organic compounds

(E)-Methyl 2-anilinomethylene-3-oxobutanoate: X-ray and density functional theory studies

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Molecules of the title compound, $C_{12}H_{13}NO_3$, are not planar and are stabilized by electrostatic interactions, as the dipole moment of the molecule is 3.76 D. They are also stabilized by intramolecular hydrogen bonds of $N \cdots O$ and $C \cdots O$ types, and by a complicated network of weak intermolecular hydrogen bonds of the $C \cdots O$ type. This paper also reports the theoretical investigation of the hydrogen bonding and electronic structure of the title compound using natural bond orbital (NBO) analysis.

Comment

Anilinomethyleneoxobutanoates belong to a large family of arylaminomethylene derivatives of active methylene compounds having two electron-withdrawing groups (acetyl, ester, cyano, nitro, etc.) on this methylene group (Hermecz et al., 1992). These compounds are frequently used for the synthesis of various 3-substituted 4-quinolones, which form a class of drugs with a broad spectrum of biological activities, such as antibacterial, anti-allergic, antiherpetic, anti-cancerogenic, etc., used in human or veterinary medicine (Milata et al., 2000). They display herbicidal, germicidal and photosynthetic activity and also inhibit photobleaching activity (Huppatz et al., 1981; Sankyo Co. Ltd, 1981; Wang et al., 1997). They are precursors for aminochinoline derivatives with broad biological activities (Palacios et al., 1999) and, according to our findings (Repický et al., 2005), they can also be used for apoptosis (programmed cell death, PCD). The title compound, (I), was synthesized and studied because it is a suitable precursor for obtaining 3-acetyl-4-quinolone, a model compound for potential drugs. Substituted anilinomethylene-oxobutanoates are suitable subjects for the study of intra-molecular hydrogen bonds between imino H atoms and the

carbonyl atoms of acetyl or alkoxycarbonyl groups (Milata et al., 1990; Couchouron et al., 1983; Michalik, 1985; Hermecz et al., 1992).

(I)
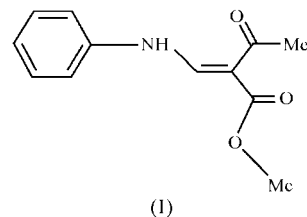
The structure of (I) is illustrated in Fig. 1 and selected geometric parameters are given in Table 1. The molecule is not planar but is stabilized by electrostatic interactions, as the dipole moment of the molecule is 3.76 D. It is also stabilized by
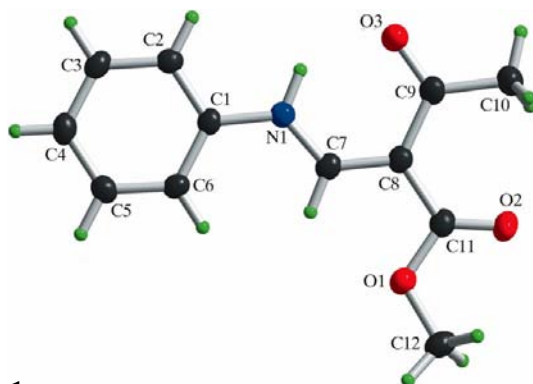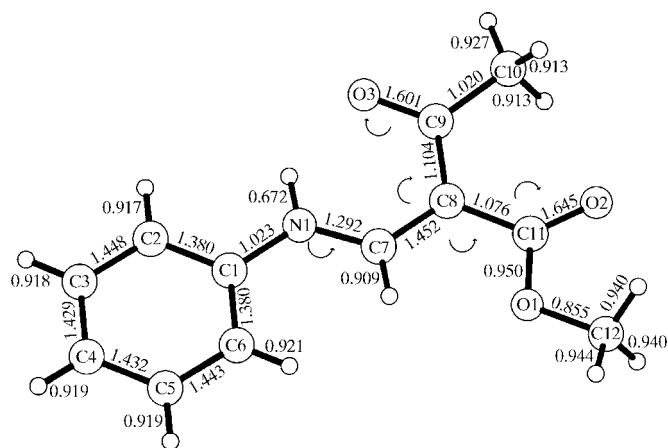

Figure 1
The numbering scheme of (I), with atomic displacement ellipsoids drawn at the 50% probability level. H atoms are shown as small spheres of arbitrary radii.
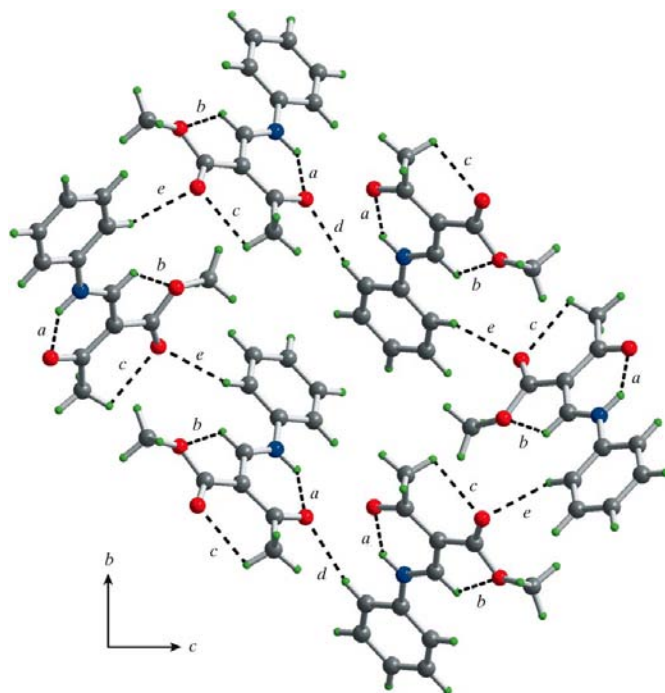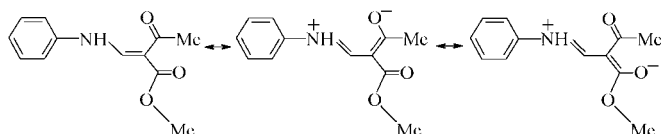

Figure 2
The hydrogen-bond pattern in the crystal structure of (I); see Table 2 for definition of symbols.

both intra- and intermolecular hydrogen bonds (Fig. 2 and Table 2). Calculations in the solid state confirm the types of hydrogen bonds found from the experiment. On the first level graph-set, as defined by Bernstein *et al.* (1995) and Grell *et al.* (1999), intramolecular $S(6)$, $S(5)$ and $S(6)$ strings are formed by hydrogen bonds *a*, *b* and *c*, respectively, and intermolecular $C(8)$ chains by hydrogen bonds *d* and *e* (hydrogen bonds *a–e* are defined in Table 2). On the second-level graph-set, $C_2^2(10)$ and $C_2^2(16)$ chains, both formed by bonds *d* and *e*, are recognized. These two hydrogen bonds, *d* and *e*, also form an $R_6^6(42)$ ring, as shown in Fig. 2.

Natural bond orbital (NBO) analysis (Foster & Weinhold, 1980) of the molecular electronic structure of (I) shows that the bond orders (Wiberg indices in Fig. 3) are very close to the expected values. The exceptions are the N1—C7 and C7—C8 bonds, the bond orders of which are between a single and a double bond, indicating delocalization of electrons. A detailed analysis of the NBO results reveals that a lone pair on atom N1 is connected through the C7═C8 double bond to electron-withdrawing groups (two –C═O groups). As a consequence, the electrons from the nitrogen lone pair are delocalized to a formally single N1—C7 bond, lending it a partial double-bond character. In addition, π electrons from the C7═C8 double bond are pulled towards the withdrawing groups through the C8—C9 and C8—C11 bonds. The possible resonance structures of compound (I) are shown in Fig. 4. Our NBO analysis shows that the most probable structure is that illustrated in the centre of Fig. 4. A similar electronic redistribution was found in 2-anilinomethylene-3-oxobutanenitrile (Langer *et al.*, 2006) and in 5-anilinomethylene-2,2-dimethyl-1,3-dioxane-4,6-dione (Smrčok *et al.*, 2007).

Experimental

The target compound, (I), was prepared by refluxing equivalent amounts (10 mmol) of aniline and methyl 2-methoxymethylene-3-oxobutanoate in toluene (20 ml) for 30 min. After cooling the reaction mixture, the crude product was filtered off and recrystallized from ethanol.

Crystal data

$C_{12}H_{13}NO_3$	$V = 1075.85\ (11)$ Å^3
$M_r = 219.23$	$Z = 4$
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation
$a = 5.3812\ (3)$ Å	$\mu = 0.10$ mm^{-1}
$b = 9.9032\ (6)$ Å	$T = 153\ (2)$ K
$c = 20.1882\ (12)$ Å	$0.48 \times 0.13 \times 0.11$ mm

Data collection

Siemens SMART CCD area-detector diffractometer	17633 measured reflections
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)	1912 independent reflections
	1627 reflections with $I > 2\sigma(I)$
$T_{min} = 0.811$, $T_{max} = 0.989$	$R_{int} = 0.037$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.035$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.100$	
$S = 1.00$	
1912 reflections	$\Delta\rho_{max} = 0.28$ e Å^{-3}
156 parameters	$\Delta\rho_{min} = -0.15$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C7—N1	1.3269 (19)	C1—N1	1.4142 (19)
C7—C8	1.388 (2)	O3—C9	1.245 (2)
C8—C11	1.467 (2)	O2—C11	1.210 (2)
C1—N1—C7—C8	−179.71 (14)	N1—C7—C8—C9	1.6 (2)
N1—C1—C2—C3	178.92 (13)		

Table 2
Comparison of experimental hydrogen-bonding geometry (Å, °) for compound (I) and results from the solid-state density functional theory calculations (calc_s).

Notation	D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
a	N1—H1$\cdots$O3	0.91	1.93	2.6149 (18)	131
	calc_s	1.04	1.80		137
b	C7—H7$\cdots$O1	0.93	2.22	2.6256 (19)	106
	calc_s	1.09	2.19		101
c	C10—H10$B\cdots$O2	0.96	2.49	2.8023 (19)	99
	calc_s	1.10	2.46		97
d	C2—H2$\cdots$O3^{i}	0.94	2.39	3.322 (2)	169
	calc_s	1.09	2.24		171
e	C6—H6$\cdots$O2^{ii}	0.93	2.52	3.3640 (19)	151
	calc_s	1.09	2.36		152

Symmetry codes: (i) $\frac{1}{2} + x, \frac{3}{2} - y, 1 - z$; (ii) $1 - x, -\frac{1}{2} + y, \frac{3}{2} - z$.

For the X-ray data, H atoms were constrained to ideal geometry using an appropriate riding model, while the distances to the parent atoms were free to refine (C—H = 0.93–0.98 Å). For the methyl groups, the C—C—H and O—C—H angles were kept fixed at 109.5°, while the torsion angles were allowed to refine, with the starting positions based on the threefold averaged circular Fourier synthesis. The isotropic displacement parameters for the H atoms were kept fixed at $1.5U_{eq}$ of the parent methyl C atom and at $1.2U_{eq}$ of the parent atom for the rest.

Figure 3
Wiberg bond orders calculated for an isolated molecule of (I) using NBO formalism. The arrows indicate predicted transfers of electronic density.

Figure 4
Probable resonance structures of the title compound.

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A theoretical investigation of the hydrogen bonds of (I) was performed using the Vienna *ab initio* simulation package *VASP* (Kresse & Hafner, 1993; Kresse & Furthmüller, 1996). The exchange-correlation functional is expressed in the localized density approximation (LDA) according to Perdew & Zunger (1981), together with the generalized gradient approximation (GGA) according to Perdew & Wang (1992). Plane waves form a basis set and calculations were performed using the projector-augmented wave method (Blöchl, 1994; Kresse & Joubert, 1999) and atomic pseudo-potentials (Kresse & Hafner, 1994). An optional energy cut-off controlling the accuracy of the calculation was set at 400 eV, representing an extended basis set and consequently highly accurate calculations. The optimization of the positions of the H atoms was achieved by the method of conjugated gradient in 8κ points (Teter *et al.*, 1989; Bylander *et al.*, 1990). NBO (natural bond orbital) calculations were carried out by means of the *NBO* program (Glendening *et al.*, 1993) included in the *GAUSSIAN98* package (Frisch *et al.*, 1998), after full optimization of the geometric parameters of the isolated molecule at the B3LYP/6-31G** level of theory.

Data collection: *SMART* (Bruker, 2003); cell refinement: *SAINT* (Bruker, 2003); data reduction: *SAINT* and *SADABS* (Sheldrick, 2003); program(s) used to solve structure: *SHELXTL* (Bruker, 2003); program(s) used to refine structure: *SHELXTL*; molecular graphics: *DIAMOND* (Brandenburg, 2007); software used to prepare material for publication: *SHELXTL*.

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