Synthesis of Ten Isomers of a Macrocyclic Polyether, Tetramethyldibenzo-18-crown-6, and their Complexes with Salts of Alkali Metals

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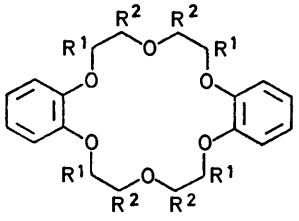
The preparation of the ten possible isomers of tetramethyldibenzo-18-crown-6 (6,10,17,21- and 7,9,18,20-tetramethyl-6,7,9,10,17,18,20,21-octahydrodibenzo[*b*,*k*][1,4,7,10,13,16]hexaoxacyclo-octadecin) (IV) and (VIII), from catechol and the ditosylates of 1,1'-oxydipropan-2-ol and 2,2'-oxydipropan-1-ol, respectively is described. The ability of the macrocycles to form crystalline complexes with some alkali and alkaline earth metals has been investigated and a number of these complexes are reported.

In continuation of our investigation of the conformational changes which macrocyclic polyethers undergo on complexation with cations, we have synthesised two sets of tetramethyldibenzo-18-crown-6 types (1) and (2). The introduction of four equivalent asym-



(1) R^1 = Me, R^2 = H
(2) R^1 = H, R^2 = Me

metric centres at positions 6, 10, 17, and 21 and at 7, 9, 18, and 20 gives rise to the possibility of five isomers in each series. The method of synthesis was based on that described by Pedersen.[1] 1,1'-Oxydipropan-2-ol and 2,2'-oxydipropan-1-ol were prepared, converted into their ditosylates (II) and (VI), and separated by fractional crystallisation into the *meso*- and racemic isomers. Each ditosylate on reaction with catechol gave a pair of isomers which were separated either by fractional crystallisation, or by making use of differences in the solubilities of the macrocycle complexes with alkali metal salts. The fifth isomer in each series was prepared by a two stage procedure. Catechol protected by monobenzylation was treated with the *meso*-ditosylate to give a bridged intermediate, and after removal of the protecting group, ring closure was effected on reaction with the racemic isomer. The reactions are summarised in Schemes 1 and 2.

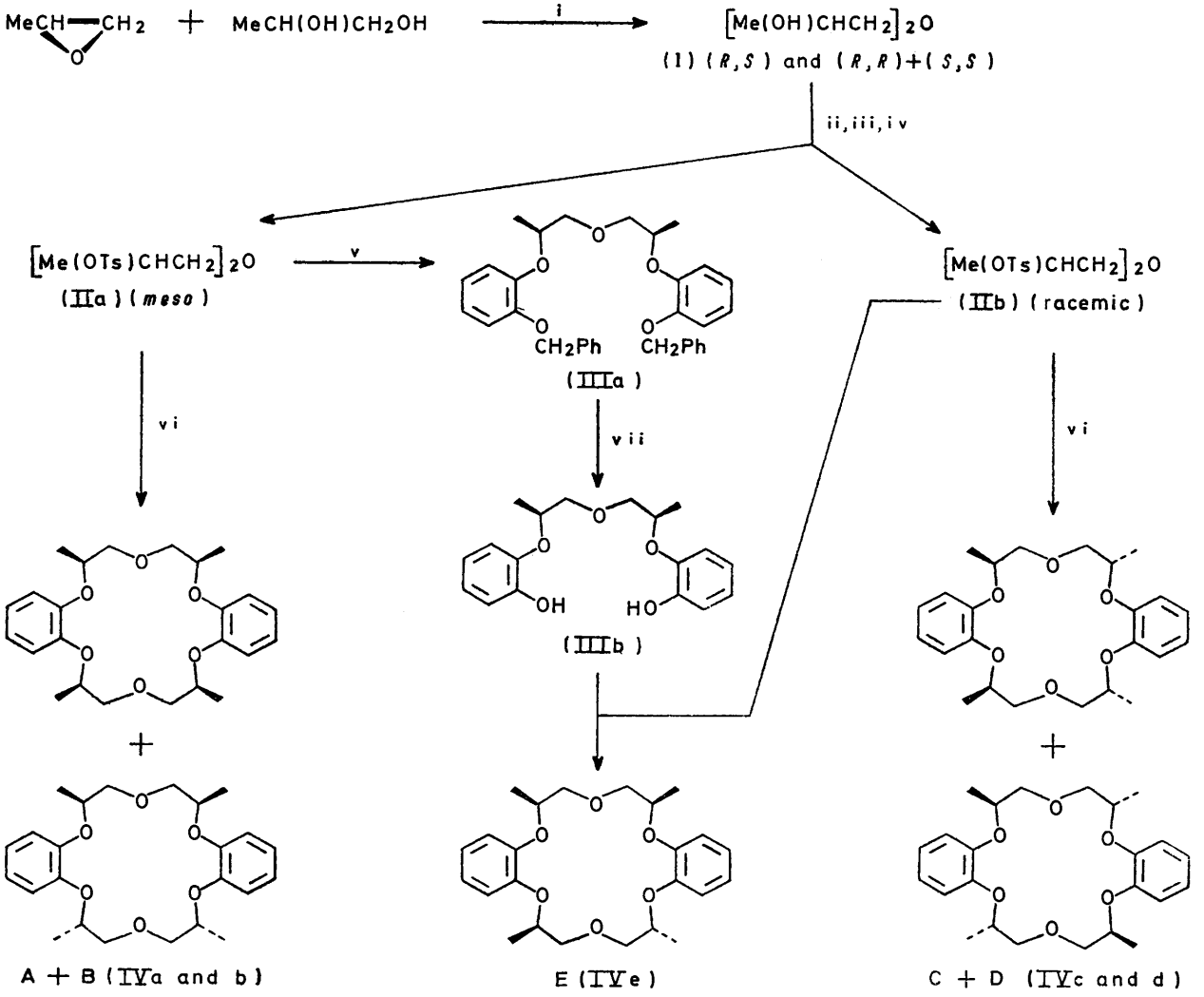
The structures of isomers E (IVe) and J (VIIIe) are known from the method of synthesis, and structures of isomers F (VIIIa) and G (VIIIb) have been obtained from *X*-ray analyses of their complexes with CsNCS.[2] The complete configurations of the remaining six isomers have not yet been determined.

All ten isomers form complexes to varying degrees with suitable salts of the alkali metals, and the isolated complexes were usually solvated, particularly those of the series (IV) isomers. This is probably because the 6-, 10-, 17-, and 21-methyl groups are restricted in their movements by the close proximity of the benzene rings and this fixes the molecule in a rather more rigid state than the series (VIII) isomers where the 7-, 9-, 18-, and 20-methyl groups are out of contact with the benzene rings and have less effect on the flexibility of the molecule. A greater degree of flexibility allows the

[1] C. J. Pedersen, *J. Amer. Chem. Soc.*, 1967, **89**, 7017.
[2] A. J. Layton, P. R. Mallinson, D. G. Parsons, and M. R. Truter, *J.C.S. Chem. Comm.*, 1973, 694.

macrocycle to attain a better fit around the cation when complexation occurs and less space is available for co-ordination of solvent molecules.

Earlier work has shown that dibenzo-18-crown-6 forms complexes of 1 : 1 stoicheiometry with sodium or rubidium thiocyanate,[1,3] but with caesium thiocyanate the preferred complex [4] contains two molecules of dibenzo-18-crown-6 and one of caesium thiocyanate. In this present series the same pattern is followed by isomer (VIIIb), but not by isomer (VIIIa),[2] which gives a 1 : 1 complex for all cations, so that it is for the largest



SCHEME 1 Reagents and conditions: i, Na; ii, low temperature crystallisation; iii, tosylation; iv, fractional crystallisation; v, *o*-$PhCH_2OC_6H_4OH$; vi, *o*-$C_6H_4(OH)_2$; vii, H_2/Pd

cation that subtle differences in the ligand produce a marked effect, as discussed in detail elsewhere.[5]

EXPERIMENTAL

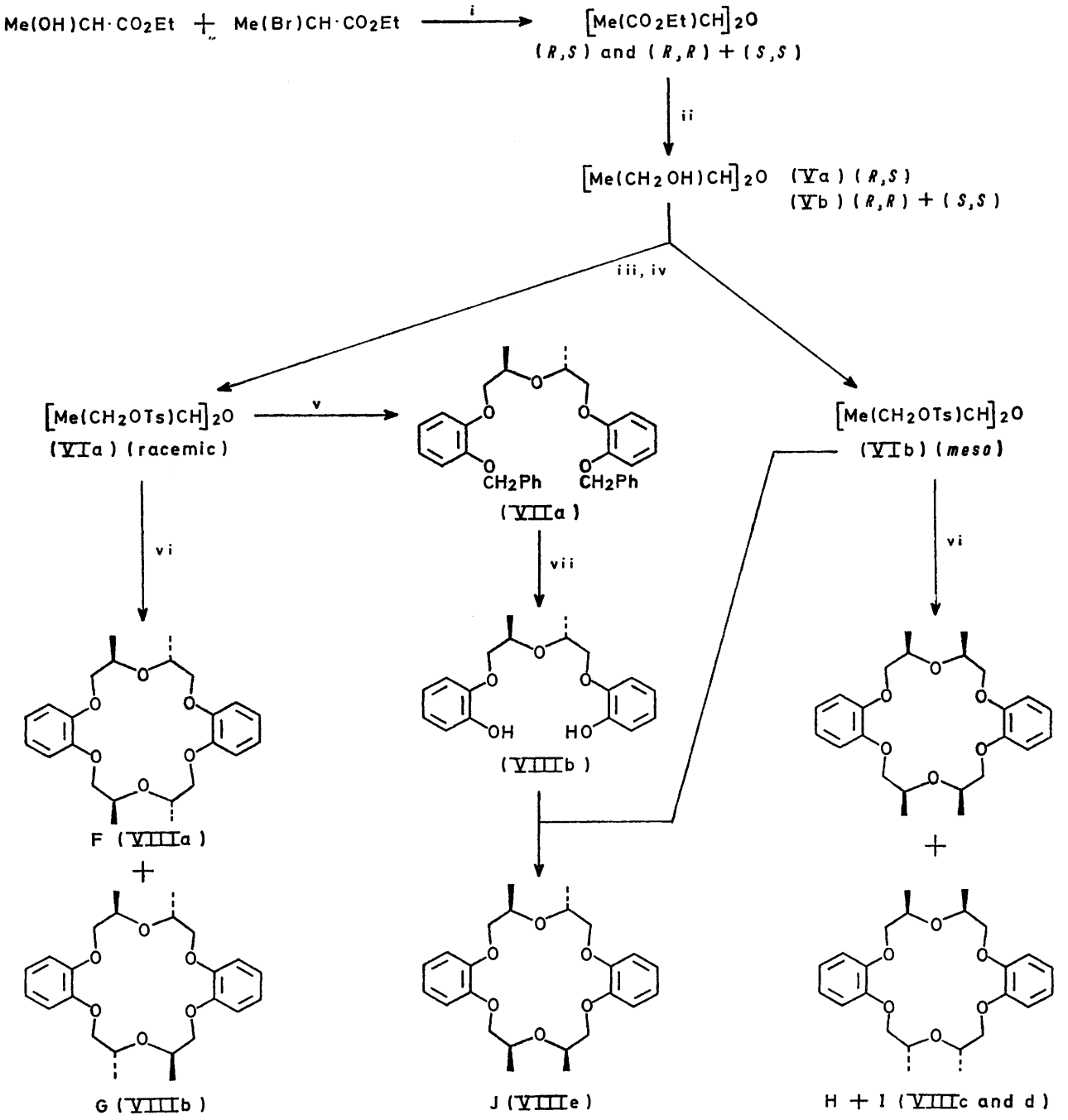
meso- *and* rac-1,1′-*Oxydipropan*-2-*ol* (I).—This was prepared by a modification of the method of Sexton and Britton.[6] Propylene glycol (2475 g) at 50° and under nitrogen was treated with sodium (11 g), the solution was stirred, warmed to 100°, and propylene oxide added at the rate (250 g h^{-1}) required to keep the reaction temperature at *ca.* 120°; in 9 h 1926 g were added. Acetic acid (30 ml) was added to the cold reaction product, and the mixture distilled at atmospheric pressure. The distillate (3600 g), b.p. 202—245°, was twice fractionally distilled using a 40 cm Vigreux column to yield a mixture (1147 g) of the *meso*- and *rac*-isomers, b.p. 215—225°. Addition of ether (1 l) and cooling to −78° gave the *meso*-isomer as waxy needles (463 g, 10·6%), m.p. 45—48°, and refractionation of the mother liquor gave the racemate (containing a little of the *meso*-isomer) as a viscous liquid (600 g, 13·7%), b.p. 218—221°.

meso-*Bis*-(2-*tosyloxypropyl*) *Ether* (IIa).—The *meso*-

[3] D. Bright and M. R. Truter, *J. Chem. Soc.* (*B*), 1970, 1544; M. A. Bush and M. R. Truter, *ibid.*, 1971, 1440.
[4] C. J. Pedersen, *J. Amer. Chem. Soc.*, 1970, **92**, 386.
[5] P. R. Mallinson, *J.C.S. Perkin II*, in the press.
[6] A. R. Sexton and E. C. Britton, *J. Amer. Chem. Soc.*, 1953, **75**, 4357.

glycol (I) (80 g) in dry pyridine (450 ml) at 10° was treated with toluene-*p*-sulphonyl chloride (300 g). After 3 days at room temperature the product was stirred into ice and water, and the ditosylate collected, washed with water, and recrystallised from ethanol (1200 ml), to give *needles* (232 g, 88%), m.p. 84—86° (Found: C, 54·6; H, 6·05. $C_{20}H_{26}O_7S_2$ requires C, 54·3; H, 5·99%), τ ($CDCl_3$) 2·2—2·8 (8H, q), 5·45 (2H, m), 6·65 (4H, d, *J* 5·5 Hz), 7·54 (6H, s), and 8·83 (6H, d, *J* 6 Hz). The doublet at τ 6·65 was replaced by the expected multiplet at τ 7·08 (4H) in benzene.

rac-*Bis*-(2-*tosyloxypropyl*) *Ether* (IIb).—This was prepared in the same manner as (IIa) but from the racemic glycol (I) (120 g) and toluene-*p*-sulphonyl chloride (450 g) in dry pyridine. The oil which separated on mixing the product with cold water was extracted with chloroform and washed with 2N-hydrochloric acid, and then water. After drying ($MgSO_4$) and concentrating under reduced



SCHEME 2 Reagents and conditions: i, Na; ii, $LiAlH_4$; iii, tosylation; iv, fractional crystallisation; v, *o*-$PhCH_2OC_6H_4OH$; vi, *o*-$C_6H_4(OH)_2$; vii, H_2/Pd

pressure, the resulting pale brown oil was dissolved in methanol (800 ml) and kept at 3°. The ditosylate which crystallised over a period of several days gave *prisms* (280 g, 71%), m.p. 47—50° (from methanol) (Found: C, 54·3; H, 5·7%) τ ($CDCl_3$) 2·2—2·8 (8H, q), 5·45 (2H, m), 6·68 (4H, q), 7·56 (6H, s), and 8·82 (6H, d, *J* 6 Hz).

rel-(6R,10S,17R,21S)- *and* rel-(6R,10S,17S,21R)-6,10,17,-21-*Tetramethyl*-6,7,9,10,17,18,20,21-*octahydrodibenzo*[b,k]-1,4,7,10,13,16-*hexaoxacyclo-octadecin, Isomers* A *and* B (IVa *and* b).—A solution of catechol (66 g, 0·6 mol) in n-butanol (150 ml) under nitrogen was treated with a solution of sodium hydroxide (25 g, 0·625 mol) in n-butanol (750 ml); the sodium catecholate formed a thick slurry. The *meso*-ditosylate (IIa) (132 g, 0·3 mol) was added in portions with stirring in 5 min. Reaction was rapid and accompanied by the separation of sodium tosylate; after the mixture had been heated for 30 min, more sodium hydroxide (25 g) in n-butanol (650 ml) was added followed by further *meso*-ditosylate (132 g) added slowly in order to prevent excessive frothing as the sodium tosylate separated. After 90 min the mixture was cooled, the sodium tosylate filtered off, and the filtrate concentrated *in vacuo* at 60—70° to yield a brown oil. This was poured into water, extracted with ether (300 ml), washed with 5% sodium hydroxide solution (4 × 100 ml) and water (4 × 100 ml), then dried ($MgSO_4$). Concentration under reduced pressure at 80—90° gave a brown oil which was dissolved in benzene (150 ml) and again concentrated, giving a brown syrup (79 g). Much of the colour was removed after dissolution in light petroleum (b.p. 60—80°) (250 ml) and treatment with charcoal; the orange syrup (65 g) obtained was dissolved in light petroleum (b.p. 60—80°)–ether (250 ml; 1 : 1 v/v) and cooled to 3°. A colourless crystalline product (13·9 g), m.p. 90—105°, was obtained. The i.r. spectrum (KBr) showed this to be a mixture containing isomers A and B in the proportion 4 : 1 [determined from the ratio of the intensities of i.r. bands at 742 cm^{-1} (isomer A) and 749 cm^{-1} (isomer B)]. Crystallisation from methanol resulted in only a small concentration of isomer A over B although a separation could be achieved on a very small scale by hand picking of the two different crystalline forms. Further attempted fractional crystallisation of isomers A and B became less effective as impurities were removed (isomers A and B have about the same solubilities in methanol and ethanol, but in the presence of polymeric impurities, the solubility of isomer B was increased more than that of isomer A). After three recrystallisations from methanol the ratio isomer A : isomer B had increased to *ca.* 9 : 1. A complete separation was achieved as follows. The mixture enriched in A (6·5 g) dissolved in hot methanol (50 ml) was treated with sodium iodide (0·5 g), and on cooling pure isomer A separated as needles (4·7 g), m.p. 109—110°. The crude mother liquors enriched in isomer B from earlier fractional crystallisations were concentrated, dissolved in benzene, treated with charcoal, and reconcentrated to give a syrup (25 g). This was dissolved in light petroleum (b.p. 60—80°) (80 ml) and was washed through an alumina column (activity I) (40 × 2 cm) with light petroleum (500 ml). After concentration of the eluate to 60 ml the solution was cooled to 3° to give a crystalline product (12·4 g), which was mainly isomer B. Recrystallisation from methanol gave pure isomer B (4·6 g). The mother liquor from this crystallisation was combined with the mother liquor from the previous crystallisation of A from sodium iodide solution and concentrated to dryness (14·0 g). The i.r. spectrum indicated roughly equal amounts of isomers A and B, and these were separated by addition of sodium iodide (2·0 g) to a solution of the mixture of isomers in ethanol (100 ml). Nearly pure isomer A obtained on cooling was combined with the previous crop, and recrystallised from ethanol to give isomer A as *needles* (8·1 g, 6·5%), m.p. 109—110° [Found: C, 69·3; H, 7·5%; *M* (by vapour pressure osmometry), 378. $C_{24}H_{32}O_6$ requires C, 69·2; H, 7·7%; *M*, 416], τ ($CDCl_3$) 3·14 (8H, s), 5·3—5·6 (4H, sext.), 6·30 (8H, d, *J* 5 Hz), and 8·78 (12H, d, *J* 6 Hz); in benzene the methylene protons gave a doublet at τ 6·4 (8H) but the methine protons centred at τ 5·5 showed a more complex splitting pattern than the sextet obtained in $CDCl_3$; $\lambda_{max.}$ (MeOH) 281 nm. Isomer B was recovered from the mother liquor after concentration to dryness, followed by decomposition of the sodium iodide complex on addition of water. The product from alcohol (50 ml) was combined with the previous crop and again recrystallised from ethanol to give isomer B as *thick needles* (6·95 g, 5·6%), m.p. 137° [Found: C, 69·1; H, 7·7%; *M* (v.p. osmometry), 420], τ ($CDCl_3$) 3·13 (8H, s), 5·3—5·7 (4H, sext.), 6·05—6·45 (8H, m), and 8·75 (12H, d, *J* 6 Hz), $\lambda_{max.}$ (MeOH) 282 nm.

rel-(6R,10R,17R,21R)- *and* rel-(6R,10R,17S,21S)-6,10,17-,21-*Tetramethyl*-6,7,9,10,17,18,20,21-*octahydrodibenzo*[b,k]-[1,4,7,10,13,16]*hexaoxacyclo-octadecin, Isomers* C *and* D (IVc *and* d).—Catechol (25 g) was added to n-butanol (240 ml) containing sodium hydroxide (9·1 g) and heated with stirring under nitrogen, and the racemic ditosylate (11b) (50 g) was then added and the mixture heated for 30 min. More sodium hydroxide (9·1 g) and racemic ditosylate (50 g) were added and heating continued for 1·5 h. The products of the reaction were isolated in the same manner as isomers A and B giving a pale orange oil (27 g). On standing for 64 h at 3°, isomer C crystallised: this was separated by dissolving the oil in light petroleum–ether (50 ml) and filtering off the solid material (2·1 g), m.p. 121—133°. Crystallisation from methanol (50 ml) and then from ethanol (50 ml) gave isomer C as *flakes* (1·42 g, 3·0%), m.p. 136—137° [Found: C, 69·4; H, 7·9%; *M* (v.p. osmometry), 419], $\lambda_{max.}$ (MeOH) 282 nm. On standing, isomer D slowly separated from the light petroleum solution. The crude material (2·3 g), m.p. 112—121°, was recrystallised from methanol and then from ethanol, giving *needles* (0·88 g), m.p. 121—122° [Found: C, 69·65; H, 7·95%; *M* (v.p. osmometry), 416].

rel-(6R,10R,17R,21S)-6,10,17,21-*Tetramethyl*-6,7,9,10,17,-18,20,21-*octahydrodibenzo*[b,k][1,4,7,10,13,16]*hexaoxacyclo-octadecin, Isomer* E (IVe).—The syrupy bis-(2-*o*-benzyloxyphenoxypropyl) ether (IIIa) (16 g), prepared from sodium o-benzyloxyphenolate and the *meso*-glycol (IIa), was debenzylated in ethanol with Pd/H_2. The diphenol (IIIb) was obtained as an oil (9·1 g), which solidified to a glass on cooling, and was used without further purification. The diphenol (IIIb) (9·0 g) in n-butanol (100 ml) was converted into its disodium salt with sodium hydroxide (2·4 g) in n-butanol (140 ml) and heated under reflux with the racemic ditosylate (IIb) (13·5 g) under nitrogen. Isolation of the product in the usual way gave a pale orange oil (11·2 g). Chromatography over alumina (30 × 2·5 cm), eluting with benzene, gave an oil (6·2 g), which was dissolved in methanol and kept at 3°. The small crop of crystals (25 mg), m.p. 95—110°, was identified from the i.r. spectrum as isomer B, and was probably formed owing to

the presence of a little of the racemic ditosylate in the *meso*-isomer. On cooling the methanolic solution to −10°, a waxy solid (2·1 g) was obtained, m.p. 75—87°. Repeated fractional crystallisation of this material from methanol afforded pure *isomer* E (0·51 g), m.p. 84—86° (Found: C, 69·6; H, 6·7%). The ^{1}H n.m.r. spectrum in $CDCl_3$ showed two sets of doublets of similar intensity for the methyl groups.

meso- *and* rac-*Diethyl 2,2′-Oxydipropionate*.—Redistilled ethyl lactate (320 g) was converted into its sodium salt in ether (1000 ml), and then treated with ethyl 2-bromopropionate (380 g). The product (200 g), b.p. 121·5—123° at 15 mmHg, represented a yield of 74% after recovery of unchanged ethyl-2-bromopropionate (95 g). G.l.c. showed the ether to be a mixture of 64·9% of the racemate and 35·1% of the *meso*-modification. Price [7] reports 28% of the *meso*-form.

In another preparation using a technical grade of ethyl lactate (140 g) and ethyl-2-bromopropionate (180 g), the yield of ester was 93·5 g (57·2%), b.p. 80—82° at 1—1·5 mmHg, the recovery of the bromo-compound being 45 g. G.l.c. indicated a mixture of 75·8% of the racemate and 24·2% of the *meso*-compound.

meso- *and* rac-2,2′-*Oxydipropan*-1-*ol* (Va *and* b).—Reduction of the foregoing mixture of racemic and meso-diesters (199 g) with lithium aluminium hydride (48 g) in ether (650 ml) gave the racemic and *meso*-glycols (99 g, 82%), b.p. 127—128° at 15 mmHg. The composition of the mixture determined by g.l.c. was 73·6% of the racemate and 25·4% of the *meso*-compound.

meso- *and* rac-*Bis*-(1-*methyl*-2-*tosyloxyethyl*) *Ether* (VIa and b).—The foregoing mixture of *meso*- and racemic glycols (98 g) in dry pyridine (300 ml) was treated with tosyl chloride (360 g) in portions, with stirring and cooling to keep the reaction temperature at 10—20°. After 3 h at 20°, the mixture of the ditosylates was obtained on precipitation into cold water. The product after washing with water was crystallised from methanol to yield the crude racemic isomer (220 g), and recrystallisation from methanol (500 ml) afforded needles of the pure rac-*isomer* (190 g), m.p. 90—91° (Found: C, 53·9; H, 6·1. $C_{20}H_{26}O_7S_2$ requires C, 54·3; H, 5·9%). The combined methanolic liquors were then subjected to a series of fractional crystallisations from methanol, in order to separate the pure *meso*-isomer, advantage being taken of the different crystalline types of the racemate (feathery needles) and the *meso*-compound (thick prisms). After eight crystallisations the meso-*compound* (42 g), m.p. 60°, was obtained (Found: C, 53·85; H, 6·0%). Another 25 g of the racemate was also obtained. The yield of the racemate was 66·5% and of the *meso*-compound 13·0%, the proportions of the racemate (83·6%) and *meso*-compound (16·4%) indicating that the recovery of the more soluble *meso*-compound was not complete.

rel-(7R,9R,18S,20S), *and* rel-(7R, 9R,18R,20R)-7,9,18,20-*Tetramethyl*-6,7,9,10,17,18,20,21-*octahydrodibenzo*[b,k][1,4,-7,10,13,16]*hexaoxacyclo-octadecin* (VIIIa) *and* (VIIIb), *Isomers F and G respectively*.—A solution of sodium hydroxide (3·5 g) in n-butanol (150 ml) was mixed with a solution of catechol (9·0 g) in n-butanol (150 ml) and stirred under nitrogen at 100°. The racemic ditosylate (VIa) (18·5 g) was added and the mixture heated under reflux for 30 min. The precipitated sodium tosylate was filtered off and more sodium hydroxide (3·5 g) in n-butanol (100 ml) was added, followed by the ditosylate (18·5 g). Heating under reflux was continued; the reaction was followed by withdrawing samples, and examining the i.r. spectrum of the ether-soluble material, the extent of the reaction being judged by the intensity of the doublet at 1170 and 1190 cm^{-1} due to the SO_2 sym. stretch of the ditosyl compound. After 6 h, reaction was complete. The filtered reaction solution was concentrated under reduced pressure to 40 ml and dissolved in chloroform (200 ml). After washing with dilute sodium hydroxide solution, and then water, the product was reconcentrated, dissolved in cyclohexane, and treated with charcoal. Filtration and reconcentration yielded a pale orange oil which slowly deposited colourless crystals. The oil was shaken with ether–cyclohexane (1 : 1 v/v) and set aside at 3°, and isomer F slowly separated (1·7 g). Recrystallisation from ethanol gave pure *isomer* F (VIIIa) (1·1 g, 6·7%), m.p. 199—200° [Found: C, 68·9; H, 7·95%; *M* (from *X*-ray data [8]), 414]. On concentration of the mother liquors second crops were obtained, and were combined and recrystallised from methanol giving prisms of *isomer* G (VIIIb) (0·62 g, 3·8%), m.p. 134° (Found: C, 68·8; H, 7·8%).

Isomer F may be obtained in two stable crystalline forms. From most solvents tried, *e.g.* methanol, acetone, chloroform, and ethyl acetate, the isomer crystallised in a monoclinic form, but from acetic acid and by sublimation a triclinic modification was obtained. A transition from the monoclinic to the triclinic form occurs at 180—185°. The two types are most easily distinguishable by differences in their i.r. spectrum especially in the C–H stretch region.

rel-(7R,9S,18R,20S)- *and* rel-(7R,9S,18S,20R)-7,9,18,20-*Tetramethyl*-6,7,9,10,17,18,20,21-*octahydrodibenzo*[b,k][1,4,-7,10,13,16]*hexaoxacyclo-octadecin, Isomers* H *and* I (VIIIc *and* d).—Catechol (12·1 g) was converted into its sodium salt in n-butanol and then treated with the *meso*-ditosylate (VIb) under conditions similar to those described for isomers F and G. Work-up of the reaction product gave a dark brown oil, and this on dilution with ether deposited dark brown polymeric material (3 g) which was discarded. The ethereal solution was washed with water until neutral; concentration under reduced pressure gave a brown oil which was dissolved in light petroleum (b.p. 60—80°) (150 ml). Treatment with charcoal and concentration gave an orange oil (19 g), and a second decolourisation gave a pale orange oil (17·5 g). The oil when dissolved in methanol (100 ml) and kept at 3° for 48 h deposited colourless flakes of isomer I (2·1 g, 8·4%). Recrystallisation from cyclohexane gave pure *isomer* I, m.p. 160° [Found: C, 69·2; H, 7·9%; *M* (from *X*-ray data), 429]. The mother liquor was reconcentrated, dissolved in light petroleum (b.p. 60—80°) (30 ml), and eluted through alumina (60 × 2·5 cm; acidic grade), with light petroleum (500 ml); concentration gave a yellow oil (9·5 g). The i.r. spectrum of this oil showed O–H stretching bands indicating the presence of considerable amounts of open-chain polymeric products which prevented the crystallisation of the macrocycle. The yellow oil (9·5 g) in methanol (75 ml) was treated with potassium thiocyanate (10 g) and warmed to give a solution, then concentrated under reduced pressure to yield a thick slurry. This mass of potassium thiocyanate plus a little of the potassium thiocyanate complex was washed with ether, then shaken with cold water. The colourless solid obtained (0·285 g),

[7] C. C. Price, M. K. Akkapeddi, B. T. BeBona, and B. C. Furie, *J. Amer. Chem. Soc.*, 1972, **94**, 3964.
[8] P. R. Mallinson, *J.C.S. Perkin II*, in the press.

m.p. 153°, was the potassium thiocyanate complex of isomer H, which was dissociated in boiling water, to yield the free isomer H as an oil which crystallised on cooling (0·195 g), m.p. 85—90°. Similar treatment of the mother liquor and ether washings gave another 0·57 g of the potassium thiocyanate complex, which after dissociation and crystallisation from methanol (10 ml) gave a total yield of *isomer* H of 0·462 g (1·9%), m.p. 92° [Found: C, 68·7; H, 7·8%; *M* (from *X*-ray data), 423]. Attempted purification of the potassium thiocyanate complex of isomer H by recrystallisation was rather difficult because of its high solubility in solvents which did not cause dissociation. The complex apparently required water to produce a stable crystalline form; thus it was found that 80 mg of the complex could be recrystallised from ethanol (3 ml) containing a trace of water. The complex on heating showed a change in crystal shape at 75—80°, lost solvent at 95°, and finally melted at 153°.

rac-*Bis*-(2-o-*benzyloxyphenoxy*-1-*methylethyl*) *Ether* (VIIa).—A mixture of sodium o-benzyloxyphenolate (30 g) and the racemic ditosylate (VIa) (30 g) was heated under reflux in benzene for 6 h. The product (17·9 g) was obtained after isolation in the manner described for the cyclic ethers. Recrystallisation from methanol gave feathery *needles* (14·1 g), m.p. 59° (Found: C, 76·9; H, 7·0. $C_{32}H_{34}O_5$ requires C, 77·1; H, 6·9%).

rac-*Bis*-(2-o-*hydroxyphenoxy*-1-*methylethyl*) *Ether* (VIIb).—Hydrogenation of a solution of the foregoing ether (VIIa) (12·2 g) in ethanol (100 ml) over 10% Pd–C (500 mg) at atmospheric pressure was complete in 6 h. The oil obtained on concentration was dissolved in ether and extracted into dilute sodium hydroxide solution. The product was recovered on acidification and extraction into ether. Washing with water, drying, and concentration *in vacuo* at 1 mmHg and 80° afforded the diphenol (VIIb) as a pale straw coloured *oil* (8·0 g) (Found: C, 67·7; H, 7·2. $C_{18}H_{22}O_5$ requires C, 68·0; H, 7·0%).

rel-(7R,9R,18R,20S)-7,9,18,20-*Tetramethyl*-6,7,9,10,17,18,20,21-*octahydrodibenzo*[b,k][1,4,7,10,13,16]-*hexaoxacyclooctadecin*, *Isomer* J (VIIIe).—A solution of the racemic diphenol (VIIIb) (7·1 g) in n-butanol (200 ml) was converted into its disodium salt and then treated with the *meso*-ditosylate (VIb) (7·7 g) dissolved in n-butanol (75 ml), added dropwise over 45 min. After heating for 5 h the i.r. spectrum of the ether-soluble product indicated that reaction was complete. The sodium tosylate was filtered off, and the filtrate concentrated under reduced pressure, dissolved in ether, and washed with water. Evaporation of the ether gave a brown oil (5·15 g); this was decolourised (charcoal) in cyclohexane (75 ml) and the product reconcentrated to yield a pale yellow oil which rapidly crystallised on cooling (4·3 g), m.p. 115—120°. Recrystallisation from methanol (30 ml) and from ethanol (25 ml) gave *isomer* J (2·89 g, 31·1%), m.p. 120—122° [Found: C, 68·5; H, 7·6%; *M* (from *X*-ray data), 406]. Reconcentration of the mother liquor gave a further 0·57 g (6·1%).

Complexes between the Crown Ethers and Salts of Alkali and Alkaline Earth Metals.—The complexes were obtained by allowing a solution of the ligand and salt in stoicheiometric proportions to evaporate slowly at room temperature. The solvents most commonly used were methanol, ethanol, and acetone; for some of the very soluble complexes ethyl acetate or n-butanol was used. In many cases where the complex was solvated, the products were obtained as syrups which crystallised slowly on standing, and evidence of complex formation was obtained from changes in the i.r. spectra. A small number of complexes crystallised from dilute solution in a form sufficiently pure for chemical analyses, and, in some cases, preliminary investigation by *X*-ray photography. Elemental analyses are given in the Table. The solvated complexes were identified from the hydroxy- or carbonyl stretching bands in the i.r. spectra which could be attributed to the solvent.

Complexes formed between crown-ethers and salts

Isomer	Salt	M.p. (°C)	Ratio [a]	Formula of complex		Calc. (%) C	Calc. (%) H	Calc. (%) N	Found (%) C	Found (%) H	Found (%) N	Formula wt. (*X*-rays) Calc.	Formula wt. (*X*-rays) Found
A	KI	200	1 : 1	$C_{24}H_{32}O_6$	KI [b]	49·5	5·5		49·5	5·4			
B	KI	180	1 : 1	$C_{24}H_{32}O_6$	KI [b]	49·5	5·5		49·45	5·65			
C	NaI	260	1 : 1	$C_{24}H_{32}O_6$	NaI [c]	50·75	5·7		51·0	5·7		566	590
C	KNCS	202	1 : 1	$C_{24}H_{32}O_6$	KNCS [c]	58·45	6·3	2·7	58·7	6·4	2·8	513	505
C	$Ca(NCS)_2$	>300 [d]	1 : 1	$C_{24}H_{32}O_6$	$Ca(NCS)_2$ [c]	54·5	5·6	4·9	54·4	5·7	4·8		
D	NaI	130	1 : 1	$C_{24}H_{32}O_6$	NaI EtAc	51·4	6·2		51·3	6·1			
F	NaNCS	198	1 : 1	$C_{24}H_{32}O_6$	NaNCS [c]	60·35	6·5	2·8	59·6	6·5	3·1	497	510
F	KNCS	185	1 : 1	$C_{24}H_{32}O_6$	KNCS [c]	58·5	6·3	2·7	57·8	6·3	2·8		
F	RbNCS	206	1 : 1	$C_{24}H_{32}O_6$	KNCS [c]	53·5	5·75	2·5	53·5	5·8	2·7	557	562
F	KI	220	1 : 1	$C_{24}H_{32}O_6$	KI [c]	49·5	5·5		49·7	5·2			
G	NaNCS	208	1 : 1	$C_{24}H_{32}O_6$	NaNCS [c]	60·3	6·5	2·8	59·8	6·6	2·8	497	495
G	KNCS	230	1 : 1	$C_{24}H_{32}O_6$	KNCS [c]	58·5	6·3	2·7	58·5	6·3	2·75		
G	CsNCS	180	1 : 2	$C_{48}H_{64}O_{12}$	CsNCS EtOH	57·2	6·2	1·3	57·5	6·6	1·3	1069	1040
D	$Ca(NCS)_2$	>300 [d]	1 : 1	$C_{24}H_{32}O_6$	$Ca(NCS)_2$ [c]	54·5	5·6	4·9	54·4	5·7	4·8		
F	$Ca(NCS)_2$	>300 [d]	1 : 1	$C_{24}H_{32}O_6$	$Ca(NCS)_2$ [c]	54·5	5·6	4·9	54·2	5·6	4·8		
F	$Ba(NCS)_2$	>300 [d]	1 : 1	$C_{24}H_{32}O_6$	$Ba(NCS)_2SH_2O$	44·3	5·1	4·0	44·0	5·0	4·3		
B	RbI	185	1 : 1	$C_{24}H_{32}O_6$	RbI [b]	45·8	5·1 (I, 20·2)		45·6	5·3 (I, 20·2)			

[a] Salt : ether. [b] After drying in vacuum. [c] Unsolvated. [d] With decomposition.

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