Trifluoromethyl-substituted Benziminazoles.

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Some trifluoromethyl-substituted benziminazoles have been synthesised and their reactions with certain metals have been studied. Those with trifluoromethyl groups in both the glyoxaline and benzene rings are appreciably acidic.

THE preparations of 4- and 5-trifluoromethylbenziminazole (Sykes and Tatlow, *J.*, 1952, 4078) and of 2-trifluoromethylbenziminazole (Smith and Steinle, *J. Amer. Chem. Soc.*, 1953, **75**, 1292) have already been described. In this paper we report the syntheses of 2 : 4- and 2 : 5-bistrifluoromethylbenziminazole by Phillip's method (*J.*, 1928, 2393) from trifluoroacetic acid and 2 : 3- and 3 : 4-diaminobenzotrifluoride, respectively. 2-Trifluoromethylbenziminazole was also made by this process.

3-Acetamido-2-nitrobenzotrifluoride (Rouche, *Bull. Acad. roy. Belg., Cl. Sci.*, 1927, **13**, 346), by catalytic hydrogenation, gave 3-acetamido-2-aminobenzotrifluoride, which underwent ring closure, with the elimination of water, when refluxed with 4N-hydrochloric acid, forming 2-methyl-4-trifluoromethylbenziminazole. This was made also from 2 : 3-diaminobenzotrifluoride and acetic acid by Phillip's method (*loc. cit.*). Diazotisation of 3-acetamido-2-aminobenzotrifluoride gave 1-acetyl-4-trifluoromethylbenzotriazole. These cyclisations are normal for monoacetylated aromatic *o*-diamines (see, for example, Saunders, "The Aromatic Diazo-compounds and Their Technical Applications," Arnold, London, 1949, p. 247; Wright, *Chem. Reviews*, 1951, **48**, 397).

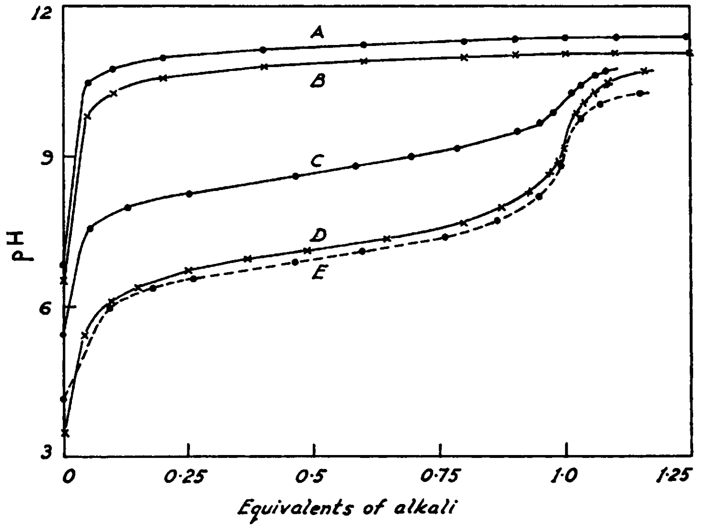
2-Phenyl-4-trifluoromethylbenziminazole was prepared from benzaldehyde and 2 : 3-diaminobenzotrifluoride by Weidenhagen's method (*Ber.*, 1936, **69**, 2263).

Lane (*Chem. and Ind.*, 1953, 798) has shown that 2-trifluoromethylbenziminazole reacts with *o*-phenylenediamine in 2-hydroxyethylamine to give 2 : 2′-dibenziminazolyl. This reaction has been confirmed, but 2 : 4- and 2 : 5-bistrifluoromethylbenziminazole did not so react. Though the fluoroalkyl group of 2-trifluoromethylbenziminazole shows this particular instability, it is not hydrolysed by 5N-sodium hydroxide, concentrated sulphuric acid, or sodium ethoxide in ethyl alcohol.

It has also been shown by Lane (*loc. cit.*) that 2-trifluoromethylbenziminazole can be titrated with dilute sodium hydroxide in the presence of thymolphthalein as indicator. We have confirmed and extended this observation (see Figure). The 2 : 4- and 2 : 5-bistrifluoromethyl compounds are quite acidic and may in fact be titrated with phenolphthalein as indicator. The 2-trifluoromethyl derivative is also appreciably acidic, though an end-point cannot be obtained with phenolphthalein. Whilst the 4- and 5-trifluoromethyl isomers give acidic reactions, they cannot actually be titrated even with thymolphthalein as indicator.

The acidity of all the trifluoromethylbenziminazoles, as compared with benziminazole which gives an alkaline reaction in aqueous solution, can be attributed to the electronegativity of the fluoroalkyl group. The greatest effect is exerted on the imino-function when the trifluoromethyl group occupies position 2 in the benziminazole nucleus; but even when located in the benzenoid ring however it still has an appreciable effect. The introduction of a second fluoroalkyl group into the benziminazole nucleus gives rise to a further increase in acidity. Rabinowitz and Wagner (*J. Amer. Chem. Soc.*, 1951, **73**, 3030) have shown that the introduction of a nitro-group into the 4- or the 5-position of the benziminazole nucleus gives the resulting compounds an acidic character. The theories advanced by these workers to explain the differing acidities of the nitrobenziminazoles appear to be equally applicable to the corresponding trifluoromethylbenziminazoles. Similarly, the increased acidity of the 2-isomer can be attributed to the electronic effect of the fluoroalkyl group, which can be transmitted to the imide group in both tautomers so that it should be more pronounced than in the 4- or the 5-isomer.

Benziminazole and substituted benziminazoles form salts with various metals, notably silver and mercury (see, for example, Welcher, "Organic Analytical Reagents," D. Van Nostrand, Co. Inc., New York, 1947, Vols. 1—4). The fluoro-compounds described here gave precipitates with some metal ions, but did not exhibit outstanding properties in this respect.



Curves were obtained by titration of aqueous-alcoholic solutions of benziminazoles with 0·0097N- (*A and B*), *or* 0·100N-*sodium hydroxide* (*C, D, and E*).

A, 4-*Trifluoromethyl*-; *B*-, 5-*trifluoromethyl*-; *C*, 2-*trifluoromethyl*; *D*, 2 : 5-*bistrifluoromethyl*-; *E*, 2 : 4-*bistrifluoromethyl-benziminazole.*

EXPERIMENTAL

2-*Trifluoromethylbenziminazole*.—*o*-Phenylenediamine (5·0 g.), trifluoroacetic acid (5·7 g.), and 4N-hydrochloric acid (33 c.c.) were refluxed together for 3 hr. The solution was neutralised (aqueous ammonia) and the precipitate recrystallised from ethyl alcohol, to give 2-trifluoromethylbenziminazole (5·5 g.), m. p. 209—210°, for which Smith and Steinle (*loc. cit.*) gave m. p. 210°.

2 : 4- *and* 2 : 5-*Bistrifluoromethylbenziminazole*.—2 : 3-Diaminobenzotrifluoride (Sykes and Tatlow, *loc. cit.*), treated as above, yielded 2 : 4-*bistrifluoromethylbenziminazole* (29%; it was crystallised with difficulty from aqueous ethyl alcohol), m. p. 151° (Found: C, 42·6; H, 1·8; F, 45·3. $C_9H_4N_2F_6$ requires C, 42·5; H, 1·6; F, 44·9%).

3 : 4-Diaminobenzotrifluoride similarly afforded 2 : 5-*bistrifluoromethylbenziminazole* (48%, from ethyl alcohol), m. p. 197° (Found: C, 42·3; H, 1·8; F, 44·7%).

2-*Methyl*-4-*trifluoromethylbenziminazole*.—3-Acetamido-2-nitrobenzotrifluoride (3·50 g.), ethyl alcohol (75 c.c.), and Raney nickel (*ca.* 0·5 g.) were shaken together at *ca.* 20°/1 atm. in hydrogen until the absorption was complete (1 hr.). The solution was filtered and evaporated *in vacuo*, and the residue recrystallised from aqueous ethyl alcohol to give 3-*acetamido*-2-*aminobenzotrifluoride* (2·10 g.), m. p. 137° (Found : C, 49·4; H, 4·0; F, 25·6. $C_9H_9ON_2F_3$ requires C, 49·5; H, 4·2; F, 26·1%).

When refluxed with 4N-hydrochloric acid, or with acetic anhydride–acetic acid, this product afforded, in almost quantitative yield, 2-*methyl*-4-*trifluoromethylbenziminazole*, m. p. 174° (Found : C, 54·0; H, 3·7; F, 28·3. $C_9H_7N_2F_3$ requires C, 54·0; H, 3·5; F, 28·5%).

2 : 3-Diaminobenzotrifluoride (3·20 g.), glacial acetic acid (1·15 c.c.), and 4N-hydrochloric acid (18·1 c.c.) were refluxed together for 45 min., the solution was neutralised with ammonia, and the resultant precipitate filtered off and recrystallised from water (charcoal). The same product (1·85 g.), m. p. and mixed m. p. 174°, was obtained.

1-*Acetyl*-4-*trifluoromethylbenzotriazole*.—Diazotisation at 0° of 3-acetamido-2-aminobenzotrifluoride (0·10 g.) in 2N-hydrochloric acid (4·0 c.c.), with sodium nitrite (0·032 g.) in water (1·0 c.c.), gave a solid. Recrystallised from ethyl alcohol, this afforded 1-*acetyl*-4-*trifluoromethylbenzotriazole* (0·056 g.), m. p. 100° (Found : C, 47·5; H, 2·3; N, 18·4. $C_9H_6ON_3F_3$ requires C, 47·2; H, 2·6; N, 18·3%).

2-*Phenyl*-4-*trifluoromethylbenziminazole*.—2 : 3-Diaminobenzotrifluoride (3·5 g.), copper acetate (8·0 g.), benzaldehyde (2·4 g.), methyl alcohol (75 c.c.), and water (50 c.c.) were refluxed together for 90 min. The solution was cooled, and the brown deposit filtered off, suspended in aqueous ethyl alcohol (3 : 1, v/v; 100 c.c.) and decomposed by hydrogen sulphide. The solution was filtered and evaporated *in vacuo*, and the residue was recrystallised from aqueous ethyl alcohol to give 2-*phenyl*-4-*trifluoromethylbenziminazole* (4·2 g.), m. p. 175° (Found : C, 64·0; H, 3·7; F, 21·3. $C_{14}H_9N_2F_3$ requires C, 64·1; H, 3·5; F, 21·7%).

Reactions of 2-*Trifluoromethyl-substituted Benziminazoles with* o-*Phenylenediamine*.—Equimolecular proportions of the iminazole and *o*-phenylenediamine were refluxed together for 4 hr. in 2-hydroxyethylamine (5 ml./0·25 g. of solids). The solution was poured into water. In the cases of 2 : 4- and 2 : 5-bistrifluoromethylbenziminazole, dilute acetic acid was added slowly to give a precipitate, which was filtered off and recrystallised to give the unchanged iminazole (*ca.* 80%), identified by m. p. and mixed m. p.

From the reaction of 2-trifluoromethylbenziminazole a white fluorine-free precipitate (65%) was obtained, which shrank but did not melt at *ca.* 400°. Lane (*J.*, 1953, 2238) observed a similar effect at 395—400°.

Formation of Precipitates.—1% Solutions of the substituted benziminazoles in ethyl alcohol were used throughout the tests. Aqueous solutions (0·4 mg./ml.) of the following ions were prepared; bismuth, cadmium, cobalt, copper(I), copper(II), gold(III), lead(II), mercury(II), silver, and thallium. The reagent solution (0·5 ml.) and the metal solution (2·0 ml.) were mixed and dilute aqueous ammonia was added to give an alkaline solution. Other tubes, containing solutions of the metal but no reagent, or the reagent solution but no metal ions, were similarly treated and used to study the behaviour of the reagent or metal ions alone. These tests were repeated for each reagent with each metal.

2-Trifluoromethylbenziminazole reacted with copper(II) and silver. The 4- and the 5-isomer gave precipitates with mercury(II) and silver. The 5-isomer formed with silver a gelatinous precipitate which did not crystallise. Only silver was precipitated by 2 : 4- and 2 : 5-bistrifluoromethylbenziminazole. 2-Methyl- and 2-phenyl-4-trifluoromethylbenziminazole reacted with lead(II), mercury(II), and silver. The latter compound also precipitated copper(II).

No precipitates were formed by these compounds in acid solution.

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