Tetrahedron Vol. 38, No. 22, pp. 3271 to 3275, 1982
Printed in Great Britain.

0040-4020/82/223271-05$03.00/0
Pergamon Press Ltd.

CONFORMATIONAL ANALYSIS—IV†

A LANTHANIDE INDUCED SHIFT (LIS) NMR INVESTIGATION OF THE CONFORMATION AND RELATIVE CONFORMER ENERGIES OF *TRANS* AND *CIS* 2-DECALONE

RAYMOND J. ABRAHAM, HELEN A. BERGEN and DEREK J. CHADWICK
The Robert Robinson Laboratories, University of Liverpool, England

(*Received in the U.K. 29 March 1982*)

Abstract—The solution conformation of *trans*-2-decalone and the conformational population of *cis*-2-decalone has been determined by LIS analysis. The angle of pucker (α) of the ketone ring in *trans*-2-decalone is 51 ± 2°, identical to that of cyclohexanone, but different from that determined for substituted decalones in the solid state, in which significant flattening of the ring occurs.

The steroidal conformer of *cis*-2-decalone, when the latter is complexed to Yb(fod)$_3$ in CDCl$_3$, is found to be preferred over the non-steroidal conformer by a ratio of 55:45, in contrast to the preference reported from the low temperature ^{13}C NMR spectrum for the non complexed ketone in CH$_2$Cl$_2$. The two determinations can be combined to give the enthalpy difference in favor of the non-steroidal conformer of *ca* 0.8 kcal mole^{-1}.

The decalin system has played an important role in the development of conformational analysis as it is both the simplest, conformationally important bicyclic system and a more realistic model for the complex alicyclic natural products such as the steroids and terpenes than cyclohexane itself. Thus the decalins and their substituted derivatives have been the subject of a number of investigations aimed at the identification of the favoured conformations and the determination of relative conformer energies.[2,3] Recently ^{13}C NMR has been extensively used to provide accurate measurements of conformer and activation energies for the decalins,[4] the inversion process of *cis* decalin being particularly well-studied.[5] However, refined conformational studies on the decalins are still infrequent, as the simple derivatives are often liquids, precluding routine crystal structure analysis, and are at the limits of complexity for electron diffraction and microwave studies.

We have demonstrated in earlier papers in this series how the LIS technique can be used to obtain, in suitable cases, both refined molecular geometries in solution[6,7] and relative conformer energies.[1,8] These investigations have concentrated on cyclic ketones, which are both suitable substrates for the LIS technique and also incorporate the co-ordinating centre as part of the cyclic system, providing optimum definition. It has proved possible to show, for example, that introduction of the 4-t-Bu group in cyclohexanone induces considerable distortion of the ring, and we have suggested that the 4-phenyl group, which produces much less distortion may be preferable as a locking group for conformational studies.[6] Here, we present the results of an extension of these studies to *cis* and *trans*-2-decalones.

trans-2-Decalone (Fig. 1) exists as a rigid chair-chair structure.[2] A combined conformational energy, vibrational analysis and electron diffraction study[9] of *trans*-2-decalone in the gas phase found both rings to be distorted chairs with the torsional angle about the C1–C2 bond = 55.3°. In a crystal structure analysis of methyl-3-oxo-*trans*-bicyclo [4.4.0] decane-1-carboxylate.[10] The chair-chair form was confirmed, although the torsional angles around bonds C2–C3 and C3–C4 of about 45° and C1–C2 of 47°, showed some flattening of the cyclohexanone ring. It was therefore thought of interest to determine the angle of pucker of the solution conformation of trans-2-decalone, a determination well-suited to the LIS method.

cis-3-Decalone has two important conformations (Fig. 1 ii). The steroidal (a) form has three gauche butane interactions. In the non-steroidal (b) form, one of these gauche interactions is replaced by a 3-alkyl ketone type interaction which is thought to have a stabilising effect: on theoretical grounds a preference for conformer (b) has been predicted.[2] The experimental evidence, however, is conflicting. The results of an ORD study of *cis*-10-methyl-2-decalone indicate the predominance of the steroid conformation,[11] whereas a ^{13}C NMR study of *cis*-2-decalone suggests a 2:1 predominance of the non-steroidal form at 186°K.[4] The presence of the non-steroidal conformer both in the solid state and solution is indicated by X-ray and CD studies on methyl *cis*-tetrahydro- α and β -santoninate.[12] The angle of pucker of the ring reported in the two crystallographic studies is markedly reduced indicating a flattening of the cyclohexane ring in the solid state. In the present LIS study of the solution conformation of *cis*-2-decalone both the angle of pucker (α) of the cyclohexanone ring and the equilibrium between the steroidal and non-steroidal forms have been determined.

In LIS analysis, the bound chemical shift (Δ) is related directly to the lanthanide-substrate complex geometry through the McConnell-Robertson equation (1).

$$\Delta = K.\ (3\cos^2\theta - 1)/R^3. \qquad (1)$$

The assumptions and procedure necessary for the application of this equation in conformational analysis have been discussed by us previously:[6] an identical approach has been adopted in the present work. The starting geometry was taken either from a crystal structure or a

---

†For Part III see Ref. 1.

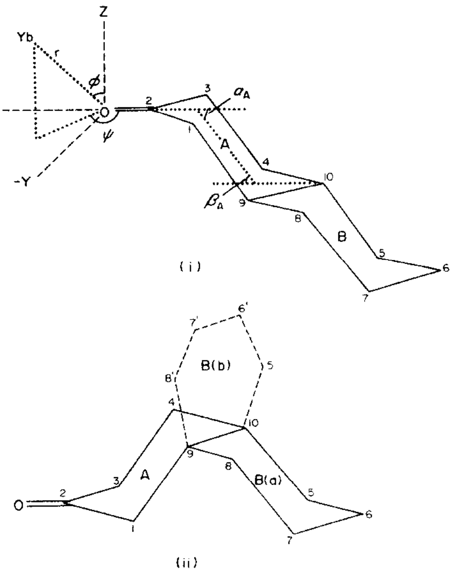

Fig. 1. Lanthanide—substrate geometry and definitions. (i) *trans*-2-decalone, (ii) *cis*-2-decalone.

molecular mechanics calculation and refined via systematic variation of the angle of pucker (Fig. 1). Program LIRAS 3[1] was used to calculate the bound chemical shifts (ΔM) from eqn (1), and to compare these with experimental values via calculation of an agreement factor R_X, eqn (2).

$$R_X = \left\{\sum(\Delta_{obs} - \Delta_{calc})^2 / \sum \Delta^2_{obs}\right\}^{1/2} \quad (2)$$

A unique and well-defined substrate geometry is indicated when variation of Rx with pucker angle yields a sharp minimum $R_x < 0.02$. The four site model for lanthanide ion binding was used in which the Yb ion is reflected in the XZ and XY planes (Fig. 1), and in which the populations of the two sites reflected about the XZ plane may be varied.

EXPERIMENTAL

The proton and ^{13}C spectra were obtained with a Bruker WH400 and Varian XL-100 (25.2 MHz) spectrometers on solns in $CDCl_3$ previously stored over molecular sieves, with TMS as internal standard. A commercial sample of 2-decalone was separated into the *cis* and *trans* isomers by preparative GLC $Yb(fod)_3$, dried *in vacuo* over P_4O_{10} for 24 h prior to use, was added in incremental quantities to the substrate soln. The observed and bound shifts are given in Tables 1 and 2. All computations were performed on the University ICL 1906 S and IBM 4341 computers.

The ^{13}C chemical shifts of the steroidal and non-steroidal isomers of *cis*-2-decalone at 186°K are given in Ref. 4. At room temp there is complete averaging of the NMR signals: however, it was possible to assign the ten sharp signals by comparison with the low temp analysis. Inspection of the resultant ΔM values provided an additional check. (A larger ΔM is expected for those carbons near to the lanthanide ion.) The ^{13}C chemical shifts of

Table 1. Observed shifts (δ) and bound shifts (ΔM) for *trans*-2-decalone-$Yb(fod)_3$[a]

ρ	C_1	C_3	C_9	C_{10}	C_4	C_5	C_8	C_6	C_7
0.0	48.54	41.65	43.28	41.51	33.62	34.20	32.67	26.11	25.58
0.0488	51.38	44.67	44.34	42.70	34.98	34.82	33.23	26.50	25.98
0.0932	53.67	46.61	45.77	43.51	36.06	35.30	33.63	26.78	26.28
0.1477	56.18	49.09	46.95	44.41	37.24	35.81	34.08	27.09	26.57
0.1943	58.40	51.29	47.99	45.20	38.28	36.26	34.46	27.32	26.81
Slope	50.31	48.64	24.67	18.65	23.76	10.48	9.09	6.18	6.25
Intercept	48.76	41.95	43.28	41.66	33.74	34.26	32.73	26.16	25.64
Corr.coeff.	0.9988	0.9979	0.9977	0.9965	0.9986	0.9979	0.9973	0.9958	0.9946
ΔM[b]	44.75	43.27	21.94	16.59	21.14	9.33	8.09	5.49	5.56

	H_{3eq}	H_{1eq}	H_{3ax}	H_{1ax}
0.0526	4.609	4.505	3.968	3.678
0.1006	6.537	6.458	5.394	5.090
0.1601	8.853	8.699	7.008	6.683
0.2161	10.906	10.722	8.472	8.134
slope	38.68	38.09	27.58	27.27
intercept	2.60	2.55	2.56	2.28
corr.coeff	0.9998	0.9997	0.9996	0.9996
ΔM[b]	38.68	38.09	27.58	27.27

[a] $[S]_o = 0.658M$ (0.509 for protons)

[b] carbon data normalized to H_{3eq} (ΔM = 43.48 from the solutions for carbon data).

Table 2. Observed shifts (δ) and bound shifts (ΔM) for *cis*-2-decalone-Yb(fod)$_3$

ρ^a	C_1	C_3	C_9	C_{10}	C_4	C_8	C_5	C_7	C_6
0.0	45.38	39.31	38.55	34.85	28.78	28.78	28.32	23.71	22.93
0.0285	46.67	40.59	39.16	35.32	29.35	29.20	28.56	23.90	23.12
0.0653	48.51	42.48	40.10	36.00	30.27	29.74	28.97	24.20	23.43
0.1070	50.71	44.66	41.17	36.82	31.35	30.41	29,45	24.54	23.80
0.1431	52.53	46.51	42.08	37.50	32.24	30.95	29.82	24.82	24.09
slope	50.31	50.67	24.91	18.65	24.49	15.24	10.65	7.82	8.19
intercept	45.31	39.23	38.50	34.82	28.72	28.77	28.29	23.70	22.92
corr.coeff	.9998	.9998	.9998	.9997	.9995	.9999	.9994	.9996	.9993
ΔM	50.31	50.67	24.91	18.65	24.49	15.24	10.65	7.82	8.19

$^a [S]_0 = 1.035$ M

trans-2-decalone were assigned by comparison with those of *trans*-2-decalol.[13] Inspection of the ΔM values confirmed the assignments.

The ^1H spectrum of *trans*-2-decalone is very complex and assignment by inspection of the unshifted spectrum proved impossible. After the first Yb(fod)$_3$ addition however, four signals (due to the 1,3 axial and equatorial hydrogens) were clearly visible and well separated, having experienced significant downfield shifts. The splitting patterns indicated the assignments of these peaks and further selective ^1H decoupling experiments confirmed these.

RESULTS AND DISCUSSION

The initial geometries chosen for *trans*-2-decalone are given in Figs. 2 and 3. The molecular mechanics calculation[9] used the forcefield of Lifson and Warshel[14] (henceforth known as the LW Forcefield geometry), adapted to include the CO group. A second geometry for the carbon skeleton of *trans*-2-decalone was derived from the crystal structure of methyl-3-oxo-*trans*-bicyclo [4.4.0] decane-1-carboxylate.[10] In addition the H atoms were taken to have a CCH of 109.47° and a C–H bond length of 1.09Å.

The two geometries differ mainly in the length of the C_9C_{10} bond and the torsional angles in ring A. The crystal structure shows a marked flattening of the ring, in contrast to the molecular mechanics geometry in which the ring torsional angles are similar to those of cyclohexanone. The results of subsequent refinement of the angle of pucker of ring A (α_A) are shown in Fig. 4. Angle β_A was unrefined as there is insufficient data to ensure reliable geometry definition for this region of the molecule. A minimum agreement factor of $R_x < 0.014$ was

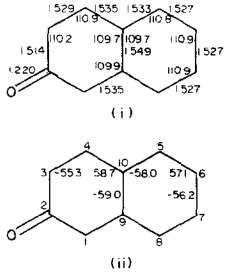

Fig. 2. (i) Bond lengths (Å) and bond angles (°), and (ii) torsional angles (°) of *trans*-2-decalone derived from the LW Forcefield Geometry.[9]

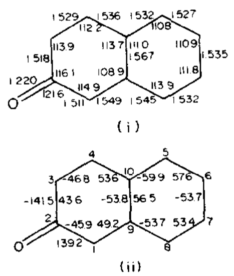

Fig. 3. (i) Bond lengths (Å) and bond angles (°), and (ii) torsional angles (°) of *trans*-2-decalone derived from the crystal structure geometry of Methyl-3-oxo-trans bicyclo [4.4.0] decane-1-carboxylate.[10]

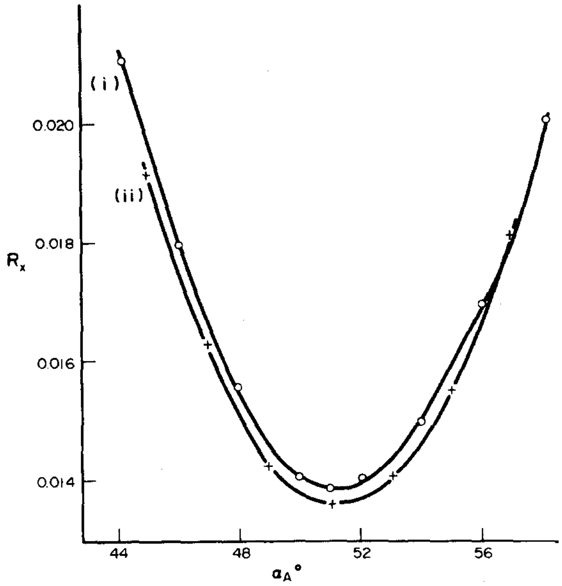

Fig. 4. The agreement factor (R_x) vs the angle of pucker (α_A) for *trans*-2-decalone. (i) LW Forcefield and (ii) crystallographic starting geometries.

Table 3. Lanthanide position for refined 2-decalone geometries

	Trans-2-decalone		Cis-2-decalone
	LW Forcefield	Crystallographic	
r (Å)	2.95	2.75 - 2.85	2.90
ϕ (°)	75,105	65-70, 115-110	75, 105
ψ (°)	140,220	145-150, 215-210	140,220
% population (+Y)	50	45	50
R_x	0.0139	0.0137	0.0139
α_A (°)	51	51	51

obtained at a value of $\alpha_A = 51°$, for both initial geometries. The well defined and sharp minima indicate the appropriateness of the 4-site model for lanthanide-ion binding. Table 3 summarises the lanthanide ion positions in the refined lanthanide substrate geometries. The lanthanide ion is well placed for maximum overlap with oxygen lone pairs and minimum steric interference with the α-hydrogens. Note that for the crystal geometry, the populations of the lanthanide ion in the sites reflected about the XZ plane are not equal. This unexpected result is a consequence of the slight asymmetry of the initial geometry. The lengths of and, in particular, the torsional angles about the C1–C2 and C2–C3 bonds are significantly different. The decrease in population of the sites on the +Y side from the expected 50% is slight, however (5%).

The angles of pucker previously measured by the LIS technique[6] are $\alpha = 49°$, $\beta = 51°$ for cyclohexanone and $\alpha = 45°$, $\beta = 47–50°$, $\alpha = 42°$, $\beta = 50°$ for the 4-phenyl and 4-t-butyl derivatives. These substituents distort and flatten the ring to a small extent. For trans-2-decalone the refined value of α_A is 51°, close to the value for cyclohexanone. In this case the substitution of ring B has very little effect on the conformation of the cyclohexanone ring A. Thus geometric considerations alone would suggest that *trans*-2-decalone is an even better model for a locked cyclohexanone ring than the 4-phenyl group we recommended previously. However, the latter is preferable if beta substitution effects are important, as in ^{13}C NMR analyses.[15]

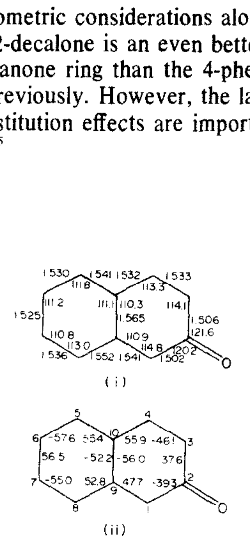

Fig. 5. (i) Bond lengths (Å) and Bond angles (°), and (ii) torsional angles (°) for the steroidal conformer of *cis*-2-decalone, derived from the crystal structure geometry of 3-oxo-cis bicyclo [4.4.0] decane-1-carboxylic acid.[10]

The other point of note is the discrepancy between the angle of pucker of ring A found in the crystal study[10] and that in the gas phase[9] and solution. Whereas the latter values are in essentially complete agreement, crystal packing forces in the solid have flattened the easily deformed cyclohexanone ring by several degrees (from 51 to 39°). This observation emphasises, yet again, the need for caution in translating the results of crystal structure analyses directly to the liquid or vapour phases.

The initial geometry chosen for the steroidal conformer [ring B in position (a)] of *cis*-2-decalone was taken from the crystal structure of 3-oxo-*cis*-bicyclo [4.4.0] decane-1-carboxylic acid.[10] The relevant bond lengths and angles are shown in Fig. 5. An identical geometry was chosen for the non-steroidal form [ring B in position (b)] with the alteration that the torsional angle $C_4C_{10}C_9C_{8'}$ is −56.0° in (b) whereas $C_4C_{10}C_9C_8$ is −179° in (a).

From our LIS analysis of the solution conformation of *trans*-2-decalone, the angle of pucker of ring A was found to be 51°. Although the crystallographic study of 3-oxo-*cis*-bicyclo [4.4.0] decane-1-carboxylic acid[10] (containing the *cis*-2-decalone skeleton) indicated a flattened ring A in the solid state (torsional angle of 37.6° and −46.1° about bonds C_2C_3 and C_3C_4 respectively), it was thought that the solution conformation of ring A in *cis*-2-decalone would be similar to that for the *trans* isomer. Thus an angle of pucker of $\alpha_A = 51°$ was assumed for *cis*-2-decalone.

Subsequent analysis of the LIS data was then concerned with the determinations of the percentage of the steroidal and non-steroidal conformers of *cis*-2-decalone present in solution. The results are shown graphically in Fig. 6. A sharp and well-defined minimum is obtained with an acceptable agreement factor of 0.0139. A slight preference for the steroidal conformer is indicated at 55%, which is independent of α_A over a small range, as shown in Fig. 6. The lanthanide ion positions are very similar to those obtained in the lanthanide *trans*-2-decalone complex (Table 3).

The preferential stability of the steroidal conformer obtained here at first sight appears to contradict the results of Browne *et al.*,[4] who, by observing ^{13}C NMR resonance of the separate "frozen out" conformers at 186°K in methylene chloride solution, found the non-steroidal form to be the more stable (favoured in the ratio 65:35). The different results may be due to the different entropies of the conformers, as it would be expected that the steroidal conformer would have the

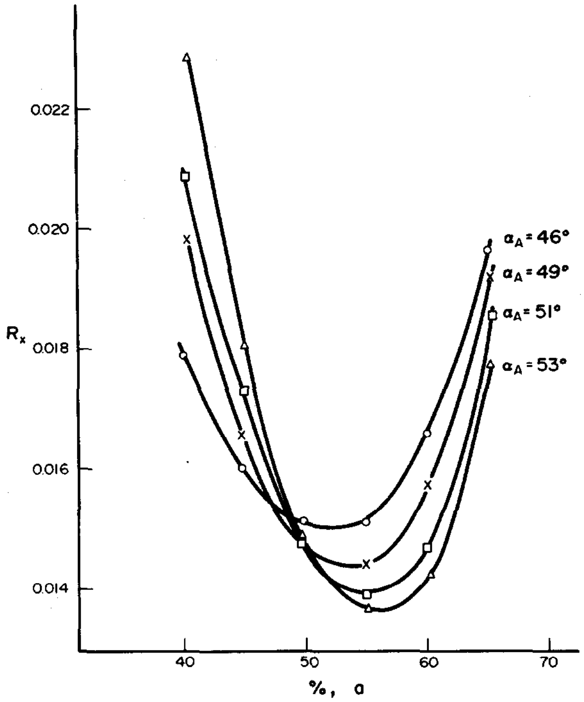

Fig. 6. The agreement factor (R_x) vs the % steroidal conformer (a) for *cis*-2-decalone with various angles of pucker (α_A).

higher entropy, the cyclohexanone ring being more flexible in this conformer. In this context it is of interest to note that the two determinations of ΔG (0.23 kcals mole^{-1} at 186°K, -0.12 kcals mole^{-1} at 298°K) when combined give values of ΔH and ΔS of 0.81 kcals mole^{-1} and 3.4 e.u.

The value of 0.8 kcals mole^{-1} in favour of the non-steroidal conformer for the enthalpy difference of the conformers is in very good agreement with the accepted values for the "3-alkyl ketone effect" (Eliel[16] quotes 0.6–0.9 kcals mole^{-1}), which supports this interpretation.

However, different solvation effects in the two experiments may also be significant. This emphasises the dangers of equating the accurate determinations of conformer populations at one temperature with enthalpy differences, and opens up the intriguing prospect of combining LIS experiments at room temperature with low temperature studies to determine accurate values of conformer enthalpy and entropy differences.

CONCLUSIONS

It is apparent that the crystal structure and molecular mechanics geometries are good starting points in the determination of the solution conformation of *trans*-2-decalone. The differences in some of the torsional angles, however, demonstrate limitations in the assumption that the solid state or theoretical geometries and the solution geometry are equivalent. We have demonstrated the usefulness of the LIS approach as a complementary method for the accurate determination of torsional angles in solution and have further shown that the technique is sufficiently refined to yield reliable thermodynamic information on conformational equilibria.

Acknowledgements—We wish to thank Dr. B. E. Mann and Dr. C. Spencer for their assistance in operating the Sheffield S.E.R.C. very high-field NMR service, and acknowledge the University of Liverpool computing facilities, and S.E.R.C. grants towards the Varian XL-100 spectrometer and for a Senior Research Assistantship (H.A.B.).

REFERENCES

[1] R. J. Abraham, D. J. Chadwick and F. Sancassan, *Tetrahedron* **38**, 1485 (1982).
[2] M. Hanack, *Conformation Theory*, Chap. 4(II). Academic Press, New York (1965).
[3] E. L. Eliel, *Stereochemistry of Carbon Compounds*, Chap. 10. McGraw-Hill, New York (1962).
[4] L. M. Browne, R. E. Klinck and J. B. Stothers. *Org. Mag. Res.* **12**, 561 (1979).
[5] B. E. Mann, *J. Magn. Res.* **21**, 17 (1976); J. W. Blunt, J. M. Coxon, N. B. Lindley and G. A. Lane, *Aust. J. Chem.* **29**, 967 (1976).
[6a] R. J. Abraham, M. J. Bovill, D. J. Chadwick, L. Griffiths and F. Sancassan, *Tetrahedron* **36**, 279 (1980); [b] R. J. Abraham, H. A. Bergen and D. J. Chadwick, *Tetrahedron Letters* 2807 (1981).
[7] R. J. Abraham, D. J. Chadwick and F. Sancassan, *Tetrahedron* **37**, 1081 (1981).
[8] R. J. Abraham, D. J. Chadwick, L. Griffiths and F. Sancassan, *J. Am. Chem. Soc.* **102**, 5128 (1980).
[9] W. Schubert, L. Schafer and G. H. Pauli, *J. Molecular Structure* **21**, 53 (1974).
[10] D. J. Chadwick and J. D. Dunitz, *J. Chem. Soc.* Perkin II, 276 (1979).
[11] C. Djerassi and D. Marshall, *J. Am. Chem. Soc.*, **80**, 3986 (1958).
[12] H. Ogura, H. Takayanagi, Y. Harada and Y. Iitaka, *J. Chem. Soc.* Perkin II, 1142 (1979).
[13] S. H. Grover and J. B. Stothers, *Can. J. Chem.* **52**, 870 (1974).
[14] S. Lifson and A. Warshel, *J. Chem. Phys.* **55**, 477 (1971).
[15] E. L. Eliel and K. M. Pietrusiewicz, *Topics in C-13 NMR Spectroscopy* **3**, 171 (1979).
[16] Ref. 3, p. 240.