Nuclear Magnetic Resonance Spectra of Adamantyl-substituted Phenols and Solvent-induced Shifts of Sterically Hindered Protons

By **Soon Ng**, Department of Chemistry, University of Malaya, Kuala Lumpur, Malaysia

The n.m.r. spectra of 2,6-di-1-adamantyl-4-alkylphenols (alkyl = Me, Et, Pr^i, Bu^t, or 1-adamantyl) have been recorded for dilute solutions in [^{2}H]chloroform, carbon disulphide, carbon tetrachloride, hexane, and [^{2}H$_6$]benzene. The internally referenced chemical shifts of the ring and phenolic protons are presented. The resonance of the sterically hindered 3- and 5-protons is shifted, relative to solutions in carbon tetrachloride or hexane, downfield in [^{2}H$_6$]benzene and in [^{2}H]chloroform, and upfield in carbon disulphide. These internally referenced solvent shifts become larger as steric hindrance of the protons increases, except in the case of solutions in [^{2}H]chloroform, for which the shift, relative to hexane solution, becomes smaller as the steric hindrance of the protons increases. Comparison with data for the corresponding 2,6-di-t-butylphenols reveals that the adamantyl group causes shielding of neighbouring protons. The chemical shifts of the sterically hindered phenolic protons of 2,4,6-tri-t-butylphenol and 2,6-di-1-adamantyl-4-t-butylphenol have been obtained for solutions in carbon tetrachloride–benzene over the whole range of mixture concentrations. The factors causing solvent shifts for the sterically hindered protons in these substituted phenols are discussed.

1-ADAMANTYL-SUBSTITUTED PHENOLS have been synthesized by Ong.[1] Following the same procedure we have synthesized a series of 2,6-di-1-adamantyl-4-alkylphenols (alkyl = Me, Et, Pr^i, Bu^t, or 1-adamantyl), and have studied the steric and magnetic shielding effects of the adamantyl group on the ring and phenolic proton magnetic resonances. The n.m.r. spectra of the adamantyl-substituted phenols have been recorded for dilute solutions in [^{2}H]chloroform, carbon disulphide, carbon tetrachloride, and [^{2}H$_6$]benzene. To compare the solvent effects of adamantyl-substitution with alkyl-substitution in phenols, the internally referenced chemical shifts of the 3-, 5-, and phenolic protons of 2,6-di-t-butyl-4-alkylphenols and 2,4,6-trimethylphenol in the same solvents were also obtained. Similar data for the 2,6-disubstituted phenols with Me, Bu^t, and Ad (adamantyl) groups in position 4 were also obtained for dilute solutions in n-hexane.

The factors causing solvent shifts for 'surface' protons are now well understood in terms of several physical effects of solute–solvent interactions, *viz.* σ_A (anisotropic effect), σ_W (van der Waals effect), and σ_E (reaction field effect), as well as chemical association effects.[2] For sterically hindered protons the physical effects would be less than or different from those for 'surface' protons. So if an internal reference such as tetramethylsilane is used, a sterically hindered proton would be expected to show an apparent shift, reflecting the shift of the reference protons in the opposite direction.[3] The sterically hindered protons of the substituted phenols mentioned show substantial internally referenced solvent-induced shifts, the magnitude of which increases with the degree of steric hindrance, except in the case of solutions in chloroform, for which the shift, relative to n-hexane solution, becomes smaller as the steric hindrance of the protons increases. The data are discussed in terms of the various factors causing solvent shifts, the effect of alkyl-substitution at the *para*-position, the magnetic deshielding of protons due to intramolecular steric interactions with proximate hydrogen atoms, and the magnetic anisotropic effect of the adamantyl group on neighbouring protons.

EXPERIMENTAL

The adamantyl-substituted phenols were prepared by heating under nitrogen at *ca.* 85 °C for 25 h, a mixture of the appropriate 4-alkylphenol, 1-bromoadamantane, and sodium (molar ratio 1 : 2 : 1) in *p*-xylene and *NN*-dimethylformamide.[1] 1-Bromoadamantane and the alkyl-substituted phenols were obtained from commercial sources and were recrystallized before use. The m.p.s of the 2,6-di-1-adamantyl-4-alkylphenols are: 4-methyl 261—263°, 4-ethyl 276°, 4-isopropyl 204—206°, 4-t-butyl 225—226°, 4-(1-adamantyl) >360°. The 4-isopropyl and 4-(1-adamantyl) compounds are described in ref. 1. Analyses are now reported for the *4-methyl* (Found: C, 86·05; H, 9·8. $C_{27}H_{36}O$ requires C, 86·1; H, 9·65%), the *4-ethyl* (Found: C, 86·25; H, 9·75. $C_{28}H_{38}O$ requires C, 86·1; H, 9·8%), and *4-t-butyl* (Found: C, 86·35; H, 10·35. $C_{30}H_{42}O$ requires C, 86·05; H, 10·1%) derivatives.

4-Ethyl-2,6-di-t-butylphenol and 4-isopropyl-2,6-di-t-butylphenol were prepared by treating 2,6-di-t-butylphenol with ethyl bromide and isopropyl bromide respectively in potassium t-butoxide.[4] The products were purified by g.l.c.

The n.m.r. spectra were recorded on a 60 MHz Hitachi–Perkin-Elmer R-20B high-resolution spectrometer, with the permanent magnet thermostatically maintained at 34 °C. The chemical shifts were measured with a Takeda Riken 3824X frequency counter to an accuracy of ±0·01 p.p.m. for the data reported in p.p.m. and to an accuracy of ±0·20 Hz for the data reported in Hz. Tetramethylsilane was used as internal reference. Spectroscopic grade solvents were used. [^{2}H]Chloroform and [^{2}H$_6$]benzene were obtained from Merck (Darmstadt).

RESULTS AND DISCUSSION

The 60 MHz spectrum of the adamantyl (Ad) protons of the 2,6-di-1-adamantyl-4-alkylphenols consists of two broad bands, one centred at δ 1·80 (12H) and the other centred at δ 2·10 ± 0·05 p.p.m. (18H) in the non-aromatic solvents ($CDCl_3$, CCl_4, and CS_2). In the

---

[1] S. H. Ong, *Chem. Comm.*, 1970, 1180.

[2] A. D. Buckingham, T. Schaefer, and W. G. Schneider, *J. Chem. Phys.*, 1960, **32**, 1227.

[3] D. H. Williams, J. Ronayne, and R. G. Wilson, *Chem. Comm.*, 1967, 1089.

[4] N. Kornblum and R. Seltzer, *J. Amer. Chem. Soc.*, 1961, **83**, 3668.

aromatic solvent (C_6D_6) the Ad protons give rise to three broad bands: a band with unresolved fine structure centred at δ 1·73 and a band centred at δ 2·03 overlapping with a band whose centre varies in position from δ 2·14 to 2·22 p.p.m. as the 4-alkyl group varies from Me to Bu^t. The band at δ 1·73 may be assigned to the six methylene δ-protons, the band at δ 2·03 to the three bridgehead γ-protons, and the third band to the six methylene β-protons. The 60 MHz spectrum of the Ad protons of 2,4,6-tri-1-adamantylphenol varies from two broad bands (in CS_2) to three broad bands with unresolved fine structure (in C_6D_6).

As already mentioned, the resonance of the methylene β-protons of the Ad groups is affected by the nature of the 4-alkyl group in C_6D_6 solution. Although hindered, the phenolic H is capable of interacting with the π-electron system of the benzene molecule (see later). In the weak H-bonded complex the methylene β-protons are near the periphery of the benzene ring, and, as a result of the ring current effect, experience slight deshielding, as observed. The 4-Me group lowers the acidity of the OH group more than does the 4-Bu^t group, so that the strength and extent of the OH ··· π interaction and therefore the deshielding effect on the methylene β-protons is greatest with the 4-Bu^t or the 4-Ad group, as observed. The effect of the 4-alkyl group on the δ value of the phenolic H is discussed later.

When used as a solvent, CS_2 (rod-shaped molecule) is expected to produce upfield shifts, whereas benzene (disc-shaped molecule) is expected to produce downfield shifts, relative to internal tetramethylsilane, for sterically hindered protons as a result of the solvent anisotropy effect (σ_A).[3] These predicted shifts are in directions opposite to those expected for internally referenced solvent-induced shifts for ' surface ' protons, and are realized in the results (Tables 1—3) for the sterically hindered 3- and 5-protons of the trisubstituted phenols. Tables 1 and 2 also list the internally referenced relative shifts in pairs of solvents. Carbon tetrachloride and n-hexane are expected to have a negligible σ_A effect.[2] The largest relative shift is observed for 2,4,6-tri-1-adamantylphenol (0·32 p.p.m. in the solvent pair, C_6D_6,n-C_6H_{14}, and 0·42 p.p.m. in the pair, C_6D_6,CCl_4). The externally referenced solvent shift for tetramethylsilane in the solvent pair, C_6H_6,CCl_4, is reported to be 0·52 p.p.m.;[5] this value may represent the largest solvent shift that could be observed for a sterically hindered proton in this solvent pair.

The solvent shifts in CS_2, C_6D_6, and CCl_4 are larger in the Ad-substituted series than in the Bu^t-substituted series, and in each series the solvent shifts become larger as the group in position 4 becomes bulkier. These results indicate that the Ad group more effectively inhibits the access of the solvent molecules to the 3- and 5-protons than does the Bu^t group. In the case of the more exposed 3- and 5-protons of 2,4,6-trimethylphenol, the $C_6D_6 - CCl_4$ shift is very small, but the $CS_2 - CCl_4$ and $CDCl_3 - CCl_4$ shifts are only slightly smaller than for the more hindered protons. The large relative $C_6D_6 - CCl_4$ shift for protons in sterically crowded sites could have important diagnostic applications in molecular structure determination.

For ' surface ' protons the van der Waals effect, σ_W, produces a low-field shift.[2] So for sterically hindered protons this effect would produce an apparent internally referenced upfield shift, with magnitudes in the order $CCl_4 > CDCl_3 >$ n-hexane solution.[3] Since CCl_4 and n-hexane have a negligible σ_A effect and possibly a small σ_E effect, the relative shift in these two solvents may give an estimate of the σ_W effect. The last columns in Tables 1 and 2 show that the $CCl_4 -$ n-C_6H_{14} relative shift amounts to 0·07 p.p.m. when the 4-alkyl group is Me, increasing to 0·10 p.p.m. with the Bu^t and Ad groups, but is negligible for the relatively more exposed 3- and 5-protons of trimethylphenol.

It is apparent that the $C_6D_6 - CCl_4$ solvent shift includes the ' downfield shift ' of the σ_A term of benzene and the ' upfield shift ' of the σ_W term of carbon tetrachloride. As n-hexane has a relatively small σ_W term, the $C_6D_6 -$ n-C_6H_{14} solvent shift gives a good estimate of the σ_A effect of benzene, as shown in the second last columns of Tables 1 and 2.

The solvent $CDCl_3$ produces downfield shifts of the 3- and 5-protons, relative to n-hexane solution, which becomes smaller as the group at position 4 increases in bulkiness (Tables 1 and 2). As chloroform has a relatively large dielectric constant (4·59 *vs.* 1·87 for n-hexane, 34 °C), the relative shifts may be attributed to the polar effect, σ_E. This solvent reaction field effect on the non-polar reference would be negligible and is expected to be reduced for less accessible protons of polar solutes. Hence the σ_E effect would be expected to give rise to actual shifts of the solute protons, and the shift would decrease as steric crowding of the protons increased, as observed.

As shown in Table 3 (also in Tables 1 and 2) the resonance of the 3- and 5-protons shifts to lower field over a range of *ca.* 0·20 p.p.m. as the 4-alkyl group increases in bulkiness in the two series of substituted phenols. This deshielding is due to intramolecular steric interactions with the proximate hydrogen atoms of the bulky substituent groups.[6] The mechanism of steric deshielding is believed to involve a van der Waals repulsion and a decrease in electron density at the deshielded site. Steric deshielding would also account for the larger δ values of the phenolic H in the Ad-substituted phenols than in the corresponding Bu^t-substituted phenols in each solvent (Table 4).

The 3- and 5-protons resonate at higher fields (0·02—0·08 p.p.m.) in the Ad-substituted than in the Bu^t-substituted series for the same 4-alkyl group in each of the solvents. This difference cannot be due to a greater ' high-field shift ' σ_W effect caused by Ad being a more effective shielding group than Bu^t, since differences of

---

[5] J. K. Becconsall, G. D. Daves, jun., and W. R. Anderson, jun., *J. Amer. Chem. Soc.*, 1970, **92**, 430.

[6] B. V. Cheney, *J. Amer. Chem. Soc.*, 1968, **90**, 5386; C. G. Cardenas, *J. Org. Chem.*, 1971, **36**, 1631.

TABLE 1

Chemical shifts * of the 3- and 5-protons of 2,6-di-1-adamantyl-4-alkyl phenols in various solvents † (0·080M-solutions at 34 °C)

	δ (p.p.m. ± 0·01)									
Alkyl	CDCl$_3$	CCl$_4$	CS$_2$	C$_6$D$_6$	Δ_B^A (p.p.m.)	Δ_C^A (p.p.m.)	Δ_B^D (p.p.m.)	Δ_E^D (p.p.m.)	Δ_C^D (p.p.m.)	Δ_A^D (p.p.m.)
Me	6·93	6·75	6·68	7·00	−0·07	+0·25	−0·14	+0·11	+0·18	−0·07
Et	6·94	6·78	6·71	7·08	−0·07	+0·30				
Pr^i	6·98	6·81	6·74	7·14	−0·07	+0·33				
Bu^t	7·15	6·98	6·90	7·35	−0·08	+0·37	−0·18	+0·07	+0·27	−0·10
Ad	7·12	6·95	6·86	7·37	−0·09	+0·42	−0·19	+0·07	+0·32	−0·10

* $\Delta_Y^X = \delta(Y) - \delta(X)$. † A, CCl$_4$; B, CS$_2$; C, C$_6D_6$; D, n-C$_6H_{14}$; E, CDCl$_3$.

TABLE 2

Chemical shifts * of the 3- and 5-protons of 2,6-di-t-butyl-4-alkylphenols and 2,4,6-trimethylphenol in various solvents † (0·080M-solutions at 34 °C)

	δ (p.p.m. ± 0·01)									
Alkyl	CDCl$_3$	CCl$_4$	CS$_2$	C$_6$D$_6$	Δ_B^A (p.p.m.)	Δ_C^A (p.p.m.)	Δ_B^D (p.p.m.)	Δ_E^D (p.p.m.)	Δ_C^D (p.p.m.)	Δ_A^D (p.p.m.)
Me	6·97	6·81	6·76	7·05	−0·05	+0·24	−0·12	+0·09	+0·17	−0·07
Et	6·98	6·84	6·78	7·11	−0·06	+0·27				
Pr^i	7·03	6·87	6·81	7·16	−0·06	+0·29				
Bu^t	7·20	7·05	6·97	7·37	−0·08	+0·32	−0·18	+0·05	+0·22	−0·10
Trimethyl–phenol	6·77	6·64	6·59	6·67	−0·05	+0·03	−0·06	+0·12	+0·02	−0·01

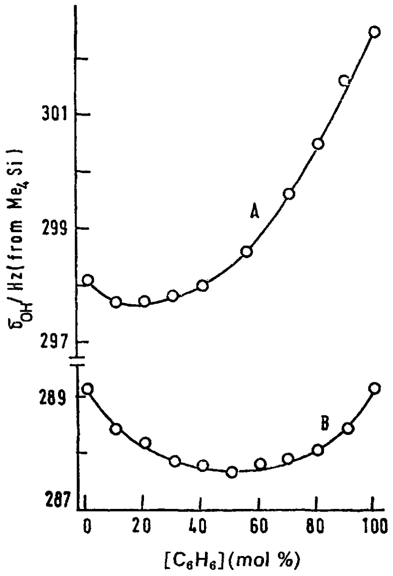
*† As Table 1.

the same magnitude are found for solutions in carbon tetrachloride and n-hexane. Further, there is an upfield shift of 0·03 p.p.m. in all the non-aromatic solvents as the group in position 4 changes from Bu^t to Ad, reversing the trend in δ values observed for the variation from Me to Bu^t in the Ad-substituted series. This is unexpected, since with the Ad group steric deshielding should be larger and more than compensate for any σ_W effect. These data therefore suggest a magnetic anisotropic effect of the Ad group on neighbouring protons. The observed shielding of the 3- and 5-protons by the Ad groups is not large; the effect is

TABLE 3

Chemical shifts of the 3-, 5-, and phenolic protons of some substituted phenols in n-hexane solution (0·04M at 34 °C)

Phenol	δ (p.p.m. ± 0·01) 3,5-H	δ (p.p.m. ± 0·01) Phenolic H
2,4,6-Me$_3$	6·65	4·02
2,6-Bu$^t_2$-4-Me	6·88	4·74
2,4,6-Bu$^t_3$	7·15	4·78
2,6-Ad$_2$-4-Me	6·82	4·90
2,6-Ad$_2$-4-Bu^t	7·08	4·95
2,4,6-Ad$_3$	7·05	4·95



Variation of the chemical shift of the phenolic H with concentration of benzene in carbon tetrachloride–benzene: A, 2,6-di-1-adamantyl-4-t-butylphenol; B, 2,4,6-tri-t-butylphenol (concentration of solute constant at 1 mol %)

TABLE 4

Chemical shifts of the phenolic protons of 2,6-di-t-butyl-4-alkylphenols (I), 2,6-di-1-adamantyl-4-alkylphenols (II), and 2,4,6-trimethylphenol in various solvents (0·080M-solutions at 34 °C)

	δ (p.p.m. ± 0·01)							
	CDCl$_3$		CCl$_4$		CS$_2$		C$_6$D$_6$	
Alkyl	(I)	(II)	(I)	(II)	(I)	(II)	(I)	(II)
Me	4·98	5·15	4·78	4·92	4·70	4·86	4·77	5·00
Et	4·99	5·16	4·80	4·95	4·72	4·88	4·78	5·02
Pr^i	5·00	5·16	4·81	4·96	4·73	4·88	4·80	5·02
Bu^t	5·00	5·18	4·83	4·96	4·74	4·89	4·82	5·03
Ad		5·18		4·97		4·89		5·05
Trimethylphenol	4·40		4·18		4·11		3·93	

presumably obscured by the larger steric deshielding and, in the case of benzene solution, by the greater σ_A effect that would be produced by the Ad groups, *vis-à-vis* the Bu^t groups.

The solvent shifts of the sterically hindered phenolic protons (Table 4) in the non-aromatic solvents are as expected, but in the aromatic solvent (C_6D_6) the δ values are identical with or slightly larger (0·06—0·08 p.p.m.) than those in carbon tetrachloride. The data for solutions in benzene reflect the OH · · · π solute–solvent association. The Figure shows that as benzene is added to a dilute solution of 2,4,6-tri-t-butylphenol in carbon tetrachloride, the resonance of the phenolic H initially shifts to low frequency (high field) as a result of the OH · · · π interaction, reaches a minimum, and then shifts to higher frequency as the ' down-field shift ' of the σ_A effect predominates when benzene becomes the major component in the solution. In neat carbon tetrachloride and [$^2H_6$]benzene the δ values happen to be identical in the Bu^t-substituted series (Table 4 and Figure). In the case of 2,6-di-1-adamantyl-4-t-butylphenol the OH is relatively more hindered, so that the OH · · · π interaction is less but the σ_A effect greater than in the case of 2,4,6-tri-t-butylphenol (top curve in Figure).

The resonance of the phenolic proton in either series is shifted slightly to low field (0·02—0·05 p.p.m.; Tables 3 and 4) as the group at position 4 varies from Me to Bu^t and Ad. As self-association is expected to be negligible, the data for the inert solvent n-hexane (Table 3) no doubt reflect the relationship between the acidity of the OH group, as affected by the 4-alkyl group, and its δ value, the more acidic OH group having the larger δ value. Judging from the data in Tables 3 and 4, the electron-releasing ability of the 4-Ad group is equivalent to that of the 4-Bu^t group.

I thank Dr. S. H. Ong for discussions and Mr. T. C. Chua for assistance in the synthesis of the adamantyl-substituted phenols.

[2/504 *Received*, 6*th March*, 1972]