

Synthesis of (+)-3,4,8,9,13,14,18,19,23,24,28,29-Dodecaethoxy-1,6,11,16,21,26-hexaazacyclotriacontane. The First D_6 -Symmetry Organic Molecule with Known Absolute Configuration

Koichiro NAEMURA,* Yuji KANDA, Masatoshi YAMANAKA, and Hiroaki CHIKAMATSU
Department of Chemistry, Faculty of Engineering Science,
Osaka University, Toyonaka, Osaka 560

The high-symmetry chiral macrocyclic polyamides and polyamines were synthesized by using (+)-tartaric acid as a chiral source. The title compound, one of the amines, is the first D_6 -symmetry organic molecule with known absolute configuration.

Among chiral organic compounds with dihedral symmetry (D_n , $n \geq 2$), a various kinds of D_2 -symmetry molecules have been prepared in optically active modifications.¹⁾ Since the first synthesis of the optically active D_3 -symmetry compound was reported by Farina,²⁾ several organic compounds belonging to this point group were synthesized¹⁾ and a few macrocyclic compounds with D_4 symmetry were also prepared in optically active forms.³⁾ But, as far as we know, there is no report described for the preparation of an organic molecule with higher dihedral symmetry than D_4 symmetry. We here report the syntheses of high-symmetry chiral¹⁾ macrocyclic polyamides and polyamines with known absolute configuration in enantiomerically pure forms, and the 30-membered hexa-amine 1 is the first organic compound with D_6 symmetry.

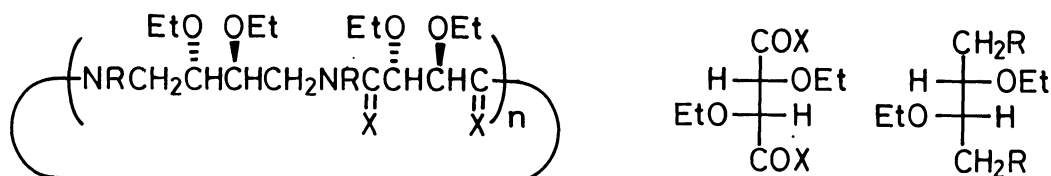
Reduction of (+)-10, bp 120-122 °C (6 mmHg (1 mmHg=133.322 Pa)); $[\alpha]_D^{29} +73.4^\circ$ (acetone), prepared from (+)-tartaric acid, with $LiAlH_4$ afforded (+)-13, bp 95 °C (0.8 mmHg); $[\alpha]_D^{30} +43.6^\circ$ (acetone), which was transformed to 14. Reaction of 14 with potassium phthalate in N,N-dimethylformamide (DMF) at 100 °C followed by treatment with hydrazine hydrate in ethanol under reflux⁴⁾ gave (-)-15, bp 104-106 °C (7 mmHg); $[\alpha]_D^{20} -39.2^\circ$ ($CHCl_3$), in 33% overall yield based upon 10. By treatment of 10 with NH_3 in methanol followed by $LiAlH_4$ reduction, the amine 15 was also prepared in a yield of 24% for two steps. Treatment of (+)-11, mp 125-126.5 °C; $[\alpha]_D^{25} +67.1^\circ$ (H_2O), with thionyl chloride and a small amount of DMF at 80 °C gave 12, bp 90-93 °C (7 mmHg). High dilution condensation of 12 with (-)-15 in benzene and triethylamine at room temperature gave the mixture of macrocyclic polyamides, which was chromatographed on alumina to afford the tetra-amide 5⁵⁾ (12% yield), mp 188-190 °C (recrystallized from ether); $[\alpha]_D^{22} +21.6^\circ$ ($CHCl_3$), and the glassy hexa-amide 4 (19%), $[\alpha]_D^{22} +69.1^\circ$ ($CHCl_3$). The structures of these amides 4 and 5 were confirmed on the basis of their mass and 1H NMR spectra as well as elemental analyses. In this reaction, the formation of a small amount of the diamide 6 was detected, but it could not be isolated.

Reaction of (+)-4 with diborane in tetrahydrofuran (THF) under reflux followed by acid hydrolysis and basification⁶⁾ afforded the free hexa-amine 1 (75%), $[\alpha]_D^{20}$

+80.1° (MeOH), as a colorless oil, which was treated with p-toluenesulfonyl chloride in ether and aqueous NaOH solution to afford 7 (glassy solid, 60%), $[\alpha]_D^{20} -77.8^\circ$ (CHCl₃). Analogously, the free tetra-amine 2 (oil, 88%), $[\alpha]_D^{20} -17.7^\circ$ (MeOH), and 8 (glassy solid, 40%), $[\alpha]_D^{25} -16.7^\circ$ (CHCl₃), were prepared from (+)-5.

In contrast with the condensation of the amine with the acyl chloride, Atkins' procedure⁷⁾ gave the 10-membered tosylamide 9 and the 20-membered tosylamide 8, and in this case, the 30-membered compound 7 did not obtained. Treatment of 15 with p-toluenesulfonyl chloride in ether and aqueous NaOH solution gave (-)-16 (86%), mp 110-112 °C (recrystallized from EtOH); $[\alpha]_D^{29} -5.88^\circ$ (CHCl₃), which was treated with sodium ethoxide in ethanol to give the disodium salt as a white solid. Reaction of 14 with the disodium salt in DMF at 95-100 °C afforded the mixture of tosylamides, which was chromatographed on alumina to give 9 (20%), mp 180-181 °C (from ether); $[\alpha]_D^{25} +70.7^\circ$ (CHCl₃), and 8 (12%). Reaction of 14 with 16 and NaH in DMF at 95-100 °C followed by chromatography also provided 8 (11%) and 9 (19%). The detosylation of 8 and 9 were performed by treatment with LiAlH₄ in THF under reflux to give 2 (55%) and 3 (oil, 51%), $[\alpha]_D^{24} +39.2^\circ$ (EtOH), respectively.

Highest attainable symmetry of the 30-membered hexa-amine 1, having one C₆ axis and six C₂ axes (dihedral axes) perpendicular to it, is D₆ and the compound is the first organic molecule with this symmetry. The 20-membered tetra-amine 2 and the 10-membered diamine 3 belong to the D₄ and D₂ point group, respectively.



1	n = 3	R = H	X = H ₂	6	n = 1	R = H	X = O	10	X = OMe	13	R = OH
2	n = 2	R = H	X = H ₂	7	n = 3	R = Ts	X = H ₂	11	X = OH	14	R = OTs
3	n = 1	R = H	X = H ₂	8	n = 2	R = Ts	X = H ₂	12	X = Cl	15	R = NH ₂
4	n = 3	R = H	X = O	9	n = 1	R = Ts	X = H ₂			16	R = NHTs
5	n = 2	R = H	X = O								

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