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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

THE FIRST OPTICALLY ACTIVE ORGANIC MOLECULE WITH T SYMMETRY AND OF KNOWN ABSOLUTE CONFIGURATION

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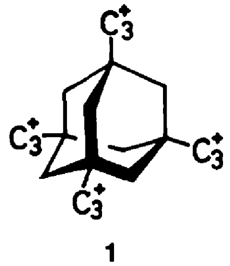
Abstract—(−)-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-Trishomocubanethanoic acid (5) of known absolute configuration and absolute rotation was converted into (+)-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-2-bromoethynyl-D_3-trishomocubane (27) of C_3 symmetry. 1,3,5,7-Tetraethynyladamantane (22), with Td symmetry, was prepared from 1,3,5,7-tetrakis(hydroxymethyl)adamantane (13). Coupling of the C_3-component 27 with the Td component 22 was successfully accomplished by Chodkiewicz and Cadiot's procedure providing (+)-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 (4) whose highest attainable static and time-averaged dynamic symmetry are T and $(C_3)^4 \wedge T$, respectively.

Organic molecules with polyhedral symmetry have been and remain a challenge to organic chemists. Among hydrocarbons based on Platonic regular polyhedra, cubane (Oh symmetry) was prepared by Eaton and Cole[1] in 1964 and dodecahedrane (Ih symmetry) was made by Paquette and co-workers[2] in 1982. Tetrahedrane (Td symmetry) itself is unknown, but the syntheses of the tetralithio[3] and the tetra-t-butyl derivative[4] were reported in 1978. These symmetry classes are not chiral.

Among molecules with chiral polyhedral symmetry (T, O, and I symmetry), the existence of molecules with conformational T symmetry has been discussed by several workers. An electron diffraction study by Bartell *et al.*[5] showed unambiguously that tetrakis(trimethyl)silane assumes a conformation of T symmetry in the gas phase. On the basis of empirical force-field calculation, Iroff and Mislow[6] showed that molecules of the type of t-Bu_4M [e.g. $C[Si(CH_3)_3]_4$ and $C[C(CH_3)_3]_4$] and tetra-t-butyltetrahedrane exist in a conformation with T symmetry in the ground state. However, as far as we know, no optically active molecules with T symmetry have been mentioned in these reports. The synthesis of an optically active molecule of chiral polyhedral symmetry is thus an interesting synthetic challenge.

Farina and Morandi[7] proposed three models by way of a potentially accessible model of T symmetry, one of which, 1, may be obtained in optically active form by placing four optically active C_3 submolecular units of the same chirality at the four apices of a tetrahedral framework such as adamantane (Td symmetry).

After we reported the preparation and absolute configuration determination of (+)-D_3-trishomocubane (2)[8] with D_3 symmetry, we explored a synthetic route to an enantiomerically pure compound of polyhedral T symmetry such as 1 using a D_3-trishomocubane derivative as the optically active C_3 submolecular unit. In 1981 we prepared (−)-1,3,5,7-tetrakis[[(2-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-D_3-trishomocubanyl)acetoxy]methyl]adamantane (3)[9] by using 1,3,5,7-tetrakis(hydroxymethyl)adamantane (13) and (−)-2-trishomocubanethanoic acid (5) and reported this as the first optically active compound with dynamic T symmetry. Soon after publication, Mislow[10] showed that the interposition of the acetoxymethyl ($CH_2CO_2CH_2$) groups destroys all threefold symmetry inherent in four trishomocubanyl groups and the highest symmetry really attainable by molecule 3 is D_2. This prompted us to replace the four acetoxymethyl groups of 3 with cylindrically symmetric groups, such as the $-(C{\equiv}C)-_n$ group. In this



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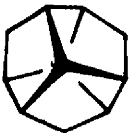

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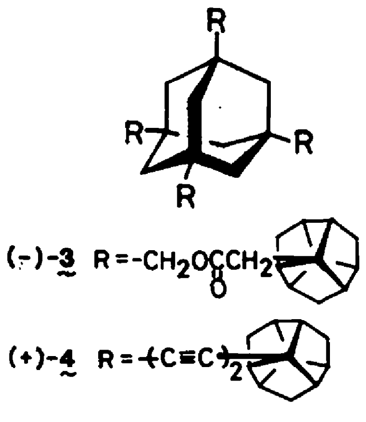


paper we wish to report the successful synthesis of (+)-1,3,5,7-tetrakis[2-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-D_3-trishomocubanylbuta-1,3-diynyl]adamantane (**4**) which has cylindrically symmetric $-(C\equiv C)-_2$ groups between the central Td-adamantane core and the C_3-trishomocubane components.

RESULTS AND DISCUSSION

As our synthetic strategy involved the coupling of the C_3-components with the Td-component, both components require functional groups as ready "handles" for the coupling reaction. We chose 2-ethynyl-D_3-trishomocubane (**12**) and 1,3,5,7-tetraethynyladamantane (**22**) as the C_3-component and the Td-component, respectively.

Preparation of the C_3*-component,* (+)*-2-ethynyl-*D_3*-trishomocubane* (**12**)

As it is indispensable for our strategy that the absolute configuration and optical purity of the C_3-component be known, we used (−)-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-trishomocubanethanoic acid (**5**), whose preparation was reported in our previous paper,[9] as the starting material for the synthesis of the optically active C_3-component, (+)-2-ethynyl-D_3-trishomocubane (**12**). Treatment of (−)-**5**, $[\alpha]_D$ −68.2° (96% optical purity),[9] with thionyl chloride gave the acyl chloride **6** which was reacted with dimethylamine to afford the (−)-dimethylamide **7** as a liquid. Reduction of (−)-**7** with $LiAlH_4$ followed by oxidation with 30% hydrogen peroxide in methanol gave the amine oxide **9**. Cope elimination of **9** was carried out at 165–170° under reduced pressure to yield (−)-2-ethenyl-D_3-trishomocubane (**10**) as a volatile solid in 60% overall yield from **5**. Bromination of (−)-**10** with a solution of bromine in carbon tetrachloride yielded the dibromide **11** as a liquid. Although dehydrobromination of **11** by heating at 190–200° with powdered KOH is rather drastic, the reaction was successfully carried out under reduced pressure, and the volatile product was removed from the reaction mixture by distillation. Further purification gave (+)-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-2-ethynyl-D_3-trishomocubane (**12**), $[\alpha]_D$ +29.2°, in 36% overall yield from **10**. Its ^1H-NMR spectrum δ 1.3–1.7 (m, 6H, CH_2), 2.04 (s, 1H, $C\equiv CH$), 1.8–2.3 (m, 6H, CH), and 2.35 (br s, 1H, CH), is consistent with the 2-substituted D_3-trishomocubane structure **12** of C_3 symmetry.

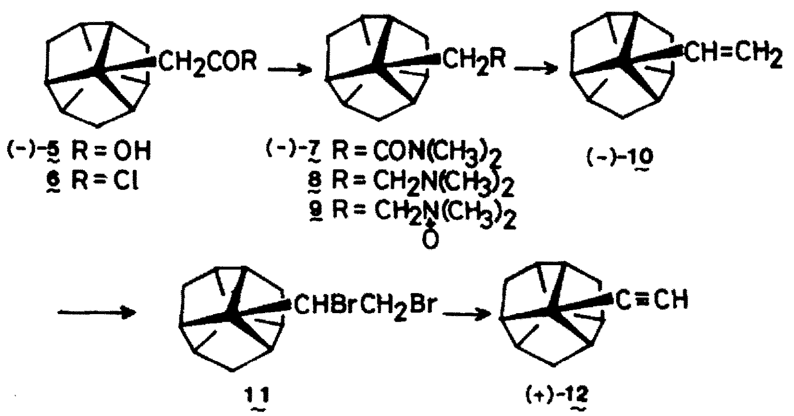
Preparation of the Td*-component,* 1,3,5,7*-tetraethynyladamantane* (**22**)

The simple synthesis of 1-ethynyladamantane from 1-bromoadamantane via 1-(2-bromoethenyl)-adamantane was reported by Stetter and Wulff.[11] However, our attempts to convert 1,3,5,7-tetrabromoadamantane[12] into 1,3,5,7-tetraethynyladamantane (**22**) according to Stetter and Wulff's procedure were not successful because 1,3,5,7-tetrabromoadamantane is scarcely soluble in vinyl bromide. We therefore decided to convert 1,3,5,7-tetrakis-(carboxymethyl)adamantane (**16**) to the Td-component **22** by the parallel sequence of conversions described for the preparation of (+)-**12**.

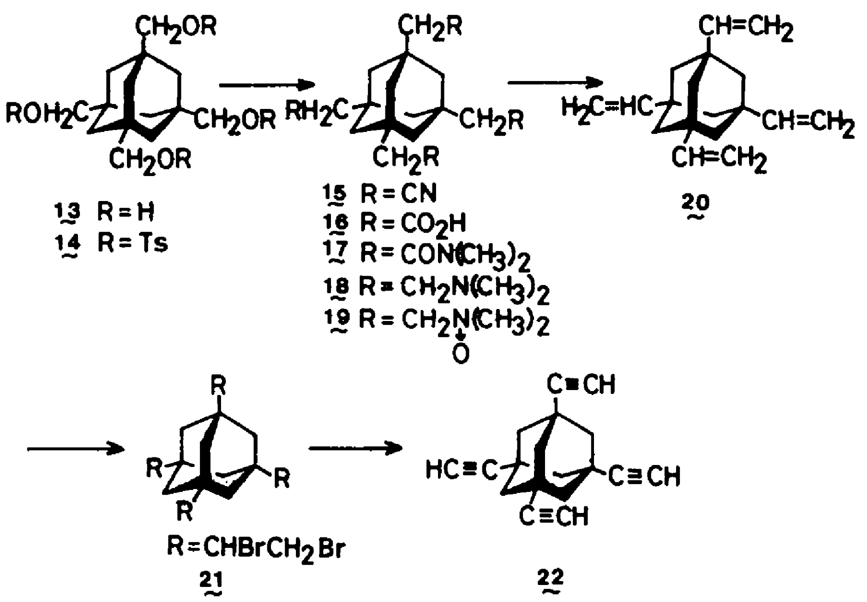
A routine homologation reaction sequence converted 1,3,5,7-tetrakis(hydroxymethyl)adamantane (**13**)[13] into **16** via the *p*-toluenesulfonate **14** and the nitrile **15**. The overall yield for the three-step conversion of **13** into **16** was 68%. Treatment of **16** with thionyl chloride followed by the reaction with dimethylamine in benzene gave amide **17** which was reduced to amine **18** with $LiAlH_4$. Oxidation of **18** with 30% hydrogen peroxide followed by pyrolysis at 165–170° yielded 1,3,5,7-tetraethenyladamantane (**20**) as a liquid in 62% overall yield from **16**. Bromination of **20** followed by dehydrobromination with KOH at 160° under reduced pressure gave 1,3,5,7-tetraethynyladamantane (**22**) as a volatile solid, m.p. 156–157° (sealed tube). The structural proof of **22** was based on the ^1H-NMR spectrum which exhibited only two singlet signals, δ 1.90 (12H) and 2.14 (4H), due to the methylene and acetylenic protons, respectively.

Model coupling reaction of the Td*-component* **22** *with* 1*-Bromo-*3,3*-dimethyl-*1*-butyne* (**23**)

The final stage of our strategy is the coupling reaction of the (+)-C_3-component **12** with the Td-component **22**. The reaction was carried out following Chodkiewicz and Cadiot's procedure.[14] Before coupling of **22** with (+)-**12**, we examined the reactivity of **22** with a rather bulky bromoalkyne under Chodkiewicz and Cadiot's reaction conditions. The coupling of **22** with 4 molar equiv of 1-bromo-3,3-dimethyl-1-butyne (**23**), prepared from 3,3-dimethyl-1-butyne[15] with sodium hypobromite, gave a complex mixture of the cross-coupling products. The presence of singly, doubly, and triply coupled products together with a small amount of the desired quadruply coupled compound **25** was revealed by mass spectral analysis. After this preliminary



Scheme 1.



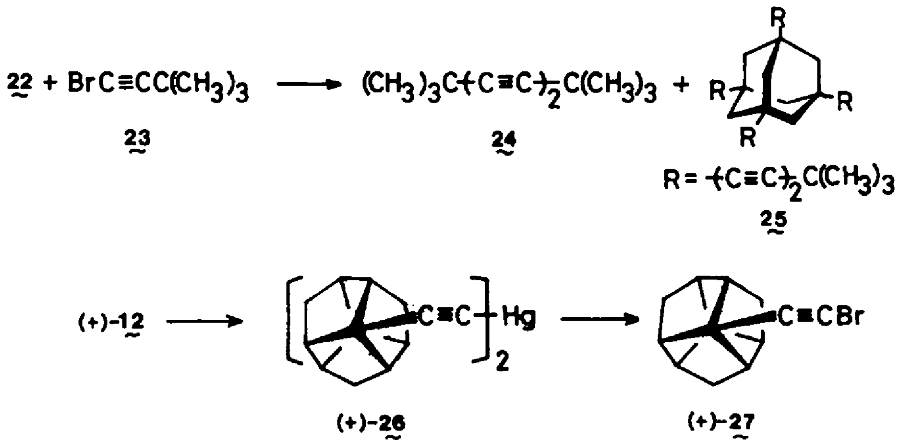
Scheme 2.

experiment, the coupling of **22** was run with large excess of **23**. Chromatographic separation afforded the known polyacetylenic compound, 2,2,7,7-tetramethyloctane-3,5-diyne (**24**) (12% yield) and the quadruply coupled compound **25** (23% yield), m.p. > 300°, which was further purified by recrystallization from pentane. Proof for structure **25** is based on the mass spectrum as well as the ^{1}H-NMR and IR spectra. The ^{1}H-NMR showed only two singlet signals, δ 1.25 (36H) and 1.82 (12H), due to methyl and methylene groups, respectively. The 3300 cm^{-1} band observed in the IR spectrum of **22** was not present in that of **25**.

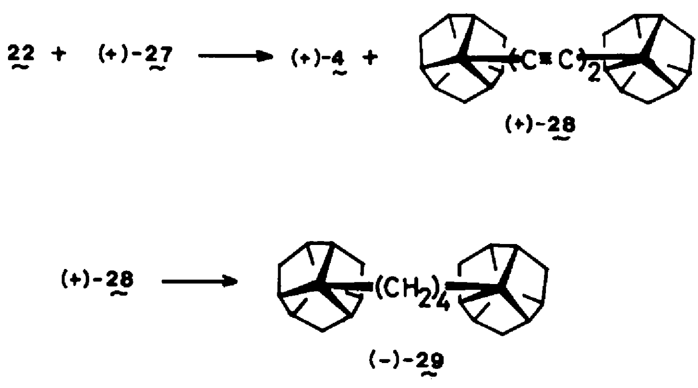
Coupling reaction of the Td-*component* **22** *with the* (+)-C_3-*component* **12**

After several attempts to convert (+)-**12** into **27** by the reaction with sodium hypobromite were unsuccessful, resulting only in recovery of the starting material **12**, the desired conversion was accomplished by Eglinton and McCrae's procedure.[16] Reaction of (+)-**12** with a solution of mercuric acetate in n-butylamine gave the mercury derivative **26** which was treated with bromine in carbon tetrachloride to give a 57% overall yield of (+)-**27** as a solid.

Chodkiewicz and Cadiot's reaction of **22** with 10 molar equiv of (+)-**27** followed by chromatographic separation on alumina gave (+)-**27** (23% recovered), the dimer (+)-**28** (28% yield), and a mixture of the cross-coupling products. The dimer (+)-**28** was further purified on sublimation. The assigned structure was confirmed on the basis of mass, UV, and ^{1}H-NMR spectra as well as the chemical reaction. On hydrogenation over PtO_2 in ethanol (+)-**28** took up 4 mol of hydrogen to afford the (−)-saturated hydrocarbon **29**, m.p. 208–210°. On the other hand, analysis of the cross-coupling products by means of mass spectroscopy revealed the presence of the doubly and the triply coupled products as well as the desired quadruply coupled product **4**. Recrystallization of the mixture from pentane removed the doubly coupled compound, it being easily soluble in hot pentane, and left a 5 : 1 mixture of the triply coupled compound and **4**. In spite of using a large excess of the bromoalkyne **27**, the coupling reaction provided the desired quadruply coupled product **4** in rather poor yield. The 5 : 1 mixture was again reacted with excess (+)-**27** by the same procedure. Alumina column chromatography of the product gave a 60% yield of (+)-**28** and **4** together with



Scheme 3.



Scheme 4.

a small amount of the triply coupled product. Recrystallization of the cross-coupling products from pentane provided (+)-4 as silky crystals. Some coloration of the crystals begins at *ca* 300°; at 350°, a dark brown coloration is evident, but melting is never observed. Structure 4 was unambiguously confirmed by analysis of the spectra (mass, UV, IR, and ^{1}H-NMR) as well as elemental analysis. The 3300 cm^{-1} band observed in the IR spectrum of the mixture of the cross-coupling products disappeared in that of 4 and bands due to $-(C{\equiv}C)_2-$ groups were observed at 2250 and 2150 cm^{-1}. The ^{1}H-NMR spectrum of 4 demonstrated the absence of acetylenic protons, whose signal at δ 2.14 was observed in that of the mixture.

Since interposition of $-(C{\equiv}C)_2-$ groups between the four C_3-trishomocubanyl groups and the central Td-adamantane framework will result in free rotation of all the C_3-components, the time-averaged dynamic symmetry[6] of this molecule is $(C_3)^4 \wedge T$. If we assume inhibition of internal free rotation of the four C_3-components, the highest static symmetry attainable by (+)-4 is T.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. IR spectral data were obtained on a Hitachi 260-10 spectrophotometer. ^{1}H-NMR spectra were obtained on a JNM-C-60 and a JNM-FX-100. Optical rotations were measured with a JASCO DIP-140 automatic polarimeter. UV spectra were measured with a Beckman DB spectrometer. Mass spectra were taken with a Matsuda-type double-focusing spectrometer equipped with a silicon emitter.[17] GLC analyses were performed on a JGC-20K equipped with an FID using a 2 m × 3 mm i.d. column of 10% PEG 20M on UniportHP. Elemental analyses were determined on a Yanagimoto CHN-Corder.

(−)-N,N-*Dimethyl-(2-*D_3*-trishomocubanyl)ethanamide* (**7**). A mixture of (−)-**5**, $[\alpha]_D$ −68.2° (96% optical purity),[9] (3.73 g, 0.0183 mol) and $SOCl_2$ (5.60 g, 0.0471 mol) was stirred for 48 h at room temp. Excess $SOCl_2$ was removed under reduced pressure to give **6** as a liquid which was dissolved in 30 ml of dry benzene. After the soln was added dropwise to a stirred soln of anhyd dimethylamine (3.80 g, 0.0843 mol) in dry benzene (15 ml) with ice cooling, the mixture was warmed gradually to room temp and further stirred for 48 h at this temp. The mixture was poured into ice–water, made acidic with aq HCl and extracted with ether. The extract was washed with $NaHCO_3$ aq and water, dried ($MgSO_4$), and concentrated to give an oily product which was distilled to furnish (−)-**7** (3.39 g, 80% yield), b.p. 127–130° (0.4 mm Hg); $[\alpha]_D^{27}$ −58.8° (*c* 0.366, EtOH); IR (neat film) 1650 cm^{-1}. (Found: C, 77.97; H, 9.13; N, 5.91. Calc for $C_{15}H_{21}ON$: C, 77.88; H, 9.15; N, 6.05%.)

(−)-*2-Ethenyl-*D_3*-trishomocubane* (**10**). A soln of (−)-**7** (3.39 g, 14.7 mmol) in dry ether (65 ml) was added to a suspension of $LiAlH_4$ (670 mg, 17.6 mmol) in dry ether (25 ml), and the mixture was refluxed for 20 h. After NaOH aq (NaOH 11.1 g, H_2O 45 ml) was carefully added to the mixture with ice cooling, an inorganic solid was filtered off and washed with ether. The washings and the original filtrate were combined, washed with water, dried ($MgSO_4$) and concentrated *in vacuo* to give **8** (3.23 g) as an oil. The amine **8** (3.23 g) was dissolved in MeOH (4 ml) and cooled in an ice bath. To the chilled and stirred soln was slowly added 30% H_2O_2 (2 ml), and the mixture was gradually warmed to room temp. After 4 and 16 h periods, the mixture was further treated with 30% H_2O_2 (each 2 ml). After being stirred for 30 h at room temp, the mixture was treated with Pt black (100 mg) to destroy the remaining H_2O_2. The catalyst was filtered off and the filtrate was concentrated to give **9** as a solid which was transferred into a distilling flask equipped with a cold trap. Pyrolysis by heating at 165–170° *in vacuo* for 3 h gave a semisolid which was dissolved in ether, washed successively with aq HCl, $NaHCO_3$ aq, and water and dried ($MgSO_4$). After removal of the solvent, the resulting solid was sublimed at 50° (5 mm Hg) to afford (−)-**10** (1.90 g, 75% yield based on 7), m.p. 53–54° (in a sealed tube); $[\alpha]_D^{27}$ −81.3° (*c* 0.508, EtOH); IR (KBr) 3100, 1635, 905 cm^{-1}. (Found: C, 90.64; H, 9.40. Calc for $C_{13}H_{16}$: C, 90.64; H, 9.36%.)

(+)-*2-Ethynyl-*D_3*-trishomocubane* (**12**). A soln of Br_2 (1.70 g, 10.6 mmol) in dry CCl_4 (4 ml) was added to a soln of (−)-**10** (1.52 g, 8.84 mmol) in dry CCl_4 (4 ml) with ice cooling. After being stirred for 3 h at room temp, the mixture was diluted with CCl_4 (20 ml), washed successively with aq sodium thiosulfate soln, $NaHCO_3$ aq, and water, dried (Na_2SO_4) and concentrated to give **11** as a pale yellow liquid (3.60 g). Crude **11** (3.06 g) was placed in a distilling flask equipped with a cold trap and mixed with powdered KOH (2.9 g) and triethylene glycol (8 ml). The mixture was heated at 190–200° for 2 h under reduced pressure (30 mm Hg), and a solid was collected in the trap. The condensate was dissolved in pentane, washed with water, and dried ($MgSO_4$). After the solvent was evaporated, the residue was chromatographed on alumina and fractions eluted with pentane gave a colorless liquid which was distilled to afford (+)-**12** (540 mg, 36% yield based on (−)-**10**), b.p. 110–115° (30 mm Hg); $[\alpha]_D^{25}$ +29.2° (*c* 0.251, EtOH); IR (neat film) 3300, 2105, 1460 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.3–1.7 (6H, m), 2.04 (1H, s), 1.8–2.3 (6H, m), 2.35 (1H, br s). (Found: C, 91.55; H, 8.19. Calc for $C_{13}H_{14}$: C, 91.71; H, 8.29%.)

1,3,5,7-*Tetrakis(cyanomethyl)adamantane* (**15**). To an ice-cooled soln of **13**[13] (5.90 g, 0.0230 mol) in pyridine (150 ml) was added *p*-toluenesulfonyl chloride (26.2 g, 0.138 mol). The mixture was stirred for 6 h with ice cooling and kept overnight at room temp. After the mixture was poured into ice–water and extracted with ether, the extract was washed successively with aq HCl, $NaHCO_3$ aq, and water, dried ($MgSO_4$) and concentrated to give **14** (19.2 g) as a solid. A mixture of crude **14** (19.2 g), NaCN (6.76 g, 0.138 mol), and DMF (110 ml) was heated at 120–130° for 14 h with stirring. After cooling, the remaining NaCN was removed by filtration and the filtrate was concentrated *in vacuo*. Addition of water (200 ml) to the residue deposited a solid which was collected and recrystallized from AcOH to afford **15** (5.20 g, 77% overall yield from **13**), m.p. 266–268°; IR (KBr) 2240 cm^{-1}. (Found: C, 73.71; H, 6.89; N, 18.87. Calc for $C_{18}H_{20}N_4$: C, 73.94; H, 6.90: N, 19.16%.)

1,3,5,7-*Tetrakis(carboxymethyl)adamantane* (**16**). A mixture of **15** (11.4 g, 0.0390 mol), conc H_2SO_4 (215 ml), and water (260 ml) was heated at 120–130° for 24 h. Cooling in an ice-bath deposited a solid which was collected, washed with water, and recrystallized from AcOH to give **16** (12.6 g, 88% yield), m.p. > 300°. (Found: C, 58.86; H, 6.53. Calc for $C_{18}H_{24}O_8$: C, 58.69; H, 6.57%.)

1,3,5,7 - *Tetrakis*(N,N - *dimethylcarbamoylmethyl*) - *adamantane* (**17**). A mixture of **16** (12.6 g, 0.0344 mol) and $SOCl_2$ (115 ml) was gently refluxed for 40 h. Removal of excess $SOCl_2$ *in vacuo* gave the acyl chloride (14.6 g) as a solid which was dissolved in dry benzene (400 ml). The soln was added to a chilled soln of anhyd dimethylamine (24.7 g, 0.549 mol) in dry benzene (100 ml). After being stirred for 6 h with ice cooling, the mixture was allowed to stand overnight at room temp. The excess dimethylamine was removed *in vacuo* and the residual benzene soln was washed with a small amount of water, dried (Na_2SO_4) and concentrated to give **17** (15.2 g, 93% yield). Bulb-to-bulb distillation (oven temp 345–350° at 0.1 mm Hg) afforded an analytical sample of **17**; IR (neat film) 1630 cm^{-1}. (Found: C, 65.80; H, 9.15; N, 11.55. Calc for $C_{26}H_{44}O_4N_4$: C, 65.51; H, 9.31; H, 11.76%.)

1,3,5,7 - *Tetrakis*(2 - N,N - *dimethylaminomethyl*) - *adamantane* (**18**). A soln of **17** (15.2 g, 0.0320 mol) in dry THF (500 ml) was added to a suspension of $LiAlH_4$ (7.30 g, 0.192 mol) in dry THF (150 ml), and the mixture was refluxed for 24 h. The same workup as described for the preparation of **8** gave **18** (11.3 g, 84% yield) as a solid which was recrystallized from hexane, m.p. 66–68°. (Found: C, 74.02; H, 12.40; N, 13.41. Calc for $C_{26}H_{25}N_4$: C, 74.22; H, 12.46; N, 13.32%.)

1,3,5,7-*Tetraethenyladamantane* (**20**). Amine **18** (11.3 g, 0.0270 mol) was treated with 30% H_2O_2 by the same procedure as described for the preparation of **9**. Amine oxide **19** was obtained as a viscous oil. Pyrolysis of **19** was carried out as described for the preparation of **10** and distillation of the product afforded **20** (5.10 g, 79% yield), b.p. 98–100° (0.2 mm Hg); IR (neat film) 3100, 1640, 1000, 910 cm^{-1}. (Found: C, 89.83; H, 10.01. Calc for $C_{18}H_{24}$: C, 89.94; H, 10.06%.)

1,3,5,7-*Tetraethynyladamantane* (**22**). Addition of Br_2 (16.0 g, 0.100 mol) to **20** (4.81 g, 0.0200 mol) was carried out as described for the preparation of **11**. Dilution with CCl_4 (100 ml) and cooling in an ice-bath deposited a solid which was collected and washed with chilled CCl_4 to afford bromide **21** (14.1 g, 80% yield), m.p. 108–110° dec. Bromide **21** (2.70 g, 3.07 mmol), powdered KOH (3.8 g), and triethylene glycol (10 ml) were placed in a distilling flask equipped with a cold trap and heated at 160° under reduced pressure (30 mm Hg) for 2.5 h. The routine workup as described for the preparation of (+)-**12** gave a solid which sublimed at 95–100° (20 mm Hg) to furnish **22** (125 mg, 18% yield), m.p. 156–157° (in a sealed tube); IR (KBr) 3300, 2100, 1450 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.90 (12H, s), 2.14 (4H, s). (Found: C, 92.97; H, 7.01. Calc for $C_{18}H_{16}$: C, 93.06; H, 6.94%.)

1-*Bromo*-3,3-*dimethyl*-1-*butyne* (**23**). A soln of 3,3-dimethyl-1-butyne[15] (2.30 g, 0.0280 mol) in THF (91 ml) was added to a mixture of Br_2 (1.58 ml), 10 N NaOH aq (7.2 ml), and ice (17 g). The mixture was vigorously stirred for 2 h with ice cooling and then for a further 3 h at room temp. After NH_4Cl aq was added to the mixture with ice cooling, the mixture was extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated to give **23** (3.49 g, 78% yield) as a colorless liquid; IR (neat film) 2970, 2940, 2900, 2870, 1470, 1365, 1260, and 1200 cm^{-1}. This unstable bromide was used in the next step without further purification.

1,3,5,7 - *Tetrakis*(t - *butyl* - 1,3 - *butadiynyl*)*adamantane* (**25**). A soln of **23** (400 mg, 2.50 mmol) in THF (0.5 ml) was added to a stirred mixture of **22** (38 mg, 0.16 mmol), cuprous chloride (2.0 mg, 0.020 mmol), 30% aq ethylamine (2 ml), and THF (0.7 ml) during 15 min under N_2, and the mixture was stirred for an additional 1 h at room temp. During this period, a small amount of solid hydroxylamine hydrochloride was added several times to keep the Cu ion in the cuprous state. After 5% KCN aq was added to the mixture, the mixture was extracted with ether. The extract was washed with water, dried ($MgSO_4$) and concentrated to give a solid which was chromatographed on alumina. The earlier fractions eluted with pentane gave **24** (25 mg, 12% yield), m.p. 129–131° (in a sealed tube) (lit.[18] m.p. 130–132°), as a volatile solid and the later fractions eluted with the same solvent afforded the cross-coupled product **25** (20 mg, 23% yield) which was recrystallized from pentane, m.p. > 300°; IR (KBr) 2150, 1450, 1360, 1280, 1190 cm^{-1}; UV (hexane) λ_{max} 217 nm (ε 2.65 × 10^3), 230 (3.04 × 10^3), 241 (2.87 × 10^3), 255 (1.96 × 10^3); ^{1}H-NMR ($CDCl_3$) δ 1.25 (36H, s), 1.82 (12H, s); MS (*m/e*) 552 (M^+). (Found: C, 91.14; H, 8.74. Calc for $C_{42}H_{48}$: C, 91.25; H, 8.75%.)

Mercury derivative of (+)-2-*ethynyl*-D_3-*trishomocubane* (**12**). A soln of mercuric acetate (537 mg, 1.69 mmol) in n-butylamine (2.1 ml) was added all at once to a soln of (+)-**12** (460 mg, 2.71 mmol) in n-butylamine (1.4 ml). After being stirred for 10 min at room temp, the mixture was poured into a 0.5 N H_2SO_4–ice mixture and extracted with EtOAc. The extract was washed with water, dried (Na_2SO_4) and concentrated *in vacuo* to give a white solid which was recrystallized from pentane to afford (+)-**26** (446 mg, 61% yield), m.p. 163–165°; $[\alpha]_D^{20}$ +27.7° (*c* 0.282, $CHCl_3$); IR (KBr) 2140, 1460, 1295, 1270 cm^{-1}. (Found: C, 57.88; H, 4.87. Calc for $C_{26}H_{26}Hg$: C, 57.93; H, 4.86%.)

(+)-2-*Bromoethynyl*-D_3-*trishomocubane* (**27**). To a soln of (+)-**26** (411 mg, 0.764 mmol) in CCl_4 (20 ml) was slowly added a soln of Br_2 (250 mg, 1.57 mmol) in CCl_4 (2.5 ml). After being stirred for 10 min at room temp, the mixture was concentrated *in vacuo*. Pentane was added to the residue, and a deposited inorganic solid was removed. The filtrate was chromatographed on alumina and fractions eluted with pentane gave (+)-**27** as a colorless solid (355 mg, 93% yield), $[\alpha]_D^{22}$ +19.6° (*c* 0.393, MeOH); IR (KBr) 2200, 1460, 1300, 1275 cm^{-1}. This crude bromide was used in the next step without further purification.

(+) - 1,3,5,7 - *Tetrakis*[2 - (1*S*,3*S*,5*R*,6*S*,8*R*,10*R*) - D_3 - *trishomocubanyl* - 1,3 - *butadiynyl*]*adamantane* (**4**). A soln of (+)-**27** (160 mg, 0.64 mmol) in THF (0.3 ml) was added to a stirred mixture of **22** (15 mg, 0.064 mmol), cuprous chloride (1.0 mg, 0.010 mmol), 30% aq ethylamine (1.5 ml), and THF (0.4 ml) over a period of 15 min under N_2. The mixture was stirred for an additional 45 min at room temp and a small amount of hydroxylamine hydrochloride was added to keep the Cu ion in the cuprous state. The same workup as described for the preparation of **25** gave an oil which was chromatographed on alumina. The earlier eluates with pentane gave the recovered bromide **27** (36 mg, 23% recovered), and the latter eluates with pentane afforded the dimer **28** (30 mg, 28% yield). The final eluates with pentane–ether (95/5, v/v) gave a mixture of cross-coupling products (40 mg) as a solid which was recrystallized from pentane (10 ml) to furnish 15 mg of a 5:1 mixture (analyzed by MS) of triple and quadruple cross-coupling products. By the same procedure as described above, this mixture (15 mg) was again treated with (+)-**27** (50 mg, 0.22 mmol), cuprous chloride (1.5 mg, 0.015 mmol), 30% aq ethylamine (1.5 ml), and THF (0.8 ml). Chromatography of the product on alumina gave **27** (10 mg, 18% recovered), **28** (22 mg, 60% yield), and a mixture of the cross-coupling products (15 mg). The mixture was recrystallized three times from hot pentane to give **4** (7.5 mg) as silky crystals, m.p. > 350°; $[\alpha]_D^{27}$ +65.3° (*c* 0.101, $CHCl_3$); UV (hexane) λ_{max} 222.5 nm (ε 2.83 × 10^3), 234 (3.17 × 10^3), 246.5 (3.06 × 10^3), 260.5 (1.69 × 10^3); IR (KBr) 2250, 2150 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.30 (12H, d, J = 10 Hz), 1.54 (12H, d, J = 10 Hz), 1.72 (12H, s), 2.00 (12H, s), 2.08 (4H, s), 2.14 (12H, s); MS (*m/e*) 905 (M^+). (Found: C, 92.68; H, 7.11. Calc for $C_{70}H_{64}$: C, 92.87; H, 7.13%.)

Dimer **28** was sublimed at 150° (0.1 mm Hg), m.p. 310° dec. (in a sealed tube); $[\alpha]_D^{25}$ +54.3° (*c* 0.181, $CHCl_3$); UV (hexane) λ_{max} 223 nm (ε 326), 234 (464), 246.5 (511), 259.5 (327); IR (KBr)

2150 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.30 (6H, d, J = 12 Hz), 1.56 (6H, d, J = 12 Hz), 2.02 (8H, br s), 2.15 (6H, s); MS (*m/e*) 338 (M^+). (Found: C, 92.20; H, 7.75. Calc for $C_{26}H_{26}$: C, 92.26; H, 7.74%.)

(−)-1,4-*Bis*(2-D_3-*trishomocubanyl*)*butane* (**29**). A mixture of (+)-**28** (25 mg, 0.074 mmol), PtO_2 (10 mg), and EtOH (20 ml) was shaken at room temp in a hydrogenation flask at 1 atm of H_2. After the H_2 absorption had ceased, the catalyst was filtered off. The filtrate was concentrated to give a white solid which was recrystallized from EtOH to furnish (−)-**29** (12 mg, 48% yield), m.p. 208–210°; $[\alpha]_D^{27}$ −24.5° (*c* 0.567, $CHCl_3$). (Found: C, 89.95; H, 9.83. Calc for $C_{26}H_{34}$: C, 90.11; H, 9.89%.)

REFERENCES

[1] P. E. Eaton and T. W. Cole, Jr., *J. Am. Chem. Soc.* **86**, 3157 (1964).

[2] R. J. Ternansky, D. W. Balogh and L. A. Paquette, *Ibid.* **104**, 4503 (1982).

[3] G. Rauscher, T. Clark, D. Poppinger and P. von R. Schleyer, *Angew. Chem. Int. Ed. Engl.* **17**, 276 (1978).

[4] G. Maier, S. Pfriem, U. Schafer and R. Matusch, *Ibid.* **17**, 520 (1978).

[5] L. S. Bartell, F. B. Clippard, Jr. and T. L. Boates, *Inorg. Chem.* **9**, 2436 (1970).

[6] L. D. Iroff and K. Mislow, *J. Am. Chem. Soc.* **100**, 2121 (1978).

[7] M. Farina and C. Morandi, *Tetrahedron* **30**, 1819 (1974).

[8] M. Nakazaki, K. Naemura and M. Arashiba, *J. Org. Chem.* **43**, 689 (1978).

[9] M. Nakazaki and K. Naemura, *J. Chem. Soc. Chem. Commun.* 911 (1980); M. Nakazaki and K. Naemura, *J. Org. Chem.* **46**, 106 (1981).

[10] K. Mislow, *J. Chem. Soc. Chem. Commun.* 234 (1981).

[11] H. Stetter and P. Goebel, *Chem. Ber.* **95**, 1039 (1962).

[12] H. Stetter and C. Wulff, *Ibid.* **93**, 1366 (1960).

[13] S. Landa and Z. Kamvcek, *Coll. Czech. Chem. Commun.* **24**, 4004 (1959).

[14] W. Chodkiewicz and P. Cadiot, *C.R. Acad. Sci. Paris* **241**, 1055 (1955); J. N. Gardmer, E. R. H. Jones, P. R. Leeming and J. S. Stephenson, *J. Chem. Soc.* 691 (1960).

[15] P. D. Bartlett and L. J. Rosen, *J. Am. Chem. Soc.* **64**, 543 (1942).

[16] G. Eglinton and W. McCrae, *J. Chem. Soc.* 2295 (1963).

[17] T. Matsuo, H. Matsuda and I. Katakuse, *Anal. Chem.* **51**, 69 (1979).

[18] F. Bohlmann, *Chem. Ber.* **86**, 657 (1953).