Chem. Mater. 1994, 6, 1282–1292

3-(3′,5′-Dinitrophenyl)-4-(2′,5′-dimethoxyphenyl)cyclobutane-1,2-dicarboxylic Acid: Engineered Topochemical Synthesis and Molecular and Supramolecular Properties

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Received January 3, 1994. Revised Manuscript Received March 11, 1994[●]

The title compound (**1b**), synthesized using the principles of crystal engineering, exhibits interesting molecular and supramolecular properties. Diacid **1b** crystallizes in the triclinic space group $P\bar{1}$, $a = 8.150(1)$, $b = 8.927(2)$, $c = 17.894(4)$ Å; $\alpha = 98.91(1)$, $\beta = 97.60(1)$, $\gamma = 110.62(2)°$, and the structure was solved and refined to an R factor of 0.063 on 2910 nonzero reflections. Intramolecular charge transfer in **1b** was studied spectroscopically. Through-bond coupling (TBC) and the resultant C–C bond elongation are observed in **1b** to a moderate extent. A more general Cambridge Structural Database (CSD) study on 1,2-diphenylethanes provides clear evidence for the molecular attributes required for TBC. Diacid **1b** forms a host–guest complex with toluene in which the orientation of the guest molecule is perfectly tuned to the steric and electronic requirements of the host. The toluene guest molecule induces a convergent supramolecular cage, while another divergent supermolecule results because of the zigzag hydrogen-bonded chains of carboxyl groups. A water molecule, seemingly inadvertently trapped in the carboxyl channels, is not involved in hydrogen bonding but is a mere space filler. A general analysis of the solvation properties of benzene, toluene, and water is presented.

A distinctive feature of modern chemistry, and one which is reflective of the coming together of the various subbranches of the subject, is the fact that a wide variety of concepts, strategies, and techniques are used in a single study. Nowhere is this more apparent than in organic materials chemistry which attempts to link synthesis, structure, and properties to obtain a clearer understanding of organic solids. Such an understanding in turn provides insight into many observed chemical, physical, and biological processes such as molecular recognition,[1] crystal engineering,[2] and supramolecular function.[3]

Molecular assembly and architecture of a wide and sophisticated variety of organic supermolecules often requires the synthesis of novel building-block molecules with desired information sites.[3] Such molecules may on occasion be difficult to synthesize conventionally. A case in point are β-truxinic acids such as **1a** which are problematic to make in solution but not so in the solid state.[4] Our attention was drawn to unsymmetrical β-truxinic acids[5] such as the title compound **1b** on account of their possible applications as clathrate hosts. These unsymmetrical derivatives are unusual and must in principle be prepared via solid-state 2+2 cycloaddition reactions of cinnamic acid molecular complexes.

In this paper we report the engineered topochemical synthesis of the title compound **1b** and show that it can be used as a model to study several interesting molecular and supramolecular properties. The methodology adopted here for the solid-state synthesis is to use donor–acceptor π–π interactions to bring together to within the topochemical threshold distance, two "potentially reactive" alkenic double bonds from two electronically distinctive cinnamic acids. This is shown in Scheme 1, from which it is clear that the product cyclobutane will have donor and acceptor groups in a cofacial relationship leading to cleft formation; this feature can be exploited for the selective binding of simple aromatic compounds. Further, the proximity of the donor and acceptor phenyl rings in **1b** makes it a good model compound for the study of intramolecular charge transfer.[6,7] Additionally, the rigid

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[●] Abstract published in *Advance ACS Abstracts,* August 15, 1994.

(1) (a) Etter, M. C.; Urbanczyk-Lipkowska, Z.; Zia-Ebrahimi, M.; Panunto, T. W. *J. Am. Chem. Soc.* **1990,** *112,* 8415. (b) Whitesides, G. M. *Angew. Chem., Int. Ed. Engl.* **1990,** *29,* 1209. (c) Rebek, J. Jr. *Angew. Chem., Int. Ed. Engl.* **1990,** *29,* 245. (d) Sharma, C. V. K.; Panneerselvam, K.; Pilati, T.; Desiraju, G. R. *J. Chem. Soc., Chem. Commun.* **1992,** 832. (e) Copp, S. B.; Subramanian, S.; Zaworotko, M. J. *J. Am. Chem. Soc.* **1992,** *114,* 8719. (f) Kickham, J. E.; Loeb, S. J.; Murphy, S. J. *J. Am. Chem. Soc.* **1993,** *115,* 7031. (g) Ashton, P. R.; Reder, A. S.; Spencer, N.; Stoddart, J. F. *J. Am. Chem. Soc.* **1993,** *115,* 5286. (h) Chang, Y.; West, M.; Fowler, F. W.; Lauher, J. W. *J. Am. Chem. Soc.* **1993,** *115,* 5991. (i) Geib, S. J.; Vicent, C.; Fan, E.; Hamilton, A. D. *Angew. Chem., Int. Ed. Engl.* **1993,** *32,* 119. (j) Yang, J.; Fan, E.; Geib, S. J.; Hamilton, A. D. *J. Am. Chem. Soc.* **1993,** *115,* 5314. (k) Biradha, K.; Sharma, C. V. K.; Panneerselvam, K.; Shimoni, L.; Carrell, H. L.; Zacharias, D. E.; Desiraju, G. R. *J. Chem. Soc., Chem. Commun.* **1993,** 1473.

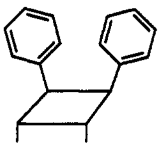
(2) Desiraju, G. R. *Crystal Engineering. The Design of Organic Solids*; Elsevier: Amsterdam, 1989.

(3) (a) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1990,** *28,* 1304. (b) Atwood, J. L.; Orr, G. W.; Bott, S. G.; Robinson, K. D. *Angew. Chem., Int. Ed. Engl.* **1993,** *32,* 1093. (c) Seto, C. T.; Whitesides, G. M. *J. Am. Chem. Soc.* **1993,** *115,* 905. (d) Anelli, P. L.; Ashton, P. R.; Ballardini, R.; Balzani, V.; Delgado, M.; Gandolfi, M. T.; Goodnow, T. T.; Kaifer, A. E.; Philp, D.; Pietraszkiewicz, M.; Prodi, L.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Vicent, C.; Williams, D. J. *J. Am. Chem. Soc.* **1992,** *114,* 193. (e) Reddy, D. S.; Panneerselvam, K.; Pilati, T.; Desiraju, G. R. *J. Chem. Soc., Chem. Commun.* **1993,** 661. (f) Reddy, D. S.; Goud, B. S.; Panneerselvam, K.; Desiraju, G. R. *J. Chem. Soc., Chem. Commun.* **1993,** 663.

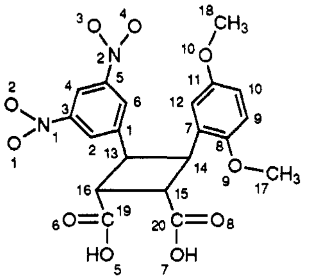
(4) Cohen, M. D.; Schmidt, G. M.; Sonntag, F. I. *J. Chem. Soc.* **1964,** 2000.

(5) Desiraju, G. R.; Sharma, C. V. K. M. *J. Chem. Soc., Chem. Commun.* **1991,** 1239.

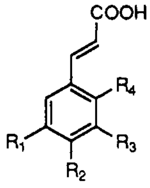
0897-4756/94/2806-1282$04.50/0



1a



1b



2a: $R_1 = R_3 = NO_2$; $R_2 = R_4 = H$
2b: $R_2 = R_4 = NO_2$; $R_1 = R_3 = H$
2c: $R_2 = R_3 = OMe$; $R_1 = R_4 = H$
2d: $R_1 = R_4 = OMe$; $R_2 = R_3 = H$
3a: **2b**:**2c**; **3b**: **2b**:**2d**; **3c**: **2a**:**2c**; **3d**: **2a**:**2d**

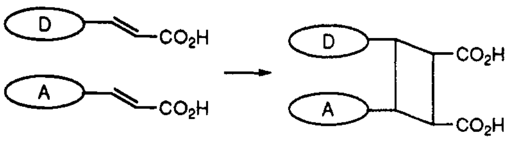
parallel orientation of phenyl groups with respect to the connecting central C–C single bond is a prerequisite for the phenomenon of through-bond coupling (TBC)[6,8] and the consequent C–C bond elongation provides a good opportunity to study this phenomenon also. We have used X-ray crystallography, semiempirical calculations, electronic spectroscopy, and the Cambridge Structural Database (CSD) to study these properties of diacid **1b**. Similar multifaceted approaches to the study of supramolecular[1,3] and materials chemistry[9] are being used in several laboratories today and were used by Etter in many thought-provoking studies. It is therefore appropriate that this paper appears in a collection which commemorates her contribution to solid-state and structural chemistry.

Experimental Section

Synthesis. The cinnamic acids **2a**, **2c**, and **2d** were prepared by Knoevenagel condensation, and the acid **2b** was prepared by Perkin condensation from the corresponding aldehydes. 3,5-Dinitrobenzaldehye was prepared by the reduction of 3,5-dinitrobenzoic acid to 3,5-dinitrobenzyl alcohol with diborane/THF at 0 °C in a N_2 atmosphere followed by oxidation with pyridinium chromyl chloride (PCC) in CH_2Cl_2.

The 1:1 mixed crystals **3b**[10] (mp 143 °C), **3c** (mp 155 °C), and **3d**[5] (mp 158 °C) were obtained from EtOH or 2:1 toluene–benzene or by simple solid-state grinding of the constituent acids.[11] Powdered, crystalline **3b**, **3c**, and **3d** were coated thinly between glass plates separately and were irradiated in sunlight at ca. 25–30 °C. Complexes **3a**[12] and **3b** showed no reactivity at all even after irradiation for 2–3 months. Complexes **3c** and **3d**, however, yielded the corresponding truxinic acids in ca. 60% yield after 5 days. Material obtained by grinding might just as easily have been used for these solid-state reactions, and there is no need to prepare single crystals of the complex by solution recrystallization in order to carry out the solid-state reaction. We irradiated both recrystallized and ground single crystals of complexes **3c** and **3d** and an intimately ground 1:1 physical mixture of the respective acids but the final products (i.e, the unsymmetrical β-truxinic acids) were obtained in similar yields in either case. The reaction products were separated by column chromatography (silica gel, 3:2 hexane–EtOAc). The topochemical product obtained exclusively from **3d** is 3-(3′,5′-dinitrophenyl)-4-(2′,5′-dimethoxyphenyl)cyclobutane-1,2-dicarboxylic acid, $C_{20}H_{18}N_2O_{10}$, **1b**. NMR ($^2H_6$-acetone) δ 3.6 (s, 3H), 3.7 (s, 3H), 4.2, 4.7 (m, 4H), 6.6 (m, 2H), 6.9 (d, 1H), 8.35 (d, 2H), 8.65 (dd, 1H); MS (*m/z*, %) 446 M^+ (2%), (M–H_2O), 428 (30%), (M–NO_2), 400 (25%), ($C_{11}H_{12}O_4$), 208 (100%), ($C_{11}H_{12}O_4$–H_2O), 190 (40%), ($C_{11}H_{12}O_4$–OMe) 177 (50%). Crystals suitable for X-ray analysis were obtained by slow evaporation from a solution of **1b** in 5:1 MeOH–toluene. These crystals (mp 210 °C) are deep yellow and have a composition $(C_{20}H_{18}N_2O_{10}):(C_7H_8)_{0.5}:(H_2O)_{0.5}$.

Scheme 1



X-ray Crystallography. $C_{20}H_{18}N_2O_{10}$: $(C_7H_8)_{0.5}$:$(H_2O)_{0.5}$, M = 509.5, triclinic, space group $P\bar{1}$, a = 8.150(1), b = 8.927(2), c = 17.894(4) Å, α = 98.91(1), β = 97.60(2), γ = 110.62(2)°, V = 1178.95 Å^3, μ(Mo Kα) = 0.71 cm^{-1}, Z = 2, D_c = 1.435 g cm^{-3}. Intensity data were collected on an Enraf-Nonius FAST area detector diffractometer using Mo Kα radiation within the range of 2Θ, 2–70°. Unit-cell parameters were determined by a least-squares fit of the settings for 25 accurately centered high-angle reflections (10° ≤ 2Θ ≤ 30°). A total of 2910 reflections were considered nonzero at the 3.0σ level out of 5475 reflections collected. The structure was solved by direct methods (SHELXS 86)[13] and the refinement was carried out with the programme SHELX 76.[14] The toluene and water molecules were found to be disordered about centers of inversion. All H atoms were located from difference Fourier maps except the H atoms in the toluene molecule. All non-H atoms were refined anisotropically and H atoms were refined isotropically barring the disordered H atoms in the toluene and water. The R value converged at 0.063 and the weighted R value at 0.072. The final difference electron density map did not reveal any significant electron density above 0.52 and below −0.25 eÅ^{-3}. The atomic coordinates and equivalent isotropic thermal parameters are given in Table 1.

Database Studies. The CSD (version 5.00, 109 861 entries)[15] was searched for 1,2-diphenylethane derivatives to study the C13–C14 bond elongation and for benzene, toluene, and water inclusion compounds to examine the nature of solvent binding. Details of the questions framed for these two distinct problems are briefly discussed.

All 1,2-diphenylethanes (see I) were retrieved from the CSD using the 3D graphics option (Table 2). The atoms C13 and C14

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(6) Anstead, G. M.; Srinivasan, R.; Peterson, C. S.; Wilson, S. R.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1991**, *113*, 1378.

(7) (a) Nakazawa, T.; Murata, I. *J. Am. Chem. Soc.* **1977**, *99*, 1996. (b) Stobbe, M.; Kirchmeyer, S.; Adiwidjaja, G.; de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 171. (c) Maslak, P.; Chopra, A. *J. Am. Chem. Soc.* **1993**, *115*, 9331.

(8) Hoffman, R. *Acc. Chem. Res.* **1971**, *4*, 1.

(9) (a) Etter, M. C.; Frankenbach, G. M. *Chem. Mater.* **1989**, *1*, 10. (b) For an overview of Etter's contribution to this area see: Harris, K. D. M.; Hollingsworth, M. D. *Nature (London)* **1989**, *341*, 19. (c) Fagan, P. J.; Ward, M. D.; Calabrese, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 1698. (d) Prasad, P. N.; Reinhardt, B. A. *Chem. Mater.* **1990**, *2*, 660. (e) Frankenbach, G. M.; Etter, M. C. *Chem. Mater.* **1992**, *4*, 272. (f) Fagan, P. J.; Ward, M. D. *Sci. Amer.* **1992**, 48. (g) Li, S.; White, H. S.; Ward, M. D. *Chem. Mater.* **1992**, *4*, 1082.

(10) Sharma, C. V. K.; Panneerselvam, K.; Pilati, T.; Desiraju, G. R. *J. Chem. Soc., Perkin Trans 2* **1993**, 2209.

(11) It has been shown that mechanical grinding is a superior method of obtaining quantitative yields of many organic donor–acceptor complexes. Naturally, only polycrystalline material is obtained. (a) Rastogi, R. P.; Singh, N. B. *J. Phys. Chem.* **1966**, *70*, 3315. (b) Scheffer, J. R.; Wong, Y. F.; Patil, A. O.; Curtin, D. Y.; Paul, I. C. *J. Am. Chem. Soc.* **1985**, *107*, 4898. (c) Patil, A. O.; Pennington, W. T.; Desiraju, G. R.; Curtin, D. Y.; Paul, I. C. *Mol. Cryst. Liq. Cryst.* **1986**, *134*, 279. (d) Etter, M. C.; Frankenbach, G. M.; Bernstein, J. *Tetrahedron Lett.* **1989**, *30*, 3617.

(12) Sarma, J. A. R. P.; Desiraju, G. R. *J. Chem. Soc., Perkin Trans 2* **1985**, 1905.

(13) Sheldrick, G. M. SHELX 86. In *Crystallographic Computing 3*; Sheldrick, G. M., Kruger, C., Goddard, R., Eds.; Oxford University Press: Oxford, U.K., 1985; pp 175–189.

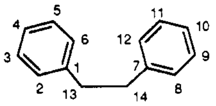
(14) Sheldrick, G. M. SHELX 76. Programme for Crystal Structure Determination, University of Cambridge, England, 1976.

(15) Allen, F. H.; Davies, J. E.; Galloy, J. J.; Johnson, O.; Kennard, O.; Macrae, C. F.; Watson, D. G. *J. Chem. Inf. Comput. Sci.* **1991**, *31*, 204.

Table 1. Fractional Coordinates and Equivalent Thermal Parameters for Diacid 1b (Esd's in Parentheses)

atom	x/a	y/b	z/c	U_{eq}
C(1)	−0.0403(4)	0.0222(4)	−0.2151(2)	0.029(2)
C(2)	−0.1751(4)	0.0555(4)	−0.1856(2)	0.037(2)
C(3)	−0.2630(4)	0.1398(4)	−0.2219(2)	0.038(2)
C(4)	−0.2238(5)	0.1930(4)	−0.2879(2)	0.040(2)
C(5)	−0.0904(4)	0.1565(4)	−0.3166(2)	0.036(2)
C(6)	−0.0007(4)	0.0723(4)	−0.2823(2)	0.033(2)
C(7)	−0.2253(5)	−0.3449(4)	−0.2504(2)	0.035(2)
C(8)	−0.2138(6)	−0.3684(5)	−0.3279(2)	0.049(2)
C(9)	−0.3698(8)	−0.4530(6)	−0.3839(2)	0.075(2)
C(10)	−0.5326(7)	−0.5117(7)	−0.3636(3)	0.083(2)
C(11)	−0.5467(6)	−0.4872(5)	−0.2877(3)	0.059(3)
C(12)	−0.3916(5)	−0.4052(4)	−0.2311(2)	0.043(2)
C(13)	0.0559(4)	−0.0748(4)	−0.1801(2)	0.032(2)
C(14)	−0.0566(4)	−0.2621(4)	−0.1903(2)	0.032(2)
C(15)	−0.0656(4)	−0.2313(4)	−0.1046(2)	0.029(2)
C(16)	0.0787(4)	−0.0550(4)	−0.0906(2)	0.030(2)
C(17)	−0.0326(9)	−0.3114(6)	−0.4217(3)	0.095(4)
C(18)	−0.7351(7)	−0.5173(6)	−0.1967(4)	0.100(4)
C(19)	0.2613(4)	−0.0336(4)	−0.0501(2)	0.031(2)
C(20)	−0.0344(4)	−0.3492(4)	−0.0590(2)	0.033(2)
N(1)	−0.4096(4)	0.1675(4)	−0.1907(2)	0.060(2)
N(2)	−0.0421(4)	0.2096(4)	−0.3872(2)	0.050(2)
O(1)	−0.4178(4)	0.1584(4)	−0.1244(2)	0.095(2)
O(2)	−0.5147(5)	0.2028(5)	−0.2311(2)	0.115(3)
O(3)	−0.0973(5)	0.3080(4)	−0.4089(2)	0.087(2)
O(4)	0.0515(4)	0.1534(4)	−0.4199(2)	0.073(2)
O(5)	0.3266(3)	−0.1357(3)	−0.0769(1)	0.045(1)
O(6)	0.3405(3)	0.0812(3)	0.0073(1)	0.041(1)
O(7)	0.0209(4)	−0.2930(3)	0.0134(1)	0.048(2)
O(8)	−0.0678(4)	−0.4927(3)	−0.0919(1)	0.051(2)
O(9)	−0.0463(4)	−0.3041(3)	−0.3417(1)	0.064(2)
O(10)	−0.7148(4)	−0.5489(5)	−0.2723(2)	0.081(3)
C(1a)	−0.4031(10)	−0.0399(9)	−0.5501(6)	0.127(7)
C(2a)	−0.4300(11)	−0.1149(9)	−0.4886(7)	0.188(7)
C(3a)	−0.5303(10)	−0.0775(9)	−0.4379(5)	0.115(6)
C(4a)[a]	−0.5689(22)	−0.1611(16)	−0.3645(10)	0.147(9)
O(w)[a]	0.5000	0.5000	0.0000	0.340(17)
H(2)	−0.206(4)	0.027(4)	−0.137(2)	0.03(1)
H(4)	−0.288(4)	0.252(4)	−0.308(2)	0.03(1)
H(6)	0.089(4)	0.049(4)	−0.303(2)	0.03(1)
H(9)	−0.351(6)	−0.472(5)	−0.435(2)	0.08(1)
H(10)	−0.636(6)	−0.565(5)	−0.404(4)	0.09(2)
H(12)	−0.408(4)	−0.384(4)	−0.175(2)	0.04(1)
H(13)	0.164(4)	−0.061(3)	−0.196(2)	0.02(1)
H(14)	0.017(3)	−0.320(3)	−0.198(1)	0.01(1)
H(15)	−0.181(3)	−0.229(3)	−0.094(1)	0.01(1)
H(16)	0.045(3)	0.030(3)	−0.064(2)	0.01(1)
H(171)	0.109(7)	−0.264(7)	−0.415(3)	0.11(2)
H(172)	−0.101(9)	−0.245(8)	−0.445(4)	0.17(3)
H(173)	−0.077(9)	−0.431(8)	−0.453(4)	0.16(2)
H(181)	−0.869(6)	−0.573(6)	−0.201(2)	0.09(2)
H(182)	−0.697(8)	−0.401(7)	−0.184(3)	0.13(2)
H(183)	−0.655(9)	−0.580(8)	−0.157(4)	0.16(3)
H(50)	0.451(6)	−0.120(5)	−0.053(2)	0.08(1)
H(70)	0.043(7)	−0.349(6)	0.037(3)	0.10(2)
H(1a)	−0.312	−0.070	−0.587	0.139
H(2a)	−0.363	−0.189	−0.491	0.139
H(4a1)[a]	−0.512	−0.251	−0.360	0.158
H(4a2)[a]	−0.716	−0.221	−0.368	0.158
H(4a3)[a]	−0.519	−0.068	−0.309	0.158
H(10w)[a]	0.555	0.454	0.011	0.409
H(20w)[a]	0.421	0.502	0.050	0.409

[a] 0.5 occupancy.



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were specified to be tetrahedral. The commands NOLN (nolinks) and NOCY (nocyclic routes) were specified for the two phenyl rings so as to retain some chemical similarity and to preserve the rotational degrees of freedom around C13–C14, C1–C13, and C7–C14. Such commands would then exclude compounds such as the cyclophanes, 1,2-(dinaphthyl)ethane, and so on. Screens −28, 35, 153, 85, and 89 were set to eliminate organometallic and disordered structures and also those entries containing no coordinates or where chemical and crystallographic connectivities are not matched. Entries where the *R* factor is greater than 0.075 would also be excluded. All 1,2-diphenylcyclopropanes were identified and eliminated manually, because these were found to be structurally quite distinct from those compounds in which TBC was observed. The numbering scheme shown above and in Table 2 will be used hereafter in the text to represent the specific bond lenghts and torsion angles in all the diphenylethanes discussed irrespective of the numbering scheme used in the original crystallographic papers.

Table 2. Sample CSD Question Generated by the Graphics 3D Option for 1,2-Diphenylethane Derivatives

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SCREEN -28 153 85 89 35
T1 *CONN
NFRAG 1
AT1 C 3
AT2 C 2
AT3 C 2
AT4 C 2
AT5 C 2
AT6 C 2
AT7 C 3
AT8 C 2
AT9 C 2
AT10 C 2
AT11 C 2
AT12 C 2
AT13 C T4
AT14 C T4
BO 1 2 5
BO 2 3 5
BO 3 4 5
BO 4 5 5
BO 5 6 5
BO 1 6 5
BO 7 8 5
BO 8 9 5
BO 9 10 5
BO 10 11 5
BO 11 12 5
BO 7 12 5
BO 1 13 1
BO 13 14 1
BO 7 14 1
NOCR 2 3 4 5 6 8 9 10 11 12
NOLN
GEOM
DEFINE TOR 1 13 14 7
SELECT TOR -45 45
DEFINE C-C 13 14
SELECT C-C 1.50 1.70
SETUP P1 1 2 3 4 5 6
SETUP P2 7 8 9 10 11 12
DEFINE P1P2 P1 P2
SCAT C-C P1P2
C OVERLAP OF CRYSTAL
    FRAGMENTS PERMITTED
C SEARCH FOR ALL
    CRYSTAL FRAGMENTS
NFRAG -99
END
QUEST T1
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Solvates containing benzene, toluene and water were obtained using the screens −28, 153, 85, and 88 to create a subsidiary IDX file which was then searched for further classification and subsequent tests. For calculating hydrogen-bond distances in the hydrates, it was specified that the $O_w \cdots RR$ distance (RR = N, O; water O atom and O or N atom of the host compound) should be between 2.5 and 3.2 Å. This distance which is longer than the normal hydrogen-bond distance of 2.8 Å was used so that some weak hydrogen bonds would not be missed. Any compound that has at least one hydrogen bond (hit) that satisfies the above relaxed distance criterion was considered to display hydrogen bonding with the water molecule. While calculating the percentage of hydrogen bonds in these hydrates, only unique hits were considered; in other words, duplicate structures were excluded.

Results and Discussion

Crystal Engineering: The 2+2 Cycloaddition Reaction. We have reported earlier[12] that the 1:1 charge-transfer complex **3a**, of 2,4-dinitrocinnamic acid (**2b**) and 3,4-dimethoxycinnamic acid (**2c**), is not photoreactive in the solid-state despite the favorable disposition of the two "potentially reactive" double bonds of the donor and acceptor molecules; namely, a mean double-bond center–center distance of 3.80 Å. We subsequently prepared another 1:1 cinnamic acid charge-transfer complex **3b** using the same acceptor **2b** and a different donor, 2,5-dimethoxycinnamic acid, **2d**. Complex **3b** is also unreactive. This unexpected lack of reactivity confirms our earlier suggestion that the nitro groups in **2b** suppress the reactivity of the alkenes toward $\pi\pi^*$-mediated reactions due to the easier accessibility of $n\pi^*$ level, which provides

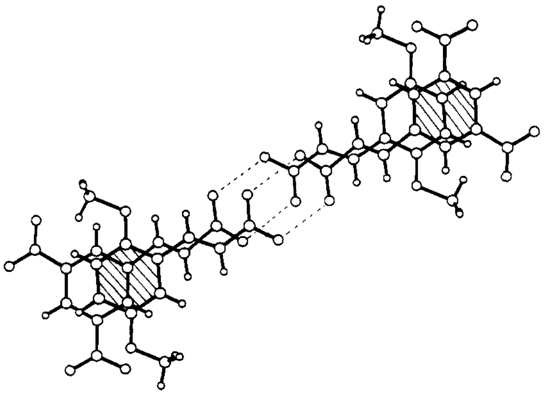

Figure 1. Molecules **2a** and **2d** in complex **3d**, related by O–H···O hydrogen bonding and π–π stacking. Diacid **1b** is formed by 2+2 cycloaddition of neighboring stacked molecules. O–H···O hydrogen bonds are shown as dashed lines.

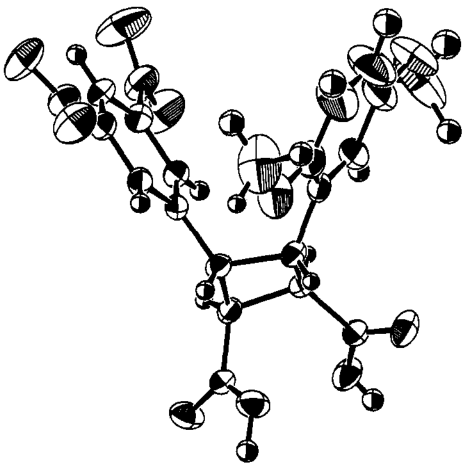

Figure 2. ORTEP diagram of the molecule of **1b**. The toluene and water molecules are not shown.

a pathway for the excited ππ* electrons to the ground state through radiationless decay without any reaction. The lack of reactivity of complexes **3a** and **3b** towards solid-state 2+2 cycloaddition suggested that it would be more appropriate to use 3,5-dinitrocinnamic acid **2a** as the acceptor component in the molecular complex selected for the solid-state reaction. Unlike in acid **2b**, the excited ππ* electrons in acid **2a** cannot access the nπ* state because the 1,3,5-substitution pattern precludes the resonance required for the ππ* → nπ* energy transfer or in other words, the nitro groups of **2a** act essentially as inductive groups only. Accordingly we prepared complexes of **2a** with **2c** (**3c**) and of **2a** with **2d** (**3d**). As we expected, these complexes are photoreactive in the solid state, and this observation is in accord with the mechanism proposed earlier by us for the photostability of complexes of acid **2b**.[12] The crystal structure of **3d** was determined, and the center–center distance between the two potentially reactive double bonds is 3.54 Å, which is within the 4.2-Å threshold distance for solid-state photochemical reactivity.[4] This is shown in Figure 1.

Molecular Structure of Diacid 1b. The crystal structure determination confirms the structure of diacid **1b**, and an ORTEP view of the molecule is shown in Figure 2. Diacid **1b** has two cofacial phenyl rings, with a mean interplanar distance of 3.77 Å,[16] a centroid–centroid distance 4.37 Å and an interplanar angle of 59.2°. These two phenyl rings have a slightly skewed conformation with the torsion angle, C1–C13–C14–C7, being 16.7°. The closest distance between the two phenyl rings is C1···C7, 3.0 Å. There are two intramolecular nonbonded C–H···O contacts[17] between the H(6) atom of the dinitrophenyl group and the O(9) atom of the dimethoxyphenyl group (C···O, 3.23 Å; Θ = 104°) and between the carboxyl oxygen atom O(5) and the diagonally located H(14) atom of the cyclobutane ring (C···O, 3.20 Å and Θ 102°). The AM1[18] optimized structure of diacid **1b** also results in two C–H···O interactions, but these are different from those observed in the crystal structure. In the crystal the cyclobutane ring is puckered with a torsion angle of 11.4°, but the ring is planar in the AM1 optimized geometry with a torsion angle of 1.4°. The carboxyl groups of **1b** are not involved in intramolecular O–H···O hydrogen bonding though they are adjacent. Instead both of them form intermolecular hydrogen bonded dimers (Figure 6a). The two carboxyl groups are partially disordered with the two C–O distances being 1.246 and 1.272 Å in one group and 1.241 and 1.272 Å in the other. The clathrated water molecule (not shown in Figure 2) is disordered and occupies a special position ($^1/_2$, $^1/_2$, 0). The two H atoms of the water molecules were found from difference Fourier maps. The H–O distances are 0.74 and 1.17 Å with the H–O–H angle being 102.6°. The disordered toluene molecule is located on another inversion center at ($^1/_2$, 0, $^1/_2$), and hence the asymmetric unit contains only half a toluene molecule (omitted in Figure 2 for clarity).

Charge Transfer. An interesting feature in the molecular structure of **1b** is the cofacial disposition of aromatic donor and acceptor groups. Such an arrangement permits intramolecular charge transfer,[6,7] the presence of which is ascertained by electronic spectroscopy. The UV spectrum of diacid **1b** in MeOH (4×10^{-5} M) was compared with those of the model compounds, 1,3-dinitrobenzene and 1,4-dimethoxybenzene in the same solvent. The UV spectrum of **1b** is red-shifted and broadened compared to the combined 1:1 spectrum of a mixture of the model compounds (Figure 3). A residual absorption near 310 nm was also noticed in the spectrum of **1b**. This band is ascribed to intramolecular charge transfer. UV spectra of **1b** recorded in MeCN and CH_2Cl_2 also showed similar features clearly indicating the presence of intramolecular charge transfer. As seen in Figure 3 the absorption maxima at 227 and 288 nm are 3 and 2 nm red shifted, compared to the composite spectrum of the model compounds. The ^1H NMR shifts ($CDCl_3$) of the two aryl moieties in **1b** also suggest mutual shielding and therefore the presence of a molecular conformation which can sustain intramolecular charge transfer. The nitro aromatic protons of **1b** are shifted upfield to δ 8.35 and 8.63 compared to the values of δ 8.78 and 9.10 in 1,3-dinitrobenzene, and similarly the aliphatic and methoxy aromatic protons in **1b** are shifted upfield to δ 3.60, 3.70, and 6.60 compared to the values of δ 3.81 and 6.9 in 1,4-dimethoxybenzene. The slight

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[16] This is defined as the mean of the two perpendicular distances from each centroid to the other ring.

[17] (a) Takusagawa, F.; Koetzle, T. F.; Srikrishnan, T.; Parthasarathy, R. *Acta. Crystallogr.* **1979**, *B35*, 1388. (b) Etter, M. C.; Panunto, T. W. *J. Am. Chem. Soc.* **1988**, *110*, 5896. (c) Steiner, T.; Saenger, W. *J. Am. Chem. Soc.* **1992**, *114*, 10146. (d) For a discussion of intramolecular C–H···N interactions see: Harlow, R. L.; Li, C.; Sammes, M. P. *J. Chem. Soc., Chem. Commun.* **1984**, 819. Avendano, C.; Espada, M.; Ocana, B.; Garcia-Granda, S.; Diaz, R. M.; Tejerina, B.; Gomez-Beltran, F.; Martinez, A.; Elguero, J. *J. Chem. Soc., Perkin Trans 2* **1993**, 1547.

[18] Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

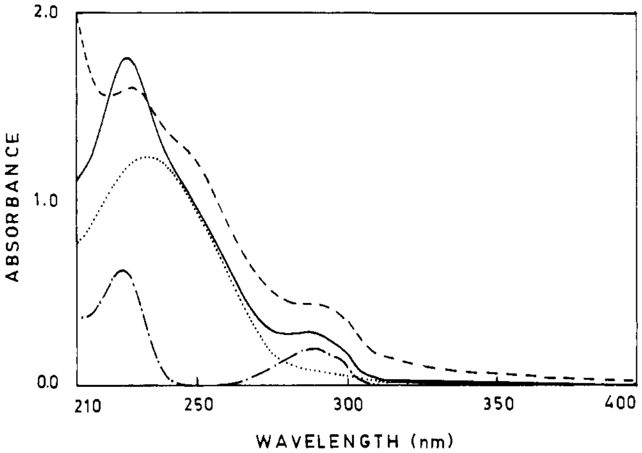
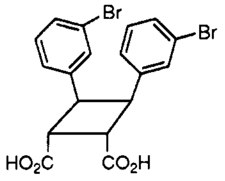


Figure 3. Electronic absorption spectra of **1b** (- - -) and the model compounds 1,3-dinitrobenzene (···) and 1,4-dimethoxybenzene (-·-) in MeOH (4 × 10^{-5}M). Spectrum (—) is a composite of the 1,3-dinitrobenzene and 1,4-dimethoxybenzene spectra.

variations in the upfield shifts of the different protons also suggest the importance of skewed conformations of **1b** in solution. The mean interplanar distance of the two phenyl rings 3.77 Å, obtained from the crystal structure, also indicates the existence of intramolecular charge transfer. This distance is slightly higher than the AM1 or MNDO optimized values of 3.64 and 3.62 Å, because of the presence of the toluene guest molecule in the crystal structure which is involved in intermolecular charge transfer with the dinitrophenyl ring of **1b**.

Through-Bond Coupling (TBC) and C–C Bond Elongation. Diacid **1b** is a good example to study the phenomenon of TBC which arises when multiple π orbitals are parallel to a σ bond which is elongated as a result.[19] The σ bond length can be diminished by through-space coupling (TSC) which opposes the TBC effect. The TBC in diphenylethanes will be a maximum if the two phenyl groups connected to the σ bond are in a trans disposition and parallel to each other, because the TSC would then be negligible and the maximum number of π orbitals can mix with σ^* orbitals. Steric constraints and a rigid molecular framework accentuate the TBC effect.[6] Substitution at the sp^3 centers may also affect the magnitude of TBC.[19a] A study of the C–C bond lengthening may reveal the process of C–C bond cleavage which is synthetically important and an estimate of the energy required for such a process.[6]

In the present example, we noticed a slight elongation in the C13–C14 (hereafter called the central C–C bond) bond length, 1.566(5) Å, compared to the "normal" bond length between C(sp^3)–C(sp^3) atoms 1.537 Å.[20] Other related structures have significantly elongated central C–C bonds. Earlier studies on indanoindane (KINCUF) which resembles **1b** closely both electronically and structurally show an elongation of the C–C bond to 1.614 Å due to TBC.[6] Two other truxinic acids, 3,4-bis(3′-bromophenyl)cyclobutane-1,2-dicarboxylic acid (**4**) and 3,4-bis(3′-chlorophenyl)cyclobutane-1,2-dicarboxylic acid (**5**), are reported in the literature[21] as having elongated central C–C bond lengths of 1.573 and 1.575 Å. Some other simple cyclobutanes which are not part of a larger rigid molecular framework such as BAHNIH[22] (1.604 Å), CMCNCB[23] (1.606 Å), SAJJAO[24] (1.594 Å), and SIKROT[25] (1.585 Å) also have elongated central C–C bonds. We carried out molecular mechanics and semiempirical MNDO and AM1 calculations to find out the effect of substituents on the central C–C bond length in diacids **1a**, **1b**, **4**, and **5**. The central C–C bond lengths, interplanar distances, and some of the torsion and interplanar angles of the phenyl groups obtained by experiment, molecular mechanics, and semiempirical methods are given in Table 3.



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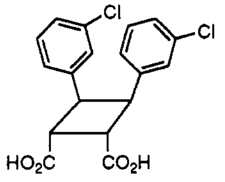

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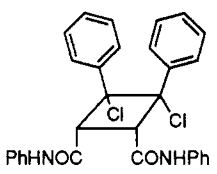
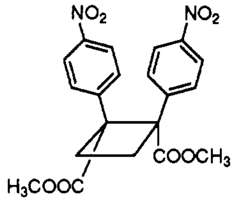
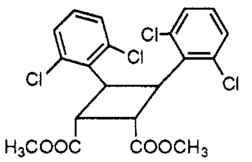


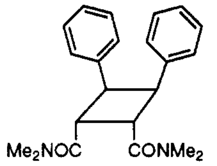
BAHNIH



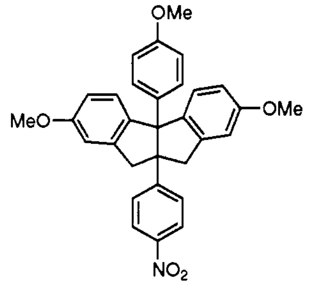
CMCNCB



SAJJAO



SIKROT



KINCUF

Table 3 shows that the central C–C bond lengths and molecular geometry are not reproduced consistently in all the three structures by the semiempirical methods.[26]

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(19) (a) Dougherty, D. A.; Schlegel, H. B.; Mislow, K. *Tetrahedron* **1978**, *34*, 1441. (b) Zhou, X.; Liu, R.; Allinger, N. L. *J. Am. Chem. Soc.* **1993**, *115*, 7525.

(20) (a) Sutton, L. E., Ed.; *Chem. Soc., Spec. Publ.* **1965**, *No. 18*, 514. (b) Allen, F. H. *Acta Crystallogr.* **1981**, *B37*, 890.

(21) Kanao, S.; Kashino, S.; Haisa, M. *Acta Crystallogr.* **1990**, *C46*, 2439.

(22) Ciechanowicz-Rutkowska, M.; Konsur, A.; Duraj, S.; Kolasa, A.; Ledibea, L. L.; Zankowska-Janinska, W. *Tetrahedron* **1981**, *37*, 3503.

(23) Carr, P.; Finney, J. L.; Lindley, P. F.; Detitta, G. T. *Acta Crystallogr., Sect B* **1977**, *33*, 1022.

(24) Ben-Efraim, D. A.; Arad-Yellin, R. *Tetrahedron*, **1988**, *44*, 6175.

(25) Caccamese, S.; Fronczek, F. R. *Tetrahedron* **1990**, *46*, 7841.

(26) However it seems that there is no conclusive evidence on the efficacy of either AM1 or MNDO approximation methods in evaluating TBC. Reference 6 states that while AM1 outperforms MNDO for calculating TBC, the MNDO method seems to work well for many other cases. See for example: Osawa, E.; Kanenmatsu, K. In *Molecular Structure and Energetics*; Studies of Organic Molecules; Liebman, J. F., Greenberg, A., Eds.; VCH; New York, 1986; Vol. 3., p 329.

Table 3. Selected Intramolecular Angles and Distances in Cyclobutanes 1a, 1b, 4, and 5 Obtained from Experiment and Calculation[a] To Probe the Effect of TBC on Central C–C Bond Elongation

			phenyl–phenyl			
		central C–C dist[b] (Å)	torsion angle[c] (deg)	interplanar angle (deg)	interplanar dist (Å)	centroid–centroid dist (Å)
1a	crystal[d]					
	MMX	1.553	18.94	56.9	3.33	4.62
	MNDO	1.573	13.79	63.2	3.43	4.85
	AM1	1.561	8.6	53.1	2.94	4.62
1b	crystal	1.566	−16.7	59.2	3.77	4.37
	MMX	1.556	−17.3	54.1	3.12	4.80
	MNDO	1.576	−8.9	63.1	3.62	4.83
	AM1	1.565	−5.9	66.1	3.64	4.42
4	crystal	1.575	20.5	61.2	3.82	4.44
	MMX	1.555	23.2	58.1	3.58	4.42
	MNDO	1.576	9.1	63.9	3.82	4.65
	AM1	1.566	12.0	61.8	3.72	4.41
5	crystal	1.573	20.8	61.1	3.81	4.45
	MMX	1.556	21.1	58.1	3.58	4.41
	MNDO	1.577	10.4	63.1	3.75	4.67
	AM1	1.568	7.7	60.6	3.61	4.37

[a] Molecular mechanics calculations were performed using the MM2 set of parameters. AM1 and MNDO optimisations were carried out with the MOPAC program.[18] [b] C13–C14. [c] C1–C13–C14–C17. [d] Crystal structure not solved.

However, the semiempirical central C–C bond lengths are slightly increased compared to the lengths obtained via molecular mechanics which does not consider electronic effects. Such differences between molecular mechanics and semiempirical values indicate the presence of TBC. Variations of the substitution patterns in the phenyl rings showed no significant effect on the central C–C bond lengths in either of the semiempirical methods. So the reason for the relatively slight elongation of the central C–C bond in **1b** compared to molecules **1a**, **4**, and **5** is not clear. However, it may be reasonable to assume that TSC is greater in **1b** than in other related cyclobutanes due to the strong intramolecular charge-transfer interaction between adjacent phenyl rings or because of the location of the guest molecule toluene in the cleft formed by the two phenyl groups.

We have also carried out a more general CSD study on all crystal structures that contain the 1,2-diphenylethane fragment. TBC is insensitive to rotation around the central C13–C14 bond,[8] whereas rotation around C1–C13 and C7–C14 will diminish the interaction between σ and π orbitals reducing the TBC effect. This CSD study is also helpful to distinguish between steric and electronic effects on the central C–C bond elongation. If steric effects were to play an important role in bond lengthening, there should not be any correlation between the C–C bond lengths and the relative orientation of phenyl rings (parallel arrangement of π orbitals). On the other hand if any such correlation is found, it is an indication of TBC. Though the torsion angle C1–C13–C14–C7 has no direct role to play in these systems, it can indirectly affect the TBC. This is so because at lower torsion angles (0–45°) the phenyl groups must be parallel while at higher torsion angles (45–90°) the phenyl groups need not be parallel. Finally, as the torsion angle increases further (90–180°), the phenyl groups will be free to take up any orientation whatsoever. To visualize the effect of torsion angle on interplanar angle more clearly, three scatterplots were drawn for C–C bond lengths versus interplanar angle of phenyl groups for three different ranges of torsion angles (Figure 4).

At smaller torsional angles (Figure 4a) most of the C–C bond lengths are long, 1.57–1.64 Å, because the interplanar angles must also be small and the TBC effect increases. In Figure 4b where the phenyl groups have rotational freedom (torsion angle 45–90°), the interplanar angles are randomly distributed. When the interplanar angles are large (70–110°), not much lengthening of the central C–C

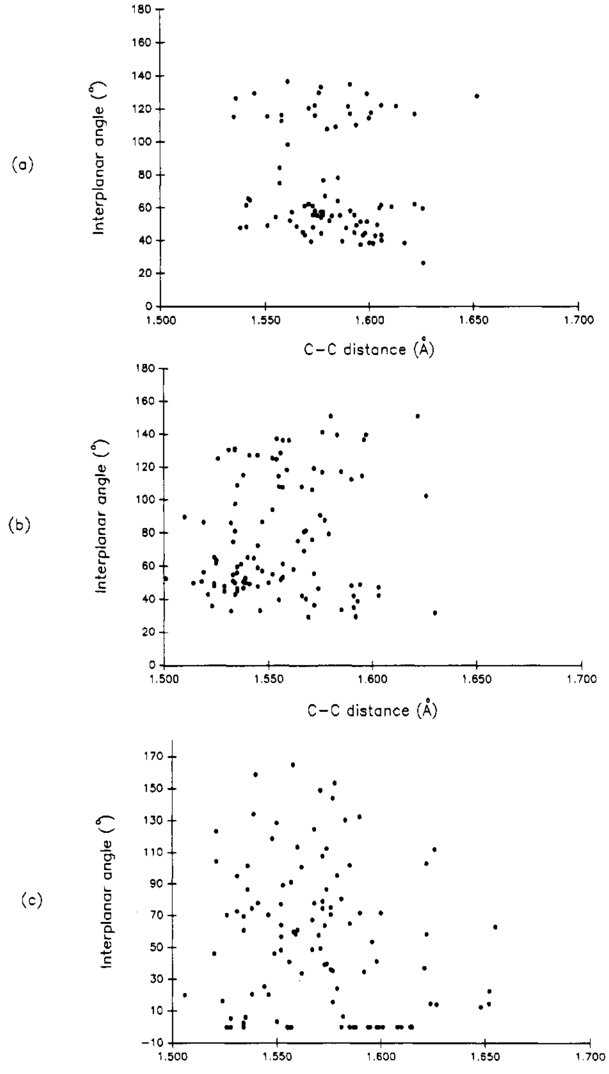

Figure 4. Scatterplots of phenyl–phenyl interplanar angle versus central C–C bond distance in 1,2-diphenylethanes retrieved from the CSD with small (a), medium (b), and large (c) torsion angles C1–C13–C14–C7 (τ) (a) $0 < \tau < 45°$; (b) $45 < \tau < 90°$; (c) $90 < \tau < 180°$.

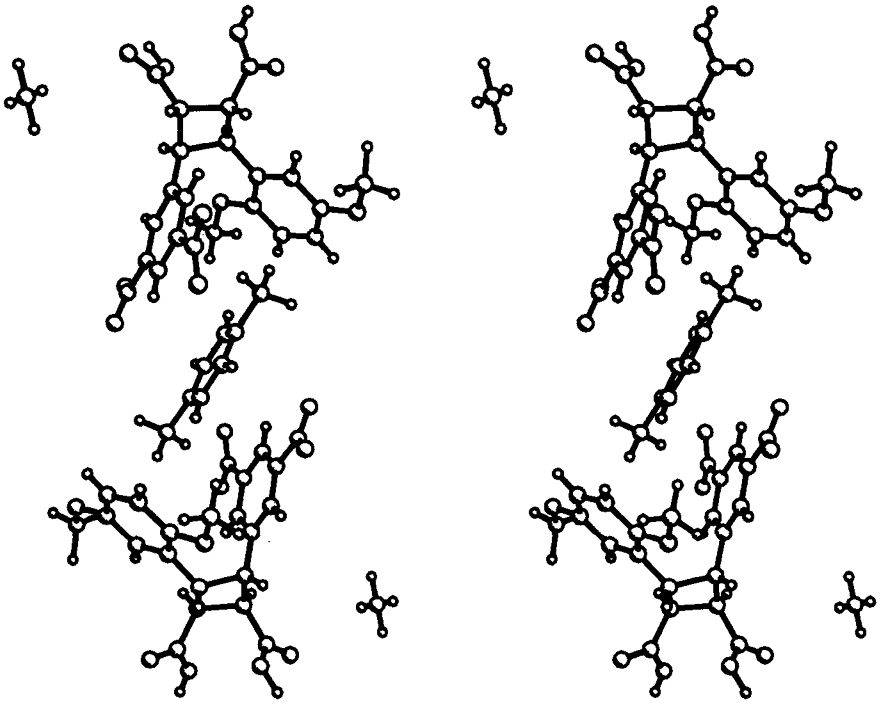

Figure 5. Stereoview of the guest–molecule induced supramolecular cage of **1b**. Notice the orientation of the toluene guest vis-à-vis the dinitrophenyl and the dimethoxyphenyl rings of the host. The water molecule is also shown. Compare this with Figure 6.

bond (1.52–1.57 Å) is noticed as would be expected. In this intermediate range of torsion angles, the larger interplanar angles between phenyl groups will be stabilized by herringbone interactions and the possibility of TBC appears to be remote. Figure 4b also indicates that small interplanar angles (0–60° and 120–180°) are crucial for C–C bond lengthening. Long central C–C bond lengths occur only when the interplanar angles are small. At higher torsion angles (Figure 4c) there is minimal interaction between phenyl rings which exist in all mutual orientations. So the C–C bond lengths have all values in the range, 1.53–1.65 Å and satisfyingly, the longer lengths (>1.60 Å) are associated with smaller interplanar angles. Surprisingly, scatterplot 4c shows a small cluster of points with short bond lengths, 1.52–1.56 Å, and small interplanar angles (<30°). This subset requires further analysis. However, in an overall sense, plots 4a–4c emphasise the importance of smaller interplanar angles for effective TBC.

Supramolecular Properties. Weber and co-workers have shown that several three- and four-membered ring compounds with phenyl and other bulky substituents are good and highly selective host materials for the formation of inclusion compounds.[27] The cavity size (between two phenyl groups) and electronic properties of diacid **1b** makes it a specific host for simple aromatics because these molecules can simultaneously satisfy the requirements of size, shape, π–π and herringbone interactions which are necessary for binding with the host. So we selected benzene, toluene, xylene, nitrobenzene, 1,4-dinitrobenzene, and anisole as possible guests for complexation with **1b**. We were successful in obtaining crystals of the host–guest complex between **1b** and toluene from 5:1 MeOH–toluene. After the X-ray analysis it was found that the **1b** crystal also includes a water molecule, with both the toluene and water molecules being disordered. Crystals of the nitrobenzene complex of **1b** obtained from CH_2Cl_2 were of a quality too poor for X-ray work.

As shown in Figure 5 two inversion-related molecules of **1b** surround the toluene molecule and form the supramolecular cavity. The toluene molecule is disordered around the same inversion center, effectively appearing like a molecule of *p*-xylene. In this way, the cavity size and shape matches the guest and also optimizes π–π interactions. Figure 5 also shows that the toluene molecule is sandwiched between the two dinitrophenyl moieties of **1b** with a stacking distance of 3.25 Å, a centroid-centroid distance of 4.6 Å and a dihedral angle of 16°, while simultaneously making an angle of 74° with the 2,5-dimethoxyphenyl moieties of **1b** with a 5.76-Å centroid–centroid distance. The electron-rich toluene molecule stacks with the electron-deficient dinitrophenyl rings and has herringbone (C–H···π) type interactions with the electron-rich dimethoxyphenyl rings of **1b**. Knowing these binding features, one may predict that *p*-xylene will bind like toluene, while nitrobenzene a molecule of roughly the same size and shape would be nearly parallel to the dimethoxyphenyl rings and inclined in a herringbone fashion to the dinitrophenyl rings.

The water molecule which is included along with toluene in crystalline **1b** is not involved in any significant hydrogen bonding (water, O_w···O 3.5 Å, C–H···O_w, 3.77, 136°). Despite the presence of a sizeable number of O atoms in the molecule, the water molecule merely occupies the channels formed by the carboxylic dimers (Figure 6a). The related diacids **4** and **5** (Figure 6b) also form similar channels and these channels are filled by disordered acetic acid and/or water molecules (not located exactly).[21] Acids **4** and **5** also do not show any significant hydrogen bonding with the included molecules (O_w···O 3.0, 2.95 Å). It seems that the solvent inclusion phenomenon is common to many other β-truxinic acids.[28] This observation raises the significant question as to whether water can act as a space filler in crystals without being involved in any specific

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[27] (a) Weber, E.; Hecker, M.; Csoregh, I.; Czugler, M. *J. Am. Chem. Soc.* **1989**, *111*, 7866. (b) Csoregh, I.; Czugler, M.; Kalman, K.; Weber, E.; Hecker, M. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2539.

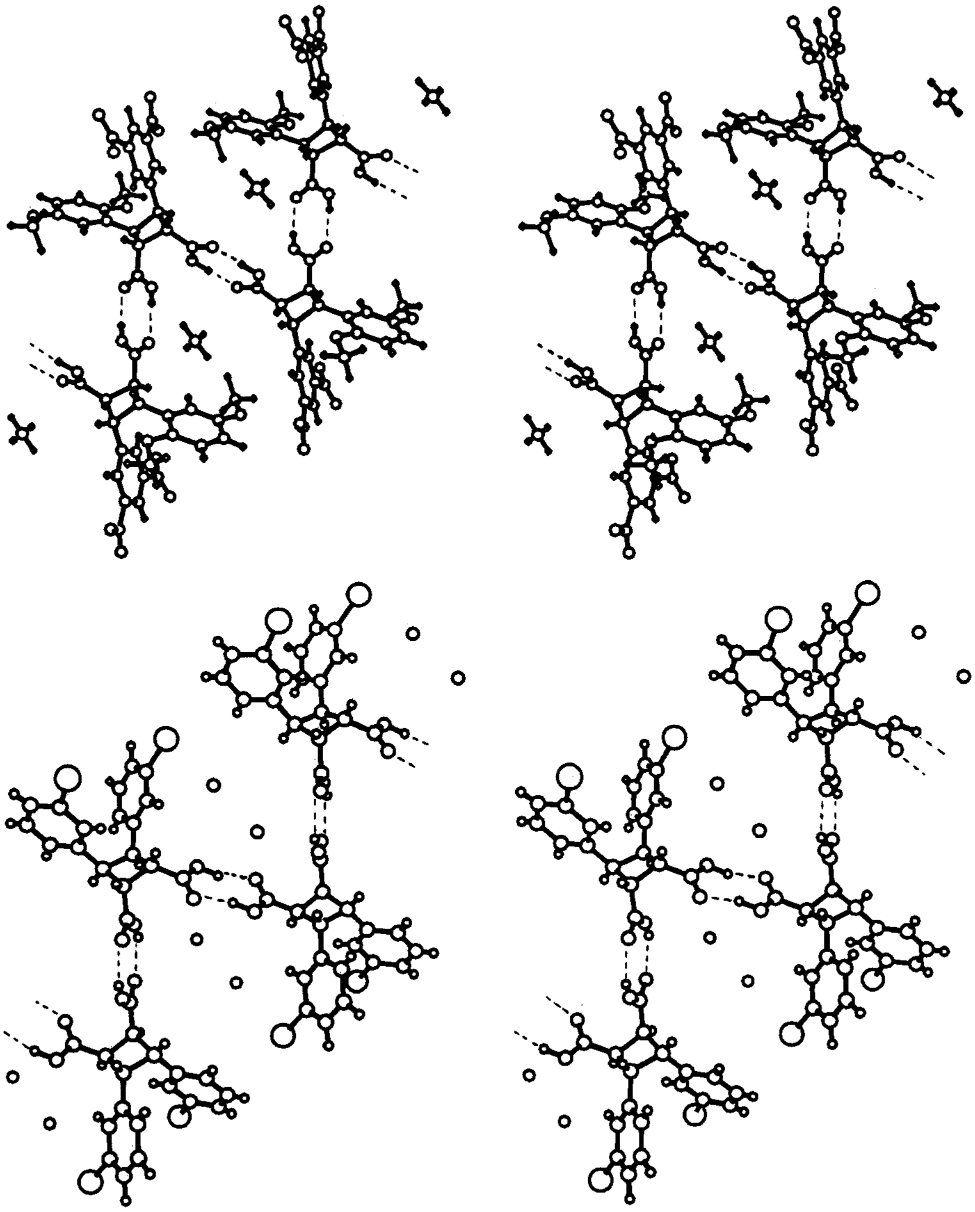

Figure 6. Stereoviews of the divergent supermolecules formed by the zigzag hydrogen-bonded chains of carboxy dimers in some cyclobutane-1,2-dicarboxylic acids: (a, top) a disordered water molecule in the cavity of **1b**; (b, bottom) two disordered water molecules (H atoms not shown) in the cavity of **4** (or **5**).

hydrogen bonding even in the presence of heteroatom containing host molecules.[29]

The crystal structure of **1b** is also interesting because it has two distinct supramolecular cages, polar and the apolar. The polar cavity is occupied by water molecules (Figure 6a) and apolar cavity by toluene molecules (Figure 5). The polar cavity is induced by the mutual recognition of carboxyl groups which form hydrogen-bonded dimers, and the apolar cavity is induced by the guest. The supramolecular assembly of carboxyl dimers is divergent forming a zigzag hydrogen-bonded chain as shown in Figure 6a. The apolar convergently assembled supermolecule is formed when two molecules of **1b** encapsulate the toluene molecule (Figure 5). The divergent polar supramolecular assembly and the clathration of water (acetic acid) molecules in it is also found in two other truxinic acids **4** and **5** (Figure 6b). But these two truxinic acids do not have a convergent supramolecular cage. The phenyl rings in diacids **4** and **5** are close-packed with a phenyl ring protruding into the cleft of the adjacent molecule without forming a cage (Figure 7). On the other hand, the guest molecules in **1b** occupy the clefts between two phenyl rings and hold two **1b** molecules together. This may be termed a guest-induced supramolecular cage. Another example of this type of guest induced cavity is the 6:1 complex of 1,3-cyclohexanedione and benzene reported by Etter and co-workers, where the benzene molecule is surrounded by six hydrogen-bonded molecules of the 1,3-diketone (Figure 8).[30] It should be mentioned here that when 1,3-cyclohexanedione is recrystallized in the absence of benzene, a divergent linear hydrogen-bonded chain is formed.

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(28) Nakanishi, F.; Nakanishi, H.; Tsuchiya, M.; Hasegawa, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3096.

(29) Jeffrey, G. A.; Saenger, W. *Hydrogen Bonding in Biological Structures*; Springer-Verlag: Berlin, 1991.

(30) Etter, M. C.; Urbanczyk-Lipkowska, Z.; Jahn, D. A.; Frye, J. S. *J. Am. Chem. Soc.* **1986**, *108*, 5871. For a discussion on cooperative hydrogen bonding and stabilization energies of 1,3-diketone aggregates and their 6:1 benzene complex see: Turi, L.; Dannenberg, J. J. *J. Phys. Chem.* **1992**, *96*, 5819.

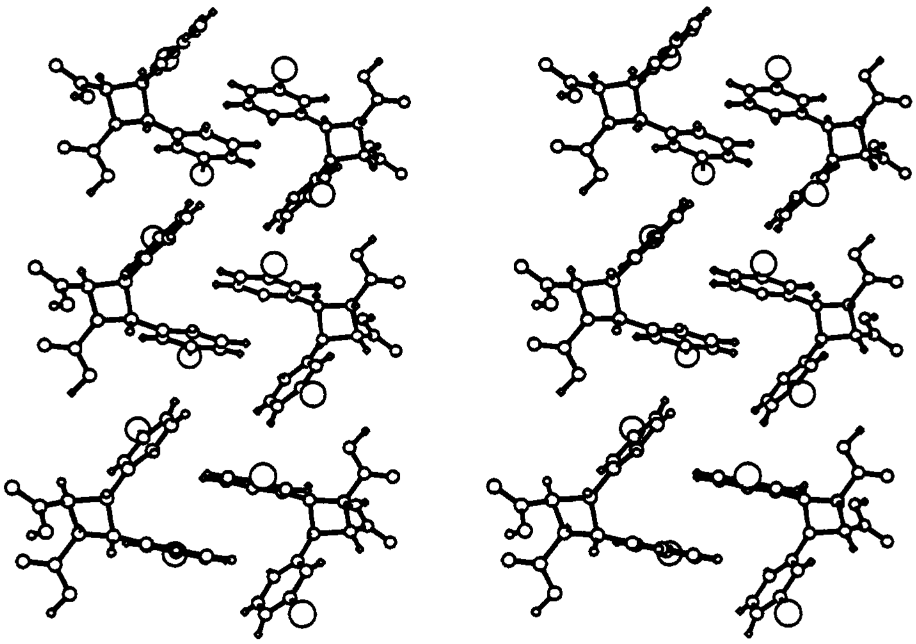


Figure 7. Stereoview of the crystal structure of diacid 4 (or 5) with phenyl rings protruding into the cavity formed by adjacent molecules. Compare this with Figure 5.

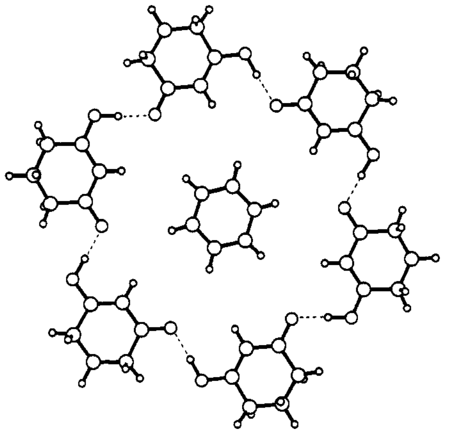
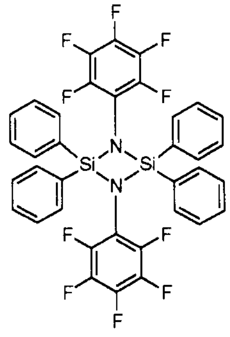


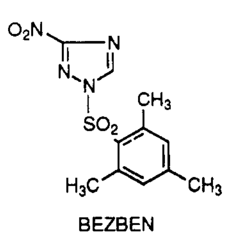
Figure 8. Benzene guest molecule in the cavity of the hydrogen-bonded hexamer of the enol form of 1,3-cyclohexanedione. $O-H\cdots O$ hydrogen bonds are shown as dashed lines.

These examples highlight the fact that one can design convergent supermolecules (or supramolecular cages) of different sizes by varying the host-to-guest molecular ratio based on the geometrical and directional properties of the host and guest.

These observations in the **1b** crystal structure prompted us to search the CSD for other solvates of benzene, toluene, and water, to investigate more thoroughly the nature of their interaction with the host and especially to ascertain the importance of these solvents as space fillers in the host network. Benzene and toluene solvates, retrieved from the CSD, may also provide an opportunity to estimate the importance of electrostatic and van der Waals forces in crystal packing in general.[31] The easiest way of approximating the significance of van der Waals interactions in such solvates is to distinguish the hosts as aromatic and nonaromatic, because nonaromatic clathrates of benzene and toluene can only be stabilized by van der Waals interactions. Of a total of 31 toluene clathrates with $R < 0.10$, toluene is clathrated by 26 aromatic and 5 nonaromatic compounds, while of a total of 177 benzene clathrates with $R < 0.10$ benzene is clathrated by 132 aromatic and 45 nonaromatic compounds. The higher percentage of nonaromatic clathrates for benzene (34%) as compared to toluene (19%) suggests that the more symmetrical and nonpolar molecule is more suited to a space-filling role. We also examined the stacking interactions in these two groups of solvates; often the guest molecules are found to stack with electron-withdrawing aromatic rings rather than with electron-donating aromatic rings. In the latter case, T-shaped geometries and herringbone interactions ($C-H\cdots\pi$) seem to be preferred. The kind of selective binding of the toluene molecule observed in **1b** is also observed in the benzene solvates of 1-(mesityl-2-sulfonyl)-3-nitro-1,2,4-triazole (BEZBEN)[32] and bis(*N*-pentafluorophenyl)tetraphenylcyclodisilazane (DUZLIT)[33] (Figure 9).



DUZLIT



BEZBEN

A total of 2437 organic hydrates were retrieved from the CSD; these hits were further classified as neutral two-residue compounds (1479), neutral three-residue com-

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(31) (a) Hunter, C. A.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5525. (b) Ferguson, S. B.; Sanford, E. M.; Seward, E. M.; Diederich, F. *J. Am. Chem. Soc.* **1991**, *113*, 5410. (c) Klebe, G.; Diederich, F. *Philos. Trans. R. Soc. London, A* **1993**, *335*, 37.

(32) Kuroda, R.; Sanderson, M. R.; Neidle, S.; Reese, C. B. *J. Chem. Soc., Perkin. Trans. 2* **1982**, 617.

(33) Clare, P.; Sowerby, D. B.; Haidul, I. *J. Organomet. Chem.* **1986**, *310*, 161.

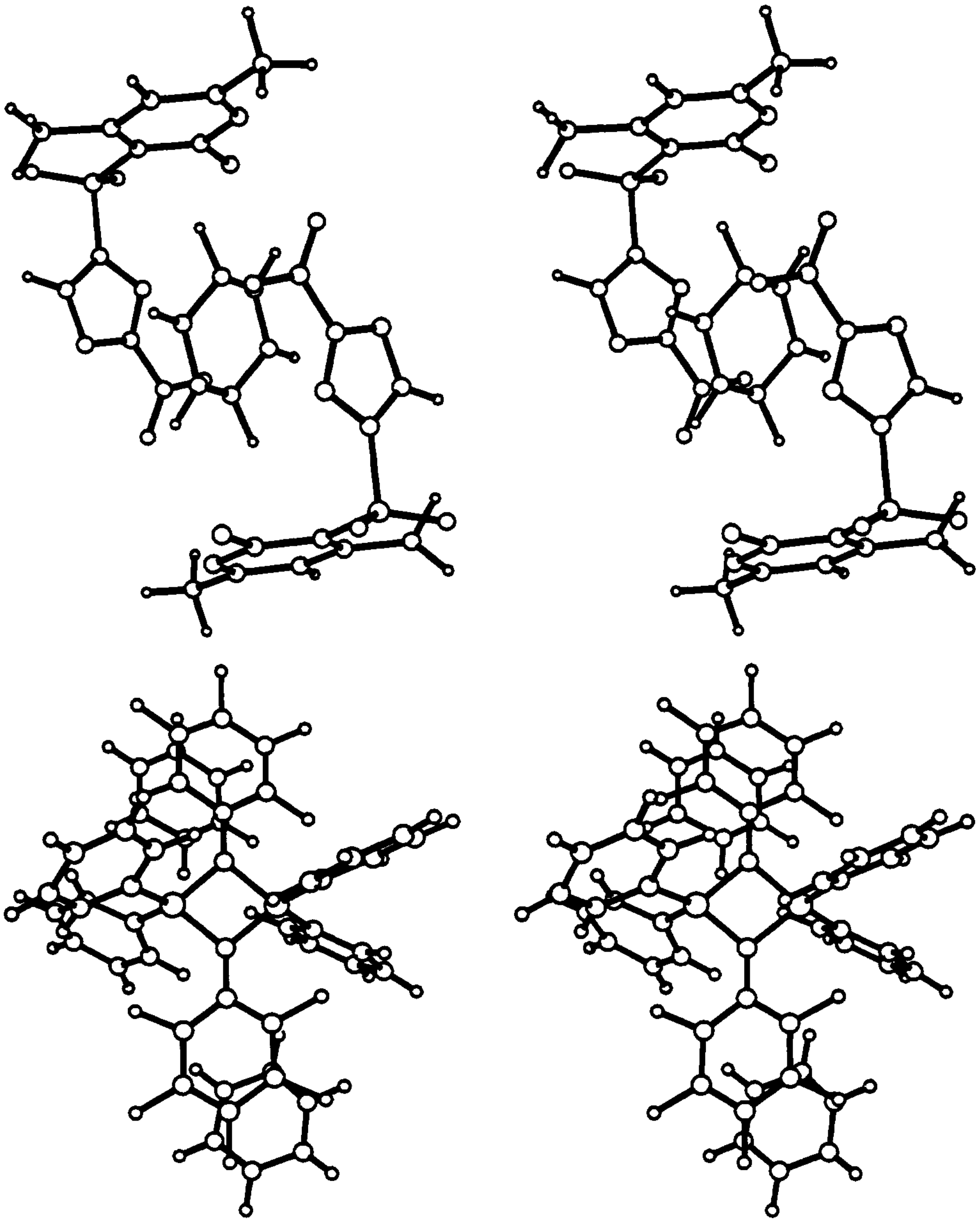

Figure 9. Benzene solvates satisfying stacking and herringbone interactions with the host molecules; (a, top) BEZBEN; (b, bottom) DUZLIT. Compare the similarity of (a) with Figure 5.

pounds (151), neutral four-residue compounds (2), and crystals containing charged molecules (805). Of these, we considered possible hydrogen bonding in the neutral two- and three-residue compounds. It is interesting to note here that the water is the most favored choice for the third residue in three-residue neutral organic compounds. Of the 176 neutral three-residue compounds in the CSD, as many as 151 compounds contain water as one of the residues, i.e, there are only 25 neutral three-residue compounds that do not contain water. What is more significant is that among these 151 hydrates, the water molecule is involved in hydrogen bonding in only 46.2% of the cases. In contrast, for the 1479 two residue hydrates, water is involved in hydrogen bonding in 66.3% of the cases. We did not find any evidence of hydrogen bonding in the remaining compounds even when we increased the $O_w \cdots (N, O)$ threshold from 3.2 to 3.5 Å. Additionally we evaluated the percentage of hydrogen bonds in both cases by imposing more rigorous restrictions such as eliminating all disordered molecules and reducing the *R* factor to be below 0.075. Even so, the trends are similar but the percentage of hydrogen-bonded compounds increased as expected for two-residue compounds to 72% (786) and for three-residue compounds to 58% (85). These results indicate that the highly polar water molecule can also act as a very good space filler, often being disordered when fulfilling this role. To provide crystal stability, it may occupy polar or apolar cavities without necessarily participating in strong hydrogen bonding. Water may act as a space filler because its small size allows it to fit easily into small voids created during the crystallization process.[34] Solvent inclusion may therefore be one of the factors that affects the crystallization process. It is pertinent to record here that water was not added to the recrystallizing solution of **1b** in 5:1 MeOH–toluene, but on the other hand, no attempt was made to carry out the recrystallization under strictly anhydrous conditions. It is reasonable to assume

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[34] However, it is possible that water is involved in weak intermolecular interactions such as C–H···O, O–H···π, and O–H···C in compounds which do not show strong hydrogen bonding. See for example: Viswamitra, M. A.; Radhakrishnan, R.; Bandekar, J.; Desiraju, G. R. *J. Am. Chem. Soc.* **1993**, *115*, 4868.

that certain molecules cannot crystallize if their shape is awkward and/or the intermolecular interactions are incompatible with close packing. Crystallization of such compounds may be facilitated by the presence of a particular solvent which is capable of being clathrated effectively.

Conclusions

The solid-state reaction reported here reveals that the principles of crystal engineering may be used to synthesize new compounds such as **1b** for a study of molecular and supramolecular properties. The CSD study on 1,2-diphenylethanes provides unambiguous crystallographic evidence for the presence of TBC.[6] The selective binding of an aromatic compound in the cavity formed by four phenyl groups (from two molecules) reveals an interesting feature in the binding process, namely, that by varying substituents on the phenyl groups one can fine-tune the orientation of the guests precisely. This example also highlights the superior selective binding features in the solid state where nondirectional, van der Waals, and directional $\pi-\pi$ and C–H$\cdots\pi$ interactions are perfectly matched.[2,10,35] The unusual absence of hydrogen bonding of the included water molecules in the **1b** crystal is an observation which seems to contradict chemical intuition especially in compounds where there is a lot of scope for hydrogen bonding. The CSD survey of hydrogen bonding in hydrates shows that the highly polar water molecule not only is good at forming hydrogen bonds but also is a good space filler; in other words, it provides thermodynamic stability to the crystal without invoking its potential hydrogen-bonding functions. The CSD search also hints that the symmetrical, nonpolar benzene molecule is more suited for a space-filling role rather than the toluene molecule. Finally it is suggested that the "correct" solvent for crystallization may be obtained by optimizing clathration effects in certain cases.

Acknowledgment. Financial support from the DST and UGC, Government of India (C.V.K.S., K.P., G.R.D.) and from NIH Grant GM 44360 (L.S., H.K., H.L.C.) is acknowledged.

Supplementary Material Available: Tables of thermal parameters, bond lengths and angles, and hydrogen-bonding scheme (4 pages); table of F_o/F_c values for the complex **1b** (14 pages).

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[35] Suzuki, T.; Fujii, H.; Miyashi, T. *J. Org. Chem.* **1992**, *57*, 6744.