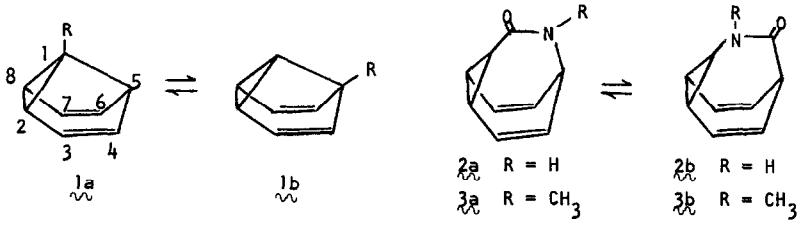
Tetrahedron Letters No. 33, pp. 3141-3144, 1971. Pergamon Press. Printed in Great Britain.

THE COPE REARRANGEMENT: SUBSTITUENT EFFECTS ON EQUILIBRIA OF BRIDGED HOMOTROPILIDENES

Grant R. Krow
Temple University, Philadelphia, Pa. 19122
and
Kermit C. Ramey
ARCO Chemical Company, Glenolden, Pa. 19036

(Received in USA 21 May 1971; received in UK for publication 19 July 1971)

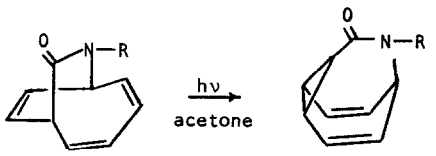
As part of a theoretical attack on the problem of reducing the energy of the Cope rearrangement to a negative number, Hoffmann and Stohrer[1] have used EH calculations to determine substituent effects on equilibrium preferences for semibullvalene tautomers 1a ⇌ 1b. In evaluating the effect of bridgehead substituents R on the strength of the cyclopropane 2-8 σ bond of 1a, specifically strong preferences were predicted for both π-electron donor and acceptor substituents.[1,2] It was shown for 1a that the Walsh orbitals of the cyclopropane interact in a π manner with π acceptors R to strengthen the 2-8 bond and with π donors to weaken this same bond. It follows for an equilibrium of the type 1a ⇌ 1b that a π acceptor, such as R = carbonyl or nitrile, will stabilize 1a, while donors, such as R = amino, alkoxy, or halogen, will destabilize 1a and then 1b will be favored. By extension of the above arguments to the equilibria for bridged lactams 2 and 3, it can be predicted that 2a[1,3] and 3a, which have the π acceptor carbonyl adjacent to the cyclopropyl ring, will be favored. Although solubility problems have precluded quantitative data for 2a,[3] we have confirmed the prediction for the N-methyl lactam 3a.



1a 1b

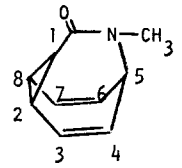
2a R = H 2b R = H
3a R = CH_3 3b R = CH_3

Lactam 3a was synthesized from 7-azabicyclo[4.2.2]deca-2,4,9-trien-8-one 4.[3]



4 R = H; 5 R = CH_3 3a R = CH_3

Treatment of 4 with sodium hydride in dimethylformamide followed by addition of methylsulfate afforded N-methyllactam 5, mp 75-76°, λ_{max} ($CHCl_3$) 1660 cm^{-1}. The nmr spectrum showed signals ($CDCl_3$) at δ 2.8 (NCH_3); δ 3.57 (CH-C=O); δ 4.0 (triplet CH-N); δ 5.2-6.5 (six vinyl protons). Acetone sensitized photolysis of 5 utilizing a 450 Watt high pressure Hanovia lamp with quartz optics afforded an N-methyllactam, mp 100-101°, λ_{max} ($CHCl_3$) 1635 cm^{-1}, shown to be 3a by interpretation of its nmr spectrum.



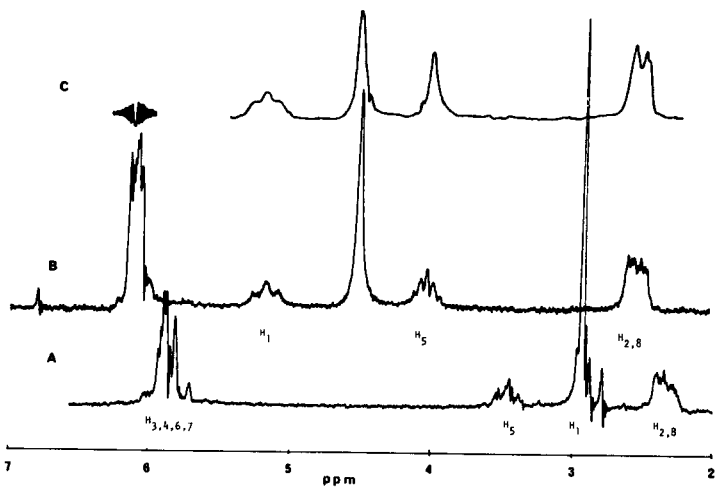


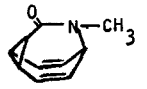
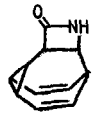
Figure 1: (A) 100 MHz spectrum of 3a; (B) 0.61 M (in $CDCl_3$) with 0.11 M $Eu(DPM)_3$ and 100 Hz offset; and (C) decoupled spectrum resulting from irradiation of the olefinic protons.

The 100 MHz spectrum of 3a is quite complex, as shown in Figure 1, and consists of two distinct and two overlapping resonances. These are assigned ($CDCl_3$) δ 2.32 = $H_{2,8}$; δ 2.88 = H_1; δ 2.92 = N-$\underline{CH_3}$; δ 3.44 = H_5; δ 5.90 = $H_{3,4,6,7}$. The nearly identical chemical shifts of the olefinic protons indicate we are dealing with a static structure or a fluctional structure in which one isomer largely predominates. The assignments are confirmed by the addition in stepwise increments of Eu $(DPM)_3$ (part B of Figure 1). Coordination of Eu $(DPM)_3$ with the amide oxygen[4] results in dramatic down-field shifts for H_1 and N-CH_3, the nearest neighbors of the carbonyl group, a slight shift of proton H_5, which is farther removed, and small change for the remaining protons. Spin decoupling of the olefinic protons (part C of Figure 1) affected the resonances of $H_{2,8,5}$ but not H_1. Collectively, the shift reagent and spin decoupling are proof that we are dealing with structure 3a having a cyclopropyl proton adjacent to carbonyl. This confirms previous assignments to systems of this type.[3]

The spectral evidence also indicates that 3a is several kcal/mole more stable than tautomer 3b. The NMR spectrum was invariant with temperature from -70°C to +140°C;[5,6] and Eu $(DPM)_3$ addition, which spread out the spectrum, did not result in the appearance of any peaks which might indicate a minor isomer 3b. If it is assumed as a minimum that we could detect 6% of 3b in an averaging process at 140°, a difference in free energy $\Delta G^\circ \geq 3.7$ kcal/mole exists for the two isomers.

Previous work (Table I) on the position of equilibria of bridged homotropilidenes has shown only small (0 - 2.0 kcal) preferences for one tautomer. Paquette[7] has shown lactam 6 to have a slight preference for the tautomer with the carbonyl on the cyclopropane side. Doering[8] has found bullvalone 7 to exhibit a temperature dependent spectrum. Doering has estimated the unassigned major tautomer, here assumed by analogy with the present work to have the carbonyl adjacent to cyclopropane, to be present about 90% at room temperature. Imino-ether 8 exists mainly with the ethoxide adjacent to the cyclopropane.[3,6] In the polarized C=N double bond the carbon end is the π acceptor, the nitrogen end the π donor to the homotropilidene system. The electronic effects are of a magnitude such that 10% of the minor isomer is present at room temperature.

Table 1. Position of Equilibria[a] of Some Bridged Homotropilidenes

	Favored tautomer	%	ΔG° kcal/mole	Ref.
3a		94 ≤ 100[b] (140°)	≥ 3.7	this work
6		64 (45°)	0.365	7
7[c]		90[d]	≈ 2.0	8
8		90	1.8 (ΔH°)	6

[a] Determined by DNMR.

[b] Minimum estimate, no minor isomer was detected.

[c] Assumed to be the more stable isomer by analogy to the present work and Ref. 1.

[d] Estimated in Ref. 8.

For lactam 3a, the powerful directing effects of the carbonyl and nitrogen functionalities have combined so that the π acceptor carbonyl is adjacent to cyclopropane and the π donor nitrogen is away. This result is confirmation of the prediction of Hoffmann and Stohrer.[1] We are investigating similar homotropilidene systems in order to further test these predictions.

Acknowledgement: We thank Badische Anilin und Soda Fabrik for the gift of cyclooctatetraene.

References

1. R. Hoffmann and W. D. Stohrer, personal communication.

2. R. Hoffmann, Tetrahedron Lett., 2907 (1970); H. Günther, Ibid., 5173 (1970).

3. L. A. Paquette and T. J. Barton, J. Am. Chem. Soc., 89, 5480 (1967); L. A. Paquette, J. R. Malpass, G. R. Krow, T. J. Barton, Ibid., 91, 5296 (1969).

4. A. R. Katritsky and R. A. Y. Jones, Chem. Ind. (London), 1961, 722 and ref. therein.

5. G. Schroder, J. Oth, R. Merenyi, Angew. Chem. internat. Edit., 4, 752 (1962) have reported barriers ≤ 13 kcal/mole for bridged homotropilidenes.

6. H. Klose and H. Günther, Chem. Ber., 102, 2230 (1969), report a barrier ≤ 15 kcal/mole for the homotropilidene rearrangement of the similar ethoxyazabullvalene.

7. L. A. Paquette, S. Kirschner, J. Malpass, J. Am. Chem. Soc., 91, 3970 (1969).

8. W. von E. Doering, B. Ferrier, E. Fossel, J. Hartenstein, M. Jones, G. Klumpp, R. Rubin, M. Saunders, Tetrahedron, 23, 3943 (1967).