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).

Phenyl-di-(*p*-N^4-acetylsulfanilamidophenyl)-arsenic.—To a solution of 3.36 g. (0.01 mole) of phenyl-di-(*p*-aminophenyl)-arsenic in 30 cc. of acetone was added 5.9 g. (0.025 mole) of *p*-acetaminobenzenesulfonyl chloride and 5 cc. of pyridine.[7] After standing for three hours the mixture was diluted with 500 cc. of water, and the oil which separated crystallized on standing. The crystals were washed successively with 5% sodium carbonate solution, 10% hydrochloric acid and water. Recrystallization from 30% ethanol gave 7 g. or a 96% yield of phenyl-di-(*p*-N^4-acetylsulfanilamidophenyl)-arsenic melting at 184°.

Anal. Calcd. for $C_{34}H_{31}O_6N_4S_2As$: N, 7.68. Found: N, 7.72.

Phenyl-di-(*p*-sulfanilamidophenyl)-arsenic.—The acetyl derivative was hydrolyzed by boiling 3.6 g. (0.005 mole) with 1 g. of sodium hydroxide in 15 cc. of water for one hour. The resulting 2.7 g. (84%) of crude hydrolysis product was recrystallized from 95% ethanol; m. p. 198°.

Anal. Calcd. for $C_{30}H_{27}O_4N_4S_2As$: N, 8.68. Found: N, 8.80.

Reaction with Phenylphosphorus Dichloride.[8]—*p*-Aminophenyllithium, prepared from 0.198 mole of *n*-butyllithium and 11.35 g. (0.066 mole) of *p*-bromoaniline, was allowed to react with 6 g. (0.033 mole) of phenylphosphorus dichloride under conditions identical with those described for the corresponding arsenic compound. The phenyl-di-(*p*-aminophenyl)-phosphorus, which separated as an oil upon neutralization of the aqueous hydrochloric acid extract, was extracted with ether, the ether solution dried over sodium sulfate, and the amine hydrochloride precipitated with hydrogen chloride. Since the hydrochloride was extremely hygroscopic and difficult to handle as such, it was suspended in dilute ammonium hydroxide. The amine was again extracted with ether and the ether removed by distillation. Distillation of the amine at 2 mm. could not be accomplished without decomposition. The yield of amine was 6 g. or 93%, based on a 70% interconversion of *p*-bromoaniline.

Anal. Calcd. for $C_{18}H_{17}N_2P$: P, 10.9. Found: P, 11.2.

Phenyl-di-(*p*-N-acetylaminophenyl)-phosphorus.—The diacetyl derivative of phenyl-di-(*p*-aminophenyl)-phosphorus, prepared by a Schotten–Baumann reaction using acetic anhydride and sodium hydroxide, melted at 169° after recrystallization from 50% ethanol.

Anal. Calcd. for $C_{22}H_{21}O_2N_2P$: N, 7.6. Found: N, 7.42.

Phenyl-di-(*p*-N^4-acetylsulfanilamidophenyl)-phosphorus.—The disulfanilamido derivative, prepared in 94% yield by a procedure similar to that used for the synthesis of the analogous arsenic compound, melted at 186–187°, after recrystallization from 30% ethanol.

Anal. Calcd. for $C_{34}H_{31}O_6N_4S_2P$: P, 4.5. Found: P, 4.72.

Phenyl-di-(*p*-sulfanilamidophenyl)-phosphorus.—The diacetyl derivative was hydrolyzed by boiling 4 g. (0.0058 mole) with 1 g. of sodium hydroxide in 25 cc. of water. Neutralization of the alkaline solution gave 3 g. (86%) of the free amine. Recrystallization from 95% ethanol gave a product melting at 202–204°.

Anal. Calcd. for $C_{30}H_{27}O_4N_4S_2P$: N, 9.3. Found: N, 9.46.

It is of interest to note that a mixed melting point of the analogous arsenic and phosphorus compounds, melting at 198° and 202–204°, respectively, showed no depression.

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The Fries Rearrangement of Esters of Hindered Acids

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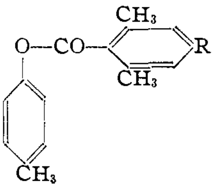
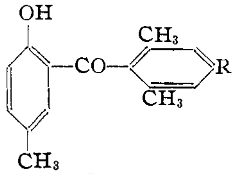
The mechanism suggested by Skraup and Poller[1] for the Fries rearrangement of aryl esters involves preliminary fission to the corresponding phenol and acid chloride. If the cleavage involves preliminary addition to the carbonyl group, steric hindrance might be expected to suppress it.

To test this idea we have heated *p*-tolyl 2,6-xylate (I, R = H) and *p*-tolyl mesitoate (I, R = CH_3) with aluminum chloride. Rearrangement took place in each case; the methyl groups ortho to the ester group had no marked effect on the ease or extent of the reaction.



I



II

Experimental

***p*-Tolyl 2,6-Xylate.**—To 3 g. of *p*-cresol was added 4.6 g. (0.025 mole) of 2,6-dimethylbenzoyl chloride. Hydrogen chloride was evolved and the reaction mixture became hot. It was shaken until the evolution of hydrogen chloride ceased, then poured into 50 cc. of a 10% sodium hydroxide solution. The upper layer was extracted with ether, and the ether solution was washed several times with water and dried over magnesium sulfate. The ester crystallized from methanol in long, white needles; yield 4.8 g.; m. p. 62.5–63°.

Anal.[2] Calcd. for $C_{16}H_{16}O_2$: C, 79.96; H, 6.72. Found: C, 80.06; H, 6.77.

***p*-Tolyl Mesitoate.**—This ester was made by a procedure similar to the foregoing. After crystallization from alcohol, it melted at 73°; yield, 85% of the theoretical amount.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.27; H, 7.13. Found: C, 80.29; H, 7.10.

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(7) Winterbottom, THIS JOURNAL, **62**, 160 (1940).

(8) The authors are grateful to Mr. G. E. Brown for the phenylphosphorus dichloride.

(1) Skraup and Poller, *Ber.*, **57**, 2033 (1924).

(2) Microanalyses by Mr. L. G. Fauble and Miss Mary S. Kreger.