

Carbon-13 Nuclear Magnetic Resonance of Unsymmetrically *ortho*-Disubstituted Benzenes. Spectral Analysis of Phthalic and Maleic Acid Monoesters †

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A simple and rapid technique for the analysis of certain ^{13}C n.m.r. spectra has now been demonstrated to be applicable to the spectra of unsymmetrically *ortho*-disubstituted benzenes. The ^1H coupled spectra of these compounds reveal characteristic differences in the splitting patterns of the protonated ring carbons. This phenomenon has been used to assign the ^{13}C n.m.r. signals of a series of phthalic acid monoesters. In addition the ^{13}C n.m.r. spectra of the structurally and electronically related maleic acid monoesters are assigned. The effects of phthalate or maleate monoesterification on the ^{13}C chemical shifts of a series of alcohols are recorded and compared to recent accounts concerning other esters. These data reveal that ^{13}C chemical shifts induced by esterification of alcohols are relatively consistent, and predictable, regardless of the group attached to the carboxy-function.

TARPLEY and GOLDSTEIN¹ have thoroughly analysed the ^1H coupled ^{13}C n.m.r. spectra of several *ortho*-dihalogeno-substituted benzenes. More recently Günther *et al.*² have noticed that the splitting pattern observed for ^{13}C n.m.r. signals in the ^1H coupled spectra of a number of symmetrically *ortho*-disubstituted benzenes differs characteristically for ring carbons in the positions α and β to the substituted carbons. In particular the β -carbons appear as a distinct doublet of doublets, while the α -carbons give rise to a doublet of broad signals, consisting of many lines. Wenkert and his co-workers³ have employed this 'fingerprinting method' to assign the chemical shifts of coumarin and benzofuran, and suggest its general applicability to unsymmetrical systems. However, its applicability to unsymmetrically, *ortho*-disubstituted benzenes has not been tested.

We have now demonstrated the general utility of this technique for the analysis of the ^{13}C n.m.r. spectra of unsymmetrically, *ortho*-disubstituted benzenes. An illustration is detailed below in the spectral analysis of phthalic acid monoesters, degradation products⁴⁻⁶ of the ubiquitous⁷ phthalate ester plasticizers, and intermediates in a resolution procedure for chiral alcohols.⁸ In addition the structurally and electronically related maleic acid monoesters were prepared to serve as model compounds for spectral studies.

EXPERIMENTAL

Natural abundance ^{13}C spectra of 1M solutions in CDCl_3 containing tetramethylsilane as internal reference were

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‡ The more obvious models, phthalic acid, dimethyl phthalate, maleic acid and dimethyl maleate, could not be used due to solubility problems in CDCl_3 , and overlapping signals in other solvents.

§ The chemical shift assignments of these compounds have been reported elsewhere,^{10,11} but the actual chemical shift values recorded herein were determined under the conditions of the present investigation.

¹ A. R. Tarpley, jun., and J. H. Goldstein, *J. Mol. Spectroscopy*, 1971, **37**, 432.

² H. Günther, H. Schmickler, and G. Jikeli, *J. Magnetic Resonance*, 1973, **11**, 344.

³ E. Wenkert *et al.*, in 'Topics in Carbon-13 N.M.R. Spectroscopy,' ed. G. C. Levy, Wiley, New York, 1976, vol 2, p. 113.

⁴ T. F. Hammargren, M.S. Thesis, Texas A & M University, 1976.

recorded on a JEOL JNM-PS-100 spectrometer operating at 25.034 MHz in the Fourier transform mode. The spectra of representative samples were also recorded on 2M solutions and a negligible dependence of chemical shifts on concentration was observed.

The phthalic and maleic acid monoesters which were used in this investigation have been reported in the literature and were prepared and purified by standard procedures⁹ with only slight modifications. These substances exhibited physical and spectral characteristics entirely consistent with the assigned structures.

RESULTS AND DISCUSSION

In the ^1H decoupled ^{13}C n.m.r. spectrum of phthalic acid monomethyl ester, the signals of the methyl group, the carbonyl carbons, and the two less intense, non-protonated ring carbons may be readily assigned by standard chemical shift theory.¹⁰ In order to differentiate between the latter two signals (C-2 and -7, Table 1), a shift comparison with analogous carbons of maleic acid monomethyl ester was carried out. ‡ These in turn were assigned by model comparisons.

The ^{13}C chemical shifts (in CDCl_3) of freshly distilled samples of methyl acrylate and acrylic acid are shown in Figure 1. § With this information the more downfield olefinic carbon shift of the maleic acid monoesters can be assigned C-3' (which is β to the carboxy group), and the more upfield shift to C-2' (Table 2). The ^{13}C n.m.r. spectra of a series of maleic acid monoesters were assigned

⁵ D. L. Stalling, J. W. Hogan, and J. L. Johnson, *Environmental Health Perspectives*, 1973, **3**, 159.

⁶ V. W. Saeger and S. E. Tucker III, *Plast. Eng.*, 1973, **29**, 46.

⁷ Cf. C. S. Giam, H. S. Chan, and G. S. Neff, *Analyt. Chem.*, 1975, **47**, 2225 and references contained therein.

⁸ J. Kenyon, *Org. Synth.*, 1964, Coll. Vol. I, 418.

⁹ E.g., see (a) W. A. Fessler and R. L. Shriner, *J. Amer. Chem. Soc.*, 1936, **58**, 1384; (b) J. F. Coggans and J. E. Copenhaver, *ibid.*, 1939, **61**, 2909; (c) S. M. Spatz and H. Stone, *J. Org. Chem.*, 1958, **23**, 1559; (d) A. Zilka and M. D. Bachi, *ibid.*, 1959, **24**, 1096; (e) B. Yu. Gordinskii, V. M. Shimanskii, and R. S. Vishnyakova, *Zhur. Prikl. Khim.*, 1967, **40**, 1881 (*Chem. Abs.*, 1967, **67**, 116520).

¹⁰ (a) G. C. Levy and G. L. Nelson, 'Carbon-13 Nuclear Magnetic Resonance for Organic Chemists,' Wiley-Interscience, New York, 1972; (b) J. B. Stothers, 'Carbon-13 N.M.R. Spectroscopy,' Academic Press, New York, 1972.

¹¹ L. F. Johnson and W. C. Jankowski, 'Carbon-13 N.M.R. Spectra,' Wiley-Interscience, New York, 1972.

by analogy to the monomethyl ester and the chemical shift data are listed in Table 2.

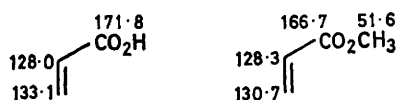


FIGURE 1 ^{13}C N.m.r. chemical shifts of acrylic acid and methyl acrylate in CDCl_3 (relative to Me_4Si)

The chemical shifts of C-2 and -7 of the phthalic acid monoesters (Table 1), which were easily distinguished from those of other ring carbons due to their weaker signals,¹⁰ were differentiated from one another by comparison to those of analogous carbon centres of the maleate derivatives (Table 2). The chemical shift assignments of C-3—6 (Table 1) were somewhat more difficult.

'crude triplets' (J_1 ca. 171 Hz). This is in accord with Günther's 'fingerprint' analysis.²

The assignments are not as straightforward in the case of phthalic acid monoesters, since being unsymmetrically *ortho*-disubstituted benzenes they possess both α and α' , and β and β' carbons (Figure 2). Since each of the β -carbon signals of the ^1H coupled spectrum of phthalic acid monomethyl ester appears as a distinct doublet

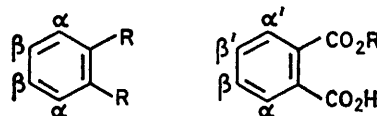
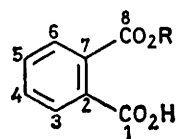


FIGURE 2 *ortho*-Disubstituted benzenes

of doublets,² they are easily distinguished from the pair of α -carbon signals.

TABLE 1

^{13}C Chemical shifts (p.p.m. from Me_4Si) of phthalic acid monoesters in CDCl_3 ^a



Carbon	R								Δ (p.p.m.) ^c
	CH_3	Et	Pr^n	Pr^t	Bu^n	Bu^s	Bu^t	$\text{C}_8\text{H}_{17}^b$	
1	172.5	172.3	172.8	172.8	172.8	172.9	173.3	172.7	0.8
2	130.0	130.1	130.1	129.9	130.0	129.9	129.9	130.1	0.1
3	129.8	129.6	129.7	129.6	129.7	129.7	129.4	129.7	0.4
4	130.8	130.8	130.7	130.6	130.7	130.6	130.3	130.7	0.5
5	132.2	132.1	132.2	132.1	132.2	132.1	132.0	132.1	0.2
6	128.6	128.7	128.8	128.7	128.8	128.6	128.8	128.6	0.2
7	133.3	133.5	133.6	134.0	133.6	134.0	134.7	133.6	1.4
8	168.6	168.2	168.1	167.6	168.1	167.7	167.0	168.3	1.4

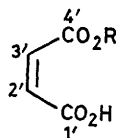
^a Chemical shifts for the R groups are reported in Table 4. ^b 2-Ethylhexyl. ^c Chemical shift difference between the methyl and *t*-butyl derivatives.

The ^1H coupled ^{13}C n.m.r. spectrum of dimethyl phthalate exhibited a distinct doublet of doublets (J_1 171.5, J_2 8.2 Hz) centred at δ 131.1 p.p.m. for the

In order to distinguish between the signals of the α - and the α' -carbons, and between the β - and the β' -carbons, shift comparisons with methyl benzoate and

TABLE 2

^{13}C Chemical shifts (p.p.m. from Me_4Si) of maleic acid monoesters in CDCl_3 ^a



Carbon	R								Δ (p.p.m.) ^c
	CH_3	Et	Pr^n	Pr^t	Bu^n	Bu^s	Bu^t	$\text{C}_8\text{H}_{17}^b$	
1'	167.3	167.0	167.2	166.9	167.1	166.4	166.6	167.2	0.7
2'	130.1	130.5	130.3	131.0	130.4	130.8	131.9	130.3	1.8
3'	133.2	133.4	133.7	133.3	133.5	133.5	133.2	133.6	0
4'	166.8	166.7	166.5	166.5	166.6	166.8	166.2	166.5	0.6

^a Chemical shifts of the R groups are reported in Table 3. ^b 2-Ethylhexyl. ^c Chemical shift difference between the methyl and *t*-butyl derivatives.

β -carbons (Figure 2), while the α -carbon resonances, centred at δ 128.9 p.p.m., appeared as a doublet of

† See footnote on p. 831.

benzoic acid were carried out (Figure 3)†. Recognition of the difficulty of extrapolation of shift parameters from monosubstituted benzenes to *ortho*-disubstituted

systems¹⁰ compelled us to use shift comparisons (and trends) between the two models rather than absolute chemical shift values.

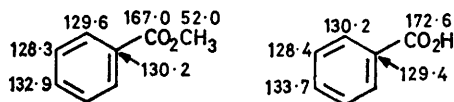


FIGURE 3 ¹³C N.M.R. chemical shifts of methyl benzoate and benzoic acid in CDCl₃ (relative to Me₄Si)

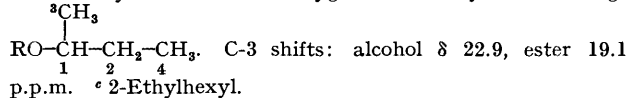
An electron-withdrawing substituent on a mono-substituted benzene ring exerts its major influence on the chemical shifts of the *ipso*-, *ortho*-, and *para*-carbons, and relatively little effect at the *meta*-carbon relative to benzene itself,¹⁰ as may be observed for methyl benzoate and benzoic acid (Figure 3). Thus, C-4 (Table 1) of

TABLE 3

¹³C Chemical shifts (p.p.m. from Me₄Si) of alcohols (ROH) and their monomaleate derivatives in CDCl₃

		R							
		CH ₃	Et	Pr ^a	Pr ⁱ	Bu ^a	Bu ^{s b}	Bu ^t	C ₈ H ₁₇ ^c
C-1 ^a	Alcohol	50.4	58.0	64.4	64.2	62.5	69.4	69.1	65.3
	Ester	53.1	62.7	68.2	70.9	66.5	75.2	84.7	69.0
C-2	Alcohol	18.2	25.9	25.3	35.0	32.1	31.2	42.1	
	Ester		13.9	21.6	21.5	30.3	28.5	27.8	38.6

^a Directly bonded to oxygen. ^b s-Butyl numbering:



phthalic acid monomethyl ester, being *para* to a methoxycarbonyl substituent should appear upfield of C-5, which is *para* to the carboxy group (δ 130.8 and 132.2 p.p.m., respectively).

Similarly the α -carbon of phthalic acid monomethyl ester is *ortho* to a carboxylate group, while the α' -carbon is *ortho* to a methoxycarbonyl group and should appear at higher field. Consequently, on comparison with the ¹³C chemical shifts of the *ortho*-carbons in methyl benzoate and benzoic acid (δ 129.5 and 130.2 p.p.m., respectively), the α -carbon is assigned the more downfield signal (δ 129.8 p.p.m.) and the α' -carbon the more upfield one (δ 128.6 p.p.m.).

The ¹³C n.m.r. spectra of a series of phthalic acid monoesters were assigned by analogy with the monomethyl prototype. The chemical shift data are recorded in Table 1.

An examination of the chemical shift data for the maleic acid monoesters in Table 2 reveals that the major variation occurs at C-2'. This could be anticipated from resonance theory and reflects, in part, changes in π -electron delocalization over C-1'—4'.

Significant chemical shift variations for the phthalic acid monoesters can be seen for C-1, -7, and -8 (Table 1). There is undoubtedly a major electronic contribution

* C-1 is bonded directly to oxygen.

¹² S. W. Pelletier, Z. Djarmati, and C. Pape, *Tetrahedron*, 1976, **32**, 995.

to the changes observed at C-7 and -8 for the various derivatives, and a significant 'through-space' interaction which produces perturbations at C-1.

Effects of Phthalate and Maleate Monoesterification upon the ¹³C Chemical Shifts of Several Alcohols.—¹³C N.M.R. spectra of a multitude of esters are well known. Literature accounts however have been at variance concerning the magnitude of the 'esterification effect' on the chemical shifts of various alcohols. Recently Pelletier and his co-workers¹² reported the ¹³C chemical shifts of 28 carboxylates and found C-1* 'esterification effects' (relative to the parent alcohols) ranging from +1.3 to +17.7 p.p.m. (a positive value represents a downfield shift). The C-2 'esterification effect' was found to be essentially constant at -3.8 (\pm 0.7) p.p.m. These workers found an upper limit of ca. 5 p.p.m. for the C-1 'esterification effect' for esters of methanol.

Tsuji *et al.*¹³ examined effects upon ¹³C chemical shifts of some simple alcohols when acetylated, methoxycarbonylated, and mesylated. For the acetyl derivatives C-1 'esterification effects' were found to range from +1.5 to +3.7 p.p.m. The C-2 shifts were relatively constant in these studies, also at ca. -3.8 (\pm 1.1) p.p.m.

For the maleic acid monoesters we found C-1 'esterification shifts' ranging from +2.7 to +15.6 p.p.m. In close agreement with the results discussed above,^{12,13} C-2 shifts were relatively constant, ranging from -3.4 to -4.7 p.p.m. These results are listed in Table 3.

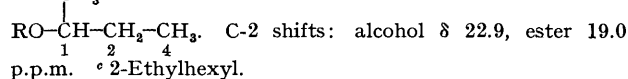
The esterification of the same alcohols with phthalic acid (to produce phthalic acid monoesters) resulted in effects on the C-1 chemical shifts which ranged from +2.4 to +13.5 p.p.m. Shift effects at C-2 ranged from -3.3 to -4.5 p.p.m. These results are catalogued in Table 4. The present work strengthens the observ-

TABLE 4

¹³C Chemical shifts (p.p.m. from Me₄Si) of alcohols (ROH) and their monophthalate derivatives in CDCl₃

		R							
		CH ₃	Et	Pr ^a	Pr ⁱ	Bu ^a	Bu ^{s b}	Bu ^t	C ₈ H ₁₇ ^c
C-1 ^a	Alcohol	50.4	58.0	64.4	64.2	62.5	69.4	69.1	65.3
	Ester	52.8	62.0	67.6	69.6	65.9	74.2	82.6	68.4
C-2	Alcohol		18.2	25.9	25.3	35.0	32.1	31.2	42.1
	Ester		13.9	21.8	21.5	30.5	28.7	27.9	38.7

^a Directly bonded to oxygen. ^b s-Butyl numbering:



ation¹² that carbon resonances in esterified alcohols are shifted by a predictable amount, regardless of the group attached to the carboxy-function.

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¹³ Y. Terui, K. Tori, and N. Tsuji, *Tetrahedron Letters*, 1976, 621.