro-3,1*H*-benzazepine, both known compounds. The imide dissolves in sodium hydroxide solution at room temperature, but the ring is quickly opened and acidification of the resulting solution precipitates only the monoamidic acid.

From the conversion to compound IIb, it appears that the seven-membered heterocycle readily accepts one double bond in addition to the aromatic bond, but refuses to move this bond into the 1,2 position and resists the acquisition of the final unsaturation of the benzazepine system in competition with side reactions. This may mean that the 3,1*H*-benzazepine structure is less stable than the methyl isoquinolines and other possible isomers and polymeric forms and may indicate also that routes to this structure which involve the stepwise introduction of double bonds at elevated temperatures are unfavorable in competition with possible stabilizing rearrangements.

With this in mind, a limited study of the dehydrogenation of N-methyl-2,3,4,5-tetrahydro-3,1*H*-benzazepine has been made. The methyl derivative was employed because it had been found by Zelinsky and Jurjew (2) that N-methylpyrrolidine could be dehydrogenated more smoothly than pyrrolidine. An attempt by Schmidt (3) to dehydrogenate hexamethylenimine with aqueous silver acetate at 180° resulted in a mixture from which a small amount of α-picoline was separated. An attempt by von Braun and Bartsch (4) to dehydrogenate 2,3,4,5-tetrahydro-1-benzazepine by distillation from silver sulfate resulted in a high recovery of unchanged starting material.

For present purposes, 2,3,4,5-tetrahydro-3,1*H*-benzazepine was prepared according to Ruggli (5) by the reductive cyclization of *o*-phenylenediacetonitrile, and was converted with formaldehyde and formic acid to N-methyl-2,3,4,5-tetrahydro-3,1*H*-benzazepine. At 270°, in 90 minutes, on 40% Pd-asbestos, hydrogen evolution was 29 mole-%, and half as many equivalents of volatile base were evolved. At 290°, in 15 minutes, hydrogen evolution was 46 mole-% and volatile base was negligible. Titration of the liquid product showed 0.56 molar-equivalent of base, pK_H *ca.* 8, corresponding to starting material; and 0.37 molar-equivalent of a base mixture, pK_H *ca.* 5, corresponding roughly to quinoline, aromatic amines, or vinyl amines. From the product, about 80% of the starting material indicated by the titration was recovered as the picrate but no pure picrates were separated from the less basic fraction. Apparently each molecule of starting material gives up one molecule of hydrogen fairly readily, but the product is subject to rearrangement and finally, more slowly, to elimination of ammonia or methylamine under prolonged contact with the catalyst. The ring may have accepted the first unsaturation, but has refused again to acquire the second one in competition with side reactions. Further study of the dehydrogenation does not promise to be profitable at this time.

In connection with some unsuccessful attempts to prepare other derivatives

of 3,1*H*-benzazepine, *o*-bis(β-hydroxyethyl)benzene has been synthesized and converted to the phenylurethan, and improvements have been made in the preparation of *o*-divinylbenzene and in the conversion of *o*-ethylbenzonitrile to *o*-ethylacetophenone. Furthermore, *o*-acetylbenzoyl chloride has been synthesized and *o*-diacetylbenzene has been converted to a bromine derivative which is probably ω,ω′-dibromo-*o*-diacetylbenzene but which, because of its peculiar sensitivity, has thus far resisted proper characterization.

EXPERIMENTAL

o-Phenylenediacetonitrile. Bromination of 530 g. of technical 90% *o*-xylene with 1700 g. of bromine added in 90 minutes at 125–130° (6) under "Photoflood" illumination gave 586 g. of crude *o*-xylylene bromide, m.p. 94–95°, which, when purified, melted at 95–96°, reported m.p. 93° (6).

The washed crude dibromide, 264 g., was added in six minutes to a vigorously stirred solution of 151 g. of potassium cyanide in 500 ml. of water and 950 ml. of ethanol, previously heated to boiling (7, 8). After refluxing 15 minutes, the solution was poured on ice and diluted with ice-water to 8 liters. Filtration and recrystallization from alcohol yielded 70% of *o*-phenylenediacetonitrile, cream colored, m.p. 59–60°, reported 60° (7). Further recrystallization removed the color without raising the melting point.

o-Phenylenediacetamide was prepared by the method of Moore and Thorpe (7). When 10.4 g. of *o*-phenylenediacetonitrile was added rapidly with stirring to 30 ml. of conc'd sulfuric acid, the temperature rose quickly to 110°. After 15 minutes the mixture was poured on ice and neutralized with ammonium hydroxide. Yield of recrystallized diamide, 85%, m.p. 198–198.5°, reported m.p. 198°.

Difficulties with this method reported by Coffey (9) were apparently associated with his control of the temperature at 60°.

o-Phenylenediacetic acid monoamide. *o*-Phenylenediacetamide was boiled for 12 hours with an equimolar quantity of aqueous sodium hydroxide. The residue from evaporation to dryness was subjected to vacuum-sublimation (180°, 3 hours, 0.05 mm.). From the sublimation residue, by acidification and repeated recrystallization from water, there was obtained the monoamidic acid, m.p. 208–209°, reported m.p. 207–208° (9).

Anal. Calc'd for $C_{10}H_{11}NO_3$: N, 7.25; Mol. wt., 193.2.

Found: N, 6.96; Neut. equiv., 193.4.

Pyrolysis of o-phenylenediacetamide. The diamide, 190 mg., was heated for 30 minutes at 30 mm. in a test tube immersed in a graphite bath at 295°. The material which had sublimed into the upper part of the tube was extracted with boiling water (45 ml.). On cooling, the solution deposited long yellow plates (83 mg., m.p. 191–192°) of *o*-phenylenediacetimide (2,3,4,5-tetrahydro-3,1*H*-benzazepin-2,4-dione). Evaporation to dryness, followed by benzene extraction, yielded an additional 15 mg., m.p. 188–190°, and left 20 mg. of crude starting material, m.p. 192–193°. Recrystallization from isopropyl alcohol gave the colorless imide, m.p. 191–192°, mixture m.p. with starting diamide, 178–181°. On a 2-g. scale the yield was 53%. At lower or higher temperatures the yields were lower, while at 0.1 mm. the diamide sublimed with little reaction. An attempt to carry out the reaction homogeneously in boiling phenyl ether gave 87% of the expected quantity of ammonia in 75 minutes, but the yield of imide was only 12%.

The *o*-phenylenediacetimide was easily soluble in acetone, insoluble in ether, and soluble in hot water, benzene, or ethanol. Heating with dilute sulfuric acid at 170° gave *o*-phenylenediacetic acid. Solution in 3 *M* sodium hydroxide, followed by immediate acidification with dilute hydrochloric acid, precipitated the *o*-phenylenediacetic acid monoamide, initially somewhat impure, identified by mixture melting point.

Anal. Calc'd for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 7.99 Mol. wt., 175.3.

Found: C, 68.50; H, 5.40; N, 8.18; Mol. wt., 164 (Menzies, chloroform).

Reduction of o-phenylenediacetimide to the lactam, 2,3,4,5-tetrahydro-3,1H-benzazepin-2-one. A solution of 0.50 g. of the imide in 5 ml. of anhydrous dioxane was added to 0.02 mole of lithium aluminum hydride in 40 ml. of boiling anhydrous ether and refluxing was continued for one hour. From the ether solution, after washing with 9 *M* sulfuric acid, there was obtained 0.19 g. of brown material from which, by washing with ether and ethanol and recrystallizing from acetone, a small sample of a cream-colored solid, m.p. 158–160°, was produced. This was presumably the lactam, reported m.p. 159–160° (10).

Reduction of the lactam to 2,3,4,5-tetrahydro-3,1H-benzazepine. Reaction of 20 mg. of the presumed lactam with 1.5 millimoles of lithium aluminum hydride in 6 ml. of dioxane under reflux for four hours followed by the addition of aqueous hydrochloric acid, concentration under reduced pressure, addition of alkali, and extraction with ether, gave a solution from which 15 mg. of N-(*p*-toluenesulfonyl)-2,3,4,5-tetrahydro-3,1*H*-benzazepine was obtained, m.p. 130–131°, mixture m.p. with an authentic sample, 131–132°.

2-Chloro-4,5-dihydro-3,1H-benzazepin-4-one. *o*-Phenylenediacetimide, 400 mg., was refluxed with 15 ml. of phosphorus oxychloride for 20 minutes. The excess reagent was removed at aspirator pressure and the brown residue was stirred with ice, giving 315 mg. of a light tan powder which, by crystallization from methanol and 2-propanol, gave colorless crystals, m.p. 153–154°. This material was slightly soluble in ether and insoluble in cold aqueous sodium hydroxide. The compound in acetone solution slowly decolorized dilute potassium permanganate and reacted rapidly with sodium iodide.

Anal. Calc'd for $C_{10}H_8ClNO$: Cl, 18.31. Found: Cl, 18.38.

N-Ethyl-2,3,4,5-tetrahydro-3,1H-benzazepine. In one hydrogenation of *o*-phenylenediacetonitrile on W-2 Raney nickel at 120 atmospheres and 135° with ethanol and ammonia present, the temperature was maintained for about an hour longer than in the usual experiment which normally produces 2,3,4,5-tetrahydro-3,1*H*-benzazepine. The principal low-boiling product was apparently N-ethyl-2,3,4,5-tetrahydro-3,1*H*-benzazepine which was isolated as the *hydrochloride*, m.p. 247–248°.

Anal. Calc'd for $C_{12}H_{18}ClN$: Cl, 16.75. Found: Cl, 16.75.

N-Methyl-2,3,4,5-tetrahydro-3,1H-benzazepine. Purified 2,3,4,5-tetrahydro-3,1*H*-benzazepine, 10.5 g., was mixed at 0° with 8 ml. of 37% aq. formaldehyde and 5.5 ml. of 98% formic acid (11) and heated for 2.5 hours on the steam-bath. The ether extract from the neutralized solution gave 10.8 g. of the nearly pure N-methyl-2,3,4,5-tetrahydro-3,1*H*-benzazepine. The pure amine, 8.8 g., b.p. 121°/20 mm., 237°/760 mm., n_D^{25} 1.541, was obtained from the recrystallized hydrochloride.

Anal. Calc'd for $C_{11}H_{15}N$: Mol. wt., 161.2. Found: Neut. equiv., 160.7.

The *hydrochloride* was precipitated in ether and recrystallized from ethanol, m.p. 253–254° dec.

Anal. Calc'd for $C_{11}H_{16}ClN$: Cl, 17.94. Found: Cl, 17.89.

The *picrate* was obtained as fine yellow needles from a relatively large volume of ethanol, m.p. 225–226° dec.

Anal. Calc'd for $C_{17}H_{18}N_4O_7$: C, 52.31: H, 4.65.
Found: C, 52.24; H, 4.26.

The *methiodide* was formed with methyl iodide in ethanol and was recrystallized from ethanol, m.p. 230–231°, reported (12) m.p. 227°.

Dehydrogenation of N-methyl-2,3,4,5-tetrahydro-3,1H-benzazepine. Palladium supported on asbestos, prepared according to Zelinsky and Borisoff (13), was used in an apparatus which permitted the measurement of hydrogen and of the gaseous, basic material evolved. At 270°, in 90 minutes, 1.62 g. of the tertiary amine produced 65 ml. (S.T.P.) of hydrogen and 0.0015 equivalent of volatile base. At 290°, in 15 minutes, 1.76 g. evolved 114 ml. of hydrogen and 0.00022 equivalent of volatile base. Potentiometric titration of 160 mg. of the product showed breaks at 0.00056 equivalent, pK_H about 8, and at 0.00093 equivalent, pK about 5. The remaining product, 1.73 g., was dissolved in 50 ml. of ether and extracted with successive portions of 0.1 *M* hydrochloric acid (50, 7 × 3, 3 × 3, 2 × 10 ml.). The individual acid extracts were treated with sodium picrate solution. The first extracts gave 1.98 g. of a bright yellow picrate, m.p. 219–221° which, after recrystallization, proved to

be derived from the starting material (m.p. 225°). A further 1.30 g. of solid picrates was obtained, but no pure compounds were isolated.

o-Bis(β-hydroxyethyl)benzene. *o*-Phenylenediacetonitrile was converted to ethyl *o*-phenylenediacetate with sulfuric acid in ethanol (14). A solution of 8.0 g. of the ester in 40 ml. of anhydrous ether was added, in 20 minutes, to a stirred, cooled solution of 0.06 mole of lithium aluminum hydride in 150 ml. of ether. After stirring 30 minutes longer at room temperature and refluxing for 15 minutes, water and excess 9 *M* sulfuric acid were added and the aqueous layer was extracted several times with ether. The ether extract was washed with water and sodium bicarbonate solution, dried, and evaporated to leave an oil which subsequently crystallized. Recrystallization from benzene gave 4.8 g. (90%) of *o*-bis(β-hydroxyethyl)benzene, colorless needles, m.p. 61–62°. The compound was soluble in alcohol, ether, and water.

Anal. Calc'd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49.
Found: C, 72.40; H, 8.71.

The *bis-phenylurethan* crystallized from benzene as rectangular plates, m.p. 168–169°.

Anal. Calc'd for $C_{24}H_{24}N_2O_4$: N, 6.93. Found: N, 6.93.

o-Divinylbenzene was produced in 90% yield by the dehydration of *o*-bis(β-hydroxyethyl)benzene on potassium hydroxide. This method supplements previous preparations (15, 16) and may be more convenient. Molten *o*-bis(β-hydroxyethyl)benzene, 8.4 g., was added in 20 minutes to 10 g. of potassium hydroxide in a distilling-flask evacuated to 60 mm. and immersed in an oil-bath at 185°. Heating was continued for 20 minutes, to yield a mixture of water and a cloudy liquid in the receiving flask. Layer separation was completed in the centrifuge. Drying and distillation of the organic layer gave 5.9 g. of *o*-divinylbenzene, b.p. 80–82°/16 mm., n_D^{27} 1.5726, d_4^{22} 0.934, constants consistent with those previously reported.

An attempt to convert the diene to a bis-bromohydrin by a procedure which works well with styrene was not successful.

Bromination of o-diacetylbenzene. *o*-Diacetylbenzene was prepared by the controlled oxidation of *o*-ethylacetophenone according to Winkler (17). Yield, 23%; recovery of starting material, 29%; m.p. 41–42°, reported 39°.

The *o*-ethylacetophenone was prepared by the route described by Birch, *et al.* (18). This procedure, however, had been worked out independently in this laboratory with a somewhat better yield in the one step involving the action of the Grignard reagent on *o*-ethylbenzonitrile. To the Grignard reagent from 8.8 g. of magnesium and excess methyl iodide was added 25.4 g. of *o*-ethylbenzonitrile. Ether was boiled off and the residue was heated for 15 minutes on the steam bath (19, 20), after which ice and acetic acid was carefully added. The resulting mixture was heated for one hour on the steam-bath and the *o*-ethylacetophenone, b.p. 104–109°/17 mm., yield 24.5 g., was isolated in the usual way. Assay by hydroxylamine hydrochloride and pyridine (21) indicated 96% purity.

In glacial acetic acid at room temperature the reaction of *o*-diacetylbenzene with bromine is too rapid for proper control. When 0.005 mole of diketone in 10 ml. of $CHCl_3$ and 0.01 mole of bromine in 5 ml. of $CHCl_3$ were separately cooled to −25°, mixed, and permitted to warm up slowly, the color rapidly faded at −18°. Washing of the solution with ice-cold sodium bicarbonate solution and water, and removal of the solvent at 40° left an orange-brown oil. In an earlier, smaller run, slow crystallization from benzene had given two crystalline species which were separated mechanically. The more abundant crystalline form, m.p. 101°, was used to seed the crystallization of the colored oil to give 1.15 g. of solid, m.p. 90–97°. Repeated recrystallization from ethyl acetate and carbon tetrachloride gave 0.68 g. of colorless needles, m.p. 102–103°. The compound reacted rapidly with sodium iodide in acetone with iodine formation and was analyzed by means of the sodium bromide precipitated. It is therefore more probably *o*-bis(bromoacetyl)benzene although the isomeric ω,ω-dibromo-*o*-diacetylbenzene is not excluded.

Anal. Calc'd for $C_{10}H_8Br_2O_2$: Br, 49.95. Found: Br, 49.9.

The colorless compound turned black after standing for one week in the dark. Tars were obtained with hydroxylamine hydrochloride in aqueous methanol and with sodium ace-

tate in aqueous ethanol. Methylamine in ethanol gave a deep purple dye-like solution. Only amorphous materials were isolated after reaction with the potassium salt of *p*-toluenesulfonamide in methanol.

o-Acetylbenzoyl chloride. Reaction of *o*-acetylbenzoic acid for 12 hours with 10% excess thionyl chloride at room temperature gave a low-melting solid. Recrystallization from petroleum ether between room temperature and −70° gave a nearly quantitative yield, presumably of the acid chloride, m.p. 57–58°. The compound was hydrolyzed back to the acid by a warm sodium bicarbonate solution and gave with aniline and ammonia, respectively, in poor yields, the *anilide*, m.p. 158–160°, and the *amide*, m.p. 117–118°, reported by Karlslake and Huston (22). Reaction with cadmiummethyl yielded dimethylphthalide as the main product. Reports of failure to isolate a product from the treatment of *o*-acetylbenzoic acid with thionyl chloride (17) and phosphorus pentachloride (22) are probably related to the heat sensitivity of the acid chloride.

SUMMARY

Syntheses are reported as follows: *o*-phenylenediacetimide; 4-chloro-2,5-dihydro-3,1*H*-benzazepin-2-one; N-ethyl-2,3,4,5-tetrahydro-3,1*H*-benzazepine; N-methyl-2,3,4,5-tetrahydro-3,1*H*-benzazepine together with its picrate and hydrochloride; *o*-bis(β-hydroxyethyl)benzene and its bis-phenylurethan; *o*-acetylbenzoyl chloride; and a compound which is probably *o*-bis(bromoacetyl)benzene.

An alternative preparation of *o*-divinylbenzene is described.

Treatment of *o*-phenylenediacetimide with phosphorus oxychloride introduces one endocyclic double bond below 120°, but fails to produce 2,4-dichloro-3,1*H*-benzazepine at higher temperatures in competition with side reactions.

Dehydrogenation of N-methyl-2,3,4,5-tetrahydro-3,1*H*-benzazepine proceeds slowly, yielding one molecule of hydrogen and subsequently forming a mixture of weak bases.

ANN ARBOR, MICHIGAN

REFERENCES

(1) GABRIEL, *Ber.*, **19**, 1653 (1881).
(2) ZELINSKY AND JURJEW, *Ber.*, **62**, 2589 (1929).
(3) SCHMIDT, *Ber.*, **55**, 1584 (1922).
(4) VON BRAUN AND BARTSCH, *Ber.*, **45**, 3376 (1912).
(5) RUGGLI, BUSSEMACHER, MUELLER, AND STAUB, *Helv. Chim. Acta*, **18**, 1388 (1935).
(6) PERKIN, *J. Chem. Soc.*, **53**, 1 (1888).
(7) MOORE AND THORPE, *J. Chem. Soc.*, **93**, 175 (1908).
(8) PERKIN AND TITLEY, *J. Chem. Soc.*, **121**, 1562 (1922).
(9) COFFEY, *Rec. trav. chim.*, **42**, 387 (1923).
(10) BAKER, *J. Chem. Soc.*, 3247 (1945).
(11) CLARKE, GILLESPIE, AND WEISSHAUS, *J. Am. Chem. Soc.*, **55**, 4571 (1940).
(12) VON BRAUN AND REICH, *Ber.*, **58**, 2765 (1925).
(13) ZELINSKY AND BORISOFF, *Ber.*, **57**, 150 (1924).
(14) *Org. Syntheses*, Coll. Vol. I, 2nd ed., 270 (1941).
(15) DELUCHAT, *Ann. chim.* [11], **1**, 181 (1934).
(16) FRIES AND BESTIAN, *Ber.*, **69**, 715 (1936).
(17) WINKLER, *Chem. Ber.*, **81**, 256 (1948).
(18) BIRCH, DEAN, FIDLER, AND LOWRY, *J. Am. Chem. Soc.*, **71**, 1362 (1949).
(19) REICHSTEIN, GRUESSNER, AND ZSCHOKKE, *Helv. Chim. Acta*, **15**, 1066 (1932).
(20) BORSCHE AND WAGNER-ROEMICH, *Ann.*, **546**, 273 (1941).
(21) SIGGIA, *Quantitative Organic Analysis via Functional Groups*, John Wiley and Sons, New York, 1949.
(22) KARLSLAKE AND HUSTON, *J. Am. Chem. Soc.*, **31**, 479 (1909).