Table I[a]

Compd	$\delta_{C\text{-}2}$	$\delta_{C\text{-}3}$	$J_{2,3}$	$J_{3,4}$	$J_{1,2}$
1a	2.94	3.18	9	9	9
1b	2.94			9	
2a	3.37	3.68	8	8	4

[a] Coupling constants given in hertz.

1a and **2a**. The chemical shifts of the carbinol protons for **2a** were assigned from the observed coupling constants, but a similar assignment was not possible for **1a**. The deuterio derivative **1b** was prepared by lithium aluminum deuteride reduction of **3** followed by hydroboration of the resulting allylic alcohol. The disappearance of the multiplet at δ 3.18 in the nmr spectrum of **1b** established the chemical shifts of the carbinol protons.

Since the absolute configuration of (−)-piperitone is known to be 6*R*,[6] the relative stereochemistry of the diols can be used to assign their absolute configurations. From these considerations, (+)-**1a** is (1*S*,2*R*,3*R*,4*R*)-2,3-dihydroxy-*p*-menthane while (+)-**2a** is (1*R*,2*S*,3*S*,4*R*)-2,3-dihydroxy-*p*-menthane.

The dibenzoate chirality rule predicts that the sign of the first Cotton effect around 230 nm is in accordance with the chirality of the dibenzoate groups of a vicinal diol.[2] This chirality is negative for **1** and positive for **2**. The dibenzoates **1c** and **2b**, prepared by treatment of the corresponding diols with excess benzoyl chloride–pyridine, have strong Cotton effects (Figure 1) whose sign is in agreement with that predicted by the rule. The molar ellipticities given in Figure 1 differ by an order of magnitude, although the curves clearly bear a mirror image relationship. The differences in the magnitude of the two effects are probably ascribable to deviations from the parallel alignment of the carbinol carbon–oxygen bond and the long axis transition moment of the benzoate, as well as differences in the relative orientation and separation of the aromatic rings.

In conclusion, the absolute configurations deduced from the CD measurements correspond with those assigned from the known absolute configuration of (−)-piperitone and the relative stereochemistry obtained from the proton nmr spectra. These results coupled with earlier studies[1] support the use of the dibenzoate chirality rule in assigning the absolute configuration of other substituted 1,2-cyclohexanediols.

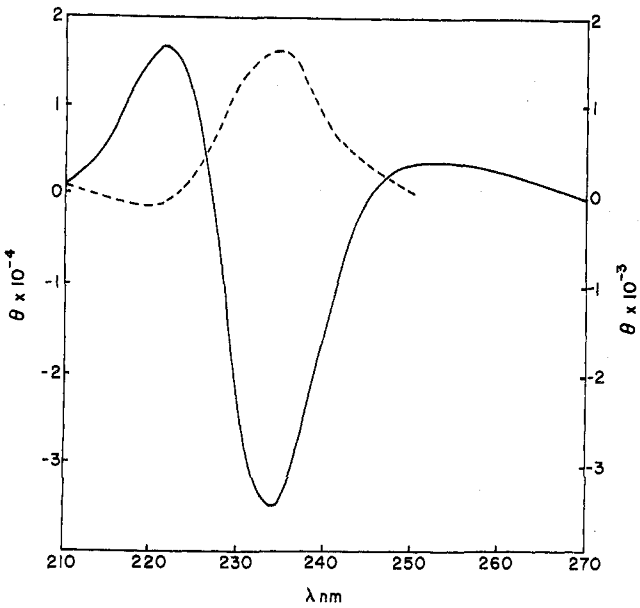

Figure 1. CD curves of diol dibenzoates. The solid line is **1c** legend on left and the dashed line is **2b** legend on right. Optical purity of dibenzoates ~40%.

Experimental Section

(−)-Piperitone, $[\alpha]_D$ −21.1° (reported[7] $[\alpha]_D$ −51.5°, *i.e.*, ~41% optically pure), was hydroborated and oxidized as described by Klein and Dunkelblum.[4] The reaction mixture was distilled and the diol fraction, bp 110–115° (0.1 mm), was collected. Chromatography on silica gel, using ethyl acetate–hexane (1:4) separated the mixture into a faster moving oil (**2a**) and a slower moving oil (**1a**). The specific rotations at the D line in chloroform for **1a** and **2a** were 47.2 and 13.3°, respectively. When these rotations are corrected for the optical purity of (−)-piperitone they become 115 and 32.4°, respectively. The dibenzoate of each diol was prepared by treating the diol in pyridine with excess benzoyl chloride, and the reaction products were purified by preparative thick layer chromatography on silica gel using ethyl acetate in hexane (1:9). The dibenzoates **1c** and **2b** were oils, $[\alpha]_D$ −74° and 42° ($CHCl_3$), respectively. The CD curves of the dibenzoates were determined in isooctane using a Cary 60 spectropolarimeter and are shown in Figure 1. The 220-MHz spectrum of **1c** in $CDCl_3$ showed absorption at δ 5.305 (t, 1 H) and 5.091 (t, 1 H) and complex aromatic absorption (10 H). The spectrum of **2b** showed absorption at δ 5.418 (d, 1 H) and 5.327 (q, 1 H) and complex aromatic absorption (10 H).

Registry No.—**1a**, 51745-19-8; **1b**, 51745-20-1; **1c**, 51705-86-3; **2a**, 51745-21-2; **2b**, 51705-87-4; **3**, 4573-50-6.

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Preparation and Purification of 18-Crown-6[1]

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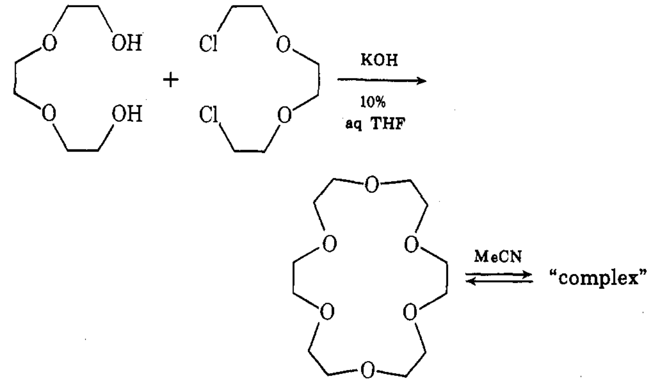
Of the many crown ethers which have been prepared[2] since the pioneering work of Pedersen[3] first appeared, 18-crown-6 is probably the simplest and most synthetically useful. Its synthesis in low yield was reported by Pedersen in his first paper.[3] Greene[4] and Dale and Kristiansen[5] have reported syntheses of 18-crown-6 from triethylene glycol and the corresponding ditosylate. A variety of bases was examined by Greene[4] but in both cases potassium *tert*-butoxide was favored. We report here a simple synthesis of 18-crown-6 from triethylene glycol and the commercially available (Eastman) 3,6-dioxa-1,8-dichlorooctane (triethylene glycol dichloride) using potassium hydroxide as base in 10% aqueous tetrahydrofuran and purification of the crown *via* its acetonitrile complex.

The Williamson ether synthesis yields crude crown in about 40% yield after a rapid distillation under high vacuum. The distilled material contains an impurity believed to be a vinyl ether and some open-chain, hydroxyl-containing material. Addition of acetonitrile to the crude



crown results in the formation of an 18-crown-6–acetonitrile adduct (complex)[6] of variable stoichiometry depending on conditions. Evaporation of the acetonitrile leaves crown of high purity. Evidence on the nature of this and other complexes of 18-crown-6 will be published elsewhere.

Experimental Section

A 3-l., three-neck flask equipped with mechanical stirrer, reflux condenser, and addition funnel was charged with triethylene glycol (112.5 g, 0.75 mol) and tetrahydrofuran (600 ml). Stirring was commenced and a 60% KOH solution (109 g of 85% KOH in 70 ml of water) was poured in. The solution warmed but did not boil. After *ca.* 15 min of stirring (the solution darkened) a solution of 3,6-dioxa-1,8-dichlorooctane (140.3 g, 0.75 mol) in THF (100 ml) was added in a stream. After the addition was complete, the solution was heated at reflux and stirred vigorously for 18 hr. The solution was allowed to cool and the bulk of the THF was evaporated under reduced pressure. The resulting thick brown slurry was diluted with 500 ml of dichloromethane and filtered. The salts removed by filtration were washed with more dichloromethane to remove adsorbed crown, and the combined organic solution was dried over $MgSO_4$, evaporated to minimum volume (aspirator vacuum), and then distilled under high vacuum. The distillation should be carried out at the lowest possible pressure; a typical fraction contained 80 g and was collected at 100-160° (0.2 mm).

To 50 g of crude 18-crown-6, bp 125-160° (0.2 mm), in a 250-ml erlenmeyer flask was added 125 ml of acetonitrile. The resulting slurry was heated on a hot plate to effect solution. A magnetic stirring bar was added and the neck was equipped with a $CaSO_4$ drying tube. The solution was stirred vigorously as it was allowed to cool to ambient temperature, and fine white crystals of crown-acetonitrile complex were deposited. The flask was finally cooled in an ice-acetone bath to precipitate as much complex as possible, and the solid was then collected by rapid filtration. The hygroscopic crystals were transferred to a 500-ml round-bottom flask equipped with a magnetic stirring bar and vacuum take-off. The acetonitrile was removed from the complex under high vacuum (0.1-0.5 mm) with gentle heating ($\leq 40°$) over 2-3 hr. The pure, colorless crown (20-30 g, 40-60%) crystallized on standing and showed no ions above *m/e* 265 in the mass spectrum and no significant hydroxyl vibration in the 3500-cm^{-1} region of the infrared. The pure crown had mp 36.5-38.0° (lit.[4] mp 39-40°); nmr (60 MHz, CCl_4) 3.56 ppm (singlet); ir (neat) 2875 (alkane CH), 1450 and 1350 (alkane CH), and 1120 cm^{-1} (ether link); mass spectrum M and M + 1 at *m/e* 264 and 265, other fragments at *m/e* 89, 87, 59, 45, 44, 43, and 31.

Registry No.—18-Crown-6, 17455-13-9; triethylene glycol, 112-27-6; 3,6-dioxa-1,8-dichlorooctane, 112-26-5.

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(2) For recent reviews see (a) C. J. Pedersen and H. K. Frensdorff, *Angew. Chem., Int. Ed. Engl.*, **11**, 16 (1972); (b) D. J. Cram and J. M. Cram, *Science*, **183**, 803 (1974); (c) F. Vögtle and P. Neumann, *Chem.-Ztg., Chem. App.*, **97**, 600 (1973).
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(6) A number of solid complexes of crown ethers are reported, including complexes of many metal ions,[2a] hydronium ion,[7] bromine,[8] thiourea,[9] and others. With the exception of the metal ions where a crystal structure has been determined, the nature of the interactions between host and guest is not clearly understood. There is an obvious possibility that different substrates interact differently with the host, affording on different occasions a complex, a solvate, and so on. Intuitively, it appears that two possible factors favor formation of a host-guest solid adduct. The large size of the 18-membered ring and its lack of rigidity might favor the interstitial trapping of other molecules to gain a more favorable crystal lattice. The second factor which probably influences the formation of such complexes is the multiplicity of electronegative heteroatoms distributed in the ring system which have the potential for interacting with and further ordering, the guest molecule in the lattice. We therefore use the term "complex" advisedly and are aware that probably only structural data derived from direct observations (*e.g.*, X-ray) will resolve the nature of the complex in individual cases.
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Fluorescence Properties of a Meisenheimer Complex[1]

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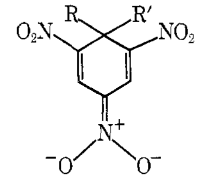
Meisenheimer complexes (below), the σ complexes which are formed as a result of the attack of nucleophilic agents on polynitroaromatic compounds, have been of interest to chemists for over 70 years.[2] Their spectroscopic (uv-visible, ir, nmr)[3,4] properties have been extensively studied, but the fluorescence behavior of these complexes has been overlooked. In view of the similarity of these complexes to the polynitrophenyl haptens used in many immunochemistry studies,[5] we decided to investigate the possibility of using these complexes as fluorescent biophysical probe molecules.[6] We report here the results of our preliminary investigations of the fluorescence properties of a Meisenheimer complex (where R = R′ = H, tetramethylammonium 1,1′-dihydro-2,4,6-trinitrocyclohexadienate) under differing environmental conditions. We believe that these results represent the first reported observations of Meisenheimer complex fluorescence.



$R = H, OH, OCH_3; R' = H, OCH_3, CN, SO_3^-$, etc.

The 1,1′-dihydro-2,4,6-trinitrocyclohexadienate anion fluoresces in acetronitrile with an emission maximum at about 670 nm. The quantum efficiency, which because of instrumental limitations must be considered only an estimate, is about 0.09. The measured lifetime is 1.8 ± 0.4 nsec. These data give a radiative lifetime of about 20 nsec.

In water, the emission maximum is shifted to the red (Figure 1) and the intensity is greatly diminished from that in acetonitrile. However, in the presence of an excess of human serum albumin (HSA) the emission spectrum (Figure 1) is similar to that in acetonitrile, although the quantum efficiency is somewhat less.

It is well known that serum albumins act as nonspecific binding agents for hydrophobic anions[7] and apparently the binding of the 1,1′-dihydro-2,4,6-trinitrocyclohexadienate anion to HSA[8] places it in a sufficiently nonaqueous environment that its emission spectrum more closely resembles that observed in acetonitrile. The lifetimes of