Heteronuclear ^{1}H–^{19}F Nuclear Overhauser Effects in Fluoro-aromatic Compounds

By R. A. BELL* and J. K. SAUNDERS

(*Department of Chemistry, McMaster University, Hamilton, Ontario, Canada*)

Summary Large positive nuclear Overhauser enhancements have been observed between ^{1}H and ^{19}F in a number of fluoro-aromatic compounds.

NUCLEAR OVERHAUSER EFFECTS (NOEs) have been used extensively in organic chemistry as an aid to structure and conformational elucidation.[1,2] Positive NOEs can be observed in such proton systems because the dominant relaxation mechanism for protons is the dipole–dipole interaction, a distance-dependant quantity. So dominant is this mechanism at normal temperatures that a valuable correlation between NOE and proton–proton internuclear distance has been obtained.[2] However, in many compounds of interest reliable NOE data cannot be obtained because of factors such as small chemical-shift differences between the protons in question or overlap of the signals with other proton absorptions. It was reasoned that in such compounds incorporation of fluorine into the molecule and use of heteronuclear NOEs would prove valuable, provided such ^{1}H–^{19}F NOEs could be obtained reliably. Moreover, the magnitude of the NOEs would provide information on the relaxation mechanisms open to ^{19}F in larger organic molecules.

A limited number of investigators,[3] studying ^{19}F nuclear relaxation in small molecules, have noted Overhauser enhancements. However, the relaxation processes of ^{19}F are generally more complex than those for protons, as mechanisms other than dipole–dipole are significant, in particular the spin-rotation interaction is regarded as important,[3,4] and although the NOE involves all relaxation mechanisms, positive effects are primarily dependant upon the interaction that couples the spins involved.

Four fluoro-aromatic compounds have been examined and the results are shown in the Table. All compounds showed an area increase of the ^{19}F signal upon saturation of the proton resonances. Reversal of the process caused an area increase in the signals corresponding to the protons *ortho* to the fluorine although this increase was smaller than expected on the basis of their internuclear distance. Clearly in all the compounds examined the dipole–dipole interaction is a significant relaxation mechanism and in fact, with the exception of *o*-fluorotoluene where spin-rotation could be important, it is the dominant relaxation process. Indeed, the value of 50% observed for ^{19}F in 1-fluoronaphthalene is close to the theoretical maximum[5] of 53% expected for a pure dipole–dipole intramolecular relaxation. Preliminary examination of the effect of temperature and magnetic field strength on the spin–lattice relaxation time supports this evidence.

^{1}H–^{19}F *Overhauser Effects*[a]

	N.O.E. %	
Compound[b]	^{1}H saturated ^{19}F observed	^{19}F saturated *ortho* ^{1}H observed
2,4-Dinitrofluorobenzene	22	10
p-Fluoronitrobenzene	45	11
1-Fluoronaphthalene	50	
	48[c]	
o-Fluorotoluene	28	
	18 (H)	
	11 (CH_3)	

[a] Spectra were recorded on a DP-IL-60 using CF_3CCl_3 as lock and NMR Specialties SD60 spin decoupler modified for use with a General Radio Type 1164 frequency synthesizer.

[b] Unless otherwise stated solutions were degassed and prepared as follows: 20% compound, 20% CCl_3CF_3 25% $(CD_3)_2SO$ 25% $CDCl_3$.

[c] $(CD_3)_2SO$ replaced by benzene.

The observation of sizeable NOEs between ^{1}H and ^{19}F implies that the technique should be of particular value in conformational analysis. As the size of the molecule increases the effect of spin-rotation is expected to decrease[6] and therefore larger molecules such as steroids should be amenable to study.

We thank the National Research Council of Canada for financial assistance and the award of a Fellowship to J.K.S.

(*Received, July* 10*th*, 1970; *Com.* 1105.)

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