Experiments in Pursuit of Pentagonal Dodecahedrane: Model Synthesis of Convex Polyquinanes†

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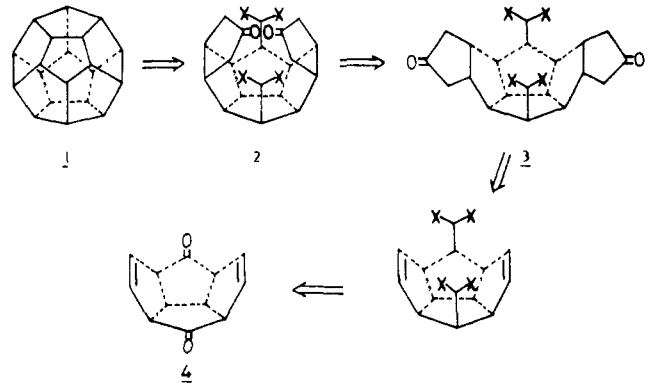
Abstract: A novel synthetic approach to dodecahedrane is described. The pivotal synthon of C_2 symmetry in this approach, tetracyclo[7.2.1.$0^{4,11}$.$0^{6,10}$]dodeca-2,7-diene-5,12-dione (tetraquinanedione **4**), has been synthesized from readily available C_5 and C_7 building blocks, 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene and 7-*tert*-butoxynorbornadiene (**14**) employing a π^4s + π^2s Diels–Alder reaction, a π^2s + π^2s photocycloaddition, and a regioselective thermal cyclobutane fragmentation as the key transformations. This photothermal metathetic approach for the synthesis of functionalized tetraquinanes has been generalized. An effective methodology for the cyclopentanone annulation of tetraquinane **5** using the dichloroketene cycloaddition–diazomethane ring expansion sequence has been established. A protocol for the projection of the newly appended *exo*-cyclopentanone rings within the cavity of the polyquinane framework as in **32** has been executed.

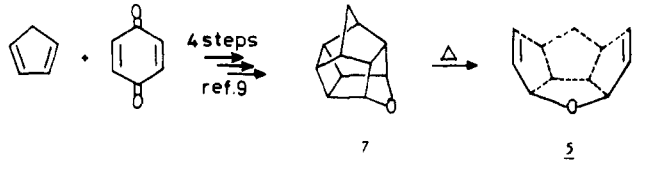
That dodecahedrane (**1**), a $C_{20}H_{20}$ hydrocarbon of I_h symmetry, is a major synthetic challenge needs little testimony. The logistics required for the creation of this "hydrocarbon football" made up of 12 five-membered rings constituted by the bonding together of 20 identical methine units and having in all 30 ring junctions, all cis and syn to each other, are at once formidable.[1] The quest for **1** which began nearly a quarter of a century ago has drawn many research groups, the world over, into the fray and has resulted in the development of imaginative strategies for assembling spheroidal polyquinanes.[2,3] Both convergent, e.g., C_{10} + C_{10} dimerization of triquinacene,[4] C_{15} + C_5 "capping" of [5]-peristylane[3a–c] among others,[5] as well as serial approaches to dodecahedrane has been pursued. While the former have been beset with unfavorable steric and entropic factors that have proved difficult to overcome despite innovative tactical manoeuvers,[4c,d] the latter have generally proved more encouraging and rely on the enormous symmetry of the target molecule. Indeed, the only successful route to **1** reported to date by Paquette charters a serial course. About 4 years ago, we initiated a modest effort at Hyderabad toward dodecahedrane, and this report details a portion of these endeavors.[6]

As is the practice in any major synthetic venture, our first step was to take the dodecahedrane molecule apart, to formulate a logical retrosynthetic approach, and to identify the key intermediates. This is depicted in Scheme I. The exercise identified the symmetrical, highly functionalized C_{20} hexaquinane (**2**) as the pivotal pretarget and the C_{12} tetraquinanedione **4** as the key starting synthon. **2**, which retains a spheroidal contour, has all 20 carbon atoms as well as two strategically placed $-CX_2$ type of functionalities for "molecular stitching" through 4-fold base-catalyzed intramolecular displacement reaction to furnish a secododecahedranedione which could be enticed into pinacolic coupling to deliver dodecahedrane framework. Thus, three subgoals that emerged in our approach to **1** are (i) development of a new methodology toward the synthesis of diverse tetraquinanes of varying complexity and in particular **4**, (ii) adaptation of a suitable cyclopentanone annulation (**4** → **3**) and ring inversion strategy (**3** → **2**), and (iii) deployment of the "molecular stitching" plan (**2** → **1**). Realization of the first subgoal and model studies related to the second are detailed below.

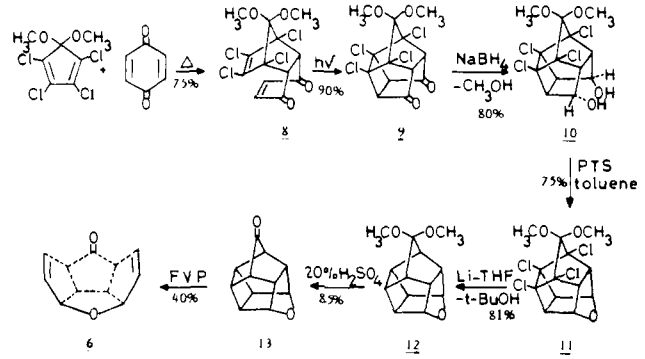
Scheme I



Scheme II



Scheme III



Synthesis of Tetraquinanes

At the time the present investigation was initiated, there were only two reported syntheses of functionalized tetraquinanes available in the literature, both of which suffered from severe limitations during scale-up processes and also did not deliver the requisite functionality.[7] Therefore, we decided to develop a de novo approach to appropriately functionalized tetraquinanes from readily and abundantly available C_5, C_6, and C_7 building blocks.

† Dedicated to Prof. Gurbakhsh Singh on the occasion of his 65th birthday.
‡ Abstracted from the Ph.D. Dissertation of Mangalam S. Nair, University of Hyderabad, 1984.

(1) Reviews: (a) Mehta, G. *J. Sci. Ind. Res.* **1978**, *37*, 256. (b) Eaton, P. E. *Tetrahedron* **1979**, *35*, 2189. (c) Paquette, L. A. *Pure Appl. Chem.* **1978**, *50*, 1291. (d) *Chem. Eng. News* **1982**, 60 (Aug 16), 25. (e) Paquette, L. A. *Top. Stereochem.* **1984**, *119*, 1.
(2) (a) Teransky, R. J.; Balogh, D. W.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 4503. (b) Paquette, L. A.; Teransky, R. I.; Balogh, D. W.; Kentgen, G. *Ibid.* **1983**, *105*, 5446 and references cited therein of pioneering and successful efforts of the Paquette group in the area.

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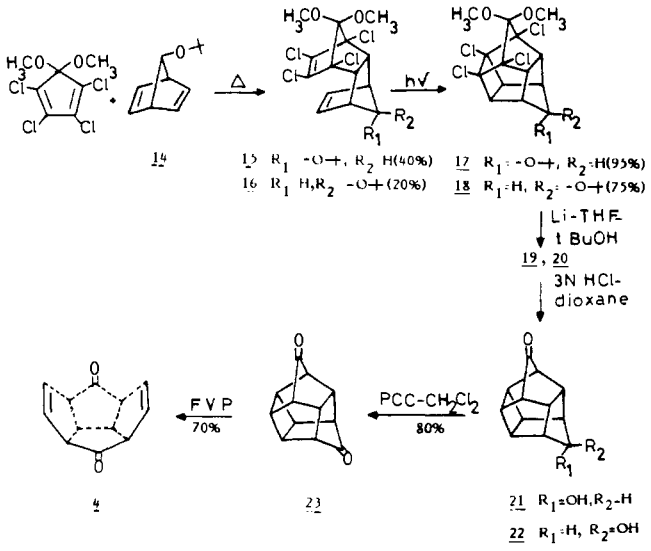
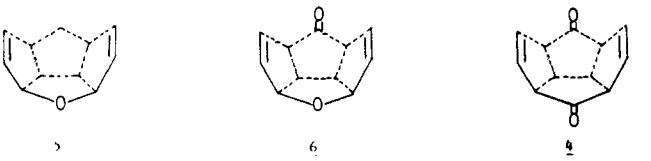
Scheme IV



To test the feasibility of our new route to tetraquinanes and to also have some of them in quantity for exploratory work, we identified three compounds, **5**, **6**, and **4**, of increasing complexity and symmetry as our objective. Synthetic routes to **4–6** were



patterned along our well-established and versatile photothermal metathesis route to triquinanes.[8] Flash vacuum pyrolysis (FVP) of readily available[8,9] hexacyclic ether **7** resulted in a facile [2 + 2]-cycloreversion and furnished the C_{12} oxatetraquinane **5** in 95% yield, and multigram quantities of it could be readily realized from 1,3-cyclopentadiene and *p*-benzoquinone (Scheme II). In an analogous manner, **6** was obtained through the FV pyrolysis of hexacyclic keto ether **13** in 40% yield. The keto ether **13**, in turn, was synthesized from 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene and *p*-benzoquinone through a series of reactions

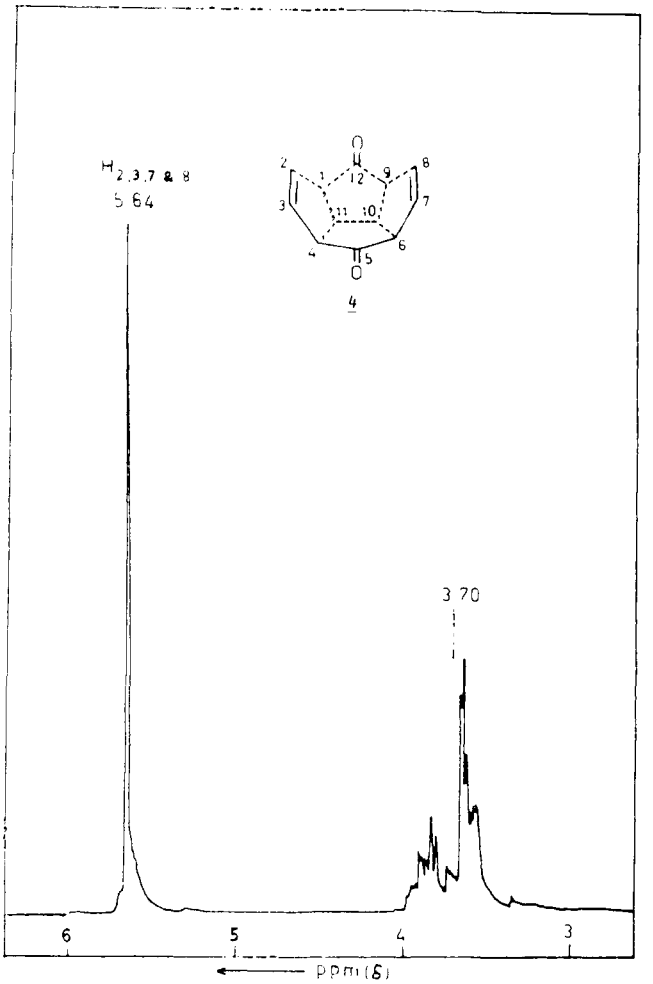


Figure 1. ^{1}H NMR spectrum (100 MHz) of tetraquinonedione **4**.

summarized in Scheme III in 30% overall yield. The most notable feature of the [2 + 2]-cycloreversion reaction in **13** was that its carbonyl group (7-ketonorbornane type) remained intact, and this was a happy augury for the synthesis of **4** to which we turned our attention next.

Diels–Alder reaction between 7-*tert*-butoxynorbornadiene (**14**) and 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene in a sealed tube (110 °C, 3 days) furnished a mixture of three [4 + 2] products from which the two required endo,endo adducts **15** (40%) and **16** (20%) were readily separated.[10] Acetone-sensitized photolysis of **15** and **16** furnished the corresponding hexacyclic-caged compounds **17** and **18**, respectively, in high yield. The redundant chlorine atoms in **17** and **18** were readily replaced by hydrogen atoms on reduction with Li/THF/*t*-BuOH milieu[11] in 80% yield to give **19** and **20**. One-step deprotection with 3 N HCl relieved **19** of the acetal and the ether functionality, and hydroxy ketones **21** and **22** were readily realized. PCC oxidation led to the hexacyclic dione **23**, mp 227–228 °C, whose three-line ^{1}H NMR (δ 3.2, 3.1, and 2.2; 2:1:2) and four-line ^{13}C NMR (δ 210.0, 48.4, 42.4, and 41.8) were fully in agreement with its formulation (Scheme IV).[11] FVP of **23** proceeded uneventfully and without the much feared decarbonylation to give **4** in ~70% yield based on recovered starting material. The same isolated yield could also be realized after two cycles.[11,12] The structure and high symmetry

(3) (a) Eaton, P. E.; Mueller, R. H.; Carlson, G. R.; Cullison, D. A.; Copper, G. F.; Chou, T.-C.; Krebs, E.-P. *Ibid.* **1977**, *99*, 2751. (b) Eaton, P. E.; Andrews, G. D.; Krebs, E.-P.; Kunai, T. *J. Org. Chem.* **1979**, *44*, 2824. (c) Eaton, P. E.; Sidhu, R. S.; Langford, G. E.; Cullison, D. A.; Pietruszewski, C. L. *Tetrahedron* **1981**, *25*, 4479. (d) McKervey, M. A.; Vibuljan, P.; Ferguson, G.; Siew, P. Y. *J. Chem. Soc., Chem. Commun.* **1981**, 912. (e) Mehta, G.; Nair, M. S. *Ibid.* **1983**, 439. (f) Baldwin, J. E.; Beckwith, P. L. M.; *Ibid.* **1983**, 279. (g) Fessner, W. D.; Prinzbach, H.; Rihs, G. *Tetrahedron Lett.* **1983**, 5857. (h) Monego, T. A. Ph.D. Dissertation, Michigan State University, 1982. Farnum, D. G.; Monego, T. A., private communication. (i) Serratosa, F., University of Barcelona, private communication. (j) Mehta, G.; Nair, M. S. *J. Chem. Soc., Chem. Commun.* **1985**, 629.

(4) (a) Woodward, R. B.; Fukunaga, T.; Kelly, R. C. *J. Am. Chem. Soc.* **1964**, *86*, 3162. (b) Jacobson, I. T. *Acta Chem. Scand.* **1967**, *21*, 2235. (c) Repic, O. Ph.D. Dissertation, Harvard University, 1976. (d) Deslongchamps, P.; Soucy, P. *Tetrahedron* **1981**, *37*, 4385. (d) Roberts, W. P.; Shoham, G. *Tetrahedron Lett.* **1981**, 4895.

(5) Paquette, L. A.; Farnham, W. B.; Ley, S. V. *J. Am. Chem. Soc.* **1975**, *97*, 7273. Paquette, L. A.; Itoh, I.; Farnham, W. B. *Ibid.* **1975**, *97*, 7280. Paquette, L. A.; Itoh, I.; Lipkowitz, K. *J. Org. Chem.* **1976**, *41*, 3524.

(6) Part of this work has been published in a preliminary report.[3e,j]

(7) McNeil, D.; Vogt, B. R.; Sudol, J. J.; Theodoropoulos, S.; Hedeya, E. *J. Am. Chem. Soc.* **1974**, *96*, 4673. Paquette, L. A.; Wyvratt, M. J. *Ibid.* **1974**, *96*, 4671. Fukunaga, T.; Clement, R. A. *J. Org. Chem.* **1977**, *42*, 270.

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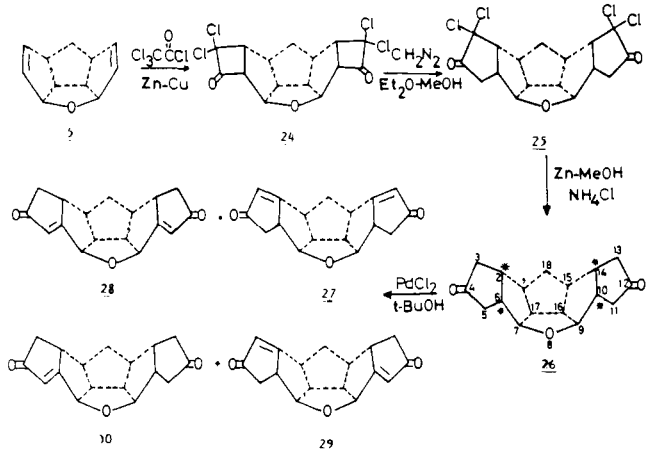
(9) Chaudhury, B. Ph.D. Dissertation, Indian Institute of Technology, Kanpur, 1979. Sasaki, T.; Eguchi, S.; Kiriyama, T.; Hiroati, O. *Tetrahedron* **1974**, *30*, 2707. Cookson, R. C.; Crundwell, E.; Hill, R. R.; Hudec, J. *J. Chem. Soc. C.* **1964**, 3062.

(10) Astin, K. B.; Mackenzic, K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1004 Byrne, L. T.; Rye, A. R.; Wege, D. *Aust. J. Chem.* **1974**, *27*, 1961.

(11) Diketone **23** has been independently prepared in Prof. H. Prinzbach's group. However, its thermal fragmentation at 700 °C led to only 1,3-cyclopentadiene, benzene, and naphthalene. Sedelmeier, G. Ph.D. Dissertation, University of Freiberg, 1979. We thank Prof. Prinzbach and Dr. W. D. Fessner for this information.

Scheme V



of **4** was manifest in its ^1H and ^{13}C NMR spectra (Figure 1). The attainment of **4** through the route depicted in Scheme IV, to date, remains the simplest practical entry into this tetraquinane ring system from commercially available C_5 and C_7 building blocks.

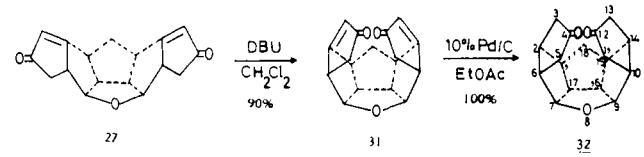
Strategy for Cyclopentanone Annulation and Ring Inversion

Having demonstrated a synthetic approach to tetraquinanes in general, and synthesized necessary quantities of **4**, **5**, and **6** in particular, the next task enroute to dodecahedrane **1** was the bis(cyclopentanone) annulation and stereochemical inversion. Since **5** was the most abundant of the three functionalized tetraquinanes synthesized, it seemed appropriate to initiate model studies of cyclopentanone annulation on this substrate. The Greene methodology[13] of dichloroketene cycloaddition and ring expansion was selected for this purpose as it would render the requisite symmetrical product.

When oxatetraquinane **5** was treated with an excess of dichloroketene generated in situ by using trichloroacetyl chloride and the Zn–Cu couple according to the procedure of Brady,[14] a bis(dichloroketene) adduct **24**, mp 238–240 °C, was obtained in 40% yield. While the regiochemical assignment to **24** follows from its ^1H and ^{13}C NMR data, the exo stereochemistry is based on the known propensity of folded polyquinanes to react from the open convex face. Reaction of the bis-adduct **24** with diazomethane in the presence of methanol furnished **25** (65%). Dechlorination of **25** to furnish **26**, mp 164 °C, 80%, was most conveniently carried out by using Zn–MeOH–NH_4Cl combination. Its 500-MHz ^1H NMR spectrum showed a characteristic proton signal at δ 4.35 (2 H, d, J = 4.3 Hz), by now a familiar feature of compounds of this series. The nine-line ^{13}C NMR with characteristic resonances at δ 218.8 (C_4 and C_{12}) and 91.4 (C_7 and C_9) further reinforced the structural formulation, Scheme V.

Even though bis(cyclopentanone) annulation of **5** had been achieved, it could be successfully utilized for the synthesis of dodecahedrane only if the two newly appended cyclopentane rings could be projected within the cavity of the polyquinane framework. This required inversion of the stereochemistry at the four starred positions in **26** and was achieved in a fairly straightforward manner. Reaction of hexaquinanedione **26** with $PdCl_2$ in refluxing *t*-BuOH transformed it into a mixture of bis-enones **27**, **28**, and **29** and the monoenone **30** in approximately equal amounts and in 65–75% yield,[15] Scheme V. Each of these compounds having closely related R_f values was separated by careful column chromatography and fractional crystallization and assigned a structure with the help of complimentary spectral data. In particular, incisive analysis of 500-MHz ^1H NMR and ^{13}C NMR data proved decisive (Scheme V).

Scheme VI



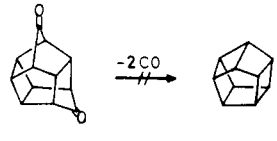
After acquiring the bis-enones **27**, **28**, and **29**, the next task was the relocation of the double bonds. As it is well-known that α,β-unsaturated carbonyl compounds equilibrate with their β,γ-isomers in the presence of base, we decided to subject the bis-enones to this treatment. In order to avoid any damage to the ether functionality present in the bis-enones, a mild base-like DBU was chosen for the purpose. Thus, exposure of **27** to a catalytic amount of DBU resulted in its smooth isomerization to **31**, mp 212–214 °C, in almost quantitative yield (Scheme VI). The structural formulation **31** was arrived at after careful comparison of its spectral data with that of **27** and analysis of the subtle differences in the two sets of spectra. For example, the deshielded protons attached to C_7 and C_9 resonated at δ 4.52 (2 H, dd, $J_1 = J_2$ = 6 Hz) in **31** and helped in assigning the structure with inversion of stereochemistry at C_6 and C_{10}. The nine-line ^{13}C NMR spectrum with its nine resonances not only assured us of its symmetry but also gave validity to the structure **31**. One could explain the formation of **31** as arising from a two-step process, viz., (i) proton abstraction by base leading to deconjugation of α,β-enone functionality to furnish a β,γ-unsaturated ketone and (ii) its reprotonation from the endo face and isomerization back to the α,β-enone system. The base catalyzed isomerization of the enone functionalities in **28** and **29** were also attempted. However, the α,β-unsaturated carbonyl system proximal to the ether linkage was found to be stable and did not undergo isomerization with DBU. Under the euphoria of having successfully obtained the spheroidal bis-enone **31** in just one step from **27**, further attempts to isomerize **28** and **29** were not made.

Catalytic hydrogenation of **31** over 10% Pd/C catalyst resulted in the projection of the two cyclopentanone units within the cavity, thus giving rise to **32**, mp 150–152 °C, in quantitative yield.[3c,d] Once again, the structure of **32** was confirmed after careful analysis and comparison of its spectral data with that of **26** in which the two cyclopentanone units were outside the central cavity. The IR spectrum (1730 cm^{-1}) and the ^1H NMR spectrum showing characteristic resonance due to protons attached to C_7 and C_9 appearing at δ 4.39 (2 H, dd, $J_1 = J_2$ = 5.3 Hz, cf., δ 4.35, 2 H, d, J = 4.3 Hz for **26**) were mainly instrumental in assigning the structural formulation **32** (Scheme VI). In this manner, our second subgoal of bis(cyclopentanone) annulation and ring inversion was successfully demonstrated with model oxatetraquinane **5**. We are now engaged in applying this methodology to **4** enroute to dodecahedrane, and these findings will be reported in due course.

Experimental Section

General Method for Flash Vacuum Pyrolysis (FVP). The flash thermolysis were carried out in a quartz vigreux column (30 cm × 1.5 cm), packed with quartz chips, connected to a vacuum line, and adapted with a collection flask and a liquid nitrogen trap. The quartz column was heated with a nichrome coil wound around it and insulated by asbestos padding. The column temperature was controlled by a variac and measured by a thermocouple (Chromel–Alumel) using a Keithley digitial

(12) Of course, formation of pentaprismane (i) on decarbonylation of **23** would have been a most welcome deviation, but such decarbonylative routes to tetraprismane (cubane) and other caged systems have failed, and therefore we did not consider it a very real possibility.



(13) Greene, A. E.; Depress, J. P. *J. Am. Chem. Soc.* **1979**, *101*, 4003.
(14) Bak, D. A.; Brady, W. I. *J. Org. Chem.* **1981**, *37*, 2949.

(15) The bis-enones **27–29** could also be obtained from **26** via either the phenylselenylation–selenoxide elimination sequence[16] or the palladium-catalyzed dehydrosilylation of the derived trimethylsilyl enol ether.[17]

multimeter. The column was preheated and equilibrated to the requisite temperature (±10 °C). The hexacyclic ethers were slowly sublimed (80–140 °C/1–7 torr) through the quartz tube. The condensate, in most cases, deposited in the collection flask and was carefully chromatographed.

5-Oxatetracyclo[7.2.1.0^{4,11}.0^{6,10}]dodeca-2,7-diene (5). 4-Oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane (**7**), (1 g, 6.25 mmol)[8b] was slowly sublimed (80 °C/7 torr) through a quartz tube heated to 620 °C (±10 °C) as described in the general method for FVP. The condensate in the receiver was carefully chromatographed over $AgNO_3$-impregnated silica gel. Elution with 20% benzene–petroleum ether furnished the starting hexacyclic ether **7** (250 mg, 25%). Further elution of the column with ether furnished 5-oxatetracyclo[7.2.1.0^{4,11}.0^{6,10}]dodeca-2,7-diene (**5**) (700 mg, 70%) and was sublimed (80 °C/15 torr) to give a white solid, mp 119.5–120.5 °C: IR (KBr) ν_{max} 3100, 1620, 740 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 5.9–5.35 (4 H, AB q with st, J = 6 Hz), 5.2 (2 H, d, J = 6 Hz), 3.68–3.3 (2 H, m), 3.24–2.9 (2 H, m), 2.18–1.5 (2 H m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 138.7 (d), 132.7 (d), 90.4 (d), 53.6 (d), 51.5 (d), 34.5 (t); mass spectrum (70 eV), m/e (rel intensity) 160 (M^+, 100), 145 (15), 131 (56), 129 (23), 117 (79), 115 (31), 104 (29), 91 (73), 78 (63), 66 (18); high-resolution mass spectrum for $C_{11}H_{12}O$ calcd m/e 160.0886, found m/e 160.0885.

1,8,9,10-Tetrachloro-11,11-dimethoxytricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione (8).[18a] A mixture of tetrachlorodimethoxycyclopentadiene dimethyl acetal (180 g, 0.69 mol) and p-benzoquinone (76 g, 0.7 mol) in dry toluene (600 mL) was refluxed for 24 h. Most of the solvent was then removed under reduced pressure and the residue diluted with hexane. On cooling, pale-yellow crystals of the Diels–Alder adduct **8** (210 g, 83%) were obtained: mp 162–163 °C [lit.[18a] 162–164 °C]; IR (KBr) ν_{max} 1760, 1640, 1620 cm^{-1}.

4,4-Dimethoxy-2,3,5,6-tetrachloropentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione (9).[18a] A solution of the Diels–Alder adduct **8** (40 g, 0.15 mol) in 840 mL of acetone was purged with nitrogen and irradiated for 4 h with a 450-W Hanovia medium-pressure mercury vapor lamp in a quartz immersion well using a Pyrex filter. The solvent was removed and the crude product crystallized from benzene–hexane to furnish the pentacyclic diketone **9** (36 g, 90%) and was sublimed to give an analytically pure sample: mp 151–152 °C [lit.[18a] 151–152.2 °C]; IR (KBr) ν_{max} 1760 cm^{-1}; ^{1}H NMR (100 MHz, acetone-d_6) δ 3.74 (3 H, s), 3.70 (3 H, s), 3.56 (4 H, br s).

4,4-Dimethoxy-2,3,5,6-tetrachloropentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-*endo*-8,*exo*-11-diol (10). A solution of a freshly sublimed sample of the pentacyclic diketone **9** (30 g, 89 mmol) in 200 mL of 95% ethyl alcohol was cooled in an ice bath, and sodium borohydride (6 g, 156 mmol) was added to it in small lots over a period of 1 h. The reaction mixture was stirred further for 5 h and most of the ethyl alcohol removed under reduced pressure. The residue was extracted with chloroform (3 × 150 mL), and the combined organic layers were washed with water and dried. Removal of solvent and crystallization from ethyl acetate–hexane furnished the pentacyclic diol **10** (24 g, 80%), mp 254–256 °C [lit.[18b] 256–257 °C); IR (KBr) ν_{max} 3400 cm^{-1} (br).

4-Oxa-1,7,8,9-Tetrachloro-12,12-dimethoxyhexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane (11). A mixture of the pentacyclic diol **10** (26 g, 70 mmol) and p-toluenesulfonic acid (2 g, added in four lots of 0.5 g each after every 12 h) in dry toluene (400 mL) was refluxed by using a Dean-Stark apparatus for 48 h, during which time 100 mL of turbid toluene was removed. The remaining solvent was evaporated under reduced pressure and the residue extracted with chloroform (3 × 150 mL). The combined organic extract was washed with water and 5% aqueous $NaHCO_3$ and dried. Removal of solvent furnished a dark-colored residue which after crystallization from ethyl acetate–hexane gave the hexacyclic ether **11** (18 g, 73%) and was recrystallized from the same solvent system: mp 188–190 °C [lit.[18b] 189–190 °C]; IR (KBr) ν_{max} 2950, 1090, 1025, 780 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 5.2 (2 H, m), 3.62 (3 H, s, $-OCH_3$), 3.56 (3 H, s, $-OCH_3$), 3.2–3.0 (4 H, m).

4-Oxa-12,12-dimethoxyhexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane (12). In a 1-L, three-necked RB flask equipped with a stirrer, a condenser, and a nitrogen inlet was placed the tetrachlorohexacyclic ether **11** (20 g, 55 mmol), 80 mL of dry *tert*-butyl alcohol, and 400 mL of dry tetrahydrofuran. The reaction mixture was vigorously stirred, and lithium metal (6.4 g, 0.8 g-atom) was added to it as small pieces over a period of 1 h such that the solution remained at a gentle reflux (external cooling was done occasionally when the reaction became too vigorous). When the exothermic reaction had subsided, the reaction mixture was refluxed for 45 min and cooled to room temperature. The unreacted lithium metal was filtered off and destroyed separately. THF was removed under reduced pressure and the product extracted with ether (3 × 100 mL). The combined ether extract was washed with water and 3% HCl and dried. Removal of solvent furnished the dimethoxyhexacyclic ether **12** (10 g, 81%) and was further purified by sublimation: mp 72 °C; IR spectrum (KBr) ν_{max} 3025, 1140, 1100 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 4.75 (2 H, br s, $-CH-O-CH-$), 3.25 (3 H, s, $-OCH_3$), 2.98 (3 H, s, $-OCH_3$), 2.64 (6 H, br s), 2.28 (2 H, br s); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 121.8, 85.8, 51.1, 50.6, 46.3, 44.0, 39.7. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.12; H, 7.21.

4-Oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecan-12-one (13). A solution of the hexacyclic dimethoxyketal **12** (10 g, 49.5 mmol) in 150 mL of ether was cooled to ~15 °C in a cold water bath, and 50 mL of 20% H_2SO_4 (v/v) was added to it dropwise over a period of 25 min. The reaction mixture was then brought to room temperature and stirred for 15 min. The ethereal layer was separated and the aqueous layer extracted with ether (3 × 40 mL). The combined ether extract was washed with water and 5% aqueous $NaHCO_3$ and dried. Removal of solvent furnished the hexacyclic keto ether **13** (7 g, 86%) and was further purified by sublimation (130 °C/8 torr): mp 239–240 °C; IR (KBr) ν_{max} 3000, 1790, 1310, 1120 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 5.2–5.0 (2 H, unresolved m), 3.0–2.4 (6 H, m), 2.3–2.1 (2 H, unresolved m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 211.7 (s, $-C=O$), 87.4 (d, 2 C, $-HC-O-CH-$), 45.9 (d, 2 C), 45.8 (d, 4 C), 35.4 (d, 2 C). Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 75.90; H, 5.69.

5-Oxatetracyclo[7.2.1.0^{4,11}.0^{6,10}]dodeca-2,7-dien-12-one (6). The hexacyclic keto ether **13** (1 g, 9.7 mmol) was slowly sublimed (130–140 °C/5 torr) through a quartz tube preheated and equilibrated to ~620 °C as elaborated in the general procedure for FVP. The pyrolysate (500 mg) collected in the receiver was carefully chromatographed over a silica gel (15 g) column. Elution with 50% benzene–petroleum ether removed all the less polar impurities. Further elution with benzene furnished the oxatetraquinane **6** (400 mg, 40%) and was sublimed (130 °C/10 torr) to give an analytically pure sample: mp 100–101 °C; IR (KBr) ν_{max} 1730, 1340, 1060, 720 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 5.9–5.6 (4 H, m, $-HC=CH-$), 5.5 (2 H, d with st, $-HC-O-CH-$, J = 6 Hz), 3.85–3.50 (2 H, m), 3.4–3.1 (2 H, m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 215.3 (s, $-C=O$), 136.4 (d, $-HC=CH$), 134.2 (d, $-HC=CH$), 92.4 (d, $-HC-O-CH-$), 60.7 (d), 46.3 (d); mass spectrum (70 eV) m/e (rel intensity) 174 (M^+, 22), 145 (11), 130 (29), 117 (100), 91 (19), 81 (40), 65 (14), 53 (15); high-resolution mass spectra for $C_{11}H_{10}O_2$ calcd m/e 174.0681, found m/e 174.0678.

Diels–Alder Reaction of 1,2,3,4-Tetrachloro-5,5-dimethoxycyclopentadiene and 7-*tert*-Butoxynorbornadiene (14).[10] Tetrachlorodimethoxycyclopentadiene (10.6 g, 0.04 mol) and 7-*tert*-butoxynorbornadiene (**14**) (6.6 g, 0.04 mol) diluted with 3 mL of carbon tetrachloride was heated in a sealed tube at 100–110 °C for a period of 72 h. The black, tarry product obtained was chromatographed over neutral alumina (120 g) using petroleum ether as eluent to furnish **15** (7 g, 40%) which was crystallized from methanol: mp 116–117 °C [lit.[10a,b] 116–117 °C]; IR (KBr) ν_{max} 1600, 1180, 1090, 710 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 5.8 (2 H, t, J = 2 Hz), 3.64 (3 H, s, $-OCH_3$), 3.48 (3 H, s, $-OCH_3$), 3.4–3.2 (2 H, m), 2.7–2.5 (2 H, m, bridgehead protons), 1.1 (9 H, s, $OC(CH_3)_3$); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 128.4, 128.2, 117.3, 89.0, 76.9, 74.2, 52.6, 51.6, 46.9, 28.5.

Further elution of the column with petroleum ether furnished **16** (3.5 g, 20%) and was crystallized from hexane, mp 125 °C [lit.[10a] 124–125 °C]; IR (KBr) ν_{max} 1610, 1180, 720 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 6.0 (2 H, unresolved m), 3.78 (1 H, unresolved m), 3.6 (3 H, s, $-OCH_3$), 3.47 (3 H, s, $-OCH_3$), 3.04 (2 H, m), 2.9 (2 H, m), 1.12 (9 H, s, $-OC(CH_3)_3$); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 127.5, 126.6, 115.6, 91.8, 76.7, 73.7, 52.5, 51.5, 48.8, 48.4, 28.1.

Continued elution of the column with petroleum ether furnished the undesired adduct along with a small amount of **16** and was purified by repeated crystallizations: mp 195–196 °C [lit.[10a] 196–197 °C]; IR (KBr) ν_{max} 1610, 1180, 710 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 6.09 (2 H, m), 4.16 (1 H, br s), 3.46 (3 H, s, $-OCH_3$), 3.44 (3 H, s, $-OCH_3$), 2.77 (2 H, q), 2.46 (2 H, s); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 135.6, 130.6, 115.1, 80.3, 75.8, 73.6, 54.6, 52.4, 51.4, 46.2, 28.5.

***anti*-4-*tert*-Butoxy-12,12-dimethoxy-1,7,8,11-tetrachlorohexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane (17).** A solution of the Diels–Alder adduct **15** (4.3 g, 10 mmol) in 180 mL of acetone was purged with a slow stream of nitrogen and irradiated by using a 450-W medium-pressure mercury vapor lamp in a quartz immersion well for 30 min. The solvent was removed under reduced pressure and the crude product chromatographed when using a silica gel (30 g) column to furnish the hexacyclic adduct **17** (4.1 g, 95%) and crystallized from dichloromethane–petroleum ether: mp 156 °C [lit.[10b] 156–157 °C]; IR (KBr) ν_{max} 2950, 1360, 1220, 790, 760 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 4.0–3.9 (1 H, m, $-HC-$

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$OC(CH_3)_3$, 3.64 (3 H, s, $-OCH_3$), 3.36 (3 H, s, $-OCH_3$), 3.36–3.2 (2 H, m), 3.0–2.86 (2 H, m), 2.8–2.6 (2 H, m), 1.44 (9 H, s, $-OC(CH_3)_3$; ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 105.8 (s), 80.8 (d), 79.4 (s), 79.1 (s), 73.9 (s), 55.9 (d), 51.7 (q), 51.1 (q), 49.9 (d), 48.3 (d), 28.3 (q).

***syn*-4-*tert*-Butoxy-12,12-Dimethoxy-1,7,8,11-tetrachlorohexacyclo-[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecane (18).** A solution of the Diels–Alder adduct **16** (1 g, 0.25 mmol) in acetone was flushed with a slow stream of nitrogen and irradiated by using a 450-W medium-pressure mercury vapor lamp in a quartz immersion well for 1 h. The solvent was removed under reduced pressure and the crude product chromatographed over a silica gel (20 g) column to furnish the hexacyclic adduct **18** (600 mg, 60%) and crystallized from dichloromethane–petroleum ether; mp 140–141 °C; IR (KBr) ν_{max} 2950, 1210, 1100, 790, 730 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 4.16 (1 H, br s, $-HC-OC(CH_3)_3$, 3.6 (3 H, s, $-OCH_3$), 3.55 (3 H, s, $-OCH_3$), 3.2 (2 H, m), 2.88 (2 H, m), 2.7 (2 H, m), 1.4 (9 H, s, $OC(CH_3)_3$); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 105.0, 80.2, 80.1, 74.6, 72.7, 52.2, 51.8, 50.6, 49.9, 47.8, 27.2.

4-*tert*-Butoxy-12,12-Dimethoxyhexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecane (19). To a magnetically stirred solution of the tetrachlorohexacyclic adduct **17** (3.8 g, 9 mmol) in 250 mL of dry tetrahydrofuran and 25 mL of dry *tert*-butyl alcohol was added lithium metal (1.25 g, 0.17 g-atom) in small pieces over a period of 45 min. The rate of addition of lithium was carefully controlled so as to retain the reaction mixture under a gentle reflux. When all the lithium had been added, the reaction mixture was refluxed for 1 h more, the unreacted lithium filtered off, and the reaction mixture carefully quenched with water. THF was removed under reduced pressure and the crude product extracted with ethyl acetate (3 × 40 mL). The combined organic extract was washed with water and 3% HCl and dried. Removal of solvent furnished 2.8 g of crude product which was chromatographed over a silica gel (30 g) column to furnish pure **19** (2.2 g, 85%) and was crystallized from dichloromethane–petroleum ether: mp 117–118 °C; IR (KBr) ν_{max} 2950, 1300, 1100, 1050 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 4.0–3.88 (1 H, m, $-HC-OC(CH_3)_3$), 3.28 (3 H, s, $-OCH_3$), 3.18 (3 H, m, $-OCH_3$), 3.0–2.86 (2 H, m), 2.84–2.64 (2 H, m), 2.64–2.4 (2 H, m), 2.2–2.04 (2 H, m), 1.16 (9 H, s, $OC(CH_3)_3$); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 120.2 (s), 82.8 (d), 72.9 (s), 50.9 (d), 50.4 (q), 49.3 (d), 48.3 (d), 42.8 (d), 40.5 (d), 28.6 (q). Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 73.30; H, 9.06. In an analogous manner, reduction of the hexacyclic compound **18** furnished the dechlorinated product **20**.

4-Hydroxyhexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]decan-12-one (21): To a solution of **19** (2.0 g, 7 mmol) in 30 mL of dioxane was added 10 mL of 3 N HCl and the reaction mixture refluxed for 3 h. Dioxane was removed under reduced pressure and the product extracted with ethyl acetate (3 × 30 mL). The combined organic extract was washed with aqueous $NaHCO_3$ and dried. Removal of solvent furnished **21** (1.0 g, 80%) and was crystallized from dichloromethane–petroleum ether: mp 182–184 °C; IR (KBr) ν_{max} 3400 (br); ^1H NMR (100 MHz, $CDCl_3$) δ 4.2 (1 H, m), 3.1–2.0 (10 H, m). In an exactly identical experiment, **20** was hydrolyzed to the hexacyclic epimeric compound **22**.

Hexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecane-4,12-dione (23). To a suspension of pyridinium chlorochromate (1.5 g, 0.8 mmol) in 20 mL of dry dichloromethane was added a solution of the hydroxy compound **21** (1.0 g, 5.5 mmol) in 20 mL of dry dichloromethane. The reaction mixture was stirred at room temperature (~32 °C) for 1 h, diluted with ether, and filtered through a short column of Florisil. Removal of solvent furnished **23** (800 mg, 80%) and was purified by sublimation: mp 227–228 °C; IR (KBr) ν_{max} 1770, 1190, 1160, 1130 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 3.2 (4 H, m), 3.05 (2 H, m), 2.15 (4 H, m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 210.0, 48.8, 42.4, 41.8. Anal. Calcd for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41. Found: C, 77.25; H, 5.52.

Tetracyclo[7.2.1.$0^{4,11}$.$0^{6,10}$]dodeca-2,7-diene-5,12-dione (4). A sample of the hexacyclic diketone **23** (200 mg, 1.1 mmol) was slowly sublimed (130 °C/5 torr) through a quartz column preheated to 580 °C (±10 °C) as elaborated in the general procedure for FVP. The pyrolysate was charged on a neutral alumina (10 g) column and eluted with 20% ethyl acetate–benzene to furnish the tetracyclic diketone **4** (60 mg, 30%). It was further purified by sublimation to give an analytically pure sample: mp 173–175 °C; IR (KBr) ν_{max} 1720, 1630, 1180, 730 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$, Figure 1) δ 5.64 (4 H, s, —*HC*=CH), 4.0–3.4 (6 H, m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 214.2, 133.5, 62.7, 43.2; mass spectrum (70 eV), *m/e* (rel intensity) 186 (M^+, 47), 130 (100), 115 (26), 92 (21), 70 (7), 65 (71); high-resolution mass spectrum for $C_{12}H_{10}O_2$ calcd *m/e* 186.0681, found *m/e* 186.0677.

Further elution of the column resulted in the recovery of the hexacyclic diketone **23** (120 mg, 60%) which was recycled.

(1*R,2*R**,5*R**,6*R**,8*S**,9*S**,12*S**,14*R**,15*S**)-3,3,11,11-Tetrachloro-7-oxahexacyclo[11.2.1.$0^{2,5}$.$0^{6,15}$.$0^{8,14}$.$0^{9,12}$]hexadecane-4,10-dione (24).** To a vigorously stirred mixture of oxatetraquinane **5** (1.0 g, 8.25 mmol) and the Zn–Cu couple (8 g, 0.12 g atom) in 400 mL of dry ether was added trichloroacetyl chloride (8 g, 44 mmol) in 400 mL of dry ether dropwise over a period of 4 h. The reaction mixture was stirred at room temperature (~26 °C) for a further period of 24 h and filtered through a Celite pad to remove unreaced Zn–Cu couple as well as zinc chloride formed during the reaction. The filtrate was diluted with water carefully, washed with water (2 × 100 mL) and saturated aqueous $NaHCO_3$ (2 × 100 mL), and dried. Removal of solvent furnished 3 g of dark viscous material which was charged on a silica gel (40 g) column. Elution with 20% benzene–petroleum ether yielded the bis(dichloroketene) adduct **24** (1.0 g, 42%) and was crystallized from dichloromethane–petroleum ether: mp 238–240 °C dec; IR (KBr) ν_{max} 1810, 1180, 1040, 760 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 4.45 (2 H, d, *J* = 5 Hz, —*HC*—O—), 4.34 (1 H, $^1/_2$ AB q, *J* = 7 Hz), 3.46 (1 H, $^1/_2$ AB q, *J* = 7 Hz), 3.3–2.8 (4 H, m), 2.66–2.1 (2 H, m), 1.95 (1 H, m), 1.4 (1 H, m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 193.7 (s, —*C*=O), 89.2 (d,—*C*H—O—), 87.8 (s, —CCl_2), 67.5 (d), 59.3 (d), 56.0 (d), 49.7 (d), 39.6 (t). Anal. Calcd for $C_{15}H_{12}Cl_4O_3$: C, 47.12; H, 3.14. Found: C, 47.25; H, 3.20.

(1*R,2*R**,6*R**,7*S**,9*R**,10*S**,14*S**,15*R**,16*R**,17*S**)-3,3,13,13-Tetrachloro-8-oxahexacyclo[13.2.1.$0^{2,6}$.$0^{7,17}$.$0^{9,16}$.$0^{10,14}$]octadecane-4,12-dione (25).** To a solution of the bis(dichloroketene) adduct **24** (1.1 g, 2.6 mmol) in 200 mL of ether maintained at 5–7 °C was added a cold ethereal solution (80 mL) of diazomethane (prepared from 3 g of nitrosmethylurea) followed by 5 mL of methanol. The reaction mixture was kept at 5–7 °C for 4 h with occasional swirling. Excess of diazomethane was destroyed with a few drops of acetic acid and the ether solution washed with water and 5% aqueous $NaHCO_3$ and dried. Most of the ether was removed on the rotary evaporator and the total product diluted with petroleum ether and refrigerated for a few hours to furnish the ring expanded product **25** (640 mg, 60%) as fine white crystals, mp 220 °C dec; IR (KBr) ν_{max} 1770, 1400, 1040, 890, 740 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 4.4 (2 H, d, *J* = 7 Hz, $-HC-O-$), 3.6–1.5 (14 H, m); ^{13}C NMR (25.0 MHz, Me_2SO-d_6) δ 201.4, 89.4, 89.1, 62.1, 56.1, 50.1, 45.0, 32.8, one resonance merged with Me_2SO signals. C, H analysis for this compound was not done as it decomposed very soon.

(1*R,2*R**,6*R**,7*S**,9*R**,10*S**,14*S**,15*S**,16*R**,17*S**)-8-Oxahexacyclo[13.2.1.$0^{2,6}$.$0^{7,17}$.$0^{9,16}$.$0^{10,14}$]octadecane-4,12-dione (26).** To a solution of the tetrachlorohexacyclic dione **25** (820 mg, 2 mmol) in 30 mL of methanol was added 500 mg of NH_4Cl and 1 g (0.015 g-atom) of zinc powder. The reaction mixture was stirred at room temperature for 1 h and filtered through a Celite pad to remove unreacted zinc as well as zinc chloride formed during the reaction. Methanol was removed under reduced pressure and the residue extracted with dichloromethane (3 × 30 mL), washed with water, and dried. Removal of solvent furnished and hexacyclic dione **26** (450 mg, 82%) and was crystallized from dichloromethane–petroleum ether: mp 163–164 °C; IR (KBr) ν_{max} 1740, 1400, 1140 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.35 (2 H, d, *J* = 4.3 Hz), 3.31 (2 H, dd, $J_1 = J_2 = 4.4$ Hz), 3.05–2.9 (4 H, m), 2.45–2.33 (6 H, m), 2.23 (2 H, d, *J* = 8 Hz), 2.1 (1 H, td, $J_1 = 14$ Hz, $J_2 = 9$ Hz), 1.87–1.83 (2 H, m), 1.17 (1 H, td, $J_1 = 14$ Hz, $J_2 = 1.5$ Hz); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 218.8, 91.4, 57.0, 54.1, 48.7, 46.9, 44.8, 39.8, 37.6; mass spectrum (70 eV), *m/e* (rel intensity) 272 (M^+, 100), 244 (21), 215 (27), 149 (44), 133 (20), 120 (14), 105 (20), 91 (46), 79 (43), 77 (22); high-resolution mass spectrum for $C_{17}H_{20}O_3$. Calcd *m/e* 272.1412, found *m/e* 272.1413.

Dehydrogenation of Hexacyclic Dione 26 Using $PdCl_2$.[19] To a solution of the hexacyclic diketone **26** (135 mg, 0.5 mmol) in 25 mL of dry *tert*-butyl alcohol was added an excess of $PdCl_2$ (225 mg, 1.25 mmol), and the reaction mixture was refluxed for 48 h. Unreacted $PdCl_2$ as well as the Pd metal formed during the reaction was filtered and kept aside for recycling. *tert*-Butyl alcohol was removed under reduced pressure and the total product (95 mg, 75%) charged on a silica gel (15 g) column. Careful elution with 40% benzene–petroleum ether furnished the hexacyclic monoenone **30** (16 mg, 17%), and it was crystallized from dichloromethane–petroleum ether: mp 148 °C; IR (KBr) ν_{max} 1740, 1715, 1640, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.95 (1 H, d, *J* = 4 Hz, —*HC*=C—), 4.87 (1 H, d, *J* = 10 Hz, —C=C—*HC*—O), 4.58 (1 H, d, *J* = 11 Hz, —*HC*—O—), 3.48–3.33 (3 H, m), 2.97–2.94 (2 H, m), 2.76 (1 H, m), 2.47–2.3 (5 H, m), 2.16–2.09 (2 H, m), 1.93–1.80 (2 H, m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 218.0, 210.2, 184.8, 124.3, 92.7, 81.1, 60.2, 58.1, 54.3, 51.3, 49.1, 47.3, 47.2, 44.7, 43.3, 39.2, 36.9; mass spectrum (70 eV), *m/e* (rel intensity) 270 (M^+, 100), 135 (21), 131 (42), 120 (23), 115 (27), 105 (23), 91 (72), 79 (38), 77 (40), 53 (29), 51 (17).

Further elution of the column furnished **28** (20 mg, 18%) and was crystallized from dichloromethane–petroleum ether, mp 216–218 °C dec; IR (KBr) ν_{max} 1705, 1620, 1400, 1020 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.0 (2 H, d, *J* = 3 Hz, —*HC*=C—), 5.06 (2 H, d, *J* = 5.5 Hz, —*HC*—O), 3.68–3.20 (4 H, m), 2.84 (1 H, d, *J* = 8 Hz), 2.70 (1 H, d, *J* = 8 Hz), 2.16–1.9 (6 H, m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 210.0,

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183.8, 125.7, 83.1, 60.2, 51.9, 47.7, 43.5, 29.7; mass spectrum (70 eV), m/e (rel intensity) 268 (M^+, 100), 240 (23), 171 (23), 159 (23), 145 (29), 133 (56), 115 (46), 105 (35), 91 (92), 77 (56), 55 (33).

Continued elution of the column with the same solvent system yielded **29** (25 mg, 20%) and was crystallized from dichloromethane–petroleum ether: mp 215 °C; IR (KBr) ν_{max} 1710, 1630, 1140, 690 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.97 (1 H, d, J = 1.5 Hz, —*H*C=CH—), 5.83 (1 H, d, J = 2.2 Hz, —*H*C=CH), 5.08 (1 H, d, J = 4.9 Hz, —C=C—*H*C—O), 4.5 (1 H, dd, J_1 = 8.2 Hz, J_2 = 4.5 Hz, —*H*C—O—), 3.62–3.43 (4 H, m), 3.23 (1 H, m), 2.84–2.78 (2 H, m), 2.72 (1 H, td, J_1 = 14.5 Hz, J_2 = 10 Hz), 2.54 (1 H, m), 2.27 (1 H, dd, J_1 = 16 Hz, J_2 = 3.8 Hz), 2.16 (1 H, dd, J_1 = 17 Hz, J_2 = 3.2 Hz), 1.82 (1 H, td, J_1 = 14.5 Hz, J_2 = 6 Hz); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 214.8, 208.9, 189.1, 184.8, 125.4, 124.8, 90.8, 84.4, 61.0, 51.3, 50.0, 49.5, 49.0, 43.9, 42.0, 40.9; mass spectrum (70 eV), m/e (rel intensity) 268 (M^+, 100), 169 (12), 158 (13), 131 (42), 115 (28), 91 (50), 79 (23), 77 (44), 65 (25), 53 (22); high-resolution mass spectrum for $C_{17}H_{16}O_3$. Calcd m/e 268.1099, found m/e 268.1096.

Further elution of the column with 60% benzene–petroleum ether furnished **27** (28 mg, 21%) and was crystallized from dichloromethane–petroleum ether: mp 217 °C dec; IR (KBr) ν_{max} 1705, 1640, 1080, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.86 (2 H, d, J = 1.2 Hz, —*H*C=C—), 4.51 (2 H, m, —*H*C—O—), 3.62–3.43 (6 H, m), 2.86 (1 H, d, J = 7.2 Hz), 2.82 (1 H, d, J = 7.2 Hz), 2.51 (1 H, td, J_1 = 14 Hz, J_2 = 10.5 Hz); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 208.9, 186.9, 125.1, 91.4, 60.2, 50.2, 49.3, 42.2, 38.2; mass spectrum (70 eV), m/e (rel intensity) 268 (M^+, 100), 240 (39), 212 (13), 148 (18), 133 (15), 115 (13), 104 (15), 91 (27), 79 (16), 77 (34), 65 (15), 51 (13); high-resolution mass spectrum for $C_{17}H_{16}O_3$. Calcd m/e 268.1099, found m/e 268.1101.

(1*R,6*R**,7*S**,9*R**,10*S**,15*R**,16*S**,17*S**)-8-Oxahexacyclo[13.2.1.0^{2,6}.0^{7,17}.0^{9,16}.0^{10,14}]octadeca-2,13-diene-4,12-dione (31).** To a solution of the symmetrical bis-enone **27** (10 mg, 0.06 mmol) in 15 mL of dry dichloromethane was added 10 mg of 1,8-diazabicyclo[5.4.0]undecane (DBU). The reaction mixture was refluxed for 5 h and diluted with 10 mL more of dichloromethane. The organic layer was washed with 5% HCl, followed by water, and dried. Removal of solvent furnished 10 mg of crude product. A quick filtration through a silica gel (5 g) column furnished the isomerized enone **31** (9 mg, 90%) and was crystallized from dichloromethane–petroleum ether: mp 212–214 °C dec; IR spectrum (KBr) ν_{max} 1710, 1630, 1090, 940 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 5.76 (2 H, s with st, *H*C=C—), 4.52 (2 H, dd, J_1 = J_2 = 6 Hz, —*H*C—O), 3.8–3.3 (4 H, m), 3.1–2.9 (2 H, m), 2.5–2.0 (4 H, m), 2.0–1.6 (2 H, m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 209.7, 189.9, 125.6, 81.6, 58.5, 51.3, 46.9, 37.8, 35.5; mass spectrum (70 eV), m/e (rel intensity) 268 (M^+, 100), 240 (33), 212 (12), 148 (12), 132 (12), 115 (12), 105 (15), 91 (21), 77 (20); high-resolution mass spectrum for $C_{17}H_{16}O_3$ calcd m/e 268.1099, found m/e 268.1101.

(1*R,2*S**,6*S**,7*S**,9*R**,10*R**,14*R**,15*S**,16*R**,17*S**)-8-Oxahexacyclo[13.2.1.0^{2,6}.0^{7,17}.0^{9,16}.0^{10,14}]octadecane-4,12-dione (32).** A solution of **31** (8 mg, 0.05 mmol) in 10 mL of dry ethyl acetate was hydrogenated (40-psi H_2 pressure) over 10% Pd/C (3 mg) for a period of 6 h. Pd/C was filtered off and the solvent removed to furnish **32** (8 mg, 100%). Crystallization from dichloromethane–petroleum ether furnished an analytically pure sample: mp 150–152 °C; IR (KBr) ν_{max} 1730, 1160, 980 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.39 (2 H, dd, J_1 = J_2 = 4.39 Hz, —*H*C—O—), 3.1–3.07 (2 H, m), 3.04–2.91 (4 H, m), 2.70–2.62 (4 H, m), 2.36–2.21 (6 H, m), 1.52–1.47 (1 H, m), 0.94–0.92 (1 H, m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 220.2, 87.8, 57.6, 50.1, 43.4, 43.2, 40.5, 38.5, 32.3; mass spectrum (70 eV), m/e (rel intensity) 272 (M^+, 100), 191 (36), 91 (26), 79 (17), 17 (14); high-resolution mass spectrum for $C_{17}H_{20}O_3$ calcd m/e 272.1412, found m/e 272.1413.

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Model Compounds for the Study of Spectroscopic Properties of Visual Pigments and Bacteriorhodopsin

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Abstract: A series of modified retinals bearing nonconjugated positive charges along the polyene were synthesized. It was found that nonconjugated charges shifted the absorption maxima of retinal chromophore as well as protonated retinal Schiff bases. The magnitude of shift observed in bacteriorhodopsin (bR), 5170 cm^{-1}, could be found in our models by the additivity of two factors: (1) interaction through space with a positive charge located in the vicinity of the ring operating in nonprotic solvents, provided that the interaction between the charge and its counteranion is weakened by a homoconjugation effect; (2) weakening the interaction of the Schiff base positively charged nitrogen with its counteranion. A shift of ca. 5000 cm^{-1} can also be achieved by interaction through space with two nonconjugated positive charges. The absorption maximum of protonated retinal Schiff base is influenced significantly by an interaction with a nonconjugated charge located in the vicinity of the ring moiety or carbon 9. The influence of a charge located in the vicinity of carbon 12 and carbon 14 is minor. Nonconjugated positive charges have a remarkable effect on C=C stretching frequencies as well. It is suggested that the different C=C stretching frequencies found in bR, visual pigments, as well as their photochemically induced intermediates, may originate from interaction with external charges. the C=N^+ stretching frequency does no exhibit similar sensitivity to external nonconjugated charges, and it is practically unaffected by them.

Color recognition is based on the different absorption maxima of visual pigments which are located in photoreceptors. The human retina contains three types of pigments absorbing at 450, 535, and 650 nm, while other vertebrates have a range of absorptions between 450 and 600 nm.[1] All these visual pigments consist of a chromophore, 11-*cis*-retinal, covalently bound to an apoprotein to the ϵ-amino terminal of a lysine residue via a protonated Schiff base (SBH^+) linkage.[2] Protonated 11-*cis*-retinal Schiff base formed from *n*-butylamine absorbs at 440 nm in methanol. The red shifts from 440 nm found in various visual pigments are due to the effects of the protein environment and were defined as "opsin shifts".[3] A retinal-based pigment, bacteriorhodopsin (bR), was found[4] in the purple membrane of the

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