Tetrahedron Vol. 49, No. 8, pp. 1511-1524, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00

General Approach for the Synthesis of Polyquinenes *via* the Weiss Reaction XV. Synthesis of the [5.5.5.5]Fenestrane System *via* the Aldol Approach and Studies Directed Toward the [5.5.6.6]Fenestranes

Xiaoyong Fu, Greg Kubiak, Weijiang Zhang, Wenching Han, Ashok K. Gupta and James M. Cook*

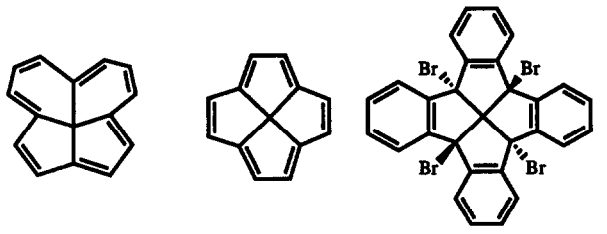
Department of Chemistry, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin 53201

(*Received in USA* 24 *November* 1992)

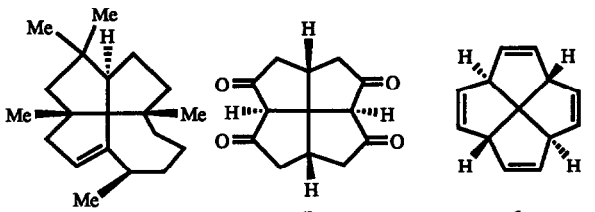
Abstract: The all *cis*-8a,12b-diacetoxytetracyclo[5.5.1.0.^{4,13}0^{10,13}]tridecane-2,6-dione **9** was successfully synthesized *via* aldolization of the diketodialdehyde **8** under conditions of equilibration, followed by trapping with acetic anhydride. Aldol cyclization of the dialdehyde **14** to provide the [5.5.6.6]fenestrane system **12** was also attempted. This resulted in the observation of tetracycle **25** with the desired ring system albeit as a minor product. The major products isolated from this approach were the undesired α,β-unsaturated aldehyde **22** and monoaldehyde **23**, the latter of which contained a configuration opposite to that of C-5 in **12**. In addition, the related bisacylation approach provided **26** as the major product with the undesired configuration at C-8. This cyclization furnished the transannular tetraone **27** at higher temperature.

In the early 1970's, Hoffmann *et al.*[1] proposed the concept of a planar tetracoordinate carbon atom based on the nature of planar methane. Calculations revealed that the energy difference between the square planar and tetrahedral methane was considerably greater than typical carbon-hydrogen and carbon-carbon bond strengths and was estimated to range from 95 to 250 kcal/mole.[2-5] Consequently, the limiting case of a molecule containing a tetracoordinate planar carbon with these ordinary bonds was not experimentally likely. However, stabilization of the planar form or destabilization of the tetrahedral form were proposed as a means through which this energy gap could be narrowed.[1] In this regard, annulenes **1**[1] and **2**[1,6] have been suggested as possible candidates to house a planar tetracoordinate carbon atom by Hoffmann[1] and Keese,[6] respectively. The [14] and [12] π annulene systems of **1** and **2** were proposed to overlap with the lone pair of electrons in the p_z orbital of the planar form of the central carbon atom thereby stabilizing this form. On the other hand, it has been suggested that the coplanar nature of the annulene system would increase the energy of the tetrahedral (central) carbon atom, also promoting rehybridization to generate the planar tetracoordinate form.[6] However, MNDO and MINDO/3 calculations by Schleyer,[7] Dewar[8] and Gleiter[9] suggested that both **1** and **2** would behave as unstable polyenes. Consequently, the calculated energies of the tetracyclo[6.6.1.0^{4,15}.0^{12,15}]pentadecane heptaene **1** and the tetracyclo[5.5.1.0^{4,13}.0^{10,13}]tridecane hexaene **2** have stimulated computational[1-9] as well as synthetic[10,11] efforts in this area. Recent syntheses and studies on the [5.5.5.5]fenestrindans with four bridgehead substituents by Kuck *et al.*[12-14] have suggested a definite flattening at the central carbon atom, although it is not overwhelming. For example, the degree of angular distortion at the central carbon α[12] was found to be 121.4° by

X-ray crystallography in the case of tetrabromofenestrindan **3**[14]. Furthermore, the unique medium ring [5.5.5.7]fenestrane diterpene laurenene **4** has recently attracted the attention of synthetic chemists.[15-17]



1 **2** **3**

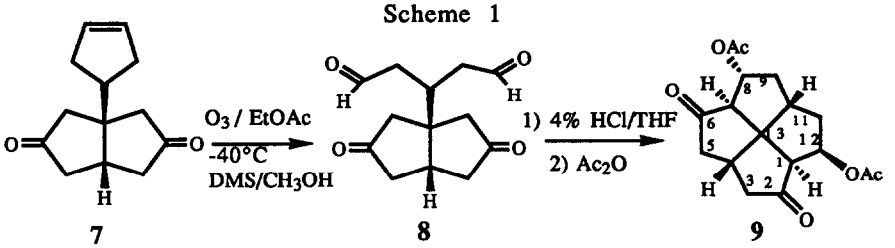


4 **5** **6**

Generation of the tetracyclo[5.5.1.0.^{4,13}0^{10,13}]tridecane-2,6,8,12-tetraone **5** *via* a bisacylation sequence from the diketo-diacid by Mitschka *et al.*[18] and its subsequent conversion into the fenestrane tetraene **6** by Deshpande *et al.*[19] in our laboratory constituted the first synthesis of the [5.5.5.5]fenestrane system. Keese then reported the first synthesis of the [5.5.5.5]fenestrane parent hydrocarbon,[10] and subsequently, Kubiak converted **6** into the parent fenestrane. In contrast, synthetic and computational studies on the [5.5.6.6] fenestranes have been limited. We wish to report the successful synthesis of bis-acetoxy[5.5.5.5]fenestrane dione derivative **9** *via* an aldol approach, and attempts to employ this process for the preparation of the [5.5.6.6] system.

The 1-(3'-cyclopenten-1'-yl)-*cis*-bicyclo[3.3.0]octane-3,7-dione **7** (Scheme 1) prepared earlier in our laboratory *via* the Weiss reaction[20] was readily oxidized to the diketodialdehyde **8** in greater than 90% yield. Initial aldolization experiments to provide the desired [5.5.5.5] system with **8** in hot acetic acid/H_2SO_4 resulted in kinetic trapping of two epimeric diketodiacetates which owe their origin to transannular cyclization.[20]

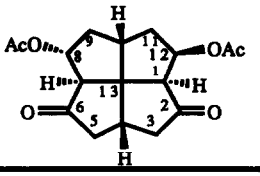
Scheme 1



7 **8** **9**

However, when **8** was stirred in tetrahydrofuran in the presence of 4% aqueous HCl under conditions of equilibration[21] (room temperature, 2 weeks), followed by trapping with excess acetic anhydride, a mixture of diketodiacetates was isolated. Based on analysis of the crude product mixture by NMR spectroscopy, the desired [5.5.5.5]fenestrane diketodiacetate **9** comprised 45% of this material. The mixture was subjected to repeated flash chromatography (silica gel, EtOAc/hexane, 1:1) to yield the desired fenestrane **9** (major product), accompanied by a small quantity of a symmetrical epimeric [5.5.5.5]fenestrane diketodiacetate **9a**. The two transannular cyclization products, the structures of which had previously been reported,[20] comprised the remainder (20%) of the mixture. The structures of the all-*cis*-[5.5.5.5]fenestrane **9** diacetate and its epimer were deduced from IR and mass spectroscopy, as well as high resolution NMR spectroscopy. The designation of **9** as all-*cis* follows from the nomenclature devised by Keese *et al.* to simplify designation of this [5.5.5.5]fenestrane

Table 1. 500 MHz ^{1}H NMR Data for the Diketodiacetate **9** in CD_3OD.



Proton	δ (ppm)		*J* (Hz)	Proton	δ (ppm)	*J* (Hz)	
H12	5.565	5	H12-H1	H3(down)	2.350	18	gem
		4	H12-H11(down)			9.5	H3(down)-H4
		1	H12-H11(up)			1.5	H3(down)-H1
H8	5.597	<1	H8-H7	H5(down)	2.415	19	gem
		5	H8-H9(up)			4	H5(down)-H4
		1	H8-H9(down)			1	H5(down)-H7
H7	3.188	1	H7-H5(down)	H5(up)	2.642	19.5	gem
		1	H7-H8(down)			8.8	H5(up)-H4
H4	2.910	8.5	H4-H3(up)	H11(up)	2.270	14	gem
		8.5	H4-H5(up)			7.5	H11(up)-H10
		4	H4-H5(down)			1	H11(up)-H12
		9	H4-H3(down)				
H10	2.847	7.5	H10-H11(up)	H9(down)	1.825	15.5	gem
		8.5	H10-H11(down)			1	H9(down)-H8
		8.5	H10-H9(up)			1	H9(down)-H10
		1	H10-H9(down)			1	H9(down)-H7
H3(up)	2.750	18.5	gem				
		8.5	H3(up)-H4				

system.[10a-d]

A COSY experiment and a series of homonuclear-decoupling experiments permitted the assignment of all the proton resonance lines of **9**, as well as the determination of coupling constants (Table 1). The presence of the two different sets of coupled CH_2-CH-CH_2- units precluded transannular cyclization across the cyclopentanone ring (for example, from carbon atom-11 to 5 or atom-11 to 3) and confirmed that diacetate **9** contained the [5.5.5.5]fenestrane skeleton. To distinguish between the structure of the all *cis*- and a *cis-cis-cis-trans*-[5.5.5.5]fenestrane, it was necessary to examine the coupling constants of the methine protons (C-1 and C-7) at the ring junctions. It was found that each of the methine protons at H-1 and H-7 were coupled with one proton of the methylene unit on the other side of the carbonyl group (CH_2-3 and CH_2-5, respectively). This long range 4-bond coupling required that the bonds involved be nearly coplanar.[22] By examination of molecular models, it was found that the junction proton could not be coplanar with either of the protons of the CH_2 group if the ring juncture was *trans*. This implied that the relative stereochemistry of the two junction protons at C-1 and C-7 must be *cis*. The configurations at carbon atoms-10 and -4 were determined in a similar manner. At this point, the nonsymmetrical nature of the structure of **9**, as evidenced by the observation of seventeen signals in the broadband decoupled ^{13}C-NMR spectrum, could be ascribed to the *trans* disposition of the two acetate functions. The structure of the symmetrical minor isomer which accompanied **9** is consistent with a diketodiacetate epimeric with **9** either at C-8 or C-12 to provide the acetate functions *cis* to one another.

Formation of the all *cis* configuration at the ring junctures in **9** rather than the *cis-cis-cis-trans*-diastereomer is in agreement with MM2 calculations, as illustrated in Figure 1. Examination of the energies of the all *cis*-**10** and the *cis-cis-cis-trans* system **11** indicates that the all-*cis* diastereomer is more stable than **11** by

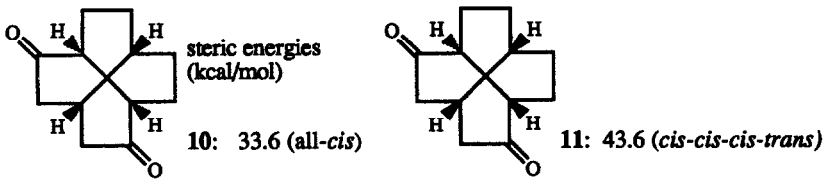


Figure 1. MM2 optimized energies for the [5.5.5.5]fenestrane derivatives **10** and **11**.

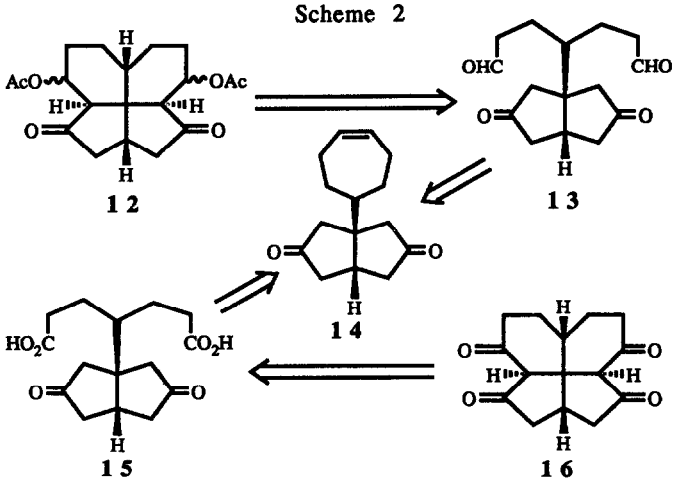
10 kcal/mol. This is in agreement with calculations reported by Keese[10b] in a related system, consequently, formation of **10** over **11** would be expected under the conditions of thermodynamic equilibrium.

The all *cis*-8α,12β-diacetoxytetracyclo[5.5.1.0.^{4,13}0^{10,13}]tridecane-2,6-dione **9** can be converted into the desired staurane tetrol on treatment with borane-THF analogous to published procedures.[19] The aldol approach to **9** provides an alternate synthesis of the staurane system which is superior to the bisacylation route if nucleophilic reagents are required in the latter stages of the route toward **2**.[23] In addition, the structure of diketodiacetate **9** permits chemospecific differentiation between carbon atoms [C(2) and C(6)] and [C(8) and C(12)] due to the reactivity of the two sets of functional groups as compared to those of the tetraone **5**.

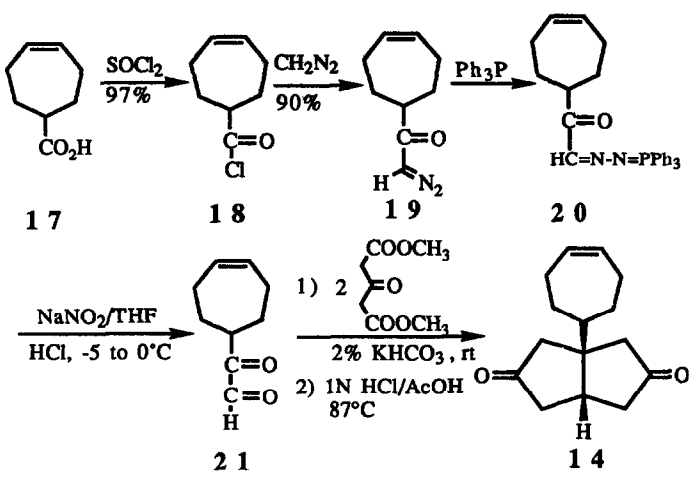
The synthesis of both the tetraone **5** *via* the bisacylation process and the preparation of the diketodiacetate **9** by aldolization proceeded through the common synthon diketoolefin **7**. From a retrosynthetic perspective (Scheme 2), the [5.5.6.6]fenestrane skeleton of the related bisketone **12** or tetraketone **16** could be prepared in a similar fashion by replacement of the cyclopentenyl-*cis*-bicyclo[3.3.0]octane-3,7-dione **7** with the cycloheptenyl-*cis*-bicyclo[3.3.0]octane-3,7-dione **14** to generate either the intermediate dialdehyde **13** or the diacid **15**, respectively.

The preparation of the cycloheptenyl-*cis*-bicyclo[3.3.0]octane-3,7-dione **14** *via* the Weiss reaction began with cycloheptenyl carboxylic acid **17**, which was prepared from cyclopentanone by the modified[24] Stork enamine[25] protocol (200 gram scale) in 36% overall yield. The carboxylic acid was converted into the diazoketone **19** by the Arndt-Eistert procedure in excellent yield (Scheme 3). Treatment of **19** with triphenylphosphine gave the light yellow colored crystalline phosphazine **20** which could be stored in a dessicator until needed. The phosphazine **20** was treated with nitrous acid at 0°C to furnish 4-cyclohepten-1-yl-glyoxal **21**, according to the method of Bestmann.[19,26] The Weiss reaction of **21** with dimethyl 3-ketoglutarate was carried out under aqueous alkaline conditions in 70% yield. Hydrolysis of the ester functions at 87°C accompanied by decarboxylation gave the key 1-(4'-cyclohepten-1-yl)-*cis*-bicyclo[3.3.0]-octane-3,7-dione **14** in 40% overall yield from phosphazine **20**. As expected from the C_s symmetry of **14**, only nine lines

Scheme 2



Scheme 3



were observed in the carbon NMR spectrum of this bicyclooctane-3,7-dione. The key intermediate **14** could be prepared directly from 4-cycloheptenyl carboxylic acid without purification of each intermediate in 10-15 gram quantities.

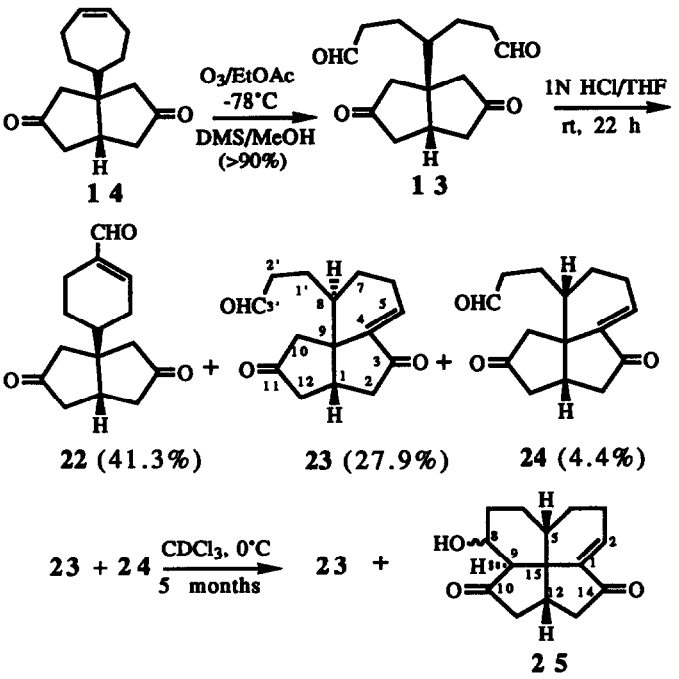
With the cycloheptenyl-*cis*-bicyclo[3.3.0] system **14** in hand, attention turned to the aldol approach to generate the [5.5.6.6]fenestrane system. Since the aldolization process yielded the desired [5.5.5.5.]fenestrane only under conditions of thermodynamic equilibrium, the analogous process was employed for the conversion of dialdehyde **13** into **12**. In this regard, scission of the olefinic bond in **14** to provide bisaldehyde **13** was readily accomplished by ozonolysis. The bisaldehyde **13** obtained by this process was subjected to an intramolecular cyclization (1N HCl/THF, r.t.,14d) and the reaction was quenched with excess acetic anhydride, as illustrated. However, monoaldehyde **22** rather than the desired [5.5.6.6]diketodiacetate was obtained from this condensation. This aldehydo-olefin comprised 50% of the mixture (GC), accompanied by at least seven other components at lesser concentrations. The structure of **22** was assigned based on IR, MS and NMR spectroscopy. In particular, signals due to the presence of three carbonyl groups and two olefinic carbon atoms with appropriate multiplicities were observed in the ^{13}C-NMR spectrum of **22**. An aldehyde proton at δ 9.42 ppm was present in the ^{1}H-NMR spectrum of **22**. Comparison of the chemical shifts which corresponded to the aldehydic carbon atom and proton (δ 193.5 and 9.42 ppm, respectively) of **22** with those of the starting dialdehyde **13** (δ 205 and 9.77 ppm, respectively) strongly suggested the carbonyl group in **22** was conjugated with a double bond. Delocalization of a carbonyl carbon atom is known to provide an aldehyde resonance at higher field with respect to the saturated congener.[22] On the other hand, the related olefinic carbon atoms and the corresponding proton resonated at relatively lower field (δ 140, 150 and 6.82 ppm) than those of **14** (δ 131.53 and 5.77 ppm). Moreover, the bridgehead proton in the bicyclo[3.3.0]octane-3,7-dione nucleus of **22** was coupled to four adjacent protons [homonuclear 2D-COSY (500 MHz) spectrum], which excluded a product of transannular cyclization.

The formation of the α,β-unsaturated aldehyde **22** arose by aldol condensation to furnish a six-membered aldol which underwent dehydration to provide the α,β-unsaturated aldehyde function. The corresponding reaction in the [5.5.5.5] series **8** would have produced an unstable four-membered ring which under the conditions of equilibration underwent a retro-aldol reaction to regenerate dialdehyde **8** rather than dehydration.

When the aldol condensation of **13** was quenched at an earlier stage (1 d), **22** accompanied by two other aldehydes **23** and **24**, was obtained in a ratio of 1.3 : 1. The unsaturated aldehyde **22** was readily separated from **23** and **24** by flash chromatography. The mixture of epimeric tricyclic aldehydes **23** and **24** was not separable

under a variety of chromatographic conditions. The structure of the major isomer **23** was determined by NMR spectroscopy. The ^{1}H-NMR spectrum was assigned based primarily on homonuclear COSY experiments. The assignments of the signals for the bicyclo[3.3.0]octane-3,7-dione unit began with the diagnostic multiplet (δ 2.89) at H-1, while assignments of the signals for the six membered ring were based on the interaction between the olefinic proton at H-5 and the proton at H-6. An AB spin system for the methylene unit at C-10 was confirmed by NOE difference spectra. It is important to note that H-2 (α) appeared as a doublet instead of a doublet of doublets, which implies that the dihedral angle between H-1 and H-2 (α) is close to 90°. A crosspeak was observed between H-1 and H-2 (α) in the relay COSY spectrum. The NMR spectral data of **23** are summarized in Table 2.

Scheme 4

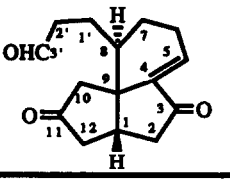


The relative configuration of C-8 was elucidated from 2D-NOESY experiments. A clear NOE was observed between protons located at H-1 and H-1' (β), and strong NOE enhancements were also observed between H-10 and H-7 as well as H-10 and H-8. These results are in agreement with the structure of **23**, as illustrated, with the proton at H-8 located in the α position. Since the aldehydic singlet at C-3' and the olefinic triplet at C-5 appeared at chemical shifts analogous to the two signals in **23**, the structure of the minor component was proposed as the desired beta epimer **24**.

The tricyclic aldehyde **23** was stable in $CDCl_3$ solution at low temperature (0°C). The signals which corresponded to the carbon atoms in **23** could be identified in the ^{13}C-NMR spectrum of a sample kept in the freezer for 5 months. This supports the configuration of H-8 as a in **23**. In contrast, all of the carbon signals for **24** disappeared in that same ^{13}C-NMR spectrum with the appearance of two new minor components. Since the yield of **24** (*vida infra* **25**) was low, the structures of these two new compounds were not unambiguously assigned. Two new methine signals (DEPT experiments) were observed at approximately 60 ppm in the carbon NMR spectrum of this mixture, therefore, it is felt that they arise from the carbon atom located at C-8 in the epimeric mixture represented by the desired [5.5.6.6] system **25**. Further studies in this area are underway.

With regard to the bisacylation approach to the [5.5.6.6]fenestrane system (Scheme 5), the diketoolefin **14** was converted into the diacid **15** in 96% yield *via* ozonolysis which was followed by Jones oxidation (Scheme 5). The diacid was treated with *p*TSA in a mixture of benzene and dioxane at reflux to provide the tricyclic monoacid **26**. The base peak (m/e 279) in the mass spectrum (CI) indicated that **26** resulted from

Table 2. NMR Spectral Data for the Tricyclic Aldehyde 23

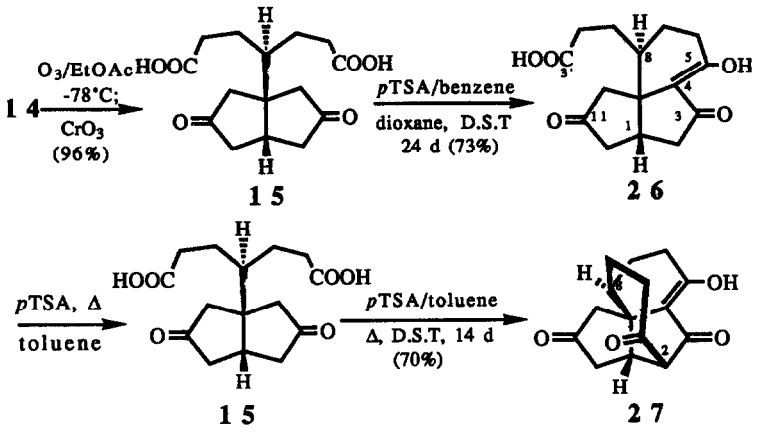


^{1}H-NMR(500 MHz, $CDCl_3$)				^{13}C-NMR	
Proton	Chemical shift(ppm)	Coupling constant (Hz)		Carbon	Chemical shift(ppm)
H-3	9.80	s		C-11	217.02
H-5	6.77	H5-H6(up)	3.42	C-3	204.09
		H5-H6(down)	3.59		
H-1	2.89	H1-H12(up)	8.93	C-3'	201.30
		H1-H12(down)	10.51		
		H1-H2(up)	8.05		
H-12(up)	2.64	gem	18.80	C-5	133.41
		H12(up)-H1	8.72		
H-2(up)	2.56	gem	18.56	C-4	140.75
		H2(up)-H1	7.07		
H-2'	2.54	m		C-10	50.34
H-2'	2.46	m		C-9	45.65
H-2(down)	2.39	gem	18.65	C-12	42.88
H-10(up)	2.34	gem	18.47	C-2	42.19
H-10(down)	2.30	gem	19.27	C-2'	41.65
H-6	2.23	m		C-1	35.89
H-6	2.13	m		C-8	35.74
H-12(down)	2.04	gem	18.80	C-6	20.96
		H12(down)-H1	11.00		
H-1'(up)	1.80	m		C-7	20.96
H-8	1.71	m		C-1'	18.99
H-7	1.71	m			
H-1'(down)	1.26	m			

monocyclization of the diacid **15**, accompanied by loss of one molecule of water. Based on this data the structure of **26** could have been either an acid anhydride or the tricyclic monoacid generated from a monoacylation process. The skeletal structure of **26** was confirmed as the latter by observation of two carbonyl signals at δ 217.7 and 206.0 ppm, two signals at δ 177.8 and 169.8 ppm and an olefinic carbon atom located at 113.4 ppm. The two carbonyl functions resonated at quite different fields; the signal at 217.7 ppm was similar to that in the starting diacid **15**, while the other signal at relatively higher field (206 ppm) implies conjugation with a double bond.[22] The relative configuration at C-8 was not unambiguously determined, but is believed to be the same as that of the monoaldehyde **23** from chemical reactivity. When the diacid **15** was heated at higher temperature, a tetracyclic tetrone **27** was obtained with the desired molecular ion (m/e, 261) for the [5.5.6.6]fenestrane tetraone (CIMS). The homonuclear COSY experiments clearly indicated the presence of the (12)CH_2-(1)CH-(2)CH coupling system. Also the unsymmetrical nature of this molecule (^{13}C-NMR spectroscopy of the product indicated the presence of three carbonyl signals at δ 215.71, 210.21 and 199.01 ppm, respectively) suggested that transannular cyclization had occurred.

In summary, a [5.5.5.5]fenestrane diketodiacetate **9** was successfully synthesized *via* aldolization of the diketodialdehyde **8** under conditions of equilibration, which was followed by trapping with acetic anhydride. This approach was also attempted to effect cyclization of the dialdehyde **14** into a [5.5.6.6]fenestrane system **12**. This has resulted in the observation of **25** with the desired ring system albeit as a very minor product. However,

Scheme 5



the major products isolated from this approach were the undesired α,β-unsaturated aldehyde **22** and monoaldehyde **23**, the latter of which contained a configuration opposite to that of C-5 in **12**. This prevented further cyclization to the desired [5.5.6.6]fenestrane system. In addition, the related bisacylation approach provided **26** as the major product with the undesired configuration at C-8. This cyclization furnished the transannular tetraone **27** at higher temperature. The difference between the geometry and stability of intermediates in the [5.5.5.5] and [5.5.6.6]fenestrane systems with regard to the formation of the all-*cis*-fenestranes has been analyzed.[27] Further work will be required, however, to determine which kinetic and thermodynamic parameters predominate in the cyclization process to **26** and **27**.

Experimental Section

The experimental details are analogous to those reported earlier.[21b] All chemicals were purchased from Aldrich Chemical Co. unless otherwise stated. The 4-cycloheptene-1-carboxylic acid **17**[24,25] and diketodialdehyde **8**[20] were prepared on large scale, according to the published procedures.

All *cis*-8α,12β-diacetoxytetracyclo[5.5.1.0.^{4,13}0^{10,13}]tridecane-2,6-dione 9. Diketodialdehyde **8** (1.0 g, 4.23 mmol) was dissolved in distilled THF (100 mL). Aqueous HCl (6N, 15 mL) was added and the mixture was stirred at room temperature under a nitrogen atmosphere for 7 d. Another portion of HCl (6N, 15 mL) was added and the mixture was stirred for an additional 7 d. Acetic anhydride (100 mL) was then added and the mixture was allowed to stir at room temperature overnight. The solvents were removed under reduced pressure to afford a pale yellow colored oil (1.5 g). The crude material was purified by flash chromatography (EtOAc/hexane, 1:1). The initial fractions contained 4-chlorobutyl acetate (from the acid-catalyzed ring opening of THF). The more polar products were purified by repeated flash chromatography to afford the major product (^{13}C-NMR) as a white solid which was purified further by recrystallization from EtOAc/hexane to provide a sample of **9** (>90% pure on NMR analysis): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.83 (1H, dddd, J=15.5, 1, 1, 1 Hz), 1.98 (3H, s), 2.02 (3H, s), 2.27 (1H, ddd, J=14, 7.5, 1 Hz), 2.35 (1H, ddd, J=18, 9.5, 1.5 Hz), 2.42 (1H, ddd, J=19, 4, 1 Hz), 2.64 (1H, dd, J=19.5, 8.5 Hz), 2.75 (1H, dd, J=18.5, 8.5 Hz), 2.85 (1H, dddd, J=8.5, 8.5, 7, 1 Hz), 2.91 (1H, dddd, J=9.0, 8.5, 8.5, 4 Hz), 3.88 (1H, dd, J=1, 1 Hz), 5.57 (1H, ddd, J=5, 4, 1 Hz), 5.60 (1H, ddd, J=5, 1, 1 Hz). ^{13}C-NMR (125.76 MHz, $CDCl_3$) δ 21.11, 21.23, 37.06, 40.74, 42.50, 44.39, 48.71, 50.65, 63.31, 63.38, 67.26, 78.91, 80.97, 169.61, 169.735, 214.19, 214.83. MS (EI, 15 eV) 320 (M^+, 13.3), 292 (17.3), 260 (70.1), 218 (100), 200 (85.3). HRMS Calcd. for $C_{15}H_{16}O_4$ (M^+-HOAc), 260.1048; Found 260.1082; Calcd. for $C_{13}H_{12}O_2$ (M^+-2HOAc), 200.0837; Found, 200.0846. The molecular ion was not observed.

4-Cycloheptene-1-carboxyl Chloride 18. The 4-cycloheptene-1-carboxylic acid **17**[24,25] (4.5 g, 0.03 mol) was dissolved in freshly distilled thionyl chloride (12.5 mL). The mixture was stirred at room temperature for 2 h and then warmed to 45 - 50°C. Dry benzene (5 mL) was then added and all the volatile material was carefully removed by aspirator pump pressure. It is important that all the excess thionyl chloride be removed. After removal of the low boiling material which provided a red colored liquid, the acid chloride (5.0 g, 98% yield) was obtained by high vacuum distillation at 74°C (0.40 mm Hg). The volatile material occasionally had to be redistilled in order to provide the above material balance; IR (neat) 3010 (s), 2980 (s), 1790 (br), 1640 (s) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.50-2.60 (8H, m), 3.00(1H, m), 5.80 (2H, t); MS (CI, CH_4) m/e (relative intensity) 161 (6%), 159 (M+1, 18%), 141 (31%), 123 (100%), 95 (8%). This material was employed directly in the next experiment.

2-(4'-Cyclohepten-1'-yl)-2-oxo-1-diazoethane 19. A mixture of 2-(2-ethoxyethoxy)-ethanol (35 mL) and ether (20 mL) was added to a solution of KOH (6 g) which had been dissolved in H_2O (10 mL). This mixture was placed in a water bath and the temperature held between 50-60°C. As the ether began to distill, a solution of Aldrich Diazald (21.5 g) in ether (200 mL) was added. This distillation was continued until collection of yellow-colored distillate ceased. The collected yellow-colored solution contained three grams of diazomethane. A solution of 4-cycloheptene-1-carboxyl chloride **18** (8.28 g, 0.05 mol) and dry ether (10 mL) was then added slowly to the mixture of etheral diazomethane (3 g, 0.07 mol) and triethylamine (4.85 g, 0.04 mol) which had been cooled in a dry ice-ethyl acetate bath (-78°C). The mixture which resulted was stirred for one hour at -78°C and then brought to room temperature for 40 minutes. The solution which resulted was stored in a refrigerator overnight. The Et_3N•HCl solid which formed was filtered from the medium at 0°C, and ether was removed from the residue under reduced pressure. The residue could be purified either by chromatography (benzene-ethyl acetate, gradient elution) or by distillation in small batches (2-3 g) at 110-115°C (0.7 mm Hg) to provide the diazoketone (7.38 g, 90%) as a viscous yellow liquid **19**: IR (neat) 3040 (s), 3010 (s), 2980 (s),2100 (s),1730 (s), 1630 (s), cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.20-3.00 (9H, m), 3.70, 4.20, 5.40 (1H, three singlets), 5.80 (2H, t); MS (CI, CH_4) m/e (relative intensity) 165 (M^++1, 66%), 137 (11%), 123,(100%), 95 (36%). **Caution**: This compound will decompose with rapid evolution of nitrogen on heating above the boiling point (0.7 mm Hg). The material was employed directly in the next experiment.

2-(4'-Cyclohepten-1'-yl)-2-keto-1-triphenylphosphazino-ethane 20. Triphenylphosphine (3.67 g, 0.014 mol) was dissolved in anhydrous ether (20 mL) and was added to a solution composed of 2-(4'-cyclohepten-1'-yl)-2-keto-1-diazoethane **19** (2.11 g, 0.013 mol) and anhydrous ether (10 mL). The mixture was allowed to stir at room temperature for 3 h. The solid which formed was filtered from the medium and recrystallized from ethyl acetate/hexane to provide **20** (4.77 g, 87%) characterized as yellow crystals: mp 117-118°C; IR (KBr) 3030 (s), 1645 (s), 1520 (s), 1485 (s), 1070 (s), 910 (s), cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.15-2.10 (8H, m), 3.40 (1H, br, m), 5.80 (2H, br, s), 7.60 (16H, m); MS (C.I., CH_4) m/e (relative intensity) 427 (M^++1, 0.4%), 349 (13%), 321 (3%), 279 (0.7%), 263 (53%), 185 (100%), 109 (10%), 165 (44%), 137 (13%), 123 (13%). Anal. Calcd. for $C_{27}H_{27}ON_2P$•1/4 hexane: C, 76.42%; H, 6.82%; N, 6.25%. Found: C, 76.83%; H, 7.33%; N, 6.71%.

4-Cyclohepten-1-yl-glyoxal 21. To a solution of 2-(4'-cyclohepten-1'-yl)-2-keto-1-triphenylphosphazinoethane **20** (2.6 g, 6.1 mmol) and freshly distilled THF (21 mL) was added sodium nitrite (17.5 mmol). The mixture was cooled to -5°C in an ice-salt bath and hydrochloric acid (12 mL, 2N) was added

dropwise. The temperature was not allowed to exceed 0°C. The mixture which resulted was stirred for 30 minutes between 0°C and 5°C and then allowed to warm to room temperature. Stirring was continued until the nitrous acid was consumed as indicated by a negative test with starch-iodide paper. The aqueous layer was separated, and the organic phase was washed with a mixture of aq. saturated sodium chloride and saturated sodium bicarbonate (4:1) solution until the acid had been removed. The organic phase (THF) was washed with brine and the solvent was removed under vacuum in the absence of heat after which the residue was taken up in ether. The ether solution was dried over anhydrous magnesium sulfate and filtered. To remove $(Ph)_3PO$, dry zinc chloride in dry ether was added to the ether solution until no more white solid [$(Ph)_3PO{\bullet}ZnCl_2$] precipitated. The ether layer was separated, washed well with brine and dried (Na_2SO_4). The ether was removed under reduced pressure in the absence of heat to provide a yellow oil. The oil was immediately chromatographed on silica gel (ethyl acetate-hexane, gradient elution) to provide 4-cyclohepten-1-yl-glyoxal as a yellow liquid (0.83 g, 90%) **21**: IR (neat) 3400 (br), 3010 (s), 2980 (s), 1715 (s), 1705 (s), 1635 (s) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.00-3.15 (9H, m), 5.80 (2H, s), 9.50 (s). MS (CI, CH_4) m/e relative intensity 153 (M^++1, 55%), 135 (100%), 123 (34%), 107 (72%), 95 (39%). This 4-cycloheptenyl-1-glyoxal **21** was subjected to steam distillation to give the semihydrate [^{1}H-NMR ($CDCl_3$) δ 1.40-2.30 (9H, m), 3.30 (2H, s, D_2O exchangeable), 4.60 (2H, s), 5.80 (2H, br, s)]. This material was employed directly in the next experiment.

Tetramethyl 1-(4'-cyclohepten-1'-yl)-*cis*-bicyclo[3.3.0]octane-3,7-dione-2,4,6,8-tetracarboxylate 14a. Dimethyl-3-ketoglutarate (9.8 g, 57 mmol) was added to an aq. solution of sodium bicarbonate (50 mL, pH8.3, 0.17M) and stirred for 20 minutes. At this point, 4-cycloheptenyl-1-glyoxal **21** (4.3 g, 28 mmol) and methanol (140 mL) were added and the mixture was stirred (mechanical stirrer) at room temperature for 7 d. Aqueous sodium bicarbonate was added from time to time to keep the pH of the mixture at 8.3 over the seven day period. Upon acidification of the mixture to pH=7.0 with cold aq. HCl (1N) and evaporation, an oil settled out of the solution and was separated. The oil was washed with methanol to provide a clean yellow liquid which was subjected to a short wash column (silica gel, ethyl acetate). The aq. solution was then extracted with $CHCl_3$ and the $CHCl_3$ layer was evaporated under reduced pressure to provide a brown residue. The residue was chromatographed on silica gel (benzene-ethyl acetate, gradient elution) to give a yellow liquid **14a** (2.1 g). The total yield of **14a** was 9.4 g (72%) obtained as a sticky yellow liquid: IR (neat) 3500-2950 (br), 1740-1620 (br ester and enol absorptions), 1260 (s) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.10-2.30 (10H, m), 3.80 (14H, 4 x OCH_3 groups overlapping with two other protons α to methoxycarbonyl groups), 5.80 (2H, br, s), 9.60 (2H, br s, D_2O exchangeable); MS (CI, CH_4) m/e (relative intensity) 505 (M^++41, 5%), 493 M^++29, 14%), 465 (M^++1, 78%), 433 (100%), 401 (16%), 375 (20%), 369 (7%). This material was employed directly in the next experiment(**14a** is the 2,4,6,8-tetramethoxycarbonyl derivative of **14**).

1-(4'-Cyclohepten-1'-yl)-*cis*-bicyclo[3.3.0]octane-3,7-dione 14. Tetramethyl-1-(4'-cyclohepten-1'-yl)-*cis*-bicyclo[3.3.0]octane-3,7-dione-2,4,6,8-tetracarboxylate **14a** (4.71 g, 0.01 mmol) was added to a solution of aq. HCl (42 mL, 10%) and glacial acetic acid (28 mL). The mixture which resulted was heated to 87°C for 6 h. The solution was cooled, brought to pH=8.0 with cold aq. $NaHCO_3$ solution (10%), and extracted with $CHCl_3$ (4 x 50 mL). The combined extracts were dried (Na_2SO_4) and concentrated under vacuum. The oil which resulted was chromatographed on silica gel (ethyl acetate-hexane, 25:75) to give the dione **14** (1.67 g, 72%): IR (neat) 3500 (br), 3030 (s), 1740 (s) cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.08 (2H, m), 1.56 (1H, m), 1.77 (2H, m), 2.00 (2H, m), 2.12 (2H, dd, J=19.30, 5.41 Hz), 2.19 (2H, d, J=18.81 Hz), 2.29 (2H, m), 2.45 (2H, d, J=18.74 Hz), 2.65 (2H, dd, J=19.30, 8.9 Hz), 2.96 (1H, m), 5.77 (2H, m); ^{13}C-NMR

(125.75 MHz,$CDCl_3$) δ 27.59 (2C, t), 28.78 (2C, t), 38.53 (1C, d), 44.82 (2C, t), 47.60 (2C, t), 49.13 (1C, d), 52.10 (1C, s), 131.53 (2C, d), 217.16 (2C, s); MS (EI, 15 eV) m/e (relative intensity) 232 (M^+, 1.9%), 204 (M^+-CO, 1.4%), 189 (10.0%), 174 (2.9%), 156 (2.5%), 137 (100%). Anal. Calcd, for $C_{15}H_{20}O_2$: C, 77.59%; H, 8.62%. Found: C, 77.53%; H, 8.66%.

Alternate procedure for the direct preparation of 1-(4'-cyclohepten-1'-yl)-*cis*-bicyclo[3.3.0]octane-3,7-dione 14 from 4-cycloheptenyl-1-carboxylic acid 17. The olefinic diketone **14** was routinely prepared on large scale from the acid **17** without purification and characterization of individual intermediates described above. The cycloheptenyl acid **17** (25 g, 0.178 mmol) was dissolved in freshly distilled thionyl chloride (75 mL) as described in the procedure for the preparation of **18.** To ensure the success of the next step, the excess thionyl chloride should be removed as completely as possible. This was done by flash evaporation of the reaction mixture with dry benzene (4 x 25 mL) under vacuum. The acid chloride (23-25 g), obtained by high vaccum distillation (<1 mmHg), was treated with etheral diazomethane (-78°C) followed by stirring with triphenylphosphine (40 g) in dry ether. The light yellow crystalline phosphazinodiazoethane **20** (45-50 g) was carefully decomposed into the substituted glyoxal with nitrous acid at a temperature lower than -2°C. The temperature was critical for this transformation. Slow addition of aq. hydrochloric acid (2N, 180 mL) into the reaction mixture which also contained $NaNO_2$ (18 g) in THF (315 mL) with rapid stirring was necessary to keep the reaction mixture about -5°C. Otherwise, the yield of the reaction was dramatically reduced. The crude cycloheptenyl glyoxal **21** (13-15 g) obtained from a wash column (silica gel) was employed directly for the Weiss reaction with dimethyl-3-ketoglutarate (40 g) under the conditions of CH_3OH (450 mL) and aq. $KHCO_3$ (2%, 150 mL). The crude oil obtained from the reaction was subjected to the acid-mediated hydrolysis and decarboxylation. Pure cycloheptenyl-*cis*-bicyclo[3.3.0]octane-3,7-dione **14** (15.5 g, 37.4% overall from **17**) was obtained by flash chromatography (ethyl acetate/hexane, 25:75). The overall yield ranged from 20-37%. The spectroscopic properties of **14** obtained in this manner were in complete agreement with those of **14** described in the previous experiment.

1-[(4'-Formyl)-cyclohex-3'-en-1'-yl]-*cis*-bicyclo[3.3.0]octane-3,7-dione 22 and 8-(3'-oxopropyl)-tricyclo[7.3.0.^{1,9}0^{4,9}]dodec-4-ene-3,11-diones 23 and 24. The olefinic diketone **14** (0.3 g, 1.29 mmol) was dissolved in ethyl acetate (80 mL) in a three neck flask (250 mL) equipped with a magnetic stirrer and a low temperature thermometer. The flask was placed in a cooling bath (dry ice-ethyl acetate) and the temperature was allowed to drop to -78°C. Ozone was generated (O_3 flow, 3.7 L/min; 115 VAC; O_2 pressure, 6.5 psi) and bubbled through the cold solution until it took on a light blue coloration. Excess ozone was purged from the reaction medium with dry nitrogen. Methanol (18 mL) and dimethyl sulfide (18 mL) were added into the cold solution. The mixture was then stirred and allowed to slowly warm to room temperature. After 16 h, the reaction was worked up by removal of solvent under reduced pressure in a fume hood, and the residue was carefully flash evaporated with toluene (3 x 20 mL) under vacuum. The oily residue which resulted was purified by a short wash column (silica gel, ethyl acetate) to provide a dialdehyde **13** the structure of which was confirmed by NMR spectroscopy [^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.49 (m), 1.83 (m), 2.10-2.75 (m), 2.95 (m), 9.77 (s)]. The dialdehyde was not purified or characterized further but directly employed in the next step.

The dialdehyde **13** was dissolved in a mixture of distilled THF (80 mL) and aq. HCl (1N, 5 mL). The mixture which resulted was stirred at room temperature under an atmosphere of argon for 22 h. Solid $NaHCO_3$ (5 g) was added to neutralize excess HCl. The mixture was then filtered and concentrated under reduced

pressure. The residue was dissolved in ethyl acetate (50 mL) and washed in succession with saturated aq. $NaHCO_3$, H_2O, brine and dried ($MgSO_4$). Removal of solvent in vacuum provided a crude oil which was purified by wash column chromatography (ethyl acetate/hexane, 8:2) to provide a colorless oil (240 mg, 75.4%). The ^{1}H-NMR spectrum of the oil clearly indicated the presence of two major aldehydic components by observation of the two major aldehydic signals at δ 9.79 and δ 9.41 ppm, respectively, in a ratio of about 1:1.3 (**23/24**:**22**). This mixture appeared as only one spot on TLC (R_f=0.40, ethyl acetate/hexane, 9:1). The two major components were separated by flash chromatography ($CHCl_3$/MeOH, 20:1) to provide **23/24** and **22**. The tricyclic aldehydes **23/24** (R_f=0.46, $CHCl_3$/MeOH, 20:1) were not separable despite repeated attempts under various conditions.

22 (41.3%) (R_f=0.68, $CHCl_3$/MeOH, 20:1): ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.20 (1H, dq, J=12.21, 5.18 Hz), 1.57 (1H, tdd, J=11.95, 4.65, 2.31 Hz), 1.74 (1H, m), 1.81 (1H, m), 2.07 (1H, dd, J=19.64, 6.24 Hz), 2.15 (1H, dd, J=19.68, 4.30 Hz), 2.19 (2H, dd, J=18.85, 4.29 Hz), 2.33 (1H, m), 2.38 (1H, dd, J=18.79, 0.93 Hz), 2.43 (1H, d, J=19.49 Hz), 2.44 (1H, m), 2.50 (1H, m), 2.60 (1H, ddd, J=19.66, 8.49, 1.27 Hz), 2.67 (1H, ddd, J=19.57, 9.33, 1.03 Hz), 2.96 (1H, m), 6.82 (1H, m), 9.42 (1H, s); ^{13}C-NMR (62.896 MHz, $CDCl_3$) δ 23.35 (1C, t), 24.42 (1C, t), 27.03 (1C, t), 38.38 (1C, d), 39.56 (1C, d), 44.18 (1C, t), 44.58 (1C, t), 46.06 (1C, t), 47.31 (1C, t), 50.46 (1C, s), 140.37 (1C, s), 150.40 (1C, d), 193.54 (1C, d), 216.33 (1C, s), 216.66 (1C, s); MS (EI, 70 eV) m/e (relative intensity) 247 (M^+ + 1, 1.7%), 246 (M^+, 9.5%), 245 (M^+ - 1, 1.4%), 228 (45.9%), 218 (12.4%), 203 (10.0%), 200 (8.2%), 188 (10.8%), 175 (8.4%), 164 (8.5%), 160 (8.5%), 149 (9.5%), 137 (100%), 136 (31.3%, 121 (16.0%), 109 (32.1%).

23 (27.9%) : ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.26 (1H, m), 1.71 (3H, m), 1.80 (2H, m), 2.04 (1H, dd, J=18.80, 11.00 Hz), 2.13 (1H, m), 2.23 (1H, m), 2.30 (1H, d, J=19.27 Hz), 2.34 (1H, d, J=18.47 Hz), 2.39 (1H, d, J=18.65 Hz), 2.48-2.54 (2H, m), 2.56 (1H, dd, J=18.56, 7.07 Hz), 2.64 (1H, dd, J=18.80, 8.72 Hz), 2.89 (1H, m), 6.77 (1H, t, J=3.50 Hz), 9.79 (1H, s); ^{13}C-NMR (62.896 MHz, $CDCl_3$) δ 18.99 (1C, t), 20.96 (2C, t), 35.74 (1C, d), 35.89 (1C, d), 41.65 (1C, t), 42.19 (1C, t), 42.88 (1C, t), 45.65 (1C, s), 50.34 (1C, t), 133.41 (1C, d), 140.75 (1C, s), 201.30 (1C, d), 204.09 (1C, s), 217.02 (1C, s); MS (EI, 70 eV) m/e (relative intensity) 246 (M^+, 75.7%) 228 (29.8%), 203 (63.8%), 188 (51.1%), 175 (30.9%), 160 (100%), 145 (68.8%), 144 (68.8%), 131 (85.1%), 120 (70.2%), 105 (93.6%).

24 (4.4%): The following signals could be identified for the minor isomer (*ca.* 12% as compared to the major isomer by integration of the ^{1}H-NMR spectrum). ^{1}H-NMR δ 9.76 (s), 6.72 (m); ^{13}C-NMR δ 21.93, 23.35, 25.50, 32.15, 4046, 41.34, 43.20, 44.73, 45.04, 128.89, 134.15. The other signals were overlapped by the signals of the major isomer **23.**

1-(4'-Heptanedioic acid)-*cis*-bicyclo[3.3.0]octane-3,7-dione 15. The 1-(4'-cyclohepten-1'-yl)-*cis*-bicyclo[3.3.0]octane-3,7-dione **14** (0.5 g, 2.1 mmol) was dissolved in dry acetone (freshly distilled over $KMnO_4$, 45 mL) and cooled in a dry ice-ethyl acetate bath to -78°C. Ozone was bubbled through the solution until the solution took on a light blue coloration (4 minutes). Dry nitrogen was passed through the solution for 25 min. to purge the excess ozone. At this point, Jones' reagent (17.5 mL, 1.2M) was added dropwise over a period of 12 minutes in such a manner as to keep the temperature below -60°C. The mixture was stirred at -78°C for 40 min., and allowed to warm to -5°C. Water (60 mL), ethyl acetate (100 mL) and solid sodium bisulfite were added to the mixture until the organic phase separated and became colorless. The aqueous phase was extracted with ethyl acetate (15 x 60 mL). The organic layers were combined and concentrated under reduced

pressure to furnish **15** (0.41 g) as an oil. The aqueous phase was subjected to continuous extraction to provide additional quantities (0.32 g) of the oil. The combined oils were recrystallized from ethyl acetate to provide 1-(4'-heptanedioic acid)-*cis*-bicyclo[3.3.0]octane-3,7-dione (0.61 g, 96%) as a white solid **15**: mp 174-176°C; FTIR (KBr) 3303 (br), 2945, 1733, 1715, 1405, 1300, 1201, 1159, 1118 cm^{-1}; ^{1}H-NMR (250 MHz, DMSO-d_6) δ 1.34 (4H, m), 1.67 (2H, m), 2.00-2.60 (11H, m), 2.86 (1H, m), 10.77 (2H, br. s); ^{13}C-NMR (62.896 MHz, DMSO-d_6) δ 25.89 (2C, t), 32.75 (2C, t), 38.06 (1C, d), 42.08 (1C, d), 43.63 (2C, t), 46.72 (2C, t), 51.12 (1C, s), 173.95 (2C, s), 217.86 (2C, s); MS (C.I., CH_4) m/e (relative intensity) 297 (M^++1, 12.9%), 279 (M^++1-H_2O, 100%), 261 (M^++1-2H_2O, 45.4%), 251 (13.5%), 233 (30.7%), 219 (10.6%), 169 (10.3%). Anal. Calcd, for $C_{15}H_{20}O_6$: C, 60.81; H, 6.76. Found: C, 60.63; H, 6.76.

6-Hydroxy-8-(2'-carboxyethyl)-tricyclo[7.3.0.^{1,9}0^{4,9}]dodec-4-ene-3,11-dione 26. The diacid **15** (1.1 g, 3.7 mmol) and dry pTSA (800 mg) were dissolved in dry dioxane (30 mL) under an atmosphere of nitrogen. Dry benzene (180 mL) was then added to the mixture *via* a double ended needle under nitrogen. The mixture which resulted was stirred and allowed to warm to reflux (oil bath temperature, 120°C) with continuous removal of water by a Dean-Stark trap for 24 d. The reaction mixture was allowed to cool to room temperature and the solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate (150 mL) and washed with water (25 mL), brine and dried ($MgSO_4$). The solution was passed through a short wash column (silica gel) which was eluted with THF/EtOAc (1:1) to provide the tricyclic monoacid (756 mg, 73.2%). **26**: FTIR (KBr); 3466, 2956 (br. s), 1750, 1708, 1420, 1307, 1257, 1187 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.25-3.00 (m), 9.75 (bs); ^{13}C-NMR (62.896 MHz, $CDCl_3$) δ 21.25, 21.92, 23.23, 31.61, 36.54, 38.13, 42.12, 42.64, 50.31, 51.07, 113.38, 169.84, 177.84, 205.95, 217.72; MS (CI, CH_4) m/e (relative intensity) 279 (M^++1, 100%), 261 (M^++1-H_2O, 15.0%).

Cyclization of the diketodiacid 15 in refluxing toluene to provide the transannular tetracyclic tetraone 27. The diketodiacid **15** (300 mg, 1.01 mmol) was added to a 100 mL flask which contained dry toluene (60 mL). The mixture which resulted was stirred and allowed to warm to reflux with continuous removal of water *via* a Dean-Stark trap under nitrogen for two weeks. The diacid went into solution upon heating. The reaction mixture was allowed to cool to room temperature. The solvent was removed under reduced pressure. The residure was dissolved in ethyl acetate and washed with water, brine and dried ($MgSO_4$). The crude material (70%) was purified by wash column chromatography (silica gel, $CHCl_3$/dioxane, 7:3) to provide a transannular tetracyclic tetraone **27** as the major isolable material: FTIR (KBr) 3431, 2959, 1747 (sh), 1736, 1704 (sh), 1181 cm^{-1};^{1}H-NMR (250 MHz, $CDCl_3$) δ 2.83 (1H, br. s), 2.71 (1H, dd, J=9.4, 19.2 Hz), 2.53 (1H, br. s), 2.50-2.37 (3H, m), 2.24 (1H, m), 2.20 (1H, dt, J=3.1, 13.5 Hz), 2.15 (1H, dd, J=9.3, 19.1 Hz), 2.06 (1H, m), 1.96 (1H, dd, J=1, 15.1 Hz), 1.94 (1H, dt, J= 1.8, 13.5 Hz), 1.85 (1H, m), 1.75 (1H, dd, J=3.5, 13.5Hz), 1.60 (1H, br. s); ^{13}C-NMR (62.896 MHz, $CDCl_3$) δ 28.31, 34.08, 36.51, 40.77, 45.05, 46.68, 47.56, 51.70, 55.65, 65.11, 104.61, 184.12, 199.01, 210.21, 215.71; MS (CI, CH_4) m/e (relative intensity) 261 (M^++1, 100%), 243 (M^++1-CO, 35.6%), 162 (12.3%).

Acknowledgement: The authors wish to thank the NSF (CHE 9111392) and the donors of the Petroleum Research Fund for generous financial support of this research.

References

1. Hoffmann, R.; Alder, R. W.; Wilcox, C. F. *J. Am. Chem. Soc.* **1970**, *92*, 4992. Hoffmann, R. *Pure Appl. Chem.* **1971**, *28*, 181.
2. Greenberg, A.; Liebman, J. F. *Strained Organic Molecules*, Academic Press, New York, **1978**.
3. Collins, J. B.; Dill, J. D.; Jemmis, E. D.; Apeloig, Y.; Schleyer, P. v. R.; Seeger, R.; Pople, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 5419.
4. Wiberg, K. B.; Ellison, G. B. *Tetrahedron* **1974**, *30*, 1573. Wiberg, K. B.; Ellison, G. B.; Wendoloski, J. J. *J. Am. Chem. Soc.* **1976**, *98*, 1212.
5. a). Durmaz, S.; Murrell, J. N.; Pedlay, J. B. *J. Chem. Soc. Chem. Commun.* **1972**, 933. Murrell, J. N.; Pedlay, J. B.; Durmaz, S. *J. Chem. Soc. Faraday Trans. 2* **1973**, *69*, 1370. b). Crans, D. C.; Snyder, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 7153. c). Krogh-Jespersen, M.-B.; Chandrasekhar, J.; Würthwein, E.-U.; Collins, J. B.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1980**, *102*, 2263. d). Monkhorst, H. *J. Chem. Soc. Chem. Commun.* **1968**, 1111. e). Olah, G.; Klopman, G. *Chem. Phys Lett.* **1971**, *11*, 604. f). Minkin, V. I.; Minyaev, R. M.; Zacharov, I. I. *J. Chem. Soc. Chem. Commun.* **1977**, 213. g). Lathan, W. A.; Hehere, W. J.; Curtiss, L. A.; Pople, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 6377.
6. Keese, R.; Pfenninger, A.; Roesle, A. *Helv. Chim. Acta* **1979**, *62*, 326.
7. Chandrasekhar, J.; Würthwein, E.-U.; Schleyer, P. v. R. *Tetrahedron* **1981**, *37*, 921.
8. Calculations by Dewar *et al.* and Schang *et al.* suggested instability for **1** and **2**. See: Bingham, R. C.; Dewar, M. J. S.; Ho, D. H. *J. Am. Chem. Soc.* **1975**, *97*, 1285, 1294.
9. Böhm, M. C.; Gleiter, R.; Schang, P. *Tetrahedron Lett.* **1979**, 2575.
10. a). Luyten, M.; Keese, R. *Tetrahedron* **1986**, *42*, 1687. b). Pfenninger, A.; Roesle, A.; Keese, R. *Helv. Chem. Acta* **1985**, *68*, 493. c). Luyten, M.; Keese, R. *Angew. Chem.* **1984**, *96*, 358. d). Thommen, M.; Gerber, P.; Keese, R. *Chimia* **1991**, *45*, 21. e). Mani, J.; Schuttel, S.; Zhang, C.; Bigler, P.; Müller, C.; Keese, R. *Helv. Chim. Acta* **1989**, *72*, 487. f). Keese, R.; Luef, W.; Mani, J.; Schuttel, S.; Schmid, M.; Zhang, C. In *Strain and its Implications in Organic Chemistry*, de Meijere, A. and Blechert, S., Kluwer Academic Publisher, **1989**, p283. g). van der Waals, A.; Keese, R. *J. Chem Soc. Chem. Commun.* **1992**, 570.
11. a). Gupta, A. K.; Fu, X.; Snyder, J. P.; Cook, J. M. *Tetrahedron* **1991**, *47*, 3665. b). Mitschka, R.; Oehldrich, J.; Takahashi, K.; Cook, J. M.; Weiss, U.; Silverton, J. *Tetrahedron* **1981**, *37*, 4521.
12. Kuck, D. In *Quasicrystals, Networks, and Molecules of Fivefold Symmetry*, Hargittai, I. (Ed.), VCH Publishers, New York, **1990**, Chapter 19.
13. Kuck, D.; Schuster, A.; Krause, R. A. *J. Org. Chem.* **1991**, *56*, 3472. b). Paisdor, B.; Kuck, D. *J. Org. Chem.* **1991**, *56*, 4753. c). Kuck, D.; Schuster, A.; Ohlhorst, B.; Sinnwell, V.; de Meijere, A. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 595. d). Kuck, D. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 508. e). Kuck, D.; Bögge, H. *J. Am. Chem. Soc.* **1986**, *108*, 8107. f). Kuck, D.; Schuster, A. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1192.
14. Kuck, D. personal communication, **1992**.
15. For the syntheses of the [5.5.5.7]fenestrane natural product laurenene **4** see references 15-17. Tsunoda, T.; Amaike, M.; Tambunan, U. S. F.; Fujise, Y.; Ito, S. *Tetrahedron Lett.* **1987**, *28*, 2537.
16. Crimmins, M. T.; Gould, L. D. *J. Am. Chem. Soc.* **1987**, *109*, 6199.
17. Wender, P. A.; von Geldern, T. W.; Levine, B. H. *J. Am. Chem. Soc.* **1988**, *110*, 4858.
18. Mitschka, R.; Cook, J. M.; Weiss, U. *J. Am. Chem. Soc.* **1978**, *100*, 3973.
19. Deshpande, M.; Venkatachalam, M.; Jawdosiuk, M.; Kubiak, G.; Weiss, U.; Cook, J. M. *J. Am Chem. Soc.* **1985**,*107*, 4786.
20. Deshpande, M. N.; Wehrli, S.; Jawdosiuk, M.; Guy, Jr., J. T.; Bennett, D. W.; Cook, J. M.; Depp, M. R.; Weiss, U. *J. Org. Chem.* **1986**, *51*, 2436.
21. a). Venkatachalam, M.; Wehrli, S.; Kubiak, G.; Cook, J. M.; Weiss, U. *Tetrahedron Lett.* **1986**, 4111. b). Gupta, A. K.; Lannoye, G. S.; Kubiak, G.; Schkeryantz, J.; Wehrli, S.; Cook, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 2169.
22. Silverstein, R. M.; Clayton, G. B.; Morrill, T. C. *Spectrometric Identification of Organic Compounds* 5th ed., John Wiley and Sons: New York, **1991**.
23. a). Han, W. C.; Takahashi, K.; Cook, J. M.; Weiss, U.; Silverton, J. V. *J. Am. Chem. Soc.* **1982**, *104*, 318. b). Eaton, P. E.; Mueller, R. H.; Carlson, G. R.; Cullison, D. A.; Cooper, G. F.; Chou, T.-C.; Krebs, E. -P. *J. Am. Chem. Soc.* **1977**, *99*, 2751.
24. Marguardt, D.; Newcomb, M. *Syn. Comm.* **1988**, *18*, 1193.
25. Stork, G.; Landesman, H. *J. Am. Chem. Soc.* **1956**, *78*, 5129.
26. Bestmann, H. J; Klein, O.; Göthlich, L.; Buckschewski, H. *Chem. Ber.* **1963**, *96*, 2259.
27. Fu, X. Ph.D. Thesis, University of Wisconsin-Milwaukee, **1992**.