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An unusual $C{=}C\cdots C{=}O$ interaction in (*Z*)-3-[(4-halogenphenyl)amino]-2-cyanoprop-2-enoates†

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Cite this: *New J. Chem.*, 2016, **40**, 85

Received (in Montpellier, France) 12th July 2015,
Accepted 18th August 2015

DOI: 10.1039/c5nj01814e

www.rsc.org/njc

An unusual $C{=}C\cdots C{=}O$ 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 $C{=}C\cdots C{=}O$ interaction is mainly dominated by dispersion and electrostatic energies, 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 atoms can act as an electron donors[6–8] as well as an electron acceptors[9] forming various kinds of noncovalent interactions, such as $C\cdots\pi$, cation$\cdots\pi$ and anion$\cdots\pi$, *etc.* Considering the complementary roles of carbon atoms, $C\cdots C$ interactions are expected to occur between electron-rich vinyl and electron-poor carbonyl fragments. Our interest in 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 studied their X-ray crystal structures.

Interestingly we have discovered a hitherto unreported $C{=}C\cdots C{=}O$ interaction in the supramolecular structure of ethyl (*Z*)-3-[(4-bromophenyl)amino]-2-cyanoprop-2-enoate, **1** (Fig. 1). As shown in the 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 $C\cdots C$ interactions between the vinyl and carbonyl groups.

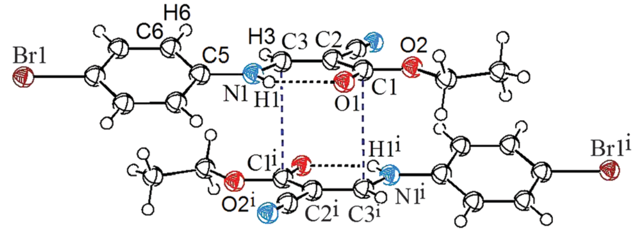
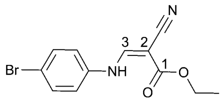


Fig. 1 The dimeric structure of ethyl (*Z*)-2-cyano-3-[(4-bromophenyl)-amino]prop-2-enoate, **1**, showing both experimentally and theoretically the formation of the $C\cdots C$ interaction between C3 and C1^{i}; the distances $C3\cdots C1^{i}$ from experimental and DFT calculations are 3.277 and 3.186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



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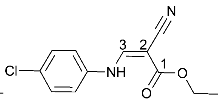

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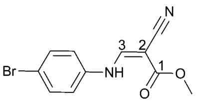

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A recent study[7] has shown the existence of $C\cdots C$ interactions. However, the only work on this subject still remains theoretical. A computational study shows that the $C\cdots C$ interactions exist between electron-deficient molecules (CO_2 or NCCN) and electron-rich molecules, such as $HC{\equiv}CH$ and $H_2C{=}CH_2$, *etc.*, and that all the dimers formed by this interaction show C_{2V} symmetry and correspond to energy minima. The $C{=}C\cdots C{=}O$ interaction in **1**, we believe, is very similar to 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 $C{=}C\cdots C{=}O$ interactions, the density functional theory (DFT) calculations at the WB97XD[10]/6-311+G(d,p) level were performed on compound **1**.

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† CCDC 952088. For crystallographic data in CIF or other electronic format see DOI: 10.1039/c5nj01814e

The monomer and the dimers formed by C═C···C═O interaction were studied. All the calculations were carried out using the GAUSSIAN 09[11] package. At this selected theoretical level, both the monomer and dimer of **1** correspond to energy minima, and are in good agreement with the crystallographically determined structure. The optimized dimer is also shown in Fig. 1. As shown in the figure, 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 −20.79 kcal 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 for 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 and Fig. 2. As 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^{-1}, 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^{-1}. The orbital interactions involving atoms C1 and C3^{i} are completely identical to the 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^{-1}. The results have theoretically confirmed that the orbital interaction between the 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

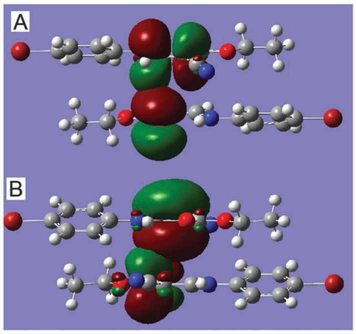

Fig. 2 Dominant orbital interactions A, π(O1^{i}═C1^{i}) → π*(C3═C2), and B, π(C2═C3) → π* (C1^{i}═O1^{i}), showing the nature of the C═C···C═O in **1**. For the sake of clarity, the same orbital interactions A′ and B′ have been omitted.

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} decreases 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 to maintain the dimer in a lower electrostatic repulsion level due to the longer distance between C2 and C2^{i}, and the latter favoring to enhance the following C–H···N≡C hydrogen bond.

In addition to the orbital interactions between the vinyl and carbonyl groups, the C═C···C═O dimer should also be stabilized by other standard energy contributions, such as dispersion, electrostatic, exchange-repulsion and polarization. To roundly explore the source of 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 the 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 occur in ethyl (*Z*)-3-[(4-bromophenyl)amino]-2-cyanoprop-2-enoate, **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 Br1 atom (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 for geometry optimization using the same methods as for **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 and C1^{i} are 3.188 and 3.218 Å, respectively. The corresponding total dimerization energies 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 are shown by the second-order perturbation theory analysis of the 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 occurred between the vinyl and carbonyl groups

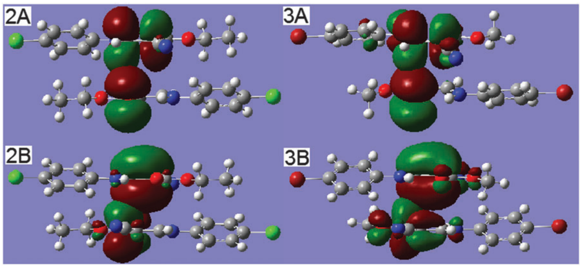

Fig. 3 The dominant NBO orbital interactions A, $\pi(\mathrm{O1^i{=}C1^i}) \rightarrow \pi^*(\mathrm{C3{=}C2})$, and B, $\pi(\mathrm{C2{=}C3}) \rightarrow \pi^*(\mathrm{C1^i{=}O1^i})$ corresponding to the C···C interaction between vinyl atom C1 and carbonyl atom $\mathrm{C3^i}$ in **2** (left) and **3**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

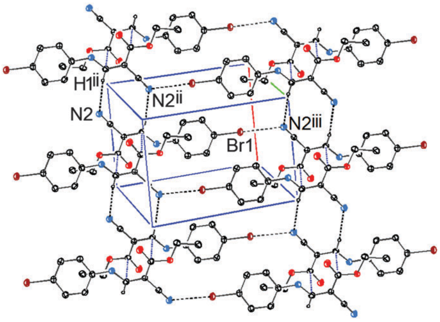

Fig. 5 Part of the crystal structure of **1**, showing the formation of a two-dimensional sheet *via* C···C, N···Br and C–H···N interactions. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Symmetry codes: (ii) −*x*, 1 − *y*, 2 − *z*; (iii) *x*, *y* + 1, *z* − 1.

despite the abundance of vinyl and carbonyl groups existing in crystal structures deposited so far in the CCDC. However, this interaction exists predominantly in (*Z*)-3-[(4-halogenphenyl)amino]-2-cyanoprop-2-enoates.

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

In addition to the C=C···C=O interactions, there are two intermolecular noncovalent interactions in **1**, one is of vinyl C–H···N≡C type (Fig. 4), and the other is of C≡N···Br type (Fig. 5). The distances of $\mathrm{H3\cdots N2^{ii}}$ and $\mathrm{N2^{iii}\cdots Br1}$ are 2.47 and 3.36 Å, respectively, and the bond angle of $\mathrm{C3{-}H3\cdots N2^{ii}}$ 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 and 4); such dimers related by translation are further linked to 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 to a sheet by N···Br interactions (Fig. 5).

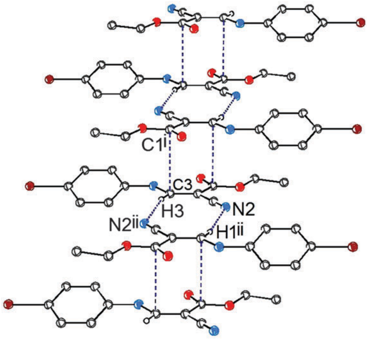

Fig. 4 Packing diagram of **1**, showing the formation of the stepped hydrogen-bonded chain along the [100] direction. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Symmetry transformations: (i) 1 − *x*, 1 − *y*, 2 − *z*; (ii) −*x*, 1 − *y*, 2 − *z*.

In conclusion, the detailed structural analysis has revealed an unusual C=C···C=O interaction existing predominantly in (*Z*)-3-[(4-halogenphenyl)amino]-2-cyanoprop-2-enoates. The DFT computations and second order perturbation theory analysis of the Fock Matrix on 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 interactions occurring between the 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) and 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 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 with inert oil on glass fibers. Data were measured using Mo-Kα radiation on a Bruker SMART 1000 CCD diffractometer. Data collection at 296 K and reduction were performed using the 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, $P\bar{1}$, a = 7.495 (1) Å, b = 7.525 (1) Å, 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, D_c = 1.579 g cm^{-3}; 6597 reflections collected, 2189 unique

(R_{int} = 0.026), 1855 observed with $I > 2(I)$; final R = 0.0309, wR_2 = 0.0770, goodness-of-fit S = 1.07.

Notes and references

1 (*a*) D. A. Dougherty, *Acc. Chem. Res.*, 2013, **46**, 885–893; (*b*) L. Strekowski and B. Wilson, *Mutat. Res.*, 2007, **623**, 3–13; (*c*) B. T. Benedetti, E. J. Peterson, P. Kabolizadeh, A. Martinez, R. Kipping and N. P. Farrell, *Mol. Pharmaceutics*, 2011, **8**, 940–948; (*d*) C. P. Selby and A. Sancar, *Biochemistry*, 1991, **30**, 3841–3849.

2 (*a*) Z. Chi, R. Liu and H. Zhang, *Biomacromolecules*, 2010, **11**, 2454–2459; (*b*) M. N. Namchuk and S. G. Withers, *Biochemistry*, 1995, **34**, 16194–16202; (*c*) D. H. Williams, E. Stephens, D. P. O'Brien and M. Zhou, *Angew. Chem., Int. Ed. Engl.*, 2004, **43**, 6596–6616.

3 (*a*) D. A. Britz and A. N. Khlobystov, *Chem. Soc. Rev.*, 2006, **35**, 637–659; (*b*) B. Rybtchinski, *ACS Nano*, 2011, **5**, 6791–6818; (*c*) D. Baskaran, J. W. Mays and M. S. Bratcher, *Chem. Mater.*, 2005, **17**, 3389–3397; (*d*) K. L. Vidale, D. M. Sherman, K. Hallenga, K. V. Wood and J. G. Stowell, *J. Am. Chem. Soc.*, 2001, **123**, 3854–3855.

4 S. S. Sheiko, F. C. Sun, A. Randall, D. Shirvanyants, M. Rubinstein, H. Lee and K. Matyjaszewski, *Nature*, 2006, **440**, 191–194.

5 G. A. DiLabio, P. G. Piva, P. Kruse and R. A. Wolkow, *J. Am. Chem. Soc.*, 2004, **126**, 16048–16050.

6 M. A. Viswamitra, R. Radhakrishnan, J. Bandekar and G. R. Desiraju, *J. Am. Chem. Soc.*, 1993, **115**, 4868–4869.

7 I. Alkorta, F. Blanco, J. Elguero, J. A. Dobado, S. M. Ferrer and I. Vidal, *J. Phys. Chem. A*, 2009, **113**, 8387–8393.

8 (*a*) Z. Zhang, Y. Wu and G. Zhang, *CrystEngComm*, 2011, **13**, 4496–4499; (*b*) J. L. Atwood, F. Hamada, K. D. Robinson, G. W. Orr and R. L. Vincent, *Nature*, 1991, **349**, 683–684.

9 (*a*) Z. Zhang, H. Tong, Y. Wu and G. Zhang, *New J. Chem.*, 2012, **36**, 44–47; (*b*) G. Bhattacharjya, G. Savitha and G. Ramanathan, *CrystEngComm*, 2004, **6**, 233–235.

10 (*a*) S. Grimme, *J. Comput. Chem.*, 2006, **27**, 1787–1799; (*b*) J.-D. Chai and M. Head-Gordon, *Phys. Chem. Chem. Phys.*, 2008, **10**, 6615–6620.

11 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz and J. Cioslowskiand D. J. Fox, *GAUSSIAN 09 revision A.02*, Gaussian, Inc., Wallingford CT, 2009.

12 E. A. Reed, L. A. Curtiss and F. Weinhold, *Chem. Rev.*, 1988, **88**, 899–926.

13 E. A. Reed and F. Weinhold, *J. Chem. Phys.*, 1983, **78**, 4066–4073.

14 L. Song, Y. Lin, W. Wu, Q. Zhang and Y. Mo, *J. Phys. Chem. A*, 2005, **109**, 2310–2316.

15 E. D. Glendening, J. K. Badenhoop, A. E. Reed, J. E. Carpenter and F. Weinhold, *NBO Version 3.1*, Theoretical Chemistry Institute, University of Wisconsin, Madison, USA, 1995.

16 M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. Su, T. L. Windus, M. Dupuis and J. A. Montgomery, *J. Comput. Chem.*, 1993, **14**, 1347–1363.

17 (*a*) H He Li Be B C N O F Ne Na Mg Al Si P S Cl Ar: E. Papajak and D. G. Truhlar, *J. Chem. Theory Comput.*, 2010, **6**, 597–601; (*b*) B–F: R. A. Kendall, T. H. Dunning Jr. and R. J. Harrison, *J. Chem. Phys.*, 1992, **96**, 6796–6806.

18 *SMART 5.0 and SAINT 4.0 for Windows NT, Area Detector Control and Integration Software*, Bruker Analytical X-Ray Systems Inc., Madison, WI, 1998.

19 G. M. Sheldrick, *SADABS: Program for Empirical Absorption Correction of Area Detector Data*, University of Göttingen, Germany, 1996.

20 G. M. Sheldrick, *SHELXTL 5.1 for Program for Windows NT: Structure Determination Software Programs*, Bruker Analytical X-Ray Systems, Inc., Madison, WI, 1997.