In a separate experiment, a solution of **1g** (340 mg, 1 mmol) and *p*-methoxyacetophenone (155 mg, 1 mmol) in benzene (200 mL) was irradiated for 2 h. Workup in the usual manner yielded 60 mg (18%) of unchanged **1g**, mp 188–189 °C (mixture melting point) (elution with a mixture (1:1) of benzene and petroleum ether), 35 mg (10%) of **5g**, mp 235–236 °C (elution with a mixture (7:3) of benzene and petroleum ether and recrystallization from a mixture (1:1) of chloroform and ethanol), and 177 mg (52%) of **4g**, mp 117–118 °C[4e] (mixture melting point) (elution with benzene and recrystallization from ethanol).

5g: IR ν_{max} (KBr) 3060, 3040 (CH) 2240 (C≡N), 1750 (C=O) and 1610 (C=C) cm^{-1}; UV ν_{max} (CH_3OH) 313 nm (ϵ 6200, sh), 301 (6750), 275 (8400), 257 (25 800), 251 (23 900, sh), 231 (28 400); ^1H NMR ($CDCl_3$) δ 6.77 (1 H, s, CH), 7.35 (10 H, m, aromatic), 8.85 and 9.30 (H^7 and H^8); mass spectrum, *m/e* (relative intensity) 335 (M^+, 23), 305 (5), 291 (5), 252 (10), 205 (100), 176 (72) and other peaks.

Anal. Calcd for $C_{23}H_{13}NO_2$: C, 82.39; H, 3.88; N, 4.18. Found: C, 82.01; H, 4.13; N, 4.27.

In another experiment, a solution of **1g** (340 mg, 1 mmol) and *p*-methoxyacetophenone (150 mg, 1 mmol) in methanol was irradiated for 3 h. Workup of the photolyzate in the usual manner yielded 70 mg (31%) of unchanged **1g**, mp 188–189 °C (mixture melting point) (elution with a mixture (1:1) of benzene and petroleum ether), and 230 mg (62%) of **10g**, mp 152–153 C (elution with a mixture (3:2) of benzene and petroleum ether and recrystallization from carbon tetrachloride).

10g: IR ν_{max} (KBr) 3060, 3020, 3000, 2930, 2900 (CH), 2215 (C≡N), 1770 (C=O) and 600 (C=C) cm^{-1}; UV ν_{max} (CH_3OH) 292 nm (ϵ 2000), 278 (2250), 254 (19 600, sh), 244 (22 800); ^1H NMR ($CDCl_3$) δ 3.25 (3 H, s, OCH_3), 3.30 (1 H, d, J = 8 Hz, CH), 5.07 (1 H, d, J = 8 Hz, CH) and 7.20 (14 H, m, aromatic).

Anal. Calcd for $C_{24}H_{19}NO_3$: C, 78.05; H, 5.15; N, 3.79. Found: C, 78.21; H, 5.01; N, 3.93.

Registry No. **1b**, 36165-25-0; **1c**, 1955-40-4; **1d**, 117252-11-6; **1e**, 1955-55-1; **1f**, 87575-49-3; **1g**, 117252-12-7; **2b**, 106552-37-8; **2c**, 24845-42-9; **2d**, 117252-13-8; **2e**, 117252-14-9; **2f**, 106552-38-9; **2g**, 117252-15-0; **4b**, 68727-79-7; **4c**, 56258-96-9; **4d**, 117252-16-1; **4e**, 117252-17-2; **4f**, 117252-18-3; **4g**, 68727-72-0; **5b**, 117252-19-4; **5c**, 117252-20-7; **5d**, 117252-21-8; **5e**, 117252-22-9; **5f**, 117252-23-0; **5g**, 117252-24-1; **10b**, 117252-25-2; **10g**, 117252-26-3; I^-, 20461-54-5; DMHD, 764-13-6; ferrocene, 102-54-5; oxygen, 7782-44-7; *p*-methoxyacetophenone, 100-06-1.

Design of Roof-Shaped Clathrate Hosts.[1] Inclusion Properties and X-ray Crystal Structures of a Free Host and of Inclusion Compounds with 1-BuOH and DMF

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A series of new clathrate hosts characteristic of a roof-shaped molecular backbone and specifically attached functional groups have been synthesized and studied with regard to their inclusion behavior (68 different inclusion species). Formation, stoichiometries, and selectivities of the clathrates depend in a systematic manner on the structural features of the hosts including the number, the nature, the flexibility, and the geometry of functional groups. X-ray structure analyses of two inclusion compounds [**1a**·1-BuOH (1:1), $P\bar{1}$, a = 11.979 (8) Å, b = 10.233 (9) Å, c = 8.974 (6) Å, α = 84.79 (4)°, β = 76.68 (6)°, γ = 68.06 (5)°, Z = 2; and **1a**·DMF (1:1), $P2_1/c$, a = 10.889 (8) Å, b = 9.126 (3) Å, c = 19.005 (13) Å, β = 98.53 (4)°, Z = 4] illustrate that cyclic H bonding between host and guest and dimer clustering of the host molecule play a fundamental role in clathrate binding. The free host **1a** shows infinite H-bonded zigzag chains in its crystal structure [$P\bar{1}$, a = 14.346 (11) Å, b = 12.496 (15) Å, c = 9.432 (6) Å, α = 113.76 (7)°, β = 78.76 (8)°, γ = 107.48 (8)°, Z = 4].

In the last years, the collection of compounds that show the unique property of clathration has increased considerably.[3] Unfortunately, many of these new host molecules have remained individual examples rather than suggesting some structural analogy or fitting in a particular class of substances. They reflect the clathrate chemistry as being rather complex. On the other hand, host compounds having a structural relationship are more conducive to throwing light upon the problem by making a thorough discussion of inclusion properties possible, e.g., based on a designed structural modification.[4,5]

Here we report on such a family of new clathrate hosts whose common feature is a roof-shaped rigid overall structure;[6] we give a demonstration of their inclusion capabilities and support by X-ray crystallographic evidence two isolated inclusion compounds and a free host.

Results and Discussion

Design Strategy. In a former paper we developed the design principle for a new host type called "coordinatoclathrand".[4b,7] The procedure involves a molecule with both a bulky basic skeleton (BS, see Figure 1) and suitably positioned (coordinating) functional groups (FG), i.e., a specific combination of topological and coordinative host–guest interactions in the solid state. Se-

(1) Weber, E. Presented in part at the 4th International Symposium on Inclusion Phenomena, Lancaster, England, July 1986; Abstract I.8.

(2) (a) University of Bonn. (b) University of Stockholm. (c) Home address: Central Research Institute for Chemistry of the Hungarian Academy of Sciences, H-1525 Budapest, Hungary.

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(4) (a) Weber, E.; Ahrendt, J.; Czugler, M.; Csöregh, I. *Angew. Chem.* **1986**, *98*, 719; *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 746. (b) Weber, E.; Csöregh, I.; Stensland, B.; Czugler, M. *J. Am. Chem. Soc.* **1984**, *106*, 3297. (c) Czugler, M.; Stezowski, J. J.; Weber, E. *J. Chem. Soc., Chem. Commun.* **1983**, 154.

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(7) Nomenclature, see: Weber, E.; Josel, H.-P. *J. Inclusion Phenom.* **1983**, *1*, 79. Weber, E. In ref 3b; Vol. 140, p 1.

0022-3263/88/1953-5831$01.50/0

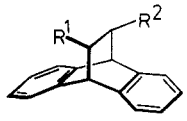
Table I. Crystalline Inclusion Compounds[a]

1a	1-PrOH (1:1), 1-BuOH (1:1), *t*-BuOH (1:1), 1-PentOH (1:1), 1-OctOH (2:1), ethylene glycol (1:2), 2-methoxyethanol (≈1:1),[b] formic acid (1:2), acetic acid (1:1), propionic acid (1:1), 2-chloropropionic acid (1:1), valeric acid (1:1), lactic acid (≈1:1),[b] tartaric acid (2:1), mercaptoacetic acid (1:1), thioacetic acid (≈2:1),[b] propionaldehyde (1:1), acetone (1:1), DMF (1:1), acetonitrile (≈1:1),[b] benzyl cyanide (1:1), DMSO (1:1), THF (1:2), dioxane (2:1), *o*-dichlorobenzene (1:1), 2,6-dimethylnitrobenzene (1:1), 2-nitrophenol (1:2)
1c	THF (2:1), dioxane (2:1)
1h	ethylene glycol (1:1), acetic acid (1:1), propionic acid (2:3)
1k	MeOH (1:1), formic acid (1:3), acetic acid (1:1), propionic acid (1:1)
1r	dioxane (1:1)
1s	dioxane (2:1)
1t	MeOH (2:1), *t*-BuOH (1:1), ethylene glycol (1:1), epichlorohydrin (2:1), diacetone alcohol (2:1), DMF (3:2), DMSO (1:1)
2a	benzyl cyanide (1:2), DMSO (1:2), dioxane (2:1)
2f	DMF (1:1), dioxane (1:1)
2n	MeOH (1:1), *t*-BuOH (1:1), cyclo-HexOH (1:1), acetic acid (1:1), 2-chloropropionic acid (1:1), lactic acid (1:1), propionaldehyde (2:1), acetone (2:1), DMF (2:1), DMSO (1:1), THF (2:1), dioxane (2:1), morpholine (1:1), piperidine (1:1), pyridine (2:1), nitrobenzene (1:1)
3a	*t*-BuOH (1:1), DMSO (1:2), dioxane (1:1)

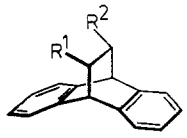
[a] See Experimental Section for method of preparation, drying standard, and characterization; stoichiometric ratios (host:guest) are given in parentheses. [b] Slightly varying stoichiometry.

lectivity is obtained by a complementarity relationship between host (lattice) and guest molecules. It was shown that constitutions being modelled on a pair of scissors (cf. A, Figure 1) are prominent representatives of this particular class of hosts.[4,8] Removal of the hatched sections in A produces B, or the basic geometry turns from a pair of scissors to a roof. We thought that this manipulation applied to a chemical constitution will not drop the net ability of inclusion formation but may have a favorable effect on the topological inclusion selectivity, e.g., by providing a different lattice cage.[3] Modifications of the substituents, i.e., the functional groups (FG), were made with regard to a chemical control of inclusion selectivity, particularly taking advantage of H bonds.[4]

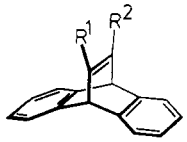
Individual compounds in this context being explored are specified by formulas **1**–**3** (a–u).



1



2



3

	R^1	R^2
a:	COOH	COOH
b:	COOMe	COOMe
c:	COPh	COPh
d:	CN	CN
e:	$-C(=O)-O-C(=O)-$	
f:	$-C(=O)-NH-C(=O)-$	
g:	COCl	COCl
h:	$CONH_2$	$CONH_2$
i:	CONH-n-Pr	CONH-n-Pr
j:	CONH-i-Pr	CONH-i-Pr
k:	CONH-t-Bu	CONH-t-Bu
l:	CONH-cyclo-Hex	CONH-cyclo-Hex
m:	$-O-C(=O)-O-$	
n:	OH	OH
o:	CH_2OH	CH_2OH
p:	CH_2OTos	CH_2OTos
q:	CH_3	CH_3
r:	COOH	COPh
s:	COOH	Ph
t:	COOH	H
u:	COOEt	H

Synthesis. All roof-shaped compounds involve a Diels–Alder addition of a corresponding ene to anthracene as the principal synthetic step.[9] Some of the additions

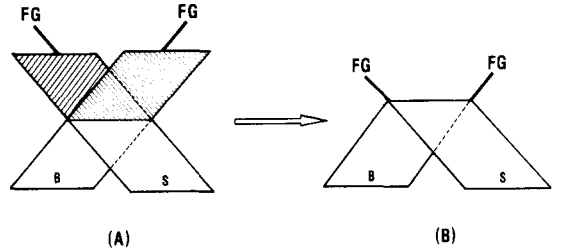


Figure 1. Geometric design concept of roof-shaped hosts (BS = bulky skeleton, FG = functional group).

give immediately the intended hosts (**1a**, **1c**, **1d**, **1s**, and **1t**). In other cases a subsequent hydrolysis (**2a**, **2n**, **3a**, and **3t**), a reduction (**1o**, **2o**, and **2q**), or other transformations (cf. **1h–l**, **1r**, and **2f**) are required to obtain the target molecules. For more details, see the Experimental Section.

Clathrate Formation. In order to show the inclusion behavior of compounds **1–3** as completely as possible, we used a broad variety of solvents, including alcohols, acids, aldehydes, nitriles, amides, amines, heterocycles, etc., of different constitution (cf. Table I),[10] for the recrystallization (clathration) experiments. The capability of the roof-type hosts in forming inclusion compounds is evident from Table I. A total of nearly 70 different lattice inclusions are specified there.

By far the most inclusions (27 different species) are related to *trans*-dicarboxylic acid **1a**. This is also the host compound displaying the highest variability in the clathration of molecules belonging to different substance classes (alcohols, acids, aprotic dipolar and rather apolar compounds). However, inclusion of low-volume substrate species rarely occurs with some of the already mentioned compound series. This is quite clearly seen in the range of unbranched alcohols: inclusion formation of **1a** does not occur with methanol or with ethanol, but only beginning with 1-propanol to higher homologues up to and including 1-octanol (Table I). Referring to the carboxylic acids, however, differences in the sizes of molecules primarily influence the inclusion stoichiometries (e.g., formic acid, 1:2, acetic acid and propionic acid, 1:1). This is perhaps a result of their proclivity to form H-bonded intersubstrate dimers.

The relevance of functional-group interaction between

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(9) Holmes, H. L. In *Organic Reactions*; Adams, R., Ed.; Wiley: New York, 1948; Vol. 4, p 60.

(10) Solvents mentioned in Table I were tested separately for all hosts. Compounds not included by **1–3** are benzene, toluene, *o*-, *m*-, and *p*-xylene, mesitylene, bromobenzene, cyclohexane, *tert*-butyl chloride, pentyl bromide, nitromethane, acetamide, acetylacetone, 1,2-dimethoxyethane.

Table II. Selective Guest Inclusion of 1a from a Two-Component Solvent System

entry	recrystn solvent compd mixture (I/II)[a]	host:I:II mol ratio[b]
1	DMF/acetic acid	1:1:0
2	DMF/1-BuOH	1:1:0
3	DMF/*t*-BuOH	1:1:0
4	DMF/1-OctOH	1:1:0
5	DMF/piperidine	1:1:0
6	DMF/dioxane	1:1:0
7	DMF/*o*-dichlorobenzene	1:1:0
8	1-PrOH/1-BuOH	1:0:1
9	1-BuOH/*t*-BuOH	1:*x*:*y*[c]
10	1-OctOH/*t*-BuOH	1:1:0
11	*t*-BuOH/ethylene glycol	1:0:1
12	1-BuOH/acetic acid	1:1:0
13	1-OctOH/acetic acid	1:0:1
14	ethylene glycol/acetic acid	1:1:0
15	formic acid/acetic acid	1:1:0
16	formic acid/propionic acid	1:1:0
17	acetic acid/lactic acid	1:1:0
18	acetic acid/acetamide	1:1:0

[a] Equimolar ratio. [b] Determined by NMR integration as specified in Table I. [c] No clear discrimination in favor of I or II.

host and guest to clathrate formation ("coordinatoclathrate" relation, see above) appears from the examples as given in the following: bivalent ethylene glycol (cf. ref 4a) yields a stable inclusion compound with **1a**; conversion into the corresponding dimethyl ether (1,2-dimethoxyethane) leads to a loss of the inclusion formation; the monomethyl ether (2-methoxyethanol) is in between, showing no clear stoichiometric ratio in the inclusion compound (Table I). On the other hand, the cyclic ethers tetrahydrofuran and dioxane render crystal inclusions of **1a** readily available, which suggests the importance of size and shape effects to crystal inclusion. Another remarkable point of the inclusions with **1a** relates to the stoichiometries (host:guest) differing in many cases from the expected ratios,[5,8] e.g., 1:1 at the inclusion compounds with dimethylformamide (half and not a full equivalent of dimethylformamide per carboxylic group). We may interpret these findings to the effect that the functional groups of **1a** are not completely available for guest binding, or can be used otherwise, e.g., for host–host interaction in order to stabilize an inclusion matrix.

Nevertheless, the inclusion of dimethylformamide in the lattice of **1a** is found to be so much favored that this inclusion compound is practically always obtained in competitive experiments (Table II, entries 1–7), even in the presence of a large excess of the second component. The results of other solvent combinations are less clear and show that steric and electronic effects between host and guest may superimpose in a way difficult to separate from one another. For instance, from a 1:1 mixture of 1-BuOH/acetic acid (entry 12), the alcohol is selectively included by **1a**, but from a mixture of 1-OctOH/acetic acid (entry 13), it is the acid that is preferred; 1-OctOH/*t*-BuOH (entry 10) yields the inclusion compound with 1-OctOH. Regarding a two-component solvent mixture of carboxylic acids, the spatially less demanding component is preferentially included by **1a**, e.g., formic acid > acetic acid or propionic acid (entries 15–17). But keep in mind that this fact contradicts the behavior of alcohols (entries 8 and 10).

Probing the effect of functional-group modification was achieved by using the compounds **1b–d**, **1h–l**, and **1o–q** for the recrystallization experiments. These compounds are expected to show functional complementarity differing from that of **1a**. Table I summarizes the results. Inclusion compounds are formed of **1c**, **1h**, and **1k**, respectively. All the other potential hosts are ineffective. Obviously the COPh groups of **1c** are not suitable for coordinative binding with protic guests, but use their bulk to form "molecular barrier clathrates"[3] with THF and dioxane. By way of contrast, the amide functions as in **1h** and **1k** allow clathrate formation with highly protic guests such as acids. Considering the series of amides, **1h** provides the highest number of amide hydrogens, while **1k** has the most bulky side groups and hence their superiority to **1i** and **1j** is founded.

Retaining one of the two COOH groups of **1a** and modification of the other one yields the unsymmetric host compounds **1r–t**. It is interesting to note that **1r** and **1s** behave much the same as **1c**, i.e., they form clathrates with dioxane, whereas **1t** forms the expected inclusion compounds with guests typical of keeping up H bonds to the carboxylic group.[4b,c,8] Thus the inclusion behavior of the carboxylic acids **1r** and **1s** is comparable to functional-group-free species[4a] with no direct host–guest contact; **1t**, however, is near to **1a** with supposed strong host–guest interactions. Considering an explanation of this remarkable behavior would necessarily lead into an analysis of the crystal packings and would require crystal structures. Another remarkable fact is the following: MeOH acts as a suitable guest for **1t** whereas long-chain alcohols are ineffective. The opposite is true for **1a**. Since EtOH, which is the next higher homologue of MeOH, does not lead to a corresponding crystal inclusion with **1t** (the same applies for **1k**), crystallization of **1t** (or **1k**) from respective solvent mixtures provides an easy way to separate MeOH from EtOH, or from other higher alcohols. The same is effective for a solvent mixture t-BuOH/1-BuOH since 1-BuOH is clearly discriminated by **1t**. Of practical interest is also the clear discrimination of acetone in a mixture with diacetone alcohol (e.g., for the separation of aldol condensation products).

The next point in question refers to the effect of sterically different positioning of the functional groups. As Table I shows clearly, the inclusion properties of the host compound **2a** having a syn instead of an anti position of the carboxylic groups (cf. **1a**) are restricted, especially in the uptake of hydroxylic guests. This suggests that intramolecular H bonding of the adjacent functional groups may have occurred, lowering host–guest interaction.

Modification of the carboxylic groups in **2a** was effected by introducing functions as in **2f** and **2m–p**. Among these compounds only **2f** and **2n** proved to be inclusion hosts (Table I). The imide **2f**, although a potential proton donor, only forms few inclusions with typical aprotic guests (DMF, dioxane) which discriminates them clearly from the amides **1h** and **1k** (see Table I). On the other hand, the diol **2n** provides relatively broad inclusion properties comparable to those of **1a**. Naturally there are some differences between the inclusion behaviors of **1a** and **2n**, most strikingly shown for the unbranched alcohols higher than methanol which are not accommodated in the lattice of **2n**.

The selective inclusion properties of **2n** (Table III, supplementary material) offer several possibilities of compound separation, of interest in analytics and for preparation purposes. The separation of MeOH from a mixture with EtOH, or of propionaldehyde from propionic acid, or 2-chloropropionic acid or lactic acid, etc., are a few examples.

The unsaturated structure **3** provides a third possibility of arranging functional sensor groups at the same roof-shaped backbone in a given geometry. Here the sensors project in a steeply upward position with respect to the

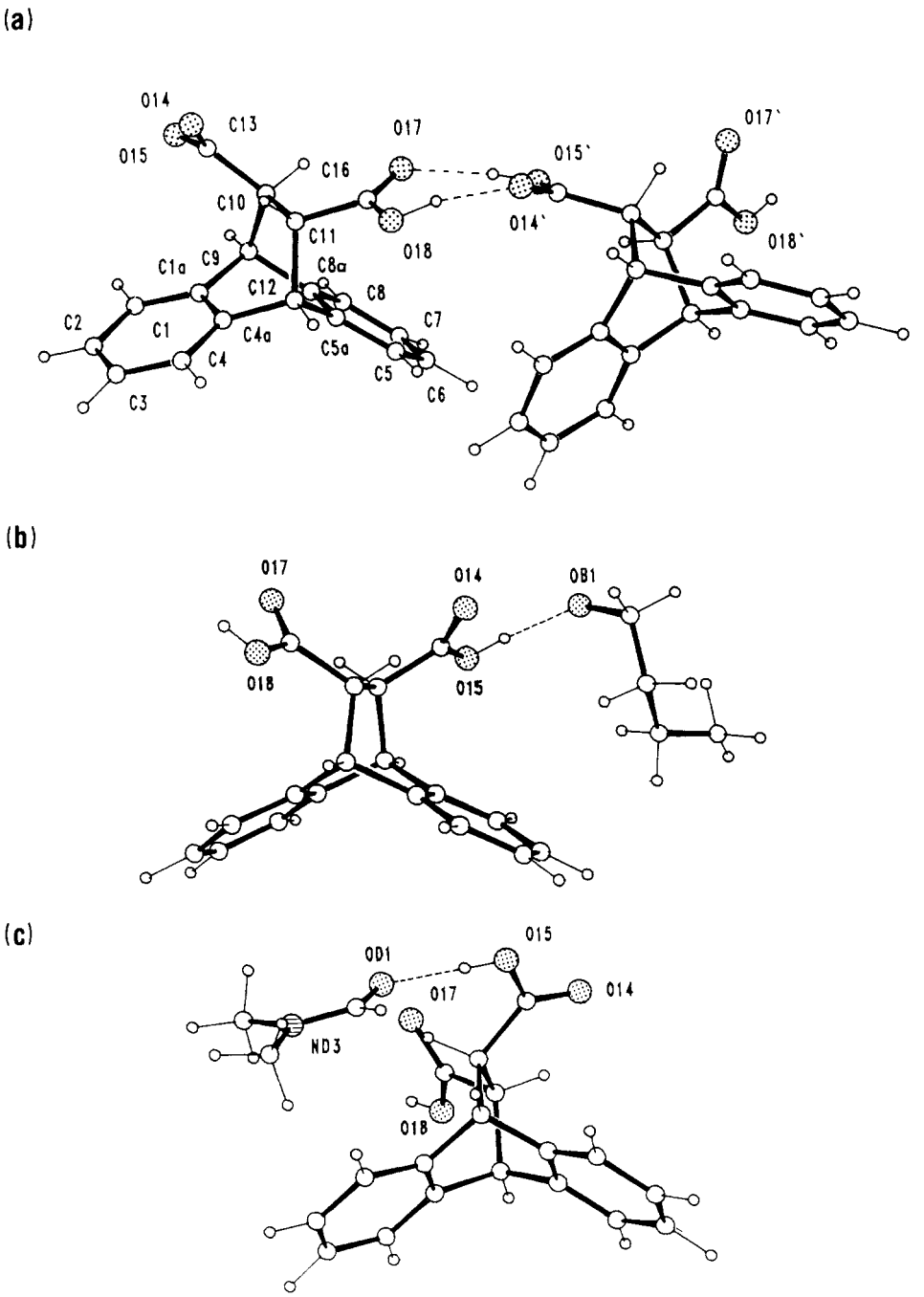

Figure 2. Perspective views of the asymmetric units: (a) **1a** (free host), (b) **1a**·1-BuOH, (c) **1a**·DMF. Solid and dashed lines represent covalent and hydrogen bonds, respectively. Complete atomic numbering is given for one host molecule only; atoms of the second host molecule are primed.

top ridge of the molecule instead of being inclined to one or both sides of the roof. In **3a**, the carboxylic groups may interact intramolecularly, comparable to **2a**. Consequently **3a** and **2a** display rather similar (and poor) inclusion properties (Table I). As contrasted with the saturated monocarboxylic acid **1t**, the unsaturated analogue **3t** completely fails in inclusion formation.

A question arises concerning the packing parameters in the crystals. In view of the superior host behavior of **1a**, a primary interest is to learn about the crystal lattices of **1a** (free host) and of its preferential inclusion compounds, e.g., with 1-BuOH and DMF.

X-ray Crystal Structure Determination of 1a, 1a·1-BuOH (1:1), and 1a·DMF (1:1). Crystal data are given in Table IV. The H-bonding dimensions are summarized in Table V. Atomic coordinates, thermal parameters, and bonding dimensions are collected in Tables VI–X (supplementary material).

(1) Molecular Structures. Perspective views of the asymmetric units of the structures of the free host **1a** and of its two coordinatoclathrates with 1-BuOH and DMF (including numbering of relevant atoms) are shown in Figure 2. The bond lengths and bond angles of the host molecules in these structures generally conform to the expected values and also agree well with those published recently.[6] It is noteworthy, however, that the C(9)–C(10) and C(11)–C(12) bond distances in the ethano bridge range between 1.565 (5) and 1.579 (4) Å in the present structures and are always longer than the usual value (1.541 ± 3 Å)[11]

(11) Kennard, O. *International Tables for X-ray Crystallography*; Kynoch: Birmingham, 1968; Vol. III, pp 275–276.

Table IV. Selected Crystal Data and Some Details of the Refining Calculations[a]

compound	**1a**	**1a**·1-BuOH	**1a**·DMF
formula	$C_{18}H_{14}O_4$	$C_{18}H_{14}O_4 \cdot C_4H_{10}O$	$C_{18}H_{14}O_4 \cdot C_3H_7ON$
formula wt, amu	294.31	368.4	367.4
space group	$P\bar{1}$	$P\bar{1}$	$P2_1/c$
cell dimens			
a, Å	14.346 (11)	11.979 (8)	10.889 (8)
b, Å	12.496 (15)	10.233 (9)	9.126 (3)
c, Å	9.432 (6)	8.974 (6)	19.005 (13)
α, deg	113.76 (7)	84.79 (4)	90.0
β, deg	78.76 (8)	76.68 (6)	98.53 (4)
γ, deg	107.48 (8)	68.06 (5)	90.0
Z	4	2	4
D_{calcd}, g cm^{-3}	1.33	1.23	1.31
$\mu_{CuK\alpha}$, cm^{-1}	7.33	6.71	7.31
total no. of unique reflctns collected	4758	3546	3323
no. of reflctns used in the refinements	3351	2771	2572
no. of variables refined	399	251	255
final agreement factor, R	0.048	0.065	0.048

[a] Esd's, where given, are in parentheses. A complete list of crystallographic information is given as Table IV of the supplementary material.

for such bonds. These elongations reflect the strain in the molecule. The dihedral angles between the phenyl rings are 53.8 (2)°/56.4 (2)° in the crystals of the free host for molecules A/B, and 57.6 (2)° and 54.9 (2)° in the structures of **1a**·1-BuOH and **1a**·DMF, respectively. Considering the geometries of the guests, larger deviations from ideal values (0.1–0.2 Å in bond lengths) were observed for 1-BuOH, in accordance with the assumed disorder of the molecule, but not for DMF, which has a more ordered structure.

(2) Packing Relations. In the structure of the free host **1a**, the asymmetric unit consists of two molecules in the form of a H-bonded dimer (Figure 2a). In some sense, this dimer may be understood as a self-inclusion complex (pseudo host–guest interaction). Each dimer is then H bonded to two other centrosymmetrically related dimers. In this way molecules are linked to form infinite zigzag chains (Figure 3a). It is apparent from the intermolecular distances (cf. Table V) that atom O(15) is engaged in two short contacts, one (2.68 Å) to O(14) within the same zigzag chain and another (2.95 Å) to O(15′) in the nearest neighboring chain. The angle O(14)···O(15)···O(15′) is 89.8 (1)°. Both these O···O distances are shorter than the sum of their van der Waals' radii. Thus, these conditions satisfy the geometric criteria of either two H bonds to O(14) and O(15′) [i.e., disordered H(15) atom] or a bifurcated H bond. This may well be the reason why the position of H(O15) could not be found from X-ray data. There are also close contacts of C–H···O type[12] between the chains (cf. Table V).

The first thing we must note in the packings of **1a**·1-BuOH (Figure 3b) and **1a**·DMF (Figure 3c) is the interhost H bond between symmetry-related COOH groups resulting in H-bonded host dimers as demonstrated in the structure of **1a** (cf. Figure 3a). Disorder of the 1-BuOH guest in structure **1a**·1-BuOH is the probable reason why the alcoholic H(OB1) atom could not be located. It is, however, apparent from the geometrical arrangement around atom O(B1) that the alcoholic oxygen functions both as a proton donor and as an acceptor (Table V). Thus, a 12-membered ring (H atoms included) is formed via H bonds with the carboxyl groups of the hosts (Figure 3b). This loop closely resembles those present in the clathrates of 1,1′-binaphthyl-2,2′-dicarboxylic acid host with MeOH, EtOH, or *i*-PrOH as guests.[4b] The H-bonded host dimers linked together by this H-bonded loop then form infinite chains with no specific interactions between them.

It was observed earlier[4,8] that DMF as a guest may be engaged in H bonding with an acid host not only in acceptor but also in donor fashion by way of a C–H···O type of interaction.[12] Usually a seven-membered H-bonded ring composed of one carboxyl and one formyl group is formed.[13] In the structure of **1a**·DMF, however, DMF is coordinated to the host molecule analogously to 1-BuOH, i.e., a "dimer" 14-membered loop of H bonds is formed around the center of symmetry including two carboxylic and two formyl groups of host and guest, respectively (Figure 3c). Here the unusual anti position of the carboxylic O–H bond is a necessary condition for maintaining the O–H···O hydrogen bond between host and guest. If the H(O15) atoms are located in the usual syn positions (cf. Figures 3a,b), the symmetry-related equivalent would have to make an impossibly close approach. Nevertheless, **1a** still maintains its characteristic H bonding to another host molecule, and so infinite chains are formed just as in its coordinatoclathrate with 1-BuOH. Close contacts of C–H···O type between the guest molecules (cf. Table V) may also contribute to stabilizing the crystal packing.

Conclusions

The experiments described here illustrate a simple and effective approach to a singular new class of clathrate hosts characteristic of a roof-shaped molecular backbone with specifically attached functional groups. They allow one to bring together within a crystal buildup different organic compounds in a very systematic manner, depending on the nature, the number, the flexibility, and the geometry of the attached functions. Most of these interact via H bonds, and it is demonstrated by the X-ray structure of the prototypical free host **1a** that a stable H-bonded framework is formed even without a guest. This high affinity of the carboxylic groups to form interhost aggregates is also expressed in the structures of the inclusion compounds of **1a** with 1-BuOH and DMF since dimer clustering of the host is retained for half the carboxylic groups present. Such a dimer, with a reduced number of functional groups for guest binding, seems to be a general feature of inclusion formation in this host family, and accounts for the common host:guest stoichiometry, 1:1, of the inherently bifunctional hosts. Likewise it may also explain the masking of potential coordinative groups observed for corresponding monofunctional and quasi-monofunctional hosts (cf. **1r**, **1s**). Nevertheless, the present hosts give a further demonstration of the usefulness of the coordinatoclathrate conception.[3b,4b]

Suitably tailored basic skeletons oriented by the overall structure of the dimer unit mentioned above are expected to be another source of new selective clathrate hosts. In addition, future experiments will show if it is possible to alter the inclusion properties of these hosts specifically by

(12) At present, there is a lively discussion on weak C–H···O interactions in host–guest complexes; cf.; Kumpf, R. A.; Damewood, J. R., Jr. *J. Chem. Soc., Chem. Commun.* **1988**, 621. See also: Taylor, R.; Kennard, O. *J. Am. Chem. Soc.* **1982**, *104*, 5063.

(13) We dispose of a great number of different inclusion compounds with DMF all showing the same or nearly the same mode of host–guest binding in the crystal (cf. ref 2a, 4, and 8).

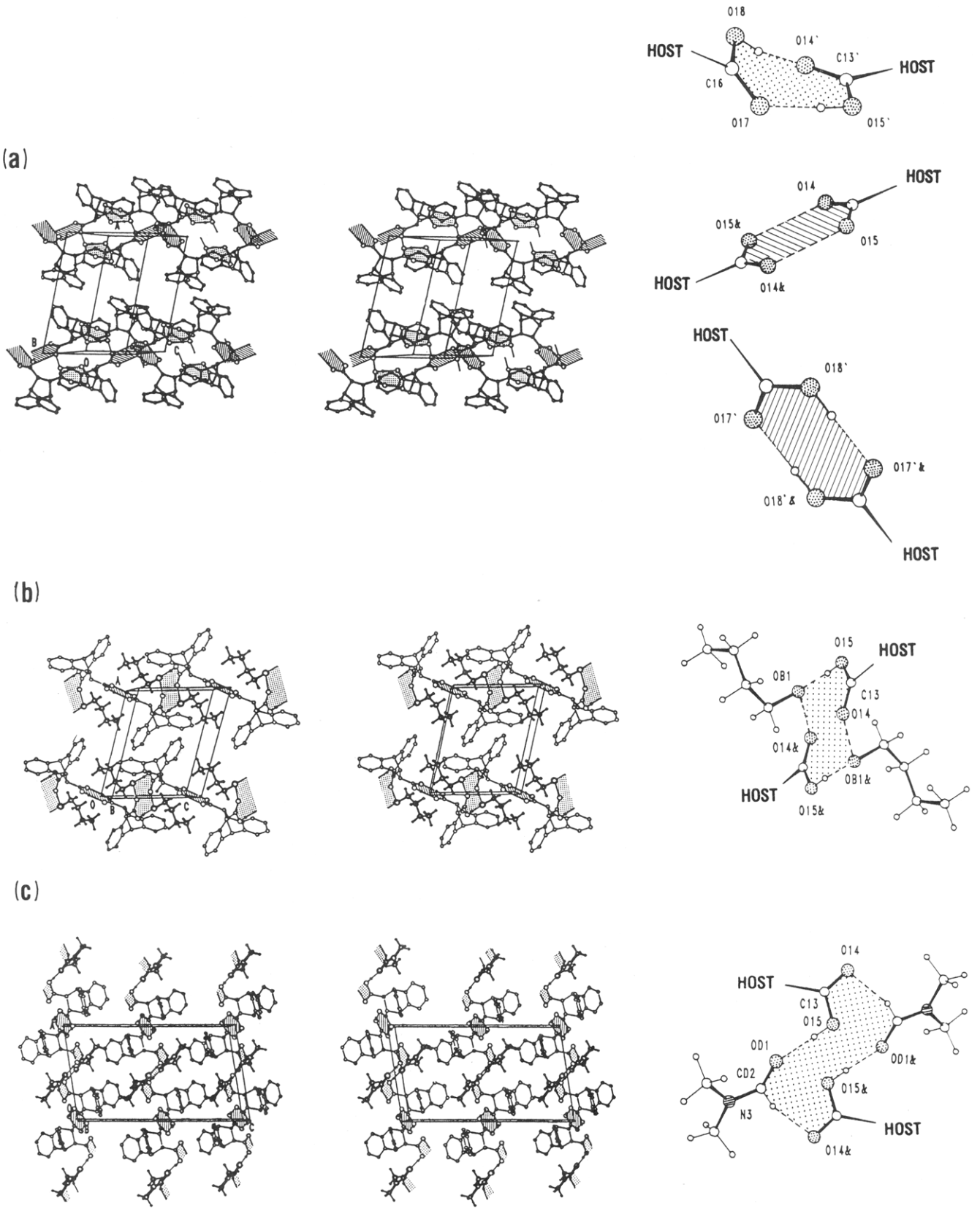

Figure 3. Stereoscopic packing diagrams and hydrogen-bonding schemes of (a) free host **1a**, (b) **1a**·1-BuOH, (c) **1a**·DMF. Interhost hydrogen-bonded ring systems (centrosymmetrically related dimers) are marked with hatching; hydrogen-bonded ring systems involving host and guest are marked with dotting. In part a, the hydrogen-bonded rings related to asymmetric dimer units of hosts (cf. Figure 2a) are also dotted, suggesting a "pseudo host–guest interaction" (see text). O, N, C, and H atoms are specified with circles of decreasing size; H atoms of the host are omitted; guest molecules are bold faced. Individual units of the hydrogen-bonded ring constitutions for each compound are shown separately, with hydrogen-bond interactions represented by dashed lines. The hatched hydrogen-bonded ring of part a (specified with H) holds also for parts b and c.

Table V. Bond Distances and Angles in Possible Hydrogen Bonds[a]

atoms involved	symmetry	bond distance, Å			angle, deg
		$O_D \cdots O_A$	O_D–H	H···O_A	O_D–H···O_A
		1a (Free Host)			
O(18)–H(18)···O(14′)	(x, y, z)	2.650 (5)	0.98	1.69	167
O(15′)–H(15′)···O(17)	(x, y, z)	2.759 (5)	0.92	1.84	173
O(18′)–H(18′)···O(17′)	(−x, −y − 1, −z + 2)	2.705 (5)	0.90	1.83	166
C(9)–H(9)···O(17)	(−x, −y, −z + 1)	3.209 (4)	1.08	2.40	131
C(10′)–H(10′)···O(18)	(x, y, z + 1)	3.433 (5)	1.08	2.36	170
O(15)–H(15)···O(14)[b]	(−x, −y, −z)	2.681 (4)			
O(15)–H(15)···O(15′)[b]	(−x, −y, −z + 1)	2.953 (5)			
		1a·1-BuOH (1:1)			
O(18)–H(18)···O(17)	(−x, −y + 1, −z + 2)	2.646 (4)	0.82	1.83	173
O(15)–H(15)···O(B1)	(−x, + 1, −y, −z + 1)	2.599 (5)	0.88	1.72	176
O(B1)–H(B1)···O(14)[b]	(x + 1, y, z)	2.741 (5)			
		1a·DMF (1:1)			
O(18)–H(18)···O(17)	(−x + 2, −y + 1, −z)	2.616 (3)	0.87	1.76	170
O(15)–H(15)···O(D1)	(x, y, z − 1)	2.623 (3)	0.89	1.74	179
C(D2)–H(D2)···O(14)	(−x + 1, −y, −z + 1)	3.240 (4)	1.04	2.25	160
C(D4)–H(D4c)···O(D1)	(−x + 1, −y + 1, −z + 2)	3.372 (6)	1.08	2.38	151

[a] Esd's, where given, are in parentheses. [b] The positions of these H atoms could not be derived from X-ray data; see the text for explanation.

introduction of substituents at the aromatic rings. Also, some of the hosts of type **1**, represent compounds of known chirality[14] and may therefore be used for optical resolution of enantiomeric guests. Studies along these lines are in progress.[15]

Experimental Section

General. Melting points were obtained on a Kofler apparatus (Reichert, Wien). The ^{1}H NMR spectra were taken on a Varian EM-360 spectrometer with Me_4Si as internal reference. IR spectra were obtained by using a Pye-Unicam SP-1100 spectrometer. Mass spectra were recorded on an A.E.I. MS-50 mass spectrometer. Starting compounds were purchased from Janssen (Nettetal-2, West Germany).

Diels–Alder Adducts 1a, 1c, 1d, 1s, 1t, 2e, 2m, 3b, and 3u. Reactions were done according to literature procedures,[16-25] in most cases. All of them involve anthracene as the diene. Specific details are given for each compound.

1a: with fumaric acid in dioxane;[16] 92% of colorless crystals; mp 242 °C (from MeOH) (lit.[16] mp 240–242 °C).

1c: with (*E*)-dibenzoylethene[17] (neat);[18] 42% of colorless crystals; mp 164–165 °C (from EtOH) (lit.[18a] mp 163–164 °C).

1d: with fumarodinitrile in xylene;[19] 80% of colorless crystals; mp 274 °C (from dioxane/H_2O, 9:1) (lit.[19] mp 200–202 °C, lit.[19b] mp 259 °C).

1s: with cinnamic acid (neat);[22] 10% of colorless crystals; mp 256 °C (from EtOH) (lit.[22] mp 248 °C).

1t: with acrylic acid (neat);[23] 76% of colorless crystals; mp 189 °C (from EtOH/H_2O) (lit.[23] mp 198 °C).

2e: with maleic anhydride in dioxane;[20] quantitative yield of colorless crystals; mp 261 °C (lit.[20a] mp 262–263 °C).

2m: with vinylene carbonate in xylene;[21] 68% of colorless needles; mp 255 °C (from benzene) (lit.[21] mp 253–254 °C).

3b: with dimethyl acetylenedicarboxylate (neat);[24] 93% of colorless crystals; mp 160–161 °C (lit.[24] mp 160–161 °C).

3u: with ethyl acetylenecarboxylate in xylene;[25] 42% of colorless crystals; mp 110 °C (lit.[25] mp 108–110 °C).

Carboxylic Acids 2a, 3a, and 3t and Diol 2n. These compounds were obtained by hydrolysis of **2e**, **3b**, **3u**, and **2m**, respectively. Specific details are given for each compound.

2a: 45% aqueous KOH;[16] 92% of colorless microcrystals; mp 264 °C (from ethyl acetate) (lit.[16] mp 264 °C).

2n: 1 N NaOH in H_2O/EtOH (1:1);[21] 92% of colorless crystals; mp 202–203 °C (from hexane/toluene) (lit.[21] mp 203 °C).

3a: 2 N NaOH in H_2O/MeOH (3:2);[24] 84% of colorless crystals; mp 216 °C (from EtOH (lit.[24] mp 215–16 °C).

3t: 1 N NaOH in MeOH;[25] 95% of colorless crystals; mp 249 °C (from acetic acid) (lit.[25] mp 250 °C).

Acid dichloride 1g: from **1a** (7.35 g, 25 mmol), thionyl chloride (6.70 g, 56 mmol), and pyridine (2.33 g, 29 mmol) in benzene (40 mL) as usual.[26a] The compound (quantitative yield) was directly used for the syntheses of **1h–1l**.

Amides 1h–l. These compounds were prepared from acid dichloride **1g** with excess NH_3 (aqueous, concentrated) or the respective amine according to the standard procedure.[27] After recrystallization (**1h–j**, and **1l** from acetic acid, **1k** from MeOH), the products were dried (12 h, 100 °C, 15 Torr). Satisfactory elemental analytical data were obtained for all compounds. Specific details are given below.

1h: 82% of a colorless powder; mp >270 °C; ^{1}H NMR (DMSO-d_6) δ 3.18 (s, 2 H, ethano), 4.67 (s, 2 H, bridgehead), 6.60–7.60 (m, 12 H, aryl, NH_2); IR (KBr) 3510, 3390 (NH), 1670 cm^{-1} (C=O); MS calcd for $C_{18}H_{16}N_2O_2$ (M^+) *m/e* 292.1208, found 292.1232.

1i: 92% of a colorless powder; mp >270 °C; ^{1}H NMR (DMSO-d_6) δ 0.97 (t, *J* = 7 Hz, 6 H, CH_3), 1.20–1.75 (m, 4 H, CH_2), 2.80–3.25 (m, 4 H, CH_2N), 3.30 (s, 2 H, ethano), 4.70 (s, 2 H, bridgehead), 7.05–7.55 (m, 8 H, aryl), 8.25 (t, *J* = 5 Hz, 2 H, NH); IR (KBr) 3360 (NH), 1645 cm^{-1} (C=O); MS calcd for $C_{24}H_{28}N_2O_2$ (M^+) *m/e* 376.2144, found 376.2151.

1j: 93% of a colorless powder; mp >270 °C; ^{1}H NMR (DMSO-d_6) δ 1.05 (d, *J* = 7 Hz, 12 H, CH_3), 3.25 (s, 2 H, ethano), 3.50–4.00 (m, 2 H, CH_2N), 4.60 (s, 2 H, bridgehead), 6.70–7.50 (m, 8 H, aryl), 7.95 (d, *J* = 6 Hz, 2 H, NH); IR (KBr) 3385 (NH),

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1650 cm^{-1} (C=O); MS calcd for $C_{24}H_{28}N_2O_2$ (M^+) m/e 376.2144, found 376.2149.

1k: 89% of colorless crystals; mp 248 °C; ^1H NMR (DMSO-d_6) δ 1.20 (s, 18 H, t-bu), 3.00 (s, 2 H, ethano), 4.62 (s, 2 H, bridgehead), 6.60–7.60 (m, 10 H, aryl, NH); IR (KBr) 3390 (NH), 1650 cm^{-1} (C=O); MS calcd for $C_{26}H_{32}N_2O_2$ (M^+) m/e 404.2456, found 404.2460.

1l: 87% of a colorless powder; mp >270 °C; ^1H NMR (DMSO-d_6) δ 0.87–2.04 (m, 20 H, CH_2), 3.15–3.65 (m, 2 H, CHN), 3.33 (s, 2 H, ethano), 4.66 (s, 2 H, bridgehead), 7.06–7.60 (m, 8 H, aryl), 8.13 (d, J = 8 Hz, 2 H, NH); IR (KBr) 3375 (NH), 1645 cm^{-1} (C=O); MS calcd for $C_{30}H_{36}N_2O_2$ (M^+) m/e 456.2768, found 456.2790.

Imide 2f. Diacid **2a** was caused to react with excess NH_3 (aqueous, concentrated) at 100 °C for 0.5 h.[28] Recrystallization from toluene gave 35% of colorless crystals, mp >270 °C (lit.[28] mp 303–304 °C).

Keto Acid 1r. Friedel–Crafts reaction of **2e** with benzene and $AlCl_3$ under usual conditions[26] (recrystallization from toluene) yielded 43% of colorless crystals, mp 242 °C (lit.[18a] mp 246 °C).

Dihydroxy compounds 1o and 2o: usual reduction of the corresponding diacids **1a** and **2a** with $LiAlH_4$ in THF;[26c] recrystallization from $MeNO_2$.

1o: 64% colorless crystals; mp 207 °C (lit.[29] mp 205–207 °C).

2o: 47% colorless crystals; mp 225 °C (lit.[29] mp 226–227 °C).

Ditosylate 2p. Diol **2o** was caused to react with TosCl in pyridine under standard conditions.[26d] Recrystallization from MeCN gave 85% of colorless crystals, mp 193 °C (lit.[29] mp 193–195 °C).

Dimethyl derivative 2q: usual reduction of **2p** with $LiAlH_4$ in THF.[26c] Recrystallization from petroleum ether (30–60) yielded 90% of colorless crystals, mp 173 °C (lit.[29] mp 173–174 °C).

Preparation of the Clathrates. The corresponding host compound was dissolved with heating in a minimum amount of the respective guest solvent (or solvent mixture). The solution was placed into a hot oil bath to prevent it from rapid cooling and to ensure slow crystallization of the clathrate. After storage for 12 h at room temperature, the crystals that formed were collected by suction filtration, washed with ether or MeOH, and dried (2 h, 15 Torr, room temperature). Host:guest stoichiometry of the isolated crystals was determined by NMR integration.[4b] Data for each compound are given in Table I.

Crystallography. (a) Sample Preparation. Crystals of the clathrate compounds 1a·1-BuOH (1:1) and 1a·DMF (1:1), suitable for crystallographic studies, were obtained as described above. Suitable crystals of the free host **1a** were prepared by recrystallization from MeOH. In order to prevent the crystals of the inclusion compounds from possible solvent evaporation during measurement, the single crystals selected for X-ray work were sealed in epoxy glue.

(b) Data Collection and Processing. The intensity data were collected on a Philips PW 1100 diffractometer at room temperature, using graphite-monochromated Cu Kα radiation (λ = 1.5418 Å, θ_{max} = 67°). The unit cell parameters were refined against accurately measured line positions from a Guinier photograph, taken with strictly monochromated Cu Kα_1 radiation (λ = 1.5406 Å) and using Si (a = 5.4309 Å at 298 K) as an internal standard. Lorentz and polarization corrections were applied during the data reduction, but the rather small absorption effects were neglected. Crystal data and experimental details are summarized in Table IV.

(c) Structure Analysis and Refinement. Initial models of the structures were derived by direct methods (MULTAN).[30] These models were completed and refined by using the SHELX[31] program system.

Only the reflections with $F > 6\sigma(F)$ were considered as observed and were used in the following calculations. Positions of the H atoms were either found in difference electron density maps and kept fixed during the calculations, or generated after each cycle of the refinement by using geometrical evidence. This applies for all except two of the H sites, which could not be determined by either method. These are a carboxylic H in **1a** and the alcoholic one in 1a·1-BuOH. In the final refinement cycles, positions of the non-hydrogen atoms were refined together with their anisotropic thermal parameters. Group isotropic temperature factors were refined for the generated H positions, while the hydrogens connected to O or N atoms had their own isotropic temperature factors refined. The methyls were refined as rigid groups. The temperature factors of the C atoms of the 1-BuOH guest in structure 1a·1-BuOH are considerably higher than those of the host molecule (Table VI), suggesting disorder on these atomic sites. Therefore, the group isotropic temperature factor (U) of the calculated H atoms of this guest was fixed at 0.32. A few reflections (five for **1a**, 23 for 1a·1-BuOH, and 12 for 1a·DMF), which appeared to be seriously affected by extinction, were excluded from the calculations of the final R values (Table IV of the supplementary material). In the refinement of the structure of the free host, the weights were calculated as $w = 1.5789/(\sigma^2(F) + 0.00111F^2)$ while the reflections of the inclusion compounds 1a·1-BuOH and 1a·DMF were given unit weight. Final atomic coordinates and thermal parameters, observed bond distances and bond angles, and calculated H positions are listed in Tables VI–X (supplementary material).

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Registry No. **1a**, 36326-57-5; 1a·1-BuOH (1:1), 116841-13-5; 1a·t-BuOH (1:1), 116841-14-6; 1a·1-PentOH (1:1), 116841-15-7; 1a·1-OctOH (2:1), 116841-16-8; 1a·ethylene glycol (1:2), 116841-17-9; 1a·2-methoxyethanol (1:1), 116841-18-0; 1a·formic acid (1:2), 116841-19-1; 1a·acetic acid (1:1), 116841-20-4; 1a·propionic acid (1:1), 116841-21-5; 1a·2-chloropropionic acid (1:1), 116841-22-6; 1a·valeric acid (1:1), 116841-23-7; 1a·lactic acid, 116863-78-6; 1a·tartaric acid (2:1), 116841-24-8; 1a·mercaptoacetic (1:1), 116841-25-9; 1a·thioacetic acid (2:1), 116841-26-0; 1a·propionaldehyde (1:1), 116841-27-1; 1a·acetone (1:1), 116841-28-2; 1a·DMF (1:1), 116841-29-3; 1a·acetonitrile (1:1), 116841-30-6; 1a·benzyl cyanide (1:1), 116841-31-7; 1a·DMSO (1:1), 116841-32-8; 1a·THF (1:2), 116841-33-9; 1a·dioxane (2:1), 116841-34-0; 1a·o-dichlorobenzene (1:1), 116841-35-1; 1a·2,6-dimethylnitrobenzene (1:1), 116841-36-2; 1a·1-Pr-OH (1:1), 116841-37-3; 1a·2-nitrophenol (1:2), 116863-79-7; **1c**, 116841-38-4; 1c·THF (2:1), 116841-39-5; 1c·dioxane (2:1), 116841-40-8; **1d**, 116841-41-9; **1g**, 116841-42-0; **1h**, 116841-43-1; 1h·ethylene glycol (1:1), 116841-44-2; 1h·acetic acid, 116841-45-3; 1h·propionic acid, 116841-46-4; **1i**, 116841-47-5; **1j**, 116841-48-6; **1k**, 116841-49-7; 1k·MeOH (1:1), 116841-50-0; 1k·formic acid (1:3), 116841-51-1; 1k·acetic acid (1:1), 116841-52-2; 1k·propionic acid (1:1), 116841-53-3; **1l**, 116841-54-4; **1o**, 41204-44-8; **1r**, 116841-55-5; 1r·dioxane (1:1), 116841-56-6; **1s**, 116841-57-7; 1s·dioxane (2:1), 116841-58-8; **1t**, 116908-92-0; 1t·MeOH (2:1), 116908-93-1; 1t·t-BuOH (1:1), 116908-94-2; 1t·ethylene glycol (1:1), 116908-95-3; 1t·epichlorohydrin (2:1), 116908-96-4; 1t·diacetone alcohol (2:1), 116908-97-5; 1t·DMF (3:2), 116908-98-6; 1t·DMSO (1:1), 116946-98-6; **2a**, 27069-21-2; 2a·benzyl cyanide (1:2), 95929-78-5; 2a·DMSO (1:2), 95929-79-6; 2a·dioxane (2:1), 95929-81-0; **2e**, 5443-16-3; **2f**, 5721-34-6; 2f·DMF (2:1), 116841-61-3; 2f·dioxane (1:1), 116841-62-4; **2m**, 5675-70-7; **2n**, 2732-95-8; 2n·MeOH (1:1), 116841-65-7; 2n·t-BuOH (1:1), 116841-66-8; 2n·cyclo-HexOH (1:1), 116841-67-9; 2n·acetic acid (1:1), 116841-68-0; 2n·2-chloropropionic acid (1:1), 116841-69-1; 2n·lactic acid (1:1), 116841-70-4; 2n·propionaldehyde (2:1), 116841-71-5; 2n·acetone (2:1), 116841-72-6; 2n·DMF (2:1), 116841-73-7; 2n·DMSO (1:1), 116841-74-8; 2n·THF (2:1), 116841-75-9; 2n·dioxane (2:1), 116841-76-0; 2n·morpholine (1:1), 116841-77-1; 2n·piperidine (1:1), 116841-78-2; 2n·pyridine (2:1), 116841-79-3; 2n·nitrobenzene (1:1), 116841-80-6; **2o**, 71991-70-3; **2p**, 103616-67-7; **2q**, 5445-53-4; **3a**, 1625-81-6; 3a·t-BuOH (1:1), 116841-81-7; 3a·DMSO (1:2), 116841-82-8; 3a·dioxane (1:1), 116841-83-9; **3b**, 1625-82-7; **3t**,

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27649-96-3; **3u**, 27649-95-2; anthracene, 120-12-7; fumaric acid, 110-17-8; (*E*)-dibenzoylethene, 959-28-4; fumarodinitrile, 764-42-1; cinnamic acid, 621-82-9; acrylic acid, 79-10-7; maleic anhydride, 108-31-6; vinylene carbonate, 872-36-6; dimethyl acetylenedicarboxylate, 762-42-5; ethyl acetylenecarboxylate, 623-47-2.

Supplementary Material Available: Specification of the selective inclusion properties of **2n** (Table III), complete list of crystallographic information (Table IV), lists of positional parameters and equivalent isotropic/isotropic temperature factors of the non-hydrogen atoms and of the hydrogen atoms (Table VI), bond lengths (Table VII) and bond angles (Table VIII) involving non-hydrogen atoms, fractional atomic coordinates of the calculated hydrogen positions (Table IX), and anisotropic thermal parameters of the non-hydrogen atoms (Table X) (23 pages). Ordering information is given on any current masthead page. Listings of observed and calculated structure factors are available directly from the author.

Studies on the Molybdenum Cofactor: Model Synthetic Routes Directed at Form B

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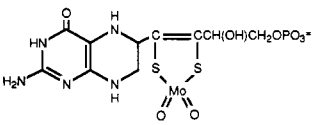
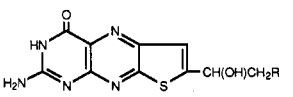
A general method for the conversion of available pyrazine intermediates to 6,7-dihydrothieno[2,3-*b*]pyrazines, and then to 6,7-dihydrothieno[3,2-*g*]pterins, has been developed as a model synthetic strategy for an approach to Form B of the molybdenum cofactor.

Molybdenum is present in trace amounts in the tissues of a broad range of biological species, including algae, fungi, bacteria, plants, animals, and humans, and has recently been recognized as an essential trace element for human health.[1] Molybdenum functions as a prosthetic metal in a number of enzymes that catalyze redox reactions; these enzymes also require a common organic cofactor for their activity, which was once thought to be a protein[2] but has recently been shown to be a novel pterin derivative with a sulfur-containing 6-alkenyl side chain.[3,4] This organic cofactor has been termed molybdopterin. The complex of molybdenum with molybdopterin, referred to as the molybdenum cofactor, has been found to be a universal cofactor for all molybdenum-containing enzymes studied with the single exception of nitrogenase, which has its own unique iron–molybdenum cofactor.[5–7] Structure **1** has been proposed for the molybdenum cofactor.

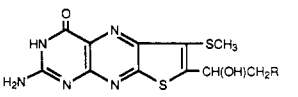
Molybdopterin differs from other organic enzyme cofactors such as FAD, biotin, pyridoxal phosphate, etc. in being extraordinarily unstable in the free form; when released from the enzyme, it is rapidly degraded to inactive products. As a consequence, its structure has been probed indirectly by EXAFS examination of the molybdenum enzyme active sites,[8,9] by chemical degradation, and by spectroscopic studies of its stable (but inactive) oxidation products.[3,10–13] One of these oxidation products is a thieno[3,2-*g*]pterin, termed Form B, for which structure **2** has been suggested. The only sulfur-containing pterin natural product previously known is the thieno[3,2-*g*]pterin derivative urothione, which was first isolated from human urine in 1940[14] and synthesized 27 years later in 0.3% yield from pteridine intermediates.[15–19] Structure **3**, which was ultimately assigned to urothione, received strong support through comparison with deoxyurothione (**4**), which we synthesized several years ago by an unambigous route,[20] and has recently been rigorously confirmed by direct comparison with (±)-urothione prepared by a new and unequivocal total synthesis.[21] The discovery that children suffering from biochemical abnormalities due to combined deficiencies of sulfite oxidase and xanthine dehydrogenase lacked the active molybdenum cofactor, and that their urine samples were devoid of urothione, confirmed that this latter compound was the urinary metabolite of the molybdenum cofactor.[3,22]



1



2, R = OPO_3H^-
5, R = OH



3, R = OH
4, R = H

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