Orthocyclophanes. 3.[1,2] Ketonands, Novel Ketonic Crowns of Polyoxo[1_n]orthocyclophane Constitution

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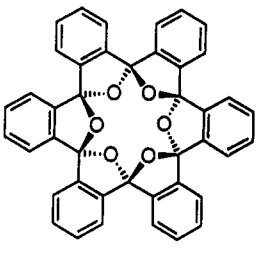
Synthetic studies of a new family of novel ketonic macrocycles are reported. Exhaustive oxidation of all of the methylenes in odd-numbered [1_n]orthocyclophanes ([1_n]OCPs) resulted in the polyoxo derivatives of a cyclopolyorthobenzoyl or polyoxo[1_n]orthocyclophane constitution. This new class of ketonic crowns is referred to as [1_n]orthocyclophanepolyones and includes [1_5]orthocyclophanepentaone, [1_7]orthocyclophaneheptaone, and [1_9]orthocyclophanenonaone. We suggest the generic name "*ketonands*" for these ketonic crowns. Structures of ketonands were confirmed by spectral and X-ray crystallographic analyses.

Introduction

The chemistry of [1_n]orthocyclophane ([1_n]OCP) is of current interest in connection with the preparation of new macrocyclic compounds.[1,2] Synthetic methods leading to [1_n]OCPs have broad applications in organic synthesis, for example, in the potential relationship between indanyl systems and C-60 (Buckminsterfullerene).[3] Systematic studies of [1_n]OCPs have shown that there are remarkable differences between the properties of odd- and even-numbered [1_n]OCPs. In our previous work, we reported that exhaustive oxidation of all of the methylenes in even-numbered [1_n]OCPs does not give the corresponding polyoxo derivative, but rather generates novel star-shaped crown ethers, such as [1_6]starand (1)[2] and [1_8]starand (2).[2,4] In contrast, the present paper describes the properties of odd-numbered [1_n]OCPs, in which case exhaustive oxidation of all methylenes generate supramolecular ketonic macrocycles.



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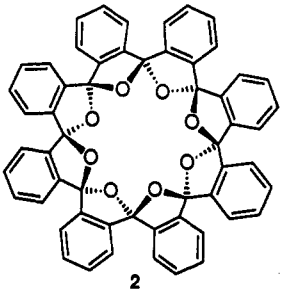

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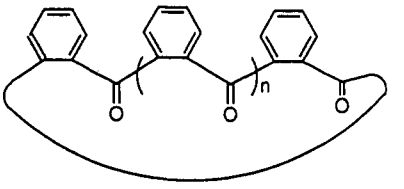
In spite of extensive studies of the synthesis and inclusion behavior of various crown compounds (crown ethers, cryptands, spherands, cavitands, calixarenes, cyclophanes, cryptophanes, and so forth) during the past two decades,[5] investigations focused on ketonic macrocycles have only recently begun. Only a few cyclic oligoketones (oxocrowns) have been reported, such as macrocyclic trioxo[3.3.3]paracylophane[6] and 1,3,9,11,17,19-hexaoxocyclotetracosane.[7] The goal of the present research was the synthesis of a new class of ketonic macrocycles by the oxidation of all methylenes in odd-numbered [1_n]OCPs, to provide oxocrowns 3 of a cyclopolyorthobenzoyl constitution. Herein, we would like to suggest a generic name, "*ketonands*", for these ligands containing ketonic functions.



n = 1,2,3...

3

Results and Discussion

During the past decade, we have devoted considerable effort to the synthesis of ketonands. We first investigated the synthesis of every size of [1_n]OCP cycle and then studied their oxidation to the corresponding polyoxo derivatives, knowing that methylenes situated between two aromatic nuclei are labile to oxidation. The synthesis of the [1_n]OCP cycle had not been fully investigated,

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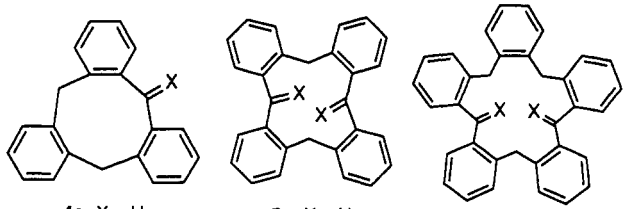
although the methoxy derivatives[8] of [1_3]- to [1_6]-OCPs were reported in the separation of the mixture of acid-catalyzed cyclization products of veratryl alcohol. Mediocycle **4a**[9] was the only known parent hydrocarbon of the [1_n]OCP type, until we reported the synthesis of [1_4]-OCP (**5a**) and [1_5]OCP (**6a**).[1]



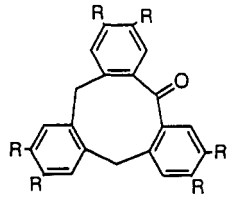
4a: X = H_2
4b: X = O

5a: X = H_2
5b: X = O

6a: X = H_2
6b: X = O

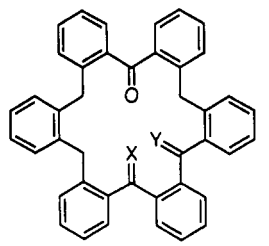
In this work, we developed synthetic routes to higher members of the odd-numbered [1_n]OCP series ($n \geq 7$) and then studied the oxidation of their benzylic methylenes. Since the oxidation products of [1_n]OCPs vary depending upon the reaction conditions,[2] various oxo derivatives, such as mono-, di-, and trioxo[1_n]OCPs, can exist. Herein, we propose the class name [1_n]orthocyclophanones for the mono-oxo derivative of [1_n]OCPs. The term [1_n]orthocyclophanone bears resemblance to the term cycloalkanone, since the two derive from the oxidation of [1_n]orthocyclophane and cycloalkane, respectively. Thus, the term [1_n]orthocyclophanepolyone applies to the polyoxo derivatives of [1_n]OCPs, such as [1_n]OCP-1,2-dione, [1_n]OCP-1,2,3-trione, and so forth, the numbers denoting the positions of ketonic functions in the polyoxo[1_n]OCPs.

From the literature, [1_3]orthocyclophanes are known to be oxidized only to monoketones **4b**[10] and **7a**;[11] further oxidation of **7a** does not give the corresponding triketone, but yields a rearranged lactone **7b**.[12] In our work,[2] we were unable to obtain ketonands from the oxidation of even-numbered [1_n]OCPs. Partial oxidation of both [1_6]-OCP-1,4-dione (**8a**)[4] and [1_6]OCP-1,3-dione (**8b**)[2] gave [1_6]-OCP-pentaone (**8c**), and exhaustive oxidation of **8c** generated an isomerized cyclopolyketal, [1_6]starand (**1**), instead of the corresponding unstable hexaone **8d**. Exhaustive oxidation of [1_8]OCP-1,3-dione also gave the isomerization product, [1_8]starand (**2**).[2] We presume this occurs via the corresponding polyketones, [1_6]ketonand (**8d**) and [1_8]ketonand, respectively. Oxidation of [1_4]-orthocyclophane-1,3-dione (**5b**)[1] gave neither the corresponding starand nor ketonand. Examination of molecular models suggests that the cycle **5** is not large enough to accommodate more than two carbonyl functions and is conformationally unable to form a "starand". A computer-generated drawing of the lowest energy structure of [1_4]-starand suggests that the distance between the oxygen

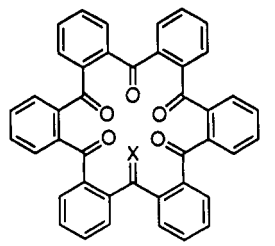


R = OCH_3
7a

R = OCH_3
7b



8a; X = O, Y = H_2
8b; X = H_2, Y = O



8c; X = H_2
8d; X = O

atoms and the center of the cavity, 1.14 Å, is shorter than the van der Waals radius of an oxygen atom, 1.4 Å.[2]

The first ketonand was prepared by modification of [1_5]-OCP (Scheme 1). Oxidation of [1_5]OCP-1,3-diol (**9**) with PCC gave [1_5]OCP-1,3-dione (**6b**),[1] which upon further oxidation with ceric ammonium nitrate (CAN) in hot acetic acid provided the corresponding pentaoxo derivative [1_5]-OCP-pentaone, or [1_5]ketonand **10**, as crystalline needles, mp 350 °C dec, in moderate yield. No other side product was produced.

In contrast to hexaketone **8d**, which presumably isomerizes spontaneously to bicyclic polyketal **1**,[4] the carbonyls in ketonand **10** were retained without internal ketalization. This can be interpreted to mean that the conformational disadvantage dictates that cyclopentaketone **10** cannot isomerize to the corresponding cyclic polyketal of the up-down-up conformation, as in the case of **8d** to **1**, since **10** has an odd number of (five) oxygen atoms.

The structure of ketonand **10** was assigned by spectral analysis. The IR absorption at 1657 cm^{-1} and the ^{13}C NMR resonance at δ 197.57 confirmed the presence of carbonyl functions. Exact mass M^+ 520.1349, obtained by HRMS, agreed with the calculated mass for $C_{35}H_{20}O_5$ (M 520.1311). The simplicity of the ^{13}C NMR spectrum, showing four signals at δ 197.57, 139.34, 130.88, and 130.80, suggested an inherent high degree of symmetry in the molecule in solution.

We wished to determine the conformation of [1_5]ketonand **10** in the crystal form. When recrystallized from CH_2Cl_2, crystals of **10** in air spontaneously decomposed to a powder, however upon addition of some methanol to a solution of **10** in CH_2Cl_2, followed by careful evaporation of the solvent, rather stable crystals were obtained as beautiful needles. However, these crystals did not contain MeOH molecules (^1H NMR and X-ray).

An X-ray analysis of **10** showed a twisted (or puckered) conformation. An ORTEP diagram of the molecular geometry is shown in Figure 1. There is little regularity in the bond angles in the crystal structure. The simplicity of the ^1H and ^{13}C NMR spectra reveals a high degree of symmetry of the molecule in solution, indicating a flexible conformation for **10** rather than a rigid conformation with a preorganized cavity.

For the synthesis of the higher members of the [1_n]-OCP series, we conducted a systematic study of the acid-

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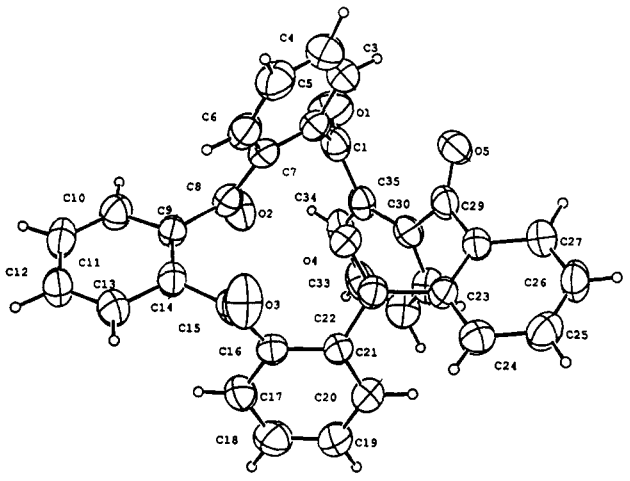
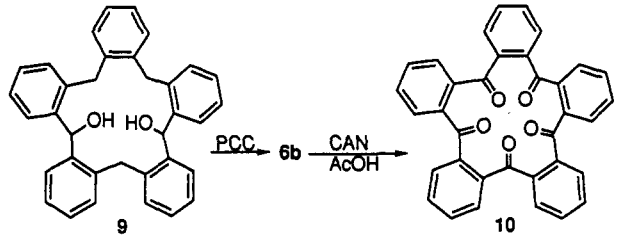


Figure 1. ORTEP Diagram of [1$_5$]ketonand **10**. There is little regularity in the bond angles. In view of the NMR spectral data, this structure has a flexible conformation in solution and so gives simple ^{1}H and ^{13}C NMR patterns.

Scheme 1



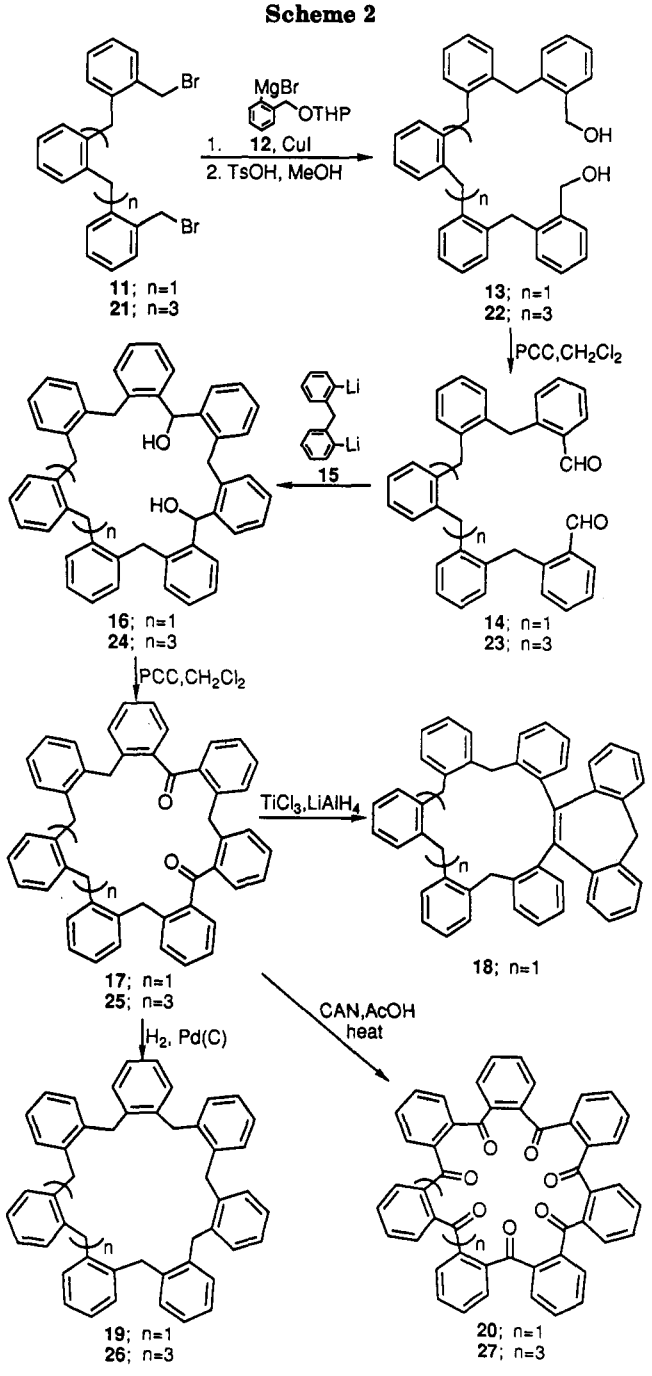
catalyzed Friedel–Craft cycloalkylation of various *o*-benzylbenzylic alcohols (*o*-BBAs), demonstrating regioselectivity in the intramolecular cyclization. Consistent with the regioselectivity rule,[13] higher representatives of [1$_n$]OCP could not be prepared by acid-catalyzed cyclization of *o*-BBA, in a one-pot reaction, though the lower homolog **4a**[9a] could be easily obtained in moderate yield.

Thus, [1$_7$]OCP cycle was prepared by a synthetic route outlined in Scheme 2. Reaction of dibromide **11**,[14] in the presence of CuI, with 2 molar equiv of Grignard reagent **12**, followed by removal of the THP protecting groups from the bis-condensation product gave an α,ω-benzylbenzylic diol **13**. Subsequent oxidation of **13** with PCC in CH_2Cl_2 provided the corresponding dialdehyde **14**.

Treatment of bis(2-bromophenyl)methane[1] with *n*-butyllithium to give dilithio reagent **15**, followed by reaction with **14** gave cyclic diol **16**, which was then oxidized with PCC to [1$_7$]orthocyclophane-1,3-dione (**17**). Treatment of **17** with McMurry reagent,[15] $TiCl_3/LiAlH_4$, gave the intramolecular reductive olefination product **18**, consistent with previous reports.[1,2] The aliphatic ^{1}H NMR signals of the bis-cyclophane **18** appear to consist of three overlapping AB quartets and two singlets, displaying 13 resonance peaks. There are at least 24 sp^2-carbon lines in the ^{13}C NMR spectrum of **18**, where a flat structure would have only 22. It is evident from the NMR data that **18** is nonplanar and conformationally constrained.

Pd-catalyzed hydrogenation of **17** afforded [1$_7$]OCP **19**, whose ^{1}H NMR spectrum showed resonances at δ 7.16–

Scheme 2



6.85 for aromatic and δ 3.56 for benzylic protons. The ^{13}C NMR spectrum possessed four simple signals at δ 138.29, 129.86, 126.35 and 36.60, denoting a high degree of symmetry of the molecule in solution. The exact mass M^+ 630.3283 agreed with the theoretical mass calculated for $C_{49}H_{42}$ (M 630.3287). Hydrocarbon **19** was soluble in conventional solvents in contrast to the insoluble lower homolog [1$_6$]OCP, but consistent with the reasonable solubility of the odd-numbered [1$_5$]OCP (**6a**).[1] The solubility difference can presumably be accounted for by the higher degree of molecular symmetry of even-numbered [1$_n$]OCPs than odd-numbered [1$_n$]OCPs; the higher the molecular symmetry, the closer the packing.

[1$_7$]Ketonand **20** was obtained by exhaustive oxidation of cyclic dione **17** with CAN in hot acetic acid. As we would predict, the seven carbonyls in **20** were stable with no isomerization (internal ketalization) to a cyclic polyketal. The IR absorption of **20** at 1665 cm^{-1} and the ^{13}C

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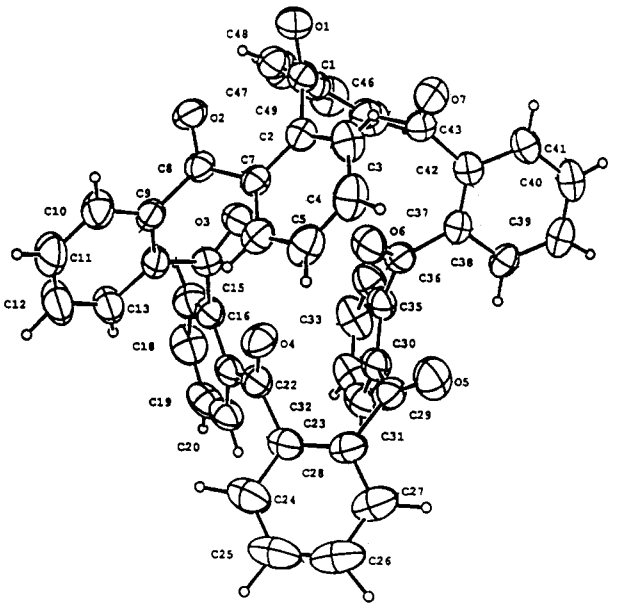

Figure 2. ORTEP Diagram of [1_7]ketonand **20**. There is little regularity in the bond angles. In view of the NMR spectrum, this structure has a flexible conformation in solution resulting in simple ^1H and ^{13}C NMR patterns.

NMR resonance at δ 195.44 revealed the presence of the carbonyl function. A high degree of symmetry of **20** in solution was exhibited (^{13}C NMR) by the presence of only four signals at δ 195.44, 138.46, 130.06, and 129.91. The exact mass (M^+ 728.1848) agreed with the theoretical value calculated for $C_{49}H_{28}O_7$ (M 728.1835). Ketonand **20** does not dissolve in MeOH, but easily dissolves in CH_2Cl_2.

For an X-ray structural analysis, crystals of ketonand **20** were grown carefully by adding some MeOH to a solution of **20** in CH_2Cl_2, followed by slow evaporation of the solvent to give crystals that are stable in air. These crystals contain MeOH molecules in the crystal lattice in a 1:1 ratio of **20** and MeOH, which was determined from the ^1H NMR spectrum and X-ray analysis. This is in contrast to crystals of the lower homolog **10**, which did not contain MeOH molecules despite being grown under the same conditions. This fact presumably demonstrates a stronger binding affinity of **20** than **10** toward MeOH molecules.

X-ray analysis disclosed that **20** has a twisted (or puckered) structure like its lower homolog **10**. An ORTEP diagram of **20** is shown in Figure 2 and a stereoview in Figure 3. In the crystal, it appears that there is little regularity in the bond angles, as is the case with **10**. In spite of the X-ray structural analysis, which shows a twisted (or puckered) conformation, ketonand **20** must have a flexible conformation in solution, since the ^1H and ^{13}C NMR spectra show very simple patterns due to a high degree of symmetry.

An attempt to synthesize a larger [1_n]OCP cycle is also illustrated in Scheme 2. Dibromide **21** was prepared by treating diol **13** with HBr gas in CH_2Cl_2. Reaction of **21** with Grignard **12** in the presence of CuI, followed by removal of the THP protecting groups in the bis-coupling product gave α,ω-benzylic diol **22**, which was oxidized with PCC to dialdehyde **23**. Treatment of **23** with dilithio reagent **15** gave diol **24**, and subsequent oxidation with PCC provided [1_9]orthocyclophane-1,3-dione (**25**). We were unable to obtain [1_9]OCP **26** by Pd-catalyzed reduction of diketone **25**.

Exhaustive oxidation of dione **25** by heating with CAN in hot AcOH generated [1_9]ketonand **27**. The presence of nine ketonic functions in **27** and its lack of isomerization to a cyclic polyketal is consistent with the properties of analogs **10** and **20**. The IR spectrum of **27** showed a carbonyl absorption at 1670 cm^{-1}, and the ^1H NMR (200 MHz) spectrum at 25 °C showed a singlet at δ 7.26 for the aromatic protons.

At 50 °C, the ^{13}C NMR spectrum of **27** showed one carbonyl signal at δ 195.75 and three at δ 138.69, 130.27, and 129.90 for aromatic carbon atoms, which is consistent with the spectra of lower analogs **10** and **20** and reveals a high degree of symmetry due to flexibility. At 25 °C, the ^{13}C NMR spectrum included two broadened signals centered at δ 138.7 and 129.9 for aromatic carbons. At much lower temperature (*e.g.*, −10 and −30 °C), these two peaks further broadened and then split into many resonances. Figure 4 demonstrates the temperature-dependence of the flexibility of ketonand **27** in solution. The ^{13}C NMR patterns of ketonands **10**, **20**, and **27** at 25 °C reveal that the flexibility of ketonands decreases as the molecular size increases.

In contrast to lower homologs **10** and **20**, the higher ketonand **27** did not show a sharp melting point, but decomposed slowly at its melting point. FAB mass spectrometry of **27** showed *m/z* 959 as a parent peak, indicating the formation of the sodiated species [M·Na^+]. The HRMS (FAB) spectrum showed an exact mass of M^+ 937.3172, which agreed with the mass of the protonated species (M·H^+) calculated for ($C_{63}H_{36}O_9$ + H). Given the X-ray and NMR results of the lower homologs **10** and **20**, ketonand **27** might also have a twist conformation in its crystal form and a flexible conformation in solution, especially at high temperature.

Ketonands **10**, **20**, and **27** are macrocyclic oxocrowns, and show characteristic binding properties for ions or neutral molecules. Qualitative experiments showed that their solutions in organic solvents have remarkable solubility for metal salts, such as alkali iodide, thus demonstrating their binding property toward metal ions. The ^1H NMR spectra of the complexes showed either changes in chemical shifts or splitting of resonances. The ^{13}C NMR spectra of the complexes also revealed chemical shift changes. For example, the singlet at δ 7.38 pertaining to the aromatic protons of **20** splitted into many peaks over a range of δ 7.54–7.34 when **20** was complexed with NaI. In the ^{13}C NMR spectrum of **20**, the ketonic carbon resonance (δ 195.44) shifted to δ 197.02 and the aromatic carbon resonances (δ 138.46, 130.06, and 129.91) shifted to δ 137.64, 131.22, and 130.19, respectively, when **20** was complexed with NaI. In some cases (*e.g.*, **10**), the metal complex precipitated from the solution, depending on the size of the metal ion (*e.g*, Na^+). A more detailed study for complexation of ketonands will be reported in the future.

Although a quantitative study of complexation has yet to be done, we can hypothesize that these ketonands will show inclusion behavior for a variety of chemical species, since they have either negative ligand oxygen or positive carbonyl carbon atoms. Moreover, in light of the flexibility of the molecules in solution (NMR), ketonands are expected to vary in their complexation behavior toward various hosts.

In conclusion, novel macrocyclic oxocrowns of the cyclopolyorthobenzoyl structure type have been prepared for the first time. Exhaustive oxidation of the methylenes

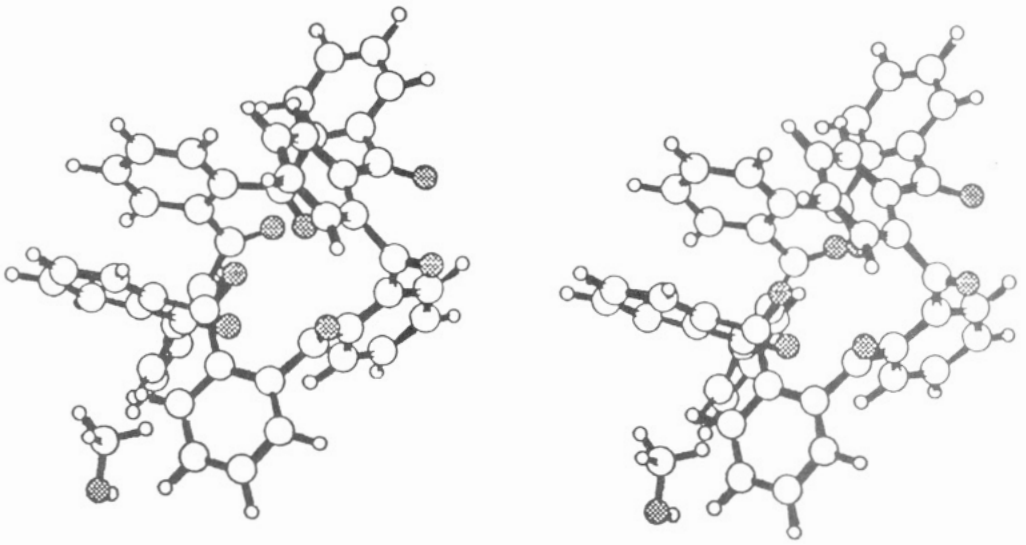

Figure 3. Stereoview of [1_7]ketonand **20**. The crystal grown in CH_2Cl_2/MeOH contains a 1:1 ratio of **20** and MeOH.

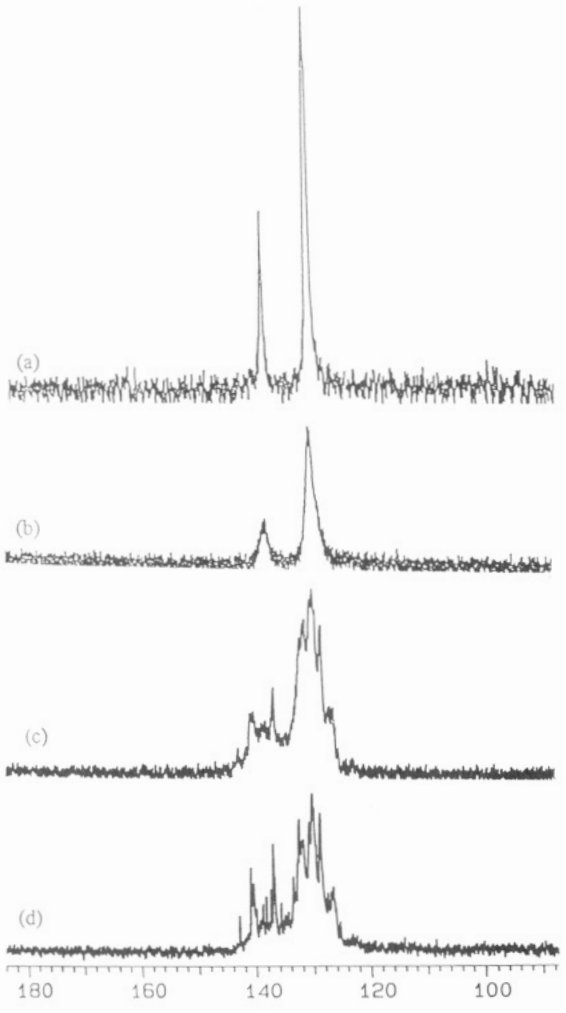

Figure 4. ^{13}C NMR spectra of [1_9]ketonand **27** at (a) 50 °C, (b) 25 °C, (c) −10 °C, and (d) −30 °C. The rigid conformation at low temperature becomes flexible as the temperature increases.

in odd-numbered [1_n]OCPs generated the corresponding oxocrowns, which are referred to as ketonands. The [1_5]-, [1_7]-, and [1_9]ketonands were prepared. The preparation of much higher homologs of [1_n]ketonands ($n \geq 11$) can also be expected from the oxidation of even-numbered [1_n]OCPs, since they can adopt a puckered conformation rather than a sterically-strained planar structure. Although the X-ray analysis of the prepared ketonands revealed puckered conformation without symmetry, a ^{13}C NMR study demonstrated that ketonands become flexible in solution as the temperature increases, to the point of having a have high degree of symmetry. The ketonands will be studied to fully ascertain their binding properties.

Experimental Section

General. All anhydrous reactions were conducted with precautions for rigorous exclusion of air and moisture. Melting points were measured on an Electrothermal Melting Point Apparatus and were uncorrected. Diethyl ether and tetrahydrofuran (THF) were purified by refluxing for a few hours with sodium benzophenone ketyl under nitrogen, followed by distilling prior to use. Dichloromethane (CH_2Cl_2) was dried by distilling over CaH_2. Flash chromatography was conducted using silica gel 60 (E. M. Merck, 0.040 mm, 230–400 mesh ASTM). IR spectra were obtained on a Perkin-Elmer Model 782 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Brucker AC-80 and/or Varian VXR-200s NMR spectrometer using $CDCl_3$ as solvent except where noted, and tetramethylsilane as internal reference. All chemical shifts (δ) are reported in parts per million and J-values are in hertz. Mass spectra were recorded on a VG-7025 with normal geometry. Chemicals were purified, when necessary, according to the reported procedure.[16]

X-ray Crystallography.[17] Data were collected at 23 ± 1 °C on an Enraf-Nonius CAD4 diffractometer using graphite-monochromated Mo Kα radiation (γ = 0.71073 Å). The crystal structure was solved and refined using the Enraf-Nonius supplied MolEN package. Direct methods (SIR) provided the complete non-hydrogen atom structures. All the hydrogen atoms except for the solvent methyl hydrogen of [1_7]ketonand **20** were located from the difference Fourier maps and refined with isotropic thermal parameters. The structures were refined by full-matrix least-squares method employing anisotropic thermal parameters for non-hydrogen atoms.

2,9,16,23,30-Pentaoxohexacyclo[29.4.0.0^{3,8}.0^{10,15}.0^{17,22}.0^{24,29}]-pentatriaconta-1(31),3(8),4,6,10(15),11,13,17(22),18,20,24(29),-25,27,32,34-pentadecaene; [1_5]Ketonand (10). To a solution of dione **6b**[1] (320 mg, 670 μmol) in AcOH (70 mL) was added ceric ammonium nitrate (CAN) (4.0 g, 7.3 mmol), and the mixture was heated at 80 °C for 1 d. A small amount of excess oxidant

(16) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: Oxford, 1988.

(17) The authors have deposited atomic coordinates for **10** and **20** with the Cambridge Crystallographic Data Centre. The coordinate can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Table 1. Crystallographic Data[a] for [1₅]ketonand 10

formula	$C_{35}H_{20}O_5$
formular weight	520.35
a, Å	14.636(4)
b, Å	8.903(2)
c, Å	19.238(6)
β, deg	91.07(2)
V, Å^3	2506.4
Z	4
space grp	$P2_1/c$
ρ, g/cm^3	1.38
μ, cm^{-1}	0.9
R (F_o), %	4.6
R_w (F_o^2), %	4.7

[a] T = 298 K, λ = 0.71073 Å (Mo Kα).

total 1 g in portions) was supplied during the oxidation. The reaction mixture was poured into water (300 mL) and extracted with CH_2Cl_2. The organic layer was washed successively with water and aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated to give the crude product, which was chromatographed (SiO_2, CH_2Cl_2/Et_2O; 1:1, v/v; $R_f \sim 0.2$) to afford 230 mg (66%) of [1₅]-ketonand **10** as crystalline needles: mp 350 °C dec; IR (KBr) 1657, 1591, and 763 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.47 (s, 20 H); ^{13}C NMR (CD_2Cl_2, 50.29 MHz) δ 197.57, 139.34, 130.88, 130.80; EIMS m/z (rel inten) 520 (M$^+$, 100), 504 (18.3), 372 (16.3), and 296 (24.7); HRMS calcd for $C_{35}H_{20}O_5$ M 520.1311, found M$^+$ 520.1349.

X-ray Analysis of 10. Crystals were grown by dissolving powdery **10** in CH_2Cl_2, followed by adding some MeOH, and carefully evaporating the solvent to afford beautiful needles. The ^{1}H NMR spectrum obtained by using this crystal did not give proton resonance for MeOH. The crystallographic data of **10** are presented in Table 1.

1,2-Bis[2-[2-(hydroxymethyl)benzyl]benzyl]benzene (13). Grignard reagent **12** was prepared by adding dropwise with stirring a solution of 2-bromobenzyl tetrahydropyran-2-yl (THP) ether (3.17 g, 11.7 mmol) in THF (50 mL) to Mg turnings (20 mmol) immersed in THF (20 mL) under nitrogen, followed by refluxing for 3 h. To a stirred solution of dibromide **11**[14] (4.00 g, 9.0 mmol) in THF (50 mL) containing CuI (0.4 g) was added Grignard **12** at 0 °C, followed by stirring the mixture overnight at 25 °C. The reaction was quenched with aqueous NH_4Cl (50 mL) and the solvent was removed *in vacuo*. The aqueous layer was extracted with CH_2Cl_2, the organic layer was washed successively with aqueous $NaHCO_3$ and water, and evaporated *in vacuo* to give a crude bis-coupling product as an oil, which was then used directly for removal of the THP protecting group.

A solution of the crude product and *p*-toluenesulfonic acid (*p*-TsOH) (1.0 g) in MeOH (60 mL) was refluxed for 6 h, followed by cooling to 25 °C. The mixture was treated with saturated aqueous $NaHCO_3$ (10 mL), and the solvent was evaporated *in vacuo* to give a crystalline solid, which was insoluble in conventional organic solvents. The crude product was thoroughly washed successively with distilled water and diethyl ether to give 3.20 g (71%) of pure **13** as a powder: mp 174–175 °C; IR (KBr) 3500–3100, 1600, 1450, 1050, and 740 cm^{-1}; ^{1}H NMR (80 MHz; $CDCl_3$ + DMSO-d_6, 3:1, v/v) δ 7.48–6.72 (m, 20 H), 4.50 (d, 4 H), 3.98 (s, 4 H), 3.90 (s, 4 H) and 2.64 (s, 2 H); EIMS m/z (rel inten) 480 (M$^+$ – H_2O, 1.2), 462 (M$^+$ – 2 H_2O, 49.8), 267 (38.6), 192 (33.8) and 179 (100).

1,2-Bis[2-(2-formylbenzyl)benzyl]benzene (14). A mixture of **13** (3.3 g, 6.6 mmol), Celite (6 g), and PCC (6 g) in CH_2Cl_2 (50 mL) was stirred for 3 h. The mixture was filtered, the filtrate was evaporated *in vacuo*, and the crude product was chromatographed (SiO_2, CH_2Cl_2), followed by recrystallization from hexane/ether (1:1, v/v) to give 2.8 g (85%) of crystalline **14**: mp 94–95 °C; IR (KBr) 1690, 1595, 1450, and 750 cm^{-1}; ^{1}H NMR (80 MHz) δ 10.0 (s, 2 H), 7.87–6.79 (m, 20 H), 4.24 (s, 4 H), and 3.83 (s, 4 H); ^{13}C NMR (50.29 MHz) δ 192.0, 142.2, 138.3, 138.1, 138.0, 134.0, 133.6, 131.9, 130.8, 129.7, 129.6, 129.53, 129.46, 126.7, 126.61, 126.58, 36.2, and 35.1; EIMS m/z (rel inten) 476 (M$^+$ – H_2O, 100), 458 (26.7), 280 (29.2), 195 (55.8), and 179 (63.9); HRMS calcd for $C_{36}H_{28}O$ (M – H_2O) 476.2140, found (M$^+$ – H_2O) 476.2208.

[1₇]Orthocyclophane-1,3-dione (17). Dilithio reagent **15** was prepared by dropwise addition of *n*-BuLi (2.5 M, 7.5 mL, 18.8 mmol) under nitrogen to a stirred solution of bis(2-bromophenyl)-methane[1] (2.60 g, 8.0 mmol) in THF (300 mL) at –30 °C, followed by stirring for 2 h at 25 °C. To this reagent **15** was added a solution of **14** (2.0 g, 4 mmol) in THF (100 mL), and the mixture was stirred at reflux for 40 h, cooled to room temperature (rt), and treated with aqueous NH_4Cl. After concentration *in vacuo*, the mixture was extracted with CH_2Cl_2, and the extract was dried ($MgSO_4$) and concentrated to give diol **16**, which was oxidized directly, without purification, because of the difficulty of separation.

A solution of crude **16** in CH_2Cl_2 (200 mL) containing Celite (12 g) and PCC (10 g) was stirred at 25 °C for 6 h. The mixture was filtered by suction through silica gel on a glass filter, followed by washing the silica gel with CH_2Cl_2. After concentration *in vacuo*, the crude product was chromatographed (SiO_2, CH_2Cl_2/n-C_6H_{14}; 1:1, v/v) to give 800 mg (31%) of crystalline **17**: mp 212–212 °C; IR (KBr) 1658, 1598, and 740 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.36–6.77 (m, 28 H), 4.30 (s, 2 H), 3.95 (s, 4 H), and 3.66 (s, 4 H); ^{13}C NMR (50.29 MHz) δ 199.67 (*C*=O), 140.81, 139.89, 139.54, 138.77, 138.66, 138.55, 137.85, 131.30, 131.25, 130.81, 130.61, 129.97, 129.80, 129.54, 129.48, 126.11, 126.06, 125.96, 125.76, 125.61, 37.86, 36.28, and 35.99; EIMS m/z (rel inten) 658 (M$^+$, 100), 464 (18.7), 255 (34.1), and 179 (45.2); HRMS calcd for $C_{49}H_{38}O_2$ M 658.2872, found M$^+$ 658.2886.

Bicyclic Bis-Cyclophane (18). McMurry Olefination of 17. A mixture of $LiAlH_4$ (152 mg, 4 mmol) and $TiCl_3$ (1.54 g, 10 mmol) in THF (60 mL) was refluxed for 30 min, followed by addition of **17** (250 mg, 380 μmol), and refluxed overnight. To this mixture was added aqueous NH_4Cl, followed by evaporation of the solvent. The mixture was extracted with CH_2Cl_2, and the extract was washed with water, dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was chromatographed (SiO_2, CH_2Cl_2/n-C_6H_{14}; 1:1, v/v) to provide 210 mg (87%) of powdery **18**: mp 302–303 °C; IR (KBr) 3015, 2920, 1485, 1050 and 740 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.61–6.47 (m, 28 H), and 4.1–3.20 (3 overlapping AB q and 2 s, 10 H); ^{13}C NMR (50.29 MHz) δ 141.02, 140.76, 140.37, 139.25, 138.44, 138.31, 138.12, 136.45, 132.98, 131.00, 130.92, 129.87, 128.93, 128.70, 128.41, 128.16, 126.71, 126.56, 126.50, 126.37, 126.25, 126.04, 125.56, 123.87, 41.29, 36.62, 36.15, and 34.90; EIMS m/z (rel inten) 626 (M$^+$, 100), 431 (21.4), 267 (47.6), and 179 (38.1); HRMS calcd for $C_{49}H_{38}$ M 626.2973, found M$^+$ 626.2949.

[1₇]Orthocyclophane (19). Pd-Catalyzed Reduction of 17. Cyclic diketone **17** (145 mg, 230 μmol) was hydrogenated by stirring with 10% Pd/C (20 mg) under H_2 gas (35–40 psi) in a mixture of EtOH (30 mL) and concd HCl (5 mL) for 3 d. After routine workup, the crude product was chromatographed (SiO_2, CH_2Cl_2/n-C_6H_{14}; 1:1, v/v) to give 74 mg (53%) of powdery **19**: mp 207–208 °C; IR (KBr) 3020, 1488, and 745 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.16–6.85 (m, 28 H), 3.56 (s, 14 H); ^{13}C NMR (50.29 MHz) δ 138.29, 129.86, 126.35, and 36.60; EIMS m/z (rel inten) 630 (M$^+$, 43.4), 345 (12.7), 269 (54.0), and 179 (100); HRMS calcd for $C_{49}H_{42}$ M 630.3287, found M$^+$ 630.3283.

2,9,16,23,30,37,44-Heptaoxooctacyclo[43.4.0^{3,8}.0^{10,15}.0^{17,22}.0^{24,29}.0^{31,36}.0^{38,43}]nonatetraconta-1(45),3(8),4,6,10-(15),11,13,17(22),18,20,24(29),25,27,31(36),32,34,38(43),39,41,-46,48-henicosaene; [1₇]Ketonand (20). A solution of dione **17** (223 mg, 340 μmol) in AcOH (60 mL) containing CAN (4.11 g, 7.5 mmol) was refluxed for 2 d. After routine workup, the crude product was chromatographed (SiO_2, CH_2Cl_2/Et_2O; 1:1, v/v; $R_f \sim 0.2$) to give 127 mg (50%) of crystalline **20**: mp 252–253 °C; IR (KBr) 3050, 1665 (C=O), 1255, 1280, 940 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.38 (s, 28 H); ^{13}C NMR (50.29 MHz) δ 195.44 (*C*=O), 138.46, 130.06, and 129.91; EIMS m/z (rel inten) 728 (M$^+$, 50.52), 369 (33.5), 262 (36.7), and 162 (100); HRMS calcd for $C_{49}H_{28}O_7$ M 728.1835, found M$^+$ 728.1848.

X-ray Analysis of 20. Crystals were grown by dissolving powdery **20** in CH_2Cl_2, followed by adding some MeOH and carefully evaporating the solvent to give beautiful needles, which contained MeOH molecules. In the ^{1}H NMR spectrum recorded by using this crystals, the ratio of the aromatic and the methyl proton resonance was 9:1, which showed that in the crystals the molecule **20** bound the MeOH molecule in the ratio 1:1. The crystallographic data of **20** are presented in Table 2.

1,2-Bis[2-[2-(bromomethyl)benzyl]benzyl]benzene (21). Into a solution of diol **13** (3.40 g, 6.82 mmol) in CH_2Cl_2 (150 mL)

Table 2. Crystallographic Data[a] for [1$_7$]ketonand 20

formula	$C_{49}H_{28}O_7$
formular weight	728.77
a, Å	9.313(1)
b, Å	12.048
c, Å	17.324
α, deg	99.52(1)
β, deg	90.84(1)
γ, deg	93.84(1)
V, Å^3	1909.2
Z	2
space grp	P-1
ρ, g/cm^{-1}	1.27
μ, cm^{-1}	0.8
R (F_o), %	7.5
R_w (F_o^2), %	7.8

[a] T = 298 K, λ = 0.71073 Å (Mo Kα).

was passed HBr gas at 25 °C until saturated, whereupon the cloudy solution turned to orange. After sufficient saturation, the reaction flask was stoppered and the mixture was stirred for 4–5 h until the mixture showed only one spot ($R_f \sim 1.0$) on TLC (SiO_2; CH_2Cl_2). After routine workup, the crude product was chromatographed (SiO_2, CH_2Cl_2) to give 3.80 g (89%) of crystalline **21**: mp 121–122 °C; IR (KBr) 1600, 1490, 1450, and 745 cm^{-1}; ^{1}H NMR (80 MHz) δ 7.32–6.67 (m, 20 H), 4.30 (s, 4 H), 3.94 (s, 4 H) and 3.83 (s, 4 H); ^{13}C NMR (50.29 MHz) δ 138.97, 138.33, 138.22, 137.67, 135.65, 130.36, 130.00, 129.61, 129.46, 128.89, 126.71, and 126.55 (Ar), and 36.16, 35.29 and 31.61 (ArCH_2); EIMS m/z (rel inten) 626, 624 and 622 (M^+, 1.88:3.79:1.78), 544 and 542 (0.92:0.66), 464 (4.74), 283 (21.6) and 269 (26.3), 179 (100).

1,2-Bis[2-[2-[2-(hydroxymethyl)benzyl]benzyl]benzyl]benzene (22) was prepared by use of the same procedure as that of **11** to **13** conversion. Reaction of Grignard **12** (7.50 mmol) with dibromide **21** (2.00 g, 3.20 mmol) in the presence of CuI (0.5 g) and removal of the THP protecting group in the coupling product, followed by usual workup, gave a solid which was insoluble in conventional organic solvents. The crude product was washed thoroughly with distilled water and diethyl ether to remove the water- and ether-soluble impurities to give 1.40 g (64%) of crystalline **22**: mp 77–78 °C; IR (KBr) 3500–3100, 1600, 1040, 1010 and 750 cm^{-1}; ^{1}H NMR (80 MHz) δ 7.31–6.63 (m, 28 H), 4.35 (d, 4 H, J = 5 Hz, ArCH_2O), 3.76 (s, 4 H), 3.71 (s, 8 H) and 1.26 (t, 2 H, J = 5 Hz); ^{13}C NMR (50.29 MHz) δ 138.73, 138.66, 138,52, 138,37, 138.25, 137.86, 129.86, 129.62, 129.56, 129.43, 129.37, 128.08, 127.83, 126.52 (Ar), and 62.96 (CH_2OH), 36.31, 36.15, 35.23 (ArCH_2); EIMS m/z (rel inten) 642 ($M^+ - 2H_2O$, 19.5), 552 (9.0), 267 (26.6) and 179 (100); HRMS (FAB) calcd for $C_{50}H_{44}$ ($M - 2H_2O$) 642.3287, found ($M^+ - 2H_2O$) 642.4327.

1,2-Bis[2-[2-(2-formylbenzyl)benzyl]benzyl]benzene (23). A mixture of diol **22** (10.6 g, 15.6 mmol), Celite (18 g), and PCC (14 g) in CH_2Cl_2 (300 mL) was stirred for 2 h. After routine workup, the crude product was chromatographed (SiO_2, CH_2Cl_2), followed by recrystallization from hexane to provide 9.91 g (94.2%) of crystalline **23**: mp 117–118 °C; IR (KBr) 1695, 1600, 1450, and 700 cm^{-1}; ^{1}H NMR (80 MHz) δ 9.96 (s, 2 H), 7.90–6.81 (m, 28 H), 4.16 (s, 4 H, CH_2ArCHO), 3.73 (s, 4 H), and 3.70 (s, 4 H); ^{13}C NMR (50.29 MHz) δ 192.00 (C=O), 142.19, 138.38, 138.14, 138.08, 137.97, 133.90, 138.64, 131.71, 130.84, 129.74, 129.49, 129.21, 126.69, 126.56, 126.45, 36.11, and 35.01; EIMS m/z (rel inten) 656 ($M^+ - H_2O$, 70.5), 267 (27.1), 195 (57.6), and 179 (100); HRMS calcd for $C_{50}H_{40}O$ ($M - H_2O$) 656.3079, found ($M^+ - H_2O$) 656.2990.

Decacyclo[57.4.0.0^{3,8}.0^{10,15}.0^{17,22}.0^{24,29}.0^{31,36}.0^{38,43}.0^{45,50}.0^{52,57}]-trihexaconta-1(59),3(8),4,6,10(15),11,13,17(22),18,20,24(29),-25,27,31(36),32,34,38(43),39,41,45(50),46,48,52(57),53,55,60,62-heptacosaene-2,16-dione (25). To dilithio reagent **15** (4.5 mmol) was added a solution of **23** (2.0 g, 3.0 mmol) in THF (100 mL), and the stirred mixture was refluxed for 36 h and cooled, followed by treating with aqueous NH_4Cl. Routine workup gave crude diol **24**, which was oxidized directly. A solution of crude **24** in CH_2Cl_2 (200 mL) containing Celite (6 g) and PCC (5 g) was stirred at 25 °C for 6 h. After routine workup, the crude product was chromatographed (SiO_2, CH_2Cl_2/n-C_6H_{14}; 1:1, v/v) to give 930 mg (37.0%) of crystalline **25**: mp 213–214 °C; IR (KBr) 1660, 1495, 1450, and 740 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.33–6.68 (m, 36 H), 4.13 (s, 2 H, CO-ArCH_2ArCO), 3.87 (s, 4 H, CO-ArCH_2Ar), 3.74 (s, 4 H), and 3.67 (s, 4 H); ^{13}C NMR (50.29 MHz) δ 199.53 (C=O), 141.03, 140.37, 139.13, 138.98, 138.81, 138.63, 138.58, 138.53, 138.44, 131.13, 131.01, 130.90, 130.70, 130.48, 130.41, 130.02, 129.75, 129.54, 129.49, 129.11, 126.31, 126.29, 126.22, 126.11, 125.70, 125.58, 36.27, 36.06, and 35.97; EIMS m/z (rel inten) 838 (M^+, 100), 820 (36.1), 341 (19.1), and 179 (63.7); HRMS (FAB) calcd for $C_{63}H_{51}O_2$ (MH) 839.3889, found (MH^+) 839.4546.

2,9,16,23,30,37,44,51,58-Nonaoxodecacyclo[57.4.0.0^{3,8}.0^{10,15}.0^{17,22}.0^{24,29}.0^{31,36}.0^{38,43}.0^{45,50}.0^{52,57}]trihexaconta-1(59),3-(8),4,6,10(15),11,13,17(22),18,20,24(29),25,27,31(36),32,34,38-(43),39,41,45(50),46,48,52(57),53,55,60,62-heptacosaene; [1$_9$]-Ketonand (27). A solution of dione **24** (650 mg, 780 μmol) in AcOH (60 mL) and H_2O (5 mL) containing CAN (15 g, 27.4 mmol) was heated at 80–100 °C for 6 d. After routine workup, the crude product was chromatographed (SiO_2, CH_2Cl_2/Et_2O; 1:1, v/v; R_f 0.15) to give 250 mg (34.6%) of powdery [1$_9$]ketonand **27**: mp 282–288 °C dec; IR (KBr) 1670 cm^{-1}; ^{1}H NMR (80 MHz) δ 7.26 (s, 36 H); ^{13}C NMR (50.29 MHz) δ 195.75, 138.69, 130.27, and 129.90; FABMS m/z (rel inten) 959 (M·Na$^+$, 5.79), 795 (7.16), 663 (60.6), 554 (36.5), 316 (68.5), 288 (100); HRMS (FAB) calcd for $C_{63}H_{37}O_9$ (MH) 937.2438, found (MH^+) 937.3172.

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Supplementary Material Available: Experimental data and copies of IR, MS, and ^{1}H and ^{13}C NMR spectra of **10**, **13**, **14**, **17–23**, **25**, and **27**. Also stereoviews of **10** and **20** (62 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.