^{13}C and ^{15}N NMR Study of Acyclic Vicinal Diastereoisomers. Conformational Effects

George C. Levy*†
Florida State University, Tallahassee, Florida 32306, USA

T. Pehk§ and E. Lippmaa
Institute of Cybernetics of the Estonian Academy of Sciences, Lenini puiestee 10, Tallinn 200 001, USSR

Conformations of aliphatic diastereoisomers with vicinal asymmetric centers (2,3-disubstituted butanes and 5,6-disubstituted *n*-decanes) are discussed in terms of their ^{13}C and, in some cases, ^{15}N chemical shifts and spin-lattice relaxation times. Solvent and protonation effects are explained by conformational changes in the isomers.

INTRODUCTION

The importance of steric effects on ^{13}C chemical shifts is well known[1] and is used with great success for analysis of various isomeric mixtures, especially alicyclic compounds.[1c] In acyclic diastereoisomers, steric effects must also have a substantial role, as demonstrated by the large differences in chemical shifts of corresponding carbon atoms in diastereomeric alkanes.[2] Standard factor analysis of chemical shifts, however, gives no means for assignment of lines to individual isomers, although chemical shift differences of corresponding carbon atoms can reach several ppm. In some cases calculations have determined mean conformations, using, in particular, shielding effects on *gauche* carbon chemical shifts.[3,4] Nevertheless, there are no simple general rules to assign aliphatic diastereomer lines to definite configurations.

It was shown by us that ^{13}C spin-lattice relaxation times of isomers can be used for the identification of individual compounds from their equimolar mixtures, especially within alicyclic stereoisomers.[5] Different mutual orientation of atoms in isomers results in variation of the effective molecular volume, leading to different effective correlation times with corresponding relaxation times. However, steric interactions and conformations of acyclic isomers are less clearly defined and variations in their physical constants are usually minimal as compared with those of cyclic isomers. The same must be predicted for spin-lattice relaxation times.

Usually an aliphatic molecule cannot be characterized by a single correlation time due to segmental motion and rotational anisotropy effects.[6] Concepts of longer or shorter relaxation times for corresponding carbon atoms in one of two isomers can be successful only when differences in segmental or anisotropic motions do not mask variations in overall tumbling rates. Despite these complications, we set up a study to evaluate ^{13}C relaxation times of corresponding carbon atoms in aliphatic diastereoisomers with the goal of connecting T_1 differences with certain preferred conformations. 2,3-Disubstituted butanes were chosen due to the relative simplicity of their conformational analysis. Only rotation around the C-2,3 bond must be considered in these cases. 5,6-Disubstituted *n*-decanes were used as medium molecular weight compounds in order to obtain information about the propagation along the main molecular chain of chemical shift and relaxation time differentials in aliphatic diastereoisomers. In 5,6-disubstituted *n*-decanes, as in the simpler 2,3-disubstituted butanes, the main differences in conformations of isomers result from rotation around the central carbon–carbon bond.

EXPERIMENTAL

Compounds **2**, **3**, and **4** (Table 1) were commercially available (Aldrich, Pfalz & Bauer) as mixtures of isomers (with some excess of the *meso* compounds, determined by GLC analysis or known chemical shifts of 2,3-dichlorobutanes[7]). Compounds **7**, **8** and **10** (Table 3) were prepared from **4** with a known ratio (3:2) of *meso* and racemic isomers. Diaminobutane (**5**), 3-amino-2-butanol (**11**) and their salts, **6** and **12**, respectively, were prepared from dimethylglyoxime.[8] The much higher solubility of the racemic salt of **6** was used for the assignment of lines to the isomers of **6** and **5**. In the case of **11**, the *erythro* configuration was assigned for the prevailing isomer, which had a higher boiling point (in analogy with *meso*-**4** and *meso*-**5** isomers). Hydrocarbons **1** and **9** were prepared by Wurtz type coupling of corresponding bromo-derivatives, made from styrene and 1-hexene. The chemical shifts of *meso* and racemic 2,3-diphenylbutanes (**1**, Table 1) fit nicely with reported values,[12] except for C-*s* of the *meso* isomer. The assignment of lines for *meso* and racemic 5,6-dimethyldecanes was based on calculated chemical shifts for 3,4-dimethylhexane isomers.[3,4] The isomers

* Author to whom correspondence should be addressed.
† Camille and Henry Dreyfus Teacher Scholar.
§ On scientific leave of absence at the Florida State University, 1979.

CCC-0030-4921/80/0014-0214$03.00

Table 1. Carbon chemical shifts and spin-lattice relaxation times of 2,3-di-X-substituted butanes

No.	Substituent (X)	Solvent concentration	Chemical shifts (δ_{TMS})[a] CH meso	CH rac	CH meso–rac	CH_3 meso	CH_3 rac	CH_3 meso–rac	T_1 (s, 308 K) CH meso	CH rac	CH_3 meso	CH_3 rac
1	Ph	2 M in $CDCl_3$	47.5	46.7	0.8	21.2	18.2	3.0	3.42	3.58	1.43	1.48
2	Cl	Pure	61.3	60.2	1.1	21.9	19.8	2.1	13.6	14.3	6.45	6.55
3a	Br	Pure	53.7	52.1	1.6	25.2	20.5	4.7	7.81	8.85	3.89	4.10
3b	Br	0.8 M in CH_3CN	55.4	54.6	0.8	24.6	22.4	2.2	11.7	12.5	7.04	7.12
3c	Br	1.3 M in DMSO	55.4	54.9	0.5	23.9	22.8	1.1	5.42	5.66	3.05	2.94
4	OH	Pure	71.0	71.6	−0.6	17.6	18.5	−0.9	0.42	0.48	0.64	0.69
5	NH_2[c]	Pure	52.0	52.9	−0.9	18.2	20.1	−1.9	5.09	5.00	2.91	2.84
6	NH_3^+[d]	2.5 M in H_2O	49.8	48.8	1.0	14.7	12.9	1.8	1.95	2.03	1.65	1.68
7	$OCOCH_3$[e]	Pure	71.2	71.3	−0.1	14.9	15.8	−0.9	2.86	2.70	2.13	1.91
8	OCH_3[f]	~4 M in butanediol monomethyl ether	80.3	78.9	1.4	15.3	13.7	1.6	10.7	11.0	5.61	5.43
9	n-C_4H_9	Pure	37.7	36.7	1.0	16.7	14.6	2.1	5.69	5.94	3.43	3.67

[a] From external $(CD_3)_2CO$ capillary; $\delta_{TMS} = 29.8$.
[b] Aromatic carbon atoms: C-*s*; *meso*, 146.6 ppm, 21.5 s; *rac*, 145.9 ppm, 23.1 s: C-*o*; *meso*, 127.8 ppm, 3.23 s; *rac*, 128.0 ppm, 3.51 s: C-*m*; *meso*, 128.5 ppm, 3.33 s; *rac*, 128.0 ppm, 3.51 s: C-*p*; *meso*, 126.2 ppm, 1.78 s; *rac*, 125.9 ppm, 2.26 s.
[c] ^{15}N; *meso* 33.3 ppm; $T_1 - 15.8$ s: *rac* 34.1 ppm; $T_1 - 15.4$ s.
[d] ^{15}N: *meso* 43.5 ppm; *rac* 44.0 ppm.
[e] $CH_3(CO)$ groups: *meso* 20.6 ppm, 6.21 s; *rac* 20.5 ppm, 5.61 s.
[f] OCH_3 groups coincide at 56.8 ppm.

of **13**, **14** and **15** (Table 4) were prepared from *cis*- and *trans*-5-decene (Pfalz & Bauer) by *trans*-addition of halogens, epoxidation and cleavage of epoxides. Reported chemical shifts and spin-lattice relaxation times (Tables 1–4) are all measured from *mixtures* in order to have *direct* comparison of shielding and relaxation effects for pairs of isomers. The use of TMS as reference compound, especially in studying medium effects, has been strongly criticized[9] and in the present study up to more than 1 ppm chemical shift differences of internal TMS from external acetone-d_6 capillary (29.0–30.3 ppm) were observed in various 2,3-butanediol solutions (Table 2). However, in most cases the TMS chemical shift was close to 29.8 ppm upfield, and this value was used to convert *external* acetone-d_6 values to the TMS scale; no susceptibility corrections were used.

Carbon-13 and ^{15}N chemical shifts and spin-lattice relaxation times were obtained using a Bruker HX-270 superconducting magnet spectrometer operating in the quadrature detection mode for ^{13}C at 67.9 and ^{15}N at 27.4 MHz. ^{15}N chemical shifts were measured from external saturated $^*NH_4NO_3$ and reported on the NH_3 scale by taking $\delta_{NH_4NO_3} = 20.7$ ppm.[10]

Spin-lattice relaxation times were measured at room temperature using the $(T\text{-}180\text{-}t\text{-}90°)_x$ pulse sequence and an on-line three parameter exponential fitting program.[11] Since the T_1 values of corresponding carbon atoms in aliphatic isomers are in many cases nearly the same, *at least two runs were made in order to confirm the small differences that were observed.* Of course, relaxation times of aliphatic isomers can be compared only from individual samples where errors due to imperfect pulsing, unequal temperature, different macroviscosities, diamagnetic and paramagnetic impurities etc. are effectively cancelled, and where

Table 2. Carbon chemicals shifts and spin lattice relaxation times of 2,3-butanediol isomers[a] in different solvents

Solvent concentration	Chemical shifts (δ_{TMS})[b] CH meso	CH rac	CH rac–meso	CH_3 meso	CH_3 rac	CH_3 rac–meso	T_1 (s, 308 K) CH meso	CH rac	CH_3 meso	CH_3 rac
CCl_4 (saturated, <5%)	70.74	72.33	1.59	16.96	19.41	2.45	2.30	2.35	2.01	2.08
$CHCl_3$, 2.5 M	70.81	72.25	1.44	16.84	19.07	2.23	2.39	2.62	1.99	2.07
CH_2Cl_2, 2.5 M	70.86	72.33	1.47	16.78	19.02	2.24	3.27	3.63	2.22	2.29
C_6H_6, 2.5 M	70.83	72.18	1.35	16.92	19.02	2.10	1.49	1.66	1.42	1.49
CH_3NO_2, 2.5 M	71.62	72.80	1.18	17.35	19.09	1.74	4.69	5.07	2.92	3.04
CH_3CN, 2.5 M	71.33	72.18	0.85	17.75	19.01	1.26	9.51	9.82	4.64	4.89
$(C_2H_5)_3N$, 2.5 M	71.08	71.82	0.74	18.39	19.36	0.97	2.35	2.79	1.93	2.13
Pure (11 M)	70.96	71.56	0.60	17.63	18.54	0.91	0.42	0.48	0.64	0.69
H_2O, 2.5 M	71.08	71.47	0.39	17.07	17.80	0.73	3.21	3.51	2.09	2.16
C_5H_5N, 2.5 M	71.30	71.64	0.34	18.64	19.00	0.36	3.62	3.99	2.35	2.48
DMF, 2.5 M	71.50	71.50	0	18.74	18.48	−0.26	4.7		2.70	2.80
DMSO, 2.5 M	71.56	71.36	−0.20	19.87	19.16	−0.71	4.28	5.02	2.57	2.90
HMPA, 2 M	71.62	71.09	−0.53	19.74	18.13	−1.61	2.68	2.92	2.37	2.55

[a] Ratio of *meso*/*rac* isomers = 3:2.
[b] From external $(CD_3)_2CO$ capillary, $\delta_{TMS} = 29.8$ ppm.

Table 3. Carbon chemical shifts and relaxation times of some 2,3-disubstituted butanes, CH_3—CHX—CHY—CH_3, with unequal substituents

No.	Substituents		Chemical shifts (δ_{TMS})[a]								Spin-lattice relaxation times, T_1 (s)							
			CHX		CHY		CH_3(CHX)		CH_3(CHY)		CHX		CHY		CH_3(CHX)		CH_3(CHY)	
No.	X	Y	*erythro*	*threo*	*erythro*	*threo*	*erythro*	*threo*	*erythro*	*threo*	*erythro*	*threo*	*erythro*	*threo*	*erythro*	*threo*	*erythro*	*threo*
10	OH	OCH_3[b]	69.7	70.4	81.7	82.0	18.9	18.4	14.2	14.4	7.58	7.98	7.23	7.62	4.08	4.12	4.70	4.64
11	OH	NH_2[c]	70.1	71.4	52.0	53.0	18.0	19.3	18.1	20.2	0.55	0.48	0.55	0.50	0.78	0.70	0.76	0.73
12	OH	NH_3^+[d]	66.6	68.2	52.2	53.5	17.9	19.5	12.3	15.1	0.49	0.47	0.47	0.45	0.61	0.59	0.72	0.69

[a] From external $(CD_3)_2CO$ capillary; assumed at δ_{TMS} = 29.8 ppm.
[b] In mixture with 2,3 dimethoxybutanes: OCH_3: *erythro* 56.5 ppm; T_1 = 11.0 s: *threo* 56.6 ppm; T_1 = 11.7 s.
[c] Without solvent, ^{15}N data: *erythro* 32.1 ppm; T_1 = 3.0 s: *threo* 33.4 ppm; T_1 = 2.7 s.
[d] Without solvent, ^{15}N data: *erythro* 43.2 ppm; T_1 = 2.5 s: *threo* 42.9 ppm; T_1 = 2.3 s.

Table 4. Carbon-13 chemical shifts and spin-lattice relaxation times of some 5,6-di-X-substituted *n*-decanes

No.	Substituent (X), solvent			Chemical shifts (δ_{TMS})					Spin-lattice relaxation times, T_1 (s)				
				C-1,10	C-2,9	C-3,8	C-4,7	C-5,6	C-1,10	C-2,9	C-3,8	C-4,7	C-5,6
13a	OH,	$CHCl_3$	*meso*	13.86	22.61	28.15	30.80	74.64			2.20	1.39	2.07
									3.95	3.14			
			rac	13.86	22.61	27.75	33.19	74.37			2.25	1.41	2.26
13b	OH,	DMSO	*meso*	14.02	22.42	27.81	32.22	73.82			1.02	0.66	1.03
									2.74	1.66			
			rac	14.02	22.38	27.95	32.14	73.17			1.07	0.74	1.08
9	CH_3,	Pure	*meso*	14.04	23.12	30.14	32.71	37.66			5.31	3.72	5.69
									7.30	6.20			
			rac	14.04	23.10	30.05	34.72	36.70			5.53	4.04	5.94
14	Cl,	$CHCl_3$	*meso*	13.70	22.01	28.12	34.34	65.89			3.03	2.11	3.77
									4.40	3.62			
			rac	13.70	22.01	28.75	34.02	65.34			2.84	2.11	3.42
15	Br,	$CHCl_3$	*meso*	13.72	21.89	28.97	36.48	59.78			3.11	2.50	4.18
									4.97	4.01			
			rac	13.72	21.80	29.82	34.48	59.49			2.93	2.39	3.99

much higher accuracy can be obtained than from comparing data from different samples.

However, the different sensitivity of isomers to paramagnetic impurities cannot be ruled out, especially for ^{15}N nuclei. An initial sample of 2,3-diaminobutanes had quite different nuclear Overhauser effects on the nitrogen atoms of the two isomers. Preferential bonding of paramagnetic impurities (probably from the metal parts of a spinning-band column) to the racemic isomer was observed. Only after redistillation from an all glass apparatus were full NOEs observed for nitrogens in both amines.

RESULTS AND DISCUSSION

Chemical shifts and spin-lattice relaxation times of measured pairs of isomers are given in Tables 1–4. As seen from these data, resonances from *meso* (*erythro*) isomers can be shifted to high, as well as to low field, as compared with resonances of the racemic (*threo*) isomers. Straightforward conformational analysis gives a satisfactory explanation of most of the chemical shift and spin-lattice relaxation data, as discussed below.

In 2,3-disubstituted butanes three conformations had to be considered for both *erythro* (*meso*) and *threo* (*rac*) isomers. In the case of equal substituents, (X = Y), two conformers (*M2* and *M3*, Fig. 1) are equivalent in the *meso* isomers. The main conformations of both isomers are determined by nonbonded interactions, which depend on the nature of substituents.

For 2,3-diphenylbutanes (**1**) conformations with *trans*-phenyl groups should be favored (*M1* and *R3*). This leads to increased shielding of methyl groups in

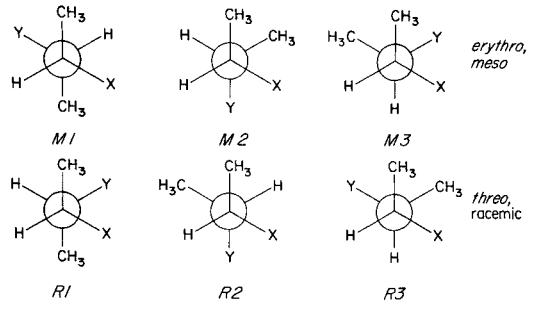

Figure 1. Conformations of 2,3-disubstituted butanes.

the racemic isomer due to methyl–methyl *gauche* interactions as compared with the *meso* isomer. Stronger steric interactions in *R3* lead to a somewhat smaller mean molecular volume; hence a shorter effective overall correlation time and longer T_1 values for corresponding carbon atoms in the racemic isomer. Shorter T_1 values are also observed for the aromatic carbon atoms of the *meso* isomer. Larger freedom of phenyl group internal rotation in the less crowded *meso* isomer should also be noted. This is indicated by the larger ratio of $T_1^{o,m}$ to T_1^{p} in the *meso* isomer (1.85) as compared with the racemic isomer (1.55).[13]

Strong mutual repulsion of heavy halogen atoms in *gauche* conformations leads to highly populated diaxial conformations of *trans*-1,2-dichloro- and dibromocyclohexanes.[14] Therefore, for 2,3-dichloro- and 2,3-dibromo-butanes (**2** and **3**) conformations *M1* and *R3* should also be favored. Chemical shifts of carbon atoms in the racemic isomers should again be shielded relative to those of the *meso* isomers. Carbon relaxation times in the racemic isomers are also longer than in the *meso* isomers, as in the case of **1**. A conformational study of 2,3-dibromobutanes on the basis of their IR spectra showed a substantial *decrease* of *M1* and *R3* conformations in acetonitrile solution as compared with the pure compound.[15] Indeed, the separation of the lines of the CH and CH_3 groups from the *meso* and racemic isomers is greatly reduced in acetonitrile and even more so in DMSO solution, but the racemic isomer still gives resonances at higher field (Table 1).

2,3-Butanediol isomers (**4**) should be quite susceptible to solvation effects and therefore a systematic study of solvents was undertaken (Table 2). The data reveal that the positions of lines from the *meso* and racemic isomers can be interchanged in the series of nonpolar solvents (CCl_4, CH_2Cl_2) through very polar solvents (DMSO, HMPA). Measured solvent effects on chemical shifts can be explained as a combination of intrinsic solvent shifts and those arising from conformational effects.

In the case of chloroform as a *solute* (which must be free from conformational effects) more than 4 ppm solvent shifts to lower field in strongly polar solvents were observed,[16] but no correlations of solvent shifts with solvent properties, including reaction field expressions or solvent polarity functions, were found. As a first assumption, changes in the positions of methyl resonances can be considered to result from conformational effects, while changes in CHOH resonances can result from both conformational and nonconformational factors. The methyl carbon resonance in *meso*-butanediol is deshielded by 2.8 ppm in HMPA and DMSO, which is explained by the conformational change from *M2* (diol in CCl_4, *intra*molecular H-bond, 1.5 *gauche* interactions per methyl group) to *M1* (diol in HMPA, *inter*molecular interactions, 1 *gauche* interaction per methyl group). At the same time, the methyl resonance of racemic butanediol is shifted by a lesser amount (1.3 ppm) to high field, which is understandable in terms of a change from *R1* to *R3*. This change is much less favorable than the conformational change of the *meso* isomer due to extra *gauche* interactions between methyl groups in *R3*.

The main conformational change in the 2,3-butanediol isomers with increasing solvent polarity is *M2* → *M1*, as viewed by the chemical shifts of the methyl groups. It is interesting to note that chloroform solvent shifts[16] correlate well with methyl group chemical shifts of *meso*-2,3-butanediol in the same solvents (Fig. 2). Thus, the same properties of solvents determine the intrinsic solvent effects (chloroform) and gradual conformational change from *M2* to *M1* (*meso*-2,3-butanediol). The smaller changes in the methyl carbon chemical shifts of the racemic isomer do not correlate with chloroform solvent shifts.

In all cases the two ^{13}C resonances of each isomer move as a pair (there is no case where crossover occurs for one type of carbon without the other carbon resonance being likewise affected).

The twentyfold spread in CH T_1s arises mainly from change in solvent viscosity. However, it should be noted that in all cases the racemic isomer has longer T_1s, indicating some additional mobility. Furthermore, the ratios observed from T_1CH_3/T_1CH allow estimation of E_a for internal methyl group rotation,[17] c. 2 kcal mol^{-1}. The data indicate no significant difference in $-CH_3$ rotation in *meso* and racemic isomers.

Contrary to the butanediols, in 2,3-diaminobutanes (**5**) spin-lattice relaxation times of *meso* isomers are (slightly) longer, while relative chemical shifts of *meso* and racemic isomers show the same trends in the diamine and diol. Close analysis of carbon and nitrogen chemical shifts in pure diamines (**5**) and their diprotonated forms (**6**) reveals that conformations different from those in the diols had to be considered in this case.[18] The preferred conformation of *meso*-amine should be *M1* with *trans*-amino groups and *R2* for the racemic isomer. *R1* is ruled out by the near equality of ^{15}N chemical shifts in *meso*- and racemic-amines; the amino group nitrogen atom in *R1* would resonate at least 5 ppm to higher field than in *M1* due to the extra *gauche* interaction between amino groups.[19] *R3* for the diamine is ruled out on the basis of large differences in carbon chemical shifts on protonation of the amine (Table 1). The methyl carbon in the *meso* isomer is shifted to high field by 3.5 ppm and in the racemic isomer by 7.2 ppm, which is explained by change of conformation for the racemic-diamine during protonation (from *R2* with one *gauche* interaction per methyl group to *R3* with two *gauche* interactions per methyl group).

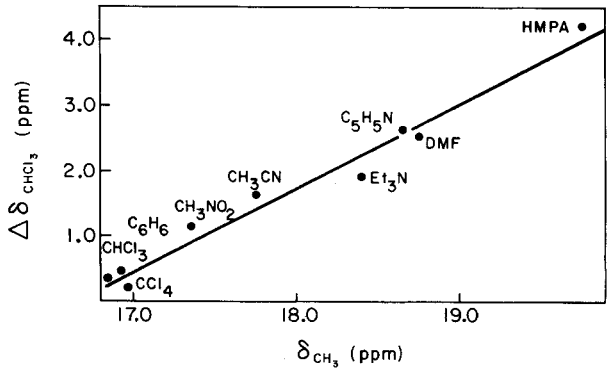

Figure 2. Comparison of chloroform and *meso*-2,3-butanediol methyl carbon chemical shifts in various solvents.

In diprotonated amines strong electrostatic repulsions between NH_3^+ groups determine the conformations for *meso* and racemic salts as *M1* and *R3*, with shielded carbons and longer observed spin-lattice relaxation times for the racemic isomer. Nitrogen chemical shifts on protonation show only minor differences between the two isomers, because the number of *gauche* interactions with the participation of the amino group does not change.

Carbon chemical shifts and relaxation times of 2,3-butanediol diacetates (**7**) behave analogously to 2,3-diamines, but 2,3-dimethoxybutanes (**8**) follow essentially the pattern observed for bulky substituents, such as phenyl, except that the CH_3 T_1s from the *meso* isomer are longer than in the racemic isomer. This could be explained by somewhat increased CH_3 rotation in the *meso* isomer or, alternatively, the effect may result from differences in overall motional anisotropy for the two isomers.

It should be noted that spin-lattice relaxation times are very useful for assigning lines in mixtures of mono- and di-methyl ethers of 2,3-butanediol. Monomethyl ethers with free OH groups have definitely shorter carbon spin-lattice relaxation times than dimethyl ethers. In the 3-amino-2-butanols (**11**, Table 3) chemical shifts and spin-lattice relaxation times behave as in diamine isomers. Preferred conformations of salts of aminoalcohols (**12**) are the same as in free aminoalcohols because there is no strong electrostatic repulsion within the molecule, observed in diprotonated diamines (**6**). Near equality of ^{15}N chemical shifts also supports this conclusion.

Isomers of 5,6-dimethyldecane (**9**) can be viewed as 2,3-disubstituted butanes; they behave in the sense of chemical shifts and spin-lattice relaxation times as if they were 2,3-disubstituted butanes with bulky substituents. No single preferred conformation can be assigned, however, for the *meso* or racemic isomer on the basis of near equality of all alkyl–alkyl *gauche* interactions (this is also consistent with a recent conformational analysis of 2,3-dimethylbutane from ^{13}C NMR spectra at low temperature[20]). Nevertheless, shorter spin-lattice relaxation times of resolved carbon atoms can be useful in analysis of this type of isomeric hydrocarbon mixture. Chemical shifts do not follow the simple pattern observed in the short carbon chain.

5,6-Decanediols in chloroform solution give results similar to those for 5,6-dimethyldecanes, but solvent change to DMSO changes the relative positions of lines from *meso* and racemic isomers at C-3,8 and C-4,7 (which can be explained conformationally, as in the case of 2,3-butanediol).

In 5,6-dibromo- and 5,6-dichloro-decanes, chemical shifts of racemic CH groups are upfield from *meso* CH groups, as in the case of the 5,6-dimethyl- or 5,6-dihydroxy-derivatives, but racemic C-3,8 are shifted downfield. This must again be explained by different predominant conformations of dihalogenodecanes relative to decanediols or dimethyldecanes. In dihalogenodecanes these should be *M1* and *R3* (Fig. 1, instead of CH_3 groups: n-C_4H_9 groups). Spin-lattice relaxation times from carbon atoms of *meso* isomers in these cases are longer than from those of racemic isomers, which is opposite to that observed for 2,3-disubstituted butanes. However, in 2,3-dibromobutane the racemic isomer has a higher density than the *meso* isomer; beginning from 3,4-dibromohexanes the *meso* isomers show higher density.[21]

CONCLUSIONS

The present study shows that various patterns of mutual chemical shifts and spin-lattice relaxation can arise for corresponding atoms in a cyclic diastereoisomers. In 2,3-disubstituted butanes all lines of one isomer are usually shifted to high or low field relative to the corresponding lines of the other isomer. In longer aliphatic chains this is no longer true. Nevertheless, mutual chemical shift patterns seem to be operative. Simple conformational considerations with the use of high-field *gauche* chemical shift effects can be applied for analysis of mixtures. (A reviewer pointed out that in complex molecules, interactions between enantiomers may result in unique spectra for racemates *vis-à-vis* pure enantiomers.[22]) Solvents play an essential role in determination of chemical shifts in mixtures of isomers, shifting conformational equilibria in some cases. Spin-lattice relaxation times can be useful in analysis of mixtures of aliphatic diastereomers, giving information not available from shielding and helping to determine preferred conformations and conformational flexibility.

Acknowledgements

We gratefully acknowledge the National Science Foundation for support of this research.

REFERENCES

1. (a) G. C. Levy and G. L. Nelson, *Carbon-13 Nuclear Magnetic Resonance for Organic Chemists*, Wiley, New York (1972); (b) F. Wehrli and T. Wirthlin, *Interpretation of Carbon-13 NMR Spectra*, Heyden, London (1976); (c) E. L. Eliel and K. M. Pietrusiewicz, *Topics in Carbon-13 NMR Spectroscopy*, Vol. 3, ed. by G. C. Levy, p. 171. Wiley, New York (1979).
2. L. P. Lindeman and J. Q. Adams, *Anal. Chem.* **43**, 1245 (1971).
3. T. J. Pehk, V. V. Salum and E. T. Lippmaa, *Abstracts of Conference on the Use of Computers in Spectroscopy of Molecules*, p. 66. Novosibirsk (1977).
4. H. Beierbeck and J. Saunders, *Can. J. Chem.* **55**, 771 (1977).
5. (a) T. Pehk and E. Lippmaa, *Proceedings of the XIXth Congress Ampère*, p. 330. Heidelberg (1976); (b) T. Pehk, *Proceedings of the XXth Congress Ampère*, p. 545. Tallinn (1979).
6. D. A. Wright, D. E. Axelson and G. C. Levy, *Topics in Carbon-13 NMR Spectroscopy*, Vol. 3, ed. by G. C. Levy, p. 103. Wiley, New York (1979).
7. C. J. Carman, A. R. Tarpley and J. H. Goldstein, *J. Am. Chem. Soc.* **93**, 2864 (1971).
8. F. H. Dickey, W. Ficket and H. J. Lucas, *J. Am. Chem. Soc.* **74**, 944 (1952).
9. D. Ziessow and M. Carroll, *Ber. Bunsenges. Phys. Chem.* **76**, 61 (1972).

10. G. C. Levy and R. L. Lichter, *Nitrogen-15 NMR Spectroscopy*, p. 32. Wiley, New York (1979).
11. J. Kowalewski, G. C. Levy, L. F. Johnson and L. Palmer, *J. Magn. Reson.* **28,** 533 (1977).
12. P. J. Gouverneur and J. M. Mulangala, *Bull. Soc. Chim. Belg.* **86,** 721 (1977).
13. G. C. Levy, J. D. Cargioli and F. A. L. Anet, *J. Am. Chem. Soc.* **95,** 1527 (1973).
14. O. A. Subbotin, N. M. Sergeev, N. S. Zefirov and L. G. Gurvich, *Zh. Org. Khim.* **11,** 2233 (1975).
15. K. Limura, *Bull. Chem. Soc. Jpn,* **42,** 3135 (1969).
16. R. L. Lichter and J. D. Roberts, *J. Phys. Chem.* **74,** 912 (1970).
17. J. R. Lyerla and D. M. Grant, *J. Phys. Chem.* **76,** 3213 (1972).
18. G. C. Levy, T. J. Pehk and E. Lippmaa, *Chem. Commun.* in press.
19. R. L. Lichter and J. D. Roberts, *J. Am. Chem. Soc.* **94,** 2495 (1972).
20. L. Lunazzi, D. Macciantelli, F. Bernardi and K. U. Ingold, *J. Am. Chem. Soc.* **99,** 4573 (1977).
21. S. Winstein and R. Wood, *J. Am. Chem. Soc.* **62,** 548 (1940).
22. T. Williams, R. G. Pitcher, P. Bommer, J. Gutzwiller and M. Uskoković, *J. Am. Chem. Soc.* **91,** 1871 (1969).

Received 18 October 1979; accepted (revised) 17 December 1979

© Heyden & Son Ltd, 1980