

STUDIES IN THE FORMATION OF HETEROCYCLIC RINGS CONTAINING NITROGEN

Part IV. The Position of Chloro Group in the 1:2-Disubstituted Benziminazole from 4-Chloro-*o*-Phenylenediamine and Benzaldehyde

BY N. V. SUBBA RAO AND C. V. RATNAM

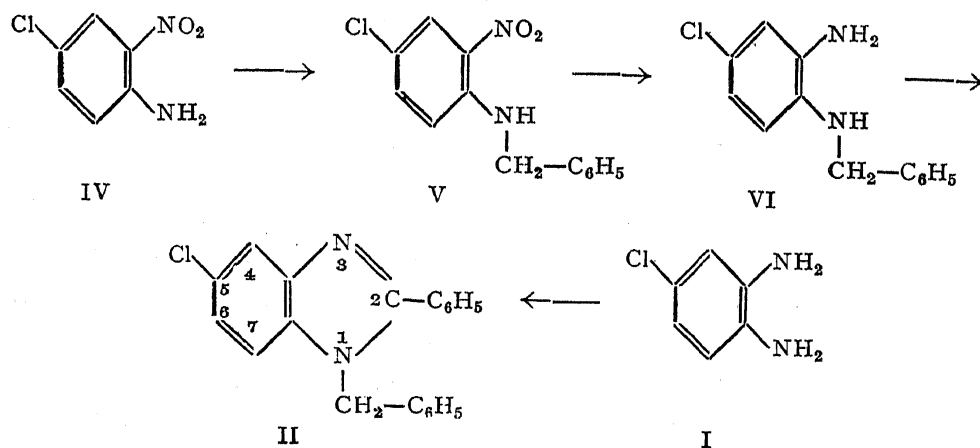
(Department of Chemistry, Osmania University, Hyderabad-Dn.)

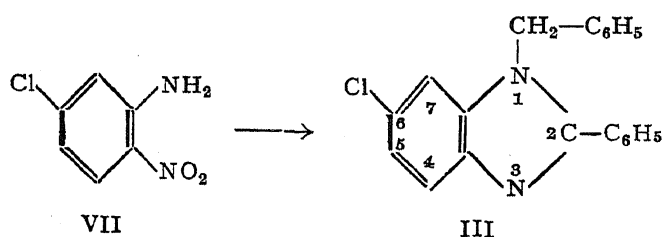
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By the condensation of 4-chloro-*o*-phenylenediamine (I) with more than three molar proportions of benzaldehyde in the absence of any solvent at 150–70°, Fischer and Limmer¹ reported the formation of N:N'-dibenzylidene-4-chloro-*o*-phenylenediamine. They stated further that this dianil, by heating above its melting point, or by boiling in acids, was transformed into the corresponding benziminazole, 'p-chloro- ω -phenyl-N-benzyl benziminazole'. Evidently, the position of the chloro group (5 or 6 position) in this benziminazole has been left unsolved.

The diamine is now condensed with two moles of benzaldehyde following the modified Hinsberg's procedure,^{2, 3} when the 1:2-disubstituted benziminazole, 2-substituted benziminazole, and a benzodiazepine derivative have been isolated. The 1:2-disubstituted benziminazole obtained by us does not agree in its melting point and other properties with that reported by Fischer and Limmer. The product may be either 1-benzyl-2-phenyl-5-chloro benziminazole (II), or 1-benzyl-2-phenyl-6-chloro benziminazole (III). With a view to establishing the structure of this compound, syntheses of the two benziminazoles (II) and (III) have been undertaken adopting a scheme similar to that made use of in the syntheses of the corresponding methyl benziminazoles.⁴





Starting from 4-chloro-2-nitro aniline (IV), the synthesis of 1-benzyl-2-phenyl-5-chloro benzimidazole (II) has been achieved as in the methyl series, through the intermediates, N-benzyl-4-chloro-2-nitro aniline (V), and N¹-benzyl-4-chloro-*o*-phenylenediamine (VI). Similarly, the 6-chloro isomer (III) has been synthesised from 5-chloro-2-nitro aniline (VII) through the corresponding benzyl derivative and diamine.

The 1:2-disubstituted benzimidazole obtained from benzaldehyde condensation has been found to be identical with 1-benzyl-2-phenyl-5-chloro-benzimidazole (II). It may be expected that in all the 1:2-disubstituted benzimidazoles formed from 4-chloro-*o*-phenylene-diamine and aromatic aldehydes, the chloro group will be in position 5.

EXPERIMENTAL

All m.p.'s are uncorrected. The micro-analyses were carried out by one of the authors (C. V. R.). The experimental procedures are dealt with in a very brief manner, since the various details are exactly similar to those given for methyl series.

I. Condensation of 4-chloro-*o*-phenylenediamine with benzaldehyde

Condensation of 4-chloro-*o*-phenylenediamine (3.6 g.) with benzaldehyde (5.3 g.) in glacial acetic acid at room temperature for a period of one hour yielded 2:3:4-triphenyl-7-(or 8)-chloro benzodiazepine (0.65 g.), 1:2-disubstituted benzimidazole (6.5 g.), and 2-phenyl-5-(or 6)-chloro benzimidazole (0.7 g.). The diazepine derivative crystallised from alcohol in rectangular rods, m.p. 125° (Found: C, 79.2; H, 5.3; N, 7.4; C₂₇H₁₉N₂Cl requires C, 79.7; H, 4.7; N, 6.9%). The crude disubstituted benzimidazole was washed with hot dilute alcohol (1:1) and recrystallised from petroleum ether and alcohol to yield prismatic rods, m.p. 171° (Found C, 74.8; H, 5.1; N, 8.5; C₂₀H₁₅N₂Cl requires C, 75.3; H, 4.7; N, 8.8%) (cf. Fischer and Limmer, white needles from alcohol, volatilising at about 225°). 2-Phenyl-5-(or 6)-chloro benzimidazole came out as plates from alcohol, m.p. 210°, and was found to be identical with the product reported in literature.⁵⁻⁷

II. Synthesis of 1-benzyl-2-phenyl-5-chloro benziminazole

(a) *N*-Benzyl-4-chloro-2-nitro aniline.—4-Chloro-2-nitro aniline (5.7 g.), prepared by the method of Crepaz,⁸ was benzylated with benzyl chloride (4 ml.), fused sodium acetate (3.0 g.), and iodine (0.07 g.) at 120° for twelve hours. The unreacted amine was separated by trituration with concentrated hydrochloric acid and the crude benzyl derivative (5.0 g.) thus obtained crystallised from petroleum ether in orange-red rhombic plates, m.p. 79° (Found: C, 59.9; H, 4.3; N, 11.2; $C_{13}H_{11}N_2O_2Cl$ requires C, 59.4; H, 4.2; N, 10.7%). Feitelson, and co-workers⁹ reported the melting point of the compound as 68°.

(b) *N*¹-Benzyl-4-chloro-*o*-phenylenediamine.—*N*-Benzyl-4-chloro-2-nitro aniline (1.0 g.), on reduction with zinc and hydrochloric acid in alcoholic medium at 40–50°, yielded crude *N*¹-benzyl-4-chloro-*o*-phenylenediamine (0.8 g.) turning brown in air. The base was characterised as its hydrochloride, tiny rectangular rods from ethyl acetate, m.p. 163° (Found: C, 57.6; H, 5.5; N, 10.8; $C_{13}H_{13}N_2Cl.HCl$ requires C, 58.0; H, 5.2; N, 10.4%).

(c) 1-Benzyl-2-phenyl-5-chloro benziminazole.—*N*¹-Benzyl-4-chloro-*o*-phenylenediamine (0.47 g.) and benzaldehyde (0.21 g.) were condensed together in alcoholic medium containing nitrobenzene (5 ml.), and the crude benziminazole (0.5 g.) was purified by repeated crystallisations from dilute alcohol, petroleum ether and finally from alcohol. The pure 1-benzyl-2-phenyl-5-chloro benziminazole was obtained as prismatic rods from alcohol, m.p. 172° (Found: C, 75.0; H, 4.9; N, 8.7; $C_{20}H_{15}N_2Cl$ requires C, 75.3; H, 4.7; N, 8.8%). The melting point was undepressed by the 1:2-disubstituted benziminazole from the condensation of 4-chloro-*o*-phenylenediamine with benzaldehyde.

III. Synthesis of 1-benzyl-2-phenyl-6-chloro benziminazole

(a) *N*-Benzyl-5-chloro-2-nitro aniline.—5-Chloro-2-nitro aniline (5.7 g.), obtained by the hydrolysis of 5-chloro-2-nitro acetanilide¹⁰ using dilute hydrochloric acid (4:1), when benzylated following the procedure used in II (a), gave the crude benzyl derivative (5.0 g.). It crystallised from petroleum ether in bright yellow needles, m.p. 101 (Feitelson and co-workers⁹; m.p. 100–101°).

(b) *N*²-Benzyl-4-chloro-*o*-phenylenediamine.—Reduction of *N*-benzyl-5-chloro-2-nitro aniline (1.0 g.) as in II (b) resulted in *N*²-benzyl-4-chloro-*o*-phenylenediamine (0.7 g.), a viscous pale brown oil. Its hydrochloride was

obtained as almost colourless leaflets from ethyl acetate, m.p. 175° (decomp.) (Found: C, 57.5; H, 5.7; N, 10.7; $C_{13}H_{13}N_2Cl \cdot HCl$ requires C, 58.0; H, 5.2; N, 10.4%).

(c) 1-Benzyl-2-phenyl-6-chloro benziminazole.—Condensation of N²-benzyl-4-chloro-*o*-phenylenediamine (0.47 g.) with benzaldehyde (0.21 g.) as in II (c) yielded the crude benziminazole (0.4 g.), which on purification came out as bushy needles from alcohol, m.p. 160° (Found: C, 74.7; H, 5.1; N, 9.1; $C_{20}H_{15}N_2Cl$ requires C, 75.3; H, 4.7; N, 8.8%). The melting point was depressed by the 1:2-disubstituted benziminazole obtained in I.

SUMMARY

5-Chloro and 6-chloro, 1-benzyl-2-phenyl-benziminazoles have been synthesised starting from 4-chloro-2-nitro aniline and 5-chloro-2-nitro aniline respectively. The 1:2-disubstituted benziminazole obtained by the condensation of 4-chloro-*o*-phenylenediamine with benzaldehyde has been found to be identical with the 5-chloro isomer.

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