Cyclopentadienone Epoxide: Synthesis and Photochemistry

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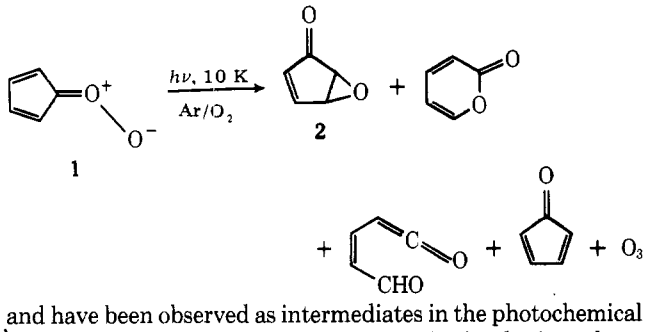
Received August 29, 1978

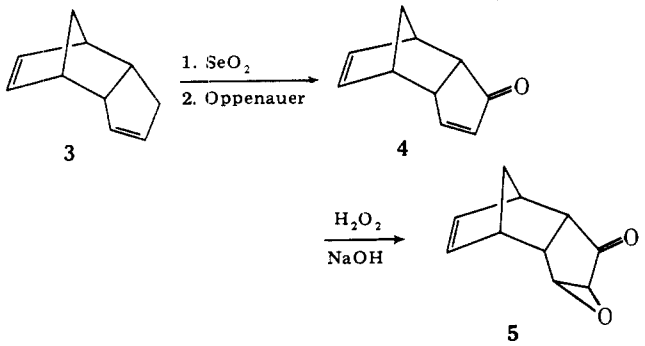
4,5-Epoxy-2-cyclopenten-1-one (**2**) was prepared by the vacuum pyrolysis of the dimethyl phthalate Diels–Alder adduct (**8**). Cyclopentadienone epoxide (**2**) was shown to be reasonably thermally stable but reactive toward nucleophilic and electrophilic reagents. Photolysis of matrix isolated **1** produces α-pyrone (**10**) and the aldehyde ene ketene (**9**).

In the course of our investigation of the photochemistry of cyclopentadienone *O*-oxide (**1**),[1] it became apparent that one of the photoproducts was the unknown cyclopentadienone epoxide (**2**). Alkyl and aryl derivatives of **2** are well-known[2–4]

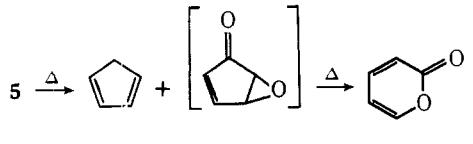


and have been observed as intermediates in the photochemical conversion of 4-pyrones to 2-pyrones. Aryl-substituted cyclopentadienone epoxides undergo reversible opening of the epoxide ring to pyrylium salts[5,6] and both alkyl- and aryl-substituted cyclopentadienone epoxides undergo irreversible isomerization to 2-pyrones[4,7–9] and 2-furaldehydes.[10,11] All attempts to prepare the parent cyclopentadienone epoxide (**2**) have been frustrated by the sensitivity of this system to acid-catalyzed rearrangement and nucleophilic attack.

We chose to use the thermal cleavage of a Diels–Alder adduct of cyclopentadienone epoxide as a means of avoiding the problems of electrophilic and nucleophilic attack. This approach has been used in the synthesis of reactive molecules[12] including the bicyclo[3.1.0]hex-3-en-2-ones.[13] Our initial approach began with dicyclopentadiene (**3**). Oxidation with

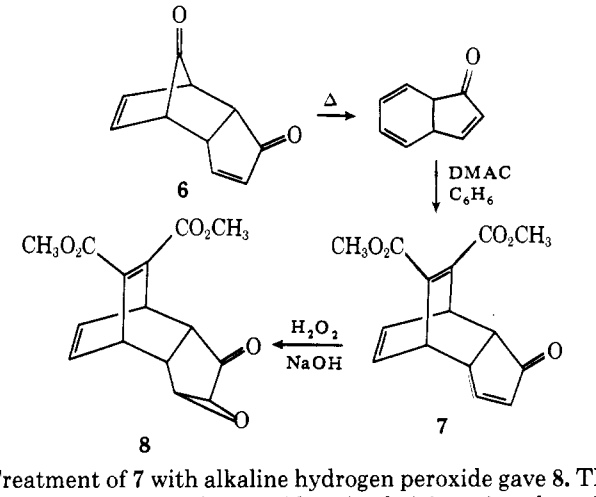


selenium dioxide followed by Oppenauer oxidation of the resulting allylic alcohols gave **4**,[14] and treatment of **4** with alkaline hydrogen peroxide gave the epoxide **5**. The epoxide (**5**) was sublimed (25 °C, 10^{-5} torr) through an oven (440 °C) and condensed onto a cesium iodide window (77 K). Infrared analysis of the condensate (77 K) showed complete conversion to cyclopentadiene and 2-pyrone. When the oven temperature was reduced to 380 °C, decomposition of the Diels–Alder adduct **5** was incomplete. The products were, however, still

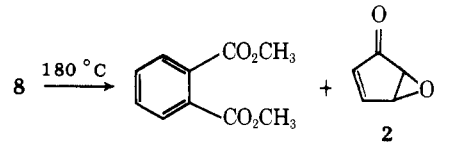


cyclopentadiene and 2-pyrone. These results directed our attention to the synthesis of an adduct of **2** which could be decomposed at a lower temperature. The experience of Fleming and Wildsmith in the synthesis of cyclobutene[15] seemed relevant, and we adopted their strategy of using an adduct which would give an aromatic compound as one product in the retro-Diels–Alder reaction.

Synthesis of the adduct **8** started from cyclopentadienone dimer (**6**).[16,17] Thermal elimination of carbon monoxide and trapping with dimethyl acetylenedicarboxylate gave **7**.



Treatment of **7** with alkaline hydrogen peroxide gave **8**. The stereochemistry of the epoxide **8** (and **5**) is assigned on the basis of attack by the hydroperoxide ion on the less hindered side (convex side) of the molecule. Vacuum thermolysis[18] of adduct **8** at an oven temperature of 180 °C followed by trapping on a cesium iodide window at 77 K gave dimethyl phthalate and a new compound with infrared bands at 1340, 1000, 853, and 794 cm^{-1} (the carbonyl region was obscured by dimethyl phthalate). When the oven temperature was raised to 410 °C, the products were dimethyl phthalate and 2-pyrone. It thus seemed probable that the product obtained at 180 °C was the desired cyclopentadienone epoxide (**2**). The identity of the product was rigorously established in an NMR experiment using the method of Anet and Squillacote.[19] Adduct **8** was decomposed at 180 °C, passed through a trap at −5 °C to



remove dimethyl phthalate, and condensed onto an aluminum surface at 77 K. Deuteriochloroform was slowly condensed onto the cold sample. Upon warming, the solution dripped into an NMR tube cooled at 77 K. The tube was then sealed and warmed to room temperature. The 200-MHz NMR spectrum of cyclopentadienone epoxide is shown in Figure 1. The ^{13}C NMR spectrum shows δ 199.2 (C=O), 155.4 (β-olefinic carbon), 133.9 (α-olefinic carbon), 53.4 and 51.1 (COC). Cy-

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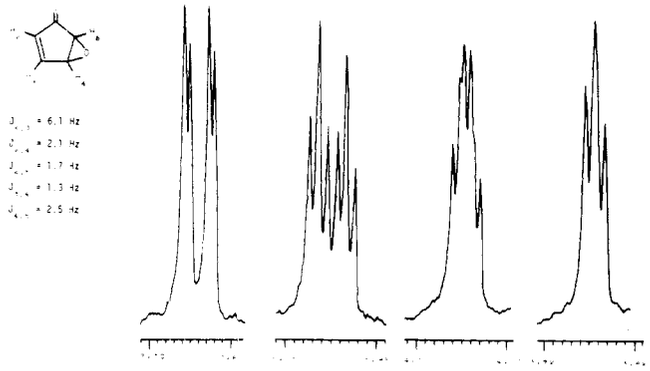
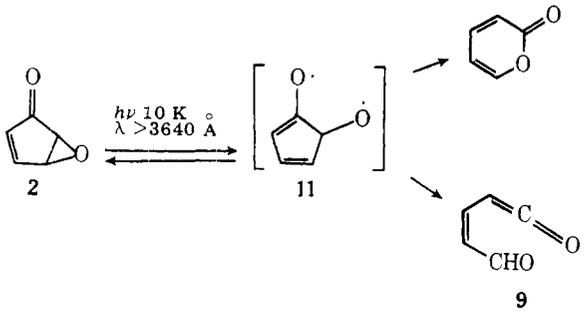


Figure 1. The 200-MHz ^1H NMR spectrum of 4,5-epoxy-2-cyclopenten-1-one. Assignments based on decoupling experiments are: δ 7.65 (H_3), 6.00 (H_2), 4.12 (H_4), and 3.67 (H_5).

clopentadienone epoxide may be isolated in 98% yield by collecting the effluent from the −5 °C trap in a silanized[20] second trap cooled to −78 °C. Cyclopentadienone epoxide in chloroform solution is stable when heated at 140 °C in a sealed tube for 12 h but is rapidly destroyed when carbon tetrachloride solutions are treated at room temperature with a trace of sodium methoxide, boron trifluoride etherate, or mineral acid.

A sample of cyclopentadienone epoxide matrix isolated in argon at 10 K has the infrared spectrum shown in Figure 2. Irradiation (λ >3640 Å) of matrix isolated **2** produces the aldehyde ene ketene **9** and 2-pyrone. It is probable that these transformations occur via the diradical **11** formed by cleavage



of the β-carbon–oxygen bond of the α,β-epoxy ketone. The identification of **9** and 2-pyrone is based on comparison of infrared spectra with the authentic materials and their photochemical conversion. 4-Cyclopentene-1,3,-dione, the product expected from α-carbon–oxygen bond cleavage in **2**, could not be observed.[21] In addition, no evidence for the existence of the oxypyrylium tautomer of the epoxide was found.

Experimental Section

4,5-Epoxytricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (5). Dicyclopentadien-3-one[14] (**4**) (7.97 g., 0.20 mol) was dissolved in 80 mL of methanol and 80 mL of dichloromethane. To this solution was added 40% hydrogen peroxide (18.0 mL) and 0.2 N sodium hydroxide (25.0 mL). The resulting two-phase system was vigorously stirred for 10 min. The layers were separated and the aqueous phase was extracted once with dichloromethane (200 mL). The combined organic layers were washed with water, dried over anhydrous sodium sulfate, and filtered. Removal of the solvent under aspirator pressure followed by sublimation gave the desired epoxide as a white solid (2.98 g, 92% yield): mp 136–139 °C (sealed tube); ^1H NMR ($CDCl_3$) δ 6.03 (m, 2 H), 3.58 (t, 1 H), 3.20 (m, 2 H), 3.10 (m, 2 H), 2.75 (m, 1 H), 1.61 (d, 1 H), 1.45 (d, 1 H); IR (CCl_4) 1745 cm^{-1}.

Anal. Calcd for $C_{10}H_{10}O_2$: C, 74.05; H, 6.21. Found: C, 73.91; H, 6.13.

Dimethyl Tricyclo[5.2.2.0^{2,6}]undeca-4,8,10-trien-3-one-8,9-dicarboxylate (7). Cyclopentadienone dimer (**6**) (3.0 g, 0.019 mol) was placed in the closed end of a 20 × 1.2 cm glass tube. The open end of the tube ended in a 14/20 male joint to which was attached a vacuum adapter inserted into a 100-mL receiving flask containing dimethylacetylene dicarboxylate (8.70 g, 0.06 mol) in benzene (40 mL). The central portion of the tube was packed with glass helices and resistively heated to 350 °C. The receiving flask was cooled to −78 °C, and the pressure in the system was reduced to 10^{-2} torr. The starting dione was sublimed (85 °C) through the hot zone, and the pyrolysate was collected in the cold trap. When sublimation was complete, the receiving flask was removed from the vacuum line, stoppered, and warmed to 45 °C for 10 h. The solvent was removed at aspirator pressure and excess dimethyl acetylenedicarboxylate was removed by heating to 100 °C under high vacuum. The orange solid which remained was recrystallized from carbon tetrachloride giving light tan needles (4.10 g., 78% yield): mp 120–121.5 °C; ^1H NMR ($CDCl_3$) δ 7.42 (dd, 1 H), 6.70 (m, 3 H), 4.39 (d, 1 H), 4.19 (m, 1 H), 3.80 (s, 6 H), 3.25 (m, 1 H), 2.64 (ddd, 1 H); IR (CCl_4) 1770 cm^{-1}.

Anal. Calcd for $C_{15}H_{14}O_5$: C, 65.70; H, 5.15. Found: C, 65.64; H, 5.26.

Dimethyl 4,5-Epoxytricyclo[5.2.2.0^{2,6}]undeca-8,10-dien-3-one-8,9-dicarboxylate (8). To a solution of the enone (**7**) (0.50 g, 1.8 mmol) in methanol (8 mL) and dichloromethane (8 mL) was added 30% hydrogen peroxide (1.3 mL) and 0.2 N sodium hydroxide (2.7 mL). The resulting two-phase system was vigorously stirred for 10 min. The layers were separated and the aqueous phase was extracted once with dichloromethane. The combined organic layers were washed with water, dried over anhydrous sodium sulfate, and passed through a short plug of silica gel and the solvent was removed under reduced pressure. Final traces of solvent were removed under high vacuum to give a white crystalline solid (0.46 g, 87% yield): mp 81–82 °C; ^1HNMR ($CDCl_3$) δ 6.42 (m, 2 H), 4.38 (m, 1 H), 4.25 (m, 1 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 3.65 (m, 1 H), 3.40 (m, 1 H), 2.90 (dd, 1 H), 2.60 (ddd, 1 H); IR (CCl_4) 1755, 1735 cm^{-1}.

Anal. Calcd for $C_{15}H_{14}O_6$: C, 62.07; H, 4.86. Found: C, 62.19; H, 4.76.

4,5-Epoxy-2-cyclopenten-1-one (2). The Diels–Alder adduct (**8**) (80.0 mg, 0.27 mmol) was sublimed (85 °C, 10^{-4} torr) through a glass helices packed tube resistively heated to 180 °C. The pyrolysate was passed through a trap cooled to −5 °C to remove the dimethyl phthalate, and the trap effluent was collected at −78 °C in a silanized second trap (26.0 mg, 98% yield): ^1HNMR ($CDCl_3$) δ 7.65 (dd, 1 H, J = 6.1, 1.3 Hz), 6.00 (ddd, 1 H, J = 6.1, 2.1, 1.7 Hz), 4.12 (m, 1 H, J = 2.5, 2.1, 1.3 Hz), 3.67 (dd, 1 H, J = 2.5, 1.7 Hz); ^{13}C NMR δ 199.2 (C=O), 155.4 (β-olefinic carbon), 133.9 (α-olefinic carbon), 53.4 and 51.1 (COC); IR (Ar matrix) 1750 (s), 1742 (m), 1558 (w), 1340 (m), 1178 (w), 1170 (w), 1002 (m), 962 (w), 940 (w), 855 (s), 828 (m), 794 (s), 738 (m), 700 (w), 450 (m), 439 (m) cm^{-1}; UV (cyclohexane) λ_{max} 221, 274

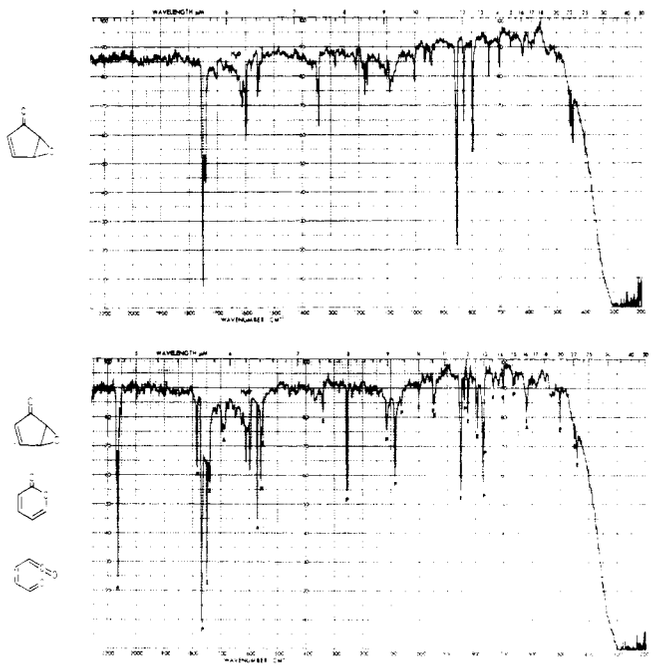


Figure 2. (Top) The infrared spectrum of 4,5-epoxy-2-cyclopenten-1-one isolated (1:1000) in an argon matrix at 10 K. (Bottom) The infrared spectrum of the same sample after irradiation (20 min, λ >3640 Å) shows 2-pyrone (P), the aldehyde ene ketene (A), and unconverted starting material (E).

(sh), 283 (shoulder tailing to ~385 nm); mass spectrum *m/e* 96 (M^+, 0.77), 68 ($C_4H_4O^+$, 1.0).

Acknowledgment. This research was supported by Grant GM-24427 from the National Institute for General Medical Sciences, U.S. Department of Health, Education and Welfare and by Grant CHE75-10939 from the National Science Foundation. The 200-MHz NMR spectrometer used in these studies was purchased with NSF Grant CHE76-05926 awarded to the Department of Chemistry, UCLA.

Registry No.—**2**, 68781-88-4; **4**, 5530-96-1; **5**, 68781-89-5; **6**, 14224-63-6; **7**, 68781-90-8; **8**, 68781-91-9; dimethyl acetylenedicarboxylate, 762-42-5.

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Metabolites of the Marine Sponge *Chondrosia collectrix*

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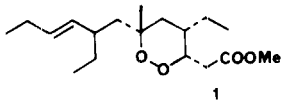
Received September 12, 1978

The Caribbean sponge *Chondrosia collectrix* contained antimicrobial metabolites when freshly collected, but these compounds were absent after storage in ethanol. The ethanol extracts contained five major metabolites, the ketal **3**, hemiketals **4** and **5**, the α,β-unsaturated ester **6**, and the diol **7**. A dichloromethane extract of lyophilized sponge contained a mixture of peroxide acids **17** and **18** together with the corresponding methyl esters **15** and **16** and the hemiketal **4**. The peroxides **15–18** were responsible for mild antibacterial activity.

During a study of Caribbean sponges, we have encountered a number of compounds which appear to be derived from fatty acids with methyl and ethyl side chains. The first example of these compounds were plakortin (**1**) and a related ketone **2** from a sample of *Plakortis halichondrioides*.[1] In this



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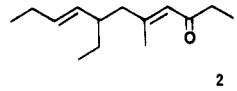

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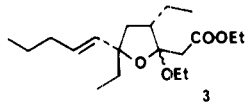

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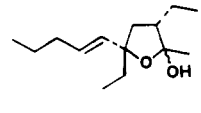

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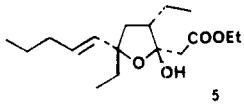

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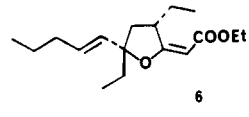

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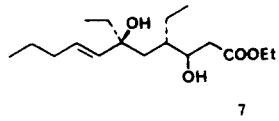

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paper we wish to report the identification of several metabolites from ethanol extracts of *Chondrosia collectrix* and different metabolites from a dichloromethane extract of the lyophilized sponge.

The ether-soluble portion of the ethanolic extract (3 months at 0 °C) of *Chondrosia collectrix*[2] was chromatographed on Florisil to obtain, in order of increasing polarity, the ketal **3** (0.4% dry weight), the hemiketal **4** (0.4% dry weight), the hemiketal ester **5** (0.9% dry weight), the ester **6** (0.2% dry weight), and the diol **7** (1.2% dry weight). The structure of the hemiketal ester **5** was determined by analysis of spectral data followed by a degradation sequence.

The hemiketal **5** had the molecular formula $C_{17}H_{30}O_4$. As expected for a hemiketal, dehydration occurred in the mass spectrometer to give $M - H_2O$ as the highest observed ion. The infrared spectrum contained hydroxyl and ester bands at 3600 and 1725 cm^{-1}, respectively. The ^{13}C NMR spectrum contained signals for an ester carbonyl at δ 171.8, two olefinic carbons at δ 135.5 (d) and 128.0 (d), a hemiketal carbon at δ 103.7 (s), two carbons bearing oxygen at δ 84.8 (s) and 60.6 (t), and 11 other carbon atoms. The ^1H NMR spectrum contained signals for an ethyl ester at δ 1.29 and 4.24 and a disubstituted olefin at δ 5.35 (d, 1 H, J = 15 Hz) and 5.55 (dt, 1 H, J = 15, 7, 7 Hz), an AB quartet at δ 2.57 and 2.76 (J = 15 Hz) assigned to the protons at C-2, and three additional methyl triplets at δ 0.86, 0.90, and 0.92.

Ozonolysis of the hemiketal **5** in ethyl acetate solution at −78 °C followed by hydrogenation of the ozonide over 10% palladium on charcoal at 0 °C gave an aldehyde **8**, which rearranged on silica gel chromatography to produce the unsaturated keto ester **9**. The keto ester **9** had the molecular formula $C_{13}H_{20}O_4$, indicating that *n*-butyraldehyde had been lost during ozonolysis. The infrared spectrum of the keto ester

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