

Synthesis of (+)-1,3,5,7-Tetrakis[2-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-*D*₃-trishomocubanylbuta-1,3-diynyl]adamantane. An Optically Active Organic Molecule with *T* Symmetry and of Known Absolute Configuration

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Coupling of 1,3,5,7-tetraethynyladamantane (**12**) with (+)-1-bromo-2-[2-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-*D*₃-trishomocubanyl]ethyne (**21**) provided the title compound (**2**) of known absolute configuration whose highest attainable static and time-averaged dynamic symmetry are *T* and (*C*₃)⁴ \wedge *T*, respectively.

The alleged dynamic *T* symmetry¹ of (–)-1,3,5,7-tetrakis[2-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-*D*₃-trishomocubanylacetoxyethyl]adamantane (**1**) whose synthesis was reported from our laboratory, has been disclaimed by Mislow² owing to the asymmetry introduced by CH₂OCOCH₂ groups connecting the *T_d*-adamantane core and the surrounding *C*₃-trishomocubane frameworks.

In this communication, we report the synthesis of (+)-(**2**) which has cylindrically symmetric C≡C–C≡C groups between the central *T_d*-adamantane core and the *C*₃-trishomocubane components.

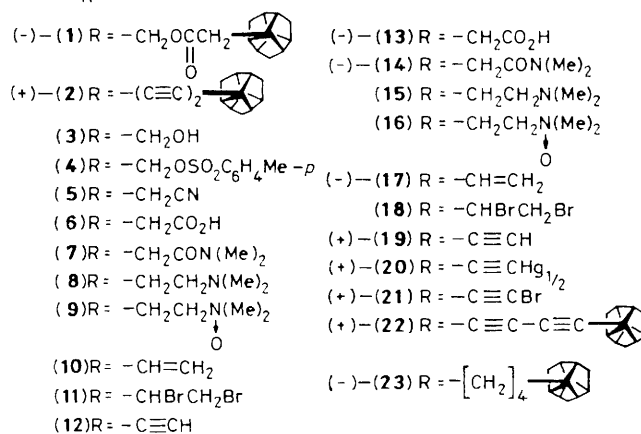
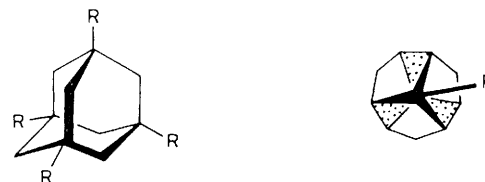
Our synthetic strategy involved the coupling of two acetylene derivatives (**12**) and (+)-(**21**), both of which were prepared *via* a parallel sequence of conversions from (**3**) and (–)-(**13**), respectively.

(–)-2-*D*₃-Trishomocubaneacetic acid (**13**) [α]_D²⁵ –68.2° (EtOH) (96% optical purity) whose 1*S*,3*S*,5*R*,6*S*,8*R*,10*R*-configuration and absolute rotation have been reported,¹ was converted into the (–)-dimethylamide (**14**),[†] b.p. 127–130 °C (0.4 mm), [α]_D²⁵ –58.8° (EtOH) which afforded the amine (**15**) on LiAlH₄ reduction. Cope elimination of the *N*-oxide (**16**) prepared from (**15**) provided the (–)-tetraethynyl derivative (**17**), m.p. 53–54 °C (in a sealed tube), [α]_D²⁷ –81.3° (EtOH) [75% yield from the amide (**14**)]. Compound (**17**) was converted into the ethyne (**19**), b.p. 110–115 °C (30 mm), [α]_D²⁵ +29.2° (EtOH)[‡] [36% yield from (**17**)] by dehydrobromination of the crude dibromide (**18**) with KOH in triethylene glycol. Finally, Eglinton's procedure³ transformed the ethyne (**19**) into the unstable (+)-bromide (**21**), [α]_D²² +19.6° (MeOH) *via* the (+)-mercuric derivative (**20**), m.p. 163–165 °C, [α]_D²⁰ +27.9° (CHCl₃).

Preparation of the *T_d*-component (**12**), 1,3,5,7-tetraethynyladamantane, began with the hydroxymethyl derivative (**3**)⁴ whose conversion into the acid (**6**), m.p. >300 °C was achieved *via* the toluene-*p*-sulphonate (**4**), m.p. 143–145 °C and the nitrile (**5**), m.p. 266–268 °C. The parallel sequence of conversions described for the *C*₃-components transformed the acid (**6**) into 1,3,5,7-tetraethynyladamantane (**12**), m.p. 156–157 °C (11% overall yield) *via* (**7**), (**8**), (**9**), (**10**), and (**11**).

Coupling of the (+)-*C*₃-component (**21**) and the *T_d*-component (**12**) was carried out following Chodkiewicz and Cadot's procedure.⁵

To a stirred mixture of (**12**) (15 mg, 0.064 mmol), copper(I) chloride (1.0 mg), 30% aq. EtNH₂ (1.5 ml), and tetrahydrofuran (THF) (0.4 ml) was added a mixture of the (+)-



bromide (**21**) (160 mg, 0.64 mmol) and THF (0.3 ml) over a period of 15 min at 27 °C in an atmosphere of nitrogen. A small amount of solid NH₂OH.HCl was added to keep the copper ion in the copper(I) state, and the mixture was stirred for an additional 45 min. Quenching with 5% aq. KCN followed by extraction with diethyl ether afforded a product mixture whose Al₂O₃ chromatography (elution with pentane) gave the recovered (+)-bromide (**21**) (36 mg), the (+)-dimer (**22**)§ (30 mg), m.p. 310 °C (decomp.), [α]_D²⁵ +54.3° (CHCl₃), and a mixture of partially coupled compounds (40 mg).

Extraction with hot pentane (30 ml) left a 5:1 mixture (from the mass spectrum) of triply and quadruply coupled compounds (15 mg) to which the second coupling reaction was performed with the (+)-bromide (**21**) (55 mg), copper(I) chloride (1.5 mg), 30% aq. EtNH₂ (1.5 ml), and THF (0.8 ml). Al₂O₃ chromatography of the product provided the recovered (+)-bromide (**21**) (10 mg), the (+)-dimer ((**22**) 22 mg), and (+)-(**2**) (15 mg) which was recrystallized from pentane to give a silky crystalline product (7.5 mg, 13% yield), m.p. >350 °C, [α]_D²⁷ +65.3° (*c* 0.101, CHCl₃), λ_{\max} nm (log ϵ) (in hexane), 222.5 (3.45), 234 (3.50), 246.5 (3.49), and 260.5 (3.23), i.r. (KBr) 2250 and 2150 cm^{–1}, *m/z* 905 (*M*⁺).¶ These

† All compounds reported in this paper were found to give satisfactory analytical and spectroscopic data.

‡ The inversion of optical rotation found on going from the (–)-ethene derivative (**17**) to the (+)-ethyne derivative (**19**) has found a parallel in the catalytic hydrogenation of the (+)-dimer (**22**) into the (–)-octahydro derivative (**23**), [α]_D²⁷ –24.5° (CHCl₃).

§ (**22**): i.r. (KBr) 2150 cm^{–1}, *m/z* 338 (*M*⁺), λ_{\max} nm (log ϵ) (in hexane) 223 (2.51), 234 (2.67), 246.5 (2.71), and 259.5 (2.51), ¹H n.m.r. (CDCl₃) δ 1.30 (6 H, d, *J* 12 Hz, CH₂), 1.56 (6 H, d, *J* 12 Hz, CH₂), 2.02 (8 H, br. s, CH), and 2.15 (6 H, s, CH).

¶ The mass spectra were measured using a Matsuda-type double-focusing spectrometer equipped with a silicon emitter (T. Matsuo, H. Matsuda, and I. Katakuse, *Anal. Chem.*, 1979, **51**, 69).

spectral data coupled with the ^1H n.m.r. results [(CDCl_3) δ 1.30 (12 H, d, J 10 Hz, CH_2 in C_3 -component), 1.54 (12 H, d, J 10 Hz, CH_2 in C_3 -component), 1.72 (12 H, s, CH_2 in adamantane core), 2.00 (12 H, s, CH in C_3 -component), 2.08 (4 H, s, central CH in C_3 -component), and 2.14 (12 H, s, CH in C_3 -component)] are consistent with the assigned structure (**2**), whose highest attainable static and time averaged dynamic symmetry⁶ are T and $(C_3)^4 \wedge T$, respectively.

Received, 9th August 1982; Com. 947

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