(12) The IR spectra were determined with Perkin-Elmer Model 237B and Beckmann Model IR-9 infrared recording spectrophotometers. The NMR spectra were determined at 60 MHz with a Jeol Model C-60H and at 100 MHz with a Varian Associates Model HA-100 NMR spectrometer. The chemical shifts are expressed in δ values (parts per million) relative to an Me_4Si internal standard. The mass spectra were obtained with a Consolidated Electronics Corp. Model 110-21B and a Varian Associates Model CH5 mass spectrometer. Gas chromatographic analyses (GLC) were performed on a Hewlett-Packard Model 402 high efficiency chromatograph with a flame ionization detector attached to a Hewlett-Packard Model 3380A integrator.

(13) M. J. Mintz and C. Walling, *Org. Synth.*, **49**, 9 (1969).

(14) D. Jentzsch, "Gas Chromatographie", Frankh'sche Verlagshandlung, Stuttgart, 1968, pp 61–62 and 98.

(15) Prepared (84%) by the acetylation (1:1 Ac_2O–pyridine) of 5-hydroxy-2-pentanone: bp 100 °C (14 torr); IR (film) 1740, 1716 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 4.13 (2 H, t, J = 7 Hz), 2.60 (2 H, t, J = 7 Hz), singlets at 2.20 (3 H, s) and 2.07 (3 H, s) that are superimposed on 1.93 (2 H, quintet, J = 7 Hz); MS *m/e* (rel intensity) 144 (M^+, 4), 101 (17), 87 (18), 84 (16), 58 (20), 43 (100).

Endoperoxides of Naphthalenes. Synthesis and Reactions of Substituted 2,3-Epoxynaphthalene 1,4-Endoperoxides

Michio Sasaoka and Harold Hart*

Department of Chemistry, Michigan State University, East Lansing, Michigan 48824

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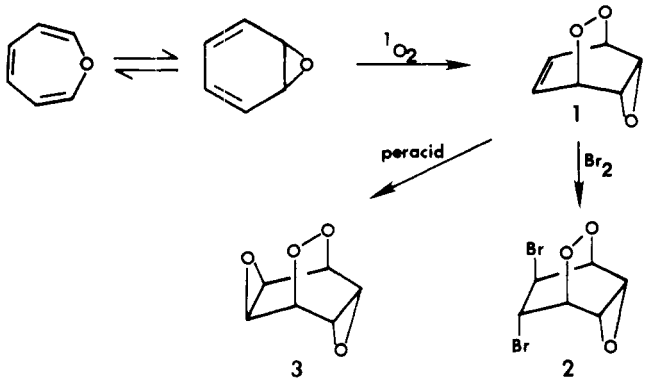
Oxidation of the 1,4-endoperoxides of 1,2,3,4-tetramethyl- or octamethylnaphthalene with *m*-chloroperbenzoic acid gave the stable, crystalline epoxy endoperoxides **8** and **9**. Epoxidation occurred predominantly syn to the peroxide bridge. The *syn*-epoxy peroxides underwent acid-catalyzed solvolytic rearrangement to the stable peroxy acetals **14** and **24**, respectively, but the *anti*-epoxy endoperoxide **8a** was recovered under similar conditions. The rearrangement involves a 1,2-aryl migration. Catalytic hydrogenolysis of **14** gave *cis*-1-acetyl-1,2,3-trimethylindan-2,3-diol (**16**), which was obtained independently from the acid-catalyzed methanolysis of the *syn*-epoxide of 1,2,3,4-tetramethylnaphthalene 1,4-endoxide (**19**). Deuterium labeling studies support the proposed mechanism for these rearrangements (Scheme II). Thermolysis of the epoxy endoperoxide **8s** occurs with O–O bond cleavage, as established by trapping the intermediate diradical with good hydrogen donors (diglyme, benzhydrol) to give the epoxydiol **10s**, synthesized independently by hydrogenolysis of **8s**. In the absence of trapping agent, thermolysis of **8s** occurs with loss of a methyl group to give the ketone **33**.

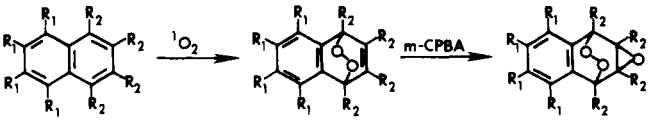
Endoperoxides of polycyclic aromatic compounds have been the subject of many investigations owing to their synthetic usefulness[1] and their biological importance.[2] Anthracenes and higher polyarenes are well known to give endoperoxides with singlet oxygen,[3] but only a few naphthalene endoperoxides have been similarly prepared.[4-6] Electron-donating groups on the 1 and 4 positions are necessary for the reaction of naphthalenes with singlet oxygen.[7]

Naphthalene endoperoxides have an isolated 2,3 double



bond which could be used for further functionalization of the molecule, and it was our purpose in this work to explore that possibility. Indeed, a similar double bond in oxepin endoperoxide **1** was found to undergo epoxidation and bromine addition.[8] More recently, the reduction of such strained double bonds by diimide without reducing the peroxide bond has been described.[9]

We were able to epoxidize the 1,4-endoperoxides of 1,2,3,4-tetramethylnaphthalene[5] and octamethylnaphthalene[6] to give extremely stable[10] epoxy peroxides **8** and **9**. We wish to report here on the synthesis and chemistry of these compounds, and in particular on their acid-catalyzed solvolysis



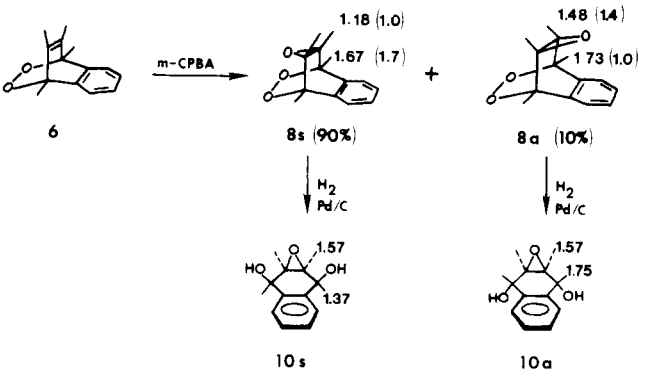
4; R_1 = H, R_2 = CH_3 **6**; R_1 = H, R_2 = CH_3 **8**; R_1 = H, R_2 = CH_3

5; R_1 = R_2 = CH_3 **7**; R_1 = R_2 = CH_3 **9**; R_1 = R_2 = CH_3

to give another class of surprisingly stable bicyclic peroxides.

Results and Discussion

Epoxy Endoperoxide of 1,2,3,4-Tetramethylnaphthalene. Oxidation of endoperoxide **6**[5] with *m*-chloroperbenzoic acid (*m*-CPBA) gave two isomeric epoxy endoperoxides in a 9:1 ratio.[1] These isomers were separated after recrystallization from ether. The major isomer formed colorless rods, and the minor isomer formed colorless cloudy plates which could be separated mechanically (tweezers). Catalytic hydrogenolysis of each isomer gave an epoxydiol. The NMR spectra of the epoxy endoperoxides and diols were consistent with the symmetry of their structures.[12] The peak assignments for the



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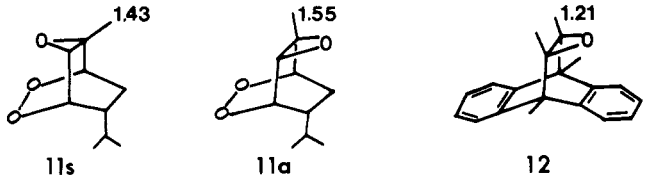
various methyl groups in 8 and 10 were made through deuterium labeling (vide infra).

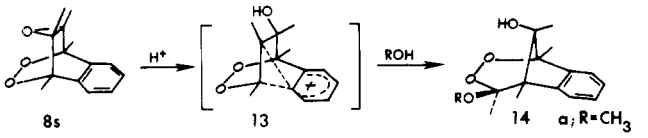
The major isomer was assigned the syn configuration and the minor isomer the anti configuration on the basis of the chemical shifts of the methyl groups on the epoxide rings, and on dipole moments.[13] The upfield chemical shift of the epoxide methyls in the syn isomer (δ 1.18) compared with those of the ascaridole epoxides 11[10] can be attributed to the shielding effect of the aromatic ring. A similar upfield shift was observed in the dibenzobarrelene epoxide 12.[14] The



11s 11a 12

downfield shift of the benzylic methyls in **10a** (δ 1.75; syn to the epoxide oxygen) relative to those in **10s** (δ 1.37; anti to the epoxide oxygen) adds support to the assignment. Finally, the dipole moments of the major (μ = 4.2 ± 0.1 D) and minor (μ = 1.7 ± 0.1 D) isomers confirm the assignment.

Acid-Catalyzed Solvolysis of 8s. When **8s** was treated with trifluoroacetic acid (TFA) in methylene chloride (0 °C, 20 min) in the presence of methanol or ethanol, a single product, assigned structure **14,** was obtained in quantitative



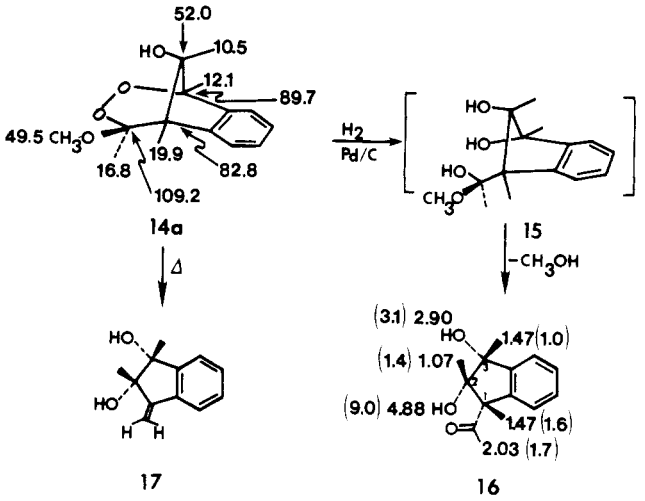
8s 13 14 a; R=CH_3 b; R=C_2H_5

yield. Although the mass spectrum of **14** did not show an M^+ peak (the highest *m/e* peak corresponded to $M^+ - H_2O$), elemental analysis and a positive test with HI in acetone suggested that the peroxide group was still present.

The ^1H NMR spectrum of **14a** showed singlets for three of the *C*-methyl groups (δ 1.10, 1.38, 1.45), but the fourth *C*-methyl group was a doublet at δ 0.75 (J = 1.4 Hz). This methyl group was coupled (verified by decoupling) with the hydroxyl proton which (at 180 MHz) appeared as a quartet at δ 5.78 (J = 1.4 Hz). This result is consistent with protonation and ring opening at the epoxide oxygen and not the peroxide oxygen, for if the latter had occurred one would expect to find a (HOO)C(CH_3)< moiety, with the hydroperoxy proton at lower field than δ 5.78, and not coupled to the geminal methyl group.[15] The lower than usual chemical shift of the hydroxyl proton in **14a** and its coupling with the geminal methyl protons can be explained by its strong hydrogen bonding with an oxygen of either the peroxide or methoxyl group (ν_{O-H} 3450 cm^{-1}). The ^1H NMR spectrum of **14b** was similar to that of **14a** (except for ethoxy signals in place of the methoxy singlet at δ 3.40).

The ^{13}C NMR spectra of **14a** and **14b** were also consistent with the assigned structures. The ^{13}C peak assignments for **14a,** shown on the structure, are based on deuterium labeling and comparison with **14b.** The unique quaternary carbon signal at δ 108.2 supports the peroxy acetal structure.[16]

To prove the structure, **14a** was subjected to catalytic hydrogenolysis. Reaction with hydrogen (Pd/C) in ethanol was complete in 30 min at room temperature and gave the acetylindandiol **16** as the sole product (the presumed intermediate hemiacetal **15** was not isolated). The alcohol and carbonyl functionalities were clear from the infrared spectrum (ν_{O-H} 3440, $\nu_{C=O}$ 1700 cm^{-1}), and the ^1H NMR spectrum showed the acetyl methyl (δ 2.03) and hydroxyl protons (δ 2.90 and 4.88) as well as singlets at δ 1.07 (3 H) and 1.47 (6 H) for the remaining methyl groups. Europium shift slopes are shown on the structure. The ^{13}C NMR spectrum of **16** showed the

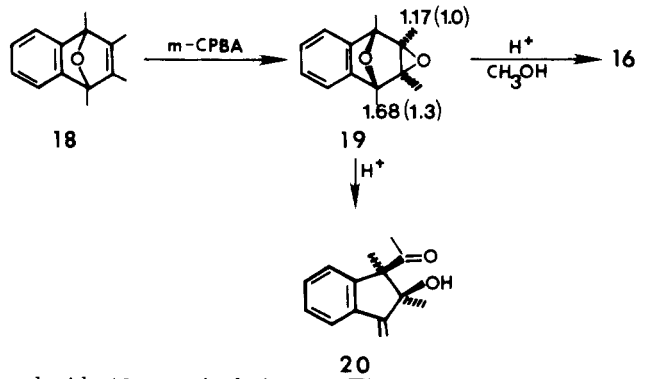


presence of four different methyl groups. The structure of **16** was confirmed by independent synthesis (vide infra).

Thermolysis of **14a** (refluxing xylene) gave an unsaturated diol assigned **17** in 22% yield. The infrared spectrum of **17** showed bands for the hydroxyl and terminal methylene groups. The ^1H NMR spectrum showed two methyl singlets (δ 1.35, 1.42), two methylene protons (δ 5.27, 5.52), and a broad singlet for the two hydroxyl protons (δ 2.53). Since the methylene protons are not equivalent, the alternative structure with the methylene group at the central carbon of the five-membered ring is eliminated. The formation of **17** from **14a** can be rationalized starting with O–O bond cleavage, although a unique mechanism cannot be specified at present.

The formation of peroxy acetal **14** from **8s** can be rationalized by protonation of the epoxide oxygen and ring opening with aryl participation to give **13.** Stereospecific reaction of **13** with the nucleophile results in **14.**[17] Consistent with this mechanism, the *anti*-epoxy endoperoxide **8a** was recovered unchanged on treatment with TFA under conditions identical with those which caused rapid conversion of **8s** to **14.**[18,19] It is perhaps surprising that the peroxy acetal **14** survived the acidic conditions of its preparation. Indeed, treatment of **14a** with TFA in ethanol did not bring about alkoxy group exchange or any other reaction.[20]

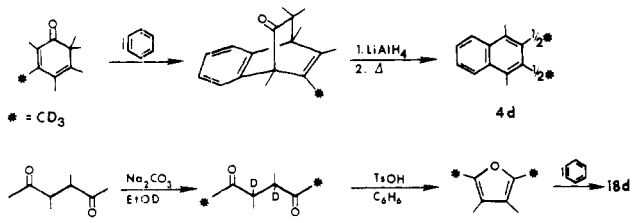
1,2,3,4-Tetramethylnaphthalene 1,4-Endoxide Epoxide. For comparison with **8s,** the naphthalene 1,4-endoxide epoxide **19** was prepared and solvolyzed in acid. Epoxidation of naphthalene 1,4-endoxide 18[21] with *m*-CPBA gave the epoxy



endoxide **19** as a single isomer. The syn stereochemistry is assigned on the basis of the chemical shifts and europium shift slopes of the methyl signals, which are nearly identical with those of **8s** and quite different from those of **8a.**

When **19** was treated with TFA and methanol under the same conditions as for **8s,** it was converted in analogous fashion to **16.** If the methanol was omitted, the product was instead the unsaturated keto alcohol **20,** whose structure was assigned from spectral data and mechanistic considerations.

Scheme I



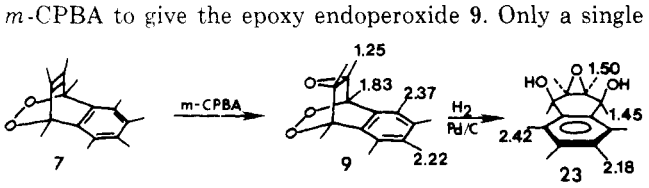
The formation of **16** or **20** from **19** can be rationalized by protonation at the epoxide oxygen and ring opening with aryl participation to give the bridged ion **21** which in the absence of nucleophile loses a proton to give **20** or in the presence of methanol is captured to give the acetal **22.** Unlike the peroxyacetal **14,** which is stable and easily isolated from the acidic medium, **22** is much more strained and solvolyzes to **16** under the reaction conditions (Scheme II).

Deuterium Labeling Studies. Deuterium labeling was used to verify structural and NMR assignments and to be sure that our mechanistic scheme for the acid-catalyzed solvolytic rearrangements of **8s** and **19** was correct. The preparation of the labeled compounds is outlined in Scheme I (for details, see the Experimental Section). The expected and observed labeling consequences are outlined in Scheme II.

Labeled tetramethylnaphthalene **4-*d*** was converted via singlet oxygen and *m*-CPBA to **8s-*d*,** which according to Scheme II should give **16** labeled at the C_1 and C_2 methyls. In fact, the peaks at δ 1.07 and 1.47 were diminished in intensity. Since the peak at δ 1.47 represented two methyl groups with accidental degeneracy, shift reagent was used and this established that it was the peak with the higher slope that was diminished in intensity. These results are consistent with the label being at C_1 (δ 1.47, slope 1.6) and C_2 (δ 1.07).

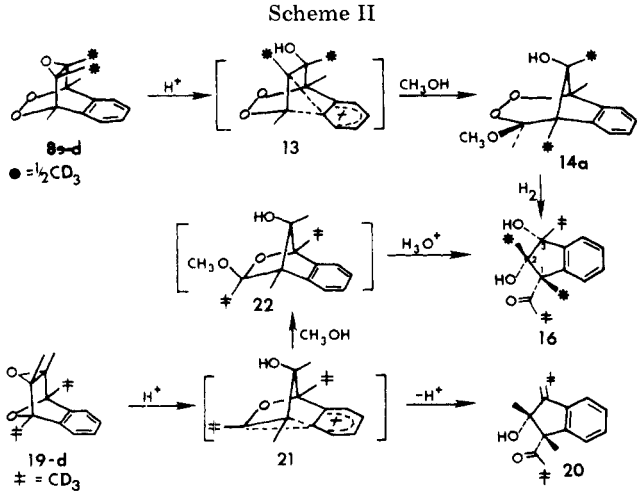
Tetramethylfuran labeled at the C_2 and C_5 methyls was converted to **19-*d*,** which with TFA and methanol gave **16** with the label at the C_3 methyl (δ 1.47, slope 1.0) and acetyl methyl (δ 2.03). Thus, the label results are entirely consistent with the mechanisms put forth in Scheme II.[22]

Epoxyoctamethylnaphthalene Endoperoxide. Octamethylnaphthalene 1,4-endoperoxide[6] was oxidized with *m*-CPBA to give the epoxy endoperoxide **9.** Only a single

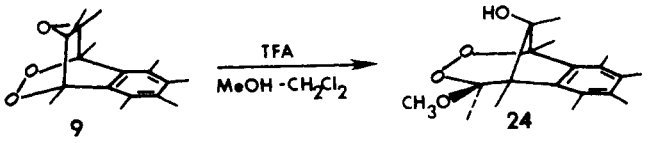


isomer, assigned the syn geometry, was isolated. The chemical shifts of the epoxide methyl groups in **9** (compare with **8s**) and

Scheme II

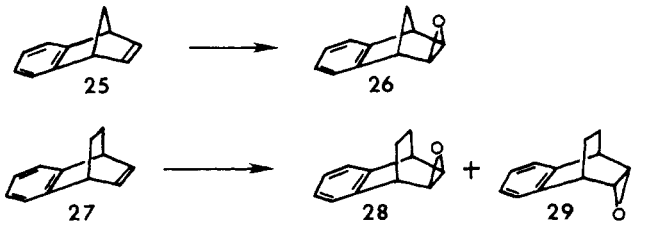


of the benzylic methyls in **23** (compare with **10s**) favor this assignment. Consistent with this stereochemistry, **9** underwent quantitative, rapid solvolytic rearrangement to the peroxy acetal **24** on treatment with TFA in methanol/methylene chloride. The compound liberated iodine instantaneously from HI in acetone, showed a parent peak at *m/e* 320 in its mass spectrum, and had a ^{1}H NMR spectrum comparable with that of **14a** except for the aromatic methyl substituents.

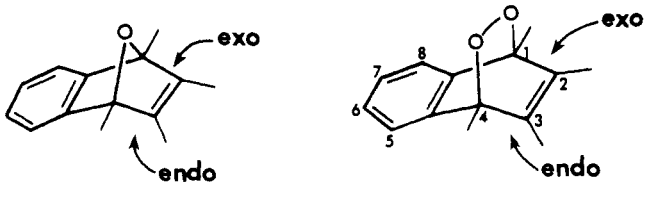


It is worth noting that in each epoxidation described here (i.e., **6, 7,** and **18**) the predominant or exclusive product was the syn isomer (corresponding to exo if the oxygen bridge is replaced by a carbon bridge). This result may be rationalized as an effect of the oxygen bridge. It is known that the direction of epoxidation can be controlled by coordination of the oxidizing agent with an oxygen atom already present in the substrate.[23] In the present case, coordination with the peroxide bridge in **6** or **7** or the endoxide bridge in **18** could account for the observed syn orientation.

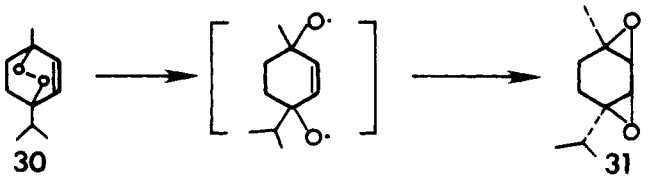
Alternatively, a steric factor may be involved, particularly with **18.** It is well known that most reagents attack bicyclic [2.2.1] systems from the exo face, thus avoiding the crowdedness of the endo face.[24] For example, epoxidation of benzonorbornadiene (**25**) gave only the *exo*-oxide **26.**[25] The [2.2.2]



alkene dihydrobenzobarrelene (**27**), on the other hand, gave equal amounts of **28** and **29.**[26] However, the steric crowdedness of the endo face of **6** and **7** may be more significant than usual for [2.2.2] bicyclic systems because of the peroxide bridge. The O–O bond length, which is shorter than a C–C single bond, tends to expand the O–C–C bond angle and contract the C_2–C_1–C_{8a} bond angle. Consequently, either the steric factor or coordination with the oxygen bridge (or both) may rationalize the syn epoxidation of **6, 7,** and **18.**

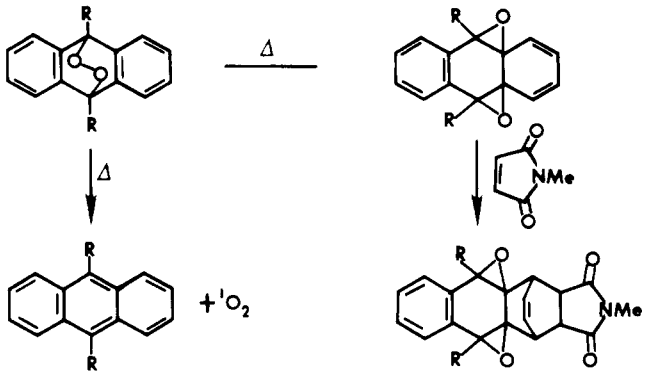


Thermolysis of Epoxy Endoperoxide 8. The thermal rearrangement of ascaridol (**30**) to the diepoxide **31** has been



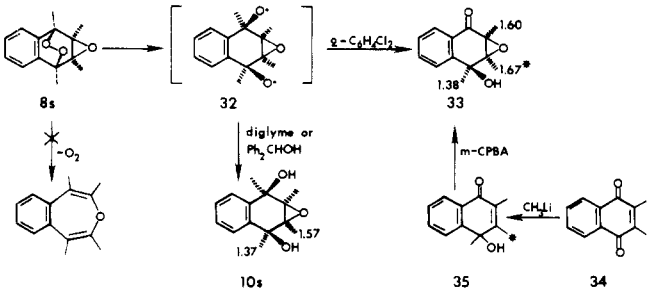
known for many years;[27] the mechanism involves rate-determining homolytic O–O bond cleavage followed by rapid addition of the oxygens to the double bond.[28] For anthracene

endoperoxides, two types of thermal reactions are known. O–O bond cleavage may give a diepoxide, which can be trapped,[29] or C–O bond cleavage may occur, with the extrusion of singlet



oxygen and reformation of anthracene.[30] Naphthalene endoperoxides, on the other hand, only extrude oxygen, the rearrangement to diepoxides so far being unkown.[31]

It was of interest to investigate the thermolysis of epoxynaphthalene endoperoxides such as **8** or **9**, for oxygen extrusion could provide a useful benzoxepin synthesis. In fact, however, decomposition of **8s** in refluxing *o*-dichlorobenzene gave instead of an oxepin a ketone assigned structure **33**.[32] The



compound showed infrared peaks for the hydroxyl, conjugated carbonyl, and epoxide functions and had an ^1H NMR spectrum with three methyl singlets and a broad singlet for the hydroxyl proton. The structure and the stereochemical relationship between the epoxide ring and the hydroxyl group (cis) were confirmed by independent synthesis.

2,3-Dimethyl-1,4-naphthoquinone (**34**) and methyllithium afforded the keto alcohol **35** which was oxidized with *m*-CPBA to give a product identical with **33** obtained from **8s**. The epoxidation of **35** should be controlled by and occur cis to the hydroxyl function.[23,33]

Although the precise mechanism for the formation of **33** is not clear, the diradical **32** seemed to be one plausible intermediate. Indeed, when the thermolysis was carried out in the presence of a good hydrogen donor (diglyme solvent), the diol **10s** was obtained in quantitative yield. Also, if the thermolysis was carried out in *o*-dichlorobenzene to which benzhydrol was added, the products were **10s** and benzophenone. Thus, **8s** seems to decompose thermally by O–O, not C–O, bond cleavage. Trapping of **32** is one of the few examples of diradical trapping by external chemical means.[34]

Experimental Section[35]

Epoxidation of 1,2,3,4-Tetramethyl-1,4-epidioxy-1,4-dihydronaphthalene (6). A methylene chloride solution (50 mL) of 85% *m*-chloroperbenzoic acid (*m*-CPBA, 4.4 g) was added dropwise at 0 °C to a solution of 6[5] (3.97 g, 18.4 mmol) in 20 mL of CH_2Cl_2. The mixture was stirred at 0 °C for 18 h, during which time *m*-chlorobenzoic acid precipitated from solution. The solid was removed by suction filtration, and the filtrate was washed with aqueous sodium sulfite. It was then washed with aqueous Na_2CO_3 and water and dried ($MgSO_4$). The solvent was removed under vacuum at room temperature to give colorless solids which showed NMR peaks due to the syn (**8s**, 90%) and anti (**8a**, 10%) isomers of 1,2,3,4-tetramethyl-2,3-epoxy-1,4-epidioxy-1,2,3,4-tetrahydronaphthalene. The solids were recrystallized from ether in a crystallizing dish covered by Parafilm. Colorless cloudy plates (**8s**; 3.42 g, 80%) and colorless rods (**8a**; 0.28 g, 7%) obtained after slow evaporation of the ether were separated mechanically.

For **8s:** mp 154–156 °C; IR (Nujol) 1125 (m), 1100 (s), 1070 (m), 865 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (s, 6 H), 1.67 (s, 6 H), 7.23 (s, 4 H); ^{13}C NMR ($CDCl_3$) 11.7, 14.2, 66.3, 79.7, 122.0, 128.3, and 140.0 ppm from Me_4Si; for europium shift data, see structure; mass spectrum, *m/e* (rel. intensity) 232 (1), 216 (1), 200 (6), 173 (100).

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.48; H, 6.94.

For **8a:** mp 174–177 °C; IR (Nujol) 1120 (s), 1075 (m), 1065 (s), 1050 (m), 870 (m), 845 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (s, 6 H), 1.73 (s, 6 H), 7.0–7.4 (m, 4 H); ^{13}C NMR ($CDCl_3$) 11.1, 15.4, 56.5, 82.7, 120.8, 128.3, and 136.0 ppm from Me_4Si; for europium shift data, see structure; mass spectrum, *m/e* (rel. intensity) 232 (0.5), 216 (2), 200 (22), 173 (100).

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.34; H, 6.91.

Epoxidation of 1,2,3,4,5,6,7,8-Octamethyl-1,4-epidioxy-1,4-dihydronaphthalene (7). A methylene chloride solution (15 mL) of 85% *m*-CPBA (897 mg) was added dropwise at 0 °C to a solution of **7** in 10 mL of CH_2Cl_2. The mixture was stirred at 0 °C for 24 h. Workup in the manner described for the preparation of **8** gave a colorless solid which was nearly pure. Recrystallization from ether/$CHCl_3$ gave pure 1,2,3,4,5,6,7,8-octamethyl-2,3-epoxy-1,4-epidioxy-1,2,3,4-tetrahydronaphthalene (**9**): mp 200–201 °C; IR (Nujol) 1120 (s), 1100 (s), 1080 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (s, 6 H), 1.83 (s, 6 H), 2.22 (s, 6 H), 2.37 (s, 6 H); UV (cyclohexane) λ_{max} 275 nm (ϵ 420), 225 (6840); mass spectrum, *m/e* (rel. intensity) 288 (6), 256 (4), 202 (100).

Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.89; H, 8.32.

Catalytic Hydrogenolysis of 8 and 9. Medium-pressure catalytic hydrogenolysis (20–30 psi of H_2) of **8s, 8a,** and **9** in ethanol with palladium on charcoal (10%, Matheson Coleman and Bell) at room temperature gave the corresponding diols **10s, 10a,** and **23** in 65, 62, and 82% yields, respectively.

For **10s:** mp 162–163.5 °C; IR (Nujol) 3450 (s), 3400 (s), 3320 (s), 1100 (s), 1090 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 (s, 6 H), 1.57 (s, 6 H), 2.27 (br s, 2 H), 7.0–7.3 (m, 2 H), 7.3–7.6 (m, 2 H); mass spectrum, *m/e* (rel. intensity) 234 (4), 200 (8), 173 (100).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.73; H, 7.76.

For **10a:** mp 161–162.5 °C; IR (Nujol) 3200 (s), 1100 (s), 1065 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (s, 6 H), 1.75 (s, 6 H), 2.60 (s, 2 H), 7.1–7.6 (m, 4 H).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.68; H, 7.75.

For **23:** mp 198–200 °C; IR (Nujol) 3590 (s), 3450 (s), 1325 (s), 1085 (s), 1065 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (s, 6 H), 1.50 (s, 6 H), 2.18 (s, 8 H, CH_3 and OH), 2.42 (s, 6 H); mass spectrum, *m/e* (rel. intensity) 290 (10), 273 (3), 257 (6), 230 (24), 229 (100).

Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.44; H, 9.03. Found: C, 74.08; H, 8.80.

4-Methoxy-1,4,5,8-tetramethyl-6,7-benzo-2,3-dioxabicyclo-[3.2.1]oct-6-en-8-ol (14a). To a solution of **8s** (900 mg) in a mixed solvent of CH_2Cl_2 (15 mL) and MeOH (3 mL) was added 6 mL of trifluoroacetic acid (TFA) dropwise over 5 min at 0 °C with stirring. After additional stirring for 15 min at 0 °C, the reaction mixture was poured into aqueous Na_2CO_3 slowly with vigorous stirring. The organic layer was separated, washed, and dried ($MgSO_4$). Evaporation of the solvent under vacuum left a colorless solid which showed NMR peaks due only to **14a**. No further purification than rinsing with petroleum ether was necessary: mp 98–100 °C; IR (Nujol) 3450 (s), 1035 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75 (d, 3 H, J = 1.4 Hz, C_8 methyl), 1.10 (s, 3 H, C_4 methyl), 1.38 (s, 3 H, C_5 methyl), 1.45 (s, 3 H, C_1 methyl), 3.40 (s, 3 H, methoxyl), 5.78 (br s, 1 H, hydroxyl), 6.7–7.3 (m, 4 H, arom); with a Bruker WH-180 spectrometer, the broad singlet at δ 5.78 was resolved to a quartet with J = 1.4 Hz; irradiation of the doublet at δ 0.75 changed this quartet to a singlet; ^{13}C NMR ($CDCl_3$) 10.5, 12.1, 16.8, 19.9, 49.5, 52.0, 82.8, 89.7, 109.2, 122.2, 123.0, 127.9, 128.7, 141.1, and 146.8 ppm from Me_4Si; UV (MeOH) λ_{max} 272 nm (ϵ 400), 265 (420), 258 (340), 252 (200); mass spectrum, *m/e* (rel. intensity) 246 (1.5, $M^+ - H_2O$), 133 (100).

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.27; H, 7.40.

4-Ethoxy-1,4,5,8-tetramethyl-6,7-benzo-2,3-dioxabicyclo-[3.2.1]oct-6-en-8-ol (14b). To a solution of **8s** (250 mg) in a mixed

solvent of CH_2Cl_2 (10 mL) and EtOH (2 mL) was added 3 mL of TFA dropwise over 5 min at 0 °C with stirring. Stirring was continued for 15 min at 0 °C. Workup in the manner described for **14a** gave a colorless oil which was nearly pure **14b** (300 mg). The colorless oil was chromatographed on silica gel with $CHCl_3$ as the eluent to give pure **14b:** IR (Neat) 3460 (s), 1045 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75 (d, 3 H, J = 1.4 Hz), 1.10 (s, 3 H), 1.28 and 1.38 (t and s, respectively, 6 H), 1.45 (s, 6 H), 3.2–4.1 (m, 2 H), 6.07 (br s, 1 H), 6.9–7.4 (m, 4 H); ^{13}C NMR ($CDCl_3$) 10.5 (q), 12.1 (q), 15.3 (q), 17.4 (q), 19.9 (q), 52.0 (s), 58.0 (t), 82.9 (s), 89.7 (s), 109.0 (s), 122.2 (d), 123.0 (d), 127.9 (d), 128.7 (d), 141.3 (s), and 146.9 (s) ppm from Me_4Si; mass spectrum, m/e (rel. intensity) 260 (0.5, $M^+ - H_2O$), 190 (13), 172 (75), 84 (100).

Addition of a small quantity of **14a** or **14b** to a solution of hydriodic acid in acetone liberated iodine.

1-Acetyl-1,2,3-trimethylindan-2,3-diol (16). Medium-pressure catalytic hydrogenolysis (24 psi of H_2) of **14a** (200 mg) in ethanol with palladium on charcoal (10%, Matheson Coleman and Bell) at room temperature for 30 min gave **16** (110 mg, 62%): mp 105–107 °C (petroleum ether); IR (Nujol) 3440 (s), 3290 (s), 1700 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 3 H), 1.47 (s, 6 H), 2.03 (s, 3 H), 2.90 (s, 1 H), 4.88 (s, 1 H), 7.0–7.4 (m, 4 H); for europium shift data, see the structure; ^{13}C NMR ($CDCl_3$) 18.8, 20.3, 20.9, 29.4, 61.0, 80.4, 86.4, 123.7, 124.4, 128.2, 129.0, 144.2, and 144.9 ppm from Me_4Si; mass spectrum, m/e (rel. intensity) 261 (2, $M^+ - H_2O$), 200 (6), 191 (3), 181 (2), 174 (51), 173 (100).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.80; H, 7.71.

1-Methylene-2,3-dimethylindan-2,3-diol (17). **14a** (400 mg) was heated in o-xylene at reflux for 10 h. Evaporation of the solvent under vacuum left a light brown residue which was purified by GLC (10% SE 30, 165 °C) to give a colorless solid. The solid was recrystallized from petroleum ether to give pure **17** (65 mg, 22%): mp 96–97°C; IR (Nujol) 3430 (s), 3320 (s), 1790 (m), 1660 (m), 900 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (s, 3 H), 1.42 (s, 3 H), 2.53 (br s, 2 H), 5.27 (s, 1 H), 5.52 (s, 1 H), 7.0–7.6 (m, 4 H); mass spectrum, m/e (rel. intensity) 190 (21), 175 (54), 172 (59), 156 (36), 129 (100).

Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.88; H, 7.44.

1,2,3,4-Tetramethyl-1,4-endoxy-1,4-dihydronaphthalene (18). A mixture of 3,4-dimethyl-2,5-hexanedione[21] (12.4 g), p-toluenesulfonic acid (catalytic amount), and benzene (80 mL) was heated under reflux for 6 h, during which time the water produced was removed azeotropically. The volatile solvent was removed under vacuum, and the brown oily residue was distilled under reduced pressure as described in the literature[21] to give pure 2,3,4,5-tetramethylfuran (9.5 g, 77%).

A mixture of tetramethylfuran (3.0 g), benzenediazonium-2-carboxylate hydrochloride (5.3 g), propylene oxide (36 mL) and 1,2-dichloroethane (100 mL) was heated gradually until gas evolution commenced. The mixture was then heated under reflux for 2 h. The volatile solvents were removed under vacuum, and the residue was dissolved in ether, washed with dilute aqueous NaOH and water, and dried ($MgSO_4$). The brown oil which remained after removal of the ether was chromatographed on silica gel with $CHCl_3$ as an eluent to give pure **18** (2.8 g, 57%).[21]

1,2,3,4-Tetramethyl-1,4:2,3-diepoxy-1,2,3,4-tetrahydronaphthalene (19). A solution of 85% m-CPBA (487 mg) in 13 mL of CH_2Cl_2 was added dropwise to a solution of **18** (400 mg) in 2 mL of CH_2Cl_2 with stirring at 0 °C. Stirring was continued for 5 h, during which time m-chlorobenzoic acid precipitated from solution. The solid was removed by suction filtration, and the filtrate was washed with aqueous Na_2SO_3, and water and dried ($MgSO_4$). The solvent was removed under vacuum at room temperature to give a colorless oily solid (420 mg) which showed NMR peaks due only to **19.** It was used for further reactions without purification: IR (Nujol) 1160 (s), 1130 (s), 1085 (s), 1070 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ1.17 (s, 6 H, $C_{2,3}$ methyls), 1.68 (s, 6 H, $C_{1,4}$ methyls), 7.03 (s, 4 H); ^{13}C NMR ($CDCl_3$) 9.1, 11.8, 68.5, 84.8, 119.7, 126.6, and 149.5 ppm from Me_4Si. For europium shift data, see structure.

Reaction of 19 with TFA in CH_2Cl_2/MeOH. TFA (1.4 mL) was added dropwise to a solution of **19** (200 mg) in a mixed solvent of methylene chloride (30 mL) and methanol (1.4 mL) with stirring at 0 °C. The mixture was stirred at 0 °C for an additional 1.5 h. After workup as in the preparation of **14,** the solvent was removed under vacuum to give a yellow oil which was chromatographed on silica gel with $CHCl_3$ as the eluent to give pure **16** (80 mg, 37%), identical with material from **14a.**

1-Methylene-3-acetyl-2,3-dimethylindan-2-ol (20). TFA (1.4 mL) was added dropwise to a solution of **19** (200 mg) in 30 mL of methylene chloride with stirring at 0 °C. After additional stirring for 1.5 h and workup as for **14,** the solvent was evaporated under vacuum to give a yellow oil whose NMR spectrum showed peaks due to **20** and some small impurities. The yellow oil was chromatographed on silica gel with $CHCl_3$ as eluent to give pure **20** as colorless needles (30%): mp 87–90 °C; IR (Nujol) 3400 (s), 1790 (m), 1700 (s), 1650 (m), 900 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (s, 3 H), 1.48 (s, 3 H), 1.82 (s, 3 H), 3.25 (s, 1 H), 5.22 (s, 1 H), 5.45 (s, 1 H), 7.0–7.6 (m, 4 H); mass spectrum, m/e (rel. intensity) 216 (5), 200 (3), 198 (4), 184 (4), 183 (4), 173 (90), 156 (100).

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.68; H, 7.35.

When **19** (420 mg) was allowed to stand in a flask for 10 days, it decomposed to a brown oil. Chromatography of this oil on silica gel with $CHCl_3$ as the eluent gave **20** (178 mg, 42%).

Deuterium Labeling Experiments. A. 1,4-Dimethyl-2,3-dimethyl-d_3-naphthalene **4-*d*** was prepared as follows. A mixture of 2,4,5,6,6-pentamethyl-3-methyl-d_3-cyclohexa-2,4-dienone[36] (6.01 g), benzenediazonium-2-carboxylate hydrochloride (6.5 g), propylene oxide (10 mL), and 1,2-dichloroethane (85 mL) was heated gradually until gas evolution commenced. After the solution became clear, the reaction mixture was heated under reflux for 1 h. The volatile solvents were removed under vacuum. The oily residue was dissolved in ether, washed with dilute aqueous NaOH and water, and dried ($MgSO_4$). The light brown residue which remained after the solvent evaporated was recrystallized from methanol to give 1,3,4,7,7-pentamethyl-2-methyl-d_3-5,6-benzobicyclo[2.2.2]octa-2,5-dien-8-one (5.23 g). This ketone (2.5 g) was reduced with lithium aluminum hydride in ether at room temperature in the usual manner to give the corresponding alcohol (2.3 g). This alcohol, without purification, was heated in o-xylene under reflux for 51 h. Evaporation of the solvent to dryness gave a colorless solid which was recrystallized from petroleum ether to give pure **4-*d*,** which showed two methyl singlets at δ 2.37 and 2.57 with relative intensities of 0.6:1.0.

Starting with **4-*d*** and using the same methods as described above, **8-*d*, 10-*d*, 14a-*d*,** and **16-*d*** were prepared. For **8s-*d*,** the ^1H NMR peak at δ 1.18 was reduced in area. For **8a-*d*,** the singlet at δ 1.48 was reduced in area. For both **10s-*d*** and **10a-*d*,** the singlet at δ 1.57 was reduced in area. For **14a-*d*,** the doublet at δ 0.75 and the singlet at δ 1.38 were reduced in their intensities. The ^{13}C NMR peaks at 10.5, 19.9, 52.0, and 82.8 ppm showed diminished intensities. For **16-*d*,** the singlets at δ 1.07 and 1.47 had reduced intensities.

B. 19-*d* was prepared as follows. A mixture of 3,4-dimethylhexane-2,5-dione (14.1 g), sodium carbonate (4.5 g), ethanol-d (31 mL), and D_2O (60 mL) was stirred at room temperature for 18 h. The mixture was poured into 250 mL of methylene chloride and washed with aqueous NaCl. Any residual base was removed with solid CO_2. After drying ($MgSO_4$), the solvent was evaporated under vacuum to give the deuterated diketone as an oil (12.35 g). The diketone was converted to deuterated tetramethylfuran by catalysis with p-toluenesulfonic acid as described for the nondeuterated compound since the reported $ZnCl_2$ method[21] resulted in deuterium loss. The 2,5-dideuteriomethyl-3,4-dimethylfuran was converted to **18-*d*** and **19-*d*** by the same method used for the unlabeled material. The ^1H NMR spectrum of **19-*d*** showed that the peak at δ 1.68 ($C_{1,4}$ methyls) was reduced in area by about 50%.

Starting with **19-*d*, 16-*d*** was prepared as with the unlabeled material. The ^1H NMR spectrum of **16-*d*** showed reduced intensity of signals at δ 1.47 and 2.03. Of the methyls which are accidentally degenerate at δ 1.47, the one which moves least with europium shift reagent was decreased in intensity.

4-Methoxy-1,4,5,8-tetramethyl-6,7-(3',4',5',6'-tetramethylbenzo)-2,3-dioxabicyclo[3.2.1]oct-6-en-8-ol (24). The reaction of **9** (150 mg) with TFA (2 mL) in the same manner as described for the preparation of **14** afforded **24** quantitatively as a colorless oil: IR (neat) 3470 (s), 1120 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77 (d, 3 H, J = 1.4 Hz), 1.12 (s, 3 H), 1.57 (s, 6 H), 2.17 (s, 6 H), 2.27 (s, 3 H), 2.31 (s, 3 H), 3.35 (s, 3 H), 5.53 (br s, 1 H); mass spectrum, m/e (rel. intensity) 320 (<1), 203 (100).

2,3,4-Trimethyl-2,3-epoxy-4-hydroxy-1,2,3,5-tetrahydronaphthalenone (33). Compound **8s** (100 mg) was heated in o-dichlorobenzene (20 mL) under reflux for 2 h. The solvent was removed under vacuum to give a brown oily residue whose NMR spectrum showed peaks due to the starting material and to **33.** Separation and purification by chromatography on silica gel with $CHCl_3$ as the eluent gave three fractions. The first fraction was starting material (27 mg). From the second fraction, **33** was obtained (18 mg): mp 113–114 °C; IR (Nujol) 3565 (s), 3460 (s), 1680 (s), 1100 (s), 1080 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (s, 3 H), 1.60 (s, 3 H), 1.67 (s, 3 H), 2.47 (br s, 1 H), 7.0–7.8 (m, 4 H); mass spectrum, m/e (rel. intensity) 218 (1), 175 (100).

Anal. Calcd for $C_{13}H_{14}O_3$: C,71.54; H, 6.47. Found: C, 71.42; H, 6.44.

Trapping of Diradical 32. A. 8s (355 mg) in 8 mL of diglyme was heated at reflux under nitrogen for 2 h. The ^1H NMR spectrum of the diglyme solution after heating showed peaks due only to **10s. B.** Evaporation of the solvent left an oily brown residue to which 3 mL of petroleum ether was added. On standing overnight in a refrigerator, colorless crystals deposited which were recrystallized from petroleum ether to give pure **10s** (220 mg, 61%).

B. A mixture of **8s** (100 mg) and benzhydrol (80 mg) was heated in 10 mL of *o*-dichlorobenzene at reflux for 7 h. The brown oil which was obtained after removal of the solvent under vacuum was chromatographed on silica gel with $CHCl_3$ as the eluent. The first fraction gave a small amount of starting material. From the second fraction, benzophenone (17 mg) was obtained and identified by its IR spectrum. From the third fraction, **10s** (30 mg) was obtained, identical with the product from hydrogenolysis of **8s.**

2,3,4-Trimethyl-4-hydroxy-1,4-dihydronaphthalenone (35). To a solution of 2,3-dimethyl-1,4-naphthoquinone[37] (558 mg) in dry ether (100 mL) was added dropwise at −78 °C under nitrogen 2.0 mL of commercial 1.77 M methyllithium (ether). The mixture was stirred for 15 min and then warmed to room temperature. After additional stirring for 1 h, water (20 mL) was added with vigorous stirring. The separated aqueous layer was extracted with ether, and the combined ether layers were washed with dilute hydrochloric acid and saturated sodium chloride solution and dried ($MgSO_4$). Removal of the ether under vacuum gave a pale yellow solid which was rinsed with petroleum ether to give colorless **35** (400 mg, 67%): mp 163–164 °C; IR (Nujol) 3420 (s), 1635 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.55 (s, 3 H, C_4 methyl), 1.87 (s, 1 H, OH), 1.92 (br s, 3 H, C_2 methyl), 2.13 (br s, 3 H, C_3 methyl), 7.2–8.0 (m, 4 H, arom); mass spectrum, *m/e* (rel. intensity) 202 (32), 187 (100).

Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.79; H, 6.36.

Treatment of **35** with excess sodium methoxide in methanol-*d* for 1 h at room temperature[36] gave labeled **35** lacking the signal at δ 2.13.

Epoxidation of 35. To a solution of **35** (202 mg) in methylene chloride (10 mL) was added 300 mg of 85% *m*-CPBA in 10 mL of the same solvent. The mixture was stirred for 7 h at room temperature, washed with aqueous sodium sulfite (2×), aqueous sodium carbonate (4×), and saturated sodium chloride (2×), and dried ($MgSO_4$). Removal of the solvent under vacuum gave a colorless residue which, after rinsing with petroleum ether (30–60 °C), gave 180 mg (83%) of pure **33** (IR, NMR, melting point, and mixture melting point were identical with the thermolysis product of **8s**). Starting with labeled **35** (vide supra), the resulting labeled **33** lacked the signal at δ 1.67 in its NMR spectrum.

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Registry No.—**4-*d***, 68437-56-9; **6**, 36230-27-0; **7**, 36230-32-7; **8a**, 68437-57-0; **8a-*d***, 68437-58-1; **8s**, 68509-51-3; **8s-*d***, 68509-52-4; **9**, 68437-59-2; **10a**, 68437-60-5; **10a-*d***, 68437-61-6; **10s**, 68509-53-5; **10s-*d***, 68509-54-6; **14a**, 68474-66-8; **14a-*d*** (isomer 1), 68437-62-7; **14a-*d*** (isomer 2), 68437-63-8; **14b**, 68474-67-9; **16**, 68437-64-9; **16-*d*** (isomer 1), 68437-65-0; **16-*d*** (isomer 2), 68437-66-1; **17**, 68437-67-2; **18**, 68437-78-3; **18-*d***, 68437-69-4; **19**, 68473-70-7; **19-*d***, 68437-71-8; **20**, 68437-72-9; **23**, 68437-73-0; **24**, 68437-74-1; **33**, 68437-75-2; **33-*d***, 68437-76-3; **34**, 2197-57-1; **35**, 68437-77-4; **35-*d***, 68437-78-5; 3,4-dimethyl-2,5-hexanedione, 25234-79-1; 2,3,4,5-tetramethylfuran, 10599-58-3; 2,4,5,6,6-pentamethyl-3-methyl-d_3-cyclohexa-2,4-dienone, 5070-43-9; 1,3,4,7,7-pentamethyl-2-methyl-d_3-5,6-benzobicyclo[2.2.2]octa-2,5-dien-8-one, 68437-79-6; 1,3,4,7,7-pentamethyl-2-methyl-d_3-5,6-benzobicyclo[2.2.2]octa-2,5-dien-8-ol, 68437-80-9; 2,5-dideuteriomethyl-3,4-dimethylfuran, 68437-81-0.

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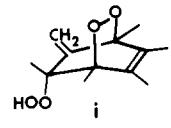

i

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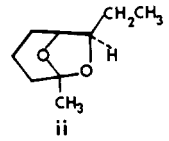
(16) The chemical shift of the acetal carbon of ii, for example, is 107.6 ppm



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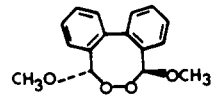
from Me_4Si: L. F. Johnson and W. C. Jankowski, "Carbon-13 NMR Spectra", Wiley-Interscience, New York, 1972, spectrum 359.
(17) A similar rearrangement was observed with dibenzobarrelene oxide **12**;[14] see also S. J. Cristol and R. K. Bly, *J. Am. Chem. Soc.*, **82**, 6155 (1960).
(18) After a prolonged reaction time, **8a** gave several unidentified products in low yield.
(19) Although a few examples of 1,3 peroxide oxygen shifts have been reported [A. P. Schaap, P. A. Burns, and K. A. Zaklika, *J. Am. Chem. Soc.*, **99**, 1270 (1977); J. Griffiths, K. Chu, and C. Hawkins, *J. Chem. Soc., Chem. Commun.*, 676 (1976); T. Wilson, *Photochem. Photobiol.*, **10**, 441 (1969)], we are not aware of 1,2 shifts such as might possibly have occurred with **8a.**
(20) There is some precedent for the acid stability of **14.** The peroxy acetal iii



iii

is also known as a stable cyclic peroxide which was produced in the acid-catalyzed methanolysis of phenanthrene ozonide: J. N. Brown, R. L. R. Towns, M. J. Kovelan, and A. H. Andrist, *J. Org. Chem.*, **41**, 3757 (1976).
(21) An improvement over literature procedures [E. Wolthuis, B. Bossenbroek, G. DeWall, E. Geels, and A. Leegwater, *J. Org. Chem.*, **28**, 148 (1963)] was developed; see Experimental Section for details.
(22) The ^1H NMR assignments in **16** were made as follows. The peak at δ 2.03 is clearly the acetyl methyl. The methyl at C_1 has an environment almost identical with that of the C_3 methyl of **20** (δ 1.47 and 1.48, respectively). The C_3 methyl is similar to that of the C_3 methyl in **17** (δ 1,47 and 1.42). The central methyl in all of these compounds comes at somewhat higher field than the benzylic methyls (δ 1.07 in **16**, δ 1.35 in **17**, and δ 1.28 in **20**; it appears at highest field in **16**, where it is not adjacent to an exocyclic methylene double bond).
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(31) The photochemical rearrangement of naphthalene endoperoxides to diepoxides is known.[4]
(32) An analogous reaction was observed when 9,10-dimethylanthracene endoperoxide iv was heated, with hydroxy ketone v being one of the products:

iv v

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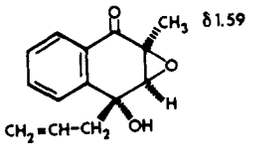
(33) NMR comparisons further support the stereochemical assignment. Treatment of **35** with CH_3ONa/CH_3OD exchanged protons on the β-enone methyl group, and epoxidation gave labeled **33** lacking the methyl signal at δ 1.67; furthermore, exchange of the OH proton of **33** in D_2O sharpened the singlet at δ 1.38. Consequently, the methyl signals in **33** are confidently assigned as shown on the structure. The chemical shift of the C_4 methyl (δ 1.38) compares favorably with the benzylic methyls of **10s** (δ 1.37) and not with those of **10a** (δ 1.75), consistent with all-cis stereochemistry. Also, the C_2 methyl shift in **33** (δ 1.60) is similar to that recently reported for vi: K. Maruyama and Y. Naruta, Chem. Lett., 431 (1978).



vi

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(35) ^1H NMR spectra were measured at 60 MHz on a Varian T-60 or at 180 MHz on a Bruker WH-180 spectrometer against tetramethylsilane as an internal standard. ^{13}C NMR spectra were determined on a Varian CFT-20 spectrometer. UV spectra were determined on a Unicam SP-800 spectrometer. IR spectra were determined on a Perkin-Elmer Model 167 spectrometer. Mass spectra were obtained with a Hitachi Perkin-Elmer Model 167 spectrometer. Mass spectra were obtained with a Hitachi Perkin-Elmer RMU-6 spectrometer. Elemental analyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, Mich. Melting points are uncorrected.
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Structures and Tautomerization Energies of Pyrrole and Some Pyrrole Derivatives

A. Karpfen and P. Schuster*

Institut für Theoretische Chemie und Strahlenchemie der Universität Wien, Währingerstr. 17, 1090 Wien, Austria

H. Berner

Sandoz-Forschungsinstitut, Wien, Austria

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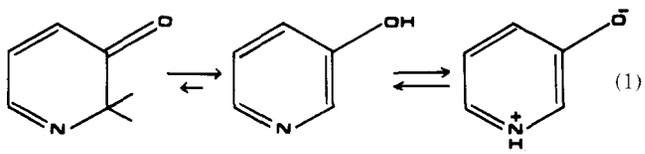
Molecular geometries, dipole moments, and isomerization energies were obtained by direct optimization of the (MINDO/3) energy surface of pyrrole, 2-methylpyrrole, 3-hydroxypyrrole, 2-methylene-Δ^4-pyrrolin-3-one, and various other substituted pyrroles and pyrrolenines. The most common tautomeric structures as well as some protonated molecules were investigated too. Solvent effects on tautomerization equilibria are discussed by means of the calculated polarities of the structures studied.

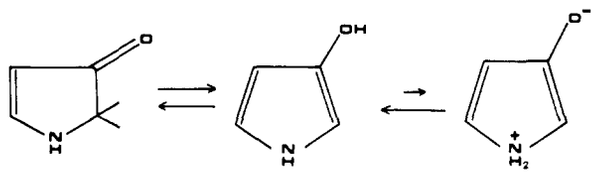
Prototropic equilibria of hydroxypyridines have been studied extensively by theoretical,[1] spectroscopic,[2] and kinetic[3] methods. 3-Hydroxypyridine (eq 1) is of special interest since the equilibrium constant K_{AC} favors most investigations in aqueous solutions ($K_{AC} \sim 1$, H_2O solvent, $T = 25$ °C). Structures of type B are characterized by high energies in the pyridine series and hence do not contribute appreciably to equilibrium mixtures. Additionally, 3-hydroxypyridine is also of interest in biochemistry as it represents an essential structural unit of vitamin B_6 compounds.



(1)

B A C

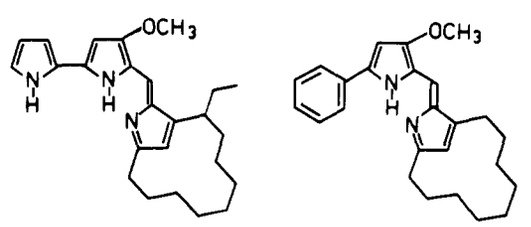
The analogous compound of the pyrrole series, 3-hydroxypyrrole (eq 2), in principle is subjected to the same kind of tautomerization equilibria. In contrast to the pyridines, structures of type C are highly disfavored energetically in the pyrrole series. Therefore, tautomerization equilibria of the type A ⇌ B are often discussed in the literature.[4]



(2)

B A

In connection with our investigations on prodigiosins,[5] we became interested in the methoxypyrrole derivative (eq 4) for reasons of pharmacological activity compared to the native biological compound, metacycloprodigiosin. Therefore, we had to look for synthetic methods which could lead to such



(3, 4)

Metacycloprodigiosin

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