474. *Addition Reactions of Heterocyclic Compounds. Part XXII.* The Nuclear Magnetic Resonance Spectra and Structures of Some Indoles*

By R. M. ACHESON

The nuclear magnetic resonance spectra of a number of indolecarboxylic esters have been measured and some structural reassignments made.

THE nuclear magnetic resonance spectra of a number of indolecarboxylic esters (II—X) are recorded in the Table. The usual[1] powerful deshielding effect of ester groups on neighbouring protons, which also extends across the 3- and 4-positions of the indole ring, is shown. The change in spectrum on addition of piperidine, to eliminate coupling of the 1-proton in the five-membered ring as has been used previously for pyrroles,[2] suggested that for the esters (II and III) weak coupling between this proton and one (not the 4-proton)

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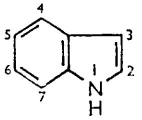
* Part XXI, R. M. Acheson, R. S. Feinburg, and J. M. F. Gagan, *J.*, 1965, 948.

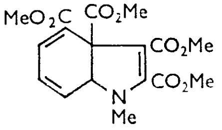
[1] P. Diehl, *Helv. Chim. Acta*, 1961, **44**, 829; L. M. Jackman, " Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, London, 1962, p. 124.

[2] S. Gronowitz, A.-B. Hörnfeldt, B. Gestblom, and R. A. Hoffman, *Arkiv Kemi*, 1962, **18**, 133.

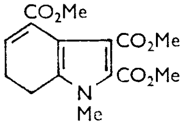
in the carbocyclic ring also took place; long-range couplings between the 3- and 7-protons of some methylindoles have been described.[3]



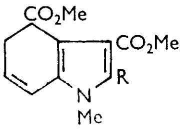
(I: 1-Me)
(II: 2-CO_2Me)
(III: 3-CO_2Me)
(VI: 4-CO_2Me-1-Me)
(V: 5-CO_2Me)
(VI: 6-CO_2Me-1-Me)
(VII: 3,4-di-CO_2Me-1-Me)
(VIII: 2,3,4-tri-CO_2Me-1-Me)
(IX: 2,3,4,5-tetra-CO_2Me-1-Me)
(X: 2,3,6,7-tetra-CO_2Me-1-Me)



(XI)
(XII: 6,7-di-H)



(XV)
(XVI: 4,5-diH)



(XIII: R = H)
(XIV: R = CO_2Me

(XVII: 2-CO_2Me)
(XVIII: 4,5-di-CO_2Me-1,2-di-Me

The assignments in the Table are mostly unambiguous and in the cases of the indoles (IX and X) confirm their structures which were previously deduced[4] from the results of degradation. For both indoles the large coupling constants require that the hydrogen atoms are *ortho* to each other and attached to the carbocyclic ring. Ester groups are therefore present at positions 2 and 3, and in conjunction with the data for the indole mono-esters, the lowest field proton of the tetra-esters can only be accommodated at position 4 thus giving a unique structure (X) for one of them. The resonance position of the more shielded proton of the isomeric indole is at too high a field for it to be *ortho* to an ester group and this again leads to a unique structure (IX).

The nuclear magnetic resonance spectrum of the adduct from 1-methylpyrrole and dimethyl acetylenedicarboxylate confirms the structure (XI) deduced[4] from chemical studies. The bridgehead hydrogen atom couples only with the adjacent proton in contrast to the tetramethyl 9*aH*-quinolizine-1,2,3,4-tetracarboxylates where the bridgehead proton couples approximately equally to the 8- and 9-protons.[5] The large difference between $J_{5,6}$ and $J_{6,7}$ is consistent with the butadiene-like character of the carbocyclic ring.[4]

Alkaline hydrolysis of the adduct (XI) gave[6] a product tentatively described as 6,7-dihydro-1-methylindole-3,4,5-tricarboxylic acid, the positions of the carboxyl groups being certain. However the nuclear magnetic resonance spectrum of the corresponding triester (XIV) showed decisively that the carbocyclic double bond was at the 6,7-position. The single proton at position 4 appears as a triplet and the methylene group as a doublet which does not appear to couple appreciably with the adjacent olefinic proton; other examples of weak coupling in this situation are known.[7] The reason that the double bond fails to remain conjugated with the 4-carboxyl group (cf. XV) is probably that the loss in resonance stabilisation is more than offset by a reduction in strain, caused by making the 4-carbon atom tetrahedral, since the three negatively charged carboxylate groups formed in the hydrolysis would otherwise be coplanar.

Selective decarboxylation and esterification of 5,6-dihydro-1-methylindole-2,3,4-tricarboxylic acid gave[6] a dihydroindole diester (XIII), the nuclear magnetic resonance spectrum of which showed that the only structural change was the loss of the 2- or 3-ester group. Dehydrogenation of the diester gave the corresponding indole (VII), also obtained[6] by the partial hydrolysis and subsequent decarboxylation of the ester (VIII). Although the difference in chemical shift of the 2- and 3-hydrogen atoms in indoles often enables an

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[3] J. A. Elvidge and R. G. Foster, *J.*, 1964, 981.

[4] R. M. Acheson and J. M. Vernon, *J.*, 1962, 1148.

[5] R. M. Acheson, R. S. Feinberg, and J. M. F. Gagan, *J.*, 1965, 948.

[6] R. M. Acheson and J. M. Vernon, *J.*, 1963, 1907.

[7] High Resolution NMR Spectra Catalog, Varian Associates, California, 1962, vol. I, Spectra Nos. 115 and 210.

Nuclear magnetic resonance spectra at 60 Mc./sec. with reference to internal tetramethylsilane

Structure[1]	Solvent[2]	Chemical shifts (τ) and J (c./sec.) for hydrogen atoms or groups at the positions indicated								
		1	2	3	3a	4	5	6	7	7a
(I)[3]	A	6·63[4]	3·18d	3·52d						
(II)	A	0·80[5]	6·04[4]	2·78d $J_{1,3} = 3$		2·26q $J_{4,5} = 7$ $J_{4,6} = 2$	2·5 ←	→	2·9m	
	B	—		2·80		2·32q $J_{4,5} = 7$ $J_{4,6} = 2$	2·5 ←	→	2·9m[14]	
(III)	A	1·2[5]	2·10d $J_{1,2} = 3·5$	6·07[4]		1·79q[7] $\Sigma J = 10$	2·5 ←	→	2·8m	
	B	—	2·10			1·82q[7] $\Sigma J = 10$	2·5 ←→	2·7m	2·80q $J_{6,7} = 6·5$ $J_{5,7} = 1·5$	
(IV)	A	6·28[4]	2·87	2·87		6·03[4]	2·05q $J_{5,7} = 1·5$	2·77t or q[8] $J_{5,6} = 7·5$	2·48q $J_{6,7} = 8$	
	C		2·45d $J_{2,3} = 3$	3·02d			2·18d[9]	2·72q $\Sigma J = 15·5$	2·18d[9]	
(V)	A	1·15[5]	2·77t[8]	3·37t[7]		1·53d $J_{4,6} = 1·5$	6·08[4]	2·08q $J_{6,7} = 8·5$	2·63d	
	B	—	2·72d $J_{2,3} = 3·5$	3·35d[7]		1·53d $J_{4,6} = 1·5$		2·06q $J_{6,7} = 8·5$	2·60d	
(VI)	A	6·21[4]	2·81d $J_{2,3} = 3$	3·46d		2·35d $J_{4,5} = 8·5$	2·13q $J_{5,7} = 1·5$	6·07[4]	1·87[5]	
	C		2·39d $J_{2,3} = 3$	3·45d[7, 10]		2·30[9]	2·30[9]		1·85[7, 10]	
(VII)	A	6·29[4]	2·33	6·15[6]		6·04[6]	2·43 ←	→	2·73m	
	C		1·81				2·24m	2·5 ←→	2·70m	
(VIII)	A	6·15[6]	6·10[6]	6·12[6]		6·05[6]	2·18q $J_{5,6} = 6·5$ $J_{5,7} = 1·5$	2·30 ←→	2·72m	
(IX)	A	6·01[6]	5·94[6]	5·98[6]		5·94[6]	5·92[6]	2·02d $J_{6,7} = 9$	2·55d	
(X)	A	6·20[6]	6·05[6]	6·05[6]		1·69d $J_{4,5} = 8·5$	2·05d	5·93[6]	5·93[6]	
(XI)	A	7·20[4]	6·21[6]	6·24[6]	6·37[4]	6·10[6]	2·94d $J_{5,6} = 5·5$	3·68q $J_{6,7} = 10·5$	4·01q $J_{7,7a} = 3$	5·17d
(XII)	A	7·20[4]	6·24[6]	6·28[6]	6·39[4]	6·12[6]	2·99t $J_{5,6} = 4$	7·78m[11]	8·06m[11]	5·99t[8] $J_{7,7a} = 5$
(XIII)	A	6·50[4]	2·78	6·30[4]		6·30[4] 5·42t	6·81d[11] $J_{4,5} = 7$	4·05d[12]	4·08[12] $J_{6,7} = 11·5$	
(XIV)	A	6·35[4]	6·17[4]	6·26[4]		6·35[4] 5·49t	6·80d[11] $J_{4,5} = 6·5$	4·06d[12] $J_{6,7} = 11$	4·09d[12]	
(XVI)	A	6·33[6]	6·16[6, 13]	6·22[6]		6·33[6] *ca.* 6·16[13]	8·05m[11]	8·05m[11]	7·46m[11]	
(XVII)	A		6·16[4]	3·06m		3·76m	3·06m			
	B		6·16[4]	3·07m[14]		3·77q $J_{3,4} = 2·5$ $J_{4,5} = 4$	3·07m[14]			
(XVIII)	A	6·46[4]	7·64[4]	5·67q[11] 8·67t[4] $J = 7$		5·72q[11] 8·70t[4] $J = 7$	2·91			

[1] Compounds were prepared by standard methods or according to refs. 4 and 6. [2] Solvents: A = $CDCl_3$, B = $CDCl_3$ with piperidine, C = Me_2SO. [3] Data from ref. 8. [4] Me group. [5] Broad. [6] Me group, assignment uncertain. [7] With some further splitting. [8] Partially obscured. [9] Almost superimposed. [10] A small amount of coupling between the 3- and 7-hydrogen atoms appears to occur, cf. ref. 3. [11] CH_2 group. [12] Assignments possibly inverted. [13] Part of an unresolved 4-proton peak. [14] Simplified in this solvent.

d = doublet. m = multiplet. q = quartet. t = triplet.

easy differentiation in the position of substitution to be made[8] in this case it proved impossible because of the deshielding effect of the 4-ester group on the hydrogen atoms at positions 2 and 3, and similar comparisons between the dihydroindole (XIII) and the

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[8] L. A. Cohen, J. W. Daly, H. Kny, and B. Witkop, *J. Amer. Chem. Soc.*, 1960, **82**, 2184.

pyrroles in the Table and others [9] were unhelpful. However, the chemical shift of the lone proton of the diester (VII) was markedly different in deuterochloroform and dimethyl sulphoxide. This is convincing evidence for the supposition, suggested earlier on analogy, that the 2-substituent had been lost as the chemical shifts of hydrogen atoms (when present) at position 2, but not at position 3, of indole, its 2- and 3-methyl and ethoxycarbonyl derivatives,[10] and almost certainly also of methyl 1-methylindole-4- and -6-carboxylates are markedly different in these solvents.

Heating the ester (XIV) with dimethyl acetylenedicarboxylate gave [6] a mixture of the tetra-ester (IX) and a pentaester; the tetra-ester is clearly formed by a Diels–Alder addition of the acetylene across the 3a,6-positions of the indole (XIV) followed by loss of methyl acrylate. Heating the indole (XIV) alone at the reaction temperature gave a glass, the nuclear magnetic resonance spectrum of which showed all the peaks of the starting material as well as a multiplet (τ 2·0—2·7) indicating some aromatisation, poorly resolved multiplets (τ 7·3 and 7·9), and a triplet (τ 3·2), consistent with the presence of some of the more conjugated indole (XV). By a similar Diels–Alder reaction the formation of pentamethyl 1-methylindole-2,3,4,6,7-pentacarboxylate from the decomposition product (XV) can be understood; the position of the single proton (τ 1·57) is consistent with, but does not prove, this formulation.

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[9] Ref. 7, Spectra Nos. 98 and 174.

[10] R. V. Jardine and R. K. Brown, *Canad. J. Chem.*, 1963, **41**, 2067.