Molecular Crystals and Liquid Crystals

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gmcl20

Syntheses and Crystal Structures of (N-Pyridylmethylene)Aminobenzamid New Building Blocks for Binary and Ternary Co-Crystals

Christer B. Aakeröy [a] , Alicia M. Beatty [b] & Keith Lorimer [c]

[a] Department of Chemistry, Kansas State University, Manhattan, KS

[b] Department of Chemistry, Mississippi State University, Mississippi State, MS

[c] SSCI, Inc., West Lafayette, IN

Version of record first published: 21 Dec 2006

To cite this article: Christer B. Aakeröy, Alicia M. Beatty & Keith Lorimer (2006): Syntheses and Crystal Structures of (N-Pyridylmethylene)Aminobenzamides: New Building Blocks for Binary and Ternary Co-Crystals, Molecular Crystals and Liquid Crystals, 456:1, 163-174

To link to this article: http://dx.doi.org/10.1080/15421400600788674

Mol. Cryst. Liq. Cryst., Vol. 456, pp. 163–174, 2006

ISSN: 1542-1406 print/1563-5287 online
DOI: 10.1080/15421400600788674

Syntheses and Crystal Structures of (*N*-Pyridylmethylene)Aminobenzamides: New Building Blocks for Binary and Ternary Co-Crystals

Christer B. Aakeröy
Department of Chemistry, Kansas State University, Manhattan, KS

Alicia M. Beatty
Department of Chemistry, Mississippi State University, Mississippi State, MS

Keith Lorimer
SSCI, Inc., West Lafayette, IN

The syntheses of four supramolecular reagents (SRs) based on (N-pyridylmethylene)-aminobenzamides are reported. The crystal structure of 4′-(N-4-pyridylmethylene) aminobenzamide is dominated by an amide-py N–H···N hydrogen bond and an amide–carbonyl N–H···O hydrogen bond. The crystal structure of 4′-(N-3-pyridyl-methylene)aminobenzamide contains the same N–H···N interaction but this time it is accompanied by an amide-imine N–H···N hydrogen bond. Finally, the crystal structure of 3′-(N-3-pyridylmethylene) aminobenzamide contains a well-known amide-amide ribbon constructed from two inequivalent N–H···O hydrogen bonds. The hydrogen-bond interactions in these three similar compounds are very different which indicates a structural flexibility that may be beneficial for successful co-crystallization reactions.

Keywords: hydrogen bonding; (N-pyridylmethylene)aminobenzamides; single-crystal X-ray diffraction; supramolecular reagents

INTRODUCTION

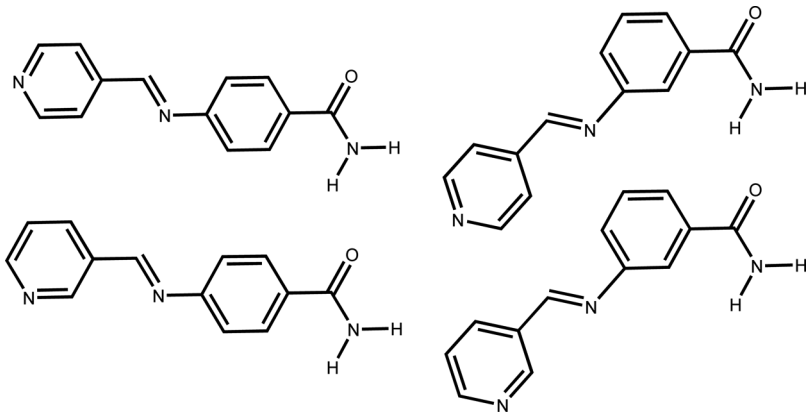
The fact that primary amides often generate self-complementary hydrogen-bond motifs [1] has meant that such functionalities have

Financial support from NSF (CHE-0316479) and Kansas State University is gratefully acknowledged.

Address correspondence to Christer B. Aakeröy, Department of Chemistry, Willard Hall, Kansas State University, Manhattan, KS 66506, USA. E-mail: aakeroy@ksu.edu

been employed as intermolecular synthetic tools in crystal engineering [2,3]. Many elegant studies have shown that a variety of extended molecular architectures can be constructed with the aid of complementary intermolecular interactions [4]. Typically, these assemblies are homomeric and despite the abundance of papers dealing with all aspects of design and assembly of organic extended networks with desirable connectivities and shapes, it remains very difficult to bring more than two different molecular species into one crystalline lattice in a predictable manner, without making or breaking covalent bonds [5,6]. In fact, there are very few examples of successful strategies for the reliable construction of ternary supermolecules [7–10]. In the first such study, *iso*nicotinamide was allowed to react with two carboxylic acids resulting in ternary supermolecules where the dominant supramolecular synthons are (1) the heteromeric carboxylic acid···pyridine hydrogen bond and (2) the heteromeric amide···acid hydrogen-bond interaction. These architectures are assembled according to a hierarchical view of intermolecular forces and, in each reported case, the stronger acid (as determined by pK_a values) interacts preferentially with the best acceptor (the pyridine nitrogen atom), and the weaker acid binds to the amide moiety. With this in mind, we want to explore the generality of our approach by making small and controllable alterations to our SR's and in this study we report on the synthesis of extended pyridyl-amide based compounds containing two different binding sites, Scheme 1.

These ligands can be synthesized via a simple one-step Schiff-base condensation [11] and they should, in principle, be capable of acting



SCHEME 1 Target ligands incorporating both pyridyl and carboxamide moieties.

as assembly platforms for ternary supermolecules. The ability to modify the length of the ligands as well as the substituent position provides important tools with which to control the metrics and shape of the resulting aggregates.

EXPERIMENTAL SECTION

Synthesis of 4′-(*N*-4-Pyridylmethylene)Aminobenzamide, 1

4-pyridinecarboxaldehyde (0.5 g, 4.7 mmol), 4-aminobenzamide (0.63 g, 4.7 mmol) and benzene (80 ml) were added to a 250 ml round-bottomed flask. A little ethanol was added to aid solubility (10 ml) and a Dean-Stark apparatus was attached. The solution was heated under reflux overnight and an orange precipitate was collected, washed with a little ethanol and dried. The orange solid was recrystallized from ethanol/water mixture to give yellow irregular crystals. Mp. 219–224°C.

Synthesis of 4′-(*N*-3-Pyridylmethylene)Aminobenzamide, 2

3-pyridinecarboxaldehyde (0.5 g, 4.7 mmol), 4-aminobenzamide (0.63 g, 4.7 mmol) and benzene (80 ml) were added to a 250 ml round-bottomed flask. A little ethanol was added to aid solubility (10 ml) and a Dean-Stark apparatus was attached. The solution was heated under reflux overnight and a pale yellow precipitate was collected, washed with ethanol and dried. Re-crystallization from methanol and water gave orange irregular crystals. Mp. 144–150°C.

Synthesis of 3′-(*N*-3-Pyridylmethylene)Aminobenzamide, 3

3-pyridinecarboxaldehyde (0.5 g, 4.7 mmol), 3-aminobenzamide (0.63 g, 4.7 mmol) and benzene (80 ml) were added to a 250 ml round-bottomed flask. A little ethanol was added to aid solubility (10 ml) and a Dean-Stark apparatus was attached. The solution was heated under reflux overnight and a pale yellow precipitate was collected, washed with ethanol and dried. Crystallization from ethanol gave yellow prisms. Mp. 132–134°C.

Synthesis of 3′-(*N*-4-Pyridylmethylene)Aminobenzamide, 4

4-pyridinecarboxaldehyde (0.5 g, 4.7 mmol), 3-aminobenzamide (0.63 g, 4.7 mmol) and benzene (80 ml) were added to a 250 ml round-bottomed flask. A little ethanol was added to aid solubility (10 ml) and a Dean-Stark apparatus was attached. The solution was heated under reflux

overnight and a pale yellow precipitate was collected, washed with ethanol and dried. Crystallization from methanol gave a yellow microcrystalline solid. Mp. 159–162°C.

X-Ray Crystallography

Crystalline samples of **1–3** were placed in inert oil, mounted on a glass pin, and transferred to the cold gas stream of the diffractometer. Crystal data were collected and integrated using a Bruker SMART 1000 system, with graphite monochromated Mo-Kα ($\lambda = 0.71073$ Å) radiation at 173 K. The structures were solved by direct methods using SHELXS-97 and refined using SHELXL-97 [12]. Non-hydrogen atoms were found by successive full matrix least squares refinement on F^2 and refined with anisotropic thermal parameters. Hydrogen atom positions were located from difference Fourier maps and a riding model with fixed thermal parameters [$u_{ij} = 1.2U_{ij}(eq)$ for the atom to which they are bonded] was used for subsequent refinements. Table 1 provides crystallographic details for **1–3**, [13] and the molecular geometries and numbering scheme are shown in Figures 1a–c.

RESULTS

Crystal Structure of 4-(*N*-4-Pyridylmethylene) Aminobenzamide, 1

The crystal structure of **1** consists of 1-D hydrogen-bonded chains generated from N–H···N interactions between amide and pyridine functionalities of adjacent molecules. The remaining N–H hydrogen bond donor of the amide group links to carbonyl oxygen acceptors of neighboring molecules to generate 2-D sheets, Figure 2 and Table 2.

In addition, short C–H···N interactions between aromatic protons and imine nitrogen atoms help bind adjacent chains together into 2-D sheets. The sheets, when viewed edge-on display a planar arrangement, Figure 3.

Crystal Structure of 4-(*N*-3-Pyridylmethylene) Aminobenzamide, 2

The crystal structure of **2** contains N–H···N hydrogen bonds between amide and pyridine functionalities of two adjacent molecules of **2**. The anti-amino hydrogen-bond donor of the amide functionality links to imine nitrogen acceptors of neighboring dimers to generate 1-D ribbons, Figure 4 and Table 3.

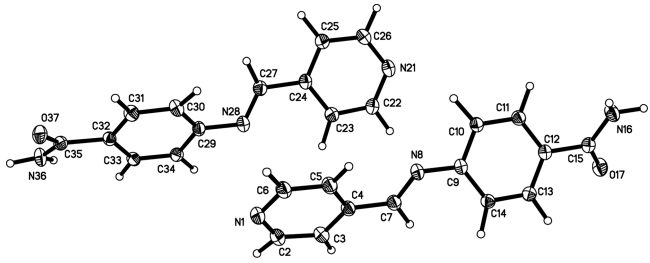
TABLE 1 Data Collection and Refinement for **1–3**

Compound	**1**	**2**	**3**
Empirical formula	$C_{13}H_{11}N_3O$	$C_{13}H_{11}N_3O$	$C_{13}H_{11}N_3O$
MW	225.25	225.25	225.25
Crystal size (mm)	$0.46 \times 0.32 \times 0.22$	$0.20 \times 0.20 \times 0.20$	$0.40 \times 0.30 \times 0.28$
Crystal system	triclinic	monoclinic	triclinic
Space group	P-1	$P2_1/c$	P-1
a (Å)	8.316(3)	20.433(6)	9.5621(10)
b (Å)	8.356(3)	4.9674(14)	9.9143(11)
c (Å)	8.436(3)	11.249(3)	12.2870(14)
α (deg)	107.304(6)	90	79.927(2)
β (deg)	99.996(6)	93.958(5)	84.163(3)
χ (deg)	94.571(6)	90	73.976(2)
Volume ($Å^3$)	545.7(3)	1139.0(5)	1100.6(2)
Z	2	4	2
D_{calc}(g cm^{-3})	1.371	1.314	1.359
F(000)	236	472	472
μ(Mo-K_α) (mm^{-1})	0.091	0.087	0.090
Temp (K)	173	173	173
$\theta - 2\theta$ scans; θ range (deg)	2.51 to 28.15	2.00–28.33	1.69 – 23.30
Range h	−10 to 10	−27 to 26	−5 to 10
Range k	−10 to 10	−5 to 6	−10 to 11
Range l	−11 to 10	−14 to 14	−12 to 13
Reflns collected	3586	7523	5828
Unique reflns	2367	2617	3156
Observed reflns ($I > 2\sigma I$)	1837	1790	2446
Data:parameter (obs. data)	11.93	11.62	7.97
Refinement	Full-matrix lsq. on F^2	Full-matrix lsq. on F^2	full-matrix lsq. on F^2
R/R_w^2 (obs data)	0.0553/0.1699	0.0465/0.1128	0.0418/0.1132
R/R_w^2 (all data)	0.0717/0.1781	0.0766/0.1247	0.0550/0.1208
$\Delta\rho_{max/min}$ (e $Å^{-3}$)	0.286/−0.266	0.204/−0.261	0.188/−0.198
S	1.129	0.984	1.067
Weighting function ($w^{-1} = [\sigma^2(F_o^2) + (g_1P)^2 + (g_2P)]$ where $P = [F_o^2 = 2\ F_c^2]/3$	$g_1 = 00817$ $g_2 = 0.3557$	$g_1 = 0.0652$ $g_2 = 0.0000$	$g_1 = 0.0661$ $g_2 = 0.1367$

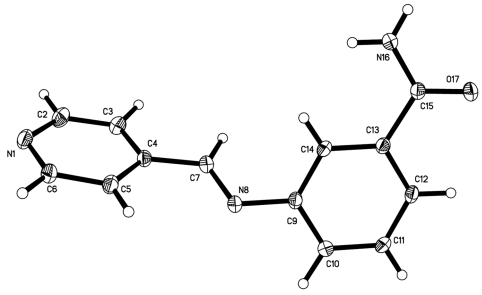
Neighboring ribbons stack on top of each other, Figure 5.

Crystal Structure of 3-(*N*-3-Pyridylmethylene) Aminobenzamide, 3

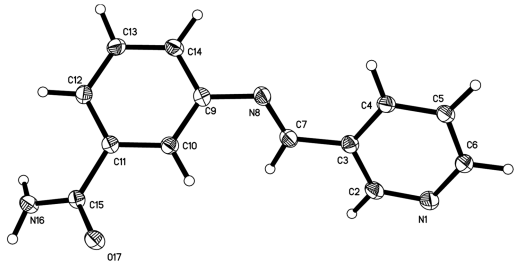
Symmetry inequivalent amide-amide N−H···O hydrogen-bond interactions generate head-to-head in the crystal structure of **3**. The remaining anti hydrogen-bond donor of the amide group links adjacent



(a)



(b)



(c)

FIGURE 1 Thermal ellipsoid plots of (a) 4-(*N*-4-pyridylmethylene)aminobenzamide, **1** (b) 4-(*N*-3-pyridylmethylene)aminobenzamide, **2** (c) 3-(*N*-3-pyridylmethylene)aminobenzamide, **3**.

dimers *via* N–H···O hydrogen bonds to form infinite 1-D ribbons, Figure 6 and Table 4.

Adjacent ribbons stack on top of each other generating infinite columns of dimers, Figure 7.

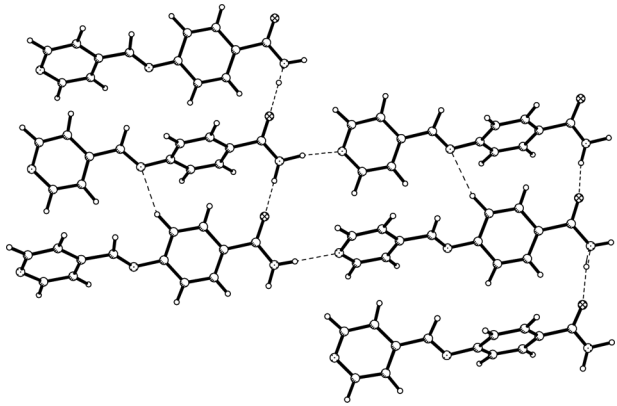


FIGURE 2 2-D sheets generated from from N–H···O and from N–H···N interactions.

DISCUSSION

The crystal structures of all three extended supramolecular reagents are dominated by N–H···O and N–H···N hydrogen bonds. There are three functional groups present in each structure: primary amides, pyridine nitrogen atoms and imine groups with a total of two donors and three acceptors capable of forming strong hydrogen bonds. Both donors come from the amide NH_2 group and therefore, as there are no other competing donors in these structures, the amide group functions as the only primary hydrogen-bond donor. Due to the unequal ratio of donors to acceptors, short C–H···O and C–H···N contacts are seen in all three structures. A summary of the primary hydrogen-bond interactions is presented in Table 5.

TABLE 2 Hydrogen Bonds for **1** [Å and deg.]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N36-H36A...N2#1	0.94	2.06	2.996(2)	172
N36-H36B...O17#2	0.99	1.97	2.927(2)	163
N16-H16A...O37#3	0.95	2.16	2.979(2)	144
N16-H16B...N1#4	1.10	1.86	2.951(2)	172
C25-H25...O37#5	1.08	2.46	3.491(2)	161

#1 x, y + 1, z − 1 #2 −x, −y + 1, −z + 3 #3 −x + 1, −y + 1, −z + 3 #4 x, y − 1, z + 1 #5 −x + 1, −y + 1, −z + 2.

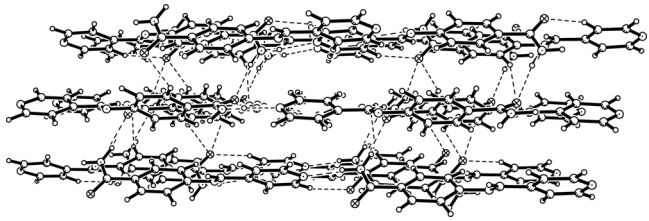


FIGURE 3 Sheets of **1** are planar when viewed edge-on.

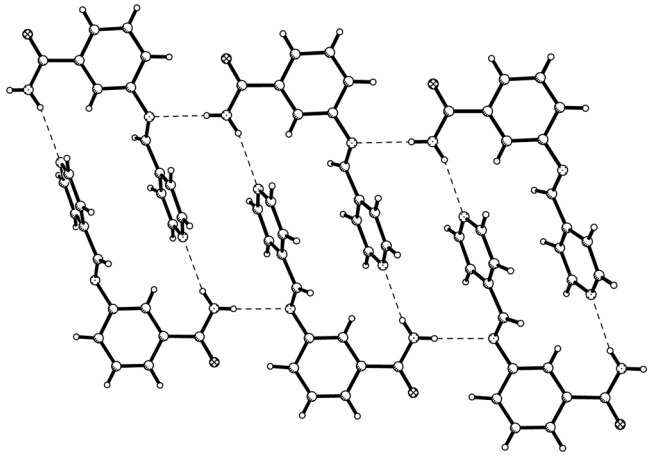


FIGURE 4 A combination of amide···pyridine and amide···imine N–H···N hydrogen bonds, produce an infinite ribbon in the crystal structure of **2**.

A detailed structural examination of **1–3** has enabled the identification of several differences, in terms of molecular recognition behavior between the three compounds. The fact that there are significant differences in the crystal structures of three closely related compounds that all contain the same primary hydrogen-bond donors

TABLE 3 Hydrogen Bonds for **2** [Å and deg.]

D-H...A	d(D-H)	d(H...A)	d(D...A)	< (DHA)
N16-H16A...N8#1	0.85	2.38	3.220(3)	173
N16-H16B...N1#2	0.86	2.39	3.236(3)	166

#1 x, y − 1, z #2 −x + 2, −y + 3, −z.

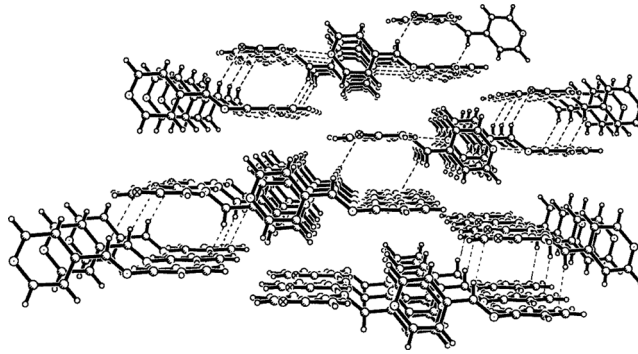


FIGURE 5 Edge-on view of 2-D layers of **2** showing N–H···O interactions.

and acceptors may actually represent an advantage when it comes to using these compounds in preparations of co-crystals via hydrogen-bond based strategies. Co-crystals are not necessarily easy to obtain

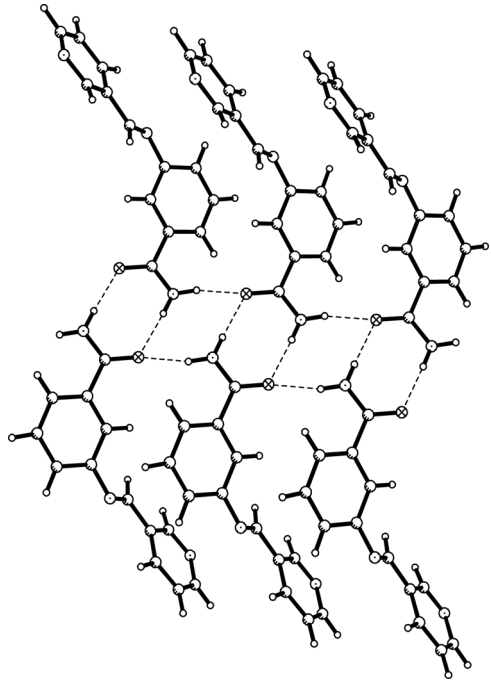


FIGURE 6 A well-known ribbon-like motif in the crystal structure of **3**.

TABLE 4 Hydrogen Bonds for **3** [Å and deg.]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N16-H16B...O17#1	0.90	2.06	2.956(2)	177
N16-H16A...O17#2	0.90	2.02	2.874(2)	158

#1 −x, −y+1, −z+2 #2 x, y − 1, z.

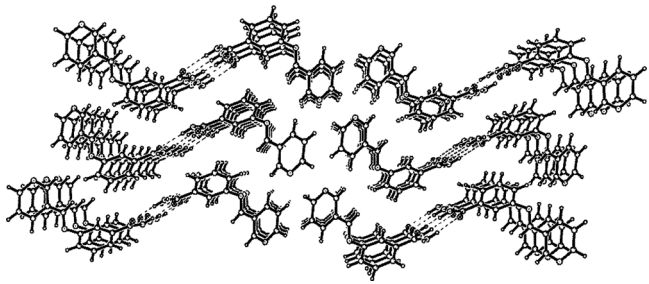


FIGURE 7 Infinite hydrogen-bonded ribbons in the crystal structure of **3**.

since binary and higher-order molecular solids are only likely to form if the heteromeric intermolecular interactions are more favorable than the alternative homomeric non-covalent forces that may take place. If a compound is capable of participating in several different robust and well-defined intermolecular interactions it may be well-suited to supporting the demands of multiple hydrogen-bond donors/acceptors on a variety of molecules. Consequently, such a compound is likely to be a good supramolecular reagent since it possesses a structural flexibility that can allow it to co-exist with different molecular species within the same crystalline lattice. This idea is akin to the notion that polymorphic compounds that display alternative packing patterns are good

TABLE 5 Primary Hydrogen-Bond Interactions for **1–3**

Compound	Interaction moieties	Hydrogen bonding interaction
1	amide-pyridine	N–H···N
	amide-amide	N–H···O
2	amide-pyridine	N–H···N
	amide-imine	N–H···N
3	amide-amide	N–H···O
	amide-amide	N–H···O

candidates for supramolecular synthesis of co-crystals as they are not energetically locked into a single type of crystalline lattice or packing mode [14].

We are currently examining the ability of **1**–**4** to act as reliable supramolecular reagents through the use of systematic co-crystallization reactions with a wide range of hydrogen-bond donors such as carboxylic acids and oximes.

REFERENCES

[1] Leiserowitz, L. & Tuval, M. (1978). *Acta Crystallogr. Sect. B*, *B34*, 1230.

[2] Desiraju, G. R. (1995). *Angew. Chem. Int. Ed. Engl.*, *34*, 2311; Desiraju, G. R. (1989). *Crystal Engineering*, Elsevier: Amsterdam; Aakeröy, C. B. (1977). *Acta Crystallogr. Sect. B*, *53*, 569; Aakeröy, C. B. & Salmon, D. J. (2005). *Cryst. Eng. Comm.*, *7*, 439; Childs, S. L., Chyall, L. J., Dunlap, J. T., Smolenskaya, V. N., Stahly, B. C., & Stahly, G. P. (2004). *J. Am. Chem. Soc.*, *126*, 13335; Remenar, J. F., Morissette, S. L., Peterson, M. L., Moulton, B., MacPhee, J. M., Guzman, H. R., & Almarsson, O. (2003). *J. Am. Chem. Soc.*, *125*, 8456; Du, M., Zhang, Z.-H., & Zhao, X.-J. (2005). *Cryst. Growth Des.*, *5*, 1199; Trask, A. V., Motherwell, W. D. S., & Jones, W. (2005). *Cryst. Growth Des.*, *5*, 1013; Lehn, J.-M. (1998). In: *Perspectives in Coordination Chemistry*, Williams, A. F., Floriani, C., & Merbach, A. E. (Eds.), VCH; Kaes, C., Katz, A., & Hosseini, M. W. (2000). *Chem. Rev.*, *100*, 3553; Cronin, L. (2004). *Ann. Rep. Prog. Chem. Sect. A: Inorg. Chem.*, *100*, 323; Ward, M. D., McCleverty, J. A., & Jeffery, J. C. (2001). *Coord. Chem. Rev.*, *222*, 251; Batten, S. R. (2005). *J. Solid State Chem.*, *178*, 2475.

[3] Aakeröy, C. B., Beatty, A. M., & Helfrich, B. A. (1998). *J. Chem. Soc. Dalton Trans.*, 1943; Aakeröy, C. B. & Beatty, A. M. (1998). *Chem. Commun.*, 1067.

[4] Papaefstathiou, G. S. & MacGillivray, L. R. (2001). *Org. Lett.*, *3*, 3835; Nguyen, T. L., Fowler, F. W., & Lauher, J. W. (2001). *J. Am. Chem. Soc.*, *123*, 11057; MacGillivray, L. R., Reid, J. L., & Ripmeester, J. A. (2000). *J. Am. Chem. Soc.*, *122*, 7817; Bhogala, B. R. & Nangia, A. (2003). *Cryst. Growth Des.*, *3*, 547; Kumar, U., Kato, T., & Frechet, J. M. J. (1992). *J. Am. Chem. Soc.*, *114*, 6630; Palmore, G. T. R., Luo, T.-J., McBride-Wieser, M.-T., Picciotto, E. A., & Reynoso-Paz, C. M. (1999). *Chem. Mater.*, *11*, 3315.

[5] Shan, S., Batchelor, E., & Jones, W. (2002). *Tet. Lett.*, *43*, 8721; Bailey Walsh, R. D., Bradner, M. W., Fleischman, S., Morales, M. A., Moulton, B., Rodriguez-Hornedo, N., & Zaworotko, M. J. (2003). *Chem. Commun.*, 186; Vishweshwar, P., Thaimattam, R., Jaskolski, M., & Desiraju, G. R. (2002). *Chem. Commun.*, 1830; Zerkowski, J. A., MacDonald, J. C., & Whitesides, G. M. (1997). *Chem. Mater.*, *9*, 1933; Kane, J. J., Liao, R. F., Lauher, J. W., & Fowler, F. W. (1995). *J. Am. Chem. Soc.*, *117*, 12003; Lehn, J.-M., Mascal, M., DeCian, A., & Fischer, J. (1990). *J. Chem. Soc. Chem. Commun.*, 479; Vishweshwar, P., Nangia, A., & Lynch, V. M. (2003). *Cryst. Eng. Comm.*, *5*, 164; Almarsson, Ö. & Zaworotko, M. J. (2004). *Chem. Commun.*, 1889.

[6] Desiraju, G. R. & Sarma, J. A. R. P. (1983). *Chemical Comm.*, 45; Huang, C., Leiserowitz, L., & Schmidt, G. M. (1973). *J. Chem. Soc. Perkin Trans.*, *2*, 503; Pan, F., Wong, W. S., Gramlich, V., Bosshard, C., & Gunter, P. (1996). *Chem. Commun.*, 2; Pedireddi, V. R., Jones, W., Chorlton, A. P., & Docherty, R. (1996). *Chem. Commun.*, 997; Aakeröy, C. B., Beatty, A. M., Nieuwenhuyzen, M., & Zou, M.

(2000). *Tetrahedron*, *56*, 6693; Dale, S. H., Elsegood, M. R. J., Hemmings, M., & Wilkinson, A. L. (2004). *Cryst. Eng. Comm.*, *6*, 207; Pedireddi, V. R., Prakasha-Reddy, J., & Arora, K. K. (2003) *Tet. Lett.*, *44*, 4857.

[7] Aakeröy, C. B., Beatty, A. M., & Helfrich, B. A. (2201). *Angew. Chem. Int. Ed.*, *40*, 3240; Aakeröy, C. B., Desper, J., & Urbina, J. F. (2005). *Chem. Commun.*, 2820; Aakeröy, C. B., Desper, J., Elisabeth, E., Helfrich, B. A., Levin, B., & Urbina, J. F. (2005). *Zeitschrift f. Krist.*, *220*, 325; Bhogala, B. R., Basavoju, S., & Nangia, A. (2005). *Cryst. Growth Des.*, *5*, 1683; Aakeröy, C. B., Desper, J., & Helfrich, B. A. (2004). *Cryst. Eng. Comm.*, *6*, 19.

[8] Koefler's complex is a solvate (pyridine), and its preparation was not based upon an explicit supramolecular strategy. Bernstein, J., Regev, H., & Herbstein, F. H. (1980). *Acta Crystallogr. Sect. B*, *36*, 1170.

[9] A three-component co-crystal based on isomorphous replacement with acridine in a 2:3 2,2′-dihydroxybiphenyl phenazine co-crystal has been reported. This approach also relies on molecular complementarity and recognition and may be effective in the future design of other ternary systems. Smolka, T., Boese, R., & Sustmann, R. (1999). *Struct. Chem.*, *10*, 429.

[10] A 3:1:1 ternary co-crystal has been reported previously although no explicit design strategy was evident. Lynch, D. E., Smith, G., Byriel, K. A., & Kennard, C. H. L. (1992). *J. Chem. Soc. Chem. Commun.*, 300.

[11] Blatter, H. M. US Pat. 3340260 19670905 (1967).

[12] Sheldrick, G. M. University of Göttingen.

[13] CCDC 285456–285458 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[14] Aakeröy, C. B., Beatty, A. M., Helfrich, B. A., & Nieuwenhuyzen, M. (2003). *Cryst. Growth & Des.*, *3*, 159.