Acknowledgment. This work was supported in part by a grant from the National Science Foundation for which I express my thanks.

NOTE ADDED IN PROOF: In a recent paper, D. K. Banerjee and T. R. Kastura, *J. Am. Chem. Soc.*, **79**, 926 (1957), describe, *inter alia,* the hydrolysis of Ib with essentially the same results as reported in the above.

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5,6-Dichloro-1-(3-dimethylaminopropyl)benzimidazole Monohydrochloride Monohydrate

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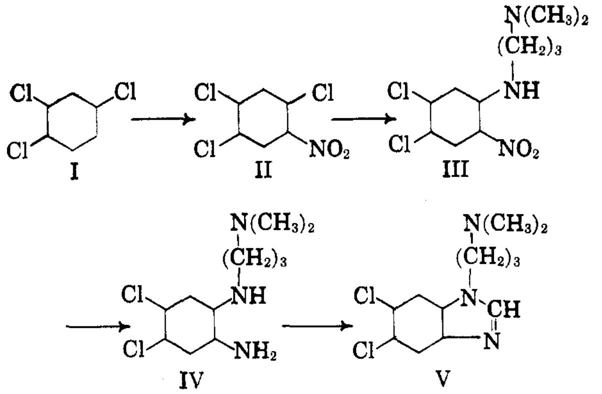
Received November 27, 1956

In the course of other work, a specimen of the title compound was desired. It was therefore synthesized by the following sequence of reactions.



2,4,5-Trichloro-1-nitrobenzene (II) was prepared by nitration of 1,2,4-trichlorobenzene (I) by a slight modification of the method of Barlow and Ing,[1] whereby the yield of crude product was raised to 90% of the theoretical; contrary to Cohn and Fischer,[2] it was readily recrystallized from hexane (3 vol.). This compound was condensed with *N,N*-dimethyl-1,3-propanediamine, essentially by Barlow's method,[3] to give III, which was isolated in crystalline form, both as the hydrochloride and as free base; of a long series of such compounds previously prepared,[1] the only one hitherto crystallized as the free base had been the 2-diethylaminoethyl analog. Compound III was then catalytically reduced to IV, and this was condensed with formic acid, in the presence of hydrochloric acid, to afford V, which was isolated as colorless crystals of its monohydrochloride monohydrate.

EXPERIMENTAL

2,4,5-Trichloro-1-nitrobenzene. Fuming nitric acid (240 ml.) was cooled in ice salt to −1.5°, and 50 ml. of 1,2,4-trichlorobenzene was added dropwise, with stirring, during 2 hr.; after stirring for a further 1 hr. at 0°, the suspension was poured onto 1 l. of crushed ice (in an ice bath) and allowed to warm slowly to room temperature overnight. The colorless crystalline product was filtered off, washed thoroughly with water, air-dried, and then dried under high vacuum. (The filtrate contained no oily material.) Yield, 88.7 g. (90% of the theoretical). It was best recrystallized from hexane (3 vol.); colorless crystals; yield of first crop, 69 g. (70% of the theoretical); m.p. 57–59°; lit. yield,[1] 50 to 60%; lit. m.p., 55°;[2] 57°;[1,4] 58°.[5,6]

N-(4,5-Dichloro-2-nitrophenyl)-N',N'-dimethyl-1,3-propanediamine hydrochloride and free base. To 7.9 g. of dry pyridine was added 10.2 g. of *N,N*-dimethyl-1,3-propanediamine (3-dimethylaminopropylamine), followed by 25 g. of 2,4,5-trichloro-1-nitrobenzene. On swirling, the mixture became colder as the crystals all dissolved and then hotter as new crystals appeared. It was placed under a reflux condenser (Drierite tube), 100 ml. of dry toluene was added, and the suspension was boiled (glycerol bath at 116°) for 3.5 hr. The crystals (5.6 g.) were removed, and the filtrate was evaporated to dryness, affording a brown syrup which was dissolved in 315 ml. of hexane and extracted with 100 ml. of 2*N* hydrochloric acid followed by three portions of water. The aqueous layers were combined and evaporated to dryness, giving orange-colored crystals (23.1 g.). Recrystallization from absolute ethanol (5 vol.) afforded hygroscopic yellow crystals (which turn orange-colored in moist air) of the title compound; m.p. 195–197°. Its infrared absorption spectrum was in agreement with the proposed structure.

Anal. Calcd. for $C_{11}H_{15}Cl_2N_3O_2.HCl$: C, 40.20; H, 4.91; Cl, 32.37; N, 12.79. Found: C, 40.16; H, 4.64; Cl, 32.69; N, 12.82.

For isolation of the free base, the hydrochloride was dissolved in water, a slight excess of aqueous sodium bicarbonate solution was added, the cloudy solution was extracted several times with ether, and the combined ether extracts were dried with anhydrous sodium sulfate, filtered, and evaporated to dryness, affording a quantitative yield of yellow crystals which were dried at high vacuum; m.p. 34–35°. The material is readily soluble in ether, pentane, or heptane, but may be recrystallized by cautious addition of water to a solution in ethanol. Its infrared absorption spectrum (of the solid and of the melt) agreed with the proposed structure.

Anal. Calcd. for $C_{11}H_{15}Cl_2N_3O_2$: C, 45.22; H, 5.18; Cl, 24.27; N, 14.38. Found: C, 45.32; H, 5.00; Cl, 24.21; N, 14.32.

5,6-Dichloro-1-(3-dimethylaminopropyl)benzimidazole monohydrochloride monohydrate. To a solution of 7 g. of the previous free base in 70 ml. of absolute ethanol was added 3 g. of 10% palladized carbon, and the suspension was shaken with hydrogen (30 lb. per sq. in.) at room temperature until the yellow color had disappeared and uptake of hydrogen ceased. The suspension was then filtered, the colorless filtrate being collected directly in a flask containing 8 ml. of concentrated hydrochloric acid. This solution was evaporated to dryness under diminished pressure and two successive 100-ml. portions of absolute ethanol were added and evaporated off, giving a purplish flaky glass. This was dissolved in 50 ml. of 4*N* hydrochloric acid; a boiling stone and 4 ml. of 98% formic acid were added, and the solution was boiled under reflux during 2 hr. and then cooled. The solution was diluted with 250 ml. of water; 0.5 g. of Nuchar was added,

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(1) R. B. Barlow and H. R. Ing, *J. Chem. Soc.*, 713 (1950).

(2) P. Cohn and A. Fischer, *Monatsh.*, **21**, 267 (1900).

(3) R. B. Barlow, *J. Chem. Soc.*, 2225 (1951).

(4) A. F. Holleman and F. E. van Haeften, *Rec. trav. chim.*, **40**, 67 (1921).

(5) F. Beilstein and A. Kurbatow, *Ann.*, **192**, 228 (1878).

(6) H. H. Hodgson, *J. Soc. Dyers Colourists*, **42**, 365 (1926).

and the suspension was boiled under reflux for 20 min. and filtered hot. To the cooled filtrate, 44 ml. of concentrated ammonia was added, and the whitish suspension was immediately extracted with six successive portions of ether. The ether extracts were combined, dried with anhydrous sodium sulfate, filtered, and the filtrate was evaporated to dryness, affording 4.4 g. of a brown syrup (A). This was dissolved in 100 ml. of absolute ethanol and concentrated hydrochloric acid was added dropwise, with gentle swirling, until the solution was faintly acid to Methyl Orange. The solution was evaporated to dryness under diminished pressure, and a further 100 ml. of absolute ethanol was added and evaporated off, affording a mass of colorless crystals which were stirred with 25 ml. of absolute ethanol and filtered off. A total of 6.5 g. of base A, treated in this way, gave (in 3 successive crops) 6.7 g. of colorless, crystalline hydrochloride monohydrate; m.p. 218–227° (dec.). Recrystallized from boiling absolute ethanol (10 vol.) by cooling, it had m.p. 232–235°. Its infrared absorption spectrum agreed with the proposed structure.

Anal. Calcd. for $C_{12}H_{15}Cl_2N_3.HCl.H_2O$: C, 44.12; H, 5.55; Cl, 32.56; N, 12.86. Found: C, 44.16; H, 5.57; Cl, 33.33; N, 12.32.

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Condensation of 4,6,7-Trimethyl-5-hydroxyisocoumaranone with Carbonyl Compounds

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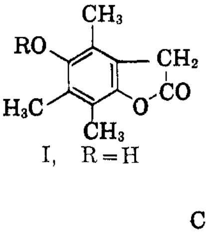
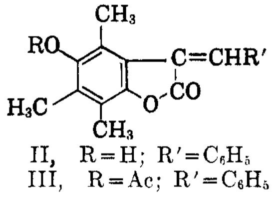
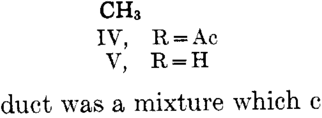
Received November 28, 1956

In connection with other work, some experiments have been made upon the condensation of the isocoumaranone I (R = H)[2] with aldehydes and ketones, leading to products having structure II. It was found that I could be condensed with aromatic aldehydes (benzaldehyde, anisaldehyde), and with cinnamaldehyde, although in the latter case the product was a mixture which could not be separated into pure compounds. Two ketones (2-pentanone and acetophenone) failed to give any reaction, and the one aliphatic aldehyde tried, butyraldehyde, gave a very low yield of the product derived from one mole of the aldehyde and two of the isocoumaranone.


I, R=H


II, R=H; R'=C_6H_5
III, R=Ac; R'=C_6H_5


IV, R=Ac
V, R=H

The reaction between I (R = H) and benzaldehyde was investigated in some detail. The product II (R = H; R' = C_6H_5) resulted in 43% yield when aniline was used as condensing agent, and in 81% yield when piperidine was used. This material was converted into the monoacetate III by action of acetic anhydride. Catalytic reduction of III gave the benzyl derivative IV, and IV was also prepared by acetylation of V, prepared by catalytic hydrogenation of II. Hydrogenation of II gave a mixture of products which could not be separated by crystallization, but from which, after acetylation, IV could be isolated. The yellow alcoholic solution of II became colorless as reduction was completed, but when this colorless solution was exposed to air, it rapidly acquired a yellow color. Doubtless reduction of II proceeded beyond the stage of V, with opening of the coumaranone ring and formation of a hydroquinone. A pure specimen of V, however, could not be obtained, either by reduction of II, or by hydrolysis of IV.

Originally it was hoped that I could be condensed with glyoxal in such a way that two molecules of I would be connected by a butadiene chain. However, all attempts in this direction met with failure—use of glyoxal in aqueous alcoholic solution, or of glyoxal bisulfite compound as a source of anhydrous glyoxal, in air or under nitrogen led to dark, opaque solutions from which only dark, high-melting, insoluble solids could be isolated in small yields. No better success was had with benzil as the dicarbonyl compound. In this case, there was apparently no reaction at all, for most of the starting materials could be isolated unchanged from the reaction mixture.

EXPERIMENTAL[3]

3-Benzal-4,6,7-trimethyl-5-hydroxyisocoumaranone (II). A solution of I (5.6 g., 0.029 mole), benzaldehyde (freshly distilled, 2.9 cc., 0.029 mole) and piperidine (8 drops) in dry ethanol (130 cc.) was heated at 55–60° under a nitrogen atmosphere for 3 days. The cooled reaction mixture deposited II (6.6 g., 81%) melting at 182.5–184.5°. The analytical sample, recrystallized three times from aqueous ethanol, formed yellow needles which melted at 184.0–184.7°.

Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.33; H, 5.95.

Substitution of aniline for piperidine in the above experiment resulted in a much lower yield (43%) of II; failure to provide an atmosphere of nitrogen, or to use anhydrous conditions, also resulted in a lower yield. The use of sodium ethoxide in place of piperidine resulted in complete failure; the product consisted of tars and unchanged starting materials.

3-Benzal-4,6,7-trimethyl-5-acetoxyisocoumaranone (III). The isocoumaranone II (1.0 g.) was added to acetic anhy-

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[1] From the Ph.D. thesis of Richard N. Hurd, University of Minnesota, September 1956.

[2] L. I. Smith and C. W. MacMullen, *J. Am. Chem. Soc.*, **58**, 629 (1936).

[3] Microanalyses by the Microanalytical Laboratory of the University of Minnesota.