European Journal of Chemistry

View Journal Online
View Article Online

Synthesis, structural elucidation and X-ray crystallographic studies of 1-(3,5-*bis*(trifluoromethyl)phenyl)-3-(dimethylamino)prop-2-en-1-one

Stability Nongrum, Susma Das, Shikpika Khanikar and Jai Narain Vishwakarma *

Organic Research Laboratory, Department of Chemical Science, Assam Don Bosco University, Tapesia Gardens, Kamarkuchi, Sonapur, 782 402 Assam, India
stabilitynongrum@gmail.com (S.N.), susmadas91@gmail.com (S.D.), shilpikakhanikar11@gmail.com (S.K.), jnvishwakarma@rediffmail.com (J.N.V.)

* *Corresponding author at: Organic Research Laboratory, Department of Chemical Science, Assam Don Bosco University, Tapesia Gardens, Kamarkuchi, Sonapur, 782 402 Assam, India.*
Tel: +91.91270.51222 Fax: +91.91270.51222 e-mail: jnvishwakarma@rediffmail.com (J.N. Vishwakarma).

RESEARCH ARTICLE

10.5155/eurjchem.10.4.381-385.1922

Received: 03 September 2019
Received in revised form: 24 September 2019
Accepted: 06 October 2019
Published online: 31 December 2019
Printed: 31 December 2019

KEYWORDS

Enaminones
Acetophenone
Trifluoromethyl
X-ray crystallography
Geometric parameters
N,*N*-Dimethylformamide dimethyl acetal

ABSTRACT

A new enaminone was synthesized by reacting 3,5-*bis*-(trifluoromethyl)acetophenones and *N*,*N*-dimethylformamide dimethyl acetal and its detailed structural and crystalline properties were studied. The crystal data were found to be as $C_{13}H_{11}F_6NO$, monoclinic, space group $P2_1/c$ (no. 14), a = 8.1556(8) Å, b = 24.877(3) Å, c = 7.6067(7) Å, β = 116.745(6)°, V = 1378.2(3) Å^3, Z = 4, T = 293(2) K, μ(MoKα) = 0.150 mm^{-1}, *Dcalc* = 1.500 g/cm^3, 40777 reflections measured (5.594° ≤ 2Θ ≤ 56.786°), 3413 unique (R_{int} = 0.1040, R_{sigma} = 0.0584) which were used in all calculations. The final R_1 was 0.0771 (I > 2σ(I)) and wR_2 was 0.2541 (all data).

Cite this: *Eur. J. Chem.* **2019**, *10(4)*, 381-385 **Journal website**: www.eurjchem.com

1. Introduction

Fluorine containing naturally occurring compounds are very few to be found [1], however, about 25% of the marketed drug molecules are embedded with fluorine atoms [2]. Fluorine, the most electronegative element in periodic table and also capable of forming hydrogen-bond, can induce a strong plorization on its neighbouring elements [1]. Hence, the presence of fluorinated groups in biologically active molecular architectures should influence the electronic and binding properties, metabolic stability and lipophilicity enhancing the drug optimization capablities of a lead molecule. Trifluoromethylated alkenes are considered very important pharmacophores and have been gaining propularity in pharmaceuticals and agro-sciences [3]. A number of fluorine substituted drugs are available in the market, which are prescribed to cure a wide range of diseases [4]. Encouraged by these advantages, a good degree of attention has been invested towards the development of newer synthetic strategies for mono-, di- and tri-fluorinated molecular entities [5,6].

Literature reveals that enaminones are very versatile predecessors for synthesizing novel heterocyclic systems as they can react with both electrophiles and nucleophiles [7,8]. They also process many biological properties like antitumor, antimicrobial, anti-inflammatory, analgesic, ulcerogenic agents [7].

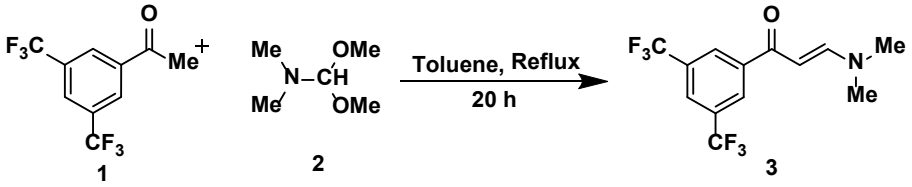
Promoted by these observations and in continuation with our earlier studies on enaminones [9,10], we decided to synthesise the title compound, the results of which are presented herein (Scheme 1).

2. Experimental

2.1. Instrumentation

^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded on Bruker AV II 300 MHz. The chemical shift (δ ppm) and the coupling constants (Hz) are reported in the standard fashion with reference to TMS as standard in $CDCl_3$. The FT-IR spectra were recorded on Perkin Elmer Spectrum II spectrophotometer. The melting point was recorded using open capillary method and is uncorrected. X-ray diffraction data of the crystal were recorded using a Bruker APEX-II CCD diffractometer [11]. The electro spray mass spectra were recorded on a THERMO Finnigan LCQ Advantage max ion trap mass spectrometer.

ISSN 2153-2249 (Print) / ISSN 2153-2257 (Online)
http://dx.doi.org/10.5155/eurjchem.10.4.381-385.1922



Scheme 1

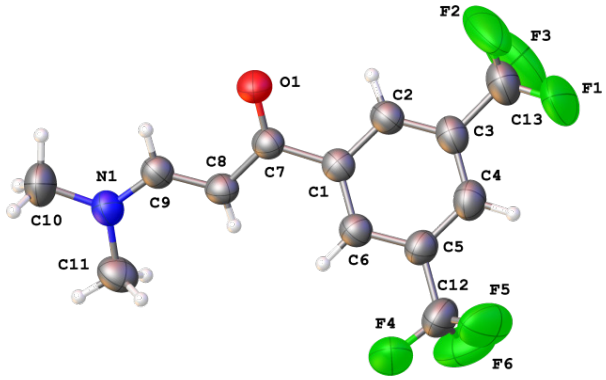


Figure 1. Molecular structure of the title compound.

2.2. Synthesis

A mixture of 3,5-*bis*-(trifluoromethyl)acetophenone (**1**) (1 mmol) and *N*,*N*-dimethylformamide dimethyl acetal (**2**) (2 mmol) in 3 mL toluene was refluxed for 20 hours. Completion of the reaction was monitored by TLC. At the end of the reaction, solvent was removed under reduced pressure to give a viscous mass which on trituration with hexane gave a practically pure yellow solid in 87% yield. Further purification was achieved by column chromatography on Silica Gel (60-120 mesh) using ethylacetate-hexane (20%) mixture as mobile phase.

1-(3, 5-Bis(trifluoromethyl)phenyl)-3-(dimethylamino)prop-2-en-1-one (**3**): Colour: Yellow. Yield: 87%. M.p.: 95-96 °C. FT-IR (KBr, ν, cm^{-1}): 1676 (C=O) (ketone), 1558 (C=C) (aromatic), 1348 (C-N) (amine), 1295 (C-F), 910 (C-H) (aromatic), 662 (C-H) (aromatic). ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 2.99 (s, 3H, CH_3), 3.22 (s, 3H, CH_3), 5.67 (d, 1H, *J* = 12 Hz, C_2H), 7.91 (d, 1H, *J* = 12 Hz, C_3H), 7.94 (s, 1H, Ar-H), 8.32 (s, 2H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 37.7 (1C, CH_3), 45.5 (1C, CH_3), 91.1 (1C, C_2), 123.5 (2C, CF_3), 124.3 (1C, C_4', Aromatic), 127.7 (2C, C_2', C_6', Aromatic), 131.7 (2C, C_3', C_5', Aromatic), 142.5 (1C, C_1', Aromatic), 155.7 (1C, C_3), 184.7 (1C, C_1). MS (ESI, *m/z* (%)): 312 ([MH]$^+$, 100%), 313, 314, 334, 335.

2.3. Crystallographic details

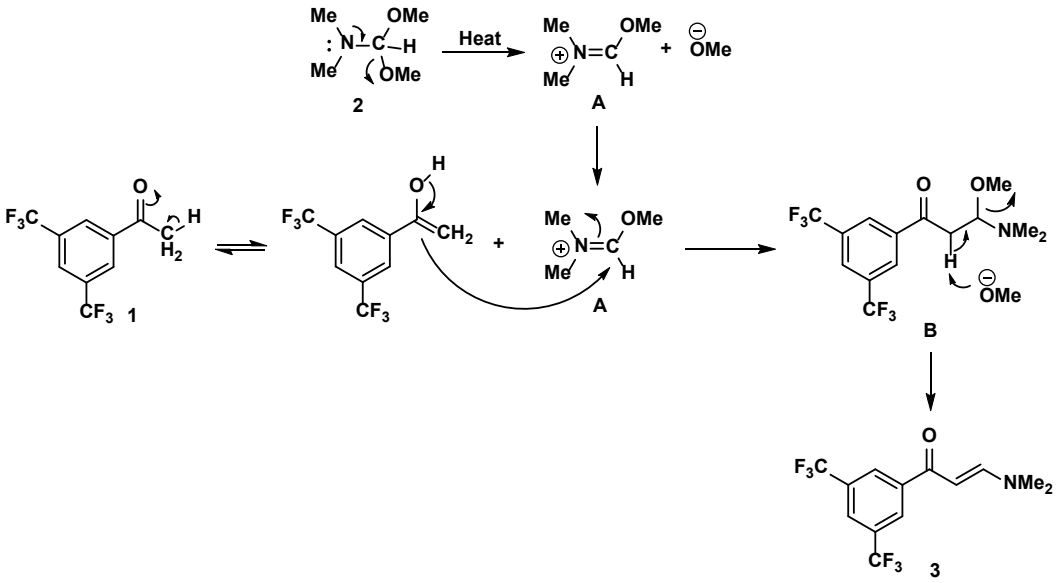
Block, colorless crystals of the compound were obtained by dissolving the compound in ethanol and then allowing it to recrystallize slowly. The structure was solved by direct methods (SHELXS97) [12] and refined by full-matrix least-squares based on F^2. All calculations were carried out using the WinGX [13] system version 1.80.05. All the non-H-atoms were refined in the anisotropic approximation. The threshold expression of F^2>2sigma(F^2) is used only for calculating R-factors (gt) etc. H-atoms were located at calculated positions. Figure 2 shows the packing pattern of the crystal, of its components in three dimensional lattice.

3. Results and discussion

3.1. Spectral analysis

The FT-IR spectra showed a bands at 1676 cm^{-1} for C=O, 1558 cm^{-1} for C=C, 1348 cm^{-1} for C-N, 1295 cm^{-1} for C-F and 910 cm^{-1} and 662 cm^{-1} for aromatic C-H bonds. The ^{1}H NMR spectra of compound **3** exhibited two distinct singlets at δ 2.99 and 3.22 ppm for the two methyl protons of NMe_2 group indicating that the two methyl groups are in different environments due the double bond character of the C-N bond. The vinylic protons resonated as doublets at δ 5.67 and 7.91 ppm with coupling constant of 12.0 Hz, thus supporting trans geometry. The aromatic protons appeared as singlets at δ 7.94 ppm for one proton and at δ 8.32 ppm for two protons. In the ^{13}C NMR spectra of compound **3**, the two methyl group carbon atoms showed signals at δ 37.7 and 45.5 ppm. The vinylic carbon atoms C_3 and C_2 resonated at δ 91.1 and 155.7 ppm, respectively. The carbonyl carbon signal was found at δ 184.7 ppm as expected. The ^{13}C NMR spectra of the aromatic ring was very interesting due to coupling pattern with fluorine atoms. Thus, the carbon atoms of the CF_3 groups gave quartet at δ 123.5 ppm with coupling constant of 270 Hz and the aromatic carbon atoms C_3' and C_5' appeared as quartet at δ 131.7 ppm with a coupling constant of 132 Hz. The C_4' of the aromatic ring resonated at δ 124.3 ppm as a septet with a coupling constant 3.75 Hz and C_2' and C_6' appeared as a doublet at δ 127.7 ppm with *J* = 3 Hz. The C_1' carbon was located at δ 142.5 ppm. The mass spectra of compound **3** showed a base peak for MH$^+$ at 312 and other peaks at 313, 314, 334 and 335 *m/z*.

Dimethylformamide-dimethylacetal undergoes cleavage under thermal conditions to give the oxo-stabilized carbenium ion **A**, which acting as an electrophile reacts with enolized acetophenone **1** to give an intermediate **B**. Assisted by the methoxide ion **B** is finally converted into the desired formaylated acetophenone **3** as shown in Scheme 2.



Scheme 2

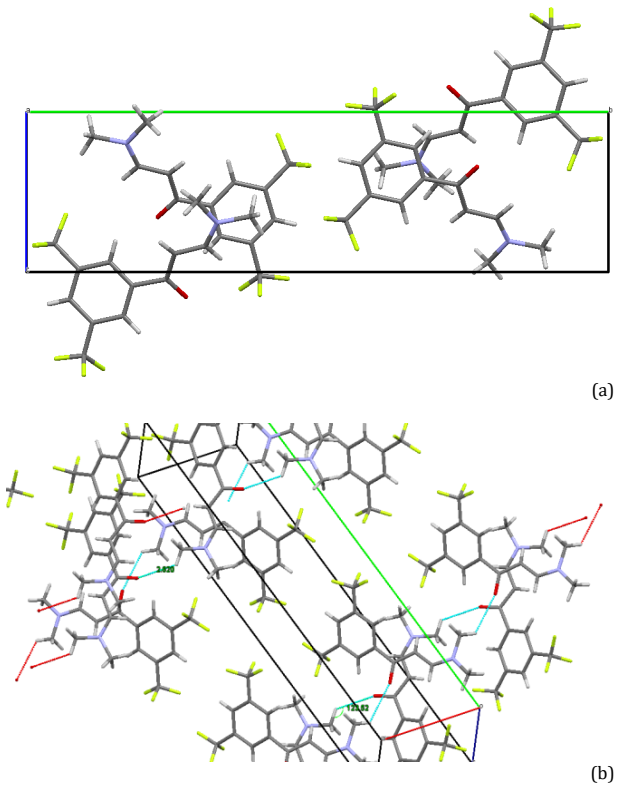
3.2. Crystal structure

The compound 1-(3,5-*bis*(trifluoromethyl)phenyl)-3-(dimethylamino)prop-2-en-1-one ($C_{13}H_{11}F_6NO$) crystallized in a monoclinic cell (space group P2(1)/*c*) obtained by phi and ω scans, refinement on F^2, $R[F^2>2\sigma(F^2)]$ = 0.0771, $wR(F^2)$ = 0.2541, 234 parameters and radiation source is from fine-focus sealed tube.

All the conditions used for the measurement of the crystal structure is shown in Table 1 and 2 along with their atomic coordinates and displacement parameters. The structural parameters including bond distances and bond angles for compound **3** are listed in Table 3. In the crystal packing structure, no significant hydrogen bond was found. However, a short intermolecular contact is observed between O1 and H6 atoms.

Table 1. Crystal data and structure refinement for the title compound.

Parameters	**Obtained specification**
CCDC No	194391
Empirical formula	$C_{13}H_{11}F_6NO$
Formula weight	311.23
Temperature (K)	293(2)
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	8.1556(8)
b (Å)	24.877(3)
c (Å)	7.6067(7)
α (°)	90
β (°)	116.745(6)
γ (°)	90
Volume (Å^3)	1378.2(3)
Z	4
ρ_{calc} (g/cm^3)	1.500
μ (mm^{-1})	0.150
F(000)	632.0
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection (°)	5.594 to 56.786
Index ranges	$-10 \le h \le 10$ $-33 \le k \le 32$ $-10 \le l \le 10$
Reflections collected	40777
Independent reflections	3413 [R_{int} = 0.1040, R_{sigma} = 0.0584]
Data/restraints/parameters	3413/0/234
Goodness-of-fit on F^2	1.051
Final R indexes [I≥2σ (I)]	R_1 = 0.0771, wR_2 = 0.2062
Final R indexes [all data]	R_1 = 0.1600, wR_2 = 0.2541
Largest diff. peak/hole (e.Å^{-3})	0.40/-0.37



(a)

(b)

Figure 2. (a) Packing of the crystal in three-dimensional lattice, (b) Short contact formed between oxygen and hydrogen.

4. Conclusion

In this article, we report the successful synthesis of a new enaminone, which may act as a building block for numerous hitherto unreported novel molecules. Its spectral characterization has been studied. Its crystalline characterization shows that it adopts trans-configuration. The bond angles of C1-C7-C8, C7-C8-C9 and C8-C9-N1 are found to be 118.4(3)°, 119.8(3)°, and 128.2(3)°, respectively. These obtained values suggested that a planer structure in the molecule.

Table 2. Fractional atomic coordinates (×10⁴) and equivalent isotropic displacement parameters (Å²×10³) for compound **3**. U_{eq} is defined as 1/3 of of the trace of the orthogonalized U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	3230(3)	2259.4(9)	6561(3)	64.4(7)
N1	-1553(4)	1721.1(11)	1929(4)	77.4(12)
F1	6340(6)	4483.3(14)	10432(5)	171.6(18)
F2	6980(5)	3681.5(16)	11068(5)	161.4(17)
F3	4873(6)	4012(2)	11429(5)	170.5(18)
F4	1000(5)	4321.5(11)	1441(4)	125.2(12)
F5	3012(5)	4859.9(12)	3341(5)	136.5(14)
F6	435(5)	4813.5(13)	3323(5)	138.7(13)
C1	2592(4)	3177.6(12)	5857(5)	47.5(8)
C2	3802(5)	3330.8(15)	7763(5)	53.2(8)
C3	4321(5)	3861.5(14)	8190(5)	57.9(9)
C4	3650(5)	4251.5(16)	6724(6)	63.3(10)
C5	2465(5)	4099.9(13)	4826(5)	56.3(9)
C6	1920(5)	3566.5(13)	4392(5)	50.8(8)
C7	2107(4)	2591.0(12)	5458(4)	46.9(8)
C8	385(4)	2451.2(14)	3854(5)	48.9(8)
C9	-43(5)	1925.1(14)	3381(5)	48.8(8)
C10	-1716(8)	1146.7(18)	1520(8)	80.9(13)
C11	-3019(6)	2067(2)	602(7)	67.4(11)
C12	1754(6)	4517.1(16)	3240(7)	56.8(8)
C13	5627(7)	4013.7(19)	10238(7)	82.7(13)

Table 3. Bond lengths and angles for compound **3**.

Atom-Atom	Bond length (Å)	Atom-Atom	Bond length (Å)
O1-C7	1.238(3)	C3-C4	1.391(5)
C8-C9	1.360(5)	C3-C13	1.487(6)
C8-C7	1.428(4)	C5-C4	1.380(5)
C2-C1	1.390(5)	C5-C12	1.496(5)
C2-C3	1.380(5)	F4-C12	1.315(5)
C9-N1	1.330(4)	F5-C12	1.310(5)
C7-C1	1.507(4)	C12-F6	1.329(5)
C1-C6	1.389(4)	C13-F1	1.283(5)
C6-C5	1.391(4)	C13-F2	1.293(5)
N1-C11	1.450(5)	C13-F3	1.304(6)
N1-C10	1.456(5)		
Atom-Atom-Atom	**Bond angles (°)**	**Atom-Atom-Atom**	**Bond angles (°)**
C9-C8-C7	119.8(3)	C6-C5-C12	120.2(3)
C3-C2-C1	120.4(3)	C4-C5-C6	120.5(3)
N1-C9-C8	128.2(3)	C4-C5-C12	119.3(3)
O1-C7-C8	124.1(3)	C5-C4-C3	119.0(3)
O1-C7-C1	117.5(3)	F4-C12-C5	114.3(3)
C8-C7-C1	118.4(3)	F4-C12-F6	104.2(4)
C2-C1-C7	118.3(3)	F5-C12-C5	113.3(4)
C6-C1-C2	119.0(3)	F5-C12-F4	106.8(4)
C6-C1-C7	122.7(3)	F5-C12-F6	105.4(4)
C1-C6-C5	120.3(3)	F6-C12-C5	112.0(4)
C9-N1-C11	121.2(3)	F1-C13-C3	115.2(4)
C9-N1-C10	120.9(3)	F1-C13-F2	106.4(4)
C11-N1-C10	117.8(4)	F1-C13-F3	104.7(4)
C2-C3-C4	120.7(3)	F2-C13-C3	113.6(4)
C2-C3-C13	119.3(4)	F2-C13-F3	102.9(5)
C4-C3-C13	120.0(3)	F3-C13-C3	112.8(4)

Acknowledgements

The authors would like to thank Rev. Fr. Dr. Stephen Mavely, Vice Chancellor, Assam Don Bosco University for providing infrastructure for the execution of this work. The authors also express their heart-full gratitude to Mr. Tridib Ranjan Nath and Mr. Biraj Jyoti Borah, SAIC, Tezpur University, Napaam for recording the XRD spectra. The authors are very much grateful to Mr. Farlando Diengdoh, Department of Chemistry, St. Anthony's College, Shillong for his generous help extended for solving the XRD spectra.

Supporting information

CCDC-194391 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/, or by e-mailing data request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033.

Disclosure statement

Conflict of interests: The authors declare that they have no conflict of interest.
Author contributions: All authors contributed equally to this work.
Ethical approval: All ethical guidelines have adhered to.
Sample availability: Samples of the compounds are available from the author.

Funding

This investigation was funded by the Department of Biotechnology, Government of India, India.

ORCID

Stability Nongrum
http://orcid.org/0000-0002-2427-6007
Susma Das
http://orcid.org/0000-0002-2391-8792

Shikpika Khanikar
http://orcid.org/0000-0001-9845-2002
Jai Narain Vishwakarma
http://orcid.org/0000-0001-9068-4554

References

[1]. Musumeci, D.; Irace, C.; Santamaria, R.; Montesarchio, D. *Med. Chem. Commun.* **2013**, *4*, 1405-1410.
[2]. Wang, J.; Sanchez-Rosello, M.; Acena, L. J.; Pozo, del C.; Sorochinsky, E. A.; Fustero, S.; Soloshonok, A. V.; Liu, H. *Chem. Rev.* **2014**, *114*, 2432-2506.
[3]. Lisi, H.; Xinkan, Y.; Gavin, C. T. *J. Org. Chem*. **2017**, *82*, 6192-6201
[4]. Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev*. **2008**, *37*, 320-330.
[5]. Champagne, A. P.; Desroches, J.; Hamel, J. D.; Vandamme, M.; Paquin, J. F. *Chem. Rev.* **2015**, *115*, 9073-9174.
[6]. Charpentier, J.; Fruh, N.; Togni, A. *Chem. Rev.* **2015**, *115*, 650-682.
[7]. Vishwakarma, J. N.; Khanikar, S.; Kalita, U.; Kaping S.; Ray, M. *Curr. Chem. Lett*. **2018**, 7, 35-44.
[8]. Mohamed, A. R.; Omran, A. O. *J. Heterocycl. Chem.* **2016**, *53*, 1121-1128.
[9]. Kalita, U.; Kaping, S.; Nongkynrih, R.; Sunn, M.; Boiss, I.; Singha, I. L.; Vishwakarma, J. N. *Med. Chem. Res.* **2015**, *24(6)*, 2742-2755.
[10]. Kalita, U.; Kaping, S.; Nellanant, J.; Helissey, P.; Vishwakarma, N. J. *Heterocyclic Lett.* **2014**, *4(1)*, 137-145.
[11]. Bruker, APEX II, Bruker AXS Inc., Madison, WI, USA, 2004.
[12]. Sheldrick, G. M. SHELXS-97 and SHELXL-97, Program for Crystal Structure Solution and Refinement, University of Gottingen, Gottingen, 1997
[13]. Farrugia, L. J. *J. Appl. Crystallogr*. **1999**, *32*, 837-838.