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464. N-*Alkyl*-2-1′-*benzimidazolylethylamines.*

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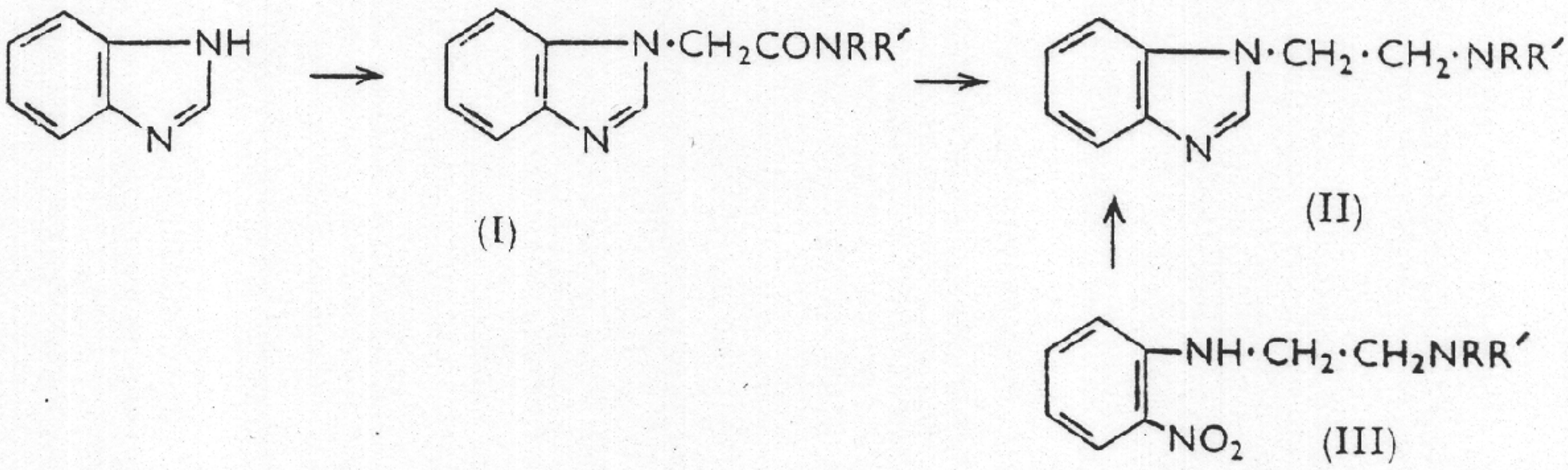
Certain *N*-alkyl-2-1′-benzimidazolylethylamines have been prepared in order to discover whether they resemble or antagonise serotonin in its pharmacological action.

2-1′-Benzimidazolyl-*N*-methylethylamine (II; R = H, R′ = Me) has been prepared from the corresponding unsubstituted compound (II; R = R′ = H) by formylation and subsequent reduction with lithium aluminium hydride, but the overall yield starting from



(I) (II) (III)

o-chloronitrobenzene is low. The same product has, however, been obtained in high yield by reducing the condensation product (I; R = H, R′ = Me) of benzimidazole and α-chloro-*N*-methylacetamide This method has been applied to the preparation of the *NN*-dimethyl and *NN*-diethyl derivatives. The latter compound has also been prepared from *NN*-diethyl-*N′*-*o*-nitrophenylethylenediamine (III; R = R′ = Et) by reduction and cyclisation.

Experimental.—2-1′-*Benzimidazolyl*-N-*methylethylamine.* (*a*) 2-1′-Benzimidazolylethylamine [1] (3·5 g.), 98—100% formic acid (10 ml.), and toluene (40 ml.) were slowly distilled on a steam-bath. After 6 hr. the residual formic acid and toluene were evaporated *in vacuo*, water (2 ml.) was added, the mixture basified with solid potassium hydrogen carbonate and extracted with chloroform. The dried (Na_2SO_4) solution gave, on evaporation, a brownish-oil which slowly solidified. 2-1′-*Benzimidazolyl*-N-*formylethylamine* was obtained after two recrystallisations from ethyl acetate as needles (15%), m. p. 148·5° (Found: C, 63·6; H, 5·9; N, 22·2. $C_{10}H_{11}ON_3$ requires C, 63·5; H, 5·8; N, 22·2%). The formyl compound (0·9 g.) was added slowly to a suspension of lithium aluminium hydride (1 g.) in tetrahydrofuran and then refluxed with stirring for 4 hr., the excess of hydride decomposed with water, and the product extracted with benzene. Evaporation gave an oil, soluble in water from which 2-1′-*benziminazolyl*-N-*methylethylamine dipicrate* was precipitated. Two crystallisations from water gave red needles (70%), decomp. *ca.* 170° (Found: C, 42·1; H, 3·2. $C_{10}H_{13}N_3,2C_6H_3O_7N_3$ requires C, 41·7; H, 3·0%).

(*b*) Benzimidazole (17·3 g.) was dissolved in ethanol (300 ml.) in which sodium (3·4 g.) had been dissolved. α-Chloro-*N*-methylacetamide [2] (16 g.) in ethanol (100 ml.) was slowly added, and the mixture refluxed for 4 hr. Sodium chloride was removed by filtration, and ethanol by evaporation. The residual oil solidified rapidly and was twice crystallised from ethyl methyl ketone to give 2-1′-*benzimidazolyl*-N-*methylacetamide* as needles (90%), m. p. 172° (Found: C, 63·7; H, 5·8. $C_{10}H_{11}ON_3$ requires C, 63·5; H, 5·9%). This compound (13·5 g.), lithium aluminium hydride (6 g.), and tetrahydrofuran (300 ml.) were refluxed for 6 hr. The excess of hydride was decomposed with tetrahydrofuran, and the combined extracts were dried ($NaSO_4$). On evaporation 2-1′-benzimidazolyl-*N*-methylethylamine was obtained as a colourless oil (95%) which rapidly became brown in the air. The infrared spectra of the dipicrates of the two products were identical.

2-1′-*Benzimidazolyl*-NN-*dimethylethylamine.* Similarly prepared from α-chloro-*NN*-dimethylacetamide,[2] 2-1′-*benzimidazolyl*-NN-*dimethylacetamide* was twice recrystallised from ethyl methyl ketone as plates, m. p. 139° (Found: C, 65·7; H, 6·9. $C_{11}H_{13}ON_3$ requires C, 65·0; H, 6·4%). 2-1′-*Benzimidazolyl*-NN-*dimethylethylamine dipicrate* recrystallised (twice) from water, forming yellow needles (60%), decomp. *ca.* 212° (Found: C, 42·3; H, 3·5. $C_{11}H_{15}N_3,2C_6H_3O_7N_3$ requires C, 42·7; H, 3·2%).

[1] Mamalis, Petrow, and Sturgeon, *J.*, 1950, 1600.
[2] Jacobs and Heidelberger, *J. Biol. Chem.*, 1915, **21**, 147.

2-1′-*Benzimidazolyl*-NN-*diethylethylamine*. (*a*) Similarly prepared from α-chloro-*NN*-diethylacetamide,[2] 2-1′-*benzimidazolyl*-NN-*diethylacetamide* was recrystallised four times from water, forming needles (50%), m. p. 124° (Found: C, 68·4; H, 7·0; N, 17·5. $C_{13}H_{17}ON_3$ requires C, 67·5; H, 7·0; N, 18·2%). 2-1′-*Benzimidazolyl*-NN-*diethylethylamine dipicrate* was recrystallised twice from water, forming yellow needles (60%), m. p. 220° (decomp.) (Found: C, 44·5; H, 3·7. $C_{13}H_{19}N_3,2C_6H_3O_7N_3$ requires C, 44·4; H, 3·7%).

(*b*) *NN*-Diethyl-*N′*-*o*-nitrophenylethylenediamine (10 g.) was catalytically reduced in alcohol (100 ml.) over Raney nickel at 5 atm. for 1 hr. The crude oily *N*-(2-diethylaminoethyl)-*o*-phenylenediamine obtained (95%) was refluxed for 40 min. with 4N-hydrochloric acid (100 ml.) and 87% formic acid (20 ml.). The product, basified with concentrated aqueous ammonia, was extracted four times with chloroform. On evaporation 2-1′-benzimidazolyl-*NN*-diethylethylamine was obtained as a brown oil from which the dipicrate, recrystallised thrice from water, was obtained as yellow needles (45%), m. p. and mixed m. p. 220—221° (decomp.) (identical infrared spectra).