Synthesis and Chiral Recognition of Novel Crown Ethers incorporating Helicene Chiral Centres

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Two novel optically active crown ethers (7) and (14) incorporating helicene molecular frameworks were prepared, and their chiral recognition properties were examined to show that (M)-(-)-(7) and (M)-(-)-(14) had opposite chiral recognition for the transport of methyl phenylglycinate or 1-phenylethylamine.

Although a large number of chiral crown ethers incorporating various chiral centres have been prepared, none possessing helicene molecular frameworks as the chiral centre have been reported. Here we report the preparation of two novel helicene crowns (7) and (14) and their chiral recognition properties. The Wittig condensation of 4-bromo-2,5-dimethylbenzaldehyde† with the bis(triphenylphosphonium) salt (2) [from the dibromide (1)²] using NaOMe-DMF (DMF = N,N-dimethylformamide) gave a mixture of stereoisomeric products (3). This was dissolved in benzene and irradiated with a high pressure mercury lamp‡ for 3 h to give (4), m.p. 227—279 °C [27% yield from (1)]. Lithiation of (4) with BunLi in tetrahydrofuran (THF) followed by formylation with DMF gave the dialdehyde (5), m.p. 280—282 °C, which was reduced with LiAlH4 to the diol (6), m.p. 227—

(1)
$$R = CH_2Br$$

(2) $R = CH_2PPh_3Br$ Me
(3) $R = CH = CH - CH$ Me
(4) $R = Br$
(5) $R = CHO$
(6) $R = CH_2OH$

(8)
$$R = CH_2Br$$
 (11) $R = Br$
(9) $R = CH_2PPh_3Br$ (12) $R = CHO$
(10) $R = CH \implies CH \implies CH \implies CH_2OH$
(M) $-(-) -(14)$ $R = CH_2OO$
 $R = CH_2OO$

229 °C. Condensation of (6) with 3,6,9,12-tetraoxatetradecane-1,14-diyl bistoluene-*p*-sulphonate³ (NaH–THF) gave the pentahelicene crown ether (7), \S m.p. 116—117 °C (26% yield) after chromatography on alumina; ¹H n.m.r. (CDCl₃) δ 0.72 (s, 2CH₃), 2.83 (s, 2CH₃), and 4.37 (q, 2ArCH₂).

The hexahelicene crown (14) was prepared in the same way from the dibromide (8).⁴ The Wittig condensation of *p*-bromobenzaldehyde with the bis(triphenylphosphonium) bromide (9) prepared from (8), gave a mixture of stereoisomers of the stilbene derivative (10). A solution of (10) containing iodine was irradiated with a high pressure mercury lamp for 3 h to yield 2,15-dibromohexahelicene (11), m.p. 246—248 °C [17% yield from (8)]. Formylation of (11) gave (12), m.p. 287—289 °C (74% yield) which was reduced with LiAlH₄ to the diol (13), m.p. 233—234 °C (50% yield). The alcohol (13) condensed with 3,6,9,12-tetraoxatetradecane-1,14-diyl bistoluene-*p*-sulphonate to afford 2,15-hexaheliceno-27-crown-6 (14), m.p. 78—80 °C (54% yield); ¹H n.m.r. (CDCl₃) 3.92 (q, 2ArCH₂O).

Optical resolution of both (\pm) -(7) and (\pm) -(14) was achieved by h.p.l.c. with a column packed with (\pm) -poly-(triphenylmethyl methacrylate);⁵ elution with methanol gave optically pure (M)-(-)-(7), (P)-(+)-(7), (M)-(-)-(14), and (P)-(+)-(14) with $[\alpha]_D^{25}$ (MeOH) -754, +748, -1269, and +1260° respectively. Comparison of their c.d. spectra

Table 1. Differential transport⁸ of enantiomeric molecules through bulk liquid membranes containing (7) and (14).^a

Host ^b	Guest	Time /h	Transport	Configura- tion of dominant enantiomer	Optical purity
(M)- $(-)$ - (7)	e	6	6	S	75
(P)-(+)-(7)	e	6	6	R	77
(M)- $(-)$ - (7)	d	5	12	R	26
(P)- $(+)$ - (7)	d	5	11	S	29
(M)- $(-)$ - (14)	c	6	2	R	26
(P)- $(+)$ - (14)	e	6	2	S	28
(M)- $()$ - (14)	d	4	5	S	20
(P)- $(+)$ - (14)	d	4	5	R	18

^aCarried out in conventional apparatus (ref. 9) which consisted of an outer cylindrical glass vessel (24.5 mm inner diameter) and a central glass tube (15.5 mm inner diameter). The 0.01 m CHCl₃ solution of the host separated the inner aqueous phase (0.1 m HCl) and the outer aqueous phase (0.08 m HCl) which contained LiPF₆ (0.4 m) and the racemic guest (0.08 m). The organic layer was stirred at a constant speed (60 r.p.m.) at 20 °C, and transport was followed by monitoring the absorbance at 262 nm and [θ]₂₆₂ of the inner aqueous phase. ^b In the absence of crown ethers, there was no detectable transfer of the substrates. ^c Methyl (\pm)-phenylglycinate hydrochloride. ^d (\pm)-1-Phenylethylamine hydrochloride.

^{† 4-}Bromo-2,5-dimethylbenzaldehyde, m.p. 59—60 °C, was prepared by oxidation [with $Me_2C=N(O)ONa$] of 2-bromo-5-bromo-methyl-p-xylene obtained by bromomethylation of 2-bromo-p-xylene.

[‡] Halos, EH-300, Eikosha Co., Osaka, Japan.

[§] Satisfactory analytical and spectroscopic data have been obtained for all new compounds.

[¶] Both (-)-(7) and (-)-(14) with M-helicity were eluted first.

with those of authentic (M)-(-)-pentahelicene**6 and (M)-(-)-hexahelicene⁷ established their absolute configurations.

Table 1 lists the chiral recognition behaviour of (7) and (14) with methyl (\pm)-phenylglycinate hydrochloride and (\pm)-1-phenylethylamine hydrochloride. Table 1 shows (a) that (7) has a higher enantiomer selectivity than (14) towards both substrates, and methyl phenylglycinate of as high as 77% optical purity was 6% transported by (7), and (b) that (7) and (14) although of the same helicity exhibit opposite chiral recognition toward both substrates. This result is compatible with examination of Corey-Pauling-Koltun models for (7) and (14) which reveal that the ether part of (M)-(-)-crown (7) has P-helicity while that of (M)-(-)-crown (14) has M-helicity.

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^{**} In contrast to optically labile (M)-(-)-pentahelicene, (M)-(-)-crown (7) was quite stable showing no optical rotation change after refluxing its methanolic solution for 24 h.