NOTES

The Hofmann Degradation of Glutaramide

By Samuel R. Aspinall

Although the Hofmann degradation has been used widely to prepare simple monoamines, its use to prepare diamines has been exploited but little. Urea, and presumably oxamide, yield elementary nitrogen when treated with alkaline hypobromite; while the use of malonamide is excluded because the anticipated product, methylenediamine, is unknown in the pure condition. Van Dam[1] states that bromine reacts on succinamide to yield a dibromo compound, but treatment of the latter with potassium or barium hydroxide fails to yield ethylenediamine, ammonia being the sole volatile product. The only records of the conversion of a diamide to a diamine by the Hofmann degradation are contained in German Patent No. 232,072 and an investigation by Von Braun and Lemke[2] which state that sodium hypohalite converts adipamide to tetramethylenediamine.

When a sample of trimethylenediamine was needed recently in this Laboratory it was found possible to prepare it easily and in good yield by the Hofmann degradation of glutaramide.

Experimental

One mole (130 g.) of pure glutaramide (prepared by ammonolysis of the ester in the usual way) was dissolved at 0° in a solution of 2 moles (320 g.) of bromine and 10 moles (660 g.) of 85% of potassium hydroxide in 3 liters of water. The solution was allowed to come to room temperature, heated at 60° for two hours, acidified with hydrochloric acid and evaporated to a small volume. The large mass of inorganic salt was filtered, washed with acetone and the filtrates evaporated to a paste. An excess of crude potassium hydroxide was mixed into the paste and a water solution of the amine was distilled, dried over metallic sodium and redistilled. It was finally obtained as a pure, water-white liquid boiling at 131° (uncor.) at 760 mm. by fractionation through a Vigreux column from a fresh piece of sodium. The yield was 56 g. (75% of theoretical). The amine was further identified as the derivatives tabulated below.

Table I

Derivatives of Trimethylenediamine

Derivative	Formula	M. p., °C.	Recrystn. solvent	Nitrogen, % Calcd.	Found, Kjeld. I	II
Dipicrate	$(HPic.NH_2CH_2)_2CH_2$	250^a	H_2O	21.05	21.10	21.00
Diphenylcarbonamido-	$(C_6H_5NHCONHCH_2)_2CH_2$	215^b	aq. EtOH	17.94	17.97	18.04
Dibenzoyl-	$(C_6H_5CONHCH_2)_2CH_2$	140^c	aq. EtOH	9.93	9.90	9.69

[a] (uncor.) With decomposition. [b] (cor.). [c] (cor.) Literature 147–8° (*Ber.* **21**, 2365 (1888)).

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[1] Van Dam, *Rec. trav. chim.*, **15**, 102 (1896).

[2] Von Braun and Lemke, *Ber.*, **55**, 3526 (1922).

The Reductive Alkylation of Hindered Aromatic Amines. II

By William S. Emerson[1] and E. L. Ringwald

In continuing a study of the reductive alkylation of hindered aromatic amines,[2] two additional halogenated amines have been examined for dehalogenation accompanying alkylation.[2a]

When 4-iodo-2,6-dibromoaniline was refluxed with zinc, hydrochloric acid and formaldehyde in glacial acetic acid, all of the halogen was removed and the amine was smoothly methylated to give N,N-dimethylaniline. While this removal from the para position showed iodine to be more reactive than bromine in these reactions, chlorine was found to be far less reactive. Under these same conditions, the reductive alkylation of 2,4-dichloro-1,3-diaminobenzene produced the tetramethyl derivative, no chlorine having been removed by the amalgamated zinc and hydrochloric acid.

Experimental

Reductive Alkylation of 2,6-Dibromo-4-iodoaniline.—After a mixture of 15 g. of 2,6-dibromo-4-iodoaniline,[3] 200

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[1] Present address: Monsanto Chemical Co., Dayton, Ohio.

[2] (a) Emerson, Dorf and Deutschman, This Journal, **62**, 2159 (1940); (b) Emerson, Neumann and Moundres, *ibid.*, **63**, 972 (1941).

[3] Sudborough and Lakhumalani, *J. Chem. Soc.*, **111**, 41 (1917).

cc. of glacial acetic acid, 25 cc. of 40% aqueous formaldehyde and 100 g. of amalgamated zinc had been heated to boiling, 200 cc. of concentrated hydrochloric acid was added over a three-hour period. Refluxing was continued for twenty-one hours more. The mixture was then cooled and the excess hydrochloric acid neutralized with sodium hydroxide before extraction with four 100-cc. portions of benzene. After the benzene was distilled from the combined extracts, the dimethylaniline distilled at 120-125° (23 mm.); yield, 3.9 g. (81%). It was identified as the picrate, m. p. 162-163° (163°).

4,6-Dichloro-1,3-diaminobenzene was obtained in 69% yield by boiling the diacetyl derivative[4] with 50% sulfuric acid for twelve hours. It was crystallized once from alcohol, m. p. 138-139° (136-137°).[4]

4,6-Dichloro-1,3-bis-dimethylaminobenzene.—When 15 g. of 4,6-dichloro-1,3-diaminobenzene was substituted for the 2,6-dibromo-4-iodoaniline in the above procedure, the product was 14 g. (71%) of 4,6-dichloro-1,3-bis-dimethylaminobenzene. It was crystallized five times from benzene, m. p. 222-223°.

Anal. Calcd. for $C_{10}H_{14}N_2Cl_2$: N, 12.0; Cl, 30.4. Found: N, 12.2; Cl, 30.0.

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[4] Morgan, *J. Chem. Soc.*, **77**, 1202 (1900).

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Introduction of Amino-Aryl Groups by the Halogen-Metal Interconversion Reaction[1]

BY HENRY GILMAN AND C. G. STUCKWISCH

The present study is an extension[2] of procedures for the introduction of water-solubilizing groups, particularly into organometallic and organometalloidal compounds.

When an ether solution of *p*-bromoaniline is allowed to react for several minutes with *n*-butyllithium; halogen-metal interconversion takes place to an extent of at least 68%: $p\text{-}NH_2C_6H_4Br + n\text{-}C_4H_9Li \rightarrow p\text{-}NH_2C_6H_4Li + n\text{-}C_4H_9Br$.[3] The yield of the *p*-aminophenyllithium derivative was determined by weighing the *p*-aminobenzoic acid obtained by carbonation; and the yield reported is minimal, for carbonation of RLi compounds is accompanied by appreciable ketone formation.[4]

Then, without isolation, the RLi derivative was treated with phenylarsenic dichloride to give a 91% yield of phenyl-di-(*p*-aminophenyl)-arsenic.

$$C_6H_5AsCl_2 + 2LiC_6H_4NH_2\text{-}p \longrightarrow C_6H_5As(C_6H_4NH_2\text{-}p)_2 + 2LiCl$$

The aminophenylarsenic compound with *p*-acetaminobenzenesulfonyl chloride gave the corresponding N^4-acetylsulfanilamidophenylarsenic compound (96% yield); and this on hydrolysis gave the *p*-sulfanilamidophenylarsenic compound.

Related transformations, in equally satisfactory yields, were effected starting with phenylphosphorus dichloride and the *p*-aminophenyllithium derivative. On the basis of other halogen-metal interconversion reactions, the reaction can undoubtedly be extended to the introduction of a variety of amino-aryl groups, as well as to types like $NH_2(CH_2)_nC\equiv CH$. The introduction of *p*-aminophenyl groups is of particular significance because of the unavailability of direct nuclear substitution reactions for introducing a *p*-amino group in the types described.

Experimental

Reaction of *p*-Bromoaniline with *n*-Butyllithium.—To a solution of 0.15 mole of *n*-butyllithium in 200 cc. of ether, cooled to −60° in a solid carbon dioxide-acetone bath, was added 8.6 g. (0.05 mole) of *p*-bromoaniline. After three, six, nine and twelve minute intervals, 50-cc. aliquots were withdrawn and each was carbonated by pouring on crushed solid carbon dioxide. The copper salt of *p*-aminobenzoic acid was isolated, and from the salt was obtained (by treatment with hydrogen sulfide) the *p*-aminobenzoic acid. The yields of acid were: 28% (3 min.); 38.4% (6 min.); 68% (9 min.); and 51% (12 min.). The yield of the *p*-aminophenyllithium derivative probably can be increased by an examination of other factors involving halogen-metal interconversion reactions.[5]

Reaction with Phenylarsenic Dichloride.—To a solution of 0.3 mole of *n*-butyllithium in 500 cc. of ether, cooled to −60° in a solid carbon dioxide-acetone bath, was added 17.2 g. (0.10 mole) of *p*-bromoaniline. After nine minutes, 11.1 g. (0.05 mole) of phenylarsenic dichloride[6] in 50 cc. of ether was added dropwise over a five-minute period. At the end of this time the bath temperature was allowed to rise to −45°. After removing the cooling bath, the solution was heated to reflux, held there for one hour, cooled, and then hydrolyzed by the dropwise addition of 10% hydrochloric acid. The basic material was precipitated from the aqueous hydrochloric acid layer by 30% sodium hydroxide solution. After crystallization from 50% ethanol, the phenyl-di-(*p*-aminophenyl)-arsenic melted at 69°. The yield was 10.8 g. or 91%, based on a 70% interconversion of *p*-bromoaniline.

Anal. Calcd. for $C_{18}H_{17}N_2As$: As, 22.8. Found: As, 22.3.

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[1] Paper XLIII in the series "Relative Reactivities of Organometallic Compounds." The preceding paper is in THIS JOURNAL, **63**, (1941).

[2] Some related recent studies are: Gilman and Banner, *ibid.*, **62**, 344 (1940); Gilman and Spatz, *ibid.*, **62**, 446 (1940); **63**, 1553 (1941); Gilman, Willis, Cook, Webb and Meals, *ibid.*, **62**, 667 (1940); Gilman and Moore, *ibid.*, **62**, 1843 (1940); Gilman and Cook, *ibid.*, **62**, 2813 (1940).

[3] Three equivalents of *n*-butyllithium were used to take care of the active hydrogens on the amino group. It is at present unknown whether both active hydrogens are replaced by lithium under these mild conditions.

[4] Gilman and Van Ess, THIS JOURNAL, **55**, 1258 (1933).

[5] Gilman and Moore, *ibid.*, **62**, 1843 (1940); Gilman, Moore and Baine, *ibid.*, **63**, 2479 (1941).

[6] Pope and Turner, *J. Chem. Soc.*, **117**, 1447 (1920).