533. *Heterocyclic Compounds of Nitrogen. Part VI.*[1] *The Structures of Some Dihydrocinnolines.*

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Dihydrocinnoline and its 4-methyl and 4-phenyl derivatives are shown by hydrogen nuclear magnetic resonance spectroscopy to have hydrazone structures.

Reduction of the heterocyclic ring of a cinnoline could yield three dihydro-compounds (I—III). Dihydrocinnoline and its 4-methyl and 4-phenyl derivative have been assigned [2-4] the 1,2-dihydro-structure (as I) because they are oxidised to the corresponding

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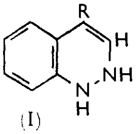
[1] Part V, Bruce, *J.*, 1962, 5302.

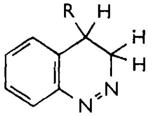
[2] Busch and Rast, *Ber.*, 1897, **30**, 521.

[3] Jacobs, in Elderfield, "Heterocyclic Compounds," Wiley and Sons, New York, 1957, Vol. VI, p. 151, and references therein.

[4] Castle and Onda, *J. Org. Chem.*, 1961, **26**, 4465.

cinnolines, and because dihydro-4-methylcinnoline forms a dibenzoyl[3] and a phthaloyl[4] derivative. This evidence, however, is not conclusive since it is known that phenylhydrazones (cf. III) are susceptible to oxidation[5] and that they can be converted into derivatives of the tautomeric hydrazine form (cf. I) by acetylation.[6]


(I)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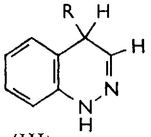
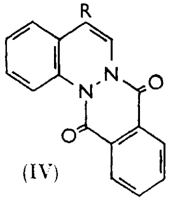

(III)


(IV)

The dihydro-compounds prepared from 3,4-diphenylcinnoline and its 7-methyl homologue are also oxidised to the parent cinnolines, but they show[7] only one active hydrogen atom when treated with methylmagnesium iodide, thus suggesting a 1,4-dihydro-structure (as III). An attempt[3] to assign a structure to dihydro-4-methylcinnoline on the basis of its ultraviolet absorption spectrum was inconclusive. The structures of three dihydrocinnolines have now been established by hydrogen nuclear magnetic resonance spectroscopy.

The dihydro-derivatives of cinnoline and 4-methyl- and 4-phenyl-cinnoline are colourless, and, as Nujol mulls or in carbon tetrachloride solution, show N–H absorption in the infrared region, thus excluding the azo-form (as II) as a sole structure. In Nujol, the dihydro-compounds have a weak, but distinct, absorption band at 1630—1632 cm.$^{-1}$, but in carbon tetrachloride this moves to 1623—1628 cm.$^{-1}$, and only in the case of dihydrocinnoline is it clearly resolved from the aromatic absorption. It suggests that the dihydro-compounds are hydrazones (as III), since C=N linkages may[8-10] absorb weakly in the 1640 cm.$^{-1}$ region, but its diagnostic value is decreased by the fact that all the parent cinnolines, in Nujol, have bands of medium intensity between 1615 and 1622 cm.$^{-1}$.

The hydrogen nuclear magnetic resonance spectrum of dihydrocinnoline in carbon tetrachloride solution shows a single band at 2·02 τ, and a doublet at 6·81, assignable, respectively, to an N–H group, and a CH_2 group coupled to an adjacent hydrogen atom. This establishes the hydrazone structure (III; R = H). Absorption by the hydrogen atom at position 3 was not distinguished; it probably[9,11] lies in the aromatic region. Dihydro-4-methylcinnoline is similarly shown to be (III; R = Me) by a singlet at 1·75 (N–H), an octet (1 : 1 : 3 : 3 : 3 : 3 : 1 : 1) centred at 6·79 due to the single hydrogen atom at position 4 coupled to the methyl group (J = 6·6 c./sec.), and further coupled to the hydrogen atom at position 3 (J = 2·4 c./sec.), and by a doublet at 8·84 (J = 6·0 c./sec.) due to the methyl group. The dihydro-derivative of 4-phenylcinnoline is also a hydrazone (III; R = Ph) since, in deuterochloroform solution, it shows N–H absorption at 2·12, and a doublet at 5·59 due to the single hydrogen atom at position 4 coupled to that at position 3.

Since solvents such as those used for the determination of the foregoing spectra may interact[12] with some amines, the hydrogen nuclear magnetic resonance spectrum of dihydro-4-methylcinnoline was measured for a solution in dioxan. Absorption by the solvent masked the octet in the 6·8 region, but the hydrazone structure (III; R = Me) was confirmed by a singlet at 1·37 (N–H), and a doublet at 8·70 (J = 6·6 c./sec.) due to the methyl group.

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[5] Lynch and Pausacker, *J.*, 1954, 3340, earlier papers in the series, and references therein; Milligan and Minor, *J. Org. Chem.*, 1962, **27**, 4663.

[6] Suvorov, Sorokina, and Sheinker, *J. Gen. Chem. U.S.S.R.*, 1958, **28**, 1058.

[7] Allen and VanAllan, *J. Amer. Chem. Soc.*, 1951, **73**, 5850.

[8] Tanner, *Spectrochim. Acta*, 1959, **15**, 20, and references therein.

[9] O'Connor, *J. Org. Chem.*, 1961, **26**, 4375.

[10] O'Connor and Rosenbrook, *J. Org. Chem.*, 1961, **26**, 5208.

[11] Curtin, Gourse, Richardson, and Rinehart, *J. Org. Chem.*, 1959, **24**, 93.

[12] Asscher and Vofsi, *J.*, 1961, 2261; Foster, *Chem. and Ind.*, 1960, 1354, and references therein.

The structures (III; R = Me or Ph) were confirmed indirectly from the hydrogen nuclear magnetic resonance spectra of their phthaloyl derivatives (IV; R = Me or Ph), neither of which absorbed in the 5—8 τ region. The methyl resonance of compound (IV; R = Me) is a singlet at 7·90, in good agreement with the value 7·86 reported[13] for α-methylstyrene.

The dihydrocinnolines are potentially tautomeric, but contributions from the hydrazine (I) and the azo-form (II) are small, since dihydro-4-methylcinnoline does not absorb near 7·9, where resonance of the methyl group in a structure (I; R = Me) would be expected, and neither dihydrocinnoline nor dihydro-4-phenylcinnoline shows bands in the 7—9 τ region where absorption by the 3-methylene group in a structure (II; R = Me or Ph) would probably occur.[9]

The aromatic hydrogen atoms in the 1,4-dihydrocinnolines cause complex absorption between 2·7 and 3·6 τ. The corresponding absorptions by the parent cinnolines are at lower field, and appear as a group of mainly strong bands centred at about 2·3, a weaker group centred at about 1·6, and, for 4-methyl- and 4-phenyl-cinnoline, additional singlets corresponding to one hydrogen atom at, respectively, 1·05 and 0·97. These singlets are assigned to the 3-hydrogen atom, since aromatic hydrogen atoms adjacent to a hetero-atom are known[14] to absorb at lower fields than those in other positions. This assignment is confirmed by the almost identical position of the singlets when the spectrum is measured at 25 Mc./sec. instead of at 60 Mc./sec., by a doublet at 0·78 in the spectrum of cinnoline (in which the absorption by the 3-hydrogen atom is split by coupling with that at position 4), and by the absence of absorption by 3,4-diphenylcinnoline in this region. Similar groups of bands appear in the spectra of 4-(2,3- and 3,4-dimethoxyphenyl)cinnoline,[15] the singlets being at, respectively, 0·93 and 0·75; extra bands in the 3 τ region are thought to arise from the hydrogen atoms in the veratrole nuclei.[16]

The phenyl-hydrogen atoms in 4-phenyl- and 1,4-dihydro-4-phenyl-cinnoline appear as singlets at, respectively, 2·55 and 2·78. The aromatic-hydrogen atoms in the phthaloyl derivatives (IV; R = Me or Ph) give rise to a complex group of bands stretching from 1·4 to 3·0.

EXPERIMENTAL

Ether was distilled from lithium aluminium hydride, and pyridine from potassium hydroxide. Phthalic anhydride was freed from phthalic acid by extraction with chloroform. Sublimation temperatures are those of the heating-bath. M. p.s are corrected. Infrared spectra were determined with a Unicam S.P. 200 spectrometer. Nuclear magnetic resonance spectra were measured at 60 Mc./sec. (unless stated otherwise) with an Associated Electrical Industries model RS2 spectrometer, with sample tubes of 4 mm. internal diameter and tetramethylsilane as internal standard. The dihydrocinnolines deteriorate on storage in air, and spectra were therefore determined for freshly prepared materials.

1,4-*Dihydrocinnoline* (III; R = H).—A mixture of cinnoline (176 mg.), lithium aluminium hydride (220 mg.), and ether (25 c.c.) was stirred and refluxed for 2 hr., cooled, and decomposed with methanol (4 c.c.) in moist ether (8 c.c.). The ethereal phase was washed with water and dried ($MgSO_4$), and the solvent was removed under nitrogen. Sublimation of the residue at 60—80°/1·3 mm., and crystallisation of the sublimate from light petroleum (b. p. 60—80°), gave 1,4-dihydrocinnoline (92 mg., 51%) as plates, m. p. 81—82·5° (lit.,[2] 87—88°) (Found: C, 73·0; H, 5·9. Calc. for $C_8H_8N_2$: C, 72·7; H, 6·1%). It had $\nu_{max.}$ (in Nujol) 3250m, 1632w, 1601m, 1593m cm.$^{-1}$, $\nu_{max.}$ (0·7% in CCl_4) 3360m, 1628w, 1608m,sh, 1598m cm.$^{-1}$, τ (20% in CCl_4) 2·02, multiplet between 2·9 and 3·6 with strongest band at 3·23, doublet at 6·81 (J = 3·6 c./sec.). An attempt to prepare a phthaloyl derivative by treatment with phthalic anhydride in pyridine was unsuccessful.

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[13] Jackman, " Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Ltd., London, 1959, p. 58.

[14] Ref. 13, p. 64; Seiffert, *Angew. Chem.*, 1962, **74**, 250.

[15] Bruce, *J.*, 1959, 2366.

[16] Allen and Bruce, *J.*, 1963, 1757.

1,4-*Dihydro*-4-*methylcinnoline* (III; R = Me).—Reduction[4] of 4-methylcinnoline as described for cinnoline gave the dihydro-compound as needles, from light petroleum (b. p. 60—80°), m. p. 63—65° (lit.,[4] 64—65°). It had $\nu_{max.}$ (in Nujol) 3215s, 1631w, 1608m,sh, 1595m cm.$^{-1}$, $\nu_{max.}$ (0·7% in CCl_4) 3370m, 1623w,sh, 1610m, 1599m cm.$^{-1}$, τ (35% in CCl_4) 1·75, multiplet between 2·8 and 3·6 with strongest band at 3·14, octet at 6·79 (J_1 = 6·6 c./sec., J_2 = 2·4 c./sec.), doublet at 8·84 (J = 6·0 c./sec.), τ (25% in dioxan) 1·37, multiplet between 2·7 and 3·5 with strongest band at 2·97, doublet at 8·70 (J = 6·6 c./sec.).

Treatment[4] of the dihydro-compound with phthalic anhydride in pyridine, sublimation of the product at 150°/5 × 10^{-5} mm., and crystallisation of the sublimate from ethanol gave the phthaloyl derivative (IV; R = Me) as orange needles, m. p. 187—187·5° (lit.,[4] 185—186°), which had $\nu_{max.}$ (in Nujol) 1665s cm.$^{-1}$, τ (20% in $CDCl_3$) multiplet between 1·5 and 2·9 with strongest band at 2·84, singlet at 7·90.

1,4-*Dihydro*-4-*phenylcinnoline* (III; R = Ph).—A mixture of 4-phenylcinnoline (1·54 g.), lithium aluminium hydride (0·63 g.), and ether (70 c.c.) was stirred and refluxed for 3 hr., cooled, and decomposed with methanol (10 c.c.) in moist ether (10 c.c.). The ethereal phase was washed with water, dried ($MgSO_4$), and evaporated. Crystallisation of the residue from light petroleum (b. p. 80—100°), sublimation of the product at 100—105°/5 × 10^{-5} mm., and recrystallisation of the sublimate gave 1,4-dihydro-4-phenylcinnoline (1·18 g., 76%) as needles, m. p. 112·5—113° (lit.,[17] 115—116°), $\nu_{max.}$ (in Nujol) 3245s, 1630w, 1607w,sh, 1597m cm.$^{-1}$, $\nu_{max.}$ (0·9% in CCl_4) 3365m, 1628w,sh, 1602m cm.$^{-1}$, τ (35% in $CDCl_3$) 2·12, multiplet between 2·7 and 3·5 with strongest band at 2·78, doublet at 5·59 (J = 3 c./sec.).

A mixture of the dihydro-compound (201 mg.), phthalic anhydride (305 mg.), and pyridine (1·5 c.c.) was refluxed for 15½ hr., cooled, and diluted with ethyl acetate (15 c.c.). The solution was washed successively with dilute hydrochloric acid, water, aqueous sodium carbonate, and water, and dried ($MgSO_4$). Removal of the solvent, sublimation of the residue at 170°/5 × 10^{-5} mm., and crystallisation of the sublimate from ethanol, afforded the *phthaloyl derivative* (IV; R = Ph) (140 mg.) as yellow plates, m. p. 178—178·5° (Found: C, 77·9; H, 4·3; N, 8·3. $C_{22}H_{14}N_2O_2$ requires C, 78·1; H, 4·2; N, 8·3%). It had $\nu_{max.}$ (in Nujol) 1654s, 1638s cm.$^{-1}$; τ (23% in $CDCl_3$) multiplet between 1·4 and 3·0 with strongest band at 2·67 (phenyl-hydrogen atoms).

Spectra of Cinnolines.—(*a*) Cinnoline (Aldrich Chemical Co., Inc) was distilled (bulb-to-bulb) at 80° (bath)/1 mm., and had $\nu_{max.}$ (in Nujol) 1622m, 1583s cm.$^{-1}$, τ (25% in CCl_4) doublet at 0·78 (J = 6·0 c./sec.), multiplets between 1·5 and 1·7, and between 2·1 and 2·4. (*b*) 4-Methylcinnoline,[18] m. p. 73—74° (lit.,[18] 73—74°) had $\nu_{max.}$ (in Nujol) 1619m, 1576s cm.$^{-1}$, τ (23% in CCl_4) singlet at 1·05, multiplets between 1·5 and 1·8, and 2·0 and 2·5, singlet at 7·49, τ (30% in CCl_4, at 25 Mc./sec.) singlet at 1·04, multiplet between 1·4 and 2·7, singlet at 7·45. (*c*) 4-Phenylcinnoline,[15] m. p. 65·5—66°, had $\nu_{max.}$ (in Nujol) 1615m, 1569s cm.$^{-1}$, τ (35% in CCl_4) singlet at 0·97, multiplets between 1·5 and 1·7, and 2·0 and 2·6 with strongest band at 2·55 (phenyl H atoms), τ (35% in CCl_4, at 25 Mc./sec.) singlet at 0·98, multiplet between 1·6 and 2·6 with strongest band at 2·56. (*d*) 4-(2,3-Dimethoxyphenyl)cinnoline,[15] m. p. 120·5—121°, had τ (20% in CCl_4) singlet at 0·93, multiplets between 1·4 and 1·6, 2·2 and 2·4, and 2·8 and 3·3, singlets at 6·08, 6·54 (MeO). (*e*) 4-(3,4-Dimethoxyphenyl)cinnoline,[15] m. p. 152·5°, had τ (20% in $CDCl_3$) singlet at 0·75, multiplets between 1·3 and 1·5, and 2·1 and 2·3, singlets at 2·90, 6·02, 6·04. (*f*) 3,4-Diphenylcinnoline,[7] m. p. 151·5—152° (lit.,[7] 151—152°), had τ (25% in $CDCl_3$) multiplets between 1·3 and 1·5, and 2·2 and 2·9.

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[17] Neber, Knöller, Herbst, and Trissler, *Annalen*, 1929, **471**, 113.

[18] Lal, *J. Indian Chem. Soc.*, 1957, **34**, 425.