

**460.** *A Modified Benziminazole Synthesis.*

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Reaction of aliphatic diamides with *o*-diamines or their salts is shown to produce bisbenziminazoles, including a number which cannot be obtained by the conventional route from the dicarboxylic acid. Some extensions of the reaction are reported.

LITTLE work has been reported on the preparation of benziminazoles from carboxyamides and *o*-diamines despite the good yields that have been obtained in this reaction (Wright, *Chem. Reviews*, 1951, **48**, 397, and references therein). In order to provide a simpler route to some difunctional benziminazole derivatives (required for metal-complex investigations), the reaction between some aliphatic diamides and *o*-diamines has been examined. Whereas oxalic acid or its esters with *o*-diamines give 2 : 3-dihydroxyquinoxalines (Phillips, *J.*, 1928, 2397), oxamide and *o*-phenylenediamine or 3 : 4-diaminotoluene have now been shown to give, respectively, 2 : 2'-dibenziminazolyl and 5 : 5'-dimethyl-2 : 2'-dibenziminazolyl. The former compound has previously been obtained by the reduction of *oo'*-dinitro-oxanilide (Hübner, *Annalen*, 1881, **209**, 339), and the latter by the reduction of *NN'*-di-(4-methyl-2-nitrophenyl)oxamide (Hübner, *ibid.*, p. 370) and by heating *NN'*-di-(2-amino-4-methylphenyl)oxamide (Hinsberg, *Ber.*, 1882, **15**, 2690). The powerful fluorescence of solutions of these compounds and particularly of their salts is now noted.

Conventional syntheses of bisbenziminazoles from dibasic acids or esters also fail in the

case of malonic acid or esters, which with *o*-phenylenediamine form *o*-phenylenemalonamide (Shriner and Boermans, *J. Amer. Chem. Soc.*, 1944, **66**, 1810; Phillips, *ibid.*, 1942, **64**, 187). Malonamide with *o*-phenylenediamine, however, gives methylenebis-2-benzimidazole. This synthesis proceeded readily when the *o*-diamine or its salts and the diamide were heated together, preferably in a high-boiling solvent, *e.g.*, ethylene glycol or glycerol. *NN'*-Di-(2-hydroxyethyl)diamides, which, in some cases, are more conveniently prepared than the unsubstituted diamides, may also be used, as may the ammonium salts of the acids. The scope of the reaction, which may be regarded as an extension of the acylation method of Galat and Elion (*J. Amer. Chem. Soc.*, 1943, **65**, 1566), is shown below.

Equimolecular quantities of *NN'*-di-(2-hydroxyethyl)oxamide and *o*-phenylenediamine under similar conditions gave, uniquely, benzimidazole-2-carboxy-2'-hydroxyethylamide. The 5-methyl homologue was similarly obtained from 3 : 4-diaminotoluene. This route to these compounds is considerably simpler than that described by Copeland and Day (*J. Amer. Chem. Soc.*, 1943, **65**, 1072) for the former compound.

#### EXPERIMENTAL

*NN'*-Di-(2-hydroxyethyl)diamides were prepared by Rauscher and Clark's method (*J. Amer. Chem. Soc.*, 1948, **70**, 438).

2 : 2'-Dibenzimidazolyl.—Oxamide (4.4 g.), *o*-phenylenediamine (10.8 g.), and ethylene glycol (10 ml.) were refluxed for 3 hr., then cooled and poured into water (200 ml.). The yellow insoluble material was filtered off (9.2 g.) and recrystallised (charcoal) from ethylene glycol, yielding 2 : 2'-dibenzimidazolyl as a yellow microcrystalline powder which shrank with decomposition at 395—400° but did not completely melt (Found : C, 71.6; H, 4.4; N, 24.0. Calc. for C<sub>14</sub>H<sub>10</sub>N<sub>4</sub> : C, 71.8; H, 4.3; N, 23.95%). Hübner (*loc. cit.*) reported that it did not melt at 300°.

Ammonium oxalate monohydrate (3.6 g.), *o*-phenylenediamine (5.5 g.), and glycerol (10 g.) were refluxed together for 2 hr., then poured into water (100 ml.), and the 2 : 2'-dibenzimidazolyl was filtered off and recrystallised from ethylene glycol (yield 2.0 g.).

5 : 5'-Dimethyl-2 : 2'-dibenzimidazolyl.—Oxamide (4.4 g.), 3 : 4-diaminotoluene (12.2 g.), and ethylene glycol (15 g.) similarly formed 5 : 5'-dimethyl-2 : 2'-dibenzimidazolyl (6.4 g.), which crystallised from ethanol as fine yellow needles, m. p. 350° (with sublimation, in an open tube) (Found : N, 22.0. Calc. for C<sub>16</sub>H<sub>14</sub>N<sub>4</sub> : N, 21.35%). Hübner (*loc. cit.*) gives m. p. "about 193°."

Ammonium oxalate monohydrate (1.7 g.), 3 : 4-diaminotoluene (3.7 g.), and glycerol (5 g.) similarly yielded this compound (2.4 g.), m. p. 345—350°.

Methylenebis-2-benzimidazole.—Malonamide (5.1 g.), *o*-phenylenediamine (10.8 g.), and ethylene glycol (15 ml.) were refluxed together for 4 hr., then poured into water, and the solid formed (5.2 g.) was filtered off. Recrystallisation (charcoal) from ethylene glycol gave colourless prisms of methylenebis-2-benzimidazole, m. p. 389° (decomp.; bath preheated to 370°) (Found : C, 72.5; H, 5.3; N, 22.2. C<sub>15</sub>H<sub>12</sub>N<sub>4</sub> requires C, 72.5; H, 4.8; N, 22.6%). The dihydrochloride crystallised from water as cubes, m. p. 330—333° (decomp.) (Found : N, 17.1; Cl, 21.7. C<sub>15</sub>H<sub>12</sub>N<sub>4</sub>·2HCl requires N, 17.4; Cl, 22.15%). Neither compound exhibited fluorescence.

*NN'*-Di-(2-hydroxyethyl)malonamide (5.7 g.) and *o*-phenylenediamine (5.4 g.) were refluxed together for 4 hr., then cooled. Addition of concentrated hydrochloric acid formed crystals, which, after recrystallisation (charcoal) from boiling water, melted at 329—333° (decomp.) and did not depress the m. p. of the hydrochloride obtained in the previous experiment.

Methylenebis-(5-methyl-2-benzimidazole) Dihydrochloride.—Similarly prepared from malonamide and 3 : 4-diaminotoluene, this salt crystallised from aqueous hydrochloric acid in feathery needles, m. p. 332° (decomp.; inserted at 310°) (Found : N, 15.7; Cl, 19.7. C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>·2HCl requires N, 16.05; Cl, 20.3%).

Tetramethylenebis-2-benzimidazole.—*NN'*-Di-(2-hydroxyethyl)adipamide (11.6 g.) and *o*-phenylenediamine (5.4 g.) were refluxed together for 6 hr. The cooled mixture was extracted with boiling water. The residue (6.6 g.), recrystallised (charcoal) from aqueous ethanol, had m. p. 265—267° (Found : N, 19.1. Calc. for C<sub>18</sub>H<sub>18</sub>N<sub>4</sub> : N, 19.3%). Shriner and Upson (*J. Amer. Chem. Soc.*, 1941, **63**, 2277) give m. p. 259—260°.

Octamethylenebis-2-benzimidazole.—*NN'*-Di-(2-hydroxyethyl)sebacamide (10.0 g.) and *o*-phenylenediamine (5.5 g.) similarly gave this compound, m. p. 275° (Found : N, 15.7. Calc. for C<sub>22</sub>H<sub>26</sub>N<sub>4</sub> : N, 16.2%). Shriner and Upson (*loc. cit.*) give m. p. 277—279°.

*2-Phenylbenziminazole*.—Ammonium benzoate (7.0 g.), *o*-phenylenediamine (5.5 g.), and glycerol (15 ml.) were refluxed for 3 hr. and poured into water. The precipitated solid (7.6 g.), recrystallised from ethanol, melted at 294° (Found: C, 80.0; H, 5.1. Calc. for  $C_{13}H_{10}N_2$ : C, 80.4; H, 5.15%) (lit., m. p. 290°).

*2-(2-Hydroxyphenyl)benziminazole*.—Salicylamide (13.7 g.), *o*-phenylenediamine dihydrochloride (18 g.) and ethylene glycol (20 ml.) were refluxed for 4 hr., then poured into water, the suspension was neutralised with sodium hydrogen carbonate, and the solid was filtered off (11 g.). Recrystallisation (charcoal) from aqueous dioxan raised the m. p. to 241—242° (Found: C, 74.6; H, 4.5; N, 13.0. Calc. for  $C_{13}H_{10}ON_2$ : C, 74.4; H, 4.8; N, 13.3%). Walter and Freiser (*Analyt. Chem.*, 1953, 25, 127) give m. p. 242°. The *hydrochloride*, recrystallised from water, had m. p. 254° (Found: N, 11.0; Cl, 14.55.  $C_{13}H_{10}ON_2 \cdot HCl$  requires N, 11.4; Cl, 14.4%).

*2-(3-Hydroxy-2-naphthyl)benziminazole*.—2-Hydroxy-3-naphthoic acid (9.4 g.), 2-hydroxyethylamine (10 g.), and *o*-phenylenediamine (5.4 g.) similarly formed the *naphthyl* compound, m. p. 298—300 (from 2-ethoxyethanol) (Found: C, 77.7; H, 4.7; N, 10.8.  $C_{17}H_{12}ON_2$  requires C, 78.3; H, 4.6; N, 10.8%). This solid has a vivid orange fluorescence in ultra-violet light.

*Benziminazole-2-carboxy-2'-hydroxyethylamide*.—*NN'*-Di-(2-hydroxyethyl)oxamide (8.8 g.) and *o*-phenylenediamine (5.4 g.) were refluxed for 2 hr., then poured into water, and the yellow solid was filtered off. Recrystallisation (charcoal) from ethanol gave the benziminazole, m. p. 221° (Found: C, 58.2; H, 5.1; N, 20.0. Calc. for  $C_{10}H_{11}O_2N_3$ : C, 58.5; H, 5.4; N, 20.5%). Copeland and Day (*loc. cit.*) give m. p. 219—220°. Alcoholic solutions of this compound (and its 5-methyl homologue; see below) were vividly fluorescent under ultra-violet light.

*5-Methylbenziminazole-2-carboxy-2'-hydroxyethylamide*.—Similarly prepared from 3:4-diaminotoluene and *NN'*-di-(2-hydroxyethyl)oxamide this *benziminazole* melted at 216° (Found: C, 60.0; H, 6.1; N, 18.8.  $C_{11}H_{13}O_2N_3$  requires C, 60.3; H, 5.9; N, 19.2%).

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