Long-Range Spin–Spin Coupling in Alkylfluorobenzenes. The Stereochemical Requirements for Coupling of Fluorine and Hydrogen Separated by Five Bonds[1]

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Abstract: Chemical shift data obtained from the nmr spectra of several series of 2,4,6-trialkylhalobenzenes enable the assignment of preferred conformation to those *ortho* alkyl groups which lack threefold symmetry. Application of these conformational preferences to the nmr spectra of a number of alkylfluorobenzenes results in the conclusion that a necessary condition for long-range spin–spin coupling of hydrogen and fluorine which are separated by five bonds is proximate orientation of the nuclei. The magnitude of this long-range spin–spin coupling (J_{H-F}^{1-5}) is shown to be extremely sensitive to the internuclear separation of the couple but rather insensitive to changes in electron density within the aromatic ring. Thus, these data appear to be compelling experimental evidence in support of a "through-space" mechanism of long-range spin-spin coupling.

The observations of spin–spin couplings between nuclei which are spatially proximate but separated by five or more chemical bonds have quite naturally raised a question concerning the importance of direct spin–spin interaction across space.[3] However, there would seem to be no clear resolution of this question despite a wealth of experimental data.

For example, the long-range couplings of hydrogen and fluorine nuclei separated by five or more chemical bonds have received considerable experimental attention. In all cases amenable to analysis, spatial proximity appears to be a necessary condition for observable spin–spin interaction.[4] Indeed, this spatial requirement has been elaborately formulated as the "converging vector rule" by Cross and Landis on the basis of their extensive studies of long-range coupling of various fluorosteroids.[4c] However, attempts by Cross to assign mechanism on the basis of these data led to the ambiguous conclusion that either "through-space" or "through-bond" coupling or a mixture of both was compatible with the data.[3c] The difficulty of mechanistic decision is further compounded by the present lack of theoretical support and the existence of apparent counter-examples in related systems.[3b]

We suggest that further attempts to assess the importance of through-space coupling should begin by finding systems where the internuclear distances between the coupling nuclei can be determined and also incrementally varied, in order that the sensitivity of the coupling constant to changes in internuclear distance can be tested. As a step in this direction, we report here studies of spin–spin coupling between *ortho* β-protons (hydrogens on β carbons of *ortho* alkyl groups) and fluorine in a number of alkylfluorobenzenes. This system permits reasonable spatial definition of the coupling nuclei as well as considerable latitude for variation of this spatial relationship. In addition, this system provides opportunities to alter electron distribution within the molecules by substituent variation at sites distant from the site of spin–spin interaction.

Results

2,4,6-Triethylfluorobenzene and 2,4,6-triisopropylfluorobenzene were synthesized by application of the Schiemann reaction. The corresponding diazonium ions were isolable as the crystalline fluoroborate salts, but, in contrast to trimethylbenzenediazonium fluoroborate which is quite stable at room temperature, these salts undergo relatively rapid decomposition at room temperature to yield the corresponding aryl fluorides. 2,4,6-Tri-*t*-butylbenzenediazonium ion could not be isolated as the fluoroborate salt. All evidence indicates that this ion has only a fleeting existence. This aryl fluoride could however be synthesized in moderate yield by low-temperature diazotization of 2,4,6-tri-*t*-butylaniline in 48% hydrofluoric acid.

Most substituents could be introduced at C-3 of 2,4,6-triethylfluorobenzene and 2,4,6-triisopropylfluorobenzene by direct electrophilic substitution reactions. Analogous introduction of 3 substituents in 2,4,6-tri-*t*-butylfluorobenzene is not so straightforward. However, it was found that nitration of 2,4,6-tri-*t*-butylfluorobenzene with 90% nitric acid in nitromethane afforded the 3-nitro derivative in modest yield (*ca.* 20%) together with the major product, 4-nitro-2,6-di-*t*-butylfluorobenzene, formed by nitrodealkylation. Other 3-

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(2) (a) National Science Foundation Undergraduate Research Scholar, 1964; (b) California Biochemical Undergraduate Research Scholar, 1965.

(3) (a) F. A. L. Anet, A. J. R. Bourn, P. Carter, and S. Winstein, *J. Am. Chem. Soc.*, **87**, 5249 (1965); (b) K. L. Servis and J. D. Roberts, *ibid.*, **87**, 1339 (1965); (c) A. D. Cross, *ibid.*, **86**, 4011 (1964); (d) S. Ng and C. H. Sederholm, *J. Chem. Phys.*, 40, 2090 (1964); (e) L. Petrakis and C. H. Sederholm *ibid.*, **35**, 1243 (1961).

(4) (a) M. Takahashi, D. R. Davis, and J. D. Roberts, *J. Am. Chem. Soc.*, **84**, 2935 (1962); (b) D. R. Davis, R. P. Lutz, and J. D. Roberts, *ibid.*, **83**, 246 (1961); (c) A. D. Cross and P. W. Landis, *ibid.*, **86**, 4005 (1964); (d) A. Lewin, *ibid.*, **86**, 2304 (1964); (e) J. Burdon, *Tetrahedron*, **21**, 1101 (1965).

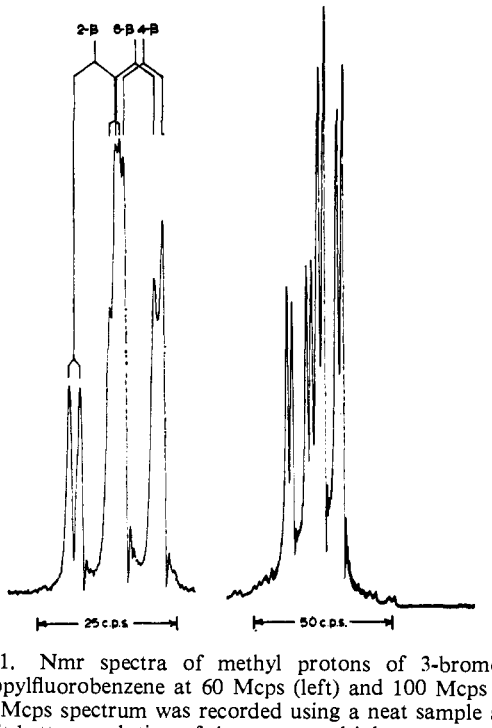


Figure 1. Nmr spectra of methyl protons of 3-bromo-2,4,6-triisopropylfluorobenzene at 60 Mcps (left) and 100 Mcps (right). This 60-Mcps spectrum was recorded using a neat sample at 100° to permit better resolution of the center multiplet.

substituted 2,4,6-tri-*t*-butylfluorobenzenes were synthesized from the 3-nitro derivative. The 4-nitro derivative offered a convenient entry to a series of 4-substituted 2,6-di-*t*-butylfluorobenzenes.

The nmr spectra of the compounds used in this study were straightforward and could be analyzed by first-order methods. The triethylfluorobenzene series presents the biggest difficulty since second-order effects are still present at 60 Mcps. As a result, detection of very small fluorine–proton couplings is difficult. These problems were resolved by examination of 100-Mcps spectra of selected compounds.

The character of many of the spectra reported here is exemplified by the spectrum of 3-bromo-2,4,6-triisopropylfluorobenzene shown in Figure 1. The methyl region at 60 Mcps consists of three multiplets with area 1:3:2. The downfield doublet is one leg of a doublet of doublets assigned to the methyl protons of the 2-isopropyl group which are spin coupled to fluorine ($J_{H-F}^{1,5}$ = 1.8 cps) as well as to the methine proton. The upfield leg of this doublet is obscured in the central multiplet. The remaining four lines are due to methyl protons of the 4- and 6-isopropyl groups. Considerable aid in making assignments was obtained from spectra of the four 2,4,6-triisopropylhalobenzenes (*vide infra*). Further confirmation of assignment is found in the slight broadening of the methyl proton lines of the 6-isopropyl group due to very small coupling with fluorine. The corresponding 100-Mcps spectrum of this compound shown in Figure 1 fully confirms the splitting assignments based on the 60-Mcps spectrum.

Spectra of the methyl protons of the 3-substituted 2,4,6-triethylfluorobenzenes are less dramatic. The spectrum of the 3-iodo derivative shown in Figure 2 has three triplets, one for each of the three sets of methyl protons. No resolvable long-range coupling is detected. The corresponding 100-Mcps spectrum (Figure 2) show the same three triplets, but at this field strength

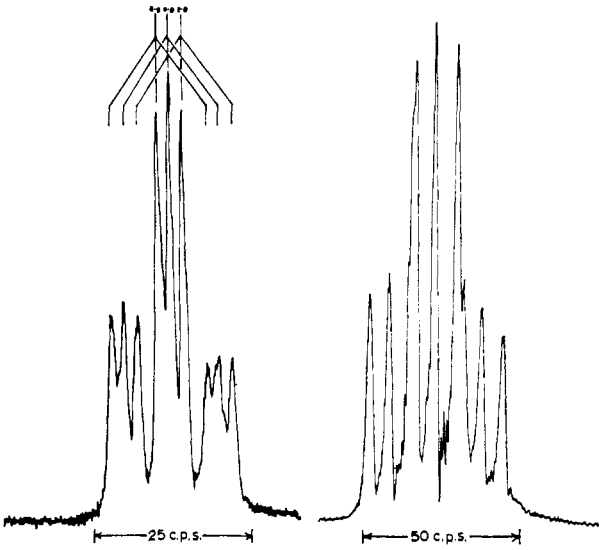


Figure 2. Nmr spectra of methyl protons of 3-iodo-2,4,6-triethylfluorobenzene at 60 Mcps (left) and 100 Mcps (right). Both spectra were recorded using the same sample, 5% by weight in CCl_4.

the chemical shifts are sufficient to cause overlapping of lines.[5] Nevertheless, the spectrum confirms the absence of strong coupling, but line widths indicate the presence of weak coupling (~0.3 cps) of the methyl

Table I. Methyl Proton Chemical Shifts (cps) and Coupling Constants at 60 Mcps[a]

X	$\nu_{2-\beta}$	$\nu_{4-\beta}$	$\nu_{6-\beta}$	$J_{H-F}^{2-\beta}$	$J_{H-F}^{6-\beta}$
A. 3-X-2,4,6-Triethylfluorobenzenes					
H	71.9	70.8	71.9	0.3[b]	0.3[b]
Cl	71.1	72.0	72.0		
Br	70.1	72.2	72.2		
I	68.6	70.6	72.5	0.3[b]	0.3[b]
B. 3-X-2,4,6-Triisopropylfluorobenzenes					
H	74.8	72.9	74.8	0.3[b]	0.3[b]
F	79.9	73.8	73.8	0.7 (triplet)	0.3
Cl	80.4	72.9	74.5	1.84	0.3
Br	80.4	72.8	74.3	1.89	0.3
I	80.2	72.5	74.6	1.94	0.3
CH_3	78.9	71.3	73.5	1.68	0.3
C. 3-X-2,4,6-Tri-*t*-butylfluorobenzenes					
H	83.0	78.1	83.0	0.93	0.93
NH_3^+[c]	101.8	95.3	88.1	1.64	1.09
NO_2	85.7	80.9	83.8	1.92	1.29
OH	93.2	83.8	79.8	2.90	1.28
NH_2	93.6	85.1	78.8	3.52	1.33
Br	99.7	93.7	81.7	4.22	1.22

X	$\nu_{2,6-\beta}$	$J_{H-F}^{2,6-\beta}$	$J_{H-F}^{3,5-ArH}$	$\nu_{3,5-ArH}$
D. 4-X-2,6-Di-*t*-butylfluorobenzenes				
t-Bu	83.0	0.93	7.4	426
NH_3^+[c]	79.9	1.03	6.1	442
NO_2	87.0	1.15	6.3	485
NH_2	79.9	0.93	6.2	381
Br	82.6	1.10	6.6	433

[a] Samples were 5% by weight in CCl_4, except where noted otherwise, and referenced to TMS. [b] Coupling constants were estimated using the technique of D. Kowalewski, *Mol. Phys.*, **9**, 319 (1965). [c] Spectrum recorded using trifluoroacetic acid as solvent.

(5) We are grateful to Dr. N. S. Bhacca, Varian Associates, for recording the 100-Mc spectra reported here.

protons of both the 2- and the 6-ethyl groups. That the methyl protons of the 2-ethyl group are the least deshielded set was confirmed by examining the spectrum of 3,5-diiodo-2,4,6-triethylfluorobenzene. This compound exhibits one triplet for its methyl protons with the center line at 68.5 cps.

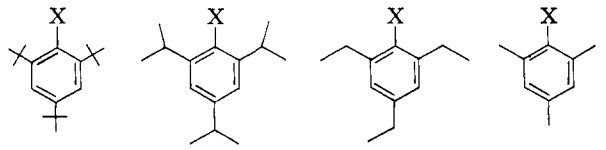
The spectra of the 2,4,6-tri-*t*-butylfluorobenzenes and the 2,6-di-*t*-butylfluorobenzenes are very straightforward showing sharp singlets or doublets for the respective *t*-butyl groups.

The chemical shift and coupling constant data for the methyl protons of the compounds studied are tabulated in Table I.

Discussion

A summary of pertinent chemical shift differences for four series of 2,4,6-trialkylhalobenzenes is given in Table II.[6] The important features of the data in Table II for the present discussion are: (1) significant

Table II. Chemical Shift Differences, $\nu_{ortho} - \nu_{para}$ (cps), at 60 Mcps[a,b]

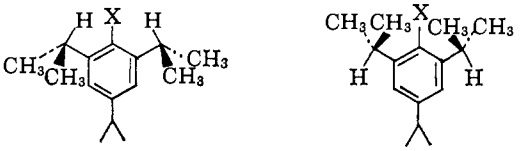


X	$\Delta\nu_{\beta-H}$	$\Delta\nu_{\beta-H}$	$\Delta\nu_{\alpha-H}$	$\Delta\nu_{\beta-H}$	$\Delta\nu_{\alpha-H}$	$\Delta\nu_{\alpha-H}$
F	5	2	21	1	5	2
Cl	13	1[c]	36	1	10	6
Br	16	1[c]	37	0	12	8
I	21	0	32	−1	12	12

[a] Samples were 5 weight % in CCl_4 and reference to TMS. [b] In all cases, the difference between the chemical shift of an α or β proton in the parent hydrocarbon and the same proton on the *para* alkyl group was no greater than 1 cps except for the halomesitylenes where deviations up to 5 cps were noted in some cases: compare with P. Diehl and G. Svegliado, *Helv. Chim. Acta*, **46**, 461 (1963), and W. A. Gibbons and V. M. S. Gil, *Mol. Phys.*, **9**, 167 (1965). [c] Neat samples of these compounds showed resolvable patterns ($\Delta\nu \sim 1$ cps) for the two different sets of β protons; however these chemical shift differences could not be detected in dilute solution.

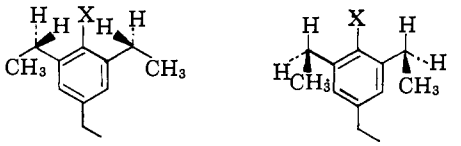
downfield shifts of *ortho* β-protons with respect to the *para* β-protons in the spectra of the 2,4,6-tri-*t*-butylhalobenzenes; (2) negligible or small shifts of *ortho* β-protons with respect to *para* β-protons of the 2,4,6-triisopropylhalobenzenes and 2,4,6-triethylhalobenzenes; (3) large downfield shift differences between *ortho* α-protons and *para* α-protons in the spectra of the 2,4,6-triisopropylhalobenzenes and, to a lesser extent, 2,4,6-triethylhalobenzenes.

The principal mode of deshielding of the *ortho* alkyl protons with respect to the *para* alkyl protons may be open to question, but all of the deshielding effects thought to be important in this situation are effectively inverse functions of the distance separating the proton and substituent.[7] Hence, the absence of significant deshielding of *ortho* β-protons of the 2,4,6-triisopropylhalobenzenes and 2,4,6-triethylhalobenzenes, but fairly strong deshielding of the *ortho* α-protons of these compounds, implies that isopropyl and ethyl groups *ortho* to a halogen spend most of their time with their respective methyl protons distant from the substituent, and their respective methine and methylene protons more proximate to the halogen function. For the triisopropylhalobenzene series, a conformation near I would appear most consistent with the data. It may be noted that the largest difference, $\Delta\nu_{\beta-H}$, in the triisopropylhalobenzene series is observed for 2,4,6-triisopropylfluorobenzene, which, having the smallest halogen substituent, should have the smallest energy difference between conformation I and the most hindered of the possible conformations, II.[8]

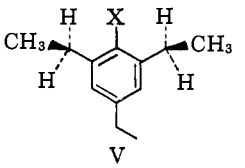


I II

Specification of the preferred conformation of the *o*-ethyl groups is more difficult since a number of conformations exist which are reasonably consistent with the chemical shift data. For example, attempts to fit the chemical shift data of the triethylhalobenzenes with that of the triisopropyl- and trimethylhalobenzenes require weighted averages of conformations III, IV, and



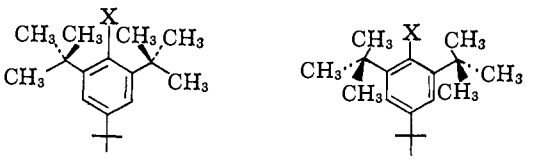
III IV



V

V. In any event, the absence of significant deshielding of *ortho* β-protons would imply that the dihedral angle between the *o*-ethyl group and the halogen substituent is on the average greater than 90°.

In contrast, *o*-*t*-butyl groups of the tri-*t*-butylhalobenzenes must have some of their β protons proximate to the halogen function. The limiting conformation, VI, seems clearly favored with respect to VII. As a result, the *ortho* β-protons are predicted to be strongly deshielded, as observed.



VI VII

(6) L. Armi and P. C. Myhre, unpublished work. A more detailed discussion of these data with special reference to chemical shifts will be presented in a subsequent paper.

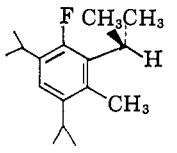
(7) (a) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp 176–183; (b) A. D. Buckingham, *Can. J. Chem.*, **38**, 300 (1960); (c) T. Schaefer, W. F. Reynolds, and T. Yonemoto, *ibid.*, **41**, 2969 (1963); (d) S. Winstein, P. Carter, F. Anet, and A. Bourn, *J. Am. Chem. Soc.*, **87**, 5248 (1965).

(8) Preliminary studies by K. L. Brown indicate a decrease in deshielding of the *ortho* α-protons of I (X = F) over the temperature range from −30 to +170°. In addition slight increases in the deshielding of the *ortho* β-protons as well as discernable line broadening (see Figure 1) are observed. Control studies indicate superimposed solvent–solute effects which, for the present, prevent anything more than very rough estimates of the energy difference between I and II, of the order of several kcal mole^{-1}.

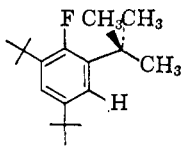
These conformational results are certainly not unexpected. Indeed, they are essentially as one would predict upon examination of models. The important point to establish is that the chemical shift would appear to be a sensitive indicator of conformational preference of *o*-alkyl groups in these systems.

Application of these conformational preferences to the spectra of the various 2,4,6-trialkylfluorobenzenes (Table I) leads to the tentative conclusion that significant coupling of *ortho* β-protons and fluorine occurs only when the β-protons are proximate to fluorine. Thus the *ortho* β-protons of tri-*t*-butylfluorobenzene show resolvable coupling ($J_{H-F}^{1,5} = 0.9_3$) while the *ortho* β-proton lines of triisopropyl- and triethylfluorobenzene are only slightly broadened indicating coupling constants of about 0.3 cps or less.

A test of this conclusion can be made by introducing a substituent larger than fluorine at C-3 of 2,4,6-triisopropylfluorobenzene. The effect of such a substitution would be an alteration of the preferred conformation with the net result that the 2-β-protons would be more proximate to fluorine. Hence, significant coupling would be predicted. In the discussion of conformational alteration, 3-methyl-2,4,6-triisopropylfluorobenzene (VIII) is a compound of particular interest, since it can be considered, in the region of interest, sterically equivalent to 2,4,6-tri-*t*-butylfluorobenzene (IX). Assuming the conformations shown in VIII



VIII



IX

and IX and that the set of *ortho* β-protons of IX distant with respect to fluorine are not appreciably deshielded by, or coupled with, fluorine, one would predict on the basis of rotational averaging that

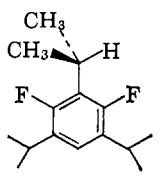
$$(\nu_{2-\beta-H} - \nu_{4-\beta-H})_{VIII} \simeq {}^3/_2(\nu_{o-\beta-H} - \nu_{p-\beta-H})_{IX} = 7.6 \text{ cps}$$

and

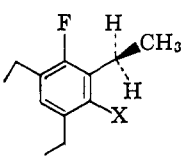
$$(J_{H-F}^{2-\beta-H})_{VIII} = {}^3/_2(J_{H-F}^{2,6-\beta-H})_{IX} = 1.5 \text{ cps}$$

Both values are in good agreement with the experimental observations, 7.5 and 1.7 cps.[9] Similar deshielding and coupling constant results are found in studies of the 3-chloro, 3-bromo, and 3-iodo derivatives of triisopropylfluorobenzene (Table I).

The symmetry of 1,3-difluoro-2,4,6-triisopropylbenzene (X) dictates that the 2-β-protons exhibit a triplet coupling pattern with fluorine. The size of the coupling



X



XI

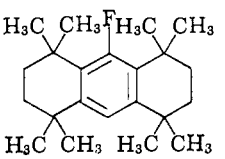
(9) Absorption lines differing by about 1 cps could not be completely resolved. Consequently the observed values of small couplings are lower than the actual value since overlapping will, in general, have the effect of bringing the peaks of two lines closer together.

constant, 0.7 cps, again indicates that coupling between β-protons and fluorine occurs only when the nuclei are proximate.

Introduction of substituents at C-3 in 2,4,6-triethylfluorobenzene should cause the 2-β-protons to be, on the average, closer to fluorine. Consideration of possible conformations indicates that the distance need not be sufficiently close for strong coupling. That is, the most favored conformation could be one with the 2-ethyl group approximately perpendicular to the ring plane (XI). Such an orientation permits the set of 2-β-protons to be neither proximate to the 3 substituent nor fluorine, and, consequently, relatively uninfluenced by them. This orientation, however, places the 2-β-protons out of the region of maximum deshielding by induced ring current. The net shielding of the 2-β-protons of the 3-halo-2,4,6-triethylfluorobenzenes (Table I) appears to be attributable to this effect.

The initial conclusion, based on the nmr spectra of the three 2,4,6-trialkylfluorobenzenes, that proximity of the *ortho* β-protons and fluorine is necessary for significant coupling seems quite convincingly reinforced by the spectra of the 3-substituted derivatives of triisopropylfluorobenzene and triethylfluorobenzene. The parallelism of these results with those found in both related and quite different systems—acyclic,[4a] alicyclic,[4b,c] and aromatic[4d,e]—strongly implies that a generally necessary condition for $J_{H-F}^{1,5}$ is spatial proximity of the coupling nuclei.[10,11]

A particularly definitive test of this conclusion would be the examination of the spectra of 2,4,6-tri-*t*-butylfluorobenzene under conditions where the rate of rotation of the *ortho* *t*-butyl groups is slower than the time of the nmr experiment. If these conditions prevail, one would anticipate seeing two different kinds of *ortho* β-protons. The protons distant (IX) should experience negligible deshielding by, or coupling with, fluorine, but the proximate protons would be strongly coupled and deshielded by fluorine. This condition has not been experimentally realized.[12] However, the molecule, 9-fluorooctamethyloctahydroanthracene (XII), possesses structural features quite similar to ones



XII

that would be obtained if the conformation shown in IX could be frozen. The nmr spectrum of XII shows the expected features. The methyl protons at C-1 and

(10) The restriction must be made that most of the bonds are single bonds. It seems quite possible that extended unsaturated systems could be found which show significant proton–fluorine coupling even though the nuclei are not proximate.

(11) It is noteworthy that the results reported here are in complete harmony with the "converging vector rule."[3o] However it must also be pointed out that none of the compounds studied which have *ortho* β-protons proximate to fluorine have nonintersecting vectors taken along the respective C–H and C–F bonds. Therefore, these data do not permit discrimination between the alternative experimental criteria for $J_{H-F}^{1,5}$ of proximity or proximity with converging vectors.

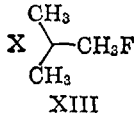
(12) The "lumpiness" of a *t*-butyl group is a question of interest. Models indicate that rotation of *ortho* *t* butyl groups in compounds such as 2,4,6-tri-*t*-butylbromobenzene should have rather severe restrictions, but to date no direct evidence of these barriers is available. The failure to detect spectral changes at temperatures as low as −110° indicates a barrier to rotation lower than about 8 kcal mole^{-1}.

C-8 are spin–spin coupled to fluorine ($J_{H-F}^{1,5}$ = 2.1 cps) and are deshielded (7 cps) with respect to methyl protons at C-4 and C-5. In contrast, the methylene protons at C-2 and C-7 are neither perceptibly coupled to fluorine nor deshielded with respect to protons at C-3 or C-6.

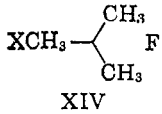
The observed requirement of proximity of coupling nuclei raises the question of mechanism of this long-range coupling. Transference of spin information by orbital overlap directly across space, rather than through the five-bond framework, is without doubt a convenient explanation of the proximity requirements. Arguments based on convenience, however, are hardly compelling, particularly when the less convenient but more conventional alternatives involving through-bond spin–spin interaction could not be disproved by earlier data.[13] Without more detailed theoretical criteria, the experimental options available are those which test the sensitivity of the long-range spin–spin coupling to effects that one would expect to discriminate between the two kinds of coupling mechanisms. For this reason, the nmr spectra of 3-substituted 2,4,6-tri-*t*-butylfluorobenzenes and 4-substituted 2,6-di-*t*-butylfluorobenzenes were studied, the expectation being that the former would further delineate the dependence of the coupling constant on changes in internuclear separation of the coupling nuclei, and the latter would test the effect of changing the electron distribution of the aromatic ring system.

The effect of substitution at C-3 of 2,4,6-tri-*t*-butylfluorobenzene is striking and qualitatively in accord with prediction, if coupling occurs through space. That is, the observed coupling constant of the 2-β-protons is markedly increased (from 60 to over 400%) by replacing hydrogen at C-3 with a larger substituent. Concomittant changes in the coupling constant of the 6-β-protons with fluorine are small (Table I). Variations of the substituent at C-4 of 2,6-di-*t*-butylfluorobenzene cause only slight changes in the observed coupling constant. The absence of marked changes in $J_{H-F}^{1,5}$ upon wide variation of substituent groups at C-4 is also expected if coupling occurs by a through-space mechanism.[3d]

The observation of large increases in the coupling constant of the 2-β-protons attendant every substitution at C-3 of 2,4,6-tri-*t*-butylfluorobenzene and the considerable spread in these values require further comment. These results are thought to reflect both direct and indirect buttressing of the 2-*t*-butyl group by the 3 substituent. Indirect buttressing is presumed to effect changes in conformational preference of the 2-*t*-butyl group. Although experimental observation of discrete rotomers has so far been elusive,[12] models very strongly suggest that the introduction of large, approximately spherical substituents at C-3 should favor conformations of the 2-*t*-butyl group closer to XIII than XIV.



XIII



XIV

(13) This question has been discussed at length by Cross.[3o] No further exposition of the variety of subtle and sometimes tortuous possibilities will be made here.

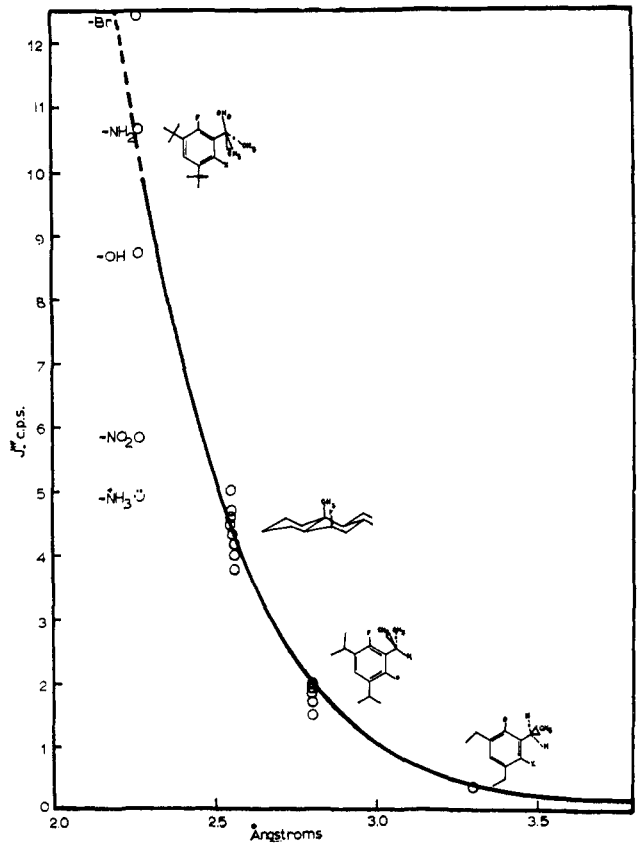


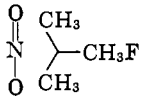
Figure 3. Plot of contributions to observed $J_{H-F}^{1,5}$ by protons on proximate methyl carbons as a function of calculated internuclear separation of fluorine and carbon. Calculated distances are based on the conformations shown. Observed $J_{H-F}^{1,5}$ data are taken from Table I and ref 4c.

If one assumes that the conformation of the 2-*t*-butyl group can be fairly accurately represented by XIII, it is possible to construct the following correlation between $J_{H-F}^{1,5}$ and internuclear separation. The data obtained from the alkylfluorobenzene systems (*vide supra*) indicate that $J_{H-F}^{1,5}$ is essentially zero when the dihedral angle between the pertinent methyl and fluorine is greater than about 90°, or, alternatively, the methyl carbon is more than 3.3 A from fluorine. Thus, the contribution of the distant methyl groups of XIII to the observed coupling must be zero and the coupling constant contribution of the proximate methyl group may be taken as three times the observed coupling constant. This would imply a truly dramatic increase in the coupling constant as one decreases internuclear separation. This increase is depicted graphically in Figure 3 where distances between the pertinent methyl carbon and fluorine are calculated on the basis of the conformations shown using normal bond lengths and bond angles. In addition to the data reported here, representative values of the coupling constant of 19 protons with 6-β-fluorine of some 6-β-fluorosteroids are included.[4c]

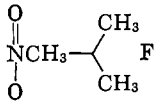
The scatter of points at small internuclear distance is nearly as dramatic as the shape of the correlation curve. This scatter indicates the approximations of the construct. Given that $J_{H-F}^{1,5}$ is strongly dependent upon internuclear separation, any error made in assessing the smaller separations will be reflected in very large deviations from the correlation curve.

Some error can undoubtedly be ascribed to faulty conformational weighting; the inclusion of some XIV is probably important, particularly for smaller substituents. Larger substituents, however, can cause large direct buttressing effects resulting in considerable deformation of bond angles. The net effect of this is expected to be actual internuclear distances which are smaller than those calculated on the basis of normal bond lengths and angles. Some indication of this direct buttressing effect may also be found in the 3-halo-2,4,6-triisopropylfluorobenzene series where the coupling constant increases slightly with increasing size of the halogen substituent.

Despite these highly adjustable parameters, several questions concerning the effect of 3 substituents arise. For example, the large increase in coupling constant when the 3 substituent is changed from a nitro group to an amino group does not seem to correlate with the size of these two substituents. A partial answer to this question is the preferred orientation of these two essentially linear groups with respect to the ring plane of this crowded alkylbenzene. Ultraviolet spectral data indicate that the nitro group of 2,4,6-tri-*t*-butylnitrobenzene assumes an orientation which is close to perpendicular with the ring while the corresponding amino function is substantially coplanar.[14] Thus, it is possible that estimates of the conformation of the 2-*t*-butyl group in 3-nitro-2,4,6-tri-*t*-butylfluorobenzene are more profitably based on consideration of conformations XV and XVI.



XV



XVI

A number of other arguments could be marshaled to rationalize some of the other data with the construct. The number of arguments required, perhaps, reflects the number of real questions which remain. However, these questions do not cloud the central point that the accumulated data are best interpreted in terms of very marked sensitivity of J_{H-F}[1,5] to changes in internuclear distance. This is and remains the central piece of experimental evidence upon which any case for a mechanism of long-range spin–spin coupling through space must rest.

Experimental Section

Melting points were taken on a calibrated Fisher-Johns apparatus. Elemental analyses were performed by Mr. C. F. Geiger, Ontario, Calif. Gas–liquid partition chromatographic analyses and preparative separations were performed, unless noted otherwise, using an Aerograph A-700 equipped with an S.E. 30 column, 10 ft × $^3/_8$ in., 200 to 260°, 150 ml min^{-1}.

Materials. 1,3,5-Triethylbenzene was obtained from K & K Laboratories and redistilled before use. Gas–liquid partition chromatography (glpc) indicated greater than 99% purity. 1,3,5-Triisopropylbenzene was isolated from "Alkazene-13," a product of the Dow Chemical Co. This material contained significant amounts of 1,2,4-triisopropylbenzene, 1-isopropenyl-3,5-diisopropylbenzene, and tetraisopropylbenzene in addition to the compound of interest. Isolation was effected by partial sulfonation and careful fractionation of the unsulfonated fraction. Material so obtained was 99% pure, bp 120° (19 mm), n^{22}D 1.4873. The principal contaminent was the unsymmetrical isomer. 1,3,5-Tri-*t*-butylbenzene was prepared by alkylation of 1,4-di-*t*-butylbenzene with *t*-butyl chloride and aluminum chloride[15] and, more recently, by low-temperature alkylation of *t*-butylbenzene with *t*-butyl chloride and aluminum chloride.[16] A sample of 3-hydroxy-2,4,6-tri-*t*-butylfluorobenzene was generously supplied by Dr. Bruce Rickborn, University of California, Santa Barbara, Calif.

2,4,6-Triisopropylfluorobenzene. Reduction of 30.0 g (0.118 mole) of 2,4,6-triisopropylnitrobenzene[17] with stannous chloride gave 55.7 g of moist 2,4,6-triisopropylanilinium hexachlorostannate.[18] The amine resulting from hydrolysis with base was diazotized at 0° with 12 g of sodium nitrite during a 15-min period. Addition of 30 g of sodium fluoroborate in 30 ml of water caused precipitation of triisopropylbenzenediazonium fluoroborate which was collected by suction filtration and dried by rotary evaporation at 25° (1 mm) for 30 min, affording 20.6 g of powdery, white crystals. The infrared spectrum (Nujol) showed a sharp band at 2240 cm^{-1}. The flask containing the salt was reattached to the rotary evaporator and evacuation was continued unattended for an additional 3 hr. During this period the salt decomposed leaving a brown liquid, 14.6 g. After extraction, washing, and drying, the material was distilled yielding 11.6 g of colorless liquid, bp 96–97° (10 mm), n^{20}D 1.4793.

Anal. Calcd for $C_{15}H_{23}F$: C, 81.03; H, 10.43. Found: C, 80.97; H, 10.28.

2,4,6-Triethylfluorobenzene. 2,4,6-Triethylaniline[19] (6.0 g, 0.034 mole) was converted to the diazonium fluoroborate in the manner described. The slightly yellow product decomposed upon remaining at room temperature overnight. The resulting product was warmed gently to effect complete decomposition, washed free of acid, and dried to yield 4.4 g of crude material, n^{20}D 1.4885. Distillation afforded 3.2 g, bp 96.5–97.2° (15 mm), n^{20}D 1.4846. Glpc indicated purity greater than 99.5%.

Anal. Calcd for $C_{12}H_{17}F$: C, 79.95; H, 9.51. Found: C, 80.14; H, 9.56.

2,4,6-Tri-*t*-butylfluorobenzene. A 120-ml polyethylene flask was charged with 3.43 g (13 mmoles) of tri-*t*-butylaniline[20] and 30 ml of 48% hydrofluoric acid. A solution of 3.0 g (44 mmoles) of sodium nitrite was added dropwise over a 45-min period to the well-stirred mixture which was cooled by means of an ice–salt bath to −5°. The reaction mixture turned black upon addition of each drop of sodium nitrite and slowly decolorized to a yellow-orange. At the end of the reaction, the dark orange liquid and gummy yellow solid were poured into ice and water, and the products were extracted with cyclohexane (*ca.* 100 ml total). The cyclohexane extracts were washed with water and saturated sodium chloride, and then dried over anhydrous sodium sulfate. Evaporation of the solvent left 3.08 g of dark brown oil. Glpc revealed six major components. Column chromatography of the oil over alumina (20 × 2.5 cm) with pentane elution afforded 1.29 g (38%) of colorless crystals, mp 117–120°. An analytical sample was prepared by recrystallization from ethanol and vacuum sublimation, mp 120–121°.

Anal. Calcd for $C_{18}H_{29}F$: C, 81.76; H, 11.00. Found: C, 81.64; H, 11.16.

1,3-Difluoro-2,4,6-triisopropylbenzene. 1,3-Dinitro-2,4,6-triisopropylbenzene was reduced to 1,3-diamino-2,4,6-triisopropylbenzene using stannous chloride in acetic acid and hydrochloric acid, mp 72–73°.

Anal. Calcd for $C_{15}H_{26}N_2$: C, 76.86; H, 11.18; N, 11.86. Found: C, 77.01; H, 11.48; N, 11.77.

Tetrazotization of 10.1 g (44 mmoles) of the diamine was effected by dropwise addition of 10 g of sodium nitrite in 25 ml of water to a cold (−4°) suspension of the diamine hydrochloride in 130 ml of 2 *N* hydrochloric acid. After filtration of the orange reaction mixture, about 60 g of sodium fluoroborate in 60 ml of water was added quickly. Precipitation of the tetrazonium fluoroborate occurred after much hectic scratching and cooling. The precipitate was collected by suction filtration and dried by rotary evaporation yielding a tan solid. The solid was allowed to decompose at room temperature yielding a 4.9 g of brown oil. Distillation afforded three fractions, 2.6 g, with essentially the same boiling

(14) J. Burgers, M. A. Hoefnagel, P. E. Verkade, H. Visser, and B. M. Wepster, *Rec. Trav. Chim.*, 77, 491 (1958).

(15) E. E. Betts and L. R. C. Barclay, *Can. J. Chem.*, **33**, 1768 (1955).

(16) T. Rieger and P. C. Myhre, unpublished results.

(17) A. Newton, *J. Am. Chem. Soc.*, **65**, 2434 (1943).

(18) L. I. Smith, "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., John Wiley and Sons, Inc., New York, N. Y., 1953, p 254.

(19) W. Dillingham and E. E. Reid, *J. Am. Chem. Soc.*, **60**, 2606 (1938).

(20) P. D. Bartlett, M. Roha, and R. M. Stiles, *ibid.*, **76**, 2349 (1954).

point, 87.8–88° (3.8 mm), n^{25}D 1.4709. Glpc indicated 97% purity. An analytical sample was prepared by preparative glpc.

Anal. Calcd for $C_{15}H_{22}F_2$: C, 74.96; H, 9.23. Found: C, 74.82; H, 9.46.

Preparations of 3-Halo-2,4,6-triisopropyl- and 3-Halo-2,4,6-triethylfluorobenzenes. The 3-halo derivatives were prepared by direct electrophilic substitution of the parent fluorobenzene using the appropriate molecular halogen together with silver perchlorate in acetic acid solvent. The following description is typical. A solution containing 3.2 g (20 mmoles) of bromine in 25 ml of acetic acid was added dropwise over a 20-min period to a magnetically stirred solution containing 4.4 g (20 mmoles) of 2,4,6-triisopropylfluorobenzene and 4.1 g (20 mmoles) of anhydrous silver perchlorate in 45 ml of acetic acid. The reaction mixture was stirred an additional 10 min and then processed by filtration, addition of water to the filtrate, and extraction of organic products with cyclohexane. After washing the organic layer with water and drying over anhydrous sodium sulfate, the cyclohexane was evaporated leaving 5.7 g of oil. Distillation of the yellow oil afforded three fractions: (1) bp 109–111° (3.5 mm), 1.0 g; (2) bp 111–111.3° (3.5 mm), 2.4 g, n^{22}D 1.5118; (3) bp 111.3° (3.5 mm), 0.9 g. Glpc indicated that fraction 2 was greater than 99% pure.

Anal. Calcd for $C_{15}H_{22}BrF$: C, 59.80; H, 7.36. Found: C, 59.92; H, 7.51.

The properties and analytical data for the related compounds are tabulated in Table III.

Table III

X	Bp, °C (mm)	nD/°C	Calcd C	Calcd H	Found C	Found H
	3-Halo-2,4,6-triethylfluorobenzenes					
Cl	96.5–98 (6.5)	1.4955/24	67.12	7.51	67.43	7.74
Br	93–98 (2.4)	1.5213/24	55.61	6.22	55.63	6.51
I	109–111 (2.4)	1.5534/23	47.08	5.27	46.74	5.39
	3-Halo-2,4,6-triisopropylfluorobenzenes					
Cl	105 (3.7)	1.4964/24	70.16	8.63	70.15	8.64
Br	111 (3.5)	1.5118/22	59.80	7.36	59.92	7.51
I	124 (3.5)	1.5374/23	51.73	6.36	51.86	6.45

3-Methyl-2,4,6-triisopropylfluorobenzene. To a flask containing 5.0 ml of *n*-butyllithium in *n*-hexane (15 %by weight) was added 1.07 g of 3-bromo-2,4,6-triisopropylfluorobenzene dissolved in 10 ml of anhydrous ether. The resulting solution was stirred magnetically for 1 hr at room temperature. Next, 3.0 ml of methyl iodide was added dropwise with stirring and external cooling. After a 1-hr period, the products were isolated by addition of water. After washing with water and saturated sodium chloride, and drying over anhydrous sodium sulfate, the organic layer was concentrated affording 1.01 g of yellow-brown oil. Glpc revealed a trace of starting material, a major component at shorter retention time, and a small amount of triisopropylfluorobenzene at even shorter retention time. Preparative glpc afforded the major component, a colorless oil, n^{20}D 1.4901.

Anal. Calcd for $C_{16}H_{25}F$: C, 81.31; H, 10.66. Found: C, 81.61; H, 10.91.

3-Nitro-2,4,6-tri-*t*-butylfluorobenzene and 4-Nitro-2,6-di-*t*-butylfluorobenzene. Thirty-one milliliters (0.66 mole) of 90% nitric acid was added dropwise in a 15-min period to a cooled (−5°) solution of 14.7 g (56 mmoles) of 2,4,6-tri-*t*-butylfluorobenzene[21] in cyclohexane–nitromethane (45 ml:40 ml). Slow evolution of nitrogen dioxide was noted after the addition. The reaction temperature was raised to 22° over a 24-hr period at which time an aliquot indicated about 70% conversion of reactant. An additional 25 ml of nitric acid was added and reaction was continued at room temperature for an additional 100 hr. Products were isolated by the addition of 100 ml of water followed by extraction with benzene. After washing the combined extracts with water and 10% sodium hydroxide and drying over anhydrous sodium sulfate, the solvent was removed by rotary evaporation yielding 13.9 g of crude product. Glpc indicated only two products which were shown by their nmr spectra to be 4-nitro-2,6-di-*t*-butylfluorobenzene (81%) and 3-nitro-2,4,6-tri-*t*-butylfluorobenzene (19%).

Fractional crystallization from ethanol–acetone (1:1) afforded 2.57 g of the 3-nitro derivative. Recrystallization and sublimation gave an analytical sample, mp 219–221°.

Anal. Calcd for $C_{18}H_{28}FNO_2$: C, 69.87; H, 9.12; N, 4.53. Found: C, 69.64; H, 9.36; N, 4.56.

Evaporation of the mother liquor from the first crystallization and subsequent recrystallization of the residue from acetone–ethanol (1:1) yielded 5.85 g of colorless crystals of the 4-nitro derivative, mp 82–82.5°.

Anal. Calcd for $C_{14}H_{20}FNO_2$: C, 66.38; H, 7.96; N, 5.53. Found: C, 66.08; H, 7.83; N, 5.22.

4-Amino-2,6-di-*t*-butylfluorobenzene. This compound was prepared by addition of 37.5 g (0.17 mole) of stannous chloride dissolved in 50 ml of concentrated hydrochloric acid to a refluxing solution of 8.08 g (32 mmoles) of the 4-nitro compound in 75 ml of acetic acid. After a 2-hr reaction period, the product was isolated by hydrolysis with base followed by extraction with benzene. A dark brown oil (6.35 g) was obtained upon evaporation of the solvent. Purification was achieved by redissolving the crude product in benzene and saturating the benzene solution with anhydrous hydrogen chloride. Snow-white crystals, 4.58 g (55%), of the amine hydrochloride were collected by suction filtration. An additional 1.81 g of partially crystalline material (crude amine) was isolated from the neutralized mother liquor. Hydrolysis of 3.99 g of the amine hydrochloride afforded 3.03 g of fan-shaped crystals, mp 48°.

Anal. Calcd for $C_{14}H_{22}FN$: C, 75.29; H, 9.93; N, 6.27. Found: C, 75.51; H, 10.01; N, 6.22.

4-Bromo-2,6-di-*t*-butylfluorobenzene. 4-Amino-2,6-di-*t*-butylfluorobenzene (0.50 g, 2.2 mmoles) was converted to the hydrobromide salt in 15 ml of 48% hydrobromic acid and was subsequently diazotized with 0.19 g (2.8 mmoles) of sodium nitrite. The resulting yellow suspension was added to a hot solution of 0.35 g of cupous bromide in 15 ml of hydrobromic acid. Nitrogen evolution ceased after 10 min of reflux. Thirty minutes later the reaction mixture was cooled, diluted with water, and neutralized with base. Extraction with cyclohexane followed by washing and subsequent evaporation of solvent afforded 0.54 g of brown, viscous oil. Glpc indicated three major components. Column chromatography (1 × 20 cm) on acid-washed alumina with pentane elution yielded 0.29 g of a two-component mixture which was separated by preparative glpc to yield 86 mg of 4-bromo-2,6-di-*t*-butylfluorobenzene, mp 57.5–59°.

Anal. Calcd for $C_{14}H_{20}BrF$: C, 58.86; H, 7.01; Br, 27.83. Found: C, 58.85; H, 7.25; Br, 26.90.

3-Amino-2,4,6-tri-*t*-butylfluorobenzene. A benzene–methanol solution (20 ml:25 ml) containing 1.49 g (4.8 mmoles) of 3-nitro-2,4,6-tri-*t*-butylfluorobenzene was heated to reflux together with 100 g of 4% sodium amalgam for 16 hr. The resulting solution was filtered and products were isolated after washing by concentrating the filtrate. Crystallization of the residue from ethanol afforded 0.81 g of a two-component mixture (glpc), 2,4,6-tri-*t*-butylaniline (10%) and 3-amino-2,4,6-tri-*t*-butylfluorobenzene (90%).[21] A portion of this material was purified by preparative glpc to yield an analytical sample, mp 160–161°.

Anal. Calcd for $C_{18}H_{30}FN$: C, 77.37; H, 10.82. Found: C, 77.35; H, 10.85.

3-Bromo-2,4,6-tri-*t*-butylfluorobenzene. A sample of the 3-amino derivative (0.57 g) containing about 10% 2,4,6-tri-*t*-butylaniline was diazotized in 27 ml of 48% hydrobromic acid at −7° with 0.56 g of sodium nitrite. Two hundred and eighty milligrams of dark brown oil was isolated with difficulty from the diluted reaction mixture by extraction with cyclohexane and benzene. Column chromatography of this material over alumina (1 × 10 cm) with pentane elution afforded a fraction, 0.10 g, whose gas–liquid partition chromatogram showed four major components at 4.6, 11.7, 12.5, and 15.1 min. Twenty-three milligrams of material with retention times 11.7 and 12.5 min was separated by preparative glpc. The retention time of 11.7 min corresponded to that of authentic tri-*t*-butylbromobenzene. Nmr spectra of the sample confirmed the presence of this contaminant. The presence of this material did not interfere with the absorption lines of the major component, 3-bromo-2,4,6-tri-*t*-butylfluorobenzene. Spectra recorded here are derived from this sample.

9-Fluoro-1,1,4,4,5,5,8,8-octamethyl-1,2,3,4,5,6,7,8-octahydroanthracene. A suspension of 9-aminooctamethyloctahydroan-

(21) This sample of aryl fluoride was shown by glpc to be contaminated with about 1–2% of the parent hydrocarbon, 1,3,5-tri-*t*-butylbenzene, a fact which became abundantly clear as the sequence of reactions progressed.

thracene[22] (2.18 g, 6.9 mmoles) in 15 ml of 48% hydrofluoric acid was cooled to −5° and diazotized by portionwise addition of an excess (2.0 g) of finely powdered sodium nitrite. After the 30-min addition period, the resulting yellow suspension was allowed to stir for an additional 15 min, and then poured on an excess of ice. After careful neutralization by addition of sodium hydroxide pellets, the resulting precipitate was collected by suction filtration and washed well with water and finally with 20 ml of cold ethanol, 2.21 g, mp 165–210°. Column chromatography over acid-washed alumina with pentane–benzene elution afforded 0.96 g of colorless prisms from the first 100-ml fraction, mp 224–225°.

Anal. Calcd for $C_{22}H_{33}F$: C, 84.02; H, 9.93. Found: C, 83.84; H, 10.14.

Spectral Measurements. Nmr spectra were recorded using a Varian Associates A-60 spectrometer operating at about 38°. Chemical shift data and coupling constants were measured, except where noted otherwise, in 5% by weight solutions of carbon tetrachloride. Calibrations were made using the usual side-band technique. A Hewlett-Packard Model 524D frequency counter and a Hewlett Packard Model 202C audiooscillator were used for this purpose.

Coupling constants were measured by repetitively sweeping at an expanded sweep width (50 cycles) and taking the average of peak to peak separations.

(22) L. R. C. Barclay and E. E. Betts, *Can. J. Chem.*, **33**, 672 (1955). The structure was not recognized at the time of this report. See, however, L. R. C. Barclay and E. E. Betts, *J. Am. Chem. Soc.*, **77**, 5735 (1955).

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The Proton Magnetic Resonance Spectra of Olefins. V. 3-Chloro- and 3-Methoxypropenes

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Abstract: The high-resolution proton magnetic resonance spectra of allyl chloride, allylidene chloride, allyl methyl ether, and acrolein dimethyl acetal have each been obtained at three or four temperatures in the range −50 to +130°, and have been analyzed in terms of chemical shifts and [H,H] coupling constants. The magnitude and temperature dependence of the coupling constants indicate which rotamer is the more stable in each case, and an approximate thermodynamic treatment yields limits for ΔH. The values deduced were: allyl chloride, $\Delta H = 100 \pm 30$ cal/mole (H-eclipsed favored); allylidene chloride, $\Delta H = 800 \pm 100$ cal/mole (H-eclipsed favored); allyl methyl ether, $\Delta H = -115 \pm 30$ cal/mole (O-eclipsed favored); acrolein dimethyl acetal, $\Delta H = -110 \pm 30$ cal/mole (O-eclipsed favored).

In a continuation of the study of rotational isomerism in substituted propenes,[1-3] we have examined the proton nmr spectra of allyl chloride, allylidene chloride, allyl methyl ether, and acrolein dimethyl acetal at several temperatures.

The expected[4-6] geometry of the rotamers of these compounds is depicted in Figure 1.

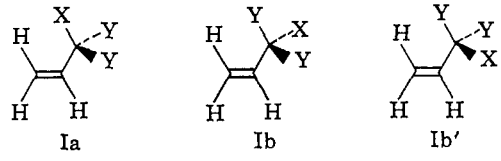

Figure 1. Expected geometry of rotamers of substituted propenes.

Interconversion between rotamers is rapid at temperatures down to −60°, so that only weighted-average values of the chemical shifts and coupling constants are observed. Thus

$$J_{HX} = p_a J_{HX}^{t} + (1 - p_a) J_{HX}^{g} \quad (1)$$

where J_{HX} is the observed coupling constant, p_a is the fractional population in form Ia, J_{HX}^{t} and J_{HX}^{g} are the (H,X) coupling constants characteristic of form Ia and Ib (or Ib′), respectively. Solving for p_a, and substituting in

$$\Delta F = -RT \ln K_{eq} = -RT \ln 2p_a/(1 - p_a) \quad (2)$$

one obtains

$$\Delta F = -RT \ln 2(J_{HX} - J_{HX}^{g})/(J_{HX}^{t} - J_{HX}) \quad (3)$$

Similarly

$$\Delta F = -RT \ln (J_{HY}^{t} + J_{HY}^{g} - 2J_{HY})/(J_{HY} - J_{HY}^{g}) \quad (4)$$

In some other studies of rotational isomerism,[7-12] it has been found or assumed explicitly that $\Delta S \sim 0$.

(1) A. A. Bothner-By and C. Naar-Colin, *J. Am. Chem. Soc.*, **83**, 231 (1961); A. A. Bothner-By, C. Naar-Colin, and H. Günther, *ibid.*, **84**, 2748 (1962).
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