Nuclear Magnetic Resonance Spectroscopy. Carbon-13 Chemical Shifts in Norbornyl Derivatives[1]

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Abstract: The ^{13}C chemical shifts for a number of norbornyl derivatives have been obtained in natural abundance. The compounds studied were the series of methylnorbornanes, methylnorbornenes, methyl-2-norbornanones, methyl-2,2-difluoronorbornanes, and a variety of exo- and endo-2-substituted norbornanes. The observed shifts have been interpreted in terms of inductive, bond length, and steric effects. The α- and β-substituent effects are shown to be dependent on the extent of substitution at both the α and β carbon atoms and changes in bond lengths have been used to rationalize the shift changes. Steric interactions between the endo-2 and endo-6 positions, and the exo-2 and syn-7 positions have been shown to generate important chemical-shift changes and these changes can be used as a semiquantitative measure of steric interactions in norbornyl derivatives. Studies with electron-withdrawing groups have revealed a new long-range cmr γ effect produced by exo-2 substituents on C-6. These shifts appear to provide a sensitive and quantitative measure of the electronic demands of a neighboring group as a function of stereochemistry. The substituent shifts obtained from the monosubstituted derivatives have been used to predict the shifts of each of the 1- and 3-methyl-2-norbornanols. The agreement between observed and calculated values is generally good and supports the general approach. Several ^{13}C–^{13}C coupling constants for norbornane, nortricyclene, and quadricyclene are reported and interpreted in terms of the s character of the C–C bonds.

As part of our continuing studies of ^{13}C nmr (cmr) spectroscopy and its application to organic chemistry we have determined the carbon chemical shifts of a series of norbornyl derivatives. These compounds were chosen because the norbornyl skeleton provides a relatively rigid and closely defined framework for the investigation of substituent effects in saturated molecules. Norbornyl derivatives have been utilized by organic chemists in a wide variety of investigations and clearly have some unusual properties.[2] In addition to providing data for elucidation of theories of ^{13}C chemical shifts, the present work shows how ^{13}C spectra can yield important evidence about steric and electronic effects in the ground state of this controversial series of substances. Many cmr substituent parameters have already been derived from studies in conformationally mobile systems and have been interpreted in terms of inductive, steric, and bond delocalization effects.[3-9] Our aim here was to investigate such substituent shift parameters as a function of substituent position and orientation on the norbornane skeleton and hence, to try to delineate further the factors which influence ^{13}C chemical shifts. Investigations of this type have only recently become very feasible as the result of several new techniques, such as the digital-sweep spectrometer[10] and noise[11] and off-resonance proton decoupling,[7,12] as developed in this and other laboratories.

A series of exo-2-substituted norbornanes were used to determine the influence of the nature of the substituent. Various methyl-substituted norbornanes, norbornenes, 2-norbornanones, and 2,2-difluoronorbornanes were studied to investigate the dependence on the position of the substituent. These substituent perturbations will be discussed in terms of α, β, and γ effects—the chemical shifts of carbon atoms further removed from the site of substitution are only slightly affected.

The compounds used in this work were commercial samples or were prepared by standard synthetic procedures (see Experimental Section) and hence their structures were known. Where possible, spectra were obtained using neat samples containing 10% dioxane as internal reference, and chemical shifts were measured with protons decoupled. In a few instances, spectra were determined on mixtures because of separation difficulties. The resonance lines due to each component in the mixture could be readily identified by their intensities because the components were present in unequal amounts in all cases (except for the 1-methylnorbornanols, see Experimental Section). The chemical shifts determined for a compound alone or as a mixture were practically identical. The shifts are considered accurate to ±0.1 ppm unless otherwise stated, and have been converted to the CS_2 scale using the relationship: $\delta_C^{CS_2} = \delta_C^{dioxane} + 125.5$ ppm.

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(1) Supported by the National Science Foundation.

(2) See, for example, P. G. Gassman, J. L. Marshall, J. G. MacMillan, and J. M. Hornback, *J. Amer. Chem. Soc.*, 91, 4282 (1969), and references cited therein.

(3) D. M. Grant and E. G. Paul, *ibid.*, 86, 2984 (1964).

(4) (a) D. M. Grant and B. V. Cheney, *ibid.*, 89, 5315 (1967); (b) B. V. Cheney and D. M. Grant, *ibid.*, 89, 5319 (1967).

(5) D. K. Dalling and D. M. Grant, *ibid.*, 89, 6612 (1967).

(6) T. D. Brown, Ph.D. Thesis, University of Utah, Salt Lake City, Utah, 1967.

(7) J. D. Roberts, F. J. Weigert, J. I. Kroschwitz, and H. J. Reich, *J. Amer. Chem. Soc.*, 92, 1338 (1970).

(8) (a) E. Lippmaa and T. Pehk, *Kem. Teollisuus*, 24, 1001 (1967); (b) E. Lippmaa and T. Pehk, *Eesti NSV Tead. Akad. Toim., Keem., Geol.*, 17, 210 (1968).

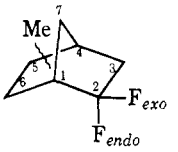
(9) W. J. Horsley, H. Sternlicht, and J. Cohen, *J. Amer. Chem. Soc.*, 92, 680 (1970).

(10) F. J. Weigert and J. D. Roberts, *ibid.*, 89, 2967 (1967); *ibid.*, 90, 3543 (1968).

(11) (a) F. J. Weigert, M. Jautelat, and J. D. Roberts, *Proc. Natl. Acad. Sci. U. S.*, 60, 1152 (1968); (b) L. F. Johnson and M. E. Tate, *Can. J. Chem.*, 47, 63 (1969).

(12) L. F. Johnson, personal communication.

Table I. ^{13}C and ^{19}F Chemical Shifts of the Methyl-2,2-difluoronorbornanes[a] and *exo*-Fluoronorbornane



Methyl of 2,2-difluoronorbornane	C-1	C-2	C-3	C-4	C-5	C-6	C-7	CH_3	F_{exo}[b]	F_{endo}[b]
None	147.6	61.4	149.8	156.3	165.1	171.7	155.6		86.2	109.3
1-	143.8	62.3	149.2	157.2	162.9	163.7	149.5	180.3	94.3	116.7
exo-3-	147.6*	61.6	145.7*	148.9	163.9	171.5	158.3	180.6	104.8	109.6
endo-3-	148.5*	63.2	146.9*	151.3	172.4	171.6	156.5	183.5	84.6	120.6
exo-5-	146.9	61.5	149.0	150.0	157.9	161.9	159.1	171.0	86.2	108.0
endo-5-	146.5	61.5	157.1	151.2	160.3	163.3	154.0	176.4	83.7	110.1
exo-6-	141.1	61.5	150.6	156.0	154.7	165.4	159.1	172.0	85.5	110.0
endo-6-	143.0	61.0	149.0	156.4	156.2	160.2	153.8	174.7	74.1	101.8
syn-7-	143.7	61.1	152.2	151.4	164.8	170.5	147.3	180.3	81.4	97.8
anti-7-	143.4	61.9	148.4	152.4	168.0	174.6	150.4	181.0	86.5	106.5
exo-2-Fluoro-norbornane	150.4	96.9	152.7	157.9	164.5	170.2	157.5		158.9	

[a] The ^{13}C shifts are in parts per million upfield from CS_2 and are considered accurate to ±0.1 ppm; the asterisks designate pairs of shifts which have been assigned for consistency with other shift data, although there is a possibility that the assignments should be interchanged. [b] The ^{19}F shifts are in parts per million upfield from $CFCl_3$ and are considered accurate to ±0.3 ppm.

Table II. ^{13}C–^{19}F Coupling Constants of the Methyl-2,2-difluoronorbornanes and *exo*-2-Fluoronorbornane[a]

Methyl of 2,2-difluoro-norbornane	C-1	C-2	C-3	C-4	C-6	C-7	CH_3
None	24.1, 22.0	253.9, 253.9	24.3, 22.0	5.4, 2.8	5.8, 5.8	4.9	
1-	21.9, 21.9	256.5, 256.5	24.7, 22.7	4.5, 2.6	6.3, 4.2	5.3	4.0
exo-3-	24.0, 21.8	258, 258	24.0, 20.3	5.6, 1.2	5.8, 5.8	4.7	14.1, 2.7
endo-3-	24.2, 22.4	259.9, 252.6	22.4, 22.1	4.4, 1.9	6.9, 5.9	5.8	1.5, 9.7
exo-5-	23.0, 21.8	255.0, 250.2	23.6, 21.6	3.2, 3.2	6.0, 6.0	5.0	<1
endo-5-	23.5, 21.3	254.0, 251.6	24.6, 21.8	4.2, 2.2	6.0, 6.0	4.0	<1
exo-6-	22.3, 20.9	255.0, 250.2	23.1, 21.1	4.6, 2.0	5.8, 5.8	5.0	~1
endo-6-	22.3, 19.1	257.3, 250.3	21.8, 21.8	*b*	3.4, 3.4	5.2	<1, 7.0
syn-7-	20.7, 20.7	253, 253	25.4, 21.6	4.0, 3.0	8.1, 6.8	5.5	4.5, <1
anti-7-	22.6, 20.6	254.5, 254.5	24.1, 21.7	3.5, 2.6	5.8, 5.8	4.3	<1
exo-2-Fluoro-norbornane	20.2	182.0	20.4	2.3	9.8	<1	

[a] All coupling constants are in hertz and are considered accurate to ±0.5 Hz, except at C-2 where the error is ±2 Hz. The couplings to C-5 were all less than 1 Hz. The first datum in each case where two are given is believed to be that for the coupling to the *exo*-fluorine. The assignments of the exo- and endo-coupling constants were subject to considerable uncertainties and attempts to establish these unequivocally by decoupling experiments were not successful. [b] Not determined because of overlapping signals.

Assignments

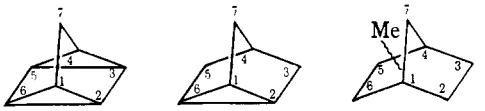
A. Fluorides and C–F Coupling Constants (Tables I and II). The observation of C–F coupling constants and their dependence on the number of intervening bonds allows a straightforward assignment of the carbons in the various methyl 2,2-difluoronorbornanes.[13] The large one-bond coupling $^1J_{CF}$ (*ca.* 250 Hz) and the large downfield shift readily identified the α carbon (C-2). The β carbons (C-1 and C-3) appeared as a pair of doublets with coupling constants of about 22 Hz. In order to differentiate these two positions, additional criteria were invoked: (i) the tertiary bridgehead carbon (C-1) absorbs downfield of the secondary carbon and (ii) substitution of a methyl group causes a downfield shift at both the α and β carbons. These facts allow an unambiguous choice between carbons 1 and 3 for all but the 3-substituted compounds where the assignments were made to achieve consistency with the other members of the series. In fact, there is no compelling reason why the shifts of C-1 and C-3 for the 3-substituted compounds may not be reversed. However, differences are small, and reversal of the assignments will have little effect on the arguments presented below.

The three-bond coupling constants $^3J_{CF}$ were different for each of the γ carbon atoms (C-4, C-6, and C-7) and thus these positions could be identified through the series. The coupling constants in *exo*-2-fluoronorbornane (see below), and the effect of methyl substitution allowed positive identification of these carbon atoms. This variation in $^3J_{CF}$ (especially the fact that only the *endo*-fluorine appears to be coupled to C-7) has important bearing on the theory of coupling constants between heavy nuclei, because it shows that a through-space interaction contributes significantly to the overall effect (presumably *via* a back-lobe overlap mechanism).[14] Carbons more than three bonds re-

(13) J. B. Dence and J. D. Roberts, *J. Amer. Chem. Soc.*, 91, 1542 (1969).

(14) M. Barfield, *J. Chem. Phys.*, 41, 3825 (1964). For a different

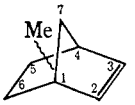
Table III. ^{13}C Chemical Shifts of Hydrocarbons Related to Norbornane[a]



Compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	CH_3
Quadricyclene	169.6	177.8	177.8	169.6	177.8	177.8	160.6	
Tricyclene	182.9	182.9	159.6	163.1	159.6	182.9	159.6	
Norbornane	156.0	162.7	162.7	156.0	162.7	162.7	154.1	
1-Methylnorbornane	148.7	155.7	161.2	154.6	161.2	155.7	147.2	171.8
exo-2-Methylnorbornane	149.3	156.0	152.6	155.5	162.5*	163.8*	157.8	170.5
endo-2-Methylnorbornane	150.6	158.2	152.1	154.6	162.2	170.4	153.9	175.4
7-Methylnorbornane	151.8	165.6	165.6	151.8	161.8	161.8	148.5	180.1

[a] See footnotes to Table I.

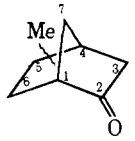
Table IV. ^{13}C Chemical Shifts of Norbornenes[a]



Compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	CH_3
Norbornene	150.6	57.3	57.3	150.6	167.3	167.3	144.0	
1-Methylnorbornene	142.9	52.8	57.0	149.5	164.8	160.2	137.8	174.8
exo-5-Methylnorbornene	150.1	55.6*	56.6*	144.1	159.8	157.8	147.8	171.1
endo-5-Methylnorbornene	149.2	55.6	60.3	145.0	159.8	158.6	142.3	173.3
syn-7-Methylnorbornene	145.0	60.4	60.4	145.0	166.9	166.9	138.1	180.3
anti-7-Methylnorbornene	146.8	55.0	55.0	146.8	171.0	171.0	139.5	178.4
Norbornadiene	141.9	49.4	49.4	141.9	49.4	49.4	117.4	

[a] See footnotes to Table I.

Table V. ^{13}C Chemical Shifts of Methyl-2-norbornanones[a]



Methyl of 2-norbornanone	C-1	C-2	C-3	C-4	C-5	C-6	C-7	CH_3
None[b]	142.7	−22.5	147.6	156.6	165.1	168.5	154.9	
1-[b]	139.2	−23.4	147.3	158.1	163.5*	161.0*	148.6	178.8
exo-3-	143.2*	−25.1	144.6*	150.9	164.4	168.9	158.4	178.7
endo-3-[b]	142.4*	−24.7	144.5*	151.9	171.6	167.2	155.5	182.1
exo-5-	142.1	−22.7	147.4	150.5	159.2	157.9*	158.6*	170.8
endo-5-	141.4	−22.1	154.1	151.9	159.8	159.3	153.5	175.6
exo-6-	136.1	−23.0	148.8	156.4	155.0*	161.5	158.6*	171.9
endo-6-	136.7	−21.0	146.9	156.7	153.9	160.1	156.5	174.0
syn-7-	137.6	−23.1	152.5	152.8	163.7	168.3	148.9	179.9
anti-7-	138.5	−22.3	145.5	152.6	167.9	171.5	150.0	180.7

[a] See footnotes to Table I. [b] The resonances and assignments agree well with those reported by E. Wenkert, A. O. Clouse, D. W. Cochran, and D. Doddrell, *Chem. Commun.*, 1433 (1969).

moved (*i.e.*, C-5 and the methyl carbons) did not appear to be coupled to the fluorines unless they were close together in space as for the *syn*-7- and *endo*-6-methyl derivatives.

The *exo*-2-fluoronorbornane coupling constants are in accord with those found for the difluorides with the exception of $^1J_{CF}$ which has a value of 180 Hz. This increase (assuming a negative sign) in the algebraic sense is in accord with other studies on the series of fluoromethanes.[15]

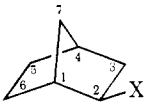
treatment of these couplings, see M. Karplus and M. Barfield, *J. Amer. Chem. Soc.*, 91, 1 (1969).

(15) S. G. Frankiss, *J. Phys. Chem.*, 67, 752 (1963).

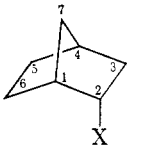
The assignments presented here clearly demonstrate the great utility of fluorine substitution for the identification of ^{13}C resonances.

B. Nonfluorinated Norbornanes (Tables III–VII). In the few examples where an element of symmetry was present, an initial (and in the case of norbornane, complete) assignment of shifts could be made on the basis of intensities. Generally, however, the off-resonance proton-decoupled spectrum provided the first step toward the assignment because this technique separates the carbons according to the number of directly attached hydrogens. Then, if the proton spectrum of the compound could be assigned, the determination of the

Table VI. ^{13}C Chemical Shifts of exo- and endo-2-Substituted Norbornanes[a]



X	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C_x
H	156.0	162.7	162.7	156.0	162.7	162.7	154.1	
CH_3	149.3	156.0	152.6	155.5	162.5*	163.8*	157.8	170.5
NH_2	147.1	137.4	150.3	156.4	163.9*	165.8*	158.5	
OH	148.3	118.4	150.4	157.0	164.0	167.9	158.2	
F	150.4	96.9	152.7	157.9	164.5	170.2	157.5	
CN	150.5	161.7	156.4	156.3	164.2*	164.3*	155.4	69.4
COOH	151.4	146.0	158.3	156.2	163.0*	163.7*	155.9	11.4
$COOCH_3$	150.9	146.3	158.5	156.4	163.8*	164.1*	156.2	17.1
CH_2OH	154.2	147.6	158.3*	156.2	162.5*	163.4*	157.4*	126.4



CH_3	150.6	158.2	152.1	154.6	162.2	170.4	153.9	175.4
NH_2	149.2	139.4	152.2*	154.8	162.1	172.2	153.8*	
OH	149.7	120.3	153.2*	155.1	162.5	172.4	155.0*	
F								
CN	152.6	162.6	157.2	155.8	163.4	167.6	154.1	70.2
COOH	151.8	146.5	160.6	155.1	163.3	167.5	152.2	12.3
$COOCH_3$	152.0	146.8	160.5	155.3	163.4	167.7	152.4	18.2
CH_2OH	154.3	149.9	158.7	155.6	162.5	169.9	152.7	128.5

[a] See footnotes to Table I.

exact proton-decoupling frequency for each carbon provides an unambiguous identification of each resonance. The specific decoupling technique was particularly useful in assigning C-2 for the compounds in Table VI (apart from 2-methylnorbornane), also C-7 and the bridgehead carbons. Thus, positive identification could be obtained for the majority of carbons in the series of molecules.

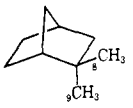
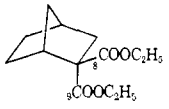
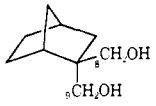
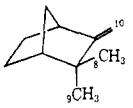
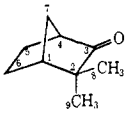
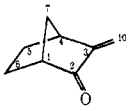
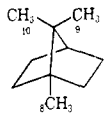
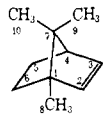
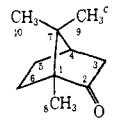
The data obtained in this way provided a framework on which the remaining assignments could be made because a number of characteristic features were evident. Thus, only the α, β, and those γ carbons which were in close proximity were affected markedly by the substituent. Second, substituent parameters were found to be transferable between reasonably related molecules and were approximately additive. Application of the substituent effects to the peaks which could not be identified directly normally permitted complete sets of assignments, except a few cases where the resonances in question had similar chemical shifts. An example of the general procedure is set out below.

Table VIII shows the observed chemical shifts, the multiplicities observed in off-resonance proton-decoupled spectra (*i.e.*, number of directly attached hydrogens) and specific proton-decoupling frequencies relative to dioxane for *endo*-5-methyl-2-norbornene. The arguments for the assignment of the particular resonances follow. The peaks at 55.6 and 60.3 ppm are immediately identified as C-2 and C-3 (but not differentiated) on the basis of the ^{13}C chemical shifts, multiplicities, and specific decoupling frequencies. The 173.3-ppm absorption appears as a quartet in the off-resonance decoupled spectrum and thus must be the methyl carbon. There are two absorptions at 158.6 and 142.3 ppm which appear as triplets when partially decoupled and must be C-6 and C-7. The large chemical-shift difference between these carbons allows their differentiation by comparison with the corresponding shifts in norbornene which are accurately known. The difference in the proton-decoupling frequencies is too small to be useful in this case. The remaining three lines at 145.0, 149.2, and 159.8 ppm must belong to C-1, C-4, and C-5, and they appear as doublets in the off-resonance spectrum. The peak at 159.8 is identified as C-5 by the proton-decoupling frequency. Now, we know that a methyl group causes a substantial downfield shift at positions β to the point of substitution, and since C-4 is β to the methyl, we can assign the peak at 145.0 to it and this leaves C-1 as the remaining absorption at 149.2. The question still remains as to how to choose between the unsaturated carbon atoms. We can see from the difference between *syn*- and *anti*-7-methylnorbornene that steric interaction between a methyl group and the π cloud of an alkene causes an upfield shift of the unsaturated carbons. In addition, the *exo*-5-methyl compound shows only a slight influence of the methyl substituent on positions 2 and 3. Thus, we conclude that steric interactions cause an upfield shift at C-3 and hence the 60.3-ppm resonance is assigned to that position. *A priori*, there is no reason why this assignment might not be reversed; however, all our present information on steric effects agrees with the assignment given.[16]

Comparison with Other Studies. The ^{13}C chemical shifts of some of the simpler members of this group of compounds have been reported by other workers.[8a,17]

(16) The suggestion has been made that the presence of an endo (or exo) substituent will cause a twisting of the norbornyl skeleton and that the major steric interaction will be between positions 2 and 5, rather than 2 and 6. This hypothesis can be ruled out by the data for the methyldifluoronorbornanes where the assignment depends on C–F coupling constants. In these compounds, the shifts clearly demonstrate that it is the endo-2,6-type interaction which is important.

Table VII. ^{13}C Chemical Shifts of Some gem-Substituted Norbornanes[a]

Compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
	144.7	155.9	145.6	154.0	164.1	167.8	154.2	161.2	165.6	
	148.9	131.4	153.8	156.0	164.7	167.5	153.0	20.9[b]	22.0[b]	
	152.5	145.6	154.6	155.6	163.7	168.0	155.0	125.3	126.6	
	144.1	150.8	27.1	145.4	163.1	166.7	155.0	163.6	168.6	93.0
	146.3	146.0	−26.6	143.6	168.1*	169.1*	157.6	169.4	171.2	
	143.6	−11.0	41.8	150.0	164.3	169.0	155.9			82.1
	145.8	156.0	164.1	146.5	164.1	156.0	147.5	177.0	173.6	173.6
	139.9*	53.0	58.5	140.1	168.0	160.9	136.2*	179.4	172.9*	173.1*
	135.4	−23.9	149.6	149.2	165.5*	162.6*	146.0	183.3	172.9*	173.5*

[a] See footnotes to Table I. [b] C_2H_5 resonances at 131.7, 132.0, 178.6, and 178.7 ppm. [c] The resonances and assignments agree well with those reported by E. Wenkert, A. O. Clouse, D. W. Cochran, and D. Doddrell, *Chem. Commun.*, 1433 (1969).

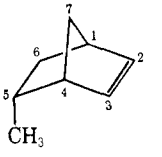
Our results are generally in satisfactory agreement with other slow passage studies. The results of Lippmaa and Pehk[8a] on the unsubstituted hydrocarbons agree with the present data within their stated error limits of ±1 ppm. Olah and White[17] have recently reported shifts of norbornane which differ from those given here by a constant factor of 1.4 ppm. This would indicate that the discrepancy is due to the choice of reference. It is perhaps worth noting that both the other groups used external references (CS_2 and TMS, respectively), and both groups report more upfield shifts than we do.

Discussion

The data presented in Tables IX–XII demonstrate that a substituent may substantially influence the chemical shift of the α (directly attached), β, and γ carbons. While the smaller and more subtle changes at positions further removed may prove to be important in the future, we will restrict our discussion here to the α, β, and γ effects.

(17) G. A. Olah and A. M. White, *J. Amer. Chem. Soc.*, 91, 3954 (1969).

Table VIII. Multiplicities and Specific Decoupling Frequencies for *endo*-5-Methylnorbornene



δ	Multiplicity[a]	Proton decoupling[b]	Assignment
55.6	Doublet	−1.2	C-2
60.3	Doublet	−1.2	C-3
142.3	Triplet	1.2	C-7
145.0	Doublet	0.3	C-4
149.2	Doublet	0.4	C-1
158.6	Triplet	1.2	C-6
159.8	Doublet	0.7	C-5
173.3	Quartet	1.4	CH_3

[a] Off-resonance. [b] Relative to dioxane in parts per million.

Table IX. Substituent Chemical Shifts for 2-Substituted Norbornanes[a]

Substituent	C-1	C-2	C-3	C-4	C-5	C-6	C-7
			exo Derivatives				
CH_3	−6.7	−6.7	−10.1	−0.5	−0.2	1.1	3.7
NH_2	−8.9	−25.3	−12.4	0.4	1.2	3.1	4.4
OH	−7.7	−44.3	−12.3	1.0	1.3	5.2	4.1
F	−5.6	−65.8	−10.0	1.9	1.8	9.5	3.4
CN	−5.5	−1.0	−6.3	0.3	1.5	1.6	1.3
COOH	−4.6	−16.7	−4.4	0.2	0.3	1.0	1.8
$COOCH_3$	−5.1	−16.4	−4.2	0.4	1.1	1.4	2.1
CH_2OH	−1.8	−15.1	−4.4	0.2	−0.2	0.7	3.3
			endo Derivatives				
CH_3	−5.4	−4.5	−10.6	−1.4	−0.5	7.7	−0.2
NH_2	−6.8	−23.3	−10.5	−1.2	−0.6	9.5	−0.3
OH	−6.3	−42.4	−9.5	−0.9	−0.2	9.7	0.9
F							
CN	−3.4	−0.1	−5.5	−0.2	0.7	4.9	0.0
COOH	−4.2	−16.2	−2.1	−0.9	0.6	4.8	−1.9
$COOCH_3$	−4.0	−15.9	−2.2	−0.7	0.7	5.0	−1.7
CH_2OH	−1.7	−12.8	−4.0	−0.4	−0.2	7.2	−1.4

[a] Substituent shifts are in parts per million relative to norbornane; a minus sign denotes a downfield shift on substitution.

Table X. Difference between Shifts of exo- and endo-2-Substituted Norbornanes[a]

Substituent	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C_{subs}
CH_3	1.3	2.2	−0.5	−0.9	−0.3	6.6	−3.9	4.9
NH_2	2.1	2.0	1.9	−1.6	−1.8	6.4	−4.7	
OH	1.4	1.9	2.8	−1.9	−1.5	4.5	−3.2	
F								
CN	2.1	0.9	0.8	−0.5	−0.8	3.3	−1.3	0.8
COOH	0.4	0.5	2.3	−1.1	0.3	3.8	−3.7	0.9
$COOCH_3$	1.1	0.5	2.0	−1.1	−0.4	3.6	−3.8	1.1
CH_2OH	0.1	2.3	0.4	−0.6	0.0	6.5	−4.7	2.1

[a] A minus sign denotes that the resonance of the endo compound is downfield of the resonance in the equivalent exo compound.

Differences between exo and endo Substituents. Differences between exo and endo substituents at C-2 for a range of compounds are shown in Table X. The corresponding data for epimeric methyl groups in several derivatives can be seen in Table XI. If data for C-6 and C-7 are excluded from the comparison—because there is a marked steric interaction at these positions (see the later discussion of γ effects)—it is clear that the orientation of the substituent has very little influence on chemical shift. The observed shift differences between epimers are an order of magnitude smaller than the α or β shifts associated with the substituents. However, it should be noted that the direction of the shift at each position is usually the same over the series and may be a direct measure of interaction between the substituent and the remote position. On the other hand, it is conceivable that these shifts reflect an overall distortion of the norbornyl skeleton, rather than being a function of the substituent itself. Thus, we conclude that whatever the underlying cause of ^{13}C chemical shifts, it is only marginally dependent on the orientation of the perturbing group (excluding, of course, direct steric interaction which is well known to be an important factor in ^{13}C shifts).

The α and β Effects. Several workers[6,8,9] have measured α-substituent effects on ^{13}C chemical shifts in simple alkanes and have interpreted their results in terms of electronegativity effects—at least for substituents composed of first-row elements. A corresponding β effect has been noted, but has defied explanation since it has been found to be essentially independent of the nature of the substituent.[3-8] Consideration of the norbornyl results presented here reveals consistent trends with substitution which suggests that a reexamination of the earlier data might be fruitful.

The α effect of both exo- and endo-2 substituents appears to be smaller (in magnitude) than the effect of the same substituent in simple alkanes. The α effect of a methyl group is essentially independent of the point of substitution with the exception of two groups of compounds. When the methyl group replaces a hydrogen which is generating a sterically induced upfield shift at the carbon in question, the α effect is always larger. The observed shift can be regarded as the sum of a normal α effect and the change in the steric shift. When the carbon adjacent to the point of substitution is fully substituted (*i.e.*, a carbonyl or CF_2 group), the observed α shift is smaller than expected.

Turning to the β effect, a substituent at C-2 always shifts C-3 more than C-1, but this shift is essentially independent of the nature of the substituent (see Table IX). In addition, the β shift induced by a methyl group in various positions is dependent on the degree of substitution at the α and β carbons, but is independent of other changes in the system (see Table XI). These observations suggest that the α and β effect in cmr are mutually dependent on the degree of substitution at both positions and that this reflects the replacement of hydrogen, rather than the nature of the incoming group. In order to check this idea, the data for substituted alkanes reported by Grant and Paul[3] and the results for substituted alcohols obtained in this laboratory[7] were considered.

Examination of the shifts for acyclic hydrocarbons and alcohols quickly revealed that the α and β shifts are dependent on the degree of substitution in a rather consistent way. The effect at the α and β positions of a hydroxyl group (Table XIII), a methyl group (Table XIV), and a methyl group when there is already a hydroxyl group at the position in question (Table XV), can be sorted according to the number of hydrogens at the α position (m) and the number at the β position. The parameter used to measure the β hydrogen effect (n) was the total number of substituents other than hydrogen on the β carbons. For example, if we are considering the effect of hydroxyl substitution at C-3 in 2-methylpentane, this would be listed in Table XIII under $m = 1$ (because there is one hydrogen remaining at C-3 after substitution) and $n = 3$ (because there are a total of three substituents at the β carbons—two at C-2 and one at C-4).

In many instances, there are several values available for particular entries in the tables which fall within a narrow range and so for these only the average value is listed. The tables show that replacement of a hydrogen at either the α or the β position results in a decrease in the magnitude of both the α and β shift by approximately 3 ppm. Although the absolute value of the shift in each table varies widely, the same trend is observed in each case and the differences between each pair of items in all three tables are nearly the same. Thus, it seems that there is a fundamental value for the

Table XI. Methyl Substitutent Effects in Norbornyl Derivatives[a]

Methyl	Designation of effect	Substrate: Alkane	Alkene	Ketone	Difluoride	Designation of effect	Substrate: Alkane	Alkene	Ketone	Difluoride
	C-1					C-2				
1-	α	−7.3	−7.7	−3.5	−3.8	β	−7.0	−4.5	−0.9	0.9
exo-3-	γ	−0.5		0.5	0.0	β	−10.1		−2.6	0.2
endo-3-	γ	−1.4		−0.3	0.9	β	−10.6		−2.2	1.8
exo-5-	γ	−0.5	−0.5	−0.6	−0.7	δ	−0.2	−1.7	−0.2	0.1
endo-5-	γ	−1.4	−1.4	−1.3	−1.1	δ	−0.5	−1.7	0.4	0.1
exo-6-	β	−6.7	−6.5	−6.6	−6.5	γ	1.1	−0.7	−0.5	0.1
endo-6-	β	−5.4	−5.6	−6.0	−4.6	γ	7.7	3.0	1.5	−0.4
syn-7-	β	−4.2	−5.6	−5.1	−3.9	γ	2.9	3.1	−0.6	−0.3
anti-7-	β	−4.2	−3.8	−4.2	−4.2	γ	−0.9	−2.3	0.2	0.5
	C-3					C-4				
1-	γ	−1.5	−0.3	−0.3	−0.6	γ	−1.4	−1.1	1.5	0.9
exo-3-	α	−6.7		−3.0	−4.1	β	−6.7		−5.7	−7.4
endo-3-	α	−4.5		−3.1	−2.9	β	−5.4		−4.7	−5.0
exo-5-	γ	1.1	−0.7	−0.2	−0.8	β	−6.7	−6.5	−6.1	−6.3
endo-5-	γ	7.7	3.0	6.5	7.3	β	−5.4	−5.6	−4.7	−5.1
exo-6-	δ	−0.2	−1.7	0.8	0.8	γ	−0.5	−0.5	−0.2	−0.3
endo-6-	δ	−0.5	−1.7	−0.7	−0.8	γ	−1.4	−1.4	0.1	0.1
syn-7-	γ	2.9	3.1	4.9	2.4	β	−4.2	−5.6	−3.8	−4.9
anti-7-	γ	−0.9	−2.3	−2.1	−1.4	β	−4.2	−3.8	−4.0	−3.9
	C-5					C-6				
1-	γ	−1.5	−2.5	−1.6	−2.2	β	−7.0	−7.1	−7.5	−8.0
exo-3-	γ	1.1		−0.7	−1.2	δ	−0.2		0.4	−0.2
endo-3-	γ	7.7		6.5	7.3	δ	−0.5		−1.3	−0.1
exo-5-	α	−6.7	−7.5	−5.9	−7.2	β	−10.1	−9.5	−10.6	−9.8
endo-5-	α	−4.5	−7.5	−5.3	−4.8	β	−10.6	−8.7	−9.2	−8.4
exo-6-	β	−10.1	−9.5	−10.1	−10.4	α	−6.7	−7.5	−7.0	−6.3
endo-6-	β	−10.6	−8.7	−11.2	−8.9	α	−4.5	−7.5	−8.4	−11.5
syn-7-	γ	−0.9	−0.4	−1.4	−0.3	γ	−0.9	−0.4	−0.2	−1.2
anti-7-	γ	2.9	3.7	2.8	2.9	γ	2.9	3.7	3.0	2.9
	C-7									
1-	β	−6.9	−6.2	−6.3	−6.1					
exo-3-	γ	3.7		3.5	2.7					
endo-3-	γ	−0.2		0.6	0.9					
exo-5-	γ	3.7	3.8	3.7	3.5					
endo-5-	γ	−0.2	−1.7	−1.4	−1.6					
exo-6-	γ	3.7	3.8	3.7	3.5					
endo-6-	γ	−0.2	−1.7	1.6	−1.8					
syn-7-	α	−5.6	−5.9	−6.0	−8.3					
anti-7-	α	−5.6	−4.5	−4.9	−5.2					

[a] Effect of methyl group in parts per million at designated position relative to norbornane, norbornene, 2-norbornanone, and 2,2-difluoronorbornane, respectively.

Table XII. Effect of 2-Keto and Difluoro Functions on Methylnorbornanes[a]

Methyl of norbornane	Relation to functional group: C-1 β	C-2 α	C-3 β	C-4 γ	C-5 δ	C-6 γ	C-7 γ	CH_3
				Ketone				
None	−13.3	−185.2	−15.1	0.6	2.4	5.8	0.8	
1-	−9.5	−179.1	−13.9	3.5	2.3	5.3	1.4	7.0 (γ)
exo-3-	−12.3	−177.7	−11.4	1.6	0.6	6.4	0.6	8.2 (γ)
endo-3-	−12.2	−176.8	−13.7	1.3	1.2	5.0	1.6	6.7 (γ)
exo-5-	−13.4	−185.2	−16.4	1.2	3.2	5.3	0.8	0.3 (ε)
endo-5-	−13.2	−184.3	−16.3	1.3	1.6	7.2	−0.4	0.2 (ε)
exo-6-	−13.2	−186.8	−13.7	0.9	2.4	5.5	0.8	1.4 (δ)
endo-6-	−13.9	−191.4	−15.3	2.1	1.8	1.9	2.6	−1.4 (δ)
sun-7-	−14.2	−188.7	−13.1	1.0	1.9	6.5	0.4	−0.2 (δ)
anti-7-	−13.3	−184.1	−16.3	0.8	2.3	5.9	1.5	0.6 (δ)
				Difluoride				
None	−8.4	−101.3	−12.9	0.3	2.4	9.0	1.5	
1-	−4.9	−93.4	−12.0	2.6	1.7	8.0	2.3	8.5 (γ)
exo-3-	−7.9	−91.0	−10.3	−0.4	0.1	9.0	0.5	10.1 (γ)
endo-3-	−6.1	−88.9	−11.3	0.7	2.0	9.4	2.6	8.1 (γ)
exo-5-	−8.6	−101.0	−14.8	0.7	1.9	9.3	1.3	0.5 (ε)
endo-5-	−8.1	−100.7	−13.3	0.6	2.1	11.2	0.1	1.0 (ε)
exo-6-	−8.2	−102.3	−11.9	0.5	2.1	9.4	1.3	1.5 (δ)
endo-6-	−7.6	−109.4	−13.2	1.8	4.1	2.0	−0.1	−0.7 (δ)
syn-7-	−8.1	−104.5	−13.4	−0.4	3.0	8.7	−1.2	0.2 (δ)
anti-7-	−8.4	−99.9	−13.4	0.6	2.4	9.0	1.9	0.9 (δ)

[a] Shifts are reported relative to appropriate methylnorbornane, *i.e.*, $\Delta = \delta_{\text{methyl ketone}} - \delta_{\text{methylnorbornane}}$.

Table XIII. The Effect of Introduction of a Hydroxyl Group as a Function of Degree of Substitution[a]

n	$m = 3$	$m = 2$	$m = 1$	$m = 0$
		Effect at α Carbon		
0	−51.3	−51.4	−47.6	−43.5
1		−48.3	−44.5	−40.7
2		−45.0	−40.7	−38.4
3		−41.4	−37.2	−36.3
4			−32.4	
5			−29.7	
		Effect at β Carbon		
0		−11.6	−9.7	−7.3
1		−10.2	−7.6	−5.0
2		−6.9	−5.2	−5.0
3		−5.0	−4.9	−4.9

[a] Here m is the number of hydrogens on the α carbon; n is the number of substituents other than hydrogen at the β carbons. All shifts are in parts per million.

Table XIV. The Effect of Introduction of a Methyl Group as a Function of Degree of Substitution[a]

n	$m = 3$	$m = 2$	$m = 1$	$m = 0$
		Effect at α Carbon		
0	−8.0	−10.2	−9.1	−2.7
1		−9.3	−5.1	−3.0
2		−7.4	−2.6	1.2
3		−5.2	−0.3	2.8
		Effect at β Carbon		
0		−9.7	−8.8	−7.2
1		−9.4	−7.1	−4.7
2		−6.2	−4.3	−4.0
3		−2.5	−2.5	−2.4

[a] See footnote to Table XIII.

Table XV. The Effect of a Methyl Group in the Presence of a Hydroxyl Group[a]

n	$m = 2$	$m = 1$	$m = 0$
	Effect at α Carbon[b]		
0			
1	−8.1	−6.4	−6.9
2		−5.3	−1.6
3		−3.1	−0.2
	Effect at β Carbon[b]		
0			
1	−6.6	−5.4	−3.7
2	−5.3	−3.6	−2.3
3	−1.9	−1.8	−1.9

[a] See footnote to Table XIII. [b] The α carbon already carries a hydroxyl substituent.

α shift and for the β shift for each substituent, which is presumably inductive in origin. These fundamental values are incremented by rather constant amounts and the number of such increments is determined by the number of substituents at the α and β carbons. More important, the amounts of these changes are surprisingly independent of whether the hydrogens are replaced at the α or β position, the nature of the replacing group, or the rotational conformation about the C_α–C_β bond. The principal systematic deviation from these correlations is the fact that a limiting value for the β shift of methyl and hydroxyl groups appears to be attained for the more highly substituted cases, that is with smaller m and larger n. There also appears to be a trend for the β carbon shift to be less sensitive to the degree of substitution than the α carbon—independent of whether substitution is at the α or β carbon.

An alternate way to correlate the results is to consider the total number of hydrogens replaced at the α and β carbons to be the important parameter. Plots of the α and β effect for methyl and hydroxyl substituents against the number of hydrogens removed, are shown in Figures 1–4. These plots clearly show that, provided one ignores the absolute scale of the chemical shifts, methyl and hydroxyl groups have equivalent effects on the α and β shifts, and that the rate of change of shift with hydrogen replacement is greater at the α than at the β position (3.5 ppm per hydrogen and 2.4 ppm per hydrogen, respectively).[18]

We conclude that there is a parameter associated with changes in the C_α–C_β bond which gives rise to the variations in the α and β shifts of substituents. In other words, the α effect consists of a basic inductive effect (which determines the scale of operation) and a variable term which is governed by the state of the C_α–C_β bond. The β effect also has a basic component plus an adjustable term determined by the C_α–C_β bond.

The question now arises as to what is the mechanism of this bond-dependent shift change. Clearly, the presence or absence of hydrogen on the carbon atoms in question is playing a vital role. Hydrogen differs from other substituents in two ways—it is the only substituent considered here which does not have p electrons to use in bonding to carbon; it is the smallest substituent and hence, allows the greatest variation in the spatial requirements of the attached carbon. At this time, we are unable to offer a theoretical justification for this phenomenon. Qualitatively, there is a quandary—whether to take as the basic inductive effect of the substituent (which defines the absolute scale of the substituent shift) the effect apparent in the fully substituted or the fully hydrogenated member of a series. If one looks at the β effect, the constant value obtained for the more substituted members suggests that this represents the true inductive effect and that introduction of hydrogen causes an increase in the magnitude of the effect. On the other hand, the α effect shows no sign of levelling off with increasing substitution. Also, if the fully substituted compound were taken as the reference point, one would expect the α effect for introduction of a substituent into ethane to be smaller (in magnitude) than for its introduction into the central carbon of isobutane, since the latter has more hydrogen substituents. The reverse is observed. If one starts with the premise that the fully hydrogenated example represents the true inductive effect, one is again faced with a dilemma. One must now accept that the inductive effect of a methyl group at the α position and the effect of a methyl or hydroxyl group at the β position are essentially the same. There is also the problem as to why the β effect attains a constant value, while the α effect steadily decreases in size with increasing substitution. It has been implicitly assumed in this discussion that the chemical shift provides a measure of the chemical inductive effect of a substituent, but the possibility cannot be overlooked that the observed effect is a combination of magnetic and chemical influences.

(18) Since this paper was submitted for publication, L. M. Jackman and D. P. Kelly, *J. Chem. Soc. B*, 102 (1970), have reported carbon shifts for a number of methyl-substituted alcohols and ketones which agree satisfactorily with those we have recently published.[7] These authors also point out the importance of the number of hydrogens attached to the β carbon atoms as a factor influencing chemical shifts.

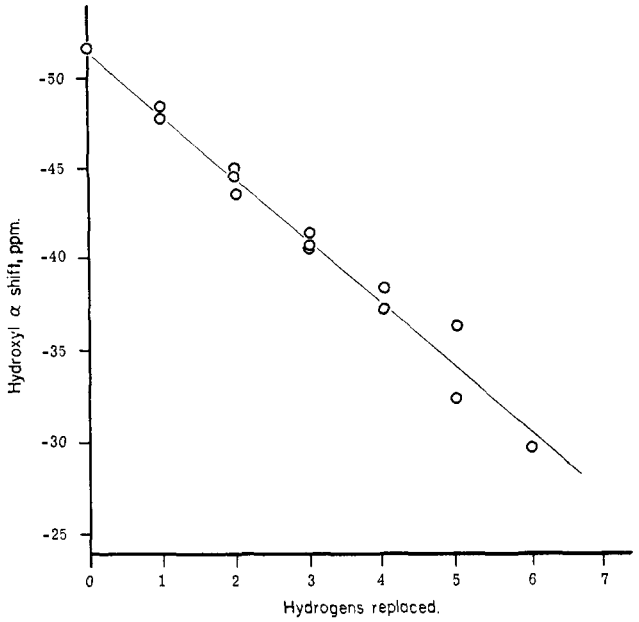


Figure 1. The α effect of a hydroxyl group as a function of the total number of hydrogens replaced at the α and β carbons.

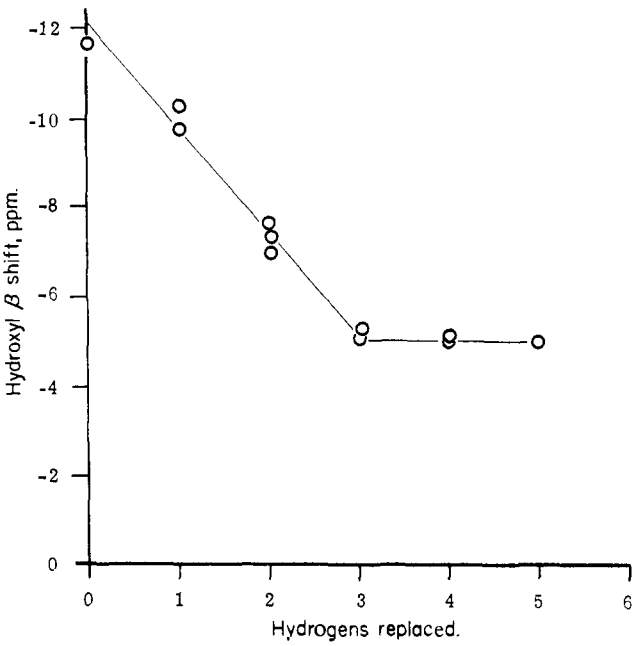


Figure 2. The β effect of a hydroxyl group as a function of the total number of hydrogens replaced at the α and β carbons.

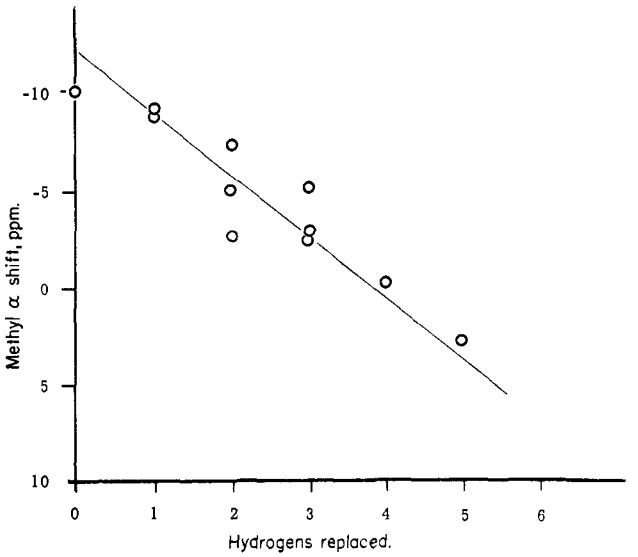


Figure 3. The α effect of a methyl group as a function of the total number of hydrogens replaced at the α and β carbons.

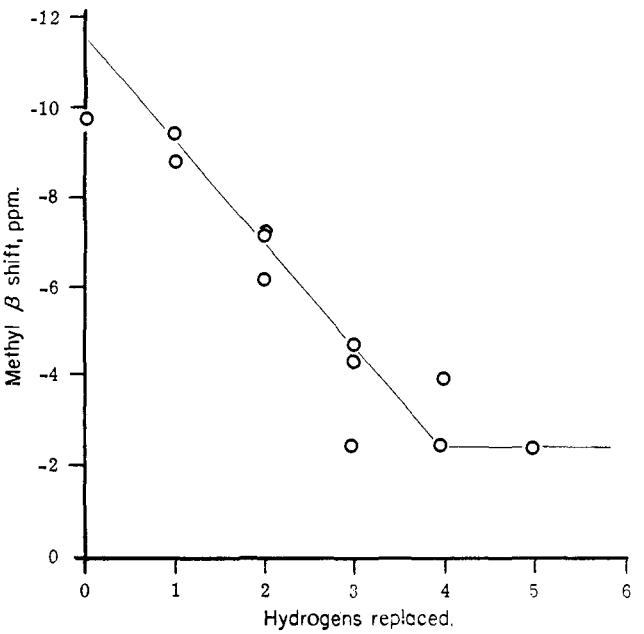


Figure 4. The β effect of a methyl group as a function of the total number of hydrogens replaced at the α and β carbons. The line here is drawn to correspond roughly to that in Figure 2 although, in this case, it is not certain that there is a break at four hydrogens replaced.

The most plausible explanation that we have so far been able to develop is as follows: addition of a substituent induces a fundamental shift which is determined by the nature of the incoming group and this shift can be measured for the introduction of the substituent into methane and ethane. In the present case, the parameters in parts per million are $\alpha_{OH} = -51.4$, $\beta_{OH} = -11.6$, $\alpha_{CH_3} = -10.2$, $\beta_{CH_3} = -9.7$. However, the presence of a substituent either at the α or β position perturbs the C_α–C_β bond which, according to the theory of Litchman and Grant[19] results in an upfield shift. This is consistent with the observation that the shift change is independent of the site of substitution. In addition, it can rationalize why the β effect reaches a limiting value but the α effect does not. The β carbon, no matter how heavily substituted itself, is influenced by the substituent operating along the C_α–C_β bond, which can only be distorted easily to a limited degree. On the other hand, the α carbon is influenced by the effect of the substituent on each of the C_α–X bonds (X $\neq$ H) and, therefore, should be more sensitive to the substituent effect. Also, one might expect the C_α-substituent bond to be more susceptible to change than the other three bonds and hence, the effect on the α position will be greater than at the β position.

(19) W. M. Litchman and D. M. Grant, *J. Amer. Chem. Soc.*, **90**, 1400 (1968).

Let us now return to the norbornyl data and the particular features noted earlier, and see how the ideas presented above can be applied here. The smaller α values observed in the 2-norbornyl series (Table II) compared with the linear alkane substituent shifts[6,8] are explicable because in the norbornanes, substitution takes place at a secondary carbon, while most of the substituent shifts so far reported for the alkanes are for substitution at primary carbons. The same applies for the β effects at C-1 and C-3. The actual magnitudes of the α effect are in the order expected if inductive effects were the main contributing mechanism to the shifts. The cyano group is the one exception and we have no rationalization of this, other than to note the presence of the triple bond. The fact that the endo substituents have a smaller effect at both α and β positions can be understood because endo substituents suffer greater overall steric interaction than exo substituents and this will cause a greater distortion of the C_α–C_β bonds, so that the basic downfield shift caused by the substituent will be diminished more with endo than with exo groups. The same type of argument can be used to explain the difference between axial and equatorial substituents in the cyclohexyl series.

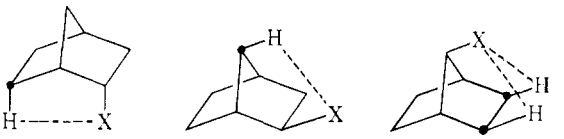
The α effects resulting from substitution of methyl at various positions in the norbornyl skeleton are larger than would be expected from the pattern found for alkanes wherein the degree of substitution at the α carbon is particularly important. If Table XIV is used to predict the methyl substituent effect in norbornanes, the observed values are too large. However, the β shifts for these norbornyl derivatives do follow the predicted behavior and one is faced with the necessity of finding some new parameter which applies to α shifts with norbornyl compounds. The rigidity of, and the strain in, the norbornyl ring system may be important here, especially if the hybridization of the carbons deviates much from sp^3.

The almost complete invariance to structural change of the chemical shift of C-2 in the ketones ($\delta = -23.0 \pm 2$) and difluorides ($\delta = 61.7 \pm 1.5$) shows that the electronic demands of a substituent can override the more subtle effects discussed above. By contrast, the β shifts in these cases follow the normal scheme, provided a larger inductive effect is utilized as the starting parameter.

The γ Effect. Since the pioneering work of Cheney and Grant,[4] the importance of steric interaction on ^{13}C chemical shifts has been verified in several studies.[5,9,20] The present work is no exception and, in fact, the sterically induced γ shift is the most easily recognized of any of the interactions studied here.

With a substituent in the 2 position, there are three γ positions—C-4, C-6, and C-7. The hydrogen attached to C-4 is far removed from the 2 position and so there can be no sizable steric interaction here. As a result, the γ shifts of this carbon are small. The situation at C-6 and C-7 is quite different. Introduction of an endo substituent at C-2 causes a marked upfield shift at C-6 and the magnitude of this shift appears to be related to the size of the substituent—there is very little change at C-7. Likewise, if an exo substituent is introduced, C-7 shows a marked upfield shift and the magnitude of the shift follows essentially the same order as for the endo substituent at C-6. In addition to the effect at C-7, an exo substituent generates an upfield shift at C-6, which appears to depend on the electronic rather than the steric nature of the substituent. This effect will be discussed later in this section.

Throughout each series of methyl-substituted compounds (Tables I, III–V), sterically induced shifts can be observed. Whenever there is an interaction of the type shown in **1**–**3**, the carbon attached to hydrogen shows an upfield shift. In all cases, the endo-2 to endo-6 type interaction **1** generates a larger upfield shift than the exo-2 to syn-7 type, **2** and **3**. The interaction with an *endo*-6-methyl group is not transmitted to



1 2 3

C-2 in the norbornanones or the difluorides. Recent work on fluorine chemical shifts[13] shows that there is a marked dependence on steric interaction for this nucleus, but this is not reflected at the adjacent carbon atom.

Grant and Cheney[4] deduced a semiempirical formula for the calculation of sterically induced ^{13}C shifts, assuming that hydrogen–hydrogen interaction was the predominant mechanism. The results, both here and from other studies, indicate that this is not the only mechanism operative because fluorine, hydroxyl, and amino groups cause equivalent, if not larger, hydrogen-transmitted chemical-shift changes at carbon.[9,20b] The chemical shifts of the unsaturated carbons in *syn*- and *anti*-7-methylnorbornene and *endo*-5-methylnorbornene show that interaction between a methyl group and a π cloud can cause the same type of upfield shift. Thus, it seems clear that the concept of the hydrogen–hydrogen interaction mechanism should be expanded and regarded as one member of the more general class of electron–electron repulsions which result in an upfield chemical shift change.

Calculations based on the equation of Grant and Cheney[4] were carried out to determine the effect of a freely rotating methyl group at each position of the skeleton. The electron-diffraction data of Bauer and coworkers[21] were used to define the positions of all but the methyl group. A C–C distance of 1.55 Å, a C–H distance of 1.09 Å, and tetrahedral angles were assumed for this group. The calculations showed: (i) a methyl group at C-1 does not interact significantly with, and is not expected to change the shift of any other carbon as the result of a steric effect; (ii) an *endo*-methyl group at C-2 should cause a large upfield shift at C-6 and a small change at C-3 (see Figure 5); (iii) an exo methyl at C-2 should cause a small upfield shift at C-7 and a small change at C-3 (see Figure 6); (iv) a methyl group at C-7 should give an equivalent small upfield shift at both C-2 and C-3 (see Figure 7). Thus, the calculations reproduce the observed behavior

(20) (a) H. J. Reich, M. Jautelat, M. T. Messe, F. J. Weigert, and J. D. Roberts, *J. Amer. Chem. Soc.*, **91**, 7445 (1969); (b) D. E. Dorman, S. J. Angyal, and J. D. Roberts, *ibid.*, **92**, 1351 (1970).

(21) J. F. Chiang, C. F. Wilcox, and S. H. Bauer, *ibid.*, **90**, 3149 (1968).

qualitatively, although the effect at C-3 will be masked by the β effect of the substituent. The calculations are, however, quite poor on a quantitative basis. It may be that either the equation proposed by Cheney and Grant is basically inaccurate, or else the model used does not represent the actual structure which may well be distorted from an idealized geometry. We are inclined to believe that the latter is probably the predominant cause, even though the semiempirical parameters of Grant and Cheney probably could be improved considerably.

Steric interactions have been invoked for many years to rationalize the rates and products of substitution reactions of norbornyl derivatives. The chemical-shift changes observed in this work provide explicit evidence for steric interactions involving substitutions on the norbornyl skeleton and it appears that the magnitude of the observed changes can be used as a semiquantitative measure of the degree of interaction. As one example we can see that a syn substituent at C-7 does, in fact, have a smaller steric influence on C-2 than an endo substituent at C-6.

The remaining γ effect at C-6 resulting from substitution of an exo substituent at C-2 cannot be explained by steric interaction. Here, the shift changes correlate with the electronegativity of the substituents in much the same manner as the α effect. The C-6 resonances do not appear to show a similar dependence on electronegativity for the endo substituents and, what little effect there may be, is masked by the sterically induced change. It should also be noted that the other γ carbons (C-4 and C-7) do not show this electronegativity effect. We must conclude that the special spatial configuration between the substituent, C-2 and C-6, has an important bearing on the mechanism of the shift changes. Recently ^{19}F chemical shift data for 4-substituted 1,1-difluorocyclohexanes[22] and 4-substituted 1-fluorobicyclo[2.2.2]octanes[23] have demonstrated a similar upfield shift of the ^{19}F resonance which is dependent on substituent orientation. This behavior is very reminiscent of that found for long-range W arrangement internuclear coupling constants and there may well be a common origin for these effects. Increasing overlap between the back lobes of the C-2 and C-6 bonding orbitals offers an especially attractive explanation for the observed changes. Expressed in valence-bond terminology, this means that there is a greater contribution than in the corresponding acyclic derivative of α,γ hyperconjugation as expressed by canonical structures such as I. These contributions should increase as the electron-withdrawing power of X is increased. The upfield shift of C-6 with increasing overlap fits nicely with the cmr work of Olah and coworkers[2,24] on bridged cations where much larger upfield shifts are observed. Thus, it appears that ^{13}C chemical shifts may provide a sensitive and quantitative probe for measuring the electronic demands of a neighboring group as a function of stereochemistry in the ground state of formally neutral molecules.

Methyl-2-norbornanols. In order to check the validity of the concepts outlined above, the shifts of the epimeric 1-, *exo*-3-, and *endo*-3-methyl-2-norbornanols

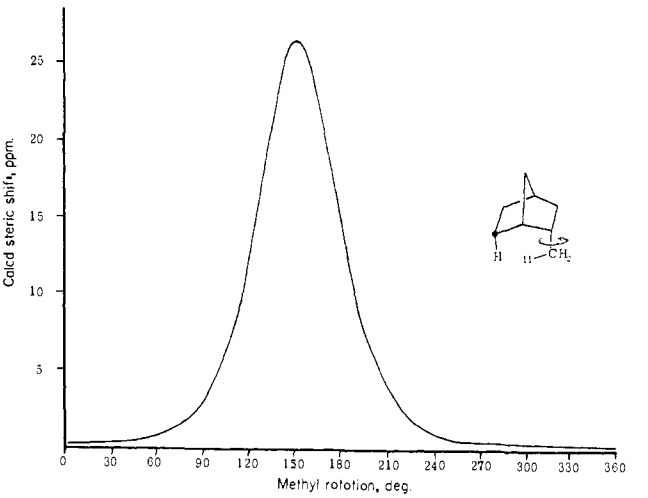
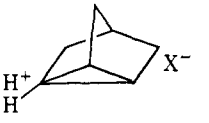


Figure 5. The calculated shift due to steric interaction between an *endo*-2-methyl group and the *endo*-hydrogen at C-6 as a function of methyl rotation.

were determined (Table XVI). Here, the concern was for (a) the generality and additivity of substituent effects, (b) the degree of independence of the shifts to



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substituent orientation, and (c) the importance of bond distortion effects. Predicted shifts were obtained by correcting the observed shifts of the *exo*- and *endo*-2-norbornanols for methyl substituent effects as calculated from the differences between corresponding carbons of the methylnorbornanes and norbornane. The resonances were assigned to specific carbons according to the methods discussed earlier. Table XVI shows that the agreement between predicted and observed shifts is good for all carbons except for those where substituents are attached. This behavior demonstrates the generality and additivity of substituent effects. The carbons immediately adjacent to the point of attachment of the OH or methyl groups are expected to absorb at higher field by approximately 3 ppm than the simple predictions because the number of β hydrogens has been reduced. This trend is rather general, although the 3-carbon resonance of *exo*-3-methyl-*endo*-2-norbornanol is only slightly affected. (It may be, in this case, that the C_2–C_3 bond has already been distorted by the *endo*-OH substituent and introduction of the *exo*-3-methyl group does not perturb the bond further.) Furthermore, where a substantial steric interaction between substituents is expected, as for the di-exo and di-endo derivatives, large upfield shifts of the 2 and 3 carbons result, which further support the idea that bond distortions are a major influence on the shifts of α and β carbon atoms.

^{13}C–^{13}C Coupling Constants. It is well known that ^{13}C–^{13}C coupling constants are a sensitive measure of the degree of s character in C–C bonds.[25–28] Table

(22) K. Grohmann and J. D. Roberts, unpublished observations.
(23) G. L. Anderson and L. M. Stock, *J. Amer. Chem. Soc.*, **90**, 212 (1968).
(24) G. A. Olah, C. L. Jeuell, and A. M. White, *ibid.*, **91**, 3961 (1969).
(25) K. Frei and H. J. Bernstein, *J. Chem. Phys.*, **38**, 1216 (1963).
(26) R. M. Lynden-Bell and N. Sheppard, *Proc. Roy. Soc., Ser. A*, **269**, 385 (1962).

Table XVI. ^{13}C Chemical Shifts of Methyl-2-norbornanols[a]

		endo-OH			*exo*-OH		
		Pred	Obsd	Diff	Pred	Obsd	Diff
1-Methyl-2-norbornanol	C-1	142.4	144.6	−2.2	141.0	144.9	−3.9
	C-2	113.3	115.7	−2.4	111.4	115.9	−4.5
	C-3	151.7	151.7	0.0	148.9	149.0	−0.1
	C-4	153.7	155.4	−1.7	155.6	156.4	−0.8
	C-5	161.0	161.0	0.0	162.5	161.9	0.6
	C-6	165.4	165.4	0.0	160.9	159.1	1.8
	C-7	148.1	147.9	0.2	151.3	152.2	−0.9
	CH_3		174.0			176.2	
exo-3-Methyl-2-norbornanol	C-1	149.2	149.0	0.2	147.8	147.4	0.4
	C-2	110.2	*b*		108.3	*b*	
	C-3	146.5	146.8	−0.3	143.7	149.0[c]	−5.3
	C-4	148.4	148.4	0.0	150.3	149.2[c]	1.1
	C-5	163.6	162.3	1.3	165.1	163.1	2.0
	C-6	172.2	172.6	−0.4	167.7	167.8	−0.1
	C-7	158.7	158.2	0.5	161.9	160.6	1.3
	CH_3		173.0			172.9	
endo-3-Methyl-2-norbornanol	C-1	148.3	148.6	−0.3	146.9	146.9	0.0
	C-2	109.7	121.1	−11.4	107.8	*b*	
	C-3	148.7	155.4	−6.7	145.9	146.1	−0.2
	C-4	149.7	149.9	−0.2	151.6	151.4	0.2
	C-5	170.2	170.6	−0.4	171.7	171.3	0.4
	C-6	171.9	172.7	−0.8	167.4	167.3	0.1
	C-7	154.8	155.7	−0.9	158.0	155.5	2.5
	CH_3		182.3			177.9	

[a] See footnotes to Table I. [b] Not surely identified separately from the resonance of other 3-methyl isomers. [c] Hidden by resonances of the endo isomer.

Table XVII. ^{13}C–^{13}C Coupling Constants

Compd	Bond	$^1J_{CC}$, Hz
Quadricyclene	1,2	12.6
	1,7	41.5
Nortricyclene	1,7	40.4
	3,4	29.8
Norbornane	1,2	33.4
	1,7	32.5

XVII shows the one-bond ^{13}C–^{13}C coupling constants determined from natural-abundance studies of norbornane, nortricyclene, and quadricyclene.[27]

The value of 12.6 Hz for the 1,2 and 1,6 bonds in quadricyclene is in close agreement with other values for cyclopropane which indicate sp^5–sp^5 type hybridization of the carbon–carbon bonding orbitals. This leaves the other two orbitals at C-1 as approximately sp^2 hybrids. The approximate relationship $J_{C_AC_B} = 550 (S_A S_B)$ has been used to relate the s character in the bonding orbital on atom A with the C_A–C_B coupling constant.[27] Application of this equation, with the assumption that $S_{C_1} = 0.333$ shows that the s character at C-7 of the orbital along the 1,7 bond is midway between sp^3 and sp^4 hybridization ($S_{C_7} = 0.226$). The 1,7 coupling constant in nortricyclene suggests that there is also similar orbital hybridization in this molecule. Comparison of the remaining coupling constants in the table with those found for simple sp^3–sp^3 bonding (ethane 34.6 Hz and neopentane 36.9 Hz) indicates that the corresponding carbon–carbon bonds of the bridged systems have greater p character than their acyclic counterparts.

Experimental Section[29]

Nmr Spectra. All nmr spectra were obtained with a Varian A56/60 spectrometer operating at 56.4 MHz. All chemical shifts were determined to internal hexafluorobenzene and converted to the $CFCl_3$ scale, with the relationship $\delta_F^{CFCl_3} = \delta_F^{C_6F_6} + 162.3$. The cmr spectra were obtained from natural-abundance ^{13}C in 10-mm tubes with a Varian DFS60 spectrometer operating at 15.08 MHz.[10] Chemical shifts were determined from spectra taken with noise decoupling which removed all ^{13}C–H couplings.[11] Dioxane was the internal standard in all cases; shifts were determined from 500 Hz or smaller sweep widths with sweep rates of 5 Hz/sec or less. Where possible, the samples were neat liquids containing 10% dioxane or saturated solutions of solids in dioxane. When only limited quantities of a compound were available, the sample volume was made up to approximately 1.5 ml with dioxane. Concentration and solvent effects were within the experimental error of ±0.1 ppm.

Cycloalkanes. Norbornane, nortricyclene, and quadricyclene were commercial samples. The methylnorbornanes and camphane[30] were prepared by hydrogenation of the corresponding cycloalkenes (see below). 2,2-Dimethylnorbornane was prepared by Wolff–Kishner reduction of camphenilone.[31–33]

Cycloalkenes. Norbornene, norbornadiene, and camphene were commercial samples. Bornylene and 1-methylnorbornene were prepared *via* the tosylhydrazones of the corresponding ketones.[34] A 45:55 mixture of *exo*- and *endo*-5-methylnorbornenes was available from the Diels–Alder reaction of propene and cyclopentadiene.[35] It was not possible to separate the mixture of epimers.

(27) F. J. Weigert and J. D. Roberts, *J. Amer. Chem. Soc.*, **89**, 5962 (1967).
(28) W. M. Litchman and D. M. Grant, *ibid.*, **89**, 6775 (1967).
(29) All melting points and boiling points are uncorrected. Preparative vapor-phase chromatographic separations were carried out on a 20-ft Carbowax W column. Infrared spectra were taken on either a Perkin-Elmer 237 Infracord or a Model 237 grating spectrophotometer.
(30) O. Aschan, *Chem. Ber.*, **33**, 1006 (1900).
(31) L. F. Fieser and M. Fieser, "Reagents for Organic Chemistry," Wiley, New York, N. Y., 1967, p 435.
(32) O. Aschan, *Chem. Zentralbl. I*, 415 (1912).
(33) S. Nametkin and A. Chuchrikoff, *Justus Liebigs Ann. Chem.*, **438**, 194 (1924).
(34) R. H. Shapiro and M. J. Heath, *J. Amer. Chem. Soc.*, **89**, 5734 (1967).
(35) K. Alder and H. J. Ache, *Chem. Ber.*, **95**, 503, 511 (1962).

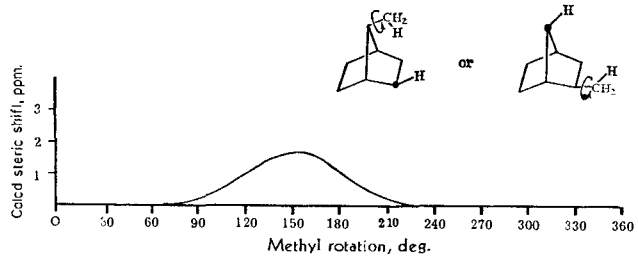

Figure 7. The calculated shift due to steric interaction between a *syn*-7-methyl group and the *exo*-hydrogen at C-2 as a function of methyl rotation.

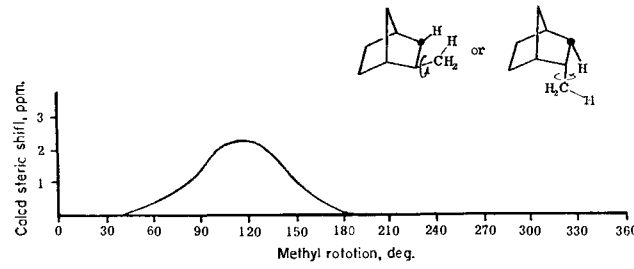

Figure 6. The calculated shift due to steric interaction between an *exo*-3-methyl group and the *exo*-hydrogen at C-2 as a function of methyl rotation.

Table XVIII. Preparation and Properties of 2,2-Difluoronorbornanes

Substituent	Reagents: Ketone, g	Sulfur tetrafluoride, g	Water, ml	Methylene chloride, ml	Reaction temp, °C	Reaction time, hr	% yield	Mp, °C	Anal.[f] C	H	F	Infrared, cm^{-1}
None	5	33.4	0.8	25	*a*	16	55	73	63.51	7.55	28.66	2990, 2890, 1480, 1460, 1440, 1350, 1315, 1185, 1140, 1105, 1065, 985, 895, 850
									63.62	7.62	28.75[g]	
1-Methyl	8	50	1.8	30	*a*	72	28	45–46	65.56	8.22	25.85	2950, 2870, 1455, 1340, 1320, 1310, 1175, 1160, 1145, 1085, 1035, 980, 895
									65.73	8.27	26.03[g]	
exo-3-Methyl	7.0	62	1.1	30	75	27	39	(125–126)[b]	65.66	8.24	25.77	2975, 1460, 1335, 1115, 1090, 980
endo-3-Methyl	14.9	91	3.6	50	70	24	10	53–54	65.99	8.35	25.84	2960, 2870, 1475, 1460, 1445, 1350, 1330, 1175, 1150, 1135, 1100, 1075, 1040, 1020, 980, 940, 920, 840
exo-5-Methyl[c] / *exo*-6-Methyl	5	50	1.0	40	60	24	30	*d*				
endo-5-Methyl	1.2	10	0.3	15	55	20	53	*d*, *e*	65.60	8.30	25.91	2960, 2890, 1470, 1455, 1440, 1380, 1350, 1305, 1250, 1190, 1155, 1100, 1065, 1025, 1000, 965, 900, 870
endo-6-Methyl	1.3	13.5	0.3	20	70	19	28	*d*, *e*	65.75	8.22	26.03	2970, 2370, 1460, 1365, 1340, 1320, 1305, 1270, 1190, 1145, 1105, 1080, 1020, 1000, 955, 905, 880
syn-7-Methyl	2.4	26	0.4	30	*a*	23	10	*d*				
anti-7-Methyl	1.5	10	0.3	20	*a*	24	52	*d*	65.88	8.23	25.96	2960, 2880, 1475, 1445, 1385, 1330, 1310, 1250, 1235, 1180, 1125, 1105, 1080, 1030, 1005, 980, 900, 870, 845
3,3-Dimethyl	8.8	74	1.3	50	90	24	8	95–97	67.62	8.97	23.27	2975, 1465, 1330, 1160, 1130, 1115, 1075, 1050, 1030, 990
									67.47	8.81	23.72[g]	
7,7-Dimethyl	1.4	12	0.3	20	80	22	8	88–91	67.38	8.75		2960, 1455, 1340, 1275, 1175, 1155, 1110, 1100, 1060, 905

[a] Room temperature. [b] Boiling point. [c] Mixture could not be separated by vpc. [d] Liquid collected by vpc. [e] Freezes just below room temperature. [f] Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan. [g] Calculated.

An authentic sample of the endo isomer was synthesized according to Berson.[36]

syn- **and** *anti-***7-Methylnorbornenes.** *syn*-7-Bromo-7-methylnorbornene was prepared by the method of Skattebøl.[37] Two additional unidentified products were obtained from this procedure besides the reported *syn*-7-bromo-7-methylnorbornene, bp 78–80° (16 mm), in 57% yield; A, bp 114–116° (16 mm), in 3% yield and B, bp 126–130° (16 mm), in 10% yield. The bromo compound (2.56 g) was dissolved in tri-*n*-butyltin hydride (7.2 ml) at room temperature and the mixture became warm. The solution was allowed to stand for 4 hr, slowly warmed to 120°, and the 7-methylnorbornenes, bp 50–52° (35 mm), 1.21 g (83%), removed by distillation. The 50:50 mixture was separated by preparative vpc at 100°. The anti form had longer retention time. The structure of the anti isomer was confirmed by oxidation to *anti*-7-methylnorbornanone[38,39] (*vide infra*) and of both isomers by hydrogenation to 7-methylnorbornane. Hydrogenation of the mixture of epimers in methanol over palladium on charcoal at room temperature for 1 hr gave 7-methylnorbornane and *syn*-7-methylnorbornene. No further change occurred over 15 hr. The hydrogenation could be completed over Adams catalyst in acetic acid.

Ketones. Norbornanone, 3-methylenenorbornanone, camphor, and camphenilone were commercial materials. 1-Methylnorbornanone was prepared by oxidation of 1-methylnorbornanol.[40] The *exo*- and *endo*-3-methylnorbornanones were synthesized by known procedures.[41,42] The remaining methyl ketones were prepared in good yield through hydroboration followed by oxidation[43,44] of the appropriate alkenes. Thus, *syn*- and *anti*-7-methylnorbornene gave *syn*- and *anti*-7-methyl-2-norbornanone, respectively. *endo*-5-Methylnorbornene gave a mixture of *endo*-5- and *endo*-6-methyl-2-norbornanones which could be separated by vpc at 180°.[29] The structure of the 6 isomer was established by comparison of its infrared spectrum with that of an authentic sample.[39,44] Hydroboration and oxidation of the mixture of *exo*- and *endo*-5-methylnorbornenes gave a mixture of the four possible ketones. Partial separation could be achieved by vpc to give *endo*-5-methyl-, a mixture of *exo*-5- and *exo*-6-methyl-, and the *endo*-6-methyl-2-norbornanones (in order of retention times). The 5-methyl isomers were in slight excess in both the exo and endo pairs. The cmr spectrum was run on the mixture of exo isomers, and peaks due to each component were selected on the basis of intensity—a 55:45 ratio of *exo*-5:*exo*-6-being present.

Difluorides. Each of the methyl-2,2-difluoronorbornanes was prepared by treatment of the corresponding ketone with sulfur tetrafluoride.[45] There was no rearranged product detected in any case. The general procedure is outlined below and Table XVIII summarizes the data concerning quantities, conditions, yields, and physical properties for each compound.

The ketone (0.05 mol), water (0.075 mol), and methylene chloride (30 ml) were placed in a stainless steel Parr bomb. The bomb was cooled to −78°, the air evacuated, and sulfur tetrafluoride (0.4 mol) was condensed in. *Care must be taken* because sulfur tetrafluoride is highly toxic. The bomb was sealed and shaken in a Parr rocker for 24 hr at room temperature (hindered ketones may require 50–70° to obtain satisfactory yields). At the end of this time, the bomb was vented in the fume hood and the contents poured into a separatory funnel containing 10% sodium bicarbonate. (Alternatively, the contents of the bomb can be poured into water (500 ml) in a beaker and solid potassium hydroxide added until the solution is basic.) The brown mixture was shaken successively with 10% sodium bicarbonate, water, and saturated sodium chloride. Ether was added as necessary to maintain the volume of the organic layer at 50 ml. The ethereal layer was separated, dried over sodium sulfate, and cautiously (many difluorides are quite volatile) distilled at room temperature. After the ether and methylene chloride had been removed, the difluoride was collected by bulb-to-bulb distillation (bp approximately 120°). Unreacted ketone was present in several preparations, especially for the more hindered examples. Final purification was achieved by preparative vpc. The compounds are quite stable (but volatile) and can be stored for extended periods in sealed ampoules.

The mixture of *exo*-5- and *exo*-6-methyl-2,2-difluoronorbornane, prepared from the mixture of ketones, could not be separated by vpc. However, since they were not present in equal amounts, their nmr and cmr spectra could be assigned readily on the basis of intensities.

2-Substituted Norbornanes. The 2-norbornylamines were available from previous work[46] and the 2-norborneols were commercial materials. *exo*-2-Fluoronorbornane was kindly supplied by Dr. C. L. Jeuell of Case Western Reserve University. The remaining monosubstituted derivatives were intermediates in the conversion of 2-cyanonorbornane into 2-methylnorbornane.[36] 2,2-Dicarboethoxynorbornane and 2,2-dihydroxymethylnorbornane were prepared by reported procedures.[47]

1-Methyl- and *exo*- **and** *endo*-**3-Methyl-***exo*- **and** -*endo*-**2-norborneols.** Mixtures of the endo and exo isomers of 1-methylnorbornanol, *endo*-3-methylnorbornanol, and *exo*-3-methylnorbornanol were prepared by aluminum isopropoxide reduction of the corresponding ketones according to the procedure of Hirsjarvi.[48] In each case, the endo isomer was *ca.* 70–80% of the mixture except for 1-methylnorbornanol where a 50–50 mixture was formed. Lithium aluminum hydride reduction of the corresponding ketones resulted in >90% formation of the endo alcohols, and the spectra of these reduction products allowed the assignment of the resonances of the endo isomer in the cmr spectra of the mixtures from the isopropoxide reductions.

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