# Resolution of Trishomocubanone: The Enantiomeric ($D_3$)-Trishomocubanes

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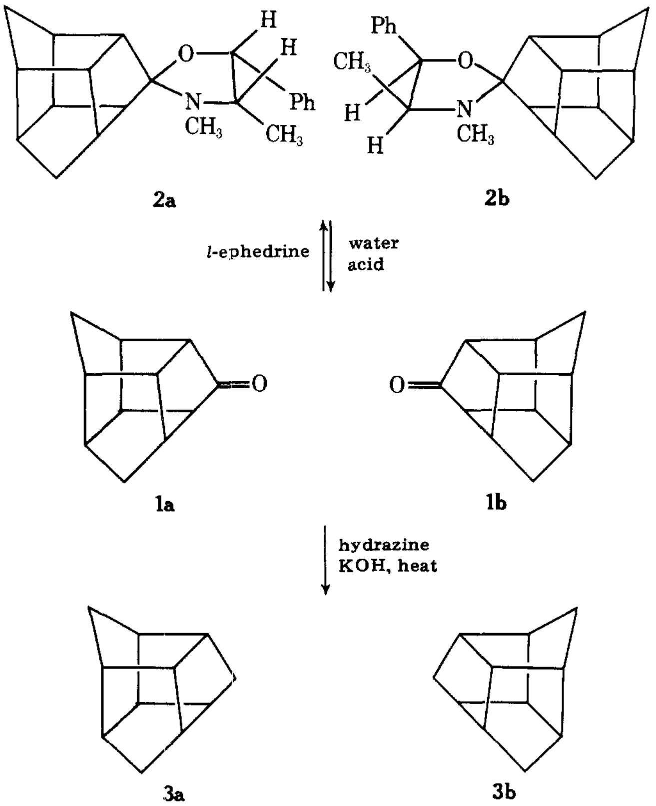
The resolution of trishomocubanone and the preparation of the enantiomeric ($D_3$)-trishomocubanes (pentacyclo[6.3.0.0$^{2,6}$.0$^{3,10}$.0$^{5,9}$]undecane) are reported. Absolute configurations are assigned.

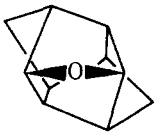
($D_3$)-Trishomocubane is a saturated pentacyclic cage compound containing neither cyclobutane nor cyclopropane rings.[1] It is very probably the most stable member of the saturated set of compounds of formula $C_{11}H_{14}$.[2] The carbon skeleton is made up of fused five-membered rings and is intrinsically chiral. Its $D_3$ point group symmetry is exceedingly rare in organic compounds.[3] In complement to our initial synthesis of this system,[1c] we report now preparation of the enantiomeric ($D_3$)-trishomocubanes and assignment of absolute configuration. Our results agree nicely with those reached by other methods and published during the course of our work.[4]

Racemic trishomocubanone (**1a,b**) is readily available by simple chemical transformations of the Diels–Alder adduct of cyclopentadiene to *p*-benzoquinone, as we have reported elsewhere.[1c] Reaction of the racemic ketone with *l*-ephedrine, available commercially, gives the mixture of isomers **2a,b** from which the individual diastereomers can be separated easily by fractional crystallization from methanol. The separation is monitored conveniently by $^1$H NMR. The benzylic proton resonances of the isomers are cleanly resolved at 270 MHz: that of isomer mp 104–105 °C is at $\delta$ 5.08 ppm (d, $J$ = 7 Hz); that of isomer mp 88–89 °C is at $\delta$ 5.20 ppm (d, $J$ = 7 Hz). Other interesting differences in the $^1$H NMR spectra of the diastereomers can be noted from the data in the Experimental Section.

Acid hydrolysis of the separated diastereomers **2a** and **2b** gives the enantiomeric ketones: **1a**, (−)-trishomocubanone, mp 162–163 °C, $[\alpha]^{20}_{\mathrm{D}}$ −98.8° (cyclohexane) from the higher melting diastereomer; and **1b**, (+)-trishomocubanone, mp 162–163 °C, $[\alpha]^{20}_{\mathrm{D}}$ +98.8° from the lower melting diastereomer.



As has been shown,[5] the absolute configuration of polycyclic ketones can be derived from the sign of the CD curve for their n–π* absorption by proper application of the octant rule. In the case at hand, examination of the "outer ring"[6] in a projection of **1a** in which the carbonyl group is held at the "point of twist"[7] leads to prediction of a positive Cotton effect for this enantiomer. As it turns out, negatively rotating trishomocubanone exhibits a positive CD absorption at 293 nm, $[\theta]$ +6.58 × 10$^3$, and is thus assigned absolute configuration **1a**, (3*S*)-trishomocubanone.[4]



**1a**

Wolff–Kishner reduction of the enantiomeric trishomocubanones using standard Huang–Minlon conditions gives the corresponding hydrocarbons in excellent yield. Negatively rotating ketone **1a** gives (−)-($D_3$)-trishomocubane (**3a**): mp 148–149 °C; $[\alpha]^{20}_{\mathrm{D}}$ −162° (cyclohexane). Positively rotating ketone gives (+)-($D_3$)-trishomocubane (**3b**): mp 148–149 °C; $[\alpha]^{20}_{\mathrm{D}}$ +162°. Thus, (−)-($D_3$)-trishomocubane is of absolute *S* configuration at position 3; the configuration at each of the other chiral centers follows by symmetry. Correspondingly, (+)-($D_3$)-trishomocubane is 3*R*.

## Experimental Section

$^1$H NMR spectra were recorded at 270 MHz of solutions in $CDCl_3$ and are referenced to internal tetramethylsilane. Melting points are not corrected. Optical rotations were taken for solutions in cyclohexane in a thermostated 1-dm cell using a Perkin-Elmer Model 141 digital polarimeter. Circular dichroism measurements were performed using a Cary Model 60 spectropolarimeter.

**Preparation and Separation of 2a and 2b.** Racemic trishomocubanone[1c] (pentacyclo[6.3.0.0$^{2,6}$.0$^{3,10}$.0$^{5,9}$]undecan-4-one, 430 mg) and *l*-ephedrine (Aldrich Chemical Co., 460 mg) were heated together for 72 h in benzene (25 mL) refluxing beneath a Dean–Stark trap. The solvent was then removed under vacuum on a rotary evaporator leaving a clear oil (810 mg) which was taken up in methanol. The diastereomers were obtained separate and pure by fractional crystallization. Two crops of the higher melting isomer **2a** (260 mg, 63%) were taken: clear cubes; mp 104–105 °C; $^1$H NMR $\delta$ 7.3–7.1 (5 H), 5.08 (1 H, d, $J$ = 7 Hz), 3.58 (1 H, p, $J$ = 7 Hz), 2.62 (1 H, m), 2.53 (3 H, s), 2.50 (1 H, m), 2.34 (1 H, sym m), 2.3–2.1 (4 H, m), 2.0 (1 H, m), 1.48 (2 H, d, $J \sim$ 10 Hz), 1.36 and 1.32 (1 H each, overlapping d, $J \sim$ 10 Hz), 0.84 ppm (3 H, d, $J$ = 7 Hz). Further concentration of the mother liquor gave isomer **2b** (200 mg, 49%): white needles; mp 88–89 °C; $^1$H NMR $\delta$ 7.3–7.1 (5 H), 5.20 (1 H, d, $J$ = 7 Hz), 3.64 (1 H, p, $J$ = 7 Hz), 2.83 (1 H, m), 2.58 (3 H, s), 2.47 (1 H, m), 2.2–2.0 (6 H, m), 1.53 and 1.49 (1 H each, overlapping d, $J \sim$ 9 Hz), 1.40 and 1.36 (1 H each, overlapping d, $J \sim$ 9 Hz), 0.93 ppm (3 H, d, $J$ = 7 Hz).

**(−)- and (+)-Trishomocubanone.** The high-melting diastereomer **2a** (230 mg) was dissolved in a mixture of benzene (5 mL), water (0.5 mL), and methanesulfonic acid (3 drops). The mixture was refluxed overnight. Water was added; the aqueous phase was separated and extracted three times with chloroform. The extract was combined with the original organic phase and concentrated in vacuo. The solid residue was sublimed (40 °C (0.5 Torr)) to give (−)-trishomocubanone, **1a** (98 mg, 81%), of good purity: mp 162–163 °C; $\alpha^{20}{}_D$ −1.211 ± 0.002°; $[\alpha]^{20}{}_D$ −98.8°; CD (*c* 0.0355, cyclohexane) $[\theta]$ 0 (340), +6.58 × $10^3$ (293), 0 (240 nm); lit.[4] mp 159 °C, $[\alpha]^{20}{}_D$ −99.1°.

A similar procedure produced the enantiomeric ketone **1b**: mp 162–163 °C; $\alpha^{20}{}_D$ +0.355 ± 0.002°; $[\alpha]^{20}{}_D$ +98.8°; CD (C 0.0298, cyclohexane) $[\theta]$ 0 (330), −6.48 × $10^3$ (293), 0 (240 nm).

**(−)- and (+)-($D_3$)-Trishomocubane.** A mixture of resolved ketone **1a** (60 mg), hydrazine hydrate (85%, 1 mL), and triethylene glycol (2.5 mL) was refluxed for 10 min and then cooled. Potassium hydroxide pellets (200 mg) were added, and the mixture was heated vigorously. The clear distillate was collected until the pot residue charred. The distillate was extracted thoroughly with pentane. The extract was washed with dilute hydrochloric acid, followed by water, and then dried. The solvent was blown off in a slow stream of nitrogen. The white residue was sublimed (25 °C (80 Torr)) to give (−)-($D_3$)-trishomocubane (**3a**, 48 mg, 88%): mp 148–149 °C; $\alpha^{20}{}_D$ −0.694 ± 0.002°; $[\alpha]^{20}{}_D$ −162°; lit.[4] mp 149 °C, $[\alpha]^{20}{}_D$ −164°.

Similarly, (+)-($D_3$)-trishomocubane (**3b**) was obtained: mp 148–149 °C; $\alpha^{20}{}_D$ +0.571 ± 0.002°; $[\alpha]^{20}{}_D$ +162°.

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**Registry No.**—**1a**, 61473-76-5; **1b**, 61473-82-3; **2a**, 65957-38-2; **2b**, 66007-13-4; **3a**, 61473-77-6; **3b**, 61473-83-4; (±)-trishomocubanone, 66007-14-5; *l*-ephedrine, 299-42-3.

## References and Notes

(1) (a) G. R. Underwood and B. Ramamoorthy, *Tetrahedron Lett.*, 4125 (1970); (b) S. A. Godleski, P. v. R. Schleyer, E. Osawa, and G. J. Kent, *Chem. Commun.*, 976 (1974); (c) P. E. Eaton, R. A. Hudson, and C. Giordano, *ibid.*, 978 (1974).

(2) G. J. Kent, S. A. Godleski, E. Ōsawa, and P. v. R. Schleyer, *J. Org. Chem.*, **42**, 3852 (1977).

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(4) G. Helmchen and G. Staiger, *Angew. Chem., Int. Ed. Engl.*, **16**, 116 (1977); M. Nakazaki, K. Naemura, and N. Arashiba, *J. Org. Chem.*, **43**, 689 (1978). Note that the latter has a misprint in the text which reverses the assignment given in the Experimental Section and in Table I.

(5) For example, M. Nakazaki, K. Naemura, and Y. Kondo, *J. Org. Chem.*, **41**, 1229 (1976); M. Nakazaki, K. Naemura, and H. Kadowaki, *ibid.*, **41**, 3725 (1976).

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# Cyclophanes. 9. Dibenzo[*def,pqr*]tetraphenylene: A Benzoannulated Cyclooctatetraene Composed of Orthogonal Aromatic Systems[1]

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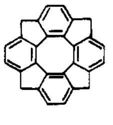
2,17-Dithia[3.3](3,3′)biphenylophane (**10**) was prepared from the coupling of 3,3′-bis(bromomethyl)biphenyl and 3,3′-bis(mercaptomethyl)biphenyl. Bridge contraction to generate the bis(methylthio) ether **14** and subsequent oxidation gave the disulfoxide **15** which undergoes thermal elimination of methylsulfenic acid to yield [2.2](3,3′)-biphenylophane-1,15-diene (**9**). Oxidative photocyclization of the diene **9** gave dibenzo[*def,pqr*]tetraphenylene (**13**), an analogue of [8]circulene. Raney nickel desulfurization of the disulfoxide **15** or thermal elimination of sulfur dioxide from the disulfone **12** produced the [2.2](3,3′)biphenylophane (**16**), which has a preferred anti geometry which is in contrast to the syn geometry of the corresponding diene **9**.

Recent investigations of the class of compounds known as circulenes[2] have provided information on the chemical and physical properties of fused aromatic macrocycles incorporating benzene, furan, and thiophen systems. Coronene or [6]circulene,[3] a tetraoxo[8]circulene,[4] a tetramethano-*o*-tetraphenylene **1**,[5] and several thia[7]circulenes[6] have provided the basis for these investigations. There is considerable interest in the fully carbocyclic aromatic molecules which are expected to be considerably more distorted from planarity than the abovementioned examples. Compounds in this category include corannulene or [5]circulene (**2**),[7] which has been shown by x-ray structure determination[8] to be bowl shaped, and the unreported higher homologs, [7]circulene (**3**) and [8]circulene (**4**). Unsuccessful attempts to synthesize these latter two compounds by the oxidative photochemical cyclization of the cyclophane dienes **5** and **6** have been recorded by ourselves[1] and others.[9] Unlike the bowl-shaped [5]circulene, [7]- and [8]circulene are expected, on the basis of molecular models, to have saddle-shaped geometries similar to that predicted for the hexa[7]circulene (**7**), which has been prepared from the corresponding cyclophane diene **8**.[10]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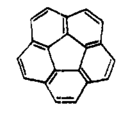
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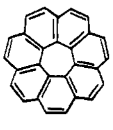
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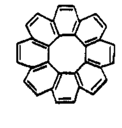
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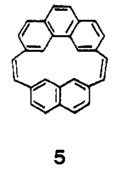
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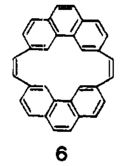
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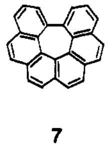
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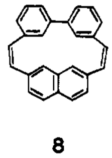
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We wish to report the synthesis of [2.2](3,3′)biphenylophane-1,15-diene (**9**) from its corresponding dithiacyclophane **10** and the successful photochemical cyclization to give dibenzo[*def,pqr*]tetraphenylene (**13**), which may be regarded as a cyclooctatetraene composed of two orthogonal phenanthrylene moieties. Thulin and Wennerstrom[11] have recently reported the synthesis of the title compound **13** by an alternative, shorter, albeit lower yielding route.

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