the reason for the lesser rate ratio k_{meso}/k_{dl} (elimination) in methanol[3,10] (40) and in acetone$_3$ (23) compared to DMF may lie in the larger population of conformer D in the less polar solvents methanol and acetone as compared to the more polar DMF.

Experimental Section

The *meso* and *dl* pair isomers of 1,2-dibromo-1,2-diphenylethane were prepared as previously described; meso, mp 249–251 °C (lit.[26] 254–255 °C dec); *dl*, mp 108–109 °C (lit.[27] mp 110–111 °C). The reported $^3J_{H/H}$ couplings were obtained in either a WP-200-SY (Department de Química Orgânica, Universidad Autônoma de Madrid, Spain) or a WM-250 (UNC) Bruker instrument from the ^{1}H-NMR spectra, looking at the ^{13}C satellites of the ^{12}CH signal centered at 5.48 (CDCl), 5.69 (CD_3OD), 5.87 (acetone-d_6) or 6.10 (Me_2SO-d_6) ppm for the *dl* pair and 5.48 ($CDCl_3$) ppm for the *meso* isomer. The distance in Hz between the two observed doublets flanking the normal, intense signal was identical, within the experimental error, with the $^1J_{C-H}$ coupling (ca. 156.5 Hz for both isomers) observed in the proton coupled ^{13}C spectra ($CDCl_3$) for the CHBrCHBr carbon signal 56.2 ppm for the *meso* isomer and at 59.1 ppm for the *dl* pair.

Acknowledgment. This work was supported by NSF Grant CHE-8314169.

Registry No. *trans*-Stilbene, 103-30-0; *meso*-α,α′-dibromobibenzyl, 13440-24-9; (±)-α,α′-dibromobibenzyl, 13027-48-0.

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(27) Buckles, R. E.; Steinmetz, W. E.; Wheeler, N. G. *J. Am. Chem. Soc.* **1950**, *72*, 2496.

Configuration of Some Para-Substituted Benzhydrols

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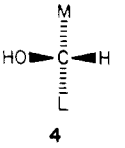
The preparation of optically active benzhydrol-2,3,4,5,6,-d_5 (**3**, phenyl(perdeuteriophenyl)carbinol, $[\alpha]^{20}_D$–0.85° (*c* 16, $CHCl_3$) from resolved (+)-4′-nitrobenzhydrol-2,3,4,5,6-d_5 (**1**) via the corresponding (−)-4′-amino compound (**2**) was reported recently.[2] The configurations of the compounds in this series (**1** → **2** → **3**) were tentatively assigned by application of the Horeau method[3] to **1**. Treatment of either (+)-**1** or the corresponding nondeuteriated compound[4] with excess *dl*-α-phenylbutyric anhydride gave recovered (+)-α-phenylbutyric acid (optical yield of 4.3–4.5%).

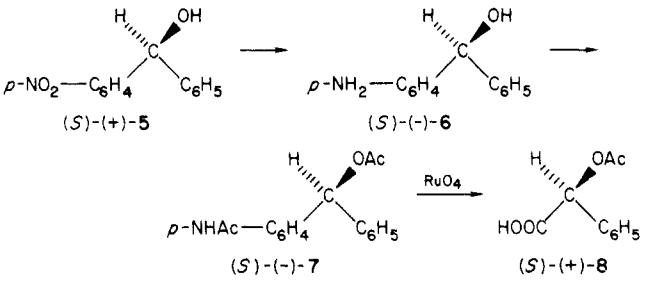
According to the empirical model developed by Horeau,[3] when (+)-α-phenylbutyric acid is recovered from this kinetic resolution, the configuration of the optically active carbinol is represented by **4**.



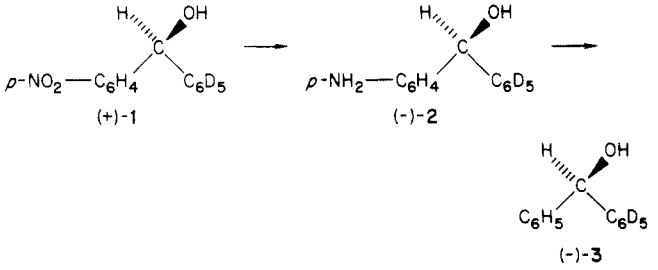
4

Without prior knowledge, one would make the reasonable assumption that the *p*-nitrophenyl group would be the L (larger) group and phenyl the M (medium) group. It would also be reasonable to assume that this steric difference might not be very great because the difference in bulk is at the para position considerably removed from the chiral center. However, recent studies by Guetté and co-workers[5,6] convincingly demonstrate that for *p*-Me, *p*-Br, *p*-OMe, and *p*-CF_3 benzhydrols, Horeau's method predicts the correct absolute configuration *when the para-substituted phenyl ring is designated M and the unsubstituted phenyl group is designated L*! This conclusion is based on a direct chemical correlation of the (+)-*p*-bromo- and (−)-*p*-methylbenzhydrols to (*S*)-(+)-mandelic acid.[5] Interpreting our results in light of Guetté's studies, we tentatively predict the absolute configurations as shown in **1** → **2** → **3**. We felt, however, that these assignments should be confirmed by a direct correlation.

Based on the ruthenium dioxide oxidation of an aromatic system as applied by Nakagawa and co-workers,[7] we studied the oxidation of (−)-*p*-acetamidobenzhydrol acetate.[8] *p*-Nitrobenzhydrol was resolved as previously reported[2,9,10] and the (+)-isomer **5** reduced (10% Pd/C) to the (−)-amine **6** that was converted to the diacetate (−)-**7**.



This was oxidized (RuO_2 + $NaIO_4$) to give (after exacting chromatographic purification) (*S*)-(+)-*O*-acetylmandelic acid (8 18% yield) which was identical (IR, NMR, mass spectrum, mixture melting point, and optical rotation) with an authentic sample. Since the chiral center is not dis-



(1) Permanent address: Shanghai Institute of Organic Chemistry, Academic Sinica, China.
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(4) The configuration of (+)-**1**, $[\alpha]^{20}_D$ +77.4° (*c* 2, $CHCl_3$), and the corresponding (+)-nondeuteriated compound,[5,6] $[\alpha]^{20}_D$ +78.2° (*c* 2, $CHCl_3$), are obviously the same since deuteriation would affect the rotation in the order of 1° out of a total of 77°.
(5) Capillon, J.; Guetté, J.-P. *Tetrahedron* **1979**, *35*, 1801.
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(8) In exploratory experiments *p*-nitrobenzhydrol acetate was oxidized by RuO_4 to *O*-acetyl-*p*-nitromandelic acid (mp 153–155 °C: Carrara, G.; Fava, F.; Martinuzzi, C.; Vecchi, A. *Gazz. Chim. Ital.* **1952**, *82*, 674). This compound is not report in optically active form. An attempt to convert it to **8** failed when hydrogenation (Pd–C) gave a complex mixture of products.
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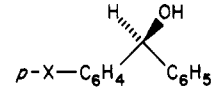
Table I. Rotations of *S* Para-Substituted Benzhydrols

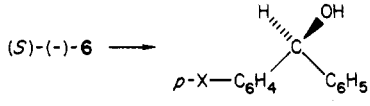


compd	X	configuration	max rotation[a] $[\alpha]_D$, deg	*t*, °C	*c*, solv	ref
6	NH_2	*S*-(−)	−32.8	22	5, C_6H_6	2,*b*
	NHAc	*S*-(−)	−16.7	19	2, EtOH	9
7[c]	NHAc[c]	*S*-(−)[c]	−41.4[c]	20	0.7, EtOH	*b*,*c*
	CH_3	*S*-(−)	−10.3	22	5, C_6H_6	5
	OCH_3	*S*-(−)	−18.8	22	5, C_6H_6	5
5	NO_2	*S*-(+)	+79.5	20	1.3, $CHCl_3$	2,9,10
9	Br	*S*-(+)	+19.8	22	5, C_6H_6	5
9	Br	*S*-(+)	+21.0	20	0.8, C_6H_6	*b*
10	Cl	*S*-(+)	+22.0	20	0.9, $CHCl_3$	*b*
10[d]	Cl[d]	*S*-(+)	+13.7	20	20, $CHCl_3$	12
	CF_3	*S*-(+)	+40.4	22	5, C_6H_6	5

[a] Rotations are given for the *S* isomer even though in some literature cases the actual determination may have been on the enantiomer. [b] Data from this paper. [c] This is the *N*,*O*-diacetyl derivative **7** made directly from **6**. [d] The maximum rotation for the (−)-enantiomer obtained by resolution[12] was reported as $[\alpha]^{20}_D$ −32.1° (*c* 6.7, $CHCl_3$), 29.9° (*c* 6.7, C_6H_6), 23.4° (*c* 6.7, EtOAc), and 18.9° (*c* 6.7, EtOH).

turbed in the sequence **5** → **6** → **7** → **8**, we can confidently assign the configurations to these compounds as shown in their formulas and in Table I.

In addition, (*S*)-(−)-*p*-aminobenzhydrol has been converted via the Sandmeyer reaction[11] into (*S*)-(+)-*p*-bromobenzhydrol (**9**) and (*S*)-(+)-chlorobenzhydrol (**10**). These compounds were prepared by Guetté and co-workers, and our results confirm their configurational assignments. Thus the configurations of the para-substituted benzhydrols **1** through **10** have been interrelated to those studied by Guetté and co-workers.[5]



(*S*)-(+)-**9**, X = Br
(*S*)-(+)-**10**, X = Cl

From the data collected in Table I, it is seen that the four para-substituted *S* benzhydrols with an activating substituent (CH_3, OCH_3, NH_2, NHAc) are levorotatory, *S*-(−); while the four *S* benzhydrols with a deactivating substituent (NO_2, Br, Cl, CF_3) in the para position are dextrorotatory, *S*-(+). This rudimentary correlation is based on sodium D line rotations; more meaningful correlations should be based on circular dichroism studies which are contemplated.

Experimental Section

Optical rotations were taken on a Rudolph Research Autopol III electronic polarimeter which records to 0.001°; readings with standard samples were reproducible to ±0.002°. Measurements were made in 1-dcm permanent-window cells thermostated at 20.0 ± 0.1 °C. Proton magnetic resonance spectra (^{1}H NMR) were taken at 300 MHz on a Nicolet, NMC instrument in Fourier transfer mode. Chemical reactions were routinely followed by thin-layer chromatography (TLC) using Analtech PGBE silica gel GF plates (250 μm). Melting points were determined between cover glasses on an aluminum block microscope hot stage. Mass spectra were taken on a Hewlett-Packard 5995B instrument using direct introduction probe.

(*S*)-(−)-*p*-Aminobenzhydrol (6). Resolved[9,10] (*S*)-(+)-*p*-nitrobenzhydrol (1.05 g) $[\alpha]^{20}_D$ +79.5° (*c* 1.3, $CHCl_3$) in methanol (15 mL) was reduced with hydrogen in the presence of 10% Pd/C (94 mg) as described for the deuteriated analogue[2] but at 0 °C instead of 25 °C. The reaction was stopped as soon as the theoretical amount of hydrogen was absorbed and no starting material remained as measured by TLC. After removal of catalyst and solvent, the residual yellow solid was recrystallized from $CHCl_3$/hexane to give white crystals (611 mg, 67% yield), mp 126–127 °C, $[\alpha]^{20}_D$ −32.8° (*c* 1.1, $CHCl_3$) [lit.[9] mp 136–137 °C, $[\alpha]^{20}_D$ −30.3° (c 1.12, $CHCl_3$)].

(*S*)-(−)-*p*-Acetamidobenzhydryl Acetate[9] (7). Acetic anhydride was added to a stirred solution of **6** [330 mg, 1.66 mmol, $[\alpha]^{20}_D$ −32.8 ± 0.5° (*c* 1.1, $CHCl_3$)] in pyridine (1 mL). The reaction was begun at 0 °C and allowed to reach 20 °C over 14 h. Water (15 mL) was added and the mixture extracted with ethyl acetate. The extracts were washed with water, dried ($MgSO_4$), and concentrated to give a white solid (433 mg) that was recrystallized (ethanol–water) to give platelets (362 mg, 77% yield), mp 128–130 °C, $[\alpha]^{20}_D$ −41.4° (*c* 0.7, EtOH) [lit.[9] mp 122 °C, $[\alpha]^{20}_D$ −41.3° (*c* 2, EtOH)].

(*S*)-(+)-*O*-Acetylmandelic Acid[13,14] (8). A solution of **7** (300 mg, 1.06 mmol) in acetone (22 mL) was added to the yellow stirred solution of ruthenium dioxide (56.5 mg, 0.42 mmol) and sodium periodate (680.3 mg, 3.18 mmol), in acetone (11 mL) and water (3.6 mL). The mixture was stirred for 4.5 h, during which time a solution of sodium periodate (14 g) in water (70 mL)/acetone (70 mL) was added portionwise at a rate to keep the reaction mixture yellow whenever darkening occurred. After the mixture was passed through a short Celite column, the solvent was evaporated and the residue extracted with ether. The ether solution was extracted with saturated $NaHCO_3$. Ether extracts of this acidified (3 N HCl) aqueous layer were washed (saturated NaCl, H_2O), dried ($MgSO_4$), and evaporated to give crude acid **8** (72.8 mg). This was purified (silica gel column, CH_2Cl_2) to give white crystals (37.3 mg, 18% yield), mp 102–104 °C, $[\alpha]^{20}_D$ +152.4° (*c* 1.8, $CHCl_3$). A mixture melting point of these crystals with an authentic sample,[13,14] mp 101–103 °C, $[\alpha]^{20}_D$ +154.4° (*c* 2.1, $CHCl_3$), was 102–104 °C. These two samples had identical ^{1}H NMR mass, and IR spectra.

(*S*)-(+)-*p*-Bromobenzhydrol[5] (9). Sodium nitrite (60.7 mg, 0.88 mmol in 1 mL H_2O) was mixed with (*S*)-(−)-**6** [151 mg, $[\alpha]^{20}_D$ −32.8° (*c* 1.1, $CHCl_3$)] in 6 N HCl (3 mL) at 0 °C. After 10 min the excess nitrite was destroyed with urea (60 mg), and the reaction mixture under nitrogen was filtered at 0 °C into acetone (12 mL). To the acetone solution were added cuprous bromide (157.8 mg, 1.1 mmol) and lithium bromide (111.2 mg, 1.25 mmol), and the mixture was stirred at 0 °C for 0.5 h. The mixture was vacuum evaporated and ether extracts of the residue were washed (H_2O, 0.2 N NaOH, H_2O), dried ($MgSO_4$), and concentrated to give crude **9** (174 mg). Recrystallization (hexane) yielded needles (100 mg, 50% yield), mp 74–76 °C, $[\alpha]^{20}_D$ +21.0° (*c* 0.8, C_6H_6) [lit.[5] mp 78 °C, $[\alpha]^{22}_D$ +19.8° (*c* 5, C_6H_6)].

(*S*)-(+)-*p*-Chlorobenzhydrol (10). By the method described above, (*S*)-(−)-**6** (152 mg) was converted to **10**, using cuprous

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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.

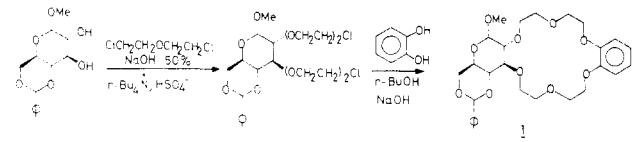
These crown ethers are obtained in good overall yields (60–70% range) from commercially available materials, permitting thus preparation at a scale large enough (20–30 g) to achieve complexation experiments. The nine chiral crown ethers presented here (Scheme II) have been derived from the following 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.

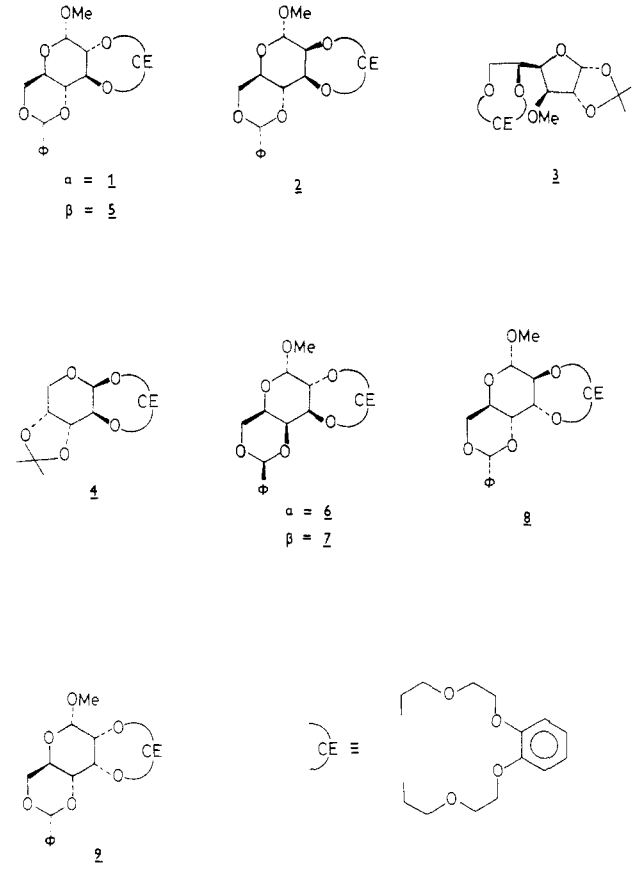
Experimental Section

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

†Unité Associée au CNRS No. 486.

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