Synthesis and Absolute Configuration of the First Optically Active Organic Molecule with *T* Symmetry; (−)-1,3,5,7-Tetrakis[2-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-D_3-trishomocubanylacetoxymethyl]adamantane

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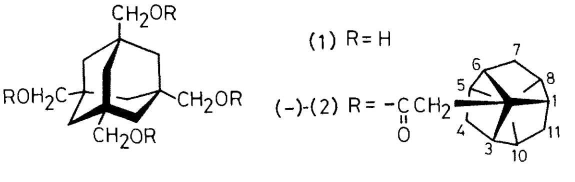
Summary Starting from the Diels–Alder adduct (**3**) between 2-methoxycarbonyl-1,4-benzoquinone and cyclopentadiene, a modified Barborak's synthesis of D_3-trishomocubane afforded (−)-2-(1*S*,3*S*,5*R*,6*S*,8*R*,10*R*)-D_3-trishomocubaneacetic acid (**11**) whose esterification with 1,3,5,7-tetrakis(hydroxymethyl)adamantane (**1**) gave (−)-(**2**), the first organic molecule of *T* symmetry with known absolute configuration.

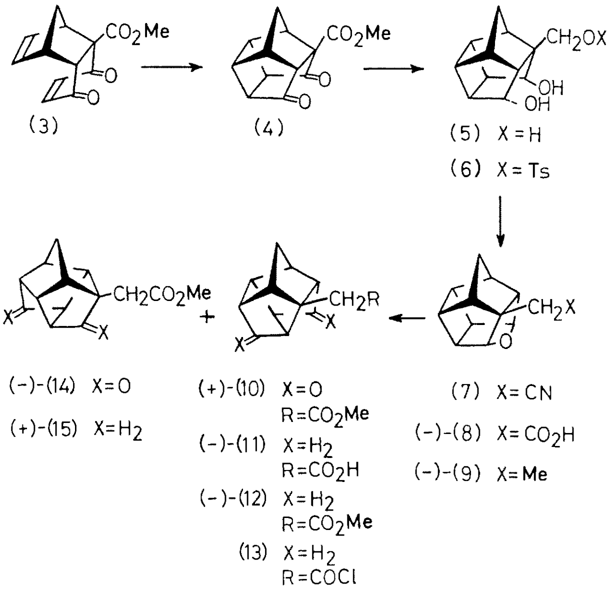
AMONG gyrochiral organic molecules synthesized so far, the ones with the highest symmetry have been D_3 symmetric molecules with symmetry number 6. In our earlier paper,[1] we reported the preparation and absolute configuration of (+)-D_3-trishomocubane with this dihedral symmetry, and we now report the synthesis of the first gyrochiral organic molecule having *T* symmetry, a polyhedral symmetry with symmetry number 12.

Our guiding principle[2] was desymmetrization of the T_d symmetry inherent to a regular tetrahedron by introducing optically active C_3-components with the same chirality on its four apexes; this was achieved by esterification of 1,3,5,7-tetrakis(hydroxymethyl)adamantane (**1**)[3] with (−)-2-D_3-trishomocubaneacetic acid (**11**).



Intramolecular photo-cyclization of the Diels–Alder product† (**3**) prepared from 2-methoxycarbonyl-1,4-benzoquinone and cyclopentadiene, gave the pentacyclic diketone (**4**), $LiAlH_4$ reduction of which yielded the triol (**5**). Tosylation to (**6**), followed by treatment with sodium cyanide in dimethylformamide converted (**5**) into the oxolan cyanide (**7**) which was hydrolysed with KOH in ethylene glycol to the (±)-carboxylic acid (**8**), m.p. 110—111 °C.

Optical resolution *via* the cinchonidine salt yielded (−)-(**8**), m.p. 109—110 °C, $[\alpha]_D^{22}$ −39·3°‡ which was converted into the ethyl derivative (**9**), $[\alpha]_D^{22}$ −21·6°. A fairly large enantiomer differential shift observed in the n.m.r. spectra of (−)-(**9**) on addition of $Eu(TFC)_3$§ indicated 97% optical purity.



Heating (−)-(**8**) at 150—160 °C with conc. sulphuric acid in acetic acid for 42 h, followed successively by saponification, diazomethane esterification, and Corey's oxidation, gave a 1 : 1 mixture of the diketo esters (**10**) and (**14**) from which (+)-(**10**) crystallized, m.p. 112—113 °C, $[\alpha]_D^{20}$ +232° ($CHCl_3$).

Removal of the carbonyl groups by Wolff–Kishner reduction afforded (−)-2-D_3-trishomocubaneacetic acid (**11**), m.p. 108—110 °C, $[\alpha]_D^{20}$ −68·9°, diazomethane esterification of which gave (−)-(**12**), $[\alpha]_D^{24}$ −68·5°.

The mother liquor of (+)-(**10**) afforded the isomeric rearrangement product (−)-(**14**) which was converted into the (+)-methyl ester (**15**), $[\alpha]_D^{24}$ +77·8°. The much simpler ^1H and ^{13}C n.m.r. spectra observed for (−)-(**12**) compared with those of (+)-(**15**), supported C_3 symmetry for (−)-(**12**) while its laevorotation[1,4] indicated a (1*S*,3*S*,5*R*,6*S*,8*R*,10*R*) configuration.

Heating (−)-(**11**) with thionyl chloride provided the acyl chloride (**13**) which was treated with (**1**) in pyridine giving (−)-(**2**), m.p. 197—198 °C, $[\alpha]_D^{20}$ −54·0° ($CHCl_3$),

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† All compounds reported in this paper exhibited correct analytical and spectroscopic data.

‡ Except otherwise notified, all optical rotations were measured in ethanolic solution.

§ Tris[3-(2,2,2-trifluoro-1-hydroxyethylidene)-(−)-camphorato]europium.

m/e 1000 (M^+) ($C_{66}H_{80}O_8$). The ^{1}H and ^{13}C n.m.r. spectra of (−)-(**2**) both confirmed its *T*-symmetric structure, and the fact that almost no discernible change was observed in the temperature-dependent ^{1}H n.m.r. spectra (−60 to +60 °C) also confirmed dynamic *T* symmetry for (−)-(**2**) in this temperature range.

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[3] S. Landa and Z. Kamycek, *Coll. Czech. Chem. Commun.*, 1959, **24**, 4004.

[4] M. Nakazaki, K. Naemura, and S. Nakahara, *J. Org. Chem.*, 1978, **43**, 4745; M. Nakazaki, K. Naemura, N. Arashiba, and M. Iwasaki, *ibid.*, 1979, **44**, 2433.