Asian Journal of Chemistry; Vol. 24, No. 9 (2012), 4163-4165

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

Synthesis and Structural Characterization of the Aminopyrazole Derived Pyrimidinone†

HEE-MOON PARK*, BONG-JUN CHANG, HANGKYO JIN and JEONG-HOON KIM

Environment and Resources Research Center, Korea Research Institute of Chemical Technology, PO Box 107, Yuseong, Daejeon 305-600, Republic of Korea

*Corresponding author: E-mail: hmpark@krict.re.kr

AJC-11345

The pyrazolo pyrimidinone was prepared by treatment of 4-amino-5-pyrazole carboxamide with 2-ethoxy benzoic acid and the product characterized using NMR, high resolution mass spectrometry and X-ray crystallography. In the crystal, the hydrogen bonds and intermolecular interactions join the bridge between O26 of one molecule and C10-H10A of another. The molecule ($C_{22}H_{30}N_6O_4S$) crystallized in the monoclinic P2(1)/c space group. Unit cell parameters for 5-(2-ethoxy-5-(4-methyl-piperazine-1-sulfonyl)-phenyl)-1-methyl-3-propyl-1,6-dihydro-pyrazolo(4,3-d)pyrimidin-7-one: a = 17.2898(4), b = 6.9755(3), c = 8.0757(2)Å, β = 100.0710(10) and Z = 4.

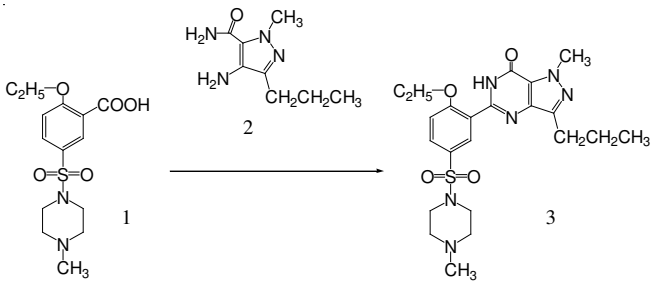
Key Words: Synthesis, Pyrazolopyrimidinone, Crystal structure, Diffractometer.

INTRODUCTION

In this work, the synthesis and the crystal structure of molecule **3** (**Scheme-I**), as determined by spectral analysis and single-crystal X-ray analysis are reported. Characterization of the molecule by NMR, high resolution mass spectrometry and X-ray crystallography revealed this product to be the 5-(2-ethoxy-5-(4-methyl-piperazine-1-sulfonyl)-phenyl)-1-methyl-3-propyl-1,6-dihydro-pyrazolo(4,3-d)pyrimidin-7-one (**3**). This molecule may be a primary moiety for the synthesis of heterocyclic multi ring compounds. Sulfonyl pyrazolo pyrimidinone is well introduced into the therapy of erectile dysfunction. The pharmaco dynamic principle of sulfonyl pyrazolo pyrimidinone is the selective inhibition of cyclic guanosine mono phosphate (cGMP)-specific phosphodiesterase type V (PDE V) predominately in the corpus cavernosum. The second messenger cGMP is located in vascular smooth muscle cells, platelets or rod photoreceptors and several side effects are described[1-4]. Nitric oxide-mediated cGMP is synthesised in the central nervous system as well; studies about animal brain regions describe several areas with production of cGMP. To the best of our knowledge, the work described here provides the first modern characterization of the pyrazolo pyrimidinone compound (**3**).

EXPERIMENTAL

The compound, sulfonyl pyrazolo pyrimidinone (250 mg, 0.581 mmol), was dissolved in DMF (1 mL) and sprayed into warm water (200 mL) while stirring vigorously. To this solution, warm sodium phosphate buffer (80 mL of pH 7.4, 500 mM) was added with stirring. The mixture was then extracted with ethyl acetate (3 mL × 80 mL), the organic extracts combined and extracted with brine (15 mL) and the organic layer then dried over magnesium sulfate. The ethyl acetate was removed by rotary evaporation and the products isolated by flash column chromatography on silica gel eluted with ethyl acetate and hexane. Compound **3** was obtained as a ivory powder (20 mg, R_f = 0.4; 20 % Hex:EtOAc) ^{1}H NMR (500 MHz, $CDCl_3$) d 8.76 (d, *J* = 2.5 Hz 1H), 7.77 (m, 1H), 7.12 (d, *J* = 8.8 Hz, 1H), 4.34 (m, *J* = 2.5 Hz, 2H), 4.24 (s, 2H), 3.07 (bs, 4H), 2.90 (t, *J* = 7.3 Hz, 2H), 2.46 (m, 4H), 2.90 (t, *J* = 7.3 Hz, 2H), 2.46 (m, 4H), 2.24 (s, 3H), 1.92 (s, 1H), 1.83 (m, 2H), 1.61 (t, *J* = 7.3 Hz, 3H), 0.99 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) d 159.39, 153.73, 147.04, 146.52, 138.45, 131.75, 131.22, 128.93, 124.57, 121.19, 113.12, 66.16, 54.13, 46.05,



Scheme-I: Synthesis of compound **3**

†Presented to The 5th Korea-China International Conference on Multi-Functional Materials and Application.

45.81, 38.30, 27.83, 22.34, 14.62, 14.13; HRMS (ESI,M + H^+) m/z calculated for $C_{22}H_{30}N_6O4_S$ 474.2049, found 474.2050. Crystals of the compound **3** were obtained by dissolving in a minimum amount of warm methanol, followed by slow evaporation over 3 day in a 2 mL glass vial. Details concerning crystal data, data collection characteristics and structure refinement are summarized in Table-1. The crystal was mounted on capillaries and transferred to a goniostat and were collected at 100(1) K under nitrogen stream. Data were collected on a Bruker CCD diffractometer with graphite-monochromated Mo-Ka radiation. A total of 22546 reflections were collected from which 5824 independent [$R_{(int)}$ = 0.0404] reflections were extracted. The structure was solved by direct methods using the SHELXTL XP[5] system and refined by a full-matrix least-squares methods based on F^2 using SHELXL97[6] using all 22456 data to final wR_2 (on F^2, all data) = 0.1408 and R_1 (on F, with [I[2r(I)]) = 0.0505. In this case, non-hydrogen atoms were refined employing anisotropic displacement parameters and the hydrogen atom positions were calculated with fixed isotropic displacement parameters.

TABLE-1
CRYSTAL DATA AND STRUCTURE REFINEMENT

Identification code	20110805lt_0m
Empirical formula	$C_{22}H_{30}N_6O_4S$
Formula weight	474.58
Temperature (K)	100(1)
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	P2(1)/c/
Unit cell dimensions	a = 17.2898(4)A α = 90° b = 16.9755(3) Å β = 100.0710(10)° c = 8.0757(2) Å γ = 90°
Volume	2333.72(9) $Å^3$
Z	4
Density (calculated)	1.351 Mg/m^3
Absorption coefficient	0.180 m m^{-1}
$F_{(000)}$	1008
Crystal size	0.22 mm × 0.16 mm × 0.07 mm
Theta range for data collection	1.69 to 28.34°
Index ranges	-21 ⇐ h ⇐ 23, -22 ⇐ k ⇐ 22, -10 ⇐ 1 ⇐ 8
Reflections collected	22546
Independent reflections	5824 [$R_{(int)}$ = 0.0404]
Completeness to θ = 28.34°	99.9 %
Absorption correction	Multi-scan
Max. and min transmission	0.9875 and 0.9614
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	5824/0/298
Goodness-of-fit on F^2	1.069
Final R indices [I > 2σ(1)]	R_1 = 0.0505, wR2 = 0.1275
R indices (all data)	R_1 = 0.0767, wR2 = 0.1408
Largest diff. peak and hole	0.794 and –0.487 e $Å^{-3}$

RESULTS AND DISCUSSION

Fig. 1 shows a perspective drawing of the compound **3** together with the selective atomic labeling and the necessary bond distances and angles are shown in Table-2. The different intermolecular interactions lead to the distorted assembles in the crystal lattice. Only one kind of intermolecular hydrogen bond is observed in the crystal (Fig. 2). The adjacent non-parallel molecules are connected by intermolecular hydrogen bonds (C10-H10A-O26). The interactions that can not be neglected are the weak C-H-O interactions, which are different from the traditional patterns. The pyrazolopyrimidinone compound **3** crystallizes with a space group of monoclinic P2(1)/c. The bond lengths and bond angles in the crystal unit are all in the normal range.

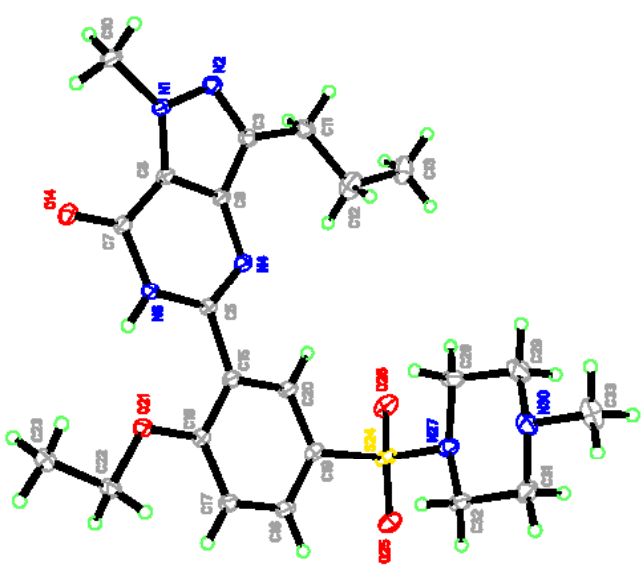


Fig. 1. An ORTEP plot of compound **3**

TABLE-2
BOND DISTANCES (Å) AND ANGLES (°) FOR COMPOUND **3**

Bond	Bond distances (Å)	Bond	Bond angles (°)
S24-O26	1.4323(15)	O26-S24-O25	120.07(9)
S24-O25	1.4348(15)	O26-S24-N27	107.12(9)
S24-N27	1.6396(18)	O25-S24-N27	107.04(9)
N27-C32	1.480(3)	O26-S24-C19	108.27(9)
N27-O28	1.484(3)	O25-S24-C19	107.44(10)
C28-C29	1.506(3)	N27-S24-C19	106.11(9)
C28-H28A	0.97	C32-N27-C28	112.65(16)
C28-H28B	0.97	C32-N27-S24	114.19(14)
C29-N30	1.453(3)	C28-N27-S24	114.90(14)
C29-H29B	0.97	N27-C28-C29	110.09(18)
N30-C33	1.456(3)	N27-C28-H28A	109.6
N30-C31	1.456(3)	C29-C28-H28A	109.6
C31-C32	1.506(3)	C29-C28-H28B	109.6
C31-H31A	0.97	C29-C28-H28B	108.2
C31-H31B	0.97	N30-C29-C28	110.71(18)
C32-H32A	0.97	N30-C29-H29A	109.5
C32-H32B	0.97	C28-C29-H29A	109.5
C33-H33A	0.96	N30-C29-H29B	109.5
C33-H33B	0.96	C28-C29-H29B	109.5
C33-H33C	0.96	H29A-C29-H29B	108.1

Conclusion

In this study, the compound **3** has been characterized by analytical, spectral and crystallo-graphic methods. Structural characterizations by single-crystal diffraction analysis has also been discussed and the pyrazolo-pyrimidinone possesses a distorted monoclinic geometry. Our next attempt will be to focus on the synthesis of different thiazolone scaffolds incorporating substituents on the hetero-acyclic ring.

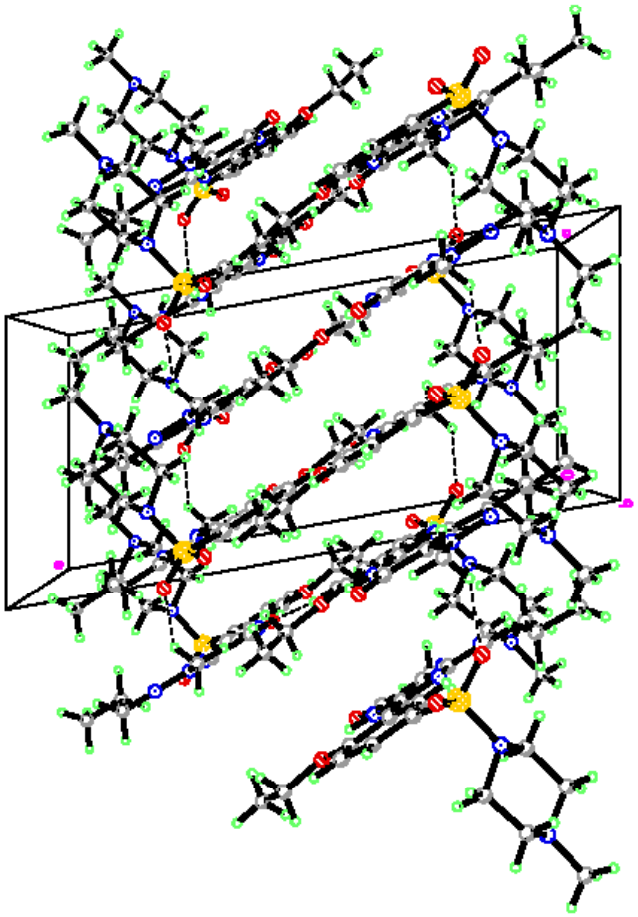


Fig. 2. C–H–O hydrogen bonds

REFERENCES

1. J.L. Goldstein, F.E. Silverstein, N.M. Agrawal, R.C. Hubbard, J. Kaiser, C.J. Maurath, K.M. Verburg and G.S. Geis, *Am. J. Gastroenterol.*, **95**, 1681 (2000).
2. R.J. Cook and D.L. Sackett, *Br. Med. J.*, **310**, 452 (1995).
3. K.S. Laitinen, K. Slovaara, S. Severgnini and J.T. Laitinen, *Brain Res.*, **755**, 272 (1997).
4. U. Walter, M. Eigenthaler, J. Geiger and M. Reinhard, *Adv. Exp. Med. Biol.*, **344**, 237 (1993).
5. G. Sheldrick, *Acta Cryst.*, **64A**, 112 (2008).
6. A. Berkessel, M. Bolte, T. Nemann and L. Seidel, *Chem. Ber.*, **129**, 1183 (1996).