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NUCLEAR MAGNETIC RESONANCE STUDIES. III. APPLICATION OF TRIS-(1,1,1,2,2,3,3-HEPTAFLUORO-7,7-DIMETHYL-4,6-OCTANEDIONATO)EUROPIUM AS A SHIFT REAGENT FOR PHENOLS[1]

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The application of β-diketone complexes of lanthanide ions as nmr shift reafents to many classes of organic compounds is a recent development of great potential and utility.[2] They were, however, considered to be inapplicable to phenols and carboxylic acids, since the pioneering work of Sanders and Williams[3] demonstrated that tris(dipivalomethanato)europium, $Eu(dpm)_3$, was decomposed by these two types of compounds. The recent interest in the use of tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)europium, $Eu(fod)_3$, as a shift reagent for 2,4-dimethyl-phenol[4] prompts us to report the results of our independent studies on alkyl- and nitrophenols.

Platzed and Demerseman have studied the effect of $Eu(dpm)_3$ on a number of weakly acidic phenols.[5] Under their conditions, however, we were unable to obtain any high resolution spectra, obviously due to the instability of $Eu(dpm)_3$ to phenols with pKa values even greater than 10. The more acidic $Eu(fod)_3$ should be less unstable and might be useful for phenols. Indeed, $Eu(fod)_3$ induced pmr spectra have been obtained for o-, m-, and p-cresol, 2,4-, 3,4-, and 3,5-dimethylphenol, phenol, thymol, and p-nitrophenol. No decomposition of the reagent has been detected. With a moderate concentration of $Eu(fod)_3$,

$Eu(fod)_3$/substrate molar ratio of 0.2 to 0.7, only the ortho proton resonance for p-nitrophenol showed significant broadening. The pertinent data are listed in Tables I and II.[7]

From Table I, it is clear that in addition to the metal-proton distance factor the induced shifts are influenced by both steric and electronic effects of substituents. Among the phenols under examination, the smallest shift was realized for the most acidic p-nitrophenol. The less acidic alkylated phenols displayed larger shifts than those of the unsubstituted one. For phenols of similar acidity, *e. g.*, 2,4-dimethylphenol vs. thymol,[8] steric hindrance at the coordination site reduced the induced shift appreciably.

A linear relationship has been observed between the induced shifts and the $Eu(fod)_3$/substrate molar ratios.[7] Extrapolation to zero concentration of $Eu(fod)_3$ gives the approximate chemical shift[9, 10] of protons of uncomplexed phenols. The excellent agreement between the extrapolated and observed values(Table II) makes it possible to estimate the chemical shift of an individual proton in a complex system with reasonable accuracy.

With the exception of o-cresol, spectral simplification can be achieved without loss of resolution provided sufficient $Eu(fod)_3$ has been added. Nonetheless, the Eu(fod)3 or $Eu(dpm)_3$ induced spectrum of the corresponding o-tolyl acetate is resolvable.[11] Consequently, although some macrocyclic germanium shift reagents have recently been found to be effective with phenols,[12] the readily available europium reagents are still the most convenient shift reagents for investigating phenols.

Table I. Normalized Lanthanide Induced Shifts for Phenols[a]

Substrate	o-CH$_3$	m-CH$_3$	p-CH$_3$	o-H	o'-H	m-H	m'-H	p-H
Phenol	-	-	-	6.59		1.71		1.24
m-Cresol	-	1.79	-	9.88	10.34	-	2.82	2.64
p-Cresol	-	-	1.14	8.72		2.26		-
			(0.66)^b	(5.02)		(1.39)		
2,4-Dimethylphenol	6.95	-	1.19	-	8.76	3.10	2.06	-
3,4-Dimethylphenol	-	1.85	1.60	11.39	10.97	-	3.21	-
3,5-Dimethylphenol	-	1.72	-	9.53		-		2.68
Thymol	2.31^c	0.46	-	-	6.44	2.43	-	1.90
p-Nitrophenol	-	-	-	(1.39)		(0.84)		-

[a] In ppm, measured in carbon tetrachloride solution unless otherwise mentioned.

[b] In deuteriochloroform(99%D) solution. [c] Methine proton of isopropyl group.

Table II. Proton Chemical Shifts for Uncomplexed Phenols[a]

Substrate	m-CH$_3$	p-CH$_3$	o-CH$_3$	o'-H	m-H	p-H
m-Cresol	2.24^b(2.27)^c	-	6.55(6.52)	(6.79)	(7.07)	(6.70)
p-Cresol	-	2.24(2.24)	6.58(6.51)		6.89(6.88)	-
3,4-Dimethylphenol	2.16(2.13)	2.16(2.18)	6.43(6.43)	6.50(6.53)	6.83(6.84)	-
3,5-Dimethylphenol	2.23(2.25)	-	6.31(6.41)		-	6.41(6.44)

[a] In ppm downfield from TMS. [b] Observed. [c] Extrapolated.

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(7) All chemical shifts were measured at 60 MHz on 0.2-0.3 M solutions of phenols with five or more different concentrations of Eu(fod)$_3$. The normalized induced shifts reported here were extrapolated from the least-squares fit with correlation coefficients greater than 0.99 in most cases, and represent hypothetical shifts at equal molar concentrations of phenols and Eu(fod)$_3$. The calculated chemical shifts of the uncomplexed substrates were also obtained by extrapolation.

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