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# The Pentaoxa[5]peristylanes. A Novel Oxa-Cage System

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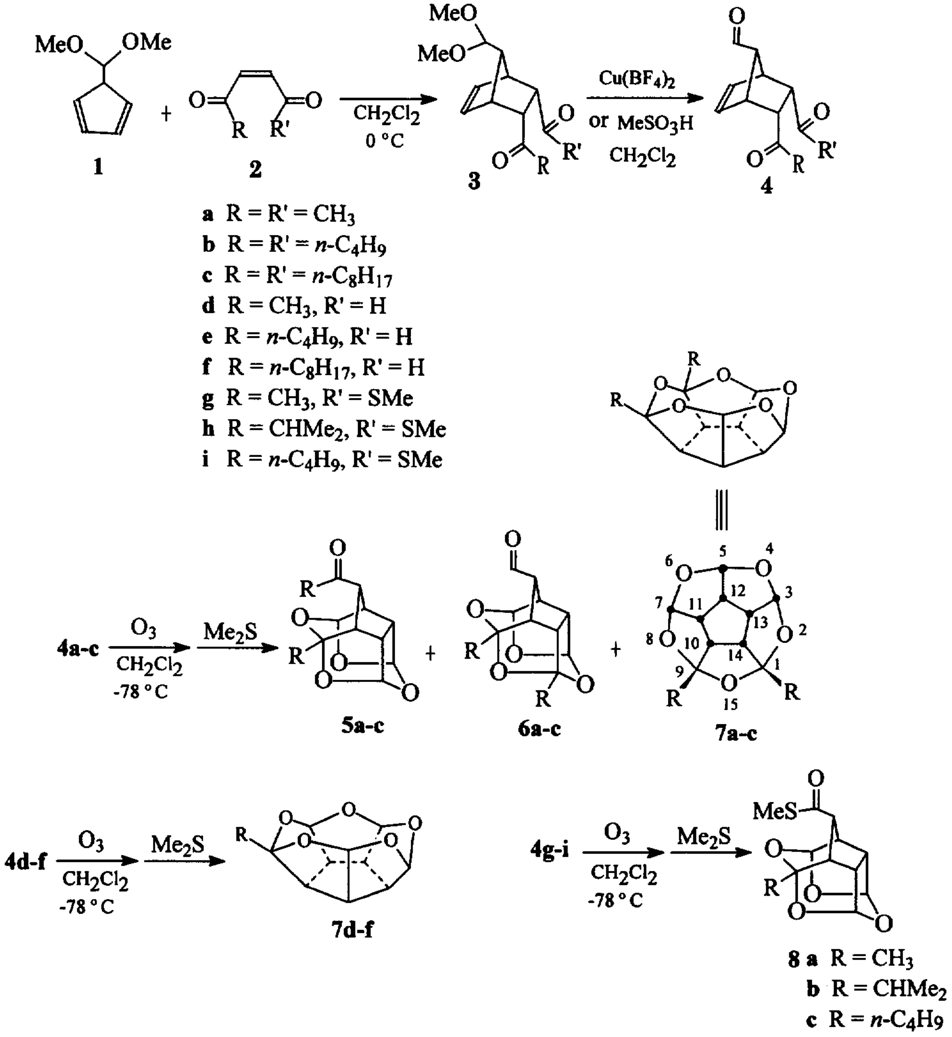
***Abstract***: The synthesis of pentaoxa[5]peristylanes, a novel oxa-cage system, has been accomplished via ozonolysis of 7-*anti*-2,3-*bis*-*endo*-triacylbicyclo[2.2.1]-5-heptenes and via a direct chemical transformation of the tetraacetal tetraoxa-cages **5a-c** and **6a-c**. © 1997 Elsevier Science Ltd.

The synthesis of peristylanes, such as [5]peristylane[1] and [4]peristylane,[2] has been accomplished and attempts to roof [5]peristylane has been made.[3] On the other hand, the synthesis of heterocyclic analogs of peristylanes has received much less attention.[4] Recently, we conceived that some heterocyclic cage systems might be viewed as novel classes of cage-backboned coronands (crown ethers) and might exhibit interesting cation-binding properties. We also visualized that the "creation" of oxa-cage compounds from carbocyclic cages might be achieved by replacing the skeletal carbon atoms with oxygen atoms at the proper positions and by extending the skeletal backbone.[5] Thus, we have accomplished the synthesis of tetraacetal tetraoxa-cages,[5,6] tetraacetal pentaoxa-cages,[7] diacetal trioxa-cages,[8] and triacetal trioxa-cages.[9] We report in this communication the synthesis of pentaoxa[5]peristylanes, a novel oxa-cage system, via ozonolysis of 2,3-*bis*-*endo*-7-*anti*-triacylnorbornenes. We also wish to demonstrate for the first time the direct transformation of tetraacetal tetraoxa-cages to pentaoxa[5]-peristylanes.

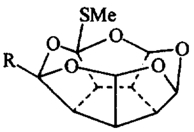
Diels-Alder reaction of compound **1**[10] with *cis*-enediones **2a-f**[5,6] in dichloromethane at 0 °C for 72 h gave the *anti-endo* adducts **3a-f** in 70-75% yields. Treatment of **3a-f** with $Cu(BF_4)_2$ or methanesulfonic acid in dichloromethane at 25 °C gave the hydrolysis products **4a-f** in 75-80% yields (Scheme 1). Compounds **4g-i** were prepared from (Z)-$\gamma$-oxo-$\alpha$,$\beta$-unsaturated thioesters **2g-i**[6a,c] by a similar sequence in 60-65% overall yields. Ozonolysis of **4a-c** in dichloromethane at -78 °C followed by reduction with dimethyl sulfide gave the tetraacetal tetraoxa-cages **5a-c** (30-34%) and **6a-c** (34-38%) and the pentaacetal pentaoxa-cages **7a-c** (18-22%), the pentaoxa[5]-peristylanes. Ozonolysis of **4d-f** under the same reaction conditions gave the pentaacetal pentaoxa-cages **7d-f** in 75-80% yields. The by-products **5d-f** and **6d-f** were too small amount to be isolated. Ozonolysis of **4g-i** under the same reaction conditions gave the tetraacetal tetraoxa-cages **8a-c** in 85-90% yields. No detectable amount of the pentaoxa[5]peristylanes **9a-c** or the tetraacetal tetraoxa-cages **10a-c** or **11a-c** was obtained. The thioester group may exhibit much less reactive than the acyl groups for the cyclization reaction.

**Scheme 1**



**a** $R = R' = CH_3$
**b** $R = R' = n\text{-}C_4H_9$
**c** $R = R' = n\text{-}C_8H_{17}$
**d** $R = CH_3, R' = H$
**e** $R = n\text{-}C_4H_9, R' = H$
**f** $R = n\text{-}C_8H_{17}, R' = H$
**g** $R = CH_3, R' = SMe$
**h** $R = CHMe_2, R' = SMe$
**i** $R = n\text{-}C_4H_9, R' = SMe$

**8 a** $R = CH_3$
**b** $R = CHMe_2$
**c** $R = n\text{-}C_4H_9$



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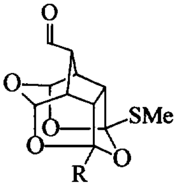

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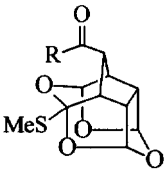

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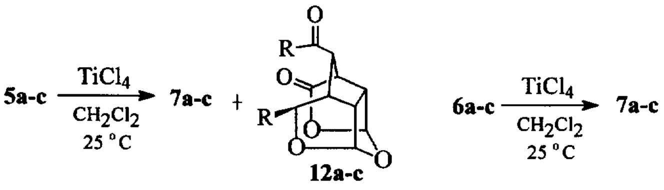
Compounds **7a-f** are white solid.[11] The IR spectra of **7a-f** lacked carbonyl absorptions and showed strong absorptions near 1050 $cm^{-1}$ for the ether C-O bonds. The $^1H$ NMR spectrum of **7a** revealed one doublet at $\delta$ 5.91 for the acetal proton on C-5 and one doublet at $\delta$ 5.85 for the two acetal protons on C-3 and C-7. The absorption at $\delta$ 2.09 (a singlet) for the methyl ketone protons of **4a** shifted to $\delta$ 1.50 for the angular methyl protons of **7a**. The $^{13}C$ NMR spectrum of **7a** lacked any carbonyl absorption and displayed one peak at $\delta$ 113.33 for the acetal carbon C-5, one peak at $\delta$ 112.46 for the acetal carbons C-3 and C-7, one singlet at $\delta$ 120.30 for the quaternary carbons, and one peak at $\delta$ 26.94 for the angular methyl carbons. The IR spectra and $^1H$ and $^{13}C$ NMR spectra of **7b-f** revealed that these compounds possess the same skeleton as **7a**.

Treatment of the tetraacetal tetraoxa-cages **5a-c** with catalytic amount of $TiCl_4$ in dichloromethane at 25 °C for 4 h gave the pentaoxa[5]peristylanes **7a-c** in 70-75% yields and the hydride rearrangement products **12a-c** in 20-15% yields (Scheme 2). Reaction of **6a-c** under the same reaction conditions gave **7a-c** in 85-90% yields. The amount of **12a-c** was too small to be isolated.

**Scheme 2**



Thus, we have accomplished for the first time the synthesis of pentaoxa[5]peristylanes, a novel and interesting oxa-cage system.

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(11) Selected spectral data for **7**. **7a**: white solid; mp 214-215 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.91 (d, J = 5.4 Hz, 1H), 5.85 (d, J = 5.1 Hz, 2H), 3.70-3.65 (m, 3H), 3.39-3.35 (m, 2H), 1.50 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 120.30 (2C), 113.33 (CH), 112.46 (2CH), 62.72 (2CH), 58.91 (2CH), 58.53 (CH), 26.94 ($2CH_3$); MS *m/z* (rel int.) 238 ($M^+$, 12), 208 (100). **7e**: white solid; mp 178-179 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.90 (d, J = 6.0 Hz, 2H), 5.86 (d, J = 5.1 Hz, 2H), 3.68-3.62 (m, 4H), 3.38-3.34 (m, 1H), 1.76-1.70 (m, 2H), 1.40-1.26 (m, 4H), 0.92 (t, J = 6.9 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 123.59 (C), 113.51 (2CH), 112.81 (2CH), 59.96 (CH), 58.76 (2CH), 58.27 (2CH), 39.30($CH_2$), 26.04($CH_2$), 22.66 ($CH_2$), 13.98 ($CH_3$); MS *m/z* (rel int.) 266 ($M^+$, 14), 209 (100).

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