A Robust Supramolecular Heterosynthon Assembled by a Hydrogen Bond and a Chalcogen Bond

Shaobin Miao, Yunfan Zhang, Linjie Shan, Mingyuan Xu, Jian-Ge Wang, Yu Zhang and Weizhou Wang *

College of Chemistry and Chemical Engineering, Luoyang Normal University, Luoyang 471934, China; miaoshaobin@126.com (S.M.); yzhfishman@126.com (Y.Z.); wzwanglab@yahoo.com (L.S.); wzwanglab@126.com (M.X.); wang_jiange2@126.com (J.-G.W.); yzhpaper@yahoo.com (Y.Z.)

* Correspondence: wzw@lynu.edu.cn; Tel.: +86-379-686-18320

Abstract: The 1:1 and 2:1 cocrystals of isophthalic acid and 2,1,3-benzoselenadiazole have been successfully synthesized and resolved; the noncovalent interactions in the crystal structures have been studied in detail by quantum chemical calculations. In both of the crystal structures, isophthalic acid and 2,1,3-benzoselenadiazole are bound together by a cyclic supramolecular heterosynthon assembled by an O–H···N hydrogen bond and a N–Se···O chalcogen bond. The crystal structures of the 1:1 and 2:1 cocrystals of isophthalic acid and 2,1,3-benzoselenadiazole and the crystal structure of pure isophthalic acid are very similar, which indicates that the [COOH]···[Se−N] cyclic heterosynthon can be an effective alternative to the strong [COOH]2 cyclic homosynthon. The quantum theory of atoms in molecules further recognizes the existence of the hydrogen bond and chalcogen bond. The results of quantum chemical calculations show that the strengths of the π⋯π stacking interactions in the 1:1 cocrystals of isophthalic acid and 2,1,3-benzoselenadiazole are almost the same as those in the 2:1 cocrystals of isophthalic acid and 2,1,3-benzoselenadiazole, and the strengths of the [COOH]···[Se−N] cyclic heterosynthons (about 9.00 kcal/mol) are less than the strengths of the much stronger [COOH]2 cyclic homosynthons (14.00 kcal/mol). These calculated results are in good agreement with those experimentally observed, demonstrating that, although not as strong as the [COOH]2 cyclic homosynthon, the [COOH]···[Se−N] cyclic heterosynthon can also play a key role in the crystal growth and design.

Keywords: supramolecular synthon; O–H···N hydrogen bond; N–Se···O chalcogen bond; π⋯π stacking interaction; quantum chemical calculation

1. Introduction

The concept of supramolecular synthon has been generally accepted and widely used in the field of crystal engineering [1,2]. In contrast to the other σ-hole bonds such as the halogen bond and chalcogen bond [3–5], the hydrogen bond has much greater strength and much stronger cooperativity, in most cases. Hence, the supramolecular synthons are always assembled with strong or weak hydrogen bonds. The [COOH]2 cyclic homosynthon I in Figure 1 is one of the most common supramolecular synthons in the Cambridge Structural Database (CSD) [6–8]. In fact, in the cornerstone paper of Desiraju [1], the first supramolecular synthon discussed is the [COOH]2 cyclic homosynthon I. The synthon I can link simple dicarboxylic acids such as isophthalic acid together to form tape structures, or link simple tricarboxylic acids such as trimesic acid together to form sheet structures [1–5]. Besides the hydrogen bonds, the other σ-hole bonds can also form cyclic homosynthon. Let us add here that, in recent years, many new types of noncovalent bonds have been uncovered and generally accepted by the chemical community [9]. As shown in Figure 1, two N–Se···N chalcogen bonds form a four-membered [Se−N]2 cyclic homosynthon II. The homosynthon II and its analogues were frequently found in the structures of crystals involving 2,1,3-benzoselenadiazoles or 1,2,5-chalcogenadiazoles [10–13]. In the homosynthon II, the N atom is an electron donor and the Se atom is an electron acceptor. Besides supramolecular...
homosynthons, there also exist supramolecular heterosynthons [14,15]. The two functional groups COOH and Se–N are complementary to each other. It is reasonable to assume that they can form the cyclic supramolecular heterosynthons in Figure 1. Evidently, heterosynthons is assembled by an O–H···N hydrogen bond and a N–Se···O chalcogen bond.

Calculations of the molecular electrostatic potentials support the above assumption. Figure 2 demonstrates the molecular electrostatic potential maps of 2,1,3-benzoselenadiazole and isophthalic acid; also shown in Figure 2 are the electrostatic potential maxima or minima on the atoms involved in the synthons in Figure 1. The computational details of the electrostatic potentials are given in Section 2.3. The positive regions of electrostatic potentials on the H atoms point to the negative regions of electrostatic potentials on the O atoms to form homosynthons; the positive regions of electrostatic potentials on the Se atoms point to the negative regions of electrostatic potentials on the N atoms to form heterosynthons; the positive regions of electrostatic potentials on the H and Se atoms point to the negative regions of electrostatic potentials on the N and O atoms, respectively, to form heterosynthons. The local electrostatic potential minimum on the N atom is close to the local electrostatic potential minimum on the O atom, whereas the local electrostatic potential maximum on the H atom is 2.68 times larger than that on the Se atom. Hence, it can be predicted that homosynthons is the strongest one among the three synthons in Figure 1, followed by heterosynthons, and homosynthons is the weakest one.

A search of the CSD (Version 5.42, February 2021) retrieved only two structures of organic cocrystals containing heterosynthons [8]. One cocrystal is formed between pentafluorobenzoic acid and 2,1,3-benzoselenadiazole, and the other cocrystal is formed between pentafluorobenzoic acid and 4,5,6,7-tetramethyl-2,1,3-benzoselenadiazole [10].
Evidently, the study of heterosynthon III is still in its infancy. In this work, we investigated the structures and properties of the [COOH]⋅⋅⋅[Se−N] cyclic heterosynthons formed between isophthalic acid and 2,1,3-benzoselenadiazole. There are two reasons why we selected the two simple organic molecules to study heterosynthon III. The first is to further develop the database of the [COOH]⋅⋅⋅[Se−N] cyclic heterosynthons in the field of crystal engineering. Secondly, considering that Tang and coworkers have reported a unique phenomenon of the simultaneously boosted fluorescence and room-temperature phosphorescence from the pure isophthalic acid crystals [16], it is significant and important to further investigate whether such a unique luminescent phenomenon can also be observed for the cocrystals between isophthalic acid and 2,1,3-benzoselenadiazole.

2. Materials and Methods

2.1. Cocrystal Synthesis

The isophthalic acid (purity 98%), 2,1,3-benzoselenadiazole (purity 98%), and the solvent methanol (analytical reagent grade) were purchased from Zhengzhou Alfa Chemical Co., Ltd., Zhengzhou, China. All of them were used as received. First of all, a 1:1 mixture of isophthalic acid (0.0166 g, 0.1 mmol) and 2,1,3-benzoselenadiazole (0.0183 g, 0.1 mmol) was dissolved in 10 mL of methanol. Upon slow evaporation of the solution at room temperature, the colorless needle-shaped cocrystal 1 for X-ray analysis was obtained after 1–2 days. Secondly, using the same experimental method, we also tried to synthesize the cocrystals of isophthalic acid and 2,1,3-benzoselenadiazole with 9:1, 8:1, 7:1, 6:1, 5:1, 4:1, 3:1, 2:1, 1:2, 1:3, 1:4, 1:5, 1:6, 1:7, 1:8 and 1:9 molar ratios. After trying many times, only the 2:1 cocrystal of isophthalic acid and 2,1,3-benzoselenadiazole was successfully synthesized. The cocrystal 2 is also colorless and needle-shaped.

2.2. X-ray Crystallography

The single-crystal data of cocrystal 1 and cocrystal 2 were collected on a Rigaku AFC10 diffractometer using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å) at room temperature. Data processing was conducted with the CrysAlisPro software. Structure solution and refinements were carried out with the SHELX-2014 program in conjunction with the Olex2.0 graphical user interface [17–19]. All the hydrogen atoms of the isophthalic acid and 2,1,3-benzoselenadiazole were placed in calculated positions with the riding model approximation. The crystallographic data of cocrystal 1 and cocrystal 2 can be obtained free of charge from the Cambridge Crystallographic Data Centre (CCDC). The CCDC deposition numbers are 2,090,234 and 2,090,225 for cocrystal 1 and cocrystal 2, respectively.

2.3. Computational Details

The molecular electrostatic potentials, energies and electron densities of the monomers and complexes considered in this study were calculated at the PBE0-D3(BJ)/def2-TZVPP level of theory [20–23]. The geometries of these monomers and complexes were not optimized and taken directly from their corresponding crystal structures. The molecular electrostatic potentials were calculated on the 0.001 au electron density isosurfaces of isophthalic acid and 2,1,3-benzoselenadiazole. The molecular electrostatic potential maps in Figure 2 were plotted using the GaussView 6.0 program [24]. The PBE0-D3(BJ)/def2-TZVPP single-point interaction energies were calculated by using the conventional supermolecule method. The basis set superposition error was eliminated with the counterpoise method [25]. Let us add here that the reliability of the PBE0-D3(BJ)/def2-TZVPP calculations for the study of weakly bound molecular complexes has been proven many times in our previous studies [26–28]. All the PBE0-D3(BJ)/def2-TZVPP calculations were carried out with the GAUSSIAN 09 software [29].

To further confirm the existence of the hydrogen bond and chalcogen bond in homosynthon I and heterosynthon III, the “atoms in molecules” (AIM) analysis has been
performed with the PBE0-D3(BJ)/def2-TZVPP electron density [30]. The AIM2000 software was employed to carry out the AIM analysis [31].

3. Results and Discussion

3.1. The Crystal Structures of Cocrystals 1 and 2

Table 1 lists the crystallographic data and structure refinement parameters for cocrystals 1 and 2. Figures 3 and 4 show the important noncovalent interactions in cocrystals 1 and 2, respectively. As shown in Figure 3, in the crystal structure of the 1:1 cocrystal 1, the isophthalic acid and 2,1,3-benzoselenadiazole molecules are connected by the heterosynthon III to form zigzag tape structures, and these infinite tapes are stacked together by the $\pi\cdots\pi$ stacking interactions between isophthalic acid and 2,1,3-benzoselenadiazole. Figure 4 shows that, in the crystal structure of the 2:1 cocrystal 2, the isophthalic acid and 2,1,3-benzoselenadiazole molecules are connected by both heterosynthon III and homosynthon I to form zigzag tape structures, and these infinite tapes are stacked together by both the $\pi\cdots\pi$ stacking interactions between isophthalic acid and 2,1,3-benzoselenadiazole, and the $\pi\cdots\pi$ stacking interactions between isophthalic acid molecules. The [COOH]···[Se−N] cyclic heterosynthons in the crystal structure of cocrystal 1 are clearly equivalent, and the [COOH]···[Se−N] cyclic heterosynthons in the crystal structure of cocrystal 2 are also equivalent. However, the H···N and Se···O interatomic distances (1.892 and 3.056 Å, respectively) of heterosynthon III in the crystal structure of cocrystal 2 are both smaller than the corresponding ones (1.916 and 3.104 Å, respectively) of heterosynthon III in the crystal structure of cocrystal 1, which indicates that the strength of heterosynthon III in the crystal structure of cocrystal 2 is stronger than the strength of heterosynthon III in the crystal structure of cocrystal 1. As can be seen in the crystal structures of cocrystals 1 and cocrystal 2 (the cif files have been included in the Supplementary Materials), besides the noncovalent interactions discussed here, the H···H contacts also exist in cocrystal 1 and the H···O contacts also exist in cocrystal 2. The binding energies of the H···H contacts in cocrystal 1 and the H···O contacts in cocrystal 2 are very small (less than 1 kcal/mol) at the PBE0-D3(BJ)/def2-TZVPP theory level, so these interactions were not discussed further.

Table 1. Crystallographic data and structure refinement parameters for cocrystals 1 and 2.

<table>
<thead>
<tr>
<th>Cocrystal</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>CCDC No.</td>
<td>2090234</td>
<td>2090225</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>$C_{14}H_{10}N_{2}O_{4}Se$</td>
<td>$C_{22}H_{16}N_{2}O_{8}Se$</td>
</tr>
<tr>
<td>Formula weight</td>
<td>349.20</td>
<td>515.33</td>
</tr>
<tr>
<td>Crystal size/mm$^3$</td>
<td>$0.27 \times 0.15 \times 0.14$</td>
<td>$0.27 \times 0.25 \times 0.22$</td>
</tr>
<tr>
<td>Crystal system</td>
<td>monoclinic</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>$P2_1/m$</td>
<td>$C2/c$</td>
</tr>
<tr>
<td>$a$/Å</td>
<td>6.9731(4)</td>
<td>10.4027(7)</td>
</tr>
<tr>
<td>$b$/Å</td>
<td>12.4491(5)</td>
<td>14.8477(7)</td>
</tr>
<tr>
<td>$c$/Å</td>
<td>8.2841(3)</td>
<td>13.9101(8)</td>
</tr>
<tr>
<td>$\alpha$/°</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>$\beta$/°</td>
<td>107.827(5)</td>
<td>101.425(6)</td>
</tr>
<tr>
<td>$\gamma$/°</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>$V$/Å$^3$</td>
<td>684.60(6)</td>
<td>2105.9(2)</td>
</tr>
<tr>
<td>$Z$</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>$\rho_{calc}$/g cm$^{-3}$</td>
<td>1.694</td>
<td>1.625</td>
</tr>
<tr>
<td>$T$/K</td>
<td>292</td>
<td>290</td>
</tr>
<tr>
<td>$2\theta$ range for data collection/°</td>
<td>6.546–56.698</td>
<td>7.054–56.898</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>49375</td>
<td>12212</td>
</tr>
<tr>
<td>Independent reflections $[R_{int}]$</td>
<td>1627 [0.0317]</td>
<td>2387 [0.0539]</td>
</tr>
<tr>
<td>$R_1$, $wR_2$ (I &gt; 2$\sigma$(I))</td>
<td>0.0318, 0.0696</td>
<td>0.0548, 0.0901</td>
</tr>
<tr>
<td>$R_1$, $wR_2$ (all data)</td>
<td>0.0406, 0.0726</td>
<td>0.0850, 0.0988</td>
</tr>
<tr>
<td>Goodness-of-fit on $R^2$</td>
<td>1.120</td>
<td>1.131</td>
</tr>
</tbody>
</table>
Reflections collected 9375 12212
Independent reflections \[R_{\text{int}}\] 1627 \[0.0317\] 2387 \[0.0539\]
\[R_{1}, wR_{2}(I > 2\sigma(I))\] 0.0318, 0.0696 0.0548, 0.0901
\[R_{1}, wR_{2}(\text{all data})\] 0.0406, 0.0726 0.0850, 0.0988
Goodness-of-fit on \(F^2\) 1.120 1.131

Figure 3. Part of the crystal structure of cocrystal 1 showing the O–H···N hydrogen bonds, N–Se···O chalcogen bonds and \(\pi\cdots\pi\) stacking interactions.

The molecular packing in the crystal structure of pure isophthalic acid follows the same pattern of the stacked zigzag infinite chains [32]. The isophthalic acid molecules are connected by homosynthon I to form zigzag tape structures, and these infinite tapes are

Figure 4. Part of the crystal structure of cocrystal 2 showing the O–H···O hydrogen bonds, O–H···N hydrogen bonds, N–Se···O chalcogen bonds and \(\pi\cdots\pi\) stacking interactions.
The molecular packing in the crystal structure of pure isophthalic acid follows the same pattern of the stacked zigzag infinite chains [32]. The isophthalic acid molecules are connected by homosynthon I to form zigzag tape structures, and these infinite tapes are stacked together by the π···π stacking interactions between isophthalic acid molecules. All these results show that heterosynthon III can play an equal role with homosynthon I in crystal growth and design. In the homosynthon I of the pure isophthalic acid crystal, the two O–H···O hydrogen bonds are not equivalent, but both of the H···O interatomic distances are smaller than the H···O interatomic distances of the homosynthon I in the crystal structure of cocrystal 2. The subtle structural differences between the pure isophthalic acid crystal and the cocrystals 1 and 2 can lead to obvious property differences. Tang and coworkers found that pure isophthalic acid crystals exhibit a unique phenomenon of simultaneously boosted fluorescence and room-temperature phosphorescence [16]. Unfortunately, in this study, we did not observe such a unique phenomenon for both the 1:1 cocrystal 1 and the 2:1 cocrystal 2. We also did not observe the fluorescence or room-temperature phosphorescence in their respective solutions. We will uncover some of the reasons by using the quantum chemical calculations.

3.2. The π···π Stacking Interactions in the Crystal Structures

There are mainly three types of noncovalent interactions in the cocrystals 1 and 2: hydrogen bond, chalcogen bond, and π···π stacking interaction. To prove that heterosynthon III is as strong as homosynthon I in crystal growth and design, the first thing is to exclude the effect of the π···π stacking interaction by comparing the π···π stacking interaction in cocrystal 1 with the π···π stacking interaction in cocrystal 2.

Only the π···π stacking interactions between isophthalic acid and 2,1,3-benzoselenadiazole exist in cocrystal 1. As can be seen in Figure 5, the π···π stacking interaction energy of the isolated dimer between isophthalic acid and 2,1,3-benzoselenadiazole is −7.17 kcal/mol. The π···π stacking interaction energy of the well-known parallel-displaced benzene dimer is about −2.70 kcal/mol [33]. The π···π stacking interaction energy of the isolated dimer between isophthalic acid and 2,1,3-benzoselenadiazole is two times more than the π···π stacking interaction energy of the parallel-displaced benzene dimer. On the other hand, the simultaneous formation of heterosynthon III will affect the strength of the π···π stacking interaction between isophthalic acid and 2,1,3-benzoselenadiazole. Figure 5 shows that the interaction energy of the five pairs of π-stacked dimers connected by heterosynthon III is −39.83 kcal/mol. Averagely, the interaction energy of each pair of π-stacked dimers is −7.97 kcal/mol. This means that the simultaneous formation of heterosynthon III significantly strengthens the π···π stacking interaction between isophthalic acid and 2,1,3-benzoselenadiazole. To obtain the precise interaction energy of one pair of π-stacked dimers, we calculated a series of π···π stacking interaction energies and plotted a graph for the correlation between the interaction energy and the number of the π-stacked dimers (see Figure 6). The values of the coefficient of determination and adjusted correlation coefficient are both equal to 1.00, which indicates that the correlation between the interaction energy and the number of the π-stacked dimers is quite strong. The slope of the fitted line is −8.17 kcal/mol, therefore the precise interaction energy of the one pair of π-stacked dimers in cocrystal 1 is −8.17 kcal/mol. In contrast to the interaction energy of −7.17 kcal/mol for the isolated dimer between isophthalic acid and 2,1,3-benzoselenadiazole, it can be concluded that the formation of heterosynthon III can stabilize one pair of π-stacked dimers by 1.00 kcal/mol.
There are two kinds of $\pi\cdots\pi$ stacking interactions in cocrystal 2, i.e., the $\pi\cdots\pi$ stacking interaction between isophthalic acid and 2,1,3-benzoselenadiazole and the $\pi\cdots\pi$ stacking interaction between two isophthalic acid molecules. Figure 7 shows the $\pi\cdots\pi$ stacking interaction energies for the complexes taken from cocrystals 1 and 2, respectively. In the complex taken from cocrystal 1, the $\pi$-stacked dimers are connected only by heterosynthon III. In the complex taken from cocrystal 2, the $\pi$-stacked dimers are connected by both homosynthon I and heterosynthon III. The interaction energy of the isolated $\pi$-stacked isophthalic acid dimer in cocrystal 2 is $-7.03$ kcal/mol, which is very close to the interaction energy of the isolated $\pi$-stacked dimer between isophthalic acid and 2,1,3-benzoselenadiazole. On the other hand, as shown in Figure 7, the $\pi\cdots\pi$ stacking interaction energy of the complex taken from cocrystal 1 is almost the same as that of the complex taken from cocrystal 2. These results clearly show that there are almost no differences between the $\pi\cdots\pi$ stacking interactions in cocrystal 1 and the $\pi\cdots\pi$ stacking interactions in cocrystal 2.

Figure 5. The interaction energies of one pair of $\pi$-stacked dimers and five pairs of $\pi$-stacked dimers connected by heterosynthon III in cocrystal 1.

Figure 6. The correlation of the interaction energy with the number of $\pi$-stacked dimers.
Figure 7. The $\pi\cdots\pi$ stacking interaction energies for the complexes in cocrystals 1 (top) and 2 (bottom).

3.3. The Nature of the Supramolecular Synthons in the Crystal Structures

In the above discussions, the existences of the hydrogen bonds and chalcogen bonds were judged according to the sum of the atomic radii of H, O, N and Se. A hydrogen bond is formed if the H···O(N) interatomic distance is less than the sum of the atomic radii of H and O(N), and a chalcogen bond is formed if the Se···O interatomic distance is less than the sum of the atomic radii of Se and O. Such a method was employed by most crystallographers. Here, we further investigate these noncovalent bonds by using quantum chemical calculations.

Bader’s AIM theory is a perfect tool for identifying the existences of the noncovalent bonds [30]. Many groups have applied the AIM theory to disclose the nature of the noncovalent bonds [34–38]. According to the AIM theory, the chemical bonding can be defined in terms of the topology of the electron density and its Laplacian. The Laplacian of the electron density ($\nabla^2 \rho$) determines where electronic charge is locally concentrated ($\nabla^2 \rho < 0$) or depleted ($\nabla^2 \rho > 0$). Hence, for the noncovalent bonds such as the hydrogen bonds and chalcogen bonds considered in this study, the electron densities at the bond critical points are quite small (about 0.01 au or less), and the corresponding Laplacians of the electron densities are positive. Figure 8 shows the molecular graphs for the complexes taken from cocrystals 1 and 2 along with the values of electron densities and their Laplacians. The values of the electron densities at the bond critical points are in the range of 0.0099–0.0330 au, and the values of the Laplacians of the electron densities at the bond critical points are in the range of 0.0358–0.1112 au. The small electron densities and positive electron density Laplacians clearly show the existences of the O–H···O hydrogen bond, O–H···N hydrogen bond and N–Se···O chalcogen bond.
Figure 8. The molecular graphs for the complexes in cocrystals 1 (a) and 2 (b,c). For clarity purposes, only the bond critical points (small red dots) are shown. The black numbers (in au) are the electron densities, and the red numbers (in au) are the Laplacians of the electron densities.

Figure 9 shows the interatomic distances and interaction energies for the three different synthons in cocrystals 1 and 2. The interatomic distances and interaction energies of heterosynthon III in cocrystal 1 are very close to the corresponding ones in cocrystal 2. This means that there is no obvious change for heterosynthon III in different cocrystals.

The interaction energy of homosynthon I is $-14.00$ kcal/mol. Evidently, the strength of homosynthon I is much stronger than the strength of heterosynthon III. Even so, heterosynthon III is still robust enough to replace homosynthon I in the crystal engineering. To further inspect the values of electron densities, interatomic distances, and interaction...
energies in Figures 8 and 9, it can be found that any two of the three quantities have a linear relationship with each other, as reported previously [37,38].

![Diagram](image_url)

**Figure 9.** The interatomic distances (black numbers, Å) and interaction energies (red numbers, kcal/mol) for the three different synthons in cocrystals 1 (a) and 2 (b).

At the PBE0-D3(BJ)/def2-TZVPP level of theory, the interaction energy of the isophthalic acid dimer in the pure isophthalic acid crystal is $-22.31$ kcal/mol, which implies that the strength of homosynthon I in the pure isophthalic acid crystal is much stronger than the strengths of heterosynthon III and homosynthon I in cocrystals 1 and 2. It is well-known that strong intermolecular forces can rigidify the molecules and are favorable for the light emission [16]. This explains, in part, why we did not observe the fluorescence or room-temperature phosphorescence of cocrystal 1 and cocrystal 2 under 300 nm UV light irradiation.

4. Conclusions

In the present study, we have successfully synthesized and resolved the 1:1 and 2:1 cocrystals of isophthalic acid and 2,1,3-benzoselenadiazole. In the 1:1 cocrystal 1, the isophthalic acid and 2,1,3-benzoselenadiazole are bound together by the $[\text{COOH}]_2-[\text{Se}−\text{N}]$ cyclic heterosynthons to form the zigzag tape structures. In the 2:1 cocrystal 2, similar zigzag tape structures of isophthalic acid and 2,1,3-benzoselenadiazole are formed by both the $[\text{COOH}]_2-[\text{Se}−\text{N}]$ cyclic heterosynthons and the $[\text{COOH}]_2$ cyclic homosynthons. These zigzag tape structures are stacked by the $\pi:\pi$ stacking interactions. The crystal structure of the 1:1 cocrystal of the isophthalic acid and 2,1,3-benzoselenadiazole, the crystal structure of the 2:1 cocrystal of the isophthalic acid and 2,1,3-benzoselenadiazole, and the crystal structure of the pure isophthalic acid are very similar, which indicates that the $[\text{COOH}]_2-[\text{Se}−\text{N}]$ cyclic heterosynthon can be an effective alternative to the much stronger $[\text{COOH}]_2$ cyclic homosynthon.

AIM analyses have been carried out to further prove the existence of the hydrogen bond and chalcogen bond in these crystal structures. The interaction energies of the $[\text{COOH}]_2-[\text{Se}−\text{N}]$ cyclic heterosynthons, $[\text{COOH}]_2$ cyclic homosynthons and $\pi:\pi$ stacking...
interactions have been calculated at the reliable PBE0-D3(BJ)/def2-TZVPP theory level. The interaction energy of the $\pi\cdots\pi$ stacking interaction between two zigzag tape structures in the 1:1 cocrystal of isophthalic acid and 2,1,3-benzoselenadiazole is almost the same as the interaction energy of the $\pi\cdots\pi$ stacking interaction between two zigzag tape structures in the 2:1 cocrystal of isophthalic acid and 2,1,3-benzoselenadiazole. The interaction energy of the $\text{[COOH]}\cdots\text{[Se}^-$-$\text{N]}$ cyclic heterosynthon is about $-9.00$ kcal/mol, and the interaction energy of the $\text{[COOH]}^2$ cyclic homosynthon is $-14.00$ kcal/mol. Both the experimental observations and theoretical calculations show that, although not as strong as the $\text{[COOH]}^2$ cyclic homosynthon, the $\text{[COOH]}\cdots\text{[Se}^-$-$\text{N]}$ cyclic heterosynthon can also play an important role in determining the structures and functions of crystals.

In contrast to the abundance of studies on the applications of the $\text{[COOH]}^2$ cyclic homosynthons in the crystal engineering, the applications of the $\text{[COOH]}\cdots\text{[Se}^-$-$\text{N]}$ cyclic heterosynths in crystal engineering are seldom studied. We are now working on this line and will report a series of cocrystals formed by the $\text{[COOH]}\cdots\text{[Se}^-$-$\text{N]}$ cyclic heterosynthons in the near future.

**Supplementary Materials:** The following are available online at https://www.mdpi.com/article/10.3390/cryst11111309/s1, cif files and checkCIF/PLATON reports for the cocrystals 2090225 and 2090234.

**Author Contributions:** S.M., Y.Z. (Yunfan Zhang), L.S. and M.X. grew the cocrystals; J.-G.W. carried out the single-crystal X-ray diffraction analyses; Y.Z. (Yu Zhang) performed the quantum chemical calculations; S.M. and W.W. designed and supervised this project; S.M. and W.W. wrote and revised the paper. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research was funded by the National Science Foundation of China, grant number 21773104.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** Data is contained within the article.

**Acknowledgments:** We thank the National Science Foundation of China for the financial support. W.W. thanks the National Supercomputing Center in Shenzhen for the computational support.

**Conflicts of Interest:** The authors declare no conflict of interest.

**References**


