

5 H, C_6H_5), 3.87 (d, 1 H, $J = 9$ Hz, CH_3OCH_2), 3.48 (d, 1 H, $J = 9$ Hz, CH_3OCH_2), 3.23 (s, 3 H, OCH_3), 1.59 (s, 3 H, CCH_3); IR (neat) 3300, 2700, 1705, 1110 cm^{-1} .

Anal. Calcd for $C_{11}H_{14}O_2$: C, 68.04; H, 7.22. Found: C, 67.98; H, 7.28.

(-)-(*S*)-1,2-Diphenyl-3-methoxy-2-methyl-1-propanone (10). To 500 mg (2.40 mmol) of methyl *O*-methyl- α -methyltropate (9) in 60-mL of dry ethyl ether at $-78^\circ C$ was added over 2 h 1.34 mL (1.8 M, 1.0 equiv) of phenyl lithium. The mixture was then poured into a cold solution of ammonium chloride. The phases were separated, and the organic layer was dried ($MgSO_4$) and concentrated. Analysis by GLC showed the presence of 1,2-diphenyl-3-methoxy-2-methyl-1-propanone (51%).

(-)-(*S*)-9 (680 mg; 3.3 mmol) $[\alpha]_D^{25} -30.8^\circ$, was converted to (-)-(*S*)-10, which was purified by preparative TLC to give 310 mg (37%) of (-)-(*S*)-10, $[\alpha]_D^{25} -122.0^\circ$ (c 1.2, $HCCl_3$), by using the above procedure with slight modification. This material was identical with 10, prepared from 7.

(-)-(*S*)-1-Hydroxy-1,2-diphenyl-2-methyl-1-propanone (7). To 2.70 g (11.3 mmol) of the propanedione 2 in 100 mL of absolute ethanol and 14.5 mL of acetic acid was added 334 mg (1.4 equiv H^-) of sodium cyanoborohydride. The solution was stirred for 16 h. The mixture was then poured into cold 10% hydrochloric acid and stirred for 5 min. The acid solution was extracted twice, with 100 mL of ether, and the combined ethereal fractions were extracted with 50 mL of saturated sodium bicarbonate. The ethereal solution was dried ($MgSO_4$) and concentrated to give a thick yellow oil which was purified by chromatography on silica gel using benzene-hexane (4:1), then benzene-ethyl acetate (4.5:5), to give 1.84 g (68%) of 1-hydroxy-1,2-diphenyl-2-methyl-1-propanone (7): NMR (CCl_4) δ 7.28 (m, 10 H, aromatic), 4.13 (d, 1 H, $J = 11$ Hz, CH_2OH), 3.53 (d, 1 H, $J = 11$ Hz, CH_2OH), 2.83 (s, 1 H, CH_2OH), 1.78 (s, 3 H, $C-CH_3$); IR (neat) 3480, 1670 cm^{-1} .

Alcohol 7 could also be purified by preparative TLC using benzene-hexane (4:1) and benzene-ethyl acetate (4.5:0.5).

Using the above procedure, 295 mg (1.24 mmol) of (-)-(*S*)-2, $[\alpha]_D^{25} -387.3^\circ$ (c 1.08, $HCCl_3$), gave 145 mg (49%) of (-)-(*S*)-7, $[\alpha]_D^{25} -223.5^\circ$ (c 0.96, $HCCl_3$).

In ethanol, sodium borohydride and 2 gave only a α -methyldeoxybenzoin (12, 74%).

Preparation of (-)-(*S*)-1,2-Diphenyl-3-methoxy-2-methyl-1-propanone (10) from 7. A. To 160 mg (0.666 mmol) of 1-hydroxy-1,2-diphenyl-2-methyl-1-propanone (7) in 30 mL of methylene chloride was added 248 mg (2.5 eq) of trimethyl-oxonium tetrafluoroborate.¹³ The reaction mixture was refluxed for 16 h followed by the addition of water. The phases were separated, and the organic layer was dried ($MgSO_4$) and concentrated. Analysis by TLC using benzene-hexane (4:1) revealed only two spots with R_f values identical with those of 7 and 10

prepared by an alternate pathway. Purification by preparative TLC using benzene-hexane (4:1) gave 50 mg (31%) of 1,2-diphenyl-3-methoxy-2-methyl-1-propanone (10): NMR (CCl_4) δ 7.2 (s, 10 H, aromatic), 3.9 (d, 1 H, $J = 9$ Hz, CH_2-OCH_3), 3.6 (d, 1 H, $J = 9$ Hz, CH_2OCH_3), 3.2 (s, 3 H, OCH_3), 1.6 (s, 3 H, CCH_3); IR (neat) 3060, 3020, 1680, 1110 cm^{-1} .

Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.32; H, 7.09. Found: C, 80.55; H, 7.00.

(-)-(*S*) alcohol 7, $[\alpha]_D^{25} -223.5^\circ$ (c 0.96, $HCCl_3$) (129 mg; 0.538 mmol), was converted to 60 mg (44%) of (-)-(*S*)-10, $[\alpha]_D^{25} -122.0^\circ$ (c 1.1, $HCCl_3$), whose spectral properties were identical with those of authentic racemic material, by using the above procedure.

B. To 65 mg (0.27 mmol) of (-)-(*S*)-7 (53% optically pure) in 3 mL of methyl iodide was added 130 mg of silver oxide. The mixture was gently refluxed for 72 h and then filtered. The filtrate was diluted with methylene chloride and extracted with water. The methylene chloride was dried ($MgSO_4$) and concentrated to give, after purification by preparative TLC, 31 mg (45%) of (-)-(*S*)-10, $[\alpha]_D^{25} -6.88^\circ$ (c 1.1, $HCCl_3$). Recovered (-)-(*S*)-7 was 1.1% optically pure, $[\alpha]_D^{25} -2.52^\circ$ (c 0.6, $HCCl_3$).

Determination of Optical Purity. All samples whose optical purities were to be determined were weighed directly into the NMR tubes. Typical sample sizes were 30–60 mg. For all determinations, carbon tetrachloride or deuterated chloroform (ca. 0.5 mL, 4% Me_4Si) was used. After preliminary analysis, the europium shift reagent $Eu(C_{11}H_{19}O_2)_3$ was added directly, and the tube was shaken until all solids were dissolved. The spectra were examined for the extent of chemical shift and diastereomeric separation, and then the diastereomeric signals were integrated five times. The chemical shifts were obtained relative to Me_4Si using a side banding technique. From the results of multiple analyses of the same sample, it was found that the relative error in determining optical purities by this method was $\pm 4\%$.

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Registry No. (\pm)-1, 70397-71-6; (*S*)-1, 59472-41-2; (\pm)-2, 70397-72-7; (*S*)-2, 66364-98-5; (\pm)-3, 31917-13-2; (*S*)-3, 59492-59-0; (*S*)-3 quinine salt, 70343-17-8; (*R*)-3, 28968-34-5; (*R*)-3 quinine salt, 70343-22-5; (\pm)-4, 70397-73-8; (*S*)-4, 59472-42-3; 5, 34009-61-5; (\pm)-6, 2328-24-7; (\pm)-7, 70398-00-4; (*S*)-7, 66365-01-3; (\pm)-8, 70397-74-9; (*R*)-8, 70343-18-9; (*S*)-8, 66365-02-4; (\pm)-9, 70397-75-0; (*R*)-9, 70343-19-0; (*S*)-9, 66365-03-5; (\pm)-10, 70397-99-8; (*R*)-10, 70343-20-3; (*S*)-10, 66365-04-6; (\pm)-12, 67737-73-9; diethyl phenylmalonate, 83-13-6; methyl iodide, 74-88-4; (\pm)-*O*-methyl- α -methyltropate, 70343-21-4.

Syntheses of Novel Gyrochiral Pentacyclic Systems with C_2 Symmetry.

(-)- C_2 -Bismethanotwistane and (\pm)- C_2 -Methanoditwistane

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Diazomethane ring expansion of C_2 -bismethanotwistane-8,12-dione (18) obtained from the cyclohexadiene-benzoquinone adduct 10 was explored to secure the synthetic route to a novel gyrochiral pentacyclic system, D_3 -tritwistane (7). Whereas D_3 -trishomocubanedione (22) was found to afford the single 23 and the double 24 ring expansion products, 18 failed to yield the expected doubly expanded product with a D_3 -tritwistane system. Preparation of the new gyrochiral pentacyclic hydrocarbons (-)- C_2 -bismethanotwistane (5) and (\pm)- C_2 -methanoditwistane (6) are reported.

Among groups of rigid pentacyclic hydrocarbons (1) which can be conceptually constructed by simultaneous

diagonal bridging between the 2,5, 3,7, and 6,8 carbon atoms of twisted D_3 -bicyclo[2.2.2]octane, cubane (2) ($k =$

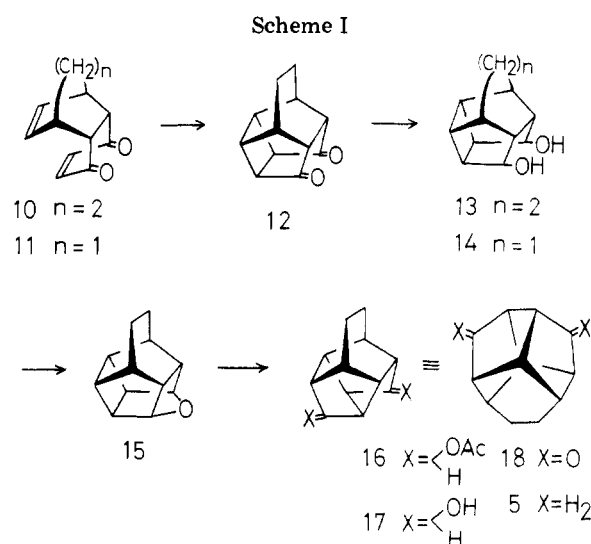
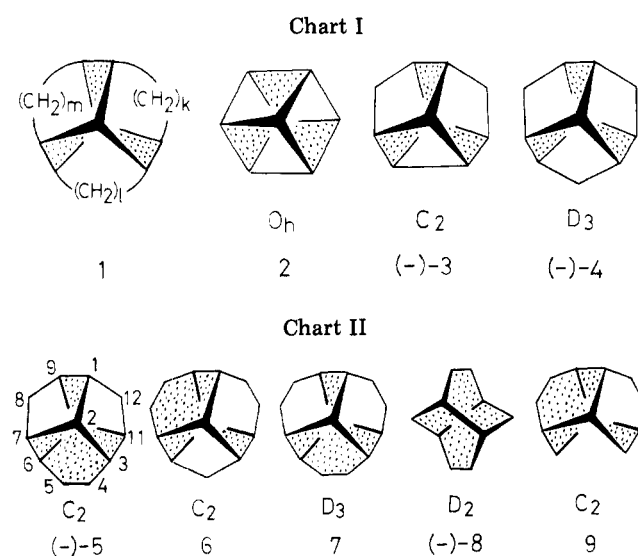


Table I. Trivial Names and Symmetries of the Pentacyclic Hydrocarbons Constructed by 2,5, 3,7, and 6,8 Diagonal Bridgings of the D_3 Twisted Bicyclo[2.2.2]octane (1)

k	l	m	trivial name	symmetry	ref
0	0	0	cubane (2)	O_h	1
0	0	1	homocubane	C_{2v}	2
0	0	2	basketane	C_{2v}	2
0	1	1	C_2 -bishomocubane (3)	C_2	3, 10
0	1	2	C_1 -homobasketane	C_1	4
0	2	2	C_2 -6,8-dehydroditwistane	C_2	5
1	1	1	D_3 -trishomocubane (4)	D_3	6, 11
1	1	2	C_2 -bismethanotwistane (5)	C_2	
1	2	2	C_2 -methanoditwistane (6)	C_2	
2	2	2	D_3 -tritwistane (7)	D_3	

$l = m = 0$) (C_8H_8 , O_h symmetry) is the simplest representative.

Table I tabulates members with this structural characteristic up to D_3 -tritwistane (7) ($k = l = m = 2$) with their trivial name and symmetry.⁷

Our continuing interests in gyrochiral⁸ cage-shaped compounds had led us to synthesize two pentacyclic hydrocarbons, (-)- C_2 -bishomocubane (3) ($k = 0$, $l = m = 1$) and (-)- D_3 -trishomocubane (4) ($k = l = m = 1$), in optically active modifications, and their absolute configuration determinations have been recently reported from our laboratory.^{10,11}

Among these two, each being made up of six twisted cyclopentane rings with the same chirality corresponding to its inherent symmetry number 6, D_3 -trishomocubane (4) makes itself especially conspicuous due to its beautiful chiral symmetry.

Stepwise ring expansion of this hydrocarbon 4, maintaining the characteristic twisted bicyclo[2.2.2]octane framework, yields a series of gyrochiral rigid pentacyclic hydrocarbons: C_2 -bismethanotwistane (5) ($k = l = 1$, $m = 2$),¹² C_2 -methanoditwistane (6) ($k = 1$, $l = m = 2$),¹² and D_3 -tritwistane (7) ($k = l = m = 2$).¹²

Logical extension of our interests in gyrochiral cage-shaped hydrocarbons has led us to explore the synthesis of D_3 -tritwistane (7) in an optically active modification with a known absolute configuration, and our enthusiasm has been further spurred by its interesting intrinsic stereochemistry: (a) corresponding to the symmetry number 6, D_3 -tritwistane (7) is composed of six twist-boat cyclohexanes with the same chirality; (b) D_3 -tritwistane ($C_{14}H_{20}$) (7) can be envisaged as the genatrix of "twist-diamond" which theoretically could be constructed by infinite outside expansion by fusing twist-boat cyclohexanes of the same chirality.

As a preliminary experiment securing a possible synthetic route to D_3 -tritwistane (7), diazomethane ring expansion¹⁶ was tried on C_2 -bismethanotwistane-8,12-dione (18) whose preparation, as well as the related syntheses of C_2 -bismethanotwistane (5) and C_2 -methanoditwistane (6), is reported in this paper.

Results and Discussion

Syntheses of (\pm)- C_2 -Bismethanotwistane-8,12-dione (18) and (\pm)- C_2 -Bismethanotwistane (5) (Scheme I).

(1) Cassar, L.; Eaton, P. E.; Halpern, J. *J. Am. Chem. Soc.* **1970**, *92*, 3515. Cassar, L.; Eaton, P. E.; Halpern, J. *Ibid.* **1970**, *92*, 6366; and references cited therein.

(2) Dauben, W. G.; Schallhorn, C. H.; Whalen, D. L. *J. Am. Chem. Soc.* **1971**, *93*, 1446. Paquette, L. A.; Beckley, R. S. *Ibid.* **1975**, *97*, 1084; and references cited therein.

(3) Chapman, N. B.; Key, J. M.; Toyne, K. J. *J. Org. Chem.* **1970**, *35*, 3860; and references cited therein.

(4) (a) Hirao, K.; Abe, E.; Yonemitsu, O. *Tetrahedron Lett.* **1975**, 4131. (b) Mauer, W.; Grimme, W. *Ibid.* **1976**, 1835. (c) Hirao, K.; Unno, S.; Yonemitsu, O. *J. Chem. Soc., Chem. Commun.* **1977**, 577.

(5) References are cited in ref 4a.

(6) (a) Underwood, G. R.; Ramamoorthy, B. *Tetrahedron Lett.* **1970**, 4125. (b) Godleski, S. A.; Schleyer, P. von R.; Osawa, E.; Kent, G. J. *J. Chem. Soc., Chem. Commun.* **1974**, 976. (c) Eaton, P. E.; Hudson, P. A.; Giordano, C. *Ibid.* **1974**, 978. (d) Blum, J.; Zlotogorski, C.; Zora, Z. *Tetrahedron Lett.* **1975**, 1117. (e) Smith, E. C.; Barborak, J. C. *J. Org. Chem.* **1976**, *41*, 1433.

(7) Members with k , l , or m higher than 2 are excluded because of their conformational mobility.

(8) Nakazaki, M.; Naemura, K.; Kadowaki, H. *J. Org. Chem.* **1976**, *41*, 3725. Nakazaki, M.; Yamamoto, K.; Tanaka, S. *Ibid.* **1976**, *41*, 4081.

(9) In this paper, all structural formulas with (+) or (-) rotational specifications are illustrated in their absolute configurations.

(10) Nakazaki, M.; Naemura, K. *J. Org. Chem.* **1977**, *42*, 2985.

(11) Nakazaki, M.; Naemura, K.; Arashiba, N. *J. Org. Chem.* **1978**, *43*, 689. For other syntheses of optically active D_3 -trishomocubane, see: Helmchen, G.; Striger, G. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 116. Eaton, P. E.; Leipzig, B. *J. Org. Chem.* **1978**, *43*, 2483.

(12) Our proposal of these trivial names is motivated by the automatic appearance of twistane (8)¹³ (D_2 symmetry) and ditwistane (9)¹⁴ (C_2 symmetry) moieties through diagonal ethano bridging¹⁵ of the bicyclo[2.2.2]octane "core". Their corresponding IUPAC names are as follows: 5, pentacyclo[7.3.0.0^{2,7}.0^{3,11}.0^{6,10}]undecane; 6, pentacyclo[7.4.0.0^{2,7}.0^{3,11}.0^{6,10}]tridecane; 7, pentacyclo[8.4.0.0^{2,7}.0^{3,12}.0^{6,11}]tetradecane.

(13) Tichy, M. *Collect. Czech. Chem. Commun.* **1974**, *39*, 2673; and references cited therein.

(14) Hirao, K.; Iwakuma, T.; Taniguchi, M.; Abe, E.; Yonemitsu, O.; Date, T.; Kotera, K. *J. Chem. Soc., Chem. Commun.* **1974**, 691.

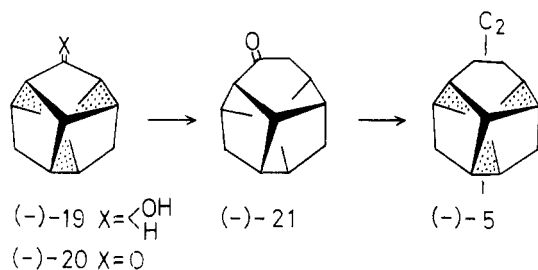
(15) Similarly, D_3 -trishomocubane may be called D_3 -tritwistbrendane, since the CH_2 diagonal bridging in the bicyclo[2.2.2]octane unit always leads to the appearance of the twist-brendane moiety.

(16) Yonemitsu¹⁶ reported the diazomethane ring expansion in the series of C_2 -bishomocubane compounds.

Table II. Diagnostic Carbonyl Absorption Bands in Pentacyclic Cage-Shaped Compounds

$\nu(\text{C}=\text{O}), \text{cm}^{-1}$ (KBr)						
18	20	21	22	23	24	25
1760	1768	1713	1750	1765	1715	1765
	1748		(1765 sh)	1713		1720

Scheme II



One of our strategies for preparing D_3 -tritwistane (7) was the double diazomethane ring expansion of the dione 18 which was prepared from the cyclohexadiene-benzoquinone adduct 10 following Barborak's approach to D_3 -trishomocubane from 11.^{6e}

Irradiation with a medium-pressure mercury lamp smoothly converted 10 into the pentacyclic dione 12 whose LiAlH_4 reduction provided the diol 13.¹⁷ The facile Wagner-Meerwein-type rearrangement observed in the diol 14,^{6e} the most elegant feature in Barborak's synthesis, failed in the higher homologue diol 13 whose heating at 120 °C in acetic acid with a small amount of concentrated sulfuric acid for 42 h afforded a 77% yield of crystals of 15, mp 182–184 °C.

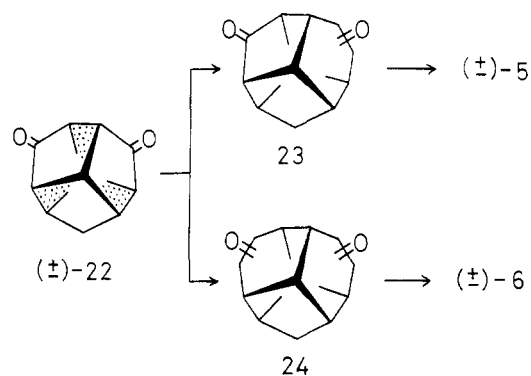
On the basis of a lack of carbonyl absorption in the IR spectrum and a broad singlet at δ 4.75 (2 H) in the ^1H NMR spectrum, we assigned the ether structure 15, which was further supported by comparison with Pachler's ^1H NMR data.¹⁸

Partial conversion to the diacetate 16 was finally achieved under more drastic conditions where the same reaction mixture was heated at 140–150 °C for 110 h. Chromatography of the product yielded, besides the ether 15 (60% yield), a 26% yield of an oil, bp 150–160 °C (5 mm).

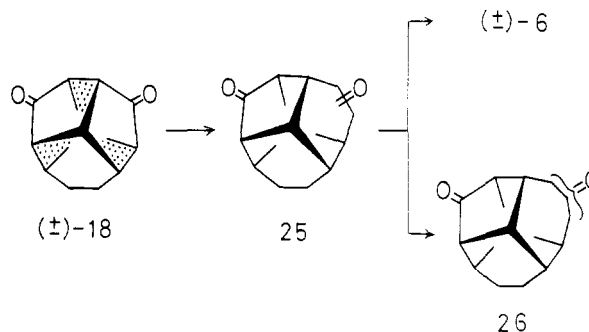
Observation of an acetyl peak (δ 2.02, 2 CH_3CO) in the ^1H NMR spectrum was sufficient for assignment of the rearranged structure 16,¹⁹ which was proved by its eventual conversion to C_2 -bismethanotwistane (5). Recycling the recovered ether 15 provided a fair yield of the diacetate 16 whose saponification followed by CrO_3 oxidation of the resulting diol 17 gave the dione 18, mp 186–188 °C, whose carbonyl absorption band observed at 1760 cm^{-1} can be compared with the 1750- cm^{-1} absorption band exhibited by D_3 -trishomocubanedione (22) (Table II).

The Wolff-Kishner reduction of the dione 18 completed the synthesis of (\pm)- C_2 -bismethanotwistane (5), mp 135 °C, the identity of which was established by the comparison with the (-) enantiomer prepared via diazomethane

Scheme III



Scheme IV



ring expansion of (-)- D_3 -trishomocubane (20) to be discussed below.

Ring Expansion of (-)- D_3 -Trishomocubane (20) and Preparation of (-)- C_2 -Bismethanotwistane (5) (Scheme II). Before carrying out double-ring expansion with diazomethane on the pentacyclic diketone 22, we first made attempts to seek the best conditions for this type of ring expansion utilizing a pentacyclic monoketone model compound, (-)- D_3 -trishomocubane (20).

Chromic acid oxidation of (-)- D_3 -trishomocubanol (19)¹¹ gave the (-)-ketone 20, mp 161–163 °C, $[\alpha]_D -49.2^\circ$, which was treated with an excess of diazomethane ether solution for 48 h at 0 °C. Workup afforded a monoketone (56% yield), mp 132–133 °C, $[\alpha]_D -120^\circ$, whose IR spectrum exhibiting a 1713- cm^{-1} carbonyl band instead of a 1750- cm^{-1} band in the starting material indicated the expanded structure 21. The Wolff-Kishner reduction of the monoketone 21 produced an 89% yield of (-)- C_2 -bismethanotwistane (5), mp 132–134 °C, $[\alpha]_D -163^\circ$, whose TLC, IR, and ^1H NMR analyses were found indistinguishable with those of (\pm)-5 secured via Scheme I.

Ring Expansion of (\pm)- D_3 -Trishomocubanedione (22) and Preparation of (\pm)- C_2 -Methanoditwistane (6) (Scheme III). Our next model of the ring expansion was a pentacyclic diketone, (\pm)- D_3 -trishomocubanedione (22). When an ether solution of the dione 22 with 2 mol of diazomethane at 0 °C was allowed to stand for 24 h, formation of dione 23,²⁰ mp 180 °C, resulted in a 40% yield. The IR spectrum exhibiting two absorption bands at 1710 and 1766 cm^{-1} with equal intensities suggested the single expansion structure 23, which was proved by its Wolff-Kishner reduction to (\pm)- C_2 -bismethanotwistane (5).

Ring expansion with a larger excess of diazomethane (14 mol, at 0 °C) gave another diketone, 24²⁰ (40% yield),

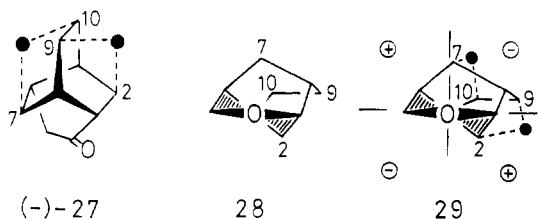
(17) Analogy to the lower homologue 14^{6a} suggests a similar stereochemistry to diol 13, with both hydroxyl groups pointing toward the inside of the cage structure.

(18) Pachler, K. G. R.; Wessels, P. L.; Dekker, J.; Dekker, J. J.; Dekker, T. G. *Tetrahedron Lett.* 1976, 3059.

(19) Although analogy to the lower homologue D_3 -trishomocubane-4,7-diol¹¹ indicates the cis stereochemistry (C_1 symmetry), of the diol 17, the trans structure with C_2 symmetry cannot be excluded because of our observation of only one singlet (δ 2.02 (CH_3CO)) exhibited by the diacetate 16.

(20) Symmetry of the starting diketone 22 demands two and three regioisomeric products for 23 and 24, respectively. Although melting points and other physical properties suggested their homogeneity, no attempt was made to ascertain the relative locations of the two carbonyl groups in 23 and 24.

Chart III



which melted at 176–177.5 °C. Replacement of the original 1750-cm⁻¹ absorption band by the 1710-cm⁻¹ band in its IR spectrum together with the *m/e* 202 M⁺ peak observed in the mass spectrum indicated the doubly expanded structure **24**, and this was found to be supported by the conversion into (±)-C₂-methanoditwistane (**6**), mp 95 °C, on Wolff–Kishner reduction.

Additional support for this novel ring system **6** was provided by its alternate preparation from C₂-bismethanotwistane-8,12-dione (**18**) (Scheme IV) as well as by the C₂-symmetrical nature revealed in the ¹³C NMR spectrum (see Experimental Section).

Ring Expansion Reaction of (±)-C₂-Bismethanotwistane-8,12-dione (18) (Scheme IV). Monitoring the process with IR spectroscopy, we were surprised to observe a much sluggish ring-expansion reaction in the diketone **18**, which required 4 days of standing at 0 °C with 14 mol of ethereal diazomethane solution to provide a 61% yield of the diketone **25**, mp 130–133 °C. The mass spectrum with *m/e* 202 M⁺ and the IR spectrum exhibiting carbonyl absorption bands at 1760 and 1710 cm⁻¹ with equal intensities (Table II) suggested the single expanded structure **25**,²¹ and this was proved by its conversion into (±)-C₂-methanoditwistane (**6**) by Wolff–Kishner reduction.

Diazomethane ring expansion to introduce a second methylene unit in the cyclopentanone moiety of the newly formed diketone **25**, thereby securing the desired D₃-tritwistane system, was unsuccessful, making a striking contrast to the observed facile double ring expansion in the diketone **22** to **24**. An oily reaction product (40% yield) obtained when **25** was allowed to stand with 35 mol of diazomethane at 0 °C for 1 week still exhibited the 1765- and 1715-cm⁻¹ carbonyl absorption bands in the IR spectrum, indicating that the cyclopentanone moiety was left intact, and the *m/e* 202 M⁺ and 216 M⁺ peaks in the mass spectrum suggested that the product was a mixture of **25** and **26**.

Table II summarizes the diagnostic carbonyl absorption bands characteristic to the cage-shaped pentacyclic ketones which are discussed in this paper.

Chiroptical Properties of (-)-C₂-Bismethanotwistan-4-one (21) and the Absolute Rotations of the Related Cage-Shaped Hydrocarbons. The known absolute configuration¹¹ of its precursor, (-)-D₃-trishomocubane (**20**), correlates the resulting (-)-C₂-bismethanotwistan-4-one (**21**) with (-)-twistan-4-one (**27**)¹³ which can be converted into the former by 2,9 and 7,10 diagonal bridging (shown in broken lines) with methylene units. Comparing the respective octant projections **28**²² and **29** of (-)-twistan-4-one and (-)-C₂-bismethanotwistan-4-one, one notices the two extra bridging methylenes located in (+)- and (-)-octant regions supposedly canceling their effects on the circular dichroism spectrum. The (-) Cotton curves of **28** and **29** exhibiting troughs at 285 nm ([θ]_{abs} 1.52 × 10³ deg cm²/dmol) and 280 nm ([θ]_{abs} 1.04

Table III. Absolute Rotations of (-)-C₂-Bismethanotwistane (**5**) and the Related Cage-Shaped Hydrocarbons (in Chloroform)

(-)-3	(-)-4	(-)-30	(-)-5
[α] _D -44°	[α] _D -165°	[α] _D -233°	[α] _D -293°

× 10³ deg cm²/dmol),²³ respectively confirm this prediction.

Calculation based on the reported absolute rotation,¹¹ [α]_D -88.5°, of (-)-D₃-trishomocubane (**20**) and the direct synthetic route from **20** to **5** (Scheme II) assign absolute rotation [α]_D -293° to (-)-C₂-bismethanotwistane (**5**).

Table III lists this absolute rotation value with those of the related cage-shaped hydrocarbons (-)-C₂-bishomocubane (**3**),^{10,24} (-)-D₃-trishomocubane (**4**),¹¹ and (-)-ditwistbrendane (**30**).^{11,24} The extrapolation of these values for **3** → **4** → **5** seems to furnish an interesting prediction that D₃-tritwistane (**7**) with the same twisted bicyclo-[2.2.2]octane “core” should be levorotatory with an absolute rotation as high as [α]_D -500°.

Experimental Section

Infrared spectra were taken with a Hitachi EPI-S2 spectrophotometer. ¹H NMR spectra were recorded on a JNM-C-60 HL, and the ¹³C NMR spectrum was recorded on a JNM FX-100. Optical rotations were measured with a JASCO-DIP-SL automatic polarimeter. Circular dichroism data were collected with a JASCO J-40 spectropolarimeter. Mass spectra were taken with a Hitachi RMS-4 spectrometer. Elemental analyses were determined on a Yanagimoto CHN-Corder, Type II. All melting and boiling points are uncorrected.

Pentacyclo[6.2.2.0^{2,7}.0^{4,10}.0^{5,9}]dodecane-3,6-dione (12). A solution of the *p*-benzoquinone and 1,3-cyclohexadiene Diels–Alder adduct **10**²⁵ (5.00 g, 5.31 mmol) in ethyl acetate (250 mL) was irradiated for 8 h with a mercury lamp (SLH-100 UV, Toshiba). Most of the solvent was evaporated in vacuo and the residue was placed in a refrigerator. A deposit was collected and recrystallized from the same solvent to give 2.80 g of **12** (56% yield); mp 253 °C (lit.²⁶ mp 256 °C). Anal. Calcd for C₁₂H₁₂O₂: C, 76.57; H, 6.43. Found: C, 76.52; H, 6.35.

Pentacyclo[6.2.2.0^{2,7}.0^{4,10}.0^{5,9}]dodecane-3,6-diol (13). A solution of **12** (11.2 g, 0.0595 mol) in dry THF (400 mL) was added to a suspension of LiAlH₄ (6.0 g, 0.158 mol) in dry THF (100 mL), and the mixture was refluxed for 10 h. Diluted sulfuric acid was carefully added to the reaction mixture with ice cooling, and an inorganic solid was filtered off. The filtrate was dried (MgSO₄) and evaporation of the solvent gave a white solid, which was recrystallized from ethyl acetate to afford 6.88 g of **13** (60% yield); mp 168–170 °C; IR (KBr) 3180, 1500, 1270, 1150, 1120, 1090, 1060, 820 cm⁻¹.

Anal. Calcd for C₁₂H₁₆O₂: C, 74.96; H, 8.39. Found: C, 74.78; H, 8.29.

Rearrangement of Pentacyclo[6.2.2.0^{2,7}.0^{4,10}.0^{5,9}]dodecane-3,6-diol (13). A solution of **13** (1.35 g, 7.11 mol) in glacial acetic acid (11.5 mL) containing concentrated sulfuric acid (0.12 g) was heated at 120 °C under reflux for 42 h. The reaction mixture was allowed to cool, then treated with 0.6 g of anhydrous sodium acetate and subsequently with activated charcoal, and filtered, and most of the solvent was evaporated in vacuo. The residue was diluted with water and extracted with ether. The

(23) The [θ] value is corrected to 100% optical purity according to its known optical purity.

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(21) No attempt was made to know the relative position of two carbonyl groups in **25** and **26**.

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extract was washed with saturated NaHCO_3 solution and water, dried (MgSO_4), and concentrated. The residue was chromatographed on neutral alumina (Woelm activity III), and elution with *n*-pentane gave 0.95 g of **15** (77% yield) as a white solid which was sublimed at 60 °C (5 mm): mp 182–184 °C (in a sealed tube); IR (KBr) 1335, 1305, 1255, 1035, 965, 915, 860 cm^{-1} ; NMR (CDCl_3) δ 1.48–1.55 (m, 4 H), 1.71 (m, half-bandwidth 9.0 Hz, 2 H), 2.2 (m, half-bandwidth 7.5 Hz, 2 H), 2.4 (m, half-bandwidth 9.0 Hz, 2 H), 2.7 (m, half-bandwidth 9.0 Hz, 2 H), 4.75 (m, half-bandwidth 6.0 Hz, 2 H).

Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}$: C, 82.72; H, 8.10. Found: C, 82.54; H, 8.01.

B. A mixture of **13** (5.18 g, 0.0269 mol), glacial acetic acid (45 mL), and concentrated sulfuric acid (0.46 g) was heated at 140–150 °C for 110 h in a sealed tube. After cooling, the reaction mixture was worked up in the same manner described above and the crude product was chromatographed on silica gel. Elution with *n*-pentane–ether (9:1 (v/v)) gave 2.80 g of **15** (60% yield) as a white solid, mp 182 °C (in a sealed tube), and subsequent elution with ether afforded an oily product which was distilled to give 1.96 g of **16** (26% yield): bp 155–160 °C (5 mm); IR (film) 1730, 1362, 1240, 1045 cm^{-1} ; NMR (CDCl_3) δ 1.52 (bs, half-bandwidth 6.0 Hz, 6 H), 2.02 (s, 6 H), 2.0–2.7 (m, 6 H), 4.75 (m, half-bandwidth 7.5 Hz, 2 H).

Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{O}_4$: C, 69.54; H, 7.30. Found: C, 69.36; H, 7.21.

Rearrangement of 15 to C_2 -Bismethanotwist-8,12-diyl Diacetate (16). A mixture of **15** (4.45 g, 0.0256 mol), glacial acetic acid (41 mL), and concentrated sulfuric acid (0.4 g) was heated at 140–150 °C for 140 h in a sealed tube. After the same workup described above, the crude product was chromatographed on silica gel. Elution with *n*-pentane–ether (9:1 (v/v)) recovered 2.90 g of **15** (65%), and elution with ether afforded 1.73 g of **16** (24% yield); bp 155–160 °C (5 mm).

C_2 -Bismethanotwistane-8,12-dione (18). A mixture of **16** (1.60 g, 5.79 mmol), KOH (2.6 g), and 50% aqueous methanol (8 mL) was refluxed for 3 h. After removal of most of the methanol in vacuo, the residue was diluted with water and extracted with CHCl_3 . The extract was washed with water, dried (MgSO_4), and concentrated to give 0.91 g of the crude diol **17**. The diol **17** (0.91 g, 4.74 mmol) was dissolved in acetone (6 mL), and an excess of Jones' reagent²⁷ was added to the solution at 0 °C. After 3 h of stirring at room temperature, the mixture was diluted with water and extracted with CHCl_3 . The extract was washed with saturated NaHCO_3 solution and water, dried (MgSO_4), and concentrated. The residue was chromatographed on neutral alumina (Woelm activity III), and elution with ether gave a solid which was recrystallized from hexane–ether to yield 0.83 g of **18** (76% yield based on **16**): mp 186–188 °C; IR (KBr) 1760, 1270, 1205, 1150, 1140, 1060, 835 cm^{-1} ; NMR (CDCl_3) δ 1.55–1.90 (m, 4 H), 2.0–2.7 (m, 8 H).

Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{O}_2$: C, 76.57; H, 6.43. Found: C, 76.67; H, 6.42.

(-)- D_3 -Trishomocubanone (20). Following the same procedure reported for preparing the (+) enantiomer,¹¹ (-)- D_3 -trishomocubyl hydrogen phthalate was converted into (-)- D_3 -trishomocubanone (**20**) via (-)- D_3 -trishomocubanol (**19**): mp 161–163 °C; $[\alpha]_D^{30}$ -49.2° (c 0.654, EtOH) (optical purity 55.6%).¹¹

Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{O}$: C, 82.46; H, 7.55. Found: C, 82.26; H, 7.50.

(-)- C_2 -Bismethanotwistane-4-one (21). To a suspension of (-)-**20** (1.25 g, 7.81 mmol), $[\alpha]_D^{30}$ -49.2°, in ether (50 mL) was added an ethereal solution of diazomethane prepared from *p*-toluenesulfonylmethyl nitrosamide (21.4 g, 0.100 mol) according to the procedure described by de Boer et al.,²⁸ and the mixture was allowed to stand for 48 h at 0 °C. After decomposition of excess diazomethane by adding glacial acetic acid, the reaction mixture was washed with saturated NaHCO_3 solution and water, dried (MgSO_4), and concentrated. The residue was chromatographed on silica gel, and elution with *n*-pentane–ether (9:1 (v/v)) gave a white solid which was sublimed at 110–120 °C (5 mm) to

give 755 mg of **21** (56% yield): mp 132–133 °C (in a sealed tube); $[\alpha]_D^{27}$ -120° (c 0.768, EtOH); CD (c 2.45×10^{-2} , isooctane) $[\theta]$ (nm) -586 (280), -586 (286), -254 sh deg cm^2/dmol (298); IR (KBr) 1713, 1460, 1400, 1350, 1305, 1270, 1232, 1222, 1180, 1165, 1085, 1050 cm^{-1} ; NMR (CDCl_3) δ 1.2–1.6 (m, 4 H), 1.7–2.2 (m, 4 H), 2.2–2.4 (m, 6 H); mass spectrum m/e 174 (M^+).

Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}$: C, 82.72; H, 8.10. Found: C, 82.46; H, 8.21.

(-)- C_2 -Bismethanotwistane (5). A mixture of (-)-**21** (320 mg, 1.84 mmol), $[\alpha]_D^{27}$ -120°, KOH (0.38 g), 80% hydrazine hydrate (0.53 g), and triethylene glycol (2 mL) was treated by a similar procedure to that described for the preparation of (\pm)-**5**. A solid obtained was sublimed at 70–80 °C (20 mm) to give 260 mg of (-)-**5** (89% yield): mp 132–134 °C (in a sealed tube); $[\alpha]_D^{28}$ -163° (c 0.725, CHCl_3); mass spectrum m/e 160 (M^+).

Anal. Calcd for $\text{C}_{12}\text{H}_{16}$: C, 89.94; H, 10.06. Found: C, 89.95; H, 9.95.

Ring Expansion of D_3 -Trishomocubanone (22) with Diazomethane. A. A mixture of **22** (530 mg, 3.05 mmol), prepared according to Barborak's method,^{6c} and an ethereal solution of CH_2N_2 prepared from *p*-toluenesulfonylmethyl nitrosamide (14.5 g, 67.8 mmol)²⁸ was kept for 48 h at 0 °C and then worked up as described for the preparation of (-)-**21**. A crude product was chromatographed on silica gel, and elution with hexane–ether (1:3 (v/v)) gave a solid which was recrystallized from hexane–ether to afford 245 mg of **24** (40% yield). A part of this was further purified by sublimation at 120–130 °C (5 mm): mp 176–177.5 °C (in a sealed tube); IR (KBr) 1715, 1405, 1350, 1270, 1230 cm^{-1} ; mass spectrum m/e 202 (M^+).

Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$: C, 77.20; H, 6.98. Found: C, 77.05; H, 7.02.

B. A mixture of **22** (3.00 g, 17.2 mmol) and an ethereal solution of CH_2N_2 prepared from *p*-toluenesulfonylmethyl nitrosamide (11.0 g, 51.4 mmol) was allowed to stand for 24 h at 0 °C and then worked up as above. Chromatography afforded a solid which was recrystallized twice from hexane–ether to give 1.29 g of **23** (40% yield). Further purification through sublimation at 130 °C (5 mm) afforded the sample for elemental analysis: mp 180 °C (in a sealed tube); IR (KBr) 1765, 1713, 1400, 1350, 1275, 1235, 1150, 1075 cm^{-1} ; mass spectrum m/e 188 (M^+).

Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{O}_2$: C, 76.57; H, 6.43. Found: C, 76.35; H, 6.61.

Ring Expansion of C_2 -Bismethanotwistane-8,12-dione (18) with Diazomethane. A solution of **18** (440 mg, 2.34 mmol) in ether containing CH_2N_2 prepared from *p*-toluenesulfonylmethyl nitrosamide (12.5 g, 58.5 mmol) was allowed to stand for 4 days at 0 °C and worked up as above. The crude product was chromatographed to yield a solid which was recrystallized twice from hexane–ether to give 290 mg of **25** (61% yield). A part of this was sublimed at 130–140 °C (7 mm) to provide the sample for elemental analysis: mp 130–133 °C (in a sealed tube); IR (KBr) 1765, 1720, 1150, 1035 cm^{-1} ; mass spectrum m/e 202 (M^+).

Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$: C, 77.20; H, 6.98. Found: C, 77.42; H, 7.17.

Ring Expansion of 25 with Diazomethane. A mixture of **25** (100 mg, 0.495 mmol) and an ethereal solution of CH_2N_2 prepared from *p*-toluenesulfonylmethyl nitrosamide (5.35 g, 25.0 mmol) was kept for 7 days in a refrigerator (0 °C) and worked up as above. The crude product was chromatographed on silica gel and elution with hexane–ether (1:1 (v/v)) gave 40 mg of a mixture of **25** and **26** as an oil: IR (film) 1765, 1715, 1700 (sh) cm^{-1} ; mass spectrum m/e (relative heights) 202 (13) (M^+), 216 (10) (M^+).

C_2 -Bismethanotwistane (5). From 18. A mixture of **18** (150 mg, 0.798 mmol), KOH (180 mg), 80% hydrazine hydrate (0.34 g), and triethylene glycol (4.2 mL) was heated in an oil bath. During 2 h, the bath temperature was gradually raised to 200 °C and this temperature was kept for an additional 3 h. A white solid was observed to condense on the inner wall of the condenser during this time. After cooling, the solid was dissolved in ether. The ethereal solution was washed with water, dried (MgSO_4), and concentrated to afford a solid which was sublimed at 40 °C (5 mm) to yield 30 mg of **5** (24% yield): mp 135 °C (in a sealed tube); IR (KBr) 1465, 1445, 1315, 1290, 1272, 1170, 965, 945, 830, 765, 750 cm^{-1} ; mass spectrum m/e 160 (M^+).

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(28) de Boer, Th. J.; Backer, H. J. "Organic Syntheses", Collect Vol. IV; Wiley: New York, N.Y., 1963; p 250.

Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 89.96; H, 10.10.

From 23. A mixture of **23** (1.20 g, 5.94 mmol), KOH (2.86 g), 80% hydrazine hydrate (4.00 g), and triethylene glycol (13 mL) was treated in a manner similar to that above. A white solid was purified by sublimation at 60–70 °C (15 mm) to afford 500 mg of **5** (53% yield); mp 132–133 °C (in a sealed tube).

Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 89.82; H, 9.95.

C_2 -Methanotwistane (6). **From 24.** A mixture of **24** (350 mg, 1.73 mmol), KOH (0.84 g), 80% hydrazine hydrate (1.20 g), and triethylene glycol (4 mL) was heated for 1.5 h at 110 °C and then for an additional 2 h at 190–200 °C. During this period a white solid was observed to condense on the inner wall of the condenser. After cooling, this was dissolved in *n*-pentane and the pentane solution was washed with water, dried ($MgSO_4$), and concentrated. Purification through sublimation at 80–90 °C (5 mm) gave 240 mg of **6** (79% yield); mp 95 °C (in a sealed tube); IR (KBr) 1460, 1445, 1325, 1292, 1280, 1170, 960, 920, 810 cm^{-1} ;

^{13}C NMR ($CDCl_3$) δ 19.7, 23.2, 30.7, 37.0, 38.2, 39.4, 41.3; mass spectrum m/e 174 (M^+).

Anal. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41. Found: C, 89.80; H, 10.25.

From 25. A mixture of **25** (150 mg, 0.743 mmol), KOH (0.36 g), 80% hydrazine hydrate (0.51 g), and triethylene glycol (2 mL) was treated by the same manner as above. Sublimation of the product afforded 84 mg of **6** (65% yield); mp 94–96 °C (in a sealed tube).

Anal. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41. Found: C, 89.74; H, 10.30.

Registry No. (–)-**3**, 62928-75-0; (–)-**4**, 61473-77-6; (–)-**5**, 70209-47-1; (±)-**5**, 70267-03-7; (±)-**6**, 70224-69-0; **10**, 69685-89-8; **12**, 712-25-4; **13**, 62111-05-1; **15**, 60749-69-1; **16**, 70209-48-2; **17**, 70209-49-3; (±)-**18**, 70209-50-6; (–)-**19**, 61393-99-5; (–)-**20**, 61473-76-5; (–)-**21**, 70209-51-7; (±)-**22**, 70209-52-8; (±)-**23**, 70224-75-8; (±)-**24**, 70224-76-9; (±)-**25**, 70224-77-0; (±)-**26**, 70209-53-9; (–)-**30**, 64727-80-6; (–)- D_3 -trishomocubyl hydrogen phthalate, 64727-85-1; diazomethane, 334-88-3.

Synthesis of the First Optically Active Anti-Bredt-Rule Compound with Known Absolute Configuration. (–)-(*S*)-Bicyclo[3.3.1]-1(2)-nonene

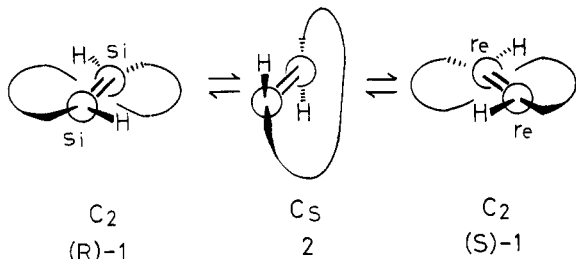
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As the first member of optically active anti-Bredt-rule compounds, (–)-(*S*)-bicyclo[3.3.1]-1(2)-nonene (**7**) was prepared from (–)-(*1R,3S*)-*cis*-3-hydroxycyclohexanecarboxylic acid (**8**).

The gyrochiral¹ conformation (*R*)-**1** of a *trans*-cyclo-



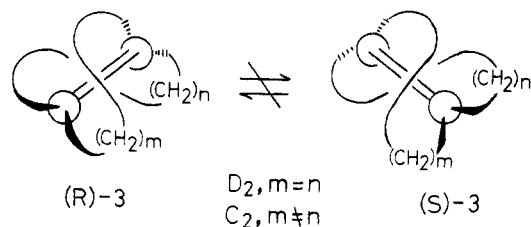
alkene with C_2 symmetry can be converted into its enantiomeric (*S*)-**1** conformation via schematically achiral planar C_2 conformation **2**. Equilibration with the opposite process results in racemization whose rate is to be determined by the height of the energy barrier which the molecule should experience in passing through the planar transition conformation **2**.

Shortening the *trans* bridge should increase the non-bonding interaction in the transition state resulting in "frozen" enantiomeric conformers which can be isolated separately, and this has been unambiguously demonstrated in Cope's classic optical resolution of *trans*-cyclooctene **6**.² Accompanying the (*R*)-**1** \rightleftharpoons (*S*)-**1** conformational transformation, simultaneous inversion of planar chirality of the double bond faces takes place as can be seen from the chirality specification change *si-si* \rightleftharpoons *re-re* for their respective outside faces.

Replacing the pair of homotopic hydrogen atoms in C_2 *trans*-cycloalkene by an extra *trans* bridge leads to for-

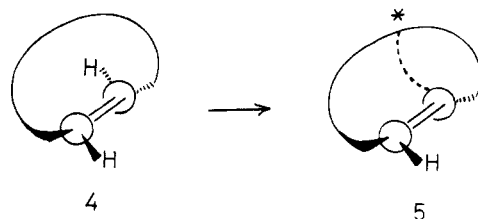
mation of the *trans* doubly bridged ethylene **3**, preparation of whose series of homologues ($m = n = 8$; $m = 8, n = 10$; $m = n = 10$) has been reported recently from our and Marshall's laboratories.³

In these *trans* doubly bridged ethylenes, the type of conformational chirality inversion observed in (*R*)-**1** \rightleftharpoons (*S*)-**1** cannot be realized; (*R*)-**3** \rightleftharpoons (*S*)-**3** inversion, being



essentially configurational rather than conformational, should only be achieved by a bond cleavage–recombination process between two *trans* bridges.

Another obvious and direct way to prevent (*R*)-**1** \rightleftharpoons (*S*)-**1** conformational inversion is provided by spanning a bridge (showed by the broken line in **5**) between the olefinic



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