Modular Design of Hosts Involving a Rigid Succinimide Framework and N-Bonded Lateral Groups. Crystalline Inclusion Properties and Crystal Structures of Inclusion Compounds with Dioxane, MeOH, and DMF

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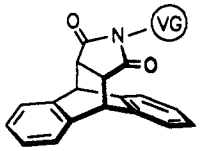
A series of crystalline host molecules comprising a characteristic 9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboxamide framework have been synthesized and studied with regard to their inclusion behavior. They follow a new design concept which is to convert a given molecule, presently of amine, aminophenol, amino alcohol, or amino acid type, by addition of a so-called "clathratogenic group" (inclusion promoting group) into a crystalline host. These hosts form crystalline inclusion compounds with a variety of uncharged organic molecules ranging from protic dipolar to rather apolar compounds (103 different inclusion species). Inclusion formation and binding modes depend on the structural features of the hosts, i.e., the type of functional groups, their number, and geometric factors. X-ray crystal structures of three inclusion species are reported: **1**·dioxane (1:1) [$P2_1/n$, a = 11.9757 (4) Å, b = 9.8442 (3) Å, c = 16.2371 (5) Å, β = 109.196 (4)°, Z = 4], **23**·MeOH (1:1) [$Pbca$, a = 8.532 (1) Å, b = 18.865 (1) Å, c = 24.074 (2) Å, Z = 8], **24**·DMF (1:1) [$P2_1/a$, a = 15.217 (1) Å, b = 11.445 (1) Å, c = 26.685 (2) Å, β = 106.15 (1)°, Z = 8]. They show the compounds to be typical coordinatoclathrates with hydrogen bond interactions between host and guest. In the crystals of **1**·dioxane (1:1), hydrophobically aggregated host molecules form rectangular cages, each with space enough for two H bonded guests. In **23**·MeOH (1:1), the guest acts both as donor and acceptor in H bonds, resulting in endless H bonded chains of alternating host and guest molecules. The finite 1:1 host–guest associates in **24**·DMF (1:1) are held together by characteristic O–H···O(C) and possibly als by (C)H···O-type interactions.

Organic compounds that form crystalline host–guest inclusions (cocrystalline structures) with secondary molecules[1] are attracting increasing attention[2] in view of practical uses. These include chemical separation, compound protection, topochemistry, or the development of new solid materials.[1-5] Unfortunately, the a priori design of a particular cocrystalline structure seems to be out of reach within the near future.[6] Nevertheless, it has been shown that some simple considerations based on geometry, polarity, and other structural attributes are useful in designing a crystalline host molecule with potential inclusion properties.[1,7] Although this approach is not fully developed, it has resulted in new important classes of crystalline inclusion compounds.[8,9] We describe here a fundamental further development of the previous design principles for crystalline hosts[7] and illustrate it with a reasonable number of compounds (**1**–**32**).

Results and Discussion

Structural Approach. Among the recently introduced crystalline hosts, molecules comprising a characteristic 9,10-dihydro-9,10-ethanoanthracene structural unit (cf. I) are significant.[10] This suggests that the rigid tetracyclic



I

VG = variable group

framework is a favorable structural element for crystalline hosts, and one could think of using it in a more general way. This development involves substitution of the building block into other functional molecules whereas the previous use of the tetracyclic framework was the other way around, i.e., incorporation of functional groups into the basic 9,10-dihydro-9,10-ethanoanthracene molecule.[10] Properly speaking, we intend to use the mentioned building block as an auxiliary substituent to transform a given molecule into a crystalline host. By analogy with the so-called "mesogenic groups" of liquid crystalline compounds,[11] we may define a group which promotes clathrate or crystalline inclusion formation a

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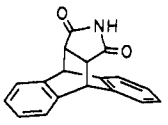
Chart I



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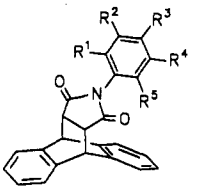
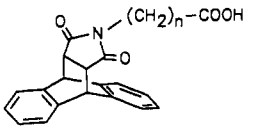


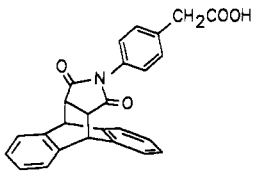
2 - 21

No	R^1	R^2	R^3	R^4	R^5
2	H	H	H	H	H
3	COOH	H	H	H	H
4	COOH	H	Me	H	H
5	COOH	H	Cl	H	H
6	COOH	H	H	Cl	H
7	COOH	H	Cl	H	Cl
8	H	COOH	H	H	H
9	H	COOH	H	H	Me
10	H	H	COOH	H	H
11	H	COOH	H	COOH	H
12	H	H	OH	H	H
13	H	H	OMe	H	H
14	H	NO_2	H	H	H
15	H	H	NO_2	H	H
16	Br	H	H	H	H
17	H	H	Br	H	H
18	Me	H	H	H	H
19	Me	Me	H	H	H
20	Me	H	H	Me	H
21	Me	H	H	H	Me



22 n = 1
23 n = 2
24 n = 3

25 n = 4
26 n = 5



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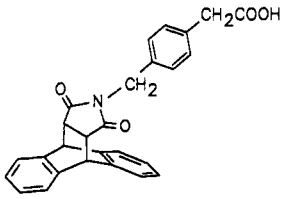

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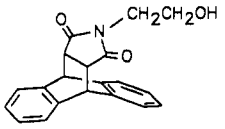

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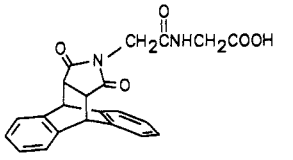

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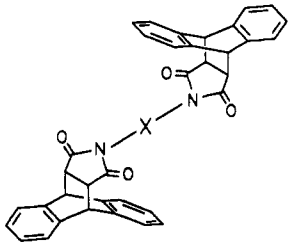
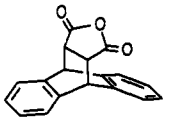


31 X = 1,4-phenylene
32 X = 4,4'-biphenyldiyl



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"clathratogenic group". Hence, we have studied the potential clathratogenic property of the 9,10-dihydro-9,10-ethanoanthracene group being connected with different amines, aminophenols, amino alcohols, and amino acids according to the general formula I (substituted dicarboximides). Individual compounds explored in this context are specified by formulae 1–32, where 1 is the parent molecule and 31 or 32 are "dimers".

Synthesis. All dicarboximides 1–32 were synthesized from anhydride 33[12] and the corresponding amines, amino alcohols, or amino acids although under slightly varied reaction conditions (see Experimental Section). The crystalline inclusion compounds were obtained by simple recrystallization of the host compound from the respective guest solvent.

Inclusion Properties. A total of 103 different inclusion compounds are specified in Table I, showing the efficiency of the new host design in general. Nevertheless, the individual dicarboximides 1–32 are rather different in their inclusion ability and demonstrate a characteristic level of selectivity. Some of the compounds, of which 8, 23, and 24 are typical examples, form inclusions in the broad sense, i.e., with molecules belonging to different substance classes (alcohols, acids, aprotic dipolar and rather apolar compounds). These hosts are carboxylic acids. Others, among them 1, 2, 13, 16, or 21, which have no carboxylic group, allow only very few (one or two) inclusions. But there are also examples of the explored group of compounds which have no host properties under the experimental conditions. They are either aprotic compounds (15, 17, 18, 20, 31, and 32) or protic substances (26, 27, and 29) but with a certain degree of flexibility in the functional arm (except 12 which is a rigid phenol). These findings show that H donating groups are an important structural feature of the present hosts.

Host–guest stoichiometric ratios determined include 4:1, 3:1, 2:1, 1:1, and 1:2, with the most frequently observed stoichiometric ratio being 1:1 (Table I). It is, however, difficult to draw conclusions from the individual stoichiometric data except for the alcohol inclusions of 8, 23, and 24 which show quite clearly that the larger guests prefer the larger host–guest ratio (2:1 vs 1:1).

With reference to the solvent molecules included, the results are as follows (Table I). DMF forms the highest number of inclusions (17) followed by dioxane (11) and pyridine (10); MeOH forms seven and benzene only one single inclusion. Evidently, the inclusion of dipolar-aprotic and proton acceptor guests are the most frequent in this host series. Alcohol guests are only efficient with carboxylic hosts, except for 13. In the same way, pyridine is only included by carboxylic hosts but not every carboxylic host is efficient with pyridine (Table I), which rules out simple salt formation[13] and demonstrates steric effects.

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Table I. Crystalline Inclusion Compounds[a,b]

1	DMF (1:1), dioxane (1:1)
2	DMF (3:1),[c] dioxane (4:1)[c]
3	DMF (1:1), diethylformamide (1:1)
4	MeOH (1:1), EtOH (1:1), DMF (1:1), DMSO (1:2),[c] pyridine (1:1)
5	MeOH (1:1), DMF (1:1), diethylformamide (1:1), DMSO (1:2),[c] pyridine (1:1)
6	acetone (4:1), methylformamide (1:1), DMF (1:1), diethylformamide (1:1), acetonitrile (2:1), nitromethane (2:1), THF (4:1), dioxane (4:1), pyridine (1:1)
7	MeOH (1:1), EtOH (1:1), acetic acid (1:1), acetone (1:1), DMF (1:1),[c] DMSO (1:1)[c]
8	MeOH (1:1), EtOH (3:1),[c] acetic acid (1:1), DMF (1:1), nitromethane (1:1), THF (1:1),[c] dioxane (2:1),[c] pyridine (1:1)
9	DMF (1:1), diethylformamide (1:1), pyridine (1:1)
10	DMF (1:1), diethylformamide (1:1), dibutylformamide (1:1), methylphenylformamide (1:1), dimethylacetamide (1:1), pyridine (1:1)
11	DMF (1:1, 1:2),[d] diethylformamide (1:1), dimethylacetamide (1:1), dioxane (1:1), pyridine (1:2)
13	MeOH (1:1)
14	DMF (1:1), THF (1:1), dioxane (1:1), pyridine (2:1)
16	dioxane (3:1)[c]
19	acetonitrile (1:1), nitromethane (1:1)
21	benzene (1:1)
22	DMF (1:1), DMSO (1:1), dioxane (2:1), pyridine (1:1)
23	MeOH (1:1), EtOH (1:1), 1-PrOH (2:1), 2-PrOH (2:1), 2-BuOH (3:1), acetic acid (2:1), propionic acid (2:1), methylformamide (1:1), DMF (1:1), diethylformamide (1:1), dimethylacetamide (1:1), acetonitrile (1:1), nitromethane (1:1), nitroethane (1:1), DMSO (1:1), THF (1:1), dioxane (2:1), 1,3-dioxolane (2:1), tetrahydropyran (2:1), pyridine (1:1)
24	MeOH (1:1), EtOH (2:1), 2-PrOH (2:1), methylformamide (1:1), DMF (1:1), dimethylacetamide (1:1), nitromethane (1:1), DMSO (2:1), THF (1:1), dioxane (2:1), pyridine (2:1)
25	EtOH (1:1), DMF (1:1), dioxane (2:1)
28	THF (2:1), DMF (1:1)
30	dioxane (2:1)

[a] See Experimental Section for method of preparation, drying standard, and characterization; stoichiometric ratios (host–guest) are given in parentheses. [b] Solvents mentioned in this table were tested separately for all hosts. Compounds not included by 1–32 are c-HexOH, butanoic acid, cyclohexanone, dihydropyrane, toluene, *o*-, *m*-, and *p*-xylene, and mesitylene. [c] Slightly varying stoichiometry. [d] Ratio dependent on recrystallization conditions (concentration of components, rate of cooling).

For instance, in the series of carboxylic acids **22–26** with alkane chains of different lengths (C_1–C_5) between the carboxylic acid and dicarboximide groups, the dependence of inclusion behavior on host structure is obvious. In **22**, which has the shortest chain length, one may assume the formation of an intramolecular seven-membered H bonded ring involving the carboxylic group and one of the imido carbonyls,[14] thus reducing the inclusion properties and preventing **22** from inclusion of alcohols. The homologous acid **23** is different. This compound is the most efficient host molecule of all structures studied. On going to the next higher homologues, **24–26**, one observes a strict decrease of the inclusion behavior with increasing chain length. That is, **24** forms a moderate number of inclusions with alcohols and other guests, including pyridine, while **25** forms only very few inclusions (exclusive of pyridine) and **26** is totally inefficient. Similar facts are true for the phenylene analogue compounds **27** and **28**. This particular behavior of hosts **22–28** suggests that, depending on the distance between the two functional sites (dicarboximide and carboxylic acid group) and on geometric constraints in the crystal, guest molecules with H donor/H acceptor properties form intra- or intermolecular contacts with complementary host functional groups (bridge- or catemer-like) which requires successful competition for complementary interactions. In principle, these relations control the inclusion properties of host molecules **22–28**.

Positioning of the carboxylic groups is also an important point for the benzoic acid derivative hosts (cf. **3**, **8**, **10**), although the formation of an intramolecular H bonded ring corresponding to that assumed for **22** is unlikely for **3–7** on steric (conformational) grounds. The addition of secondary substituents (Cl, Me; cf. **3–9**) allows further differentiation of the inclusion behavior. However, as can be seen from **4** and **5**, methyl and chloro substituents at identical positions on the phenyl ring behave similarly, which is reasonable since these substituents are of comparable sizes. On the other hand, one extra methyl or chloro substituent is crucial for the individual inclusion behavior (cf. **3–5**). In the series of noncarboxylic hosts, the introduction of one single substituent (Me, NO_2, Br) is decisive for being or not being a host under the given experimental conditions (cf. **2** vs **18**).

Another remarkable finding is that both hydroxy compounds, phenol **12** and alcohol **29**, yield no inclusion, unlike their carboxylic acid analogues **10** and **23**. This again shows the superiority of the carboxylic hosts. The inclusion of unsubstituted dicarboximide **1** is possibly caused by the acidic imide hydrogen, whereas the presence of two dicarboximido groups such as in **31** and **32** gives rise to rather balanced structures which do not meet the requirements of a host molecule.[7]

In view of the mentioned problems regarding the host–guest interaction modes, and in order to investigate the packing principles of the new inclusion family, we studied the crystal structures of three selected inclusion species: **1**·dioxane (1:1), **23**·MeOH (1:1), and **24**·DMF (1:1), which are inclusion compounds formed between different proton donor and acceptor components.

X-ray Analysis: Structure Description of 1·Dioxane (1:1), 23·MeOH (1:1), and 24·DMF (1:1). Views of the molecular and packing structures are presented in Figures 1–4 (including numbering schemes of the atoms). Crystal data are given in Table II. Hydrogen bond dimensions are shown in Table III. Lists of final atomic coordinates, covalent bond distances and intramolecular angles involving the non-hydrogen atoms, fractional atomic coordinates for the hydrogen atoms, bond distances and angles involving the hydrogen atoms located from difference electron density maps, as well as lists of the anisotropic thermal parameters of the non-hydrogen atoms are deposited (supplementary material).

(1) Molecular Structures. It is seen in Figure 1a–c that the dihydroethanoanthracenedicarboximido moiety is rigid, possessing analogous conformations in the different structures. Only the flexible N-bound lateral groups in hosts **23** and **24** are affected by the variation of packing forces. The corresponding bond lengths (Table IX, supplementary material) and bond angles (Table X, supplementary material) in different host molecules of the present three structures are comparable with each other within experimental error, and together with the remaining ones they conform to the expected values, with a few exceptions. Inspection of the atomic thermal parameters (Table XIII, supplementary material) shows that the carboxy oxygen atoms in both **23** and **24** have considerably higher atomic displacement parameters than the other non-hydrogen atoms of the hosts, indicating disorder for these atoms. The B_{eq} values are 15.8 Å^2 for O(19) and 9.0

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Table II. Selected Crystal Data and Some Details of the Refinement Calculations

compd	1·dioxane (1:1)	23·MeOH (1:1)	24·DMF (1:1)
formula unit	$C_{22}H_{21}NO_4$	$C_{22}H_{21}NO_5$	$C_{25}H_{26}N_2O_5$
formula wt, amu	363.41	379.41	434.49
crystal size, mm	0.30 × 0.45 × 0.40	0.55 × 0.36 × 0.20	0.38 × 0.40 × 0.53
space group	$P2_1/n$	$Pbca$	$P2_1/a$
cell dimension			
a, Å	11.9757 (4)	8.532 (1)	15.217 (1)
b, Å	9.8442 (3)	18.865 (1)	11.445 (1)
c, Å	16.2371 (5)	24.074 (2)	26.685 (2)
α, deg	90.0	90.0	90.0
β, deg	109.196 (4)	90.0	106.15 (1)
γ, deg	90.0	90.0	90.0
V_c, Å^3	1807.8 (1)	3875.0 (5)	4464.0 (6)
Z	4	8	8
D_c, g cm^{-3}	1.33	1.30	1.29
$F(000)$	768	1600	1840
$\mu_{CuK\alpha}$, cm^{-1}	7.09	7.21	7.02
N_{obs} (unique, nonzero)	2955	2918	6735
N_{ref} with the limit	2020 $F/\sigma(F) > 6$	1948 $F/\sigma(F) > 2$	4363 $F/\sigma(F) > 6$
$N_{variables,tot}$	258	259	597[b]
final agreement factors			
$R = \sum\|\Delta F\|/\sum\|F_o\|$	0.070	0.063	0.106
$R_w = [w\|\Delta F\|^2/\sum w\|F_o\|^2]^{1/2}$ [c]	0.110	0.079	0.158

[a] Esd's, where given, are in parentheses. [b] In the case of 24·DMF "blocked full-matrix" refinement technique,[35] have been used; two blocks, each with 301 variables, were refined in consecutive cycles. [c] Weights of the structure factors in SHELX[35] are estimated as $w = \text{const}/(\sigma^2(F) + g\cdot F^2)$ with g = 0.010 84, 0.0005, and 0.000 25 for 1·dioxane, 23·MeOH and 24·DMF, respectively.

Table III. Bond Lengths (Å) and Bond Angles (deg) of Possible Hydrogen Bonds in 1•Dioxane (1:1), 23•MeOH (1:1), and 24•DMF (1:1)[a]

atoms involved	symmetry	distance donor··· acceptor	D–H	H···A	angle <D–H··A
1·dioxane (1:1)					
N(14)–H(14)···O(D1)	x, y, z	2.940 (5)	0.96	2.04	155
23·MeOH (1:1)					
O(29)–H(20)···O(M)	x, y, z	2.610 (7)	1.02	1.59	176
O(M)–H(OM)···O(15)	$^1/_2 - x, ^1/_2 + y, z$	2.718 (6)	0.93	1.79	177
24·DMF (1:1)					
O(20)–H(20)···O(D)	x, y, z	2.624 (9)	1.00	1.67	158
O(20′)–H(20′)··O(D′)	x, y, z	2.687 (9)	1.06	1.55	167

[a] The esd's, where given, are in parentheses. The H atom positions are not refined.

Å^2 for O(20) in 23; in 24 they are 9.1/9.9 Å^2 for O(19) and 9.6/11.0 Å^2 for O(20) in molecules A/B, respectively. The high thermal mobility gives rise to unusually short bond lengths for the carboxy C=O groups not involved in hydrogen bonding in the present structures: 1.17 (1) Å in 23 and 1.17 (1)/1.18 (1) Å in 24 for molecules A/B, respectively.

In the ethano bridge, the C(9)–C(10) and C(11)–C(12) bonds are slightly elongated while the C(10)–C(11) distance has the normal value for such a bond.[10] The calculated mean distance for the elongated bonds in the present four crystallographically independent host molecules (with rms deviation in angular brackets) is 1.563 [13] Å, the mean C(10)–C(11) bond length is 1.534 [2] Å, and the average dihedral angle between the two phenyl ring planes in the tricyclic dihydroanthracene moiety is 123 [5]°, all in accordance with our earlier observations concerning the

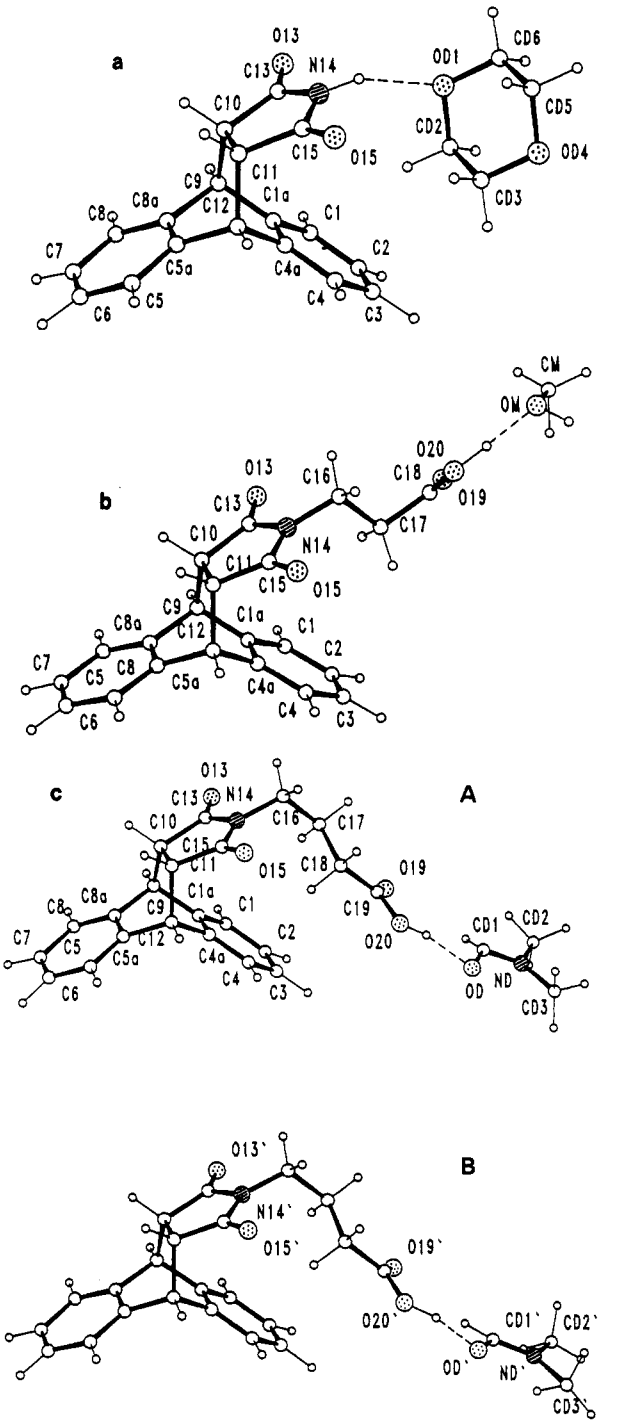

Figure 1. Perspective views of the asymmetric units including atom numbering for (a) 1·dioxane (1:1), (b) 23·MeOH (1:1), and (c) 24·DMF (1:1) showing the two crystallographically independent host–guest associations (A and B). Solid and dashed lines represent covalent and hydrogen bonds, respectively; heteroatoms are shaded.

dihydroethanoanthracene skeleton.[10] The flat succinimide ring is fused to the ethano bridge so that it is tilted through almost exactly 60° with respect to the plane of the C(9)–C(10)–C(11)–C(12) bridging atoms (the calculated mean value for the present four molecules is 60.9 [5]°).

(2) Packing Relations and Host–Guest Interactions. In 1·dioxane (1:1), each aprotic dioxane guest is hydrogen-bonded to the imide N atom of a host molecule, forming a 1:1 host–guest aggregate. The hosts, held together by hydrophobic interactions only, are arranged so as to form nearly rectangular cages with space comfortable

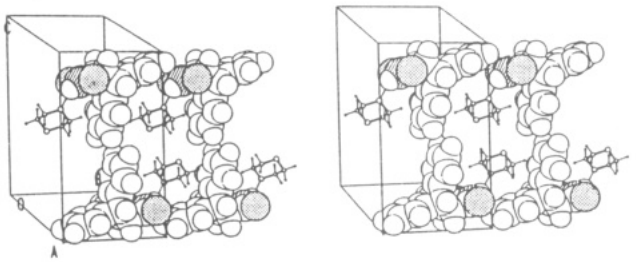

Figure 2. Stereoscopic packing diagram of **1**·dioxane (1:1). The host molecule is in van der Waals, the guest molecule in ball-and-stick representation. O atoms of the host are dotted, N atoms are hatched; O atoms of the guest are specified by larger spheres. The host–guest H bond is indicated by a thin line.

for inclusion of two chair-shaped dioxane guests (Figure 2).

The special feature in **23**·MeOH (1:1) is as follows. Besides the host–COOH and guest –OH functions, one of the carbonyl groups of the dicarboximido moiety is also involved in the hydrogen bond scheme. Thus, in the endless H bonded chains of alternating host and guest molecules (Figure 3), which run in the crystallographic *b* direction, each –COOH group functions as proton donor only, whereas the alcoholic proton is accepted by the carboximido oxygen, O(13). At the same time, each carboxy C=O group seems to be involved in an interhost interaction with a carboximido C=O group from a neighboring H bonded chain, related by the symmetry operation $^{-1}/_{2} + x$, $^{1}/_{2} - y + 1$, $-z + 1$ (Figure 4a): the observed 2.97 (1) Å for the C(15)···O(19) distance is somewhat less than the commonly accepted value of 3.1 Å for the sum of the van der Waals' radii.[16] The C(18)–=O(19)···C(15) angle is 136.1 (7)°. This relatively short nonbonded contact occurs between two carbonyl groups where the strongly dipolar nature of the C=O bonds is enhanced by electron-withdrawing neighbors, such as the imide N(14) atom on the one hand and the carboxy O(20)–H group on the other. Accordingly, this contact appears to be a dipole–dipole interaction of the type discussed by Bolton[17,18] and by Silverman et al.[19] and found in organic crystals containing several carbonyl groups.[18,19] This interaction, linking together the hydrogen-bonded chains pairwise, also leads to a fairly short intermolecular contact distance between O(19) and C(11) [O(19)···C(11)$_{-1/2+x,1/2-y+1,z+1}$ = 2.987 (9) Å]. Besides the dipole–dipole interaction, there are only weak van der Waals' type forces between the hydrophobic dihydroanthracene moieties of different chain pairs.

From previous studies of DMF inclusion compounds of different carboxylic hosts[10a,20,21] it is obvious that besides (O)H···O hydrogen bonding, the formyl group may also be involved in a (C)H···O-type interaction with the host carboxyl function. Nevertheless, in the present **24**·DMF (1:1) inclusion, the –CHO groups act only as proton acceptors toward the hosts in both crystallographically independent host–guest associates (A and B in Figure 1c). This is somewhat surprising, because the least-squares plane of the DMF molecule is only slightly inclined to the plane of the carboxyl group to which it is H-bonded [the dihedral angles are 21.2(5) and 19.2(5)° for the A and B aggregates, respectively], and the formyl hydrogens point in the direction of the respective carbonyl O(19) atom. However, the H(D1)···O(19) distances (3.06 Å in A and 2.71 Å in B) are significantly longer than the sum of the Van der Waals' radii (2.4 Å),[16] thus clearly showing that in the present structure the formyl groups do not take advantage of a (C)H···O type of interaction with the host carboxyl group.

There are two interactions between symmetry related 1:1 host–guest associates in **24**·DMF worth mentioning (Figure 4b). Each of these interactions involves one of the dicarboximido carbonyl groups of a host and one of the *N*-methyl groups of a guest: the C(D3)–H(D31)···O(13′)$_{-x,-y,-z}$ contact has the parameters C···O = 2.95 (2) Å, H···O = 2.24 Å, ∠ C–H···O = 122° and ∠ H···O=C = 140°, whereas the C(D2′)–H(D24)···O(13)$_{1/2-x,1/2+y,1-z}$ interaction has C···O = 3.05 (2) Å, H···O = 2.50 Å, C–H···O = 110 and ∠ H···O=C = 145°. These contacts are possible (C)H···O type interactions, first discussed by Sutor[22] and later by Taylor and Kennard,[23] Berkovitch-Yellin and Leiserowitz,[24] and Desiraju[6,25] among others. Despite the fact that crystallographic results usually show one of the methyl H atoms pointing in the direction of a potential proton acceptor (most often an oxygen), the ability of a methyl group to act as proton donor in an attractive (C)H···O type interaction is still somewhat controversial.[10b,26-28] In the present case it must be stressed, however, that the proton donor ability of the CH_3 group is enhanced by the electron-withdrawing effect of the neighboring amide nitrogen atom. Moreover, this methyl···O interaction can possibly be the reason why the formyl (C)H···O interaction does not occur in this structure. On the other hand, because of the relatively high level of random error in the data on **24**·DMF (1:1), due to the limited quality of the crystals, and also because of the high uncertainty generally in X-ray-determined methyl H positions, it is not possible to arrive at a definite conclusion. More accurate data from structures with this type of interaction, and investigations also with other methods than X-ray diffraction, are necessary to prove the proton donor ability of methyl groups.

Conclusions

Using the rigid tetracyclic 9,10-dihydro-9,10-ethanoanthracene framework as a means to increase the bulkiness of a given molecule has proved to make accessible new crystalline inclusion hosts with novel structures. They are compounds where a dicarboximido unit is used to connect the characteristic tetracyclic framework to the particular molecules. These are various amines, aminophenols, amino alcohols, amino acids, or simply ammonia to give the corresponding dicarboximido analogues **1**–**32** with and without proton donating groups.

They form crystalline inclusions with a variety of uncharged organic molecules ranging from protic dipolar to rather apolar compounds (103 different examples, Table I). Inclusion formation depends on structural parameters of the host, the type and number of functional groups, and

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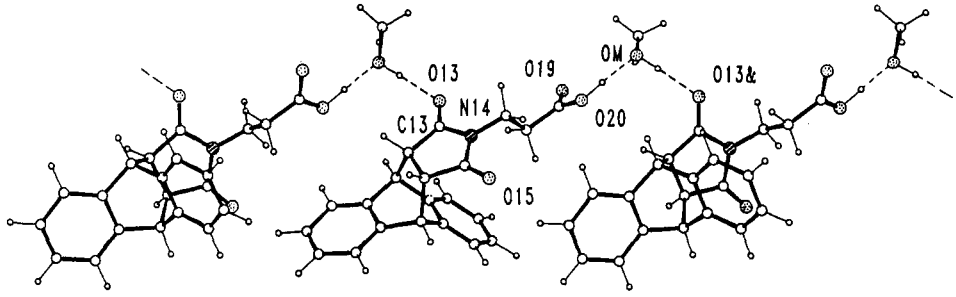

Figure 3. Packing excerpt of **23**·MeOH (1:1) showing the endless host–guest H bonded supramolecular chains which run in the crystallographic *b* direction. Heteroatoms are shaded; H bonds are indicated by dashed lines.

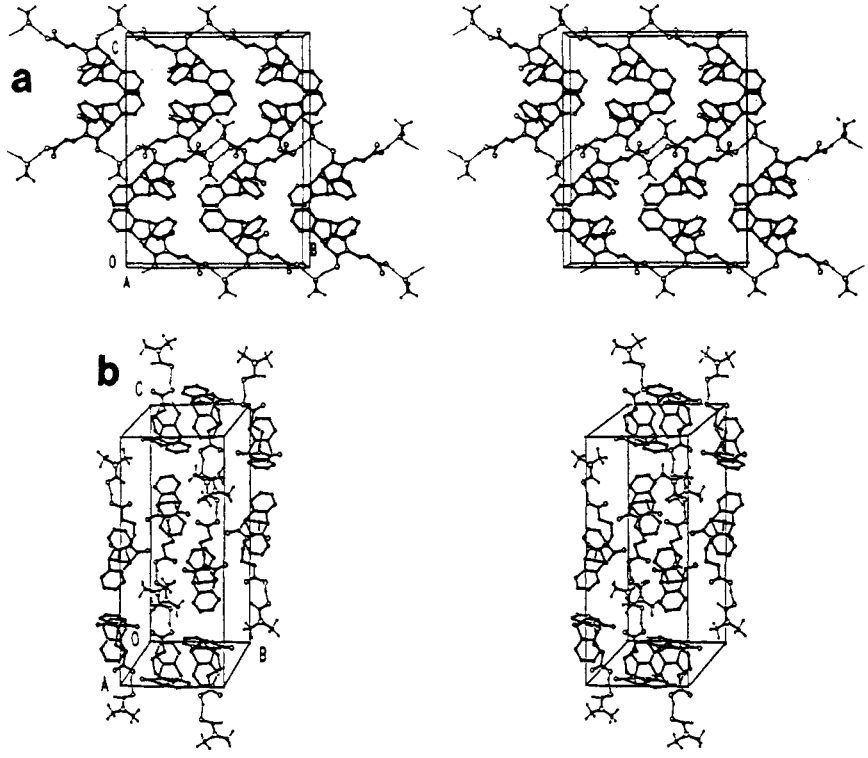

Figure 4. Stereoscopic packing diagrams of (a) **23**·MeOH (1:1) and (b) **24**·DMF (1:1). Heteroatoms are specified by larger spheres. H atoms of the hosts are omitted, except those involved in H bonds, which are indicated as thin lines.

geometric factors being the most important. These parameters also determine the mode of interaction between host and guest, as supported by crystallographic evidence in three cases.

The results show that a new approach for the design of a crystalline host based on the introduction of a so-called "clathratogenic group" (inclusion-promoting group) could be successfully applied to the given sector of compounds. The new approach seems capable of development to become a general strategy for designing crystalline hosts.

Experimental Section

General. Spectroscopic (IR, ^{1}H NMR, MS) and elemental analytical data for all new compounds are given in the supplementary material (Tables IV–VII).

***cis*-9,10-Dihydro-9,10-ethanoanthracene-11,12-dicarboximide (1).** Procedure of Bachmann and Cole;[29] recrystallization from toluene; 35%; colorless powder; mp > 290 °C (lit.[29] mp 303–304 °C).

Syntheses of N-Substituted 9,10-Dihydro-9,10-ethanoanthracene-11,12-dicarboximides 2–32. General Procedures 1–3. Procedures used and specific details for each compound are given below.

Procedure 1. A mixture of anhydride **33**[12] (5.52 g, 20.0 mmol) and the corresponding amine (20.0 mmol) (see below) in DMF (50 mL) was heated at reflux[30] (*reaction time from 2 h to 7 d*; DC-control). After being cooled to room temperature, the solution was added to ice–water (200 mL) to yield a precipitate which was collected, filtered, washed (H_2O), and dried. In some cases an oil was obtained which solidified on standing for several h at 5 °C. The crude products were purified by recrystallization from acetone or EtOH to yield colorless powders unless otherwise stated.

Procedure 2.[29] Anhydride **33**[12] (5.52 g, 20.0 mmol) was dissolved in refluxing dioxane (75 mL). While hot (60 °C), a solution of the corresponding amino acid (30.0 mmol) (see below) in 20% aqueous Na_2CO_3 (10 mL) was added. The mixture was held at 90 °C for 4 h. After being cooled to room temperature it was diluted with H_2O (50–100 mL). Acidification (dilute HCl) of the resulting clear solutions precipitated colorless solids which were collected, washed (H_2O), and recrystallized from EtOH to yield colorless powders unless otherwise stated.

Procedure 3. Equimolar amounts (30.0 mmol) of anhydride **33**[12] and the corresponding amine (see below) were mixed together and slowly heated to the boiling temperature of the amine.[31] An

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exothermic reaction occurred. The mixture was allowed to cool to room temperature. The crude products were purified by recrystallization from acetone to yield colorless powders.

2: procedure 1; aniline; recrystallization from $MeNO_2$; 70%; mp 242 °C (lit.[32] mp 203 °C).

3: procedure 1; anthranilic acid; 94.5%; mp 273–274 °C.

4: procedure 1; 2-amino-5-methylbenzoic acid; 83%; mp 233 °C.

5: procedure 1; 2-amino-5-chlorobenzoic acid; 88.5%; mp > 290 °C.

6: procedure 1; 2-amino-4-chlorobenzoic acid; 72%; mp > 290 °C.

7: procedure 1; 2-amino-3,5-dichlorobenzoic acid; 45.5%; mp 273–274 °C.

8: procedure 1; 3-aminobenzoic acid; 70%; mp 288–290 °C.

9: procedure 1; 3-amino-4-methylbenzoic acid; 69.5%; mp > 290 °C.

10: procedure 1; 4-aminobenzoic acid; 95%; mp > 290 °C.

11: procedure 1; 5-aminoisophthalic acid; 64.5%; mp > 290 °C.

12: procedure 1; 4-hydroxyaniline; 57%; mp > 290 °C (lit.[31] mp 334–335 °C).

13: procedure 1; 4-methoxyaniline; 88%; mp 258 °C.

14: procedure 1; 3-nitroaniline; 79%; mp 248 °C.

15: procedure 1; 4-nitroaniline; 45%; mp > 290 °C.

16: procedure 1; 2-bromoaniline; 76.5%; mp 224 °C.

17: procedure 1; 4-bromoaniline; 91%; mp 229 °C.

18: procedure 3; 2-methylaniline; 89%; mp 248 °C.

19: procedure 3; 2,3-dimethylaniline; 91%; mp 246 °C.

20: procedure 3; 2,5-dimethylaniline; 81%; mp 219 °C.

21: procedure 3; 2,6-dimethylaniline; 90%; mp 216 °C.

22: procedure 2; glycine; recrystallization from acetonitrile; 72%; mp 270 °C (lit.[29] mp 269–270 °C).

23: procedure 2; β-alanine; 80.5%; mp 218 °C.

24: procedure 2; 4-aminobutanoic acid; 86%; mp 206 °C.

25: procedure 1; 5-aminovalerianic acid; 75.5%; mp 198 °C.

26: procedure 1; 6-aminocaproic acid; 84%; mp 183 °C.

27: procedure 1; 4-aminophenylacetic acid; 74%; mp > 290 °C.

28: procedure 1; 4-(aminomethylbenzoic acid; 81.5%; mp 280 °C.

29: procedure 3; aminoethanol; 45%; mp 218 °C (lit.[31] mp 218–220 °C).

30: procedure 2; diglycine; 80.5%; mp 239 °C.

31: procedure 1; 1,4-diaminobenzene; 89.5%; mp > 300 °C.

32: procedure 1; benzidine; 86.5%; mp > 300 °C.

Preparation of the Crystalline Inclusion Compounds. General Procedure. The host compound was dissolved by heating in a minimum amount of the guest solvent. After storage for 12 h at room temperature, the crystals formed were colled by suction filtration, washed with an inert solvent (*n*-pentane, Et_2O, or MeOH), and dried (2 h, room temperature (15 Torr)). Host–guest stoichiometry was determined by ^1H NMR integration. Data for each compound are given in Table I.

Crystallography. (a) Sample Preparation and Data Collection. Single crystals of 1·dioxane (1:1), **23**·MeOH (1:1), and **24**·DMF (1:1) were obtained from a solution of the host compound in the respective solvent as described above. The selected single crystals, of reasonable quality, of 1·dioxane and **23**·MeOH were put in glass capillaries in order to protect them from possible evaporation during the data collection. In the case of **24**·DMF, a great number of individual crystals, sealed in epoxy glue, were tested on the diffractometer. However, no high-quality crystal for X-ray single-crystal diffraction studies was found. Nevertheless, the best crystal out of those tested was selected for data collection.

Intensity data were obtained with a STOE/AED2 diffractometer at room temperature, using graphite-monochromatized CuKα radiation (λ = 1.5418 Å) up to a Θ limit of 70° for 1·dioxane and **23**·MeOH and 65° for **24**·DMF. The monitor reflections, measured approximately every hour, showed no systematic intensity variation. Data reduction included corrections for background, Lorentz, and polarization effects. Despite the low calculated absorption coefficients of the **23**·MeOH crystals (cf. Table II), significant absorption effects were detected in all probability due to the mother liquor content of the capillary. Therefore, the data reduction in the case of **23**·MeOH included correction also for absorption effects. The applied empirical absorption correction was based on Ψ scans of six reflections with $70° < \chi < 84°$ and $21° < 2\Theta < 93°$. The transmission factor varied between 49% and 83%.

The unit cell parameters, listed in Table II, were refined against 2Θ values of strong, well-centered reflections ($63_{[27<2\Theta<48°]}$ for 1·dioxane, $42_{[29<2\Theta,49°]}$ for **23**·MeOH, and $54_{[30<2\Theta<64°]}$ for **24**·DMF).

(b) Structure Analysis and Refinement. Direct methods, using the SHELXS[33] program system, gave reasonable models for 1·dioxane and **23**·MeOH, but not for **24**·DMF. Good structure factor estimates for this latter structure were obtained with a randomly oriented and positioned dihydroethanoanthracenedicarboximide moiety, which was used in the calculation of the *E* values. The largest 400 *E* values ($E > 1.95$) were then put into the direct-method calculations with the MULTAN[34] program system. From the best set of phases, reliable positions could be deduced for most of the non-hydrogen atoms of the two crystallographically independent host molecules. The few remaining non-H positions of the hosts, together with the two guest molecules, were found by weighted Fourier recycling calculation.[34]

The preliminary structural models were refined by full-matrix least-squares procedures according to Sheldrick (SHELX).[35] The hydrogen atoms were either located from difference electron density calculations, and their positions were held riding on their respective "mother" atoms during the subsequent calculations (all H atoms of the host 1, but only the carboxylic one of the hosts **23** and **24**, together with the alcoholic H of the MeOH and the formyl H of the DMF guests), or were assumed to have ideal, geometrically predictable positions, which were recalculated after each cycle of the refinement (H atoms of the dioxane guest as well as all the carbon-bonded H positions in **23**·MeOH and **24**·DMF, except the formyl hydrogens of the DMF guests). In the last stage of the refinements, the non-hydrogen atomic positions were refined together with their anisotropic thermal parameters. Individual isotropic temperature factors were refined for the H atoms located from difference electron density calculations, and common isotropic temperature factors for the calculated ones. The methyl groups were treated as rigid groups, with three rotational parameters refined for each of them. Crystal data and some details of the refinement calculations, together with the final *R* values, are given in Table II.

In the case of the **24**·DMF structure, the asymmetric crystallographic unit contains two host and two guest molecules. Because of the great number of variables, the "blocked full-matrix" technique[35] had to be used in the last stage of the refinement. Accordingly, the parameters were divided into two blocks: the two 1:1 host–guest aggregates were refined by the full-matrix least-squares method in consecutive cycles. Moreover, as seen in Table II, the refinement of this latter structure resulted in relatively high *R* values, in all probability due to the random errors in the observed data, which in turn may depend on the rather poor quality of the crystal. A structure factor calculation, based on the final refined structural model yielded an R_w value of 0.184 for all the 6735 unique nonzero reflections. The highest residual electron density for this structure was 0.368 e Å^{-3}.

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Registry No. 1·dioxane (1:1), 137092-83-2; 1·DMF (1:1), 137092-84-3; **2**, 137092-85-4; 2·DMF (3:1), 137092-86-5; 2-dioxane (4:1), 137092-87-6; **3**, 137092-88-7; 3·DMF (1:1), 137092-89-8; 3·diethylformamide (1:1), 137092-90-1; **4**, 137092-91-2; 4·MeOH (1:1), 137092-92-3; 4·EtOH (1:1), 137092-93-4; 4·DMF (1:1), 137092-94-5; 4·DMSO (1:2), 137092-95-6; 4·pyridine (1:1), 137092-96-7; **5**, 137092-97-8; 5·MeOH (1:1), 137092-98-9; 5·DMF (1:1), 137092-99-0; 5·diethylformamide (1:1), 137093-00-6; 5·DMSO (1:2), 137093-01-7; 5·pyridine (1:1), 137093-02-8; **6**, 137093-03-9; 6·acetone (4:1), 137093-04-0; 6·methylformamide (1:1), 137093-05-1; 6·DMF (1:1), 137093-06-2; 6·diethylformamide (1:1), 137093-07-3; 6·acetonitrile (2:1), 137093-08-4; 6·nitromethane (2:1), 137093-09-5; 6·THF (4:1), 137093-10-8; 6-dioxane (4:1), 137093-11-9; 6·pyridine (1:1), 137093-12-0; **7**, 137093-13-1; 7·MeOH (1:1), 137093-14-2; 7·EtOH (1:1), 137093-15-3; 7·acetic acid (1:1), 137093-16-4; 7·acetone (1:1), 137093-17-5; 7·DMF (1:1), 137093-18-6; 7·DMSO (1:1), 137093-19-7; **8**, 137093-20-0; 8·MeOH (1:1), 137093-21-1; 8·EtOH (3:1), 137093-22-2; 8·acetic acid (1:1), 137093-23-3; 8·DMF (1:1), 137093-24-4; 8·nitromethane (1:1), 137093-25-5; 8·THF (1:1), 137093-26-6; 8·dioxane (2:1), 137093-27-7; 8·pyridine (1:1), 137093-28-8; **9**, 137093-29-9; 9·DMF (1:1), 137093-30-2; 9·diethylformamide (1:1), 137093-31-3; 9·pyridine (1:1), 137143-55-6; **10**, 137093-32-4; 10·DMF (1:1), 137093-33-5; 10·diethylformamide (1:1), 137093-34-6; 10·dibutylformamide (1:1), 137093-35-7; 10·methylphenylformamide (1:1), 137093-36-8; 10·dimethylacetamide (1:1), 137093-37-9; 10·pyridine (1:1), 137093-38-0; **11**, 137093-39-1; 11·DMF (1:1), 137093-40-4; 11·DMF (1:2), 137093-41-5; 11·diethylformamide (1:1), 137093-42-6; 11·dimethylacetamide (1:1), 137093-43-7; 11·dioxane (1:1), 137093-44-8; 11·pyridine (1:1), 137093-45-9; **12**, 137093-46-0; **13**, 137093-47-1; 13·MeOH (1:1), 137093-48-2; **14**, 137122-26-0; 14·DMF (1:1), 137122-27-1; 14·THF (1:1), 137122-28-2; 14·dioxane (1:1), 137122-29-3; 14·pyridine (2:1), 137122-30-6; **15**, 137093-49-3; **16**, 137093-50-6; 16·dioxane (3:1), 137093-51-7; **17**, 137093-52-8; **18**, 137093-53-9; **19**, 137093-54-0; 19·acetonitrile (1:1), 137093-55-1; 19·nitromethane (1:1), 137093-56-2; **20**, 137093-57-3; **21**, 137093-58-4; 21·benzene (1:1), 137093-59-5; **22**, 137093-60-8; 22·DMF (1:1), 137093-61-9; 22·DMSO (1:1), 137093-62-0; 22·dioxane (2:1), 137093-63-1; 22·pyridine (1:1), 137093-64-2; **23**, 137093-65-3; 23·MeOH (1:1), 137093-66-4; 23·EtOH (1:1), 137093-67-5; 23·1-PrOH (2:1), 137093-68-6; 23·2-PrOH (2:1), 137093-69-7; 23·2-BuOH (3:1), 137093-70-0; 23·acetic acid (2:1), 137093-71-1; 23·propionic acid (2:1), 137093-72-2; 23·methylformamide (1:1), 137093-73-3; 23·DMF (1:1), 137093-74-4; 23·diethylformamide (1:1), 137093-75-5; 23·dimethylacetamide (1:1), 137093-76-6; 23·acetonitrile (1:1), 137122-31-7; 23·nitromethane (1:1), 137093-77-7; 23·nitroethane (1:1), 137093-78-8; 23·DMSO (1:1), 137093-79-9; 23·THF (1:1), 137093-80-2; 23·dioxane (2:1), 137093-81-3; 23·1,3-dioxolane (2:1), 137093-82-4; 23·tetrahydropyran (2:1), 137093-83-5; 23·pyridine (1:1), 137093-84-6; **24**, 137093-85-7; 24·MeOH (1:1), 137093-86-8; 24·EtOH (2:1), 137093-87-9; 24·2-PrOH (2:1), 137093-88-0; 24·methylformamide (1:1), 137093-89-1; 24·DMF (1:1), 137093-90-4; 24·dimethylacetamide (1:1), 137093-91-5; 24·nitromethane (1:1), 137093-92-6; 24·DMSO (2:1), 137093-93-7; 24·THF (1:1), 137093-94-8; 24·dioxane (2:1), 137093-95-9; 24·pyridine (2:1), 137093-96-0; **25**, 137093-97-1; 25·EtOH (1:1), 137093-98-2; 25·DMF (1:1), 137093-99-3; 25·dioxane (2:1), 137094-00-9; **26**, 137094-01-0; **27**, 137094-02-1; **28**, 137094-03-2; 28·THF (2:1), 137094-04-3; 28·DMF (1:1), 137094-05-4; **29**, 137094-06-5; **30**, 137094-07-6; 30·dioxane (2:1), 137094-08-7; **31**, 137122-32-8; **32**, 137094-09-8; **33**, 103515-22-6; aniline, 62-53-3; anthranilic acid, 118-92-3; 2-amino-5-methylbenzoic acid, 2941-78-8; 2-amino-5-chlorobenzoic acid, 635-21-2; 2-amino-4-chlorobenzoic acid, 89-77-0; 2-amino-3,5-dichlorobenzoic acid, 2789-92-6; 3-aminobenzoic acid, 99-05-8; 3-amino-4-methylbenzoic acid, 2458-12-0; 4-aminobenzoic acid, 150-13-0; 5-aminoisophthalic acid, 99-31-0; 4-hydroxyaniline, 123-30-8; 4-methoxyaniline, 104-94-9; 3-nitroaniline, 99-09-2; 4-nitroaniline, 100-01-6; 2-bromoaniline, 615-36-1; 4-bromoaniline, 106-40-1; 2-methylaniline, 95-53-4; 2,3-dimethylaniline, 87-59-2; 2,5-dimethylaniline, 95-78-3; 2,6-dimethylaniline, 87-62-7; glycine, 56-40-6; β-alanine, 107-95-9; 4-aminobutanoic acid, 56-12-2; 5-aminovalerianic acid, 660-88-8; 6-aminocaproic acid, 60-32-2; 4-aminophenylacetic acid, 1197-55-3; 4-(aminomethyl)benzoic acid, 56-91-7; aminoethanol, 141-43-5; diglycine, 556-50-3; 1,4-diaminobenzene, 106-50-3; benzidine, 92-87-5.

Supplementary Material Available: Spectroscopic (IR, ^{1}H NMR, MS) and elemental analytical data of the new compounds (Tables IV–VII), positional parameters of the non-hydrogen atoms (Table VIII), intramolecular bond lengths and bond angles involving non-hydrogen atoms (Table IX and X), positional parameters for the hydrogen atoms (Table XI), intramolecular bond lengths and bond angles involving hydrogen atoms (located from difference electron density maps; Table XII), and anisotropic temperature factors of the non-hydrogen atoms (Table XIII) (33 pages); tables of observed and calculated structure factors (44 pages). Ordering information is given on any current masthead page. A listing of observed and calculated structure factors is available directly from the authors.

Synthesis of Quinolines via Ortho-Lithiated *N*-Acylanilines. A Modified Friedländer Synthesis[1,2]

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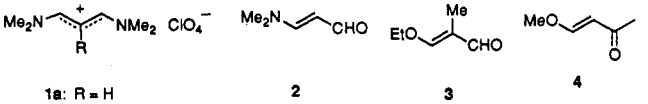
A new variation of the Friedländer quinoline synthesis was devised based on the sequential reaction of ortho-lithiated *N*-*t*-Boc-anilines or *N*-pivaloylanilines with masked malondialdehyde derivatives [e.g., vinamidinium salts **1a** and **1b**, 3-(dimethylamino)acrolein (**2**), and 3-ethoxymethacrolein (**3**)] and subsequent acid-induced cyclization.

The Friedländer quinoline synthesis involves the condensation of an aromatic *o*-amino aldehyde or *o*-amino ketone with an aldehyde or a ketone containing at least one methylene group α to the carbonyl moiety.[5-7] The

Scheme I



1a: R = H
1b: R = Ph

2 3 4

process is one of considerable breadth, but until recently (see below) a major limitation was that the *o*-amino car-

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(3) Syntex Research Postdoctoral Fellow, 1989–1990.
(4) Syntex Research Postdoctoral Fellow, 1991–.
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(6) Cheng, C.-C.; Yan, S.-J. *Org. React.* **1982**, *28*, 37.

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