$(H_2O)](PF_6)_2$ (a = NH_3);[22] the products were separated by FPLC.[23] The singly modified product was characterized by differential pulse polarography; the heme($Fe^{3+/2+}$) reduction potential is 275 mV (NHE); the reduction potential of the $a_5Ru(His62)^{3+/2+}$ moiety is 75 mV (NHE), as expected.[24] The $Ru^{2+} \rightarrow Fe^{3+}$ ($-\Delta G° = 0.2$ eV) ET rate was measured by using the $[Ru(bpy)_3]^{2+}$/EDTA flash photolysis technique.[24] Electron transfer was monitored by the increase in absorbance at 550 nm, attributable to reduction of the heme iron. The kinetics were first order over three half-lives ($\sigma = 0.98$),[25] with $k_{obsd} = 1.7$ (1) s^{-1}.

A simple exponential edge-edge distance dependence [$\exp[-\beta(d - d_0)]$, with $\beta = 0.9$ Å^{-1} and no correction for difference in reorganization energy or driving force][6a] predicts a $Ru^{2+} \rightarrow Fe^{3+}$ ET rate for the N62H mutant of 0.4-2.0 s^{-1} relative to the 30 s^{-1} observed[24] for a_5Ru(His33)cytochrome c.[26] In the a_5Ru-(His33) derivative of horse heart cytochrome c, the ET pathway consists only of aliphatic residues.[2b,27] The finding that the rate for the ruthenated N62H mutant agrees strikingly with that calculated relative to horse heart cytochrome c suggests that the mere presence of aromatic residues and/or polarizable sulfur atoms along the pathway for electron transfer does not necessarily create conditions for significantly stronger donor-acceptor electronic coupling through the protein medium.[28]

Beratan and Onuchic have proposed a theoretical framework for long-range donor-acceptor coupling involving pathways that are combinations of covalent-bond, hydrogen-bond, and through-space interactions.[29] Using this approach, we have estimated the pathways of strongest coupling between the ruthenated histidine and the heme for N62H (mutant, see Figure 1) and for His33 (horse heart cytochrome c).[30] A comparison of the best pathways gives $k_{ET(His62)} = k_{ET(His33)}[H_{ab(His62\text{-}Met64)}/H_{ab(His33\text{-}Pro30)}]^2 = 0.4$ s^{-1} relative to 30 s^{-1} for His33 (horse heart cytochrome c).[31] This value also agrees well with the observed rate for the ruthenated N62H mutant.

Acknowledgment. We thank Professor Judith L. Campbell, Dr. Guy Guillemette, Dr. Alfred Gartner, and Professor A. G. Mauk for helpful discussions and Dr. Adrienne Raphael for assistance with the electrochemical (differential pulse polarography) measurements. Large-scale fermentations were done with the aid of Dr. Tom Sutherland at the UCLA Molecular Biology Institute. B.E.B. acknowledges the Medical Research Council (Canada) for a postdoctoral fellowship. This research was supported by National Science Foundation Grant CHE88-14222.

(22) Callahan, R. W.; Brown, G. M.; Meyer, T. J. *Inorg. Chem.* **1975**, *14*, 1443-1453.

(23) N62H cytochrome c (50 mg) was reacted with a 40-fold excess of $[a_5Ru(H_2O)](PF_6)_2$ (80 mg, 0.16 mmol) in 16 mL of deoxygenated HEPES, pH 7.0, for 45 min in an argon atmosphere. The reaction was terminated by separating the protein from the unreacted ruthenium complex on a Sephadex G-25 column. The protein was oxidized with [CoEDTA]$^-$ prior to FPLC purification.

(24) Nocera, D. G.; Winkler, J. R.; Yocom, K. M.; Bordignon, E.; Gray, H. B. *J. Am. Chem. Soc.* **1984**, *106*, 5145-5150.

(25) Flash conditions were as follows: 100 mM sodium phosphate, pH 7.0, 8.3 mM EDTA, 65 μM $[Ru(bpy)_3]^{2+}$, and 2 μM ruthenated N62H cytochrome c. No concentration dependence of k_{obsd} was seen over a 4-fold concentration range.

(26) The range for k_{His62} was obtained by using $d_{His62} = 14.7$-15.6 Å (ref 10); $d_{His33} = 10.8$-11.7 Å (ref 6a).

(27) Meade, T. J.; Gray, H. B.; Winkler, J. R. *J. Am. Chem. Soc.* **1989**, *111*, 4353-4356.

(28) Kuki and Wolynes came to a similar conclusion after making an extensive theoretical analysis of the long-range ET pathway in a ruthenated myoglobin: Kuki, A.; Wolynes, P. G. *Science (Washington, D.C.)* **1987**, *236*, 1647-1652.

(29) (a) Beratan, D. N.; Onuchic, J. N. *Photosynth. Res.*, in press. (b) Beratan, D. N.; Onuchic, J. N.; Hopfield, J. J. *J. Chem. Phys.* **1987**, *86*, 4488-4498. (c) Cowan, J. A.; Upmacis, R. K.; Beratan, D. N.; Onuchic, J. N.; Gray, H. B. *Ann. N.Y. Acad. Sci.* **1989**, *550*, 68-84.

(30) Optimal pathways were determined by using a computer program written by J. N. Betts. The calculated pathway for horse heart cytochrome c (His33-Leu32-Asn31-Pro30-His18-Fe) is abbreviated His33-Pro30.

(31) No range is reported for the rate calculation based on the pathway model, since the best pathway (not a range of pathways) from His62 of the N62H mutant is being compared with the best pathway from His33 (horse heart cytochrome c).

Radical Cation Cope Rearrangement of 1,5-Hexadiyne to 1,2,4,5-Hexatetraene (Bis(allene)) at 77 K

Sheng Dai, Robert S. Pappas,† Guo-Fei Chen, Qing-Xiang Guo, Jih Tzong Wang, and Ffrancon Williams*

Department of Chemistry, University of Tennessee Knoxville, Tennessee 37996-1600

Received August 10, 1989

Although the formation of chair cyclohexane-1,4-diyl radical cation intermediates in the oxidation of 1,5-hexadienes[1,2] can be regarded as the first step in a Cope-like reaction, the subsequent retrocyclization required to complete the rearrangement is quite unlikely to occur in degenerate or nearly degenerate systems in view of the manifestly greater stability of the cyclic intermediate.[1] Indeed, this return step was previously calculated to be endothermic by 34 kcal mol^{-1} for the parent 1,5-hexadiene.[3] The identification of cycloolefinic and aromatic products in these oxidations[1,4] also clearly points to this irreversibility. It therefore seems likely that some,[2] if not all,[5] of the previously reported radical cation induced Cope rearrangements of aryl-substituted 1,5-hexadienes[2,5] actually proceed through back electron transfer[2] to form neutral cyclohexane-1,4-diyl precursors which can easily undergo the necessary cleavage to the rearranged 1,5-hexadienes.[4] At any rate, a Cope-type rearrangement has not hitherto been demonstrated exclusively at the radical cation stage, and here we report the first direct observation of such a reaction.

Acetylenic Cope processes leading to allenes[6] provide examples of extremely nondegenerate systems with an appreciable net driving force that should be augmented in the radical cation because of the higher ionization potentials associated with acetylenes.[7] In studying the radiolytic oxidation of 1,5-hexadiyne (**1**) in Freon matrices, we observed an intense and well-defined ESR pattern (Figure 1a) in several haloethanes (CF_3CCl_3, CF_2ClCCl_3, $CF_2ClCFCl_2$, and $CFCl_2CFCl_2$) which is readily analyzed as a quintet (a(4H) = 28.6 G) of triplets (a(2H) = 3.8 G) with a g factor of 2.0024. This is clearly the spectrum of a symmetrically delocalized species, and since the corresponding spectrum (b) from 1,6-dideuterio-1,5-hexadiyne is a simple quintet[8]

† Undergraduate research participant from Indiana University Southeast, New Albany, IN 47150.

(1) (a) Guo, Q.-X.; Qin, X.-Z.; Wang, J. T.; Williams, F. *J. Am. Chem. Soc.* **1988**, *110*, 1974. (b) Williams, F.; Guo, Q.-X.; Bebout, D. C.; Carpenter, B. K. *J. Am. Chem. Soc.* **1989**, *111*, 4133.

(2) Miyashi, T.; Konno, A.; Takahashi, Y. *J. Am. Chem. Soc.* **1988**, *110*, 3676.

(3) Bauld, N. L.; Bellville, D. J.; Pabon, R.; Chelsky, R.; Green, G. *J. Am. Chem. Soc.* **1983**, *105*, 2378.

(4) Adam, W.; Grabowski, S.; Miranda, A. A.; Rübenacker, M. *J. Chem. Soc., Chem. Commun.* **1988**, 142.

(5) Lorenz, K.; Bauld, N. L. *J. Catal.* **1983**, *95*, 613. In this reference, the photoassisted, zeolite-catalyzed rearrangement of 1,3,4-triphenyl-1,5-hexadiene to 1,3,6-triphenyl-1,5-hexadiene is attributed to a radical cation Cope process. A referee has pointed out that this reaction should have enough thermodynamic driving force to outweigh the barrier imposed by the intrinsic stability of the cyclic 1,4-diyl radical cation structure, this driving force coming from the development of the conjugation energy from two styrene-like systems in the product radical cation compared to only one such system in the reactant radical cation. The above-referenced study also reports, however, that the attempted hole catalysis of this rearrangement using the tris(p-bromophenyl)aminium hexachloroantimonate reagent failed to take place although this reagent is an effective catalyst for radical cation Diels-Alder processes (Reynolds, D. W.; Bauld, N. L. *Tetrahedron* **1986**, *42*, 6189). We conclude that the precise stage of back electron transfer, and therefore the reaction pathway, in the photoassisted, zeolite-catalyzed Cope rearrangement of 1,3,4-triphenyl-1,5-hexadiene is conjectural.

(6) Viola, A.; Collins, J. J.; Filipp, N. *Tetrahedron* **1981**, *37*, 3765.

(7) Kimura, K.; Katsumata, S.; Achiba, Y.; Yamazaki, T.; Iwata, S. *Handbook of HeI Photoelectron Spectra of Fundamental Organic Molecules*; Japan Scientific Societies Press: Tokyo, 1981; pp 57-71.

(8) The minor spectral components present between the lines of the quintet in Figure 1b belong to a quartet (a(3H) = 28.6 G) of triplets (a(1D) = 4.4 G) pattern that can be assigned to the isotopic radical cation in which one of the four strongly coupled hydrogens has been replaced by deuterium. This species is presumably produced either from a small amount of the correspondingly labeled **1** or from **1**-d_2 as the result of H-D exchange during the radical cation rearrangement. In the latter case, the expected broadening from the deuterium hfs may obscure the small hfs to one hydrogen.

0002-7863/89/1511-8759$01.50/0

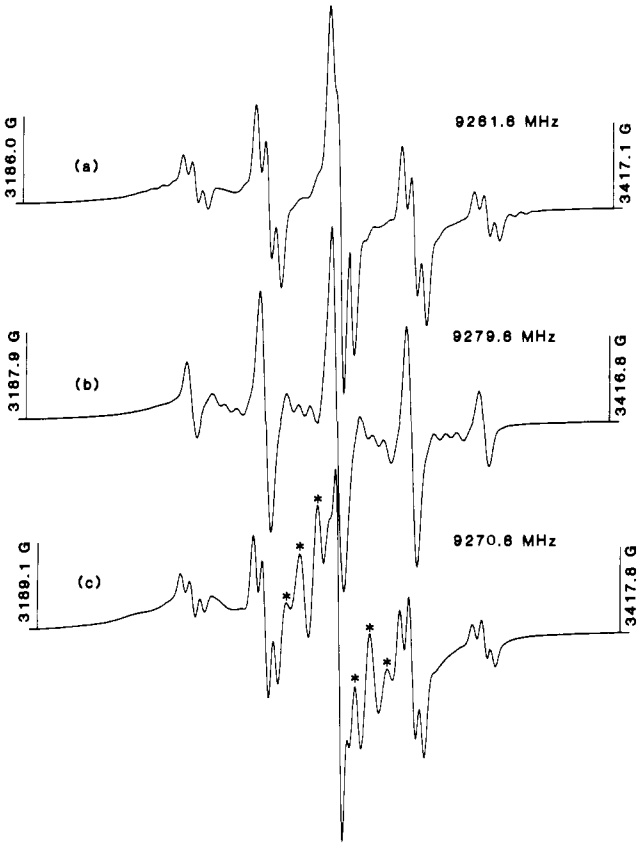
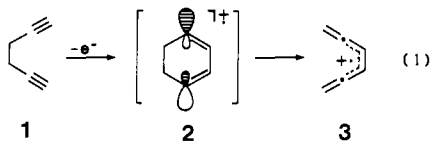


Figure 1. ESR spectra assigned to 1,2,4,5-hexatetraene radical cations obtained from γ-irradiated (dose, ca. 0.25 Mrad) CF_3CCl_3 solutions of (a) 1,5-hexadiyne, (b) 1,6-dideuterio-1,5-hexadiyne, and (c) 1,2,4,5-hexatetraene at 130 K. The concentrations were ca. 1 mol %, and the samples were irradiated at 77 K. Only reversible spectral changes resulting from line narrowing were observed between 77 K and the matrix softening point of ca. 150 K. The spectral components denoted by asterisks in c originate from other radicals.

with the same hyperfine splitting, the two sets of equivalent hydrogens are preserved in forming the radical cation. However, the very large difference between the observed hydrogen couplings is totally inconsistent with the 6–12-G range of values to be expected for the bicyclo[2.2.0]hexa-1,3-diene radical cation, a cyclobutadiene-like species[9] of high energy (Table I) that would result from bonding at the 1,6- and 2,5-positions of a highly strained $\mathbf{1}^{\bullet+}$.



As illustrated in reaction 1, a Cope rearrangement of $\mathbf{1}^{\bullet+}$ through the cyclic six-membered transition structure **2** would produce **3**, the radical cation of 1,2,4,5-hexatetraene (**4**). It was therefore of interest to obtain **3** directly from **4**,[10] and a comparison of the dominant patterns in spectra a and c of Figure 1 leaves no doubt that the same signal carrier is generated in haloethanes[10b] by the oxidation of both **1** and **4**. The ESR parameters are as expected for **3**,[11] and the assignment is further corroborated by

Scheme I

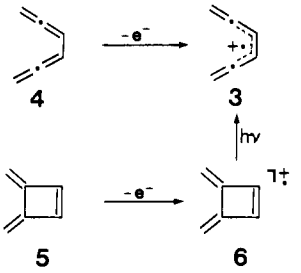


Table I. Heats of Formation of 1,5-Hexadiyne Radical Cation and Its Possible Isomers at 298 K

radical cation isomer	point group used in calcn[a] or exptl determinatn[b]	ΔH_f, kcal mol^{-1}
1,5-hexadiyne ($\mathbf{1}^{\bullet+}$)	C_{2h} (anti, planar)	328.4
	C_{2v} (syn, planar)	327.5
	exptl	329 ± 2[b]
bicyclo[2.2.0]hexa-1,3-diene	C_{2v}	348.6
3,4-dimethylenecyclobutene (**6**)	C_{2v}	294.7
5,6-dihydro-1,4-benzyne (**2**)	C_{2v}	319.6[c]
		312.0[d]
	C_s	311.9
1,2,4,5-hexatetraene (**3**)	C_{2v} (s-cis)	282.2
	exptl	295 ± 5[b,e]

[a] AM1-UHF method (ref 11). [b] From ΔH_f of neutral molecule and gas-phase ionization potential: Rosenstock, H. M.; McCulloh, K. E.; Lossing, F. P. *Adv. Mass Spectrom.* **1978**, *7B*, 1260. [c] Symmetrical charge distribution. [d] Unsymmetrical charge distribution. [e] Based on estimated ΔH_f for neutral molecule.

our finding that this spectrum grows in with high intensity upon the photolysis of the 3,4-dimethylenecyclobutene radical cation (**6**) with visible light (Scheme I), the transformation of **6** to **3** being precisely analogous to the radical cation photoconversion of cyclobutene to butadiene.[12]

In keeping with our opening remarks, a necessary corollary to the occurrence of reaction 1 is that it should be progressively exothermic. This is shown to be the case by AM1 calculations and gas-phase data on the heats of formation of the isomeric C_6H_6 radical cations (Table I). Even allowing that radical cations are involved, the finding of a Cope-type transformation at 77 K is remarkable[13] and reflects the great reactivity of ionized bis(acetylenes). A natural extension would be to study radical cations from ene–diyne systems[14] of considerable current interest.[15]

(9) (a) Courtneidge, J. L.; Davies, A. G. *Acc. Chem. Res.* **1987**, *20*, 90. (b) Shiotani, M. *Magn. Reson. Rev.* **1987**, *12*, 333.

(10) (a) Hopf, H. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 732. Hopf, H.; Bohm, I.; Kleinschroth, J. *Org. Synth.* **1981**, *60*, 41. We thank Professor Hopf for supplementary details regarding the isolation of **4**. (b) Whereas **3** is not produced from **1** in the $CFCl_3$ matrix, it is generated from **4** in both the $CFCl_3$ and haloethane matrices. Apparently, either the solubility of **1** in $CFCl_3$ is too low for efficient oxidation to occur, or the greater rigidity of the $CFCl_3$ matrix prevents the Cope rearrangement of $\mathbf{1}^{\bullet+}$.

(11) AM1-UHF (Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902) calculations on **3** in C_{2v} symmetry gave hydrogen 1s spin densities of 0.0503 (4H) and 0.0013 (2H) corresponding to couplings of 25.5 and 0.7 G based on the atomic value of 506.7 G for hydrogen. Using the AM1 optimized geometry for **3**, INDO (Pople, J. A.; Beveridge, D. L. *Approximate Molecular Orbital Theory*; McGraw-Hill: New York, 1970) calculations also predict the expected $a_2(\pi)$ SOMO (qualitatively similar to that of *s-cis*-butadiene radical cation) with couplings of 44.8 (4H) and −1.6 G (2H), the INDO conversion factor from spin density being 540 G.

(12) (a) Brauer, B.-E.; Thurnauer, M. C. *Chem. Phys. Lett.* **1987**, *133*, 207. (b) Miyashi, T.; Wakamatsu, K.; Akiya, T.; Kikuchi, K.; Mukai, T. *J. Am. Chem. Soc.* **1987**, *109*, 5270. (c) Gerson, F.; Qin, X.-Z.; Bally, T.; Aebischer, J.-N. *Helv. Chim. Acta* **1988**, *71*, 1069. For theoretical considerations, see: Haselbach, E.; Bally, T.; Lanyiova, Z. *Helv. Chim. Acta* **1979**, *62*, 577. Dunkin, I. R.; Andrews, L. *Tetrahedron* **1985**, *41*, 145. Belville, D. J.; Chelsky, R.; Bauld, N. L. *J. Comput. Chem.* **1982**, *3*, 548.

(13) The neutral Cope rearrangement of **1** to **4** is generally considered[6,10a] to be the rate-determining stage in the thermal rearrangement of **1** to **5**. This process, which provided us with **5**, occurs with an activation energy of 34.4 kcal mol^{-1}, the first-order rate constants being 0.8×10^{-4} s^{-1} at 483 K and 1.81×10^{-2} s^{-1} at 570 K: Huntsman, W. D.; Wristers, H. J. *J. Am. Chem. Soc.* **1967**, *89*, 342. With these data, the calculated $t_{1/2}$ at 77 K is ca. 10^{78} years.

(14) Bergman, R. G. *Acc. Chem. Res.* **1973**, *6*, 25. Lockhart, T. P.; Comita, P. B.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 4082. Lockhart, T. P.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 4091.

(15) For biological interest, see: Magnus, P.; Carter, P. A. *J. Am. Chem. Soc.* **1988**, *110*, 1626. Danishefsky, S. J.; Mantlo, N. B.; Yamashita, D. S.; Schulte, G. *J. Am. Chem. Soc.* **1988**, *110*, 6890.

Acknowledgment. We are greatly indebted to Professor Stephen F. Nelsen for his incisive calculations which suggested that the final stage of the oxidation pathway from 1,5-hexadiyne goes to the bis(allene) radical cation. We also thank Professor James L. Adcock, Professor John E. Bartmess, Huimin Luo, and Terry Sumpter for the use of preparative gas chromatographs and experimental assistance. This research was supported by the Division of Chemical Sciences, Office of Basic Energy Sciences, U.S. Department of Energy (Grant DE-FG05-88ER13852). R.S.P. was the recipient of a 1989 Summer Undergraduate Research Fellowship from The Science Alliance under the State of Tennessee's Centers of Excellence Program.

Trisnorsqualene Cyclopropylamine: A Reversible, Tight-Binding Inhibitor of Squalene Epoxidase

Stephanie E. Sen† and Glenn D. Prestwich*

Department of Chemistry
State University of New York
Stony Brook, New York 11794-3400

Received July 17, 1989

The epoxidation of squalene to (3*S*)-2,3-oxidosqualene by squalene epoxidase (SE) and its subsequent cyclization by vertebrate oxidosqualene cyclase (OSC) to lanosterol are the key steps in cholesterol biosynthesis.[1] The best hypocholesteremic drugs available at present (e.g., mevinolin and its congeners) decrease steroid levels by reducing mevalonate production via the inhibition of HMG-CoA reductase.[2] In contrast, our strategy has been the development of inhibitors of SE and OSC.[3] Recently, we[4] and others[5] described the inhibition of SE by compounds derived from modification of the terminal isopropylidene group of squalene. We now report the first example of a cyclopropylamine-containing squalene analogue which acts as a highly selective, slow tight-binding inhibitor[6] of pig liver squalene epoxidase.

Squalene analogues containing the cyclopropylamine moiety were synthesized as follows. Analogue **1** was prepared from trisnorsqualene aldehyde[4] and cyclopropylamine, by the procedure of Borch et al.[7] Reductive amination of **1** with aqueous formaldehyde, followed by hydrogen peroxide oxidation,[8] provided cyclopropylamine analogues **2** and **2b**. Cyclopropylamine **3** was prepared by reductive amination of tetranorsqualene aldehyde.[9]

Cyclopropylamine analogues **1–3** could function in three ways. First, in their protonated forms, the amines could simply interact ionically with either of the two enzymes. Second, the amines could undergo oxidation to the corresponding *N*-oxides, thus acting as prodrugs for a functionality known to be a transition-state mimic of OSC epoxide opening.[10] Third, the amines could be oxidized by a one-electron process and thus act as mechanism-based inactivators[11] to irreversibly inactivate SE or OSC. A variety of cyclopropylamines are potent mechanism-based inactivators of mitochondrial monoamine oxidase, plasma amine oxidase, and cytochrome P-450 enzymes.[12] Although SE is believed to be an external flavoprotein monooxygenase,[13] the mechanism by which the delivery of one oxygen atom to squalene occurs is poorly understood. Squalenoid cyclopropylamines may address these mechanistic questions.

Because oxidation of squalene might be initiated at either the C-2 or C-3 position, both the N-2 (trisnorsqualene) analogue **1** and the N-3 (tetranorsqualene) cyclopropylamine analogue **3** were required. The *N*-methyl analogue **2** and *N*-methyl *N*-oxide **2b** test for procyclase inhibitory activity (secondary amines **1** and **3** would be converted to hydroxylamines).

Compounds **1–3** and **2b** were tested for pig liver SE and OSC inhibition. The results are presented in Table I. Secondary amine **1** is one of the most potent inhibitors of vertebrate SE known, with $IC_{50} = 2\ \mu M$.[14] Interestingly, amine **3**, bearing one less methylene

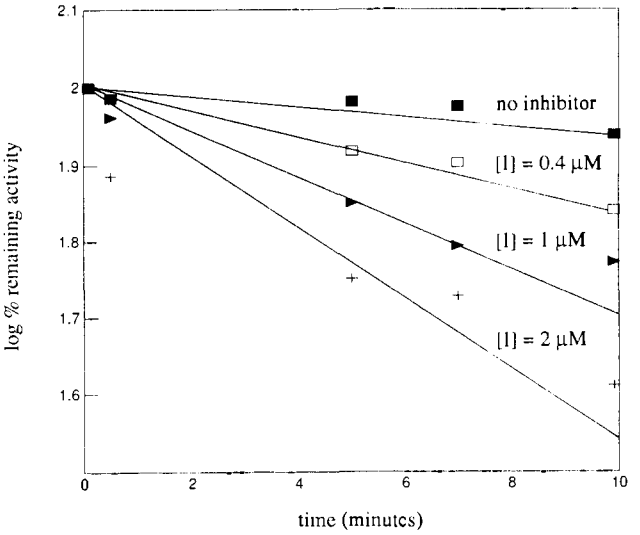
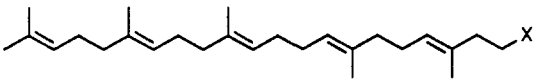


Figure 1. Time dependency of inactivation of trisnorsqualene cyclopropylamine (**1**). Incubations of 0.5, 5, 7, and 10 min were performed with inhibitor concentrations of 0, 0.4, 1, and 2 μM.

Table I. IC_{50} Values of SE and OSC Inhibition for Compounds **1–8**[a]



compd	X	IC_{50} (SE), μM	IC_{50} (OSC), μM
1	CH_2NH-c-C_3H_5	2	ni
2	$CH_2N(CH_3)$-c-C_3H_5	100	ni
2b	$CH_2N(O)(CH_3)$-c-C_3H_5	200	40
3	NH-c-C_3H_5	4	ni
4	CH_2NHEt	200	ni
5	$CH_2NH(i\text{-}Pr)$	ni	ni
6	$CH_2N(CH_3)_2$	20	ni
7	CH_2OH	4	ni
8	CH_2NH_2	200	ni

[a] The abbreviation ni represents no inhibition at [I] = 400 μM. IC_{50} values for OSC were calculated by subtracting SE inhibitory effects from inhibition in mixed OSC + SE assays. 2-Aza-2,3-dihydrosqualene (**6**), trisnorsqualene alcohol (**7**), and trisnorsqualene amine (**8**) were previously reported as SE inhibitors (see ref 4a and 14).

† Present address: Department of Molecular Biology, Scripps Clinic and Research Foundation, La Jolla, CA 92307.

(1) Mulheirn, L. J.; Ramm, P. J. *Chem. Soc. Rev.* **1972**, 259–291.
(2) Endo, A. *J. Med. Chem.* **1985**, *28*, 401–410.
(3) Attempts have previously been made to develop inhibitors of SE and OSC. See: Cattel, L.; Ceruti, M.; Viola, F.; Delprino, L.; Balliano, G.; Duriatti, A.; Bouvier-Navé, P. *Lipids* **1986**, *21*, 31–38 and references therein.
(4) (a) Sen, S. E.; Prestwich, G. D. *J. Am. Chem. Soc.* **1989**, *111*, 1508–1510. (b) Sen, S. E.; Prestwich, G. D. *J. Med. Chem.* **1989**, *32*, 2152–2158.
(5) Ceruti, M.; Viola, F.; Grosa, G.; Balliano, G.; Delprino, L.; Cattel, L. *J. Chem. Res., Synop.* **1988**, 18–19; *J. Chem. Res., Miniprint* **1988**, 239–260.
(6) Schloss, J. V. *Acc. Chem. Res.* **1988**, *21*, 348–353.
(7) Borch, R. F.; Bernstein, M. D.; Durst, H. D. *J. Am. Chem. Soc.* **1971**, *93*, 2897–2904.
(8) Ceruti, M.; Balliano, G.; Viola, F.; Cattel, L.; Gerst, N.; Schuber, F. *Eur. J. Med. Chem.—Chim. Ther.* **1987**, *22*, 199–208.
(9) van Tamelen, E. E.; Pedlar, A. D.; Li, E.; James, D. R. *J. Am. Chem. Soc.* **1977**, *99*, 6778–6780.
(10) Ceruti, M.; Delprino, L.; Cattel, L.; Bouvier-Navé, P.; Duriatti, A.; Schuber, F.; Benveniste, P. *J. Chem. Soc., Chem. Commun.* **1985**, 1054–1055.
(11) Silverman, R. B. *Mechanism-Based Enzyme Inactivation: Chemistry and Enzymology*; CRC Press: Boca Raton, 1988; Vol. 2.
(12) In each case, one-electron oxidation of the nitrogen center can produce a cyclopropylamine radical cation which rapidly rearranges to give a homoallyl iminium radical. See: (a) Hanzlik, R. P.; Tullman, R. H. *J. Am. Chem. Soc.* **1982**, *104*, 2048–2050. (b) Macdonald, T. L.; Zirvi, K.; Burka, L. T.; Peyman, P.; Guengerich, F. P. *J. Am. Chem. Soc.* **1982**, *104*, 2050–2052. (c) Silverman, R. B.; Hoffman, S. J.; Catus W. B., III *J. Am. Chem. Soc.* **1980**, *102*, 7126–7128. (d) Silverman, R. B. *J. Biol. Chem.* **1983**, *208*, 14766–14769.
(13) Ono, T.; Ozasa, S.; Hasegawa, F.; Imai, Y. *Biochim. Biophys. Acta* **1977**, *486*, 401–407.

0002-7863/89/1511-8761$01.50/0