

406. *The Reactions of Certain Nitrogen-containing Compounds derived from Benzotrifluoride.*

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Diazotised *m*-aminobenzotrifluoride with dimethylaniline, phenol, and β -naphthol, gave the expected azo-compounds, and with the parent amine gave 3 : 3'-bistrifluoromethyldiazoaminobenzene which could not be rearranged. 3 : 3'-Bistrifluoromethylazobenzene gave the azoxy-compound on oxidation, and, when treated with sodium amalgam and then with mineral acids, afforded 2 : 2'-bistrifluoromethylbenzidine. 2 : 2'-Bistrifluoromethylhydrazobenzene was fairly stable; it was converted into the corresponding benzidine derivative under drastic conditions.

THIS paper describes the application of certain classical reactions to some nitrogenous aromatic compounds containing trifluoromethyl groups. *m*-Aminobenzotrifluoride (Swarts, *Bull. Acad. roy. Belg.*, 1898, [iii], 35, 375) was diazotised in the usual way and was coupled with phenol, β -naphthol, and dimethylaniline to give the expected azo-compounds. The structure of that derived from the tertiary amine was confirmed by reductive cleavage and acetylation of the fragments; this azo-compound has been mentioned by Miller, Sapp, and Miller (*Cancer Research*, 1949, 9, 652). Diazotisation and self-coupling of *m*-aminobenzotrifluoride proceeded readily in the absence of an excess of mineral acid, the structure of the product, 3 : 3'-bistrifluoromethyldiazoaminobenzene, being proved by hydrogenolysis to ammonia and the parent amine. This diazoamino-compound could not be rearranged to the aminoazo-product; unless complete decomposition was induced, the starting material was recovered. The diazoamino-structure is stabilised, evidently, by the presence of trifluoromethyl substituents, and the recovery of the starting material from an attempted rearrangement in the presence of acid and dimethylaniline suggests that initial rupture of the nitrogen chain is difficult.

3 : 3'-Bistrifluoromethylazobenzene was first made by Swarts (*Bull. Acad. roy. Belg.*, 1922, 8, 343) as a by-product of the oxidation of *m*-aminobenzotrifluoride with chromic acid; Gonze (*Bull. Soc. chim. Belg.*, 1934, 43, 504; *Bull. Acad. roy. Belg.*, 1934, 20, 809) prepared from it the corresponding hydrazo-compound which was somewhat less easily oxidised than the analogous toluene derivative. Gonze found that the hydrazo-compound did not readily undergo the benzidine transformation, 10% hydrochloric acid giving mainly a mixture of the parent amine and azo-compound, though a small amount of unidentified solid was isolated also. We prepared 3 : 3'-bistrifluoromethylazobenzene by reduction of *m*-nitrobenzotrifluoride, either with zinc dust and sodium hydroxide (*idem, loc. cit.*), or electrolytically. Oxidation of the azo-compound with hydrogen peroxide-acetic acid

afforded the analogous azoxy-derivative, of which the structure was confirmed by reduction to *m*-aminobenzotrifluoride. Reduction of the 3 : 3'-azo-compound, in alcohol, by sodium amalgam gave a colourless solution containing Gonze's hydrazo-compound. When this solution was added directly to warm sulphuric acid (50% by volume), there were obtained, after removal of the regenerated azo-compound, two bases, m. p. 180—182° and 141° (conversions of 11% and 1.5%) respectively, each of which had a correct analysis for a diaminobistrifluoromethyldiphenyl. The product having m. p. 180—182° was shown to be the benzidine derivative, 4 : 4'-diamino-2 : 2'-bistrifluoromethyldiphenyl, since, after tetrazotisation, and reduction with hypophosphorous acid, 2 : 2'-bistrifluoromethyldiphenyl was obtained, as was shown by its conversion with hot sulphuric acid (Le Fave's process, *J. Amer. Chem. Soc.*, 1949, **71**, 4148) into 9-oxofluorene-4-carboxylic acid, which is known to be formed from diphenic acid, the expected primary product, under these conditions (Graebe and Aubin, *Ber.*, 1887, **20**, 845). Complete proof of the structure of the benzidine was afforded by its identity with the product obtained by Pettit and Tatlow (*J.*, 1951, 3459) via an Ullmann reaction upon 2-iodo-5-nitrobenzotrifluoride. The second product, m. p. 141°, is as yet unidentified, though, from the usual course of rearrangements of hydrazobenzenes, it may well be 2 : 4'-diamino-4 : 2'-bistrifluoromethyldiphenyl. In this particular benzidine transformation, disproportionation occurs to a considerable extent, confirming Gonze's original conclusions (*loc. cit.*).

Electrolytic reduction of *o*-nitrobenzotrifluoride gave 2 : 2'-bistrifluoromethylazobenzene, which, with sodium amalgam, afforded 2 : 2'-bistrifluoromethylhydrazobenzene which by hydrogenolysis gave *o*-aminobenzotrifluoride. The 2 : 2'-bistrifluoromethyl derivative is relatively stable for a hydrazo-compound; it was not, apparently, oxidized appreciably in air, and was recovered after treatment with dilute mineral acids under conditions which cause rearrangements of many hydrazo-compounds. More concentrated sulphuric acid (2 : 1 H₂SO₄-H₂O by vol.), however, did effect a transformation. A small amount of 2 : 2'-bistrifluoromethylazobenzene was formed, but the main product was 4 : 4'-diamino-3 : 3'-bistrifluoromethyldiphenyl: this and its bistrifluoroacetyl derivative were identical with the compounds prepared by Pettit and Tatlow (*loc. cit.*) through an Ullmann reaction on 5-iodo-2-nitrobenzotrifluoride.

It appears that trifluoromethyl substituents in aromatic nuclei hinder the two types of acid-catalysed transformations considered in this investigation. The conversion of a diazoamino- into an aminoazo-compound is usually thought to proceed intermolecularly, following reaction with a proton (cf. Hughes and Ingold, *Quart. Reviews*, 1952, **6**, 34), and the benzidine transformation intramolecularly, after addition of two protons to the hydrazo-derivative (*idem, loc. cit.*; Hammond and Shine, *J. Amer. Chem. Soc.*, 1950, **72**, 220). Presumably the presence of trifluoromethyl groups causes proton additions to proceed less readily than with unsubstituted compounds. Though there are few reports of the effect it appears that the presence of other electrophilic substituents hinders these rearrangements, since Zettel (*Ber.*, 1893, **26**, 2471) found that tetrachlorodiazaminobenzene was unusually stable to acids, and Carlin and Forshey (*J. Amer. Chem. Soc.*, 1950, **72**, 793) had to use drastic conditions to effect transformations of 3 : 3' : 5 : 5'-tetrachloro- and -bromohydrazobenzene (see also Meyer, Meyer, and Taeger, *Ber.*, 1920, **53**, 2034), steric effects not being the complete explanation. Similar stability is shown by 2 : 2'-dichloro- (Dey, Govindachari, and Rajagopalan, *J. Sci. Ind. Res., India*, 1946, **4**, 645) and 2 : 2' : 5 : 5'-tetrachloro-hydrazobenzene (*idem, ibid.*, 1946, **5**, B, 75). Though trifluoromethyl substituents will reduce the basicity of the >NH groups, the actual reactions of protons with the latter may not be the rate-determining steps in these transformations. However, 2 : 2'-bistrifluoromethylhydrazobenzene apparently did not form salts with acids at all readily.

EXPERIMENTAL

Coupling of Diazotised m-Aminobenzotrifluoride with Dimethylaniline.—*m*-Aminobenzotrifluoride (5.00 g.) was warmed with concentrated hydrochloric acid (7.8 c.c.) and water (7.8 c.c.) to give a solution which was stirred mechanically and cooled to 0° whilst sodium nitrite (2.25 g.) in water (10.0 c.c.) was added, followed by dimethylaniline (3.76 g.) in hydrochloric acid (5.8 c.c.; 6N), and sodium acetate (5.0 g.) in water (12.0 c.c.). The resultant precipitate was washed and

recrystallised, first from ethyl alcohol made very slightly alkaline with aqueous potassium hydroxide, and then from light petroleum (b. p. 60—80°), to give orange-red 4-dimethylamino-3'-trifluoromethylazobenzene (3.98 g.), m. p. 81—82° (Found : C, 61.5; H, 5.0; F, 18.8. Calc. for C₁₅H₁₄N₃F₃ : C, 61.4; H, 4.8; F, 19.4%). Miller, Sapp, and Miller (*loc. cit.*) gave m. p. 77—79°.

This azo-compound (2.00 g.), Raney nickel (*ca.* 0.5 g.), and ethyl alcohol (25.0 c.c.) were shaken together in hydrogen until absorption (325 c.c.) was complete (80 min.). After filtration and evaporation, the product was distilled *in vacuo*, to give a fraction (a), b. p. 115—160° (bath)/17 mm., and a residue (b). Fraction (a), acetic acid (1.0 c.c.), and acetic anhydride (1.2 c.c.) were heated to 100° for 3 min., to give, after isolation as usual, *m*-acetamidobenzotrifluoride (1.07 g.), m. p. and mixed m. p. 104°, for which Swarts (*loc. cit.*, 1898) gave m. p. 103°. The residue (b), after similar treatment, afforded, after two recrystallisations of the product from water, *p*-acetamido-*NN*-dimethylaniline (0.18 g.), m. p. and mixed m. p. 128—130°.

Coupling of Diazotised m-Aminobenzotrifluoride with Phenol and with β-Naphthol.—(a) The amine (2.50 g.), in water (12 c.c.) and concentrated hydrochloric acid (3.9 c.c.), was diazotised at 0° with sodium nitrite (1.13 g.), in water (5 c.c.), and the solution was treated with phenol (1.60 g.), in aqueous sodium hydroxide, the solution being made slightly alkaline. The precipitate, after being washed, dried, and recrystallised from carbon tetrachloride, gave yellow 4-hydroxy-3'-trifluoromethylazobenzene (2.91 g.), m. p. 110—111° (Found : C, 58.5; H, 3.4; F, 21.1. C₁₃H₉ON₂F₃ requires C, 58.65; H, 3.4; F, 21.4%).

(b) A similar reaction in which the amine was diazotised and coupled with β-naphthol at pH 7—8 afforded, after recrystallisation from ethyl alcohol, the red 3-trifluoromethylphenylazo-β-naphthol (60%), m. p. 165—166° (Found : C, 64.7; H, 3.2; F, 17.8. C₁₇H₁₁ON₂F₃ requires C, 64.5; H, 3.5; F, 18.0%).

Diazotisation and Self-coupling of m-Aminobenzotrifluoride.—(a) The amine (3.22 g.), concentrated hydrochloric acid (2.6 c.c.), and water (5.2 c.c.) were warmed together until homogeneous, and then stirred mechanically and cooled to 0—5°. Sodium nitrite (0.72 g.) in water (5.0 c.c.) was added dropwise, followed by sodium acetate (3.0 g.) in water (6.0 c.c.), and after 10 min. the precipitate was removed, washed, and dried. Recrystallisation from light petroleum (b. p. 60—80°) afforded yellow 3 : 3'-bistrifluoromethyldiazoaminobenzene (2.67 g.), m. p. 117—118° (Found : C, 50.5; H, 2.8; F, 33.9. C₁₄H₉N₃F₆ requires C, 50.5; H, 2.7; F, 34.2%).

(b) (By Earl's process, *Chem. and Ind.*, 1936, 55, 192.) *m*-Aminobenzotrifluoride (5.0 g.), saponin (0.1 g.), potassium chromate (0.2 g.), sodium nitrite (1.2 g.), and water (50 c.c.) were shaken together mechanically in an atmosphere of carbon dioxide (12" Hg pressure) for 1 hr. The precipitate, after recrystallisation from *n*-hexane, had m. p. and mixed m. p. 117—118° (yield 3.25 g.).

(c) This diazoamino-compound was unaffected when heated with *m*-aminobenzotrifluoride and its hydrochloride, with the amine and hydrogen chloride in methyl alcohol, with concentrated hydrochloric acid, with dimethylaniline and a little concentrated hydrochloric acid, or with acetic acid or trifluoroacetic acid, alone or containing the parent amine, except that prolonged heating caused decomposition.

Reduction of 3 : 3'-Bistrifluoromethyldiazoaminobenzene.—This material (2.90 g.), light petroleum (30 c.c., b. p. 60—80°), and Raney nickel (*ca.* 2 g.) were shaken for 6 hr. at 130—140° in a rocking autoclave in hydrogen (120 atm.). Ammonia was present at the end of the reaction. After filtration of the product, a little concentrated hydrochloric acid was added to the filtrate, the petroleum was evaporated *in vacuo*, and the residual salt was taken up in water, diazotised, and coupled with β-naphthol as described before, to give 3-trifluoromethylphenylazo-β-naphthol (3.21 g.), m. p. and mixed m. p. 165°.

3 : 3'-Bistrifluoromethylazobenzene from m-Nitrobenzotrifluoride.—The apparatus comprised a cylindrical porous pot, which carried a sheet-lead anode (*ca.* 110 sq. cm.), was filled with saturated aqueous sodium carbonate, and was contained in a beaker (capacity 1 l.) which held also a lead cathode (*ca.* 110 sq. cm.) To the cathode compartment were added *m*-nitrobenzotrifluoride (35.8 g.), ethyl alcohol (350 c.c.), water (30 c.c.), and sodium acetate (10 g.). The cathode solution was stirred mechanically, and current was passed (at 12 v, this rose to 10 amp. after 1 hr.; the voltage was then reduced progressively to 7 to keep the amperage at 10) until appreciable evolution of hydrogen occurred (*ca.* 2½ hr.). The temperature rose to about 60° during the reaction, a little alcohol being added to the cathode compartment and water to the anode compartment to replace losses. Air was drawn through the cathodic solution for 20 min., and the deposited solid was washed and recrystallised from aqueous alcohol, affording

red 3: 3'-bistrifluoromethylazobenzene (17.3 g.), m. p. 82° (Found: C, 52.9; H, 2.6; F, 35.6. Calc. for $C_{14}H_8N_2F_6$: C, 52.8; H, 2.5; F, 35.8%), for which Swarts (*loc. cit.*, 1922) gave m. p. 82.3°.

3: 3'-Bistrifluoromethylazoxybenzene.—3: 3'-Bistrifluoromethylazobenzene (2.00 g.), acetic acid (75 c.c.), and hydrogen peroxide solution (10 c.c., 100-vol.) were heated at 80° for 20 hr., further portions of hydrogen peroxide (3×5 c.c.) being added at intervals of 5 hr. The solution was poured into excess of water and the precipitate was washed and recrystallised from aqueous ethyl alcohol, to give 3: 3'-bistrifluoromethylazoxybenzene (1.82 g.), m. p. 47° (Found: C, 50.4; H, 2.4. $C_{14}H_8ON_2F_6$ requires C, 50.3; H, 2.4%).

The azoxy-compound (0.50 g.), ethyl alcohol (5 c.c.) and Raney nickel (*ca.* 1 g.) were shaken together in hydrogen until absorption was complete. The solution was filtered, a little concentrated hydrochloric acid was added, and the alcohol was evaporated *in vacuo*. The residual salt was diazotised in the usual way and then β -naphthol (0.45 g.), in aqueous sodium hydroxide, was added. The precipitate, recrystallised from ethyl alcohol, gave 3-trifluoromethylphenylazo- β -naphthol (0.56 g.), m. p. and mixed m. p. 165—166°.

4: 4'-Diamino-2: 2'-bistrifluoromethyldiphenyl.—3: 3'-Bistrifluoromethylazobenzene (5.00 g.), ethyl alcohol (75 c.c.), water (5.0 c.c.), and sodium amalgam (Na, 1.5 g.; Hg, 70 g.) were shaken together vigorously until the solution was colourless (*ca.* 5 min.), and then poured into 1: 1 (vol.) sulphuric acid—water (200 c.c.) at 40—50°. A red precipitate was deposited, and after being recrystallised from aqueous alcohol this regenerated starting material (1.40 g.) had m. p. and mixed m. p. 79°. The aqueous layer was neutralised with sodium hydroxide (5N) and extracted with ether, and the extracts were washed, dried ($MgSO_4$), and evaporated, leaving a semi-solid residue. After the addition of a little light petroleum (b. p. 40—60°) the solution (A) was filtered and the solid was recrystallised from aqueous ethyl alcohol, to give 4: 4'-diamino-2: 2'-bistrifluoromethyldiphenyl (0.55 g.), m. p. 180—182°, not depressed in admixture with the product described by Pettit and Tatlow (*loc. cit.*) (Found: C, 52.4; H, 3.1. Calc. for $C_{14}H_{10}N_2F_6$: C, 52.5; H, 3.1%). Treatment, in ether, with excess of trifluoroacetic anhydride (Bourne, Henry, Tatlow, and Tatlow, *J.*, 1952, 4014) gave the bistrifluoroacetyl derivative (84%) m. p. 209—210° (Found: C, 42.4; H, 1.7. $C_{18}H_8O_2N_2F_{12}$ requires C, 42.2; H, 1.6%). The sulphate of this benzidine, and that of the 3: 3'-bistrifluoromethyl isomer, are fairly soluble in water.

Concentration of the solution (A) gave a mixture of oil (1.87 g.) and crystals; the crystals were separated, washed with light petroleum (b. p. 40—60°), and recrystallised from ethyl alcohol. The product (0.078 g.) had m. p. 141°, depressed in admixture with the above benzidine derivative (Found: C, 52.4; H, 3.4. $C_{14}H_{10}N_2F_6$ requires C, 52.5; H, 3.1%).

2: 2'-Bistrifluoromethyldiphenyl.—4: 4'-Diamino-2: 2'-bistrifluoromethyldiphenyl (2.50 g.) was tetrazotised, using sodium nitrite (1.2 g.), concentrated hydrochloric acid (4.0 c.c.), and water (20 c.c.). Hypophosphorous acid (16 c.c., 30%) was added, and after 1 hr. at 0° and 2 hr. at 15° the mixture was distilled in steam, the distillate was ether-extracted, the extracts were dried ($MgSO_4$) and evaporated, and the residue was distilled, to give 2: 2'-bistrifluoromethyldiphenyl (1.34 g.), b. p. 230°, m. p. 32° [after nucleation with a solid specimen prepared by an Ullmann reaction on *o*-iodobenzotrifluoride (Pettit and Tatlow, unpublished results)] (Found: C, 58.2; H, 2.8. $C_{14}H_8F_6$ requires C, 57.9; H, 2.8%).

2: 2'-Bistrifluoromethyldiphenyl (0.204 g.) was stirred mechanically with concentrated sulphuric acid (2.0 c.c.) at 90° for $\frac{1}{2}$ hr. and at 100° for 3 hr. The mixture was poured into ice-water, the aqueous phase was extracted with ether, and the ethereal extracts were washed with aqueous alkali. The ethereal phase retained a neutral substance (0.06 g.), later shown to be 4-trifluoromethylfluorenone (Pettit and Tatlow, unpublished). The alkaline washings were acidified (H_2SO_4) and extracted with fresh ether, and these ethereal layers were washed, dried ($MgSO_4$), and evaporated, to give, after recrystallisation from ethyl alcohol, 9-oxofluorene-4-carboxylic acid (0.050 g.), m. p. and mixed m. p. 226—227° (Found: C, 74.8; H, 3.6. Calc. for $C_{14}H_8O_3$: C, 75.0; H, 3.6%). Graebe and Aubin (*loc. cit.*) gave m. p. 227°.

2: 2'-Bistrifluoromethylazobenzene.—*o*-Nitrobenzotrifluoride (Jones, *J. Amer. Chem. Soc.*, 1947, 69, 2346), (6.50 g.) was reduced electrolytically (5 amp.) as described for the *m*-isomer, a smaller apparatus being used. The solid product, recrystallised from aqueous ethyl alcohol, afforded red 2: 2'-bistrifluoromethylazobenzene (1.41 g.), m. p. 126—128° (Found: C, 52.6; H, 2.5; F, 35.4. $C_{14}H_8N_2F_6$ requires C, 52.8; H, 2.5; F, 35.8%).

2: 2'-Bistrifluoromethylhydrazobenzene.—(a) *Preparation*. The 2: 2'-bistrifluoromethylazo-compound (1.0 g.), ethyl alcohol (30 c.c.), water (2.0 c.c.), and sodium amalgam (Na, 1.0 g.; Hg, 50 g.) were shaken together until the red colour was discharged (*ca.* 2 min.); then the solution was poured into concentrated hydrochloric acid (50 c.c.) containing ice (50 g.). The precipitate, recrystallised from aqueous alcohol, afforded colourless 2: 2'-bistrifluoromethyl-

hydrazobenzene (0.90 g.), m. p. 122—123° (depressed in admixture with the starting material) (Found : C, 52.5; H, 3.0; F, 35.3. $C_{14}H_{10}N_2F_6$ requires C, 52.5; H, 3.1; F, 35.6%).

The hydrazo-compound (0.50 g.) was hydrogenated and the product was coupled as described for 3 : 3'-bistrifluoromethylazoxybenzene, to give, after recrystallisation from ethyl alcohol, red 2-trifluoromethylphenylazo- β -naphthol (0.58 g.), m. p. 157—158°, alone and in admixture with the product prepared directly from *o*-aminobenzotrifluoride (Pettit, Stacey, and Tatlow, unpublished) (Found : C, 64.5; H, 3.2; F, 17.9. $C_{17}H_{11}ON_2F_3$ requires C, 64.5; H, 3.5; F, 18.0%).

The hydrazo-compound was insoluble in cold aqueous acids, and it could not be diazotised and coupled with β -naphthol.

(b) *Benzidine transformation*. The 2 : 2'-hydrazo-compound (0.42 g.) was heated with sulphuric acid (8 c.c.) and water (4 c.c.) at 90° for 2 hr. with stirring. The reddish insoluble material, recrystallised from aqueous alcohol, gave 2 : 2'-bistrifluoromethylazobenzene (0.01 g.), m. p. and mixed m. p. 125°. The acid solution was neutralised with aqueous sodium hydroxide; extraction with ether followed by drying ($MgSO_4$) and evaporation of the extracts afforded a solid, which, after three recrystallisations from aqueous alcohol, gave 4 : 4'-diamino-3 : 3'-bistrifluoromethyldiphenyl (0.15 g.), m. p. and mixed m. p. 115° (Found : C, 52.2; H, 3.0. Calc. for $C_{14}H_8N_2F_6$: C, 52.5; H, 3.1%). Treatment of the product, in ether, with excess of trifluoroacetic anhydride, followed by evaporation *in vacuo* with several portions of carbon tetrachloride, afforded the bistrifluoroacetyl derivative, m. p. (unchanged by recrystallisation) and mixed m. p. 201°. Pettit and Tatlow (*loc. cit.*) gave m. p. s 115—116.5° and 202° respectively.

The authors thank Professor M. Stacey, F.R.S., for his interest, the Imperial Smelting Corporation Ltd. for an award to one of them (R. A. C.) and for gifts of benzotrifluoride, and Miss C. Ullmann for experimental assistance.

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[Received, February 19th, 1953.]
