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^{13}C Nuclear Magnetic Resonance Studies on Phenols; Effects of a Lanthanide Shift Reagent and Triethylamine[1]

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^{13}C Nuclear magnetic resonance (^{13}C-NMR) spectra of 16 phenolic compounds were recorded and the Eu(fod)$_3$ and triethylamine induced shifts of their carbon resonances were measured. Generally, these shift reagents are useful for analyzing ^{13}C-NMR spectra of phenols. By means of Eu(fod)$_3$, aromatic carbons of phenols were shifted in the order; *ortho*, *meta* and *para* carbons to a phenolic group. Some anomalous shifts were observed on using Eu(fod)$_3$, the upfield shift for the C-6 nucleus in 2-methoxyphenol and the relatively large downfield shifts for the C-6 nuclei in *ortho*-alkylphenols. Triethylamine induced a downfield shift for the C-1, C-2 and C-6 nuclei, and an upfield shift for the C-3, C-4 and C-5 nuclei of phenols with exception of 2-methoxyphenol.

Keywords——^{13}C-NMR; ^{13}C chemical shift; lanthanide shift reagent; Eu(fod)$_3$; triethylamine; phenols; deuterated phenols; alkyl phenols; methoxy phenols

Recently the application of lanthanide shift reagents(LSR) for phenols in ^{1}H nuclear magnetic resonance (^{1}H-NMR) spectroscopy was demonstrated by Shoffner[3] and Liu.[4] However, ^{13}C-NMR data of LSR induced effects for phenols have not been reported except *p*-cresol.[5] In the present paper, we report the ^{13}C-NMR spectra of 16 phenolic compounds and their shifted spectra upon addition of tris-(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate)europium(III)[Eu(fod)$_3$] and triethylamine(Et$_3$N), and the usefulness of these shift reagents for the assignment of carbon resonances of phenol compounds. ^{13}C Chemical shifts of alkyl- and methoxy-substituted phenols were examined(Table I), and their Eu(fod)$_3$ and Et$_3$N induced shifts are presented in the Table II and III.

Phenol and Anisol

The ^{13}C resonances of phenol and anisol have been assigned.[6] On using Eu(fod)$_3$ for phenol, the magnitude of the induced downfield shifts decreased in the order of C–1, C–2(6), C–3(5), and C–4 in inverse proportion to the distance between each carbon atom and a hydroxyl group. The C–1 peak was significantly broadened, since Eu atom may affect the relaxation time of the C–1 carbon atom. On the other hand, Eu(fod)$_3$ induced small shifts for the ^{13}C signals of anisol. Generally, an ethereal oxygen acts as a very poor donor toward LSR,[7] so that a methoxy oxygen of anisol would coordinate very weakly to Eu(fod)$_3$. It is difficult to assign phenolic and ethereal aromatic carbon signals in a molecule, since these carbons resonate at the same field. However, the addition of Eu (fod)$_3$ enables us easily to assign their carbon signals because of the larger induced shifts of phenolic carbons.

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[3] J.P. Shoffner, *J. Am. Chem. Soc.*, **96**, 1599 (1974); *Anal. Chem.*, **47**, 341 (1975).

[4] K-T. Liu, M-F. Hsu, and J-S. Chen, *Tetrahedron Letters*, **1974**, 2179.

[5] K. Tori and Y. Yoshimura, *Tetrahedron Letters*, **1973**, 3127.

[6] J.B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press, New York, 1972, p. 196.

[7] A.F. Cockerill, G.L.O. Davis, R.C. Harden, and D.M. Rackham, *Chem. Rev.*, **73**, 553 (1973).

In the presence of Et_3N, the C–1 and C–2(6) peaks of phenol moved downfield. On the contrary, the C–3(5) and C–4 peaks shifted upfield. Et_3N had no influence on the chemical shifts of anisol.

TABLE I. ^{13}C Chemical Shifts of Substituted Phenols[a)]

Substituent	C–1	C–2	C–3	C–4	C–5	C–6	$-OCH_3$	$-CH_3$
Nil	155.3	115.5	129.8	121.0				
2–OCH_3	145.8	146.7	110.9	120.2	121.5	114.7	55.9	
3–OCH_3	156.7	101.7	160.8	106.6	130.3	108.1	55.6	
4–OCH_3	149.7	116.3	115.1	153.6	115.1	116.3	56.0	
2–CH_3	153.7	123.9	131.1	120.8	127.1	115.0		15.7
3–CH_3	155.3	116.2	140.0	121.8	129.5	112.4		21.3
4–CH_3	153.1	115.2	130.1	130.1	130.1	115.2		20.4
2,3-diCH_3	153.5	122.6	138.4	122.5	126.1	112.8		(2)11.4 (3)20.0
2,4-diCH_3	151.5	123.7	131.7	130.0	127.4	114.9		(2)15.7 (4)20.4
2,5-diCH_3	153.6	120.6	130.8	121.5	137.1	115.8		(2)15.3 (5)20.9
2,6-diCH_3	152.2	123.1	128.6	120.3	128.6	123.1		(2)15.8 (6)15.8
							↓ $-C(CH_3)_3$	↓ $-C(CH_3)_3$
2-*t*-Bu	154.2	136.2	127.0	120.7	127.0	116.6	34.5	29.7
3-*t*-Bu	155.2	112.4[b)]	153.4	117.9	129.2	112.7[b)]	34.6	31.2
4-*t*-Bu	153.0	114.9	126.5	143.7	126.5	114.9	34.1	31.5
2,6-di-*t*-Bu	153.9	136.0	124.9	119.7	124.9	136.0	34.3	30.4
							↓ $-CH(CH_3)_2$	↓ $-CH(CH_3)_2$
2,6-diisoPr	150.0	133.7	123.5	120.7	123.5	133.7	27.2	22.8

a) chemical shifts in ppm for TMS
b) ambiguous assignment

TABLE II. $Eu(fod)_3$ and Et_3N Induced Shifts for Methoxyphenols[a)]

Substituent		C–1	C–2	C–3	C–4	C–5	C–6	$-OCH_3$
Nil	ΔE[b)]	3.5	1.1	0.6	0.5	0.6	1.1	
	ΔN[c)]	2.4	0.7	−0.3	−2.0	−0.3	0.7	
(Anisol)	ΔE	0.3	0.2	0.1	0.1	0.1	0.2	0.3
	ΔN	0.1	0.0	0.0	0.0	0.0	0.0	−0.1
2–OCH_3	ΔE	4.4	2.0	0.5	0.7	0.5	−0.2	2.6
	ΔN	1.1	1.2	0.4	−0.7	−0.2	1.2	−0.3
3–OCH_3	ΔE	2.2	0.7	0.6	0.4	0.4	0.7	0.3
	ΔN	2.4	0.5	0.3	−1.9	−0.4	0.6	−0.3
4–OCH_3	ΔE	3.4	1.2	0.8	0.9	0.8	1.2	0.5
	ΔN	1.9	0.6	−0.3	−0.8	−0.3	0.6	−0.3

a) Observed shifts in ppm, plus value indicates a downfield shift.
b) $Eu(fod)_3$ (0.1 mmol) induced shift $\Delta E = \delta_{Eu(fod)_3} - \delta$
c) Et_3N (2 mmol) induced shift $\Delta N = \delta_{Et_3N} - \delta$

Alkyl Phenols

The ^{13}C chemical shifts of cresols,[8,9] 2,6-dimethylphenol,[8] 2-*t*-butylphenol[9] and 2,6-diisopropylphenol[8] have been reported previously. Although there are small discrepancies (0.1—1.0 ppm) between the early data and ours, these may depend on differences in experimental conditions.

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[8] E. Breitmaier and W. Voelter, "^{13}C NMR Spectroscopy," Verlag Chemie, Weinheim, 1974, p. 171.

[9] L.F. Johnson and W.C. Jankowski, "Carbon-13 NMR Spectra," John Wiley and Sons, New York, 1972, Spectrum No. 247, 385, and 438.

Other alkylphenols were assigned by the use of the off-resonance decoupling technique and considering substituent effects of hydroxyl (C_{subst}; +26.9, C_{ortho}; −12.7, C_{meta}; +1.4, C_{para}; −7.3)[10] and alkyl groups (methyl: C_s; +8.9, C_o; +0.7, C_m; −0.1, C_p; −2.9, *t*-butyl: C_s; +20.5, C_o; −3.3, C_m; −0.3, C_p; −2.9)[6,10] on each benzene ring. Some carbons bearing a hydrogen were further confirmed by refferring the ^{13}C spectra of *ortho* and *para* deuterated phenols in the experimental section.

Generally, the trend of $Eu(fod)_3$ and Et_3N induced differential shifts of alkylphenols is parallel to that of phenol. For example, the induced shifts of phenol and 4-methylphenol are 3.5, 1.1, 0.6, and 0.5, and 3.4, 1.1, 0.6, and 0.6 ppm for each C–1, C–2, C–3, and C–4 nucleus respectively. In 2-methylphenol, the $Eu(fod)_3$ induced differential shift for the C–6 nucleus (ΔE 1.1) is much larger than that for the C–2 nucleus (ΔE 0.6). This finding may suggest that the coordination of $Eu(fod)_3$ to 2-methylphenol is sterically hindered by a methyl group. In order to clarify the steric factor of the alkyl group, more hindered phenols were examined. The magnitude of the differential shifts of 2,6-dimethylphenol is one third at C–1 (ΔE 1.1) and a half at C–2, C–3, and C–4 (ΔE 0.6, 0.3, and 0.3) relative to that of phenol. $Eu(fod)_3$ induced shifts for the C–1, C–2, and C–6 nuclei in 2-*t*-butylphenol are much smaller, while the corresponding signals of carbon in 3- and 4-*t*-butylphenol shift considerably. Furthermore, $Eu(fod)_3$ induced shifts were scarcely observed in 2,6-diisopropylphenol and 2.6-di-*t*-butylphenol. This implies that the formation of the phenol-$Eu(fod)_3$ adduct may be very sensitive to the steric factor, and that the geometry of the adduct may change when an *ortho*-position of the hydroxyl group is substituted by a bulky group.

TABLE III. $Eu(fod)_3$ and Et_3N Induced Shifts for Alkylphenols[a]

Substituent		C–1	C–2	C–3	C–4	C–5	C–6	$-CH_3$		$-\overset{\downarrow}{C}(CH_3)_3$	$-C(\overset{\downarrow}{C}H_3)_3$
2–CH_3	ΔE[b]	2.1	0.6	0.5	0.4	0.5	1.1	0.7			
	ΔN[c]	2.0	1.7	−0.2	−1.7	−0.5	0.3	0.6			
3–CH_3	ΔE	3.7	1.2	0.6	0.6	0.6	1.1	0.2			
	ΔN	2.3	0.8	−0.6	−1.8	−0.3	0.6	0.2			
4–CH_3	ΔE	3.4	1.1	0.6	0.6	0.6	1.1	0.2			
	ΔN	2.2	0.7	−0.2	−2.1	−0.2	0.7	0.0			
2,3-diCH_3	ΔE	2.3	0.7	0.5	0.4	0.5	1.2	(2)0.8	(3)0.2		
	ΔN	1.9	1.5	−0.4	−1.6	−0.5	0.3	0.3	0.1		
2,4-diCH_3	ΔE	2.4	0.7	0.5	0.5	0.6	1.2	(2)0.8	(4)0.2		
	ΔN	1.9	1.7	−0.1	−1.9	−0.5	0.3	0.6	0.1		
2,5-diCH_3	ΔE	2.7	0.7	0.6	0.5	0.6	1.4	(2)0.9	(5)0.1		
	ΔN	1.9	1.7	−0.2	−1.6	−0.9	0.4	0.6	0.1		
2,6-diCH_3	ΔE	1.1	0.6	0.3	0.2	0.3	0.6	(2)0.5	(6)0.5		
	ΔN	0.9	2.3	−0.2	−0.1	−0.2	2.3	0.6	0.6		
2-*t*-Bu	ΔE	0.5	0.2	0.1	0.2	0.1	0.3			0.2	0.1
	ΔN	2.2	0.7	−0.4	−1.9	−0.4	0.0			0.2	−0.1
3-*t*-Bu	ΔE	2.4	0.9	0.5	0.4	0.5	0.7			0.2	0.2
	ΔN	2.2	0.5	−0.6	−1.9	−0.3	0.6			0.0	0.2
4-*t*-Bu	ΔE	3.9	1.2	0.7	0.5	0.7	1.2			0.3	0.1
	ΔN	2.2	0.5	−0.3	−2.2	−0.3	0.5			−0.1	0.1
2,6-di-*t*-Bu	ΔE	0.1	0.1	0.0	0.0	0.0	0.1			0.0	0.0
	ΔN	0.1	0.1	0.0	0.1	0.0	0.1			0.1	0.0
										$-\overset{\downarrow}{C}H(CH_3)_2$	$-CH(\overset{\downarrow}{C}H_3)_2$
2,6-diisoPr	ΔE	0.5	0.3	0.2	0.2	0.2	0.3			0.2	0.1
	ΔN	0.5	1.7	−0.2	−0.1	−0.2	1.7			−0.1	0.2

See Table II for footnotes *a*) to *c*).

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[10] G.C. Levy and G.L. Nelson, "Carbon-13 Nuclear Maguetic Resonance for Organic Chemists", Wiley-Interscience, New York, 1972, p. 81.

In ^{1}H-NMR of *o*-xylenols, Shoffner[3] reported that ring protons and methyl protons situated in the 3-*meta* position undergo a greater induced shift than those in the 5-*meta* position, and that the result may be attributed to the difference in orientation of the protons with respect to the principal magnetic axis of the metal atom. However, on ^{13}C induced shifts of *o*-xylenols, there was no difference between 3- and 5-*meta* carbons whether they are aromatic or methyl. In addition, it is interesting that the magnitude of the shift of 6-*ortho* carbons was almost twice that of 2-*ortho* carbons. This shows that the mechanism responsible for the induced shift would be more complicated. It seems to be difficult to ascertain the relationship between each carbon atom in phenol molecules and the magnitude of the induced shift.

A methyl carbon *ortho* to a phenolic group was easily distinguished from methyl ones at the *meta*- and *para*-positions on comparison between the induced shifts of the former (ΔE 0.7) and of the latters(ΔE 0.1—0.2).

On the other hand, Et_3N induced relatively large shifts for the C–2 nucleus in 2-methyl phenols(ΔN 1.7—2.3). It seems plausible that the above shifts would be contributed by the hyperconjugation effect of an *ortho*-methyl group enhanced with Et_3N. A steric effect was observed in the Et_3N induced shifts of 2,6-dialkylphenols. The differential shifts for the C–1, C–2, and C–6 nuclei decreased orderly for the series; 2,6-dimethyl, diisopropyl, and di-*t*-butylphenol. The shifts for the C–4 nucleus were extremely small in 2,6-dialkylphenols.

Methoxy Phenols

The ^{13}C chemical shifts of 3-methoxy- and 4-methoxyphenol were mostly predictable on the basis of the chemical shifts of phenol and of additivity of substituent parameters on a methoxy group (C_s; +31.4, C_o; −14.4, C_m; +1.0, C_p; −7.7)[10] and a hydroxy group. For 2-methoxyphenol, comparison between the observed chemical shifts and the calculated ones did not give good agreement.

The induced shifts of 2-methoxyphenol were somewhat different from those of the other phenols examined here. The larger downfield shifts for the C–1, C–2, and methoxy carbon nuclei, and the upfield shift for the C–6 nucleus were observed. These can not be simply explained by means of the pseudo-contact term. The upfield shift for the C–6 nucleus seems to suggest the existence of contact interaction on the analogy of lanthanide-induced contact shifts observed in the ^{13}C-NMR spectra of amines,[11,12] alcohols,[13] and ketones.[14]

In methoxyphenols, Et_3N induced greatly a downfield shift for the C–1 nucleus and a upfield shift for the C–4 nucleus like phenol, although its induced shifts of 2-methoxyphenol were rather anomalous. In addition of Et_3N, methoxy-substituted carbon signals of methoxyphenols shifted to lower field than aromatic carbon signals in the corresponding position of phenol. This substituent effect would be explainable by the presumption that the increase of solvent polarity in the presence of Et_3N would enhance the electron donating effect of a methoxy group.

Experimental

Materials——The phenols and triethylamine were obtained from Tokyo Chemical Industry Co., Ltd., Tokyo. Eu(fod)$_3$ was purchased from Dojin Co., Ltd., Kumamoto.

Following deuterated compounds were prepared by heating in sealed tubes at 100° for 12 hr with sodium deuteroxide[15]; 2-methoxyphenol-4,6-d_2, 3-methoxyphenol-2,4,6-d_3, 4-methoxyphenol-2,6-d_2, 2-methyl-

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[11] R.J. Cushley, D.R. Anderson, and S.R. Lipsky, *J. Chem. Soc. Chem. Commun.*, **1972**, 636.

[12] M. Hirayama, E. Edagawa, and Y. Hanyu, *J. Chem. Soc. Chem. Commun.*, **1972**, 1343.

[13] G.E. Hawkes, D. Leibfritz, D.W. Roberts, and J.D. Roberts, *J. Am. Chem. Soc.*, **95**, 1659 (1973).

[14] D.J. Chadwick and D.H. Williams, *J. Chem. Soc. Chem. Commun.*, **1974**, 128.

[15] A.F. Thomas, "Deuterium Labeling in Organic Chemistry," Appleton-Century-Crofts, New York, 1971, p. 204.

phenol-4,6-d_2, 2,3-dimethylphenol-4,6-d_2, 2,4-dimethylphenol-6-*d*, 2,5-dimethylphenol-4,6-d_2, 2,6-dimethylphenol-4-*d*, 2-*t*-butylphenol-4,6-d_2, 3-*t*-butylphenol-2,4,6-d_3, 4-*t*-butylphenol-2,6-d_2. Deuterium content in the deuterated compounds was checked by ^{1}H–NMR.

^{13}C-NMR Measurements——^{13}C Spectra were recorded on a Varian XL-100-12 spectrometer at 25.16 MHz, equipped with a Varian 620/L computer using 8 k data points. Computer measured chemical shifts were corrected to ±0.05 ppm and narrow peaks as close as 0.1 ppm could be resolved.

Each sample (1 mmole) was dissolved into $CDCl_3$ (1 ml) in a 10 mm sample tube and then TMS (0.1 ml) was added as an internal standard. $Eu(fod)_3$ varying from 0.025 to 0.1 mmol, or Et_3N from 0.5 to 2 mmole were added to the solution.