Reaction of Enedione Epoxides with Base[1]

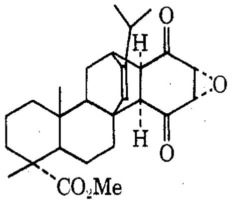
Werner Herz,* V. S. Iyer, and M. Gopal Nair

Department of Chemistry, The Florida State University, Tallahassee, Florida 32306

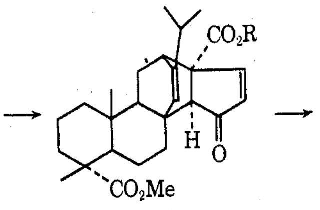
Received July 8, 1975

Epoxides of bridged enediones, such as adducts of cyclopentadiene and cyclohexadienes with *p*-benzoquinones, undergo Favorskii-type ring contraction to γ-carbethoxy-α,β-unsaturated cyclopentenones on treatment with ethanolic sodium hydroxide. Thermal decarboxylation of the corresponding acids to α,β-unsaturated cyclopentenones involves an anionic-type transition state. Epoxides of unbridged enediones, i.e., adducts of butadienes with *p*-benzoquinone, do not undergo Favorskii-type ring contraction with ethanolic sodium hydroxide, but nucleophilic displacement to yield hydroxybenzoquinones.

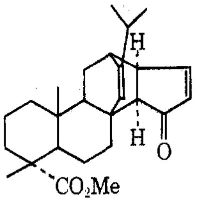
In the course of earlier work[2] we transformed the epoxide 1 to **2a** by treatment with base and thence, by hydrolysis and decarboxylation, to the cyclopentenone **3**. It occurred to us that this series of reactions, whose first step involved the Favorskii rearrangement of an enedione epoxide, might offer a general route to alicyclic systems incorporating a cyclopentenone moiety, since the starting materials are readily prepared by the Diels–Alder reaction. In the present paper we report our study of this procedure with some model compounds.



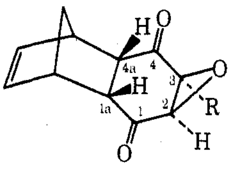
1



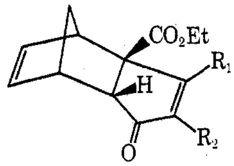
2a, R = Et
b, R = H



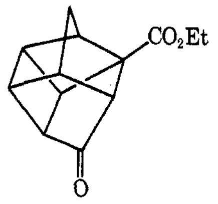
3



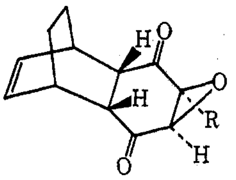
4a, R = H
b, R = Me



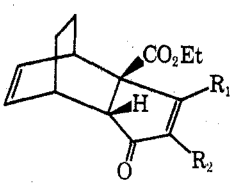
5a, R₁, R₂ = H
b, R₁ = Me; R₂ = H
c, R₁ = H; R₂ = Me



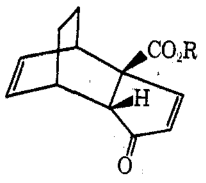
6



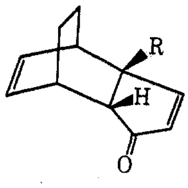
7a, R = H
b, R = Me



8a, R₁, R₂ = H
b, R₁ = Me; R₂ = H
c, R₁ = H; R₂ = Me



9a, R = H
b, R = D



10a, R = H
b, R = D

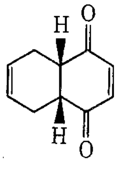
Reaction of **4a** and **7a** with a small amount of sodium hydroxide in ethanol indeed resulted in rearrangement to esters **5a** and **8a** in high yield. In the case of **5a**, the stereochemistry of the rearrangement product was verified by photolytic conversion to the cage isomer **6** and is in accord with the discussion presented earlier.[2]

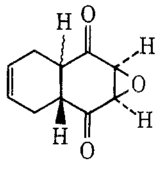
Rearrangement of **4b** afforded two isomeric esters in the ratio 3:2. The major product **5c** and the minor product **5b** were easily distinguishable by NMR spectrometry, since the cyclopentenone vinyl proton of **5c** should resonate at lower field than that of **5b** (7.1 vs. 5.8 ppm) and since these signals can be identified readily by being coupled allylically to the vinyl methyl group. Similarly, rearrangement of **7b** gave **8c** and **8b** in the ratio 3:2, the distinction being made on the same grounds (6.9 vs. 5.9 ppm).

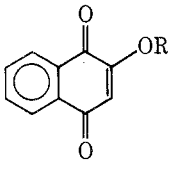
In terms of the Loftfield mechanism for the Favorskii rearrangement, **5b** and **8b** arise through displacement of an oxirane bond by the enolate of C_{7a} and **5c** and **8c** by the enolate at C_{4a}. In contrast to the situation prevailing in the case of **1**, there is obviously little regioselectivity in the simple substances under discussion here, although the products arising from attack of enolate on the tertiary center are formed in somewhat larger amounts.

The hydrolysis and decarboxylation step was examined in the case of **8a**. Hydrolysis to **9a** followed by pyrolysis afforded **10a** in excellent yield. We have not previously commented on the details of the decarboxylation step, which, because it results in the exclusive formation of an α,β- instead of a β,γ-unsaturated cyclopentenone, is not likely to proceed via the cyclic mechanism of Linstead[3] and Barton[4] or the β-carbonium ion mechanism of Johnson.[5] We assume that the presence of the ketone group is responsible for this departure from the path by which β,γ-unsaturated acids normally undergo decarboxylation and that, in the case of **2b** and **9a**, pyrolytic decarboxylation is initiated by (for steric reasons) intermolecular proton transfer from the carboxyl to the ketone group. Subsequent decarboxylation would lead to an incipient carbanion (stabilized to some extent by the protonated carbonyl) which is in turn protonated exclusively at the γ position by a second intermolecular proton transfer.[6]

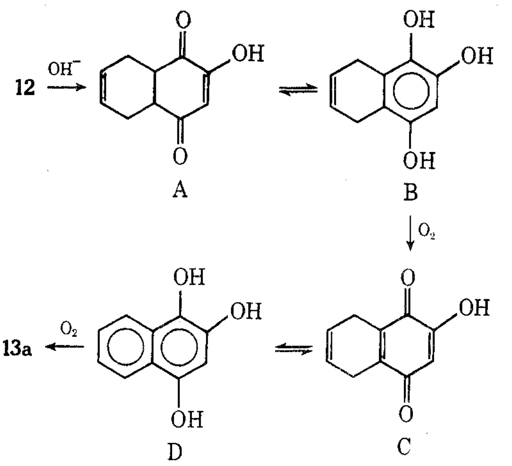
Evidence against a mechanism involving initial formation of a β,γ-unsaturated cyclopentenone was also provided by the following experiment. Pyrolysis of **9b** afforded a substance **10b** containing the deuterium label exclusively at the γ position, as evidenced in the NMR spectrum by collapse of the H-2 and H-3 doublets of doublets to doublets. Any series of steps involving intra- or intermolecular proton transfer from the carboxyl group to C-2 and subsequent double bond isomerization to an α,β-unsaturated cyclopentenone would have resulted in scrambling of label between C-2 and C-4.


11

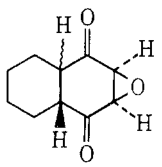

12a, β-H
b, α-H

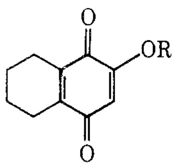

13a, R = H
b, R = Me

Under the conditions successfully used for the rearrangement of **4a, 4b, 7a,** and **7b, 12a** and the more stable trans isomer **12b** were recovered unchanged. Use of excess sodium hydroxide in aqueous ethanol resulted in formation of a highly colored aromatic substance identified as **13a** by methylation to **13b.** This is obviously the result of bimolecular nucleophilic displacement by external hydroxide ion and subsequent elimination in the manner demonstrated earlier[7,8] for the reaction of **4** and **7** with thiols. In base, the initially formed hydroxyenedione A tautomerizes to the anion of B which may undergo air oxidation to C. Further tautomerization to D and another oxidation step would lead to **13a.** Thus, exclusion of air resulted in formation of a yellow intermediate, possibly A or B, but exposure to air during work-up again produced **13a.**



Similarly, reaction of **14a** and **14b** obtained from **12a** by hydrogenation (ethyl acetate–10% Pd/C) and subsequent isomerization gave **15a** which was characterized as **15b.**


14a, β-H
b, α-H


15a, R = H
b, R = Me

Thus bridged enedione epoxides uniformly undergo the Favorskii rearrangement with base, possibly because of steric interference with approach of the nucleophile from the endo side, whereas unbridged relatively unhindered enedione epoxides like **12** and **14** react by the bimolecular displacement–elimination pathway. This behavior would seem to limit severely the utility of enedione epoxides as precursors of substituted cyclopentenones, although increased substitution on the epoxidic carbon atoms might conceivably direct the reaction into the Favorskii rearrangement path.[10]

Experimental Section

Epoxidations. Epoxidations of the Diels–Alder adducts of cyclopentadiene and cyclohexadiene with p-benzoquinone and methyl-p-benzoquinone were carried out as described in the literature[7,8,12] to give **4a, 4b, 7a,** and **7b** in essentially quantitative yield.

Epoxidation of the butadiene-p-benzoquinone adduct required low temperature and short reaction time and was carried out as follows. To a solution of 8 g of **11** in 20 ml of acetone immersed in a freezing mixture was added with stirring (N_2 atmosphere) 10 ml of ice-cold freshly prepared 20% sodium carbonate solution followed immediately by 40 ml of 30% hydrogen peroxide. After 3 min of stirring at low temperature, the mixture was diluted with water and extracted with ether. The washed and dried ether layer was evaporated and the residue crystallized from petroleum ether, yield 5 g (68%) of **12a** after recrystallization from petroleum ether, mp 72°, NMR signals at 5.6 br (vinyl protons), 3.55 (protons under epoxide), 3.25 m (protons at ring junction), and 2.1 in (methylenic protons).

Anal. Calcd for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66; O, 26.94. Found: C, 67.00; H, 5.62; O, 27.28.

Chromatography of 1 g of **12a** over alumina and elution with chloroform produced a 3:1 mixture of **12b** and **12a.** Recrystallization of the mixture from chloroform–ether afforded **12b,** mp 172°, NMR signals at 5.6 c (vinyl protons) and 3.65 ppm (epoxidic protons). The methylene and methinyl region was complex.

Anal. Calcd for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66, O, 26.94. Found: C, 67.38; H, 5.62; O, 27.28.

Favorskii Rearrangements. Rearrangements of **4a, 4b, 7a,** and **7b** were carried out as described below for **1a.** To a solution of 2 g of **4a** in 30 ml of absolute ethanol was added 0.5 ml of saturated sodium hydroxide solution. After 0.5 hr, the highly colored solution was evaporated and reduced pressure, diluted with water, and extracted with ether. The washed and dried ether layer was evaporated and the residue was chromatographed over Florisil to furnish 1.8 g of gummy **5a** which had ir bands at 1720 (ester), 1695, and 1640 cm^{-1} (conjugated cyclopentenone); λ_{max} 230, 325 nm (ϵ 12600, 60), NMR signals at 7.50 d ($J \simeq 5$ Hz, β proton), 5.95 d (AJ, α proton), 6.00 (2 H, vinylic protons of bridge), 4.27 q (J = 7 Hz, $-OCH_2CH_3$), 3.00 br (methine), 1.82 (center of AB system, J = 11 Hz, methylene), 1.30 t ppm (7, methyl).

Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47; O, 21.99. Found: C, 71.20; H, 6.46; O, 21.89.

Rearrangement of **4b** gave a quantitative yield of **5b** and **5c** (2:3 ratio). The two compounds were separated by preparative TLC (chloroform–ethyl acetate, 9:1). The less polar substance (**5b**) was a gum: ir bands at 1725, 1690, and 1640 cm^{-1}; λ_{max} 240, 330 nm (ϵ 12800, 70); NMR signals at 6.05 br (2 H, vinyl protons of bridge), 5.8 br (α-vinyl proton), 4.25 q (2 H, $-OCH_2CH_3$), 3.4 br (proton α to carbonyl) 3.2 br (bridgehead protons), 2.00 br (vinyl methyl), 1.8 (center of AB, J = 12 Hz, methylene) 1.30 ppm t (7, $-OCH_2CH_3$).

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94; O, 20.60. Found: C, 72.50; H, 6.85; O, 20.40.

The more polar product (**5c**) was a gum: ir bands at 1725, 1690, 1635 cm^{-1}; λ_{max} 235, 325 nm (ϵ 12500, 70); NMR signals at 7.1 br (β proton), 6.00 br (bridge vinyl protons), 4.25 q (J = 7 Hz, $-OCH_2CH_3$), 3.3 br (3 H, bridgehead proton and proton α to carbonyl), 1.8 (center of AB, J = 12 Hz, methylenes), 1.65 (α-vinyl methyl), 1.30 ppm t (7, $-OCH_2CH_3$).

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94; O, 20.60. Found: C, 72.00; H, 6.70; O, 20.59.

Rearrangement of **7a** gave **8a** as a gum in 95% yield: ir bands at 1720, 1700, and 1640 cm^{-1}; NMR signals at 7.41 d and 6.05 d (J = 6 Hz, β and α protons of cyclopentenone), 5.95 (J = 3 Hz, 2 vinyl protons of bridge), 4.15 q and 1.25 ppm t (J = 7 Hz, ethoxyl).

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 71.88; H, 6.90.

Hydrolysis of **8a** with 10% methanolic sodium hydroxide solution, removal of solvent at reduced pressure, acidification of the residue, and recrystallization from methanol afforded **9a:** mp 134–135°; ir bands at 3300 (broad) and 1710 (carboxyl), 1705, and 1645 cm^{-1} (cyclopentenone); NMR signals similar to those of **8a** except for the absence of the ethoxyl.

Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.92. Found: C, 70.99; H, 6.10.

Rearrangement of **7b** in the same manner gave a mixture of gummy **8b** and **8c** (90%, 2:3 ratio) which was separated by preparative TLC as described for **5b** and **5c.** The less polar substance **8b** had ir bands at 1725, 1695, and 1635 cm^{-1}; λ_{max} 238, 328 nm (ϵ 12000, 70); NMR signals at 5.9 m (superimposed α-vinyl and vinyl bridge protons), 2.00 ppm br (β-vinyl methyl), and the usual ethoxyl resonances.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37; O, 19.49. Found: C, 72.83; H, 7.38, O, 19.72.

The more polar product **8c** had ir bands at 1720, 1690, 1635 cm^{-1}; λ_{max} 235, 330 nm (ε 11800, 68); NMR signals at 6.90 br (β-vinyl proton), 5.9c (two vinyl protons), 1.7 ppm br (α-vinyl methyl), and the usual ethoxyl resonances.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37, O, 19.49. Found: C, 72.89; H, 7.51; O, 19.49.

Catalytic Reduction of 12a and 12b. A solution of 2 g of **12a** in 30 ml of ethyl acetate was hydrogenated for 24 hr in the presence of 0.2 g of Pd/C. Filtration, evaporation at reduced pressure, and recrystallization from ether–hexane afforded **14a** in quantitative yield: mp 60–61°; ir band at 1720 cm^{-1}; NMR signals at 3.65 (2 H, epoxidic protons), 3.15 m (proton at ring junction), 1.58 ppm m (methylenes).

Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71; O, 26.64. Found: C, 66.75; H, 6.77; O, 26.37.

Reduction of **12b** in the same fashion and recrystallization of the crude product from hexane afforded **14b**, mp 53–54°, ir band at 1720 cm^{-1}. The same substance was obtained by chromotography of **14a** over alumina and elution with chloroform.

Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71; O, 26.64. Found: C, 67.00; H, 6.70; O, 26.30.

Reactions of 12 and 14 with Base. Reaction of **12a** with base under the conditions described for **4a, 4b, 7a,** and **7b** resulted in recovery of starting material **12a** and **12b**; hence excess base was employed. To a solution of 1.0 g of **12a** in 30 ml of 95% ethanol was added with stirring at ice bath temperature (nitrogen atmosphere) 15 ml of 10% sodium hydroxide solution. After 20 min, the mixture was diluted with water, acidified with HCl, and filtered. Methylation of the brown solid **13a** with diazomethane in the usual fashion afforded 0.9 g of **13b**, mp 183° (lit.[13] mp 183.5°). Treatment of **12b** with base followed by methylation also gave **13b** in 90% overall yield.

Reaction of **14a** or **14b** with base in the manner described in the previous paragraph followed by methylation of the crude product with diazomethane gave **15** in 90% yield, mp 170–171° (lit.[14] mp 171°, 172°).

Photocyclization of 5a. A solution of 0.5 g of **5a** in 50 ml of methanol was irradiated for 20 hr in a photochemical reactor with a Hanovia 450 lamp using a Pyrex filter. The solution was evaporated at reduced pressure and the residue chromatographed over 20 g of alumina. Elution with benzene afforded 0.45 g of noncrystalline **6**: ir band at 770 cm^{-1} (strained cyclopentanone); λ_{max} 285 nm (ε 68); NMR signals at 4.20 q (2 H) and 1.28 t (3 H, J = 7 Hz, ethoxyl), 2.2–3 ppm c (9 H, methinyl and methylene protons).

Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47; O, 21.99. Found: C, 71.25; H, 6.40; O, 21.80.

Decarboxylation of 9a. Decarboxylation was achieved by heating the substance in a slow stream of nitrogen at 150° for 15 min until CO_2 evolution had ceased. Trituration of the product (**10**) with methanol resulted in crystallization. The material, mp 103°, was homogeneous on TLC, and had significant NMR signals at 7.60 dd (J = 6 Hz, 3, β proton) and 6.30 ppm dd (J = 6 Hz, 2, α proton).

Anal. Calcd for $C_{11}H_{12}O$: C, 87.46; H, 7.55. Found: C, 82.78; H, 7.51.

A solution of 0.1 g of **9a** in 3 ml of $CDCl_3$ was mixed with 2 ml of D_2O and stirred thoroughly. After 15 min, a portion of the mixture was transferred to an NMR sample tube; the NMR spectrum exhibited no OH absorption. The mixture was dried by addition of anhydrous sodium sulfate, filtered, and evaporated. The residue (**9b**) was pyrolyzed as described in the preceding paragraph. The NMR spectrum of the crude product (**10b**) now displayed the β- and α-cyclopentenone protons as doublets at 7.60 and 6.30 ppm (J = 6 Hz). On thin layer examination, **10b** exhibited R_f values identical with those of **10a**.

Registry No.—**4a**, 15052-12-7; **4b**, 15052-13-8; **5a**, 56689-06-6; **5b**, 56689-07-7; **5c**, 56689-08-8; **6**, 56689-09-9; **7a**, 56711-55-8; **7b**, 56711-56-9; **8a**, 56689-10-2; **8b**, 56689-11-3; **8c**, 56689-12-4; **9a**, 56689-13-5; **10a**, 56689-14-6; **11**, 35043-92-6; **12a**, 56689-15-7; **12b**, 56711-57-0; **14a**, 56689-16-8; **14b**, 56711-58-1.

References and Notes

(1) Supported in part by grants from the National Science Foundation (GP-12582) and the donors of the Petroleum Research Fund, administered by the American Chemical Society.
(2) W. Herz and M. G. Nair, *J. Org. Chem.*, **34**, 4016 (1969).
(3) R. P. Linstead, *J. Chem. Soc.*, 1603 (1930).
(4) D. H. R. Barton and C. J. W. Brooks, *J. Chem. Soc.*, 257 (1951).
(5) W. S. Johnson and W. E. Heinz, *J. Am. Chem. Soc.*, **71**, 2913 (1949).
(6) This view was originally supported by the observation that if a few drops of sulfuric acid are added to an ethanol solution of **2a**, the decarboxylation proceeds smoothly at the boiling point.[2]
(7) D. F. O'Brien and J. W. Gates, Jr., *J. Org. Chem.*, **30**, 2593 (1965).
(8) H. S. Wilgus III, E. Frauenglass, P. P. Chiesa, G. H. Nawn, F. J. Evans, and J. W. Gates, *Can. J. Chem.*, **44**, 603 (1966).
(9) It should be noted that bimolecular nucleophilic displacement reactions of **4** and **7** with mercaptans[7,8] were very slow.
(10) R. W. Mouk, K. M. Patel, and W. Reusch, *Tetrahedron*, **31**, 13 (1975).
(11) For experimental details see W. Herz, M. G. Nair, and D. Prakash, *J. Org. Chem.*, **40**, 1017 (1975).
(12) K. Alder, F. H. Flock, and H. Beumling, *Chem. Ber.*, **93**, 1896 (1960).
(13) L. F. Fieser, *J. Am. Chem. Soc.*, **48**, 2922 (1926).
(14) E. Hecker and R. Lattrell, *Justus Liebigs Ann. Chem.*, **662**, 48 (1963); J. Cunningham, E. Haslam, and R. D. Haworth, *J. Chem. Soc.*, 2875 (1963).

Epoxydiazo Ketones. Synthesis and Reactions

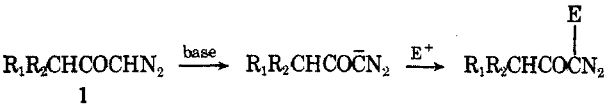
Neil F. Woolsey* and Mohammed H. Khalil

Department of Chemistry, University of North Dakota, Grand Forks, North Dakota 58202

Received May 27, 1975

Darzens condensation of 3-chloro-1-diazopropanone with nonenolizable aldehydes and base in equal molar amount yielded 1-diazo-4-R-3,4-epoxy-2-butanones (**7**) [**a**, R = Ph; **b**, R = 4-$NO_2C_6H_4$; **c**, R = 4-$CH_3OC_6H_4$; **d**, R = (*E*)-PhCH=CH; **e**, R = 2-thienyl]. Under conditions of higher base and excess aldehyde molar ratios, **7** and diadducts of 2-diazo-1,5-di-R-4,5-epoxy-1-hydroxy-3-pentanones (**8**) were produced. The reactions of **7a–c** with hydrogen chloride gas in ether generated α-chloro ketones and opened the epoxide ring in the case of **7a** and **7c**. Photolysis of **7a** in methanol gave methyl 4-hydroxy-4-phenyl-2-butenoate (**32**). Pyrolysis of **7a** in refluxing methanol gave 1,1-dimethoxy-4-phenyl-3-buten-2-one (**34**).

Previous work has established that diazomethyl ketones undergo a variety of base-catalyzed reactions in a nondestructive manner[1], i.e., the diazo ketone moiety is maintained in the products. For the most part these reactions result from the facile formation of an anion at the diazomethyl carbon followed by reaction with electrophile (reaction 1).



$$R_1R_2CHCOCHN_2 \xrightarrow{\text{base}} R_1R_2CHCO\bar{C}N_2 \xrightarrow{E^+} R_1R_2CHCO\overset{E}{\overset{|}{C}}N_2 \quad (1)$$

1

In cases where anion formation could take place at either the diazomethyl or the 3 carbon, the greater acidity of the diazomethyl hydrogen directed condensation to this posi-