Synthesis of Diacetal Trioxa-Cage Compounds via a Sequential Cyclization Reaction of Norbornene Derivatives Induced by Electrophiles

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The synthesis of diacetal trioxa-cage compounds via a sequential cyclization reaction of norbornene derivatives induced by electrophiles in a short sequence is reported. Treatment of the norbornene derivatives 2a–d and 10b with I$_2$ in aqueous THF in the presence of KI at 25 °C regioslectively gave the iodo-cage compounds 3a–d and 11 in 80–90% yields, respectively, via an iodine-induced sequential cyclization reaction. No detectable amount of other regiosomers or monocyclization products was obtained. The synthesis of trioxa-cages 14a–e was accomplished from 3a–d and 11 in a two-step sequence. Treatment of diacetylnorbornenes 15a–f with I$_2$ in aqueous THF at 25 °C regioslectively and stereoselectively gave the sequential cyclization products 16a–f, respectively, which were converted in one step to the diacetal trioxa-cages 24a–f in high yields. The structure of these trioxa-cages was proven by X-ray analysis of the crystalline compound 14f. Other electrophiles, such as bromine, m-CPBA, and Hg(OAc)$_2$, were also found to be effective for the sequential cyclization reaction. Oxymercuration of 15a–f and 2a–c with Hg(OAc)$_2$ in aqueous THF followed by reduction with NaBH$_4$ at 25 °C gave compounds 28a–f and 30b–d in high yields, respectively.

Introduction

The synthesis and chemistry of polycyclic cage compounds have attracted considerable attention in recent years. The vast majority of the work reported in this area has dealt with carbocyclic cage compounds. On the other hand, the synthesis and chemistry of heterocyclic cage compounds have received less attention. However, there are some reports regarding the chemistry of syntheses of oxa-cage compounds in the literature. This class of heterocyclic cage compounds is synthesized by intramolecular alkene–oxirane (2–2π) photocycloadDITION, by transannular cyclization of suitable compounds, by tandem cyclization, by dehydration of diols having the proper stereochemistry, by base-promoted rear-

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There are some reports regarding the electrophile-induced lactonization of norbornene derivatives. Recently, we discovered an iodine-induced sequential cyclization reaction of norbornene derivatives by the ring closure with participation of carbonyl and thioether groups leading to the formation of novel iodo-cage compounds. In this paper we report the full details of this sequential cyclization reaction of norbornene derivatives induced by several electrophiles. As part of a program that involves the synthesis and chemistry of new heterocyclic cage compounds, we also report here for the first time the application of the sequential cyclization reaction for the synthesis of diacetal trioxa-cages (type C).

**Results and Discussion**

Oxidation of 2-(methylthio)-5-alkylfurans 1a–d with 2 equiv of pyridinium chlorochromate (PCC) in dichloromethane at 25 °C followed by addition of cyclopentadiene gave the endo-adducts 2a–d in 65–70% yield. Treatment of 2a–d with I2 in aqueous THF in the presence of KI at 25 °C for 6 h gave the iodo-cage compounds 3a–d in 80–85% yields (Scheme 2). No detectable amount of the other regioisomer 4 was obtained. Also, no detectable amount of the monocyclization products 5 or 6 was obtained.

A mechanism is proposed for the formation of the iodo-cage compounds 3a–c (Scheme 3). Electrophilic attack of an iodine molecule at the alkene bond of 2 from the exo face gives the iodonium ion 7. Sequential intramolecular nucleophilic addition of the exo acyl group to the iodonium ion followed by addition of water molecule gives the intermediate 9. Loss of the methylthio group of 9 leads to the lactones 3. Since only the regioisomers 3a–d are obtained, we propose that the exclusive regioselective cleavage of the partial carbon–iodine bond of 7 may be preferentially affected through space by the acyl carbonyl group rather than by the thioether group.

To compare the nucleophilic cyclization of an ester group with that of an acyl group to the iodonium ion, compounds 10a,b were prepared. Treatment of 10a,b with I2 in aqueous THF in the presence of KI at 25 °C for 6 h gave the iodo-cage compounds 11a and 11b in 80% yields, respectively (Scheme 4). No detectable amount of other regioisomers and monocyclization products was obtained. Thus, we propose that the regioselective cleavage of the partial carbon–iodine bond may be preferentially affected by the acyl group rather than by the ester group.

The synthesis of diacetal trioxa-cage compounds (type C in Scheme 1) was accomplished from 3 and 11 by a two-step sequence. Reduction of the iodo-cage compounds 3a–d and 11 with NaBH4 in methanol at 0 °C for 4 h gave the hemiacetals 12a–e, instead of the stereoisomers 13a–e, in 70–80% yields, respectively (Scheme 5). The 1H NMR spectrum of 12a revealed one doublet at δ 5.42 (J = 2.4 Hz) for the hemiacetal proton on C3. The small coupling constant implies that the proton on C3 is trans to the proton on C2. The stereochemistry of the hydroxy group of 12 was also determined by NOE experiments of 12a. Irradiating the acetal proton on C3 of 12a (δ 5.42) gives 12.3% enhancement for the C9 proton absorptions and 5.7% enhancement for the C1 proton absorptions. Irradiating the C9 proton (δ 4.23) gives 9.9% enhancement for the acetal proton peak, 4.4% enhancement for the C1 proton peak, and 3.3% enhancement for the C8 proton peak. Nucleophilic addition of NaBH4 to the lactone carbonyl group of 3 and 11 may take place from the less hindered exo face, leading to formation of the stereoisomers 13a–e, which, followed by anomerization, gave the thermodynamical products 12a–e. Treatment of 12a–e with KH in dry THF at 0 °C for 2 h gave the diacetal trioxa-cage compounds 14a–e in 90% yield, respectively. The structure of the diacetal trioxa-cages 14 was proven by X-ray analysis of the crystalline compound 14e. A mechanism was proposed.

![Scheme 2](image1)

![Scheme 3](image2)

![Scheme 4](image3)
for the conversion of 12a–e to the trioxa-cages 14a–e via the base-promoted anomerization intermediates 12A, 12B, and 13A (Scheme 5).

To extend the iodine-induced sequential cyclization of norbornene derivatives and the synthesis of diacetal trioxa-cage compounds, the bis-endodiacylnorbornenes 15a–g were prepared. Treatment of 15a–d with I₂ in aqueous THF in the presence of KI at 25 °C for 6 h gave the iodo-cage compounds 16a–d in 80–90% yields (Scheme 6). The stereochemistry of the hydroxy group of 16a–d was determined on the basis of NOE experiments of 16a. Irradiating the C₉ proton (δ 4.42) gives 8.4% enhancement for the intensity of the angular methyl proton on C₁₃₂, 2.2% enhancement for the C₈ proton peak, and 3.2% enhancement for the C₁ proton absorption. Quantities of the other stereoisomers 17a–d were too small to be isolated. No detectable amount of the monocyclization product 18 was obtained. Reaction of 15e,f with I₂ under the same reaction conditions gave the iodo-cages 12a,c in 80% yields. For the cases of reactions of 15d–f with I₂, the other regioisomers 19d–f were formed in too small amounts to be isolated. Treatment of compound 15g with I₂ under the same reaction conditions gave the dehydration iodo-cage 20 in 80% yield. Oxidation of 12a,c and 16d with PCC in CH₂Cl₂ at 25 °C gave 3a,c and 21 in 80% yields, respectively.

A reaction mechanism is proposed for the formation of 16 from 15 (Scheme 7). Electrophilic attack of iodine molecule to the alkene bond of 15 from the exo face gives the iodonium ion 22. Sequential intramolecular nucleophilic addition of the endo acyl groups to the iodonium ion gives the oxonium ion 23. Addition of a water molecule to 23 from the less hindered convex face, followed by loss of a proton, gave the observed product 16.

The synthesis of diacetal trioxa-cages was accomplished from 16 by a one-step procedure. Reaction of 16a–d with KH in dry THF at 0 °C for 2 h gave the diacetal trioxa-cage compounds 24a–d in 90% yields (Scheme 8). A mechanism via the base-promoted anomerization, similar to Scheme 5, was proposed for the conversion of 16 to 24. Thus, we have developed a general method for the synthesis of diacetal trioxa-cages via a sequential cyclization of diacylnorbornenes induced by iodine in a short sequence.

We have also tried with other electrophiles to induce the sequential cyclization reaction of norbornene derivatives. Reaction of 15a with bromine or NBS in aqueous THF at 25 °C for 2 h gave the bromo-cage compound 25 in 85% yield. Treatment of 25 with KH in dry THF at 0 °C for 2 h gave the trioxa-cage 24a in 90% yield (Scheme 9). Reaction of 15a,b with m-CPBA in dichloromethane at 25 °C gave compounds 26a,b, in 80% yields, which were converted to the tosylates 27a,b. Treatment of 27a,b with KH in dry THF at 0 °C gave the trioxa-cages 24a,b in 80% yields. Thus, the sequential cyclization was also effective with bromine or m-CPBA as electrophiles.

Oxymercuration of 15a–f with Hg(OAc)₂ in aqueous THF at 25 °C followed by reduction with NaBH₄ gave the sequential cyclization compounds 28a–f in 70–80% yields (Scheme 10). For the case of reactions of 15d–f with Hg(OAc)₂, the other regioisomers 29d–f were formed in amounts too small to be isolated. The regiochemistry of the alkyl group of 28d–f was confirmed by the following chemical transformation. Oxidation of 28d–f with PCC in CH₂Cl₂ at 25 °C gave the lactones 30a–c in 80% yields. The 1H NMR spectrum of 28e revealed one singlet at δ 5.36 for the hemiacetal proton on C₁₃. The coupling constant (J = 0 Hz) implies that
the proton on C₂ is trans to the proton on C₃. The stereochemistry of the hydroxyl group of 28 was also determined by NOE experiments of 28a and 28e. Irradiating the acetol proton on C₃ of 28e (δ 5.36) gives 4.9% enhancement for the intensity of the endo proton Hₐ on C₉ and 2.3% enhancement for the C₇ proton peak. Irradiating the C₁ proton of 28a (δ 2.27) gives 3.8% enhancement for the intensity of the angular methyl protons on R'. Alkoxymercuration of 15a with Hg(OAc)₂ in methanol at 25 °C followed by reduction with NaBH₄ gave 31 in 75% yield. Reaction of 15a with Hg(OAc)₂ in acetonitrile at 25 °C, followed by reduction with NaBH₄, gave 32 in 70% yield. Oxymercuration of 2a with Hg(OAc)₂ in aqueous THF at 25 °C followed by reduction with NaBH₄ gave the lactones 30b,c and 30d. Thus, the sequential cyclization was also effective with Hg(OAc)₂ as the electrophile.

Conclusions

In summary, we have demonstrated a sequential cyclization reaction of norbornene derivatives induced by electrophiles, and we have accomplished for the first time the synthesis of diacetal trioxa-cage compounds in a short sequence via this sequential cyclization reaction. In each case of the sequential cyclization, no detectable amount of monocyclization products was obtained. For unsymmetric norbornenes, the sequential cyclization was found to be highly regioselective. We found that the exclusive regioselective deavage of the partial carbon—iodine bond of the iodonium ion 7 may be preferentially affected through space by the acyl group rather than by the thiol ester group or the ester group. For the diacyl-norbornenes 15a–d, the stereochemistry of the hydroxyl group of 16a–d was found to be highly stereoselective. The structure of the diacetal trioxa-cases 14a–e and 24a–d was proven by X-ray analysis of the crystalline compound 14e. Other electrophiles, such as bromine, m-CPBA, and Hg(OAc)₂, were found to be also effective for the sequential cyclization reaction. Oxymercuration of 2 and 15 with Hg(OAc)₂ followed by reduction with NaBH₄ gave the corresponding dioxa-cages 30 and 28.

Experimental Section

General. Melting points were determined in capillary tubes with a Laboratory Devices melting point apparatus and are uncorrected. Infrared spectra were recorded in CHCl₃ solutions or on neat thin films between NaCl disks. ¹H NMR spectra were determined at 300 MHz, and ¹³C NMR spectra were determined at 75 MHz on Fourier transform spectrometers. Chemical shifts are reported in ppm relative to TMS in the solvents specified. The multiplicities of ¹³C signals were determined by DEPT techniques. High-resolution mass values were obtained with a high resolution mass spectrometer at the Department of Chemistry, National Tsing Hua University. Elemental analyses were performed at the microanalysis laboratory of National Taiwan University. X-ray analyses were carried out on a diffractometer at the Department of Chemistry, National Sun Yat Sen University. For thin-layer chromatography (TLC) analysis, precoated TLC plates (Kieselgel 60 F²₅₄) were used, and column chromatography was done by using Kieselgel 60 (70–230 mesh) as the stationary phase. THF was distilled immediately prior to use from sodium benzophenone ketyl under nitrogen. CH₂Cl₂ was distilled from CaH₂ under nitrogen.

General Procedure for the Sequential Cyclization Reactions of Norbornene Derivatives 2a–d. To a solution of 2a (0.50 g, 2.4 mmol) in THF (2 mL) and H₂O (20 mL) were added I₂ (3.0 g, 11.8 mmol) and KI (2.0 g, 12 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 6 h. To this solution was added saturated Na₂S₂O₃ (30 mL) for reducing unreacted iodine and the mixture was extracted with ether (3 × 30 mL). The organic layer was washed with brine, dried over MgSO₄, and evaporated, and the residue was purified by column chromatography to give the iodo-lactone cage compounds 30a (0.59 g, 80%).

Spectral data for 3a: white solid; mp 107–108 °C; ¹H (CHCl₃) 2990, 1770, 1100 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.94 (d, J = 4.8 Hz, 1H), 4.01 (d, J = 3.0 Hz, 1H), 3.19 (dd, J = 9.9 Hz, J = 4.5 Hz, 1H), 3.11 (dd, J = 9.9 Hz, J = 5.1 Hz, 1H), 2.94–2.92 (m, 1H), 2.50–2.46 (m, 1H), 2.05–2.01 (m, 1H), 1.63 (s, 3H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 174.26 (C), 116.10 (C), 91.31 (CH), 51.04 (CH), 49.61 (CH), 48.56 (CH), 48.33 (CH), 40.49 (CH), 27.88 (CH).
2.45 (CH3); LMRSm/z (rel inten) 306 (M−, 9), 179 (100), 135 (41); HRMS (EI) calc for C12H12O5 305.9753, found 305.9759.

**General Procedure for the Sequential Cyclization Reactions of the Esters 10a,b.** The same reaction conditions and procedure for the iodine-induced sequential cyclization of 2a−d were applied to the cyclization reaction of 10a,b to give compounds 3a and 11.

**Spectral data for 11:** yield 80% white solid; mp 112−113 °C; IR (CHCl3) 2990, 1776, 1605, 1100, 755 cm−1; 1H NMR (300 MHz, CDCl3) δ 7.45−7.36 (m, 5H), 5.19 (d, J = 4.8 Hz, 1H), 4.18 (d, J = 2.4 Hz, 1H), 3.31−3.25 (m, 2H), 3.13−3.10 (m, 1H), 3.02−3.00 (m, 1H), 2.56−2.52 (m, 1H), 2.07−2.03 (m, 1H); 13C NMR (75 MHz, CDCl3, DEPT) δ 174.29 (C=O), 137.75 (C), 129.18 (2CH), 128.40 (2CH), 125.16 (CH), 116.22 (C), 91.91 (CH3), 53.98 (CH), 49.41 (CH), 48.88 (CH), 40.75 (CH3), 27.67 (CH); LMRSm/z (rel inten) 368 (M+1, 100); 241 (100); 153 (54); HRMS (EI) calc for C31H26O2 567.0900, found 567.0912.

**General Procedure for the Reduction of 3a−d and 11 with NaBH4.** To a solution of 3a (0.05 g, 1.6 mmol) in methanol (30 mL) was added NaBH4 (0.30 g, 7.9 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 4 h. After addition of saturated NH4Cl (30 mL) and extraction with ether (4 × 50 mL), the organic layer was washed with brine, dried over MgSO4, and evaporated, and the residue was purified by column chromatography to give the hexadiace 12a (0.41 g, 80%).

**Spectral data for 12a:** highly viscous liquid; IR (CHCl3) 3400, 2990, 1100 cm−1; 1H NMR (300 MHz, CDCl3) δ 4.52 (d, J = 2.4 Hz, 1H), 4.81 (d, J = 4.8 Hz, 1H), 4.32 (s, 1H), 4.23 (d, J = 2.4 Hz, 1H), 2.98−2.86 (m, 2H), 2.70−2.65 (m, 2H), 2.35−2.31 (m, 1H), 1.87−1.83 (m, 1H), 1.57 (s, 3H); 13C NMR (75 MHz, CDCl3, DEPT) δ 117.38 (C), 98.36 (CH), 90.93 (CH), 54.97 (CH), 50.92 (CH), 49.58 (CH), 47.28 (CH), 39.62 (CH), 29.29 (CH), 25.22 (CH); LMRSm/z (rel inten) 306 (M+, 1), 181 (100), 135 (43); HRMS (EI) calc for C18H14O2 297.0990, found 297.0991.

**Spectral data for 12b:** yield 70% highly viscous liquid; IR (CHCl3) 3400, 2990, 1380, 1100 cm−1; 1H NMR (300 MHz, CDCl3) δ 5.45 (d, J = 3.0 Hz, 1H), 4.84 (d, J = 5.1 Hz, 1H), 4.22 (d, J = 2.4 Hz, 1H), 3.72 (d, J = 3.0 Hz, 1H), 2.97−2.92 (m, 1H), 2.78−2.75 (m, 1H), 2.72−2.61 (m, 2H), 2.35−2.32 (m, 1H), 2.01−1.96 (m, 1H), 1.86−1.84 (m, 1H), 0.98 (d, J = 6.9 Hz, 3H), 0.96 (d, J = 6.9 Hz, 3H); 13C NMR (75 MHz, CDCl3, DEPT) δ 122.05 (C), 98.15 (CH), 90.37 (CH), 54.54 (CH), 49.73 (CH), 47.40 (CH), 47.22 (CH), 39.62 (CH), 34.32 (CH), 29.97 (CH), 17.36 (CH3), 17.12 (CH3); LMRSm/z (rel inten) 336 (M+, 24), 209 (100), 191 (48); HRMS (EI) calc for C26H22O4 456.0586, found 456.0578.

**General Procedure for the Synthesis of Diacetal Trioxa-Cage Compounds 14a−e.** To a solution of 12a (0.31 g, 1.0 mmol) in dichloromethane (50 mL) was added PCC (0.42 g, 2.0 mmol) at 25 °C. The reaction mixture was stirred for 25 °C for 3 h. The reaction mixture was filtered and the solvent was evaporated. The residue was purified by column chromatography to give the iodo-lactone 3a in 80% yield. The same reaction conditions and procedure were applied for the oxidation of 16d to give 21 in 80% yield.

**Spectral data for 21:** white waxy solid; mp 55−56 °C; IR (CHCl3) 2980, 1770, 1240, 1100 cm−1; 1H NMR (300 MHz, CDCl3) δ 4.95 (d, J = 5.4 Hz, 1H), 4.04 (d, J = 2.6 Hz, 1H), 3.18−3.04 (m, 2H), 2.95−2.91 (m, 2H), 2.48 (d, J = 11.7 Hz, 1H), 2.00 (d, J = 11.7 Hz, 1H), 1.88−1.80 (m, 2H), 1.40−1.20 (m, 12H), 0.88 (t, J = 6.6 Hz, 3H); 13C NMR (75 MHz, CDCl3, DEPT) δ 174.49 (C=O), 118.30 (C), 91.31 (CH), 49.68 (CH), 49.42 (CH), 48.86 (CH), 48.50 (CH), 40.67 (CH2), 36.50 (CH), 31.75 (CH2), 29.35 (CH), 29.32 (CH), 29.06 (CH), 28.00 (CH), 23.46 (CH), 27.58 (CH), 14.06 (CH2); LMRSm/z (rel inten) 404 (M+, 6), 233 (100); HRMS (EI) calc for C19H19O5 404.0848, found 404.0845.

**General Procedure for the Synthesis of Diacetal Trioxa-Cage Compounds 24a−d.** The same reaction conditions and procedure for the preparation of trioxa-cages 14a−e were applied for the synthesis of diacetal trioxa-cage compounds 24a−d.

**4-Methyl-3,5,7-trioxapentacyclo[7,2.1.02.8.013.6.019.1]dodecane (24a):** yield 80%; white waxy solid; 70−71 °C; IR (CHCl3) 2990, 1100 cm−1; 1H NMR (300 MHz, CDCl3) δ 4.25 (brs, 2H), 2.83 (brs, 2H), 2.76 (brs, 2H), 1.83−1.73 (m, 2H), 1.60 (s, 6H); 13C NMR (75 MHz, CDCl3, DEPT) δ 115.81 (2C), 80.29 (2CH), 56.66 (2CH2), 46.99 (2CH2), 31.61 (CH3), 22.19 (2CH3); LMRSm/z (rel inten) 194 (M+, 27), 138 (100); HRMS (EI) calc for C16H16O3 224.0949, found 224.0948. Anal. Calc'd for C16H16O3: C, 58.61; H, 7.27, found: C, 58.62; H, 7.30.

**Reaction of Bis-endiacylindonorborne 15a with Br2 or N-Br-Chlorocarbene.** To a solution of bis-endiacylindonorborne 15a (0.26 g, 0.9 mmol) in dry THF (2 mL) and H2O (20 mL) was added Br2 (0.64 g, 4.0 mmol) or N-bromosuccinimide (0.72 g, 4.0 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 2 h. To this solution was added saturated Na2S2O3 (30 mL) for reducing unreacted Br2.
and the mixture was extracted with ether (4 × 30 mL). The organic layer was washed with brine, dried over MgSO4, and evaporated, and the residue was purified by column chromatography to give the bromo-cage compound 25 (0.88 g, 80%): highly viscous liquid; IR (CHCl3) 3400, 2995, 1015 cm⁻¹; 1H NMR (300 MHz, CDCl3) δ 4.64 (d, J = 4.5 Hz, 1H), 4.37 (d, J = 2.4 Hz, 1H), 3.05–3.00 (m, 1H), 2.96–2.91 (m, 1H), 2.67–2.62 (m, 1H), 2.34–2.27 (m, 1H), 1.72–1.67 (m, 1H), 1.57 (s, 3H), 1.55 (s, 3H), 1.46–1.44 (m, 1H); 13C NMR (75 MHz, CDCl3, DEPT) δ 117.09 (C), 103.92 (C), 89.88 (CH), 56.60 (CH), 53.34 (CH), 52.47 (CH), 48.97 (CH), 45.94 (CH), 37.67 (CH2), 25.87 (CH3), 24.35 (CH3); LRMS m/z (rel inten) 274 (M+1, 18), 195 (46), 177 (65), 151 (100).

**Reaction of 25 with KH.** The same reaction conditions and procedure for the preparation of 24a from 16a were applied for the reaction of 25 with KH to give 24a in 90% yield.

**Sequential Cyclization of Bis-endo-diacylnorbornenes 15a,b.** Mediated by mCPBA. To a solution of 15a (0.18 g, 1.00 mmol) in dichloromethane (30 mL) was added pCPBA (0.14 g, 1.37 mmol) and extraction with dichloromethane (3 × 30 mL), the organic layer was washed with saturated NaHCO3 and brine, dried over MgSO4, and evaporated, and the residue was purified by column chromatography to give the sequential cyclization product 26a (0.28 g, 80%): viscous liquid; IR (CHCl3) 3090, 2980, 2880, 1450, 1430, 1370, 1350 cm⁻¹; 1H NMR (300 MHz, CDCl3) δ 7.95–7.93 (m, 1H), 7.87–7.83 (m, 1H), 7.59–7.56 (m, 1H), 7.42 (dd, J = 6.0 Hz, 1H, 7.0 Hz, 1H), 4.21 (s, 1H), 4.15 (d, J = 4.8 Hz, 1H), 3.01–2.93 (m, 2H), 2.69–2.65 (m, 1H), 2.42 (brs, 1H), 2.18 (d, J = 10.8 Hz, 1H), 1.74 (s, 3H), 1.57 (s, 3H), 1.55–1.51 (m, 1H); 13C NMR (75 MHz, CDCl3, DEPT) δ 162.79 (C), 138.19 (CH), 131.41 (CH), 129.80 (CH), 128.90 (C), 127.33 (CH), 118.83 (C), 113.41 (C), 89.15 (CH), 74.33 (CH), 52.52 (CH), 51.76 (CH), 47.82 (CH), 44.01 (CH), 35.31 (CH3), 24.83 (CH3), 19.15 (CH3); LRMS m/z (rel inten) 352, 350 (M+1, 5), 195 (100).

**Tosylation of 26a,b.** To a solution of 26a (0.25 g, 0.71 mmol) in pyridine (10 mL) was added p-toluenesulfonyl fluoride (0.16 g, 0.85 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 12 h. The reaction mixture was worked up, and the residue was purified by column chromatography to give the tosylate 27a (0.32 g, 90%): yellow oil; IR (CHCl3) 1780, 1670, 1610, 1590 cm⁻¹; 1H NMR (300 MHz, CDCl3) δ 7.92–7.79 (m, 4H), 7.57–7.35 (m, 4H), 4.76 (d, J = 1.2 Hz, 1H), 4.24 (d, J = 4.8 Hz, 1H), 2.98–2.92 (m, 2H), 2.70–2.62 (m, 2H), 2.44 (s, 3H), 2.11–2.05 (m, 1H), 1.65 (s, 3H), 1.62–1.58 (m, 1H), 1.54 (s, 3H); 13C NMR (75 MHz, CDCl3, DEPT) δ 196.10 (C), 162.79 (C), 141.52 (C), 133.62 (C), 133.54 (C), 129.98 (CH2), 129.85 (CH), 129.10 (CH), 128.70 (C), 127.60 (CH), 127.22 (CH), 118.91 (C), 112.86 (C), 86.31 (CH), 83.66 (CH), 52.14 (CH), 51.74 (CH), 47.91 (CH), 42.71 (CH), 35.14 (CH2), 24.49 (CH3), 21.53 (CH3), 18.80 (CH3); LRMS m/z (rel inten) 506, 504 (M+2, 349, 100).

**Conversion of the Tosylates 27a,b to the Trioxa-Cages 24a,c.** To a solution of 27a (0.59 g, 1.00 mmol) in dry THF (40 mL) was added KH (0.080 g, 2.0 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 6 h. To this reaction mixture was dropwise added H2O (10 mL) at 0 °C to destroy the excess KH. After addition of saturated NH4Cl (10 mL) and extraction with ether (3 × 30 mL), the organic layer was washed with brine, dried over MgSO4, and evaporated, and the residue was purified by column chromatography to give the trioxa-cage 24a in 70% yield.

**General Procedure for Oxymercuration–Demercuration of Bis-endo-diacylnorbornenes 15a–f.** To a solution of 15a (0.18 g, 1.00 mmol) in anhydrous methanol (20 mL) was added Hg(OAc)2 (0.35 g, 1.1 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 2 h. To this solution was added NaH2PO4 (0.20 g, 1.1 mmol) and the reaction mixture was stirred at 25 °C for another 2 h. The solvent was evaporated and saturated NH4Cl (20 mL) was added. After extraction with ether (3 × 30 mL), the organic layer was washed with brine, dried over MgSO4, and evaporated, and the residue was purified by column chromatography to give the cyclization product 16a (0.23 g, 75%): pale yellow oil; IR (CHCl3) 2980, 2880, 1600 cm⁻¹; 1H NMR (300 MHz, CDCl3) δ 4.44 (dd, J = 8.1 Hz, J = 4.5 Hz, 1H), 3.00–2.80 (m, 3H), 2.55–2.50 (m, 1H), 2.27 (brs, 1H), 1.90 (dd, J = 14.1 Hz, J = 3.6 Hz, 1H), 1.68–1.55 (m, 1H), 1.52 (s, 3H); 13C NMR (75 MHz, CDCl3, DEPT) δ 116.69 (C), 104.51 (C), 81.21 (CH), 52.73 (CH), 53.79 (CH), 49.37 (CH), 39.60 (CH), 36.60 (CH), 33.82 (CH2), 26.36 (CH3), 23.99 (CH3); LRMS m/z (rel inten) 196 (M+1, 42), 179 (100); HRMS (EI) calcld for C14H20O2 196.1099, found 196.1091. Anal. Calcld for C14H20O2: C, 73.29; H, 8.95; found: C, 73.18; H, 8.89.
General Procedure for Oxymercuration–Demercuration of 2a–c. The same reaction conditions and procedure for the oxymercuration of 15a–f were applied for oxymercuration–demercuration of 2a–c to give the sequential cyclization product 30b–d in 70–80% yields.

Spectral data for 30d: yield 75%; pale yellow oil; IR (CHCl₃) 2970, 1767, 1250, 1107 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.62 (dd, J = 6.6 Hz, J = 6.6 Hz, 1H), 3.10–3.03 (m, 2H), 2.90–2.86 (m, 1H), 2.69 (s, 1H), 2.12–2.05 (m, 1H), 1.83–1.66 (m, 4H), 1.01 (d, J = 7.2 Hz, 3H), 0.98 (d, J = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 176.34 (C=O), 120.73 (C), 81.52 (CH), 49.78 (CH), 48.77 (CH), 40.80 (CH₂), 39.31 (CH), 35.85 (CH₂), 34.04 (CH), 16.70 (CH₃), 16.60 (CH₃); LRMS m/z (rel inten) 208 (M⁺, 12), 164 (100); HRMS (EI) calcld for C₁₂H₁₆O₃: 208.1099, found 208.1094. Anal. Calcld for C₁₂H₁₆O₃: C, 69.19; H, 7.75; found: C, 69.10; H, 7.81.

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Supporting Information Available: ¹H and ¹³C NMR spectra data of 3b–d, 12c–e, 14b–e, 16b–d, 16b–d, 24b–d, 26b, 27b, 28b–f, and 30a–c (23 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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