Substituent Effects on the ^{13}C Relaxation Time along Aliphatic Chains. Application to a Prostaglandin

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Summary The ^{13}C spin–lattice relaxation behaviour of decan-1-oic acid is similar to that of decan-1-ol while in the absence of intermolecular hydrogen bonding various 1-decane derivatives exhibit a characteristic T_1 minimum near the middle of the chain.

THIS study was intended to obtain basic information on the variation of ^{13}C spin–lattice relaxation times along aliphatic chains, which could be of use in the determination of the sequence of biomolecules.

The behaviour of decan-1-oic acid is similar to that reported by Allerhand *et al.*[1] for decan-1-ol; the molecules are strongly bonded by intermolecular hydrogen bonding of the CO_2H groups, their overall motion being therefore restricted, whereas segmental motion has more freedom of movement, away from the centre of the aggregate, along the aliphatic chains. When diluted in a non-polar solvent such as CCl_4, decan-1-oic acid shows a large increase in T_1, related to its greater mobility due to dissociation of the aggregates.

The behaviour of methyl decan-1-oate is similar to that of dilute solutions of decan-1-oic acid. In the absence of intermolecular hydrogen bonding T_1 values increase markedly while they exhibit a characteristic minimum near the middle of the chain. A comparison of the magnitude of the T_1 and τ_C values and their distribution in decan-1-ol, decan-1-oic acid, 1-aminodecane, and decane-1-thiol indicates very weak intermolecular association for the latter two compounds.

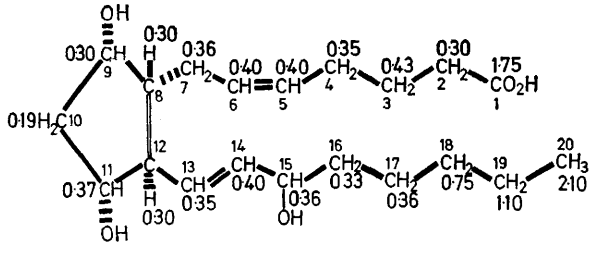
Allerhand and his co-workers[2] have reported a progressive increase in T_1 values along the side chain of cholesteryl chloride and related it to increasing segmental mobility. A similar effect might be expected for other less bulky substituents which would be also easier to introduce into a specific site. We have therefore investigated the relaxation behaviour of 1-bromo-1-iodo-, and 1-phenyl-decane and the Table shows the influence of the mass of the terminal group of all the studied compounds on the mean value of τ_C along the aliphatic chain. The relatively small difference of 15% in $\bar{\tau}_C$ between 1-aminodecane (mass 30) and 1-iododecane (mass 141) is unexpected. The comparative small value of $\bar{\tau}_C$, found for n-decane, suggests however that association effects cannot be completely excluded for such polar compounds. The $\bar{\tau}_C$ value for 1-phenyldecane, higher than predicted from the mass of the benzene ring, is a consequence of the association of the phenyl rings demonstrated by dilution effects in CCl_4.

TABLE

^{13}C Relaxation times (T_1/s) for substituted decanes[a]

Terminal group R	R	2	3	4	5	6	7	8	9	10	τ_C	Mass of terminal group
*CH_2OH[b]	0·6	0·7	0·7	0·8	0·8	0·8	1·1	1·2	1·6	3·0	27·3	30
CO_2H	—	0·4	0·6	0·8	0·8	0·8	1·2	1·4	1·9	3·0	28·8	45
CO_2H[c]	—	1·6	1·8	2·3	2·3	2·3	2·6	3·6	3·9	4·5	9·8	45
CO_2*CH_3	5·3	2·6	2·5	2·2	2·2	2·2	2·2	3·6	3·9	5·3	9·05	59
*CH_2NH_2	2·8	2·8	2·5	2·2	2·2	2·2	2·4	3·1	3·7	4·0	8·9	30
*CH_2SH	3·0	2·6	2·6	2·4	2·1	2·1	2·4	3·1	3·4	3·8	9·0	47
*CH_2Ph	1·4	1·2	1·1	1·1	1·1	1·3	1·3	1·8	2·8	3·0	17·2	91
*CH_2Br	2·8	2·7	1·9	2·0	2·1	2·1	2·2	3·1	3·9	5·3	9·55	94
*CH_2I	2·4	2·2	1·9	1·9	2·0	2·0	2·1	2·7	3·6	3·9	10·3	141
*CH_3	5·6	6·0	5·2	4·8	4·3	4·3	4·8	5·2	6·0	5·6	4·6	15

[a] Chemical shifts agree with calculated values,[4] and will be reported elsewhere. Reproductibility of the measured T_1 values was better than ± 5%. [b] In agreement with values obtained by Allerhand and Doddrell.[1] [c] In 33% CCl_4 solution.



T_1 values for $PGF_{2\alpha}$ (in s).

From the above results, it is clear that amongst the substituents (mass <150) only hydroxy- and carboxy-groups are able to generate long range relaxation effects which might be useful for sequencing in biomolecules.

We *have also* examined whether these effects shown by the various substituted decanes could be observed in molecules of biological interest and we report here, as an example, results for prostaglandin $PGF_{2\alpha}$.†

The substituted cyclopentane ring of $PGF_{2\alpha}$ with its two adjacent double bonds forms a rigid framework. T_1 for C-10 is about half of that for the two adjacent carbon atoms which bear a single hydrogen atom. The side chain attached to C-12 shows increased mobility from the C-15 oxymethine carbon to the terminal methyl group. As for decan-1-oic acid, greater segmental motion would be expected for the acid side chain from C-1 to C-7. However, this effect seems to be compensated by the rigid part of the chain (C-5 to C-8), and as a consequence the maximum T_1 value is observed for C-3.

These results are consistent with previous assignments[3] for $PGF_{2\alpha}$ based on chemical shift considerations. However, owing to the combination of various effects, this example shows clearly that care should be exercised when using spin–lattice relaxation measurements to differentiate CH and CH_2 type carbons in a different chemical environment.

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† Results on various other biological molecules will be reported elsewhere.

[1] D. Doddrell and A. Allerhand, *J. Amer. Chem. Soc.*, 1971, **93**, 1558.
[2] A. Allerhand and D. Doddrell, *J. Amer. Chem. Soc.*, 1971, **93**, 2777; A. Allerhand, D. Doddrell, and R. Komorosky, *J. Chem. Phys.*, 1971, **55**, 189.
[3] G. Lukacs, F. Piriou, S. D. Gero, D. A. van Dorp, E. W. Hagaman, and E. Wenkert, *Tetrahedron Letters*, 1973, 515; G. F. Cooper and J. Fried, *Proc. Nat. Acad. Sci. U.S.A.*, 1973, **70**, 1579.
[4] J. B. Stothers, 'Carbon-13 N.M.R. Spectroscopy,' Academic Press, New York, 1972.