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SYNTHESIS, CHARACTERIZATION AND CRYSTAL STRUCTURE OF 1-[5-(4-BROMOPHENYL)-3-(4-FLUOROPHENYL)-4, 5-DIHYDRO-1*H*-PYRAZOL-1-YL]-2-CHLOROPROPAN-1-ONE

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ABSTRACT

The title compound 1-[5-(4-Bromophenyl)-3-(4-Fluorophenyl)-4, 5-dihydro-1*H*-Pyrazol-1-yl]-2-Chloropropan-1-one (2) was synthesized by reacting chalcone, (2*E*)-3-(4-Bromophenyl)-1-(4-Fluorophenyl) prop-2-en-1-one (1) with hydrazine hydrate in the presence of 2-chloro propionic acid. It has been crystallizes using ethanol by using slow evaporation process in the orthorhombic space group $P2_12_12_1$ with unit cell parameters a = 8.1984(9), b = 11.1417(22), c = 19.2217(10) Å, α=β=ϒ=90.00(0)º. The molecule is essentially planar except the pyrazoline ring which is slightly deviated and adopts normal *envelope* conformation. The methyl group attached to pyrazoline ring through the carbon atoms C10 and C11 is disordered over two positions C12/C12A with site occupancy ratio of 50:50. The crystal structure features the presence of inter-molecular [C-H…F] and intra-molecular [C-H…N] hydrogen bonds, as well as π–π interactions [between the Pyrazoline ring and Fluorophenyl ring], which contributes to the stabilization of the crystal structure. The structure of the compound is characterized by elemental analysis, ^{1}H NMR spectra and Single crystal XRD.

Keywords: 2-Pyrazoline, Crystal Structure, Direct Method, Intermolecular interaction, Confirmation.

INTRODUCTION

Pyrazolines are well known as important nitrogen-containing five-membered heterocyclic compounds whose derivatives have been found to possess considerable biological activities. Pyrazolines have played a crucial part in the development of theory in heterocyclic chemistry and also used extensively in organic synthesis[1,2] stimulates enormous research activity in this field[3]. In particular, they are used as antitumor, antibacterial, antifungal, antiviral, anti-parasitic, anti-tubercular and insecticidal agents[4,5]. Some of these compounds also possess anti-inflammatory, anti-diabetic, anaesthetic and analgesicproperties[6,7]. Dueto these interesting activities of diversely substituted pyrazolines and the considerable attention these materials have received in the recent years, we report the synthesis and crystal structures of 1-[5-(4-Bromophenyl)-3-(4-Fluorophenyl)-4,5-dihydro-1*H*-Pyrazol-1-yl]-2-Chloropropan-1-one(2)(Figure1).

EXPERIMENTAL

Materials and Method

Melting point was taken in open capillary tube and was uncorrected. The purity of the compound was confirmed by thin layer chromatography using Merck silica gel 60 F_{254}-coated aluminium plates using ethyl acetate : n-hexane (1:3, v/v) as solvent system. ^{1}H NMR (400 MHz) spectra was recorded on a Bruker AMX 400 spectrometer, with 5 mm PABBO BB-1H TUBES with TMS as internal standard. Elemental analysis was carried out using VARIO EL-III (ElementarAnalysensystem GmBH).

Procedure for the synthesis of 1-[5-(4-bromophenyl)-3-(4-fluorophenyl)-4, 5-dihydro-1h-pyrazol-1-yl]-2-chloropropan-1-one (2)

The synthetic route for the title compound is shown in Figure 1**.**A mixture of 3-(4-Bromophenyl)-1-(4-Fluorophenyl)prop-2-en-1-one (3.05g,0.01 mol) and hydrazine hydrate (0.5 mL, 0.01 mol) in 25 mL 2-chloro propionic acid was refluxed for 8 h. The reaction mixture was cooled and poured into 50 ml ice-cold water. The precipitate was collected by filtration and purified by recrystallization from ethanol. The crystals were grown by the slow evaporation method. Pale yellow crystals obtained with 42% yield. M.p. 142–144 °C; Analytical data: Found (Cald): C%:52.74 (52.77); H%: 3.72 (3.69); N%: 6.81 (6.84). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 1.57 (d, 3H, CH_3), 3.17 (dd, 1H, H_A, J_{AB} =18.0Hz, J_{AX} =4.8 Hz), 3.88 (dd, 1H, H_B, J_{BA} = 18.2 Hz, J_{BX} = 11.8 Hz), 5.56 (dd, 1H, H_X, J_{XA}= 4.8 Hz, J_{XB}= 11.6 Hz), 5.48 (q, 1H, CH), 7.14-7.90(m, 8H, Ar–H).

X-Ray Intensity Data Collection

X-ray intensity data of the crystal (0.20 X 0.20 X 0.10 mm) having well-defined crystal morphology were collected at 293(2)*K* on *X'calibur* CCD area-detector X-ray Diffractometer[8] equipped with Mo*Kα* radiation (*λ*=0.71073Å). The intensities were measured by employing *ω* scan mode for the diffraction angle ranging from 3.66 to 25.00°. A total number of 4328 reflections were measured of which 2910 were found to be unique. The criterion *(I >2σ (I)*) was employed to the unique data set and hence 1113 reflections were treated as observed. Data were corrected for Lorentz and Polarization factors. The structure was solved by direct methods using SHELXS97[9]. All non-hydrogen atoms of the molecule were located in the best E-map and Full-matrix least-squares refinement was carried out using SHELXL97[9].The final refinement cycles converged to R = 0.1076and wR(F^2) = 0.2164 for 1113 observed reflections. A relatively large value of the R-factor could be due the presence of three halogen atoms and partly also due to the thermal disorder present in the methyl group. The residual electron density ranges from -0.573 to0.449 eÅ^{-3}. Atomic scattering factors were taken from International Tables for X-ray Crystallography (1992, Vol. C, Tables- 4.2.6.8 and 6.1.1.4).

The crystallographic data are summarized in Table-1. Some selected bond angles which play an important role in collating the structural properties of this molecule with the related structures are presented in Table-2. An ORTEP[10] view of the molecule with atomic labeling is shown in Figure-2. The geometry of the molecule was calculated using the PLATON[11] and PARST[12]software.**CCDC-1419962**contains the supplementary crystallographic data for the structure.

RESULTS AND DISCUSSION

The molecular structure of the title compound (Figure-1) has also been confirmed by ^{1}H NMR spectral data. The formation of 2-pyrazoline ring was confirmed by the appearance of ABX pattern in ^{1}H NMR spectra due to germinal-vicinal coupling between protons H_A and H_B at C-4 and H_X at C-5. The signal due to proton H_A appeared as a doublet of doublet around δ 3.17 ppm (J_{AB} =18.0Hz, J_{AX} =4.8 Hz). The proton H_B appeared as a doublet of doublet around δ 3.88 ppm (J_{BA} = 18.2 Hz, J_{BX} = 11.8 Hz).While, H_X appeared as a doublet of doublet around δ 5.56 ppm (J_{XA}= 4.8 Hz, J_{XB}= 11.6 Hz).

X-ray diffraction studies reveal that the molecule comprises three rings, viz. Florophenlyring [A], Bromophenyl ring [B] and Pyrazoline ring[C], respectively. All the bond lengths and angles are normal and correspond to those observed in related structures, except the bond length for C6-F1=1.50(2) Å, which is significantly larger than the values reported for some related structures[13-15]. The reason for a relatively large value for this bond could be due to the involvement of F1 in two C-H…F inter-molecular hydrogen bonds. The presence of keto group [C10=O1] is confirmed with its bond length of 1.261(18) Å. This is slightly more than the standard value for carbonyl bonds[16] (1.210 Å) but is in good agreement with the values observed for some related structures[13, 15]. The endocyclic bond angles in Florophenyl (Ring A) and Bromophenyl (Ring B) moieties indicate perfect aromatic character[16].

The ring A and ring B (Fluorophenyl and Bromophenyl) are perfectly planar with maximum deviation for the atom F1 [0.0338(9) Å] and Br1 [-0.0069(25) Å], respectively. The pyrazoline ring (C) adopts *envelope confirmation* with C3, being the pivotal atom, indicating deviation of -0.0348 Å and the asymmetry parameter[17] ΔC_s (C3) =1.148.

Table- 1: Crystal data and other experimental detail

CCDC Number	1419962
Crystal description	Block
Crystal size	0.20 x 0.20 x 0.10 mm
Empirical formula	$C_{18}H_{15}BrCl\ F\ N\ O$
Formula weight	409.68
Radiation, Wavelength	Mo *K*α, 0.71073 Å
Unit cell dimensions	a = 8.1984(9), b = 11.142(2), c =19.222(4) Å α= β =ϒ = 90.00(5)˚
Crystal system, Space group	Orthorhombic, $P2_1\ 2_1\ 2_1$
Unit cell volume	1755.8(5)Å^3
No. of molecules per unit cell, Z	4
Absorption coefficient	2.510mm^{-1}
F(000)	824
θ range for entire data collection	3.66< θ < 25.00º
Reflections collected / unique	4328 /2910
Reflections observed I > 2σ(I))	1113
Range of indices	h= -9 to 6, k= -10 to 13, l= -22 to 10
No. of parameters refined	217
Final R-factor	0.1076
wR(F2)	0.2164
Rint	0.0690
Rsigma	0.2130
Goodness-of-fit	0.986
(Δ/σ)max	0.001
Final residual electron density	-0.573<Δρ>0.449 eÅ^{-3}

Table- 2: Selected Bond Lengths and Bond angles

Bond Lengths (Å)		Bond Angles(˚)	
F1-C6	1.50(2)	F1-C6-C7	118.4(2)
Cl1-C11	1.72(2)	F1-C6-C5	119.5(1)
Br1-C16	1.84(2)	Br1-C16-C15	119.8(1)
O1-C10	1.26(2)	Br1-C16-C17	120.5(2)
N1-N2	1.34(2)	N1-N2-C3	111.0(1)
N1-C1	1.27(2)	N1-N2-C3	109.7(1)

The methyl group located at C11 is disordered over two positions, i.e., C12 and C12A with site occupancy of 50:50. The disordered methyl group adopts *anti-clinical* (+) orientation with respect to ring B and it is confirmed by the magnitude of torsion present at both the positions of C12-atom (C12/C12A) [N2-C10-C11-C12=139(2)ºand N2-C10-C11-C12A=108(2)º], respectively. The atom F1 plays a key role in the stabilization of crystal structure as it participates in two inter-molecular hydrogen bonds. F1 acts as the hydrogen bond acceptor via atoms H12C and H12E to the atoms C12 and C12A, respectively. The nitrogen atom N1 is involved in the formation of an intra-molecular hydrogen bond [C11-H11…N1],

resulting into the occurrence of a *virtual* five-membered ring S(5)[18][consisting of atomN1, N2, C10, C11 and H11].The packing view of the molecule represents a *zig-zag* network [Figure-3].The crystal packing features the presence of π–π interactions between ring C and A [Centeroid separation = 4.0135(9) Å, inter-planar spacing = 3.53 Å and Centeroid shift = 1.9 Å; symmetry codes: x-1/2,- y+1/2, -z+1]. These interactions also contribute to the stabilization of the crystal structure. The geometry of hydrogen bonding is presented in Table-3.

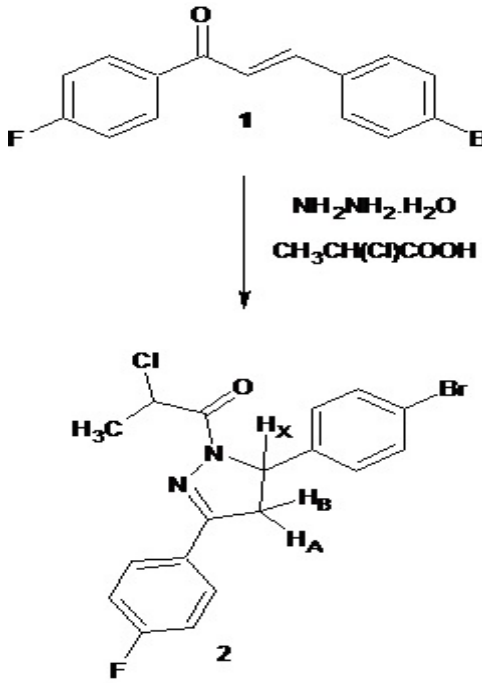

Fig. -1: Scheme of the Reaction

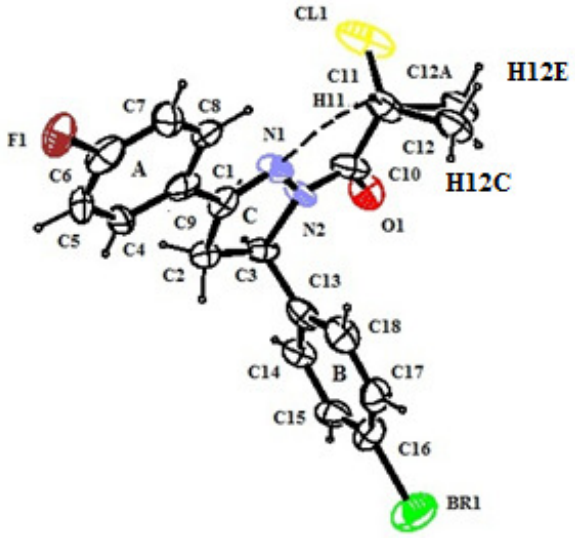

Fig.-2:Ortep view of the molecules with displacement ellipsoids at the 40% probability level.
H atoms shown as small spheres of arbitary radii. The broken lines show the intermolecular hydrogen bonds forming S(5) motif.

Table-3: Geometry of Intra and Inter molecular Hydrogen bonds

D-H…A	D-H (Å)	H…A(Å)	D…A(Å)	θ[DH…A(°)]
C11-H11…N1	0.98(2)	2.4(3)	2.8(2)	105
C12- H12C…F1^{i}	0.98(3)	2.4(8)	3.2(4)	131.98
C12A-H12E…F1^{i}	0.94(3)	2.6(8)	3.5(5)	172.65

Symmetry codes: (i) –x+1/2+2,-y, -z+1/2

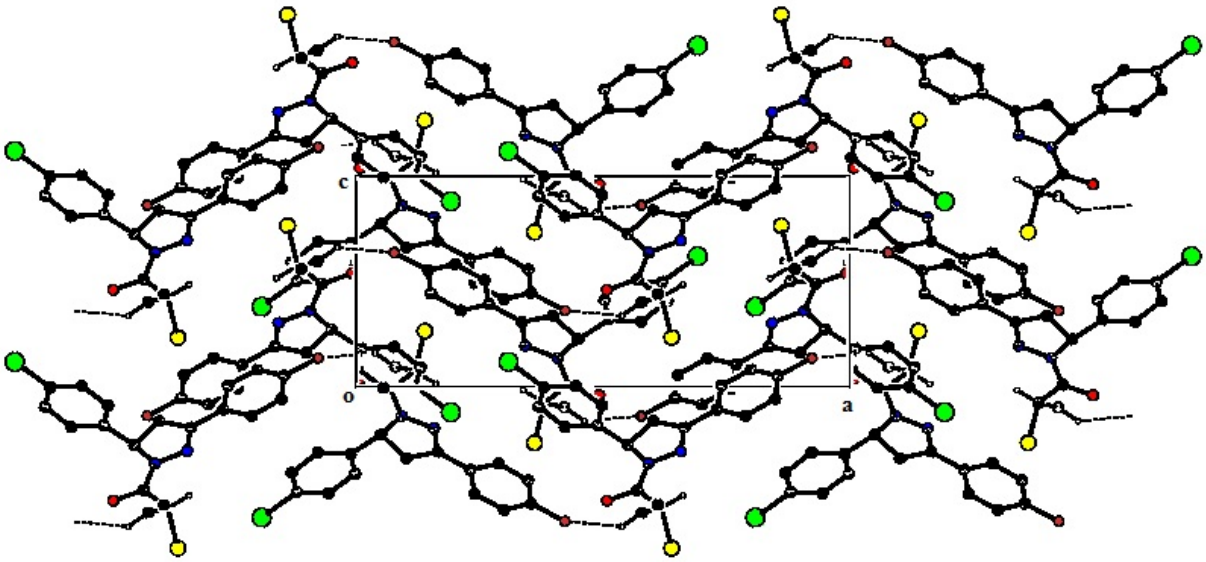

Fig.- 3:Packing of the molecules viewed down the b-axis. The dotted lines indicate an Inter-molecular interaction.

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REFERENCES

1. E. I. Klimova, M. Marcos, T. B. Klimova, A. T. Cecilio, A. T. Ruben and R. R. Lena, *J. Organomet. Chem.,* **585**, 106(1999).
2. D. Bhaskarreddy, B. N. Chandrasekhar, V. Padmavathi and R. P. Sumathi, *Synthesis,* **3**, 491(1997).
3. R. V.Hes, K. Welling and A. C.Grosscurt, *J. Agric. Food Chem*., **26,**915(1978).
4. D. Azarifar and M. Shaebanzadeh,*Molecules*, **7**, 885(2002).
5. M. Amir, H. Kumar, and S. A. Khan, *Bioorg. Med. Chem. Lett.,* **18**, 918(1978).
6. B. K.Sarojini, M.Vidyagayatri, C.G.Darshanraj, B. R. Bharathand H. Manjunatha, *Lett. Drug Des. Discovery*, **7**, 214(2010).
7. H. A. Regaila, A. K. El-Bayonk and M. Hammad, *Egypt. J. Chem*., **20**,197(1979).
8. Oxford Diffraction. *CrysAlis PRO* and *CrysAlis RED*. Oxford Diffraction Ltd, Yarnton, England, (2010).

9. G. M. Sheldrick, *ActaCryst*., **A64**, 112(2008).
10. L. J. Farrugia, *J. Appl. Cryst.,* **32**, 837(1999).
11. A. L. Spek, *ActaCryst.,* **D65,** 148(2009).
12. M. Nardelli,*J. Appl. Cryst.*, **28**, 659(1995).
13. H. K. Fun, W. S.Loh, M. Sapnakumari, B. Narayanab and B. K. Sarojinic, *ActaCryst.,***E68**, o2655(2012).
14. H. K. Fun, T. S. Chia, M. Sapnakumari, B. Narayanab and B. K. Sarojini, *ActaCryst.,* **E68**, o2680(2012).
15. P. J.Jasinski, C. J. Guild, S. Samshuddin, B. Narayanab and H. S. Yathirajan, *ActaCryst.,***E66**, o1948(2010).
16. F. Allen, O. Kennard, D.G. Watson, L. Brammer and A. G. Orpen, *Taylor, R., J. Chem. Soc., Perkin Trans-II,* **S1**, (1987).
17. W. L. Duax, and D. A. Norton, *Atlas of Steroid Structures*, New York: Plenum Press, **1,** (1975).
18. J. Bernstein, R. E. Davis, L. Shimoni and N. L. Chang NL (1995) *Angew Chem Int Ed Engl*.,**34,** 1555(1995).

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