filtrate was concentrated in vacuo to afford 13.09 g (84%) of **6a** as a yellow oil: IR (neat) 3465 (s), 3365 (s), 3220 (m), 3065 (m), 3045 (m), 3015 (m), 2955 (s), 2830 (s), 1620 (s), 1600 (s), 1120 (s), 1075 (s), 800 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.57 (s, 3 H, CH_3), 3.47 (s, 3 H, OCH_3), 3.67 (br s, 2 H, NH_2), 6.58 (d, 2 H, J = 7 Hz, *p*-NH_2ArH), 7.30 (d, 2 H, J = 7 Hz, *p*-NH_2ArH), 7.21-7.41 (m, 3 H, ArH), 7.44-7.64 (m, 2 H, ArH); ^{13}C NMR ($CDCl_3$) δ 3.5, 51.0, 114.4, 127.7, 129.5, 134.3, 135.7, 148.0; EIMS, *m/e* (relative intensity) 244 (P + 1, 12.2), 243 (P, 55.3), 228 (P - Me, 74.0); high-resolution mass spectrum, *m/e* 243.1086 ($C_{14}H_{17}NOSi$ requires *m/e* 243.1079.

(4-Aminophenyl)methylphenylsilanol (7a). A solution of 4-(methoxymethylphenylsilyl)benzenamine (**6a**) (9.370 g, 38.56 mmol) in 50 mL of 1:1 acetone-water was stirred for 2 days at 80 °C. The mixture was concentrated under reduced pressure, and $CHCl_3$ (30 mL) was added. The reaction mixture was washed with H_2O (30 mL). The aqueous layer was then washed with $CHCl_3$ (3 × 30 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo to afford 8.237 g (93%) of (4-aminophenyl)methylphenylsilanol (**7a**) as a dark red, viscous oil: IR (neat) 3625-3100 (br s), 3065 (m), 3045 (m), 3015 (m), 2960 (m), 1620 (s), 1600 (s), 1505 (s), 1430 (s), 1260 (s), 1120 (s), 1065 (br m), 1000 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.55 (s, 3 H, CH_3), 3.42 (s, 2 H, NH_2), 6.51 (d, 2 H, J = 8 Hz, *p*-NH_2ArH), 7.16 (d, 2 H, J = 8 Hz, *p*-NH_2ArH), 7.18-7.35 (m, 3 H, ArH), 7.38-7.58 (m, 2 H, ArH); FAB-MS, *m/e* (230, P + 1).

4,4'-(1,3-Dimethyl-1,3-diphenyl-1,3-disiloxanediyl)bis(benzenamine) (8a). A solution of (4-aminophenyl)methylphenylsilanol (**7a**) (2.276 g, 9.939 mmol) in 3 mL of CH_3CN was treated dropwise with 0.18 mL (0.18 mmol) of 1.0 M aqueous $Bu_4N^+OH^-$. The mixture was stirred for 2 days at ambient temperature, concentrated under reduced pressure, and treated with $CHCl_3$ (30 mL). The reaction mixture was washed with $CHCl_3$ (3 × 30 mL). The combined organic extracts were washed with H_2O until the color of the organic layer turned from green to brown. The organic extract was dried over $MgSO_4$ and concentrated in vacuo to afford 1.96 g (90%) of 4,4'-(1,3-dimethyl-1,3-diphenyl-1,3-disiloxanediyl)bis(benzenamine) (**8a**) as a dark red oil: IR (neat) 3465 (m), 3375 (s), 3205 (m), 3060 (m), 3040 (m), 3010 (s), 2950 (m), 1620 (s), 1595 (s), 1500 (s), 1425 (s), 1115 (s), 1050 (br s), 785 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.50 (s, 6 H, CH_3), 3.66 (br s, 4 H, NH_2), 6.54 (d, 4 H, J = 8 Hz, *p*-NH_2ArH) 7.12-7.36 (m, 10 H, *p*-NH_2ArH + ArH), 7.39-7.56 (m, 4 H, ArH); ^{13}C NMR ($CDCl_3$) δ 0.4, 114.3, 127.5, 129.2, 133.3, 133.9, 135.4, 138.5, 147.6; CIMS, *m/e* (relative intensity) 497 (P + 57, 16.4), 441 (P + 1, 100.0), 348 (P - C_6H_6N, 53.7). Anal. Calcd for $C_{26}H_{28}N_2OSi_2$: C, 70.87; H, 6.42; N, 6.36. Found: C, 70.60; H, 6.49; N, 6.29.

1,3-Bis(4-isocyanatophenyl)-1,3-dimethyl-1,3-diphenyldisiloxane (1a). A solution of phosgene (ca. 40 mL) in chlorobenzene (25 mL) at 0 °C was treated dropwise with a solution of 4,4'-(1,3-dimethyl-1,3-diphenyl-1,3-disiloxanediyl)bis(benzenamine) (**8a**) (1.96 g, 4.45 mmol) in chlorobenzene (50 mL). The mixture was heated to reflux and maintained at that temperature for 4.5 h while phosgene gas was slowly passed through the reaction mixture. The solution was purged with N_2 (gas) for 45 min and then cooled to ambient temperature. The volatiles were removed in vacuo to afford 2.03 g (93%) of 1,3-bis(4-isocyanatophenyl)-1,3-dimethyl-1,3-diphenyldisiloxane (**1a**) as a dark brown oil: IR (neat) 3070 (m), 3050 (w), 3025 (w), 2960 (m), 2275 (br s), 1595 (s), 1515 (m), 1430 (s), 1260 (s), 1115 (s), 1095 (s), 1060 (br s), 795 (s), 735 (s), 700 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.58 (s, 6 H, CH_3), 7.05, (d, 4 H, J = 8 Hz, *p*-OCNAr*H*), 7.23-7.67 (m, 14 H, *p*-OCNAr*H* + ArH).

Registry No. **1a**, 102368-11-6; **1b**, 102368-12-7; **2**, 106-40-1; **3**, 63911-87-5; **4**, 5089-33-8; **5a**, 102368-04-7; **5b**, 69185-17-7; **6a**, 102368-05-8; **6b**, 102368-06-9; **7a**, 102368-07-0; **7b**, 102368-08-1; **8a**, 102368-09-2; **8b**, 102368-10-5.

Formation of the Tetracyclo[5.4.2.0^{2,6}.0^{2,9}]tridecane Ring System by a Novel Transannular Aldolization Reaction[1]

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Attempts to employ the "aldol approach"[5] to convert 1-(1,5-dioxopentyl)-*cis*-bicyclo[3.3.0]octane-3,7-dione (**7**) into the corresponding [5.5.5.5]fenestrane derivative **8b** were thwarted when the dialdehyde **7** underwent transannular cyclization instead to provide the two diastereomeric diketodiacetates **18a** and **18b**. The structures of the trans,trans isomer **18a** and its cis,trans diastereomer **18b** were assigned, on the basis of 1D and 2D NMR (COSY and ^1H-^{13}C correlated) experiments; moreover, the structure of **18a** was confirmed by X-ray crystallography. The difference between the mode of cyclization of the diacid **5** to provide the [5.5.5.5]fenestrane **6** as compared to the transannular cyclization of dialdehyde **7** to furnish the [5.4.2.0^{2,6}.0^{2,9}] system in **18** is discussed.

The synthesis of saturated [4.4.4.4] and unsaturated [5.5.5.5] derivatives of [*m.n.o.p.*]fenestranes[2-4] has received much attention recently in particular with respect to the deformation of the central carbon atom toward a planar

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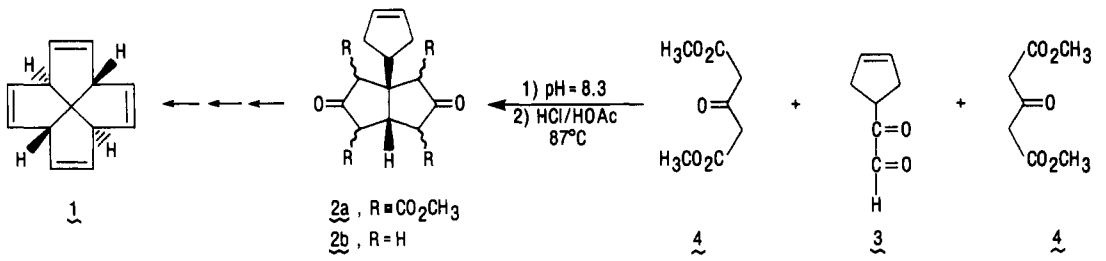
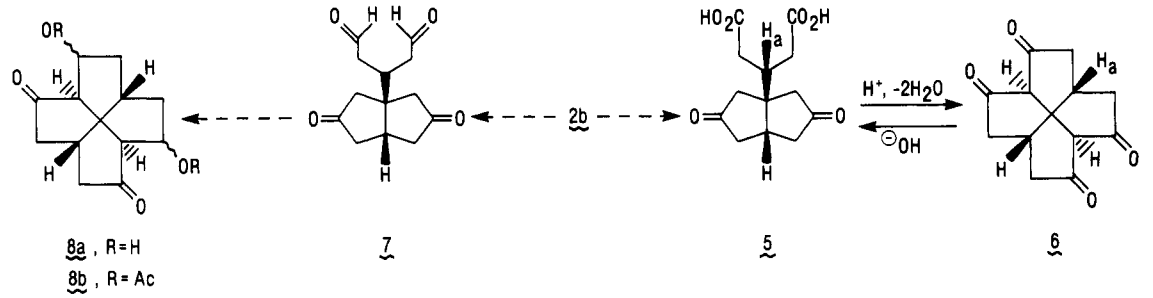
0022-3263/86/1951-2436$01.50/0

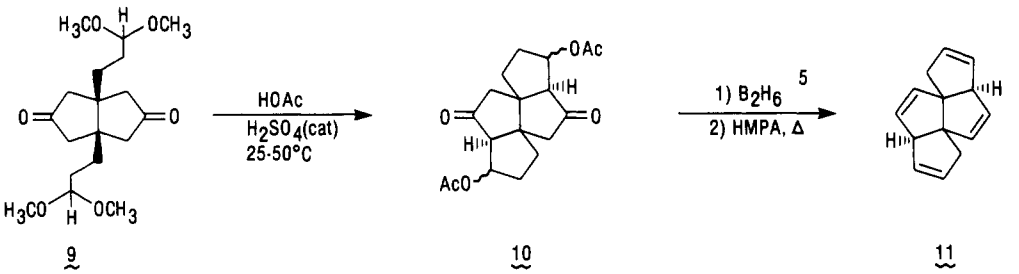
Scheme I



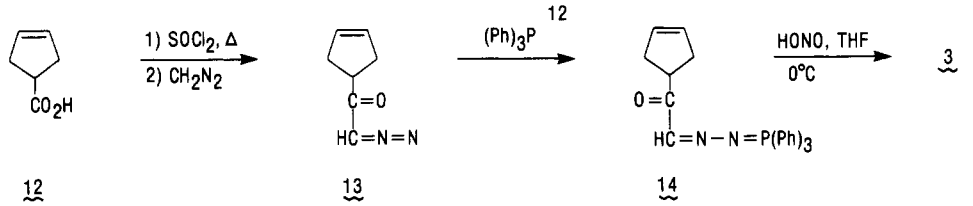
Scheme II



Scheme III



Scheme IV



geometry.[3,4] Although the possibility of such distortion is still controversial,[3a-g] several laboratories have been involved in attempts to synthesize the [5.5.5.5]fenestranehexaene system in order to provide a route to severely strained carbon atoms which have been deformed from the normal tetrahedral bond angle of 109.5°; such a phenomenon has been termed the planarization of carbon by Keese.[3g] Synthetic efforts in our own laboratory have centered on the preparation of unsaturated derivatives of the [5.5.5.5]fenestrane system, for example stauran-2,5,8,11-tetraene **1**.[4f] In this report aspects of this research which have resulted in the unexpected formation of compounds derived from the tetracyclo[5.4.2.0^{2,6}.0^{2,9}]tridecane ring system are described.

Retrosynthetic analysis of the highly symmetrical **1** indicates that synthetic entry into such a system might be accomplished from the corresponding 1-(3-cyclopentenyl)-*cis*-bicyclo[3.3.0]octane-3,7-dione derivative **2a**, available in gram quantities[1] from condensation of 3-cyclopenteneglyoxal **3** with 2 equiv of dimethyl 3-oxoglutarate (**4**) (Scheme I). Acidic hydrolysis of this 1:2 adduct **2a**, accompanied by decarboxylation, would then yield **2b**, the pivotal intermediate for the present discussion. This intermediate **2b** (Scheme II) could be converted into the diacid **5**, followed by cyclization to stauran-2,5,8,11-tetrone **6**; the latter reaction has been previously reported.[4a] Alternatively, the cyclopentene-substituted *cis*-bicyclo[3.3.0]octane-3,7-dione **2b** could presumably be converted into dialdehyde **7**, to be cyclized subsequently to the [5.5.5.5]fenestrane systems **8a** or **8b** by a double intramolecular aldol cyclization. The latter approach has recently been termed the "aldol approach".[5]

Earlier, it had been demonstrated that β-diketones of the *cis*-bicyclo[3.3.0]octane-2,8-dione series, e.g., **6**, are readily cleaved by nucleophiles via processes related to retro-Claisen reactions.[6] These ring scissions have been observed by Eaton[7] and Dauben[8] as well as in our labo-

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ratories.[6,9] The lability of compounds such as **6** toward nucleophiles prompted the close examination of the aldol route **2b** → **7** → **8a** to [5.5.5.5]fenestranes (Scheme II). This sequence appeared particularly attractive, since Venkatachalam et al.[5] have recently converted the diketo diacetal **9** into the corresponding polyquinane **10** via the aldol approach. The key feature of this conversion (Scheme III) rested on trapping of the resulting aldols as the diacetates; this prevented ring cleavage via a retroaldol reaction. Reduction of **10** with diborane, followed by dehydration, gave the desired tetraene **11**. Studies directed toward the analogous conversion of dialdehyde **7** into tetraene **1** therefore appeared worthy of active investigation.

The synthesis of 3-cyclopenteneglyoxal **3** began with 3-cyclopentenecarboxylic acid (**12**), as illustrated in Scheme IV. This material can be prepared readily by a simple three-step procedure, according to the method reported by Schmid[10a] and Murdock.[10b] This sequence has been significantly improved by the reaction of disodiomalonic ester with *trans*-1,4-dichloro-2-butene.[10a] The vinyl cyclopropane diethyl ester i (see ref 11) produced in this process undergoes a vinylcyclopropane rearrangement to provide the malonate ii,[11] from which **12** was obtained on hydrolysis.[1]

From the acid **12**, the desired diazo ketone **13** was prepared in high yield by an Arndt-Eistert reaction, as shown in Scheme IV. The diazo ketone **13** was purified by careful Kugelrohr distillation under high vacuum. *Caution: The diazo ketone **13** will decompose explosively if the distillation is not carried out under high vacuum at temperatures below 80 °C.* The ^{13}C NMR spectrum of **13** contained only five lines, as expected for structure **13**. Moreover, bands in the IR spectrum of **13** at 2105 cm^{-1} (C=N=N) and 1731 cm^{-1} (C=O) fully supported the assignment of the structure as shown.

The diazo ketone was stirred with triphenylphosphine to give a 93% yield of the crystalline phosphazine **14**, according to a method previously reported by Bestmann.[12] A sample of the crude diazo ketone **13** could be employed directly in this step, since only slightly better results were obtained when **14** was obtained from distilled **13**. The structure of **14** was confirmed by IR, NMR, and mass spectroscopy.[1] Conversion of **14** into the desired 3-cyclopenteneglyoxal **3** was effected by treatment with nitrous acid[12] at 0 °C. Moffett et al.[13] have reported that alicyclic glyoxals were hygroscopic oils which decompose upon distillation and polymerize on standing; however, Kugelrohr distillation of **3** under high vacuum (0.1–0.05 mm Hg) provided the yellow compound **3** in moderate yield. The glyoxal **3**, moreover, could be obtained in pure form by flash chromatography in yields ranging from 60% to 85%. Apparently, **3** exists as a mixture of the anhydrous compound and its semihydrate, analogous to the cases reported by Moffett[14] and Han.[15] This phenomenon resulted in a complex ^{13}C and ^{1}H NMR spectrum of **3**; however, the bis(2,4-dinitrophenylhydrazine) derivative of **3** was a crystalline solid which gave acceptable carbon and hydrogen data on elemental analysis. A detailed analysis of the spectra of **3** is contained in the Experimental Section and in ref 1.

Because of its lability, **3** was reacted immediately with 2 equiv of dimethyl 3-oxoglutarate (**4**), at pH 8.3, as illustrated in Scheme I. The yields of tetramethyl 3,7-dioxo-1-(3-cyclopentenyl)-*cis*-bicyclo[3.3.0]octane-2,4,6,8-tetracarboxylate (**2a**) ranged from 70% to 90%; at pH 5.6 only 50% was obtained in agreement with earlier work reported on this condensation.[16] The chemical ionization mass spectrum of the desired tetraester **2a** contained a parent ion at 437 (M + 1) amu, followed by ions which corresponded to the consecutive loss of three molecules of methanol, analogous to earlier reports by Biemann[17] and Mitschka[18] for similar systems. The IR, ^{1}H NMR, and ^{13}C NMR spectra of **2a** were very similar to those of previous tetraesters[16] and confirmed the structural assignment.[1] Tetraester **2a** was hydrolyzed at 87 °C under conditions similar to those previously reported[16] to provide the key intermediate, 1-(3-cyclopentenyl-*cis*-bicyclo[3.3.0]-octane-3,7-dione (**2b**), in 90–96% yield.

Initial attempts to oxidize the cyclopentene unit of **2b** to the desired 3-substituted glutaraldehyde derivative **7** included the following: $OsO_4/NaIO_4$; O_3, acetone, −75 °C, dimethyl sulfide (DMS); O_3, CH_3OH, −75 °C, DMS; O_3, EtOAc, H_2/Pd. From the reaction of ozone with **2b** in either acetone or ethyl acetate,[19] it was possible to isolate a stable, crystalline ozonide (mp 155–156 °C). Unfortunately, on reduction of this material at −20 to 25 °C a complex mixture of products was obtained. Since some of the desired dialdehyde **7** appeared to be present in the mixture (see below), it is felt **7** underwent partial cyclization, and this rendered the material unsuitable for purification.[19] In view of this it was decided to protect both carbonyl groups of **2b** by ketalization with ethylene glycol. This was accomplished in excellent yield to provide the bis(ethylene ketal) **15**, as illustrated in Scheme V. Treatment of **15** with ozone (CH_3OH, −70 °C), followed by reductive workup (Pd/C, H_2 or $NaBH_4$) furnished a mixture of products from which only the lactone iii[20] could

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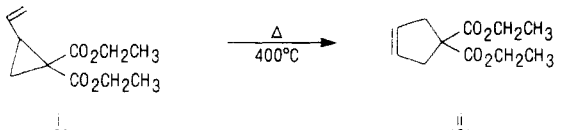
(11) The rearrangement (300-g scale) is carried out at 400 °C by percolating i through a column packed with glass beads. The crude material from this reaction is recycled through the column until conversion of i into ii is complete.



i ii

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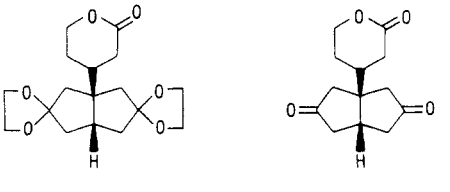
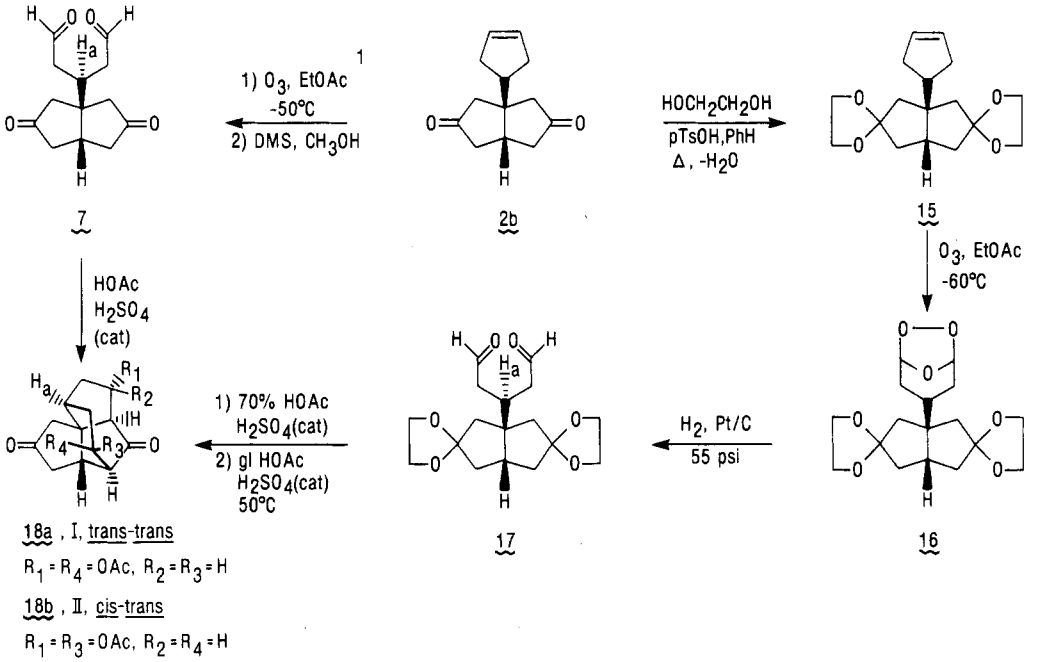
(20) The lactones iii and iv were isolated from the reactions of **15** and **2b**, respectively, with ozone followed by reductive workup (see ref 1 for spectral data and experimental details).



iii iv

Scheme V



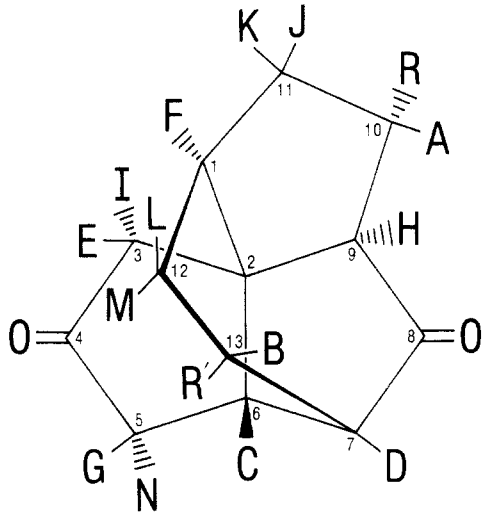
be isolated. The structure of the lactone was deduced from spectral data and elemental analysis.[1] The formation of lactones related to iii has been reported to occur via the radical decomposition of an intermediate hydroperoxide during the hydrogenolysis of ozonides[21a] especially when the reaction medium is not kept at low temperature. Fischer et al.[21b] had reported that cyclopentene was cleanly oxidized with ozone in ethyl acetate. This procedure worked well in our hands for the bisketal **15** was converted into a stable ozonide (O_3, EtOAc, –60 °C) and then reduced (H_2, Pt/C, EtOAc) to the dialdehyde **17** in excellent yield. Similar results were observed with **2b** when ethyl acetate (–50 °C) was employed as the solvent (see below) followed by reduction with DMS (CH_3OH, –50 °C).

It was anticipated that conversion of **15** into a diketo dialdehyde, followed by intramolecular aldolization, would furnish 2,6-dihydroxystaurane-8,12-dione **8a**, thus avoiding the labile β-diketone functionality encountered earlier.[6] The initial attempts to cyclize the diketal dialdehyde **17** to the desired [5.5.5.5]fenestrane system **8a** were carried out with aqueous hydrochloric acid in THF,[1] in a fashion similar to the conditions successfully employed for the preparation of triquinacene.[22] This method was unsuccessful, presumably because of the facile retroaldol reactions which can occur in [5.5.5.5]fenestrane systems such as **8a**. Attempts, reported by Keese,[23] to prepare a related [5.5.5.5]fenestrane system through formation of the final ring via aldolization were similarly unsuccessful. This reversibility is not surprising given the ease with which *cis*-bicyclo[3.3.0]octane-2,8-dione systems have been shown to undergo retro-Claisen reactions.[6-9]

It was felt, however, that trapping of the intermediary β-hydroxy ketone **8a** as the acetate **8b** would prevent retroaldolization and thus yield the desired [5.5.5.5]fenestrane system. Heathcock,[24] Deslongchamps,[25] and Burke[26] had synthesized β-hydroxy ketones by trapping them as stable β-ketoacetates, when related aldol cyclizations were carried out in acetic acid in the presence of a mineral acid, and Venkatachalam[5] in our laboratory had successfully accomplished the cyclization **9** → **10** in a similar polyquinane (see Scheme III). The diketal dialdehyde **17** was therefore stirred at room temperature for 14 h in 70% acetic acid in the presence of a catalytic amount of sulfuric acid. This treatment effected hydrolysis of the ketal functions, accompanied by partial cyclization.[1] After several experiments[1] it was found that complete aldol cyclization could be accomplished by stirring the diketal dialdehyde **17** in 70% acetic acid (H_2SO_4, catalyst) for 14 h, followed by heating the crude reaction product at 50–55 °C for 3 days in glacial acetic acid, again in the presence of a catalytic amount of sulfuric acid. The product from this sequence was purified by flash chromatography on silica gel. Use of this technique resulted in the isolation of two dione diacetates [CI mass spectrum, *m/z* 321 (M + 1), 261 (–HOAc), 201 (–HOAc, 100)], present in a ratio of 3:2, in a combined yield of 75%. When these dione diacetates were subjected to high resolution proton or carbon-13 NMR spectroscopy, it was immediately obvious that the spectra obtained could not be those of a symmetrical substance such as **8b**; the cyclization had evidently occurred in an unexpected direction.

The carbon skeletons and the relative stereochemistries of both dione diacetates **18a(I)** and **18b(II)** were assigned by employing 1D and 2D NMR techniques (decoupling, COSY, ^1H–^{13}C correlated experiments). Proton spectra (250 MHz) were run in $CDCl_3$ as well as C_6D_6 in order to resolve the proton signals which overlapped and to permit the measurement of coupling constants. A standard ^1H 2D correlated experiment [COSY][27] was performed to obtain cross peaks between protons which had coupling constants ≥2.4 Hz. A modified COSY spectrum was then run by using a 0.3-s pulse delay before acquisition;[27] this

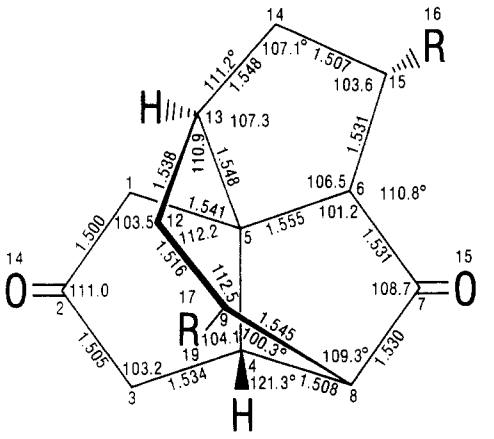
(21) (a) Winslow-White, R.; King, S. W.; O'Brien, J. L. *Tetrahedron Lett.* **1971**, *39*, 3587. (b) Fischer, F. G.; Düll, H.; Ertel, L. *Chem. Ber.* **1932**, *65*, 1467.
(22) Bertz, S.; Lannoye, G.; Cook, J. M. *Tetrahedron Lett.* **1985**, *26*, 4695.
(23) Keese, R., private communication.
(24) Heathcock, C. H.; Tice, C. M.; Germroth, T. C. *J. Am. Chem. Soc.* **1982**, *104*, 6081.
(25) Belanger, A.; Poupant, J.; Deslongchamps, P. *Tetrahedron Lett.* **1968**, 2127.
(26) Burke, S. D.; Murtiashaw, C. W.; Oplinger, J. A. *Tetrahedron Lett.* **1983**, *24*, 2949.
(27) Shoolery, J. N. *J. Nat. Prod.* **1984**, *47*, 226.



18a I=R=R′=OAc

18b II, R′ and B are interchanged R=R′=OAc

IUPAC numbering system



18a, R=OAc

Crystallographic numbering system

Important Bond Angles

C1–C5–C13=120.0° C
C4–C5–C6=104.4°
C1–C5–C6=113.3°
C4–C5–C13=112.6°
C6–C5–C13=102.5°
C1–C5–C4=103.5°
C4–C8–C9=109.3°
C7–C8–C9=107.5°
C5–C13–C14=107.3°
C5–C13–C12=110.9°

Figure 1.

permitted the detection of most of the long-range coupling between protons. The signals for the carbon atoms were assigned occasionally from the off-resonance carbon-13 NMR spectra but generally were obtained from 2D, ^1H–^{13}C correlated experiments.

As mentioned above, the proton and carbon-13 NMR spectra of isomers **18a(I)** and **18b(II)** ruled out symmetrical structures which would arise from a [5.5.5.5]fenestrane system **8b** since the two protons [see Figure 1 and Figures 3–6 (supplementary material)] A and B adjacent to the acetate groups [**18a**, 4.72 (B), 5.26 (A); **18b**, 5.12 (B), 5.42 (A)] in each diastereomer appeared at two different chemical shifts. These shifts were, however, in the region of those observed in **10** reported earlier by Venkatachalam et al.[5] This fact supports the presence of the β-acetoxyketo functionality. Examination of the proton spectra of **18a** indicated the presence of signals which appeared as an AB pattern [δ 2.33 (d, 1 H, J_{EI} = 19 Hz), 2.73 (d, 1 H, J = 19 Hz)] and represented an isolated methylene unit (protons E and I, see Figure 1). This supported the transannular nature of **18a(I)** and ruled out other possible structures considered in ref 1.

Since it was known (see Figure 1) that protons termed A and B in **18a** were bound to the carbons bearing the acetate groups, their cross peaks [see Experimental Section and Figures 3 and 4 (supplementary material, COSY spectrum)] were employed to locate the position of protons J and K (δ 2.02) and L and M (δ 1.90, 1.72), respectively. This analysis also resulted in the assignment of junction protons D (δ 2.75) and H (δ 2.37). The assignment of protons C, G, and N was slightly more difficult because of signal overlap. These signals gave rise to an "AMX"-type of spectrum in which the largest coupling constant (J_{GN} = 18.5 Hz) could be attributed to the geminal coupling of the two methylene protons G and N, while the two smaller coupling constants (J_{GC} = 8.5 Hz and J_{NG} = 12 Hz) were assigned to vicinal couplings. As a consequence, the chemical shifts of methine proton C and methylene protons G and N were determined to be δ 2.91, 2.57, and 1.83, respectively. These assignments were supported by the results of the ^1H–^{13}C correlated experiment. The methine carbon (see Figures 3 and 4, supplementary material) was observed at δ 38.00; moreover, this signal had a unique cross peak at the frequency of proton C (δ 2.91). The methylene carbon, on the other hand, gave rise to two cross peaks located at δ2.57 and 1.83, which permitted the unambiguous assignment of the position of protons G and N.

In the COSY experiment (Figure 5, supplementary material) on **18a(I)** which employed C_6D_6 as a solvent, the cross peak between D and H did indicate a small long-range coupling between these two protons. In **18a(I)** this would be a four-bond coupling which is consistent with the four-bond coupling between methylene protons α to a carbonyl group and is well documented in cyclopentanone systems.[28] Other long-range couplings were seen in the modified COSY experiment. The coupling observed between E or I and G or N ($J \simeq 1$ Hz) is of the same type as the one between D and H, in agreement with structure **18a(I)**. Finally, in a simple decoupling experiment, it was found that proton H couples slightly to F, while D does not. This fact indicates that proton H is the junction proton belonging to the five-membered ring. Since protons A and H are coupled with each other, they are contained in the same five-membered ring.

The ^1H spectra of **18b(II)** in $CDCl_3$ or C_6H_6 are very similar to those of **18a(I)**. In particular, the proton spectrum of isomer **18b** (see Figure 6) also contains one isolated methylene group [E (δ 2.75), I (δ 2.35)], which gives rise to an AB (J_{EI} = 19 Hz) spectrum. Although there are some changes in chemical shift between the spectra of the trans,trans isomer **18a(I)** and the cis,trans diastereomer **18b(II)**, the major difference stems from the coupling of proton B with the adjacent protons. In the trans,trans isomer **18a(I)** the signal from proton B appears as a triplet

(28) Jackman, L. M.; Sternhell, S. *Application of NMR Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon: New York, 1969; p 334.

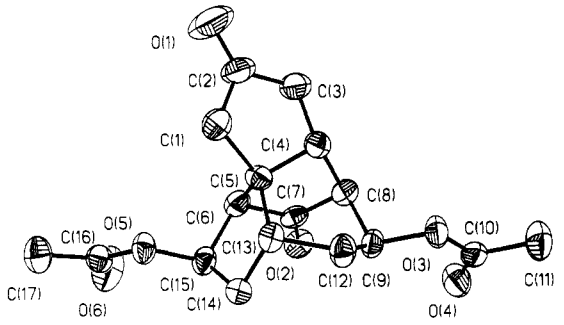


Figure 2. Ortep drawing of **18a**.

of doublets, while in **18b(II)** it is observed as a quartet. This indicates that the difference between the two isomers consists in the stereochemistry of the acetate groups attached to the carbons bearing proton B. In Dreiding models of **18a** the dihedral angle between B and D is close to 90°; hence, the coupling constant is small (J_{BD} = 2.2 Hz). The dihedral angle between B and D in **18b** is smaller, which results in a larger coupling constant (J_{BC} = 5.75 Hz). The chemical shifts of the other protons in isomers **18a** and **18b** are consistent with the structure of **18b(II)** as reported. The protons which are the most dissimilar between **18a** and **18b**, respectively, are those which are in close proximity to the epimeric center; these protons are designated B (δ 5.12), C (δ 2.58), J and L (δ 2.40), and M (δ 1.13). Although the structures of the trans,trans dione diacetate **18a(I)** and the cis,trans diastereomer **18b(II)** based on the COSY NMR experiments have been communicated recently,[4f] **18a** has been subjected to single-crystal X-ray analysis in order to obtain detailed information on the geometry of the quaternary carbon atom. The crystal structure [Figures 1 and 2 (Ortep)] completely confirms the structure of **18a(I)** reported earlier[4f] and also supports the structure of **18b(II)** as described here. In Figure 1 the bond lengths and some of the bond angles are reported for **18a**, while an Ortep drawing is depicted in Figure 2. Crystallographic parameters can be found in the Experimental Section, and complete tables of atom coordinates, bond lengths, etc., are contained in the supplementary material.

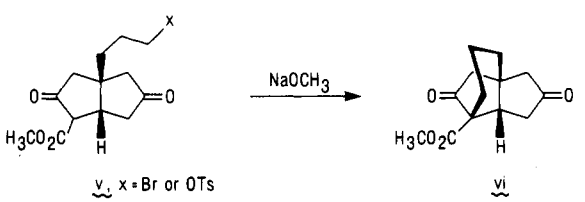
It is clear that dialdehyde **17** has undergone transannular cyclization to provide **18** in preference to the desired cyclization to **8b**. This is interesting for a variety of reasons. Examination of Dreiding models indicates that the staurane ring system **8b** should be less strained, in terms of angle strain, than the transannular products **18a,b** which were isolated; this interpretation is supported by the X-ray data on **18a**. The bond angles, in regard to strain at the central carbon atom of **18a**, are depicted in Figure 1. The bond angle for carbon atoms C_1–C_5–C_{13} has been distorted to 120°, while the corresponding angle for atoms C_4–C_5–C_6 has been compressed to 104.4°. Other bond angles in **18a** have also been compressed to compensate for the opening of the C_1–C_5–C_{13} angle. In contrast, the bond angles in the more symmetrical staurane tetraketone **6** have been reported to be 115.1° for C_2–C_1–C_8 and 117.5° for C_5–C_1–C_{11}.[6] If the degree of angle opening obtained from X-ray data [**18a** (120°), **6** (117.5°)] and strain estimated from Dreiding models are any measure of stability, the expected **8b** should have formed in preference to the observed **18a(I)** and **18b(II)**. Furthermore, none of the desired staurane system **8b** was isolated from the HOAc–H_2SO_4 reaction mixture.

The mode of cyclization of **17** (also of **7**, see below) to dione diacetates **18a** and **18b** is not entirely without precedent. Recently, Pattenden et al.[29] reported a similar type of transannular cyclization, V → VI, in an alkylation reaction directed toward the synthesis of quadrone. In that case, however, the transannular cyclization was promoted by an ester group which had been installed initially at C_4 in order to direct the alkylation toward that carbon atom. The conditions used for the intramolecular cyclization of **17**, acetic acid–sulfuric acid, are analogous to those employed[5] in the case of **9** → **10**, where the reaction proceeded by the expected mode of intramolecular aldol cyclization. No transannular cyclization was observed in that system even when the reaction was run under conditions analogous to those employed for preparation of **18**. Evidently, in **17**, the glutardialdehyde side chain directs the two consecutive intramolecular aldolizations toward the transannular products **18a,b**, while in the 1,5-disubstituted *cis*-bicyclo[3.3.0]octane-3,7-dione system **9**, cyclization occurs as envisaged to provide **10**.[5] More importantly, the diketo diacid **5** (Scheme II) which bears a glutaric acid side chain cyclizes to provide staurane tetraketone **6** with a stereochemistry (H_a = β) opposite to that required for formation of **18a**.

The dichotomy between successful cyclization of the glutaric *acid* **5** (H_a = β) to the desired *all-cis*-[5.5.5.5]-fenestrane system **6** (H_a = β) vs. rotation and aldolization of the glutar*aldehyde* side chain in **17** → **18** (H_a = α) with the opposite stereochemistry is intriguing. The two reactions are run at very different temperatures and in different reaction media; moreover, the oxidation state of the carbons involved in the cyclization is not the same. Simple comparisons are therefore difficult to make. It was initially felt that the difference in reaction temperature in the cyclization reaction of diketal dialdehyde **17** (50°) on the one hand and the diacid **5** (160°) on the other might have been a significant factor in formation of the transannular products **18a** and **18b**. This possibility was eliminated: when the dialdehyde **17** was heated at reflux in a mixture of acetic and sulfuric acids (catalyst), the same two dione diacetates **18a** and **18b** were obtained. In order to determine whether the ketal groups of **17** might influence the cyclization, the diketo dialdehyde **7** was prepared.[30] When the 3-cyclopentene-substituted bicyclo[3.3.0]octane-3,7-dione **2b** was treated with ozone in ethyl acetate at −50 °C a crystalline ozonide was isolated in 98% yield.[30] Treatment of the ozonide with DMS in methanol at low temperature furnished a 95% yield of the diketo dialdehyde **7**. None of the lactone iv (ref 20) previously formed by other procedures was obtained from this workup at low temperature. Diketo dialdehyde **7**, however, when reacted with acetic acid–sulfuric acid at 25 or 50 °C or at reflux gave only the two transannular products **18a** and **18b**. The ratio of these two materials was still approximately 3:2, with **18a(I)** predominating.

Comparing the two processes **5** → **6** vs. **7** → **18** in Dreiding models fails to explain the difference between the two reaction pathways. This difference must be associated with different conformational orientations of the C_5 side chain in the two processes: in reaction **5** → **6**, the orien-

(29) Cooper, K.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* 1984, 799.



v, X = Br or OTs vi

(30) Venkatachalam, M.; Deshpande, M. N.; Jawdosiuk, M.; Kubiak, G.; Wehrli, S.; Weiss, U.; Cook, J. M. *Tetrahedron* **1986**, *42*, 1597.

tation of the hydrogen at $C_{3'}$ of this side chain must be β (see **5**, Scheme II), while it is required to be α in **7** → **18** (see Scheme V).

Although the structures of the transannular cyclization products **18a(I)** and **18b(II)** are interesting in their own right, the more intriguing question concerns their mode of formation to the exclusion of any detectable [5.5.5.5]-fenestrane **8b**. Studies to understand better the stereochemistry of the transannular cyclization **7** → **18** are under way. Even though a second route, "the diborane approach", to staurane tetraene **1** has recently proven successful,[4f] it remains to be seen whether conditions for aldolization can be found which will yield the [5.5.5.5]-fenestrane system rather than the transannular product **18**.

Experimental Section

Microanalyses were performed on an F and M Scientific Corp. Model 185 carbon, hydrogen, and nitrogen analyzer. Melting points were taken on a Thomas-Hoover melting point apparatus; they are uncorrected. Low-resolution NMR spectra were recorded on Varian T-60 and EM-360 spectrometers. Chemical ionization (CI) mass spectra and electron impact (EI) mass spectra were obtained on a Finnigan GC/MS or a Hewlett-Packard 5985 gas chromatograph–mass spectrometer. The infrared spectra were obtained on a Beckmann Acculab-1 or a Nicolet MX-1 instrument.

Analytical TLC plates were E. Merck Brinkman UV active silica gel or alumina on plastic. Flash chromatography was performed according to the method of Still using 4–63 μm silica gel. The spray reagent was composed of 2,4-dinitrophenylhydrazine, ethanol, and sulfuric acid. The citrate/phosphate buffer (pH 5.6) was prepared by dissolving disodium hydrogen phosphate heptahydrate (11.67 g) and citric acid (3.68 g) in water (900 mL). THF, benzene, and ether were distilled from sodium–benzophenone as needed. All high-resolution NMR spectra were recorded on a Bruker WM 250 spectrometer. COSY spectra were recorded with the sequence $(90°\text{-}t_1\text{-}45°\text{-}t_2)_n$.[31] In addition, 256 experiments were acquired with a size of 512 data points and with a sweep width of 1250 Hz. Each dimension was zero-filled once before 2D processing. The window used in the 2D processing was a pure sine bell, and the matrix was symmetrized before plotting.

The ^1H–^{13}C correlated experiments were recorded with the sequence given in ref 32. The delay Δ was $1/(2^1J_{CH}) = 3.6$ ms, which gave the connection between the carbon atoms and the protons directly attached to them. Sixty-four experiments were acquired with a size of 1K data points and a sweep width of 3000 Hz. For the first dimension the sweep width was 1250 Hz. For the 2D processing each dimension was zero-filled once, and the window employed was a sine bell shifted by $\pi/2$.

The experimental procedure for conversion of 1-(3-cyclopentenyl)-*cis*-bicyclo[3.3.0]octane-3,7-dione (**2b**) into the corresponding stable ozonide, followed by reductive workup (DMS, CH_3OH) to provide 1-(1,5-dioxo-3-pentyl)-*cis*-bicyclo[3.3.0]octane 3,7-dione (**7**) has been reported elsewhere (see ref 30 for details).

3-Cyclopentene-1-carboxylic Acid (12). The carboxylic acid **12** was synthesized according to the procedure reported by Murdock.[10b] The boiling point [70–71 °C (0.7 mm)], IR, and NMR were identical with those reported for **12** in the literature.[10]

2-(3-Cyclopentenyl)-2-oxo-1-diazoethane (13). A sample of 3-cyclopentenecarboxylic acid (**12**, 27 g, 0.24 mol) was heated in thionyl chloride (47.6 g, 0.40 mol) for 1–4 h at reflux. Excess thionyl chloride was removed under reduced pressure, followed by distillation of the corresponding acid chloride to yield 3-cyclopentenylcarbonyl chloride (27.4 g, 85%): bp 50–52 °C (12 mm) [lit.[10] bp 95–96 °C (55 mm)]; n^{27}_D 1.4725 (lit.[10] n^{23}_D = 1.4744); ^1H NMR (neat) 2.67 (d, 4 H, J = 8 Hz), 3.53 (q, 1 H, J = 8 Hz), 5.57 (s, 2 H); ^{13}C NMR (neat) 36.6 (t), 53.8 (d), 128.7 (d), 175.9 (s). This material was immediately employed for the preparation of 2-(3-cyclopentenyl)-2-oxo-1-diazoethane (**13**). A solution of 3-cyclopentenylcarbonyl chloride (27.4 g, 0.21 mol) in anhydrous ether (50 mL) was slowly added, with stirring, to a cold (−30 °C) solution of triethylamine (20 g, 27.5 mL, 0.20 mol) and ethereal diazomethane (20 g, 0.198 mol). The diazomethane was prepared[33] by addition of a solution of Diazald (86 g, 0.40 mol) in ether (800 mL) to a stirred mixture of 2-(2-ethoxyethoxy)ethanol (140 mL), potassium hydroxide (24 g), water (40 mL), and ether (150 mL). The addition was carried out at 65–70 °C accompanied by simultaneous distillation of etheral diazomethane. After the solution which resulted had been stirred overnight, triethyl ammonium hydrochloride was filtered from the medium, and the filtrate was concentrated under vacuum at room temperature. The residual brown oil was distilled under high vacuum to provide 2-(3-cyclopentenyl)-2-oxo-1-diazoethane (**13**, 26.8 g, 87%): bp 63–65 °C (0.6 mm); n^{28}_D 1.5233; IR (FT, neat) 3062, 2931, 2852, 2105, 1731, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.53 (d, 4 H, J = 8 Hz), 3.00 and 3.15 (2 overlapping t, 1 H, J = 8 Hz), 5.56 (s, 2 H), 5.65 (s, 1 H); ^{13}C NMR (neat) δ 36.5 (t), 47.6 (d), 53.7 (d), 129.4 (d), 191.2 (s); mass spectrum (15 eV), m/e (relative intensity) 136 (20, M^+), 107 (70), 95 (50), 79 (78), 66 (100).

Anal. Calcd for $C_7H_8N_2O$: C, 61.76; H, 5.88; N, 20.59. Found: C, 61.40; H, 5.61; N, 19.92.

When this reaction was carried out on a smaller scale (10 g) yields of diazo ketone **13** as high as 94% were obtained.

2-(3-Cyclopentenyl)-2-oxo-1-(triphenylphosphazino)-ethane (14). A solution of 2-(3-cyclopentenyl)-2-oxo-1-diazoethane (**13**, 26.8 g, 0.20 mol) in anhydrous ether (100 mL) was added to a well-stirred solution of triphenylphosphine (52.4 g, 0.20 mol) dissolved in anhydrous ether (250 mL).[12] The mixture was stirred at room temperature for 1.0 h. The yellow solid which precipitated was filtered from the mixture and washed with anhydrous ether to provide **14** (73.7 g, 92.6%, mp 118–119 °C): mp 119–120 °C (ethyl acetate–hexane); IR (KBr) 3058, 2939, 2917, 2851, 1648, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.15–2.80 (m, 4 H), 3.87 (t, 1 H), 5.53 (br s, 2 H), 7.20–7.90 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 30.3 (d), 36.2 (t), 48.1 (d), 125.1 (s), 128.5 (d), 129.1 (d), 131.8 (s), 132.7 (d), 133.2 (d), 133.7 (d), 134.2 (d), 146.3 (d), 148.6 (d), 185.3 (s); mass spectrum (CI, CH_4), m/e (relative intensity) 399 (M + 1, 3), 263 (55), 185 (44), 137 (100), 109 (19).

Anal. Calcd for $C_{25}H_{23}N_2OP$: C, 75.36; H, 5.82; N, 7.03. Found: C, 75.58; H, 6.04; N, 6.97.

The phosphazine **14** is quite sensitive to moisture and should be used immediately; however, it can be stored in a vacuum desiccator for several days if kept in the presence of a drying agent ($CaSO_4$).

3-Cyclopentene-1-glyoxal (3). A solution of 2-(3-cyclopentenyl)-2-oxo-1-(triphenylphosphazino)ethane (**14**, 8.0 g, 0.02 mol) in THF (70 mL, distilled) was cooled in a three-neck flask by complete immersion in an ice–salt bath. After addition of sodium nitrite (4.0 g, 0.058 mol), aqueous hydrochloric acid (2.0 N, 40 mL) was added dropwise at −5 to 0 °C. The mixture was stirred for 30 min, while the temperature was held between 0 and 5 °C, after which it was allowed to warm to room temperature, according to the procedure of Bestmann.[12] Stirring was continued until the nitrous acid was consumed, as indicated by a negative test with starch iodide paper. The organic layer was then separated and dried ($MgSO_4$), and **3** was isolated by Kugelrohr distillation under reduced pressure. Since various hydrated forms of the glyoxal **3** are present,[14] the boiling point cannot be determined precisely. The anhydrous form of **3** boils at 48–50 °C (bath temperature) at 0.5 torr and was collected as a yellow oil in a receiver immersed in dry ice–acetone. The material which distilled was then dissolved in methanol and used immediately for the next experiment. In order to distill the hydrated form of the glyoxal **3**, the temperature of the bath was increased from 50 to 110 °C and held at this temperature until decomposition of the dark residue began.

Alternatively, the organic layer from the initial separation was concentrated under reduced pressure (room temperature) to provide a yellow oil. This material was dissolved in ether and washed with water and brine until the aqueous layer was neutral to litmus paper. The organic layer was then concentrated under reduced pressure at room temperature, after which the residue was taken up in anhydrous ether. A suspension of zinc chloride in anhydrous ether was added to the ether layer until no more

(31) Bax, A.; Freeman, R. *J. Magn. Reson.* **1981**, *44*, 542.
(32) Bax, A.; Morris, G. A. *J. Magn. Reson.* **1981**, *42*, 501.
(33) de Boer, T. J.; Baker, H. J. *Organic Synthesis*; Wiley: New York, 1963; Collect. Vol. 4, p 250.

solid [$(Ph)_3PO{\cdot}ZnCl_2$] precipitated. The precipitate was filtered from the ether layer, and the filtrate was washed with water and brine until the aqueous layer was neutral to litmus paper. The ethereal extract was dried (Na_2SO_4) and concentrated under reduced pressure. The oil which resulted was chromatographed (flash) at once on silica gel (benzene–ether, eluent) to provide the desired glyoxal **3** (1.5 g, 53%) followed by its hydrated form (1.0 g, 35%): IR (neat) 3450, 2925, 2858, 1726, 1442, 1282 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.63 (d, 4 H, J = 7 Hz), 3.53 (t, 1 H), 4.67 (br s, 1 H, D_2O exchangeable), 5.63 (s, 2 H): mass spectrum (CI, CH_4), m/e (relative intensity) 125 (M + 1, 100), 107 (80), 97 (90); ^{13}C NMR ($CDCl_3$) δ 35.4 (t), 45.1 (d), 128.8 (d), 181.3 (s), 189.0 (s). The glyoxal was converted with 2,4-dinitrophenylhydrazine into the solid derivative: 3-cyclopenteneglyoxal bis(2,4-dinitrophenylhydrazone) (mp 248–250 °C dec).

Anal. Calcd for $C_{19}H_{16}N_8O_8$: C, 47.10; H, 3.33. Found: C, 47.14; H, 3.47.

Preparation of Tetramethyl 1-(3-Cyclopentenyl)-*cis*-3,7-dioxobicyclo[3.3.0]octane-2,4,6,8-tetracarboxylate (2a) at pH 5.8. A solution of citrate/phosphate buffer (pH 5.6, 180 mL) was added to 3-cyclopenteneglyoxal monohydrate (**3**, 10 g, 70 mmol) which had been dissolved in methanol (200 mL). Dimethyl 3-oxoglutarate (**4**, 28.5 g, 160 mmol) was then added to the mixture, followed by addition of the buffer (pH 5.6) until the solution became slightly turbid. After the mixture was stirred for 12 h much of the tetraester **2a** had precipitated from the medium; however, stirring was continued at room temperature under N_2 for an additional 40–50 h, to permit complete precipitation of the 1:2 adduct. This solid was filtered off to yield the tetramethyl tetraester (17 g, 56%). The mother liquor was concentrated under vaccum at room temperature to furnish a dark-brown oil. Fractional crystallization of the oil (methanol) and column chromatography (EtOAc/hexane) afforded more of the tetraester (6.7 g, 22% yield); the combined yields of **2a** were 78%. Recrystallization of the material from methanol gave an analytical sample of **2a**: mp 144–145 °C; IR (KBr) 3062, 3050, 3032, 2957, 2930, 2857, 1737, 1676, 1445, 1329, 1265, 1244, 1212, 1195, 1165 cm^{-1}; ^{1}H NMR ($CDCl_3$), 60 MHz) δ 2.25 (d, 4 H, J = 8 Hz), 3.00–4.00 (17 H, sharp singlets at δ 3.57 and 3.72 which overlapped with complex signals) 5.73 (s, 2 H), 11.28 (br s, 0.6 H, D_2O exchangeable); ^{13}C NMR ($CDCl_3$) δ 32.8, 35.1, 45.4, 46.2, 51.4, 51.6, 52.2, 52.4, 56.2, 58.0, 60.4, 104.4, 105.2, 129.4, 130.6, 169.7, 170.1, 170.7, 171.3, 172.8; mass spectrum (CI, CH_4), m/e (relative intensity) 437 (M + 1, 58), 405 (100), 373 (20).

Anal. Calcd for $C_{21}H_{24}O_{10}$: C, 57.80; H, 5.50. Found: C, 58.12; H, 5.73.

Preparation of 2a at pH 8.3. A solution of **3** (25 g, 0.18 mol) in methanol (500 mL) was added to a well-stirred mixture of **4** (71.2 g, 0.40 mol) which had been previously dissolved in aqueous potassium bicarbonate solution (100 mL, 1%). After dissolution of **3**, an additional amount of potassium bicarbonate solution (1%) was added to the reaction mixture until the solution became slightly turbid. After 6 h the tetraester **2a** began to precipitate from the medium; however, stirring was continued under nitrogen at room temperature for an addition 40 h. The tetraester which precipitated was filtered from the medium, after which the filtrate was cooled to 4 °C with ice and the pH brought to 6 on addition of ice-cold aqueous hydrochloric acid (10%). An additional amount of **2a** precipitated, and the same process was repeated again until the pH was adjusted to 2. The remainder of the tetraester **2a** which precipitated was filtered from the medium and the combined solids were crystallized from methanol to provide an 83% yield of **2a**: mp 144–145 °C, identical with **2a** obtained from the previous experiment. When this reaction was repeated on a smaller scale (1–2 g) a 90% yield of **2a** was realized.

1-(3-Cyclopentenyl)-*cis*-bicyclo[3.3.0]octane-3,7-dione (2b). The tetramethyl ester (**2a**, 20 g, 46 mmol) was added to a solution of glacial acetic acid (125 mL) and aqueous HCl [188 mL, concentrated HCl–H_2O (1:9)]. The mixture was heated to 87 °C over a 20-min period with vigorous stirring and held at 87 ± 1 °C until the evolution of CO_2 gas ceased (8 h). The solution was cooled to room temperature, filtered, and CH_2Cl_2 (300 mL) was added to the filtrate. The solution was cooled to 5 °C, and the pH was adjusted to 8.0 with a saturated solution of Na_2CO_3. The organic layer was separated and the aqueous layer was reextracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4). The solvent was removed under reduced pressure, and the product obtained was triturated with ether to give **2b** (8.4 g, 90%). Chromatography of **2b** through a short wash column (SiO_2, $CHCl_3$–eluent) afforded white crystalline **2b**. Recrystallization of the material from EtOAc/hexane gave an analytical sample of **2b**: mp 119–120 °C; IR (KBr) 3447, 3047, 2958, 1731, 1398, 1248, 1205, 1187 cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 2.00–2.83 (overlapping signals, 14 H), 5.63 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 35.2, 39.9, 44.0, 44.4, 47.1, 50.5, 129.9, 216.9; mass spectrum (CI, CH_4), m/e (relative intensity) 205 (M + 1, 100), 187 (28.2), 137 (8.5).

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.64; H, 7.80.

1-(3-Cyclopentenyl)-*cis*-bicyclo[3.3.0]octane-3,7-dione Bis(ethylene ketal) (15). A mixture of 1-(3-cyclopentenyl)-*cis*-bicyclo[3.3.0]octane-3,7-dione (**2b**, 10 g, 0.05 mol), anhydrous benzene (250 mL), *p*-toluenesulfonic acid (2.0 g), and distilled ethylene glycol (60 mL, 1 mol) was heated to reflux. The system, which was equipped with a condenser and a Dean–Stark trap, was held at this temperature for 24 h. The reaction mixture was subsequently cooled to room temperature and the organic layer was separated. The benzene phase was washed consecutively with aqueous sodium bicarbonate solution (10%, 3 × 40 mL), water (2 × 40 mL), and brine and dried ($MgSO_4$). The solvent was removed under reduced pressure to provide an oil, which was chromatographed on silica gel (hexane–ethylacetate, gradient elution). This gave the crystalline diketal **15** (14 g) in 98% yield. A pure sample of the diketal **15** was also obtained in 77% yield by distillation of the crude material under vacuum: bp 145–148 °C (0.5 mm); mp 46–48 °C; IR ($CHCl_3$) 3040, 2920, 2870 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.60–2.80 (m, 14 H), 3.80 (s, 8 H), 5.60 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 30.00, 31.10, 42.45, 43.20, 44.00, 45.10, 63.97, 64.36, 117.17, 129.60; mass spectrum (CI, CH_4), m/e (relative intensity) 293 (M + 1, 100).

Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.86; H, 8.27. Found: C, 70.31; H, 8.28.

1-(1,5-Dioxo-3-pentyl)-*cis*-bicyclo[3.3.0]octane-3,7-dione Bis(ethylene ketal) (17). A stream of ozone was passed through a solution of diketal **15** (2.5 g, 8.6 mmol) in anhydrous ethyl acetate (120 mL) at −60 °C until a faint blue color developed. Nitrogen was passed through the solution for 15 min, after which the ethyl acetate was removed under reduced pressure to provide the ozonide **16** (2.91 g, 100): IR (FT, $CHCl_3$) 2958, 2939, 2885, 1339, 1332, 1114, 1083, 1050, 1032, 1017 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.30–2.40 (m, 14 H), 3.85 (s, 8 H), 5.70 (s, 1 H), 5.80 (s, 1 H); ^{13}C NMR ($CDCl_3$) 30.19 (d), 32.01 (t), 41.25 (t), 41.46 (d), 45.02 (t), 51.04 (s), 63.91 (t), 64.27 (t), 98.84 (d), 117.46 (s); mass spectrum (CI, CH_4), m/e (relative intensity) 341 (M + 1, 71), 323 (38), 295 (100), 267 (58).

Anal. Calcd for $C_{17}H_{24}O_7$: C, 60.00; H, 7.10. Found: C, 59.76; H, 7.46.

The ozonide from above (**16**, 1.6 g, 5.5 mmol), dissolved in ethyl acetate (75 mL), was stirred under hydrogen gas (50–55 psi) in the presence of Pt–C (5%, 0.2 g) at room temperature for 2 h. The catalyst was removed by filtration, and the filtrate was evaporated under reduced pressure to give a colorless oil. This material was obtained in 98% yield and characterized as **17** (1.6 g): oil; IR (KBr) 3430 (br), 2990, 2920, 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.70–2.50 (m, 14 H), 4.00 (s, 8 H), 9.79 (low intensity); ^{13}C NMR ($CDCl_3$) δ 31.8, 41.0, 44.7, 45.2, 50.7, 63.7, 64.0, 98.6, 117.0, 201.7; mass spectrum (CI, CH_4), m/e (relative intensity) 325 (M + 1, 70), 307 (100).

***trans*,*trans*- and *cis*,*trans*-4,8-Dioxotetracyclo[5.4.2.0^{2,6}.0^{2,9}]tridecyl 10,13-Diacetates [18a(I) and 18b(II)].** A solution of 1-(1,5-dioxo-3-pentyl)-*cis*-bicyclo[3.3.0]octane-3,7-dione bis(ethylene ketal) (**17**, 2.5 g, 7.3 mmol, or the corresponding methyl hemiacetal derivative of **17**, 2.5 g, 7.0 mmol) was stirred in 70% acetic acid (200 mL) under nitrogen at room temperature in the presence of concentrated H_2SO_4 (1 mL) for 14 h. The mixture was brought to pH 4.0, and the solution which resulted was concentrated to dryness under reduced pressure (room temperature). The residue was triturated with ethyl acetate (100 mL) and the solid filtered off. Removal of the solvent from the filtrate under reduced pressure gave an oil, which was placed under high vacuum (0.1 mm) at 45–50 °C for 12 h to provide a very viscous oil free of ethylene glycol and its acetate. The oil was dissolved in glacial acetic acid (200 mL) and stirred (N_2) at 50–55 °C for

3 days in the presence of concentrated H_2SO_4 (1 mL). The procedure could also be carried out at room temperature (4 days) with similar results. The solution was then brought to pH 4.0 with aqueous sodium bicarbonate, followed by removal of acetic acid under reduced pressure. The residue was then dissolved in cold water (35 mL), and the aqueous layer was extracted with ethyl acetate (4 × 25 mL). The organic layers were washed consecutively with cold aqueous sodium bicarbonate (5%, 3 × 20 mL), cold water (3 × 20 mL), and brine (2 × 20 mL) and then dried ($MgSO_4$). The ethyl acetate was removed under reduced pressure to provide an oil (2.3 g). The crude dione diacetate **18** obtained in this fashion was purified by flash chromatography (20% hexane–ethyl acetate, gradient elution) to provide the two diastereomers trans,trans (1.08 g, 46.2%) and cis,trans (0.67 g, 28.7%) as white crystalline solids.

18a(I) (trans,trans): mp 170 °C; IR (FT, KBr) 2977.34, 2936.00, 2900.55, 2882.10, 1760.17, 1740.80 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.72 (m, 1 H, M), 1.83 (q, 1 H, N, J_{GN} = 18.5 Hz, J_{NC} = 12.0 Hz), 1.90 (m, 1 H, L), 1.97 (s, 3 H), 2.02 (overlapping s, $COCH_3$, and m, J, K, 5 H), 2.33 (d, 1 H, I, J_{EI} = 19 Hz), 2.37 (br s, 1 H, H), 2.57 (q, 1 H, G, J_{GN} = 18.5 Hz, J_{GC} = 8.5 Hz), 2.62 (m, 1 H, F), 2.73 (d, 1 H, E, J_{EI} = 19 Hz), 2.76 (br s, 1 H, D), 2.91 (q, 1 H, C, J_{CG} = 8.5 Hz, J_{CN} = 12 Hz), 4.92 (t of d, 1 H, B, J_{BL} = J_{BM} = 7 Hz, J_{BD} = 2.2 Hz), 5.26 (q of d, 1 H, A, J_{AJ} = 3.5 Hz, J_{AK} = 6.2 Hz, J_{AH} = 0.7 Hz); ^{13}C NMR ($CDCl_3$) δ 20.98 (q), 21.04 (q), 32.24 (t), 38.00 (d), 39.49 (d), 41.59 (t), 41.78 (t), 48.67 (t), 56.08 (d), 56.60 (s), 61.22 (d), 70.59 (d), 77.44 (d), 169.43 (s), 169.78 (s), 214.53 (s), 214.99 (s); mass spectrum (CI, CH_4) m/e (relative intensity) 321 (M + 1, 30), 261 (56), 201 (100); high-resolution mass spectrum calcd for $C_{17}H_{20}O_6$ 320.1260, found 320.1295.

Anal. Calcd for $C_{17}H_{20}O_6$: C, 63.75; H, 6.25. Found: C, 63.64; H, 6.19.

18b(II) (cis,trans): mp 159–160 °C; IR (FT, KBr) 2965.82, 2920.50, 1751.49, 1737.09 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (d of q, 1 H, M, J_{ML} = 15 Hz, J_{MB} = 7 Hz, J_{MF} = 5.5 Hz), 1.88 (q, 1 H, N, J_{NG} = 18.5 Hz, J_{NC} = 12 Hz), 2.00 (m overlapping with other signals, 1 H, K), 2.03 (s, 3 H), 2.06 (s, 3 H), 2.35 (d, 1 H, I, J_{EI} = 19 Hz), 2.38 (br s, 1 H, H), 2.40 (m, 2 H, overlapping, J, L) 2.58 (overlapping q and m, 3 H, F, C, G, J_{GN} = 18.50 Hz, J_{GC} = 7.59 Hz, J_{CN} = 12 Hz), 2.75 (d, 1 H, E, J_{EI} = 19 Hz), 2.95 (d, 1 H, D, J_{BD} = 5.75 Hz), 5.12 (d of t, 1 H, B, J_{BD} = 5.75 Hz, J_{BL} = 7.00 Hz, J_{BM} = 7.00 Hz), 5.42 (q of d, 1 H, A, J_{AJ} = 7.00 Hz, J_{AK} = 5.50 Hz, J_{AH} = 1.50 Hz); ^{13}C NMR ($CDCl_3$) δ 21.06 (q), 21.07 (q), 32.14 (t), 41.87 (t), 41.97 (d), 42.78 (t), 48.15 (t), 53.61 (d), 56.39 (s), 61.39 (d), 72.32 (d), 77.30 (d), 170.15 (s), 170.29 (s), 214.73 (s), 214.94 (s); mass spectrum (CI, CH_4) m/e (relative intensity) 321 (M + 1, 72), 261 (83), 201 (100).

Anal. Calcd for $C_{17}H_{20}O_6$: C, 63.75; H, 6.25. Found: C, 63.55; H, 6.15.

Preparation of *trans,trans*- and *cis,trans*-4,8-Dioxotetracyclo[5.4.2.0^{2,6}.0^{2,9}]tridecyl 10,13-Diacetates [18a(I) and 18b(II)] from Diketone 2b by Reaction with Ozone, Followed by Treatment with Zinc and Acetic Acid. Ozone was passed through a solution of the diketone **2b** (1 g, 4.9 mmol) in anhydrous methylene chloride (80 mL) at −78 °C (dry ice–acetone) until the reaction mixture became light blue. After removal of the methylene chloride under reduced pressure, the solid, powdery ozonide which was obtained was dissolved in glacial acetic acid (30 mL). Zinc dust (2 g) was then added in small portions at 10 °C. The solution was stirred at room temperature for 12 h and then at 80 °C for 4 h. The mixture was cooled to room temperature and filtered. The filtrate which resulted was stirred at 50 °C for 3 days in the presence of concentrated H_2SO_4 (0.5 mL). At this point sodium bicarbonate was added to the solution, and the pH was brought to 4.0. After the removal of acetic acid under reduced pressure, the residue was stirred in the presence of ethyl acetate (50 mL) and then filtered. The organic layer was extracted consecutively with cold aqueous $NaHCO_3$ solution (3 × 20 mL), cold water (3 × 20 mL), and brine (2 × 20 mL) and then dried ($MgSO_4$). Removal of the solvent provided a brown oil (1.1 g), which was purified by flash chromatography (hexane–ethyl acetate) to provide a mixture of diacetates **18a(I)** and **18b(II)** as white crystalline solids. These two isomers **18a** and **18b** were identical with those obtained from the previous experiment.

Aldol Condensation of Dialdehyde 7 at High Temperature. A sample of 1-(1,5-dioxo-3-pentyl)-*cis*-bicyclo[3.3.0]octane-3,7-dione (**7**, 0.1 g, 4.0 × 10^{-1} mmol) was dissolved in glacial acetic acid (20 mL), and a drop of concentrated sulfuric acid was added to the solution. The solution was refluxed under a N_2 atmosphere for 2 h. The reaction mixture was then allowed to cool to room temperature and brought to pH 4.0 with solid sodium bicarbonate. The acetic acid was removed under reduced pressure, and the residue which formed was dissolved in cold water (10 mL), followed by extraction with ethyl acetate (3 × 20 mL). The organic layer was washed consecutively with cold, aqueous sodium bicarbonate solution (5%, 3 × 10 mL), cold water (3 × 10 mL), and brine (2 × 10 mL) and then dried ($MgSO_4$). The product obtained from this sequence was identical with the mixture of diacetates **18a(I)** and **18b** (TLC, 20% hexane–ethyl acetate, double elutions R_f 0.45 and 0.54) produced in the previous experiment.

Crystallographic Data of 18a. The crystal habit was found to be monoclinic with cell dimensions a = 7.8695 (26) Å, b = 23.0502 (39) Å, c = 8.4940 (18) Å, and β = 98.918 (23)° belonging to the space group P_{21}/C.[34] All reflections within a 2θ range of 3–45° with indices h, k, $\pm l$ were collected with 2 check reflections for every 48 measured, yielding 2222 unique reflections of which 1568 were coded observed ($F_0 > 3\sigma F_0$).

The crystallographic data were collected by omega scans at ambient temperature on a Nicolet P3/F diffractometer using molybdenum radiation and a graphite monochromator. All atoms were located on successive difference Fourier maps by using the program SHELXTL. All non-hydrogen atoms were refined anisotropically, and all hydrogen atoms were allowed to ride on the corresponding carbon atom and refined isotropically with a common temperature factor. The final residuals were R = 0.0611 and R_w = 0.0627, $W = 1/(\sigma^2F + 0.0009F^2)$. The atom coordinates (Table 1), bond lengths (Table 2), bond angles (Table 3), anisotropic temperature factors (Table 4), the hydrogen coordinates and temperature factors (Table 5), for all atoms are contained in the supplementary material. The data with regard to the observed and calculated structural factors for **18a(I)**, as well as torsion angles, are available from the author (J.M.C.).

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Supplementary Material Available: Tables of atom coordinates, bond lengths, bond angles, anisotropic temperature factors, hydrogen coordinates, and temperature factors for all atoms. COSY NMR spectra ($CDCl_3$) of **18a** (Figures 3, 4, supplementary material) and **18b** (Figures 5, 6, supplementary material) as well as the COSY spectra run in C_6D_6 (Figures 7–10, supplementary material) (10 pages).

(34) *International Tables for Crystallography*; D. Reidel: Boston, 1983; Vol. A, p 174.