chloride and lithium chloride. After initial, partial purification by preparative TLC, the crude product (112 mg, 67% yield) was crystallized (hexane) to give **10** (64.5 mg), needles, mp 60–61 °C, $[\alpha]^{20}_D$ +22.0° (*c* 0.9, $CHCl_3$) [lit.[12] mp 50–54 °C, $[\alpha]^{20}_D$ +13.7° (*c* 20, $CHCl_3$)].

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Registry No. **5**, 33149-64-3; **6**, 101402-02-2; **7**, 101402-03-3; **8**, 7322-88-5; **9**, 73773-07-6; **10**, 101402-04-4; *p*-nitrobenzhydrol acetate, 101402-05-5; *o*-acetyl-*p*-nitromandelic acid, 29898-08-6.

Enantiomeric Differentiation of Racemic Organic Salts by Chiral Crown Ethers Derived from Sugars

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Chiral crown ethers have been derived from (*R*)- and (*S*)-binaphthol[1,2] and carbohydrate residues[3,4] which differentiate between enantiomers of racemic substrates. We have recently developed an easy and new method[5] to prepare benzo-18-crown-6 ethers exhibiting chirality due to the presence of a carbohydrate moiety as an inexpensive source of asymmetry. This method is outlined in Scheme I.

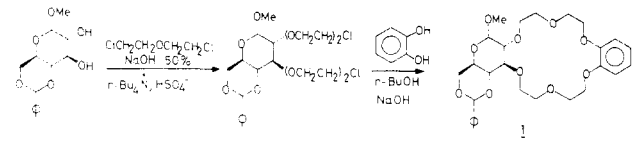
These crown ethers are obtained in good overall yields (60–70% range) from commercially available materials, permitting thus preparation at a scale large enough (20–30 g) to achieve complexation experiments. The nine chiral crown ethers presented here (Scheme II) have been derived from the following diols: methyl 4,6-*O*-benzylidene-α- and -β-D-glucopyranosides,[6] **1** and **5**, methyl 4,6-*O*-benzylidene-α- and -β-D-galactopyranosides,[6] **6** and **7**, methyl 4,6-*O*-benzylidene-α-D-mannopyranoside,[7] **2**, 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose,[8,9] **3**, 3,4-*O*-isopropylidene-β-D-arabinofuranose,[10] **4**, methyl 4,6-*O*-benzylidene-α-D-altropyranose, **8**, prepared from **1** by closure and opening of the 2,3-epoxide[11] and methyl 4,6-*O*-benzylidene-α-D-alloyranoside, **9**, obtained from **1** by benzoylation at the C-2 position and oxidation and reduction[12,13] at the C-3 position.

We want to report here on the complexing behavior of these ethers toward primary alkylammonium salts and especially salts of α-amino acid esters. First, they are all able to dissolve the salts in aprotic organic solvents. Quantitative assessment of both complexing power and enantiomeric differentiation was obtained by using a NMR spectroscopic method,[14] because significant changes were observed in the spectra of both the crown and the salt when they were mixed indicating thus the formation of complexes.

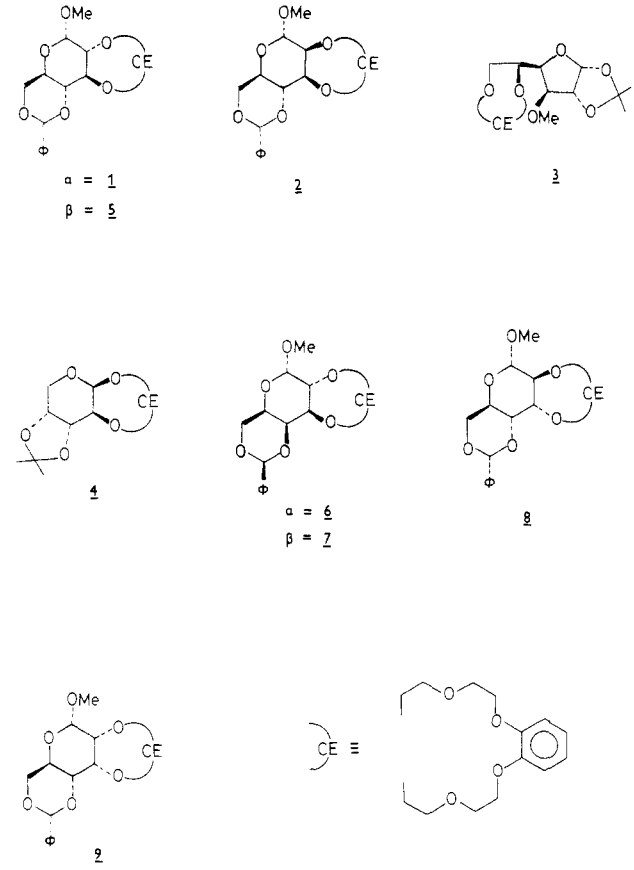
Experimental Section

a. Preparation of the Crown Ethers. A representative procedure is as the following. Methyl 4,6-*O*-benzylidene-2,3-[1,2-benzenediylbis((oxyethoxy)ethyl)]-*O*-α-D-glucopyranoside, **1**. A solution of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (20 g, 71 mmol) and tetra-*n*-butylammonium hydrogen sulfate

Scheme I



Scheme II



(24.1 g, 71 mmol) in bis[2-chloroethyl ether] (300 mL) is vigorously stirred at room temperature with 50% aqueous sodium hydroxide to yield after 4 h methyl 4,6-*O*-benzylidene-2,3-*bis*-*O*-[(2-chloroethoxy)ethyl]-α-D-glucopyranoside which crystallizes from ethanol [26.3 g (75%), mp 62–63 °C, $[\alpha_D]^{20}$ +43° (*c* 2, $CHCl_3$)]. This derivative (25 g, 50 mmol) is then treated with catechol (5.5 g, 50 mmol) in 1-butanol containing dry sodium hydroxide powder (4 g, 100 mmol) by stirring at reflux for 8 h under an inert atmosphere. Crystallization from benzene/petroleum ether affords **1** [17.5 g (65%), mp 130 °C, $[\alpha]_D^{20}$ +15° (*c* 1, $CHCl_3$)].

b. General Method. In a typical experiment a 0.15 M solution

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Table I. Complexation and Discrimination Data for the Interaction of Crown Ethers 1-9 with Ammonium Salts[a]

crown ether	equlbrm values	phenylethylamine	phenylglycine	Ala	Val	Phe	Tyr	Trp	Met
1	R[b]	0.65	0.98	0.89	0.80	1.00	1.00	1.00	0.93
	CRF[b]	1.50	2.30	1.50	2.70	2.00	1.50	1.60	1.60
	major enantmr	*R*	D	D	D	D	D	D	D
2	R	0.70	1.00	0.98	0.90	1.00	1.00	1.00	0.93
	CRF	1.30	1.80	1.10	1.40	1.30	1.15	1.30	1.05
	major enantmr	*S*	L	L	L	L	L	L	L
3	R	0.35	0.50	0.40	0.45	0.50	0.40	0.30	0.30
	CRF	1.10	1.10	1.00	1.05	1.10	1.00	1.00	1.00
	major enantmr	*S*	L	–	L	L	–	–	–
4	R	0.60	0.90	0.80	0.80	0.85	0.50	0.40	0.60
	CRF	1.20	1.00	1.00	1.00	1.05	1.00	1.00	1.00
	major enantmr	*S*	–	–	–	L	–	–	–
5	R	0.70	0.95	0.98	1.00	1.00	1.00	1.00	1.00
	CRF	1.50	2.00	1.80	1.80	2.10	2.00	1.80	1.70
	major enantmr	*R*	D	D	D	D	D	D	D
6	R	0.70	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	CRF	1.50	2.10	1.40	1.80	1.70	2.00	2.00	1.10
	major enantmr	*R*	D	D	D	D	D	yd	D
7	R	0.60	0.95	0.90	1.00	1.00	1.00	1.00	1.00
	CRF	1.60	2.10	1.70	2.60	2.00	1.50	1.50	1.80
	major enantmr	*R*	D	D	D	D	D	D	D
8	R	0.50	0.60	0.50	0.70	0.70	0.75	0.75	0.60
	CRF	1.20	1.50	2.10	1.70	1.20	1.50	1.40	1.00
	major enantmr	*R*	D	D	D	D	D	D	D
9	R	0.60	0.90	0.90	0.90	0.80	1.00	1.00	1.00
	CRF	1.40	2.00	1.70	2.50	2.00	1.50	2.00	1.50
	major enantmr	*R*	D	D	D	D	D	D	D

[a] Hexafluorophosphates for the amino acid methyl ester and thiocyanate for the phenylethylamine. [b] R is the molar ratio crown-ether/salt in the organic phase; CRF (chiral recognition factor) is the ratio L/D (or D/L) always in the organic phase according to ref 14.

(2 mL) of 1 in $CDCl_3$ was shaken at room temperature with a 1 M solution of D,L-phenylglycine methyl ester hydrochloride in D_2O (1 mL) which was 4 M in $LiPF_6$ and adjusted to pH 4 with a sufficient amount of lithium deuteriohydroxide. The layers were centrifuged and separated carefully, the meniscus being discarded. The ^1H and ^{13}C spectra of the organic layers were then recorded. The relative concentrations of salt to crown ether were determined by integration of the appropriate signals. Since diastereoisomeric complex formation is accompanied by small chemical shift differences between originally coincident signals arising from the previously recorded racemic salts, enantiomeric differentiation (i.e., the D/L ratios) was deduced by integration on expanded spectra (5 Hz/cm). Extraction experiments were also performed with pure D and L enantiomers, allowing configurational assignments to be made.

In another set of experiments, by progressively increasing the ratio of salt vs. crown, we checked by ^1H NMR that the diastereoisomeric complexes were 1:1 in all the cases.

The shifting NMR signals we relied upon were the following: for the crown ether, the anomeric proton of the sugar moiety; for the salt, depending upon its nature, the ^1H signal of the methyl groups for phenylethylamine, valine, and alanine, the signal of the protons on the asymmetric carbon atom for phenylglycine, and the ^{13}C signal of the ester carbonyl group for the others. Our results are summarized in the Table I.

c. Physical and Spectral Data. **5**: mp 120–122 °C (from benzene–hexane); $[\alpha]_D^{25}$ –51.6° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 7.42–7.52 (m, 2 H, C_6H_5), 7.28–7.40 (m, 3 H, C_6H_5), 6.9 (s, 4 H, C_6H_4), 5.52 (s, 1 H, CHC_6H_5), 4.35 (d, 1 H, H-1, J_{1-2} = 7.5 Hz), 4.32 (dd, 1 H, H-6′, $J_{6-6'}$ = 12 Hz), 3.55–4.25 (m, 19 H, H-3, H-4, H-6, CH_2CH_2), 3.54 (s, 3 H, OCH_3), 3.36 (m, 1 H, H-5, J_{5-6} = 5 Hz), 3.22 (t, 1 H, H-2, J_{2-3} = 8.5 Hz).

6: gum; $[\alpha]_D^{25}$ +82° (*c* 1.02, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 7.65–7.80 (m, 2 H, C_6H_5), 7.30–7.40 (m, 3 H, C_6H_5), 6.89 (s, 4 H, C_6H_4), 5.55 (s, 1 H, CHC_6H_5), 4.79 (d, 1 H, H-1, J_{1-2} = 3.5 Hz), 4.10–4.40 (m, 3 H, H-5, H-6′), 3.55–4.0 (m, 19 H, H-2, H-3, H-4, CH_2CH_2), 3.38 (s, 3 H, OCH_3).

7: mp 138–139 °C (from benzene–hexane); $[\alpha]_D^{25}$ +33.5° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 7.48–4.58 (m, 2 H, C_6H_5), 7.26–7.38 (m, 3 H, C_6H_5), 6.89 (s, 4 H, C_6H_4), 5.52 (s, 1 H, CHC_6H_5), 4.35 (dd, 1 H, H-6, $J_{6-6'}$ = 12 Hz), 4.21 (d, 1 H, H-1, J_{1-2} = 7.5 Hz), 3.57–4.18 (m, 19 H, H-3, H-4, H-5, CH_2CH_2), 3.55 (s, 3 H, OCH_3), 3.48 (dd, 1 H, H-2, J_{2-3} = 9 Hz).

8: gum; $[\alpha]_D^{25}$ + 39.1° (*c* 1.05, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 7.65–7.75 (m, 2 H, C_6H_5), 7.30–7.40 (m, 3 H, C_6H_5), 6.89 (s, 4 H, C_6H_4), 5.52 (s, 1 H, CHC_6H_5), 4.58 (s, 1 H, H-1), 4.05–4.35 (m, 4 H, H-3 (H-4), H-5, H-6, H-6′), 3.40–4.05 (m, 18 H, H-2, H-4 (H-3), CH_2CH_2), 3.35 (s, 3 H, OCH_3).

9: mp 50–51 °C (from benzene); $[\alpha]_D^{25}$ +82.5° (*c* 0.91, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 7.75–7.80 (m, 2 H, C_6H_5), 7.35–7.50 (m, 3 H, C_6H_5), 6.91 (s, 4 H, C_6H_4), 5.50 (s, 1 H, CHC_6H_5), 4.72 (d, 1 H, H-1, J_{1-2} = 4 Hz), 3.99–4.20 (m, 3 H, H-3, H-5, H-6), 3.48–3.94 (m, 18 H, H-4, H-6′, CH_2CH_2), 3.42 (dd, 1 H, H-2, J_{2-3} = 5.2 Hz), 3.39 (s, 3 H, OCH_3).

Satisfactory analytical data have been obtained for the compounds **5–9** (±0.35 for C, 0.16 for H, and 0.65 for O).

Discussion

Table I shows that some of our ethers form strong complexes with primary alkylammonium salts. More interesting is their ability to discriminate between enantiomers, especially when they contain a phenyl group. Inspection of CPK space-filling molecular models suggests that both the catechol residue and, to a less extent, the 4,6-*O*-benzylidene ring play an important role in enantiomeric differentiation due to electronic interactions between them and the salt as they may act as dipole–dipole interaction acceptors. On another hand, the catechol residue tends to rigidify the crown which adopts a well-defined conformation. The 4,6-benzylidene acetal, which locks the conformation of the pyranose ring, acts in the same way. It is of interest to note that a majority of crown ethers forms stronger complexes with D enantiomers whereas crown ether **2** does it with the L enantiomers of the same aminoacid ester salts. Molecular model examination does not provide sufficient data to explain this behavior, especially as our crown ethers are heterotopic, i.e., can form two different diastereoisomeric complexes accroding to the side of the ring on which the complexation takes place.

In order to understand more precisely how the complexation takes place, we are collecting X-ray diffraction data on **1**: D-phenylglycine methyl ester hexafluoro-

phosphate complex. We already know that its space group is $P2^1$, a = 18.016 (4), b = 8.622 (2), and c = 13.420 (3) Å.

On another hand, we are checking the use of these chiral crown ethers to separate enantiomers when covalently fixed on silica gel and to induce enantiomeric excess in carbanionic reactions performed by phase-transfer catalysis.

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Dinitrogen Sulfide

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The thermal decomposition of 5-phenyl-1,2,3,4-thiatriazole (**1**) has been the subject of several studies.[2,3] In the most recent investigation,[3] four possible routes, A–D, were considered (Scheme I). Routes A and B were excluded on the grounds that no kinetic isotope effect was observed when the nitrogen atom in position 2 was substituted for ^{15}N. However, the introduction of ^{15}N in position 4 gave rise to a kinetic isotope effect of 1.04, in excellent agreement with a calculated isotope effect 1.041 for N(3)–N(4) bond breaking. However, N_2S was not detectable as a product of the decomposition, and route C was, therefore, excluded. It was concluded[3] that the reaction proceeded via reversible ring opening to thiobenzoyl azide (**2**) (not observed), which then rapidly decomposes to benzonitrile, N_2, and S. On the product side, benzonitrile was formed in virtually 100% yield at temperatures below 100 °C, and in ca. 96% yield together with ca. 4% phenyl isothiocyanate (PhNCS) on gas-phase pyrolysis at 300 °C.[3]

We now wish to report that, contrary to the above conclusion, N_2S is indeed formed as a reactive intermediate in the thermal decomposition of **1**.

1 was subjected to flash vacuum pyrolysis in an apparatus with contact times of ca. 1 ms and permitting the isolation of the products at 77 K or in Ar matrix at 20 K for IR spectroscopic examination. Pyrolyses were carried out at temperatures between 300 and 400 °C. Two prominent products, absorbing at 2228 (benzonitrile) and 2030 cm^{-1}, respectively, were observed. In addition, weak bands at 2175 and 2120 cm^{-1} are ascribed to traces of phenyl isothiocyanate. The IR spectrum resulting from a 400 °C pyrolysis with Ar matrix isolation at 20 K is shown in Figure 1.

The intensity of the 2030 cm^{-1} band decreased relative to that of benzonitrile as the pyrolysis temperature was increased from 300 to 400 °C and above, thereby indicating

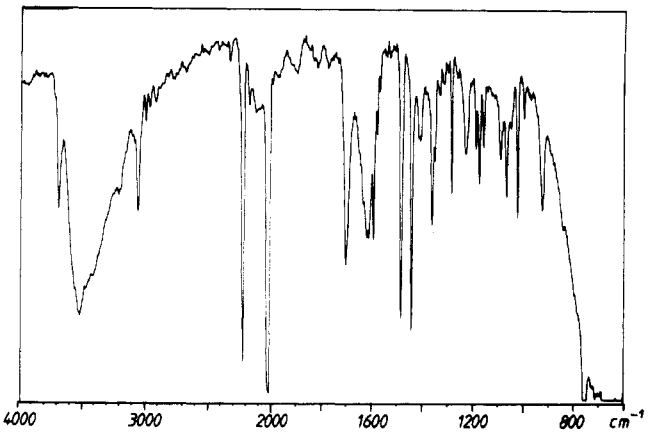

Figure 1. IR spectrum of the products of pyrolysis of **1** at 400 °C (Ar matrix, 20 K).

Scheme I

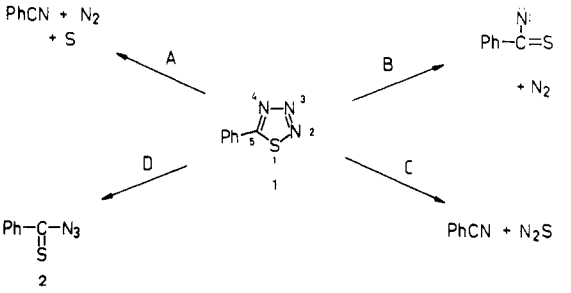

Table I. Infrared, Electronegativity, and Ionization Data for Diazonium Betaines

compd					
a		b	$\bar{\nu}$, cm^{-1} [a]	EN_X [b]	IP, eV [c]
$N{\equiv}N^+C^-H_2$	↔	$N^-{=}N^+{=}CH_2$	2050	2.5	9.0
$N{\equiv}N^+N^-H$	↔	$N^-{=}N^+{=}NH$	2130	3	11.5
$N{\equiv}N^+O^-$	↔	$N^-{=}N^+{=}O$	2224	3.5	12.9
$N{\equiv}N^+S^-$	↔	$N^-{=}N^+{=}S$	2030	2.5	10.4 [d]

[a] From IR spectrum. [b] Electronegativity of affixed atom X in N_2X. [c] First ionization potential, experimental values, from ref 7a, unless otherwise stated. [d] MNDO calculated value, from: Sensarma, S., Turner, A. G. *Inorg. Chim. Acta* **1982**, *64*, L 161.

that the 2030 cm^{-1} species is unstable and thermally decomposes. Although stable in the solid state at 77 K, this species disappeared on slow warming to 160 K. At the same time, the previously light yellow and transparent solid faded and became opaque, presumably due to the formation of sulfur. After further warming to room temperature, benzonitrile and sulfur were isolable, each in nearly quantitative yield.

An IR spectrum very similar to the one shown in Figure 1 was also obtained on Ar matrix photolysis of **1** at 310 ± 11 nm (2228 (w), 2030 cm^{-1} (m)). Photolysis was very slow at this wavelength. Photolysis was faster with 254-nm light, giving the 2228 and 2230 cm^{-1} bands with equal intensity, and, in addition, very weak bands at 2190 and 2120 cm^{-1} due to phenyl isothiocyanate.

The important 2030 cm^{-1} species cannot be due to benzonitrile sulfide (PhCNS), which we have shown in other work to absorb at 2270 cm^{-1},[4] and in agreement with Holm,[3] no PhCNS is formed in the thermal decomposition of **1**. Thiobenzoyl azide (**2**) is not a good candidate either, since azides generally absorb near 2130 cm^{-1} in the IR, although the thioacyl group may cause a shift toward lower

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