

Synthesis and Crystal Structure of 2-(4-Methoxyphenyl)-3-(3,4,5-trimethoxyphenyl)acrylonitrile

Chandagirikoppal V. KAVITHA,* G. SARALA,** S. NAVEEN,** Sridhar M. ANANDALWAR,**†
 J. Shashidhara PRASAD,** and Kanchugarakoppal S. RANGAPPA*

*Department of Studies in Chemistry, University of Mysore, Mysore 570006, India

**Department of Studies in Physics, University of Mysore, Mysore 570006, India

A new dipolarophile, used to construct bioactive heterocycles, 2-(4-methoxyphenyl)-3-(3,4,5-trimethoxyphenyl)-acrylonitrile, $C_{19}H_{19}NO_4$, was synthesized by base-catalyzed reaction of 3,4,5-trimethoxybenzaldehyde with (4-methoxyphenyl)acetonitrile. The compound crystallizes in the monoclinic space group $P2_1/c$ with cell parameters $a = 7.2880(4)\text{\AA}$, $b = 8.1030(9)\text{\AA}$, $c = 28.460(3)\text{\AA}$, $\beta = 94.018(5)^\circ$, $Z = 4$. The structure exhibits both inter and intramolecular hydrogen bonds of the type C-H...O and C-H...N.

(Received June 26, 2006; Accepted September 13, 2006; Published on web November 16, 2006)

The use of the nitrile function for the C-C bond formation reaction occupies an important position in organic chemistry. 2,3-Disubstituted acrylonitriles represent an interesting class of biologically active compounds, which are capable of undergoing many useful organic transformations. Many have been transformed into bioactive heterocycles.¹ The title compound was designed as an analog of Combretastatin A-4 (II),² in which the 3-hydroxy-4-methoxy phenyl moiety was replaced by the 4-methoxy phenyl moiety and an olefinic bond-carrying nitrile group. Recently, the crystal structures of some bioactive heteroarylacrylonitriles, which reflect the olefinic bond geometry, and other structural details of the molecules have been reported.³ We found from the literature that the olefinic bond had the *Z*-configuration irrespective of the size of the substituents on the heterocyclic rings. In order to confirm the olefinic bond geometry connected to (4-methoxyphenyl)acetonitrile and 3,4,5-trimethoxyphenyl rings and to obtain the structural conformation details of the molecule, its X-ray structure determination was carried out.

To a well-stirred suspension of 3,4,5-trimethoxybenzaldehyde (1.33 g, 6.8 mmol) in a 5% NaOH (10 ml) solution, 4-methoxyphenylacetonitrile (1 g, 6.8 mmol) was added along with catalytic amount of tertiarybutylammonium bromide. The mixture was stirred at room temperature for 50 min, saturated with a sodium chloride solution and extracted with diethyl ether (3×15 ml). The combined organic layer was dried over

anhydrous sodium sulfate and evaporated under a vacuum to obtain a crude mass, which upon recrystallization with methanol gave a colorless crystalline solid. Melting point, 103°C . Single crystals suitable for the structural analysis were obtained by a slow evaporation technique using methanol as a solvent. A schematic diagram of the molecule is shown in Fig.

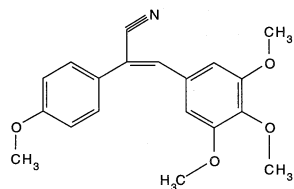


Fig. 1 Schematic diagram.

Table 1 Crystal data and structure refinement table

Empirical formula	$C_{19}H_{19}NO_4$
Formula weight	325.35
Temperature	293(2)K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	$P2_1/c$
Cell dimensions	$a = 7.2880(4)\text{\AA}$ $b = 8.1030(9)\text{\AA}$ $c = 28.460(3)\text{\AA}$ $\beta = 94.018(5)^\circ$
Volume	$1676.6(3)\text{\AA}^3$
<i>Z</i>	4
D_c	1.289 Mg/m ³
Absorption coefficient	0.091 mm ⁻¹
F_{000}	688
θ_{\max}	25.68°
Reflections collected	4006
Independent reflections	2343 [$R(\text{int}) = 0.0258$]
Data/restraints/parameters	2343/0/222
Goodness-of-fit on F^2	1.129
Final <i>R</i> indices [$I > 2\sigma(I)$]	$R1 = 0.0744$, $wR2 = 0.2246$
<i>R</i> indices (all data)	$R1 = 0.0853$, $wR2 = 0.2512$
$(\Delta f)_{\max}$	0.000
$(\Delta\rho)_{\max}$	0.364 e.Å ⁻³
$(\Delta\rho)_{\min}$	-0.389 e.Å ⁻³
Refinement method	full-matrix least-squares on F^2
Measurement	DIPLabo
Program system	Denzo
Structure determination	SHELXS-97
Refinement	full-matrix: SHELXL-97
CCDC	285311

† To whom correspondence should be addressed.
 E-mail: mas@physics.uni-mysore.ac.in

Table 2 Atomic coordinates and equivalent thermal parameters of the non-hydrogen atoms

Atom	x	y	z	U_{eq}
C1	-0.5694(4)	0.6101(5)	0.4081(2)	0.0640(9)
C2	-0.6012(4)	0.6549(5)	0.45366(9)	0.0615(9)
C3	-0.4711(4)	0.7446(5)	0.47928(9)	0.0692(1)
C4	-0.3119(4)	0.7937(5)	0.45889(9)	0.0639(1)
C5	-0.2799(4)	0.7542(4)	0.41303(8)	0.0549(8)
C6	-0.4128(4)	0.6583(5)	0.38791(9)	0.0631(9)
O7	-0.7651(3)	0.6045(3)	0.46947(7)	0.0761(8)
C8	-0.8063(5)	0.6542(6)	0.5156(2)	0.086(2)
C9	-0.1163(4)	0.8186(4)	0.39079(9)	0.0551(8)
C10	-0.0082(4)	0.9348(5)	0.4195(2)	0.0700(2)
N11	0.0728(5)	1.0272(6)	0.4426(2)	0.1029(14)
C12	-0.0730(4)	0.7877(4)	0.34653(9)	0.0565(9)
C13	0.0728(4)	0.8569(4)	0.31925(9)	0.0524(8)
C14	0.2249(4)	0.9409(4)	0.33930(9)	0.0553(9)
C15	0.3460(4)	1.0151(4)	0.31109(9)	0.0548(8)
C16	0.3208(4)	1.0041(4)	0.26209(9)	0.0519(8)
C17	0.1740(3)	0.9132(4)	0.24199(8)	0.0497(8)
C18	0.0503(4)	0.8409(4)	0.27043(9)	0.0524(8)
O19	0.1650(3)	0.9071(3)	0.19393(6)	0.0619(7)
C20	0.0272(5)	0.8091(6)	0.17083(1)	0.0824(13)
O21	0.4335(3)	1.0868(3)	0.23368(6)	0.0614(7)
C22	0.6079(4)	1.0104(6)	0.2300(2)	0.077(1)
O23	0.4942(3)	1.1065(3)	0.32759(7)	0.0735(8)
C24	0.5084(5)	1.1505(6)	0.3758(2)	0.0800(2)

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij}(a_i^* a_j^*)(a_i a_j).$$

1.

A single crystal of the title compound with dimensions of 0.3 × 0.27 × 0.25 mm was chosen for an X-ray diffraction study. The data were collected on a DIPLabo Image Plate system equipped with a normal-focus, 3 kW sealed X-ray source (graphite monochromated Mo K_{α}). The crystal-to-detector distance was fixed at 120 mm with a detector area of 441 × 240 mm². Thirty six frames of data were collected at room temperature by an oscillation method. Each exposure of the image plate was set to a period of 400 s. Successive frames were scanned in steps of 5° per min with an oscillation range of 5°. Image processing and data reduction were performed using Denzo.⁴ All of the frames could be indexed using a primitive monoclinic lattice. The structure was solved by direct methods using SHELXS-97. All of the non-hydrogen atoms were revealed in the first Fourier map, itself. A least-squares refinement using SHELXL-97 with isotropic temperature factors for all the non-hydrogen atoms converged the residual R1 to 0.1751. Subsequent refinements were carried out with anisotropic thermal parameters for non-hydrogen atoms. After eight cycles of refinement the residuals converged to 0.0744. The hydrogen atoms were fixed at chemically acceptable positions and were allowed to ride on their parent atoms. The details of the crystal data and refinement are given in Table 1.

The final atomic coordinates and equivalent thermal parameters for all of the non-hydrogen atoms are given in Table 2. The bond lengths and angles of all the non-hydrogen atoms are given in Table 3, which are in good agreement with the standard values. Figure 2 represents an ORTEP diagram of the molecule with thermal ellipsoids drawn at 50% probability.

The dihedral angle between the methoxyphenyl ring and the trimethoxyphenyl ring is 18.16(16)°. The olefinic bond connecting the 4-methoxyphenylacrylonitrile and 3,4,5-trimethoxyphenyl groups has the Z geometry. Significant deviations from the ideal bond-angle geometry around the Csp² atoms of the double bond were observed. The bond angles C9-C12-C13=130.5(3)°, C12-C9-C5=125.7(3)° and C10-C9-C5

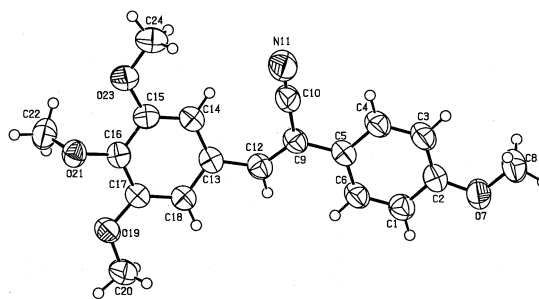


Fig. 2 ORTEP diagram of the molecule at 50% probability.

=114.3(2)° are distorted due to a steric hindrance of the double bond linking the two ring systems. The olefinic double bond bearing the three conjugated substituents has a length of 1.343(4)Å, which is slightly less than the corresponding value of 1.353(3)Å and greater than 1.304(4)Å reported for (Z)-2-(3-thienyl)-3-(3,4,5-trimethoxyphenyl)acrylonitrile,⁵ and 2-styrylbenzimidazole,⁶ indicating some delocalization in the unsaturated bridging units. The torsion angle of -160.60(33)° for C9-C12-C13-C18 indicates a deviation of the 3,4,5-trimethoxyphenyl ring from the plane of the olefinic double bond. The torsion angle values of 2.34(52)°, -10.73(47)° and -5.18(46)° for C3-C2-O7-C8, C14-C15-O23-C24 and C18-C17-O19-C20, respectively, indicate that the methoxy groups are in the plane of their respective phenyl rings, while the methoxy group at O21 deviates by 78.46(37)° [C15-C16-O21-C22] from the plane of its respective phenyl plane. The structure exhibits both inter and intramolecular hydrogen bonds of the type C-H...O and C-H...N. The intermolecular hydrogen bonds are C6-H6...O21, which has a length of 3.501(3)Å and an angle of 163°, and C12-H12...O19, which has a length of 3.343(4)Å and an angle of 143° with symmetry code -x, -1/2+y, 1/2-z. The molecules form hydrogen-bonded dimers.

Acknowledgements

The authors would like to express their thanks to DST, Government of India for financial assistance under the projects SP/I2/FOO/93 and SR/SO/HS-58/2003.

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