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Articles

Synthesis and Characterization of Coronanes: Multicyclopropane-Fused Macrocyclic Arrays

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Stepwise macrocyclization of the all *syn-trans*-1,15-quinquecyclopropanedimethanol (**4**) with iso- and terephthaloyl chlorides and 4,4′-methanediyl-dibenzoic acid (**28**) gave the corresponding coronanes **22**, **23**, and **32**. The same protocol was used with all *syn-trans*-1,21-septecyclopropanedimethanol (**5**) and 2,3-naphthalenedicarboxylic acid to obtain the macrolide **27**. Direct macrocyclization of diol **4** and 1,10-phenanthroline-2,9-dicarbonyl chloride (**33**) and 2,2′-bipyridine-4,4′-dicarbonyl chloride (**35**) gave the coronanes **34** and **36**, respectively. Ring closing metathesis (RCM) of the diene **42** using $Cl_2(Cy_3P)_2Ru{=}CHPh$ (**48**) (Grubbs's catalyst) gave the macrocyclic lactone **45**. The structures of coronanes **22**, **23**, **32**, **34**, **36**, and **45** were confirmed by X-ray crystallographic studies which showed the cyclopropyl chain to adopt very differing conformations throughout the series. Several of the macrocycles have significant free pathways through their ring centers, and in the case of compound **34** there is a water molecule hydrogen bonded within the ring. This latter compound has the potential to act as a chiral ligand to metal centers.

Introduction

In 1990, Yoshida et al. in the Fujisawa laboratories in Japan, reported the isolation and partial structural elucidation of FR-900848 (**1**) from a fermentation broth of *Streptoverticillium fervens*.[1] The full stereochemical assignment of this substance was proven both by degradation[2] and total synthesis.[3] FR-900848 (**1**) shows potent, selective activity against filamentous fungi such as *Aspergillus niger*, *Mucor rouxianus*, *Aureobasidium pullans*, and various *Trichophyton sp.*, etc.[1] The fatty acid side chain of FR-900848 (**1**) bears a striking resemblance to the side chain of U-106305 (**2**), a cholesteryl ester transfer protein inhibitor isolated from *Streptomyces sp.* by workers at Upjohn Laboratories[4] and also first synthesized in our laboratories.[5] Both fatty acid side chains of FR-900848 (**1**) and U-106305 (**2**) contain all *syn-trans*-disubstituted quarter- and quinquecyclopropane systems which undoubtedly conformationally restrict these lipophilic domains. Indeed, we have shown by extensive crystallography that *all-syn-trans*-disubstituted cyclopropane oligomers with 3−7 rings are helical, at least in the solid state.[2,5] We questioned whether the preference for an extended helical structure was principally dictated by crystal packing since examination of molecular models shows considerable conformational mobility. Indeed we were intrigued by the possibility of utilizing an all *syn-*

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(1) (a) Yoshida, M.; Ezaki, M.; Hashimoto, M.; Yamashita, M.; Shigematsu, N.; Okuhara, M.; Kohsaka, M.; Horikoshi, K. *J. Antibiot.* **1990**, *43*, 748. (b) Yoshida, M.; Horikoshi, K. EP 286 330, 1988, US Patent, 4 803 074, 1989; *Chem. Abstr.* **1989**, *110*, 210961.

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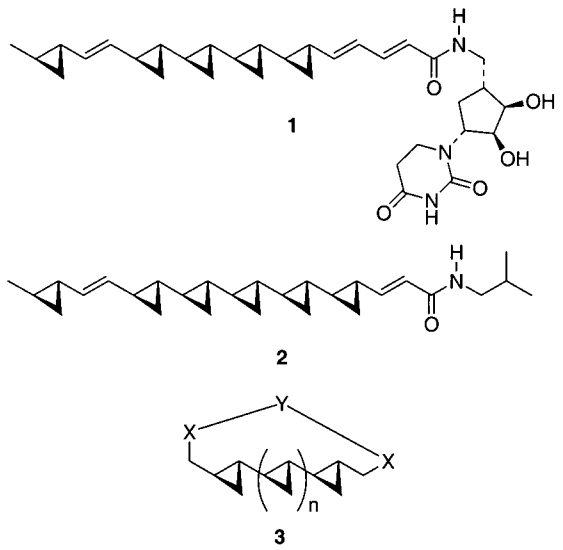
trans-cyclopropene oligomer to conformationally restrict a macrocyclic ring system as generically depicted by structure **3** (X−Y−X = lactone or dilactone entity), and this would clearly not be possible with an extended helical conformation.



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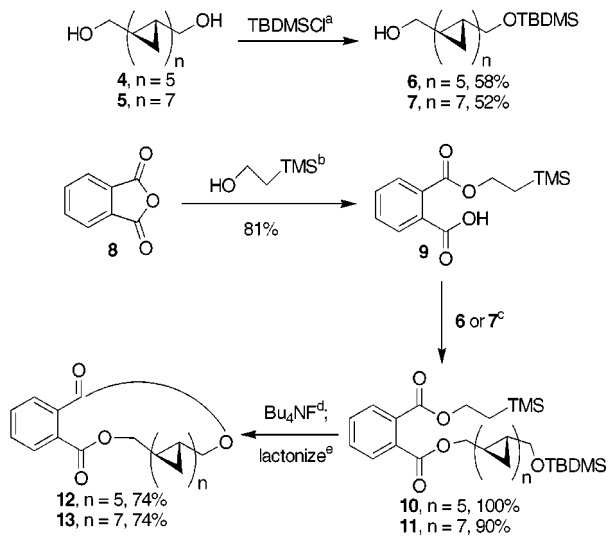
2

3

To explore these conformational issues, we examined the conversion of quinquecyclopropane **4**[5b] and septecyclopropane **5**[5b] into the macrocyclic lactone systems **3**. Condensation of diol **5** with phthaloyl chloride (DMAP, pyridine, CH_2Cl_2, THF) gave a macrocyclic dilactone **13** in poor yield (10%) and consequently a higher yielding, stepwise approach was devised (Scheme 1).[6] In the same stepwise fashion, diol **4** was converted into the lower homologue dilactone **12** with a macrocyclization yield of 74%. Both coronanes[7] **12** and **13** are symmetrical compounds (^{13}C NMR) exhibiting the correct molecular weight (EI MS), and the structure of the quinquecyclopropane system **12** was unequivocally established by X-ray crystallography.[6]

Scheme 1[a]



[a] Key: (a) TBDMSCl, imidazole, CH_2Cl_2; (b) $TMS(CH_2)_2OH$, NaH, THF; (c) **6** or **7**, DCC, DMAP, CH_2Cl_2; (d) Bu_4NF, THF; (e) 2,4,6-$Cl_3C_6H_2COCl$, Et_3N, THF; DMAP, PhMe, Δ.

Herein we report the synthesis and the full characterization of seven new coronanes, six with symmetrical dilactone structures and prepared either via the same stepwise procedures outlined above or directly from diol **4** and a diacyl dichloride under high dilution conditions. The seventh coronane prepared was a nonsymmetrical lactone and was synthesized using a ring closing metathesis (RCM) reaction.

Result and Discussion

Coronanes **22** and **23**, which are regioisomers of the known dilactone **12**, were synthesized following the same stepwise procedure. Isophthaloyl **14** and terephthaloyl chlorides **15** were esterified with 2-trimethylsilylethanol to give the diesters **16** and **17** which were half deprotected by reaction with tetrabutylammonium fluoride (1 equiv) in THF. The unsymmetrical diesters **20** and **21** were obtained following the Steglich-esterification[8] of (2-trimethylsilylethyl) iso- and terephthalate with alcohol **6**.[5b] After double deprotection, the resultant hydroxy acid was macrocyclized under Yamaguchi[9] conditions to provide coronanes **22** and **23**. It was notable that yields for final macrocyclization of these compounds were both excellent (91 and 95%, respectively) (Scheme 2), which suggests that the structure of quinquecyclopropane array was flexible and of amenable conformation for facile macrocyclic ring closure. Recrystallization of coronanes **22** and **23** afforded crystals suitable for X-ray structure determinations (vida infra).

We have sought to prepare additional septecyclopropane coronanes since the parent macrocycle **13** was not obtained crystalline. The analogous naphthalene-2,3-dicarboxylic coronane **27** was prepared in the standard stepwise fashion from alcohol **7**[6] (Scheme 3). Unfortu-

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(3) (a) Barrett, A. G. M.; Kasdorf, K., *Chem. Commun.* **1996**, 325. (b) Barrett, A. G. M.; Kasdorf, K. *J. Am. Chem. Soc.* **1996**, *118*, 11030. (c) For a second total synthesis, see Falck, J. R.; Mekonnen, B.; Yu, J.; Lai, J.-Y. *J. Am. Chem. Soc.* **1996**, *118*, 6096.

(4) Kuo, M. S.; Zielinski, R. J.; Cialdella, J. I.; Marschke, C. K.; Dupuis, M. J.; Li, G. P.; Kloosterman, D. A.; Spilman, C. H.; Marshall, V. P. *J. Am. Chem. Soc.* **1995**, *117*, 10629.

(5) (a) Barrett, A. G. M.; Hamprecht, D.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1996**, *118*, 7863. (b) Barrett, A. G. M.; Hamprecht, D.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 8608. (c) For a second total synthesis see Charette, A. B.; Lebel, H. *J. Am. Chem. Soc.* **1996**, *118*, 10327.

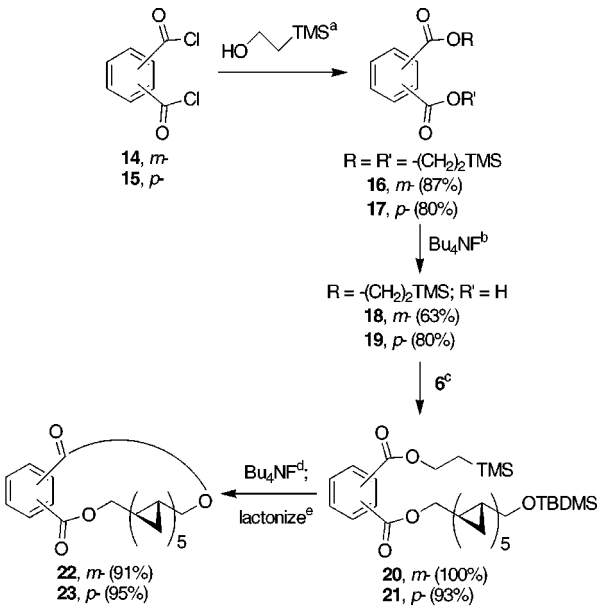
(6) Barrett, A. G. M.; Gross, T.; Hamprecht, D.; Ohkubo, M.; White, A. J. P.; Williams, D. J. *Synthesis* **1998**, 490.

(7) Fitjer and co-workers have introduced the term coronane as the name for cyclic alkanes globally fused to another cycloalkane; for examples, see: Wehle, D.; Fitjer, L. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 130.

(8) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522.

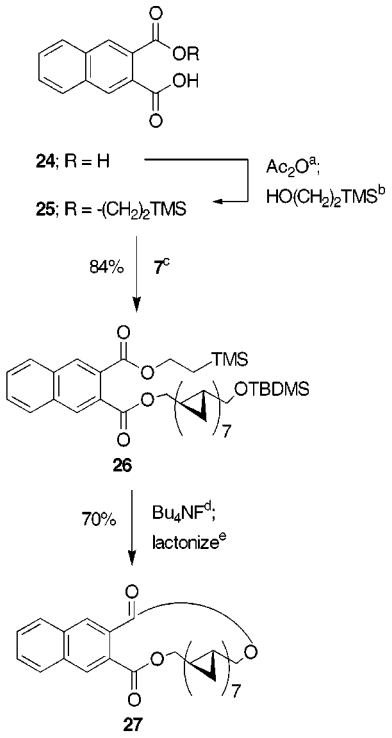
(9) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989.

Scheme 2[a]



[a] Key: (a) $TMS(CH_2)_2OH$, pyridine, CH_2Cl_2; (b) Bu_4NF (1 equiv), THF; (c) **6**, DCC, DMAP, CH_2Cl_2; (d) Bu_4NF, THF; (e) 2,4,6-$Cl_3C_6H_2COCl$, Et_3N, THF; DMAP, PhMe, Δ.

Scheme 3[a]

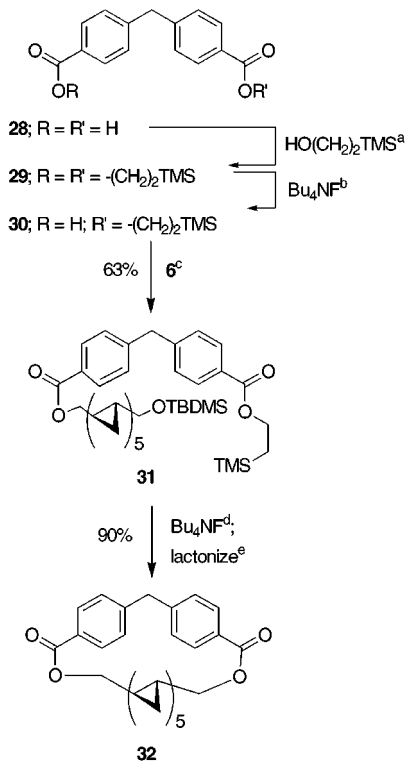


[a] Key: (a) Ac_2O, Δ; (b) $TMS(CH_2)_2OH$, NaH, THF; (c) **7**, DCC, DMAP, CH_2Cl_2; (d) Bu_4NF, THF; (e) 2,4,6-$Cl_3C_6H_2COCl$, Et_3N, THF; DMAP, PhMe, Δ.

nately, coronane **27** also did not give crystals suitable for an X-ray structural determination.

The synthesis of a novel macrocyclic lactone, having a 1,1-diphenylmethane group spacer between both lactone systems, was also undertaken. The initial step in this synthesis involved the reaction of acid **28** with trimethylsilylethanol to provide diester **29** in 57% yield (Scheme 4). The next step, involving mono-deprotection of diester **29**, proved more problematical. A moderate yield (49%)

Scheme 4[a]



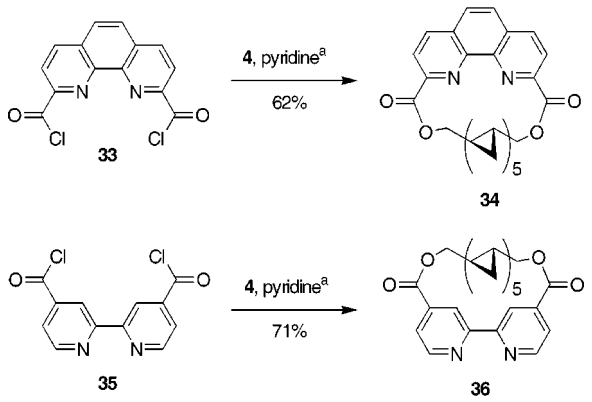
[a] Key: (a) $TMS(CH_2)_2OH$, DCC, DMAP, THF; (b) Bu_4NF (1 equiv), THF; (c) 2,4,6-$Cl_3C_6H_2COCl$, Et_3N, PhMe; **6**, DMAP, Δ; (d) Bu_4NF, THF; (e) 2,4,6-$Cl_3C_6H_2COCl$, Et_3N, THF; DMAP, PhMe, Δ.

of monoester **30** was obtained by reaction with tetrabutylammonium fluoride (1 equiv) in THF along with complete deprotection to provide starting diacid **28**. Various alternative reactions conditions were investigated in an attempt to optimize the yield for this transformation. Careful saponification of dimethyl terephthalate has been reported to provide the monomethyl ester in quantitative yield.[10] However, with this procedure, only conversion of diester **29** to the diacid **28** was observed. Mono-deprotection using potassium trimethylsilanolate[11] was attempted, but this reaction was also found to be ineffective with only diester **29** being recovered unchanged. As a consequence of the failure of these optimization techniques, the synthesis of **32** was continued utilizing the moderate yielding tetrabutylammonium fluoride mediated mono-deprotection. Coupling of monoester **30** with alcohol **6** using DCC and DMAP proceeded in only modest yield (53%) as did use of the more reactive coupling agent EDCI (47%). The optimal yield for this esterification was achieved via formation of the mixed anhydride, using 2,4,6-trichlorobenzoyl chloride, which provided the macrocyclization precursor **31** in 63% yield. Deprotection of ester **31** provided the hydroxy-acid which was used without purification. Yamaguchi macrocyclization gave the desired coronane **32** in excellent yield (90%) as a crystalline solid suitable for an X-ray crystallographic study (vide infra).

At this point, we decided to synthesize novel coronanes bearing phenanthroline and bipyridine as spacers and bidentate ligands. Such coronane ligands may undergo

(10) Godfrey, C. R. A. Ph.D. Thesis, Imperial College, London, 1980.
(11) Laganis, E. D.; Chenard, B. L. *Tetrahedron Lett.* **1984**, *25*, 5831.

Scheme 5[a]



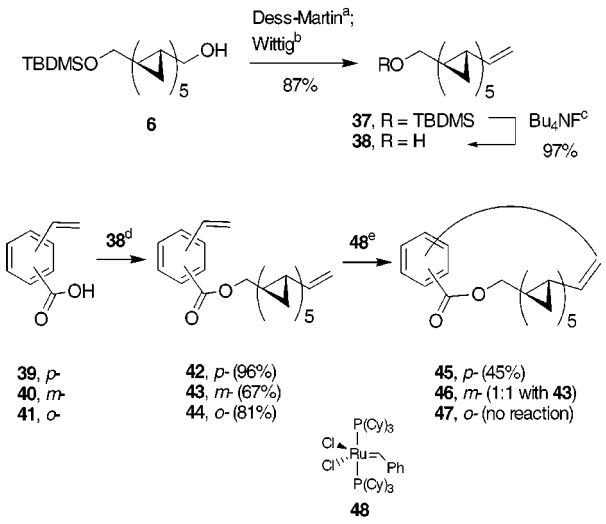
[a] Key: (a) 4, pyridine, CH_2Cl_2 (high dilution).

considerable conformational change and/or form higher order cyclopropane systems on metal ion complexation. Chandler et al. have reported that the inclusion of a larger polycyclic aromatic residue into a macrocyclic framework increases the yield of the ring closure reaction.[12] Accordingly, we examined the direct one-step synthesis of coronane **34**, using diacid chloride **33**[13] and the diol **4** as starting materials. Macrocyclization[12a,13c] in dry toluene at reflux and in high dilution gave the coronane **34** but in very low yield. In contrast, lactonization in dichloromethane in the presence of pyridine proceeded in superior yield. In the optimum procedure, reaction of diol **4** (0.75 equiv) with dichloride **33** in the presence of pyridine (2 equiv) proceeded in 62% yield (Scheme 5). In this procedure, the addition of **4** in dichloromethane was dropwise, and the reaction carried out at high dilution at room temperature. The structure of the coronane **34** was unequivocally established by an X-ray crystallographic study (vide infra).

This direct approach was extended to the synthesis of the corresponding bipyridine coronane **36** (Scheme 5). Excess of dichloride **35**, freshly synthesized[14] from the corresponding diacid, and pyridine were required in order to consume all the diol **4**. The reaction was again carried out at room temperature at high dilution conditions in dichloromethane solution. The yield of coronane **36** obtained was remarkable (71%). Again the coronane **36** was isolated as a crystalline solid suitable for an X-ray crystallographic study (vide infra).

Finally, ring closing metathesis (RCM)[15] was examined as a method for coronane synthesis. Fürstner and others have widely applied RCM in concise, elegant syntheses of macrocyclic natural products.[16] We considered that in

Scheme 6[a]



[a] Key: (a) Dess−Martin reagent, pyridine, CH_2Cl_2; (b) Ph_3PCH_3Br, *t*-BuOK, THF; (c) Bu_4NF, THF; (d) 38, DCC, DMAP, CH_2Cl_2; (e) $Cl_2(Cy_3P)_2Ru{=}CHPh$ (48, 20% mol), PhMe, Δ.

the presence of Grubbs's catalyst **48**, dienes **42**−**44** could potentially undergo macrocyclization via RCM to provide coronanes **45**−**47** (Scheme 6). Alkene **38** was synthesized from alcohol **6** by Dess−Martin oxidation, Wittig olefination, and desilylation. Alcohol **38** was subjected to DCC-mediated coupling with the vinylbenzoic acids **39**−**41**[17,18] to provide dienes **42**−**44** as the metathesis precursors (Scheme 6). Diene **42** was subjected to RCM using 5 mol % complex **48** in dichloromethane solution and with the gradual addition of both diene **42** and catalyst.[19] However, with this procedure no reaction was observed, and diene **42** was recovered intact (>95%) from the reaction mixture. A similar lack of reactivity was also observed at higher temperature in toluene at reflux. Gratifyingly, use of increased catalyst loading (20 mol % **48**) proved more successful with formation of the desired macrocycle **45** being observed, albeit in moderate yield (45%). The remaining mass balance consisted of unreacted diene **42**. The presence of unreacted starting material presented an additional problem in that starting material **42** and product **45** were of similar polarity thereby precluding the use of chromatography for purification. Fortunately, macrocycle **45** was readily purified by recrystallization, and the structure was unequivocally established by X-ray crystallography (vide infra) showing the *cis* stereochemistry of the double bond.

This ring closing metathesis protocol was also applied to diene **44**. In this instance no reaction was observed and unreacted diene **44** was recovered in near quantitative yield. This failure was possibly due to the proximity of the styrene unit to the carbonyl residue. Such effects are precedented in macrocyclic reaction.[15,19] Addition of titanium tetraisopropoxide has been reported to overcome the suppression of macrocyclization by proximal Lewis basic sites in the diene.[20] However, attempted RCM in the presence of titanium tetraisopropoxide gave intractable mixtures of products. The ring closing metathesis

(12) (a) Chandler, C. J.; Deady, L. W.; Reiss, J. A. *J. Heterocycl. Chem.* **1986**, *23*, 1327. (b) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017.

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(15) For recent reviews see the following for leading references: (a) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (b) Fürstner, A. *Top. Catal.* **1997**, *4*, 285. (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036. (d) Fürstner, A. *Top. Organomet. Chem.* **1998**, *1*, 37. (e) Ivin, K. J.; Mol, J. C. *Olefin Metathesis and Metathesis Polymerization*, 2nd ed.; Academic Press: New York, 1997.

(16) Fürstner, A.; Seidel, G.; Kindler, N. *Tetrahedron* **1999**, *55*, 8215 and references therein.

(17) Leebrick, J. R.; Ramsden, H. E. *J. Org. Chem.* **1958**, *23*, 935.

(18) Dale, W. J.; Starr, L.; Strobel, C. W. *J. Org. Chem.* **1961**, *26*, 2225.

(19) Fürstner, A.; Langemann, K. *Synthesis* **1997**, 793.

(20) Fürstner, A.; Langemann, K. *J. Am. Chem. Soc.* **1997**, *119*, 9130.

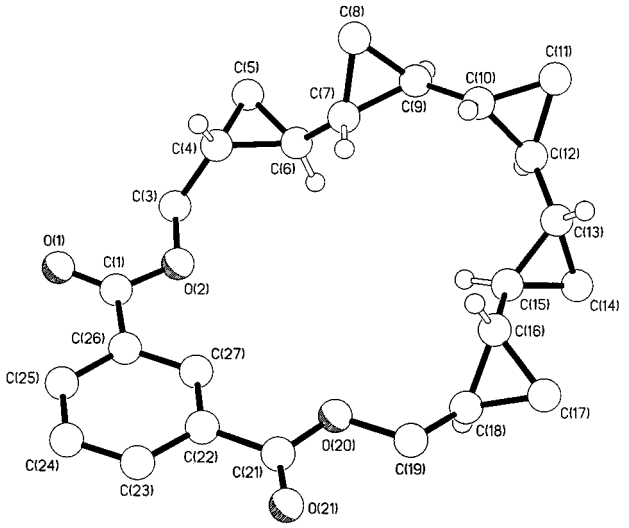

Figure 1. The molecular structure of **22** showing atomic numbering.

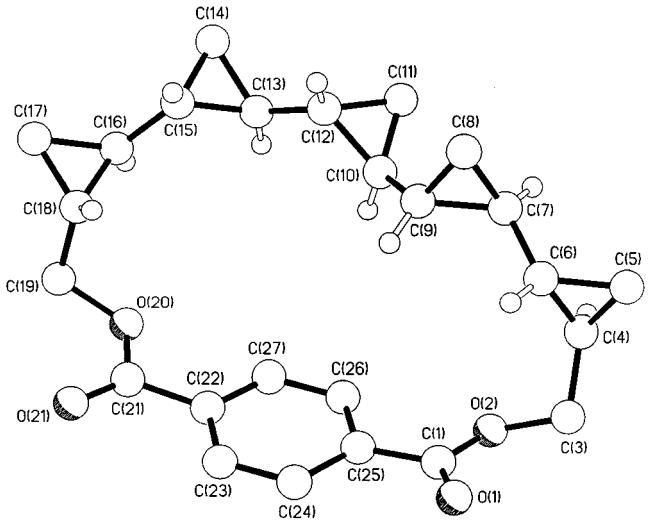

Figure 2. The molecular structure of **23** showing atomic numbering.

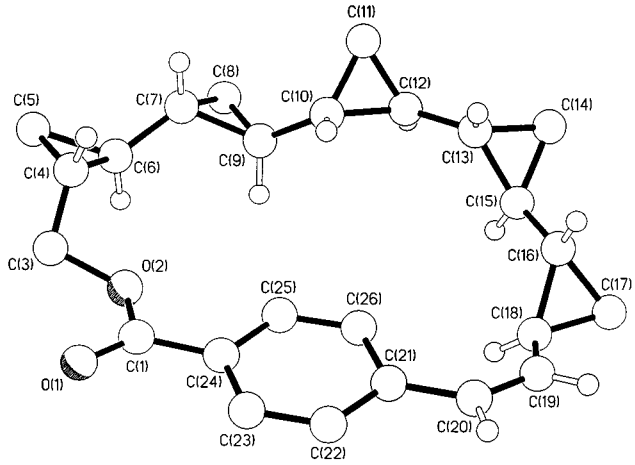

Figure 3. The molecular structure of **45** showing atomic numbering.

of **43** was also attempted. As in the case of diene **42**, RCM of diene **43** gave approximately a 1:1 mixture of starting material **43** and coronane **46** (Scheme 6). Unfortunately, neither chromatography nor recrystallization were useful methods of purification.

X-ray Crystallography. The crystal structures of compounds **22**, **23**, **32**, **34**, **36**, and **45** have been determined. All of the compounds are macrocyclic and contain chains comprised of five cyclopropyl units, each of the same chirality, that act as a link between the ends of aromatic-based nuclei. The torsional twists about the bonds in each cyclopropyl ring that form part of the macrocyclic backbone, are, as would be expected, very similar and, with one exception [the C(10)−C(12) bond in compound **32** which has a rotation of −160°], are in the range −132 to −147°, though in general these angles are less than the analogous angle (ca. 144°) in cyclopropane.[21] In contrast, the torsional twists about the bonds linking adjacent cyclopropyl rings show wide variations, giving rise to substantial differences in the geometries of the different macrocycles.

In all the structures except **45** (which has an unsymmetric spacer unit), the conformations adopted by the macrocycles are, to a large extent, controlled by the *syn* or *anti* dispositions of the pair of ester carbonyl groups. In **45** it is the *syn* or *anti* geometry of the C(20) methine hydrogen atom and the O(1) ester carbonyl that exercises the same control. In molecules with a "*syn*" conformation the macrocycle will tend to be open whereas in those with an "*anti*" geometry the cyclopropyl chain will tend to be directed over the aromatic spacer unit, creating a basketlike conformation.

In the solid-state structure of **22** (Figure 1) the ester carbonyl groups are *syn* and directed away from the linking cyclopropyl chain. The macrocycle consequently adopts an open (but folded) conformation, with the cyclopropyl chain looping out of the plane of, and away from, the isophthalate unit which is planar to within 0.09 Å; C(3) and C(19) lie only 0.07 and 0.06 Å, respectively, out of this plane. There is a small free pathway of ca. 2.4 Å diameter through the ring center. All of the carbon atoms of the cyclopropyl backbone lie "above" the plane of the isophthalate unit [peaking at 2.90 Å for C(10)] with the exception of C(18) which lies 0.16 Å "below" this plane. The molecules pack to form offset stacks, the phenyl ring on one overlaying the O(1)−C(1)-O(2)−C(3) portion of the next with a mean interplanar separation of ca. 3.5 Å. This stacking results in the formation of restricted channels that extend along the crystallographic *a* direction.

The crystal structure of **23** has the isophthalate unit replaced by a terephthalate unit (Figure 2), with the carbonyl oxygen atoms again *syn* and oriented away from the macrocyclic ring center. The conformation is again folded, the cyclopropyl chain looping out of the plane of the terephthalate unit which is distinctly bowed with the C(1)−C(25) and C(21)−C(22) bonds subtending an angle of 17°. There are also small, but significant, torsional twists (3 and 9°) about the ester−phenyl linkages. As in **22**, all of the carbon atoms of the cyclopropyl backbone lie "above" the plane of the terephthalate unit [peaking at 3.95 Å for C(12)]. As a consequence of the change from a *meta* to a *para* substitution on the aromatic ring together with the folding of the cyclopropyl chain back toward the terephthalate unit, the macrocycle is self-filling. Adjacent molecules are linked by weak C−H···O hydrogen bonds between one of the C(19) methylene

(21) Nijveldt, D.; Vos, A. *Acta Crystallogr. B* **1988**, *44*, 296.

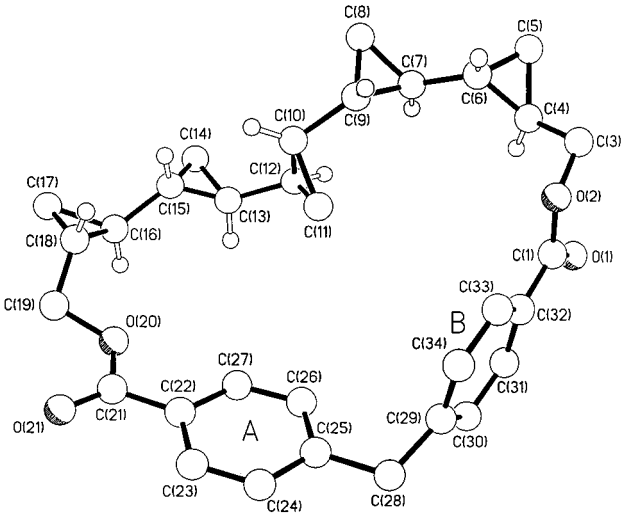

Figure 4. The molecular structure of **32** showing atomic numbering.

hydrogen atoms in one molecule and the O(21) carbonyl oxygen in another to form helical chains that are generated by the crystallographic 2_1 screw axis; the C···O and H···O distances are 3.37, 2.45 Å with a C−H···O angle of 160°.

Compound **45** (Figure 3), which has a *cis*-olefinic linkage in place of one of the ester CO_2CH_2 units of **23**—and thus has a chain that is one methylene carbon shorter—adopts a distinctly flatter conformation with the largest deviation for any of the backbone carbon atoms from the plane of the phenyl ring being only 1.42 Å [for C(10)]. Although the *syn* relationship between the ester carbonyl oxygen and the C(20) methine hydrogen atom results in the cyclopropyl chain looping away from the aromatic unit, the shortening of the chain length coupled with the *para* substitution of the phenyl ring results in the macrocycle being self-filling. As in the case of the terephthalate structure **23**, there are small, but significant, torsional twists (6 and 11°) about the bonds linking the phenyl ring to the ester and olefinic functions. The molecules pack to form offset stacks in the crystallographic *a* direction but with only marginal $\pi-\pi$ overlap between the aromatic rings; the mean interplanar separation is 3.40 Å, but the ring centroid···ring centroid distance is 5.38 Å.

Figure 4 shows the crystal structure of compound **32** to have approximate C_2 symmetry about an axis passing through C(11) and C(28). Despite the folded nature of the extended "aromatic spacer unit" and the potential to form an open macrocyclic geometry, the diphenylmethane unit adopts a near orthogonal geometry (torsional twists of 25 and 84° about the C(25)−C(28) and C(28)−C(29) bonds), and this coupled with a folding back on itself toward the aromatic rings of the linking cyclopropyl chain results in a self-filling conformation. It is notable that in this structure we see the largest deviation from ideal (of ca. 16°) in one of the "invariant" cyclopropyl torsion angles, that about C(10)−C(12). Adjacent molecules in the crystal form offset stacks along the crystallographic *a* direction with rings **A** and **B** of one molecule only marginally overlapping their counterparts in the next; the **A**···**A** and **B**···**B** mean interplanar separations are 3.10 and 3.56 Å, respectively, with ring centroid···ring centroid distances of 5.66 Å in each case.

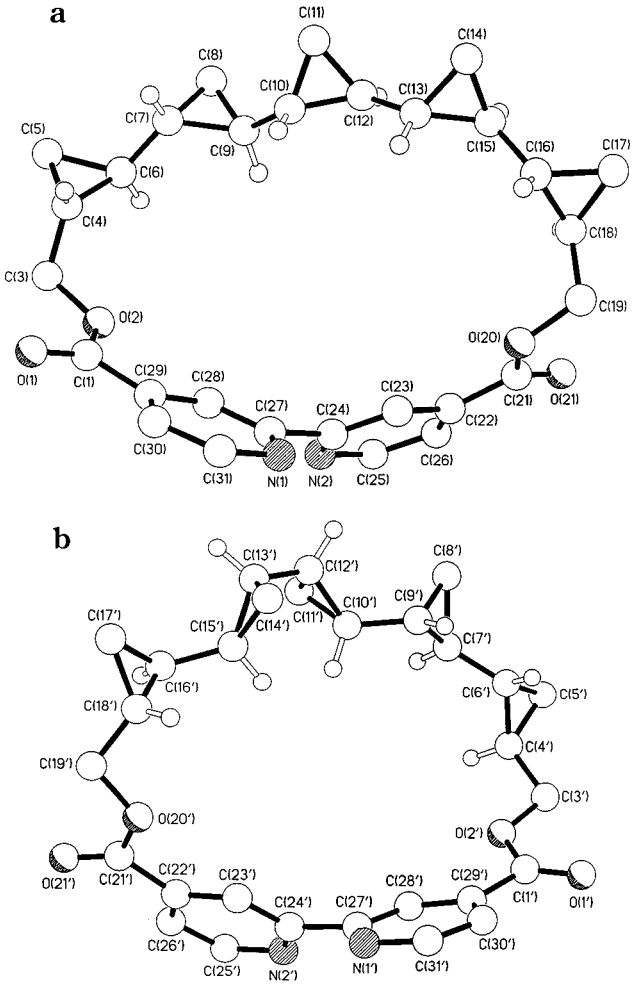

Figure 5. The molecular structures of the two independent molecules **36a** and **36b** showing atomic numbering.

Compound **36** crystallizes with two crystallographically independent molecules, **36a** and **36b**, in the asymmetric unit, each with a distinctly different conformation (shown in Figures 5a and 5b, respectively). Both molecules have their carbonyl oxygen atoms in an *anti* orientation, thus directing the cyclopropyl chains over the bipyridyl ring system creating basketlike conformations. In each case the bipyridyl unit has a distinctly twisted conformation with a ca. 135° torsion angle about the bond linking the two ring systems, the pyridyl nitrogens being in an *anti* geometry with respect to each other. Despite major differences in the torsional twists within the cyclopropyl linkages between the two independent molecules, e.g. 159° about C(12)−C(13) in **36a** cf. 0° for its counterpart in **36b**, both molecules have open conformations with free pathways of ca. 6.0 × 2.6 Å and 5.6 × 2.8 Å in **36a** and **36b**, respectively, through their macrocyclic ring centers. It is interesting to note that whereas molecule **36a** has approximate C_2 symmetry about an axis passing through C(11) and the center of the C(24)−C(27) bond, molecule **36b** does not. Possibly the most striking difference between the two molecules, however, is the enantiomeric relationship between the bipyridyl-diester units, i.e., the structure contains two interconvertible diastereomers. The two independent molecules form **-A-B-A-B-** stacks with one of the pyridyl rings of one molecule overlaying one of the next ad infinitum, the pyridyl rings of one

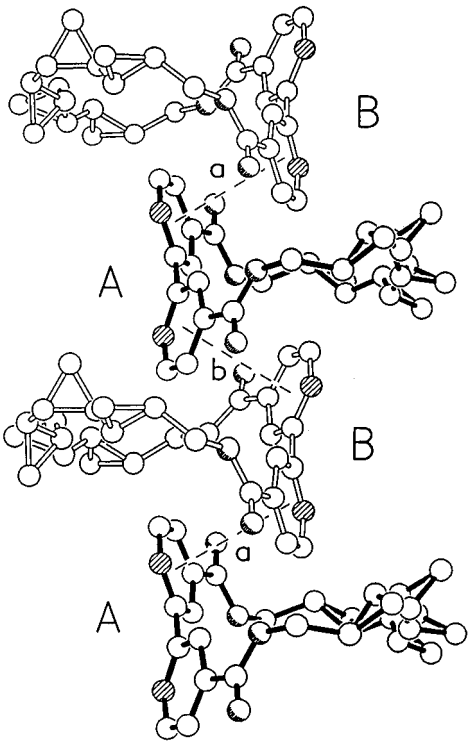

Figure 6. One of the **-A-B-A-B-** stacks of independent molecules **36a** and **36b**. The mean interplanar and centroid··· centroid separations (Å) are (a) 3.41, 3.60, and (b) 3.25, 3.55.

molecule inserting into the macrocyclic cavities of the next (Figure 6).

Compound **34** also crystallizes with two crystallographically independent molecules, **34a** and **34b**, in the asymmetric unit, each again having a distinctly different conformation (shown in Figures 7a and 7b, respectively). Unlike in compound **36** where the ester carbonyl units were oriented *syn* in each independent molecule, here in one (**34a**) they are *anti*—with one being directed into the macrocyclic ring center and the other away—whereas in the other (**34b**) they are *syn*, both being directed outward. Molecule **34a** has an open, folded conformation with all of the backbone carbon atoms lying above the plane of the phenanthroline ring system, peaking at 4.50 Å for C(10). There are significant out of plane twists [ca. 13° about C(1)−C(31) and ca. 20° about C(21)−C(22)] of the ester functions out of the phenanthroline ring plane. Within the macrocyclic cavity is located a water molecule which lies within hydrogen bonding distance of O(1), O(20), N(1), and N(2), Figure 7a. In contrast, molecule **34b** has a distinctly twisted conformation with C(9′) lying 2.09 Å above, and C(16′) 1.61 Å below, the phenanthroline ring plane. There are again significant out of plane twists [ca. 32° about C(1′)−C(31′) and ca. 19° about C(21′)−C(22′)] of the ester functions out of the phenanthroline ring plane. Despite these marked differences in conformation, molecule **34b** still has a distinctly open conformation, and again traps a water molecule within its ring center, being positioned within hydrogen bonding distance of O(2′), O(20′), N(1′), and N(2′), Figure 7b. The two independent molecules form continuous **-A-B-A-B-** stacks with the phenanthroline ring of one molecule π-stacking with its counterpart in the next (Figure 8); the mean

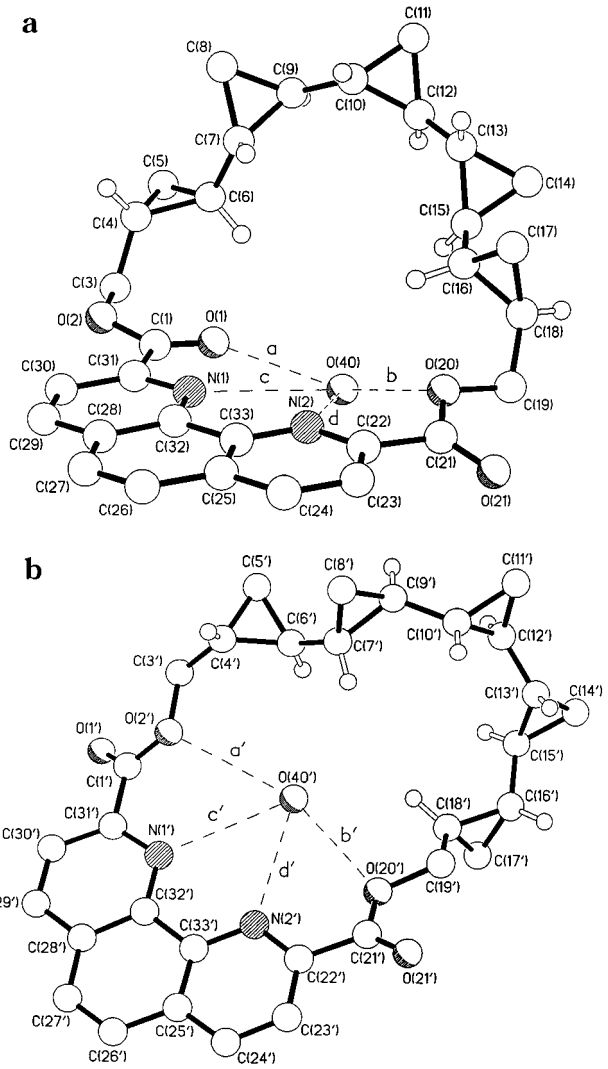

Figure 7. The molecular structures of the two independent molecules **34a** and **34b** showing atomic numbering. The hydrogen bonding O···X contacts (Å) are (a) 2.85, (b) 2.94, (c) 3.19, (d) 3.19, (a′) 3.07, (b′) 2.96, (c′) 3.14, and (d′) 3.22 (the water hydrogen atoms were not located).

interplanar separations are 3.35 and 3.43 Å, the rings being inclined by ca. 2°. The conformations of the molecules, particularly that adopted by **34b**, are ideally tailored for chelation to a metal center, the molecule acting as a chiral tetradentate ligand. This potential is currently being explored.

Conclusions

We have synthesized seven new coronanes bearing all *syn-trans* cyclopropane oligomers. Macrocycles **22**, **23**, **27**, and **32** were obtained via stepwise double esterification in excellent yields in the macrocyclization step. Coronanes **34** and **36** were prepared by the direct macrocyclization from diol **4** at high dilution conditions and in excellent yields. Finally, ring closing metathesis was successfully used to obtain macrolide **45**. Six of these macrocycles yielded crystals suitable to carry out X-ray crystallographic studies. We are currently examining the metal ion complexing abilities of macrocycles **34** and **36** and the host−guest chemistry of related coronanes. This research will be reported in due course.

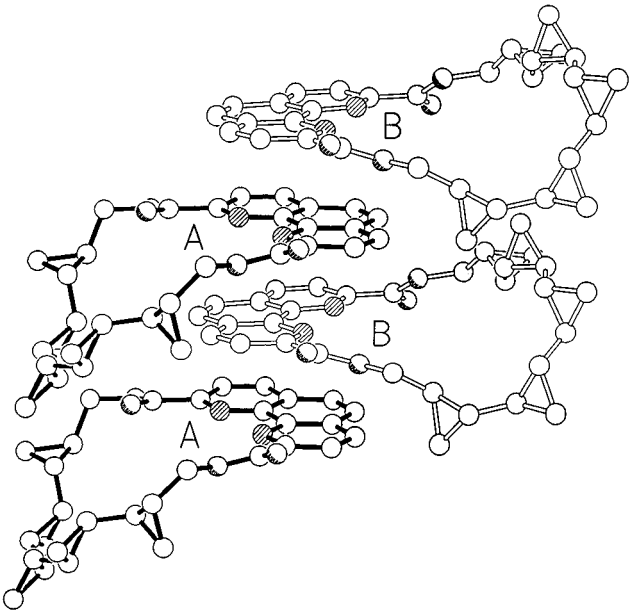

Figure 8. One of the **-A-B-A-B-** stacks of independent molecules **34a** and **34b**.

Experimental Section

General Procedures. All reactions were carried out in an atmosphere of dry nitrogen or argon at room temperature unless otherwise stated. Reaction temperatures other than room temperature were recorded as bath temperatures unless otherwise stated. Chromatography was carried out on BDH silica 60, 230−400 mesh ASTM, using flash techniques[22] (eluants are quoted in parentheses). Analytical thin-layer chromatography (TLC) was performed on Merck precoated silica 60 F_{254} plates. Petroleum bp 40−60 °C (hexanes) used as a chromatography eluant was distilled; all other chromatography eluants were BDH GPR grade and undistilled. The following reaction solvents/reagents were purified by distillation: benzene (PhH) (P_2O_5, N_2), dichloromethane (CH_2Cl_2) (CaH_2, N_2), 1,2-dimethoxyethane (DME) (CaH_2, N_2), pyridine (CaH_2, N_2), and tetrahydrofuran (THF) (Ph_2CO/K, N_2). All other organic solvents and reagents were obtained from commercial sources and used without further purification. Organic extracts were concentrated using a rotary-evaporator at ≤40 °C bath temperature. Nonvolatile oils and solids were vacuum-dried at <2 mmHg.

Bis[2-(trimethylsilyl)ethyl] 1,3-Benzenedicarboxylate (16). Pyridine (0.55 mL, 6.84 mmol) was added dropwise to a mixture of isophthaloyl chloride (464 mg, 2.28 mmol) and 2-(trimethylsilyl)ethanol (0.66 mL, 4.57 mmol) in CH_2Cl_2. After stirring overnight, saturated aqueous NH_4Cl was added, and the mixture was extracted with CH_2Cl_2, dried (Na_2SO_4), and evaporated in vacuo. Chromatography (hexanes:EtOAc 95:5) gave **16** (728 mg, 87%) as a colorless oil: R_f 0.55 (hexanes: EtOAc 9:1); IR (film) 1724 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.70 (dd, 1H, J = 1.7, 1.7 Hz), 8.23 (dd, 2H J = 1.8, 7.8 Hz), 7.54 (dd, 1H, J = 7.8, 7.8 Hz), 4.43−4.49 (m, 4H), 1.13−1.19 (m, 4H), 0.11 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 133.6, 131.1, 130.6, 128.5, 63.6, 17.5, −1.4; MS (CI) m/z 384 $(M + NH_4)^+$; HRMS (CI) calcd for $C_{18}H_{34}NO_4Si_2$: $(M + NH_4)^+$ 384.2026, found: $(M + NH_4)^+$ 384.2050; Anal. Calcd. for $C_{18}H_{30}O_4Si_2$: C, 58.97; H, 8.25. Found: C, 59.10; H, 8.23.

Hydrogen 2-(Trimethylsilyl)ethyl 1,3-Benzenedicarboxylate (18). Bu_4NF in THF (1M; 1.87 mL, 1.87 mmol) was added to **16** (687 mg, 1.87 mmol) in THF (15 mL). After stirring overnight, Et_2O (50 mL) and 1 N HCl (5 mL) were added in sequence, and the organic layer was separated, dried (Na_2SO_4), and evaporated in vacuo. Chromatography (CH_2Cl_2: MeOH 100: 0 to 97:3) gave **18** (315 mg, 63%) as a white solid: mp 101−103 °C (hexanes and CH_2Cl_2); R_f 0.52 (CH_2Cl_2: MeOH 9:1); IR (film) 2500−3200, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 8.79 (dd, 1H, J = 1.5, 1.5 Hz), 8.30−8.33 (m, 2H), 7.60 (dd, 1H, J = 7.8, 7.8 Hz), 4.45−4.51 (m, 2H), 1.16−1.27 (m, 2H), 0.12 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 165.8, 134.6, 134.2, 131.3, 129.7, 128.7, 63.8, 17.5, −1.4; MS (CI) m/z 284 $(M + NH_4)^+$; HRMS (CI) calcd for $C_{13}H_{22}NO_4Si$: $(M + NH_4)^+$) 284.1318, found: $(M + NH_4)^+$ 284.1299. Anal. Calcd. for $C_{13}H_{18}O_4Si$: C, 58.62; H, 6.81. Found: C, 58.54; H, 6.90.

(1*R*,3*S*,4*R*,6*S*,7*R*,9*R*,10*S*,12*R*,13*S*,15*R*)-15-[(*tert*-Butyldimethylsilyloxy)methyl]-1-quinquecyclopropanemethyl 2-(Trimethylsilyl)ethyl 1,3-Benzenedicarboxylate (20). A mixture of acid **18** (47.8 mg, 0.179 mmol), alcohol **6** (57.8 mg, 0.154 mmol), DCC (63.4 mg, 0.307 mmol), and DMAP (8.9 mg, 0.073 mmol) in CH_2Cl_2 (1 mL) was stirred overnight, when CH_2Cl_2 (10 mL) and H_2O (2 mL) were added. The organic layer was separated, dried (Na_2SO_4), and evaporated in vacuo. Chromatography (hexanes:Et_2O 10:0 to 9:1) gave **20** (96 mg, 100%) as a colorless oil: R_f 0.53 (hexanes: EtOAc 9:1); $[\alpha]^{25}_D$ = −91.2 (*c* 1.0, $CHCl_3$); IR (film) 1724 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.71 (dd, 1H, J = 1.5, 1.5 Hz), 8.24 (dd, 2H, J = 1.5, 7.7 Hz), 7.55 (dd, 1H, J = 7.7, 7.7 Hz), 4.44−4.50 (m, 2H), 4.15 (d, 2H, J = 7.3 Hz), 3.42−3.46 (m, 2H), 1.15−1.21 (m, 2H), 0.91−1.01 (m, 1H), 0.90 (s, 9H), 0.87−0.89 (m, 1H), 0.62−0.74 (m, 2H), 0.36−0.61 (m, 8H), 0.20−0.26 (m, 2H), 0.11 (s, 9H), 0.05 (s, 6H), 0.03−0.19 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 133.6, 131.1, 131.0, 130.7, 128.5, 69.4, 66.7, 63.6, 26.0, 19.5, 19.0, 18.6, 18.5, 18.3, 18.2, 17.9, 17.5, 15.9, 8.9, 8.3, 8.2, 8.1, −1.4, −5.1; MS (CI) m/z 642 $(M + NH_4)^+$; HRMS (CI) calcd for $C_{36}H_{60}NO_5Si_2$: $(M + NH_4)^+$ 642.4010, found: $(M + NH_4)^+$ 642.4011.

Coronane 22. A mixture of diester **20** (71.8 mg, 115 μmol) and Bu_4NF in THF (1 M; 575 μL, 575 μmol) in THF (2 mL) was stirred for 1 h, when Et_2O (20 mL) and saturated aqueous NH_4Cl were added. After the mixture was stirred for a few min, 1 N HCl was added, and the organic layer was separated. The aqueous layer was extracted with Et_2O (3 × 10 mL), and the combined organic layer was dried (Na_2SO_4) and evaporated in vacuo. The residue was dissolved in THF (3 mL), Et_3N (22.8 μL, 161 μmol) and 2,4,6-trichlorobenzoyl chloride (24 μL, 150 μmol) were added, and the mixture was stirred for 2 h. After filtration, the filtrate was diluted with PhMe (40 mL) and added to DMAP (84 mg, 688 μmol) in PhMe (10 mL) at reflux over 3.5 h using a syringe pump. After the mixture was allowed to cool to room temperature, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The separated organic layer was dried (Na_2SO_4) and evaporated in vacuo. Chromatography (hexanes: Et_2O from 10:1 to 1:1) gave **22** (41 mg, 91%) as white crystals: mp 64−67 °C (Et_2O and EtOH); R_f 0.65 (hexanes:EtOAc 4:1); $[\alpha]^{25}_D$ = +61.8 (*c* 0.5, $CHCl_3$); IR (film) 1723 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.79 (dd, 1H, J = 1.6, 1.6 Hz), 8.26 (dd, 2H, J = 1.7, 7.8 Hz), 7.58 (dd, 1H, J = 7.7, 7.7 Hz), 4.81 (dd, 2H, J = 3.7, 11.2 Hz), 3.59 (dd, 2H, J = 11.1, 11.1 Hz), 1.12−1.27 (m, 2H), 0.49−1.00 (m, 4H), 0.39−0.47 (m, 4H), 0.16−0.34 (m, 8H), 0.06−0.10 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 133.7, 131.6, 129.8, 128.6, 70.1, 22.6, 21.5, 21.1, 17.8, 9.3, 8.8, 8.2; MS (CI) 410 $(M + NH_4)^+$, 393 $(M + H)^+$; HRMS (CI) calcd for $C_{25}H_{29}O_4$: $(M + H)^+$ 393.2066, found: $(M + H)^+$ 393.2059; Crystal data for **22**: $C_{25}H_{28}O_4$, M = 392.5, orthorhombic, $P2_12_12_1$ (no. 19), a = 5.317(1), b = 11.882(2), c = 35.118(6) Å, V = 2218.7(6) Å^3, Z = 4, D_c = 1.175 g cm^{-3}, μ(Cu−Kα) = 6.28 cm^{-1}, F(000) = 840, T = 293 K; clear thin platy needles, 0.80 × 0.37 × 0.07 mm, 2058 independent measured reflections; refinement based on F^2 to give R_1 = 0.057, wR_2 = 0.147 for 1512 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 124°$] and 263 parameters. The absolute structure was assigned by internal reference to the known chirality of the pentacyclopropyl chain.

Coronane 23. Compound **23** was obtained as a white solid from **21** in 95% yield (40 mg) as described for **22**: mp 148−150 °C (Et_2O and EtOH); R_f 0.61 (hexanes:EtOAc 8.5:1.5); $[\alpha]^{25}_D$ = +6.5 (*c* 0.8, $CHCl_3$); IR (film) 1714 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.29 (s, 4H), 4.98 (dd, 2H, J = 4.7, 11.2 Hz), 3.59 (dd, 2H, J = 11.1, 11.1 Hz), 1.23−1.27 (m, 2H), 0.55−

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0.62 (m, 4H), 0.26−0.29 (m, 2H), −0.05−0.18 (m, 10H), −0.23-(−)0.19 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 135.0, 129.9, 69.5, 22.1, 21.6, 21.1, 20.3, 18.9, 10.5, 9.0, 6.3; MS (CI) *m*/*z* 393 $(M + H)^+$. HRMS (CI) calcd for $C_{25}H_{29}O_4$: $(M + H)^+$ 393.2066, found: $(M + H)^+$ 393.2066; Anal. Calcd. for $C_{25}H_{28}O_4$: C, 76.50; H, 7.19. Found: C, 76.36; H, 7.28; Crystal data for **23**: $C_{25}H_{28}O_4$, M = 392.5, monoclinic, $P2_1$ (no. 4), a = 9.852(1), b = 10.659(1), c = 10.526(1) Å, β = 98.77(1)°, V = 1092.4(2) Å^3, Z = 2, D_c = 1.193 g cm^{-3}, μ(Cu−Kα) = 6.37 cm^{-1}, F(000) = 420, T = 293 K; clear hexagonal plates, 0.93 × 0.33 × 0.30 mm, 1920 independent measured reflections; refinement based on F^2 to give R_1 = 0.055, wR_2 = 0.148 for 1821 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \le 128°$] and 263 parameters. The absolute structure was assigned by internal reference to the known chirality of the pentacyclopropyl chain.

Coronane 27. Macrolactone **27** was obtained as a colorless oil from diester **26** in 70% yield (44 mg) as described for **22**: R_f 0.63 (hexanes: EtOAc 4:1); $[\alpha]^{25}_D$ = −44.1 (*c* 2.2, $CHCl_3$); IR (film) 1724 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (s, 2H), 7.94−7.97 (m, 2H), 7.61−7.66 (m, 2H), 4.88 (dd, 2H, J = 5.0, 11.3 Hz), 3.62 (dd, 2H, J = 9.7, 11.3 Hz), 1.25−1.34 (m, 2H), 0.52−0.62 (m, 4H), 0.30−0.49 (m, 12H), 0.19−0.27 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 133.4, 130.2, 129.1, 128.6, 128.5, 70.0, 22.2, 21.7, 21.7, 20.0, 17.3, 10.8, 10.6, 10.0, 9.4; MS (CI) *m*/*z* 523 $(M + H)^+$; HRMS (CI) calcd for $C_{35}H_{39}O_4$: $(M + H)^+$ 523.2848, found: $(M + H)^+$ 523.2846. Anal. Calcd for $C_{35}H_{38}O_4$: C, 80.43; H, 7.33. Found: C, 80.27; H, 7.30.

Coronane 32. Compound **32** was obtained as white crystals from **31** in 90% yield (45.7 mg) as described for **22** after chromatography (hexanes: EtOAc 5:1): mp 146−149 °C (Et_2O); R_f 0.63 (hexanes: EtOAc 5:1); IR ($CHCl_3$) 1712 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, 4H, J = 8.3 Hz), 7.23 (d, 4H, J = 8.2 Hz), 4.80 (dd, 2H, J = 4.3, 11.3 Hz), 4.09 (s, 2H), 3.44 (t, 2H, J = 11.0 Hz), 0.96−1.05 (m, 2H), 0.82−0.89 (m, 2H), 0.46−0.52 (m, 2H), 0.36−0.44 (m, 4H), 0.32−0.35 (m, 2H), 0.03−0.12 (m, 4H), −0.03−0.02 (m, 2H), −0.24 (t, 2H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 146.3, 130.0, 128.9, 128.8, 68.5, 41.9, 20.7, 19.6, 18.9, 17.8, 17.7, 9.4, 9.1, 7.7; MS (CI) *m*/*z* 500 $(M + NH_4)^+$, 483 $(M + H)^+$; HRMS (CI) calcd for $C_{32}H_{35}O_4$: $(M + H)^+$ 483.2535, found $(M + H)^+$ 483.2541. Anal. Calcd for $C_{32}H_{34}O_4$: C, 79.63; H, 7.11. Found: C, 79.86; H, 7.03; Crystal data for **32**: $C_{32}H_{34}O_4$, M = 482.6, monoclinic, $P2_1$ (no. 4), a = 5.655(1), b = 12.154(2), c = 19.727(2) Å, β = 90.46(1)°, V = 1355.6(3) Å^3, Z = 2, D_c = 1.182 g cm^{-3}, μ(Cu−Kα) = 6.07 cm^{-1}, F(000) = 516, T = 293 K; clear blocks, 0.30 × 0.27 x 0.27 mm, 2344 independent measured reflections; refinement based on $F2$ to give $R1$ = 0.098, $wR2$ = 0.271 for 1392 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \le 127°$] and 325 parameters. The absolute structure was assigned by internal reference to the known chirality of the pentacyclopropyl chain.

Coronane 34. Diol **4** (16.1 mg, 61.6 μmol) and pyridine (13.3 μL, 163.8 μmol) in dry CH_2Cl_2 (20 mL) were added dropwise with stirring to chloride **33** (25 mg, 81.9 μmol) in dry CH_2Cl_2 (60 mL). After 24 h, the solvent was removed under reduced pressure, and the product was purified by chromatography (CH_2Cl_2:MeOH 90:1) to give **34** (18.7 mg, 62%) as a white solid: mp 116−118 °C (hexanes and CH_2Cl_2); R_f 0.25 (CH_2Cl_2:MeOH 90:1); $[\alpha]^{25}_D$ = +54 (*c* 1.41, $CHCl_3$); IR (film) 1715 cm^{-1}; UV−vis ($CHCl_3$:MeOH 3:1) λ_{max} (log ϵ): 242.7 (2.03), 249.9 (1.73), 281.7 (1.56) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (s, 4H), 7.97 (s, 2H), 4.54 (dd, 2H, J = 7.7, 11.2 Hz), 4.20 (dd, 2H, J = 6.2, 11.2 Hz), 1.42 (m, 2H), 0.78 (m, 2H), 0.68 (m, 2H), 0.32−0.57 (m, 10H) 0.03−0.15 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 149.1, 145.6, 137.3, 130.5, 128.2, 123.9, 70.3, 22.8, 21.8, 21.5, 19.1, 17.5, 11.3, 10.3, 9.9; MS (EI) *m*/*z* 494 ($M^{+\bullet}$); HRMS (EI) calculated for $C_{31}H_{30}N_2O_4$: ($M^{+\bullet}$) 494.2205 found: ($M^{+\bullet}$) 494.2193. Anal. Calcd for $C_{31}H_{30}N_2O_4$: C, 75.28; H, 6.11; N, 5.66. Found: C, 75.06; H, 6.15; N, 5.51; Crystal data for **34**: $C_{31}H_{30}N_2O_4 \cdot H_2O$, M = 512.6, monoclinic, $P2_1$ (no. 4), a = 7.034(1), b = 35.773(2), c = 11.172(1) Å, β = 104.13(1)°, V = 2725.9(2) Å^3, Z = 4 (there are two crystallographically independent molecules in the asymmetric unit), D_c = 1.249 g cm^{-3}, μ(Cu−Kα) = 6.86 cm^{-1}, F(000) = 1088, T = 293 K; clear platy needles, 0.63 × 0.43 × 0.07 mm, 4598 independent measured reflections; refinement based on F^2 to give R_1 = 0.046, wR_2 = 0.116 for 3961 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \le 128°$] and 686 parameters. The absolute structure was assigned by internal reference to the known chirality of the pentacyclopropyl chain.

Coronane 36. Compound **36** was obtained from **35** (80 mg, 284.4 μmol) in CH_2Cl_2 (80 mL), **4** (15 mg, 56.8 μmol) and pyridine (92 μL, 1.14 mmol) in CH_2Cl_2 (20 mL) as described for **34** and was purified by chromatography (CH_2Cl_2:MeOH 30:1) to give **36** (19 mg, 71%) as a white solid: mp 141−142 °C (hexanes); R_f 0.29 (CH_2Cl_2:MeOH 30:1); $[\alpha]^{25}_D$ = −3.5 (*c* 0.38, $CHCl_3$); IR (film) 1727 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.02 (d, 2H, J = 4.9 Hz), 8.45 (s, 2H), 7.99 (d, 2H, J = 4.9 Hz), 4.83 (dd, 2H, J = 4.7, 11.4 Hz), 3.65 (t, 2H, J = 10.7 Hz), 1.16 (m, 2H), 0.68 (m, 2H), 0.14−0.54 (m, 14H) 0.07 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 157.5, 151.2, 139.2, 123.0, 121.4, 70.4, 20.9, 20.8, 20.5, 20.4, 17.4, 9.4, 9.3, 9.0; MS (CI) *m*/*z* 471 $(M + H)^+$; HRMS (CI) calculated for $C_{29}H_{31}N_2O_4$: $(M + H)^+$ 471.2284 found: $(M + H)^+$ 471.2285. Anal. Calcd for $C_{29}H_{30}N_2O_4$: C, 74.02; H, 6.43; N, 5.95. Found: C, 73.99; H, 6.46; N, 5.97; Crystal data for **36**: $C_{29}H_{30}N_2O_4$, M = 470.6, tetragonal, $P4_3$ (no. 78), $a = b$ = 11.006(1), c = 41.345(2) Å, V = 5008.5(3) Å^3, Z = 8 (there are two crystallographically independent molecules in the asymmetric unit), D_c = 1.248 g cm^{-3}, μ(Cu−Kα) = 6.69 cm^{-1}, F(000) = 2000, T = 293 K; clear needles, 0.53 × 0.30 × 0.30 mm, 4216 independent measured reflections; refinement based on F^2 to give R_1 = 0.043, wR_2 = 0.107 for 3611 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \le 128°$] and 632 parameters. The absolute structure was assigned by internal reference to the known chirality of the pentacyclopropyl chain.

(1*R*,3*S*,4*R*,6*S*,7*R*,9*S*,10*R*,12*S*,13*R*,15*S*)-1-[(*tert*-Butyldimethylsilyloxy)methyl]-15-ethenyl-quinquecyclopropane (37). Dess−Martin reagent (116 mg, 0.274 mmol) was added to a mixture of **6** (86 mg, 0.228 mmol) and pyridine (37 μL, 0.556 mmol) in CH_2Cl_2 (3 mL). After stirring for 1.5 h, a mixture of saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ was added at 0 °C, and the mixture was extracted with Et_2O (20 mL). The organic layer was washed with saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), and concentrated in vacuo. Chromatography (hexanes:Et_2O 95:5) gave the corresponding aldehyde which was dissolved in THF (2 mL) and added to a solution of methylenetriphenylphosphorane [prepared in situ from methyltriphenylphosphonium bromide (135 mg, 0.378 mmol) and *t*-BuOK in THF (1M; 0.4 mL, 0.4 mmol)] in THF (5 mL) at 0 °C. After stirring for 1 h at room temperature, saturated aqueous NH_4Cl was added, the mixture was extracted with Et_2O, dried (Na_2SO_4), and evaporated in vacuo. Chromatography (hexanes:Et_2O 97:3) gave **37** (74 mg, 87%) as a colorless oil: R_f 0.55 (hexanes:EtOAc 20:1); $[\alpha]^{25}_D$ = −164.1 (*c* 1.0, $CHCl_3$); IR (film) 1636, 1254, 1089, 837 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.31−5.43 (m, 1H), 5.00 (dd, 1H, J = 1.7, 17.0 Hz), 4.82 (dd, 1H, J = 1.7, 10.2 Hz), 3.39−3.48 (m, 2H), 1.13−1.18 (m, 1H), 0.91 (s, 9H), 0.83−0.87 (m, 1H), 0.64−0.75 (m, 2H), 0.42−0.60 (m, 8H), 0.18−0.29 (m, 2H), 0.06 (s, 6H), 0.04−0.13 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 111.1, 66.7, 30.3, 26.0, 22.3, 21.3, 19.6, 18.6, 18.5, 18.4, 18.3, 18.2, 18.1, 11.8, 8.3, 8.2, 8.1, 7.8, −5.1; MS (CI) *m*/*z* 390 $(M + NH_4)^+$; HRMS (CI) calculated for $C_{24}H_{44}NOSi$: $(M + NH_4)^+$ 390.3192 found: $(M + NH_4)^+$ 390.3192. Anal. Calcd for $C_{24}H_{40}$-OSi: C, 77.36; H, 10.83. Found: C, 77.14; H, 10.84.

(1*R*,3*S*,4*R*,6*S*,7*R*,9*S*,10*R*,12*S*,13*R*,15*S*)-15-Ethenyl-1-quinquecyclopropanemethanol (38). Bu_4NF in THF (1M; 1.288 mL, 1.288 mmol) was added to quinquecyclopropane **37** (240 mg, 644 μmol) in THF (5 mL). The mixture was stirred at room temperature for 1 h when Et_2O (5 mL) and saturated aqueous NH_4Cl (3 mL) were added. The mixture was stirred for a further 5 min, and 1 N HCl (5 mL) was added, and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (hexanes:EtOAc 3:1) gave alcohol **38** (0.164 g, 97%) as colorless crystals: mp 38 °C (hexanes and Et_2O); R_f 0.38 (hexanes:EtOAc 3:1); IR ($CHCl_3$) 1633, 1032, 928, 897 cm^{-1}; ^{1}H NMR

(300 MHz, $CDCl_3$) δ 5.32−5.42 (m, 1H), 5.00 (dd, 1H, J = 1.7, 17.0 Hz), 4.81 (dd, 1H, J = 1.7, 10.2 Hz), 3.35−3.46 (m, 2H), 1.09−1.18 (m, 1H), 0.78−0.88 (m, 2H), 0.67−0.77 (m, 1H), 0.41−0.59 (m, 8H), 0.24−0.29 (m, 2H), 0.02−0.12 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 111.1, 66.9, 22.3, 21.2, 19.8, 18.6, 18.4, 18.3, 18.1, 18.0, 11.8, 8.3, 8.2, 8.1, 7.8; MS (CI) *m*/*z* 276 $(M + NH_4)^+$, 258 $(M)^+$; HRMS (CI) calcd for $C_{18}H_{30}NO$: $(M + NH_4)^+$ 276.2327, found: $(M + NH_4)^+$ 276.2320. Anal. Calcd for $C_{18}H_{26}O$: C, 83.66; H, 10.15. Found: C, 83.57; H, 10.13.

(1*R*,3*S*,4*R*,6*S*,7*R*,9*S*,10*R*,12*S*,13*R*,15*S*)-15-(Ethenyl)-1-quinquecyclopropanemethyl 4-Ethenylbenzoate (42). DCC (68 mg, 0.33 mmol) and DMAP (10 mg, 0.08 mmol) were added to 4-ethenylbenzoic acid **39** (30 mg, 0.20 mmol) and alcohol **38** (45 mg, 0.174 mmol) in CH_2Cl_2 (6 mL), and the mixture was stirred overnight. H_2O (3 mL) was added, layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), concentrated in vacuo, and chromatographed (hexanes: EtOAc, 10:0 to 10:1) to provide ester **42** (65 mg, 96%) as a colorless oil: R_f 0.66 (hexanes: EtOAc 10:1); IR ($CHCl_3$) 1709 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, 2H, J = 8.3 Hz), 7.48 (d, 2H, J = 8.3 Hz), 6.77 (dd, 1H, J = 10.9, 17.6 Hz), 5.88 (d, 1H, J = 17.6 Hz), 5.40 (d, 1H, J = 10.9 Hz), 5.31−5.43 (m, 1H), 5.01 (dd, 1H, J = 1.7, 17.0 Hz), 4.81 (dd, 1H, J = 1.7, 10.2 Hz), 4.06−4.19 (m, 2H), 1.04−1.19 (m, 1H), 0.95−1.02 (m, 1H), 0.82−0.90 (m, 2H), 0.35−0.59 (m, 10H), 0.04−0.14 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 141.9, 136.1, 129.9, 129.7, 126.1, 116.4, 111.1, 68.9, 30.4, 22.3, 21.3, 19.0, 18.6, 18.4, 18.4, 18.1, 18.0, 16.0, 11.8, 8.8, 8.3, 8.2, 7.8; MS (FAB) *m*/*z* 388 $(M^{+\bullet})$; HRMS (FAB) calcd for $C_{27}H_{32}O_2$: $(M^{+\bullet})$ 388.2402, found: $(M^{+\bullet})$ 388.2377. Anal. Calcd for $C_{27}H_{32}O_2$: C, 83.45; H, 8.31. Found: C, 83.23; H, 8.34.

Coronane 45. Grubbs's catalyst **48** (18 mg, 20 mol %) was added to a solution of diene **42** (42.5 mg, 0.109 mmol) in PhMe (100 mL) and the mixture heated to reflux overnight. The solution was cooled and concentrated in vacuo, and the residue was suspended in hexanes and filtered through silica to provide a pale yellow solution. This solution was concentrated in vacuo and chromatographed (hexanes:Et_2O 20:1) to provide crude **45** as a white solid. Recrystallization from hexanes gave pure coronane **45** (23.9 mg, 45%) as colorless crystals; R_f 0.31 (hexanes:Et_2O 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, 2H, J = 8.3 Hz), 7.66 (d, 2H, J = 8.3 Hz), 6.40 (d, 1H, J = 11.3 Hz), 5.36 (dd, 1H, J = 8.0, 11.3 Hz), 5.02 (dd, 1H, J = 4.5, 10.9 Hz), 3.32 (t, 1H, J = 11.0 Hz), 1.73−1.79 (m, 1H), 1.08−1.16 (m, 1H), 0.97−1.01 (m, 2H), 0.81−0.86 (m, 1H), 0.71−0.76 (m, 1H), 0.65−0.69 (m, 1H), 0.57−0.62 (m, 1H), 0.36−0.44 (m, 3H), 0.29−0.34 (m, 1H), 0.16−0.22 (m, 2H), 0.05−0.16 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 142.5, 137.5, 129.6, 129.0, 128.7, 128.0, 69.1, 25.3, 23.0, 22.7, 22.0, 21.7, 20.9, 20.8, 19.6, 18.8, 18.4, 16.9, 11.3, 9.9, 8.1, 7.3; MS (CI) *m*/*z* 378 $(M + NH_4)^+$, 361 $(M + H)^+$; HRMS (CI) calcd for $C_{25}H_{29}O_2$: $(M + H)^+$ 361.2168, found: $(M + H)^+$ 361.2164. Anal. Calcd for $C_{25}H_{28}O_2$: C, 83.28; H, 7.83. Found: C, 83.05; H, 7.66; Crystal data for **45**: $C_{25}H_{28}O_2$, M = 360.5, monoclinic, $P2_1$ (no. 4), a = 5.379(1), b = 19.524(3), c = 10.077(1) Å, β = 102.60(1)°, V = 1032.7(3) Å^3, Z = 2, D_c = 1.159 g cm^{-3}, μ(Cu−Kα) = 5.57 cm^{-1}, F(000) = 388, T = 293 K; clear blocky needles, 0.83 × 0.17 × 0.17 mm, 1754 independent measured reflections; refinement based on F^2 to give R_1 = 0.088, wR_2 = 0.214 for 1135 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 128°$] and 244 parameters. The absolute structure was assigned by internal reference to the known chirality of the pentacyclopropyl chain.

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Supporting Information Available: Experimental procedures and characterization data for **17**, **19**, **21**, **25**, **26**, **29**, **30**, **31**, **43**, and **44**. Copies of ^{1}H NMR of **20** and **22** and X-ray data of **22**, **23**, **32**, **34**, **36**, and **45**. This material is available free of charge via the Internet at http://pubs.acs.org.

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