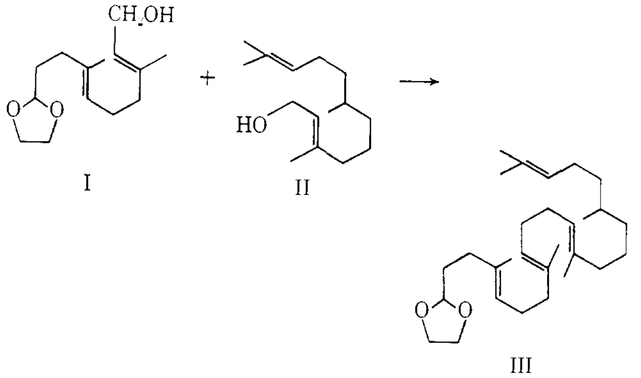
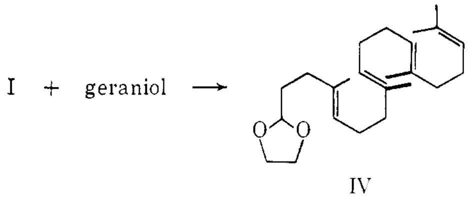
to room temperature was permitted during the course of 10 min, and refluxing (80–82°) for 15 min was utilized to ensure completion of the reaction. The hydrocarbon product was isolated by addition of water, petroleum ether (bp 60–80°) extraction, and silica gel chromatography. The entire reaction can be executed within a few hours and provides hydrocarbon consisting of C-1–C-1′:C-1–C-3′ coupled material in the ratio 7:1 (71% yield, 80% yield based on starting material consumed). In various modifications, *n*-butyl-, *t*-butyl-, or phenyllithium could be substituted for methyllithium without disadvantage; however, greater proportions of this reagent substantially lower the yield of coupled product. The success of mixed couplings depends on the molar proportion of the starting allyl alcohols. In a reaction involving equimolar amounts of geraniol and farnesol, a statistical (1:2:1) ratio of products resulted. Nonspecific coupling also was observed with geraniol–crotyl alcohol. However, by using an excess of one of the different allyl alcohols, a good yield of cross product can be realized (see below).

In addition, other related transformations have been carried out. Through the use of the above experimental procedure, *meso*-hydrobenzoin was reduced to *trans*-stilbene in 31% (88%)[4] yield. As expected, benzyl alcohol was transformed into bibenzyl without difficulty and in good yield, *i.e.*, 68% (78%).[4,5]

In order to demonstrate the adaptability of the synthesis scheme, we describe the preparation of 4-^{3}H-labeled *trans,trans,trans*-18,19-dihydrosqualene 2,3-oxide (V), required in this laboratory in a different connection.[1] After synthesis of the two required allyl alcohols I and II by conventional means,[6,7] the unsymmetrical coupling was carried out under conditions described above (70% yield), the dihydrofarnesol being present in $\sim$10 *M* excess. Through isolation–purification by thiourea clathrate formation, followed by chromatography over a silver nitrate column, there was secured the desired all-*trans* acetal III, a colorless oil which exhibited one peak on vpc and possessed ir, nmr, and mass spectral properties in agreement with the assigned structure. After hydrolysis (perchloric acid in aqueous tetrahydrofuran) to the corresponding aldehyde, the tritium label was introduced by exchange in acidic tritium oxide–tetrahydrofuran.[8] Production of V, the desired final product, was achieved by treatment of the labeled aldehyde with diphenylsulfonium isopropylide.[8] Similarly, the allyl alcohol I[7] was converted to the cross-coupling product IV by employing geraniol as the second, more abundant alcoholic component.





Acknowledgment. The authors are indebted to the National Science Foundation for grant support (NSF GP 5556).

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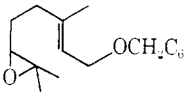
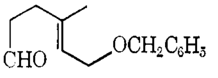
(4) Second yield based on starting material consumed.

(5) With the metal valence change II → IV in mind,[2] the other direct reductive coupling experiments were carried out. Although vanadium dichloride in refluxing glyme or dioxane served to convert benzyl alcohol to bibenzyl in 25–35% yield, the reaction was found to be erratic and therefore was not pursued. In exploratory experiments, titanium dichloride in refluxing glyme or hexamethylphosphoramide effected conversion of benzyl alcohol to small amounts (≤5%) of bibenzyl.

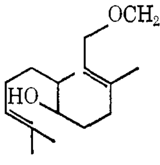
(6) Synthesis of *trans*-6,7-dihydrofarnesol: *trans*-geraniol was protected by O-benzylation (sodium hydride followed by benzyl chloride, all in glyme), after which the 6,7-oxide i was prepared by successive treatment with N-bromosuccinimide in aqueous *t*-butyl alcohol and base [E. E. van Tamelen and T. J. Curphey, *Tetrahedron Letters*, 121 (1962)]; perchloric acid in aqueous tetrahydrofuran effected conversion to glycol, which was cleaved to the aldehyde ii by means of sodium metaperiodate. The carbon chain was then established by reaction with 6-methylhept-5-enyl-2-magnesium chloride; the resulting alcohol iii was tosylated in pyridine in methylene dichloride. Lithium aluminum hydride reduction afforded the dihydrofarnesyl benzyl ether, which was cleaved by treatment with lithium in liquid ammonia.



i

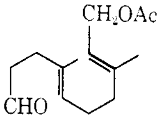


ii



iii

(7) Synthesis of the ethylene acetal of 10-acetoxy-4,8-dimethyldeca-4,8-dienal: successive treatment of the terminal epoxide of farnesyl acetate [E. E. van Tamelen, A. Storni, E. J. Hessler, and M. Schwartz, *J. Am. Chem. Soc.*, **85**, 3295 (1963)] with perchloric acid–aqueous tetrahydrofuran and sodium metaperiodate produced the expected aldehyde iv, which was converted to the corresponding ethylene acetal in an oxalic acid catalyzed reaction with ethylene glycol. Saponification was carried out with potassium carbonate in methanol. The structures of all new substances described in this manuscript were consistent with nmr, ir, and/or mass spectral data.



iv

(8) R. Nadeau and R. Hanzlik, *Methods Enzymol.*, in press.

(9) National Institutes of Health Predoctoral Fellow, 1964–1967.

(10) National Science Foundation Fellow, 1966–1967.

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Substituent Effects on Fluorine-19 Chemical Shifts in Saturated Systems[1]

Sir:

Previous work by our group[2] has shown that the effects of substituents on side chains in aromatic sys-

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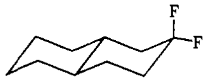
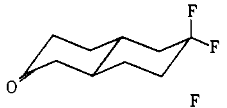
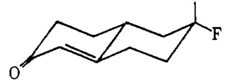
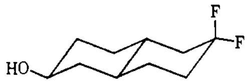
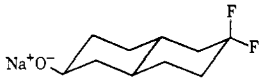
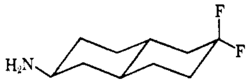
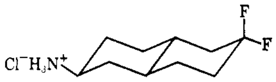
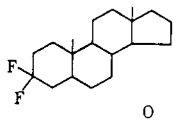
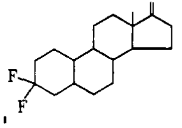
(1) This work was supported by the Air Force Office of Scientific Research through Grant No. AF-AFOSR-1050-67.

Table I. ^{19}F Nmr Spectra of Some Saturated 1,1-Difluoro Compounds

Compound	Solvent^a	Chemical Shift^b Axial	Chemical Shift^b Equat	SCS^c Axial	SCS^c Equat
	DMF	−768	−1471	0	0
	Acetone	−751	−1458	0	0
	DMF	−759	−1408	+9	+63
	Acetone	−745	−1391	+6	+67
	DMF	−603	−1294	+165	+177
	Acetone	−584	−1281	+167	+177
	DMF	−773	−1452	−5	+19
	DMF	−774	−1449	−6	+22
	DMF	−779	−1462	−11	+9
	MeOH	−732	−1419	(0)	(0)^d
	DMF	−779	−1449	−11	+22
	MeOH	−733	−1401	(−1)^d	(+18)^d
	DMF	−769	−1445	−1	+26
	DMF	−768	−1445	0	+26

^{a} All solutions contain 20% w/w solute with 5% TCTFB internal standard. ^{b} In cycles per second downfield from TCTFB. ^{c} Substituent chemical shifts relative to *trans*-2,2-difluorodecalin in corresponding solvent. ^{d} Relative to the free amine in methanol.

tems in general, and on the ^{19}F nmr chemical shifts of aryl fluorides in particular, can be interpreted in terms of two effects, one involving π polarization by mesomeric or π-inductive mechanisms, and one involving direct electrostatic interactions across space (field effect). While, however, this work seemed to indicate unambiguously the importance of such long-range electrostatic interactions, the results were naturally complicated by the concomitant effects of π polarization; it would obviously be better if one could get similar data for saturated systems where mesomeric effects would be absent.

Evidence of this kind has been presented by Stock and his collaborators[3] for the effects of substituents on chemical reactions of side chains in saturated systems, but very little work has been reported on analogous effects on ^{19}F chemical shifts. The few data reported refer moreover to small monocyclic systems from which no general conclusions can be drawn concerning long-range effects.[4] We have accordingly prepared the compounds listed in Table I and measured their ^{19}F nmr spectra.[5] Table I lists chemical shifts for the axial and equatorial fluorine atoms in these compounds, and also substituent chemical shifts[2] (SCS), *i.e.*, the differences in chemical shift between a given compound and one in which the substituent is replaced by hydrogen.

Several surprising conclusions follow from these results. In the first place, equatorial fluorines in the 2 position of decalin are shielded (rather than deshielded) by +I substituents in the 6 position, while the effect on axial fluorine is small (except in 6,6-difluoro-$\Delta^{1,9}$-2-octalone). If the substituents act by electrostatic polarization of C–F σ bonds, one would expect[2] their effect to be greater on equatorial fluorine than on axial fluorine; however, one would expect the resulting shifts to be in the opposite direction to that observed.

Secondly, no detectable effect is transmitted between the 3 and 17 positions of androstane, although the distance between them is comparable with that between the 3 and 4″ positions in terphenyl. The FM expression[2] for SCS in aromatic compounds predicts significant field effects at this distance, and effects of this kind were observed[2] in 3″-substituted 4-fluoroterphenyls.

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(2) M. J. S. Dewar and P. J. Grisdale, *J. Am. Chem. Soc.*, **84**, 3539, 3541, 3546, 3548 (1962); M. J. S. Dewar and A. P. Marchand, *ibid.*, **88**, 354, 3318 (1966); W. Adcock and M. J. S. Dewar, *ibid.*, **89**, 379, 386 (1967); M. J. S. Dewar and Y. Takeuchi, *ibid.*, **89**, 390 (1967).

(3) See H. D. Holtz and L. M. Stock, *ibid.*, **86**, 5183, 5188 (1964); **87**, 2404 (1965); R. Golden and L. M. Stock, *ibid.*, **88**, 5928 (1966).

(4) See, *e.g.*, J. W. Emsley, *Mol. Phys.*, **9**, 381 (1965); J. Feeney, L. H. Sutcliffe, and S. M. Walker, *ibid.*, **11**, 117, 129 (1966).

(5) All the compounds gave satisfactory analyses, and their other properties (including their proton nmr spectra) were in accordance with the assigned structures; details of their syntheses will be given in the main paper. The ^{19}F nmr spectra were measured at 56.4 MHz with a Varian DP-60 spectrometer, using 5% (w/w) 1,1,2,2-tetrachloro-3,3,4,4-tetrafluorocyclobutane as internal standard and a Hewlett–Packard 200JR oscillator for calibration.

Thirdly, the effects in decalin cannot be due to simple electrostatic polarization, for, if they were, one would expect the SCS of the hydroxy- and aminodecalins to change very greatly on passing to the corresponding salts (RO^- and RNH_3^+) where a neutral dipole has been replaced by a group with a full formal charge. These changes in fact were small, less than that due to replacement of methylene by carbonyl.

These observations seem to suggest that in this system the effects of substituents on the chemical shifts of fluorine are stereochemical rather than electronic, being due to conformational distortion of the decalin skeleton. This would also account for the large SCS of the axial fluorine in the octalone system. Here the ring containing the fluorine is distorted considerably from a normal chair conformation so that the axial fluorine is forced into rather severe steric interaction with protons in the 8 and 10 positions.

In the work[2] on aryl fluorides, it was shown that substituents apparently exercise two different effects, one involving π polarization, the other a direct electrostatic interaction across space on the C–F bond. The results reported here show, however, that this second effect does *not* involve polarization of the C–F σ bond as was previously[2] assumed. The solution of this apparent dilemma lies in the incorrect assumption that has commonly been made, that the effect of a substituent on an adjacent π system depends on localized interactions (π-inductive or mesomeric) *via* the adjacent atom in the ring. In fact, the electrostatic effects of a charged or polar substituent will extend over the whole of an adjacent conjugated system. When a fluorine atom is attached to a conjugated system, the p electrons of the strongly electronegative fluorine will not normally be delocalized into the π system to any great extent, *i.e.*, the C–F bond will have a π bond order of almost zero and the fluorine atom will have a π charge density close to two. Any polarization of the C–F π bond will therefore involve orbitals that are largely concentrated on fluorine. Consequently, if such a polarization is to be brought about by the direct electrostatic (field) effect of a distant polar group, the dominant factor will be the electrostatic field it sets up at the fluorine atom. The field effect of the earlier paper therefore refers to π polarization, not σ polarization, so no corresponding effect is observed in the case of saturated fluorides.

Acknowledgment. We are extremely grateful to Dr. B. A. Shoulders of the University of Texas for his help and advice in obtaining the ^{19}F nmr spectra. We are also indebted to Dr. Pierre Crabbé of Syntex for supplying us with isoandrosterone.

(6) National Science Foundation Postdoctoral Fellow, 1966–1967.

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Received August 28, 1967

Chemical Shifts for Bicyclic Fluorides[1,2]

Sir:

Fluorine chemical shifts may be quite reasonably interpreted within the framework of conventional bond property theory because the paramagnetic term of the Ramsey equation is dominant.[3] This notion and the utility of the magnetic resonance method underlie investigations of substituent effects on ^{19}F resonance.[4] The focus of this work is, quite naturally, directed toward the interpretation of substituent chemical shifts (SCS) for aryl fluorides. Somewhat conflicting views have been expressed concerning the importance of electric field effects on ^{19}F resonance. Thus, Taft[4d–g] has suggested that these effects are small. Dewar, on the other hand, recently proposed that the field effect plays a relatively important role in the determination of the SCS.[4h–j] Emsley, *et al.*,[4k–n] report that the SCS for substituted fluorocarbons are compatible with the electric field theory advanced by Buckingham.[5] Our interest in the origin and transmission of the polar effect[6] prompted this investigation of the influence of sterically remote, unconjugated substituents on the chemical shifts of substituted and unsubstituted bicyclic fluorides.[7] An important feature of the magnetic resonance of bridgehead fluorine atoms is discussed first as a prelude to the interpretation of the substituent effects that were also examined.[8] The results for some *tertiary* fluorides are presented in Table I.

Table I. Chemical Shifts for Some Tertiary Fluorides

Compound	^{19}F chemical shift, ppm[a]
t-Butyl[b]	132
1-Adamantyl[c]	132
1-Bicyclo[2.2.2]octyl[d]	148
1-(4-Carbethoxybicyclo[2.2.2]octyl)[d]	152
1-(4-Carbethoxybicyclo[2.2.2]oct-2-enyl)[d]	164
1-Dibenzobicyclo[2.2.2]octa-2,5-dienyl[d]	191
1-Apocamphyl[d,e]	194

[a] The chemical shifts are reported for the compound in carbon tetrachloride solution relative to fluorotrichloromethane as an external reference. [b] N. Muller and D. T. Carr, *J. Phys. Chem.*, **67**, 112 (1963). [c] R. W. Taft, private communication. [d] This study. [e] A sample of this compound was generously provided by P. Beak.

Table II. Chemical Shifts for Derivatives of 1-Fluorobicyclo[2.2.2]octane

4-Substituent	Substituent chemical shift, ppm[a]
H	0.00
$CO_2C_2H_5$	+4.47
F	+9.23

[a] For carbon tetrachloride.

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(1) Chemistry of the Bicyclo[2.2.2]octanes. VIII. This research was supported by a grant from the National Science Foundation.

(2) We are indebted to M. J. S. Dewar and T. Squires, *J. Am. Chem. Soc.*, **90**, 200 (1968), for delaying publication of their work in order that the results of these parallel studies could appear simultaneously.

(3) M. Karplus and T. P. Das, *J. Chem. Phys.*, **34**, 1683 (1961).

(4) (a) H. S. Gutowsky and C. J. Hoffman, *ibid.*, **19**, 1259 (1951); (b) H. S. Gutowsky, D. W. McCall, B. R. McGarvey, and L. H. Meyer, *J. Am. Chem. Soc.*, **74**, 4809 (1952); (c) L. H. Meyer and H. S. Gutowsky, *J. Phys. Chem.*, **57**, 481 (1953); (d) R. W. Taft, *J. Am. Chem. Soc.*, **79**, 1045 (1957); (e) R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson, and G. T. Davis, *ibid.*, **85**, 709 (1963); (f) R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson, and G. T. Davis, *ibid.*, **85**, 3146 (1963); (g) R. W. Taft and L. D. McKeever, *ibid.*, **87**, 2489 (1965); (h) M. J. S. Dewar and A. P. Marchand, *ibid.*, **88**, 3318 (1966); (i) M. J. S. Dewar and W. Adcock, *ibid.*, **89**, 379 (1967); (j) M. J. S. Dewar and Y. Takeuchi, *ibid.*, **89**, 390 (1967); (k) N. Boden, J. W. Emsley, J. Feeney, and L. H. Sutcliffe, *Mol. Phys.*, **8**, 133 (1964); (l) N. Boden, J. W. Emsley, J. Feeney, and L. H. Sutcliffe, *ibid.*, **8**, 467 (1964); (m) J. W. Emsley, *ibid.*, **9**, 381 (1965); (n) J. Feeney, L. H. Sutcliffe, and S. M. Walker, *ibid.*, 11, 117, 129, 137, 145 (1966).

(5) A. D. Buckingham, *Can. J. Chem.*, **38**, 300 (1960).

(6) (a) H. D. Holtz and L. M. Stock, *J. Am. Chem. Soc.*, **86**, 5188 (1964); (b) R. Golden and L. M. Stock, *ibid.*, **88**, 5928 (1966); (c) F. W. Baker, R. C. Parish, and L. M. Stock, *ibid.*, **89**, 5677 (1967).

(7) The new compounds were identified and characterized by the mode of preparation, by spectroscopic study, and by microanalysis.