Singlet Oxygen Photooxygenation of Tricyclo[4.3.0.0^{1,3}]nona-6,8-dienes and Bicyclo[4.3.0]nona-1(6),7-dienes: Characterization of the Primary Reaction Products and Subsequent Transformations

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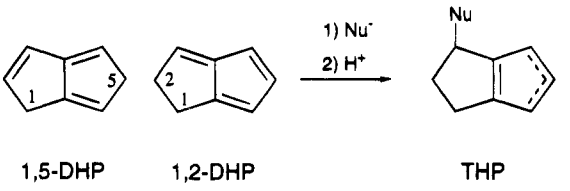
Received September 6, 1994®

Ring expansion of 3-methyl-1-phenyl-1,2-dihydropentalene **1** using a sequence of cyclopropanation and acid-catalyzed vinylcyclopropane rearrangement in the presence of nucleophilic trapping reagents led to bicyclo[4.3.0]nona-1(6),7-dienes **8** and **9** in good yields and with high diastereoselectivity. Photooxygenation of these compounds, as well as the secondary product tricyclo[4.3.0.0^{1,3}]-nona-6,8-diene **2**, afforded the unstable endoperoxides **3** and **11** both with high (but completely inverse) diastereofacial selectivity. Both endoperoxides underwent Kornblum–De La Mare reaction in the presence of triethylamine to give the hydroxy enones **4** and **15**. X-ray structure analyses of **4a** and **15** confirmed the proposed reaction topicities. The thermal rearrangement of **11** afforded a series of products (bis-epoxide **12**, epoxy enone **13**, and epoxy enal **14**) following the well-known peroxide homolysis protocol, whereas **3** thermally rearranged into the cyclooctene dione **5** and the cycloheptenone aldehyde **6**, by cleavage of the central bicyclo[3.3.0]octane bond and competing 1,2-hydrogen and 1,2-alkyl shifts, respectively.

Introduction

The photooxygenation of cyclic 1,3-dienes is a valuable method for the synthesis of polyoxyfunctionalized target molecules.[1] This type of singlet oxygen addition reaction is the fastest bimolecular Diels–Alder reaction known and leads to thermally and photochemically unstable bicyclic peroxides (endoperoxides). With and without external reagents, these endoperoxides can be rearranged or easily transformed into various oxidation products. If additionally the diastereofacial selectivity can be controlled, singlet oxygen photooxygenation can serve as an excellent and mild synthetic methodology.[2]

Our synthesis of 1,2- and 1,5-dihydropentalenes (DHP)[3] and their corresponding tetrahydro- and octahydro-isomers constitutes as a versatile approach to numerous reactive building blocks and thus is a starting point for the synthesis of terpenoid compounds.[4] Whereas hydrogen shifts are relatively slow for 1,2- and 1,5-DHP (which can therefore be separated and investigated independently), tetrahydropentalenes underwent rapid 1,5-hydrogen migrations and are in rapid equilibrium at room temperature. We therefore used a method to convert 1,2-DHP into the tetrahydro-isomers (THP) with concomitant protection against hydrogen migration. Nucleophilic addition to the electrophilic C3–C4 double bond of pentafulvene-like 1,2-DHP might supply this protection.



Herein we report the synthesis of cyclopropanation products and subsequent transformations of the corresponding endoperoxides. Cyclopropanation of the C3–C4 double bond not only serves as a method of protection but also as an approach to ring expansion products. Thus, we additionally investigated several methods for ring expansion of the tricyclo[4.3.0.0^{1,3}]nona-6,8-diene skeleton to bicyclo[4.3.0]nona-1(6),7-dienes and further conversion of these compounds into polyoxyfunctionalized products.

Results

Tricyclo[4.3.0.0^{1,3}]nona-6,8-dienes. The use of oxosulfonium ylides for selective cyclopropanation of pentafulvenes has been reported by Schröer and Friedrichsen.[5] We doubted whether this method would also work for 1,2-dihydropentalenes because of our experiences with pronounced selectivity differences between pentafulvenes and dihydropentalenes in cycloaddition reactions.[6] Fortunately, 1,2-dihydropentalene **1** proved to behave quite similarly in its reactivity toward the sulfur ylide, showing strong preference for addition to the C3–C4 double bond.

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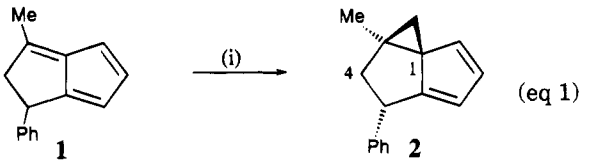
Thus, cyclopropanation using trimethyloxosulfonium iodide/NaH proceeded smoothly at 0 °C with the formation of only one diastereoisomeric tricyclo[4.3.0.0^{1,3}]nona-6,8-diene **2**.[7] As already observed for the lithium aluminum hydride reduction of **1**,[4] a phenyl substituent at C-1 completely shields the *syn*-side of the reactive C3–C4 double bond against attack by the ylide reagent. An NOE enhancement of 3.5% for the proximate cyclopropane methylene hydrogen 2-H$_{syn}$ on saturation of 5-H (vice versa 8.4%) was indicative of the relative configuration of compound **2**.



(eq 1)

(i) $Me_3SO^+I^-$, NaH, DMSO, 0°C, 82%

In order to learn more about the structural distortion induced by the annulated cyclopropane ring, we studied the photooxygenation of **2** which serves as a precursor for the following reaction steps. Singlet oxygen was generated by photosensitization using tetraphenylporphyrin as sensitizer in methylene chloride at −65 °C. The DABCO (quenching) test[8] and the limonene (product pattern) test[9] clearly proved that exclusively Type II photooxygenation (i.e. singlet oxygen) occurs under the conditions described. The endoperoxide **3** is stable in solution at temperatures lower than at −50 °C and could be characterized by NMR. Within the limits of NMR resolution, only one diastereoisomer was observed, to which we assigned the *anti*-phenyl configuration. This assignment was proven by the product stereochemistry of the thermal and base-catalyzed rearrangements of endoperoxide **3**. Surprisingly, after treatment with triethylamine (Kornblum–De La Mare reaction[10]) two products were formed in a ratio of 39:61. These compounds could be separated and fully characterized. Both molecules are γ-hydroxy enones (**4a**,**b**) and differ only in their respective configuration at C-5.

The crystal structure analysis[18] of the minor diastereoisomer **4a** was performed in order to unambigously establish the relative configuration of C-1, C-5, and C-6. In the crystal lattice, every molecule of **4a** shows two hydrogen bonds to two other hydroxy enones (183 pm H···O). In agreement with the *trans*-arrangement between the phenyl substituent at C-5 and the cyclopropane methylene group C-2 are the similar proton NMR chemical shifts for 2-H$_{anti}$ and 2-H$_{syn}$ (1.55 and 1.63 ppm) for **4a**. In **4b**, where the phenyl substituent is pointing toward the 2-H$_{syn}$, this hydrogen atom is anisotropically shielded and its resonance is shifted to 1.06 ppm. The inverse chemical shift effect could be observed for the methyl group at C-3. The formation of **4b** (which must a be secondary product) indicates that after heterolytic cleavage of the peroxide bond, epimerization at C-5 can compete with protonation of the primary formed alkoxy oxygen, which terminates the whole reaction sequence. Treatment of either **4a** or **4b** with base (triethylamine

(7) All compounds are racemic. Only one enantiomer is drawn.
(8) Ouannès, C.; Wilson, T. *J. Am. Chem. Soc.* **1968**, *90*, 6527.
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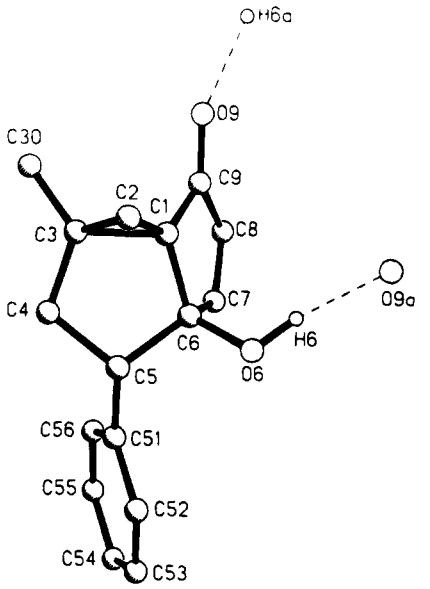
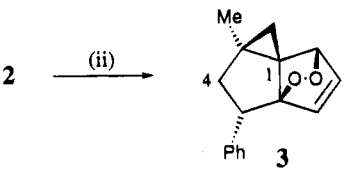
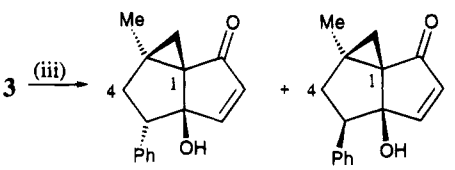


Figure 1. X-ray structure **4a** (minor diastereomer from the base catalyzed rearrangement of endoperoxide **3**)

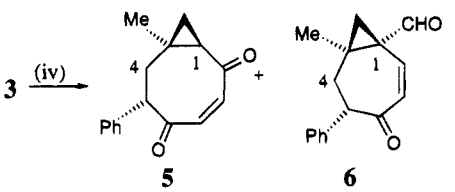
or sodium hydride) does not lead to such an epimerization. Therefore, we assume that a previously unreported (and unusual) process leads to partial inversion of configuration at C-5.



(eq 2)



(eq 3)



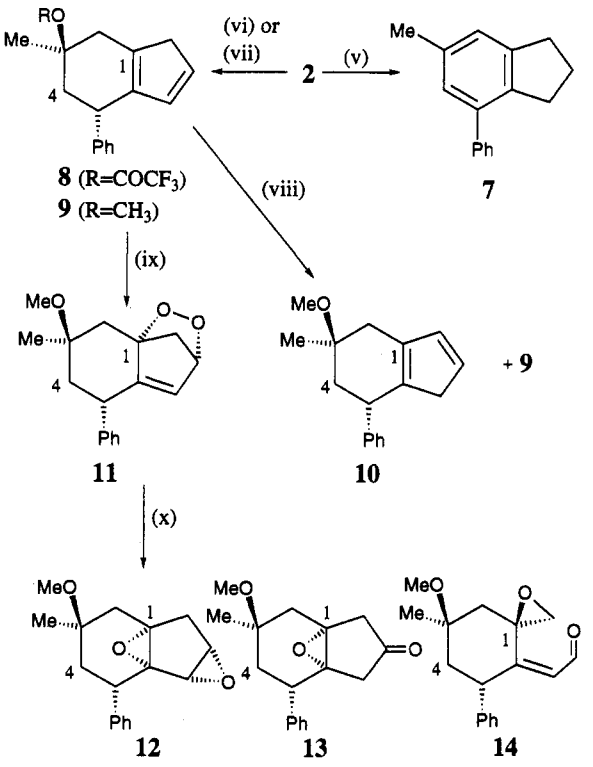
(eq 4)

(ii) TPP, CH_2Cl_2, $^3O_2$, hv, -65°C, 100%;
(iii) 8 eq. NEt_3, CH_2Cl_2, -20°C, 73%; **4a**:**4b** = 39:61;
(iv) CH_2Cl_2, r.t., 2h, 80%, **5**:**6** = 80:20.

A surprising result was the thermal rearrangement of endoperoxide **3**. To the best of our knowledge,[1] there is no example known of the thermolysis of a bicyclic endoperoxide leading to the direct formation of an enedione system by consecutive C–C cleavage and 1,2-hydrogen (or 1,2-alkyl) migration. Cyclic conjugated enediones can, however, be generated via a sequence of photooxygenation, base-catalyzed ring opening, and oxidation of the γ-hydroxy enone starting from the corresponding cyclo-1,3-dienes.[11] When substrate **3** was warmed in solution to 0 °C, the *direct* rearrangement was complete in 5 h and **5** was formed with ca 20% **6** as an

(11) Kayama, Y.; Oda, M.; Kitahara, Y. *Chem. Lett.* **1974**, 345.

Scheme 1



(v) HCl, CH_2Cl_2, 0°C, 95%;

(vi) 1.0 eq. CF_3COOH, CH_2Cl_2, 0°C, 90%, d.r.> 96:4;

(vii) 1.0 eq. CF_3COOH, CH_3OH, 0°C, 91%, d.r. = 87:13;

(viii) 1.5 eq. NaH, Et_2O, -20°C, 2h, then r.t., 0.5 h, than NH_4Cl, H_2O, 95%; (ix) TPP, CH_2Cl_2, $^3O_2$, hv, -25°C, 100%;

(x) CH_2Cl_2, r.t., 7d, 85%, **12**:**13**:**14** = 30:40:30.

additional product as a result of competing 1,2-H and 1,2-alkyl shifts.

Bicyclo[4.3.0]nona-1(6),7-dienes. There are several methods known by which vinylcyclopropanes of the spiro-[4.2]heptadiene-type can be transformed into ring-enlarged products.[12] For compound **2**, thermolysis under vacuum flash conditions (550 °C/0.1 Torr) gave rise to a complex product mixture (not shown). NMR analysis indicated that at least two bicyclo[4.3.0]nonatrienes were formed as major products. An alternative method for the rearrangement of vinylcyclopropanes is acid catalysis. After treatment of a solution of **2** in methylene chloride at 0 °C with gaseous HCl for 3 min, the formation of indane **7** was complete. Product **7** results from a sequence of protonation/deprotonation steps, which leads to the most stable C_9-compound. When an equimolar amount of trifluoroacetic acid in methylene chloride was utilized, only one product was formed with remarkably high stereoselectivity. In analogy to the trapping products described later, we assign the *trans* configuration to this product **8** (Scheme 1). Protonation occurred exclusively at C-9, with formation of the cyclopropylallyl cation, which subsequently underwent cyclopropyl ring opening and (simultaneous?) cation trapping by the trifluoroacetate anion. The analogous experiment in methanol gave a 87:13 mixture of the diastereoisomeric methanol addition products **9**.

The major product (the only one drawn in Scheme 1) was the *trans* 3-methoxy product, as indicated by NOE measurements. When sterically more demanding alcohols (e.g. 2-propanol, not shown) were used, even in high molar excess, the corresponding trapping products were always formed with the trifluoroacetic acid addition product **8** as byproduct. This disadvantage, however, was counterbalanced by the fact that sterically more demanding alcohols gave rise to the formation of diastereoisomerically pure trapping products.[13]

Surprisingly, **9** was formed as only one constitutional (cyclopentadiene) isomer, in contrast to the results obtained when tetrahydropentalenes were synthesized from their 1,2-dihydropentalene precursors.[4] The 1,5-hydrogen shifts are relatively fast with 1,2-dialkyl-substituted cyclopentadienes[14] and also with 1,2,3,*n*-tetrahydropentalenes, even at room temperature. Compound **9**, however, showed no tendency to isomerize, even when heated to 60 °C in dimethyl sulfoxide (higher temperatures could not be applied because of di- and oligomerization). When the sodium cyclopentadienyl anion generated from **9** by treatment with 1.5 equiv of NaH in ether was quenched with water, the two bicyclo-[4.3.0]nonadiene tautomers **9** and **10** were isolated in a 2:1 ratio. No trace of the isomeric 2,3-disubstituted cyclopentadiene isomer could be detected. Similar behavior for the protonation of bicyclic sodium cyclopentadienyls was reported by Reinarz and Fonken for the unsubstituted bicyclo[4.3.0]nonadiene.[15] Our results clearly show that **9** and **10** are separated by at least a 30 kcal/mol activation barrier. 1,5-Hydrogen migration obviously seems to be complicated by the substituents at C-3 and C-5 and, consequently, we expected these substituents also to exhibit a pronounced effect on the side-selectivity of cycloaddition reactions with **9**.

The photooxygenation of the 87:13 diastereoisomeric mixture of **9** was complete in methylene chloride at −25 °C after less than 1 h. A 87:13 mixture of endoperoxides **11** resulted (only the major diastereoisomer is shown in Scheme 1), indicating that every substrate diastereoisomer had been added to by 1 equiv of singlet oxygen with high face-selectivity. From NOE measurements, no unequivocal decision about the relative configuration could be made. Our initial idea was that, similar to **2**, the phenyl substituent at C-5 plays the decisive role in the photooxygenation of **9**. As already indicated in Scheme 1 this assumption proved to be wrong (*vide infra*). When the mixture of diastereoisomeric endoperoxides was kept in solution for 7 days at room temperature (which also indicates the much higher thermal stability of **11** compared with **3**), the thermal rearrangement was complete. Eight products were formed, of which only the major ones are shown in Scheme 1. As with other known tricyclic endoperoxides derived from substituted cyclopentadienes, three decomposition pathways operate, all initiated by homolysis of the O−O bond. The "least motion" product **12** requires only radical addition of one of the oxygen radicals to the C−C double bond and subsequent C−O bond formation at the 1,3-biradical stage. 1,2-Hydrogen migration after formation

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Table 1. ^{1}H NMR Spectroscopic Data for Compounds in this Study[a]

compd	1-H	2-H	4-H	5-H	7-H	8-H	9-H	Me	Ph
2		1.91 (d,1H, J = 4.1), 1.95 (d, J = 4.1)	2.56 (dd, 1H, J = 12.5, J = 2.7), 2.74 (dd, 1H, J = 12.5 J = 6.9)	3.87 (t, 1H, J = 7.9)	5.85 (s, 1H)	6.55 (dd, 1H, J = 5.1, J = 2.1)	6.26 (d, 1H, J = 5.1)	1.49 (s, 3H)	7.24–7.38 (m, 5H)
3		0.91 (d, 1H, J = 5.8), 0.96 (d, 1H, J = 5.8)	2.50–2.58 (m, 2H)	3.22 (dd, 1H, J = 9.9, J = 8.0)	6.57 (dd, 1H, J = 5.6, J = 1.2)	6.71 (dd, 1H, J = 5.6, J = 2.2)	5.18 (dd, 1H, J = 2.2, J = 1.2)	1.34 (s, 3H)	7.25–7.46 (m, 5H)
4a		1.55 (d, 1H, J = 5.8), 1.63 (d, 1H, J = 5.8)	2.03 (dd, 1H, J = 14.0, J = 11.2), 2.40 (dd, 1H, J = 14.0, J = 8.6)	3.18 (dd, 1H, J = 11.2, J = 8.6)	6.92 (d, 1H, J = 6.0)	6.06 (d, 1H, J = 6.0)		1.09 (s, 3H)	7.16–7.32 (m, 5H)
4b		1.06 (dd, 1H, J = 3.9, J = 1.1), 1.50 (d, 1H, J = 3.9)	2.21 (dd, 1H, J = 11.8, J = 6.4), 2.69 (ddd, 1H, J = 11.8 J = 10.8 J = 1.2)	2.99 (dd, 1H, J = 10.8, J = 6.4)	7.46 (d, 1H, J = 5.9)	6.14 (d, 1H, J = 5.9)		1.56 (s, 3H)	7.18–7.34 (m, 5H)
5	1.84 (dd, 1H, J = 7.6, J = 6.5)	0.81 (dd, 1H, J = 7.6, J = 5.1), 1.38 (dd, 1H, J = 6.5, J = 5.1)	2.07 (dd, 1H, J = 15.0, J = 8.3), 2.36 (dd, 1H, J = 15.0, J = 8.4)	4.15 (t, 1H, J = 8.4)	6.29 (d, 1H, J = 13.1)	6.56 (d, 1H, J = 13.1)		1.22 (s, 3H)	7.19–7.24 (m, 5H)
6		1.90 (d, 1H, J = 5.6), 2.23 (d, 1H, J = 5.6)	2.35 (dd, 1H, J = 15.7, J = 3.0), 2.82 (dd, 1H, J = 15.7, J = 12.2)	3.73 (dd, 1H, J = 12.2, J = 3.0)	7.20–7.45 (m_c)	6.14 (d, 1H, J = 13.0)	9.26 (s, 1H)	1.47 (s, 3H)	7.20–7.45 (m, 5H)
8		2.63 (dd, 1H, J = 18.7, J = 3.8), 3.21 (d, 1H, J = 18.7)	1.72 (dd, 1H, J = 13.9, J = 11.4), 2.76 (ddd, 1H, J = 13.9, J = 5.4 J = 2.2)	3.72 (m, 1H)	6.25 (d, 1H, J = 5.4)	6.06 (d, 1H, J = 5.4)	2.95–3.01 (m, 2H)	1.71 (s, 3H)	7.14–7.36 (m, 5H)
9[b]		2.42 (dd, 1H, J = 18.1, J = 3.8), 2.68 (d, 1H, J = 18.1)	1.59 (dd, 1H, J = 13.7, J = 11.5), 2.26 (ddd, 1H, J = 13.7, J = 5.3, J = 2.1)	3.75 (m, 1H)	6.20 (d, 1H, J = 5.3)	6.06 (ddd, 1H, J = 5.3, J = 3.0, J = 1.5)	2.90–3.01 (m, 2H)	1.27 (s, 3H), 3.29 (s, OMe)	7.16–7.35 (m, 5H)

[a] 250 MHz, $CDCl_3$, shifts in δ, coupling constants in Hz. [b] Minor diastereoisomer: δ 2.81 (m, 1H), 3.10 (m, 1H).

Table 2. ^{1}H NMR Spectroscopic Data for Compounds in This Study[a]

compd	2-H	4-H	5-H	7-H	8-H	9-H	Me	OMe	Ph
11	2.10 (m, 1H), 2.53 (d, 1H, J = 15.5)	1.64 (dd, 1H, J = 13.5, J = 12.6), 2.10 (m, 1H)	3.82 (ddd, 1H, J = 12.6 J = 6.2, J = 2.2)	5.82 (br s, 1H)	5.22 (br s, 1H)	2.10 (m, 2H)	1.29 (s, 3H)	3.29 (s, 3H)	7.19–7.35 (m, 5H)
12	1.67 (d, 1H, J = 16.0), 2.29 (d, 1H, J = 16.0)	1.51 (dd, 1H, J = 14.1, J = 12.0), 1.89 (ddd, 1H, J = 14.1, J = 5.0, J = 2.2)	3.39 (dd, 1H, J = 12.0, J = 5.0)	3.30 (d, 1H, J = 2.9)	3.68 (t, 1H, J = 2.9)	1.74 (dd, 1H, J = 15.5, J = 2.9), 2.04 (dd, 1H, J = 15.5, J = 2.2)	1.10 (s, 3H)	3.25 (s, 3H)	7.25–7.46 (m, 5H)
13	1.93 (d, 1H, J = 15.7), 2.13 (dd, 1H, J = 15.7, J = 2.3)	1.62 (dd, 1H, J = 14.1, J = 12.1), 1.82 (ddd, 1H J = 14.1, J = 4.8, J = 2.3)	3.24 (dd, 1H, J = 12.1, J = 4.8)	2.27 (d, 1H, J = 19.3), 2.39 (d, 1H, J = 19.3)		2.45 (d, 1H, J = 19.4), 2.62 (d, 1H, J = 19.4)	1.10 (s, 3H)	3.18 (s, 3H)	7.15–7.33 (m, 5H)
14	1.96 (1H, covered), 2.35 (1H, covered)	1.93 (1H, covered), 2.35 (1H, covered)	4.34 (ddd, 1H, J = 12.8, J = 3.7, J = 1.6)	5.24 (dd, 1H, J = 7.9, J = 1.6)	9.96 (d, 1H, J = 7.9)	2.97 (d, 1H, J = 4.4), 3.04 (d, 1H, J = 4.4)	1.21 (s, 3H)	3.22 (s, 3H)	7.17–7.31 (m, 5H)
15[b]	1.97 (d, 1H, J = 15.2), 2.26 (d, 1H, J = 15.2)	2.08 (dd, 1H, J = 5.6 J = 1.2), 2.38, (d, 1H, J = 12.6)	3.95 (ddd, 1H, J = 12.6, J = 5.6, J = 1.6)	5.55 (d, 1H J = 1.6)		2.43 (br s, 2H)	1.24 (s, 3H)	3.11 (s, 3H)	7.15–7.26 (m, 5H)

[a] 250 MHz, $CDCl_3$, shifts in δ, coupling constants in Hz. [b] Minor diastereoisomer: δ 3.27 (s, 3H, OMe), 5.25 (d, 1H, J = 1.8)

Table 3. ^{13}C NMR Spectroscopic Data for Compounds in This Study[a]

compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	Me	OMe	Ph
2	56.0 (s)	27.4 (t)	36.6 (s)	51.2 (t)	41.1 (d)	161.3 (s)	130.7 (d)	133.4 (d)	118.2 (d)	21.5 (q)		126.5 (d),128.2 (d), 128.3 (d), 142.1 (s)
3	65.1 (s)	15.7 (t)	26.2 (s)	42.5 (t)	41.2 (d)	101.1 (s)	139.5 (d)	133.7 (d)	82.2 (d)	17.7 (q)		12€.7 (d), 128.1 (d),128.2 (d), 137.3 (s)
4a	51.9 (s)	32.6 (t)	36.4 (s)	41.5 (t)	42.6 (d)	88.4 (s)	155.7 (d)	139.5 (d)	201.6 (s)	17.9 (q)		127.5 (d), 128.9 (d), 129.1 (d), 137.2 (s)
4b	50.6 (s)	20.8 (t)	37.2 (s)	39.4 (t)	51.4 (d)	90.2 (s)	159.5 (d)	135.6 (d)	203.5 (s)	18.8 (q)		127.3 (d), 128.7 (d), 138.7 (s)
5	38.8 (d)	20.4 (t)	27.3 (s)	38.3 (t)	54.3 (d)	205.6 (s)	137.1 (d)	138.0 (d)	204.0 (s)	28.0 (q)		127.6 (d), 128.7 (d), 128.8 (d), 139.2 (s)
6	42.2 (s)	32.9 (t)	39.5 (s)	37.8 (t)	54.6 (d)	203.2 (s)	139.9 (d)	127.8 (d)	198.4 (d)	21.5 (q)		127.1 (d), 128.1 (d), 128.7 (d), 140.8 (s)
8	135.6 (s)	43.1 (t)	87.6 (s)	36.5 (t)	39.3 (d)	139.5 (s)	130.6 (d)	132.7 (d)	43.8 (t)	25.2 (q)	112.5 (CF_3), 154.4 (C=O)	126.5 (d); 128.0 (d), 128.6 (d), 143.6 (s)
9	137.4 (s)	43.3 (t)	74.0 (s)	36.4 (t)	39.5 (d)	139.6 (s)	129.8 (d)	133.2 (d)	43.5 (t)	24.4 (q)	49.3 (q)	126.1 (d), 128.1 (d), 128.4 (d), 145.1 (s)
10	140.9 (s)	31.9 (t)	73.9 (s)	35.4 (t)	39.5 (d)	136.9 (s)	41.5 (t)	133.6 (d)	131.7 (d)	24.5 (q)	49.2 (q)	126.1 (d), 128.1 (d), 128.4 (d), 146.0 (s)
11	90.8 (s)	41.3 (t)	73.6 (s)	33.4 (t)	38.5 (d)	150.5 (s)	126.2 (d)	84.5 (d)	56.1 (t)	24.5 (q)	49.5 (q)	126.5 (d), 127.9 (d), 128.4 (d), 144.3 (s)
12	64.5 (s)	38.8 (t)	72.6 (s)	37.3 (t)	37.2 (d)	72.0 (s)	62.9 (d)	54.0 (d)	33.1 (t)	24.0 (q)	49.0 (q)	126.8 (d), 128.2 (d), 128.7 (d), 141.1 (s)
13	62.6 (s)	37.0 (t)	72.3 (s)	36.9 (t)	39.5 (d)	67.0 (s)	46.5 (t)	211.7 (s)	43.6 (t)	23.9 (q)	49.0 (q)	127.0 (d), 128.0 (d), 128.7 (d), 141.5 (s)
14	56.6 (s)	43.3 (t)	74.4 (s)	43.0 (t)	44.5 (d)	165.1 (s)	125.7 (d)	190.4 (d)	53.8 (t)	24.6 (q)	49.4 (q)	127.3 (d), 128.3 (d), 128.7 (d), 139.2 (s)
15[b]	76.5 (s)	48.1 (t)	73.7 (s)	37.3 (t)	40.3 (d)	181.3 (s)	129.3 (d)	206.6 (s)	52.3 (t)	25.9 (q)	49.0 (q)	126.7 (d), 128.0 (d), 128.7 (d), 142.7 (s)

[a] 63 MHz, $CDCl_3$, shifts in δ. [b] Minor diastereoisomer: δ 23.9 (q), 42.7 (t), 44.8 (d), 47.7 (t), 49.3 (q), 51.8 (t), 72.8 (s), 75.2 (s), 127.5, 128.6, 128.9, 131.9 (all d), 140.9 (s).

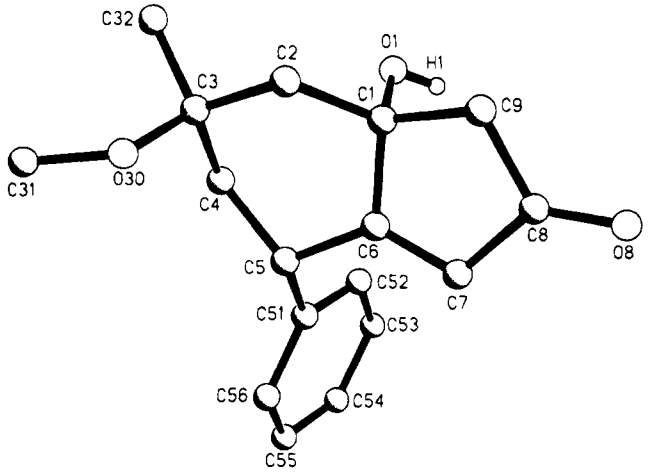

Figure 2. X-ray structure **15** (product of the base-catalyzed rearrangement of endoperoxide **11**).

of the higher substituted oxirane ring leads to the epoxy ketone **13**, and cleavage of a C−C single bond following the primary homolytic step leads to the enol epoxide **14**. NMR analysis indicated a *ca.* 87:13 (±5%) ratio for all product types. Additionally, the geometric isomers of **14** were detected, probably due to secondary isomerization. Using flash chromatography, the bis-epoxides **12** could be separated, and enriched samples of epoxy ketones **13** were obtained. The enol epoxides were not stable under these conditions.

When the endoperoxide **11** was treated with triethylamine in methylene chloride, quantitative Kornblum–De La Mare reaction was observed. Again, the ratio of diastereoisomeric hydroxy enones **15** exactly matched the diastereoisomeric ratio of the starting material **11**.

After chromatographic separation of the diastereoisomers **15**, crystallization from methyl *tert*-butyl ether gave colorless crystals of the major diastereoisomer (minor not shown in Figure 2) suitable for X-ray structure analysis.[18] The *cis*-arrangement of the methyl, phenyl, and hydroxy group in the major diastereoisomer **15** reveals (a) methanol trapping of the protonated tricyclo[4.3.0.0^{1,3}]nona-6,8-diene **2** had occurred mainly *anti* to the side of the phenyl substituent, and (b) singlet oxygen addition had exclusively taken place *syn* with respect to the phenyl substituent. No secondary rearrangement, as observed in the case of the endoperoxide ring opening product **4a** (*vide supra*), was detected for **13**.

Discussion

Two experimental facets of our study on photooxygenation and secondary transformations of endoperoxides are remarkable: (a) the high face-selectivity of the singlet oxygen addition reaction with the dienes **3** and **9**. For **3** the phenyl group directs the *anti* $^1O_2$-addition, and for **9** *syn* $^1O_2$-addition is controlled by the alkoxy group; (b) the pronounced chemoselectivity difference in the thermal rearrangement of endoperoxides **3** and **11**. In general, the stereoselectivity of nucleophilic addition reactions toward the C3−C4 double bond of 1,2-dihydropentalenes (e.g. the cyclopropanation of **1** to give **2**), as well as electrophilic addition reactions toward the diene system of tetrahydropentalenes,[4] is strictly controlled by the phenyl substituent at C-1 which effectively shields one side of the olefinic part of the substrate. In contrast, the phenyl group is located in an equatorial position in substrates like **8** and **9** (as indicated by force field calculations as well from inspection of the X-ray structure of **15**) and therefore does not exhibit strong diastereofacial control. As a consequence of this conformational fixation, the methoxy group in (the major diastereoisomer of) **9** is located in an axial position and shields the attack of singlet oxygen from this side. The thermal rearrangement of endoperoxide **11** follows the well-known protocol of O−O bond homolysis and competing radical addition toward the C=C double bond (to give **12**) as well as 1,2-hydrogen migration (to give **13**) and bond cleavage of one proximate C−C bond (to give **14**). Many bicyclic endoperoxides follow this pathway, i.e. the parent compound from 1,3-cyclopentadiene.[16] In contrast, endoperoxide **3** rearranges with much higher selectivity to give mainly the ene dione **5**. As the X-ray structure analysis of **4a** indicates, the C1-C6 bond is the most strained proximate single bond with respect to the 1,5-biradical formed after O−O homolysis. Consequently this bond breaks, giving rise to the formation of a cyclopropyl radical. This radical is incapable of conversion to an allylic radical[17] and consequently a 1,2-hydrogen or (less effective) 1,2-alkyl-shift terminates this reaction sequence.

Experimental Section

General Aspects. IR spectra were recorded on a Perkin-Elmer 1420 ratio recording infrared spectrometer and NMR spectra on a Bruker AC 200 and Bruker AC 250 with $CDCl_3$ as solvent and TMS as internal standard. Melting points were taken on a Reichert Thermovar Kofler apparatus. Combustion analyses were performed by the Microanalytical Division of the Institute of Inorganic Chemistry, and mass spectra were carried out in the Institute of Organic Chemistry (Finnigan MAT 8200). The X-ray analyses were carried out with a Siemens R3m/V diffractometer by using a Mo K_α radiation and a graphite monochromator; the SHELXTL PLUS program, run on a MicroVAX-II station, was used for structural analyses. Photooxygenations were performed in test tubes of 3-cm diameter, equipped with a gas inlet tube for the passage of a slow stream of dried oxygen gas. The test tube was placed in a cooling bath connected to a cryostat and irradiated by two 150-W sodium lamps. Solvents and commercially available chemicals were purified by standard procedures or used as bought.

3-Methyl-5-phenyltricyclo[4.3.0.0^{1,3}]nona-6,8-diene (2). To a solution of 6.03 g (27.0 mmol) of trimethyloxosulfonium ylide and 0.66 g (27.5 mmol) of sodium hydride in 30 mL of DMSO under nitrogen at 0 °C was added a solution of 5.00 g (25.7 mmol) of **1**[3] in 10 mL of DMSO within 10 min. After stirring for 2 h at 20 °C and 1 h at 50 °C the reaction mixture was poured on 85.0 mL of ice−water and extracted with ether (3 × 40 mL). Evaporation of the solvent and crystallization from MeOH gave 4.38 g (82%) of **2** as yellow powder: mp 44–45 °C; IR ($CHCl_3$, cm^{-1}) 3020, 2880, 2810, 1460, 1160, 690. Anal. Calcd for $C_{16}H_{16}$: C, 92.25; H, 7.74. Found: C, 91.86; H, 7.83.

Photooxygenation of 2. A 0.50 g (2.40 mmol) amount of **2** was dissolved in 5 mL of $CDCl_3$ with 0.5 mg of tetraphenyl porphyrin (TPP) and cooled to −65 °C while a constant stream of dry oxygen was applied. After irradiation with a sodium lamp for 50 min, the reaction was completed (TLC-control). NMR analysis at −35 °C showed that endoperoxide **3** was the sole product.

3-Methyl-5-phenyl-6-hydroxytricyclo[4.3.0.0^{1,3}]non-7-en-9-one (4a,b). To a solution of 0.30 g (1.25 mmol) of **3** in 3

(16) Schulte-Elte, K. H.; Willhalm, B.; Ohloff, G. *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 985.
(17) Beckwith, A. L. J. *Chem. Soc. Rev.* **1993**, 143.
(18) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

mL of CH_2Cl_2 at −65 °C was added 1.12 g (11.07 mmol) of Et_3N. The mixture was allowed to stand overnight at −20 °C. After evaporation of the solvent and chromatography (silica gel, 1:1 PE/EtOAc, R_f = 0.55) 220 mg (73%) of a mixture of the diastereoisomers **4a** and **4b** in a ratio of 39:61 was obtained. Further chromatography (silica gel, 2:1 PE/MTB) yielded 110 mg (37%) of **4b** as the first fraction (colorless plates, mp 148−149 °C) and 60 mg (20%) of **4a** as the second fraction (colorless needles, mp 108−110 °C); IR ($CHCl_3$, cm^{-1}) **4a** 3585, 3060, 29220, 1705, 1595, 1440, 1365, 850; **4b** 3580, 3060, 2920, 1715, 1445, 1170, 700. Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found for **4a**: C, 79.92; H, 7.03. Found for **4b**: C, 79.94; H, 6.94.

1-Methyl-8-phenylbicyclo[6.1.0]non-5-ene-4,7-dione (5) and 6-Formyl-1-methyl-3-phenylbicyclo[5.1.0]oct-5-en-4-one (6). A 0.070 g (0.336 mmol) amount of endoperoxide **3** in $CDCl_3$ was allowed to stand at 20 °C for 2 h. ^{1}H-NMR analysis showed complete conversion of **3**. After chromatography (silica gel, 1:1 PE/EtOAc R_f = 0.53) 50 mg (63%) of **5** and 12 mg (17%) of **6** were isolated as yellow oils. Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found for **5**: C, 80.05; H, 6.70. Found for **6**: C, 79.88; H, 6.65.

3-Methyl-1-phenylindane (7). A 0.040 g (0.190 mmol) amount of **2** was dissolved in 5 mL of CH_2Cl_2, and a stream of gaseous HCl was passed through until the solution became colorless. After 3 min the solution turned blue and was stirred for another 15 min. The reaction mixture was quenched with 5 mL of aqueous K_2CO_3 and extracted with CH_2Cl_2 (2 × 5 mL). After evaporation of the solvent, inspection by NMR spectroscopy showed that indane **7** was the sole product.

^{1}H-NMR: 2.08 (t, 7.3 Hz, 2H), 2.41 (s, 3H), 2.98 (t, 7.3 Hz, 4H), 7.10 (d, 8.6 Hz,2H), 7.24−7.52 (m, 5H). ^{13}C-NMR: 21.5 (q), 26.2 (t), 32.7 (t), 33.4 (t), 124.5 (d), 127.0 (d), 127.6 (d), 128.5 (d), 128.8 (d), 136.5 (s), 138.3 (s), 139.2 (s), 141.8 (s), 145.5 (s).

3-(Trifluoroacetyl)-3-methyl-5-phenylbicyclo[4.3.0]nona-1(6),7-diene (8). A 0.380 g (1.80 mmol) amount of **2** was dissolved in 10 mL of CH_2Cl_2, and 0.205 g (1.80 mmol) of CF_3-COOH in 2 mL of CH_2Cl_2 was added dropwise. After stirring the reaction mixture for 3 h at 20 °C 20 mL aqueous K_2CO_3 solution was added and extracted with CH_2Cl_2 (3 × 10 mL). Evaporation of the solvent yielded 0.526 g (90%) of **8** as a yellow oil: IR ($CHCl_3$, cm^{-1}) 2880, 1755, 1350, 1205, 1150; HRMS m/z [M^+] calcd 322.1181, obsd 322.1175.

3-Methoxy-3-methyl-5-phenylbicyclo[4.3.0]nona-1(6),7-diene (9). A 1.90 g (9.12 mmol) amount of **2** was dissolved in 50 mL of MeOH and 10 mL of CH_2Cl_2, and 1.04 g (9.12 mmol) of CF_3COOH in 5 mL of CH_2Cl_2 was added in portions. The reaction mixture was stirred at 20 °C for 2 h, poured into a 100 mL aqueous K_2CO_3 solution, and extracted with ether (3 × 50 mL). Evaporation of the solvent yielded a 87:13 mixture of the diastereoisomers **9** as an orange oil. After chromatography (silica gel, 20:1 PE/EtOAc, R_f = 0.25) 2.01 g (91%) of a yellow oil was obtained: IR ($CHCl_3$, cm^{-1}) 3020, 2920, 2890, 1470, 1350, 1070, 685. Anal. Calcd. for $C_{17}H_{20}O$: C, 84.96; H, 8.39. Found: C, 85.17; H, 8.55.

Base-Induced Isomerization of 9. A 0.250 g (1.04 mmol) sample of **9** was dissolved in 10 mL of dry diethyl ether and cooled to 0 °C. After the addition of 0.036 g (1.50 mmol) of sodium hydride, the solution was stirred for 2 h. The solution was then hydrolyzed with 10 mL of aqueous ammonium chloride solution and extracted with diethyl ether (2 × 10 mL) and dried. After evaporation, a yellow oil resulted which consisted of a 2:1 mixture of **9** and **10**.

Photooxygenation of 9. A 0.310 g (1.29 mmol) amount of **9** and 1 mg of TPP were dissolved in 30 mL of CH_2Cl_2 and cooled to −25 °C. After irradiation with a sodium lamp for 20 min the solvent was evaporated and NMR analysis showed that only one product, endoperoxide **11**, had been formed.

Thermal Rearrangement of 11. A 0.100 g (0.37 mmol) amount of **11** was allowed to stand at 20 °C for 7 days. The ^{1}H-NMR spectra indicated a product mixture of **12**, **13**, and **14** in a ratio of 3:3:1. Chromatography (silica gel, 2:1 PE/EtOAc) yielded a fraction R_f = 0.38 that contained 40 mg (40%) of **13** and **14** and a fraction R_f = 0.31 containing 45 mg (45%) of **12** and **14**. Crystallization (3:1 PE/MTB) yielded 37 mg (37%) of the bis-epoxide **12** as colorless needles: mp 118−119 °C; IR ($CHCl_3$, cm^{-1}) **12** 2950, 2910, 1355, 1100, 1070, 900, 695. Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found for **12**: C, 75.36; H, 7.65. Found for **13** and **14**: C, 74.60; H, 7.61.

1-Hydroxy-3-methoxy-3-methyl-5-phenylbicyclo[4.3.0]-non-6-en-8-one (15). To a solution of 0.220 g (0.81 mmol) of endoperoxide **11** in 20 mL of CH_2Cl_2 at 0 °C was added 0.506 mg (5.00 mmol) of Et_3N, and the mixture was stirred at 0 °C for 24 h. Evaporation of the solvent and chromatography (silica gel, 1:1 PE/EtOAc, R_f = 0.28) yielded 150 mg (68%) of a yellow oil. Crystallization from MTB gave 130 mg (59%) of **15** as colorless needles: mp 93−95 °C; IR ($CHCl_3$, cm^{-1}) 3420, 2940, 2900, 1690, 1660, 1595, 1065. Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.30; H, 7.51.

Acknowledgment. Financial support for this study was provided by the Deutsche Forschungsgemeinschaft (Sonderforschungsbereich 347 "Selektive Reaktionen Metall-aktivierter Moleküle", located at the University of Würzburg).

JO941525A