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Dialkylation by Means of Dimethylformamide (DMF) 2-Dimethylaminobenzimidazoles (1)

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In an attempt to prepare 5(or 6)-nitro-2-diphenylaminobenzimidazole and its 5(or 6)-chloro analog, 2-chloro-5(or 6)-nitrobenzimidazole and 2,5(or 6)-dichlorobenzimidazole were refluxed with diphenylamine in dimethylformamide which was used as a solvent. In both cases the sole benzimidazole isolated was the 2-dimethylaminobenzimidazole resulting from the reaction of the 2-chlorobenzimidazole with the solvent.

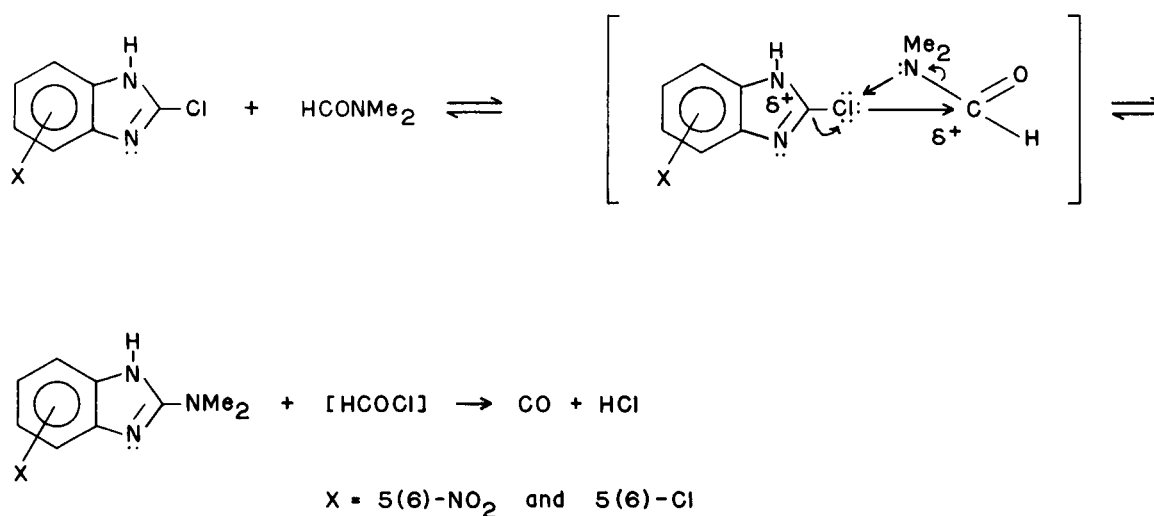
There have been no reports in the literature of the preparation of amino-substituted 2-aminobenzimidazoles from the reaction between 2-chlorobenzimidazoles and *N*-substituted amides. Dimethylformamide has been used as a dimethylamino inserting agent in connection with other compounds. Coppinger (3) used DMF to prepare *N,N*-dimethylbenzamide from benzoyl chloride, *N,N*-dimethylacetamide and *N,N*-dimethylsuccinamic acid from the respective anhydrides, and *N,N*-dimethylbenzylamine from benzyl chloride. Schmerling (2) treated chloro- and bromoaromatic compounds with monoalkylformamides at elevated temperature and pres-

sure to obtain monoalkylaminoaromatic compounds. Deorha and Sharma (5), and Wakae and Hamano (6) further demonstrated the use of DMF as a means of replacing a halogen atom in halonitrobenzenes by the dimethylamino group.

Recently, the reaction between 2-chlorobenzothiazole and DMF to give 2-dimethylaminobenzothiazole has been described and a mechanism proposed for this reaction (7).

2-Dimethylaminobenzimidazole has been prepared in good yield in a sealed tube reaction (8). We have prepared substituted 2-dimethylaminobenzimidazoles by the same reaction in better yields than by the DMF reaction since we did not attempt to determine the optimum conditions for this reaction.

The reaction between 2-chlorobenzimidazoles and DMF results in the formation of carbon monoxide and hydrogen chloride which are believed to arise by the mechanism shown in Chart I, similar to that proposed by D'Amico, *et al.* (7).



EXPERIMENTAL (9)

2-Chlorobenzimidazole (I).

This compound was prepared by the method of Harrison, Ralph and Smith (10). Yield, melting point and infrared spectra agreed with the prior investigators. Ultraviolet bands, λ max (Ethanol), $m\mu$ (log ϵ): 280 (3.95); 274 (3.85).

2,5(or 6)-Dichlorobenzimidazole (II).

Compound II was prepared by a similar method, yield, 54%, m.p. 203°. Ultraviolet bands, λ max (Ethanol), $m\mu$ (log ϵ): 288 (3.86); 245 (3.74); 208 (4.57). Infrared bands ν max, (KBr, cm^{-1}): 3076(s), 2941(s), 2857(s), 2778(s), 2703(s), 2632(s), 2564(s), 2439(m), 1613(m), 1575(w), 1449(s), 1429(s), 1408(s), 1333(m), 1325(m), 1282(w), 1266(s), 1220(m), 1205(w), 1163(w), 990(s), 917(s), 855(m), 840(ms), 806(s), 800(s), 746(w), 706(m), 704(m).

Anal. Calcd. for $\text{C}_7\text{H}_4\text{N}_2\text{Cl}_2$: C, 44.94; H, 2.16; Cl, 37.92. Found: C, 45.23; H, 2.38; Cl, 37.68.

2-Chloro-5(or 6)-nitrobenzimidazole (III).

Compound III was previously prepared by Harrison, *et al.* (10). We used a similar method and the physical constants of our product agreed with those given by these authors. Ultraviolet bands, λ max (Ethanol), $m\mu$ (log ϵ) 305 (3.89); 237 (4.25); 260 sh (3.92).

2-Dimethylaminobenzimidazole (IV).

(a) Compound IV was prepared as described by Efros, *et al.* (8), m.p. 312-314°; lit. (8) m.p. 314-316°. Ultraviolet bands, λ max (Ethanol), $m\mu$ (log ϵ) 289 (4.05); 250 (3.29). Infrared bands ν max (KBr, cm^{-1}): 3000(s), 2930(s), 2850(s), 2800(s), 2740(s), 2600(s), 2550(m), 1620(s), 1600(s), 1570(s), 1455(s), 1430(s), 1400(s), 1350(w), 1330(m), 1280(s), 1255(s), 1230(s), 1200(m), 1180(m), 1140(m), 1100(w), 1075(m), 1035(s), 1010(s), 935(s), 920(s), 900(m), 825(m), 765(m), 740(s), 735(s), 730(s), 705(m).

(b) To 1.5 g. (0.01 mole) of 2-chlorobenzimidazole, oven-dried at 110° for several hours was added 45 ml. of redistilled, Baker, reagent grade dimethylformamide. The mixture was heated under reflux for 14 hours. The reaction mixture was filtered hot (charcoal) and adjusted to pH 7 with ammonium hydroxide to obtain a white precipitate. This was recrystallized from ethanol, yield 45%. The physical constants of this product agreed with those given in (a).

2-Dimethylamino-5(or 6)-chlorobenzimidazole (V).

(a) The compound was prepared by the method described in Reference 8 to give a yield of 80% and a m.p. of 230-243°. Recrystallized from aqueous alcohol it gave a m.p. of 236.8-237.8°. Ultraviolet bands, λ max (Ethanol), $m\mu$ (log ϵ) 298 (4.16); 256 (3.99); 219 (4.68). Infrared bands, ν max (KBr, cm^{-1}): 3050(s), 3000(s), 2930(s), 2850(s), 2750(s), 2600(s), 2550(m), 1750(m), 1700(ms), 1675(ms), 1635(s), 1570(s), 1560(s), 1460(s), 1455(s), 1410(s), 1400(s), 1350(m), 1310(m), 1280(s), 1255(s), 1220(m), 1200(m), 1140(w), 1120(w), 1080(m), 1050(m), 1030(m), 935(s), 925(s), 885(w), 870(mw), 840(m), 815(m), 800(ms), 750(w), 710(m), 700(m).

Anal. Calcd. for $\text{C}_9\text{H}_{10}\text{N}_3\text{Cl}$: C, 55.24; H, 5.16. Found: C, 55.94; H, 5.44.

(b) The same compound was prepared in 25% yield by treatment of the 2,5(or 6)-dichlorobenzimidazole with dimethylformamide as described in IV(b), resulting in a compound m.p. 237-239° and having U.V. and I.R. spectra identical to those obtained with the compound prepared in (a).

2-Dimethylamino-5(or 6)-nitrobenzimidazole (VI).

(a) This compound was prepared by the method described in Reference 8 in a yield of 90% and with a m.p. of 242-243°. Ultraviolet bands, λ max (Ethanol), $m\mu$ (log ϵ) 267 (4.22); 231 (4.10); 338 (3.93) (0.01 N HCl); 252 (4.23); 222 (4.25). Infrared bands, ν max (KBr, cm^{-1}): 3100(s), 3050(s), 2850(s), 2750(s), 2650(s), 2550(m), 1630(s), 1600(s), 1580(s), 1480(s), 1455(s), 1440(s), 1400(s), 1370(s), 1320(s), 1280(s), 1260(s), 1230(s), 1140(m), 1120(m), 1060(s), 1030(m), 940(m), 925(s), 870(m), 850(m), 820(s), 760(s), 735(s), 714(m).

Anal. Calcd. for $\text{C}_9\text{H}_{10}\text{N}_4\text{O}_2$: C, 52.41; H, 4.88. Found: C, 52.84; H, 5.25.

(b) The same compound was prepared by treating 2-chloro-5(or 6)-nitrobenzimidazole with dimethylformamide as described in IV(b) resulting in a compound m.p. 238-240° (yield 59%) and having identical U.V. and I.R. spectra with the compound prepared by method (a).

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