191. *Monomethyl-indoles, -benzofurans, and -benzothiophens, their Long-range and Other Proton–proton couplings, and the Non-equivalence of Methylene Protons in some Intermediate Diethyl Acetals.*

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Monomethyl derivatives of indole, benzofuran, and benzothiophen have been prepared and purified, and their proton magnetic resonance spectra measured at 60 Mc./sec. The data not relevant to a (future) consideration of the aromaticity of the bicyclic systems are here presented, and the possible mechanisms of the long-range and other couplings are discussed.

The non-equivalence of the methylene protons in some intermediate diethyl acetals and related compounds receives comment.

APPRECIABLE coupling (*ca.* 0·4 to 1·3 c./sec.) has been detected between protons on different rings of a number of fused-ring systems. The following couplings (in c./sec.) have been reported: 5,7-dichloro- and 5,7-dimethyl-quinoline,[1] and 7-ethylquinoline,[1a] $J_{4,8}$ 0·8; quinoline, $J_{4,8}$ 1·0;[1a] *N*-benzylthieno[3,2-*b*]pyrrole, $J_{2,5}$ 1·3 and $J_{3,6}$ 0·5;[2] indenes, $J_{3,7}$ 0·7; benzofuran, $J_{3,7}$ 0·9;[3] acridine, $J_{4,9}$ 0·9 and $J_{1,9}$ 0·4; acridone, $J_{1,10}$ 0·4; Acridine Yellow, $J_{4,9}$ 0·8;[4] 1,3-diaminoisoquinoline, $J_{4,8}$ 0·8.[5] We now provide further examples of long-range coupling in indole, which has $J_{3,7}$ 0·7 c./sec., in some monomethyl-indoles, monomethylbenzofurans, and in 2-methylbenzothiophen, which has $J_{3,7}$ 0·9 c./sec. Two further possible examples are mentioned below.

The various methyl-indoles, -benzofurans, and -thiophens have been prepared and their proton resonance spectra measured in extension of studies on aromaticity.[6] The methyl-group resonances, and conclusions, will be reported separately. Here we describe the chemistry involved and, in particular, those features of the proton resonance spectra of the bicyclic compounds (Tables 1 and 2) and of intermediates, etc., which are not relevant to the discussion on aromaticity.

[1] Anet, *J. Chem. Phys.*, 1960, **32**, 1274.
[1a] Schaefer, *Canad. J. Chem.*, 1961, **39**, 1864.
[2] Gutowsky and Porte, *J. Chem. Phys.*, 1961, **35**, 839.
[3] Elvidge and Foster, *J.*, 1963, 590.
[4] Kokko and Goldstein, *Spectrochim. Acta*, 1963, **19**, 1119.
[5] Cox, Elvidge, and Jones, *J.*, 1964, in the press.
[6] Elvidge and Jackman, *J.*, 1961, 859.

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TABLE 1.

Proton resonance results for indole and monomethyl-indoles, -benzofurans, and -benzothiophens.

Line positions in c./sec. (and τ), and coupling constants, J (c./sec.) * (10% solutions in CCl_4, containing 0·2% of $SiMe_4$).

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Indoles	2-H	3-H	$J_{1,2}$	$J_{1,3}$	$J_{2,3}$	$J_{3,7}$
Unsubst.	391·0(3·48) †	377·5(3·71) †	2·4	2·1	3·3	0·7
4-Me	399·0(3·35)	384·0(3·60)	2·4	2·1	3·3	0·8
5-Me	395·0(3·42)	374·5(3·76)	2·4	2·0	3·2	0·6
6-Me	400·0(3·33)	380·5(3·66)	*ca.* 2·4	2·1	3·3	1·0
7-Me	400·0(3·33)	379·5(3·69)	2·3	2·15	3·3	

Benzofurans						
2-Me ¶		375·0(3·75)				1·0
3-Me ‖	‡					
4-Me-	460·5(2·34)	403·0(3·28)			2·15	0·8
5-Me	450·5(2·49)	395·5(3·41)			2·2	0·8
6-Me	448·5(2·53)	397·0(3·38)			2·2	1·0
7-Me	453·0(2·45) §	400·0(3·33) §			2·2	

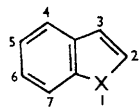| Benzothiophens						
2-Me ¶		413·0(3·12)				0·9
3-Me ‖	414·0(3·10)					

* The calibration of the Varian A 60 spectrometer was checked. The sweep rate was 0·2 c. per sec. per sec. and the scale 0·2 c. per sec. per mm. † These multiplet signals were appropriately collapsed by irradiation at a point 75 c./sec. to low field of their mean position. Hence $\tau_{NH} = ca.$ 2·35. We are indebted to Dr. D. W. Turner for this decoupling result. ‡ Not identifiable because of overlap with the aromatic band. § These figures correct those previously given.[3] ¶ $J_{2\text{-Me},3\text{-H}} = 1\cdot2$ c./sec. ‖ $J_{2\text{-H},3\text{-Me}} = 1\cdot2$ c./sec.

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TABLE 2.

Additional coupling constants (c./sec.).

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	$J_{1,2}$	$J_{1,3}$	$J_{1\text{-H},2\text{-Me}}$	$J_{2\text{-Me},3\text{-H}}$	$J_{1\text{-H},3\text{-Me}}$	$J_{2\text{-H},3\text{-Me}}$
2-Me-indene		*ca.* 2	0·7	1·5		
3-Me-indene	1·7				2·1	1·5

Inter-ring Couplings.—In the spectrum of indole (I; $X = NH$) at 60 Mc./sec., the 2-proton signal (identified from the splitting, and the chemical shifts in 2- and 3-methyl-indole [7]) approximates to a triplet; it is really two overlapping doublets in which the two inner lines are not quite coincident. The signal from the 3-proton is analogous except that each line of the two overlapping doublets is finely split into a doublet. The multiplet patterns are " first-order " [see Figure (A)] and provide the 2,3-, 1,2-, 1,3-, and 3,7-coupling constants directly. Removal of the 1,2- and 1,3-coupling by 1-deuteration results in an *AB* pattern [see Figure (B)] in which each line of the high-field signal (from the 3-proton) is further split into a doublet. That this extra splitting is caused by coupling of the 3- to the 7-proton is confirmed by the spectrum of 7-methyl[1-²H]indole in which the 2- and 3-proton signals appear as a simple *AB* quartet [see Figure (C)]. The long-range 3,7-coupling is discernible once more in the spectra of 4-, 5-, and 6-methylindole. The value of $J_{3,7}$ is not constant, as in the indenes,[3] but varies a little from compound to compound (see Table 1). A similar situation is encountered with the methylbenzofurans (I; $X = O$).

The benzothiophens (I; $X = S$) with a methyl substituent on the benzene ring give spectra in which the complex aromatic band completely masks the signals from the 2- and 3-protons. The inductive effect of a methyl group in the five-membered ring, however, shifts the signal of the adjacent proton to the high-field side of the aromatic band, so that the multiplet pattern can be examined. The 2-proton signal from 3-methylbenzothiophen appears as a quadruplet, as expected. On the other hand, 2-methylbenzothiophen gives

[7] Cohen, Daly, Kny, and Witkop, *J. Amer. Chem. Soc.*, 1960, **82**, 2184.

a 3-proton signal which appears as a quintuplet, like the 3-proton signal of 2-methyl-benzofuran. These quintuplet signals are really overlapping double quadruplets, the quadruplet splitting arising from coupling to the protons of the 2-methyl group and the doubling from coupling to the 7-proton. This explanation is confirmed by the spectra of 2,7-dimethylbenzothiophen and 7-methylbenzofuran. The 3-proton signal in the former appears as a quadruplet because there is now only coupling to the 2-methyl group, and in the latter as a doublet (*i.e.*, half of an AB quartet) because there is only 2,3-coupling.
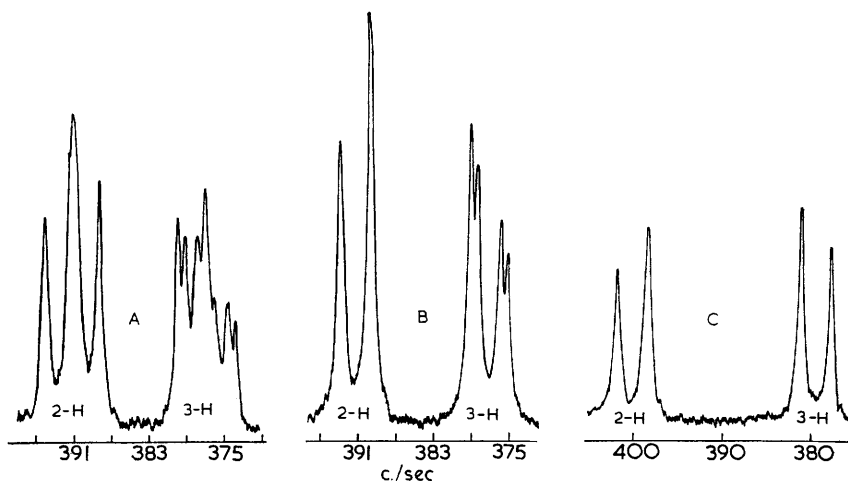
The 2- and 3-proton signals of (A) indole, (B) [1-^{2}H]indole, and (C) 7-methyl-[1-^{2}H]indole.

The long-range inter-ring coupling in the indenes,[3] indoles, benzofurans, and benzo-thiophens disappears on replacement of either the 3- or the 7-proton by a methyl group. This is a difference from coupling across an allylic system, for which a hyperconjugative mechanism has been proposed.[8] In the thienopyrrole, mentioned above, the inter-ring couplings were considered to involve the π-electron system.[2] On this basis, the correlation of electron spins, which leads to proton-spin coupling, requires delocalisation of π electrons between those orbitals which embrace the carbon atoms carrying the coupled protons. In valence-bond terms, there must be conjugation between those positions to which the coupled protons are attached. This implies that either a fair proportion of the canonical forms contain the particular conjugated pathway or that there is a preferential weighting of such forms. Of the eight canonical forms for indene (of which six bear single separated charges not on adjacent positions), there are four in which the 3- and the 7-position are conjugated. Hence coupling between the protons attached to these positions is to be expected. However, the foregoing reasoning does not provide a sufficient explanation. Thus in four of the canonical forms for indene there is a conjugated path between the 3- and the 5-position, yet 3,5-coupling is not detectable. It appears that the conjugated path must usually be over bonds which are disposed in a near-perfect zig-zag or all-*trans* configuration. This leads to best overlap not only of π orbitals but also of the σ-bond orbitals. The electrons of the latter may well be involved, additionally, in the trans-mission of the proton spin-state information. Consideration of the canonical forms for the other rigidly planar fused-ring systems serves only to reinforce these conclusions.

Previously,[3] we gave evidence for 1,7-coupling in indene, based on the fact that the methylene-group signal from each of the monomethylindenes was ragged and of greater line-width than the clean triplet signal from 7-methylindene. The components of the

[8] Hoffman, *Mol. Phys.*, 1958, **1**, 326; Hoffman and Gronowitz, *Acta Chem. Scand.*, 1959, **13**, 1477.

triplet signal from the last compound were slightly broader than those observed by Elleman and Manatt [9] when they recorded the 1-methylene signal from indene whilst decoupling the aromatic protons. That there is appreciable 1,4-coupling can, however, be discounted because we find that the 1-methylene signal from 4,7-dimethylindene has the same line-width as that [3] from 7-methylindene.

Intra-ring Couplings.—Coupling in indole between the NH-proton and the 2- and the 3-proton was mentioned above. The values are $J_{1,2}$ 2·4 and $J_{1,3}$ 2·1 c./sec. Analogous couplings are observed in the spectra of 4-, 5-, 6-, and 7-methylindole. The position of the NH resonance for indole was located by a decoupling technique.

Coupling between the 2- and the 3-proton in the present bicyclic systems varies to a greater extent than do the other couplings with change in the group at the 1-position. Thus we find that $J_{2,3}$ for indene is 5·8, for indole 3·3, and for benzofuran 2·15 c./sec. The 2,3-coupling for benzothiophen was not obtained, for a reason already given, so it is uncertain yet whether the size of $J_{2,3}$ bears a simple relation to the electronegativity of the adjacent 1-group and hence to the π-bond order and polarisation of the 2,3-bond.

In 2-methylindene, the coupling between the protons of the methyl group and those of the 1-methylene group, which are four bonds apart, $J_{\text{1-H, 2-Me}}$, is 0·7 c./sec. In 3-methylindene, the coupling $J_{\text{1-H, 3-Me}}$ is 2·1 c./sec. (Table 2) (cf. ref. 9a), which is three times larger, in spite of there being five intervening bonds. Couplings of a similar (unexpected) size have been detected between the methyl group and the allylic methylene proton(s) in 5-methyl-1-thiacyclopent-4-en-2-one,[10] in cyclopentenones,[11] and in compounds of the santonin series.[12]

In indene, the 1,3-coupling, across four bonds, is of about the same size, 1·95 c./sec. Hoffman, having earlier observed the similarity in size between couplings across homo-allylic and allylic systems, proposed a hyperconjugation mechanism for the transmission of spin-state information.[8] Certainly there can be no hyperconjugation between the 1-methylene and 2-methyl protons in 2-methylindene, so that, on this basis, the small value for $J_{\text{1-H, 2-Me}}$ is reasonable. Pinhey and Sternhell [12] obtained evidence for the homoallylic coupling [between H^a and H^b in the system (II)] being a maximum when there is a dihedral angle of about 90° between the terminal C–H^b bond and the plane of the rest of the system. This agrees with a coupling mechanism involving interaction (contact or overlap) between the σ orbitals of the two terminal C–H bonds and the π orbital of the intervening double-bond. The electron correlation, and thence proton-spin coupling, effectively occurs through only three orbitals, and not *via* the electrons of five bonds. The size of the homoallylic coupling is therefore comprehensible.

$$CH^a_3-C=C-CH^b-\ (II) \qquad\qquad H^c-C=C-\overset{|}{\underset{|}{C}}-H^b\ (III)$$

Removal of the terminal methyl group, to give the allylic system (III), *e.g.*, as in indene, does not materially alter the size of the coupling, although the number of bonds between the coupled protons, now H^c and H^b, has decreased from five to four. This is to be expected because if there is contact or overlap between the σ orbital of the C–H^b bond and the π orbital of the double bond, as the stereochemical dependence of J indicates,[13] then the electron correlation is still through three orbitals. The third is the σ orbital of the :C–H^c bond, the electrons of which correlate with those of the adjacent π orbital through an exchange interaction.[14] In 2-methylindene, the coupling between

[9] Elleman and Manatt, *J. Chem. Phys.*, 1962, **36**, 2346.
[9a] Bergson and Weidler, *Acta Chem. Scand.*, 1963, **17**, 862.
[10] Hoffman and Gronowitz, *Arkiv. Kemi*, 1960—1961, **16**, 471.
[11] Lyons, *Diss. Abs.*, 1962, **22**, 3404.
[12] Pinhey and Sternhell, *Tetrahedron Letters*, 1963, 275.
[13] Whipple, Goldstein, and McClure, *J. Amer. Chem. Soc.*, 1960, **82**, 3811; Bothner-By, Naar-Colin, and Günther, *ibid.*, 1962, **84**, 2748.
[14] McConnell, *J. Chem. Phys.*, 1959, **30**, 126.

the 1-methylene protons and those of the methyl group is necessarily through four single bonds and so is bound to be smaller.

Preparations.—(*a*) *Indenes.* Previously, we assigned configurations to the two isomeric methylindanones, obtained from the cyclisation of β-*m*-tolylpropionic acid, on the basis of chromatographic behaviour and infrared and proton magnetic resonance data.[3]   On the assignment, depended the orientation of 4- and 6-methylindene.   We have now confirmed our conclusions by an unambiguous synthesis of the 5-methylindanone, achieved by cyclising *p*-(α-bromopropionyl)toluene by use of aluminium chloride (cf. ref. 15). Independently, House and Schellenbaum [16] have separated the 5- and 7-methylindanones by chromatography on silica gel and have synthesised the 7-isomer by an unambiguous route.

4,7-Dimethylindene was obtained by an extension of our route [3] to the monomethyl-indenes.   β-*p*-Xylylpropionic acid was cyclised by use of hydrogen fluoride to 4,7-di-methylindanone, which was reduced to the dimethylindanol.   The latter gave methyl resonances at τ 7·89 and 7·82, whereas in the indanone one methyl group was relatively deshielded, as expected, the signals being at τ 7·81 and 7·53.   Dehydration of the dimethyl-indanol did not lead solely to the indene, as with the monomethyl compounds, but gave a mixture which was separated by distillation.

The volatile component was the required liquid 4,7-dimethylindene.[17]   The signals in the proton resonance spectrum of this compound, from the olefinic and benzenoid protons severally, appeared as double triplets and as an *AB* quartet.   The line positions and couplings are given in the Experimental section.   The important finding was the absence of detectable long-range (inter-ring) coupling in this compound.

$$(J_{5,6} = J_{5',6'} = 8 \ c./sec.)$$
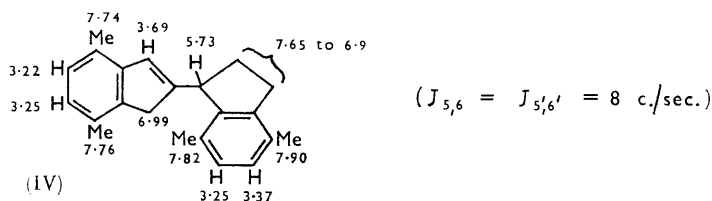
The relatively involatile residue from distillation of the 4,7-dimethylindene was a solid, m. p. 122°, with the same elemental composition.   It had an indene chromophore (ultra-violet absorption), and the C–H deformation frequency was correct for a 1,2,3,4-tetra-substituted benzene.   That it was the 1,2′-linked dimer (IV) was indicated by the appended proton resonance results (τ in CCl_4).   An analogous dimeric product has been reported from the dehydration of 1,4,5-trimethylindanol.[18]

(*b*) *Indoles.* The 4-, 5-, 6-, and 7-methylindoles were prepared unambiguously by cyclising the appropriate *N*-formylxylidenes by use of molten potassium t-butoxide (cf. ref. 19).   The parent xylidine invariably contaminated the product but was removed by repeated acid extraction.   [1-²H]Indoles were obtained for proton resonance study by shaking the carbon tetrachloride solutions with a few drops of alkaline heavy water.

(*c*) *Benzofurans.* The 5- and 7-methylbenzofurans were obtained by a route analogous to that used for the indenes,[3] namely cyclisation of *p*- and *o*-cresoxyacetic acid by use of hydrogen fluoride to the methylbenzofuran-3-ones, followed by reduction with lithium aluminium hydride to the benzofuranols (which were not isolated), and dehydration by repeated distillation.   The physical properties of the products and the intermediate

[15] Layer and MacGregor, *J. Org. Chem.*, 1956, **21**, 1120.
[16] House and Schellenbaum, *J. Org. Chem.*, 1963, **28**, 34; see also p. 31.
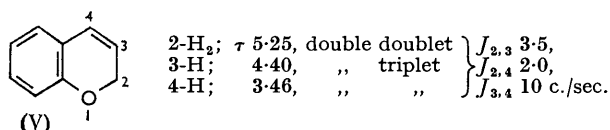[17] Herz, *J. Amer. Chem. Soc.*, 1953, **75**, 73.
[18] Herz and Rogers, *J. Amer. Chem. Soc.*, 1953, **75**, 4498.
[19] Tyson, *Org. Synth.*, 1943, **23**, 42.

benzofuranones agreed with those reported,[20,21] but we found higher melting points for the starting cresoxyacetic acids (cf. ref. 21) and therefore determined their elemental composition. The cyclisation of *m*-cresoxyacetyl chloride by use of aluminium chloride gave, as expected, a mixture of 4- and 6-methylbenzofuran-3-one (m. p.s 58 and 86°), which was separated by steam-distillation. The orientation was ascertained by comparison of the C–H deformation frequencies with those for the correspondingly orientated 7- and 5-methylindan-1-one. Furthermore, the derived 4- and 6-methylbenzofuran had similar frequencies to the corresponding indenes.[3] Also in support of the assignments were the proton resonance results, the methyl group in the lower-melting methylbenzofuranone being deshielded, relatively, indicating its proximity to the carbonyl group. Furthermore, the higher-melting isomer showed a doublet signal from a single proton, on the low-field side of the signals from the other benzenoid protons. This signal (τ 2·55, J 8 c./sec.) can only be assigned to the 4-proton in the 6-methyl structure. A similar low-field one-proton signal (τ 2·41, J 8 c./sec.) appears in the spectrum of the analogous 5-methylindan-1-one.

2-Methylbenzofuran was obtained satisfactorily by treating *o*-(2,3-dibromopropyl)-phenyl acetate with alkali,[22] although this reaction, which presumably involves attack of phenoxide ion upon the side-chain, might be expected to yield benzopyrans. Indeed, we found, from the olefinic region of the proton resonance spectrum, that the product before purification contained some 5% of 2*H*-chromen (2*H*-1-benzopyran) (V). The results which demonstrated the presence of (V) are as shown.

2-H$_2$; τ 5·25, double doublet $\left.\begin{array}{l}\end{array}\right\}$ $J_{2,3}$ 3·5,
3-H; 4·40, ,, triplet $\left.\begin{array}{l}\end{array}\right\}$ $J_{2,4}$ 2·0,
4-H; 3·46, ,, ,, $\left.\begin{array}{l}\end{array}\right\}$ $J_{3,4}$ 10 c./sec.

(V)

It appears that there may be weak 4,8-coupling in this chromen (V) because the lines of the double triplet at τ 3·46 are broadened. In the related 3,3′-dichloro-2,2′-bi-2*H*-chromen the signal from the two equivalent 4-protons was a fine doublet, whereas that from the 2-protons was a singlet,[23] so there must be inter-ring coupling and again this may be 4,8-coupling.

(*d*) *Benzothiophens.* For the preparation of the methylbenzothiophens, we found that cyclisation of the three (tolylthio)acetic acids, by use of aluminium chloride or hydrogen fluoride,[24,25] was inefficient; moreover, the thiobenzofuranone products oxidised in the air to the thioindigos. We found Tilak's route[26] much more satisfactory. This involves cyclisation, by use of polyphosphoric acid, of the (tolylthio)acetaldehyde diethyl acetals, obtained from the thiocresols and bromoacetal. The product from the cyclisation was always contaminated with the parent thiocresol but this was relatively easily removed by chromatography on alumina. The cyclisation of the (*m*-tolylthio)acetaldehyde acetal was reported by Tilak[26] to give 6-methylbenzothiophen as an oil, in conflict with Tarbell and Fukushima's claim[25] that this compound was a solid, m. p. 42—43°. We found from the proton magnetic resonance spectrum of the oil, which had been freed from thiocresol, that it was a 2 : 1 mixture of 6- and 4-methylbenzothiophen. A derived picrate behaved as a single compound and, after recrystallisation, had m. p. 115°, in agreement with Tilak's finding. Decomposition of this picrate on a column of alumina then afforded the benzothiophen which, after sublimation, was obtained as colourless needles, m. p.

[20] Pappalardo and Duro, *Boll. sci. Fac. Chim. ind. Bologna*, 1952, **10**, 168.
[21] Higginbotham and Stephen, *J.*, 1920, **117**, 1534.
[22] Adams and Rindfusz, *J. Amer. Chem. Soc.*, 1919, **41**, 648.
[23] Parham, Fritz, Soeder, and Dodson, *J. Org. Chem.*, 1963, **28**, 577.
[24] Tarbell, Fukushima, and Dam, *J. Amer. Chem. Soc.*, 1945, **67**, 1643.
[25] Tarbell and Fukushima, *J. Amer. Chem. Soc.*, 1946, **68**, 1456.
[26] Tilak, *Proc. Indian Acad. Sci.*, 1951, **32**, A, 390; Tilak and Sunthankar, *ibid.*, p. 396.

42—43°, agreeing with Tarbell and Fukushima's description of the 6-methyl compound. We then prepared 4-methylbenzothiophen by an unambiguous route,[27] and confirmed that the product was an oil which gave a picrate, m. p. 135—136°. The C–H out-of-plane bending modes for the 4- and 6-methylbenzothiophen compared well with the frequencies shown by 4- and 6-methylindene, respectively.

Difficulty was, initially, experienced in obtaining satisfactory elemental analyses for the methylbenzothiophens; this was only partly due to their volatility, and it was found necessary to repeat the purification procedures several times beyond the stage at which the melting point or refractive index had become constant.

Non-equivalence of the Methylene Protons in some Diethyl Acetals.—The proton resonance spectra of the three (tolylthio)acetaldehyde diethyl acetals (used in preparation of the benzothiophens) each show the expected doublet signal from the β-methylene protons next to the sulphur atom, a triplet from the α-proton, and a triplet from the methyl protons of the two ethoxyl groups (Table 3). The signal from the two methylene protons

TABLE 3.

Proton resonance results for the (tolylthio)acetaldehyde diethyl acetals and
other ethoxy-compounds (*ca.* 10% in CCl$_4$).

(Tolylthio)acetaldehyde diethyl acetals

τ						
o-cpd.	*m*-cpd.	*p*-cpd.	Intensity	Multiplicity	*J* (c./sec.)	Assignment
8·84	8·84	8·85	6	triplet	7	CH$_3$'s of ethoxy-groups
7·63	7·68	7·71	3	singlet		CH$_3$ on aryl ring
7·01	7·00	7·06	2	doublet	5·5	CH$_2$ of S·CH$_2$·CH$<$
6·45	6·46	6·49	4	double quadruplet	7, *ca.* 2·5	CH$_2$'s of ethoxy-groups
5·43	5·45	5·49	1	triplet	5·5	CH of S·CH$_2$·CH$<$
3·0 to 2·6	3·2 to 2·8		4	complex		aryl protons
		3·02	2	} *AB* quartet	8	aryl H's *o* to CH$_3$
		2·78	2			aryl H's *o* to S

Bromoacetaldehyde diethyl acetal

τ	Intensity	Multiplicity	*J* (c./sec.)	Assignment
8·80	6	triplet	7	CH$_3$'s of ethoxy-groups
7·56	2	doublet	5·5	CH$_2$ of Br·CH$_2$·CH$<$
6·41	4	double quadruplet	7, *ca.* 2	CH$_2$'s of ethoxy-groups
5·38	1	triplet	5·5	CH of Br·CH$_2$·CH$<$

Diethyl sulphate

8·61	6	triplet	} 7·2	CH$_3$'s
5·75	4	quadruplet		CH$_2$'s

Diethyl carbonate

8·70	6	triplet	} 7·2	CH$_3$'s
5·87	4	quadruplet		CH$_2$'s

Potassium ethyl xanthate (in D$_2$O with t-butyl alcohol as internal reference)

8·62	3	triplet	} 7·2	CH$_3$
5·56	2	quadruplet		CH$_2$

of the ethoxyl groups, however, is complex. The increased multiplicity cannot be ascribed to coupling across oxygen to the α-proton of the aldehyde moiety, because of the simple signal from this latter proton. In each case, the complex methylene signal approximates to a double quadruplet which can be derived from an *AB* pattern by splitting each line into a quadruplet (through coupling to the adjacent methyl protons). Eight lines appear rather than sixteen, because of overlap. The observed multiplet, however, is not really " first-order " because an extra combination line is apparent at higher field and there are signs of other weak lines. Nevertheless, pending full analysis of the spectra, it seems safe to state that the methylene protons of the ethoxyl groups in each of the three acetals are non-equivalent.

[27] Kloetzel, Little, and Frisch, *J. Org. Chem.*, 1953, **18**, 1511.

A similar complexity was noticed by Finegold [28] in the methylene signal from diethyl sulphite. The multiplet pattern in this case was analysed by Kaplan and Roberts [29] as arising from an ABC_3 spin-coupled system (see also ref. 30). Our acetals appear to provide further examples: J_{AC} and J_{BC} are evidently numerically equal because of the sharp triplet from the methyl protons. Yet another example is bromoacetaldehyde diethyl acetal (Table 3).

It seems that the non-equivalence of the methylene protons in these acetals results from an intrinsic *internal* asymmetry of the acetal grouping (IV), and not ultimately from restricted rotation. To the protons a and b of one (or other) methylenoxy group, the
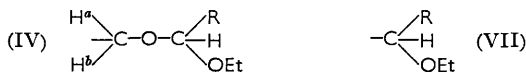
attached group (VII) is asymmetric. The environment of each of the protons a and b in each rotational conformer is consequently distinct. Each therefore experiences a different average environment from the other even though rapid rotation may equalise the populations of the separate conformers. A study of the dependence of the multiplet patterns upon temperature would, of course, determine whether restricted rotation was additionally contributing to the non-equivalence of the methylenoxy protons in a given acetal (cf. ref. 31).

In the spectra of diethyl sulphate, diethyl carbonate, and potassium ethyl xanthate, the methylene protons give rise in each case to a simple $1:3:3:1$ quadruplet signal, as expected for two equivalent protons coupled to the three protons of a methyl group. In each of these three ethoxy-derivatives, there is a plane of symmetry through the attached moiety ($-SO_2-OR$, $-CO-OR$, $-CS-S^-$), and, with free rotation of the groups, the methylenoxy protons have identical average environments and thus are equivalent. The simple seven-line A_2X_3 spectra are therefore to be expected.

EXPERIMENTAL

Incidental proton resonance results are included here.

Unambiguous Synthesis of 5-Methylindanone (cf. Refs. 3 and 15).—p-α-Bromopropionyl-toluene [32] (3 g.) was heated with aluminium chloride (6 g.) at 150° for 7 hr. The melt was cooled, water was added cautiously, and the mixture steam-distilled. The 5-methylindanone crystallised from the distillate, and was recrytallised from light petroleum (b. p. 40—60°) to give plates, m. p. 70—71°, undepressed by admixture with the sample obtained from cyclisation of β-*m*-tolylpropionic acid.[3]

4,7-Dimethylindene (cf. Refs. 3 and 33) and its Dimer.—p-Xylene (30 g.) was chloromethylated to 2,5-dimethylbenzyl chloride [34] (14·7 g.), b. p. 92—102°/8 mm., which with diethyl sodiomalonate provided a diethyl ester [35] (10·8 g.), hydrolysis of which to the di-acid followed by decarboxylation afforded β-2,5-dimethylphenylpropionic acid [36] (5·6 g.), m. p. 44—45° (from light petroleum). Cyclisation [3] gave 4,7-dimethylindanone [37] (4·2 g.), m. p. 77—78° (from light petroleum), which had τ (in CCl$_4$) 7·81, 7·53 (4-, 7-Me); ca. 7·67, ca. 7·27 (2-, 3-H$_2$; complex); 3·20, 2·94 (5-, 6-H; *AB* quartet, $J_{5,6}$ 7·5 c./sec.).

Reduction [3] of the indanone afforded 4,7-dimethylindanol (3 g.), having τ (in CCl$_4$) ca. 8·15, 7·3 (2-, 3-H$_2$; complex); 7·89, 7·82 (4-, 7-Me); 6·4 (OH; removed by deuteration);

[28] Finegold, *Proc. Chem. Soc.*, 1960, 283.
[29] Kaplan and Roberts, *J. Amer. Chem. Soc.*, 1961, **83**, 4666.
[30] Pritchard and Lauterbur, *J. Amer. Chem. Soc.*, 1961, **83**, 2105.
[31] Gutowsky, *J. Chem. Phys.*, 1962, **37**, 2196.
[32] Sanchez, *Bull. Soc. chim. France*, 1929, [4], **45**, 284.
[33] Elsner and Parker, *J.*, 1957, 592.
[34] v. Braun and Nelles, *Ber.*, 1934, **67**, 1094; Fuson and McKeever, *Org. Reactions*, 1947, **1**, 69.
[35] Hoch, *Compt. rend.*, 1931, **192**, 1464; cf. Wagner-Jauregg, Arnold, and Hüter, *Ber.*, 1942, **75**, 1293.
[36] Westfahl and Gresham, *J. Amer. Chem. Soc.*, 1954, **76**, 1076.
[37] Plattner and Wyss, *Helv. Chim. Acta*, 1941, **24**, 483.

5·27 (1-H; complex); 3·30, 3·27 (5-, 6-H; *AB* quartet, $J_{5,6}$ 8 c./sec.), which was dehydrated [3] with toluene-*p*-sulphonic acid in boiling benzene. Fractionation of the product gave: (i) 4,7-dimethylindene,[17] b. p. 94°/11 mm., n_D^{22} 1·5600 (Found: C, 91·55; H, 8·3. Calc. for $C_{11}H_{12}$: C, 91·6; H, 8·4%), τ (in CCl_4) 7·77, 7·66 (7-, 4-Me; singlets, showing signs of very fine splitting), 6·89 (1-H_2; overlapping double doublet); 3·64, 3·18 (2-, 3-H; double triplets, $J_{2,3}$ 5·7, $J_{1,2}$ 1·95, $J_{1,3}$ 1·90 c./sec.); 3·27, 3·20 (6-, 5-H; *AB* quartet, $J_{5,6}$ 8 c./sec.); and (ii) a residue which crystallised when cold; recrystallisation of this solid from light petroleum and sublimation at 110°/0·5 mm. gave needles, m. p. 121—122°, of the *dimer* (IV) (Found: C, 92·0; H, 8·45. $C_{22}H_{24}$ requires C, 91·6; H, 8·4%), $\lambda_{max.}$ (in EtOH) 232 (infl.), 265, 275 (sh), 291, and 302 mμ [10^{-3} ε 8·9, 8·6, 6·95, 1·87, and 1·34], $\nu_{max.}$ (Nujol) 860 cm.$^{-1}$.

Monomethylindoles (cf. Ref. 19).—The *N*-formylxylidine (27 g.) (from 2,3-, 2,4-, 2,5-, and 2,6-dimethylaniline) was added to t-butyl alcohol (150 c.c.) containing potassium t-butoxide (from 7·1 g. of potassium), and the excess of the alcohol was removed by distillation in a stream of purified nitrogen. The temperature was raised to 320—330° for 25 min., so that the residue refluxed. After being cooled, the product was treated with water and steam-distilled. The distillate was extracted (3 times) with ether, and the ethereal solution was washed several times with dilute hydrochloric acid, and water, and dried ($MgSO_4$), and then evaporated. Distillation under reduced pressure gave the crude indole. When the indole was a solid, it was recrystallised from light petroleum (b. p. 40—60°). When it was a liquid, it was taken up in ether, and the solution washed with dilute hydrochloric acid, and water, dried, and evaporated, and the residue distilled under reduced pressure.

Monomethylindoles [38] (Calc. for C_9H_9N: C, 82·4; H, 6·9; N, 10·7%).

Compound	B. p./mm.	M. p.	n_D (Temp.)	Found (%)		
				C	H	N
4-Me	90°/15		1·5629 (27°)	82·2	6·95	10·2
5-Me		59—60°		82·3	6·9	10·7
6-Me	70°/0·3		1·6051 (24°)	82·3	7·1	10·5
7-Me		84—85°		82·7	6·8	10·8

Monomethylbenzofurans.—*o*-, *m*-, and *p*-Cresol were each converted by Higginbotham and Stephen's method [21] into the cresoxyacetic acid. Recrystallisation of the respective products from ethanol–water gave *o*-, m. p. 156—157° (Found: C, 64·8; H, 6·1%), *m*-, m. p. 104·5—105·5° (Found: C, 65·0; H, 6·4%), and *p*-cresoxyacetic acid, m. p. 139—140° (Found: C, 64·8; H, 5·8. Calc. for $C_9H_{10}O_3$: C, 65·05; H, 6·1%). The m. p.s were all higher than previously recorded.[21] The *m*-compound was subsequently obtained in higher yield by a procedure analogous to that described by Tarbell and Fukushima [25] for the thio-compound.

m-Cresoxyacetic acid (64 g.) was converted, by use of thionyl chloride (90 c.c.; freshly distilled from quinoline), into the acid chloride, b. p. 128°/14 mm. (55 g.). This acid chloride (25 g.) was added slowly to a vigorously stirred suspension of powdered aluminium chloride in purified light petroleum (b. p. 60—80°) (100 c.c.) which was being refluxed. After 30 min., the mixture was cooled in ice, water was added cautiously, and then sufficient dilute hydrochloric acid was added to dissolve the solids. The petroleum layer was separated and evaporated, and the residue steam-distilled, giving a distillate (700 c.c.) which contained a yellow oil, *A*, that remained mobile at 0°, and a similar following distillate from which the oil crystallised at 0°. Recrystallisation of the solid from light petroleum (b. p. 40—60°) afforded needles (3 g.), m. p. 85—86°, of 6-methylbenzofuran-3-one, as described by Higginbotham and Stephen.[21] The compound had $\nu_{max.}$ (Nujol) 818 cm.$^{-1}$, and τ_{Me} (in CCl_4) 7·58 (5-methylindanone has $\nu_{max.}$ 813 cm.$^{-1}$ and τ_{Me} 7·57).[3]

The oil *A* (14 g.) in ether was chromatographed on a column (64 × 4 cm.) of alumina (Spence, type H) and the yellow band was eluted with 1 : 1-chloroform–hexane (500 c.c.). Evaporation of the eluate afforded yellow, oily crystals, m. p. 50—56° (2 g.). Re-chromatography on a shorter column (12 × 1 cm.) gave almost colourless crystals which sublimed at 40°/0·5 mm. to give needles, m. p. 57—58°, of 4-*methylbenzofuran-3-one* (Found: C, 72·8; H, 5·4. $C_9H_8O_2$ requires C, 73·0; H, 5·4%), $\nu_{max.}$ (Nujol) 780 cm.$^{-1}$, τ_{Me} (in CCl_4) 7·46 [7-Methyl-indanone has $\nu_{max.}$ 778 cm.$^{-1}$, τ_{Me} 7·43].[3]

[38] Marion and Oldfield, *Canad. J. Res.*, 1947, **25B**, 1.

5- and 7-Methylbenzofuran-3-one [21] were prepared by cyclisation of *p*- and *o*-cresoxyacetic acid by use of hydrogen fluoride (cf. ref. 3).

Each of the foregoing four methylbenzofuran-3-ones was reduced with lithium aluminium hydride (cf. ref. 3) to the methylbenzofuranol, distillation of which gave the methylbenzofuran [4- and 6-, $v_{max.}$ (film) 765 and 810 cm.$^{-1}$, respectively]. 3-Methylbenzofuran was obtained by distillation (dehydration) of the benzofuranol obtained from methylmagnesium iodide and benzofuran-3-one.[39] 2-Methylbenzofuran was synthesised by treating *o*-2,3-dibromopropyl-phenyl acetate [22] with alkali; the product, before fractionation, contained about 5% of 2*H*-chromen, as shown (above) from its proton magnetic resonance spectrum.

Monomethylbenzofurans [20] (Calc. for C_9H_8O: C, 81·8; H, 6·1%).

Compound	B. p./mm.	n_D (Temp.)	Found (%) C	H
2-Me	81°/14	1·5610 (23°)	81·8	6·1
3-Me	90°/23	1·5569 (21°)	81·85	6·35
4-Me	87°/21	1·5569 (20°)	81·9	6·4
5-Me	86°/20	1·5550 (26°)	81·6	6·3
6-Me	88°/23	1·5562 (26°)	82·0	6·3
7-Me	83°/20	1·5559 (26°)	81·8	6·1

Monomethylbenzothiophens (*cf. Ref.* 26).—*o*-, *m*-, and *p*-Thiocresol were prepared from the corresponding toluidines by Tarbell and Fukushima's method.[25] The thiocresol (8·6 g.) was added to ethanol (50 c.c.) containing sodium ethoxide (from 1·6 g. of sodium) and the solution cooled with solid carbon dioxide whilst bromoacetaldehyde diethyl acetal (12·5 g.) was added gradually with stirring. The mixture was refluxed for 3 hr. and then evaporated, and the residue treated with water. Extraction with ether, and distillation, finally under reduced pressure, gave the (tolylthio)acetaldehyde diethyl acetal (15 g.) (*o*, b. p. 164—166°/15 mm., $n_D^{19°}$ 1·5261; *m*, b. p. 164—166°/13 mm., $n_D^{24°}$ 1·5200; *p*, b. p. 168—169°/15 mm., $n_D^{24°}$ 1·5191) (cf. ref. 40).

Purified nitrogen was passed for 15 min. through polyphosphoric acid (40 c.c.; 1 : 1 H_3PO_4–P_2O_5) heated on a steam-bath. Then with the acid at 180°/0·3 mm., the cold (tolylthio)acetaldehyde acetal (5 g.) was added *beneath the surface*, during 20 min. Heating was continued for a further 10 min. In each case the product distilled out rapidly, and was collected in a cold trap (solid CO_2), and then taken up in ether, and the solution was dried ($MgSO_4$) and evaporated. The oil was chromatographed in hexane on a column (20 × 1 cm.) of alumina (Spence, type H), to remove thiocresol, and the eluate (200 c.c.) was evaporated.

The product from the *o*-tolylthio-compound was distilled under reduced pressure to give 7-methylbenzothiophen [25] (2·2 g.). The product from the *p*-tolylthio-compound was crystall-ised from aqueous ethanol and then sublimed at 25°/0·5 mm. to give 5-methylbenzothiophen [24] (2 g.). The oily product (5 g.) from the *m*-sulphide (17 g.) [shown by proton magnetic resonance (above) to be a 2 : 1 mixture of 6- and 4-methylbenzothiophen], in ethanol, was mixed with warm saturated ethanolic picric acid (8·5 g.) and the solution cooled. The picrate had m. p. 115—115·5° (from ethanol). The picrate in benzene was run on to a column (22 × 1 cm.) of alumina (Spence, type H) and the benzothiophen was recovered from the eluate (100 c.c.) by evaporation (1·8 g.; m. p. 38—40°). Recrystallisation from methanol–water, and two sublim-ations at 30—35°/0·5 mm., gave 6-methylbenzothiophen [25] as needles, m. p. 42—43°, $v_{max.}$ (Nujol) 812 cm.$^{-1}$ (6-methylindene has $v_{max.}$ 827 cm.$^{-1}$).[3]

4-Methylbenzothiophen [27] (picrate, m. p. 135—136°) had $v_{max.}$ (liquid film) 760 cm.$^{-1}$ (4-methylindene has $v_{max.}$ 775 cm.$^{-1}$).[3]

3-Methylbenzothiophen [41] was obtained by cyclodehydration of (phenylthio)propan-2-one, and 2-methylbenzothiophen [42] from α-[*o*-carboxy(phenylthio)]propionic acid.

2,7-Dimethylbenzothiophen.—This compound, b. p. 120°/16 mm., prepared from 7-methyl-benzothiophen by Shirley and Cameron's procedure,[43] had τ (in CCl_4) 7·54 and 7·49 (2-, 7-Me; doublet, singlet); 3·2 (3-H; quadruplet, $J_{2-Me,3-H}$ 1·2 c./sec.).

[39] Friedländer, *Ber.*, 1899, **32**, 1867.
[40] Banfield, Davies, Ennis, Middleton, and Porter, *J.*, 1956, 2603.
[41] Werner, *Rec. Trav. chim.*, 1949, **68**, 509.
[42] Hansch and Blondon, *J. Amer. Chem. Soc.*, 1948, **70**, 1561.
[43] Shirley and Cameron, *J. Amer. Chem. Soc.*, 1952, **74**, 664.

Monomethylbenzothiophens (Calc. for C_9H_8S: C, 72·9; H, 5·4; S, 21·6%).

Compound	M. p.	B. p./mm.	n_D (Temp.)	C	H	S
				Found (%)		
2-Me	52·5—53·5°			73·2	5·7	21·8
3-Me		104°/9	1·6232 (20°)	72·8	5·3	22·0
4-Me		120°/18	1·6260 (24°)	72·6	5·4	22·0
5-Me	35·5—36°			72·6	5·4	21·4
6-Me	42—43°			72·9	5·4	21·4
7-Me		112°/16	1·6193 (21°)	73·1	5·2	21·35

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