solution was evaporated to dryness and crystallized from water to give 0.99 g (76%) of **5**: mp 149–150°; $[\alpha]^{25}D$ −36° (*c* 0.5, water); $\lambda_{max}$ (pH 1) 258 nm ($\epsilon$ 12,000); $\lambda_{min}$ 231 nm ($\epsilon$ 3700), 280 s (7100); $\lambda_{max}$ (pH 11) 256 nm ($\epsilon$ 14,000), $\lambda_{min}$ 229 nm ($\epsilon$ 4200), 280 s (7900); NMR (DMSO-$d_6$ + $D_2O$) $\delta$ 3.5–4.4 (broad m), 5.18 (s, 2, $CH_2C_6H_5$), 5.68 (d, 1, H-1′, $J_{1',2'}$ = 6.0 Hz), 7.18 (broad s, 5, $CH_2C_6H_5$), 7.89 (s, 1, H-8). The compound was homogeneous by TLC, paper chromatography, and paper electrophoresis.

Anal. Calcd for $C_{17}H_{19}N_5O_5$: C, 54.68; H, 5.13; N, 18.76. Found: C, 54.37; H, 5.34; N, 18.34.

**Debenzylation of $N^3$-Benzyluridine (2).** Sodium naphthalene in dioxane (7.7 ml, 2.7 mmol) was added to **2** (100 mg, 0.30 mmol) in dioxane (20 ml) under nitrogen, and the mixture was stirred for 3 hr, after which time TLC indicated complete disappearance of **2**. The solution was left open to the atmosphere until the green color disappeared and then evaporated to dryness. The solid was washed with diethyl ether (3 × 10 ml) to remove the naphthalene and then taken up in water and treated with Amberlite IR 120 ($H^+$) to remove the sodium ions. The resin was removed by filtration and washed with water (10 ml), and the combined filtrates were evaporated to a solid that was recrystallized from water–methanol to give **2** (78 mg, 84%) which was identical in all respects with uridine.

**Debenzylation of $N^1$-Benzylguanosine (5).** The debenzylation of **5** (50 mg, 0.13 mmol) in THF (20 ml) with sodium naphthalene in THF (3.3 ml, 1.2 mmol) was carried out as described for $N^3$-benzyluridine (**2**) except that sodium ions were removed with Dowex 50 (pyridinium), yield 28 mg (76%).

**Ion-Exchange Chromatography.** Samples of $N^3$-benzyluridine (**2**, 5 mg) and $N^1$-benzylguanosine (**5**, 5 mg) were applied to analytical ion-exchange (Dowex 1, $OH^-$) columns as described by Dekker.[15] $N^3$-Benzyluridine was readily eluted in 50% methanol–water and $N^1$-benzylguanosine in 70% methanol–water.

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**Registry No.**—**1**, 58-96-8; **2**, 14985-34-3; **3**, 118-00-3; **4**, 55043-74-8; **5**, 55043-75-9; *N,N*-dimethylformamide dibenzyl acetal, 2016-04-8.

## References and Notes

(1) N. Imura, T. Tsuruo, and T. Ukita, *Chem. Pharm. Bull.*, **16**, 1105 (1968).
(2) E. Shaw, *J. Am. Chem. Soc.*, **80**, 3899 (1958).
(3) J. Žemlička, *Collect. Czech. Chem. Commun.*, **28**, 1060 (1963).
(4) A. Holý, S. Chládek, and J. Žemlička, *Collect. Czech. Chem. Commun.*, **34**, 253 (1969).
(5) J. Žemlička, *Collect. Czech. Chem. Commun.*, **35**, 3572 (1970).
(6) A. Holý, R. Bald, and N. D. Hong, *Collect. Czech. Chem. Commun.*, **36**, 2658 (1971).
(7) H. Brechbühler, H. Büchi, E. Hatz, J. Schreiber, and A. Eschenmoser, *Helv. Chim. Acta*, **48**, 1746 (1965).
(8) J. Žemlička, R. Gasser, J. V. Freisler, and J. P. Horwitz, *J. Am. Chem. Soc.*, **94**, 3213 (1972).
(9) J. Žemlička, *Collect. Czech. Chem. Commun.*, **33**, 3796 (1968).
(10) K. D. Philips, J. Žemlička, and J. P. Horwitz, *Carbohydr. Res.*, **30**, 281 (1973).
(11) P. B. Farmer, A. B. Foster, M. Jarman, and M. J. Tisdale, *Biochem. J.*, **135**, 203 (1973).
(12) J. Žemlička and A. Holý, *Collect. Czech. Chem. Commun.*, **32**, 3159 (1967).
(13) W. D. Closson, P. Wriede, and S. Bank, *J. Am. Chem. Soc.*, **88**, 1581 (1966).
(14) J. C. Philips and C. Perianayagam, personal communication.
(15) C. A. Dekker, *J. Am. Chem. Soc.*, **87**, 4027 (1965).

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# Photochemical Reaction of α,β-Epoxy Esters in Protic Solvent

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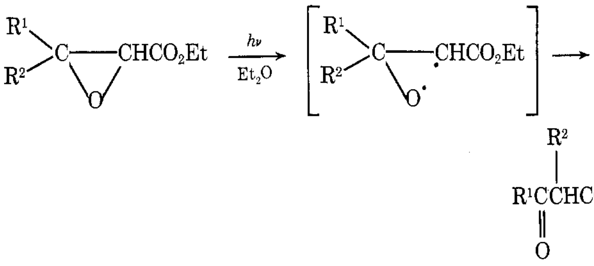
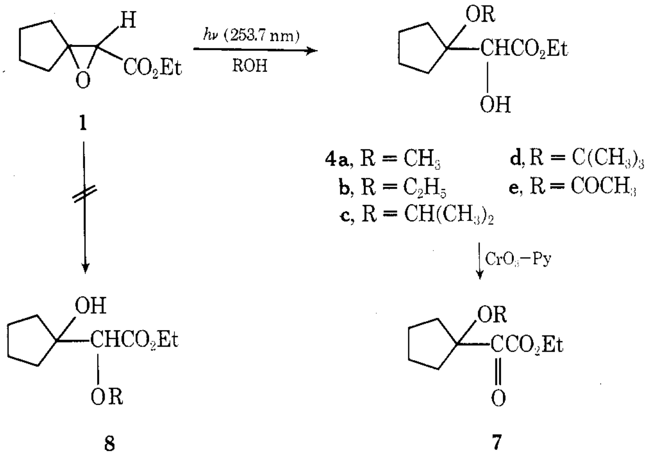
It was previously reported that α,β-epoxy esters with simple alkyl substituents were rearranged to the corresponding β-keto esters when they were irradiated in an aprotic solvent such as diethyl ether and carbon tetrachloride.[1] These transformations have been also reported in various types of α,β-epoxy ketones, and the mechanism involved may well be a homolytic fission of α carbon–oxygen bond followed by a transfer of β-alkyl substituent.[2] The present investigation was undertaken to determine whether homolytic fission of the epoxy ring would preferentially occur even when irradiated in a protic solvent.



Irradiation of ethyl 1-oxaspiro[2,4]heptane-2-carboxylate (**1**) in methanol with 253.7-nm light produced α-hydroxy ester **4a** in a 67% yield. The structure of **4a** was determined by NMR spectroscopy and an oxidation reaction. The NMR spectrum of **4a** in DMSO-$d_6$ exhibits a doublet at $\delta$ 5.47 ($J$ = 5.8 Hz) attributable to the hydroxyl proton, which indicates the presence of a secondary hydroxyl group.[3] Oxidation with chromium trioxide–pyridine complex yielded α-keto ester **7a**. Acid-catalyzed thermal reaction of **1** in methanol produced **4a** and ethyl 2-hydroxy-2-(1-cyclopentenyl)acetate. From these results it is concluded that the alternative product (**8**) is not produced in this reaction. Dark reaction of **1** in methanol for 15 days was confirmed not to provide a detectable amount of **4a**. Irradiation of **1** with a high-pressure mercury vapor lamp produced only a small amount of **4a** because of the secondary photolytic decomposition of the product.



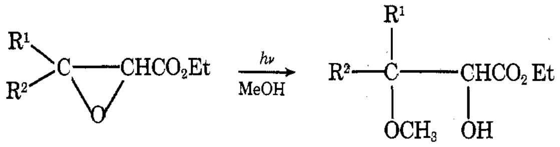
Irradiation of **1** in several protic solvents produced the corresponding α-hydroxy esters (**4a–e**). These results are summarized in Table I. Dark reaction in acetic acid under the same conditions produced a 75% yield of **4e** in a 31% conversion. The lower yield of **4e** in the photochemical reaction is due to the fast photolytic decomposition of the product. On the other hand, the lower yields of **4c** and **4d**[4] are probably due to the weak nucleophilicities of 2-propanol and 2-methyl-2-propanol, because the acid-catalyzed thermal reactions in both solvents produced low yields of **4c** and **4d**.

Ethyl 1-oxaspiro[2,5]octane-2-carboxylate (**2**) and ethyl 3-methyl-3-ethyl glycidate (**3**) also produced the corresponding α-hydroxy-β-methoxy esters **5a** (26%) and **6a** (34%) in 66 and 96% conversions, respectively, when irra-

### Table I
### Photochemical Reaction of Ethyl 1-Oxaspiro[2,4]heptane-2-carboxylate in Various Solvents[a]

| Solvent | Product | Conversion, % | Yield, %[b] |
|---|---|---|---|
| Methanol | 4a | 72 | 67 |
| Ethanol | 4b | 30 | 57 |
| 2-Propanol | 4c | 10 | Trace |
| 2-Methyl-2-propanol | 4d | 18 | Trace |
| Acetic acid | 4e | 47 | 30 |

[a] Irradiated for 74 hr. [b] Based upon epoxy ester consumed.



**1–3** **4a–6a**

**1**, **4a**, $R^1 = R^2 = -(CH_2)_4-$
**2**, **5a**, $R^1 = R^2 = -(CH_2)_5-$
**3**, **6a**, $R^1 = C_2H_5$; $R^2 = CH_3$

diated in methanol with 253.7-nm light. The product **6a** involved nearly equal amounts of diastereomers.

Although some reports concerning a photochemical ionic reaction of an oxirane ring are available,[5-7] the exact natures of these reactions are unknown. Photolysis of methanol in the presence of oxygen was reported to yield an acidic substrate, which initiated the ionic reaction.[7] However, irradiation of **1** in methanol under nitrogen, oxygen atmosphere, or vacuum ($1 \times 10^{-4}$ mm) produced almost the same yields of **4a** with similar conversions. Rather than the effect of oxygen, some acidic substrate produced photochemically probably plays an important role in these reactions. Irradiation of **1** in the presence of sodium carbonate in methanol was confirmed not to yield **4a**. Consequently, although it is unknown as to what the nature of the acidic substrate is, heterolytic cleavage of the $\beta$ carbon–oxygen bond to give **4–6** with no detectable formation of the alternative product such as **8** indicates that these reactions probably proceed via a photochemical protonation and not via an excitation of ester carbonyl followed by homolytic fission of the $\alpha$ carbon–oxygen bond.

Although the photochemical transformation of $\alpha,\beta$-epoxy ester to $\beta$-keto ester was quenched by a triplet quencher,[1] the photochemical ionic reaction of **1** to give **4** was not affected by an addition of piperylene, benzene, and naphthalene in concentrations ranging from 0.02 to 0.2 *M*.

## Experimental Section

Gas–liquid chromatographic analyses were carried out with a Hitachi K-53 and preparative works were done with a Varian Autoprep 700. Infrared spectra were obtained with a Hitachi EPI-G22, and nuclear magnetic resonance spectra were measured with a Jeol 3H-60 using tetramethylsilane as an internal standard. Mass spectra were obtained with a Hitachi RM-50 GC. Quantitative GLC analyses were carried out by an internal standard method. All melting points and boiling points are uncorrected.

The starting $\alpha,\beta$-epoxy esters **1**, bp 106.0–106.5° (12 mm) [lit.[8b] bp 90–95° (3–4 mm)], **2**, bp 124.5° (15 mm) [lit.[8a] bp 134–137° (21 mm)], and **3**, bp 84–86° (12 mm) [lit.[8c] bp 91–95° (17 mm)], were prepared using the procedure of Johnson et al.[8a] and distilled before use. Methanol, ethanol, 2-propanol, and 2-methyl-2-propanol were dried over calcium oxide.

**Photochemical Reactions.** A mixture of $\alpha,\beta$-epoxy ester (**1–3**) and protic solvent (0.08 *M*) in a quartz tube was cooled in water and externally irradiated with a 15-W low-pressure mercury vapor lamp. Nitrogen gas was allowed to pass through the mixture during the irradiation. The products were separated by distillation and preparative GLC, and identified from ir, NMR, and mass spectral data.

**Ethyl 2-hydroxy-2-(1-methoxycyclopentyl)acetate** (**4a**) had $n^{26}\mathrm{D}$ 1.4576; ir ($CCl_4$) 3510, 1725, 1100 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.28 (t, 3), 1.68 (m), 3.15 (s, 3), 4.17 (q, 2), 2.76 (s, 1, OH), 3.95 (s, 1); NMR (DMSO-$d_6$) $\delta$ 1.18 (t, 3), 1.60 (m, 8), 3.10 (s, 3), 4.06 (q, 2), 5.47 (d, 1, OH, $J$ = 5.8 Hz), 4.16 (d, 1, $J$ = 5.8 Hz); mass spectrum *m/e* (rel intensity) 129 (21), 99 (100), 67 (72). Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.33; H, 9.12.

Oxidation of **4a** with the mixture of chromium trioxide and pyridine[9] produced **ethyl (1-methoxycyclopentyl)glyoxalate** (**7a**): bp 110–111° (11.5 mm); ir ($CCl_4$) 1745, 1725 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.36 (t, 3), 1.75 (m, 4), 1.92 (m, 4), 3.18 (s, 3), 4.29 (q, 2); mass spectrum *m/e* 200 ($M^+$), 99, 67, 55, 45, 41. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.76; H, 7.94.

**Ethyl 2-hydroxy-2-(1-ethoxycyclopentyl)acetate** (**4b**) had $n^{25}\mathrm{D}$ 1.4530; ir ($CCl_4$) 3500, 1722, 1112 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.07 (t, 3), 1.32 (t, 3), 1.71 (s, 8), 3.46 (q, 2), 4.23 (q, 2), 2.93 (s, 1, OH), 4.01 (s, 1); mass spectrum *m/e* (rel intensity) 143 (17), 113 (100), 85 (95), 67 (76). Anal. Calcd for $C_{11}H_{20}O_4$; C, 61.09; H, 9.32. Found: C, 61.07; H, 9.29.

**Ethyl 2-hydroxy-2-(1-acetoxycyclopentyl)acetate** (**4e**) had $n^{20}\mathrm{D}$ 1.4530; ir ($CCl_4$) 3580, 3500, 1720, 1745, 1230 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.30 (t, 3), 2.12 (s, 3), 1.70 (s, 8), 4.21 (q, 2), 2.80 (s, 1, OH), 4.82 (s, 1); mass spectrum *m/e* (rel intensity) 188 (11), 170 (5), 104 (100), 97 (53), 85 (36), 76 (36). Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.29; H, 7.90.

**Ethyl 2-hydroxy-2-(1-methoxycyclohexyl)acetate** (**5a**) had $n^{20}\mathrm{D}$ 1.4664; ir ($CCl_4$) 3520, 1725, 1087 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.32 (t, 3), 3.20 (s, 3), 1.50 (s, 10), 4.23 (q, 2), 2.90 (s, 1, OH), 3.93 (s, 1); mass spectrum *m/e* (rel intensity) 113 (100), 81 (83). Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 60.82; H, 9.24.

**Ethyl 2-hydroxy-3-methoxy-3-methyl valerate** (**6a**) had $n^{20}\mathrm{D}$ 1.4383; ir ($CCl_4$) 3515, 1720, 1095 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.88 (t, 3), 1.30 (t, 3), 1.15 and 1.09 (s, 3, diastereomer), 3.17 (s, 3), 4.22 (q, 2), 1.60 (m, 2), 2.90 (s, 1, OH), 3.91 (s, 1); mass spectrum *m/e* (rel intensity) 161 (4), 87 (100), 55 (58). Anal. Calcd for $C_9H_{18}O_4$: C, 56.82; H, 9.54. Found: C, 56.60; H, 9.66.

**Thermal Reaction of 1 in Methanol.** A solution of 0.63 g of **1** in 40 ml of methanol was refluxed with 25 $\mu$l of concentrated HCl for 1 hr. The resulting mixture was treated in the usual way. GLC analysis of the ethereal solution (Carbowax 20M, 190°) indicated the presence of **1**, **4a**, and ethyl 2-hydroxy-2-(1-cyclopentenyl)acetate in a ratio of 10:81:9. Preparative GLC gave ethyl 2-hydroxy-2-(1-cyclopentenyl)acetate: ir ($CCl_4$) 3515, 3045, 1733 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.28 (t, 3), 1.93 (m, 2), 2.27 (m, 4), 4.22 (q, 2), 5.70 (s, 1), 3.15 (s, 1), 4.60 (s, 1); mass spectrum *m/e* (rel intensity) 170 ($M^+$, 65), 124 (55), 97 (100), 79 (66), 67 (69). Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.20; H, 8.50.

Spectral data of **4a** isolated from a thermal reaction were completely identical with those of the photochemical one.

**Registry No.**—**1**, 6975-15-1; **2**, 6975-17-3; **3**, 3647-33-4; **4a**, 55043-44-2; **4b**, 55043-45-3; **4e**, 55043-46-4; **5a**, 55043-47-5; **6a** diastereomer a, 55043-18-0; **6b** diastereomer b, 55043-19-1; **7a**, 55043-48-6; ethyl 2-hydroxy-2-(1-cyclopentenyl)acetate, 33487-18-2.

## References and Notes

(1) M. Tokuda, M. Hataya, J. Imai, M. Itoh, and A. Suzuki, *Tetrahedron Lett.*, 3133 (1971).

(2) (a) N. R. Bertoniere and G. W. Griffin, "Organic Photochemistry", Vol. 3, O. L. Chapman, Ed., Marcel Dekker, New York, N.Y., 1973, p 142; (b) H. E. Zimmerman, B. R. Cowley, C. Y. Tseng, and J. W. Wilson, *J. Am. Chem. Soc.*, **86**, 947 (1964); (c) C. S. Marcos and W. Reusch, *ibid.*, **89**, 3363 (1967).

(3) O. L. Chapman and R. W. King, *J. Am. Chem. Soc.*, **86**, 1256 (1964).

(4) Identities of **4c** and **4d** were established by comparison of GLC retention times and mass spectra of GC–mass with those of the acid-catalyzed reaction products.

(5) (a) K. Tokumaru, *Bull. Chem. Soc. Jpn.*, **40**, 242 (1967); (b) M. Hisaoka and K. Tokumaru, *Chem. Lett.*, 351 (1973).

(6) I. Saito, M. Takami, T. Konoike, and T. Matsuura, *Tetrahedron Lett.*, 2689 (1972).

(7) (a) G. Roussi and R. Bengelmans, *Tetrahedron Lett.*, 1333 (1972); (b) S. J. Cristol, G. A. Lee, and A. L. Noreen, *ibid.*, 4175 (1971).

(8) (a) R. H. Hunt, L. J. Chinn, and W. S. Johnson, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 459; (b) M. S. Newmann, *J. Am. Chem. Soc.*, **57**, 732 (1935); (c) R. P. Linstead and J. T. W. Mann, *J. Chem. Soc.*, 2070 (1930).

(9) P. J. Pasto and C. R. Johnson, "Organic Structure Determination", Prentice-Hall, Englewood Cliffs, N.J., 1969, p 361.