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THREE BOND CARBON-13-PROTON COUPLING AS A STRUCTURAL AID. METHYLATED BENZENE AND BENZOIC ACID DERIVATIVES

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Long-range $^{13}C-^{1}H$ coupling constants have been determined to assist in assignment of signals in CMR spectra, to evaluate the magnitude and sign of these coupling constants and, to a more limited extent, in conformational analysis of selected compounds.[1] Most of these measurements have been of compounds with known structures. The experimental procedures for aromatic compounds are especially difficult as a result of overlapping aromatic signals and multiple couplings of nuclear carbon atoms to ring protons[2,3] and involve special procedures such as heteronuclear decoupling, spin-tickling,[1] deuterium labelling,[2] and off-resonance irradiation.[4] We wish to report a simple, straightforward procedure in which three bond $^{13}C-^{1}H$ couplings ($^{3}J_{C-H}$) are used to distinguish positional isomers of substituted aromatic compounds and therefore should be applicable as a general structural tool.[5]

The CMR spectra of methylated benzene and benzoic acid derivatives show the substituent carbon atom resonances at frequencies removed from the main aromatic resonances and are readily located. Since $^{3}J_{C-H}$ is substantially larger than $^{4}J_{C-H}$,[8] the additional multiplicity of methyl quartets or the multiplicity of carboxylic acid carbon resonances in undecoupled CMR spectra are a direct indication of the number of protons situated ortho to the carbon atoms in question For example, the methyl quartet ($^{1}J_{C-H}$ = 127 Hz) in the undecoupled CMR spectrum of o-cresol shows additional $^{3}J_{C-H}$ splitting to provide a quartet of doublets as a result of a coupling interaction with one ortho proton.

Data for representative compounds is presented in the Table. First-order coupling of the substituent carbon atom to ortho protons was observed in most cases, with a coupling constant in the range $^{3}J_{C-H}$ = 3.5-5.5 Hz. The three bond couplings do not always provide unambiguous assignments for isomeric structures, but invariably narrow the structural possibilities. The utility of this technique can be seen from the CMR spectra of the six isomers of dimethylphenol shown in Figure 1. Only the 2,3-dimethyl isomer shows a quartet of doublets and a quartet without further coupling for the two methyl carbon resonances. The 2,6-dimethyl isomer shows the equivalent methyl carbon atoms as a single quartet of doublets, while two quartet of doublets are apparent in the spectrum of the 3,4-dimethyl isomer. Likewise the CMR spectrum 3,5-dimethylphenol is unique since it is the sole isomer which exhibits a single quartet of triplets for the equivalent methyl carbon atoms. Both 2,4-dimethyl- and 2,5-dimethylphenol show a quartet of doublets and a quartet of triplets for the methyl carbon atoms and hence cannot be differentiated by this procedure.

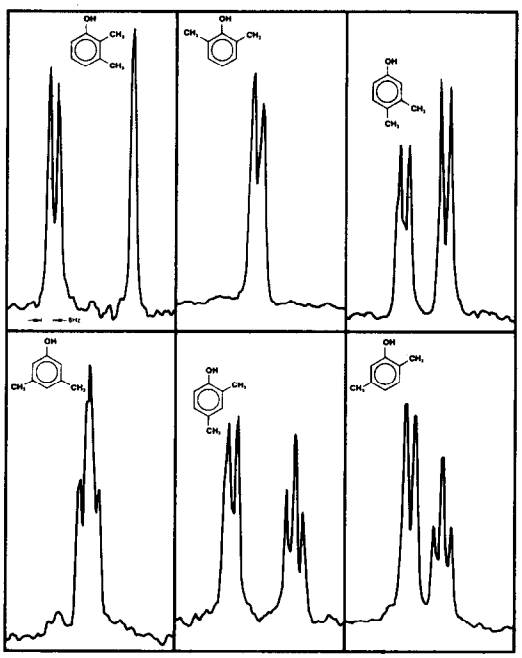

Figure 1. Scale expansion of methyl region in CMR spectra of isomeric dimethylphenols

In the case of toluene, o-xylene, p-xylene and 2,6-dimethylbenzoic acid the long-range couplings are more complex, giving rise to broad ($W_{1/2}$ = 8-10 Hz) or non-first-order signals. This has been found to be characteristic of substituent carbon atoms when the adjacent proton is situated ortho to another proton with similar chemical shift.[9] Thus the complexity as well as the multiplicity of spin-spin couplings can serve to provide useful structural information for distinguishing isomers of substituted aromatic compounds.

Work is currently in progress to assess the applicability of these long-range couplings in structural analysis of other aromatic systems and of other aromatic substituents.

Table

CMR Data for Aromatic Substituents

Compound	Solvent	Chemical Shift[a]	$^3J_{C-H}$ Multiplicity[b]
toluene	$CDCl_3$	21.2	B
o-cresol	DMSO-d_6	16.0	D
m-cresol	DMSO-d_6	21.6	T
p-cresol	$CDCl_3$	20.2	T
o-xylene	$CDCl_3$	19.5	B
m-xylene	$CDCl_3$	21.1	T
p-xylene	$CDCl_3$	20.5	–[c]
2,3-dimethylphenol	DMSO-d_6	11.5 (C-2 CH_3)	S
		19.8 (C-3 CH_3)	D
2,6-dimethylphenol	$CDCl_3$	15.5	D
3,4-dimethylphenol	$CDCl_3$	18.5	D
		19.6	D
3,5-dimethylphenol	DMSO-d_6	21.1	T
2,4-dimethylphenol	$CDCl_3$	15.3 (C-2 CH_3)	D
		20.0 (C-4 CH_3)	T
2,5-dimethylphenol	$CDCl_3$	15.1 (C-2 CH_3)	D
		20.7 (C-5 CH_3)	T
benzoic acid	$CDCl_3$	172.4	T
2-methylbenzoic acid	DMSO-d_6	21.8 (CH_3)	?
		169.4	D
3-methylbenzoic acid	$CDCl_3$	21.0 (CH_3)	T
		172.7	T
4-methylbenzoic acid	DMSO-d_6	21.3 (CH_3)	T
		167.6	T
2-amino-3-methylbenzoic acid	DMSO-d_6	17.7 (CH_3)	D
		170.5	D
2-amino-4-methylbenzoic acid	DMSO-d_6	21.4 (CH_3)	T
		169.8	D
2-amino-5-methylbenzoic acid	DMSO-d_6	20.0 (CH_3)	T
		169.9	D
3-amino-4-methylbenzoic acid	DMSO-d_6	17.8 (CH_3)	D
		168.5	T
2,4-dimethylbenzoic acid	$CDCl_3$	21.2 (C-4 CH_3)	T
		21.9 (C-2 CH_3)	D
		173.5	D
2,5-dimethylbenzoic acid	DMSO-d_6	20.5 (C-5 CH_3)	T
		21.2 (C-2 CH_3)	D
		169.1	D[d]
2,6-dimethylbenzoic acid	DMSO-d_6	19.7 (CH_3)	–
		171.3	S[e]
3,4-dimethylbenzoic acid	DMSO-d_6	19.3 (CH_3)	–
		19.5 (CH_3)	
		167.7	T
3,5-dimethylbenzoic acid	$CDCl_3$	20.5 (CH_3)	T
		169.2	T

[a] ppm relative to TMS
[b] S = singlet, D = doublet, T = triplet, B = broad single band
[c] poorly resolved five line pattern
[d] poorly resolved three line pattern
[e] two overlapping doublets

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5) Compounds were obtained from commercial sources and were used without further purification. Pulse FT CMR spectra were recorded of concentrated solutions in either $CDCl_3$ or DMSO-d_6 in 10 mm tubes with a Varian model CFT-20 spectrometer. Chemical shifts were obtained relative to TMS by taking the solvent's central ^{13}C peak as 39.6 ppm (DMSO-d_6) or 76.9 ppm ($CDCl_3$).[6] It was possible to acquire good quality undecoupled spectra in 4-6 hours by using a gated decoupling technique[7] and a sweep width of 4 KHz with 8,192 data points.

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