Reversal of Stereospecificity during Allylic Hydroperoxidation of 3-Norcarene and Bicyclo[4.2.0]oct-3-ene Derivatives Arising from Structurally Enforced Quenching of Singlet Oxygen by the Hydrazide Functionality

Sir:

The importance of the singlet ($\Delta_g$) state of oxygen to synthetic, mechanistic, and environmental chemistry is now well recognized. The wide ranging reactivity of $\text{O}_2$ is witnessed in its ability to effect allylic hydroperoxidation of simple olefins, 1,2-cycloaddition to alkenes of low ionization potential, and 1,4-endoperoxidation of conjugated dienes.\(^1\) Without exception, the first of these reactions has been found to proceed with cis stereochemistry, being characterized by an exacting dependence on steric factors and the availability of an in-plane allylic hydrogen. The other pair of transformations proceed with equally impressive stereocontrol, full retention of stereochemistry occurring in every reported example.

We have now investigated a heretofore unexplored parameter of singlet oxygen behavior, viz., rigid fixing of a functional group capable of quenching the $\Delta_g$ state within suitable proximity to the favored site of oxygenation. Since the observed end result is unprecedented redirection of $\text{O}_2$ attack to the more sterically congested surface of the molecule, the synthetic value of such a scheme is made evident, particularly if the functionality which causes singlet oxygen deactivation can later be extruded from the molecule. In this communication, attention is given to the allylic hydroperoxidation of 3-norcarene and bicyclo[4.2.0]oct-3-ene ring systems. The accompanying paper\(^2\) describes a comparable assessment of the $\text{O}_2$ endoperoxidation of related norcadienes and presents a unifying molecular orbital basis for the markedly contrasting observations made. The reader should recognize that our treatment is extra-mechanistic and therefore independent of the precise mechanistic details of the specific type of oxygenation, some of which remain highly controversial.

$^1$H NMR studies have indicated 3-norcarene to be capable of facile interconversion between boat conformations \(\text{la}\) and \(\text{lb}\).\(^3\) These two forms are clearly not isoequivalent and stereochemical considerations suggest that \(\text{la}\) with its quasi-equatorial cyclopropane ring should be somewhat favored over \(\text{lb}\). However, models reveal the conformational equilibrium to be rather delicately balanced and to be expectedly sensitive to substitution on the cyclopropane ring and elsewhere. Of importance to the photooxygenation reaction, \(\text{la}\) and \(\text{lb}\) share the common stereoelectronic feature of having two equivalent allylic C–H bonds properly aligned with the \(p_z\) orbitals of the double bond, as emphasized in the formulas. On a more general note, electrophilic attack on \(\text{la}\) and \(\text{lb}\) from the less hindered

<table>
<thead>
<tr>
<th>Compd</th>
<th>Epoxidation (^b)</th>
<th>Bromohydrin formation (^c)</th>
<th>Photo-oxygenation (^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percentage composition (sym:anti)(^a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{la})</td>
<td>61.6:38.4</td>
<td>87.4:12.6</td>
<td>100:0</td>
</tr>
<tr>
<td>(\text{lb})</td>
<td>25.6:74.4</td>
<td>16.5:83.5</td>
<td>0:100</td>
</tr>
<tr>
<td>(\text{lc})</td>
<td>0:100</td>
<td>0:100</td>
<td>0:100</td>
</tr>
<tr>
<td>(\text{ld})</td>
<td>69:31</td>
<td>93:7</td>
<td>100:0</td>
</tr>
<tr>
<td>(\text{le})</td>
<td>35:65</td>
<td>—</td>
<td>0:100</td>
</tr>
<tr>
<td>(\text{lf})</td>
<td>7:84(^e)</td>
<td>15:70(^e)</td>
<td>91:9(^f)</td>
</tr>
</tbody>
</table>

\(^a\) The points of stereochemical reference are the cyclopropane ring and the attacking reagent. \(^b\) n-Chloroperbenzoic acid in \(\text{CH}_2\text{Cl}_2\) buffered with solid sodium bicarbonate, 25°C; yields determined by VPC analysis except where noted. \(^c\) N-Bromosuccinimide in aqueous glyme, 25°C; yields determined by VPC analysis after conversion to epoxides with sodium hydride in refluxing tetrahydrofuran. \(^d\) 10% Methanol in \(\text{CH}_2\text{Cl}_2\), containing 10\(^{-8}\) M rose bengal; product analysis made subsequent to NaBH\(_4\) reduction of the hydroperoxides. \(^e\) Isolated yields determined after column chromatography on silica gel. \(^f\) Lack of epimeric contamination determined by TLC analysis. \(^g\) Independent synthesis achieved by phenylselenide anion promoted opening of the stereochemically related epoxide and \(\text{H}_2\text{O}_2\) treatment.

Direction leads unambiguously to different products, \(\text{la}\) serving as progenitor to the syn isomer and \(\text{lb}\) to the anti counterpart. These expectations need not be borne out, however, in more highly substituted derivatives where additional steric factors may gain subtle importance.\(^4\)

The stereochemical consequences of direct epoxidation and bromohydrin formation of several 3-norcanes (Table I) reveal \(\text{I}\) and \(\text{4}\) to be more disposed to attack from the direction syn to the cyclopropane ring. In contrast, the structural features in \(\text{2, 3, 5,}\) and \(\text{6}\) are such that approach of the electrophile from the anti direction is kinetically preferred. That epoxidation and bromohydrin formation proceed with like stereoselectivity (although generally more accentuated when \(\text{Br}^+\) is the electrophile) was established by base-promoted cyclization of the bromohydrins. The major epoxide isolated from each of these experiments was invariably the epimer of that obtained by the more direct procedure. Structural assignments to the individual epoxides follow from their respective \(^1\)H NMR spectra and supportive Eu(fod)\(_3\) pseudocontact shifting in selected cases.
The photooxidations of 1–6 were conducted in a dichloro-
methane–methanol (9:1) solvent system with rose bengal or
methylene blue as sensitizer (comparable stereochemical
results). For characterization the hydroperoxides were reduced
(NaBH₄) without purification to the respective allylic alcohols.
Lithium diethylamide promoted ring opening of the epimeric
epoxides provided the authentic samples necessary for estab-
lishment of stereochemical configuration. With reference to
Table I, the data for hydrocarbons 1–5 are seen to parallel
precisely the previously established stereoselectivities and reflect
the anticipated enhanced attack of the less congested face of the olefinic plane.¹

\[ \text{CH}_3 \text{N=O} + \text{O}_2 \rightarrow \text{CH}_3 \text{N=O} \]

Like photooxygenation of 6 proceeds at a much slower rate
than 5 and gives rise only to the product of opposite configu-
rations. This most unusual stereochemical reversal involving
\(^1\text{O}_2\) attack from the more sterically encumbered direction
appears to be a general reactivity pattern of hydrazides of this
type. Thus, the \(N\)-methyl congener of 6 and the bishomocu-
bane derivative 7 behave comparably! ¹

Pertinent to an understanding of these results are the report
by Ouannis and Wilson that \(^1\text{O}_2\) is efficiently quenched by amines ⁶
and the finding by Ogryzlo and Tang that there exists
a good correlation between the quenching efficiency of the
amine and its ionization potential.⁷ Briefly summarized, an
increase in electron availability is conducive to an increase in
\(k_Q\). Since the \(pK_a\) of a nitrogen base parallels in magnitude its
IP and hydrazines are characterized by low \(pK_a\)'s,⁸ such
molecules can be expected to be efficient quenchers. Indeed,
their effectiveness toward photoexcited ketones has recently
been established by Cohen.⁹ Because the capability of hydra-
zides to cause electronic relaxation of \(^1\text{O}_2\) appears to be a general reactivity pattern of hydrazides of this
type, the \(N\)-methyl congener of 6 and the bishomocu-
bane derivative 7 behave comparably! ¹

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References and Notes

(1) (a) K. Gollnick, Adv. Photochem., 6, 1 (1968); (b) S. K. Foote, Acc. Chem.
Res., 1, 104 (1968); (c) D. R. Kearns, Chem. Rev., 71, 385 (1971); (d) R.
(2) L. A. Paquette, D. G. Liotta, C. C. Liao, T. G. Wallis, L. Eickman, J. Clardy,
and R. Glei1, following paper in this issue.
(3) W. D. Kumler, B. Bokleff, B. Bruck, and S. Weinstein, J. Am. Chem.
(4) The epoxidation of \(+\)-3-carene is a case in point: P. Kropp, J. Am. Chem.
(1974).
(8) D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution".
(1972).
(1974).
(10) In related work, the capability of hydrazides (e.g., ii) to appreciably reduce
\(^1\text{O}_2\) reactivity in binary mixed solutions (CHCl₃-CH₂OH, CHCl₃-CH₂CN,
CH₃OH) with ii has been demonstrated.

Endoperoxidation of Conformationally Fixed
Norcaradienes by Singlet Oxygen. Frontier Molecular
Orbital Basis for the Operability of \(^1\text{O}_2\)
Quenching by Hydrazides

Sir:

Just as study of the allylic hydroperoxidation of various
3-norcarnenes has revealed the capability of hydrazides to
quench \(^1\text{O}_2\) oxygen as it functions in this reaction,¹ so the en-
doperoxidation of structurally related norcaradienes should
similarly lend itself to an evaluation of a possible hydrazide
directive effect on such \(4\) cycloadditions. Significantly, the
stereochemical outcome of the two oxygenation modes
should not be identical if the conditions of HMO perturbation
theory are rigorously adhered to.

The stereospecificity of norcaradiene endoperoxidation has
been experimentally assessed in five different systems (Table
I), two of the illustrated examples (1b, 2) having been inde-
pendently studied by others.²³ To facilitate product identifi-
cation, the first-formed endoperoxides were thermally rear-
anged to their trishomobenzene dioperoxide isomers without
loss of configuration.⁴ Because \(^1\text{H}\) NMR data revealed the
cyclopropyl protons in the dioperoxides to be only marginally
shielded, the oxygen atoms are assumed to be anti to the
three-membered ring. This important stereochemical point was
established conclusively by x-ray crystal structure analysis of
8 (Figure 1), the crystals of which form in the orthohombic
system with \(a = 13.404, b = 15.147 (3), \) and \(c = 16.020 \) (4)
A. Systematic extinctions in 0kl (absent if \(k = Zn + l\)), h0l
(absent if \(l = Zn + l\)), and hkl (absent if \(h = Zn + l\)) sug-

Communications to the Editor

Referential Notes

(1) (a) K. Gollnick, Adv. Photochem., 6, 1 (1968); (b) S. K. Foote, Acc. Chem.
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CH₃OH) with ii has been demonstrated.

(11) R. Glei1, private communication.
(12) For example, 5 undergoes complete allylic hydroperoxidation in 2 h while
6 reacts only to 67% completion after 22 h.

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