Tetrahedron Letters No. 46, pp 4045 - 4048, 1974. Pergamon Press. Printed in Great Britain.

LANTHANIDE INDUCED SHIFT NMR STUDIES OF SOME BICYCLO-[6·1·0]-NONA-2,4,6-TRIENE DERIVATIVES

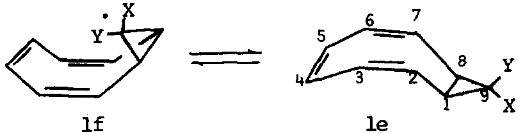
Clair J. Cheer and William Rosen*
Department of Chemistry, University of Rhode Island
Kingston, Rhode Island 02881

and

J. John Uebel
Department of Chemistry, University of New Hampshire
Durham, New Hampshire 03824

(Received in USA 24 July 1974; received in UK for publication 8 October 1974)

The chemical behavior of bicyclo-[6·1·0]-nona-2,4,6-triene and its derivatives has been the subject of many investigations.[1] Much of the activity has been concerned with mechanistic studies of the thermolytic reactions of this system leading to the 8,9-dihydroindene system.[2] Most current mechanistic schemes invoke a pre-equilibrium between the two possible conformers, **1e** and **1f**, as precursors to subsequent thermolytic events. If steric constraints prevent attainment of the folded conformation, **1f**, (Y≠H), then energetics dictate a profile which is different from the sterically unencumbered situation when the extended form, **1e**, (Y=H), has ready access to **1f**.[3,4] To date little evidence is available bearing on the equilibrium between **1e** and **1f**. We, therefore, wish to address ourselves to this conformational problem by showing that the extended conformation is preferred.



1f **1e**

2a X=CH_2OH; Y=H **3s** X=H; Y=CO_2CH_3
2s X=H; Y=CH_2OH **4a** X=CN; Y=H
3a X=CO_2CH_3; Y=H **5a** X=$CO_2C_6H_4$-p-Br; Y=H

Five 9-substituted bicyclo-[6·1·0]-nona-2,4,6-triene derivatives were studied. The anti- and syn- carbomethoxy derivatives, **3a** and **3s** respectively, were prepared and separated by standard procedures.[5] The corresponding hydroxymethyl derivatives, **2a** and **2s**, were then obtained from **3a** and **3s** by reduction with $LiAlH_4$.[6,7] The anti-nitrile, **4a**, was prepared as described in the literature.[8,9]

The lanthanide induced shift (LIS) NMR studies were conducted on 0.5 to 1.0 M solutions of the materials in $CDCl_3$, utilizing either $Eu(dpm)_3$ or $Eu(fod)_3$ as the shift reagents.[10] Table I displays the least squares slopes of the lines generated when the shift (in ppm) of a specific proton is plotted against the mole ratio of shift reagent to substrate, and subsequently standardized to H_9, so that the similarities and differences are easily discernible. The shifts are observed to be nearly independent of shift reagent used as shown by the values obtained for **3a** and **3s**. This allows a direct comparison of all the structures.

Table I

Shifts Relative to H_9 Shifts

Compound Ratio	**2a**[a]	**2s**[a]	**3a**[a]	**3s**[a]	**3a**[b]	**3s**[b]	**4a**[b]
Hx/H_9	1.74	1.56	1.06	0.75	1.14	0.73	----
H_9/H_9	1.00	1.00	1.00	1.00	1.00	1.00	1.00
$H_{1,8}/H_9$	0.68	0.38	1.03	0.43	1.02	0.50	0.65
$H_{2,7}/H_9$	0.32	0.57	0.32	0.74	0.33	0.77	0.34
$H_{3,6}/H_9$	0.13	0.17	0.13	0.22	0.11	0.29	0.11
$H_{4,5}/H_9$	0.12	0.14	0.01	0.25	0.01	0.21	0.11
Scale Factor[c]	15.17	17.14	14.04	13.46	12.91	7.10	4.88

[a] $Eu(dpm)_3$ used. [b] $Eu(fod)_3$ used. [c] Multiplication of the relative shifts by the scale factor produces the observed gradients in $CDCl_3$.

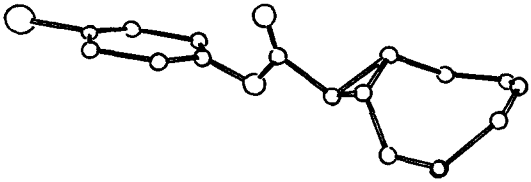
Table II represents the best fits of the data with respect to the theoretically possible structures i.e. either folded, **1f**, or extended, **1e**. The procedure followed was to locate the Eu atom with respect to the cyclopropyl protons, $H_{1,8,9}$, and then calculate[11] the expected shifts of the remaining protons, H_{2-7}, assuming either a folded or extended conformation. For carbinols **2a** and

Table II

Reliability of Folded and Extended Structures

Derivative & Shift Reagent	%^{R}Folded (1f)	%^{R}Extended (1e)
2a + Eu(dpm)$_3$	13.4	3.4
2s + Eu(dpm)$_3$	96.2	7.0
3a + Eu(dpm)$_3$ [or Eu(fod)$_3$]	36.3 [36.8]	9.6 [9.6]
3s + Eu(dpm)$_3$ [or Eu(fod)$_3$]	90.9 [94.3]	6.9 [6.6]
4a + Eu(fod)$_3$	23.8	4.9

2s the methylene shifts (Hx) were also used to locate the Eu atom. The discrepancies between the calculated and observed values are displayed in terms of a reliability factor[12] (R) and listed in Table II. In all cases the extended conformation gives significantly superior fits, indicating that in solution all five compounds exist primarily in the extended conformation. In the solid state the *p*-bromophenyl ester 5a has also been found to exist in the extended conformation with its carbonyl *anti* to H_9 (see figure).[13] The same is true for *anti*-carbomethoxy ester 3a in solution as judged from the LIS data.



The extended conformation is to be expected for 2s and 3s since placement of the substituent in the cavity of the ring would be sterically prohibitive.[1,4] The extended conformation exhibited by 2a, 3a, and 4a has been intuitively assumed until now and it is satisfying to have confirmatory evidence. Only in the case of the *anti*-ester 3a with Eu(dpm)$_3$ was it possible to affect a modest improvement in the fit by averaging some of the folded conformation (5%) into the calculations. Since the errors associated with this procedure are large and the improvements marginal, we feel that a significant extent (<5%) of the folded conformation is not present in any of the *anti* isomers.

In locating the Eu atom several assumptions were made. In all cases the metal was assumed to lie in the symmetry plane of the molecule. For the nitrile 4a, it was assumed to lie along the C≡N bond[14] axis and for the esters it was assumed to lie along the C=O bond axis.[10] For carbinols 2a and 2s the Eu-O distance and the C-O-Eu angle were adjusted. It is interesting to note that for 2s the X group adopts a conformation with the oxygen *syn* to H_9 while with 2a the oxygen is *anti* to H_9 as found in the crystalline state.[13] Molecular models suggest that the O/$H_{2,7}$ interactions are probably responsible for this reversal in 2s.

References

1. S. W. Staley, *Intra. Sci. Chem. Rep.*, *5*, 149 (1971).
2. J. E. Baldwin, A. H. Andrist and R. K. Pinschmidt, Jr., *J. Amer. Chem. Soc.*, *94*, 5845 (1972).
3. P. Radlick and W. Fenical, *ibid.*, *91*, 1560 (1969); A. G. Anastassiou and R. C. Griffith, *ibid.*, *93*, *3083* (1971) and *95*, 2379 (1973); L. A. Paquette and M. J. Epstein, *ibid.*, *95*, 6717 (1973).
4. S. W. Staley and T. J. Henry, *ibid.*, *91*, 7787 (1969).
5. M. B. Sohn, M. Jones, Jr., and B. Fairless, *ibid.*, *94*, 4774 (1972).
6. T. L. Burkoth, *J. Org. Chem.*, *31*, 4259 (1966).
7. 2a is a low melting solid, mp=52-3°, in contrast to the literature report of an oil,[6] while 2s is an oil having physical properties consistent with its structure: nmr (τ): 4.0 (m, 6H), 6.30 (d, 2H), 8.43 (m, 3H); u.v. EtOH λmax=247 (log ε-3.46).
8. A. G. Anastassiou and R. C. Griffith, *Tetrahedron Lett.*, 3067 (1973).
9. Attempts to obtain the *syn*-nitrile yielded only a small amount which was unsuitable for our purposes. We wish to thank Prof. A. G. Anastassiou for the procedures leading to 4a.
10. Obtained from commercial sources and purified by repeated sublimations. See A. F. Cockrill, G. L. O. Davies, R. C. Harden and D. M. Rackham, *Chem. Rev.*, *73*, 553 (1973).
11. The calculations were performed using the Robertson-McConnell equation using the Eu-X bond as the principal magnetic axis.
12. M. R. Willcott III, R. E. Lenkinski and R. E. Davis, *J. Amer. Chem. Soc.*, *94*, 1742 (1972).
13. The ester, 5a, mp=79-9°, crystallizes in the orthorhombic space group $Pca2_1$ with unit cell dimensions a = 14.63Å, b = 5.83Å, c = 16.74Å and four molecules per unit cell(ρ obsd = 1.48, ρ calcd = 1.47 g/cc). Intensities of 848 independent reflections were estimated visually from multiple film Weissenberg photographs (cu-Kα), corrected for Lorentz and polarization effects, solved utilizing the heavy atom method by Patterson and Fourier techniques and refined by least squares to R = 0.14.
14. R. E. Davis, M. R. Willcott III, R. E. Lenkinski, W. E. Doering and L. Birladeanu, *J. Amer. Chem. Soc.*, *95*, 6846 (1973).
15. We thank the University of Rhode Island Research Committee and the University of New Hampshire Computer Center for financial support.