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Chemistry of Cage-shaped Hydrocarbons. The Oxidation of Heptacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,11}.0^{5,9}.0^{10,14}]tetradecane

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Oxidative ring opening reactions enabled disassembly of the cage structure of the title compound. Stepwise oxidations were achieved through radical intermediates using lead tetracetate and iodine. The regioselectivity of bond fission is rationalized by comparing the relative strains of each bond. Multiple cleavages of C-C bond were accomplished by photolysis with HgO and iodine under UV. The oxidative effect of Ce(IV) ion on a cage-shaped diketone is examined. New skeletons of polyquinanes are obtained from these reactions.

INTRODUCTION

The title compound, heptacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,11}.0^{5,9}.0^{10,14}]tetradecane (HCTD), is prepared in one step by heating norbornadiene with metal carbonyls.[1] The cage-shaped structure consists of eight five-membered rings, therefore belonging to the family of polyquinanes. By virtue of its ready accessibility, HCTD is utilized to form other polyquinane derivatives such as triquinane, tetraquinane, and pristylane.[2] Some structures are of high symmetry, therefore particularly useful for theoretical studies.[3] In this report we describe sequence of oxidations of this compound and its related chemical modifications. The mechanism and regio-selectivity of the reactions are discussed.

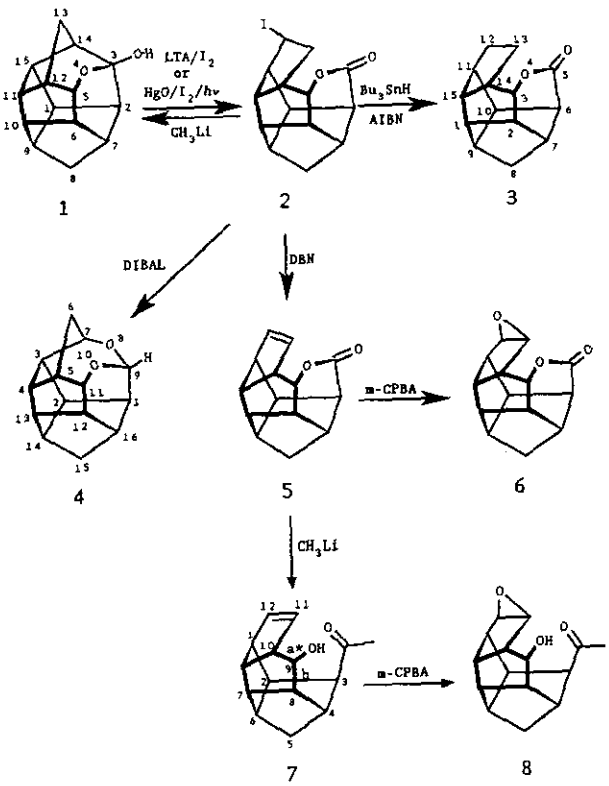
RESULTS

Oxidation via Hypoiodite Intermediate

Oxidations of HCTD were performed with selective C-C bond cleavages. The conversion of hemiketal **1** to **2** was accomplished with oxidants of two kinds, i.e., either a combination of lead tetracetate and iodine[4,5] (yield of **2** is 85%) or photolysis of mercuric oxide in the presence of iodine[6] (yield 88%) (Scheme I). Both reactions proceed through hypoiodite intermediates, and their regio-selectivities were similar.

β-Fission of secondary alkoxy radicals may occur at either adjacent C-C bond. Homolytic cleavage of C(3)-C(14) followed by iodination yielded **2**, whereas cleavage of C(2)-C(3) yielded its structural isomer. Molecular simulation with a force field indicates that the latter product reverts to **1** more readily. The polycyclic geometries of **1** and **2** carry nonbonded strain to varying degrees. Reduction of **2** with methyl lithium closes the ring to **1** in high yield. The structure **2** was confirmed by its spectral and chemical properties. The ^{1}H NMR absorption of **2** at δ 4.28 ppm couples

Scheme I



Dedicated to Professor Sung-Mao Wang (王松茂) on the occasion of his seventieth birthday.

with the ^{13}C signal at δ 21.14 ppm in a 2-D ^{1}H-^{13}C correlation spectrum, characteristic of an iodomethylene (-CHI-) group. In ^{1}H-^{1}H plot the δ 4.28 signal couples with a pair of hydrogens at δ 2.47 (1H) & 2.86 (1H) ppm of the adjacent -CH_2- moiety.

Reductive dehalogenation of **2** with tributyltin hydride in the presence of azoisobutyronitrile (AIBN) yielded **3**. Treatment of **2** with DIBAL in dichloromethane, followed by hydrolysis yielded acetal **4**. The latter structure maintains the shape of a cage of which the carbonyl at C(9) is protected by two *cisoid*-oriented hydroxyl groups through intramolecular ketal formation. The three carboxyl hydrogens arise at δ 4.29 (t, J = 9 Hz), 4.41 (t, J = 7 Hz), and 5.39 (d, J = 9 Hz), which are consistent with the assigned geometry.

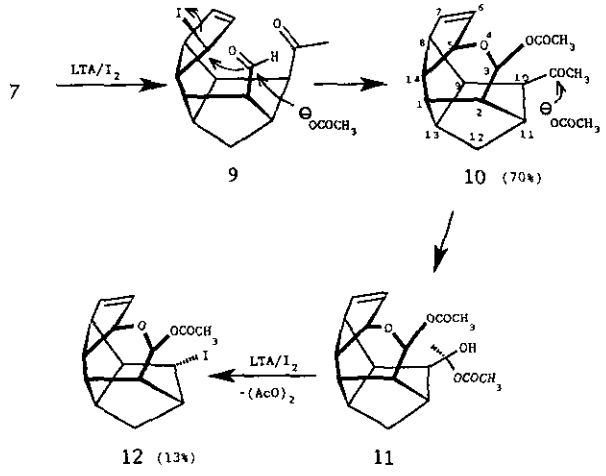
Base-induced dehydroiodination of **2** with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in benzene gave olefin **5** in good yield. The olefinic hydrogens show in the ^{1}H NMR spectrum as two multiplets at δ 5.60 and 5.69 ppm. The allylic hydrogen H(14) at δ 3.45 ppm couples with H(3) which is a triplet at δ 4.94 ppm. The ^{13}C signals for olefinic carbons C(12) and C(13) overlap to give a singlet at δ 135.6 ppm, indistinguishable even under large magnetic field (i.e. 125.8 MHz). In a ^{1}H-^{13}C 2-D plot the latter signal couples with both olefinic hydrogens.

Epoxidation of **5** with m-chloroperbenzoic acid (m-CPBA) yielded **6**. As spectra of **6** bear similarities with that of **3**, their comparison is instructive. In ^{1}H NMR spectra of **3** there is only one signal at δ > 3.0 ppm (i.e. δ 4.82 ppm, triplet, J = 9 Hz), whereas for **6** there are four low field signals (δ > 3.10) shown at δ 3.30 (triplet, J = 8 Hz), 3.44 (m), 3.59 (m), and 5.12 ppm (triplet, J = 8 Hz). The latter triplet at δ 5.12 ppm is assigned to H(3) and the two multiplets are assigned to epoxyl hydrogens H(12,13). Comparison of their ^{13}C NMR spectral patterns indicates that the lines at δ 56.81 and 59.44 ppm of **6** are derived from the epoxyl carbons, whereas the corresponding ethylene lines of **3** appear at δ 26.51 and 30.34 ppm.

Methylation of **5** using methyl lithium in THF at -78 °C opened the lactone ring. Methyl lithium was used in large excess to ensure completion of conversion to **7**. In the IR spectrum the acetyl group of **7** produces an absorption at ν 1702 cm^{-1}. The olefinic carbons give two distinct signals at δ 131.5 and 131.7 ppm in the ^{13}C NMR spectrum, but the corresponding hydrogens appear as a singlet at δ 5.71 ppm in ^{1}H spectrum. Epoxidation of **7** with m-CPBA resulted in the corresponding epoxide **8**. The epoxyl group is evident from the two multiplets at δ 3.41 and 3.69 ppm in the ^{1}H NMR spectrum and those at δ 59.03 and 60.59 ppm in ^{13}C spectra.

Further oxidation of **7** using LTA/I_2 yielded two products. The NMR spectrum of the major product (yield 70%) displays features consisting of an acetyl group, an acetate group, an allylic alkyloxyl moiety, and an acetal moiety. The structure of **10** complies well with these characteristics, whereas its formation can be deduced from the primary product **9** (Scheme II) although the presence of the latter was not identified on purification. The minor product (yield 13%) **12** is less polar than **10** and was purified on a silica gel chromatograph. Comparison of NMR spectra of **12** and **10** shows a few characteristics: the signals corresponding to the acetyl group of **10** disappear, while a triplet at δ 4.32 ppm in the ^{1}H spectrum and a doublet at δ 26.62 ppm in ^{13}C emerge for **12**. These features indicate that the acetyl group at C(10) of **10** is substituted by iodide. The transformation of **10** to **12** is rationalized in a sequence shown in Scheme II.

Scheme II



Oxidation by Ceric Ammonium Nitrate

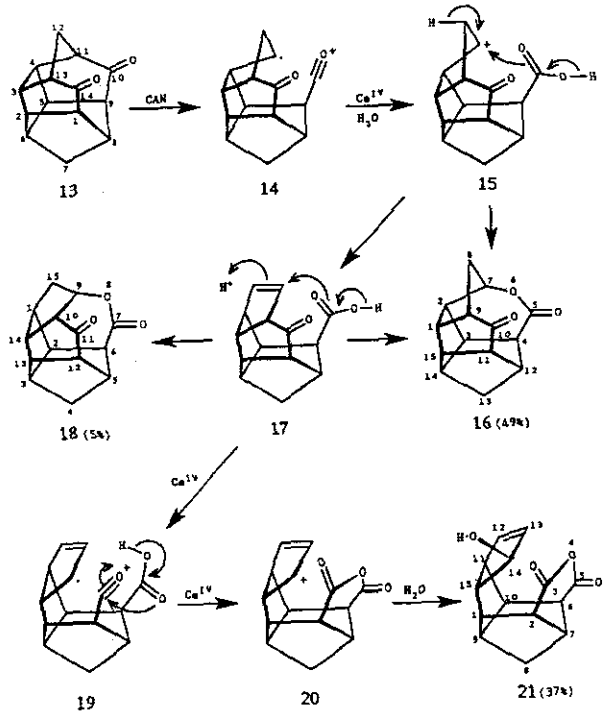
Oxidation of **1** with the Jones reagent yielded diketone **13**.[2] As the two carbonyl groups are separated by a narrow distance (2.9 Å), a transannular electronic interaction was detected. Detailed theoretical analysis of such orbital correlations is reported.[3a] Several characteristic chemical reactions are also outlined.[1b,3c]

Oxidation of Bayer-Villiger type of **13** with m-CPBA yielded a monolactone. In the ^{13}C NMR spectrum the doublet at δ 83.97 ppm and two singlets at δ 170.54 and 220.66 are most informative. The regio-selectivity of C-C bond breakage is not self-evident.[7] Two isomers of **16** may be derived, for which the lactone oxygen is located either between bond C(9)-C(10) of **13** or between C(10)-C(11). In the ^{1}H NMR spectrum the product displays a multiplet at δ 4.97 ppm due to the proton of the methinyl group directly connected to the carboxylate. In a 2D ^{1}H-^{1}H COSY plot this

signal couples with a -CH_2- moiety, a feature consistent with structure **16**.

Oxidation of **13** to **16** may be achieved by Ce(IV) ion. Ceric ion abstracts one electron at a time from the reactant to produce a radical cation intermediate (Scheme III). The reaction **13** with ceric ammonium nitrate was less selective than with m-CPBA in that three products were isolated from a mixture (total yield 91%). The structure of **18** resembles closely that of **16**, whereas a 1,2-shift occurs on the lactone moiety. There are 14 ^{13}C absorptions in NMR including two triplets and three relatively low field signals at δ 80.9, 173.8, and 215.3 ppm. A methinyl ^1H signal (δ 4.92 ppm for H(9)) couples with two hydrogens on secondary carbon C(15). The formation of **18** was depicted as proceeding though acid **17** that is an intermediate common for **16**, **18** and **21**.

Scheme III



Four molar equivalents of ceric ion is required for conversion of **13** to **21**, and two moles of water are consumed. The carbonyls appear in ^{13}C at δ 168.9 and 169.7 ppm, the olefinic peaks at δ 133.9 and 136.6 ppm, and the allyl C(14) at δ 75.1 ppm. Two absorptions of the anhydrous moiety appear in IR spectra at 1793 and 1751 cm^{-1}. The identification of compounds **16**, **18**, and **21** in this reaction allows us to deduce a full reaction mechanism for Ce(IV) oxidation of **13**. The numbering in Scheme III for compounds **13**, **16**, **18**, and **21** differ from each other (similar situation applies in Scheme I) because of variations in their polycyclic ring connectivities.

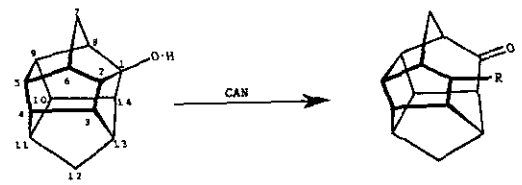
Tertiary alcohol **22** was oxidized by ceric ion to form nitrate **23a**. The regio-selectivity of bond breakage in this reaction is identical to that of a hypoiodite (**23b**).[2] Reactions of both types are known to proceed through free-radical intermediates.

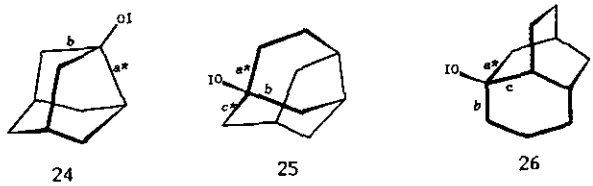
DISCUSSION

Regio-selectivity in the Fragmentation of Hypoiodite

The direction of β-fission of alkoxy radicals that result from thermolysis of hypoiodites generally depends on the relative stability of resulting radicals.[8] For instance, tertiary alkyl radicals are generally more stable than secondary ones, and secondary than primary ones. In the case of polycyclic systems the variation of the total strain energy of the system needs to be considered. The regio-selectivity of C-C bond cleavage has been rationalized by the changes of steric energy on going from the alkoxy radicals to the carbonylalkyl radicals.[5]

The observed selectivity for thermolysis of hypoiodites **24**, **25**, and **26** complies well with predictions; i.e. bonds labeled with asterisk (*) were broken to yield products with lower strain. It is noted that for **26** a primary radical is formed in preference to a secondary one (to open bond c). An inconsistency is observed for the diamantane alkoxy radical **27**, for which homolysis appeared at a bond of





smaller strain (bond a). The stability of **28** is estimated to be better than the alternate primary radical, but it is believed that **28** undergoes the reversible process readily to **27**.[4]

In our studies of compounds **1**, **7**, and **22** the direction of β-fission can be analyzed in a similar way, i.e. by comparing the relative strains of each product. However, an alternate criterion is employed to simplify the prediction on regio-selectivity. For radical reactions the regio-selectivity is generally governed by an early stage transition state which resembles closely the structure of the reactant.[9] This condition is particularly true for kinetic-controlled mechanisms. The relative strains of the bond undergoing β-fission may be properly reflected in their bonding strains that can be estimated according to force field models.[10] The more distorted is the bond, the more readily it is torn apart. In Table 1 we summarize stretching energies of all β-bondings for seven alkyoxy radicals. In most cases the experiments agree well with the predicted order of bonding strain, except compounds **7** and **27**. The explanation for **7** is similar to that for **27**; i.e. the radical of lower energy undergoes a reversible process.

It is found that the regio-selectivity of C-C fission is invariant for the two reagents, i.e. combination of LTA and I_2 or irradiation of HgO/I_2 with UV light. Both processes proceed with similar mechanisms. A major distinction between the two methods is that the latter may result in two consecutive C-C bond cleavages in one treatment. An example is shown in Scheme IV for oxidation of adamantanol **29**, in which iodo-formate **30** is produced directly with excess reagents.[6] An alternate sequence utilizing Bayer-Villiger oxidation of ketone **31** followed by reduction of **32** to **33** requires four steps. In our cage system, the conversion of **22** to **2** through **1** might be completed in one operation with this photochemical procedure.

Scheme IV[6a]

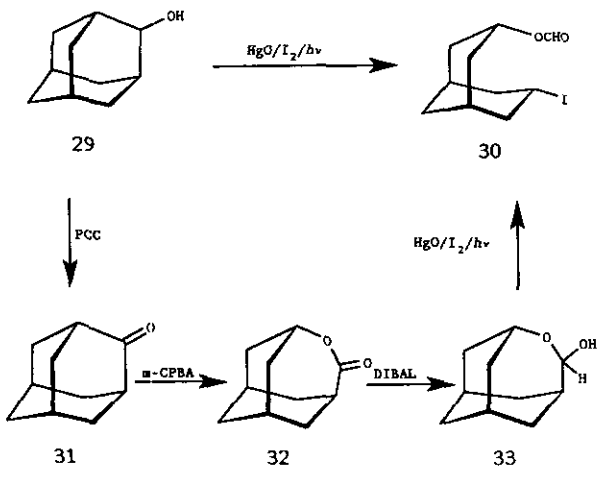


Table 1. Stretching Energy of C-C Bonds Undergoing β-Fission of the Corresponding Alkoxy Radicals.[a] The Bonds Labeled with a, b, and c are Referred to the Structures in Schemes. The Ones Marked with Asterisk (*) Undergo Fission in Thermolysis

Compd. bond	**1**	**7**	**22**	**24**[b]	**25**	**26**	**27**[b]
a	2.45*	0.011*	0.544*	2.327*	2.186*	2.420*	1.520*
b	1.89	0.274	0.242	1.127	1.622*	2.199	1.963
c			0.070		1.287	1.728	

[a] The stretching energy is calculated by the equation: $E\ (KJ/mol) = 1324 \times (R - R_o)^2(1 - 2.000 \times (R - R_o))$, which is implanted in the force field model MM2(91) developed by Allinger.[10]
[b] The two symmetrical bonds were averaged.

The Mechanism of Ceric Oxidation

Ceric ion in various coordinated forms is a strong oxidizing agent for alcohols, aldehydes and ketones.[11] It is known that Ce(IV) ion forms 1:1 complexes with alcohols which rapidly collapse to products. It is used in colorimetric and quantitative detection of alcohols. Under more drastic conditions, carbonyl compounds are also vulnerable to Ce(IV) ions. The first step of oxidation is complex formation, followed by C-C cleavage to form a radical intermediate.[12] The radical is unbonded, i.e. not associated with the metal, and may be further oxidized such as in reaction of **13**, or be trapped by ligands or solvent such as in formation of **23a**.

The observation of compounds **16**, **18** and **21** in oxidation of **13** can be combined into one mechanism shown in Scheme III. Both **16** and **18** are derived from common intermediate **17**. The relative feasibility for the two different paths of lactone formation depends on the strain of products. The strain of **16** (163 KJ/mol) is estimated to be 55 KJ lower than that of **18** (218 KJ/mol),[10] whereas the yield of **16** (49%) was about 10 times that of **18** (5%). During reaction of **13** to **17**, two molar equivalents of ceric ion is consumed. Prolonged reaction of **17** with further two moles of Ce(IV) yielded **21** in 37%.

The two C-C bond cleavages of **13** appear at C(10)-C(11) and C(13)-C(14) with high regio-selectivity. The selectivity in transformation of **13** to **16** is similar to the reaction using m-CPBA. The relative yields of **16**, **18**, and **21** may be further optimized separately.

CONCLUSION

Alcohols of polycyclic hydrocarbons were oxidized through radical intermediates formed by fragmentation of hypoiodite. The regio-selectivity of β-fission of alkoxy

radicals are determined by the following factors: (a) the relative strain of the bonds undergoing homolysis, (b) the stability of the resulting radical, and (c) the reversibility of bond recombination. The reaction mechanisms are similar with either the reagent LTA/I_2 or photolysis with HgO/I_2.

Ce(IV) is a stronger oxidant toward poly-ketones than m-CPBA. Multi-step oxidative processes are accomplished in one operation. The regio-selectivity of C-C bond fission is high along with its high reactivity. The product distribution is determined by either their relative stabilities or their rates of reactions.

EXPERIMENTAL SECTION

General

^1H and ^{13}C NMR spectra were recorder on either a Bruker AMX-500 FT or AC-200 FT spectrometer. Chemical shifts of ^1H were measured downfield from TMS in δ units, whereas those of ^{13}C were recorded with the central line of $CDCl_3$ at δ 76.90 ppm as internal reference. Infrared spectra were recorded on a Perkin-Elmer 882 infrared spectrophotometer. Elemental analyses were obtained on a Perkin-Elmer 2400 CHN instrument. Mass spectra were carried out on a VG Analytical 70-250 S/SE spectrometer. Melting points (Yanaco MICRO mp apparatus model MP-S3) are uncorrected.

Benzene and pyridine were freshly distilled over sodium and CaH_2 respectively.

12-Iodo-4-oxahexacyclo[7.6.0.0^{2,7}.0^{3,14}.0^{6,10}.0^{11,15}]pentadecan-5-one (2)

This reaction was accomplished by two methods: method A utilizes reagents of $Pb(OAc)_4$ and I_2; method B uses UV irradiation with HgO and I_2.

Method A: To a two-necked (100 mL round-bottom) flask fitted with a condenser was added $Pb(OAc)_4$ (1.26 g, 2.84 mmol). The flask was evacuated and purged with nitrogen three times. Compound **1** (213 mg, 1.00 mmol) and I_2 (678 mg) were dissolved in benzene (100 mL), and the solution was injected with syringe into the flask. The mixture was stirred with a magnetic bar at room temperature for 85 min. It was filtered and extracted with ether. The ether portions were combined and washed with saturated $Na_2S_2O_3$ (60 mL × 2), distilled water (60 mL × 2), and saturated $NaHCO_3$ (60 mL × 3). The solvent was dried over anhydrous $MgSO_4$ and evaporated *in vacuo* to produce pale yellow oil. Iodolactone **2** (290 mg, 0.848 mmol, 85%) was recrystallized from chloroform/hexane as colorless crystals, mp 154.5-155 °C. IR ($CDCl_3$) ν 1720, 1735 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ 1.67 (1H, d, J = 11 Hz), 1.74 (1H, d, J = 11 Hz), 2.34 (1H, m), 2.45-2.50 (1H, dt, J = 7.5, 15 Hz), 2.60-2.70 (4H, m), 2.70-2.74 (1H, q, J = 8 Hz), 2.78-2.84 (1H, m), 2.84-2.88 (1H, dd, J = 7.5, 15 Hz), 3.05-3.13 (1H, m), 3.20-3.26 (1H, m), 4.26-4.30 (1H, td, J = 2.5, 8 Hz, -CHI-), 4.77 (1H, t, J = 9 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.14 (d, -CHI-), 39.84 (d), 39.99 (t), 44.74 (d), 44.33 (d), 45.85 (d), 47.08 (t), 51.27 (d), 52.22 (d), 53.06 (d), 55.65 (d), 63.45 (d), 82.48 (d), 174.29 (s). MS (30 eV) *m/z* (relative intensity) 343 (M^+, 3%), 215 (M^+-I, 100%), 187 (10%), 169 (22%). Anal. calcd for $C_{14}H_{15}O_2$: C 49.14, H 4.42; found: C 49.07, H 4.21. HRMS calcd: 342.0117; found: *m/z* 342.0114.

Method B: Pyridine was distilled over CaH_2 first and degassed 15 min in a container by purging nitrogen in an ultrasonic bath. To a Pyrex (50 mL round-bottom) flask containing a magnetic stirring bar was added **1** (25 mg, 0.116 mmol) , HgO (65 mg), and I_2 (78 mg), followed by benzene (40 mL) and pyridine (0.1 mL). The mixture was irradiated with UV light for 10 h at room temperature. The resulting mixture was worked up as previously described. Colorless crystals of **2** were collected in 88% yield (35 mg).

Reduction of 2 by Methyl Lithium

A three-necked flask (50 mL round-bottom) containing a magnetic bar was fitted with a dropping funnel and a nitrogen inlet/outlet; to it was added compound **1** (70 mg, 0.21 mmol) and THF (15 mL) while the system was cooled to -78 °C in an acetone/dry ice bath under nitrogen atmosphere. A solution of methyl lithium in ether (5%, 2 mL) was added dropwise to the mixture through a funnel, and the resulting solution was stirred magnetically for 1 h. The reaction was quenched on adding saturated NH_4Cl (3 mL); then the mixture was partitioned three times between water and ether. The organic layers were combined and dried over anhydrous $MgSO_4$. An oily product was collected after evaporating the solvent. Compound **1** was purified in 91% yield (40 mg, 0.19 mmol) by passing through a silica gel chromatographic column using hexane/ethyl acetate (3/2 v/v) as eluent. Its spectral characteristics were identical to those of an authentic sample.

4-Oxahexacyclo[7.6.0.0^{2,7}.0^{3,14}.0^{6,10}.0^{11,15}]pentadecan-5-one (3)

To a flask (round-bottom) containing toluene (15 mL) was added **2** (30 mg, 0. 087 mmol), followed by tributyltin hydride (0.25 mL) and azoisobutyronitrile (AIBN) in catalytic amount. The solution was stirred for 3 h and quenched on addition of saturated sodium bicarbonate. The resulting mixture was extracted several times with ether, dried over

anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The product was purified by silica gel chromatograph (hexane/ethyl acetate 3/1 as eluent) to give an oil (13 mg, 0.060 mmol, 70%). IR ($CDCl_3$) ν 1711 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.55-1.85 (6H, m), 2.05-2.20 (1H, t, J = 8 Hz), 2.32-2.38 (1H, m), 2.40-2.52 (1H, m), 2.58-2.68 (2H, m), 2.72 (1H, t, J = 3 Hz), 2.72-2.85 (3H, m), 4.82 (1H, t, J = 9 Hz). ^{13}C NMR ($CDCl_3$) δ 26.51, 30.34, 40.12 (2C), 44.83, 45.21, 46.13, 48.59, 51.77, 53.78, 54.58 (2C), 83.30, 175.39; MS (38 eV) *m/z* (relative intensity) 216 (M^+, 100%), 188 (M^+-CO, 25%), 170 (22%), 144 (20%), 129 (22%). HRMS calcd for $C_{14}H_{16}O_2$: 216.1150; found: *m/z* 216.1147.

8,10-Dioxaheptacyclo[7.7.0.0^{2,14}.0^{3,7}.0^{4,13}.0^{5,11}.0^{12,16}]-hexadecane (4)

To a two-necked (50 mL round-bottom) flask fitted with a septum and a drying tube under a nitrogen atmosphere was added **2** (40 mg, 0.117 mmol) and freshly distilled CH_2Cl_2 (10 mL). The solution was cooled in a methanol-dry ice bath (-78 °C), then to it was injected slowly with syringe DIBAL-H (1.0 M, 3.75 mL). The mixture was stirred for 2 h at -78 °C and quenched by the addition of MeOH (1 mL). It was filtered through celite, dried over anhydrous $MgSO_4$, and evacuated *in vacuo*. The crude product was purified by HPLC (hexane/ethyl acetate 9/1 as eluent) to give a white solid (23 mg, 0.106 mmol, 90%). ^1H NMR ($CDCl_3$) δ 1.63 (2H, m), 1.85-1.96 (2H, m), 2.02-2.10 (1H, m), 2.15-2.20 (1H, m), 2.21-2.30 (1H, m), 2.41-2.52 (1H, m), 2.55-2.85 (5H, m), 4.29 (1H, t, J = 9 Hz), 4.41 (1H, t, J = 7 Hz), 5.39 (1H, d, J = 9 Hz). ^{13}C NMR ($CDCl_3$) δ 33.92 (d), 34.03 (d), 34.65 (d), 39.13 (t), 42.11 (t), 45.42 (d), 47.25 (d), 50.90 (d), 53.40 (d), 56.23 (d), 74.50 (d), 76.55 (d), 92.62 (d); MS (36 eV) *m/z* (relative intensity) 216 (M^+, 100), 198 (M^+-H_2O, 8), 188 (M^+-CO, 48), 170 (15).

4-Oxahexacyclo[7.6.0.0^{2,7}.0^{3,14}.0^{6,10}.0^{11,15}]pentadecan-12-en-5-one (5)

A two-necked (100 mL round-bottom) flask containing a magnetic stirring bar fitted with a condenser and a septum was evacuated and flushed with nitrogen three times. To this flask under nitrogen was added **2** (180 mg, 0.526 mmol), followed by freshly distilled benzene (30 mL) and 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) (0.30 mL). The benzene solution was stirred and heated to reflux for 24 h. The resulting mixture was evaporated *in vacuo*, the pale yellow solids were purified by passing through silica-gel flash column chromatograph (hexane/ethyl acetate 3/2 as eluent). Olefin **5** was collected as white solid in 91% yield (102 mg, 0.48 mmol). IR ($CDCl_3$) ν 1732, 1718 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.67-1.72 (1H, d, J = 11 Hz), 1.77-1.83 (1H, d, J = 11 Hz), 2.30 (1H, br), 2.40-2.47 (1H, m), 2.50-2.60 (1H, m), 2.70-2.83 (2H, m), 2.90-2.97 (1H, m), 3.10-3.20 (2H, m), 3.40-3.48 (1H, m), 4.90-4.99 (1H, t, J = 9 Hz), 5.60-5.62 (m, 1H), 5.68-5.70 (1H, m); ^{13}C NMR ($CDCl_3$) δ 38.21 (t), 38.72 (d), 43.05 (d), 45.68 (d), 47.29 (d), 48.82 (d), 54.30 (d), 54.70 (d), 54.77 (d), 58.75 (d), 80.61 (d), 135.58 (2C, d), 175.83 (s); MS (70 eV): *m/z* (rel. int.) 214 (M^+, 100%), 186 (M^+-CO, 38), 132 (22), 158 (16), 142 (10), 141 (10), 129 (25); HRMS calcd for $C_{14}H_{14}O_2$: 214.0993; found: *m/z* 214.0990.

Epoxidation of 5

Olefin **5** (50 mg, 0.23 mmol) was stirred under nitrogen with excess m-chloroperbenzoic acid (m-CPBA) (85%, 190 mg, 0.94 mmol) and $NaHCO_3$ (28 mg) in CH_2Cl_2 (30 mL) at room temperature for 6 h. The mixture was filtered through celite, and the filtrate was washed three times with saturated Na2S03 soln followed by three times with saturated $NaHCO_3$ solution. The solution was dried over anhydrous $MgSO_4$, evaporated *in vacuo*, and the resulting mixture was passed through a silica-gel HPLC (hexane/ethyl acetate 2/3 as eluent). Epoxide **6** was collected as solid in 58% yield (31 mg, 0.14 mmol, 58%). IR ($CDCl_3$) ν 1723 cm^{-1}; ^1H NMR ($CDCl_3$), δ 1.72-1.87 (2H, m), 2.36 (1H, br), 2.58 (1H, t, J = 7.5 Hz), 2.68-3.05 (6H, m), 3.30 (1H, t, J = 8 Hz), 3.44 (1H, s), 3.59 (1H, s), 5.12 (1H, t, J = 8 Hz); ^{13}C NMR ($CDCl_3$), δ 39.36 (t), 39.47 (t), 44.16 (d), 44.78 (d), 46.95 (d), 48.19 (d), 50.02 (d), 51.08 (d), 53.71 (d), 54.63 (d), 56.81 (d), 59.44 (d), 82.25 (d), 175.27 (s, CO); MS (50 eV): *m/z* (rel. int.) 230 (M^+, 13%), 214 (10%), 202 (M^+-CO, 100%), 184 (12%), 174 (86%), 156 (23%); HRMS calcd for $C_{14}H_{14}O_3$: 230.0943, found: *m/z* 230.0939.

3-Acetyl-9-hydroxypentacyclo[5.5.1.0^{2,6}.0^{4,8}.0^{10,13}]tridecan-11-ene (7)

A two-necked (25 mL round-bottom) flask containing a magnetic stirring bar fitted with a condenser and a septum was evacuated and flushed with nitrogen three times. To this flask under nitrogen atmosphere was injected **5** (100 mg, 0.467 mmol) in freshly distilled THF (40 mL) followed by methyl lithium (5% in ether, 40 mL) at -78 °C. The solution was sirred 3 h at -78 °C and was warmed up to room temperature for further 2 h. The reaction was quenched on addition of saturated NH_4Cl (10 mL) and water (30 mL). The resulting mixture was extracted with ether (50 mL × 3), dried over anhydrous $MgSO_4$ and filtered; the filtrate was evaporated *in vacuo*. The resulting oil was purified by passing through silica-gel column chromatograph (hexane/ethyl acetate 3/2 as eluent). Product **7** was collected in 78% yield (85 mg, 0.37 mmol), mp 113-114 °C. IR ($CDCl_3$) ν 3436,

1702, 1210 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47-1.49 (2H, m), 2.08 (3H, s), 2.40-2.45 (2H, m), 2.45-2.65 (3H, m), 2.86 (1H, br), 3.00-3.36 (3H, m), 4.54-4.64 (1H, t, J = 9 Hz), 5.71 (2H, m); ^{13}C NMR ($CDCl_3$) δ 38.36 (q), 38.38 (d), 39.19 (t), 44.68 (d), 46.84 (d), 52.04 (d), 53.37 (d), 54.65 (d), 55.21 (d), 55.42 (d), 55.98 (d), 75.99 (d), 131.51 (d), 131.70 (s), 210.80 (s); MS (30 eV): *m/z* (rel. int.) 230 (M^+, 25%), 204 (100%), 186 (21%), 137 (20%); HRMS calcd for $C_{15}H_{18}O_2$: 230.1307; found: *m/z* 230.1313.

Epoxidation of 7

Olefin **7** (17 mg, 0.074 mmol) was stirred under nitrogen with excess amount of *m*-chloroperbenzoic acid (*m*-CPBA) (85%, 49 mg, 0.24 mmol) and $NaHCO_3$ (8.0 mg) in CH_2Cl_2 (10 mL) at room temperature for 4 h. The mixture was filtered through celite, and the filtrate was washed three times with saturated Na_2SO_3 solution followed by three times with saturated $NaHCO_3$ solution. The solution was dried over anhydrous $MgSO_4$ and evaporated *in vacuo*; the resulting mixture was passed through a silica gel HPLC (hexane/ethyl acetate 2/3 as eluent). Epoxide **8** was collected in 77% yield (14 mg, 0.057 mmol). ^1H NMR ($CDCl_3$) δ 1.31-1.47 (2H, AB pattern, J = 11 Hz), 1.57 (1H, s, -OH), 2.16 (3H, s), 2.47 (2H, m), 2.50-2.57 (1H, m), 2.60-2.65 (2H, m), 2.70-2.80 (1H, m), 2.77-2.88 (1H, q, J = 8 Hz), 3.03-3.13 (2H, m), 3.41 (1H, d, J = 2 Hz), 3.69 (1H, m), 4.68 (1H, t, J = 10 Hz); ^{13}C NMR ($CDCl_3$) δ 28.35, 37.97, 40.03, 41.95, 48.13, 49.26, 50.11, 51.52, 51.63, 52.66, 54.14, 59.03, 60.59, 73.57, 209.6; MS (46 eV): *m/z* (rel. int.) 246 (M^+, 100%), 228 (80%), 203 (80%), 201 (78%), 198 (65%), 187 (45%), 185 (75%).

3-Acetyloxy-10-acetyl-4-oxaheptacyclo[6.5.1.$0^{2,11}$.$0^{5,14}$.$0^{9,13}$]tetradecan-6-ene (10) and 3-Acetyloxy-10-iodo-4-oxaheptacyclo[6.5.1.$0^{2,11}$.$0^{5,14}$.$0^{9,13}$]tetradecan-6-ene (12)

To a two-necked (100 mL round-bottom) flask fitted with a condenser was added $Pb(OAc)_4$ (940 mg, 2.12 mmol) under a nitrogen atmosphere. The flask was evacuated and purged with nitrogen for 15 min. Compound **7** (50 mg, 0.22 mmol) and I_2 (240 mg, 0.94 mmol) were dissolved in benzene (50 mL), and the solution was injected through a syringe into the flask. The mixture was stirred with a magnetic bar at 0 °C for 2 h. It was filtered and extracted with ether; the ether portions were combined and washed with saturated $Na_2S_2O_3$ (50 mL × 3) followed by distilled water (50 mL × 3) and saturated $NaHCO_3$ (50 mL × 3). The solvent was dried over anhydrous $MgSO_4$ and evaporated *in vacuo*, and the resulting mixture was passed through a silica gel HPLC (hexane/ethyl acetate 3/2 as eluent). Product **10** was collected in 70% yield (44 mg, 0.153 mmol) along with a minor amount of **12** (11 mg, 0.030 mmol, 13%). Physical data of **10** ^1H NMR ($CDCl_3$, 200 MHz) δ 1.27 (1H, d, J= 11 Hz), 1.50 (1H, d, J = 11 Hz), 1.76 (1H, dt, J = 3, 11 Hz), 2.03 (3H, s), 2.06 (3H, s), 2.33-2.38 (1H, dt, J = 5, 10 Hz), 2.41 (1H, br), 2.45-2.48 (1H, q, J = 9 Hz), 2.71-2.78 (2H, m), 2.87 (1H, m), 3.18-3.28 (1H, m), 4.54 (1H, dd, J= 2, 8 Hz), 5.82-5.87 (1H, m), 5.94-5.98 (1H, dd, J = 3, 6 Hz), 6.12 (1H, d, J = 2 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.13 (q), 28.46 (q), 32.64 (d), 36.64 (t), 40.35 (d), 40.43 (d), 41.75 (d), 44.81 (d), 50.92 (d), 54.80 (d), 55.10 (d), 73.63 (d), 92.48 (d), 133.30 (d), 136.77 (s), 169.87 (s), 209.58 (s). Physical data of **12**: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.54-1.59 (1H, d, J = 11 Hz), 1.81-1.89 (1H, td, J = 3, 11 Hz), 2.06 (3H, s), 2.21-2.26 (1H, d, J = 11 Hz), 2.27-2.45 (1H, dt, J = 5, 10 Hz), 2.50 (1H, br), 2.64-2.76 (1H, q, J = 8 Hz), 2.72-2.82 (1H, m), 2.81-2.88 (1H, m), 2.98-3.06 (1H, tm, J = 7 Hz), 4.32 (1H, t, J = 2 HZ), 4.55-4.60 (1H, dd, J = 2, 8 Hz), 5.84-5.89 (1H, m), 6.04-6.09 (1H, dd, J = 3, 6 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.13 (q), 26.62 (d), 32.11 (d), 38.23 (t), 40.89 (d), 41.24 (d), 48.90 (d), 55.52 (d), 55.80 (d), 56.66 (d), 74.00 (d), 91.84 (d), 133.48 (d), 135.71 (d), 169.75 (s).

6-Oxahexacyclo[7.6.0.0^{2,7}.0^{3,14}.0^{4,12}.0^{11,15}]pentadecan-5,10-dione (16), 8-Oxahexacyclo[7.5.1.0^{2,6}.0^{3,13}.0^{5,12}.0^{10,14}]pentadecan-7,11-dione (18) and 14-Hydroxy-4-oxapentacyclo[7.6.0.0^{2,7}.0^{6,10}.0^{11,15}]pentadecan-12-en-3,5-dione (21)

To a flask (150 mL round-bottomed) containing ceric ammonium nitrate (950 mg, 1.73 mmol) in distilled water (15 mL) was added with stirring a solution of dikeone **13** (106 mg, 0.49 mmol) in CH_3CN (2 mL). The mixture was stirred at room temperature until all diketone was consumed as monitored by TLC. The reaction was quenched on addition of distilled water, and extracted with CH_2Cl_2 (2 × 25 mL). The organic layers were combined, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The products were purified by passing through silica gel HPLC (ethyl acetate/hexane 8/1 as eluent). The lactones **16** (56 mg, 0.24 mmol, 49%), **18** (6 mg, 0.026 mmol, 5%) and **21** (45 mg, 0.18 mmol, 37%) were collected as white solids. Physical data of **16**: mp 260.5-261.5 °C; IR ($CHCl_3$) ν 1728 (s) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.70-1.72 (2H, s), 2.10-2.21 (1H, m), 2.50-2.58 (2H, m), 2.65-2.90 (2H, m), 2.95-2.98 (3H, m), 3.02-3.11 (2H, m), 3.19-3.26 (1H, m), 4.94-5.01 (1H, dd, J = 6, 8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.51 (d), 42.11 (d), 42.20 (d), 42.42 (t), 43.05 (t), 44.16 (d), 45.59 (d), 52.50 (d), 55.11 (d), 55.18 (2C, d), 83.97 (d), 170.54 (s), 220.66 (s); MS (70 eV) *m/z* (rel. int.) 230 (M^+, 100%), 202

(M^+-CO, 48%), 201 (32%), 186 (M^+-CO_2, 16%), 184 (12%), 174 (12%), 173 (16%); HRMS calc. for $C_{14}H_{14}O_3$: 230.0943; found: *m/z* 230.0946. Physical data of **18**: IR ($CHCl_3$) ν 1730, 1705 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.58-1.73 (2H, AB pattern, J = 11 Hz), 2.02-2.07 (2H, m), 2.40 (1H, m), 2.58-2.63 (1H, m), 2.62-2.69 (1H, m), 2.78-2.87 (3H, m), 3.23-3.30 (3H, m), 4.92 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.72 (t), 42.44 (2C, dt), 43.72 (d), 45.26 (d), 49.48 (d), 50.70 (d), 52.62 (d), 53.08 (d), 57.07 (d), 59.33 (d), 80.87 (d), 173.75 (s), 215.34 (s); MS (70 eV) *m/z* (rel. int.) 230 (M^+, 62%), 202 (M^+-CO, 69%), 184 (M^+-CO-H_2O, 13%), 174 (10%), 157 (52%), 156 (55%); HRMS calcd for $C_{14}H_{14}O_3$: 230.0943; found: 230.0937. Physical data of **21**: mp 181.5-182.5 °C; IR ($CHCl_3$) ν 3360, 3300 (br), 1793, 1751 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.60-1.64 (2H, AB pattern), 1.79 (1H, br, -OH), 2.57 (1H, s), 2.68-2.69 (1H, d, J = 3 Hz), 2.75-3.00 (5H, m), 3.70 (1H, m), 4.91 (1H, s), 5.73-5.84 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.28 (t), 39.63 (d), 42.20 (d), 42.33 (d), 42.95 (d), 44.01 (d), 52.76 (d), 53.94 (d), 55.92 (d), 75.10 (d), 133.86 (d), 136.62 (d), 168.92 (d), 169.69 (d); MS (70 eV) *m/z* (rel. int.) 246 (M^+, 5.6%), 228 (M^+-H_2O, 5.7%), 218 (M^+-CO, 21%), 200 (M^+-CO-H_2O, 79%), 172 (M^+-2CO-H_2O, 100%), 155 (56%); Anal. calcd for $C_{14}H_{14}O_4$: C 68.28, H 5.73; found: C 68.00, H 5.73.

An alternative preparation of **16** using *m*-CPBA gave a more selective result. Diketone **13** (76 mg, 0.355 mmol) and a little toluenesulfonic acid (2 mg) was dissolved in freshly distilled benzene (15 mL) in a flask (round-bottom), to the stirred solution was added slowly excess *m*-CPBA (85%, 500 mg, 2.4 mmol). The reaction was monitored by TLC until starting materials were all consumed, and then worked-up as previously described. Compound **16** was isolated in 67% yield (55 mg, 0.24 mmol). Its spectral features are identical to those of the material collected from CAN oxidation.

14-Nitrohexacyclo[6.6.0.0^{2,6}.0^{3,13}.0^{4,11}.0^{5,9}]tetradecan-10-one (23a)

Oxidation with ceric ammonium nitrate was performed as previously described. Organic nitrate **23a** was purified as a colorless solid, mp 110-111 °C; IR ($CHCl_3$) ν 1724 (s), 1629 (s), 1282 (s), 1216 (s) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.72 (2H, s), 1.99-2.14 (1H, td, J = 7, 13 Hz), 2.40-2.48 (1H, m), 2.54-2.70 (5H, m), 2.79-2.96 (3H, m), 3.07-3.21 (2H, m), 4.75 (1H, d, J = 2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 42.36 (t), 42.76 (d), 46.23 (t), 47.75 (d), 51.61 (d), 51.95 (d), 53.94 (d), 54.71 (d), 55.25 (d), 56.18 (d), 56.58 (d), 57.08 (d), 92.55 (d), 226.69 (s); Anal. calcd for $C_{14}H_{15}NO_4$: C 64.61, H 5.42, N 5.10; found: C 64.81, H 5.65, N 5.10.

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Key Words

Heptacyclotetradecane; Hypoiodite oxidation; Ceric oxidation; Cage compounds; Polyquinanes.

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