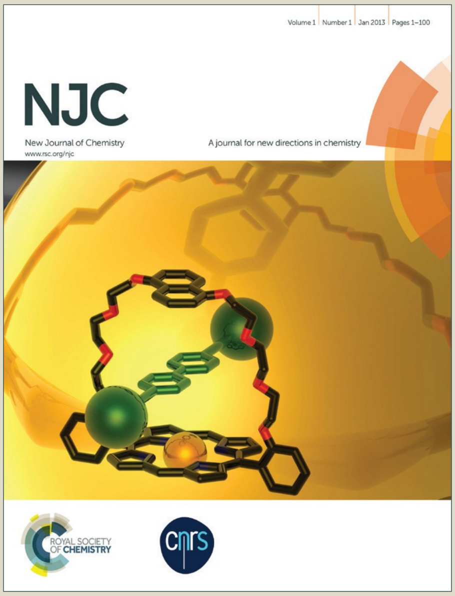

Volume 1 | Number 1 | Jan 2013 | Pages 1–100
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An Unusual C=C···C=O Interaction in (Z)-3-[(4-halogenphenyl)amino]-2-cyanoprop-2-enoates

Received 00th January 20xx,

Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

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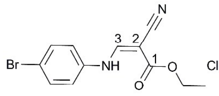
An unusual C=C···C=O interaction has been discovered in (Z)-3-[(4-halogenphenyl)amino]-2-cyanoprop-2-enoates and rationalized by the density functional theory calculations. Second order perturbation theory analysis based on the NBO method and LMOEDA energy decomposition further reveals that the C=C···C=O interaction is dominated mainly by dispersion, electrostatic and two orbital interactions.

Noncovalent interactions play a dominant role in Chemical interactions between a protein and a drug,[1] or an enzyme and its substrate,[2] self-assembly of nanomaterials,[3] and even some chemical reactions[4,5]. A complete understanding of these chemical interactions will often demand a complete understanding of the noncovalent interactions too. Therefore, it is not surprising that a great deal of interest has been generated in the study of noncovalent interactions. Experimental and theoretical results have shown that unsaturated carbon atom can act as an electron donor[6-8] as well as an electron acceptor[9] forming various kinds of noncovalent interactions, such as C···π, cation···π and anion···π etc. Considering the complementary roles of carbon atom, C···C interactions are expected to occur between electron-rich vinyl and electron-poor carbonyl fragments. Our interest in the β-enamino esters, (Z)-3-[(4-halogenphenyl)amino]-2-cyanoprop-2-enoates, mainly stems from this expectation. In this context, we have prepared a series of such β-enamino esters, and examined their X-ray crystal structures.

Interestingly we have discovered a hitherto unreported C=C···C=O interaction in the supramolecular structure of ethyl (Z)-3-[(4-bromophenyl)amino]-2-cyanoprop-2-enoate, **1** (Fig. 1). As is shown in Figure, the vinyl atom C3 resides orthogonally above the pseudotrigonal axis of the ester carbonyl group. The distance between C3 and C1^{i} is only 3.277(3) Å, which is significantly shorter than the sum of van der Waals radii, 3.4 Å. The characteristic geometry suggests a pair of C···C interactions between vinyl and carbonyl groups.



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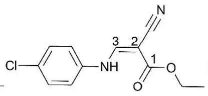

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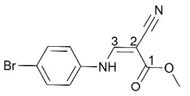

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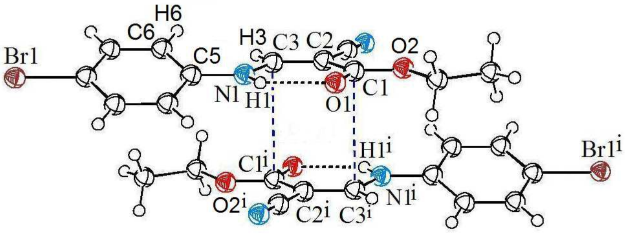

Fig. 1 The dimeric structure of ethyl (Z)-2-cyano-3-[(4-bromophenyl)-amino]prop-2-enoate, **1**, showing both experimentally and theoretically the formation of the C···C interaction between C3 and C1^{i}; the distances C3···C1^{i} from experimental and DFT calculations are 3.277 and 3.186 Å, respectively. Symmetry code: (i) 1-x, 1-y, 2-z.

Recent study[7] has shown the existence of C···C interactions. However, the only work on this subject still remain theoretical. Computational study shows that the C···C interactions exist between electron-deficient molecule (CO_2 or NCCN) and electron-rich molecule, such as HC≡CH and $H_2C=CH_2$ etc., and that all the dimers formed by this interaction show $C2_V$ symmetry and correspond to energetic minima. The C=C···C=O interaction in **1**, we think, is very similar with the $CH_2=CH_2\cdots CO_2$ interaction, though the formed dimers differ in parameters and symmetry.

To quantitatively evaluate the strength of the C=C···C=O interactions, the density functional theory (DFT) calculations at

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† CCDC reference number 952088. For crystallographic data in CIF or other electronic format see DOI: 10.1039/x0xx00000x

the WB97XD[10]/6-311+G(d,p) level were performed on compound **1**. The monomer and the dimers formed by C=C···C=O interaction were studied. All the calculations were carried out by using GAUSSIAN 09[11] package. At this selected theoretical level, both monomer and dimer of **1** are found to be the energy minima, and are in good agreement with the crystallographically determined structure. The optimized dimer is also shown in Fig. 1. As the Figure shows, the atom C3 approaches the atom $C1^i$ perpendicularly to the ester carbonyl plane, and the distance between C3 and $C1^i$ is 3.186 Å. The total dimerization energy is -20.79kcal.mol^{-1}, showing theoretically that the C=C···C=O interaction is thermodynamically most favorable.

It is widely accepted that the natural bond orbital (NBO) theory[12,13] is quite useful in analyzing intermolecular interactions.[14] In order to further characterize the C=C···C=O interaction via orbital interactions, we have also performed NBO analysis on the C=C···C=O dimer with NBO version 3.1[15] incorporated in the G09 package using the optimized ground-state geometries. Interestingly, we have found that there are four intermolecular orbital interactions corresponding to the C=C···C=O interaction, out of which only the strongest interactions (as well as strongest between the dimer), A and B, are shown in Table 1 & Figure 2. As is shown in the Table and Figure, the π-orbital of the carbonyl $O1^i$=$C1^i$ interacts with the π*-antibonding orbital of the vinyl C3=C2, with a concomitant second-order stabilization energy of $E^{(2)}$ = 0.27 kcal/mol, and on the other hand, the π-orbital of C2=C3 interplays with the π*-antibonding orbital of the $C1^i$=$O1^i$ bond, with a second-order energy of 0.26 kcal/mol. The orbital interactions involving the atoms C1 and $C3^i$ are completely identical with ones involving $C1^i$ and C3. The total stabilization energy that attributed to the C=C···C=O interactions is approximately 1.36 kcal/mol. The results have theoretically confirmed that the orbital interaction between vinyl and carbonyl groups, though weak, can actually occur, and may be of vital importance in controlling the directionality and geometrical details.

Table 1 Stabilization energies for selected NBO pairs in **1**, as given by second order perturbation theory analysis of the Fock Matrix in the NBO basis, obtained from WB97XD[10]/6-311+G(d,p).

Pair name	donor NBO	acceptor NBO	E(2) energy (kcal.mol-1)
A	π ($O1^i$=C^i)	π* (C3=C2)	0.27
B	π (C2=C3)	π* ($C1^i$=$O1^i$)	0.26
A’	π (O1=C1)	π* ($C3^i$=$C2^i$)	0.27
B’	π ($C2^i$=$C3^i$)	π* (C1=O1)	0.26

Here the C=C···C=O interaction, though being bidirectional charge-transfer, leads to a redistribution of charge within the dimer. NBO calculations have revealed that during the formation of the C=C···C=O bond, the positive charge on the carbonyl atom $C1^i$ decrease from 0.821 to 0.810 *e*, the charge (0.182*e*) on the partner atom C3 is, however, nearly unchanged, thus reducing the repulsion component between C3 and $C1^i$. Conversely, the negative charges on atoms C2 and N2 increase from -0.384 and -0.340 *e* to -0.397 and -0.363 *e*, respectively, the former favoring keeping the dimer in a lower electrostatic repulsion levels due to the longer distance between C2 and $C2^i$, and the latter favoring enhancing the following C–H···N≡C hydrogen bond.

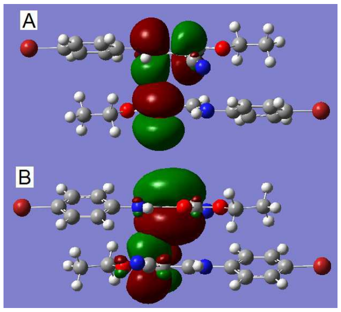

Fig. 2 Dominant orbital interactions **A**, π($O1^i$=$C1^i$)→π*(C3=C2), and **B**, π(C2=C3)→π*($C1^i$=$O1^i$), showing the nature of the C=C···C=O in **1**. For the sake of clarity, the same orbital interactions A’ and B’ have been omitted.

In addition to the orbital interactions between vinyl and carbonyl groups, the C=C···C=O dimer should be also stabilized by other standard energy contributions, such as dispersion, electrostatic, exchange-repulsion and polarization. To roundly explore the source of the dimerization energy (-20.79 kcal.mol^{-1}), we employed the localized molecular orbital energy decomposition analysis (LMOEDA) approach of Su and Li[16] to decompose the C=C···C=O interaction energy into electrostatic, exchange, repulsion, polarization, and dispersion components. The LMOEDA computations have been performed using the GAMESS package at MP2/maug-cc-pVTZ level.[17] The results shows that the C=C···C=O interaction is mainly dominated by dispersion energy and electrostatic energy, which contribute 66.6% and 25.4%, respectively, to the total dimerization energy.

Given that the C=C···C=O interactions occure in ethyl (Z)-3-[(4-bromophenyl)amino]-2-cyanoprop-2-enoa te, **1**, it is very probable to find this kind of interactions in ethyl (Z)-3-[(4-chlorophenyl)amino]-2-cyanoprop-2-enoate, **2** and methyl (Z)-3-[(4-bromophenyl)amino]-2-cyanoprop-2-enoate, **3**.

Keeping our motivation in mind, we replace the atom Br1 (Fig. 1) with a Cl1 atom, and the O2-ethyl with methyl to build the monomer and dimer of **2** and **3**, respectively, for the evaluation of C=C···C=O interactions. The DFT calculations were performed to the geometry optimization using the same methods as **1**. Interestingly, in the optimized dimers **2** and **3**, the main geometry parameters are in perfect accordance with those found in **1** (Fig. 1); the atom C3 approaches the atom $C1^i$ perpendicularly to the ester carbonyl plane; the distances between C3 to $C1^i$ are 3.188 and 3.218 Å, respectively. The corresponding total dimerization energy are -20.76 and 19.18 kcal.mol^{-1}, respectively. The main orbital interactions involved in the C=C···C=O interaction are A, π($O1^i$=$C1^i$)→ π*(C3=C2), and B, π(C2=C3)→π*($C1^i$=$O1^i$) (Fig. 3), which is shown by second-order perturbation theory analysis of Fock Matrix. The results reveals that the C=C···C=O interactions do exist universally in (Z)-3-[(4-halogenphenyl)amino]-2-cyanoprop-2-enoates.

The C=C···C=O interaction is very scarce. Searches of the Cambridge Structural Database (CSD) showed that no such interaction occurs between vinyl and carbonyl despite of the abundance of vinyl and carbonyl groups existing in crystal structures deposited so far in the CCDC. However, this interaction exists widespread in (Z)-3-[(4-halogenphenyl)amino]-2-cyanoprop-2-enoates.

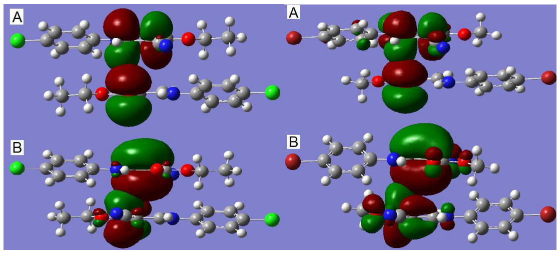

Fig. 3 The dominant NBO orbital interactions A, π(O1^i=C1^i)→π*(C3=C2), and B, π (C2=C3)→π*(C1^i=O1^i) corresponding to the C···C interaction between the vinyl atom C1 and the carbonyl atom C3^i in **2** (left) and **3** (right). For the sake of clarity, the same orbital interactions between the atoms C3 and C1^i have been omitted.

The crystal structure of **1** also exhibits a strong intramolecular N–H···O hydrogen bond and a strong H···H van der Waals repulsion (Fig. 1). The distance N1–H1···O1 is 2.01Å and the associated angle 133°. The H3···H6 distance and the C3–N1–C5–C6 torsion angle are 2.25 Å and 21°, respectively, suggesting a strong van der Waals repulsion between the C3–H and C6–H. Combination of these two interactions leads to a nearly planar conformation to the molecule's main skeleton. This conformation sets the stage for the C=C···C=O interactions observed within the crystal lattice.

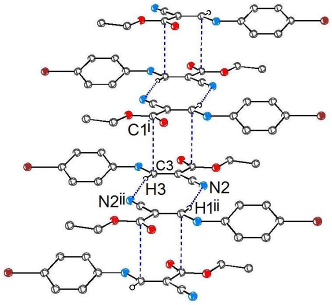

Fig.4 Packing diagram of 1, showing the formation of the stepped hydrogen-bonded chain along [100] direction. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Symmetry transformations: (i) 1-x, 1-y, 2-z; (ii) -x, 1-y, 2-z.

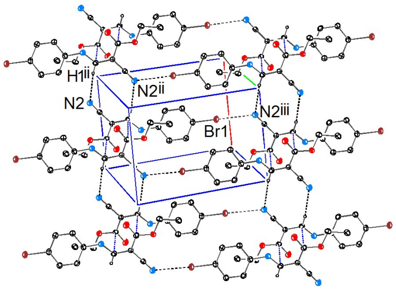

Fig. 5 Part of crystal structure of **1,** showing the formation of a two-dimensional sheet via C···C, N···Br and C–H···N interactions. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Symmetry codes: (ii) -x, 1-y, 2-z; (iii) x, y+1, z-1

In addition to the C=C···C=O interactions, there are two intermolecular noncovalent interactions in **1**, one of vinyl C–H···N≡C type (Fig. 4), and one of C≡N···Br type (Fig. 5). The distances H3···N2^{ii} and N2^{iii}····Br1 are 2.47 and 3.36 Å, respectively, and the bond angle C3-H3···N2^{ii} is 168°. These noncovalent interactions synergistically constitute a stepped (011) sheet, the formation of which can be understood in the following way: the inversion-related molecules form a dimer via a pair of C=C···C=O interactions (Fig. 1 & 4); such dimers related by translation are further linked into a stepped molecular chain parallel to [100] via a pair of equivalent C–H···N hydrogen bonds (Fig. 4); chains of this type are laterally linked into a sheet by N···Br interactions (Fig. 5).

In conclusion, the detailed structural analysis has revealed an unusual C=C···C=O interaction existing widespread in (Z)-3-[(4-halogenphenyl)amino]-2-cyanoprop-2-enoates. DFT computations and second order perturbation theory analysis of the Fock Matrix in the NBO basis at the WB97XD/6-311+G (d, p) level provided effective support to the interaction. The present work, we believe, may be the first systematic study on C···C interaction occurring between vinyl and carbonyl fragments.

Experimental

Synthesis of ethyl (Z)-3-[(4-bromophenyl)amino]-2-cyanoprop-2-enoate, 1

A mixture of 4-bromoaniline (0.02 mol), ethyl 2-cyano-3-ethoxyacrylate (0.02 mol) in toluene (10 ml) was refluxed for ca. 10 min. The reaction mixture was then cooled to room temperature. The precipitate was collected by filtration and washed with ethanol. Crystals suitable for an X-ray analysis were obtained by slow cooling of a hot toluene solution of the crude product.

X-Ray structure determination

The selected crystal was mounted in inert oil on glass fibers. Data were measured using Mo-Ka radiation on a Bruker SMART 1000 CCD diffractometer. Data collection at 296 K and reduction were performed using SMART and SAINT software.[18] Absorption correction was applied using the multi-scan method (SADABS).[19] The crystal structure of **1** was solved by direct methods and refined by full matrix least-squares on F^2 using the SHELXTL program package.[20] All non-hydrogen atoms were subjected to anisotropic refinement, and all H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms.

Crystal data

$C_{12}H_{11}BrN_2O_2$, M = 295.13, triclinic, P-1, a = 7.495 (1), b = 7.525 (1), c = 12.065(1) Å , α = 80.285(2), β = 86.767(2), γ = 67.729(2)°, V = 620.7(2) Å^3, Z = 2, T = 293(2) K, Dc = 1.579 g cm^{-3}; 6597 reflections collected, 2189 unique (Rint = 0.026), 1855 observed with $I > 2(I)$; final R = 0.0309, wR2 = 0.0770, goodness-of-fit S = 1.07.

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