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Synthesis and Theoretical Characterization of an Acetylene-Ammonia Cocrystal

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The cocrystallization of different kinds of molecules is to be understood as supramolecular heterogeneous synthesis. It is a part of the field of crystal engineering. In contrast to chemical synthesis of molecules, here weak noncovalent interactions such as hydrogen bridges are utilized to create supramolecular aggregates. Employing the concept of supramolecular heterosynthons[1] representing the most relevant intermolecular contacts, it is hoped that cocrystals can be constructed in a systematic manner. This would have an important impact for pharmaceutical applications.[2] However, there is no reliable set of rules which would allow us to predict formation, stoichiometry, and structure of a cocrystal. While we are still far from a deeper understanding of the formation processes of crystals, an understanding of the resulting structure(s) seems to be an achievable goal, in particular for crystals of small molecules. Cocrystallization of compounds with low melting and boiling points, however, is a great experimental challenge, in particular if single crystals are required to determine the crystal structure by X-ray diffraction. The prerequesite for this particular kind of noncovalent synthesis is special equipment which allows cocrystallization of the components in situ (directly in the diffractometer) at low temperatures and elevated pressure. The crystal growth itself is perfomed within a capillary flushed by cold nitrogen. Local heating occurs by an IR laser beam focused onto the capillary and controlled in position and intensity with a computer program.[3]

Here this technology is applied to produce an acetylene−ammonia crystal. A straightforward expectation for the synthon of such a cocrystal is a dumbbell shaped arrangement of two ammonia molecules at both ends of the acetylene governed by CH$\cdots$N interactions. Surprisingly, a 1:1 cocrystal was obtained consisting of antiparallel planes of zigzag chains (Figure 1). In accordance with the symmetry requirements of the crystal in space group *Ima*2 the ammonia H-atoms are disordered. Correspondingly, the N-lone pair is directed alternatively to one or the other H-atom of the two neighboring acetylene molecules. The structure closely resembles that of the known acetylene−pyridine 1:1 cocrystal which also displays zigzag chains.[4]

This unexpected finding prompts the following questions: (i) whether similar synthons can also be found in small clusters of acetylene and ammonia, and (ii) what is the stability of such mixed aggregates as compared to pure acetylene and ammonia clusters. Note that the corresponding small molecular aggregates might play an important role at the very infant stages of crystal formation. They can readily be treated as isolated entities in high-level ab initio calculations. Figure 2 displays the structures, stabilization energies, and harmonic zero-point vibrational energy (ZPVE) corrections for representative aggregates containing up to four molecules.

Structures and ZPVE corrections were extracted from valence-only second-order Møller−Plessett (MP2) calculations made with TURBOMOLE,[5] employing the aug-cc-pVTZ basis set[6] and making use of the resolution-of-the-identity approximation with the corresponding auxiliary basis set.[7] Stabilization energies subsequently were obtained with MOLPRO[8] by single and double excitation coupled-cluster theory including a perturbative triple excitation correction (CCSD(T)). Here all electrons were correlated using aug-cc-pCVnZ (n = T, Q) basis sets.[6] The complete basis set (cbs) limits of the CCSD(T) stabilization energies were estimated with extrapolation[9] of the basis set dependence of their MP2 contributions after applying the counterpoise correction of the basis set superposition error (cf. SI). For the aggregates considered here this level of theory is generally accepted to be most reliable.

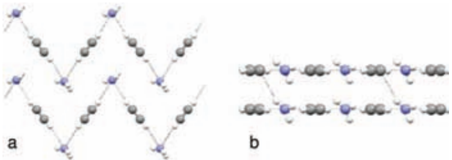

Figure 1. Acetylene−ammonia cocrystal in the solid state with idealized hydrogen geometries (Supporting Information, SI) in the alternating orientation at the N-atoms: (a) the zigzag chains within a plane (0 0 1), N$\cdots$C distances 3.387 Å, C$\cdots$N$\cdots$C angle 69.5°; (b) two planes of zigzag chains (010) above each other, N$\cdots$C distance between planes 3.549 Å.

The dimer of acetylene is known to have a T-shaped minimum structure,[10] while the acetylene trimer and tetramer were found to have cyclic structures.[11] Structures (1), (4), and (10) in Figure 2 are consistent with these findings and the results of previous ab initio calculations.[12] The minimum structure of the ammonia dimer has been the topic of a long debate.[13] Structure (2) represents the minimum of a very nonrigid dimer with a flat potential energy surface in the well region. Within the given error bars its stabilization energy agrees with the results of previous high-level ab initio studies.[14] For the ammonia trimer and tetramer experiment and theory indicate cyclic minimum structures.[15] Structures (5) and (11) are compatible with the previous findings. Finally, the linear structure (3) of the mixed acetylene−ammonia dimeric system and its dissociation energy have been determined by spectroscopy and ab initio calculations.[16] In addition to the signatures of (3) in one of these studies[16e] IR bands have been observed which, based on ab initio calculations, were tentatively assigned to the mixed trimeric system (6), while the alternative structure (7) was found to be a high-lying local minimum. We are not aware of a study of the remaining mixed trimeric and tetrameric acetylene−ammonia aggregates.

While the acetylene dimer (1) with its CH$\cdots\pi$ interaction is roughly half as stable as the ammonia dimer (2) with its NH$\cdots$N contact, the hydrogen bridge between the acidic CH group and the N-atom present in the acetylene−ammonia dimer (3) is more stable. The calculated equilibrium distance between the two CC bond midpoints (CC$_{bm}$) in (1) is $\sim$0.12 Å shorter than the vibrationally averaged value of 4.40−4.41 Å derived from spectroscopy.[10a,b] From Quantum Monte Carlo (QMC) calculations of the vibrational ground states on a model potential for the very nonrigid acetylene dimer one infers a nonharmonic ZPVE correction of 1.6 kJ/mol,[17]

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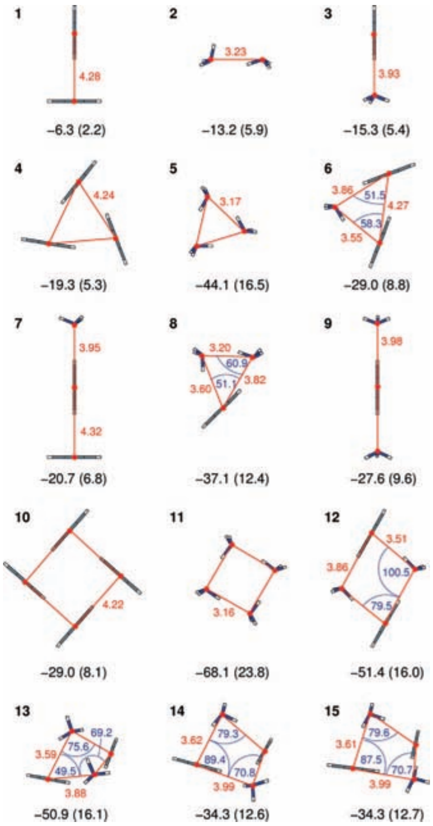

Figure 2. Optimized aggregate geometries. Point group symmetries are C_{2v} for (1); C_s for (2), (6−8), (13−15); C_{3v} for (3); C_{3h} for (4, 5); D_{3d} for (9); C_{4h} for (10, 11); and C_{2h} for (12). Distances (red) in Å; angles (blue) in deg. Stabilization energies (accurate to ±0.2 for (1−3), ±0.6 for (4−9), and ±1.0 for (10−15); SI) and harmonic ZPVE corrections (in parentheses) in kJ/mol.

suggesting a scaling factor of 0.73 to be applied to our harmonic ZPVE correction. The resulting energy of dissociation into the monomers of 4.7 ± 0.2 kJ/mol agrees well with an estimate of 4.8 kJ/mol derived from IR spectroscopy.[10c] From a model potential which essentially reproduces the spectroscopical findings for the ammonia dimer, one extracts an equilibrium distance of 3.31 Å between the two N-atoms, a well depth of −12.2 kJ/mol, and a nonharmonic ZPVE correction of 4.6 kJ/mol.[13c] Using this value, which corresponds to scaling our harmonic correction with 0.78, our estimate for the energy of dissociation of (2) into monomers is 8.6 ± 0.2 kJ/mol, i.e., ∼1 kJ/mol higher than the direct value from the model potential. In the case of the mixed dimeric system (3), analysis of microwave spectra suggests a vibrationally averaged distance of ∼4.00 Å between the CC_{bm} and the N-atom.[16a] A recent state-specific vibrational predissociation investigation finds a dissociation energy of 10.8 ± 0.1 kJ/mol.[16f] Using our value of −15.3 kJ/mol for the well depth we derive a nonharmonic ZPVE correction of 4.5 kJ/mol, corresponding to a scaling factor of 0.83 to be applied to the harmonic ZPVE correction. We conclude that the mixed dimer (3) is favored by at least 2 kJ/mol over (2). It thus is the dimeric aggregate which is most likely to form in a 1:1 acetylene−ammonia mixture.

A naive expectation for the stabilization energy of the acetylene trimer (4) would be −18.9 kJ/mol, i.e., three times that of (1). In fact, the calculated value is only 0.4 kJ/mol (2%) lower because of a partial cancelation of overall attractive nonadditive three-body interactions and stabilization energy loss due to deviation from the ideal T-shaped geometry in the two-body contribution. In the ammonia trimer (5) the orientation of the ammonia monomers is very close to that found in the dimer (2), and the two-body contribution per monomer in (2) and (5) is virtually identical.[15c] Three-body effects, which are expected to be important for clusters containing molecules with sizable dipole moments, thus lead to a magnitude for the stabilization energy of (5) which is 11% larger than three times that of (2). Note also that the cooperativity of the interactions in (5) leads to a sizable contraction of the distance between the N-atoms by 0.06 Å as compared to (2), while the distances between the CC_{bm} of the acetylene molecules contract somewhat less, by 0.04 Å, between (1) and (4). A trimeric system composed of one ammonia and two acetylenes may arrange in a linear fashion, as shown by structure (7). Its stabilization energy, however, is 0.9 kJ/mol higher than the value −21.6 kJ/mol obtained by summing up the results for (1) and (3). This is a consequence of an unfavorable arrangement of the dipole moment of ammonia and the quadrupole moment of the acetylene at the bottom. Anticooperative effects also become visible in elongations of the distances between the CC_{bm} of the central acetylene and that of the other acetylene and the N-atom, respectively. While (7) represents a local minimum, the cyclic structure (6) with its additional $NH\cdots\pi$ interaction is more stable by 8.3 kJ/mol. This energy difference is significantly smaller than the 11.2 kJ/mol found in previous, lower level calculations.[16e] The cooperativity of the interactions in (6) is reflected by considerable shortening of the $CC_{bm}\cdots N$ distance. The trimeric system composed of one acetylene and two ammonia molecules may also arrange to a cyclic and linear structure. Again, the cyclic structure (8) is far more stable (by 9.5 kJ/mol) than the linear one (9). In (9) the unfavorable arrangement of the dipole moments of the two ammonia molecules leads to a stabilization energy 3 kJ/mol higher than −30.6 kJ/mol, i.e., two times that of (3), accompanied by a significant elongation of the $CC_{bm}\cdots N$ distances. It becomes clear why a 2:1 dumbbell-shaped arrangement is not the preferred synthon. The cooperative nature of the interactions in (8) is also indicated by the contracted $CC_{bm}\cdots N$ and $N\cdots N$ distances.

The most stable of all trimeric systems is (5), while (4) is the least stable. We note that the sum of the stabilization energies of (4) and (5) is −63.4 kJ/mol and, thus, 2.7 kJ/mol higher than the sum of −66.1 kJ/mol of the stabilization energies of the mixed trimers (6) and (8). Adding the unscaled ZPVE corrections this energy difference is slightly increased to 3.3 kJ/mol. The nonharmonic ZPVE correction as obtained from QMC calculations for (4) is 4.3 kJ/mol,[17] i.e., ∼80% of the harmonic value (Figure 2). Using a scaling factor of 0.8 for the ZPVE corrections of all trimeric systems changes their energy difference by 0.1 kJ/mol only. We conclude that formation of a 2:1 and a 1:2 mixed aggregate is preferred over that of two one-component trimers by ∼3 kJ/mol.

Tetramers (10) and (11) may be considered to be composed of two dimers in an antiparallel side-by-side arrangement. This also holds for the most stable mixed cluster (12). The dimers and heterodimers, respectively, contract somewhat upon formation of the tetrameric aggregates: the distances between two CC_{bm}, two N-atoms, and one CC_{bm} and a N-atom, respectively, consistently reduce by 0.06−0.07 Å. This is due to additional attractive two- and three-body interactions in the tetrameric aggregates. Note that four-body interactions are known to be of minor importance.[15c] The cooperativity of the additional interactions becomes also manifest in the large stabilization energies of (10) and (11): they are roughly 5-fold more stable than (1) and (2), respectively. In the mixed acetylene−ammonia aggregate (12), on the other hand, two acetylene−ammonia complexes are held together by relatively weak $NH\cdots\pi$ interactions, so that it is only about three times as stable as the dimeric aggregate (3). In (12) the destabilizing ZPVE

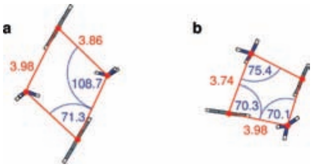

Figure 3. Subunits of the experimental crystal structure.

correction is also only three times larger than that in (3), while in (10) and (11) it is about four times as large as that in (1) and (2), respectively, in agreement with the number of $CH\cdots\pi$ and $NH\cdots N$ contacts in these complexes. All in all, the 1:1 mixed aggregate (12) is less stable than the pure ammonia tetramer (11), in contrast to the situation for the corresponding dimers. However, the magnitude of the stabilization energy of the mixed 1:1 tetrameric aggregate (12) is 2.9 kJ/mol larger than that of the average of the stabilization energies of the pure components, (10) and (11). The nonharmonic ZPVE correction for (10) was 6.4 kJ/mol,[17] suggesting application of a scaling factor of 0.8 to our harmonic ZPVE corrections. Using this for (11) and (12) as well the mixed aggregate (12) remains ~3 kJ/mol more stable than the average of (10) and (11), which, together with the analogous findings for the dimeric and trimeric aggregates, can be a first indication for the preferential formation of a cocrystal.

Figure 3 contains two different subunits of the experimental crystal structure. Comparison with Figure 2 reveals a close correspondence of the ab initio optimized aggregate (12) to subunit (a), which is a part of two coplanar neighboring acetylene−ammonia zigzag chains. In the crystal structure, the $CC_{bm}\cdots N$ distances for the $CH\cdots N$-bridged pairs are longer by 0.12 Å and those for the $NH\cdots\pi$-bridged pairs are even longer by 0.35 Å, while the $N\cdots CC_{bm}\cdots N$ angle reduces by 8°. For the most part these discrepancies are due to the fact that the ammonia molecules cannot adopt the same orientation as they have in the cluster because simultaneously they have to optimize their contacts with further neighbors in the crystal. This becomes particularly evident by considering structure element (b), which is a subunit of the crystal structure consisting of a zigzag acetylene-ammonia element of one plane and an ammonia of a neighboring plane. Its basic features are also found in the isolated 1:1 aggregates (13−15). While in these clusters the on-top ammonia may orient perfectly to optimize the $NH\cdots\pi$ contacts, in the crystal its three H-atoms have a choice between six π-systems: four from the acetylenes in the antiparallel layers below and above, and two from acetylenes in the same plane. This explains the disorder of the H-atoms in the crystal. Nevertheless, there is a remarkable agreement between important geometrical parameters of the aggregates (13−15) and subunit (b): in all of these aggregates, the two acetylenes are coplanar and in (14) and (15) the N-atom of one ammonia is located in the same plane, similar to (b). The $CC_{bm}\cdots N$ distances and the $CC_{bm}\cdots N\cdots CC_{bm}$ angle of the coplanar arrangement in (14) and (15) agree nearly perfectly with the corresponding geometrical parameters of the crystal structure subunit (b). However, in (14) and (15) the orientation of the out-of-plane ammonia is opposite to that of subunit (b), whereas in (13) it points to the correct direction. This enables an additional $NH\cdots N$ hydrogen bridge which is not present in the crystal, since in the crystal the acceptor atom is already involved in hydrogen bridges with acetylene molecules. The relatively strong $NH\cdots N$ hydrogen bridge leads to an out-of-plane distortion of the acetylene−ammonia−acetylene subunit, accompanied by a shortening of the $CC_{bm}\cdots N$ distances, but the $CC_{bm}\cdots N\cdots CC_{bm}$ angle remains very close to the 70° found in the crystal. Note that (13) is calculated to be only slightly less stable than (12), so that in view of the ± 1.0 kJ/mol uncertainty of the cbs estimated stabilization energies they should be considered as isoenergetic. They might form in equal amounts in cold mixtures of acetylene and ammonia. Both clusters are able to retain important stuctural characteristics upon addition of further molecules.

All in all the results of the ab initio calculations lead to the hypothesis that formation of a cocrystal is initially driven by the larger stability of mixed agregates as compared to a mixture of separate single-component aggregates. This is supported by the finding that important supramolecular synthons of the crystal are already present in the very small aggregates as considered here.

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Supporting Information Available: Crystal structure measurement/refinement and ab initio calculation details. Crystallographic data, tables with ab initio energies and structures, complete ref 8. This material is available free of charge via the Internet at http://pubs.acs.org.

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