EC00098-05. We wish to thank Dr. James Franzen for his help with the CD measurements.

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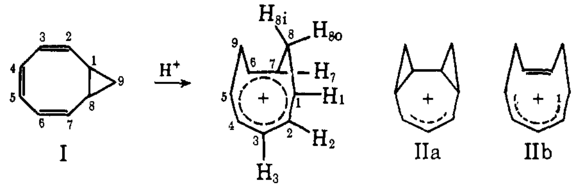
Received September 18, 1970

Protonated *cis*-Bicyclo[6.1.0]nona-2,4,6-triene, a Monocyclic 1,3-Bishomotropylium Ion

Sir:

We have recently reported[1] a series of bicyclic 1,4-bishomotropylium ions,[2] all of which possess considerable homoaromatic character. We now wish to communicate our results on a second type of bishomotropylium ion—a 1,3-bishomotropylium species, II,[2] which represents the first monocyclic bishomotropylium ion.



I II IIa IIb

When a solution of I[3] in CD_2Cl_2 was extracted into a 1:4 (v/v) mixture of FSO_3H–SO_2ClF at *ca.* −125°, there resulted an orange-red solution which gave a quite clean nmr spectrum (Figure 1).[4] A priori, I could have protonated at any one or more of five positions—C_1 ($\equiv C_8$), C_2 ($\equiv C_7$), C_3 ($\equiv C_6$), C_4 ($\equiv C_5$), or C_9. However, based on relative nucleophilicities, one would expect protonation at one or more of the double bond positions, only. Protonation at C_2, C_3, or C_4 would give a 1,2-, 1,3-, or 1,4-bishomotropylium ion, respectively. It is noteworthy that the nmr spectrum of II (Figure 1) is consistent only with C_3 protonation (*i.e.*, a 1,3-bishomotropylium ion), to give what should be the most stable of the three possible bishomotropylium ions.[5] All chemical shifts and coupling constants were unambiguously assigned *via* decoupling experiments; the nmr parameters are summarized in Table I.

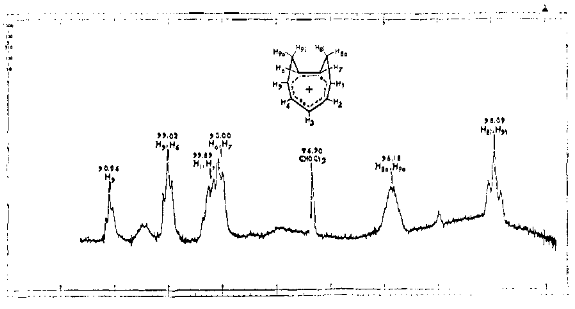


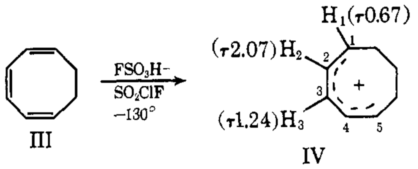
Figure 1. 100-MHz nmr spectrum of protonated *cis*-bicyclo[6.1.0]nona-2,4,6-triene (II) at *ca.* −125° (sweep width = 1000Hz).

Table I. Nuclear Magnetic Resonance Data for Protonated *cis*-Bicyclo[6.1.0]nona-2,4,6-triene (II)[a]

Proton	Chem shift,[b] τ	Coupling constants, Hz
H_3	0.94	$J_{2,3} \equiv J_{3,4} = 6.0 \pm 0.5$
H_2, H_4	2.02	$J_{1,2} \equiv J_{4,5} = 9.0 \pm 0.5$
H_1, H_5	2.82	$J_{1,8o} \equiv J_{5,9o} = 9.0 \pm 0.5$
H_6, H_7	3.00	$J_{7,8o} \equiv J_{6,9o} = 9.0 \pm 0.5$
H_{8o}, H_{9o}	6.18	$J_{1,8i} \equiv J_{5,9i} = 11.0 \pm 0.5$
H_{8i}, H_{9i}	8.09	$J_{8i,8o} \equiv J_{9i,9o} = 12.0 \pm 0.5$
		$J_{7,8i} \equiv J_{8,9i}$ = small

[a] In FSO_3H–SO_2ClF (1:4, v/v) at *ca.* −125°. [b] Chemical shifts measured relative to internal $CHDCl_2$ (τ 4.70).

The nmr data of Table I are compatible, we believe, only with the arrangement of carbons and hydrogens shown in II;[6] however, there remains the problem of the electronic structure of II. Besides the bishomotropylium representation, II, the tricyclic structure, IIa, and the noninteracting monocyclic structure, IIb, are conceivable. It is immediately possible to eliminate IIa as an adequate representation for II, since the $|J_{\text{gem}}| = 12$ Hz is far too large for a cyclopropane ring.[7] Also, the charge distribution at C_2, C_3, and C_4 observed for II is the opposite of what one would expect for IIa.[8,9] Structure IIb, with a simple pentadienyl unit and an isolated double bond, is not easily dismissed without recourse to models. Therefore, 1,3,5-cyclooctatriene (III) was protonated to yield the cyclooctadienyl cation IV.



III IV

$J_{1,2} = 8.1 \pm 0.2$ Hz
$J_{2,3} = 7.2 \pm 0.2$ Hz

A comparison of the nmr data for II and IV immediately reveals that IIb is not an adequate representation for II. In particular, H_1 and H_5 in II are each shifted some 2 ppm to higher field relative to their counterparts in IV. If this upfield shift is really due

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[1] P. Ahlberg, D. L. Harris, and S. Winstein, (a) *J. Amer. Chem. Soc.*, **92**, 2146 (1970); (b) *ibid.*, **92**, 4454 (1970); (c) M. Roberts, H. Hamberger, and S. Winstein, *ibid.*, **92**, 6346 (1970).

[2] The two segments of a 1,4-bishomotropylium ion consist of three and four carbons, while those of a 1,3-bishomotropylium ion consist of five and two carbons; for a further discussion of nomenclature, see S. Winstein, *Quart. Rev., Chem. Soc.*, **23**, 141 (1969).

[3] R. Rieke, M. Ogliaruso, R. McClung, and S. Winstein, *J. Amer. Chem. Soc.*, **88**, 4729 (1966).

[4] When the probe temperature was raised to *ca.* −90°, decomposition took place with a half-life of *ca.* 15 min.

[5] This is true because, in the 1,3-bishomotropylium ion, the charge resides on the *longest* linearly conjugated carbon segment (neglecting homoconjugation). This is the overriding factor when one considers overall energy (neglecting strain contributions, which probably change less than the electronic factors in the isomeric ions in question).

[6] The possibility that the methylene bridges are trans to one another, rather than cis as shown, is deemed unlikely on the basis of the charge distribution observed for II, as well as the chemical-shift difference between inner and outer protons; this will be discussed in a full paper. In order to further confirm this interpretation, a bicyclic 1,3-bishomotropylium ion is being studied in these laboratories.

[7] See the discussion in P. Warner, D. L. Harris, C. H. Bradley, and S. Winstein, *Tetrahedron Lett.*, 4013 (1970).

[8] For studies of allylic ions, see (a) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1969, p 252; (b) G. A. Olah and J. M. Bollinger, *J. Amer. Chem. Soc.*, **90**, 6082 (1968); (c) P. Warner, Ph.D. Dissertation, U.C.L.A., 1970, p 153; (d) A. F. Diaz, D. L. Harris, M. Sakai, and S. Winstein, submitted for publication.

[9] For studies of allylic ions conjugated with cyclopropane rings, see (a) N. C. Deno, H. G. Richey, Jr., J. S. Liu, D. N. Lincoln, and J. O. Turner, *J. Amer. Chem. Soc.*, **87**, 4533 (1965); (b) M. Roberts, H. Hamberger, and S. Winstein, *ibid.*, **92**, 6346 (1970); (c) P. Warner and S. Winstein, submitted for publication.

to charge removal from the pentadienyl unit, it ought to be reflected in a downfield shift of the protons of the double bond (H_6, H_7) relative to an appropriate model. Two possible models are cyclohexene[10] (vinyl protons at τ 4.41) and 1,4,7-cyclononatriene[11] (vinyl protons at τ 4.66). It is clear that H_6 and H_7 of II are both deshielded significantly relative to either model; we attribute this to charge delocalization onto C_6 and C_7. Thus, there can be little doubt that charge is dispersed onto the double bond from the pentadienyl unit to yield the 1,3-bishomotropylium ion, II, although the amount of charge transfer appears to be less than in the 1,4-bishomotropylium ions[1] (where charge is dispersed from an allyl moiety to a butadiene segment).

In light of the ring current which would be expected for II, it is interesting to examine the inner and outer methylene protons. These were differentiated on the basis of the larger $J_{1,8i}$ (J_{trans}) relative to $J_{1,8o}$ (J_{cis}).[12] Also, $J_{7,8i}$ is quite small. Examination of models indicates that the repulsion between H_{8i} and H_{9i} forces the methylene carbons apart, whereby a proper dihedral angle for the observed small coupling constant is achieved.[12,13] The methylene protons of 1,4,7-cyclononatriene appear to be an appropriate model for comparison with those of II.[14] As reported,[10] the chemical-shift difference between the methylene protons of the former is 1.50 ppm. Close scrutiny of the nmr pattern[14] reveals that the inner protons of 1,4,7-cyclononatriene are at lower field than the outer ones. As seen in Table I, this situation is reversed for II.[12] Therefore, the relatively small chemical-shift difference of 1.9 ppm between the inner and outer protons of II is not a true reflection of the size of the ring current in II; a $\Delta\delta$ of 3.4 ppm might give a more accurate picture.[12]

Of considerable interest, with regard to the protonation of I, is the stereochemistry of the process. Unlike cyclooctatetraene, which was found to stereoselectively (80%) deuterate on the endo side to give the monohomotropylium ion with the deuteron mostly inside,[15] I showed stereoselective (70%) deuterium incorporation on the exo side to yield II-d_1, with the deuterium atom mainly on the outside.[14] Obviously, the small change in energy (less than 1 kcal/mol) required to produce this switch in stereochemistry could come from subtle conformational factors.

Acknowledgment. We are grateful to Dr. D. L. Harris for help in obtaining the 100-MHz spectra, and for valuable discussions regarding their interpretation.

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[10] K. B. Wiberg and B. J. Nist, *J. Amer. Chem. Soc.*, **83**, 1226 (1961).

[11] P. Radlick and S. Winstein, *ibid.*, **85**, 344 (1963).

[12] A referee has questioned the basis of our assignments of H_{8i} and H_{8o}, as well as our analysis of the chemical-shift difference between inner and outer methylene protons (particularly the use of 1,4,7-cyclononatriene as a model). While we feel that a full discussion should be reserved for a full paper, we give the following analysis. The C_8–C_9 distance in II (relative to the comparable distance in 1,4,7-cyclononatriene) is shortened by the flattening of the pentadienyl unit of II (as seen in models). When this distance is restored, the approximate dihedral angles obtained from either Dreiding or Framework molecular orbital models are $\angle 1,8i = 160°$, $\angle 1,8o = 20°$, $\angle 7,8i = 120°$, $\angle 7,8o = 0°$. While these angles cannot be precisely related to coupling constants, it is clear that the $\angle 7,8i$ is consistent with the small $J_{7,8i}$. Therefore, we cannot reconcile the data with a reversed assignment of the methylene hydrogens. Further, the models show that, in both 1,4,7-cyclononatriene and II, the inner methylene hydrogens are not in the shielding area above the double bonds. The geometry change incurred on going from 1,4,7-cyclononatriene to II does not seem to appreciably affect the position of the inner methylene hydrogens with respect to the double bonds. Lastly, the van der Waals deshielding effect on the inner methylene protons of II should be more severe than in 1,4,7-cyclononatriene. Therefore, our estimate of $\Delta\delta = 3.4$ ppm is, we feel, a lower limit.

[13] E. Garbisch, Jr., *J. Amer. Chem. Soc.*, **86**, 5561 (1964).

[14] From the analysis of a 60-MHz nmr spectrum, $|J_{\text{gem}}| = 12.5 \pm 0.5$ Hz, $J_{\text{trans}} = 9.0 \pm 0.5$ Hz, and $J_{\text{cis}} = 6.3 \pm 0.5$ Hz. The inner protons resonate at τ 6.32, while the outer ones appear at 7.82.

[15] S. Winstein, H. D. Kaesz, C. G. Kreiter, and E. C. Friedrich, *J. Amer. Chem. Soc.*, **87**, 3267 (1965).

[16] Address correspondence to this author at the Department of Chemistry, Yale University, New Haven, Conn. 06520.

[17] National Science Foundation Predoctoral Fellow, 1966–1970.

[18] Deceased Nov 23, 1969.

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Received August 28, 1970

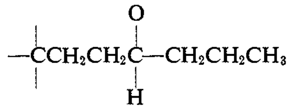
Oudenone, a Novel Tyrosine Hydroxylase Inhibitor from Microbial Origin

Sir:

In the course of the studies on enzyme inhibitors produced by microorganisms in our laboratories, oudenone was discovered in a culture filtrate of *Oudemansiella radicata* very recently,[1] and it showed inhibition of tyrosine hydroxylase and exhibited significant hypotensive effect.[1]

We report herein the structural elucidation and total synthesis of oudenone (**1**), which undergoes a dynamic skeletal change to afford the β-trione **2b** through **2a** by simple addition of water.

Oudenone (**1**), soluble not only in usual organic solvents but also in water, has the formula $C_{12}H_{16}O_3$ (M^+ 208.112), and shows: mp 77–78°; $[\alpha]^{21}D$ $-10.8°$ (c 0.69, EtOH); pK_a = 4.1; $FeCl_3$ test positive; CHI_3 test positive; uv max [MeOH] 285 (ϵ 19,000), 220 (ϵ 12,000) [0.1–1 N NaOH], 247 (ϵ 23,000), 270 mμ (sh); ir (KBr) 3440 (w), 1715 (w), 1662 (s), 1563 (s), 1198 (m), 1018 (m); (CCl_4) 3420 (w), 1735 (w), 1673 (s), 1578 (s), 1185 (m), 1007 cm^{-1} (m). The nmr spectrum is shown in Figure 1. The unique signals of ABXY system at δ 3.19 and 3.57 are assigned to the geminal methylene (H_A, H_B) adjacent to the double bond. The large geminal coupling constant and relatively low chemical shift suggest that the methylene is adjacent to exo or endo unsaturation of a five- or six-membered ring[2] and under the influence of a carbonyl group,[3] respectively. The unsymmetrical triplet signal at δ 0.98 suggests the presence of a side chain longer than ethyl.[4] The lowest signal at δ 4.91 (quintet, J = 6.0 Hz) is reasonably assigned to a hydrogen on the carbon attached to the ether linkage. A partial structure



$$-\overset{|}{\underset{|}{C}}CH_2CH_2\overset{O}{\underset{H}{\overset{|}{\underset{|}{C}}}}-CH_2CH_2CH_3$$

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[1] H. Umezawa, T. Takeuchi, H. Iinuma, K. Suzuki, M. Ito, M. Matsuzaki, T. Nagatsu, and O. Tanabe, *J. Antibiot.*, **23**, 514 (1970).

[2] R. Cahill, R. C. Cookson, and T. A. Crabb, *Tetrahedron*, **25**, 4711 (1969), and references contained therein.

[3] L. M. Jackman and S. Sternhell, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, London, 1969, p 207.

[4] For such virtual coupling, see, for instance, ref 3, pp 143–150.