Stable endoperoxide of 4,5,6,8,16-pentamethyl[2.2]metacyclophane; structural analysis and deoxygenation

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Photooxygenation of 4,5,6,8,16-pentamethyl[2.2]meta-cyclophane 6 gives [2.2]metacyclophane endoperoxide 7; its X-ray crystallographic analysis and stability in the thermal deoxygenation reaction are reported.

Photochemically generated singlet oxygen ($^1O_2$) cycloadds to conjugated dienes and arenes to give endoperoxides.[1] The endoperoxides are important intermediates in photo-oxidation reactions, but, in most cases, are too unstable to isolate in order to study their structure.
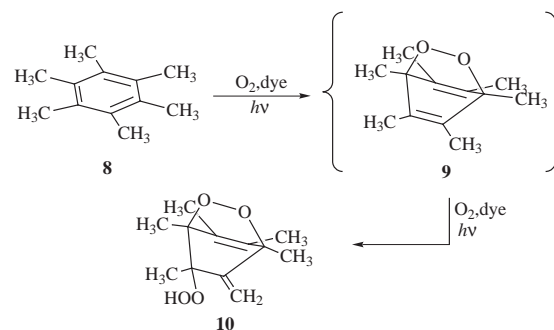
On the other hand, it is known that strained aromatic rings in cyclophanes, such as in the [2.2.2.2](1,2,4,5)cyclophane[2] and the [2.2]paracyclophane diene,[3] readily undergo photocycloaddition with $^1O_2$ in the presence of photosensitizing dyes. Recently, it was reported that the photoirradiation of a mono-(Dewar benzene)† isomer of the [1.1]metacyclophane gave the corresponding endoperoxide.[4] In this case, no additional sensitizer was used. This result suggests that the strained metacyclophanes are reactive in photocycloaddition reactions with $^1O_2$. Here, we report the preparation and X-ray crystal structure of a stable endoperoxide of a pentamethyl[2.2]metacyclophane and its deoxygenation. To the best of our knowledge, it is the first unequivocal example of an X-ray crystallographic analysis of an endoperoxide of an isolated 6-membered aromatic ring system.

4,5,6,8,16-Pentamethyl[2.2]metacyclophane 6‡ was prepared by the sulfur method analogous to the preparation of 8,16-dimethyl[2.2]metacyclophane.[5] Irradiation of [2.2]metacyclophane 6 using a high pressure mercury lamp produced endoperoxide 7. The reaction proceeds in different solvents such as acetone (72% yield), ethanol, or hexane in high yields (Scheme 1). Although no additional photosensitizer was added, the reaction leading to 7 is thought to proceed *via* $^1O_2$. Thus, the reaction was slowed remarkably by addition of 1,4-diazabicyclo-[2.2.2]octane, a known $^1O_2$ quencher. It may well be possible that the [2.2]metacyclophane 6 itself acts as sensitizer in the reaction.

The similarly substituted hexamethylbenzene 8 itself is inert under the irradiation conditions mentioned above, although it has been reported that the formation of the unstable endoperoxide 9 can be detected by ^1H NMR spectroscopy in the reaction mixture, when methylene blue was used as a photosensitizer. Epidioxy hydroperoxide 10 is the final product *via* a subsequent ene reaction of 9 (Scheme 2).[6]
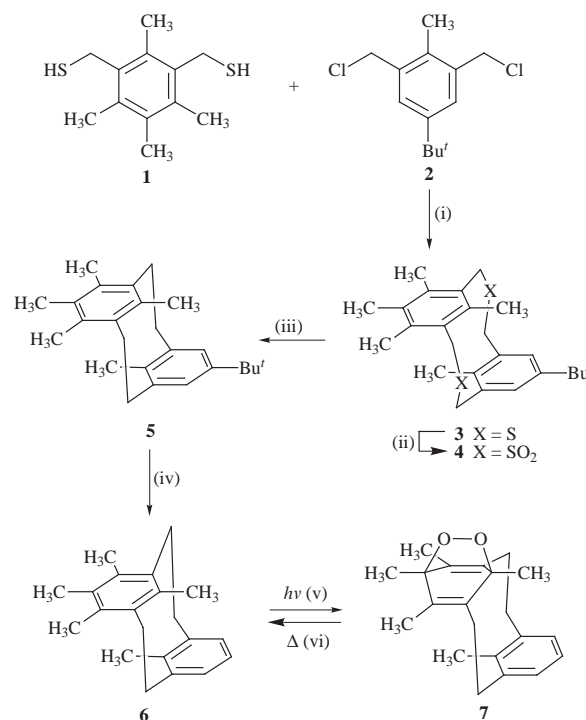
Scheme 1 *Reagents and conditions:* (i) KOH, NaBH$_4$, EtOH, 35%; (ii) H$_2$O$_2$, AcOH, 84%; (iii) 400 °C, 0.6 torr, 79%; (iv) benzene, AlCl$_3$/CH$_3$NO$_2$, 40%; (v) acetone, *hv* (high pressure mercury lamp), air, 72%; (vi) see Fig. 1

Scheme 2

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† 'Dewar' benzene is bicyclo[2.2.0]hexadiene.
‡ Data for **6**, mp 145–147 °C (Found: C, 90.75; H, 9.56. C$_{21}$H$_{26}$ requires C, 90.59; H, 9.41%). δ_H(270 MHz; CDCl$_3$) 0.48 (3 H, s, CH$_3$), 0.49 (3 H, s, CH$_3$), 2.16 (3 H, s, CH$_3$), 2.32 (6 H, s, CH$_3$), 2.50 (2 H, ddd, *J* 4.5, 12.0 and 13.1, CH$_2$), 2.70 (2 H, ddd, *J* 3.9, 12.0 and 12.2, CH$_2$), 2.84 (2 H, ddd, *J* 3.0, 4.5 and 12.5, CH$_2$), 3.26 (2 H, ddd, *J* 3.0, 3.9 and 13.1, CH$_2$), 6.87 (1 H, t, *J* 7.3, arom. H), 7.01 (2 H, d, *J* 7.3, arom. H); *m/z* 278 (M$^+$, 60%), 248 (M$^+$ − 30, 100).

Compared to **9**, endoperoxide **7** is stable enough to be recrystallized from hexane. The half-life of **7** is 10 hours at 45 °C. On the other hand, endoperoxide **9**, which was not isolated, was reported to decompose completely at 40 °C in 1 hour as monitored by ^1H NMR spectroscopy. Thermal deoxygenation of **7** was also monitored by ^1H NMR spectroscopy (Fig. 1). The enthalpy and entropy of activation in the deoxygenation
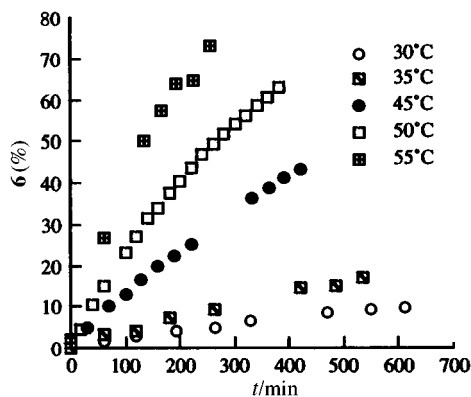
Fig. 1 Variation of the formation of [2.2]metacyclophane **6** from endoperoxide **7** with reaction time at 30, 35, 45, 50 and 55 °C in CDCl₃
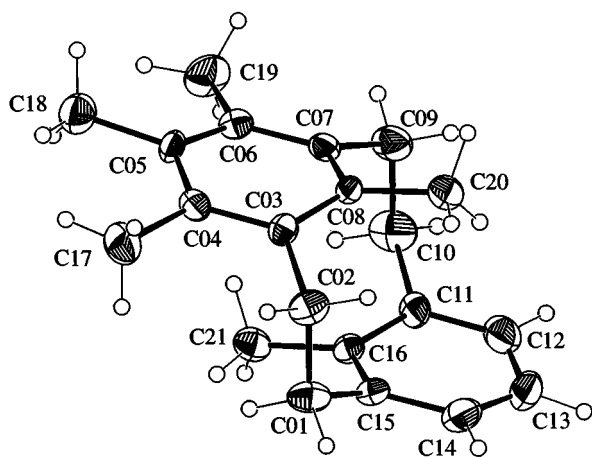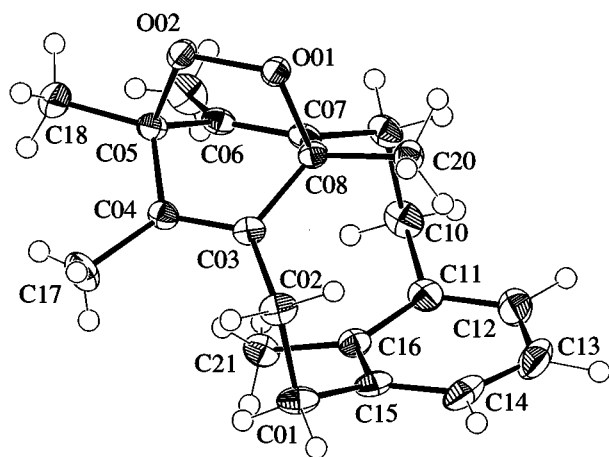

Fig. 2 ORTEP View of metacyclophane **6**

Fig. 3 ORTEP View of endoperoxide **7**

reaction were determined to be $\Delta H^{\ddagger} = 27.4 \pm 1.1$ kcal mol⁻¹, $\Delta S^{\ddagger} = 6.06 \pm 1.7$ eu,§ respectively. From these results, it can be seen that the kinetic stability of endoperoxide **7** is larger than that of the endoperoxide of 1,4-dimethylnaphthalene ($\Delta H^{\ddagger} = 24.2 \pm 0.2$ kcal mol⁻¹, $\Delta S^{\ddagger} = 2 \pm 1$ eu), and smaller than that of the endoperoxide of 9,10-diphenylanthracene ($\Delta H^{\ddagger} = 32.5 \pm 0.2$ kcal mol⁻¹, $\Delta S^{\ddagger} = 9.6 \pm 0.5$ eu).[7]

X-Ray crystallographic analyses of **6** and **7** are shown in Figs. 2 and 3, respectively. In the case of endoperoxide **7**, the selected bond distances (Å) and bond angles (°) are: O01–O02

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§ 1 eu = 4.184 J K⁻¹ mol⁻¹.

1.470(2), C05–O02 1.489(3), C08–O01 1.497(3); O02–C05–C04 105.8(2), C04–C05–C06 111.4(2), O01–C08–C03 104.3(2), C07–C08–C03 111.4(2). The O01–O02 bond length [1.470(2) Å] of endoperoxide **7** is found to be elongated which may be caused by the electronic repulsion between lone pairs of electrons on the oxygen atoms in an eclipsed configuration, the dihedral angle of C08–O01–O02–C05 being only 2.1°. Incidentally, elongated bond lengths of the O–O bonds are not so uncommon in cyclic peroxides, and can be found in tetra-benzo[*de,hi,op,st*]pentacene endoperoxide [1.496(5) Å],[1a] 7,12-dimethylbenz[*a*]anthracene endoperoxide (1.480 Å),[8a] benzo-[1,2,3-*kl*:4,5,6-*k′l′*]dixanthene endoperoxide (1.50 Å),[8b] and thioxanthenol[1′,9′:4,5,6]benzoxanthene endoperoxide (1.48 Å).[8c] Remarkable, however, is the change in the distance between C08 and C16 going from **6** to **7** (2.82 *vs.* 3.28 Å). It is evidence that strain is released at the carbon atoms located on the internal positions of **7** by a change in their hybridization modes from sp² to sp³. This, in turn, may be one of the factors which contribute to the stability of **7**.

Experimental

All melting points are uncorrected. IR spectra were measured as KBr pellets. ¹H NMR spectra were determined in CDCl₃ at 270 MHz with a JEOL EX-270 instrument. *J* Values are given in Hz. Mass spectra were measured on a JEOL JMS-01-SG-2 machine at 75 eV using a direct inlet system. Elemental analysis was performed on a Yanako MT-5 instrument.

Photooxygenation of [2.2]metacyclophane 6

A solution of **6** (100 mg, 0.36 mmol) in acetone (100 ml) was irradiated with a 100 W high pressure mercury lamp (Riko Kagaku Sangyo Co.) for 6 h at RT in air. A pyrex filter was used. The reaction mixture was evaporated under reduced pressure and the residue was chromatographed on silica gel (Wako gel C-300) using dichloromethane as eluent. The eluate was evaporated and the residue was recrystallized from hexane, giving endoperoxide **7** (81 mg, 72%), mp 73 °C (decomp.) (Found: C, 81.11; H, 8.27. C₂₁H₂₆O₂ requires C, 81.25; H, 8.44%); δ_H(270 MHz, CDCl₃) 0.12 (3 H, s, CH₃), 1.47 (3H, s, CH₃), 1.92 (6 H, s, CH₃), 2.00 (3 H, s, CH₃), 1.91–2.02 (2 H, m, CH₂), 2.55 (2 H, ddd, *J* 3.1, 4.0 and 12.5, CH₂), 2.70 (2 H, ddd, *J* 3.1, 3.6 and 12.7, CH₂), 3.16 (2 H, ddd, *J* 4.0, 12.5 and 12.7, CH₂), 6.96–7.07 (3 H, m, arom. H); *m/z* 310 (M⁺, 27%).

X-Ray crystal structure determination of 6¶

Crystal data. C₂₁H₂₆, *M* = 278.42, monoclinic, *a* = 14.628(4), *b* = 7.871(4), *c* = 14.646(4) Å, β = 108.27(2)°, *V* = 1601.3(10) Å³, (by least-squares refinement on diffractometer angles for 25 automatically centered reflections, λ = 1.541 84 Å), space group *P*2₁/*c* (No. 14), *Z* = 4, D_x = 1.155 g cm⁻³, colorless plate, crystal size 0.37 × 0.27 × 0.03 mm, μ(Cu-Kα) = 4.5 cm⁻¹.

Data collection and processing. CAD4 FR590 diffractometer, $\omega - 2\theta$ mode with ω scan width = (0.6 + 0.410 tan θ°, scan speed 2 to 20 deg min⁻¹, graphite-monochromated Cu-Kα radiation; 1747 reflections were measured (3.18 ≤ θ ≤ 75.67°, −*h*, *k*, ±*l*). 1651 Unique [merging *R* = 0.0334 after empirical absorption correction (max., min. transmission factors = 0.9927, 0.7617)] was used.

Structure analysis and refinement. The structure was solved by direct methods (SIR92[9]). Full-matrix least-squares refine-

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¶ Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/198.

ment on F^2 with all non-hydrogen atoms anisotropic and hydrogens in calculated positions with $U_{iso} = 1.3$ times of U(bonded atoms) was done. The weighting scheme is $w = 1/[\sigma^2(F_o^2) + (0.1687P)^2 + 26.0206P]$ where $P = (F_o^2 + 2F_c^2)/3$. Final R and R_w values for 190 parameters are 0.0672, 0.1851, $S = 1.02$. All calculations were performed on a MicroVAX3100 and IBM RISC System/6000 3100 using MolEN [10] and SHELXL-93.[11]

X-Ray crystal structure determination of 7¶

Crystal data. $C_{21}H_{26}O_2$, $M = 310.42$, monoclinic, $a = 14.529(5)$, $b = 15.949(5)$, $c = 7.328(5)$ Å, $\beta = 103.99(1)°$, $V = 1647.7(14)$ Å^3, (by least-squares refinement on diffractometer angles for 25 automatically centered reflections, $\lambda = 1.54184$ Å), space group $P2_1/n$ (No. 14), $Z = 4$, $D_x = 1.251$ g cm^{-3}, colorless, prism, crystal size $0.40 \times 0.40 \times 0.20$ mm, μ(Cu-Kα) = 5.8 cm^{-1}.

Data collection and processing. CAD4 FR590 diffractometer, $\omega - 2\theta$ mode with ω scan width = $(1.4 + 0.270 \tan \theta)°$, scan speed 4 to 20 deg min^{-1}, graphite-monochromated Cu-Kα radiation; 2911 reflections were measured ($4.19 \leqslant \theta \leqslant 64.98°$, $+h$, $+k$, $\pm l$). 2795 Unique [merging $R = 0.0835$ after empirical absorption correction (max., min. transmission factor = 0.9754, 0.7512)] was used.

Structure analysis and refinement. The structure was solved by direct methods (SIR92 [9]). Full-matrix least-squares refinement on F^2 with all non-hydrogen atoms anisotropic and hydrogens in calculated positions with $U_{iso} = 1.3$ times of U(bonded atoms) was done. The weighting scheme is $w = 1/[\sigma^2(F_o^2) + (0.1687P)^2 + 26.0206P]$ where $P = (F_o^2 + 2F_c^2)/3$. Final R and R_w values for 246 parameters are 0.0679, 0.1803, $S = 1.04$. All calculations were performed on a MicroVAX3100 and IBM RISC System/6000 3100 using MolEN [10] and SHELXL-93.[11]

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