hydrazone) was added, with stirring, to a solution of 2 ml. of glacial acetic acid in 5 ml. of benzene. The red color of the bisdiazo compound was discharged instantaneously. The reaction mixture was extracted twice with aqueous sodium bicarbonate and the aqueous layers were backwashed with ether. The ether–benzene solution was dried (magnesium sulfate) and evaporated to give a yellow oil which solidified upon standing in the refrigerator. This solid was recrystallized from pentane to give white crystals with an infrared band at 5.70 μ and m.p. 45–49°, lit.[12] m.p. 47°. The yield was 0.10 g. (11.4%).

1,4-Bis(α-diazomethyl)benzene Bisphosphazine (VII).—A solution of 1,4-bis(α-diazomethyl)benzene (prepared from 0.958 g., 5.9 mmoles of dihydrazone) in 125 ml. of benzene was added, over a period of 5 hr., to a solution of 3.04 g. (11.5 mmoles) of triphenylphosphine in 50 ml. of benzene. The system was under a nitrogen atmosphere and the reaction solution was magnetically stirred. The bisphosphazine, which precipitated as a yellow solid, was filtered off and washed with dry ether. A nitrogen atmosphere was maintained over the filter funnel to prevent moisture from decomposing the bisphosphazine. The solid was recrystallized from ether–chloroform and dried *in vacuo;* it had m.p. 192–195° dec. The yield was 1.20 g. (30%).

Anal. Calcd. for $C_{44}N_{36}N_4P_2$: C, 77.5; H, 5.3; N, 8.22. Found: C, 77.7; H, 5.4; N, 7.82.

4,4′-Dibenzoylbiphenyl.—To a stirred slurry of 79.8 g. (0.6 mole) of aluminum chloride in 150 ml. of carbon disulfide, heated to gentle reflux, was added dropwise a solution of 69.2 ml. (84.6 g., 0.6 mole) of benzoyl chloride in 50 ml. of carbon disulfide. A solution of 20 g. (0.13 mole) of biphenyl in 60 ml. of carbon disulfide then was added to the stirred mixture over a period of 6 hr. The dark-colored reaction mixture then was poured into ice-cold concentrated hydrochloric acid. The reaction mixture was extracted with methylene chloride. The extracts were washed with dilute aqueous sodium hydroxide, dried (magnesium sulfate), and evaporated to give a white solid. This solid was recrystallized from ethanol to give pearl-white plates, m.p. 214–216°, lit.[13] m.p. 216°. The yield was 2.34 g. (4.96%). The major product of the reaction mixture was monobenzoyl biphenyl.

4,4′-Dibenzoylbiphenyl Dihydrazone.—A solution of 1.94 g. (5.38 mmoles) of 4,4′-dibenzoylbiphenyl, 125 ml. of absolute ethanol, and 33.7 g. of 95% hydrazine (32.0 g., 1.0 mole hydrazine) was refluxed under argon for 24 hr. The solution was concentrated on the rotary evaporator and stored in the refrigerator. The tan-colored solid which formed was filtered off and recrystallized from benzene–cyclohexane. The white crystals formed had m.p. 200–203° (taken rapidly).

Anal. Calcd. for $C_{26}H_{22}N_4$: C, 80.0; H, 5.7; N, 14.4. Found: C, 80.4; H, 5.9; N, 14.0.

4,4′-Bis(α-diazobenzyl)biphenyl (IV).—An erlenmeyer flask was charged with 0.39 g. (1 mmole) of 4,4′-dibenzoylbiphenyl dihydrazone, 100 ml. of anhydrous ether, 5 g. of sodium sulfate, 0.86 g. (10 mmoles) of manganese dioxide, and 0.5 ml. of ethanol saturated with potassium hydroxide. The reaction mixture was stirred vigorously for 70 min. The reaction mixture was filtered and the ether was evaporated to give a sticky red solid, which when triturated with methylene chloride gave red crystals, m.p. 132–134° dec. The crystals were dichroic and had a strong infrared band at 4.81 μ.

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(12) E. Grimaux, *Ann.*, **155**, 342 (1870).

(13) W. Schlenk and M. Brauns, *Ber.*, **48**, 716 (1915).

Reactions of Indoles with Benzyne

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The postulation of benzyne has led to numerous investigations designed to prove the existence of this short-lived intermediate and to establish factors which affect is generation from precursors such as monohalobenzenes, *o*-dihalobenzenes, diphenyliodonium salts, *o*-benzenediazonium carboxylate, 1,2,3-benzothiadiazole 1,1-dioxide, di-*o*-iodophenylmercury, and *o*-chlorobenzophenone.[1] However, less attention has been given to the exploration of benzyne chemistry from the point of view of arylation reactions on carbon, which might be of synthetic interest. Thus, the only reports are on the arylation of carbanions derived from compounds with acidic hydrogen,[2] particularly in cyclization reactions,[3] the addition to olefins,[4] acetylenes,[5] and reactive dienes,[6] and the benzyne arylation of enamines.[7] This paper describes a partially successful attempt to extend this aspect of benzyne chemistry.

Indoles, like enamines, present a bidentate system to electrophiles, which may be attacked on nitrogen or on carbon at the 3-position. When benzyne (I) was generated from bromobenzene with sodium amide in liquid ammonia in the presence of the sodium salt of indole (IIa), N-phenylindole (III, 5%) and 3-phenylindole (IV, 15%) were formed, together with aniline, diphenylamine, and triphenylamine. Under the same conditions, benzyne formation in the presence of N-methylindole (V) did not lead to any N-methyl-3-phenylindole (VI) but only to the aryl amines derived from reaction of benzyne with the solvent.

The reaction products were identified by thin layer and vapor phase chromatographic comparison with authentic samples. Isolation of 3-phenylindole (IV), triphenylamine, and aniline (as picrate) was accomplished by preparative column chromatography.

Benzyne arylation of the indole sodium salt on nitrogen and predominantly on carbon may be contrasted with the corresponding methylation which leads only to nitrogen alkylation under the same conditions.

When the indole lithium salt (IIb) was treated with benzyne (I), generated from *o*-bromofluorobenzene and magnesium in tetrahydrofuran, N-phenylindole (III, 0.5%), 3-phenylindole (IV, 1%), and 2,3-phenylenedihydroindole (VII, 8%) were formed. N-Methylindole (V) and benzyne, generated under the same conditions, produced N-methyl-3-phenylindole (VI, 4%).

In the absence of a proton source, nucleophilic attack of the phenyl anion on the indolenine system of the intermediate VIII leads to the more stable anilide anion, corresponding to 2,3-phenylenedihydroindole (VII), which is then protonated on work-up. With the N-methyl immonium salt IX, abstraction of a more acidic proton and generation of 3-phenylindole (VI) is preferred over cyclization to a dihydroindole.

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(1) For reviews, see G. Wittig, *Angew. Chem.*, **69**, 245 (1957); G. Wittig, *ibid.*, **74**, 479 (1962); R. Huisgen and J. Sauer, *ibid.*, **72**, 91 (1960); E. F. Jenny, M. C. Caserio, and J. D. Roberts, *Experientia*, **14**, 349 (1958); J. F. Bunnet, *Quart. Rev.* (London), **12**, 1 (1958); H. Heany, *Chem. Rev.*, **62**, 2 (1962); J. F. Bunnet and B. F. Hrutfiord, *J. Org. Chem.*, **27**, 4152 (1962); R. S. Berry, G. N. Spokes, and M. Stiles, *J. Am. Chem. Soc.*, **84**, 3570 (1962); and E. LeGoff, *ibid.*, **84**, 3786 (1962).

(2) F. W. Bergstrom and R. Agostinho, *ibid.*, **67**, 2152 (1945); W. W. Leake and R. Levine, *ibid.*, **81**, 1169, 1627 (1959); P. H. Dirstine and F. W. Bergstrom, *J. Org. Chem.*, **11**, 55 (1946); F. Scardiglia and J. D. Roberts, *Tetrahedron*, **3**, 197 (1958).

(3) J. F. Bunnett and B. F. Hrutfiord, *J. Am. Chem. Soc.*, **83**, 1691 (1961); J. F. Bunnett and J. A. Skorcz, *J. Org. Chem.*, **27**, 3836 (1962); J. F. Bunnett, *ibid.*, **28**, 1 (1963).

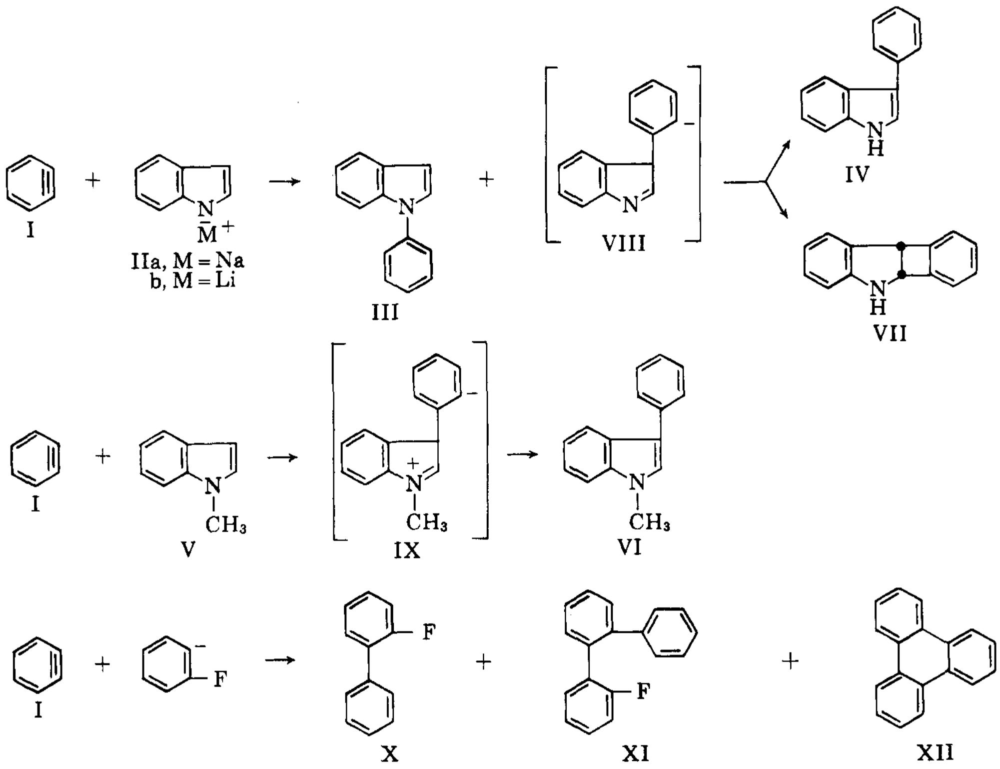
(4) H. E. Simmons, *J. Am. Chem. Soc.*, **82**, 1657 (1961).

(5) M. Stiles, U. Burckhardt, and A. Haag, *J. Org. Chem.*, **27**, 4715 (1962).

(6) G. Wittig and E. Knauss, *Ber.*, **91**, 895 (1958); G. Wittig, E. Knauss, and K. Niethammer, *Ann.*, **630**, 10 (1960).

(7) M. E. Kuehne, *J. Am. Chem. Soc.*, **84**, 837 (1962).

SCHEME I

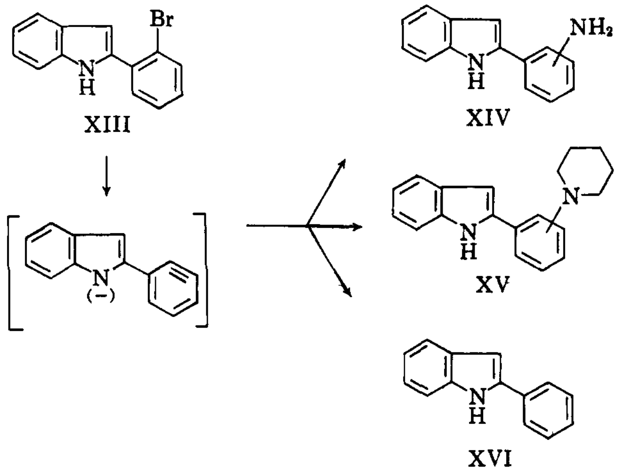


2,3-Phenylenedihydroindole (VII), isolated by column chromatography, showed ultraviolet absorption consistent with an *o*-alkyl N-alkylaniline and a mass spectrum with main peaks at 193 and 165 m/e corresponding to the molecular ion and loss of CH_2N, perhaps due to formation of a fluorene fragment. Large peaks were not found for the masses of benzyne or indole.

The only other well-defined products of these reactions were 2-fluorobiphenyl (X), 2-fluoro-2′-phenylbiphenyl (XI), and triphenylene (XII), derived from benzyne and the *o*-fluorophenyl anion. In addition, unstable amorphous materials were formed which could be shown to consist of several components by thin layer chromatography. Pyrolysis of these materials regenerated indole and N-methylindole, respectively.

For a possible synthesis of 1,2- and 2,3-phenyleneindoles, 2-(2′-bromophenyl)indole (XIII) was prepared by a Fischer indole synthesis and treated with strong bases. From the reaction with sodium amide, only a 2-aminophenylindole (XIV) was isolated as major product. When piperidyllithium was used, a 2-piperidinophenylindole (XV) and 2-phenylindole (XVI) were obtained. A reaction with *n*-butyllithium yielded mostly 2-phenylindole. The observed dehalogenation may be analogous to the formation of benzene and N-ethylethyleneimine from fluorobenzene and lithium diethylamide, which proceeds by a benzyne reduction.[8]

SCHEME II



Experimental

An Aerograph Model A-90-P instrument was used in all vapor-phase chromatographic experiments. In each case a 20-ft. column was used with a flow rate of 56 ml./min. at a pressure of 21 lb. of helium and other experimental conditions as indicated. All R_f values and colors in thin layer chromatographic experiments and all vapor phase chromatographic retention times which are described for specified compounds were compared with duplicate values obtained with authentic samples. All isolated compounds were compared by infrared spectra and, when solid, by mixture melting points with authentic samples.

Reactions of Indole and N-Methylindole with Benzyne in Liquid Ammonia. Formation of N-Phenylindole (III), 3-Phenylindole (IV), Aniline, Diphenylamine, and Triphenylamine.—A solution of sodium amide was prepared by adding 1.99 g. (0.085 g.-atom) of sodium over 30 min. to a stirred solution of 0.2 g. of ferric chloride in 200 ml. of liquid ammonia. After 1 hr. 2.78 g. (0.025 mole) of indole in 10 ml. of dry ether and then 4.80 g. (0.030 mole) of bromobenzene were added to the decolorized solution. After 30 min., the reaction was quenched by addition of 5.2 g. (0.10 mole) of ammonium chloride, the ammonia was evaporated, 50 ml. of water was added, and the mixture was extracted with ether. Washing with water, drying over magnesium sulfate, and concentration gave 5.00 g. of oil.

Vapor phase chromatogram of 6.9 mg. of the oil on a Dow 11 column (temperatures: column 252°, collector 263°, detector 295°, injector 267°) showed the following retention times: aniline, 1.1 min.; indole, 2.7 min.; diphenylamine, 6.4 min.; N-phenylindole, 10.4 min.; triphenylamine, 17.1 min.; and 3-phenylindole, 20.5 min. A quantitative estimate calculated from areas and compared to authentic samples was 260 mg. of N-

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[8] G. Wittig, H. J. Schmidt, and H. Renner, *Ber.*, **95**, 2377 (1962).

phenylindole[9] (5% yield) and 750 mg. of 3-phenylindole[10] (15% yield).

Thin layer chromatogram on Merck Alumina G with cyclohexane–benzene (1:1) showed the following R_f values and colors with sulfuric acid spray: 3-phenylindole, 0.09–0.14, yellow; indole, 0.14–0.27, red; diphenylamine, 0.45–0.55, blue; and N-phenylindole, 0.77–0.89, violet-red.

Chromatography of 4.93 g. of the oil on 30 g. of alumina (Woelm neutral II) gave the following amounts of products: 3.8 g. of oil (100 ml. of pentane), 0.2 g. of oil (100 ml. of 5:1 pentane–benzene), 0.52 g. of product with m.p. 75–78° (200 ml. of benzene), and 0.30 g. of product with m.p. 50–60° (200 ml. of methylene chloride). Recrystallization of the last two fractions gave a pure sample of 3-phenylindole identified by m.p. and m.m.p. 86–87°. Distillation of the first two eluates gave 0.40 g. of product, b.p. 110–130° (20 mm.), which was converted to aniline picrate, m.p. and m.m.p. 186–187° dec. (lit.[11] 181° dec.), which was recrystallized from ether–petroleum ether b.p. 30–60°) to give 2.45 g. of product with b.p. 130–170° (20 mm.), 0.6 g. of product with b.p. 170–210° (20 mm.), and 0.20 g. of residue. From the second fraction, 1.0 g. of indole and 0.20 g. of triphenylamine, m.p. 128–129°, could be crystallized from ether and petroleum ether.

Under the same conditions N-methylindole, prepared from indole in liquid ammonia with sodium amide and methyl iodide,[12] gave no detectable amount of N-methyl-3-phenylindole[13] (vapor phase chromatogram under above conditions requires a retention time of 20.7 min.; thin layer chromatography, alumina G, 1:1 benzene–cyclohexane, requires R_f 0.6–0.7). Only aniline, 1.1 min.; N-methylindole, 2.6 min.; diphenylamine, 6.5 min.; and triphenylamine, 18.4 min., could be detected by vapor phase chromatography. By thin layer chromatography, diphenylamine, R_f 0.6–0.7, could be detected under the above conditions.

Reaction of Indolyllithium with Benzyne. Formation of N-Phenylindole (III), 3-Phenylindole (IV), 2,3-Phenylenedihydroindole (VII), 2-Fluorobiphenyl (X), 2-Fluoro-2′-phenylbiphenyl (XI), and Triphenylene (XII).—To a solution of phenyllithium, prepared under a helium atmosphere from 0.55 g. (0.080 g.-atom) of lithium and 6.32 g. (0.040 mole) of bromobenzene in 30 ml. of anhydrous ether was added 3.51 g. (0.030 mole) of indole in 10 ml. of dry ether. After stirring for 1 hr. the solution was added under helium dropwise, over 1 hr., to a warmed and stirred mixture of 0.732 g. (0.030 g.-atom) of magnesium and 5.25 g. (0.030 mole) of *o*-bromofluorobenzene in 30 ml. of tetrahydrofuran, shortly after reaction of the metal and dihalobenzene had started. After an additional hour the solvents were removed *in vacuo,* 50 ml. of 5% aqueous hydrochloric acid was added, and the mixture was extracted with ether to give 5.83 g. of oil. Only traces of material were obtained from the acid solution on addition of excess sodium carbonate.

Analytical vapor phase chromatogram on a Dow 11 column (temperatures: column 255°, collector 267°, detector 297°, injector 274°) showed the following retention times: indole, 2.6 min.; 2-fluorobiphenyl, 3.3 min.; N-phenylindole (0.5% yield), 10.6 min.; 2-fluoro-2′-phenylbiphenyl (less than 4% yield), 11.5 min.; 2,3 phenylenedihydroindole (8% yield), 12.2 min.; 3-phenylindole (1% yield), 21.7 min.; and triphenylene, 55 min.

The reaction was repeated with triple amounts and 14.4 g. of oily product was obtained. Solution in 50 ml. of benzene and the dropwise addition to 150 ml. of pentane gave a yellow precipitate which was filtered, redissolved in 10 ml. of benzene, and reprecipitated by addition to 50 ml. of pentane to give 0.60 g. of powder, m.p. 173–210°. Chromatography of the powder on 20 g. of Woelm neutral II alumina gave a material, m.p. 166–168°, eluted with benzene and 8:2 benzene–dichloromethane, which by thin layer chromatography in benzene on alumina or silica gel showed several components but no indole. However, by vapor phase chromatography indole was produced as the main component by pyrolysis at 242°. The material was reactive with air, giving a new substance, m.p. 200–210°. The original benzene–pentane-soluble material was chromatographed on 85 g. of Woelm neutral II alumina, giving these eluates: 4 g. (200 ml. of pentane), 4 g. (300 ml. of cyclohexane), and 3 g. (200 ml. of benzene). From the third fraction 0.50 g. of 2,3-phenylenedihydroindole was obtained, m.p. 251–252° when recrystallized from ethanol. Ultraviolet absorption was at $\lambda_{\max}^{\mathrm{MeOH}}$ 250 mμ (log ε 3.1) and 290 (2.8) and mass spectral peaks were at 193 and 165 *m/e*.

Anal. Calcd. for $C_{14}H_{11}N$: C, 87.03; H, 5.74; N, 7.29. Found: C, 86.75; H, 5.55; N, 7.19.

Treatment of the second fraction with petroleum ether gave 2.0 g. of recovered indole. Rechromatography of the combined mother liquors of the second fraction and the first fraction on 30 g. of Woelm basic I alumina gave 0.8 g. of indole, eluted with pentane and cyclohexane, and 0.3 g. of 2-fluorobiphenyl, m.p. 62–64°, eluted with pentane. A sample recrystallized from pentane showed m.p. 70–71°, undepressed by an authentic sample, and the same infrared spectrum as an authentic sample.[14]

Combination of the remaining eluate fractions and distillation gave 1.4 g. of material with b.p. to 145° (20 mm.) and 2.5 g. of residue, which was fractionated by thin layer chromatography on Merck Alumina G with petroleum ether. The most rapidly moving fraction of 0.60 g. was subjected to successive preparative vapor phase chromatography (Dow 11 column; temperatures: column 252°, collector 263°, detector 295°, injector 267°) to give 0.10 g. of crude, then 0.050 g. of pure, 2-fluoro-2′-phenylbiphenyl, distilled at 135–140°, bath (3 mm.). The ultraviolet absorption was at $\lambda_{\max}^{\mathrm{hexane}}$ 230 mμ (log ε 3.1). The mass spectrum showed peaks at 248 and 228 *m/e* for molecular peak and fragment after loss of HF.

Anal. Calcd. for $C_{19}H_{13}F$: C, 87.07; H, 5.27. Found: C, 87.19; H, 5.18.

From the second thin layer chromatographic fraction, 0.050 g. of triphenylene,[15] m.p. and m.m.p. 192–194°, was obtained.

Reaction of N-Methylindole with Benzyne. Formation of N-Methyl-3-phenylindole (VI), 2-Fluorobiphenyl (X), 2-Fluoro-2-phenylbiphenyl (XI), and Triphenylene (XII).—A solution of 3.87 g. (0.030 mole) of N-methylindole in 20 ml. of tetrahydrofuran was added dropwise, with stirring over 1 hr., to a reacting mixture of 0.80 g. (0.033 g.-atom) of magnesium and 5.78 g. (0.030 mole) of *o*-bromofluorobenzene, heated in 70 ml. of tetrahydrofuran under an atmosphere of helium. After an additional hour the solvent was removed *in vacuo;* 2 ml. of water, 20 ml. of acetone, 150 ml. of dichloromethane, and, after 30 min., anhydrous magnesium sulfate were added. Filtration and concentration gave 6.33 g. of oil.

A vapor phase chromatogram of 7.0 mg. on a Dow 11 column (temperatures: column 252°, collector 263°, detector 295°, injector 272°) showed the following retention times: N-methylindole, 2.6 min.; 2-fluorobiphenyl, 3.3 min.; 2-fluoro-2′-phenylbiphenyl, 11.2 min.; N-methyl-3-phenylindole (3.3% yield), 20.7 min.; and triphenylene, 54.2 min.

Solution of the product in 10 ml. of benzene and addition to 200 ml. of petroleum ether gave 180 mg. of precipitate, m.p. 100–120°, which was purified to 130 mg., m.p. 140–145°, by three reprecipitations. This material showed several compounds on thin layer chromatography but no N-methylindole. Pyrolytic distillation at 140° (20 mm.) gave an oil showing ten components by vapor phase chromatography, the most abundant being N-methylindole. Concentration of the benzene–petroleum ether solution yielded 0.15 g. of triphenylene, recrystallized from ethanol, m.p. and m.m.p. 191–192°. Chromatography of the remaining oil on Merck Alumina G gave 5.0 g. of cyclohexane eluate from which 0.20 g. of 2-fluorobiphenyl, m.p. 70°, could be isolated in early fractions. Removel of material to b.p. 145° (20 mm.) left 2.5 g. of oil residue which was chromatographed on 50 g. of Woelm neutral II alumina. Fractions eluted with 1:1 petroleum ether–cyclohexane and cyclohexane gave 1.3 g. of oil enriched in 2-fluoro-2′-phenylbiphenyl. Repeated preparative vapor phase chromatography gave 0.10 g. of this product, distilled at 140–145°, bath (3 mm.).

2-(2′-Bromophenyl)indole (XIII).—A mixture of 3.98 g. (0.020 mole) of *o*-bromoacetophenone and 2.16 g. (0.020 mole) of phenylhydrazine was heated at 50° for 3 hr. The crude phenyl-

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(9) E. Fischer and O. Hess, *Ber.*, **17**, 559 (1884).

(10) F. Henle, *ibid.*, **38**, 1362 (1905).

(11) O. Silberrad and G. Rotter, *J. Chem. Soc.*, **89**, 167 (1906).

(12) W. J. Hickinbottom, "Reactions of Organic Compounds," Richard Clay and Co., Ltd., London, 1957, p. 409.

(13) W. H. Ince [*Ann.*, **253**, 35 (1889)] reports m.p. 64–65°, picrate m.p. 90°.

(14) G. Schiemann and W. Roselius, *Ber.*, **62**, 1809 (1929).

(15) G. Wittig and E. Benz, *ibid.*, **91**, 882 (1958).

hydrazone (no infrared carbonyl absorption) was heated in 30 g. of polyphosphoric acid at 100° for 3 hr. and at 170° for 3 min. Dilution with 150 ml. of water, addition of excess ammonia, and extraction with ether gave 4.0 g. of an oil from which 1.0 g. of the crude indole compound (XIII), m.p. 60–64°, was obtained by crystallization from ether–petroleum ether. A pure sample had m.p. 76–77°.

Anal. Calcd. for $C_{14}H_{10}BrN$: C, 61.86; H, 3.71; N, 5.15. Found: C, 61.85; H, 3.71; N, 5.19.

Alternatively, 3.0 g. of crude phenylhydrazone was heated for 5 min. at 170° with 20 g. of powdered zinc chloride and 40 g. of sand. Addition of 10 ml. of concentrated hydrochloric acid, extraction with ether, concentration, and chromatography on 25 g. ot Woelm neutral I alumina in benzene gave 1.5 g. of crude product, m.p. 68–70°.

2-(3′-Bromophenyl)indole (XVII).—A solution of 8.2 g. (0.020 mole) of *m*-bromoacetophenone and 4.5 g. (0.020 mole) of phenylhydrazine in 5 ml. of ethanol deposited 10.4 g. of phenylhydrazone, m.p. 100–101° after recrystallization from ethanol. This compound decomposed to a black tar on standing in air for 3 days. A solution of 10.0 g. of the phenylhydrazone in 100 g. of polyphosphoric acid was heated at 80–90° for 2 hr. and at 135° for 5 min. Dilution with water, filtration, and crystallization from ethanol gave 7.0 g. of XVII, m.p. 152–154°, recrystallized to m.p. 157–158°.

Anal. Calcd. for $C_{14}H_{10}BrN$: C, 61.80; H, 3.71; N, 5.15. Found: C, 61.95; H, 3.83; N, 5.06.

Reaction of 2-(2′-Bromophenyl)indole (XIII) with Sodium Amide.—Within 10 min. a solution of 0.65 g. (2.4 mole) 2-(2′-bromophenyl)indole in 10 ml. of dry ether was added dropwise to a stirred solution of sodium amide, prepared from 0.30 g. (0.012 g.-atom) of sodium in 150 ml. ot liquid ammonia. After 20 min., 0.80 g. (0.015 mole) of ammonium chloride was added, the ammonia was evaporated, the residue was dissolved in methylene chloride, and the solution was washed with 5% aqueous hydrochloric acid and evaporated.

Preparative thin layer chromatography of 0.4 g. of residual oil on Merck alumina G with 1:1 benzene–cyclohexane gave 0.150 g. of recovered starting material, 0.10 g. of an aminophenylindole (XIV) (m.p. 165–167°, recrystallized from dichloromethane and cyclohexane), and 120 mg. of dark oils in three fractions. Mass spectrum of the crystalline compound showed *m/e* 208 for the molecular peak.

Anal. Calcd. for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.47. Found: C, 80.62; H, 6.04; N, 13.27.

Reaction of 2-(2′-Bromophenyl)indole (XIII) with Piperidyllithium.—A solution of piperidyllithium, made by adding 2.7 ml. of a 13% solution of *n*-butyllithium in cyclohexane to 0.35 ml. of piperidine in 20 ml. of dry ether, was added to 0.54 g. of 2-(2′-bromophenyl)indole in 30 ml. of ether under nitrogen. After stirring for 18 hr., 1 ml. of water was added, the solvent was removed *in vacuo*, the residue was dissolved in dichloromethane, and the filtered solution was evaporated to 0.80 g. of oil. Successive preparative thin layer chromatography on Merck alumina G with 7:3 and 1:2 benzene–cyclohexane gave 0.25 g. of 2-phenylindole, m.p. and m.m.p. 176–178°, and 0.09 g. of a 2-piperidinophenylindole (XV), m.p. 86–87°; ultraviolet absorption showed $\lambda_{\max}^{\text{methanol}}$ 230 mμ (log ε 4.52), 320 (4.20).

Anal. Calcd. for $C_{19}H_{10}N_2$: C, 82.00; H, 7.30; N, 10.14. Found: C, 82.40; H, 7.50; N, 9.95.

Reaction of 2-(2′-Bromophenyl)indole with *n*-Butyllithium.—To a stirred solution of 0.85 g. (0.0031 mole) of 2-(2-bromophenyl)-indole in 50 ml. of dry tetrahydrofuran was added, under nitrogen, 20 ml. of ether containing 3.6 ml. of 14% butyllithium in cyclohexane. After refluxing for 18 hr., 1 ml. of water was added, the solvent was removed *in vacuo*, the residue was extracted with acetone, and the concentrate (0.75 g.) was subjected to preparative thin layer chromatography on Merck alumina G with 1:1 benzene–cyclohexane to give 0.43 g. of 2-phenylindole, m.p. and m.m.p. 175–178°, and several small oily fractions.

Acknowledgment.—We thank Professor Klaus Biemann, Massachusetts Institute of Technology, and Dr. Francis Johnson, Dow Chemical Company, for mass spectra; and the National Institutes of Health for support under USPHS Grant No. GM-09381.

The Oxidation of Phenylhydrazides to Carboxylic Acids with Manganese Dioxide.
II. By-products[1]

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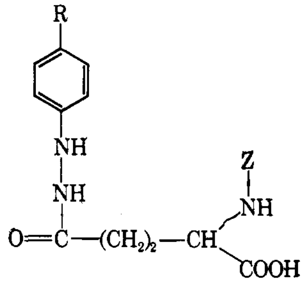
In a recent publication,[2] the smooth oxidation of phenylhydrazides to carboxylic acids with manganese dioxide was reported. The reaction is carried out in aqueous acetic acid at room temperature and is completed within 30 min. The γ-phenylhydrazide and the γ-(*p*-tolylhydrazide) of N-carbobenzoxy-L-glutamic acid (Ia and Ib, respectively), and dipeptides thereof, were found to undergo this reaction in good yield[3a] leaving protecting carbobenzoxy and ester groups intact and without racemization. These results prompted the suggestion that the phenylhydrazide group might well be used as a protective group in peptide chemistry.[2]



Ia, R = H; Z = $PhCH_2OCO$
b, R = CH_3; Z = $PhCH_2OCO$

In the present paper we report some investigations which have resulted in the discovery of essentially all of the products of the reaction and, consequently, have shed light on the mechanism.[3] All experiments were carried out on Ia under the conditions described in the preceding paper.[2]

Careful measurement of the nitrogen, which is rapidly evolved during the course of the reaction, showed that the nitrogen of the phenylhydrazide group is totally eliminated as elementary nitrogen within 30 min. Thus, obvious limitations are placed on the type of mechanism in operation.[3b]

In order to determine the fate of the aromatic ring of the phenylhydrazide group, we resorted to analysis of reaction mixtures by gas chromatography. The following three aromatic products were detected in the yields indicated: benzene (30%), phenol (27%), and phenyl acetate (41%). It has already been demonstrated that the N-carbobenzoxy group survives intact the conditions of the reaction[2,3a] and, moreover, none of these products could be detected by gas chromatography when N-carbobenzoxyglycine was submitted to the reaction conditions. Therefore, the aromatic products and the nitrogen have their origin in the

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(1) For the preceding paper, see ref. 2.

(2) R. B. Kelly, *J. Org. Chem.*, **28**, 453 (1963).

(3) (a) Yields of 80–90% of crystalline acids have been obtained (ref. 2); (b) see ref. 6d.