Solvent Trapping of Photochemically Generated Pyran-4-one-Derived Oxyallyls: A Convenient Cyclopentannulation Method

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Dedicated with best wishes to Professor Howard Zimmerman in recognition of his many important contributions to the field of organic photochemistry

Abstract: Fused bicyclic pyran-4-ones $2\mathbf{a}-\mathbf{f}$ are readily available via one-step annulation with diketene or diketene equivalents. Irradiation of $2\mathbf{b}-\mathbf{e}$ in methanol furnished ring-contracted solvent adducts **4** in moderate yields, whereas irradiation in aqueous H₂SO₄ gave the corresponding glycols **8** and **9**. The unusual predominance of *cis*-fused product **8b** appears to result from in situ acid-catalyzed equilibration. Substrate **2f** could also be trapped in aqueous acid, and displayed a modest stereoselectivity that may derive from conformational control by the methyl group on the starting material's stereogenic center.

Key Words: annulations, bicyclic compounds, diols, heterocycles, photochemistry, ring contractions

Pyran-4-ones undergo efficient photochemical ring contraction to transient epoxy-fused oxyallyl zwitterions 1 (Scheme 1), in analogy to the better known 2,5-cyclohexadienones.¹ We have shown that these intermediates can then be trapped by a variety of pendant nucleophiles to furnish polycyclic products.² The short lifetime of the zwitterion suggested that the corresponding intermolecular processes would not be efficient, with the possible exception of trapping by nucleophilic solvent. Indeed, Pavlik and Barltrop demonstrated that alcoholic solvents could intercept the oxyallyl intermediates derived from simple polyalkyl pyran-4-ones to give 5-alkoxy-4-hydroxy-2-cyclopenten-1-ones.³ In a preliminary study, we extended this process to fused bicyclic pyran-4-ones 2, whose intermediate zwitterions could be trapped by solvent methanol to give ring-contracted bicyclic products in which both bridgehead positions would be oxygenated, but attempts to accomplish the analogous trapping with water proceeded in low efficiency.⁴ Here we report the full details of zwitterion trapping by methanol, as well as an improved procedure for aqueous trapping of fused bicyclic pyran-4-ones to furnish dihydroxylated products. The overall procedure functions as a two-step cyclopentannulation method.

As described previously, the pyran-4-one substrates 2a-d could be easily prepared from diketene and the morpholine enamines of cyclic ketones following the procedure of Hünig (Scheme 2).⁵ An alternative method employing



Scheme 1

diketene equivalent 2,2,6-trimethyl-1,3-dioxin-4-one⁶ gave significantly higher yields of 2d while the more highly substituted 2,2,5,6-tetramethyl-1,3-dioxin-4-one allowed access to the fully substituted pyranone 2e. In order to examine the effect of a stereogenic center within the adjacent ring, methyl-substituted example 2f was also prepared, via the pyrrolidine enamine of methylcyclohexanone and 2,2,6-trimethyl-1,3-dioxin-4-one.

hν

MeOH

Nu



Scheme 2

Extended irradiation of cyclopentane-containing pyranone 2a in methanol failed to significantly consume the substrate, a result that we attribute to unacceptable levels of ring strain in the hypothetical oxyallyl zwitterion 3a

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Scheme 3

that would result (Scheme 3). However, the larger ring substrates **2b-d** all gave solvent trapping products, albeit in variable yield. The six-membered case 2b provided only minor amounts of the expected methanol adducts 4b and only in the presence of sulfuric acid. Seven- and eight-membered substrates 2c,d gave better yields, although the product mixture in the case of 2c was complicated by the presence of both diastereomeric methanol adducts 4c and 5c, as well as the apparent reduction product 7c. Finally, tetrasubstituted pyranone 2e was irradiated and yielded roughly equal amounts of regioisomeric methanol adducts 4e and 6e. The preference for trans addition in these cases parallels previous studies employing simple monocyclic pyranones, as does the regioselectivity in favor of attack at the more substituted terminus of the oxyallyl system.3,7 The regiochemical mixture seen with 2e was expected, since the two termini are equally substituted. The formation of 7c is most readily explained by competing trapping at the less substituted terminus followed by a secondary Norrish type II cleavage to furnish 7c and formaldehyde.⁸ However, we were not able to isolate any of putative precursor, 6c.

Irradiation of pyranones 2 in neutral aqueous solution gave complex mixtures, further complicated by the low aqueous solubility of the starting materials. The previously noted benefit of catalytic amounts of sulfuric acid in the methanol trapping experiments with **2b** suggested further examination of this effect. Prior reports by Barltrop⁹ and Pavlik¹⁰ indicated that 4-hydroxypyrilium cations, resulting from protonation of pyran-4-one carbonyl oxygens, underwent smooth photochemical rearrangement in analogy to their neutral counterparts. In the case of substrates 2b-d, we found that 10% aqueous sulfuric acid provided an effective medium for the desired transformation (Scheme 4). In contrast to the methanol trapping process discussed above, significant amounts of both cis- and trans-fused diastereomers 8b-d and 9b-d were isolated, and in the case of six-membered substrate 2b, the less strained *cis*-isomer was predominant. The ratio of **8b** and 9b was found to be dependent upon the concentration of H₂SO₄, suggesting the possibility of in situ isomerization. In fact, trans-fused isomer 9b underwent partial isomerization to 8b under the reaction conditions, presumably via a retro-aldol/aldol mechanism.11,12



Scheme 4

Definitive stereochemical assignment of cis- and transisomers was challenging. Single crystal x-ray diffraction analysis of 4e confirmed the expected trans relationship of the angular hydroxy and methoxy groups,¹³ and other methanol adducts were assigned by analogy. In the cases of glycols 8 and 9, the ability to form acetonides 11b, c from 8b, c with no comparable acetonide formation from 9b, c had been used to support a tentative assignment (Scheme 5).⁴ However, we were reluctant to rely on a negative result and also were concerned about possible acid catalyzed isomerization under the ketalization conditions (vide supra). Fortunately, a significant difference in the NMR chemical shifts of the hydroxyl protons could be used to distinguish the cis- and trans-isomers. In 0.01 M CDCl₃ solution, *cis*-isomers **8b–d** all displayed one downfield hydroxyl resonance ($\delta = 2.99 - 3.52$ ppm) and a second one further upfield (approx. 2.6 ppm), suggestive of internal hydrogen bonding between the two neighboring hydroxyls. In contrast, the hydroxyl resonances of 9b, c both appeared in the typical chemical shift range for isolated alcohols (1.45–1.83 ppm).¹⁴ X-ray crystallographic analysis of 8d confirmed the cis ring fusion and the presence of an internal hydrogen bond,¹³ in support of the NMR trends described above.

Finally, substrate 2f was examined to determine whether the stereogenic center within the cyclohexyl ring would exert any influence on ring contraction to the oxyallyl zwitterion. Assuming that the methyl group adopts a pseudoequatorial disposition, formation of zwitterion 3f might be favorable over that of its diastereomer 3g (Scheme 6). In the event, irradiation of 2f in dilute aqueous acid¹⁵ provided three products in a combined 39% yield. The major product was a crystalline solid, and x-ray diffraction analysis confirmed that it was the all-*cis*-isomer **8f**.¹³ A second product was assigned as the other *cis*-fused isomer **8g**, based upon ¹H NMR evidence for internal hydrogen bonding by the glycol moiety. The third product is presumed to be one of the two possible *trans*-isomers, and we have tentatively assigned it as **9f**. Thus, it appears that the methyl group exerts a modest effect on zwitterion formation.

Fused bicyclic pyran-4-ones are easily prepared from enamines and either diketene or dioxinone, and irradiation in methanol or aqueous acid leads to ring contraction with solvent incorporation. This two-step route functions as an overall cyclopentannulation method, with stereoselectivity in favor of the *trans*-isomers **4** and **9** in most cases. A pre-existing stereocenter in the ring adjacent to the pyranone led to a modest selectivity (approx. 2:1) in zwitterion formation. Intramolecular trapping of similar diastereomeric zwitterions is under study and will be reported elsewhere.







Scheme 6

Reactions were conducted in oven-dried (120°C) or flame-dried glassware under a positive atm of N2 unless otherwise stated. Transfer of anhyd solvents or air-sensitive reagents was accomplished with oven-dried syringes or cannulae. Solvents were distilled before use: CH₂Cl₂ from CaH₂, Et₂O and THF from Na-benzophenone ketyl. Commercial reagents and solutions were used as received unless otherwise stated. TLC was performed on plates of silica precoated with 0.25 mm Kieselgel 60 F_{254} (Merck). Flash columns were packed with 230-400 mesh silica gel (Merck or Baxter). Radial chromatography was performed on a Harrison Research Chromatotron Model 7924T with plates of silica precoated with 1, 2 or 4 mm silica gel 60 F₂₅₄ containing gypsum (EM Science). Mps were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected. ¹H NMR spectra were recorded on a 300 MHz Varian Unity or 500 MHz Varian VXR instrument. ¹³C NMR spectra were obtained at 75 MHz (Unity) or at 125 MHz (VXR). IR spectra were measured with a Mattson FT-IR 3000 spectrophotometer. Mass spectra were determined on a VG Micromass 7050E mass spectrometer equipped with a VG 2000 data system. Elemental analyses were carried out at Atlantic Microlabs based in Norcross, Georgia.

Bicyclic Pyranones 2

Substrates **2a,b** were previously described by Hünig and coworkers.⁵ All others were prepared using the Hünig procedure (Method A) or the dioxinone procedure (Method B).¹⁶

Method A: 3-Methyl-2-oxabicyclo[5.4.0]undeca-3,6(1)-dien-5one (2c); Typical Procedure

1-Morpholinocycloheptene (17.3 g, 95 mmol) was placed in a 250 mL 3-neck round bottom flask fitted with magnetic stirring bar, reflux condenser with a nitrogen inlet, thermometer and an addition funnel charged with diketene (15 mL, 190 mmol). The flask was warmed to 65°C and the diketene was added dropwise over 1 h. (Caution: do not allow the internal temperature to rise above 75 °C. Rapid addition of diketene can provoke an exotherm with associated pressure build-up.) Following addition, the reaction was allowed to stand at 70 °C for 2 h, then at ambient temperature for 24 h, after which the flask was fitted with a distillation head and the red oil was distilled under reduced pressure (2 mm, 100-160°C). The crude distillate was diluted with CH₂Cl₂ (100 mL) and the solution was washed with 2 N NaOH/sat. NaCl (500 mL each), dried (MgSO₄), filtered, and concentrated to give 14.7 g of yellow solid. Fractional crystallization (cyclohexane, activated charcoal) gave 7.0 g (41%) of 2c as a colorless crystalline solid.

Mp 104–105°C; R_f 0.49 (EtOAc).

IR (thin film): v = 3061, 2920, 1663, 1611 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): $\delta = 6.05$ (q, 1H, J = 0.7 Hz), 2.72 (t, 2H, J = 5.5 Hz), 2.64 (t, 2H, J = 5.6 Hz), 2.22 (d, 3H, J = 0.7 Hz), 1.81 (app. pent., 2H, J = 5.6 Hz), 1.68 (2H, app. p, J = 5.5 Hz), 1.55 (app. p, 2H, J = 5.6 Hz).

¹³C NMR (75 MHz, CDCl₃): δ = 178.4, 167.7, 163.5, 125.8, 112.3, 33.6, 31.5, 25.8, 24.5, 21.5, 19.4.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.13; H, 7.93.

Method B: 3-Methyl-2-oxabicyclo[6.4.0]dodeca-3,6(1)-dien-5one (2d); Typical Procedure

1-Morpholinocyclooctene (4.8 g, 24 mmol) and 2,2,6-trimethyl-1,3-dioxin-4-one (6.4 mL, 49 mmol; 2 equiv.) were mixed in an open 100-mL round bottom flask equipped with a magnetic stirring bar. The vigorously stirred mixture was placed in an oil bath preheated to 120-130 °C and heated for 1.5 h. After cooling to r.t., the reaction mixture was diluted with CHCl₃ (200 mL) and washed with 2 N NaOH/sat. NaCl (100 mL each). The organic layer was dried (Na₂SO₄), concentrated, and purified by flash chromatography (silica gel; 6 cm × 15 cm column; Et₂O-CH₂Cl₂-hexanes, 2:1:2) to give 4.1 g (88%) of **2d** as a pale yellow crystalline solid.

Mp 89–91 °C; R_f 0.22 (Et₂O–CH₂Cl₂–hexanes, 2:1:2).

IR (KBr): v = 1660, 1600 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 6.04 (br s, 1H), 2.66–2.62 (m, 2H), 2.57–2.52 (m, 2H), 2.20 (br s, 3H), 1.78–1.70 (m, 2H), 1.67–1.59 (m, 2H), 1.51–1.38 (m, 4H).

 ^{13}C NMR (75 MHz, CDCl₃): δ = 178.9, 165.5, 164.4, 123.9, 113.0, 30.6, 29.0, 29.0, 26.2, 26.1, 22.3, 19.8.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.09; H, 8.44.

3,4-Dimethyl-2-oxabicyclo[4.4.0]deca-3,6(1)-dien-5-one (**2e**) Prepared via Method B (71%): colorless crystalline solid, mp 54– 55° C; R_f=0.31 (EtOAc–hexanes, 1:1).

IR (thin film): v = 2986, 1663, 1605 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 2.39 (tt, 2H, *J* = 6.4, 1.5 Hz), 2.32 (tt, 2H, *J* = 6.2, 1.5 Hz), 2.14 (s, 3H), 1.81 (s, 3H), 1.73–1.63 (m, 2H), 1.63–1.52 (m, 2H).

¹³C NMR (75 MHz, CDCl₃): δ = 178.8, 161.9, 159.8, 119.8, 118.8, 27.0, 21.6, 21.3, 20.6, 17.4, 9.5.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.98; H, 7.97.

3,4,10-Trimethyl-2-oxabicyclo[4.4.0]deca-3,6(1)-dien-5-one (**2f**) Prepared via Method B, except using 6-methyl-1-pyrrolidinocyclohexene (55%): yellow crystalline solid, mp 65–67°C; R_f =0.25 (EtOAc–hexanes, 1:1).

IR (KBr): v = 1660, 1605 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): $\delta = 6.03$ (q, 1H, J = 1.0 Hz), 2.70 (dq, 1H, J = 13.5, 7.0 Hz), 2.44–2.36 (m, 2H), 2.22 (d, 3H, J = 1.0 Hz), 1.91 (dddd, 1H, J = 13.4, 11.0, 5.5, 2.5 Hz), 1.73–1.66 (m, 1H), 1.64–1.57 (m, 1H), 1.54–1.48 (m, 1H), 1.24 (d, 3H, J = 7.0 Hz).

¹³C NMR (75 MHz, CDCl₃): δ = 180.1, 166.7, 164.8, 121.6, 112.9, 32.4, 30.9, 21.6, 20.1, 19.5, 18.9.

Table Photoproducts from Solvent Trapping of 2b-f

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.01; H, 7.93.

Solvent Trapping of Pyranones 2

Photochemical reactions were carried out using a Hanovia 450W medium pressure Hg lamp in a water-cooled jacket. For small scale reactions, a quartz tube clamped 10 cm from the outer edge of the cooling jacket was used, and for large scale reactions an immersion well was used. All photochemical reaction mixtures were deoxygenated with a slow stream of dry N_2 for 15–30 min.

Product	R _f /phys. descr.	IR v (cm ⁻¹)	¹ H NMR δ ^a	13 C NMR δ^{b}	EA (%)	HRMS (m/z)
4b	0.39 (Et ₂ O– CH ₂ Cl ₂ –hex, 4:3:3)/ oil	3437, 1709, 1608	5.83 (q, 1H, <i>J</i> = 1.5), 3.18 (s, 3H), 2.09 (d, 3H, <i>J</i> = 1.5), 2.10–1.90 (m, 1H), 1.89–1.76 (m, 1H), 1.74–1.62 (m, 2H), 1.61–1.36 (m, 5H)	204.5, 175.4, 127.9, 82.3, 79.5, 51.3, 25.1, 19.6, 18.6, 18.4, 14.2		calcd for C ₁₁ H ₁₆ O ₃ 196.1099. Found: 196.1098
4c	0.40 (hex– EtOAc, 1:1)/ solid (mp 111– 112°C)	3414, 1688, 1614	5.78 (q, 1H, <i>J</i> = 1.5), 3.15 (s, 3H), 2.20–2.0 (m, 1H), 2.09 (d, 3H, <i>J</i> = 1.5), 1.90–1.50 (m, 10H)	204.4, 176.9, 127.1, 85.1, 83.9, 51.4, 29.3, 25.3, 25.0, 24.7, 20.1, 14.1	Calcd for C ₁₂ H ₁₈ O ₃ : C, 68.54; H, 8.63. Found: C, 68.68; H, 8.67	
5c	0.54 (hex– EtOAc, 1:1)/ oil	3501, 1707, 1628	5.87 (q, 1H, $J = 1.2$), 3.87 (d, 1H, J = 1.5), 3.37 (s, 3H), 2.20–1.92 (m, 2H), 2.07 (d, 3H, $J = 1.2$), 1.88–1.76 (m, 2H), 1.70–1.20 (m, 6H)	203.5, 181.1, 127.6, 82.4, 81.1, 51.8, 34.5, 30.9, 26.8, 22.5, 22.0, 14.0		calcd for C ₁₂ H ₁₈ O ₃ 210.1256. Found: 210.1263
7c	0.33 (hex– EtOAc, 1:1)/ oil	3422, 1696, 1643	3.70 (s, 1H), 2.64–2.50 (m, 1H), 2.55 (s, 2H), 2.50–2.36 (m, 1H), 2.36–2.17 (m, 2H), 1.85–1.70 (m, 2H), 1.70–1.57 (m, 2H), 1.56–1.45 (m, 2H), 1.43 (s, 3H)	204.9, 177.5, 142.7, 76.1, 51.4, 31.8, 27.5, 27.2, 26.7, 26.6, 23.3		calcd for C ₁₁ H ₁₆ O ₂ 180.1158. Found: 180.1154
4d	0.43 (Et ₂ O– CH ₂ Cl ₂ –hex, 2:1:1)/ oil	3320, 1680, 1610	5.78 (q, 1H, <i>J</i> = 1.4), 3.09 (s, 3H), 2.00 (d, 3H, <i>J</i> = 1.5), 1.91–1.68 (m, 6H), 1.59–1.19 (m, 7H)	204.6, 178.0, 127.2, 82.3, 65.8, 52.1, 30.1, 28.7, 27.4, 24.0, 23.5, 23.3, 14.5	Calcd for C ₁₃ H ₂₀ O ₃ : C, 69.61; H, 8.99. Found: C, 69.63; H, 9.00	
4e	0.60 (hex– EtOAc, 1:1)/ solid (mp 136– 137°C)	3458, 1696, 1632	3.10 (s, 3H), 2.15–1.93 (m, 2H), 1.96 (q, 3H, <i>J</i> =1.1), 1.90–1.78 (m, 2H), 1.71 (q, 3H, <i>J</i> =1.1), 1.70–1.58 (m, 3H), 1.58–1.48 (m, 2H)	204.7, 166.4, 134.8, 81.4, 78.7, 51.4, 25.3, 19.6, 18.7, 18.4, 11.5, 8.0	Calcd for C ₁₂ H ₁₈ O ₃ : C, 68.55; H, 8.63. Found: C, 68.64; H, 8.68	
6e	0.42 (hex– EtOAc, 1:1)/ oil	3451, 1703, 1645	3.43 (s, 3H), 2.50–2.25 (m, 2H), 2.20– 2.00 (m, 2H), 1.90 (br s, 1H), 1.80– 1.50 (m, 4H), 1.38 (s, 3H), 1.33 (s, 3H)	204.4, 171.8, 135.5, 84.3, 80.7, 52.6, 22.5, 22.0, 21.9, 21.4, 19.5, 15.6		calcd for C ₁₂ H ₁₈ O ₃ 210.1256. Found: 210.1262
8b	0.58 (EtOAc)/ oil	3401, 1709, 1618	5.87 (q, 1H, <i>J</i> = 1.4), 3.84 (br s, 1H), 3.65 (br s, 1H), 2.22–2.12 (m, 1H), 2.07 (d, 3H, <i>J</i> = 1.4), 1.78–1.45 (m, 7H)	207.5, 178.7, 127.2, 77.7, 76.9, 32.2, 30.8, 19.9, 19.8, 14.4		calcd for $C_{10}H_{14}O_3$ 182.0945. Found: 182.0944
9b	0.50 (EtOAc)/ solid (mp 152– 153 °C)	3383, 3310, 1709, 1607	5.89 (q, 1H, <i>J</i> =1.5), 2.16–1.94 (m, 1H), 2.11 (d, 3H, <i>J</i> =1.5), 1.83 (br s, 1Hs), 1.83–1.58 (m, 7H), 1.45 (br s, 1H)	205.9, 175.7, 128.4, 79.0, 77.9, 24.9, 24.1, 19.6, 18.6, 14.2	Calcd for C ₁₀ H ₁₄ O ₃ : C, 65.92; H, 7.74. Found: C, 65.82; H, 7.75	

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Table	Photoproducts	from Solvent	Trapping of 2b-f	(continued)
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Product	R _f /phys. descr.	IR v (cm ⁻¹)	1 H NMR δ^{a}	13 C NMR δ^{b}	EA (%)	HRMS (m/z)
8c	0.49 (hex– EtOAc, 1:1)/ gum	3410, 1705, 1624	5.93 (q, 1H, $J = 1.3$), 3.68 (br s, 1H), 3.24 (br s, 1H), 2.10 (d, 3H, $J = 1.3$), 2.02 (dd, 1H, $J = 13.6$, 9.2), 1.85 (dd, 1H, $J = 13.6$, 8.9), 1.80–1.51 (m, 5H), 1.45–1.28 (m, 3H)	208.1, 181.6, 127.4, 81.4, 78.6, 34.9, 34.3, 30.6, 22.8, 22.6, 14.5		calcd for C ₁₁ H ₁₆ O ₃ 196.1099. Found: 196.1103
9c	0.41 (hex– EtOAc, 1:1)/ solid (mp 172– 174°C)	3399, 3337, 1701, 1618	5.80 (q, 1H, <i>J</i> = 1.4), 2.07 (d, 3H, <i>J</i> = 1.4), 2.05–1.90 (m, 1H), 1.89–1.65 (m, 11H)	209.4, 179.9, 127.5, 84.1, 81.8, 29.9, 27.3, 26.4, 26.3, 26.0, 14.1	Calcd for C ₁₁ H ₁₆ O ₃ : C, 67.32; H, 8.22. Found: C, 67.28; H, 8.20	
10c	0.15 (hex– EtOAc, 1:1)/ solid (mp 98– 101 °C)	3400, 1701, 1638	4.28 (s, 1H), 3.91 (br s, 1H), 3.36 (br s, 1H), 2.62 (ddd, 1H, <i>J</i> = 16.3, 8.2, 2.9), 2.48 (ddd, 1H, <i>J</i> = 16.3, 7.9, 3.2), 2.38–2.20 (m, 2H), 1.84–1.70 (m, 2H), 1.64–1.52 (m, 2H), 1.56–1.40 (m, 2H), 1.29 (s, 3H)	202.9, 176.5, 139.1, 82.1, 79.0, 31.2, 27.3, 26.5, 26.2, 23.2, 22.6		calcd for C ₁₁ H ₁₆ O ₃ 196.1099. Found: 196.1093
8d	0.53 (hex– EtOAc, 1:1)/ gum	3342, 1713	5.87 (q, 1H, J = 1.5), 4.77 (br s, 1H), 4.02 (br s, 1H), 2.08 (d, 3H, J = 1.5), 1.89–1.80 (m, 2H), 1.73–1.60 (m, 4H), 1.54–1.39 (m, 4H), 1.29–1.24 (m, 2H) (500 MHz, d^6 acetone)	206.4, 181.2, 127.3, 81.3, 78.9, 32.6, 28.9, 26.2, 25.6, 24.4, 23.4, 14.1 (125 MHz, acetone- <i>d</i> ₆)		
9d	0.63 (hex– EtOAc, 1:1)/ solid (mp 193– 194°C)	3449, 1699, 1640	5.68 (q, 1H, <i>J</i> =1.4), 2.05 (d, 3H, <i>J</i> =1.2), 2.01–1.70 (m, 12H), 1.61 (s, 1H), 1.51 (s, 1H)	210.1, 181.5, 127.2, 82.6, 79.3, 31.4, 29.3, 29.0, 28.4, 25.2, 24.6, 14.5		calcd for C ₁₂ H ₁₈ O ₃ 210.1256. Found: 210.1253
8f	0.50 (hex– EtOAc, 1:1)/ solid (mp 198– 201 °C)	3590, 1709	5.85 (q, 1H, J = 1.5), 4.83 (br s, 1H), 3.86 (br s, 1H), 2.17 (d, 3H, J = 1.5), 1.66–1.61 (m, 2H), 1.54–1.48 (m, 2H), 1.43–1.28 (m, 2H), 1.15 (d, 3H, J = 6.5), 1.13–1.08 (m, 1H) (500 MHz, d^6 acetone)	204.4, 181.2, 127.7, 80.8, 79.5, 41.8, 30.3, 29.4, 21.3, 16.8, 16.2 (125 MHz, ace- tone- <i>d</i> ₆)		
8g	0.45 (hex– EtOAc, 1:1)/ oil ^e	3564, 1717	6.00 (q, 1H, J = 1.0), 4.72 (br s, 1H), 4.04 (br s, 1H), 2.18–2.13 (m, 1H), 2.10 (d, 3H, J = 1.0), 1.93 (dt, 1H, J = 13.0, 5.5), 1.72–1.66 (m, 1H), 1.62–1.58 (m, 1H), 1.53–1.48 (m, 1H), 1.32–1.23 (m, 1H), 1.22–1.15 (m, 1H), 0.85 (d, 3H, J = 7.5) (500 MHz, d^6 acetone)	204.8, 177.4, 129.8, 81.7, 77.9, 36.7, 29.5, 27.9, 18.2, 17.8, 16.2 (125 MHz, ace- tone- <i>d</i> ₆)		
9f	0.45 (hex– EtOAc, 1:1)/ oil ^e		partial spectrum: 5.91 (q, 1H, <i>J</i> = 1.5), 3.31 (br s, 2H), 2.20 (d, 3H, <i>J</i> = 1.5), 2.20–2.11 (m, 2H), 1.52–1.46 (m, 1H), 1.48–1.46 (m, 1H), 1.26–1.22 (m, 1H), 1.16 (d, 3H, <i>J</i> = 7.0) (500 MHz, CDCl ₃)	206.2, 181.2, 127.3, 79.9, 79.1, 38.5, 30.1, 29.2, 19.2, 16.5, 16.2 (125 MHz, CDCl ₃)		

^a All ¹H NMR data were acquired at 300 MHz in CDCl₃ unless otherwise indicated. Coupling constants (*J*) are given in Hz.

^b All ¹³C NMR data were acquired at 75 MHz in CDCl₃ unless otherwise indicated.

^c Products **8g** and **9f** were isolated as an inseparable mixture. Careful iterative chromatography provided an enriched sample of **8g** for IR and NMR analysis. Partial NMR data for **9f** were obtained from the mixture.

Methanol Trapping: 1-Hydroxy-8-methoxy-11-methylbicyclo[6.3.0]undec-10-en-9-one (4d); Typical Procedure

Pyranone **2d** (105 mg, 0.55 mmol) was dissolved in dry MeOH (95 mL) in a quartz tube equipped with a magnetic stirring bar and rubber septum. The solution was purged with a stream of dry N_2 and

irradiated. Following complete consumption of **2d** (1.5 h; determined by TLC), the reaction mixture was concentrated and the residue was purified by flash chromatography (silica gel; $2 \text{ cm} \times 15 \text{ cm}$ column; Et₂O–CH₂Cl₂–hexanes, 2:1:1) to give 72 mg (59%) of **4d** as a pale yellow oil. See Table for characterization data.

Aqueous Trapping: 1,8-Dihydroxy-11-methylbicyclo-[6.3.0]undec-10-en-9-one (9d); Typical Procedure

Pyran-4-one **2d** (50 mg, 0.28 mmol) was dissolved in a 10% solution of H_2SO_4 (50 mL) in a polished quartz tube equipped with a magnetic stirring bar and rubber septum. The solution was purged with a stream of dry N_2 and irradiated for 1.5 h. The resulting solution was neutralized with solid Na_2CO_3 and extracted with EtOAc (2 × 100 mL). The organic layers were combined and dried (MgSO₄), then concentrated to give a yellow oil. Purification via radial disk chromatography (silica gel, 1 mm plate; EtOAc–hexanes, 1:4) gave 6 mg (10%) of **9d** as a white paste and 24 mg (41%) of **8d** as a white solid. See Table for characterization data.

References and Notes

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- (11) Molecular mechanics calculations (AM1)indicate that *cis*isomer **8b** is more stable than *trans*-isomer **9b** by as much as 12 kcal/mol.
- (12) In contrast, *trans*-isomers **9c** and **9d** did not undergo any isomerization under the reaction conditions.
- (13) X-ray diffraction data for 4e, 8d and 8f have been deposited with the Cambridge Crystallographic Data Centre (deposition numbers CCDC 158715, CCDC 158907 and CCDC 158908, respectively).
- (14) Hydroxyl proton assignments were confirmed by D_2O exchange. In acetone- d_6 , the hydroxyl protons of both *cis*-**8** and *trans*-**9** all appeared downfield of 4 ppm.
- (15) Higher concentrations of H_2SO_4 led to variable product ratios, presumably via acid-catalyzed isomerization as noted with **8b/9b**.
- (16) The UV absorbance data for known compounds **2a,b** have been previously reported: **2a** (MeOH): $\lambda_{max} 252 \text{ nm} (\varepsilon = 12.6 \times 10^3 \text{ cm}^{-1}\text{M}^{-1})$; **5 b** (MeOH): $\lambda_{max} 252 \text{ nm} (\varepsilon = 13.6 \times 10^3 \text{ cm}^{-1}\text{M}^{-1})$; **5 b** (EtOH): $\lambda_{max} 252 (\varepsilon = 5.6 \times 10^3 \text{ cm}^{-1}\text{M}^{-1})$.¹⁷ The data for **2c–f** are: **2c** (MeOH): $\lambda_{max} 256 \text{ nm} (\varepsilon = 10.2 \times 10^3 \text{ cm}^{-1}\text{M}^{-1})$; **2d** (MeOH): $\lambda_{max} 256 \text{ nm} (\varepsilon = 10.2 \times 10^3 \text{ cm}^{-1}\text{M}^{-1})$; **2d** (MeOH): $\lambda_{max} 256 \text{ nm} (10^{-5} \text{ M}; \varepsilon = 11.4 \times 10^3 \text{ cm}^{-1}\text{M}^{-1})$; **2e** (MeOH): $\lambda_{max} 266 \text{ nm} (10^{-5} \text{ M}; \varepsilon = 11.1 \times 10^3 \text{ cm}^{-1}\text{M}^{-1})$; **2f** (EtOH): $\lambda_{max} 262 \text{ nm} (\varepsilon = 7.5 \times 10^3 \text{ cm}^{-1}\text{M}^{-1})$.
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