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REFINEMENT OF THE SOLUTION STRUCTURE OF BICYCLO[3.1.0]HEXAN-3-ONE BY ^{1}H- AND ^{13}C-LANTHANIDE INDUCED SHIFT (L.I.S.) ANALYSIS

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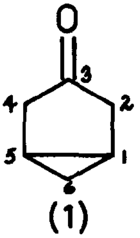
Although lanthanide shift reagents have rightly become a routine tool in n.m.r. spectroscopy, the decline in the number of publications dealing with their detailed structural application perhaps reflects a growing disenchantment with their utility arising from the assumptions implied in their use. Surprisingly, after the early work of R.J.P. Williams and co-workers on the determination of the conformations of AMP and TMP in aqueous solution[1], there has been little effort expended in attempts to use L.I.S.'s in the same sort of way as X-ray diffraction data i.e., as a tool for refinement of structure and conformation[2]. The fundamental problem associated with this kind of application is shortage of data: the system is often underdetermined. Perhaps for this reason, investigators have shown more concern for the additional problems of choice of a correct shift reagent-substrate model and the reliability of the McConnell-Robertson equation than for the intrinsically more important structural applications.

We demonstrate here that by utilisation of L.I.S.'s for ^{1}H and ^{13}C nuclei, use of a physically reasonable model for lanthanide binding and restriction of the number of variables defining the conformation of the system under study to a minimum, it is possible to refine, with a high degree of confidence, the solution structure of bicyclo[3.1.0]hexan-3-one (1).



(1)

A starting geometry for (1) was derived from the X-ray crystal structure of N'-isopropylidenebicyclo[3.1.0]hexan-6-exo-carbohydrazide[3] and the published geometry for cyclopropane[4]. L.I.S.'s were measured for all carbon (XL-100, 25.2 MHz) and hydrogen atoms (R-34, 220 MHz) (on the same solutions) by incremental addition of $Yb(fod)_3$ to a 0.9M solution of the substrate in $CDCl_3$. The slopes of the least-squares linear plots of induced shift *versus* the molar ratio of shift reagent to substrate (correlation coefficients 0.997 or better) were assumed to correspond to the bound shifts (ΔM values, see Table).

A modified version of the computer programme METALSEARCH[5] was used to calculate values of the bound shifts for all carbon and hydrogen nuclei: only the carbonyl carbon atom C(3) was excluded from the analysis since it is vulnerable to diamagnetic and contact shift effects[6]. Crucial to the success of the analysis was the assumption that the Yb ion populates equally sites symmetrically disposed with respect to the mirror plane bisecting the C(2)-C(3)-C(4) angle (we have previously stressed the importance of lanthanide ion binding into lone-pair electron density as implied by this double-site model[7]). The Yb ion positions were varied by incremental scanning of the polar variables (Figure 1) in the ranges 'r' 2.60-3.40 Å in 0.02 Å steps, ϕ $70-110^0$ and ψ $110-150^0$ in 2^0 steps. Best ion positions, as judged by calculation of a crystallographic agreement (R) factor between calculated and observed bound shifts, were determined for a range of conformations of the substrate (1), obtained by variation of the angle of pucker, α, at C(2) and C(4) (Figure 1), in 5^0 steps in the range $170-215^0$. The results of this analysis are summarised in Figure 2, which demonstrates that the overall best fit between calculated and experimental data is obtained with a flattened boat conformation, angle of pucker 195 ± 12^0 in close agreement with previous results , from different approaches. in analogous thujane derivatives[8]. The lanthanide ion positions corresponding to this best fit ($r = 3.16-3.20$ A, $\phi = 80-82^0$, $\psi = 128-130^0$ and $232-230^0$) are entirely reasonable in the light of our earlier work on ketone-lanthanide shift reagent complexes[6].

The results of this study strongly support the reliability of conformational analysis by L.I.S. experiments provided that (i) the degree of determination of the system can be optimised by simultaneous use of ^1H- and ^{13}C-induced shifts, (ii) the number of variables defining the conformation is restricted (in this case to one) and (iii) reasonable assumptions concerning the lanthanide ion binding are made.

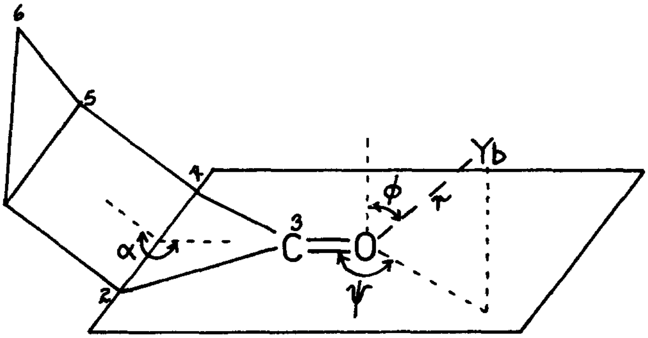


Figure 1

TABLE

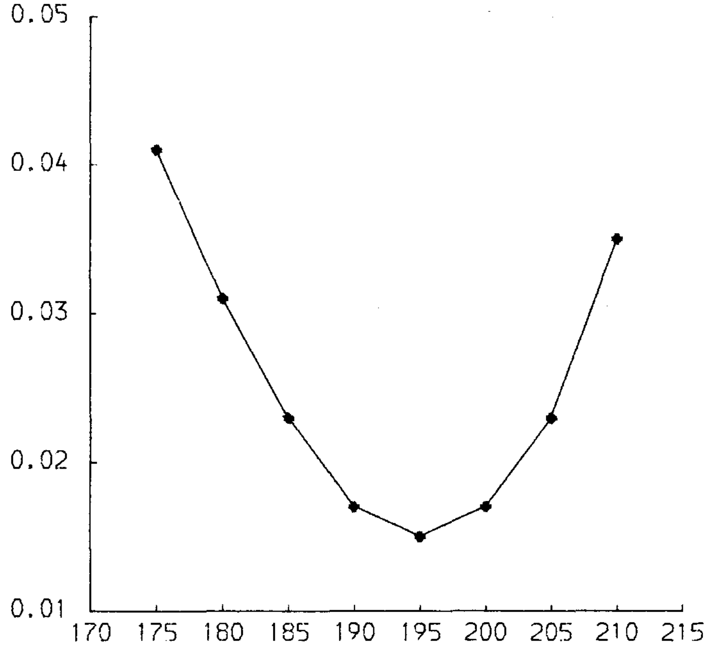
Observed and bound shifts for bicyclo [3.1.0] hexan-3-one

$\rho \times 10^{-2}$,[a]	H(2,4)endo	H(2,4)exo	H(1,5)	H(6)endo	H(6)exo	C(3)	C(2,4)	C(1,5)	C(6)
0 [b]:	2.148	2.594	1.539	-.060	0.908	218.26	41.06	12.22	13.30
3.58	3.376	3.720	1.968	0.576	1.225	222.48	42.67	12.99	13.93
9.71	5.128	5.304	2.561	1.456	1.666	228.25	44.93	14.07	14.72
12.58	5.929	6.019	2.831	1.867	1.867	-	-	-	-
15.66	6.816	6.816	3.123	2.302	2.080	-	-	-	-
slope :	29.50	26.67	10.01	14.93	7.42	101.9	39.5	18.9	14.5
correlation:	.9994	.9993	.9991	.9992	.9991	.9981	.9986	.9984	.9966
ΔM[c]:	29.50	26.67	10.01	14.93	7.42	97.8	37.9	18.1	13.9

[a] $\rho = [L]_o/[S]_o$; $[S]_o$ = 0.8941M.

[b] shifts are in p.p.m. relative to internal T.M.S.

[c] carbon data normalised to H(2,4)exo (three points) ΔM = 27.69.



Agreement (R) factors for best solutions <u>versus</u> angle of pucker

Figure 2

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