

25. Union of Aryl Nuclei. Part II. Chloro-, Bromo-, and Nitro-fluorenones.

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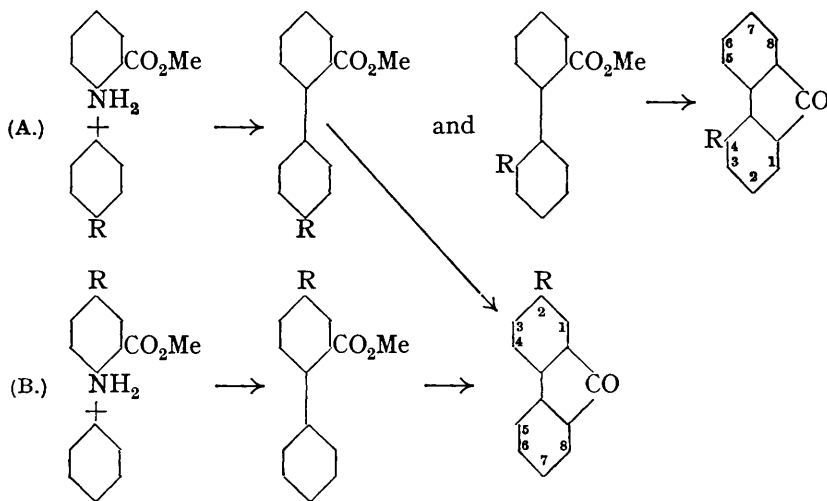
By means of the reaction due to Gomberg and his collaborators (*J. Amer. Chem. Soc.*, 1924, **46**, 2339; 1926, **48**, 1372), diazotised methyl anthranilate (or a derivative) and a neutral aromatic liquid being used, nuclear-substituted diphenyl-2-carboxylic acids become readily available, from which the corresponding substituted fluorenones may be obtained quantitatively on ring closure. Various alternative methods of procedure which present themselves are investigated.

It has long been known that derivatives of fluorenone may be prepared either by direct substitution or by substitution in fluorene, followed by oxidation. If the substituting agent is kationoid in type, the substituent atom or group first enters the 2-position, and then position 7 and to a smaller extent position 5. The scope of both these methods is thus limited. Moreover, when these methods are used, mixtures of mono- and di-substitution products, often contaminated with unsubstituted material, are frequently encountered, from which it is difficult to separate pure products (Courtot and Vignati, *Bull. Soc. chim.*, 1927, **41**, 58; *Compt. rend.*, 1927, **184**, 1179; Korczynski, Karlowska, and Kierzek, *Bull. Soc. chim.*, 1927, **41**, 65; Thurston and Shriner, *J. Amer. Chem. Soc.*, 1935, **57**, 2164). Alternative methods for the preparation of substituted fluorenones have been reviewed recently by Miller and Bachman (*J. Amer. Chem. Soc.*, 1935, **57**, 2443).

It has been shown (preceding paper) that by means of the procedure due to Gomberg and his co-workers (*J. Amer. Chem. Soc.*, 1924, **46**, 2339; 1926, **48**, 1372) it is possible to obtain diphenyl-2-carboxylic acid (or its methyl ester) from diazotised methyl anthranilate and benzene in the presence of alkali. This reaction is now utilised to provide chloro-, bromo-, and nitro-diphenyl-2-carboxylic acids, from which the corresponding substituted fluorenones are derived by ring closure—a long-known method of preparing fluorenones (Fittig and Ostermayer, *Annalen*, 1873, **166**, 376; Graebe and Aubin, *Ber.*, 1887, **20**, 845; Weger and Döring, *Ber.*, 1903, **36**, 881).

By means of this method monosubstituted derivatives of diphenyl-2-carboxylic acid

may be obtained either from diazotised methyl anthranilate and a monosubstituted benzene derivative (A), or from the diazotised methyl ester of a monosubstituted anthranilic acid and benzene (B).



In the former process a mixture of diphenyl-2-carboxylic esters results, as indicated above, where R may be either a so-called ortho-para-directing or meta-directing group or atom (cf. Grieve and Hey, J., 1934, 1797), from which two fluorenes are obtained on ring closure. The latter procedure gives a single product and is therefore preferred.

From the reactions between diazotised methyl 4-chloro- and 4-bromo-anthranilate and benzene, 5-chloro- and 5-bromo-diphenyl-2-carboxylic acids were obtained, which were converted quantitatively by ring closure with concentrated sulphuric acid at 50° into 3-chlorofluorenone and 3-bromofluorenone respectively. Similarly, diazotised methyl 5-chloro- and 5-bromo-anthranilate and benzene yielded 4-chlorodiphenyl-2-carboxylic acid and the 4-bromo-analogue, from which 2-chloro- and 2-bromo-fluorenone respectively were obtained. Further, from the reaction between the diazotised methyl ester of 5-nitroanthranilic acid and benzene, 4-nitrodiphenyl-2-carboxylic acid was obtained; this was converted into 2-nitrofluorenone. On the other hand, no product could be isolated from the reaction between diazotised methyl anthranilate and nitrobenzene. The reaction between diazotised methyl anthranilate and either chloro- or bromo-benzene gave mixtures of probably 2'- and 4'-halogenodiphenyl-2-carboxylic acids; these yielded mixtures of the 4- and 2-halogenofluorenes, which could not be separated completely (cf. Miller and Bachman, *loc. cit.*). The combined yields of the mixed acids resulting from these reactions (method A) were less satisfactory than the yields of the single acids resulting from the reactions using a substituted methyl anthranilate and benzene (method B).

The 2-chlorofluorenone obtained from 4-chlorodiphenyl-2-carboxylic acid was identical with a specimen obtained from the ring closure of 4'-chlorodiphenyl-2-carboxylic acid, which was prepared from 4'-chloro-2-methyldiphenyl by oxidation. The latter was obtained from the reaction between diazotised *p*-chloroaniline and toluene, which yielded some 4'-chloro-4-methyldiphenyl but mainly 4'-chloro-2-methyldiphenyl. A similar result was recorded by Gomberg and Pernert (*J. Amer. Chem. Soc.*, 1926, **48**, 1378) for the reaction between diazotised *p*-bromoaniline and toluene.

EXPERIMENTAL.

Preparation of Substituted Anthranilic Esters.—Methyl 5-chloroanthranilate was prepared by the direct chlorination of methyl anthranilate (Freundler, *Bull. Soc. chim.*, 1911, **9**, 605). Methyl 5-bromoanthranilate was obtained by bromination of methyl trichloroethylidene-anthranilate, as recommended by Freundler (*loc. cit.*; cf. Wheeler, *J. Amer. Chem. Soc.*, 1909,

31, 565). The 4-halogenoanthranilic esters were prepared by the following sequence of reactions: 2-nitro-*p*-toluidine \rightarrow 4-halogeno-2-nitrotoluene \rightarrow 4-halogeno-*o*-toluidine \rightarrow 4-halogenoaceto-*o*-toluidide \rightarrow 4-halogeno-2-acetamidobenzoic acid \rightarrow methyl 4-halogeno-2-aminobenzoate (cf. Friedländer, Bruckner, and Deutsch, *Annalen*, 1912, **388**, 23; Cohn, *Monatsh.*, 1901, **22**, 473; Robertson and Waters, *J.*, 1931, 72; Frejka and Vymetal, *Coll. Czech. Chem. Comm.*, 1935, **7**, 436). The reduction of the nitro-group was effected with stannous chloride, and the oxidation of the methyl group with neutral potassium permanganate. Methyl 5-nitroanthranilate was prepared by nitration of acetylanthranilic acid, followed by hydrolysis and esterification (cf. Rupe, *Ber.*, 1897, **30**, 1097; Baly, Tuck, and Marsden, *J.*, 1910, **97**, 1502; Bogert and Scatchard, *J. Amer. Chem. Soc.*, 1919, **41**, 2065).

3-Chlorofluorenone.—A paste of methyl 4-chloroanthranilate (18.5 g., 0.1 mol.), hydrochloric acid (30 c.c., *d* 1.16), and water (10 c.c.) was diazotised in the normal manner with aqueous sodium nitrite. Aqueous sodium hydroxide (9 g. in 30 c.c.) was gradually added to a vigorously stirred mixture of the ice-cold diazonium solution and benzene (150 c.c.). Stirring was continued for 10 hours while the temperature was raised to 25°. The benzene layer was separated, washed with concentrated hydrochloric acid and with water, dried, and distilled. After removal of the excess of benzene the crude 5-chlorodiphenyl-2-carboxylic ester was collected under reduced pressure (b. p. 180–190°/20 mm.; yield 25%, calculated on weight of methyl 4-chloroanthranilate). The crude ester was boiled under reflux for 4 hours with 20% aqueous sodium hydroxide, and the solution diluted with water, filtered, and acidified. The precipitated 5-chlorodiphenyl-2-carboxylic acid crystallised from dilute alcohol in needles, m. p. 152° (Found: C, 67.1; H, 4.3. $C_{13}H_9O_2Cl$ requires C, 67.1; H, 3.9%).

The acid (or ester) was warmed to 50° with ten times its weight of concentrated sulphuric acid and kept at that temperature for 10 minutes. When the solution was poured into water, 3-chlorofluorenone separated as a yellow precipitate, which after crystallisation from alcohol melted at 157° (Found: C, 72.8; H, 3.3. $C_{13}H_7OCl$ requires C, 72.7; H, 3.3%).

The following reactions were carried out in similar manner except where otherwise stated.

2-Chlorofluorenone.—Crude methyl 4-chlorodiphenyl-2-carboxylate (b. p. 185–195°/20 mm., 320°/760 mm.) was obtained in 29% yield from diazotised methyl 5-chloroanthranilate (46.5 g., 0.25 mol.) and benzene. Hydrolysis of the ester gave 4-chlorodiphenyl-2-carboxylic acid, which crystallised from dilute alcohol in needles, m. p. 157° (Found: C, 67.4; H, 4.0. $C_{13}H_9O_2Cl$ requires C, 67.1; H, 3.9%). Ring closure gave 2-chlorofluorenone, m. p. 123° (Found: C, 73.2; H, 3.5; Cl, 16.3. Calc. for $C_{13}H_7OCl$: C, 72.7; H, 3.3; Cl, 16.5%). Courtot and Vignati (*Compt. rend.*, 1927, **184**, 1179) and Courtot (*Ann. Chim.*, 1930, **14**, 5) record m. p. 123° and Chanussot (*Anal. Asoc. Quím. Argentina*, 1927, **15**, 216) records m. p. 125–126°.

3-Bromofluorenone.—Diazotised methyl 4-bromoanthranilate (23 g., 0.1 mol.) and benzene gave crude methyl 5-bromodiphenyl-2-carboxylate (b. p. 185–195°/20 mm.) in 25% yield, which on hydrolysis yielded 5-bromodiphenyl-2-carboxylic acid; this separated from dilute alcohol in needles, m. p. 172° (Found: C, 56.4; H, 3.2. $C_{13}H_9O_2Br$ requires C, 56.3; H, 3.2%). Ring closure yielded 3-bromofluorenone, m. p. 161° (Found: C, 60.0; H, 2.8. Calc. for $C_{13}H_7OBr$: C, 60.2; H, 2.7%). Montagne and van Charante (*Rec. trav. chim.*, 1913, **32**, 172) describe two forms of 3-bromofluorenone, m. p. 162.5° and 165.5°. Bardout (*Anal. Asoc. Quím. Argentina*, 1934, **22**, 123) gives m. p. 165°, Miller and Bachman (*loc. cit.*) m. p. 162°.

2-Bromofluorenone.—From diazotised methyl 5-bromoanthranilate (57.5 g., 0.25 mol.) and benzene, crude methyl 4-bromodiphenyl-2-carboxylate (b. p. 185–200°/20 mm.) was obtained in 29% yield. The free 4-bromodiphenyl-2-carboxylic acid obtained on hydrolysis melted, after crystallisation from dilute alcohol, at 164° (Found: C, 56.5; H, 3.1. Calc. for $C_{13}H_9O_2Br$: C, 56.3; H, 3.2%). Courtot (*Ann. Chim.*, 1930, **14**, 137) gives m. p. 165°. The 2-bromofluorenone obtained on ring closure melted at 150° (Found: C, 60.5; H, 2.7. Calc. for $C_{13}H_7OBr$: C, 60.2; H, 2.7%). Schmidt and Bauer (*Ber.*, 1905, **38**, 3751, 3767) record m. p. 134°, Courtot and Vignati (*Bull. Soc. chim.*, 1927, **41**, 58) m. p. 142–143°, Gomberg and Pernert (*loc. cit.*) m. p. 149°, and Thurston and Shriner (*loc. cit.*) m. p. 146°.

2-Nitrofluorenone.—The reaction between diazotised methyl 5-nitroanthranilate (49 g., 0.25 mol.) and benzene gave crude methyl 4-nitrodiphenyl-2-carboxylate in 7% yield. Double the usual quantity of hydrochloric acid was used during the diazotisation, which was effected with solid sodium nitrite. The crude nitrodiphenylcarboxylic ester was extracted from the product, after removal of the excess of benzene, with light petroleum (b. p. 80–100°). Evaporation of this extract left a residue of the crude ester, which on hydrolysis yielded 4-nitrodiphenyl-2-carboxylic acid; this, purified by sublimation in a vacuum, separated from

dilute alcohol in needles, m. p. 173° (Found: C, 64.1; H, 3.6. $C_{13}H_9O_4N$ requires C, 64.2; H, 3.7%). Ring closure gave 2-nitrofluorenone, m. p. 219° (Found: C, 69.2; H, 3.0. Calc. for $C_{13}H_7O_3N$: C, 69.3; H, 3.1%). Schultz (*Annalen*, 1880, 203, 103) records m. p. 220°, Ullmann and Mallet (*Ber.*, 1898, 31, 1696) m. p. 218.5° (corr.), and Diels (*Ber.*, 1901, 34, 1759) m. p. 222—223° (corr.).

Action of Diazotised Methyl Anthranilate on Chloro- and Bromo-benzene.—Reactions were carried out, as described above, methyl anthranilate (50 g., 0.33 mol.) being used with chloro- and bromo-benzene. In the former case a mixture of methyl 2'- and 4'-chlorodiphenyl-2-carboxylates (b. p. 180—200°/20 mm.) was obtained in 17% yield. The mixture of acids obtained on hydrolysis was converted by ring closure into a mixture of 4- and 2-chlorofluorenone. In similar manner the reaction with bromobenzene gave a mixture of methyl 2'- and 4'-bromodiphenyl-2-carboxylate (b. p. 180—200°/20 mm.) in 13% yield. A mixture of the two acids was obtained on hydrolysis and, on ring closure, a mixture of 4- and 2-bromofluorenone. Attempts to separate the constituents of these mixtures were only partly successful.

4'-Chloro-2-methyldiphenyl.—*p*-Chloroaniline (25.5 g.), diazotised in the normal manner, was added to toluene (250 c.c.), and the mixture vigorously stirred at about 5° while aqueous sodium hydroxide (30% solution) was added gradually until alkaline. Steam-distillation of the product gave, in addition to recovered toluene, a mixture of chloromethyldiphenyls, from which 4'-chloro-4-methyldiphenyl (m. p. 122°) separated. Redistillation of the liquid residue, which comprised the greater part of the product, gave 4'-chloro-2-methyldiphenyl as a clear refractive liquid, b. p. 288—290° (Found: C, 77.1; H, 5.3. $C_{13}H_{11}Cl$ requires C, 77.0; H, 5.4%). A portion of this chlorohydrocarbon was boiled under reflux with aqueous potassium permanganate for 10 hours. After treatment of the solution with sulphur dioxide 4'-chlorodiphenyl-2-carboxylic acid separated, which crystallised from dilute alcohol in needles, m. p. 161° (Found: C, 67.2; H, 4.2. $C_{13}H_9O_2Cl$ requires C, 67.1; H, 3.9%). Ring closure with sulphuric acid at 50° gave 2-chlorofluorenone, m. p. 123° alone and in admixture with the compound derived from 4-chlorodiphenyl-2-carboxylic acid.

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