Steric Hindrance in Substituted Dibenzofurans

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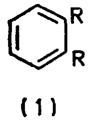
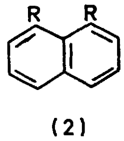
Ten alkyl-substituted dibenzofurans (3) have been synthesized by irridiation of the corresponding diphenyl ethers (4). ^{13}C Chemical shift analysis indicates that some of the highly substituted compounds (3d, g—i) are probably twisted out of the molecular plane due to steric interaction of the substituents in the 1 and 9 positions.

THE *ortho*- or *peri*-interaction in substituted aromatic compounds (1) or (2) is of considerable interest.[1,2] The close proximity of the substituents in the 1 and 9 positions of dibenzofurans has been pointed out recently by Tokura and his co-workers[3] who measured a nuclear Overhauser enhancement of 38% in 1,2,3,4-tetramethyldibenzofuran (3f) between the methyl group at C-1 and the proton at C-9, a value comparable with that found in 1,2,3,4-tetramethylphenanthrene.[4] Inspection of the molecular structure of dibenzofuran[5] shows that the molecule as a whole has a small deviation from planarity. The distance between the methyl group carbon atoms in



(1)



(2)

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[1] N. K. Wilson and J. B. Stothers, *J. Magnetic Resonance*, 1974, **15**, 31.

[2] E. L. Motell, D. Lauer, and G. Maciel, *J. Phys. Chem.*, 1973, **77**, 1865.

[3] T. Keumi, Y. Oshima, and N. Tokura, *Bull. Chem. Soc. Japan*, 1975, **48**, 1065.

[4] R. H. Martin and J. C. Nouls, *Tetrahedron Letters*, 1968, 2727.

[5] O. Dideberg, L. Dupont, and J. M. Andre, *Acta Cryst.*, 1972, **28B**, 1002.

1,9-dimethyldibenzofuran estimated by using the molecular frame of the parent compound, is only 2.4 Å. Therefore much steric hindrance in 1,9-disubstituted dibenzofurans is expected.

TABLE 1

Physical data for dibenzofurans (3) and ethers (4)

Ether *	Yield (%)	M.p. (°C) or b.p. (°C) at *p*/Torr †	Dibenzofuran	Substituents	Yield (%)	M.p. (°) †	δ($CDCl_3$)
			(3a)	None	55	86—87	7.1—8.25 (m, ArH),
(4b)	40	47 (50) [a]	(3b)	2,8-Me_2	45	67 (68—69) [b]	2.39 (6 H, s, CH_3) 6.97—7.52 (m, 6 ArH)
(4c)	35	137 at 9 (160 at 15) [a]	(3c)	2,6-Me_2	45	56—57	2.39 (3 H, s, CH_3), 2.50 (3 H, s, CH_3), 6.97—7.65 (m, 6 ArH)
(4d)	60	165 at 13	(3d)	1,4,6,9-Me_4	35	103—104	2.52 (6 H, s, CH_3), 2.84 (6 H, s, CH_3), 6.98 (AB, *J* 8 Hz, 4 ArH)
(4e)	74	151—153 at 10	(3e)	1,4-Me_2	39	17 (17—18) [c]	2.50 (3 H, s, CH_3), 2.69 (3 H, s, CH_3), 6.90—7.94 (m, 6 ArH)
(4f)	68	175—178 at 14	(3f)	1,2,3,4-Me_4	40	112 (112) [d]	2.27, 2.29 (6 H, CH_3), 2.48 (3 H, s, CH_3), 2.67 (3 H, s, CH_3), 7.17—8.10 (m, 4 ArH)
(4g)	56	66—67	(3g)	1,2,3,4,6,9-Me_6	40	112—113	2.29, 2.31, 2.51, 2.54, 2.77, 2.83 (18 H, CH_3), 6.97 (AB, *J* 8 Hz, 4 ArH)
(4h)	48	162	(3h)	1,2,3,4,6,7,9-Me_7	36	151—152	2.34, 2.36, 2.46, 2.50, 2.77, 2.81 (27 H, CH_3), 6.87 (s, 1 ArH)
(4i)	46	119	(3i)	1,2,3,4,6,7,8,9-Me_8	34	174—175	2.24, 2.26 (12 H, CH_3), 2.46 (6 H, s, CH_3), 2.62 (6 H, s, CH_3)
(4j)	37	155—160 at 13	(3j)	1-Pr^i-4-Me	25	Oil	1.37 (6 H, d, *J* 7 Hz, Pr^i), 2.52 (3 H, s, CH_3), 3.7 (1 H, septet, Pr^i), 6.98—8.0 (m, 6 ArH)
(4k)	34	200—204 at 11	(3k)	1-Pr^i-4,6,7,8,9-Me_5	5	86—88	1.36 (6 H, d, *J* 7 Hz, Pr^i), 2.49, 2.53, 2.60 (15 H, CH_3), 3.9 (1 H, septet, Pr^i), 7.11 (s, 2 ArH)
(4l)	39	71—72	(3l)	1,3-Bu^t_2	20	Oil	1.40 (9 H, s, Bu^t), 1.61 (9 H, s, Bu^t), 7.12—8.2 (m, 6 ArH)
(4m)	80	137—140 at 0.01	(3m)	1,3-Bu^t_2-6,7,8,9-Me_4	0		

* Substituents as in corresponding dibenzofuran. † Literature values in parentheses.

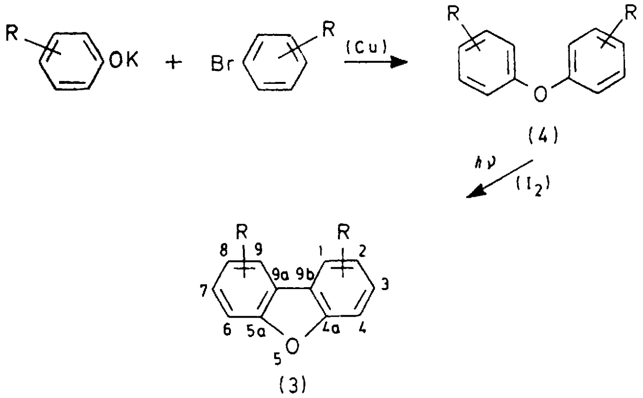
[a] M. Tomita, *J. Pharm. Soc. Japan*, 1937, **57**, 391. [b] R. Gerdil and E. A. C. Lucken, *J. Amer. Chem. Soc.*, 1965, **87**, 213. [c] S. Tripett, *J. Chem. Soc.*, 1957, 419. [d] T. Keumi, Y. Oshima, and N. Tokura, *Bull. Chem. Soc. Japan*, 1975, **48**, 1065.

Our new synthesis of dibenzofurans [6] gave access to various substituted compounds. We have chosen these molecules for a systematic study of the effects of substitution on a system consisting of three condensed aromatic rings. By monitoring the ^{13}C chemical shifts of the methyl groups we hoped to measure the steric strain in the compounds synthesized.

Synthetic Procedure.—The preparation of alkylated dibenzofurans usually requires multistep procedures.[7] By the recently developed photochemical synthesis of dibenzofurans from diaryl ethers [6] a variety of polyalkylated derivatives becomes accessible. The substituted diphenyl ethers (4) necessary for dehydrocyclisation can readily be obtained by an Ullmann reaction.[8] The dibenzofurans (3) prepared by this sequence are listed in Table 1.

Due to the steric interaction between the 1- and 9-positions the yield of (3k) was only 5% and in the case of (4m) no photochemical cyclisation could be observed.

^{13}C *Chemical Shift Assignments of the Alkyl Groups.*—The assignment of the carbon chemical shifts of the alkyl groups in the dibenzofurans (3b—l) is best approached by comparing (3c) with (3b). Obviously, the methyl group at C-6 resonates at higher field than the one at C-2. This shielding of a methyl group on an aromatic ring *ortho* to an oxygen linkage is known from the pair toluene and *o*-cresol.[9] Consequently (see Figure 1) in compound (3d) the methyl groups at C-1 and -9 are the most deshielded and the same assignments hold in (3e). Further substitution of (3e) by two more methyl groups in the same aromatic ring [(3f)] gives the usual upfield shift due to steric crowding.[10] It is quite substantial (3 p.p.m.) for both methyl groups in (3e). The assignment for (3f) has been confirmed using a single frequency decoupling experiment which follows the proton chemical



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[6] K.-P. Zeller and H. Petersen, *Synthesis*, 1975, 532.

[7] W. E. Parham, in 'Heterocyclic Compounds,' ed. R. L. Elderfield, Wiley, New York, 1951, vol. 2, S. 123.

[8] A. A. Moroz and M. S. Shvartsberg, *Russ. Chem. Rev.*, 1974, **43**, 679.

[9] J. B. Stothers, 'Carbon-13 N.M.R. Spectroscopy,' Academic Press, New York, 1972, p. 202.

[10] Ref. 9, p. 203.

shift assignment of Tokura.[3] Compound (3f) has substituents in one benzene ring only. By further substitution in the other ring dramatic effects can be seen in the chemical shifts of the methyl groups. Only the methyl group at C-4 does not experience a chemical shift. The 6-methyl group signal is 2.6 p.p.m. downfield from that of 4-methyl at the same position that the signals for 4- or 6-Me have in compounds (3c—e). On simple arguments one would expect a further upfield shift for the methyl groups at C-1 on going from (3f) to (3g). However, a downfield shift of 4.4 p.p.m. is observed. At the same time, the methyl group at C-9 resonates at 25.4 p.p.m., 0.6 p.p.m. to lower field than the corresponding methyl group in (3d). Very clearly, the difference of 4.6 p.p.m. between the methyl group signals at C-9 and -1 in (3g) is due to steric crowding between the methyl groups in the fully substituted ring.

TABLE 2

^{13}C Chemical shifts (δ) of the side chain carbon atoms of the dibenzofurans (3)

Dibenzofuran	C-1	C-2	C-3	C-4	C-6	C-7	C-8	C-9
(3b)		21.2					21.2	
(3c)		21.3			15.2			
(3d)	24.7			15.0	15.0			24.7
(3e)	19.5			15.0				
(3f)	16.4	16.4	15.5	12.4				
(3g)	20.8	16.6	16.4	12.4	15.1			25.4
(3h)	20.7	16.6	16.4	12.4	11.5	19.0		25.3
(3i)	21.7	16.5	16.3	12.4	12.4	16.4	16.5	21.7
(3j)	30.2 [a] 22.6 [b]			15.0				
(3k)	31.1 [d] 24.9 [b]			15.0	12.4	16.4	16.7	21.0
(3l)	35.7 [c] 31.6 [b]		35.3 [c] 29.9 [b]					

[a] CH<. [b] CH_3. [c] -C≤.

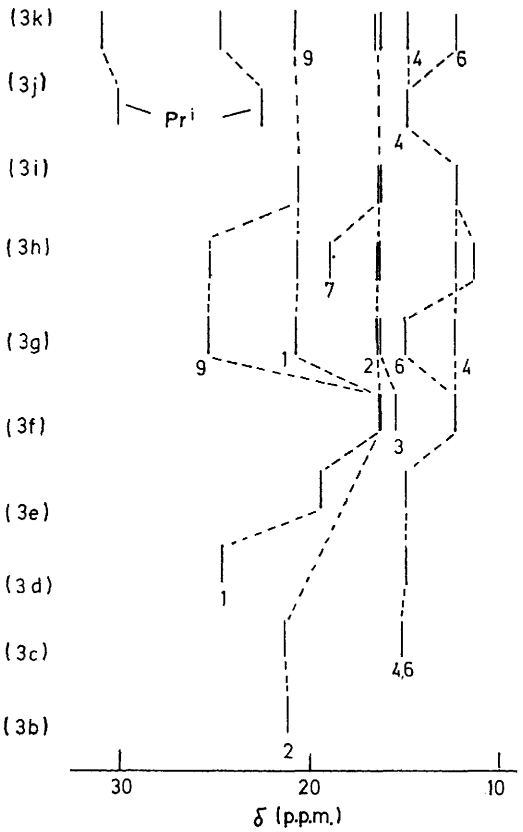

FIGURE 1 ^{13}C Chemical shifts of substituents in dibenzofurans (3)

However, the downfield shift of the methyl group at C-1 going from (3f) to (3g) must have another reason. Such a large effect across five bonds has not, to our knowledge, been observed: the situation here is reminiscent of that observed in other systems where severe steric interaction across four bonds also causes large downfield shifts.[1] While no theoretical explanation has been forwarded for this effect it seems attractive, in the dibenzofurans, to suggest that the downfield shifts may be a manifestation of molecular plane twisting.

In principle, similar arguments hold for the isopropyl substituted compounds (3j and k). Comparing the isopropyl group resonances going from (3j) to (3k) we again find downfield shifts, which we also feel are probably an indication of molecular plane twisting.

^{13}C *Chemical Shifts of the Ring Carbon Atoms.*—Assignment of the ^{13}C chemical shifts of the aromatic ring carbon atoms of the dibenzofurans (3) is rather difficult. Due to the unsymmetrical substitution of most of the compounds all 12 carbon atoms have different chemical shifts. Furthermore, in the more highly substituted compounds nearly all the carbon atoms have the same multiplicity. The assignments described here are done with the usual methods, especially off resonance decoupling and the use of shift increments. Signals closer than 1 p.p.m. with the same multiplicity are assigned tentatively. Within the scope of this work further effort seemed unnecessary.

The ^{13}C chemical shifts for dibenzofuran (3a) are best compared with those of benzofuran.[11] Straightforward is the assignment of C-4a and -5a at 156.2 p.p.m. From the remaining signals the quaternary C-9a and -9b are found by off resonance decoupling at 124.2 p.p.m. The resonance at highest field belongs to C-4 and -6. They are shielded due to their β-position with respect to the oxygen atom. Comparing (3b) with (3a) proves the

[11] N. Platzer, J.-J. Basselier, and P. Demerseman, *Bull. Soc. chim. France*, 1974, 905.

TABLE 3

^{13}C Chemical shifts [δ (p.p.m.) from Me_4Si] of the ring carbon atoms of dibenzofurans (3) [a]

Dibenzofuran	C-1	C-2	C-3	C-4	C-6	C-7	C-8	C-9	C-9b	C-4a	C-5a	C-9a
(3a)	120.6	122.6	127.0	111.6	111.6	127.0	122.6	120.6	124.2	156.2	156.2	124.2
(3b)	120.4	131.8	127.9	111.0	111.0	127.9	131.8	120.4	124.3	154.9	154.9	124.3
(3c)	117.9	131.9	127.9	111.1	121.7	127.9	122.4	120.6	123.6	155.3	154.4	124.6
(3d)	129.4	125.1	127.3	119.2	119.2	127.3	125.1	129.4	123.6	154.9	154.9	123.6
(3e)	130.7	122.4	126.2	119.0	111.5	127.8	123.7	122.3	122.3	155.0	156.0	125.4
(3f)	129.0	128.0	134.4	116.9	111.2	125.5	122.0	122.0	119.7	153.4	155.9	125.7
(3g)	129.1	127.2	134.2	117.0	119.0	126.8	125.2	129.3	122.1	153.5	155.1	124.2
(3h)	129.0	126.8	134.2	116.8	117.2	133.6	127.2	128.1	121.9	153.4	155.4	122.0
(3i)	129.3	126.9	133.5	116.7	116.7	133.5	126.9	129.3	122.3	153.5	153.5	122.3
(3j)	141.9	118.3	126.1	119.0	111.6	128.1	122.7	122.5	121.2	155.0	156.1	124.6
(3k)	141.5	119.2	127.2	118.4	117.0	134.0	127.4	129.6	121.8	153.5	154.8	122.8
(3l)	146.2	117.0	150.8	106.6	111.5	125.7	125.6	121.9	118.8	156.4	157.6	123.8

[a] Signals of the same multiplicity <1 p.p.m. apart are assigned tentatively.

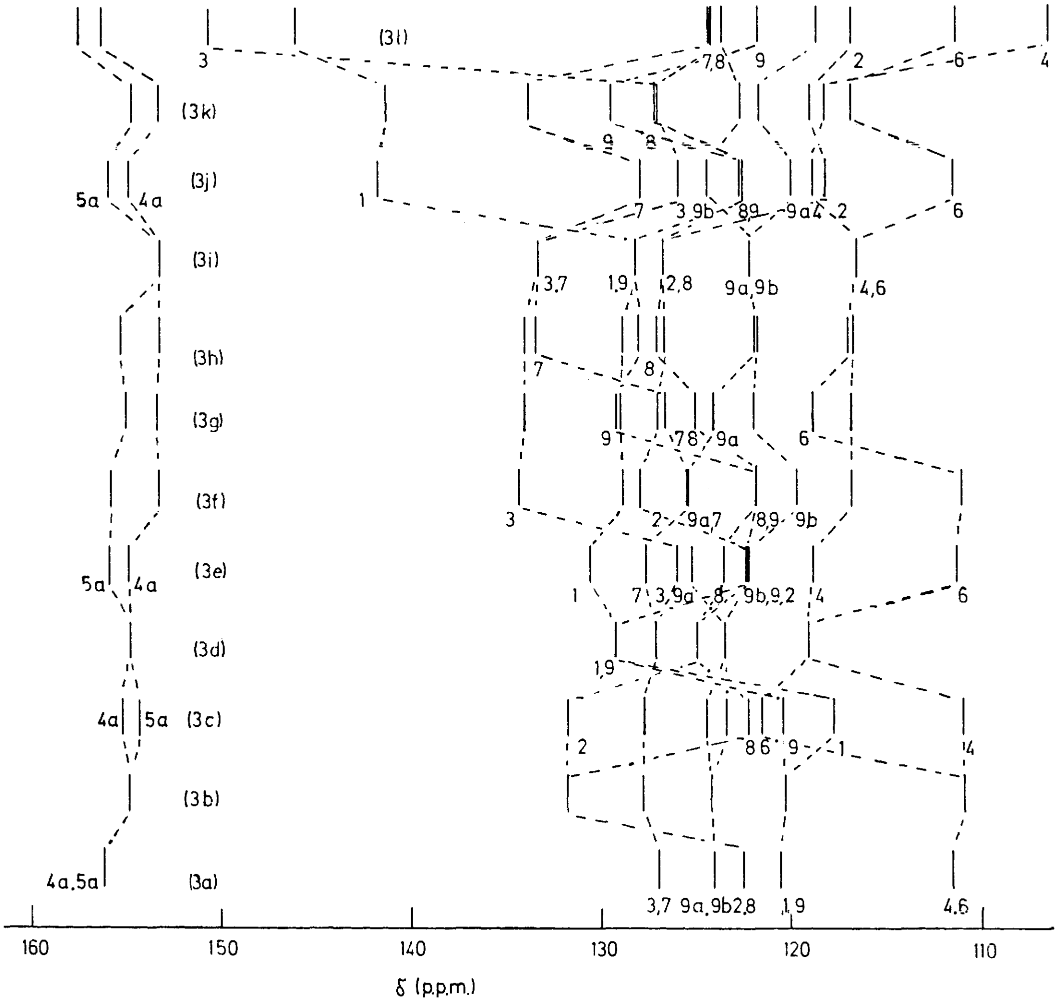

FIGURE 2 ^{13}C Chemical shifts of ring atoms in dibenzofurans (3)

assignment for C-2 and -8, since in (3b) only, one signal is deshielded significantly by an increment due to substitution by a methyl group.[12] Discrimination between the pairs C-7 and -3 and C-9 and -1 is carried out by comparison with the spectrum of (3d). Again, the shift increment for methyl group substitution fits only the assignment of C-9 and -1 in (3a) at 120.6 p.p.m. These assignments are in full agreement with the results of Platzer [11] for benzofuran.

Compound (3c) is the first example of an unsymmetrically substituted molecule in our series. The spectrum may be constructed from those for (3b and d), respectively. Discrimination between C-4a and -5a is based on an intensity argument although we are aware of the

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[12] G. B. Savitsky and K. Nakimawa, *J. Phys. Chem.*, 1964, **68**, 1956.

problems involved. However, C-5a has a longer relaxation time than C-4a due to its greater distance from the next proton. This intensity pattern holds for all unsymmetrically substituted dibenzofurans studied here, except (3g, h, k, and l), where this differentiation is based on assuming no overlapping of the corresponding signals. From the other pairs of signals C-9 remains at the shift position it maintains in (3a), whereas C-1 is somewhat shielded due to the introduction of a methyl group at its neighbour C-2. This carbon atom holds its shift position compared with (3b) whereas C-8 returns to its shift value in (3a). The pair C-7 and -3 does not split at all in (3c) and accordingly these carbon atoms maintain their chemical shift position compared with (3b). The pair C-4 and -6 is easily identified by off resonance decoupling; again C-6 is deshielded by a methyl group increment. Whereas (3c) is unsymmetric due to substitution at different positions in both benzene rings, (3e) is unsymmetric since only one aromatic ring is substituted by methyl groups. C-1 Is again at lowest field whereas C-9 resonates at about the shift position it maintains in (3a—c). In (3e) C-2, -8, and -9 have the same multiplicity and resonate too close together for specific assignment. We assume that C-2 is a little bit more shielded than C-8 due to the methyl group at C-1. The same argument holds for the distinction between C-3 and -7. The pair C-4 and -6 is again easily assigned. The relatively large splitting between the signals of C-9a and -9b is remarkable and is even higher in the more sterically hindered compound (3f). The relative assignment within the pair C-9a and -9b is based on the argument that C-9b should be somewhat more shielded by the methyl group at its neighbour C-1. Going from (3e) to (3f) we find C-2 and -3 deshielded by a methyl group increment, all the other chemical shift values remaining unchanged or somewhat shielded by effects of steric crowding. A rigid distinction between the signals of C-1 and -2 however is difficult. Further substitution in (3g) deshields C-9 and -6. In (3h) only one carbon atom signal appears as a doublet with off resonance decoupling and C-7 is again deshielded by another methyl group increment. The splitting in corresponding pairs is rather small and hence the relative assignment is tentative due to the rather slight asymmetry of this compound. The chemical shifts in (3i) can be easily worked out by joining the corresponding pairs in (3h). A comparison between the fully methylated compound (3i) and the parent dibenzofuran (3a) shows that the sequence of some signals is reversed. C-1 and -9 now resonate at lower field than C-2 and -8, whereas C-9a and -9b are more shielded. This again is most likely a consequence of the assumed non-planarity in (3i), which of course must effect positions 1, 9, 9a, and 9b most strongly. Compound (3j) has about the same chemical shifts as (3e) except for C-1 and -2, since here a methyl group is replaced by an isopropyl group. Similar arguments hold for the pair (3k and g). The assignment for compound (3l) is relatively easy. Using the shift increments of a t-butyl group we find the resonances at 150.8 and 146.2 p.p.m. belong to C-1 and -3 respectively. C-4 Is more shielded than C-2 due to a t-butyl group and an oxygen atom in the β-positions. The resonances in the unsubstituted ring remain almost the same as those of (3a).

Conclusions.—We have shown that steric effects can cause considerable deshielding of carbon atoms which are separated by five bonds. In view of the current discussion [13] on the direction of the δ-effect, we feel that the deshielding in case of steric overcrowding between carbon atoms in γ,[2] δ,[1] and now ε positions may result from one general cause. Further work is in progress.

EXPERIMENTAL

General Procedure for Ullmann Condensation.—A phenol (0.05 mol) and powdered potassium hydroxide (0.05 mol) were mixed and heated to *ca*. 100° for 1 h. Water formed was removed *in vacuo* (10 Torr) by heating for 4 h at 150° in an oil-bath. To the dry salt was added a catalytic amount of copper powder and an aryl bromide (0.05 mol). The reaction flask was fitted with an air condenser and the mixture gradually heated to 200° and maintained at 200° for 6—10 h. After extraction several times with hot benzene, the ether was obtained pure either by vacuum distillation or by filtration over silica gel (100 g) with benzene as eluant and recrystallisation from hexane–ethyl acetate (see Table 1). All new compounds gave satisfactory elemental analysis.

Dibenzofurans (3).—Alkylated dibenzofurans were obtained from the corresponding diphenyl ethers by our photochemical method.[6] All new compounds gave satisfactory elemental analysis.

N.m.r. Measurements.—^{1}H Spectra were taken on a Varian HA-100 spectrometer at 100 MHz for $CDCl_3$ solutions with tetramethylsilane as internal reference and lock signal. ^{13}C–^1H Noise decoupled spectra were taken on a Varian XL-100-15 spectrometer at 25.16 MHz for $CDCl_3$ solutions with tetramethylsilane as internal reference. The solvent provided the lock signal. The spectrometer was equipped with a 5 mm insert in a Varian V-4412 probe and a Varian 620-L 16k computer.

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[13] H. Pearson, *J.C.S. Chem. Comm.*, 1975, 912.