Chiral Recognition by Configurationally Chiral Cryptands

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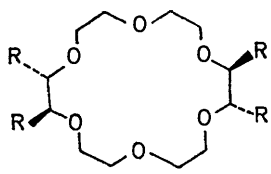
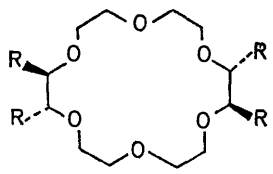
Summary 1,1′,4,4′-Tetra-*O*-triphenylmethyl-2,2′:3,3′-bis-*O*-oxydiethylenedi-L-threitol [LL-(**3**)] and 1,2:1′,2′:5,6:5′,6′-tetra-*O*-isopropylidene-3,3′:4,4′-bis-*O*-oxydiethylenedi-D-mannitol [DD-(**4**)] exhibit enantiomeric differentiation in complexation equilibria towards (±)-(*RS*)-α-phenylethylammonium hexafluorophosphate.

RECENTLY the first steps have been taken by chemists[1,2] towards synthesizing organic catalysts which will exhibit the characteristics of regioselectivity and stereoselectivity in catalysing chemical reactions that are normally associated with enzyme-catalysed transformations found in Nature. The availability[3] of optically pure configurationally chiral cryptands LL-(**1**)—(**3**) and DD-(**4**)—(**6**) which are derived from relatively inexpensive sources of chirality and which complex primary alkylammonium cations has prompted us to examine their chiral recognition properties towards (+)-(*R*)-, (−)-(*S*)-, and (±)-(*RS*)-α-phenylethylamine [(+)-(*R*)-(**7**), (−)-(*S*)-(**7**), and (±)-(*RS*)-(**7**)] salts.

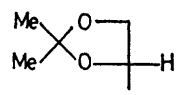
Cryptands (**1**)—(**6**) all have D_2 symmetry and consequently the two faces of the chiral host cycles are homotopic. This means that complexation of achiral or optically pure guests to either face affords identical complexes. However, complexation of enantiomeric guests results in the formation of diastereomeric complexes. An n.m.r. spectroscopic method[4,5] was used to identify the diastereomeric complexes and obtain their relative proportions at equilibrium. In all cases three experiments were performed in which the guest was partitioned betwen D_2O and $CDCl_3$ in the presence of the chiral host. In type (i) experiments, 0·126 mmol of host was dissolved in 0·7 ml of $CDCl_3$ and shaken for 1 min at room temperature with 0·8 ml of D_2O



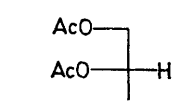
LL-(1) R = CH_2OCH_2Ph
LL-(2) R = CH_2OAc
LL-(3) R = CH_2OCPh_3



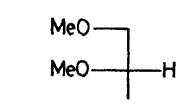
DD-(4) R =



DD-(5) R =



DD-(6) R =



containing 0·745 mmol of (±)-(*RS*)-(**7**)·HCl, and 0·745 mmol of $LiPF_6$. The ^1H n.m.r. spectrum of the $CDCl_3$ layer was then recorded and integrated. In experiments (ii) and (iii), (+)-(*R*)-(**7**).HCl and (−)-(*S*)-(**7**).HCl, respectively,

TABLE. ^{1}H N.m.r. spectroscopic data for the $CDCl_3$ layer in chiral recognition experiments on hosts LL-(**1**)—(**3**) and DD-(**4**)—(**6**) with guests (+)-(*R*)-(**7**).HPF_6, (−)-(*S*)-(**7**).HPF_6, and (±)-(*RS*)-(**7**).HPF_6.

Host[a]	$\tau(J/Hz)$[b] (*R*)-Guest-[Me][c]	$\tau(J/Hz)$[b] (*S*)-Guest-[Me][c]	[Guest]/[Host][d]	Enantiomeric differentiation (*R*)-Guest : (*S*)-Guest
(+)-LL-(**1**)	8·53 (6·8)	8·56 (6·8)	1·0	50 : 50
(−)-LL-(**3**)[e]	8·72 (6·6)	8·75 (6·6)	1·0	40 : 60
(+)-DD-(**4**)	8·38 (7·0)	8·33 (7·0)	1·3	62 : 38
(+)-DD-(**5**)	8·36 (7·0)	8·34 (7·0)	1·4	50 : 50

[a] Hosts (−)-LL-(**2**) and (+)-DD-(**5**) exhibited insufficient splittings between the methyl doublets of the racemic guests to permit reliable calculations of the enantiomeric differentiation. The guest to host ratios for (−)-LL-(**2**) and (+)-DD-(**5**) were 0·9 and 1·7, respectively. [b] The spectra were recorded on a Varian HA100 spectrometer with Me_4Si as 'lock' and internal standard. [c] Assignments were made on the basis of type (ii) and type (iii) experiments. [d] Guest to host ratios in excess of 1·0 indicate the presence of some 2 : 1 complex formation which could arise through hydrogen bonding of a second guest to oxygens in the side chains of the host. [e] ^{1}H n.m.r. spectra recorded at 70 °C in order to obtain better resolution.

replaced (±)-(*RS*)-(**7**).HCl. Although diastereomeric complex formation is accompanied by significant changes in the ^{1}H n.m.r. spectra of the hosts,‡ it manifests itself most noticeably in small chemical shift differences between originally coincident signals arising from the previously

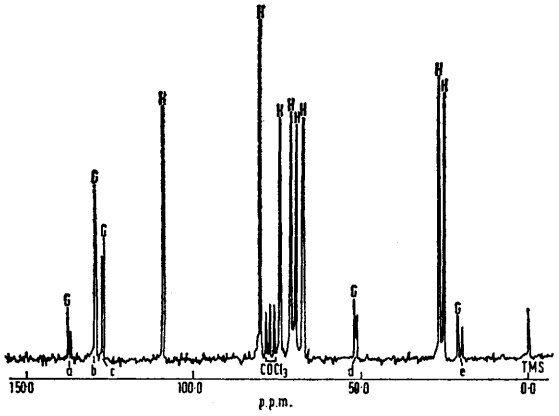


FIGURE 1. The noise-decoupled ^{13}C n.m.r. spectrum of DD-(**4**)-(*RS*)-(**7**).HPF_6: H indicates host signals‡ and G indicates guest signals. Guest signals are assigned from low field to high as (a) substituted carbons in the (*R*) and (*S*) phenyl rings, (b) *meta* and *para* carbons in the phenyl rings, (c) *ortho* carbons in the (*S*) and (*R*) phenyl rings, (d) (*R*) and (*S*) methine carbons, and (e) (*R*) and (*S*) methyl carbons.

enantiomeric guests. In the case of cryptands (+)-LL-(**1**), (−)-LL-(**3**), (+)-DD-(**4**), and (+)-DD-(**6**) two doublets were observed in type (i) experiments for the methyl groups of the guests in the diastereomeric complexes formed between the hosts and the racemic guests. The configurational assignments to the diastereomeric complexes was made on the basis of type (ii) and type (iii) experiments with optically pure guests. The molar ratios of guest to host were obtained directly from integration and the enantiomeric differentiations were deduced by line shape analysis on expanded spectra (50 Hz sweep width) using a suitable computer program. The results are summarised in the Table. The enantiomeric differentiation of 62 : 38 exhibited by DD-(**4**) towards (*RS*)-(**7**).HPF_6 in favour of the (*R*)-isomer is confirmed qualitatively but convincingly in the noise-decoupled ^{13}C n.m.r. spectrum (Figure 1) obtained for a type (i) experiment.

Chiral recognition is observed when the substituent groups on the configurationally chiral 18-crown-6 cycle are bulky. With the L-series host LL-(**3**), complex LL-(**3**)-(*S*)-(**7**).HPF_6 is *ca.* 240 cal mol^{-1} more stable than complex LL-(**3**)-(*R*)-(**7**).HPF_6. With the D-series host DD-(**4**), com-

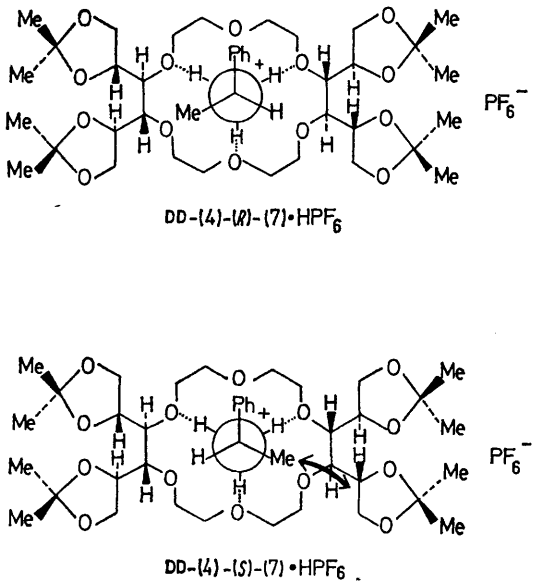


FIGURE 2. Three-point binding models for the diastereomeric complexes DD-(**4**)-(*R*)-(**7**).HPF_6 and DD-(**4**)-(*S*)-(**7**).HPF_6.

plex DD-(**4**)-(*R*)-(**7**).HPF_6 is *ca.* 300 cal mol^{-1} more stable than complex DD-(**4**)-(*S*)-(**7**).HPF_6. Although the free energy differences are small they are in accord with expectation arising out of inspection of molecular models. Assuming a three-point binding model[2,3,6] for the 1 : 1 complexes formed between DD-(**4**) and (*R*)-(**7**).HPF_6, and DD-(**4**) and (*S*)-(**7**).HPF_6, and selecting the Newman projection which places the phenyl group over a region of the 18-crown-6 cycle free of substituent groups, the methyl group of the guest is seen (Figure 2) to interact more severely with a side chain in the DD-(**4**)-(*S*)-(**7**).HPF_6 complex. In the L-series the situation is reversed and the LL-(**3**)-(*R*)-(**7**).-HPF_6 complex experiences this destabilising interaction.

‡ The fact that no duplication of the signals for the hosts are observed means that exchange between guest and host is fast on the n.m.r. time scale.

Although optically active configurationally chiral cryptands have been reported previously,[5,7] the chiral recognition exhibited by LL-(**3**) and DD-(**4**) is novel and puts them on a par with the simple conformationally chiral cryptands[2] obtained from 2,2′-dihydroxy-1,1′-binaphthyl. Stereoselectivity in complexation is one important requirement for an organic catalyst. Another requirement is functionality[2,8] and hosts derived from carbohydrate precursors are well-endowed with functional groups.

We thank Dr. B. F. Taylor for recording the ^{13}C n.m.r. spectra on a Jeol PS100 spectrometer.

(*Received, 11th August* 1975; *Com.* 933.)

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