Carbon-13 Chemical Shifts of Substituted Nortricyclenes

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Abstract—^{13}C NMR spectra of a series of substituted nortricyclene derivatives have been measured, and the ^{13}C chemical shifts interpreted in terms of α, β, γ and δ-effects. The nature of these substituent shifts is discussed together with some analytical possibilities. The substituent shifts provide valuable data about the steric effects in strained molecules and can be used as increments for structural analysis, particularly for the determination of orientations of substituent groups.

INTRODUCTION

THE NORBORNYL skeleton provides a rigid and moderately strained framework of reasonably well known geometry that is very suitable for the study of various electronic, steric, magnetic and field effects, both in magnetic resonance and in organic reactivity. The substituent effects in norbornyl derivatives have been investigated by ^{1}H and particularly by ^{13}C NMR (CMR) spectroscopy in several laboratories.[1 to 6]

In extension of this work we have now studied the same effects in the related but yet more strained tricyclo-[2,2,1,0^{2,6}]-heptane (nortricyclene) skeleton. The object of this study was to establish the substituent influence in terms of α, β, γ and δ-effects.

The differences in bond lengths and angles of norbornane and nortricyclene derivatives are well known from the ED studies,[7 to 10] as well as from various theoretical calculations.[10 to 13] Changes in molecular geometry result in differences in physical properties and in chemical reactivity. For example, the formation of 3,5-hydroxy-acids in nortricyclene, but not in norbornane, is explained by the much longer distance between the C-3 and C-5 carbons as compared to that in norbornane.[14]

EXPERIMENTAL

The ^{13}C spectra were determined on liquids at 15·1 MHz and room temperature using a frequency-swept universal NMR spectrometer as described in our previous communication on norbornane derivatives.[2] The ^{13}C chemical shifts were measured in ppm downfield from internal methylene chloride (15 to 20%) and converted to the TMS scale using the relation $\delta_{TMS} = 53{\cdot}9 + \delta_{CH_2Cl_2}$. The interatomic distances, various angles and interaction energies were calculated from the ED data of Bauer *et al.* on norbornane and 4-chloronortricyclene.[8,9] For methyl derivatives and alcohols the bond between the methyl carbon or hydroxyl oxygen and the ring carbon was taken to be directed along the corresponding CH bond in the unsubstituted parent compound. In numerical calculations all the C—CH$_3$ distances were taken to be equal to 1·54 Å and the C—O distance to equal 1·43 Å. The authors acknowledge the help of Mrs V. Salum in writing the programs for these calculations on a M-32 computer.

RESULTS

The ^{13}C chemical shifts of all the nortricyclene derivatives measured are given in Table 1 and the structures in Scheme 1.

1. Hydrocarbon derivatives of nortricyclene

1.1. *Nortricyclene* (**1**). In this case the line assignments follow unambiguously from line intensities and signal multiplicities in the off-resonance decoupled spectra. Our data agree with those reported by Roberts *et al.*,[3] taking $\delta_{CS_2} = 193{\cdot}1 - \delta_{TMS}$.[2]

The high-field line at 10·3 ppm corresponds to the cyclopropyl carbons that always display the very characteristic large diamagnetic shifts. The chemical shift of the C-3,5,7 carbons in nortricyclene (33·4 ppm) is very close to the mean value of the chemical shifts of the corresponding carbon atoms in norbornane (33·5 ppm). At the same time the C-4 shift in nortricyclene is more diamagnetic than in norbornane by 7·4 ppm. This relative shift may be due to stronger nonbonded interactions of C-4 in nortricyclene. Indeed, the distance of C-4 from the cyclopropyl carbons is 2·28 Å in nortricyclene and the corresponding mean distance in norbornane is 2·41 Å. Although the difference in interatomic distances is only 0·13 Å, it can lead to significant diamagnetic shifts if one takes into account that the diamagnetic shift corresponding to a shortening of the C—C interatomic distance from 2·9 Å to 2·8 Å leads to a diamagnetic shift equal to about 3 ppm (see Fig. 1).

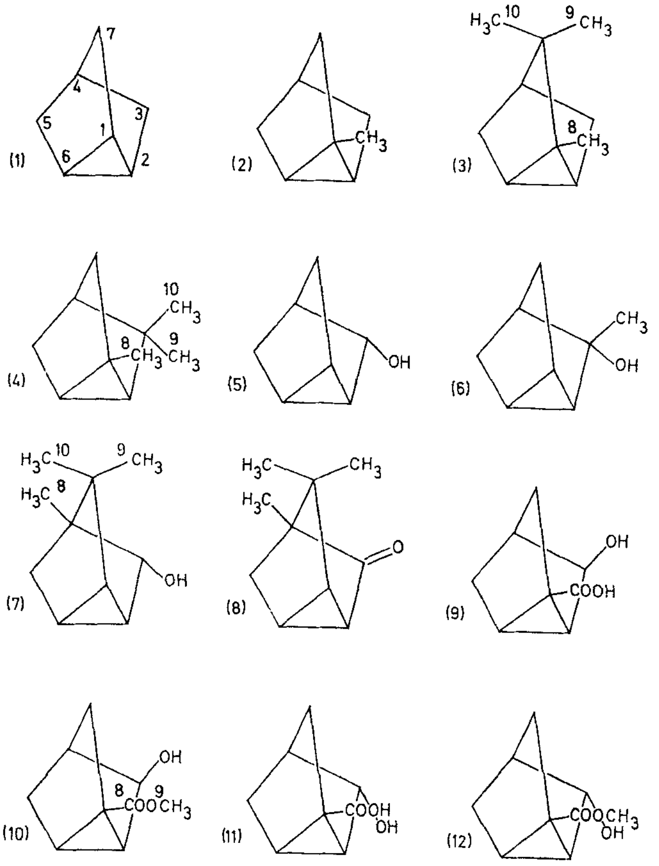
Another possibility to explain the high-field shift of C-4 in nortricyclene is by the diamagnetic anisotropy of the cyclopropyl ring. The 0·3 to 0·33 ppm difference in H-4 proton chemical shifts between norbornane and nortricyclene has been explained on the basis of this shielding effect by Patel *et al.*[18] and by Forsen.[19] This explanation is clearly untenable for the carbon shifts, however. Assuming the usual R^{-3} dependence of the relative chemical shifts upon diamagnetic anisotropy, the resulting diamagnetic shift of C-4 in nortricyclene relative to that in norbornane should be only 1·0 ppm, or nearly an order of magnitude less than the observed value of 7·4 ppm. Calculation by the formula given by Tori *et al.*[20] gives 0·58 ppm for the diamagnetic shift of H-4 and 2·0 ppm for that of C-4. Clearly, magnetic effects are not important in carbon resonance and may easily be overemphasised in proton resonance as well, as was shown to be the case for norbornane derivatives.[2]

1.2. 1-*Methylnortricyclene* (**2**). From the two lines of double intensity in the ^{13}C spectrum of this compound the high-field resonance must belong to the cyclopropyl carbons C-2 and C-6, and the low-field line to C-3 and C-5. The very low intensity of the 18·9 ppm line allows its unambiguous assignment to the substituted C-1 carbon of the three-membered ring. The line at 39·6 ppm forms a triplet in the off-resonance decoupled spectrum and consequently belongs to the C-7 methylene

TABLE 1. CARBON-13 CHEMICAL SHIFTS OF SUBSTITUTED NORTRICYCLENES

No.	Compound	^{13}C chemical shifts in ppm, measured downfield from external TMS[a] C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
(1)	Nortricyclene	10·3	10·3	33·4	29·9	33·4	10·3	33·4			
(2)	1-Methylnortricyclene	18·9	18·0	34·6	32·6	34·6	18·0	39·6	15·9		
(3)	Tricyclene (1,7,7-Trimethylnortricyclene)	26·9	20·3	32·0	42·7	32·0	20·3	43·8	11·1	21·2	21·2
(4)	Cyclofenchene (1,3,3-Trimethylnortricyclene)	20·3	30·3	43·2	43·2	33·4	20·3	38·4	16·8	23·5	23·5
(5)	3-Nortricyclenol	13·2	15·9	77·0	35·6	29·4	10·7	30·6			
(6)	3-Methyl-3-nortricyclenol	13·0	21·5	81·6	40·6	31·9	13·0	31·9	22·0		
(7)	Pericyclobornanol (4,7,7-Trimethyl-3-nortricyclenol)	27·4	19·9	79·3	45·6	33·3	13·8	42·9	7·9	19·9	21·8
(8)	Pericyclocamphanone	33·3	20·9	213·6	47·8	35·9	20·3	43·0	5·6	20·9	20·3
(9)	*cis*-3-Hydroxynortricyclene-1-carboxylic acid (solution in pyridine)	27·3	28·9	76·8	37·7	31·1	25·5	30·1	176·5		
(10)	*cis*-3-Hydroxynortricyclene-1-carboxylic acid methyl ester										
	(solution in CH_2Cl_2)	27·0	28·9	76·8	37·3	31·1	25·9	29·7	174·4	51·5	
	(solution in pyridine)	27·1	29·2	76·7	37·6	31·1	25·9	30·0	174·3	51·4	
(11)	*trans*-3-Hydroxynortricyclene-1-carboxylic acid										
	(solution in pyridine)	28·4	27·2	75·9	37·4	30·1	23·1	30·7	175·9		
(12)	*trans*-3-Hydroxynortricyclene-1-carboxylic acid methyl ester										
	(solution in CH_2Cl_2)	28·5	27·3	76·0	37·3	30·1	23·5	30·7	173·8	51·5	
	(solution in pyridine)	28·4	27·7	76·0	37·5	30·1	23·5	30·8	173·7	51·3	

[a] $\delta_{TMS} = 53{\cdot}9 + \delta_{CH_2Cl_2}$.



SCHEME 1. The structures of nortricyclene derivatives described in Table 1.

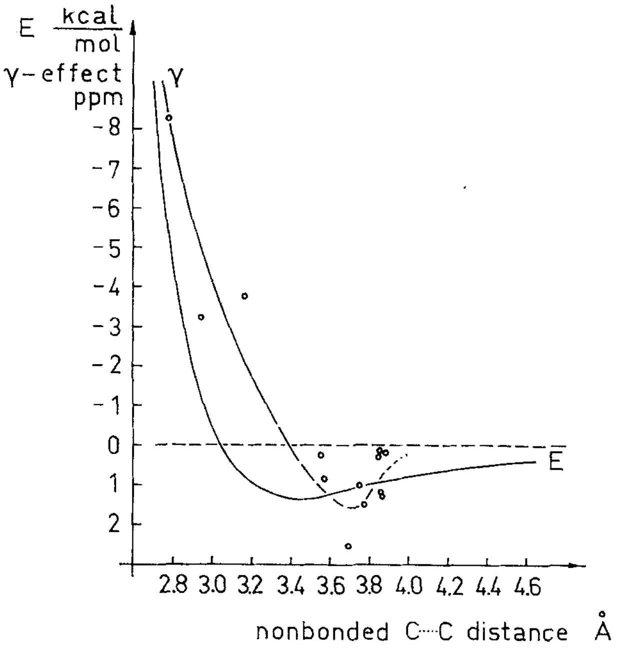


FIG. 1. Relation between the nonbonded C···C interatomic distance in Å, the van-der-Waals energy E (in kcal/mol) and the γ-effect (in ppm).

carbon. From the remaining two lines the peak at 32·6 ppm belongs to C-4 and that at 15·9 ppm to the methyl carbon.

1.3. *Tricyclene* (**3**). The weak lines at 26·9 ppm and 43·8 ppm are singlets in single resonance spectra and can be assigned to C-1 and C-7, respectively. The doublet at 42·7 ppm and the quartet at 11·1 ppm, both of unit intensity, correspond to C-4 and the 1-methyl carbon. Lines of double intensity at 32·0 ppm, 21·2 ppm and 20·3 ppm can be unambiguously assigned to C-3, C-5, the *gem*-methyl groups and to C-2, C-6 on the basis of signal multiplicities in off-resonance decoupled spectra.

1.4. *Cyclofenchene* (**4**). Assignment of the singlet (C-1, C-3) and triplet peaks (C-5, C-7) is obvious. The doublet at 43·2 ppm can only belong to C-4. Of the two high-field doublets, the 20·3 ppm resonance can be assigned to C-6 and the 30·3 ppm resonance to C-2 on the basis of the paramagnetic influence of the *gem*-methyl groups at C-3. The shift of the 1-methyl group must be close to that in **2** and so the peak at 16·8 ppm is assigned to it. The remaining line at 23·5 ppm corresponds to the *gem*-methyl carbons at C-3. There is no measurable difference between the chemical shifts of the two *gem*-carbons, although the distances to the 1-methyl group are different, 4·52 Å and 6·05 Å respectively. These distances are clearly large enough to preclude any interaction between the methyl groups. In tricyclene (**3**), where the distances are smaller, all methyl resonances are shifted upfield. The effect is most pronounced on the 1-methyl carbon (Δ = −4·8 ppm) and very close to that in bornane (Δ = −4·9 ppm).[2] These relative shifts are very nearly equal, as could be expected for the methyl-methyl distances that differ only by 0·03 Å. The 0·9 ppm difference between the 1-methyl shifts in **2** and **4** may be caused by small differences in the overall molecular geometry. Chemical shift of the *gem*-methyl carbons in tricyclene is 1·7 ppm downfield from those in bornane. This may be the result of less pronounced 1,4-nonbonded interactions between the ring methylene carbons and the *syn*-methyl groups, because the corresponding distance is 3·03 Å in tricyclene and 2·94 Å in bornane. Some confirmation of this assumption is provided by the corresponding −2·6 ppm and −2·5 ppm diamagnetic shifts of the γ-CH_2 carbons in both compounds. The presence of a three-membered ring in tricyclene may, however, also be a contributing factor.

The various interactions between the carbon atoms in bornane, tricyclene and cyclofenchene are illustrated in Table 2.

TABLE 2. THE ^{13}C CHEMICAL SHIFT CHANGES, CAUSED BY THE INTRODUCTION OF A *gem*-DIMETHYL GROUP INTO 1-METHYLNORBORNANE AND 1-METHYLNORTRICYCLENE

	Bornane		Tricyclene		Cyclofenchene
Carbon atom	C—C distance Å	Effect[a] ppm	C—C distance Å	Effect[a] ppm	Effect[a] ppm
α-C	1·54	−0·4	1·54	+4·2	+8·6
β-CH	2·59	+8·5	2·62	+10·1	+10·6
β-CH[b]					+12·3
β-C[b]	2·59	+2·7	2·59	+8·0	
γ-C[b]					+1·4
γ-CH[b]			3·31; 3·82	+2·3	+2·3
γ-CH_2	2·94; 3·84	−0·1[c]			−1.2
γ-CH_2	2·94; 3·84	−2·5[d]	3·03; 3·86	−2·6	−1·2
γ-CH_3	3·05	−4·9	3·02	−4·8	
δ-CH_3					+0·9

[a] Diamagnetic relative shifts upon introduction of the *gem*-methyl groups are shown with a negative sign.

[b] Three-membered ring in tricyclene and cyclofenchene.

[c] C-2, C-6.

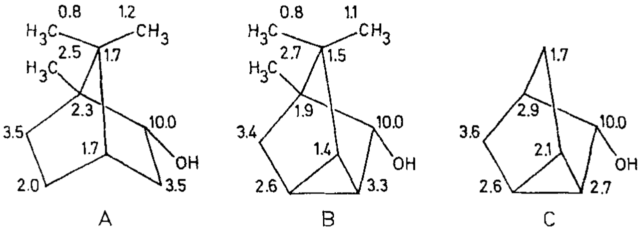
[d] C-3, C-5.

There are substantial differences in the α,β and γ-effects in norbornane and nortricyclene derivatives. The low-field α-effects in tricyclene and cyclofenchene are unusual for norbornane derivatives and must be somehow connected with the increased molecular strain. The β-effects are about the same in both series of compounds, but the γ-effects, caused by the 1,4-nonbonded *gauche* interactions, are very different for the carbons of the three-membered ring and for all the other carbons. The γ-effect on C-3 in bornane is diamagnetic (Δ = −2·5 ppm) and very close to the corresponding effect in tricyclene (Δ = −2·6 ppm).

The influence of the *gem*-methyl groups on C-2 in bornane is perturbed by the 1-methyl group and thus the diamagnetic shift is only 0·1 ppm. In tricyclene the distance from C-2 to the 7-*syn* methyl group is extended from 2·94 Å to 3·31 Å, that is into the range where the 1,4-interactions result in paramagnetic shifts. In addition the dihedral angles between the 7-methyl carbons and C-2 in norbornane (65° and 172°) and tricyclene (91° and 154°) are different. The 2·3 ppm low-field shift is rather large and may contain some additional influences.

2. Derivatives of Nortricyclene with Polar Substituents

2.1. 3-*Nortricyclenol* (**5**). The assignment of C-3 and C-4 is straightforward on the basis of signal multiplicities and the very characteristic chemical shifts. The high-field triplet at 29·4 ppm can be assigned to C-5 on the basis of the 1,4-*gauche* interaction that always leads to relative diamagnetic shifts at distances less than 3 Å. This assignment leaves the other triplet at 30·6 ppm to C-7. From the cyclopropyl carbons C-2 could be expected to resonate at the lowest field because of the paramagnetic β-effect of the hydroxyl group. C-1 and C-6 shifts were assigned on the basis of the lanthanide-induced shifts. The resulting shift changes upon addition of $Eu(DPM)_3$ to a CH_2Cl_2 solution of the alcohol are shown in Scheme 2, together with similar data for pericyclobornanol (**7**) and borneol.[5] All the induced shifts are paramagnetic and normalised to a C-3 shift equal to 10 ppm.



SCHEME 2. Lanthanide-induced carbon shifts of borneol (A), pericycloborneol (B) and 3-nortricyclenol (C). The lanthanide-induced shift of C-3 is taken to equal 10 ppm.

2.2. 3-*Methyl*-3-*hydroxynortricyclene* (**6**). Accidental equality of the C-1 and C-6 as well as of the C-5 and C-7 chemical shifts makes the spectral assignments self-evident. Signal multiplicities were used to differentiate between some closely spaced lines. The accidental equality of the shifts of both of the symmetrically placed pairs of carbons once more underlines the very near equality of the γ-effects caused by the methyl and hydroxyl groups (see Table 1 of the substituent parameters for norbornane derivatives in Ref. 2). At the same time the shift values show that the two γ-effects are non-additive.

2.3. *Pericyclobornanol* (**7**). In this compound the assignment of C-3, C-5 and 4-CH_3 is obvious. Weak singlets at 45·6 ppm and 42·9 ppm correspond to quaternary carbons, and are assigned on the basis of the lanthanide-induced shifts (see Scheme 2) and by analogy with borneol.[2,5] All other shifts could likewise be assigned with the aid of the induced shifts and this technique provided the only straightforward means of assignment of the *gem*-methyl resonances. At the same time these assignments are consistent with the expected influence of the methyl groups, which can lead to only paramagnetic shifts on the symmetrically spaced C-6 and C-2, with approximate conservation of the characteristic shift difference of these carbons in **5** and **7**.

2.4. *Pericyclocamphanone* (**8**). The same arguments and techniques were used for the assignments. Of course, the assignment of the two CH-2 and CH-6 groups as well as of the *geminal* methyl groups with very close shifts is not unambiguous. The most pronounced peculiarity of the ^{13}C shifts in this compound is the large paramagnetic shifts of the cyclopropyl carbons C-1 and C-6 in β-position to the carbonyl group. Such paramagnetic shifts are caused by conjugation of the three-membered ring with the carbonyl group. For example, the difference in β-cyclopropyl carbon shifts between cyclopropyl phenyl carbinol and cyclopropyl phenyl ketone is 8 ppm; a difference very close to that between the γ-carbon resonances in allyl alcohol and acrolein. Only oxygen resonance, however, can provide unequivocal evidence of cyclopropyl conjugation with a carbonyl group. A study of ^{17}O resonance of cyclopropyl ketones showed that in dicyclopropyl ketone the paramagnetic shift of β-cyclopropyl carbons is matched by a significant diamagnetic shift of the oxygen resonance, as one could expect in the case of a charge redistribution. If one takes the ^{17}O shift in acetone to be zero, then the same resonance is shifted upfield by 34 ppm in di-isopropyl ketone and significantly more, by 100 ppm in dicyclopropyl ketone.

2.5. cis-3-*Hydroxynortricyclene*-1-*carboxylic acid* (**9**), *the methyl ester* (**10**), trans-3-*Hydroxytricyclene*-1-*carboxylic acid* (**11**) *and the methyl ester* (**12**). An investigation of these isomers by proton resonance has been reported previously.[21] The acids were measured as solutions in pyridine, using methylene chloride as internal standard. The esters were measured both in methylene chloride solution and with the addition of about 50% pyridine to compensate for any possible solvent effects in the spectra of the acids.

The assignment of the carboxyl, methoxyl and C-3 carbons is unambiguous in all cases. The only singlets in the spectra of all four compounds must belong to the cyclopropyl C-1 carbons carrying the carboxyl groups and are easily assigned. The low-field doublets correspond to C-4. Of the remaining cyclopropyl carbons, C-2 must resonate at a lower field due to the β-effect of the hydroxyl group. The C-5 and C-7 carbons were assigned by means of the selective decoupling experiments. Although the distance between the hydroxyl oxygen and the carboxyl carbon exceeds 4 Å in the *cis* and 5 Å in the *trans* isomer, the shift difference between the isomers is remarkably large (0·6 ppm). The chemical shifts of the acid and ester in the same solvent have only minor differences in the cyclopropyl carbons. In fact, the shift differences between the carboxyl carbon of the acid and ester are about the smallest described thus far, being only 2·2 ppm against the usual 5 to 7 ppm.[22,23,24] The solvent shifts between methylene chloride and pyridine are also small. The shifts do not exceed those observed in the proton spectra, but may be indicative of the solvent-solute interaction via the hydroxyl group, as discussed by Paasivirta.[21]

All the measured ^{13}C chemical shifts are quite regular and prove that the α-acid must be the *cis* and β-acid the *trans* isomer. This conclusion was drawn from a comparison of the chemical shifts of cyclopropyl carbons. If one makes the reasonable assumption that β-effects of the carboxyl group on cyclopropyl carbons are equal in both isomers, then the differences in the chemical shifts of C-1 and C-6 must be caused by the influence of the hydroxyl group on these carbons. Both the C-1 resonance in the *trans* isomer and the C-6 resonance in the *cis* isomer must be shifted by 2·5 ppm downfield. The experimental shift differences between the isomers are 1·5 ppm on C-1 and 2·4 ppm on C-6, i.e. very close to the expected values. The C-5, C-7 shifts also behave as expected, the carbon closest to the hydroxyl oxygen showing a distinct diamagnetic shift. Other shift differences between the isomers (C-2 and C-3) are too small to discuss at present.

DISCUSSION

Exactly as for norbornane derivatives,[2] substituted nortricyclenes provide numerous examples of the very sensitive and analytically significant dependence of the ^{13}C chemical shifts upon the molecular geometry. The general character of the α, β and γ-effects is the same as in aliphatic compounds, the first two being paramagnetic and the third mostly diamagnetic (see Table 4 in Ref. 2). Although the various substituent effects are not strictly additive, the limited additivity is usually sufficient for an analytical identification of the various isomers as well as for the analysis of complicated mixtures that cannot be separated by rectification or chromatography.

The *gauche*-1,4-interaction is the most important single factor that determines the ^{13}C chemical shift dependence upon conformational factors and the molecular structure. At the same time the exact mechanism of this interaction is quite unknown although there has been no lack of proposed theoretical explanations.

As follows from the general theory of magnetic shielding developed by Ramsey[25] and modified by Saika and Slichter,[26] the ^{13}C screening constant can be subdivided into three atomic contributions—the diamagnetic term, the paramagnetic term and the term which includes all magnetic screening influences of other parts of the molecule.

The influence of the diamagnetic term is insignificant. The recent proposal of Mason[27] to include the α-carbon atoms in its calculation leads to larger values and to important substituent effects, but is quite artificial. After all, there is no logical reason not to include the β-atoms and so on, winding up with truly astronomical σ_d values. If, however, one assumes that the ^{13}C shifts depend primarily upon the paramagnetic term σ_p, then only changes in the immediate electronic environment of the carbon atom are important. It follows then from the Ramsey theory that the presence of low-lying excited states leads to a decrease in ΔE and to a relative paramagnetic shift, while any increase in electron density under the influence of some substituent group or steric polarisation along the H—C bond[27] increases the average orbital radius and a diamagnetic shift results. Deviations from the classical perfect pairing bond structures have been shown to result in either diamagnetic or paramagnetic shifts.[28]

At the same time it is known that the ^{13}C shift changes in the γ-position (the 1,4-*gauche* effect) show the following regularities:

1. The effect is generally diamagnetic and increases with decreasing interatomic distance between the first and the fourth heavier atoms, not counting the hydrogens. At greater distances, however, paramagnetic γ-effects are common (see Table 3).

The sign of the γ-effect at short distances is such that

TABLE 3. 1,4-*gauche*-EFFECTS ON ^{13}C CHEMICAL SHIFTS IN SOME METHYL-SUBSTITUTED RIGID HYDROCARBONS

Compound	Interacting carbon atoms	C_1—C_4 distance Å	Dihedral angle between the C_1C_2 and C_3C_4 planes	Distance in Å between the methyl hydrogen (H_1) and the closest H_4 atom[a]		1,4-effect in ppm, calculated from the formula of Grant and Cheney[b]		1,4-effect in ppm, experimental value[c]
				min	max	min	max	
1-Methyladamantane	γ-CH ↔ CH_3	3·88	180°	4·57	5·58	+0·001	+0·006	+0·3
1-Methylnorbornane	3-CH_2 ↔ CH_3	3·86	154°	4·35	5·32	+0·001	+0·008	+1·3
1-Methylnortricyclene	3-CH_2 ↔ CH_3	3·86	138°	4·06	5·08	+0·001	+0·003	+1·2
2-exo-Methylnorbornane	6-CH_2 ↔ CH_3	3·85	170°	4·19	4·75	+0·001	+0·008	+0·1
7-Methylnorbornane	6-CH_2 ↔ *anti*-CH_3	3·84	172°	4·56	5·06	+0·002	+0·006	+0·5
2-endo-Methylnorbornane	7-CH_2 ↔ CH_3	3·77	152°	4·58	4·83	+0·002	+0·007	+1·5
1-Methylnortricyclene	4-CH ↔ CH_3	3·70	180°	3·91	4·44	+0·001	+0·006	+2·7
2-endo-Methylnorbornane	4-CH ↔ CH_3	3·55	121°	3·43	4·48	+0·001	+0·014	+0·8
2-exo-Methylnorbornane	4-CH ↔ CH_3	3·55	121°	3·43	4·49	+0·001	+0·029	+0·2
2-exo-Methylnorbornane	7-CH_2 ↔ CH_3	3·17	85°	2·22	4·00	−0·001	−2·02	−3·8
7-Methylnorbornane	2-CH_2 ↔ *syn*-CH_3	2·94	65°	2·02	3·92	+0·030	−1·82	−3·2
2-endo-Methylnorbornane	6-CH_2 ↔ CH_3	2·77	48°	1·35	3·32	−0·100	−33·5	−8·3

[a] The effect caused by the other, more distant hydrogen atom is smaller and in all cases negligible in comparison with the experimental value.
[b] D. M. Grant and B. V. Cheney, *J. Amer. Chem. Soc.* **89,** 5315 (1967).
[c] Difference between the γ-C chemical shifts in the substituted and the unsubstituted hydrocarbon, in ppm.

diamagnetic −3 to −6 ppm ^{13}C shifts result irrespective of the nature of the other nucleus which may be carbon, oxygen, fluorine, nitrogen, chlorine, etc. An important exception has been found by Grant *et al.*[15] in 2-*tert*-butyl-1,3-dioxanes, however, where in the 5,5-dimethyl isomer the *cis* (axial and closer to the oxygen atoms) methyl group is the less shielded one. This difference is even larger in isomeric *cis-trans* pairs of 2-*tert*-butyl-5-methyl-1,3-dioxanes and 2,5-di-*tert*-butyl-1,3-dioxanes.[15] The abnormal ^{13}C shifts have been interpreted by pointing out that an axial substituent at C-5 in the *cis*-1,3-dioxanes has no *syn* axial hydrogen with which to interact, but rather appears to be deshielded by the ring oxygen atoms, which thus cause a downfield shift of the 5-axial substituents.[15] This explanation is, however, not quite convincing, since it leaves unexplained the significant diamagnetic shift of both methyl resonances in *cis*- and *trans*-2-*tert*-butyl-5-methyl-1,3-dioxanes relative to 1,1-dimethylcyclohexane. It is also important to note that the nonprotonated oxygen atoms cause very regular diamagnetic shifts of −3·0 ppm and −4·1 ppm of the corresponding γ-carbons in the cyclohexane ring of 1,1-*gem*-dihydroxycyclohexane diacetate and in the ketal formed from cyclohexanone and ethylene glycol.

2. The sign and magnitude of the γ-effect bear some relation to the van-der-Waals energy E between two nonbonded atoms (see Fig. 1). The van-der-Waals energies have been calculated according to Hill.[32] Indeed, the calculated distances from the sterically influenced carbon atoms to methyl carbons and hydrogens are in several cases smaller than the sum of the van-der-Waals radii of the two interacting carbons (3·4 Å) or carbon and hydrogen (2·9 Å)[32] (see Table 3). The same applies to the equilibrium distances of isolated atoms as given by Kitaigorodsky (3·8 Å for C—C and 3·15 Å for the C—H distance).[33]

3. Approximate linearity exists between the calculated C_4—C_{methyl} and C_4—H_{methyl} distances, see Fig. 2. This linear dependence simplifies any empirical interpretation of the steric interactions, because only C—C, C—H or even H—H distances can be considered, although the other distances can be the really important ones.

4. There is a very pronounced angle dependence of the magnitude of the γ-effect. It is not easy to distinguish between the distance and the angle effects, however, and it is impossible to find any obvious angle dependence for the γ-effects in strained hydrocarbons (see Table 3).

5. The number of interacting heavier atoms and not just the distance between the ends of the interacting chain, is important. The δ and ε-effects between the carbon atoms are usually paramagnetic,[2] even at short distances where the H· · ·H interactions are strong, as is the case for the methyl carbons of 1,8-dimethylnaphthalene[45] and veratrol.[27] In 1,8-dimethylnaphthalene the methyl shift is 7·3 ppm to lower field relative to 1-methylnaphthalene, whereas in *o*-xylene, where the 1,4-interaction is possible, this shift (1·8 ppm) is diamagnetic relative to toluene.[45]

6. Very similar, but larger diamagnetic γ-effects appear in the spectra of ^{15}N, ^{17}O, ^{19}F, ^{31}P and other nuclei.[2,3] No effects of this type appear in proton spectra. The γ-proton shifts are in many cases opposite to the γ-carbon

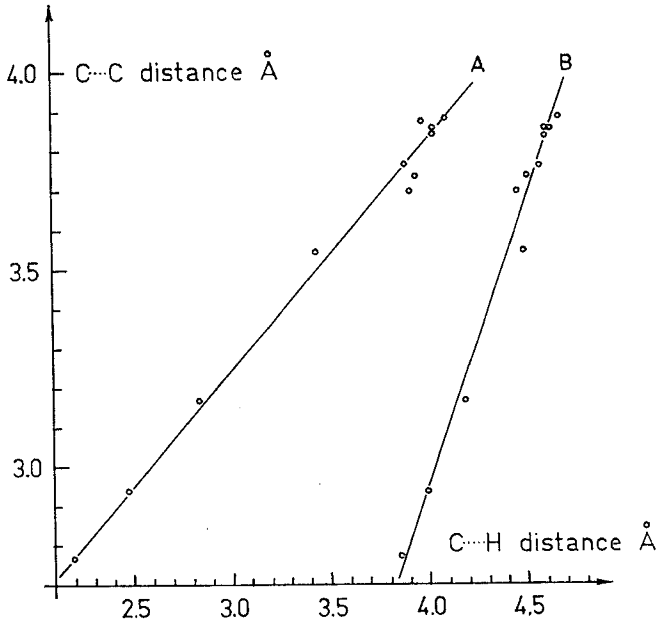


FIG. 2. Relation between the calculated C_4—C_{methyl} and the C_4—H_{methyl} distances. A—minimum value. B—maximum value.

shifts[2] and in aliphatic chains parallel those anticipated on the basis of inductive effects propagating along the chain, showing no peculiarities in the γ-position.

7. The γ-effect parallels the changes in ultraviolet spectra. There is a marked difference between the ^{13}C shifts and the ultraviolet band positions and intensities of *cis*- and *trans*-alkenes.[30] The σ—σ^* transition of the C—C bond electrons in *n*-butane occurs at 70400 cm^{-1} for the *trans*- and at 75000 cm^{-1} for the *gauche*-conformer,[31] thus showing a very pronounced change in the molecular excited states as a result of steric interactions in the *gauche* form.

8. There is practically no correlation between the magnitude of the γ-effect and the corresponding long-range proton-proton coupling constant through five bonds. In fact, large effects have been found between atoms that do not have a *W*-arrangement of the intervening bonds (C-6 and *endo*-2-methyl group in norbornane derivatives, α-CH$_2$ groups in *cis*-unsaturated compounds, etc.).

9. The 1,4-interaction is non-additive and not reciprocal. It is very different for different nuclei and can be unequal even for nuclei of the same type (^{13}C) in different positions in the same molecule.

10. The magnitude of the γ-effect bears no simple relation to the C—H, C—Cl or C=O bond polarisabilities, but rather strongly depends on carbon hybridisation.

Even though the 1,4-interactions usually involve short H· · ·H distances and changes in the corresponding C—H bonds have been held responsible for the observed diamagnetic effects,[27] the presence of hydrogen atoms is by no means essential. The critical C-6 and C-7 carbon shifts in *endo*- and *exo*-norbornanols show only quite insignificant changes (0·0 to 0·7 ppm) upon silylation when the hydroxyl hydrogen is replaced by the very bulky trimethylsilyl group. Likewise, very characteristic ^{13}C shift differences between *cis*- and *trans*-isomers have been found in halogen-substituted acrylic acids where the only interacting groups were halogens and the carboxyl group.[16]

11. The long-range γ-effects in carbon shielding may be related to the abnormal effects encountered in the transmission of nonconjugative substituent effects in rigid strained molecules, showing both angle dependence and reversed attenuation effects.[34,35] Such chemical effects have been very successfully explained by the field model and have cast some doubt on the general validity of the σ-inductive model in organic chemistry.

12. Last, but not least—the introduction of substituents into the molecule can lead to changes in the overall molecular geometry and to significantly changed rotational barriers, even to the point of replacing the repulsive forces with those of attraction, as it is common for the oxygen-containing groups.[32,36]

Even in the cases where all direct γ-interactions between the carbon or hydrogen atoms are geometrically very unfavourable and the first (α and β) neighbours are the same, the methyl and the α-carbon shifts can show significant variations. These methyl shifts are 31·1 ppm in 1-methyladamantane, only 21·4 ppm in 1-methylnorbornane and 27·7 ppm in 1-methyl[3,2,1]bicyclooctane. Formation of a 'superchair' from an ordinary chair conformation in 1,3-dioxanes[46] can and does likewise lead to significant carbon shift changes, both in the ring and for the substituents.[15]

Grant and Paul were the first to mention the very characteristic diamagnetic γ-effects in alkanes.[37,38] It was shown that although magnetic anisotropy effects could be used for the explanation and were considered at first,[37] the necessary anisotropy value $\Delta\chi_{CC}$ would be too large by at least two orders of magnitude.[38] Of course, any such explanation would also be in conflict with the observed proton shifts. The observed effects were attributed to the admixture of higher paramagnetic orbitals, alteration in the degree of bond delocalisation at the ^{13}C atom and changes in hybridisation due to deviations from tetrahedral symmetry.

Similar effects were found in cyclohexane derivatives[39] and proposed as a new method for conformational analysis of alicyclic compounds, but without any theoretical interpretation. In the same year diamagnetic interactions between *ortho*-methyl groups in methylbenzenes were described.[40] Deviations from perfect pairing in the two closely positioned CH bonds as well as additional π-electron delocalisation with the interacting methyl groups were held responsible for the relative diamagnetic shifts. Soon afterwards the sterically induced diamagnetic shifts were observed in isomeric normal alkenes and later in isomeric halogen-substituted acrylic acids[16] and attributed to the changes in the mean excitation energy ΔE.[30] Indeed, the ultraviolet spectra of *cis*- and *trans*-alkenes, as well as those of the *gauche*- and *trans*-conformers of alkanes are always different and a diamagnetic relative shift for the interacting carbon atoms in the more strained *cis*-isomer or *gauche*-conformer is predicted on this basis, in full agreement with the experiment. Too little is known about the ultraviolet spectra and the excited states of complicated isomeric molecules, however, to allow any quantitative calculations.

After the study of alkylbenzenes, sterically perturbed carbon atoms were found to be shifted to higher fields in cyclohexane derivatives as well.[41,42] This diamagnetic shift was ascribed to induced polarisation of charge along the sterically perturbed CH bond.[27] A semi-empirical formula for predicting the angular and distance dependence of such relative diamagnetic ^{13}C shift was proposed by Grant and Cheney.[27,28] The formula has been reasonably successful for predicting the ^{13}C shifts in methyl-substituted cyclohexanes,[27,42] but fails quantitatively for norbornane[3] and tricyclene derivatives (see Table 3), although the qualitative predictions are correct. As already pointed out by us[16] and by Roberts *et al.*[3] the assumption that the diamagnetic γ-effects are caused by repulsive hydrogen-hydrogen interaction is clearly insufficient, since similar diamagnetic shifts are caused by many other groups that do not contain hydrogens, particularly carbonyl, hydroxyl, the ether oxygen and the halogens.[16]

The study of nortricyclene derivatives did not lead to new conclusions about the nature of the γ-effect. It was once again shown that the C· · ·O interactions at close distances lead to relative diamagnetic ^{13}C shifts and that the H· · ·H interactions as well as the magnetic effects can be safely disregarded as a possible cause of the γ-effect, even in compounds containing the highly anisotropic cyclopropyl ring. Bond polarisability could play an important role, but calculations using the proposed formula[27,28] lead in some cases to unsatisfactory results and leave the question open why some β and δ-shifts are not diamagnetic either. The long-range field effect could provide a very attractive solution to the problem, but the expected angular dependence does not fit the expermental data, and the close similarity between the effects caused by methyl and hydroxyl groups with quite different electrical dipoles remains unexplained. While it is true that strain leads to changes in atomic charges and quite good relations of the ^{13}C shifts with the calculated charges can be found, such data is not available for large molecules which are of primary interest in this field. The same applies to the excited states and the interpreted ultraviolet spectra of norbornane and nortricyclene derivatives.

In general the situation with the diamagnetic nonbonded-1,4-effects is very similar to that of the barriers of rotation about the single bonds.[44] The problem is actually even more complicated, because the molecular excited states also play an important role. Only a full numerical quantum-chemical calculation might accurately predict the measured γ-effect, but at the inevitable price of mathematical complexity. At the same time the various simplified relations clearly describe only one and possibly not always the most important facet of the phenomenon. Even though a full understanding of the interaction is difficult, there is no question about the analytical usefulness of the simple fact that in yet another case the more crowded alicyclic structure has also the greater diamagnetic ^{13}C chemical shifts.

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