Alanine-derived Hosts Comprising a Roof-shaped Carbonimide Framework. Synthesis, Inclusion Formation and X-Ray Crystal Structures of Racemic and Optically Resolved Free Hosts, and their Crystalline Complexes with 3-Methylcyclohexanone

Edwin Weber,*[a] Christiane Reutel,[a] Concepción Foces-Foces*[b] and Antonio L. Llamas-Saiz[b]

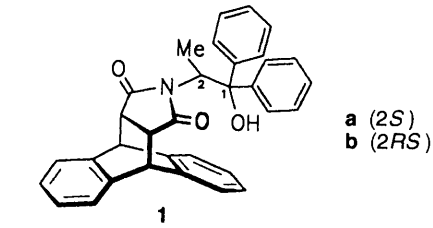
[a] *Institut für Organische Chemie der Technischen Universität Bergakademie Freiberg, Leipziger Str. 29, D-09596 Freiberg/Sa., Germany*

[b] *U.E.I. de Cristalografía, Instituto de Química-Física 'Rocasolano', CSIC, Serrano 119, E-28006 Madrid, Spain*

A chiral crystalline host molecule derived from the amino acid alanine comprising a characteristic 9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboximide framework as an inclusion-promoting group has been synthesized in optically resolved and racemic forms and studied with regard to their inclusion behaviour. Dependent on the optical resolution state, this host forms crystalline inclusion compounds with a great variety of uncharged organic molecules ranging from protic dipolar to rather apolar compounds (78 different inclusion species) with the racemic host being more efficient. X-Ray crystal structures of the optically resolved and racemic uncomplexed host species and of their 1:1 inclusion complexes with 3-methylcyclohexanone are reported. The host hydroxy groups are always involved in O–H ··· O=C intramolecular hydrogen bonds. The crystal packings of both complexes are analogous, showing similar cell dimensions and space groups $P2_1$ and $P2_1/a$. Moreover, the two independent molecules in the resolved complex are almost related by a pseudo centre of symmetry.

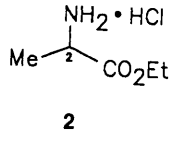
Organic supramolecular solid state chemistry[1] including clathrate formation[2] and crystal engineering[3] are a great challenge owing to the potential uses in compound and isomer separation,[4] in topochemical reactions[5] and in materials sciences.[6] With reference to the latter field, very recently, clathrates have attracted attention as sensor coatings.[7] This has stimulated development of new strategies in cocrystallization and motivated the design of novel host types.[1,2] Coordination-assisted clathrate formation between functionalized hosts and polar guest components is one particular entry[8] and among the many new types of polar host structures,[2] compounds that feature a molecular roof are prominent examples.[9] In fact, the roof-shaped 9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboximide framework has proved an efficient 'clathratogenic group'.[10] On the other hand, the design of crystalline chiral selectors based on optically active natural compounds is very challenging.[11]

We report here amalgamation of the principles, as shown by formula **1** where the characteristic imide skeleton from above and a particular building block derived from amino acid alanine are brought together. We describe synthesis and crystal inclusion properties, considering both the optically resolved and racemic forms of compound **1** (**1a** and **1b**), and present crystal structures of free host compounds and of inclusion compounds with 3-methylcyclohexanone. This makes possible correlation of the inclusion properties and of the packing principles with chirality.



a (2*S*)
b (2*RS*)

1



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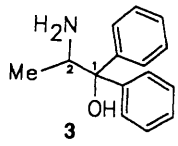

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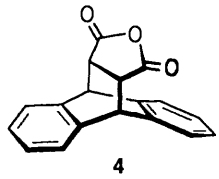

a (2*S*)
b (2*RS*)

4

Results and Discusion

Synthesis.—Host compounds **1a** and **1b** were synthesized in three steps from L- and D,L-alanine, respectively, in 33 and 30% overall yields, by conversion of the amino acids into the corresponding ethyl ester hydrochlorides **2** (**a**, **b**) followed by Grignard reaction with bromobenzene to give aminopropanols **3** (**a**, **b**) and reaction with anhydride **4**. The crystalline inclusion compounds were obtained by single recrystallization of the host compound from the respective guest solvent.

Inclusion Properties.—A total of 78 different inclusion compounds are specified in Table 1, showing the efficiency of the new host design in general. Nevertheless, the racemic host **1b** is much more effective in the enclathration of polar and apolar organic molecules as compared to the optically resolved species **1a**. This is particularly obvious for the hydroxylic guests where **1b** forms numerous inclusion compounds with alcohols of different size and shape while **1a** yields only very few inclusions (with cyclohexanol and 2-methylcyclohexanol) under

Table 1 Crystalline inclusion compounds

Guest solvent	Host compound **1a**	**1b**
PrOH	—	2:1
Pr^{i}OH	—	2:1
Bu^{i}OH	—	2:1
Bu^{s}OH	—	2:1
Bu^{t}OH	—	3:2
OctOH	—	1:2
1-PhCH$_2$CH$_2$OH	—	2:1
2-PhCH$_2$CH$_2$OH	—	2:1
C_5H_9OH	—	2:1
$C_6H_{11}OH$	1:1	1:1
2-Me-$C_6H_{10}OH$	1:1	2:3
3-Me-$C_6H_{10}OH$	—	1:1
PrNH$_2$	—	2:1
Bu^{i}NH$_2$	—	2:1
Bu^{s}NH$_2$	—	2:1
Bu^{t}NH$_2$	1:1	1:2
$C_5H_9NH_2$	1:1	1:1
$C_6H_{11}NH_2$	1:1	1:1
2-Me-$C_6H_{10}NH_2$	1:1	1:1
3-Me-$C_6H_{10}NH_2$	—	2:1
Pr$_2$NH	—	4:1
Pr$^i_2$NH	—	2:1
Bu$^i_2$NH	—	4:1
Piperidine	1:1	1:1
2-Methylpiperidine	—	2:1
3-Methylpiperidine	—	2:1
Pyrrolidine	—	1:1
Morpholine	2:1	1:1
Pyridine	1:1	1:1
2-Picoline	—	3:1
3-Picoline	—	3:1
4-Picoline	1:1	3:1
Acetone	—	2:1
Cyclopentanone	1:1	1:2
3-Methylcyclopentanone	1:1	1:1
Cyclohexanone	1:1	1:1
2-Methylcyclohexanone	1:1	1:1
3-Methylcyclohexanone	1:1	1:1
Cycloheptanone	1:1	1:1
(+)-Fenchone	1:1	1:1
(−)-Fenchone	1:1	1:1
(+)-Pulegone	—	2:1
(+)-Limonene	—	4:1
(−)-Menthone	—	3:2
(+)-Carvone	—	4:1
Acetic acid	—	2:1
DMF	—	1:1
Propionitrile	—	2:1
Butyronitrile	1:1	1:1
Nitroethane	—	2:1
Me$_2$SO	—	2:1
THF	1:1	1:1
Dioxane	2:1	2:1
Benzene	1:1	1:1
Toluene	—	4:1
Xylene	—	4:1

the same conditions. On the other hand, **1b** still demonstrates selectivity to alcohols: small alcohols (MeOH and EtOH) and alcohols that comprise a butyl chain (BuOH, pentan-2-ol) are inefficient. To some degree, this is also true for the amine guests, although **1a** is rather efficient here, in particular with alicyclic primary amines whereas secondary amines fail, without exception.

With reference to the ketone guests, **1a** and **1b** are similar,

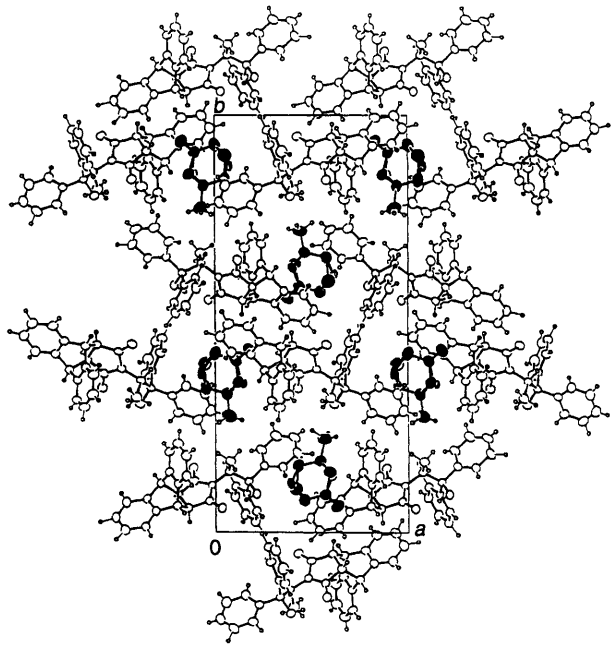

Fig. 1 An ORTEP view down the *c* axis of the crystal packing of compound **1a**-$C_7H_{12}O$. The guest molecule is shaded; methylene hydrogens of the guest molecule are omitted. In Figs. 1–5 the ellipsoids are drawn at 30% probability level.

except for acetone and most of the more complex terpene-type ketones that are inefficient with **1a**. Moreover acetic acid, dimethylformamide (DMF), nitroethane and Me$_2$SO all are inefficient with **1a**, unlike **1b**. Another remarkable finding is that **1a** enclathrates benzene, but not toluene and xylene; all are enclathrated by **1b**.

Host–guest stoichiometric ratios determined for the inclusion compounds of **1a** and **1b** (*cf.* Table 1) are also worthy of comparison. By far the most frequently observed stoichiometric ratio for the inclusions of **1a** is 1:1, only two cases show a 2:1 ratio. However, in the case of **1b**, the host–guest stoichiometric ratio 2:1 is just as frequent as 1:1, and there is also a rather high quota of 4:1 and 3:1, and to a lesser degree of 2:3 and 1:2, stoichiometries at inclusion formation. It is not easy to draw conclusions from the individual stoichiometric data. Nevertheless, some general trend is quite evident, that is, within a certain class of guest compounds the larger guests prefer the larger host–guest ratio demonstrating steric effects. The 2:1 stoichiometric ratio of the inclusion compounds formed between **1a** and dioxane or morpholine may be explained by the bivalency of the guest molecules.[12] The high stoichiometric ratio of 4:1 determined for some of the inclusion compounds of **1b** with apolar and rather shielded secondary amines (see Table 1) suggests cluster formation of host molecules in the solid cocrystalline state.[13] On the other hand, the 1:1 stoichiometric ratio preferred of the inclusion compounds **1a** is indicative of the formation of concrete host–guest complexes.[8b]

In order to learn the building principles and interaction modes of the new clathrate family including elucidation of stereochemical effects, we studied the crystal structures of two selected inclusion compounds formed between **1a** or **1b** with 3-methylcyclohexanone where **1a** and **1b** are stereochemically different species (optically resolved and racemic) of the same host constitution.

X-Ray Analysis: Structure Description of Free Host (**1a**, **1b**) *and of Inclusion Compounds* (**1a** *or* **1b** *with* 3-*Methylcyclohexanone*).—A numbering scheme indicating relevant atoms is shown in Fig. 3(*a*). Views of the structures are presented in Figs.

Table 2 Summary of crystal data and experimental parameters

Compound	**1a**	**1b**	**1a**·$C_7H_{12}O$	**1b**·$C_7H_{12}O$
Formula	$C_{33}H_{27}NO_3$	$C_{33}H_{27}NO_3$	$C_{33}H_{27}NO_3 \cdot C_7H_{12}O$	$C_{33}H_{27}NO_3 \cdot C_7H_{12}O$
Space group	$P2_1$	$P\bar{1}$	$P2_1$	$P2_1/a$
Z	4	2	4	4
Unit cell dimensions				
a/Å	21.1027(16)	9.3126(6)	13.0454(6)	13.0402(11)
b/Å	14.3572(8)	11.8349(20)	28.1359(34)	28.2841(44)
c/Å	8.6446(3)	13.2646(9)	8.7936(3)	8.7615(7)
α/°	90	110.655(12)	90	90
β/°	93.306(5)	108.465(8)	94.114(3)	94.605(6)
γ/°	90	97.583(9)	90	90
V/Å^3	2614.7(3)	1247.7(3)	3219.3(4)	3221.1(6)
D_c/g cm^{-3}	1.234	1.293	1.233	1.233
$F(000)$	1024	512	1272	1272
μ/cm^{-1}	5.87	6.15	5.88	5.87
θ/Cu-Kα	65	60	65	60
Number of reflections				
Independent	4633	3652	5607	4744
Observed [$3\sigma(I)$]	4202	2637	4710	3336
Final R and R_w	0.050, 0.068	0.056, 0.063	0.055, 0.062	0.107, 0.118
Final ΔF peaks/e Å^{-3}	±0.16	±0.32	±0.22	±0.74

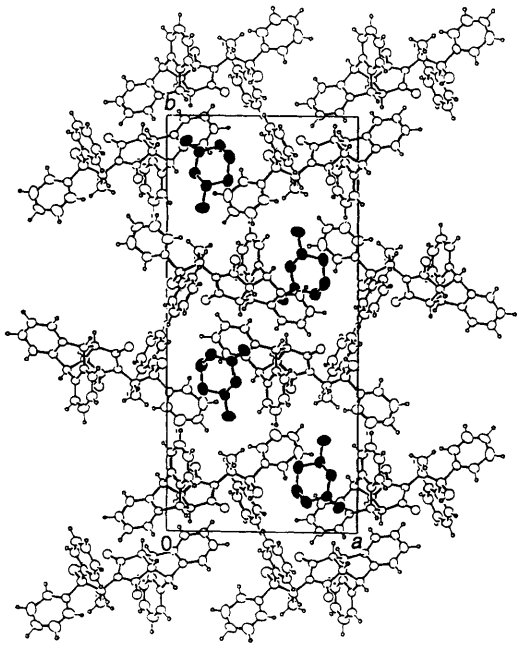

Fig. 2 Crystal packing of compound **1b**·$C_7H_{12}O$, down the c axis. The guest molecule is shaded; hydrogens of the guest molecule are omitted.

1–7. Crystal data are given in Table 2. Geometrical parameters including hydrogen bonding are shown in Tables 3 and 4 (atomic coordinates have been deposited at the Cambridge Crystallographic Data Centre).

Molecular Structures.—The host molecules are conformationally rigid with the hydroxy group involved in an intramolecular hydrogen bond (*cf.* Table 4). Some degree of delocalization was found in the O=C–N fragment of the succinimide ring involved in the intramolecular hydrogen bond. Considerable strain is indicated by deviations of some bond distances and angles (*cf.* Table 3). The C(33)–C(37) and C(34)–C(44) distances are elongated as compared to the tabulated[14] Csp^3–Csp^3 bond of 1.542(11) Å. However, these bonds and the angle between the succinimide ring and the ethano bridge are consistent with those of the literature[10] for the dihydroethanoanthracenedicarboximide skeleton [mean values of 1.560(4), 60.6(1) *vs.* 1.563(13) Å, 60.9(5)°]. The C(1)–C(2) distances are in the 1.503(9)–1.563(6) Å range, those of the free hosts being larger than the weighted mean of 1.546(4) Å previously reported for the lactic acid derivative.[11c] The length of this bond is closely related to the conformation of the molecule around it: the longer the C(1)–C(2) bond the lower the C(11)–C(1)–C(2)–N(5) torsion angle (*cf.* Table 3).

Packing Relations.—The packing arrangements for **1a**·$C_7H_{12}O$ and **1b**·$C_7H_{12}O$ are quite similar and they are presented in Figs. 1 and 2. The cell dimensions are analogous and it is worth noting that the space groups are $P2_1$ and $P2_1/a$ and, in addition, the two independent molecules in $P2_1$ are related by a pseudo-symmetry centre at (0.270, 0.496, 0.531). If the small differences in the relative disposition of the two parts of the molecule around the N(5)–C(2) bond (*cf.* Table 3) are neglected and the H(2) and –C(1)OHPh$_2$ interchange their positions in molecule B the structure of **1b**·$C_7H_{12}O$ could be obtained [Figs. 3(*a*) and 3(*b*)]. Moreover, the C–H · · · phenyl interactions joining both independent molecules are close to those found for the racemic complex, that is, a pair of molecules crystallographically related by a symmetry centre at (0.50, 0.50, 0.50) (see Fig. 3 and Table 4). These 'dimers' do not bear any significant interactions among them or between them and guest molecules.

The cell dimensions and global packing of **1a** and **1b** are completely different between them and with respect to their complexes (Figs. 4 and 5). Although both independent molecules in **1a** are related by a pseudo-symmetry centre at (0.246, 0.108, 0.246) their relative dispositions are different from those of the complexes [Fig. 3(*c*)]. However, in **1b**, the two centrosymmetrically related molecules [Fig. 3(*d*)] almost resemble the situation previously observed in the complexes [Figs. 3(*a*) and 3(*b*)] but the equivalent C–H · · · phenyl interactions between them are missing.

Size and Shape of Cavities in the Crystals.—A model of interpenetrating spheres of van der Waals radii has been used for the location of cavities in the crystals.[15] The guest molecules in the resolved complex (almost centrosymmetrically related) and in the racemate are allocated in two waved channels along the a axis (Fig. 6). The total packing coefficients for compounds **1a**, **1b**, **1a**·$C_7H_{12}O$ and **1b**·$C_7H_{12}O$ are 0.66, 0.68, 0.66 and 0.65 [$C_k^{all} = (V_{host} + V_{guest})$/unit cell vol.]. The presence of spherical voids of volume 23.4, 13.2 and 12.4 Å^3 in all the

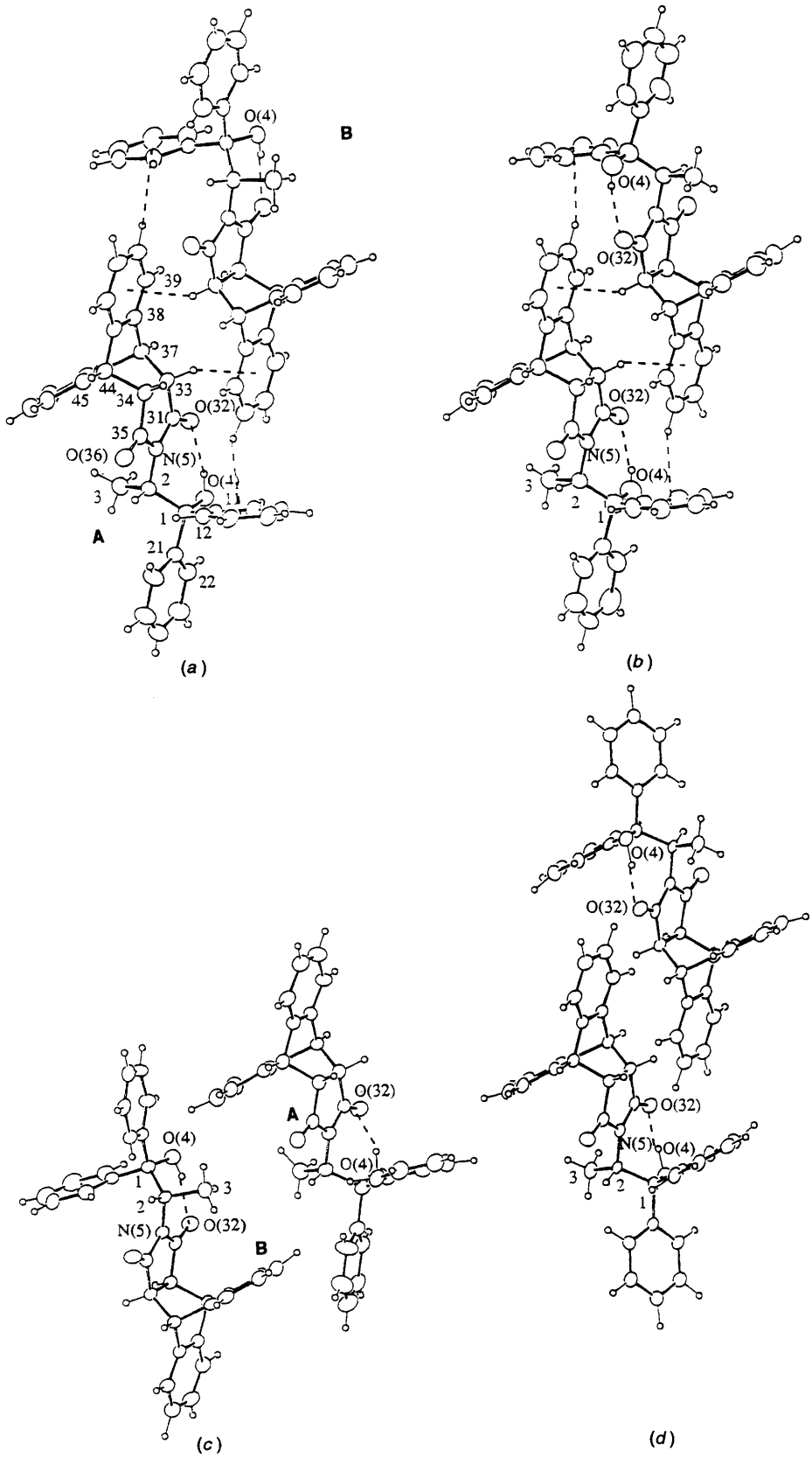

Fig. 3 Perspective views of the two independent host *S*-molecules in (*a*) **1a**·$C_7H_{12}O$, the two host enantiomers through a symmetry centre in (*b*) **1b**·$C_7H_{12}O$ and of compounds (*c*) **1a** and (*d*) **1b**, similar to (*a*) and (*b*). Dashed lines indicate O–H · · · O=C and C–H · · · phenyl interactions. The same projection has been used for all compounds in order to show the similarities between all pairs of molecules.

structures except **1b** is consistent with the previously mentioned packing coefficient values. The lack of intermolecular interactions between host and guest together with the statistical disorder observed in both complexes agree with the low values of their local packing coefficients of 0.45 and 0.42 ($C^1_k = V_{guest}/V_{hole}$).

Table 3 Selected geometrical parameters (Å/°)

Compound	**1a** Mol A	**1a** Mol B	**1b**	**1a**·$C_7H_{12}O$ Mol A	**1a**·$C_7H_{12}O$ Mol B	**1b**·$C_7H_{12}O$
C(1)–C(2)	1.563(6)	1.552(5)	1.558(5)	1.537(6)	1.548(6)	1.503(9)
N(5)–C(31)	1.388(4)	1.384(5)	1.372(4)	1.389(5)	1.372(5)	1.387(7)
N(5)–C(35)	1.400(4)	1.404(4)	1.408(3)	1.410(5)	1.407(6)	1.396(6)
C(31)–O(32)	1.211(5)	1.216(5)	1.220(3)	1.210(5)	1.217(6)	1.212(6)
C(35)–O(36)	1.207(5)	1.207(5)	1.203(4)	1.204(6)	1.208(6)	1.214(7)
C(2)–N(5)–C(31)	126.6(2)	128.1(3)	126.9(3)	126.3(3)	128.6(4)	126.2(4)
C(2)–N(5)–C(35)	121.8(2)	119.9(3)	120.6(3)	121.6(3)	119.3(3)	121.5(4)
O(4)–C(1)–C(2)–C(3)	46.7(5)	45.7(4)	41.1(4)	52.4(5)	48.0(5)	56.3(7)
O(4)–C(1)–C(2)–N(5)	−78.8(4)	−80.3(4)	−85.6(3)	−73.9(4)	−76.4(4)	−77.2(6)
C(11)–C(1)–C(2)–N(5)	44.5(4)	43.5(4)	36.8(4)	49.8(5)	47.2(5)	49.3(7)
C(21)–C(1)–C(2)–N(5)	165.1(3)	162.5(3)	157.5(3)	170.0(3)	167.4(4)	165.6(5)
C(31)–N(5)–C(2)–C(3)	−66.5(4)	−68.8(5)	−70.7(4)	−61.2(5)	−72.4(4)	−67.5(7)
C(35)–N(5)–C(2)–C(3)	107.7(4)	106.0(4)	103.5(4)	107.5(4)	96.4(4)	100.1(6)
C(1)–C(2)–N(5)–C(31)	61.1(4)	58.8(5)	57.9(4)	67.3(5)	54.3(6)	69.2(7)

Table 4 Intra- and inter-molecular hydrogen bonding (Å/°)

Intramolecular contact

Compound	O(4)···O(32)	H(4)···O(32)	O(4)–H(4)	O(4)–H(4)···O(32)
1a (mol A)	2.705(4)	1.99(6)	0.73(6)	168(6)
1a (mol B)	2.734(4)	2.02(5)	0.74(5)	160(5)
1b	2.759(4)	1.83(5)	1.00(5)	152(3)
1a·$C_7H_{12}O$ (mol A)	2.695(4)	1.87(3)	0.85(3)	166(3)
1a·$C_7H_{12}O$ (mol B)	2.680(5)	1.88(4)	0.84(4)	160(4)
1b·$C_7H_{12}O$	2.681(6)	1.99(–)	0.74(–)	161(–)

Intermolecular contact

	X–H···centroid[a]	X–H	X···Y	H···Y	X–H···Y	Symmetry
1a	C(33B)–H(33B)···C(21–26)B	0.98(4)	3.826(4)	2.93(4)	151(3)	$1-x,-\frac{1}{2}+y,1-z$
1b	C(14)–H(14)···C(21–26)	0.96(5)	3.521(5)	2.62(5)	156(4)	$-x,1-y,-z$
1a·$C_7H_{12}O$	C(33A)–H(33A)···C(38–43)B	0.98(4)	3.673(5)	2.86(4)	142(3)	x,y,z
1a·$C_7H_{12}O$	C(40A)–H(40A)···C(11–16)B	0.96(5)	3.729(6)	2.84(5)	155(4)	x,y,z
1a·$C_7H_{12}O$	C(34B)–H(34B)···C(38–43)A	0.90(4)	3.711(5)	2.94(4)	144(4)	x,y,z
1a·$C_7H_{12}O$	C(41B)–H(41B)···C(11–16)A	1.00(5)	3.555(7)	2.73(5)	140(4)	x,y,z
1b·$C_7H_{12}O$	C(33)–H(33)···C(38–43)	0.95(5)	3.704(6)	2.90(5)	143(4)	$1-x,1-y,1-z$
1b·$C_7H_{12}O$	C(40)–H(40)···C(11–16)	1.00(8)	3.601(7)	2.70(8)	151(6)	$1-x,1-y,1-z$

[a] C(11–16), C(21–26), C(38–43) and C(45–50) stand for the centroids of the corresponding rings.

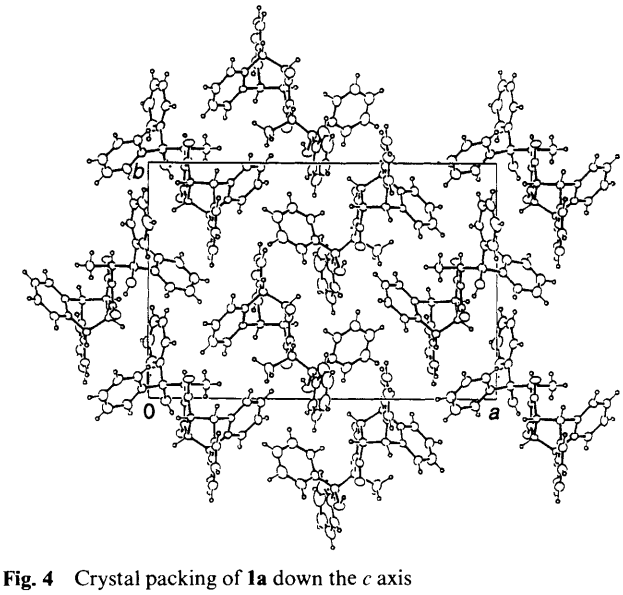

Fig. 4 Crystal packing of **1a** down the *c* axis

Summary and Conclusions.—The amino acid alanine, both in optically resolved and racemic form, when modified by the introduction of a rigid tetracyclic 9,10-dihydro-9,10-ethanoanthracene framework as a clathrate-promoting group[10] yields host compounds **1a** and **1b** that form crystalline inclusions with numerous organic molecules ranging from protic dipolar to apolar compounds (78 different examples). The composition of the inclusion materials and inclusion efficiencies depend on the optical form of the host. Certainly, there is no guest molecule enclathrated by the optically resolved host **1a** that does not undergo crystalline inclusion with racemic **1b**, but **1b** yields inclusions in a much broader sense (56 *vs.* 22 inclusion species). Corresponding inclusion compounds formed of **1a** and **1b**, in most cases, show the same stoichiometric ratio indicating similar packing behaviour in the cocrystalline state.

Indeed, the crystal structures of the 1:1 complexes between **1a** or **1b** and 3-methylcyclohexanone are similar, with the two independent molecules, in case of **1a**, almost related by a symmetry centre and host–host inter C–H···phenyl interactions closely related in both cases. By way of contrast, only one C–H···phenyl interaction is present in the structures of the uncomplexed host compounds **1a** and **1b** indicating an unfavourable packing state. Moreover, the crystal packings of uncomplexed host compounds **1a** and **1b** are different with regard to relative molecular dispositions, and hence the different inclusion behaviour. The host hydroxy groups are

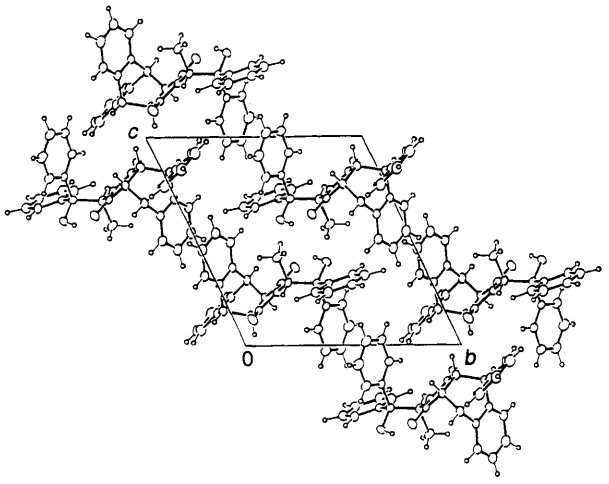

Fig. 5 Crystal packing of **1b** down the *a* axis

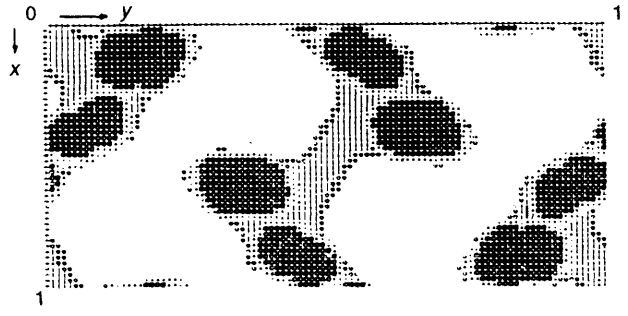

Fig. 6 A section through $z = 0$ of the continuous channel of **1b**·$C_7H_{12}O$ (two in the unit cell) that accommodate the guest molecules. A 0.3 Å grid for the holes search and a rolling sphere of 1.4 Å radius were used for smoothing the host clefts which are drawn in grey while the van der Waals interior of atoms are shown in black.

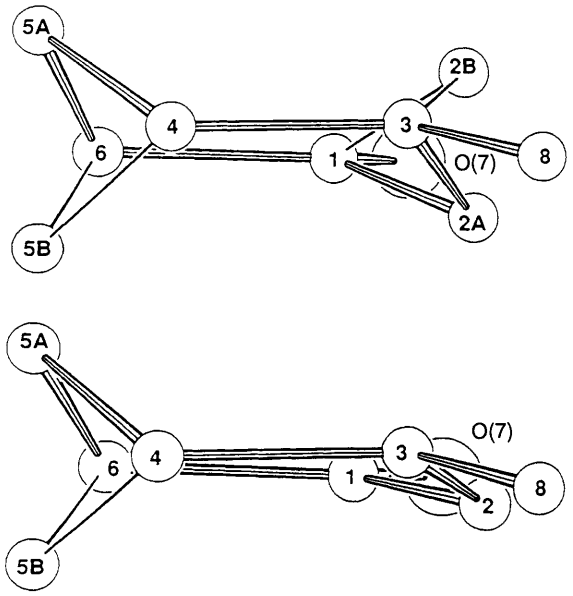

Fig. 7 A view of the guest molecule showing the *R*/*S* configurational (**1a**·$C_7H_{12}O$) and conformational (**1b**·$C_7H_{12}O$) disorder and the numbering system

always involved in O–H · · · O intramolecular hydrogen bonds showing the host molecules already to be in a favourable binding state that renders superfluous a significant host–guest contact. This is a critical point for future host development along the line presently introduced including chiral selectors.[11]

Experimental

cis-9,10-*Dihydro*-9,10-*ethanoanthracene*-11,12-*dicarboxylic acid anhydride* **4**. Procedure of Diels–Alder;[16] colourless crystals (43%), m.p. 260–262 °C (from acetone) (lit.,[16] 262 °C).

Alanine ethyl ester hydrochlorides **2a**, **2b**. Prepared by the modified procedure of Boissonnas *et al.*[17] To a suspension of the amino acid (39.2 g, 0.44 mol) in anhydrous EtOH (260 cm^3) thionyl chloride (50 cm^3, 0.68 mol) was added at room temp. The mixture was heated at reflux for 2 h. After being cooled to room temp., the solvent was removed under reduced pressure. The crude product was dissolved in EtOH and Et_2O was added for crystallization. **2a**: colourless crystals (62.7 g, 93%), m.p. 78 °C (lit.,[18] 76 °C); $[\alpha]_D^{20}$ +2.8 (*c* 7.37 in H_2O) [lit.,[18] +3.1 (*c* 2.5 in H_2O)]. **2b**: colourless crystals (65.2 g, 97%), m.p. 84–85 °C (lit.,[19] 86.5–87 °C).

2-*Amino*-1,1-*diphenylpropan*-1-*ols* **3a**, **3b**. Grignard reaction as described for **3a**;[20] using a fivefold excess of Grignard reagent instead of an eightfold excess. **3a**: colourless powder (57%), m.p. 100–102 °C (lit.,[21] 101.5–102.5 °C); $[\alpha]_D^{20}$ −85.9 (*c* 2.77 in $CHCl_3$) [lit.,[20] −82.4 (*c* 0.814 in $CHCl_3$)]. **3b**: colourless powder (46%), m.p. 94–98 °C.

2-(9,10-*Dihydro*-9,10-*ethano*-11,12-*dicarboximido*)-1,1-*diphenylpropan*-1-*ols* **1a**, **1b**. A mixture of anhydride **4** (27.6 g, 0.1 mol) and the corresponding aminopropanol (**3a**, **3b**) (22.7 g, 0.1 mol) in DMF (250 cm^3) was heated at reflux[22] for 6 h. After being cooled to room temp., the solution was added to ice–water (1 dm^3) to yield a white precipitate which was collected, filtered, washed (H_2O), and dried. **1a**: colourless crystals (14.8 g, 61%), m.p. 206–208 °C (from EtOH) (Found: C, 81.35; H, 5.68; N, 2.95. $C_{33}H_{27}NO_3$ requires C, 81.63; H, 5.60; N, 2.88%); $[\alpha]_D^{20}$ −54.9 (*c* 5.015 in $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3350 (OH), 2960 (CH), 1768 and 1688 (C=O), 1455 and 1405 (CH, OH), 1356, 1163 (CO), 1119, 1026, 906 (OH) and 754 and 701 (Ar); δ_H(250 MHz; $CDCl_3$) 0.39 (3 H, d, *J* 7 Hz, Me), 2.76, 2.98 (2 H, dd, *J* 9 and 4 Hz, CH), 4.66, 4.74 (2 H, d, *J* 4 Hz, CH), 4.99 (1 H, q, *J* 7 Hz, NCH), 5.89 (1 H, s, OH) and 6.99–7.57 (18 H, m, ArH); δ_C(62.89 MHz; $CDCl_3$) 11.06, 45.16, 45.44, 46.66, 55.44, 78.61, 124.05, 124.78, 124.85, 124.91, 125.37, 126.62, 126.93, 127.04, 127.80, 128.02, 138.26, 138.40, 140.87, 141.01, 144.08, 145.74, 176.49 and 180.09; *m*/*z* (FAB; mNBA) 486.2 (M + H). **1b**: colourless powder (16.5 g, 68%), m.p. 199–200 °C (from EtOH) (Found: C, 81.38; H, 5.67; N, 2.90. $C_{33}H_{27}NO_3$ requires C, 81.63; H, 5.60; N, 2.88%); spectroscopic data of the racemic compound **1b** correspond to the optically resolved species **1a**.

Preparation of the Crystalline Inclusion Compounds. General Procedure.—They were obtained by recrystallization of the corresponding host compound from a minimum amount of the respective guest solvent. The crystals formed were collected by suction filtration, washed with an inert solvent (MeOH), and dried (1 h, 15 Torr, room temp.). Host–guest stoichiometry was determined by ^1H NMR integration. Data for each compound are given in Table 1.

Crystallography. (*a*) *Sample preparation.* Suitable crystals for X-ray diffraction were prepared by the slow cooling of a solution of the corresponding host compound in the guest solvent (3-methylcyclohexanone). Single crystals of the free hosts were obtained from EtOH for **1a** and from BuOH for **1b**.

(*b*) *X-Ray structure determination.* The experimental details and the most relevant parameters of the refinement are given in Table 2. All crystals were sealed in Lindemann glass capillaries to prevent decomposition during data collection. Two standard reflections monitored every 90 min exhibited a linear decrease of 4, 1, 1 and 12% for compounds **1a**, **1b**, **1a**·$C_7H_{12}O$ and **1b**·$C_7H_{12}O$, respectively. The structures were solved by direct methods, SIR88[23] and DIRDIF92.[24] The non-hydrogen atoms were refined anisotropically and the hydrogen atoms were included as isotropic. Five and six reflections for compounds **1a**

and **1b**·$C_7H_{12}O$, respectively, were affected by secondary extinction and were considered as unobserved in the last cycles of refinement. Most of the calculations were performed on a VAX6410 computer using the XRAY80 system.[25] The atomic scattering factors were taken from the *International Tables for X-Ray Crystallography*, vol. IV.[26] All the guest molecules appear to be disordered. The structure of **1b**·$C_7H_{12}O$ was not determined as precisely as those of the other compounds owing to disorder and to the quality of the crystals. The two independent molecules in **1a**·$C_7H_{12}O$ are disordered in such a way that both enantiomers are present in the same cavity sharing all atoms except 2 and 5. The occupancy factors are 0.73(2)/0.27(2) for *R*/*S* enantiomers and analogously 0.71(2)/0.29(2) for *S*/*R* ones. However, only conformational disorder is present in **1b**·$C_7H_{12}O$, the population parameters being 0.67(2) and 0.37(2) (Fig. 7). H atoms were found directly in difference maps except some of guest molecules. The absolute configuration was not determined since it was known by synthesis.

Supplementary Data.—Atomic coordinates for the structures of Table 2 have been deposited with the Cambridge Crystallographic Data Centre. For details of the CCDC deposition scheme see 'Instructions for Authors (1994),' *J. Chem. Soc., Perkin Trans. 2*, issue 1.

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