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Supramolecular Inclusion Hosts Based on Amino Acid Compound Sources: Design, Synthesis and Crystalline Inclusion Behaviour. X-Ray Crystal Structures of Two Inefficient Host Compounds

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Abstract. A new design of crystalline hosts derived from amino acids, characterised by an aminoethanol functional unit or its carbonamide structural derivative and appended aromatic residues including secondary substituents, is reported. The syntheses of corresponding compounds (**1**–**15**) are described. Crystalline inclusion formation is shown and discussed with reference to structural parameters of the host molecules. X-Ray crystal structures of compounds **3** and **11** have been determined in order to suggest reasons for their failure to show inclusion ability.

Key words: host synthesis, aminoethanol derivatives, crystalline inclusion compounds, X-ray structure analysis

Supplementary Data relating to this article (structure factors, isotropic and anisotropic displacement parameters, bond distances and angles) have been deposited with the British Library at Boston Spa, Wetherby, West Yorkshire, U.K., as Supplementary Publication No. SUP 82243 (18 pages).

1. Introduction

Host design based on rigid bulky groups and making use of hydroxyl functions has proved very profitable in the formation of crystalline inclusion complexes [1–4]. Compounds of this type are mostly diols having the hydroxyl group incorporated into a crowded diarylhydroxymethyl residue [5]. Others are bulky diols that derive from natural chiral compounds such as tartaric [6] lactic [7] or mandelic acid [8] typical of the hydroxyl functions in adjacent positions. These hosts not only are specific chiral selectors [3, 9] and sensor materials [10] as well as supports for enantioselective solid-solid reactions [3, 11] but make possible crystalline inclu-

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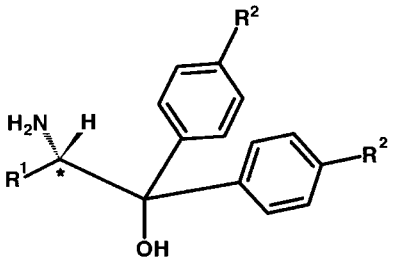
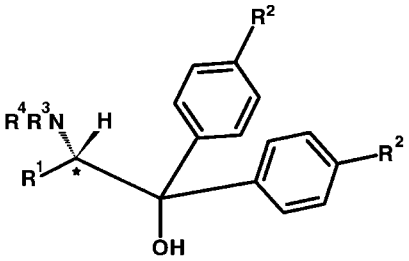


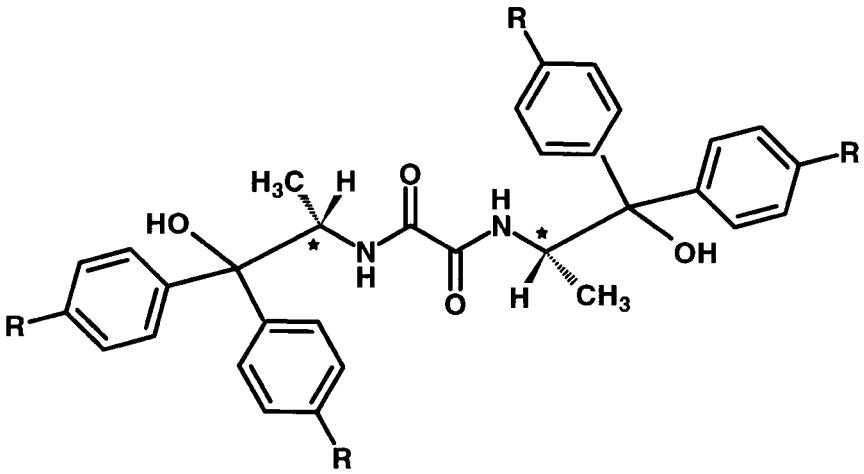
	R^1	R^2
1	CH_3	H
2	CH_3	CH_3
3	CH_3	$C(CH_3)_3$
4	CH_3	Cl
5	C_6H_5	H
6	$CH_2C_6H_5$	H



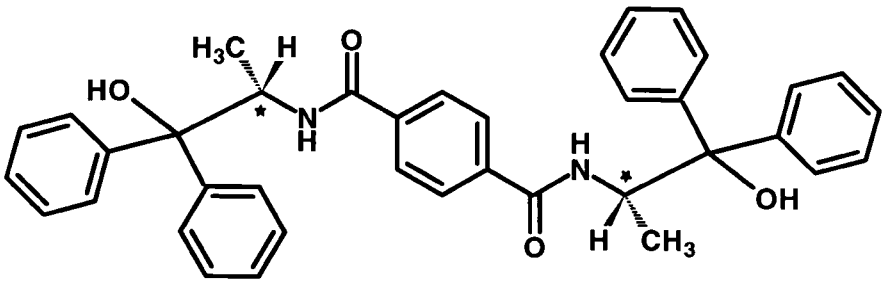
	R^1	R^2	R^3	R^4
7	CH_3	H	H	$C(O)C_6H_5$
8	CH_3	H	H	$2,4\text{-}(NO_2)_2C_6H_3$
9	CH_3	H	H	$2,4\text{-}(NO_2)_2\text{-}5\text{-}(NH_2)C_6H_2$
10	C_6H_5	H	H	$C(O)C_6H_5$
11	CH_3	H	$CH_2C_6H_5$	$CH_2C_6H_5$
12	CH_3	H	$1,2\text{-}(CO)_2C_6H_4$	

Scheme 1.

sion formation with organic compounds at a remarkably broad level [6–8]. In this nexus, bulky host analogues where one of the adjacent hydroxyl groups is substituted by an amino function, i.e., compounds that derive from amino acids instead of hydroxycarboxylic acids, would be a promising structural modification considering inclusion selectivity. Moreover, both bulky dicarboximide derivatives of common amino acids [12] and dipeptides [13] have already been shown to be efficient host compounds. Consequently, we now report a similar host design typical of a bulkily substituted 2-aminoethanol structure. The preparation of specific compounds **1**–**15**, tests of the inclusion properties and examination of selected X-ray crystal structures of two case studies of compounds exhibiting remarkably inefficient host properties are reported here.



13 R = H
14 R = $C(CH_3)_3$



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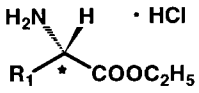
Scheme 2.

2. Experimental

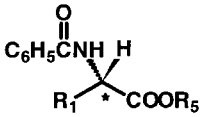
2.1. SYNTHESIS

2.1.1. *General*

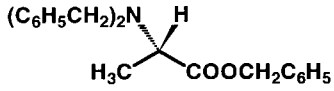
All temperatures are uncorrected. Melting points were obtained with a Kofler apparatus (Reichert, Wien). Optical rotations were determined with a Perkin Elmer 241 polarimeter. Infrared spectra (IR) were recorded on a Perkin Elmer 1600 FT-IR spectrometer. ^{1}H-NMR spectra were taken with EM-360 (60 MHz, Varian), AW-80 (80 MHz, Bruker) and AC-200 (200 MHz, Bruker) spectrometers in the solvent as indicated. ^{13}C-NMR spectra were recorded with AC-200 (50.32 MHz, Bruker)



		R'
16	**a**	CH_3
	b	C_6H_5
	c	$CH_2C_6H_5$



		R^1	R^5
17	**a**	CH_3	C_2H_5
	b	C_6H_5	CH_3



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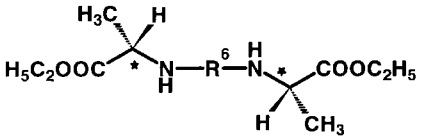

		R^6
19	**a**	C(O)C(O)
	b	1,4-$(CO)_2C_6H_4$

Scheme 3.

and WM-250 (62.89 MHz, Bruker) spectrometers. Chemical shifts are reported in ppm downfield from tetramethylsilane as internal reference. The mass spectra (MS) were recorded with an MS-50 spectrometer (A.E.I., Manchester); the FAB-MS spectra were obtained with a Concept 1H instrument (Kratos, Manchester).

2.1.2. *Starting Compounds and Intermediates*

Amino Acid Ethyl Ester Hydrochlorides **16**(**a**–**c**) were synthesized from the respective amino acids by a modified literature procedure [14] as described previously [12].

16a: colourless crystals; m.p. 78 °C, $[\alpha]_D^{20}$ +2.8° (c 7.37, H_2O)
16b: colourless crystals; m.p. 196–199 °C, $[\alpha]_D^{20}$ +91.0° (c 1.93, H_2O)
16c: colourless crystals; m.p. 153–154 °C, $[\alpha]_D^{20}$ −7.5° (c 1.71, H_2O).

N-Benzoyl-L-alanine Ethyl Ester (**17a**) was prepared from **16a** and benzoyl chloride in pyridine as usual [15]. Recrystallization from toluene gave 69% yield of

colourless crystals; m.p. 93–95 °C (lit. [16] 95 °C); $[\alpha]_D^{20}$ +40.84 ° (c 2.135, $CHCl_3$), $[\alpha]_D^{20}$ −8.35 ° (c 1.70, ethanol).

N-Benzoyl-L-phenylglycine Methyl Ester (**17b**) was synthesized in two steps from L-phenylglycine via *N*-benzoylation and subsequent ester formation.

N-benzoylation of L-phenylglycine with benzoyl chloride and NaOH was performed under usual Schotten-Baumann conditions [15] to give 62% yield of colourless crystals; m.p. 195–196 °C (lit. [17] 195.5–196.5 °C); $[\alpha]_D^{20}$ +119.5 (c 0.94, ethanol).

Esterification of *N*-benzoylphenylglycine was carried out with borontrifluoride etherate and methanol following a literature procedure [18]. Recrystallization from petroleum ether (60–90 °C) gave 85% yield of colourless crystals; m.p. 98–100 °C (lit. [19] 101.5 °C); $[\alpha]_D^{20}$ +103.8 ° (c 1.33, ethyl acetate).

N,N-Dibenzyl-L-alanine Benzyl Ester (**18**). To a stirred solution of L-alanine (12.6 g, 0.14 mol) in ethanol (140 mL) were added H_2O (70 mL) and 7 N aqueous KOH (42 mL). The mixture was heated to reflux and excess benzyl chloride (70 mL, 0.61 mol) was added dropwise during 5 min. The mixture was heated to reflux for 1 h. Then the alcohol was distilled off. On acidification with acetic acid an oil separated which was extracted with chloroform. Evaporation of the solvents including benzyl alcohol (obtained from hydrolysis of excess benzyl chloride) in vacuum at 120 °C yielded the crude product which was purified by column chromatography [SiO_2, 63–100 μm; Et_2O-petroleum ether (40–60 °C), 1 : 1] to give 27.2 g (54%) of a colourless oil; $[\alpha]_D^{20}$ −85.22 ° (c 8.71, MeOH); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.42 (d, $^3J_{(H,H)}$ = 7.0 Hz, 3H; CH_3), 3.62 (q, $^3J_{(H,H)}$ = 7.0 Hz, 1H; CH), 3.70 (d, $^3J_{(H,H)}$ = 14.0 Hz, 2H; CH_2), 3.90 (d, $^2J_{(H,H)}$ = 14.0 Hz, 2H, CH_2), 5.21 (d, $^2J_{(H,H)}$ = 12.6 Hz, 1H; CH_2), 5.30 (d, $^2J_{(H,H)}$ = 12.6 Hz, 1H; CH_2), 7.22–7.52 (m, 15H, Ar-H); ^{13}C-NMR (62.89 MHz, $CDCl_3$), δ 14.85 (CH_3), 54.31, 56.10 (3 CH_2), 65.92 (CH), 126.85, 128.14, 128.23, 128.29, 128.34, 128.48, 128.55 (15 CH), 136.06 (Cq), 139.73 (2 Cq), 173.44 (CO); MS (FAB, *m*NBA) m/z 360.1 $(M + H)^+$ *calcd.* for $C_{24}H_{25}NO_2$ (359.47).

Diethyl N,N′-Oxalylbis(L-alaninate) (**19a**). Oxalyl dichloride (5.0 g, 40 mmol), was dropped into a suspension of ethyl L-alaninate hydrochloride (**16a**) (11.0 g, 70 mmol) in dry toluene (125 mL) and heated to reflux for 4 h. On cooling a precipitate formed which was filtered, dried and recrystallized from ethanol to yield 5.5 g (54%) colourless crystals; m.p. 125–127 °C (lit. [20] m.p. 126 °C); $[\alpha]_D^{20}$ +2.88 ° (c 2.19, $CHCl_3$); ^{1}H-NMR (60 MHz, $CDCl_3$) δ 1.25 (t, 6H; CH_3), 2.42 (d, 6H; CH_3), 4.13 (q, 4H; OCH_2), 4.50 (m, 2H; NCH), 7.75 (br, 2H; NH).

Diethyl N,N′-Terephthaloylbis(L-alaninate) (**19b**). Ethyl L-alaninate hydrochloride (**16a**) (7.6 g, 50 mmol) was dissolved in pyridine (40 mL). Terephthaloyl dichloride (7.0 g, 35 mmol) was added and the mixture was stirred for 4 h at room temperature.

Diluted HCl (350 mL) was added and the mixture was stirred for an additional 3 h. The precipitate formed was collected and dried (70 °C, vac.) to give 7.1 g (79%) colourless powder; m.p. 155–158 °C; ^{1}H-NMR (80 MHz, [D_6]DMSO) δ 1.20 (t, 6H; CH_3), 1.37 (d, 6H; CH_3), 4.10 (q, 4H; OCH_2), 4.45 (m, 2H, NCH), 7.92 (s, 4H; Ar-H), 8.85 (d, 2H; NH); MS (70 eV) m/z 364 (M^+) *calcd.* for $C_{18}H_{24}N_2O_6$(364.40).

2.1.3. *Host Compounds and Analogues*

2-Amino Alcohols **1**–**6** were synthesized from **16**(**a**–**c**) via Grignard reaction as described in the literature [12].

1: colourless powder; m.p. 100–102 °C; $[\alpha]_D^{20}$ −85.9 °C (c 2.77, $CHCl_3$).

2: (isolated as the hydrochloride): colourless powder; m.p. 235–238 °C; $[\alpha]_D^{20}$ +47.8 ° (c 4.28, MeOH).

3: colourless crystals; m.p. 217–218 °C (from EtOH); $[\alpha]_D^{20}$ −47.1 ° (c 3.03, $CHCl_3$).

4: colourless powder; m.p. 106–109 °C; $[\alpha]_D^{20}$ −81.9 ° (c 3.01, $CHCl_3$).

5: colourless powder; m.p. 128–130 °C; $[\alpha]_D^{20}$ −241.3 ° (c 2.42, $CHCl_3$).

6: colourless powder; m.p. 140–143 °C; $[\alpha]_D^{20}$ −82.9 ° (c 3.07, $CHCl_3$).

N-Benzoyl-substituted Amino Alcohols **7** and **10**. They were synthesized from *N*-benzoylamino acid esters **17a** or **17b** and phenyl magnesium bromide (prepared from bromobenzene and Mg in dry THF) using the common Grignard procedure [21]. Specific details for each compound are given below.

7: Evaporation of the solvent and recrystallization from 1-propanol gave 80% yield of colourless crystals; m.p. 220–222 °C; $[\alpha]_D^{20}$ −101.72° (c 4.83, DMF); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.18 (d, $^3J_{(H,H)}$ = 6.2 Hz, 3H; CH_3), 3.12 (s, 1H; OH), 5.28 (dq, $^3J_{(H,H)}$ = 6.2 Hz, 1H; NCH), 6.58 (d, $^3J_{(H,H)}$ = 8.9 Hz, 1H; NH) 7.10–7.56 (m, 15H; Ar H); ^{13}C-NMR (50.32 MHz, $CDCl_3$/[D_6]DMSO) δ 15.41 (CH_3), 50.95 (CH), 79.24 (Cq), 125.02, 125.60, 125.89, 126.17, 126.85, 127.59, 127.64, 127.80, 130.69, 134.88 (15 CH), 134.88, 145.51, 146.73 (3 Cq) 166.37 (CO); IR (KBr) 3407.5 (s; OH), 2977.2 (w; CH), 1625.5 (vs; C=O), 1527.5 (vs), 1486.8 (m), 1444.5 (m; Ar), 1343.0 (m; CH, OH), 1160.7 (m; CO), 751,2 (w), 697.1 (s; monosubst. Ar) cm^{-1}; MS (FAB, *m*NBA + DMSO) m/z 332.1 $(M + H)^+$ *calcd.* for $C_{22}H_{21}NO_2$(331.41). *Anal. calcd.* for $C_{22}H_{21}NO_2$: C, 79.73; H, 6.39; N, 4.23. *Found:* C, 79.78; H, 6.41; N, 4.30.

10: The solid which formed from the organic layer was collected, dried (vac.) and recrystallized from toluene to give 87% yield of colourless crystals; m.p. 273–274 °C; $[\alpha]_D^{20}$ −281.8° (c 0.90, DMF); ^{1}H-NMR (200 MHz, [D_6]DMSO) δ 6.15 (d, 1H; NCH), 6.24 (s, 1H; OH), 6.98–7.72 (m, 20H; Ar-H), 8.67 (d, 1H; NH); ^{13}C-NMR (50.32 MHz, [D_6] DMSO) δ 59.62 (CH), 79.85 (Cq), 125.83, 126.14, 126.45, 126.79, 126.88, 127.13, 127.43, 128.09, 128.39, 129.23, 131.35 (20 CH),

134.71, 139.50, 144.87, 146.83 (4 Cq), 166.01 (CO). *Anal. calcd.* for $C_{27}H_{23}NO_2$ (393.48): C, 82.42; H, 5.89; N, 3.56. *Found*: C, 82.79; H, 5.96; N, 3.77.

N-Aryl-substituted 2-Amino Alcohols **8** and **9**. They were synthesized from **1** and the corresponding fluorobenzenes following literature procedures ([22] for **8** and [23] for **9**).

(2S)-N-(2,4-Dinitrophenyl)-2-amino-1,1-diphenylpropan-1-ol (**8**). A mixture composed of **1** (3.7 g, 16.4 mmol), solutions of sodium hydrogencarbonate (2 g) in water (20 mol) and of 2,4-dinitrofluorobenzene in ethanol (40 mL) was stirred at room temperature for 3 h. Glycine (0.4 g, 5.4 mmol) was added and the mixture was stirred for an additional 2 h. The solvent was evaporated under vacuum and the residue extracted into water (50 mL). The aqueous layer was extracted with three 50 mL portions of diethyl ether, dried (Na_2SO_4) and evaporated. Recrystallization from ethanol yielded the 2:1 inclusion compound of **8** with ethanol. Treatment of the complex at 70 °C in vacuum for 2 d gave 4.2 g (65%) of desolvated pure **8** as yellow powder; m.p. 120–122 °C; $[\alpha]_D^{20}$ +254.0° (c 3.41, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.30 (d, $^3J_{(H,H)}$ = 7.3 Hz, 3H; CH_3), 2.81 (br, 1H; OH), 4.78 (dq, $^3J_{(H,H)}$ = 9.1 Hz, $^3J_{(H,H)}$= 7.3 Hz, 1H; NCH), 6.96 (d, $^3J_{(H,H)}$ = 8.7 Hz, 1H; Ar-H), 7.08–7.51 (m, 10H; Ar-H), 8.19 (dd, $^3J_{(H,H)}$ = 8.7 Hz, $^4J_{(H,H)}$ = 3.6 Hz, 1H; Ar-H), 9.04 (d, $^4J_{(H,H)}$ = 3.6 Hz, 1H; Ar-H), 9.13 (d, $^3J_{(H,H)}$ = 9.1 Hz, 1H; NH); ^{13}C-NMR (62.89 MHz, $CDCl_3$) δ 15.55 (CH_3), 55.06 (CH), 80.17 (Cq), 113.71, 124.60, 125.50, 125.72, 127.58, 127.73, 128.54, 128.66, 130.25 (13 CH), 135.52, 143.71, 147.35 (5 Cq); IR (KBr) 3526.6 (m; NH), 3331.4 (m; OH), 3055.3 (w; CH), 1618.4 (s), 1582.7 (s; Ar). 1498.3 (s; N=O), 1419.5 (s; CH, OH), 1327.6 (vs; N=O), 1139.3 (s; CO), 741.7 (m), 696.3 (s; monosubst. Ar) cm^{-1}; MS (FAB, *m*NBA) m/z 393.2 (M^+) *calcd*. for $C_{21}H_{19}N_3O_5$ (393.40). *Anal. calcd*. for $C_{21}H_{19}N_3O_5$: C, 64.12; H, 4.87; N, 10.68. *Found*: C, 63.85; H, 4.95; N, 10.54.

(2S)-N-(5-Amino-2,4-dinitrophenyl)-2-amino-1,1-diphenylpropan-1-ol (**9**). A mixture composed of **1** (4.2 g, 18 mmol), sodium hydrogencarbonate (2.2 g, 26 mmol), 5-fluoro-2,4-dinitroaniline (4.7 g, 23 mmol) and ethanol (100 mL) was heated to reflux for 2 h. The solvent was removed in vacuum and the residue equilibrated between water (100 mL) and ethanol (100 mL). The aqueous layer was separated and extracted with diethyl ether (2 × 50 mL). The organic layers were combined, dried (Na_2SO_4) and evaporated. Recrystallization from ethanol yielded the 2:1 inclusion compound of **9** with ethanol. Treatment of the complex at 70 °C in vacuum for 3 d gave 3.8 g (51%) of desolvated pure **9** as yellow powder; m.p. 208–211 °C; $[\alpha]_D^{20}$ +23.9 ° (c 4.27, acetone); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.20 (d, 3H; CH_3), 2.67 (s, 1H; OH), 4.53 (m, 1H; NCH), 5.90 (s, 1H; Ar-H), 6.42 (br, 2H; NH_2), 7.12–7.50 (m, 10H; Ar-H), 8.80 (d, 1H; NH), 9.15 (s, 1H; Ar-H); ^{13}C-NMR (62.89 MHz, $CDCl_3$) δ 15.09 (CH_3), 54.48 (CH), 80.23 (Cq), 94.64 (CH), 123.86, 125.39 (2 Cq), 125.74 (2 CH), 125.81 (2 CH), 127.62, 127.66 (2 CH), 128.59 (4

CH), 129.45 (CH), 143.99, 144.22, 147.26, 148.89 (4 Cq); IR (KBr) 3479.8 (s; NH), 3354.3 (s; OH), 1626.8 (vs; NH_2), 1592.5 (s), 1562,9 (s; CO), 818.4 (w; Ar), 746.2 (m), 698,7 (m; monosubst. Ar) cm^{-1}; MS (FAB, *m*NBA + NaOAc) *m*/*z* 409.1 $(M + H)^+$, 431.1 $(M + Na)^+$ *calcd*. for $C_{21}N_{20}N_4O_5$ (408.41). *Anal. calcd*. for $C_{21}H_{20}N_4O_5$: C, 61.76; H, 4.94; N, 13.72. *Found*: C, 61.45; H, 5.01; N, 13.79.

(2S)-N,N-Dibenzyl-2-amino-1,1-diphenylpropan-1-ol (**11**). Benzyl alaninate **18** (28.1 g, 80 mmol) in dry THF (200 mL) was reacted with phenylmagnesium bromide [from bromobenzene (24.7 g, 0.24 mol) and Mg (10.2 g, 0.42 mol)] in dry THF (300 mL) under usual Grignard conditions [15] and work-up. Recrystallization from methanol yielded 15.3 g (47%) of colourless crystals; m.p. 134–136 °C; $[\alpha]_D^{20}$ −62.22° (c 3.44; $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.27 (d, $^3J_{(H,H)}$ = 7.2 Hz, 3H; CH_3, 3.29 (d, $^2J_{(H,H)}$ = 12.9 Hz, 2H; CH_2), 3.64 (d, $^2J_{(H,H)}$ = 12.9 Hz, 2H; CH_2), 3.86 (q, $^3J_{(H,H)}$ = 7.2 Hz, 1H; NCH), 5.28 (s, 1H; OH), 7.13-7.44 (m, 18H; Ar-H), 7.59 (m, 2H; Ar-H); ^{13}C-NMR (62.89 MHz, $CDCl_3$) δ 8.57 (CH_3), 55.08 (2 CH_2), 60.57 (CH), 78.47 (Cq), 126.67, 127.05, 127.20, 127.51, 127.56, 127.74, 128.37, 129.19 (20 CH), 139.01 (2 Cq), 144.57, 145.95 (2 Cq); IR (KBr) 3320.2 (m; OH), 3021.8 (m), 2841.7 (m; CH), 1596.4 (w), 1491.2 (m; Ar), 1446.6 (m; CH), 1346.2 (m; OH), 1143.5 (m; CO), 748.0 (s), 695.2 (vs; monosubst. Ar) cm^{-1}; MS (FAB, *m*NBA) *m*/*z* 408.2 $(M + H)^+$ *calcd*. for $C_{29}H_{29}NO$ (407.55). *Anal. calcd.* for $C_{29}H_{29}NO$: C, 85.47; H, 7.17; N, 3.44. *Found*: C, 85.28; H, 7.19; N, 3.76.

(2S)-2-Phthalimido-1,1-diphenylpropan-1-ol (**12**). Synthesis was performed following a procedure for preparation of 2-phthalimido-1-propanol [24]. To an ice-cooled suspension of **1** (7.1 g, 30 mmol) in THF (20 mL) was dropped a solution of *N*-(ethoxycarbonyl)phthalimide [25] in THF (25 mL). Stirring was continued at room temperature overnight. The solvent was removed under reduced pressure. Recrystallization from methanol yielded 8.8 g (79%) colourless crystals; m.p. 136–139 °C; $[\alpha_D]^{20}$ −116.87° (c 2.52, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.29 (d, $^3J_{(H,H)}$ = 6.9 Hz, 3H; CH_3), 5.57 (q, $^3J_{(H,H)}$ = 6.9 Hz, 1H; NCH), 5.99 (s, 1H; OH), 6.95-7.77 (m, 14H; Ar-H); ^{13}C-NMR (62.89 MHz, $CDCl_3$) δ 14.06 (CH_3), 55.82 (CH), 80.08 (Cq), 124.12, 125.64, 126.25, 127.35, 127.44, 128.74, 128.91, 131.91, 134.92 (10 CH, 4 Cq), 145.21, 146.59 (2 CO); IR (KBr) 3403.7 (m; OH), 2990.1 (w; CH), 1771.1 (m), 1696.3 (vs; C = O), 1406.4 (m), 1352.5 (m; CH, OH), 1040.6 (m; CO), 769.7 (w), 748.4 (w; 1,2-subst. Ar), 707.8 (m; monosubst. Ar) cm^{-1}; MS (FAB, *m*NBA) *m*/*z* 358.1 $(M + H)^+$ *calcd*. for $C_{23}H_{19}NO_3$ (357.41). *Anal. calcd*. for $C_{23}H_{19}NO_3$: C, 77.29; H, 5.36; N, 3.92. *Found*: C, 77.27; H, 5.37; N, 3.85.

Bis-Amides **13**–**15**. They were synthesized from diesters **19a** or **19b** via Grignard addition using the common procedure [21]. Specific details for each compound are given.

(2S,2′S)-N,N′-Oxalylbis(2-amino-1,1-diphenylpropan-1-ol (**13**). **19a** (8.7 g, 30 mmol) in dry THF (200 mL) and phenylmagnesium bromide [from bromobenzene (37.6 mL, 0.36 mol) and magnesium (9.1 g, 0.37 mol) in dry THF (300 mL)] were reacted. Recrystallization from ethanol yielded 2.2 g (14%) colourless powder; m.p. 252–255 °C; $[\alpha]_D^{20}$ −134.3° (c 1.36, DMF); ^{1}H-NMR (250 MHz, [D$_6$]DMSO) δ 0.91 (d, $^3J_{(H,H)}$ = 5.9 Hz, 6H; CH_3), 4.90 (dq, $^3J_{(H,H)}$ = 9.3 Hz, $^3J_{(H,H)}$ = 5.9 Hz; NCH), 6.29 (s, 2H; OH), 7.06–7.48 (m, 20H; Ar-H), 8.48 (d, $^3J_{(H,H)}$ = 9.3 Hz, 2H; NH); ^{13}C-NMR (50.32 MHz, [D$_6$]DMSO) δ 15.37 (2 CH_3), 51.21 (2 CH), 78.80 (2 Cq), 125.27 (4 CH), 125.44 (4 CH), 126.38 (2 CH), 126.50 (2 CH), 127.93 (4 CH), 128.10 (4 CH), 145.64 (2 Cq), 146.35 (2 Cq), 158.84 (2 CO); IR (KBr): 3340.3 (s; OH), 3060.0 (w; CH), 1654.1 (vs; C = O), 1519.1 (s), 1447.7 (s; Ar), 1168.1 (m; CO), 750.7 (w), 697.4 (s; monosubst. Ar) cm^{-1}; MS (FAB, *m*NBA + DMSO) *m*/*z* 509.2 (M + H)$^+$, 587.2 (M + H + DMSO)$^+$ *calcd.* for $C_{32}H_{32}N_2O_4$ (508.62). *Anal. calcd.* for $C_{32}H_{32}N_2O_4$: C, 75.57; H, 6.34; N, 5.51. *Found*: C, 75.09; H, 6.08; N, 5.56.

(2S,2′S)-N,N′-Oxalylbis[2-amino-1,1-bis(4-tert-butylphenyl]propan-1-ol (**14**). **19a** (8.7 g), 30 mmol) in dry THF (200 mL) and 4-tert-butylphenylmagnesium bromide [from 4-tert-butylbromobenzene (76.7 g, 0.36 mol) and magnesium (9.1 g, 0.37 mol) in dry THF (300 mL) were reacted. Recrystallization from ethanol yielded 10.0 g (46%) colourless powder; m.p. 307-308 °C; $[\alpha]_D^{20}$ −124.5 ° (c 2.58, DMF); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.05 (d, $^3J_{(H,H)}$ = 6.6 Hz, 6H; CH_3), 1.30 (s, 18H; $C(CH_3)_3$), 1.23 (s, 18H; $C(CH_3)_3$), 3.12 (br, 2H; OH), 4.96 (dq, $^3J_{(H,H)}$ = 9.5 Hz, $^3J_{(H,H)}$ = 6.6 Hz, 2H; NCH), 7.20 - 7.37 (m, 16H; Ar-H), 7.86 (d, $^3J_{(H,H)}$ = 9.5 Hz, 2H; NH); ^{13}C-NMR (62.89 MHz, $CDCl_3$) δ 16.11 (2 CH_3), 31.31 (12 CH_3), 34.35 (4 Cq), 51.92 (2 CH), 87.14 (2 Cq), 125.11, 125.23, 125.41, 125.55 (16 CH), 141.58 141.77, 149.72, 149.86 (4 Cq), 159.19 (2 CO); IR (KBr) 3372.2 (m; OH), 2961.8 (vs), 2869.2 (w; CH), 1659.3 (vs; C = O), 1507.6 (vs; Ar), 1403.0 (w), 1363.1 (w; *t*-Butyl), 1269,1 (w; OH), 1108.6 (w; CO), 829.7 (m; 1,4-subst. Ar) cm^{-1}. *Anal. calcd.* for $C_{48}H_{64}N_2O_4$ (733.05): C, 78.65; H, 8.80; N, 3.82. *Found*: C, 78.37; H, 8.83; N, 4.08.

(2S,2′S)-N,N′-Terephthaloylbis(2-amino-1,1-diphenylpropan-1-ol (**15**). **19b** (5.5 g, 15 mmol) in dry THF (100 mL) and phenylmagnesium bromide [from bromobenzene (18.8 mL, 0.18 mol) and Mg (4.6 g, 0.19 mol) in dry THF (100 mL)] were reacted. Recrystallization from 1-propanol yielded 3.5 g (39%) colourless powder; m.p. 285–286 °C; $[\alpha]_D^{20}$ −91.6 ° (c 1.51, DMF); ^{1}H-NMR (250 MHz, [D$_6$]DMSO) δ 1.01 (d, $^3J_{(H,H)}$ = 6.4 Hz, 6H; CH_3), 5.20 (dq, $^3J_{(H,H)}$ = 8.7 Hz, $^3J_{(H,H)}$ = 6.4 Hz, 2H; NCH), 5.92 (s, 2H; OH), 7.03–7.61 (m, 24H; Ar-H), 7.97 (d, $^3J_{(H,H)}$ = 8.7 Hz, 2H; NH); ^{13}C-NMR (50.32 MHz, [D$_6$]DMSO) δ 15.63 (2 CH_3), 51.17 (2 CH), 79.47 (2 Cq), 125.30, 125.68, 126.31, 126.42, 127.03, 127.84, 128.10 (20 CH), 137.03 (2 Cq), 145.80 (2 Cq), 146.84 (2 Cq), 165.31 (2 CO); IR (KBr) 3405.1 (s, br; OH), 3059.3 (w), 2984.4 (w; CH), 1630.0 (vs; C=O), 1532.3 (vs), 1492.9

(s), 1449.4 (m; Ar), 1347.9 (m; CH), 1164.5 (m; CO), 860.8 (w; 1,4-subst. Ar), 750.0 (m), 700.7 (s; monosubst. Ar) cm^{-1}; MS (FAB, *m*NBA + DMSO) m/z 585.2 $(M + H)^+$ *calcd*. for $C_{38}H_{36}N_2O_4$ (584.71). *Anal. calcd.* for $C_{38}H_{36}N_2O_4$: C, 78.06; H, 6.21; N, 4.79. *Found*: C, 77.59; H, 6.39; N, 5.02.

2.1.4. *Crystalline Inclusion Compounds*

The corresponding host compound was dissolved under heating in a minimum amount of the respective guest solvent. After storage for 12 h at room temperature, the crystals which formed were collected, washed with diethyl ether or methanol and dried (1 h, 15 Torr, room temperature). Host:guest stoichiometric ratios were determined by ^{1}H-NMR integration. Data for each compound are given in Table I.

2.2. CRYSTALLOGRAPHY

2.2.1. *Sample Preparation*

Single crystals of compounds **3** and **11** were obtained by dissolution in ethanol and saturating the solution by slow evaporation at room temperature.

2.2.2. *X-ray Structure Determination*

Details of data collection and refinement procedure are given in Table II. All crystals were enclosed in a Lindemann capillary to prevent decomposition. Two data sets were collected for **3**, at room temperature and at 150 K using an Oxford Cryostream device [26] for cooling the sample. Only the results corresponding to the low temperature data set are reported. The structures were solved by direct methods using the SIR92 program [27] and the refinement was carried out by full matrix least squares procedures on F_o using the XRAY80 [28] and XTAL3.2 Systems [29]. Several crystals were tested because most of them were clearly twinned. The one used for data collection shows narrow peaks in the $\omega/2\theta$ scan mode. However, two very close peaks could be observed in the 200 reflection, although both peaks could be measured simultaneously employing a scan width even smaller than that used for data collection. No fissure could be detected by visual inspection of the sample, supporting the supposition that the crystal could be partially twinned. In spite of its quality, we proceeded for data collection of this crystal due to the lack of any better sample. The hydrogen atoms were mainly located in the corresponding difference Fourier synthesis and were included in the refinement, although all of them had to be kept fixed for **3** because of the poor crystal quality of the sample, which is correlated with the high displacement parameters displayed by the *t*-butyl groups. A disorder model for these groups could be obtained using room temperature data, however, no residual electron density is observed for these positions when low temperature data is employed. Two and three low angle reflections affected by strong secondary extinction had been marked as not observed for **3** and **11**, respectively. The weighting scheme was calculated with the aid of

Table I. Crystalline inclusion compounds (host:guest stoichiometric ratios)[a]

Guest solvent	Host compound				
	5	**6**	**8**	**9**	**14**
MeOH	[b]	–	1 : 1	[c]	–
EtOH	2 : 1	–	2 : 1	1 : 1 (1 : 2)	–
n-PrOH	–	–	1 : 1	[b]	1 : 1
i-PrOH	–	–	2 : 1	[b]	–
i-BuOH	–	–	2 : 1	–	–
t-BuOH	–	–	1 : 1	[b]	–
n-$PrNH_2$	–	3 : 1	1 : 1	[b]	–
n-Pr_2NH	1 : 1	–	[b]	[b]	–
n-Pr_3N	2 : 1	[b]	[b]	[b]	[b]
Piperidine	[b]	2 : 3	1 : 2	[b]	1 : 2
Pyridine	1 : 1	–	–	1 : 2	2 : 1
Morpholine	1 : 1	–	1 : 1	2 : 1	1 : 1
Acetonitrile	–	–	[b]	1 : 1	–
Acetone	–	–	1 : 1	[b]	–
Cyclohexanone	–	–	[b]	[b]	2 : 3
DMF	–	–	1 : 1	1 : 1	1 : 2
DMSO	–	–	2 : 1	1 : 1	1 : 2
THF	[b]	1 : 1	1 : 1	2 : 1	2 : 1
1,4-Dioxane	–	[b]	[b]	2 : 1	1 : 1
Toluene	–	–	–	[c]	3 : 1
Xylene	–	–	2 : 1	[c]	6 : 1

[a] Crystalline inclusion compounds (host : guest stoichiometric ratio) are also formed between **4** and *n*-Pr_2NH (2 : 1); **6** and *c*-$HexNH_2$ (1 : 1); **14** and 2-$BuNH_2$ (3 : 2), 1-$PhEtNH_2$ (1 : 1).
[b] Difficult to crystallize.
[c] Low solubility.

the PESOS [30] program. Geometrical data were extracted using the PARST [31] program. The absolute configuration of atom C(2) in both compounds was known by synthesis. The atomic scattering factors were taken from the literature [32]. The final fractional coordinates of the non-hydrogen atoms are listed in Tables III and IV.

Table II. Crystal analysis parameters

Crystal data	**3**	**11**
Formula	$C_{23}H_{33}ON$	$C_{29}H_{29}ON$
Crystal habit	Colourless, prism	Colourless, hexagonal plate
Crystal size (mm)	0.67 × 0.57 × 0.33	0.67 × 0.43 × 0.13
Symmetry	Orthorhombic, $P2_12_12_1$	Monoclinic, $P2_1$
Unit cell determination:	Least-squares fit from 31 and 92 reflexions ($\theta < 45°$)	
Unit cell dimensions (Å,°)	a = 29.470(4)	a = 10.923(1)
	b = 10.546(1)	b = 10.025(1)
	c = 6.449(1)	c = 10.779(1)
	90, 90, 90	90, 94.958(4), 90
Packing V(Å^3), Z	2004.1(4), 4	1175.779(9), 2
D_c (g/cm^3), M, F(000)	1.125, 339.52, 744	1.151, 407.55, 436
μ(cm^{-1})	0.512	0.528
T (K)	150	295
Experimental data		
Technique	Four circle diffractometer: Philips PW1100, Bisecting geometry.	
	Graphite oriented monochromator: $\omega/2\theta$ scans.	
	Detector apertures 1 × 1°. CuKα radiation, θ_{max} 65°.	
	1/2 min./reflex.	1 min/reflex
Scan width:	1.5°	1.5°
Number of reflexions:		
Measured	2039	2244
Independent	2013	2127
Observed	1274 (2σ(I))	2040 (3σ(I))
Standard reflexions:	2 reflexions every 90 minutes. No decay.	
Extinction coeff. (× 10^4)	0.82(13)*	
Solution and refinement		
Solution	Direct methods: Sir92	
Refinement:	Least-Squares on F_{obs}, Full matrix	
Parameters:		
Number of variables	226*	395
Degrees of freedom	1048	1645
Ratio of freedom	4.6	4.2
H atoms	From difference synthesis*	
Weighting-scheme	Empirical as to give no trends in $\langle w\Delta^2 F\rangle$ vs $\langle\|F_{obs}\|\rangle$ and $\langle\sin\theta/\lambda\rangle$	
Max. thermal value (Å^2)	U22[C(29)] = 0.092(12)	U11[C(44)] = 0.160(4)
Final ΔF peaks (eÅ^{-3})	−0.79/0.96	±0.18
Final R and wR	0.120, 0.138	0.042, 0.042

* See experimental.

Table III. Fractional atomic coordinates and equivalent isotropic displacement parameters of the non-hydrogen atoms of compound **3**. The esds are given in parentheses

Atom	x/a	y/b	z/c	U_{eq}/Å^2
C(1)	−0.0006(4)	0.2073(8)	0.440(1)	0.027(3)
C(2)	0.0036(4)	0.3513(9)	0.476(1)	0.034(3)
C(3)	0.0479(4)	0.392(1)	0.573(2)	0.040(4)
O(4)	0.0022(3)	0.1495(5)	0.6446(1)	0.032(2)
N(5)	−0.0347(3)	0.3862(8)	0.614(1)	0.036(3)
C(11)	0.0433(3)	0.159(1)	0.324(2)	0.027(3)
C(12)	0.0515(4)	0.207(1)	0.121(2)	0.043(4)
C(13)	0.0919(4)	0.175(1)	0.025(2)	0.037(4)
C(14)	0.1230(4)	0.097(1)	0.108(2)	0.034(3)
C(15)	0.1135(4)	0.045(1)	0.300(2)	0.038(4)
C(16)	0.0727(4)	0.078(1)	0.405(2)	0.038(4)
C(17)	0.1677(4)	0.057(1)	−0.003(2)	0.041(4)
C(18)	0.1792(4)	0.151(1)	−0.179(2)	0.050(4)
C(19)	0.1633(4)	−0.075(1)	−0.084(2)	0.051(4)
C(20)	0.2088(4)	0.062(1)	0.154(2)	0.053(4)
C(21)	−0.0433(3)	0.170(1)	0.330(2)	0.034(4)
C(22)	−0.0639(4)	0.068(1)	0.406(2)	0.036(3)
C(23)	−0.1105(4)	0.034(1)	0.316(2)	0.039(4)
C(24)	−0.1274(4)	0.101(1)	0.143(2)	0.040(4)
C(25)	−0.1016(4)	0.202(1)	0.074(2)	0.035(3)
C(26)	−0.0613(4)	0.234(1)	0.161(2)	0.039(4)
C(27)	−0.1732(4)	0.066(1)	0.043(2)	0.041(4)
C(28)	−0.1658(4)	0.046(1)	−0.196(2)	0.048(4)
C(29)	−0.2072(5)	0.171(2)	0.074(3)	0.071(6)
C(30)	−0.1923(4)	−0.058(1)	0.130(2)	0.055(4)

3. Results and Discusion

3.1. HOST DESIGN AND SYNTHESIS

The principal host design of this work involves a rigid molecular framework comprising bulky residues and having hydroxy and amino functions attached to neighbouring carbon atoms, i.e., formation of a bulkily substituted aminoethanol structure. This integrated functionality derives from the amino acid compound source and can readily be supplied via the addition of an organometallic reagent to an amino acid ester. Using this general method, compounds **1**–**6** have been obtained by reaction of the esters **16**(**a**–**c**) with the corresponding Grignard reagents [12].

Table IV. Fractional atomic coordinates and equivalent isotropic displacement parameters of the non-hydrogen atoms of compound **11**. The esds are given in parentheses

Atom	x/a	y/b	z/c	$U_{eq}/Å^2$
C(1)	0.4609(2)	0.2820(3)	0.3516(2)	0.0429(6)
C(2)	0.5565(2)	0.3965(3)	0.3798(2)	0.0449(7)
C(3)	0.5196(3)	0.5332(4)	0.3293(2)	0.0556(8)
O(4)	0.5161(2)	0.1629(3)	0.4032(1)	0.0502(5)
N(5)	0.6799(2)	0.3500(-)	0.3503(2)	0.0492(6)
C(11)	0.4281(2)	0.2628(3)	0.2114(2)	0.0464(6)
C(12)	0.3600(2)	0.3571(4)	0.1405(2)	0.0517(7)
C(13)	0.3373(3)	0.3423(4)	0.0123(2)	0.0640(9)
C(14)	0.3792(4)	0.2312(5)	−0.0452(3)	0.0823(12)
C(15)	0.4430(4)	0.1251(5)	0.0235(3)	0.0858(13)
C(16)	0.4670(3)	0.1504(4)	0.1516(3)	0.0634(9)
C(21)	0.3458(2)	0.3037(3)	0.4224(2)	0.0450(6)
C(22)	0.2304(2)	0.2624(4)	0.3731(2)	0.0590(8)
C(23)	0.1282(3)	0.2717(5)	0.4407(3)	0.0742(11)
C(24)	0.1397(3)	0.3209(4)	0.5599(3)	0.0714(10)
C(25)	0.2531(3)	0.3609(4)	0.6112(3)	0.0665(9)
C(26)	0.3557(2)	0.3519(4)	0.5443(2)	0.0557(8)
C(31)	0.7108(2)	0.3831(4)	0.2237(2)	0.0579(9)
C(32)	0.8191(2)	0.3067(4)	0.1851(2)	0.0576(8)
C(33)	0.9115(3)	0.3711(5)	0.1277(3)	0.0739(12)
C(34)	1.0096(3)	0.3014(7)	0.0886(3)	0.0921(17)
C(35)	1.0191(3)	0.1667(7)	0.1069(3)	0.0918(17)
C(36)	0.9286(4)	0.0995(5)	0.1640(4)	0.0900(14)
C(37)	0.8290(3)	0.1701(5)	0.2020(3)	0.0762(11)
C(41)	0.7759(2)	0.4019(4)	0.4430(2)	0.0596(9)
C(42)	0.7794(2)	0.3318(4)	0.5670(2)	0.0596(8)
C(43)	0.7421(4)	0.3946(5)	0.6714(3)	0.0813(12)
C(44)	0.7493(5)	0.3308(6)	0.7861(3)	0.1056(18)
C(45)	0.7977(5)	0.2038(6)	0.7971(4)	0.1022(17)
C(46)	0.8327(3)	0.1389(5)	0.6943(4)	0.0905(15)
C(47)	0.8226(2)	0.2006(4)	0.5788(3)	0.0682(10)

Compounds **7**, **10** and **11** were synthesized analogously from **17**(**a**,**b**) and phenyl magnesium bromide.

On the other hand, the *N*-aryl substituted derivatives **8** and **9** are the result of a nucleophilic aromatic substitution of 2,4-dinitrofluorobenzene (Sanger reagent) or 2,4-dinitro-5-fluoroaniline with **1**. The phthalimido derivative **12** was obtained from **1** and Nefkens reagent [*N*-(ethoxycarbonyl)phthalimide] [24]. Compounds **13**–**15**, i.e. the bisamides of amino-ethanols **1** and **3**, were synthesized from Grignard reaction of **19a** and **19b**, respectively.

As a result of this structural design, 15 potential host compounds differing in substitution, bulkiness, molecular size and functionality, but all based upon the aminoethanol building block have been synthesized. They will enable a reasonable investigation of the crystalline inclusion behaviour on comparative terms.

3.2. INCLUSION PROPERTIES

A total of 45 different crystalline inclusion compounds are specified in Table I showing the efficiency of the new host design. Nevertheless it is also obvious from Table I that only a limited number of the synthesized compounds behave as hosts. Furthermore these hosts are rather different both in their efficiency and the property of forming inclusion compounds with particular classes of guests. This is particularly obvious for host compounds **4** and **8** being the extreme cases of efficiency, in that **4** only yields an inclusion compound with *n*-Pr_2NH while **8** is rather broad in guest acceptance, and for the alcohols, dipolar aprotic solvents (e.g., DMF, DMSO) or aromatic hydrocarbon guests that show affinity to selected hosts. No guest compound can be included by each of the hosts but there are several uniquely included by one host only.

On the other hand, the host-guest stoichiometric ratios determined for the inclusion compounds are rather complex in their distribution which makes it difficult to draw conclusions, although 1 : 1 and 2 : 1 stoichiometric ratios are favoured and a high quota of guests are rare. In contrast, unusually high host quota can be found, e.g. 3 : 1 or 6 : 1 in the case of host **14**, generally suggesting that only a small lattice space is provided by this host.

The most important findings, however, come from a structural comparison including all potential host compounds. Considering, e.g., the alanine derived aminoethanols **1**–**4**, these compounds are probably not sufficiently bulky. Even the most bulkily substituted representative of this series of compounds (**3**) does not form a crystalline inclusion and only **4**, comprising a polar chloro substituent, yields one single inclusion compound under the experimental conditions. The latter property is perhaps a consequence of a weak chloro interaction [33] which is known to exercise a specific influence on the crystal packing [34] and as such also affects the clathrate structure [35].

As shown with compounds **5** and **6**, which derive from phenylglycine or phenylalanine, enlargement of the amino side of the molecule leads to the start of inclu-

sion behaviour in particular with amine guests, and logically the more rigid host **5** is more efficient. On the other hand, substitution at the amino nitrogen has a rather different bearing on the host property. While transformation of the amino group to a carbonamide (**7**, **10**) or carbonimide function (**12**) as well as changing to a dibenzylic tertiary amino group (**11**) involve loss of the inclusion ability which, in some ways, is different from previous findings [12, 36], substitution by a dinitrofluorobenzene or dinitrofluoroaniline residue such as in **8** and **9** is very promising (Table I). Here the effectiveness of inclusion formation may stem from the presence of the highly polar functions being either binding sites for the guests or "sticky" groups to stabilize the host lattice [2b].

Similar results are found for the bisamides **13**–**15** showing again that bulky secondary substituents are essential to yield an inclusion host (cf. **14**) while the size of the dicarboxamide spacer elements (oxalyl or terephthaloyl) is at the most a marginal parameter. Typical features of host **14** are the ability to form inclusion compounds with aprotic guests including aromatic hydrocarbons and the noticably high host:guest stoichiometric ratios suggesting 'true' clathrate formation [37].

Compared with the analogous diol hosts derived from hydroxycarboxylic acids, e.g. lactic acid [7, 9] compared to alanine or mandelic acid [8] compared to phenylglycine, the present compounds are of remarkably low efficiency, except for **8** and **9** which, however, profit from a particular motif (see above). This weakness in inclusion formation also involves chiral guests giving rise to no enantioseparation worth mentioning. Wishing to get an idea of the reasons for the unexpectedly low inclusion power of this compound family prompted us to determine the crystal packings. Hence the crystal structures of compounds **3** and **11**, which are typical examples of the new design which failed in inclusion formation, were studied making a reasonable comparison to the previous diol hosts [7–9] and to related dicarboximide hosts [12] possible.

3.3. STRUCTURAL STUDIES

3.3.1. *Molecular Structures*

The molecular structures of **3** and **11** display big differences as far as the common skeleton is concerned (Figure 1 and Table V), adopting in **3** a conformation similar to that shown by the related bulky alanine derivatives already reported [12]. The main differences arise from the intramolecular OH···N hydrogen bond present in **11** (Figure 1b), which changes the O(4)—C(1)—C(2)—N(5) torsion angle [45.5(3)° versus −59.4(9)° in **3**]. The last value is close to those displayed by 11 related compounds [12] (16 crystallographically independent molecules), which range between −73.3(6)° and −86.1(5)°. In all molecules, the almost coplanarity of O(4) and the two phenyl rings attached to C(1) [measured by the O(4)—C(1)—C(ϕ)—C(ϕ) torsion angle that ranges from 1.4° to 37.2°] is sustained by C—H···O intramolecular interactions, Table V. The only exception is presented by phenyl C(21)–C(26) in **11** [O(4)—C(1)—C(21)—C(22) = −97.3(3)°] where this weak

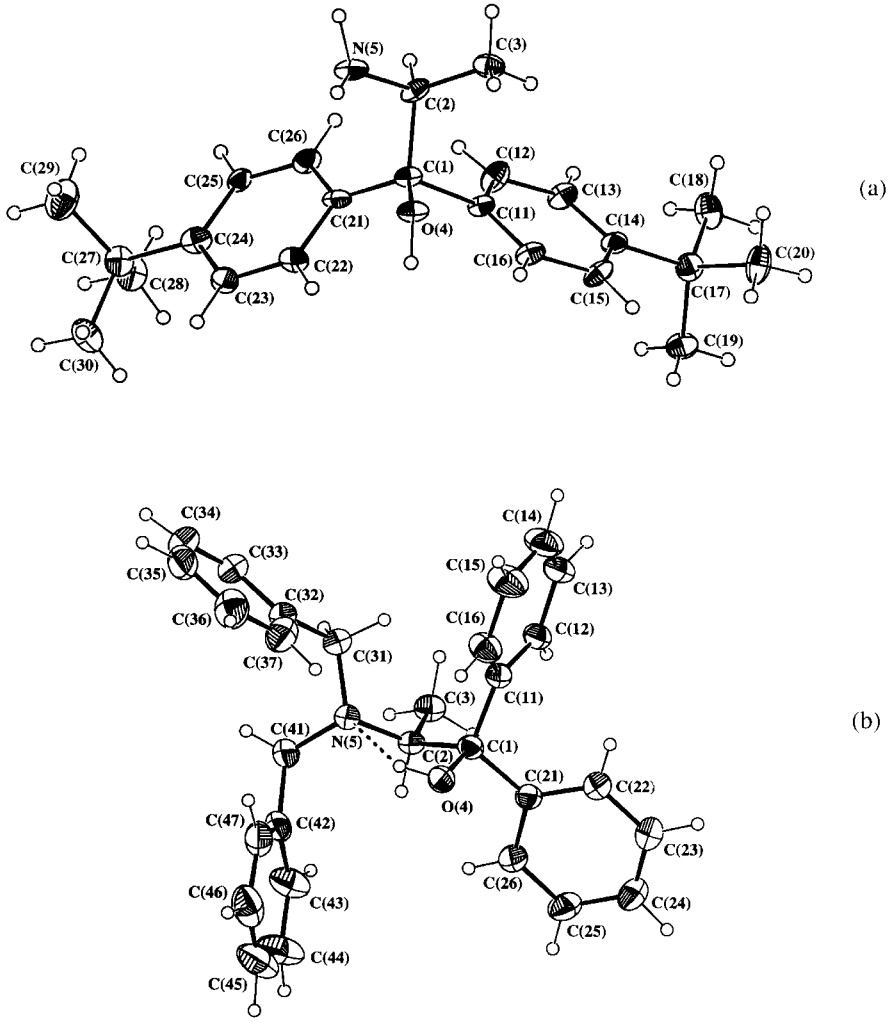

Figure 1. Perspective views of the independent molecules of **3** (a) and **11** (b) showing the numbering system. The anisotropic displacement parameters are shown at 30% probability level. The dotted line in **11** indicates a hydrogen bond.

C—H···O intramolecular interaction is replaced by two intermolecular ones; one is retained with O(4) but of a neighbouring molecule and the other with the centroid of a phenyl ring (Table V). The *t*-butyl substitution at the *para* position on the phenyl rings of **3** closes the intracyclic *ipso* angles in agreement with the values reported by Domenicano and Murray-Rust [38].

3.3.2. *Packing Structures*

While the crystal structure of **11** consists of discrete molecular units (Figure 2b) packed together by weak hydrogen bond interactions that of **3** is constituted by

Table V. Selected geometrical parameters for compounds **3** and **11** (Å,°)

Molecule	**3**		**11**	
C(1)—C(2)	1.541(12)		1.564(4)	
C(1)—O(4)	1.546(10)		1.429(4)	
C(1)—C(11)	1.580(15)		1.534(3)	
C(1)—C(21)	1.494(16)		1.542(3)	
C(2)—C(3)	1.512(16)		1.516(5)	
C(2)—N(5)	1.487(14)		1.487(3)	
N(5)—C(31)	–		1.472(3)	
N(5)—C(41)	–		1.479(3)	
C(2)—N(5)—C(31)/H(5A)	116.6(-)		114.3(1)	
C(2)—N(5)—C(41)/H(5B)	127.8(-)		110.4(1)	
C(31)/H(5A)—N(5)—C(41)/H(5B)	108.3(-)		109.9(1)	
C(12)—C(11)—C(16)	118.7(10)		118.0(3)	
C(22)—C(21)—C(26)	115.7(10)		117.4(2)	
C(33)—C(32)—C(37)	–		117.8(3)	
C(43)—C(42)—C(47)	–		118.4(3)	
C(13)—C(14)—C(15)	117.3(10)		120.0(4)	
C(23)—C(24)—C(25)	116.4(11)		119.2(3)	
O(4)—C(1)—C(11)—C(12)	−175.9(9)		172.2(2)	
O(4)—C(1)—C(11)—C(16)	3.0(13)		−8.4(3)	
O(4)—C(1)—C(21)—C(22)	−14.2(14)		−97.3(3)	
O(4)—C(1)—C(21)—C(26)	162.2(10)		75.8(3)	
O(4)—C(1)—C(2)—N(5)	−59.4(9)		45.5(3)	
O(4)—C(1)—C(2)—C(3)	61.4(10)		178.0(2)	
C(1)—C(2)—N(5)—C(31)/H(5A)	−163.9(-)		93.5(2)	
C(1)—C(2)—N(5)—C(41)/H(5B)	49.8(-)		−142.0(2)	
Hydrogen interactions	X—H	H···X	X···Y	X—H···Y
3:				
O(4)—H(4)···N(5)($-x$, $y-1/2$, $3/2-z$)	0.92(-)	2.68(-)	3.324(10)	128(-)
C(16)—H(16)···O(4)	0.93(-)	2.31(-)	2.698(14)	104(-)
C(16)—H(16)···N(5)($-x$, $y-1/2$, $3/2-z$)	0.93(-)	2.96(-)	3.870(15)	166(-)
C(22)—H(22)···O(4)	0.94(-)	2.39(-)	2.745(13)	102(-)
N(5)—H(5a)···O(4)($-x$, $y+1/2$, $3/2-z$)	0.97(-)	2.65(-)	3.324(10)	127(-)
C(3)—H(3a)···O(4)($-x$, $y+1/2$, $3/2-z$)	0.96(-)	2.94(-)	3.582(13)	126(-)
N(5)—H(5a)···C(11–16)($-x$, $y+1/2$, $1/2-z$)	0.97(-)	2.95(-)	3.594(10)	125(-)
C(3)—H(3a)···C(21–26)($-x$, $y+1/2$, $1/2-z$)	0.96(-)	2.80(-)	3.438(12)	125(-)
11:				
O(4)—H(4)···N(5)	0.85(4)	2.08(4)	2.687(3)	128(4)
C(16)—H(16)···O(4)	0.97(4)	2.32(4)	2.722(3)	104(3)
C(3)—H(031)···O(4)($1-x$, $y+1/2$, $1-z$)	1.04(3)	2.74(3)	3.216(3)	108(2)
C(26)—H(26)···O(4)($1-x$, $y+1/2$, $1-z$)	0.90(4)	2.95(4)	3.445(5)	116(3)
C(43)—H(43)···O(4)($1-x$, $y+1/2$, $1-z$)	1.03(7)	2.98(6)	3.929(5)	154(5)
C(31)—H(311)···C(11–16)	1.02(3)	2.86(3)	3.828(3)	158(2)
C(23)—H(23)···C(32–37)($x-1$, y, z)	0.98(4)	2.99(4)	3.766(3)	137(3)

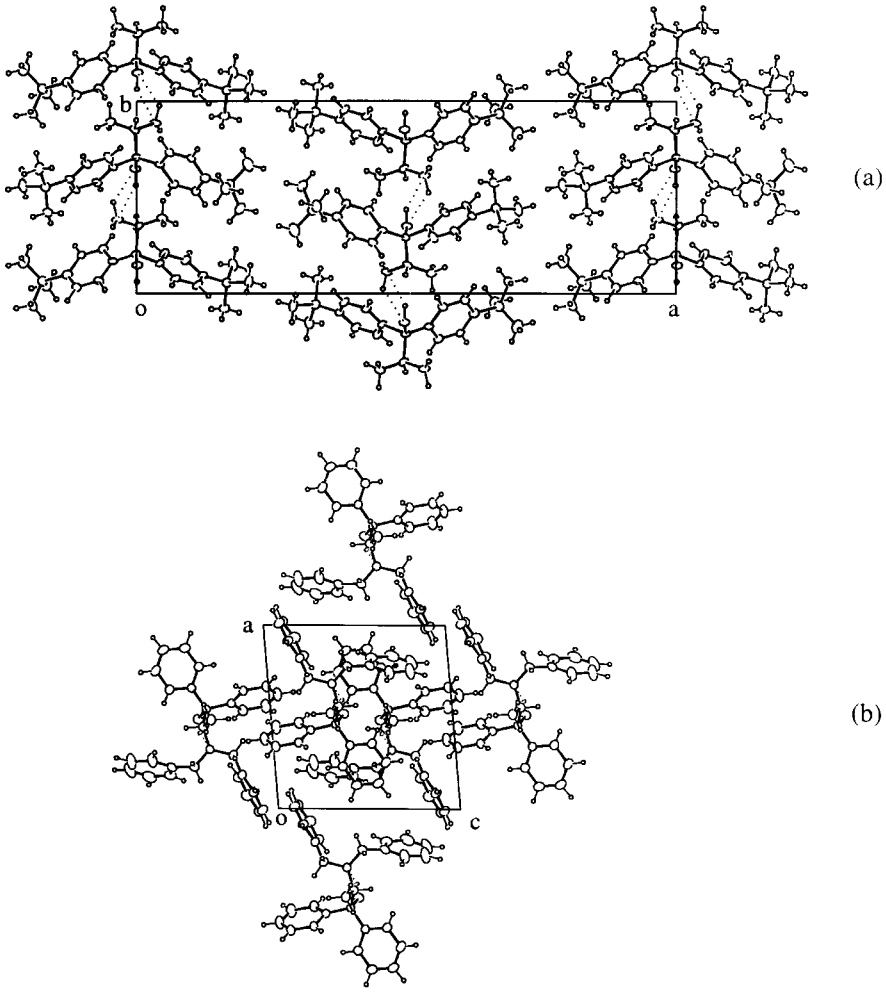

Figure 2. Packing diagrams of **3** (a) and **11** (b) viewed along the *b* and *c* axes, respectively. The two shortest intermolecular hydrogen bonds in **3** (cf. Table V) have been marked using dotted lines.

chains of molecules related by a 2_1 axis along *b* and joined by four hydrogen bonds (Table V and Figure 2a). These chains pack together by two hydrogen interactions involving the π electron cloud of the phenyl rings in a way that highly hydrophobic regions are formed by the amalgamation of all *t*-butyl groups at both sides of *bc* planes located at $x = 0.25$ and $x = 0.75$. The total packing coefficients for **11** and **3** are 0.65 and 0.66, respectively.

There are two spherical voids [39] related by a 2_1 axis and located at (0.10., 0.21, 0.83) and (0.90, 0.71, 0.17) in the unit cell of **11**, the volume of each being 16.83 $Å^3$ which is large enough to encapsulate a water molecule. However, no inclusion complexes of any kind have been obtained using **11** as a potential host

compound. This may be due to the hydrogen bond self-saturation principle pointed out by us in the inclusion behaviour of the structurally related hosts derived from alanine [12].

4. Conclusions

Considering the previously studied diol hosts derived from lactic [7, 9] and mandelic acid [8], the analogous use of the aminoethanol functional building block of amino acids to give the presently synthesized compounds is less productive. Whilst the two hosts that stem from lactic and mandelic acid provide a large number and a great variety of crystalline inclusion compounds [7–9], the present compounds derived from alanine, phenylglycine and phenylalanine are rather poor hosts unless highly polar groups (e.g. **8**, **9**) or a second structural element of aminoethanol (e.g. **14**) are involved. Obviously the structural bulk required for the formation of an inclusion host is much higher for the aminoethanol than for the diol type of hosts, which is perhaps a consequence of the weaker hydrogen donorship of the amino group when taking part in hydrogen bonding [40]. Moreover intramolecular H-bonding, as provided in the structure of **11** (Table V), is a further restrictive feature, although it is present in the diol case [7, 9].

Correspondingly more bulkiness seems also a potential requirement for the carbonamide and carbonimide structural modifications (**7**, **10**, **12**–**15**) to create a good host. This is exactly met with the closely related roof-shaped carbonimide hosts being determined by the bulky 9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboximide framework [12] which has proven an effective inclusion-promoting group [41]. Therefore the incorporation of particularly bulky and rigid units typical of host design is a promising way of development in this field of compounds.

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