Laticyclic Conjugated Polyenes. Study on Diels−Alder Cycloadditions of a Facially Dissymmetric Maleic Anhydride

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Received February 17, 1999

The tetracyclic ring-fused, facially dissymmetric maleic anhydride **2** was synthesized from compound **9** obtained from the Diels−Alder cycloaddition of the bicyclic ring-fused cyclohexadiene **1** and acetylenedicarboxylate. Maleic anhydride **2** readily underwent the Diels−Alder cycloadditions with anthracene, 1,3-diphenylisobenzofuran, cyclopentadiene, 1,3-cyclohexadiene, 6,6-dimethylfulvene, and *o*-quinodimethane. All the cycloadditions occurred exclusively on the π-face syn to the etheno bridge of **2**, thereby in cases of the cycloadditions with anthracene, cyclopentadiene, 1,3-cyclohexadiene, and 6,6-dimethylfulvene producing the corresponding adducts **11a**, **18b**, **22b**, and **23b** that contain three double bonds aligned in parallel. The structures of **18b** and **22b** were unequivocally established by the X-ray structural determinations. The molecular structure of maleic anhydride **2** was analyzed by X-ray crystallography to have a pyramidalized dienophilic double bond, which appeared to correlate well with the observed π-facial selectivity.

Introduction

The synthetic endeavor toward the rigid polycyclic molecules of specially designed architecture has been actively demonstrated in the search for new structure systems that may possess specific functions of various interests. For example, rigid and often symmetric molecules are capable of functioning as "spacers" for use as probes to evaluate the intramolecular nonconjugated orbital interactions in terms of through-space and through-bond mechanisms[1] and electron-transfer phenomenon with regard to the dependence of distance and orientation between donor and acceptor groups.[2] They are also capable of functioning as "templates" for use as a synthetic tactic to direct specific bond formation.[3] Recently, intense research activity on supramolecular chemistry has also attracted much interest in the synthesis of rigid polycyclic spacer molecules for use as complementary components for molecular recognition directed self-assembly to construct supermolecules.[4] A variety of ring systems have been used as basic building blocks to construct the polycyclic spacer molecules. Among them, acene,[5] 1,4-cyclohexadiene,[6] cyclobutane,[7] norbornane,[8] and 7-oxabicyclo[2.2.1]heptane[9] are most notable examples. Toward the synthesis of these types of polycyclic molecules, the most commonly employed strategy is based on the concept of repetitive Diels−Alder cycloadditions using appropriate bis-dienes and bis-dienophiles.

Our interest in the synthesis of polycyclic molecules containing π-bonds arranged in laticyclic topology[10] led us to prepare 1,8,9,10-tetrachlorotricyclo-11,11-dimethoxy-[6.2.1.0^{2,7}] undeca-3,5,9-triene (**1**) for use as a synthon for *cis*-9,10-dihydronaphthalene.[11] We utilized triene **1** as a bis-cyclohexadiene to stereoselectively construct polycyclic molecules that hold two syn-concatenated bicyclo[2.2.2]octene units by the method of sequential Diels−Alder cycloadditions.[12] As we continue to exploit

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(1) (a) Gleiter, R.; Schafer, W. *Acc. Chem. Res.* **1990**, *23*, 369−375. (b) Hunig, S.; Martin, H.-D.; Mayer, B.; Peters, K.; Prokschy, F.; Schmitt, M.; von Schnering, H. G. *Chem. Ber.* **1987**, *120*, 195−201. (c) Martin, H.-D.; Mayer, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 283−314. (d) Hoffmann, R. *Acc. Chem. Res.* **1971**, *4*, 1−9. (e) Hoffmann, R.; Imamura, A.; Hehre, W. J. *J. Am. Chem. Soc.* **1968**, *90*, 1499−1509.

(2) (a) Paddon-Row, M. N.; Jordan, K. D. In *Modern Models of Bonding and Delocalization*; Libman, J. F., Greenberg, A., Eds.; VCH Publishers: New York, 1988; Chapter 3, pp 115−194. (b) Lawson, J. M.; Craig, D. C.; Oliver, A. M.; Paddon-Row, M. N. *Tetrahedron* **1995**, *51*, 3841−3864. (c) Kumar K.; Tepper, R. J.; Zeng, Y.; Zimmt, M. B.; *J. Org. Chem.* **1995**, *60*, 4051−4066. (d) Jordan, K. D.; Paddon-Row, M. N. *Chem. Rev.* **1992**, *92*, 395−410. (e) Paddon-Row, M. N.; Cotsaris, E.; Patney, H. K. *Tetrahedron* **1986**, *42*, 1779−1788. (f) Paddon-Row, M. N. *Acc. Chem. Res.* **1982**, *15*, 245−251. (g) Paddon-Row, M. N.; Patney, H. K.; Brown, R. S.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 5575−5577.

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(5) (a) Kenny, P. W.; Miller, L. L.; Rak, S. F.; Jozefiak, T. H.; Christopfel, W. C.; Kim, J.-H.; Uphaus, R. A. *J. Am. Chem. Soc.* **1988**, *110*, 4445−4446. (b) Thomas, A. D.; Miller, L. L. *J. Org. Chem.* **1986**, *51*, 4160−4169. (c) Patney, H. K. *J. Org. Chem.* **1988**, *53*, 6106−6109.

(6) Graham, R. J.; Paquette, L. A. *J. Org. Chem.* **1995**, *60*, 5770−5777.

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(8) (a) Margetic, D.; Johnston, M. R.; Tiekink, E. R. T.; Warrener, R. N. *Tetrahedron Lettt.* **1998**, *39*, 5277−5280 and earlier papers from this group. (b) Warrener, R. N.; Butler, D. N. *Aldrichim. Acta* **1997**, *30*, 119−130. (c) Paddon-Row, M. N. *Acc. Chem. Res.* **1994**, *27*, 18−25.

(9) (a) Philp, D.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1154−1196. (b) Warrener, R. N.; Wang, S.; Russell, R. A. *Tetrahedron* **1997**, *53*, 3975−3990.

(10) Goldstein, M. J.; Hoffmann, R. *J. Am. Chem. Soc.* **1971**, *93*, 6193−6204.

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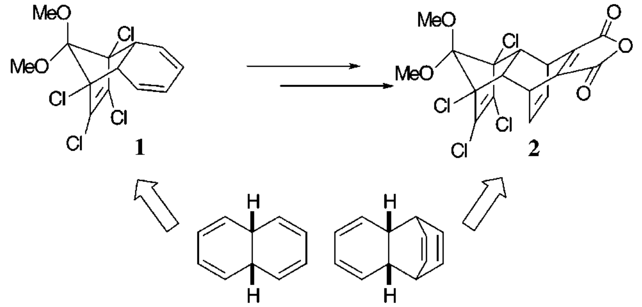
10.1021/jo990256r CCC: $18.00

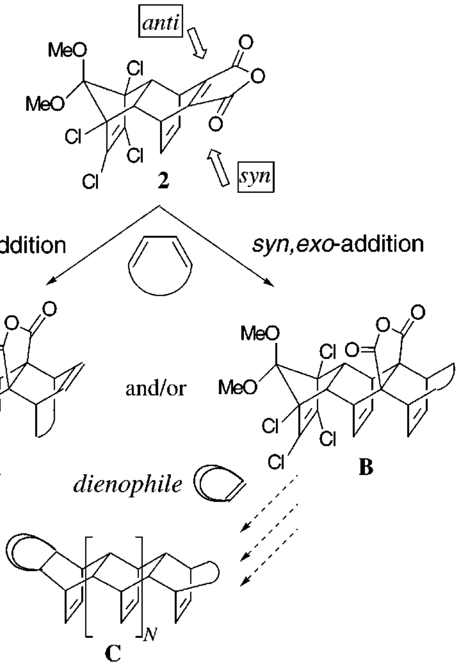
the application of tricyclic triene **1** for the synthesis of bicyclo[2.2.2]octene-based rigid polycyclic spacer molecules, we have undertaken the preparation of 3,4,5,6-tetrachloro-13,13-dimethoxytetracyclo[6.2.2.$1^{3,6}$.$0^{2,7}$]trideca-4,9,11-triene-9,10-dicarboxylic anhydride (**2**) from **1**.[13] Anhydride **2** is of synthetic interest not only as a dienophile but also as a cyclic diene component for use in Diels−Alder cycloadditions, because it contains an activated double bond and a masked cyclohexadiene moiety that can be generated by a dechlorination−deacetalization−decarbonylation process.[12]



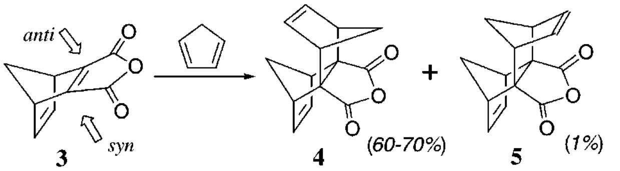
Maleic anhydride **2** has laticyclic conjugated double bonds and is facially dissymmetric. Initially, we anticipated simply based upon consideration of steric factors that the Diels−Alder cycloadditions would likely proceed via syn-side (relative to the etheno bridges in **2**) attack of the cyclic diene upon **2** to produce syn,endo and/or syn,exo cycloadducts (**A** and/or **B**; Scheme 1).[14] Cycloadducts **B**, for example, thus formed could subsequently be subjected to the unmasking of cyclohexadiene substructure (protection of anhydride moiety may deem necessary) for further elaboration of linearly syn-concatenated bicyclo[2.2.2]octenes having double bonds arranged for laticyclic conjugation as shown by generic structure **C** (Scheme 1).[15]

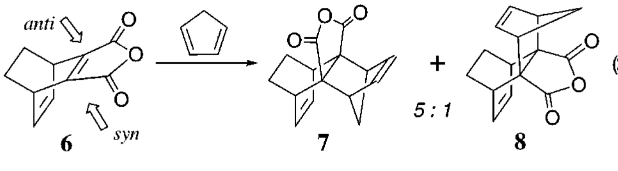
This anticipation of facial selectivity is contrary to the behavior of bicyclo[2.2.1]heptadienyl (norbornadienyl) systems. It is well documented that Diels−Alder cycloadditions to norbornadienyl systems occur predominately or exclusively upon the face anti to the etheno bridge.[16,17]

Scheme 1



Stille and Frey in 1959 reported the Diels−Alder cycloaddition of cyclopentadiene to norbornadiene and established the major 1:1 adduct to be presumably formed by anti-face attack of cyclopentadiene onto dienophile.[17e] Such a mode of addition was observed nearly 10 years later by Edman and Simmon in their study of the Diels−Alder cycloadditions of bicyclic dicarboxylic anhydride **3** with various dienes.[18] Two 1:1 adducts **4** (60−70%) and **5** (1%) were isolated from the cycloaddition of cyclopentadiene with maleic anhydride **3**, which were established to result from exclusive anti-face attack of cyclopentadiene onto **3** (eq 1). However, additions of a diene onto bicyclo[2.2.2]octa-2,5-dienyl systems are known to take place preferentially at the syn face.[19] Williams et al. investigated the Diels−Alder cycloaddition of cyclopentadiene with bicyclic dicarboxylic anhydride **6** and observed pronounced syn-facial selectivity.[19a,b] Only two of the four possible steroisomeric adducts **7** and **8** were formed in a ratio of 5:1 (eq 2).





The distinct preference for attack of a diene on the syn face of bicyclo[2.2.2]octadienyl systems is even reinforced in the Diels−Alder cycloadditions of more elaborated, facially dissymmetric maleic anhydride **2**. The cycload-

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(12) (a) Lin, C.-T.; Wang, N. J.; Tseng, H. Z.; Chou, T.-C. *J. Org. Chem.* **1997**, *62*, 4857−4861. (b) Lin, C.-T.; Wang, N. J.; Yeh, Y.-L.; Chou, T.-C. *Tetrahedron* **1995**, *51*, 2907−2928. (c) Lin, C.-T.; Hwang, B.-P.; Chou, T.-C. *J. Chin. Chem. Soc. (Taipei)* **1993**, *40*, 159−167. (d) Chou, T.-C.; Hong, P.-C.; Lin, C.-T. *Tetrahedron Lett.* **1991**, *32*, 6351−6354. (e) Lin, C.-T.; Chou, T.-C. *J. Org. Chem.* **1990**, *55*, 2252−2254. (f) Chou, T.-C.; Chuang, K.-S.; Lin, C.-T. *J. Org. Chem.* **1988**, *53*, 5168−5170.

(13) Chou, T.-C.; Jiang, T. S.; Hwang, J. T.; Lin, C.-T. *Tetrahedron Lett.* **1994**, *35*, 4165−4168.

(14) Syn and anti refer to the relative side of the attachment of diene and the existing etheno bridge in **2,** and endo and exo refer to the orientation of the anhydride moiety relative to the newly formed bicyclic ring nucleus in accordance with the Alder endo rule.

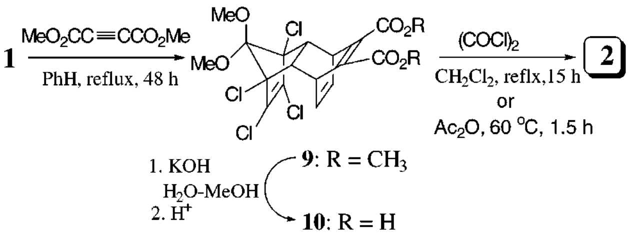
(15) For a different approach to the class of laticyclic conjugated polyenes of generic structure **C**, see: (a) Grimme, W.; Gossel, J.; Lex, J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 473−475. (b) Grimme, W.; Reinhart, G. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 617−618.

(16) Exo and endo are frequently used in designating facial selectivity in norbornenyl systems. To be consistent within the present paper, we replace exo and endo with anti and syn, respectively, to denote the face with respect to the existing etheno bridge.

(17) (a) Bartlett, P. D.; Blakeney, A. J.; Kimura, M.; Watson, W. H. *J. Am. Chem. Soc.* **1980**, *102*, 1383−1390. (b) Huisgen, R.; Ooms, P. H. J.; Mingin, M.; Allinger, N. L. *J. Am. Chem. Soc.* **1980**, *102*, 39513953. (c) McCulloch, R.; Rye, A. R.; Wage, D. *Tetrahedron Lett.* **1969**, 5163−5166. (d) Cave, M. P.; Scheel, F. M. *J. Org. Chem.* **1967**, *32*, 1304−1307. (e) Stille, J. K.; Frey, D. A. *J. Am. Chem. Soc.* **1959**, *81*, 4273−4275. (f) Soloway, S. B. *J. Am. Chem. Soc.* **1952**, *74*, 1027−1209.

(18) Edman, J. R.; Simmons, H. E. *J. Org. Chem.* **1968**, *33*, 3808−3816.

Scheme 2



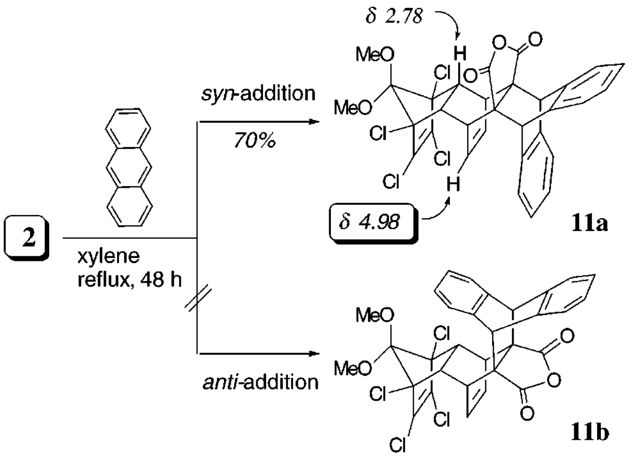
ditions proceeded with the attack of cyclic dienes exclusively upon the activated double bond of **2** via the face syn to the etheno bridge, thereby affording cycloadducts having stereostructures **A** and/or **B** (Scheme 1).[13] The syn-facial addition is exclusive for all cases investigated in this study! In this paper, we wish to report the results of study in full account, along with comment on the syn-facial selectivity based on the X-ray structural analysis of maleic anhydride **2**.

Results and Discussion

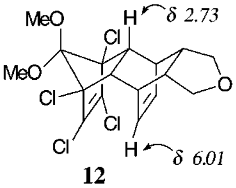
The preparation of facially dissymmetric maleic anhydride **2** as presented in Scheme 2 starts from the readily available tricyclic triene **1**[11] following the established procedure with modification. Thus, a solution of triene **1** and dimethyl acetylenedicarboxylate in benzene was refluxed for 48 h, thereby furnishing Diels–Alder adduct **9** in 83% yield. The reaction proceeded with the dienophile approaching **1** exclusively from the less hindered exo face, as expected by known facts,[12] to yield the adduct **9**. Dehydration of maleic acid **10**, obtained from hydrolysis of adduct **9**, with oxalyl chloride in refluxing dichloromethane for 15 h[20] or by heating with acetic anhydride at 60 °C for 1.5 h[19a] afforded maleic anhydride **2** in nearly 60% overall yield from **1**.[21] The presence of two characteristic absorption bands at 1777 and 1840 cm^{-1} in the infrared spectrum of **2** confirmed the formation of anhydride ring moiety. The structure is further supported by the X-ray structural determination (vide infra).

Diels–Alder Cycloadditions of 2 with Endocyclic Dienes. The electronically activated double bond present in maleic anhydride **2** readily undergoes the Diels–Alder cycloadditions with various endocyclic dienes.[22] The results of Diels–Alder cycloadditions of maleic anhydride **2** with anthracene, 1,3-diphenylisobenzofuran, cyclopentadiene, cyclohexadiene, and 6,6-dimethylfulvene are outlined in Schemes 3–7. To determine the composition of the crude product mixture (number of isomeric adducts and ratio), thin-layer chromatographic and ^{1}H NMR spectral analyses were performed immediately after the workup procedure without further separation and purification. Elemental and mass analyses were used to establish the 1:1 nature of the resulting cycloadducts. All the adducts obtained from the reactions have inherent C_s symmetry as evident from their rather simple ^{1}H and ^{13}C NMR spectra, which are consistent with the structural assignments. The stereostructures of the adducts were assigned principally on the basis of ^{1}H NMR spectral analyses[23] and by comparison with similar adducts prepared in our laboratory.

Scheme 3



Thus, the Diels–Alder cycloaddition of **2** with anthracene (3 equiv) in refluxing xylene for 2 days afforded only one of two possible 1:1 adducts (i.e., syn adduct **11a** and anti adduct **11b**, Scheme 3) in 70% yield after recrystallization from CHCl$_3$. The ^{1}H NMR spectrum of this adduct exhibits a signal (pseudo-dd, part of an AA′XX′ system) centered at δ 4.98 ascribed to the vinyl hydrogens of the etheno bridge: an upfield shift of 1.03 or 1.14 ppm with respect to that of ether **12** (at δ 6.01)[12a] or anhydride **13** (at δ 6.12),[12f] respectively. The upfield shift is attributed to the consequence of a strong anisotropic shielding effect on vinyl hydrogens by the proximal, face-to-face benzene ring and double bond and is best demonstrated by comparison of the vinyl hydrogen absorption signals in bicyclo[2.2.2]octadienes **14**,[24] **15**,[12c,24] and **16**.[15b] This observation led us to suggest that the reaction occurred via addition of anthracene to the syn face of **2** to form an adduct having the stereostructure **11a**, in which the etheno bridge is sandwiched face-to-face by a benzene ring and a chlorine-substituted double bond.[25]



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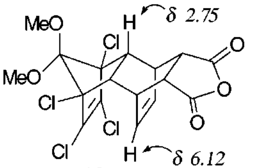

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The cycloaddition of 1,3-diphenylisobenzofuran (1 equiv) to maleic anhydride **2** was carried out by stirring the reaction mixture in dichloromethane at room temperature for 30 min. Out of four possible stereoisomeric 1:1 adducts (i.e., *syn,endo*-**17a**, *syn,exo*-**17b**, *anti,endo*-**17c**, and *anti,exo*-**17d**, Scheme 4), only one adduct was ob-

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[19] (a) Williams, R. V.; Todime, M. M. R.; Enemark, P.; van der Helm, D.; Rizvi, S. K. *J. Org. Chem.* **1993**, *58*, 6740–6744. (b) Williams, R. V.; Edwards, W. D.; Gadgil, V. R.; Colvin, M. E.; Seidl, E. T.; van der Helm, D.; Hossain, M. B. *J. Org. Chem.* **1998**, 63, 5268–5271. (c) Bertsch, A.; Grimme, W.; Reinhardt, G.; Rose, H.; Warner, P. N. *J. Am. Chem. Soc.* **1988**, *110*, 5112–5117.

[20] Pokkuluri, P. R.; Scheffer, J. R.; Trotter, J.; Yap, M. *J. Org. Chem.* **1992**, *57*, 1486-1494.

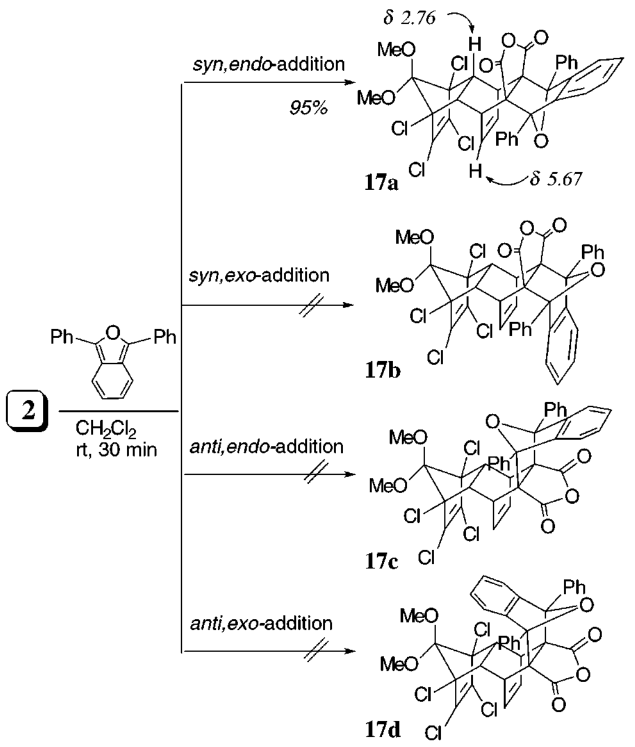
[21] Maleic anhydride **2** is rather stable. On heating **2** in toluene under reflux for 3 days, there was no detectable retro-Diels–Alder fragmentation of **2**. Decomposition, however, became observable at the temperature of refluxing xylene (140 °C).

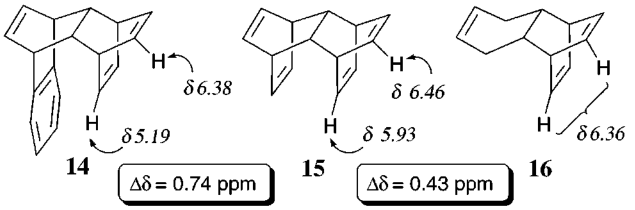
[22] The electronically activated double bond in maleic ester **9**, however, does not undergo Diels–Alder cycloadditions with various dienes, including 1,3-diphenylisobenzofuran and cyclopentadiene, under classical or catalytic conditions.

[23] Marchand, A. P. *Stereochemical Applications of NMR Studies in Rigid Bicyclic Systems*; Verlag Chemie International: New York, 1982.

[24] Melder, J. P.; Wahl, F.; Fritz, H.; Prinzbach, H. *Chimia* **1987**, *41*, 426–428.

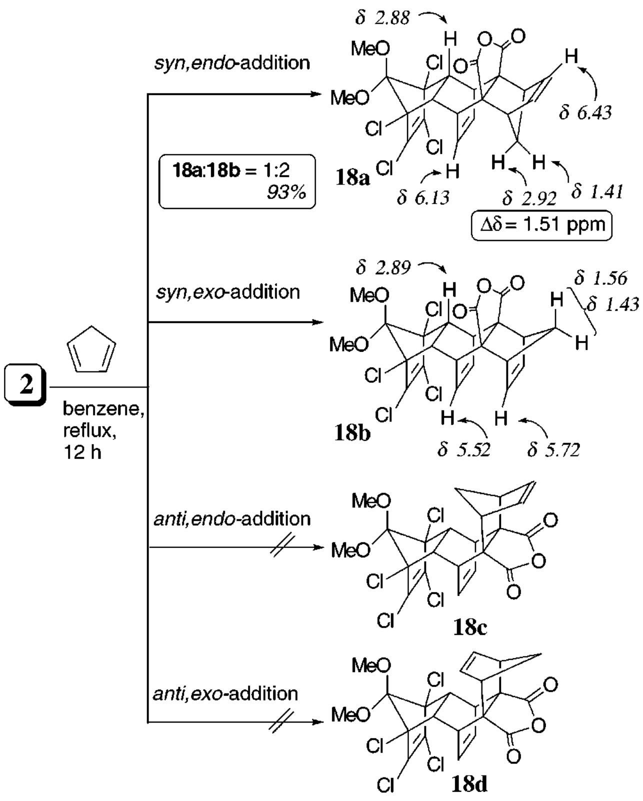
Scheme 4





14 **15** **16**

Scheme 5



tained in 95% yield after recrystallization from EtOAc. In the ^{1}H NMR spectrum of this adduct, an absorption signal centered at δ 5.67 (pseudo-dd) due to the etheno-bridge hydrogens indicates the absence of a proximal, face-to-face benzene ring. An upfield shift of 0.34 or 0.45 ppm, as compared, respectively, to the signals of the etheno-bridge hydrogens of **12** (at δ 6.01) or anhydride **13** (at δ 6.12), can only be attributed to the result of a shielding effect on the double bond by the proximal oxygen bridge.[26] On the basis of this information, the syn,exo isomer **17b** was eliminated as the product, which would be expected to show an ^{1}H NMR spectrum having a signal for the etheno-bridge hydrogens at much higher field, similar to that of **11a** (at δ 4.98). The ^{1}H NMR spectrum also contains a broad singlet assigned to the tertiary hydrogens at the ring junction at 2.76, which is nearly same as that in adducts **11a** (br s at δ 2.78), **12** (br s at δ 2.73), and **13** (br s at δ 2.75). The small difference in chemical shifts indicates that the two tertiary hydrogens in this adduct are syn to the anhydride moiety as in the adduct **11a**, rather than syn to an oxygen atom or benzene ring as in the other adducts (i.e., *anti,endo*-**17c** or *anti,exo*-**17d**) that would be formed, if addition of 1,3-diphenylisobenzofuran had occurred upon the anti face of **2**.[25] The stereostructure of this adduct is therefore assigned to have the syn,endo stereochemistry as depicted in **17a** (Scheme 4), which results from syn-side attack of 1,3-diphenylisobenzofuran upon the dienophile **2** and endo addition in accordance with the Alder rule. When a solution of maleic anhydride **2** in benzene was refluxed in the presence of excess cyclopentadiene (5 equiv) for 12 h, the reaction furnished two isomeric 1:1 cycloadducts in a ratio of 2:1. These two adducts were separated by column chromatography and recrystallized from CH_2Cl_2 and $CHCl_3$ to give adducts **18a** and **18b**, respectively, in a total of 93% yield (Scheme 5).

The syn,exo structure **18b** is assigned to the major product, for among the four possible stereoisomeric adducts (**18a**−**d**) only **18b** displays the ^{1}H NMR spectrum with absorption signals centered at δ 5.72 (pseudo-t) and δ 5.52 (pseudo-dd). The signals are ascribed to respective vinyl hydrogens of two mutually shielded double bonds of bicyclo[2.2.1]heptene and bicyclo[2.2.2]octene substructures in **18b**, in which the vinyl hydrogens of central double bond (at δ 5.52) is further shielded by the flanking chlorinated double bond. Groups of vinyl hydrogens displaying comparable chemical shifts have been noted in laticyclic conjugated trienes **19**[12a] and **20**,[25] thereby supporting our assignment for **18b**.[27] To confirm our structural assignment, an X-ray single-crystal structure of **18b** was determined.[28]

On the other hand, in the ^{1}H NMR spectrum of minor product, the corresponding etheno-bridge hydrogens ap-

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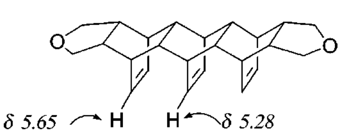
(25) In the anti-addition adduct **11b**, one of the benzene rings is placed above the hydrogens at the ring junction and is expected to cause a large upfield shift of their absorptions, which is inconsistent with thier occurrence at the observed δ value (δ 2.78). For example, in tetrahydrogenated **14**, the two pairs of hydrogens at the ethano bridge proximal to the benzene ring experience shielding effects and, hence, display anomalous upfield chemical shifts (δ 0.57/ δ 0.75): Grimme, W.; Pohl, K.; Wortmann, J.; Frowein, D. *Liebigs Ann.* **1996**, 1905−1916. See also: Butler, D. N.; Barrette, A.; Snow, R. A. *Synth. Commun.* **1975**, *5*, 101−106.

(26) A shielding effect of the double bond by the proximal oxygen-bridge in rigid oxa analogues of the norbornylogue skeleton has been noted. LeGoff, E.; Slee, J. D. *J. Org. Chem.* **1970**, *35*, 3897−3901.

(27) This kind of consequence is typical for *endo,endo*-dimethanonaphthalene and other related homologous systems. Astin, K. B.; Mackenzie, K. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1004−1010.



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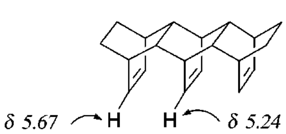

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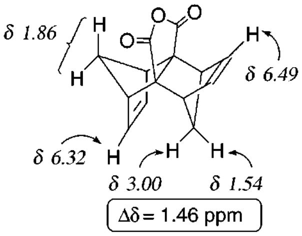
pear at δ 6.43 (pseudo-t) and δ 6.13 (pseudo-dd), the former being comparable to vinyl hydrogens of *endo*- or *exo*-bicyclo[2.2.1]hept-2-ene-5,6-dicarboxylic anhydride substructure in **4**[18] and the latter in compound **13**. This reveals that all three of the other stereoisomers (**18a**, **18c**, and **18d**, Scheme 5) are possible. A diagnostic feature that led us to eliminate isomers **18c**/**18d** and assign stereostructure **18a** for this minor adduct is the unusual absorption of an AB pattern ($J = 10$ Hz) generated by the two hydrogens on the methano bridge.



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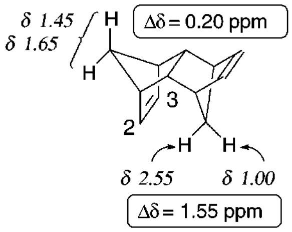
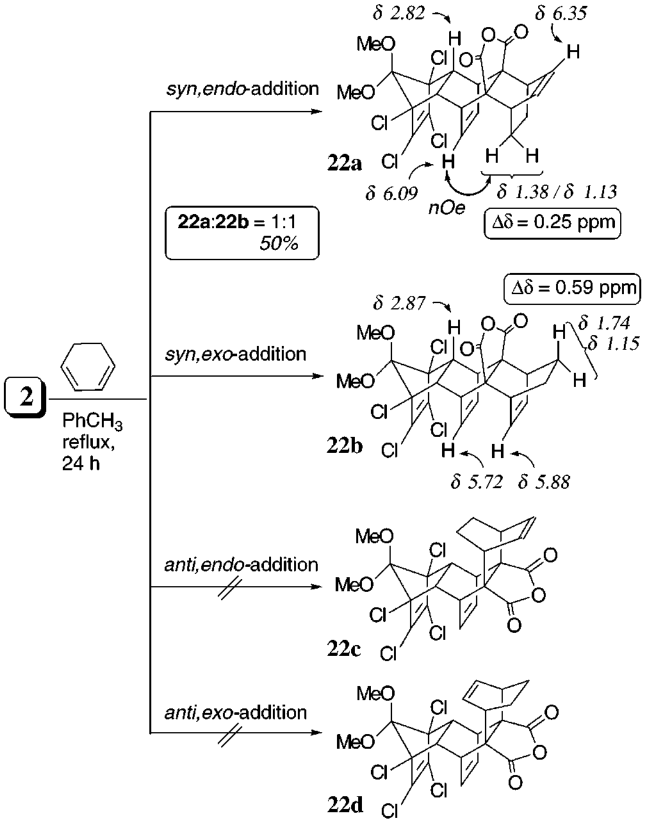


21

The ^{1}H NMR spectral assignments in ring systems composed of fused norbornyl fragments are well-documented in the literature.[23] In norbornene itself, the hydrogens of methano-bridge resonance at δ 1.08 and 1.33 ($\Delta\delta = 0.25$ ppm), with the hydrogen syn to the double bond being shielded and absorbing at higher field (lower δ).[29] Extending to the two fused norbornyl systems, the assignments of relative absorption positions of the hydrogens at two environmentally different methano bridges of dechlorinated insecticide aldrin **21**[29,30] and its derivative **4** are demonstrative for our stereochemical determination of adduct **18a**. For compound **21**, a separation of $\Delta\delta = 1.55$ ppm is observed for the two geminal hydrogens that are on the bridge proximal to the $\Delta^{2,3}$ double bond. Similar behavior is observed for the corresponding protons in **4** with a separation of $\Delta\delta = 1.46$ ppm. On the basis of steric compression against the π cloud of the double bond,[31] the hydrogen directly facing the $\Delta^{2,3}$ double bond in **4** and **21** experiences a very strong deshielding effect and thus displays a large downfield shift to appear at δ 3.00 and 2.55, respectively. The other pair of bridge hydrogens in **4** and **21** behaves rather normally, comparable to that of norbornene[29] and anhydride derivatives[18] (and **18b**), with values in the range of less than $\Delta\delta = 0.25$ ppm for the separation of these two hydrogens. Thus, among three stereoisomeric adducts (**18a**, **18c**, and **18d**), only stereostructure **18a** can most probably exhibit, by its two hydrogens on the methano bridge, an absorption of the AB pattern (δ 2.92/δ 1.41) with a large difference in chemical shfits ($\Delta\delta = 1.51$ ppm) and an unusual downfield absorption for one of these two hydrogens. The establishment of the stereostructures of both adducts **18a** and **18b** suggests that the cycloaddition of cyclopentadiene to maleic anhydride **2** takes place exclusively on the syn face of **2**.

Scheme 6



A comparable result was found for Diels–Alder cycloaddition of 1,3-cyclohexadiene (1.2 equiv) with maleic anhydride **2**, when the reaction mixture in toluene was heated under reflux for 24 h. The reaction produced two 1:1 cycloadducts in about equal amounts, which were separated by column chromatography and recrystallized from CH$_2$Cl$_2$ to give syn,endo adduct **22a** and syn,exo adduct **22b** in a total yield of 50% (Scheme 6). Stereostructural determination of syn,exo adduct **22b** is evidently supported by the presence of absorption signals at δ 5.72 (pseudo-dd) and δ 5.88 (pseudo-dd) in its ^{1}H NMR spectrum, which are due to vinyl hydrogens of two parallel aligned, mutually shielded double bonds closely resembling those of **18b**. In particular, the differences in chemical shifts are nearly the same (**22b**, $\Delta\delta = 0.16$ ppm vs **18b**, $\Delta\delta = 0.19$ ppm), indicating the distances between two etheno bridges in **18b** and **22b** are about equal. The stereostructure of **22b** was unequivocally established by an X-ray structural analysis[32] that revealed the structural similarity to that of **18b**.[33]

The ^{1}H NMR spectrum of second adduct (**22a**) shows two absorption signals at δ 6.35 and 6.09, indicative of two bicyclo[2.2.2]octene moieties that are differently situated in the molecular framework. The geminal hydrogens on the ethano bridge appear at δ 1.38 and 1.13 with a separation of $\Delta\delta = 0.25$ ppm, comparable to those in bicyclo[2.2.2]octene (δ 1.50/δ 1.27, $\Delta\delta = 0.23$ ppm) and

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(28) Crystal data of **18b**: C$_{22}$H$_{18}$Cl$_4$O$_5$, FW = 504.19, monoclinic, $P2_1/c$; $a = 14.616(3)$ Å, $b = 10.989(3)$ Å, $c = 15.194(3)$ Å, $\beta = 118.440(10)°$, $V = 2145.8(9)$ Å^3, $Z = 4$, $D_{\text{calc}} = 1.561$ Mg m^{-3}, $F(000) = 1031.92$. Of 3016 reflections measured, refined to convergence with $R_F = 0.040$, $R_w = 0.035$, and GOF = 2.12 for 1890 reflections having $I > 2\sigma(I)$. (The details of the X-ray analysis are provided as Supporting Information.)

(29) Marchand, A. P.; Rose, J. E. *J. Am. Chem. Soc.* **1968**, *90*, 3724–3731 and references therein.

(30) Haywood-Farmer, J.; Malkus, H.; Battiste, M. A. *J. Am. Chem. Soc.* **1972**, *94*, 2209–2218 and references therein.

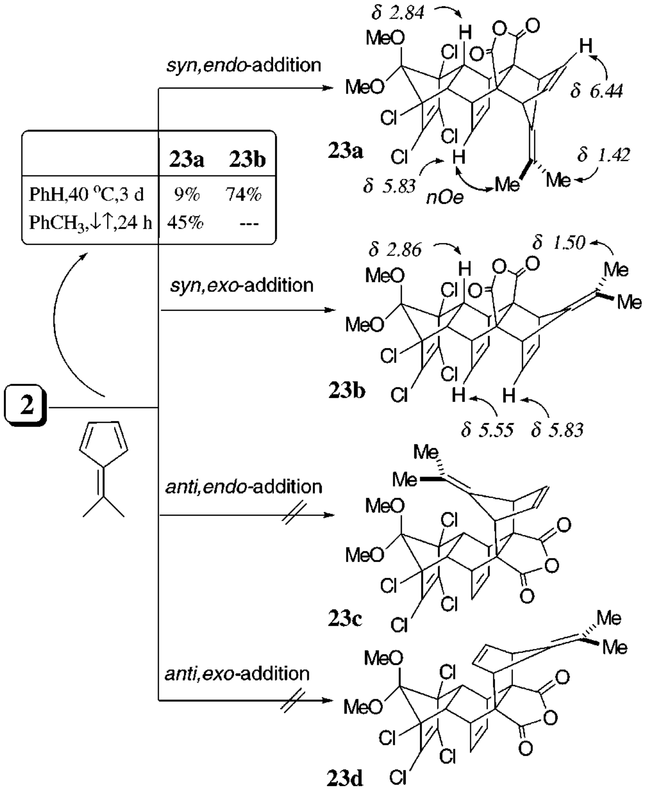
(31) Winstein, S.; Carter, P.; Anet, F. A. L.; Bourn, A. J. R. *J. Am. Chem. Soc.* **1965**, *87*, 5247–5249.

endo-bicyclo[2.2.2]oct-2-ene-5,6-dicarboxylic anhydride (δ 1.62/δ 1.43, $\Delta\delta = 0.19$ ppm).[34] These spectral data alone cannot clearly discriminate among isomeric adducts **22a**, **22c**, and **22d**. Recourse is thus made to the broad singlet displayed by the tertiary hydrogens at the ring junction, which appears at δ 2.82 and is nearly the same as that of **22b** (δ 2.87) and **18a**/**18b** as well. The similarity in chemical shifts implies that the anhydride moiety in this second adduct (**22a**) is syn to the tertiary hydrogens at the ring junction, like the relative orientation of corresponding moieties in **22b** and **18a**/**18b**, rather than in other isomers **22c** and **22d**.[35] The assignment of stereostructure **22a** is supported by the NOE spectrum in which enhancement of the absorption signal due to the hydrogens of the etheno bridge is observed, when the "inside" hydrogens of the ethano bridge in **22a** are irradiated. Again, maleic anhydride **2** displayed syn-facial selectivity in the Diels–Alder cycloaddition with cyclohexadiene, thereby affording syn,endo adduct **22a** and syn,exo adduct **22b**.

The Diels–Alder cycloaddition of maleic anhydride **2** with 6,6-dimethylfulvene (5.5 equiv) in benzene at 40 °C for 3 days furnished, after separation by chromatography, adducts **23a** and **23b** in 9% and 74% yields, respectively. When the reaction was performed by heating the reaction mixture in toluene under reflux for 24 h, **23a** was obtained in 45% yield as sole product (Scheme 7). Apparently, adduct **23b** is thermodynamically less stable than **23a**. In fact, upon heating a solution of **23b** in benzene, retro-Diels–Alder reaction occurred to produce **2**, **23a**, and 6,6-dimethylfulvene. The ^{1}H NMR spectrum of the adduct **23a** exhibits two absorption signals at δ 6.44 (pseudo-t) and δ 5.83 (pseudo-dd) ascribed to the vinyl hydrogens of two etheno bridges. The upfield shift of the vinyl hydrogens on the central etheno bridge (at δ 5.83) is attributed to the shielding by contiguous parallel- and perpendicular-oriented double bonds. These absorption signals, together with a broad singlet at δ 2.84 displayed by the tertiary hydrogens at the ring junction, suggest that this adduct possesses stereochemistry like that of **18a** and **22a** and is formed by the syn,endo addition mode of cycloaddition. An NOE was observed at δ 5.83 for the etheno-bridge hydrogens when the isopropylidene methyl hydrogens (at δ 1.42) were irradiated, further supporting the structural assignment of adduct **23a**.

The syn,endo adduct **23b** is identified to have three etheno bridges aligned in parallel and in close spatial proximity, just like those in **18b** and **22b**. This stereostructure is evident from the absorption signals at δ 5.83 (pseudo-t) and δ 5.55 (pseudo-dd) due to the vinyl hydrogens of two etheno bridges and a broad singlet at δ 2.86 ascribed to the tertiary hydrogens at the ring junction.

Scheme 7



	23a	23b
PhH,40 °C,3 d	9%	74%
PhCH$_3$,↓↑,24 h	45%	---

Diels–Alder Cycloaddition of 2 with *o*-Quinodimethane. As anticipated at the beginning based upon consideration of the ethano bridge being sterically more demanding than the etheno bridge, the exclusive cycloadditions of endocyclic dienes onto the syn face of maleic anhydride **2** are realized in all cases (Schemes 3–7).[36] This consideration led us to undertake the investigation of Diels–Alder cycloadditions of **2** with a less sterically demanding exocyclic diene, *o*-quinodimethane (**24**), with the expectation of observing any degree of change in the π-facial selectivity of **2**.

To this end, maleic anhydride **2** was subjected to the Diels–Alder cycloaddition with **24** (2 equiv) generated in situ by pyrolysis of 1,4-dihydro-2,3-benzoxatin[37] in toluene at 95 °C for 6 h. The reaction produced only one of the two possible stereoisomeric adducts in 73% yield (**25a**/**25b** or **25c**/**25d**, Scheme 8). The ^{1}H NMR spectrum of this adduct displays a broad singlet at δ 2.87 due to the tertiary hydrogens at the ring junction and an A_2B_2 quartet at δ 3.09 and 2.70 with $J = 14.3$ Hz that are ascribed to two pairs of benzylic hydrogens. Together with the observed NOE enhancement of absorption signal at δ 6.27 upon irradiation of one pair of the benzylic hydrogens (at δ 2.70), this adduct could be assigned the stereostructure **25a** or **25b**. Structures **25a** and **25b** are conformational isomers and could be formed by either syn,endo or syn,exo addition of *o*-quinodimethane onto

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(32) Crystal data of **22b**: $C_{23}H_{20}Cl_4O_5$, FW = 518.19, monoclinic, $P2_1/n$; $a = 14.822(4)$ Å, $b = 11.593(2)$ Å, $c = 14.960(3)$ Å, $\beta = 119.60(2)°$, $V = 2235.1(9)$ Å^3, $Z = 4$, $D_{\text{calc}} = 1.540$ Mg m^{-3}, $F(000) = 1064$. Of 2926 reflections collected, refined to convergence with $R_F = 0.0490$, $R_w = 0.1366$, and GOF = 0.965 for 2926 reflections having $I > 2\sigma(I)$. (The details of the X-ray analysis are provided as Supporting Information.)

(33) The distances from the outlying CCl=CCl and CH=CH bonds to the central CH=CH bond are 2.892 and 3.056 Å in **18b** and 2.942 and 2.957 Å in **22b**, respectively. We have observed that the [2 + 2] photocyclization of **18b** and **22b** takes place predominately between the dichlorinated C=C and the central C=C bonds.

(34) Tori, K.; Takano, Y.; Kitahonoki, K. *Chem. Ber.* **1964**, *97*, 2798–2815.

(35) The tertiary hydrogens at ring junction in **22c** should appear at lower field due to the effect of steric compression by the ethano-bridge hydrogens, and those in **22d** should appear at higher field because of the shielding effect of the proximal double bond.

(36) To our disappointment, maleic anhydride **2** was unable to undergo the Diels–Alder cycloaddition with diene **1** to produce adduct of generic structure **C** under conventional, catalytic, or pressurized (up to 4 Kbar) conditions.

(37) Hoey, M. D.; Dittmer, D. C. *J. Org. Chem.* **1991**, *56*, 1947–1948.

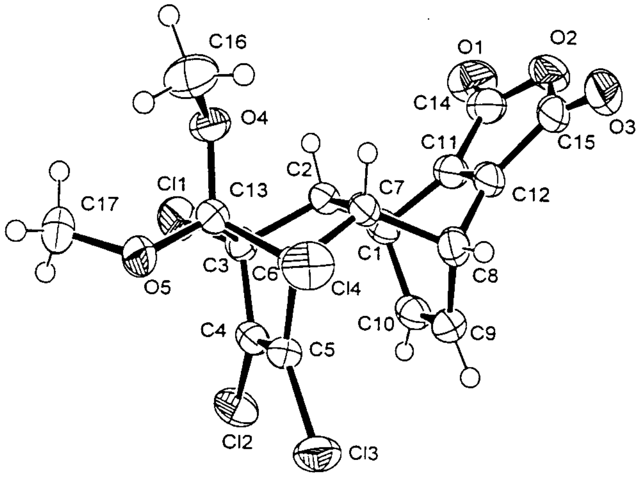
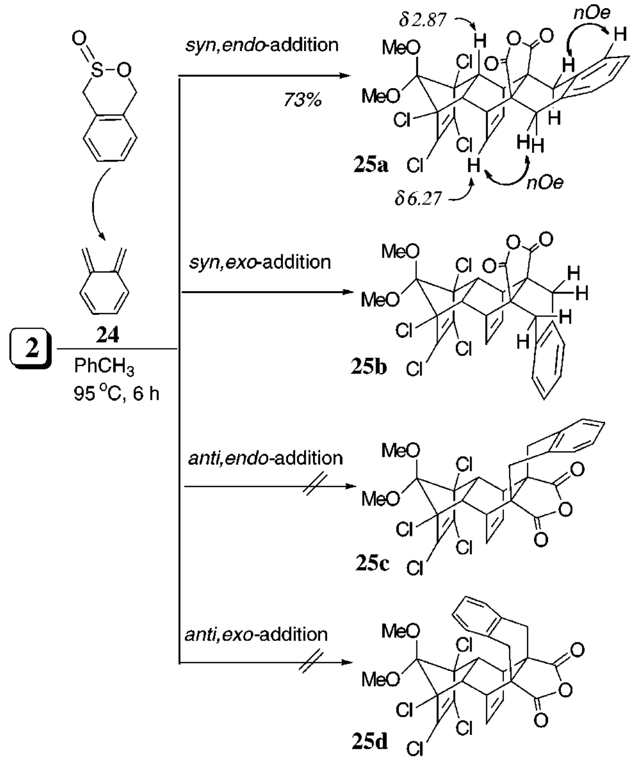


Figure 1. ORTEP drawing of the X-ray structure of **2**.

Scheme 8



dienophile **2**.[38] The appearance of vinyl hydrogens at δ 6.27 indicates the absence of a benzene ring in close proximity to the etheno bridge, and thus, the adduct adapts itself to the sterically more favored conformation **25a**. The syn-facial selectivity of **2** still prevails over the anti-facial selectivity in the Diels–Alder cycloaddition with *o*-quinodimethane.

Crystal Structure of 2. An ORTEP drawing of a single molecule of anhydride **2** is shown in Figure 1. Analysis of the crystal data reveals the molecule to have an approximate mirror symmetry. The overall geometry of the tetrachlorinated bicylo[2.2.1]heptenyl substructure is, in general, comparable to that in structures **18b** and **22b**, with elongated C3–C13 (1.577 Å) and C6–C13 (1.573 Å) bonds and a compressed C3–C13–C6 bond angle (90.33°). The distance between C4–C5 and C9–C10 double bonds is averaged to be 2.961 Å. In the bicyclo[2.2.2]octadienyl ring, the elongations of the bonds between the bridgehead (C1/C8) and ethano-bridge (C2/C7) carbon atoms (C1–C2, 1.573 Å, and C7–C8, 1.567 Å) are also observed in the present case as in structure **6** (1.580 and 1.578 Å).[19b] The bicyclo[2.2.2]octadienyl substructure is composed of three equilateral trapezoids, which are formed by the carbon atoms of the C2–C7, C9–C10, and C11–C12 bonds with the common bridgehead carbon atoms (C1 and C8).[39] As illustrated in Figure 2, these three equilateral trapezoids form dihedral angles of 124.3°, 122.4°, and 113.3° with each other, such that the boat conformation of the C1–C2–C7–C8–C12–C11 six-membered ring is puckered and the other two are slightly flattened. The five-membered anhydride ring is slightly twisted with the C14–C11–C12–C15 torsional angle of 1.1° and is not coplanar with the C1–C11–C12–C8 trapezoid as indicated by the C1–C11–C12–C15 and C8–C12–C11–C14 dihedral angles being −175.7° and 176.6°, respectively.[40] That the C2–C1–C8–C15 and C7–C8–C1–C14 dihedral angles are −111.2° and 111.5°, which are about 2° smaller than the dihedral angles of C2–C1–C8–C12 (−113.4°) and C7–C8–C1–C11(113.2°), respectively, also reflects this noncoplanarity. This difference of 2° in dihedral angles indicates that both the C14 and C15 carbon atoms on the anhydride ring are located out of the C1–C11–C12–C8 plane on the same side as the C2–C7 bridging atoms, with deviations of 0.081 and 0.107 Å, respectively. These deviations translate into an inclination of approximately 3.2° and 4.2° for the respective C11–C14 and C12–C15 bonds with the C1–C11–C12–C8 trapezoid plane of the bicyclo[2.2.2]-octadienyl system. It is also interesting to note that the dichlorinated double bond in **2** is not planar. The C6–C5–C4–Cl(2) and C3–C4–C5–Cl(3) dihedral angles are −175.0° and 175.3°, respectively.

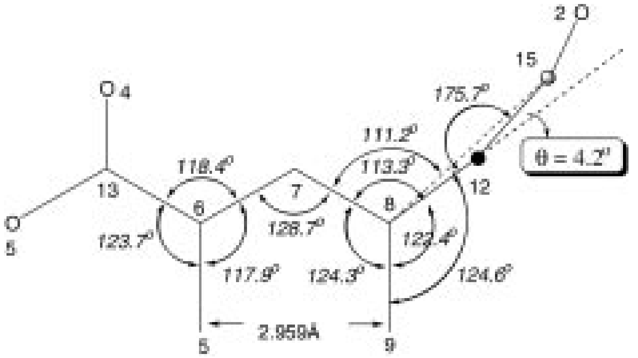


Figure 2. Nonplanarity of the C11–C12 double bond and the dihedral angles between least-squares planes in **2**. Projection on the plane containing C13, O2, O4, and O5.

The rationales for the facial selectivity of the norbornenyl and norbornadienyl systems have been intensively

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[38] Endo and exo refer to the orientation of the anhydride moiety relative to the benzene ring as depicted in Scheme 8 and by no means refer to the courses of addition as defined by the Alder rule, which is not applicable to the unsubstituted exocyclic 1,3-butadienes. No effort was undertaken to study thermal equilibrium between the conformers **25a** and **25b**, so as to gain information on the courses of addition, i.e., endo vs exo.

[39] The dihedral angles (C1–C11–C12–C8, C1–C10–C9–C8, and C1–C2–C7–C8) are about 0.2°.

[40] The C10–C1–C8–C15 and C9–C8–C1–C14 dihedral angles are 124.6° and −124.2°, which are about 2° larger than C9–C8–C1–C11 (−122.5°) and C10–C1–C8–C12 (122.3°), respectively.

deliberated and debated.[41] The anti-facial selectivity is presumably to be the result of factors such as torsional effects,[42] greater π electron density,[43] and disrotatory orbital tilting[44] that overcome the unfavorable steric effects on the more crowded anti face of the π-system and, hence, dictate the additions of dienes to the anti face of norbornenyl and norbornadienyl systems. Correlation between the π-facial selectivity and the pyramidalization of the double bond in norbornene and norbornadiene has also been noted.[45]

On the contrary, there are fewer explanations for the π-facial stereoselectivity in cycloadditions of bicyclo[2.2.2]-octadiene and related species. Steric factors certainly play an important role in determining the course of reactions. However, since differential steric effects are much less significant in bicyclo[2.2.2]octadienes **2** and **6** (ethano vs etheno bridges) than in norbornadiene (methano vs etheno bridges), the expectation of dominant Diels−Alder anti attack on the bicyclo[2.2.2]octadienyl dienophile is obviously contemplated by analogy with norbornenyl systems. Nevertheless, in the case of the Diels−Alder cycloaddition of cyclopentadiene with dienophile **6** there is a distinct preference for syn addition along with some anti addition products observed (eq 2). Very recently, Williams et al. analyzed the molecular structure of maleic anhydride **6** by both ab initio calculations and X-ray structural determination.[19b] With the structural data, they proposed that a combination of the double-bond pyramidalization and minimization of steric interactions is responsible for the π-facial selectivity observed in bicyclo[2.2.2]octadienyl dienophile **6**.

In our cases of the Diels−Alder cycloaddtions of maleic anhydride **2** with cyclopentadiene and other various dienes, the face syn to the etheno bridge of **2** is the exclusive face to be attacked by dienes (Schemes 3−8). The observed syn-facial selectivity of maleic anhydride **2** in Diels−Alder cycloadditions seems to be in concord with its crystal structure. The syn-facial selectivity is likely the consequence of a pyramidalized anhydride olefinic bond (ca. 3.6° pyramidalization) and the more severe steric hindrance on the side of the ethano bridge (the anti face of the π system) due to the larger degree of folding of the C1−C2−C7−C8−C12−C11 boat conformation.[46]

Conclusion

The results of the present study demonstrate that the laticyclic conjugated, facially dissymmetric maleic anhydride **2** undergoes the Diels−Alder cycloadditions with various dienes exclusively from the π face syn to its etheno bridge. The observed π-facial selectivity is more enforced relative to that of bicyclo[2.2.2]octadienyl dienophile **6** and entirely opposite to that of norbornadienyl systems, such as anhydride **3**. The π-facial selectivity seems to agree with the X-ray crystal structure of **2**, which reveals pyramidalization (ca. 3.6°) of the anhydride double bond. However, the consequence of laticyclic conjugation and hence the presence of a remote double bond in influencing the π-facial selectivity of **2** await further evaluation by both experimental work and computational analysis. Nevertheless, the results of the present investigation indicate that maleic anhydride **2** is a potential synthon for the synthesis of linearly syn-concatenated bicyclo[2.2.2]octene-based spacer molecules having double bonds arranged for laticyclic conjugation as shown by generic structure **C** (Scheme 1).

Experimental Section

Melting points were determined on a capillary apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a 200, 300, or 400 MHz spectrometer using $CDCl_3$ as solvent (unless otherwise specified). All chemical shifts were expressed in δ (ppm) with reference to $CDCl_3$ (δ 7.26 for ^1H NMR and δ 77.0 for ^{13}C NMR). The number of attached hydrogens on the carbon atom was determined by the DEPT analysis. Infrared (IR) spectra were recorded as KBr pellets on an FT-IR spectrophotometer. Mass (MS) spectra were obtained by the EI mode unless otherwise indicated. Column chromatography was performed with E. Merck Kieselgel 60 (230−400 mesh). All solvents used were either reagent grade or were distilled prior to use. Microanalyses were performed by the Analytical Center of Cheng-Kung University, Tainan, Taiwan.

Dimethyl ($1\alpha,2\alpha,3\beta,6\beta,7\alpha,8\alpha$)-3,4,5,6-Tetrachloro-13,13-dimethoxytetra cyclo[6.2.2.1^{3,6}.0^{2,7}]trideca-4,9,11-triene-9,10-dicarboxylate (9). A solution of triene **1** (15.0 g, 43.8 mmol) and dimethyl acetylenedicarboxylate (6.2 g, 43.8 mmol) in benzene (200 mL) was stirred and heated under reflux for 48 h. The reaction mixture was concentrated to give a crude product that was recrystallized from diethyl acetate−hexane to afford pure dicarboxylate **9** (17.8 g, 83%) as a colorless solid: mp 162−163 °C; IR (cm^{-1}) 1735, 1714, 1642, 1604; ^1H NMR (200 MHz) δ 6.30 (pseudo-dd, $J = 4.5$, 3.3 Hz, 2H), 4.04 (pseudo-t, $J = 3.3$ Hz, 2H), 3.80 (s, 6H), 3.56 (s, 3H), 3.49 (s, 3H), 2.92 (br s, 2H); ^{13}C NMR (75 MHz) δ 165.6, 146.1, 130.1, 127.6, 115.6, 76.4, 52.7, 52.3, 51.6, 51.5, 38.6; MS (12 eV) m/z (relative intensity) 453 ($M^+ - OMe$, 32), 449 ($M^+ - Cl$, 10), 253 (100), 207 (61), 179 (25). Anal. Calcd for $C_{19}H_{18}Cl_4O_6$: C, 47.14; H, 3.75; Cl, 29.29. Found: C, 47.31; H, 3.76; Cl, 29.28.

($1\alpha,2\alpha,3\beta,6\beta,7\alpha,8\alpha$)-3,4,5,6-Tetrachloro-13,13-dimethoxytetracyclo [6.2.2.1^{3,6}.0^{2,7}]trideca-4,9,11-triene-9,10-dicarboxylic Acid (10). To a solution of dicarboxylate **9** (8.0 g, 16.5 mmol) in ethanol (100 mL) was added dropwise an aqueous solution of NaOH (9.6 M, 300 mL) at 0 °C. The resulting mixture was heated under reflux for 4 h and then cooled to room temperature. Water (500 mL) was added, and the solution was washed with diethyl ether (300 mL) to remove any unchanged diester **9**. The aqueous solution was acidified at 0 °C by slow addition of concentrated HCl until the precipitate was formed. The mixture was extracted with diethyl ether (300 mL × 3) and the organic layers were washed with water (300 mL × 2). After being dried over $MgSO_4$, the solvent was evaporated in vacuo to give a solid residue that was purified by recrystallization from acetonitrile to give diacid **10** (6.3 g, 81%) as a colorless solid: mp 217−219 °C dec; IR (cm^{-1}) 2300−3500 (br), 1715, 1606, 1589; ^1H NMR (acetone-d_6, 200 MHz) δ 6.34 (pseudo-dd, $J = 4.5$, 3.6 Hz, 2H), 4.27 (pseudo-t, $J = 3.3$ Hz, 2H), 3.58 (s, 3H), 3.48 (s, 3H), 3.02 (br s, 2H); ^{13}C NMR (acetone-d_6, 75 MHz) δ 166.6, 148.5, 131.0, 128.5, 116.8, 77.6, 52.9, 52.2, 52.1, 40.3; MS (12 eV) m/z

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(41) (a) Watson, W. H. *Stereochemistry and Reactivity of Systems Containing π Electrons*; Verlag Chemie International: Deerfield Beach, FL, 1983.

(42) (a) Schleyer, P. v. R. *J. Am. Chem. Soc.* **1967**, *89*, 701−000. (b) Brown, F. K.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 1971−1978.

(43) Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, *98*, 4054−4059.

(44) Gleiter, R. *Pure Appl. Chem*. **1987**, *59*, 1585−1594 and references therein.

(45) Houk, K. N.; Rondan, N. G.; Brown, F. K.; Jorgensen W. L.; Madura, J. D.; Spellmeyer, D. C. *J. Am. Chem. Soc.* **1983**, *105*, 5980−5988 and references therein.

(46) A systematic quantum-chemical semiempirical analysis of the Diels−Alder cycloaddition of cyclopentadiene to maleic anhydride **2** (Scheme 5) with computations using MNDO, AM1, and PM3 methods confirms the experimental finding of *syn*,*endo*-**18a** and *syn*,*exo*-**18b** being the results of both thermodynamic and kinetic control (Kuo, L.-H.; Slanina, Z.; Chou, T.-C. *Z. Naturforsch.* **1996**, *51a*, 1134−1138). However, the prevalent syn-facial selectivity under the condition of either thermodynamic or kinetic control, as evident from the outcome of the Diels−Alder cycloaddition of 6,6-dimethylfulvene to maleic anhydride **2** (Scheme 7), suggests that the facial selectivity is kinetically controlled.

(relative intensity) 421 ($M^+ - Cl$, 10), 253 (100), 207 (70), 179 (40). This material was used for the next reaction without further purification.

(1α,2α,3*β*,6*β*,7α,8α)-3,4,5,6-Tetrachloro-13,13-dimethoxytetracyclo [6.2.2.1^{3,6}.0^{2,7}]trideca-4,9,11-triene-9,10-dicarboxylic Anhydride (2). Method A. To a solution of dicarboxylic acid **10** (6.8 g, 14.9 mmol) in freshly distilled CH_2Cl_2 (100 mL) was rapidly added oxalyl chloride (4.8 mL, 55.2 mmol) under an atmosphere of nitrogen. The reaction mixture was heated under reflux until a clear solution appeared (ca. 15 h). Removal of solvent left a gray residue that was recrystallized from benzene−hexane (1:4) to furnish maleic anhydride **2** (5.5 g, 84%). **Method B.** A solution of dicarboxylic acid **10** (2.5 g, 5.4 mmol) in acetic anhydride (8.3 g, 81.4 mmol) was heated at 60 °C for 1.5 h. The solution was cooled to room temperature, and the resulting precipitate was collected by filtration to afford anhydride **2** (2.0 g, 85%) as a colorless solid. Repeated recrystallization from benzene−hexane provided an analytical sample of **2** as colorless crystals: mp 178−183 °C dec; IR (cm^{-1}) 1840, 1777, 1609; ^{1}H NMR (300 MHz) δ 6.37 (pseudo-dd, $J = 4.5$, 3.3 Hz, 2H), 4.19 (pseudo-t, $J = 3.3$ Hz, 2H), 3.55 (s, 3H), 3.49 (s, 3H), 2.88 (br s, 2H); ^{13}C NMR (75 MHz) δ 159.8, 158.4, 130.0, 127.8, 115.9, 76.0, 52.8, 52.1, 51.7, 34.4; MS (12 eV) *m*/*z* (relative intensity) 403 ($M^+ - Cl$, 15), 253 (100), 207 (72), 179 (41). Anal. Calcd for $C_{17}H_{12}Cl_4O_5$: C, 46.61; H, 2.76; Cl, 32.37. Found: C, 46.64; H, 2.74; Cl, 32.37.

General Procedure for the Diels−Alder Cycloadditions of 2 with Dienes. Maleic anhydride **2** (1.0 g, 2.3 mmol) was allowed to react with a diene in a previously dried solvent under an atmosphere of N_2 for a period of time. The molar equivalent of diene and solvent used and the reaction temperature and time for the specific cycloaddition are indicated in the text and in Schemes 3−8. At the conclusion of each reaction, the solvent was removed in vacuo and the resulting solid residue was immediately analyzed by thin-layer chromatographic and ^{1}H NMR spectroscopic methods to determine the composition (number of isomeric adducts and ratio). The crude product mixture was then separated and purified by chromatography (silica gel) followed by recrystallization.

Cycloaddition with Anthracene. Formation of (1α,2*β*,3α,6α,7*β*,8α,9α,10*β*,13*β*, 14α)-4:5,17:18-Dibenzo-10,11,12,13-tetrachloro-19,19-dimethoxyhexacyclo[6. 6.2.2^{3,6}.1^{10,13}.0^{2,7}.0^{9,14}]-nonadeca-4,11,15,17-tetraene-2,7-dicarboxylic Anhydride (11a). Colorless crystals (yield 70%): mp 280−281 °C (ethyl acetate, dec); IR (cm^{-1}) 1865, 1771, 1606; ^{1}H NMR (acetone-d_6, 300 MHz) δ 7.34−7.28 (m, 4H), 7.19−7.15 (m, 4H), 4.98 (pseudo-dd, $J = 4.5$, 3.3 Hz, 2H), 4.70 (br s, 2H), 3.50 (s, 3H), 3.42−3.39 (s and m, 5H), 2.78 (br s, 2H); ^{13}C NMR (acetone-d_6, 75 MHz) δ 174.3, 141.9, 140.9, 128.8, 128.5, 128.2, 126.5, 126.2, 121.9, 114.7, 77.7, 64.1, 53.1, 52.2, 50.7, 49.7, 37.2; MS (12 eV) *m*/*z* (relative intensity) 616 (M^+, 2), 581 ($M^+ - Cl$, 34), 253 (86), 207 (37), 178 (100). Anal. Calcd for $C_{31}H_{22}Cl_4O_5$: C, 60.41; H, 3.60; Cl, 23.01. Found: C, 60.44; H, 3.64; Cl, 22.89.

Cycloaddition with 1,3-Diphenylisobenzofuran. Formation of (1α,2*β*,3α,6α, 7*β*,8α,9α,10*β*,13*β*,14α)-17-Oxa-4:5-benzo-10,11,12,13-tetrachloro-18,18-dimethoxy-3,6-diphenylhexacyclo[6.6.2.1^{3,6}.1^{10,13}.0^{2,7}.0^{9,14}]octadeca-4,11,15-triene-2,7-dicarboxylic Anhydride (17a). Colorless crystals (yield 95%): mp 278−279 °C (ethyl acetate, dec); IR (cm^{-1}) 1857, 1832, 1778, 1605, 1019; ^{1}H NMR (acetone-d_6, 300 MHz) δ 7.99−7.97 (m, 4H), 7.68−7.56 (m, 6H), 7.35−7.32 (m, 4H), 5.67 (pseudo-dd, $J = 4.2$, 3.3 Hz, 2H), 3.51 (s, 3H), 3.40 (s, 3H), 3.28 (dd of pseudo-t, $J = 4.2$, 3.3 Hz, 2H), 2.76 (br s, 2H); ^{13}C NMR (acetone-d_6, 75 MHz) δ 171.7, 145.7, 135.1, 129.9, 129.8, 129.7, 128.9, 126.9, 126.1, 121.7, 114.7, 92.3, 77.6, 72.1, 53.2, 52.2, 49.1, 35.3; MS (12 eV) *m*/*z* (relative intensity) 673 ($M^+ - Cl$, 42), 270 (100), 253 (82), 207 (57). Anal. Calcd for $C_{37}H_{26}Cl_4O_6$: C, 62.73; H, 3.70; Cl, 20.02. Found: C, 62.74; H, 3.80; Cl, 20.15.

Cycloaddition with Cyclopentadiene. Formation of (1α,2*β*,3α,6α,7*β*,8α,9α, 10*β*,13*β*,14α)- and (1α,2*β*,3*β*,6*β*,7*β*, 8α,9α,10*β*,13*β*,14α)-10,11,12,13-Tetrachloro-18, 18-dimethoxyhexacyclo[6.6.2.1^{3,6}.1^{10,13}.0^{2,7}.0^{9,14}]octadeca-4,11,15-triene-2,7-dicarboxylic Anhydride (18a and 18b). Colorless crystals (total yield 93%; **18a**/**18b** = 1:2). **18a**: mp 196 °C (CH_2Cl_2, dec); IR (cm^{-1}) 1853, 1772, 1604; ^{1}H NMR (300 MHz) δ 6.43 (pseudo-t, $J = 1.8$ Hz, 2H), 6.13 (pseudo-dd, $J = 4.5$, 3.3 Hz, 2H), 3.54 (s, 3H), 3.47 (s, 3H), 3.44 (dd of pseudo-t, $J = 4.2$, 3.3 Hz, 2H), 3.10 (pseudo-quintet, $J = 1.8$ Hz, 2H), 2.92 (d of pseudo-t, $J = 10$ Hz, 1H), 2.88 (br s, 2H), 1.41 (d of pseudo-t, $J = 10$ Hz, 1H); ^{13}C NMR (75 MHz) δ 173.5, 140.5, 128.1, 127.7, 113.8, 76.8, 64.2, 52.8, 51.7, 50.2, 50.1, 48.9, 34.7; MS (12 eV) *m*/*z* (relative intensity) 504 (M^+, (1), 469 ($M^+ - Cl$, 24), 253 (100), 207 (34), 66 (77). Anal. Calcd for $C_{22}H_{18}Cl_4O_5$: C, 52.41; H, 3.60; Cl, 28.13. Found: C, 52.38; H, 3.60; Cl, 28.18. **18b**: mp 203 °C (ethyl acetate, dec); IR (cm^{-1}) 1855, 1770, 1605, 1338; ^{1}H NMR (300 MHz) δ 5.72 (pseudo-t, $J = 1.8$ Hz, 2H), 5.52 (pseudo-dd, $J = 4.5$, 3.3 Hz, 2H), 3.54 (s, 3H), 3.44 (s, 3H), 3.32 (dd of pseudo-t, $J = 4.2$, 3.3 Hz, 2H), 3.21 (pseudo-quintet, $J = 1.8$ Hz, m, 2H), 2.89 (br s, 2H), 1.56 (d, $J = 10.2$ Hz, 1H), 1.43 (d, $J = 10.2$ Hz, 1H); ^{13}C NMR (75 MHz) δ 175.7, 136.8, 128.2, 126.0, 113.7, 76.7, 62.1, 52.8, 51.7, 51.0, 49.5, 48.3, 34.6; MS (12 eV) *m*/*z* (relative intensity) 504 (M^+, 10), 469 ($M^+ - Cl$, 24), 253 (100), 207 (17), 115 (68), 66 (45). Anal. Calcd for $C_{22}H_{18}Cl_4O_5$: C, 52.41; H, 3.60; Cl, 28.13. Found: C, 52.14; H, 3.64; Cl, 28.01.

Cycloaddition with 1,3-Cyclohexadiene. Formation of (1α,2*β*,3α,6α,7*β*,8α, 9α,10*β*,13*β*,14α)- and (1α,2*β*,3*β*,6*β*,7*β*,8α, 9α,10*β*,13*β*,14α)-10,11,12,13-Tetrachloro-19,19-dimethoxyhexacyclo[6.6.2.2^{3,6}.1^{10,13}.0^{2,7}.0^{9,14}]nonadeca-4,11,15-triene-2,7-dicarboxylic Anhydride (22a and 22b). Colorless crystals (total yield 50%; **22a**/**22b** = 1:1). **22a**: mp 227 °C (CH_2Cl_2, dec); IR (cm^{-1}) 1859, 1772, 1605; ^{1}H NMR (300 MHz) δ 6.35 (pseudo-dd, $J = 4.5$, 3.3 Hz, 2H), 6.09 (pseudo-dd, $J = 4.5$, 3.3 Hz, 2H), 3.53 (s, 3H), 3.46 (s, 3H), 3.18 (pseudo-t, $J = 3.9$ Hz, 2H), 2.85 (m, 2H), 2.82 (br s, 2H), 1.38 (m of d, $J = 9.9$ Hz, 2H), 1.13 (m of d, $J = 9.9$ Hz, 2H); ^{13}C NMR (75 MHz) δ 174.9, 136.2, 128.1, 122.5, 113.9, 76.9, 58.9, 52.8, 51.7, 48.5, 35.7, 35.5, 19.9; MS (12 eV) *m*/*z* (relative intensity) 518 (M^+, <1), 483 ($M^+ - Cl$, 15), 253 (100), 207 (15), 80 (21). Anal. Calcd for $C_{23}H_{20}Cl_4O_5$: C, 53.31; H, 3.89; Cl, 27.37. Found: C, 53.34; H, 3.97; Cl, 27.26. **22b**: mp 230 °C (CH_2Cl_2, dec); IR (cm^{-1}) 1859, 1773, 1606; ^{1}H NMR (300 MHz) δ 5.88 (pseudo-dd, $J = 4.5$, 3.3 Hz, 2H), 5.72 (pseudo-dd, $J = 4.5$, 3.3 Hz, 2H), 3.54 (s, 3H), 3.44 (s, 3H), 3.20 (pseudo-t, $J = 3.9$ Hz, 2H), 2.87 (m with a br s, 4H), 1.74 (m of d, $J = 9.9$ Hz, 2H), 1.15 (m of d, $J = 9.9$ Hz, 2H); ^{13}C NMR (75 MHz) δ 176.0, 132.5, 128.0, 127.5, 113.4, 76.8, 59.6, 52.8, 51.7, 48.2, 37.1, 36.3, 22.8; MS (12 eV) *m*/*z* (relative intensity) 518 (M^+, 3), 483 ($M^+ - Cl$, 32), 253 (100), 207 (12), 80 (20). Anal. Calcd for $C_{23}H_{20}Cl_4O_5$: C, 53.31; H, 3.89; Cl, 27.37. Found: C, 53.63; H, 4.11; Cl, 27.24.

Cycloaddition with 6,6-Dimethylfulvene. Formation of (1α,2*β*,3α,6α,7*β*,8α, 9α,10*β*,13*β*,14α)- and (1α,2*β*,3*β*,6*β*,7*β*,8α, 9α,10*β*,13*β*,14α)-10,11,12,13-Tetrachloro-18,18-dimethoxy-17-dimethylmethylidenehexacyclo[6.6.2.1^{3,6}.1^{10,13}.-0^{2,7}.0^{9,14}]octadeca-4,11,15-triene-2,7-dicarboxylic Anhydride (23a and 23b). Method A (benzene, 40 °C, 3 days): total yield 81%; **23a**/**23b** = 1:8. **Method B** (toluene, reflux, 24 h): 45% yield of **23a** only. **23a** (colorless solids): mp 195−196 °C dec; IR (cm^{-1}) 1844, 1774, 1605; ^{1}H NMR (300 MHz) δ 6.44 (pseudo-t, $J = 2.0$ Hz, 2H), 5.83 (pseudo-dd, $J = 4.8$, 3.0 Hz, 2H), 3.54 (s, 3H), 3.46 (s, 3H), 3.45−3.43 (m, 2H), 3.41−3.38 (m, 2H), 2.84 (br s, 2H), 1.42 (s, 6H); ^{13}C NMR (50 MHz) δ 173.2, 147.0, 138.6, 128.1, 124.6, 113.5, 112.4, 76.6, 63.8, 52.8, 51.7, 49.5, 48.6, 34.7, 19.6; MS (12 eV) *m*/*z* (relative intensity) 544 (M^+, 21), 509 (28), 253 (61), 207 (16), 106 (100). Anal. Calcd for $C_{25}H_{22}Cl_4O_5$: C, 55.17; H, 4.07; Cl, 26.06. Found: C, 55.11; H, 4.03; Cl, 25.92. **23b** (colorless crystals): mp 178−179 °C; IR (cm^{-1}) 1847, 1811, 1770, 1654, 1604; ^{1}H NMR (200 MHz) δ 5.83 (pseudo-t, $J = 2.0$ Hz, 2H), 5.55 (pseudo-dd, $J = 4.8$, 3.2 Hz, 2H), 3.70 (pseudo-t, $J = 2.0$ Hz, 2H), 3.53 (s, 3H), 3.43 (s, 3H), 3.34 (m, 2H), 2.86 (br s, 2H), 1.50 (s, 6H); ^{13}C NMR (50 MHz) δ 174.8, 141.9, 135.9, 128.1, 126.1, 115.2, 113.6, 76.6, 62.1, 52.8, 51.7, 51.2, 49.6, 34.2, 19.4; MS (12 eV) *m*/*z* (relative intensity) 544 (M^+, 7), 509 (25), 253 (100), 207 (20), 106 (77). Anal. Calcd for $C_{25}H_{22}Cl_4O_5$: C, 55.17; H, 4.07; Cl, 26.06. Found: C, 55.12; H, 4.11; Cl, 26.08.

Cycloaddition with *o*-Quinodimethane. Formation of (1α,2*β*,7*β*,8α,9α,10*β*,13*β*, 14α)-4:5-Benzo-10,11,12,13-tetrachloro-17,17-dimethoxypentacyclo[6.6.2.1^{10,13}. 0^{2,7}.0^{9,14}]-

heptadeca-4,11,15-triene-2,7-dicarboxylic Anhydride (25a). A solution of 1,4-dihydro-2,3-benzoxathin-3-oxide in dry toluene was added dropwise in 10 min to a solution of maleic anhydride **2** in dry toluene heated at 95 °C to generate *o*-quinodimethane in situ. Then the general procedure was followed, and the reaction furnished, after chromatography, adduct **25a** in 73% yield as a colorless solid: mp 287−288 °C; IR (cm^{-1}) 1854, 1782, 1604; ^{1}H NMR (300 MHz) δ 7.18−7.15 (m, 2H), 7.05−7.02 (m, 2H), 6.27 (pseudo-dd, $J = 4.4$, 3.3 Hz, 2H), 3.54 (s, 3H), 3.48 (s, 3H), 3.24 (pseudo-t, $J = 2.6$ Hz, 2H), 3.09 (d, $J = 14.3$ Hz, 2H), 2.87 (br s, 2H), 2.70 (d, $J = 14.3$ Hz, 2H); ^{13}C NMR (50 MHz) δ 174.7, 133.1, 128.5, 128.3, 128.3, 127.9, 113.7, 76.7, 58.9, 52.9, 51.8, 47.6, 37.0, 36.9; MS (FAB) m/z (relative intensity) 543 (M$^+$ + H, 3), 154 (100), 138 (99), 137 (99), 136 (99). Anal. Calcd for $C_{25}H_{20}Cl_4O_5$: C, 55.38; H, 3.72. Found: C, 55.16; H, 3.70.

X-ray Crystallographic Study. Crystals of **2**, $C_{17}H_{12}Cl_4O_5$ (FW = 438.07), are triclinic, space group *P*-1, with cell data: $a = 8.293(2)$ Å, $b = 10.018(2)$ Å, and $c = 11.137(2)$ Å, $\beta = 86.570(10)°$, $V = 872.8(3)$ Å^3, $Z = 2$, $D_{\mathrm{calc}} = 1.667$ Mg m^{-3}, $F(000) = 444$. A crystal of dimensions 0.68 × 0.46 × 0.44 mm was used for the data collection with an Enraf-Nonius CAD-4 diffractometer at 293(2) K and using graphite-monochromated Mo Kα radiation ($\lambda = 0.71069$ Å) from θ values of 1.86−24.97°. Of 3231 reflections collected, 3060 reflections had $I > 2\sigma(I)$. The structure was solved by direct methods using NRCVAX and refined by full-matrix least-squares methods (based on F^2) using SHELXL-93. All non-hydrogen atoms were refined with anisotropic displacement parameters, and all hydrogen atoms were contrained to geometrically calculated positions. The final agreement factors were $R_{\mathrm{F}} = 0.0299$ (0.0350 for all data), $R_{\mathrm{w}} = 0.0816$ (0.0844 for all data), and GOF = 1.021.

Acknowledgment. Financial support was generously provided by the National Science Council of Taiwan (NSC 86-2113-M194-002 and NSC 87-2113-M194-001).

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of new compounds shown in Schemes 2−8, together with X-ray crystallographic details for **2**, **18b**, and **22b.** This material is available free of charge via the Internet at http://pubs.acs.org.

JO990256R