Acta Cryst. (1999). B**55**, 432–440

Chiral recognition between host and guest: a binaphthyl-18-crown-6 host with D-phenylglycinium methyl ester perchlorate guest. A difficult structure solved with *CRUNCH*

Donald J. Cram,[a] R. A. G. de Graaff,[b] Carolyn B. Knobler,[a] David S. Lingenfelter,[c] Emily F. Maverick[a]* and Kenneth N. Trueblood[a]†

[a]*Department of Chemistry and Biochemistry, University of California, Los Angeles, CA 90095-1569, USA,* [b]*X-ray Department, Gorlaeus Laboratories, PO Box 9502, 2300 RA Leyden, The Netherlands, and* [c]*97 Shoreline Court, Richmond, CA 94804-7432, USA. E-mail: maverick@chem.ucla.edu*

(*Received 27 May 1998; accepted 15 October 1998*)

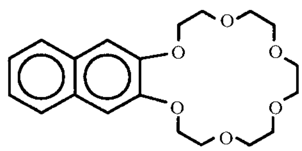
Abstract

The complex between (*R*)-4,5,7,8,10,11,13,14,16,17-decahydro-2,19-diphenyldinaphtho[2,1-*q*:1′,2′-*s*][1,4,7,-10,13,16]hexaoxa[2,5,8,11,14,17,19]cycloicosaheptene {*Chemical Abstracts* name: (*R*)-4,5,7,8,10,11,13,14,16,17-decahydro-2,19-diphenyldinaphtho[2,1-*q*:1′,2′-*s*][1,4,7,-10,13,16]hexaoxacycloicosin} and D-2-phenylglycinium methyl ester perchlorate, $C_9H_{12}NO_2^+.ClO_4^-.C_{42}H_{40}O_6.$-$H_2O$, crystallizes in the orthorhombic space group $P2_12_12_1$ with two $C_9H_{12}NO_2^+.C_{42}H_{40}O_6$ complexes, two ClO_4^- ions and two molecules of water in the asymmetric unit. Crystal data: M_r = 924.44, a = 23.048 (7), b = 34.383 (6), c = 11.992 (6) Å, V = 9503 (6) Å^3, Z = 8, D_x = 1.292 Mg m^{-3}, $F(000)$ = 3904, μ(Cu $K\alpha$) = 1.261 mm^{-1}, T = 175 K, R = 0.0896 for all 7784 reflections, 1208 parameters refined in three blocks with 29 restraints. Nearly twenty years elapsed between the first data collection and the solution of the structure with the direct-methods program *CRUNCH*. The structural details are of interest because enantiomers of this host show a high degree of discrimination between enantiomers of α-amino acids and their esters. The crystal structure demonstrates the influence of C—H···O and C—H···π interactions on the unexpected orientation of the guest in the host cavity. The same orientation is found in both of the unique complexes, and the geometric details are in agreement with solution studies.

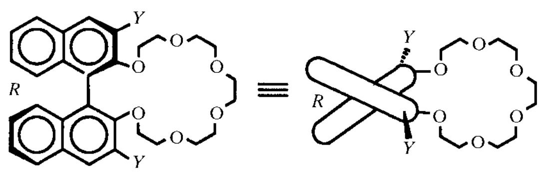
1. Introduction

This structural study was begun in 1979, when systematic scrutiny of ground-state chiral recognition in solution had just started (Lingenfelter *et al.*, 1981, and references cited therein). The hosts in Fig. 1 contain O-atom arrangements similar to that of 18-crown-6, but were designed to have a higher degree of preorganization for binding alkylammonium ions than the parent corand. Hosts (2) and (3) also have a chiral cavity. The structure of the complex of (*R*)-(3) with D-phenylglycinium methyl ester perchlorate is reported here.

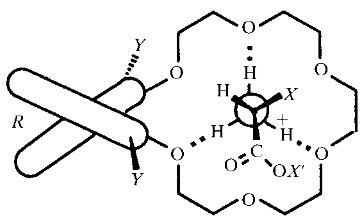
The binaphthyl group, because of its inherent high barrier to inversion, confers chirality on the host. The barrier was systematically increased by adding bulky groups (*Y* in Fig. 1) to the binaphthyl moiety. Structure determinations of both the empty host and the cationic



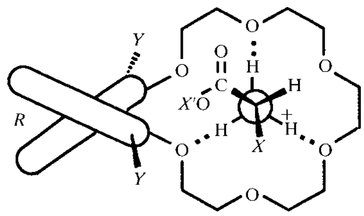
(1)



(2): Y = CH_3; (3): Y = C_6H_5



Proposed (1981)



Found for (3), X = C_6H_5, X' = CH_3

Fig. 1. Structural formulas for hosts (1), naphthyl-18-crown-6 (Cram & Trueblood, 1981); (2) and (3), Y_2-binaphthyl-20-crown-6, Y = CH_3 and Y = C_6H_5, respectively. Also shown are the proposed conformation for the complex of Y_2-binaphthyl-20-crown-6 and $X'O_2CCHXNH_3^+$ (Lingenfelter *et al.*, 1981) and that found for the present complex of (3), Y = C_6H_5, X' = CH_3 and X = C_6H_5.

† Deceased 7 May 1998.

ISSN 0108-7681

Table 1. *Free energy of binding XNH_3^+ (picrates: Lingenfelter et al., 1981) and EDCs (perchlorates: Lingenfelter et al., 1981; Peacock et al., 1978) for chiral hosts*

	$-\Delta G^\circ$ (kJ mol^{-1})			EDC†
Host‡	Guest: HNH_3^+	Guest: $CH_3NH_3^+$	Guest: $(CH_3)_3CNH_3^+$	Guest: XCH(CO_2CH_3)NH_3^+
(1), Nap$(OEOEO)_2$E	40	31	29	Host not chiral
(2), $(CH_3)_2$D$(OEOEO)_2$E	37	29	27	(3.3)§
(3), $(C_6H_5)_2$D$(OEOEO)_2$E	33	26	19	19.5 (7.7)§
(4), $(CH_3)_2$D$(OEOEO)_2$D	31	18	11	22
(5), D$(OEOEO)_2$D	23	16	11	2.4
(6), $(CH_3)_2$T$(OEOEO)_2$T			14¶	10.2

† EDC = $[G_1]_{org}[G_2]_{aq}/[G_2]_{org}[G_1]_{aq}$ where $[G_1]$ is the concentration of the more strongly complexed and $[G_2]$ is the concentration of the less strongly complexed guest enantiomer. Org and aq refer to the organic and aqueous layers in the extraction–complexation procedure, respectively. ‡ Shorthand for condensed structural formulas: Nap = naphthyl, E = $-CH_2CH_2-$, D = binaphthyl, T = bitetralyl. For structural formulas see Figs. 1 and 2. § Values in parentheses: $X = (CH_3)_2CH$. All others: $X = C_6H_5$. ¶ Estimated from K_e values given in Peacock *et al.* (1978). The counterion was hexafluorophosphate.

complex with $Y = CH_3$, (2), established the structural preorganization of the host and the mode of binding of $(CH_3)_3CNH_3^+$ to the chirally organized O atoms of the crown ring (Goldberg, 1980).

Cationic complexes formed by corand hosts (1)–(3) are readily extracted (with counterion) into relatively nonpolar solvents. The degree of preorganization produced by substituting a binaphthyl group for a CH_2CH_2 group in 18-crown-6 was measured by standardized extraction procedures (Helgeson *et al.*, 1979). The free energies of binding of related hosts with a series of ammonium-ion guests are compared in Table 1. In the standard extraction procedure the anion, picrate, is extracted into chloroform along with the complex cation, and its UV absorbance at 380 nm provides a convenient method of observing the rate of extraction and measuring the strength of binding of the complex. The data in Table 1 show that the present host, (3), binds ammonium guests less strongly than (2) and the nonchiral host (1) but more strongly than hosts containing two binaphthyl or bitetralyl chiral units [(4), (5), (6); see Fig. 2]. Structures of (5) and (6) with phenylglycinium methyl ester and phenylglycinium guests, respectively, have been determined (Goldberg, 1977; Knobler *et al.*, 1988).

Chiral-recognition experiments (Lingenfelter *et al.*, 1981) gave the following results. With amino-acid or amino-acid-ester guests, the best discrimination between enantiomeric guests by hosts containing one binaphthyl group was obtained with (3) ($Y = C_6H_5$). In Table 1, enantiomer distribution constants (EDCs) for selective complexation of D- and L-amino-acid methyl ester guests are given for hosts (2)–(6). The EDC of (3) is nearly as high as that for the most discriminating host with two binaphthyl groups, (4). The discrimination was significantly better when X of the XCH(CO_2X')NH_3^+ guest was phenyl rather than isopropyl, but did not depend strongly on whether the guest was the amino acid (X' = H) or the amino-acid ester ($X' = CH_3$). A binding conformation for (3) was proposed (Lingenfelter *et al.*, 1981) in which the X group avoids, but the carboxylate contacts, Y of the host (Fig. 1). The current study was undertaken to help correlate structure with binding and stereoselectivity.

2. Experimental

2.1. *Crystals*

Many attempts were made to grow suitable crystals of completely enantiomerically resolved complexes of (3),

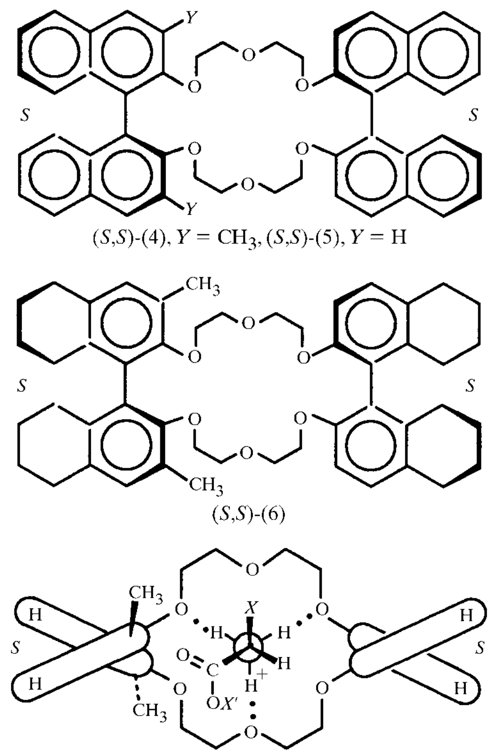


Fig. 2. Structural formulas for hosts (4), (5) and (6), 22-crown-6 hosts containing two binaphthyl or two bitetralyl groups. Also shown is the conformation of the complex (*S,S*)-(6)∪L-$C_6H_5CH(CO_2H)NH_3^+$ (Knobler *et al.*, 1988).

Table 2. *Experimental details*

Crystal data	
Chemical formula	$C_9H_{12}NO_2^+.ClO_4^-.C_{42}H_{40}O_6.H_2O$
Chemical formula weight	924.44
Cell setting	Orthorhombic
Space group	$P2_12_12_1$
a (Å)	23.048 (7)
b (Å)	34.383 (6)
c (Å)	11.992 (6)
V (Å^3)	9503 (6)
Z	8
D_x (Mg m^{-3})	1.292
Density measured by	Flotation in carbon tetrachloride/benzene (295 K; see text)
Radiation type	Cu $K\alpha$
Wavelength (Å)	1.5418
No. of reflections for cell parameters	25
θ range (°)	7.95–10.0
μ (mm^{-1})	1.261
Temperature (K)	175
Crystal form	Cut needle
Crystal size (mm)	0.39 × 0.20 × 0.18
Crystal color	Colorless
Data collection	
Diffractometer	Rigaku AFC-5*R*
Data collection method	$\theta/2\theta$ scans
Absorption correction	None
No. of measured reflections	7823
No. of independent reflections	7821
No. of observed reflections	6928
Criterion for observed reflections	$I > 2\sigma(I)$
θ_{max} (°)	60.09
Range of h, k, l	$0 \rightarrow h \rightarrow 25$ $0 \rightarrow k \rightarrow 38$ $0 \rightarrow l \rightarrow 13$
No. of standard reflections	3
Frequency of standard reflections	Every 147 reflections
Intensity decay (%)	4
Refinement	
Refinement on	F^2
$R[F^2>2\sigma(F^2)]$	0.0793
$wR(F^2)$	0.2112
S	1.010
No. of reflections used in refinement	7784
No. of parameters used	1208
H-atom treatment	H atoms riding; fixed C—H distances, $<u^2>_H = 1.2 \times U_{eq}$ of attached C, except for CH_3 and NH_3^+ groups, for which factor was 1.5; CH_3 groups rotating about O—C bond; NH_3^+ groups rotating about C—N bond
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.1470P)^2 + 18.9318P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	0.287
$\Delta\rho_{max}$ (e Å^{-3})	1.032
$\Delta\rho_{min}$ (e Å^{-3})	−0.590
Extinction method	*SHELXL*93 (Sheldrick, 1993)
Extinction coefficient	0.00111 (12)
Source of atomic scattering factors	*International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
Computer programs	
Data collection, cell refinement and data reduction	*UCLA Crystallographic Package* (1984)
Structure solution	*CRUNCH* (pre-production version, de Graaff, 1998)
Structure refinement	*SHELXL*93 (Sheldrick, 1993)
Preparation of material for publication	Local programs
Molecular graphics	*SHELXTL* (Sheldrick, 1995)

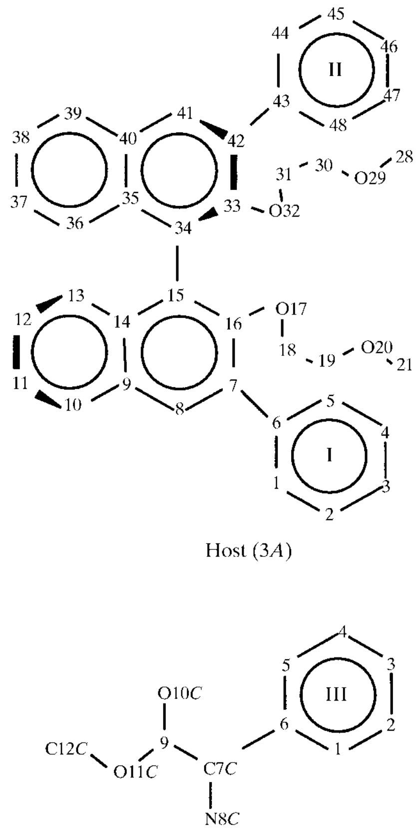
with the hope of preparing complexes of one host (*R* or *S*) with guests of each configuration. Although the complexes could be isolated, the only crystals of host (3) (Y = C_6H_5) suitable for X-ray analysis were obtained with (*R*)-(3), the strongly favored guest D-$C_6H_5CH(CO_2CH_3)NH_3^+$, and ClO_4^-. Several other anions were tried, including picrate, without success.

Crystals for the X-ray structural study were prepared as follows. Solutions of D-phenylglycine methyl ester perchlorate and (*R*)-(3) dissolved in boiling ethyl acetate were combined. The precipitate isolated from the cooled mixture was dissolved in hot methanol; small crystals formed upon cooling the solution and were isolated and recrystallized from methanol. The crystals so prepared contain two formula units and two H_2O molecules, a total of 132 non-H atoms and 108 H atoms, in the asymmetric unit in $P2_12_12_1$. The point at which water entered the preparation is not known, but the measured density at room temperature, 1.261 Mg m^{-3} (V = 9753 Å^3), is in agreement with this formula. Despite the fact that we collected an apparently good data set at room temperature, we were not able to solve the structure at that time, with *MULTAN* and its accompanying suite of programs (*YZARC*, *RANTAN* and others) (Declercq *et al.*, 1979), nor at intervals over the next 15 years as the *SHELX* (Sheldrick, 1990) programs became available. In 1985, new crystals were grown by J. Chappuis, using the original conditions, but the data collected at that time did not yield a solution. In 1995, data were collected on one of the Chappuis crystals, both at room temperature and at 175 K, on a Rigaku AFC-5*R* diffractometer with a rotating anode and Cu $K\alpha$ radiation. Data were limited to θ_{max} = 60° by instrument geometry. These data, especially those taken at 175 K, were more intense than those in previous measurements; however, structure solution still eluded us although we tried many different approaches and programs.

2.2. *Solution*

The structure was finally solved by a pre-production version of the program *CRUNCH* (de Gelder *et al.*, 1993; de Graaff, 1998). *CRUNCH* is based on two principles: the Maximum Determinant Rule as formulated by Tsoucaris (1970) and careful evaluation and extension of the partial models obtained from the phases calculated using this rule. The size of a matrix that may be useful for phase determination is limited by the number of atoms in the cell. Generally matrices of orders larger than $N/3$ are too large. A significant amount of redundancy in the matrix is also required. This obviously limits the number of independent reflections that can be phased in one matrix by maximizing the determinant as a function of the phases. To overcome this problem, *CRUNCH* allows for the concurrent maximization of more than one determinant. The matrices are linked to avoid arriving at a set of phases which contains subsets derived from different origins, since the value of the determinant of a Karle–Hauptman matrix is a structure invariant.

Solution of the phase problem was not routine; the structure was solved by inspection of the results of 100 random trials. *CRUNCH* uses the conventional $R2$ to evaluate atomic models at various stages of the process of solution. The model with the lowest final value of $R2$ was used to generate new phases as input to the phase refinement by simultaneous maximization of three Karle–Hauptman determinants. This approach is somewhat reminiscent of the well known Shake and Bake procedure (Weeks *et al.*, 1994). After a few cycles, a fairly complete model of the structure resulted. It is worth noting that the current version of *CRUNCH* (de Graaff, 1998) solves the structure with default parameters.



Host (3*A*)

Cation guest of (3*A*) (C1*C etc.*)

Fig. 3. Atomic numbering scheme for cation (3*A*), (R)-(3)∪D-$C_6H_5CH(CO_2CH_3)NH_3^+$. Roman numerals I, II and III designate the centroids of the phenyl-ring planes C1–C6, C43–C48 and C1*C*–C6*C*, respectively. Host–guest (3*B*) is numbered the same, *modulo* 50, and the roman numerals IV, V and VI designate the centroids of the ring planes C51–C56, C93–C98 and C51*C*–C62*C*, respectively.

2.3. *Refinement*

During the early refinement stages large displacement parameters of the atoms in one perchlorate ion and extra peaks in the vicinity suggested disorder. In the final model for this region we used three Cl atoms and 11 O atoms with isotropic displacement parameters and restrained distances and angles, for a total occupancy of 1.0 Cl and 4.0 O. Similarly, one water O atom is modeled with two atoms (O2*W*, anisotropic, and O3*W*, isotropic), for a total occupancy of 1.0, and one O atom in the more ordered ClO_4^- ion is modeled with two isotropic atoms (O2*A* and O2*A*′). Other non-H atoms were refined anisotropically. Final refinement cycles included all atomic positions and displacement parameters in three overlapping blocks of 124, 553 and 563 parameters, respectively. H atoms for water were not located.

The maximum shift/error of 0.287 in the last cycle was for the torsion angle for the methyl group C62*C*, and the maximum shift in position was 0.02 Å for H62*E*. The highest peak in the electron-density synthesis (1.032 e $Å^{-3}$) is in the disordered perchlorate region, 1.28 Å from Cl16 and 0.67 Å from O17*A*. The next highest peak (0.90 e $Å^{-3}$) is between O4*A* of perchlorate and O2*W*, perhaps indicating another minor position for disordered water. Experimental details are given in Table 2, and fractional coordinates and U_{eq} or U_{iso} values are given in Table 3†.

3. Results

3.1. *Configuration and conformation of host and guest*

The crystal study reported here confirms the absolute configurations (Flack, 1983) of host (3) and its guest, but not the proposed binding conformation (Fig. 1). The numbering scheme for the crystal structure is given in Fig. 3. The atoms for cationic complex (3*A*) are numbered 1 through 48, 1*C* through 12*C*, and those for complex (3*B*) are numbered the same, *modulo* 50. Fig. 4 is a stereoview of the asymmetric unit, and Figs. 5 and 6 are views of each of the cations looking down the

† Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR0005). Services for accessing these data are described at the back of the journal.

Table 3. *Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)*

Site occupancies for disordered regions are: Cl1*A*, O3*A*, O4*A*, O5*A* 1.0; O2*A* and O2*A*′ 0.50, for a total of one Cl_1O_4; Cl11, O13*A*, O14*A*, O15*A* 0.55; Cl16, O17*A*, O18*A*, O19*A*, O20*A* 0.20; Cl21, O22*A*, O23*A*, O24*A* 0.25; O12*A* 0.80 (bound to both Cl11 and Cl21), for the second Cl_1O_4. Occupancies for the two H_2O molecules in the asymmetric unit are: O1*W* 1.0; O2*W* 0.85; O3*W* 0.15. See text.

$$U_{\rm eq} = (1/3)\Sigma_i\Sigma_j U^{ij}a^i a^j \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$U_{\rm iso}/U_{\rm eq}$
C1	0.7311 (3)	0.2966 (2)	0.4886 (7)	0.039 (2)
C2	0.7375 (4)	0.2920 (2)	0.3761 (7)	0.047 (2)
C3	0.7098 (4)	0.2612 (2)	0.3214 (7)	0.047 (2)
C4	0.6750 (4)	0.2365 (2)	0.3824 (6)	0.040 (2)
C5	0.6687 (3)	0.2413 (2)	0.4955 (6)	0.034 (2)
C6	0.6961 (3)	0.2717 (2)	0.5517 (7)	0.034 (2)
C7	0.6888 (3)	0.2789 (2)	0.6732 (6)	0.0286 (14)
C8	0.6822 (3)	0.3165 (2)	0.7095 (6)	0.0289 (15)
C9	0.6756 (3)	0.3254 (2)	0.8241 (6)	0.0297 (15)
C10	0.6714 (3)	0.3643 (2)	0.8611 (7)	0.036 (2)
C11	0.6650 (4)	0.3730 (2)	0.9717 (6)	0.040 (2)
C12	0.6621 (3)	0.3428 (2)	1.0505 (7)	0.041 (2)
C13	0.6662 (3)	0.3046 (2)	1.0173 (6)	0.033 (2)
C14	0.6735 (3)	0.2951 (2)	0.9037 (5)	0.0252 (14)
C15	0.6816 (3)	0.2560 (2)	0.8658 (6)	0.0261 (14)
C16	0.6884 (3)	0.2486 (2)	0.7567 (6)	0.0244 (14)
O17	0.6970 (2)	0.21010 (12)	0.7224 (4)	0.0277 (10)
C18	0.7562 (3)	0.2017 (2)	0.6933 (7)	0.030 (2)
C19	0.7606 (3)	0.1579 (2)	0.6906 (7)	0.035 (2)
O20	0.7181 (2)	0.14019 (13)	0.6206 (4)	0.0319 (10)
C21	0.7290 (3)	0.1451 (2)	0.5038 (6)	0.037 (2)
C22	0.6787 (3)	0.1282 (2)	0.4427 (6)	0.039 (2)
O23	0.6276 (2)	0.15005 (14)	0.4673 (4)	0.0345 (11)
C24	0.5774 (3)	0.1364 (2)	0.4099 (6)	0.037 (2)
C25	0.5292 (3)	0.1642 (2)	0.4290 (7)	0.042 (2)
O26	0.5171 (2)	0.16630 (14)	0.5462 (4)	0.0357 (11)
C27	0.4698 (3)	0.1926 (2)	0.5691 (7)	0.037 (2)
C28	0.4588 (3)	0.1929 (2)	0.6927 (7)	0.038 (2)
O29	0.5096 (2)	0.20781 (14)	0.7497 (5)	0.0346 (11)
C30	0.4997 (3)	0.2131 (2)	0.8643 (6)	0.033 (2)
C31	0.5557 (3)	0.2256 (2)	0.9180 (6)	0.0301 (15)
O32	0.5964 (2)	0.19441 (12)	0.9111 (4)	0.0276 (10)
C33	0.6470 (3)	0.1972 (2)	0.9747 (5)	0.0254 (14)
C34	0.6887 (3)	0.2246 (2)	0.9516 (6)	0.0270 (14)
C35	0.7424 (3)	0.2234 (2)	1.0115 (6)	0.0291 (15)
C36	0.7874 (3)	0.2511 (2)	0.9957 (7)	0.033 (2)
C37	0.8375 (3)	0.2491 (2)	1.0573 (7)	0.040 (2)
C38	0.8461 (3)	0.2195 (2)	1.1353 (6)	0.038 (2)
C39	0.8040 (3)	0.1919 (2)	1.1508 (6)	0.035 (2)
C40	0.7511 (3)	0.1935 (2)	1.0925 (6)	0.031 (2)
C41	0.7066 (3)	0.1666 (2)	1.1132 (6)	0.0313 (15)
C42	0.6544 (3)	0.1680 (2)	1.0585 (6)	0.0276 (14)
C43	0.6090 (3)	0.1388 (2)	1.0876 (6)	0.031 (2)
C44	0.5507 (3)	0.1493 (2)	1.1095 (6)	0.035 (2)
C45	0.5106 (3)	0.1221 (2)	1.1413 (6)	0.040 (2)
C46	0.5274 (3)	0.0834 (2)	1.1560 (6)	0.042 (2)
C47	0.5836 (4)	0.0726 (2)	1.1349 (7)	0.043 (2)
C48	0.6246 (3)	0.1003 (2)	1.1037 (6)	0.035 (2)
C1*C*	0.5014 (3)	0.0779 (2)	0.6655 (7)	0.037 (2)
C2*C*	0.4435 (3)	0.0700 (2)	0.6948 (8)	0.044 (2)
C3*C*	0.4222 (3)	0.0798 (2)	0.7986 (8)	0.041 (2)
C4*C*	0.4585 (3)	0.0980 (2)	0.8763 (7)	0.039 (2)
C5*C*	0.5160 (3)	0.1060 (2)	0.8459 (7)	0.035 (2)
C6*C*	0.5372 (3)	0.0961 (2)	0.7430 (6)	0.0293 (15)
C7*C*	0.5989 (3)	0.1063 (2)	0.7106 (6)	0.0299 (15)

Table 3 (*cont.*)

	x	y	z	$U_{\rm iso}/U_{\rm eq}$
N8*C*	0.6066 (2)	0.1496 (2)	0.7042 (5)	0.0306 (13)
C9*C*	0.6429 (3)	0.0907 (2)	0.7937 (7)	0.031 (2)
O10*C*	0.6726 (2)	0.11054 (14)	0.8516 (4)	0.0380 (12)
O11*C*	0.6442 (2)	0.05208 (15)	0.7893 (6)	0.051 (2)
C12*C*	0.6847 (4)	0.0328 (2)	0.8657 (9)	0.055 (2)
C51	1.1974 (3)	0.0186 (2)	0.2335 (7)	0.039 (2)
C52	1.1913 (3)	0.0075 (2)	0.1237 (7)	0.043 (2)
C53	1.1424 (3)	0.0180 (2)	0.0647 (7)	0.040 (2)
C54	1.0997 (3)	0.0396 (2)	0.1160 (6)	0.036 (2)
C55	1.1055 (3)	0.0509 (2)	0.2259 (6)	0.031 (2)
C56	1.1549 (3)	0.0415 (2)	0.2876 (7)	0.035 (2)
C57	1.1656 (3)	0.0544 (2)	0.4030 (6)	0.0315 (15)
C58	1.2181 (3)	0.0705 (2)	0.4299 (7)	0.036 (2)
C59	1.2333 (3)	0.0814 (2)	0.5384 (7)	0.033 (2)
C60	1.2874 (3)	0.1007 (2)	0.5618 (7)	0.040 (2)
C61	1.3009 (3)	0.1103 (2)	0.6691 (7)	0.042 (2)
C62	1.2633 (3)	0.1019 (2)	0.7568 (8)	0.048 (2)
C63	1.2106 (3)	0.0837 (2)	0.7379 (7)	0.043 (2)
C64	1.1934 (3)	0.0746 (2)	0.6257 (7)	0.035 (2)
C65	1.1374 (3)	0.0594 (2)	0.5984 (6)	0.031 (2)
C66	1.1242 (3)	0.0513 (2)	0.4908 (6)	0.032 (2)
O67	1.0665 (2)	0.04193 (12)	0.4669 (4)	0.0318 (11)
C68	1.0535 (3)	0.0017 (2)	0.4456 (8)	0.037 (2)
C69	0.9885 (3)	−0.0020 (2)	0.4540 (9)	0.047 (2)
O70	0.9586 (2)	0.02497 (13)	0.3811 (5)	0.0364 (11)
C71	0.9595 (3)	0.0149 (2)	0.2651 (7)	0.041 (2)
C72	0.9317 (3)	0.0476 (2)	0.2011 (7)	0.043 (2)
O73	0.9668 (2)	0.08071 (14)	0.2125 (4)	0.0351 (11)
C74	0.9457 (3)	0.1133 (2)	0.1526 (6)	0.042 (2)
C75	0.9870 (4)	0.1461 (2)	0.1632 (6)	0.039 (2)
O76	0.9901 (2)	0.15769 (14)	0.2778 (4)	0.0346 (11)
C77	1.0264 (3)	0.1909 (2)	0.2914 (7)	0.040 (2)
C78	1.0313 (3)	0.2008 (2)	0.4126 (7)	0.035 (2)
O79	1.0564 (2)	0.16852 (13)	0.4696 (4)	0.0337 (11)
C80	1.0689 (3)	0.1780 (2)	0.5848 (6)	0.034 (2)
C81	1.0922 (3)	0.1427 (2)	0.6411 (7)	0.037 (2)
O82	1.0456 (2)	0.11497 (13)	0.6502 (4)	0.0314 (10)
C83	1.0529 (3)	0.0812 (2)	0.7134 (6)	0.032 (2)
C84	1.0937 (3)	0.0535 (2)	0.6904 (5)	0.0304 (15)
C85	1.0922 (3)	0.0169 (2)	0.7468 (6)	0.035 (2)
C86	1.1309 (3)	−0.0141 (2)	0.7230 (7)	0.042 (2)
C87	1.1257 (4)	−0.0490 (2)	0.7762 (7)	0.046 (2)
C88	1.0827 (4)	−0.0554 (2)	0.8556 (8)	0.048 (2)
C89	1.0444 (3)	−0.0268 (2)	0.8804 (7)	0.041 (2)
C90	1.0478 (3)	0.0105 (2)	0.8285 (6)	0.035 (2)
C91	1.0095 (3)	0.0405 (2)	0.8533 (6)	0.040 (2)
C92	1.0112 (3)	0.0762 (2)	0.8022 (6)	0.035 (2)
C93	0.9692 (4)	0.1067 (3)	0.8332 (7)	0.046 (2)
C94	0.9877 (5)	0.1448 (3)	0.8550 (7)	0.059 (3)
C95	0.9461 (5)	0.1734 (3)	0.8856 (7)	0.068 (3)
C96	0.8873 (5)	0.1606 (4)	0.9006 (8)	0.070 (3)
C97	0.8699 (4)	0.1233 (3)	0.8828 (8)	0.064 (3)
C98	0.9111 (4)	0.0973 (3)	0.8519 (7)	0.052 (2)
C55*C*	0.9155 (3)	0.1664 (2)	0.5960 (6)	0.0305 (15)
C54*C*	0.9043 (3)	0.2056 (2)	0.6199 (6)	0.034 (2)
C53*C*	0.8759 (3)	0.2287 (2)	0.5420 (6)	0.035 (2)
C52*C*	0.8588 (3)	0.2131 (2)	0.4426 (7)	0.037 (2)
C51*C*	0.8705 (3)	0.1743 (2)	0.4168 (6)	0.035 (2)
C56*C*	0.8994 (3)	0.1513 (2)	0.4944 (6)	0.0275 (14)
C57*C*	0.9118 (3)	0.1094 (2)	0.4668 (6)	0.0304 (15)
N58*C*	0.9752 (2)	0.1025 (2)	0.4493 (5)	0.0304 (12)
C59*C*	0.8908 (3)	0.0807 (2)	0.5530 (7)	0.038 (2)
O60*C*	0.9218 (2)	0.06103 (15)	0.6092 (5)	0.0425 (13)
O61*C*	0.8327 (2)	0.0810 (2)	0.5589 (5)	0.0479 (14)
C62*C*	0.8062 (4)	0.0559 (3)	0.6419 (8)	0.056 (2)
Cl1*A*	0.66440 (9)	0.01254 (5)	0.4372 (2)	0.0546 (5)

Table 3 (*cont.*)

	x	y	z	U_{iso}/U_{eq}
O2*A*†	0.7178 (9)	0.0287 (6)	0.4802 (18)	0.090 (6)
O2*A*′†	0.7168 (6)	0.0354 (4)	0.4325 (13)	0.055 (3)
O3*A*	0.6168 (4)	0.0333 (2)	0.4805 (10)	0.101 (3)
O4*A*	0.6683 (5)	−0.0254 (2)	0.4733 (11)	0.131 (4)
O5*A*	0.6608 (6)	0.0099 (4)	0.3164 (9)	0.139 (4)
O1*W*	0.7958 (3)	0.0915 (2)	0.2974 (7)	0.081 (2)
O2*W*	0.7432 (4)	0.0455 (2)	0.1498 (8)	0.078 (2)
O3*W*†	1.3175 (14)	0.1045 (9)	1.0344 (27)	0.036 (7)
Cl11†	0.8483 (2)	0.33241 (10)	0.7379 (3)	0.0620 (10)
O12*A*†	0.8241 (2)	0.29351 (12)	0.7383 (6)	0.066 (2)
O13*A*†	0.8040 (3)	0.3601 (2)	0.7057 (8)	0.066 (3)
O14*A*†	0.8960 (3)	0.3342 (2)	0.6593 (8)	0.156 (10)
O15*A*†	0.8694 (5)	0.3419 (2)	0.8487 (5)	0.119 (7)
Cl16†	0.9087 (4)	0.2968 (2)	0.8110 (7)	0.052 (2)
O17*A*†	0.9591 (5)	0.2726 (4)	0.8314 (15)	0.039 (6)
O18*A*†	0.8586 (5)	0.2723 (5)	0.7904 (17)	0.054 (7)
O19*A*†	0.8979 (9)	0.3211 (5)	0.9077 (13)	0.064 (9)
O20*A*†	0.9192 (8)	0.3212 (5)	0.7145 (13)	0.068 (9)
Cl21†	0.8784 (2)	0.3129 (2)	0.7637 (5)	0.040 (2)
O22*A*†	0.9261 (3)	0.2859 (4)	0.7486 (18)	0.103 (11)
O23*A*†	0.8774 (6)	0.3263 (6)	0.8783 (8)	0.069 (8)
O24*A*†	0.8859 (6)	0.3458 (4)	0.6896 (15)	0.077 (8)

† Refined isotropically.

naphthyl-to-naphthyl bond. Tables 4 and 5 give hydrogen-bond information and selected non-bonded interactions for the two independent complexes. Some of the intra-complex interactions are shown in Fig. 7.

3.2. *Proposed and observed conformation*

The guest 'perches' on one face of the macroring. (We use the symbol ⊍ to denote 'perching' or 'nesting' complexes, to distinguish them from ⊙, for complexes in which the guest is completely surrounded by the host.) The N—H$^+$···O bonds in an observed tripod arrangement between guest and host are the same as those found from CPK model† examination and from the earlier crystal structure of (2)⊍$(CH_3)_3CNH_3^+$ (Goldberg, 1980). However, in contrast to the proposed conformation for (3)⊍guest (Fig. 1), the carbonyl group of the guest in (3*A*) and (3*B*) forms an O···H—C contact with the crown ring, while the C_6H_5 group of the guest interacts with the C_6H_5 group of the host in a C—H···π fashion. In addition, the phenyl ring of the guest is positioned above O—CH_2CH_2—O protons of the crown ring, providing a C—H···π interaction with H28*B* (2.86 Å) in one complex and H78*B* (2.66 Å) in the other. These interactions are shown in Table 5, where the closest contacts of the centroids of each of the six unique benzene rings are tabulated. Previous evidence for C—H···π interactions has been reported by Madhavi *et al.* (1997), and neutron diffraction evidence is given by Steiner *et al.* (1997), who call them 'aromatic hydrogen bonds'.

† Corey–Pauling–Koltun space-filling molecular model (Koltun, 1965).

C—H···O contacts also influence the structure in ways that were unexpected (Table 4). First, the N—C—H proton of the guest, instead of being oriented towards the binaphthyl group as originally proposed, binds in cation (3*B*) to a water molecule, and in cation (3*A*) to O of perchlorate. This type of interaction of the α H atom in amino acids has been noted in other structures (for examples, see Steiner, 1995). In addition, some CH_2 groups of the crown rings participate in C—H···O interactions with O atoms of their own and neighboring guests (Table 4).

3.3. *Comparison of the two independent complexes*

The two cationic complexes in the asymmetric unit share the same general conformation, but differ from each other slightly in details. The most significant of these follow. (i) As noted above, the N—C—H proton of one guest (guest *A*) contacts a perchlorate O atom, whereas the N—C—H proton in the other guest (guest *B*) makes a shorter contact with a water O atom (Table 4). The same proton in both complexes is also close to an O atom in the crown ring (H7*C*···O23, H57*C*···O73). (ii) The angle between plane normals of the binaphthyl group in host (3*A*) is 106.1 (1)°, and in host (3*B*) the same angle is 88.2 (1)° (visible in Figs. 5 and 6). A related effect is the difference in the distance between O atoms in the 20-crown-6 moieties attached directly to binaphthyl groups, O17···O32 3.284 (6) Å for host *A* and O67···O82 3.372 (7) Å for host *B*.

The two cations are linked by an N—C—H···O(water)···perchlorate···H—C—N chain (Fig. 4, Tables 4 and 5). Thus the two anions in the asymmetric unit are in quite different environments. The second, severely disordered perchlorate ion contacts protons in the host of (3*A*) and the guest of (3*B*). Presumably the disorder arises because several similar contacts are possible, *e.g.* O14*A* (occupancy 0.55)···H25*B* 2.38 Å, and O24*A* (occupancy 0.25)···H25*B* 2.68 Å.

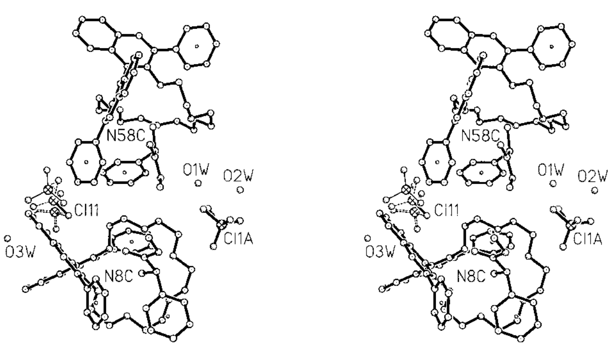


Fig. 4. A stereoview of the asymmetric unit, including two cationic complexes, two perchlorate anions, and two water O atoms [O1*W*, O2*W* (occupancy 0.85) and O3*W* (occupancy 0.15)]. H atoms and most labels are omitted for clarity. Circles indicate the centroids of the phenyl-ring planes.

Table 4. *Comparison of the two independent complex cations (3A) and (3B) in the asymmetric unit (Å, °)*

	Host–guest (3*A*)	Host–guest (3*B*)
Distance of guest N from plane of the three hydrogen-bonded O atoms	0.615 (5)	0.560 (5)
Angle of normal to the three-O-atom plane with guest C—N vector	17	13
N—H···O angle	153 (2), 163 (2), 167 (2)	156 (2), 158 (2), 170 (2)
Average	161	161
N···O distance	2.778 (7), 2.859 (8), 2.930 (8)	2.816 (7), 2.818 (8), 2.936 (8)
Average	2.856	2.857
Other N···O distances	2.952 (7), 2.882 (8), 3.050 (7)	2.943 (8), 2.950 (7), 2.969 (7)
Average	2.961	2.954
O···H—C interactions: O···H distance, O···H—C angle	O10*C*···H19*B*—C19: 2.53, 130 O11*C*′†···H71*A*—C71: 2.45, 152 O3*A*···H7*C*—C7*C*: 2.84, 154 O23···H7*C*—C7*C*: 2.82, 115	O60*C*···H69*B*—C69: 2.55, 128 O61*C*···H21*A*—C21: 2.52, 139 O1*W*···H57*C*—C57*C*: 2.55, 147 O73···H57*C*—C57*C*: 2.91, 116

† O11*C*′ is related to O11*C* by the operation $\frac{3}{2} - x, -y, -\frac{1}{2} + z$.

4. Discussion

4.1. *Influence of anion on binding*

Both cations in the asymmetric unit have the same host–guest binding conformation. It was not possible to prepare crystals of the complex with other anions, nor was it possible to crystallize the same host with the guest of opposite L configuration. Results of solution studies had indicated that the choice of anion was important for hosts (4), (5) and (6) (Peacock *et al.*, 1978; Kyba *et al.*, 1978): for these hosts, PF_6^- provided a larger EDC than ClO_4^- with the phenylglycinium methyl ester guest. These facts suggest that even in solution in an organic solvent the slightly acidic N—C—H proton is oriented outward toward the anion, and that the anion may affect the strength of binding and enantiomer distribution of the guest by helping to orient the guest in the host cavity.

That anion and water are involved in complexation should not have been a surprise, because structures of many crown-type hosts with and without guests have shown that solvent and/or anion moieties often play very specific roles in crystallization and binding. For example, water is bound to the cation guests Cs^+ and K^+ in cryptahemispherand complexes (Maverick *et al.*, 1997), and picrate is bound to $CH_3NH_3^+$ or Rb^+ in the presence of hemispherand hosts (Tucker *et al.*, 1989). The solvent and the anion were difficult to take into account in the CPK model examination studies that guided the synth-

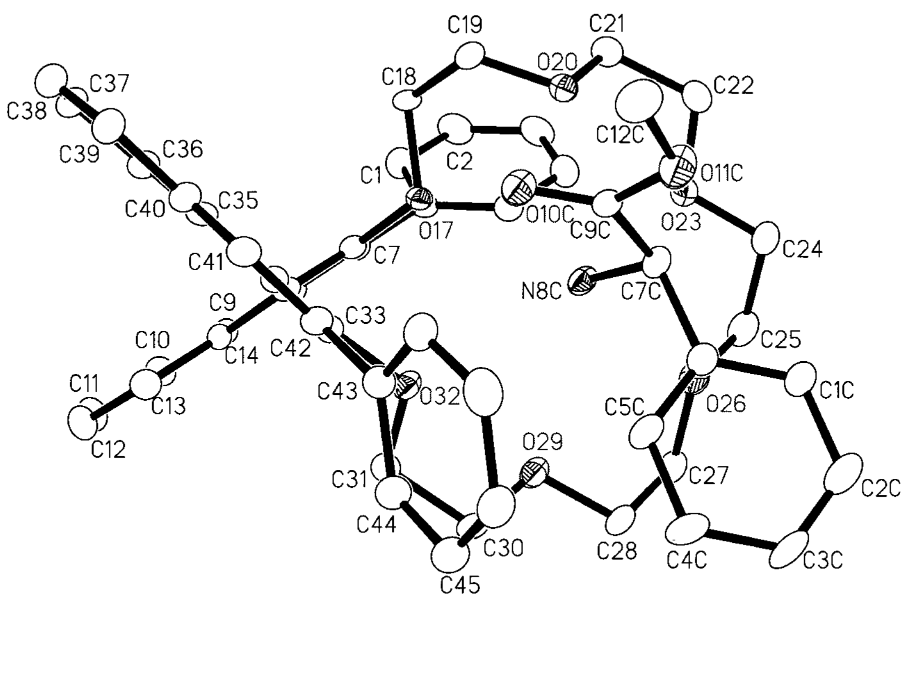


Fig. 5. Host-guest (3*A*), looking down the naphthyl–naphthyl bond. Atomic displacement ellipsoids enclose 30% probability. H atoms and some labels are omitted.

Table 5. *Host–guest C—H···π interactions and possible hydrogen bonds involving water (Å, °)*

For phenyl-ring centroid designations I–VI see Fig. 3.

	Host–guest (3*A*)	Host–guest (3*B*)
Intra-complex		
π···H—C	II···H5*C*—C5*C*: 2.79, 137	V···H55*C*—C55*C*: 2.70, 140
	III···H28*B*—C28: 2.86, 154	VI···H78*B*—C78: 2.66, 156
Intermolecular†		
π···H—C	I′···H80*B*—C80: 2.73, 157	IV′···H10—C10: 3.03, 133
	II′···H24*B*—C24: 2.66, 156	V′···H74*B*—C74: 2.67, 145

Possible hydrogen bonds O atoms	O···O distances	Angle
O5*A*†···O2*W*···O4*A*′	3.015 (15), 3.018 (16)	142.9 (5)
O1*W*···O2*W*···O5*A*	2.664 (12), 3.015 (15)	95.0 (4)
O1*W*···O2*W*···O4*A*′	2.664 (12), 3.018 (6)	107.1 (4)
O2*W*···O1*W*···O61*C*	2.664 (12), 3.270 (10)	133.6 (4)

† O4*A*′ is related to O4*A* by the operation $\frac{3}{2} - x, -y, -\frac{1}{2} + z$. I′ is related to I by the operation $\frac{1}{2} + x, \frac{1}{2} - y, 1 - z$. II′ and V′ are related to II and V, respectively, by the operation $x, y, z - 1$. IV′ is related to IV by the operation $x - \frac{1}{2}, \frac{1}{2} - y, 1 - z$.

eses of the hosts and the choice of guests. In the solution studies that established scales of binding, the extent of the influence of the picrate and of the water common to all the experiments is not well known. While their use standardizes the experiments, their influence on the structures, and therefore the binding, of the complexes presumably varies, in perhaps subtle ways.

4.2. *C—H···π interactions between host and guest*

The phenyl rings on the bonded faces of the hosts, II (see Figs. 3 and 7) and the analogous V, make very similar contacts with the phenyl rings of the guests, III and VI (Table 5). These contacts may be assumed to be dictated by the 'fit' of host to guest. This result is fully consistent with the solution ^{1}H NMR spectrum of the complex, in which it is observed that the *ortho* protons of the C_6H_5 group of the guest in diastereomerically related complexes are shielded differentially [δ = 6.58 p.p.m. for (*S*) (L) or (*R*) (D) *versus* 6.95 p.p.m. for (*S*) (D) or (*R*) (L); Lingenfelter *et al.*, 1981]. This upfield shift of 0.37 p.p.m. for the *ortho* protons of the favored guest results from the shielding region of the aromatic ring of the host (Peacock *et al.*, 1978).

In contrast, I and IV, the phenyl rings on the non-bonding faces of (3*A*) and (3*B*), which contact neighboring molecules, are in quite different surroundings (Table 5). The latter interactions are presumably not influenced by bonding of host to guest but by crystal packing.

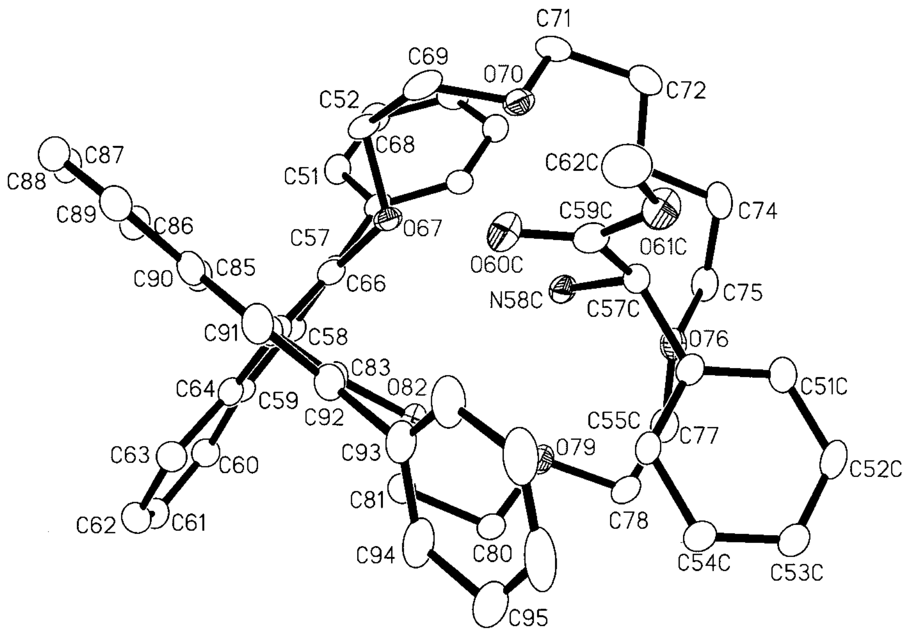


Fig. 6. Host–guest (3*B*) viewed as in Fig. 5.

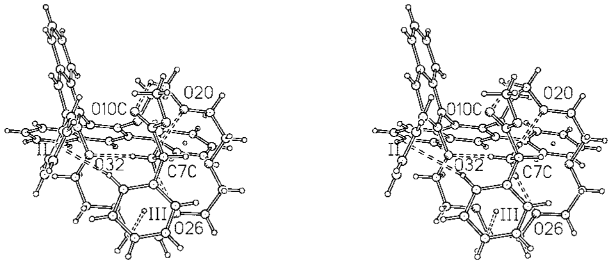


Fig. 7. Stereoview of host–guest (3*A*), looking down the guest C—N bond. N—H···O, C—H···O and C—H···π interactions between host and guest are indicated by dashed lines. See Tables 4 and 5.

4.3. *Comparison with the phenylglycinium complexes of (5) and (6)*

Does the crystal structure show why host (3) is both a stronger binder and a stronger discriminator between enantiomers than either (5) or (6) (Table 1)? Comparison of (3) with the crystal structures of (5) (Goldberg, 1977) and (6) (Knobler *et al.*, 1988) is partial because the complex of (5) contains PF_6^- rather than ClO_4^-. In addition, the complex of (5) is the 'wrong' or less stable diastereomer, and the complex of (6) contains the phenylglycinium ion rather than phenylglycinium methyl ester as guest. Nevertheless, the following observations help to explain the differences in binding and EDCs presented in Table 1.

(i) In (5) with the less favored guest, the N—H···O bonds are less linear than those in the present structure (Table 4), and the N atom at 1.63 Å is farther out of the plane of the three hydrogen-bonded O atoms. The N—C—H···O interaction with the crown ring is present, but the orientation of the guest in the cavity prevents contact of this proton with the anion.

(ii) In (6) with phenylglycinium ion guest one of the N—H···O bonds is bifurcated, and in this structure as well, no N—C—H···O contact with the anion is possible, because the anion is hydrogen-bonded to the carboxyl H atom of the guest.†

(iii) Both (5) and (6) are strained because in order to accommodate the guest the two binaphthyl or bitetralyl groups must spread apart on the binding surface. As a result these bulky groups contact one another on the opposite face of the host.

Thus we may conclude that (3) is preorganized for favorable N—H···O geometry, and that C—H···π and C—H···O interactions aid in its ability to discriminate between phenylglycinium enantiomers. Though (4), presumed to be similar in structure to (6), is a slightly better discriminator between enantiomeric amino acids than is (3), the fact that the hosts with two chiral centers are poorer binders renders (3) a more generally useful agent for separating those enantiomers.

† The H atoms in the structure of (6) are not well located but the positions of the O atoms of guest and anion indicate hydrogen bonding.

The authors are grateful to J. Chappuis for growing the crystals. We thank the National Science Foundation and the National Institutes of Health (GM 12640) for support.

References

Cram, D. J. & Trueblood, K. N. (1981). *Top. Curr. Chem.* **98**, 43–106.
Declercq, J. P., Germain, G. & Woolfson, M. M. (1979). *Acta Cryst.* A**35**, 622–626.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Gelder, R. de, de Graaff, R. A. G. & Schenk, H. (1993). *Acta Cryst.* A**49**, 287–293.
Goldberg, I. (1977). *J. Am. Chem. Soc.* **99**, 6049–6057.
Goldberg, I. (1980). *J. Am. Chem. Soc.* **102**, 4106–4113.
Graaff, R. A. G. de (1998). *CRUNCH. Program for Solution of Crystal Structures.* X-ray Department, Gorlaeus Laboratories, 2300 RA Leyden, The Netherlands. (*CRUNCH* is available without charge to the scientific community from http://chemb0b.leidenuniv.nl:80/~rag/)
Helgeson, R. C., Weisman, G. R., Toner, J. T., Tarnowski, T. L., Chao, Y., Mayer, J. T. & Cram, D. J. (1979). *J. Am. Chem. Soc.* **101**, 4928–4941.
Knobler, C. B., Gaeta, F. C. A. & Cram, D. J. (1988). *J. Chem. Soc. Chem. Commun.* pp. 330–333.
Koltun, W. L. (1965). *Biopolymers*, **3**, 665–679.
Kyba, E. P., Timko, J. M., Kaplan, L. J., de Jong, F., Gokel, G. W. & Cram, D. J. (1978). *J. Am. Chem. Soc.* **100**, 4555–4568.
Lingenfelter, D. S., Helgeson, R. C. & Cram, D. J. (1981). *J. Org. Chem.* **46**, 393–406.
Madhavi, N. N. L., Katz, A. K., Carrell, H. L., Nangia, A. & Desiraju, G. R. (1997). *J. Chem. Soc. Chem. Commun.* pp. 1953–1954.
Maverick, E. F., Knobler, C. B., Trueblood, K. N. & Ho, S. P. (1997). *Acta Cryst.* C**53**, 1822–1827.
Peacock, S. C., Domeier, L. A., Gaeta, F. C. A., Helgeson, R. C., Timko, J. M. & Cram, D. J. (1978). *J. Am. Chem. Soc.* **100**, 8190–8202.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures.* University of Göttingen, Germany.
Sheldrick, G. M. (1995). *SHELXTL.* Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Steiner, T. (1995). *J. Chem. Soc. Perkin Trans.* 2, pp. 1315–1319.
Steiner, T., Mason, S. A. & Tamm, M. (1997). *Acta Cryst.* B**53**, 843–848.
Tsoucaris, G. (1970). *Acta Cryst.* A**26**, 492–499.
Tucker, J. A., Knobler, C. B., Goldberg, I. & Cram, D. J. (1989). *J. Org. Chem.* **54**, 5460–5482.
UCLA Crystallographic Package (1984). J. D. McCullough Laboratory of X-ray Crystallography, University of California, Los Angeles, USA.
Weeks, C. M., DeTitta, G. T., Hauptman, H. A., Thuman, P. & Miller, R. (1994). *Acta Cryst.* A**50**, 210–220.