^{13}C Nuclear Magnetic Resonance Studies. 38.[1] Examination of the Long-range Shielding Effects of the Hydroxyl Group in Alicyclic Systems

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The substituent effects of the hydroxyl group on the ^{13}C shieldings of the *trans*-decalols and the 10-methyl-*trans*-decalols have been determined. The shifts for the carbons three and four bonds from the site of substitution depend strongly on their orientation with respect to the hydroxyl group. While the latter have not been widely recognized, these δ effects are valuable for spectral analysis and stereochemical assignments since these range up to 3.4 p.p.m. In direct contrast to the well established trends for γ effects, steric crowding of δ nuclei causes marked downfield shifts. The corresponding effects in several steroids are illustrated.

On a déterminé les effets de substituent du groupe hydroxyle sur le blindage du ^{13}C des *trans*-décalols et des méthyl-10 des *trans*-décalols. Le déplacement des carbones qui se trouve à trois et quatre liens du site de la substitution montre une grande dépendance sur l'orientation par rapport au groupe hydroxyle. Même si ces derniers effets n'ont pas été reconnus d'une façon générale jusqu'à maintenant les effets sont très utiles pour l'analyse spectrale et la détermination stéréochimique puisqu'ils ont des valeurs allant jusqu'à 3.4 p.p.m. L'encombrement stérique des noyaux cause un déplacement chimique marqué vers les bas champs et ceci en opposition directe avec les tendences bien établies pour les effets γ. On illustre enfin des correspondents dans plusieurs stéroides. [Traduit par le journal]

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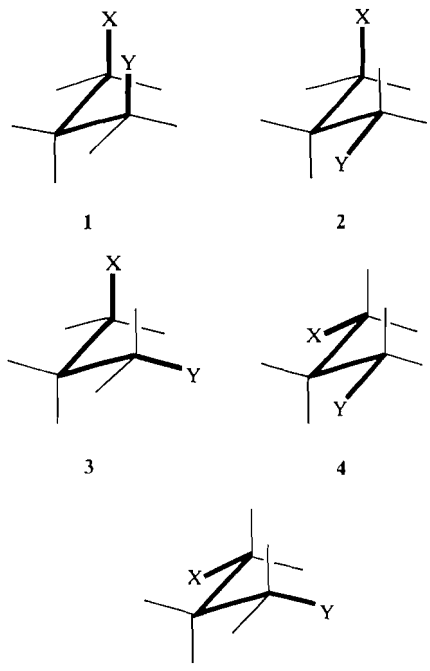
Introduction

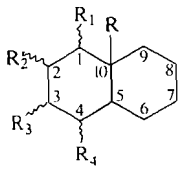
One of the earliest findings in ^{13}C n.m.r. investigations of organic compounds was the discovery of remarkably consistent shielding effects exerted by an array of substituents within families of compounds (1). Because of their reproducibility, a knowledge of these substituent effects for a given system often can permit the direct assignment of ^{13}C signals in the spectra of related compounds (2). While the early work with aromatic systems showed that these effects clearly reveal the presence of steric inhibition of resonance (3), it was not until the results for alicyclic systems were available that the existence of pronounced steric effects in σ-bonded systems was established (4, 5). For example, the effect of a substituent group separated by three bonds from a given carbon depends on its relative orientation; if *gauche* or eclipsed, the carbon is shielded relative to that in the corresponding *anti* arrangement. This general behavior has been utilized for stereochemical purposes in a wide variety of systems (6) and a theoretical model rationalizing the geometrical features in terms of interacting proximate hydrogen atoms for hydrocarbons has been presented (7).

The general conclusion that ^{13}C shieldings increase as the extent of steric crowding increases appears to have no exceptions for interactions be-



[1]Part 36, ref. 34; Part 37, ref. 35.

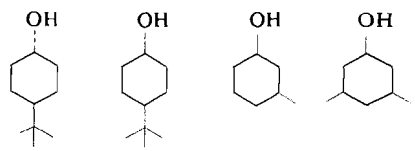
[2]Holder of NRCC scholarship, 1968–1971.



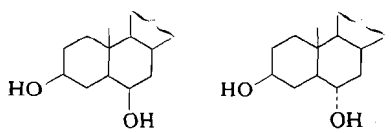
Compound	R	R_1	R_2	R_3	R_4
6	H	β-OH	H	H	H
7	H	α-OH	H	H	H
8	H	H	α-OH	H	H
9	H	H	β-OH	H	H
10	CH_3	β-OH	H	H	H
11	CH_3	α-OH	H	H	H
12	CH_3	H	α-OH	H	H
13	CH_3	H	β-OH	H	H
14	CH_3	H	H	β-OH	H
15	CH_3	H	H	α-OH	H
16	CH_3	H	H	H	α-OH
17	CH_3	H	H	H	β-OH

tween substituents and carbons *separated by three bonds*. Appreciable longer range effects have been found in cyclohexane systems (5, 8) and these were also found to be shielding (*i.e.* producing upfield shifts) and have been interpreted in terms of inductive parameters with negligible steric contributions. For groups separated by four bonds, however, a variety of orientations may be adopted and the initial work did not involve examinations of all possibilities **1–5**. Of these, the *syn*-axial **1** (with either or both X and Y = C) is particularly interesting since the separation of X and Y is comparable to that for *gauche* interactions. The overwhelming majority of cyclic model systems examined, however, lack cases having *syn*-axial **1** interactions. For acyclic systems, these represent only minor contributors to the observed shifts since more stable orientations are favored. In the initial report of the effects of molecular symmetry on ^{13}C shieldings (9) it was noted that significant *deshielding* effects occur over four bonds and in the course of a structural elucidation using ^{13}C n.m.r. (10) it was found that *syn*-axial methyl–methyl interactions were accompanied by marked downfield shifts.

A systematic study, therefore, seemed warranted to include examples having each of the arrangements **1–5**. For this purpose we have determined the ^{13}C spectra of the *trans*-decalols **6–9**, the eight 10-methyl-*trans*-decalols **10–17**,[3] a few substituted cyclohexanols **18–21**, as well as the cholestan-3β,6-diols **22** and **23**. Comparison of these data with those for the corresponding hydrocarbons permitted the assessment of the shielding effects of the hydroxyl group at the neighboring carbons. In this way definitive evidence of appreciable downfield shifts for *syn*-axial interactions was obtained. This finding is in striking contrast to the general trend for *gauche* interactions and clearly violates the general premise which associates steric crowding with upfield shifts. These examples were chosen because unequivocal assignments for most of the nuclei are straightforward and, since the general equivalence of the effects of hydroxyl and methyl groups has been recognized (11), the trends should be indicative of 1,5 Me···Me interactions which are commonly encountered in more complex systems. A preliminary report of some of these results has appeared (12).



18 **19** **20** **21**



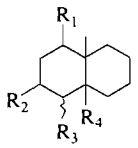
22 **23**

[3]The numbering scheme given in **10** has been employed to simplify comparisons with related systems such as steroids.

Experimental

Materials

The parent hydrocarbons and most of the steroids examined are commercially available compounds. The



Compound	R_1	R_2	R_3	R_4
24	=O	H	H	α-H
25	H	=O	H	α-H
26	H	=O	=	
27	H	H	α-OH	β-H
28	H	H	β-OH	β-H
29	H	H	=O	H

trans-decalols were prepared by combinations of published procedures as outlined below.

trans-1- and -2-Decalols (6–9)

Stereospecific reductions of *trans*-1-decalone, which was obtained by treatment of a commercial mixture of *cis*- and *trans* isomers with MeO^-–MeOH (13), were employed to prepare the *trans*-1-decalols. The $LiAlH_4$–$AlCl_3$ method of Eliel and Nasipuri (14) furnished **6** while the $IrCl_4$ reagent (15) gave 7. By fractional distillation of a commercial mixture of *trans*-2-decalyl acetates, a sample rich in the 2β isomer was obtained. Hydrolysis gave crude **9** which was purified by recrystallization from petroleum ether and sublimation. The equatorial isomer was obtained by mixed hydride equilibrium (14) of the alcohols from hydrolysis of the *trans*-2-decalyl acetates; recrystallization from petroleum ether gave pure **8**. The physical properties of the four decalols agreed well with published data (16).

10-Methyl-trans-decal-1-ols (10 and 11)

The preparation of 10-methyl-*trans*-decal-1-one (**24**) from *trans*-1-decalone via the 2-furfurylidene derivative (17) gave crude 10-methyl-*trans*-decal-1α-ol (**11**) before the oxidation step. A portion of this material crystallized on standing in the cold and recrystallization from petroleum ether gave **11**, m.p. 56–57°. $LiAlH_4$ reduction of **24** gave a 4:1 mixture of **10** and **11**, from which the required spectral data were readily obtained since pure **11** was available.

10-Methyl-trans-decal-2-ols (12 and 13)

These alcohols were prepared from 10-methyl-*trans*-decal-3-one (**25**) which was obtained from 2-methylcyclohexanone and methyl vinyl ketone via published procedures (18, 19). Bromination (20) of **25** gave the 3α-bromo derivative which with $LiAlH_4$ furnished 2β,3β-oxido-10-methyl-*trans*-decalin (21) and, subsequently, **13** (22) which was purified by recrystallization from pentane, m.p. 56–59° (lit. (22), m.p. 57.5–58.5°).

Oxidation of **13** with Jones' reagent followed by mixed hydride reduction (14) gave **12**, m.p. 44–47° (lit. (22), b.p. ~ 140°/0.4 m).

10-Methyl-trans-decal-3-ols (14 and 15)

Reduction of **25** with the $IrCl_4$ reagent (15) gave **15** in 75% yield, m.p. 86–88°. In the preparation of **25**, the reduction of 10-methyl-Δ^4-octal-3-one (**26**) with Li–NH_3 gave a mixture of **25** and the corresponding decalols. A second treatment with Li–NH_3 converted the mixture entirely to alcohols which were oxidized by Jones' reagent to **25**. It was found that partial oxidation, with insufficient reagent, furnished a mixture from which **14** was readily separated by fractional distillation. Recrystallization of this material from petroleum ether gave **14**, m.p. 71–73°.

10-Methyl-trans-decal-4-ols (16 and 17)

Since attempts to isolate pure samples of each of these alcohols were unsuccessful, mixtures of different compositions were prepared using different procedures. Detailed comparisons of the n.m.r. spectra of these mixtures, together with the knowledge of their mode of formation, permitted the characterization of each.

Hydroboration (23) of 10-methyl-Δ^4-decalin, prepared from **26** via its ethylene thioketal (19) gave a mixture of three decalols whose methyl protons absorbed at 0.85, 0.96, and 1.03 p.p.m. A mixture containing only two of these was produced by catalytic hydrogenation of 10-methyl-Δ^5-decal-4α-ol (24). The major component, having methyl shieldings of δ_H 0.96 and δ_C 27.9, and the minor component with methyl shieldings of δ_H 0.85 and δ_C 16.8, are the *cis*- and *trans*-alcohols **27** and **16**, respectively; the methyl ^{13}C shieldings clearly identify each isomer since the geometry of the ring junction markedly affects angular methyl shieldings (25). Thus, the third decalol from hydroboration, the major product, with methyl shieldings of δ_H 1.03 and δ_C 28.1, is **28**. It is interesting that both hydrogenation and hydroboration preferentially occur at the 4-(5-)double bond on the same side as the methyl group.

To obtain mixtures containing **17**, the *trans*-axial isomer, the mixture from hydroboration was oxidized with Jones' reagent to obtain a mixture of 10-methyl-4-decalones (**29**), in which the *cis*-isomer was predominant. Treatment with the $IrCl_4$ reagent proceeded to only a limited extent but the major component of the alcohol fraction exhibited methyl absorption at δ_H 1.07 and δ_C 19.1, values different from each of the other isomers, and its carbinyl proton signal at 3.80 p.p.m. had a width at half-height of 8.0 Hz, consistent with the equatorial orientation expected for **17**. $LiAlH_4$ reduction of **29** afforded a mixture of the four decalols **16**, **17**, **27**, and **28**, with **16** present in the smallest amounts but readily identified by its methyl n.m.r. absorptions.

Cholestan-3β,6-diols (22 and 23)

Hydrogenation of cholestan-3β-ol-6-one over platinum oxide (26) gave, after recrystallization from methanol, **22** in 68% yield, m.p. 189–192° (lit. (26) m.p. 188–190°). Reduction of the same cholestanone with sodium in alcohol (27) gave **23**, from methanol, m.p. 219–221° (lit. (27) m.p. 216–217°).

Spectra

The proton spectra were obtained with Varian T60 and HA100 spectrometers using $CDCl_3$ solutions. The ^{13}C spectra were determined on a Varian XL-100-15 system operating in the Fourier transform mode as described previously (28). All shieldings were measured relative to internal TMS with 20% (w/v) solutions in $CDCl_3$ using either 5 or 10 mm sample tubes and the appropriate receiver inserts. The precision of the individual shielding values is ±0.05 p.p.m.

Results and Discussion

The shielding data for the *trans*-decalols **6–17** are listed in Table 1 together with the results for *trans*-decalin and 10-methyl-*trans*-decalin. The

TABLE 1. ^{13}C Shieldings[a] of *trans*-decalin, 10-methyl-*trans*-decalin, and the *trans*-decalols **6–17**

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	Me
trans-Decalin	34.3	26.9	26.9	34.3	43.7	34.3	26.9	26.9	34.3	43.7	
6	74.6	35.8	24.1	(33.5)	41.2	(33.7)	(26.4)	(26.2)	29.1	50.4	
7	70.4	34.3	20.0	(33.8)	35.6	33.9	(26.8)	(26.4)	29.6	47.4	
8	43.0	70.2	35.6	32.0	42.3	(33.8)	(26.5)	(26.3)	(33.3)	41.2	
9	40.4	66.6	(33.9)	27.6	43.2	(33.8)	26.7	26.7	32.9	36.4	
10-Methyl-*trans*-decalin	42.1	22.1	27.2	29.3	45.8	29.3	27.2	22.1	42.1	33.9	15.7
10	79.6	30.4	24.4	28.1	44.2	28.1	26.8	21.7	37.3	39.2	9.8
11	75.2	(28.5)	20.4	(28.8)	37.5	(28.8)	26.7	21.8	34.8	38.3	16.1
12	50.9	66.9	36.4	27.9	44.9	28.1	26.9	21.2	41.6	34.7	16.6
13	47.8	67.6	34.1	24.0	45.9	28.7	27.0	21.2	41.9	33.5	17.9
14	40.0	31.2	71.0	38.1	43.1	28.8	26.7	21.9	41.1	33.0	15.7
15	35.6	28.6	66.6	36.0	37.8	28.8	27.0	21.9	41.5	33.7	14.7
16	41.2	20.4	36.6	70.0	52.4	23.0	26.7	21.7	41.9	34.8	16.8
17	43.7	16.9	34.1	71.8	48.5	26.0	27.3	21.9	41.7	33.7	19.1

[a]In p.p.m. from TMS in $CDCl_3$ solutions. Similar values in parentheses may be interchanged.

TABLE 2. ^{13}C Shieldings[a] of some cyclohexanols, sterols, and the related hydrocarbons

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	Me
t-Butylcyclohexane											
18	70.9	36.0	25.6	47.2	25.6	36.0					27.6[b]
19	65.7	33.4	20.9	48.1	20.9	33.4					27.5[b]
Methylcyclohexane	32.9	35.6	26.6	26.5	26.6	35.6					22.9
20	70.6	44.6	31.4	34.1	24.2	35.4					22.3
21	70.0	44.0	30.8	41.2	30.8	44.0					22.3
Cholestane	38.7	22.2	26.9	29.1	47.1	29.1	32.3	35.6	54.9	36.3	12.3[c]
Pregnane	38.9	22.3	26.9	29.2	47.2	29.2	32.4	35.7	55.3	36.4	12.3[c]
Androstane	38.8	22.2	26.9	29.1	47.1	29.1	32.6	36.0	55.1	36.4	12.3[c]
Cholestan-3β-ol (**30**)	37.1	31.6	71.2	38.3	45.0	28.8	32.1	35.6	54.4	35.5	12.4[c]
Pregnan-3β-ol-20-one (**31**)	37.0	32.0	71.0	38.1	44.8	28.6	31.4	35.4	54.2	35.4	12.3[c]
Pregnan-3β,20-diol (**32**)	37.5	32.5	70.5	39.2	45.3	29.2	32.5	35.7	54.8	35.8	12.5[c]
Androstan-3β-ol-17-one (**33**)	36.9	31.4	70.9	38.0	44.8	28.4	30.9	35.0	54.4	35.6	12.3[c]
Androstan-3β,17β-diol (**34**)	37.5	(32.0)	70.5	39.2	45.3	29.1	(32.3)	35.8	54.9	35.8	12.5[c]
Androstan-3α,17β-diol (**35**)	32.1	29.8	65.5	36.9	39.5	29.1	32.1	36.0	55.0	36.6	11.6[c]
Androstan-3α-ol-17-one (**36**)	30.9	29.0	66.3	36.3	39.2	28.3	32.2	35.1	54.5	35.8	11.2[c]
22	38.5	31.5	71.5	35.4	47.3	71.9	39.6	30.4	54.2	35.4	15.8[c]
23	37.3	31.3	71.1	32.3	51.6	69.3	41.7	34.3	53.7	36.2	13.5[c]

[a]In p.p.m. from TMS in $CDCl_3$ solutions. Values in parentheses may be interchanged.
[b]Quaternary carbons appeared at 32.2 p.p.m.
[c]C-19.

shieldings for the cyclohexanols **18–21**, the cholestanediols **22** and **23**, and the steroids **30–36** are given in Table 2. Since the reason for including these steroids was for comparison with the decalols, the data are limited to those for the A and B rings in these systems. The results for the parent hydrocarbons of the alcohols in Table 2 are also included. Although the results for some of these materials have been reported by other workers, the data were remeasured in $CDCl_3$ solutions to obtain results for a common solvent for more precise comparisons of the hydroxyl substituent effects.

Signal Assignments

The present results for *trans*-decalin and 10-methyl-*trans*-decalin agree reasonably well with those recently reported (29). Although most of the deviations are ~0.3 p.p.m., the differences between the two sets of data range from 0.05–0.8

TABLE 3. Substituent effects[a] of the hydroxyl group in cyclohexanols **18–21** and decalols **6–17**

	A Ring				B Ring			
Compound	α	β	γ	δ	γ	δ	ε	ζ
6	40.3	8.9, $6.7_{(CH)}$	−2.8, $-2.5_{(CH)}$	−0.8	−5.2	−0.6, −0.7	−0.5	
7	36.1	7.4, 3.7	−6.9, −8.1	−0.4	−4.7	−0.4, −0.5	−0.1	
8	43.3	8.7, 8.7	−2.3, $-2.5_{(CH)}$	$-1.4_{(CH)}$		−1.0	−0.5, −0.6	−0.4
9	39.7	6.1, 7.0	−6.7, −7.3	−0.5		−1.4	−0.5, −0.2	*a*−0.2
10	37.5	8.3, $5.3_{(C)}$	$-2.8, -1.6_{(CH)} -5.9_{(Me)}$	−1.2	−4.8	−1.2, −0.4	−0.4	
11	33.1	6.4, 4.4	−6.8, −8.3 +0.4	−0.5	−7.3	−0.5, −0.3	−0.5	
12	44.8	8.8, 9.2	$-1.4, +0.8_{(C)}$	$-0.9_{(CH)} +0.9_{(Me)}$		−0.5	−1.2, −0.9	−0.3
13	45.5	5.7, 6.9	−5.3, −0.4	+0.1 +2.2		−0.2	−0.6, −0.9	−0.2
14[b]	43.8	9.1, 8.8	$-2.1, -2.7_{(CH)}$	−0.9[c]		−0.5	−0.5, −1.0	−0.2
15[b]	39.4	6.5, 6.7	−6.5, −8.0	−0.2		−0.5	−0.2, −0.6	−0.2
16	40.7	9.4, $6.6_{(CH)}$	$-1.7, +0.9_{(C)}$	$-0.9, +1.1_{(Me)}$	−6.3	−0.5, −0.2	−0.4	
17	42.5	6.6, 2.7	−5.2, −0.2	+1.6, +3.4	−3.3	+0.1, −0.4	−0.2	
18								
19								
20[c]	44.0	9.0, 8.9	−1.5(CH), −2.4	−1.5, −0.6(Me)				
21[c]	(44.5)[d]	(10.5)[d]	(−1.0)[d]	(−2.3)[d]				

[a]Values represent $\delta_C^{ROH}-\delta_C^{RH}$ for corresponding carbons in each case; the carbon with the lower number is listed first in the tabulation for the same effects. Carbons other than methylenes are noted.
[b]The ε effects at the methyl carbon are 0.0 (**14**) and −1.0 p.p.m. (**15**).
[c]Comparing C-1 in **20** with C-3 in methylcyclohexane, C-2 (**20**) *vs.* C-2, -3 (**20**) *vs.* C-1, etc.
[d]Shieldings for *cis*-1,3-dimethylcyclohexane estimated from methyl substituent effects from methylcyclohexane assuming simple additivity.

p.p.m., indicating the existence of small solvent effects and the necessity of employing a common solvent in the present study.

With the results for the parent hydrocarbons and the cyclohexanols (11), the problem of individual assignments for the decalols was reduced. The signals of methylene carbons were distinguished from the others by off-resonance decoupling and then assigned by consideration of the expected substituent effects of the hydroxyl group. It had been established that the hydroxyl group deshields both the carbon to which it is bonded and its immediate neighbors; these have been termed α and β effects, respectively. Carbons three and four bonds removed from the oxygen atom tend to experience upfield shifts (8, 11) with the most pronounced effects found for *gauche* arrangements of γ carbons. More remote carbons are expected to be little affected by the hydroxyl group and this series permits characterization of the ε and ζ effects.

For decalols **6–9**, the carbinyl signal was readily identified as the lowest field signal, while the signals for C-6, -7, and -8 were taken as those closest to the values for the corresponding carbons in *trans*-decalin, although C-7 and -8 could not be uniquely identified in **6–8**. Of the remaining methylene signals, those at lowest field were assigned to the β carbons, *i.e.* C-2 in **6** and **7** and C-1, -3 in **8** and **9**. The 29 p.p.m. signal for each of **6** and **7** was assigned to C-9 since this carbon is *gauche* to the hydroxyl group and a shift of *ca.* −5 p.p.m. is expected to result. The pair of methylene signals remaining for **6–9** were assigned directly from their observed positions relative to the corresponding carbons in *trans*-decalin taking into account the upfield shift expected for those *gauche* to the axial hydroxyl group in **7** and **9**. For **6** and **7** the less shielded methine signal must arise from C-10 while the more shielded methine signal for **9** is from C-10 because of the γ effect of the axial hydroxyl. For **8** the methine signals were assigned from the fact that equatorial hydroxyl groups shield the γ carbon more than the δ carbon (8, 11). Thus, the assignments were completed.

For the methyldecalols **10–17**, the carbinyl, methyl, methine, and quaternary signals were easily identified. For **12–15**, the methylene carbons of the unsubstituted ring should be little affected by the hydroxyl group and so were assigned as listed. The assignments for C-7, -8, and -9 in **16** and **17** and C-6, -7, and -8 in **10** and **11** were based on similar grounds; for the latter the least shielded methylene signal arises from C-9, leaving only C-2, -3, and -4 unassigned. Since C-2 and -4 will be most and least affected, respectively, by the hydroxyl group, the assignments in Table 1 follow. The expected β-effect of *ca.* 10 p.p.m. permitted assignment of the β-methylene carbons for **12–17** and the remaining methylene signals were readily associated with specific carbons, with the distinctive differences for the γ carbons in the axial and equatorial cases taken into account.

The results for cholestane and androstane are in good agreement with those reported (30, 31) and the data for pregnane are very similar, as one would expect since detailed study of several steroids has established that substitution at C-17 has little effect on the A and B ring carbon shieldings (30). As in the case of the decalols, consideration of the shielding trends found for the cyclohexanols led to the assignments listed in Table 2. The five 3β-hydroxy derivatives exhibited closely similar patterns as did the pair of 3α-hydroxyandrostane derivatives. For each steroid the methine (C-5, -8, and -9), quaternary (C-10), and methyl (C-19) signals were identified by off-resonance decoupling and the carbinyl signals were characteristically shifted to the region, 65–72 p.p.m. Comparison of the cholestanediol spectra with that for cholestan-3β-ol led to the assignments listed with no apparent ambiguities.

Shielding Trends

With these assignments in hand, the observed trends can be considered in more detail. The consistency of the trends lends strong support to the present assignments, but, in any event, the emphasis is directed toward those centers for which the assignments are certain. In complex spectra a complete analysis may not be possible without an array of suitable model compounds for comparison but signals arising from methyl, carbinyl, quaternary, and, often, methine carbons are readily distinguished. To simplify discussion, the observed substituent effects in the decalols and cyclohexanols have been collected in Table 3; for each epimeric pair, the equatorial epimer is listed first.

Some general trends are apparent from comparison of the results for each epimeric pair. The α effects of equatorial hydroxyl groups are larger, unless the axial hydroxyl is *syn*-axial with the 10-methyl group (**13** and **17**). In all cases, the β effects produced by the equatorial hydroxyls are consistently larger than those found for their axial

counterparts and the magnitude of the downfield shifts depends on the degree of substitution of the affected carbon with methylene carbons undergoing greater shifts. This tendency was initially noted in a detailed examination of several norbornyl derivatives and possible interpretations of the trend were proposed (32). As already noted, greater upfield shifts were anticipated and are exhibited by the skeletal γ carbons in the axial epimers. The opposite trend for the methyl carbon in **12** and **13** is a consequence of the fact that it is γ *gauche* with respect to the equatorial hydroxyl (**12**) and *anti* relative to the axial hydroxyl (**13**). The attenuated α and β effects and enhanced upfield γ shifts found for the axial epimers are exactly analogous to the trends exhibited by a variety of substituents (2) and it is precisely this trend which led to the generalization that steric crowding enhances the shieldings of the carbons involved in the fragment containing the γ *gauche* groups.

The γ effects operative at the methylene carbon in the unsubstituted ring of **6**, **7**, **10**, **11**, **16**, and **17** are interesting since these vary from −3.3 to −7.3 p.p.m. although each arises from a similar γ *gauche* interaction with the hydroxyl group. Presumably the variation in these shifts results from different degrees of skeletal twisting associated with minimizing the steric interactions between the methyl and hydroxyl groups. The fact that the γ effects at C-9 in **6** and **7** are comparable lends credence to this interpretation since **6** and **7** would be expected to have very similar geometries. For the other two pairs, the γ effect at this methylene is smaller in the epimer having *syn*-axial methylhydroxyl interactions, *e.g.* **17** *vs.* **16**, and **10** *vs.* **11**. A consistent variation in the γ effects experienced by methylene and methine carbons is also apparent for **7**, **9**, **11**, and **15** with the methine carbon more strongly affected. It seems reasonable to propose that this tendency results from the somewhat greater freedom of the methylenes to minimize *gauche* interactions with the hydroxyl group since these alcohols are presumably less flexible at the ring junction. Similar variations in γ effects for methyl *vs.* methylene carbons have been noted in a series of methylcyclohexanes (33).

The results in the last few columns of Table 3 show that even the more remote carbons are slightly affected by the hydroxyl group. It seems reasonable to attribute the ε and ζ effects to slight geometrical alterations of the decalyl skeleton and it is interesting that the general tendency is toward higher field for these nuclei. A particularly striking example is the difference found for the methyl carbons in **14** and **15**. Although the hydroxyl and methyl groups are separated by five bonds and are on opposite faces of the molecule in **15**, its methyl carbon exhibits the larger shift. Perhaps the twist associated with minimizing the interactions of the hydroxyl group on the α face of the molecule tends to increase the γ *gauche* interactions experienced by the β-methyl carbon.

Within the series **6–17**, each of the arrangements **2–5**, with X = oxygen and Y = carbon, occurs several times while **1** occurs only twice. With few exceptions, the arrangements **2–5** are associated with upfield shifts while **1** produces relatively large (2–3 p.p.m.) downfield shifts. This deshielding influence is in direct contrast to the trend normally associated with sterically crowded carbons although of the possible arrangements **1–5** for δ groups, these groups are closest in **1**. Clearly, the interpretation relating steric crowding with upfield shifts through steric polarization of the interacting bonds (7) is inadequate to account for these *syn*-axial effects. It should be noted that the exceptions to the general trend for the α effects, mentioned earlier, are those having *syn*-axial OH···Me interactions, **13** and **17**. In each of these, the α effect is accentuated such that the axial hydroxyl group deshields the carbinyl carbon more than its equatorial counterpart. Thus, the generalization regarding attenuated α effects for axial hydroxyls, proposed earlier (4), is shown to have exceptions. The magnitude of the δ effects for *syn*-axial arrangements of substituents, however, is sufficiently large to render these useful for stereochemical analysis. At the same time, these trends show that the interpretation of small shifts in the spectra of complex molecules in conformational terms may be difficult since steric crowding can produce both upfield *and* downfield shifts.

To obtain additional examples of the hydroxyl substituent effects in related polycyclic systems, the sterols **22**, **23**, **30–36** were examined and the substituent effects observed are listed in Table 4. The data for **30–34** demonstrate both the general consistency of these effects and the fact that each varies by *ca.* ±0.5 p.p.m. These results are expected to be comparable to those for **14** while the data for **35** and **36** compare favorably with those for **15**. In these sterols it is again apparent that the more remote carbons in the **B** ring experience small effects of the hydroxyl group. As in the decalols, the methine carbons exhibit slightly

TABLE 4. Substituent effects[a] of 3- and 6-hydroxyl groups in some steroids

	A Ring							B Ring			
Compound	α (C-3)	β (C-2, C-4)		γ (C-1, C-5)		δ (C-10)	ε (C-19)	δ (C-6)	ε (C-7, C-9)		ζ (C-8)
30	44.3	9.4	9.2	−1.6	−2.1	−0.8	0.1	−0.3	−0.2	−0.5	0.0
31	44.1	9.7	8.9	−1.9	−2.4	−1.0	0.0	−0.6	−1.0	−1.1	−0.3
32	43.6	10.2	10.0	−1.4	−1.9	−0.6	0.2	0.0	0.1	−0.5	0.0
33	44.0	9.2	8.9	−1.9	−2.3	−0.8	0.0	−0.7	−1.7	−0.7	−1.0
34	43.6	9.8	10.1	−1.3	−1.8	−0.6	0.2	0.0	−0.3	−0.2	−0.2
35	38.6	7.6	7.8	−6.7	−7.6	0.2	−0.7	0.0	−0.5	−0.1	0.0
36	39.4	6.8	7.2	−7.9	−7.9	−0.6	−1.1	−0.8	−0.4	−0.6	−0.9

	B Ring							A Ring			
	α (C-6)	β (C-5, C-7)		γ (C-8, C-10)		δ (C-9, C-19)		γ (C-4)	δ (C-1, C-3)		ε (C-2)
23[b]	40.5	6.6	9.6	−1.3	0.7	−0.7	1.1	−6.0	0.2	−0.1	−0.3
22[b]	43.1	2.3	7.5	−5.2	−0.1	−0.2	3.4	−2.9	1.4	0.3	−0.1

[a]Values obtained from $\delta_C^{ROH} - \delta_C^{RH}$ for the corresponding carbons in each case.
[b]Values obtained by comparing 22 and 23 with cholestan-3β-ol.

greater γ effects than the methylene carbons and the angular methyl carbons in **35** and **36** are shielded relative to the C-19 absorption for androstane even though the hydroxyl group is five bonds away and on the opposite face of these molecules. The angular methyl absorptions for **22** and **23**, relative to **30**, exhibit the same shifts as those for **16** and **17** indicating the consistency of the δ effect of the hydroxyl group. It is interesting that the methyl shifts for **23**, **16**, and **12** are downfield since the orientation of the methyl and hydroxyl groups corresponds to **2**, X = CH_3, Y = OH. Similar orientations for methylene and hydroxyl groups in the other decalols lead to upfield shifts but it may be unwise to compare the effects for skeletal methylene carbons with those for methyl carbons since there are two bonded pathways between the hydroxyl and methylene groups. The somewhat smaller δ effect at the methyl carbon in **13** may be due to the greater ease with which the *syn*-axial Me···OH interaction can be reduced by skeletal twist. It may be noted that the other individual hydroxyl effects in **22** and **23** agree remarkably well with those for **16** and **17**, in particular, the γ effects at C-4 and the α, β, and γ effects in the substituted rings.

In summary, the hydroxyl group exerts comparable effects at the neighboring carbons in the *trans*-decalols, 10-methyl-*trans*-decalols, and sterols. Although the individual effects at the α, β, γ, and δ carbons can vary by *ca.* 0.5 p.p.m., the shifts are sufficiently distinctive to identify specific centers and should be valuable for signal assignments in a wide variety of terpenes and steroids. The steric dependence of the γ and δ effects clearly characterizes sterically crowded carbons and even though a theoretical interpretation of the opposite effects of γ *gauche* and *syn*-axial interactions is lacking these trends are qualitatively useful. From these and other results (12) the general tendency for downfield shifts arising from *syn*-axial arrangements of substituents shows that conformational interpretations of differences for complex systems must be approached cautiously. The sensitivity of carbon shieldings to minor changes in molecular geometry is illustrated by the small, but readily measurable, shifts found for centers five and six bonds removed from the hydroxyl group.

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