Photooxygenation of 1,3,5-Cycloheptatriene: Transformations of Endoperoxides[1]

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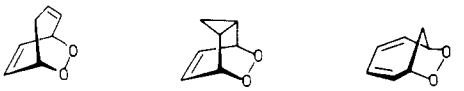
Abstract: The chemistry of the tropilidene (2+4)- and (2+6)- and the norcaradiene (2+4)-cycloadducts, respectively **2a**, **2c**, and **2b**, of 1,3,5-cycloheptatriene with singlet oxygen was studied, including their thermolysis, photolysis, rearrangement in methanol, and triphenylphosphine deoxygenation. The respective oxygen diradicals are postulated as precursors to the thermal and photochemical products. In the course of this investigation, the stereospecific syntheses of the bisepoxides **4a** and **3c** of tropilidene and the bisepoxide **3b** of norcaradiene were accomplished.

In a recent communication[3] we described the isolation and characterization of the tropilidene-derived endoperoxides **2a** and **2c** and the norcaradiene-derived endoperoxide **2b** in the



2a 2b 2c

singlet oxygenation of 1,3,5-cycloheptatriene (**1**). Prior to our work only the stable **2a** had been isolated and characterized[4] and the labile **2c** was postulated[5] as an intermediate in order to rationalize certain products in the singlet oxygenation of cycloheptatriene **1**. The norcaradiene endoperoxide **2b** went fully unnoticed.

In connection with our studies on the characterization of these endoperoxides, we observed[3] that on thermolysis **2a** led to the epoxyenone **3a**, while **2b** afforded the hitherto still missing[6] norcaradiene bisepoxide isomer **3b**. In view of the

3a 3b

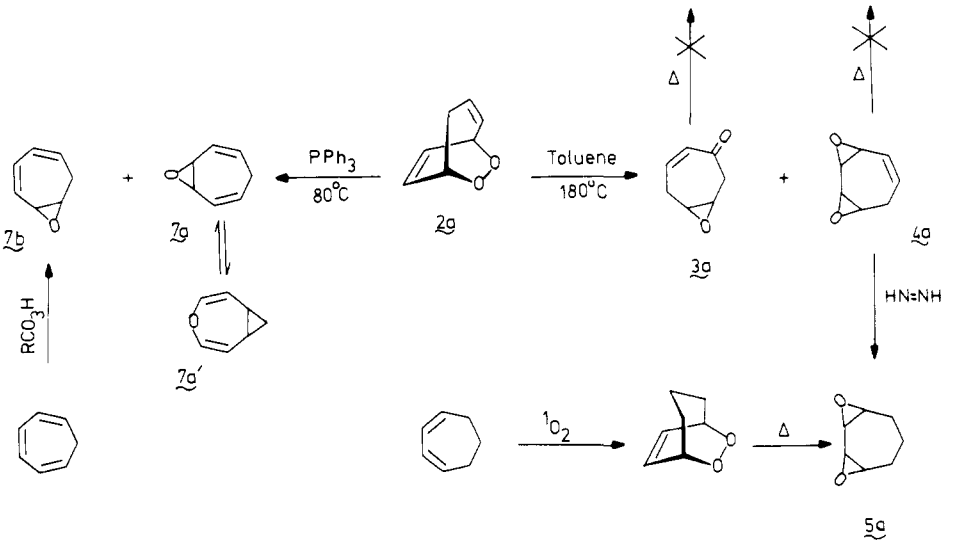
mechanistic insight to be gained on the behavior of these intriguing bicyclic peroxides and the synthetic value of the products, we felt that it would be important to examine the full scope of the transformation of the endoperoxides **2**. Herein we report the details of this investigation, including the thermolysis, photolysis, triphenylphosphine deoxygenations, and methanolysis.

Results and Discussion

Transformations of the Endoperoxide 2a. In Scheme I the chemistry of the tropilidene (2+4)-adduct **2a** is summarized. As can be seen, the thermal stability of endoperoxide **2a** is quite high and heating at 180–190 °C in toluene for 45 min was essential to destroy it completely. The major product of the thermolysis was the epoxy enone **3a** (67% yield) and the minor product was the expected bisepoxide **4a** (11% yield). Both are new compounds and were rigorously characterized by satisfactory elemental analysis, parent ion peak in the MS, and the IR and NMR spectral data (cf. Experimental Section). Furthermore, the bisepoxide **4a** could be reduced with diimide in CH_2Cl_2[7] to afford the *syn*-bisepoxide **5a** quantitatively; however, attempted catalytic hydrogenation over Pd/C was problematic because, besides saturation, also hydrogenolysis of the epoxide ring occurred. An authentic sample of the latter was readily prepared (Scheme I) by singlet oxygenation of cycloheptadiene[8] and subsequent thermal rearrangement of the known cycloheptadiene endoperoxide to the *syn*-bisepoxide **5a** in 95% yield.[9] Spectral data and physical constants completely matched between the two samples of the *syn*-bisepoxide **5a**.

As to the mechanism of formation of the epoxyenone **3a** and the ene-bisepoxide **4a** in the thermolysis of endoperoxide **2a**, control experiments reveal that both **3a** and **4a** are stable when submitted to the thermolysis conditions. Therefore, the diradical A (eq 1) either transposes an alkoxy α hydrogen by β

Scheme I



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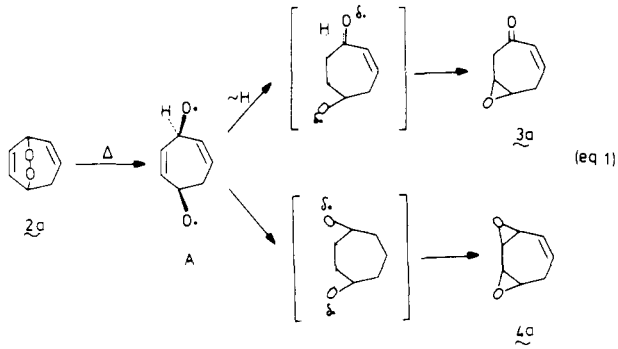


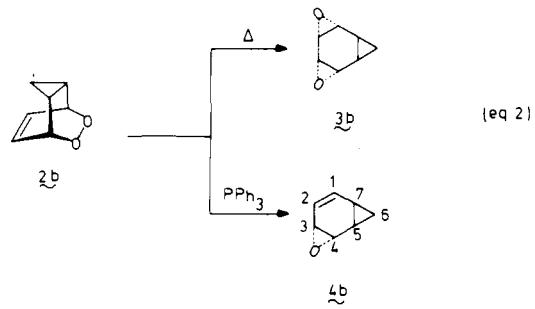
(eq 1)

scission affording epoxyenone **3a** (major path), or cycloadds into ene-bisepoxide **4a** (minor path). Not necessarily do these two transformations of diradical A have to take place via the concerted transition states shown in eq 1; however, the relatively simple and clean product mixture obtained from the thermolysis of endoperoxide **2a** presupposes that the diradical A is well behaved. Stepwise transformations leading to subsequent diradicals would be expected to generate a more complex product mixture.

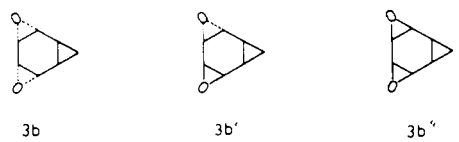
The triphenylphosphine deoxygenation of endoperoxide **2a** in $CHCl_3$ at 80 °C led to a mixture of 3,4-epoxy-1,5- and 5,6-epoxy-1,3-cycloheptadienes, respectively **7a** and **7b.** At room temperature the epoxydiene **7a** was in equilibrium with its valence tautomer **7a'** (Scheme I), as confirmed by NMR. This tautomeric equilibrium was already described by Grimme et al.[10a] Our ^1H NMR spectral data were identical with those reported.[10]

Endoperoxide **2a** is stable in polar and protic solvents such as methanol even at reflux temperature. Thus, the polar transformations of **2a** could not be investigated.

Transformations of the Endoperoxide 2b. In eq 2 is summarized the chemistry of the norcaradiene (2+4)-adduct **2b.** Compared with the tropilidene (2+4)-adduct **2a,** this endoperoxide isomer is considerably simpler in its chemistry. Thus, on heating at 100 °C in CCl_4, endoperoxide **2b** was quantitatively transformed into the *syn*-bisepoxide **3b.** In fact, this is the missing isomer of the three possible norcaradiene bisepoxides since **3b'** and **3b''** were prepared by Vogel et al.[6]



(eq 2)

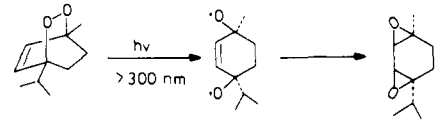


The structural assignment of the bisepoxide **3b** is secured on the basis of correct elemental analysis and parent ion peak in the MS. The ^1H NMR spectral data were particularly decisive. Thus, all four epoxide protons form a singlet at 2.95 ppm, while the cyclopropyl protons constitute multiplets at 1.1–1.5, 0.7–1.0, and 0.25–0.55 ppm, respectively assigned to the bridgehead, endo, and exo protons. Double resonance experiments were particularly helpful in this assignment. Comparison with the published ^1H NMR data on the bisepoxide isomers **3b'** and **3b''** permitted us to confirm the syn geometry **3b** for our bisepox.[1-]

The triphenylphosphine deoxygenation of endoperoxide **2b** in $CHCl_3$ at 0 °C gave the norcaradiene monoepoxide **4b** in 69% yield. The structural assignment rests on correct elemental analysis, a parent ion fragment in the MS, and IR and ^1H NMR spectral data. The latter was particularly decisive since double resonance experiments were essential to unravel the complex ^1H NMR. Thus, the olefinic protons H_1 and H_2 form complex multiplets at 5.7–6.0 and 5.2–5.5 ppm, respectively. The H_1 proton is coupled of course to H_2 ($J_{1,2}$ = 9.66 Hz), but in addition also to the cyclopropyl bridgehead proton at 0.9–1.4 ppm ($J_{1,7}$ = 3.77 Hz) and to the epoxy proton H_3 at 2.6–2.9 ppm ($J_{1,3}$ = 1.3 Hz). The other olefinic proton, H_2, consists of a doublet of doublets as expected from coupling to H_1 ($J_{1,2}$ = 9.66 Hz) and H_3 ($J_{2,3}$ = 3.66 Hz). Irradiation of H_3 at 2.75 ppm collapses the H_2 resonance into a doublet, i.e., B portion of the AB pattern. The H_3 proton is further coupled ($J_{3,4}$ = 4.50 Hz) to the other epoxy proton H_4 at 3.4–3.6 ppm, which in turn is coupled ($J_{4,5}$ = 1.75 Hz) to the bridgehead cyclopropyl proton H_5 at 1.5–1.9 ppm. It is important to emphasize that the assignment of the epoxy protons H_3 and H_4, respectively to the high field signal at δ 2.6–2.9 ppm and the low field signal at δ 3.4–3.6 ppm, was secured by double resonance experiments. The *endo*- and *exo*-methylenic cyclopropyl protons H_6 are located at 0.6–0.9 and 0.9–1.4 ppm, respectively. They are complex multiplets for which it was not possible to obtain coupling constant data on our 60-MHz spectrometer. However, the small $H_{4,5}$ coupling ($J_{4,5}$ = 1.75 ppm) and the other ^1H NMR data confirm the anti geometry of the epoxide and cyclopropane rings, as suggested by inspection of Dreiding models. In fact, this geometry obliges a planar cyclohexene ring. X-ray analysis is in progress for the corresponding ene-epoxide **4b** derived from 7-cyano-1,3,5-cycloheptatriene.[11]

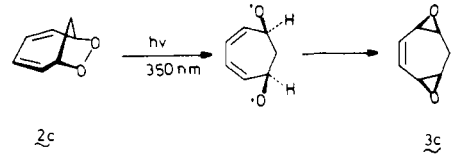
Transformation of Endoperoxide 2c. As can be appreciated from Scheme II, the tropilidene (2+6)-adduct **2c** is the most complex of the three endoperoxides in its chemistry. The simplest transformation is its photolysis and, therefore, we shall discuss it first.

Irradiation of endoperoxide **2c** in benzene at its λ_{max} 294 nm, i.e., $\pi \rightarrow \pi^*$ excitation of the dienic moiety, resulted in recovery of the endoperoxide even after 14 h. However, irradiation at 350 nm, presumably the $n \rightarrow \pi^*$ transition originating at the peroxide moiety, cleanly converted **2c** into the *syn*-bisepoxide **3c** in 56.8% yield. It is known[12] that the endoperoxide–bisepoxide rearrangement requires excitation at >300 nm and triplet n,π^* sensitization is even more effective. This photochemical behavior of such endoperoxides is consistent with that reported of simple dialkyl peroxides at long wavelengths,[13] and the diradical mechanism, illustrated in eq 3 for ascaridole, was proposed.[14]



(eq 3)

We suggest a similar mechanism for the photochemical transformation **2c** → **3c** (eq 4).

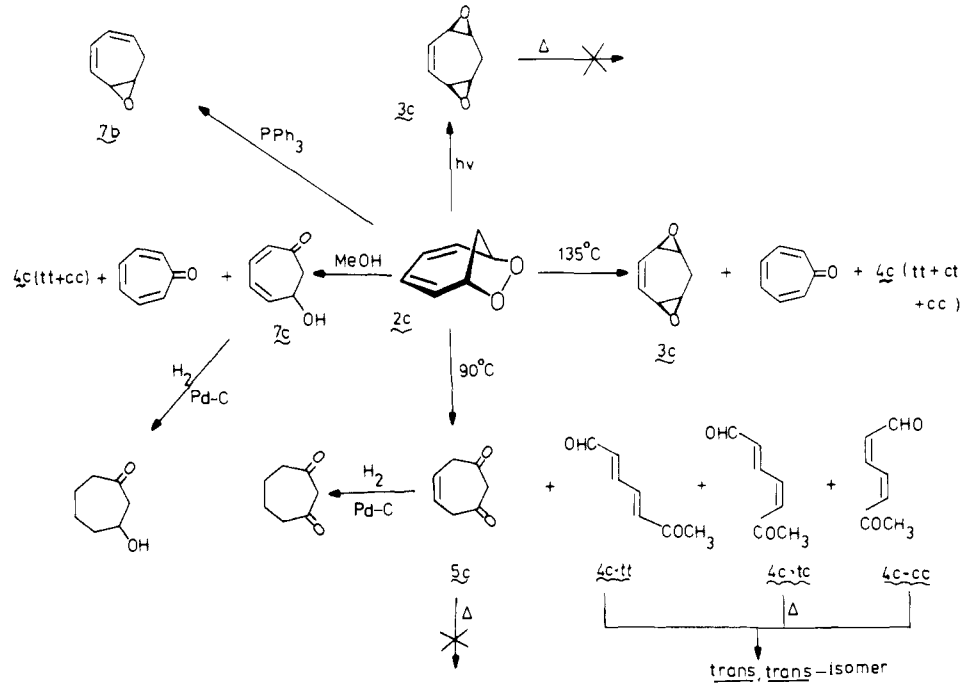


(eq 4)

In the absence of further experimental data, concerted photochemical mechanisms for **2c** → **3c** are entirely feasible.

The characterization[4b] of the bisepoxide **3c** was made on the basis of its correct elemental analysis, molecular ion peak in the MS, and characteristic IR and ^1H NMR spectra. Thus, the ^1H NMR exhibited a singlet for the olefinic protons at 5.65 ppm and a multiplet for the epoxide protons at 3.0–3.3 ppm,

Scheme II

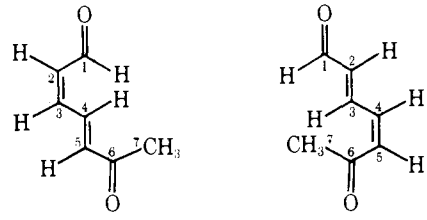


which were coupled to the endo proton of the methylene group, located at 1.0–1.4 ppm. Irradiation at 3.1 ppm collapsed the 1.0–1.4-ppm multiplet into a doublet consisting of the A portion of the AB pattern of the methylenic proton (J = 11.6 Hz). The *exo*-methylenic proton was located at 2.3–2.8 ppm as a multiplet.

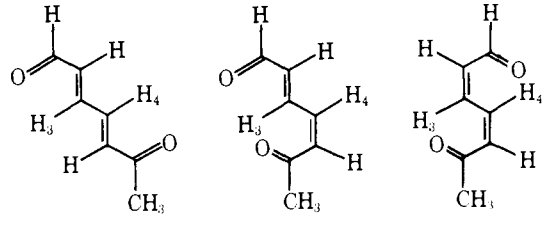
The thermolysis of endoperoxide **2c**, on the other hand, was messy. Depending on the temperature, different products were obtained and their composition altered. For example, thermolysis of **2c** at 135 °C in toluene for 3.5 h gave the expected bisepoxide **3c** in 32% yield, 6–8% tropone, and the three of the four possible ring-opening dienes *trans,trans*-, *trans,cis*-, and *cis,cis*-**4c** in 24, 12, and 8% yields, respectively. Control experiments showed that the *trans,trans*-diene isomer **4c** was stable under the thermolysis conditions, but the cis,cis isomer did isomerize into the cis,trans and the trans,trans isomers on heating. The dienes were not derived from the bisepoxide **3c** since the latter was stable to heating under the thermolysis conditions of **2c**.

The isolation, purification, and identification of the three diene isomers **4c** from the thermolysate of **2c** was no trivial task. They were obtained as a mixture by elution with $CHCl_3$ on silica gel chromatography. Careful silica gel chromatography of this diene isomer mixture at 25 °C, eluting with $CHCl_3$/*n*-pentane (3:1), permitted the separation of the cis,trans isomer as the first fraction and the trans,trans isomer as last fraction. Further purification was achieved by Kugelrohr distillation. These isomers gave correct elemental analyses and exhibited parent ions in the MS.

The IR and ^1H NMR spectral data of the three diene isomers and their assignments are summarized in Table I. Detailed double resonance experiments were essential in assigning the ^1H NMR spectra (Table I). The most troublesome was the cis,trans isomer **4c** because two geometrical arrangements of the CHO and $COCH_3$ groups are plausible, namely, the **2Z:4E** and **2E:4Z** configurations. The trans configuration of the aldehyde bearing double bond, i.e., isomer **2E:4Z**, could be secured on the basis of the large coupling constant between the H_2 and H_3 protons ($J_{2,3}$ = 14.82 Hz). For example, irradiation of the aldehydic proton H_1 at 9.36 ppm caused a collapse of the doublet of doublets of the olefinic proton H_2 at 6.1 ppm into a doublet, due to coupling by the olefinic proton H_3 ($J_{2,3}$ = 14.82 Hz). The coupling constant between the aldehydic proton H_1 and olefinic proton H_2 was established as $J_{1,2}$ = 6.49 Hz.

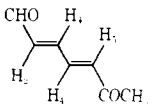
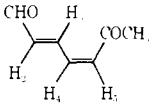
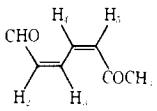


Another structurally significant feature concerns the relative chemical shifts of the olefinic protons H_3 and H_4 of the diene isomers. For example, in the trans,trans isomer **4c**, the H_3 and H_4 resonances constitute an unresolved multiplet at 6.7–7.25 ppm; but for the cis,trans- and the cis,cis isomers **4c**, the H_3 and H_4 protons constitute separate multiplets, of which the H_3 proton multiplet is displaced to lower field compared with the H_4 proton multiplet, i.e., 7.95 vs. 6.2 ppm for the cis,trans isomer and 7.8 vs. 7.14 ppm for the cis,cis isomer (Table I). More significant, the H_3 protons of both the cis,trans and cis,cis isomers are displaced to lower field ($\Delta\delta$ ca. 0.7 ppm) compared with the H_3 proton of the trans,trans isomer. We translate this spectral information into the structural details exhibited in the rotamers below.



In the cis,trans and cis,cis isomers, the H_3 protons sit in the deshielding cone of the acetyl carbonyl group. Furthermore, in the cis,cis isomer also the H_4 proton is deshielded by the anisotropy effect of the aldehyde carbonyl group. In the trans,trans isomer this deshielding effect is less pronounced. Dreiding models imply that the bulky methyl group should be turned anti to the H_3 protons in the cis,trans and cis,cis isomers due to unfavorable steric interactions. This also explains the

Table 1. Spectral Data for Dienes **4c**

diene	NMR ($CDCl_3$) type	δ	multiplicity	J, Hz	IR, cm^{-1} [a] ν_{CHO}	$\nu_{C=O}$	$\nu_{C=C}$
	H_1	9.35	d	$J_{1,2}$ 6.52	2820 w	1690 s	1590 s
	$H_{2,5}$	6.0–6.6	m		2720 w		
	$H_{3,4}$	6.7–7.25	m				
	CH_3	2.26	s				
	H_1	9.36	d	$J_{1,2}$ 6.49	2805 w	1690 s	1620 m
	H_2	6.1	dd	$J_{2,3}$ 14.82	2705 w		1570 s
	H_3	7.95	dd	$J_{3,4}$ 9.16			
	H_4	6.2	m	$J_{4,5}$ 10.9			
	H_5	6.4	d				
	CH_3	2.2	s				
	H_1	9.93	d	$J_{1,2}$ 6.83	2860 w	1685 s	1615 m
	H_2	5.99	dd	$J_{2,3}$ 10.99	2720 w		1565 s
	H_3	7.8	t	$J_{3,4}$ 11.32			
	H_4	7.14	t	$J_{4,5}$ 10.66			
	H_5	6.2	d	$J_{3,5}$ 0.66			
	CH_3	2.22	s	$J_{2,4}$ 0.60			

[a] All in CCl_4 except the cis,cis isomer, which was taken in $CHCl_3$.

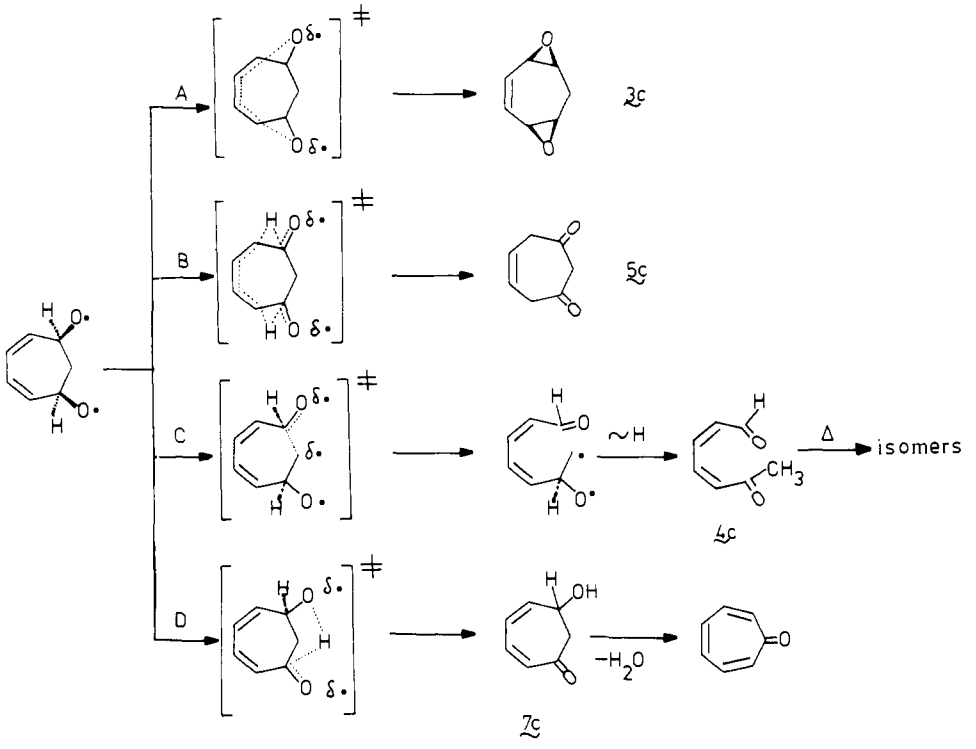
greater relative displacement of the H_3 vs. H_4 proton in the cis,cis isomer.

Returning to the thermolysis of the endoperoxide **2c**, in CCl_4[14] at 90 °C for 5 h the dienes **4c** are also formed in relative yields 20, 10, and 10% for trans,trans, cis,trans, and cis,cis isomers, respectively, by NMR. However, instead of the expected bisepoxide **3c**, the ene-dione **5c** was obtained in 40% yield. Even at 50 °C in $CHCl_3$ during 3 days the ene-dione **5c** is formed slowly. However, at 105 °C in $CHCl_3$ an approximate 1:1 mixture of ene-dione **5c** (ca. 25%) and bisepoxide **3c** (ca. 25%) is obtained, besides the dienes **4c** (ca. 50%).

Unquestionably, this is mechanistically speaking interesting but puzzling, especially since control experiments convincingly demonstrate that none of these products interconvert thermally; i.e., **3c** ⇄ **4c**, **3c** ⇄ **5c**, and **4c** ⇄ **5c** do *not* take place under the conditions of the thermolysis of **2c** between 50 and 135 °C. In the absence of further experimental data, we postulate that, like in the photolysis of endoperoxide **2c** (eq 4), the oxygen diradical serves as precursor to the observed thermolysis products, i.e., the bisepoxide **3c**, the isomeric dienes **4c**, the ene-diene **5c**, and the tropone (Scheme III). Whether the various transformations of the diradical are concerted as indicated in the transition states is an open ended question at this point, but it is a convenient mechanistic rationale to account for the observed products. Further mechanistic scrutiny will be necessary and is in progress.

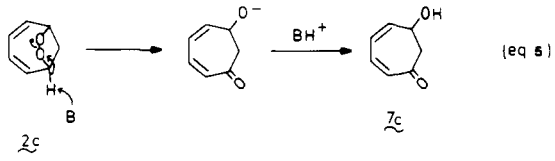
Most intriguing is the formation of ene-dione **5c** via path B since this twofold hydrogen migration is preferred at lower temperature. Furthermore, path C must give first the cis,cis isomer of the diene **4c**, which then isomerizes into the cis,trans and trans,trans isomers, as confirmed by control experiments. The formation of tropone by dehydration of the ketol **7c** (path C) could be confirmed by control experiments. Thus, authentic **7c**, prepared independently from endoperoxide **2c** by methanolysis (Scheme II), dehydrated readily under the thermolysis conditions at 135 °C to afford tropone.

Scheme III



The methanolysis of endoperoxide **2c** at 30 °C afforded within 90 min the *cis,cis*- and *trans,trans*-dienes **4c** in 8 and 2% yields, respectively (the cis,cis isomer converts into the trans,trans isomer in methanol as confirmed by control experiments), 9% tropone, and 57% ketol **7c**. As already pointed out, ketol **7c** readily dehydrates into tropone, especially on silica gel chromatography unless special care is taken. The ketol **7c** could be completely characterized on the basis of correct elemental analysis, IR and NMR spectra (cf. Experimental Section), and catalytic hydrogenation over Pd/C to the known[5] 3-hydroxycycloheptanone.

The formation of the ketol **7c**, the major product in the methanolysis of endoperoxide **2c**, can be rationalized in terms of the base-catalyzed isomerization shown in eq 5.[17]



2c 7c (eq 5)

The polar and protic methanol appears to be sufficiently basic to execute this isomerization. Similar results were observed in the thiourea reduction of endoperoxide **2c** in acetone, affording ketol **7c** (55%) and the *trans,trans*-diene **4c** (16%). Control experiments confirmed that thiourea isomerized the *cis,cis*-diene **4c** quantitatively into the trans,trans isomer, presumably via a reversible Michael-type process.

Treatment of endoperoxide **2c** with triphenylphosphine at 0 °C in $CHCl_3$ gave a complex mixture of products in which the presence of cycloheptatriene epoxide **7b** could be established by NMR.[10b]

Experimental Section

Boiling points and melting points are uncorrected. Infrared spectra were taken on a Perkin-Elmer Model 283 spectrophotometer, ^1H NMR spectra on an Hitachi Perkin-Elmer R-24B spectrometer, and mass spectra on an Hitachi Perkin-Elmer RMS-4 spectrometer. The elemental analyses were performed by the Atlantic Analytical Laboratories, P.O. Box 80569, Atlanta, Ga. 30366. Commercial reagents and solvents were purified to match reported physical and spectral data. Known compounds used in this research were either purchased from standard suppliers (if available) or prepared according to the literature procedures and purified to match the reported physical and spectral data.

Thermolysis of Endoperoxides 2. A 0.5–1.0 M solution (5 mL) of the endoperoxide **2** in CCl_4 (<100 °C) or in toluene (>100 °C) was placed into a constricted test tube, sealed under vacuum, and heated in an oil bath for the appropriate time. After cooling to room temperature, the solvent was rotoevaporated (ca. 20 °C at 15 Torr) and the residue analyzed by ^1H NMR to assure complete transformation of endoperoxide **2**. The thermolysate was submitted to silica gel chromatography, fractional distillation, sublimation, and/or recrystallization to isolate and purify the individual products. Their structure identification is based on spectra data, elemental analyses, independent synthesis, or comparison with literature data.

Endoperoxide 2a. Heating a 1 M solution of **2a** in toluene at 180–190 °C for 45 min, followed by silica gel chromatography at −20 °C, eluting with CH_2Cl_2/*n*-pentane, afforded as second eluate the epoxyenone **3a** in 67% yield, colorless liquid, bulb-to-bulb distilled at 60 °C (bath temperature) and 1.0 Torr, $n^{20}D$ 1.5109; satisfactory elemental analysis based on the $C_7H_8O_2$ empirical formula. The spectral data are: ^1H NMR (CCl_4, Me_4Si, ppm) δ 2.2–3.5 (6 H, multiplet) and 5.5–6.5 (2 H, AB system, J_{AB} = 11.8 Hz); IR (CCl_4, cm^{-1}) 3030 and 3010 (olefinic C–H), 2960 (aliphatic C–H), 1690 (C=O), 1580 (C=C), and 1440 (CH_2 bending); MS (70 eV) *m/e* 124.

As first eluate, the bisepoxide **4a** was isolated in 11% yield, colorless crystals, mp 26–27 °C from CH_2Cl_2/*n*-C_5H_{12} (1:3); satisfactory elemental analysis based on the $C_7H_8O_2$ empirical formula. The spectral data are: ^1H NMR (CCl_4, Me_4Si, ppm) δ 2.1–3.5 (6 H, multiplet) and 5.3–5.8 (2 H, multiplet); IR (CCl_4, cm^{-1}) 3010 (olefinic C—H), 3000, 2985 (aliphatic C—H), 1550 (C=C), 1440 (CH_2 bending), 1250, 1220; MS (70 eV) *m/e* 124.

Diimide Reduction of Bisepoxide 4a. A solution of 0.15 mmol of **4a** in 5 mL of CH_2Cl_2 was reduced at 0 °C with a 20-fold molar excess of diimide, generated in situ as described,[7] affording the saturated bisepoxide **5a** in 95% yield, mp 46–47 °C, colorless needles from ether/*n*-hexane (1:2); satisfactory elemental analysis based on the $C_7H_{10}O_2$ empirical formula. The spectral data are: ^1H NMR (CCl_4, Me_4Si, ppm) δ 1.0–2.5 (6 H, multiplet) and 2.95 (4 H, broad singlet); IR (CCl_4, cm^{-1}) 2980, 2940 (aliphatic C—H), 1480, 1310, 950, 905, 845; MS (70 eV) *m/e* 126.

Thermal Stability of Products 3a and 4a. Heating of 0.2 M solution of epoxyenone **3a** or of bisepoxide **4a** in toluene at 220 °C for 45 min did not result in any changes of these products, as confirmed by ^1H NMR and/or IR.

Endoperoxide 2b. Heating a 0.5 M solution of **2b** in CCl_4 at 100 °C for 30 min afforded the bisepoxide **3b** in 100% yield, colorless liquid, $n^{20}D$ 1.5062; satisfactory elemental analysis based on the $C_7H_8O_2$ empirical formula. The spectral data are: ^1H NMR (CCl_4, Me_4Si, ppm) δ 0.25–0.55 (1 H, multiplet), 0.7–1.0 (1 H, multiplet), 1.1–1.5 (2 H, multiplet), and 2.95 (4 H, singlet); IR (CCl_4, cm^{-1}) 3070 (cyclopropyl C—H), 2990 (aliphatic C—H), 1455 and 1420 (CH_2 bending), and 1235 (C—O); MS (70 eV) *m/e* 124.

Endoperoxide 2c (Thermolysis at 135 °C in Toluene). On heating a 0.3 M solution of **2c** in toluene at 135 °C for 3.5 h afforded a very complex thermolysate mixture, as confirmed by ^1H NMR. The individual products were isolated by silica gel chromatography at 25 °C, eluting with $CHCl_3$.

As first eluate, the bisepoxide **3c** was isolated in 32% yield, colorless needles, mp 55–56 °C, from *n*-hexane/ether 2:1; satisfactory elemental analysis based on the $C_7H_8O_2$ empirical formula. The spectral data are: ^1H NMR (CCl_4, ppm), for the numbering refer to Scheme II, δ_7 (endo) 1.0–1.4 (1 H, multiplet), δ_7 (exo) 2.3–2.8 (1 H, multiplet), $\delta_{1,2,5,6}$ 3.0–3.3 (4 H, multiplet), and $\delta_{3,4}$ 5.65 (2 H, singlet); IR (CCl_4, cm^{-1}) 3030 (olefinic C—H), 2980, 2940 (aliphatic C—H), 1480 (CH_2 bending), 990, 975, 935, 865; MS (70 eV) *m/e* 124.

As second eluate a mixture of the dienes *trans,trans*-, *cis,trans*-, and *cis,cis*-**4c** was isolated in 24, 12, and 8% yields, respectively, colorless oil; satisfactory elemental analysis based on the $C_7H_8O_2$ empirical formula. On further silica gel chromatography, using $CHCl_3$/*n*-C_5H_{12} as solvent, the dienes eluted in the order cis,trans > cis,cis > trans,trans. The cis,trans and cis,cis are colorless oils, while the trans,trans isomer is crystalline, mp 48 °C (lit.[16] 42 °C). For convenience, the NMR, IR, and MS spectral data are summarized in Table I.

Endoperoxide 2c (Thermolysis at 90 °C in CCl_4). Heating a 0.5 M solution of **2c** in CCl_4 at 90 °C for 5 h led to a complex product mixture, consisting of the isomeric dienes **4c** and the dione **5c**, as confirmed by ^1H NMR. The isomer composition of the dienes **4c** was 20% trans,trans, 10% cis,trans, and 10% cis,cis by NMR. The dione **5c** (40%) could conveniently be isolated by first destroying the dienes **4c** on heating at 90 °C for 14 h. The resulting reaction mixture was chromatographed on Florisil, eluting with CH_2Cl_2 at room temperature. The dione **5c** was obtained in 28% yield, colorless liquid, bp 110 °C at 0.9 Torr, satisfactory elemental analysis based on the $C_7H_8O_2$ empirical formula. The spectral data are: ^1H NMR ($CDCl_3$, Me_4Si, ppm) δ 3.12 (4 H, doublet, J = 4.25 Hz), 3.46 (2 H, singlet), and 5.6 (2 H, multiplet); IR (CCl_4, cm^{-1}) 3020 (olefinic C—H), 2920 (aliphatic C—H), 1710–1730 (C=O), 1580 (C=C), 1440 (CH_2 bending), 1395, 1260, 1240; MS (70 eV) *m/e* 124. Catalytic reduction of **5c** in ethyl acetate over Pd/C (10%) afforded quantitatively 1,3-cycloheptadienone; identical ^1H NMR and IR data with authentic material.[17]

Thermal Stability of Bisepoxide 3c. On heating of a 0.5 M solution of **3c** in toluene at 135 and at 180 °C for 6 h, this bisepoxide was recovered quantitatively, as confirmed by ^1H NMR and IR.

Thermal Stability of Dienes 4c. On heating 0.2 M solutions of the pure *trans,trans*-**4c** diene (isolated by silica gel chromatography at 25 °C, eluting with $CHCl_3$/*n*-pentane 3:1) in toluene at 135 °C for 3.5 h, no isomerization occurred, as confirmed by NMR. When a 0.2 M solution of the pure *cis,cis*-**4c** diene (isolated by silica gel chromatography at 25 °C, eluting with 3:1 $CHCl_3$/*n*-C_5H_{12}) in toluene was heated at 135 °C for 3 h, extensive cis-trans isomerization occurred, as confirmed by NMR.

Photolysis of Endoperoxide 2c. A 10-mL cylindrical Pyrex vessel was charged with 0.75 mmol of endoperoxide **2c** in 6 mL of benzene,

sealed with a rubber septum, and irradiated in a Rayonet photoreactor (Model PR-100), provided with a merry-go-round, at 350 nm for 6 h. The solvent was rotoevaporated (ca. 15 °C at 20 Torr) and the product confirmed as bisepoxide **3c** by ^{1}H NMR, IR, and TLC (silica gel, CH_2Cl_2/n-C_5H_{12} as eluant), formed in 57% yield. Control experiments showed that **2c** was photostable at 295-300 nm.

Methanolysis of Endoperoxide 2c. A solution of 2 mmol of **2c** in 10 mL of MeOH was allowed to stand at room temperature (ca. 30 min) and monitored by ^{1}H NMR. After 90 min the endoperoxide **2c** was completely transformed into a complex mixture of products. Rotoevaporation (ca. 25 °C at 15 Torr) of the MeOH and by silica gel chromatography at 25 °C, eluting with $CHCl_3$, the individual products were isolated and purified.

As first eluate, the *cis,cis*-**4c** and *trans,trans*-**4c** dienes were obtained in 8 and 2% yields, respectively, as confirmed by ^{1}H NMR and IR. A control experiment showed that *cis,cis*-**4c** isomerized into *trans,trans*-**4c**. As second eluate, 9% tropone was obtained.

As third eluate, the ketol **7c** was isolated[4a] in 57% yield, pale yellow liquid, which on attempted distillation at 110 °C (bath temperature) and 1 Torr partially dehydrated into tropone. The spectral data are: ^{1}H NMR ($CDCl_3$, Me_4Si, ppm) δ 2.5-3.25 (2 H, multiplet, J_{AB} = 15.67 Hz), 3.5 (1 H, multiplet, exchanged with D_2O), 4.3-4.7 (1 H, multiplet), and 5.4-6.6 (4 H, multiplet); IR ($CHCl_3$, cm^{-1}) 3590, 3360 (OH), 3010 (olefinic C—H), 2990 (aliphatic C—H), 1650 (C=O), 1635 (C=C), 1575 (CH_2 bending); MS (70 eV) *m/e* 124. Catalytic reduction of ketol **7c** over Pd/C (10%) in MeOH afforded the known[5] 3-hydroxycycloheptanone, colorless liquid, bp 90 °C at 1 Torr.

On the silica gel column, the ketol **7c** partially dehydrated to form tropone.

Triphenylphosphine Deoxygenations of Endoperoxides 2. A 10-mL, one-necked, round-bottomed flask, provided with a magnetic spinbar, was charged with 0.5 mmol of endoperoxide **2** in 5 mL of $CHCl_3$. While stirring magnetically, 0.5 mmol of triphenylphosphine in 2 mL of $CHCl_3$ was added dropwise and allowed to stir 30 min at room temperature. The solvent was rotoevaporated (ca. 25 °C at 15 Torr), the residue was triturated with 2 mL of cold ether, the solid triphenylphosphine oxide removed by filtration, the solvent rotoevaporated, and the product bulb-to-bulb distilled at 50 °C and 0.1 Torr.

Endoperoxide 2a. Deoxygenation of **2a** at 80 °C afforded a mixture of epoxydiene **7a**, its valence isomer **7a'**, and epoxydiene **7b** in 57% total yield, confirmed by ^{1}H NMR and IR which were identical with the authentic compounds.[10]

Endoperoxide 2b. The ene-epoxide **4b** was obtained in 69% yield at 0 °C, colorless liquid, satisfactory elemental composition by high resolution mass spectrometry. The spectral data are: ^{1}H NMR (CCl_4, Me_4Si, ppm), for numbering refer to eq 2, $\delta_{6_{endo}}$ 0.6-0.9 (1 H, multiplet), $\delta_{6_{exo},7}$ 0.9-1.4 (2 H, multiplet), δ_5 1.5-1.9 (1 H, multiplet), δ_3 2.6-2.9 (1 H, multiplet), δ_4 3.4-3.6 (1 H, multiplet), δ_2 5.2-5.5 (1 H, multiplet), and δ_1 5.7-6.0 (1 H, multiplet), $J_{1,3}$ = 1.30, $J_{4,5}$ = 1.75, $J_{2,3}$ = 3.66, $J_{1,7}$ = 3.77, $J_{3,4}$ = 4.50, and J_{12} = 9.66 Hz; IR (CCl_4, cm^{-1}) 3010 (olefinic C—H), 3040 (cyclopropyl C—H), 2970 (aliphatic C—H), 1665 (C=C).

Endoperoxide 2c. At 0 °C a complex reaction mixture was obtained, whose NMR clearly showed the presence of cycloheptatriene epoxide **7b**, prepared by peracetic acid epoxidation of cycloheptatriene.[10b]

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Mechanism of Biaryl Synthesis with Nickel Complexes

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Abstract: The mechanism of the nickel-catalyzed coupling of aryl halides to afford biaryls is examined by focusing on the reactions of arylnickel(II) halide as the important organometallic intermediate. A variety of triethylphosphinenickel(II) complexes, *trans*-**Ar**NiX$(PEt_3)_2$ (**1**), are synthesized and found to yield biaryls only upon treatment with aryl halide (ArX). Biaryl formation is shown to involve a radical-chain process in which paramagnetic nickel(I) and arylnickel(III) species are reactive intermediates. The propagation steps include the oxidative addition of ArX to nickel(I) to produce the reactive arylnickel(III) species, which undergoes aryl transfer with **1** to afford a diarylnickel(III) intermediate, followed by reductive elimination of biaryl and the regeneration of nickel(I). This series of chain reactions provides an efficient mechanism for the cross coupling of **1** and ArX selectively to **Ar**Ar, except for a competition from a halogen exchange process which, in effect, scrambles aryl groups between **1** and an arylnickel(III) species. The initiation of the catalytic cycle is associated with electron transfer from **1** to ArX, and it can be manipulated by a rational choice of initiators and inhibitors. In the course of biaryl formation, the triethylphosphine ligand reacts with excess ArX to produce arylphosphonium salts, $ArPEt_3^+$, by a second catalytic process induced by the nickel(I) intermediate. The phosphine levels in the reaction are critical to initiation and inhibition of both of these catalytic or chain processes, which are discussed in relation to nickel ligation.

Introduction

Synthetic procedures for the preparation of biaryls by the classical Ullmann reaction[1] have, in recent years, been supplanted by the use of zerovalent nickel to effect the reductive coupling of aryl halides under homogeneous conditions.

$$2ArX \xrightarrow{+2e} ArAr + 2X^-$$

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