^{13}C- and ^{1}H-NMR Shielding Effects in Aliphatic *gauche/trans* Fragments

Hans-Jörg Schneider*, Ulrich Buchheit, Volker Hoppen, and Günther Schmidt

Fachrichtung Organische Chemie der Universität des Saarlandes, D-6600 Saarbrücken 11 (FRG)

Received July 26, 1988

Keywords: NMR shielding mechanisms / Steric effects / Hybridization

On the basis of improved calculation models, of new NMR measurements with bicyclo[2.2.1]heptyl and cyclohexyl compounds, and of literature data it is shown that classical mechanisms of sterically induced charge polarizations, of linear electric field, and of anisotropy effects can account for many substituent-induced shielding (SIS) differences. The rôle of steric distortions on α- and β-SIS is discussed; bond angle variations generated by a methyl group introduction at C-α and subsequent hybridization changes are correlated with Cα-Me SIS values as well as with the eq/ax shielding in cyclohexanes.

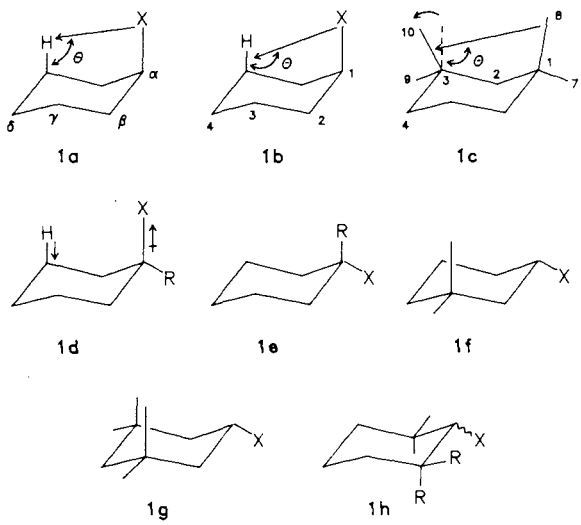
^{13}C- und ^{1}H-NMR-Abschirmungseffekte in aliphatischen *gauche/trans*-Fragmenten

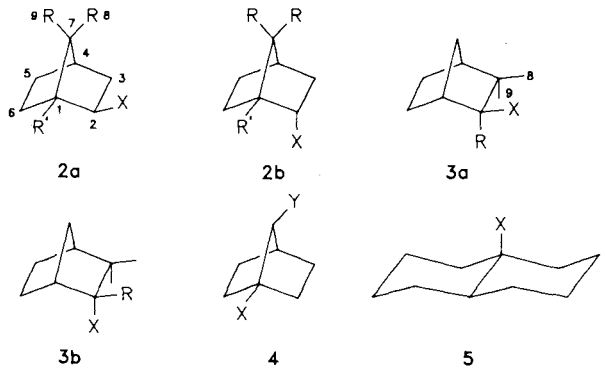
Auf der Basis von verbesserten rechnerischen Modellen, von neuen NMR-Messungen an Bicyclo[2.2.1]heptan- und an Cyclohexanverbindungen sowie von Literaturdaten wird gezeigt, daß klassische Mechanismen von sterisch induzierten Ladungspolarisierungen, von linearen elektrischen Feldeffekten und Anisotropieeffekten zahlreiche Unterschiede bei Substituenteneffekten erklären. Die Rolle sterischer Geometriestörungen auf α- und β-Effekte wird diskutiert; die durch Einführung von α-Methylsubstituenten induzierten Bindungswinkeländerungen an C-α und die daraus berechneten Hybridisierungsdifferenzen lassen sich sowohl mit den sehr unterschiedlichen Cα-Me-Substituenteneffekten wie auch mit den entsprechenden Differenzen zwischen äquatorialen und axialen Susbtituenten korrelieren.

The significant shielding differences between *gauche* and *trans* orientations in aliphatic frameworks have initiated many publications, particularly in the field of ^{13}C-NMR spectroscopy[1]. The advent of high-field and of 2D NMR makes ^{1}H-NMR shifts a similarly promising tool even for complicated frameworks such as saturated steroids[2], and allows for the first time a mechanistic comparison of complementary proton and carbon shieldings.

Stereochemical applications of ^{13}C-NMR shifts have been largely based on the shielding of γ-carbon atoms by a *syn (gauche)* alkyl substitutent[1], which has been rationalized by Grant and Cheney[3] with sterically induced charge polarization along a *syn*-axial C–H bond. On the basis of more realistic model geometries and of a different equation derived a recognized force-field parametrization we have shown[4a] that these steric effects not only correctly predict the substituent induced shieldings (SIS) by X = Me on *syn*-γ atoms such as C-3 in **1a**/**1b**, **1d**, C-7 in **2a** (R = R′ = H), or C-6 in **2b**, or *syn*-methyl carbons in **3a**, **3b** (Table 1) and similarly in steroids[4b], but also *do* allow for *de*shielding effects on ϑ-carbon atoms[1a,b,5], such as on C-10 in **1c**[6] or C-8 in **2a**[7] (R = Me, Table 1). As a necessary consequence of the angular dependence of the polarizing gradient, *de*shielding at γ-carbon atoms will occur for $\theta < 90°$, which is the case for several interactions in ϑ groups such C-8 in **2a** (R′ = R = Me)[4a].

If one places the point of action for the steric forces not arbitrarily at the hydrogen end of the polarized C–H bond as it has been done earlier[3,4a] (model **1a**), but more towards carbon (model **1b**) – which is a better representation of the polarized electron cloud – it becomes clear, why with





  0009–2940/89/0202–0321 $ 02.50/0

Table 1. ^{13}C-NMR shifts in bicyclo[2.2.1]heptanes (δ values, internal standard: TMS, 10–40% solutions, $T = 300 \pm 10$ K); the symbols *, •, $^+$ refer to exchangeable signals

Nr.	Me in Pos.	X (in Pos.)	cf. Ref.	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10 (R)
2a, b	7,7 (R′ = H)	H	7g	43.86	29.46					46.04	21.20		
2a	7,7 (R′ = H)	x-2-Me	–[a]	50.14	38.90	39.39	44.98	28.05*	31.46*	46.28	23.04•	22.94•	
2b	7,7 (R′ = H)	n-2-Me	–[a]	49.07	31.88	38.74	44.98	29.83	21.06*	47.84	20.96*	21.90*	
2a, b	1,7,7	H	7a, 7b[b]	47.0	37.1	29.1	46.6	29.1	37.1	45.4	19.6		16.2
2a	1,7,7	x-2-Cl	–[a]	49.9	67.4	42.5	46.1	27.0	36.4	47.4	20.1	20.1	13.3
2b	1,7,7	n-2-Cl	–[a]	51.2	67.4	40.7	45.6	28.5	28.5	48.3	18.9	20.8	13.5
2a	1,7,7	x-2-Br	–[a]	49.3	60.8	43.0	46.7	27.0	36.5	47.8	20.5*	20.2*	15.4
2b	1,7,7	n-2-Br	–[a]	50.6	62.1	40.8	45.0	28.0	30.3	46.7	18.5	20.8	29.0
2a	1,7,7	x-2-NH_2[d]	–[a], 7g[c]	48.2	60.2	40.6	45.1	27.4	36.4	46.6	21.0*	20.4*	11.9
2b	1,7,7	n-2-NH_2[d]	–[a], 7g[c]	49.1	56.5	39.4	45.1	29.7	26.4	48.2	18.6	20.4	13.5
2a	1,7,7	x-2-Me[d,e]	–[a]	47.35*	41.79	39.81	45.66	27.59	38.51	46.73*	21.09•	20.70•	12.77
2b	1,7,7	n-2-Me[d,f]	–[a]	48.62*	37.44	38.12	45.66	28.70$^+$	28.01$^+$	47.87*	20.65•	19.92•	14.04
3a, b	3,3 (R = H)	H	7a, 7b[b]	38.8	47.2	36.9	48.1	25.1	28.7	38.7	31.7	27.3	
3a	3,3 (R = H)	x-2-OH	–[a], 7d[c]	46.1	83.2	42.6	47.9	24.7	23.6	35.0	23.0	26.0	
3b	3,3 (R = H)	n-2-OH	–[a], 7d[c]	43.9	79.5	37.8	48.2	24.7	18.3	33.8	30.6	20.3	
3a	3,3 (R = H)	x-2-Me	–[a]	46.34	48.68	40.1	49.59	24.55	30.03	35.68	25.00	27.93	
3b	3,3 (R = H)	n-2-Me	–[a]	44.13	44.85	36.79	49.27	24.94	20.02	37.31	32.35	21.50	
3a	2,3,3	2-x-Cl	–[a]	54.92	84.79	44.90	50.43	23.95	23.95	35.73	25.31	23.36	(2)30.78
3a	2,3,3	2-x-OH	–[a]	51.30	79.40	43.60	49.40	23.70	23.70	34.20	25.30	23.70	(2)21.50
3b	2,3,3	2-n-OH	–[a]	50.08	77.80	41.90	49.60	21.20	24.00	34.60	27.00	21.90	(2)26.40

[a] This work. – [b] Average values from ref.[7a,7b]. – [c] Similar literature values available. – [d] Measured as epimeric mixtures (**2a** + **2b**). – [e] X = Mc: 19.70. – [f] 15.60.

syn-γ C-H/alkyl interactions always strong shielding is observed, inasmuch as θ is significantly increased in this more realistic calculational model[8]. Furthermore, it becomes understandable why replacement of the *syn*-γ C–H bond by a C–C bond leads to weakening or even sign reversal of the corresponding γ substituent effect such as in **1c** and **2a** (R = Me, R′ = H or Me, see Table 1), as the point of action for the steric forces now must be around the center of an also longer polarized bond (model **1c**). Together with a bending-out reflex effect[6b] this leads to θ values around 90°, resulting in small shift effects of negative or positive sign. Since at the same time the bond angles in such arrangements can become significantly distorted (e.g. C1–C2–C3 in **1c** by 8° in comparison to cyclohexane[6b]) a reliable calculation of the many small shielding variations is not feasible at the present time. The often found generalization[9] that "steric crowding" leads to shielding at γ positions and to deshielding at δ positions is obviously not justified. In spite of the ambiguities which plague all computations of nonbonded interactions[10], however, a remarkably unambigous and well-fitting representation of sterically induced polarization on γ-carbon atoms is obtained not only for conformationally fixed alkanes but also for *n*-butane rotamers[11].

A strong support for the given rationalization of sterically induced ^{13}C shielding must be seen in the recently observed ^1H-NMR shifts in cyclohexanoid frameworks[2] which similar to the syn-γ effect of an axial methyl group in cyclohexane (+0.25 ppm)[12] does show the expected (opposite!) sign and magnitude compared to the complementary γ- ^{13}C shifts[8]; the calculated steric forces agree with a sensitivity of about 0.1 ppm/μdyn (^1H) as compared to about 2 ppm/μdyn found for ^{13}C[13]. In summary, the arguments put forward against[1b,9,14] the sterically induced shielding model seem to ignore necessary consequences of the angular force gradient dependence as well as of geometry distortions; they are moreover partially based on observations with *syn*-γ heterosubstitutents which clearly must work through entirely different mechanisms[4a,15] (see below).

Polar Substituent Effects on γ Positions

Although substitutents such as X = F exert *no* steric forces on *syn*-axial C–H bonds in conformations such as **1a**/**1b**[4a], even stronger shielding is observed compared to the effect of a more bulky methyl group (e.g. –7.2 vs –6.5 ppm).

The *syn*-γ effects of polar groups[2b,16] vary in cyclohexanes **1a**, e.g. from –7.2 (X = F) over –6.3 (X = OMe), –5.1 (X = CN), –1.1 (X = $SnMe_3$), to +2.3 (X = HgAc); in closer proximity such as for C-6 in *endo*-2-bicyclo-[2.2.1]heptanes **2b**, **3b** etc. the increment can exceed –10 ppm (Table 1). Obviously, all this is at variance with statesments[14a,17] that the *syn*-γ effect is nearly independent of the nature of the X substituent, and demonstrates, that a formal scheme explaining the *syn*-γ effect in essence by removal of hydrogen at the β substituent[14] is insufficient. Also, the presence of any hydrogen atoms at the inducing substituent X[1b,14a] is obviously no prerequisite for these effects.

In contrast to earlier assumptions[18], γ-shielding effects of substituents such as halogen or oxygen in *gauche*-X–C–C–C–H fragments in normal frameworks are totally unrelated to any geometry changes[4a]. Only if the *syn*-γ C–H bond is replaced by a C–C bond, reflex effects with concomitant bond angle changes are noted (**1c**)[6b], which can be responsible for the observed *syn*-γ *de*shielding effects for X = Me (see above) as well as for X = Hal, OR, NR_2 etc. (Table 1).

The deshielding of *protons* by polar substituents in *syn*-diaxial X−C−C−C−*H arrangements such as in **1a**, **1d** is evolving as the most prominent shift effect in alicyclic frameworks[2] and may well play a similar rôle in assignments as the corresponding *syn*-γ carbon SIS after 2D NMR and high-field spectroscopy makes such ^{1}H shifts routinely accessible. Sign and magnitude of the ^{1}*syn*-γ ^{1}H-SIS are correctly predicted by calculated linear electric field (LEF) and anisotropy (AN) contributions[2] (Table 2), although the latter are complicated by uncertain C−X bond susceptibility values[19] (for this reason and in view of additional ambiguities involved with OH-group calculations, several shielding calculations in Table 2 were omitted). Since in such *syn*-H−C−C−C−X arrangements the γ carbons are shielded and the terminal protons are deshielded, and since the difference involved (Table 2) corresponds roughly to the different sensitivity of carbon and proton against charge density variation (a factor of 10−20), it seems likely, that the major screening contributions here stems indeed from the C−X dipole-induced Cγ-Ha charge polarization (model **1d**). This would be also in line with the above-mentioned variation of the *syn*- ^{13}C shielding from X = F to X = metal (that for X = $PbMe_3$, $SnMe_3$ etc. still shielding – although to a much lesser degree – is observed must be ascribed to the Cα◀H dipole replaced here by another C◀M dipole). However, LEF and AN calculations (Table 2) make clear, that the charge variations resulting from LEF for *syn*- ^{1}H represent only a part of the effect and for *syn*- ^{13}C even show a sign *opposite* to the observed shielding.

Table 2. Substituent-induced shifts, electric field and anisotropy effects, and charge variations for γ-C−H groups[a]

X	γ-^{1}H, axial exp.[b]	LEF[c]	AN[c]	γ-^{13}C exp.[d]	q[e]
a-F	0.46	0.20	0.22	−7.2	4.2
a-Cl	0.63	0.06	0.32	−6.9	2.6
a-Br	0.68			−6.3	2.0
a-I	0.66	0.14	0.50	−4.5	1.1
a-OH	0.47	–	–	−6.9	–
e-F	0.10	0.04	−0.18	−3.4	−1.4
e-Cl	0.12	0.12	−0.24	−0.5	−0.7
e-Br	0.14	0.04	−0.30	+0.7	−0.5
e-I	0.13	0.03	−0.39	+2.4	−0.2
e-OH	0.05	–	–	−2.3	

[a] For Cγ hydrogen, γ-carbon atoms in cyclohexanoid structures. – [b] Averaged SIS [ppm] values from 3-×-substituted 5α-androstan-17-ones[2]. – [c] Linear electric field effects (LEF) and anisotropy effects (AN) calculated with procedures and parametrization as described earlier[2], effect of X = H subtracted. – [d] SIS [ppm] from substituted cyclohexanes (**1d**, **1e**, R = H)[14]. – [e] Calculated charge variations (X = H subtracted) in 10^{-3} elementary electron charge units.

Carbon atoms in γ positions are not only exposed to polarization of Cβ−Cγ bonds, which due to inhomogeneity of the electric fields are not amenable to LEF calculations, but also to a strong through-bond effect of small charge variations at Cβ. We have shown earlier[4b] that a charge accumulation of only a few % at Cβ, e.g. by back donation from F etc., could lead to the observed shielding effects at C-γ. However, any quantification of the necessarily complex mechanistic contributions to C-γ seems to be impossible, also in view of additional high-order effects (see below). This also makes all correlations of the γ-carbon shifts with properties of *anti*-γ substitutents to a speculative enterprise. Shielding by *anti*-γ first-row elements cannot be the accounted for by hyper-conjugation[20], an often repeated concept[21] in spite of contradictions[16,22] which have been acknowledged by the original proponents[1d]. For practical applications it is important, too, to note that the presence of axial C−C instead of C−H bonds in α *or* γ position leads to sign reversal[22] for X = F, OR, NR_2 [see e.g. **1e**, (R = Me)[16], **1f**/**g** (Table 3), **2b** (Table 1)].

Table 3. ^{13}C-NMR shifts in 3,3-Dimethyl- and 3,3,5,5-tetramethylcyclohexyl derivatives[a]

	1f							
X	C-1 α	C-2 β	C-3 γ	C-4 ϑ	C-5 γ	C-6 β	e-Me ϑ	a-Me ϑ
Cl	34.15	10.99	2.91	−1.15	0.15	11.09	−0.85	0.61
Br	26.06	11.86	3.78	−1.24	1.21	11.95	−0.85	0.32
I	1.56	14.10	5.00	−1.43	2.40	14.04	−0.91	2.08
OH	44.71	9.36	1.82	−0.39	−1.24	9.36	−0.46	1.56
$OOCCH_3$	47.97	5.33	1.69	−0.52	−1.50	5.66	−1.11	1.75
OTMS	46.02	9.94	1.82	−0.52	−1.43	9.82	−0.78	1.88
H	22.49	39.39	30.42			26.58	33.80	24.05

	1g					
X	C-1 α	C-2/6 β	C-3/5 γ	C-4 ϑ	e-Me ϑ	a-Me ϑ
Cl	35.75	9.75	2.20	−2.08	−9.91	0.13
Br	26.97	11.90	3.11	−1.10	−0.71	0.19
I	8.64	14.11	3.64	−1.43	−0.84	0.13
OH	45.30	9.10	1.36	−1.06	−0.26	0.97
OCH_3	55.11	5.49	0.97	−0.39	−0.45	1.17
H	19.76	39.45	31.33	52.45	35.81	27.04

[a] Substituent-induced shifts (δ values) relative to X = H; shifts for X = H relative to internal TMS. Measurements in (20±3)% $CFCl_3$ solutions at ambient temperature. All compounds predominate (>95%) in the eq-X conformation. Reported[22b] ^{13}C shifts for **1f** (R = H, X = Cl, Br, I, OH) agree only roughly, in particular for X = I at C-α, due to large solvent effects (cf. H.-J. Schneider, W. Freitag, *J. Chem. Soc., Perkin Trans. 2*, **1979**, 1337).

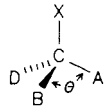
^{13}C-SIS in α and β Position – Steric Distortions and High-Order Effects

Whitesell et al.[23] have recently claimed a "fundamental shift effect" in ^{13}C-NMR spectroscopy, consisting of interactions of vicinal hydrogens at C-α and C-β which only for an *anti*-H−C−C−H orientation are believed to give rise to deshielding at C-α and C-β. The authors, however, seem to ignore besides some earlier experimental[24] and general[4a,6b,11c,16,18,22a,25] work several findings which are at variance with their proposal: the upfield shift usually observed for the sterically more hindered structure at C-α and C-β is retained in geometries with *no* alternative *gauche*/antiperiplanar H−C−C−H orientations, such as in

bicyclo[2.2.1]heptanes **3a** and **3b** (for R = H, C-α and C-β are upfield for **3b** by about 2 ppm[1a]; even larger epimeric differences are observed for carbon atoms which bear no hydrogen at all, such as C-3 in **3a**/**3b** (X = Me, OH). In cyclohexanes, where the H−C−C−H *gauche*/*anti* alternative in most cases is just a consequence of the eq/ax alternative, the shielding increments on C-α and/or C-β are found upfield for axial as compared to equatorial substituents even in structures such as **1d**, **1e** (R = Me)[16] or such as **1h** (R = H or Me)[6b], although *neither* C-α *nor* C-β does carry any hydrogen. The pitfalls of generalizations based on insufficient NMR data are illustrated by one other example: Whitesell et al. ascribe the 1.2-ppm upfield shift of cyclopentane relative to cyclohexane to the presence of more *anti*-HCCH orientations in the latter compound; but cycloheptane, which by the same token also should be shielded is *down*field from cyclohexane by 1.7 ppm.

The invariably larger deshielding effect of equatorial groups on C-β as compared to the axial epimers is not[4a,26] associated with Cα−Cβ−Cγ bond angle or bond length changes, as assumed earlier[18,27]. The strong variation of Cβ-SIS with the nature of polar but less bulky substitutents (see e.g. Tables 1, 3) – which again is at variance with assumptions in the literature[28] – points to a dominating electronic or polar origin, and the corresponding shifts have been quantitatively described by high-order square electric field effects[15a,22a,29]. It has been shown, that for quaternary Cβ atoms a larger LEF contribution – due to the Cβ−C bond polarizibility – will counteract the deshielding square field[6a], and that weak flattening of a cyclohexanoid geometry will have the same effect[22a]. The smaller effect of an axial substituent X on C-β can originate in a larger effective distance r between the center of polarizibility at C−X and C-β, which however is difficult to evaluate in view of the steep r^{-6} dependence and the parametrization problems[8,15a] involved.

Another problem here is the possible change of bond length, angles, and hybridization which is not only expected between eq/ax or *endo*/*exo* epimers, but also between different structures exhibiting a differing steric hindrance between substrate skeleton and substituent. Apart from some model calculations on halomethanes[25] a quantitative assessment of these geometry/hybridization changes and of their impact on NMR shifts in aliphatic frameworks has not been tried until now. We understook such an analysis after finding out that the introduction of a methyl substitutent into different stereochemical environments seems to generate systematic bond angle θ distortions at C-α.



$$\lambda^2_{C-X} = \cos\Theta_{ACB}/(\cos\Theta_{ACX} \cdot \cos\Theta_{BCX}) \quad (1)$$

$$\%s = 100/(1 + \lambda^2_{C-X}) \quad (2)$$

The bond angles θ were taken from MM2 force field[10] calculations; the hybridization index λ^2 and from this the s character (% s) for the substituted C−X bond were evaluated using Coulsons[30] equations [(1) and (2)].

Table 4. Hybridization and Me-SIS at C-α of different methylcycloalkanes[a]

	Δδ exp.	$\bar{s}_{X=H}$ (%)	$\bar{s}_{X=Me}$ (%)	$\Delta\bar{s}_{Me-H}$ (%)	Δδ(calcd.)
1d (R = H)	0.13	23.1	26.8	3.7	1.7
1e (R = H)	5.66	23.6	26.3	2.7	4.5
1d (R = Me)	−2.90	21.6	25.7	4.1	0.6
2a (R = R′ = H)	6.7	25.4	29.3	3.9	1.2
2b (R = R′ = H)	4.5	28.8	32.7	3.9	1.2
2b (R = Me)	0.34	26.5	30.3	3.8	1.5
2a (R = Me)	4.69	25.2	29.7	4.5	0.5
3b (R = H)	−2.35	28.1	32.0	3.9	1.2
3a (R = H)	1.48	24.4	27.9	3.5	2.3
4 (X = H)	5.6	32.7	35.3	2.6	4.8
4 (Y = H)	7.3	39.8	40.7	0.9	9.6
5	−9.44	20.9	27.6	6.7	−6.7

[a] Hybridization degree calculated with eq. (1) on the basis of MM2-optimized geometries; Δδ from regression analysis (Figure 1).

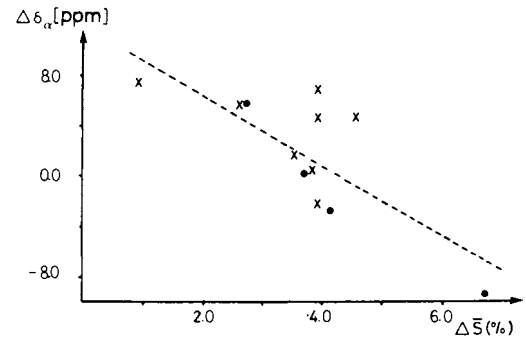


Figure 1. Methyl SIS values on C-α vs. calculated hybridization changes (see text); filled circles: cyclohexanoid structures (used for regression line), other points: bicycloheptanes (for identification see Table 4)

Average $\bar{s}$ values were obtained from the available bond angles at Cα for 12 compounds with X = H and X = Me (Table 4). A fairly linear correlation between the experimental ^{13}C-SIS and the calculated hybridization change $\Delta\bar{s}$ accompanying the substitution R−H→R−Me was observed (Figure 1) with r = 0.969 for cyclohexanoid systems [**1d**, **1e** (R = H, Me) **5**], decreasing to r = 0.76 if all compounds are included; the major deviations due to the 2-*exo*-substituted bicyclo[2.2.1]heptane **2a** are not associated with particular bond length or torsional angle changes, but possibly to deficiencies of the force field in the prediction of small geometry variations with the more strained bicyclic frameworks. It is gratifying that the fundamental C-α shift difference between axial and equatorial cyclohexane is in line with the correlation, and that the abscissa value of 12±2 ppm (for $\Delta\bar{s}=0$) agrees with the "fundamental methyl group shift" of 10.2 ppm, which has been proposed 17 years ago by Roberts et al.[7a] for strainfree systems.

This work was supported by the *Deutsche Forschungsgemeinschaft*, Bonn, and the *Fonds der Chemischen Industrie*, Frankfurt.

Experimental

^{13}C-NMR spectra were recorded at 22.62 MHz on Bruker HX90 and WH90 instruments, usually with 0.02 ppm digital resolution.

Measuring conditions see footnotes to tables and references given there. ^{13}C shift assignments were secured by off-resonance decoupled spectra. ^{1}H-NMR spectra were usually measured at 90 MHz using 10% $CDCl_3$ solutions; for fully analyzed ^{1}H-spectra with 2D techniques see ref.[2].

Compounds were commercially available or prepared as described below; all compounds were checked by ^{13}C-NMR (Tables 1, 3).

3,3-Dimethyl- and 3,3,5,5-Tetramethylcyclohexyl Derivatives **1f**, **1g**: *Chlorides* and *bromides* were obtained from the hydroxy compounds **1f**[31], **1g**[32] (X = OH) by reaction with dihalocarbens under phase-transfer conditions[33]; byproducts found (^{13}C-NMR analysis) were usually up 20% dihalonocaranes, up to 10% formates, besides about 10–20% of unreacted alcohol (reactions with different epimeric monoalkylcyclohexanoles (2-, 3-, and 4-methyl- and 4-*tert*-butylcyclohexanol[16] showed that the halide formation from the dihaloformate intermediates occurs largely with retention of configuration). Typically, 0.1 mol of hydroxy compound (**1f**, **1g**, X = OH) and 20 ml of dichloromethane were added to 100 ml of 50% sodium hydroxide solution containing 0.4 g of triethylbenzylammonium chloride. 80 ml of chloroform was added with stirring at a rate that the temperature was 50–60% (about 2 hours); after further 2 hours of stirring about 1 l of water was added; the organic material was extracted with three 100-ml $CHCl_3$ portions, dried with $MgSO_4$, and fractionated after distilling off the solvent in vacuum; yields (not optimized) and boiling points were: **1f**, X = Cl: 30%, b.p. (14 Torr) = 59 °C; **1g**, X = Cl: 37% b.p. (2.5 Torr) = 60.5 °C; **1f**, X = Br: 15%, b.p. (14 Torr) = 74 °C; **1g**, X = Br 37%, b.p. (2.3 Torr) = 60.5 °C.

Iodides from **1f**, **1g** (X = OH) were prepared by reaction with *o*-phenylen phosphorochloridite to yield the corresponding esters and by subsequent treatment with iodine following literature procedures[34]. The method yields, as also found with monoalkylcyclohexanols[16], up to 35% of isomeric cyclohexy iodides from hydride shifts (^{13}C-NMR analysis); the iodides **1f**, **1g** (X = I) were, after distillation in vacuum, pure enough for ^{13}C-NMR studies.

Acetates Trimethylsilyl Ethers, Methyl Ethers were obtained by standard procedures[35] from alcohol reactions with acetic anhydride, chlorotrimethylsilane, or methyl iodide.

Fenchanes **2a**, **2b** (R = Me, R′ = H, X = Me) were obtained from α-fenchene by hydrogenation over platinium-charocal[36]; the epimer ratio was 75% of *exo*-2-methyl and 25% of *endo* (^{13}C-NMR).

Methylbornanes (**2a**, **2b**, R = R′ = X = Me) were prepared similarly to fenchanes from 2-methylenebornane[37] [2-methylene-, 1,7,7-trimethylbicyclo(2.2.1)heptane]; after reaction of 2.2 g (0.011 mol) of olefin with 0.12 g of platinum-charcoal (10% Pt) (added in 2 portions) in 30 ml of methanol during 3 the hydrogenation was complete (> 99%); after removal of the catalyst and the solvents with intermediate extraction with $CHCl_3$ the residue showed 72% of *exo* (**2a**) and 88% of *endo* compound **2b**. – ^{1}H-NMR (15% in $CDCl_3$) for **2a**: δ = 0.81; 0.86; 0.89; **2b**: δ = 0.73, 0.94, 0.98 (Me signals).

Bornyl Halides[38] and *-amines*[39] (**2a**, **2b**, R = R′ = Me, X = Cl, Br, NH_2) were prepared as described earlier; ^{1}H-NMR data for:

2b, R = R′ = Me, X = Br: 0.97, 0.87, 0.86 (Me), 4.23 broad m (2-H);

2b, R = R′ = Me, X = Cl: 0.93, 0.71, 0.71 (Me), 4.10 broad m (2-H);

2a, R = R′ = X = Br: 1.15, 1.03, 0.88 (Me), 4.07 (2-H).

Camphenilyl Derivatives **3a**/**3b** (R = H, X = OH, Me) have been described earlier[40]; all attempts to prepare the corresponding halides **3a**/**3b** (R = H, X = Cl, Br) by reactions of the hydroxy educts with gaseous HCl and HBr, with $:CCl_2$ and $:CBr_2$ (see above), with $SOCl_2$ in pyridine, as well as by tosylate reactions with LiBr in acetone were unsuccessful, leading to several rearranged products (^{13}C-NMR analysis). The camphene derivatives **3a**/**3b**, R = Me, X = OH and **3a** R = Me, X = Cl have been described earlier[41].

CAS Registry Numbers

1f (X = Cl): 35188-27-3 / **1f** (X = Br): 25090-98-6 / **1f** (X = I): 35188-29-5 / **1f** (X = OH): 767-12-4 / **1f** (X = OAc): 25866-66-4 / **1f** (X = O-TMS): 117408-29-4 / **1f** (X = H): 590-66-9 / **1g** (X = Cl): 117408-30-7 / **1g** (X = Br): 117408-31-8 / **1g** (X = I): 117408-32-9 / **1g** (X = OH): 2650-40-0 / **1g** (X = OMe): 117408-33-0 / **1g** (X = H): 24770-64-7 / **2a** (R′ = H; X = Me): 42836-45-3 / **2a** (R′ = Me; X = Cl): 559-45-5 / **2a** (R′ = Me; X = Br): 30462-54-5 / **2a** (R′ = Me; X = NH_2): 2223-67-8 / **2a** (R′ = X = Me): 57905-87-0 / **2b** (R′ = H; X = Me): 42836-46-4 / **2b** (R′ = Me; X = Cl): 464-41-5 / **2b** (R′ = Me; X = Br): 54825-45-5 / **2b** (R′ = Me; X = NH_2): 464-42-6 / **2b** (R′ = X = Me): 57905-88-1 / **2ab** (R′ = X = H): 2034-53-9 / **2ab** (R′ = Me; X = H): 464-15-3 / **3a** (R = H; X = OH): 515-28-6 / **3a** (R = H; X = Me): 20536-41-8 / **3a** (R = Me; X = Cl): 22768-67-8 / **3a** (R = Me; X = OH): 13429-40-8 / **3b** (R = H; X = OH): 640-54-0 / **3b** (R = H; X = Me): 20536-40-7 / **3b** (R = Me; X = OH): 13429-57-7 / **3ab** (R = X = H): 6248-85-7 / 2-methylenebornane: 27538-47-2

---

[1] For reviews see [1a] N. K. Wilson, J. B. Stothers, *Top. Stereochem.* **8** (1974) 1. – [1b] H. Duddeck, *ibid.* **16** (1986) 219 (substituent effects). – [1c] N. M. Sergeev, O. A. Subbotin, *Russ. Chem. Rev. (Engl. Transl.)* **47** (1978) 265. – [1d] E. L. Eliel, K. M. Pietrusiewicz, *Top. Carbon-13 NMR Spectrosc.* **3** (1979) 171.

[2] H.-J. Schneider, U. Buchheit, N. Becker, G. Schmidt, U. Siehl, *J. Am. Chem. Soc.* **107** (1985) 7027, and references cited therein.

[3] D. M. Grant, B. V. Cheney, *J. Am. Chem. Soc.* **89** (1967) 5315.

[4] [4a] H.-J. Schneider, E. F. Weigand, *J. Am. Chem. Soc.* **99** (1977) 8362. – [4b] H.-J. Schneider, W. Gschwendtner, E. F. Weigand, *ibid.* **101** (1979) 7195.

[5] Deshielding effects on C atoms in "crowded" environment were mainly reported for OH substituents: W. A. Ayer, L. M. Brown, S. Fung, J. B. Stothers, *Org. Magn. Reson.* **11** (1978) 73, and references cited therein.

[6] [6a] G. Mann, E. Kleinpeter, H. Werner, *Org. Magn. Reson.* **11** (1978) 561. – [6b] H.-J. Schneider, W. Freitag, *Chem. Ber.* **112** (1979) 16.

[7] For other ^{13}C-NMR measurements on related norbornanes see ref. [1a] and [7a] J. B. Grutzner, M. Jautelat, J. B. Dence, R. A. Smith, J. S. Roberts, *J. Am. Chem. Soc.* **92** (1970) 7107. – [7b] E. Lippmaa, T. Pehk, J. Paasivirta, N. Belikova, A. Platé, *Org. Magn. Reson.* **2** (1970) 581. – [7c] H.-J. Schneider, W. Bremser, *Tetrahedron Lett.* **1970**, 5197. – [7d] J. B. Stothers, C. T. Tan, K. C. Teo, *Can. J. Chem.* **54** (1976) 1211. – [7e] E. Lippmaa, T. Pehk, N. A. Belikova, A. A. Bobyleva, A. Kalinichenko, M. D. Ordubadi, A. F. Platé, *Org. Magn. Reson.* **8** (1976) 74. – [7f] K. B. Wiberg, W. E. Pratt, W. F. Bailey, *J. Org. Chem.* **45** (1980) 4936. – [7g] R. M. Carman, K. L. Greenfield, *Austr. J. Chem.* **37** (1984) 1785.

[8] H.-J. Schneider, G. Schmidt, *J. Chem. Soc., Perkin Trans. 2*, **1985** 2027; the proton positions in Table 3 of that paper should throughout be replaced by the following sequence: βe, βa; γe, γa; δe, δa.

[9] See e.g. A. P. Marchand, *Stereochemical Applications of NMR Studies in Rigid Bicyclic Systems* p. 26, 27, Verlag Chemie International, Deerfield Beach, Florida 1982.

[10] See e.g. U. Burkert, N. L. Allinger, *Molecular Mechanics*, American Chemical Society, Washington 1982.

[11] For experimental *n*-butane rotamer shifts see [11a] D. M. Grant, E. G. Paul, *J. Am. Chem. Soc.* **86** (1964) 2984. – [11b] H.-J. Schneider, W. Freitag, *ibid.* **98** (1976) 478. – For earlier INDO calculations see [1fc] K. Seidman, G. E. Maciel, *ibid.* **99** (1977) 659.

[12] D. Danneels, M. Anteunis, *Org. Magn. Reson.* **6** (1974) 617.

[13] Similar results have been reported even with aromatic systems: B. V. Cheney, *J. Am. Chem. Soc.* **90** (1968) 5386.

[14] [14a] H. Beierbeck, J. K. Saunders, J. W. ApSimon, *Can. J. Chem.* **55** (1977) 2813. – [14b] H. Beierbeck, J. K. Saunders, *ibid.* **54** (1976) 2985.

[15] [15a] H.-J. Schneider, W. Freitag, *J. Am. Chem. Soc.* **99** (1977) 8363. – [15b] H.-J. Schneider, W. Freitag, W. Gschwendtner, G. Maldner, *J. Magn. Reson.* **36** (1979) 273.
[16] H.-J. Schneider, V. Hoppen, *J. Org. Chem.* **43** (1978) 3866.
[17] J. K. Whitesell, B. Hildebrandt, *J. Org. Chem.* **50** (1985) 4975.
[18] D. E. Gorenstein, *J. Am. Chem. Soc.* **99** (1977) 2254.
[19] [19a] A. K. Davis, D. W. Mathieson, P. D. Nicklin, J. R. Bell, K. J. Toyne, *Tetrahedron Lett.* **1973**, 413. – [19b] W. Gschwendtner, H.-J. Schneider, *J. Org. Chem.* **45** (1980) 3507.
[20] E. L. Eliel, W. F. Bailey, L. D. Kopp, R. C. Willer, D. M. Grant, R. Bertrand, K. A. Christensen, D. K. Dalling, W. M. Duch, E. Wenkert, F. M. Schell, D. W. Cochran, *J. Am. Chem. Soc.* **97** (1975) 322.
[21] See e.g. [21a] N. Chandrakumar, S. Subramanian, *Modern Techniques in High-Resolution FT-NMR*, Springer Verlag, New York 1987. – [21b] H.-O. Kalinowski, S. Berger, S. Braun, *^{13}C-NMR-Spektroskopie*, Thieme Verlag, Stuttgart 1984.
[22] [22a] H.-J. Schneider, W. Ansorge, *Tetrahedron* **33** (1977) 265. – [22b] T. P. Forrest, Thiel, *J. Can. J. Chem.* **59** (1981) 2870. – [22c] J. B. Stothers, C. T. Tan, *ibid.* **55** (1977) 841. – [22d] J. R. Wiseman, H. O. Krabbenhoft, *J. Org. Chem.* **42** (1977) 2240; for further literature see ref.[1b].
[23] J. K. Whitesell, M. A. Minton, *J. Am. Chem. Soc.* **109** (1987) 225.
[24] Low-temperature ^{13}C-NMR studies with methylcyclohexane have been carried out earlier: [24a] F. A. L. Anet, C. H. Bradley, G. W. Buchanan, *J. Am. Chem. Soc.* **93** (1971) 258. – [24b] H. Booth, J. R. Everett, *J. Chem. Soc., Perkin Trans. 2*, **1980** 255. – [24c] H. Booth, *Kem.-Kenzi* **7** (1980) 5. – All ^{13}C-shift increments for methylcyclohexane were also available from earlier work: see, e.g. ref.[16] and [24d] H.-J. Schneider, R. Price, G. Keller, *Angew. Chem.* **83** (1971) 759; *Angew. Chem. Int. Ed. Engl.* **10** (1971) 730.
[25] D. Purdela, *J. Magn. Reson.* **5** (1971) 23, 37.
[26] G. M. Schwenzer, *J. Org. Chem.* **43** (1978) 1079.
[27] J. D. Roberts, F. J. Weigert, J. I. Kroschwitz, H. J. Reich, *J. Am. Chem. Soc.* **92** (1970) 1338.
[28] H. Beierbeck, J. K. Saunders, *Can. J. Chem.* **53** (1975) 1307.
[29] For earlier calculations see [29a] W. T. Raynes, A. D. Buckingham, H. J. Bernstein, *J. Phys. Chem.* **36** (1962) 3481. – [29b] J. Feeney, L. H. Sutcliffe, Walker, *J. Mol. Phys.* **11** (1966) 117.
[30] C. A. Coulson, *Valence*, Oxford University Press, London 1953.
[31] A. W. Crossley, N. Renouf, *J. Chem. Soc.* **87** (1905) 1494.
[32] G. Chiurdoglu, A. Maquetian, *Bull. Soc. Chim. Belg.* **63** (1954) 357.
[33] I. Tabushi, Z. Yoshida, N. Takahashi, *J. Am. Chem. Soc.* **93** (1971) 1820.
[34] E. J. Corey, J. E. Anderson, *J. Org. Chem.* **32** (1967) 4160.
[35] *Organikum*, 12. Ed., VEB Deutscher Verlag der Wissenschaften, Berlin 1973.
[36] Cf. W. Hückel, D. Volkmann, *Liebigs Ann. Chem.* **664** (1963) 31.
[37] J.-M. Conia, J.-C. Limasset, *Bull. Soc. Chim. Fr.* **1967**, 1936.
[38] Cf. [38a] W. Hückel, E. Gelchsheimer, *Liebigs Ann. Chem.* **625** (1959) 12. – [38b] H. Meerwein, J. Vorster, *J. Prakt. Chem.* **147** (1963) 83. – [38c] E. F. Weigand, H.-J. Schneider, *Chem. Ber.* **112** (1979) 3031.
[39] W. Hückel, P. Rieckmann, *Liebigs Ann. Chem.* **625** (1959) 1.
[40] Cf. [40a] S. Beckmann, B. Geiger, *Chem. Ber.* **94** (1961) 1910. – [40b] W. Hückel, *Liebigs Ann. Chem.* **549** (1941) 95, 186.
[41] [41a] W. Hückel, H.-J. Schneider, H. Schneider-Bernlöhr, *Liebigs Ann. Chem.* **1975**, 1690. – For ^{1}H-NMR data see [41b] H.-J. Schneider, N. Franklin, W. Hückel, *ibid.* **745** (1971) 1, and references cited therein.

[213/88]