

Synthesis and Chiral Recognition of Optically Active Crown Ethers incorporating a *trans* Doubly-bridged Ethylene Framework

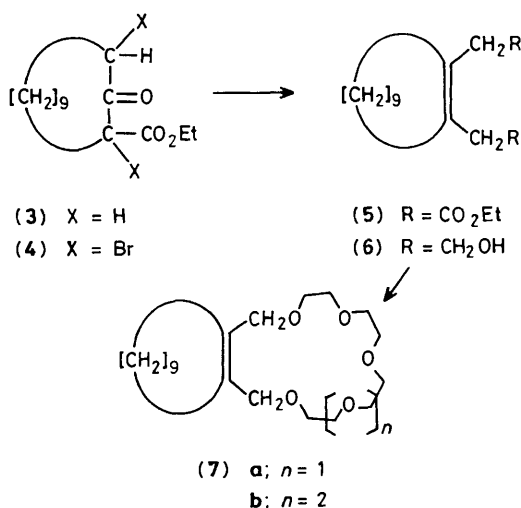
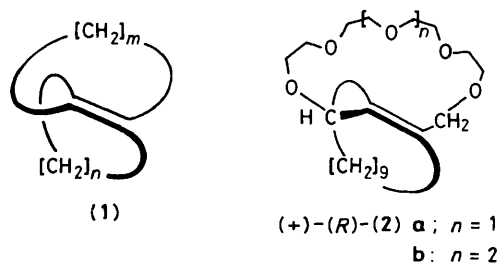
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Two novel optically active crown ethers (**2a**) and (**2b**) having a *trans* doubly-bridged ethylene framework were prepared, and examination of their chiral recognition behaviour showed that (+)-(*R*)-(**2a**) has a high enantiomer selectivity for methyl α -phenylglycinate.

Our interest in chiral twisted π -electron systems¹ has led us to report the first synthesis of *trans* doubly-bridged ethylene (**1**).² As a natural extension of these studies, we report here the preparation and chiral recognition properties of a novel optically active crown ether (+)-(*R*)-(**2a**) and (+)-(*R*)-(**2b**) incorporating a *trans* doubly-bridged ethylene framework.

Bromination of 2-ethoxycarbonylcyclododecanone (**3**)³ with bromine in carbon tetrachloride followed by the Favorskii rearrangement using sodium methoxide gave the *cis* ester (**5**) [b.p. 139–141 °C (0.1mm)] which was reduced with LiAlH₄ to the *cis* alcohol (**6**)† [m.p. 61.5–62.5 °C, 36% yield from (**1**)]. Condensation of (**6**) with 3,6,9-trioxaundeca-1,11-diyl bis(toluene-*p*-sulphonate) (NaH-tetrahydrofuran) afforded the *cis* doubly-bridged ethylene crown ether (**7a**) (m.p. 56–57 °C, 68% yield); ¹H n.m.r. (CDCl₃) δ 1.35 (br.s, 14H), 2.30 (t, 4H), 3.62 (s, 16H), and 4.06 (s, 4H). A cyclohexane solution of (**7a**) was irradiated with a low-pressure mercury lamp‡ under nitrogen. Monitoring the reaction by h.p.l.c. indicated that irradiation for 3 h yielded a 1:5 mixture of the *cis* and *trans* isomers. Separation of these isomers was



† Satisfactory analytical and spectroscopic data have been obtained for all new compounds.

‡ HALOS, PIL-30, Eikosha Co., Osaka.

achieved by a chemical method which made use of the expected inertness of the *trans* isomer toward dichlorocarbene owing to the buried nature of the double bond.^{2a} The isomeric mixture when stirred with 50% aqueous NaOH, CHCl₃, and cetyltrimethylammonium chloride yielded (preparative t.l.c.) the unchanged (\pm)-*trans*-crown-5 (**2a**) (m.p. 41–42 °C, 48% yield); ¹H n.m.r. (CDCl₃) δ 0.80–1.80 (m, 14H), 2.10–2.62 (m, 4H), 3.61 (s, 16H), and 4.24 (AB quartet, J_{ab} 17 Hz, 4H), and the dichlorocarbene adduct of the *cis* isomer (**7a**) (m.p. 53–54 °C, 9% yield).

The (\pm)-*trans*-crown-6 (**2b**) was prepared in the same way from (**6**). The alcohol (**6**) condensed with 3,6,9,12-tetraoxatetradecane-1,14-diyl bis(toluene-*p*-sulphonate) to afford the *cis*-crown-6 (**7b**) (m.p. 48–49 °C, 65% yield); ¹H n.m.r. (CDCl₃) δ 1.35 (br.s, 14H), 2.30 (t, 4H), 3.62 (s, 20H), and 4.06 (s, 4H). Irradiation (3 h) of (**7b**) with the low-pressure mercury lamp yielded a 1:5 mixture (*cis*:*trans*) which was treated with dichlorocarbene as described for the preparation of (**2a**). Preparative silica gel t.l.c. gave a 42% yield of (\pm)-*trans*-crown-6 (**2b**), colourless oil; ¹H n.m.r. (CDCl₃) δ 0.80–1.80 (m, 14H), 2.20–2.65 (m, 4H), 3.61 (s, 20H), and 4.24 (AB quartet, J_{ab} 18 Hz, 4H).

Optical resolution of both (\pm)-(**2a**) and (\pm)-(**2b**) achieved by h.p.l.c. with a column packed with (+)-poly(triphenylmethyl methacrylate),⁴ on elution§ with methanol gave optically pure (+)-(*R*)-(**2a**), (–)-(*S*)-(**2a**), (+)-(*R*)-(**2b**), and (–)-(*S*)-(**2b**)¶ with $[\alpha]_D^{25}$ (MeOH) +31.6°, –30.8°, +29.3°, and –28.4° respectively.

Table 1. Differential transport⁶ of enantiomeric molecules through bulk liquid membranes containing (+)-(*R*)-(**2a**) and (+)-(*R*)-(**2b**).^a

Host	Guest	Time/h	% Transport	Configuration of dominant enantiomer	% E.e.
(+)-(<i>R</i>)-(2a)	b	1.5	4.5	(<i>S</i>)	27
	c	1.0	6.1	(<i>R</i>)	61
(+)-(<i>R</i>)-(2b)	b	1.5	4.6	(<i>S</i>)	24
	c	1.0	6.5	(<i>R</i>)	39

^a Carried out in conventional apparatus⁷ 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 $[\theta]_{262}$ of the inner aqueous phase. ^b (\pm)-1-Phenylethylamine hydrochloride. ^c Methyl (\pm)-phenylglycinate hydrochloride.

§ Both (+)-(**2a**) and (+)-(**2b**) were eluted first.

¶ The (*R*) configurations of (+)-(**2a**) and (+)-(**2b**) were determined by comparison of their c.d. spectra with that of authentic (–)-(*R*)-[8.8]betweenanene (**1**, $m = n = 8$).^{2b,5}

Table 1 lists the chiral recognition behaviour of (**2a**) and (**2b**) with methyl (\pm)-phenylglycinate hydrochloride and (\pm)-1-phenylethylamine hydrochloride. These results indicate that (**2a**) has a higher enantiomer selectivity than (**2b**) towards both substrates, and methyl phenylglycinate of as high as 61% enantiomeric excess (e.e.) was transported by (+)-(*R*)-(**2a**).

Received, 8th July 1985; Com. 973

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