6 H, C(11-13)H_2, C(11'-13')H_2], 0.88 [t, 1.5 H, J = 6.7 Hz, C(10)H_3 or C(10')H_3], 0.83 [t, 1.5 H, J = 7.3 Hz, C(10)H_3 or C(10')H_3]; ^{19}F-NMR ($CDCl_3$) δ 4.36, 4.06.

(*R*)-MTPA ester of synthetic (±)-erythro model mono-THF (14-er): ^{1}H-NMR (500 MHz, $CDCl_3$, TMS reference) δ 7.59-7.56 (2 H, Ar*H*), 7.40 (3 H, Ar*H*), 5.31-5.25 [m, 1 H, C(15)*H*O, C(15')*H*O], 3.96 [m, 0.5 H, C(16)*H*O or C(16')*H*O], 3.90 [m, 0.5 H, C(16)*H*O or C(16')*H*O], 3.82 [m, 0.5 H, C(19)H_aO or C(19')H_aO], 3.73 [m, 0.5 H, C(19)H_bO or C(19')H_bO], 3.64 [m, 1 H, C(19)H_aH_bO or C(19')H_aH_bO], 3.57 (s, 1.5 H, MeO-15 or MeO-15'), 3.55 (s, 1.5 H, MeO-15' or MeO-15), 1.92-1.62 [m, 4 H, C(17,18)H_2, C(17',18')H_2], 1.64 [m, 1 H, C(14)H_aH_b or C(14')H_aH_b], 1.59 [m, 1 H, C(14)H_aH_b or C(14')H_aH_b], 1.38-1.20 [m, 6 H, C(11-13)H_2, C(11'-13')H_2], 0.88 [t, 1.5 H, J = 7.0 Hz, C(10)H_3 or C(10')H_3], 0.85 [t, 1.5 H, J = 7.1 Hz, C(10)H_3 or C(10')H_3]; ^{19}F-NMR ($CDCl_3$) δ 4.46, 4.37.

(S)-MTPA ester of synthetic model (β-hydroxyalkyl)butenolide (15): ^{1}H-NMR (500 MHz, $CDCl_3$, TMS reference) δ 7.48 (2 H, Ar*H*), 7.41 (3 H, Ar*H*), 6.98 [brd, 1 H, J = 1.2 Hz, C(35)*H*], 5.41 [m, 1 H, C(4)*H*O], 4.90 [qq, 1 H, J = 6.8, 1.3 Hz, C(36)*H*CH_3], 3.48 (d, 3 H, J = 1.0 Hz, MeO-4), 2.68 [dddd, 1 H, J = 15.4, 7.8, 1.2, 1.2 Hz, C(3)H_aH_b], 2.60 [dddd, 1 H, J = 15.4, 4.6, 1.7, 1.7 Hz, C(3)H_aH_b], 1.35 [d, 3 H, J = 6.3 Hz, C(5)H_3], 1.34 [d, 3 H, J = 6.8 Hz, C(37)H_3]; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.27, 165.81, 152.21, 131.84, 129.65, 128.98, 128.46, 127.44, 123.26 (q, J = 289 Hz, *C*F_3), 77.67, 71.52, 55.18, 31.22, 19.45, 18.84; ^{19}F-NMR ($CDCl_3$) δ 4.33; IR (neat) 3072, 2985, 2938, 2849, 1755, 1655, 1493, 1452, 1377, 1320, 1271, 1169, 1121, 1081, 1022 cm^{-1}; TLC R_f = 0.3 (2:1 hexane/EtOAc).

(*R*)-MTPA ester of synthetic model (β-hydroxyalkyl)butenolide (15): ^{1}H-NMR (500 MHz, $CDCl_3$, TMS reference) δ 7.52 (2 H, Ar*H*), 7.41 (3 H, Ar*H*), 6.66 [br d, 1 H, J = 1.2 Hz, C(35)*H*], 5.34 [m, 1 H, C(4)*H*O], 4.73 [qq, 1 H, J = 6.8, 1.2 Hz, C(36)*H*CH_3], 3.56 (d, 3 H, J = 1.2 Hz, MeO-4), 2.57 [m, 2 H, C(3)H_aH_b], 1.42 [d, 3 H, J = 6.3 Hz, C(5)H_3], 1.28 [d, 3 H, J = 6.8 Hz, C(37)H_3]; ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.30, 165.75, 152.26, 132.42, 129.54, 128.63, 128.40, 127.06, 123.26 (q, J = 289 Hz, *C*F_3), 77.58, 71.49, 55.41, 30.99, 19.77, 18.72; ^{19}F-NMR ($CDCl_3$) δ 4.46; IR (neat) 3070, 2985, 2950, 2850, 1752, 1655, 1492, 1452, 1377, 1320, 1271, 1169, 1121, 1081, 1024 cm^{-1}; TLC R_f = 0.3 (2:1 hexane/EtOAc).

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The Pagodane Route to Dodecahedranes: Highly Functionalized, Saturated, and Unsaturated Pentagonal Dodecahedranes via Aldol-Type Cyclizations

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Abstract: Pentagonal dodecahedranes with four (**69**), six (**67** and **83**), and eight (**79**) skeletal positions being functionalized are made available from dimethyl 14,19-dioxopagodane-4-*syn*,9-*syn*-dicarboxylate **7** as a common precursor. Key steps are the installation of the two carbonyl functions of **7** into the expeditiously available pagodane 4-*syn*,7-*syn*-diester, the $2\sigma \rightarrow 2\pi$ pagodane isomerization into the respective bissecododecahedradiene (**46**), and two transannular C,C bond formations. The implied oxidation of two unactivated methylene groups is brought about by a Barton reaction of unusual complexity (at least 14 bond breaking/bond forming events), conveniency (one-pot reaction), and performance (nearly quantiative yield). The subsequent cyclobutane opening ($2\sigma \rightarrow 2\pi$) in **7** and several model systems by bromine addition and bromine elimination is found to be complicated by heavy skeletal substitution but is efficiently effected for **7** by an intriguing detour (isododecahedranes **48**, secododecahedradienes **50**). Thus, for the 20(21) steps between isodrin and the various dodecahedranes, total yields of 12-16% are achieved. Under acid catalysis the two (exothermic) cyclization steps are kinetically sufficiently differentiated to allow the selective generation of intermediate secododecahedranes (**66** and **78**). Limitations of this aldol type route are the cyclizations calculated to be endothermic and which could not be executed irreversibly. Dodecahedrenes (**67**) with their highly bent C=C double bond (ψ ca. 46°) are found to be kinetically surprisingly stable; from mass spectra, indications for the existence of even higher unsaturated dodecahedranes and leads for further functional group manipulations are derived. In the X-ray determinations, the doubly epoxyannulated dodecahedrane **79a** is found to be slimmer by ca. 0.5 Å than the parent dodecahedrane skeleton of **69a**.

Introduction

The $(CH)_{20}$ pentagonal dodecahedrane (**C**)—here synonymously called dodecahedrane—has been an outstanding target in organic synthesis.[1] Of the numerous strategies perceived for the construction of this fascinating molecular skeleton, to date only two have been successfully completed. In the pioneering synthesis by the group of Paquette,[2] the readily available [C10(C5 + C5) + C4] cycloadduct **A** is linearly transformed into C_{20} seco precursor **B**, which for the ultimate cyclization **B** → **C** necessitated dehydrogenative C,C bond forming methodology. The synthesis developed in our laboratory[3] starts from the commercial [C7(C5 + C2) + C5] composite **D** (isodrin), from which the C_{20} [1.1.1.1]pagodane framework **E** is built up by making inter alia use of an earlier discovered [6 + 6] photocyclization reaction.[4] Thanks to a highly optimized protocol, a remarkable 24% yield of parent pagodane was accomplished in large scale preparations.[5]

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(2) Paquette, L. A. *Pure Appl. Chem.* **1978**, *50*, 1291. Paquette, L. A. In *Organic Synthesis-Today and Tomorrow*; Trost, B. M., Hutchinson, C. R., Eds.; Pergamon Press: New York, 1981; p 335. Paquette, L. A. In *Strategies and Tactics in Organic Synthesis*; Lindberg, T., Ed.; Academic Press: New York, 1984; p 175. Paquette, L. A.; Doherty, A. M. In *Polyquinane Chemistry, Synthesis and Reactions*; Springer Verlag: Heidelberg, 1987. 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.

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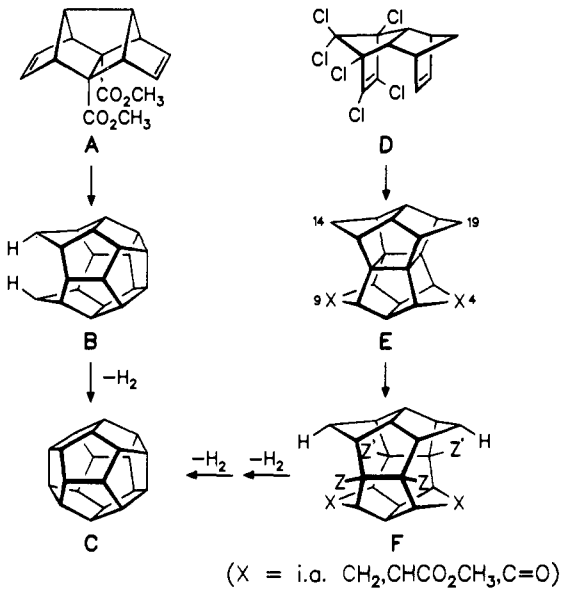
0002-7863/92/1514-10213$03.00/0

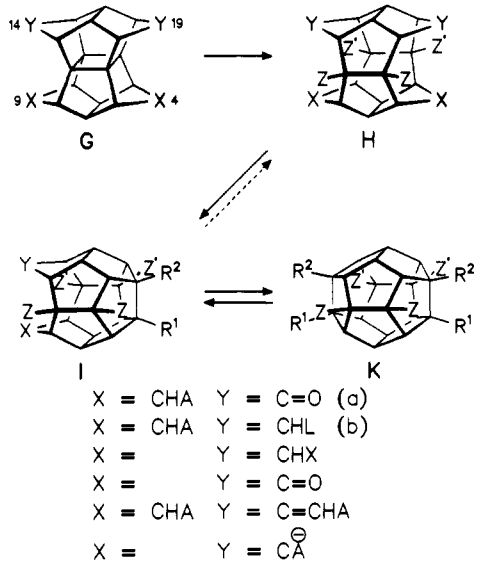
Scheme I



The close structural similarity between the parent structures **C** (I_h) and **E** (X = CH_2, D_{2h}) and a very favorable energy relationship originally had nourished the hope for a simple, thermodynamically driven "one-step" isomerization process implicating in toto the hydrogenative scission and dehydrogenative formation of two C,C bonds (route A in our original tactical scheme).[6,7]

The 8% of dodecahedrane reproducibly obtained from the Lewis acid mediated gas-phase reactions with pagodane (in collaboration with the groups of Schleyer and Maier)[8,9] was an exhilarating achievement at the time but clearly could not meet our early defined goals. The failure to observe any dodecahedrane in response of pagodane to superacids (in collaboration with the group of Olah) was a severe blow but was adequately compensated for by the discovery of the pagodane dication with its unique bonding situation.[10-12] Of the two more laborious, stepwise routes (B/C),[6,7] which were consequently elaborated for the conversion **E** → **C**, the route **B**, implying dehydrogenative formation of the two missing C,C bonds with the bisseco compounds **F** as intermediates (cf. Scheme I), brought a significant improvement with up to 58% total yield of dodecahedranes.[8,13-15] Similar to the "one-step" route A, transannular C,C bond formation and 1,2-dehydrogenation of potentially hyperstable bisseco intermediates **F** were recognized as major detracting pathways. As the most challenging limitation, partial or total removal of functional groups as a consequence of the forcing dehydrocyclization conditions—

Scheme II



well-known from studies in the adamantane area[9,16]—deprived this **B** route from its originally conceived and highly valued potential for chemical modification of the ultimate dodecahedrane sphere by functionalities which had been installed at earlier stages of the synthesis.

Program: The Aldol-Type Route

Obviously, to save our pagodane → dodecahedrane concept, specifically route **B**, as an alley to broadly functionalized and structurally modified dodecahedranes, the dehydrocyclization stratagem at the stage of bissecododecahedranes **F** had to be given up for more "tolerant" bond forming techniques. Already at an early stage of the project, the availability of pagodane-1,6-dione (**E**, X = C=O)[5,14] had encouraged the application of photochemical or carbenoid ring closure procedures to bissecodiones of type **F**—with no success, though, for varying reasons. Specifically the photochemical homo-Norrish cyclopentane formation—successfully applied in the Paquette synthesis and of great appeal since it tolerates a broad substitution pattern and creates manipulable hydroxyl functions—turned out as ineffective because of the unfavorable orientation between the C=O and C–H bonds.[15]

The conceptual way out of this dilemma is displayed in Scheme II: Needed are pagodanes **G** which are activated at all four methylene positions in a way that can be deliberately adjusted to the needs of the subsequent pagodane → bissecododecahedrane (**H**) → secododecahedrane (**I**) → dodecahedrane (**K**) transformations, during which the strict preservation or the selective transformation of the respective functionalities R/Z is demanded. There is not much methodological choice for the $2\sigma \rightarrow 2\pi$ cyclobutane opening, which makes up the entry into the **H** series. In earlier studies with substrates of type **E**, sequential bromine photoaddition/bromine elimination had been found as the only workable procedure.[13] However, there were good reasons to be concerned about the question as to how the additional functionalities in **G** would influence course and selectivity of this step. For the impending lateral cyclizations **H** → **I** → **K**, several more or less standard ring forming methodologies had been envisaged. It must be added as an essential prerogative, that the functionalities as abstracted in Scheme II have to be introduced already at the pagodane (**G**) stages. Mainly for steric reasons, chemical manipulation of syn functional groups is strongly limited in the lateral half-cages of bisseco structures (**H**).[14]

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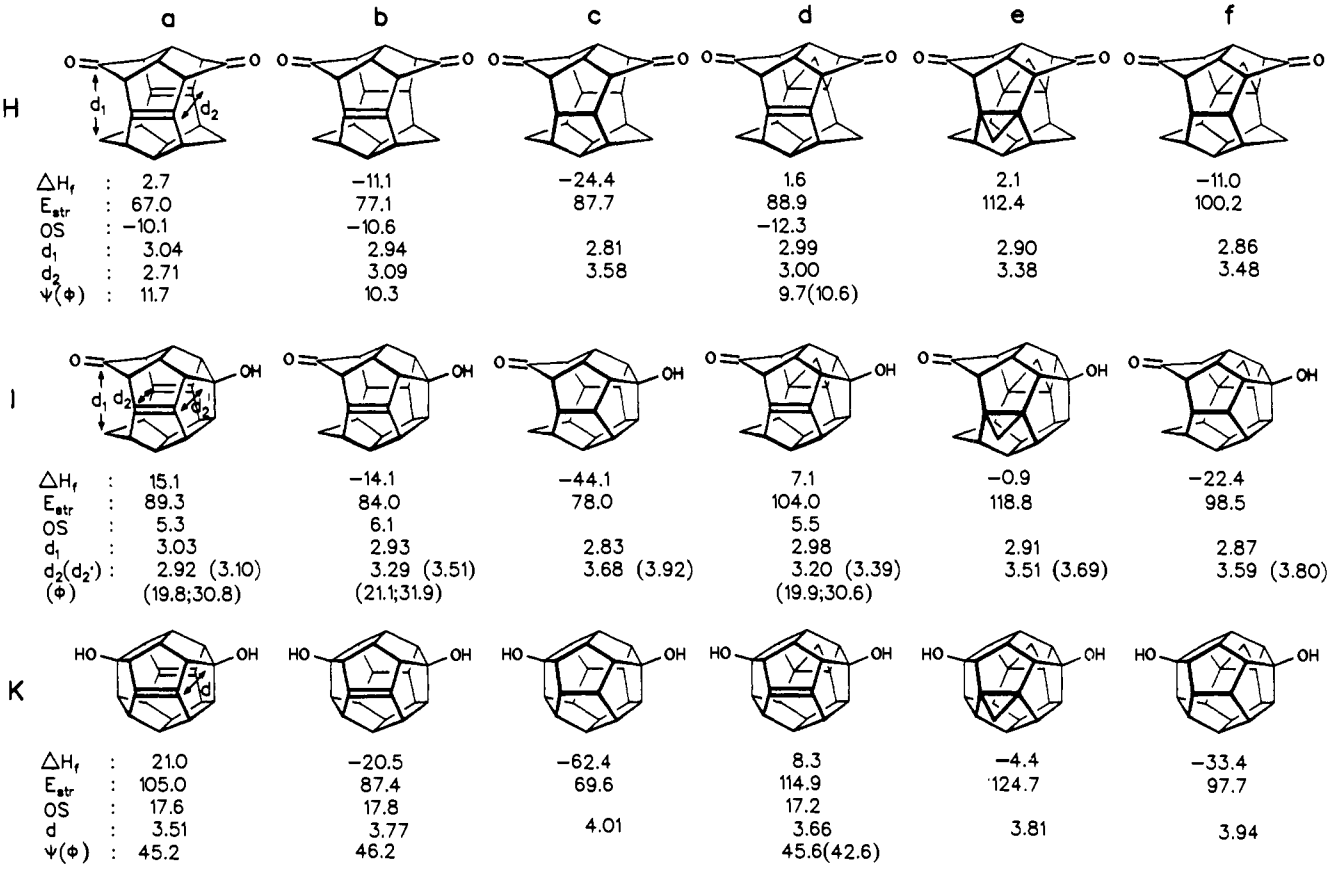
Chart I



	a	b	c	d	e	f
H						
ΔH_f	2.7	−11.1	−24.4	1.6	2.1	−11.0
E_{str}	67.0	77.1	87.7	88.9	112.4	100.2
OS	−10.1	−10.6		−12.3		
d_1	3.04	2.94	2.81	2.99	2.90	2.86
d_2	2.71	3.09	3.58	3.00	3.38	3.48
$\Psi(\Phi)$	11.7	10.3		9.7(10.6)		
I						
ΔH_f	15.1	−14.1	−44.1	7.1	−0.9	−22.4
E_{str}	89.3	84.0	78.0	104.0	118.8	98.5
OS	5.3	6.1		5.5		
d_1	3.03	2.93	2.83	2.98	2.91	2.87
$d_2(d_2')$	2.92 (3.10)	3.29 (3.51)	3.68 (3.92)	3.20 (3.39)	3.51 (3.69)	3.59 (3.80)
(Φ)	(19.8;30.8)	(21.1;31.9)		(19.9;30.6)		
K						
ΔH_f	21.0	−20.5	−62.4	8.3	−4.4	−33.4
E_{str}	105.0	87.4	69.6	114.9	124.7	97.7
OS	17.6	17.8		17.2		
d	3.51	3.77	4.01	3.66	3.81	3.94
$\Psi(\Phi)$	45.2	46.2		45.6(42.6)		

In this paper, we detail our activities which were centered around the aldol-type approach[17] and thus to the synthesis of pagodanes **G** with carbonyl functions at C-14(19) and hydrogen-activating groups at C-4(9) (a). The preparative-synthetic potential of this route is outlined in Chart I with representative skeletons stripped of the A substituents for calculations.[18] After $2\sigma \rightarrow 2\pi$ opening to give the bissecodienes **Ha**, chemical modification of the C=C double bonds is utilized to provide the bisseco substrates **Hb–f**, from which in turn the series of unsaturated and saturated secododecahedranes **Ia–f** and dodecahedranes **Ka–f** are derived.[19]

In other contexts,[3,13-15] we have commented on the predictive value of the MM2 calculations[20,21] as presented in Chart I. As more and more X-ray crystallographic data became available for comparison,[10,22-24] a generally satisfying agreement for the structural data could be observed. With respect to energies, the discrepancies to experimentally determined heats of formation[25] are rather large. Still, the energy trends within these closely related structures are generally rather reliable. Prominent exceptions, expectedly, are the bisseco dienes **Ha**, where the well-known underestimation[26] of transannular π,π antibonding interaction (1.9–2.2 eV π,π splitting)[27] results in transannular π,π distances too small by up to 0.2 Å[24] and $\Delta H_f°$ values too small by at least 5 kcal/mol. The omission of the acceptor substituents in the calculations should not significantly influence the relative energies; the contribution of these groups to the molecular strain are expected to be comparable in the pagodane and secododecahedrane series. Pertinent to our synthetic project are the following interpretations and conclusions.

The $2\sigma \rightarrow 2\pi$ isomerization **G** → **Ha** profits from the carbonyl functions in that the angle strain resulting from the small C–CO–C angles in structures **G** (ca. 99°) and, supposedly, the transannular π,π repulsion in **Ha** are reduced.

Within the bisseco series **H**, the distances (d_1) between the carbon centers to become connected are decreasing with increasing sp^3 character of the central, former cyclobutane, carbon atoms. The carbonyl groups should inductively weaken the deleterious propensity for transannular bond formation via intermediate carbocations or radicals.

Two (**a** and **d**) out of the six transformations **H** → **I** → **K** are endothermic by a significant margin and thus are unattainable under reversible cyclization conditions.

The olefin strain (OS) in the unsaturated bisseco compounds (**Ha**, **Hb**, and **Hd**) as a measure for the reactivity of the respective C=C double bonds[28] qualifies these olefins as only slightly less hyperstable than the parent compounds. Originally it was hoped that the reduction in torsional and compressional H/H strain as a consequence of the CH_2 vs CO replacements should be such as to allow also the hydrogenative saturation of **Hb**/**Hd** for which hyperstability is not, as in **Ha**, counteracted by the transannular π,π destabilization.

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(19) Nomenclature and numbering are secured from the POLCYC program by Rücker, G.; Rücker, C. *Chimia* **1990**, *44*, 116–120. Some of the earlier used names[18] had to be corrected.
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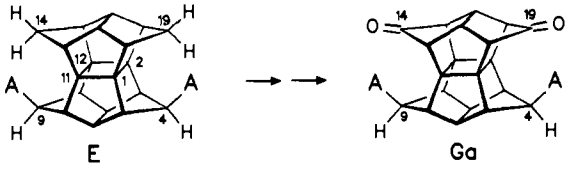
The seco olefins **Ib/Id** are not hyperstable; hydrogenative saturation, not possible in **Hb/Hd**, should be feasible at this stage.

The tilt of the C=C double bonds as expressed by the pyramidalization angles $\psi(\phi)$ dramatically increases on going from **H** to **I** to **K** olefins.[29] No olefins with $\psi(\phi)$ values of the order calculated for the unsaturated dodecahedranes **Ka,b,d** had been found to be stable enough for isolation. As judged by the OS criterium,[28] these olefins (OS = 17.2–17.8 kcal/mol) were expected to be capable of existence only at low temperatures.

4-*syn*,9-*syn*-Disubstituted Pagodane-14,19-diones (Ga). The experimental realization of the program abstracted in Chart I was bound to the ready availability of pagodane-14,19-diones **Ga** with activating substituents in the syn position at C-4(9). This latter stereochemical condition was the consequence of the highly efficient steric protection provided in the lateral half-cages of bisseco compounds **F** and later similarly experienced in the **G** and **H** series, that makes any functional group manipulation, and even syn deprotonation, difficult if not impossible at these stages.

For the preparation of the **Ga** substrates, three synthetic alternatives were scrutinized: (i) oxidation of available 4-syn,9-syn-disubstituted pagodanes **E**; (ii) de novo synthesis commencing with appropriately substituted isodrin analogs, and (iii) intramolecular functionalization (group transfer) in available **E** substrates.

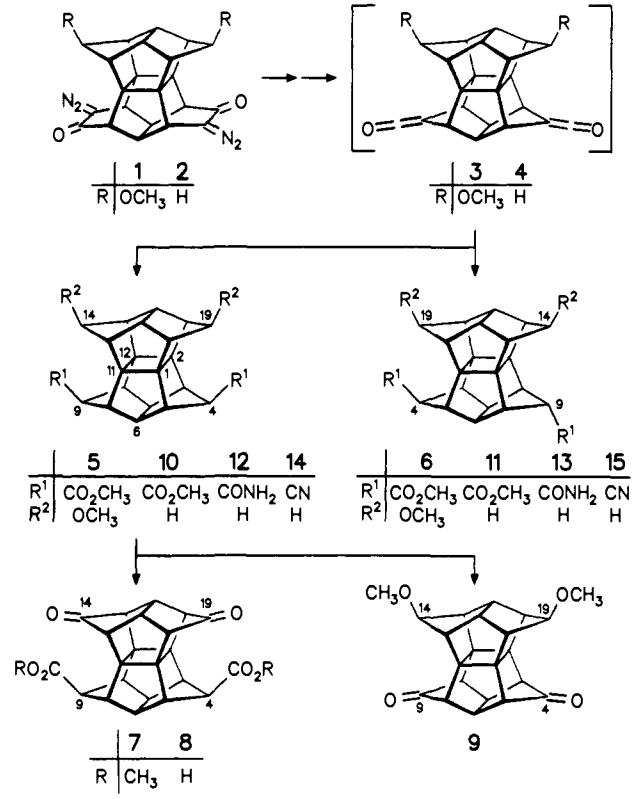
(i) Oxidation of Pagodanes E. With several 4-syn,9-syn-disubstituted pagodanes **E** at hand as direct, high-yield offsprings of the original pagodane synthesis,[5] the chances for their selective hydroxylation (oxidation) at C-14(19) to provide ultimately pagodanediones **Ga** had to be probed, even though the chances for an exclusive chemical attack at the nonactivated methylene groups seemed remote and would need strong assistance from nearby syn functionalities at C-4(9). Being at this stage ca. 40 steps away from the starting material (isodrin), it is easily understood, that only a highly expeditious solution for this problem was acceptable.



Not a trivial postulate, if one considers the preference for attack at tertiary C–H bonds with most manmade reagents reported for useful oxidation of nonactivated C–H bonds.[30] In addition, to preserve the advantage offered by the symmetry inherent to the substrates **E**, both CH_2 groups should possibly be functionalized in one step, a prerequisite which can only enhance the chance for competing processes. Still, the fact that bridgehead norbornane type C–H bonds are not attacked by peracids, raised some hope. Prior experience with related hydrocarbons or the very recently reported regiospecific oxidation of Binor S at one of its two methylene carbons by a Gif-type oxidation system,[31] with the 8% yield of monoketone being bound to a very low (10%) conversion, stresses the problem. In fact, exploratory experimentation with several standard reagents for the hydroxylation of paraffins (peracids[32] and *N*-oxides[33]) only verified the complexity of the task; the activated C–4(9)–H bonds and the highly strained cyclobutane ring in pagodanes **E** were generally the primary points of attack.

The preference for secondary C–H bonds in microbial oxidations of polycyclic hydrocarbons and directing effects by functional groups in such oxidations[34] had encouraged a study with selected pagodanes **E** and a great variety of otherwise proven microbial strains. This study, somewhat perturbed by solubility problems, turned, however, into a true exercise in futility. In no case, could a significant conversion be achieved.[35]

(ii) De Novo Synthesis. The decision to seek access to pagodanes **Ga** by more or less duplicating the original synthesis **D** → **E** with 11,12-bisalkoxylated isodrin analogs as starting materials promised inter alia the advantage that the ultimate products (e.g., **5**) could also be utilized for the S_N2 ring closure route (b in Scheme II). As reported,[36] the total yield of 14-*anti*,19-*anti*-dimethoxypagodane 4,9-diesters **5/6**, isolated as an ca. 10:1 (separable) mixture after a demanding 14-step reaction sequence, could not be lifted above a meager 6.5% total yield (cf. ca. 30% for **10** and **11**[5]). From **5**, the *syn,syn*-dione diester **7** and the *anti,anti*-dimethoxydione **9** were obtained following proven procedures. With **7**, the ideal (vide infra) substrate of type **Ga** was in our hands. Yet, the amount of labor necessary to procure a 5-g lot of **7** meant a clear limitation for its utilization as starting material in an extended program.



(iii) Intramolecular Functionalization. In the pagodanes **E**, the steric situation around syn-oriented substituents at C-4(9) is generally such that their chemical transformation is not decisively impeded—in contrast to what is observed after ring opening in the bisseco structures.[13,14] Still, the transannular distances between the A groups and the opposite syn hydrogens at C-14(19) fall into a range which seemed favorable for intramolecular hydrogen abstraction. For the pagodane-4-*syn*,9-*syn*-diol **16a** and the 4-*syn*,9-*syn*-bismethylol **17a**, as exemplary cases, transannular O–H 14(19) distances of 2.5 and 2.4 Å, respectively, have been calculated (MM2). Disappointingly enough, along several lines, as e.g., thermolysis of the bishypoiodites **16b/17b**,[37] photolysis of the

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(31) Barton, D. H. R.; Eaton, P. E.; Liu, W.-G. *Tetrahedron Lett.* **1991**, *32*, 6263–6266.

(32) Schneider, H.-J.; Müller, W. *J. Org. Chem.* **1985**, *50*, 4609–4615, and cit. lit.

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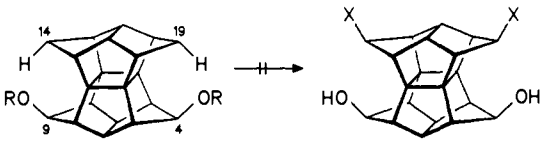
respective bisnitrites **16c/17c**,[38] or $Pb(OAc)_4$ oxidation of **17a**,[39] no sizable quantities of 14,19-bisactivated derivatives were produced. There are indications for the involvement of the more reactive tertiary C–H bonds with O–H distances of 2.7–2.8 Å.[40]



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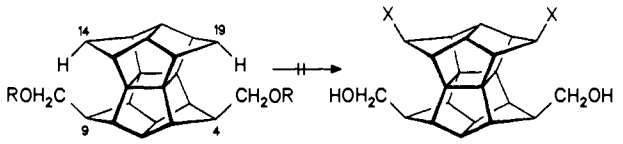


17

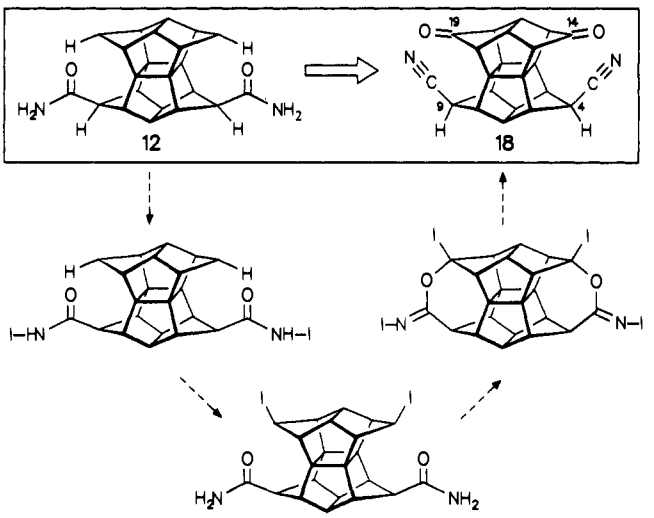
	a	b	c
R	H	I	NO

The breakthrough came from the application of the Barton–Beckwith methodology[41] for intramolecular lactone formation from carboxamides to the pagodane-4-*syn*,9-*syn*-dicarboxamide **22**. After extensive optimization work, a truly intriguing protocol is now available which allows the one-pot and near to quantitative transformation of **12** into the 14,19-dioxo-4-*syn*,9-*syn*-dicarbonitrile **18**. To this end, the suspension of **12** in CH_2Cl_2 is first exposed to ca. 6.5 equiv of iodine for several days, a treatment which for whatever reasons was found to be complementary to the final outcome. Then it was irradiated with a 500-W day light lamp whilst ca. 10 equiv of $Pb(OAc)_4$ were added in portions within 1 h to the now boiling reaction mixture with **18** being dissolved. After a simple workup procedure, crystalline **18** (mp > 320 °C) is secured in yields of, if not better than, 94% on a 2-g (25 mmol) scale.[40] From the coloration of the evaporated solvent, partial consumption of iodine by reaction with CH_2Cl_2 is manifested.

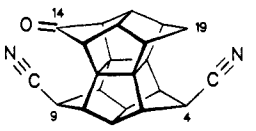
Characteristic spectral features of **18** are the five ^1H and seven ^{13}C NMR signals (C_{2v}), the norbornanone type C=O IR frequency of 1765 cm^{-1}, and the parent MS peak at m/z 282 ($M^+ - 2$ CO). It is to be noted that with δ 62.9, the ^{13}C shift of the central cyclobutane carbons, when compared to that of parent pagodane (62.9) or related 4,9-disubstituted derivatives (e.g., 63.5 for **10**;[14] cf. 62.6 for **7**), turned out as practically independent of the various functionalities. The configuration at C-4(9) was typically ascertained by the 4a(9a)-H singlet signal at δ 2.97.

In the course of the optimization efforts, ketodinitrile **19** ($\nu_{C=O}$ = 1760 cm^{-1}, $\delta_{C\text{-}1(2)}$ = 60.0, $\delta_{C\text{-}11(12)}$ = 66.2) and lactam **20** (up to 20%, distinguished from iminolactone **21** on spectroscopic grounds) could be isolated. Attempts to identify other intermediates or side products in experiments taken to partial conversion only demonstrated the rapid appearance of **18** and thus the rapid consumption of any intermediate. There can only be speculation on the mechanistic details,[41,42] number and nature of intermediates, and the actual sequence of events. Thus, with a total of at least 14 bond forming/bond breaking steps being involved, the symmetrical intermediates formulated in Scheme III can only serve

Scheme III



as aides for balancing the complex procedure. With respect to the postulated and isolated singly (**20**) or doubly bridged pagodanes, subsequent investigations have provided information as to the relative reactivity of the corresponding mono- and bislactones.[40] Oxidations ("double substitutions") under the influence of $Pb(OAc)_4/I_2$ combinations are frequently used,[30,41] and nitriles have been detected as minor components in photolysis mixtures from iodoamides.[42] Yet, the efficiency of the rather uncommon ϵ-hydrogen abstractions, of the iodine and oxygen transfers on the way from **12** to **18**, is certainly without any parallel. At all stages, steric (cage) and stereoelectronic effects must be cooperating in a very fortuitous manner.



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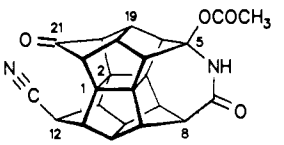

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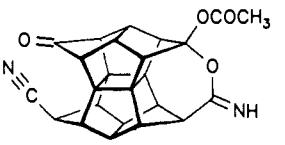

21

At this point, there was enough motivation to search for a more convenient and expeditious access to the now pivotal *syn,syn*-dicarboxamide **12** which before had been prepared in a standard four-step sequence from *syn,syn*-diester **10**. A real improvement came from a modification of our original pagodane synthesis:[5] the mixture of isomeric bisdiazoketones **2** (the C_s isomer is not shown) is photolyzed with a high-pressure Hg lamp (Pyrex vessel) at −78 °C in a ca. 10^{-2} M CH_2Cl_2/NH_3 solution (ca. 3:2). With averaged 80% of **12** and 10% of the syn,anti isomer **13** on an ca. 10-mmol scale, the result only slightly deviated from that of the methanolysis reaction. For the separation of **12** from **13** the following procedure proved workable: From methanol ca. 70% of the less soluble symmetrical **12** crystallizes in pure form; the remaining ca. 1:1 mixture of **12/13**, separable only with great material loss, is dehydrated into the respective dinitriles **14/15** (90%), which can cleanly be separated by chromatography. **14** was retransformed into **12** bringing the total yield of isolated **12** close to the 80% present in the crude product mixture. By treating a DMF solution of **14/15** with NaH for 3 days at room temperature, the *anti,anti*-dinitrile is obtained, whose NMR data are given for comparison in the Experimental Section.

The arguments will be presented below as to why hydrolysis of diketo dinitrile **18** into diketo diester **7** became of utmost

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(39) Mihailovic, M. L.; Cekovic, Z. *Synthesis* **1970**, 209–224. Criegee, R. In *Oxidation in Organic Chemistry*; Wiberg, K. B., Ed.; Academic Press: New York, 1965.

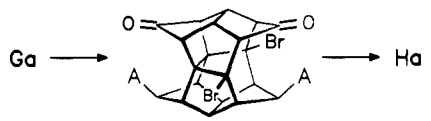
(40) Pinkos, R. Dissertation, University of Freiburg, 1990. Pinkos, R.; Rihs, G.; Prinzbach, H. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 303–305. Pinkos, R.; Melder, J.-P.; Fritz, H.; Prinzbach, H. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 310–313.

(41) Barton, D. H. R. *Aldrich. Acta* **1990**, *23*, 3–10. Barton, D. H. R.; Beckwith, A. J. L. *Proc. Chem. Soc.* **1963**, 335.

(42) Baldwin, J. E.; Barton, D. H. R.; Dainis, I.; Perreira, J. L. C. *J. Chem. Soc. (C)* **1968**, 2283–2289.

importance. It was therefore pleasing to learn that, protected by the given set of substituents, the normally acid-sensitive pagodane skeleton survived largely even the extended (24 h) refluxing in concentrated HCl/HOAc, which was necessary for the conversion of **18** into diacid **8** (85%). Esterification of **8** to give **7** with diazomethane was quantitative. Thus, with a total yield of 15–18% of **7** based on isodrin, as compared with the ca. 6.5% (based on the isodrin analogs) in the de novo synthesis,[36] the grounds were laid for the pursuit of our preparative program.

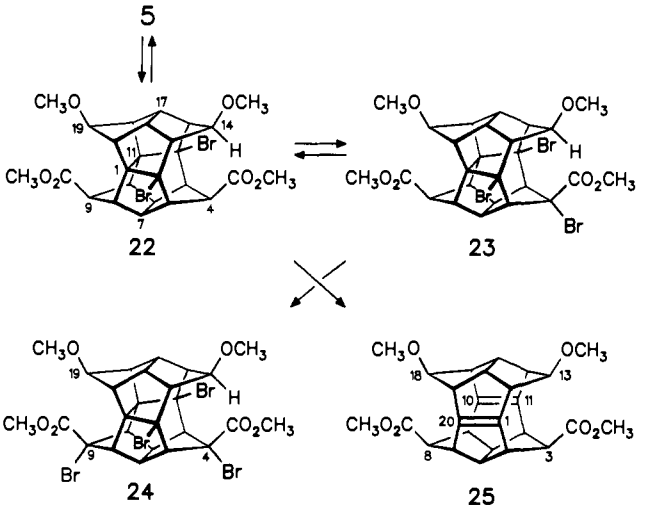
Bissecododecahedra(die)nes Ha–Hf, Secododecahedra(die)nes Ia–If, and isododecahedranes. The isomerization of the highly functionalized pagodanes **Ga** (**7** and **18**) into the respective bissecodienes **Ha** had to be considered as a rather critical step in our synthetic scheme, especially with high yields being mandatory. It is the extreme rigidity of the pagodane skeleton which generally excludes, for kinetic reasons, the direct thermal $2\sigma \rightarrow 2\pi$ pathway, even if it is thermodynamically feasible. For the isomerization by 1,4-addition (**Ga** → **N**) and 1,4-elimination of bromine (**N** → **Ha**)—with better than 90% over both steps in case of the parent hydrocarbons[13]—our prior work with the 4,9-di(tetra) functionalized pagodanes **E** signaled more or less disturbing consequences for pagodanes carrying functionalities at all four methylene positions. (i) The carbonyl functions in 4,9-dione **E** (X = C=O) had been found to significantly retard the bromine addition but otherwise not to influence the overall efficiency (85% dienedione). (ii) The functionalities in 4-*syn*,9-*syn*-diester **E** (X = $CHCO_2CH_3$) had much less impact on the rate of bromine addition but promoted α-bromination at the activated C-4(9) positions. (iii) The four chlorine atoms in 4,4,9,9-tetrachloropagodane **E** (X = CCl_2) made this compound resistant toward bromine. Clearly, bromine addition to **7** and **18** with their special concentration of functionalities was not at all guaranteed. With the oxidation potential (1.2 V for parent pagodane, 1.4 V for 4,9-dione **E**, 1.9 V for **7**, 2.1 for **9**, 2.3 V for **18**) as a heuristic criterium for the ease of bromine addition,[44] the prospects looked better for diketo diester **7** than for diketo dinitrile **18**.



N

To further define "scope and limitations" of this two-step access to the bissecodienediones **Ha**—variously functionalized dienes of this type are wanted for other investigations[27,44]—first the results with presumably less deactivated tetrafunctionalized pagodanes, the *anti,anti,syn,syn*-dimethoxy diester **5**, the *anti,anti*-dimethoxydione **9**, and the all-*syn*- and the *syn,syn,anti,anti*-dimethoxy dinitrile **35** and **38**, are summarized.

Dimethoxy diester **5** added bromine under standard conditions (irradiation of an anhydrous CH_2Cl_2 solution with excess of bromine at −10 °C, 150-W day light lamp, Duran vessel). Already at low conversion, however, tribromide **23** (mp 254–255 °C) was the main product, which very slowly transformed into tetrabromide **24** (mp 256–258 °C). Careful TLC and ^1H NMR monitoring did not reveal any higher substituted bromide. The kinetic differentiation for the α-bromination (C-4) in **22** and (C-9) in **23** was indeed sufficient for the highly selective production of the respective bromides. Thus, with 70 equiv of bromine and irradiation times of 30 min or 3 h, respectively, 92% of pure **23** or 88% of pure **24** could be isolated. The methoxy groups obviously retard somewhat the 1,4-bromine addition to **5** and protect the C-14(19) positions against bromination but do otherwise not influence the regio- and stereoselectivities governing the formation of **23** and **24**. The loss of C_s symmetry, as manifested in the NMR spectra of **23** and **24**, is due to restricted rotation imposed on the α-brominated *syn*-ester groups on the open side (**23**) or on both sides (**24**), hence to the existence of rotamers at ca. 30 °C.



In the generation of bissecodiene **25** directly from tribromide **23** or tetrabromide **24**, the bromine atoms at C-4(9) caused complications, and only mediocre yields were achieved. For that reason, prior reduction to dibromide **22** was mandatory. In **23**, the activated and sterically easily accessible 4-*anti*-bromine lent itself to hydrogenolytic elimination over platinum at 1 atm of H_2 (CH_2Cl_2). In fact, with complete retention at C-4, and without any loss of material, dibromide **22** (mp 224–225 °C, dec; $J_{3,4} \approx J_{4,5}$ = 5.0 Hz) was obtained. 1,4-Bromine elimination from **22** under somewhat modified conditions (Zn, NaI, Na_2SO_3, boiling DMF)[40] yielded **25** as the exclusive product (92%, mp 209–210 °C; $\nu_{C=O}$ = 1720, $\nu_{C=C}$ = 1610 cm^{-1}). It was only at lower reaction temperatures that reformation of **5** became detractive. With respect to the steric situation in the lateral half-cages of **25** it is to be noted, that the *syn*-ester functions in diene **25** are rotationally not impeded, with the consequence of six skeletal ^1H and seven ^{13}C NMR signals (C_s symmetry). The olefinic ^{13}C shift ($\delta_{C\text{-}1(10,11,20)}$ = 154.5) proved only slightly different from that of parent diene (155.4) or methoxyfree diene diester (155.4).[14]

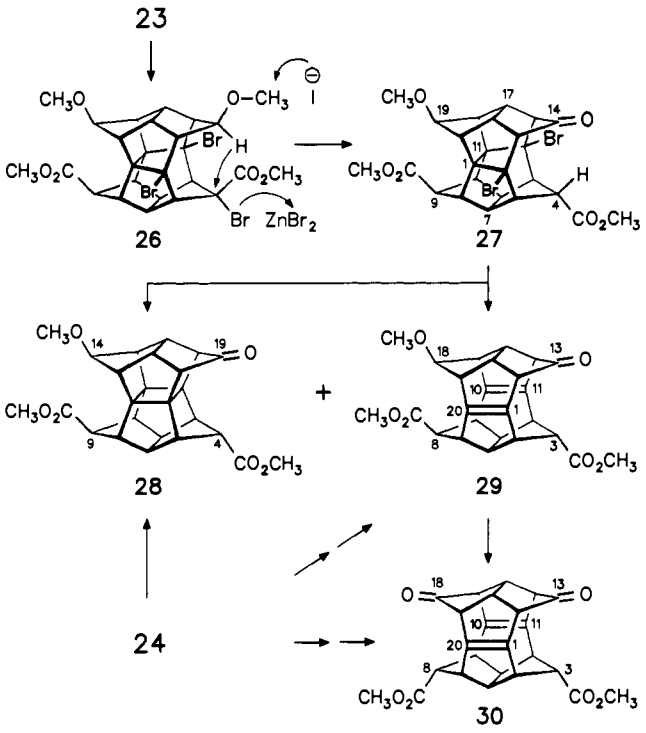
Remarkable in the context of transannular assistance provided by the secopagodane half-cage is the selective formation of bissecodienone **29** (87%; mp 226–227 °C; $\nu_{C=O}$ = 1730, $\nu_{C=C}$ = 1620 cm^{-1}, $\delta_{3\text{-}H}$ = 3.49, $\delta_{8\text{-}H}$ = 2.53, $\delta_{C1(11)}$ = 158.4, $\delta_{C10(20)}$ = 155.3) besides 8% of pagodane **28**, when tribromide **23** was exposed to the same debromination conditions. Given the steric situation in the seco half-cage and the anti configuration at C-3 in **29**, internal hydride transfer as formulated in **26** seems reasonable. That the redox step to give **27**, as formulated, precedes the 1,4-bromine elimination, is concluded from the presence of **28**. Trigonalization at C-14 and epimerization at C-4 as in **27** remove much of the steric congestion of **23** and thus provide the necessary driving force.

The fate of tetrabromide **24** under similar debromination conditions (Zn, NaI, Na_2SO_3, DMF, 140 °C, 10 min) with 51% of bisseco *anti,anti*-dienedione diester **30**, 19% of **29**, and 5% of **28** fits into this picture: Because of less severe steric compression and less favorable distances on the closed side of **24** (C9–C19), the bromine at C-9 is partially lost without concomitant hydride transfer. In **30** (mp 223–225 °C; $\nu_{C=O}$ = 1730, $\nu_{C=C}$ = 1630 cm^{-1}, $\delta_{3(8)\text{-}H}$ = 3.46 (s), $\delta_{C1(10,11,20)}$ = 160.6) the carbonyl groups apparently cause a diamagnetic shift of 0.95 ppm for the 3(8)-H signal and a paramagnetic shift of 5.6 ppm for the olefinic ^{13}C signal when compared with 4.41 and 154.2 in parent *anti,anti*-diene diester and 161.2 in ester free dienedione.[14]

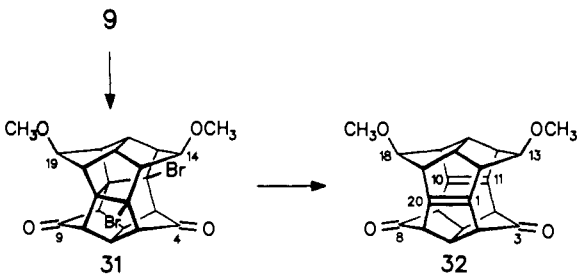
anti,anti-Dimethoxydione **9**, in line with its oxidation potential of 2.1 V,[44] reacted much more slowly than **5** under standard bromination conditions. Even with a very large excess of bromine (ca. 160 equiv, −15 °C), only ca. 50% were converted after ca. 3-h irradiation time; nevertheless, dibromide **31** was the exclusively formed product (TLC, ^1H NMR), with 44% of **9** being recovered

(43) Prinzbach, H.; Murty, B. A. R. C.; Fessner, W.-D.; Mortensen, J.; Heinze, J.; Gescheidt, G.; Gerson, F. *Angew. Chem.* **1987**, *99*, 488–490.

(44) Prinzbach, H.; Lutz, G.; Weber, K.; Heinze, J., manuscript in preparation.

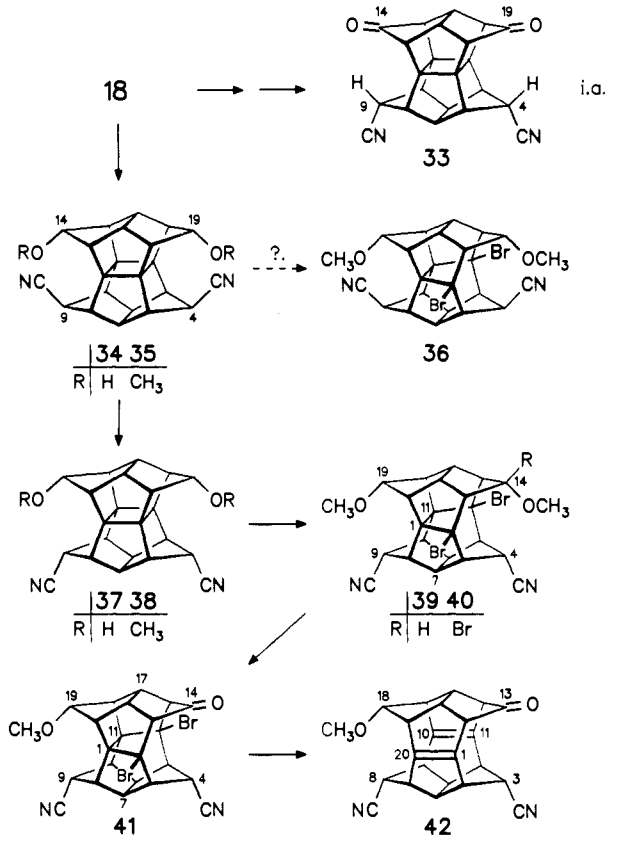


chromatographically. Longer irradiation times (total conversion after 5–7 h) led to increasingly complex mixtures resulting inter alia from bromination of the OCH_3 substituents. **31** tended much less than **22** to hydrolysis and survived chromatography without notable decomposition. Irradiation of **31** under the conditions of its formation or heating in chloroform induced rapid reformation of **9**. The necessity for the vast amount of reagent is thus understandable. $\nu_{C(4)=O}$ = 1730 and $\nu_{C(9)=O}$ = 1770 cm^{-1} give evidence to the strain differences on the two sides. Reductive 1,4-bromine elimination using the modified version (Zn, NaI, Na_2SO_3, DMF) at 140 °C was complete within a few minutes whereupon crystalline *anti,anti*-dimethoxy bissecodienedione **32** (mp 276–277 °C, $\nu_{C=O}$ = 1720 cm^{-1}) was isolated in 87% yield in addition to at most 5% of **9**. For this result, addition of **31** to the preheated heterogeneous DMF suspension is essential. The markedly reduced sensitivity of **32** toward oxygen has precedence.[14]



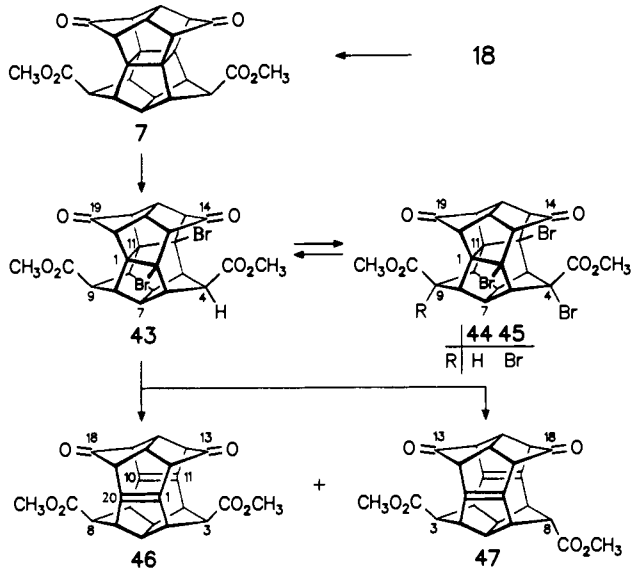
With *all-syn*-dimethoxy dinitrile **35**, produced from **18** by straightforward reduction ($NaBH_4$, 96%) to **34** and methylation (95%), photobromination set in only after raising the reaction temperature above 0 °C and then resulted in a very complex mixture of products, with dibromide **36** acting at best as a very minor component. A hint as to detracting reaction channels came from the bromination (15 °C) of the syn,syn,anti,anti isomer **38**. Isolation of 85% of dibromosecoketone **41** is explained once again in terms of an anti selective bromination, here, in secodibromide **39** to give tribromide **40**. Standard conditions transformed **41** cleanly into bissecodienone **42** (mp 235 °C; $\nu_{C=O}$ = 1725 cm^{-1}, $\delta_{C\text{-}1(11)}$ = 158.3, $\delta_{C\text{-}10(20)}$ = 157.3). With the latter, the preparatively interesting possibility for differentiation of the two lateral sides in bissecodienes is offered.

As a further demonstration of a preparatively useful cage effect, the exclusive formation of the anti,anti isomers **37(38)** upon treatment of **34(35)** with *t*-BuONa/*t*-BuOH (160 °C, 2 h) or

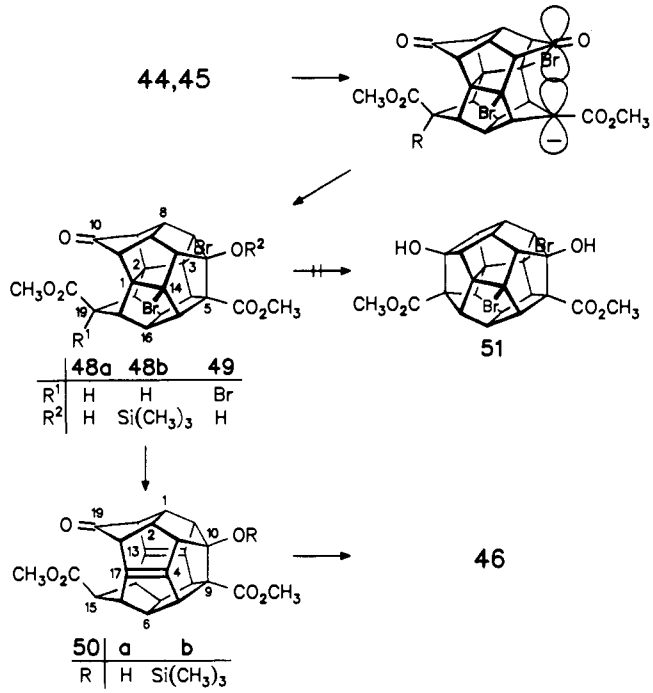


NaH/THF (50 °C, 30 min) deserves notice. *syn,syn*-Diketo dinitrile **18**, under the same equilibrating conditions, isomerized into a mixture with *anti,anti*-dinitrile **33** (secured from **37** by straightforward PCC oxidation) and their syn,anti isomer. More steric pressure is supposedly lost by the syn → anti epimerization for the tetragonal α-cyano carbanions[45] derived from **34(35)**. Relevant to this topic is the behavior of **35** and **38** under treatment with LDA/CH_3I (THF, −20 °C). **35** reacted to an insoluble salt, which dissolved upon addition of the alkylhalide to give 92% of the 4-*anti*,9-*anti*-dimethyl derivative, whilst **38** was not even deprotonated.

In the decisive bromination experiments with the **Ga** pagodanes **7** and **18**, both were expectedly found to respond only to very forcing reaction conditions. From **18**—as well as from its anti,anti isomer **33** and in contrast to, e.g., the bromination course with the similarly resistant dimethoxydione **9**—product mixtures too complex to be analyzed resulted even from small conversion runs. To our good fortune, the prediction for **7** as to be more ready for 1,4-bromine addition also materialized: As in the case of dimethoxy diester **22**, the formation of the dibromide **43** was rapidly followed by substitution to give the tribromide **44** (mp 204–206 °C, $\nu_{C=O}$ = 1770, 1730 cm^{-1}). In fact, by TLC and NMR monitoring, **43** could never be observed. Again, the bromination at C-9 of **44** leading to tetrabromide **45** (mp 219–220 °C, $\nu_{C=O}$ = 1770, 1730 cm^{-1}) was slow enough to allow the isolation of practically pure **44**, if only up to ca. 60% conversion. In totally converted runs, the ratio **44**:**45** averaged ca. 2:1. Since especially the step **44** → **45** was speeded up by higher reaction temperatures, the preparative brominations directed at the selective generation of **44** were conducted at −15 °C in immersion type irradiation vessels (ca. 1-cm thick solutions, enhanced light absorption). Trace components additionally discovered in large scale bromination experiments were later identified as **48a** and **49**. Separation of **44** from **7** was effected cleanly by chromatography through a short pad of silica gel and with an average yield of 92% based on conversion. Analogously to the situation in **23** and **24**, the α-bromines in **44** and **45** restrict the rotational freedom of the ester groups to such an extent that at ambient temperatures rotamers are seen in the NMR spectra (Figure 1).



The one-step reductive elimination of all bromines in **44** or **45** to give the desired bissecodienedione diester **46** was again complicated by the activated bromines at C-4(9), though for different reasons. Experiments with pure **44** yielded, after chromatographic workup, only 50–60% of **46** besides 5% of its syn,anti isomer **47** and oligomeric material. A third component, discernible by NMR in the crude bromination solution (up to 20%, later identified as secododecahedradiene **50a**), had obviously been transformed into **46** during the chromatographic separation procedure. Attempts to circumvent these complications, as practiced with **23**, by prior selective hydrogenolysis **44** → **43** (Pt, 1 atm of H_2, ambient temperature, CH_2Cl_2) resulted in a quantitative yield of a C_s symmetrical dibromide (MS), which, however, turned out not to be **43** but isomeric dibromoisododecahedrane **48a**.[46a] The latter, for protection and better solubility, was silylated to **48b**. In line with the relatively stable C9–Br bond, the tetrabromide **45** under the same set of conditions transformed neatly into tribromoisododecahedrane **49**. The obvious ease of the secopagodane →



isododecahedrane cyclizations is in line with the energies calculated for the respective parent hydrocarbons (ΔE_{str} = 9.4 kcal/mol, $\Delta H_f°$ = –0.5 kcal/mol). Dibromide **43**, prepared by bromine addition to **46**, when exposed to $CH_3ONa(CH_2Cl_2)$ at ambient temperature, underwent rapid and complete cyclization into **48a**. It can be speculated whether the debrominative cyclizations **44** (**45**) → **48a** do not rather follow a radical pathway. That during the bromination of **7**, more specifically from the C-4 radical en route from dibromide **43** to tribromide **44**, isododecahedrane, if at all had emanated only in trace amounts, is ascribed to the very rapid radical interception in the presence of the vast excess of bromine.

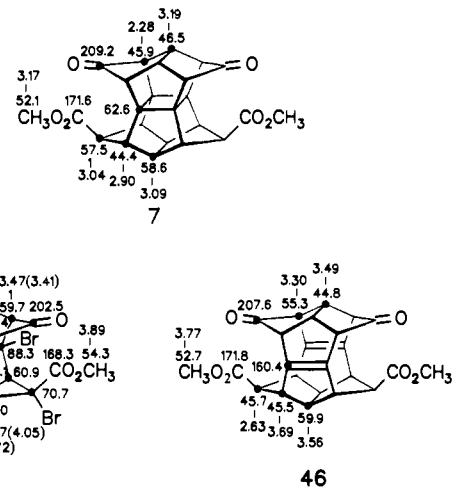


Figure 1. ^1H and ^{13}C NMR assignments ($CDCl_3$) for **44** and **46** (**7** for comparison).

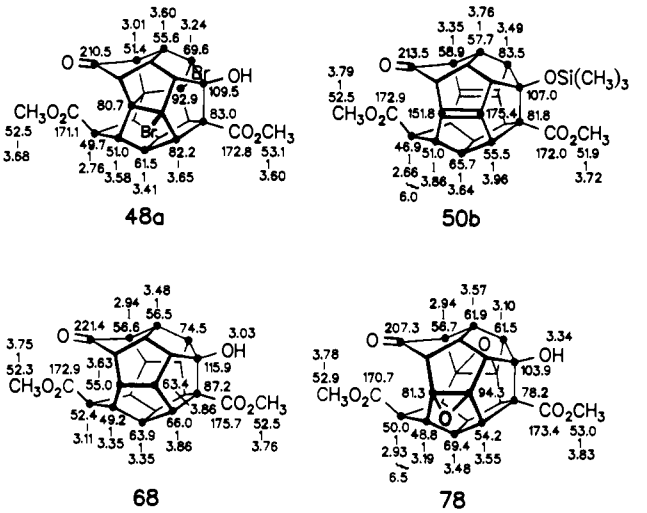


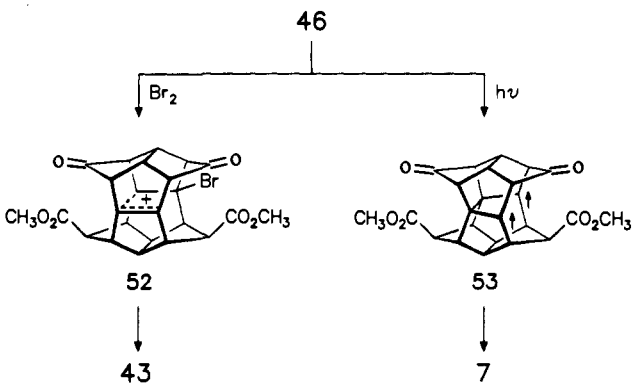
Figure 2. ^1H and ^{13}C NMR assignments ($CDCl_3$) for isododecahedrane **48a** and secododecahedranes **50b**, **68**, and **78**.

The dehydrododecahedrane **51** with its so far unknown carbon skeleton is an eyecatching species. Yet, transannular cyclization on the closed side (C10–C19) of **48a** seemed out of reach for geometrical ($d_{C10-C19}$ = ca. 3.6 Å) as well as thermochemical reasons (E_{str} for **51** ca. 150 kcal/mol). In fact, when **48a** was exposed to more forcing cyclization conditions, only decomposition occurred.

Ease and selectivity in the preparation of **48a** suggested an alternative access to bissecodiene **46** via the high-energy precursor secododecahedradiene **50a**. After 1,4-bromine elimination, the implied ring opening step **50a** → **46** should profit from a high gain in energy and strain (cf. $\Delta\Delta H_f°$ = –12.4 kcal/mol, ΔE_{str} = –22.3 kcal/mol for **Ia** → **Ha**, Chart I). Indeed, after treatment of **48a** with Zn/DMF at 120 °C and aqueous workup (pH 8), **46** was isolated in very high yield (90%)—an increase of a remarkable 35% as compared to the route via reduction of tribromide **44**—or a total of 91% based on pagodane **7**. In a nonaqueous workup procedure, the secododecahedradiene **50a** partly survived in a 1:2 mixture with **46**, from which it was separated chromatographically and fully analyzed. Bromine elimination from the "protected" precursor **48b** led almost quantitatively to **50b**.

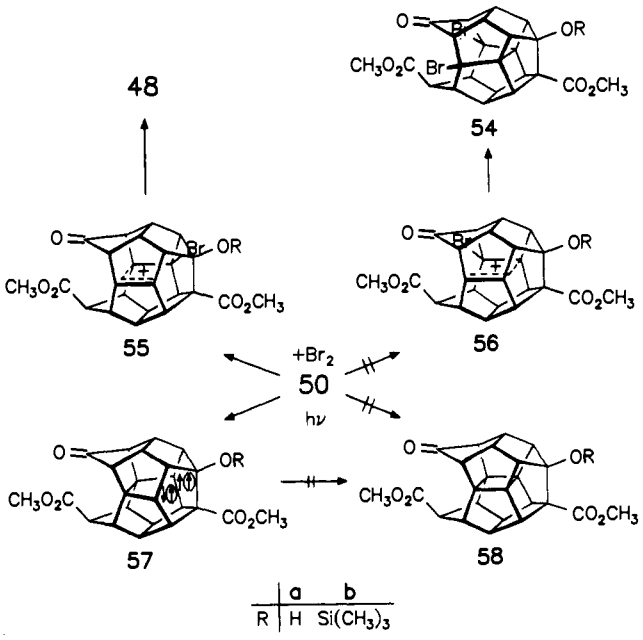
Notable NMR details for **46** (Figure 1)—as compared with the anti,anti isomer **30**—are the high field shift of only 0.83 ppm for the 3(8)-H signal (cf. the 1.88 ppm difference for the carbonyl-free *syn,syn*- (2.53) and *anti,anti*-diesters (4.41)) and a similarly large chemical shift of 160.4 ppm for the olefinic carbons. For the secodiene **50b** (Figure 2) the ^{13}C shift for the olefinic carbons (175.4 ppm) on the closed side (ϕ = 30.8° in **Ia**) is even larger. The zwitter character of the isododecahedrane skeleton in **48a,b** and **49**, being composed of (seco)pagodane and dodecahedrane "halves", is verified by the NMR analyses such as that of **48a** presented in Figure 2.

Typical for the proximate C=C double bonds in rigid bissecodienes of type **Ha** (d_2 = 2.7 Å; **25**, **29**, **30**, **32**, **42**, **46**, **47**) are



a long wavelength UV absorption, the regiospecific homoconjugate addition of acids and halogens and the [π2 + π2] cycloaddition upon direct or sensitized excitation.[14] For **46**, as an exemplary case, the UV spectrum exhibits this absorption in the form of a shoulder at 270 nm; the reactivity toward bromine, like toward oxygen, was reduced as compared to the unsubstituted diene, but the stereochemical course to give via homoconjugated cation **52** quantitatively the directly not accessible dibromide **43** was retained. Irradiation in acetone (high-pressure Hg lamp) delivered uniformly pagodane **7**; there is obviously no competition in intermediate triplet diradical **53** to cyclization.[47]

In case of the secododecahedradienes **Ia**, represented by **50a,b** with their syn periplanar yet nonparallel C=C double bonds (d_1 = 2.9, d_2 = 3.1 Å), UV shoulders between 250 and 270 nm are registered; the homoconjugative stabilization for the ions derived from primary attack at C-4(12) (**55**) or C-13(17) (**56**) is that



much in favor of the former, that exclusive addition of bromine leading back to **48** was highly probable and was indeed experimentally corroborated for **50b** (no **54b**). Photochemically, the tremendous energy increase on the way to the dehydroisododecahedranes (dehydropagodanes) **58** ($\Delta\Delta H_f°(\Delta_{Estr})$ with respect to **Ia** (Chart I) = 50.4 (88.9) kcal/mol, and the large distance between the radical centers in the plausible singlet (triplet) intermediates **57** (cf. **53**) made such a [π2 + π2] cycloaddition highly improbable.[48] And indeed, contrasting to the neat conversion **46** → **7**, direct or sensitized irradiation (acetone) of **50a(b)** caused only polymerization.

The preparation of bisseco substrates of type **Hb–Hf** (Chart I) from dienedione **46** attested to earlier experiences. Some gradual reactivity differences with respect to the parent systems[14] and to the 3,8-diester and 3,8-diketo analogs[13,14] are primarily related to the stronger inductive effect exerted by the two ϵ-keto ester units.

Hydrogenation of **46** with diimide, assisted by the destabilizing π,π interaction, was somewhat slowed down and even with an excess of reagent (up to 50 equiv of $(NCO_2K)_2/(CH_3CO_2H$, 0 °C) ended with the hyperstable monoene **60**, which was isolated in 88% yield (mp 261–263 °C) after crystallization from CH_2Cl_2/ethyl acetate. Under the more vigorous conditions directed at the formation of **59** and approaching the limiting thermal stability of the reagent (preferably set free from N_2H_4/HgO), beyond 50% conversion, **60** was accompanied by secondary products (not **59**; one (ca. 15%) being later identified as **69a**). Clearly, when compared to the parent systems, the decrease of vicinal H/H interactions in the ketonic substrate, or the small reduction in olefinic strain increase calculated for the step **Hb** → **Hc**, is not sufficient to overturn the resistance to hydrogenative saturation.

Characteristic spectral data for **60** are the ^1H multiplet signal for the newly introduced 10(11)-hydrogens (δ = 3.88) with coupling constants of ca. 10 Hz to the vicinal 12(17)-hydrogens and the δ = 151.8 signal for the slightly pyramidalized olefinic carbons. A weak IR band at 1620 cm^{-1} is provisionally assigned to the C=C stretching vibration.

In the epoxidation of **46**, the two consecutive steps are kinetically differentiated to such an extent that eneepoxide **61** (mp 279–280 °C) could be selectively (95%) approached with 4.2 equiv of *m*-chloroperbenzoic acid at ambient temperature ($\nu_{C=O}$ = 1725 cm^{-1}, $\delta_{C\text{-}1(20)}$ = 87.8, C-10(11) = 155.4, *m/z* 420 (M^+, 100%), 364 (96%)). To proceed comparably fast toward diepoxide **63** (mp 274–275 °C; 92%), a temperature of around 80 °C was found necessary, with the product fortunately being sufficiently resistant against acid catalyzed transformation. The epoxidation of hyperstable **60** with *m*-chloroperbenzoic acid to give saturated epoxide **62** was complicated by the parallel formation of diepoxide **63** (up to 10%). Dehydrogenations of the type **60** → **46** as implicit in the formation of **63**, profiting from a decrease in strain (cf. Δ_{Estr} = −10.1 kcal/mol for **Hb** → **Ha**, Chart I), are frequently observed under such oxidizing conditions and had been reported for a secododecahedrene.[46b] This complication was circumvented by making use of benzoyl peroxycarbamic acid.[49] The epoxide **62** (>90%) was utilized without characterization, when purification experiments could not be performed without partial transformation (see below).

Cyclizations H → I → K. (Seco)dodecahedranes. With the bissecododecahedradiene **46** and its conveniently accessible de-

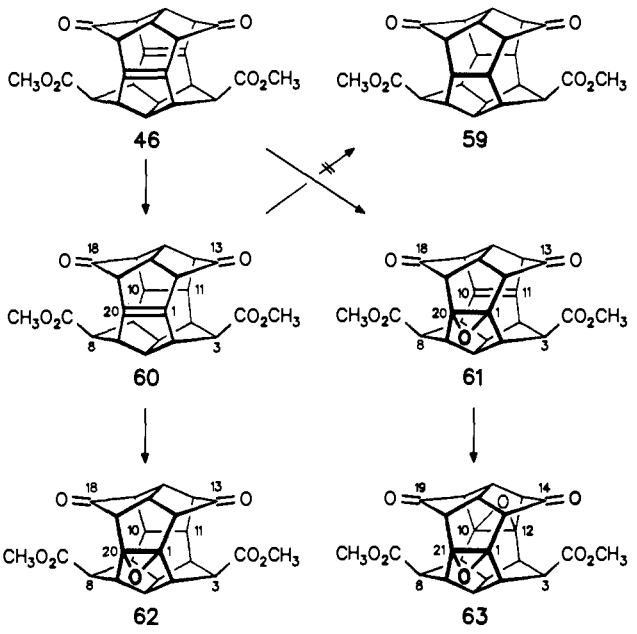
(45) Periasamy, M. P.; Walborsky, H. M. *J. Am. Chem. Soc.* **1977**, *99*, 2631–2638. Walborsky, H. M.; Motes, J. M. *J. Am. Chem. Soc.* **1970**, *92*, 2445–2450. Walborsky, H. M.; Hornyak, F. M. *J. Am. Chem. Soc.* **1955**, *77*, 6026–6029.

(46) (a) A methyl substituted isododecahedrane had been described: Paquette, L. A.; Ternansky, R. J.; Balogh, D. W.; Taylor, W. J. *J. Am. Chem. Soc.* **1983**, *105*, 5441–5446. (b) Paquette, L. A.; Miyahara, Y.; Doecke, C. W. *J. Am. Chem. Soc.* **1986**, *108*, 1716–1718. (c) Paquette, L. A.; Weber, J. C.; Kobayashi, T.; Miyahara, Y. *J. Am. Chem. Soc.* **1988**, *110*, 8591–8599.

(47) Meier, H. In *Methoden der Organischen Chemie*; Thieme: Stuttgart, 1975; Houben-Weyl, Photochemie 1, Vol. 1V/5a, Part 1, p 222.

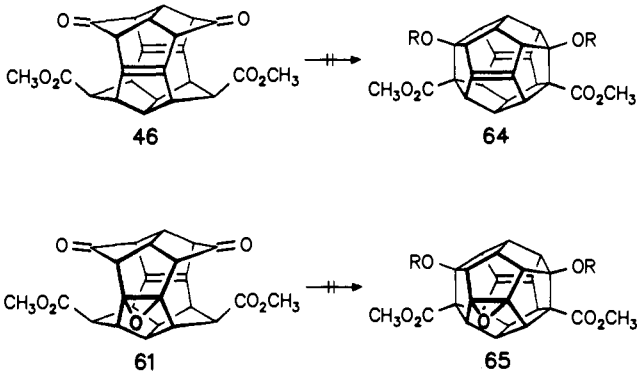
(48) Osawa, E.; Aigami, K.; Inamoto, Y. *J. Org. Chem.* **1977**, *42*, 2621–2626.

(49) Ede, W.; Kopf, H. *Methoden der Organischen Chemie*; Thieme: Stuttgart; Houben-Weyl-Müller, Bd. E13,1, p 905. Höpf, E.; Gauschow, S. *Prakt. Chem.* **1972**, *314*, 145.



rivatives **60–63**, the scene was set for the experimental realization of a greater part of the program outlined in Chart I.

The bissecodiene → dodecahedradiene cyclization **Ha** → **Ka** ($\Delta\Delta H_f°$ = +18.3, ΔE_{str} = 28.0 kcal/mol) undoubtedly is the most spectacular but also the most critical case. In view of the high endothermicity, success seemed a priori bound to the application of irreversible reaction conditions.[50] Another risky point was suspected in the reactivity of the highly pyramidalized C=C double bonds in **Ka** molecules toward oxygen and possibly toward the reagents needed for the cyclization procedure.[29] For the unfavorable thermodynamics, the reversion under base catalysis of secodiene **50a** into bissecodiene **46** was a first attest. And indeed, treatment of **46** with various base systems (NaH, LiH, $NaN(SiMe_3)_2$, partially selected for their ability to stabilize the newly created β-hydroxyester arrangements by complexation, also



in the presence of electrophiles (TMSCl, CH_3I), did not furnish any (seco)dodecahedradienes **64** (**50a**) or respective O-alkylated derivatives. The interception of very small equilibrium concentrations is certainly hampered by the increase in steric compression between the strictly ecliptical vicinal pairs of substituents. In the recuperated **46**, the configuration at C-4(9) was retained, in line with the known preference for anti protonation of the respective carbanions.

To finish off with the unsuccessful attempts: The second, though less, endothermic case in Chart I is made up by the cyclizations of type **Hd** → **Id** → **Kd**. In line with $\Delta\Delta H_f°$ = 6.7 and ΔE_{str} = 26.0 kcal/mol for the cyclopropanated models (Chart I), the epoxyene **61**, under the conditions applied to diene **46**, resisted

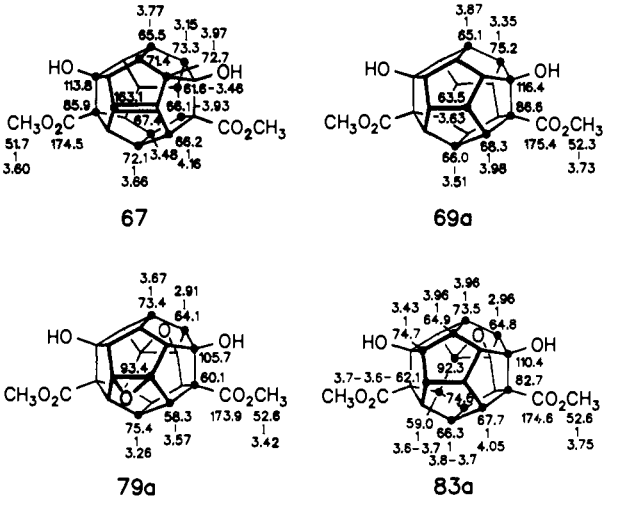
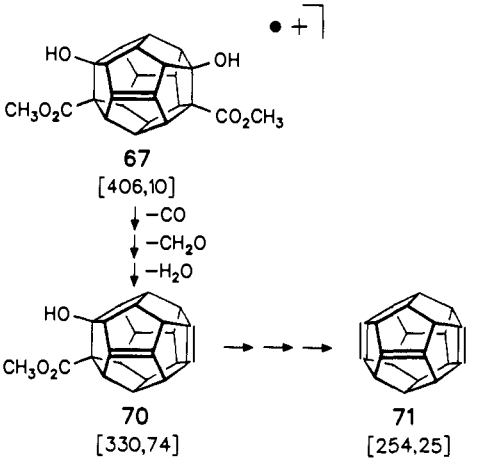


Figure 3. ^1H and ^{13}C NMR assignments for dodecahedranes **67** [D_8]THF, **69a**, **79a** ($CDCl_3/CH_3OD$), and **83a** ($CDCl_3$).

Scheme IV



cyclization; no secoepoxyene and particularly no epoxydodecahedrene **65** could be discovered.

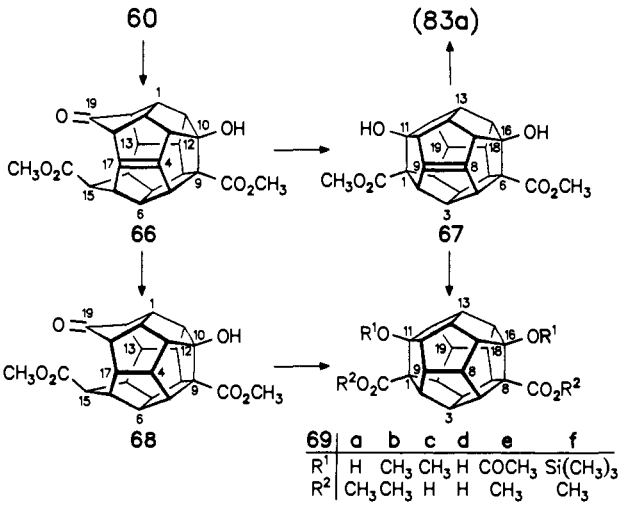
The behavior of bissecomonoene **60**, in contrast, fully lived up to the expectations derived from the exothermicity and strain release calculated for cyclizations of type **Hb** → **Kb** ($\Delta\Delta H_f°$ = −9.4, ΔE_{str} = +10.3 kcal/mol). Stirring of **60** over NaH in anhydrous THF under strict exclusion of oxygen at 25 °C induced the rapid and practically quantitative cyclization to the bissodium salt of **67**. In wet THF, within minutes, occasionally slower, bishydroxydodecahedrene diester **67** (six skeletal positions are functionalized) was formed. The base system CH_3ONa/CH_3OH could similarly be used without the base being added to the highly reactive C=C double bond in **67**. For the latter, when exposed to air, addition of water (*m/z* 422) and oxidation (*m/z* 422 = epoxide,[51] *m/z* 438 = 1,2-dioxetane[52]) were qualitatively ascertained by MS analysis. In THF solutions, nonhyperstable **67** was rapidly and neatly hydrogenated (Pd/C) to provide saturated dodecahedrane **69a**—not accessible from **46** due to the hyperstability of monoene **60**—and epoxidized (peroxycarbamic acid, ambient temperature, **83a**).

The highly strained dodecahedrene **67** remained unchanged for days at room temperature in degassed, ca. 10^{-2}–10^{-1} molar THF solution. Upon heating under reflux, only oligomeric material of an unknown nature separated out. Under inert atmosphere,

(50) Evans, D. A.; Nelson, J. V.; Taber, T. R. Stereoselective Aldol Condensations. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Wilen, S. H., Eds.; Wiley: New York, 1982; pp 1–115. Mukaiyama, T. *Org. React.* **1982**, *28*, 203.

(51) Wiberg, K. B.; Matturro, M. G.; Okarma, P. J.; Jason, M. E. *J. Am. Chem. Soc.* **1984**, *106*, 2194–2200. Wiberg, K. B.; Adams, R. D.; Okarma, P. J.; Matturro, M. G.; Segmüller, B. *J. Am. Chem. Soc.* **1984**, *106*, 2200–2206. Viavattene, R. L.; Greene, F. D.; Cheung, L. D.; Majeste, R.; Trefonas, L. M. *J. Am. Chem. Soc.* **1974**, *96*, 4342–4343.

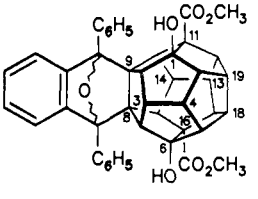
(52) Toda, M.; Okada, K.; Oda, M. *Tetrahedron Lett.* **1988**, *29*, 2329–2332.



67 could be crystallized (CH_2Cl_2/CH_3OH) without notable deterioration; the melting point, though, could not be determined because of concomitant decomposition. The NMR spectra (Figure 3)—in line with C_s symmetry nine ^1H and twelve ^{13}C framework signals—reveal some typical features: Vicinal H,H coupling constants of 6.5 Hz on the ene side, significantly smaller than on the saturated side, as a direct expression of the skeletal flattening enforced by the C=C double bond (cf. Table II in ref 14). The ^{13}C shift of the olefinic carbons (163.1 ppm), when compared to the 154.5 ppm measured for bissecodiene **25**, is supposedly linked to the increased pyramidalization (cf. the 146.0 ppm for the planar bicyclo[3.3.0]oct-1(5)-ene,[53] 150.7 ppm for the selenatricyclo-[3.3.3.0^2,7]undec-3(7)-ene,[54] and 164.5 ppm for the parent dodecahedrene[55]). The EI MS spectrum of **67** (Scheme IV) deserves a closer look in that it offers first hints as to the existence of multiply unsaturated dodecahedranes. Via the rather unusual successive elimination of CO (m/z 378, 25%), CH_2O (m/z 348, 100%), and H_2O (m/z 330, 74%) the seemingly rather stable diene radical cation **70** is produced which via an analogous sequence of events fragments into triene radical cation **71** (m/z 254, 25%).

No dimeric compounds had originated from thermal activation of **67**. Both, formation as well as stabilization of the potential 1,4-diradicals of type **O** (Scheme V) either by cyclization (**P**) or hydrogen transfer (**Q**)—preparatively interesting, known dimerization pathways for highly pyramidalized olefins[56,57]—should indeed be inhibited if not totally prohibited by very strong H,H compression illustrated in Scheme V[58] for the calculated (MM2) parent systems.

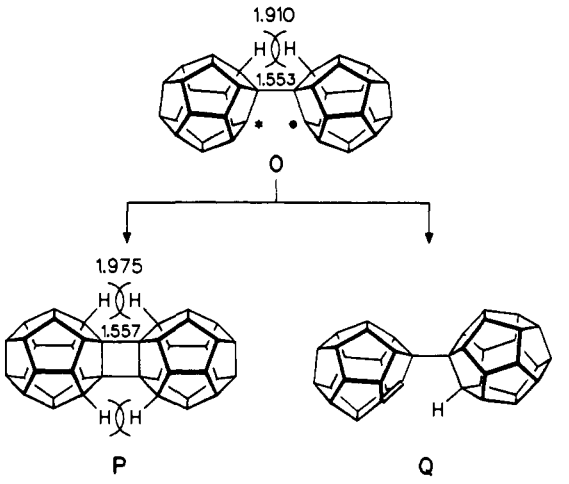
The dienophilic quality of dodecahedrenes, on the other hand, is not similarly restricted. **67** for example added diphenylisobenzofuran instantaneously at ambient temperature. The differentiation of the two isomeric cycloadducts **72** and **73**, isolated



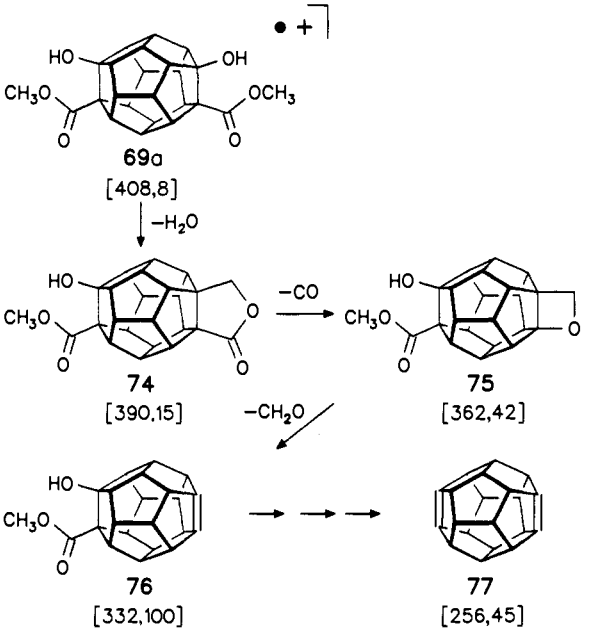
72(73)

as a 4:1 mixture (92%), was mainly based on the anisotropic deshielding effect exerted by the etheral oxygen upon the nearby 3- (**72**) or **14**-hydrogens (**73**). The regioselective attack on the OH-substituted side of **67** should primarily have steric reasons.

Scheme V



Scheme VI



The appearance of 1,6,11,16-tetrafunctionalized dodecahedrane **69a** as one of the secondary products in the enforced diimide reduction of **46** disclosed the operation of the energetically plausible sequence of hydrogenation, cyclization, hydrogenation, and cyclization steps **Ha** → **Hb** (OS, −10.6 kcal/mol) → **Ib** (OS, 6.1 kcal/mol) → **Ic** → **Kc**. The thereby suggested one-pot protocol for the conversion of **60** into **69a** (**60** → **66a** → **68a** → **69a**) was indeed expeditiously realized in the treatment of a CH_2Cl_2/CH_3OH solution of **60** with equimolar amounts of $Pd/C/H_2$ and CH_3ONa. After a simple workup procedure, filtration through a cation exchange column, the yield of crystalline **69a** was nearly quantitative (97%).

Under mild acid catalysis (silica gel, ambient temperature), the first cyclization step **60** → **66** is kinetically sufficiently differentiated from the second, that secododecahedrene **66** (mp 208–210 °C) could be uniformly attained after ca. 75% conversion (5 days). The latter's relative insensitivity toward oxygen made its chromatographic separation from **60** and spectral characterization an easy matter. Other than the 400 MHz ^1H NMR spectrum with several signals being superimposed, the ^{13}C spectrum allowed a complete analysis. As noted for secodiene **50b** (Figure 2), of the two olefinic ^{13}C signals the one (163.4 ppm) belonging to the more pyramidalized carbon on the closed side (C-4, Φ = 31.9° in **Ib**) has a significantly larger shift than that (143.2 ppm) belonging to the open side carbon (C-17, Φ = 21.1°).

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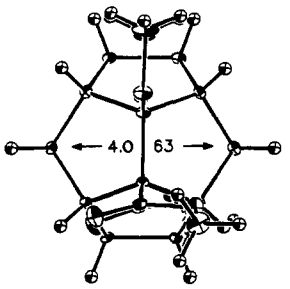


C8 · · C18 : 4.063(9)
C9 · · C19 : 4.064(9)

C1 · · C6 : 4.072(9)
C11 · · C16 : 4.064(9)

C3 · · C14 : 4.062(9)
C4 · · C13 : 4.058(9)

Figure 4. Functional group orientations and transannular distances (Å) in **69b** (M1).

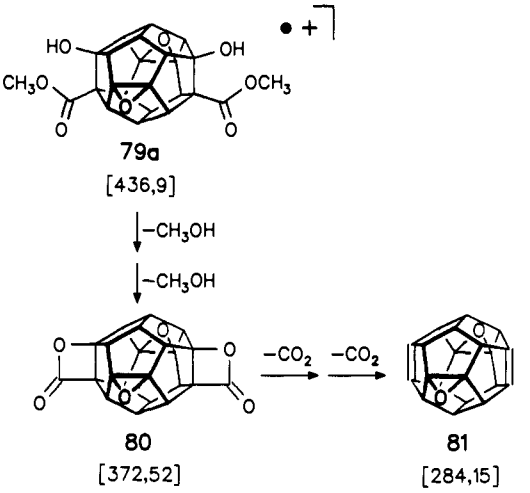
Contrary to the hyperstable bissecoene **60**, secoene **66** was rapidly hydrogenated ($Pd/C/H_2$) to give secododecahedrane **68**. In its completely analyzed ^1H and ^{13}C NMR spectra (Figure 2), the change in chemical shift of the former (**50b**) allylic carbons is remarkable: +10.5 ppm for C-5(8) and −1.8 ppm for C-14(16). From the MS spectrum (EI, i.a., *m/z* (rel intensity) 408 (M^+, 16), 390 (14), 362 (40), 332 (100)) the preferential loss of the vicinal OH/CO_2CH_3 substituents in a way illustrated for **69a** in Scheme VI becomes apparent. With especially favorable steric and energetical prerequisites, the cyclization **68** → **69a** with CH_3OH/CH_3ONa at room temperature proceeded rapidly and quantitatively.

Dodecahedrane **69a** is well soluble in CH_2Cl_2/CH_3OH mixtures, only slightly in CH_3OH or ethyl acetate. Somewhat erratic is the outcome of the etherification with CH_3I/NaH with 75–93% **69b**. Retroaldol type cleavage is supposedly interfering. Derivatization with acetic anhydride/pyridine/DMAP to the diacetate **69e** at 100 °C was slow but uniform, bissilylation with $(CH_3)_3SiCl$ to give **69f** was obviously less hindered (complete after 24 h at ambient temperature).

In the NMR spectra of the C_{2v} symmetrical dodecahedranes **69a–f**—five ^1H and seven ^{13}C NMR skeletal signals—the trends discussed already in detail by Paquette et al. for a series of monosubstituted dodecahedranes **49**[46c]—are recognized: E.g. a deshielding effect of the CO_2R groups upon the β- and γ-positions and of the OH groups upon the γ-positions and a shielding effect of the OH groups upon β-positions. Thus, for **69a** (Figure 3) the 2(5,7,20)-H signal becomes the lowest, the 10(12,15,17)-H signal the highest one, shifted by +0.6 (−0.03) ppm with respect to parent dodecahedrane (3.38). Similarly, the ^{13}C shifts are understood in terms of positive β- and negative γ(ε)-effects measured for these two functionalities (66.9 for parent dodecahedrane[60]). The EI-MS spectrum of **69a** (Scheme VI) corresponds to that of **67** (Scheme IV) in that olefinic radical cations (**76** and **77**) resulting from the elimination of vicinal OH/CO_2CH_3 groups are manifested by intensive signals. Probably due to subtle conformational differences with respect to the vicinal functionalities, the latter are cleaved off in two sequences consisting of the sequential loss of H_2O, CO, and CH_2O, with γ-lactones (e.g., **74**) and oxetanes (e.g., **75**) as plausible intermediates. In fact, it was in the *m/z* 256 (45%) peak, that a dodecahedradiene had surfaced for the first time.

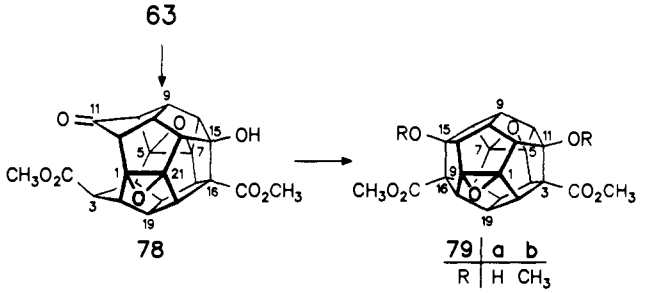
A prominent topic in the chemistry of polyfunctionalized dodecahedranes is concerned with the response of the molecular skeleton to the specific substitution and annulation pattern and with the steric and energetic consequences arising for the specific functionalities themselves, especially if forced into close distance.[62] For **69b** (Figure 4) and **79b** (Figure 5) X-ray structural analyses[23] provide information extending that collected by the Paquette group. Only the most salient features are abstracted here.

Scheme VII



Steric compression between the vicinal functionalities is minimized by nearly orthogonal CH_3O-C/C-C(O)OCH_3 planes with syn (M1, approximately C_s, Figure 4) or anti orientation (M2, approximately C_2, not shown here) of the ester groups. The average length of the thirty C–C bonds (1.554 (1.552) Å) is somewhat greater than the 1.538, 1.543, and 1.546 Å measured for the parent hydrocarbon[63,64] and its carbomethoxy[65] and 1,16-dimethyl derivatives.[66] The longest bonds in M1 with 1.578 (9)/1.579 (9) Å are the twice substituted bonds, in M2 with 1.57 (1)/1.569 (9) Å the C1–C2 and C6–C7 bonds. The pentagon angles (107.1 (5) to 108.9 (6)°) as well as the transannular distances and the ψ values (63.1–63.4°) document only minimal distortions of the dodecahedrane skeleton by the type of substitution present in **69b**.

For the formation of bicyclopropanated dodecahedranes **Ke** starting from the bishomodienes **He**, the energetical situation ($\Delta\Delta H_f° = -7.6$, $\Delta E_{str} = +12.3$ kcal/mol) pretty much corresponds to that of the successful cyclizations of type **Hb** → **Kb**. Good chances were therefore attributed to the preparation of tetrasubstituted diepoxydodecahedrane **79a**; eight skeletal positions are functionalized, from bissecodiepoxide **63**. In practice, standard conditions for 2-fold cyclization (NaH or CH_3ONa or $(CH_3)_3OK$; ambient temperature) provided nonoptimized 82% of **79a**, crystallized from CH_2Cl_2/ethylacetate (mp > 320 °C). The expectedly slow etherification to **79b** (NaH/CH_3I, 36 h at ambient temperature or 8 h at 60 °C) had no competition by ring opening to face.



Catalysis by silica gel once again allowed the enrichment of the seco intermediate **78**; it was isolated chromatographically from an ca. 2:1 mixture with **79a** obtained after 16 h stirring at room temperature (mp 252–253 °C; $\nu_{C=O} = 1725$ cm^{-1}, *m/z* 436 (M^+, 14%), 404 (100)). The structural resemblance of its open side to precursor **63** and of its closed side to **79a** finds its expression

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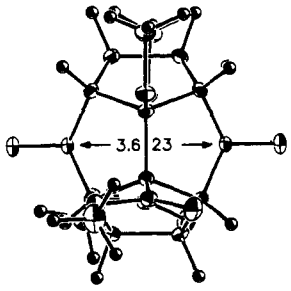


C1 · · C5 : 3.622(5)
C7 · · C21 : 3.625(5)

C3 · · C16 : 4.121(5)
C11 · · C15 : 4.120(5)

C9 · · C18 : 4.160(5)
C13 · · C19 : 4.163(6)

Figure 5. Functional group orientations and transannular distances (Å) in **79b**.

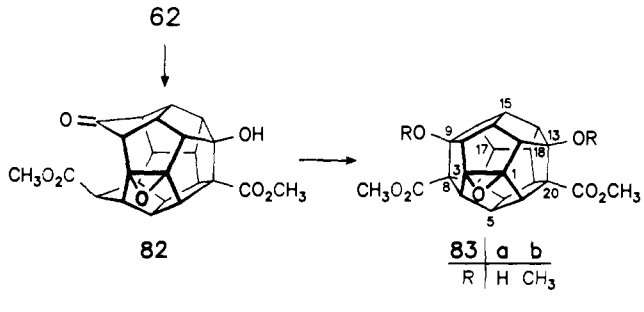
in the close correspondence of the respective ^1H and ^{13}C NMR data (Figure 2).

The flattening of the bisepoxy skeleton **79** as a result of the ethylene-like hybridization of epoxide carbons—cf. the X-ray structure analysis (Figure 5)—is responsible for the relatively small coupling constants of 7–8 Hz (Figure 3) for the vicinal 2(4,17,20)- and 8(10,12,14)-hydrogen pairs, increased strain for the relatively low field epoxide carbon signal with δ 93.4 (δ 96.3 for parent bisepoxide,[61] δ 84.0 for parent bisseco bisepoxide,[14] δ 85.1 for **63**).

Compared with **69a**, the ^{13}C NMR signals of the substituted quarternary carbons (C-2(4,17,20) and of the carbons β to the epoxide rings (C-8(10,12,14) are shifted to higher field (6.5/9.7 and 10.0/11.1 ppm, respectively), and of the carbons γ to the epoxide rings (C-9(13), C-18(19)) to lower field (8.3/9.4 ppm). The MS fragmentation pattern of **79a** again is informative with respect to the observability of multiply unsaturated dodecahedranes and reveals a third mechanism for the elimination of the functional groups. Expulsion on both sides of CH_3OH (bis-β-lactone **80**) followed by 2-fold loss of CO_2 causes the m/z 284 (40%) signal which attests to the existence of diepoxydodecahedradiene **81**. The latter is structurally not far off the highly attractive D_{2h} 1,4,10,16-dodecahedratetraene[55,61] (cf. the 0.064 Å difference in transannular (π,π) distance for the tricyclo[4.2.2.2^{2,5}]dodeca-1,5-diene and its bisepoxide).[51]

Diepoxide **79b** crystallized from CH_2Cl_2 as the approximately C_s symmetrical syn rotamer (Figure 5). As in C_s symmetrical **69b**, the longest bonds are those flanked by the substituents (av 1.608 Å), the eight bonds α to these carbons are relatively short (av 1.554 Å), the β-bonds significantly longer (av 1.568 Å). Except the inner angle of the epoxybicyclo[3.3.0]octane units, all other framework angles lie between 106.5 (2) and 108.2 (3)°. The 2-fold epoxy annulation (av for the geminal C–C bonds 117.45°) causes a shortening of the transannular distances between symmetry related epoxide carbons by ca. 0.5 Å with respect to the orthogonal transannular distances. The latter details and the ψ angles for the epoxide carbons of 47.4–47.7° at present approximate best the situation in the related, highly desired 1,16-dodecahedradiene with its syn periplanar π bonds (ψ = 45.6° calculated), for which no structural data could be secured, yet.

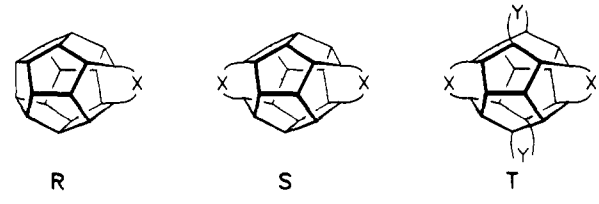
High driving force for conversions of type **Hf** → **If** → **Kf** ($\Delta\Delta H_f°$ = −22.4, ΔE_{str} = −2.5 kcal/mol, Chart I) has already been experienced during the preparation of the saturated epoxy substrate **62**. When the latter was exposed to basic cyclization conditions (NaH in THF) at ambient temperature, rapid 2-fold cyclization to give epoxydodecahedrane **83a**—six skeletal carbons are substituted—was observed by TLC and ^1H NMR control. After total conversion and chromatography, the yield ran up to 91% (mp 278–279 °C). Etherification to give **83b** (mp 227–228 °C) followed that of **69a**.



C_s symmetry of **83a(b)** and formal structural composition of one side each of **69a(b)** and of **79a(b)** follow directly from the NMR analysis—a few ^1H signals (at 400 MHz) are superimposed; the 12 ^{13}C signals, however, are cleanly separated and individually assigned. The "halves" **69a/79a** in **83a** are also reflected in the MS fragmentation pattern with significant intensities for the signals attributed to unsaturated dodecahedranes as once more the outstanding lesson.

Summary and Outlook

Value and esteem granted to a synthetic scheme, particularly if lengthy and costly, rise with its functional and structural variability. For the pagodane → dodecahedrane scheme, the access to 4,9,14,19-tetrasubstituted pagodanes (**Ga**) as presented here, provides this potential. The implied elaboration of two unactivated methylene groups into ketonic functions is unique with respect to complexity (at least 14 bond forming/bond breaking steps), to convenience (one-pot reaction), and to performance (nearly quantitative yield). Via the corresponding bissecododecahedradienes (**Ha**), dodecahedranes with four to eight functionalized skeletal positions become available in total yields ranging from 80 to 90% for the four(five) steps departing from the pagodane intermediate (**7**), and the respective protocols, restricted to 0.1 to 1.0 mmol scale to date, are generally not even optimized. Still, with 15–18% total yield for the route from isodrin to **7**, the yields for the full length route from isodrin to the dodecahedranes amount to a remarkable 10–16% or to an average yield of better than 90% for every one of the 20(21) steps. As emphasized earlier,[5,36] though, two time-consuming bottlenecks make the production of decagram quantities of pagodanes still a labor intensive undertaking. Given the nature of the various functionalities sofar introduced, the scope for chemical modifications of the dodecahedrane sphere and for transformations of the parent skeleton itself is obviously enormous. A notable detail is the kinetic stability of dodecahedrenes (**67**), which came as somewhat of a surprise,[67] and strongly furthered our activities directed toward dodecahedranes with more than just one of these highly reactive C=C double bonds. Special structure/reactivity and (homo)conjugational phenomena are challenging topics related to the high bent and specific orientation of these π bonds in the neutral as well as in derived charged species.[68] As argued above, inter alia mass spectral data strengthen our confidence in the ultimately successful generation of such dodecahedrapolyenes. In this context, the failure to irreversibly perform the endothermic cyclizations ending with the tetrasubstituted 1,16-dodecahedradienes (**64**) meant a hardfelt limitation. Yet, in preliminary notes we have outlined alternatives, by which the here presented 4,9,14,19-tetrafunctionalized pagodanes can be exploited for the preparation of **Ka** type dodecahedradienes.[61] A beneficial offspring of these activities encompasses preparative routes to nonpentagonal dodecahedranes with one (**R**),[69,70] two (**S**),[70] and four C–C bonds (**T**)[71] of the original dodecahedrane carbon skeleton being exchanged for



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bridges of varying nature—highly rewarding extensions indeed for the pagodane → dodecahedrane project.

Experimental Section

Melting points (mp), Bock Monoscop M; Anal. TLC, Merck silica gel plates with F_{254} indicator; IR, Perkin-Elmer 457, Philips PU 9706; UV, Perkin-Elmer Lambda 15; ^{1}H NMR, Bruker WM 250, AM 400; if not specified differently, the 250 MHz spectra are given; ^{13}C NMR, Bruker WP 80, WM 250, AM 400. Chemical shifts relative to TMS (δ = 0), coupling constants in Hz; for signal assignment standard techniques such as homo and heteronuclear decoupling experiments or 2D FT COSY or C/H heterocorrelation spectra were employed; assignments indicated with * can be interchanged. Whenever necessary, NOE measurements were performed to elucidate stereochemical (transannular) relationships; MS, Finnigan MAT 44S.

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*-dicarboxamide (12). To a solution of **2** (3.0 g, 8.14 mmol) in dry CH_2Cl_2 (250 mL), cooled under N_2 to −78 °C, was condensated dry NH_3 (50 mL). The solution was irradiated with a 150-W Hg high-pressure lamp (Duran) for 4 h, and NH_3 was allowed to evaporate. Concentration and crystallization of the crude solid (ca. 8:1 mixture of **12** and **13**, ^{1}H NMR) from methanol (5 mL) gave pure **12** (av 2.10 g, 75%), mp > 320 °C. Filtration of the mother liquor (silica gel, CH_2Cl_2/ethyl acetate/methanol 10:1:1) and again crystallization gave ca. 560 mg (ca. 20%) of a ca. 1:1 mixture of **12** and **13**. The latter proved inseparable and were transformed into the respective dinitriles **14/15** ($SOCl_2$, pyridine) which could be separated on silica gel (cyclohexane/ethyl acetate). **14** was transformed via the diacid chloride into **12** (ca. 90%). **12**: IR (KBr) 3155 (N-H), 2940, 2880 (C-H), 1655 (C=O) cm^{-1}; ^{1}H NMR ([D$_6$]DMSO) δ 6.87 (brs, NH), 6.69 (brs, NH), 2.73 (m, 6-, 7-H), 2.67 (s, 4a-, 9a-H), 2.56 (m, 3-, 5-, 8-, 10-, 16-, 17-H), 2.17 (m, 13-, 15-, 18-, 20-H), 1.68 (d, 14a-, 19a-H), 1.43 (d, 14s-, 19s-H); $J_{14a,14s}$ = 10.5 Hz. Anal. Calcd for $C_{22}H_{22}O_2N_2$ (346.4): C, 76.28; H, 6.40. Found: C, 75.94; H, 6.44.

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 (14). A suspension of **12** (100 mg, 0.29 mmol) and Burgess reagent[72] (1.00 g, 4.2 mmol) in CH_2Cl_2 (15 mL) was stirred for 15 h at ambient temperature. The then homogenous solution was filtered through a short pad of silica gel and concentrated: 82 mg of colorless crystals (91%), mp > 270 °C (sublimation); IR (KBr) 2995, 2950, 2880 (C-H), 2220 (C≡N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.82 (m, 6-, 7-H), 2.78 (s, 4a-, 9a-H), 2.77 (m, 16-, 17-H), 2.73 (m, 3-, 5-, 8-, 10-H), 2.74 (m, 14s-, 19s-H), 2.40 (m, 13-, 15-, 18-, 20-H), 1.70 (m, 14a, 19a-H); ^{13}C NMR ($CDCl_3$) δ 121.3 (C≡N), 64.0 (C-1, -2, -11, -12), 60.0 (C-16, -17), 58.5 (C-6, -7), 46.7 (C-4, -9), 41.8 (C-13, -15, -18, -20), 41.6 (C-3, -5, -8, -10), 40.5 (C-14, -19). Anal. Calcd for $C_{22}H_{18}N_2$ (310.4): C, 85.13; H, 5.85. Found: C, 84.83; H, 5.87.

Mixture of 14/15 from 12/13. A suspension of bisamides **12/13** (1.2 g of crude mixture, 3.46 mmol) in pyridine (9 mL) is cooled to 0 °C and treated with thionylchloride (3 mL). After stirring for 16 h at 50 °C, the solution is concentrated in vacuo, the residues dissolved in CH_2Cl_2 (50 mL) and filtered through silica gel. After evaporation of the solvent, the solid residue (ca. 8:1 mixture of **14** and **15**, 970 mg, 90%) is separated by flash chromatography (cyclohexane/ethyl acetate 5:2; R_f (**14**) = 0.21, R_F (**15**) = 0.41).

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-*anti*-dicarbonitrile (15). Mixture of 15 and Anti,Anti Isomer from 14/15. The solution of **14/15** (ca. 9:1, 50 mg, 0.16 mmol) in anhydrous DMF (3 mL) is treated with NaH (17 mg, 0.7 mmol) for 3 days at room temperature. After 3 days, aqueous NaOH is added, and then it is neutralized with formic acid. After dilution with CH_2Cl_2 and extraction with aqueous NH_4Cl, the organic phase is dried ($MgSO_4$), filtered, and concentrated in vacuo. The 50 mg of crude product consisting of **15** (42 mg, 84%) and of *anti,anti*-dinitrile (15 mg, 15%) is separated by chromatography.

15: colorless crystals, mp 242 °C; IR 2946, 2870 (C-H), 2228 (C≡N), 1464, 1287; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.51 (m, 19a-H), 1.67 (m, 14a-H), 1.72 (m, 14s-H), 2.37 (m, 13-, 15-H)*, 2.44 (m, 18-, 20-H)*, 2.48 (m, 19s-H), 2.69 (m, 8-, 10-H), 2.73 (m, 4a-, 3-, 5-H), 2.80 (m, 16-, 17-H), 2.91 (m, 9-H), 3.15 (m, 6-, 7-H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 121.2 (C4-C≡N) (4), 120.4 (C9-C≡N) (9), 63.4 (C-1, -2), 63.2 (C-11, -12), 59.6 (C-16, -17), 57.8 (C-6, -7), 47.2 (9), 46.2 (4), 42.0, 41.9, 41.8, 41.6, 41.5, 41.3. Anal. Calcd for $C_{22}H_{18}N_2$ (310.4): C, 85.13; H, 5.85; N, 9.03. Found: C, 85.00; H, 5.82; N, 8.99.

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-*anti*,9-*anti*-dicarbonitrile: colorless crystals, mp 274 °C; IR (KBr) 2966, 2944, 2872 (C-H), 2226 (C≡N), 1460, 1271 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.57 (m, 14a-, 19a-H), 1.70 (m, 14s-, 19s-H), 2.36 (m, 13-, 15-, 18-, 20-H), 2.68 (m, 16-, 17-H), 2.73 (m, 3-, 5-, 8-, 10-H), 2.76 (m, 4s-, 9s-H), 3.44 (m, 6-, 7-H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 120.3 (C≡N), 62.8 (C-1, -2, -11, -12), 53.3 (C-16, -17), 57.3 (C-6, -7), 46.9 (C-4, -9), 42.7 (C-13, -15, -18, -20), 42.2 (C-14, -19), 41.9 (C-3, -5, -8, -10); MS *m/z* (rel intensity) 310 (M$^+$, 100).

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*-dicarbonitrile (18). A suspension of **12** (2.0 g, 5.77 mmol) and iodine (9.6 g, 38 mmol) in CH_2Cl_2 (500 mL, freed from methanol) was, after standing for 6 days, irradiated with a 500-W day light lamp bringing it to reflux, and then a solution of lead tetraacetate (27.4 g, 62 mmol) in CH_2Cl_2 (200 mL) was added with stirring in portions over 1 h. After an additional 5 h of irradiation, the solid was filtered and washed with CH_2Cl_2 (150 mL). The combined CH_2Cl_2 phase was extracted with aqueous Na_2SO_3 solution until the iodine color had disappeared, washed with water and 1 N aqueous KOH, and then concentrated in vacuo to ca. 50 mL. After addition of ethyl acetate (ca. 3 mL) to this oily, yellowish residue ca. 70% of **18** crystallized. Chromatography of the mother liquor (silica, CH_2Cl_2/ethyl acetate, 10:1) gave additional 24–26% of **18** (total of ca. 1.84 g, 94%): mp > 320 °C; IR (KBr) 2975, 2950 (C-H), 2225 (C≡N), 1765 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.34 (m, 16-, 17-H), 3.15 (m, 6-, 7-H), 3.02 (m, 3-, 5-, 8-, 10-H), 2.97 (m, 4a-, 9a-H), 2.53 (m, 13-, 15-, 18-, 20-H); ^{13}C NMR ($CDCl_3$) δ 206.8 (C=O), 118.2 (C≡N), 62.9 (C-1, -2, -11, -12), 58.5 (C-6, -7), 46.9 (C-16, -17), 46.8 (C-3, -5, -8, -10), 45.3 (C-13, -15, -18, -20), 40.6 (C-4, -9); MS (EI) *m/z* (rel intensity) 338 (M$^+$, 22), 282 (100), 191 (10). Anal. Calcd for $C_{22}H_{14}O_2N_2$ (338.4): C, 78.09; H, 4.17. Found: C, 78.08; H, 4.18.

14-Oxoundecacyclo[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 (19): colorless crystals, mp > 320 °C; IR (KBr) 2965 (C-H), 2230 (C≡N), 1760 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.97 (m, 6-, 7-H), 2.90 (m, 16-, 17-H), 2.90 (m, 9a-H), 2.85 (m, 3-, 5-H)*, 2.83 (m, 8-, 10-H)*, 2.81 (m, 4a-H), 2.71 (m, 13-, 15-H), 2.50 (m, 19s-H), 2.43 (m, 18-, 20-H), 1.63 (m, 19a-H); ^{13}C NMR ($CDCl_3$) δ 210.0 (C-14), 120.5 (C≡N), 118.5 (C≡N), 66.2, 60.0 (C-1, -2, -11, -12), 58.3 (C-6, -7), 52.1 (C-16, -17), 46.8 (C-3, -5)*, 46.3 (C-8, -10)*, 45.7 (C-18, -20), 43.2 (C-13, -15), 40.8 (C-9), 39.6 (C-4), 35.7 (C-19).

5-*anti*-Acetoxy-7,21-dioxo-6-azadodecacyclo[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 (20): colorless crystals, mp 265–267 °C (gas evolution); IR (KBr) 3305 (N-H), 2955 (C-H), 2250 (C≡N), 1760, 1635 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.40 (m, NH), 3.22 (m, 18-, 19-H), 3.18 (m, 10-, 14-H), 3.14 (m, 8-H), 3.02 (m, 11-, 13-H), 3.00 (m, 12-H), 2.93 (m, 4-, 17-H), 2.62 (m, 9-, 15-H), 2.57 (m, 20-, 22-H), 2.09 (s, CH_3); ^{13}C NMR ($CDCl_3$) δ 210.1 (C-21) 169.4 (C=O), 118.7 (C≡N), 99.2 (C-5), 62.5 (C-2, -13)*, 59.0 (C-1, -16)*, 61.8 (C-8), 59.1 (C-10, -14), 50.1 (C-18, -19), 49.1 (C-4, -17), 48.2 (C-11, -13), 46.2 (C-20, -22), 43.1 (C-9, -15), 41.4 (C-12), 21.1 (CH_3) C-7 not detectable; MS (EI) *m/z* (rel intensity) 398 (M$^+$, 60), 338 (100).

Dimethyl 2,12-Dibromo-14-*anti*,19-*anti*-dimethoxydecacyclo[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 (22). **23** (200 mg, 0.30 mmol) and PtO_2 (20 mg, 0.08 mmol) in dry CH_2Cl_2 (20 mL) were stirred under a H_2 atmosphere (1 atm) at ambient temperature to total conversion (6 h, TLC control). Filtration (silica gel, 2 cm, CH_2Cl_2/ethyl acetate 5:1) and concentration in vacuo gave **22** (170 mg, 95%): colorless crystals, mp 224–225 °C dec; IR (KBr) 2980 (C-H), 2940 (C-H), 1725 (C=O), 1240 (C-O), 1100 (C-O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (m, 14-H), 3.83 (s, OCH_3), 3.79 (s, OCH_3), 3.74 (m, 19-H), 3.72 (m, 3-, 5-H), 3.31 (m, 8-, 10-H), 3.28 (m, 13-, 15-H), 3.28 (m, 16-, 17-H), 3.25 (s, OCH_3), 3.21 (s, OCH_3), 3.00 (m, 6-, 7-H), 2.97 (m, 18-, 20-H), 2.65 (m, 9-H), 2.51 (t, 4-H); $J_{3,4} = J_{4,5} \simeq 5$ Hz; ^{13}C NMR ($CDCl_3$) δ 172.3 (CO_2CH_3), 171.9 (CO_2CH_3), 96.2 (C-2, -12), 85.8 (C-19), 84.3 (C-14), 77.6 (C-1, -11), 56.9 (OCH_3), 56.8 (C-13, -15), 56.6 (C-16, -17), 56.1 (OCH_3), 54.8 (C-6, -7), 54.1 (C-4), 52.2 (OCH_3), 52.1 (C-3, -5), 51.9 (OCH_3), 50.5 (C-9), 48.4 (C-18, -20), 47.4 (C-8, -10); MS (EI) *m/z* (rel intensity) 597, 595, 593 (M$^+$, 8), 565 (8), 517, 515 (100, 96), 485, 483 (26, 24), 436 (56).

Dimethyl 2,4-*anti*-12-Tribromo-14-*anti*,19-*anti*-dimethoxy-decacyclo[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 (23). A solution of **5** (250 mg, 0.57 mmol) and bromine (2 mL, 39.0 mmol) in dry CH_2Cl_2 (50 mL) was irradiated with a halogen lamp (150 W) (Duran) while being stirred in an immersion apparatus at −10 °C to total conversion (30 min, TLC control, CH_2Cl_2/ethyl acetate, 5:1). Concentration in vacuo and filtration over silica gel (3/20 cm) gave with CH_2Cl_2 in a first fraction remaining bromine and then with CH_2Cl_2/ethyl acetate (5:1) **23** (355 mg, 92%, R_f 0.82): mp 254–255 °C; IR (KBr) 2990 (C-H), 2820 (C-H), 1725 (C=O), 1240 (C-O), 1090 (C-O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.08 (dd, 3-H)*, J = 6.0

(72) Burgess, E. M.; Penton, Jr., H. R.; Taylor, E. A.; Williams, W. M. *Organic Syntheses*; 1977; Collect. Vol. VI, pp 788–791.

Hz, 3.95 (dd, 5-H)*, J = 6.0 Hz, 3.93 (s, OCH_3), 3.80 (s, OCH_3), 3.74 (m, 19-H), 3.70 (m, 14-H), 3.53 (m, 6-H)*, 3.48 (m, 7-H)*, 3.35 (m, 8-H)*, 3.33 (m, 10-H)*, 3.26 (m, 13-, 15-, 16-, 17-H), 3.25 (OCH_3), 3.21 (OCH_3), 2.94 (m, 18-H), 2.92 (m, 20-H), 2.69 (m, 9-H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 172.2 (CO_2CH_3), 169.4 (CO_2CH_3), 92.4 (C-2)*, 91.8 (C-12)*, 85.8 (C-19), 84.3 (C-14), 77.7 (C-1, -11), 74.8 (C-4), 60.9 (C-3)*, 60.8 (C-5)*, 58.9 (C-6)*, 57.6 (C-7)*, 56.9 (OCH_3), 56.7 (C-13)*, 56.4 (C-15)*, 56.0 (OCH_3), 54.9 (C-16)*, 54.8 (C-17)*, 53.4 (OCH_3), 52.0 (OCH_3), 50.3 (C-9), 48.0 (C-18)*, 47.9 (C-20)*, 47.0 (C-8)*, 46.9 (C-10)*; MS (EI) m/z (rel intensity) 675, 673 (M^+, <1), 597, 595 (22, 42), 501, 499 (72, 70), 436 (21), 421 (28), 420 (100).

Dimethyl 2,4-*anti*,9-*anti*,12-Tetrabromo-14-*anti*,19-*anti*-dimethoxydecacyclo[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 (Atropisomers) (24). A solution of **5** (250 mg, 0.57 mmol) and bromine (2 mL, 39.0 mmol) in dry CH_2Cl_2 (50 mL) was irradiated with a halogen lamp (150 W) (Duran) at −10 °C for 3 h (TLC control, CH_2Cl_2/ethyl acetate, 10:1). Workup analogous to **23** gave **24** (380 mg, 88%): mp 256–258 °C; IR (KBr) 2980 (C-H), 2940 (C-H), 1730 (C=O), 1240 (C-O), 1110 (C-O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.11 (m, 3-H)*, 4.01 (m, 5-H)*, 3.95 (s, OCH_3), 3.92 (m, 8-, 10-H), 3.89 (s, OCH_3), 3.73 (m, 19-H), 3.67 (m, 14-H), 3.56 (m, 6-H)*, 3.43 (m, 7-H)*, 3.25 (OCH_3), 3.24 (m, 13-, 15-, 16-, 17-H), 3.21 (OCH_3), 2.96 (m, 18-H)*, 2.91 m, 20-H)*; ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.4 (2 CO_2CH_3), 91.7, 91.2, 91.1, 90.6 (C-2, -12), 85.1 (C-19), 84.2 (C-14), 76.6, 76.3 (C-1, -11), 74.1 (C-4), 67.9 (C-9), 60.7 (C-3)*, 60.4 (C-5)*, 59.7 (C-8)*, 59.4 (C-10)*, 58.4, 57.1, 56.5, 56.3, 56.2, 56.1, 55.9, 55.0, 54.8, 54.6, 53.5, 53.3, 53.0, 52.9, 52.8 (10C), 48.0 (C-18)*, 47.9 (C-20)*; MS (EI) m/z (rel intensity) 675, 673 (M^+ − Br, 30), 579 (100), 500 (38), 420 (18), 404 (26), 391 (20), 359 (20), 299 (12), 226 (17), 165 (22), 115 (30), 96 (58), 94 (60).

Dimethyl 13-*anti*,18-*anti*-Dimethoxynonacyclo[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 (25). **22** (400 mg, 0.67 mmol) was converted and worked up analogously to **23**. Crystallization from CH_2Cl_2/ethyl acetate (1:1) gave **25** (270 mg, 92%): mp 209–210 °C; IR (KBr) 2970 (C-H), 2930 (C-H), 2810 (C-H), 1720 (C=O), 1610 (C=C), 1240 (C-O), 1205 (C-O), 1090 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.89 (m, 13-, 18-H), 3.79 (s, 2 OCH_3), 3.58 (m, 15-, 16-H), 3.47 (m, 2-, 4-, 7-, 9-H), 3.37 (m, 5-, 6-H), 3.25 (s, 2OCH_3), 3.12 (m, 12-, 14-, 17-, 19-H), 2.48 (t, 3-, 8-H, J = 4.0 Hz); ^{13}C NMR ($CDCl_3$) δ 173.7 (2CO_2CH_3), 154.5 (C-1, -10, -11, -20), 82.2 (C-13, -18), 59.3 (C-5, -6), 57.1 (2OCH_3), 55.7 (C-15, -16), 51.8 (2OCH_3), 50.5 (C-12, -14, -17, -19), 47.9 (C-3, -8), 45.4 (C-2, -4, -7, -9); MS (EI) m/z (rel intensity) 436 (M^+, 100), 405 (18), 376 (14).

1,4-Bromine Elimination from 23. **23** (350 mg, 0.52 mmol) was added under N_2 to a mixture of NaI (300 mg, 2.0 mmol), Na_2SO_3 (300 mg, 2.4 mmol), and Zn powder (900 mg, 13.8 mmol) in dry DMF (4 mL) preheated at 140 °C and stirred to decolorization of the initially brown solution (10 min). It was cooled to ambient temperature, diluted with CH_2Cl_2 (100 mL), washed with H_2O (4 × 50 mL), dried ($MgSO_4$), concentrated in vacuo, and purified by chromatography (silica gel, CH_2Cl_2/ethyl acetate, 5:1) to give **29** (190 mg, 87%, R_f 0.66) and **28** (17 mg, 8%, R_f 0.53).

Dimethyl 19-methoxy-14-oxoundecacyclo[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-*anti*-dicarboxylate (28): colorless crystals, mp 197–198 °C; IR (KBr) 2970 (C-H), 1755 (C=O), 1725 (C=O), 1230 (C-O), 1110 (C-O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.66 (s, OCH_3), 3.59 (s, OCH_3), 3.35 (m, 19-H), 3.22 (s, OCH_3), 3.13 (m, 16-, 17-H), 3.13 (m, 6-, 7-H), 2.96 (m, 4-H), 2.77 (m, 3-, 5-H), 2.71 (m, 9-H), 2.56 (m, 18-, 20-H)*, 2.52 (m, 8-, 10-H)*, 2.21 (m, 13-, 15-H); ^{13}C NMR ($CDCl_3$) δ 213.0 (C-13), 173.3 (CO_2CH_3), 172.9 (CO_2CH_3), 88.0 (C-19), 62.7 (1C), 59.9 (1C), 58.6 (2C), 58.0 (2C), 57.5 (1C), 56.9 (2C), 51.7 (2C), 51.0 (2C), 46.2 (2C), 45.4 (2C), 44.7 (2C), 44.6 (2C); MS (EI) m/z (rel intensity) 420 (M^+, 100), 392 (20).

Dimethyl 18-methoxy-13-oxononacyclo[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-*anti*,8-*syn*-dicarboxylate (29): colorless crystals, mp 226–227 °C; IR (KBr) 2960 (C-H), 1730 (C=O), 1620 (C=C), 1210 (C-O), 1080 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 18-H), 3.82 (s, OCH_3), 3.66 (s, OCH_3), 3.59 (m, 5-, 6-H), 3.59 (m, 7-, 9-H), 3.52 (m, 15-, 16-H), 3.49 (m, 3-H), 3.42 (m, 2-, 4-H), 3.42 (m, 17-, 19-H), 3.30 (s, OCH_3), 3.19 (m, 12-, 14-H), 2.53 (m, 8-H); ^{13}C NMR ($CDCl_3$) δ 213.7 (C-13), 174.3 (CO_2CH_3), 173.4 (CO_2CH_3), 158.4 (C-1, -11)*, 155.8 (C-10, -20)*, 79.2 (C-18), 60.4 (C-5, -6), 56.0 (OCH_3), 55.5 (C-12, -14), 52.7 (C-2, -4), 52.0 (OCH_3), 51.9 (OCH_3), 51.4 (C-15, -16), 48.7 (C-17, -19), 45.6 (C-7, -9), 45.6 (C-8), 45.3 (C-3); MS (EI) m/z (rel intensity) 420 (M^+, 100), 392 (20).

1,4-Bromine Elimination from 24. The conversion of **24** (350 mg, 0.46 mmol), analogously to **23**, after chromatography (silica gel, CH_2Cl_2/ethyl acetate, 5:1), gave **30** (95 mg, 51%), **29** (36 mg, 19%), and **28** (10 mg, 5%).

Dimethyl 13,18-dioxononacyclo[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-*anti*,8-*anti*-dicarboxylate (30): colorless crystals, mp 223–225 °C; IR (KBr) 2975 (C-H), 1730 (C=O), 1630 (C=C), 1180 (C-O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.78 (m, 5-, 6-H), 3.70 (m, 15-, 16-H), 3.66 (s, 2OCH_3), 3.58 (m, 2-, 4-, 7-, 9-H), 3.46 (s, 3-, 8-H), 3.37 (m, 12-, 14-, 17-, 19-H); ^{13}C NMR ($CDCl_3$) δ 207.6 (C-13, -18), 173.8 (2CO_2CH_3), 160.6 (C-1, -10, -11, -20), 61.7 (C-5, -6), 55.9 (C-12, -14, -17, -19), 52.2 (2OCH_3), 48.8 (C-2, -4, -7, -9), 47.2 (C-3, -8), 44.0 (C-15, -16); MS (EI) m/z (rel intensity) 404 (M^+, 72), 344 (34), 224 (34), 165 (60), 115 (100), 103 (48), 59 (58).

2,12-Dibromo-14-*anti*,19-*anti*-dimethoxydecacyclo[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-4,9-dione (31). A solution of **9** (250 mg, 0.72 mmol) and bromine (6 mL, 117 mmol) in dry CH_2Cl_2 (50 mL) was irradiated with intensive stirring in an immersion apparatus at −15 °C with a 150-W halogen lamp from the inside and a 300-W Osram Ultra-Vitalux lamp from the outside to a conversion of ca. 50% (ca. 3 h, NMR monitoring). After warming up to ambient temperature the solution was concentrated to ca. 5 mL and purified by chromatography (silica gel). Elution with CH_2Cl_2 gave an excess of bromine, with CH_2Cl_2/ethyl acetate (10:1) pure **31** (190 mg, 52%) and with CH_2Cl_2/ethyl acetate (1:1) remaining **9** (110 mg, 44%). **31**: mp 252–253 °C; IR (KBr) 2990 (C-H), 2930 (C-H), 1770 (C=O), 1730 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.31 (m, 14-H), 4.07 (m, 19-H), 3.51 (m, 16-, 17-H), 3.47 (m, 3-, 5-H), 3.40 (m, 6-, 7-H), 3.35 (m, 13-, 15-H), 3.33 (s, OCH_3), 3.29 (s, OCH_3), 3.14 (m, 18-, 20-H), 2.97 (m, 8-, 10-H); ^{13}C NMR ($CDCl_3$) δ 207.9 and 206.9 (C-4, -9), 89.4 (C-2, -12), 84.6 (C-19), 83.4 (C-14), 76.5 (C-1, -11), 60.5 (C-3, -5), 57.2 (OCH_3), 56.6 (OCH_3), 56.9 (C-16, -17), 56.8 (C-13, -15), 49.2 (C-8, -10), 48.0 (C-18, -20); MS (EI) m/z (rel intensity) 429, 427 (M^+−Br, 18), 348 (38), 145 (32), 115 (34), 103 (26), 75 (100), 57 (46).

13-*anti*,18-*anti*-Dimethoxynonacyclo[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-3,8-dione (32). **31** (190 mg, 0.37 mmol) was added under N_2 to a mixture of NaI (225 mg, 1.5 mmol), Na_2SO_3 (235 mg, 1.9 mmol), and Zn powder (710 mg, 10.9 mmol) in dry DMF (3 mL) preheated at 140 °C and stirred to decolorization of the initially deep brown mixture 10 min. After cooling to ambient temperature the mixture was diluted with CH_2Cl_2 (50 mL), washed with water (5 × 20 mL), dried ($MgSO_4$), concentrated in vacuo, and purified by chromatography (silica gel, CH_2Cl_2/ether 2:1) to give **32** (112 mg, 87%, R_f 0.65) and **9** (6 mg, 5%). **32**: mp 276–277 °C; IR (KBr) 2960 (C-H), 2920 (C-H), 1720 (C=O), 1100 (C-O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.34 (s, 13-, 18-H), 3.80 (m, 15-, 16-H)*, 3.74 (m, 5-, 6-H)*, 3.33 (s, 2OCH_3), 3.26–3.32 (m, 2-, 4-, 7-, 9-, 12-, 14-, 17-, 19-H); MS (EI) m/z (rel intensity) 348 (M^+, 54), 292 (18), 115 (30), 103 (28), 75 (100).

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 (34). A solution of **18** (418 mg, 1.24 mmol) and $NaBH_4$ (200 mg, 5.3 mmol) in ethanol (20 mL) was stirred at ambient temperature for 30 min. Hydrolysis with NH_4Cl solution, concentration in vacuo, and continuous extraction with CH_2Cl_2/water gave crystalline **34** (405 mg, 96%): mp 294 °C; IR (KBr) 3340 (O-H), 2965, 2920 (C-H), 2225 (C≡N) cm^{-1}; ^1H NMR ($CDCl_3$/[D_6]DMSO 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 ([D_6]DMSO) δ 120.5 (C≡N), 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*-Dimethoxyundecacyclo[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 35. To a solution of **34** (100 mg, 0.29 mmol) in THF (5 mL) was added NaH (28 mg, 12 mmol) and methyl iodide (0.5 mL), and the mixture was stirred at ambient temperature for 14 h. Hydrolysis with water and extraction with CH_2Cl_2 gave **35** (104 mg, 96%): colorless crystals, mp 279–280 °C; IR (KBr) 2960, 2850, 2820 (C-H), 2220 (C≡N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.79 (m, 14a-, 19a-H), 3.28 (s, 2OCH_3), 2.99 (s, 4a-, 9a-H), 2.87 (m, 6-, 7-H), 2.77 (m, 3-, 5-, 8-, 10-H), 2.63 (m, 16-, 17-H), 2.49 (m, 13-, 15-, 18-, 20-H). Anal. Calcd for $C_{22}H_{22}O_2N_2$ (370.5): C, 77.81; H, 5.99. Found: C, 77.73; H, 6.00.

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-*anti*,9-*anti*-dicarbonitrile (37). A solution of **18** (179 mg, 0.53 mmol) and $NaBH_4$ (80 mg, 2.1 mmol) in ethanol (6 mL) was stirred at ambient temperature in a glass bomb tube for 2 h and then concentrated in vacuo. The solid was removed mechanically from the glass walls, then *tert*-butyl alcohol (5 mL) and sodium *tert*-butylate (50 mg) were added, and the mixture was heated to 160 °C for 2 h. Continuous extraction with CH_2Cl_2/water gave crystalline **37** (181 mg, 98%): mp > 320 °C; IR (KBr) 3390 (O-H), 2960 (C-H), 2235 (C≡N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.25 (m, 14a-, 19a-H), 3.97 (m, 4s-, 9s-H), 3.58 (m, 6-, 7-H), 2.73 (m, 3-, 5-, 8-, 10-H), 2.66

(m, 16-, 17-H), 2.66 (m, 13-, 15-, 18-, 20-H), 1.75 (brs, 2OH). Anal. Calcd for $C_{22}H_{18}O_2N_2$ (342.4): C, 77.18; H, 5.30. Found: C, 76.49; H, 5.35.

14-*syn*,19-*syn*-Dimethoxyundecacyclo[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-*anti*,9-*anti*-dicarbonitrile (38). A solution of **35** (10 mg, 0.03 mmol) in *tert*-butyl alcohol (3 mL) was heated with sodium *tert*-butylate (5 mg) in a glass bomb tube to 130 °C for 10 min. Filtration over a short pad of silica gel (CH_2Cl_2/ethyl acetate 10:1) gave pure (^{1}H NMR) **38**.

To a solution of **37** (100 mg, 0.29 mmol) in THF (5 mL) were added NaH (28 mg, 12 mmol) and methyl iodide (0.5 mL), and the mixture was stirred at ambient temperature for 14 h. Hydrolysis with water and extraction with CH_2Cl_2 gave crystalline **38** (108 mg, 100%): mp 232–235 °C; IR (KBr) 2950, 2810 (C-H), 2230 (C≡N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.74 (m, 14a-, 19a-H), 3.67 (m, 4s-, 9s-H), 3.55 (m, 6-, 7-H), 3.22 (s, 2OCH_3), 2.68 (m, 3-, 5-, 8-, 10-H), 2.62 (m, 16-, 17-H), 2.40 (m, 13-, 15-, 18-, 20-H); ^{13}C NMR ($CDCl_3$) δ 121.4 (C≡N), 90.8 (C-14, -19), 63.6 (C-1, -2, -11, -12), 57.4 (C-6, -7)*, 56.9 (2OCH_3), 50.2 (C-16-, -17)*, 46.3 (C-13, -15, -18, -20)*, 44.9 (C-3, -5, -8, -10), 41.8 (C-4, -9); MS (EI) m/z (rel intensity) 370 (M$^+$, 100), 339 (24).

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-*anti*,9-*anti*-dicarbonitrile (33). To a suspension of **37** (30 mg, 0.09 mmol) in CH_2Cl_2 (3 mL) was added pyridinium chlorochromte (100 mg). After standing at ambient temperature for 24 h it was filtered over a short pad of silica gel (CH_2Cl_2/ethyl acetate 2:1) to give **33** (18 mg, 60%): mp > 320 °C; IR (KBr) 2970, 2920 (C-H), 2230 (C≡N), 1765 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.77 (m, 6-, 7-H), 3.38 (m, 16-, 17-H), 3.00 (m, 3-, 5-, 8-, 10-H), 2.75 (brs, 4s-, 9s-H), 2.40 (m, 13-, 15-, 18-, 20-H). Anal. Calcd for $C_{22}H_{14}O_2$ (338.4): C, 78.09; H, 4.17. Found: C, 78.27; H, 4.20.

2,12-Dibromo-19-*syn*-methoxy-14-oxodecacyclo[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-*anti*,9-*anti*-dicarbonitrile (41). A solution of **38** (50 mg, 0.13 mmol) in CH_2Cl_2/CH_3CN (10:1, 1 mL) was irradiated with bromine (0.1 mL) at 15 °C for 30 min (TLC control). Concentration in vacuo and crystallization from CH_2Cl_2/ether gave **41** (59 mg, 85%): mp 232–235 °C dec; IR (KBr) 2920 (C-H), 2235 (C≡N), 1730 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.23 (m, 9s-H), 3.83 (m, 4s-H), 3.78 (m, 6-, 7-H), 3.72 (m, 19a-H), 3.63 (m, 3-, 5-H), 3.46 (s, OCH_3), 3.37 (m, 8-, 10-, 13-, 15-H), 3.20 (m, 18-, 20-H), 3.08 (m, 16-, 17-H); ^{13}C NMR ($CDCl_3$) δ 208.1 (C=O), 119.3 (C≡N), 118.4 (C≡N), 88.3 (C-2, -12), 83.2 (C-19), 79.4 (C-1, -11), 60.0 (C-13, -15), 57.6 (OCH_3), 57.4 (C-6, -7), 55.8 (C-3, -5), 49.6 (C-18, -20), 49.0 (C-8, -10), 47.2 (C-16, -17), 37.7 (C-4), 35.5 (C-9); MS (EI) m/z (rel intensity) 515, 513 (M$^+$, 6), 435, 433 (76), 354 (100).

18-*syn*-Methoxy-13-oxononacyclo[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-*anti*,8-*anti*-dicarbonitrile (42). **41** (152 mg, 0.30 mmol) was added under N_2 to a boiling suspension of Zn powder (77 mg, 1.2 mmol), NaI (177 mg, 1.2 mmol), and Na_2SO_3 (149 mg, 1.2 mmol) in DMF (5 mL). After 3 min (decolorization) it was cooled, diluted with CH_2Cl_2, and extracted with CH_2Cl_2/water. The organic phase was concentrated in vacuo and filtered over a short pad of silica gel (CH_2Cl_2/ethyl acetate 2:1) to give crystalline **42** (100 mg, 95%): mp 235 °C; IR (KBr) 2980, 2940 (C-H), 2230 (C≡N), 1725 (C=O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$/C_6D_6, 1:1) δ 5.08 (m, 8s-H), 3.81 (m, 5-, 6-H), 3.51 (m, 3s-H), 3.02 (s, OCH_3), 3.01 (m, 2-, 4-, 7-, 9-H), 2.92 (m, 17-, 19-, 18a-H), 2.80 (m, 15-, 16-H), 2.74 (m, 12-, 14-H); ^{13}C NMR ($CDCl_3$/C_6D_6, 1:1) δ 211.4 (C=O), 158.3 (C-1, -11)*, 157.3 (C-10, -20)*, 122.1 (C≡N), 120.5 (C≡N), 79.9 (C-18), 60.3 (C-5, -6), 57.5 (OCH_3), 54.7 (C-12, -14), 50.6 (C-2, -4), 49.1 (C-7, -9), 48.8 (C-15, -16), 48.0 (C-17, -19), 33.8 (C-3), 31.6 (C-8). Anal. Calcd for $C_{23}H_{18}O_2N_2$ (354.4): C, 77.95; H, 5.12. Found: C, 77.60; H, 5.09.

Bromination of 7. (a) A solution of **7** (0.8 g, 1.98 mmol) and bromine (46.8 g, 292.9 mmol) in dry CH_2Cl_2 (50 mL) and dry acetonitrile (2 mL) was irradiated in an immersion apparatus with intensive stirring at −15 °C with a 150-W halogen lamp from the inside and with a 300-W Osram Ultra-Vitalux lamp from the outside to ca. 60% conversion (NMR monitoring, 4 h). The solution was warmed to ambient temperature, concentrated to ca. 10 mL, and purified by chromatography (silica gel, 3/20 cm). Elution with CH_2Cl_2 gave remaining bromine, with CH_2Cl_2/ethyl acetate (10:1) nearly pure tribromide **44** (0.75 g, 59%), and with CH_2Cl_2/ethyl acetate (2:1) starting material **7** (0.30 g, 38%). Crystallization from ethyl acetate gave pure **44** (0.73 g, 92%, based on conversion).

(b) A solution of **7** (0.5 g, 1.24 mmol) and bromine (60.0 g, 750.85 mmol) in dry CH_2Cl_2 (100 mL) was irradiated with a 300-W lamp and heated to reflux to total conversion (DC control). Concentration in vacuo and chromatography (silica gel, 3/30 cm, CH_2Cl_2/ethyl acetate 10:1) gave besides **48a** and **49** (2–3%) tetrabromide **45** (250 mg, 28%), tribromide **44** (360 mg, 45%), and a mixture of **44** and **45** (160 mg, ca. 15%).

Dimethyl 2,4-*anti*,12-tribromo-14,19-dioxodecacyclo[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*,4-*syn*-dicarboxylate (44): colorless crystals, mp 219–220 °C; IR (KBr) 2995 (C-H), 2950 (C-H), 1770 (C=O), 1730 (C=O), 1250 (C-O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) Figure 1; ^{13}C NMR ($CDCl_3$) Figure 1; MS (EI) m/z (rel intensity) 643 (M$^+$, 1), 611, 613 (2), 563 (100), 484 (50), 343 (36), 227 (38).

Dimethyl 2,4-*anti*,9-*anti*,12-tetrabromo-14,19-dioxodecacyclo[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 (45): colorless crystals, mp 204–206 °C; IR (KBr) 2990 (C-H), 2800 (C-H), 1770 (C=O), 1730 (C=O), 1250 (C-O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (m, 3-H)*, 4.09 (m, 5-H)*, 4.09 (m, 6-H)*, 4.03 (m, 7-H)*, 3.90 (s, OCH_3), 3.83 (s, OCH_3), 3.69 (m, 8-H, 10-H), 3.47 (m, 13-H)*, 3.40 (m, 15-H)*, 3.18 (m, 16-, 17-H), 2.95 (m, 18-, 20-H); ^{13}C NMR ($CDCl_3$) δ 204.7 (C-14)*, 201.9 (C-19)*, 168.1 (CO_2CH_3), 167.8 (CO_2CH_3), 87.3 (C-2)*, 86.8 (C-12)*, 76.9 (C-1, -11), 69.9 (C-4), 64.6 (C-9), 60.4 (C-3)*, 60.1 (C-5)*, 60.0 (C-6)*, 59.4 (C-13)*, 59.1 (C-15)*, 58.5 (C-7)*, 54.4 (OCH_3), 54.0 (OCH_3), 53.0 (C-8, -10), 48.9 (C-18, -20), 44.0 (C-16)*, 43.8 (C-17)*; MS (EI) m/z (rel intensity) 719, 721, 723 (M$^+$, 2), 643, 641 (100), 562 (40), 226 (98).

1,4-Bromine Elimination from 44 and 48a. (a) **44** (300 mg, 0.47 mmol) was added under N_2 to a mixture of NaI (300 mg, 2.0 mmol), Na_2SO_3 (300 mg, 2.4 mmol), and Zn powder (900 mg, 13.8 mmol) in dry DMF (4 mL) at 150 °C and stirred for 15 min. After cooling to ambient temperature, the mixture was diluted with CH_2Cl_2 (100 mL), washed with water (4 × 50 mL), dried, and concentrated in vacuo. The remaining mixture (160 mg, 85%) was separated by chromatography (silica gel, CH_2Cl_2/ethyl acetate, 2:1) to give **47** (8 mg, 5%, R_f 0.77) and crystalline **46** (105 mg, 54%, R_f 0.58). **50a** (ca. 20%; R_f 0.42), detected in the raw mixture by ^{1}H NMR, had been converted to **46** on silica gel.

(b) **48a** (1.1 g, 1.95 mmol) was added under N_2 to Zn powder (5.0 g, 60.0 mmol) in dry DMF (30 mL) at 120 °C and stirred for 2 h. After cooling to ambient temperature, the mixture was diluted with dry CH_2Cl_2 (200 mL) and filtrated over kieselguhr (3 cm). Concentration in vacuo gave a crystalline mixture of **46** and **50a** (2:1, 756 mg, 96%).

(c) After cooling to room temperature, the mixture from (b) was diluted with CH_2Cl_2 (200 mL) and washed with water (4 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo. Crystallization from CH_2Cl_2/ethyl acetate gave pure **46** (650 mg, 83%). Chromatography of the mother liquor (silica gel, CH_2Cl_2/ethyl acetate 2:1) gave additional **46** (55 mg, 7%).

Dimethyl 13,18-dioxononacyclo[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 (46): colorless crystals, mp > 320 °C; **46** is very soluble in CH_2Cl_2 and $CHCl_3$, but only sparingly in DMF and THF (ca. 5 mg/mL); IR (KBr) 2940 (C-H), 1740 (C=O), 1630 (C=C?), 1250 (C-O) cm^{-1}; UV (CH_3CN) $\lambda_{max}(\epsilon)$ 314 sh (60), 270 sh (90), 216 (1300); ^{1}H NMR (400 MHz, $CDCl_3$) Figure 1; ^{13}C NMR ($CDCl_3$) Figure 1; MS (EI) m/z (rel intensity) 404 (M$^+$, 56), 348 (100), 285 (9), 229 (22), 165 (32), 115 (26).

After addition of Br_2 to a $CDCl_3$ solution of **46**, only **44** is observed by TLC and ^{1}H NMR. Irradiation of **46** in a 10^{-2} M acetone solution with a high-pressure Hg lamp in Pyrex vessel led quantitatively to **9**.

Dimethyl 13,18-dioxononacyclo[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-*anti*-dicarboxylate (47): colorless crystals, mp 196–198 °C; IR (KBr) 2940 (C-H), 1730 (C=O), 1620 (C=C?), 1245 (C-O), 1200 (C-O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, OCH_3), 3.69 (s, OCH_3), 3.69 (m, 5-, 6-H), 3.69 (m, 2-, 4-H), 3.64 (m, 15-, 16-H), 3.56 (m, 7-, 9-H), 3.49 (m, 8-H), 3.36 (m, 17-, 19-H), 3.31 (m, 12-, 14-H), 2.68 (m, 3-H); ^{13}C NMR ($CDCl_3$) δ 211.1 (C-18), 208.0 (C-13), 174.0 (CO_2CH_3), 171.9 (CO_2CH_3), 161.5 (C-1, -11), 159.5 (C-10, -20), 60.9 (C-5, -6), 55.9 (C-17, -19), 55.3 (C-12, -14), 52.7 (OCH_3), 52.1 (OCH_3), 48.7 (C-7, -9), 46.0 (C-15, -16), 45.8 (C-2, -4), 45.7 (C-3), 43.9 (C-8); MS (EI) m/z (rel intensity) 404 (M$^+$, 50), 348 (100), 165 (30).

Dimethyl 3,14-Dibromo-6-hydroxy-10-oxoundecacyclo[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 (48a). **44** (1.2 g, 1.87 mmol) and PtO_2 (0.1 g, 0.44 mmol) in dry CH_2Cl_2 (100 mL) were stirred in a H_2 atmosphere at ambient temperature to total conversion (ca. 16 h, TLC control). Filtration (silica gel, 2 cm, CH_2Cl_2/ethyl acetate 4:1) and concentration in vacuo gave **48a** (1.0 g, 95%): colorless crystals, mp 265–267 °C; IR (KBr) 3480 (O-H), 2980 (C-H), 1810 (C=O), 1765 (C=O), 1725 (C=O), 1690 (C=O), 1245 (C-O) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) Figure 2; ^{13}C NMR ($CDCl_3$) Figure 2; MS (EI) m/z (rel intensity) 564 (M$^+$, 8), 532 (8), 485 (98), 483 (100), 453 (80), 451 (78), 421 (40), 419 (35), 372 (60), 343 (25).

Dimethyl 3,14-Dibromo-6-[(trimethylsilyl)oxy]-10-oxoundecacyclo[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 (48b). A solution of **48a** (170 mg, 0.3 mmol) and chlorotrimethylsilane (3.26 g, 30.0 mmol) in CH_2Cl_2 (10 mL) and pyridine (4

mL) was stirred under N_2 at ambient temperature for 3 h. Concentration in vacuo and filtration (silica gel, 2 cm, CH_2Cl_2) gave **48b** (185 mg, 97%): colorless crystals, mp 207–208 °C; IR (KBr) 2945 (C-H), 1770 (C=O), 1730 (C=O), 1240 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.83 (m, 4-, 15-H), 3.76 (s, OCH_3), 3.68 (s, OCH_3), 3.57 (m, 18-, 20-H), 3.56 (m, 8-, 12-H), 3.34 (m, 16-, 17-H), 3.27 (m, 7-, 13-H), 3.03 (m, 9-, 11-H), 2.74 (m, 19-H), 0.14 (s, $Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 210.6 (C-10), 171.2 (CO_2CH_3), 170.6 (CO_2CH_3), 112.5 (C-6), 94.6 (C-3, -14), 86.9 (C-5), 80.7 (C-1, -2), 69.0 (C-7, -13), 61.1 (C-4, -15), 60.7 (C-16, -17), 55.2 (C-8, -12), 52.4 (OCH_3), 52.3 (OCH_3), 51.5 (C-9, -11), 51.2 (C-18, -20), 49.7 (C-19), 1.4 ($Si(CH_3)_3$); MS (EI) *m/z* (rel intensity) 636 (M^+, 3), 621 (14), 557 (8), 525 (6), 461 (6), 270 (20), 73 (100); MS (DCI, NH_3) *m/z* (rel intensity) 654 (M^+ + 18, 12), 494 (6), 90 (100).

Dimethyl 3,14,19-*anti*-Tribromo-6-hydroxy-10-oxoundecacyclo[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 (49). **45** (100 mg, 0.14 mmol) was converted analogously to **44**. Filtration (silica gel, CH_2Cl_2/ethyl acetate, 4:1) and concentration in vacuo gave exclusively (TLC) **49** (82 mg, 92%): colorless crystals, mp 208–210 °C; IR (KBr) 3450 (O-H), 2950 (C-H), 1770 (C=O), 1730 (C=O), 1240 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, OCH_3), 3.79 (s, OCH_3), 3.79 (m, 16-, 17-H), 3.77 (m, 18-, 20-H), 3.68 (m, 4-, 15-H), 3.59 (m, 8-, 12-H), 3.23 (m, 7-, 13-H), 2.99 (m, 9-, 11-H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 210 (C-10), 172.7 (CO_2CH_3), 168.0 (CO_2CH_3), 109.6 (C-6), 92.1 (C-3, -14), 83.4 (C-5), 79.7 (C-1, -2), 69.5 (C-7, -13), 64.7 (C-19), 62.3 (C-16, -17), 61.8 (C-4, -15), 56.9 (C-18, -20), 55.5 (C-8, -12), 53.8 (OCH_3), 53.2 (OCH_3), 51.2 (C-9, -11); MS (EI) *m/z* (rel intensity) 646, 644, 642, 640 (M^+, 5), 614, 612, 610, 608 (18), 563 (100), 531 (80), 499 (40), 471 (46), 226 (98), 113 (98).

Dimethyl 19-Oxo-10-[(trimethylsilyl)oxy]decacyclo[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 (50b). **48b** (150 mg, 0.24 mmol) was added under N_2 to a suspension of Zn powder (1.5 g, 22.94 mmol) in dry DMF (10 mL) at 120 °C, and the mixture was stirred to total conversion (1 h). Dilution with dry CH_2Cl_2 (100 mL), filtration over kieselguhr (1 cm), and concentration in vacuo gave crystalline, nearly pure **50b** (105 mg, 92%). For analytical purposes it was crystallized from CH_2Cl_2: mp 180–181 °C; IR (KBr) 2950 (C-H), 1740 (C=O), 1240 (C-O), 1220 (C-O) cm^{-1}; UV (CH_3CN) $\lambda_{max}(\epsilon)$ = 270 sh (240), 261 sh (280), 250 sh (420); ^1H NMR (400 MHz, $CDCl_3$) Figure 2; ^{13}C NMR ($CDCl_3$) Figure 2; MS (EI) *m/z* (rel intensity) 476 (M^+, 58), 461 (90), 372 (25), 224 (20), 73 (100).

Dimethyl 13,18-Dioxononacyclo[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 (60). To a solution of **46** (720 mg, 1.78 mmol) in CH_2Cl_2 (350 mL) was added finely powdered potassium azodicarboxylate (18.0 g, 92.57 mmol). Then with vigorous stirring at 0 °C a solution of acetic acid (11.1 g, 185.14 mmol) in methanol (60 mL) was added dropwise within 6 h. Stirring was continued at ambient temperature until the yellow color of the azo compound had disappeared (12 h). Addition of water (100 mL), separation of the phases, extraction of the aqueous phase with CH_2Cl_2 (4 × 50 mL), washing of the combined organic phases with saturated $NaHCO_3$ solution, drying ($MgSO_4$), and concentration in vacuo gave **60** (635 mg, 88%) consisting of colorless crystals, which were used directly for the following reaction. From CH_2Cl_2/ethyl acetate pure **60**: mp 261–263 °C; IR (KBr) 2950 (C-H), 1726 (C=O), 1620 (C=C?), 1250 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.88 (m, 10-, 11-H), 3.76 (s, $2OCH_3$), 3.53 (m, 2-, 7-H), 3.28 (m, 14-, 19-H), 3.13–2.96 (series of m, 8 H), 2.84 (m, 12-, 17-H); ^{13}C NMR ($CDCl_3$) δ 214.3 (C-13, -18), 172.3 ($2CO_2CH_3$), 151.8 (C-1, -20), 60.3 (C-5)*, 59.5 (C-10, -11), 58.9 (C-6)*, 55.6 (C-14, -19), 54.9 (C-12, -17), 54.1 (C-4, -9), 52.6 ($2OCH_3$), 46.7 (C-16)*, 44.9 (C-2, -7), 44.0 (C-3, -8), 42.5 (C-15)*; MS (EI) (rel intensity) 406 (M^+, 40), 378 (40), 350 (100), 318 (30), 290 (20), 231 (30), 215 (25), 167 (50), 165 (80), 115 (70).

Dimethyl 13,18-Dioxo-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 (61). To a solution of **46** (50 mg, 0.12 mmol) in CH_2Cl_2 (5 mL) was added dropwise a solution of *m*-chloroperbenzoic acid (100 mg, 85%, 0.50 mmol pure peracid) in the same solvent (2 mL). After 15 min at ambient temperature the mixture was extracted twice with aqueous Na_2SO_3 and twice with saturated $NaHCO_3$ solution, dried ($MgSO_4$), and filtered over silica gel (CH_2Cl_2/ethyl acetate, 2:1). Crystallization from CH_2Cl_2 gave **61** (49 mg, 95%): colorless crystals, mp 279–280 °C; IR (KBr) 2945 (C-H), 1725 (C=O), 1255 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, $2OCH_3$), 3.65 (m, 4-, 9-H), 3.41 (m, 12-, 17-H), 3.26 (m, 5-H), 3.10 (m, 16-H), 3.08 (m, 3-, 8-H), 3.01 (m, 2-, 7-H), 2.93–3.00 (m, 6-, 15-H), 2.76 (m, 14-, 19-H); ^1H NMR (400 MHz, $CDCl_3/C_6D_6$, 1:1) δ 3.65 ($2OCH_3$), 3.32 (m, 4-, 9-H), 3.13 (m, 12-, 17-H), 2.79 (m, 2-, 7-H), 2.70 (m, 5-H), 2.62 (m, 14-, 19-H), 2.57 (m, 3-, 8-H), 2.57 (m, 6-H), 2.53 (m, 16-H), 2.45 (m, 15-H); ^{13}C NMR ($CDCl_3$) δ 207.5 (C-13, -18), 171.2 ($2CO_2CH_3$), 155.5 (C-10, -11), 87.9 (C-1, -20), 62.8 (C-6), 58.1 (C-5), 55.4 (C-12, -17), 54.3 (C-3, -8), 52.8 ($2OCH_3$), 52.6 (C-14, -19), 48.0 (C-15), 45.4 (C-4, -9), 44.6 (C-2, -7), 43.1 (C-16); ^{13}C NMR ($CDCl_3/C_6D_6$, 1:1) δ 207.1 (C-13, -18), 171.0 ($2CO_2CH_3$), 155.4 (C-10, -11), 87.8 (C-1, -20), 62.8 (C-6), 57.9 (C-5), 55.3 (C-12, -17), 54.1 (C-3, -8), 52.7 (C-14, -19), 52.5 ($2OCH_3$), 48.0 (C-15), 45.3 (C-4, -9), 44.6 (C-2, -7), 42.9 (C-16); MS (EI) *m/z* (rel intensity) 420 (M^+, 100), 392 (66), 364 (96), 245 (22), 202 (30), 153 (48).

Dimethyl 14,19-Dioxo-11,22-dioxaundecacyclo[14.7.0.0^{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 (63). (a) A solution of **61** (10 mg, 0.02 mmol) and *m*-chloroperbenzoic acid (20 mg, 85%, 0.1 mmol pure peracid) in $CDCl_3$ (0.5 mL) was heated in a NMR tube to 80 °C for 30 min. ^1H NMR control showed complete and nearly uniform conversion to **63**. Workup analogously to (b).

(b) A solution of **46** (100 mg, 0.25 mmol) and *m*-chloroperbenzoic acid (500 mg, 85%, 2.45 mmol) in $CHCl_3$ (10 mL) was heated to reflux to total conversion (4 h, TLC control, SiO_2, CH_2Cl_2/ethyl acetate; 2:1, R_f(**63**) 0.55). After cooling to ambient temperature the mixture was diluted with CH_2Cl_2 (20 mL), washed repeatedly with aqueous Na_2SO_3 (2 × 10 mL) and saturated $NaHCO_3$ solution (2 × 10 mL), and dried ($MgSO_4$). The raw material (100 mg, 92%) was used directly for the following reaction. For analytical purposes **63** was crystallized from CH_2Cl_2/ethyl acetate, 1:2, mp 274–275 °C; IR (KBr) 2950 (C-H), 2850 (C-H), 1732 (C=O), 1260 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, $2OCH_3$), 3.14 (m, 5-, 6-H), 3.11 (m, 2-, 4-, 7-, 9-H), 3.02 (m, 16-, 17-H), 2.93 (m, 13-, 15-, 18-, 20-H), 2.93 (t, 3-, 8-H, J = 5.8 Hz); ^{13}C NMR ($CDCl_3$) δ 204.7 (C-14, -19), 170.6 ($2CO_2CH_3$), 85.1 (C-1, -10, -12, -21), 63.1 (C-5, -6), 53.7 (C-13, -15, -18, -20), 52.9 ($2OCH_3$), 50.0 (C-3, -8), 48.8 (C-16, -17), 44.7 (C-2, -4, -7, -9); MS (EI) *m/z* (rel intensity) 436 (M^+, 51), 406 (25), 405 (27), 376 (100), 348 (29).

Dimethyl 19-Oxo-10-hydroxydecacyclo[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 (66). (a) A solution of **60** (5 mg, 0.012 mmol) in $CDCl_3$ (1 mL) with silica gel (50 mg) was treated in a NMR tube at ambient temperature with ultrasound. ^1H (^{13}C) NMR control showed slow but uniform cyclization to **66**. After 5 days ca. 80% of **60** were converted.

(b) A solution of **60** (50 mg, 0.12 mmol) in CH_2Cl_2 (20 mL) was stirred with silica gel (500 mg) under N_2 at ambient temperature for 5 days (TLC control). Filtration, followed by thorough elution with CH_2Cl_2/ethyl acetate and then concentrated of the filtrate in vacuo, gave a solid residue which was purified by chromatography (silica gel, CH_2Cl_2/ethyl acetate, 1:1). The first fraction (R_f 0.55) gave **60** (9 mg, 18%), the second (R_f 0.42) crystalline **66** (38 mg, 76%): mp 208–210 °C; IR (KBr) 2940 (C-H), 1725 (C=O), 1220 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.83–3.14 (series of m, 14 H), 3.77 (s, OCH_3), 3.74 (s, OCH_3), 2.92 (t, 15-H, J = 6.0 Hz), 2.79 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 217.8 (C-19), 175.1 (CO_2CH_3), 172.4 (CO_2CH_3), 163.4 (C-4), 145.2 (C-17), 111.9 (C-10), 86.5, 71.3, 65.9, 65.4, 63.5, 63.2, 61.4, 59.9, 58.5, 57.4, 57.1, 56.0, 55.1, 52.4, 51.6, 50.8, 48.6 (18C); MS (EI) *m/z* (rel intensity) 406 (M^+, 58), 374 (100), 342 (64), 330 (74), 286 (56), 165 (84), 115 (96).

Dimethyl 11,16-Dihydroxyundecacyclo[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 (67). (a) **66** (20 mg, 0.05 mmol) (dried by heating in vacuo) was partially dissolved in dry [D_8]THF (0.5 mL) in an inert atmosphere by slight warming in an NMR tube (NMR control). After addition of sodium hydride (5 mg, 0.20 mmol), gas evolution began, and the mixture became nearly homogeneous by treating with ultrasound. In case the reaction did not begin (no gas evolution), it could be initiated by addition of a drop of wet [D_8]THF against a stream of N_2. After complete conversion (ca. 15 min) the homogeneous sample (excess of NaH settled at the bottom) was analyzed by NMR.

(b) A suspension of sodium hydride (12 mg, 80% in mineral oil, 0.40 mmol) under N_2 was washed with dry hexane in a 5-mL Schlenk tube with glass filter and dried in vacuo. After the addition of dry THF (2 mL) with bubbling N_2 through, finely powdered **60** (50 mg, 0.12 mmol) was added. In the case of no spontaneous gas evolution, the reaction could be started by addition of wet THF (1–2 drops). After complete conversion (TLC control, silica gel, CH_2Cl_2/ethyl acetate, 2:1; R_f(**60**) 0.65, R_f(**67**) 0.22) the mixture was diluted with dry benzene (2 mL), and an excess of sodium hydride was filtered off. Concentration in vacuo gave nearly pure, crystalline **67**, which was used directly for analytical purposes and for the following reactions: IR (KBr) 3480 (O-H), 2940 (C-H), 1695 (C=O), 1430, 1320, 1290, 1220, 1040, 910 cm^{-1}; ^1H NMR (400 MHz, [D_8]THF) Figure 3; $J_{3,4} = J_{4,5} = J_{5,18} = J_{12,13} = J_{13,14} = J_{13,17}$ = 11.5 Hz; $J_{2,3} = J_{3,7} = J_{10,14} = J_{14,15}$ = 6.5 Hz; ^{13}C NMR ([D_8]THF) Figure 3; MS (EI) *m/z* (rel intensity) 406 (M^+, 10), 390 (21), 378 (26), 348 (94), 330 (74), 314 (35), 302 (49), 272 (58), 254 (18).

Dimethyl 10-Hydroxy-19-oxodecacyclo[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 (68). A solution of **66** (35 mg, 0.08 mmol) in dry methanol (10 mL) was stirred with Pd/C (5%, 10 mg) under a H_2 atmosphere (atmospheric pressure) at ambient temperature for 2 h. Filtration and concentration in vacuo gave **68** (35 mg, quantitative): colorless crystals, mp 259–260 °C; IR (KBr) 3460 (O-H), 2950 (C-H), 1725 (C=O), 1260 (C-O), 1220 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) Figure 2; ^{13}C NMR ($CDCl_3$) Figure 2; MS (EI) *m/z* (rel intensity) 408 (M^+, 16), 390 (14), 362 (40), 332 (100), 300 (26), 272 (12), 256 (20).

Dimethyl 11,16-Dihydroxyundecacyclo[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 (69a). (a) To a solution of **68** (30 mg, 0.07 mmol) in dry THF (5 mL) under N_2, sodium methanolate (5 mg, 0.09 mmol) was added, and the mixture was stirred at ambient temperature for 5 min. After complete conversion (TLC control, silica gel, CH_2Cl_2/ethyl acetate, 1:1) dry methanol (10 mL) was added. After addition of cation-exchange resin (100 mg, AC 50W-X8, 100–200 mesh, hydrogen form), the mixture was stirred until a slightly acidic pH value had been reached. Filtration, concentration in vacuo, and crystallization from methanol/CH_2Cl_2 gave **69a** (28 mg, 93%), colorless crystals.

(b) To **60** (500 mg, 1.23 mmol) and Pd/C (5%, 50 mg) in dry methanol/CH_2Cl_2 (100 mL, 4:1) in a H_2 atmosphere (ambient pressure) was added a solution of sodium (60 mg, 2.60 mmol) in dry methanol (2 mL), and the mixture was stirred at ambient temperature to total conversion (2 h, TLC control). Addition of cation-exchange resin (500 mg) and workup analogously to (a) gave crystalline **69a** (485 mg, 97%): mp 315 °C; IR (KBr) 3454 (O-H), 2944 (C-H), 1698 (C=O), 1293 (C-O), 1211 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) Figure 3; ^{13}C NMR ($CDCl_3$) Figure 3; 75.2 (C-10, -12, -15, -17, J_{C-H} = 134 Hz), 68.3 (C-2, -5, -7, -20, J_{C-H} = 136 Hz), 66.0 (C-3, -4, J_{C-H} = 136 Hz), 65.1 (C-13, -14, J_{C-H} = 137 Hz), 63.5 (C-8, -9, -18, -19, J_{C-H} = 135 Hz), 52.3 (2OCH_3, J_{C-H} = 146 Hz); MS (EI) *m/z* (rel intensity) 408 (M^+, 8), 390 (15), 362 (42), 332 (100), 314 (20), 286 (46), 256 (45).

Dimethyl 11,16-Dimethoxyundecacyclo[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 (69b). (a) A suspension of NaH (20 mg, 50% in mineral oil, 0.42 mmol) under N_2 was washed three times with hexane. After the addition of a solution of **68** (30 mg, 0.07 mmol) in dry THF (5 mL), followed by CH_3I (70 mg, 0.49 mmol), the mixture was stirred at ambient temperature to total conversion (24 h, TLC control). Excess NaH was cautiously hydrolyzed with water (10 mL) and the mixture extracted with CH_2Cl_2 (4 × 10 mL). Drying ($MgSO_4$) and concentration in vacuo gave a solid residue which was dissolved in CH_2Cl_2 and filtrated over silica gel (2 cm, CH_2Cl_2/ethyl acetate, 2:1) to give **69b** (28 mg, 87%), colorless crystals from CH_2Cl_2.

(b) To **69a** (200 mg, 0.49 mmol) and NaH (50 mg, 2.08 mmol) (freed from mineral oil) in dry THF (20 mL) under N_2 was added CH_3I (350 mg, 2.46 mmol), and the mixture stirred at ambient temperature for 36 h. Workup analogously to (a) and crystallization from CH_2Cl_2 gave **69b** (200 mg, 93%): colorless crystals, mp 234–235 °C; IR (KBr) 2948 (C-H), 2918 (C-H), 2814 (OC-H), 1721 (C=O), 1291 (C-O), 1191 (C-O), 1080 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.04 (m, 2-, 5-, 7-, 20-H), 3.67 (m, 8-, 9-, 18-, 19-H), 3.67 (m, 2OCH_3), 3.57 (m, 10-, 12-, 15-, 17-H), 3.56 (m, 13-, 14-H), 3.44 (m, 3-, 4-H), 3.18 (s, 2OCH_3); ^1H NMR (400 MHz, $C_6D_6/CDCl_3$, 1:1) δ 4.02 (m, 2-, 5-, 7-, 20-H), 3.55 (m, 8-, 9-, 18-, 19-H), 3.43 (m, 10-, 12-, 15-, 17-H), 3.33 (m, 13-, 14-H), 3.31 (m, 3-, 4-H), 3.07 (s, 2OCH_3); ^{13}C NMR ($CDCl_3$) δ 175.4 (2CO_2CH_3), 123.2 (C-11, -16), 87.7 (C-1, -6), 67.6 (C-10, -12, -15, -17), 67.5 (C-2, -5, -7, -20), 65.6 (C-3, -4), 64.5 (C-8, -9, -18, -19), 64.4 (C-13, -14), 52.0 (2OCH_3), 51.9 (2OCH_3); MS (EI) *m/z* (rel intensity) 376 (M^+ – 60, 34), 346 (69), 316 (100), 286 (42), 256 (63); MS (DCI, isobutane) *m/z* (rel intensity 437 (M + H^+, 44), 405 (100), 373 (42), 345 (50), 315 (10), 256 (5).

11,16-Dimethoxyundecacyclo[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-dicarboxylic Acid (69c). **69b** (200 mg, 0.46 mmol) was converted analogously to **69a**. After 16 h the mixture was concentrated in vacuo, and the residue dissolved in water (20 mL) at 50–60 °C and acidified with 20% hydrochloric acid until pH 1 was reached. The colorless residue was removed by filtration (0 °C), washed with water (0 °C), and dried in vacuo to give **69c** (172 mg, 92%): mp > 320 °C; IR (KBr) 3495 (O-H), 2960 (C-H), 1690 (C=O), 1240 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.86 (m, 2-, 5-, 7-, 20-H), 3.48 (m, 13-, 14-H), 3.48 (m, 10-, 12-, 15-, 17-H), 3.48 (m, 8-, 9-, 18-, 19-H), 3.33 (m, 3-, 4-H), 3.09 (s, 2OCH_3); ^{13}C NMR ($CDCl_3$) δ 175.2 (2CO_2H), 122.5 (C-11, -16), 87.0 (C-1, -6), 67.2 (C-2, -5, -7, -20), 67.1 (C-13, -14), 67.0 (C-10, -12, -15, -17)*, 65.0 (C-3, -4), 63.9 (C-8, -9, -18, -19)*, 51.1 (2OCH_3). Anal. Calcd for $C_{24}H_{24}O_6$ (408.5): C, 70.58; H, 5.92. Found: C, 70.12; H, 6.42.

11,16-Hydroxyundecacyclo[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-dicarboxylic Acid (69d). A solution of **69a** (220 mg, 0.54 mmol) in methanol (40 mL) was heated with KOH (400 mg, 7.13 mmol) in water (4 mL) at reflux for 16 h. After dilution with methanol (100 mL), the mixture was stirred with cation-exchange resin (1.5 g, AC 50W-X8, 100–200 mesh, hydrogen form, washed repeatedly with methanol) till an acidic pH value was attained. Filtration and concentration in vacuo gave **69d** (205 mg, quantitative): mp > 320 °C; IR (KBr) 3370 (O-H), 2930 (C-H), 1680 (C=O) cm^{-1}; ^1H NMR (400 MHz, [D_6]DMSO) δ 3.85 (m, 2-, 5-, 7-, 20-H), 3.62 (m, 13-, 14-H), 3.45 (8-, 9-, 18-, 19-H), 3.34 (m, 3-, 4-H), 3.24 (m, 10-, 12-, 15-, 17-H); ^{13}C NMR ([D_6]DMSO) δ 175.9 (2CO_2H), 116.1 (C-11, -16), 86.5 (C-1, -6), 74.7 (C-10, -12, -15, -17), 67.3 (C-2, -5, -7, -20), 65.1 (C-3, -4), 64.2 (C-13, -14), 63.3 (C-8, -9, -18, -19). Anal. Calcd for $C_{22}H_{20}O_6$ (380.4): C, 69.46; H, 5.30. Found: C, 69.18; H, 5.50.

Dimethyl 11,16-Diacetoxyundecacyclo[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 (69e). **69a** (50 mg, 0.12 mmol) and a catalytic amount of *p*-(dimethylamino)pyridine in dry pyridine/acetic anhydride (1:1, 1 mL) were stirred with exclusion of moisture at 100 °C for 6 h. After cooling to ambient temperature the mixture was poured onto water/ice (10 mL) and extracted repeatedly with CH_2Cl_2. The combined organic phases were washed with diluted hydrochloric acid and then with saturated $NaHCO_3$ solution. Drying ($MgSO_4$), concentration in vacuo, and chromatography (silica gel, CH_2Cl_2/ethyl acetate, 2:1) gave crystalline **69e** (44 mg, 75%, R_f 0.66) and monoacetate (8 mg, 15%, R_f 0.40): colorless crystals, mp 259–260 °C; IR (KBr) 2970 (C-H), 2915 (C-H), 1720 (C=O), 1245 (C-O), 1200 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.02 (m, 2-, 5-, 7-, 20-H), 4.02 (m, 13-, 14-H), 3.70 (s, 2OCH_3), 3.60 (m, 8-, 9-, 18-, 19-H), 3.55 (m, 10-, 12-, 15-, 17-H), 3.47 (m, 3-, 4-H), 1.95 (s, 2$OCOCH_3$); ^{13}C NMR ($CDCl_3$) δ 174.7 (2CO_2CH_3), 169.6 (2$OCOCH_3$), 121.9 (C-11, -16), 86.6 (C-1, -6), 71.6 (C-10, -12, -15, -17), 67.6 (C-2, -5, -7, -20), 65.8 (C-13, -14), 65.3 (C-3, -4), 63.9 (C-8, -9, -18, -19), 52.1 (2OCH_3), 21.8 (2$OCOCH_3$); MS (EI) *m/z* (rel intensity) 492 (M^+ – 60,4), 372 (25), 313 (10), 270 (30), 255 (26); MS (DCI,NH_3) *m/z* (rel intensity) 510 (M^+ + 18,40), 450 (100), 433 (12).

Dimethyl 11,16-Bis[(trimethylsilyl)oxy]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 (69f). A solution of **69a** (50 mg, 0.12 mmol) and chlorotrimethylsilane (2.0 mL, 15.70 mmol) in pyridine (1 mL) and CH_2Cl_2 (3 mL) was stirred at ambient temperature with exclusion of moisture for 24 h (TLC control, silica gel, CH_2Cl_2). After concentration in vacuo the residue was dissolved in dry CH_2Cl_2 and filtered quickly over a short pad of silica gel (1 cm). Crystallization from CH_2Cl_2 gave **69f** (61 mg, 92%): mp 238–240 °C; IR (KBr) 2970 (C-H), 2940 (C-H), 1725 (C=O), 1205 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.00 (m, 2-, 7-, 5-, 20-H), 3.70 (m, 13-, 14-H), 3.67 (m, 8-, 9-, 18-, 19-H), 3.63 (s, 2OCH_3), 3.40 (m, 10-, 12-, 15-, 17-H), 3.40 (m, 3-, 4-H), 0.07 (s, 2$Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 175.3 (2CO_2CH_3), 119.5 (C-11, -16), 89.3 (C-1, -6), 74.6 (C-10, -12, -15, -17), 66.9 (C-2, -5, -7, -20), 65.5 (C-3, -4), 64.7 (C-8, -9, -18, -19), 63.7 (C-13, -14), 51.7 (2OCH_3), 1.5 (2$Si(CH_3)_3$); MS (EI) *m/z* (rel intensity) 552 (M^+, <1%), 537 (M^+ – 15 100), 389 (8), 313 (9), 255 (40).

Diphenylisobenzofuran Adducts to Dimethyl 11,16-Dihydroxyundecacyclo[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 (72/73). To a solution of **67** (50 mg, 0.12 mmol) in dry CH_2Cl_2 (10 mL) under N_2 was added a solution of diphenylisobenzofuran (40 mg, 0.15 mmol) in dry CH_2Cl_2 (50 mL) at ambient temperature. The yellow color of the isobenzofuran disappeared immediately. After total conversion the solution with a pale yellow fluorescence was concentrated and purified by chromatography (silica gel, CH_2Cl_2/ethyl acetate, 2:1) to give a crystalline mixture of the isomers **72/73** (4:1, 78 mg, 92%): mp > 320 °C (dec above 270 °C); IR (KBr) 3540 (O-H), 3050 (arC-H), 1710 (C=O), 1610 (arC-C), 1230 (C-O) cm^{-1}. **72**: ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.90 (m, 4 H), 7.45 (m, 4 H), 7.36 (2 H), 7.32 (m, 2 H), 7.16 (m, 2 H), 3.90 (d, 2-, 7-H), 3.87 (q, 13-H)*, 3.80 (s, 2OCH_3), 3.79 (m, 5-, 20-H), 3.70 (q, 14-H)*, 3.59 (m, 18-, 19-H), 3.26 (m, 12-, 17-H), 3.18 (q, 4-H)*, 3.06 (d, 6-, 20-H), 2.90 (q, 3-H)*; ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ = 175.3 (2CO_2CH_3), 146.2 (2C), 137.8 (2C), 128.3 (4), 127.5 (2C), 126.6 (2C), 126.3 (4C), 121.0 (2C), 116.0 (C-11, -16), 94.0 (C-8, -9), 93.5 (2C), 85.7 (C-1, -6), 75.6 (C-10, -15), 75.3 (C-12, -17), 71.4 (C-3)*, 69.5 (C-5, -20), 68.2 (C-13)*, 67.0 (C-2, -7), 64.7 (C-4)*, 64.7 (C-14)*, 63.4 (C-18, -19), 52.3 (2OCH_3); MS (DCI, NH_3) *m/z* (%) = 677 (M^+, 8), 659 (4), 271 (100).

Dimethyl 15-Hydroxy-11-oxo-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 (78). A solution of **63** (60 mg, ca. 0.14 mmol, crude material) in CH_2Cl_2 (20 mL) was stirred with silica gel (500 mg) under N_2 at ambient temperature for 16 h (TLC control). Filtration (silica gel, thorough elution with CH_2Cl_2/ethyl acetate) and concentration in vacuo gave a solid residue, which was separated by chromatography (silica gel, CH_2Cl_2/ethyl acetate, 2:1). The first fraction (R_f 0.35) gave **78** (35 mg, 58%), the second (R_f 0.15) crystalline **79a** (15 mg, 26%).

78: colorless crystals, mp 252–253 °C; IR (KBr) 3450 (O-H), 2950 (C-H), 1725 (C=O), 1250 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) Figure 2; ^{13}C NMR ($CDCl_3$) Figure 2; MS (EI) *m/z* (rel intensity) 436 (M^+, 14), 404 (100).

Dimethyl 11,15-Dihydroxy-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 (79a). (a) A solution of **78** (30 mg, 0.07 mmol) in dry THF (3 mL) was stirred under N_2 with sodium *tert*-butylate (17 mg, 0.15 mmol) at ambient temperature to complete conversion (5 min, TLC control) and then it was diluted with CH_2Cl_2 (15 mL), extracted with water (2 × 5 mL), and dried ($MgSO_4$). Concentration in vacuo gave colorless crystals (28 mg, 94%).

(b) **63** (30 mg, ca. 0.07 mmol, crude material) was converted analogously to **78**. Crystallization from CH_2Cl_2/ethyl acetate (1:1) gave **79a** (25 mg, 82%): mp > 320 °C; IR (KBr) 3450 (O-H), 2950 (C-H), 2850 (C-H), 1725 (C=O), 1260 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3/CD_3OD$, 1:1) Figure 3; ^{13}C NMR ($CDCl_3/CD_3OD/C_6D_6$) Figure 3; MS (EI) *m/z* (rel intensity) 436 (M^+, 9), 404 (100), 372 (52), 328 (30), 284 (40), 256 (15).

Dimethyl 11,15-Dimethoxy-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 (79b). (a) **63** (20 mg, 0.05 mmol, crude material) and NaH (50 mg, 2.08 mmol) (freed from mineral oil) in THF (20 mL) were stirred under N_2 with CH_3I (35 mg, 2.46 mmol) at ambient temperature for 36 h. Workup analogously to **69b** and crystallization from CH_2Cl_2 gave pure **79b** (16 mg, 76%).

(b) **78** (20 mg, 0.05 mmol) was converted analogously to **63** to give **79b** (17 mg, 82%): colorless crystals, mp 305–307 °C; IR (KBr) 2960 (C-H), 1725 (C=O), 1220 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.82 (m, 9-, 13-H), 3.79 (m, 2-, 4-, 17-, 20-H), 3.72 (m, 18-, 19-H), 3.72 (s, 2OCH_3), 3.21 (m, 8-, 10-, 12-, 14-H), 3.18 (2OCH_3); ^1H NMR (400 MHz, $CDCl_3/C_6D_6$) δ 3.77 (m, 2-, 4-, 17-, 20-H), 3.61 (s, 2OCH_3), 3.51 (m, 18-, 19-H), 3.51 (m, 9-, 13-H), 3.09 (m, 8-, 10-, 12-, 14-H), 2.99 (2OCH_3); ^{13}C NMR ($CDCl_3$) δ 172.4 (2CO_2CH_3), 111.3 (C-11, -15), 93.4 (C-1, -5, -7, -21), 79.4 (C-3, -16), 74.9 (C-18, -19), 72.5 (C-9, -13), 58.0 (C-2, -4, -17, -20), 57.7 (C-8, -10, -12, -14), 52.5 (2OCH_3), 52.0 (2OCH_3); MS (EI) *m/z* (rel intensity) 464 (M^+, 100), 436 (46), 404 (24), 374 (30), 344 (8), 343 (12), 313 (20), 285 (15), 284 (5).

Dimethyl 9,13-Dihydroxy-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 (83a). (a) A solution of **67a** (50 mg, 0.12 mmol) and peroxycarbamic acid (30 mg, ca. 90%, 0.15 mmol) in CH_2Cl_2 (20 mL) was stirred at ambient temperature for 20 min (total conversion, TLC control). The mixture was washed with aqueous Na_2SO_3 solution (2 × 10 mL), dried ($MgSO_4$), and concentrated in vacuo, and remaining benzamide removed by sublimation (10^{-2} Torr/40 °C). The residue was crystallized from CH_2Cl_2/ethyl acetate to give **83a** (45 mg, 90%).

(b) A solution of **60** (50 mg, 0.12 mmol) and peroxycarbamic acid (60 mg, ca. 90%, 0.30 mmol) in $CHCl_3$ (25 mL) was heated to reflux for 16 h. After cooling to ambient temperature it was washed twice with aqueous Na_2SO_3 solution, dried ($MgSO_4$), and concentrated in vacuo, and remaining benzamide removed by sublimation (10^{-2} Torr/40 °C). The residue was dissolved in dry THF (10 mL), stirred with NaH (15 mg, 0.60 mmol, freed from mineral oil) with exclusion of moisture at ambient temperature for 20 min, and then poured onto ice/water (10 mL). After repeated extraction with CH_2Cl_2, the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to give a raw material (55 mg), which after chromatography (silica gel; CH_2Cl_2/ethyl acetate, 1:1) gave **83a** (46 mg, 91%), mp 278–279 °C; IR (KBr) 3420 (O-H), 2940 (C-H), 1695 (C=O), 1230 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) Figure 3; ^{13}C NMR ($CDCl_3$) Figure 3; MS (EI) *m/z* (rel intensity) 422 (M^+, 24), 390 (100), 372 (12), 346 (20), 344 (58), 314 (46), 270 (22).

Dimethyl 9,13-Dimethoxy-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 (83b). **83a** (20 mg, 0.05 mmol) and NaH (5 mg, 0.20 mmol, freed from mineral oil) in dry THF (3 mL) were stirred under N_2 with CH_3I (50 mg, 0.35 mmol) at ambient temperature for 36 h. Workup analogously to **69b** and crystallization from CH_2Cl_2 gave pure **83b** (16 mg, 75%): colorless crystals, mp 227–228 °C; IR (KBr) 2960 (C-H), 2820 (C-H), 1720 (C=O), 1220 (C-O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.12 (m, 7-, 19-H), 3.73–3.55 (series of m, 4-, 5-, 6-, 11-, 14-, 15-, 16-, 17-, 18-, 21-H), 3.69 (s, 2OCH_3), 3.16 (m, 10-, 12-H), 3.16 (s, 2OCH_3); ^{13}C NMR ($CDCl_3$) δ 173.9 (2CO_2CH_3), 116.9 (C-9, -13), 93.4 (C-1, -3), 83.5 (C-8, -20), 74.2 (C-5), 72.5 (C-11), 67.4 (C-14, -16), 67.0 (C-7, -19), 65.9 (C-6), 64.1 (C-15), 63.1 (C-17, -18), 58.6 (C-4, -21), 58.1 (C-10, -12), 52.2 (2OCH_3), 51.9 (2OCH_3); ^1H NMR (400 MHz, $C_6D_6/CDCl_3$, 10:1) δ 4.08 (m, 7-, 19-H), 3.82 (d, 4-, 21-H), 3.50 (s, 2OCH_3), 3.41 (m, 17-, 18-H), 3.33 (m, 5-H), 3.28 (m, 14-, 16-H), 3.23 (m, 6-H), 3.17 (m, 11-H), 3.08 (m, 15-H), 3.02 (d, 10-, 12-H), $J_{4,5} = J_{10,11} = 7.0$, $J_{6,7} = J_{5,6} = J_{14,15} = J_{18,19} = 10.5$ Hz; MS (EI) *m/z* (rel intensity) 450 (M^+, 55), 422 (100), 390 (35), 360 (37), 330 (48), 270 (16).

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