Synthesis, Static Structure, and Kinetic Stability of a *syn*-Sesquinorbornatriene[1]

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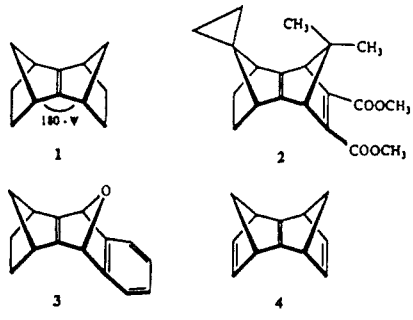
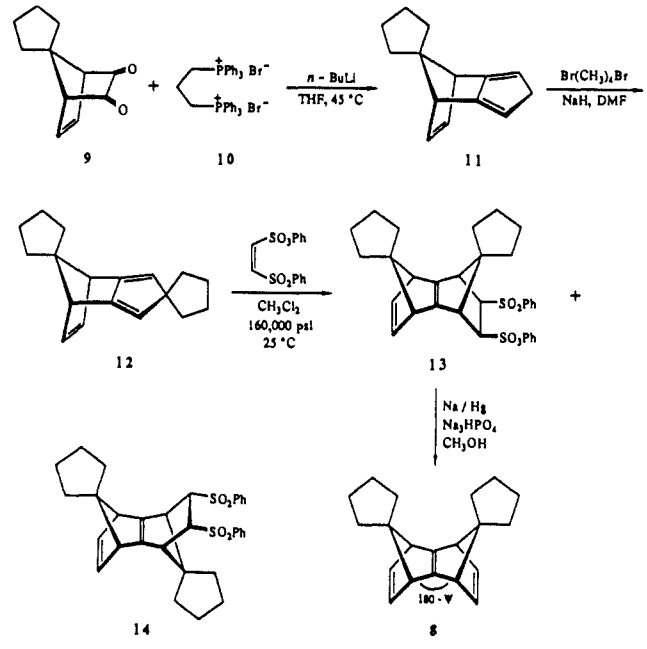
Abstract: The bisspiro *syn*-sesquinorbornatriene **8** has been synthesized and shown to be recalcitrant to attack by several reactive reagents, in contrast to the parent system **4**. The spectral properties of **8** compare closely to those of **4**, especially the pronounced downfield chemical shift of the internal pyramidalized olefinic carbons (172 ppm). On this basis, the two molecules appear to share a close conformational relationship. The greatly diminished reactivity of **8** has permitted X-ray crystallographic analysis. These data show the central flap angle to be 157.3 (4)° and the relevant pyramidalization angle to be 32.4°. This overall geometric profile constitutes an extreme level of distortion for an isolable pyramidalized alkene. For comparison purposes, several monospirocyclopentyl *syn*-sesquinorbornatrienes were also prepared. These were found to be uniformly air-sensitive, signaling that both apical carbons need to be suitably substituted to achieve kinetic stability.

As extensive as the studies dealing with the chemical reactivity of norbornenes and norbornadienes have been, only in the last decade has it come to be recognized that the π bonds in these molecules are bent downward to an extent at times exceeding 8°.[2] Theoretical studies of the phenomenon now abound.[3] The level of endo pyramidalization is enhanced to 16–18° when the two norbornyl systems are fused together in syn fashion across a double bond as in **1**.[4] The ability of these molecules to fold still further has been discerned following introduction of a second (peripheral) double bond. Removal of a pair of endo protons as in **2** and **3** is accompanied by increases in ψ to 21.8°[5] and 22.1°,[6] respectively. More recently, *syn*-sesquinorbornatriene (**4**) has yielded to synthesis.[7] Although the spectral characteristics of this maximally unsaturated hydrocarbon have been delineated,[7,8] its very high reactivity toward oxygen[9] has precluded determination of its molecular structure. The intense deshielding experienced by the central olefinic carbons in **4** (172.1 ppm) relative to those in *syn*-sesquinorbornadiene (157.4 ppm) and **1** (151.6 ppm), while striking, gives little hint regarding the degree of hingelike folding present in its ground-state structure. Computational studies of **4** suggested that angle deformation would not be substantially different from that witnessed in the diene.[10]



1 2 3 4

Scheme I



9 10 11 12 13 14 8

The present study was therefore undertaken in order to obtain fundamental structural information about a *syn*-sesquinorbornatriene.[11] Since **4** is especially susceptible to exo attack by O_2 and other reagents, it was imperative to sterically impede approach to this face. However, our intent was not to encumber the target molecule to such a degree that structural deformation beyond that already embodied in **4** would materialize concurrently.

The strategy ultimately adopted was dictated by two observations reported some time ago by Alder[12] and by Klumpp.[13] In these investigations, it was shown that **5** reacts with excess phenyl azide at room temperature to deliver bis-adduct **6**, while **7** is unreactive to this reagent. Accordingly, the 7-spirocyclopropane

(1) Paper 49 in the series dealing with isodicyclopentadienes and related molecules. For part 48: Paquette, L. A.; O'Doherty, G. A.; Miller, B. L.; Rogers, R. D.; Rheingold, A. L.; Geib, S. L. *Organometallics* **1989**, *8*, 2167.

(2) For example: (a) Pinkerton, A. A.; Schwarzenbach, D.; Stibbard, J. H. A.; Carrupt, P.-A.; Vogel, P. *J. Am. Chem. Soc.* **1981**, *103*, 2095. (b) Paquette, L. A.; Schaefer, A. G.; Blount, J. F. *Ibid.* **1983**, *105*, 3642. (c) Mackenzie, K.; Miller, A. A.; Muir, K. W.; Manojlovic-Muir, Lj. *Tetrahedron Lett.* **1983**, *24*, 4747.

(3) 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 and the many relevant references cited therein.

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(5) Paquette, L. A.; Green, K. E.; Gleiter, R.; Schafer, W.; Galucci, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 8232.

(6) (a) Bartlett, P. D.; Combs, G. L., Jr. *J. Org. Chem.* **1984**, *49*, 625. (b) Watson, W. H.; Galloy, J.; Grossie, D. A.; Bartlett, P. D.; Combs, G. L. *Acta Crystallogr.* **1984**, *C40*, 1050.

(7) (a) Paquette, L. A.; Künzer, H.; Green, K. E. *J. Am. Chem. Soc.* **1985**, *107*, 4788. (b) Paquette, L. A.; Künzer, H.; Green, K. E.; De Lucchi, O.; Licini, G.; Pasquato, L.; Valle, G. *Ibid.* **1986**, *108*, 3453.

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(10) Houk, K. N. Private Communication.

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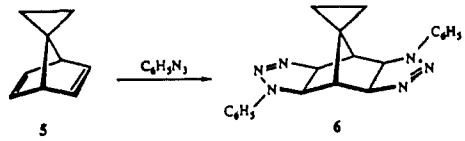
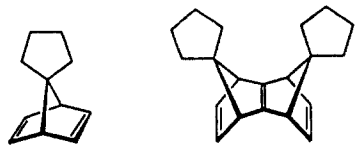
substituent seemingly does not confer as adequate a level of steric blockade to exo [3 + 2] cycloaddition as does the spirocyclopentane ring.



5 6

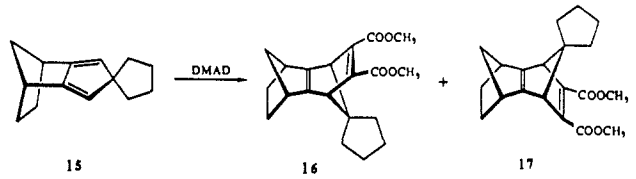


7 8

Since MOPAC calculations involving **8**[14] indicated that the closest approach between the two nearest nonbonded cyclopentyl methylene groups was well beyond van der Waals contact when ψ was still modest (>15°), this derivative of **4** was specifically targeted for investigation.

Synthesis and Structural Determination of 8. The synthetic protocol began by Wittig annulation of α-diketone **9**[15] with the bisphosphonium salt **10**[16] and spiroalkylation of the resultant tricyclo[5.2.1.$0^{2,6}$]deca-2,5,8-triene **11** with 1,4-dibromobutane and sodium hydride in dimethylformamide as solvent[17] (Scheme I). At this point, construction of the *syn*-sesquinorbornatriene framework was dependent on successful Diels–Alder capture of **12** from its endo surface. Earlier work had established that diene **15** enters into [4 + 2] cycloaddition with dienophiles such as maleic anhydride, *N*-phenylmaleimide, *p*-benzoquinone, phenyl vinyl sulfone, and *N*-methyltriazolinedione to give above-plane adducts exclusively.[4c] Only in the case of dimethyl acetylenedicarboxylate were two adducts seen, but **16** still dominated over **17** by a factor of 3:1.

On a more encouraging note, **12** was recognized to have an etheno bridge on its endo surface and consequently to be somewhat less sterically congested below plane. At the same time, the apically positioned spirocyclopentane ring in **12** can be counted on to induce a certain level of kinetic retardation to exo addition, especially in the Alder stereochemical mode preferred by **15**.[4c] In addition, (*Z*)-1,2-bis(phenylsulfonyl)ethylene,[18] the dienophile in question, is known to have large steric demands during cycloaddition to isodicyclopentadienes.[7,19]



15 16 17

For cycloaddition of the disulfone to **12**, recourse was made to high-pressure conditions. By maintenance of dichloromethane solutions of the two reactants at 160 000 psi and ambient temperature for 6 days, **13** and **14** could be isolated in yields of 77% and 11%, respectively, following chromatography. The relative stereochemistries of the adducts could be clearly discerned from their ^{1}H NMR spectra. For example, the olefinic, norbornadienyl bridgehead, and α-sulfonyl protons of **13** (in $CDCl_3$) appear at δ 6.28, 2.88, and 2.68, chemical shift values that compare favorably with those exhibited by the nonspirocyclic parent system (δ 6.47, 3.20, 2.73), which has supporting X-ray confirmation available.[7] The analogous absorptions in anti isomer **14** are seen at δ 6.79, 3.48, and 2.99 as expected.[7,19] The presence of a symmetry plane in both isomers was indicated by their 19-line ^{13}C NMR spectra.

Reductive desulfonylation[20] of **13** with buffered 1.5% sodium amalgam furnished **8** as large, colorless prisms following re-

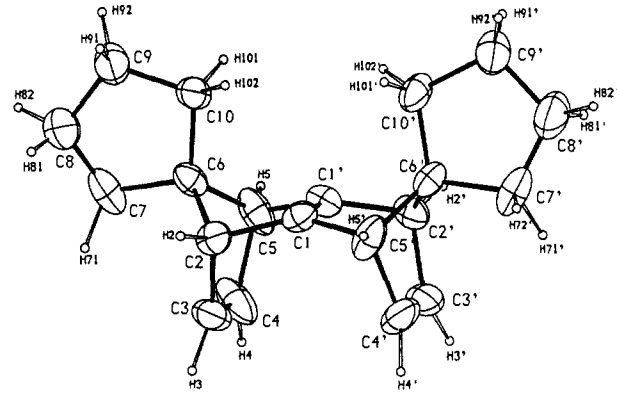


Figure 1. Computer-generated perspective drawing of the final X-ray model of **8**. The non-hydrogen atoms are represented by 30% probability thermal ellipsoids. The hydrogen atoms are drawn with an artificial radius.

Table I. Crystallographic Details for **8**

formula	$C_{20}H_{24}$
molecular weight	264
space group	C^2/c (No. 15)
molecule/unit cell	4
a, Å	21.004 (7)
b, Å	7.782 (2)
c, Å	9.972 (2)
β, deg	114.28 (2)
volume, Å^3	1485.42
ρ_{calcd}, g/cm^3	1.180
crystal dimensions, mm	0.375 × 0.075 × 0.175
diffractometer	Enraf-Nonius CAD4
radiation	Mo Kα
μ, cm^{-1}	0.6
temperature, °C	−45
scan range, 2θ	4–55
scan mode	ω–2θ
unique data	1699
unique data with $I > 3\sigma(I)$	730
variable parameters	91
R_F	0.083
R_{wF}	0.116
GOF	3.654

Table II. Bond Distances (Å) for **8**

C1–C2	1.529 (4)	C5–C6	1.574 (6)
C1′–C5	1.502 (5)	C6–C7	1.538 (5)
C2–C3	1.526 (8)	C7–C8	1.465 (10)
C2–C6	1.558 (5)	C8–C9	1.463 (8)
C3–C4	1.286 (10)	C9–C10	1.502 (6)
C4–C5	1.565 (9)	C1–C1′	1.325 (5)

Table III. Selected Bond Angles (deg) for **8**

C1–C2–C3	105.4 (3)	C2–C6–C7	114.2 (3)
C1′–C1–C2	107.4 (3)	C2–C6–C10	115.6 (3)
C1–C1′–C5	107.7 (3)	C5–C6–C7	115.7 (4)
C1–C2–C6	98.2 (3)	C5–C6–C10	116.9 (4)
C3–C2–C6	99.2 (3)	C7–C6–C10	103.7 (3)
C2–C3–C4	108.7 (5)	C6–C7–C8	105.6 (4)
C3–C4–C5	107.3 (5)	C7–C8–C9	110.2 (4)
C1′–C5–C4	104.9 (4)	C8–C9–C10	106.5 (5)
C1′–C5–C6	98.9 (3)	C6–C10–C9	108.0 (3)
C4–C5–C6	98.2 (4)	C2–C1–C5′	138.5 (2)
C2–C6–C5	91.3 (3)		

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(19) (a) Paquette, L. A.; Gugelchuk, M. *J. Org. Chem.* **1988**, *53*, 1835. (b) Paquette, L. A.; Künzer, H.; Kesselmayer, M. A. *J. Am. Chem. Soc.* **1988**, *110*, 6521. (c) Gugelchuk, M.; Paquette, L. A. *Isr. J. Chem.* in press.
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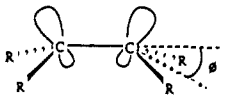
crystallization from methanol. The most notable NMR feature of this triene is the highly deshielded position of its central olefinic carbons (172.00 ppm), which falls within experimental error of the value recorded for the same atoms in **4** (172.14 ppm).[7] Although insufficient data points are available to warrant a high level of reliability,[7,8] the identity of these values suggests that the extent of pyramidal distortion in the two molecules is very closely comparable.

X-ray diffraction analyses of **8** were performed at 228 K[21] (Figure 1, Tables I–III) and at 100 K; the latter was in an attempt to gain information on electron distribution within the central double bond.[22] Unfortunately, both structural refinements clearly revealed disorder to exist at atoms C3, C4, and C8. As a consequence, the highly refined data necessary for the electron density calculations were unobtainable. On the other hand, full matrix refinement[23] clearly indicated **8** to be monoclinic (space group $C2/c$) and to possess a 2-fold crystallographic analysis. The final X-ray model revealed **8** to possess a central flap angle (ψ) of 157.3 (4)°, a record deformation level for these systems.

In recent years, pyramidalized alkenes have been discussed most often in terms of their pyramidalization angle ϕ, as defined by[24,25]

$$\cos \phi = -\cos (\text{R–C–C})/\cos \tfrac{1}{2}(\text{R–C–R})$$

with ϕ being defined as in **18**. Calculations by Hrovat and Borden

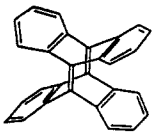
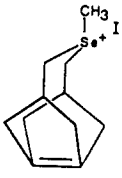


18

indicated that while HOMO energies are affected little by an increase in ϕ, LUMO levels are lowered dramatically.[26] This dichotomy has been rationalized in terms of the rather profound alterations in hybridization and overlap within the atomic orbitals from which these MO's are constructed. The ease of alkene pyramidalization gives every computational indication of being critically dependent on the bond angles at the doubly bonded carbons.[27,28] As Wiberg has noted,[29] pyramidalization within an alkene in which the R–C–C bond angles are constrained to be small has the companion effect of reducing the large R–C–R angle in the planar molecule to a more normal value.

At 32.4°, the ϕ value for **8** exceeds that of 9,9′,10,10′-tetradehydrodianthracene (**19**),[30] tricyclo[4.2.2.2^{2,5}]dodeca-1(2),5-(6)-diene (**20**),[31] the methiodide of 10-selenatricyclo[3,3,3,0^{3,7}]-undec-3(7)-ene (**21**),[32] and tetracyclo[8,2.2.2^{2,5}.2^{6,9}]octadeca-1,5,9-triene (**22**)[33] (Table IV). In both **19** and **20**, the spatial gap between the two double bonds is small, i.e., less than the π–π C···C van der Waals contact. At this distance, strong through-space repulsion between the π clouds can be expected to enhance pyramidalization despite possible amelioration of the intensity by through-bond interaction.[34] This is not the case in **8**.

Table IV. Ground State Structural Parameters for Kinetically Stable Pyramidalized Alkenes

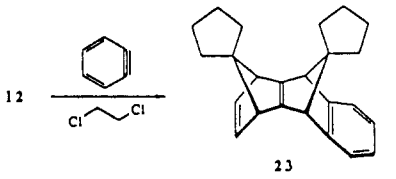
compd	ψ, deg	ϕ, deg
 **19**	44.9	19.7
 **20**	35.6	27.3
 **21**	46.2 42.1	20.3 12.3
 **22**	7.8	7.0

When a comparison is made on the basis of the flap angle ψ, then **8** is seen not to be as distorted from planarity as certain other molecules in Table I. Only when proper account is taken of the *total geometric profile* of its central olefinic carbons do the impressive structural features of the *syn*-sesquinorbornatriene framework become clearly apparent.

While solutions of parent triene **4** in chloroform are converted to the monoepoxide within minutes at room temperature when exposed to air,[7,8] **20** requires approximately overnight to undergo the analogous oxidation.[34] This transformation, one that is common to pyramidalized alkenes,[9] provides a limited view of their relative kinetic reactivity.

Noteworthily, **8** exhibits no sensitivity to atmospheric oxygen under normal circumstances, nor is reaction seen between **8** and buffered ($NaHCO_3$) *m*-chloroperbenzoic acid in dichloromethane at room temperature during 24 h. The unreactivity of the triene is further reflected in its total inertness to both phenyl azide (CH_2Cl_2, room temperature, 2 days) and diazomethane (Et_2O, 0 °C/4 h → room temperature/16 h).

In an attempt to correlate the extent of hingelike folding within the structure, triene **12** was treated with benzyne, as generated from benzendiazonium-2-carboxylate hydrochloride and propylene oxide in refluxing ethylene dichloride.[35] The benzofused derivative **23** was obtained in 77% yield as a colorless solid. Unfortunately, all attempts to grow X-ray quality crystals of this hydrocarbon were to no avail. Consequently, the precise geometric features of **23** remain unknown.



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Is One Spirocyclopentane Substituent Adequate To Realize Kinetic Stability? The previously demonstrated inertness of **7** prompted examination of several monospirocyclopentyl *syn*-sesquinorbornatrienes for the purpose of assessing the impact of

(21) J. A. Krause at the Ohio State University.
(22) Dr. R. Boese at the Institut für Anorganische Chemie der Univesität Essen.
(23) The full compilation of data can be found in the supplementary material associated with ref 11.
(24) Volland, W. V.; Davidson, E. R.; Borden, W. T. *J. Am. Chem. Soc.* **1979**, *101*, 533.
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(28) Hess, B. A., Jr.; Allen, W. D.; Michalska, D.; Schaad, L. J.; Schaefer, H. F., III *J. Am. Chem. Soc.* **1987**, *109*, 1615.
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(31) Wiberg, K. B.; Adams, R. D.; Okarma, P. J.; Maturro, M. G.; Segmuller, B. *J. Am. Chem. Soc.* **1984**, *106*, 2200.
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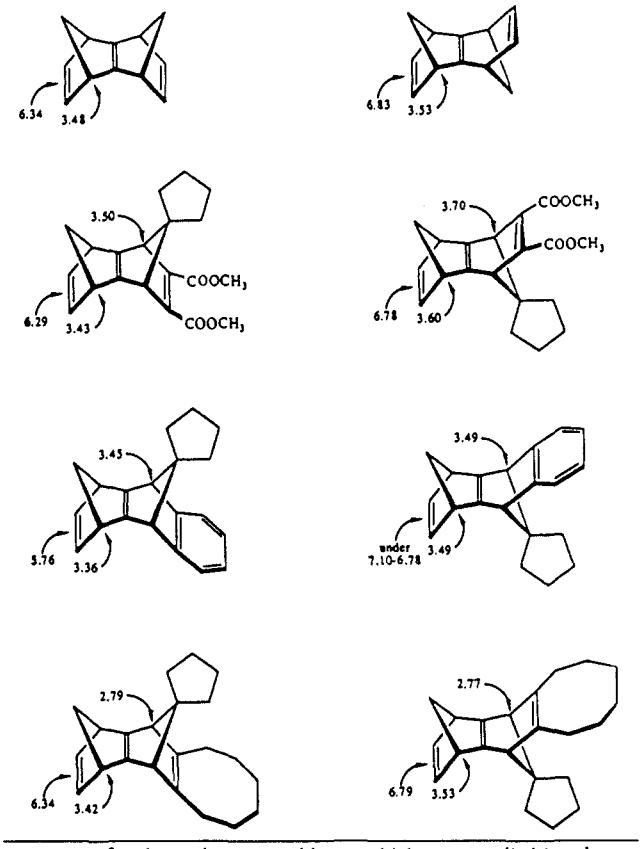
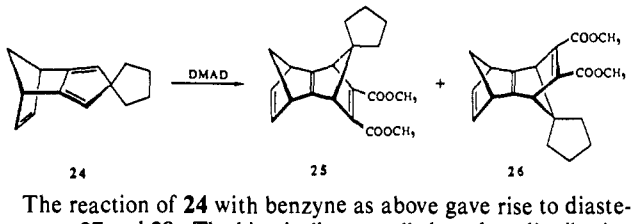
(34) Wiberg, K. B.; Matturro, M. G.; Okarma, P. J.; Jason, M. E. *J. Am. Chem. Soc.* **1984**, *106*, 2194.
(35) Friedman, L. Unpublished results. For analogy: Hart, H.; Oku, A. *J. Org. Chem.* **1972**, *37*, 4269.

Table V. ^{1}H NMR Chemical Shift Assignments To Select *syn*- and *anti*-Sesquinorbornatriene Isomer Pairs (δ Values, 300 MHz, $CDCl_3$ Solution)[a]



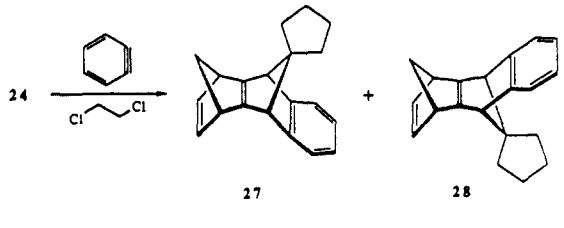
[a] Except for the cyclooctyne adducts, which were studied in toluene-d_8.

rather substantial distortion from planarity in the latter on reactivity. Initially, the Diels–Alder cycloaddition of dimethyl acetylenedicarboxylate to **24** was carried out in CD_2Cl_2 solution. After 18 h at room temperature, ^{1}H NMR analysis showed conversion to a 4:1 mixture of **25** and **26** to be complete. When the solution was exposed to air, both adducts rapidly underwent oxidation to give a complex array of products.



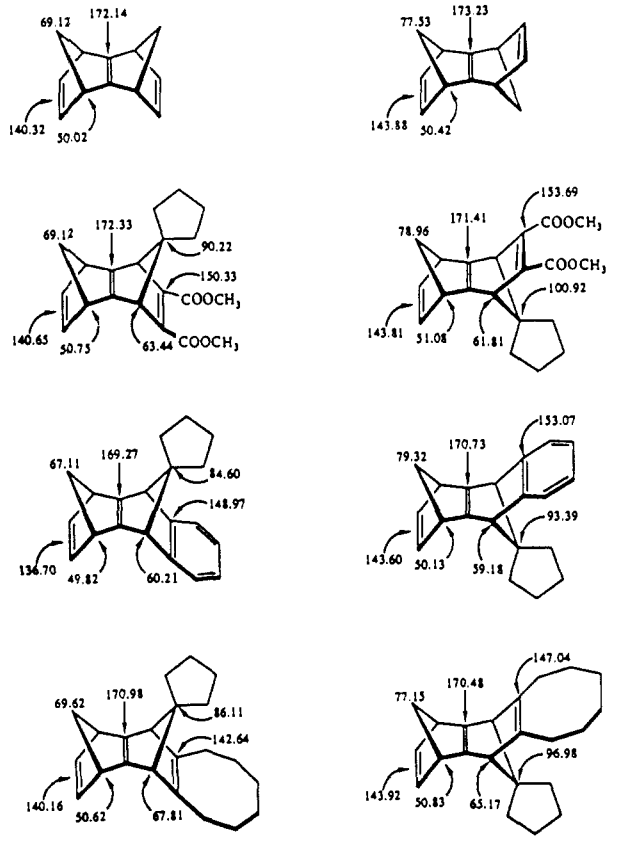
24 25 26

The reaction of **24** with benzyne as above gave rise to diastereomers **27** and **28**. The kinetically controlled product distribution was determined to be 4:3 on the basis of the integrated ratios of the clearly separated benzylic and doubly allylic bridgehead protons of the syn and anti adducts (Table V). Under carefully controlled oxygen-free conditions, the two isomers could be separated by medium-pressure liquid chromatography on silica gel. The structural assignments follow convincingly from their respective ^{1}H and ^{13}C NMR spectra (Tables V and VI). When **27** was admitted into the air, ready oxidation took place to give several unidentified compounds (TLC analysis). Anti isomer **28** proved to be less reactive toward oxygen.



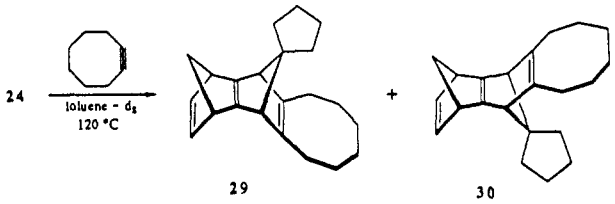
27 28

Table VI. ^{13}C NMR Chemical Shift Assignments To Select *syn*- and *anti*-Sesquinorbornatriene Isomer Pairs (ppm, 75 MHz, $CDCl_3$ Solution)[a]



[a] Except for the cyclooctyne adducts, which were studied in toluene-d_8.

When **24** was heated with cyclooctyne in toluene-d_8 at 120 °C under anaerobic conditions, there was produced a 6.5:1 mixture of **29** and **30** (^{1}H NMR analysis). Upon subsequent admission of air, the syn isomer was seen to be consumed at a considerably faster rate than **30**.



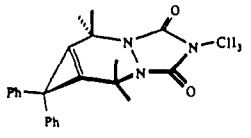
29 30

Discussion

The double bond folding (ψ) in *syn*-sesquinorbornene (**1**) amounts to 16–18°, with the pyramidalization angle (ϕ) at the olefinic carbons ranging from 24 to 26°. These values represent substantive increases in pyramidalization above those determined crystallographically for a wide selection of norbornenes and norbornadienes. The geometries of two representative *syn*-sesquinorbornadienes show the deviation from planarity to be increased somewhat more (ψ = 21–22°), but the increment is not enormous. In the present study, it is demonstrated that the inner double bond in *syn*-sesquinorbornatriene **8** is only marginally more folded than that in **2** and **3**. Thus, we must conclude that **23** may well represent the maximum extent to which the *syn*-sesquinorbornatriene framework can distort. In the case of **8**, adoption of this equilibrium geometry (ϕ = 32.4°) has the effect of positioning the key methylene protons on the exo surface (H10 and H10′) at a closer distance (3.001 Å) than either the trigonal carbons (C3–C4′ and C3′–C4 = 3.442 Å) or the vinylic hydrogens (H3–H4′ and H4–H3′ = 3.790 Å) present on the endo surface. Thus, although in principle heightened compression could materialize

on the molecular underside before van der Waals interactions gain importance, this does not occur.

The relatively small size of the "hole" extant above the π system clearly contributes in a significant way to the greatly attenuated reactivity of triene **8**.[36] Not unexpectedly, therefore, steric effects can be profitably utilized to gain access to chemically persistent alkenes. Ando and co-workers have taken advantage of extensive substitution about the double bond in **31** to preserve it from reactivity.[37] X-ray analysis has shown ψ in 31 to be 18° and the six-membered ring to be planar. As a consequence, the observed olefin pyramidalization cannot be attributed to an environment of low symmetry. The prognosis for future use of steric screening therefore seems bright. A particularly notable application could surface in the course of preparing stable members of the lower homologous series **32** and **33**.[38]

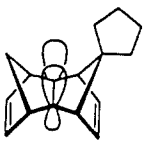


31

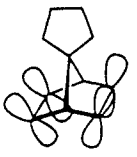
32

33

Finally, the appreciable reactivity of the monospiroalkylated *syn*-sesquinorbornatrienes can be attributed to the greater availability of exo π-electron density in systems of type **34** relative to the situation in **35**. When ψ is large as it is in **34**, lateral attack at the somewhat expanded exo p lobes[39] is made feasible.



34



35

Experimental Section

Wittig Annulation of 9. To a suspension of 1,3-trimethylenebis(triphenylphosphonium) dibromide (4.13 g, 5.69 mmol) in anhydrous tetrahydrofuran (35 mL) was added dropwise 7.3 mL of 1.55 M *n*-butyllithium in hexanes at room temperature under an atmosphere of argon. After 10 h of stirring, a solution of **9** (1.00 g, 5.68 mmol) in 25 mL of anhydrous tetrahydrofuran was introduced dropwise to the red mixture, which was then stirred for 2 h at room temperature and for 3 days at 45 °C. The cooled reaction mixture was poured into water and extracted with pentane. The combined organic phases were washed with water and brine, dried, and concentrated. Silica gel chromatography with petroleum ether as eluant furnished 320 mg (31%) of **11** as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.30 (t, J = 1.9 Hz, 2 H), 5.68 (m, 2 H), 3.26 (t, J = 1.5 Hz, 2 H), 3.06 (t, J = 1.8 Hz, 2 H), 1.71 (t, J = 7.0 Hz, 2 H), 1.52 (m, 4 H), 1.31 (t, J = 7.0 Hz, 2 H); ^{13}C NMR (63 MHz, $CDCl_3$) ppm 154.73, 137.98, 115.03, 79.55, 52.76, 46.11, 33.01, 32.18, 25.39 (1 C not observed); MS m/z (M^+) calcd 184.1252, obsd 184.1243.

Spiroalkylation of 11. To a magnetically stirred suspension of sodium hydride (800 mg, 33 mmol) in dry dimethylformamide (50 mL) was added a solution of **11** (639 mg, 3.47 mmol) in a mixture of tetrahydrofuran (2 mL) and dimethylformamide (10 mL) at −25 °C under an atmosphere of argon. After being stirred for 2 h, the resulting salt was treated with a solution of 1,4-dibromobutane (800 mg, 3.7 mmol) in 10 mL of dry dimethylformamide and then stirred at −10 °C for 25 h and at room temperature for 3.5 days. Water was added, the product was extracted into pentane, and the combined organic layers were washed with water and brine prior to drying. Solvent evaporation and chromatography of the residue on silica gel (elution with petroleum ether) provided **12** (334 mg, 40%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.24 (t, J = 1.9 Hz, 2 H), 5.59 (d, J = 0.4 Hz, 2 H), 2.95 (t, J = 1.7 Hz, 2 H), 1.83–1.32 (m, 16 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 149.71, 137.38, 125.33, 78.07, 70.68, 52.45, 34.39, 32.97, 32.88, 31.94, 25.55, 25.38 (2 C not observed); MS m/z (M^+) calcd 238.1722, obsd 238.1734.

Diels–Alder Cycloaddition of (*Z*)-1,2-Bis(phenylsulfonyl)ethylene to 12. Triene **12** (334 mg, 1.40 mmol) and (*Z*)-1,2-bis(phenylsulfonyl)-ethylene (1.73 g, 5.61 mmol) were dissolved in dichloromethane (12 mL) and maintained under a pressure of 160000 psi for 6 days. After solvent evaporation, the residual solid was purified by sequential column chromatography and MPLC (silica gel, elution with 2:1 petroleum ether–ethyl acetate). There was isolated 590 mg (77%) of **13** and 85 mg (11%) of **14** as colorless solids.

For **13**: colorless crystals; mp 208–209.5 °C (from dichloromethane–hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (m, 4 H), 7.64–7.50 (m, 6 H), 6.28 (t, J = 1.9 Hz, 2 H), 3.29 (s, 2 H), 2.88 (m, 2 H), 2.68 (s, 2 H), 2.42 (t, J = 6.8 Hz, 2 H), 1.79–1.33 (m, 14 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.28, 142.37, 138.13, 133.14, 128.85, 128.02, 93.06, 69.12, 65.99, 57.48, 55.72, 33.54, 33.34, 33.25, 30.14, 25.53, 25.47, 24.80, 23.83; MS m/z (M^+) calcd 546.1899, obsd 546.1872.

Anal. Calcd for $C_{32}H_{34}O_4S_2$: C, 70.30; H, 6.27. Found: C, 69.97; H, 6.43.

For **14**: colorless crystals; mp 216–218 °C (from dichloromethane–hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (m, 4 H), 7.72–7.51 (m, 6 H), 6.79 (t, J = 1.9 Hz, 2 H), 4.08 (s, 2 H), 3.48 (t, J = 1.7 Hz, 2 H), 2.99 (s, 2 H), 1.87–1.29 (m, 16 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 161.77, 142.73, 141.10, 133.08, 128.91, 128.15, 97.38, 72.73, 72.53, 60.12, 57.45, 37.33, 34.85, 34.76, 33.96, 26.62, 25.93, 25.79, 25.59; MS m/z ($M^+ - SO_2C_6H_5$) calcd 405.1888, obsd 405.1851.

Anal. Calcd for $C_{32}H_{34}O_4O_2{\cdot}CH_2Cl_2$: C, 62.75; H, 5.74. Found: C, 62.72; H, 5.80.

Bisspiro(cyclopentane)-*syn*-sesquinorbornatriene (8). To a magnetically stirred mixture of **13** (1.32 g, 2.41 mmol) and disodium hydrogen phosphate (2.41 g, 17.0 mmol) in methanol (40 mL) was added portionwise 42.0 g of 1.5% sodium analgam under an atmosphere of argon over a 6.5-h period. After an additional 15.5 h of stirring, the insolubles were separated by filtration and the filtrate was extracted with dichloromethane. The combined organic phases were washed with water and brine, dried, and concentrated. Preparative thin layer chromatographic purification of the residue (silica gel, elution with petroleum ether) gave **8** (403 mg, 63%) as colorless crystals: mp 86 °C (from methanol); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.29 (t, J = 1.7 Hz, 4 H), 3.19 (t, J = 1.7 Hz, 4 H), 1.84–1.44 (m, 16 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 172.00, 141.31, 90.46, 59.94, 34.23, 26.10, 25.40 (1 C not observed); MS m/z (M^+) calcd 264.1878, obsd 264.1872.

For X-ray crystallographic data, consult ref 11.

Bisspiro(cyclopentane)-*syn*-benzosesquinorbornatriene (23). To a refluxing solution of **12** (204 mg, 0.856 mmol) in ethylene dichloride (10 mL) were added 160 mg (0.867 mmol) of benzenediazonium-2-carboxylate hydrochloride and 1 mL of propylene oxide under an atmosphere of nitrogen. After 1 h, an additional 160 mg of the diazonium salt and 1 mL of propylene oxide were added to the dark green solution. The reaction mixture was refluxed 2 h longer and concentrated. Purification by preparative thin-layer chromatography on silica gel (elution with petroleum ether) furnished **23** (208 mg, 77%) as a colorless solid: mp 68–70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 (dd, J = 5.0, 3.0 Hz, 2 H), 6.69 (dd, J = 5.0, 3.0 Hz, 2 H), 5.69 (t, J = 1.8 Hz, 2 H), 3.42 (s, 2 H), 3.10 (t, J = 1.5 Hz, 2 H), 1.94 (t, J = 7.0 Hz, 2 H), 1.80 (t, J = 7.0 Hz, 2 H), 1.64–1.33 (m, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 169.75, 149.58, 137.17, 123.33, 122.90, 88.95, 84.65, 60.62, 59.45, 34.06, 33.91, 33.38, 32.88, 25.96, 25.92, 25.32, 25.28; MS m/z (M^+) calcd 314.2034, obsd 314.2057.

Anal. Calcd for $C_{24}H_{26}$: C, 91.67; H, 8.33. Found: C, 91.30; H, 8.39.

Spiroalkylation of Tricyclo[5.2.1.0^{2,6}]deca-2,5,8-triene. To a suspension of sodium hydride (3.55 g, 148 mmol) in distilled dimethylformamide (150 mL) was added dropwise a solution of tricyclo[5.2.1.0^{2,6}]deca-2,5,8-triene (2.00 g, 15.4 mmol) in a mixture of tetrahydrofuran (3 mL) and dimethylformamide (20 mL) at −50 °C under an argon atmosphere. The stirred mixture was allowed to warm to room temperature gradually during 2 h and then recooled to −50 °C. A solution of 1,4-dibromobutane (3.55 g, 16.4 mmol) in 20 mL of diethylformamide was next introduced, and stirring was maintained at 0 °C for 3.5 h and at room temperature for 41 h. Following the addition of water at 0 °C, the product was extracted into pentane and the combined organic phases were washed with water and brine, dried, and evaporated. The residue was chromatographed on silica gel (elution with petroleum ether) to give 908 mg (32%) of **24** as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.29 (t, J = 1.5 Hz, 2 H), 5.59 (s, 2 H), 3.38 (t, J = 1.5 Hz, 2 H), 2.19 (dt, J = 8.0, 1.5 Hz, 1 H), 1.93 (d, J = 8 Hz, 1 H), 1.83–1.64 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 149.25, 137.58, 124.88, 71.34, 57.90, 43.32, 34.24, 32.81, 25.64, 25.56; MS m/z (M^+) calcd 184.1252, obsd 184.1263.

(36) A listing of nonisolable olefins of this type can be found in ref 25.
(37) Ando, W.; Hanyu, Y.; Toshikazu, T.; Ueno, K. *J. Am. Chem. Soc.* **1984**, *106*, 2216.
(38) Johnson, C. A. *J. Chem. Soc., Chem. Commun.* **1983**, 1135.
(39) An independent study has shown the density maximum in a *syn*-sesquinorbornene to be shifted only by 0.1 Å from the internuclear line: Irngartinger, H.; Deuter, J.; Charumilind, P.; Paquette, L. A. *J. Am. Chem. Soc.*, in press.

Cycloaddition of Dimethyl Acetylenedicarboxylate to 24. Into an NMR tube was placed a solution of **24** (54.9 mg, 0.298 mmol) and dimethyl acetylenedicarboxylate (46.6 mg, 0.328 mmol) in 0.5 mL of CD_2Cl_2 and the tube was sealed in vacuo. After 18 h at room temperature, reaction was complete (^1H NMR analysis) and a 4:1 mixture of **25** and **26** was produced. When exposed to the air, both adducts were oxidized. The following spectra were derived from the mixture.

For **25**: ^1H NMR (80 MHz, CD_2Cl_2) δ 6.29 (t, J = 1.7 Hz), 3.59 (s), 3.50 (s), 3.43 (t, J = 1.7 Hz), 2.25-1.13 (series of m); ^{13}C NMR (75 MHz, CD_2Cl_2) ppm 172.33, 166.52, 150.33, 140.65, 90.22, 69.12, 63.44, 51.99, 50.75, 34.31, 32.84, 25.88, 25.51.

For **26**: ^1H NMR (80 MHz, CD_2Cl_2) δ 6.78 (t, J = 1.8 Hz), 3.76-3.54 (m), 3.65 (s), 2.25-1.13 (series of m); ^{13}C NMR (75 MHz, CD_2Cl_2) ppm 171.41, 166.39, 153.69, 143.81, 100.92, 78.96, 61.81, 52.03, 51.08, 34.87, 34.07, 25.70, 25.40.

Benzyne Addition to 24. A 155-mg (0.841-mmol) sample of **24** was reacted with benzenediazonium 2-carboxylate hydrochloride and propylene oxide in ethylene dichloride exactly as described above. Analogous purification afforded 106 mg of a pale yellow viscous oil, which consisted of a 4:3 mixture of syn and anti adducts. This mixture was separated by MPLC on silica gel (elution with petroleum ether) to give 29.7 mg (14%) of **27** and 39.1 mg (18%) of **28**, both as colorless oils.

For **27**: ^1H NMR (300 MHz, $CDCl_3$) δ 6.88-6.67 (m, 4 H), 5.76 (t, J = 1.7 Hz, 2 H), 3.45 (s, 2 H), 3.36 (m, 2 H), 2.12-1.28 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 169.27, 148.97, 136.70, 123.42, 123.11, 84.60, 67.11, 60.21, 49.82, 33.26, 32.60, 25.64, 25.20.

For **28**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.10-6.78 (m, 6 H), 3.49 (m, 4 H), 2.18-1.21 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.73, 153.07, 143.60, 123.63, 121.22, 93.39, 79.32, 59.18, 50.13, 34.14, 33.60, 25.47, 25.19; MS m/z (M^+) calcd 260.1565, obsd 260.1532.

Diels-Alder Reaction of Cyclooctyne with 24. Into an NMR tube was placed a solution of **24** (67.4 mg, 0.37 mmol) and cyclooctyne (42.9 mg, 0.40 mmol) in 0.5 mL of toluene-d_8, and the tube was sealed in vacuo. After 14.5 h of heating at 120 °C, reaction was shown to be complete (^1H NMR analysis) and to consist of a 6.5:1 mixture of **29** and **30**. The following spectra were derived from the mixture.

For **29**: ^1H NMR (300 MHz, toluene-d_8) δ 6.34 (t, J = 1.7 Hz), 3.42 (t, J = 1.6 Hz), 2.79 (s), 2.28-1.35 (series of m); ^{13}C NMR (75 MHz, toluene-d_8) ppm 170.98, 142.64, 140.12, 86.11, 69.62, 67.81, 50.62, 34.76, 33.92, 30.23, 26.41, 26.10, 25.80 (1 C not observed).

For **30**: ^1H NMR (300 MHz, toluene-d_8) δ 6.79 (t, J = 1.7 Hz), 3.53 (t, J = 1.7 Hz), 2.77 (s), 2.28-1.35 (series of m); ^{13}C NMR (75 MHz, toluene-d_8) ppm 170.48, 147.04, 143.92, 96.98, 77.15, 65.17, 50.83, 35.26, 35.23, 29.48, 27.01, 26.41, 25.89 (1 C not observed).

Acknowledgment. We are grateful to the National Institutes of Health for their support of this work (Grant CA-12115) and to Dr. Roland Boese (Universität Essen) and Jeanette Krause (The Ohio State University) for the X-ray crystallographic data.

Registry No. 8, 119594-09-1; **9**, 60526-44-5; **11**, 119594-06-8; **12**, 119594-07-9; **13**, 119594-08-0; **14**, 119677-31-5; **23**, 124382-48-5; **34**, 85222-07-7; **25**, 85222-29-3; **26**, 85280-15-5; **27**, 124382-50-9; **28**, 124440-58-0; **29**, 124382-51-0; **30**, 124440-59-1; $Ph_3P^+(CH_2)_3P^+Ph_3 \cdot 2Br^-$, 7333-67-7; 1,4-dibromobutane, 110-52-1; (*Z*)-1,2-bis(phenylsulfonyl)ethylene, 963-15-5; benzenediazonium-2-carboxylate hydrochloride, 124382-49-6; tricyclo[5.2.1.$0^{2,6}$]deca-2,5,8-triene, 6675-71-4; dimethyl acetylenedicarboxylate, 762-42-5; cyclooctyne, 1781-78-8.

Supplementary Material Available: Tables VII-X, listing positional parameters and anisotropic thermal parameters for **8** (4 pages); Table XI listing structure factors for **8** (8 pages). Ordering information can be found on any current masthead page.

Asymmetric Total Synthesis of Atisine via Intramolecular Double Michael Reaction

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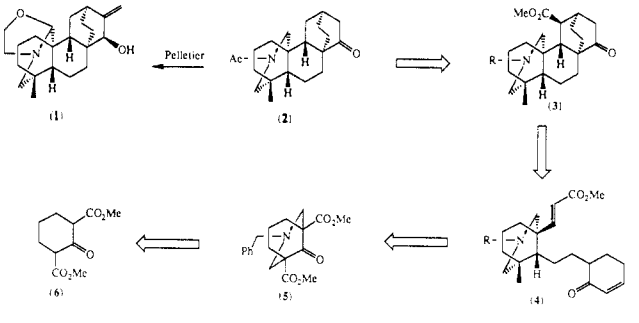
Contribution from the Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan, and Instrumental Analysis Center for Chemistry, Faculty of Science, Tohoku University, Aobayama, Sendai 980, Japan. *Received June 26, 1989*

Abstract: The bridged, pentacyclic intermediate **2** for atisine (**1**) was synthesized in a naturally occurring enantiomeric form from dimethyl cyclohexanone-2,6-dicarboxylate (**6**). The synthesis is composed of the following key steps: (1) formation of the azabicyclo[3.3.1]nonane by a double Mannich reaction, (2) enantioselective conversion by a lipase-catalyzed acylation, (3) stereoselective hydroboration in the presence of $BF_3 \cdot Et_2O$, and (4) construction of the bicyclo[2.2.2]octane ring system by an intramolecular double Michael reaction.

Diterpene alkaloids[1] are widely distributed in the plant world and have long been of interest due to their physiological properties and architectural features. Atisine (**1**), the predominant alkaloid of *Aconitum heterophyllum*,[2] has a relatively uncomplicated hexacyclic structure including azabicyclo[3.3.1]nonane and bicyclo[2.2.2]octane rings. The absolute stereochemistry was elucidated by interrelating the degradation products with those of the related diterpene alkaloids and diterpenes,[3,4] Since the stereostructure had been determined, the alkaloid has attracted the attention of organic chemists as a target molecule. Three different routes[5,6] have been successful in reaching Pelletier's synthetic intermediates[7] for atisine, although only racemates were synthesized. A major obstacle in the synthesis is the problem of constructing azabicyclo[3.3.1]nonane and bicyclo[2.2.2]octane ring systems. We envisioned assembly of the bicyclo[2.2.2]octane

Scheme I



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