# Mechanism of Oxaziridine Fragmentation by Amines

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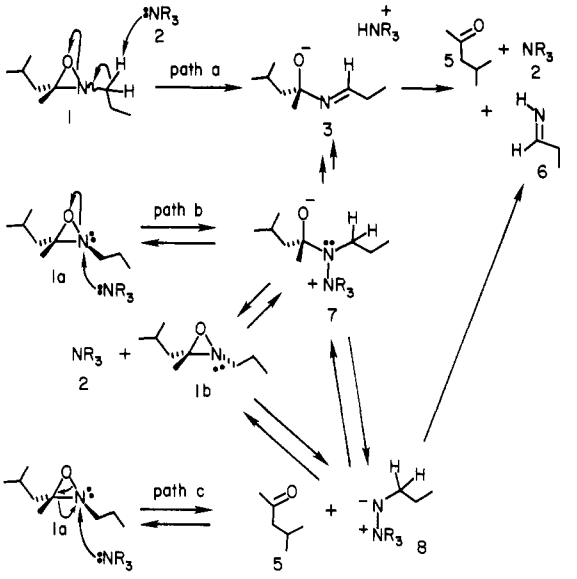
The mechanism of fragmentation of 2-*n*-propyl-3-isobutyl-3-methyloxaziridine (1) by amines is examined. A kinetic isotope effect observed in the fragmentation and the apparent irreversibility of the initial step of the reaction point to a general-base-catalyzed process for destruction of 1. No evidence is found for attack of amines at the ring nitrogen of 1 as has been observed with less hindered oxaziridines.

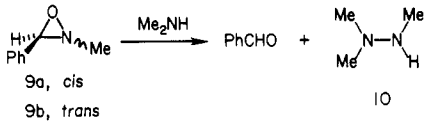
Oxaziridines represent a class of reactive three-membered heterocycles which remain the object of considerable study.[2] Of particular interest is the transfer of oxygen from oxaziridines to a variety of substrates.[3] The early report[4] of oxygen transfer from 2-*n*-propyl-3-isobutyl-3-methyloxaziridine (**1**, Scheme I) to the tertiary amine, brucine, however, has been shown[5] to be incorrect. Rather, brucine induces the fragmentation of **1** into methyl isobutyl ketone (**5**) and aldimine **6**.[6] We have suggested[5] that the fragmentation is initiated by $\alpha$ proton abstraction and rupture of the oxaziridine N–O bond (path a, Scheme I). Herein we report studies which help distinguish between this and alternate fragmentation pathways (Scheme I).

**Three Pathways.** Path a for oxaziridine fragmentation (Scheme I) finds direct precedent[7,8] in the chemical literature. However, alternate paths b and c must be considered in light of the recent work of Hata and Watanabe[9] on the amine-induced reactions of *cis*- and *trans*-2-methyl-3-phenyloxaziridines (**9a,b**, Scheme II). Upon treatment with dimethylamine, oxaziridines **9a,b** are reported[9] to yield benzaldehyde and trimethylhydrazine (**10**). The latter product may arise via initial attack of the amine at oxaziridine nitrogen. Analogous nitrogen-centered mechanisms for the attack of brucine on oxaziridines **1a,b** are depicted in Scheme I (paths b and c).

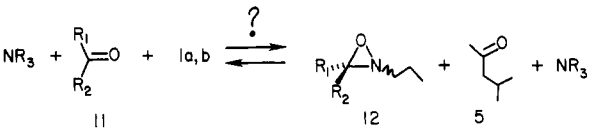
Scheme I




Scheme II




Scheme III




**Strategy.** What is the catalytic role of brucine in the fragmentation of oxaziridines **1a,b**? A broad range of possibilities is offered by Scheme I. At the outset we wished to distinguish between the general-base-catalyzed reaction (path a) and the family of mechanisms characterized by nucleophilic catalysis (e.g., paths b and c). More subtle differences in the timing of bond-forming and bond-breaking steps, as represented by paths b and c, might also be distinguished. Our strategy directed toward these goals is outlined below.

Regardless of pathway, a C–H bond $\alpha$ to oxaziridine nitrogen must be broken in the conversion of **1** into products. The timing of C–H bond breaking relative to the rate-determining step of the fragmentation might be probed to provide evidence on the mechanism. For path a, the C–H bond breaks in the initial base-induced formation of imine **3**. The disappearance of isotopically

(1) Alfred P. Sloan Fellow 1980–1982.

(2) For reviews, see the following: (a) Schmitz, E. *Adv. Heterocycl. Chem.* **1963**, *2*, 83. (b) Emmons, W. D. *Heterocycl. Comp.* **1964**, *19*, 624. (c) Paquette, L. A. "Principles of Modern Heterocyclic Chemistry"; W. A. Benjamin: New York, 1968; p 63. (d) Spence, G. G.; Taylor, E. C.; Buchardt, O. *Chem. Rev.* **1970**, *70*, 231.

(3) (a) Davis, F. A.; Jenkins, R., Jr.; Yocklovich, S. G. *Tetrahedron Lett.* **1978**, 5171. (b) Davis, F. A.; Mancinelli, P. A.; Balasubramanian, K.; Nadir, U. K. *J. Am. Chem. Soc.* **1979**, *101*, 1044. (c) Davis, F. A.; Jenkins, R., Jr.; Rizvi, S. Q. A.; Panunto, T. W. *Chem. Commun.* **1979**, 600. (d) Davis, F. A.; Abdul-Malik, N. F.; Awad, S. B.; Harakal, M. E. *Tetrahedron Lett.* **1981**, 917.

(4) Emmons, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 5739.

(5) Rastetter, W. H.; Frost, J. W. *Tetrahedron Lett.* **1979**, 3353.

(6) Identified as the (2,4-dinitrophenyl)hydrazone derivative. Boyd and co-workers have isolated imines from the base-catalyzed fragmentation of oxaziridines. See: (a) Boyd, D. R.; Hamilton, R. H.; Thompson, N. T.; Stubbs, M. E. *Tetrahedron Lett.* **1979**, 3201. (b) Boyd, D. R.; McCombe, K.; Sharma, N. D.; manuscript in preparation.

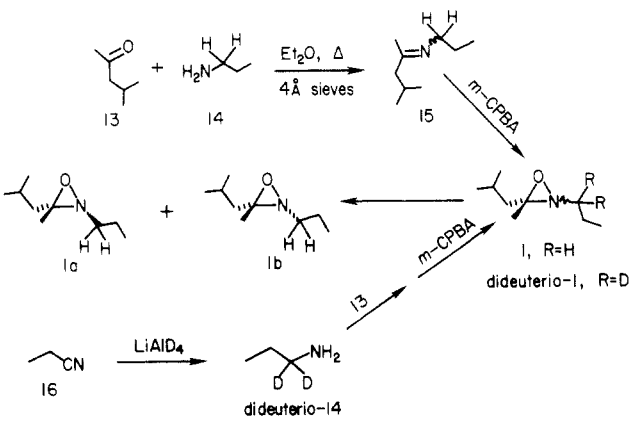
(7) The mechanism of path a was suggested by Emmons (ref 4) for the fragmentation of oxaziridines by aqueous alcoholic hydroxide. This mechanism has often been used to rationalize oxaziridine fragmentation. (a) Dinizo, S. .; Watt, D. S. *J. Am. Chem. Soc.* **1975**, *97*, 6900. (b) Boyd, D. R.; Hamilton, R.; Thompson, N. T.; Stubbs, M. E. *Tetrahedron Lett.* **1979**, 3201. (c) Yijima, C.; Hino, F.; Suda, K. *Ibid.* **1980**, 4725.

(8) Path a is directly precedented by the base-mediated rearrangement of epoxides to allylic alcohols; see references cited in ref 7a and the following: (a) Cope, A. C.; Brown, M.; Lee, H.-H. *J. Am. Chem. Soc.* **1958**, *80*, 2855. (b) Cope, A. C.; Berchtold, G. A.; Peterson, P. E.; Sharman, S. H. *Ibid.* **1960**, *82*, 6370. (c) Cope, A. C.; Heeren, J. K. *Ibid.* **1965**, *87*, 3125. (d) Crandall, J. K.; Chang, L.-H. *J. Org. Chem.* **1967**, *32*, 435, 532. (e) Rickborn, B.; Thummel, R. P. *Ibid.* **1969**, *34*, 3582. (f) Thummel, R. P.; Rickborn, B. *J. Am. Chem. Soc.* **1970**, *92*, 2064. (g) Thummel, R. P.; Rickborn, B. *J. Org. Chem.* **1971**, *36*, 1365. (h) Yasuda, A.; Tanaka, S.; Oshima, K.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 6513. (i) Apparu, M.; Barrelle, M. *Tetrahedron* **1978**, *34*, 1541. (j) Yamamoto, H.; Nozaki, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 169. (k) Corey, E. J.; Marfat, A.; Falck, J. R.; Albright, J. O. *J. Am. Chem. Soc.* **1980**, *102*, 1433.

(9) Hata, Y.; Watanabe, M. *J. Am. Chem. Soc.* **1979**, *101*, 6671.

0022-3263/82/1947-0419$01.25/0 

Scheme IV




substituted dideuterio 1 (see Scheme IV) along path a should be subject to a primary kinetic isotope effect.[10] Along path b or c the breaking of the $\alpha$ C–H bond occurs subsequent to the attack of amine at the oxaziridine nitrogen. A primary kinetic isotope effect would be seen for disappearance of dideuterio 1 along path b or c only if the initial N–N bond forming step (1 ⇄ 7 or 1 ⇄ 5 + 8) were reversible under reaction conditions.

The possible intermediacy of zwitterion 7 or of ylide 8 can be used to probe for the reversibility of the N–N bond-forming steps of paths b and c. Oxaziridines, unlike acyclic amines, do not readily undergo nitrogen inversion.[11] Isomeric oxaziridines **1a** and **1b**, thus, should be distinct isolable entities. Stereochemical information from **1a** or **1b**, however, would be lost upon formation of intermediates 7[12] or 8. Were path b or c reversible, isomerization of 1, **1a** ⇄ **1b**, would be expected during the amine-catalyzed fragmentation reaction. By constrast, isomerization would not be expected along path a, where the initial proton abstraction is likely irreversible. Thus, isomerization of 1 by brucine would effectively rule out path a; the observation of a primary isotope effect without isomerization of 1 would rule out paths b and c.

Nucleophilic paths b and c are closely related, yet ylide 8 is an obligate intermediate only along path c. The ylide formed reversibly along either path b or c might be detected through a trapping experiment. Brucine-induced fragmentation of oxaziridines **1a,b** in the presence of a large excess of a ketone other than methyl isobutyl ketone (5) might serve to trap ylide 8, forming a second oxaziridine (8 + 11 → 12, see Scheme III). Detection of 12 in the reaction mixture of partially fragmented oxaziridines **1a,b** would provide strong support for the intermediacy of 8 in a reversible path b or c.

## Results and Discussion

**Synthesis.** Oxaziridines **1a,b** were made by a modification of Emmons' route[4] as depicted in Scheme IV. Isomers **1a** and **1b** are formed in a ratio of approximately 7:1.[13] Separation of the isomers was achieved by silica gel column chromatography. The deuterated oxaziridines (dideuterio 1) were made from the corresponding labeled amine, dideuterio 14. The latter is available by reduction of propionitrile (16) with $LiAlD_4$.[14]

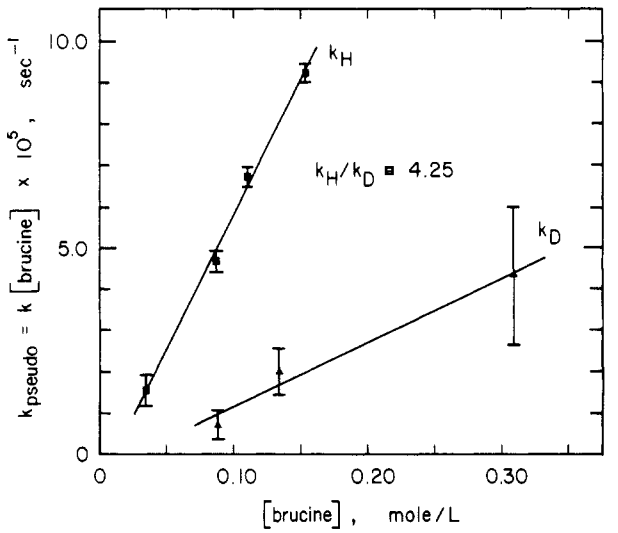



**Figure 1.** Plot of the pseudo-first-order rate constant, $k_{pseudo}$, for the fragmentation of oxaziridines **1a,b** (■) and dideuterio **1a,b** (▲) at constant brucine concentration vs. the concentration of brucine (see Table II). The error bars represent the 95% confidence limits for the values of $k_{pseudo}$. The slopes of the plots are as follows: $k_H = 6.62 \times 10^{-4}$ L mol$^{-1}$ s$^{-1}$, $k_D = 1.56 \times 10^{-4}$ L mol$^{-1}$ s$^{-1}$.

**Reactivity Studies.** The fragmentations of oxaziridines **1a,b** and dideuterio **1a,b** were performed in refluxing acetonitrile at various concentrations of catalyst (see Table II). The disappearance of the oxaziridines follows pseudo-first-order kinetics. The rate constants, $k_{pseudo} = k$[brucine], for the fragmentation of oxaziridines **1a,b** and for the slower reaction of dideuterio **1a,b** are shown in Table II. The second-order rate constants for fragmentation of **1a,b** and dideuterio **1a,b** are obtained by plotting the values of $k_{pseudo}$ vs. the concentration of brucine as shown in Figure 1. The ratio of the slopes of the plots in Figure 1 represents the kinetic isotope effect, $k_H/k_D = 6.62 \times 10^{-4}$ L mol$^{-1}$ s$^{-1}$ ÷ $1.56 \times 10^{-4}$ L mol$^{-1}$ s$^{-1}$ = 4.25, for oxaziridine fragmentation.

Minor oxaziridine isomer **1b** is stable for several hours in refluxing acetonitrile in the absence of brucine. Oxaziridine **1b** was fragmented by the action of brucine in refluxing acetonitrile to the point of 43% conversion into products. $^1$H NMR and chromatographic analysis of the remaining oxaziridine showed no isomerization of **1b**[13] to its presumably more stable isomer **1a** (cf. Scheme I, paths b and c).

Oxaziridines **1a,b** were decomposed by brucine in refluxing acetonitrile in the presence of 5, 10, and 70 equiv of methyl ethyl ketone (cf. Scheme III). Gas–liquid chromatographic (GLC) analysis through the point of 60% conversion of **1a,b** into products showed no formation of 2-*n*-propyl-3-methyl-3-ethyloxaziridine (path c, Scheme I, product of ylide 8 + methyl ethyl ketone).

The lack of isomerization for oxaziridine **1b** under reaction conditions and the failure to trap ylide 8 in the reaction medium strongly point to an irreversible fragmentation of 1 by brucine. The kinetic isotope effect seen for destruction of 1 vs. dideuterio 1, thus, *is most consistent with path a for oxaziridine fragmentation.* The

(10) For examples of primary isotope effects in the rearrangements of epoxides, see Stirling, C. J. M. *Chem. Rev.* **1978**, *78*, 517, especially pp 524, 527, 528.

(11) Numerous oxaziridine optical or geometrical isomers related by nitrogen inversion have been prepared; see the following: (a) Boyd, D. R. *Tetrahedron Lett.* **1968**, 4561. (b) Montauari, F., Moretti, I.; Torre, G. *J. Chem. Soc., Chem. Commun.* **1968**, 1694. (c) *Ibid.* **1969**, 1086. (d) Boyd, D. R.; Grahm, R. *J. Chem. Soc. C* **1969**, 2648. (e) Boyd, D. R.; Spratt, R.; Jerina, D. M. *Ibid.* **1969**, 2650. (f) Montauari, F.; Moretti, I.; Torre, G. *Gazz. Chem. Ital.* **1973**, *103*, 681. (g) Belzecki, C.; Mostowicz, D. *J. Org. Chem.* **1975**, *40*, 3878. (h) Boyd, D. R.; Neill, D. C.; Watson, C. G.; Jennings, W. B. *J. Chem. Soc., Perkins Trans. 2* **1975**, 1813. (i) Bucciarelli, M.; Forni, A.; Moretti, I.; Torre, G. *Ibid.* **1977**, 1339.

(12) Nitrogen inversion should be rapid in acyclic zwitterion 7.

(13) The minor isomer (**1b**) is assumed to have the cis relationship of the *N*-propyl and isobutyl ring substituents.

(14) Friedman, L.; Jurewicz, A. T. *J. Org. Chem.* **1968**, *33*, 1254.

Table I. Competitive Fragmentation Mass Spectral Isotopic Analysis

| % oxaziridine conversion[a] | mass ratio $m/e$ 157:159[b] |
|---|---|
| 0 | 1.18 ± 0.04 |
| 45 ± 5 | 0.70 ± 0.03 |
| 60 ± 5 | 0.50 ± 0.04 |

[a] Determined by $^1$H NMR. [b] For unreacted oxaziridines **1a,b** and dideuterio **1a,b**.

reaction of brucine with oxaziridine **1**, unlike the reaction of Scheme II,[9] appears not to be initiated by attack of the amine at oxaziridine nitrogen.

To examine the possible role of the amine in a change of mechanism for oxaziridine fragmentation, we have reacted a mixture of oxaziridines **1** and dideuterio **1** with an excess of dimethylamine under the conditions reported by Hata and Watanabe[9] (cf. Scheme II). The competitive rates of fragmentation of the oxaziridines were monitored by electron-impact mass spectrometry by measuring the intensity of the parent ion peaks for **1** ($m/e$ 157) and for dideuterio **1** ($m/e$ 159). The results are shown in Table I. A kinetic isotope effect[15] is clearly seen for the reaction of oxaziridines **1** and dideuterio **1** with dimethylamine. Further, product analysis shows the absence of hydrazine **17**, the product expected[9] from attack of dimethylamine at the nitrogen atom of oxaziridine **1** (cf. Scheme II). These data remain consistent with path a for fragmentation of **1** by dimethylamine.

The results presented herein on the fragmentation of oxaziridine **1** (Scheme I) and the results presented by Hata and Watanabe on oxaziridine **9**[9] (Scheme II) suggest a spectrum of reactivity for this class of strained heterocycles. Relatively unhindered oxaziridine **9** apparently undergoes attack by dimethylamine at ring nitrogen, while the more substituted oxaziridine **1** reacts with amines by proton abstraction at the less hindered position $\alpha$ to nitrogen. The difference parallels the $S_N2/E2$ spectrum of reactivity seen for the reaction of alkyl halides with basic nucleophiles.[16] Similar effects of steric hindrance on the ratio of attack of nucleophiles at oxaziridine nitrogen vs. oxygen have also been noted.[17]

## Experimental Section

**General Procedures.** $^1$H NMR spectra were obtained on a Varian T-60 (60 MHz), Perkin-Elmer R-24B (60 MHz), or Bruker WM-250 (250 MHz) NMR spectrometer. Chemical shifts are reported downfield from tetramethylsilane ($Me_4Si$) on the $\delta$ scale. Internal $Me_4Si$ reference was utilized at 60 MHz and residual $CHCl_3$ reference was utilized at 250 MHz. Infrared spectra were recorded on a Perkin-Elmer 283B grating infrared spectrometer. Mass spectra were obtained on a CEC 110B Mattauch-Herzog (Du Pont Instruments) high-resolution mass spectrometer. Gas–liquid chromatographic (GLC) analyses were carried out on a Varian Series 3700 chromatograph using He as carrier gas. An 8 ft × $^1/_8$ in. 4.1% Carbowax column on Chromosorb G and a flame-ionization detector were used. The GLC column temperature was programmed at 5 °C/min from 90 to 150 °C. Peaks were identified by coinjection with authentic samples.

**Synthesis of Oxaziridines 1a,b.** Methyl isobutyl ketone (**5**; 87.0 g, 0.869 mol) and *n*-propylamine (102.3 g, 1.73 mol) in $Et_2O$ (500 mL) were refluxed over activated 4 Å molecular sieves (100 g) for 16 h. Filtration, removal of solvent in vacuo, and distillation (58–60 °C, 20 mmHg) provided imine **15**[4] as a colorless liquid (120.6 g, 98%): $^1$H NMR (60 MHz, $CDCl_3$) 0.80–1.15 (9 H, m), 1.35–2.35 (5 H, m), 1.77 (3 H, s), 3.18 (2 H, t); IR (neat, NaCl) 2960, 2870, 1655, 1460, 1365, 1340, 1285, 1240, 1195, 1165 cm$^{-1}$.

Imine **15** (50.0 g, 0.354 mol) in $CH_2Cl_2$ (100 mL) at 0 °C was oxidized with 85% *m*-chloroperbenzoic acid (73.7 g, 0.363 mol of active oxygen) over a period of 90 min. The mixture was filtered and washed sequentially with $NaHSO_3$ (saturated aqueous, 2 × 50 mL), $NaHCO_3$ (saturated aqueous, 2 × 50 mL), and $H_2O$ (50 mL). Drying ($MgSO_4$), concentration of the organic layer, and distillation of the residue (68–70 °C, 10 mmHg) afforded the mixture of oxaziridine isomers **1a,b** (33.1 g, 59%).

Separation of oxaziridine isomers **1a** and **1b** (1.00 g) was achieved by silica gel (70–230 mesh, 100 g) column chromatography (3% EtOAc/hexane). The separation afforded 672 mg of **1a**[13] ($R_f$ 0.55) and 140 mg of **1b** ($R_f$ 0.50). Data for **1a**: $^1$H NMR (250 MHz, $CDCl_3$) 0.930 (6 H, t), 0.998 (3 H, t), 1.407 (1 H, dd), 1.511 (3 H, s), 1.56–1.74 (3 H, m), 1.74–1.88 (1 H, m), 2.56–2.67 (1 H, m), 2.74–2.85 (1 H, m); IR (neat, NaCl) 2960, 2940, 2880, 1460, 1380, 1365, 1340, 1290, 1245, 1235, 1210, 1170, 1130 cm$^{-1}$; exact mass calcd for $C_9H_{19}NO$ ($M^+$) $m/e$ 157.14666, found 157.14770. Data for **1b**: $^1$H NMR (250 MHz, $CDCl_3$) 0.994 (3 H, t), 0.988 (6 H, d), 1.414 (3 H, s), 1.55–1.79 (4 H, m), 1.89–1.98 (1 H, m), 2.51–2.62 (1 H, m), 2.78–2.89 (1 H, m); IR (neat, NaCl) 2960, 2880, 1460, 1380, 1365, 1340, 1290, 1245, 1235, 1210, 1170, 1130 cm$^{-1}$; exact mass calcd for $C_9H_{19}NO$ ($M^+$) $m/e$ 157.14666, found 157.14756.

**Synthesis of Dideuterio 1a,b.** 1,1-Dideuterio-*n*-propylamine (dideuterio **14**) was prepared by reduction of proprionitrile (120 mmol) in 15% yield as outlined by Friedman and Jurewicz.[14] The dideuterio amine was converted into the corresponding imine (cf. **15**) by reaction with methyl isobutyl ketone (see procedure for **15** above). Oxidation of the imine (cf. **15** → **1a,b** above) with *m*-chloroperbenzoic acid yielded dideuterio **1a,b**. Data for the dideuterio imine: $^1$H NMR (60 MHz, $CDCl_3$) 0.80–1.15 (9 H, m), 1.35–2.35 (5 H, m), 1.77 (3 H, s); IR (neat, NaCl) 2960, 2930, 2870, 2650, 1455, 1365 cm$^{-1}$. Data for dideuterio **1a,b**: $^1$H NMR (250 MHz, $CDCl_3$) as for **1a,b** but lacking absorptions in the region $\delta$ 2.51–2.89; IR (neat, NaCl) 2960, 2940, 2880, 1460, 1380, 1365, 1335, 1290, 1245, 1215, 1170, 1135 cm$^{-1}$; exact mass calcd for $C_9H_{17}D_2NO$ ($M^+$) $m/e$ 159.15922, found 159.16073.

Table II. Fragmentation Kinetic Runs

| oxaziridine (M)[a] | brucine·2$H_2O$, M | $10^5 k_{pseudo}$, $s^{-1}$[b] |
|---|---|---|
| **1a,b** (0.090) | 0.035 | 1.55 ± 0.63[c] |
| **1a,b** (0.129) | 0.087 | 4.67 ± 0.27[c] |
| **1a,b** (0.083) | 0.110 | 6.73 ± 0.25[c] |
| **1a,b** (0.086) | 0.153 | 9.25 ± 0.50[c] |
| dideuterio **1a,b** (0.039) | 0.088 | 0.70 ± 0.32[c] |
| dideuterio **1a,b** (0.039) | 0.134 | 2.00 ± 0.58[c] |
| dideuterio **1a,b** (0.039) | 0.309 | 4.33 ± 1.68[c] |

[a] 2.6 mL of $CH_3CN$ solvent used in each run. [b] Determined by linear regression analysis (linear least-squares fit). [c] 95% confidence limit.

**Reaction of Oxaziridines 1a,b with Brucine.** The mixtures of oxaziridines **1a,b** and the labeled analogues, dideuterio **1a,b**, were fragmented by the action of brucine dihydrate in refluxing acetonitrile. Table II summarizes the conditions of four kinetic runs with **1a,b** and three runs with dideuterio **1a,b**. Aliquots were removed from the reactions by syringe and analyzed by GLC vs. dodecane internal standard. The mole fraction of remainining oxaziridine **1a,b** and dideuterio **1a,b** at various reaction times between $t_0$ and 240 min were plotted to determine the pseudo-first-order rate constants shown in Table II.

**Fragmentation of Minor Oxaziridine Isomer 1b.** Oxaziridine **1b** (20.0 mg, 0.127 mmol), brucine dihydrate (98.6 mg, 0.229 mmol), and dodecane (10.0 $\mu$L) were refluxed in acetonitrile (1.46 mL). After 1 h, GLC analysis showed 43% consumption of oxaziridine **1b**. The reaction mixture was concentrated in vacuo and filtered through silica gel (3.0 g) with 3% EtOAc in hexanes to separate the oxaziridine(s) from dodecane and brucine. Column fractions were collected and analyzed by TLC (silica gel, 3% EtOAc in hexanes, phosphomolybdic acid char visualization). No

(15) The data from Table II lie on the line $k_H/k_D = 2.5$ in the plot of percent oxaziridine conversion vs. mass ratio $m/e$ 157:159. Thus, given the small number of determinations, the kinetic isotope effect for fragmentation of **1a,b** (dideuterio **1a,b**) by dimethylamine likely falls in the range $k_H/k_D = 2.0$–3.0.

(16) For a discussion, see March, J. "Advanced Organic Chemistry Reactions, Mechanisms, and Structure"; McGraw-Hill: New York, 1977; p 914.

(17) Hata, Y.; Watanabe, M. *J. Org. Chem.* **1981**, *46*, 610.

fraction nor the crude reaction mixture showed the presence of isomer **1a**. Early blank fractions through all fractions showing the slower eluting isomer **1b** were combined and analyzed by 250-MHz $^1$H NMR. The NMR spectrum of recovered oxaziridine was indistinguishable from that of pure starting isomer **1b** (vide supra). The ratio of isomers **1a/1b** is easily determined by high-field $^1$H NMR by measurement of the methyl absorptions at $\delta$ 1.511 and 1.414, respectively. The chromatographed oxaziridine from the isomerization experiment showed no isomerization, **1b** $\rightleftarrows$ **1a**, within the limits of FT NMR detection (<1% isomer **1a** present).

In a control run performed as above but omitting brucine, isomer **1b** was shown to be stable (TLC, $^1$H NMR) in refluxing acetonitrile over the period (1 h) of the isomerization experiment.

**Methyl Ethyl Ketone Trapping Experiment.** Oxaziridines **1a,b** were fragmented by the action of brucine dihydrate in refluxing acetonitrile in the presence of 5.0, 10.0, and 70.4 equiv of methyl ethyl ketone. The experiment performed with 10.0 equiv of trapping ketone is representative. Oxaziridines **1a,b** (15.8 mg, 0.10 mmol), brucine dihydrate (50.0 mg, 0.116 mmol), methyl ethyl ketone (72.1 mg, 1.00 mmol), and dodecane (8.0 $\mu$L) were refluxed in acetonitrile (1.3 mL). The reaction was monitored for 2 h through the point of 60% conversion of **1a,b** into products (GLC vs. dodecane internal standard). No 2-*n*-propyl-3-methyl-3-ethyloxaziridine (**12**, $R_1$ = Me, $R_2$ = Et; Scheme III) was detected.[18]

**Reaction of Oxaziridines 1a,b with Dimethylamine.** A stock solution of oxaziridines **1a,b** (51.4 mg, 0.33 mmol) and dideuterio oxaziridines **1a,b** (52.5 mg, 0.33 mmol) was prepared in $CDCl_3$ (1.2 mL). The molecular ion cluster in the low-resolution mass spectrum of the mixture was measured and averaged over 10 consecutive scans. The ratio of the *m/e* 157 to *m/e* 159 mass peaks ($M^+$, oxaziridine-$d_0$/$M^+$, oxaziridine-$d_2$) for the stock solution was 1.18 ± 0.04 (see Table I).

Two 5-mm NMR tubes were charged with the stock solution (0.5 mL) of oxaziridines and cooled to 0 °C. Dimethylamine (0.3–0.5 mL) was added to each tube, and the tubes were sealed and warmed to ambient temperature. The fragmentation in each tube was monitored by $^1$H NMR. The first tube was opened after 8 h (45% conversion) and the second after 24 h (60% conversion). The ratio of remaining **1a,b** to dideuterio **1a,b** was determined by mass spectrometry (vide supra). The results are presented in Table I (see text).

Oxaziridines **1a,b** (250 mg, 1.59 mmol) in $CDCl_3$ (0.5 mL) were cooled to 0 °C. To this solution was added dimethylamine (approximately 0.6 mL) and the tube was sealed. The mixture was warmed to ambient temperature and monitored by $^1$H NMR. At approximately 50% reaction the tube was opened and the reaction mixture was analyzed by GLC. No 1,1-dimethyl-2-*n*-propylhydrazine[19] nor its air-oxidation product, *N,N*-dimethyl-*n*-propylhydrazone,[20] was detected.

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**Registry No.** **1a**, 80160-86-7; dideuterio-**1a**, 80160-87-8; **1b**, 80160-88-9; dideuterio-**1b**, 80160-89-0; **5**, 108-10-1; **14**, 107-10-8; **15**, 26524-34-5.

(18) An authentic sample of **12** for coinjection was prepared from *n*-butylamine and methyl ethyl ketone by the procedure used for **1a,b**.

(19) Made by $LiAlH_4$ reduction of *N,N*-dimethyl-*n*-propylhydrazone.

(20) Made by condensation of *N,N*-dimethylhydrazine and propionaldehyde. 1,1-Dimethyl-2-*n*-propylhydrazine was seen to revert slowly to the hydrazone upon standing (also see ref 9).

# Regioselectivities in the Di-$\pi$-methane Photorearrangement of 2-Methylbenzonorbornadienes Carrying Methoxy- and Cyanoaryl Substituents. The Vinyl Methyl Effect

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The triplet-state photoisomerizations of 2-methylbenzonorbornadiene and all eight possible aryl cyano- and methoxy-substituted derivatives have been investigated. The parent hydrocarbon underwent di-$\pi$-methane rearrangement with preferential (81%) benzo–vinyl bridging to C-3 ($\beta$ bridging). The 5-$CH_3O$, 6-$CH_3O$, 5-CN, and 7-CN examples represent cases where the substituent effects should work cooperatively, and a single photoproduct was formed in each instance. In the remaining four examples, the substituents are positioned to direct in an antagonist fashion. Interestingly, the product ratios for the 7-$CH_3O$ and 7-CN systems are within experimental error of those determined on the basis of perfect substituent additivity effects. As concerns the 8-$CH_3O$ and 8-CN derivatives, the apparent directing effect of methyl for $\beta/\alpha$ bridging is seen to be slightly higher (96:4) than usual. Probable causes for this phenomenon are presented. Because of its role as a moderate controller of excited-state regioselectivity, the methyl substituent has proven to be a useful probe of such reactions. Synthetic approaches to the alkyl-substituted benzonorbornadienes are also detailed.

Perhaps as a result of its preeminent position as the most widely encountered photoisomerization process,[1] the di-$\pi$-methane rearrangement is rapidly developing into a useful tool for the elucidation of excited-state substituent effects. The dramatic regioselectivities which have been observed to this time point up the need for further investigation, not only to determine their generality but also to gain information concerning their relative efficiencies. The latter phenomenon can be most easily studied by internal competition, where at least two substituents are made to vie for control of different bonding pathways. This technique has been applied in the present experimental undertaking.

(1) Hixson, S. S.; Mariano, P. S.; Zimmerman, H. E. *Chem. Rev.* **1973**, *73*, 531.

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