

766. Heterocyclic Compounds of Nitrogen. Part VIII.¹ Proton Magnetic Resonance Spectra of Some 4-Cinnolones.

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"4-Hydroxycinnoline" and its 6,7-dimethoxy-derivative are shown to exist predominantly as 4-cinnolones in dimethyl sulphoxide solution, and to be acetylated at the 1-position by acetic anhydride.

THE ultraviolet absorption spectra of several "4-hydroxycinnolines" have been used to show² that in some cases the cinnolone form (as I; R = H) exists exclusively, whereas in others there may be a contribution from the cinnoline structure (as II; R = H), but the results are not conclusive since a model compound thought to be 1-methyl-4-cinnolone (I; R = Me) has recently been shown³ not to have this structure. The acetyl derivatives, although they are usually colourless, have been described⁴ as "presumably" 4-acetoxycinnolines (as II; R = Ac) except for that of the 6-nitro-compound which has been formulated² as 1-acetyl-6-nitro-4-cinnolone. Two "4-hydroxycinnolines" and their acetyl derivatives have now been further examined.



"4-Hydroxycinnoline" and its 6,7-dimethoxy-derivative are colourless as the solid and in common organic solvents, and their infrared spectra show strong absorptions which may be due to hydrogen-bonded carbonyl groups. The proton magnetic resonance spectrum of "4-hydroxycinnoline" in dimethyl sulphoxide is markedly different from that⁵ of a cinnoline, and consists of a group of bands between τ 1.6 and 2.7 containing only one singlet, at 2.12, of intensity corresponding to one proton. This is assigned to the 3-proton in the cinnolone (I; R = H) since the corresponding resonance from a cinnoline occurs⁵ at lower field (for 4-methylcinnoline in dimethyl sulphoxide it is at τ 0.65), and because there is no corresponding band in the otherwise similar spectrum of the 3-carboxylic acid. The remainder of the spectrum contains a doublet showing unresolved fine structure at τ 1.83 ($J = 8.5$ c./sec.) assignable to the 5-proton which is deshielded⁶ by the carbonyl group, and a quartet at 2.57 ($J_1 = 7$ c./sec., $J_2 = 2$ c./sec.) probably due to the 8-proton which is shielded⁶ by the NH group. 6,7-Dimethoxy-4-cinnolone gives singlets at τ 2.23, 2.54, and 2.94, the former being assigned to the 3-proton since this will be little influenced by substituents in the benzenoid ring, and the others to the 5- and 8-protons, respectively.

¹ Part VII, Besford and Bruce, preceding Paper.

² Hearn, Morton, and Simpson, *J.*, 1951, 3318.

³ Ames and Kucharska, *J.*, 1963, 4924.

⁴ Simpson, in Weissberger, "The Chemistry of Heterocyclic Compounds," Interscience Publ., Inc., New York, 1953, Vol. V, p. 23.

⁵ Besford, Allen, and Bruce, *J.*, 1963, 2867.

⁶ Corio and Dailey, *J. Amer. Chem. Soc.*, 1956, **78**, 3043; Diehl, *Helv. Chim. Acta*, 1961, **44**, 829.

Absorption in the τ 0—1 region was not detected in either case, indicating that contributions from the 4-hydroxycinnoline form are small.

The infrared spectrum of the monoacetyl derivative ⁷ of 4-cinnolone shows two distinct bands in the carbonyl-stretching region, suggesting the cinnolone structure (I; R = Ac). This was confirmed by the proton magnetic resonance spectrum of a solution in dimethyl sulphoxide, which in the aromatic region contains a singlet at τ 2.04 assignable to the 3-proton, a quartet at 1.84 ($J_1 = 8$ c./sec., $J_2 = 2$ c./sec.) due to the 5-proton (cf. the corresponding bands for 4-cinnolone at, respectively, 2.12 and 1.83), and a doublet, showing unresolved fine structure and corresponding to one proton, at 1.09 ($J = 9$ c./sec.). The latter is at much lower field than any band in the spectrum of 4-cinnolone, and is probably due to the 8-proton which is deshielded by the 1-acetyl group. This assignment is supported by a comparison of the spectra of 3-phenyl- and 1-acetyl-3-phenyl-oxindole in dimethyl sulphoxide. In the former the nine aromatic protons give a complex group of bands between τ 2.4 and 3.2, whereas in the latter only eight lie in this region, the ninth being accounted for by a quartet at 1.76 ($J_1 = 7$ c./sec., $J_2 = 2$ c./sec.) which is attributed to the 7-proton.

6,7-Dimethoxy-4-cinnolone also affords an acetyl derivative which shows two bands in the carbonyl-stretching region of its infrared spectrum, and three singlets in the aromatic region of its proton magnetic resonance spectrum. Those at τ 2.11 and 2.52 are assigned, respectively, to the 3- and 5-protons (cf. the values 2.23 and 2.54 for 6,7-dimethoxy-4-cinnolone), and that at 1.49 to the 8-proton.

Evidence that the deshielding of the 8-proton in the acetylcinnolones is not due to a solvent effect was obtained by measuring the spectra for solutions in deuteriochloroform: the aromatic resonances are of the same form, although spread over a slightly larger field range. Similarly 1-acetyl-3-phenyloxindole in carbon tetrachloride gives a quartet at much lower field than the rest of the aromatic resonances, but the 1-methyl-compound shows only a single group of bands. A deshielding effect of similar magnitude has been reported ⁸ for the 8-proton in some 1-acetylnaphthalenes.

The product obtained by treatment ⁹ of 4-cinnolone with a mixture of phosphorus pentachloride and phosphorus oxychloride has a proton magnetic resonance spectrum which in the aromatic region is very similar to that of 4-methylcinnoline, confirming that the compound is 4-chlorocinnoline.

EXPERIMENTAL

Sublimation temperatures are those of the heating-bath. M. p.s are corrected. Infrared spectra, in Nujol, were determined with a Unicam S.P. 200 spectrometer. Proton magnetic resonance spectra were measured at 60 Mc./sec. with a Varian A-60 spectrometer except for those of 1-acetyl- and 1-methyl-3-phenyloxindole in carbon tetrachloride which were obtained with an Associated Electrical Industries model RS2 spectrometer. Tetramethylsilane was used as an internal standard.

4-Cinnolone.—This was sublimed at 150°/0.01 mm., and then crystallised from dioxan to give needles, m. p. 237° (lit.,¹⁰ 227—229°); ν_{\max} . 1560—1590s cm.⁻¹; τ (17% in Me₂SO) 2.12, 1.83 (doublet, $J = 8.5$ c./sec., with fine structure), 2.57 (quartet, $J_1 = 7$ c./sec., $J_2 = 2$ c./sec.) in the ratio 1 : 1 : 1, and multiplets between 2.17 and 2.7 with strongest band at 2.22

4-Cinnolone-3-carboxylic Acid.—This had m. p. 268° (decomp.) (lit.,⁷ 268—268.5°), and τ (6% in Me₂SO) 1.69 (doublet, $J = 9$ c./sec., with fine structure), 2.31 (quartet, $J_1 = 6$ c./sec., $J_2 = 2$ c./sec.), and multiplets between 1.9 and 2.5 with strongest band at 2.02.

6,7-Dimethoxy-4-cinnolone.—2-Amino-4,5-dimethoxyacetophenone was diazotised,¹¹ and the precipitate was collected and decomposed by stirring at room temperature with aqueous sodium hydrogen carbonate. The product was twice crystallised from ethanol to give the cinnolone, m. p. 305—306° (lit.,¹¹ 271—272°), which had ν_{\max} . 1500, 1520, 1545, 1585, and 1620 cm.⁻¹ all

⁷ Schofield and Simpson, *J.*, 1945, 512.

⁸ Dudek, *Spectrochim. Acta*, 1963, **19**, 691.

⁹ Keneford and Simpson, *J.*, 1947, 917, and references therein.

¹⁰ Schofield and Simpson, *J.*, 1945, 520.

¹¹ Castle and Kruse, *J. Org. Chem.*, 1952, **17**, 1571.

strong and incompletely resolved, and τ (7% in Me₂SO) 2·23, 2·54, 2·94, and 5·97, 6·02 in the ratio 1 : 1 : 1 : 3 : 3.

1-Acetyl-4-cinnolone.—4-Cinnolone (50 mg.) and acetic anhydride (0·5 c.c.) were refluxed for 90 min., the solvent was removed, and the residue sublimed at 100°/0·01 mm. to give the acetyl derivative, m. p. 130·5—131° (lit.,⁷ 127—128°). Identical (m. p., mixed m. p., infrared spectrum) material was obtained by crystallisation⁷ of the product from aqueous ethanol. It had ν_{\max} . 1605, 1660, and 1735s cm.⁻¹; τ (11% in Me₂SO) 1·09 (doublet, $J = 9$ c./sec., with fine structure), 1·84 (quartet, $J_1 = 8$ c./sec., $J_2 = 2$ c./sec.), and 2·04 in the ratio 1 : 1 : 1, and additional multiplets between 1·95 and 2·6; and τ (9% in CDCl₃) 0·97 (doublet, $J = 8$ c./sec., with fine structure), 1·69 (quartet, $J_1 = 8$ c./sec., $J_2 = 2$ c./sec.), 2·16, 7·23 in the ratio 1 : 1 : 1 : 3, and additional multiplets between 2·0 and 2·7.

1-Acetyl-6,7-dimethoxy-4-cinnolone.—6,7-Dimethoxy-4-cinnolone (150 mg.) and acetic anhydride (1 c.c.) were refluxed for 90 min., the solvent was removed, and the residue sublimed at 180°/0·01 mm. Crystallisation of the sublimate from aqueous acetic acid gave the cinnolone (110 mg.) as needles, m. p. 215° unchanged by further treatment with acetic anhydride and sublimation at 160°/0·01 mm. (Found: C, 58·0; H, 5·1; N, 11·2. C₁₂H₁₂N₂O₄ requires C, 58·1; H, 4·9; N, 11·3%). It had ν_{\max} . 1615, 1670, and 1725s cm.⁻¹; τ (6% in Me₂SO) 1·49, 2·11, and 2·52 in the ratio 1 : 1 : 1; and τ (7% in CDCl₃) 1·33, 2·20, 2·38, 5·97, and 7·22 in the ratio 1 : 1 : 1 : 6 : 3.

Spectra of Oxindoles.¹²—(a) 3-Phenyl-, τ (14% in Me₂SO) multiplets between 2·4 and 3·2 (benzenoid H), 5·20 (3-H). (b) 1-Acetyl-3-phenyl-, τ (14% in Me₂SO) 1·76 (quartet, $J_1 = 7$ c./sec., $J_2 = 2$ c./sec.) (7-H), multiplets between 2·4 and 3·0 (remaining benzenoid H), 4·85 (3-H); τ (35% in CCl₄) 1·80 (quartet, $J_1 = 7$ c./sec., $J_2 = 2$ c./sec.) (7-H), multiplets between 2·7 and 3·1 (remaining benzenoid H), 5·47 (3-H), 7·55 (Ac). (c) 1-Methyl-3-phenyl-, τ (17% in CCl₄) multiplets between 2·8 and 3·4 (benzenoid H), 5·63 (3-H), 6·94 (Me).

4-Chlorocinnoline.—This had m. p. 74° (lit.,⁹ 78—79°), and τ (12% in CCl₄) 0·67, multiplets between 1·25 and 1·60, and between 1·70 and 2·35, in the ratio 1 : 1 : 3. Cf. 4-methylcinnoline, τ (15% in CCl₄) 0·98, and groups at 1·4—1·8 and 2·0—2·5, in the ratio 1 : 1 : 3

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¹² Bruce and Sutcliffe, *J.*, 1957, 4789.