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Co-crystals with Acetylene: Small Is not Simple!

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Dedicated to Yitzhak Apeloig on occasion of his 65th birthday

Abstract: Acetylene is an amazingly versatile component for the formation of co-crystals. It requires careful handling and special techniques for crystallisation, but the efforts seem to be rewarding when attaining co-crystals with small molecules as partners. Many basic questions such as the dominance of specific heterogeneous intermolecular interactions, their driving force for the formation of multicomponent crystals instead of neat ones are expected to be easily analysed. The underlying packing patterns and resulting stoichiometries based on the known supramolecular synthons seem to be straightforward for such small molecules and crystal engineering, considered as the prototype of supramolecular synthesis, should be a simple task. Nineteen co-crystals with acetylene are presented in this paper, some of which have been previously reported individually. An attempt has been made to find features shared by the groups of co-crystals, including those that could not be co-crystallised. But in spite of clear ideas and experiences from previous experiments, surprisingly almost none of systems reached our expectations. Our intuitive approach was not fulfilled, which demonstrates that multicomponent crystals even of small molecules will remain a great challenge for theoretical methods and the crystal structures shown herein represent good candidates for future testing. On the other hand, we wish to encourage other groups to present their views on the crystal structures with an unbiased approach that may offer a better explanation than we are able to outline in this article.

Keywords: acetylene · aggregation · crystal packing · molecular interactions · X-ray diffraction

Introduction

Organic chemical synthesis in the last century was successful in designing methods for the production of nearly any small organic molecule needed by mankind. This is especially evident in the field of pharmaceutics, but also true of many small compounds with hidden chemical applications in everyday life. The resolution of a difficult task often results in an even more difficult task. Nowadays it is expected that new materials are either all-rounders or have additional functionalities. Functionality implies differentiation, which can lead to multicomponent supermolecules that self-organise. In terms of synthesis, this emphasises weaker intermolecular interactions with binding energies of 5–20 kJ mol^{-1}, which are weak enough to be formed and broken as needed but strong enough, in concert and if designed well, to maintain aggregation of the aggregate. This vision is, of course, inspired by Nature's biochemical examples. Even the key properties of simpler materials are governed by weak intermolecular forces. The study and classification of intermolecular forces as well as their use for assembling molecular aggregates is a new, developing field of research.

Co-crystals are a first step in such multicomponent supramolecular aggregates. They may also be seen as model compounds that are easier to prepare and analyse. The crystallisation of a co-crystal of defined stoichiometry represents a prototype of supramolecular synthesis.[1] In contrast to molecular synthesis, there is no breaking or forming of covalent bonds, everything relies on weak interactions only. To produce multicomponent solids by co-crystallisation might seem anti-intuitive at first because crystallisation is often employed for purification. Therefore the formation of a co-crystal from a mixture of organic materials is rare, even though mixed crystals and solvates are commonplace in inorganic chemistry and mineralogy. This new synthetic approach is still not well understood in terms of strategy or systematic development but it is gaining interest in several industrially important areas.

Pharmaceutical co-crystals are prominent among these areas. In the last decade the development of new active in-

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gredients takes increasingly more time and is shifting towards biochemical methods. The slow down in development is partly due to increasing costs within the development itself, but also a result of the testing, marketing and legal procedures, especially the settlement of patent claims in the USA. On this basis, it is not surprising that a substantial amount of pharmaceutical research is devoted to the modification of known active ingredients, including the modification by co-crystallisation.

By co-crystallisation, different molecules with different functionalities or functional groups can be brought together relatively easily compared with the effort of designing a covalently bound molecule with both functions combined. The partners are free to self-organise into an optimal intermolecular arrangement to yield a co-crystal. This might take the form of a molecular complex with ordered molecules in a fixed stoichiometric ratio or a host–guest complex in which the guest fits into the cavities of a host network: it is often disordered and has only partial occupancy.[2] Whereas the mixing of compounds is usually favoured by entropy, the formation of a co-crystal still depends on it being thermodynamically stable relative to the crystals of the neat compounds but it may also be kinetically preferred. As mentioned above, crystallisation from mixtures may be used for purification under which circumstances a co-crystal is not the desired result.

The product of a successful co-crystallisation can be analysed by X-ray diffraction, preferably by single-crystal diffraction if a crystal of appropriate dimensions and quality can be grown. Thus, a three-dimensional structure of the molecules and their relative positions would be available and be the result of all the intermolecular forces acting at the time of crystallisation. To separate the effects of all such forces it has been suggested to select small molecules, which have a lower number of permutations amongst all the possible interactions. This is also attractive in theoretical chemistry in which a smaller number of atoms in a calculation leads to significantly better results at the same time. Co-crystals of small molecules may therefore be considered as model compounds for the study of intermolecular interactions. Unfortunately, small molecules have low melting points and can even be gases under ambient conditions and therefore they must be crystallised at low temperatures or increased pressures. This necessitates special experimental instrumentation and methods as will be outlined below.

The analysis of the packing of a co-crystal is governed by two complementary questions. First, the specialities and geometrical details of the interactions in the co-crystal have to be evaluated. Can those intermolecular interactions that predominantly influence the packing be identified? For this it is important to compare structures with similar functional groups and similar interactions to find patterns and rank their relative robustness. This can be done by studying homologous series of compounds.[3] Highly robust patterns of intermolecular interactions are termed synthons, which suggests their usefulness in supramolecular synthesis.[4] Secondly, the detected principles can be generalised with the aim of predicting the packing of so far unknown co-crystals. Theoretical methods are being developed to help in the prediction and multicomponent systems will be the next great challenge.

For a better understanding of co-crystal formation we decided to use small molecules that only have a few functionalities. Our strategy focused on the combination of a Lewis acid and a Lewis base, which results in the formation of a hydrogen bridge. Although hydrogen bridges are weak in comparison with covalent or ionic bonds, they themselves are divided into strong, medium strong and weak hydrogen bridges.[5] The weak bridges are all bonds from a hydrogen atom attached to a carbon atom with the acceptor usually an oxygen, nitrogen or halogen atom. The chemical bond has so many meanings for chemists that the term hydrogen bond might be misinterpreted whereas the term hydrogen bridge is free of prejudices and is "perhaps a better descriptor", as expressed by Desiraju.[5b]

An ideal co-crystal component with a minimum of functional groups should form co-crystals with a large number of partner molecules. These partner molecules should be small and sparse in their functionality. One of the most versatile molecules in respect of weak intermolecular interactions is probably acetylene. Acetylene is an ellipsoidal molecule rather than rod-shaped, the long axis is 5.5 Å. As a C–H donor it is bifunctional and simultaneously it can act as a π acceptor. This enables acetylene to form networks. The hydrogen bridges from acetylene are expected to be close to linear, however, the flat energy profile allows for a high variation of the C–H···A angle, which increases the flexibility of the networks. Suitable compounds for co-crystallisation with acetylene should show good acceptor abilities and ideally have more acceptors than donors and/or only weaker C–H donor functionalities.

Acetylene: Owing to the carbon≡carbon triple bond and the high positive energy of formation, acetylene is an unstable, highly reactive unsaturated hydrocarbon.[6] The C≡C triple bond and C–H bond lengths are 1.176 and 1.025 Å, respectively.[7]

Under normal conditions acetylene is a colourless, nontoxic and narcotic gas; it is slightly lighter than air. The critical temperature and pressure are 308.32 K and 6.139 MPa. The triple point at 128.3 kPa is 192.4 K. The formation of acetylene is strongly endothermic ($\Delta H_f = +227.5\ kJ\,mol^{-1}$ at 298.15 K).

Self-decomposition can be initiated when certain pressure limits above atmospheric pressure are exceeded. Solid acetylene is not critical with regard to decomposition provided it is the only material involved. The crystalline structure of solid acetylene changes at −140.15 °C from a cubic to an orthorhombic phase. The solubility coefficients of acetylene in organic solvents are listed in Table 1.[8] Acetylene is well-suited to co-crystallisation studies because it dissolves well in various organic solvents, which indicates its versatility in intermolecular interactions.

Table 1. Solubility coefficients of C_2H_2 in various solvents.[8]

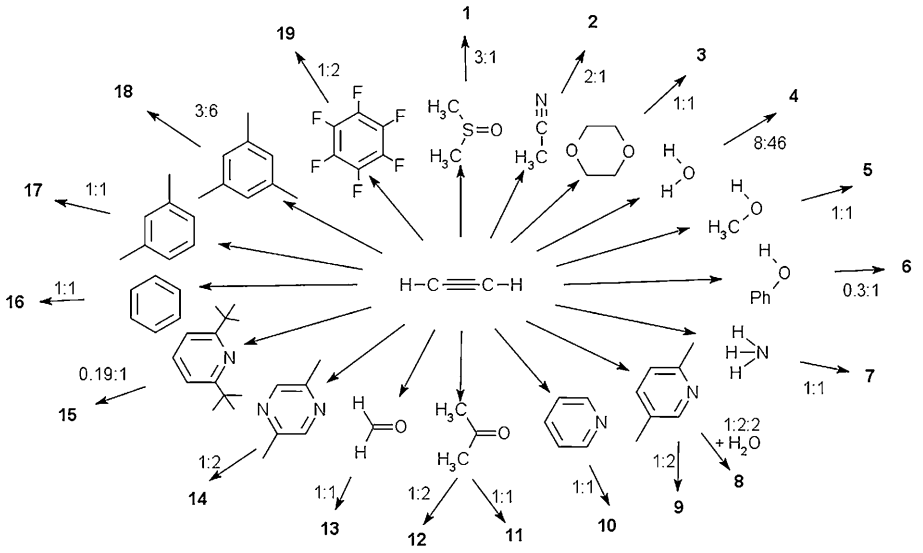
Solvent	C_2H_2 pressure [bar]	Solubility coefficient [mol kg^{-1} bar^{-1}]	
		20 °C	25 °C
methanol	0.98	1.979	0.569
ethanol	0.98	0.851	0.318
n-hexane	6.90	0.523	0.264
benzene	0.98		0.225
toluene	0.98	0.619	0.214
xylene (tech.)	0.98	0.528	0.189
triethyleneglycol	0.98		0.205
acetone	0.98	4.231	1.069
N-methyl-2-pyrrolidone	0.98	5.687	1.319
N,*N*-dimethylformamide	0.98	5.096	1.501
dimethyl sulfoxide	0.98		1.001
ammonia	0.98	7.052	2.229

Acetylene is used in several processes in chemical engineering and as a welding gas. Because of its tendency to easily deflagrate or to detonate under pressure, acetylene cannot be compressed and stored in gas cylinders like most other gases. To desensitise the gas, acetylene stored in gas cylinders is dissolved in a solvent in which the acetylene is very soluble. This solvent is mostly dispersed in a porous solid that fills the gas cylinder completely. The porous material in the cylinder arrests any local acetylene decomposition when induced, for instance, by flashback. Acetone and dimethylformamide are the preferred solvents for acetylene in cylinders. Owing to the difficulty in the preparation of co-crystals formed by acetylene and these solvents, any study of the underlying interactions were prevented until recently, when the difficulties were overcome by in situ cryocrystallisation techniques.

An overview: Before the results are discussed a generalised experimental method for the preparation of acetylene co-crystals is given and the special difficulties of their growth are discussed. The results (Scheme 1) are arranged not according to their chemical classification but by the similarities of the coordination sphere of the acceptor, starting from a tetrahedral sphere, through distorted octahedral and trigonal-bipyramidal spheres, to an aromatic linear arrangement. This one-by-one presentation of results is interrupted by ad hoc discussions of special features common to a sub-group and exemplified by the structure at hand. The ratio of acetylene-to-acceptor molecules and the distinction of molecular complexes and clathrates are discussed with the example of DMSO. The importance of comparisons with the packing of the neat components is discussed in the section on dioxane. The lengths of the acetylene hydrogen bridges are given in the acetonitrile section. A comparison with the structures of bromine is discussed in the section on methanol. The importance of polymorphism is discussed with the structures of acetone, which was found to be polymorphic. Five of the structures are clathrates, which are discussed in the text when chemically appropriate and in the context of the clathrate of hexafluorobenzene. The discussion is completed by a list of compounds that did not lead to co-crystals.

General experimental procedure: Acetylene is a gas at ambient pressure and temperature and condenses at 189 K. Direct co-crystallisation at ambient pressure therefore is not possible.

To trap the corresponding solutions and to grow single crystals of the complexes, acetylene was condensed at −196 °C in a vacuum line into a quartz capillary (0.3 mm diameter) already filled with the second component, flame-sealed and transferred to the diffractometer, a Bruker Smart1000 CCD-System with an XSTREAM LT device (MSC). The latter provides a very stable cold stream of gas along the omega axis. The goniometer head was equipped with an additional arc and an *x*,*y*,*z* slide, which allows alignment of the capillary along the omega axis. This is used as the scanning axis for data collection with a fixed or at least highly constrained ϕ angle, as provided by the Siemens SMART three-axis platform. The capillary, which withstands pressures of up to about 100 bar, was then cooled to −155 °C and a crystal was grown by our in situ crystallisation technique, that is, by moving an intensity controlled, focused infrared laser beam along the capillary (OHCD).[9] The diffusion processes at the gas/liquid/solid interfaces do not lead to the formation of one single crystal that fills the entire capillary as we usually achieve for neat compounds. Multiple heating/cooling cycles of the acetylene system usually produce several crystals in the same area. They are so close to



Scheme 1. Overview of the co-crystals formed with acetylene.

each other that all of them diffract simultaneously in the primary X-ray beam. Consequently, the collected data correspond to a superposition of diffraction patterns of several crystals. In a laborious hand-selection and systematic separation procedure utilising the RLATT program in the Bruker-AXS software, we then extracted consistent data sets and indexed, integrated and merged them to refinement. The ease with which this is possible has increased considerably in recent years since we started this procedure with acetylene. Programs like cell_now, twinabs and the twin-handling algorithms in SAINT of the Bruker-AXS suite allow for easy processing of non-merohedral twins. We feel that the procedure we coined "oligo-diffractometry" in 2003 has now evolved into a mature form between single crystal and powder work.[10]

Results and Discussion

Tetrahedral

Dimethyl sulfoxide: The molecular complex **1** of acetylene with dimethyl sulfoxide (DMSO) is a good example of the versatility of acetylene co-crystals.[10] In the crystal the molar ratio of acetylene to DMSO is 2:1. This should not be confused with the three different molecules in the unit cell as two acetylene molecules are placed at a centre of symmetry. The first molecule of acetylene links the DMSO molecules in a zigzag chain, with one short, nearly linear and one longer, side-on C–H···O hydrogen bridge (Figure 1). This zigzag chain is comparable to the zigzag chain in the β-form of the co-crystal with acetone.

The second acetylene molecule forms a two-dimensional network by cross-linking of the chains with two side-on C–H···O hydrogen bridges. This pseudo-hexagonal two-dimensional network of triple acetylene-bridged DMSO oxygen atoms is heavily corrugated. So even when neighbouring layers interlock, they still leave cavities for a third molecule of acetylene that does not participate in C–H···O hydrogen-bridging (C–H···O, $d=5.006$ Å) but is clathrated into the packing (Figure 2). The shortest intermolecular distances are to the other acetylene molecules (C–H···π, $d=2.871$ and 2.877 Å), but the are still above the sum of the van der Waals radii.

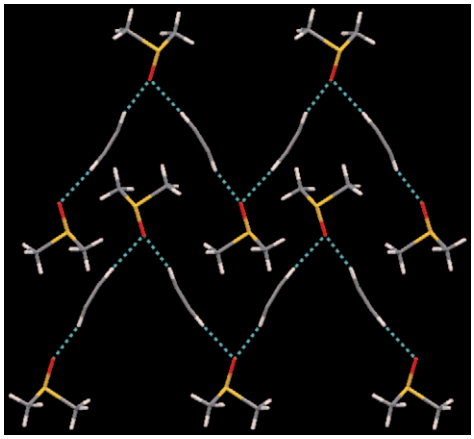


Figure 1. Part of the packing of the 2:1 acetylene/dimethyl sulfoxide co-crystal (**1**). The interaction of the first acetylene is characterised by a zigzag chain (C–H···O, $d=2.085$ Å, $D=3.135$ Å, $\theta=162°$; S=O···C, $\theta=165°$; C–H···O, $d=2.174$ Å, $D=3.252$ Å, $\theta=173°$; S=O···C, $\theta=123°$).

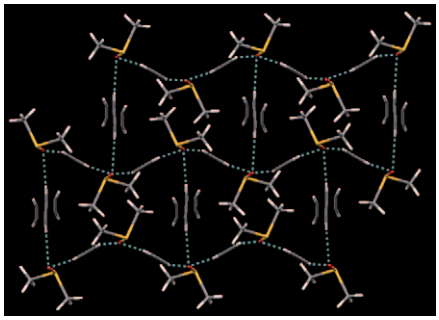


Figure 2. Packing of the 2:1 acetylene/dimethyl sulfoxide co-crystal (**1**). The second acetylene (central vertical) forms cross-links with the zigzag chains (three, horizontal) into a 2D net (C–H···O, $d=2.135$ Å, $D=3.179$ Å, $\theta=161°$; S=O···C, $\theta=120°$). A third molecule of acetylene (left and right vertical) is not incorporated into the network but fills a void.

The molecular complex with DMSO (**1**) examples the ambivalent character inherent in interactions of acetylene. Acetylene is a hydrogen-bridge donor, albeit a weak one. When acceptors are available, it will try to form two interactions. Although this is energetically favourable, it puts geometrical strain on the packing as acetylene is a slim molecule and something has to occupy the space along its side. The situation worsens when more than one acetylene molecule per acceptor must be accommodated. Intermolecular interactions with acetylene generate hollows and produce a need for bumps, otherwise the packing density and subsequently the lattice energy decrease. With DMSO half a molecule of acetylene is clathrated into the hollow that is formed by three molecules forming three hydrogen bridges to the DMSO oxygen atom.

This demonstrates that acetylene is versatile in its interactions. The geometry of the hydrogen bridge is equally variable in the angle to the triple bond (157–178°) and the hydrogen-to-acceptor distance (2.085–2.482 Å). Both sides of the acetylene molecule can be active. Within the structures observed an acetylene molecule can be employed in two, one or no hydrogen bridge. If more than one molecule of acetylene is present, each may be in a different arrangement. If more than one molecule of acetylene binds to a single acceptor molecule, the geometries of the interactions tend to be different. DMSO binds three molecules of acetylene, the highest number of acetylene molecules we found to be bound to a single acceptor atom. There are two acetylene molecules bound to the acceptor atom in the molecular complexes with pyridine and acetone (β-form). In the molecular complexes with ammonia, acetonitrile and formaldehyde the two binding acetylenes are symmetry equivalent.

Furthermore, if other donors are present they may compete with acetylene for acceptor atoms. When classifying our results the role of the acetylene molecule as a hydrogen-bridge donor is therefore less relevant and we concentrated on the acceptor and the number and geometrical arrangement of its (inter- and intramolecular) bonding contacts.

The oxygen atom of DMSO in the molecular complex **1** has four contacts: the sulfur is covalently bonded and three acetylene molecules bind intermolecularly. The four contacts adopt an arrangement that is closest to tetrahedral. A coordination number of four and a similar tetrahedral geometry are found in molecular complexes with acetonitrile (**2**), dioxane (**3**), methanol (**5**), ammonia (**7**) and a hydrate of 2,5-dimethylpyridine (**8**).

If there are five contacts, especially in a planar structure with three in-plane contacts and one each above and below the plane, the coordination geometry is trigonal-bipyramidal, as in the molecular complexes formed with formaldehyde (**13**) and 2,5-dimethylpyrazine (**14**).

2,5-Dimethylpyridine (**9**), pyridine (**10**) and acetone (**11**/**12**) form molecular complexes with six contacts to the acceptor leading to a distorted octahedral geometry.

The aromatic π system is special in its acceptor abilities as it usually will accept one hydrogen-bridge donor on each side to form a linear aromatic arrangement.

A final option for the packing of acetylene with other small molecules, especially if no acceptors are available for acetylene, is a clathrate. In the molecular complex with DMSO, the enclathration of one molecule of acetylene is a consequence of the packing of the other two molecules. With water, phenol, 2,6-di-*tert*-butylpyridine and hexafluorobenzene, clathrates are also formed.

Acetonitrile: In the molecular complex with acetonitrile the molar ratio of acetylene to acetonitrile (**2**) is 2:1. The three molecules form a finite aggregate through two hydrogen bridges from the acetylene to the nitrogen atom of the acetonitrile ($d = 2.443$ Å). The C-N···C angle is 120.6°.

The aggregates are linked by aliphatic sp^3-C–H···N ($d = 2.703$ Å, $D = 3.519$ Å, $\theta = 132°$) hydrogen bridges. Therefore the nitrogen atom has four contacts (one covalent, two acetylenes and one methyl) in a distorted tetrahedral arrangement (Figure 3). The situation is comparable to the oxygen atom in the molecular complex formed with DMSO (**1**).

The second acetylene hydrogen atoms do not bind to any acceptor. This is not a unique observation and can be seen in the molecular complexes formed with methanol (**5**) and xylene (**17**). As a consequence the network dimension is generally not predictable. The interactions with acetonitrile (**2**), methanol (**5**) and *m*-xylene (**17**) all have a comparably long C–H···X hydrogen bridge (2.376, 2.412 and 2.443 Å, respectively).

The distribution of C–H···X distances is bimodal and it varies between 2.258 and 2.363 Å (Figure 4). The molecular complexes with only half-active acetylenes belong to the group with the longest distances. This group also includes ammonia (**7**; 2.363 Å), 2,5-dimethylpyridine hydrate (**8**; 2.375 Å), pyridine (**10**; 2.464 and 2.482 Å) and *β*-acetone (**11**; 2.379 Å). As a longer distance usually means a weaker interaction, these co-crystals must compensate for this either by other especially strong interactions or an overall dense packing. Although this might be argued for the other co-crystals, it is not immediately clear for the co-crystal with acetonitrile.

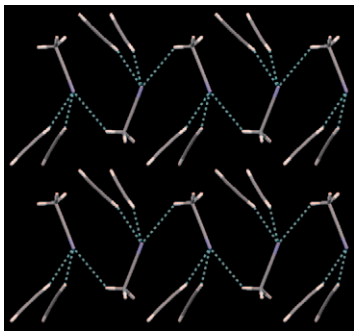


Figure 3. Co-crystal of acetylene with acetonitrile (**2**) (C–H···N, $d = 2.443$ Å, $D = 3.490$ Å, $\theta = 162°$).

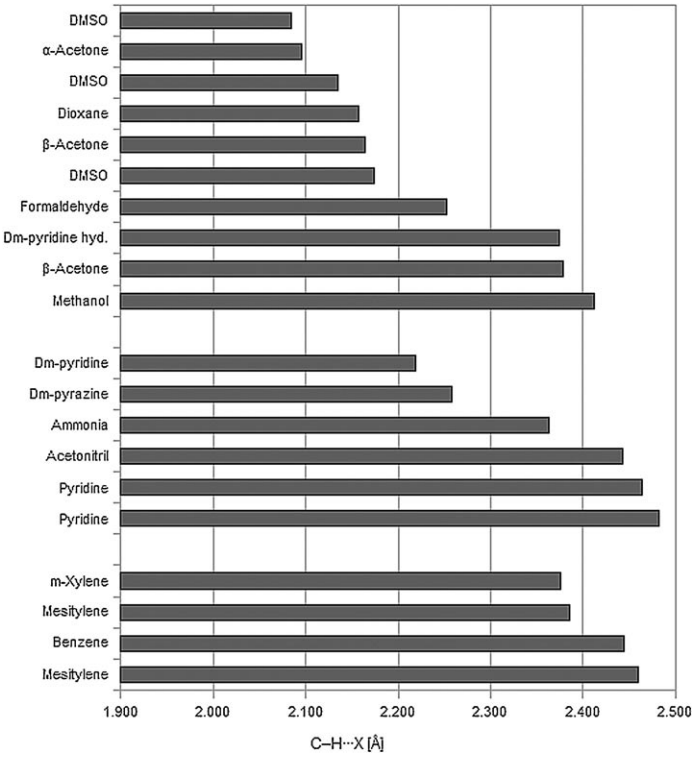


Figure 4. Intermolecular C–H···X hydrogen bridge lengths to oxygen and nitrogen atoms and π acceptors. The distribution for oxygen- and nitrogen-atom acceptors is bimodal with a distinct increase in bridge distances beginning with dimethylpyridine hydrate and ammonia.

The shorter and probably stronger hydrogen bridges are found in the molecular complexes with DMSO (**1**; 2.085, 2.135 and 2.174 Å), dioxane (**3**; 2.157 Å), 2,5-dimethylpyridine (**9**; 2.219 Å), *β*-acetone (**11**; 2.164 Å), *α*-acetone (**12**; 2.096 Å), formaldehyde (**13**; 2.253 Å) and 2,5-dimethylpyrazine (**14**; 2.258 Å).

Dioxane: Acetylene and dioxane (**3**) form a 1:1 linear chain (Figure 5).[11] The C–H···O hydrogen bridge is tilted 20° out of the C–O–C plane and 8° out of the plane of bisection of the molecule. The dioxane molecules are stacked in columns. Very weak hydrogen bridges are formed between the oxygen atoms and the methylene hydrogen atoms in the next molecules in the column. In total, the oxygen atoms have four contacts (two intramolecular, one acetylene and one methylene hydrogen) in a distorted tetrahedral geometry.

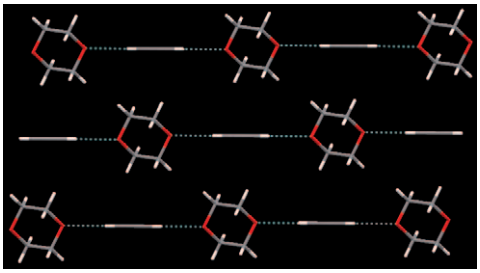


Figure 5. Linear chains of dioxane and acetylene molecules **3** linked by C–H···O ($d=2.160$ Å, $D=3.240$ Å, $\theta=179°$).

The similarities with the packing in neat dioxane are clear; columns are also formed and the layer arrangement is similar. This similarity in the structural motifs between the neat compound and the molecular complex with acetylene is found in several molecular complexes, for example, in methanol (**5**) the O–H···O chains and their stacking in layers, in 2,5-dimethylpyridine (**9**) the C–H···N hydrogen bridge from the *para*-hydrogen atom, in acetone (**12**) the *anti* arrangements of CO dipoles and the sidewise C–H···O bridge from the methyl group.

From the viewpoint of crystal engineering and co-crystallisation there is a fundamental conclusion: the packing motifs of the neat component can be maintained even in co-crystals in which rather strong interactions are present. Of course this is not a general principle: in those cases in which the strong acceptor is blocked by acetylene the previous donors have to find new acceptors, as in pyridine (**10**), or otherwise stay inactive.

Water (clathrate hydrate): The smallest molecule with an oxygen atom as acceptor is water. In hexagonal ice each water molecule acts as hydrogen-bridge acceptor and a donor, which results in a tetrahedral environment of hydrogen bridges around the oxygen atoms. This leads to the rather loose packing of ice in the hexagonal tridymite lattice with unoccupied cavities of 1.5–2.8 Å diameter, low density, and other properties that make the water/ice system "so nice to live in".

These features facilitate the formation of cages in the presence of small guest molecules and results in the encapsulation of the guest.[2] All cages are built of nearly planar, hydrogen-bridged four-, five- and six-membered rings with O···O distances between 2.725 and 2.791 Å. The cages are linked within the host framework by the sharing of common faces.

The structures of the hydrates depend on the size of the guest molecules so that the regular cages will only accommodate molecules up to a maximum size. On the other hand, if not enough guests of the appropriate size are present, the cage structure becomes unstable and hexagonal ice will form. In short, water will form a solid through good interactions (ice) or good space-filling (clathrate hydrate).

Three main structural types of clathrate hydrates have been characterised in their single crystals by using neutron or X-ray diffraction techniques: structure I, $6X{\cdot}2Y{\cdot}46H_2O$, structure II, $8X{\cdot}16Y{\cdot}136H_2O$, and the hexagonal structure H, $1X{\cdot}3Y{\cdot}2Z{\cdot}34H_2O$, in which X, Y and Z represent the different types of cages in the clathrate hydrates.[2] The cages are filled with guest molecules that stabilise the host network.

Structure I is formed when water is co-condensed with acetylene ($Pm\bar{3}n$ space group, $a=11.877(3)$ Å at 123(2) K).[2] Dodecahedral cages are formed by the oxygen atoms (Figure 6) and adopt a nearly body-centred arrangement with the central dodecahedron turned by 90°. The surrounding tetrakaidecahedra form columns along their hexagonal faces arranged vertically, horizontally and out of the plane.

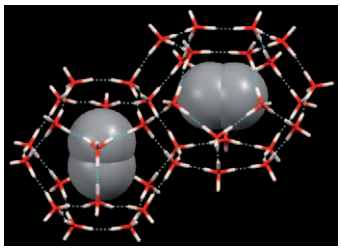


Figure 6. A tetrakaidecahedron and a dodecahedron in structure I clathrate hydrate with acetylene **4** as guest. Each water molecule is disordered; the disorder of the acetylene molecules is not shown.

The low occupation factor 0.6(1) in the dodecahedral cage corresponds to the fact that molecules that are too large to fit easily within the cage will have a lower stoichiometry. The tetrakaidekahedral cage is fully occupied with acetylene.

In the clathrate hydrate with water acetylene is not involved in a hydrogen bridge. Water is the stronger donor and acceptor. Furthermore the number of donors and acceptors match, so the participation of acetylene is not needed. A co-crystal is only formed as a clathrate as the packing density of the O–H···H network is optimised with the enclathration of small molecules. As the same clathrates are also formed with other molecules of gas any special donor abilities of acetylene are not relevant.

We can distinguish between clathrates, in which there is no special interaction between acetylene and the strong host network, intercalates, in which there is a (weak) interaction

to a strong network, and molecular complexes, in which acetylene is incorporated into a network of interactions with its partner. All these are co-crystals.

Methanol: If methanol is thought to be derived from water by substitution of one hydrogen atom by a methyl group, the matching of donor and acceptor numbers in water is broken. Methanol may still accept two hydrogen bridges but has only one hydrogen atom to form a hydrogen bridge to another molecule of methanol. In the (disordered) β-form of methanol the O–H···O chain is formed.[12] Co-crystallised **5** with acetylene, methanol also forms chains in [100] with O–H···O hydrogen bridges (d=1.690 Å, D=2.666 Å, θ=171°).[12] Here the packing motif of the neat compound is retained. The acetylene molecules are intercalated into the otherwise intact methanol β-structure and hydrogen-bridged to the oxygen atoms (d=2.399 Å, D=3.358 Å; θ=147°) side-on to the chain (≈45°). Interestingly, only one acetylene hydrogen atom is used for a hydrogen bridge with methanol in the 1:1 molecular complex (Figure 7). The closest contact of the other hydrogen atom of acetylene is to the π system of another acetylene molecule, but the distance is greater than the sum of the van der Waals radii (d=2.823 Å, D=3.857 Å, θ=160°). In total the oxygen atoms have four contacts (two intramolecular, one acetylene and one intermolecular methanol). The arrangement is distorted tetrahedral.

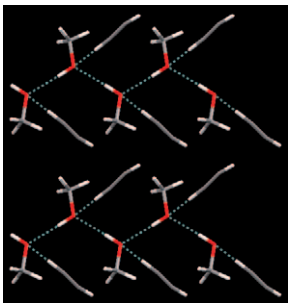


Figure 7. Chain of methanol molecules in the molecular complex with acetylene (**5**) forming a O–H···O chain (d=1.690 Å, D=2.666 Å, θ=171°). Side-on the acetylene is intercalated by weaker C–H···O interactions (d=2.399 Å, D=3.358 Å, θ=147°).

The relationship between the β-phase of methanol and the complex with acetylene is emphasised by a comparison of the cell parameters. The cell axes representing the methanol layer are comparable in length: 4.647/4.565 and 7.220/7.3135 Å. Perpendicular to the methanol layer the distance increases from 6.401 to 13.165 Å to accommodate the acetylene molecules.

The weight ratio of host-to-guest is 1.23 for acetylene/methanol, which is more efficient than in any other co-crystal with acetylene. The co-crystal features both a host network of strong hydrogen bridges enclathrating guests and a molecular complex in which each guest is strongly attached to another molecule.

Methanol and bromine form a similar complex.[13] In the 1:2 molecular complex of methanol with bromine, bromine binds to two molecules of methanol. In this molecular complex the periodicity of the methanol chain is not two (one up, one down) but four (two up, two down), rather similar to the chain of water molecules in the co-crystal of the 1:2:2 acetylene and 2,5-dimethylpyridine hydrate. But although there are some differences in the intermolecular interactions, the similarity of the co-crystals of acetylene and bromine is noteworthy, especially because the nature of the underlying interactions (hydrogen bridge vs. charge transfer) seems to be different. Although the size of both molecules is similar, the similarity in the interactions is supported by the gas-phase measurements of bimolecular complexes formed with Lewis bases. In the crystal structures, even the slight tendency to less linear arrangements of the hydrogen bridge, which was found in gas-phase bimolecular complexes, was reproduced.[14]

Two other molecular complexes of acetylene have counterparts with bromine. The molecular complex of bromine with acetone forms a symmetrical zigzag chain, which in this respect is closer to the co-crystal of acetylene with formaldehyde (**13**). Bromine with dioxane forms a 1:1 chain. The general packing is comparable to the co-crystal formed with acetylene and dioxane (**3**).

Phenol: In methanol an imbalance in the donor-to-acceptor ratio leads to the inclusion of acetylene. This is not necessarily so with all alcohols, as the example of phenol shows.

The co-crystal of acetylene with phenol (**6**) is dominated by a molecular aggregate of 12 molecules of phenol. Six phenol molecules are linked by O–H···O hydrogen bridges (d=1.728/1.729 Å, D=2.702/2.703 Å, θ=170/170°) into a hexagonal ring system. Half of the aromatic systems of these six-membered rings are linked with each other by C–H···π interactions (d_{plane}=2.884 Å) into a "hexagonal prism" (Figure 8). The hexagonal prisms of 12 molecules are arranged in hexagonal close packing. Further C–H···π interactions are found between phenol molecules (d_{plane}=2.866/2.860/2.898 Å).

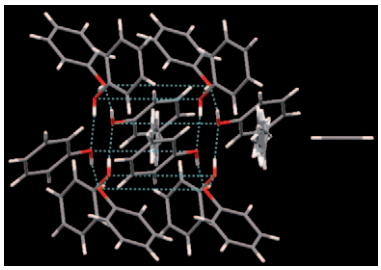


Figure 8. Co-crystal of phenol with acetylene (**6**). Twelve molecules of phenol form a hexagonal prism by O–H···O (d=1.728/1.729 Å, D=2.702/2.703 Å, θ=170°/170°) and C–H···π (d_{plane}=2.884 Å) interactions.

The acetylene molecules are incorporated into two of the cavities of this packing structure of phenol. Within the hex-

agonal prism one disordered molecule of acetylene (A) is enclathrated. The free diagonal distance between two phenol oxygen atoms is 4.4 Å and too short for the molecule to from a hydrogen bridge. It is therefore stacked flat between the hexagonal ring systems. The second cavity is longer and holds 0.90(2) of an acetylene molecule (B) at both ends, again disordered coplanar to the hexagonal ring system, and 0.77(2) of an acetylene molecule (C) perpendicular to the hexagonal ring systems and the disordered acetylene molecule B. The free cavity distance between two acetylene molecules B is 7.06 Å and too short for two molecules of acetylene, the molecule C is then disordered over two sites forming a C–H···π interaction (d_{plane} = 2.367 Å, D_{plane} = 3.450 Å) to molecule B. The ratio of acetylene to phenol is 2.28:2.

Phenol forms a clathrate with acetylene. The strong enclathrating interactions are the O–H···O hydrogen bridge and the edge-to-face phenyl interaction. Although this leaves oxygen atom acceptor positions open, the cavities in the host framework do not allow for hydrogen bridges from acetylene to phenol.

Ammonia: A change in the donor-to-acceptor ratio is also achieved when adding a third hydrogen atom, as in ammonia. The acceptor position takes the form of a single lone-pair which is especially attractive to hydrogen bridges.

At 143 K ammonia forms a 1:1 zigzag chain with acetylene (**7**) through a C–H···N hydrogen bridge (d = 2.362 Å;[15] Figure 9, top). The molecular ratio of acetylene to ammonia is 1:1. Further N–H···C hydrogen bridges can be identified (d = 2.668/2.819/2.899 Å). The ammonia is disordered over two orientations. In each orientation the lone-pair is pointing towards an acetylene molecule (Figure 9, bottom). If only one of the orientations of disorder is considered, the nitrogen atom adopts a tetrahedral sphere (three intramolecular contacts and one to acetylene).

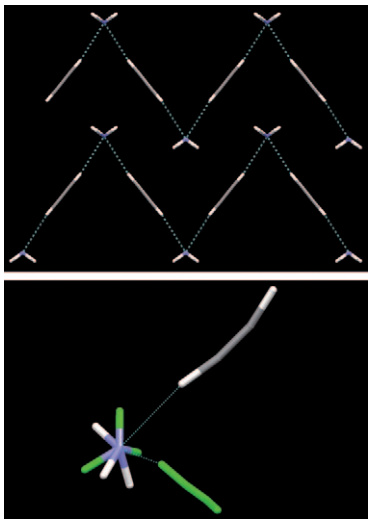


Figure 9. Co-crystal of ammonia with acetylene (**7**). Top: Each ammonia accepts two intermolecular hydrogen bridges and a zigzag chain is formed. Bottom: The ammonia is disordered over two orientations (grey, green). If only one of the orientations of disorder is considered, the tetrahedral sphere of the nitrogen atom is seen.

The 1:1 stoichiometry of the molecular complex is surprising as we expected to find a 2:1 ratio with one hydrogen bridge per lone-pair. The experimental result indicates that the electrostatic component prevails in the interaction. A linear directionality is not necessary for a stable acetylene hydrogen bridge. As other nitrogen-acceptor atoms do only accept one acetylene molecule this means that the dimensionality of the network may not be predicted reliably. Similarly, the dimensionality of oxygen acceptor networks cannot be rationalised before the measurement.

The molecular complex of acetylene with ammonia, $C_2H_2 \cdot NH_3$, is the smallest known organic molecular complex. Although methane with water, $CH_4 \cdot H_2O$, or acetylene with water, $C_2H_2 \cdot H_2O$, would be smaller (or lighter), they form a clathrate hydrate.

2,5-Dimethylpyridine hydrate: 2,5-Dimethylpyridine is hygroscopic and unsurprisingly a 1:2:2 co-crystal dihydrate (**8**) was found even without the purposeful addition of water.[16] The dihydrate **8** in space group $P2_1/c$ has one molecule of acetylene, two molecules of 2,5-dimethylpyridine and two molecules of water in the asymmetric unit. The water molecules form a chain along the O–H···O hydrogen bridges (d = 1.874/1.954 Å, D = 2.827/2.919 Å, θ = 163°/166°) in the [001] direction. 2,5-Dimethylpyridine molecules are attached to this chain through strong O–H···N hydrogen bridges (d = 1.954/1.953 Å, D = 2.931/2.936 Å, θ = 172/177°). This leaves one acceptor site for each water molecule open to accept hydrogen bridges from acetylene. Being bifunctional, one molecule of acetylene connects two chains of water molecules to produce a layer in (010). Owing to the space requirements of 2,5-dimethylpyridine, the chains are separated by 8.243 Å, which is only 0.4 Å less than the sum of the van der Waals radii of the oxygen atoms and the length of the acetylene molecule. It is asymmetrically linked with a shorter and a longer hydrogen bridge (Figure 10).

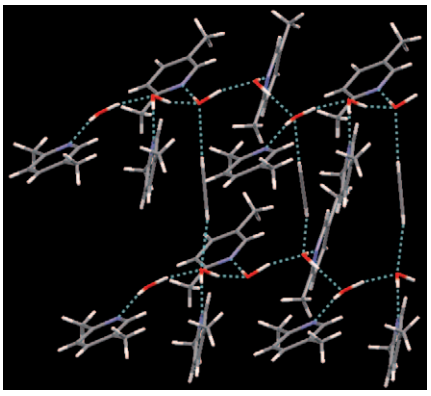


Figure 10. Co-crystal of the dihydrate **8**. Two chains of water molecules with attached molecules of 2,5-dimethylpyridine (O–H···N, d = 1.954/1.953 Å, D = 2.931/2.936 Å, θ = 172/177°) are linked by acetylene molecules (C–H···O, d = 2.375/2.574 Å, D = 3.437/3.656 Å, θ = 167/177°).

The oxygen atom in the molecular complex **8** has a tetrahedral sphere of contacts: two intramolecular contacts to its water hydrogen atoms, one intermolecular hydrogen bridge along the water chain and the intermolecular hydrogen bridge from acetylene.

The packing of the dihydrate demonstrates how the equilibrium of hydrogen bridges changes when stronger donors than acetylene are introduced. Acetylene is forced out of its interaction with the strongest acceptor, the nitrogen atom. Its new role depends on the number and character of acceptors added. In this case (adding water) the acceptor-to-donor ratio stays the same and acetylene attaches to the oxygen atom as the second strongest remaining acceptor. This indicates that hydrates of acetylene complexes are possible.

Distorted octahedral

2,5-Dimethylpyridine: If 2,5-dimethylpyridine is crystallised with acetylene but without water the situation of the donors and acceptors changes.[16] The pyridine nitrogen atom is the strongest acceptor, acetylene the strongest donor and they form a hydrogen bridge. No chain is formed but a 1:2 molecular complex (**9**) similar to the 1:2 complex formed with acetone. The hydrogen bridge is not perfectly aligned to the lone-pair, 25° above the plane of the aromatic system and 21° from the molecular axis. The other side of the nitrogen atom is involved in an aromatic C–H···N hydrogen bridge with the aromatic *para*-hydrogen atom. Both the acetylene C–H···N and aromatic C–H···N bridges form a two-dimensional honeycomb network in the (−102) layer (Figure 11).

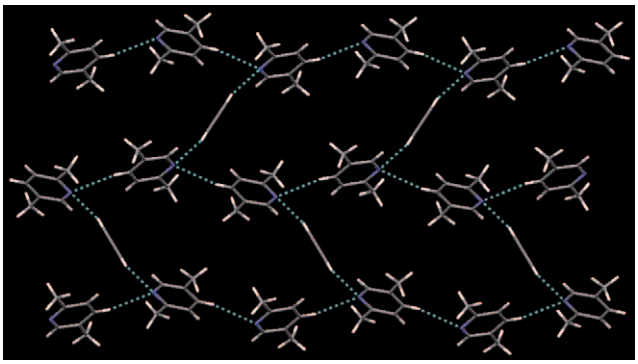


Figure 11. Co-crystal of 2,5-dimethylpyridine and acetylene (**9**) without water. With weak acetylenic C–H···N (d = 2.223 Å, D = 3.261 Å, θ = 160°) and aromatic C–H···N (d = 2.693 Å, D = 3.671 Å, θ = 151°) hydrogen bridges a honeycomb network is formed.

Although the nitrogen atom is the strongest acceptor and its lone-pair accepts two C–H hydrogen bridges, the aromatic system of the pyridine can also accept hydrogen bridges and two weak C–H···N (d = 2.877/2.979 Å) links are formed from aliphatic methyl groups to the nitrogen atom in the aromatic system. The nitrogen atom has six contacts (two intramolecular and four intramolecular, one with acetylene C–H, one aromatic C–H and two aliphatic C–H). The coordination geometry is distorted octahedral.

There seems to be a distinction between the interactions of acetylene with a heteroaromatic system and a pure aromatic system. Although the latter often have perpendicular interactions of acetylene to benzene, the nitrogen heteroatom forms one or two interactions to acetylene along the axis of the lone-pair. Acetylene then does not interact further with the aromatic system.

Pyridine: In the high-pressure form of benzene, C–H···π interactions govern the packing in a herringbone arrangement. In neat pyridine, the *ortho*-hydrogen atoms are engaged in C–H···N hydrogen bridges whereas the C–H···π interactions involve *meta*- and *para*-hydrogen atoms that cannot form a herringbone pattern. With the incorporation of acetylene into the co-crystal with pyridine (**10**) the *ortho*-hydrogen atoms are forced out of the C–H···N interaction by the stronger and more versatile acetylene C–H donor so that the heterocycle returns to the herringbone pattern of benzene.[16] In this respect this co-crystal might be compared with the case of methanol in which during intercalation of acetylene the packing is retained. Here, acetylene is intercalated into the packing of benzene with pyridine taking the place of benzene. Also the hydrogen-bridge distances are the longest found in all the molecular complexes with acetylene and there are rather large cavities in the intercalated layer of acetylene.

In the co-crystal of acetylene and pyridine (**10**) one molecule of pyridine is opposed by two half-molecules of acetylene leading to a 1:1 composition. A chain of hydrogen bridges C–H···N (d = 2.485/2.467 Å, D = 3.440/3.336 Å, θ = 147/144°) involving the nitrogen atom of the pyridine and the hydrogen atoms of the acetylene is formed comparable to the chain found in the 1:1 complex of acetone and acetylene (**12**; Figure 12). Here, we find a more side-on interaction (43° out-of-plane) and another more in-plane interaction (−28° out-of-plane).

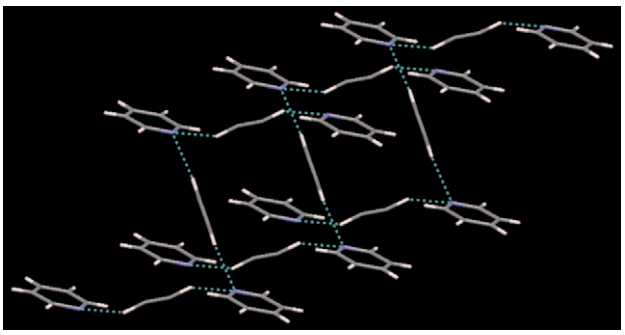


Figure 12. Co-crystal of pyridine with acetylene (**10**) with zigzag chain (C–H···N, d = 2.485/2.467 Å, D = 3.440/3.336 Å, θ = 147°/144°).

The coordination sphere is very much comparable to that of 2,5-dimethylpyridine (**9**). Six contacts (two intramolecular, two intermolecular to acetylene and two intermolecular

to aromatic C–H in pyridine) resemble a distorted octahedral.

Acetone (1:1): The packing and the interactions of the molecular complexes of acetylene with 2,5-dimethylpyridine (**9**) and pyridine (**10**) are governed by the shape and functionality of the acceptor molecule. They are flat molecules with a dipole. Acetone is similar in both respects. It also forms a (strongly distorted) octahedral sphere of contacts, even though the acceptor is changed from an aromatic nitrogen atom to a double-bonded oxygen. Furthermore, acetone forms two molecular complexes **11** and **12** with different stoichiometries.

In the β-phase (**11**) the ratio of acetylene to acetone is 1:1.[10] The molecules are arranged in a zigzag chain with two hydrogen bridges to the oxygen atom of each acetone molecule (as in the complex with pyridine). One of these hydrogen bridges is nearly linear with respect to the carbonyl group whereas the other occurs side-on (Figure 13).

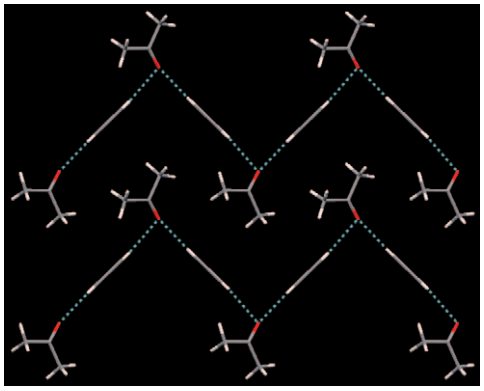


Figure 13. β-Phase of the co-crystal of acetone with acetylene (**11**). The crystal is characterised by a zigzag chain. At the acceptor oxygen atom there is a head-on and a side-on hydrogen bridge (C–H···O, $d=2.164$ Å, $D=3.246$ Å, $\theta=177°$; C=O···C, $\theta=160°$; C–H···O, $d=2.379$ Å, $D=3.431$ Å, $\theta=163°$; C=O···C $\theta=111°$).

The acetone molecule is rather flat and offers a positive polarised carbon atom. A molecule of acetylene is stacked above and below the acetone molecule. On one side the molecules are collinear, the intermolecular C···C distance is short ($D=3.491$ Å). On the other side of the acetone molecule the acetylene is perpendicular lying across the methyl groups and therefore further away from the carbon atom ($D=3.938$ Å).

Another C–H···O hydrogen bridge should be mentioned. It originates from a methyl group ($d=2.629$ Å) and with a second forms a doubly bound circular dimer. This is a packing motif found very often in the packing of neat acetone and in both molecular complexes with acetylene. Although there are other contacts with longer distances these six contacts (one intramolecular, two intermolecular to acetylene C–H, one intermolecular to methyl and two intermolecular to acetylene-π above and below) form a distorted octahedral sphere.

Acetone (1:2): In the α-phase (**12**) the ratio of acetylene to acetone is 1:2 and features a tripart molecular complex with a dumb-bell shape and two almost linear C–H···O hydrogen bridges.[10] The dumb-bells are stacked on one another so that the dipole moments of the acetone molecules are anti-parallel (Figure 14). Basically this anti-parallel arrangement of the linear acetylene–acetone molecular complex can also be seen in the β-form (**11**). There, however, they are not directly on top of each other but somewhat shifted.

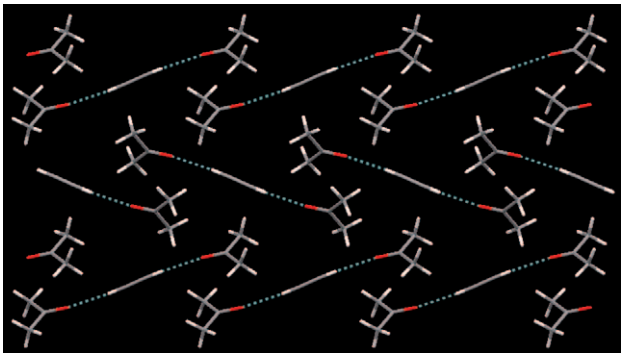


Figure 14. Packing of 1:2 acetylene and acetone α-co-crystal (**12**). The packing is characterised by a 1:2 dumb-bell-shaped molecular complex. (C–H···O, $d=2.096$ Å, $D=3.172$ Å, $\theta=172°$; C=O···C, $\theta=172°$).

Again we find the ring of the methyl C–H···O ($d=2.777$ Å) and a second C–H···O ($d=2.632$ Å) from a methyl group and an acetylene molecule ($D_{CC}=3.986$ Å). These five contacts, together with the intramolecular sixth, form a distorted octahedron.

Polymorphism of co-crystals is important because of its relationship to single-component crystals. This indicates that the phenomenon exists in the co-crystal; the situation of intermolecular interactions is in principle the same. Our result indicates that the phenomenon found in single-component crystals also exists in co-crystals, the situation of intermolecular interactions is in principle the same. Specifically, we may analyse the co-crystals of acetylene as model compounds and conclusions from them may be transferred to all crystalline systems, although with some caution.

The two different stoichiometries of the molecular complex with acetone raises the question of whether different stoichiometries for the other co-crystals may be expected. Furthermore, if there are different stoichiometries, can there also be a clathrate, an intercalate and a molecular complex at the same time? At the moment these questions must remain unanswered. During the preparation of capillaries for co-crystallisation we unintentionally varied the ratio of compounds as our method does not allow for quantitative measurement of the amounts introduced. Often some capillaries would give co-crystals whereas others would not. Sometimes when we obtained co-crystals of a lower quality in one capillary the next would give better quality co-crystals of the same type. In general capillaries with higher amounts of acetylene would grow co-crystals more easily

than those with less acetylene. In one case (2,5-dimethylpyrazine) we felt that a different stoichiometry should be possible and tried to vary the content of acetylene, that is, by adding more acetylene, but to no avail.

The molecular complexes formed with acetone do have a practical importance as acetylene for welding is usually shipped in steel cylinders filled with acetone. At 12 bar in the cylinder the molecular ratio is about 2:3. It is quite likely that the motifs discussed here are also found in solution.

Trigonal bipyramidal

Formaldehyde: For acetone the methyl groups are essential for the packing in both the neat compound and in the molecular complexes. Formaldehyde must interact with acetylene without additional methyl C–H···O hydrogen bridges and chooses a far simpler packing system. In fact, the packing of formaldehyde with acetylene is such as would be expected by most experts based on crystal engineering principles. With formaldehyde small is simple!

In the molecular complex with formaldehyde the molar ratio of acetylene to formaldehyde is 1:1, the molecules are positioned with *mm* symmetry for formaldehyde and with $-1m$ symmetry for acetylene. The structure is a straightforward zigzag chain with two equal C=O···C angles ($\theta = 125°$). The molecules of the planar chain are interdigitated. The adjacent planes are stacked with a shift of half a chain width (Figure 15).

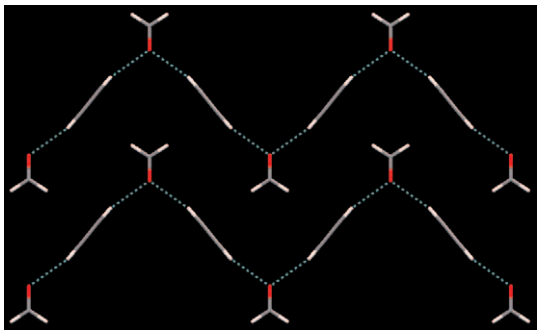


Figure 15. Packing of the 1:1 acetylene and formaldehyde co-crystal (**13**), characterised by a zigzag chain (C–H···O, $d = 2.253$ Å, $D = 3.314$ Å, $\theta = 166°$; C=O···C, $\theta = 129°$). The chains are ordered into layers with an interlayer distance of 2.715 Å.

Each oxygen atom has one intramolecular contact to a carbon atom and two intermolecular contacts to acetylene C–H···O ($d = 2.253$ Å). These form a triangle that is capped above and below by the next molecule of formaldehyde C–H···O ($D_{cc} = 3.379$ Å). The coordination geometry is that of a distorted trigonal-bipyramid.

2,5-Dimethylpyrazine: The only other molecular complex of acetylene that crystallises in planar sheets is the molecular complex with 2,5-dimethylpyrazine (**14**).[16] This molecular complex has a number of features that are special. One of the pyrazine molecules together with the acetylene molecule forms a one-dimensional linear chain along the [$\bar{1}$11] direction (Figure 16). The acetylene molecule is only 1° out of the plane of the aromatic system although it is 10° out of line with the lone-pair forming a C–H···N hydrogen bridge ($d = 2.261$ Å, $D = 3.337$ Å, $\theta = 174°$).

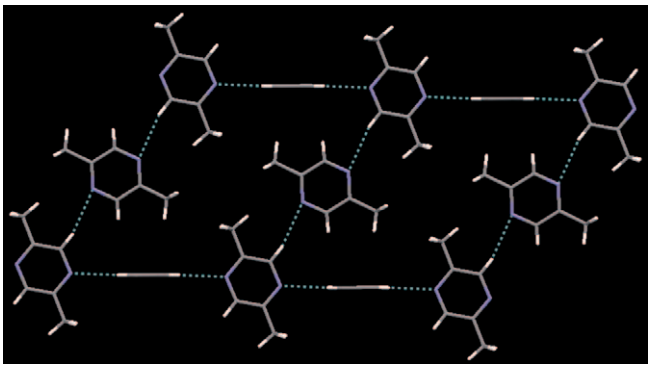


Figure 16. Packing of the co-crystal of 2,5-dimethylpyrazine with acetylene (**14**). The acetylene forms a hydrogen bridge ($d = 2.261$ Å, $D = 3.337$ Å, $\theta = 174°$) to only one of the pyrazine molecules.

The second molecule of dimethylpyrazine does not interact with acetylene. This is the only example in which the acceptor molecules in a co-crystal are simultaneously bound and unbound to acetylene. This is comparable to the situation of the clathrated acetylene in the molecular complex formed with DMSO (**1**).

The molecules are stacked and the molecular planes are tilted by only 7° with a minimum distance of 3.337 Å between them, which indicates a strong π-stacking interaction. The molecules are turned 43° against each other to avoid steric crowding of the methyl substituents and to achieve an optimal arrangement for the quadrupole interactions. An additional hydrogen bridge of the methyl group to the nitrogen atom can be identified in the π-stacked molecule C–H···O ($d = 2.974$ Å).

Similar to formaldehyde, 2,5-dimethylpyrazine forms a planar packing. There are two intramolecular contacts and one intermolecular contact with acetylene, which form a trigonal base. The π system of a pyrazine molecule on one side and a C–H···N hydrogen bridge on the other form the apexes of a trigonal-bipyramid.

2,6-Di-tert-butylpyridine: Neat 2,6-di-*tert*-butylpyridine crystallises in space group $P2_1/c$. There are no hydrogen bridges due to the steric requirement of the *tert*-butyl substituents that shield the acceptor.

We co-crystallised this compound with acetylene in the hope of synthesising a strong molecular complex (**15**). We found space group $P\bar{4}2_1c$ with the nitrogen atom and the *para*-carbon atom located on a two-fold axis and the *para*-hydrogen atom in a position to form a weak hydrogen bridge C–H···N ($d = 2.968$ Å).[16] According to the tetragonal

symmetry, each chain is surrounded by four others and weak sp^3-C–H···π interactions form the dominant motif.

Surrounded by eight molecules, spherical cavities are formed. Each has a volume of 49 $Å^3$ and a mean diameter of 4.5 Å.[17] Within the cavity residual electron density is found with an almost spherical distribution of 5.3 electrons. Attributing this to acetylene, it equates to 0.38 molecules per cavity or a molecular ratio of 0.19:1 acetylene to 2,6-di-*tert*-butylpyridine. The co-crystal is a clathrate (Figure 17).

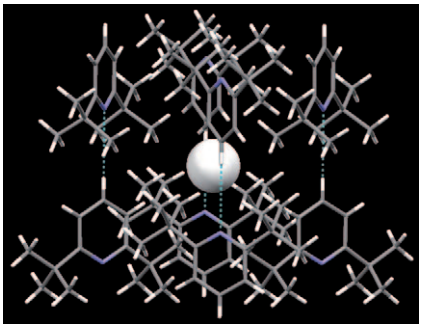


Figure 17. Co-crystal of 2,6-di-*tert*-butylpyridine with acetylene (**15**). The pyridine molecules form chains with weak C–H···N interactions (d = 2.968 Å, D = 4.051 Å, θ = 180°), the position of the disordered acetylene molecule is indicated by the white sphere.

Linear aromatic

Benzene: The following four systems are different from an acceptor point of view. They are pure aromatics and the acceptor is the π system on both sides of the aromatic ring. An additional heteroaromatic acceptor, as in pyridine, pyrazine and their derivatives, is not available. Each side may accept one hydrogen bridge from an acetylene molecule. The variation in this group of co-crystals stems from the competition between acetylene C–H and other aliphatic or aromatic C–H donors rather than different octahedral/tetrahedral geometries or different donor-to-acceptor ratios.

In the co-crystal with benzene (**16**) the molecular ratio is 1:1 and both sides of the benzene ring form a C–H···π interaction with acetylene.[18] The benzene ring lies in a special position with space group $R\bar{3}m$ and D_{3d} point-group symmetry, whereas the acetylene molecule lies on an axis perpendicular to the centre of the benzene plane, also in a special position.

The acetylene molecule reveals an unusually short triple bond. The equally unusual expansion of the C–C bond distance at lower temperature (1.097(10) Å at 201 K and 1.152(4) Å at 123 K) suggests an essentially dynamic disorder in which the acetylene molecule rotates along a double cone between benzene molecules. Assuming 1.20 Å as the "real" triple-bond length, the deviation from the axial position is 24° at 201 K and 15° at 123 K.

The crystal packing is shown in Figure 18. The distance between parallel benzene molecules corresponds to the length of the cell c axis so that, based on the X-ray intramolecular bond distances for the acetylene molecule, the C–H···π bridge (centroid) distance is 2.447 Å at 123 K and 2.462 Å at 201 K (normalised C–H distances applied). The closest intermolecular C···C distances for the benzene molecules are 5.724 Å (123 K) and 5.839 Å (201 K) and the C-(sp^2)···C(sp) contacts are 3.853 Å (123 K) and 3.918 Å (201 K).

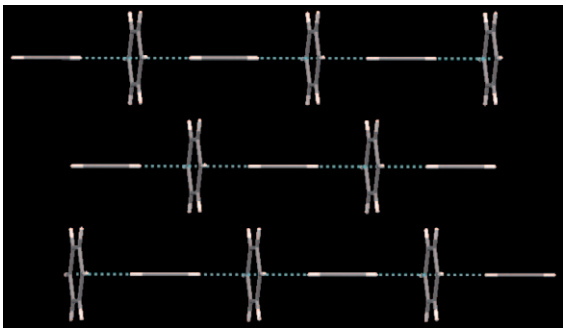


Figure 18. Co-crystal of benzene with acetylene (**16**). The high symmetry leads to a linear arrangement of the molecules. The rotational disorder does not allow the hydrogen-bridge distances to be measured directly.

1,3-Xylene: In the 1:1 co-crystal with 1,3-xylene (**17**) the acetylene forms a zigzag-chain of C–H···π interactions (2.757 Å, 3.812 Å, 165°). The other side of each acetylene is bonded by an aromatic C–H···π interaction (d_{rc} = 2.378 Å, D = 3.421 Å, θ = 161°) to the centre of a xylene molecule (Figure 19).

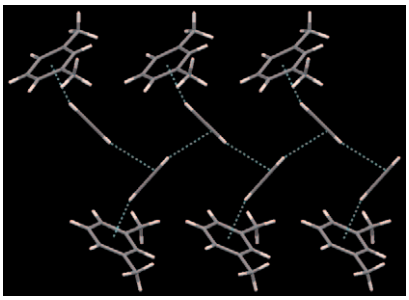


Figure 19. Co-crystal of 1,3-xylene with acetylene (**17**). The homogenic zigzag chain is formed of the C–H···π interaction (2.757 Å, 3.812 Å, 165°) as well as the heterogenic C–H···π interaction (d_{rc} = 2.378 Å, D = 3.421 Å, θ = 161°).

This is somewhat different to the situation in benzene. Although acetylene and benzene both have C–H donor and π acceptor abilities, in benzene they form heterogenic interactions. In xylene, however, they form heterogenic (acetylene–xylene) and homogenic (acetylene–acetylene and xylene–xylene) interactions. This shows that the interaction energies are in the same range and, depending on the steric requirements of the participating molecules, may be interchanged.

Mesitylene: In the co-crystal with mesitylene (**18**) we find two molecules of acetylene in two rather different environ-

ments of weak hydrogen-bridge interactions. The first is directly comparable to benzene as it forms hydrogen bridges to two π systems, pointing nearly perpendicular (d_{rc} = 2.386 Å, θ = 159°; d_{rc} = 2.460 Å, θ = 163°) to the centre of the benzene planes. The angle between planes is 23.29°. The length of the C–C bond at 153 K is 1.144(4) Å.

In the packing with benzene, the benzene hydrogen atoms surround the acetylene and lead to a hexagonal space group. In mesitylene this kind of packing is sterically impossible due to the methyl groups. Instead, the second acetylene bridges the π system of the first acetylene. The C–H···C distance is short (2.700/2.746 Å, 167/164°). The length of the C≡C triple bond is 1.115(8) Å. A third mesitylene molecule forms another C–H···π hydrogen bridge (2.714 Å, 160°) with the first acetylene molecule to complete the molecular complex of three molecules of acetylene and six molecules of mesitylene (Figure 20). Further aromatic and aliphatic (i.e., from the methyl group) C–H···π interactions might be identified.

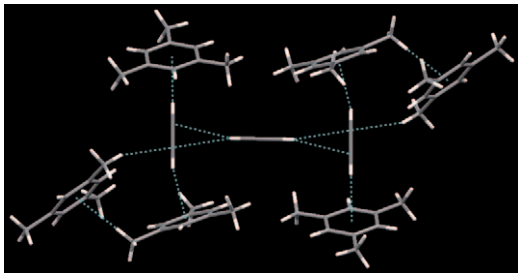


Figure 20. Co-crystal of mesitylene with acetylene (**18**). Please see the text for the length of intermolecular interactions.

The molecular complex of mesitylene with acetylene is the most complex so far. The asymmetric unit contains two molecules of acetylene and three molecules of mesitylene. The two molecules of acetylene form different types of interactions, one to the mesitylene the other to acetylene. Similarly, the three molecules of mesitylene form different types of interactions. Two accept hydrogen bridges from acetylene on one side of the π system but differ in the aromatic and aliphatic character of the donor to the other side of the π system. The third molecule does not accept any acetylene donor but only aliphatic C–H···π interactions from the other two mesitylene molecules.

Hexafluorobenzene: Methyl substituents change the packing of co-crystals of aromatic compounds with acetylene as the geometrical strain is increased and more elaborate modes of interaction are explored in the structures. But by substitution of the aromatic system there is also an influence on the strength and character of the bridge itself.

In the packing of the 1:2 co-crystal of acetylene with hexafluorobenzene (**19**) the acetylene is trapped in a cage of eight molecules of hexafluorobenzene (Figure 21). There are no hydrogen bridges between the molecules. The structure therefore is closer to a clathrate if the weak interactions

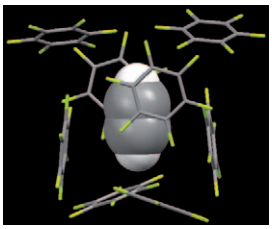


Figure 21. Co-crystal of hexafluorobenzene with acetylene (**19**). The co-crystal is a clathrate with the guest molecule tightly surrounded by eight molecules and therefore is ordered.

could be said to form a clathrating network. The C–F···C distance is 3.195 Å.

In hexafluorobenzene the six fluoro substituents exert a strong influence on the π system by withdrawing electron density. This has a marked effect on the acceptor properties of hexafluorobenzene as the charge transfer stabilisation in the molecular complex with benzene exemplifies.[19] The diminished acceptor ability of hexafluorobenzene would weaken a hydrogen bridge in a possible co-crystal with acetylene. A clathrate is therefore formed featuring typically weak C–F···π interactions, which form a loose host network in which acetylene is enclathrated without any short interactions to the host (C–H···F d = 3.252 Å, C···C D = 3.542 Å). The main difference to most other clathrates of acetylene discussed before is that the cage is small and fits closely around the guest. Therefore the acetylene is not disordered.

The five co-crystallisation partners to form a clathrate with acetylene are DMSO (**1**), water (**4**), phenol (**6**), 2,6-*tert*-butylpyridine (**15**) and hexafluorobenzene (**19**). These are rather different molecules in terms of both their size and intermolecular contacts. The extremes are water, which forms a strongly hydrogen-bridged O–H···O network into which disordered guest molecules of different sizes are inserted, and hexafluorobenzene, which forms a weakly bound host with cavities just large enough to fit acetylene. The other three are intermediate situations. Another clathrate of acetylene with hydroquinone is known from the literature.[20]

DMSO forms a two-dimensional C–H···O bridged network (**1**) with acetylene. The void between two DMSO and six acetylene molecules is filled with an additional molecule of acetylene that is ordered. Two C–H···π interactions to the other acetylene molecules are to be found but with rather small intermolecular angles (d=2.871/2.877 Å, D = 3.677/3.571 Å, θ = 131/122°). The clathration of acetylene in DMSO is closest to a molecular complex.

In the clathrate with 2,6-*tert*-butylpyridine (**15**), acetylene is fully disordered in a cavity of 4.5 Å mean diameter. 2,6-Di-*tert*-butylpyridine forms a weak C–H···N hydrogen-bridged one-dimensional network but otherwise there is no strong intermolecular network as with water or DMSO. The clathrate is not stable without the guest. The disorder demonstrates that there is no specific hydrogen-bridge interaction between guest and host. The only requirement on the guest is to be of appropriate size to fit into the cavity left by the host.

Phenol does not form a strong O−H···O intermolecular network but hexagonal prisms of 12 molecules. Acetylene is incorporated into the cages like a water cage and into the voids between prisms as in 2,6-di-*tert*-butylpyridine. The molecules are disordered over more than one orientation in their respective positions.

Compounds that did not form co-crystals: When analysing the packing of co-crystals it is always advisable to compare compounds with only small variations in chemical composition. The relative similarities and differences between them are more conclusive than absolute features of single unrelated structures. This is especially evident when looking at homologous series of compounds.[3] For co-crystallisation with acetylenes we tried to prepare analogues: formaldehyde–acetone–DMSO, ammonia–water–methanol–phenol, benzene–xylene–mesitylene and the N-heterocyclic family. It is one of the difficulties that these families of chemically similar compounds co-crystallise into rather different molecular complexes or even clathrates.

However, some compounds would not form co-crystals with acetylene. Usually we made some effort to force unyielding compounds into a co-crystal by variation of the ratio of acetylene or by changing the temperature of crystallisation but for some we were unexpectedly unsuccessful. This is especially frustrating for the preparative crystallographer as there is no rule to predict co-crystallisation partners. Even closely related compounds might yield different results: toluene, *o*- and *p*-xylene do not co-crystallise, but benzene, *m*-xylene and mesitylene do. Benzonitrile does not, acetonitrile does. Ethanol does not, methanol does. Dioxane does form a co-crystal with acetylene, furan was predicted by theoretical calculations and spectroscopic evidence to give a molecular adduct but did not yield a co-crystal.[21] In the same way diethyl ether, diacetyl, ethyleneglycol, carbon dioxide, bromine and chloroform do not co-crystallise.

The most probable explanation for this behaviour is the lattice energies of the neat compounds relative to the co-crystal. If the co-crystallisation partner has a low-energy structure of its own the formation of a co-crystal is less favourable.

To save some time in the preparative effort we used Raman spectroscopy. In general the spectra showed marked band shifts when complexes were found. On the other hand, for example, furan did not have an effect on the spectra of co-condensation, which hints that a co-crystal is not formed by our method.

Conclusion

The most respected principle in chemical structural sciences is the prediction of structures from structural knowledge. At the moment this turns out to be an impossible task for co-crystals of acetylene even if only general features of the packing are considered.

The difficulty starts with the predictability of complex formation. At present it is unclear which substances will co-crystallise and which will prefer to form one-component crystals. The difference in melting points does not seem to be an important factor. The solubility of acetylene in the corresponding neat compound is probably a good indicator. Binary mixtures with gases pose additional problems due to phase segregation at the boundary interface. As a rule, compounds forming distinct molecular complexes with strong interactions tend to form mixtures without a visible phase interface which makes the growth of single crystals easier.

Further, the chosen stoichiometry of the molecular complexes cannot be rationalised as they are a consequence of the versatility and size of acetylene to fit the available donors and optimise the overall packing. In some cases we felt that other stoichiometric ratios should be available but, except in the molecular complexes with acetone, we were not able to find conditions to synthesise different forms, usually not by lack of effort. On the other hand, although some compounds easily yield co-crystals in seemingly any ratio of mixture, temperature and growth conditions, others have to be carefully coerced maintaining specific conditions, as is well known with other co-crystallisation systems. Generally we feel that acetylene is a very convenient co-crystal former.

Acetylene forms hydrogen bridges with the strongest available acceptor that is not incorporated into stronger hydrogen bridges. Acetylene may act as a bifunctional donor or only with one side. The angle at the hydrogen atom is usually linear but may deviate from linearity as the C−H hydrogen bridge from acetylene is weaker and less directional than O−H and N−H hydrogen bridges. Equally, the distance may vary in the range between 2.085 and 2.482 Å. We found a bimodal distribution in intermolecular bridge distances with oxygen and nitrogen atoms, the aromatic partners form longer bridges above 2.36 Å.

Furthermore, acetylene is a small molecule that might be enclathrated into cavities to stabilise a host network. Owing to the size and versatility of acetylene in its interactions the molecular complexes formed and the dimensionality of the network are not predictable at present. On the other hand, because of this the packing motifs are optimised with regard to intermolecular interactions. This allows a detailed study of the interplay of weak and strong hydrogen bridges.

When classifying the molecular complexes by their coordination spheres at the acceptor site we focused on the geometrical availability of binding sites. For the most common type of coordination sphere, which is the tetrahedral, we find four contacts around the acceptor, one or two intramolecular and one to three of them intermolecularly form acetylene. The remaining are other intermolecular contacts from neighbouring molecules. The molecular complexes with acetone, pyridine and 2,5-dimethylpyridine might also be classified as tetrahedral in a simplified approach. Taking a more detailed view, two further intermolecular contacts upgrade the acceptor sphere to a distorted octahedron. The reason for an increased number of intermolecular contacts is the

overall flatness of the acceptor molecules permitting additional perpendicular approaches to the acceptor. The same happens with formaldehyde and 2,3-dimethylpyrazine, which have three contacts in a trigonal arrangement in-plane and two additional contacts from above and below the plane leading to a trigonal-bipyramidal arrangement.

Special cases are the molecular complexes with the aromatic compounds benzene, mesitylene and xylene. They are quite different from the N-heteroaromatic systems and accept one hydrogen bridge donor on each side of the π system. The structures gain versatility by using aliphatic and aromatic C–H as donors for hydrogen bridges in competition with acetylenic C–H.

In conclusion we feel that it is not possible at the moment to predict the structure of acetylene co-crystals from a few simple rules. For true crystal structure prediction of the structures presented here, the results are too different and the geometry around acetylene as a co-crystal former is probably too variable. The classification applied above simply indicates that some of the possible alternatives for structures of new co-crystals exist, but in general the results are too unexpected. The prediction of the experimental structure from a bundle of ab initio calculated, energetically similar structures seems to be as impossible as any other intuitive approach. However, the molecular complexes are suggested as benchmarks and as a challenge for theoretical methods and simulations because acetylene is small and has no intramolecular flexibility, as are most of the partners selected for our experiments, as demonstrated with the acetylene–ammonia case.

Table 2. Crystal data for new co-crystals.

	2	**6**	**13**	**17**	**18**	**19**
partner of acetylene	acetonitrile	phenol	formaldehyde	xylene	mesitylene	hexafluorobenzene
SG	$Cmc2_1$	$R\bar{3}$	$Cmcm$	$Pnma$	$P\bar{1}$	$I4_1/a$
a [Å]	11.616(3)	16.4516(3)	5.429(12)	5.964(5)	8.4511(13)	15.536(2)
b [Å]	8.239(2)	16.4516(3)	6.346(15)	10.677(10)	11.3288(15)	15.536(2)
c [Å]	7.5017(19)	21.8494(4)	11.69(3)	14.036(14)	14.796(2)	11.173(3)
α [°]	90	90	90	90	85.351(4)	90
β [°]	90	90	90	90	75.488(2)	90
γ [°]	90	120	90	90	80.641(3)	90
V [Å^3]	718.0(3)	5121.37(16)	402.6(16)	893.8(14)	1351.9(3)	2696.9(9)
Z	4	6	4	4	3	4
ρ [g cm^{-3}]	0.861	1.189	0.925	0.982	0.982	1.897
T [K]	159(2)	143(2)	123(2)	168(2)	153(2)	213(2)
reflections	358	32394	564	3314	5472	5591
data	358	3082	179	1008	4468	1732
parameters	49	161	15	53	271	116
μ [mm^{-1}]	0.052	0.079	0.069	0.055	0.055	0.228
abs. corr.	multi-scan	multi-scan	none	multi-scan	multi-scan	multi-scan
T_{min}	0.86	0.79	–	0.86	0.85	0.68
T_{max}	0.97	0.86	–	0.98	0.98	0.93
R_1	0.0328	0.0955	0.1019	0.1739	0.1177	0.0960
wR_2	0.0719	0.1564	0.1338	0.1267	0.2186	0.0921
GOF	1115	1045	968	947	1023	988
r^+ [e Å^{-3}]	0.092	0.604	0.211	0.228	0.343	0.143
r^- [e Å^{-3}]	−0.067	−0.322	−0.206	−0.166	−0.219	−0.147
CCDC no.[a]	735040	735041	735042	735043	735044	735045

[a] The CCDC references contain 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.

Experimental Section

The crystals were usually grown and measured inside a 0.3 mm quartz capillary with a SMART1000 CCD system with $Mo_{K\alpha1}$ radiation. Cell determination, data collection and reduction was performed with APEX2 (versions from 2004 to 2008). Multiscan absorption correction was performed with SADABS 2004/2008, solution and refinement with SHELXLT 12.1 ($F_o = 4\sigma(F)$, LS against F^2) and the preparation of figures with Mercury 2.[22] Hydrogen atoms were refined in riding positions except for acetylenic hydrogen where possible. Further crystal data are collected in Table 2.

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