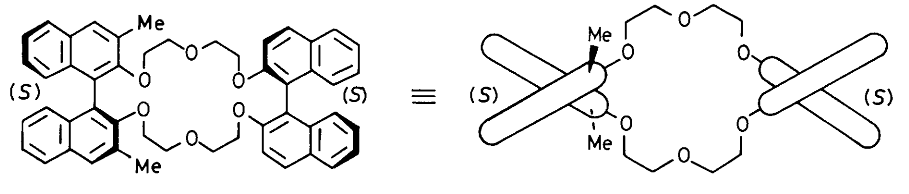
Source of Chiral Recognition in Coraplexes with Phenylglycine as Guest

Carolyn B. Knobler, Fred C. A. Gaeta, and Donald J. Cram*

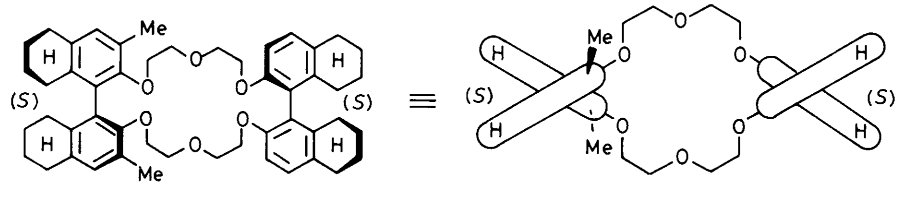
Department of Chemistry and Biochemistry, University of California at Los Angeles, Los Angeles, California 90024, U.S.A.

Crystal structures of L-$PhCH(CO_2H)NH_3ClO_4\cdot$($SS$)-$Me_2T(OEOEO)_2T$ (**4**) (T = bitetralyl component, E = $-CH_2CH_2-$) demonstrate that high chiral recognition in complexation between hosts and amino acid guests is subject to design.

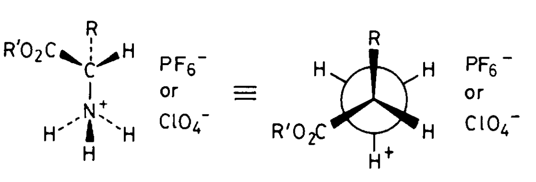
The chiral binaphthyl host (*SS*)-(**1**)[1] was shown to complex L-$PhCH(CO_2Me)NH_3PF_6$ 1.9 kcal mol^{-1} (1 kcal = 4.184 kJ) more strongly than the D-enantiomer (a factor of 31 at 0 °C) in $CDCl_3$,[2] and to complex L-$PhCH(CO_2H)NH_3ClO_4$ 1.4 kcal mol^{-1} more strongly than the D-enantiomer (a factor of 14 at 0 °C) in MeCN in $CHCl_3$ (0.45 mol fraction).[3] The very similarly shaped bitetralyl host (*SS*)-(**2**) complexed L-$PhCH(CO_2Me)NH_3ClO_4$ 1.3 kcal mol^{-1} more strongly than the D-enantiomer,[2] whereas the mixed binaphthyl–bitetralyl host (*RR*)-$Me_2D(OEOEO)_2T$ (D = binaphthyl component, T = bitetralyl component, E = $-CH_2CH_2-$) (not formulated) complexed D-$PhCH(CO_2Me)NH_3PF_6$ 1.9 kcal mol^{-1} more



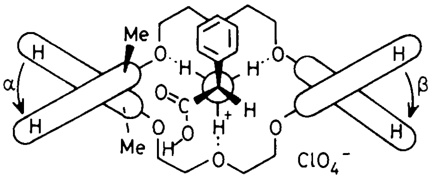
(SS)-(**1**) or (SS)-$Me_2D(OEOEO)_2D$



(SS)-(**2**) or (SS)-$Me_2T(OEOEO)_2T$

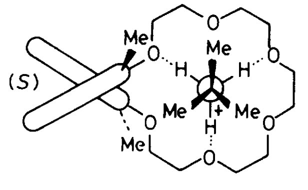


L-(**3**)



(SS)-L-(**4**) or

(SS)-L-$Me_2T(OEOEO)_2T \cdot PhCH(CO_2H)NH_3ClO_4$



(S)-(**5**) or (S)-$Me_2D(OEOEO)_2E \cdot Bu^tNH_3^+$

strongly than the L-enantiomer in $CDCl_3$ at 0 °C (a factor of 31). A variety of interchanges between bitetralyl and binaphthyl modules and between amino acid and ester salts such as (**3**) provided a body of internally consistent results anticipated and rationalized on the basis of Corey–Pauling–Koltun (CPK) molecular model examination. Structures such as (*SS*)-L-(**4**) (usually the guest was rotated 180° with respect to the host) explained the direction of the chiral bias, and the large differences in chemical shifts in the ^{1}H n.m.r. spectra of diastereoisomeric complexes.

Although racemic (**1**) had been easily resolved by crystallization of favoured diastereoisomeric complexes with pure enantiomers of $PhCH(CO_2H)NH_3ClO_4$, crystals suitable for *X*-ray structure determination of (*SS*)-L, or (*RR*)-D configurations eluded us. A complex 'designed not to form' between (*SS*)-$D(OEOEO)_2D$ and D-$PhCH(CO_2Me)NH_3PF_6$ (thermodynamically less stable diastereoisomer) did provide suitable crystals,[2] and had a structure in which CO_2Me to naphthyl π–π binding was visible, but $^+NH \cdots O$ and $^+N \cdots O$ binding was inefficiently used.[4] The expected tripod binding was observed for the complex (*S*)-$Me_2D(OEOEO)_2E \cdot Me_3CNH_3ClO_4$, (*S*)-(**5**),[5] whose CPK models corresponded very well with the crystal structure.[6] Complex (*SS*)-L-(**4**) had formed crystals by 1977 that provided excellent diffraction patterns, but the unit cell contained two independent complexes and one mole of EtOAc to give a total of 298 atoms. Solution of the crystal structure resisted 10 years of intermittent effort involving a variety of approaches. This paper reports the elucidation of the structures of the two independent complexes.†

Figure 1 shows macroring face and edge stereoviews of the two structures labelled (**4a**) and (**4b**). They are very similar

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† Compound (**4**)·$0.5MeCO_2CH_2Me$ crystallizes in small, colourless, irregularly shaped plates from $CHCl_3$–$MeCO_2CH_2Me$.

Crystal data: monoclinic, space group $P2_1$, a = 10.054(3), b = 24.075(7), c = 22.414(6) Å, β = 98.52(2)°, U = 5365(3) Å^3, Z = 4 (two host–guest complexes, two ClO_4^-, one ethyl acetate/asymmetric unit). The crystal was examined on a Syntex P$\bar{1}$ diffractometer using Mo-K_α radiation at 115 K. The structure was determined by direct methods (SHELX86). Refinement, using a modified version of SHELX 76, of four blocks containing 90, 231, 231, and 90 parameters, respectively, for 4961 reflections with $I > 3\sigma(I)$ gave R = 0.0741, R_w = 0.080 (error of fit 2.04). Perchlorate atoms refined anisotropically, all other non-H atoms isotropically, host H atoms riding or in rigid methyl groups with C–H distances fixed at 1.08 Å, carboxyl H (guest) positions refined. All H atoms had fixed isotropic displacement parameters based on the displacement parameters of the attached atoms. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

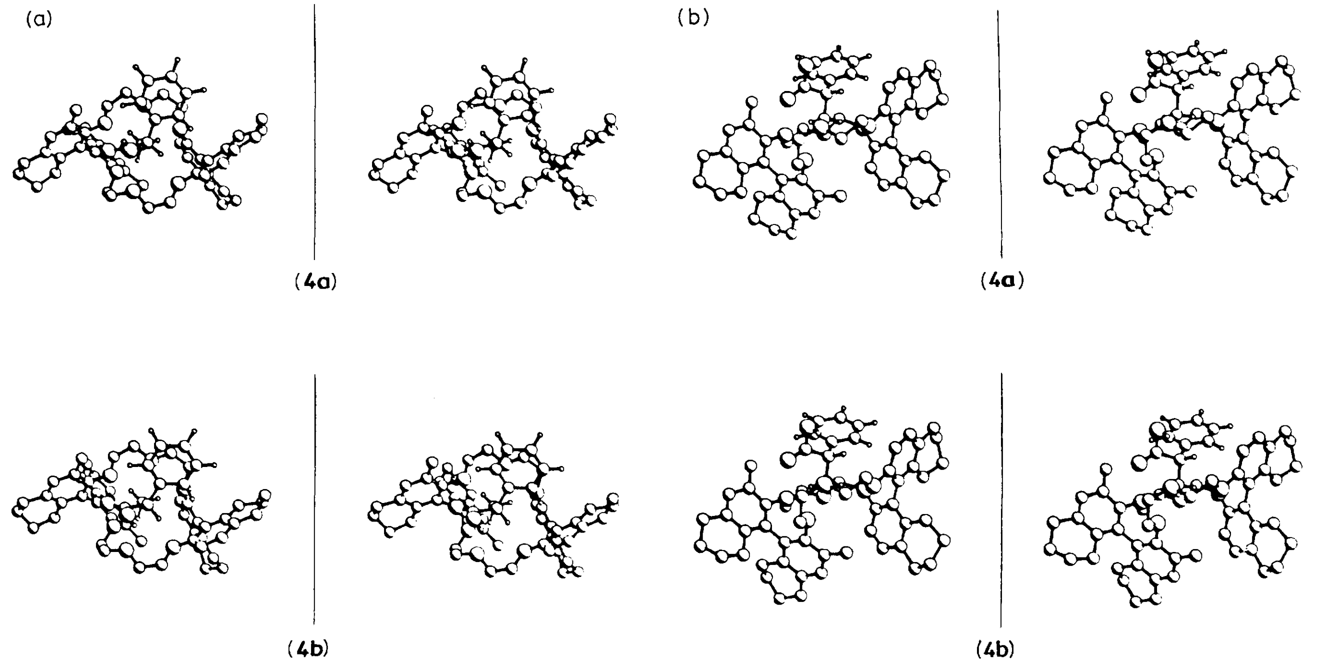

Figure 1. Stereoviews of crystal structures of (*SS*)-L-(**4**) (ClO_4^- omitted); (a) face and (b) edge views.

Table 1. Distances and bond angles in (**4a**) and (**4b**).

N···O/Å[a]	(4a)	(4b)
Average[b]	3.00 ± 0.11	3.02 ± 0.28
2 o'clock	2.89	2.92
4 o'clock	3.25	3.30
6 o'clock	2.96	3.11
8 o'clock	2.91	2.85
10 o'clock	2.88	2.81
12 o'clock	3.11	3.14
NH···O/Å[a]		
Average[b]	1.95 ± 0.15	1.93 ± 0.27
2 o'clock	1.8	1.8
6 o'clock	2.1	2.2
8 o'clock	2.0	2.0
10 o'clock	1.9	1.7
Angles/°		
C–N vector to 6 O's best plane	68	66
Ar–C–N–H dihedral	59	52
MeAr–ArMe dihedral (α)[c]	75	78
HAr–ArH dihedral (β)[c]	88	82.5

[a] Oxygens and N–H hydrogens are labelled clockwise in face views of (**4a**). [b] Average ± extremes. [c] For α and β definitions and for clock locations for oxygens, see (*SS*)-L-(**4**) formula.

even though their environments in the unit cell are different. Thus their structures appear to originate in the stereoelectronic complementarity of the host and guest. Table 1 shows the principal structural parameters and identifies the similarities and differences.

The face views of Figure 1 suggest that pole–dipole attractions between $^+NH\cdots O$ and $^+N\cdots O$ are the main binding forces between host and guest. In (**4a**) and (**4b**), the average of $(N\cdots O)_6$ distances are 3.00 ± 0.11 and 3.02 ± 0.28 Å (extremes), respectively. The four oxygens at 2, 6, 8, and 10 o'clock participate in hydrogen bonding to provide averages of $(NH\cdots O)_4$ distances of 1.95 ± 0.15 and 1.93 ± 0.27 Å (extremes) for (**4a**) and (**4b**), respectively. These average distances are shorter than the $(NH\cdots O)_3$ average distance of 2.0 Å in (*S*)-(**5**). The hydrogen bonds to oxygens in (**4**) at 6 and 8 o'clock are bifurcated, and consequently are about 0.3 to 0.5 Å longer than those at 2 and 10 o'clock, which average 1.8 Å in the two structures. The $NH\cdots O$ angles are 165° (a_{av}) and 177° (b_{av}) for the ordinary, and 134° (a_{av}) and 132° (b_{av}) for the bifurcated bonds. Molecular model examination of host (**2**) indicates that of the six oxygens, only those at 8 and 10 o'clock are conformationally locked into binding conformations by the aryl methyl groups before complexation. This preorganization of the host for binding prior to complex formation[7] correlates with the $N\cdots O$ distances in (**4a**) and (**4b**) being the shortest of the 12 measured [$(N\cdots O)_4$ average is 2.86 ± 0.05 Å]. The MeAr–ArMe dihedral angles (α) are 75 and 78° for (**4a**) and (**4b**), respectively, as compared to the HAr–ArH dihedral angles (β), which are considerably greater at 88 and 82.5°, respectively. Thus the oxygens at 8 and 10 o'clock behave as if they were the most basic of the six of the host.

The edge views of Figure 1 provide a visual impression of guest posture with respect to host. The angle at which the C–N bond vector intersects the best plane of the six oxygens in many alkylammonium coraplexes is close to 90° [*e.g.*, 88° in (*S*)-(**5**)].[8] In (**4a**) and (**4b**) this angle is 68 and 66°, respectively, which gives the phenyl group of the guest just enough space to occupy the cavity centred roughly above the oxygens at 12 o'clock [face views of (**4a**) and (**4b**)]. The Ar–C–N–H dihedral angle in (**4a**) is 59° and in (**4b**) is 52°, close to the 50—60° comparable dihedral angles previously observed for eight alkylammonium coraplexes[8] [*e.g.*, the Me–C–N–H dihedral angle in (*S*)-(**5**) is 53°). Particularly striking in the edge views of (**4a**) and (**4b**) is the splaying open of the cavities on the top to accommodate the guest, and the synchronous closing of the cavities on the bottom owing to the two tetralyl units approaching each other. The distances between the Ar–Me carbon and the nearest carbon atoms of the transannular aryl plane on the bottoms of (**4a**) and (**4b**) are 3.5 and 3.7 Å, and 3.4 and 3.6 Å, respectively, which are approximately contact distances. All of the conformations of the $O-CH_2-CH_2-O$ groups are *gauche*, and the orbitals of the unshared electron pairs all face inward, upward, or downward, but not outward.

Three types of possible host–guest binding interactions appear to be absent in (**4a**) and (**4b**). (i) The O–H groups of the guest in (**4a**) and (**4b**) are oriented differently from one another, and are too distant from any of the host's six oxygens or four aryl groups to be hydrogen bonded 'intramolecularly'. In (**4a**), this hydrogen is 2.1 Å from a perchlorate oxygen. (ii) The same absence of intramolecular hydrogen bonding applies to the slightly acidic NC–H hydrogen of the guest. (iii) The π–π host–guest attractions between the CO_2Me and naphthyls visible in the much deformed (*SS*)-D-$D(OEOEO)_2D{\cdot}PhCH(CO_2Me)NH_3PF_6$ complex[2,4] are absent in (**4a**) or (**4b**). The CO_2H and aryl planes are too distant from one another to interact.

The crystal structures of (**4a**) and (**4b**) are fully compatible with the ^1H n.m.r. chemical shifts observed for both hosts and guests in complexes (*SS*)-L-$Me_2D(OEOEO)_2D{\cdot}PhCH(CO_2Me)NH_3^+$ and (*SS*)-L-$Me_2D(OEOEO)_2D{\cdot}PhCH(CO_2H)NH_3^+$ in solution.[2,3] The crystal structures further substantiate the basic premise upon which most host–guest complexation studies are based, *i.e.*, that CPK molecular models coupled with physical organic principles can be used to design complexes with a useful degree of confidence. The source of the chiral recognition in (**4**) and related complexes is the stereoelectronic complementarity of the host–guest binding sites located in the interior of the complex, coupled with chiral complementarity of steric barriers in the host with the arrangement of substituents of the guest.

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