was added 0.208 mL (0.164 M) aqueous CTAC, 0.240 mL of aqueous substrate (1.425×10^{-2} M), and 2.891 mL of phosphate buffer. To initiate the reaction, a 0.081-mL aliquot of catalyst, freshly prepared in DMF, was then added to this solution, with rapid stirring. Final concentrations of substrate were typically 1×10^{-3} M. Final concentrations of the catalyst and surfactant used in each reaction were as noted in the text. Reaction temperatures were maintained at 25.0 ± 0.1 °C through the use of a constant-temperature water bath. Reactions were carried out with constant stirring and were allowed to run to 80% or greater hydrolysis while data were collected automatically. Rate constants, k_{obs}, were calculated either with an exponential fitting routine or through linear regression analysis of ln ($[\text{fluoride}]_{inf} - [\text{fluoride}]_t$) vs time. Infinity-point values, predicted by the exponential fitting routine, were in good agreement with observed final fluoride concentrations. Reproducibility for duplicate runs was good and is indicated by standard deviation values provided in the text.

Enzyme Inhibition Studies. To confirm the results obtained in the kinetic runs and to demonstrate loss of enzyme inhibition activity (decontamination) for the organophosphorus substrates, selected hydrolysis runs were tested for loss of AChE inhibition activity at various time points during the reaction. To carry out these studies, an assay procedure for enzymatic inhibitory activity was developed which made use of a Titertek Multiscan MCC plate reader (Flow Laboratories) and 96-well plates.[25] The assay is based on the hydrolysis of acetylthiocholine by uninhibited and inhibited AChE, with subsequent production of absorbance at 414 nm via reaction of the liberated thiocholine with DTNB. Plots of log (percent control enzyme activity) vs [inhibitor] provide standard curves from which unknown concentrations of inhibitor (substrate) could be determined at various times during an experiment.

For experiments in which the release of hydrogen ion was followed as a function of time, pH electrodes were standardized at pH 7.0 and 10.0. For each set of runs, standardized 0.01 M potassium hydroxide was used to maintain a constant pH during the course of the titration. KOH solutions were standardized with 0.01 M potassium acid phthalate, in triplicate. All reactions were carried out under a blanket of nitrogen to prevent adsorption of CO_2. In a typical reaction, an appropriate amount of sodium chloride solution at the required ionic strength was added to the reaction chamber (thermostated at 25.0 ± 0.1 °C) and titrated to pH 7.5. Surfactant (in aqueous solution) and catalyst in dimethylformamide (or substrate) were then added and titrated to pH 7.5, with the amount of base required for each step recorded. (In cases where substrate was added first, a background hydrolysis rate could be followed for several minutes prior to addition of the catalyst.) To initiate the catalyzed reaction, an aliquot of substrate in aqueous solution (or catalyst) was then added. The rate of base addition required to maintain a constant pH was recorded as a function of time. The amount of base required for any given reaction was less than 10% of the total volume, thus limiting the effects of dilution on the reaction rate. Reactions were typically allowed to proceed to at least 80% total theoretical proton production. Rate constants were derived through analysis, using a nonlinear regression routine,[14] of volume of base added (or the amount of proton titrated) as a function of time or were derived through linearization of the data (ln [substrate] vs time), followed by linear regression analysis.

Reactions on the ion exchange resins were carried out in a manner similar to the above studies and were followed with an ion specific electrode. Typically, 0.50 g of the modified resin was suspended in 55.5 mL of 0.1 M $NaCHO_3$ aqueous buffer, held in an ultrafiltration cell; to this rapidly stirred suspension was added 4.5 mL of 1.425×10^{-2} M substrate. Periodically, samples of filtrate and slurry were removed for fluoride analysis.

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Registry No. 1a, 330-13-2; **1b**, 311-45-5; **3**, 107556-72-9; **4a**, 96-64-0; **4c**, 107-44-8; **4d**, 77-81-6; **5a**, 304-91-6; **5b**, 89031-96-9; **5d**, 23330-00-9; **6a**, 84280-67-1; **6b**, 117203-79-9; **6c**, 104807-59-2; **6d**, 104807-60-5; **6e**, 107164-49-8.

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New Host Family Based on Small-Ring Compounds

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Abstract: Three- and four-membered ring compounds with functional groups and bulky substituents have proved to be a rewarding new source of inclusion hosts. These hosts form clathrates with a variety of uncharged organic molecules ranging from protic dipolar to apolar compounds (168 different inclusion species). Formation and selectivity depend in a systematic manner on structural parameters of the host, such as the nature, number, and position of functional groups, the substituents, and ring size. X-ray structure analyses of two inclusion compounds [**1**·*t*-BuOH (1:1): $P2_12_12_1$; $a = 9.782$ (1), $b = 11.376$ (1), $c = 17.603$ (1) Å; $Z = 4$. **17**·MeCN (1:1): *Pbcn*; $a = 12.314$ (1), $b = 16.074$ (1), $c = 12.938$ (1) Å; $Z = 4$] and of a free host molecule [**1**: $P2_1$; $a = 7.339$ (2), $b = 11.657$ (4), $c = 9.149$ (3) Å; $\beta = 110.07°$; $Z = 2$] are reported, revealing the building principles of the new clathrate family. The structures exhibit linear chains of inter-/intramolecular H bridges between carboxylic groups in the free host **1** and H-bridge aggregation of host and guest molecules in infinite helical chains for the **1**·*t*-BuOH (1:1) inclusion. In **17**·MeCN (1:1), the guest molecules are tightly enclosed by the host framework without further specific interactions.

Host–guest complexes[1] including clathrates[2] are expected to play an important role in the solution of theoretical and practical problems in chemistry and related fields.[3] The applicability may depend on designed host molecules becoming available in wide variety. We describe here the first examples **1–25** (see Table I) of a new host family possessing selective clathrate-forming properties. Their structures are based on a central small-ring

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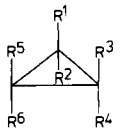
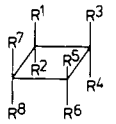
Table I.



1-23



24,25

cmpd no.	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
1	Ph	Ph	COOH	H	COOH	H		
2	*p*-MeC_6H_4	*p*-MeC_6H_4	COOH	H	COOH	H		
3	*p*-ClC_6H_4	*p*-ClC_6H_4	COOH	H	COOH	H		
4	2,2′-biphenyldiyl		COOH	H	COOH	H		
5	Ph	Ph	COOH	H	H	COOH		
6	*p*-MeC_6H_4	*p*-MeC_6H_4	COOH	H	H	COOH		
7	2,2′-biphenyldiyl		COOH	H	H	COOH		
8	Ph	COOH	Ph	COOH	H	H		
9	Ph	Ph	COOH	COOH	H	H		
10	Ph	Ph	COOH	CN	H	H		
11	Ph	Ph	COOH	H	H	H		
12	Ph	H	Ph	H	COOH	H		
13	Ph	H	H	Ph	COOH	H		
14	Ph	Ph	COPh	H	H	COPh		
15	*p*-MeC_6H_4	Ph	COPh	H	H	COPh		
16	*p*-$NO_2C_6H_4$	Ph	COPh	H	H	COPh		
17	*p*-MeC_6H_4	*p*-MeC_6H_4	COPh	H	H	COPh		
18	*p*-ClC_6H_4	*p*-ClC_6H_4	COPh	H	H	COPh		
19	2,2′-biphenyldiyl		COPh	H	H	COPh		
20	Ph	Ph	Ph	H	H	COPh		
21	2,2′-biphenyldiyl		Ph	H	H	COPh		
22	Ph	Ph	CN	CN	CN	CN		
23	2,2′-biphenyldiyl		CN	CN	CN	CN		
24	Ph	H	Ph	H	H	COOH	H	COOH
25	Ph	H	COOH	H	H	Ph	H	COOH

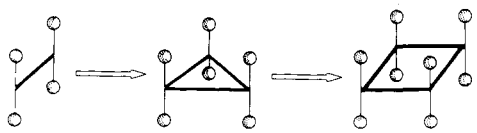


Figure 1. Design concept of the new hosts (schematic representation; the spheres stand for replaceable groups).

element (e.g., three- or four-membered ring) with various substituents in different positions. Substituents can be nonpolar and bulky (aryl) as well as polar groups (COOH, COPh, CN), i.e., capable of forming H bonds.

Other recent host designs[4-8] may be thought of as a rigid molecular axis with suitable substituents at both ends. Thus, from a topological point of view, the new host molecules extend this scheme as diagrammatically illustrated in Figure 1. By this means, both new basic conditions and new possibilities for a broad modification of host structures are opened, e.g., as far as the number and arrangement of specific groups is concerned (cf. Figure 1).

Synthesis. All three-membered ring compounds (except **8** and **10**) involve a 1,3 dipolar cycloaddition of a diazo compound to an ene as the principal synthetic step[9] (pyrazolines are intermediates; for more details, see the Experimental Section). Cyclopropane **8** was obtained by carbene addition of ethyl α-chlorophenylacetate to ethyl α-phenylacrylate in the presence of NaH, and subsequent hydrolysis.[10] Compound **10** was synthesized from ethyl 1-cyano-2-phenylcinnamate and trimethylsulfoxonium iodide upon treatment with NaH in DMSO, and subsequent hydrolysis.[11] Cyclobutanes **24** and **25** were prepared by solid-state photodimerization[12,13] of β- and α-*trans*-cinnamic acid, respectively. Clathrates were obtained by recrystallization of the host compound in the respective guest solvent or solvent mixture (competitive solvent).

Inclusion Properties. Considering the simple constitutions of **1-25**, a remarkably large number of stoichiometric crystalline inclusion compounds (a total of 168) are obtainable by recrystallization from alcohols, carboxylic acids, and dipolar aprotic and relatively apolar solvents (Table II).[14] Nevertheless, each molecular species has a characteristic level of selectivity. Some of the compounds, of which **1**, **2**, **8**, and **22** are typical examples, readily form inclusions in the broad sense; others (**7**, **17**, **20**, and **24**) allow only very few inclusions, while compounds **11-13**, **15**, **18**, and **21** have no host properties at all. For instance, **2** (*cis*-dicarboxylic acid) yields 21 inclusions (Table II) including EtOH (not MeOH), 1-PrOH, 2-PrOH, 1-BuOH, 2-BuOH, *t*-BuOH, HCOOH, MeCOOH, EtCOOH, BuCOOH, DMF (but not *N*-methylformamide or *N*,*N*-diethylformamide), DMSO, $MeNO_2$, MeCN, Me_2CO, THF, and dioxane. On the other hand, **6** (*trans*-dicarboxylic acid) forms inclusions with MeOH and *N*-

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(14) Most of the isolated clathrates are stable under ambient conditions (cf. Experimental Section) and allow storage in air over a long period with no appreciable loss of solvent. They decompose on heating to 80 °C under reduced pressure (15 Torr).

Table II. Crystalline Inclusion Compounds[a,b]

1	EtOH (1:1), 1-PrOH (1:1), 2-PrOH (1:1), 2-BuOH (1:1), *t*-BuOH (1:1), *N*-methylformamide (1:1), DMF (1:1), *N,N*-diethylformamide (1:1), DMSO (1:1), THF (1:1), 1,4-dioxane (1:1), morpholine (1:2)
2	HCOOH (2:1), MeCOOH (1:1), EtCOOH (1:1), BuCOOH (1:1), EtOH (1:1), 1-PrOH (1:1), 2-PrOH (1:1), 1-BuOH (1:1), 2-BuOH (1:1), *t*-BuOH (1:1), DMF (1:1), MeCN (1:1), EtCN (2:1), $MeNO_2$ (1:1), $EtNO_2$ (2:1), DMSO (1:1), Me_2CO (2:1), THF (1:1), 2-Me-THF (1:1), 1,3-dioxolane (2:1), 1,4-dioxane (1:1)
3	MeCOOH (2:1), EtOH (1:1), 1-PrOH (1:1), 2-PrOH (1:1), 2-BuOH (1:1), *t*-BuOH (2:1), DMSO (1:1), 1,4-dioxane (1:1)
4	EtOH (1:1), 2-PrOH (1:1), *t*-BuOH (1:1), *N*-methylformamide (1:1), DMF (1:1), DMSO (1:1), Me_2CO (1:1), THF (1:1), 1,4-dioxane (1:1)
5	MeCOOH (3:1), 2-PrOH (1:1), *t*-BuOH (1:2), *N*-methylformamide (1:2), DMF (1:1/1:2)[c], DMSO (1:2), THF (1:1), 1,4-dioxane (1:1)
6	MeOH (1:2), EtOH (1:2), *t*-BuOH (1:2), *N*-methylformamide (1:2), DMF (1:2), DMSO (1:2), 1,4-dioxane (1:1)
7	2-BuOH (1:2), *N,N*-dimethylacetamide (1:1), DMSO (1:2), 1,4-dioxane (1:2)
8	MeCOOH (1:1), EtCOOH (1:1), MeOH (1:1), EtOH (1:1), 1-PrOH (1:1), 2-PrOH (1:1), 1-BuOH (1:1), 2-BuOH (1:1), *t*-BuOH (1:1), *N*-methylformamide (1:1), DMF (1:1), *N,N*-dimethylacetamide (1:1), MeCN (2:1), $MeNO_2$ (1:1), DMSO (1:1), Me_2CO (1:1), THF (1:1), 1,3-dioxolane (1:1), 1,4-dioxane (1:1/2:1)[c], CH_2Cl_2 (1:1)
9	EtOH (1:1), 1-PrOH (1:1), 2-PrOH (1:1), *t*-BuOH (1:1), DMF (1:1), DMSO (1:1), THF (1:1), 1,3-dioxolane (1:1), 1,4-dioxane (1:1)
10	2-PrOH (1:1), *t*-BuOH (1:1), DMF (1:1), *N,N*-diethylformamide (1:1), *N,N*-dimethylacetamide (1:1), DMSO (1:1), THF (1:1), 1,4-dioxane (2:1)
14	MeCN (1:1), $MeNO_2$ (1:1), $EtNO_2$ (3:2), 1,3-dioxolane (3:2/2:1)[c], 1,4-dioxane (1:1), benzene (1:1), bromobenzene (1:1), *p*-xylene (1:1/2:1)[c]
16	1,4-dioxane (1:1), pyridine (1:1), benzene (1:1), toluene (1:1), *p*-xylene (2:1)
17	MeCN (1:1), 1,3-dioxolane (3:2)
19	MeCN (1:1), THF (3:1), 1,3-dioxolane (2:1), pyridine (1:1), benzene (1:1), bromobenzene (1:1), toluene (1:1), *o*-xylene (1:1)
20	1,3-dioxolane (2:1), 1,4-dioxane (2:1), pyridine (2:1), benzene (2:1)
22	MeOH (1:2), 2-BuOH (2:1), *N*-methylformamide (1:1), DMF (1:2), *N,N*-diethylacetamide (2:3), MeCN (1:1), $ClCH_2CN$ (2:1), EtCN (1:1), PrCN (1:2), PhCN (1:1), $MeNO_2$ (1:1), DMSO (1:2), Me_2CO (1:1), THF (1:1), 2-Me-THF (1:1), 1,3-dioxolane (2:1), 1,4-dioxane (2:1), toluene (3:1), *o*-xylene (1:1), *p*-xylene (3:1/1:1)[c]
23	MeCOOH (3:2), DMF (1:2), MeCN (1:2), $MeOCH_2CN$ (2:1), $EtNO_2$ (1:1), Me_2CO (2:1), 1,4-dioxane (1:2), *p*-xylene (3:1)
24	DMF (1:1), 1,4-dioxane (1:1)
25	MeOH (1:2), DMF (1:2), *N,N*-dimethylacetamide (1:2), *N*-methylformamide (1:1/2:3)[c], DMSO (1:2)

[a] Stoichiometries, host:guest, in parentheses. [b] Solvents mentioned in this table were tested separately for all hosts, as fast as possible (restriction: the carboxylic hosts were not fully tested with aromatic and heteroaromatic solvents, the ketone hosts were not fully tested with alcohols and acids, for reasons of solubility). Compounds not included by **1–25** are cyclopentane, cyclohexane, 1-phenylethanol, 2-phenylethanol, 2-picoline, 4-picoline, mesitylene, and cyclohexane. A more detailed specification is given in Table I of the supplementary material. [c] Ratio dependent on recrystallization conditions (concentration of components, rate of cooling).

methylformamide, but not with acids, 1-PrOH, 2-PrOH, $MeNO_2$, or MeCN. Compound **1** (lower homologue of **2**) gave no inclusions with acids. Host **7** (bridged derivative of **5**) only yields inclusions with 2-BuOH, dimethylacetamide, DMSO, and dioxane; **24** (cyclobutano host) forms inclusions with dioxane and DMF (no others).

Unlike the acids (**1–10**), the corresponding benzoyl derivatives (**14**, **16**, **17**, **19**, and **20**) do not allow inclusions with hydroxylic guests, but only with dipolar aprotic and apolar molecules (Table II) according to a complementary host–guest relationship.[3b,8c] The monofunctional compounds (**11–13**, **20**, and **21**) are either totally inactive or much poorer as inclusion formers than their bifunctional counterparts (e.g., **1**, **5**, **8**, **9**, **14**, and **19**). Nevertheless, of all hosts discussed here, **17** and **24** make available the lowest number of inclusion compounds with reference to the tested series of solvents (Table II), thus providing high clathrate formation specificity.

Inclusion selectivities derived from solvent competition experiments (two-component solvent systems) are summarized in Table III. For the carboxylic hosts it appears that DMF and DMSO are usually favored over other solvents (cf. **1**, **4**, and **25**). However, it is also possible to discriminate between DMF and DMSO, since DMSO is preferentially selected by **1** and DMF by **4**. Moreover, *t*-BuOH is easily separated from other alcohols by clathrate formation with **10**, etc. (see Table III). The noncarboxylic hosts also offer several analytically useful possibilities of compound separation.[15] The separation of *p*-xylene, or of *o*-xylene from *m*- and *p*-xylene, is an example (cf. **14** and **19**). Evidently, there are several factors (the nature, number, and position of functional groups, the substituents, ring size) controlling the inclusion properties of the new hosts.

X-ray Studies. In order to learn the building principles of the new clathrate family, we studied the X-ray crystal structures of **1**·*t*-BuOH (1:1), i.e., (protic host)·(protic guest compound), and of **17**·MeCN (1:1), i.e., (aprotic host)·(aprotic guest compound). For obvious reasons,[8c] the crystal structure of a free host compound, i.e., **1**, was also determined (Figures 2 and 3, parts a–c).

Table III. Selective Guest Inclusion from a Two-Component Solvent System (Representative Examples)[a]

host no.	recrystn solvent compd mixture (I/II)[b]	host:I:II mole ratio[c]
1	DMF/2-BuOH	1:1:0
	DMF/dioxane	1:1:0
	DMSO/2-BuOH	1:1:0
	DMSO/DMF	1:1:0
	dioxane/2-BuOH	1:1:0
	dioxane/THF	1:1:0
4	DMF/DMSO	1:1:0
	DMF/acetone	1:1:0
5	DMF/acetic acid	1:1:0
	dioxane/THF	1:1:0
10	*t*-BuOH/MeOH	1:1:0
	t-BuOH/2-PrOH	1:1:0
	t-BuOH/acetone	1:1:0
	DMF/*t*-BuOH	1:1:0
	DMSO/*t*-BuOH	1:1:0
	dioxane/2-PrOH	2:1:0
14	MeCN/benzene	1:1:0
	p-xylene/MeCN	2:1:0
	p-xylene/*o*-xylene	2:1:0
	p-xylene/*m*-xylene	2:1:0
19	benzene/toluene	1:1:0
	benzene/*o*-xylene	2:1:0
	o-xylene/*m*-xylene	1:1:0
	o-xylene/*p*-xylene	1:1:0
25	DMF/MeOH	1:2:0
	DMF/MeCN	1:2:0
	DMSO/MeOH	1:2:0

[a] A more detailed list of guest preferences is given in Table II in the supplementary material. [b] Equimolar ratio. [c] Determined by NMR integration of the isolated crystals (method of preparation and drying standard, cf. Experimental Section).

In the host molecule **1** (Figure 2, parts a and b) the cis positioning of the two carboxyl groups makes possible a rather short intramolecular H bond between them [O(21)···O(17) = 2.513 (3) and 2.552 (5) Å, O(21)–H(21) = 0.97 and 0.99 Å, H(21)···O(17) = 1.57 and 1.57 Å, O(21)–H(21)···O(17) = 162 and 170°, observed in the structures of the unsolvated host **1** and of the inclusion compound **1**·*t*-BuOH (1:1), respectively]. This H bond locks the

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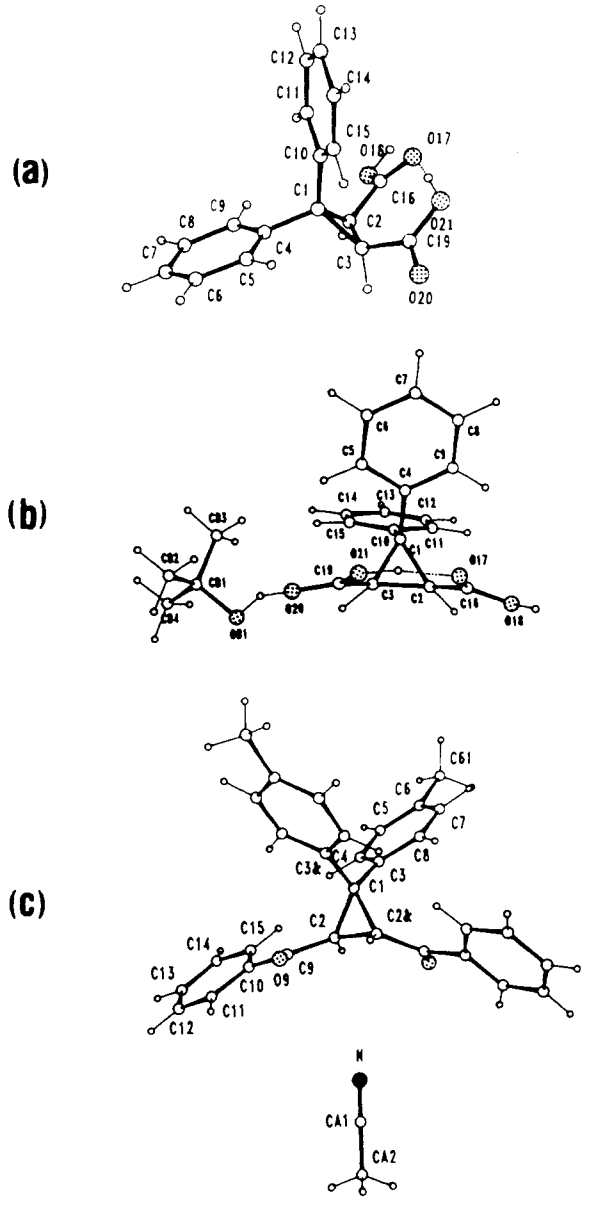

Figure 2. Molecular structures including atom numbering: (a) unsolvated **1**, (b) **1**·*t*-BuOH (1:1), (c) **17**·MeCN (1:1). Solid and dashed lines represent covalent and hydrogen bonds, respectively. O atoms are dotted; N atom is hatched.

COOH groups in a rigid conformation by closing a seven-membered ring (including the H atoms), fused to the cyclopropane. Dicarboxylic acids form extended, H-bonded chains in crystals, almost without exception.[16] A cyclic pair of O–H···O bonds is the most commonly observed coupling between carboxyl groups.[16] Nevertheless, in the structure of unsolvated host **1**, which contains an intramolecular H bond between the two neighboring carboxyl groups, the molecules may be interlinked only by the more rarely encountered catemer[16] motif: strong linear H bonds [O(18)···O-(20)$_{1+x,y,z}$ = 2.590 (3) Å, O(18)–H(18) = 1.00 Å, H(18)···O(20) = 1.60 Å, O(18)–H(18)···O(20) = 180°] unite successive molecules in the crystallographic *a* direction into endless chains (Figure 3a). Adjacent chains, related by 2_1 (twofold screw axis) symmetry, are separated from each other by C–(H)··O contacts of >3.4 Å [C(13)···O(17)$_{1-x,1/2+y,2-z}$ = 3.405 (5) Å, C(14)···O(20)$_{-x,1/2+y,2-z}$ = 3.460 (5) Å].

Earlier X-ray studies revealed that inclusions of different alcoholic guests by carboxylic hosts, such as 1,1′-binaphthyl-2,2′-dicarboxylic acid[4] or *trans*-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboxylic acid,[7] are characterized by the basic structural pattern of extended closed loops of H bonds. Inclusion of the alcoholic guest by host **1** in **1**·*t*-BuOH (1:1), however, does not result in closed rings but in infinite helical chains (Figure 3b). In these supramolecular H-bonded helices, host and guest molecules alternate [O(18)···O(1B)$_{1/2+x,1/2-y,1-z}$ = 2.566 (6) Å, O-(18)–H(18) = 1.11 Å, H(18)···O(1B) = 1.52 Å, O(18)–H-(18)···O(1B) = 155°, and O(1B)···O(20)$_{x,y,z}$ = 2.861 (6) Å, O(1B)–H(1B) = 1.06 Å, H(1B)···O(20) = 1.94 Å, O(1B)–H-(1B)···O(20) = 144°]. All the helices in the structure have the same sense, so as to yield the enantiomorphous space group $P2_12_12_1$. One may see in the structure cooperative self-organization of a supramolecular unit. Interactions of this type are of current interest.[17]

Host **17** in its MeCN clathrate displays exact crystallographic twofold (C_2) rotation symmetry with atom C(1) on the rotation axis (Figure 2c). Also the "linear" acetonitrile molecule, except the methyl H atoms, which are each distributed on two half-occupied general sites, has been located along the twofold crystallographic axis. Accordingly, the crystallographic asymmetric unit contains only half a host and half a guest molecule. The packing structure of **17**·MeCN (1:1) (Figure 3c) shows the guest molecules to be held in the host framework by steric barriers only. These are, however, completely efficient in forming a tight enclosure of the guest molecules. Molecules that are but slightly larger than MeCN, or slightly different in shape, would not fit into the present crystal cavity. On the other hand, the extremely high selectivity of **17** for MeCN (besides MeCN, only a comparatively weak inclusion[14] of 1,3-dioxolane is obtainable) suggests that other suitable packings in the crystal hardly exist for this bulky host molecule.

Conclusions. A new class of host molecules has been found and shown to efficiently enclathrate organic molecules. These hosts are superior to known clathrate formers[2] in more than one respect. They are readily available by common synthetic methods. They allow structural modification in many ways [e.g., changes in the number of bulky or functional groups or both around the ring (cf. Figure 1), introduction of other substituents, or variation of the substitution pattern].[18] As a rule, the inclusions are highly selective and their crystal quality is excellent, which makes isolation easy. The crystal structures illustrate that inclusions of very different character (H-bonded complexes and true lattice-type clathrates)[19] are possible within the new host family. Since some compounds among the hosts (e.g., **5**, **8**, **16**, **20**) may be prepared in optically active form, there is also a potential for resolution of racemic guests (cf. ref 2b, Vol. 140). Thus, the new host family is promising for practical applications.[20]

Experimental Section

(1) General Procedures. 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 determined on a Pye-Unicam SP-1100 spectrometer. Mass spectra were recorded on an AEI MS-50 mass spectrometer. Satisfactory elemental analytical data (±0.3% for C, H, and N) were obtained for all new compounds. Starting materials were purchased from Janssen (Nettetal-2, West Germany).

(2) Synthesis. Host compounds 1–4 (cis-acids) were obtained from maleic anhydride and the corresponding diaryldiazomethane following the method of van Alphen.[21] A representative procedure is given for the preparation of **2**.

Bis(4-methylphenyl)diazomethane[22] (12.8 g, 58 mmol) and maleic anhydride (5.65 g, 58 mmol) were dissolved in dry diethyl ether (200 mL). The precipitate of pyrazoline that formed was collected, dissolved in benzene, and heated to reflux. The solvent was removed and the

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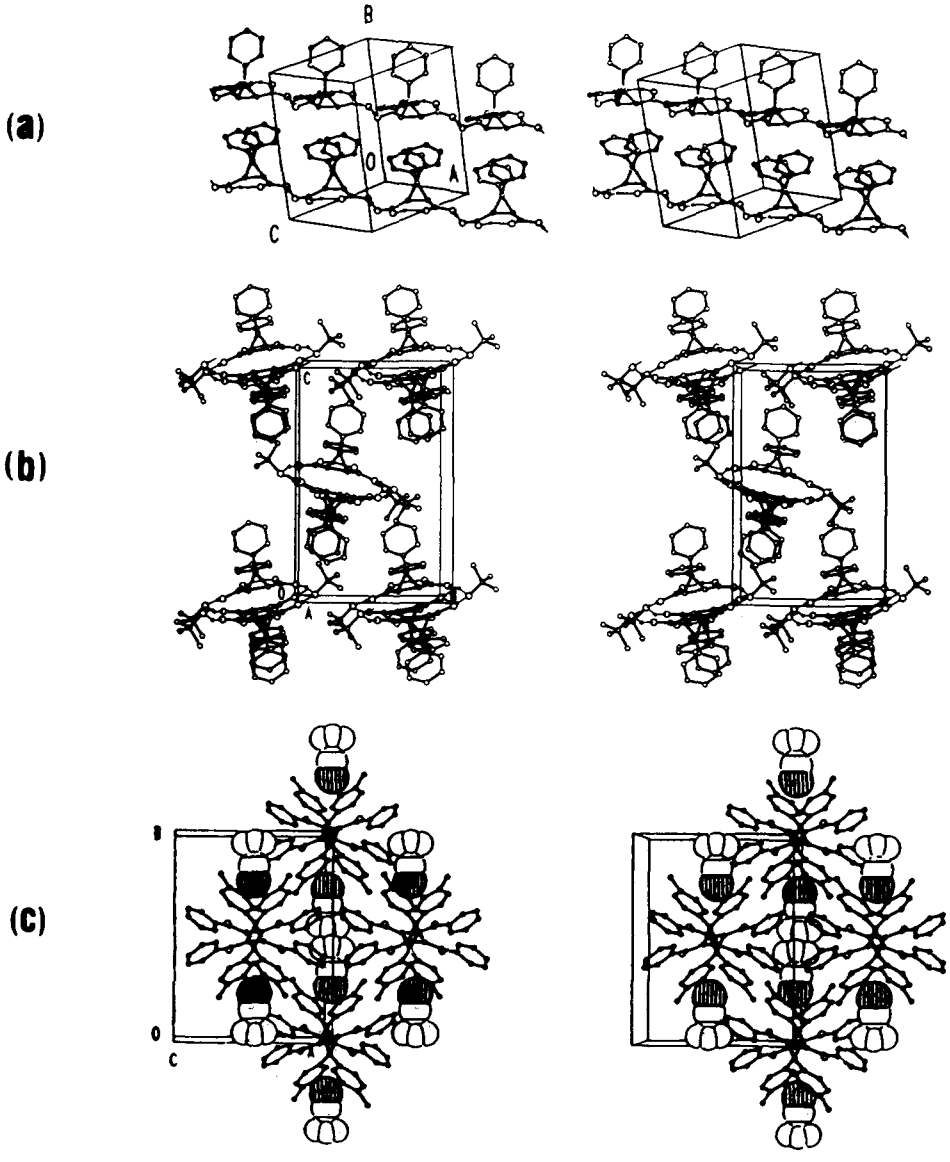

Figure 3. Stereoscopic packing diagrams: (a) unsolvated **1**, (b) **1**·*t*-BuOH (1:1), (c) **17**·MeCN (1:1). O atoms are specified by larger spheres; H atoms are omitted, except those involved in H bonds. H bonds are indicated as thin lines. In (c), the host molecule is in ball-and-stick, the guest molecule in van der Waals representation; N atoms are hatched.

residue treated with warm 2 N aqueous KOH. Filtration and acidification by dilute HCl gave the product as a colorless powder (overall yield 31%). Recrystallization from EtOH yielded the 1:1 inclusion compound of **2** as colorless crystals (mp 110–112 °C). Crystals of unsolvated **2** could not be obtained from any solvent. Specific details for each compound are given below.

(a) 3,3-Diphenylcyclopropane-*cis*-1,2-dicarboxylic acid (1): From diphenyldiazomethane[23] with maleic anhydride; 21%; recrystallization from acetone/H_2O gave colorless crystals, mp 204–206 °C dec (lit.[21] mp 204 °C).

(b) 3,3-Bis(4-methylphenyl)cyclopropane-*cis*-1,2-dicarboxylic acid (2): See procedure. ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 2.28 (s, 6 H, CH_3), 2.80 (s, 2 H, cyclopropane H), 7.02–7.48 (m, 8 H, aryl), 12.7 (s, br, 2 H, COOH); MS *m/e* 292 ($M^+ - H_2O$).

(c) 3,3-Bis(4-chlorophenyl)cyclopropane-*cis*-1,2-dicarboxylic acid (3): From bis(4-chlorophenyl)diazomethane[22,23] with maleic anhydride; 38%; recrystallization from EtOH gave the 1:1 inclusion compound with EtOH; mp >110 °C dec. Unsolvated **2** was obtained by dissolution in aqueous KOH and acidification with dilute HCl. The precipitate was collected and dried (15 Torr, 50 °C): ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 2.88 (s, 2 H, cyclopropane H), 7.21–7.58 (m, 8 H, aryl), 11.8 (s, br, 2 H, COOH); MS *m/e* 304 ($M^+ - CO - H_2O$).

(d) Spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid (4): From 9-diazofluorene[24] with maleic anhydride; 50%; recrystallization from acetic acid gave colorless crystals, mp 226–227 °C dec (lit.[25] mp 229 °C dec; lit.[26] mp 192 °C dec).

Host compounds 5–7 (trans-acids) were obtained from diethyl fumarate and the corresponding diaryldiazomethane following the method of Staudinger.[27,28] The procedure is the same as specified for **2**. Details for each compound are given below.

(a) 3,3-Diphenylcyclopropane-*trans*-1,2-dicarboxylic Acid (5). Diphenyldiazomethane[23] was reacted; 61% yield; recrystallization from acetonitrile gave colorless crystals, mp 299–301 °C (lit.[21] 290 °C).

(b) 3,3-Bis(4-methylphenyl)cyclopropane-*trans*-1,2-dicarboxylic Acid (6). Bis(4-methylphenyl)diazomethane[22] was reacted; 43% yield; recrystallization from acetonitrile gave colorless crystals: mp 284–286 °C; ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 2.29 (s, 6 H, CH_3), 3.12 (s, 2 H, cyclopropane H), 7.11, 7.40 (AA′BB′, J_{AB} = 8 Hz, 8 H, aryl), 11.5 (s, br, 2 H, COOH); HR MS, *m/e* calcd for $C_{19}H_{18}O_4$ (M^+) 310.1200, found 310.1214.

(c) Spiro[cyclopropane-1,9′-fluorene]-*trans*-2,3-dicarboxylic Acid (7). 9-Diazofluorene[24] was reacted; 62% yield; recrystallization from acetic acid gave colorless crystals, mp >300 °C dec (lit.[27] mp >270 °C; lit.[26] mp >250 °C).

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***cis*-1,2-Diphenylcyclopropane-1,2-dicarboxylic Acid (8).** Reaction[29] of ethyl α-phenylacrylate[30] with ethyl α-chlorophenylacetate[31] and NaH in dry toluene followed by saponification of the corresponding ester yielded (51%) colorless crystals (from chloroform), mp 183–184 °C (lit.[29] mp 183–184 °C).

2,2-Diphenylcyclopropane-1,1-dicarboxylic Acid (9). Reaction[32] of ethylene-1,1-dicarboxylic acid[33] with diphenyldiazomethane[23] in petroleum ether and saponification of the corresponding ester yielded (93%) a white powder. Recrystallization from acetonitrile gave colorless crystals: mp 111–115 °C dec; ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 2.59 (s, 2 H, cyclopropane H), 7.10–7.55 (m, 10 H, aryl), 8.1 (s, br, 2 H, COOH); HR MS m/e calcd for $C_{17}H_{14}O_4$ (M^+) 282.0888, found 282.0897.

1-Cyano-2,2-diphenylcyclopropane-1-carboxylic Acid (10). Reaction[11] of ethyl 1-cyano-2-phenylcinnamate[34] with trimethylsulfoxonium iodide and NaH in dry DMSO followed by saponification of the corresponding ester yielded (80%) colorless crystals (from acetone), mp 177–179 °C (lit.[11] mp 177–178 °C).

Monoacids 11–13 were synthesized from the respective alkene with ethyl diazoacetate in benzene on addition of anhydrous copper sulfate and subsequent saponification of the corresponding ester following the procedure of Blatchford and Orchin.[35]

(a) 2,2-Diphenylcyclopropanecarboxylic Acid (11). 1,1-Diphenylethylene was reacted; 55%; colorless crystals (from MeOH/H_2O); mp 170 °C (lit.[36] mp 170–171 °C).

(b) 2*t*,3*t*-Diphenylcyclopropane-1*r*-carboxylic Acid (12). (*Z*)-Stilbene was reacted; 81%; colorless crystals (from EtOH/H_2O); mp 151–153 °C (lit.[35] mp 154.5–155.5 °C).

(c) 2*c*,3*t*-Diphenylcyclopropane-1*r*-carboxylic Acid (13). (*E*)-Stilbene was reacted; 77%; colorless crystals (from MeOH/H_2O); mp 155–157 °C (lit.[35] mp 157–158 °C).

Benzoyl-substituted cyclopropanes 14–21 were obtained from the respective alkene on treatment with the corresponding diazo compound following the procedures of Smith and Howard,[37] and Horner and Lingnau.[26] Specific details for each compound are given below.

(a) *trans*-2,3-Dibenzoyl-1,1-diphenylcyclopropane (14): From (*E*)-1,2-dibenzoylethylene with diphenyldiazomethane;[23] 30%; colorless crystals (from ethyl acetate/petroleum ether); mp 177–178 °C (lit.[37] mp 179 °C).

(b) *trans*-2,3-Dibenzoyl-1-(4-methylphenyl)-1-phenylcyclopropane (15): From (*E*)-1,2-dibenzoylethylene with (4-methylphenyl)phenyldiazomethane[38] in $CHCl_3$; recrystallization from acetonitrile yielded (10%) colorless crystals: mp 212–213 °C; ^{1}H NMR ($CDCl_3$) δ 2.21 (s, 3 H, CH_3), 4.55 (s, 2 H, cyclopropane H), 6.82–8.16 (m, 19 H, aryl); IR (KBr) 3090 (CH, cyclopropane), 1680 (C=O), 1605, 1590, 1500 (aryl) cm^{-1}; HR MS m/e calcd for $C_{30}H_{24}O_2$ (M^+) 416.1770, found 416.1767.

(c) *trans*-2,3-Dibenzoyl-1-(4-nitrophenyl)-1-phenylcyclopropane (16): From (*E*)-1,2-dibenzoylethylene with (4-nitrophenyl)phenyldiazomethane[39] in $CHCl_3$; recrystallization from acetonitrile yielded (38%) colorless crystals: mp 234–236 °C; ^{1}H NMR ($CDCl_3$) δ 4.63 (s, 2 H, cyclopropane H), 7.28–8.19 (m, 19 H, aryl); IR (KBr) 3100 (CH, cyclopropane), 1675 (C=O), 1605, 1530 (aryl) cm^{-1}; HR MS m/e calcd for $C_{29}H_{21}NO_4$ (M^+) 447.1465, found 447.1473.

(d) *trans*-2,3-Dibenzoyl-1,1-bis(4-methylphenyl)cyclopropane (17): From (*E*)-1,2-dibenzoylethylene with bis(4-methylphenyl)diazomethane[22] in $CHCl_3$; recrystallization from acetone yielded (46%) colorless crystals: mp 229–231 °C; ^{1}H NMR ($CDCl_3$) δ 2.30 (s, 6 H, CH_3), 4.77 (s, 2 H, cyclopropane H), 7.25–8.61 (m, 8 H, aryl); IR (KBr) 3090 (CH, cyclopropane), 1670 (C=O), 1605, 1590, 1520 (aryl) cm^{-1}; HR MS, m/e calcd for $C_{31}H_{26}O_2$ (M^+) 430.1926, found 430.1950.

(e) *trans*-2,3-Dibenzoyl-1,1-bis(4-chlorophenyl)cyclopropane (18): From (*E*)-1,2-dibenzoylethylene with bis(4-chlorophenyl)diazomethane[22,23] in $CHCl_3$; recrystallization from acetonitrile yielded (8.5%) colorless crystals: mp 240–242 °C; ^{1}H NMR ($CDCl_3$) δ 4.55 (s, 2 H, cyclopropane H), 7.03–8.09 (m, 18 H, aryl); IR (KBr) 3100 (CH, cyclopropane), 1670 (C=O), 1605, 1590, 1500 (aryl) cm^{-1}; HR MS, m/e calcd for $C_{29}H_{20}Cl_2O_2$ (M^+) 470.0836, found 470.0838.

(f) *trans*-2,3-Dibenzoylspiro[cyclopropane-1,9′-fluorene] (19): From (*E*)-1,2-dibenzoylethylene with 9-diazofluorene[24] in benzene; 95%; colorless crystals (from acetonitrile); mp 203 °C (lit.[38] mp 203 °C).

(g) *trans*-3-Benzoyl-1,2,2-triphenylcyclopropane (20): From chalcone with diphenyldiazomethane[23] in benzene; recrystallization from acetonitrile yielded (35%) colorless crystals: mp 100–103 °C; ^{1}H NMR ($CDCl_3$) δ 4.18 (s, 2 H, cyclopropane H), 7.10–8.27 (m, 20 H, aryl); IR (KBr) 3100 (CH, cyclopropane), 1670 (C=O), 1605, 1590, 1505 (aryl) cm^{-1}; HR MS m/e calcd for $C_{28}H_{22}O$ (M^+) 374.1665, found 374.1688.

(h) *trans*-2-Benzoyl-3-phenylspiro[cyclopropane-1,9′-fluorene] (21): From chalcone with 9-diazofluorene[24] in benzene; 51%; colorless crystals (from acetonitrile); mp 186–188 °C (lit.[26] mp 186 °C).

Tetracyanocyclopropanes 22 and **23** were synthesized following the procedure of Franz.[40]

(a) 3,3-Diphenyl-1,1,2,2-cyclopropanetetracarbonitrile (22): From tetracyanoethylene in benzene/acetonitrile (4:1) with diphenyldiazomethane[23] in diethyl ether; 93%; colorless crystals (from EtOH); mp 271–272 °C dec (lit.[40] mp 276–278 °C dec; lit.[41] mp 265–266 °C dec).

(b) Spiro[cyclopropane-1,9′-fluorene]-2,2,3,3-tetracarbonitrile (23): From tetracyanoethylene in benzene/acetonitrile (4:1) with 9-diazofluorene[24] in diethyl ether; 78%; colorless crystals (from MeOH); mp 245–248 °C dec; IR (KBr) 3100 (CH, cyclopropane), 2260 (C=N) cm^{-1}; HR MS, m/e calcd for $C_{19}H_8N_4$ (M^+) 292.0748, found 292.0747.

Cyclobutanecarboxylic acids 24 and **25** were obtained by solid-phase photodimerization of (*E*)-cinnamic acids in accordance with literature procedures.[12,13]

(a) 3*t*,4*t*-Diphenylcyclobutane-1*r*,2*c*-dicarboxylic Acid (β-Truxinic Acid) (24). Finely ground (*E*)-cinnamic acid (β-modification)[42] was suspended in water and irradiated (Pyrex apparatus) by a Hg high-pressure lamp for 7 days. The solid was collected, dried, and extracted with ether to remove unreacted (*E*)-cinnamic acid. Recrystallization from EtOH gave (28%) colorless crystals, mp 207–209 °C (lit.[13] mp 210 °C).

(b) 2*c*,4*t*-Diphenylcyclobutane-1*r*,3*t*-dicarboxylic acid (α-truxillic acid) (25): From (*E*)-cinnamic acid analogously to **24**; 35%; colorless crystals (from EtOH); mp 290–292 °C (lit.[12] mp 290–292 °C; lit.[43] mp 283–284 °C).

(3) Preparation of the Clathrates. General Procedure. The corresponding host compound was dissolved under 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 an inert solvent (ether, MeOH, or CH_2Cl_2), and dried (1 h, 15 Torr, room temperature). Host:guest stoichiometry of the isolated crystals was determined by NMR integration. Data for each compound are given in Table II.

(4) Crystallography. (a) Data Collection and Processing. Crystals of the compounds suitable for X-ray crystallography were obtained as described above. In order to prevent the crystals of the inclusion compounds from possible solvent evaporation during measurement they were sealed in epoxy glue.

The intensity data were obtained on a Siemens STOE/AED2 diffractometer equipped with a graphite monochromator and Cu Kα radiation (λ = 1.5418 Å, θ_{max} = 70°) by the ω–2θ scan technique. Data reduction included correction for background, Lorentz, and polarization effects, but the rather low absorption effects were neglected. The unit cell parameters were refined against angular settings of well-centered strong reflections [23 for **1**, 24 for **1**·*t*-BuOH (1:1), and 60 for **17**·MeCN (1:1)], measured on the diffractometer within the range 28° < 2 θ < 60°.

Crystal data: 1 (unsolvated): $C_{17}H_{14}O_4$, M_w = 282.295, monoclinic, $P2_1$, a = 7.339 (2) Å, b = 11.657 (4) Å, c = 9.149 (3) Å, β = 110.07 (4)°, Z = 2, ρ_c = 1.275 g cm^{-3}, μ = 7.10 cm^{-1}. Final R = 0.048 and R_w = 0.064 for 1312 reflections.

1·*t*-BuOH (1:1): $C_{17}H_{14}O_4$·$C_4H_{10}O$, M_w = 356.418, orthorhombic, $P2_12_12_1$, a = 9.782 (1) Å, b = 11.376 (1) Å, c = 17.603 (1) Å, Z = 4, ρ_c = 1.208 g cm^{-3}, μ = 6.63 cm^{-1}. Final R = 0.052 and R_w = 0.072 for 1157 observations.

17·MeCN (1:1): $C_{31}H_{26}O_2$·C_2H_3N, M_w = 471.598, orthorhombic, $Pbcn$, a = 12.314 (1) Å, b = 16.074 (1) Å, c = 12.938 (1) Å, Z = 4, ρ_c

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= 1.223 g cm^{-3}, μ = 5.54 cm^{-1}. Final R = 0.054 and R_w = 0.088 for 1698 reflections.

(b) Structure Analysis and Refinement. The structures were solved by direct methods (SHELXS)[44] and refined by full-matrix least-squares treatments based upon F (SHELX).[45] The carboxylic hydrogens in the unsolvated host molecule **1**, the carboxylic and alcoholic H atoms in structure **1**·*t*-BuOH (1:1), and all hydrogens except those of the methyl group of the host in the **17**·MeCN (1:1) clathrate were located from difference electron density calculations, and their positions were kept riding on their respective mother atoms during the refinements. The remaining, carbon-bonded H atoms in the free host molecule and in the inclusion compound with *t*-BuOH and the methyl hydrogens of the host in **17**·MeCN (1:1) were given assumed positions, calculated after each cycle of the refinements. The C, O, and N atom positions were refined together with their anisotropic thermal parameters; an isotropic group temperature factor was refined for the H atoms in the unsolvated host molecule **1** and in the inclusion compound with *t*-BuOH, respectively, and individual temperature factors were refined for the non-methyl H positions in the structure of **17**·MeCN (1:1). The methyl groups in this latter structure, both of the host and of the guest, were treated as rigid groups with free rotation, and one isotropic group temperature factor was refined for each of them. Only data with $F > 6\sigma(F)$ were used in the refinement calculations. Final R values are included with the crystal data for each compound. Weights of the structure factors were calculated as w = const/$[\sigma^2(F) + g(F^2)]$ with const = 1.0, and the g value was refined to 0.060 12 for unsolvated **1**, 0.009 82 for **1**·*t*-BuOH (1:1), and 0.015 07 for **17**·MeCN (1:1). Final atomic coordinates and thermal parameters, observed bond distances, and bond angles are listed in Tables III-VI (supplementary material).

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Supplementary Material Available: Complete lists of isolated inclusion compounds including specification of solvents not allowing inclusion formation for each host (Table I) and of guest preferences (Table II) and crystallographic data for compounds **1**, **1**·*t*-BuOH (1:1), and **17**·MeCN (1:1) such as fractional atomic coordinates of the non-hydrogen atoms, bond distances and bond angles, and anisotropic thermal parameters of the non-hydrogen atoms (Tables III-VI) (21 pages). Ordering information is given on any current masthead page.

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Unifying the Solution Thermochemistry of Molecules, Radicals, and Ions[1]

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Abstract: A general cycle was developed that defines the thermodynamics for all of the homolytic and heterolytic cleavage reactions of a hydrocarbon, R-R′, in solution. Only seven experimental parameters were needed in order to define the energetics for all 11 of the possible cleavage reactions of R-R′. These parameters were the oxidation and reduction potentials of R-R′, R$^\bullet$, and R′$^\bullet$ and the homolytic, R-R′, bond energy. The utility of this approach was demonstrated for the case where R was an arylmethyl group and R′ was hydrogen. The oxidation and reduction potentials of the arylmethyl radicals were measured by modulation voltammetry in acetonitrile, and the homolytic C-H bond energies of the corresponding hydrocarbons were measured by photoacoustic calorimetry. The cycle was also extended to a case where R-R′ was a radical rather than a closed-shell molecule.

In the gas phase, the thermodynamic relationships between molecules and their related ions are easily understood and are well-defined in terms of familiar parameters. Homolytic bond dissociation enthalpies relate the thermochemical properties of molecules to those of radicals while ionization potentials and electron affinities tie the thermochemistry of neutral species to those of their corresponding ions. These properties have been studied extensively, and there is an abundant literature that describes them.[2]

The solution equivalents of ionization potentials and electron affinities are the electrochemical oxidation and reduction potentials. A number of thermochemical cycles have appeared in the literature in which combinations of homolytic bond energies and electrochemical potentials have been used to calculate other thermodynamic properties. These have included pK_a values for hydrocarbons[3,4] and for radical cations[5,6] and pK_R values for carbocations.[7] Most of the recent activity has focused on the interplay between hydrocarbon acidities, carbanion oxidation potentials, and homolytic bond energies[8] (eq 1-3).

$$\text{R-H} \rightarrow \text{R}^- + \text{H}^+ \quad (1)$$

$$\text{R}^- \rightarrow \text{R}^\bullet \quad (2)$$

$$\text{R-H} \rightarrow \text{R}^\bullet + \text{H}^\bullet \quad (3)$$

In this work, we have established a general scheme that links the thermochemical properties of a compound R-R′ to those of

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(2) For example, see: Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data* **1988**, *17*, supplement 1.

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