reaction mixture was heated at 90 °C until the ketene had been consumed, as evidenced by the disappearance of the ketene band at 2080 cm^{-1} in the infrared spectrum, about 2 h. There was obtained 2.3 g (65%) of the cyclobutanone at 58–62 °C at 0.25 mm by using a short-path distillation apparatus: IR 1770 cm^{-1} (C=O); NMR (CCl_4 with $CHCl_3$ as a reference) δ 0.1 (s, 9 H), 2.85 (s, 1 H), 3.3 (s, 12 H); mass spectrum, *m/e* (relative intensity) parent peak 262 (no M found), 247 (17, M–15), 189 (68), 127 (71), 95 (100), 93 (84.3).

Anal. Calcd for $C_{11}H_{22}O_5Si$: C, 50.38; H, 8.4. Found: C, 49.98; H, 8.66.

(b) 3,4,4-Trimethoxy-2-cyclobutenone (5a). A 2.3-g (8.7 mmol) portion of the cyclobutanone **3a** was heated about 24 h at 95 °C to give 1.39 g (80%) of the cyclobutenone **5a** at 58–62 °C (0.25 mm): IR and NMR data were consistent with the literature;[6b] mass spectrum, *m/e* (relative intensity) 158 (3.3, M, parent peak), 143 (100, M - 15), 127 (20, M - 31), 115 (63), 99 (43).

Cycloaddition of (Trimethylsilyl)ketene with Tetraethoxyethylene. (a) 3,3,4,4-Tetraethoxy-2-(trimethylsilyl)-cyclobutanone [3b]. This cycloaddition was accomplished by employing the same procedure as described above. From 3.0 g (26 mmol) of the ketene and 5.3 g (26 mmol) of **2b** there was obtained 5.6 g (68%) of **3b** at 75–80 °C (0.15 mm): IR 1770 cm^{-1} (C=O); NMR (CCl_4 with $CHCl_3$ as reference) δ 0.05 (s, 9 H), 1.05 (t, 12 H), 2.80 (s, 1 H), 3.50 (q, 8 H); mass spectrum *m/e* (relative intensity) parent peak 318 (no M found), 303 (3.4, M - 15), 289 (100, M - 29), 273 (15.3), 245 (6.8), 217 (15.3), 215 (42.4), 187 (39.0), 171 (69.5).

Anal. Calcd for $C_{15}H_{30}O_5Si$: C, 56.60; H, 9.43. Found: C, 56.83; H, 9.38.

(b) 3,4,4-Triethoxy-2-cyclobutenone (5b). Heating 5.6 g (17.6 mmol) of **3b** as described above resulted in the formation of 3.0 g (86%) of **5b** at 90–95 °C (0.1 mm) [lit.[6b] 75 °C (0.02 mm)]; the IR and NMR data were consistent with that reported in the literature; mass spectrum, parent peak at *m/e* 200.

3,4,4-Tri-*n*-propoxy-2-cyclobutenone, 5c. A 2.0-g (17.54 mmol) portion of the ketene was added dropwise to 4.56 g (17.54 mmol) of tetra-*n*-propoxyethylene. When the addition was complete, the reaction mixture was heated at 90–95 °C overnight. There was obtained 2.1 g (50%) of **5c** at 90–95 °C (0.1 mm): IR 1770, 1585, 1470, 1340, 1200, 1080 cm^{-1}; NMR δ 1.19 (m, 9 H), 1.3 (m, 6 H), 3.35 (t, 4 H), 3.9 (t, 2 H), 5.15 (s, 1 H); mass spectrum, *m/e* (relative intensity) 242 (1.7 M parent peak), 199 (5.9), 157 (27.1), 115 (100), 103 (9.3), 99 (24.5), 87 (7.6), 69 (93.2).

Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.5; H, 9.1. Found: C, 64.76; H, 9.03.

Conversion of a Mixture of 3b and 5b to 5a. A 1.0-g mixture of **3b** and **5b** in 20 mL of absolute methanol containing a few drops of concentrated HCl was stirred overnight under a nitrogen atmosphere. Upon evaporation of the solvent, the distilled product was only **5a** as evidenced by comparison of spectral data.

(c) 3-Hydroxy-3-cyclobutene-1,2-dione, 6. Semisquaric Acid. To a solution containing 1 g (6.3 mmol) of **5a** in 20 mL of THF was added 15 mL of 18% HCl. This solution was stirred for 1 h at 45 °C. All of the liquids were removed under reduced pressure, and the residual solid was purified by sublimation to give 0.62 g (100%) of product: mp 145–150 °C dec (lit.[6] mp 145–150 °C dec); IR and NMR data were identical with those in the literature.[10]

The NMR spectrum of **6** in acetone-d_6 revealed two singlets at 2.1 and 8.7 ppm in a ratio of 1.

Semisquaric acid was also obtained from **5b** as described above for **5a**.

Typical Procedure for the Reaction of (Trimethylsilyl)-ketene with Tetraalkoxyethylene at Room Temperature. A 1.0-g (8.7 mmol) portion of (trimethylsilyl)ketene was added dropwise to a solution of 1.29 g (8.7 mmol) of **2a** under a nitrogen atmosphere and stirred at room temperature for 3–5 days, depending on the tetraalkoxyethylene.

Acknowledgment. The authors express appreciation to the Robert A. Welch Foundation and to the North Texas State University Faculty Research Committee for support of this investigation.

Registry No. 1, 4071-85-6; **2a**, 1069-12-1; **2b**, 40923-93-1; **2c**, 40923-94-2; **3a**, 72332-21-9; **3b**, 72332-22-0; **5a**, 68057-55-6; **5b**, 68057-58-9; **5c**, 72332-23-1; **6**, 31876-38-7.

(10) Scharf, H. D.; Frauenrath, H.; Pinske, W. *Chem. Ber.* **1978**, *111*, 168.

Thermally Induced Cyclobutyl–Cyclopropylcarbinyl-Type Rearrangement of 2-Oxabicyclo[4.2.0]octan-3-ones

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It has been well-known that cyclobutyl derivatives rearrange to cyclopropylcarbinyl ones through disrotatory opening of the cyclobutane ring.[1] More recently, the acid-catalyzed rearrangement of highly constrained polycyclic lactones such as cagelike compounds has been reported.[2] However, this type of thermally induced rearrangement is little known as yet.[3] In a continuation of studies on the transformation of readily available [*n*.3.2]propellanes into other important polycarbocyclic ring systems,[4] we previously reported the acid-catalyzed cyclobutyl–cyclopropylcarbinyl-type rearrangement of 2-oxabicyclo[4.2.0]octan-3-ones **2**, **8**, and **9** (δ-lactones) to the corresponding γ-lactones **11**, **14**, and **15** (Chart I) as a preliminary report.[4c] We describe here a novel thermally induced rearrangement of the δ-lactones **1–4**, **8**, and **9** to the γ-lactones **10–15** which may be considered to proceed in a concerted manner.[5] Interestingly, the obtainable γ-lactones in the present reactions will serve as useful intermediates for the synthesis of polycyclic substrates involving the spiro-α-methylene-γ-butyrolactone skeleton which have been shown to display antitumor activity.[6,7]

The δ-lactones **1–9** were prepared by the Baeyer–Villiger oxidation (H_2O_2/AcOH or MCPBA/$CHCl_3$) of the corresponding ketones in good yields. The thermal reaction was carried out by heating an *o*-dichlorobenzene solution of δ-lactones in a sealed tube at 240 °C for 72 h or passing a hexane solution of **1–9** through a Pyrex column heated at 350 °C (contact time ca. 20 s). The results are summarized in Table I along with those under the acidic conditions.

(1) Olah, G. A.; Schleyer, P. v. R. "Carbonium Ions"; Wiley-Interscience: New York, 1972; Vol. III, Chapter 26.

(2) (a) Büchi, G.; Goldman, I. M. *J. Am. Chem. Soc.* **1957**, *79*, 4741. (b) Hirao, K.; Miura, H.; Hoshino, H.; Yonemitsu, O. *Tetrahedron Lett.* **1976**, 3895. (c) Mehta, G.; Singh, V.; Duddeck, H. *Ibid.* **1978**, 1223.

(3) Only one example is known: Yamashita, Y.; Sato, K.; Mukai, T. "Abstracts of Papers", 37th Annual Meeting of the Chemical Society of Japan, Yokohama, Apr 1–4, 1978; Vol. 2, p 633.

(4) (a) Tobe, Y.; Kimura, K.; Odaira, Y. *J. Org. Chem.* **1979**, *44*, 639. (b) Tobe, Y.; Doi, A.; Kimura, K.; Odaira, Y. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 639. (c) Tobe, Y.; Kakiuchi, K.; Kawakami, Y.; Sakai, Y.; Kimura, K.; Odaira, Y. *Chem. Lett.* **1978**, 1027. (d) Sakai, Y.; Toyotani, S.; Tobe, Y.; Odaira, Y. *Tetrahedron Lett.*, **1979**, 3855.

(5) A concerted mechanism for this type of rearrangement has likewise been proposed for some highly strained compounds. References 2a and 3. McDonald, R. N.; Davis, G. E. *J. Org. Chem.* **1969**, *34*, 1916.

(6) (a) Rodriquez, E.; Towers, G. H. N.; Mitchell, J. C. *Phytochemistry* **1976**, *15*, 1573. (b) Grieco, P. A.; Noguez, J. A.; Masaki, Y.; Hiroi, K.; Nishizawa, M.; Rosowsky, A.; Oppenheim, S.; Lazarus, H. *J. Med. Chem.* **1977**, *20*, 71.

(7) For an example, we have prepared an α-methylene γ-lactone from **11** by the usual method,[6b] and its biological activity is now under investigation.

0022-3263/80/1945-0729$01.00/0

Chart I

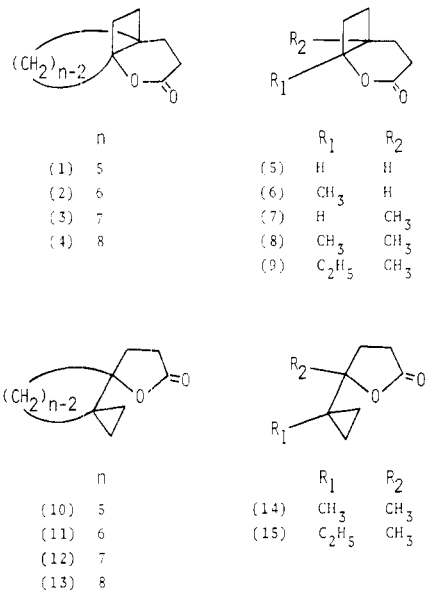


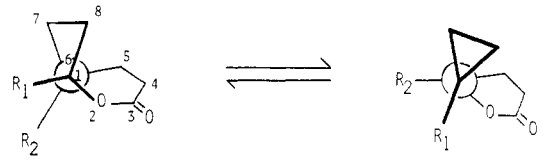
Table I. Thermally Induced Cyclobutyl-Cyclopropylcarbinyl-Type Rearrangement of δ-Lactones 1-9

	δ-lactone:γ-lactone ratio[a]		
	solution[b]	vapor phase[c]	acid[d]
1	89:11	88:12	100:0
2	15:85	21:79	14:86
3	88:12	81:19	100:0
4	94:6	94:6	100:0
5	100:0	100:0	100:0
6	100:0	100:0	100:0
7	100:0	100:0	100:0
8	74:26	51:49	80:20
9	84:16[e]	82:18[e]	86:14

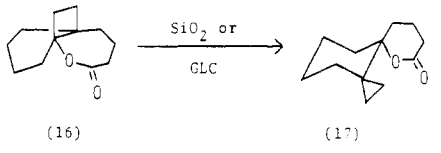
[a] Yields were almost quantitative unless otherwise noted. [b] Heated at 240 °C for 72 h in *o*-dichlorobenzene solution. [c] Heated at 350 °C for ca. 20 s under nitrogen. [d] Heated at reflux in acetic acid for 72 h. See ref 4c. [e] Small amounts of unidentified products were obtained.

In the case of the bicyclic system, unsubstituted and monomethyl-substituted δ-lactones **5–7** were recovered unchanged, whereas the dimethyl- and ethylmethyl-substituted ones **8** and **9** gave 16–49% of the corresponding γ-lactones, **14** and **15**. With the tricyclic system, the δ-lactone **2** rearranged readily to afford 79–85% of **11**. These results exhibited a trend similar to that observed in the acid-catalyzed reaction, as shown in Table I. However, it is noteworthy that the thermal rearrangement of **1**, **3**, and **4** took place to afford the desirable γ-lactones **10**, **12**, and **14**, respectively, though the rearrangement did not occur at all under the acidic conditions. Moreover, in order to examine the possibility of reverse rearrangement of γ-lactones to δ-lactones, we heated an *o*-dichlorobenzene solution of some γ-lactones, such as **11** and **14**, at 240 °C. Significantly, the reverse rearrangement proceeded gradually with the lapse of time, and finally the quantities of both lactones achieved a state of equilibrium. Namely, the ratio of **2** to **11** and that of **8** to **14** were in the ratios of 15:85 and 56:44 after about 12 and 250 h, respectively.[8,9] The above fact infers that the present cyclobutyl–cyclopropylcarbinyl-type rearrangement may proceed by a concerted mechanism rather than by a stepwise cationic one.

The distinction of reactivity for the rearrangement in a series of the δ-lactones may be attributed to the steric effect of the substituents on the conformation of cyclobutane ring of δ-lactones. Namely, inspection of molecular models of δ-lactones indicates clearly that the cyclobutane ring of dialkyl-substituted δ-lactones has a more puckered geometry compared with that of unsubstituted and monoalkyl-substituted ones, owing to 1,2-dialkyl interaction of the substituents. Such a geometry of the cyclobutane ring may permit an antiperiplanar arrangement of the two migrating bonds (C-1, O-2 and C-6, C-7 bonds) which is desirable for concerted rearrangement to γ-lactones. This is the case especially in **2** because of the steric requirement of the cyclohexane ring fused to the bridgehead positions to adopt the chair conformation.



As an extention of the present, the possibility of the rearrangement of ε-lactone to δ-lactone has been checked for the tricyclic ε-lactone **16**. Interestingly, the rearrangement of **16** proceeded more readily to lead to the formation of the corresponding δ-lactone **17** even under silica gel column chromatography or under GLC conditions (10% FFAP on Uniport B, 180 °C).



Experimental Section

Melting points are uncorrected. Infrared spectra were recorded by using a JASCO IR-G spectrometer and liquid films unless otherwise stated. ^{1}H NMR spectra were obtained on a JEOL JNM-PS-100 spectrometer, using Me_4Si as an internal standard and CCl_4 as a solvent. Mass spectra were measured with a Hitachi RMU-6E spectrometer. Analytical GLC was carried out on a Hitachi 163 gas chromatograph, and preparative GLC separation was conducted on a Varian Aerograph 90-P or a Varian Aerograph 920 gas chromatograph.

Tricyclic ketones and 1,5-dimethylbicyclo[3.2.0]heptan-2-one were prepared as previously described.[4b] Bicyclo[3.2.0]heptan-2-one[10] and the 1-methyl-,[11] 5-methyl-,[11] and 1-ethyl-5-methyl-substituted derivatives were prepared in 30–71% yields by photocycloaddition of the corresponding cyclopentenones to ethylene in a similar manner to that above. 1-Ethyl-5-methylbicyclo[3.2.0]heptan-2-one: IR 1710 cm^{-1}; NMR δ 0.75 (t, 3 H), 1.22 (s, 3 H), 1.40–2.80 (m, 10 H); MS *m/e* 152 (M^+); semicarbazone, mp 198–199.5 °C. Anal. Calcd for $C_{11}H_{19}ON_3$: C, 63.12; H, 9.15; N, 20.08. Found: C, 62.86; H, 9.15; N, 20.14. Cyclopentenone[12] and its 2-methyl-[11] and 3-methyl-substituted[13] derivatives were prepared according to the literature procedures, and the 2-ethyl-3-methyl derivative was prepared by a method similar to that for the 2,3-dimethyl one.[14] 2-Ethyl-3-methylcyclopentenone: IR 1680, 1640 cm^{-1}; NMR δ 0.90 (t, 3 H),

(8) Thermolysis of the δ-lactones **2** and **8** under similar conditions gave the same results.

(9) In addition, when an acetic acid solution of the γ-lactone **11** was refluxed, the equilibrium mixture of both lactones was also obtained (**2**/**11** ratio of 14:86) after about 72 h.

(10) Cantrell, T. S.; Solomon, J. S. *J. Am. Chem. Soc.* **1970**, *92*, 4656.
(11) Gassman, P. G.; Pascone, J. M. *J. Am. Chem. Soc.* **1973**, *95*, 7801.
(12) Teribs, W.; Franke, G.; Leichsenring, G.; Roder, H. *Ber. Dtsh. Chem. Ges.* **1953**, *86*, 616.
(13) Acheson, R. M.; Robinson, R. *J. Chem. Soc.* **1952**, 1127.
(14) Varech, D.; Ouannes, C.; Jacques, J. *Bull. Soc. Chim. Fr.* **1965**, 1162.

2.00–2.50 (m, 9 H); MS m/e 124 (M^+); semicarbazone, mp 216–217 °C. Anal. Calcd for $C_9H_{15}ON_3$: C, 59.64; H, 8.34; N, 23.19. Found: C, 59.65; H, 8.30; N, 23.17.

Preparation of δ-Lactones. δ-Lactones **1–9** were prepared by the Baeyer–Villiger oxidation of the corresponding ketones in two methods.

Procedure A. A solution of the ketone and a 20-fold excess of 30% aqueous hydrogen peroxide in acetic acid was stirred at room temperature, and the progress of the reaction was monitored by GLC. The solution was poured into water and extracted with ether, and the ether extract was washed with saturated sodium carbonate solution and brine and dried (Na_2SO_4). The solvent was removed in vacuo, and the residue was distilled under reduced pressure. δ-Lactones **1–9** were obtained in 35–80% yields and purified by preparative GLC.[15]

Procedure B. A solution of the ketone and a 2.5-fold excess of 85% *m*-chloroperbenzoic acid (MCPBA) in chloroform was stirred at room temperature. The solution was washed with saturated sodium sulfite solution and water and dried (Na_2SO_4). The products were isolated as described above (40–90%).

1: IR 1720 cm^{-1}; NMR δ 1.30–2.20 (m, 12 H), 2.30–2.50 (m, 2 H); MS m/e 166 (M^+), 138. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.90; H, 8.78.

2: IR 1720 cm^{-1}; NMR δ 1.00–2.15 (m, 14 H), 2.20–2.50 (m, 2 H); MS m/e 180 (M^+), 152. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.11; H, 9.13.

3: mp 34–36 °C; IR (KBr) 1720 cm^{-1}; NMR δ 1.20–2.20 (m, 16 H), 2.50–2.70 (m, 2 H); MS m/e 194 (M^+), 166. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.92; H, 9.44.

4: IR 1720 cm^{-1}; NMR δ 1.00–2.20 (m, 18 H), 2.50–2.70 (m, 2 H); MS m/e 208 (M^+), 180. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.70; H, 9.74.

5: IR 1720 cm^{-1}; NMR δ 1.50–2.80 (m, 9 H), 4.76 (q, 1 H); MS m/e 126 (M^+), 98.

6: IR 1720 cm^{-1}; NMR δ 1.40 (s, 3 H), 1.40–2.50 (m, 9 H); MS m/e 141 ($M^+ + 1$), 43. Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.31; H, 8.72.

7: IR 1720 cm^{-1}; NMR δ 1.24 (s, 3 H), 1.40–2.60 (m, 8 H), 4.32 (q, 1 H); MS m/e 141 ($M^+ + 1$), 99. Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.22; H, 8.77.

8: IR 1720 cm^{-1}; NMR δ 0.96 (s, 3 H), 1.14 (s, 3 H), 1.40–2.70 (m, 8 H); MS m/e 155 ($M^+ + 1$), 126. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.05; H, 9.25.

9: IR 1720 cm^{-1}; NMR δ 0.99 (t, 3 H), 1.12 (s, 3 H), 1.50–2.50 (m, 10 H); MS m/e 169 ($M^+ + 1$), 140. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.06; H, 9.98.

Thermal Rearrangement of δ-Lactones 1–9. (a) In Solution. A solution of the δ-lactone in *o*-dichlorobenzene was heated in a sealed tube at 240 °C for 72 h. After evaporation of the solvent in vacuo, the residue was analyzed by GLC (10% FFAP), and the γ-lactones were separated by column chromatography (SiO_2, 10% ether–petroleum ether) and purified by preparative GLC. The results are summarized in Table I.

(b) In the Vapor Phase. A hexane solution of the δ-lactone was passed through a Pyrex column (80 cm) heated at 350 °C in nitrogen stream (contact time ca. 20 s) and collected in a dry ice–acetone trap. Similar workup as above gave a mixture of δ- and γ-lactones. The results are summarized in Table I.

10: IR 1765 cm^{-1}; NMR δ 0.10–0.90 (m, 4 H), 1.40–2.20 (m, 8 H), 2.20–2.50 (m, 2 H); MS m/e 166 (M^+), 111. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.88; H, 8.56.

11: mp 32–34 °C; IR 1765 cm^{-1}; NMR δ 0.15–1.00 (m, 4 H), 1.20–2.20 (m, 10 H), 2.30–2.50 (m, 2 H); MS m/e 180 (M^+). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 72.98; H, 9.03.

12: IR 1765 cm^{-1}; NMR δ 0.10–1.00 (m, 4 H), 1.10–2.20 (m, 12 H), 2.30–2.60 (m, 2 H); MS m/e 194 (M^+), 166. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.33; H, 9.59.

13: IR 1765 cm^{-1}; NMR δ 0.10–1.10 (m, 4 H), 1.10–2.20 (m, 14 H), 2.30–2.60 (m, 2 H); MS m/e 208 (M^+), 180. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H. 9.68. Found: C, 75.13; H, 9.56.

14: IR 1765 cm^{-1}; NMR δ 0.49 (m, 2 H), 0.67 (t, 2 H), 1.10 (s, 3 H), 1.40 (s, 3 H), 1.80–2.60 (m, 4 H); MS m/e 155 ($M^+ + 1$). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.87; H, 9.27.

15: IR 1765 cm^{-1}; NMR δ 0.25–0.68 (m, 4 H), 0.80 (t, 3 H), 1.40 (s, 3 H), 1.50 (q, 2 H), 1.80–2.60 (m, 4 H); MS m/e 169 ($M^+ + 1$). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.13; H, 9.69.

(15) In the cases of **2**, **8**, and **9**, 10% of **11** and traces of **14** and **15** were also obtained, besides the respective δ-lactones. These may be derived from initially formed δ-lactones by the rearrangement.

Registry No. **1**, 68157-80-2; **2**, 68157-81-3; **3**, 68157-82-4; **4**, 68157-83-5; **5**, 71221-74-4; **6**, 72331-80-7; **7**, 72331-81-8; **8**, 72331-82-9; **9**, 72331-83-0; **10**, 72331-84-1; **11**, 68197-38-6; **12**, 72331-85-2; **13**, 72331-86-3; **14**, 68157-84-6; **15**, 68157-85-7; tetrahydro-3a,6a-ethano-1*H*,4*H*-pentalen-1-one, 5202-23-3; hexahydro-3a,7a-ethano-1*H*-inden-1-one, 42540-17-0; hexahydro-3a,8a-ethano-1*H*,4*H*-azulen-1-one, 70386-90-2; octahydro-3a,9a-ethano-1*H*-cyclopentacyclooctan-1-one, 70386-91-3; bicyclo[3.2.0]heptan-2-one, 29268-42-6; 1-methylbicyclo[3.2.0]heptan-2-one, 50459-43-3; 5-methylbicyclo[3.2.0]heptan-2-one, 50459-35-3; 1,5-dimethylbicyclo[3.2.0]heptan-2-one, 70386-92-4; 1-ethyl-5-methylbicyclo[3.2.0]heptan-2-one, 72331-87-4; 1-ethyl-5-methylbicyclo[3.2.0]heptan-2-one semicarbazone, 72331-88-5; 2-ethyl-3-methylcyclopentenone, 5682-72-4; 2-ethyl-3-methylcyclopentenone semicarbazone, 72331-89-6.

Alkaline Hydrolysis of 7,8-Dimethyl-10-(formylmethyl)isoalloxazine. A Kinetic Study

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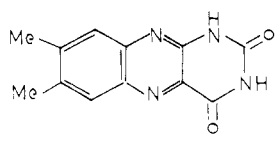
7,8-Dimethyl-10-(formylmethyl)isoalloxazine (**1**) is an important intermediate product in the photolysis of riboflavin (**2**).[2] Marked changes in the distribution of lumichrome (**3**) and lumiflavin (**4**), both major products of the photolysis of **2**, are known to occur in moving from neutral to alkaline media.[3] A possible explanation lies in the alkaline hydrolysis of **1**, formed initially in the photolysis of **2**. A previous study of the side-chain hydrolysis of **1** in the dark reported that **4** was the major product.[4]

1, R = CH_2CHO
2, R = $CH_2(CHOH)_3CH_2OH$
4, R = CH_3



3

In the present study, we report kinetic data on the dark hydrolysis of **1** in the pH range 9–12. It is shown that both **3** and **4** are major products and that their relative proportions are pH dependent.

Results and Discussion

The hydrolysis of **1**[5] (10^{-4} M) was carried out in unbuffered solutions at various pH values at 25 ± 1 °C (pH

(1) To whom correspondence should be addressed.
(2) E. C. Smith and D. E. Metzler, *J. Am. Chem. Soc.*, **85**, 3285 (1963).
(3) O. Warburg and W. Christian, *Naturwissenschaften*, **20**, 980 (1932); P. Karrer, H. Solomon, K. Schopp, E. Schlitter, and H. Fritzsche, *Helv. Chim. Acta*, **17**, 1010 (1934).
(4) P. S. Song, E. C. Smith, and D. E. Metzler, *J. Am. Chem. Soc.*, **87**, 4181 (1965).
(5) **1** was prepared as described previously by H. H. Fall and H. G. Petering, *J. Am. Chem. Soc.*, **78**, 377 (1956).

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