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SYNTHESIS OF NOVEL CROWN ETHER INCORPORATING THE (-)-(5S,6R,13S,14R)-5,6,13,14-TETRAHYDRO-5,13-METHANOCYCLOOCTA[1,2-a:5,6-a']-DINAPHTHALENE-6,14-DIOL SUBUNIT AS THE C_2-SYMMETRIC CHIRAL CENTER

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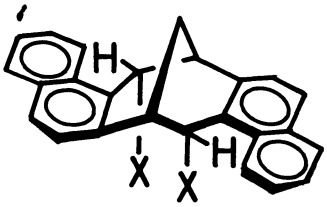
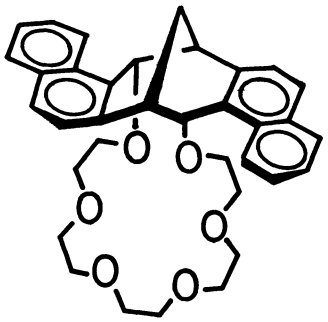
(-)-5,6,13,14-Tetrahydro-5,13-methanocycloocta[1,2-a:5,6-a']-dinaphthalene-6,14-diol was synthesized and its absolute configuration was established. Optically active crown ether was prepared by using this glycol as a source of chirality and its chiral recognition property was examined.

Various kinds of optically active crown ethers have been synthesized by using chiral molecules of C_2 symmetry as source of chirality.[1] In this communication we report synthesis and determination of absolute configuration of (-)-5,6,13,14-tetrahydro-5,13-methanocycloocta[1,2-a:5,6-a']dinaphthalene-6,14-diol (1), and also synthesis and chiral recognition property of the novel crown ether 3 incorporating this (-)-glycol molecular framework as the C_2-symmetric chiral center.



(-)-1 R=OH
(-)-2 R=OAc



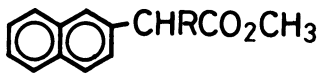
(-)-3

Our first task is the preparation of 2,4-di(2-naphthyl)glutaric acid (7) in optically active form. Methyl 2-naphthylacetate (4) was treated with dimethyl oxalate and sodium methoxide to give dimethyl 2-naphthylmalonate (5) in 75% yield. Treatment of 5 with methylene iodide and sodium methoxide followed by hydrolysis

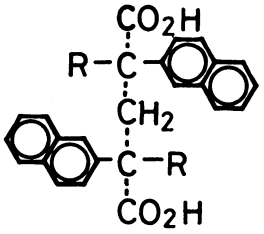
with potassium hydroxide[2] gave 6, which was in turn heated at 140-160 °C under reduced pressure to yield a mixture of (±)-2,4-di(2-naphthyl)glutaric acid (7) and its meso-isomer. Fractional recrystallization of the mixture from diethyl ether gave (±)-7,[3] mp 209-210 °C, in 25% overall yield from 5. Optical resolution was accomplished by working with (-)-α-phenylethylamine as the resolving agent. Recrystallization from ethanol gave a sparingly soluble salt, $[\alpha]_D^{28}$ +89.6° (EtOH), from which (+)-7,[4] $[\alpha]_D^{26}$ +200° (acetone), was obtained by treatment with hydrochloric acid.

The absolute configuration of 7 was determined unambigously by chemical correlation with (-)-(2R,4R)-2,4-diphenylpentane (12),[2] from which the optically active relay substance 11 with known absolute configuration was prepared. Friedel-Crafts reaction of (-)-12, $[\alpha]_D^{30}$ -38.2° ($CHCl_3$), with ethyl 3-chloroformylpropionate and aluminum chloride in 1,1,2,2-tetrachloroethane (stirred at room temperature for 1 h and at 80-100 °C for additional 30 min) gave an oily product which was hydrolyzed with sodium hydroxide to give a 58% yield of (-)-13, $[\alpha]_D^{29}$ -15.9° (EtOH), mp 178-179 °C (crystallized from methanol). Clemmensen reduction of (-)-13 gave 14, a part of which was converted, with diazomethane, into (-)-15, $[\alpha]_D^{28}$ -27.7° ($CHCl_3$); bp 203 °C (0.05 mmHg). Treatment of 14 with phosphorous pentachloride in benzene (stirred at room temperature for 1.5 h and at 80 °C for additional 30 min) followed by cyclization with stannic chloride in benzene (stirred at -10 °C for 2 h and at room temperature for additional 2 h) provided (-)-16 in 65% yield, $[\alpha]_D^{27}$ -16.9° ($CHCl_3$) after chromatography (Al_2O_3, eluted with benzene). Reduction of (-)-16 with $LiAlH_4$ in dry ether gave a solid, which was heated with 20% H_2SO_4 at 100 °C for 4 h to yield (-)-17 in 48% yield after chromatography (Al_2O_3, hexane) as a colorless oil, $[\alpha]_D^{28}$ -61.3° ($CHCl_3$). Dehydrogenation of 17 by heating with sulfur at 230-240 °C for 30 min resulted in the formation of the relay substance, (-)-(2R,4R)-2,4-di(2-naphthyl)pentane (11), $[\alpha]_D^{26}$ -130° ($CHCl_3$). On the other hand, transformation of (+)-7 into the relay substance 11 was rather straightforwardly accomplished as follows. Treatment of (+)-7 with diazomethane gave (+)-8, $[\alpha]_D^{20}$ +249° ($CHCl_3$); mp 112-113 °C (methanol), which was reduced with $LiAlH_4$ in dry THF to provide (+)-9, $[\alpha]_D^{21}$ +322° ($CHCl_3$) in 60% overall yield. Mesylation of 9 gave the mesylate 10, $LiAlH_4$ reduction of which furnished (+)-11 in 69% yield, $[\alpha]_D^{23}$ +287° ($CHCl_3$); bp 190-192 °C (0.1 mmHg). Its ^1H NMR and IR spectra and TLC behavior were identical with those of (-)-11. This enantiomeric relation between two 2,4-di(2-naphthyl)-pentane immediately indicates the 2S,4S absolute configuration to (+)-7.

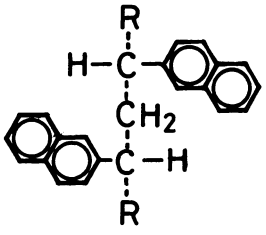
The dicarboxylic acid (+)-7 was converted, with phosphorous pentachloride in benzene (stirred at room temperature for 2.5 h and at 80 °C for additional 30 min), into the corresponding acyl chloride, which was then treated with stannic chloride in benzene (stirred at -10 °C for 1 h and at room temperature for additional 2 h) to furnish (-)-18 in 83% yield, $[\alpha]_D^{28}$ -1618° ($CHCl_3$); mp 212-214 °C (ethanol). The enantiomeric excess of this specimen was determined to be >98% by means of HPLC with a chiral column.[5)]



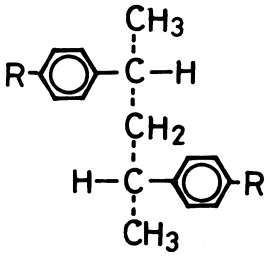
4 R = H
5 R = CO_2CH_3



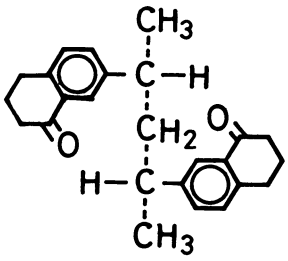
6 R = CO_2H
(+)-**7** R = H



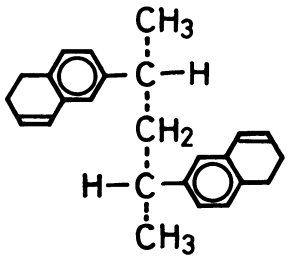
(+)-**8** R = CO_2CH_3
(+)-**9** R = CH_2OH
10 R = CH_2OMs
(+)-**11** R = CH_3



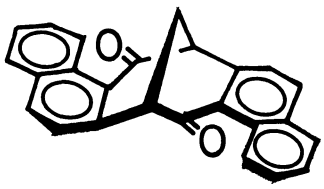
(-)-**12** R = H
(-)-**13** R = $CO(CH_2)_2CO_2H$
14 R = $(CH_2)_3CO_2H$
(-)-**15** R = $(CH_2)_3CO_2CH_3$



(-)-**16**



(-)-**17**



(-)-**18**

Reduction of (-)-18 with $LiAlH_4$ in dry THF at 0 °C for 2 h gave (-)-1 in 64% yield, $[\alpha]_D^{24}$ -437° ($CHCl_3$); mp 227-229 °C (benzene-hexane), a part of which was converted, with acetic anhydride, into (-)-2, $[\alpha]_D^{27}$ -405° ($CHCl_3$); mp 253 °C (dec.) (ethanol). In analogy with $LiAlH_4$ reduction of 2,3:6,7-dibenzobicyclo[3.3.1]nona-2,6-dien-4,8-dione[2)] together with the absolute configuration of (+)-7, we have assigned the 5S,6R,13S,14R configuration to the glycol (-)-1. The ^1H NMR spectrum

of (-)-2 supports this configuration of C_2 symmetry.

High dilution condensation of (-)-1 with pentaethyleneglycol ditosylate and NaH in dry THF (stirred and refluxed for 33 h) provided (-)-3 in 40% yield after chromatography (Al_2O_3, $CHCl_3$) followed by crystallization from benzene-hexane, mp 155-158 °C; $[\alpha]_D^{25}$ -266° ($CHCl_3$). Chiral recognition property of (-)-3 in transport of (±)-1,2-diphenylethylamine hydrochloride and methyl (±)-phenylglycinate hydrochloride was investigated and the results are given in Table 1. Enantiomer differential transport was carried out in a conventional apparatus which consisted of an outer glass vessel and a central glass tube. The 0.005 M (1 M=1 mol dm^{-3}) $CHCl_3$ solution (10 mL) of (-)-3 separated the inner aqueous phase (0.1 M HCl, 10 mL) and the outer aqueous phase (0.08 M HCl, 10 mL) which contained $LiPF_6$ (0.4 M) and the racemic guest (0.04 M). The $CHCl_3$ solution was stirred at a constant speed at 20 °C.

Table 1. Differential transport of enantiomeric molecules

Guest	Time h	Transported %	Configuration of dominantly transported enantiomer	Optical purity %
(±)-1,2-Diphenylethylamine	8	16	S	53
Methyl (±)-phenylglycinate	6	18	R	19

References

1) G. W. Gokel and S. H. Koreniowski, "Macrocyclic Polyether Systems," Springer-Verlag, Berlin, Heidelberg, and New York (1982).

2) H. Tatemitsu, F. Ogura, Y. Nakagawa, M. Nakagawa, K. Naemura, and M. Nakazaki, Bull. Chem. Soc. Jpn., 48, 2473 (1975).

3) All new compounds gave satisfactory elemental analyses and spectral data (^1H NMR and IR). Spectral data for the selected compounds are as follows, 2: ^1H NMR ($CDCl_3$) δ 2.08 (s, 6H, CH_3), 2.42 (t, J=3 Hz, 2H, CH_2), 4.00 (br s, 2H, CH), 7.12 (d, J=9 Hz, 2H, CHO-), 6.9-7.9 (m, 12H, aromatic); 3: ^1H NMR ($CDCl_3$) δ 2.18 (t, J=3 Hz, 2H, CH_2), 2.7-3.5 (m, 20H, $-OCH_2CH_2O-$), 3.84 (br s, 2H, CH), 5.82 (d, J=8 Hz, CHO-), 7.2-8.4 (m, 12H, aromatic); 18: IR (KBr) 1670 cm^{-1}; CD (EtOH) $[\theta]_{279}$ -2.96×10^4, $[\theta]_{295}$ 0, $[\theta]_{315}$ $+5.75\times10^4$, $[\theta]_{333}$ 0, $[\theta]_{351}$ -9.23×10^4, $[\theta]_{366}$ -8.36×10^4, $[\theta]_{379}$ -5.18×10^4(sh); ^1H NMR ($CDCl_3$) δ 3.12 (t, J=3 Hz, 2H, CH_2), 4.16 (t, J=3 Hz, 2H, CH), 7.2-9.5 (m, 12H, aromatic).

4) All structural formulas in this communication with (+) or (-) signs are presented in their absolute configuration.

5) H. Yuki, Y. Okamoto, and I. Okamoto, J. Am. Chem. Soc., 102, 6356 (1980); Y. Okamoto, S. Honda, I. Okamoto, and H. Yuki, ibid., 103, 6971 (1981).

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