J Chem Crystallogr (2011) 41:1214–1217
DOI 10.1007/s10870-011-0075-x

ORIGINAL PAPER

The Crystal Structures of (*Z*)-Ethyl 2-(4-chlorophenyl)-3-(2,4-difluorophenyl-amino)acrylate and its Analogues

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Received: 27 November 2008 / Accepted: 15 April 2011 / Published online: 27 April 2011

Abstract The title compound, $C_{17}H_{14}ClF_2NO_2$, crystallizes in monoclinic space group $P2_1/c$ with unit cell dimension of $a = 16.276(3)$ Å, $b = 7.5030(15)$ Å, $c = 13.812(3)$ Å, $\alpha = 90°$, $\beta = 111.11(3)°$, $\gamma = 90°$ and $Z = 4$. The structure of the title compound reveals a *Z* configuration with respect to the C=C double bond in aminoacrylate fragment. The molecule is stabilized by intramolecular N–H···F and N–H···O hydrogen bonds. In the ethyl 2-aryl-3-arylaminoacrylates, electronic properties of the substituents in the aniline motif clearly affected the attached C–N bond length, and such effect is very little relative to *Z*-/*E*-configuration with respect to the C=C double bond.

Keywords Enamine · Acrylate · Crystal structure · Conjugation

Introduction

A 2-aryl-3-arylaminoacrylate contains characteristic N–C=C bond and is therefore identified as enamine. It is well known that *Schiff* base harbors a N=C–C bond, which indicates that an enamine is the tautomeric isomer of the correspond *Schiff* base. Enamines, as to their *Schiff* bases [1–3], show good antimicrobial activities [4–7], especially against bacterium. On the other hand, an enamine is the key intermediate for anticancer agents, 3-arylquinolone and 3-arylquinoline [8–10]. In a continuation of our work on the structural characterization of enamine derivatives, we report herein the crystal structure of the title compound, (*Z*)-ethyl 2-(4-chlorophenyl)-3-(2,4-difluorophenylamino)acrylate **9**.

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Experimental

Reagents and Techniques

2-(4-Chlorophenyl)acetic acid was purchased from Aldrich (USA) and the other chemicals were purchased from Sinopharm Chemical Reagent Co., Ltd (China). Melting points (uncorrected) were determined on a XT4 MP apparatus (Taike Corp., Beijing, China). EI mass spectra were obtained on a Waters GCT mass spectrometer, and ^{1}H NMR spectra were recorded on a Bruker AV-300 spectrometer at 25 °C with TMS and solvent signals allotted as internal standards. Chemical shifts were reported in ppm (δ). Elemental analyses were performed on a CHN–O-rapid instrument and were within ±0.4% of the theoretical values.

Synthesis of (Z)-Ethyl 2-(4-chlorophenyl)-3-(2,4-difluorophenyl-amino)acrylate

Equimolar quantities (6 mmol) of ethyl 2-(4-chlorophenyl)-3-oxopropanoate (1.36 g, synthesized according to the literature procedure [11]) and 2,4-difluorobenzenamine (0.77 g) in absolute alcohol (18 mL) were heated at 75 °C for 2 h. The excess solvent was removed under reduced pressure. The residue was purified by a flash chromatography

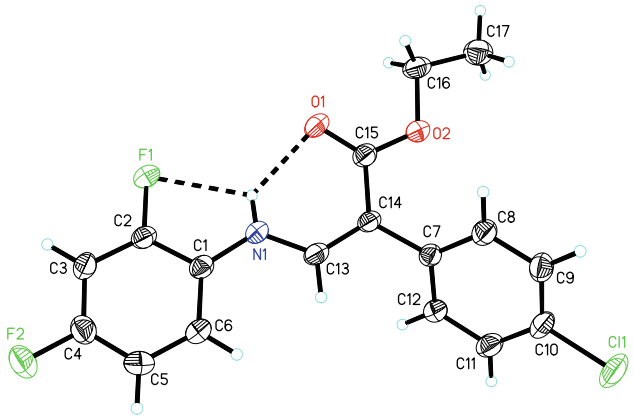


Fig. 1 The molecule structure of compound **9** (30% probability ellipsoids)

Table 1 Crystal data and experimental crystallographic details

Empirical formula	$C_{17}H_{14}ClF_2NO_2$
Formula weight	337.74
Temperature (K)	293(2)
Wavelength (Å)	0.71073
Crystal system	Orthorhombic
Space group	$P2_1/c$
Cell dimensions	
a (Å)	16.276(3)
b (Å)	7.5030(15)
c (Å)	13.812(3)
α (°)	90
β (°)	111.11(3)
γ (°)	90
Volume (Å^3)	1573.5(5)
Z	4
Density (calculated) (mg/m^3)	1.426
Absorption coefficient (/mm)	0.272
F_{000}	696
Crystal size (mm)	0.3 × 0.1 × 0.1
θ range for data collection (°)	1.34–25.25
Index ranges	$-19 \le h \le 18$
	$-9 \le k \le 0$
	$0 \le l \le 16$
Reflections collected	2957
Unique reflections	2824 [$R_{int} = 0.0270$]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2824/0/213
Goodness-of-fit on F^2	0.989
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0648$, $wR_2 = 0.1465$
R indices (all data)	$R_1 = 0.1238$, $wR_2 = 0.1703$
Largest diff. peak and hole (e/Å^3)	0.258/−0.289

with EtOAc-petrolum ether (1:6, v/v) to afford two fractions. The first fraction, after partial solvent evaporated, furnished colorless blocks of **9** suitable for single crystal structure determination. Yield of 37%, mp 131–132 °C, ^{1}H NMR (300 MHz, d_6-DMSO): 1.22 (t, $J = 7.0$ Hz, 3H); 4.20 (q, $J = 7.3$ Hz, 2H); 7.08 (t, $J = 7.8$ Hz, 1H); 7.36 (d, $J = 8.6$ Hz, 3H); 7.40 (d, $J = 8.8$ Hz, 2H); 7.68 (m, 1H); 7.73 (d, $J = 12.5$ Hz, 1H); 10.43 (d, $J = 12.2$ Hz, 1H); MS (ESI): 338.1 ($C_{17}H_{15}ClF_2NO_2$, $[M+H]^+$). Anal. Calcd for $C_{17}H_{14}ClF_2NO_2$: C, 60.45; H, 4.18; N, 4.15; Found: C, 60.26; H, 4.17; N, 4.18.

X-ray Diffraction Analysis

The crystal structure with the formula $C_{17}H_{14}ClF_2NO_2$ is shown in Fig. 1. The compound crystallizes in the monoclinic $P2_1/c$ space group. Crystallographic data, experimental details and the refinement procedures are given in Table 1. The intensity data were collected on CCD area detector diffractometer with graphite-monochromated Mo-Kα radiation ($\lambda = 0.71073$ Å) at room temperature. A crystal with dimensions 0.3 × 0.1 × 0.1 mm was used. The structure was solved by the direct method using the SHELXS-97 program [12] and refined by the full-matrix least-squares method using the SHELXL-97 program [13]. The H atom bonded to N1 was located in a difference Fourier map and all other H atoms were placed at chemically acceptable positions and were not refined. Selected

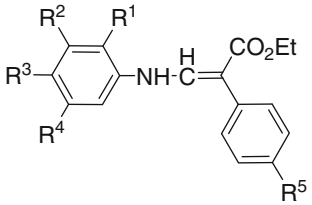
Table 2 Selected bond lengths (Å) and angles (°) with esd's in parentheses

Bond lengths			
C(1)–N(1)	1.394(4)	C(14)–C(7)	1.489(4)
N(1)–C(13)	1.344(4)	C(15)–O(1)	1.225(4)
C(13)–C(14)	1.348(5)	C(15)–O(2)	1.333(4)
C(14)–C(15)	1.463(4)		
Bond angles			
C(1)–N(1)–C(13)	126.4(3)	C(15)–C(14)–C(7)	122.4(3)
N(1)–C(13)–C(14)	127.8(3)	C(14)–C(15)–O(1)	124.3(3)
C(13)–C(14)–C(7)	118.7(3)	C(14)–C(15)–O(2)	113.2(3)
C(13)–C(14)–C(15)	119.0(3)	O(1)–C(15)–O(2)	122.4(3)

Table 3 Hydrogen-bond geometry in the title compound (Å, °)

D–H···A	D–H	H···A	D···A	D–H···A
N1–H18···F1	0.83(3)	2.29(3)	2.674(3)	108(3)
N1–H18···O1	0.83(3)	2.07(3)	2.675(4)	129(3)

Table 4 C–N bonds in some aminoacrylate crystals



Compound	Configuration	R^1	R^2	R^3	R^4	R^5	C1–N1	C13–N1	References
1	Z	H	H	OH	H	OCH_3	1.417(3)	1.340(4)	[4]
1	E	H	H	OH	H	OCH_3	1.414(3)	1.337(4)	[4]
2	Z	H	F	H	F	Cl	1.398(5)	1.344(5)	[4]
3	E	H	Cl	H	Cl	Cl	1.404(4)	1.352(4)	[4]
4	Z	H	H	F	H	Cl	1.400(7)	1.347(7)	[6]
5	E	H	OCH_3	H	OCH_3	Cl	1.418(3)	1.353(3)	[6]
6	Z	F	H	F	H	OCH_3	1.395(3)	1.343(3)	[14]
7	E	F	H	H	H	OCH_3	1.400(3)	1.364(3)	[15]
8	E	H	H	F	H	OCH_3	1.408(3)	1.359(3)	[16]
9	Z	F	H	F	H	Cl	1.394(4)	1.344(4)	–

geometrical parameters from X-ray data are given in Table 2.

Results and Discussion

Amioacrylate moiety is essentially planar with mean deviation of 0.0413 Å. This plane makes a dihedral angle of 8.7(1)° with the 2,4-difluorophenyl ring, which indicates that the two planes are almost coplanar. To the contrary, the dihedral angle between the aminoacrylate plane and *p*-chlorophenyl ring is significantly different. They forms a dihedral angle of 47.5(1)°, and the possible conjugation is disrupted. The molecule is stabilized by two intramolecular hydrogen bonds (Table 3) which form a five-membered pseudo-ring and a six-membered one, respectively. The former closed by the intramolecular N–H···F hydrogen bond is almost planar with mean deviation of 0.0032° which is coplanar with the fused C1–C6 benzene ring, and the latter closed by the intramolecular N–H···O hydrogen bond is also planar with mean deviation of 0.0357 Å (Fig. 1).

The bond length of C13–N1 (1.344(4) Å) is shorter than standard C–N single bond (1.48 Å) but longer than C=N double bond (1.28 Å), which may be the result of the conjugation of the *p* orbital of N1 with the π molecular orbital of C13=C14 double bond. For the same reason, C1–N1 is single bond with some double bond character. However, compared to C13–N1, the bond length of C1–N1 (1.394(4) Å) is more close to single bond. In order to explore what the structural factors are that lead to the variation of N–C bond length, ten congeners (Table 4) with different substituents and patterns of substitution were synthesized. Their structures were subsequently determined by X-ray diffraction analysis. As shown in Table 4, the Ar–N (C1–N1) bond length is found to be sensitive to the electronic property of the substituent in aniline motif. Compared with crystals **1** and **5**, **4** and **2** displayed longer C1–N1 bond lengths, which indicates that the electronic-donating group lengthens the Ar–N bond. Furthermore, such effect is uninfluenced irrespective of where the substituent is placed in the aniline moiety, and is very little relative to *Z*-/*E*-configuration with respect to the C=C double bond. This is supported by comparison of structures **2** and **1*Z*** with **9** and **1*E***, respectively. In fact, the coplanarity of the amino group and the attached benzene ring permitted the conjugation across the C1–N1 bond, which is prone to shorten C1–N1 bond; however, the electronic-donating group leaned to push the lone-pair electrons on N1 away from the central benzene ring. This weakened the bond between aromatic moiety and amino group. To the contrary, the electronic property of the substituent in the other aromatic ring, which in the cases of **6** and **9**, could not affect on the C13–N1 bond due to the significant twist between acrylate fragment and the mentioned benzene ring. It is clearly different for the carboxyl group, which considerably shortened the bond length of C13–N1 through conjugation together with its strong electron-withdrawing property. All of which may reason the bond length of C13−N1 generally shorter than that of C1–N1.

Supplementary Material

CCDC-711259 contains the supplementary crystallographic data for this article. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html

[or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: 44(0)1223-336033; e-mail: deposit@ccdc.cam.ac.uk.

Acknowledgments The study was financed by Scientific Research Fund of Hunan Provincial Education Department (Project 09B083) of China, by a grant (Project JSDXKYZZ0801) from Jishou University for talent introduction, China and by aid program for Science and Technology Innovative Research Team (Chemicals of Forestry Resources and Development of Forest Products) in Higher Educational Institutions of Hunan Province.

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