A Modified Benziminazole Synthesis. Part II. A Route to Unsymmetrically Substituted* 2 : 2′-*Dibenziminazolyls and Methylenebis*-2-*benziminazoles.*

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The mechanism of the formation of 2 : 2′-dibenziminazolyls and methylenebis-2-benziminazoles from *o*-diamines and oxamide and malonamide respectively is discussed, and the preparation of some unsymmetrically substituted compounds, which support the proposed mechanism, described.

Whereas oxalic acid or its esters react with *o*-phenylenediamine to form 2 : 3-dihydroxyquinoxaline (I*a*; R = H), yet it was shown in Part I * that the use of oxamide in this reaction gave 2 : 2′-dibenziminazolyl (III; R = H) as the chief product. Further experimental work has now indicated that 2 : 3-dihydroxyquinoxaline is, in fact, formed first and that this reacts with another molecule of diamine to form (III; R = H). Thus, with one equivalent of *o*-phenylenediamine dihydrochloride, oxamide reacted to form (I*a*; R = H), and with two equivalents (III; R = H) was formed (see Part I). Preformed (I*a*; R = H) similarly reacted with *o*-phenylenediamine dihydrochloride, giving (III; R = H). Further evidence was obtained from reaction of oxamic acid with first one, and then two, equivalents of *o*-phenylenediamine, the main products being respectively (I*a*; R = H) and (III; R = H). The conversion of a quinoxaline ring system into that of a benziminazole ring has not hitherto been noted but it seems likely that this reaction is another example of Galat and Elion's method of acylation (*J. Amer. Chem. Soc.*, 1943, **65**, 1566). Thus, if (I*a*; R = H) is regarded as reacting in its diketo-form (I*b*; R = H) with *o*-phenylenediamine, it can undergo a form of " ammonolysis " with the formation of

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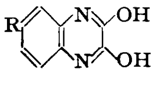
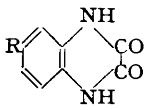
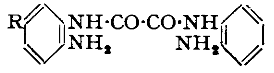
* The communication " A Modified Benziminazole Synthesis," *J.*, 1953, 2238, is regarded as Part I.

the highly labile compound (II; R = H) which is spontaneously dehydrated and cyclised to form (III; R = H). The latter step is, of course, a well-known feature of the formation of 2-substituted benziminazoles by reduction of acylated *o*-nitroanilines.

This reaction sequence has been used for the preparation of an unsymmetrically substituted 2 : 2′-dibenziminazolyl, since 2 : 3-dihydroxy-6-methylquinoxaline (I*a*; R = Me) and *o*-phenylenediamine dihydrochloride reacted to form 5-methyl-2 : 2′-dibenziminazolyl (III; R = Me). The identity of the product was confirmed by comparison of the *X*-ray powder photograph of its diacetate with those of samples prepared by two alternate routes from 2-trifluoromethyl-substituted benziminazoles (Lane, *J.*, 1955, 534). The main product from the new reaction is heavily contaminated with highly-coloured products of type (IV) (see Hinsberg, *Ber.*, 1896, **29**, 784). Acid solutions of these types of compound are brilliantly fluorescent in ultra-violet light, but the fluorescent colour (yellow-green) is quite different from that of the dibenziminazolyls (blue) and this enables one type of compound to be detected in the presence of the other. Although another route to unsymmetrically substituted benziminazoles is now provided, this contamination by difficultly removable by-products renders it of little synthetic use in comparison with the route *via* 2-trifluoromethyl-substituted benziminazoles. Furthermore, there are limitations to the scope of the reaction; *e.g.*, 2 : 3-dihydroxyquinoxaline failed to react with the salts of either 3 : 4-diaminotoluene or 4-nitro-*o*-phenylenediamine.


(I*a*)


(I*b*)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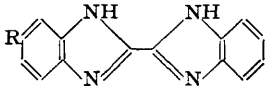
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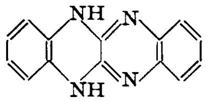
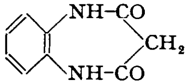
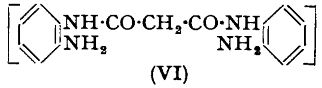

(IV)

In an analogous way, the formation of methylenebis-2-benziminazoles from *o*-diamines and malonamide (cf. Part I) is believed to involve *o*-phenylenemalonamide (V) as an intermediate product. By reaction of (V) with a further molecule of *o*-phenylenediamine dihydrochloride, methylenebis-2-benziminazole (VII) has been obtained, presumably *via* the intermediate compound (VI). This interesting conversion of a 7- into a 5-membered ring system is of greater synthetic value than the previous example since there are no coloured by-products, and the reaction has been extended to include the preparation of the unsymmetrical compound 4 : 7-diethoxymethylenebis-2-benziminazolyl from *o*-phenylenemalonamide and 2 : 3-diaminoquinol diethyl ether hydrochloride.


(V)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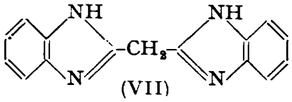
(VII)

It is noteworthy that whereas both the 2 : 2′-dibenziminazolyls and the methylenebis-2-benziminazoles formed diacetates and/or dihydrochlorides, the former group of compounds behaved only as monofunctional bases towards perchloric acid in glacial acetic acid. Although some functions are not always fully developed during titrations in glacial acetic acid, it is probable that this is a further example of steric interference with salt formation. Similar behaviour has been noted in the cases of *o*-phenanthroline, 2 : 2′-dipyridyl, and certain analogues of 2 : 2′-dipyridyl containing *iso*quinoline and thiazole rings (Knott and Breckenridge, *Canad. J. Chem.*, 1954, **32**, 512) which form only monopicrates. Like 2 : 2′-dibenziminazolyl, *o*-phenanthroline and 2 : 2′-dipyridyl behave only as monoacid bases towards perchloric acid in glacial acetic acid.

EXPERIMENTAL

The equivalent weights of the benziminazoles were determined by titration with 0·1N-perchloric acid in glacial acetic acid, crystal-violet being used as indicator (Fritz, "Acid-Base Titrations in Nonaqueous Solvents," G. F. Smith Chemical Co., Columbus, 1952).

2 : 2′-*Dibenziminazolyl.*—2 : 3-Dihydroxyquinoxaline (3·24 g.), *o*-phenylenediamine (2·16 g.), and ethylene glycol were refluxed for 8 hr., during which crystalline material slowly separated. The mixture was poured into water, and the yellow solid filtered off. The above base, crystallised from ethylene glycol (carbon), formed yellow needles which did not melt below 400° (Found : C, 72·1; H, 4·7; N, 23·6%; equiv., 232. Calc. for $C_{14}H_{10}N_4$: C, 71·8; H, 4·3; N, 23·95%; equiv., 234). The *diacetate* (pale yellow needles from glacial acetic acid) had no definite m. p. (Found : C, 60·6; H, 4·7; N, 15·3. $C_{18}H_{18}O_4N_4$ requires C, 61·0; H, 5·1; N, 15·8%).

Reaction of Oxamic Acid with o-*Phenylenediamine.*—Equimolecular quantities (0·05 mole) of this acid and base when refluxed in ethylene glycol for 5 hr. gave a 64% yield of 2 : 3-dihydroxyquinoxaline (fine cream needles from ethylene glycol), m. p. 386° (Found : C, 59·1; H, 3·6; N, 17·4. Calc. for $C_8H_6O_2N_2$: C, 59·2; H, 3·7; N, 17·3%. Repetition of this experiment with twice the quantity of *o*-phenylenediamine gave 2 : 2′-dibenziminazolyl (51%) as bright yellow needles (ethylene glycol) (Found : N, 24·0%; equiv., 235).

5-*Methyl*-2 : 2′-*dibenziminazolyl*—2 : 3-Dihydroxy-6-methylquinoxaline (2 g.), *o*-phenylenediamine dihydrochloride (2 g.), and ethylene glycol (15 ml.) similarly gave the above base (2·3 g.) as yellow crystals (aqueous ethanol), melting indistinctly at 380—390° (decomp.). The *diacetate* (Found : C, 62·0; H, 5·3; N, 15·2. $C_{19}H_{20}O_4N_4$ requires C, 61·9; H, 5·4; N, 15·2%), the *sulphate* (Found : C, 39·8; H, 3·75; N, 12·9. $C_{15}H_{12}N_4,2H_2SO_4$ requires C, 40·5; H, 3·6; N, 12·6%), and the *monopicrate* (Found : N, 20·9. $C_{21}H_{15}O_7N_7$ requires N, 20·55%) had indefinite m. p.s (cf. Lane, *loc. cit.*).

Methylenebis-2-*benziminazole.*—*o*-Phenylenemalonamide (1·76 g.), *o*-phenylenediamine dihydrochloride (2·0 g.), and ethylene glycol were refluxed for 4 hr. The mixture was poured into water, neutralised with ammonia, and filtered. The base melted at 380—390° (decomp.) (see Part I) (Found : C, 72·0; H, 4·8; N, 22·3%; equiv., 124. Calc. for $C_{15}H_{12}N_4$: C, 72·5; H, 4·8; N, 22·6%; equiv., 124). The *dipicrate* melted at 246—247° (alcohol, dimethylformamide) (Found : N, 20·2%; equiv., 354. $C_{27}H_{18}O_{14}N_{10}$ requires N, 19·7%; equiv., 353). The equivalent was determined by Clark and Wang's method (*Analyt. Chem.*, 1954, **26**, 1230).

4 : 7-*Diethoxymethylenebis*-2-*benziminazolyl.*—2 : 3-Diaminoquinol diethyl ether hydrochloride (Lane and Williams, *J.*, 1953, 4187) (2·3 g.), *o*-phenylenemalonamide (1·76 g.), and ethylene glycol (15 ml.) were refluxed for 2 hr., and worked up as before. The above *base* (2·9 g.) formed a straw-yellow powder (ethylene glycol; carbon) shrinking with decomposition at 270° with no definite m. p. (Found : C, 68·2; H, 6·1; N, 16·6%; equiv., 165. $C_{19}H_{20}O_2N_4$ requires C, 67·8; H, 5·95; N, 16·65%; equiv., 168). The *dihydrochloride* (cream prisms) decomposed, when slowly heated to 270°, without melting (Found : N, 14·2; Cl, 17·6. $C_{19}H_{20}O_2N_4,2HCl$ requires N, 13·7; Cl, 17·4%).

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