Tetrahedron Letters,Vol.25,No.45,pp 5209-5210,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

LONG-RANGE DEUTERIUM ISOTOPE EFFECTS ON FLUORINE-19 CHEMICAL SHIFTS OF 4-SUBSTITUTED BICYCLO[2.2.2]OCTYL- AND BICYCLO[2.2.1]HEPTYL-1-FLUORIDES : DEUTERIUM AS A SUBSTITUENT

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Summary: $^2H/^1H$ isotope effects on the ^{19}F chemical shifts of 4-substituted bicyclo[2.2.2]oct-1-yl and bicyclo[2.2.1]hept-1-yl fluoride are significantly shielding and deshielding, respectively. This result is consistent with deuterium being viewed as an electronegative substituent relative to hydrogen when attached to an sp^3 hybridised carbon.

In recent papers[1,2] we have shown that the ^{19}F substituent chemical shifts (SCS; σ-electron density monitors) of 4-substituted bicyclo[2.2.2]oct-1-yl fluorides (1) and the corresponding bicyclo[2.2.1]hept-1-yl fluorides (2) are strongly regulated by the electronegativity influence of the substituent. The origin of this unusual long-range substituent factor, which effects opposing contributions to the ^{19}F SCS of 1 and 2, has been ascribed to "through-bond" and "through-space" σ-electron delocalization phenomena. More recently[3], our investigations have revealed that the "through-three-bond" or σ-resonance effects of MMe_3 substituents (M=C, Si, Ge, Sn, and Pb) in 1 parallel the order of hyperconjugative electron release of CH_2MMe_3 groups attached to aromatic systems. Thus, in view of several recent studies[4] which have established that long-range deuterium isotope effects in benzylic systems (neutral and charged) arise from isotopic perturbation of hyperconjugation (σ-π) and are transmitted via the π-system, we decided to examine the effect of deuterium as a substituent in 1 and 2 for two main reasons. Firstly, the propagation of intrinsic secondary isotope effects through more than three bonds in aliphatic systems are, in general, essentially zero.[5] Thus, the observation of significant isotope effects in 1 and 2 would be strong corroborative evidence for the transmission of substituent electronegativity effects by σ-electron delocalization mechanisms in these saturated systems. Secondly, model systems 1 and 2, being rigid substrates which provide ^{19}F SCS unencumbered by steric and conformational effects, offer a unique opportunity to unequivocally ascertain the electronegativity of deuterium attached to a sp^3 hybridised carbon in the neutral ground state. This is important in connection with the rationalization of long-range intrinsic isotope effects within the framework of the organic chemists' conventional substituent effect model (Halevi approach)[6]. On the basis of their vibrational origins, the complexities of predicting these effects presents a daunting problem[7].

The deuterium derivatives (X=D) of 1, 2, and 1-substituted (X)-4-(p-fluorophenyl)bicyclo[2.2.2]octane (3) were prepared by a standard procedure (R_3SnD/AIBN)[8,9] from the corresponding bromo compounds[1,2,10]. The latter compound (3,X=D) was required in order to define precisely the electrostatic field influence of the deuterium substituent (σ_F effect). It is known that the ^{19}F SCS of 3 provide an excellent measure of σ_F parameters (ρ_F(c-C_6H_{12}) = 2.70)[1,10]. The ^{19}F SCS (ppm)[11] of 1, 2, and 3 (X=D) in c-C_6H_{12} are -0.060, 0.055, and -0.003, respectively.

The latter SCS leads to a σ_F value for deuterium of -0.001, a result which is in remarkably good agreement with a value (-0.0011)[12] previously determined by Tafts' fluorophenyl tag methodology. Thus, within experimental error (± 0.002 ppm), the polar field due to C-D relative to C-H is effectively *zero*. Clearly, the large *upfield* (or shielding) and *downfield* (or deshielding) $^2H/^1H$ isotope shifts observed for 1 and 2 (vide supra), respectively, which are the largest isotope shifts over five and four bonds ever observed in neutral systems and which are invariant to solvent (c-C_6H_{12}, $CDCl_3$, or DMF), can be ascribed exclusively to σ-electron delocalization phenomena (vide supra).

Most importantly, the pattern of the $^2H/^1H$ isotope shifts in 1 and 2 (*negative* and *positive* , respectively) is identical to that induced in these systems by electronegative substituents. Hence, deuterium is behaving inductively as an electron withdrawing substituent relative to hydrogen. Although this conclusion is not in accord with several other observations[6,7,13], it parallels the decreased hyperconjugative electron donation of the benzylic C-D bond relative to the C-H bond[4]. Furthermore, it is in accord with a previous conclusion[14] based on the observation that inductively induced *vicinal* ^{19}F SCS of deuterium and electronegative groups in saturated fluorides have the same sign (negative) and angular dependence (maximized in the antiperiplanar arrangement). We believe that the observed upfield $^2H/^1H$ isotope shifts on ^{19}F shielding in 1 and vicinal systems (H(D)-C-C-F) suggests a common origin for both perturbations, namely, charge transfer out of σ_{CF}* by σ-electron delocalization[1,2] on replacing H with the more electronegative D atom i.e. perturbation of σ_{CF}^*-σ_{CC}-σ_{CH} and σ_{CF}^*-σ_{CH} hyperconjugation in the former and latter systems, respectively.

References and Notes

1. W. Adcock and A.N. Abeywickrema, *Tetrahedron Lett.* 1981, 22, 1135; W. Adcock and A.N. Abeywickrema, *J.Org.Chem.*, 1982, 47, 2957.
2. W. Adcock, A.N. Abeywickrema and G.B. Kok, *Tetrahedron Lett.* 1982, 23, 3615; W. Adcock, A.N. Abeywickrema, and G.B. Kok, *J.Org.Chem.*, 1984, 49, 1387.
3. W. Adcock and V.S. Iyer, *J.Org.Chem.*, submitted for publication.
4. K.L. Servis and F.F. Shue, *J.Am.Chem.Soc.*, 1980, 102, 7233; D.A. Forsyth, P. Lucas, and R.M. Burk, *J.Am.Chem.Soc.*, 1982, 104, 240; L. Ernst, S. Eltamany and H. Hopf, *J.Am.Chem.Soc.*, 1982, 104, 299; J.R. Wesener and H. Günther, *Tetrahedron Lett.* 1982, 23, 2845; L. Ernst, H. Hopf, and D. Wullbrandt, *J.Am.Chem.Soc.*, 1983, 105, 4469; D.A. Forsyth and M.M. MacConnell, *J.Am.Chem.Soc.*, 1983, 105, 5920.
5. (a) R. Aydin and H. Günther, *J.Am.Chem.Soc.*, 1981, 103, 1301. (b) J.L. Jurlina and J.B. Stothers, *J.Am.Chem.Soc.*, 1982, 104, 4677.
6. E.A. Halevi, *Prog.Phys.Org.Chem.*, 1963, 1, 109.
7. (a) H. Batiz-Hernandez and R.A. Bernheim, *Prog.Nucl.Magn.Resonance Spectrosc.*, 1967, 3, 63. (b) M. Wolfsberg, *Accounts Chem.Res.*, 1972, 5, 225.
8. H.G. Kuivila, *Accounts Chem.Res.*, 1968, 1, 299; K. Kuhlein, W.P. Neumann, and H. Mohring, *Angew.Chem.Int.Ed.Engl.*, 1968, 7, 455; E.W. Della and H.K. Patney, *Synthesis* 1976, 251.
9. (a) The ^1H, ^2H, and ^{13}C nmr spectra of 1 and 2 (X=D) were in accord with their assigned structures. J_{DF} values for 1 and 2 (X=D; 0.85 and 0.2-0.3 Hz, respectively) were obtained from the ^2H spectra. Based on $\gamma_{^1H}/\gamma_{^2H}$ = 6.5145, the J_{DF} values lead to calculated J_{HF} parameters (5.57 and $\simeq$ 2.0 Hz) for 1 and 2 (X=H), respectively, which agree well with observed parameters (5.6 and 1.9 Hz). (b) M. Barfield, E.W. Della, P.E. Pigou and S.R. Walter, *J.Am.Chem.Soc.*, 1982, 104, 3549.
10. W. Adcock and T.C. Khor, *J.Am.Chem.Soc.*, 1978, 100, 7799.
11. ^{19}F nmr spectra (digital resolution, 0.06 Hz) were obtained as described in previous papers[1,2]. A *negative* sign implies shielding.
12. W.R. Young and C.S. Yann, *J.Am.Chem.Soc.*, 1969, 91, 4581.
13. A. Streitwieser and H.S. Klein, *J.Am.Chem.Soc.*, 1963, 85, 2759.
14. J.B. Lambert and L.G. Greifenstein, *J.Am.Chem.Soc.*, 1974, 96, 5120.

(Received in UK 1 August 1984)