Abstract

The thesis entitled “Molecular Recognition Study of Some Amino Derivatives of Pyrimidines and Triazines” was carried out to explore the molecular recognition between nitrogen based heterocyclic compounds and carboxylic acids, for the creation of exotic supramolecular assemblies. In this endeavor, supramolecular architectures, in the form of host-guest complexes, helices, interpenetrated networks etc., that have been obtained by co-crystallization of various pyrimidine and triazine containing amines, with aliphatic and aromatic carboxylic acids, are summarized into four chapters. Chapter 1 gives an introduction to supramolecular chemistry and its applications in various materials and pharmaceutical sectors. In Chapter 2, supramolecular architectures formed by the molecular adducts of 2,4-diamino-6-methyl-1,3,5-triazine and 2,4-diamino-6-phenyl-1,3,5-triazine with various aliphatic dicarboxylic acids are discussed. In Chapter 3, the supramolecular assemblies of 2,4-diamino-6-methyl-1,3,5-triazine 2,4-diamino-6-phenyl-1,3,5-triazine and 2,4,6-triaminopyrimidine, with various aryl and aralkyl acids (benzoic, phthalic, isophthalic, terephthalic acids, 1,3-phenylenediacidic acid and 1,4-phenylenediacidic acid) are discussed. Finally in Chapter 4, supramolecular architectures formed by melamine, 2,4-diamino-6-methyl-1,3,5-triazine and 2,4,6-triaminopyrimidine, with some dinitro substituted aromatic acids (3,5-dinitrobenzoic acid, 3,5-dinitro-o-toluic acid and 3,5-dinitro-p-toluic acid) have been discussed.
Abstract

Chapter 1

J. M. Lehn, the Nobel Laureate, stated that supramolecular chemistry is the 'chemistry beyond the molecules', considering the fact that atoms are held together by covalent bonds in molecules, while supermolecules are due to the noncovalent interactions formed between the molecules. In the molecular recognition studies, among the wide range of noncovalent interactions, the hydrogen bonds play a significant role as evident by a vast reports appeared in the literature. Nevertheless, because of the directionality and multipoint recognition features, etc., the other noncovalent bonds such as halogen bonds, \( \pi \)-interactions have also been explored to form a variety of network structures. Such studies are, indeed, not only superb to create supramolecular assemblies of exotic architectures with tailor-made properties, but also to understand functions of several biological processes, such as nucleic acid transcription and translation, enzymatic functions and antibody specificity etc. Recently, the molecular recognition studies have been well considered in pharmaceutics, under the umbrella of pharmaceutical co-crystallization, providing unprecedented developments in the intellectual property as well as bio aspects of drugs, etc. A detailed discussion of such features of supramolecular chemistry would be presented in Chapter 1.

Chapter 2

Melamine forms an exotic supramolecular assembly with cyanuric acid, in the form of rosette, which served as a representative example to illustrate the efficacy of intermolecular interactions in the formation of robust solid materials. In order to
explore such features with the derivatives of melamine, exploration of co-crystals of 2,4-diamino-6-methyl-1,3,5-triazine, 1, and 2,4-diamino-6-phenyl-1,3,5-triazine, 2, with various aliphatic acids has been carried out.

Triazine 1 forms host-guest complexes in all its co-crystals, with various aliphatic dicarboxylic acids, as illustrated in Chart 1.

<table>
<thead>
<tr>
<th>reactants</th>
<th>products &amp; ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>1.CH_3OH, 1:1</td>
</tr>
<tr>
<td>(1) + (a)</td>
<td>1a.CH_3OH, 2:1:1</td>
</tr>
<tr>
<td>(1) + (b)</td>
<td>1b.H_2O, 2:1:4</td>
</tr>
<tr>
<td>(1) + (c)</td>
<td>1c, 2:1</td>
</tr>
<tr>
<td>(1) + (d)</td>
<td>1d, 2:1</td>
</tr>
<tr>
<td>(1) + (e)</td>
<td>1e.H_2O, 2:1:1</td>
</tr>
<tr>
<td>(1) + (f)</td>
<td>1f, 2:1</td>
</tr>
<tr>
<td>(1) + (g)</td>
<td>1g, 2:1</td>
</tr>
<tr>
<td>(1) + (h)</td>
<td>1h.H_2O, 2:1:1</td>
</tr>
<tr>
<td>(1) + (i)</td>
<td>1i, 2:1</td>
</tr>
</tbody>
</table>

Analysis of the structural data of all the complexes reveals that, depending upon the $pK_a$ of the aliphatic dicarboxylic acids, two types of host-guest complexes were formed, such that if the $pK_a$ of acid is > 3, the acid molecules act as guests in the host network exclusively formed by the molecules of 1. However, if the $pK_a$ is < 3.0, the acids along with triazine 1 constitute a host network, incorporating molecules of solvent of crystallization as guests. The representative examples of host-guest complexes of 1 with acids having $pk_a < 3$ and $pk_a > 3$ are shown in Figure 1 and a detailed account of all the structures is given in this Chapter.
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Figure 1. Molecular adduct of 2,4-diamino-6-methyl-1,3,5-triazine with (a) oxalic acid having $pK_a < 3$ and (b) fumaric acid having $pK_a > 3$

However, triazine 2, an analogue of 1 with the replacement of methyl group by phenyl moiety, did not yield exclusively host-guest assemblies with various aliphatic dicarboxylic acids, illustrated in Chart 2.

<table>
<thead>
<tr>
<th>Chart 2</th>
<th>Reactants</th>
<th>Products &amp; ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a)</td>
<td>(2)</td>
<td>2a, 2:1</td>
</tr>
<tr>
<td>(b)</td>
<td>(2) + (a)</td>
<td>2b, 1:1</td>
</tr>
<tr>
<td>(c)</td>
<td>(2) + (b)</td>
<td>2c, 1:1</td>
</tr>
<tr>
<td>(d)</td>
<td>(2) + (c)</td>
<td>2d, $H_2O$, 2:1:4</td>
</tr>
<tr>
<td>(e)</td>
<td>(2) + (d)</td>
<td>2e, 2:1</td>
</tr>
<tr>
<td>(f)</td>
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<td>(g)</td>
<td>(2) + (f)</td>
<td>2g, 2:1</td>
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<td>(h)</td>
<td>(2) + (g)</td>
<td>2h, 2:1</td>
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<td>(i)</td>
<td>(2) + (h)</td>
<td>2i, 2:1</td>
</tr>
<tr>
<td>(i)</td>
<td>(2) + (i)</td>
<td>2j, 2:1</td>
</tr>
</tbody>
</table>

The structural features of the co-crystals, thus, obtained with 2 are however, quiet intriguing with a variety of architectures being formed in the form of tapes, cyclic network, helices, host-guest structures, etc. Typical examples of tape and network structures are shown in Figure 2 and the structural features of all other adducts have been discussed in this chapter.
Figure 2. Molecular arrangement in the adducts of 2 with (a) malonic acid and (b) diglycolic acid

Chapter 3

Chart 3
Abstract

Co-crystallization studies of 2,4-diamino-6-methyl-1,3,5-triazine, 2,4-diamino-6-phenyl-1,3,5-triazine and 2,4,6-triaminopyrimidine has been carried out with various aryl and aralkyl carboxylic acids, as illustrated in Chart 3, have been discussed in Chapter 3.

The adducts have been found to be yielding a variety of supramolecular architectures as illustrated in the representative examples formed by melamine and 2,4-diamino-6-methyl-1,3,5-triazine with isophthalic acid, as shown in Figures 3 and 4, respectively. In the adduct of melamine, a six membered cyclic host is formed by the constituting molecules with cavities of dimensions 8 × 12 Å², which are being filled by water molecules. It is noteworthy to mention that the incorporation of water molecules in the cavities is facilitated due to the polar nature of the void space because of the protrusion of amino groups into the void space.

Figure 3. Six member host network observed in the co-crystals of melamine and isophthalic acid, filled by water molecules.

In the adduct of 2,4-diamino-6-methyl-1,3,5-triazine also, an ensemble of six membered cyclic network was observed. However, further aggregation of those
ensembles, establishing interactions by N-H\cdots N hydrogen bonds, yielded void space, being occupied by the molecules of methanol, as shown in Figure 4.

**Figure 4.** Aggregates of ensembles of six membered cyclic networks, yielding void space, being occupied by methanol molecules.

It is interesting to observe that cavities within the six membered ensembles are non-polar, unlike in the adduct of melamine described above, due to the protrusion of methyl groups from the triazine molecules as well as from the methanol molecules in the adjacent layers, as shown in Figure 5. The detailed discussion of all those structures is given in this Chapter 3.

**Figure 5.** Methyl groups of methanol molecules, in the ten member cyclic network, protruding into the six member cyclic network
Chapter 4

It is well known from the literature that while \(-\text{COOH}\) shows affinity to form intermolecular interactions with pyridyl nitrogens through \(\text{O-H}^{\cdots}\text{N}\) hydrogen bonds, which was also illustrated through Chapters 2 and 3, amino groups have profound tendency to interact with nitro groups through different types of \(\text{N-H}^{\cdots}\text{O}\) hydrogen bonds. Since amino pyrimidines and triazines possess both pyridyl nitrogen atoms as well as amino groups, co-crystallization of such molecules with compounds containing both nitro and carboxylic acid functional groups would be of great advantage, to study the impact of multiple functional groups in the supramolecular synthesis. Thus, co-crystals of melamine, 2,4-diamino-6-methyl-1,3,5-triazine and 2,4,6-triaminopyrimidine with various dinitrobenzoic acids have been prepared.

Chart 4

![Chart 4](image)
Abstract

In most of the structures, quartet ensembles formed through N-H\textsuperscript{−}\textsuperscript{−}\textsuperscript{−}O hydrogen bond, between the constituents, as illustrated in the typical example of 2,4-diamino-6-methyl-1,3,5-triazine and 3,5-dinitrobenzoic acid, as shown in the Figure 6.

![Figure 6](image)

**Figure 6.** (a) Quartet ensemble observed in the crystal structure of co-crystals of 2,4-diamino-6-methyl-1,3,5-triazine and 3,5-dinitrobenzoic acid (b) Aggregation of adjacent quartet ensembles through N-H\textsuperscript{−}\textsuperscript{−}N and C-H\textsuperscript{−}\textsuperscript{−}O hydrogen bonds.

References:


Abstract


