# Reaction of 1,2,4,5-Tetramethyl-1,4-cyclohexadiene with Ozone − Competition between Oxidative Cleavage and Oxydehydrogenation

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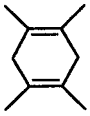
Treatment of 1,2,4,5-tetramethyl-1,4-cyclohexadiene (**1**) on polyethylene and in pentane with excess ozone afforded mixtures of the oxydehydrogenation product **2** and of the oxidative cleavage product **4** in ratios of 0.5:1 and 19:1, respectively. Epoxidation of **1** followed by ozonolysis of the epoxide **6** provided the epoxyozonide **7**.

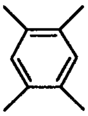
## Introduction

Ozonolysis reactions of substrates incorporating the 1,3-cyclohexadiene moiety, such as 1,3-cyclohexadiene itself,[1,2] 1,4-disubstituted-1,3-cyclohexadienes,[3,4] naphthalene[5] and substituted naphthalenes,[5,6] have been examined under a variety of aspects and conditions. The course and the products of such reactions are in agreement with the Criegee mechanism of olefin ozonolysis.[7a] The work described below was carried out in order to examine whether ozone treatment of a nonconjugated cyclohexadiene also follows this pattern.

## Results and Discussion

1,2,4,5-Tetramethyl-1,4-cyclohexadiene (**1**) was treated with 0.7 molar equivalents of ozone in methanol at ambient temperatures and the crude product was admixed with triphenylphosphane in order to reduce peroxidic components. $^1$H NMR analysis of the ensuing reaction mixture showed the presence of 24% of residual **1**, 49% of 1,2,4,5-tetramethylbenzene (**2**) and 27% of the unsaturated diketone **3**. Compounds **2** and **3** have been isolated in yields of 41% and 11%, respectively, and characterized by their $^1$H NMR and mass spectra. These results reveal that in the reaction of ozone with **1** in methanol, oxydehydrogenation competes favorably with oxidative double bond cleavage and that the latter reaction occurs by sequential rather than by simultaneous attack of ozone at the two double bonds of **1**.


**1**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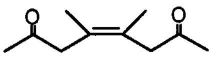
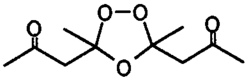

**3**

The hitherto unknown oxydehydrogenation of **1** by ozone is not restricted to reactions in the protic solvent methanol. Treatment of **1** with excess ozone on polyethylene at −78 °C afforded a mixture containing 35% of **2** and 65% of the diketoozonide **4**; the latter was isolated in a yield of 23%. Treatment of **1** with excess ozone at −78 °C in pentane gave a mixture containing 95% of **2** and only 5% of **4**, i.e. oxydehydrogenation of **1** became the predominant reaction. For the apparent solvent effect upon the ratio of oxydehydrogenation and oxidative cleavage, *viz.* 65:35 in methanol and 95:5 in pentane, there is a priori no plausible explanation. The fact that ozonide **4** was obtained in considerably higher yield on polyethylene than in pentane is in line with the experience that ozonolysis of olefins on polyethylene is conducive to ozonide formation probably due to immobilization of the Criegee fragments at their place of origin.[8]

The structure of the liquid ozonide **4** was established by its $^1$H and $^{13}$C NMR spectra, by reduction with triphenylphosphane to give the expected diketone **5**, and by independent preparation through ozonolysis of the unsaturated diketone **3** on polyethylene. The stereochemical identity of **4** was not proven. We assume, however, that ozonide formation occurs upon cleavage of the first double bond of **1** and that, hence, ozonide **4** has a *cis* geometry.


**4**


**5**

Ozone cleavage of the second double bond of **1** to generate the two carbonyl groups of **4** is not in line with the Criegee mechanism, since it cannot account for the third oxygen atom of ozone. Such abnormal ozonolysis reactions are, however, not unprecedented. Thus, ozonolysis of norbornenes possessing dimethyl-substituted double bonds afforded the corresponding 1,3-diacetylcyclopentanes as the major and the expected ozonides as the minor products.[9] Furthermore, the thermal decomposition of such ozonides yielded substantial proportions of the corresponding 1,3-diacetylcyclopentanes.[9] It is, therefore, conceivable that **4** may have been formed by the spontaneous decomposition of an unstable diozonide of **1**.

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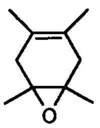
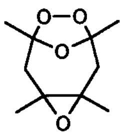
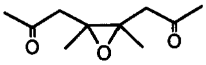
The reason for the abnormal behavior of substituted norbornenes and of **1** in ozonolysis reactions may be steric hindrance in the ozonides of such norbornenes or in the diozonide of **1.** This steric hindrance may even prevent ozone cleavage of double bonds and instead lead to epoxides.[7b] A case in point is the ozonolysis of 1,2,3,4-tetramethylcyclopenta-1,3-diene on polyethylene, which provided the corresponding epoxyozonide to the exclusion of the expected diozonide.[10] In order to test whether the crude product from the ozonolysis of **1** contains the corresponding epoxyozonide **7**, we have independently prepared **7**. Thus, treatment of **1** with *m*-chloroperbenzoic acid provided epoxide **6** in a yield of 62%. Subsequent ozonolysis of **6** on polyethylene at −78 °C gave a mixture containing 84% of **7** and 16% of **8**, from which **7** was isolated in a yield of 38%. Its structure was established by $^1$H and $^{13}$C NMR spectroscopy and by reduction with triphenylphosphane to give the expected epoxy-diketone **8**. With the help of the $^1$H NMR spectroscopic data of **7** we could show that it was not formed in detectable amounts in the ozonolysis of **1**.


**6**


**7**


**8**

## Experimental Section

**General:** NMR spectra were obtained in $CDCl_3$ with TMS as internal reference on a Bruker AC 250 instrument. Mass spectra were obtained on a Hewlett−Packard instrument 5985B and IR spectra on a Beckman 4260 instrument. Products were isolated by flash chromatography[11] on silica gel at 0.5 bar. Ozonolysis reactions on polyethylene (Microthene FN 500, spherical particles, maximum size 20 µm; supplier: Serva Feinbiochemica, Heidelberg, FRG) were performed according to a known procedure.[12]

**Ozonolysis of 1,2,4,5-Tetramethyl-1,4-cyclohexadiene (1) in Methanol:** A solution of **1** (0.68 g, 5.00 mmol) in 30 mL of methanol was treated with 0.70 molar equivalents of ozone at ambient temperatures, admixed with triphenylphosphane (1.15 g, 4.40 mmol) and left standing overnight. $^1$H NMR analysis showed the presence of **1** (24%; $\delta = 2.52$), **2** (49%; $\delta = 2.19$) and **3** (27%; $\delta = 1.76$). The solvent was evaporated at reduced pressure and the residue (2.30 g) was separated (column: 4 × 50 cm, 120 g of silica gel, pentane/ether, 7:3) to give 190 mg (41%) of **2** and 65 mg (11%) of **3**.

**1,2,4,5-Tetramethylbenzene (2):** Colorless solid. − $^1$H NMR: $\delta = 2.19$ (s, 12 H), 6.90 (s, 2 H). − EI-MS: *m*/*z* (%) = 134 (37) [M$^+$], 119 (100) $[M - CH_3]^+$.

**4,5-Dimethyl-4-octene-2,7-dione (3):** Colorless liquid. − $^1$H NMR: $\delta = 1.76$ (s, 6 H), 2.13 (s, 6 H), 3.15 (s, 4 H). (ref.[13] $^1$H NMR: $\delta = 1.66$, 2.08, 3.12). − $^{13}$C (BB) NMR: $\delta = 19.84$, 29.36, 49.94, 126.30, 206.52. − CI-MS: *m*/*z* (%) = 169 (35) $[M + H]^+$.

**Ozonolysis of 1,2,4,5-Tetramethyl-1,4-cyclohexadiene (1) on Polyethylene:** Compound **1** (0.68 g, 5.00 mmol) on 68.0 g of polyethylene was treated with ozone at −78 °C for 8 h. The products were extracted with ether and the ether was evaporated at reduced pressure to leave 1.34 g of a liquid residue which contained 35% of **2** and 65% of **4** according to $^1$H NMR spectroscopy. Separation (column 2.5 × 50 cm, 80 g of silica gel, pentane/ether, 7:3) afforded 134 mg (20%) of **2** and 248 mg (23%) of **4**.

**3,5-Dimethyl-3,5-bis(2-propanone)-1,2,4-trioxolane (4):** Colorless liquid. − $^1$H NMR: $\delta = 1.57$ (s, 6 H), 2.23 (s, 6 H), AB-System with $\delta_A = 2.81$, $\delta_B = 2.89$ ($J_{AB} = 14.4$ Hz, 4 H). − $^{13}$C NMR: $\delta = 23.28$, 31.41, 51.03, 108.32, 203.93. − IR (neat): $\tilde{\nu} = 1724$ cm$^{-1}$ (C=O).

**Reduction of Ozonide 4:** A solution of **4** (25 mg, 0.10 mmol) in 0.60 mL of $CDCl_3$ was admixed with triphenylphosphane at ambient temperature. $^1$H NMR analysis after 4 days showed that **5** was formed as the sole detectable reduction product: $\delta = 2.04$ (s, 6 H), 2.23 (s, 2 H).

**Ozonolysis of 1,2,4,5-Tetramethyl-1,4-cyclohexadiene (1) in Pentane:** A solution of **1** (0.20 g, 1.50 mmol) in 5 mL of pentane was treated with ozone at −78 °C until it turned blue. Excess ozone was flushed out with nitrogen and the solvent was evaporated at reduced pressure. $^1$H NMR analysis of the residue (0.26 g) showed the presence of 95% of **2** [$\delta = 2.19$ (s), 6.91 (s)] and 5% of **4** [$\delta = 1.57$ (s), 2.24 (s), 2.87 (q)].

**Ozonolysis of 4,5-Dimethyl-4-octene-2,7-dione (3) on Polyethylene and Reduction of the Ozonolysis Product 4:** Compound **3** (0.20 g, 1.19 mmol) on 20 g of polyethylene was treated with ozone at −78 °C for 3 h. The products were extracted with ether and the ether was then evaporated at reduced pressure to leave 0.45 g of a liquid residue which contained ozonide **4** as the sole product according to $^1$H NMR analysis. A solution of the residue in 0.6 mL of $CDCl_3$ was admixed with triphenylphosphane at ambient temperature. $^1$H NMR analysis after 4 days showed that **5** was formed as the sole detectable reduction product.

**Epoxidation of 1,2,4,5-Tetramethyl-1,4-cyclohexadiene (1):** A solution of **1** (1.00 g, 7.35 mmol) in 5 mL of ether was added dropwise to a stirred solution of *m*-chloroperbenzoic acid (1.00 g, 5.88 mmol) in 60 mL of ether at 0 °C and stirring was continued for 1 h at 0 °C. The solution was then sequentially washed with a 5% solution of aqueous NaOH and water and dried with $MgSO_4$. Evaporation of the solvent at reduced pressure left 1.60 g of a solid residue, from which **6** (0.74 g, 62%) was isolated (column 2.5 × 50 cm, 80 g of silica gel, pentane/ether, 95:5).

**1,3,4,6-Tetramethyl-7-oxa-bicyclo[4,1,0]-3-heptene (6):** Colorless solid, m.p. 51−52 °C. − $^1$H NMR: $\delta = 1.35$ (s, 6 H), 1.57 (s, 6 H), AB-System with $\delta_A = 2.29$, $\delta_B = 2.38$ ($J_{AB} = 17.6$ Hz, 4 H). − $^{13}$C (BB) NMR: $\delta = 18.53$, 19.43, 38.87, 61.59, 121.57. − EI/MS: *m*/*z* (%) = 152 (6) [M$^+$], 137 (37) $[M - CH_3]^+$, 109 (100) $[M - CH_3CO]^+$, 43 (29) $[CH_3CO]^+$. − $C_{10}H_{16}O$ (152.24): calcd. C 78.90, H 10.59; found C 78.91, H 10.43.

**Ozonolysis of 1,3,4,6-Tetramethyl-7-oxabicyclo[4,1,0]-3-heptene (6) on Polyethylene:** Compound **6** (0.70 g, 4.60 mmol) on 100 g of polyethylene was treated with ozone at −78 °C for 3 h. The products were extracted with ether and the ether was then evaporated at reduced pressure to leave 0.92 g of a residue which contained 84% of **7** and 16% of **8**, according to $^1$H NMR analysis. Separation (column 2.5 × 50 cm, 80 g of silica gel, pentane/ether, 90:10) afforded 64 mg (38%) of **7**.

**1,3,5,7-Tetramethyl-4,8,9,10-tetraoxatricyclo-[5.2.1.0$^{3,5}$]-decane (7):** Colorless solid, m.p. 73−74 °C. − $^1$H NMR: $\delta = 1.33$ (s, 6 H), 1.51 (s, 6 H), AB-system with $\delta_A = 2.28$, $\delta_B = 2.48$ ($J_{AB} = 16.1$ Hz, 4 H). − $^{13}$C (BB) NMR: δ = 22.47, 24.47, 45.69, 61.71, 108.36. − $C_{10}H_{16}O_4$ (200.24): calcd. C 59.99, H 8.05; found C 60.10, H 7.90.

**Reduction of Ozonide 7:** A solution of **7** (20 mg, 0.10 mmol) in 0.6 mL of $CDCl_3$ was admixed with triphenylphosphane at ambient temperature. $^1$H NMR analysis after 1 day showed that **8** was formed as the sole detectable reduction product: δ = 1.40 (s, 6 H), 2.20 (s, 6 H), AB-System with $\delta_A = 2.64$, $\delta_B = 2.76$ ($J_{AB} = 16.4$ Hz, 4 H).

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