Interactions in Molecular Crystals, Part 152[+]

Supramolecular Principles: Conformational Changes in the Hydrogen-Bonded Host Lattice of *N*,*N*′-Ditosyl-*p*-phenylenediamine Support the Inclusion of Rigid Guest Molecules

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Dedicated to Professor Manfred Eigen

Abstract: Crystals of thirteen novel inclusion compounds with a host lattice of *N*,*N*′-ditosyl-*p*-phenylenediamine were investigated. The conformational flexibility and the acidic hydrogens of the sulfonamide links enable the incorporation of a variety of guest molecules within the cavities of the host matrix. The crystalline host–guest aggregates can be subdivided into clathrates with weak interactions between host and guest and lattice inclusion compounds with energetically favorable host···guest hydrogen bonds; the clathrates might be further classified according to their sulfonamide···sulfonamide hydrogen bond motifs as well as to the *N*,*N*′-ditosyl-*p*-phenylenediamine conformations within the host lattices containing different cavities for guest molecule insertion.

Keywords: crystal engineering · diamines · host–guest chemistry · hydrogen bonds · supramolecular chemistry

Introduction

Host–guest molecular aggregates, as prototype examples of multicomponent self-organization,[1,2] constitute an essential link between chemistry and molecular biology[3] and open up multifaceted areas of application stretching from enantiomer separation through polymerization in matrices to the protection of sensitive pharmaceuticals.[4]

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[+] Part 151: H. Bock, Z. Havlas, K. Gharagozloo-Hubmann, M. Sievert, *Angew. Chem.* **1999**, *111*, 2379–2382; *Angew. Chem. Int. Ed.* **1999**, *38*, 2240–2243. See also ref. [1].

Crystallization and structure determination: On optimizing the crystallization of *N*,*N*′-ditosyl-*p*-phenylendiamine, a useful synthesis intermediate, from various solvents,[5a] we serendipitously discovered its ability to act as a hydrogen-bonded host lattice and have since isolated 13 inclusion compounds with a variety of guest molecules as single crystals and characterized them structurally (Figure 1).[5a–d] In addition, eight inclusion compounds of *N*,*N*′-di(4-ethylphenylsulfuryl)- and *N*,*N*′-di-(nitrobenzosulfuryl)-*p*-phenylenediamine derivatives have been reported up to now.[1f]

The crystalline host–guest aggregates (Figure 1) can be unequivocally subdivided into clathrates with weak interactions between host and guest (Figure 2: type I and II) and lattice inclusion compounds with energetically favorable host ···guest hydrogen bonds (Figure 2: type III). The clathrates might be further classified according to their sulfonamide··· sulfonamide hydrogen bond motifs as well as to the *N*,*N*′-ditosyl-*p*-phenylenediamine conformations within the host lattices containing different cavities for guest molecule insertion (Figure 2A and B, shaded areas). Two classes of isostructural inclusion compounds can be distinguished, represented here with acetone/tetrahydrofuran (Figure 2A, type I) and benzene (Figure 2B, type II).[5b, c] The inclusion compound with dimethyl sulfoxide is selected as example for the crystal packing dominated by host···guest hydrogen bonds (Figure 2C, type III).[5d]

In the crystal structure of guest-free *N*,*N*′-ditosyl-*p*-phenylenediamine[5a] and its numerous clathrates[5b–d] (Figure 2A and B) the dominant intermolecular interactions are sulfonamide···sulfonamide hydrogen bonds. A search in the Cambridge Structural Database[6] reveals that both H bond motifs, sulfonamide catemer chains (Figure 2B, ③) and eight-membered ring dimers (Figure 2A, ③), are of comparable abundance. Their largely matching distances as well as angles and density functional theory (DFT) calculations suggest that the energies of both should be about equally favorable.

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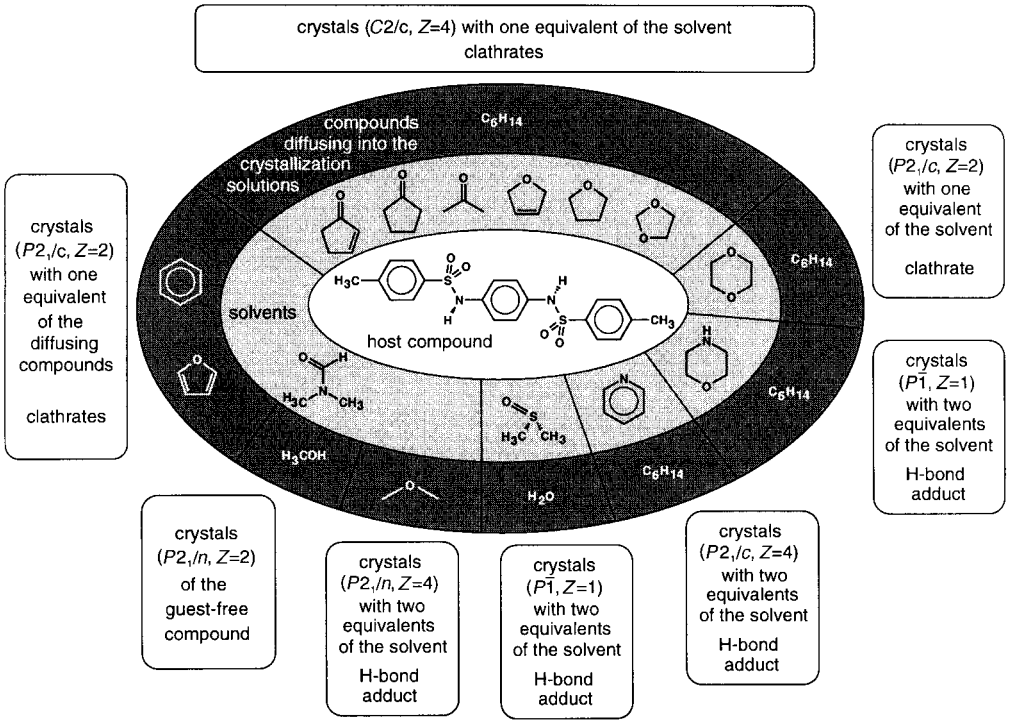

Figure 1. Crystallization conditions and structure details of the 13 inclusion compounds of *N*,*N*′-ditosyl-*p*-phenylenediamine so far isolated as single crystals (unshaded: host compound; light shading: solvents; dark shading: molecules diffused into the crystallization solutions; C_6H_{14}; *n*-hexane; boxes: crystal characterization).

In the acetone clathrate (Figure 2A, ①–④), which is isostructural with five other ones of ketones and ethers (Figure 1 and 2A, ⑤),[5b] the guest molecules are deposited in the channels available in the host matrix fixed by cyclic sulfonamide ··· sulfonamide H bond dimers (Figure 2A, ②). The ketone and ether guests each form two additional weak H bonds to the surrounding *N*,*N*′-ditosyl-*p*-phenylenediamine host molecules (Figure 2A, ④ and ⑤). Crystals of these channel clathrates, therefore, weather outside the mother liquor rather fast to microcrystalline guest-free *N*,*N*′-ditosyl-*p*-phenylenediamine, characterized by powder diffraction.[5b]

In the benzene clathrate (Figure 2B) as well as in the one isostructural with furan[5c] (Figure 1), single guest molecules are encapsulated in cages of the host matrix fixed by catemer-type sulfonamide ··· sulfonamide hydrogen bonds (Figure 2B, ③). The walls of the benzene cages consist of two phenylene and six tolyl rings, arranged similarly to the crystal packing in the high-pressure modification of benzene.[7] The crystals, therefore, decompose more slowly when stored outside the mother liquor.[5c]

The third type of host–guest inclusion compounds of *N*,*N*′-ditosyl-*p*-phenylenediamine presented are the hydrogen-bond adducts to suitable acceptor guest molecules (Figure 1) such as dimethyl sulfoxide, which is inserted into host lattice channels in double stacks parallel to the crystallographic *a* axis (Figure 2C, ①).[5d] Each *p*-phenylenediamine unit is hindered by two energetically favorable hydrogen bonds to dimethylsulfoxide molecules (Figure 3C, ②) to form a hydrogen-bonded sulfonamide host matrix. Altogether, the five hydrogen-bond adducts investigated differ in their crystal packing, especially of the host matrices with their specific cavities, and in the conformation of the *N*,*N*′-ditosyl-*p*-phenylenediamine building blocks.[5d] The host–guest aggregates with dioxane or morpholine, which exhibit rather complex intermolecular interactions, cannot be unequivocally assigned to any of the three categories.

Discussion

The spatial filling of the 14 different crystals of *N*,*N*′-ditosyl-*p*-phenylenediamine, which can be characterized by the packing coefficient C_K,[8] differs only slightly and fits in the expected range for crystals of organic molecules (Figure 4). Obviously (Figure 4), guest-free *N*,*N*′-ditosyl-*p*-phenylenediamine possesses a packing coefficient close to the center of the distribution and, therefore, excludes a low packing density as origin of the clathrate formation (Figure 1). The additional intermolecular interactions such as hydrogen bonds to adjacent oxygen centers C–H ··· O, contacts C–H ··· π between adjacent phenyl rings, and weak van der Waals attractions and repulsions are comparable both in number and in energy contribution. For the apparently energetically favorable clathrate formation of *N*,*N*′-ditosyl-*p*-phenylenediamine, therefore, the conformational changes of the host molecule documented in the 14 crystal structure determinations (Figure 3A) are the most likely of other possible reasons. This fact may also be important for the crystallization of the hydrogen-bond adducts. The conformation of the host molecule with its center of inversion in all crystal structures (Figure 1 and 2) can be unequivocally defined using only the three torsional angles around the sulfonamide bonds S–N, S–C and N–C (Figure 3).

The density functional theory (DFT) energy profiles[9] for the rotations around the sulfonamide bonds have been

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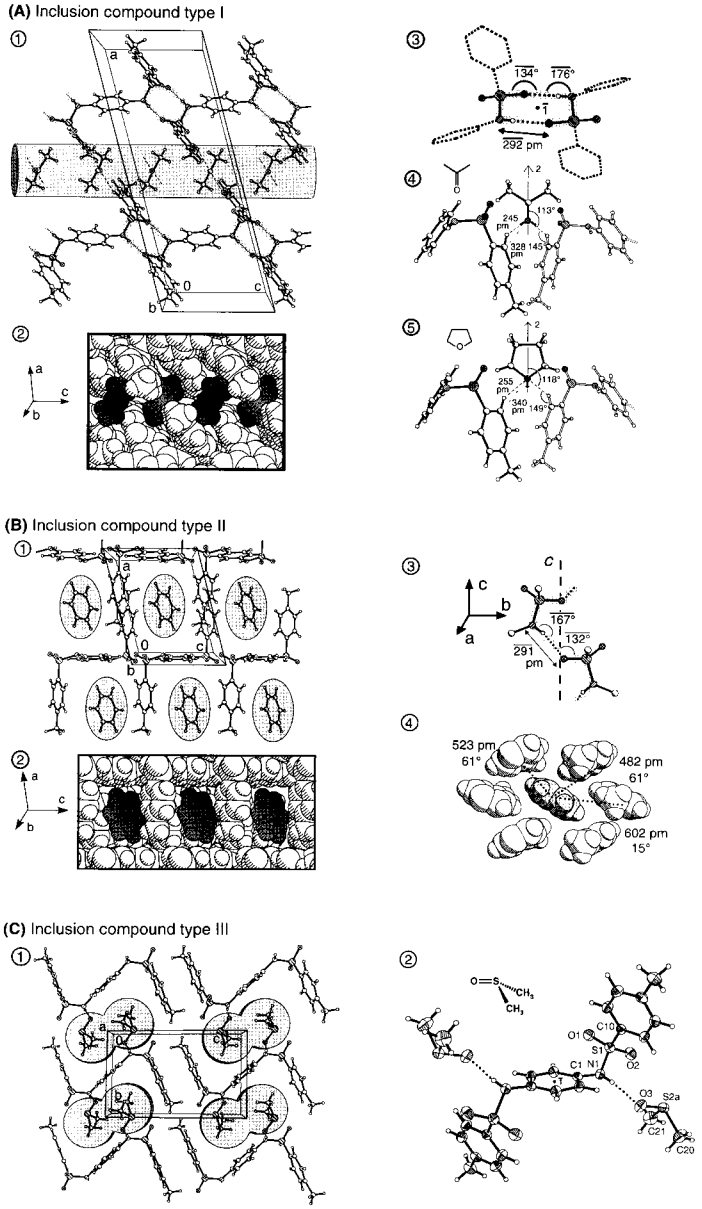

Figure 2. Representative crystal structures selected from the 13 host–guest inclusion components in different hydrogen-bonded *N*,*N*′-ditosyl-*p*-phenylenediamine lattices at 200 K:[5] **(A)** Type I with acetone as guest molecule:[5b] ① unit cell (monoclinic, $C2/c$, $Z=4$), ② space-filling representation, ③ hydrogen-bond motif of the cyclic sulfonamide dimers, ④ arrangement of the acetone guest molecules and ⑤ isostructural example with tetrahydrofuran;[5b] **(B)** Type II with benzene as guest molecule:[5c] ① unit cell (monoclinic, $P2_1/c$, $Z=2$), ② space-filling representation, ③ catemer hydrogen-bond motif along the sulfonamide chains and ④ space-filling representation of the benzene guest molecule in the cage formed by phenylene and toluene six-membered rings; **(C)** Type III containing hydrogen-bond fixed dimethyl sulfoxide as guest molecule: ① unit cell (triclinic, $P\bar{1}$, $Z=1$) and ② structural details of the H bonds at both sides of *N*,*N*′-ditosyl-*p*-phenylenediamine (50% thermal ellipsoids).

performed for smaller model molecules to avoid the tremendous CPU times required for the large parent system, namely, for *N*-methyl methanesulfonamide (Figure 3B, ω_1(CN–SC)), *N*-methyl benzenesulfonamide (Figure 3C, ω_2(NS–CC)) and *N*-phenyl methanesulfonamide (Figure 3D, ω_3(SN–CC)). The results are supported by crystal structure statistics of sulfonamide conformations in the Cambridge Structural Database:[5a, 6] For a rotation around the central bond N–S, two pronounced minima at $\omega_1 = -60 \pm 20^\circ$ and $100 \pm 20^\circ$ result (Figure 3B, nitrogen *R* configuration; for *S* configuration sign change) and for those around S–C or N–C flatter minima, which correspond to easily movable sulfonamide substituents. It is, therefore, the altogether flexible sulfonamide group of the *N*,*N*′-ditosyl-*p*-phenylenediamine that permits the impressive conformational changes (Figure 3A) of the backbone, despite the rather rigid (N–S) bond (Figure 3B), and thus the adaptation of the hydrogen-bonded host matrix to the spatial demand of the guest molecules. The conformational changes are supported by the correlated intermolecular interactions in the variety of inclusion aggregates formed (Figure 1).

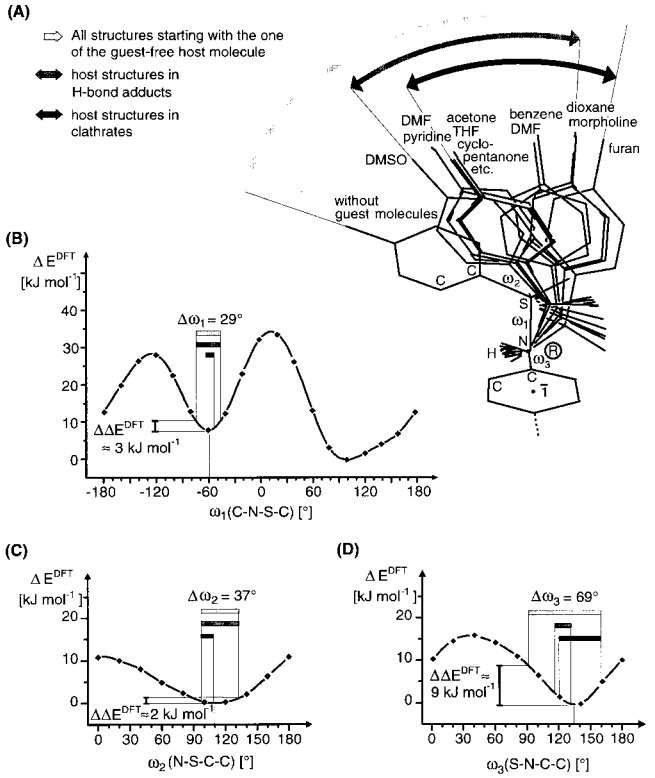

Figure 3. The differing conformations of *N*,*N*′-ditosyl-*p*-phenylenediamine in guest-free and in host–guest crystals as likely origin of the clathrate formation: **(A)** superposition of the experimentally determined conformations of 15 crystallographically independent host molecules showing the distribution range of the three torsional angles ω_1(CN–SC), ω_2(NS–CC) and ω_3(SN–CC), as well as **(B, C, D)** density functional theory (DFT) energy profiles[9] for the rotation around the bonds S–N, S–C, and N–C in model compounds (cf. text).

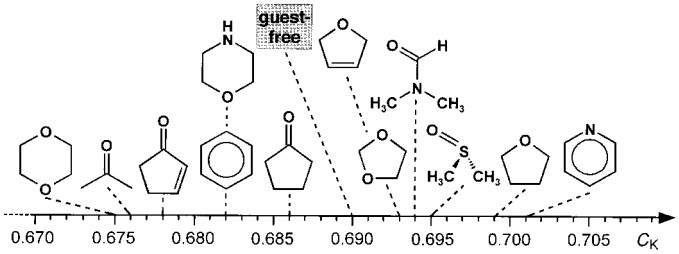

Figure 4. The packing coefficients C_K for 14 different crystal structures of *N*,*N*′-ditosyl-*p*-phenylenediamine with and without guests.

Conclusion and Perspectives

To summarize, thirteen serendipitously discovered novel inclusion compounds in the host lattices of *N*,*N*′-ditosyl-*p*-phenylenediamine have been presented. Because of the rather unfavorable conformation determined in the guest-free crystal, the conformational flexibility and the acidic hydrogens of the sulfonamide links, diverse guest molecules crystallize within the cavities of the host matrices. We hope that the multitude of information provided will stimulate further investigations of analogous self-recognition and self-organization phenomena[10] and, above all, will contribute to the present efforts concerning details of seeding formation[11, 12] in the crystallization of organic molecules.

Acknowledgments

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[2] See, for example, a) J.-M. Lehn, *Supramolecular Chemistry — Concepts and Perspectives*, VCH, Weinheim, **1995**; b) *The Crystal as a Supramolecular Entity* (Ed.: G. R. Desiraju), Wiley, Chichester, **1995**; c) F. Vögtle, *Supramolekulare Chemie*, Teubner, Stuttgart, **1992**, and references therein.

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[5] a) H. Bock, N. Nagel, C. Näther, *Z. Naturforsch. B* **1998**, *52*, 1389 – 1400, b) H. Bock, N. Nagel, C. Näther, *Z. Naturforsch. B* **1998**, *52*, 1401 – 12, c) H. Bock, N. Nagel, C. Näther, *Z. Naturforsch. B* **1998**, *52*, 1413 – 24; d) H. Bock, N. Nagel, C. Näther, *Z. Naturforsch. B* **1998**, *52*, 1425 – 39; cf. ref. [1d – g]. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-103238 (Figure 2 A, ①–④), 103242 (Figure 2 A, ⑤), 103245 (Figure 2 B, ①–④) and Refcode ZAYVAW (ref. [1g]; Figure 2 C, ①–②). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[6] The Cambridge Structural Database (version 5.10) contains 245 non-ionic crystal structures of open-chain sulfonamide fragments (C–N(H)–S(O_2)–C) with their atomic coordinates, the statistical analysis of which yields sulfonamide hydrogen bond chains (graph set description $C(4)$) and cyclic eight-membered hydrogen-bonded dimers (graph set description $R_2^2(8)$) in comparable abundance.

[7] R. Fourme, D. Andre, M. Renaud, *Acta Crystallogr. B* **1971**, 27, 1275.

[8] Packing coefficients and channel volumes in the unit cell have been calculated from the crystal structures with normalized bond lengths C–H of 108 pm as well as N–H and O–H of 100 pm by the caps and spheres model with the program OPEC.[5b, c]

[9] Density functional theory calculations have been performed using the program package GAUSSIAN 94 at the B3LYP level with the basis sets 6-31G* to 6-311G** starting from crystal structure data for which the geometry had first been completely optimized (cf. H. Bock, Z. Havlas, V. Krenzel, *Angew. Chem*. **1998**, *110*, 3305; *Angew. Chem. Int. Ed*. **1998**, *37*, 3163, and references therein). For the subsequent hypersurface calculations the torsional angles ω_1, ω_2, and ω_3 were each varied in 20° steps keeping all others constant and optimizing only bond lengths and angles. The calculations were carried out on a Silicon Graphics PowerChallenge (10 MIPS processors R10000: 190 MHz, 4 GB central memory) of the Hochschulrechenzentrum University Frankfurt/Main.

[10] See ref. [2a] and references therein.

[11] See, for example, J. Hulliger, *Angew. Chem.* **1994**, *106*, 151 – 171; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 143 – 162, and references therein, especially T. P. Martin, *The Physics and Chemistry of Finite Systems: From Clusters to Crystals, Vols. I and II* (Eds.: P. Jena, S. N. Khanna, B. K. Rao), Plenum, New York, USA, **1991/92**.

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