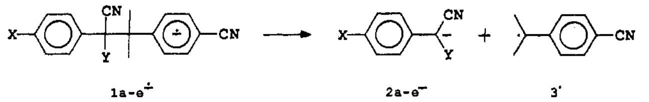

a: X = H Y = Me
b: X = OMe Y = Me
c: X = CF$_3$ Y = Me
d: X = OMe Y = CN
e: X = H Y = CN

spectroscopy. These data also indicated that the radical anions decay at a submicrosecond time scale[16] (see below).

A Stern–Volmer analysis[17] of the quantum yield for disappearance of **1a–e** is shown in Figure 1. At low concentrations of **1**, only TMB$^3$ is quenched, yielding triplet ion pairs (TMB$^{\bullet+}$,**1**$^{\bullet-}$). The fragmentation of **1**$^{\bullet-}$, or ion separation (see below), competes with BET. Since the BET is spin-forbidden, the overall reaction is relatively efficient. At higher concentrations of **1**, more excited state molecules of TMB are quenched, but an increasing fraction of them is in the singlet state. This fraction gives singlet ion pairs, within which BET is more efficient. The overall efficiency of the photoreaction, therefore, does not increase linearly with increasing concentration of **1**.

The reactions are efficiently quenched by *p*-dicyanobenzene (DCB). The quenching is due to two processes. The first one involves direct quenching of excited states of TMB, which can be independently measured and corrected for. The second process, assumed to be diffusion-limited,[18] corresponds to electron transfer from **1**$^{\bullet-}$ to DCB. Thus, the ratio of the corrected to the measured quantum yield ($\Phi_{\mathrm{corr}}/\Phi_{\mathrm{m}} - 1$) as a function of DCB concentration provides a measure of the radical anion cleavage rates[17] (Table I). Approximately 50% of **1a**$^{\bullet-}$ and **1b**$^{\bullet-}$ are intercepted by 0.04 mM and 0.4 mM DCB, respectively. **1c–e**$^{\bullet-}$ cannot be intercepted even by 5 mM DCB, implying a rate of cleavage faster than $10^8$ s$^{-1}$.

The quantum yields for disappearance of **1a,b** are identical (Figure 1), but the measured rates of mesolysis for **1a**$^{\bullet-}$ and **1b**$^{\bullet-}$ differ by a factor of 10. This observation requires that the measured quantum yields for these compounds reflect a competition between BET and ion separation. The rate of ion separation[19] in acetonitrile is ca. $5 \times 10^8$ s$^{-1}$, confirming this analysis and indicating a BET rate within the triplet ion pairs[17] of $3 \times 10^9$ s$^{-1}$. The quantum yield for disappearance of **1c** is higher than that for **1a,b**, which requires that the rate of cleavage of **1c**$^{\bullet-}$ be comparable to the rate of ion separation. Assuming that the rates of BET are the same for all radical anions,[13] the rate of mesolysis of **1c**$^{\bullet-}$ can be estimated to be $4 \times 10^8$ s$^{-1}$, indeed, very close to the rate of ion separation. In a similar fashion, the cleavage rates of **1d,e**$^{\bullet-}$ can be estimated (Table I).

In summary, the design of self-destructive acceptors based on thermodynamic considerations has proven very successful, leading to photoreactions with overall efficiencies approaching unity for acceptors with highly negative free energies of mesolysis. The rates of cleavage confirmed our earlier conclusion[3,11] that the "intrinsic" barriers in mesolytic reactions are quite low, even for near-thermoneutral reactions. The prepared acceptors are convenient molecular clocks for probing ET reactions and ion-pairing phenomena in photoinduced charge-transfer processes.

**Acknowledgment.** This research was supported by grants from the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society. The work at the Notre Dame Radiation Laboratory (Contribution No. NDRL-3331) was sponsored by the Office of Basic Energy Science of the Department of Energy.

**Supplementary Material Available:** The Stern–Volmer kinetic scheme and DCB quenching data (3 pages). Ordering information is given on any current masthead page.

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[16] For a description of the experimental setup, see: Chateauneuf, J. E. *J. Phys. Chem.* **1990**, *94*, 7177. At $3 \times 10^{-4}$ M **1** in CH$_3$CN, the fragments are produced with $10^6$–$10^7$ s$^{-1}$ rates (limited by concentration of **1**). Radical **3**$^{\bullet}$ absorbs ($\lambda_{\max}$) at ca. 295 nm, and the anions absorb at 325 nm (**2a**$^-$), 370 nm (**2c**$^-$), and 300 nm (**2d,e**$^-$). In the latter case the anions and the radical can be distinguished by their different decay rates. The measurements of the absolute rates of C–C bond scission are in progress.

[17] The kinetic scheme used in the Stern–Volmer analysis and DCB quenching data are provided in the supplementary material.

[18] The ET between **1**$^{\bullet-}$ and DCB is exothermic by 17 kcal/mol.

[19] The rate of separation of aromatic radical ions in CH$_3$CN is structure insensitive: (a) Gould, I. R.; Moser, J. E.; Ege, D.; Farid, S. *J. Am. Chem. Soc.* **1988**, *110*, 1991. (b) Gould, I. R.; Ege, D.; Mattes, S. L.; Farid, S. *J. Am. Chem. Soc.* **1987**, *109*, 3794. (c) Gould, I. R.; Ege, D.; Moser, J. E.; Farid, S. *J. Am. Chem. Soc.* **1990**, *112*, 4290.

[20] Compare: Zamkanei, M.; Kaiser, J. H.; Brikhofer, H.; Beckhaus, H.-D.; Rüchardt, C. *Chem. Ber.* **1983**, *116*, 3216.

[21] The required reversible redox potentials for **1a–e** and **2a–e**$^-$ were obtained by using a modified cyclic voltammetry method (Klingler, R. J.; Kochi, J. K. *J. Am. Chem. Soc.* **1982**, *104*, 4186) or by a second-harmonic ac voltammetry technique (Arnett, E. M.; Harvey, N. G.; Amarnath, K.; Cheng, J.-P. *J. Am. Chem. Soc.* **1989**, *111*, 4143. Arnett, E. M.; Amarnath, K.; Harvey, N. G.; Cheng, J.-P. *J. Am. Chem. Soc.* **1990**, *112*, 344).

[22] Sim, B. A.; Milne, P. H.; Griller, D.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1990**, *112*, 6635.

[23] Quantum yields were measured by using ferric oxalate actinometry: Parker, C. A. *Proc. R. Soc.* (*London*) **1953**, *A220*, 104.

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# Lack of a Secondary β-Deuterium Kinetic Isotope Effect in the Solvolysis of 2-Chloro-3-hydrosqualene. A Case of Extended π-Participation and Indication of Concerted Biomimetic Polycyclization

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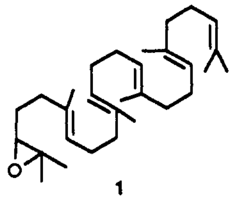
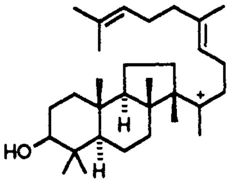
*Received July 25, 1990*

We report herein about an extended participation involving at least two double bonds in a biomimetic solvolytic reaction of a squalene derivative.

In nature, steroid hormones arise from 2,3-epoxysqualene (**1**) in an enzymatic, probably concerted, polycyclization reaction.[1,2] In the biomimetic counterpart of this reaction (Lewis acid epoxy-ring opening with **1**), tricyclic products derived from carbocation **2** are formed.[3] As with other biomimetic cyclizations, the question arises as to the reaction mechanism: is the (poly)cyclization a "stepwise" or a "concerted" process, and if the latter is operative, how many double bonds are involved in the rate-determining step?



**1**



**2**

Unfortunately, the product composition in this case as in other cases of biomimetic cyclizations is not very indicative of the reaction mechanism. A stepwise (poly)cyclization can yield acyclic and (poly)cyclic products. If the reaction is concerted and proceeding through a (nonclassical) carbonium ion, the extensive delocalization of the positive charge allows for nucleophilic attack on several centers yielding the same products as in the stepwise process.

Of the two pioneers in this field, Johnson[4] considers that the concerted mechanism is possible while in the opinion of van Tamelen[1,5] only monocyclization might be a concerted process and

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[1] (a) van Tamelen, E. E. *Acc. Chem. Res.* **1968**, *1*, 111–120; (b) **1975**, *8*, 152–158.

[2] Clayton, R. B. *Q. Rev. Chem. Soc.* **1965**, *19*, 168–200.

[3] van Tamelen, E. E.; Willet, J.; Schwartz, M.; Nadeau, R. *J. Am. Chem. Soc.* **1966**, *88*, 5937–5938.

[4] (a) Johnson, W. S. *Acc. Chem. Res.* **1968**, *1*, 1–8; (b) *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 9–16; (c) *Bioorg. Chem.* **1976**, *5*, 51–98.

[5] van Tamelen, E. E. *J. Am. Chem. Soc.* **1982**, *104*, 6480–6481.

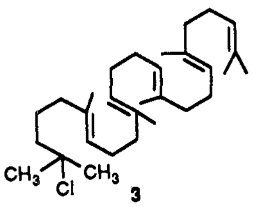
**Table I.** Relative Solvolysis Rates, Secondary $\beta$-Deuterium KIEs, and Relative Activation Parameters of Some Tertiary Chlorides Related to Squalene in 80% (v/v) Aqueous Ethanol[a]

| compd | $k_u/k_s$[b] | $k_H/k_D$[c] | $\Delta\Delta H^{\ddagger}$,[d] kJ mol$^{-1}$ | $\Delta\Delta S^{\ddagger}$,[d] J mol$^{-1}$ K$^{-1}$ |
|---|---|---|---|---|
| **4**[e] | | 1.82 (4) | 93.3 (2.1)[f] | −30.5 (6.3)[f] |
| **6**[g] | 19 | 1.37 (3) | −15.7 | −23.9 |
| **7**[h] | 1.1 | 1.01 (4) | −26.2 | −80.4 |
| **3** | 0.75 | 1.02 (1) | 3.9 | 12.9 |

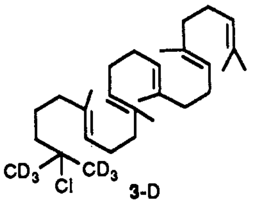
[a] The uncertainty of the last reported figures (standard deviation of the mean) is shown in parentheses. [b] Rate of unsaturated vs the corresponding saturated chloride at 25 °C. [c] At 50 °C. [d] Difference between activation parameters of unsaturated and the corresponding saturated chlorides. [e] The reaction rate at 50 °C is $k = (1.39 \pm 0.04) \times 10^{-4}$ s$^{-1}$. [f] $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$. [g] Reference 12. [h] Reference 14.

further cyclization should be stepwise. In the literature there is evidence for both stepwise[6] and concerted[7] mechanisms of polycyclization. It should be mentioned that MINDO/3 calculations of Dewar[8] and the theory of laticyclic interactions of Goldstein and Hoffmann[9] favor a mechanism in which only the first (mono)cyclization should be concerted.

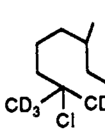
Concerted mechanisms inevitably involve $\pi$-participation of double bond(s) in the rate-determining step. Therefore we set out to investigate kinetically the solvolysis mechanism of 2-chloro-2,3-dihydrosqualene (**3**) (2-chloro-2,6,10,15,19,23-hexamethyl-6,10,14,18,22-tetracosapentaene). Since in acid-catalyzed epoxy-ring opening of **1** formally an initial tertiary cation is generated at C-2, our model substrates were chosen so as to fulfill the same criterion. Thus tertiary chloride **3**, its deuterated analogue **3**-D, and saturated reference compounds **4** and the deuterated analogue **4**-D were prepared.



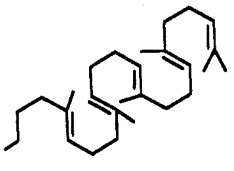
**3**



**3-D**



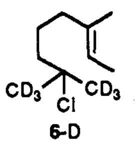
**4-D**



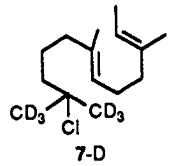
**5a**: X = OH
**b**: X = Br

The parent alcohol of **3** was obtained by reductive epoxy-ring opening of **1**[10] with LiAlH$_4$. Alcohol **5a** was prepared by the previously reported procedure[11] and converted to bromide **5b** with Ph$_3$P/CBr$_4$, which was then treated with powdered lithium in refluxing THF in an ultrasonic bath (30 kHz). In the cooled resulting reaction mixture, acetone-$d_6$ was added dropwise, yielding the parent alcohol of **3**-D. For obtaining saturated reference compounds **4** and **4**-D, alcohol **5a** was exhaustively hydrogenated and by the same procedure as described above converted to the parent alcohols of **4** and **4**-D with acetone and acetone-$d_6$, respectively. Chlorination of all parent alcohols was carried out with SOCl$_2$ in the usual manner.

Solvolysis rates of the prepared substrates were measured titrimetrically in 80% (v/v) aqueous ethanol (80 EtOH) by means of a pH-stat. Ratios of rate constants of unsaturated ($k_u$) and saturated ($k_s$) chlorides, secondary $\beta$-deuterium kinetic isotope effects (KIEs), and the relative activation parameters ($\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$) were calculated and are presented in Table I, as well as those of reference compounds **6** (**6**-D)[12,13] and **7** (**7**-D)[13,14] described previously.



**6-D**



**7-D**

We pointed out that only large rate enhancements ($k_u/k_s \gg 1$) can be taken as a valid proof of neighboring-group participation, but that small or even inverse rate effects can conceal some considerable assistance.[12] Therefore the relative rate obtained (0.75) with **3** vs **4** is rather ambiguous. Secondary $\beta$-deuterium KIEs are a more sensitive and a more reliable probe for $\pi$-participation.[15] With saturated tertiary substrates in 80% EtOH, a positive charge is generated at C-2, hyperconjugative stabilization is important, and large KIEs occur. On the other hand, if $\pi$-participation is operative, secondary $\beta$-deuterium KIEs are reduced in magnitude because of charge delocalization away from the reaction center and hence diminished hyperconjugative electron demand.[15] The secondary $\beta$-deuterium KIE in solvolysis of the squalenyl derivative **3** (**3**-D) is nearly unity. KIEs for saturated reference compounds do not depend on the size of the side chain since $(CD_3)_2C(Cl)CH_2CH_3$,[16] the saturated analogue of chloride **6**-D, and **4**-D give practically the same values ($k_H/k_D$ = 1.79, 1.80, and 1.82, resp.).

Chloride **6**-D solvolyzes with a significantly reduced KIE, which was interpreted as due to participation of the double bond.[12] This KIE is, however, larger by as much as 35% than the effect obtained with the squalenyl derivative **3**-D. Thus, although the chloride **3** solvolyzes without a rate enhancement, the lack of a KIE indicates $\pi$-participation of at least two double bonds, as was also concluded for the doubly unsaturated chloride **7** (**7**-D).[14] It seems that the solvolysis rates of saturated tertiary chlorides with a long side chain differ from those of the $k_c$ process of unsaturated analogues, so that they cannot be used for estimating $k_\Delta$.[17]

It should be mentioned that all unsaturated substrates used in this and previous solvolytic investigations are analogous to reactions where cyclic products were isolated.[1,3,4]

On first sight it seems that activation parameters for solvolysis of **3** are not in accord with the proposed extended $\pi$-participation mechanism, as they are with reference compounds **6**[12] and **7**.[14] In the latter cases the lowering of $\Delta H^{\ddagger}$ (over)compensates a large negative $\Delta S^{\ddagger}$.

On the basis of regioselectivity toward an oxidizing agent, van Tamelen[1a] proposed that squalene and some other polyenes assume a coiled conformation in polar solvents. Since 80% EtOH is a solvent of high polarity, it is likely that the investigated substrate assumes one of the many coiled conformations in which, by

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(6) (a) Stork, G.; Burgstahler, A. *J. Am. Chem. Soc.* **1955**, *77*, 5068–5077. (b) Nishizawa, M.; Takenaka, H.; Hayashi, Y. *J. Am. Chem. Soc.* **1985**, *107*, 522–523.

(7) (a) Bartlett, P. A.; Braumann, J. I.; Johnson, W. S.; Volkamnn, R. A. *J. Am. Chem. Soc.* **1973**, *95*, 7502–7504. (b) Macco, A. A.; Buck, H. M. *J. Org. Chem.* **1981**, *46*, 2655–2660. (c) Kronja, O.; Polla, E.; Borčić, S. *J. Chem. Soc., Chem. Commun.* **1983**, 1044–1045. (d) Nan-hui, H.; le Noble, W. J. *J. Org. Chem.* **1989**, *54*, 2018–2021.

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(9) Goldstein, M. J.; Hoffmann, R. *J. Am. Chem. Soc.* **1971**, *93*, 6193–6203.

(10) van Tamelen, E. E.; Sharpless, K. B. *Tetrahedron Lett.* **1967**, 2655–2659.

(11) Kronja, O.; Borčić, S.; Humski, K.; Foote, C. S. *Croat. Chem. Acta* **1990**, *63*, 81–89.

(12) Orlović, M.; Humski, K.; Borčić, S.; Polla, E. *J. Chem. Soc., Chem. Commun.* **1986**, 263–264.

(13) Orlović, M.; Kronja, O.; Humski, K.; Borčić, S.; Polla, E. *J. Org. Chem.* **1986**, *51*, 3253–3256.

(14) Borčić, S.; Humski, K.; Imper, V.; Kronja, O.; Orlović, M.; Polla, E. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1861.

(15) For summary with references, see: Sunko, D. E.; Borčić, S. Secondary Deuterium Isotope Effects and Neighboring Group Participation. In *Isotope Effects in Chemical Reactions*; Van Nostrand Reinhold Co.: New York, 1970.

(16) Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1953**, *75*, 2925–2929.

(17) $k_c$ and $k_\Delta$ are the rate constants of the unassisted and neighboring-group-assisted processes, respectively.

contrast to **7**, a necessary degree of order for participation is achieved already in the ground state. Extended participation would therefore be favored since there is no requirement for the loss of many degrees of freedom in the transition state.

Having in mind that in biomimetic cyclization of **1** tricyclic products were isolated, and according to our kinetic measurements, it is possible that even concerted tricyclization is operative in reactions of some squalene derivatives in highly polar solvents.

**Acknowledgment.** This research has been partly financed by the American-Yugoslav Board for Scientific and Technological Cooperation (Research Council of Croatia and the NSF). We thank Prof. Vernon J. Shiner, Jr., of Indiana University for useful discussions.

**Registry No. 1**, 7200-26-2; **3**, 131974-28-2; **3** alcohol, 14031-38-0; **3**-*D*, 132017-39-1; **3**-*D* alcohol, 131974-32-8; **4**, 102736-14-1; **4** alcohol, 131974-31-7; **4**-*D*, 131974-34-0; **4**-*D* alcohol, 131974-33-9; **5a**, 118599-19-2; **5b**, 132017-40-4; **6**, 131974-29-3; **6**-*D*, 131974-35-1; **7**, 131974-30-6; **7**-*D*, 131974-36-2; acetone, 67-64-1; acetone-$d_6$, 666-52-4.

**Supplementary Material Available:** IR and $^{13}C$ NMR spectra of the alcohols corresponding to **3**, **3**-D, and **4**, $^1H$ NMR spectra of the alcohols corresponding to **3**, **3**-D, **4**, and **4**-D, and mass spectra of the alcohols corresponding to **3**, **3**-D, and **4**-D (13 pages). Ordering information is given on any current masthead page.

## *N*-Nitrosoaziridinium Ion Isomerization: Dihydrodiazete *N*-Oxides and Azoxyalkenes from Aziridine Nitrosation

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*123 Chemistry, Columbia, Missouri 65211*

*Received August 3, 1990*

*N*-Nitrosoaziridines are unstable compounds which readily lose $N_2O$ to give an alkene.[1] Some years ago we sought to determine whether *N*-nitrosoaziridinium ions produced from the nitrosation of 1-substituted aziridines would undergo a similar chelotropic loss of $[RNNO]^+$.[2] The nitrosation of *cis*-1-butyl-2,3-diphenylaziridine (**1**, R = nBu) in glacial HOAc at 60 °C gives among other products a compound whose structure was assigned as (*Z*)-1-(*N*-butylnitrosamino)-1,2-diphenylethene.[2] While this structure was consistent with an extensive body of spectroscopic data, its failure to give a positive *N*-nitroso test created uncertainty about its structural assignment. A recent X-ray crystallographic diffraction analysis showed this substance to be an $\alpha,\beta$-unsaturated azoxy compound[3] (Figure 1). 1-Azoxyalkenes constitute a growing class of antibiotic agents,[4-7] and this reaction represents a new synthetic route to these compounds and a highly novel course for an amine nitrosation. We show here that the azoxyalkene **3** is produced by the electrocyclic ring opening of a novel dihydrodiazete *N*-oxide produced from the isomerization of a *N*-nitrosoaziridinium ion, and we discuss our experimental and theoretical probing of this process.

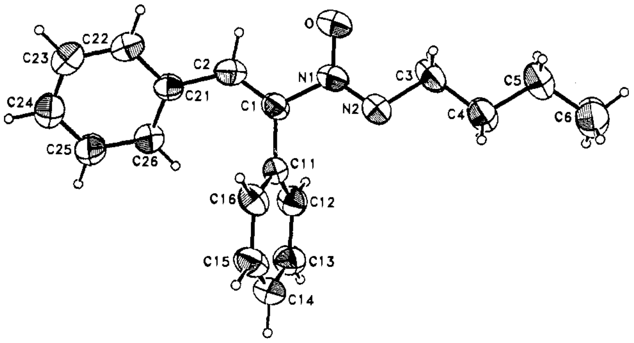


Figure 1. The X-ray crystal structure of the azoxyalkene **3**, R = nBu.

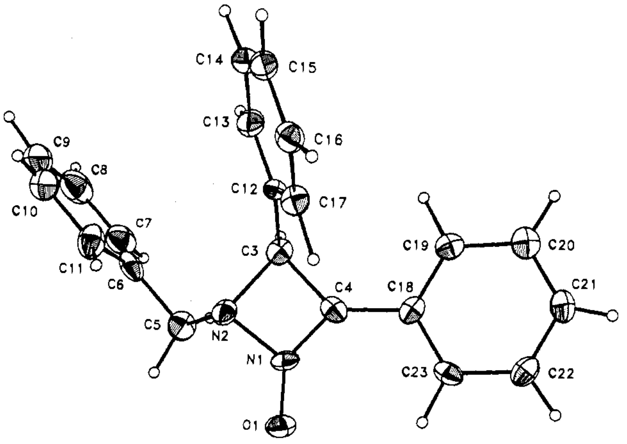
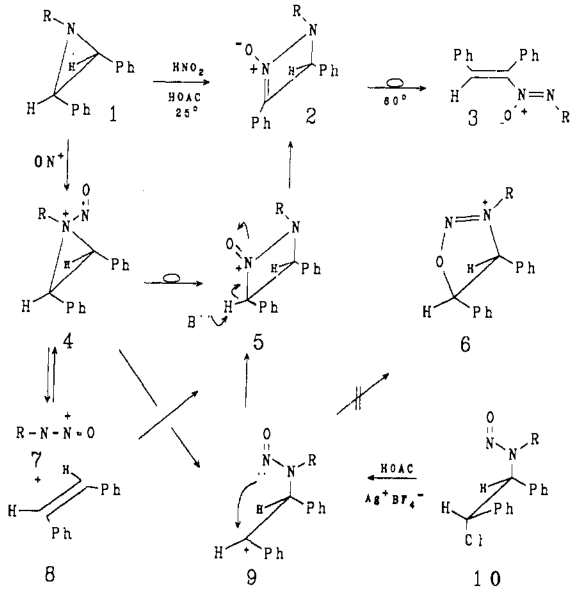


Figure 2. The X-ray crystal structure of the dihydrodiazete *N*-oxide **2**, R = Bn.

**Scheme I**



In order to shed light on the mechanism of azoxyalkene formation, we have undertaken a reinvestigation of the aziridine nitrosation and independently synthesized the nitrosenamine[8] by a modification of the procedure of Seebach and Enders.[9] HPLC analysis of the reaction mixture from the nitrosation (25 °C, HOAc) of *cis*-1-alkyl-2,3-diphenylaziridine (alkyl = butyl or benzyl) reveals, in addition to those products reported previously and the respective azoxyalkene, the generation of a major product whose GCMS characteristics (retention time and mass spectrum) are identical with those of the azoxyalkene, but whose $^1H$ NMR spectrum is significantly different.[8,10] The presence of a singlet at $\delta$ 4.7, the MS, and the origin of the substance suggest the

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[1] Clark, R. D.; Helmkamp, G. K. *J. Org. Chem.* **1964**, *29*, 1316 and references in ref 2.

[2] Loeppky, R. N.; Smith, D. H. *J. Org. Chem.* **1976**, *41*, 1578.

[3] Details of the X-ray crystallographic determination are given in the supplementary material.

[4] Stevens, C. L.; Gillis, B. T.; Haskell, T. H. *J. Am. Chem. Soc.* **1959**, *81*, 1435.

[5] Yamato, M.; Iinuma, H.; Naganawa, H.; Yamagishi, Y.; Hamada, M.; Masuda, T.; Umezawa, H.; Abe, Y.; Hori, M. *J. Antibiot.* **1986**, *39*, 184-191.

[6] Takahashi, Y.; Nakayama, M.; Watanabe, I.; Deushi, T.; Ishiwata, H.; Shiratsuchi, M.; Otani, G. *J. Antibiot.* **1989**, *42*, 1541-1546.

[7] Giencke, W.; Ort, O.; Stark, H. *Liebigs Ann. Chem.* **1989**, 671-676.

[8] See supplementary material for experimental details.

[9] Seebach, D.; Enders, D. *Chem. Ber.* **1976**, *108*, 1293-1320.

[10] The vinyl proton of **3** appears at $\delta$ 7.85 while the ring C-H singlet of **2** occurs at $\delta$ 4.7.

0002-7863/91/1513-2308$02.50/0