The Pagodane Route to Dodecahedranes: Highly Functionalized, Saturated and (Bis-)Unsaturated Pentagonal Dodecahedranes via S_N2 Cyclizations

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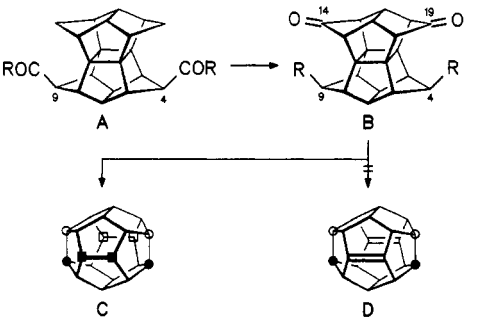
Abstract: Through S_N2 substitutive transannular cyclizations in either bisseco (**21** and **30–34**) or seco precursor substrates (**25** and **35–39**), (bis-)unsaturated, epoxy-annulated, and saturated dodecahedranes featuring novel substitution patterns—two (**45**), four (**42** and **44**), and six (**40**, **41**, and **43**) skeletal positions being pairwise functionalized—are synthesized starting from 14,19-dioxopagodane-4-*syn*,9-*syn*-dicarbonitrile (**4**). Crucial stages on the way from **4** to the key 1,16-dodecahedradiene **40** are the installation of anti-positioned leaving groups at C14(19) via pagodane bislactone (**4** → **5b** → **7b** → **11** → **3**, overall average 75%) and the pagodane → bisseco diene isomerization (**3** → **18** → **17** → **21**, overall average 80%). A shorter but less expeditious route to **40** is utilized for the preparation of secododecahedradiene **25** (**3** → **18** → **25**, derivatives **35–39**). X-ray analyses provide definite structural data on highly functionalized secopagodanes (**17**), isododecahedranes (**23**), and secododecahedradienes (**25**). The ϕ angle of 35.3° measured in **25** for C4(12) represents the strongest pyramidalization of olefinic carbon experimentally determined to date. The enormously bent C=C double bonds (ψ ca. 45°) in the unsaturated dodecahedranes (**40–42**) confer high chemical reactivity (e.g., toward oxygen, electrophiles, and 1,3-dienes) but do not impair the isolability of these olefins; intermolecular thermal reactions occur only under very forcing reaction conditions. Direct (sensitized) excitation of dienes **21**, **25**, and **40** with their perfectly synperiplanar π bonds (π,π distances ca. 2.6, 2.8/3.0, and 3.5 Å (MM2)) does induce transannular bond (cyclobutane) formation in **21** but not, however, in **25** and **40** (slow polymerization instead). Bromine addition does proceed in the homoconjugate fashion in **21** and **25** but not, however, in **40**. There is ample MS evidence for the existence of higher unsaturated dodecahedranes and for the operation of $C_{20} \rightarrow C_{11} + C_9$ and $C_{20} \rightarrow C_{15} + C_5$ fragmentation pathways.

Introduction

The synthetic route to pentagonal dodecahedranes, as reported by the Paquette group,[1] as well as the first pagodane → dodecahedrane transformations communicated from this laboratory[2] relies on catalytic dehydrogenation methodologies for the last C,C bonds to be formed. A major drawback inherently tied to this methodology is its intolerance toward functionalities on the molecular skeleton.[1,3-5] In a preceding paper in this journal,[6] we have described a way out of this dilemma; the aldol-type variant for the conversion of pagodanes into dodecahedranes (Scheme I), based on the incredibly expeditious one-pot preparation of 14,19-dioxopagodane-4-*syn*,9-*syn*-dicarbonitrile (**B**) (R = CN) from pagodane-4-*syn*,9-*syn*-dicarboxamide (**A**) (R = NH_2),[7] has paved the way to a vast array of dodecahedranes **C** in which four to eight skeletal positions are functionalized pairwise. Still, a limitation had to be accepted in that endothermic cyclizations—particularly to give higher unsaturated dodecahedranes, e.g., the highly desired 1,16-dodecahedradienes **D**—could not be effected. Obviously, the application of strictly irreversible C,C bond formation methodologies to appropriate precursor substrates should provide a remedy. Of the various methodological alternatives considered for this purpose (Scheme II in ref 6), the S_N2 variant, as abstracted in Scheme II, was pursued with high priority. In principle, pagodanes **E** with activating groups at C4(9) and leaving groups at C14(19) are isomerized into the respective bissecododecahedradienes **F**, which then are cyclized to dodecahedradienes **G**. Dodecahedrenes **I** and dodecahedranes **L** can be generated either directly from dienes **G** or after chemical manipulation of the C=C double bonds from the respective **H** and **K** bisseco precursors.

Scheme I



Yet, for the experimental realization, there are, again, a number of prerequisites, complications, and risks. (i) As was earlier commented upon,[5,6] the A and L groups needed in the bisseco intermediates **F**, **H**, and **K** have to be introduced prior to the pagodane stage **E**. The progressively tighter steric situation in the lateral half-cages on going from **F** to **H** to **K** structures, as expressed by the increasingly shorter lateral distances (the values

(1) Paquette, L. A. *Chem. Rev.* **1989**, *89*, 1051–1065. Paquette, L. A. The [n]Peristylane-Polyhedrane Connection. In *Cage Hydrocarbons*; Olah, G. A., Ed.; Wiley: New York, 1990; pp 313–332.

(2) Prinzbach, H.; Fessner, W.-D. Novel Organic Polycycles—An Adventure in Molecular Architecture. In *Organic Synthesis: Modern Trends*; Chizhov, O., Ed.; Blackwell: Oxford, 1987; pp 23–42. Fessner, W.-D.; Prinzbach, H. The Pagodane Route to Dodecahedrane. In *Cage Hydrocarbons*; Olah, G. A., Ed.; Wiley: New York, 1990; pp 353–405.

(3) Fessner, W.-D.; Murty, B. A. R. C.; Spurr, P. R.; Pinkos, R.; Melder, J.-P.; Fritz, H.; Prinzbach, H. *Chem. Ber.* **1992**, *125*, 1697–1717.

(4) Murty, B. A. R. C.; Pinkos, R.; Spurr, P. R.; Fessner, W.-D.; Lutz, G.; Fritz, H.; Hunkler, D.; Prinzbach, H. *Chem. Ber.* **1992**, *125*, 1719–1739.

(5) Lutz, G.; Pinkos, R.; Murty, B. A. R. C.; Spurr, P. R.; Fessner, W.-D.; Wörth, J.; Fritz, H.; Knothe, L.; Prinzbach, H. *Chem. Ber.* **1992**, *125*, 1741–1751.

(6) Melder, J.-P.; Pinkos, R.; Fritz, H.; Wörth, J.; Prinzbach, H. *J. Am. Chem. Soc.* **1992**, *114*, 10213–10231.

(7) Pinkos, R. Dissertation, University of Freiburg, 1990. For preliminary communications, see: Pinkos, R.; Rihs, G.; Prinzbach, H. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 303–305. Cf. ref 8.

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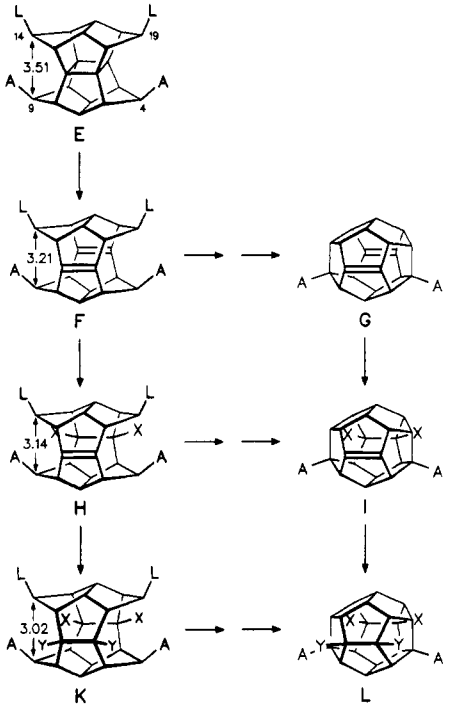
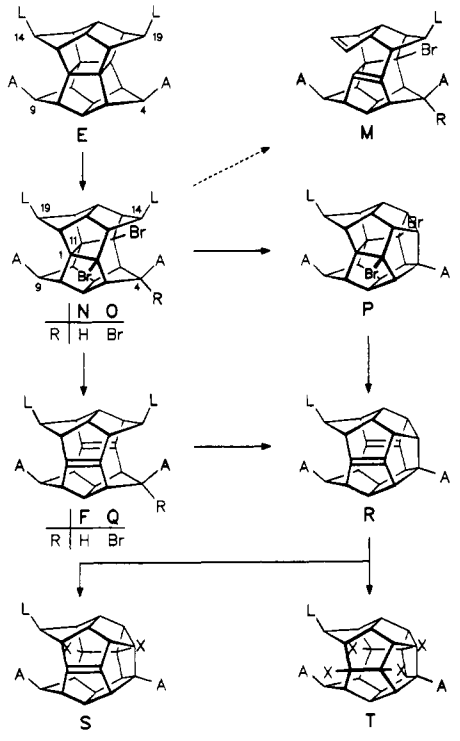
Scheme II



Scheme III



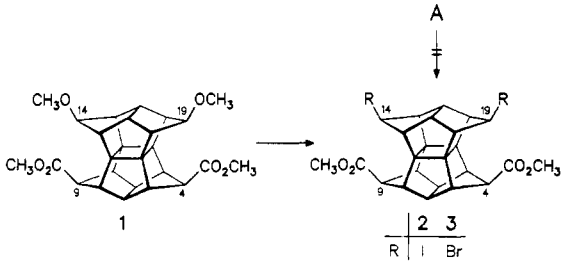
given in the formula are the MM2 values of the parent hydrocarbons[3]), impedes, if not totally prohibits, the manipulation of syn-functional groups and even the abstraction of syn-positioned protons within the lateral half-cages. (ii) For pagodane → bissecododecahedradiene transformations of type **E** → **F**, the sequential photoaddition (**N**) and Zn-promoted elimination of bromine (**F**) (Scheme III) had been singled out as the preparatively rewarding procedure. Yet, high substitution of the pagodane skeleton by electronegative substituents was reason to fear strong retardation or even preclusion of bromine addition to the 4-membered ring.[4] (iii) Under more forcing conditions, the A groups make bromination at C4(9) highly probable, both in **E** as well as in **N** substrates (e.g., **O**).[4,6] (iv) With respect to the eliminations **N** → **F** (**O** → **F** (**Q**)), the leaving group at C19 introduces a risk in that it potentially opens a competitive fragmenting 1,4-elimination pathway (e.g., **M**).

Not all potential complications, though, must necessarily be unprofitable. It had already been demonstrated for the aldol route how the complication in the photobromination of pagodanes resulting from unavoidable overbromination to give higher bromides of type **O** (iii) could be exploited for the directed preparation of secododecahedradienes.[6] This pathway from **E** to **R** via "isododecahedranes" **P** as intermediates, in principle, corresponds to route C of our original tactical pagodane → dodecahedrane scheme (Scheme I in ref 3), which we had failed to experimentally realize for the parent hydrocarbons. Route C, in fact, promises practical advantages in that the complication in the fragmenting 1,4-bromine elimination **N** → **F** by cyclization back to **E** is circumvented and that seco dienes **R** with their larger transannular π,π distance are generally less prone than the bissecodienes **F** (**Q**) to detracting transannular reactions. Interest in the actual isolation of seco dienes **R** stems mainly from their capacity as geometrical links between the nearly flat and strongly through-space homoconjugated bisseco dienes **F** and the more ball-shaped, highly pyramidalized and, in all probability, only weakly homoconjugated dodecahedradienes **G**. The derivatives **S** and **T** serve mainly as models for their **H**/**I** and **K**/**L** counterparts.

In this paper, we present the full account of our activities focused on the synthetic goals, as outlined in Schemes II and III.[7,8]

Results and Discussion

4-*syn*,9-*syn*,14-*anti*,19-*anti*-Tetrafunctionalized Pagodanes E. Pagodanes **A** with syn functionalities at C4(9)[9] are direct offsprings of our original pagodane synthesis which began from isodrin.[10] When several attempts to utilize these "neighboring" functionalities for the introduction of anti-positioned leaving groups at the "nonactivated" opposite C14(19) methylene units (cf. formula **E**) proved insufficiently rewarding or had totally failed, a *de novo* synthesis was specifically developed for the construction of 4-*syn*,9-*syn*,14-*anti*,19-*anti*-tetrafunctionalized pagodanes,[11] with the dimethyl *anti*,*anti*-dimethoxypagodane-*syn*,*syn*-dicarboxylate **1** as the prominent example. Substitution of the anti-methoxy groups at C14(19) by potent nucleofugues with retention of configuration was an easy task. Refluxing of **1** with a large excess of trimethylsilyl iodide (TMSI) led to a nearly quantitative yield of *anti*,*anti*-diiodide **2**—a convincing



reflection of the back-side protection and anchimeric assistance provided by the syn-ester groups at C4(9). Anti,anti-configuration at C14(19) was similarly retained in dibromide **3**, which had resulted from the reaction of **2** with excess bromine. Thus, with **2** and **3**, promising substrates of type **E** as entries into the S_N2

(8) Melder, J.-P. Dissertation, University of Freiburg, 1990. Melder, J.-P.; Pinkos, R.; Fritz, H.; Prinzbach, H. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 95–99.

(9) Nomenclature and numbering of all polycycles presented in this paper are secured from the POLCYC program. See: Rücker, G.; Rücker, C. *Chimia* **1990**, *44*, 116–120.

(10) Fessner, W.-D.; Sedelmeier, G.; Spurr, P. R.; Rihs, G.; Prinzbach, H. *J. Am. Chem. Soc.* **1987**, *109*, 4626–4642.

(11) Melder, J.-P.; Prinzbach, H. *Chem. Ber.* **1991**, *124*, 1271–1289.

route were at hand. Yet, to our dismay, the amount of labor needed for the preparation of **3** in gram quantities along this *de novo* route could not be brought into harmony with a broad synthetic application. In addition, diiodide **2** was found not to be amenable to the standard pagodane → bisseco diene isomerization methodology.[4]

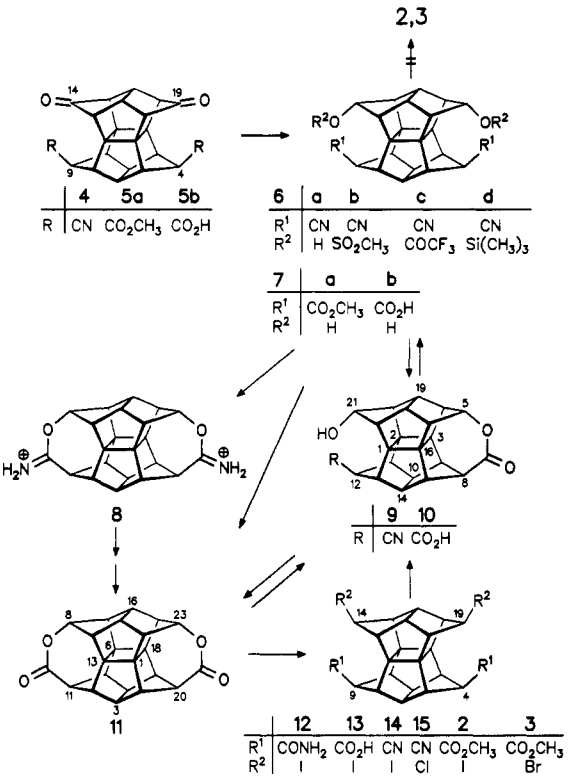
In the meantime, the 4-*syn*,9-*syn*-disubstituted pagodane-14,-19-diones **4** and **5**, representatives of intermediate **B** in Scheme I, had become available in a clearly more economical way.[7] Thus, the routes to **3** (**2**), illustrated in Scheme IV, with the sequences **4** → **6** → **14** → **2** and **5** → **7** → **11** → **3** were explored. Both, in principle, asked for anti hydride transfer to C14(19) and S_N2 substitution of appropriate syn nucleofugues. Diones **4** and **5a** could indeed be regiospecifically reduced to the respective *syn,syn*-diols **6a** (96%) and **7a** (88%), **4** with $NaBH_4$/ethanol and **5a**—to avoid partial ester reduction—with BH_3·THF.[12] It is noteworthy that in the latter case, no lactones were observed after acidic workup. Transformation of diol **6a** into the sterically somewhat encumbered dimesylate **6b**, ditriflate **6c**, and bis(trimethylsilyl) ether **6d** was, nevertheless, straightforward. Disappointingly, yet understandable after an inspection of the potential reaction channels, the potent nucleofugues in **6b,c** resisted all attempts for their substitution by Br^- or I^- ions; prolonged boiling in DMSO produced not even trace amounts of, e.g., diiodo dinitrile **14**. At best, 12% of dichloro dinitrile **15** could be isolated from the reaction of **6a** with $SOCl_2$/pyridine.

In this situation, bislactone **11** gained central importance. The two lactone bridges are part of conformationally rigid *Z* caprolactone units[13] and add significantly to the strain energy which is already present in the pagodane skeleton (E_{str} ca. 135 kcal/mol).[2] Access to **3** (**2**) through O-alkyl cleavage of the lactone rings therefore seemed promising.[14] With respect to the accessibility and stability of **11**, the expectation was experimentally verified in that both lactonizations, starting from the dihydroxy diacid **7b**, would greatly profit from an ideal "spatioelectronic" situation[15] but that hydrolytic cleavage[16] of the lactones produced would be rapid. After unsatisfactory results with various protocols for acid-catalyzed lactonization of, e.g., dihydroxy diacid **7b**,[17] which generally ended in complex mixtures of **11**, monolactone **10**, and hydroxy acids, a uniform generation of **11** was achieved along a somewhat modified procedure consisting of the treatment of **7b** with oxalyl chloride in CH_2Cl_2 instead of in benzene/DMF.[7] On a gram scale, a practically quantitative yield of **11** was attained after crystallization from CH_2Cl_2/ethyl acetate. Eventual loss of material is ascribed to hydrolysis during the workup procedure. Highly strained **11** proved, indeed, extremely prone to hydrolysis, which in control runs was shown to exclusively occur through CO–O cleavage to give, first, monolactone **10** and then dihydroxy diacid **7b**. C_{2v} symmetry of high-melting **11** (mp > 320 °C) is manifested in the six-line ^1H and eight-line ^{13}C NMR spectra with typical ^3J values of 5.2 and 4.2 Hz for the two lowest ^1H NMR triplet signals (H8(23), H11(20)).

In a parallel study directed toward the construction of nonpentagonal dodecahedranes, interest arose in monolactones of type **9**/**10**. In fact, the two steps **11** → **10** and **10** → **7b** were found to be kinetically sufficiently differentiated to allow a high accumulation of monolactone **10**.[18]

It fits into the picture of cage-driven lactonization that protonation of the nitrile functions in **6a** with strong nonnucleophilic acids did induce the rapid transannular addition of the very closely placed OH groups to give the C_{2v} symmetrical bislactone bisiminium salt **8** (^1H and ^{13}C NMR). Under appropriate conditions (F_3CO_2H/CH_2Cl_2, pyridine/water), bislactone **11** was isolated in better than 90% yield after crystallization (10-mg scale). Monolactone **9** could be selectively obtained (90%, 5% of **11**) after exposure of **6a** to boiling glacial acetic acid.

Scheme IV



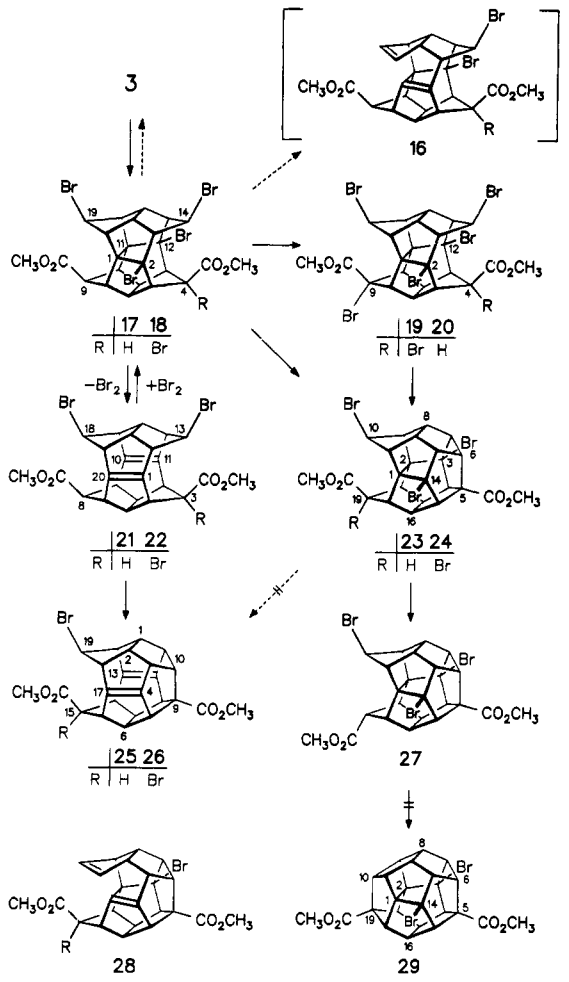
TMSI is a proven reagent for the O-alkyl cleavage of lactones.[19] With an excess of this reagent, at ambient temperature, after hydrolysis and esterification, exclusive formation of diiodide **2** (93%) from **11** was confirmed by TLC/NMR monitoring (93% after crystallization). Strain release in both ring-opening steps is apparently sufficient to also allow this double substitution with the less reactive TMSBr,[20] though only after prolonged heating to reflux of the $CHCl_3$ solution. A bonus of the TMSBr reagent stems from the observation that under defined reaction conditions, the preparatively useful bromo lactone intermediate can be attained.[21]

As a first résumé, it can be stated that the primary task, installation of anti leaving groups at C14(19) into dioxopagodane diester **5a**, could be adequately solved with the help of bislactone **11**. For the four-step route leading to *anti,anti*-dibromopagodane *syn,syn*-diester **3** (**4** → **5b** → **7b** → **11** → **3**), the overall yield runs up to an average of 75%. It adds to the economy of our project at large that with **4**, aldol-type and S_N2 variants share a common starting material.

Bissecododecahedradienes F, Isododecahedranes P, and Secododecahedradienes R. The next stage in Scheme II requires the transformation of pagodanes **E** into bissecododecahedradienes **F**, here (Scheme V) of **3** into **21** via photoaddition of bromine (tetrabromide **17**) and Zn-mediated fragmenting 1,4-elimination of bromine. It has been pointed out above that given the type of substitution in **3** and **17**, a selective conversion might constitute a rather problematic endeavour. In the reaction of **3** with bromine, the formation of **17** has to face parallel and subsequent competition

(12) Lane, C. F. *Chem. Rev.* **1976**, *76*, 773.
(13) Huisgen, R.; Ott, H. *Tetrahedron* **1959**, *6*, 253–267. Allinger, N. L. *Pure Appl. Chem.* **1982**, *54*, 2515–2522.
(14) Paquette, L. A.; Wyvratt, M. J.; Schallner, O.; Muthard, J. L.; Bergley, W. J.; Blankenship, R. M.; Balogh, D. *J. Org. Chem.* **1979**, *44*, 3616–3623.
(15) Dorigo, A. E.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 3698–3708.
(16) Wiberg, K. B.; Waldron, R. F. *J. Am. Chem. Soc.* **1991**, *113*, 7697–7705.
(17) Adam, W.; Baezu, J.; Liu, J. C. *J. Am. Chem. Soc.* **1972**, *94*, 2000–2006.
(18) Pinkos, R.; Melder, J.-P.; Fritz, H.; Prinzbach, H. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 310–313.
(19) Ho, T.-L.; Olah, G. A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 774. Drechsler, K. *Synthesis* **1983**, 459. Olah, G. A.; Husain, A.; Singh, B. P.; Mehrotra, A. K. *J. Org. Chem.* **1983**, *48*, 3667–3672.
(20) Kricheldorf, R. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 689.
(21) Weber, K. Dissertation, University of Freiburg, 1993.

Scheme V



by bromination of the activated and easily accessible anti-4(9) positions. In the case that addition of bromine to give **17** were to be, indeed, the initial step, subsequent attack at anti-H4 to give pentabromide **18** should be faster than at H9 to give isomer **20** for angular reasons, while attack at the barely accessible syn-14 and syn-19 hydrogens would be unlikely. With respect to the transformation **17** → **21**, it must be remembered that the generally competing re-formation of pagodanes (**17** → **3**) could be circumvented by raising the reaction temperatures to 150 °C or above. The uncertainty, though, remained whether the alternative 1,4-fragmentation to give **16** (cf. **M** in Scheme III) would complicate the picture.

An explorative bromination study with **3** under standard conditions (anhydrous CH_2Cl_2 solution, 5 equiv of bromine, 150-W Ultra Vitalux daylight lamp, Duran vessel)[4] made it rapidly clear that the rate of conversion was indeed comparably slow and that a selective generation of tetrabromide **17** was out of reach. Already after small conversions, a pentabromide (*m/z* = *inter alia* 773 (<1) [M^+], 253 (100), **18**) appeared, and after total conversion, even a hexabromide (*m/z* = *inter alia* 852 (4) [M^+], 771 (100), **19**) was present, if only in minute amounts. In the ultimately perceived protocol (millimolar scale, refluxing CH_2Cl_2 solution, ca. 20 equiv of bromine, daylight lamp), the reaction was stopped after ca. a 60-min irradiation time and the crude reaction mixture consisting of 92% of **18** and 5% of **19** was separated by chromatography. The greatly reduced propensity of these higher substituted secopagodane bromides toward hydrolysis at C2(12) is essential in this context.

With pentabromide **18** (mp 225–230 °C dec) at our disposal, we first probed its potentially most economical utilization, the one-pot conversion into bromosecododecahedradiene **25** by sequential or parallel 1,4- (**22**) and 1,5-bromine elimination. When rapidly added to a boiling suspension of 1 equiv each of Zn, NaI, and Na_2SO_3 in DMF,[4] **18** was completely consumed after ca. 30 s with the result, however, that besides polymeric material only two small monomeric fractions (ca. 10 and 5%) could be secured and identified as **25** (mp 184–187 °C) and isododecahedrane **23** (mp 220–221 °C). After some optimization efforts, a protocol using ca. 3 equiv of reagents and, consequently, a reaction time shortened to seconds provided 57% of **25** and 12% of **23** which were separated chromatographically from polymers. Control experiments (*vide infra*) excluded **23** as the precursor of **25** but did not definitely establish **22** as such instead. The ca. 10-min reaction time needed in the case of the 14,19-dimethoxy and 14,19-dioxo analogs lends credibility to a remarkable accelerating influence by the anti-bromine substituents in **18** (**22**). The ring closure **22** → **25** presumably involves the Zn organyl of **22** (C3). Sensitivity of diene **22** (**21**), more than that of diene **25**, toward Lewis acids, which are unavoidable in the reaction mixture, is responsible for at least part of the material loss by polymerization. In addition, the relatively numerous olefinic ^1H signals in the NMR spectrum of the crude reaction mixture could indeed be an indication of a competing Br2(12)–Br19 elimination (**16**).

With seco diene **25**, an attractive precursor of dodecahedradienes **G** was conveniently available, if only in a not totally satisfying yield. In order to avoid the detrimental side path leading to **23**, reduction of pentabromide **18** to the directly unobtainable **17** became mandatory and dibromo bisseco diene **21**, therefore, the next target. And indeed, of the four types of bromine substituents in **18**, the activated one at C4 could exclusively be eliminated by treatment with Pt/H_2 at ambient temperature, which paved the way to a nearly quantitative yield of tetrabromide **17** (mp 231–240 °C dec). Obviously, transannular C4–C14 bond formation, as postulated above for the Zn organyl of **22** or as observed under analogous conditions (Pt/H_2) with the respective 14,19-diketone,[6] did not interfere. The ensuing fragmenting bromine elimination **17** → **21**, however, ran into complications. From a series of experiments carried out under the conditions applied to **18** (boiling DMF, ca. 90% conversion after 5 s), crystalline diene **21** (mp 162–163 °C) could be isolated albeit only somewhat erratically in 55–60% yield after separation from **17** and polymeric material. Use of powdered iron instead of zinc in the otherwise standard procedure (boiling DMF) brought about the decisive improvement.[21] In spite of the necessity for much longer reaction times (ca. 10 min for total conversion), a yield of 90% of **21** was reproducibly achieved on a gram scale. It can be argued that the $FeBr_2$ produced in the reaction does less harm to product **21** than the stronger Lewis acid $ZnBr_2$, as was indeed verified experimentally. It should be recalled that such bisseco dienes form rather stable transannularly stabilized homoallylic cations upon addition of electrophiles.[22]

With a total yield of 80–85% for the three steps from **3** leading to bissecododecahedradiene **21**, stage **F** in the programmatical Scheme II was reached in a better than satisfactory manner.

With respect to the general alternatives outlined in Scheme III, it remained to be checked whether isododecahedranes of type **P** would be helpful in opening up a selective access to secododecahedradienes **R**. It was therefore pleasing to discover that the lateral cyclization **18** → **23**, which at 150 °C is only a minor reaction channel running parallel to the rapid fragmentation **18** → **22**, can be established as the almost exclusive pathway simply by lowering the reaction temperature to ca. 100 °C. After total conversion (5 min), it proved an easy matter to separate the ca. 85% of **23** from traces of seco diene **25** (resulting from **22**?). Hexabromide **19**, under the same set of reducing conditions, smoothly yielded tetrabromoisododecahedrane **24** (80% isolated), with the anti-bromine at C19 (bond angle C18–C19–C20 in **23** is 95.5(4)°, Figure 3) obviously being as resistant as that at C9

(22) Prakash, G. K. S.; Fessner, W.-D.; Olah, G. A.; Lutz, G.; Prinzbach, H. *J. Am. Chem. Soc.* **1989**, *111*, 746–748.

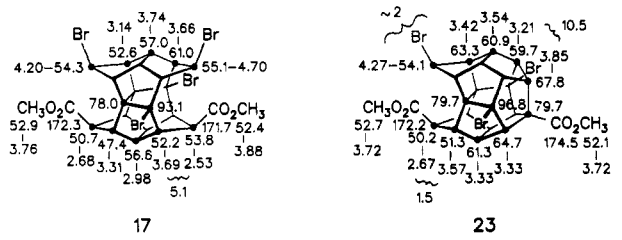


Figure 1. ^1H and ^{13}C NMR assignments ($CDCl_3$, δ, J (Hz)) for secopagodane **17** and isododecahedrane **23**.

of **19** (**20**). It should be added that **23** was also and almost quantitatively produced from **17** under base catalysis (NaH/THF) at ambient temperature.

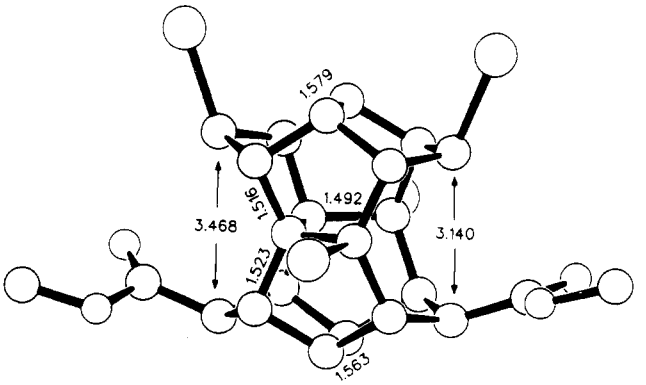
With such highly productive ways to the isododecahedranes **23** and **24**, it was highly disappointing to find out that they behave quite differently from **17** and **18** under the conditions for fragmenting 1,4-bromine elimination. In varied attempts at 150–160 °C during the zinc or iron protocol, **23** and **24** were recovered largely unchanged with, at best, traces of a diene (**25** and **26**) being detectable. More stringent reaction conditions (reaction times of 10–90 min and still incomplete conversion) led only to decomposition (via highly strained **28**?). We can only speculate about the reduced reactivity of **23** (**24**), particularly in view of the straightforward fragmentation in the related 10-oxo substrate.[6]

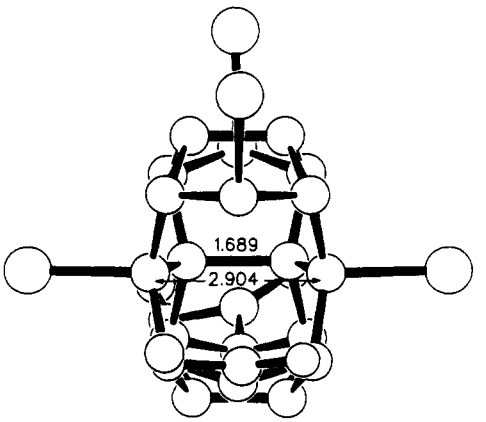
The stability noted for **24** under the given conditions of its formation from **19** and the failure to bring about cyclization **23** → **29** (cf. Scheme IX) under more vigorous basic conditions (NaH(KH)/boiling THF) were not much of a surprise given the transcaveal C10–C19 distance of 3.61 Å (Figure 3) and the extreme strain in the bisdehydrododecahedrane skeleton (E_{str} ca. 150 kcal/mol). Epimerization at C19 to give **27** (mp 225–230 °C) was induced, instead.

The brominated secopagodanes play a central part in our pagodane → dodecahedrane scheme. There is therefore a vast amount of spectral data at hand for comparison (Figures 2–7 in ref 3, Figure 1 in ref 6) in the confirmation of structures **17**–**20**. For **17**, as a representative case, the assignment of the 10 ^1H and 12 ^{13}C NMR signals is given in Figure 1. NMR analysis of **18** and **19** is complicated by the loss of the C_s symmetry; in a way typical for the high steric constraint, particularly in the "open" secopagodane half-cages, the buttressing influence of the α-bromine retards the rotation of the syn ester group at C4 sufficiently to make rotamers discernible.

Earlier attempts to collect experimental structural data for 2,12-dibromosecopagodanes, e.g., for 2,12-dibromo 4,9-dione,[3] had failed because of crystallographic disorder (cf. the 2,12-dimethoxy structure in ref 22). Crystals of **17** now proved suitable for such an analysis,[23] of which some relevant details are reproduced in Figure 2. The length of the C1–C11 bond of 1.689(15) Å represents one of the longest C,C single bonds found in cage structures,[24] and together with the rather unusual bond angles around the central carbon atoms C1(11) (100.0(8)–130.4(9)°) and C2(12) (103.5(7)–129.6(9)°) gives evidence to the high geometrical constraint in these skeletons. The differences with respect to transannular distances and internal bond angles on the "open" (C4–C14) and the "closed" side (C9–C19) are main references when it comes to explaining the differences in the rates of the Zn- and base-induced lateral cyclizations.

The isododecahedrane carbon skeleton of **23**, **24**, and **27**, formally a composite of pagodane and dodecahedrane "halves",





C2-C1-C8	105.2(8)	C3 -C4 -C-5	106.0(8)
C2-C1-C11	115.1(8)	C8 -C14-C10	96.8(8)
C8-C1-C11	100.0(8)	C13-C14-C15	104.8(8)
C8-C1-C20	130.4(9)	C18-C19-C20	98.0(8)
C1-C2-C3	106.9(9)	Br-C2 -C1 -C11	179.4(7)
C3-C2-C15	129.6(9)	Br-C2 -C1 -C20	70.0
Br-C2-C1	103.5(7)		

Figure 2. Selected X-ray structural data (bond lengths, transannular distances (Å), and bond and torsional angles (deg)) of secopagodane **17**.

is rather unusual.[6,25] For the individual assignment of the 9 ^1H and 12 ^{13}C skeletal NMR signals compiled for **23** in Figure 1, the comparison with the additionally C6-substituted analogs (cf. Figure 2 in ref 6) was especially helpful. An X-ray structural analysis for **23** (Figure 3)[26] provided definite structural information and allowed the evaluation of the calculational data. With 1.691 Å as the C1–C2 bond length and with angles around C1(2) between 99.9° and 135.7° (100.2–135.2°), the geometrical situation in this central part of the molecule is not much different from that in **17** (Figure 2) and gives no hint as to the resistance to bromine elimination. There are typical discrepancies to be noted for the two structural "halves" (pagodane vs dodecahedrane) with respect to the form of the cyclopentane units (torsion angles of -5.2(6)° for C15–C5–C4–C17 and of 54.5(6)° for C16–C20–C19–C18) and to the peripheral H–C–C–H torsion angles (cf. $J_{6,7}$ = 10.5, $J_{9,10}$ = 1.5, and $J_{18,19}$ = 2 Hz). The lateral C10–C19

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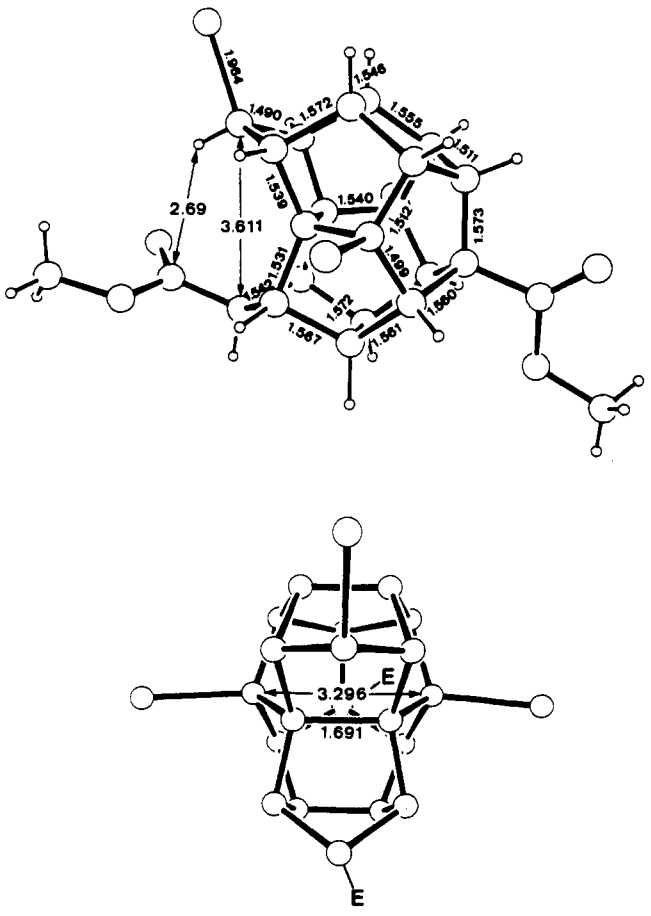

C2 -C1 -C11	100.5(4)	H6 -C6 -C7 -H7	12.8(7)
C2 -C1 -C14	121.3(5)	H6 -C6 -C13-H13	11.4(6)
C2 -C1 -C20	101.0(4)	H9 -C9 -C10-H10	57.3(7)
C11-C1 -C14	101.2(4)	H10-C10-C11-H11	60.2(6)
C11-C1 -C20	135.7(5)	H18-C18-C19-H19	57.4(7)
C14-C1 -C20	99.9(4)	H19-C19-C20-H20	62.3(6)
C9 -C10-C11	98.1(5)	H12-C12-C13-H13	14.0(6)
Br -C14-C1	110.3(4)	H15-C15-C16-H16	10.0(7)
Br -C14-C13	112.0(4)		
Br -C14-C15	110.4(4)		
C1 -C14-C13	103.7(4)		
C1 -C14-C15	104.6(5)		
C13-C14-C15	115.3(5)		
C18-C19-C20	95.5(4)		

Figure 3. Functional group orientation and selected X-ray structural data (bond lengths, transannular distances (Å), and bond and torsional angles (deg)) of isododecahedrane **23**.

distance of 3.611 Å, larger than the C9–C19 distance in **17** by 0.14 Å, is a qualitative measure for the reduced steric compression in the lateral half-cage and a reason for the failure in bringing about the lateral cyclization to give didehydrododecahedranes (**29**).

The bissecododecahedradiene diester, parent of **21**, features a pyramidalization angle of ca. 10° for the olefinic carbons and proves highly sensitive to oxygen.[3,8] Electron-attracting functionalities at the methylene positions had been found to significantly reduce this sensitivity. The electrochemically determined oxidation potential of 1.84 V for **21** is higher by 0.78 V than that measured for the bromine-free diene diester (1.06 (reversible)/1.51 (irreversible) V),[9,27] which can be taken as a measure of the additional inductive stabilization exerted by the two bromines. And indeed, **21** turned out to be slightly sensitive to oxygen; still, it should be handled under an inert atmosphere. With 155.7 ppm (Figure 5), the chemical shift of the olefinic carbons is practically that of the parent diene (155.4)[8] and thus, once more,[4,6] stands for its insensitivity to functionalities.[28] The long-wavelength UV maximum measured in CH_3CN at 287 nm (ϵ 140) (Figure 6) documents a slight red shift due to the bromines and is the standard evidence for homoconjugation between the synperiplanar and very proximate C=C double bonds. Unfortunately, as experienced with other such dienes, crystals of **21** (**22**) were of insufficient quality for an X-ray crystal structure analysis.[29]

The salient structural feature of the seco diene skeleton in **25** as a "Zwitter" of the nearly flat bisseco diene (**F**) and the more ball-shaped dodecahedradiene (**G**) skeletons finds direct expression *inter alia* in the transannular π,π distances, in the pyramidalization and chemical shift of the olefinic carbons (Figure 5), and in the UV absorption. Fortunately enough, crystals of **25** proved suitable and stable enough for an X-ray crystal structural analysis (Figure 4).[26] The compressional situation on the seco side is mirrored in the H19–C21 (2.30 Å) and C15–C19 (3.281 Å) distances which are shorter than the respective van der Waals contacts. The skeletal strain (E_{str} = 95.0 kcal/mol for the parent skeleton)[4] shows up in the C9–C10 bond of 1.603-Å length. The measured π,π distances of 2.849 and 3.195 Å, in line with weakend π,π interaction, agree fairly well with the calculated values (2.82 and 3.03 Å, MM2).[4] The lengths of these C=C double bonds (1.324 and 1.319 Å) are slightly shorter than those in bicyclo[3.3.0]-oct-1(5)-ene (1.345 Å)[31] and bridged derivatives thereof. With δ 175.4, the chemical shift of the C4(12) signal (Figure 5) is somewhat larger than that found for the olefinic carbons of dienes **D** (Figure 7). The ϕ angle at C13(17) of 15.5° (calcd 15.9°)[4] is slightly larger than that calculated for parent bisseco diene **B** (11.7°),[28] and the ϕ angle at C4(12) with 35.3° (calcd 29.5°) approaches that of parent dodecahedradiene **D** (42.9°).[8] To our knowledge, the 35.3° still makes up the strongest crystallographically determined pyramidalization of olefinic carbon.[31-33] The UV absorption maximum at 263 nm (CH_3CN, ϵ 270) places **25** into the predicted position between **21** and **40** (Figure 6). With respect to the interpretation of this absorption as a qualitative measure for π,π homoconjugation as in **21**, it has to be taken into account that increasing pyramidalization produces a decrease of the HOMO/LUMO gap.[34]

A short comment is appropriate with respect to some intriguing consistencies in the MS spectra of the secopagodanes, bissecododecahedranes and isododecahedranes of Scheme V. Initial 1,4-bromine elimination from (**17–20**)$^{\bullet+}$ and from (**23**, **24**, and

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(29) The recently determined C=C double-bond distances and ϕ angles for dioxodiene diester **i** and diene bislactone **ii** can be taken as reference values.[30]

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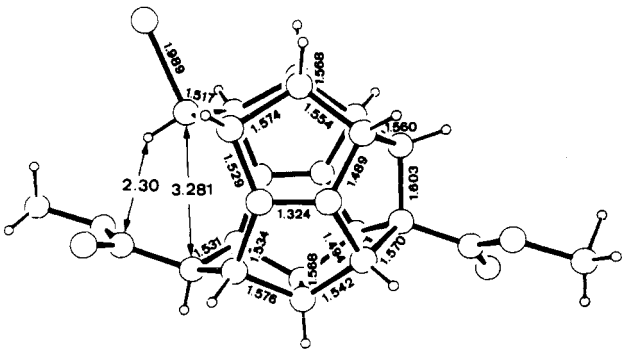
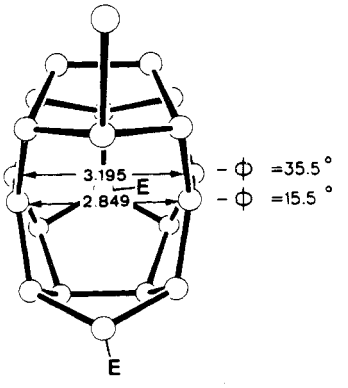




C8 -C12-C11	117.4(2)	H1-C1-C11-H11	11.4(3)
C8 -C12-C13	114.7(2)	H7-C7-C8 -H8	9.4(3)
C11-C12-C13	115.9(2)	H3-C3-C10-H10	9.9(3)
C12-C13-C14	110.8(2)		
C12-C13-C20	110.2(2)		
C14-C13-C20	137.3(2)		
C14-C15-C16	104.6(2)		

Figure 4. Functional group orientations and selected X-ray structural data (bond lengths, transannular distances (Å), and bond, torsional, and pyramidalization angles (deg)) of seco diene **25**.

27)$^{\bullet+}$ closely relates their fragmentation patterns to those of (**21** and **22**)$^{\bullet+}$ and (**25** and **26**)$^{\bullet+}$. Subsequent sequential loss of (H)-Br and $CH_3CO_2(H)$ units generally gives rise to intensive and partly very intensive signals for $C_{20}H_{14}$, $C_{20}H_{12}$, and even $C_{20}H_{10}$ ions and for the corresponding doubly-charged ions. Implying dodecahedral structures for these triene, tetraene, and pentaene species (*vide infra*) would amount to their formation being a synthetic alternative to the aldol-type and S_N2 variants for lateral C,C bond formation by radical/radical recombination or radical substitution. The intensity of some of the fragments derived from the C_{20} skeletons, considered typical for individual unsaturated dodecahedranes (cf. Schemes XV and XVI), can indeed be held indicative of dodecahedral intermediates.

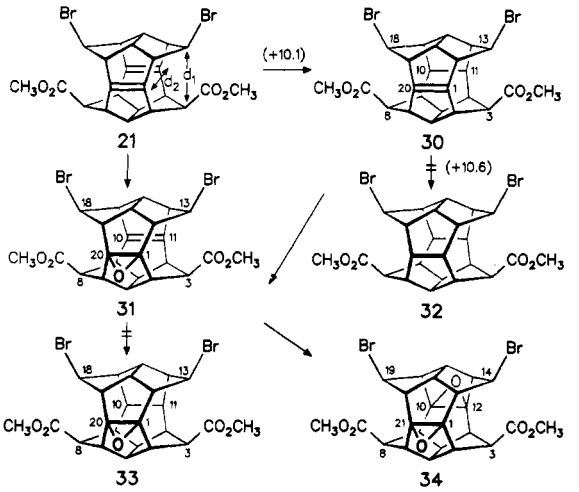
To return to Schemes II and III, for the conversion of tetrafunctionalized pagodanes **E** into tetrafunctionalized bissecododecahedradienes **F**, the three-step protocol **3** → **18** → **17** → **21** with a total yield of ca. 80% on the gram scale was a good basis for progression along the projected program. The on-first-sight even more attractive two-step protocol **3** → **18** → (**22**) **25** is, with at best 50% overall yield, an uncompetitive alley to dodecahedranes but has preparative value as a directed route to secododecahedradienes. A convincing explanation is still lacking as to why the latter should not be accessible via fragmenting 1,4-bromine elimination in isododecahedranes (**23** and **24**). The X,Y functionalities provisioned for dodecahedranes **I** and **L**, in principle, could be attached at either the diene **F** or diene **G** stage. In view of the rather diverging changes in enthalpy and strain tied to the "saturation" of the C=C double bonds in bisseco- (**F** and **H**), seco- (**R** and **S**), and dodecahedra(di)enes (**G** and **I**),[6] it appeared more advantageous to approach, particularly, the less symmetrically functionalized dodecahedranes (cf. **41**, **42**, and **44**) via their (bis)seco precursors. For that reason, the latter's preparation from dienes **21** and **25** is addressed next.

Bissecododecahedra(e)nes H(K) and Secododecahedra(e)nes S(T). Unsaturated bissecododecahedranes of type **F** and **H** have been calculated (MM2/MM3)[3] to be hyperstable. The high rate of the monohydrogenation **F** → **H** could be convincingly explained by the concomitant loss of destabilizing π,π interaction. "Saturation" of the C=C double bonds in the **F** and **H** structures by irreversible, "high-driving-force" reactions like epoxidation, carbene addition, and vicinal bis-hydroxylation, on the other hand, had posed no problem. In contrast, the seco olefins of type **R** and **S** in theory and experiment had been found to not be hyperstable.[4,6]

The attempts at "saturation" of bisseco diene **21** and seco diene **25** were limited to hydrogenation by diimide (N_2H_2) and epoxidation by benzoylpercarbamic acid. The choice of these reagents was dictated by the strong steric protection of the tetrasubstituted C=C double bonds and by the high propensity of the homoconjugated dienes to undergo acid-catalyzed skeletal rearrangements.

The response of diene **21** toward N_2H_2 ($(NCO_2K)_2/CH_3CO_2H$, CH_3OH/CH_2Cl_2, 0 °C) was unexceptional, and there was clean hydrogenation to seco ene **30** (96%, mp 163 °C). Again, the latter proved to be truly hyperstable, resisting even a very large excess of the reagent under relatively harsh reaction conditions. In fact, replacement of hydrogen atoms by large functionalities like bromine should increase the hyperstability, as it results from steric compression along the molecular surface. On the other hand, as was noted earlier,[6] the lessening of steric compression by ketonic functionalities at C13(18) had no significant impact on the course of the hydrogenation experiments.

Scheme VI



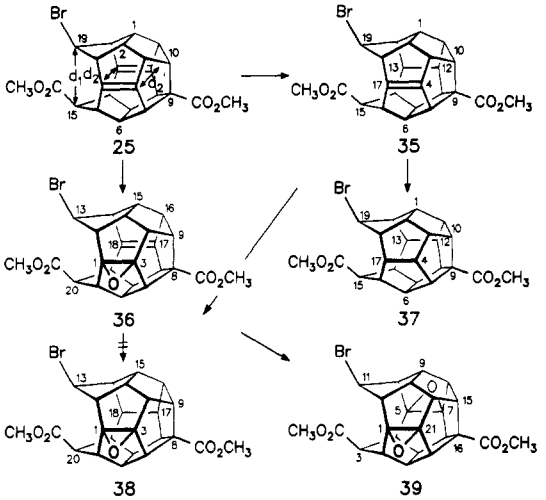
	21	30	32
d_1	3.21	3.14	3.02
d_2	2.62	2.98	3.47

Epoxidation of **21**, apart from smaller and not specifically analyzed rate discrepancies, closely corresponded to prior observations, particularly with the analogous 13,18-diketo diesters.[6] The first double bond is oxidized so much faster (**21** → **31**) than the second (**31** → **34**) that the practically exclusive generation of ene epoxide **31** (100%, mp 191 °C) was unproblematic (1 equiv of reagent, room temperature). After prolonged reaction times (24 h) and with excess reagent, however, diepoxide **34** could neatly be secured, in line with a much smaller increase in strain as compared to that in the hydrogenation **30** → **32**. Like in **30**, the C=C double bond in **31** resisted saturation by N_2H_2 to give

33. Epoxidation of **30** to **33** should be even more inhibited than that of **31**; indeed, with 4 equiv of benzoylperoxycarbamic acid, it took 6 h at ambient temperature for a ca. 75% conversion. **33** was the only product. Using *m*-chloroperbenzoic acid and a reaction time of ca. 20 h (total conversion), besides 70% of **33** and substantial amounts of polymers, we detected ca. 5% of diepoxide **34**. As an example in the catalytic hydrogenation experiments, dehydrogenation (**30** → **21**) is an interfering pathway.

Seco olefins **25** and **35** lived up to expectations. Exposure of **25** to a large excess of N_2H_2 induced the neat double hydrogenation to give secododecahedrane **37**. From a hydrogenation experiment interrupted at ca. 50% conversion and proving the presence of only a few percent of **35** besides **25** and **37**, an even greater rate for the second hydrogenation step can be concluded. A similar rate situation was noted for the epoxidation of **25**. Excess percarbamic acid at ambient temperature exclusively delivered seco diepoxide **39**. In control experiments, the second step **36** → **39** was found to be too rapid to allow the enrichment and isolation of ene epoxide **36**. The latter was therefore approached through cyclization of conveniently attainable bisseco ene epoxide **31**; after ca. 40% conversion, uniformly produced **36** was chromatographically separated. Under epoxidizing conditions, seco ene **35** differed again from bisseco ene **30** in that dehydrogenation (→ **25**) did not interfere with the smooth oxidation to yield **38**.

Scheme VII



	25	37
d_1	2.849	3.04
$d_2(d_2')$	3.195	3.60(3.89)

The structures, particularly the substitution patterns, of the (bis)seco derivatives presented in Schemes VI and VII were confirmed by spectral data, even though in some cases not all ^1H (^{13}C) NMR signals could be individually assigned. For better comparison with prior analyses of the bisseco (cf. Figures 3–7 in ref 3, Figure 1 in ref 6) and the seco structures (cf. Figure 2 in ref 6), the NMR assignments for dienes **21** and **25** and their derivatives **33**, **37**, and **38** are pictured in Figure 5. It may suffice to point out some typical substituent effects and some common regularities: the singlet (triplet) character of the α-bromine (ester) ^1H NMR signals, the para- (dia-)magnetic influence of the epoxide rings upon the α (β) ^1H (^{13}C) NMR signals, and the shift difference for the central carbons (corresponding to C4(12) and C13(17)) in seco diene **25**. The MS spectra, as for dienes **21** and **25**, provide evidence that the loss of (H) Br and CH_2CO_2 (H) might result in the formation of dodecahedranes with two to four C=C double bonds (*m*/*z* 256–252) and nicely complement the fragmentation patterns presented in the next section for the

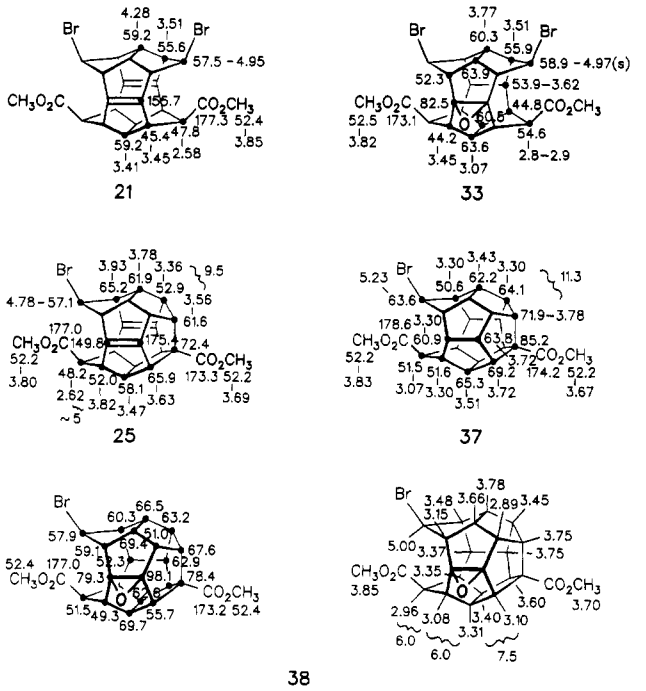


Figure 5. ^1H and ^{13}C NMR assignments ($CDCl_3$, δ, *J* (Hz)) for bisseco- (**21** and **33**) and secododecahedranes (**25**, **37** (500 MHz), and **38**).

respective dodecahedranes. Recent X-ray structural analyses for the 13,18-dioxo analogues of bisseco ene **30** and bisseco ene epoxide **31** convincingly demonstrate the changes in transcaveal distances and pyramidalization as calculated consequences for the "saturation" of one of the double bonds in **21**.[29]

Unsaturated (G and I) and Saturated Dodecahedranes (L). With (bis)seco dienes **21** and **25** and their derivatives, a broad collection of precursors for the generation of saturated (**L**) and unsaturated dodecahedranes (**G** and **I**) was at hand. With respect to the unsaturated members, we had learned from the tetrafunctionalized mono enes produced along the aldol route that thermal stability can be remarkable in spite of the high pyramidalization of the olefinic carbons (ψ 45–47°) and of the high olefin strain. The four allylic hydrogen atoms flanking the C=C double bonds apparently guarantee enough steric protection in order to block dimerizing stabilization pathways such as cyclobutane formation and ene addition.[32] The problem in handling these compounds is their extreme reactivity toward oxygen.

It is appropriate to start with the one-pot double cyclization **21** → (**25**) → **40** (E_{str} ca. 105 kcal/mol, ψ ca. 45°) as the most challenging case (Scheme VIII, the $\Delta H_f°$ (E_{str}) values (kcal/mol) and the geometrical data given are—again for **42**—that calculated for the respective unsubstituted skeletons[3,8]). The originally raised suspicion about risks arising from the relatively long distances between the carbons to be bridged and from the sharp increase in strain had been at least partially offset by the ease noted for the Zn-promoted cyclization **22** → **25**. The enolate formula **21**$^-$ and **25**$^-$ should illustrate that both cyclizing substitutions profit from very favorable, nearly colinear orbital alignment; a probably nonplanar geometry around the enolate α-carbons, as a consequence[35] of the small inner valency angles of ca. 105° in **21** and **25**, should even boost the driving force for S_N2 substitution.

For the preparation of the highly strained diene diester **40**, under the aspects of sensitivity of the product toward oxygen and potentially toward strong nucleophiles, and hence of an appropriate isolation procedure, several base systems were tested. The

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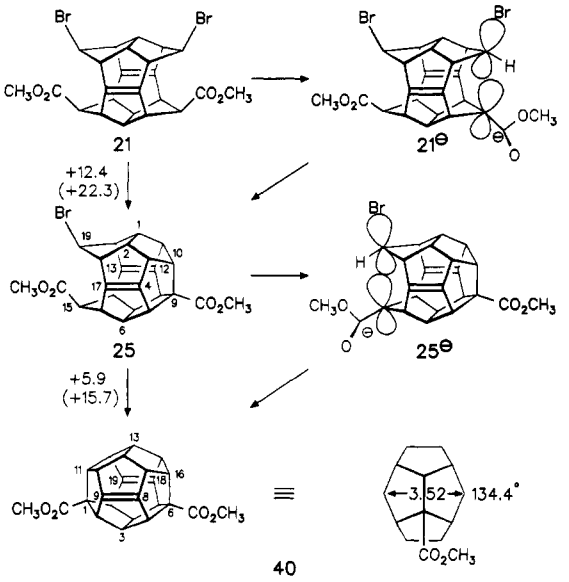
Scheme VIII



MS: m/z i.a. 372(M^+,100), 313(M−CH_3CO_2,64), 312(M−CH_3CO_2H,100), 254(M−2CH_3CO_2,42), 253(M−CH_3CO_2(H),59), 252(M−2 CH_3CO_2H,74), 127(254^{++},68), 126(252^{++},96), 125(250^{++},125).

originally used bases NaH(KH)/THF (which need a trace of water) as well as CH_3ONa/CH_3OH/THF at temperatures between −30 and 25 °C induced transformation into **25** and, depending on base concentration, slower, into **40**. During various workup procedures, partial loss of **40** by oxidation could not be avoided. Schwesinger's *t*-Bu-P_4 base[36] proved to be the one of choice. In a typical experiment, executed in all phases under careful exclusion of oxygen and moisture (glovebox), 0.2 mmol of **21** in 3 mL of THF was treated with ca. 4 equiv of base in 2 mL of THF at room temperature; after total conversion (ca. 15 min), rapid filtration through sharply dried silica gel, and concentration, practically pure **40** was isolated in reproducible 90–92% yield. In deoxygenated benzene, THF, and CH_2Cl_2 (ca. 60 mg/mL), **40** is readily soluble and stable for hours; as a ca. 10^{-2} M benzene solution, it even survived heating to 80 °C for several hours. In the crystalline state, it is stable for days under argon. For analytical purposes, **40** was recrystallized from carefully deoxygenated CH_2Cl_2/CH_3OH. After heating the colorless solid in a sealed tube, no melting or decomposition was noted, but the residue of a sample heated to 330 °C was established as oligomeric in nature (MS, no olefinic ^{13}C NMR signals) and insoluble in all common organic solvents.

In solution, **40** indeed turned out to be highly sensitive toward oxygen. The complex mixture of largely oligomeric oxidation products resulting from the exposure of a benzene solution to air did not contain diepoxide **43**. Because of unavoidable partial decomposition, the UV spectrum (Figure 6) was only qualitatively recorded; the beginning of the absorption (ca. 260 nm) and the shoulder at 253 nm define the differences to the absorption of the more "proximate" (bis)seco dienes **21** and **25**.[37,38] The ^1H NMR spectrum, as measured in standard $CDCl_3$ (Figure 7), was not totally resolved (2:4:2:6), yet in benzene-d_6, the five ^1H (4:2:2:4:2) and the seven ^{13}C NMR skeletal signals (4:2:2:2:4:2:4) expected for C_{2v} symmetry are neatly separated. The spread of the skeletal ^1H NMR shifts between 4.05 and 3.41 ppm and of

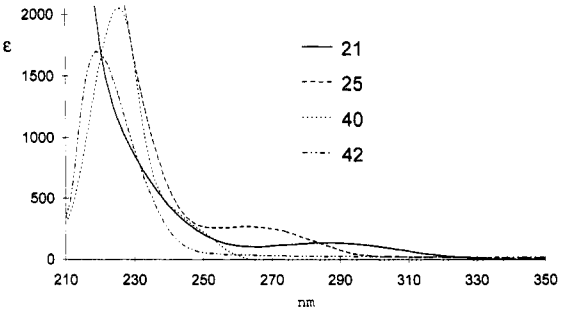


Figure 6. UV absorption curves (CH_3CN) of dienes **21**, **25**, and **40** and mono ene **42** (the latter two only qualitative).

the nonolefinic ^{13}C NMR shifts between 75.1 and 61.6 ppm—cf. 3.38 (66.9) ppm for parent dodecahedrane, the 0.35 ppm paramagnetic displacement for β-protons, and 13.5 (17.6) ppm for β- (γ-) carbons in the methoxycarbonyl derivative[39]—mirror typical substituent effects. The coupling constants of 10.4 Hz for the H11(16) triplet signal and of 4–5 (^3J) and ca. 2 Hz (^4J) estimated for the other protons are in line with the respective interplanary H/H angles as calculated for the "flattened" faces of the parent 1,16-dodecahedradiene.[4-6] The shift of the olefinic carbons—very similar to that of the parent diene (170.5)[4]—is larger by some 5–7 ppm than that found in related mono enes[6] (cf. **41** and **42**). The ca. 15 ppm larger chemical shift of the olefinic signals as compared with that in bisseco diene **21** (Figure 5) is general for these two series of compounds. The MS spectrum (EI, weak signals *m/z* 387 (4), 386 (10) point to traces of oxidized derivatives of which none is **41**) discloses the extrusion of CH_3-CO_2 (H) units from an obviously rather stable molecular entity. With reference to similar interpretations in the aldol series,[6] the relatively intensive *m/z* 255–250 signals (doubly charged at *m/z* 127 (68), 126 (96), 125 (35)) are provisionally ascribed to (protonated) dodecahedranes with up to five C=C double bonds. The $C_{11}H_7/C_9H_5$ signals (*m/z* 139 (18)/113 (24)) are speculatively assigned to a ring fragmentation similar to that specified below for **45** in Scheme XV.

Replacement of one C=C double bond in **40** by an epoxide unit, as in epoxydodecahedrene diester **41** (Scheme IX), only moderately alters the geometrical situation. The transannular distance is lengthened by ca. 0.1 ppm, and, with ψ values of 53.4° (46.0°) for the epoxide (olefinic) carbons, the molecular shape remains, consequently, rather "flat". To recall, in the aldol series,[6] the epoxydodecahedrene related to **41** had been the second unattainable "endothermic case". When bisseco ene epoxide **31** was exposed to the same set of cyclization conditions as those applied for **40**, the practically quantitatively formed and similarly oxygen-sensitive **41** was isolated after filtration as colorless needles. From qualitative rate comparisons in the epoxidation of dienes **25** and **40**, this route to **41** emerged as superior to the alternative **40** → **41** (→ **43**). During attempts to cyclize **31** with NaH/THF (trace of water), a potential complication introduced by proximate ene/epoxide arrangement surfaced. Transannular S_N2' hydrolysis, either in **31** or **36**, caused the appearence of small amounts of a side product which was spectroscopically identified as the 3,14-dihydroxy analog of isododecahedrane **23**; in **41**, the distance between the C=C double bond and the epoxide ring is sufficiently large enough to prevent this type of ene/epoxide reactivity. Consequently, **41** was neatly epoxidized by *m*-chloroperbenzoic acid to diepoxide **43**; with air, on the other hand, only oligomeric products were formed (as with **40**). For analytical purposes, a sample of **41** was recrystallized from deoxygenated THF/ethyl acetate and melted at 228 °C. The resolidified melt consisted of practically pure monomeric **41**. Symmetry reduced to C_s shows up in the complexity of the ^1H NMR spectrum (five of the nine

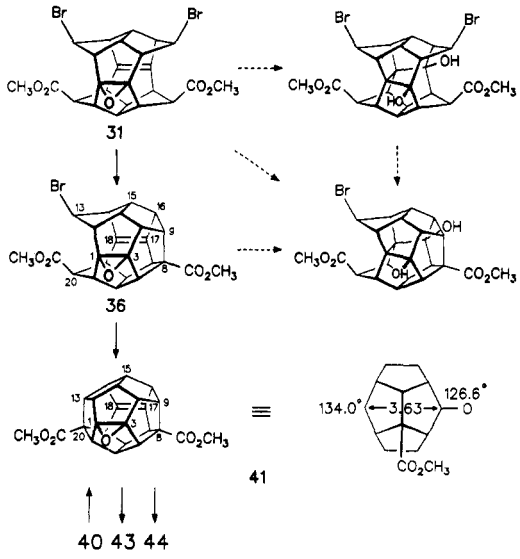
(36) 1-*tert*-Butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino)-phosphoranylideneamino]-2^2,4^2-catenadi(phosphazene). See: Schwesinger, R. *Chimia* **1985**, *39*, 269–272. Schwesinger, R.; Schlemper, H. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1167. Schwesinger, R. *Nachr. Chem. Tech. Lab.* **1990**, *38*, 1214–1215.

(37) Scheumann, K. Dissertation, University of Freiburg, 1993.

(38) Shea, K. J.; Greeley, A. C.; Nguyen, S.; Beauchamp, P. D.; Aue, D. H.; Witzeman, J. S. *J. Am. Chem. Soc.* **1986**, *108*, 5901–5908.

(39) Paquette, L. A.; Ternansky, R. J.; Balogh, D. W.; Kentgen, G. *J. Am. Chem. Soc.* **1983**, *105*, 5446–5450. Paquette, L. A.; Weber, J. C.; Kobayashi, T.; Miyahara, Y. *J. Am. Chem. Soc.* **1988**, *110*, 8591–8599.

Scheme IX

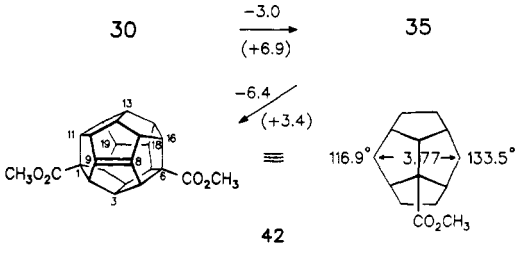


MS: m/z i.a. 388(M^+,80), 360(M−CO,14), 357(8), 329(M−CH_3CO_2,35), 328(M−CH_3CO_2H,100), 301(M−CO−CH_3CO_2,10), 269(M−CH_3CO_2(H),16), 241(M−CH_3CO_2(H),−CO,24), 120(240^{++},9).

signals are identified) and of the completely analyzed 12-signal ^{13}C NMR spectrum (2:2:1:1:2:1:1:2:2:2:2:2) (Figure 7), which typically features the molecular "halves" of diene **40** and diepoxide **43** with the olefinic (not the epoxide) carbon signals somewhat displaced to higher field (ca. 5 ppm). There is no UV evidence for transannular ene/epoxide [$\pi_2 + \sigma_2$] conjugation.[41] The MS spectrum (EI) is suggestive of parallel epoxide- and ester-induced fragmentation channels—expulsion of CO from the epoxide unit with disrupture[42] and of (H)CO_2CH_3 with retention of the molecular skeleton. There are only relatively weak signals manifesting intact ester-free dodecahedranes, e.g., *m/z* 269 assigned to $C_{20}H_{13}O$ epoxydodecahedratriene intermediates.

Dodecahedrene diester **42** (ψ = 46.5°) was analogously generated with P_4 base from bisseco ene **30** and again isolated by simple filtration in repeatedly better than 90% yield. Recrystallized from carefully deoxygenated THF/ethyl acetate, it melted unchanged at 174 °C. In experiments with NaH/DMF, up to 10% of saturated **45** was produced besides **42**. Addition

Scheme X



MS: m/z i.a. 374(M^+,100), 315(24), 315(M−CH_3CO_2,42), 314(M−CH_3CO_2H,34), 257(20), 255(M−CH_3CO_2(H),28), 141(10), 128(14), 115(17).

of stronger bases such as NaH to strongly bent C=C double bonds as in **42** has ample analogies.[32] As for **41**, reduced symmetry and additionally reduced functionalization cause the 400-MHz ^1H NMR spectrum in $CDCl_3$ (Figure 7) to present itself as a complex nonresolved multiplet (between 3.2 and 4.0 ppm). A change to benzene-d_6, (THF-d_8, pyridine-d_5) as solvent allowed at least partial identification. $J_{3,4}$ = 9.8 and $J_{10,14}$ = 6.0 Hz, in agreement with the respective interplanary H/H angles, are manifestations for the differing degree of bulging at the olefinic

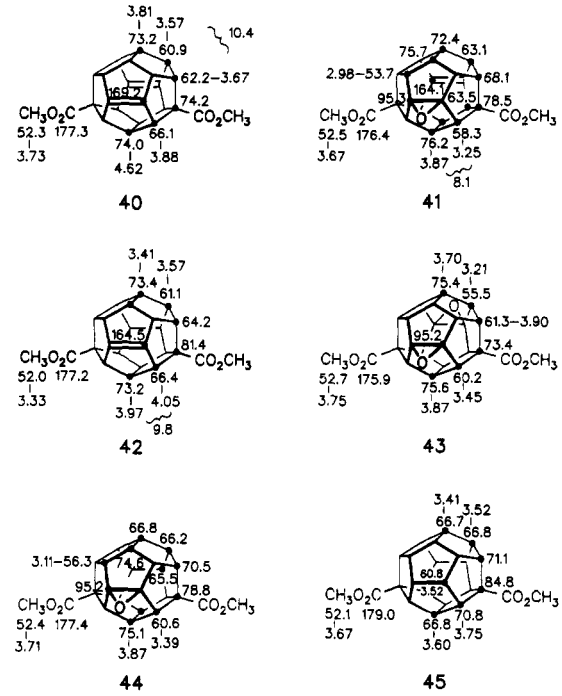


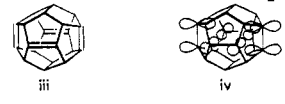
Figure 7. ^1H and ^{13}C NMR assignments of dodecahedranes **40–45**.

and saturated sides. Similarly, of the 12 skeletal ^{13}C NMR signals, only a few could be individually assigned. The MS spectra (EI), taken for various samples, as noted for **40**, have never been totally free of some weak signals demonstrating the incorporation of oxygen (e.g., *m/z* 390 (18), 406 (6)). The fragmentation pattern closely resembles that of **40**; the loss of both ester groups by β-elimination seems, however, less pronounced, and the signals for a $C_{20}H_{14}$ triene (*m/z* 254) seem to be relatively weak. In the UV spectrum, like that of **40** only qualitatively recorded (Figure 6), besides the maximum at 219 nm, no longer wave absorption is detectable. A broad UV absorption band peaking at 245 ± 15 nm has been claimed as typical for the comparably pyramidalized (ϕ = 47.8°, MM2), matrix-isolated tricyclo[3.3.2.$0^{3,7}$]dec-3(7)-ene (1557 cm^{-1} frequency for the C=C stretch).[43]

C_{2v} diepoxide **43**, thermally and air stable and with a ca. 3.6-Å (cf. X-ray in ref 6) distance between the two epoxide rings that are chemically not very sensitive, was approached in two standard and equally straightforward ways: from **40** and excess *m*-chloroperbenzoic acid and from seco diepoxide **39** with NaH/THF. After filtration over silica gel, **43** melted unchanged at 280–283 °C. Under the influence of the two epoxide oxygens, the five ^1H (2:2:2:4:4) and seven ^{13}C NMR signals (4:2:2:2:2:4:4) (Figure 7) were sufficiently separated to be unequivocally indentified. $J_{8,15}$ = 11.2 Hz is typically somewhat larger than in the more "flattened" **40**. The MS fragmentation is typically governed by parallel and consecutive extrusion of CH_3CO_2 (CH_3CO_2H) and CO units with *m/z* 285 standing for protonated diepoxydodecahedradienes.

Epoxydodecahedrane **44** (mp 182 °C) was gained through epoxidation of **42** as well as through cyclization of bisseco epoxide

(40) Present activities are directed toward the preparation of D_{2h} tetraene **iii** and its 8c–6e dication **iv**.



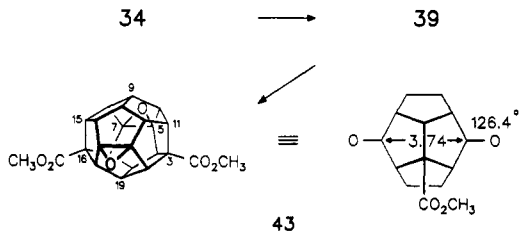
iii iv

(41) Prinzbach, H.; Klaus, M. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 276. Prinzbach, H.; Auge, W. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 209. Paulson, D. R.; Murray, A. S.; Fornoret, E. J. *J. Org. Chem.* **1978**, *43*, 2010–2013. Sedelmeier, G. Dissertation, University of Freiburg, 1979.

(42) Porter, R. N. *Mass Spectrometry of Heterocyclic Compounds*; Wiley: New York, 1985; Chapter 1.

(43) Yin, T.-K.; Radziszewski, J. G.; Renzoni, G. E.; Downing, J. W.; Michl, J.; Borden, W. T. *J. Am. Chem. Soc.* **1987**, *109*, 820–822.

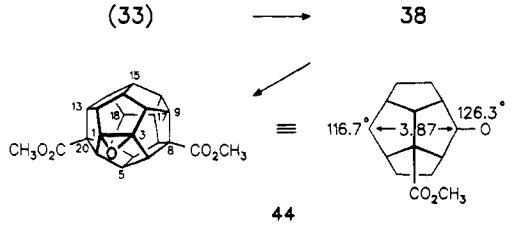
Scheme XI



43

MS: m/z i.a. 404(M^+,100), 376(M−CO,15), 344(M−CH_3CO_2H,40), 317(M−CH_3CO_2,−CO,14), 285(M−CH_3CO_2(H),21), 257(M−CH_3CO_2(H),−CO,26).

Scheme XII



44

MS: m/z i.a. 390(M^+,100), 362(M−CO,13), 331(M−CH_3CO_2,24), 330(M−CH_3CO_2H,52), 302(M−CH_3CO_2H−CO,17), 270(M−2CH_3CO_2H,7), 243(M−CH_3CO_2(H)−CO,19).

33. As noted for **35** → **38**, the epoxidation reaction is rapid enough to exclude the competing dehydrogenation **42** → **40** (no diepoxide **43**). In the 400-MHz ^1H NMR spectrum ($CDCl_3$) stretching from δ 3.85 to 3.0, of the seven signals expected for C_s symmetry (Figure 7), only the two highest multiplets belonging to the four α-epoxy protons H4(21) and H10(12) appeared individually. In contrast, the 12 skeletal ^{13}C NMR signals between 95.2 (C1,3) and 56.3 ppm (C10,12) could be individually attributed. Much like **41** and **43**, **44** responded to electron impact by CH_3CO_2 (CH_3CO_2H) and CO elimination in various sequences; again, potentially dodecahedral intermediates resulting from two ester eliminations are represented by only weak signals (e.g., *m/z* 271, protonated epoxydodecahedradiene).

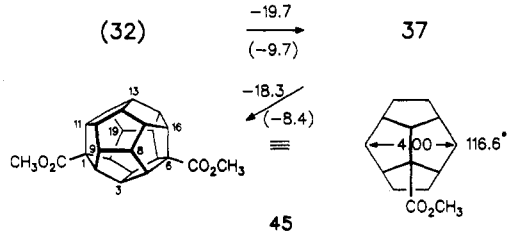
The C=C double bonds in unsaturated dodecahedranes (**40**, **41**, and **42**) are calculated not to be hyperstable. Indeed, dodecahedrane diester **45** was rapidly formed upon exposure of **40** or **42** to Pd/H_2. For preparative purposes (gram scale), a protocol was worked out starting from bisseco diene **21**;[44] after hydrogenation with diimide (96% **30**), double cyclization (**42**) and hydrogenation (H_2/Pd) are conveniently combined into a one-pot operation (90–92% of **45** isolated). In the hydrogenation of **21** with diimide, besides **30**, a trace (ca. 2%) of pagodane **3** (most probably not present in **21**) was found, for reasons not understood.

Diester **45**, very soluble in CH_2Cl_2, benzene, or THF, was recrystallized from CH_2Cl_2/ethyl acetate and melted at 190–192 °C without any notable change; at 140 °C/10^{-2} Torr, it can be sublimed. The narrow ($\Delta\delta$ ca. 0.35) ^1H NMR spectrum (Figure 7) is split into four multiplets (6:2:8:2) belonging to the β- (4 + 2), γ- (2 + 4 + 4) and δ- (2) protons (C_s). Of the ^{13}C signals, the α (2) and β (4) signals show the expected downfield displacement. The behavior under MS conditions is discussed below.

Unsaturated Dodecahedranes as Dienophiles. The highly bent C=C double bonds with correspondingly high strain and low LUMO energies should make the unsaturated dodecahedranes powerful participants in cycloaddition reactions—with restrictions due to the front-side protection exerted by the allylic hydrogens. While an account of the preparative implications of the special

(44) Wahl, F. Dissertation, University of Freiburg, 1993.

Scheme XIII

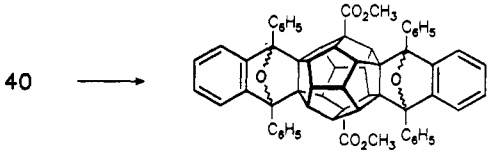


45

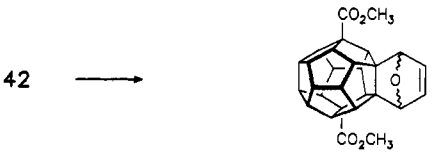
MS: m/z i.a. 376(M^+,15), 317(M−CH_3CO_2,32), 316(M−CH_3CO_2H,100), 258(24), 257(M−CH_3CO_2(H),58), 256(M−2CH_3CO_2H,34).

nature of these double bonds will be given in a broader context, two examples should suffice to demonstrate the usefulness of dodecahedrenes as dienophiles.

The measures described above for the preparation of pure crystalline samples of the unsaturated dodecahedranes **40–42** were somewhat demanding. For subsequent reactions with base-stable participants, the generation from the respective precursors (**21**, **30**, and **31**) was simplified by making use of conventional base systems. Thus, treatment of **21** with NaH/THF or **30** with CH_3ONa/CH_3OH/THF in the presence of an excess of diphenylisobenzofuran or of furan at room temperature formed the [4 + 2] adducts **46** (mixture of all three possible isomers **46 a–c**, ^1H NMR, MS) and **47** (ca. 1:1 mixture of the two isomers separated by chromatography, ^1H and ^{13}C NMR, MS) rapidly and they were isolated in high yields (90 and 93%).[45] Thermally reversible additions of this type are of great interest as "protecting" measures along the road to higher unsaturated dodecahedranes. Under this latter aspect, it should be noted that the bisseco and seco olefins (here **21**/**30** and **25**/**35**) generally are much less dienophilic, with the consequence that "protection" of this sort cannot be provided prior to the stage when the double bonds acquire their extreme oxygen sensitivity.



46a–c



47a,b

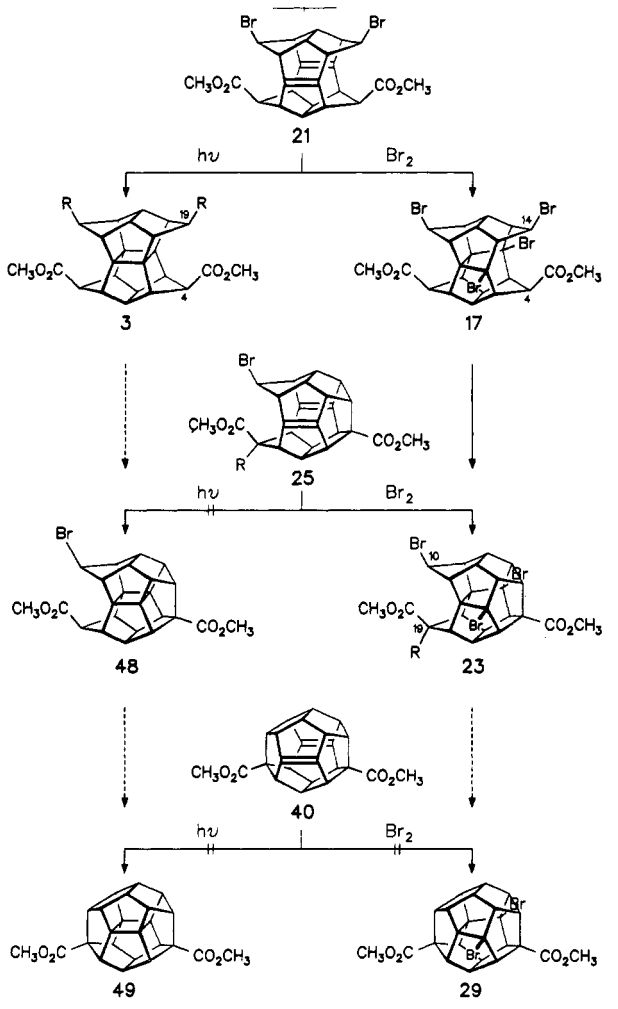
Transannular Reactivity in Bisseco-,Seco-, and Dodecahedradienes. The courses of photochemical and of addition reactions, particularly their discrepancies, for bisseco- (**21**), seco- (**25**), and 1,16-dodecahedradienes (**40**), are of particular relevance in the context of π,π interactions in this sequence of synperiplanar dienes of distinctly differing π,π distances (Scheme XIV).

The unusually proximate diene **21** (*d* ca. 2.8 Å[29]) upon direct and sensitized (acetone) excitation uniformly underwent the expected [$\pi_2 + \pi_2$] cycloaddition back to pagodane **3**. With regard to mechanisms, the transition state for the synchronous [$2_s + 2_s$] process[46] is well approximated in the rigid ground state. Bromine was rapidly added in the known regiospecific, homoconjugate fashion to yield precursor **17** via the strongly hyperconjugated 2-secopagodyl cation.[22]

(45) Weber, K.; Fritz, H.; Prinzbach, H. *Tetrahedron Lett.* **1992**, *33*, 619–622.

(46) Palmer, I. P.; Olivucci, M.; Bernardi, F.; Robb, M. A. *J. Am. Chem. Soc.* **1992**, *57*, 5081–5087; cited literature.

Scheme XIV



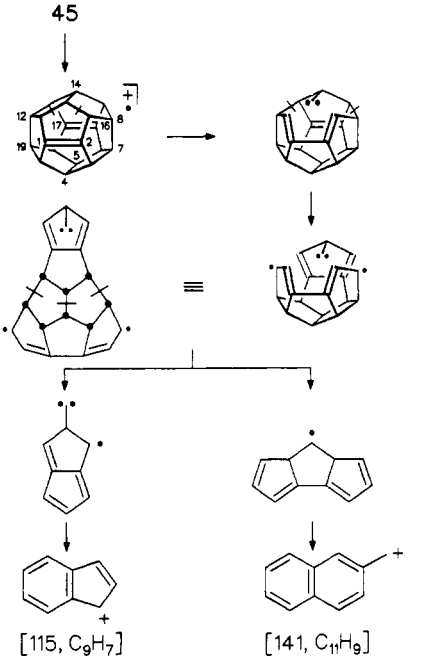
In diene **25**, both distances between the nonparallel double bonds (2.849 and 3.195 Å, Figure 4) on first sight seemed well suited for the $[\pi_2 + \pi_2]$ photocycloaddition. Yet, irradiation into the long-wavelength absorption as well as acetone sensitization ended in polymeric material. A presumptive intermediate diradical arising from initial C13–C17 bond formation obviously avoids the highly endothermic ring closure to didehydropagodane **48** ($\Delta\Delta H_f°$ = 130.3, ΔE_{str} = 176.4 kcal/mol). In contrast, addition of bromine again uniformly followed the path via the C13–C17 bridged homoconjugate cation to yield isododecahedrane **23**.

For dodecahedradiene **40**, a ca. 3.5-Å π,π distance in a very rigid carbon skeleton *a priori* qualified transannular C,C bond formation as highly unlikely. Indeed, photoexcited **40**, like **25**, produced only polymers. There is reason to assume transannular interaction in the excited states or intermediates, but procession to the tetradehydropagodane (tetradehydrododecahedrane) **49** ($\Delta H_f°$ (E_{str}) = 218.7 (258.3) kcal/mol (MM2)) would imply an even larger input of energy and strain than for **25** → **48**. The response toward bromine, under various conditions, differed from that of **21** and **25** insofar as instantaneous evolution of HBr took place. Dibromide **29** is absent from the complex mixture of tetrabromides and higher bromides formed. A high tendency for allylic substitution was also noted for the bromination of **42**,[21] and, in fact, under the given geometrical situation, allylic stabilization for cations, anions, and radicals on the dodecahedrane sphere should be very effective. These aspects will be addressed in detail in a forthcoming paper.

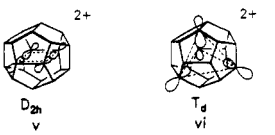
Fragmentation Pathways. Saturated dodecahedranes are thermally extremely stable, and the rigidity of their carbon skeleton counteracts any tendency for relief of strain by homolytic C,C bond cleavage. As a consequence, no fragmentation pattern was recognizable in the MS spectrum of the parent $(CH)_{20}$ hydrocarbon.[1] Even parent 1,16-diene with its strain energy of 105.3 kcal/mol ("diene strain" = 36.3 kcal/mol) survived its high-temperature VFP generation (ca. 500 °C).[8] Evidence pertaining to potential thermal stabilization pathways attainable to dodecahedranes of differing levels of dehydrogenation, and of relevance when it comes to the latter's preparation under FVP conditions, is suspected in the MS fragmentation behavior of various bisseco-, seco-, iso-, and dodecahedranes. Two exemplary cases are outlined here—with due reservation as to the still largely speculative nature of the given interpretation.

The MS spectrum (EI) of **45** is dominated by the signals arising from the parallel extrusion of CH_3CO_2 and CH_3CO_2H units with $C_{20}H_{16}^+$ and $C_{20}H_{16}^{2+}$ ions, ascribed *inter alia* to the 1,16-diene isomer, finding their expression with m/z 256 (38) and 128 (17).[47] Based on the here admittedly only rather weak $C_{11}H_9/C_9H_7$ lines (m/z 141 (8), 115 (18))—they are of higher intensity in the MS spectra of parent 1,16-dodecahedradiene itself and of its precursor bis-β-lactone but of only small intensity in the spectra of monoenes[21]—it is formulated in Scheme XV how by homolysis of allylically and bis-allylically activated C,C bonds the $C_{20} \rightarrow C_{11} + C_9$ fragmentation could proceed, with the intervention of increasingly less strained and conformationally more mobile nona-, hepta-, and pentaquinane intermediates. A somewhat concerted fission of the two allylic bonds flanking the first carbon—in the sense of a cheletropic retro-1,4-addition of carbenes to cisoid 1,3-dienes[48]—is probably helpful in order to overcome the restorative skeletal forces. The m/z 115 C_9H_7 ion (indenyl or

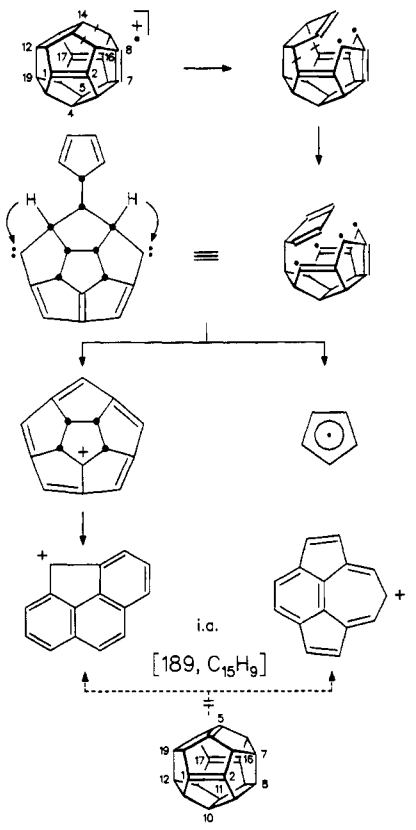
Scheme XV



(47) From calculations (R. Herges), the D_{2h} and T_d symmetrical $C_{20}H_{18}$ homoaromatic 4c–2e dications **v** and **vi** emerge as intriguing candidates. For the latter, Schleyer's 1,3-dehydro-5,7-adamantdiyl dication is the obvious prototype. See: Bremer, M.; Schleyer, P. v. R.; Schötz, K.; Kausch, M.; Schindler, M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 761. Kutzelnigg, W. *Isr. J. Chem.* **1980**, *19*, 173. Schindler, M.; Kutzelnigg, W. *J. Chem. Phys.* **1982**, *76*, 1919–1933. Schindler, M. *J. Am. Chem. Soc.* **1987**, *109*, 1020–1033.



Scheme XVI



related structure) has been identified as the main MS fragment of $(CH)_{10}$ triquinacene, the classical structural half of $(CH)_{20}$ dodecahedrane,[49] and correlated to a fragmentation route commencing with a similar cleavage of bis-allylic C,C bonds.[50]

In the MS spectra of those secopagodanes (**17**, **18**, and **53**), bisseco- (**21**), seco- (**25**), iso- (**23**), and dodecahedranes (**40** and **42**) which by virtue of their specific functionalization can be expected to deliver, at least in part, the 1,7,16-dodecahedratriene ion, the generally rather strong m/z 254 ($C_{20}H_{14}$) or m/z 253 ($C_{20}H_{13}$) signal is typically accompanied by a m/z 189 ($C_{15}H_9$) signal of varying intensity. This signal is found to be of negligible intensity for the 1,4,16-dodecahedratriene isomer[51] and for dienes (m/z 256) as well as monoenes (m/z 258). Eye-catching in the $C_{20} \rightarrow C_{15} + C_5$ fragmentation route proposed in Scheme XVI is the 10π C_{15} cation which, similarly to decadehydro[5]peristylane and the closely related C_5 symmetrical dodecahedrapentaene, should profit from significant delocalization energy.[52] Rather straightforward bond reorganizations transform this species into $C_{15}H_9$ ion(s) which are known to be stable.[53] For this fragmentation route to occur, one would again assume a certain degree of concertedness in the initiating rupture of the two bis-allylic C,C bonds, in the sense of a [4 + 2] cycloreversion, as well as in consecutive steps. Some of the attraction of such $C_{20} \rightarrow C_{15} + C_5$ fragmentations stems from their relationship to the $C_{15} + C_5$ strategy for the construction of dodecahedranes, as pioneered by Eaton.[54] Some of the compressional obstacles, which ultimately forced various research groups to abandon this approach, are helpful in the reverse direction.

Summary, Comments, and Outlook

For the parent dodecahedrane, the Paquette group has reported an impressive range of chemical transformations, such as electrophilic monosubstitutions, regiospecific 1,16-difunctionalizations under superacid conditions (together with Olah), annulation of rings (indano, cyclopropa), and ring expansions (one carbon, one nitrogen).[1] Recently, for the bromo- and phenylseleno derivatives, substitutions with intervention of the dodecahedryl radical have been demonstrated.[55] Yet, the complexity in product composition connected with multiple functionalization of the parent skeleton (cf. the calculated isomer distributions[25,44,56]) draws very narrow limits for directed syntheses.[44,57] The aldol and S_N2 variants of our pagodane → dodecahedrane scheme had been entered with the expectation that dodecahedranes with broad, modifiable substitution patterns would be attainable through the intermediacy of adequately functionalized pagodanes. This goal has indeed been met to full satisfaction. The preparative scope, as already inherent to the aldol approach (**C**), could be significantly extended with the S_N2 route (**U**), providing access to dodecahedranes pairwise functionalized at two (**45**), four (**42** and **44**), and six skeletal positions (**40**, **41**, and **43**) and particularly to the expeditious production of 1,16-dodecahedradienes of type **G** (**40**).

C U

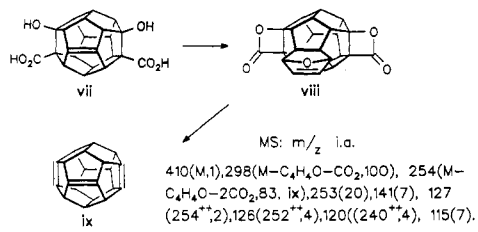
The 51–54% total yield for the eight steps leading from the common starting material **4** to **40** lends credit to the repeated assistance by stereodirecting cage effects and to the beneficial consequence of the substitution of zinc by iron in the critical pagodane → bissecododecahedradiene isomerization (**3** (**17**) → **21**). Still, the preparative hardships associated with the 15–18% total yield achieved for the 15-step sequence leading from isodrin to **4** remain. As stated before,[6] continuous supply of research material is vitally linked to well-organized logistics including a competent technical staff and industrial support in the form of kilogram quantities of an early intermediate.[10]

(48) Prinzbach, H.; Hartenstein, J. H. *Angew. Chem.* **1963**, *75*, 639–640. Jefford, C. W.; Mareda, J.; Gehret, J.-C. E.; Kabengele, T.; Graham, W. D.; Burger, U. *J. Am. Chem. Soc.* **1976**, *98*, 2585–2593.

(49) Müller, D. M. *Chem. Weekbl.* **1963**, *59*, 334. Woodward, R. B.; Fukunaga, T.; Kelly, R. C. *J. Am. Chem. Soc.* **1964**, *86*, 3162–3164. Jacobson, I. T. *Acta Chem. Scand.* **1967**, *21*, 2235–2246. Fu, X.; Cook, J. M. *J. Org. Chem.* **1992**, *57*, 5121–5128.

(50) Fukunaga, T.; McEwen, C. N.; Simmons, H. E.; deMeijere, A. *Int. J. Mass Spectrom. Ion Phys.* **1982**, *44*, 277–284. Scott, L. T.; Agopian, G. K. *J. Am. Chem. Soc.* **1974**, *96*, 4325–4326.

(51) This 1,4,16-triene (**ix**) has been cleanly generated in the mass spectrometer from the bislactone–furan adduct **viii** which had been obtained from the "aldol" product **vii**.[6] The MS spectrum, with only three strong lines, documents the rapid loss of CO_2 and furan and the relatively high kinetic stability of the triene ion. The triene itself could not be isolated in the way successfully followed for the 1,16-diene.[21]



(52) McEwen, A. B.; Schleyer, P. v. R. *J. Org. Chem.* **1986**, *51*, 4357–4368.

(53) The respective $C_{15}H_{10}$ methanofluorene has recently been identified as a trapping product when fullerenes were prepared in the presence of hydrogen donors. See: Chang, T.-M.; Naim, A.; Ahmed, S. N.; Goodloe, G.; Shevlin, P. B. *J. Am. Chem. Soc.* **1992**, *114*, 7603–7604.

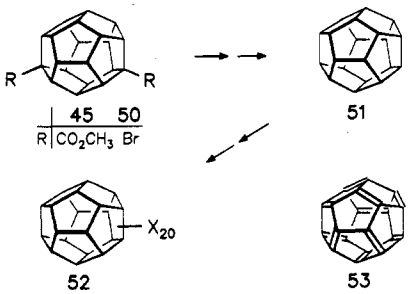
(54) Eaton, P. E. *Tetrahedron* **1974**, *35*, 2189–2223. Eaton, P. E.; Andrews, G. D.; Krebs, E.-P.; Kunai, A. *J. Org. Chem.* **1979**, *44*, 2824–2834. Eaton, P. E.; Bunelle, W. H. *Tetrahedron Lett.* **1984**, *25*, 23–26. Eaton, P. E.; Bunelle, W. H.; Engel, P. *Can. J. Chem.* **1984**, *62*, 2612–2626. Paquette, L. A. Recent Synthetic Developments in Polyquinane Chemistry. In *Topics in Current Chemistry*; Springer: Berlin, 1984; pp 135–146.

(55) Paquette, L. A.; Lagerwall, D. R.; Korth, H.-G. *J. Org. Chem.* **1992**, *57*, 5413–5419.

(56) Schulmann, J. M.; Venanzi, T.; Disch, R. *J. Am. Chem. Soc.* **1975**, *97*, 5335–5339. Balasubramanian, K. *Chem. Rev.* **1985**, *85*, 599.

(57) Wahl, F.; Prinzbach, H. Manuscript in preparation.

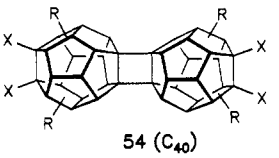
Notwithstanding, the mere installation of a multitude of functionality patterns onto the dodecahedrane periphery, the defined primary target of the aldol and S_N2 approaches, could not be our ultimate perspective. That and just to what extent the functionalities present in the aldol and S_N2 products **C** and **U** can be put to further preparative use are easily perceived and need no elaborate comment. Various functional modifications, mostly based on radical methodologies, have already been communicated.[45,58] They are instrumental, e.g., for the transfer of chirality and water solubility (glycosides) and for the construction of ansa-type bridges (remote functionalization) upon dodecahedranes. Exemplary annulations of 3- (cf. **41**, **43**, and **44**), 4-, 5-, and 6-membered rings *inter alia* via Diels–Alder (cf. **46**/**47**) and dipolar cycloadditions and metal complexations with unsaturated dodecahedranes, expansions of the C_{20} carbon skeleton to give a range of novel carbo- heteropolycycles, nonpentagonal dodecahedranes,[59] have been executed. A prominent example for preparative utilization of "S_N2-derived" dodecahedranes and for the efficient trapping of dodecahedryl radicals is the novel, highly expeditious access to the parent hydrocarbon **51** which consists of the degradation of 1,6-diester **45** via 1,6-dibromide **50**.[44,60] Intensive activities presently are going into the generation of higher unsaturated dodecahedranes with the C_{20} fullerene **53**[61] as a dim light on the horizon. To this end, perhalogenation of **51**, ultimately to $(CX)_{20}$ compounds **52** (X = F, Cl, and Br), is high on our list. In fact, from experiments executed with **51** under extremely forcing, light-assisted chlorination/bromination conditions, spectral evidence (MS, NMR) is derived which makes the substitution of all 20 hydrogens highly probable ($C_{20}Cl_{16}$, $C_{20}Br_{20}$); fragmentation patterns with m/z 240 (doubly charged at m/z 120) as a prominent signal could indeed be first indications for the existence of **53**—extending the MS evidence pointing to the potential accessibility of multiply unsaturated dodecahedranes (cf. $C_{20}H_{14}$ trienes,[51] $C_{20}H_{10}$ pentaenes[44]). Dodecahedrane **51** as icosahydrofullerene **53**?

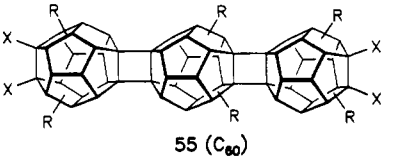


The high thermal stability of all unsaturated dodecahedranes so far known (mono-,[6] 1,16-dienes[8]) is one of the outstanding, in its extent, really surprising features[32,62] in the chemistry of these compounds. From recent experimentation,[21] it is concluded that the resistance toward dimerizing cyclobutane formation can be overruled by application of very forcing thermal activation. Access to broadly functionalized C_{40} and eventually C_{60} polycyclic skeletons of type **54** and **55** (Chart I) adds a new dimension to the pagodane → dodecahedrane project.[63]

A good part of the prominence attributed to the seco dienes of type **R** and to the dodecahedradienes of type **G** stems from their topological relationship with the bisseco dienes of type **F**. In the case of the latter, hyperconjugation approaching classical

Chart I





π,π conjugation,[64] unusual kinetic stability of the respective radical cations[65] and dications, and σ-homoaromaticity[66] are some of the intriguing phenomena directly related to their very special architecture. The question was posed as to what extent the progressive π,π distance on going from **F** to **R** to **G** dienes would sustain transannular π,π interaction and electron delocalization or even bond formation. With **25** and **40** (and parent diene[8]) now available, answers to this question are sought on the basis of the established chemical and spectroscopic diagnostics.[32] Even though in dodecahedradiene **40** cross-ring bridging (**29** and **49**) expectedly does not occur, electrochemical and spectroscopic studies as well as calculations[67] justify the conclusion that the two rather distant C=C double bonds experience notable through-space interaction and that electron delocalization is operative through the dodecahedrane cage.[68]

Experimental Section

Experimental data were recorded using the following: melting points (mp), Bock Monoscop M; analytical TLC, Merck silica gel plates with F_{254} indicator; IR, Perkin-Elmer 457 and Philips PU 9706; UV, Perkin-Elmer Lambda 15; ^{1}H NMR, Bruker WM 250, AM 400 (if not specified otherwise, the 250-MHz spectra are given); ^{13}C NMR, Bruker WP 80, WM 250, AM 400, (if not specified differently, the 100.6-MHz spectra are given); MS, Finnigan MAT 445. Chemical shifts were recorded relative to TMS ($\delta = 0$), and coupling constants are in hertz. For signal assignment, standard techniques such as homo- and heteronuclear decoupling experiments or 2D FT COSY or heterocorrelation spectra were employed; assignments indicated with *(+) can be interchanged. Generally, the H,H and C,H connectivities were established by two-dimensional homo- and heteronuclear correlated spectra. Whenever necessary, NOE measurements were performed to elucidate stereochemical (transannular) relationships.

Dimethyl 14-*anti*,19-*anti*-Diiodoundecacyclo[9.9.0.0^{1,5}.0^{2,12}.0^{2,18}.0^{3,7}.0^{6,10}.0^{8,12}.0^{11,15}.0^{13,17}.0^{16,20}]icosane-4-*syn*,9-*syn*-dicarboxylate (2). To a solution of **11** (100 mg, 0.29 mmol) in CH_2Cl_2 (3 mL) was added TMSI (0.3 mL). After 17 h at ambient temperature, the mixture was concentrated *in vacuo* and, after solvolysis with methanol (1 mL), again concentrated and then diluted with CH_2Cl_2 (5 mL). To this suspension was added diazomethane in ether dropwise, until a homogeneous, yellow solution had formed. Excess diazomethane was destroyed with formic acid. Concentration *in vacuo*, filtration over silica gel (CH_2Cl_2/ethyl acetate, 19:1), and crystallization from CH_2Cl_2/ethyl acetate gave **2** (170 mg, 93%): mp 220–223 °C dec; IR (KBr) 2970, 2945 (C—H),

(58) Scheumann, K.; Wahl, F.; Prinzbach, H. *Tetrahedron Lett.* **1992**, *33*, 615–618.
(59) Pinkos, R.; Voss, T.; Prinzbach, H. Manuscript in preparation.
(60) Wahl, F.; Wörth, J.; Prinzbach, H. Manuscript in preparation.
(61) Bakowies, D.; Thiel, W. *J. Am. Chem. Soc.* **1991**, *113*, 3704–3714. Parasuk, V.; Almlöf, J. *Chem. Phys. Lett.* **1991**, *184*, 187–189.
(62) Eaton, P. E. *Tetrahedron* **1974**, *35*, 2189–2223.
(63) The first dimers of type **54** (X = H, R = CO_2CH_3) have been secured in good yield by heating **42** up to 350 °C. See: Weber, K.; Voss, T.; Prinzbach, H. Manuscript in preparation.
(64) Elsässer, D.; Martin, H.-D.; Mayer, B.; Lutz, G.; Prinzbach, H. *Chem. Ber.* **1991**, *124*, 2863–2869.
(65) Prinzbach, H.; Murty, B. A. R. C.; Fessner, W.-D.; Mortensen, J.; Heinze, J.; Gescheidt, G.; Gerson, F. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 457.
(66) Prakasch, G. K. S.; Krishnamurthy, V. V.; Herges, R.; Bau, R.; Yuan, H.; Olah, G. A.; Fessner, W.-D.; Prinzbach, H. *J. Am. Chem. Soc.* **1988**, *110*, 7764–7772. Herges, R.; Schleyer, P. v. R.; Schindler, M.; Fessner, W.-D. *J. Am. Chem. Soc.* **1991**, *113*, 3649–3656.
(67) In collaboration with Prof. Dr. J. Heinze (Freiburg), Prof. Dr. H.-D. Martin, Dr. B. Mayer (Düsseldorf), and Doz. Dr. R. Herges (Erlangen).
(68) Weber, K.; Prinzbach, H.; Schmidlin, R.; Gerson, F.; Gescheidt, G. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 875–877.

1725 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.70 (m, 14s-, 19s-H), 3.63 (s, OCH_3), 3.59 (m, 16-, 17-H), 2.92 (m, 4a-, 9a-H), 2.77 (m, 6-, 7-H), 2.74 (m, 3-, 5-, 8-, 10-H), 2.63 (m, 13-, 15-, 18-, 20-H); ^{13}C NMR ($CDCl_3$) δ 172.9 (C=O), 62.2 (C-1, -2, -11, -12), 60.9 (C-16, -17), 57.7 (C-4, -9), 57.5 (C-6, -7), 51.8 (CH_3), 49.2 (C-13, -15, -18, -20), 43.8 (C-3, -5, -8, -10), 35.0 (C-14, -19); MS (EI) *m/z* (relative intensity) *inter alia* 628 (M^+, 50), 501 (84), 469 (5), 441 (4), 374 (45), 314 (12), 255 (15), 254 (14), 253 (12), 191 (100), 190 (14), 189 (15), 108 (21), 127 (17), 115 (13).

Dimethyl 14-*anti*,19-*anti*-Dibromoundecacyclo[9.9.0.$0^{1,5}$.$0^{2,12}$.$0^{2,18}$.$0^{3,7}$.$0^{6,10}$.$0^{8,12}$.$0^{11,15}$.$0^{13,17}$.$0^{16,20}$]icosane-4-*syn*,9-*syn*-dicarboxylate (3). A solution of **11** (1.0 g, 2.90 mmol) in $CHCl_3$ (5 mL) was heated with TMSBr (3 mL) at reflux for 4 days. Concentration *in vacuo*, solvolysis with methanol (1 mL), concentration again, and then addition of CH_2Cl_2 (15 mL) gave a suspension to which diazomethane in ether was added dropwise until a homogeneous, yellow solution had formed. Destruction of excess diazomethane with formic acid, concentration in vacuo, filtration over silica gel (CH_2Cl_2/ethyl acetate, 19:1), and crystallization from CH_2Cl_2/ethyl acetate gave **3** (1.4 g, 90%): mp 235–236 °C; IR (KBr) 2970, 2940 (C—H), 1725 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.84 (br s, 14s-, 19s-H), 3.65 (s, OCH_3), 3.59 (m, 16-, 17-H), 2.91 (s, 4a-, 9a-H), 2.81 (m, 6-, 7-H), 2.75 (m, 3-, 5-, 8-, 10-H), 2.60 (m, 13-, 15-, 18-, 20-H); ^{13}C NMR ($CDCl_3$) δ 173.0 (C=O), 62.8 (C-1, -2, -11, -12), 60.1 (C-16, -17), 58.6 (C-14, -19), 57.8 (C-4, -9), 57.7 (C-6, -7), 51.9 (OCH_3), 48.5 (C-13, -15, -18, -20), 43.9 (C-3, -5, -8, -10); MS (EI) *m/z* (relative intensity) *inter alia* [536 (64), 534 (100), 532 (63), M^+], 254 (11), 253 (13), 249 (13), 189 (11), 128 (16).

14,19-Dioxoundecacyclo[9.9.0.$0^{1,5}$.$0^{2,12}$.$0^{2,18}$.$0^{3,7}$.$0^{6,10}$.$0^{8,12}$.$0^{11,15}$.$0^{13,17}$.$0^{16,20}$]icosane-4-*syn*,9-*syn*-dicarboxylic Acid (5b). A solution of **4** (2.0 g, 5.9 mmol) in glacial acetic acid (30 mL)/concentrated HCl (30 mL) was refluxed for 24 h (total conversion). After addition of water (30 mL), filtration, and neutralization, the solid was dried *in vacuo* over P_2O_5 (1.89 g, 85%): mp > 320 °C; IR (KBr) 3460 (O—H), 2985, 2910 (C—H), 1765, 1695 (C=O) cm^{-1}; ^1H NMR δ 9.96 (br s, COOH), 3.10 (m, 6-, 7-H)*, 3.01 (m, 16-, 17-H)*, 3.00 (s, 4a-, 9a-H), 2.67 (m, 3-, 5-, 8-, 10-H), 2.16 (m, 13-, 15-, 18-, 20-H). Anal. Calcd for $C_{22}H_{16}O_6$ (376.4): C, 70.21; H, 4.29. Found: C, 70.22; H, 4.38.

14-*syn*,19-*syn*-Dihydroxyundecacyclo[9.9.0.$0^{1,5}$.$0^{2,12}$.$0^{2,18}$.$0^{3,7}$.$0^{6,10}$.$0^{8,12}$.$0^{11,15}$.$0^{13,17}$.$0^{16,20}$]icosane-4-*syn*,9-*syn*-dicarbonitrile (6a). A solution of **4** (418 mg, 1.24 mmol) in ethanol (20 mL) was stirred with $NaBH_4$ (200 mg, 5.3 mmol) at ambient temperature for 30 min. Hydrolysis with NH_4Cl solution, concentration *in vacuo*, and continuous extraction with CH_2Cl_2/water gave crystalline **6a** (405 mg, 96%): mp 294 °C; IR (KBr) 3340 (O—H), 2965, 2920 (C—H), 2225 (CN) cm^{-1}; ^1H NMR ($CDCl_3$/DMSO-d_6 2:1) δ 4.71 (d, OH), 4.06 (m, 14a-, 19a-H), 3.00 (m, 4a-, 9a-H), 2.89 (m, 6-, 7-H), 2.76 (m, 3-, 5-, 8-, 10-H), 2.58 (m, 16-, 17-H), 2.28 (m, 13-, 15-, 18-, 20-H); ^{13}C NMR (DMSO-d_6) δ 120.5 (CN), 80.4 (C-14, -19), 64.0 (C-1, -2, -11, -12), 58.8 (C-6, -7), 50.2 (C-16, -17), 47.4 (C-13, -15, -18, -20), 44.9 (C-3, -5, -8, -10), 40.1 (C-4, -9). Anal. Calcd for $C_{22}H_{18}O_2N_2$ (342.4): C, 77.18; H, 5.30. Found: C, 76.89; H, 5.33.

14-*syn*,19-*syn*-Bis((methylsulfonyl)oxy)undecacyclo[9.9.0.$0^{1,5}$.$0^{2,12}$.$0^{2,18}$.$0^{3,7}$.$0^{6,10}$.$0^{8,12}$.$0^{11,15}$.$0^{13,17}$.$0^{16,20}$]icosane-4-*syn*,9-*syn*-dicarbonitrile (6b). A solution of **6a** (20 mg, 0.06 mmol) in CH_2Cl_2 (5 mL) and pyridine (0.5 mL) was stirred with mesyl chloride (0.1 mL) for 5 h to give pure (^1H NMR) **6b**: mp 265–269 °C; IR (KBr) 2960 (C—H), 2220 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.88 (m, 14a-, 19a-H), 3.01 (s, 4a-, 9a-H), 2.88 (m, 6-, 7-H), 2.80 (m, 3-, 5-, 8-, 10-, 16-, 17-H), 2.52 (m, 13-, 15-, 18-, 20-H), 2.14 (s, $2CH_3$). Anal. Calcd for $C_{24}H_{22}O_6N_2S_2$ (498.6): C, 57.82; H, 4.45. Found: C, 58.09; H, 4.49.

14-*syn*,19-*syn*-Bis(trifluoroacetoxy)undecacyclo[9.9.0.$0^{1,5}$.$0^{2,12}$.$0^{2,18}$.$0^{3,7}$.$0^{6,10}$.$0^{8,12}$.$0^{11,15}$.$0^{13,17}$.$0^{16,20}$]icosane-4-*syn*,9-*syn*-dicarbonitrile (6c). A solution of **6a** (20 mg, 0.06 mmol) in CH_2Cl_2 (5 mL) and pyridine (0.5 mL) was stirred with trifluoroacetic anhydride (0.1 mL) for 10 min to give pure (^1H NMR) **6c**: mp 285 °C; IR (KBr) 2975 (C—H), 2235 (CN), 1765 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.87 (s, 14a-, 19a-H), 3.04 (s, 4a-, 9a-H), 2.93 (m, 6-, 7-H)*, 2.93 (m, 16-,17-H)*, 2.90 (m, 3-, 5-, 8-, 10-H)*, 2.85 (m, 13-, 15-, 18-, 20-H)*. Anal. Calcd for $C_{26}H_{16}O_4N_2F_6$ (534.4): C, 58.44; H, 3.09. Found: C, 59.21; H, 3.15.

14-*syn*,19-*syn*-Bis(trimethylsiloxy)undecacyclo[9.9.0.$0^{1,5}$.$0^{2,12}$.$0^{2,18}$.$0^{3,7}$.$0^{6,10}$.$0^{8,12}$.$0^{11,15}$.$0^{13,17}$.$0^{16,20}$]icosane-4-*syn*,9-*syn*-dicarbonitrile (6d). To a solution of **6a** (20 mg, 0.06 mmol) in CH_2Cl_2 (5 mL) and pyridine (0.5 mL) were added NaCl (50 mg), K_2CO_3 (50 mg), and TMSCl (0.1 mL), and the mixture was stirred for 12 h. The only product (^1H NMR) was **6d**: mp 277 °C; IR (KBr) 2960, 2945 (C—H), 2225 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.08 (s, 14a-, 19a-H), 2.99 (s, 4a-, 9a-H), 2.84 (m, 6-, 7-H), 2.77 (m, 3-, 5-, 8-, 10-H), 2.58 (m, 16-, 17-H), 2.25 (m, 13-, 15-, 18-, 20-H), 0.15 (s, $6CH_3$). Anal. Calcd for $C_{28}H_{34}O_2N_2Si_2$ (486.8): C, 69.09; H, 7.04. Found: C, 68.93; H, 7.01.

Dimethyl 14-*syn*,19-*syn*-Dihydroxyundecacyclo[9.9.0.$0^{1,5}$.$0^{2,12}$.$0^{2,18}$.$0^{3,7}$.$0^{6,10}$.$0^{8,12}$.$0^{11,15}$.$0^{13,17}$.$0^{16,20}$]icosane-4-*syn*,9-*syn*-dicarboxylate (7a). To a solution of **5a** (100 mg, 0.25 mmol) in dry THF (25 mL) was added, under N_2, a borane·THF complex (Aldrich, 1 M in THF, 1.0 mL, 1.0 mmol), and the mixture was stirred at ambient temperature to total conversion (24 h, TLC control). After addition of water (30 mL) and acetic acid (1 mL), the mixture was extracted continuously (CH_2Cl_2, 16 h). Concentration *in vacuo* gave a residue, which was purified by chromatography on silica gel (CH_2Cl_2/ethyl acetate/methanol, 10:1:1) to give **7a** (90 mg, 88%): colorless crystals: mp 242–243 °C; IR (KBr) 3565 (O—H), 3480 (O—H), 3390 (O—H), 2970 (C—H), 2950 (C—H), 2850 (C—H), 1710 (C=O), 1690 (C=O), 1250 (C—O) cm^{-1}; ^1H NMR (CD_3OD/$CDCl_3$) δ 4.03 (m, 14a-, 19a-H), 3.52 (s, $2OCH_3$), 2.89 (m, 16-, 17-H), 2.84 (m, 4a-, 9a-H), 2.78 (m, 3-, 5-, 8-, 10-H), 2.58 (m, 6-, 7-H), 2.22 (m, 13-, 15-, 18-, 20-H). Anal. Calcd for $C_{24}H_{24}O_6$ (408.5): C, 70.58; H, 5.92. Found: C, 70.42; H, 5.90.

14-*syn*,19-*syn*-Dihydroxyundecacyclo[9.9.0.$0^{1,5}$.$0^{2,12}$.$0^{2,18}$.$0^{3,7}$.$0^{6,10}$.$0^{8,12}$.$0^{11,15}$.$0^{13,17}$.$0^{16,20}$]icosane-4-*syn*,9-*syn*-dicarboxylic Acid (7b). A solution of **5b** (500 mg, 1.33 mmol) in ethanol (70 mL) was stirred with $NaBH_4$ (550 mg) at ambient temperature for 30 min. Hydrolysis with diluted acetic acid, concentration to 10 mL *in vacuo*, dissolution of the residue in 1 N NaOH, precipitation of the acid with concentrated hydrochloric acid and stirring (pH < 1!), filtration, washing of the white crystals to neutrality, and drying *in vacuo* over P_2O_5 gave **7b** (480 mg, 95%): mp > 320 °C; IR (KBr) 3400 (O—H), 2960 (C—H), 1685 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.85 (m, 14a-, 19a-H), 3.33 (OH), 2.78 (m, 16-, 17-H)*, 2.68 (m, 4a-, 9a-H), 2.53 (m, 3-, 5-, 8-, 10-H)*, 2.44 (m, 6-, 7-H)*, 2.07 (m, 13-, 15-, 18-, 20-H)*. Anal. Calcd for $C_{22}H_{20}O_6$ (380.4): C, 69.47; H, 5.30. Found: C, 67.86; H, 5.44.

9,22-Dioxatridecacyclo[11.11.0.$0^{1,18}$.$0^{2,20}$.$0^{3,12}$.$0^{4,19}$.$0^{5,11}$.$0^{6,13}$.$0^{6,18}$.$0^{7,16}$.$0^{8,14}$.$0^{15,24}$.$0^{17,23}$]tetracosane-10,21-diiminium Difluoroborate (8). In a solution of **6a** (20 mg, 0.06 mmol) in $CDCl_3$ (0.2 mL) and CF_3COOH (0.2 mL), after 24 h, >90% of **8** (^1H NMR) was isolated by filtration: sensitive toward hydrolysis; mp 98 °C; IR (KBr) 3300 (N—H), 2980 (C—H), 1680 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$/CF_3COOH 1:1) δ 9.42 (br s, 2NH), 8.75 (br s, 2NH), 5.57 (m, 8-, 23-H), 3.81 (m, 11-, 20-H), 3.55 (m, 3-, 4-H), 3.24 (m, 15-, 16-H), 3.02 (m, 7-, 14-, 17-, 24-H), 2.92 (m, 2-, 5-, 12-, 16-H); ^{13}C NMR ($CDCl_3$/CF_3COOH, 1:1) δ 184.7 (C=N), 103.0 (C-8, -23), 62.0 (C-1, -6, -13, -18), 61.3 (C-3, -4), 60.1 (C-11, -20), 52.8 (C-15, -16), 46.8 (C-7, -14, -17, -24), 45.8 (C-2, -5, -12, -19).

21-*syn*-Hydroxy-7-*oxo*-6-oxadodecacyclo[11.9.0.$0^{1,16}$.$0^{2,11}$.$0^{2,20}$.$0^{3,9}$.$0^{3,16}$.$0^{4,19}$.$0^{5,17}$.$0^{8,15}$.$0^{10,14}$.$0^{18,22}$]docosane-12-*syn*-carbonitrile (9). A solution of **6a** (500 mg, 1.46 mmol) in glacial acetic acid was heated to reflux for 5 min. Concentration *in vacuo* and chromatography (CH_2Cl_2/ethyl acetate/methanol, 10:1:1) gave crystalline **9** (451 mg, 90%) and **11** (25 mg, 5%). **9**: IR (KBr) 3420 (O—H), 2960 (C—H), 2225 (CN), 1695 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.77 (m, 5-H), 4.30 (m, 21a-H), 3.32 (m, 8-H), 3.07 (m, 12a-H), 3.03 (m, 10-, 11-, 13-, 14-H), 2.81 (m, 18-, 19-H), 2.63 (m, 20-, 22-H), 2.46 (m, 9-, 15-H), 2.41 (m, 4-, 17-H); ^{13}C NMR ($CDCl_3$) δ 174.0 (C=O), 120.3 (CN), 92.5 (C-5), 81.7 (C-21), 63.9 (C-1, -2)*, 62.1 (C-3, -16)*, 61.2 (C-8), 59.4 (C-10, -14), 51.5 (C-18, -19), 51.0 (C-20, -22), 48.6 (C-11, -13), 44.6 (C-4, -17), 42.1 (C-12), 42.0 (C-9, -15); MS (EI) *m/z* (relative intensity) *inter alia* 343 (M^+, 100).

9,22-Dioxatridecacyclo[11.11.0.$0^{1,18}$.$0^{2,20}$.$0^{3,12}$.$0^{4,19}$.$0^{5,11}$.$0^{6,13}$.$0^{6,18}$.$0^{7,16}$.$0^{8,14}$.$0^{15,24}$.$0^{17,23}$]tetracosane-10,21-dione (11). (a) From 7b. To a suspension of powdered and dried **7b** (5.00 g, 3.14 mmol) in anhydrous CH_2Cl_2 (600 mL) under a N_2 atmosphere was added oxalyl chloride (50.4 mL). The mixture was heated to reflux until the solution became homogenous (3–6 h). After concentration, the solid residue was freed from included oxalyl chloride by heating at 46–50 °C/10^{-2} Torr for 2 h. The solid was then taken up in anhydrous CH_2Cl_2, and this solution was poured onto an aqueous K_2CO_3 solution. In this way, the HCl formed from residual oxalyl chloride was efficiently destroyed. After concentration of the dried CH_2Cl_2 solution in vacuo, the pure crystalline **11** was isolated in practically quantitative yield: mp > 320 °C; IR (KBr) 2960 (C—H), 1700 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.93 (t, 8-, 23-H), 3.47 (t, 11-, 20-H), 3.22 (m, 15-, 16-H), 3.00 (m, 3-, 4-H), 2.70 (m, 7-, 14-, 17-, 24-H), 2.65 (m, 2-, 5-, 12-, 19-H); $J_{7,8}$ = 5.2, $J_{5,11}$ =

4.2 Hz; ^{13}C NMR ($CDCl_3$) δ 173.8 (C=O), 94.0 (C-8, -23), 63.9 (C-11, -20), 61.8 (C-1, -6, -13, -18), 59.5 (C-15, -16), 52.4 (C-3, -4), 47.1 (C-7, -14, -17, -24), 47.1 (C-2, -5, -12, -19); MS (EI) *m/z* (relative intensity) *inter alia* 344 (M^+, 100).

(b) From 6a. To a suspension of **6a** (20 mg, 0.06 mmol) in CH_2Cl_2 (0.2 mL) was added CF_3COOH (0.2 mL). When a homogenous solution had formed (ca. 10 min), it was concentrated in vacuo and pyridine (2 mL) and water (0.01 mL) were added. After 14 h, the mixture was concentrated *in vacuo* and filtrated over silica gel (CH_2Cl_2/ethyl acetate, 2:1) to give **11** (19 mg, 95%).

14-*syn*,19-*syn*-Diiodoundecacyclo[9.9.0.0^{1,5}.0^{2,12}.0^{2,18}.0^{3,7}.0^{6,10}.0^{8,12}.0^{11,15}.0^{13,17}.0^{16,20}]icosane-4-*syn*,9-*syn*-dicarbonitrile (14). **11** (50 mg, 0.15 mmol) was converted to **13** with TMSI (cf. **2**). Without purification, the solid residue, after addition of benzene (10 mL), was converted with DMF and oxalyl chloride (1 mL) to give the diacid chloride. Concentration *in vacuo*, dissolving of the brown residue in CH_2Cl_2, introduction of NH_3 gas, and filtration of the reaction mixture over silica gel (CH_2Cl_2/ethyl acetate/methanol, 10:1:1) gave **12** as a white, amorphous powder, which was suspended in CH_2Cl_2 (6 mL) and stirred with Burgess reagent (1 g, 4.2 mmol) for 4 h. A clear solution formed, which was purified by chromatography (CH_2Cl_2) to give **14** (51 mg, 65%): mp > 320 °C; IR (KBr) 2955 (C—H), 2225 (CN) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.97 (s, 14s-, 19s-H), 3.77 (m, 16-, 17-H), 2.88 (s, 4a-, 9a-H), 2.81 (m, 3-, 5-, 6-, 7-, 8-, 10-H), 2.78 (m, 13-, 15-, 18-, 20-H). Anal. Calcd for $C_{22}H_{16}N_2I_2$ (562.2): C, 47.00; H, 2.87. Found: C, 48.71; H, 2.89.

14-*anti*,19-*anti*-Dichloroundecacyclo[9.9.0.0^{1,5}.0^{2,12}.0^{2,18}.0^{3,7}.0^{6,10}.0^{8,12}.0^{11,15}.0^{13,17}.0^{16,20}]icosane-4-*syn*,9-*syn*-dicarbonitrile (15). To a solution of **6a** (100 mg, 0.29 mmol) in pyridine (5 mL) was added thionyl chloride (10 mL) dropwise, and the mixture was heated to reflux for 5 h. Concentration *in vacuo*, dissolving the residue in CH_2Cl_2, and filtration over silica gel (CH_2Cl_2) gave crystalline **15** (13 mg, 12%): mp > 320 °C; IR (KBr) 2970 (C—H), 2225 (CN) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.14 (m, 14s-, 19s-H), 3.68 (m, 14-, 16-H), 2.87 (m, 6-, 7-H), 2.84 (s, 4a-, 9a-H), 2.81 (m, 3-, 5-, 8-, 10-H), 2.67 (m, 13-, 15-, 18-, 20-H). Anal. Calcd for $C_{22}H_{16}Cl_2N_2$ (379.3): C, 69.67; H, 4.25. Found: C, 69.52; H, 4.24.

Dimethyl 2,12,14-*anti*,19-*anti*-Tetrabromodecacyclo[9.9.0.0^{1,8}.0^{2,15}.0^{3,7}.0^{5,12}.0^{6,10}.0^{11,18}.0^{13,17}.0^{16,20}]icosane-4-*syn*,9-*syn*-dicarboxylate (17). Through a suspension of **18** (200 mg, 0.26 mmol), PtO_2 (30 mg), and dry molecular sieves (4 Å, 200 mg) in CH_2Cl_2 (20 mL) was passed H_2 with stirring for 6 h. Filtration and concentration *in vacuo* gave **17** (180 mg, 100%): mp 231–240 °C dec; IR (KBr) 2985, 2940 (C—H), 1720 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.70 (br s, 14s-H), 4.20 (br s, 19s-H), 3.85 (s, OCH_3), 3.76 (s, OCH_3), 3.74 (m, 16-, 17-H), 3.69 (m, 3-, 5-H), 3.66 (m, 13-, 15-H), 3.31 (m, 8-, 10-H), 3.14 (m, 18-, 20-H), 2.98 (m, 6-, 7-H), 2.68 (m, 9a-H), 2.53 (t, 4a-H); $J_{3,4}$ = 5.1 Hz; ^{13}C NMR ($CDCl_3$) δ 172.3 (C=O), 171.7 (C=O), 93.1 (C-2, -12), 78.0 (C-1, -11), 61.0 (C-13, -15), 57.0 (C-16, -17), 56.6 (C-6, -7), 55.1 (C-14), 54.3 (C-19), 53.8 (C-4), 52.9 (OCH_3), 52.6 (C-18, -20), 52.4 (OCH_3), 52.2 (C-3, -5), 50.7 (C-9), 47.4 (C-8, -10). Anal. Calcd for $C_{24}H_{23}O_4Br_4$ (695.1): C, 41.47; H, 3.34. Found: C, 41.17; H, 3.30.

Dimethyl 2,4-*anti*,12, 14-*anti*,19-*anti*-Pentabromo- and Dimethyl 2,4-*anti*,9-*anti*,12,14-*anti*,19-*anti*-Hexabromodecacyclo[9.9.0.0^{1,8}.0^{2,15}.0^{3,7}.0^{5,12}.0^{6,10}.0^{11,18}.0^{13,17}.0^{16,20}]icosane-4-*syn*,9-*syn*-dicarboxylate (Mixtures of Rotamers) (18 and 19). A solution of **3** (100 mg, 1.87 mmol) and bromine (2 mL, 38 mmol) in CH_2Cl_2 (10 mL) was heated to reflux and irradiated in a round-bottom flask for 60 min (TLC control!). Chromatography over silica gel (CH_2Cl_2/CCl_4, 1:1) gave **19** (8 mg, 5%) and **18** (133 mg, 92%). **18**: mp 225–230 °C dec; IR (KBr) 3000, 2940 (C—H), 1725 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.64 (m, 14s-H), 4.22 (m, 19s-H), 4.07 (m, 3-H)*, 3.98 (m, 5-H)*, 3.96 (s, OCH_3), 3.80 (s, OCH_3), 3.77 (m, 16-, 17-H), 3.65 (m, 13-, 15-H), 3.50 (m, 6-, 7-H), 3.37 (m, 8-, 10-H), 3.15 (m, 18-, 20-H), 2.75 (m, 9a-H); ^{13}C NMR ($CDCl_3$) δ 172.0 (C=O), 169.3 (C=O), 89.7, 89.2 (C-2, -12), 78.1, 78.0 (C-1, -11), 73.4 (C-4), 60.9, 60.8 (C-3, -5, -13*), 60.6 (C-15)*, 58.5, 57.2 (C-6, -7), 57.2, 56.9 (C-16, -17), 54.8 (C-14), 53.9 (OCH_3), 53.7 (C-19), 52.4 (OCH_3), 52.1, 52.0 (C-18, -20), 50.4 (C-9), 46.8 (C-8, -10); MS (EI) *m/z* (relative intensity) *inter alia* 773 (M^+, <1), 695 (19), 693 (30), 691 (20), 614 (11), 612 (11), 535 (17), 533 (30), 531 (16), 452 (11), 253 (100), 252 (85), 239 (47), 226 (38), 189 (64), 128 (45), 126 (65), 59 (96).

19: mp 287–292 °C dec; IR (KBr) 2985, 2940 (C—H), 1730 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.63 (br s, 14s-H), 4.13 (br s, 20s-H), 4.08 (m, 3-H)*, 3.98 (s, OCH_3), 3.98 (m, 5-H)*, 3.88 (s, OCH_3), 3.88 (m, 6-, 7-H), 3.75 (m, 16-, 17-H), 3.61 (m, 13-, 15-H), 3.57, 3.45 (m, 8-, 10-H), 3.15, 3.11 (m, 18-, 20-H); ^{13}C NMR ($CDCl_3$) δ 169.3 (C=O), 169.3 (C=O), 89.3, 88.8, 88.7, 88.2 (C-2, -12), 77.3, 77.9, 76.8, 77.6 (C-1, -11), 72.7 (C-4), 67.0 (C-9), 60.7, 60.5, 60.4, 60.3, 59.9, 59.3, 59.0, 58.0, 57.3, 57.2, 57.0, 56.7, 54.5, 54.1, 53.7, 53.1, 53.0, 52.9, 52.8, 52.8, 52.1, 52.0, 52.0; MS (EI) *m/z* (relative intensity) *inter alia* 852 (M^+, 4), 775 (51), 773 (99), 771 (100), 769 (52), 692 (23), 613 (62), 611 (62), 531 (18), 307 (25), 252 (70), 189 (30), 126 (50).

Dimethyl 2,9-*anti*,12,14-*anti*,19-*anti*-Pentabromodecacyclo[9.9.0.0^{1,8}.0^{2,15}.0^{3,7}.0^{5,12}.0^{6,10}.0^{11,18}.0^{13,17}.0^{16,20}]icosane-4-*syn*,9-*syn*-dicarboxylate (20). Through a suspension of **19** (100 mg, 0.12 mmol), PtO_2 (30 mg), and dry molecular sieves (4 Å, 200 mg) in CH_2Cl_2 (10 mL) was passed H_2 with stirring for 4 h. Filtration and concentration *in vacuo* gave crystalline **20** (81 mg, 100%): mp 235–240 °C; IR (KBr) 2980, 2940 (C—H), 1725 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.75 (m, 14s-H), 4.17 (m, 19s-H), 3.89 (s, 2OCH_3), 3.77 (m, 2H), 3.75 (m, 2H), 3.57 (m, 1H), 3.44 (m, 2H), 3.42 (m, 1H), 3.21 (m, 1H), 3.16 (m, 1H), 2.63 (m, 4a-H). Anal. Calcd for $C_{24}H_{21}O_4Br_5$ (773.9): C, 37.24; H, 2.87. Found: C, 36.88; H, 2.79.

Dimethyl 13-*anti*,18-*anti*-Dibromononacyclo[12.6.0.0^{2,6}.0^{4,11}.0^{5,9}.0^{7,20}.0^{10,17}.0^{12,16}.0^{15,19}]icosa-1(20),10-diene-3-*syn*,8-*syn*-dicarboxylate (21). **17** (1.01 g, 1.45 mmol) was added (N_2 atmosphere) to a boiling suspension of NaI (102 mg, 0.68 mmol), Na_2SO_3 (99 mg, 0.78 mmol), and powdered iron (82 mg, 1.47 mmol) in anhydrous DMF (10 mL). After total conversion (the deep red color had disappeared, ca. 10 min), the mixture was cooled to ambient temperature, diluted with CH_2Cl_2, and washed with 10% aqueous NH_4Cl solution. The organic phase was dried ($MgSO_4$), filtered, and concentrated, and after filtration over silica gel (CH_2Cl_2/ethyl acetate, 19:1), **21** crystallized from CH_2Cl_2/ethyl acetate (675 mg, 87%): mp 162–163 °C; IR (KBr) 2935 (C—H), 1720 (C=O) cm^{-1}; UV (CH_3CN) λ_{max} (ε) 287 nm (140); ^{1}H NMR ($CDCl_3$) δ 4.95 (s, 13s-, 18s-H), 4.28 (m, 15-, 16-H), 3.85 (s, 2OCH_3), 3.51 (m, 12-, 14-, 17-, 19-H), 3.45 (m, 2-, 4-, 7-, 9-H), 3.41 (m, 5-, 6-H), 2.58 (m, 3-, 8-H); ^{13}C NMR ($CDCl_3$) δ 173.3 (C=O), 155.7 (C-1, -10, -11, -20), 59.2 (C-5, -6, -15, -16), 57.5 (C-13, -18), 55.6 (C-12, -14, -17, -19), 52.4 (OCH_3), 47.5 (C-3, -8), 45.4 (C-2, -4, -7, -9); MS (EI) *m/z* (relative intensity) *inter alia* 536 (M^+, 47), 534 (93), 532 (47), 455 (16), 454 (23), 453 (17), 256 (53), 255 (54), 254 (68), 253 (100), 252 (65), 249 (65), 239 (73), 189 (84), 141 (282^{2+}, 42), 128 (256^{2+}, 98), 127 (254^{2+}, 58), 126 (252^{2+}, 45), 115 (88).

Dimethyl 3,10-*anti*,14-Tribromoundecacyclo[9.9.0.0^{1,14}.0^{2,9}.0^{2,18}.0^{3,7}.0^{4,17}.0^{5,15}.0^{6,13}.0^{8,12}.0^{16,20}]icosane-5,19-*syn*-dicarboxylate (23). **18** (100 mg, 0.13 mmol) was added under N_2 to a suspension of Zn powder (24 mg, 0.37 mmol) and Na_2SO_3 (20 mg, 0.16 mmol) in dry DMF (3 mL) at 100 °C. After 5 min, the mixture was cooled to ambient temperature, diluted with CH_2Cl_2, washed with water, concentrated *in vacuo*, and filtered over silica gel (CH_2Cl_2/ethyl acetate, 2:1). Crystallization from CH_2Cl_2/ethyl acetate gave **23** (68 mg, 85%): mp 220–221 °C; IR (KBr) 3000, 2975 (C—H), 1730 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27 (m, 10s-H), 3.85 (t, 6-H), 3.77 (s, OCH_3), 3.72 (s, OCH_3), 3.57 (m, 18-, 20-H), 3.54 (m, 8-, 12-H), 3.42 (m, 9-, 11-H), 3.33 (m, 4-, 15-, 16-, 17-H), 3.21 (m, 7-, 13-H), 2.67 (m, 19a-H); $J_{6,7}$ = 10.5, $J_{18,19a} \approx 2$, $J_{9,10}$ = 1.5 Hz; ^{13}C NMR ($CDCl_3$) δ 174.5 (C=O), 172.2 (C=O), 96.8 (C-3, -14), 79.7 (C-1, -2, -5), 67.8 (C-6), 64.7 (C-4, -15), 61.3 (C-16, -17), 60.9 (C-8, -12), 59.7 (C-7, -13), 56.3 (C-9, -11), 54.1 (C-10), 52.7 (OCH_3), 52.1 (OCH_3), 51.3 (C-18, -20), 50.2 (C-19); MS (EI) *m/z* (relative intensity) *inter alia* (M^+ not detectable), 535 (53), 533 (100), 531 (53), 473 (13), 454 (12), 452 (12), 313 (17), 254 (33), 253 (69), 252 (47), 189 (17), 126 (36).

Dimethyl 3,10-*anti*,14,19-*anti*-Tetrabromoundecacyclo[9.9.0.0^{1,14}.0^{2,9}.0^{2,18}.0^{3,7}.0^{4,17}.0^{5,15}.0^{6,13}.0^{8,12}.0^{16,20}]icosane-5,19-*syn*-dicarboxylate (24). **19** (100 mg, 0.12 mmol) was added to a suspension of Zn powder (24 mg, 0.16 mmol) and Na_2SO_3 (20 mg, 0.16 mmol) in dry DMF (3 mL) at 100 °C. After 5 min, the mixture was cooled to ambient temperature, diluted with CH_2Cl_2, washed with water, concentrated *in vacuo*, and filtered over silica gel (CH_2Cl_2/ethyl acetate, 2:1). Crystallization from CH_2Cl_2/ethyl acetate gave **24** (65 mg, 80%): mp 150 °C; IR (KBr) 2945, 2915, 2800 (C—H), 1730 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (m, 10s-H), 3.89 (t, 6-H), 3.88 (s, OCH_3), 3.74 (s, OCH_3), 3.74 (m, 16-, 17-, 18-, 20-H), 3.56 (m, 8-, 12-H), 3.42 (m, 9-, 11-H), 3.36 (m, 4-, 15-H), 3.20 (m, 7-, 13-H); $J_{6,7}$ = 10.5 Hz; ^{13}C NMR ($CDCl_3$) δ 174.1 (C=O), 169.3 (C=O), 96.1 (C-3, -14), 80.3 (C-1, -2)*, 78.9 (C-5)*, 68.0 (C-6), 64.4 (C-19), 64.1 (C-4, -15), 62.3 (C-18, -20), 60.9 (C-8, -12), 59.4 (C-7, -13), 57.4 (C-16, -17), 56.2 (C-9, -11), 53.4 (OCH_3), 53.1 (C-10), 52.9 (OCH_3); MS (EI) *m/z* (relative intensity) *inter alia* 692 (M^+, 3), 615 (35), 613 (100), 611 (99), 609 (33), 253 (26), 252 (26), 189 (7), 126 (14).

Dimethyl 19-*anti*-Bromodecacyclo[9.9.0.0^{2,18}.0^{3,10}.0^{4,17}.0^{5,9}.0^{6,16}.0^{7,14}.0^{8,12}.0^{13,20}]icosa-4(17),12-diene-9,15-*syn*-dicarboxylate (25). **18** (60 mg, 0.08 mmol) was added to a suspension of Zn powder (20 mg, 0.3 mmol), NaI (46 mg, 0.3 mmol), and Na_2SO_3 (39 mg, 0.31 mmol) in DMF (2 mL) at 130 °C. After 5 s, the mixture was cooled to ambient temperature, diluted with CH_2Cl_2, washed with water, and concentrated *in vacuo*. Chromatography (CH_2Cl_2) gave **23** (6 mg, 12%) and crystalline **25** (20 mg, 57%): mp 184–187 °C; IR (KBr) 2935, 2800 (C—H), 1720 (C=O) cm^{-1}; UV (acetonitrile) λ_{max} (ϵ) 263 (270) nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.78 (m, 19s-H), 3.93 (m, 18-, 20-H), 3.82 (m, 14-, 16-H), 3.80 (s, OCH_3), 3.78 (m, 1-, 2-H), 3.69 (s, OCH_3), 3.63 (m, 5-, 8-H)*, 3.56 (t, 10-H), 3.47 (m, 6-, 7-H)*, 3.36 (m, 3-, 11-H), 2.62 (t, 15-H); $J_{3,10}$ = 9.5, $J_{14,15} \approx$ 5 Hz; ^{13}C NMR ($CDCl_3$) δ 177.0 (C=O), 173.3 (C=O), 172.2 (C-4, -12), 149.8 (C-13, -17), 72.4 (C-9), 65.9 (C-5, -8)*, 65.2 (C-18, -20), 61.9 (C-1, -2), 61.6 (C-10), 58.1 (C-6, -7)*, 57.1 (C-19), 52.9 (C-3, -11), 52.2 (OCH_3), 52.0 (C-14, -16), 48.2 (C-15); MS (EI) *m/z* (relative intensity) *inter alia* [454 (100), 452 (96), M$^+$], 394 (14), 392 (13), 313 (31), 254 (41), 253 (78), 252 (51), 189 (16), 126 (31).

Dimethyl 3,10-*anti*,14-Tribromoundecacyclo[9.9.0.0^{1,14}.0^{2,9}.0^{2,18}.0^{3,7}.0^{4,17}.0^{5,15}.0^{6,13}.0^{8,12}.0^{16,20}]icosane-5,19-*anti*-dicarboxylate (27). To a solution of **23** (10 mg, 0.02 mmol) in dry THF were added NaH (10 mg) and potassium *tert*-butoxide (10 mg), and the mixture was stirred for 1 h (TLC control). Then, NH_4Cl (30 mg) was added and the residue removed by filtration. The only product (^{1}H NMR) was **27**: mp 225–230 °C; IR (KBr) 2980 (C—H), 1725 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.59 (br s, 10s-H), 3.87 (t, 6-H), 3.73 (s, OCH_3), 3.68 (s, OCH_3), 3.57 (m, 8-, 12-H), 3.47–3.53 (m, 9-, 11-, 16-, 17-, 18-, 20-H), 3.36 (m, 4-, 15-H), 3.20 (m, 7-, 13-H); $J_{6,7}$ = 10.5 Hz.

Dimethyl 13-*anti*,18-*anti*-Dibromononacyclo[12.6.0.0^{2,6}.0^{4,11}.0^{5,9}.0^{7,20}.0^{10,17}.0^{12,16}.0^{15,19}]icos-1(20)-ene-3-*syn*,8-*syn*-dicarboxylate (30). To a solution of **21** (160 mg, 0.30 mmol) in CH_2Cl_2 (100 mL) and methanol (20 mL) were added dipotassium azodicarboxylate (5 g, 25 mmol) and then, with vigorous stirring and cooling with ice, slowly acetic acid (3 mL, 53 mmol). After the addition, the mixture was stirred further at ambient temperature till the yellow color had disappeared (12 h). Then, water (100 mL) was added and, after separation of the phases, the aqueous phase extracted twice with CH_2Cl_2 (20 mL). The combined organic phases were dried ($MgSO_4$), filtrated, and concentrated *in vacuo* to give colorless cyrstals (155 mg, 96%; in addition, ca. 2% of **3**), which could be used directly for subsequent reactions. From CH_2Cl_2/ethyl acetate, pure **30** was obtained: mp 163 °C; IR (KBr) 2938 (C—H), 1716 (C=O), 1213 (C—O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.93 (s, 13s-, 18s-H), 3.82 (s, OCH_3), 3.78 (m, 15-, 16-H), 3.51 (m, 10-, 11-H), 3.32 (m, 2-, 7-, 14-, 19-H), 3.06 (m, 4-, 9-, 12-, 17-H), 2.95 (m, 3a-, 5-, 6-, 8a-H); ^{13}C NMR ($CDCl_3$) δ 173.6 (C=O), 151.0 (C-1, -20), 62.6 (C-13, -18), 60.1 (C-6)*, 58.9 (C-15)$^+$, 58.2 (C-16)$^+$, 57.4 (C-5)*, 56.8 (C-10, -11), 55.3 (C-12, -17), 54.3 (C-14, -19), 54.2 (C-3, -8), 52.3 (OCH_3), 44.3 (C-4, -9), 44.3 (C-2, -7); MS (EI) *m/z* (relative intensity) *inter alia* 536 (M$^+$, 6), 457 (100), 455 (99), 315 (39), 257 (17), 256 (23), 255 (54), 254 (6), 253 (9), 252 (7), 251 (6), 250 (5), 165 (30), 128 (60), 115 (33), 44 (32).

Dimethyl 13-*anti*,18-*anti*-Dibromo-21-oxadecacyclo[12.7.0.0^{1,20}.0^{2,6}.0^{4,11}.0^{5,9}.0^{7,20}.0^{10,17}.0^{12,16}.0^{15,19}]henicos-10-ene-3-*syn*,8-*syn*-dicarboxylate (31). A solution of **21** (30 mg, 0.06 mmol) and benzoylpercarbamic acid (10 mg, 0.06 mmol) in CH_2Cl_2 (2 mL) was stirred for 20 min and then concentrated *in vacuo*. The benzamide which had been formed was removed by sublimation at 100 °C/1 Torr to give uniformly (^{1}H NMR) **31**: mp 191 °C; IR (KBr) 2942 (C—H), 1722 (C=O), 1240 (C—O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.86 (br s, 13s-, 18s-H), 3.89 (15-H)*, 3.84 (s, OCH_3), 3.73 (m, 16-H)*, 3.45 (m, 12-, 17-H)*, 3.40 (m, 4-, 9-H)*, 3.08 (m, 6-H)*, 2.91 (m, 3-, 5-*, 8-H), 2.86 (m, 2-, 7-, 14-, 19-H); ^{13}C NMR ($CDCl_3$) δ 172.8 (C=O), 155.8 (C-10, -11), 85.0 (C-1, -20), 62.0 (C-15), 61.6 (C-6), 57.7 (C-16), 57.2 (C-5), 54.4 (C-13, -14, -18, -19), 54.2 (C-3, -8), 53.7 (C-12, -17), 52.6 (OCH_3), 44.9 (C-4, -9)*, 44.4 (C-2, -7)*. Anal. Calcd for $C_{24}H_{22}O_5Br_2$ (550.2): C, 52.39; H, 4.03. Found: C, 52.72; H, 4.16.

Dimethyl 13-*anti*,18-*anti*-Dibromo-21-oxadecacyclo[12.7.0.0^{1,20}.0^{2,6}.0^{4,11}.0^{5,9}.0^{7,20}.0^{10,17}.0^{12,16}.0^{15,19}]henicosane-3-*syn*,8-*syn*-dicarboxylate (33). To a solution of **30** (16 mg, 0.03 mmol) and benzoylperoxycarbamic acid (21 mg, 0.12 mmol) in CH_2Cl_2 (2 mL), stirred at ambient temperature for 6 h, was added silica gel (250 mg). The mixture was filtrated and concentrated *in vacuo*. The residue was purified by chromatography on silica gel to give, besides **31** (4 mg, 25%), **33** (10 mg, 61%): colorless crystals; mp 188 °C dec; IR (KBr) 2942 (C—H), 1717 (C=O), 1255 (C—O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.97 (s, 13s-, 18s-H), 4.01 (m, 15-H), 3.82 (OCH_3), 3.77 (16-H), 3.62 (10-, 11-H), 3.14–3.29 (m, 4-, 7-, 9-, 12-H), 3.07 (m, 6-H), 2.80–2.93 (m, 2-, 3a-, 4-, 5-, 7-, 8a-, 9-H); ^{13}C NMR ($CDCl_3$) δ 173.1 (C=O), 82.5 (C-1, -20), 63.9 (C-15), 63.3 (C-6), 60.3 (C-16), 60.0 (C-5), 58.9 (C-13, -18), 55.9 (C-12, -17), 54.6 (C-3, -8), 53.9 (C-10, -11), 52.5 (OCH_3), 52.3 (C-14, -19), 44.8 (C-4, -9), 44.2 (C-2, -7); MS (EI) *m/z* (relative intensity) *inter alia* 552 (M$^+$, <1), 521 (10), 474 (25), 473 (99), 472 (26), 471 (100), 439 (9), 271 (11), 243 (11), 179 (11), 166 (332^{2+}, 8), 165 (330^{2+}, 15), 152 (304^{2+}, 9), 129 (258^{2+}, 10), 128 (256^{2+}, 12), 115 (230^{2+}, 17).

Dimethyl 14-*anti*,19-*anti*-Dibromo-11,22-dioxaundecacyclo[13.7.0.0^{1,21}.0^{2,6}.0^{4,12}.0^{5,9}.0^{7,21}.0^{10,12}.0^{10,18}.0^{13,17}.0^{16,20}]docosane-3-*syn*,8-*syn*-dicarboxylate (34). To a dried ($MgSO_4$) and filtered solution of *m*-chloroperbenzoic acid (95 mg, 0.55 mmol) in CH_2Cl_2 (5 mL) was added NaH_2PO_4 (100 mg, 0.70 mmol) and diene **21** (19 mg, 0.04 mmol). The mixture was stirred at ambient temperature for 24 h, washed twice with aqueous K_2CO_3 solution, dried ($MgSO_4$), filtrated, and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (CH_2Cl_2/ethyl acetate, 19:1) to give **34** (12 mg, 60%): colorless crystals; mp 228 °C dec; IR (KBr) 2942 (C—H), 1723 (C=O), 1241, 1216 (C—O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.86 (br s, 14s-, 19s-H), 3.86 (s, OCH_3), 3.78 (m, 16-, 17-H), 2.96 (m, 2-, 4-, 7-, 9-, 13-, 15-, 18-, 20-H), 2.93 (m, 5-, 6-H), 2.74 (t, 3a-, 8a-H); $J_{2,3a}$ = 4.9 Hz; ^{13}C NMR ($CDCl_3$) δ 172.2 (C=O), 83.6 (C-1, -10, -12, -21), 62.6 (C-16, -17), 62.3 (C-5, -6), 53.8 (2 signals, C-14, -19), 53.5 (C-13, -15, -18, -20), 52.7 (OCH_3), 50.2 (C-3, -8), 44.4 (C-2, -4, -7, -9); MS (EI) *m/z* (relative intensity) *inter alia* 566 (M$^+$, <1), 537 (14), 535 (29), 502 (18), 488 (25), 487 (100), 486 (26), 485 (98), 455 (16), 453 (18), 425 (9), 258 (6), 257 (9), 229 (12), 215 (10), 166 (14), 165 (32), 152 (14), 129 (258^{2+}, 11), 128 (256^{2+}, 13), 115 (230^{2+}, 20), 114 (228^{2+}, 6), 59 (35). Anal. Calcd for $C_{24}H_{22}O_6Br_2$ (566.3): C, 50.91; H, 3.34. Found: C, 50.58; H, 3.41.

Dimethyl 19-*anti*-Bromodecacyclo[9.9.0.0^{2,18}.0^{3,10}.0^{4,17}.0^{5,9}.0^{6,16}.0^{7,14}.0^{8,12}.0^{13,20}]icos-4(17)-ene-9,15-*syn*-dicarboxylate (35). A mixture of **30** (100 mg, 0.19 mmol) and NaH (40 mg, 0.42 mmol) in THF (4 mL) was stirred in an inert atmosphere. After ca. 40% conversion (TLC control, cyclohexane/ethyl acetate, 4:1, $KMnO_4$), the mixture was filtrated and concentrated *in vacuo*. Chromatography (silica gel, cyclohexane/ethyl acetate, 4:1) yielded first **30** (59 mg) and then **35** (31 mg, 89% based on conversion): mp 216 °C; IR (KBr) 2948 (C—H), 1716 (C=O), 1213 (C—O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.88 (s, 19s-H), 3.80 (s, OCH_3), 3.77 (m, 2H), 3.67 (m, 2H), 3.66 (s, OCH_3), 3.60 (m, 2H), 3.42 (m, 2H), 3.36 (m, 6-H), 3.31–3.21 (series of m, 5H), 3.16 (t, 15a-H); $J_{14,15}$ = 5.6 Hz; ^{13}C NMR ($CDCl_3$) δ 177.2 (C=O/9), 173.9 (C=O/15), 164.8 (C-4), 144.1 (C-17), 82.4 (C-9), 70.7, 67.1, 65.3, 65.1, 63.4, 63.3, 62.6, 62.0, 61.6, 60.8, 59.3, 58.5, 56.4, 54.3, 52.9, 52.3 (OCH_3), 52.2 (OCH_3), 51.8, 51.5, 50.1; MS (EI) *m/z* (relative intensity) *inter alia* [457 (6), 456 (23), 455 (7), 454 (26), M$^+$], 425 (20), 424 (17), 423 (20), 376 (57), 375 (100), 343 (14), 316 (13), 315 (54), 256 (22), 255 (57), 254 (6), 253 (8), 239 (10), 179 (11), 165 (14), 153 (11), 142 (284^{2+}, 8), 141 (282^{2+}, 15), 128 (256^{2+}, 23), 127 (254^{2+}, 13), 126 (252^{2+}, 9), 120 (240^{2+}, 9), 115 (22), 114 (228^{2+}, 8), 113 (226^{2+}, 6), 101 (202^{2+}, 6).

Dimethyl 13-*anti*-Bromo-2-oxaundecacyclo[10.9.0.0^{1,3}.0^{3,10}.0^{4,8}.0^{5,21}.0^{6,19}.0^{7,17}.0^{9,16}.0^{11,15}.0^{14,18}]henicos-17-ene-8,20-*syn*-dicarboxylate (36). To a solution of **31** (20 mg, 0.04 mmol) in THF (2 mL) was added dropwise, under an inert atmosphere, sodium methanolate in methanol, until no more educt was detectable (TLC cyclohexane/ethyl acetate 2:1, $KMnO_4$). The solution was diluted with CH_2Cl_2 (15 mL), washed with water, dried (Na_2SO_4), filtrated, and concentrated *in vacuo*. Chromatography (cyclohexane/ethyl acetate, 2:1) gave **36** (12 mg, 70%): sensitive against air and acid; mp 131 °C; IR (KBr) 2952 (C—H), 1723 (C=O), 1245 (C—O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.79 (s, 13s-H), 3.67–3.91 (m, 4H), 3.83 (s, OCH_3), 3.71 (s, OCH_3), 3.52–3.67 (m, 2H), 3.38–3.52 (m, 2H), 3.30 (m, 1H), 3.01–3.10 (m, 3H), 2.83 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 175.7 (C=O), 172.9 (C=O), 167.5 (C-17), 146.2 (C-18), 100.2 (C-3), 80.0 (C-1), 77.3 (C-8), 69.1, 68.3, 65.5, 64.8, 64.6, 62.1, 59.1, 58.8, 55.9, 53.8, 53.7, 52.5 (OCH_3), 52.2, 51.8, 49.5, 49.1. Anal. Calcd for $C_{24}H_{21}O_5Br$ (469.3): C, 61.42; H, 4.51. Found: C, 61.28; H, 4.44.

Dimethyl 19-*anti*-Bromodecacyclo[9.9.0.0^{2,18}.0^{3,10}.0^{4,17}.0^{5,9}.0^{6,16}.0^{7,14}.0^{8,12}.0^{13,20}]icosane-9,15-*syn*-dicarboxylate (37). A solution of **25** (50 mg, 0.11 mmol) in CH_2Cl_2 (3 mL) and methanol (3 mL) was converted as usual with dipotassium azodicarboxylate (0.5 g, 2.6 mmol) and acetic acid (310 mg, 5.2 mmol). Workup as usual gave **37** (48 mg, 95%): mp 197–198 °C; IR (KBr) 2945 (C—H), 1715 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.23 (s, 19s-H), 3.83 (s, OCH_3), 3.78 (t, 10-H), 3.72 (m, 5-, 8-H), 3.72 (m, 4-, 12-H), 3.67 (s, OCH_3), 3.51 (m,

6-, 7-H), 3.43 (m, 1-, 2-H), ≈3.3 (m, 3-, 11-, 13-, 14-, 16-, 17-, 18-, 20-H), 3.07 (m, 15-H); $J_{3,10}$ = 11.3 Hz; ^{13}C NMR ($CDCl_3$) δ 178.6 (C=O), 174.2 (C=O), 85.2 (C-9), 71.9 (C-10), 69.2 (C-5, -8), 65.3 (C-6, -7), 64.1 (C-3, -11)*, 63.8 (C-4, -12)*, 63.6 (C-19), 62.2 (C-1, -2), 60.9 (C-13, -17)*, 52.2, 52.2 (OCH_3), 51.6 (C-14, -16), 51.5 (C-15), 50.6 (C-18, -20)*; MS (EI) *m/z* (relative intensity) *inter alia* 458, 456 (M^+, 12), 377 (100), 317 (46), 257 (38).

Dimethyl 13-*anti*-Bromo-2-oxaundecacyclo[10.9.0.0^{1,3}.0^{3,10}.0^{4,8}.0^{5,21}.0^{6,19}.0^{7,17}.0^{9,16}.0^{11,15}.0^{14,18}]henicosane-8,20-*syn*-dicarboxylate (38). A solution of **35** (20 mg, 0.04 mmol) and benzoylpercarbamic acid (8 mg, 0.04 mmol) in CH_2Cl_2 (2 mL) was stirred for 15 min and then concentrated *in vacuo*. The benzamide which had formed was removed by sublimation at 100 °C/0.1 Torr to give uniformly (^{1}H NMR) **38**: mp 207 °C; IR (KBr) 2950 (C—H), 1720 (C=O), 1213 (C—O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.00 (br s, 13s-H), 3.85 (s, OCH_3), 3.75 (m, 9-, 15-, 17-H), 3.70 (s, OCH_3), 3.66 (m, 11-H), 3.60 (m, 7-H), 3.45 (m, 14-, 16-H), 3.40 (m, 6-H), 3.37 (m, 18-H)*, 3.35 (m, 19-H)*, 3.31 (m, 5-H), 3.15 (br d, 12-H), 3.10 (d, 4-H), 3.08 (t, 21-H), 2.96 (t, 20-H), 2.89 (dd, 10-H); $J_{4,5}$ = 7.5, $J_{5,21}$ = 6.0, $J_{9,10}$ = 10.5, $J_{10,11}$ = 7.5, $J_{11,12}$ = 6.0, $J_{19,20}$ = 6.0, $J_{20,21}$ = 6.0 Hz; ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 177.0 (C=O/8), 173.2 (C=O/20), 98.1 (C-3), 79.3 (C-1)*, 78.4 (C-8)*, 69.7 (C-5), 69.4 (C-11), 67.6 (C-9)$^+$, 66.5 (C-15)$^+$, 65.1 (C-7), 63.2 (C-16)**, 62.9 (C-17)**, 62.6 (C-6)**, 60.3 (C-14)**, 59.1 (C-12), 57.9 (C-13), 55.7 (C-4), 52.4 ($2OCH_3$), 52.3 (C-18)$^{2+}$, 51.5 (C-20), 51.0 (C-10), 50.8 (C-19)$^{2+}$, 49.3 (C-21). Anal. Calcd for $C_{24}H_{23}O_5Br$ (471.3): C, 61.16; H, 4.92. Found: C, 61.04; H, 4.79.

Dimethyl 11-*anti*-Bromo-6,22-dioxadodecacyclo[10.10.0.0^{1,21}.0^{2,19}.0^{4,18}.0^{5,7}.0^{5,10}.0^{7,17}.0^{8,15}.0^{9,13}.0^{14,21}.0^{16,20}]docosane-3-*syn*,16-dicarboxylate (39). A solution of **25** (20 mg, 0.04 mmol) and benzoylperoxycarbamic acid (50 mg, 0.25 mmol) in CH_2Cl_2 (2 mL) was stirred for 1 h and concentrated in vacuo. Volatile components were removed by sublimation at 100 °C/0.4 Torr to give pure (^{1}H NMR) **39**: mp 207–208 °C; IR (KBr) 2950, 2840 (C—H), 1720 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.91 (s, 11-H), 3.89 (s, OCH_3), 3.85 (t, 15-H), 3.76 (m, 9-, 13-H), 3.75 (s, OCH_3), 3.41 (m, 18-, 19-H), 3.21 (m, 2-, 4-H), 3.00 (m, 8-, 14-H), 2.83 (t, 3a-H); $J_{8,9}$ = 10.5, $J_{2,3}$ = 6.0 Hz; ^{13}C NMR ($CDCl_3$) δ 175.5 (C=O), 172.2 (C=O), 98.2 (C-7, -21), 78.9 (C-1, -5), 73.4 (C-16), 69.1 (C-18, -19), 68.9 (C-9, -13), 61.3 (C-15), 59.2 (C-17, -20), 54.9 (C-10, -12), 52.9 (C-11), 52.7 (OCH_3), 52.6 (OCH_3), 49.9 (C-8, -14), 49.8 (C-3), 49.7 (C-2, -4); MS (EI) *m/z* (relative intensity) *inter alia* 486, 484 (M^+, 10), 405 (100), 345 (16), 285 (10), 257 (52), 165 (22), 128 (13), 115 (15).

Dimethyl Undecacyclo[9.9.0.0^{2,9}.0^{3,7}.0^{4,20}.0^{5,18}.0^{6,16}.0^{8,15}.0^{10,14}.0^{12,19}.0^{13,17}]-icosa-8,18-diene-1,6-dicarboxylate (40). (a) To a solution of **21** (100 mg, 0.19 mmol) in dry THF (3 mL) was added, in an inert atmosphere with exclusion of moisture (glovebox), a solution of *t*-Bu-P_4 (450 mg, 0.71 mmol) in dry THF (2 mL) at room temperature. The mixture was stirred for 15 min and then rapidly filtered through silica gel (2 cm × 2 cm). Elution with dry, deoxygenated benzene (ca. 12 mL) and concentration of the eluate *in vacuo* gave colorless crystals (80 mg), very sensitive to air, which contained traces of base (^{1}H NMR). Further purification was accomplished by crystallization from deoxygenated THF/ethyl acetate. The colorless crystalline material did not melt upon heating (sealed tube) to 330 °C. The ^{13}C NMR spectrum of the recovered insoluble sample did not show any olefinic signals. (b) To a solution of **25** (15 mg, 0.03 mmol) in THF-d_8 (0.3 mL) under N_2 was added NaH (2 mg, 0.08 mmol). After 20 min, the uniform reaction to **40** was complete (^{1}H NMR): UV (acetonitrile, only qualitatively registered) λ_{max} 253 (sh?), 220 nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.02 (m, 3-, 4-H), 3.88 (m, 2-, 5-, 7-, 20-H), 3.81 (m, 13-, 14-H), 3.76–3.47 (m, 10-, 11-, 12-, 15-, 16-, 17-H), 3.73 (s, OCH_3); (benzene-d_6) δ 4.05 (m, 2-, 5-, 7-, 20-H), 3.97 (m, 3-, 4-H), 3.67 (t, 11-, 16-H), 3.57 (m, 10-, 12-, 15-, 17-H), 3.41 (m, 13-, 14-H), 3.33 (s, $2OCH_3$); $J_{10,11}$ = 10.4 Hz; ^{13}C NMR ($CDCl_3$) δ 177.3 (C=O), 169.2 (C-8, -9, -18, -19), 74.2 (C-1, -6), 74.0 (C-3, -4), 73.2 (C-13, -14), 66.1 (C-2, -5, -7, -20), 62.2 (C-11, -16), 60.9 (C-10, -12, -15, -17), 52.3 (OCH_3); (THF-d_8) δ 176.8 (C=O), 169.9 (C-8, -9, -18, -19), 75.1 (C-1, -6), 74.8 (C-3, -4), 74.1 (C-13, -14), 66.7 (C-2, -5, -7, -20), 63.1 (C-11, -16), 61.6 (C-10, -12, -15, -17), 52.2 (OCH_3); (benzene-d_6) δ 176.5 (C=O), 169.5 (C-8, -9, -18, -19), 74.6 (C-1, -6), 74.3 (C-3, -4), 73.4 (C-13, -14), 66.4 (C-2, -5, -7, -20), 62.5 (C-11, -16), 61.1 (C-10, -12, -15, -17), 51.8 (OCH_3); MS (EI) *m/z* (relative intensity) *inter alia* 373 (56), 372 (M^+, 100), 313 (64), 312 (100), 257 (27), 255 (21), 254 (42), 253 (99), 252 (74), 251 (17), 250 (21), 240 (6), 239 (16), 226 (20), 156 (312^{2+}, 33), 140 (280^{2+}, 11), 139 (278^{2+}, 27), 128 (13), 127 (254^{2+}, 68), 126 (252^{2+}, 96), 125 (250^{2+}, 35), 120 (240^{2+}, 19), 115 (25), 113 (226^{2+}, 51), 112 (224^{2+}, 12), 42 (100), 41 (98).

Dimethyl 2-Oxadodecacyclo[10.9.0.0^{1,3}.0^{3,10}.0^{4,8}.0^{5,21}.0^{6,19}.0^{7,17}.0^{9,16}.0^{11,15}.0^{13,20}.0^{14,18}]henicos-17-ene-8,20-dicarboxylate (41). To a solution of **31** (30 mg, 0.05 mmol) in dry THF (1 mL) was added, in an inert atmosphere with exclusion of moisture (glovebox), a solution of *t*-Bu-P_4 (150 mg, 0.24 mmol) in dry THF (2 mL) at room temperature. The mixture was stirred for 15 min and then filtered through a well-dried column of silica gel (1 cm × 3 cm). Elution with dry, deoxygenated benzene (ca. 7 mL) and concentration of the eluate *in vacuo* gave colorless crystals (20 mg, 95%), sensitive to air, which were practically pure (^{1}H NMR) **41**; recrystallization from deoxygenated CH_2Cl_2/CH_3OH provided an analytically pure sample: mp 228 °C; UV (acetonitrile, only qualitatively registered) λ_{max} 220 nm; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.96 (m, 7-, 19-H), 3.86 (m, 5-H), 3.60–3.82 (series of m, 6H), 3.67 (s, OCH_3), 3.53 (dt, 11-H), 3.25 (d, 4-, 21-H), 2.98 (dd, 10-, 12-H); $J_{4,5}$ = 8.1, $J_{9,10}$ = 10.4, $J_{10,11}$ = 8.0, $J_{11,15}$ = 10.7 Hz; ^{13}C NMR ($CDCl_3$) δ 176.4 (C=O), 164.1 (C-17, -18), 95.3 (C-1, -3), 76.2 (C-5)*, 75.7 (C-11)*, 75.5 (C-8, -20), 72.9 (C-6)$^+$, 72.4 (C-15)$^+$, 68.1 (C-9, -13), 63.5 (C-7, -19), 63.1 (C-14, -16), 58.3 (C-4, -21), 53.7 (C-10, -12), 52.5 (OCH_3); MS (EI) *m/z* (relative intensity) *inter alia* 389 (21), 388 (M^+, 80), 360 (14), 357 (8), 329 (35), 328 (100), 301 (10), 269 (16), 241 (24), 240 (15), 239 (27), 120 (240^{2+}, 9), 119 (238^{2+}, 7), 113 (226^{2+}, 7), 97 (16), 85 (15), 83 (17), 71 (24), 57 (41), 55 (29), 43 (36).

Dimethyl Undecacyclo[9.9.0.0^{2,9}.0^{3,7}.0^{4,20}.0^{5,18}.0^{6,16}.0^{8,15}.0^{10,14}.0^{12,19}.0^{13,17}]icos-8-ene-1,6-dicarboxylate (42). (a) To a solution of **30** (14 mg, 0.03 mmol) in THF-d_8 (0.4 mL) under N_2 was added NaH (2 mg, 0.08 mmol). The reaction to **42** was complete and uniform after 10 min (^{1}H NMR). (b) To a solution of **30** (30 mg, 0.06 mmol) in dry THF (1 mL) was added, in an inert atmosphere with exclusion of moisture (glovebox), *t*-Bu-P_4 (146 mg, 0.23 mmol) in dry THF (1 mL) at ambient temperature. The mixture was stirred for 15 min and then filtered through a well-dried column of silica gel (1 cm × 3 cm). Elution with dry THF (ca. 5 mL) and concentration *in vacuo* gave colorless crystals (25 mg), sensitive to air, which contained traces of base (^{1}H NMR). For analytical purposes, they were recrystallized from deoxygenated THF/ethyl acetate: mp 174 °C; UV (CH_3CN) λ_{max} 219 nm; ^{1}H NMR (400 MHz, (THF-d_8) δ 3.93 (m, 2-, 7-H), 3.82 (m, 3-H), 3.79–3.25 (series of m, 4-, 5-, 10-, 11-, 12-, 13-, 14-, 15-, 16-, 17-, 18-, 19-, 20-H), 3.64 (s, OCH_3); (benzene-d_6) δ 4.13 (m, 2-, 7-H), 3.82 (dt, 3-H), 3.52–3.76 (m, 4-, 5-, 10-, 11-, 15-, 16-, 20-H), 3.35 (s, OCH_3), 3.30 (m, 14-H), 3.03–3.22 (m, 12-, 13-, 17-, 18-, 19-H); $J_{2,3}$ = 6.8, $J_{3,4}$ = 10.7 Hz; (pyridine-d_5) δ 4.11 (m, 2-, 7-H), 3.88 (m, 3-H), 3.54–3.80 (m, 4-, 5-, 10-, 11-, 15-, 16-, 20-H), 3.64 (s, OCH_3), 3.41 (m, 14-H), 3.16–3.33 (m, 12-, 13-, 17-, 18-, 19-H); $J_{3,4}$ = 9.8, $J_{10,14}$ = 6.0 Hz; ^{13}C NMR (THF-d_8) δ 177.2 (C=O), 164.5 (C-8, -9), 81.4 (C-1, -6), 73.2 (C-3)*, 72.4 (C-14)*, 69.0, 69.0, 68.5, 68.4, 68.3, 64.9, 64.7, 64.2 (C-10, -15), 52.0 (OCH_3); MS (EI) *m/z* (relative intensity) *inter alia* 374 (M^+, 100), 316 (27), 315 (42), 314 (34), 257 (20), 255 (28), 141 (10), 128 (14), 115 (17) (weak signals *inter alia* *m/z* 406 (6), 390 (18) are indications of the partial oxidation of **42**).

Dimethyl 6,22-Dioxatridecacyclo[10.10.0.0^{1,21}.0^{2,19}.0^{3,11}.0^{4,18}.0^{5,7}.0^{5,10}.0^{7,17}.0^{8,15}.0^{9,13}.0^{14,21}.0^{16,20}]docosane-3,16-dicarboxylate (43). To a solution of **39** (15 mg, 0.03 mmol) in THF (2 mL) was added NaH (10 mg, 0.4 mmol). The mixture was stirred for 20 min, diluted with CH_2Cl_2 (5 mL), and filtrated over silica gel (CH_2Cl_2/ethyl acetate, 2:1) to give pure **43** (^{1}H NMR): mp 280–283 °C; IR (KBr) 2955, 2920 (C—H), 1725 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (t, 11-, 15-H), 3.87 (m, 18-, 19-H), 3.75 (s, $2OCH_3$), 3.70 (m, 9-, 13-H), 3.45 (m, 2-, 4-, 17-, 20-H), 3.21 (m, 8-, 10-, 12-, 14-H); $J_{8,15}$ = 11.2 Hz; ^{13}C NMR ($CDCl_3$) δ 175.9 (C=O), 95.2 (C-1, -5, -7, -21), 75.6 (C-18, -19), 75.4 (C-9, -13), 73.4 (C-3, -16), 61.3 (C-11, -15), 60.2 (C-2, -4, -17, -20), 55.5 (C-8, -10, -12, -14), 52.7 (OCH_3); MS (EI) *m/z* (relative intensity) *inter alia* 404 (M^+, 100), 376 (15), 344 (40), 317 (14), 285 (21), 257 (26), 229 (36), 165 (32), 145 (15), 128 (19), 115 (27), 59 (28).

Dimethyl 2-Oxadodecacyclo[10.9.0.0^{1,3}.0^{3,10}.0^{4,8}.0^{5,21}.0^{6,19}.0^{7,17}.0^{9,16}.0^{11,15}.0^{13,20}.0^{14,18}]henicosane-8,20-dicarboxylate (44). To a solution of **30** (100 mg, 0.19 mmol) in THF (5 mL) and methanol (2 mL) was added, under an inert atmosphere, a 2 M solution of sodium methanolate in methanol (2 mL). After the solution was stirred for 10 min, formic acid (100 mg, 2.22 mmol) was added and the mixture was concentrated *in vacuo* to dryness. The residue was dissolved in a dried ($MgSO_4$) solution of *m*-chloroperbenzoic acid (80 mg, 0.46 mmol) in CH_2Cl_2 (20 mL). After being stirred for 5 min, the solution was washed twice with aqueous K_2CO_3 solution, dried ($MgSO_4$), and concentrated *in vacuo*. Chromatography of the residue over silica gel (CH_2Cl_2) gave pure **44** (48 mg, 65%): mp 182 °C; IR (KBr) 2940 (C—H), 1717 (C=O), 1203 (C—O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72–3.85 (series of m, 5-, 7-, 9-, 13-, 15-, 19-H), 3.71 (s, OCH_3), 3.52–3.64 (series of m, 6-, 11-, 14-, 16-,

17-, 18-H), 3.39 (m, 4-, 21-H), 3.11 (m, 10-, 12-H); ^{13}C NMR ($CDCl_3$) δ 177.4 (C=O), 95.2 (C-1, -3), 78.8 (C-8, -20), 75.1 (C-5)*, 74.6 (C-11)*, 70.5 (C-9, -13), 67.0 (C-6), 66.8 (C-15), 66.2 (C-14, -16), 66.0 (C-7, -19), 65.5 (C-17, -18), 60.6 (C-4, -21), 56.3 (C-10, -12), 52.4 (OCH_3); MS (EI) *m/z* (relative intensity) *inter alia* 391 (28), 390 (M^+, 100), 262 (13), 359 (7), 332 (5), 331 (24), 330 (52), 303 (12), 302 (17), 271 (27), 270 (7), 269 (5), 244 (6), 243 (19), 242 (8), 241 (12), 239 (10), 228 (11), 227 (9), 226 (8), 215 (13), 202 (12), 179 (16), 178 (15), 166 (10), 165 (330^{2+}, 29), 153 (12), 152 (14), 141 (15), 135 (270^{2+}, 7), 129 (14), 128 (17), 121 (242^{2+}, 6), 115 (31), 113 (226^{2+}, 5), 91 (14), 81 (11), 77 (14), 69 (16), 59 (38), 57 (20), 55 (24), 43 (19), 41 (19). Anal. Calcd for $C_{24}H_{22}O_5$ (390.4): C, 73.83; H, 5.67. Found: C, 73.07; H, 5.62.

Dimethyl Undecacyclo[9.9.0.0^{2,9}.0^{3,7}.0^{4,20}.0^{5,18}.0^{6,16}.0^{8,15}.0^{10,14}.0^{12,19}.0^{13,17}]icosane-1,6-dicarboxylate (45). (a) To a solution of **37** (15 mg, 0.03 mmol) in THF (2 mL) was added NaH (10 mg, 0.4 mmol), and the mixture was stirred for 20 min, diluted with CH_2Cl_2 (5 mL), and filtered over silica gel (CH_2Cl_2/ethyl acetate, 2:1) to give pure **45**. (b) A solution of **30** (600 mg, 1.12 mmol) in dry THF (130 mL) and methanol (40 mL) was stirred with Pd/C (10%, 100 mg) in a H_2 atmosphere at ambient pressure for 15 min. Then, a solution of sodium methanolate (700 mg, 13.0 mmol) in methanol (10 mL) was added and the mixture stirred at ambient temperature until no more H_2 was consumed (2 h). Then, the mixture was filtrated, poured into saturated aqueous NH_4Cl solution, and extracted three times with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to give a crystalline raw material. Chromatography on silica gel with CH_2Cl_2 gave **45** (380 mg, 90%, R_f 0.50, mp 190–192 °C) and **3** (14 mg, 2%, R_f 0.56). **45**: IR (KBr) 2940, 2840 (C—H), 1720 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (m, 2-, 5-, 7-, 11-, 16-, 20-H), 3.67 (s, OCH_3), 3.60 (m, 3-, 4-H), 3.52 (m, 8-, 9-, 10-, 12-, 15-, 17-, 18-, 19-H), 3.41 (m, 13-, 14-H); ^{13}C NMR ($CDCl_3$) δ 179.0 (C=O), 84.4 (C-1, -6), 71.1 (C-11, -16), 70.8 (C-2, -5, -7, -20), 66.8 (C-8, -9, -18, -19), 66.8 (C-10, -12, -15, -17), 66.8 (C-3, -4)*, 66.7 (C-13, -14)*, 52.1 (OCH_3); MS (EI) *m/z* (relative intensity) *inter alia* 376 (M^+, 15), 317 (32), 316 (100), 258 (24), 257 (58), 256 (34), 141 (8), 129 (13), 128 (17), 115 (15).

Dimethyl 8,9:27,28-Dibenzo-1,7,10,26-tetraphenyl-29,30-dioxapentacyclo[24.2.1.1^{7,10}.0^{2,16}.0^{2,25}.0^{3,23}.0^{4,15}.0^{5,22}.0^{6,11}.0^{6,14}.0^{11,21}.0^{12,19}.0^{13,17}.0^{18,25}.0^{20,24}]triaconta-8,27-diene-4,20-dicarboxylates 46a–c. To a solution of **40** (5 mg, 0.01 mmol) in THF (1 mL) was added diphenylisobenzofuran (14 mg, 0.05 mmol). After 5 min, it was concentrated in vacuo and the residue purified by chromatography (CH_2Cl_2) to give a solid identified as a mixture of **46a–c** (11 mg, 90%): IR (KBr) 3055, 2920 (C—H), 1725 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98–7.71 (28 arom H), 2.61–4.10 (14H), 3.92 (s, OCH_3), 3.50 (s, OCH_3); MS (DCI) *m/z* (relative intensity) *inter alia* 913 (M^+ + 1, 2), 436 (54), 228 (100).

Dimethyl 25-Oxatridecacyclo[20.2.1.0^{2,6}.0^{2,21}.0^{3,13}.0^{4,11}.0^{5,9}.0^{7,20}.0^{8,18}.0^{10,17}.0^{12,16}.0^{14,21}.0^{15,19}]pentacos-23-ene-4,15-dicarboxylate (Mixture of Isomers) (47a,b). To a solution of **30** (200 mg, 0.37 mmol) and furan (2 mL) in THF (5 mL) and methanol (2 mL) was added a 2 M solution of sodium methanolate in methanol (2 mL), and the mixture was stirred for 2 h. Then, it was neutralized with formic acid, diluted with CH_2Cl_2, and washed with water. The organic phase was dried ($MgSO_4$), filtrated, and concentrated *in vacuo*. Filtration over silica gel (CH_2Cl_2/ethyl acetate, 10:1) gave colorless crystals (153 mg, 93%): IR (KBr) 2950 (C—H), 1725 (C=O), 1215 (C—O) cm^{-1}. The two isomers **47a,b** can be partially separated by chromatography (silica gel, CH_2Cl_2/ethyl acetate, 19:1). **47a**: mp 253 °C (229 °C dec); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.49 (t, 23-, 24-H), 4.60 (t, 1-, 22-H), 3.80 (m, 2H), 3.59–3.74 (m, 3H), 3.67 (s, OCH_3), 3.34–3.57 (m, 7H), 3.26 (t, 3-, 14-H)*, 2.98 (m, 6-, 20-H); $J_{1,24}$ = 0.9, $J_{3,13}$ = 11.2 Hz; ^{13}C NMR ($CDCl_3$) δ 178.6 (C=O), 136.0 (C-23, -24), 91.5 (C-2, -21), 87.6 (C-1, -22), 75.6 (C-4, -15), 71.8, 70.8, 70.7, 70.0, 69.6, 69.5, 66.5, 66.4, 66.4, 66.1, 52.3 (OCH_3); MS (EI): *m/z* (relative intensity) *inter alia* 442 (M^+, <1), 414 (3), 375 (9), 374 (100), 315 (30), 314 (76), 257 (8), 256 (14), 255 (25), 254 (6), 253 (6), 68 (6). **47b**: mp 181 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.47 (t, 23-, 24-H), 4.61 (t, 1-, 22-H), 3.82 (m, 1H), 3.65–3.78 (m, 3H), 3.68 (s, OCH_3), 3.57 (m, 1H), 3.38–3.57 (m, 7H), 3.26 (m, 3-, 14-H), 2.73 (m, 6-, 20-H); $J_{1,24}$ = 0.9 Hz. Anal. Calcd for $C_{28}H_{26}O_5$ (442.5): C, 76.00; H, 5.92. Found: C, 75.91; H, 5.90.

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