Synthesis and Chiral Recognition of an Optically Active Bis-crown Ether incorporating a Diphenanthrylnaphthalene Moiety as the Chiral Centre

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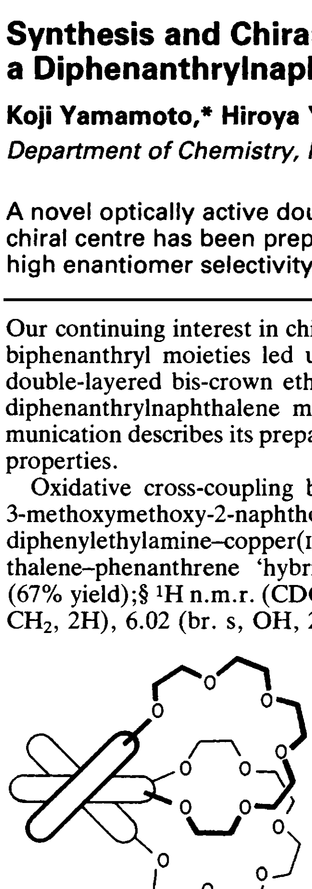
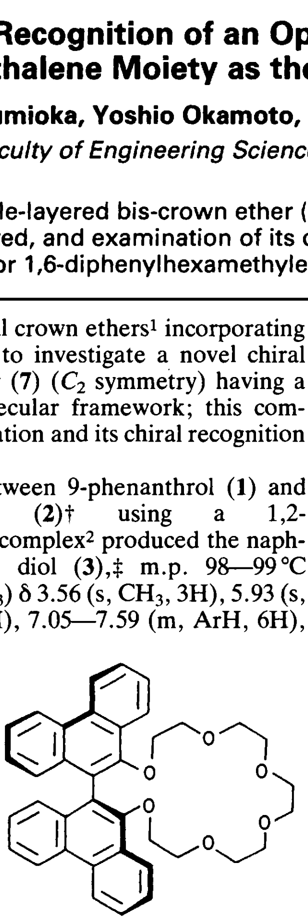
A novel optically active double-layered bis-crown ether (−)-(*S,S*)-(**7**) with a diphenanthrylnaphthalene moiety as the chiral centre has been prepared, and examination of its chiral recognition behaviour showed that (−)-(*S,S*)-(**7**) has a high enantiomer selectivity for 1,6-diphenylhexamethylene-1,6-diamine.

Our continuing interest in chiral crown ethers[1] incorporating biphenanthryl moieties led us to investigate a novel chiral double-layered bis-crown ether (**7**) (C_2 symmetry) having a diphenanthrylnaphthalene molecular framework; this communication describes its preparation and its chiral recognition properties.

Oxidative cross-coupling between 9-phenanthrol (**1**) and 3-methoxymethoxy-2-naphthol (**2**)† using a 1,2-diphenylethylamine–copper(II) complex[2] produced the naphthalene–phenanthrene 'hybrid' diol (**3**),‡ m.p. 98—99 °C (67% yield);§ ^{1}H n.m.r. ($CDCl_3$) δ 3.56 (s, CH_3, 3H), 5.93 (s, CH_2, 2H), 6.02 (br. s, OH, 2H), 7.05—7.59 (m, ArH, 6H), 7.62—7.96 (m, ArH, 4H), and 8.36—8.95 (m, ArH, 3H). Optical resolution of (±)-(**3**) was achieved by h.p.l.c. on a column packed with (+)-poly(triphenylmethyl methacrylate)[3] on silica gel (elution with methanol), giving optically pure (−)-(*S*)-(**3**)¶ and (+)-(*R*)-(**3**)‖ with $[\alpha]_D^{26}$ (MeOH) −74.8 and +74.6°, respectively. Condensation of (−)-(*S*)-(**3**) with 3,6,9,12-tetraoxatetradecane-1,14-diyl bistoluene-*p*-sulphonate (Bu^tOK–tetrahydrofuran) afforded the mono-crown ether (−)-(*S*)-(**4**) whose hydrolysis [in conc. HCl–$CHCl_3$–MeOH (1 : 40 : 80) at 25 °C (2 h)] produced (−)-(*S*)-hydroxy-crown ether (**5**) {m.p. 100—101 °C, $[\alpha]_D^{25}$ −65.3° ($CHCl_3$), 68% yield from (−)-(**3**)}. Stereoselective oxidative cross-coupling between the two phenols (−)-(*S*)-(**5**) and (**1**) using the (−)-(*R*)-1,2-diphenylethylamine–copper(II) complex[2] gave an 8 : 1 stereoisomeric mixture of the cross-coupling products, (*S,S*)- and (*R,S*)-(**6**), which was separated by h.p.l.c. on a column packed with (+)-poly(triphenylmethyl methacrylate)[3] on silica gel (elution with methanol)[3] to yield (−)-(*S,S*)-(**6**){m.p. 122—124 °C, 46% yield, $[\alpha]_D^{25}$ −102° ($CHCl_3$)} and its (−)-(*R,S*) isomer {m.p. 87—88 °C, 6% yield, $[\alpha]_D^{25}$ −12.6° ($CHCl_3$)}, respectively. Final condensation of



(−)-(*S,S*)-(**7**)



(−)-(*S*)-(**8**)

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† 3-Methoxymethoxy-2-naphthol (**2**) was derived from 2,3-dihydroxynaphthalene by reaction with chloromethyl methyl ether (Bu^tOK–tetrahydrofuran).

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

§ Two additional products have been obtained by this cross-coupling reaction; 10,10′-dihydroxy-9,9′-biphenanthryl[1] (12% yield) and 2,2′-dihydroxy-3,3′-dimethoxymethoxy-1,1′-binaphthyl (4% yield).

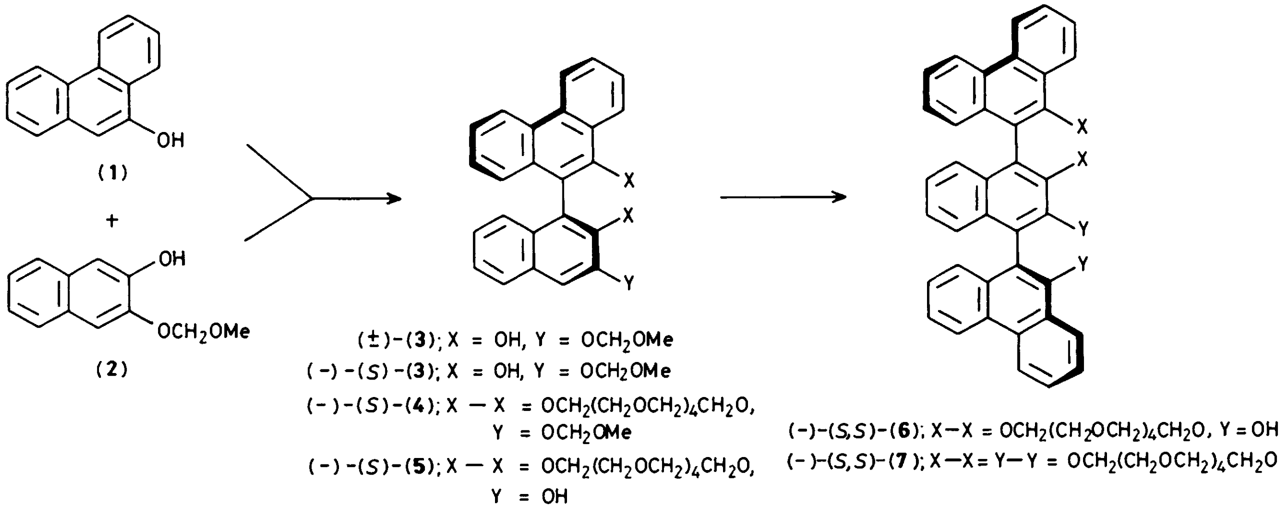
¶ (−)-(*S*)-(**3**) was the first moving fraction. Stereoselective oxidative cross-coupling between (**1**) and (**2**) using the (−)-(*R*)-1,2-diphenylethylamine–copper(II) complex[2] gave (−)-(*S*)-(**3**) {m.p. 95—96 °C, 65% yield, $[\alpha]_D^{26}$ −59.7° ($CHCl_3$), 80% optical purity}.

‖ The absolute configuration of (+)-(**3**) was determined by the application of a chiral recognition method developed by Miyano and co-workers.[4] The intermolecular cyclization of (+)-(**3**) with (±)-1,1′-binaphthyl-2,2′-dicarbonyl dichloride followed by hydrolysis gave recovered (+)-(**3**) and (+)-(*R*)-1,1′-binaphthyl-2,2′-dicarboxylic acid {m.p. 259—264 °C, $[\alpha]_D^{25}$ + 34° (0.1 M NaOH), 31% optical purity}. This result unequivocally indicates that (+)-(**3**) has the same *R* configuration.

Table 1. Differential transport[6] of enantiomeric molecules through bulk liquid membranes containing (−)-(*S*,*S*)-(**7**) and (−)-(*S*)-(**8**).[a]

Host[b]	Guest	Time/ h	Transport (%)	Configuration of dominant enantiomer	Optical purity (%)
(−)-(*S*,*S*)-(**7**)	c	1.0	3.5	L(*R*,*R*)	66
	d	0.5	3.9	(*S*,*S*)	82
(−)-(*S*)-(**8**)	c	22	3.4	L(*R*,*R*)	18
	d	10	3.6	(*S*,*S*)	26

[a] Differential transport of the hexafluorophosphate salt of racemic guests with optically active crown ethers was carried out in conventional apparatus[7] consisting 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 $CHCl_3$ solution of the host separated the inner aqueous phase (0.1 M HCl) and the outer aqueous phase (0.08 M HCl), which contained $LiPF_6$ (0.4 M) and the racemic guest (0.08 M). The organic layer was stirred at a constant speed (60 r.p.m.), and transport was followed by monitoring the absorbance at 248 (for guest c) and 260 nm (for guest d), and $[\theta]_{248}$ and $[\theta]_{262}$ of the inner aqueous phase. [b] In the absence of crown ethers, there was no detectable transfer of the substrates. [c] (±)-Cystine dimethyl ester dihydrochloride. [d] (±)-1,6-Diphenylhexamethylene-1,6-diamine dihydrochloride.



(1)

(2)

(±)-(3); X = OH, Y = OCH_2OMe

(−)-(S)-(3); X = OH, Y = OCH_2OMe

(−)-(S)-(4); X — X = $OCH_2(CH_2OCH_2)_4CH_2O$, Y = OCH_2OMe

(−)-(S)-(5); X — X = $OCH_2(CH_2OCH_2)_4CH_2O$, Y = OH

(−)-(S,S)-(6); X—X = $OCH_2(CH_2OCH_2)_4CH_2O$, Y = OH

(−)-(S,S)-(7); X—X = Y—Y = $OCH_2(CH_2OCH_2)_4CH_2O$

(−)-(*S*,*S*)-(**6**) with 3,6,9,12-tetraoxatetradecane-1,14-diyl bis-toluene-*p*-sulphonate afforded the desired bis-crown ether (−)-(*S*,*S*)-(**7**) after chromatography on alumina; m.p. 86—88 °C, 32% yield, $[\alpha]_D^{25}$ −179° ($CHCl_3$); ^1H n.m.r. ($CDCl_3$) δ 2.96—4.32 (m, CH_2, 40H), 7.06—8.04 (m, ArH, 16H), and 8.28—8.92 (m, ArH, 4H).

Examination of the Corey–Pauling–Koltun molecular model of (*S*,*S*)-(**7**) led us to select potential guest molecules containing two bindable functional groups to be located between two binding sites of host (**7**) in a complementary manner. The bifunctional host (−)-(*S*,*S*)-(**7**) was compared with the monofunctional host (−)-(*S*)-(**8**)[1] in its chiral recognition abilities. Table 1 shows the chiral recognition behaviour of (**7**) and (**8**) with two guests, (±)-cystine dimethyl ester dihydrochloride[4] and (±)-1,6-diphenylhexamethylene-1,6-diamine dihydrochloride.** These experiments indicate that the host (**7**), containing two binding sites, has a higher enantiomer selectivity than the monofunctional host (**8**) towards both guests, and 1,6-diphenylhexamethylene-1,6-diamine of up to 82% optical purity was 3.9% transported by (−)-(*S*,*S*)-(**7**).

Received, 11th September 1986; Com. 1303

** $LiAlH_4$ reduction of the dioxime derived from 1,4-dibenzoylbutane followed by h.p.l.c. separation employing a column packed with cellulose tris(3,5-dimethylphenyl carbamate) on silica gel[5] [elution with hexane–ethanol (7 : 3)] gave *meso* (m.p. 57—58 °C) and racemic 1,6-diphenylhexamethylene-1,6-diamine (m.p. 39—40 °C), respectively. Optical resolution of the racemic diamine was also achieved by h.p.l.c. on a similarly packed column [elution with hexane–ethanol (8 : 2)] to afford optically pure (−)-(*R*,*R*)-{$[\alpha]_D^{26}$ −10.8° (MeOH), $[\theta]_{260}$ -3.36×10^2 (0.1 M HCl)} and (+)-(*S*,*S*)-diamine {$[\alpha]_D^{26}$ + 10.6° (MeOH), $[\theta]_{260}$ $+3.35 \times 10^2$ (0.1 M HCl)}, respectively. Comparison of their c.d. spectra with that of authentic (−)-(*S*)-1-phenylethylamine established their absolute configurations.

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