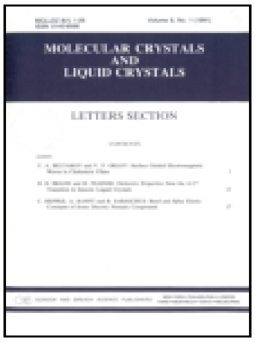

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ISSN: 1542-1406 (Print) 1563-5287 (Online) Journal homepage: http://www.tandfonline.com/loi/gmcl20

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To cite this article: Dajie Mao, Chongbo Hu, Weiwei Wang, Xiaohua Du & Zhenyuan Xu (2015) Synthesis and Crystal Structure Characterization of (E)-Methyl 2-(Methoxyimino)-2-(2-((3-(6-(Trifluoromethyl) Pyridin-3-yl) Phenoxy) Methyl) Phenyl) Acetate, Molecular Crystals and Liquid Crystals, 607:1, 264-271, DOI: 10.1080/15421406.2014.939599

To link to this article: http://dx.doi.org/10.1080/15421406.2014.939599

Mol. Cryst. Liq. Cryst., Vol. 607: pp. 264–271, 2015

ISSN: 1542-1406 print/1563-5287 online
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Synthesis and Crystal Structure Characterization of (*E*)-Methyl 2-(Methoxyimino)-2-(2-((3-(6-(Trifluoromethyl) Pyridin-3-yl) Phenoxy) Methyl) Phenyl) Acetate

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The title compound, (E)-methyl 2-(methoxyimino)-2-(2-((3-(6-(trifluoromethyl)pyridin-3-yl) phenoxy) methyl) phenyl) acetate was synthesized and characterized by ^{1}*H and* ^{13}*C NMR, IR, and MS spectroscopy. Its molecular structure was investigated by X-ray crystallography. The crystal structure analysis revealed that the two independent molecules interact via C—H···O to form a dimer, which is further connected by weak interaction with another dimer to constitute a four molecular crystal packing. At the same time, two molecules are linked by weak intermolecular C13-O3 and O3-H15 interactions to constitute a ring involving six atoms (C13/C12/C14/C15/H15/O3), which are not in the same plane. Compound (**5**) crystallizes in a monoclinic system, space group* $P_1 21/c_1$*,* $a = 7.2024(4)$ *Å,* $b = 8.4592(6)$ *Å,* $c = 35.389(2)$ *Å.*

Keywords (E)-Methyl 2-(methoxyimino)-2-(2-((3-(6-(trifluoromethyl) pyridin-3-yl) phenoxy) methyl) phenyl) acetate; single crystal; synthesis; X-ray diffraction

Introduction

Suitably substituted methoxyacrylates, such as azoxystrobin, kresoxim-methyl, and picoxystrobin derived from natural strobilurin A [1], are employed as broad-spectrum agricultural fungicides with a unique mode of action [2–4]. Subsequently, a series of highly active fungicidal compounds such as pyraoxystrobin (SYP-3343) and pyrametostrobin (SYP-4155) were discovered through variation of substituents around the methoxyacrylate moiety [5–9]. In this paper, we wish to report a new designed compound (*E*)-methyl

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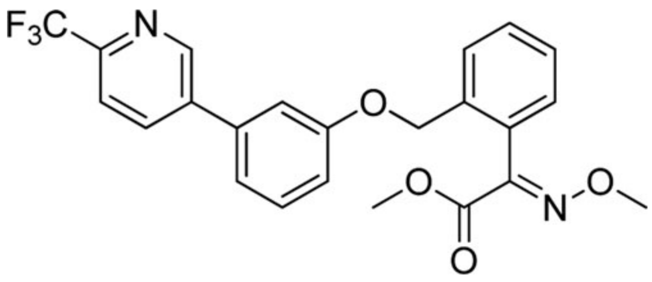

Figure 1. Structure of title compound.

2-(methoxyimino)-2-(2-((3-(6-(trifluoromethyl) pyridin-3-yl) phenoxy) methyl) phenyl) acetate (**3**). Fungicidal activities test showed that compounds (**5**) (Fig. 1) have significant inhibitory rate against *Pseudoperonospora cubensis*, *Rhizoctonia solani*, and *Botrytis cinerea*, they are 97.7%, 65.0%, and 64.3% under the concentration of 50 mg/l, respectively. The title compound can be obtained via suzuki cross-coupling reaction and nucleophilic substitution (Fig. 2). It was synthesized and characterized by ^1H and ^{13}C NMR, infrared spectroscopy (IR), and electrospray ionization (ESI) mass spectroscopy. Its crystal structure was investigated by single-crystal X-ray diffraction (XRD) analysis.

Experimental

The melting point was determined on a BÜCHI B-545 melting point apparatus and was uncorrected. The infrared (IR) spectra was recorded using a Bruker EQUINOX 55 series instrument. ^1H and ^{13}C NMR were recorded in $CDCl_3$ on Bruker AVANCE III (500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR). Proton chemical shifts (δ) are relative to tetramethylsilane (TMS, $\delta = 0.0$) as internal standard and expressed in parts per million. Spin multiplicities are given as s (singlet), d (doublet), t (triplet), and q (quartet) as well as b (broad). Coupling constants (J) are given in hertz. Infrared spectra were measured with KBr disks using a Bruker Equinox 55 instrument. ESI mass spectra were recorded using Thermo LCQ fleet mass spectrometer.

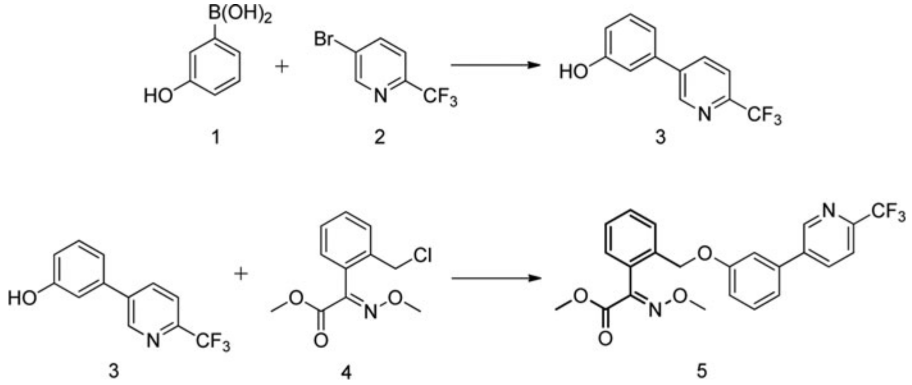

Figure 2. Synthetic route of title compound.

Synthesis of Methyl 3-(6-(Trifluoromethyl)Pyridin-3-yl)Phenol (3)

A mixture of 5-bromo-2-(trifluoromethyl)pyridine **(2)** (1.92 g, 10 mmol), (3-hydroxyphenyl) boronic acid **(1)** (1.66 g, 12 mmol), K_3PO_4 (4.25 g, 20 mmol), and 50% isopropanol (50 ml) was stirred at 85°C for 6 hr. The mixture was added to brine (40 ml) and extracted four times with ethyl acetate (40 × 3 ml). The solvent was concentrated in vacuo and the product **(3)** was obtained by recrystallizing with ethanol.

Synthesis of Title Compound (5)

3-(6-(Trifluoromethyl)pyridin-3-yl)phenol (478 mg, 2 mmol) was dissolved in 10 ml of dimethylformamide (DMF), 60% sodium hydride (120 mg, 3 mmol) and 18-crown ether-6

Table 1. Crystal data and structure refinement parameters of compound (**5**)

Parameter	Value
CCDC deposition number	CCDC 989103
Empirical formula	$C_{23}H_{19}F_3N_2O_4$
Formula weight	444.40
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P_121/c_1
Cell dimensions	$a = 7.2024(4)$ Å $b = 8.4592(6)$ Å $c = 35.389(2)$ Å $\alpha = 90.00$ $\beta = 93.192(1)^\circ$ $\gamma = 90.00$
Volume	2152.8(2) $Å^3$
Z	4
Density (calculated)	1.371 Mg/m^3
Absorption coefficient	0.111 mm^{-1}
F_{000}	920.0
Crystal size	0.40 × 0.36 × 0.17 mm
Theta range for data collection	3.00° to 26.00°
Index ranges	$-7 \leq h \leq 8$ $-10 \leq k \leq 10$ $-43 \leq l \leq 43$
Reflections collected	18181
Independent reflections	4225 [$R_{int} = 0.0598$]
Absorption correction	$T_{min} = 0.8725$, $T_{max} = 0.8842$
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4225/0/291
Goodness of fit on F^2	1.004
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0529$, $\omega R_2 = 0.1115$
R indices (all data)	$R_1 = 0.1147$, $\omega R_2 = 0.1490$
Extinction correction	None
Largest diff. peak and hole	0.284 and −0.194 e.$Å^{-3}$

Table 2. Atomic coordinates and equivalent thermal parameters of the nonhydrogen atoms (Å^2). $U_{\mathrm{eq}} = (1/3) \sum i \sum j\ Uij \mathrm{a}_i{}^* \mathrm{a}_j{}^* (\mathrm{a}_i . \mathrm{a}_j)$

Atom	*x*	*y*	*z*	U_{eq}
C13	0.2727(4)	0.3873(3)	0.1106(7)	0.0527(7)
C19	0.8197(3)	0.6616(3)	0.16907(7)	0.0461(6)
C6	0.4986(3)	0.7624(3)	0.18081(7)	0.0504(7)
C7	0.4112(4)	0.6502(3)	0.15252(8)	0.0597(8)
C8	0.4245(4)	0.3762(3)	0.13597(8)	0.0533(7)
C1	0.6918(3)	0.7704(3)	0.18772(7)	0.0485(6)
C20	0.8980(3)	0.5252(4)	0.19132(7)	0.0525(7)
C12	0.2203(4)	0.2580(3)	0.08771(7)	0.0533(7)
C14	0.0510(4)	0.2661(3)	0.06162(7)	0.0531(7)
C15	−0.1083(4)	0.3405(4)	0.07197(8)	0.0608(8)
C9	0.5232(4)	0.2371(4)	0.13943(9)	0.0685(8)
C5	0.3886(4)	0.8662(4)	0.20026(9)	0.0681(9)
C17	−0.2538(4)	0.2689(4)	0.01303(7)	0.0574(7)
C16	−0.2646(4)	0.3419(4)	0.04734(7)	0.0625(8)
C18	0.0442(4)	0.1939(4)	0.02645(8)	0.0651(8)
C2	0.7657(4)	0.8798(4)	0.21343(8)	0.0634(8)
C3	0.6535(5)	0.9828(4)	0.23175(8)	0.0754(9)
C21	1.0377(5)	0.2727(4)	0.18958(9)	0.0814(10)
C11	0.3228(4)	0.1190(4)	0.09119(9)	0.0688(8)
C22	0.8855(5)	0.8234(5)	0.08129(8)	0.0863(11)
C23	−0.4138(5)	0.2674(4)	−0.01570(9)	0.0739(9)
C10	0.4747(4)	0.1093(4)	0.11709(10)	0.0753(9)
C4	0.4639(5)	0.9755(4)	0.22538(9)	0.0767(10)
F1	−0.5670(3)	0.3321(3)	−0.00340(5)	0.0922(6)
F2	−0.4649(3)	0.1226(3)	−0.02594(7)	0.1295(10)
F3	−0.3794(3)	0.3430(4)	−0.04675(6)	0.1347(10)
N1	−0.1032(4)	0.1940(3)	0.00212(6)	0.0668(7)
N2	0.8811(3)	0.6768(3)	0.13589(6)	0.0511(6)
O1	0.4808(3)	0.4953(2)	0.16018(5)	0.0634(5)
O2	0.9089(3)	0.5247(3)	0.22521(5)	0.0834(7)
O3	0.9564(3)	0.4086(2)	0.17005(5)	0.0653(6)
O4	0.8062(3)	0.8095(3)	0.11760(5)	0.0687(6)

(53 mg, 0.2 mmol) were then added to the solution. The solution was stirred at room temperature for 0.5 hr, and (*E*)-methyl 2-(2-(chloromethyl)phenyl)-2-(methoxyimino)acetate (**4**) (580 mg, 2.4 mmol) was then added. The reaction mixture was stirred at 64°C and monitored by thin-layer chromatography (TLC). After completion of the reaction (3 hr), the mixture was added to 30 ml of water and extracted with ethyl acetate (30 × 3 ml). The combined extracts were washed with brine, dried (anhydrous magnesium sulfate), and filtered. The filtrate was evaporated, and the crude product was purified via silica gel column chromatography using a 1:12 (v/v) mixture of acetone and cyclohexane as the eluting solution to obtain compound (**5**) as a white solid: 0.58 g (yield of 64.5%), m.p. 134.1°C–134.6°C.

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.91 (s, 1H, Py-2-H), 8.01 (d, $J = 8.0$ Hz, 1H, Py-4-H), 7.76 (d, $J = 8.1$ Hz, 1H, Py-5-H), 7.57 (d, $J = 7.4$ Hz, 1H, Ph-H), 7.47 (td, $J = 7.5$, 1.4 Hz, 1H, Ph-H), 7.39–7.44 (m, 2H, Ph-H), 7.24 (dd, $J = 7.5$, 1.3 Hz, 1H, Ph-H), 7.19 (d, $J = 7.6$ Hz, 1H, Ph-H), 7.11 (s, 1H, Ph-H), 7.00 (dd, $J = 8.3$, 2.1 Hz, 1H, Ph-H), 5.05 (s, 2H, PhCH$_2$), 4.03 (s, 3H, CNOCH$_3$), 3.84 (s, 3H, COOCH$_3$); ^{13}C NMR (CDCl$_3$, 125 MHz): δ 163.35, 159.16, 149.48, 148.51, 139.33, 137.81, 135.67, 134.95, 130.50, 129.73, 129.49, 128.76, 128.04, 127.82, 122.81, 120.63, 120.51, 120.18, 115.24, 114.12, 68.63, 63.92, 53.06; IR (KBr, cm^{-1}): ν 2922, 2377, 1719, 1652, 1562, 1460, 1371, 1336, 1134, 1064, 1015, 788 cm^{-1}; MS (ESI) *m/z* (%): 445.38 $[M + 1]^+$.

Crystal Structure Analysis

The crystal structure of the title compound was solved by direct methods and was refined by a full matrix least-square method on F^2. A summary of the salient crystallographic data is given in Table 1.

A single crystal suitable for XRD obtained by recrystallizing from ethanol was colorless and block. The single crystal XRD of the crystal was collected on a PROCESS-AUTO [10] diffractometer at 296(2) K using graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The cell was refined on a PROCESS-AUTO [10] and the data were reducted on a crystal structure [11] and corrected for absorption using multi-scan [12]. The structure was solved by direct methods using SHELXS-97 and refined by a full-matrix least-square procedure using the program SHELXL-97 [13]. Subsequent refinements were carried out with anisotropic thermal parameters for nonhydrogen atoms. H atoms were placed in calculated positions with C—H = 0.96 Å (sp^3), C—H = 0.93 Å (aromatic). All H atoms included in the final cycles of refinement using a riding model, with $U_{\mathrm{iso}}(\mathrm{H}) = 1.5\ U_{\mathrm{eq}}(sp^3)$

Table 3. Bond lengths (Å)

Atoms	Length	Atoms	Length
C13-C8	1.389(4)	C13-C12	1.392(4)
C5-C4	1.373(4)	C19-N2	1.284(3)
C19-C1	1.483(3)	C19-C20	1.490(4)
C6-C5	1.390(4)	C6-C1	1.401(3)
C6-C7	1.493(4)	C7-O1	1.423(3)
C8-O1	1.370(3)	C8-C9	1.377(4)
C1-C2	1.384(4)	C20-O2	1.198(3)
C20-O3	1.324(3)	C12-C11	1.390(4)
C12-14	1.489(4)	C14-C15	1.376(4)
C14-C18	1.385(4)	C15-C16	1.384(4)
C17-N1	1.332(4)	C17-C16	1.368(4)
C17-C23	1.493(4)	C18-N1	1.329(4)
C2-C3	1.375(4)	C3-C4	1.373(4)
C21-O3	1.448(3)	C11-C10	1.390(4)
C22-O4	1.440(3)	C23-F3	1.307(4)
C23-F1	1.326(4)	C23-F2	1.324(4)
N2-O4	1.390(3)		

Table 4. Bond angles (°)

Atoms	Angle	Atoms	Angle
C8-C13-C12	120.1(3)	C8-C13-H13	120.0
C12-C13-H13	120.0(9)	N2-C19-C1	126.8(2)
N2-C19-C20	115.0(0)	C1-C19-C20	118.1(2)
C5-C6-C1	118.1(2)	C5-C6-C7	120.2(2)
C1-C6-C7	121.7(2)	O1-C7-C6	109.0(2)
O1-C7-H7A	109.9	C6-C7-H7A	109.9
O1-C7-H7B	109.9	C6-C7-H7B	109.9
H7A-C7-H7B	108.3	O1-C8-C9	116.1
O1-C8-C13	123.8(2)	C9-C8-C13	120.0(3)
C2-C1-C6	119.3(2)	C2-C1-C19	118.8(2)
C6-C1-C19	121.9(2)	O2-C20-O3	124.2(3)
O2-C20-C19	122.3(3)	O3-C20-C19	113.6(2)
C11-C12-C13	119.2(3)	C11-C12-C14	120.4(3)
C13-C12-C14	120.3(2)	C15-C14-C18	116.9(3)
C15-C14-C12	121.5(2)	C18-C14-C12	121.6(2)
C14-C15-C16	119.8(2)	C14-C15-H15	120.1
C16-C15-H15	120.1	C10-C9-C8	120.5(3)
C10-C9-H9	119.7	C8-C9-H9	119.7
C4-C5-C6	122.0(3)	C4-C5-H5	119.0
C6-C5-H5	119.0	N1-C17-C16	124.0(3)
N1-C17-C23	114.1(3)	C16-C17-C23	121.9(3)
C17-C16-C15	118.1(3)	C17-C16-H16	121.0
C15-C16-H16	121.0	N1-C18-C14	124.7(3)
N1-C18-H18	117.7	C14-C18-H18	117.7
C3-C2-C1	121.3(3)	C3-C2-H2	119.4
C1-C2-H2	119.4	C4-C3-C2	119.9(3)
C4-C3-H3	120.0	C2-C3-H3	120.0
O3-C21-H21A	109.5	O3-C21-H21B	109.5
H21A-C21-H21B	109.5	O3-C21-H21C	109.5
H21A-C21-H21C	109.5	H21B-C21-H21C	109.5
C10-C11-C12	120.2(3)	C10-C11-H11	119.9
C12-C11-H11	119.9	O4-C22-H22A	109.5
O4-C22-H22B	109.5	H22A-C22-H22B	109.5
O4-C22-H22C	109.5	H22A-C22-H22C	109.5
H22B-C22-H22C	109.5	F3-C23-F1	105.9(3)
F3-C23-F2	106.6(3)	F1-C23-F2	104.3(3)
F3-C23-C17	113.2(3)	F1-C23-C17	113.4(3)
F2-C23-C17	112.7(3)	C9-C10-C11	119.9(3)
C9-C10-H10	120.0	C11-C10-H10	120.0
C5-C4-C3	119.3(3)	C5-C4-H4	120.3
C3-C4-H4	120.3	C18-N1-C17	116.5(2)
C19-N2-O4	111.3(2)	C8-O1-C7	118.0(2)
C20-O3-C21	117.0(2)	N2-O4-C22	108.6(2)

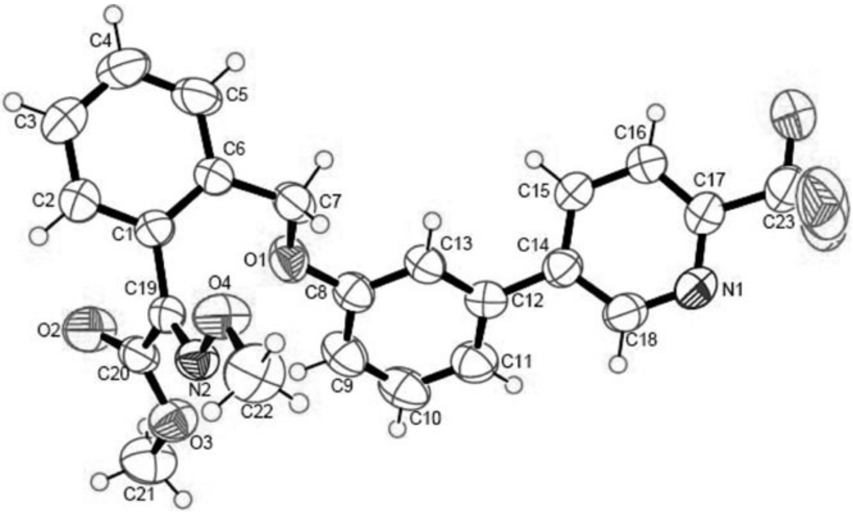

Figure 3. ORTEP of the molecule (**5**) with thermal ellipsoids drawn at 50% probability.

or 1.2 U_{eq} of the carrier atoms. A molecular plot was prepared with ORTEP-3 for Windows [14]. The software used to prepare material for publication was WINGX [15]. Table 2 gives the atomic coordinates and equivalent thermal parameters of the nonhydrogen atoms. Tables 3 and 4 give the list of bond lengths and bond angles, respectively.

The ORTEP of the molecule with thermal ellipsoids drawn at 50% probability is shown in Fig. 2. The crystal structure analysis reveals that two molecules are linked by weak intermolecular C13-O3 and O3-H15 interactions to constitute a ring involving six atoms (C13/C12/C14/C15/H15/O3), which are not in the same plane. All atoms on oximinoacetate group are on the same side of the mean plane of the benzene ring (C8···C13) and the distance of N2 and O3 atoms to the mean plane of the benzene ring (C8···C13) are 2.922 Å and 1.659 Å, respectively. The C19–N2 and C20–O2 bonds are double bonds with bond lengths of 1.284 Å and 1.198 Å, respectively. In addition, the bond angles of C7-O1-C8 and C19-N2-O4 are 117.99° and 111.26°, respectively. The conformation of the attachment of oxime ether group and the ester group to the benzene ring is well described by the torsion angle

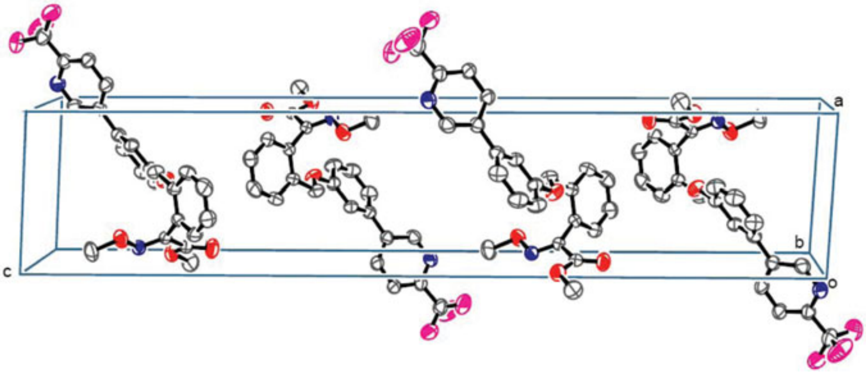

Figure 4. The crystal packing of the title compound (**5**).

values of −2.35° and −177.96° for C1-C19-N2-O4 and C20-C19-N2-O4, respectively. The benzene ring(C8···C13) makes an angle of 20.26° and 7° with the mean plane of pyridine ring(C14···C17/N1/C18) and another benzene ring(C1···C6), respectively. The crystal structure analysis shows that four molecules form a close packed structure. The two independent molecules interact via C—H···O to form a dimer, which was further connected by weak interaction with another dimer.

Conclusion

The title compound *(E)-methyl 2-(methoxyimino)-2-(2-((3-(6-(trifluoromethyl) pyridin-3-yl) phenoxy) methyl) phenyl) acetate* (**5**), was synthesized and characterized by ^{1}H NMR, ^{13}C NMR, ESI mass spectroscopy, and infrared spectroscopy. We summarize the results from XRD measurements for compound (**5**) single crystal (Fig. 3). X-ray analysis revealed that the two independent molecules interact via C—H···O to form a dimer, which is further connected by weak interaction with another dimer to constitute a four molecular crystal packing (Fig. 4). At the same time, two molecules are linked by weak intermolecular C13-O3 and O3-H15 interactions to constitute a ring involving six atoms (C13/C12/C14/C15/H15/O3), which are not in the same plane.

Acknowledgment

Authors thank Prof. Jian-Ming Gu of Zhejiang University for the help.

Supplementary Information

CCDC 989103 contains the supplementary crystallographic data for this article. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html, or from The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44(0)1223-336033. E-mail: deposit@ccdc.cam.ac.uk.

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