[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF STANFORD UNIVERSITY]

The Action of Bases on Organic Halogen Compounds. IV. The Action of the Lithium Salts of Aliphatic Amines on some Organic Halogen Compounds

BY C. H. HORNING[1] AND F. W. BERGSTROM

Aromatic amines are formed in fair yield by the action of a solution of an alkali amide upon an aryl halide in liquid ammonia,[2,3] but this reaction is sometimes accompanied by a rearrangement to the ortho position.[3] In the present article is reported the results of a preliminary investigation of the action of lithium dialkylamides (the lithium alcoholates of the ammonia system) on a number of aliphatic and aromatic halides dissolved in diethyl ether.

Lithium dialkylamides may readily be made by the method of Ziegler and Ohlinger[4] who added a dialkylamine to a solution of phenyllithium or butyllithium in ether, or by the procedure of Gilman and co-workers[3c] who used methyllithium.

n-Butyl bromide reacts with lithium diethylamide to give diethyl-*n*-butylamine in 51% yield. Ethyl iodide is converted to ethylene and a tar, while methyl iodide seems to give tar exclusively.

Chlorobenzene and bromobenzene both react with lithium diethylamide to form diethylaniline in yields of 35–56%, that is to say, of the same magnitude as the ones recently reported by Gilman and his co-workers.[3c] The lithium salts of di-*n*-butylamine and of piperidine behave similarly to yield, respectively, di-*n*-butylaniline and N-phenylpiperidine. *p*-Chlorotoluene reacts somewhat more slowly than do the phenyl halides with lithium diethylamide to give a diethylaminotoluene, which seems largely to be the para compound, though its homogeneity has not been established. Weaker bases of the type of triphenylmethyllithium or lithium acetonitrile do not react with the aryl halides in ether at ordinary temperatures.

It is interesting to find that N-phenylpiperidine may be prepared in 70% yield (see equation 1) by refluxing metallic lithium with phenyl bromide in anhydrous piperidine as a solvent. Phenyllithium is presumably an intermediate.

$$2C_6H_5Br + 2Li + C_5H_{10}NH = 2LiBr + C_6H_5NC_5H_{10} + C_6H_6 \quad (1)$$

One half of the aryl halide is converted to the corresponding hydrocarbon. It has long been known[5] that sodium reacts with a solution of phenyl chloride in liquid ammonia to form benzene, di- and triphenylamines.

Experimental

The general method of carrying out the reaction between a lithium dialkylamide and an aryl or alkyl halide is described below.

An ethereal solution of phenyllithium (about 300 cc.) was prepared in a 500-cc. 3-necked round-bottomed flask, equipped with a mercury-sealed stirrer, a dropping funnel and a reflux condenser, following the method of Gilman, Zoellner and Shelby (a nitrogen atmosphere was maintained in the flask, though this may not have been necessary).[6] The dialkylamine (about 1.25 equivalents) was added with stirring, followed in about half an hour by the aryl or alkyl halide. Stirring was continued for the time specified in Table I, after which water (100 cc.) was intro-

TABLE I

THE ACTION OF LITHIUM DIALKYLAMIDES ON ALKYL- AND ARYL HALIDES

All temperatures are uncorrected and all boiling points were determined at about 760 mm. unless otherwise noted.

Halide, mole	Lithium, dialkylamide, mole	Time of reaction, hr.	Product	Yield, %	Notes
n-C_4H_9Br, 0.25	$LiNEt_2$, 0.25	1	*n*-$C_4H_9NEt_2$	53	[a]
C_6H_5Cl, 0.33	$LiNEt_2$, 0.33	1	$C_6H_5NEt_2$	56	[b]
C_6H_5Br, 0.50	$LiNEt_2$, 0.50	1	$C_6H_5NEt_2$	44	[b]
C_6H_5Br, 0.25	$LiNC_5H_{10}$, 0.14	2	$C_6H_5NC_5H_{10}$	42	[c]
C_6H_5Br, 0.33	$LiN(C_4H_9\text{-}n)_2$, 0.33	2	$C_6H_5NBu_2$	36	[d]
p-$CH_3C_6H_4Cl$, 0.20	$LiNEt_2$, 0.20	4.5	$CH_3C_6H_4NEt_2$	21	[e]

[a] Boiling point, 136–139°. Ethyl iodide was added to a benzene solution of the amine and allowed to stand for thirty-six hours. White crystals separated from the cooled benzene solution, after concentration. *Anal.* Calcd. for $C_4H_9(C_2H_5)_3NI$: I, 44.5. Found: I, 44.9. [b] The yields were somewhat variable and were often around 35%. The diethylaniline boiled at 210–218°, and was identified by its refractive index (lit. 1.5410; found, two expts., 1.5439, 1.5488), and as its *p*-bromo derivative, m. p. 32–33° [33°, Claus and Howitz, *Ber.*, **17**, 1327 (1884)]. Miss Stelck (Thesis, Stanford University) obtained a 30.5% yield of diethylaniline in this reaction. [c] The N-phenylpiperidine boiled at 245–255° and was identified as the picrate, m. p. 145–146° [148°, von Braun, *Ber.*, **40**, 3920 (1907)]. The yield is calculated on the basis of the piperidyllithium. [d] B. p. 255–275°; picrate, m. p. 122–123° [125°, Reilly and Hickinbottom, *J. Chem. Soc.*, **113**, 103 (1918)]. Miss Stelck (Thesis, Stanford University) obtained a 42% yield of di-*n*-butylaniline in repeating this work. [e] B. p. 223–229°; hydrochloride, m. p. 154–156°. The m. p. of the hydrochloride of diethyl-*p*-toluidine is 157° [Schmidt, *J. prakt. Chem.*, (2) **48**, 48 (1893)]. It was not determined whether or not the *o*- and *m*-isomers were present.

---

(1) From the Doctor's thesis of C. H. Horning; *cf. Chem. Rev.*, **20**, 437 (1937).

(2) (a) Bergstrom, Wright, Chandler and Gilkey, *J. Org. Chem.*, **1**, 170–178 (1936); (b) Wright and Bergstrom, *ibid.*, **1**, 179–188 (1936); (c) C. H. Horning, Thesis, Stanford University 1939.

(3) (a) Gilman and Avakian, THIS JOURNAL, **67**, 349–351 (1945); (b) Urner and Bergstrom, *ibid.*, **67**, 2108 (1945); (c) Gilman and co-workers, *ibid.*, **67**, 2106 (1945).

(4) Ziegler and Ohlinger, *Ann.*, **495**, 84–112 (1932), and numerous patents documented in *Chem. Rev.*, **20**, 451–452 (1937).

(5) G. F. White, THIS JOURNAL, **45**, 779–784 (1923).

(6) Gilman, Zoellner and Shelby, *ibid.*, **55**, 1252–1257 (1933).

duced. The ether layer was separated, dried over potassium hydroxide and slowly run into a small warmed flask through a dropping funnel, in such a manner as to get rid of the ether by distillation without having too large a container for the amine. The residual products were generally distilled at atmospheric pressures.

We have obtained 2-diethylaminoquinoline by the action of lithium diethylamide on 2-chloroquinoline, in agreement with the results of Gilman and co-workers.[3c] Triphenylmethyllithium, prepared by treating an ethereal solution of lithium diethylamide with triphenylmethane, did not react with phenyl bromide in two days in ether at room temperatures, nor was any phenylacetonitrile similarly formed from the lithium salt of acetonitrile and bromobenzene.

N-Phenylpiperidine.—Piperidine (45 g., dried over sodium ribbon and distilled) and bromobenzene (18.1 g.) were placed in a 500-cc. 3-necked flask with ground joints. A reflux condenser and a mercury-sealed stirrer were attached to the flask; the third opening, used for the introduction of lithium, was closed with a glass stopper.

Lithium (0.923 g. in several small slices) was introduced and the mixture refluxed gently for three hours; 0.055 g. of the metal was recovered unchanged at the end. The flask was then heated in an oil-bath and most of the piperidine boiled off and condensed; a solid, probably $LiBr\cdot xC_5H_{10}NH$, remained. Water was added, after cooling, and the resulting aqueous solution and oil extracted several times with benzene. The latter was distilled to obtain N-phenylpiperidine, b. p. 245–255°, in a yield of 6.4 g., or 70%, based on equation (1).

N,N-Diethylaniline.—In a similar fashion, N,N-diethylaniline (b. p. 207–212°) was obtained in 33% yield from bromobenzene, diethylamine and lithium. The reaction was much more rapid than in the preceding case, but was greatly hindered at the end by the formation of a coating of $LiBr\cdot x(C_2H_5)_2NH$ over the lithium.

Summary

Lithium diethylamide, lithium N-piperidyl- and lithium di-*n*-butylamide react with phenyl chloride or phenyl bromide in ether at ordinary temperatures to form diethylaniline, N-phenylpiperidine and di-*n*-butylaniline, respectively. Metallic lithium reacts with phenyl bromide in piperidine or in diethylamine to give N-phenylpiperidine or N,N-diethylaniline, respectively.

STANFORD UNIVERSITY, CALIF.

RECEIVED SEPTEMBER 14, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WASHINGTON UNIVERSITY]

A Comparison between Certain Reactions of the Aloins and those of Glucose

BY JOHN H. GARDNER[1]

Some years ago, it was shown that, under a variety of conditions, the aloins yield formaldehyde and furfural, although in extremely small amounts.[2] The formation of formaldehyde from glucose and other sugars during the distillation of neutral, acid and alkaline solutions was reported earlier by Klein,[3] and Rosenthaler[4] obtained it as a product of the oxidation of glucose and other sugars and of barbaloin with potassium permanganate in the presence of sulfuric acid. An indication of the possible formation of furfural from a mixture of sucrose and invert sugar was obtained by Englis and Hale.[5] It has now been found that glucose, like the aloins, yields a very small quantity of formaldehyde on treatment with sodium perborate, with a considerable increase when the reaction is followed by acidification to 12% hydrochloric acid before distillation. The acidified solution also yields furfural. With borax alone, glucose gives only a trace of formaldehyde and no furfural. When the borax hydrolyzate is adjusted to 12% hydrochloric acid before distillation, both furfural and formaldehyde are found in the distillate. The aloins gave formaldehyde from the acidified hydrolyzate only, and no furfural after borax hydrolysis with or without acidification. Glucose also yields both formaldehyde and furfural on distillation with 12% hydrochloric acid.

The glucose was Mallinckrodt C. P. anhydrous. The hydrolyses were carried out with the same concentrations and conditions that were previously used for the decompositions of the aloins.[2] Formaldehyde was detected as formaldimethone which was dried, weighed and then recrystallized from alcohol. The purified samples all melted between 188 and 191°, and showed no depression in melting point when mixed with an authentic sample of formaldimethone, m. p. 189–191°. Furfural was detected by the addition of a freshly prepared, filtered solution of 1 g. of 2,4-dinitrophenylhydrazine in 10 cc. of concd. hydrochloric acid and 60 cc. of water. The precipitate was filtered out, dried and weighed. For proof of identity, the product was converted into furfural acetyl 2,4-dinitrophenylhydrazone,[6] since Bredereck has shown that furfural 2,4-dinitrophenylhydrazone is commonly formed as a mixture of two stereoisomers with no definite melting point. We have found indications that the same thing is true of the *p*-nitrophenylhydrazone. The products obtained from the glucose hydrolyzates melted between 166 and 172°, showing no depression when mixed with an authentic sample of furfural acetyl 2,4-dinitrophenylhydrazone, m. p. 171–171.5°. The results of the individual experiments, together with the earlier results of Gardner and Campbell on aloin, are collected in Table I.

---

(1) Present address, J. T. Baker Chemical Co., Phillipsburg, N. J.

(2) J. H. Gardner and J. A. Campbell, THIS JOURNAL, **64**, 1378 (1942).

(3) G. Klein, *Biochem. Z.*, **169**, 132 (1926).

(4) L. Rosenthaler, *Arch. Pharm.*, **251**, 587 (1913).

(5) D. T. Englis and C. Hale, THIS JOURNAL, **47**, 446 (1925).

(6) H. Bredereck, *Ber.*, **65**, 1833 (1932).