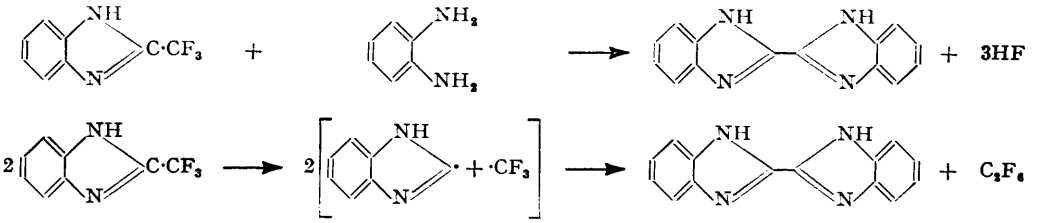
*The Reactivity of the Perfluoroalkyl Groups in 2-(Perfluoroalkyl)-benziminazoles.**

By E. S. Lane.

[Reprint Order No. 5544.]

Examples of a new reaction whereby 2-trifluoromethylbenziminazoles and *o*-diamines give 2 : 2′-dibenziminazolyls are provided. The reaction is extended to 2-heptafluoropropylbenziminazole which also reacts with *o*-phenylenediamine to give 2 : 2′-dibenziminazolyl. The significance of these reactions and some possible mechanisms are discussed.

It has recently been shown that certain 2-substituted benziminazoles can be prepared by the action of *o*-diamines on carboxylic amides or *N*-2-hydroxyethylamides (Lane, *J.*, 1953, 2238). In an attempt to prepare 2-trifluoromethylbenziminazole by this method from *o*-phenylenediamine and trifluoro-*N*-2-hydroxyethylacetamide a fluorine-free compound was obtained which gave analytical figures corresponding to $C_{14}H_{10}N_4$ and was identified as 2 : 2′-dibenziminazolyl. The following reaction mechanisms could have led to this compound :



Analysis of the reaction mixture gave a 96% overall recovery of fluorine as fluoride ion, so that, in view of the well-known stability of hexafluoroethane, the second mechanism may

* For a preliminary note on some of the work now reported see *Chem. and Ind.*, 1953, 798.

be disregarded. The same reaction also took place between 2-trifluoromethylbenziminazole and *o*-phenylenediamine in boiling ethylene glycol containing 2-hydroxyethylamine as acid acceptor. In a similar manner several 2 : 2′-dibenziminazolyls have been prepared from *o*-diamines and 2-trifluoromethyl-substituted benziminazoles, including, for the first time, some unsymmetrically substituted types; *e.g.*, 5-methyl-2 : 2′-dibenziminazolyl has been prepared from 2-trifluoromethylbenziminazole and 3 : 4-diaminotoluene and also from 5-methyl-2-trifluoromethylbenziminazole and *o*-phenylenediamine. These reactions conclusively support the reaction mechanism proposed above.

The 2-trifluoromethylbenziminazoles required for these syntheses were prepared by conventional methods and show several interesting properties. Microanalyses tended to show high values for hydrogen. Table 1 indicates that progressive replacement of the hydrogen atoms in 2-alkylbenziminazoles by fluorine causes a marked increase in the melting point: association of 1-unsubstituted benziminazoles (Hunter and Marriott, *J.*, 1941, 777), owing to the hydrogen bonding of the 1-hydrogen atoms, can be expected to increase with increasingly acidic nature of the hydrogen atoms involved. The 1-hydrogen atoms in 2-(perfluoroalkyl)benziminazoles are definitely more acidic than those of the corresponding alkyl compounds. Many of them, for example, exhibit an acid reaction in water and some can be titrated with aqueous alkali. The same effect is observed when the 2-positions of two benziminazole ring systems are joined by a (substantially) perfluorinated methylene chain, *e.g.*, in heptafluoroadipoylbis-2-benziminazole. This compound was prepared from heptafluoroadipic acid (from oxidation of intermediates kindly supplied by Mr. E. J. P. Fear, of the Ministry of Supply). The remaining hydrogen atom is believed to be in the α-position. *N*-Methylation of 2-trifluoromethylbenziminazole, however, depresses the melting point to below that of 1 : 2-dimethylbenziminazole, and this is obviously due to the removal of the more powerful counter-effects of the acidic hydrogen atoms and the tautomerism of the system.

TABLE 1. *Melting points of 2-substituted benziminazoles.*

Substituents	M. p.	Substituents	M. p.
2-Trifluoromethyl-	210°	2-Methyl-[1]	175°
2-Pentafluoroethyl-[2]	214—214·5	2-Ethyl-[3]	177—178
2-Heptafluoropropyl-	225—225·5	2-*n*-Propyl-[4]	157—159
Heptafluoroadipobis-2-benziminazole	283	Adipobis-2-benziminazole[5]	259—260
1-Methyl-2-trifluoromethylbenziminazole	97—97	1 : 2-Dimethyl-[6]	110—111

[1] Phillips (*J.*, 1928, 175). [2] Smith, jun., and Steinle, jun. (*J. Amer. Chem. Soc.*, 1952, **75**, 1292). [3] Hinsberg and Funcke (*Ber.*, 1894, **27**, 2189). [4] Weidenhagen (*Ber.*, 1936, **69**, 2763). [5] Shriner and Upson (*J. Amer. Chem. Soc.*, 1941, **63**, 2277). [6] Elderfield and McCarthy (*ibid.*, 1951, **73**, 975).

The well-known effect of the perfluoroalkyl group in reducing the basicity of the heterocyclic nitrogen system into which it is introduced is shown in this series by the failure of 2-(perfluoroalkyl)benziminazoles to form either hydrochlorides or picrates in aqueous solution. In glacial acetic acid crystalline perchlorates are sometimes formed on addition of perchloric acid, but these are not ideal for characterisation since they are frequently thermally unstable. In water, they also revert to the free base.

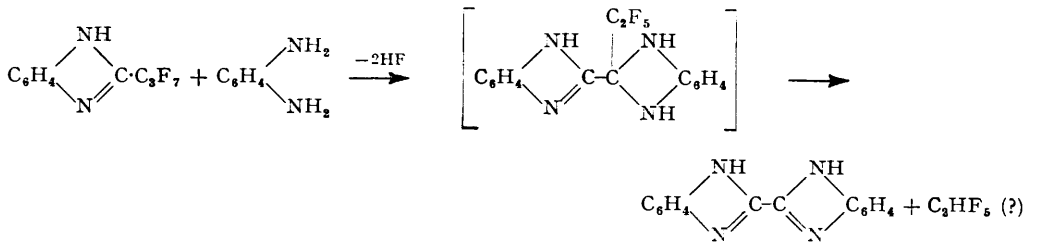
Introduction of the strongly negative trifluoromethyl groups into the 2-position of the benziminazole system does not alter the directing influence of the iminazole ring towards nitration of the benzene ring. Benziminazole itself is normally nitrated in the 5-position (van der Want, *Rec. Trav. chim.*, 1948, **67**, 45; contrast Wooley, *J. Biol. Chem.*, 1944, **152**, 225). 2-Trifluoromethylbenziminazole is similarly nitrated in the 5-position, giving a product identical with that formed in the conventional manner from trifluoroacetic acid and 5-nitro-*o*-phenylenediamine.

The new synthesis of 2 : 2′-dibenziminazolyls described above is not, however, of universal application since certain *o*-diamines fail to react in this manner; *e.g.*, 2-trifluoromethylbenziminazole did not react with 5-nitro-*o*-phenylenediamine and 5-nitro-2-trifluoromethylbenziminazole did not react with either *o*-phenylenediamine or 3 : 4-diaminotoluene. The reaction does, however, appear to be the first example of the reaction of a trifluoromethyl

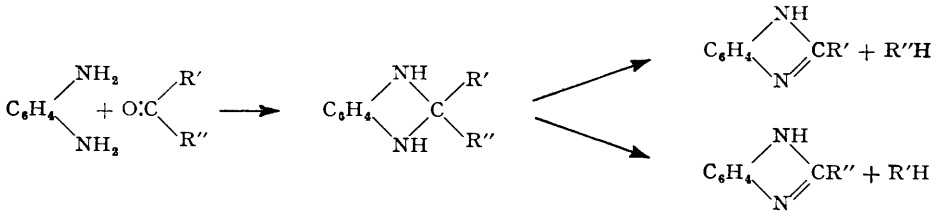
group with primary amines. It also provides a new method for the formation of a benziminazole ring and in this respect should be compared with the preparation of benziminazole itself from *o*-phenylenediamine, chloroform, and potassium hydroxide (Grassi-Cristaldi and Lambardi, *Gazzetta*, 1895, **25**, 225).

The unusual reactivity of the trifluoromethyl groups is probably due to its position adjacent to the nitrogen atom in a heterocyclic base, and provides an interesting parallel to the well-known aldol-type condensations of methyl groups in compounds such as α-picoline, quinaldine, and indeed, 2-methylbenziminazole itself (Bamberger and Berlé, *Annalen*, 1893, **273**, 315).

It was obviously of interest to determine whether the benziminazole ring system altered the reactivity of higher perfluoroalkyl groups in the 2-position. When 2-heptafluoropropylbenziminazole reacted with *o*-phenylenediamine under similar conditions, the product was again 2 : 2′-dibenziminazolyl. Here, in addition to the hitherto unrecorded example of the reaction of primary amine groups with a perfluoroalkyl group it will be noted that a C–C bond in a normally very stable perfluoroalkyl group has been broken. This new reaction is presumed to proceed *via* an unstable intermediate which later disproportionates:



There are certain similarities between this reaction and those leading to benziminazole formation by the reaction of unsymmetrical ketones with *o*-diamines (Elderfield and McCarthy, *J. Amer. Chem. Soc.*, 1951, **73**, 975):



In this case the C–C bond which is broken is the one proceeding from the carbon atom having the greater degree of substitution, so that in the intermediate benziminazoline the pentafluoroethyl group would be expected to be expelled in preference to that of the 2-benziminazolyl residue. Elderfield and McCarthy noticed that *N*-substitution in the *o*-diamine facilitated elimination of the expelled grouping, which is in direct contrast to results in this particular reaction where *N*-substitution completely inhibits the reaction, neither *N*-methyl- nor *N*-phenyl-*o*-phenylenediamine reacting with 2-trifluoromethylbenziminazole. This, however, is probably due to the failure of the initial reaction between fluorine atoms in the perfluoroalkyl group and the hydrogen atoms of the substituted amino-group, so that the unstable benziminazoline structure is not actually formed. Some factors, not yet elucidated, govern the reactivity of amino-groups with perfluoroalkyl groups in this reaction since, although several *o*-diamines have successfully undergone this reaction, no primary aromatic amines have been made to react under these general conditions.

The 2 : 2′-dibenziminazolyls described below contain the same specific grouping as found in the well-known organic reagents for iron, *o*-phenanthroline and 2 : 2′-dipyridyl. None, however, gave colours with iron or with copper salts. Their inactivity is presumably due

to the low basicity of the benziminazole nitrogen atoms and is of interest in view of the recently reported metal-complexing activity of 2-2′-pyridylbenziminazole and 2-2′-pyridyldihydroglyoxaline, both of which possess the same complexing grouping but with one of the heterocyclic nitrogen atoms of the grouping having greater basicity. The failure of the related 2-2′-pyridylbenzoxazole to form complexes with metals has similarly been attributed to the low basicity of the oxazole-nitrogen atom (Walter and Freiser, *Analyt. Chem.*, 1954, **26**, 217).

Experimental

Determination of the Equivalent Weight of Benziminazoles.—(*A*) The 2-(perfluoroalkyl)-benziminazoles can be accurately titrated in dimethylformamide solution with standardised sodium methoxide in methanol–benzene, thymol-blue being used as indicator (Fritz, *Analyt. Chem.*, 1952, **24**, 674).

(*B*) 2 : 2′-Dibenziminazolyls can be accurately titrated with standardised perchloric acid in glacial acetic acid with crystal-violet as indicator (Pifer and Wollish, *ibid.*, p. 300). Dilution of the titration mixture with ether precipitates the perchlorate of the base, which is filtered off. Traces of indicator are removed by washing, and the residue, after drying, is suitable for microanalysis.

The equivalents recorded below were carried out by these methods. Some compounds were suitable for determination by both methods and the letters in parentheses indicate which particular method has been used in individual cases.

2-*Trifluoromethylbenziminazole.*—This was prepared by Smith and Steinle's method (*loc. cit.*), except that it was recrystallised from dilute hydrochloric acid; it had m. p. 210° [Found : equiv. (*A*), 186·5. Calc. for $C_8H_5N_2F_3$: equiv., 186]. The *perchlorate* melted at 297° (decomp.) (Found : N, 10·4; Cl, 12·6. $C_8H_6O_4N_2ClF_3$ requires N, 9·8; Cl, 12·75%).

5-*Methyl*-2-*trifluoromethylbenziminazole.*—Similarly obtained from trifluoroacetic acid and 3 : 4-diaminotoluene, this *base* crystallised in colourless cubes, m. p. 185·5—187° (from dil. aqueous hydrochloric acid) [Found : N, 14·1%; equiv. (*A*), 199. $C_9H_7N_2F_3$ requires N, 14·0%; equiv., 200].

1-*Methyl*-2-*trifluoromethylbenziminazole.*—Similarly prepared from trifluoroacetic acid and *N*-methyl-*o*-phenylenediamine hydriodide (Brown and Le Roi Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 24), this *base* was isolated as colourless diamond-shaped plates, m. p. 95—97° (from aqueous acetic acid) (Found : C, 53·9; H, 4·0; N, 13·9. $C_9H_7N_2F_3$ requires C, 54·0; H, 3·5; N, 14·0%). The *perchlorate* melted at 233—235° (decomp.) (from acetic acid) (Found : N, 9·1; Cl, 12·2. $C_9H_8O_4N_2F_3Cl$ requires N, 9·3; Cl, 12·2%).

5-*Nitro*-2-*trifluoromethylbenziminazole.*—(*a*) 4-Nitro-*o*-phenylenediamine sulphate (12·6 g.), trifluoroacetic acid (5·7 g.), and 4N-hydrochloric acid (100 ml.) were refluxed together for 24 hr. After cooling, the solid product was filtered off, including a deposit from the condenser walls (10·5 g.), and the *base* recrystallised from dilute hydrochloric acid in fine, pale yellow needles, m. p. 152—154° (slow heating) [Found : C, 39·5, 39·6; H, 2·4, 2·36; N, 16·5, 16·8%; equiv. (*A*), 250. $C_8H_4O_2N_3F_3,H_2O$ requires C, 38·6; H, 2·4; N, 16·9%; equiv., 249]. It gives a yellow colour with aqueous alkalis.

(*b*) 2-Trifluoromethylbenziminazole (5 g.) was dissolved in concentrated sulphuric acid (25 ml.) and cooled in an ice-bath whilst fuming nitric acid (15 ml.) was added dropwise with efficient stirring. The mixture was kept at room temperature for 2 hr. and then poured into a large excess of cold water. The precipitated solid was filtered off (4·3 g.) and recrystallised from dilute hydrochloric acid. After drying for 2 hr. *in vacuo* at 100°, the ***anhydrous*** compound melted at 155°. In admixture with the sample (*a*) it melted at 152—154° (Found : N, 17·9. $C_8H_4O_2N_3F_3$ requires N, 18·2%).

4 : 7-*Diethoxy*-2-*trifluoromethylbenziminazole.*—Prepared by the procedure detailed above from trifluoroacetic acid and a mixture of 2 : 3- and 2 : 5-diaminoquinol diethyl ether (Lane and Williams, *J.*, 1953, 4187), this *base* melted at 216° (ethanol) [Found : C, 52·7; H, 5·15; N, 10·6%; equiv. (*A*), 276. $C_{14}H_{13}O_2N_2F_3$ requires C, 52·5; H, 4·7; N, 10·2%; equiv., 274].

2-*Heptafluoropropylbenziminazole.*—Heptafluorobutyric acid (10·7 g.) and *o*-phenylenediamine (5·4 g.) were refluxed together in 4N-hydrochloric acid (100 ml.) for 96 hr. After cooling, 2-*heptafluoropropylbenziminazole* was filtered off (5 g.). Further material was obtained by continued refluxing of the mother-liquor but the reaction was very slow. On recrystallisation from aqueous ethanol (charcoal) the base melted at 225—225·5° (with sublimation; in open tube) [Found : C, 42·2; H, 2·8; N, 9·9%; equiv. (*A*), 285. $C_{10}H_5N_2F_7$ requires C, 42·0; H, 1·75; N, 9·8%; equiv., 286].

Heptafluoroadipobis-2-benziminazole.—Heptafluoroadipic acid (5·5 g.) and *o*-phenylenediamine (4·3 g.) were refluxed together for 12 hr. in 4N-hydrochloric acid (25 ml.). The mother-liquor was then decanted from a pale green, plastic residue which gradually became granular on continued trituration in cold water (3·1 g.). The *base*, obtained crystalline with some difficulty on recrystallisation from 50% aqueous acetic acid (charcoal), had m. p. 283° (decomp.) (Found: C, 51·7; H, 3·9; N, 12·8. $C_{18}H_{11}N_4F_7$ requires C, 51·9; H, 2·65; N, 13·5%).

2 : 2′-*Dibenziminazolyl.*—(*a*) Trifluoroacetic acid (11·4 g.) was refluxed for 5 min. with 2-hydroxyethylamine (20 g.); *o*-phenylenediamine (10·8 g.) and ethylene glycol (10 ml.) were then added, and the mixture refluxed for a further 6 hr. during which crystalline material separated out and caused severe "bumping." The contents of the flask were emptied into cold water, and the pale yellow solid which separated was filtered off (9·7 g.). Recrystallisation from ethylene glycol yielded the base in pale, primrose-yellow needles which did not melt at 400° [Found: N, 23·3%; equiv. (*B*), 232. Calc. for $C_{14}H_{10}N_4$: N, 23·9%; equiv., 234].

(*b*) 2-Trifluoromethylbenziminazole (1·86 g.), *o*-phenylenediamine (1·1 g.), and 2-hydroxyethylamine (5 g.) were refluxed together in ethylene glycol (25 ml.) for 6 hr. After cooling, the needle-shaped crystals which had separated were filtered off (1·5 g.) and recrystallised from ethylene glycol, yielding the base (Found: C, 71·5; H, 4·1; N, 24·2. Calc. for $C_{14}H_{10}N_4$: C, 71·8; H, 4·3; N, 23·95%). A similar preparation from 0·400 g. of 2-trifluoromethylbenziminazole was carried out. The reaction mixture was then transferred to a flask and steam-distilled from concentrated sulphuric acid at 140°, and the distillate analysed for fluoride ion by Belcher, Caldas, and Clark's method (*Analyst*, 1952, **77**, 602). The amount of fluoride ion detected was 96% of theory. A duplicate experiment on 2-trifluoromethylbenziminazole indicated that all the fluorine in this compound remained in the covalent form under these experimental conditions.

(*c*) The procedure above was repeated with 2-heptafluorobenziminazole (1·0 g.), *o*-phenylenediamine (0·4 g.), and 2-hydroxyethylamine (0·5 g.). The product was recrystallised from ethylene glycol and did not melt at 400°. It was identified as 2 : 2′-dibenziminazolyl (Found: N, 23·8%; equiv., 233).

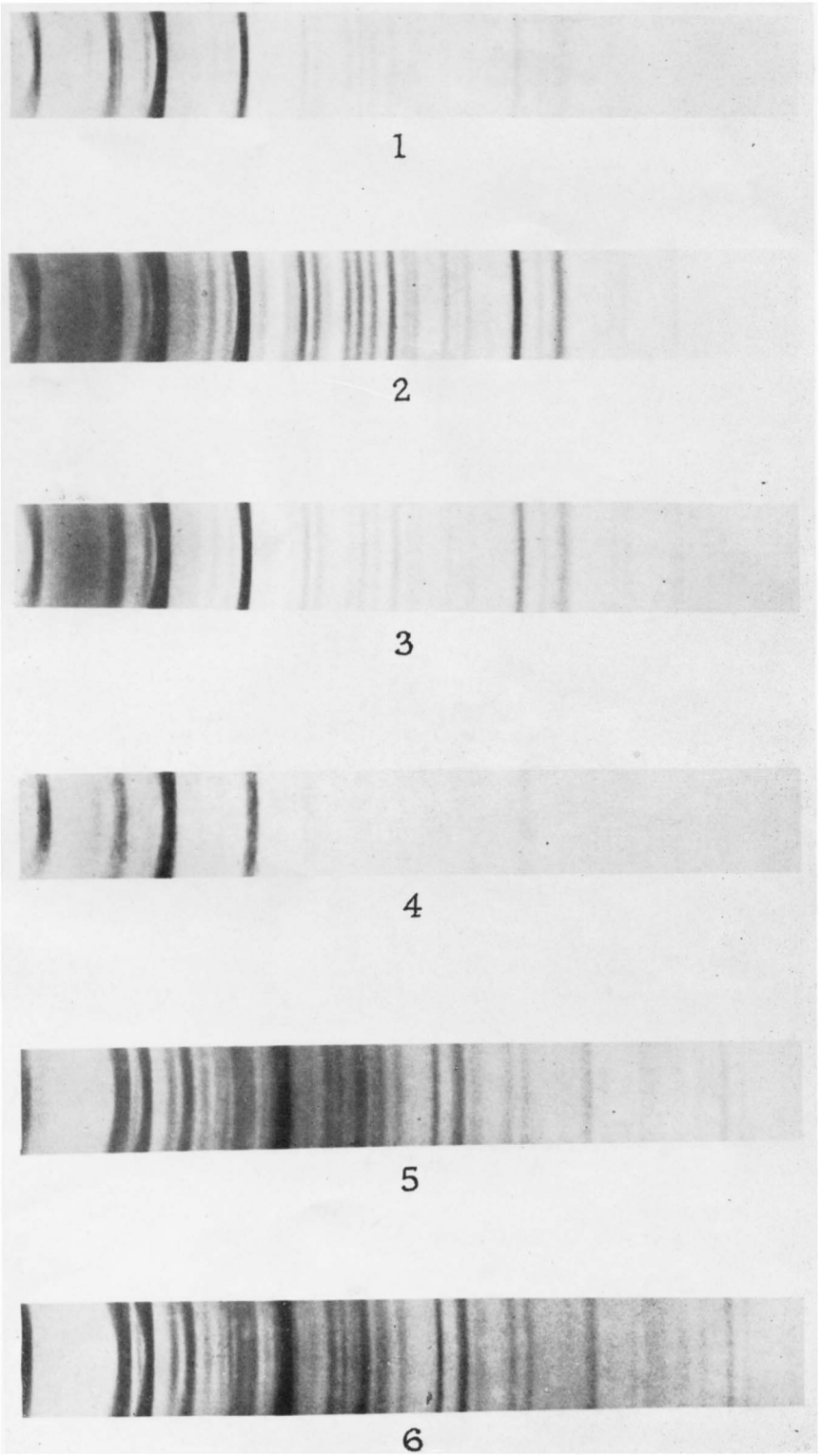
4 : 4′ : 8 : 8′-*Tetraethoxy*-2 : 2′-*dibenziminazolyl.*—2 : 3-Diaminoquinol diethyl ether (Lane and Williams, *loc. cit.*) (1·96 g.), ethyl trifluoroacetate (0·71 g.), and 2-hydroxyethylamine (2 ml.) were refluxed together for 6 hr. (Separation of a crystalline solid caused bumping.) The mixture was poured into water, and the pale yellow solid filtered off (0·9 g.). This highly insoluble material was recrystallised with difficulty from boiling nitrobenzene, the *base* forming a white, microcrystalline powder, m. p. 353° (decomp.), which gave a brilliant orange colour with mineral acids and did not fluoresce under ultra-violet light (Found: C 63·9; H, 6·5; N, 13·9. $C_{22}H_{26}O_4N_4$ requires C, 64·5; H, 6·35; N, 13·7%).

4 : 8-*Diethoxy*-2 : 2′-*dibenziminazolyl.*—Similarly prepared from 2-trifluoromethylbenziminazole (1·9 g.) and 2 : 3-diaminoquinol diethyl ether (2·0 g.), this *base* melted at 352° (decomp.) (from ethylene glycol). It gave orange colours with mineral acids [Found: C, 66·4; H, 5·2; N, 17·7%; equiv. (*B*), 322. $C_{18}H_{18}O_2N_4$ requires C, 67·0; H, 5·6; N, 17·4%; equiv., 322].

5-*Methyl*-2 : 2′-*dibenziminazolyl.*—(*a*) Prepared as above from 2-trifluoromethylbenziminazole (1·86 g.) and 3 : 4-diaminotoluene (1·22 g.), this *base* formed pale yellow crystals (from aqueous alcohol), melting indistinctly at >390° with decomposition and sublimation [Found: C, 71·6; H, 5·15; N, 21·9%; equiv. (*B*), 246. $C_{15}H_{12}N_4$ requires C, 72·5; H, 4·8; N, 22·6%; equiv., 248]. This compound is remarkably soluble in alcohol compared with the related symmetrical compounds 2 : 2′-dibenziminazolyl and 5 : 5′-dimethyl-2 : 2′-dibenziminazolyl (Lane, *loc. cit.*). Acid solutions of the base showed a vivid blue fluorescence under ultra-violet light. The *diacetate* was obtained on crystallising the base from glacial acetic acid as pale yellow needles without a definite m. p. (Found: C, 62·0; H, 5·0; N, 15·2. $C_{15}H_{12}N_4,2C_2H_4O_2$ requires C, 61·9; H, 5·4; N, 15·2%).

(*b*) This was also prepared as above in quantitative yield from 5-methyl-2-trifluoromethylbenziminazole (2·0 g.) and *o*-phenylenediamine (1·1 g.) and identified as the diacetate (Found: C, 62·4; H, 5·45; N, 15·2%).

Characterisation of 2 : 2′-*Dibenziminazolyl and* 5-*Methyl*-2 : 2′-*dibenziminazolyl.*—In view of the unusual nature of the reactions described above it was felt desirable to have as complete a characterisation as possible of these compounds. The former compound for example has no definite m. p. below 400° and is very stable towards common reagents, and the acetates of both compounds are not ideal for characterisation purposes as they have no definite melting point but slowly lose acetic acid on heating. Dr. J. Adam kindly took a number of *X*-ray powder photographs of these compounds, using a 19-cm. camera with filtered Cu-K_α radiation. The Plate shows the powder diffraction patterns obtained, and despite the poor crystallinity of some



1, 2 : 2′-Dibenziminazolyl prepared by Hübner's method (*loc. cit.*).
2, 2 : 2′-Dibenziminazolyl, from $CF_3 \cdot CO_2H$, $NH_2 \cdot CH_2 \cdot CH_2 \cdot OH$, and o-$C_6H_4(NH_2)_2$.
3, 2 : 2′-Dibenziminazolyl, from 2-trifluoromethylbenziminazole and o-$C_6H_4(NH_2)_2$.
4, 2 : 2′-Dibenziminazolyl, from 2-heptafluoropropylbenziminazole and o-$C_6H_4(NH_2)_2$.
5, 5-Methyl-2 : 2′-dibenziminazolyl acetate from 5-methyl-2-trifluoromethylbenziminazole and o-$C_6H_4(NH_2)_2$.
6, 5-Methyl-2 : 2′-dibenziminazolyl acetate from 2-trifluoromethylbenziminazole and 3 : 4-diaminotoluene.

[*To face p.* 538.

of the specimens there is little doubt as to the identity of the samples. 2 : 2′-Dibenziminazolyl prepared by the reactions above shows an identical powder diffraction pattern with that from an authentic specimen prepared by Hübner's method (*Annalen*, 1881, **209**, 339) from *oo*′-dinitrooxanilide. The powder-diffraction patterns obtained from the two samples of the diacetate of 5-methyl-2 : 2′-dibenziminazolyl prepared by the two different methods described above also confirmed their identity.

The author is indebted to Dr. F. Howlett (British Nylon Spinners, Pontypool) who recommended the methods used for the determination of the equivalent weights of these compounds, and to Dr. J. Adam (A.E.R.E.) who took the *X*-ray photographs.

A.E.R.E., HARWELL, NEAR DIDCOT, BERKS. [*Received, July 10th*, 1954.]