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Carbon-13 Chemical Shifts and Conformations of Dimethylcyclohexanols

T. Pehk, H. Kooskora and E. Lippmaa*
Institute of Cybernetics of the Estonian Academy of Sciences, Tallinn 200001, USSR

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Abstract—Carbon-13 chemical shifts of all twenty-two dimethylcyclohexanols, formed by the hydrogenation of isomeric xylenols, have been measured and assigned. Conformational peculiarities of dimethylcyclohexanols are discussed on the basis of their carbon-13 chemical shifts.

INTRODUCTION

WELL known regularities of the carbon-13 chemical shifts of methylcyclohexanes[1–3] and methyldecalins[4–6] can be used for the determination of conformational equilibria, particularly the preferred axial or equatorial orientation of the methyl groups on the 6-membered ring, together with the corresponding thermodynamic parameters.

The conformational energy of the methyl group is large ($-\Delta G^{\circ}_{CH_3} \approx 1.8$ kcal/mol[7]) and because of this large energy difference between alternative conformations (≥ 1.8 kcal/mol), only one conformer predominates. The conformational equilibration is more complicated in polymethylcyclohexanes, but even in the case of non-geminal trimethylcyclohexanes, the energy difference between any two conformers is less than 1.8 kcal/mol in only two cases.[3] Substitution of a methyl group in trimethylcyclohexanes with a hydroxyl group substantially complicates the stereochemistry of the dimethylcyclohexanols obtained. Instead of the nine trimethylcyclohexanes, there are 22 isomeric non-geminal dimethylcyclohexanols. The conformational energy of the hydroxyl group is lower than that of the methyl group[7] and the mutual conformational energy of vicinal methyl and hydroxyl groups depends on their orientation.[8]

As a starting point for the analysis of ^{13}C chemical shifts of dimethylcyclohexanols, the effects of axial and equatorial hydroxyl groups on the chemical shifts of carbons of the cyclohexane ring had to be determined. For this purpose, the ^{13}C chemical shifts of cyclohexanol were measured in various solvents at room temperature and at temperatures of conformationally frozen molecules (< -80 °C). For the determination of the effects of hydroxyl substitution, the ^{13}C chemical shifts of isomeric methylcyclohexanols[9] were remeasured and literature data about carbon chemical shifts of the conformationally fixed *trans*-decalols as well as 9-methyl-*trans*-decalols were also used.[10]

EXPERIMENTAL

Proton decoupled ^{13}C FT NMR spectra were measured at 15·1 MHz on the universal spectrometer,[11] connected to a NIC-1085 computer with 20 K core memory. ^{13}C chemical shifts were measured from internal cyclohexane and tetramethylsilane (TMS). For the calculation of substituent effects, the former is more convenient and was actually used. The chemical shift between TMS and cyclohexane was somewhat different in various samples, but remained in the 27·2 ± 0·2 ppm range. Other values reported are 26·9 ppm,[1] 27·4 ppm,[14] 27·5 ppm[12] and 27·7 ppm,[1] corrected in Ref. 13.

The chemical shifts were measured for neat mixtures of isomeric alcohols without solvent and some samples of isomers, partially separated by preparative gas-liquid chromatography (GLC), were also run as solutions in methylene chloride. The differences between ^{13}C chemical shifts in the pure compounds and the mixtures did not exceed ±0·2 ppm. All results are given in Table 1 (overleaf) and correspond to ^{13}C chemical shifts of isomeric alcohols in their mixtures.

The methylcyclohexanols and dimethylcyclohexanols were prepared by hydrogenation of the corresponding cresols and xylenols on a PtO_2 catalyst in acetic acid at about 5 atm pressure. The cyclohexanols obtained were analysed by GLC on PPE and PEG capillary columns, and separated on a preparative scale gas chromatograph, equipped with an Apiezon on Chromosorb column. Complete separation was not achieved in many cases, but resolution was sufficient for unambiguous assignment of all spectral lines of the isomers.

In some cases, additional isomerisation of the dimethylcyclohexanols with Al-isopropoxide was used, in order to vary the composition of isomeric mixtures having nearly equal concentrations and retention times of the components.

^{13}C NMR spectra were used for the identification of the synthesised dimethylcyclohexanols. The relative retention times are given in Table 2.

TABLE 2. RELATIVE RETENTION TIMES (RT) ON PPE[a] AND PEG[b] COLUMNS AND THE COMPOSITION OF DIMETHYLCYCLOHEXANOLS, OBTAINED BY HYDROGENATION OF XYLENOLS ON PtO_2 CATALYST IN CH_3COOH

Dimethyl-cyclo-hexanols	Isomers (more stable conformation)[c]											
	aee			eee			eea			eae		
	RT		%	RT		%	RT		%	RT		%
	PPE	PEG		PPE	PEG		PPE	PEG		PPE	PEG	
3,5-	1·0	1·0	23	1·06	1·19	70	1·19	1·35	7			
2,6-	1·0	1·0	67	1·0	1·11	10	1·18	1·44	23			
2,3-	1·0	1·0	11	1·03	1·14	10	1·19	1·43	9	1·25	1·55	70
2,4-	1·0	1·0	51	1·04	1·17	41	1·17	1·37	3	1·23	1·47	5
2,5-	1·0	1·0	20	1·02	1·15	25	1·15	1·39	5	1·20	1·54	50
3,4-	1·0	1·0	9	1·06	1·17	25	1·22	1·45	56	1·22	1·40	10

[a] Polyphenyl ether.
[b] Polyethylene glycol.

[c] First letter indicates orientation of the hydroxyl group, second and third the orientation of methyl groups in the preferred conformation.

RESULTS AND DISCUSSION

In order to assign and to analyse the ^{13}C spectra of methylcyclohexanols, parameters similar to those of methyl substitution[3] are needed. In the case of methylcyclohexanes, methylcyclohexane is a good model for the compound with an equatorial methyl group, but for cyclohexanol the axial conformer cannot be simply

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* Author to whom correspondence should be addressed.

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Table 1. Carbon chemical shifts of cyclohexanol, methylcyclohexanols and dimethylcyclohexanols from internal cyclohexane[a]

									Methyl groups		Conformational energies[d]				
No.	Substituents	Preferred conformation[b]	C−1	C−2	C−3	C−4	C−5	C−6	A[c]	B	Stable conformer	Unstable conformer	Δ	Effective $-\Delta G$[e]	$\Sigma\delta^{13}C$
(A) Methylcyclohexanols with high conformational homogeneity ($\Delta\Delta G \geq 1{\cdot}65$ kcal/mol)															
(1)	*t*-2-Methyl	ee	48·7	13·1	7·1	−1·1	−1·6	8·6	−8·2		0·38	2·85	2·47	0·42	66·6
(2)	*c*-3-Methyl	ee	42·8	17·3	4·6	8·1	−2·6	7·4	−4·6		0	3·82	3·82	0	73·0
(3)	*t*-4-Methyl	ee	43·1	8·4	6·7	5·0	6·7	8·4	−5·0		0	2·85	2·85	0	73·2
(4)	*t*-2-*c*-3-Dimethyl	eee	48·5	19·9	10·8	8·2	−2·8	8·9	−11·8	−7·0	1·28	5·64	4·36	1·28	74·7
(5)	*c*-2-*t*-3-Dimethyl	aee	44·3	16·1	5·0	8·2	−6·7	6·7	−10·8	−7·2	2·61	4·43	1·82	2·69	55·6
(6)	*c*-2-*c*-3-Dimethyl	eae	46·3	13·2	7·7	0·4	−2·8	1·2	−22·0	−7·7	3·53	5·38	1·85	3·61	36·3
(7)	*t*-2-*t*-4-Dimethyl	eee	48·8	12·7	16·1	5·4	7·2	8·5	−8·1	−4·9	0·38	6·55	6·17	0·38	85·7
(8)	*c*-2-*c*-4-Dimethyl	aee	42·2	9·8	10·1	5·8	1·3	6·7	−8·2	−4·4	1·71	6·33	4·62	1·71	63·3
(9)	*t*-2-*c*-5-Dimethyl	eee	48·5	12·7	6·8	7·9	5·2	17·6	−8·3	−4·7	0·38	5·62	5·24	0·38	85·7
(10)	*c*-2-*t*-5-Dimethyl	aee	43·3	9·5	1·3	8·3	−1·5	15·7	−8·5	−4·7	1·71	4·43	2·72	1·74	63·4
(11)	*c*-2-*c*-5-Dimethyl	eae	45·1	6·6	3·8	1·4	5·0	10·6	−16·1	−4·7	2·63	4·48	1·85	2·71	51·7
(12)	*t*-2-*t*-6-Dimethyl	eee	54·7	13·0	7·6	−1·2	7·6	13·0	−8·0	−8·0	0·76	6·55	5·79	0·76	78·7
(13)	*c*-2-*c*-6-Dimethyl	aee	47·6	10·8	0·5	−0·9	0·5	10·8	−8·3	−8·3	2·37	7·16	4·79	2·37	52·7
(14)	*t*-3-*c*-4-Dimethyl	aee	39·1	14·7	5·9	11·9	2·0	5·5	−7·1	−7·1	1·95	3·60	1·65	2·05	64·9
(15)	*c*-3-*t*-4-Dimethyl	eee	43·1	17·6	10·7	11·5	6·9	8·8	−6·9	−7·5	0·90	5·62	4·72	0·90	84·2
(16)	*c*-3-*c*-4-Dimethyl	eea	43·3	10·8	6·8	5·2	4·5	2·5	−7·4	−15·4	2·70	4·72	2·02	2·77	50·3
(17)	*t*-3-*t*-5-Dimethyl	aee	39·4	14·3	−0·9	17·4	−0·9	14·3	−4·3	−4·3	1·01	5·50	4·49	1·01	75·0
(18)	*t*-3-*c*-5-Dimethyl	eae	38·6	13·3	1·3	13·6	−0·9	17·8	−7·7	−4·3	1·80	3·82	2·02	1·86	71·7
(19)	*c*-3-*c*-5-Dimethyl	eee	42·6	17·0	4·0	16·6	4·0	17·0	−4·0	−4·0	0	8·50	8·50	0	93·2
(B) Cyclohexanols with low conformational homogeneity ($\Delta\Delta G \leq 1{\cdot}05$ kcal/mol)															
(20)	—	e	42·5	8·3	−2·6	−1·2	−2·6	8·3			0	1·05	1·05	0·15	52·7
(21)	*c*-2-Methyl	ae	43·5	9·2	2·2	−2·5	−5·7	5·4	−10·4		1·71	2·63	0·92	1·87	41·7
(22)	*t*-3-Methyl	ae	38·7	14·4	−0·7	7·4	−5·1	5·9	−6·9		1·05	1·80	0·75	1·22	53·7
(23)	*c*-4-Methyl	ae	39·1	5·0	2·2	4·3	2·2	5·0	−5·4		1·05	1·80	0·75	1·22	52·4
(24)	*t*-2-*t*-3-Dimethyl	eea	44·6	14·4	4·7	3·8	−6·8	5·1	−11·3	−13·4	3·01	3·75	0·74	3·18	41·1
(25)	*t*-2-*c*-4-Dimethyl	eea	47·8	7·6	11·2	0·1	3·2	2·4	−8·6	−7·4	2·18	2·85	0·67	2·34	56·3
(26)	*c*-2-*t*-4-Dimethyl	eae	45·0	7·0	12·5	−1·3	5·7	1·8	−14·6	−5·4	2·63	3·51	0·88	2·79	50·7
(27)	*t*-2-*t*-5-Dimethyl	eea	44·3	10·6	0·7	3·4	0·7	12·1	−9·1	−6·7	2·18	2·85	0·67	2·34	56·0
(28)	*t*-2-*c*-6-Dimethyl	eea	50·3	6·6	4·9	−6·9	3·8	6·4	−8·7	−13·3	3·01	3·47	0·46	3·15	43·1
(29)	*t*-3-*t*-4-Dimethyl	eae	38·5	14·0	5·6	7·1	0·6	6·8	−12·8	−9·6	2·70	3·75	1·05	2·85	50·2

[a] $\delta_{TMS} = 27{\cdot}2 + \delta C_6H_{12}$.

[b] The first letter represents the orientation of the hydroxyl group, the second, the orientation of the methyl group connected to the ring carbon with the lowest number.

[c] A represents the methyl group connected to the ring carbon with the lowest number.

[d] Conformational energies, calculated on the basis of the following parameters: $CH_{3ax} = 1{\cdot}80$ kcal/mol, $OH_{ax} = 1{\cdot}05$ kcal/mol; vicinal interactions: $CH_3, CH_3 = 0{\cdot}9$ kcal/mol, $CH_{3eq}, OH_{eq} = 0{\cdot}38$ kcal/mol, $CH_{3ax}, OH_{eq} = 0{\cdot}83$ kcal/mol, $CH_{3eq}, OH_{ax} = 0{\cdot}66$ kcal/mol; 1,3-diaxial interactions: $CH_3,CH_3 = 3{\cdot}7$ kcal/mol, $CH_3,OH = 2{\cdot}4$ kcal/mol.

[e] The part of less stable conformer included.

ruled out. From the myriad of reported $-\Delta G^\circ$ values (0·3 to 1·25 kcal/mol[7]) the best seem to centre around 1·0 kcal/mol, depending somewhat on the solvent used.[15] In Ref. 15 the comparison of intensities of CHOH proton lines at −80 °C was used to determine $-\Delta G^\circ$. The same principle of integration was utilised in ^{13}C NMR by Subbotin and Sergeyev,[16] as well as Schneider and Hoppen.[17] The main advantage of ^{13}C NMR spectra is the possibility of comparing intensities of the signals from all carbon atoms. On the other hand, the influence of non-uniform NOE values and ^{13}C relaxation times affects the accuracy of results obtained. The $-\Delta G^\circ$ value determined for the hydroxyl group by Schneider and Hoppen[17] exceeded 1·4 kcal/mol. This was explained by a strong association of the equatorial conformer with the solvent. Unfortunately, signals of the axial conformer could not be registered at −93 °C. We succeeded in measuring the ^{13}C signals of both conformers, including the axial, in the same solvent at about −80 °C (Table 3). The results found in Ref. 17 can be explained by a very low solubility of the axial conformer in CF_2Cl_2. The difference in solubilities of axial and equatorial conformers of chlorocyclohexane was actually used for isomeride separation at low temperatures.[18] The different solubility of conformers appears to be an additional source of error in using the integration of ^{13}C NMR spectra for the determination of $-\Delta G$ values.

In order to examine the solvent dependence of conformational equilibria, the ^{13}C chemical shifts of cyclohexanol in various solvents at room temperature and at −80 °C were measured (see Table 3). The largest solvent dependence at room and at low temperatures is observed at the α- and β-positions. At the γ-positions the ^{13}C shift differences between solutions in different solvents are smaller. On the other hand, the γ-positions are most sensitive to the orientation of substituents and therefore the C-3,5 chemical shifts can be used for the estimation of conformational energies.

The near invariability of cyclohexanol chemical shifts (with the exception of the substituted C-1) in the neat compound with those in methanol and ethanol solutions is remarkable and shows that this conformational equilibrium is unaffected by the molecular environment. Differences between the C-3,5 chemical shifts in the axial and equatorial conformers are slightly different in methanol (4·79 ppm), ethanol (4·95 ppm), carbon disulphide (4·90 ppm) and CF_2Cl_2 (4·60 ppm), but the corresponding differences in $-\Delta G$ values are not large, as calculated from these chemical shifts and the room temperature values. The $-\Delta G$ value for cyclohexanol is 1·1 kcal/mol and there are no large differences between these values for solutions in aprotic and protic solvents, although such effects have been predicted.[19] The averaged carbon chemical shifts can be used for the determination of conformational energies, if the intrinsic temperature dependence of the chemical shifts of individual conformers can be neglected. From the chemical shifts of dimethylcyclohexanes at room and at low temperatures (see Table 4), the temperature effects on the ring carbons can be estimated to be about 0·1 ppm, which results in an additional uncertainty of the conformational energy. In the case of cyclohexanol, this error margin is ±0·1 kcal/mol for $-\Delta G$ values calculated from the C-3,5 shift values. The conformational energy of cyclohexanol, as calculated from the C-3,5 shift, lies at the higher limit of reported values and is in accordance with the latest ^{1}H NMR data, 1·05 kcal/mol in CD_3OD.[15] The close values of the chemical shifts of neat cyclohexanol and its solutions in methanol and ethanol justify the use of this value for the interpretation of the ^{13}C spectra of undiluted samples of cyclohexanol derivatives. The substituent effects of axial and equatorial hydroxyl groups in cyclohexanol were used for signal assignments in methyl- and dimethylcyclohexanols. From the 29 cyclohexanols, 19 appear to be conformationally nearly homogeneous (>94% content of a single conformer at room temperature) on the grounds of the conformational energies for methyl (1·8 kcal/mol) and hydroxyl (1·05 kcal/mol) groups, as well as the conformational energies of vicinal methyl–methyl (0·90 kcal/mol), methyl–hydroxyl (eCH_3, eOH = 0·38 kcal/mol; aCH_3, eOH = 0·83 kcal/mol; eCH_3, aOH = 0·66 kcal/mol[8]) and 1,3-diaxial interactions (CH_3, CH_3 = 3·7 kcal/mol; CH_3, OH = 2·4 kcal/mol[7]). For the calculation of the mean hydroxyl group effects in conformationally homogeneous cyclohexanols, chemical shifts of methylcyclohexane and dimethylcyclohexanes were used, as measured from internal cyclohexane (see Table 4).

In methylcyclohexane the methyl group is about 95% equatorial at room temperature. Therefore, for the purely equatorial conformer, only a minor modification of the methylcyclohexane chemical shifts is needed and this can be achieved through the use of the methyl parameters.[3] An additional problem arises with *cis*-1,2-, *cis*-1,4- and *trans*-1,3-dimethylcyclohexanes, which at room temperature give averaged spectra, but

TABLE 3. CARBON CHEMICAL SHIFTS OF CYCLOHEXANOL[a] FROM INTERNAL CYCLOHEXANE IN VARIOUS SOLVENTS

	Mixture of conformers				Equatorial conformer				Axial conformer			
Solvent	C_1	$C_{2,6}$	$C_{3,5}$	C_4	C_1	$C_{2,6}$	$C_{3,5}$	C_4	C_1	$C_{2,6}$	$C_{3,5}$	C_4[b]
—	42·5	8·3	−2·6	−1·2								
CH_3OH	42·99	8·33	−2·63	−1·3	43·35	8·57	−2·04	−1·36	38·76	5·30	−6·83	
C_2H_5OH	42·8	8·3	−2·6	−1·3	43·16	8·54	−1·91	−1·33	38·44	5·53	−6·86	
CS_2	42·0	8·12	−2·75	−1·2	42·2	8·1	−2·0	−1·4	37·4	5·1	−6·9	
CF_2Cl_2	42·9	8·6	−2·4	−1·2	43·4	8·8	−1·8	−1·2	38·8	5·9	−6·4	
$(C_2H_5)_2O$	42·1	8·8	−2·7	−1·0	42·87	9·00	−1·84	−1·16				
$C_6H_5CH_3$	42·7	8·5	−2·6	−1·2								
CH_2Cl_2	43·0	8·6	−2·7	−1·4								

[a] About 15 vol % of cyclohexanol in the solvent, at 30 °C and at −80 °C, for CF_2Cl_2 at −40 °C and −80 °C.

[b] The signal from C-4 in the axial conformer was masked by strong signals of the equatorial conformer.

TABLE 4. CARBON CHEMICAL SHIFTS OF METHYLCYCLOHEXANE AND DIMETHYLCYCLOHEXANES FROM INTERNAL CYCLOHEXANE δC_6H_{12}

		Temperature	Carbon atoms[a]							
Substituent	Solvent	°C	C−1	C−2	C−3	C−4	C−5	C−6	$CH_{3(eq)}$	$CH_{3(ax)}$
Methyl	—	25	5·89	8·54	−0·45	−0·55	−0·45	8·54	−4·30	
Methyl	CH_2Cl_2	25	5·88	8·55	−0·44	−0·58	−0·44	8·55	−4·30	
Methyl (eq)	CH_2Cl_2	−85	6·11	8·47	−0·26	−0·61	−0·26	8·47	−3·5	
Methyl (eq)[b]	—	25	6·1	8·7	−0·1	−0·5	−0·1	8·7	−4·1	
trans-1,2-Dimethyl	—	25	12·39	12·39	8·90	−0·10	−0·10	8·90	−6·96	
	CH_2Cl_2	25	12·38	12·38	8·89	−0·06	−0·06	8·89	−6·90	
	CH_2Cl_2	−85	12·36	12·36	8·77	−0·10	−0·10	8·77	−6·31	
cis-1,2-Dimethyl	—	25	7·31	7·31	4·30	−3·46	−3·46	4·30	−11·35	
	CH_2Cl_2	25	7·29	7·29	4·30	−3·43	−3·43	4·30	−11·29	
	CH_2Cl_2	−85	6·18	8·19	1·49	0·10	−6·89	6·80	−6·31	−15·43
	CH_2Cl_2	−86[c]	7·19	7·19	4·15	−3·50	−3·50	4·15	−10·87	
	—	25[d]	6·3	8·3	1·6	0	−7·0	7·0	−6·8	−15·9
trans-1,3-Dimethyl	—	25	0·26	14·26	0·26	6·80	−6·21	6·80	−6·47	
	CH_2Cl_2	25	0·27	14·21	0·27	6·75	−6·17	6·75	−6·53	
	CH_2Cl_2	−85	1·13	13·88	−0·55	8·87	−6·21	4·43	−3·46	−8·80
	CH_2Cl_2	−85[c]	0·29	13·88	0·29	6·65	−6·21	6·65	−6·13	
	—	25[d]	1·1	14·3	−0·6	9·0	−6·2	4·6	−3·8	−9·1
cis-1,3-Dimethyl	—	25	5·95	17·63	5·95	8·15	−0·49	8·15	−4·24	
	CH_2Cl_2	25	5·90	17·56	5·90	8·11	−0·49	8·11	−4·25	
	CH_2Cl_2	−85	5·86	17·21	5·86	7·93	−0·55	7·93	−3·79	
trans-1,4-Dimethyl	—	25	5·66	8·54	8·54	5·66	8·54	8·54	−4·50	
	CH_2Cl_2	25	5·64	8·50	8·50	5·64	8·50	8·50	−4·49	
	CH_2Cl_2	−85	5·63	8·32	8·32	5·63	8·32	8·32	−4·01	
cis-1,4-Dimethyl	—	25	3·20	3·79	3·79	3·20	3·79	3·79	−6·96	
	CH_2Cl_2	25	3·18	3·77	3·77	3·18	3·77	3·77	−6·97	
	CH_2Cl_2	−85	−0·10	4·82	2·36	6·57	2·36	4·82	−3·69	−9·58
	CH_2Cl_2	−85[c]	3·33	3·59	3·59	3·33	3·59	3·59	−6·64	
	—	25[d]	−0·1	5·0	2·6	6·5	2·6	5·0	−4·0	−9·9

[a] Numbering of the ring carbon atoms starts with the carbon bearing the axial substituent.

[b] Calculated from the room temperature spectrum by the use of differences in equatorial and axial methyl group effects, given in Ref. 3.

[c] Mean values for interchanging positions.

[d] Calculated values from the differences between chemical shifts of interchanging positions at −85 °C, and the room temperature mean values.

for the conformationally homogeneous methylcyclohexanols the chemical shifts of the frozen methylcyclohexanes have to be used. For the *cis*-1,2- and *cis*-1,4-isomers the low temperature ^{13}C spectra were measured by Schneider, Price and Keller.[20] Dalling, Grant, and Johnson[21] measured these chemical shifts and those of *trans*-1,3-dimethylcyclohexane at somewhat higher temperatures. Quite large differences between these data must be noted. In order to have consistent data about the temperature effects in all the isomers, ^{13}C chemical shifts of methylcyclohexane and the dimethylcyclohexanes are given in Table 4. The solvent, methylene chloride, has a negligible influence on the chemical shifts of hydrocarbons. The temperature dependence is characterised by only small effects on ring carbons, which as a rule do not exceed 0·1 ppm. The largest effect was observed at C-2 in *cis*-1,3-dimethylcyclohexane (0·35 ppm). The methyl carbons are shifted by 0·4 to 0·6 ppm to lower fields at low temperatures. Room temperature values for the a,e isomers were obtained from the chemical shift differences of interchanging carbon atoms and the mean values of ^{13}C chemical shifts at room temperature. The average effects of axial and equatorial hydroxyl groups were calculated (Fig. 1) from the data for methylcyclohexanols **1** to **19** (Table 1) and the methylcyclohexanes (Table 4). Parameters for accounting for the interactions of vicinal methyl and hydroxyl groups were derived.

Long range shielding effects of the hydroxyl group in *trans*-decalols and sterols have been noted.[10] Mean values for these effects are also given in Fig. 1.

From the parameters of Fig. 1 and the chemical shifts of methylcyclohexanes (Table 4), the carbon chemical shifts of alcohols **1** to **19** (Table 1) can be predicted with high accuracy ($r = 0{\cdot}9996$, $s = 0{\cdot}45$ ppm). The same analysis of the chemical shifts of **1** to **19** with the aid of the methyl parameters[3] results in only insignificant differences in the effects of the hydroxyl group (Fig. 1, values in parentheses) and the predictability of

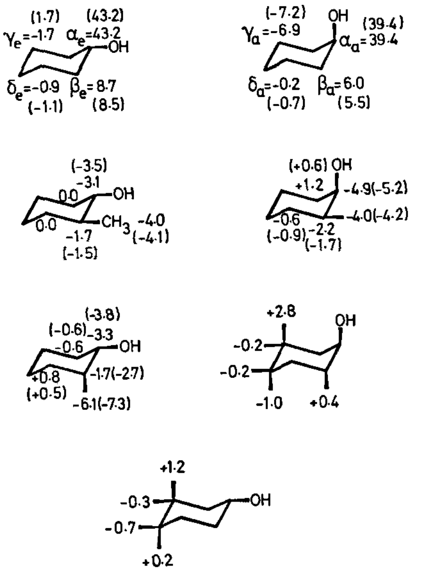

FIG. 1. Hydroxyl group effects on the chemical shifts of cyclohexane and methylcyclohexanes. Values in parentheses were used with the methyl parameters given in Ref. 3.

the chemical shifts of compounds **1** to **19** on this basis is practically the same ($r = 0{\cdot}9996$, $s = 0{\cdot}45$). The tentative assignment of C-2,6 and C-3,5 chemical shifts of *trans*-4-methylcyclohexanol[9] had to be reversed on the basis of parameters from Fig. 1, but assignments of the carbinyl carbon atoms of four 3,4-dimethylcyclohexanols[9] is in accordance with our results. The error in the chemical shift of C-4 of **19** (Table 1), given in Ref. 10 has to be noted.

Using the parameters in Fig. 1, the ^{13}C chemical shifts of both conformers in conformationally interconverting methylcyclohexanols can be calculated. As a rule the experimental shift values lay between those of both conformers, being nearer to those of the more stable form. From the experimental and predicted chemical shifts the equilibrium constants can be evaluated. Although the standard error in calculating the ^{13}C chemical shifts is not large, in the cases where differences of carbon chemical shifts of both conformers are small, large errors in equilibrium constant values result from these minor differences between the experimental and calculated chemical shifts. Analysis of the chemical shifts of the cyclohexanols **20** to **29** (Table 1) shows that at room temperature these compounds exist mainly (65 to 85%) in the conformations given in Table 1. Conformational inhomogeneity in methylcyclohexanols **20** to **29** is well documented by their carbon chemical shifts.

The sum of the chemical shifts of all carbon atoms in mono- and dimethylcyclohexanols must characterise their thermodynamic stability,[5,6,22] because conformers having 1,3-diaxial interactions are practically ruled out. In fact, good correlation is observed between the predicted conformational energies and the sums of ^{13}C chemical shifts in six methylcyclohexanols ($r = 0{\cdot}9988$ for the comparison with the conformational energies of the more stable conformers and $r = 0{\cdot}9993$ for the effective conformational energies. In the latter case, the content of less stable conformer at room temperature was also taken into account) and in the 22 dimethylcyclohexanols ($r = 0{\cdot}984$, Fig. 2). The sum of the ^{13}C chemical shifts is about −15 ppm for every 1 kcal/mol conformational energy in the molecule. Such correlations are also observed within individual isomers, as is illustrated by comparison of the conformational energies from the experimental equilibration of isomeric 2,3-dimethylcyclohexanols[23] with their carbon chemical shifts (Fig. 3).

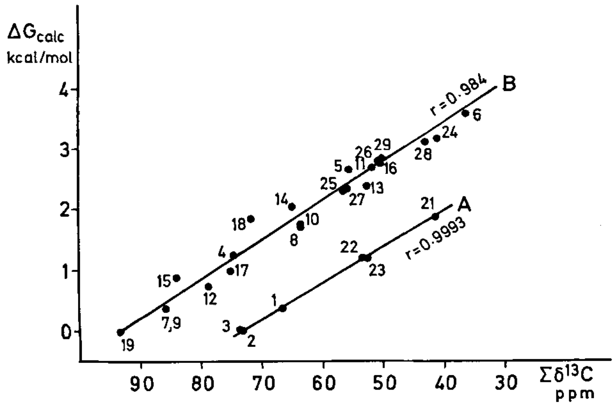

FIG. 2. Comparison of calculated conformational energies with the sums of carbon chemical shifts in mono- and dimethylcyclohexanols. Numbering of compounds according to Table 1. (A) methylcyclohexanols, (B) dimethylcyclohexanols.

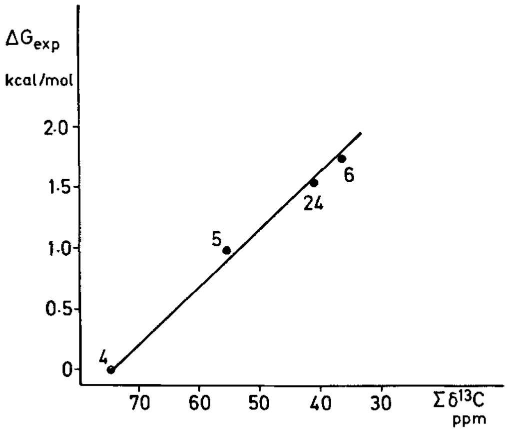

FIG. 3. Comparison of experimental thermodynamic stability, of isomeric 2,3-dimethylcyclohexanols with the corresponding sums of carbon chemical shifts. Numbering of compounds according to Table 1.

It was experimentally found that in the 3,4-dimethylcyclohexanols compounds **16** and **29** (Table 1) have a practically equal conformational energy ($-\Delta G = 0{\cdot}14$ kcal/mol).[24] This is confirmed by the equality of the total shieldings of carbon atoms in these isomers. In another pair of isomers (**14** and **15**) the latter is the more stable one, which is in accordance with the carbon chemical shifts. It was concluded in Ref. 8 that the equilibrium data given in[26] for 2,5-dimethylcyclohexanols do not correspond to a real equilibrium. The same conclusion can be drawn from carbon chemical shift data for these isomers.

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