

James W. Pavlik*, Steven J. Kirincich and Richard M. Pires

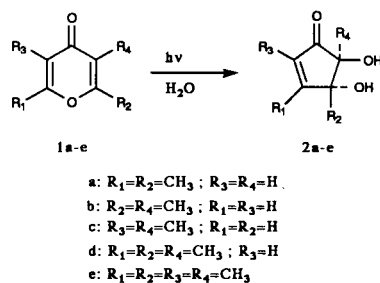
Department of Chemistry, Worcester Polytechnic Institute,
Worcester, Massachusetts 01609
Received December 21, 1990

Irradiation of 2-ethyl-3-methyl-4-pyrone **3** in aqueous solution led to the formation of *trans*-4-ethyl-5-methyl-4,5-dihydroxycyclopent-2-enone **4** and *trans*-2-methyl-3-ethyl-4,5-dihydroxycyclopent-2-enone **5**. In the latter case ¹H nmr analysis confirmed the *trans*-configuration at C₄ and C₅. These results are consistent with trapping of a photochemically generated oxabicyclohexenyl zwitterion by nucleophilic attack of both sides of the oxally system along a path *anti* to the epoxide ring.

J. Heterocyclic Chem., **28**, 537 (1991).

Work in this and in other laboratories [1-5] has shown that 4-pyrones undergo photo-ring contraction with nucleophilic addition of solvent upon irradiation in water or in alcohol solvents. More recent work has revealed that 4-pyrones bearing hydroxyalkyl side-chains can undergo photo-ring contraction with intramolecular nucleophilic addition to yield synthetically interesting bicyclic cyclopentenone ethers [6].

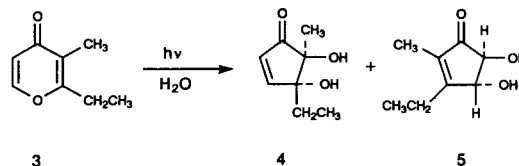
Although this photo-ring contraction was found originally to be general to a variety of methyl substituted-4-pyrones, the observed regiochemistry of the reaction was perplexing. Thus, in the case of 2,3-dimethyl-4-pyrone **1b** and 2,3,6-trimethyl-4-pyrone **1d**, the only regioisomer detected possessed the hydroxyl groups on the more highly substituted side of the molecule. Since it seemed plausible that the reaction should also yield the regioisomer having the hydroxyl groups on the less substituted side of the molecule, the regiochemistry of the photo-ring contraction reaction in water was re-investigated. To accomplish this, we selected to study the photochemistry of the unsymmetrically substituted 4-pyrone, 2-ethyl-3-methyl-4-pyrone **3**.



Preliminary analytical irradiations at 254 nm of a 2.0 x 10⁻⁴ M aqueous solution of **3** [λ max 260 nm (ε = 10,650) and 215 nm (ε = 7,300)] were monitored by uv-absorption spectroscopy. Consecutive 5 second irradiations were accompanied by a decrease in the optical density at 260 and 215 nm due to **3** and the formation of a final product with λ max at 220 nm, similar in position to the absorption maxima of known 4,5-dihydroxycyclopentenones [7].

Preparative scale photolysis was carried out by irradiating 100 ml of a 1.0 x 10⁻² M aqueous solution of **3** in a

Rayonet reactor at 254 nm until uv-analysis indicated 75 percent consumption of the 4-pyrone reactant. Work up of the resulting solution provided a crude product from which 4-ethyl-5-methyl-4,5-dihydroxycyclopentenone **4** was crystallized and identified by its elemental analysis and spectroscopic properties. As in previous cases, this is the regioisomeric dihydroxycyclopentenone bearing the hydroxyl groups on the more highly substituted side of the molecule. The residue from the crystallization was subjected to careful preparative layer chromatography to provide additional **4** and a second white crystalline compound whose elemental analysis and spectroscopic properties confirmed that its structure is 2-methyl-3-ethyl-4,5-dihydroxycyclopentenone **5**, the regioisomer bearing the hydroxyl groups on the less highly substituted side of the molecule.

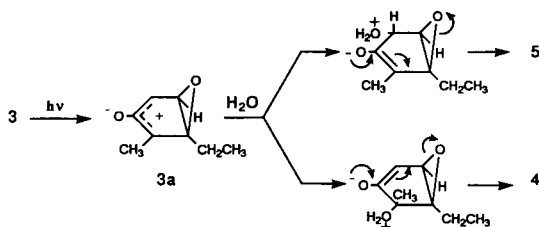


Of particular interest in the ¹H nmr spectrum of **5** are the signals in the 4.0-6.0 ppm region of the spectrum. In anhydrous dimethylsulfoxide-d₆ the two hydroxyl protons appear as a pair of overlapping doublets in the 6.0 ppm region of the spectrum, as expected for two secondary alcohol groups, a broad one proton signal at 4.65 ppm assigned to the C-4 proton, and two doublets in the 4.1-4.2 ppm region of the spectrum, assigned to the C-5 proton. Addition of deuterium oxide was accompanied by the disappearance of the signals due to the hydroxyl protons while the C-4 proton absorption remains a broad, although somewhat sharpened, one proton signal. As demanded by the assigned structure, the resonance due to the C-5 proton was observed to collapse to a clearly observable doublet at 4.17 ppm due to its coupling with the C-4 proton. The measured H₄-H₅ vicinal coupling constant of 2.7 Hz is consistent with a *trans*-configuration of the C-4 and C-5 protons. Indeed, an energy minimized structure [8] of the

cis-dihydroxycyclopentenone predicts a dihedral angle of 18° and a H_4-H_5 vicinal coupling constant of 9.0 Hz. Alternatively, an energy minimized structure of the *trans*-dihydroxycyclopentenone predicts a dihedral angle of 124° corresponding to a calculated H_4-H_5 vicinal coupling constant of 3.1 Hz, in reasonable agreement with the experimental value. These stereochemical results confirm the *trans*-configuration previously suggested by analysis of the hydroxyl region of the infrared spectrum. Of the various dihydroxycyclopentenone products isolated from photo-ring contraction of a 4-pyrone, this is the first example which has hydrogens on both carbinol carbons and thus is the first example which allows the *trans*-stereochemistry to be confirmed by nmr analysis.

These results are entirely consistent with our previous mechanistic suggestion [1] for the photo-ring contraction. Thus (Scheme 1), photochemical excitation is suggested to result in electrocyclic ring closure leading to the bicyclic zwitterion **3a**. Intermolecular nucleophilic attack by water could occur at either end of the oxyallyl system but would occur mainly at the more highly substituted side leading to the dihydroxycyclopentenone with the hydroxyl groups on the more highly substituted side of the molecule as the major product. To a lesser extent, water would attack at

Scheme 1



the less substituted side of the allyl system leading to the dihydroxycyclopentenone with the hydroxyl groups on the less substituted side of the molecule as the minor product. In either case, it would be expected that water would attack **3a** from the less hindered side - *anti* to the epoxide ring - establishing the *trans*-stereochemistry observed in the product.

EXPERIMENTAL

Melting points were determined on a MeL Temp capillary melting point apparatus and are uncorrected. 1H (200 MHz) and ^{13}C (50.3 MHz) nmr spectra were recorded in the solvent indicated on a Bruker AC-200 spectrometer. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. Infrared spectra were recorded in potassium bromide disks on a Perkin-Elmer 1720 FT spectrometer. Ultraviolet absorption spectra were recorded on a Shimadzu UV 2100 U Recording Spectrometer. Mass spectra were obtained on a Hewlett-Packard 5988 spectrometer equipped with a direct inlet probe. Preparative layer chromatography was carried out on 20 x 20 cm

glass plates precoated with a 2 mm layer of Kieselgel 60 F₂₅₄. Elemental analyses were determined by Desert Analytics, Tucson, AZ.

2-Ethyl-3-methyl-4*H*-pyran-4-one **3** was prepared by the condensation of propanoic anhydride with vinyl acetate in 60% perchloric acid [9,10].

Irradiation Procedure.

A solution of 0.276 g (2.00 mmoles) of **3** in distilled water (100 ml) in a quartz tube (24 mm id x 330 mm long) sealed with a rubber septum was purged with nitrogen (20 minutes) and then irradiated at 254 nm in a Rayonet reactor (18 lamps) (~2.5 hours). The solutions resulting from 7 such irradiations were combined, extracted with ether (3 x 50 ml), and the remaining aqueous phase concentrated *in vacuo* to provide 1.15 g of a yellow residue. This material was dissolved in diethyl ether, treated with decolorizing carbon, and concentrated. Crystallization provided 0.200 g (12%) of **4**, mp 106-107°; 1H nmr (deuterium oxide): δ 0.95 (t, 3H, J = 7.5 Hz), 1.31 (s, 3H), 1.55 (d of t, 1H, J = 14.8 Hz and 7.5 Hz), 1.89 (d of t, 1H, J = 14.8 Hz and 7.5 Hz), 6.40 (d, 1H, J = 6.0 Hz), 7.70 (d, 1H, J = 6.0 Hz); in anhydrous dimethyl sulfoxide-*d*₆ additional signals at δ 5.21 (s, 1H) and 5.32 (s, 1H), exchangeable with deuterium oxide, were observed due to the C₄ and C₅ hydroxyl protons; ^{13}C nmr (deuteriochloroform): δ 210.9 (C-1), 166.1 (C-3), 129.9 (C-21), 82.9 and 82.5 (C-4 and C-5), 31.0 (CH₃), 22.6 and 7.64 (CH₂CH₃); ir (potassium bromide): 3332 (O-H), 1712 (C=O), and 1595 (C=C) cm^{-1} ; ms: m/e (%) 156 (0.5), 138 (32), 127 (29), 123 (24), 99 (22), 95 (25), 85 (19), 67 (13), 57 (32), 43 (100).

Anal. Calcd. for C₈H₁₂O₃: C, 61.52; H, 7.75. Found: C, 61.35; H, 7.81.

The residue from the crystallization (0.53 g) was subjected to preparative layer chromatography using dichloromethane: diethyl ether (60:40) as the eluant. The major band (R_f = 0.12) was extracted with ether and concentrated. Crystallization provided 0.13 g (7.6%) of **5**, mp 94-95°; 1H nmr (dimethyl sulfoxide-*d*₆): δ 1.39 (t, 3H, J = 7.0 Hz), 1.95 (s, 3H), 2.74 (q, 2H, J = 7.0 Hz), 4.16 (d of d, 1H, J = 6.5 Hz, J = 2.3 Hz), 4.65 (br s, 1H), 5.96 and 6.00 (d, 1H, J = 6.5 Hz), both exchangeable with deuterium oxide; ^{13}C nmr (deuteriochloroform): δ 204.1 (C-1), 171.9 (C-3), 134.3 (C-2), 80.8 and 76.0 (C-4 and C-5), 20.5 (CH₃), 11.5 and 7.8 (CH₂CH₃); ir (potassium bromide): 3340 (O-H), 1720 (C=O), and 1590 (C=C) cm^{-1} ; ms: m/e (%) 156 (15.7), 138 (37.3), 127 (19.0), 110 (32.0), 109 (14.5), 95 (100), 85 (11.1), 83 (25.3), 81 (23.2), 79 (11.2), 67 (28.1), 55 (16.21), 53 (17.1), 43 (15.4).

Anal. Calcd. for C₈H₁₂O₃: C, 61.52; H, 7.75. Found: C, 61.78; H, 8.00.

Acknowledgement.

We are pleased to acknowledge the Camille and Henry Dreyfus Foundation for partial support for the purchase of the NMR spectrometer and to the Perkin-Elmer Corporation for support in the form of equipment grants.

REFERENCES AND NOTES

- [1] J. W. Pavlik and L. T. Pauliukonis, *Tetrahedron Letters*, 1939 (1976).
- [2] E. B. Keil and J. W. Pavlik, *J. Heterocyclic Chem.*, **13**, 1149 (1976).
- [3] J. W. Pavlik and A. P. Spada, *Tetrahedron Letters*, 4441 (1979).
- [4] J. A. Bartrop, A. C. Day and C. J. Samuel, *J. Am. Chem. Soc.*, **101**,

7521 (1979).

[5] J. W. Pavlik, T. E. Snead, J. R. Tata, *J. Heterocyclic Chem.*, **18**, 1481 (1981).

[6] F. G. West, P. V. Fisher and C. A. Willoughby, *J. Org. Chem.*, **55**, 5936 (1990).

[7] Dihydroxycyclopentenones reported in references [1-5] have λ max between 214-229 nm.

[8] Energy minimized structure were obtained using the semiempirical MO method MNDO.

[9] E. Kuznetsov, A. Pyshcher and G. Dorofeenko, *Khim. Geterotsikl. Soedin.*, **2**, 152 (1972).

[10] J. A. Barltrop, J. C. Barrett, Roger W. Carder, A. C. Day, J. R. Harding, W. E. Long and C. J. Samuel, *J. Am. Chem. Soc.*, **101**, 7510 (1979).