Molecular LEGO. 1. Substrate-Directed Synthesis via Stereoregular Diels-Alder Oligomerizations†

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Abstract: The diastereoselective synthesis and structural characterization of a wide range of wholly-synthetic cyclic and acyclic polyacene derivatives has been achieved. These novel compounds are notable for (i) their rigidity, (ii) their highly-ordered structures, and (iii) the high stereochemical precision which governs their formation. A key feature in the success of the synthetic methodology described is the development of a repetitive Diels-Alder reaction sequence in which three distinct levels of diastereoselectivity are expressed during each cycloaddition involving bisdiene and bisdienophilic building blocks, i.e., each cycloaddition occurs with treble diastereoselectivity. Both the bisdienes and bisdienophiles are based upon the (7-oxa)bicyclo[2.2.1]heptane ring system in which the stereoelectronic characteristics, that are inherent within this rigid bicyclic framework, are used to dictate their subsequent modes of reaction. Importantly, the bisdienes **7** and **18** exhibit different rates of mono- and bisaddition of dienophiles to their two exocyclic *s-cis*-butadiene units. Therefore, a rational, stepwise oligomerization procedure for the synthesis of [12]cyclacene derivatives has been employed in which sequential use is made of thermally-promoted and high pressure-promoted cycloadditions to assemble the desired molecular structures. The exceptionally high solubilities exhibited by many of these adducts in organic solvents have (i) assisted in their isolation and purification by chromatography, (ii) aided their structural characterization by spectroscopic techniques, and (iii) enhanced their potential for further synthetic elaboration. Extending the size of the bisdiene building block from **7** to **26** has allowed the synthesis of a family of undecacene derivatives which are capable of forming [14]cyclacene derivatives. The treble diastereoselectivity that is observed in each cycloaddition between the bisdiene and bisdienophilic building blocks is identified as a kinetically-controlled transition state phenomenon. Bond formation proceeds with the maximum staggering of the bonds under construction with respect to the vicinal bonds located at the bridgehead positions on the bisdienophiles and, subsequently, with the minimization of torsional strain within the rigid bicyclic framework of the dienophile in the transition state. The potential importance of these molecular beltlike compounds as precursors to a wide range of novel hydrocarbon molecules—such as the cyclacenes, the collarenes, and the beltenes—is illustrated by the synthetic progression from the [12]cyclacene derivative we have dubbed kohnkene **13** to [12]collarene **55**. Finally, it is suggested that, by extending the role played in the design processes of molecular structures to include information—such as stereoelectronic factors and pyramidalization—that is inherently present within certain structural types, both the controlled creation of chirality and the rapid assembly of highly-ordered three-dimensional molecular structures may be preprogramed.

Introduction

The advent[1] and rapid development[2] of supramolecular chemistry has served to focus the minds of synthetic chemists on methods for elaborating molecular architectures and for improving many aspects of molecular design, organization, and assembly of chemical compounds. The outcome of this effort has been the synthesis[3] of a wide range of molecular structures of very different structural types. These molecules usually incorporate special stereoelectronic features that (i) encourage the selective binding[4] of guest molecules and then often preside over the catalysis[5] of reactions on the bound species, (ii) increase the macroscopic expression[6,7] of a particular molecular recognition event, or (iii) allow the investigation of interfacial[8] and transport[9] phenomena. However, if the gap between these model systems and the well-known supramolecular information storage and expression systems—such as the nucleic acids, proteins, and glyco-

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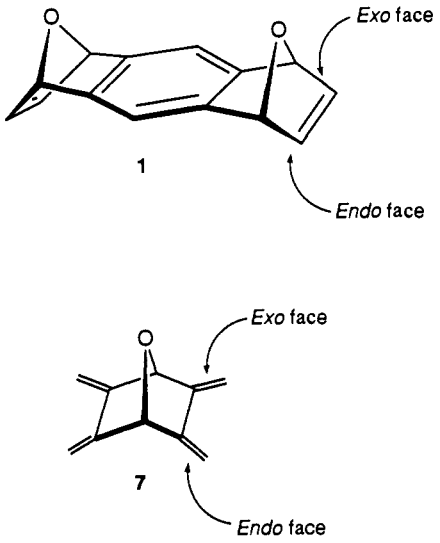
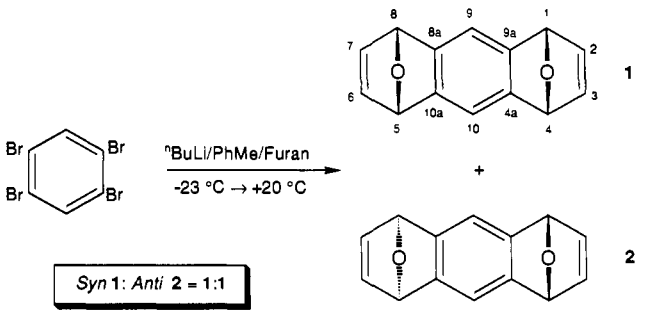


Figure 1. The concave and convex faces of both the Diels–Alder building blocks—the bisdienophile **1** and bisdiene **7**—render each compound structurally-capable of forming a closed macropolycyclic structure. The π-facial diastereoselectivities exhibited[12,13] in cycloadditions involving these species are such that Diels–Alder reaction occurs preferentially at the *exo*-face of the bisdienophile **1** and at the endo-face of the bisdiene **7**.

conjugates—is to be bridged successfully, techniques that will allow a rapid, but flexible, progression to be made from simple building blocks to complex molecular structures must be developed.[10]

With this goal in mind, synthetic studies based upon a repetitive Diels–Alder methodology involving bisdienes and bisdienophiles have much to commend[11] them. However, in those cases where stereogenic centers are created during the cycloaddition process, some stereochemical uncertainties associated with isomer production and consequent oligomer/polymer heterogeneity at a configuration level is often encountered. By the utilization of stereoelectronic information "preprogramed" into the π-systems of bicyclic bisdienophiles and bisdienes, we have shown[12] that they undergo successfully repetitive Diels–Alder reactions in a trebly diastereoselective[13] fashion at their diastereotopic π-faces. Not

Scheme I. Synthesis of the *syn*- and *anti*-Bisdienophiles, **1** and **2**, Respectively[a]



[a] Synthesis proceeds via the bisaryne equivalent generated from 1,2,4,5-tetrabromobenzene. Unambiguous confirmation of the relative configurations (i.e., syn and anti) of the endoxide bridges was provided by single crystal X-ray structural analyses.

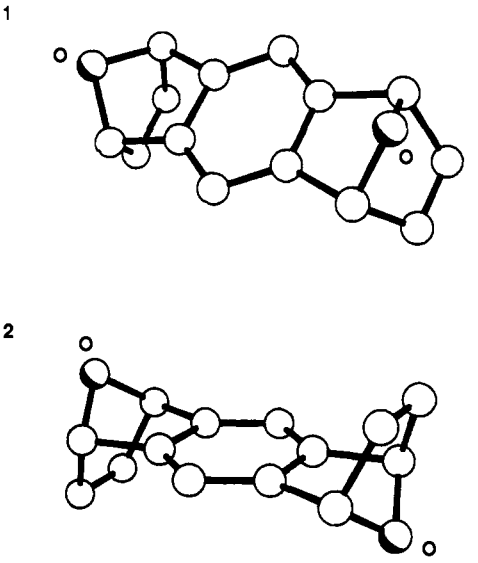


Figure 2. X-ray crystal structure of the *syn*- and *anti*-bisdienophiles, **1** and **2**, respectively. The concave/convex nature of the *syn*-bisdienophile **1** is clearly visible. A full structural characterization of these Diels–Alder building blocks was vital before their use in repetitive cycloadditions was aimed—as in the case of the *syn*-bisdienophile **1**—toward macropolycyclic compounds.

only is complete diastereoselectivity expressed with respect to each component but also, mutually, between the components themselves. This paper presents a blueprint for the design and synthesis of unnatural products that are substrate-directed, i.e., the relative stabilities of transition states dictate the outcome of the individual steps in a Diels–Alder reaction sequence which is subject to overall kinetic control.

Furthermore, macropolycyclic compounds such as **13** represent potential precursors of an intriguing range of novel hydrocarbons, particularly [12]cyclacene **57**, a beltlike compound in which the plane of the macropolycycle is orthogonal to the mean plane of the bent benzene rings—each of which is obliged to adopt boatlike conformations. Deformation of the benzene nucleus has already been demonstrated,[14] notably in the [*n*]paracyclophane series ($4 < n < 8$) amongst others. Tantalizing predictions,[15] relating to

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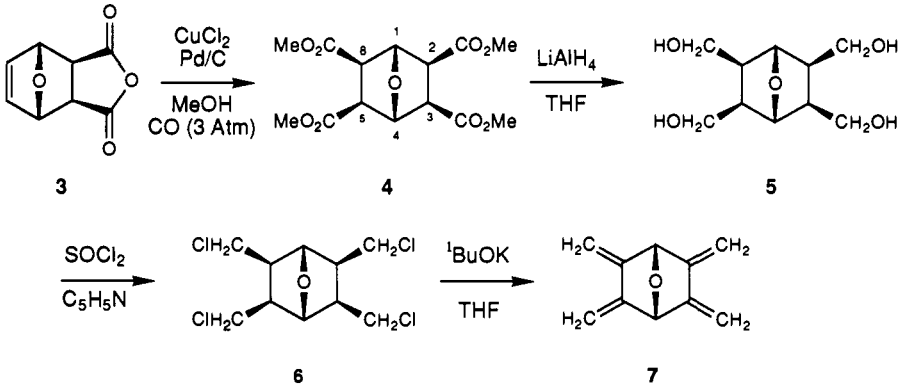
Scheme II. Synthesis of the Bisdiene 7[a]



3 4 5 6 7

[a] Carbomethoxylation of **3** affords the tetraester **4** with the all-exo configuration. The reaction sequence (**3** → **4** → **5** → **6** → **7**) can be performed on a large scale, thus providing access to significant quantities of **7**.

the physical and electronic properties of systems such as the [*n*]cyclacenes, make them potentially very important synthetic targets. The results described herein present the first stage of our research program directed toward the development of a rational, flexible synthetic approach to the design and production of complex unnatural products—an approach which is inherently substrate-directed.

Results and Discussion

Substrates as Directors of Reactivity and Selectivity. Observations from the recent literature[16-32] on the face selectivities that pertain during cycloadditions involving the π-systems associated with the 7-oxabicyclo[2.2.1]heptane framework suggested strongly to us that the stereoelectronic features, which characterize this particular rigid bicyclic structure, could provide an ideal means of controlling stereochemically the Diels–Alder reactivity of (i) the endocyclic dienophilic units present in the bisdienophile **1** such that cycloaddition occurs preferentially at the exo faces of its π-systems and (ii) the exocyclic *s-cis*-butadiene units present in the bisdiene **7** such that cycloaddition occurs preferentially at the endo faces of its π-systems.

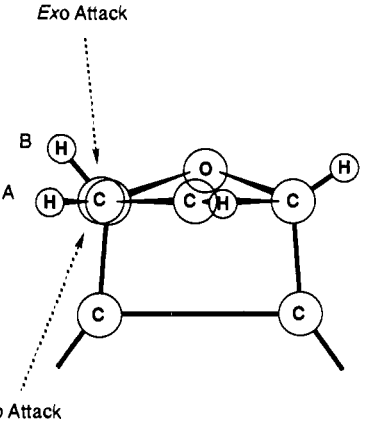


Figure 3. A Newman projection along a selected carbon (olefinic)—carbon (bridgehead) bond in a structural fragment of the *syn*-bisdienophile **1**. This shows the torsional interaction associated with the olefinic (A) and the adjacent bridgehead (B) hydrogen atoms. More important in the context of the trebly diastereoselective Diels–Alder reaction is the staggering of the bonds under construction at the exo face and the vicinal bonds located on the bridgehead carbon atoms.

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(32) Perturbations that lead to small distortions in the ground state can result in large energy differences between competing transition states for reaction. See, for example: (a) Bürgi, H.-B.; Dunitz, J. D. *Acc. Chem. Res.* **1983**, *16*, 153–161. (b) Bürgi, H.-B.; Dunitz, J. D. *J. Am. Chem. Soc.* **1987**, *109*, 2924–2926.

The exo face diastereoselectivity and exceptional reactivity exhibited during the cycloadditions of dienophilic units, such as those present in the bisdienophile **1**, have been discussed[16,17] at some length in the literature. The synthesis (Scheme I) of **1** proceeds via the trapping in situ of the bisaryne equivalent[18] generated by lithiation of 1,2,4,5-tetrabromobenzene at −23 °C. Approximately equal amounts of the two diastereoisomeric adducts **1** and **2** were isolated after silica gel chromatography. Unambiguous assignments[19] of the relative configurations of **1** and **2** were provided by X-ray crystallography. The solid state structures, shown in Figure 2, confirm that the diastereoisomer **1** has the syn configuration[19b] whilst **2** has the anti configuration.[19a,20]

Both molecular orbital calculations[17,21-24] and solid state structural analyses[25] have indicated a significant degree of pyramidalization of the alkene units in bisdienophiles, such as **1**. The distortion[26] of the olefinic hydrogen atoms in the direction of the endo face has been attributed[17,21,22,24,28,29] to the minimization of the torsional strain interaction between these particular hydrogen atoms and those situated on the adjacent bridgehead carbon atoms. One immediate consequence of this pyramidalization is to effect a disrotatory tilt of the π_x-orbitals situated on the olefinic carbon atoms. This action induces[17,29-31] an asymmetry in the frontier orbital electron densities associated with the diastereotopic π-faces. As a consequence, the electron density on the endo face is decreased and concomitantly that on the exo face is increased. However, the allylic torsional interaction, which is evident as pyramidalization in the ground state, can exhibit a more profound effect[32] in the transition state of a cycloaddition. As illustrated in the Newman projection in Figure 3, the transition state for exo face bond formation is associated with an almost perfect staggering of the bonds under construction relative to those sited on the vicinal bridgehead carbon atoms. This situation does not pertain for bond formation at the endo face. By contrast, it occurs via an almost completely eclipsed geometry.[33] Therefore, in the light of both experimental observations[28-31] and the theoretical rationalizations,[17,21,24] the Diels–Alder reactivity of the bisdienophile **1** could be predicted to proceed via cycloaddition at the exo faces of its π-systems.

The choice of **7** as the bisdiene building block was also made in the knowledge[34-45] of (i) the preferential cycloaddition to the endo faces of the exocyclic *s-cis*-butadiene units in **7** and similar systems and (ii) the differential rates observed for mono- and bisadditions to the π-systems in **7**. Thus, a controlled oligomerization sequence could be established in which thermally-promoted cycloadditions would generate monoadducts of **7** and high pressure-promoted cycloadditions would generate subsequently the bisadducts. The synthesis (Scheme II) of the bisdiene **7** followed that reported[34] by Vogel. Carbomethoxylation[35] of **3** proceeds with simultaneous esterification of the anhydride ring to afford the all-exo tetraester **4** with high diastereoselectivity.[36] Reduction ($LiAlH_4$) of **4** to the tetraol **5**, followed by its chlorination ($SOCl_2$/pyridine), afforded the tetrachloride **6** in good yield. The bisdiene **7** could be obtained in quantitative yield by treatment of **6** with base (^{t}BuOK) to effect the necessary β-elimination.

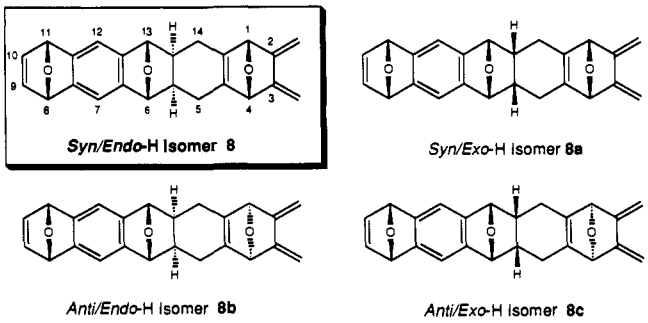


Figure 4. The four diastereoisomeric 1:1 adducts that are attainable in principle from the reaction of the bisdienophile **1** with the bisdiene **7**. The stereoelectronic control operating during the reaction is such that only the syn/endo-H diastereoisomer **8** has been detected. The "remote" stereochemical descriptors—syn and anti—refer to the relative configurations of the endoxide bridges across the newly-formed cyclohexene ring. The "close" stereochemical descriptors—exo and endo—refer to the relative configurations adopted by the hydrogen atoms at the ring junctions associated with the newly-created chiral centers.

The endo face diastereoselectivity exhibited by exocyclic *s-cis*-butadiene units, such as those present in **7**, as a result of the stereoelectronic influences inherent within the rigid 7-oxabicyclo[2.2.1]heptane framework, has been the subject[37-42] of much discussion and investigation both theoretically and experimentally. The most compelling rationalization for the endo face cycloaddition exhibited by **7** is that offered[41,43] by Paquette and Gleiter. Their calculations have revealed that a significant interaction occurs between the σ-orbitals of the bicyclic framework and the diene π_s (SHOMO) orbital. The disrotatory tilt of the π_x-orbital on the exocyclic methylene carbon atoms induced by such an interaction increases the frontier orbital electron density on the exo face while concomitantly decreasing that on the endo face of the molecule. Approach of a dienophile to the exo face of such an exocyclic *s-cis*-butadiene unit is then associated with a strongly-destabilizing antibonding interaction[44] which develops between the dienophile HOMO and the modified π_s orbital (SHOMO) of the diene. Therefore, the endo face diastereoselectivity exhibited[45] during cycloadditions experienced by **7**, and related systems, can be interpreted successfully as a kinetically-controlled interaction between the occupied orbitals of the reactants.

Although understanding and predicting the stereoselectivities exhibited in chemical reactions is a difficult and delicate activity,[46]

(33) The difference in the free energies of competing transition states with perfectly eclipsed and staggered geometries has been calculated[28] to be approximately 6 kcal mol^{-1}.

(34) (a) Vogel, P.; Florey, A. *Helv. Chim. Acta* **1974**, *57*, 200–204. (b) Mahaim, C.; Carrupt, P.-A.; Hagenbuch, J.-P. *Helv. Chim. Acta* **1980**, *62*, 1149–1157.

(35) James, D. E.; Stille, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 1810–1823.

(36) The relative configuration of **4**, which has been deduced to be all-exo by ^{1}H NMR spectroscopy, was established unequivocally by X-ray crystallography. See: Kohnke, F. H.; Stoddart, J. F.; Slawin, A. M. Z.; Williams, D. J. *Acta Crystallogr.* **1988**, *C44*, 736–737.

(37) Vogel, P. *Stereochemistry and Reactivity of Systems Containing π-Electrons*; Watson, W. H., Ed.; Verlag-Chemie: Deerfield Beach, FL, 1983; pp 147–201.

(38) (a) Tornare, J.-M.; Vogel, P. *J. Org. Chem.* **1984**, *49*, 2510–2511. (b) Metrel, J.-L.; Vogel, P. *Helv. Chim. Acta* **1985**, *68*, 334–337.

(39) Paquette, L. A. *Stereochemistry and Reactivity of Systems Containing π-Electrons*; Watson, W. H., Ed.; Verlag-Chimie: Deerfield Beach, FL, 1983; pp 41–73.

(40) (a) Avenati, M.; Hagenbuch, J.-P.; Mahaim, C.; Vogel, P. *Tetrahedron Lett.* **1980**, 3167–3170. (b) Avenati, M.; Carrupt, P.-A.; Quarroz, D.; Vogel, P. *Helv. Chim. Acta* **1982**, *65*, 188–203. (c) Mahaim, C.; Vogel, P. *Helv. Chim. Acta* **1982**, *65*, 866–886.

(41) (a) Paquette, L. A.; Carr, R. V. C.; Böhm, M. C.; Gleiter, R. *J. Am. Chem. Soc.* **1980**, *102*, 1186–1188. (b) Böhm, M. C.; Carr, J. V. C.; Gleiter, R.; Paquette, L. A. *J. Am. Chem. Soc.* **1980**, *102*, 7218–7228. (c) Paquette, L. A.; Carr, R. V. C.; Arnold, E.; Clardy, J. *J. Org. Chem.* **1980**, *45*, 4907–4913. (d) Paquette, L. A.; Charumilind, P.; Kravetz, T. M.; Böhm, M. C.; Gleiter, R. *J. Am. Chem. Soc.* **1983**, *105*, 3126–3135. (e) Paquette, L. A.; Schaefer, A. G.; Blount, J. F. *J. Am. Chem. Soc.* **1983**, *105*, 3642–3649. (f) Paquette, L. A.; Green, K. E.; Hsu, L.-Y. *J. Org. Chem.* **1984**, *49*, 3650–3652.

(42) (a) Paquette, L. A.; Bellamy, F.; Böhm, M. C.; Gleiter, R. *J. Org. Chem.* **1980**, *45*, 4913–4922. (b) Paquette, L. A.; Carr, R. V. C.; Charumilind, P.; Blount, J. F. *J. Org. Chem.* **1980**, *45*, 4922–4926.

(43) Studies of the π-facial diastereoselectivity of fused fulvene systems, in which their is most likely no distortion of the exocyclic positions reveal the same propensity for endo face reactivity. See: Paquette, L. A.; Kravetz, T. M.; Böhm, M. C.; Gleiter, R. *J. Org. Chem.* **1983**, *48*, 1250–1257.

(44) The calculated magnitude of this effect is a destabilization of exo face reaction of 3–4 kcal mol^{-1}. See: Gleiter, R.; Paquette, L. A. *Acc. Chem. Res.* **1983**, *16*, 328–334.

(45) The only consistent exceptions to endo face attack are highly reactive dienophiles such as benzynes, DMAD, and TCNE. See, for example: (a) Tornare, J.-M.; Vogel, P.; Pinkerton, A. A.; Schwarzenbach, D. *Helv. Chim. Acta* **1985**, *68*, 2195–2215. (b) Metrel, J.-L.; Lauterwein, J.; Vogel, P. *Helv. Chim. Acta* **1986**, *69*, 1287–1309. (c) Burnier, G.; Schwager, L.; Vogel, P. *Helv. Chim. Acta* **1986**, *69*, 1310–1322.

(46) Menger, F. M.; Sherrod, M. J. *J. Am. Chem. Soc.* **1990**, *112*, 8071–8075.

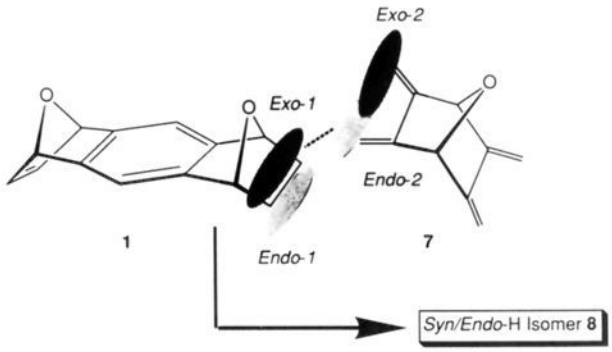
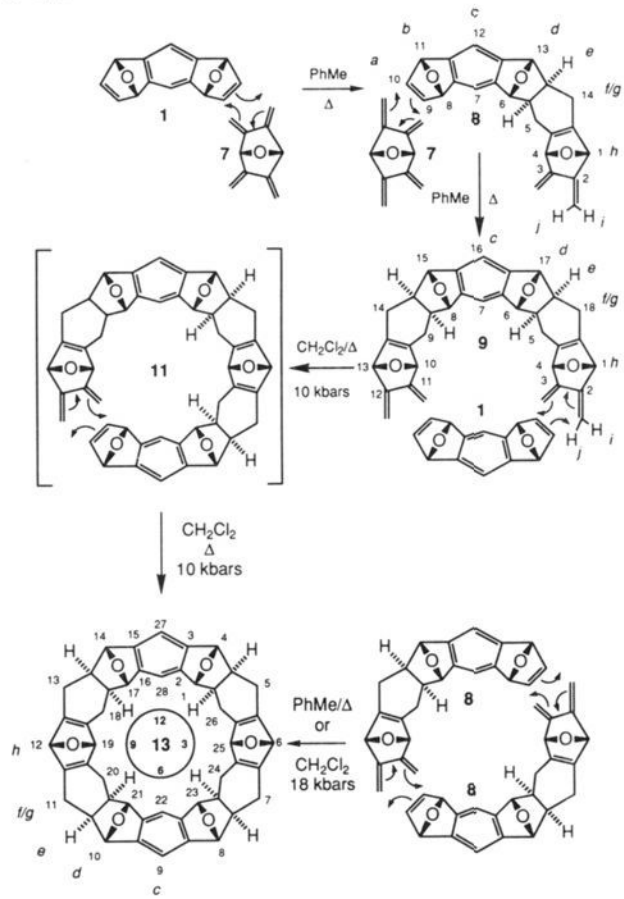


Figure 5. By uniting the factors which govern the reactivities and selectivities of the building blocks **1** and **7**, a qualitative understanding of the origin of the diastereoselectivities exhibited in their mutual reaction can be acquired. Combining π-faces of high (dark) and low (light) electron densities in a manner that allows reaction at the exo face (exo-1) of the bisdienophile **1** and at the endo face (endo-2) of the bisdiene **7** generates the observed 1:1 adduct **8**, with syn/endo-H stereochemistry across the newly-formed cyclohexene ring via a syn/exo-1/endo-2 transition state. The only other mode by which this stereochemistry could be attained would be by reaction between exo faces on both the bisdienophile **1** and the bisdiene **7**, i.e., via a syn/exo-1/exo-2 transition state. Apart from bringing two π-faces of high electron density together, this transition state would have to encounter very serious steric interactions between the two endoxide bridges in the two reactants. Steric interactions presumably disfavor the only other transition state—viz. the anti/exo-1/endo-2 one—that would allow reaction to take place between the exo face (exo-1) of the bisdienophile **1** and the endo face (endo-2) of the bisdiene **7**. Note that the "1" and "2" following exo and endo refer to "ene" and "diene", respectively.

the arguments detailed for the bisdienophile **1** and the bisdiene **7** are such that the stereochemical outcome of their mutual cycloaddition is totally predictable. The presence of diastereotopic π-faces in both **1** and **7** means that there are four possible cycloaddition products (Figure 4) which are attainable through eight discrete transition states. The "close" stereochemical descriptors—exo and endo—refer to the configuration adopted by the methine hydrogen atoms at the ring junction associated with the newly-created chiral centers. The "remote" stereochemical descriptors—syn and anti—refer to the relative configurations adopted by the endoxide bridges across the newly-formed cyclohexene rings during cycloaddition. In both **1** and **7**, the exo faces of the respective π-systems are associated with increased frontier electron densities. One would expect reaction to occur between faces of high and low electron density, leading to either an exo-1/endo-2 or an endo-1/exo-2 interaction. Incorporating the strong preferences for cycloadditions at the exo faces of the bisdienophile **1** and cycloadditions at the endo faces of the bisdiene **7** would favor (Figure 5) strongly the former exo-1/endo-2 interaction and, consequently, the generation of the syn/endo-H stereochemistry across the newly-formed cyclohexene rings during cycloaddition. Thus, the stereoselectivity which is exhibited during these particular cycloadditions can be viewed on three distinct levels. These are the diastereoselectivities associated with (i) the diastereotopic π-faces (exo-1 versus endo-1) of the bisdienophile **1**, (ii) the diastereotopic π-faces (exo-2 versus endo-2) of the bisdiene **7**, and (iii) the relative orientations—syn or anti—adopted by the endoxide bridges during the cycloaddition. The unique combination of three acts of high diastereoselectivity being expressed simultaneously during one concerted reaction has encouraged us to refer[12,13] to the cycloaddition between **1** and **7**, and many of the cycloadditions discussed throughout this paper, as exhibiting treble diastereoselectivity. Thus, the stereochemical outcome of the reaction between **1** and **7** would appear to be dictated only by the stereoelectronic information inherent within the structural frameworks of the starting materials.

The Substrate-Directed Synthesis of [12]Cyclacene Derivatives. The series of Diels–Alder reactions leading toward the synthesis[12,13] of the [12]cyclacene derivative **13** is summarized in Scheme III. Thermally-promoted cycloadditions between equimolar amounts

Scheme III. Molecular LEGO Set Used for the Synthesis of the [12]Cyclacene Derivative **13**[a]



[a] We have dubbed it kohnkene. Both the thermally-promoted and high pressure-promoted cycloadditions exhibit the same treble diastereoselectivity. The clock-face shown on structure **13** provides a convenient frame of reference for the discussion of its structural features.

of the bisdienophile **1** and the bisdiene **7** afforded[47] exclusively only one of the four possible diastereoisomeric 1:1 adducts, i.e., **8**, in 24% yield and only one of the ten possible diastereoisomeric 2:1 adducts, i.e., **9**, in 61% yield. Use of 2.5 molar equiv of **7** increases the yield of the more synthetically useful 2:1 adduct **9** to over 80%. In the case of both **8** and **9**, the cycloadditions have proceeded to generate exclusively the predicted syn/endo-H stereochemistry across all of the newly-formed cyclohexene rings. The overall C_s molecular symmetry proposed for the 1:1 adduct **8** is supported by the observation of (i) 10 signals in the ^{1}H NMR spectrum for all 10 sets of heterotopic hydrogen atoms and (ii) 11 resonances in the broadband-decoupled ^{13}C NMR spectrum, with two of them overlapping at 143.1 ppm, for the 12 types of heterotopic carbon atoms. The endo-H stereochemistry assigned to the methine hydrogen atoms, 5a,13a-H, is consistent with the observation of a sharp singlet in the ^{1}H NMR spectrum of **8** at δ 4.91 for the adjacent bridgehead hydrogen atoms, 6,13-H, which shows no observable coupling constant between these hydrogen atoms and the vicinal methine hydrogen atoms.

Confirmation of the structure of **8** was provided by X-ray crystallography of a single crystal of the monoadduct **10** formed between **8** and anthracene. Positive-ion FABMS gave a peak at m/z 535 for $[M + H]^+$ for the anthracene adduct **10**. The X-ray crystal structure analysis revealed (Figure 6) the presence of two crystallographically-independent molecules, **10a** and **10b**. However, both have the same relative configuration, i.e., one that is consistent with the original 1:1 adduct **8** having the syn/endo-H

(47) Kohnke, F. H.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 892–894.

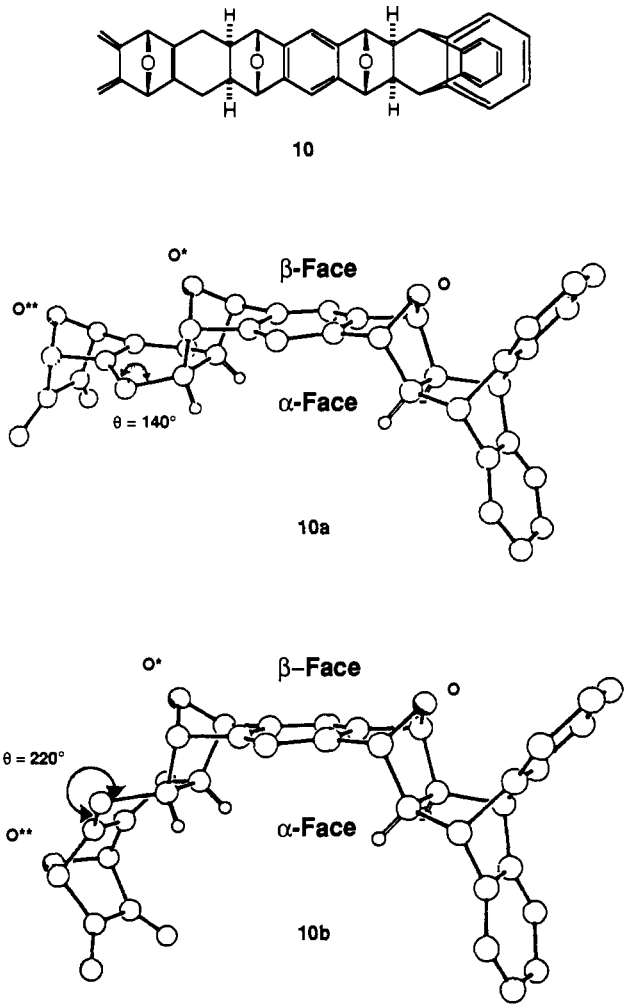


Figure 6. The X-ray structures of both crystallographically-independent molecules of the anthracene adduct **10** of the 1:1 adduct **8**. Both molecules **10a** and **10b** are consistent with the original 1:1 adduct **8** having the syn/endo-H stereochemistry across its one cyclohexene ring, and, therefore, being the product of a trebly diastereoselective Diels–Alder reaction. The significant solid state difference between the molecules **10a** and **10b** is the conformation of the cyclohexene boat folded toward the β-face in **10a** and the α-face in **10b**.

configuration.[48] Clearly, the 1:1 adduct **8**, which assumes a conformation similar to that observed (Figure 6) for molecule **10b** in the solid state structure of the anthracene adduct **10**, possesses the stereoelectronic requirements for a successful head-to-tail dimerization.

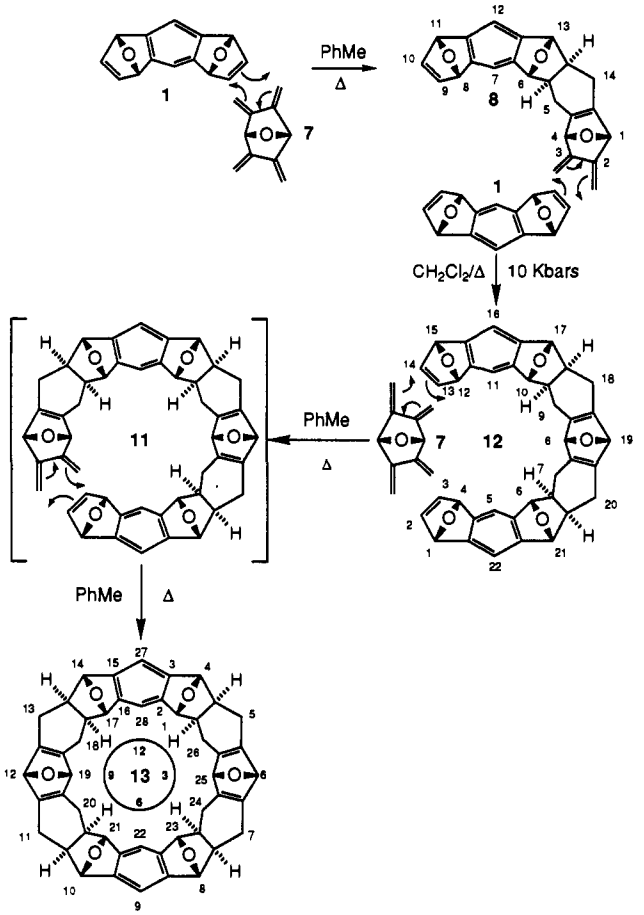
In both diastereoisomeric conformations **10a** and **10b**, the bridging O** atoms are tilted a few degrees (4–6°) more toward the exocyclic *s-cis*-butadiene unit than they are toward the endocyclic double bond. In related situations, this tilting has been attributed[37,40] to the repulsive interaction between the π-electron density associated with the endocyclic π-bond, which is pyramidalized onto the exo face, and the syn-related oxygen lone pair. The extra strain required to restore the endoxide bridge to a more symmetrical position during cycloaddition to the remaining diene unit has been invoked[37,40] to account for the reduced reactivity of the exocyclic *s-cis*-butadiene units in compounds such as **8** and **9** with respect to that exhibited in the first cycloaddition to compounds such as the bisdiene **7**. It should also be noted that anthracene reacts with the dienophilic units in **1**, **2**, and **8** in a highly diastereoselective manner. In both diastereoisomeric conformations **10a** and **10b**, the second pair of methine hydrogen atoms, 5a,17a-H, adopt the endo configuration as a consequence of the cycloaddition of **8** with anthracene. This observation emphasizes further that cycloaddition at the exo face is the preferential mode of reaction for dienophilic units such as that present in **8**. The endo-H configurations at C-5a,17a and at C-8a,14a in **10a** and **10b** are also evident from an inspection of the ^{1}H NMR spectrum of the anthracene adduct **10**. Sharp singlets are observed at δ 4.86 and 4.87 for 6,7-H and 8,15-H, respectively. It is interesting to note that, in the ^{1}H NMR spectra of the bisadducts between anthracene and (i) the syn isomer **1** and (ii) the anti isomer **2**, singlets were reported,[18] both resonating at δ 4.80. These observations indicate that, in the case of both **1** and **2**, the Diels–Alder reactions proceed with high exo diastereoselectivity to afford only the bisadducts with endo-H configurations. The reported ^{13}C NMR spectroscopic data,[18] which lists 11 resonances for both bisadducts, is also consistent with their molecular symmetries, i.e., C_{2v} and C_{2h} for **1** and **2**, respectively.

Having established the relative stereochemistry of the 1:1 adduct **8** beyond any doubt, the evidence suggesting that the 2:1 adduct **9** is formed directly from **8**, with the same treble diastereoselectivity and hence the syn/endo-H stereochemistry across both cyclohexene rings, is considerable. The C_{2v} molecular symmetry which is thereby implied for the 2:1 adduct **9**, with the syn/endo-H–syn/endo-H configuration, is supported fully by the observation of (i) eight signals in the ^{1}H NMR spectrum for the eight sets of heterotopic hydrogen atoms and (ii) nine signals in the broadband-decoupled ^{13}C NMR spectrum for the nine types of heterotopic carbon atoms. The observation in the ^{1}H NMR spectrum of a sharp singlet for the bridgehead hydrogen atoms, 6,8,15,17-H, implies that the adjacent methine hydrogen atoms, 5a,8a,14a,17a-H, have the endo-H configuration. The fact that the relative configurations of the endoxide bridges in the 2:1 adduct **9** are syn is implied by the success of the subsequent macropolycyclization of this 2:1 adduct **9** with a further equivalent of the bisdienophile **1** to afford the [12]cyclacene derivative **13**. The observation that the thermally-promoted Diels–Alder reactions between **1** and **7** are arrested so completely upon the production of the 2:1 adduct **9** illustrates an important feature of the reactivity exhibited by the bisdiene **7**. This compound is reported[34,37,38,49] to undergo mono- and bisaddition at very different rates, especially during cycloadditions with moderately reactive dienophiles such as benzoquinone and methyl vinyl ketone. Rate differences of the order of 100–300 times, in favor of monoaddition over the subsequent addition of a second dienophile to the remaining diene unit, have been documented in the literature.[34,37,38,49] This rate difference is believed to arise[37] as a result of the introduction, during monoaddition, of the endocyclic double bond (C_{4a}–C_{14a}) diammetrically-opposed to the remaining *s-cis*-butadiene unit. The major consequence of this differential reactivity exhibited by the two diene units in **7** is that a stepwise repetitive Diels–Alder oligomerization sequence can be envizaged in which alternate use is made of mild and forcing conditions to promote the respective cycloadditions. Although thermally-promoted bisaddition to the two diene units in **7** can be effected, the high temperatures necessary to achieve any significant conversion to products lead to degradation of both the starting materials and the products. This outcome is illustrated (Scheme III) during the thermally-promoted cyclodimerization carried out with **8** to yield **13**. In a solution of xylene heated under reflux, the cyclodimerization of the 1:1 adduct **8** to **13** proceeds[47] in an isolated yield of 3.5%. Cyclodimerization of **8** under 18 kbars pressure at 50 °C proceeds much more successfully to give the product **13** in 47% yield after 72 h. However, the synthetic route of choice toward the preparation of **13** is that which proceeds via the 2:1 adduct **9**. Macropoly-

(48) The only significant structural difference between the molecules **10a** and **10b** is in the conformations of their substituted cyclohexene rings. Both these rings adopt boat conformations, but, whereas in molecule **10a** the hinge angle (θ) in the six-membered ring is 140°, in the molecule **10b** the hinge angle in the six-membered ring is 220°. The consequence of these two opposite modes of folding is to contract the O*–O** distance in molecule **10a** with respect to that observed in molecule **10b**. Furthermore, the effect of this difference in geometries is to impart upon molecule **10b** an increased overall curvature to that exhibited by molecule **10a**.

(49) (a) Carrupt, P.-A.; Vogel, P. *Tetrahedron Lett.* **1979**, 4533–4536. (b) Bessiere, Y.; Vogel, P. *Helv. Chim. Acta* **1980**, *63*, 232–243. (c) Tornare, J.-M.; Vogel, P. *Helv. Chim. Acta* **1985**, *68*, 1069–1077.

Scheme IV. An Alternative Molecular LEGO Set for the Synthesis of the [12]Cyclacene Derivative, Kohnkene **13**[a]



[a] High pressure is required to accelerate the cycloaddition of the bisdienophile **1** to the 1:1 adduct **8** to afford the nonacene derivative **12**. However, macropolycyclization of **12** with the bisdiene **7** proceeds under thermally-promoted conditions to afford the [12]cyclacene derivative **13**.

cyclization of **9** can be achieved[47] by reaction with a molar equivalent of the bisdienophile **1** in a high pressure-promoted cycloaddition, that presumably affords the intermediate **11** which immediately undergoes a rapid intramolecular ring-closure. The overall yield of this high pressure-promoted macropolycyclization process is 36%. The isolation of no identifiable products other than kohnkene **13** from this reaction dictates that these high pressure-promoted cycloadditions between **1** and the 2:1 adduct **9** are proceeding with the same treble diastereoselectivity as the thermally-promoted reactions between **1** and the bisdiene **7**. In another different approach to **13**, the 1:1 adduct **8** was reacted under high pressure with 1 molar equiv of the bisdienophile **1** to afford (Scheme IV) the nonacene derivative **12**. Macropolycyclization of this 2:1 adduct **12** was then achieved by reaction with 1 molar equiv of the bisdiene **7** under only thermally-promoted conditions. Whereas in previous cases, high pressure was required to facilitate bisaddition to either **7** or **9**, the intramolecular nature of the final cycloaddition coupled with the favorable juxtaposition of the reactive termini immediately prior to ring closure in the proposed intermediate **11** are clearly features that favor macropolycyclization.

The observation of (i) six signals in the ^{1}H NMR spectrum of **13** for the six sets of heterotopic hydrogen atoms and (ii) seven signals in the broadband-decoupled ^{13}C NMR spectrum of **13** for the seven types of heterotopic carbon atoms is consistent with the high molecular symmetry (D_{2h}) of the macropolycycle. The constitution of **13** was confirmed by the observation in the positive-ion FABMS of a molecular ion at 713 for $[M + H]^+$. The lack of any significant fragmentation pattern for this molecular ion is undoubtedly a consequence of the high stability associated

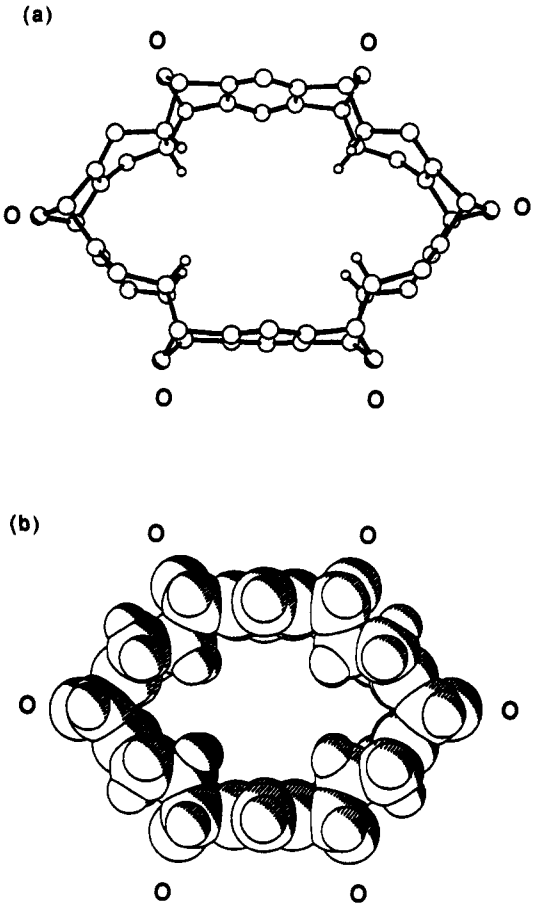


Figure 7. The X-ray crystal structure of the [12]cyclacene derivative that we have dubbed kohnkene **13**. The closed macropolycyclic structure is clearly visible in the (a) ball-and-stick and (b) space-filling representations.

with the macropolycyclic structure. Final confirmation of the macropolycyclic structure of **13** was provided[47,50] by the X-ray crystallographic analysis (Figure 7). Since the molecule of **13** possesses a crystallographic center of symmetry, the two benzene rings situated opposite to each other across the cavity at 6 and 12 o'clock with an interplanar separation of 7.9 Å are necessarily parallel. The four sets of *endo*-methine hydrogen atoms associated with the benzo-fused 7-oxabicyclo[2.2.1]heptane ring systems are directed toward the center of the cavity of the molecule, which is flanked on its outer rim by the six oxygen atoms. The interplanar separation (7.9 Å) of the aromatic rings is of the appropriate magnitude to accommodate an aromatic guest molecule positioned orthogonally with respect to the two aromatic rings at 6 and 12 o'clock. Indeed, stabilizing edge-to-face interactions[51] could be invoked between the aromatic portions of the cavity and an electron-deficient aromatic guest molecule. Although ^{1}H NMR spectroscopic studies have not provided any evidence for such an interaction, piezoelectric quartz crystal detection of nitrobenzene using **13** as the detector coating have demonstrated[52] a very sensitive, reversible, and selective response.

(50) The very high instability of the crystals of kohnkene **13** can be explained by examination of the packing of the unit cell contents. The macropolycyclic rings do not form continuous channels in the crystal. Instead, they are arranged in parallel edge-to-face layers with 12 disordered chloroform molecules sandwiched in between them in 16 discrete orientations. Upon removal of the crystals from their mother liquor, these molecules of solvation are lost spontaneously, and the crystalline form collapses to that of an amorphous powder. The instability of the crystals is such that crystallographic data had to be collected, whilst they were maintained under an atmosphere of chloroform.

(51) (a) Gould, R. O.; Gray, A. M.; Taylor, P.; Walkinshaw, M. D. *J. Am. Chem. Soc.* **1985**, *107*, 5921–5927. (b) Burley, S. K.; Petsko, G. A. *Science* **1985**, *229*, 23–28.

(52) Elmosalamy, M. A. F.; Moody, G. J.; Thomas, J. D. R.; Kohnke, F. H.; Stoddart, J. F. *Anal. Proc.* **1989**, *26*, 12–15.

Table I. Comparison of the ^1H NMR Chemical Shifts[a] of Structurally-Related Hydrogen Atoms[b]

^1H	a	b	c	d	e	f/g	h	i	j
8	7.02	5.63	7.08	4.91	1.82 to 1.89	2.23 to 2.63	4.97	5.08	4.98
	(dd, 2 H)	(dd, 2H)	(s, 2 H)	(s, 2 H)	(m, 2 H)	(m, 4 H)	(br s, 2 H)	(s, 2 H)	(s, 2 H)
9			6.99	4.92	1.78 to 1.86	2.28 to 2.68	4.97	5.09	4.99
	(s, 2 H)	(s, 4 H)	(m, 4 H)	(m, 8 H)	(br s, 4 H)	(s, 4 H)	(s, 4 H)		
13			6.98	4.89	1.60 to 1.62	2.25 to 2.70	5.08		
			(s, 4 H)	(s, 8 H)	(m, 8 H)	(m, 16 H)	(s, 4 H)		
21			6.90	4.80	1.86 to 1.92	2.20 to 2.60	3.10		
			(s, 4 H)	(s, 8 H)	(m, 8 H)	(m, 16 H)	(t, 4 H)		
52			6.84	5.09	1.02 to 1.08	2.62 to 2.64	6.69		
			(s, 4 H)	(s, 8 H)	(m, 8 H)	(m, 16 H)	(br s, 4 H)		

[a] The spectra were recorded at ambient temperature on either a Bruker AM 250 or WH 400 spectrometer using Me_4Si as the internal standard. The solvent in all cases was $CDCl_3$. [b] This provides a useful means of assessing the structural similarities and differences of the Diels–Alder oligomerization adducts. The alphabetic descriptors correspond with those shown on the schemes throughout the [12]cyclacene derivative series.

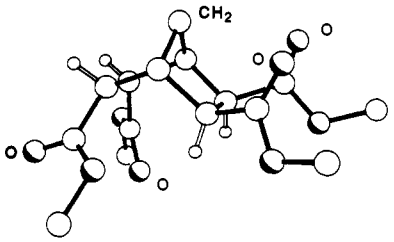


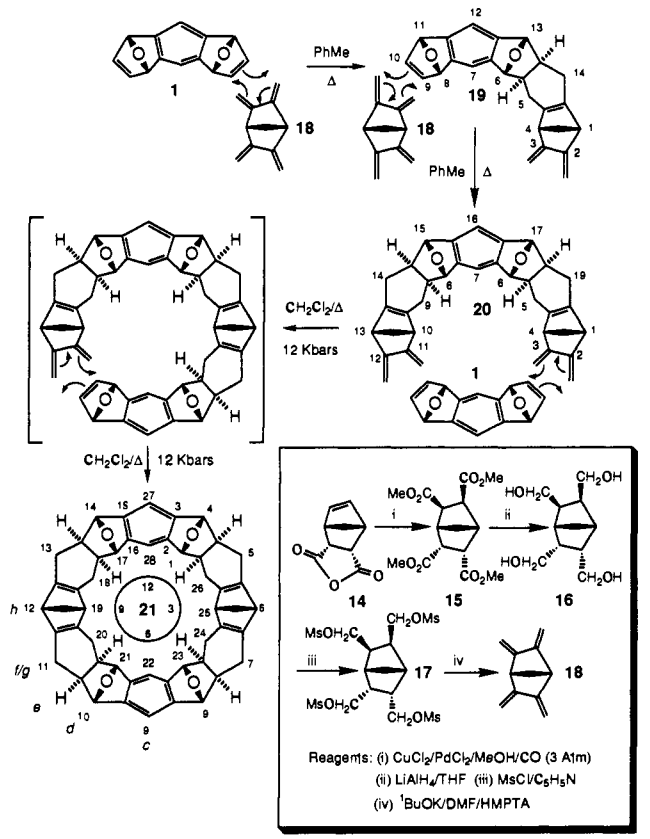
Figure 8. The X-ray crystal structure of the exo/endo-tetraester **15**.

Adding a Methylene-Bridged Bisdiene to the Molecular LEGO Set. Preliminary attempts to introduce transition metals into the cavity of kohnkene **13** were unsuccessful because the endoxide bridges in the six-membered rings at 3 and 9 o'clock are susceptible to deoxygenation. Therefore, we introduced norbornadiene units into **13** at 3 and 9 o'clock. The stereoelectronic repercussions of such a change were also of great interest to us. The synthesis of the methylene-bridged bisdiene **18** followed that described by Vogel[53] and involved (Scheme V) a sequence analogous (Scheme II) to that used for the synthesis of **7**. By contrast with the *all-exo*-anhydride, which is obtained from the reaction between maleic anhydride and furan, the Diels–Alder reaction between maleic anhydride and cyclopentadiene affords[53] the *endo*-anhydride **14**.

Carbomethoxylation of **14** using a stoichiometric amount of $PdCl_2$ afforded the exo/endo tetraester **15**. As in the carbomethoxylation of **3**, addition to the double bond occurs diastereoselectively at the exo face. The exo/endo configuration of **15** was confirmed[54] by an X-ray crystallographic analysis on a single crystal of **15** grown by slow concentration of a solution of the tetraester at room temperature. Reduction of **15** ($LiAlH_4$) afforded the tetraol **16**, which was subsequently mesylated ($MsCl/C_5H_5N$) to give the tetramesylate **17**. Treatment of **17** with base (^{t}BuOK) afforded the bisdiene **18**.

Thermally-promoted cycloaddition between the bisdienophile **1** and 2 molar equiv of the methylene-bridged bisdiene **18** afforded (Scheme V) only a single 1:1 adduct **19** (15%) and a single 2:1 adduct **20** (66%). In both cases, spectroscopic structural characterization (Table I) of the adducts was confirmed by X-ray crystallographic analysis (Figure 9). The solid state structures confirm the retention of the syn/endo-H stereochemistry generated

Scheme V. The Molecular LEGO Set Used for the Synthesis of the [12]Cyclacene Derivative **21**[a]



[a] The replacement of the oxygen bridges in **7** by a methylene bridge to give the bisdiene **18** has no effect upon the treble diastereoselectivity exhibited in the subsequent cycloadditions. The synthesis of the methylene-bridged bisdiene **18**, which is illustrated in the box, follows a procedure similar to that employed for the synthesis of the oxygen-bridged bisdiene **7**.

across each newly-formed cyclohexene ring in the cycloadditions between **1** and **18**. As noted previously (Scheme III) for **9**, the reactivity of the bisdiene **18** is such that the thermally-promoted cycloaddition process between **1** and **18** is arrested completely upon production of the 2:1 adduct **20**. However, high pressure-promoted macropolycyclization between **20** and a further equivalent of the bisdienophile **1** affords the [12]cyclacene derivative **21** in 38%

(53) Florey, A.; Vogel, P. *Helv. Chim. Acta* **1975**, *58*, 1488–1492.
(54) Giuffrida, D.; Kohnke, F. H.; Mathias, J. P.; Stoddart, J. F.; Slawin, A. M. Z.; Watts, D. J.; Williams, D. J. *Acta Crystallogr.* Submitted for publication.

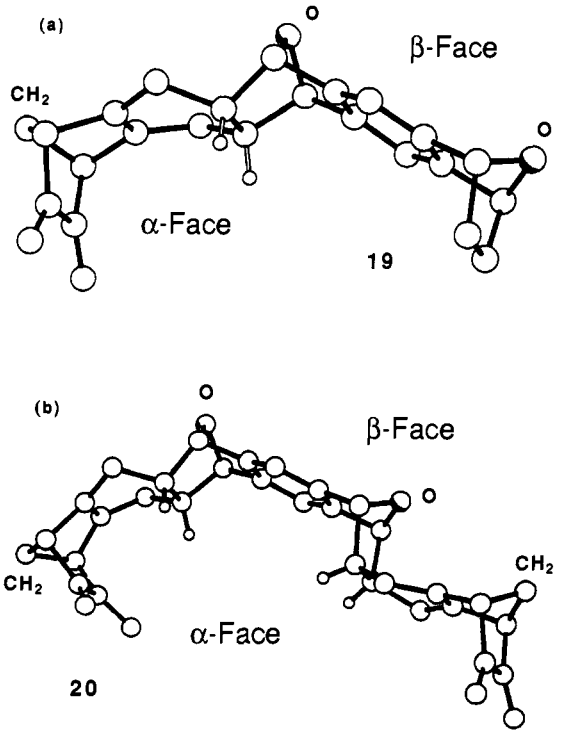


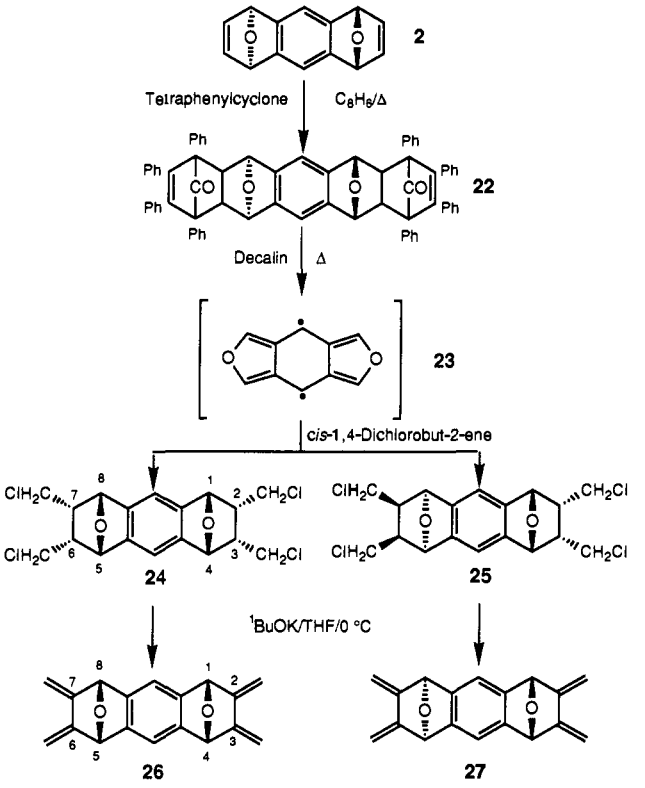
Figure 9. X-ray crystal structure of (a) the 1:1 adduct **19** and (b) the 2:1 adduct **20** incorporating the methylene-bridged bisdiene **18**. The stereochemistry across each newly-formed cyclohexene ring is clearly syn/endo-H as the result of a trebly diastereoselective Diels–Alder reaction.

yield. The structural characterization of **21** was aided by the high molecular symmetry (D_{2h}) it shares with the original [12]cyclacene derivative **13**. The observation of (i) seven signals in the ^{1}H NMR spectrum for the seven sets of heterotopic hydrogen atoms, (ii) eight signals in the broadband-decoupled ^{13}C NMR for the eight types of heterotopic carbon atoms, and (iii) the lack of any signals for either the olefinic or *s-cis*-butadiene reactive termini is consistent with the closed macropolycyclic structure **21**. The constitution of **21** was confirmed by the observation in the positive-ion FABMS of a molecular ion at m/z 709 for $[M + H]^+$. The lack of any significant fragmentation of the molecular ion once again supports the high stability attributed to the closed macropolycyclic structure. The successful synthesis of the [12]cyclacene derivative **21** from the bisdienophile **1** and the methylene-bridged bisdiene **18** demonstrates that the treble diastereoselectivity exhibited in the cycloadditions between **1** and **7** is retained in the repetitive Diels–Alder reactions between **1** and **18** outlined in Scheme V.

Extending the Bisdiene. The power of any synthetic methodology lies ultimately in the possibilities it creates for the synthesis of a wide range of different molecular structures. The success of the repetitive Diels–Alder oligomerization process for the rapid assembly of the [12]cyclacene derivatives **13** and **21** raises many questions concerning the flexibility and generality of such a synthetic approach toward the preparation of a family of macropolycyclic structures. With macropolycyclic adducts containing more than 12 laterally-fused six-membered rings in mind, the extended bisdiene **26** was identified as a suitable Diels–Alder building block.

Employing a literature procedure,[55] the pentacene derivative **22** was decomposed thermolytically[56] to generate (Scheme VI) the bisisobenzofuran **23**. The (presumed) planar nature of this bisisobenzofuran **23** renders the relative configuration of the endoxide bridges in the starting material of no stereochemical consequence subsequently. Trapping of the extremely reactive

Scheme VI. Synthetic Strategy Used To Prepare the Syn and Anti Extended Bisdienes **26** and **27**, Respectively[a]



[a] As a consequence of the (presumed) planar nature of the bisisobenzofuran intermediate **23**, the *anti*-bisdienophile **2** can be used as the original starting material. Trapping of **23** with 2 molar equiv of *cis*-1,4-dichlorobut-2-ene in situ affords an equimolar mixture of the *syn*- and *anti*-tetrachlorides, **24** and **25**, respectively. All the relative configurations have been confirmed by solid state structural analyses.

bisdiene equivalent **23** with 2 molar equiv of *cis*-1,4-dichlorobut-2-ene in situ afforded[57] a diastereoisomeric mixture of *syn*- and *anti*-tetrachlorides, **24** and **25**, respectively, in equimolar ratios in a combined isolated yield of 65%. The observation in the ^{1}H NMR spectrum of both **24** and **25** of a coupling constant (J = 4 Hz) between the signals for the bridgehead hydrogen atoms 1,4,5,8-H and the vicinal methine hydrogen atoms 2,3,6,7-H indicates[58] that the latter have adopted the exo configuration during the cycloadditions, i.e., the chloromethyl groups occupy endo positions. This observation indicates that there is a high measure of diastereoselectivity inherent within the reactions between **23** and the dienophile with respect to each furan ring, which leads to the chloromethyl groups occupying the endo configuration exclusively. Confirmation of these stereochemical assignments, in addition to the unambiguous determination of the relative configurations of the endoxide bridges in both **24** and **25**, was provided[59] by X-ray crystallographic analysis of single crystals of **24** and **25**. The *syn*- and *anti*-bisdienes, **26** and **27**, were obtained by stereospecific elimination of the diastereoisomers **24** and **25**, respectively, in quantitative yields. X-ray crystallographic analyses (Figure 10) confirmed[60] the assignment of the relative syn and anti configurations to **26** and **27**, respectively.

The presence of sp^2 character in the bonds diammetrically opposite the diene units in **26** and **27** is associated with a reduction

(55) (a) Luo, J.; Hart, H. *J. Org. Chem.* **1988**, *53*, 1341–1343. (b) Luo, J.; Hart, H. *J. Org. Chem.* **1989**, *54*, 1762–1764.

(56) For a discussion of isobenzofurans and their reactivity, see: Rodrigo, R. *Tetrahedron* **1988**, *44*, 2093–2135.

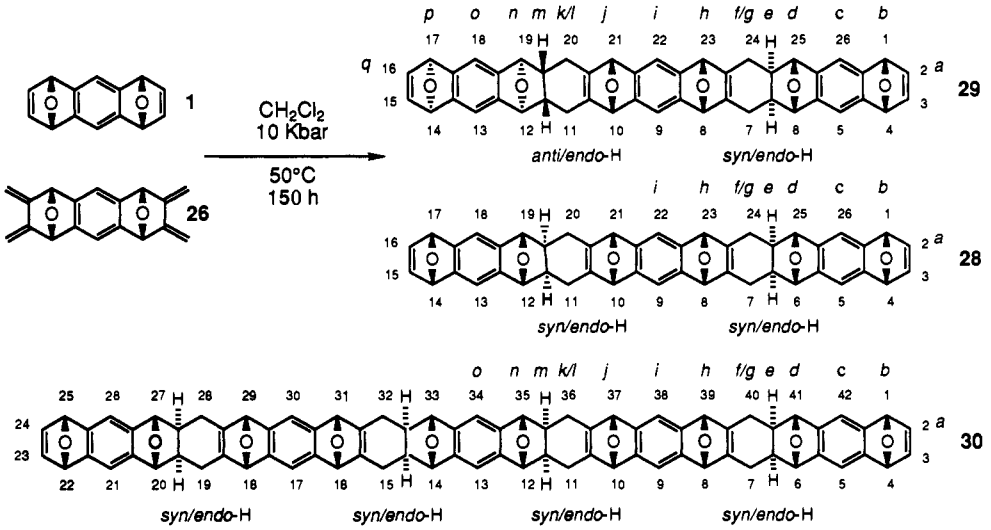
(57) Ashton, P. R.; Isaacs, N. S.; Kohnke, F. H.; Mathias, J. P.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1258–1261.

(58) (a) Luo, J.; Hart, H. *J. Org. Chem.* **1987**, *52*, 4833–4835. (b) Wittig, G.; Reuther, W. *Ann. Chem.* **1972**, *761*, 20–24. (c) Takeshita, H.; Mori, A.; Sano, S.; Fujise, Y. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1661–1662.

(59) Kohnke, F. H.; Mathias, J. P.; Stoddart, J. F.; Slawin, A. M. Z.; Williams, D. J. *Acta Crystallogr.* **1990**, *C46*, 1043–1046.

(60) (a) Kohnke, F. H.; Mathias, J. P.; Stoddart, J. F.; Slawin, A. M. Z.; Watts, D. J.; Williams, D. J. *Acta Crystallogr.* **1990**, *C46*, 1046–1049. (b) Kohnke, F. H.; Mathias, J. P.; Stoddart, J. F.; Slawin, A. M. Z.; Watts, D. J.; Williams, D. J. *Acta Crystallogr.* **1990**, *C46*, 1049–1052.

Scheme VII. High Pressure-Promoted Reaction of the *syn*-Bisdienophile **1** and the Extended *syn*-Bisdiene **26**[a]



[a] This reaction has afforded three isolated products. The major product of the reaction was the 2:1 adduct **28** with syn/endo-H stereochemistry across both of the newly-formed cyclohexene rings. The isolation of a minor 2:1 isomer **29** with anti/endo-H–syn/endo-H stereochemistry suggests the existence of a second, less favorable, reaction pathway within the Diels–Alder oligomerization process. The gross conformation of the 3:2 adduct **30** is believed to be that of a "Swiss-roll-like" coil in which the terminal dienophilic units overlap with each other.

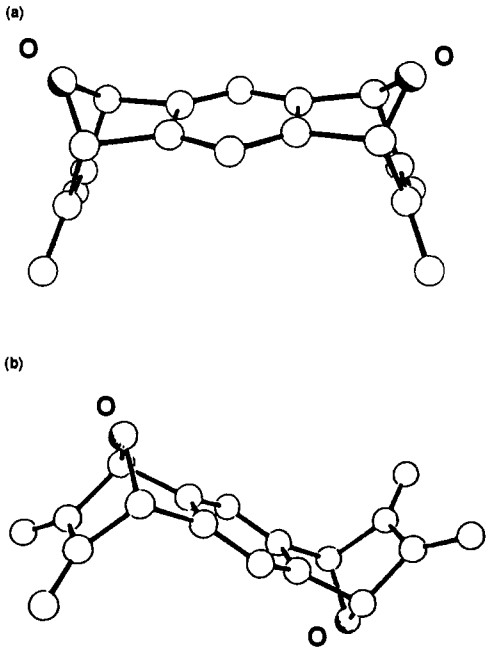


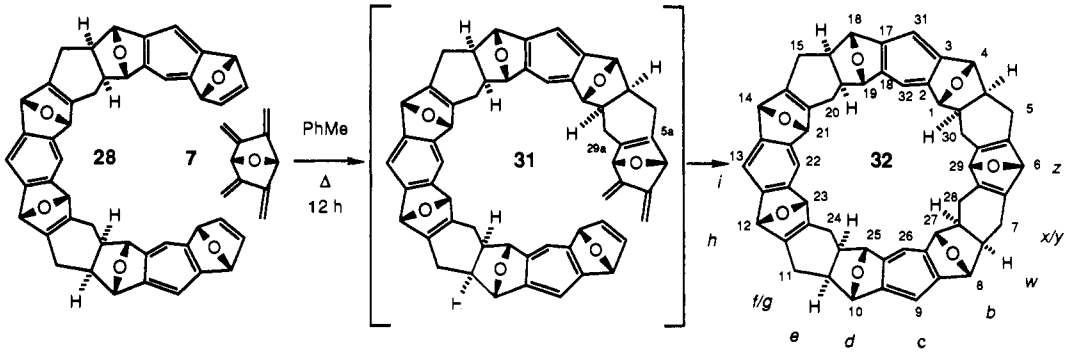
Figure 10. X-ray crystal structures of (a) the syn and (b) the anti extended bisdienes, **26** and **27**, respectively. The concave/convex nature of the *syn*-bisdiene **26** is clearly visible.

in their Diels–Alder reactivity as bisdienes. Consequently, high pressure was required to promote their cycloaddition with the *syn*-bisdienophile **1**. Reaction (Scheme VII) of **26** with 2 molar equiv of **1** in dichloromethane solution under 10 kbars of pressure afforded three products after silica gel chromatography. The major product of this reaction was characterized[57] as the 2:1 adduct **28**. The observation of (i) nine signals in the ^{1}H NMR spectrum for the nine sets of heterotopic hydrogen atoms and (ii) 12 resonances in the broadband-decoupled ^{13}C NMR spectrum for the 12 types of heterotopic carbon atoms are consistent with the C_{2v} molecular symmetry of the 2:1 adduct **28**. In particular, the presence of three different resonances in the ^{1}H NMR spectrum at δ 5.59, 5.32, and 4.90 corresponding to the bridgehead hydrogen atoms 1,4,14,17-H, 8,10,21,23-H, and 6,12,19,25-H respectively, reinforces our structural characterization of **28**. The observation of both a vicinal and allylic coupling constant in the signal centered on δ 5.59 ($J_{1,2}$, $J_{1,3}$ = 1.3 Hz) for 1,4,14,17-H confirms the presence of the dienophilic units at the termini of **28**. The lack of any multiplicity in the signals for the bridgehead hydrogen atoms 6,12,19,25-H dictates that the adjacent methine hydrogen atoms, 6a,11a,19a,24a-H, at the newly-formed ring junctions have adopted the endo configuration. Therefore, the high pressure-promoted cycloadditions between **1** and **26** exhibit the same treble diastereoselectivity observed in the syntheses of the [12]cyclacene derivatives **13** and **21**. The conversion of **28** into the [14]cyclacene derivatives **32**, **33**, and **37** subsequently provides further irrefutable evidence that the stereochemistry generated across the newly-formed cyclohexene rings in **28** is syn/endo-H.

Uniquely, the 2:1 adduct **28** is accompanied by a trace amount of another diastereoisomer that has been characterized[57] as the undecacene derivative **29**. The anti/endo-H stereochemistry present across one of the newly-formed cyclohexene rings in **29** must be a result of a second reaction pathway operating in the Diels–Alder oligomerization, wherein the mode of approach is exo with respect to both the diene and dienophilic units. This observation suggests that the stereoelectronic control which has operated previously on the π-systems of both the diene and dienophile has been relaxed with respect to one of the diene units in the extended bisdiene **26**. HPLC analysis of the crude reaction mixture reveals a ratio of 18:1 in favor of **28** over **29**. The lower molecular symmetry (C_s) associated with structure **29** is supported by the observation of (i) 17 signals in the ^{1}H NMR spectrum (see Table II) for the 17 sets of heterotopic hydrogen atoms, with six of these signals at δ 5.58, 5.56, 5.32, 5.31, 4.91, and 4.90 attributable to six discrete bridgehead hydrogen atom environments and (ii) 23 signals in the broadband-decoupled ^{13}C NMR spectrum for the 23 types of heterotopic carbon atoms. The retention of endo-H stereochemistry for the methine hydrogen atoms 6a,11a,19a,24a-H is confirmed by the observation in the ^{1}H NMR spectrum of no multiplicity in the signals at δ 4.91 and 4.90 for the bridgehead hydrogen atoms, 6,12,19,25-H. The observation in the positive-ion FABMS of a molecular ion at m/z 682 for $[M + H]^+$ confirms that the constitution of **29** is indeed identical to that of **28**. The origin of **29**—is it obtained as a result of a kinetically-controlled reaction pathway competing with that which produces **28**, or is thermodynamic control operating in the equilibration of diastereoisomers—is discussed later.

The final product isolated from the reaction between **1** and **26** under high pressure was characterized[57] as the 3:2 adduct **30**. The observation of molecular ions at m/z 1153 for $[M - H]^-$ by negative-ion FABMS and at m/z 1155 for $[M + H]^+$ by positive-ion FABMS confirm the constitution proposed for **30**. The C_{2v} molecular symmetry exhibited by **30** is consistent with the

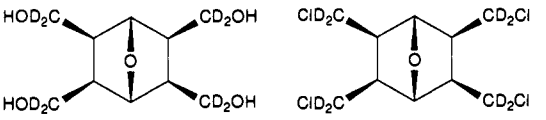
Scheme VIII[a]



[a] High pressure is not always necessary! Macropolycyclization of the 2:1 adduct **28** with the bisdiene **7** affords the [14]cyclacene derivative **32** in a remarkably facile thermally-promoted reaction. The acyclic 2:2 adduct **31** is presumably an intermediate. No trace of this compound has ever been detected. Although the final ring-closure will be accelerated as a consequence of its intramolecularity, some acceleration could also originate in the stereoelectronic complementarity of the substrates **7** and **28**.

observation of (i) 15 signals in the ^{1}H NMR spectrum (see Table II) for the 15 sets of heterotopic hydrogen atoms and (ii) 20 signals in the broadband-decoupled ^{13}C NMR spectrum for the 20 types of heterotopic carbon atoms. The presence of five discrete hydrogen bridgehead environments in **30** is indicated by the observation in the ^{1}H NMR spectrum of five signals at δ 5.42, 5.35, 5.32, 4.92, and 4.85 for the hydrogen atoms 1,4,22,25-H, 8,18,29,39-H, 10,16,31,37-H, 12,14,33,35-H, and 6,20,27,41-H, respectively. The signal centered upon δ 5.42 exhibits both a vicinal and allylic coupling constant ($J_{1,2}$, $J_{1,3}$ = 1.3 Hz), confirming the presence of the dienophilic groups at the termini of **30**. The lack of any multiplicity in the signals centered on δ 4.92 and 4.85 confers the endo configuration upon the methine hydrogen atoms adjacent to these bridgehead positions. These spectroscopic observations all support fully the assignment of syn/endo-H stereochemistry across each of the four newly-formed cyclohexene rings in the 3:2 adduct **30** and, therefore, the operation of treble diastereoselectivity throughout this Diels–Alder oligomerization sequence. The curvature that is inherent within the 19 laterally-fused six-membered rings that constitute the structure of **30** must result in some degree of mutual overlap between the opposite reactive termini of the molecule. Indeed, the appearance of the signal at lower frequencies by 0.36, 0.16, and 0.07 ppm for the hydrogen atoms 2,3,23,24-H, 1,4,22,25-H, and 5,21,26,42-H, respectively, suggests that **30** adopts a "Swiss roll-like" conformation wherein the six-membered rings at the termini of the oligomeric chain are brought into a close proximity, such that the hydrogen atoms identified above in the two laterally-fused six-membered rings at the ends of the oligomer come under the mutual influence of the shielding cones of the penultimate aromatic rings located symmetrically at the opposite termini of the molecule.

The degree of overlap suggested by these ^{1}H NMR spectroscopic observations on **30**, when taken together with the failure to isolate a [16]cyclacene derivative, either (i) directly from the high pressure-promoted cycloadditions between **1** and **26** or (ii) by reaction of the 2:1 adduct **28** with a further molar equivalent of the extended bisdiene **26**, indicates that the optimum ring size for a macropolycyclic structure incorporating **28** must be closer to 14 laterally-fused six-membered rings. Such a [14]cyclacene derivative resulted from the reaction of the 2:1 adduct **28** with the bisdiene **7**. Initially, we envisaged that this macropolycyclization might proceed by a formal two step mechanism (Scheme VIII) in which the intermolecular Diels–Alder cycloaddition between **7** and **28** is thermally-promoted, leaving the subsequent intramolecular ring-closure of **31** requiring high pressure promotion. However, to date no trace of the acyclic intermediate **31** has ever been detected during the thermally-promoted reaction between **7** and **28**. Instead, the [14]cyclacene **32** is isolated[57] directly from the thermally-promoted process in 78% yield without the need for high pressure. The remarkable acceleration of the final cycloaddition can be ascribed, at least in part, to its intramolecularity. However, probably of equal importance is the perfect stereoelectronic match between the reactive termini of the complementary substrates **7** and **28**, that renders them ideal reactive partners[61] and allows the bisdiene **7** to be inserted easily into place, yielding the [14]cyclacene derivative **32**. The observation of a molecular ion by positive-ion FABMS at m/z 829 for $[M + H]^+$, which exhibits no significant fragmentation pattern, is consistent with the macropolycyclic constitution proposed for **32**. The C_{2v} molecular symmetry of the [14]cyclacene derivative **32** is confirmed by the observation of (i) 12 signals in the ^{1}H NMR spectrum (see Table II) for the 12 sets of heterotopic hydrogen atoms and (ii) 15 signals in the broadband-decoupled ^{13}C NMR spectrum of 15 types of heterotopic carbon atoms. The lack of any multiplicity in the signals in the ^{1}H NMR spectrum at δ 5.31, 5.04, 4.92, and 4.87 associated with the bridgehead hydrogen atoms 12,14,21,23-H, 6,29-H, 10,16,19,25-H, and 1,4,8,27-H, respectively, indicates that the adjacent methine hydrogen atoms at the ring junctions can be assigned the endo configuration. It follows that the syn/endo-H stereochemistry has been generated across the newly-formed cyclohexene rings during both the high pressure-promoted and thermally-promoted cycloadditions leading to the preparation of **32**. The analogous [14]cyclacene derivatives **33** and **37** have been



34 **35**

prepared (Scheme IX) by reaction of the 2:1 adduct **28** with the methylene-bridged bisdiene **18** and the octadeuterated bisdiene **36**, respectively. The macropolycyclic compounds **33** and **37** were obtained, in 86% and 78% yields, respectively, in an equally facile manner to **32**, without the need for high pressure. The constitutions assigned to **33** and **37** are supported by the observation of molecular ions by positive-ion FABMS at (i) m/z 827 for $[M + H]^+$ for **33** and (ii) m/z 837 for $[M + H]^+$ for **37**. Both **33** and **37** exhibit NMR spectroscopic characteristics (Table II) which support fully their structural and stereochemical features in a fashion similar to those described previously for **32**. The success of the macropolycyclizations summarized in Scheme IX reinforces the notion that the bicyclic bisdienes, based upon the bicyclo-[2.2.1]heptane framework, represent an ideal stereochemical match for the dienophilic reactive termini of the 2:1 adduct **32**.

Incorporating a Disubstituted Bisdienophile into the Molecular LEGO Set. The addition of aliphatic substituents onto the Diels–Alder building blocks might be expected to influence the physical and chemical properties of their adducts. Substitution

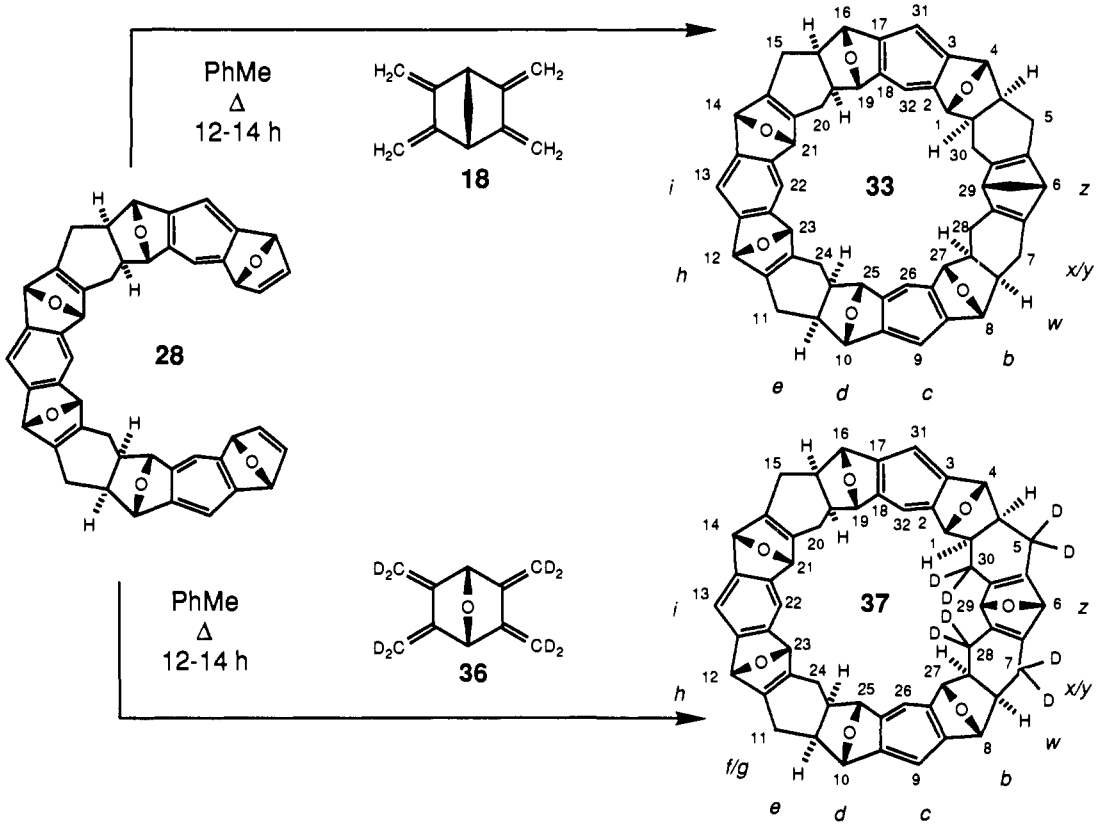
(61) This observation is in accordance with the situation that pertains in the synthesis of kohnkene **13** from the nonacene derivative **12** and the bisdiene **7**, which also proceeds directly to the macropolycycle **13**, presumably via the intermediate **11**, without any requirement for high pressure.

Table II. Comparison of the ^1H NMR Chemical Shifts[a] of Structurally-Related Hydrogen Atoms[d]

^1H[b]	q	p	o	n	m	k/l	j	i	h	f/g	e	d	c	b	a	w	x/y	z
29	6.95	5.58	7.06	4.91	1.72	2.30	5.32	7.07	5.31	2.30	1.72	4.90	7.04	5.56	6.91			
		or	or	or	to	to	or		or	to	or	or	or	or				
		5.56	7.04	4.90	1.90	2.60	5.31		5.32	2.60	1.90	4.91	7.06	5.58				
	(dd, 2 H)	(dd, 2 H)	(s, 2 H)	(s, 2 H)	(m, 2 H)	(m, 4 H)	(s, 2 H)	(s, 2 H)	(s, 2 H)	(m, 4 H)	(m, 2 H)	(s, 2 H)	(s, 2 H)	(dd, 2 H)	(dd, 2 H)			
28								7.08	5.32	2.35	1.78	4.90	7.05	5.59	6.85			
										to	to							
										2.53	1.82							
								(s, 2 H)	(s, 4 H)	(m, 8 H)	(m, 4 H)	(s, 4 H)	(s, 4 H)	(dd, 4 H)	(dd, 4 H)			
30[c]			7.08	4.92	1.60	2.35	5.35	7.05	5.32	2.35	1.60	4.85	**6.98**	**5.42**	**6.52**			
					to	to	or		or	to	to							
					1.67	2.55	5.32		5.35	2.55	1.69							
			(s, 2 H)	(s, 4 H)	(m, 4 H)	(m, 8 H)	(s, 4 H)	(s, 4 H)	(s, 4 H)	(m, 8 H)	(m, 4 H)	(s, 4 H)	(s, 4 H)	(dd, 4 H)	(dd, 4 H)			
32								7.12	5.31	2.30	1.80	4.92	6.95	4.87		1.58	2.30	5.04
										to	to					to	to	
										2.76	1.94					1.74	2.76	
								(s, 2 H)	(s, 4 H)	(m, 8 H)	(m, 4 H)	(s, 4 H)	(s, 4 H)	(s, 4 H)		(m, 4 H)	(m, 8 H)	(s, 2 H)
33								7.11	5.30	2.20	1.80	4.92	6.97	4.82		1.55	2.20	3.10
										to	to					to	to	
										2.70	1.90					1.65	2.70	
								(s, 2 H)	(s, 4 H)	(m, 8 H)	(m, 4 H)	(s, 4 H)	(s, 4 H)	(s, 4 H)		(m, 4 H)	(m, 8 H)	(t, 2 H)
37								7.11	5.30	2.30	1.80	4.92	6.94	4.86		1.62		5.01
										to	to							
										2.67	1.87							
								(s, 2 H)	(s, 4 H)	(m, 8 H)	(m, 4 H)	(s, 4 H)	(s, 4 H)	(s, 4 H)		(br s, 4 H)		(s, 2 H)
40								7.11	5.34	2.41	1.80	4.98		5.69	6.91			
										to	to							
										2.56	1.86							
								(s, 2 H)	(s, 4 H)	(m, 8 H)	(m, 4 H)	(s, 4 H)		(dd, 4 H)	(dd, 4 H)			
41								7.08	5.28	2.22	1.73	4.94		4.89		1.56	2.22	4.99
										to	to					to	to	
										2.75	1.86					1.69	2.75	
								(s, 2 H)	(s, 4 H)	(m, 8 H)	(m, 4 H)	(s, 4 H)		(dd, 4 H)		(m, 4 H)	(m, 8 H)	(s, 2 H)
44								7.11	5.30	2.10	1.70		6.77		6.50			
										to	to							
										2.48	1.76							
								(s, 2 H)	(s, 4 H)	(m, 8 H)	(m, 4 H)		(s, 4 H)		(s, 4 H)			

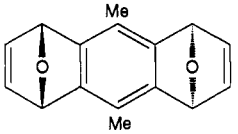
[a] The spectra were recorded at ambient temperature on either a Bruker AM 250 or WH 400 spectrometer using Me_4Si as the internal standard. The solvent in all cases was $CDCl_3$. [b] In many cases, it is not possible to differentiate with certainty assignments of hydrogen atoms to signals with very similar δ values. [c] The δ values (recorded in boldface) for protons a, b, and c are all shifted to higher field relative to those for the "same" hydrogen atoms in **28** and **29**. [d] These data provide a useful means of assessing the structural similarities and differences of the Diels–Alder oligomerization adducts. The alphabetic descriptors correspond with those shown on the schemes throughout the [14]cyclacene derivative series.

Scheme IX[a]



[a] Analogous macropolycyclizations to that reported for the preparation of the [14]cyclacene derivative **32** have been performed on the 2:1 adduct **28** with the methylene-bridged bisdiene **18** and the octadeuterated bisdiene **36** to afford the [14]cyclacene derivatives **33** and **37**, respectively. In both cases, thermally-promoted cycloadditions lead to the isolation of the products in greater than 80% yield.

of aromatic rings is often accompanied by an increase in the solubility of a compound in organic solvents. Aromatic methyl groups in a cyclacene, or on a hydrocarbon derived therefrom, would also be amenable to oxidation, thus opening up the potential for further synthetic elaboration. The lithiation of 1,2,4,5-tetrabromo-*p*-xylene at −23 °C with 2 molar equiv of *n*-butyllithium in PhMe, followed by trapping of the bisaryne equivalent thus generated in situ with 2 molar equiv of furan, afforded a clear pale yellow gum after workup and removal of the solvent in vacuo. Trituration with Me_2CO, followed by filtration, gave a white crystalline solid, which was subsequently characterized on the basis of a preliminary X-ray crystallographic analysis[62] as the *anti*-bisdienophile **39**. Column chromatography of the filtrate on silica



39

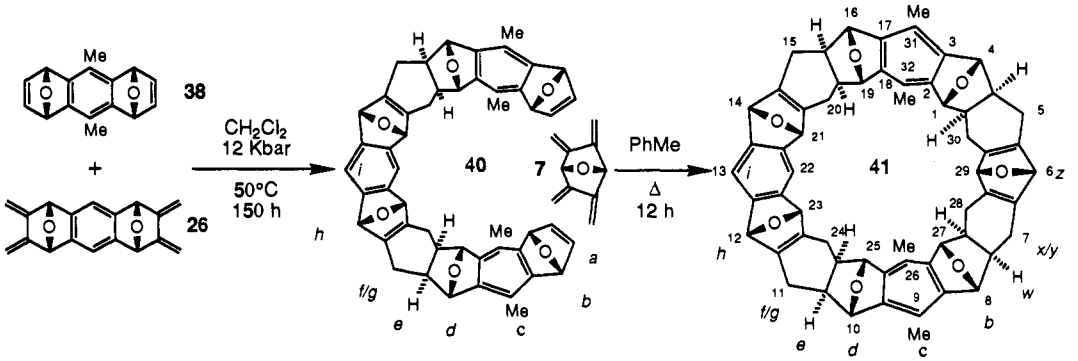
gel, using CH_2Cl_2 as the eluant, afforded the chromatographically less mobile diastereoisomer which, it was concluded, had to be the *syn*-bisdienophile **38**. Reaction of the extended *syn*-bisdiene **26** with 2 molar equiv of the *syn*-bisdienophile **38** in CH_2Cl_2 under 12 kbars of pressure at 50 °C for 150 h afforded (Scheme X), after column chromatography on silica gel, using $CHCl_3$ containing 1% MeOH as the eluant, the expected 2:1 adduct **40** in 55% yield. The observation of (i) nine signals for all nine sets of heterotopic hydrogen atoms in the ^1H NMR spectrum and (ii) 13 signals for the 13 types of heterotopic carbon atoms in the broadband-decoupled ^{13}C NMR spectrum is consistent with the overall C_{2v} molecular symmetry of **40**. In addition, the appearance at δ 4.98 in the ^1H NMR spectrum of a sharp singlet, that exhibits no observable coupling to the bridgehead hydrogen atoms, 6,12,19,25-H, confirms the endo configuration adopted by the adjacent methine hydrogen atoms, 6a,11a,19a,24a-H. Negative-ion FABMS using a mixed 18-crown-6/15-crown-5 matrix, as described[63] in the procedure employed by Kanematsu, revealed an intense molecular ion at m/z 737 for $[M - H]^-$. The ability of the crown ether matrix to capture a proton from the sample is thought to be responsible for the marked improvement in signal intensity and renders the negative-ion FABMS technique an excellent method for the detection of this and similar molecular strips. Final confirmation of the structure of **40** was provided by the successful closure of this bisdienophile with the bisdiene **7** when the two compounds were heated as reactants under reflux in PhMe, affording (Scheme X) the [14]cyclacene derivative **41**. This reaction proceeded smoothly, in a manner similar to those described for the syntheses of other [14]cyclacene derivatives, such as **32**, **33**, and **37**, to afford the tetramethyl[14]cyclacene derivative **41** in 89% yield, after column chromatography on silica gel using CH_2Cl_2 containing 2% ^{i}PrOH as the eluant. The presence of the syn/endo-H stereochemistry across both of the newly-formed cyclohexene rings in **41** is indicated by the observation in the ^1H NMR spectrum of singlets at δ 4.89 and 4.94 for the bridgehead hydrogen atoms, 1,4,8,27-H and 10,16,19,25-H, respectively. The observation of a molecular ion for **41** in the positive-ion FABMS at m/z 885 for $[M + H]^+$ provides additional supporting evidence for its assigned structure.

The Effect of Bridgehead Substitution upon Treble Diastereoselectivity. The effect of increasing steric bulk on the bridgehead positions in the bisdienophile would be expected to exert an effect

(62) This result was obtained in conjunction with Mr. H. Adams and the University of Sheffield X-Ray Crystallography Services. Although the structure of **39** is slightly disordered, the assignment of the anti configuration to the two endoxide bridges is unambiguous.

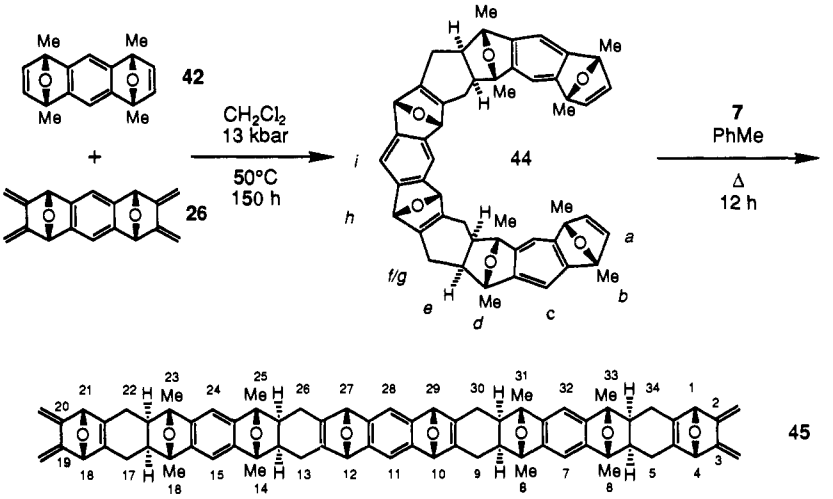
(63) Fujii, I.; Isobe, R.; Kanematsu, K. *J. Chem. Soc., Chem. Commun.* **1985**, 405–406.

Scheme X[a]



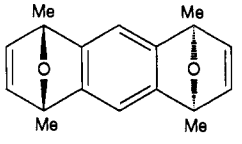
[a] Analogous macropolycyclizations to that reported for the preparation of the [14]cyclacene derivative **32** have been performed on the 2:1 adduct **40**—derived from the bisdiene **26** and the disubstituted bisdienophile **38**—with the bisdiene **7** to afford the [14]cyclacene derivative **41**. Thermally-promoted cycloadditions lead to the isolation of the product in greater than 80% yield.

Scheme XI[a]



[a] In stark contrast to the macropolycyclization reported for the undecacene derivatives **28** and **40**, the bridgehead-substituted undecacene derivative **44** reacts with the bisdiene **7** to afford an acyclic adduct **45** in the form of the acyclic pentadecacene derivative.

upon the reactivity of the adjacent π-system and, therefore, on the treble diastereoselectivity exhibited in the Diels–Alder reactions of such compounds. The synthesis of the bisdienophiles **42** and **43** was performed in an analogous fashion to that used for the preparation of **1** and **2**. The relative orientations of the endoxide bridges were determined[64] unambiguously by X-ray structural analysis (Figure 11) of single crystals of both **42** and **43**.



43

The introduction of substituents into bridgehead positions on **42** and **43** might be expected to exert some influence upon the reactivities of the adjacent dienophilic π-systems and consequently alter the diastereoselectivities observed during their cycloadditions. Indeed, it is interesting to note that the signal in the ^{1}H NMR spectra of both **42** and **43** for the olefinic hydrogen atoms, 2,3,6,7-H, is shifted upfield by 0.24 ppm to δ 6.78 relative to the signal which resonates at δ 7.02 for the "equivalent" hydrogen atoms in the unsubstituted bisdienophiles **1** and **2**, indicating a degree of perturbation is experienced by the dienophilic π-systems.

Reaction of 2 molar equiv of the bisdienophile **42** with 1 molar equiv of the extended bisdiene **26** in CH_2Cl_2 under 13 kbar pressure at 50 °C for 150 h afforded (Scheme XI), after column chromatography on silica gel using $CHCl_3$ as the eluant, a product which was characterized as the 2:1 adduct **44** in 54% yield. The C_{2v} molecular symmetry proposed for structure **44** is consistent with (i) the observation of nine signals in the ^{1}H NMR spectrum for the nine sets of heterotopic hydrogen atoms and (ii) the observation in the broadband-decoupled ^{13}C NMR spectrum of signals for all of the 14 types of heterotopic carbon atoms.

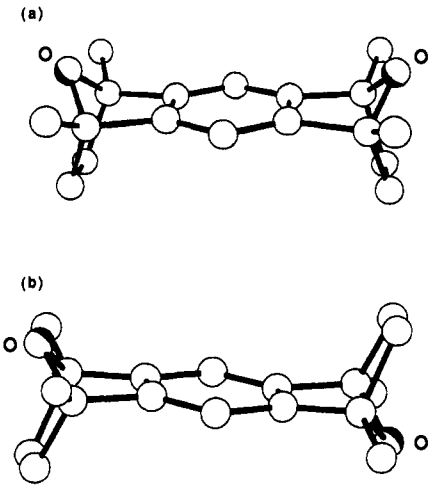
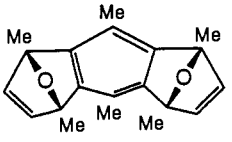


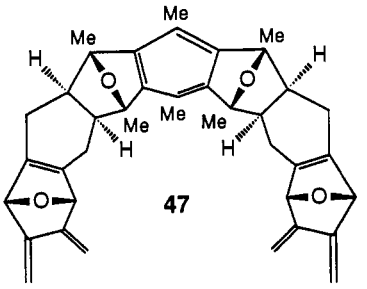
Figure 11. X-ray crystal structures of (a) the syn and (b) the anti bridgehead-substituted bisdienophiles, **42** and **43**, respectively. The concave/convex nature of the *syn*-bisdienophile **42** is again clearly visible.

(64) Kohnke, F. H.; Mathias, J. P.; Stoddart, F. J.; Slawin, A. M. Z.; Williams, D. J. *Acta Crystallogr.* To be submitted.

Substitution of the hydrogen atoms at the bridgehead positions C-6,12,19,25 by methyl groups removes the opportunity to assign the relative configuration of the adjacent ring junction methine hydrogen atoms on the basis of the magnitude of vicinal coupling constants. Thus, the relative stereochemistry generated across the newly-formed cyclohexene rings cannot be deduced directly from ^{1}H NMR spectroscopy. However, indirect evidence for the establishment of syn/endo-H stereochemistry in the reactions of bridgehead methyl substituted bisdienophiles comes from X-ray crystallography performed on the heptacene derivative **47** obtained from the reaction[65] of a 2.5 molar equiv of bisdiene **7** with a molar equivalent of *syn*-1,4:5,8-diepoxy-1,4,5,8,9,10-hexamethylanthracene **46**.



46

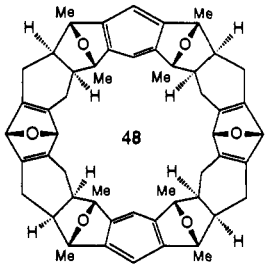


47

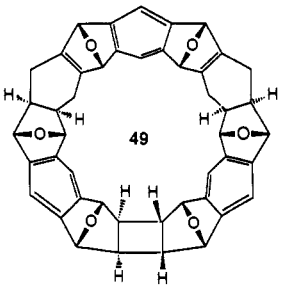
The reaction mixture obtained from a high pressure reaction between **26** and **44** was subjected to HPLC analysis under conditions identical to those used to determine the relative ratios of the 2:1 adducts **28** and **29** (Scheme VII). However, this analysis revealed no evidence for the formation of a minor configurational isomer of **44**. This observation suggests that the bridghead substitution of hydrogen atoms by methyl groups in **44** enhances the treble diastereoselectivity associated with each Diels–Alder reaction involving such building blocks.[66]

When an attempt was made to prepare the octamethyl[14]-cyclacene derivative **48** by heating **44** under reflux in PhMe with the bisdiene **7**, the reaction proceeded (Scheme XI) quite differently from those which had previously yielded the [14]cyclacene derivatives **32**, **33**, **37**, and **41**. The rate of this Diels–Alder reaction involving **44** was reduced significantly relative to that involving **28**, and the product which was isolated, after column chromatography on silica gel using CH_2Cl_2 containing 3% ^{i}PrOH as the eluant, was characterized (Scheme XI) as the acyclic adduct **45**. Thus, cycloaddition of the bisdiene unit **7** takes place at both of the terminal dienophilic units in the 2:1 adduct **44**. A strong molecular ion was revealed by positive-ion FABMS at m/z 1087 for $[M + H]^+$. This observation is consistent with the constitution shown in structure **45**. Although unexpected, this result can be related to the upfield shift of the signals observed in **44** for the hydrogen atoms 2,3,15,16-H which resonate at δ 6.50 ppm in the ^{1}H NMR spectrum. This upfield shift of the signals for the terminal hydrogen atoms can be rationalized in a manner similar to that used to explain the same phenomenon already identified in the 3:2 adduct **30** (Scheme VII), i.e., in terms of the influence on the chemical shifts of the olefinic hydrogen atoms as a result of them coming under the shielding influence of the aromatic ring at the opposite terminus of the molecule. This explanation implies an increase in the extent of the curvature of the adduct **44**—relative to that for the similar compounds such as **28** and **40**—which brings the two dienophilic ends into a much closer mutual proximity. Reaction of **44** with the bisdiene **7** would consequently place the potentially reactive termini in a less favorable position for the final intramolecular macropolycyclization, thus encouraging a further cycloaddition of a second equivalent of the bisdiene to the remaining dienophilic π-system. This observation necessarily brings into question the original stereochemical assignments conferred upon **44** and **45**. After all, a failure to achieve macropolycyclization could be ascribed to a different configuration for **44**—like that present in **29**—which would render macropolycyclization impossible. However, further studies[65] have revealed that bisdienophiles bearing bridgehead substituents do exhibit the same degree of treble diastereoselectivity in each cycloaddition, generating exclusively the syn/endo-H configuration across each newly-formed cyclohexene ring. The observation of (i) nine signals in the ^{1}H NMR spectrum for the nine sets of heterotopic hydrogen atoms and (ii) 12 signals in the broad-band-decoupled ^{13}C NMR spectrum for the 12 types of heterotopic carbon atom confirm that the molecular symmetry of **44** is C_{2v}, indicating that the stereochemistry across both of the newly-formed cyclohexene rings must be the same. So, unless a different stereochemistry has been generated exclusively across both cyclohexene rings, the assignment of the expected syn/endo-H stereochemistry would seem to be perfectly valid. A further inference can be drawn from these experiments. It is that the stereoelectronic match, required for efficient macropolycyclization, has to meet extremely exacting geometrical criteria. In the case of **7** and **44**, these criteria are clearly not being fulfilled.

In an effort to clarify this situation, the photochemical [2π + 2π] ring closure of **44** was attempted. Employing a procedure[67] identical to that used for the production of quadricyclane from bicyclo[2.2.1]heptadiene, **44** was irradiated with a 650 W Hanovia lamp in acetone using benzophenone as the sensitizer. However, none of the expected [2 + 2] cycloaddition product **49** could be isolated.



48



49

The ability to obtain the *syn*-bisdienophile **42**, without having to resort to chromatography, and its subsequent marked propensity for the syn/endo-H mode of cycloaddition in reactions with bisdienes, indicates that it could be a particularly valuable building block in further repetitive Diels–Alder oligomerizations.

Kinetic Versus Thermodynamic Control. The isolation (Scheme VII) of the minor 2:1 adduct **29**, with anti/endo-H-syn/endo-H stereochemistry, alongside the major 2:1 adduct **28** with syn/endo-H-syn/endo-H stereochemistry, represented the first evidence for the existence of a second, less favorable, reaction pathway operating within the set of closely-related cycloadditions. Since the reversibility of the Diels–Alder reaction is well-documented,[68] this observation raised questions concerning the mode of control operating in the formation of the diastereoisomers **28** and **29**, i.e.,

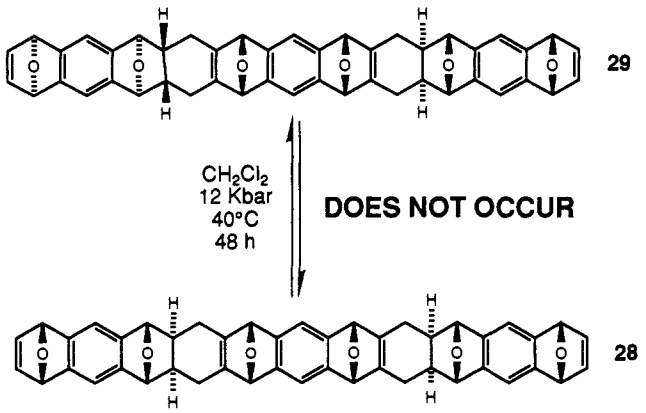
(65) Brown, G. R.; Smith, D. R.; Stoddart, J. F.; Williams, D. J. Unpublished results.

(66) Indeed, Friedrichsen has reported a significantly increased diastereoselectivity for the Diels–Alder reaction between benzo[*c*]furan and 1,4-epoxy-1,4-dimethylnaphthalene compared to that between 1,4-epoxy-1,4-dihydronaphthalene and benzo[*c*]furan, which shows no diastereoselectivity. The 7:1 ratio observed in favor of the *syn/endo*-H isomer in the Diels–Alder reaction involving 1,4-epoxy-1,4-dimethylnaphthalene is clearly of great relevance to the behavior of compounds such as **42** and **43** when they enter into cycloadditions. See: Friedrichsen, W. *Adv. Het. Chem.* **1980**, *26*, 135–241.

(67) Smith, C. D. *Org. Synth. 51*, 133–136.

(68) Thermochemical studies have confirmed the inherently exothermic nature of the Diels–Alder reaction. Thus, for the cycloreversion process to occur, one would expect a moderately high enthalpy of activation. The high pressures employed successfully in many of these syntheses also mitigate strongly against the retro-Diels–Alder process which possesses a positive molar volume of activation.

Scheme XII[a]



[a] Subjecting the minor 2:1 adduct **29** to ultrahigh pressure fails to produce any of the major 2:1 adduct **28**. If the formation of these adducts occurs under thermodynamic control, the minor isomer **29** must be the less stable and therefore it should equilibrate to give the more stable adduct **28**.

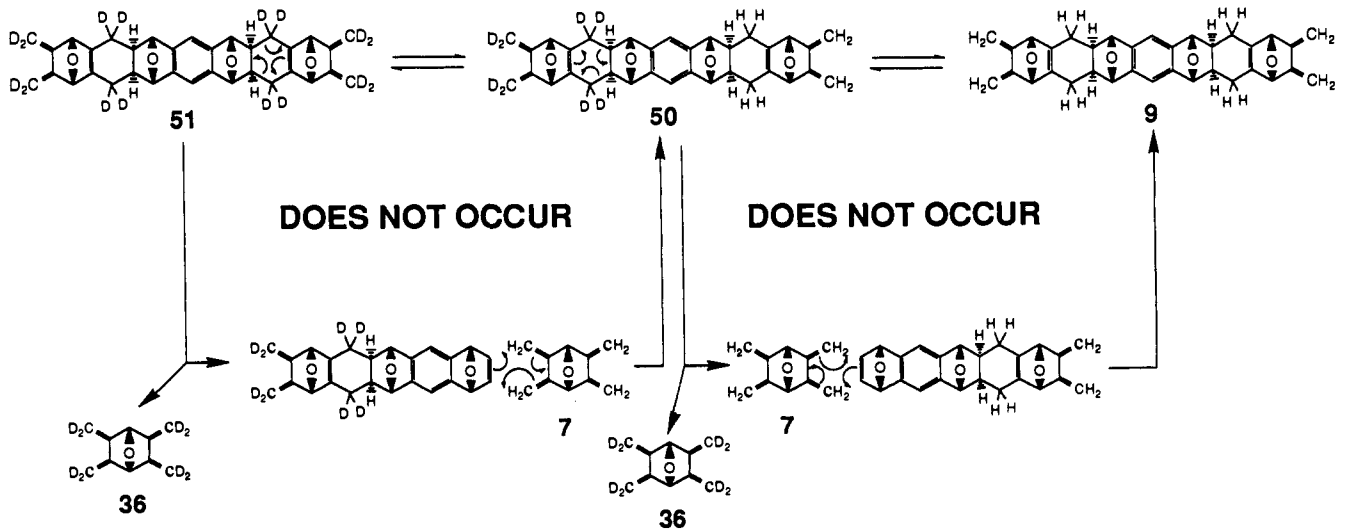
is it kinetic or thermodynamic control which is operating in these reactions and what is determining the origin of the treble diastereoselectivity exhibited in the cycloadditions under both thermally-promoted and high pressure-promoted conditions. Three possible scenarios can be envisaged. If kinetic control is in operation, the treble diastereoselectivity observed in each cycloaddition must be a consequence of a single reaction pathway—and hence a single transition state—being favored over the other competing reaction pathways. Alternatively, the treble diastereoselectivity may be a manifestation of the relative thermodynamic stability of the major syn/endo-H–syn/endo-H isomer **28** over the other possible diastereoisomeric products. A rapid retro Diels–Alder process, followed by recombination, may be occurring throughout the reaction until the most stable adducts predominate. Finally, the 2:1 adducts formed may represent both the kinetically and thermodynamically preferred product.

In order to gain a more complete knowledge of the mechanistic basis for the reactions in question and the origin of the treble diastereoselectivity they exhibit, two types of experiments were undertaken. If thermodynamic control is in operation, then pressurization (Scheme XII) of the minor 2:1 isomer **29** alone, under conditions identical to those employed in its own synthesis, should favor its reversion, via a retro-Diels–Alder process followed by a cycloaddition again, to yield the observed and therefore presumably equilibrium ratio of 18:1 in favor of **28**. HPLC analysis of such a reaction mixture provided no evidence for the formation of **28** or any retro-Diels–Alder products derived from **29**. This negative observation implies very strongly that the origin of the Diels–Alder adducts lies in a kinetically-controlled reaction pathway. In a second experiment, the hexadecadeuterated 2:1 adduct **51** was prepared from the bisdienophile **1** and the octadeuterated bisdiene **36** in a manner analogous to that used for the synthesis of the 2:1 adduct **9**. The observation of a molecular ion at m/z 519 for $[M + H]^+$ by positive-ion FABMS is consistent with the presence of 16 deuterium atoms shown (Scheme XIII) in the structural formula of **51**. ^1H NMR and ^2H NMR spectroscopies are also in complete agreement with **51** as the structural formula. The hexadecadeuterated 2:1 adduct **51** was then heated under reflux in PhMe with a 10 molar equiv of the unlabeled bisdiene **7** for 48 h until evidence of thermally-promoted degradation became obvious. If thermodynamic equilibration was occurring via retro-Diels–Alder reactions of **51**, followed by scrambling of the labeled and unlabeled bisdienes, **36** and **7**, respectively, prior to recombination, then the vast excess of the unlabeled bisdiene **7** should favor its preferential incorporation into the labeled 2:1 adduct **51**. The overall process is summarized in Scheme XIII. Examination of the reaction mixture by ^1H NMR spectroscopy and positive-ion FABMS showed no trace of either the octadeuterated 2:1 adduct **50** or the unlabeled 2:1 adduct **9**.

Both of these experimental observations are consistent with the lack of any thermodynamically-driven equilibration process operating in the course of these Diels–Alder oligomerizations. Once the products are formed under kinetic control there is no pathway open to them for re-equilibration. These conclusions validate further the arguments, based upon transition state geometries, used to explain the origins of the treble diastereoselectivity exhibited in the cycloadditions discussed in this paper.

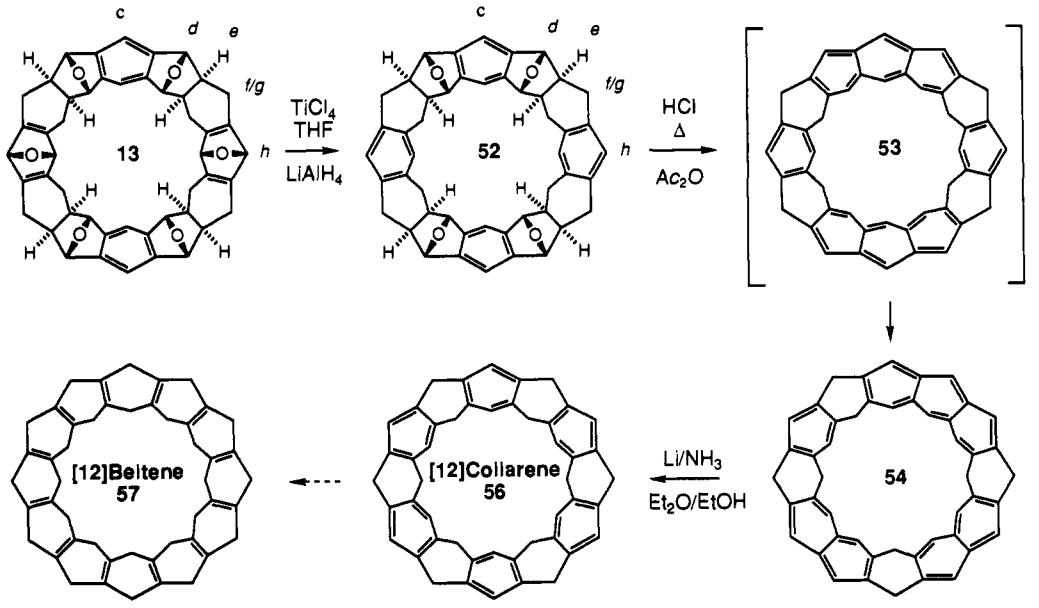
Further Synthetic Elaboration of the Molecular Belts. Apart from being appealing and novel synthetic targets in their own right, the [12]cyclacene derivatives **13** and **21**, and the [14]cyclacene derivatives **32**, **33**, **37**, and **41** represent ideal compounds for the preparation of a whole series of exotic hydrocarbons, including the [*n*]beltenes, the [*n*]collarenes, and ultimately the [*n*]cyclacenes themselves. Deoxygenation (Scheme XIV) of both the 7-oxabicyclo[2.2.1]heptane moieties located in **13**, using a low valent titanium[69] reagent, proceeds smoothly to afford[70] the [12]cyclacene

Scheme XIII[a]



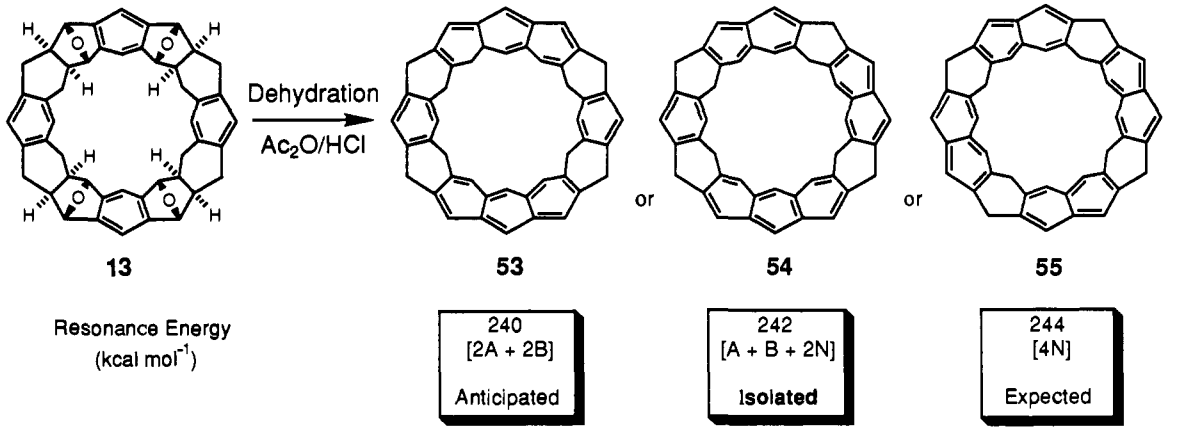
[a] If the repetitive Diels–Alder reaction products were formed under conditions of thermodynamic control, heating the hexadecadeuterated 2:1 adduct **51** under reflux in PhMe in the presence of a 10 molar excess of the unlabeled bisdiene **7** should give rise to a range of compounds, comprising the hexadecadeuterated 2:1 adduct **51**, the octadeuterated 2:1 adduct **50**, and the unlabeled 2:1 adduct **9**. No such outcome was observed—suggesting strongly that these Diels–Alder adducts are the products of kinetic control.

Scheme XIV[a]



[a] The synthetic route to [12]collarene **56** progresses via deoxygenation of kohnkene **13** to afford dideoxykohnkene **52**. Acid-catalyzed dehydration of **52** gives a mixture of isomeric hydrocarbons from which the constitutionally-asymmetric compound **54** was isolated as the major product.

Scheme XV[a]



[a] The isolation of **54** from the dehydration of **52** may be a consequence of both its resonance energy and the reduced macroring starin in comparison with the other constitutional isomers **53** and **55**. The descriptors A, B, and N refer to the anthracene, benzene, and naphthalene aromatic nuclei present in the constitutional isomers **53**, **54**, and **55**. The calculated resonance stabilization for each adduct has been derived from the values for the respective anthracene, benzene, and naphthalene nuclei.

derivative **52** in 34% yield after silica gel chromatography. Positive-ion FABMS revealed the presence of a strong molecular ion peak at m/z 680 corresponding to $[M]^+$ for **52**. The observation of (i) six signals in the ^{1}H NMR spectrum for the six sets of heterotopic hydrogen atoms and (ii) seven signals in the broadband-decoupled ^{13}C NMR spectrum for the seven types of heterotopic carbon atoms is fully consistent with the D_{2h} molecular symmetry present in the macropolycyclic compound **52**. The *endo*-methine hydrogen atoms experience a greater shielding upon the introduction of two further aromatic residues into the cavity. The signals for these hydrogen atoms are shifted upfield by 0.73 ppm from δ 1.85 in **13** to δ 1.12 in **52**.

Confirmation of the structure of **52** was provided by an X-ray structural analysis (Figure 12) of single crystals grown by vapor diffusion of chloroform into a methanolic solution of **52**. The rigid "Celtic cross-like" nature of the cavity in **52** provides a most striking solid state feature. The separation of the mean planes of the aromatic rings located at 3 and 9 o'clock is 8.9 Å. The interplanar separation of the parallelly-disposed aromatic residues at 6 and 12 o'clock in the macropolycyclic framework increases from 7.9 Å in **13** to 9.6 Å in **52**. Although it is too remote to enter into stabilizing interactions with any site on the inner surface of the cavity, a highly-disordered water molecule is situated at the crystallographic center of symmetry of **52** in the solid state. It is notable that the hinge angle (θ) is reduced to 123°, providing a qualitative indication of the increase in macroring strain associated with the incorporation of the two aromatic residues.

Acid-catalyzed dehydration of **52** afforded[70] a mixture of isomeric hydrocarbons from which **54** was isolated as the major product (56%) after chromatography. The observation of four anisochronous AB systems in the ^{1}H NMR spectrum for the four constitutionally-heterotopic 1,4-cyclohexadiene units is consistent with the asymmetric constitution proposed for **54** rather than two other possible (Scheme XV) constitutional isomers **53** and **55**. The observation in the ^{1}H NMR spectrum of resonances at δ 7.77 and 6.91 for the hydrogen atoms located on the central benzenoid ring of the one anthracene unit and the single benzene ring, respectively, provide further evidence in favor of structure **54** over either **53** or **55**. The significant upfield shift of the former signal from its

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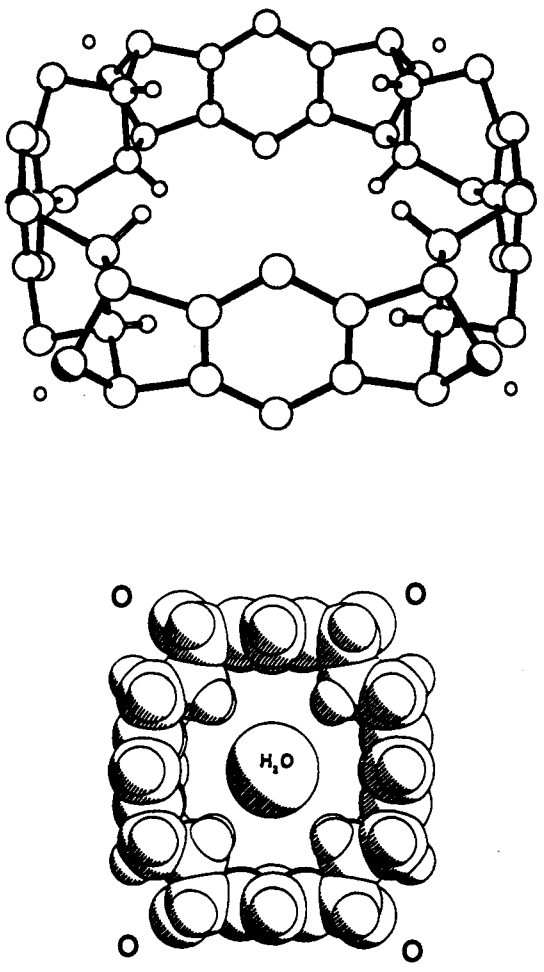

Figure 12. The X-ray structure of the [12]cyclacene derivative **52** dubbed dideoxykohnkene. The extremely rigid macropolycyclic structure and the striking "Celtic cross-like" cavity are clearly visible in both the ball-and-stick and space-filling representations. Intriguingly, a highly-disordered water molecule resides at the crystallographic center of symmetry of **52** in the solid state, although it is too remote from the inner cavity wall for any stabilizing interactions to be invoked.

more usual chemical shift value (~8.2 ppm) may be a result of the deformation of this anthracene ring and its lower aromatic character as a consequence. In an attempt to prepare [12]beltene **57**, a Birch reduction was performed on **54**. However, this reaction ceases upon production[70] of the highly-symmetrical [12]collarene **56** for which desorption EIMS revealed clearly a molecular ion at m/z 612 for $[M]^+$ with little fragmentation. This observation is consistent with the extremely high stability of the compound **56**. High field ^1H NMR spectroscopy showed the presence of only one AB system associated with the homotopic 1,4-cyclohexadiene units.[71] The identification of only one long range allylic coupling constant is a manifestation of the rigid boat-like conformation adopted by the highly-strained 1,4-cyclohexadiene units.[71]

Conclusions

The preparation of the [12]cyclacene derivatives, **13** and **21**, and the [14]cyclacene derivatives **32**, **33**, and **37**, and **41**, represent a significant contribution to the synthesis of polyacene and cyclacene derivatives. Moreover, the utilization of the bisdienophilic building blocks **1**, **38**, and **48**, in conjunction with the bisdienic building blocks **7**, **18**, **26**, and **36** in trebly-diastereoselective Diels–Alder oligomerizations, demonstrates the applicability and flexibility of this substrate-directed approach to the synthesis of outwardly-complex structural targets. The lack of any evidence for reversibility in the oligomerizations reinforces the conclusion that kinetic control is operating under the conditions employed in the syntheses and, therefore, that the origin of the treble diastereoselectivity exhibited in these oligomerizations resides in the transition states of the reaction. Finally, the potential of these macropolycyclic compounds to function as ideal precursors for the preparation of a family of novel hydrocarbon structures has been demonstrated by the conversion of kohnkene **13** into [12]-collarene **55**. The design and substrate-directed synthesis of increasingly elaborate molecular structures can be envisaged.

(71) *Conformational Analysis of Cyclohexenes, and Cyclohexadienes*; Rabideau, P. W., Ed.; Verlag Chemie: New York, 1989; pp 89–126.

(72) Sheldrick, G. M. SHELXTL *An Integrated System for Solving, Refining, and Displaying Crystal Structures from Diffraction Data*; Revision 5.2, 1985, University of Göttingen, Germany.

Experimental Section

General Methods. Tetrahydrofuran (THF) was distilled from sodium benzophenone. Benzene, toluene, and hexane were dried using sodium wire prior to use. Decalin and furan were distilled from calcium hydride prior to use. High pressure reactions were performed using CH_2Cl_2 as the solvent in a PTFE high pressure reaction vessel. The press was a fully automated 20 kbars reaction system supplied by PSIKA Pressure Systems Limited, Derbyshire, England. Thin-layer chromatography (TLC) was performed on aluminum sheets coated with Merck 5554 Kieselgel 60F, visualization being by an ultraviolet (UV) lamp, iodine vapor, or $Ce(SO_4)_2$–H_2SO_4 reagent followed by heating to ca. 100 °C in an oven. Column chromatography was performed at the bench using Kieselgel 60 (40–63 mm mesh, Merck 9385). Normal phase high pressure liquid chromatography (HPLC) was performed using both a Gilson 714 system and a Waters system fitted with UV and refractive index detectors. Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Microanalyses were performed by the University of Sheffield Microanalytical Service. Mass spectra (MS) were obtained from a Kratos MS80RF instrument. This instrument is equipped with a fast atom bombardment (FABMS) facility, operating at 8 KeV using a Xenon primary atom beam. The matrix used was either 3-nitrobenzyl alcohol (NOBA) or a mixture of 15-crown-5 and 18-crown-6. Low resolution MS were obtained on a Kratos MS 25 mass spectrometer using either electron impact mass spectrometry (EIMS) or chemical ionization mass spectrometry (CIMS), using ammonia as a carrier gas. Unless specifically stated, ^1H nuclear magnetic resonance (NMR) spectra were recorded with either Bruker WH 400 (400 MHz) or Bruker AM 250 (250 MHz) spectrometers, using tetramethylsilane as internal standard. All chemical shifts are quoted in ppm on the δ scale with all coupling constants expressed in Hertz (Hz). ^2H NMR spectra were recorded with a Bruker WH 400 (61.4 MHz) spectrometer. ^{13}C NMR spectra were recorded with a Bruker AM 250 (62.9 MHz) spectrometer using the JMOD pulse sequence.

X-ray Crystallography. X-ray diffraction measurements were performed on a Nicolet R3m diffractometer with graphite monochromated Cu Kα radiation using ω-scans. Crystal data and data collection parameters are given in Table III. Lattice parameters were determined by least squares from 18 to 22 centered reflections. Intensities were corrected for the decay of two controlled reflections, measured every 50 reflections, and for Lorentz and polarization factors, but not for absorption, with the exception of compounds **24** and **25**, for which a numerical calculation was performed. The structures were solved by direct methods and refined by full-matrix least squares. Reflections with $|F_o| > 3\sigma(|F_o|)$ were considered to be observed and were included in the refinements based upon F_o. A weighting function of the form $\omega^{-1} = \sigma^2(F) + pF^2$ was applied. Where possible, hydroxyl hydrogen atoms were located from ΔF maps and refined isotropically. Leading hydrogen atoms on methyl groups attached to sp^2 carbon atoms were located from ΔF maps where possible. All methyl groups were refined as idealized rigid bodies. Depending on data quality and the data/parameter ratio, hydrogens were either included in the refinement or placed in calculated positions (C–H distance 0.96 Å) and allowed to ride on their parent carbon atoms [$U(H) = 1.2U_{eq}(C)$]. Parameters refined were the overall scale factor, positional and anisotropic thermal parameters for non-hydrogen atoms, and positional isotropic thermal parameters for hydroxyl hydrogen atoms where located. Refinements converging with shift/error ratios were less than unity for all variables, except occasionally for disordered atoms. Final difference Fourier maps showed no significant features. All calculations were done using the SHELXTL program system.[72]

***rel*-(1*R*,4*S*,5*R*,8*S*)-1,4:5,8-Diepoxy-1,4,5,8-tetrahydroanthracene (1) and *rel*-(1*R*,4*S*,5*S*,8*R*)-1,4:5,8-Diepoxy-1,4,5,8-tetrahydroanthracene[18,19] (2).** ^{n}BuLi (220 mmol, diluted with 150 mL of anhydrous C_6H_{14}) was added dropwise over a period of 5 h to a stirred solution of 1,2,4,5-tetrabromobenzene (9.85 g, 25 mmol) and furan (30 mL, 413 mmol) in anhydrous PhMe (350 mL) at −23 °C under an atmosphere of argon.

Table III. Crystal Data and Data Collection Parameters

data	1	2	4	10	13	15	19	20[a]	24[a]	25	26	27	42	43	52
formula	$C_{14}H_{10}O_2$	$C_{14}H_{10}O_2$	$C_{14}H_{18}O_9$	$C_{38}H_{30}O_3$	$C_{48}H_{40}O_6$	$C_{15}H_{20}O_8$	$C_{25}H_{22}O_2$	$C_{14}H_{10}O_2$	$C_{18}H_{18}Cl_4O_2$	$C_{18}H_{18}Cl_4O_2$	$C_{18}H_{18}O_2$	$C_{18}H_{14}O_2$	$C_{18}H_{18}O_2$	$C_{18}H_{18}O_2$	$C_{48}H_{40}O_4$
solvent				$ClCH_2CH_2Cl$	$6(CHCl_3)$				$xCHCl_3$						H_2O
formula wt	210.2	210.2	330.3	633.6	1429.1	328.3	354.4	498.5	408.2	262.3	262.3	262.3	266.3	266.3	698.9
lattice type	monoclinic	monoclinic	orthorhombic	triclinic	monoclinic	monoclinic	monoclinic	monoclinic	hexagonal	triclinic	monoclinic	monoclinic	monoclinic	monoclinic	orthorhombic
space group	$P2_1/n$	$P2_1/c$	$F2dd$	$P\bar{1}$	$P2_1/c$	$P2_1/a$	$P2_1/a$	$P2_1/a$	$P6_3$	$P\bar{1}$	$P2_1/n$	$P2_1/n$	$P2_1$	$P2_1/n$	$Pbca$
T, K	293	293	293	293	293	293	293	293	293	293	293	293	293	293	293
cell dimensions															
a, Å	8.046 (1)	6.120 (2)	5.065 (1)	14.399 (4)	12.250 (5)	12.833 (3)	9.977 (2)	13.353 (3)	13.738 (3)	6.884 (2)	10.567 (2)	10.442 (5)	7.734 (2)	8.062 (4)	12.026 (10)
b, Å	14.573 (3)	6.996 (2)	13.632 (3)	15.220 (7)	21.247 (12)	9.309 (2)	9.307 (2)	12.369 (3)		7.782 (2)	8.149 (2)	5.691 (2)	10.216 (2)	9.142 (3)	12.511 (10)
c, Å	8.718 (1)	12.122 (3)	43.636 (9)	17.274 (8)	14.279 (11)	13.502 (4)	20.518 (4)	15.969 (5)	17.947 (4)	9.216 (2)	16.128 (3)	11.467 (4)	9.347 (3)	9.767 (4)	23.890 (15)
α, deg				86.29 (4)						101.32 (2)					
β, deg	95.47 (1)	104.14 (2)		79.63 (3)	110.59 (5)	105.01 (2)	100.97 (2)	94.97 (3)		93.03 (2)	104.33 (2)	96.69 (3)	100.93 (2)	100.07 (2)	
γ, deg				66.38 (3)						115.24 (2)					
V, Å^3	1018	503	3013	3412	3479	1558	1870	2628	2934	433	1346	677	725	709	3594
Z	4	2	8	4	2	4	4	4	6	1	4	2	2	2	4
D_c, g cm^{-3}	1.37	1.39	1.45	1.23	1.36	1.40	1.37	1.39		1.57	1.29	1.29	1.22	1.25	1.29
$F(000)$	440	220	1392	1296	1448	696	752	1064	1308	210	552	276	284	284	1480
μ, mm^{-1}	0.70	0.70	1.02	2.00	7.02	0.93	0.58	0.55	5.70	6.43	0.63	0.62	0.58	0.60	0.62
θ range, deg	58	58	58	50	50	58	58	58	58	58	58	58	58	58	50
no. of unique reflcns															
measd	1371	683	574	7013	3924	2095	2515	2694	2814	1173	1817	906	1052	1061	1808
obsd	1304	654	572	4582	1689	2025	1979	2358	2378	1144	1632	857	1043	895	1043
no. of variables	146	82	111	826	361	229	245	343	244	126	198	100	192	91	245
R	0.040	0.042	0.048	0.14	0.196	0.041	0.084	0.15	0.13	0.040	0.053	0.046	0.036	0.275	0.128
R_w	0.054	0.059	0.052	0.128	0.182	0.055	0.099			0.051	0.061	0.056	0.040	0.275	0.110
weighting factor p	0.00020	0.00022	0.00036	0.00010	0.00050	0.00030	0.00295			0.00029	0.00091	0.00120	0.00053		0.00080

[a] Disordered but configuration definitive.

Upon completion of the addition, the reaction mixture was allowed to warm to room temperature whilst being stirred overnight. The reaction was quenched with H_2O (5 mL) and stirred vigorously for 20 min. The organic phase was washed with H_2O (3 × 50 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting orange-red gum was subjected to column chromatography on silica gel, using EtOAc–light petroleum (bp 60–80 °C) (1:2 v/v) as eluant, to afford, in order of elution, a white crystalline solid, which was subsequently characterized as the anti isomer **2** (1.44 g, 6.8 mmol, 22%), followed by a white crystalline solid, which was characterized as the syn isomer **1** (1.44 g, 6.8 mmol, 22%).

Anti Isomer 2: mp 255–257 °C (from Me_2CO) (lit.[18] 245 °C); EIMS, m/z 210 for $[M]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 5.63 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 1,4,5,8-H), 7.02 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 2,3,6,7-H), and 7.18 (2 H, s, 9,10-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 82.3 (C-1,4,5,8), 114.1 (C-9,10), 143.4 (C-2,3,6,7), and 147.9 (C-4a,8a,9a,10a). Anal. Calcd for $C_{14}H_{14}O_4$: C, 79.98; H, 4.76. Found: C, 79.69; H, 4.97. Crystals of **2** suitable for X-ray structural analysis were obtained by vapor diffusion of light petroleum (bp 60–80 °C) into an EtOAc solution of **2** at room temperature.

Syn Isomer 1: mp 191–193 °C (from EtOAc) (lit.[18,19b] 191–193 °C); EIMS, m/z 210 for $[M]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 5.63 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 1,4,5,8-H), 7.02 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 2,3,6,7-H), and 7.18 (2 H, s, 9,10-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 82.0 (C-1,4,5,8), 113.6 (C-9,10), 143.3 (C-2,3,6,7), and 147.6 (C-4a,8a,9a,10a). Anal. Calcd for $C_{14}H_{14}O_4$: C, 79.98; H, 4.76. Found: C, 80.13; H, 4.96. Crystals of **1** suitable for X-ray structural analysis were obtained by vapor diffusion of light petroleum (bp 60–80 °C) into an EtOAc solution of **1** at room temperature.

Methyl *rel*-(2*R*,3*S*,5*R*,6*S*)-7-Oxabicyclo[2.2.1]heptane-2,3,5,6-tetracarboxylate[34] (4). Anhydrous $CuCl_2$ (162 g, 1.2 mol), NaOAc (200 g, 2.4 mol), and 10% Pd/C (2.3 g, 2.15 mmol) were suspended in anhydrous MeOH (600 mL) in a Pyrex Fischer–Porter vessel before addition of *rel*-(3a*R*,7a*S*)-4,7-epoxy-3a,4,7,7a-tetrahydroisobenzofuran-1,3-dione[34] (**3**) (50 g, 300 mmol). After degassing carefully, the reaction mixture was pressurized with CO (3 atm) and stirred vigorously for 8 h at room temperature. After degassing completely, to remove all the dissolved CO, and removal of solvent in vacuo, the residue was partitioned between H_2O (250 mL) and $CHCl_3$ (250 mL), and the solid residues were removed by filtration through Hyflo Supercel. The organic phase was washed repeatedly with dilute aqueous $NaHCO_3$ until no blue coloration was observed in the aqueous extract. It was then dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting yellow solid was stirred with $MeOH/Et_2O$ (100 mL, 2:1 v/v), and the white suspension was collected by filtration. Drying in vacuo afforded a white crystalline solid, which was characterized as the product **4** (69.9 g, 212 mmol, 71%): mp 159–160 °C (from MeOH) (lit.[34] 156–157 °C); EIMS, m/z 330 for $[M]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 3.01 (12 H, s, 2a,3a,5a,6a-OCH_3), 3.70 (4 H, s, 2,3,5,6-H), and 5.26 (2 H, s, 1,4-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 51.0 (C-2a,3a,5a,6a-OMe), 52.2 (C-2,3,5,6), 80.3 (C-1,4), and 170.2 (C-2a,3a,5a,6a). Anal. Calcd for $C_{14}H_{18}O_4$: C, 50.91; H, 5.45. Found: C, 50.83; H, 5.46. Single crystals of **4** suitable for X-ray structural analysis[36] were obtained by slow concentration of a $CHCl_3$ solution of **4** at room temperature.

***rel*-(2*R*,3*S*,5*R*,6*S*)-2,3,5,6-Tetrakis(hydroxymethyl)-7-oxabicyclo[2.2.1]heptane[34] (5).** A suspension of the tetraester **4** (31.2 g, 94 mmol) in anhydrous THF was added, over a period of 5 h, to a vigorously stirred suspension of $LiAlH_4$ (10 g, 258 mmol) in anhydrous THF (300 mL) maintained at −5 °C under an atmosphere of nitrogen. The reaction mixture was allowed to warm up to room temperature before being heated under reflux for a further 4 h. After cooling, the reaction was quenched with H_2O (60 mL), followed by heating under reflux for 1 min before being filtered immediately through a bed of silica gel (180 g). The solid was extracted from the silica with boiling MeOH (3 × 150 mL), and the filtrates were combined, cooled, and filtered. The resultant filtrate was concentrated in vacuo to a volume of 40 mL and left to stand at 0 °C. The crystals obtained were isolated by filtration to afford a product which was characterized as the product **5** (9.4 g, 43 mmol, 46%): mp 208 °C (from EtOH) (lit.[34] 208–209 °C); EIMS, m/z 218 for $[M]^+$; ^1H NMR (250 MHz, D_2O) δ 2.05–2.21 (4 H, m, 2,3,5,6-H), 3.25–3.58 (8 H, m, 2a,3a,5a,6a-CH_2), and 4.23 (2 H, s, 1,4-H); ^{13}C NMR (62.9 MHz, D_2O) δ 47.1 (C-2,3,5,6), 59.9 (C-2a,3a,5a,6a), and 81.7 (C-1,4). Anal. Calcd for $C_{10}H_{18}O_5$: C, 55.37; H, 8.45. Found: C, 55.05; H, 8.26.

***rel*-(2*R*,3*S*,5*R*,6*S*)-2,3,5,6-Tetrakis(chloromethyl)-7-oxabicyclo[2.2.1]heptane[34] (6).** The tetraol **5** (5.1 g, 23 mmol) was added portionwise, without cooling, to a stirred solution of anhydrous pyridine (7.5 mL, 68 mmol) and $SOCl_2$ (8.5 mL, 85 mmol). Upon completion of the addition, further $SOCl_2$ (13 mL, 15 mmol) was added, and the mixture was heated to 60–70 °C for 2 h. After cooling the mixture to room temperature, CH_2Cl_2 (180 mL) was added, and the reaction was

quenched at 0 °C by careful addition of H_2O (15 mL). The organic extract was washed with H_2O (3 × 15 mL), dried over $MgSO_4$, filtered, and then concentrated in vacuo. This afforded a white crystalline solid which was characterized as the product **6** (5.56 g, 19 mmol, 83%): mp 150–151 °C (from $CHCl_3$) (lit.[34] 149 °C); EIMS, m/z 292 for $[M]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 2.27–2.42 (4 H, m, 2,3,5,6-H), 3.36–3.64 (8 H, m, 2a,3a,5a,6a-H_2), and 4.51 (2 H, s, 1,4-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 42.5 (C-2a,3a,5a,6a), 49.1 (C-2,3,5,6), and 83.5 (C-1,4). Anal. Calcd for $C_{10}H_{14}Cl_4O_4$: C, 41.12; H, 4.80; Cl, 48.59. Found: C, 41.16; H, 4.83; Cl, 48.61.

2,3,5,6-Tetramethylidene-7-oxabicyclo[2.2.1]heptane[34] **(7).** Solid ^{t}BuOK (8.6 g, 76 mmol) was added portionwise over 30 min to a stirred solution of the tetrachloride **6** (2.40 g, 8.2 mmol) in anhydrous THF (50 mL) at 0 °C, under an atmosphere of nitrogen in the absence of light. The reaction was quenched after 14 h by the dropwise addition of H_2O (24 mL) until the KCl formed during the reaction had been completely dissolved. After concentration in vacuo, the product was extracted with C_5H_{12} (3 × 50 mL). The combined organic extracts were washed with H_2O (3 × 50 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to afford colorless crystalline needles which were characterized as the product **7** (1.04 g, 89%): mp 34–36 °C (from $CHCl_3$) (lit.[34] 35–37 °C); ^1H NMR (220 MHz, $CDCl_3$) δ 4.85 (2 H, br s, 1,4-H), 4.95 (4 H, br s, 2a,3a,5a,6a-H_Z), and 5.15 (4 H, br s, 2a,3a,5a,6a-H_E); ^{13}C (62.9 MHz, $CDCl_3$) δ 85.6 (C-1,4), 102.7 (C-2a,3a,5a,6a), and 145.7 (C-2,3,5,6).

***rel*-(1*R*,4*S*,5a*S*,6*S*,8*R*,11*S*,13*R*,13a*R*)-1,4:6,13:8,11-Triepoxy-1,4,5,5a,6,8,11,13,13a,14-decahydro-2,3-bismethylidenepentacene (8) and *rel*-(1*R*,4*S*,5a*S*,6*S*,8*R*,8a*R*,10*R*,13*S*,14a*S*,15*S*,17*R*,17a*R*)-1,4:6,17:8,15:10,13-Tetraepoxy-1,4,5,5a,6,8,8a,9,10,13,14,14a,15,17,-17a,18-hexadecahydro-2,3,10,11-tetramethylideneheptacene**[47] **(9).** A solution of the *syn*-bisdienophile **1** (2.43 g, 11.5 mmol) and the bisdiene **7** (3.37 g, 23.1 mmol) in anhydrous PhMe (245 mL) was heated under reflux for 14 h in a nitrogen atmosphere. After cooling and removal of the solvent in vacuo, the light yellow residue was subjected to column chromatography on silica gel, using a gradient elution with EtOAc–light petroleum (bp 60–80 °C)–$CHCl_3$ (1:1:0 → 1:0:1 v/v), to afford a white solid, which was characterized as **8** (1.00 g, 2.81 mmol, 24%) followed by another white solid which was characterized as **9** (3.63 g, 7.23 mmol, 61%).

Compound 8: mp, > 300 °C dec; EIMS, m/z 356 for $[M]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 1.82–1.89 (2 H, m, 5a,13a-H), 2.23–2.36 and 2.51–2.63 (2 × 2 H, 2 × m, 5,14-CH_2), 4.91 (2 H, s, 6,13-H), 4.97 (2 H, br s, 1,4-H), 4.98 (2 H, s, 2a,3a-H_Z), 5.08 (2 H, s, 2a,3a-H_E), 5.63 (2 H, dd, $J_{8,9} = J_{8,10} = 1.3$ Hz, 8,11-H), 7.02 (2 H, dd, $J_{8,9} = J_{8,10} = 1.3$ Hz, 9,10-H), and 7.08 (2 H, s, 7,12-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.7 (C-5,14), 43.2 (C-5a,13a), 82.3 (C-1,4), 85.1 (C-8,11), 85.3 (C-6,13), 100.9 (C-2a,3a), 112.0 (C-7,12), 143.3 (C-9,10), 143.1, 144.2, and 148.6 (C-2,3,4a,6a,7a,11a,12a,14a). Anal. Calcd for $C_{24}H_{20}O_3$: C, 80.87; H, 5.65. Found: C, 80.71; H, 5.24.

Compound 9: mp > 300 °C dec; EIMS, m/z 502 for $[M]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 1.78–1.86 (4 H, m, 5,9,14,18-H), 2.28–2.38 and 2.57–2.68 (2 × 4 H, 2 × m, 5a,8a,14a,17a-CH_2), 4.92 (4 H, s, 6,8,15,17-H), 4.97 (4 H, s, 1,4,10,13-H), 4.99 (4 H, s, 2a,3a,11a,12a-H_Z), 5.09 (4 H, s, 2a,3a,11a,12a-H_E), and 6.99 (2 H, s, 7,16-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.7 (C-5,9,14,18), 43.2 (C-5a,8a,14a,17a), 85.0 (C-1,4,10,13), 85.3 (C-6,8,15,17), 100.9 (C-2a,3a,11a,12a), 110.2 (C-7,16), 143.1 and 144.2 (C-2,3,4a,9a,11,12,13a,18a), 144.6 (C-6a,7a,15a,16a). Anal. Calcd for $C_{34}H_{30}O_4$: C, 81.25; H, 6.01. Found: C, 81.01; H, 6.04.

***rel*-(5a*R*,6*R*,8*S*,8a*S*,10*S*,13*R*,14a*R*,15*R*,17*S*,17a*S*)-6,17:8,15:10,13-Triepoxy-5,5a,6,8,8a,9,10,13,14,14a,15,17,17a,18-tetradecahydro-5,18-benzo-11,12-bismethylideneheptacene**[47] **(10).** A solution of the dienophile **8** (150 mg, 0.42 mmol) and anthracene (235 mg, 1.32 mmol) in xylene (5 mL of an isomeric mixture) was heated under reflux for 48 h under an atmosphere of nitrogen. After cooling, removal of solvent in vacuo afforded a yellow solid which was subjected to column chromatography on silica gel, using $CHCl_3/Et_2O$ (4:1 v/v) as eluant to yield a white crystalline solid, with a higher R_f value than **8**, which was characterized as the product **10** (25 mg, 0.047 mmol, 11%): mp > 300 °C dec; positive-ion FABMS, m/z 535 $[M + H]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 1.65–1.72 (2 H, m, 8a,14a-H), 2.18–2.20 (2 H, m, 5,18-H), 2.23–2.36 and 2.51–2.63 (2 × 2 H, 2 × m, 9,14-H_2), 4.41 (2 H, br s, 5a,17a-H), 4.86 (2 H, s, 6,17-H), 4.87 (2 H, s, 8,15-H), 4.95 (2 H, s, 11a,12a-H_Z), 4.96 (2 H, br s, 10,13-H), 5.06 (2 H, s, 11a,12a-H_E), 6.94 (2 H, s, 7,16-H), 6.99–7.03, 7.11–7.15, 7.20–7.24, and 7.25–7.29 (4 × 2 H, 4 × m, 1,2,3,4,19,20,21,22-H). Single crystals of **10** suitable for X-ray structural analysis were obtained by vapor diffusion of light petroleum (bp 60–80 °C) into a $CHCl_3/ClCH_2CH_2Cl$ solution (1:1 v/v) of **10**.

***rel*-(1*R*,4*S*,6*R*,6a*R*,8*s*,9a*S*,10*S*,12*R*,15*S*,17*R*,17a*R*,19*r*,20a*S*,-21*S*)-1,4:6,21:8,19:10,17:12,15-Pentaepoxy-1,4,6,6a,7,8,9,9a,10,12,-15,17,17a,18,19,20,20a,21-octadecahydrononacene (12).** A solution of the *syn*-bisdienophile **1** (210 mg, 11 mmol) and the 1:1 adduct **8** (356 mg, 1 mmol) in CH_2Cl_2 (20 mL) was introduced into a PTFE high-pressure reaction vessel and subjected to a pressure of 10 kbars for 200 h, with the temperature maintained at 40 °C. After cooling and depressurization, the solvent was removed in vacuo and the grey-white residue subjected to column chromatography on silica gel, using $CHCl_3$ containing 3% MeOH as eluant, to yield a white solid, which was characterized as the product **12** (150 mg, 0.15 mmol, 20%): mp > 300 °C dec; positive-ion FABMS, m/z 566 for $[M]^+$; ^1H NMR (250 MHz, $CDCl_3$) d 1.83 (4 H, m, 6a,9a,17a,20a-H), 2.38–2.50 (8 H, m, 7,9,18,20-H_2), 4.87 (4 H, s, 6,10,17,21-H), 4.95 (2 H, s, 8,19-H), 5.59 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 1,4,12,15-H), 6.98 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 2,3,13,14-H), and 7.09 (4 H, s, 5,11,16,22-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) d 27.7 (C-7,9,18,20), 41.9 (C-6a,9a,17a,20a), 82.8 (C-8,19), 87.0 (C-6,10,17,21), 87.2 (C-1,4,12,15), 112.4 (C-5,11,16,22), 143.7 (C-2,3,13,14), 144.2, 149.3, and 150.1 (C4a,5a,7a,8a,10a,-11a,15a,16a,18a,19a,21a,22a).

***rel*-(1*R*,4*S*,4a*S*,6*r*,7a*R*,8*R*,10*S*,10a*S*,12*r*,13a*R*,14*R*,17*S*,17a*S*,-19*r*,20a*R*,21*R*,23*S*,23a*S*,25*r*,26a*R*)-1,4:6,25:8,23:10,21:12,19:14,17-Hexaepoxy-1,4,4a,5,6,7,7a,8,10,10a,11,12,13,13a,14,17,17a,18,19,20,-20a,21,23,23a,24,25,26,26a-octacosahydro-2,16:3,15-dimethenoundecacene**[47] **(13). Method A.** A solution of the 1:1 adduct **8** (70 mg, 0.196 mmol) in xylene (4 mL of an isomeric mixture) was heated under reflux for 48 h in a nitrogen atmosphere. After cooling to room temperature, the solvent was removed in vacuo to afford an orange solid which was subjected to column chromatography on silica gel, using a gradient elution with $CHCl_3/C_6H_{14}$/MeOH (50:50:0 → 90:0:10 v/v), to yield a white solid which was characterized as the product **13** (5 mg, 0.007 mmol, 3.6%).

Method B. A solution of the 1:1 adduct **8** (50 mg, 0.14 mmol) in CH_2Cl_2 (10 mL) was introduced into a PTFE high-pressure reaction vessel and subjected to a pressure of 18 kbars for 72 h, with the temperature maintained at 50 °C. After cooling and depressurization, the solvent was removed in vacuo, and the grey-white residue was subjected to column chromatography on silica gel, using $CHCl_3$ containing 5% MeOH as eluant, to yield a white solid, which was characterized as the product **13** (24 mg, 0.033 mmol, 48%).

Method C. A solution of the nonacene derivative **12** (40 mg, 0.072 mmol) and the bisdiene **7** (10 mg, 0.068 mmol) in anhydrous PhMe (30 mL) was heated under reflux for 7 h under a nitrogen atmosphere before cooling to room temperature. The solvent was removed in vacuo to afford an orange solid which was subjected to column chromatography on silica gel, using a solution of CH_2Cl_2 containing 5% MeOH as the eluant, to yield a white solid which was characterized as the product **13** (35 mg, 0.0049 mmol, 69%).

Method D. A solution of the *syn*-bisdienophile **1** (155 mg, 0.74 mmol) and the bisdiene **9** (373 mg, 0.74 mmol) in CH_2Cl_2 (20 mL) was introduced into a PTFE high-pressure reaction vessel and subjected to a pressure of 10 kbars for 200 h, with the temperature maintained at 55–60 °C. After cooling and depressurization, the solvent was removed in vacuo, and the grey-white residue was subjected to column chromatography, using $CHCl_3$ containing 2% MeOH as eluant, to yield a white solid, which was characterized as the product **13** (105 mg, 0.15 mmol, 20% after recrystallization from $CHCl_3$): mp > 300 °C dec; positive-ion FABMS, m/z 713 for $[M + H]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 1.60–1.62 (8 H, m, 4a,7a,10a,13a,17a,20a,23a,26a-H), 2.25–2.38 and 2.58–2.70 (2 × 8 H, 2 × m, 5,7,11,13,18,20,24,26-CH_2), 4.89 (8 H, s, 1,4,8,10,14,17,21,23-H), 5.08 (4 H, s, 6,12,19,25-H), and 6.98 (4 H, s, 9,22,27,28-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.1 (C-5,7,11,13,18,20,24,26), 44.2 (C-4a,7a,10a,13a,17a,20a,23a,26a), 84.8 (C-1,4,8,10,14,17,21,23), 86.6 (C-6,12,19,25), 110.1 (C-9,22,27,28), 144.6 and 152.5 (C-2,3,5a,6a,8a,9a,11a,12a,15,16,18a,19a,21a,22a,-24a,25a). Anal. Calcd for $C_{48}H_{40}O_6$: C, 80.9; H, 5.65. Found: C, 79.9; H, 5.96. Single crystals of **13** suitable for X-ray structural analysis were obtained by slow concentration of a $CHCl_3$ solution of **13** at room temperature. The crystals were stable only as long as they were maintained in an atmosphere of $CHCl_3$. Upon filtering and drying, they collapsed to give an amorphous powder.

Methyl *rel*-(2*R*,3*S*,5*S*,6*R*)-Bicyclo[2.2.1]heptane-2,3,5,6-tetracarboxylate[53] **(15).** Anhydrous $CuCl_2$ (288 g, 2.14 mol) and $PdCl_2$ (5 g, 28 mmol) were suspended in anhydrous MeOH (1000 mL) in a Pyrex Fischer–Porter vessel before addition of *rel*-(3a*R*,7a*S*)-4,7-methylene-3a,4,7,7a-tetrahydroisobenzofuran-1,3-dione[34] **(14)** (56.6 g, 340 mmol). After degassing carefully, the reaction mixture was pressurized with CO (4 atm) and stirred vigorously for 48 h at room temperature. After degassing completely, to remove all the dissolved CO, and removal of solvent in vacuo, the residue was partitioned between H_2O (250 mL) and $CHCl_3$ (250 mL), and the solid residues were removed by filtration through Celite. The organic phase was washed with dilute aqueous

$NaHCO_3$ (3 × 50 mL) until no blue coloration was observed in the aqueous extract. It was then dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting yellow solid was recrystallized from MeOH to afford a crystalline solid, which was characterized as the tetraester **15** (72 g, 220 mmol, 64%): mp 84–86 °C (from MeOH) (lit.[53] 182–183 °C); CIMS, m/z 329 $[M + H]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 1.40–1.50 (1 H, m, 7-$H_{(anti)}$), 2.20–2.30 (1 H, m, 7-$H_{(syn)}$), 2.85 (2 H, s, 1,4-H), 3.08 (2 H, s, 2,3-H), 3.44 (2 H, d, 5,6-H), 3.62 and 3.67 (2 × 6 H, 2 × s, 2a,3a,5a,6a-OCH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 37.3 (C-7), 43.3 (C-1,4), 45.3 (C-5,6), 45.9 (C-2,3), 51.2 (C-2a,3a,5a,6a-OMe), and 171.5 and 172.5 (C-2a,3a,5a,6a). Anal. Calcd for $C_{15}H_{20}O_8$: C, 54.9; H, 6.14. Found: C, 55.4; H, 6.30. Single crystals of **15** suitable for X-ray structural analysis[54] were obtained by slow concentration of a $CHCl_3$ solution of **15** at room temperature.

***rel*-(2*R*,3*S*,5*S*,6*R*)-2,3,5,6-Tetrakis(hydroxymethyl)bicyclo[2.2.1]heptane**[53] **(16).** A suspension of the tetraester **15** (31.4 g, 96 mmol) in anhydrous THF (300 mL) was added, over a period of 15 h, to a vigorously stirred suspension of $LiAlH_4$ (10.4 g, 275 mmol) in anhydrous THF (300 mL) maintained at 0 °C under an atmosphere of nitrogen. The reaction mixture was allowed to warm up to room temperature before being heated under reflux for a further 15 h. After cooling, the reaction was quenched with H_2O (20 mL), followed by heating under reflux for 1 min before being filtered immediately through a bed of silica gel (180 g). The solid was extracted from the silica with boiling MeOH (3 × 150 mL), and the filtrates were combined, cooled, and filtered. The resultant filtrate was concentrated in vacuo, and the residue recrystallized from MeOH to afford colorless crystals which were characterized as the product **16** (14 g, 65 mmol, 68%): mp 164–165 °C (from MeOH) (lit.[53] mp 164–165 °C); CIMS, m/z 216 for $[M]^+$; ^1H NMR (250 MHz, D_2O) δ 1.24 (1 H, m, 7-$H_{(anti)}$), 1.57 (1 H, m, 7-$H_{(syn)}$), 1.97–2.22 (6 H, m, 1,2,3,4,5,6-H), and 3.35–3.76 (8 H, m, 2a,3a,5a,6-CH_2); ^{13}C NMR (62.9 MHz, D_2O) δ 33.1 (C-7), 38.4 (C-1,4), 38.4 (C-5,6), 41.1 (C-2,3), and 58.4 and 60.6 (C-2a,3a,5a,6a). Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.07; H, 9.32. Found: C, 61.20; H, 9.20.

***rel*-(2*R*,3*S*,5*S*,6*R*)-2,3,5,6-Tetrakis(mesyloxymethyl)bicyclo[2.2.1]heptane**[53] **(17).** Freshly distilled MsCl (11.4 g, 100 mmol) was added dropwise to a stirred solution of the tetraol **16** (2.16 g, 10 mmol) in anhydrous C_5H_5N (30 mL) under an atmosphere of nitrogen, maintaining the temperature at 0 °C throughout. The mixture was heated to 50 °C for 60 h before being poured slowly onto a vigorously stirred mixture of ice/water (100 g). The precipitate was removed by filtration, washed with further ice water (50 mL), and recrystallized from MeCN to afford a white solid which was characterized as the product **17** (1.9 g, 3.5 mmol, 36%): mp 170–171 °C (from $CHCl_3$) (lit.[53] 170–171 °C); EIMS, m/z 528 for $[M]^+$; ^1H NMR (250 MHz, CD_3CN) δ 1.35–1.50 (1 H, m, 7-$H_{(anti)}$), 1.70–1.85 (1 H, m, 7-$H_{(syn)}$), 2.30–2.45 (2 H, m, 1,4-H), 2.50–2.60 (4 H, m, 2,3,5,6-H), 3.05 (12 H, s, S-CH_3), and 4.10–4.40 (8 H, m, 2a,3a,5a,6a-CH_2); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 35.1 (C-7), 37.67 (C(Ms)), 38.2 (C-1,4), 40.4 (C-5,6), 43.7 (C-2,3), and 68.6 and 70.6 (C-2a,3a,5a,6a). Anal. Calcd for $C_{15}H_{28}O_{12}S_4$: C, 34.1; H, 5.23; S, 24.3. Found: C, 34.1; H, 5.35; S, 23.5.

2,3,5,6-Tetramethylidenebicyclo[2.2.1]heptane[53] **(18).** Solid ^{t}BuOK (9 g, 80 mmol) was added portionwise over 30 min to a stirred solution of the tetramesylate **17** (3 g, 5.7 mmol) in anhydrous DMF (90 mL) and HMPTA (15 mL) at 0 °C, under an atmosphere of nitrogen in the absence of light. The mixture was then heated to 80 °C for 72 h. After cooling, the reaction was quenched by the dropwise addition of H_2O (50 mL). After concentration in vacuo, the product was extracted with C_5H_{12} (4 × 50 mL). The combined organic extracts were washed with H_2O (5 × 100 mL), filtered through a short column of Florisil, and concentrated in vacuo to afford colorless crystalline needles which were characterized as the product **18** (520 mg, 3.6 mmol, 63%): mp 25–27 °C; (lit.[53] 28–30 °C); EIMS, m/z 144 for $[M]^+$; ^1H NMR (220 MHz, $CDCl_3$) δ 1.50 (2 H, s, 7-H_2), 3.27 (2 H, s, 1,4-H), 4.98 (4 H, br s, 2a,3a,5a,6a-H_Z), and 5.10 (4 H, br s, 2a,3a,5a,6a-H_E).

***rel*-(1*R*,4*S*,5a*S*,6a*S*,8*R*,11*S*,13*R*,13a*R*)-6,13:8,11-Diepoxy-1,4-methylene-1,4,5,5a,6,8,11,13,13a,14-decahydro-2,3-bismethylidenepentacene (19)** and ***rel*-(1*R*,4*S*,5a*S*,6*S*,8*R*,8a*R*,10*R*,13*S*,14a*S*,15*S*,17*R*,17a*R*)-6,17:8,15-Tetraepoxy-1,4:10,13-dimethylene-1,4,5,5a,6,8,8a,9,10,13,14,14a,15,17,17a,18-hexadecahydro-2,3,10,11-tetramethylideneheptacene (20).** A solution of the bisdienophile **1** (151 mg, 0.72 mmol) and the bisdiene **18** (230 mg, 1.59 mmol) in anhydrous PhMe (65 mL) was heated under reflux for 10 h, under an atmosphere of nitrogen. After cooling and removal of the solvent in vacuo, the residue was subjected to column chromatography on silica gel, using CH_2Cl_2 containing 1% EtOAc as the eluant, to afford in order of elution a white solid, which was characterized as **19** (38 mg, 0.11 mmol, 15%) followed by another white solid, which was characterized as **20** (240 mg, 0.48 mmol, 66%).

Compound 19: mp > 300 °C dec; CIMS, m/z 355 for $[M + H]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 1.50–1.57 (2 × 1 H, 2 × t, $J_{1,1a(anti)} = J_{1,1a(syn)}$ = 2.5 Hz, 1a-H_2), 1.80–1.89 (2 H, m, 5a,13a-H), 2.20–2.36 and 2.50–2.66 (2 × 2 H, 2 × m, 5,14-H_2), 3.13 (2 H, t, $J_{1,1a(anti)} = J_{1,1a(syn)}$ = 2.5 Hz, 1,4-H), 4.84 (2 H, s, 2a,3a-H_E), 4.88 (2 H, s, 6,13-H), 4.91 (2 H, s, 2a,3a-H_Z), 5.63 (2 H, dd, $J_{8,9} = J_{8,10}$ = 1.3 Hz, 8,11-H), 7.02 (2 H, dd, $J_{8,9} = J_{8,10}$ = 1.3 Hz, 9,10-H), and 7.08 (2 H, s, 7,12-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 25.7 (C-5,14), 43.2 (C-5a,13a), 47.9 (C-1a), 53.7 (C-1,4), 85.1 (C-8,11), 85.3 (C-6,13), 100.9 (C-2a,3a), 112.0 (C-7,12), 143.3 (C-9,10), 143.1, 143.4, 144.2, and 148.6 (C-2,3,4a,6a,7a,11a,12a,14a). Single crystals of **19** suitable for X-ray crystallographic analysis were obtained by vapor diffusion of $^iPr_2O$ into a $CHCl_3$ solution of **18** at room temperature.

Compound 20: mp > 300 °C dec; EIMS, m/z for 498 $[M]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 1.50–1.57 (2 × 1 H, 2 × t, $J_{1,1a(anti)} = J_{1,1a(syn)}$ = 2.5 Hz, 1a,10a-H_2), 1.80–1.86 (4 H, m, 5,9,14,18-H), 2.20–2.60 (8 H, m, 5a,8a,14a,17a-H_2), 3.13 (4 H, t, $J_{1,1a(anti)} = J_{1,1a(syn)}$ = 2.5 Hz, 1,4,10,13-H), 4.85 (4 H, s, 2a,3a,11a,12a-H_Z), 4.88 (4 H, s, 6,8,15,17-H), 5.02 (4 H, s, 2a,3a,11a,12a-H_E), and 6.98 (2 H, s, 7,16-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 28.0 (C-5,9,14,18), 43.2 (C-5a,8a,14a,17a), 48.6 (C-1a,10a), 54.2 (C-1,4,10,13), 85.8 (C-6,8,15,17), 99.8 (C-2a,3a,11a,12a), 110.1 (C-7,16), 142.4, 144.8 and 149.6 (C-2,3,4a,6a,7a,9a,11,12,13a,15a,16a,18a). Single crystals of **20** suitable for X-ray crystallographic analysis were obtained by vapor diffusion of $^iPr_2O$ into a $CHCl_3$ solution of **20** at room temperature.

***rel*-(1*R*,4*S*,4a*S*,6*r*,7a*R*,8*R*,10*S*,10a*S*,12*r*,13a*R*,14*R*,17*S*,17a*S*,19*r*,20a*R*,21*R*,23*S*,23a*S*,25*r*,26a*R*)-1,4:8,23:10,21:14,17-Tetraepoxy-6,25:12,19-dimethylene-1,4,4a,5,6,7,7a,8,10,10a,11,12,13,13a,14,17,17a,18,19,20,20a,21,23,23a,24,25,26,26a-octacosahydro-2,16:3,15-dimethenoundecacene (21).** A solution of the bisdiene **20** (230 mg, 0.46 mmol) and *syn*-bisdienophile **1** (96 mg, 0.46 mmol) in CH_2Cl_2 (20 mL) was introduced into a PTFE high-pressure reaction vessel and subjected to a pressure of 12 kbars for 200 h, with the temperature maintained at 50 °C. After cooling and depressurization, filtration afforded a white solid which was characterized as the product **21** (125 mg, 0.17 mmol, 38%): mp > 300 °C dec; positive-ion FABMS, m/z 709 for $[M + H]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 1.51 (4 H, t, $J_{6,6a(anti)} = J_{6,6a(syn)}$ = 2.5 Hz, 6a,12a-H_2), 1.86–1.92 (8 H, m, 4a,7a,10a,13a,17a,20a,23a,26a-H), 2.20–2.60 (16 H, m, 5,7,11,13,18,20,24,26-H_2), 3.10 (4 H, t, $J_{6,6a(anti)} = J_{6,6a(syn)}$ = 2.5 Hz, 6,12,19,25-H), 4.80 (8 H, s, 1,4,8,10,14,17,21,23-H), 6.90 (4 H, s, 9,22,27,28-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 29.2 (C-6a,12a), 29.7 (C-5,7,11,13,18,20,24,26), 44.3 (C-4a,7a,10a,13a,17a,20a,23a,26a), 56.2 (C-6,12,19,25), 85.1 (C-1,4,8,10,14,17,21,23), 109.9 (C-9,22,27,28), 144.8 and 150.0 (C-2,3,5a,6a,8a,9a,11a,12a,15,16,18a,19a,21a,22a,24a,25a). Anal. Calcd for $C_{50}H_{44}O_4$: C, 84.70; H, 6.27. Found: C, 83.13; H, 6.21.

1,4:8,11-Dicarboxy-5,14:7,12-diepoxy-4a,5,7,7a,11a,12,14,14a-octahydro-1,2,3,4,8,9,10,11-octaphenylpentacene[55] **(22).** A solution of the *anti*-bisdienophile **2** (1.8 g, 8.6 mmol) and 1,2,3,4-tetraphenylcyclopentadienone (6.61 g, 17.2 mmol) in anhydrous C_6H_6 (125 mL) was heated under reflux for 12 h, during which time the purple coloration disappeared completely. Removal of the solvent in vacuo, followed by trituration with cold MeOH (30 mL), and filtration afforded a copious white solid, which was characterized as the product, **22** (8.19 g, 8.54 mmol, 99%): mp > 300 °C dec; (lit.[55] mp > 300 °C); positive-ion FABMS, m/z 979 for $[M + H]^+$. Anal. Calcd for $C_{72}H_{50}O_4$: C, 88.42; H, 5.15. Found: C, 88.45; H, 5.30.

***rel*-(1*R*,2*S*,3*R*,4*S*,5*R*,6*S*,7*R*,8*S*)-2,3,6,7-Tetrakis(chloromethyl)-1,4:5,8-diepoxy-1,2,3,4,5,6,7,8-octahydroanthracene (24) and *rel*-(1*R*,2*S*,3*R*,4*S*,5*S*,6*R*,7*S*,8*R*)-2,3,6,7-Tetrakis(chloromethyl)-1,4:5,8-diepoxy-1,2,3,4,5,6,7,8-octahydroanthracene**[55,57,59] **(25).** A solution of *cis*-1,4-dichlorobut-2-ene (0.63 mL, 6 mmol) in decalin (50 mL) was heated under reflux in an atmosphere of argon, and a suspension of the pentacene derivative **22** (2.8 g, 3 mmol) in decalin (200 mL) was added over a period of 3 h, maintaining reflux temperature at all times. Upon completion of the addition, the reaction mixture was cooled and the solvent was removed in vacuo to afford a yellow-orange solid. Column chromatography on silica gel, using $CHCl_3/CCl_4$ (1:1 v/v) as eluant, yielded, in order of elution, a white crystalline solid, which was characterized as the *anti*-tetrachloride **25** (330 mg, 0.8 mmol, 27%), followed by another white crystalline solid, which was characterized as the *syn*-tetrachloride **24** (360 mg, 0.9 mmol, 30%).

Anti isomer 25: mp 220 °C dec (EtOH) (lit.[59] 220 °C); EIMS, m/z 408 for $[M]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 2.41–2.45 (4 H, m, 2,3,6,7-H), 3.00–3.30 (8 H, m, 2a,3a,6a,7a-CH_2), 5.53 (4 H, d, $J_{1,2}$ = 4 Hz, 1,4,5,8-H), and 7.51 (2 H, s, 9,10-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 43.6 (C-2a,3a,6a,7a), 47.3 (C-2,3,6,7), 82.4 (C-1,4,5,8), 113.2 (C-9,10), and 145.0 (C-4a,8a,9a,10a). Anal. Calcd for $C_{18}H_{14}Cl_4O_2$: C, 52.96; H, 4.45; Cl, 34.74. Found: C, 52.98; H, 4.61; Cl, 34.82. Single crystals of **25** suitable for X-ray structural analysis[59] were obtained by

vapor diffusion of C_5H_{12} into a CH_2Cl_2 solution of **25** at room temperature.

Syn isomer 24: mp 192–194 °C (from EtOH) (lit.[59] 192–194 °C); EIMS, *m/z* 408 for $[M]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 2.40–2.44 (4 H, m, 2,3,6,7-H), 3.00–3.28 (8 H, m, 2a,3a,6a,7a-CH_2), 5.50 (4 H, d, $J_{1,2}$ = 4 Hz, 1,4,5,8-H), and 7.52 (2 H, s, 9,10-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 42.1 (C-2a,3a,6a,7a), 44.3 (C-2,3,6,7), 82.3 (C-1,4,5,8), 115.3 (C-9,10), and 142.1 (C-4a,8a,9a,10a). Anal. Calcd for $C_{18}H_{14}Cl_4O_2$: C, 52.96; H, 4.45; Cl, 34.74. Found: C, 52.88; H, 4.61; Cl, 34.78. Single crystals of **24** suitable for X-ray structural analysis[59] were obtained by vapor diffusion of C_6H_{14} into a CH_2Cl_2 solution of **24** at room temperature.

***rel*-(1*R*,4*S*,5*R*,8*S*)-1,4:5,8-Diepoxy-1,4,5,8-tetrahydro-2,3,6,7-tetramethylideneanthracene**[57,60] **(26)**. Solid ^{t}BuOK (294 mg, 9.5 mmol) was added portionwise over 15 min to a stirred solution of the *syn*-tetrachloride **24** (420 mg, 1.03 mmol) in anhydrous THF (35 mL) at 0 °C. The reaction was quenched after 10 h by dropwise addition of H_2O (5 mL). The solvent was removed in vacuo, and the residue was partitioned between CH_2Cl_2 (20 mL) and H_2O (20 mL). The organic extract was washed with further H_2O (2 × 15 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to afford a white crystalline solid which was characterized as the product **26** (260 mg, 9.9 mmol, 96%): mp > 228 °C dec (from CH_2Cl_2); EIMS, *m/z* 262 for $[M]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 5.20 (4 H, br s, 1,4,5,8-H), 5.32 (4 H, s, 2a,3a,6a,7a-H_Z), 5.50 (4 H, s, 2a,3a,6a,7a-H_E), and 7.25 (2 H, s, 9,10-H). Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.4; H, 5.4. Found: C, 82.6; H, 5.2. Single crystals of **26** suitable for X-ray structural analysis were obtained by obtained by vapor diffusion of diisopropyl ether into a dichloromethane solution of **26** at room temperature.

***rel*-(1*R*,4*S*,5*S*,8*R*)-1,4:5,8-Diepoxy-1,4,5,8-tetrahydro-2,3,6,7-tetramethylideneanthracene**[57,60] **(27)**. The procedure used for the synthesis of the title compound (**27**) was identical to that used for the synthesis of its stereoisomer **26**. Reaction of solid ^{t}BuOK (400 mg, 3.5 mmol) with the *anti*-tetrachloride **25** (156 mg, 0.38 mmol) in anhydrous THF (10 mL) at 0 °C afforded a white crystalline solid, which was characterized as the product **27** (98 mg, 0.37 mmol, 98%): mp > 240 °C dec (from CH_2Cl_2); EIMS, *m/z* 262 for $[M]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 5.20 (4 H, br s, 1,4,5,8-H), 5.30 (4 H, s, 2a,3a,6a,7a-H_Z), 5.55 (4 H, s, 2a,3a,6a,7a-H_E), and 7.28 (2 H, s, 9,10-H). Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.41; H, 5.38. Found: C, 82.60; H, 5.22. Single crystals of **27** suitable for X-ray structural analysis were obtained by vapor diffusion of C_5H_{12} into a CH_2Cl_2 solution of **27** at room temperature.

***rel*-(1*R*,4*S*,6*R*,6a*R*,8*S*,10*R*,11a*S*,12*R*,14*S*,17*R*,19*S*,19a*R*,-21*S*,23*R*,24a*S*,25*S*)-1,4:6,25:8,23:10,21:12,19:14,17-Hexaepoxy-1,4,6,6a,7,8,10,11,11a,12,14,17,19,19a,20,21,22,24,24a,25-eicosahydroundecacene (29)**, ***rel*-(1*R*,4*S*,6*R*,6a*R*,8*S*,10*R*,11a*S*,12*S*,14*R*,17*S*,-19*R*,19a*R*,21*S*,23*R*,24a*S*,25*S*)-1,4:6,25:8,23:10,21:12,19:14,17-Hexaepoxy-1,4,6,6a,7,8,10,11,11a,12,14,17,19,19a,20,21,22,24,24a,25-eicosahydroundecacene (28)**, and ***rel*-(1*R*,4*S*,6*R*,6a*R*,8*S*,10*R*,11a*S*,12*S*,-14*R*,14a*R*,16*S*,18*R*,19a*S*,20*S*,22*R*,25*S*,27*R*,27a*R*,29*S*,31*R*,32a*S*,-33*S*,35*R*,35a*R*,37*S*,39*R*,40a*S*,41*S*)-1,4:6,41:8,39:10,37:12,35:14,33:16,31:18,29:20,27:22,25-Decaepoxy-1,4,6,6a,7,8,10,11,11a,12,14,-14a,15,16,18,19,19a,20,22,25,27,27a,28,29,31,32,32a,33,35,35a,36,37,-39,40,40a,41-hexatriacontahydrononadecacene**[57] **(30)**. A solution of the bisdienophile **1** (1.67 g, 9.79 mmol) and the bisdiene **26** (1.04 g, 3.98 mmol) in CH_2Cl_2 (45 mL) was introduced into a PTFE high-pressure reaction vessel and subjected to a pressure of 10 kbars for 150 h, with the temperature maintained at 50–55 °C. After cooling and depressurization, the solvent was removed in vacuo and the yellow residue was subjected to column chromatography on silica gel, using $CHCl_3$ containing 2% MeOH as the eluant, to yield in order of elution, a white solid, which was characterized as the product **29** (40 mg, 0.058 mmol, 1.5%), another white solid which was characterized as the product **28** (696 mg, 1.02 mmol, 25%), and yet another white solid, which was characterized as the product **30** (48 mg, 0.042 mmol, 2%).

Compound 29: mp > 300 °C dec; positive-ion FABMS, *m/z* 705 $[M + Na]^+$, 682 $[M]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 1.72–1.80 and 1.82–1.90 (2 × 2 H, 2 × m, 6a,11a,19a,24a-H), 2.30–2.60 (8 H, m, 7,11,20,24-CH_2), 4.90 and 4.91 (2 × 2 H, 2 × s, 6,12,19,25-H), 5.32 (4 H, s, 8,10,21,23-H), 5.56 and 5.58 (2 × 2 H, 2 × dd, $J_{1,2} = J_{1,3} = J_{14,15} = J_{14,16}$ = 1.3 Hz, 1,4,14,17-H), 6.91 and 6.95 (2 × 2 H, 2 × dd, $J_{1,2} = J_{1,3} = J_{14,15} = J_{14,16}$ = 1.3 Hz, 2,3,15,16-H), 7.04 and 7.06 (2 × 2 H, 2 × s, 5,13,18,26-H), and 7.07 (2 H, s, 9,22-H); ^{13}C NMR (62.9 MHz, $CDCl_3$), 26.4 and 26.5 (C-7,11,20,24), 40.3 and 40.4 (C-6a,11a,19a,24a), 82.2 and 82.3 (C-1,4,14,17), 84.6 and 84.7 (C-8,10,21,23), 86.7 and 86.8 (C-6,12,19,25), 111.9 (C-9,22), 112.2 and 112.3 (C-5,13,18,26), 143.1 and 143.4 (C-2,3,15,16), 143.7 (C-7a,10a,20a,23a), 147.7, 147.9, 148.2, 148.2, 148.6, and 146.8 (C-4a,5a,8a,9a,12a,13a,17a,18a,21a,22a,-25a,26a).

Compound 28: mp > 300 °C dec; negative-ion FABMS, *m/z* 681 for $[M - H]^-$, positive ion FABMS, *m/z* 705 for $[M + Na]^+$, 682 for $[M]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 1.78–1.82 (4 H, m, 6a,11a,19a,24a-H), 2.35–2.42 and 2.46–2.53 (2 × 4 H, 2 × m, 7,11,20,24-H_2), 4.90 (4 H, s, 6,12,19,25-H), 5.32 (4 H, s, 8,10,21,23-H), 5.59 (4 H, dd, $J_{1,2} = J_{1,3}$ = 1.3 Hz, 1,4,14,17-H), 6.85 (4 H, dd, $J_{1,2} = J_{1,3}$ = 1.3 Hz, 2,3,15,16-H), 7.05 (4 H, s, 5,13,18,26-H), and 7.08 (2 H, s, 9,22-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 26.5 (C-7,11,20,24), 40.4 (C-6a,11a,19a,24a), 82.3 (C-1,4,14,17), 84.6 (C-8,10,21,23), 86.7 (C-6,12,19,25), 111.9 (C-5,13,18,26), 112.3 (C-9,22), 143.3 (C-2,3,15,16), 143.5 (C-7a,10a,20a,23a), 147.9, 148.3, and 148.7 (C-4a,5a,8a,9a,12a,-13a,17a,18a,21a,22a,25a,26a).

Compound 30: mp > 300 °C dec; negative-ion FABMS, *m/z* 1153 for $[M - H]^-$, positive-ion FABMS, *m/z* 1178 for $[M + Na]^+$, 1154 for $[M]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 1.60–1.69 (8 H, m, 6a,11a,14a,19a,27a,32a,35a,40a-H), 2.35–2.55 (16 H, m, 7,11,15,19,28,32,36,40-H_2), 4.85 (4 H, s, 6,20,27,41-H), 4.92 (4 H, s, 12,14,33,35-H), 5.35 and 5.32 (2 × 4 H, 2 × s, 8,10,16,18,29,31,37,39-H), 5.42 (4 H, dd, $J_{1,2} = J_{1,3}$ = 1.3 Hz, 1,4,22,25-H), 6.52 (4 H, dd, $J_{1,2} = J_{1,3}$ = 1.3 Hz, 2,3,23,24-H), 6.98 (4 H, s, 5,21,26,42-H), 7.05 (4 H, s, 9,17,30,38-H), and 7.08 (2 H, s, 13,34-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 26.7 and 26.7 (C-7,11,15,19,28,32,36,40), 38.1 and 41.9 (C-6a,11a,14a,19a,27a,32a,35a,40a), 82.1 (C-1,4,22,25), 84.8 and 84.8 (C-8,10,16,18,29,31,37,39), 86.7 (C-6,20,27,41), 88.4 (C-12,14,33,35), 110.4 (C-13,34), 111.9 (C-5,21,26,42), 112.3 (C-9,17,30,38), 143.2 (C-2,3,23,24), 143.6, 145.3, 146.7, 147.6, 148.1, 148.5, and 149.4 (C-4a,5a,7a,8a,9a,10a,12a,13a,15a,16a,17a,18a,20a,21a,25a,26a,28a,-29a,30a,31a,33a,34a,36a,37a,38a,39a,41a,42a).

***rel*-(1*R*,4*S*,4a*S*,6*r*,7a*R*,8*R*,10*S*,10a*S*,12*R*,14*S*,15a*R*,16*R*,19*S*,-19a*S*,21*R*,23*R*,24a*S*,25*R*,27*S*,27a*S*,29*s*,30a*R*)-1,4:6,29:8,27:10,25:12,23:14,21:16,19-Heptaepoxy-1,4,4a,5,6,7,7a,8,10,10a,11,12,14,15,-15a,16,19,19a,20,21,23,24,24a,25,27,27a,28,29,30,30a-triacontahydro-2,18:3,17-dimethenotriadecacene**[57] **(32)**. A solution of the bisdiene **7** (13 mg, 0.09 mmol) and the 2:1 adduct **28** (55 mg, 0.08 mmol) in anhydrous PhMe (60 mL) was heated under reflux for 12 h, in an atmosphere of argon in the absence of light. After cooling to room temperature and removal of solvent in vacuo, the light brown residue was subjected to column chromatography on silica gel, using $CHCl_3$ containing 2% MeOH as the eluant, affording a white solid, which was characterized as the [14]cyclacene derivative **32** (51 mg, 0.062 mmol, 78%): mp > 300 °C dec; positive-ion FABMS, *m/z* 829 for $[M + H]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 1.58–1.74 (4 H, m, 4a,7a,27a,30a-H), 1.80–1.94 (4 H, m, 10a,15a,19a,24a-H), 2.30–2.76 (16 H, m, 5,7,11,15,20,24,28,30-CH_2), 4.87 (4 H, s, 1,4,8,27-H), 4.92 (4 H, s, 10,16,19,25-H), 5.04 (2 H, s, 6,29-H), 5.31 (4 H, s, 12,14,21,23-H), 6.95 (4 H, s, 9,26,31,32-H), and 7.12 (2 H, s, 13,22-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 26.3 (C-11,15,20,24), 27.3 (C-5,7,28,30), 40.5 (C-10a,15a,19a,24a), 42.8 (C-4a,7a,27a,30a), 84.2 (C-12,14,21,23), 85.3 and 85.9 (C-1,4,8,10,16,19,25,27), 86.4 (C-6,29), 110.3 (C-9,26,31,32), 112.2 (C-13,22), 144.5 and 144.7 (C-5a,6a,11a,14a,20a,23a,28a,29a), 148.1, 148.4, and 151.1 (C-2,3,8a,9a,12a,13a,17,18,21a,22a,25a,26a).

***rel*-(1*R*,4*S*,4a*S*,6*s*,7a*R*,8*R*,10*S*,10a*S*,12*R*,14*S*,15a*R*,16*R*,19*S*,-19a*S*,21*R*,23*S*,24a*S*,25*R*,27*S*,27a*S*,29*r*,30a*R*)-1,4:8,27:10,25:12,23:14,21:16,19-Hexaepoxy-6,29-methylene-1,4,4a,5,6,7,7a,8,10,10a,11,-12,14,15,15a,16,19,19a,20,21,23,24,24a,25,27,27a,28,29,30,30a-triacontahydro-2,18:3,17-dimethenotriadecacene (33)**. The preparation of the title compound was identical to that used for the synthesis of the [14]cyclacene derivative **32**. Reaction of the bisdiene **18** (30 mg, 0.21 mmol) with the bisdienophile **28** (100 mg, 0.14 mmol) afforded, after chromatography on silica gel, using CH_2Cl_2 containing 2% ^{i}PrOH, a white solid, which was characterized as the product **33** (99 mg, 0.12 mmol, 86%): mp > 300 °C dec; positive-ion FABMS, *m/z* 827 for $[M + H]^+$; ^1H NMR (250 MHz, $CDCl_3$) δ 1.50 (2 H, s, 6a-CH_2), 1.55–1.65 (4 H, m, 4a,7a,27a,30a-H), 1.80–1.90 (4 H, m, 10a,15a,19a,24a-H), 2.20–2.70 (16 H, m, 5,7,11,15,20,24,28,30-CH_2), 3.10 (2 H, s, 6,29-H), 4.82 (4 H, s, 1,4,8,27-H), 4.92 (4 H, s, 10,16,19,25-H), 5.30 (4 H, s, 12,14,21,23-H), 6.97 (4 H, s, 9,26,31,32-H), and 7.11 (2 H, s, 13,22-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 26.3 (C-11,15,20,24), 29.3 (C-5,7,28,30), 40.5 (C-10a,15a,19a,24a), 43.0 (C-4a,7a,27a,30a), 55.8 (C-6,29), 84.3 (C-12,14,21,23), 85.5 and 86.1 (C-1,4,8,10,16,19,25,27), 110.2 (C-9,26,31,32), 112.8 (C-13,22), 144.3 and 145.0 (C-5a,6a,11a,14a,20a,23a,28a,29a), 148.1, 148.4, and 148.4 (C-2,3,8a,9a,12a,13a,17,18,21a,22a,25a,26a).

***rel*-(2*R*,3*S*,5*R*,6*S*)-2a,2a,3a,3a,5a,5a,6a,6a-Octadeuterio-2,3,5,6-tetrakis(hydroxymethyl)-7-oxabicyclo[2.2.1]heptane (34)**. The preparation of the title compound **34** was identical to that used for the synthesis of the tetraol **5**. Reaction of the tetraester **4** (5 g, 15 mmol), with $LiAlD_4$ (2 g, 41 mmol), afforded a white crystalline solid after recrystallization from ethanol, which was characterized as the product **34** (1.4 g, 6.2 mmol, 42%): mp 206–208 °C (from ethanol); CIMS, *m/z* 227 for [M

+ H]$^+$; ^{1}H NMR (250 MHz, D_2O) δ 2.39 (4 H, s, 2,3,5,6-H), and 4.30 (2 H, s, 1,4-H); ^{2}H NMR (61.4 MHz, H_2O) δ 3.10 and 3.40 (2 × br s, 2a,3a,5a,6a-CD_2). Anal. Calcd for $C_{10}H_{10}D_8O_5$: C, 53.1 Found: C, 52.9.

***rel*-(2*S*,3*R*,5*S*,6*R*)-2a,2a,3a,3a,5a,5a,6a,6a-Octadeuterio-2,3,5,6-tetrakis(chloromethyl)-7-oxabicyclo[2.2.1]heptane (35).** The preparation of the title compound **35** was identical to that used for the synthesis of the tetrachloride **6**. Chlorination of the tetraol **34** (800 mg, 3.5 mmol) afforded a white crystalline solid after recrystallization from ethanol, which was characterized as the product **35** (900 mg, 3 mmol, 86%): mp 150–151 °C (from ethanol); CIMS, *m/z* for 300 [M]$^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.39 (4 H, s, 2,3,5,6-H), and 4.55 (2 H, s, 1,4-H); ^{2}H NMR (61.4 MHz, $CHCl_3$) δ 3.35 and 3.55 (2 × br s, 2a,3a,5a,6a-CD_2); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 41.9 (C-2a,3a,5a,6a), 50.0 (C-2,3,5,6), and 83.5 (C-1,4). Anal. Calcd for $C_{10}H_6D_8Cl_4O$: C, 39.6. Found: C, 40.0.

2a,2a,3a,3a,5a,5a,6a,6a-Octadeuterio-2,3,5,6-tetramethylidene-7-oxabicyclo[2.2.1]heptane (36). The preparation of the title compound **36** was identical to that used for the synthesis of the bisdiene **7**. Reaction of the tetrachloride **35** (600 mg, 2 mmol), with ^{t}BuOK (1.8 g, 16 mmol), afforded a white crystalline solid, which was characterized as the product **36** (301 mg, 1.95 mmol, 98%): mp 36–37 °C; EIMS, *m/z* 154 for [M]$^+$.

***rel*-(1*R*,4*S*,4a*S*,6*r*,7a*R*,8*R*,10*S*,10a*S*,12*R*,14*S*,15a*R*,16*R*,19*S*,-19a*S*,21*R*,23*S*,24a*S*,25*R*,27*S*,27a*S*,29*s*,30a*R*)-1,4:6,29:8,27:10,25:-12,23:14,21:16,19-Heptaepoxy-5,5,7,7,28,28,30,30-octadeuterio-1,4,4a,6,7a,8,10,10a,11,12,14,15,15a,16,19,19a,20,21,23,24,24a,25,-27,27a,29,30a-hexacosahydro-2,18:3,17-dimethenotriadecacene (37).** The preparation of the title compound was identical to that used for the synthesis of the [14]cyclacene derivative **32**. Reaction of the bisdienophile **28** (200 mg, 0.3 mmol), with the octadeuteriobisdiene **36** (140 mg, 9.1 mmol), afforded, after column chromatography on silica gel, using CH_2Cl_2 containing ^{i}PrOH as the eluant, a white solid, which was characterized as the product **37** (180 mg, 0.22 mmol, 72%): mp > 300 °C dec; positive-ion FABMS, *m/z* 837 for [M + H]$^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.62 (4 H, br s, 4a,7a,27a,30a-H), 1.80–1.87 (4 H, m, 10a,15a,19a,24a-H), 2.30–2.67 (8 H, m, 11,15,20,24-H_2), 4.86 (4 H, s, 1,4,8,27-H), 4.92 (4 H, s, 10,16,19,25-H), 5.01 (2 H, s, 6,29-H), 5.30 (4 H, s, 12,14,21,23-H), 6.94 (4 H, s, 9,26,31,32-H), and 7.11 (2 H, s, 13,22-H); ^{2}H NMR (61.4 MHz, $CHCl_3$), 2.1–2.9 (2 × br s, 5,7,28,30-D_2); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 26.3 (C-11,15,20,24), 40.1 (C-10a,15a,19a,24a), 42.6 (C-4a,7a,27a,30a), 84.3 (C-12,14,21,23), 85.3 and 86.0 (C-1,4,8,10,16,19,25,27), 86.3 (C6,29), 110.3 (C-9,26,31,32), 112.3 (C-13,22), 144.5 and 145.7 (C-5a,6a,11a,14a,20a,23a,28a,29a), 148.1, 148.4, and 151.1 (C-2,3,8a,9a,12a,13a,17,18,21a,22a,25a,26a). Anal. Calcd for $C_{56}H_{36}D_8O_7$: C, 80.5. Found: C, 73.6.

***rel*-(1*R*,4*S*,5*R*,8*S*)-1,4:5,8-Diepoxy-1,4,5,8-tetrahydro-9,10-dimethylanthracene (38) and *rel*-(1*R*,4*S*,5*S*,8*R*)-1,4:5,8-Diepoxy-1,4,5,8-tetrahydro-9,10-dimethylanthracene[18] (39).** The preparation of the title compounds followed a procedure which was similar to that used for the synthesis of **1** and **2**. A reaction starting from 1,2,4,5-tetrabromo-*p*-xylene (24.5 g, 58 mmol), furan (70 mL, 960 mmol), and ^{n}BuLi (147 mmol, diluted with 100 mL of anhydrous C_6H_{14}) in PhMe (800 mL) afforded, after concentration of the reaction mixture in vacuo, a yellow gum. This was triturated with Me_2CO (40 mL) to afford a white crystalline solid after filtration, which was characterized as the *anti*-bisdienophile **39** (3.4 g, 14.3 mmol, 25%). The filtrate was concentrated in vacuo before being subjected to column chromatography on silica gel, using CH_2Cl_2 as eluant, to afford a white crystalline solid, which was characterized as the *syn*-bisdienophile **38** (3.7 g, 15.5 mmol, 27%).

Anti isomer 39: mp 217–219 °C dec (lit.[18] 205 °C) (from Et_2O); EIMS, *m/z* 238 for [M]$^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.25 (6 H, s, 9,10-CH_3), 5.71 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 1,4,5,8-H), and 7.03 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 2,3,6,7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.5 (C-9,10-Me), 81.1 (C-1,4,5,8), 121.6 (C-9,10), 143.2 (C-2,3,6,7), and 146.4 (C-4a,8a,9a,10a). Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.57; H, 5.77. Crystals of **39** suitable for X-ray crystallographic analysis[62] were obtained by vapor diffusion of C_6H_{14} into a $CHCl_3$ solution of **39** at room temperature.

Syn isomer 38: mp 178–180 °C dec (from Et_2O); EIMS, *m/z* 238 for [M]$^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.25 (6 H, s, 9,10-CH_3), 5.72 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 1,4,5,8-H), and 7.05 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 2,3,6,7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.5 (C-9,10-Me), 81.1 (C-1,4,5,8), 121.4 (C-9,10), 143.4 (C-2,3,6,7), and 146.4 (C-4a,8a,9a,10a). Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.42; H, 6.03.

***rel*-(1*R*,4*S*,6*R*,6a*R*,8*S*,10*R*,11a*S*,12*S*,14*R*,17*S*,19*R*,19a*R*,-21*S*,23*R*,24a*S*,25*S*)-1,4:6,25:8,23:10,21:12,19:14,17-Hexaepoxy-1,4,6,6a,7,8,10,11,11a,12,14,17,19,19a,20,21,23,24,24a,25-eicosahydro-5,13,18,26-tetramethylundecacene (40).** The preparation of the title compound followed a procedure which was similar to that used for the synthesis of the 2:1 adduct **28**. Reaction of the bisdiene **26** (100 mg, 0.38 mmol) and the bisdienophile **38** (182 mg, 0.76 mmol) in CH_2Cl_2 (14 mL) under a pressure of 12 kbar for 150 h at 50 °C afforded, after column chromatography on silica gel, using $CHCl_3$ containing 1% MeOH as eluant, a white solid which was characterized as the product **40** (154 mg, 0.21 mmol, 55%): mp > 300 °C dec; negative-ion FABMS, *m/z* 737 for [M − H]$^-$; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.80–1.86 (4 H, m, 6a,11a,19a,24a-H), 2.20 (12 H, s, 5,13,18,26-CH_3), 2.41–2.50 (8 H, m, 7,11,20,24-CH_2), 4.98 (4 H, s, 6,12,19,25-H), 5.34 (4 H, s, 8,10,21,23-H), 5.69 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 1,4,14,17-H), 6.91 (4 H, dd, $J_{1,2} = J_{1,3} = 1.3$ Hz, 2,3,15,16-H), and 7.11 (2 H, s, 9,22-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.8 (C-5,13,18,26-Me), 26.6 (C-7,11,20,24), 40.0 (C-6a,11a,19,24a), 81.0 (C-8,10,21,23), 84.5 and 85.3 (C-1,4,6,12,14,17,19,25), 112.4 (C-9,22), 119.5 (C-5,13,18,26), 142.2 (C-2,3,15,16), 143.2 (C-7a,10a,20a,23a), 146.8, 147.9, and 148.3 (C-4a,5a,8a,9a,12a,13a,17a,18a,21a,22a,25a,26a).

***rel*-(1*R*,4*S*,4a*S*,6*r*,7a*R*,8*R*,10*S*,10a*S*,12*R*,14*S*,15a*R*,16*R*,19*S*,-19a*S*,21*R*,23*S*,24a*S*,25*R*,27*S*,27a*S*,29*s*,30a*R*)-1,4:6,29:8,27:10,25:-12,23:14,21:16,19-Heptaepoxy-1,4,4a,5,6,7,7a,8,10,10a,11,12,14,15,-15a,16,19,19a,20,21,23,24,24a,25,27,27a,28,29,30,30a-triacontahydro-9,26,31,32-tetramethyl-2,18:3,17-dimethylmethenotriadecacene (41).** The preparation of the title compound followed a procedure which was similar to that used for the synthesis of the [14]cyclacene derivative **32**. Reaction of the bisdiene **7** (10 mg, 0.068 mmol) with the bisdienophile **40** (14.2 mg, 0.019 mmol) afforded, after column chromatography on silica gel, using CH_2Cl_2 containing 2% ^{i}PrOH as the eluant, a white solid which was characterized as the [14]cyclacene derivative **41** (15 mg, 0.017 mmol, 89%): mp > 300 °C; positive-ion FABMS, *m/z* 885 for [M + H]$^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.56–1.69 (4 H, m, 4a,7a,27a,30a-H), 1.73–1.86 (4 H, m, 10a,15a,19a,24a-H), 2.09 (12 H, s, 9,26,31,32-CH_3), 2.22–2.75 (16 H, m, 5,7,11,15,20,24,28,30-H_2), 4.89 (4 H, s, 1,4,8,27-H), 4.94 (4 H, s, 10,16,19,25-H), 4.99 (2 H, s, 6,29-H), 5.28 (4 H, s, 12,14,21,23-H), and 7.08 (2 H, s, 13,22-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.8 (C-9,26,31,32-Me), 26.5 (C-11,15,20,24), 27.4 (C-5,7,28,30), 39.9 (C-10a,15a,19a,24a), 42.3 (C-4a,7a,27a,30a), 84.1, 84.2, and 84.8 (C-1,4,8,10,12,14,16,19,21,23,25,27), 86.4 (C-6,29), 112.2 (C-13,22), 117.8 (C-9,26,31,32), 143.0 and 143.2 (C-5a,6a,11a,14a,20a,23a,28a,29a), 148.1, 148.4, and 151.3 (C-2,3,8a,9a,12a,13a,17,18,21a,22a,25a,26a).

***rel*-(1*R*,4*S*,5*R*,8*S*)-1,4:5,8-Diepoxy-1,4,5,8-tetramethylanthracene (42) and *rel*-(1*R*,4*S*,5*S*,8*R*)-1,4:5,8-Diepoxy-1,4,5,8-tetramethylanthracene[18,64] (43).** The preparation of the title compounds followed a procedure which was similar to that used for the synthesis of the bisdienophiles **1** and **2**. Reaction of 1,2,4,5-tetrabromobenzene (23 g, 58 mmol), 2,5-dimethylfuran (70 mL, 658 mmol), and *n*-butyllithium (150 mmol, diluted with 100 mL of anhydrous C_6H_{14}) in PhMe (900 mL) afforded, after concentration of the reaction mixture in vacuo, a clear gum. This was triturated with acetone (40 mL) to afford a white crystalline solid after filtration, which was characterized as the *anti*-bisdienophile **43** (5.1 g, 19 mmol, 33%). The filtrate was concentrated in vacuo before trituration with petroleum ether (bp 60–80 °C) to afford, after filtration, a white crystalline solid, which was characterized as the *syn*-bisdienophile **42** (5.3 g, 20 mmol, 34%).

Anti isomer 43: mp 172–174 °C dec (from $CHCl_3$); EIMS, *m/z* 266 for [M]$^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.87 (12 H, s, 1,4,5,8-CH_3), 6.76 (4 H, s, 2,3,6,7-H), and 6.97 (2 H, s, 9,10-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 15.3 (C-1,4,5,8-Me), 88.7 (C-1,4,5,8), 110.6 (C-9,10), 147.2 (C-2,3,6,7), and 151.1 (C-4a,8a,9a,10a). Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 80.74; H, 6.53. Crystals of **43** suitable for X-ray crystallographic analysis[64] were obtained by vapor diffusion of C_5H_{12} into a CH_2Cl_2 solution of **43** at room temperature.

Syn isomer 42: 151–153 °C dec (from acetone); EIMS, *m/z* 266 for [M]$^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.86 (12 H, s, 1,4,5,8-CH_3), 6.78 (4 H, s, 2,3,6,7-H), and 6.96 (2 H, s, 9,10-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 15.4 (C-1,4,5,8-Me), 88.6 (C-1,4,5,8), 110.2 (C-9,10), 147.4 (C-2,3,6,7), and 151.1 (C-4a,8a,9a,10a). Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.16; H, 6.90. Crystals of **42** suitable for X-ray crystallographic analysis[64] were obtained by vapor diffusion of C_5H_{12} into a CH_2Cl_2 solution **42** at room temperature.

***rel*-(1*R*,4*S*,6*R*,6a*R*,8*S*,10*R*,11a*S*,12*S*,14*R*,17*S*,19*R*,19a*R*,21*S*,-23*R*,24a*S*,25*S*)-1,4:6,25:8,23:10,21:12,19:14,17-Hexaepoxy-6a,7,8,10,11,11a,19a,20,21,23,24,24a-dodecahydro-1,4,6,12,14,17,19,25-octamethylundecacene (44).** The preparation of the title compound **44** followed a procedure which was similar to that used for the 2:1 adduct **28**. Reaction of the bisdiene **26** (74 mg, 0.28 mmol) and the bisdienophile **42** (150 mg, 0.56 mmol) in CH_2Cl_2 (12 mL) under a pressure of 13 kbar for 150 h at 50 °C afforded, after column chromatography on silica gel using chloroform as eluant, a white solid, which was characterized as the product **44** (115 mg, 0.15 mmol, 54%): mp > 300 °C dec; positive-ion FABMS, *m/z* 795 for [M + H]$^+$; ^{1}H NMR (250 MHz,

$CDCl_3$) δ 1.62 (12 H, s, 6,12,19,25-CH_3), 1.70–1.76 (4 H, m, 6a,11a,19a,24a-H), 1.80 (12 H, s, 1,4,14,17-CH_3), 2.10–2.48 (8 H, m, 7,11,20,24-CH_2), 5.30 (4 H, s, 8,10,21,23-H), 6.50 (4 H, s, 2,3,15,16-H), 6.77 (4 H, s, 5,13,18,26), and 7.11 (2 H, s, 9,22-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.9 and 15.4 (C-1,4,6,12,14,17,19,25-Me), 29.7 (C-7,11,20,24), 45.5 (C-6a,11a,19,24a), 84.5 (C-8,10,21,23), 86.3 and 88.5 (C-1,4,6,12,14,17,19,25), 108.7 (C-5,13,18,26), 112.4 (C-9,22), 142.2 (C-2,3,15,16), 147.3 (C-7a,10a,20a,23a), 147.9, 149.4, and 152.3 (C-4a,5a,8a,9a,12a,13a,17a,18,21a,22a,25a,26a).

***rel*-(1*R*,4*S*,5a*S*,6*S*,8*R*,8a*R*,10*S*,12*R*,13a*S*,14*S*,16*R*,16a*R*,18*R*,-21*S*,22a*S*,23*S*,25*R*,25a*R*,27*S*,29*R*,30a*S*,31*S*,33*R*,33a*R*)-1,4:6,33:8,31:10,29:12,27:14,25:16,23:18,21-Octaepoxy-1,4,5,5a,6,8,8a,9,10,12,13,13a,14,16,16a,17,18,21,22,22a,23,25,25a,-26,27,29,30,30a,31,33,33a,34-dotriacontahydro-6,8,14,16,23,25,31,33-octamethyl-2,3,19,20-tetramethylidenepentadecacene (45).** The preparation of the title compound followed a procedure which was similar to that used for the synthesis of the [14]cyclacene **32**. Reaction of the bisdiene **7** (33 mg, 0.225 mmol) with the bisdienophile **44** (60 mg, 0.075 mmol) afforded, after column chromatography on silica gel, using CH_2Cl_2 containing 1% MeOH as the eluant, a white solid, which was characterized as the product **45** (63 mg, 0.058 mmol, 77%): mp > 300 °C; positive-ion FABMS, *m/z* 1087 for $[M + H]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 1.60–1.65 (32 H, m, 5a,8a,13a,16a,22a,25a,30a,33a-H and 6,8,14,16,23,25,31,33-CH_3), 2.20–2.60 (16 H, m, 5,9,13,17,22,26,30,34-CH_2), 5.00 and 5.08 (2 × 4 H, 2 × s, 2a,3a,19a,20a-H_E, 2a,3a,19a,20a-H_Z), 5.32 and 5.38 (2 × 4 H, 2 × s, 1,4,10,12,18,21,27,29-H), and 7.01 (6 H, s, 7,11,15,24,28,32-H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.5 and 15.3 (C-6,8,14,16,23,25,31,33-Me), 29.7 (C-5,9,13,17,22,26,30,34), 38.4 (C-5a,8a,13a,16a,22a,25a,30a,33a), 84.1 and 85.4 (C-1,4,10,12,18,21,27,29), 86.0 and 86.5 (C-6,8,14,16,23,25,31,33), 107.5 (C-7,11,15,24,28,32), 144.4, 147.6, 148.5, 148.8, 149.0, and 151.0 (C-2,2a,3,3a,4a,6a,7a,9a,10a,11a,12a,14a,15a,17a,19,19a,20,20a,21a,-23a,24a,26a,27a,28a,29a,31a,32a,34a).

Attempted Equilibration of *rel*-(1*R*,4*S*,6*R*,6a*R*,8*S*,10*R*,11a*S*,-12*R*,14*S*,17*R*,19*S*,19a*R*,21*S*,23*R*,24a*S*,25*S*)-1,4:6,25:8,23:10,21:12,19:14,17-Hexaepoxy-1,4,6,6a,7,8,10,11,11a,12,14,17,19,19a,20,21,-22,24,24a,25-eicosahydroundecacene (29) and *rel*-(1*R*,4*S*,6*R*,6a*R*,8*S*,10*R*,11a*S*,12*S*,14*R*,17*S*,19*R*,19a*R*,21*S*,23*R*,-24a*S*,25*S*)-1,4:6,25:8,23:10,21:12,19:14,17-Hexaepoxy-1,4,6,6a,7,8,10,11,11a,12,14,17,19,19a,20,21,22,24,24a,25-eicosahydroundecacene (28). A solution of the 2:1 adduct **28** (20 mg, 0.03 mmol), in CH_2Cl_2 (10 mL) was introduced into a high-pressure reaction vessel and subjected to 12 kbars pressure for 48 h maintaining the temperature at 40 °C. Upon cooling and depressurization, the homogeneous solution was examined by HPLC using CH_2Cl_2 containing 1% MeOH as eluant. No trace of the less chromatographically-mobile 2:1 adduct **28** or any other decomposition products of **29** were observed.

***rel*-(1*R*,4*S*,5a*S*,6*S*,8*R*,8a*R*,10*R*,13*S*,14a*S*,15*S*,17*R*,17a*R*)-1,4:6,17:8,15:10,13-Tetraepoxy-2a,2a,3a,3a,5,5,9,9,11a,11a,12a,12a,-14,14,18,18-hexadecadeutero-1,4,5a,6,8,8a,10,13,14a,15,17,17a-dodecahydro-2,3,11,12-tetramethylideneheptacene (51).** A solution of the bisdienophile **1** (200 mg, 0.95 mmol) and the octadeuteriobisdiene **36** (300 mg, 1.9 mmol) in anhydrous PhMe (60 mL) was heated under reflux for 12 h, under an atmosphere of argon in the absence of light. After removal of solvent in vacuo, the residue was subjected to column chromatography on silica gel, using CH_2Cl_2 containing 2% methanol as eluant, to afford a white solid, which was characterized as the product **51** (275 mg, 0.053 mmol, 41%): mp > 300 °C dec; positive-ion FABMS, *m/z* 541 for $[M + Na]^+$, 519 for $[M + H]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ 1.17 (4 H, br s, 5a,8a,14a,17a-H), 4.90 (4 H, s, 6,8,15,17-H), 4.98 (4 H, s, 4 H, 1,4,10,13-H), and 6.98 (2 H, s, 7,16-H); ^2H NMR (61.4 MHz, $CHCl_3$) δ 2.25 and 2.55 (2 × br s, 5,9,14,18-CD_2), 4.85–5.15 (2 × m, 2a,3a,11a,12a-CD_2); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 43.1 (C-5a,8a,14a,17a), 85.04 (C-1,4,10,13), 85.40 (C-6,8,15,17), 110.3 (C-7,16), 143.2, 144.1, and 144.7 (C-2,3,4a,6a,7a,-9a,11,12,13a,15a,16a,18a). Anal. Calcd for $C_{34}H_{14}D_{16}O_4$: C, 78.7. Found: C, 76.1.

Attempted Incorporation of 2,3,5,6-Tetramethylidenebicyclo[2.2.1]-heptane (7) into the Hexadecadeuterio 2:1 Adduct (51). A solution of the bisdiene **7** (150 mg, 1 mmol) and the hexadecadeuteriobisdiene **51** (50 mg, 0.1 mmol) in anhydrous PhMe (50 mL) was heated under reflux, in an atmosphere of argon, for 24 h in the absence of light. After concentration in vacuo, the residue was subjected to column chromatography on silica gel using CH_2Cl_2 as eluant. Both high field ^1H NMR spectroscopy and positive-ion FABMS showed no incorporation of signals associated with the production of the unlabeled 2:1 adduct **9** and indicated only an unchanged starting material **51**.

***rel*-(1*R*,4*S*,4a*S*,7a*R*,8*R*,10*S*,13a*R*,14*R*,17*S*,17a*S*,20a*R*,21*R*,-23*S*,23a*S*,26a*R*)-1,4:8,23:10,21:14,17-Tetraepoxy-1,4,4a,5,7a,8,10,10a,11,13,13a,14,17,17a,18,20,20a,21,23,23a,24,26,26a-tetracosahydro-2,16:3,15-dimethenoundecacene[70] (52).** $TiCl_4$ (1.9 mL, 17.3 mmol, freshly distilled) was added to THF (110 mL) with vigorous stirring at 0 °C, under an atmosphere of nitrogen, followed by $LiAlH_4$ (350 mg, 9.21 mmol). The resultant mixture was heated under reflux for 5 min. After cooling to 0 °C, a suspension of the macropolycycle **13** (315 mg, 0.44 mmol) in THF (15 mL) was added dropwise over 30 min. The reaction mixture was stirred at room temperature for 18 h and worked up by addition of Et_3N (1.65 mL, 0.012 mmol) followed by pouring into a 20% aqueous solution of KCl (200 mL). After extraction into CH_2Cl_2, drying over $MgSO_4$, and concentration in vacuo, the residue was subjected to column chromatography on silica gel, using $CHCl_3$ containing 3% MeOH as eluant, to afford a white crystalline solid after recrystallization from $CHCl_3$ which was characterized as the product **52** (128 mg, 0.19 mmol, 43%): mp > 250 °C; positive-ion FABMS, *m/z* 680 for $[M]^+$; ^1H NMR (400 MHz, CD_2Cl_2) δ 1.02–1.08 (8 H, m, 4a,7a,10a,13a,17a,20,23a,26a-H), 2.62 and 2.64 (2 × 8 H, 2 × m, 5,7,11,13,18,20,24,26-CH_2), 5.09 (8 H, s, 1,4,8,10,14,17,21,23-H), 6.69 (4 H, br s, 6,12,19,25-H), and 6.84 (4 H, s, 9,22,27,28-H); ^{13}C NMR (62.9 MHz, CD_2Cl_2) δ 31.8 (C-5,7,11,13,18,20,24,26), 47.0 (C-4a,7a,10a,13a,17a,20a,23a,26a), 83.5 (C-1,4,8,10,14,17,21,23), 110.6 (C-9,22,27,28), 125.6 (C-6,12,19,25), 138.1 and 146.2 (C-2,3,5a,6a,8a,9a,11a,12a,15,16,18a,19a,21a,22a,24a,25a).

1,4,7,10,14,17,21,24-Octahydro-2,6:3,15-dimetheneoundecacene[70] (54). The [12]cyclacene derivative **52** (100 mg, 0.147 mmol) was suspended, with ultrasonification, in a solution of Ac_2O and HCl (5:1 v/v) and heated under reflux for 16 h in an atmosphere of argon. After concentration in vacuo, the residue was partitioned between saturated aqueous $NaHCO_3$ (5 mL) and CH_2Cl_2 (100 mL), under ultrasonification for 30 min. The organic extract was dried over $MgSO_4$, filtered, and concentrated in vacuo. The yellow residue was dissolved in boiling C_6H_6 (80 mL) and heated under reflux for 30 min whilst subjected to ultrasonification. The hot solution was filtered onto a silica gel column packed with C_6H_6 and subjected to column chromatography on silica gel, using hot C_6H_6 as the eluant, to afford a white solid, after sublimation at 450 °C/10^{-3} Torr, which was characterized as the product **54** (50.4 mg, 0.083 mmol, 56%): mp > 600 °C; EIMS, *m/z* 608 $[M]^+$, 304 $[M]^{2+}$; ^1H NMR (400 MHz, CD_2Cl_2) δ 3.57–4.23 (16 H, 4 × AB, 4 × J_{AB} = 2 Hz, 1,4,7,10,14,17,21,24-CH_2), 6.91 (2 H, m, 27,28-H), 7.25 (8 H, m, 5,6,8,9,22,23,25,26-H), 7.40 (4 H, m, 11,13,18,20-H), and 7.77 (2 H, m, 12,19-H).

1,4,6,8,10,12,14,17,19,21,23,28-Dodecahydro-2,16:3,15-dimethenoundecacene[70] (56). A suspension of the [12]cyclacene derivative **54** in anhydrous Et_2O (3 mL) was added to a solution of Li (150 mg) in NH_3 (50 mL) containing EtOH (0.5 mL). The reaction mixture was stirred at −78 °C for 45 min before warming to room temperature, during which time the NH_3 evaporated off. Excess of lithium was destroyed by addition of further EtOH, and the product was partitioned between H_2O (10 mL) and C_6H_6 (20 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated in vacuo to afford a white solid which was characterized as the product **56**: mp > 300 °C; positive-ion FABMS, *m/z* 613 $[M + H]^+$; ^1H NMR (400 MHz, CD_2Cl_2) δ 3.48–3.67 (24 H, AB, J_{AB} = 15 Hz, 1,4,6,8,10,12,14,17,19,21,23,25-CH_2) and 6.92 (12 H, s, 5,7,9,11,13,18,20,22,24,26,27,28-H).

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