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Synthesis and Molecular Structure of (*E*)-Methyl 3-(2-Hydroxyphenyl)-2-(Piperidine-1-Carbonyl) Acrylate Stabilized by Hydrogen Bonding and C-H…π Interactions

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Authors' contributions

This work was carried out in collaboration between all authors. Author IK designed the study and wrote the manuscript. Author AI performed the experiments and managed the analysis. Authors BL and AAA surveyed the literature and co-wrote the first draft. Author JMW determined the crystal structure and wrote the relevant discussion. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

The crystal and molecular structure of (*E*)-methyl 3-(2-hydroxyphenyl)-2-(piperidine-1-carbonyl)acrylate, synthesized by one-pot three component reaction of salicylaldehyde, diethyl malonate and piperidine, has been reported. The title compound **4** crystallizes from a mixture of petroleum ether/ethyl acetate in the monoclinic space group P21/n with lattice parameters a = 8.0099(3) Å, b = 19.6227(7) Å, c = 9.6322(4) Å, β = 107.004(4)°, V = 1447.77(10) Å^3 and Z = 4. The molecules of the target compound **4** form H-bonded dimers in the crystal lattice. These dimers are held together by C-H…π interactions, between the piperidine equatorial α-hydrogen and the aromatic ring and C-H…O interactions between the axial α-piperidine hydrogen and the hydroxyl oxygen.

Keywords: Acrylate; crystal structure; hydrogen bonding; π-interactions.

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1. INTRODUCTION

The acrylate scaffold has been described as privileged structure since members of this structural class are one of the best candidates of transparency coating materials [1]. These have been extensively used as a benchmark protocol for the discovery of new palladium catalysts and to demonstrate new advances in Heck arylation [2,3]. Conjugate addition to acrylate derivatives has been studied by Tong and co-workers [4] using different diamine derivatives as a catalyst. Acrylate derivatives have also been found as antifungal agents [5] and used to develop fluorescent dyes [6]. Recent literature investigations have revealed that these structures find enormous applications in agrochemicals and medical because of their good environmental profile.

In view of the versatility and synthetic importance of acrylate structures, we report the synthesis and X-ray crystal structure of (*E*)-methyl 3-(2-hydroxyphenyl)-2-(piperidine-1-carbonyl)acrylate which is stabilized by hydrogen bonding, C-H…π and C-H…O interactions.

2. MATERIALS AND METHODS

2.1 General

All reagents were of analytical grade or chemically pure. The melting point was determined on a Stuart melting point apparatus (SMP3) in open capillary tube and remains uncorrected. The progress of the reaction was monitored by thin layer chromatography using pre-coated silica gel plates (Kieselgel 60 F_{254} from Merck) and the chromatogram was visualized under UV light at 254 and 365 nm. The infra-red spectrum was recorded on a Bruker Optics Alpha FTIR Spectrophotometer. ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) spectra were recorded using Bruker AV-300 spectrometer in $CDCl_3$ solution using residual solvent signal as the reference. Chemical shift values are expressed in ppm. Mass spectrum was recorded on a Finnigan MAT-311A (Germany) mass spectrometer operating at an ionization potential of 70 eV. CHN analysis was performed on a Carlo Erba Strumentazion-Mod-1106 Italy.

2.2 Synthesis

2.2.1 Synthesis of (*E*)-methyl 3-(2-hydroxyphenyl)-2-(piperidine-1-carbonyl)acrylate 4

To a cold mixture of salicylaldehyde **1** (0.1 mol) and dimethyl malonate **2** (0.1 mol) was added piperidine **3** (0.3 mol) by rapid shaking. The solid separated was filtered and washed with diethyl ether to afford the title acrylate [7]. The compound **4** was recrystallized from a mixture of petroleum ether and ethyl acetate.

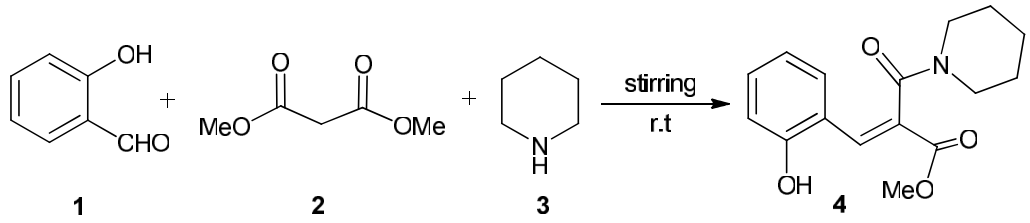
Yield: 81 %, m.p 119-120 ºC; IR (neat, cm^{-1}): 3341 (OH), 3043 (C_{sp2}-H), 2972, 2862 (C_{sp3}-H), 1727 ($C=O_{ester}$), 1699 ($C=O_{amide}$), 1602, 1508 ($C=C_{Ar}$), 1224 (C-O); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.90 (s, 1H, C-H), 7.27 (d, 1H, ^{3}J = 8.4 Hz, Ar-H), 7.21-7.19 (m, 1H, Ar-H), 7.17 (s, 1H, OH), 6.57 (dd, 2H, ^{3}J = 8.4 Hz; ^{4}J = 2.4 Hz, Ar-H), 4.01-3.95 (m, 4H, NCH_2), 3.85 (s, 3H, OCH_3), 2.04-1.98 (m, 6H, CH_2); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 165.4, 157.7, 146.8, 144.5, 133.5, 131.1, 129.7, 120.6, 119.1, 116.5, 55.8, 47.7, 29.9, 26.5. EIMS: m/z 289 [M^{+}]. Elemental analysis Calcd. for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.21; H, 6.48; N, 4.63.

2.3 X-Ray Structure Determination

A suitable crystal of (*E*)-methyl 3-(2-hydroxyphenyl)-2-(piperidine-1-carbonyl)acrylate **4** having dimensions of 0.34 × 0.30 × 0.18 mm was selected and all the reflection data were collected on an Oxford SuperNova CCD diffractometer using Mo-Kα (λ = 0.71073 Å) radiation at 130 K. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using *SHELX*-97 [8].

3. RESULTS AND DISCUSSION

The preparation of the target compound, (*E*)-methyl 3-(2-hydroxyphenyl)-2-(piperidine-1-carbonyl)acrylate **4** in an impressive yield of 81% was accomplished by the reaction of salicylaldehyde **1**, dimethyl malonate **2** and piperidine **3** as sketched in Scheme 1. The crystals of **4** were grown during the purification step from a saturated solution of petroleum ether/ethyl acetate [7].



Scheme 1. Synthesis of (*E*)-methyl 3-(2-hydroxyphenyl)-2-(piperidine-1-carbonyl)acrylate 4

The title compound was characterized by analytical and spectroscopic data. The IR spectrum showed characteristic stretching bands corresponding to C=O (ester) and C=O (amide) at 1727 and 1699 cm^{-1} respectively. The presence of hydroxyl group was confirmed by O-H stretching vibration band at 3341 cm^{-1}. Similarly, disappearance of CHO absorption frequency at 2850 and 2750 cm^{-1} indicated the formation of compound **4**. Moreover, the appearance of stretching bands for CH_2 at 2972 and 2862 cm^{-1} also indicated the formation of the title compound. In ^{1}H-NMR spectrum of compound **4**, additional resonances assigned to the methine proton at 7.90 ppm was observed which confirmed the condensation between salicylaldehyde and dimethyl malonate. In addition, the upfield signals for methylene groups between 4.01-1.98 ppm and the singlet at 7.17 ppm for hydroxyl proton also confirmed the formation of the required product. Other peaks were observed at appropriate chemical shifts and integral values. The signals resonated at 165.4 and 157.7 ppm in the ^{13}C-NMR spectrum of compound **4** assigned for C=O(ester) and C=O(amide), respectively, confirmed the formation of the title compound. Other signals resonated at their corresponding chemical shift values. The title compound was further confirmed by mass spectrometry affording molecular ion peak at m/z = 289. The elemental analysis justified the purity of the synthesized compound.

The molecular structure of **4** was fully established by a single crystal X-ray diffraction analysis. A thermal ellipsoid plot at the 40% probability level for compound **4** is presented in Fig. 1. The crystal and instrumental parameters used in the unit cell determination, the data collection, and structure refinement parameters are presented in Table 1.

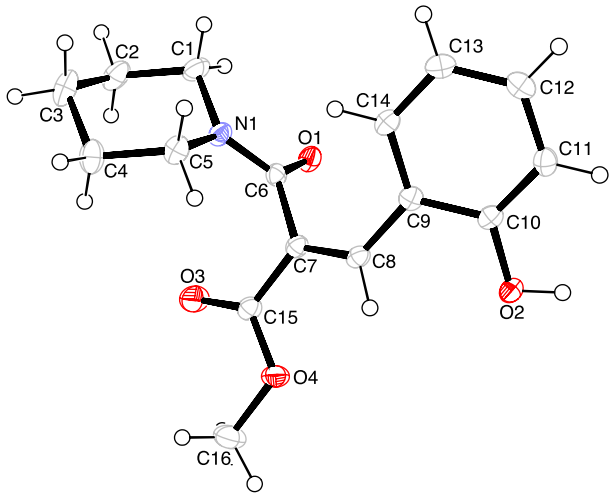


Fig. 1. Thermal ellipsoid plot for compound 4. Ellipsoids are shown at the 40% probability level

Table 1. Crystal data and structure refinement for compound 4

Empirical formula	$C_{16}H_{19}NO_4$
Formula weight	289.32
Temperature	130.0(1) K
Wavelength	0.7107 Å
Crystal system	Monoclinic
Space group	P21/n
Unit cell dimensions	*a* = 8.0099(3) Å
	b = 19.6227(7) Å
	c = 9.6322(4) Å
	β = 107.004 (4)°
Volume	1447.77(10) $Å^3$
Z	4
Density (calculated)	1.327 mg/m^3
Absorption coefficient	0.095 mm^{-1}
F(000)	616
Crystal size	0.34 × 0.30 × 0.18 mm^3
Theta range for data collection	2.85 to 25.00∞
Index ranges	-9<=h<=9, -23<=k<=22, -11<=l<=11
Reflections collected	12923
Independent reflections	2547 [R(int) = 0.0341]
Completeness to theta = 25.00∞	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.77717
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2547 / 0 / 195
Goodness-of-fit on F^2	1.074
Final R indices [I>2σ(I)]	R_1 = 0.0420, wR_2 = 0.1012
R indices (all data)	R_1 = 0.0493, wR_2 = 0.1040
Largest diff. peak and hole	0.272 and -0.199 e.$Å^{-3}$

The piperamide moiety in compound **4** is essentially co-planer with the root mean square (RMS) deviation of the fitted atoms of this group; C1, N1, C5, C6, O1 and C7 = 0.029°, with maximum deviation = 0.046 Å for C7. This group is, however, orthogonal to the alkene moiety (O1-C6-C7-C15 = -94.2(2)°, this conformation, which is necessary to avoid steric interactions between the piperamide group and the carbonyl oxygen O3 and the aromatic substituent, brings this group out of conjugation with the alkene double bond C7-C8. In contrast, the ester carboxyl (O3, C14, O4) is coplanar with the C7-C8 double bond; (O3-C15-C7-C8 = 173.8(2)°), these conformational differences result in significant differences in the sp^2-sp^2 single bonded distances between the alkene carbon (C7) and the amide and ester carbonyl carbons (C6 and C15); C7-C6 1.513(2) Å and C7-C15 1.478(2) Å respectively.

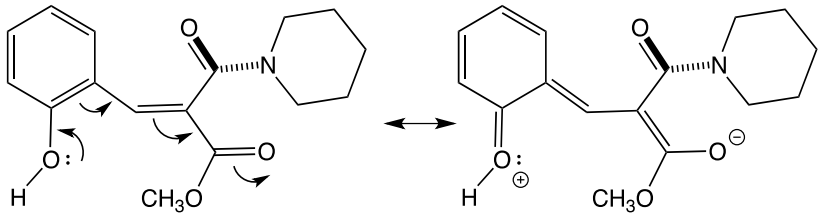


Fig. 2. Delocalization of electron density from the ortho-hydroxyl group onto the ester group

These structural differences reflect the delocalization of electron density from the ortho-hydroxyl substituent (O2) onto the ester carbonyl O3 as exhibited by the right hand side (RHS) resonance form (Fig. 2). Further support for the contributions of the RHS resonance form to the ground state structure are provided by the pattern of C-C bond distances within the aromatic ring: C9-C10 1.402(2) Å, C10-C11 1.385(2) Å C11-C12 1.379(2) Å C12-C13 1.381(2) Å C13-C14 1.376(2) Å and C9-C14 1.399(2) Å.

Molecules of **4** form H-bonded dimers in the crystal lattice as shown in Fig. 3 by O2-H 0.89(3) Å, H2…O1 1.78(3) Å, O2…O1 2.653(2) Å, and O2-H…O1 169(2)°, the second molecule is related by the symmetry transformation; -x+2,-y,-z+1.

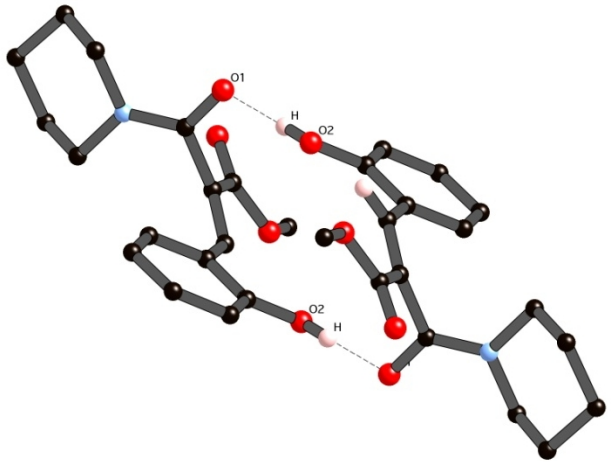


Fig. 3. H-bonded dimer units of compound 4

The H-bonded dimers shown in Fig. 3, are themselves held together by C-H...π interactions, between the piperidine equatorial *α*-hydrogen and the aromatic ring; H5B...C10 2.72 Å, this is 0.187 Å shorter than the sum of the Van der Waals radii for C and H. (Fig. 4).

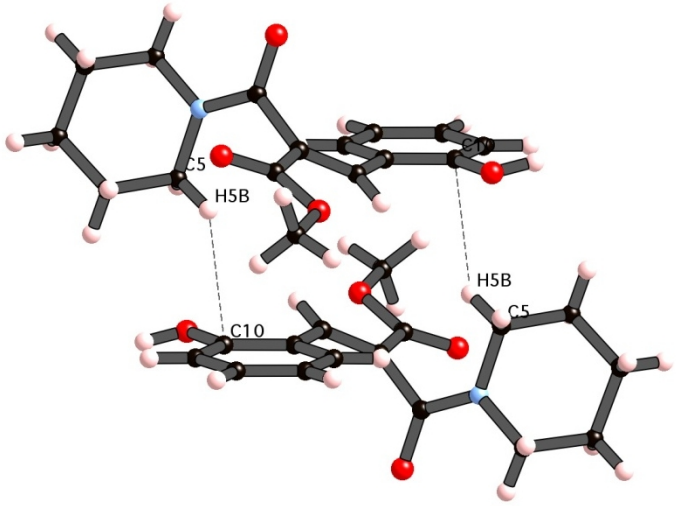


Fig. 4. C-H…π dimeric units of compound 4

The combination of the hydrogen bonding and C-H…π interactions result in the formation of columns of 4 extending down the X-axis as presented in Fig. 5.

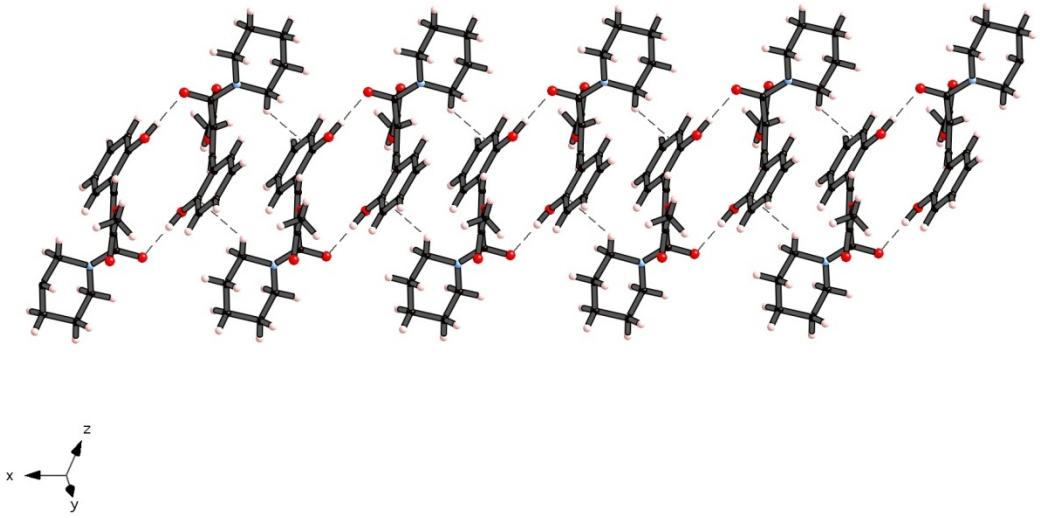


Fig. 5. Columns of compound 4, stabilized mainly by hydrogen bonding and C-H…π interactions

Adjacent columns of compound **4** are also held together by weak C-H…O interactions between the axial *α*-piperidine hydrogen H1B and the hydroxyl oxygen (O2); H1B…O2(x,y,1+z) 2.699 Å, C1-H1B…O2 137(2)° (Fig. 6).

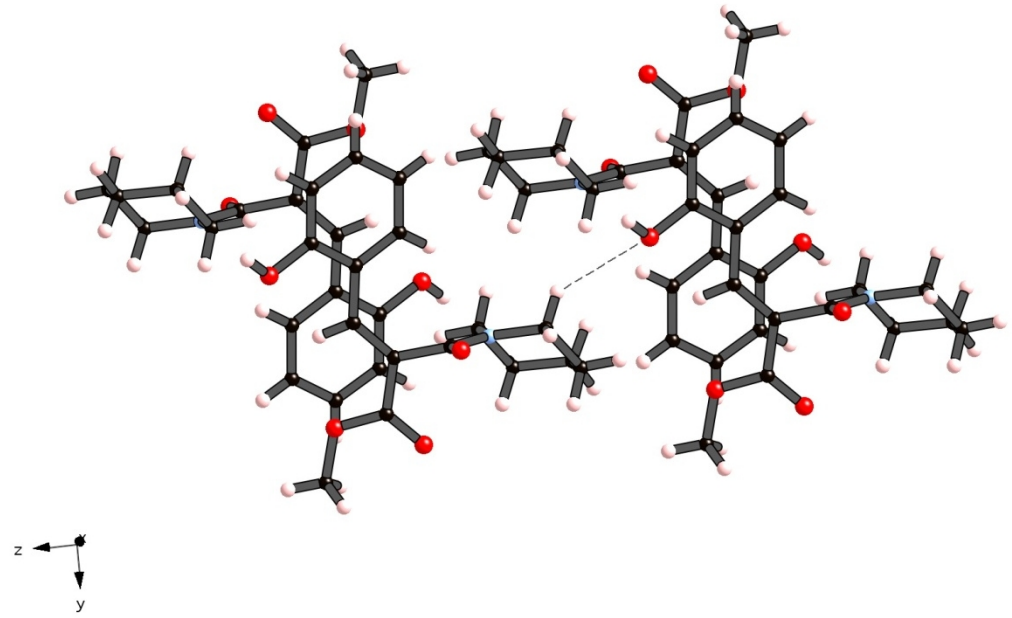


Fig. 6. C-H...O interactions between parallel columns of compound 4

4. CONCLUSION

Synthesis, spectroscopic characterization and X-ray crystal and molecular structure of (*E*)-methyl 3-(2-hydroxyphenyl)-2-(piperidine-1-carbonyl)acrylate, have been reported. The molecules of **4** are stabilized by hydrogen bonding and C-H…π interactions. The title compound may also be used as an important synthon in heterocyclic chemistry along with some industrial and biological applications.

SUPPLEMENTARY DATA

CCDC 885498 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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