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AROMATIC SOLVENT-INDUCED SHIFTS (ASIS) IN CARBON-13 NMR SPECTROSCOPY

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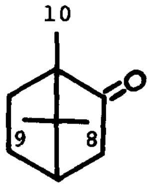
Abstract: A new method is proposed for the estimation of aromatic solvent-induced shifts(ASIS) in carbon-13 NMR spectroscopy. The observed C-13 ASIS are shown to be useful for studing the structure elucidation.

Aromatic solvent-induced shifts(ASIS) in ^{1}H NMR spectroscopy have proven to be a powerful tool in the elucidation of structural, stereochemical, and conformational problems.$^{1)}$ In particular, the ASIS observed for carbonyl compounds have been well investigated, because they can be explained in terms of an empirical rule, the so-called "carbonyl reference plane rule"$^{2)}$. However, the utility of the ASIS in ^{13}C NMR spectroscopy remains unknown. Since ^{13}C chemical shifts occur over a far greater range than ^{1}H chemical shifts, contributions due to solvent anisotropies become ralatively insignificant in ^{13}C NMR. For a specific solvent-solute interaction, however, the effects of solvent anisotropies on ^{13}C chemical shifts may not be neglected.$^{3)}$ We now report a new method for the estimation of the ^{13}C ASIS. Furthermore, a successful application of the observed ^{13}C ASIS to a structure elucidation is presented.

The ^{13}C chemical shifts of the methyl carbons of camphor 1 and pulegone 2 were measured in nonpolar solvents containing benzene-d_6 and hexafluorobenzene (Table 1). In ^{1}H NMR, the ASIS can be defined by the solvent shifts [$\Delta\delta$ = δ(aromatic solvent) – δ(CCl_4 or $CDCl_3$)]. However, for the observed ^{13}C chemical shifts, this solvent shift method does not serve reliable results for ^{13}C ASIS, probably because the anisotropy effects of C_6D_6 and C_6F_6 solvents are not major contribution of the ^{13}C solvent shifts; for example, all the methyl carbon shifts of 1 and 2 induced by C_6F_6 relative to CCl_4 (the ASIS in C_6F_6) always result in large downfield shifts(see Table 1), regardless of the spatial relationship of the given methyl carbons with respect to the carbonyl group (carbonyl dipole).



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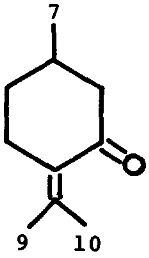

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We propose a chemical shift comparison method for the estimation of the ^{13}C ASIS. In order to detect the ^{13}C ASIS masked by other factors (such as van der Waals interactions), the observed ^{13}C chemical shifts of the methyl carbons of **1** and **2** are plotted against those of the α carbon of *tert*-butylcyclohexane(see Fig. 1 and note (4)), which were selected for the reference chemical shifts, in the corresponding solvents. In these plots, factors other than the anisotropy effects of C_6D_6 and C_6F_6 should cancel each other, and the solvent sensitivity is related to the slopes of these plots. Indeed, as shown in Fig. 1, the excellent linear correlations are obtained, except for the aromatic solvents. The significant deviations observed for C_6D_6 and C_6F_6, therefore, can be attributed to the ^{13}C ASIS. Thus, the nature of the ^{13}C ASIS is characterized by the direction and magnitude of the deviations from the plots(see Fig. 1).

In order to ascertain the validity of the obtained ^{13}C ASIS, the nature of these ASIS is compared with that of the corresponding ^1H ASIS, because the ASIS are expected to produce the same magnitude of contribution both on ^1H and ^{13}C nuclei, if these two atoms have the same geometrical relationship with respect to the solvated aromatic solvent molecules around the carbonyl dipole. The camphor molecule **1** with a rigid skeleton is adequate for this purpose.[5)] As can be seen from the ^{13}C ASIS obtained for **1**(see Fig. 1), the ^{13}C ASIS for the 8- and 9-methyl carbons show an opposite direction to that for the 10-methyl carbon. These significant variations of the ^{13}C ASIS upon the geometrical relationship of three methyl carbons with respect to the carbonyl group (dipole) are in good agreement with those of the established ^1H ASIS[5)] [Δδ(ppm): -0.21(8Me), -0.29(9Me), and +0.07(10Me) in C_6D_6, and +0.07(8Me), +0.16(9Me), and -0.06(10Me) in C_6F_6]. Additionally, the direction of the ^{13}C ASIS with C_6D_6 is found to be opposite to

Table 1. ^{13}C chemical shifts[a)] of the methyl carbons of camphor and pulegone, and of the C_α of *t*-butylcyclohexane in nonpolar and aromatic solvents

Solvent	(1) Hexane	(2) Heptane	(3) CD_2Cl_2	(4) $ClCH_2CH_2Cl$	(5) $CDCl_3$	(6) CCl_4	(7) C_6D_6	(8) C_6F_6
Camphor b)								
8 Me	19.95	19.96	19.90	19.81	19.79	19.68	19.66	20.57
9 Me	19.39	19.41	19.25	19.20	19.18	19.14	19.05	19.97
10 Me	9.49	9.48	9.39	9.39	9.25	9.23	9.53	9.81
Pulegone c)								
7 Me	22.13	22.12	21.90	22.01	21.77	21.74	21.78	22.63
9 Me	22.13	22.12	22.09	21.89	22.09	21.89	21.78	22.34
10 Me	23.00	23.00	22.98	22.93	22.99	22.80	23.04	23.07
t-butylcyclohexane								
C-α	49.29	49.21	48.84	48.73	48.50	48.30	48.68	50.87

a) ^{13}C chemical shifts are given in δ ppm from internal TMS; the spectra were measured with an ANELVA NV-21 spectrometer operating at 22.6 MHz; probe temperature ca. 30°; spectral width 5.5 KHz; pulse width 10 μsec (flipping angle ca. 15°); acquisition time 0.727 sec; data points 8K; reproducibility < 0.07 ppm; [solute] ca. 15 mol%. For the solvents, (1), (2), (4), (6), and (8), a deuteron signal of D_2O sealed in a capillary inserted into 8 mm o.d. tube was employed for the lock signal. b) For assignments in $CDCl_3$, see E. Lippmaa *et al.*, *Org. Mag. Res.*, 2, 581 (1970). c) For assignments in $CDCl_3$, see Ref (8).

that with C_6F_6. This feature is also similar to that noted recently in ^1H ASIS studies.[5c,6] From these results, the ^{13}C ASIS obtained from the new method are found to be applicable to problems in organic chemistry,[7] as with ^1H ASIS.

In pulegone, the assignment of the 9- and 10-methyl carbon resonances is difficult because of the small difference in the shifts, although the 7-methyl carbon was differentiated from the other two methyl carbons by the aid of the selective proton decoupling.[8] The upfield resonance was tentatively assigned to the 10-carbon by Jautelat *et al.*,[8] assuming the upfield shift arising from the steric interaction between the 10-carbon and the carbonyl group. On the other hand, the ^{13}C ASIS method allows a straightforward assignment of the 9- and 10-methyl carbons. As anticipated from the carbonyl reference rule, the direction of

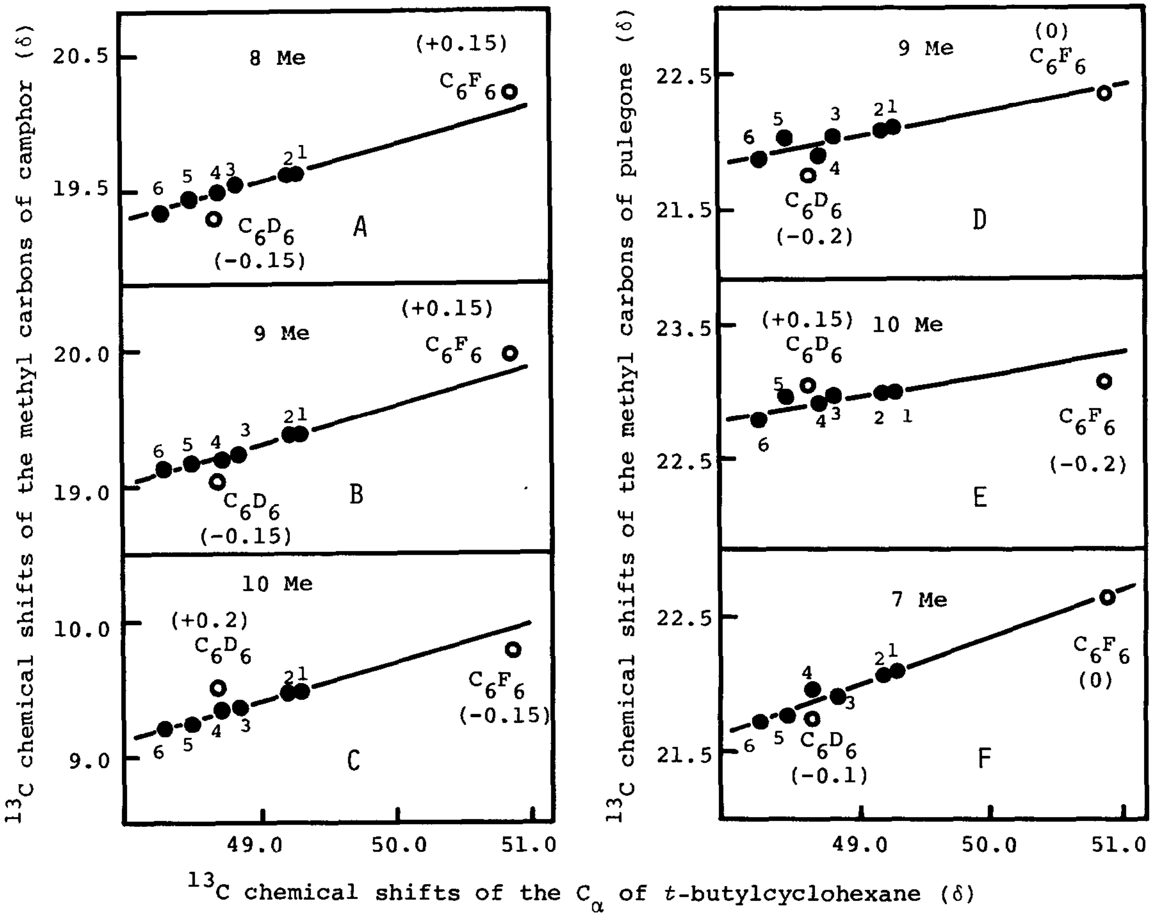

Figure 1. ^{13}C chemical shifts of the methyl carbons of camphor(A-C) and pulegone (D-F) plotted against ^{13}C chemical shifts of the C_α of *t*-butylcyclohexane in the corresponding solvents. Numbers refer to the solvents as designated in Table 1. The values(ppm) in parentheses indicate the magnitude of deviation. The plus and minus signs mean the downfield and upfield deviations, respectively.

the ^{13}C ASIS for the 9-carbon should be opposed to that for the 10-carbon; thus the 9-carbon lying behind the reference plane is expected to produce the upfield shift in C_6D_6 and the downfield shift in C_6F_6, whereas the 10-carbon lying in front of it is expected to show the reverse ^{13}C ASIS. On the basis of the ^{13}C ASIS obtained from Fig. 1(D and E), the upfield resonance can be unequivocally assigned to the 9-methyl carbon. This assignment is in contradiction with that anticipated from the steric interaction. Furthermore, the assignment of the 7-methyl carbon is also supported by the observed ^{13}C ASIS(see Fig. 1(F)).

Finally, for the estimation of the ^{13}C ASIS induced by "C_6D_6", we recommend the use of the solvent shift method with $ClCH_2CH_2Cl$ (rather than CCl_4 or $CDCl_3$) as a reference solvent, because this solvent shift, Δ, corresponds to the direction and magnitude of the deviation observed for C_6D_6 in Fig. 1.$^{9)}$

$$^{13}\mathrm{C\ ASIS\ }(C_6D_6)\quad \Delta = \delta(C_6D_6) - \delta(ClCH_2CH_2Cl)$$

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4) The C-13 chemical shift of the C_α of *t*-butylcyclohexane is logical selection for the reference shift, because (a) *t*-butylcyclohexane does not contain polar groups and has a relatively rigid skeleton, (b) the C_α shift is very sensitive to the change of solvents, and (c) the C_α shift seems to be hardly affected by a specific solvent-solute interaction, as anticipated from the geometrical position(sterically crowded site) in the molecule.
5) The ^{1}H NMR spectrum of camphor is most frequently refered to discuss the nature of the ^{1}H ASIS. (a) J. D. Connolly and R. McCrindel, *J. Chem. Soc. (c)*, 1613 (1966); (b) E. M. Engler and P. Laszlo, *J. Am. Chem. Soc.*, 93, 1317 (1971); (c) K. Nikki and N. Nakagawa, *Chem. Lett.*, 699 (1974).
6) (a) R. D. Bertrand, R. D. Compton, and J. D. Verkade, *J. Am. Chem. Soc.*, 92, 2702 (1970); (b) K. Nikki, N. Nakahata, and N. Nakagawa, *Tetrahedron Lett.*, 3811 (1975); (c) I. Horibe, H. Shigemoto, and K. Tori, *Tetrahedron Lett.*, 2849 (1975); (d) K. Nikki and N. Nakagawa, *Bull. Chem. Soc. Jpn.*, 51, 3267 (1978); (e) S. Ueji, *Bull. Chem. Soc. Jpn.*, 51, 1799(1978).
7) The magnitude of the C-13 ASIS differs slightly from that of the H-1 ASIS . This fact is presumably attributable to the difference in the method for the estimation of the ASIS and to the small difference in geometrical factors between the ^{1}H and ^{13}C nuclei in the given methyl group with respect to the solvated aromatic solvent molecule around the carbonyl dipole.
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9) The details of these results will be published elsewhere.

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