

Synthesis of Heteryl Amino Derivatives of Bis[5-Cyano-1,6-Dihydro-6-Imino-2-Isopropyl-4-(Methylthio) Pyrimidine] Diazene

Girish Deshmukh^{*1}, Chanda Gawande²

¹Department of Chemistry, Shankarlal Agrawal Science College, Salekasa, Maharashtra, India

²Department of Chemistry, S. Chandra Mahila Mahavidyalaya, Amgaon, Maharashtra, India

ABSTRACT

Study of the synthesis of heteryl amino derivatives of bis[5-cyano-1,6-dihydro-6-imino-2-isopropyl-4-(methylthio) pyrimidine] diazene we have obtained low yield at room temperature than the reaction carried out at the reflux condition.

I. INTRODUCTION

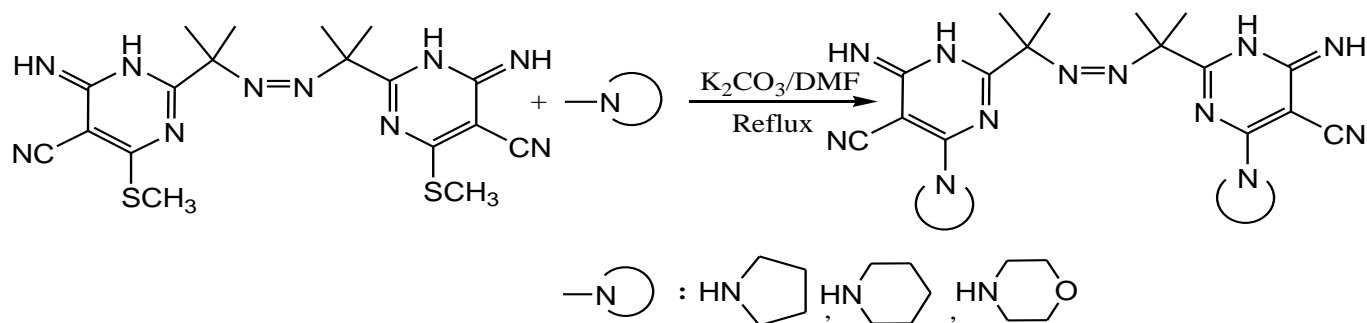
The understanding of principles of drug design and development of the drug molecules is important study the physicochemical properties of chemical compounds used to develop novel pharmacologically active compounds. The biological activities, mechanism of actions, possible biological activities of the metabolites and significance of stereochemistry for molecules are important factors for new drug design [1]. All these principles are based on the basic organic chemistry, physical chemistry and biochemistry. Heterocyclic compounds contain, one or more atoms of other elements apart from carbon, common hetero atoms are sulphur, nitrogen and oxygen [2]. The heterocyclic compounds having less common atoms such as silicon, bromine, phosphorus, tin, boron are much investigated in recent years. The heterocycles with five or six atoms in the ring are the most important [3]. The practice of medicinal chemistry is devoted to the research in development of new disease treating agent. The process of finding a new drug is complex and involves talent of people from variety of disciplines [4]. The important aspect of medicinal chemistry is to establish a relationship between pharmacological activity and chemical structure [5].

Pyrimidine is a six membered cyclic compound containing 2 nitrogen and 4 carbon atoms which is pharmacologically inactive however its substituted derivatives shows an important place in modern medicine [6]. Pyridazine 1, oxygenated derivative-pyridazinone 2 and benz fused pyridazine or phthalazine 3 are heterocyclic compounds that contain two adjacent nitrogen atoms (1,2-diazine) in the ring structure [7]. They show a high range of pharmacological activities and are found in different natural compounds with different biological activities [8]. Many heterocyclic compounds obtained from synthetic as well as natural sources, generally in practice have one or more nitrogen in the heterocyclic ring system. Diazines (1,2/1,3/1,4) are important heterocyclic rings. Recently, much attention has been focused on diazine derivatives for their broad-spectrum pharmacological activities [9].

II. PRESENT WORK

The newly synthesised molecule possesses two methylthio groups which can be easily substituted with heteryl amines that can be remarked.

Heteryl amino derivatives of can be prepared by reacting it with substituted heteryl amines in 1:2 proportion using DMF solvent and anhydrous K_2CO_3 catalyst to yield compounds .



Scheme: Synthesis of heteryl amino derivatives of bis[5-cyano-1,6-dihydro-6-imino-2-isopropyl-4-(methylthio) pyrimidine] diazene

III. RESULTS AND DISCUSSION

In the study of optimization of reaction condition and solvent for the synthesis of heteryl amino derivatives of bis[5-cyano-1,6-dihydro-6-imino-2-isopropyl-4-(methylthio) pyrimidine] diazene we have obtained low yield at room temperature than the reaction carried out at the reflux condition.

IV. EXPERIMENTAL SECTION

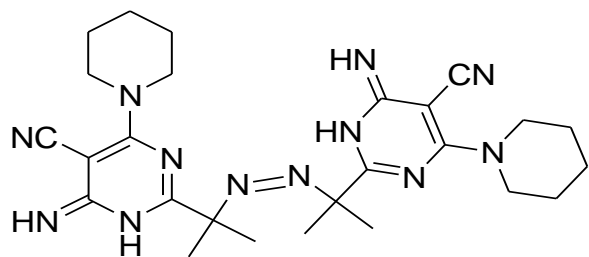
All chemicals procured from spectrochem, Alfa Aesar, SDFine, Sigma Aldrich were used without further purification. The IR spectra were recorded with Shimadzu FTIR. The melting points were recorded using Veego digital melting point apparatus. The NMR spectra were recorded with Bruker 400MHz using DMSO-d6 solvent.

V. GENERAL PROCEDURE

Compound (0.442 g, 1 mmol) and different heteryl amines, (1 mmol) in 1:2 proportion using 15 ml of DMF as solvent and catalyst anhydrous K_2CO_3 as catalyst (10 mg) reflux for 5-7 hours, the progress of reaction was monitored by TLC. The reaction mixture was cooled to room temperature and poured into ice cold water. The separated solid product was filtered off, washed many times with water and recrystallized from ethanol.

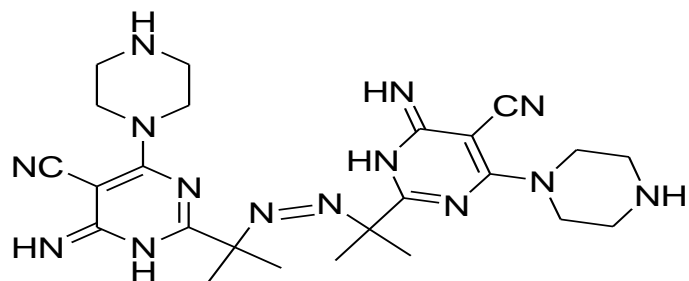
VI. SPECTRAL DATA

1) bis[5-cyano-1,6-dihydro-6-imino-2-isopropyl-4-(piperidiny) pyrimidine] diazene



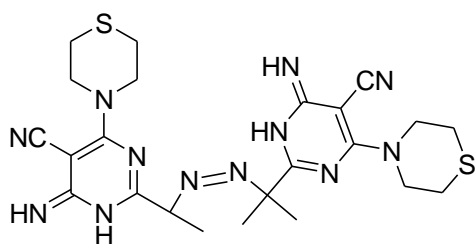
- **Molecular Formula** : C₂₆H₃₆N₁₂
- **Mol. Weight (g/mol)** : 516.6
- **IR(KBr) (cm⁻¹)** : 3300(=NH), 2198 (CN), 1616 (C=N)
- **¹H NMR (δ, ppm)** : 1.24 (q, 8H), 1.36 (s, 12H), 2.82 (t, 8H), 3.86 (s, 2H),
(DMSO-d₆) 9.21(s, 2H)
- **Mass (m/z)** : 372.2, 516.4 (M⁺)

2) bis[5-cyano-1,6-dihydro-6-imino-2-isopropyl-4-(p-piperazinyl) pyrimidine] diazene



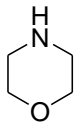
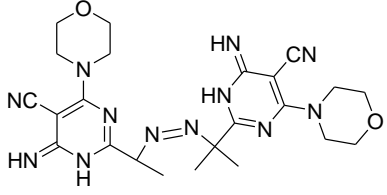
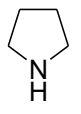
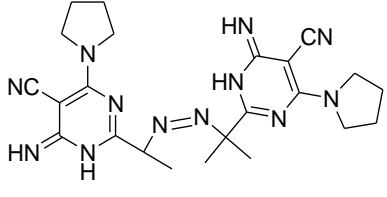
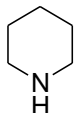
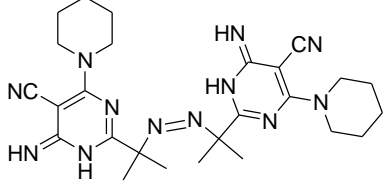
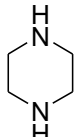
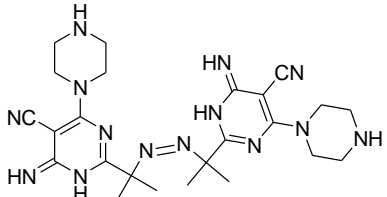
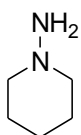
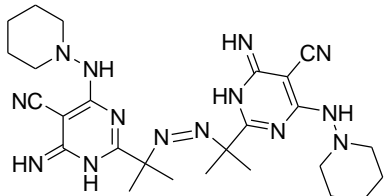
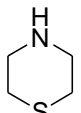
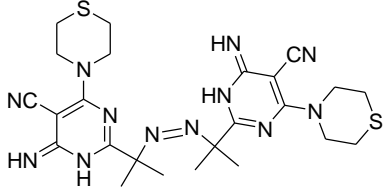
- **Molecular Formula** : C₂₄H₃₄N₁₄
- **Mol. Weight (g/mol)** : 518.6
- **IR(KBr) (cm⁻¹)** : 3309 (=NH), 2204 (CN), 1610 (C=N)
- **¹H NMR (δ, ppm)** : 1.35 (s, 12H), 3.08 (t, 8H), 3.10 (t, 8H), 3.82 (s, 2H),
(DMSO-d₆) 8.00 (s, 2H)
- **Mass (m/z)** : 332.6, 518.9(M⁺)

3) bis[5-cyano-1,6-dihydro-6-imino-2-isopropyl-4-(4-thiomorpholino) pyrimidine] diazene



- **Molecular Formula** : C₂₄H₃₂N₁₂S₂
- **Mol. Weight (g/mol)**: 552.7
- **IR(KBr) (cm⁻¹)** : 3301 (=NH), 2198 (CN), 1606 (C=N)
- **Mass (m/z)** : 477.1, 552.6 (M⁺)

Table: Synthesis of heteryl amino derivatives of bis[5-cyano-1,6-dihydro-6-imino-2-isopropyl-4-(methylthio)pyrimidine] diazene

Entry	Substrate	Product	Reaction Time (h)	Yield (%)	M.P. (°C)
a			5.0	74	194
b			5.5	70	186
c			6.5	67	180
d			4.5	78	203
e			5.0	79	178
f			6.5	83	182

VII. REFERENCES

- [1]. A. Kossel, H. Steudel, *Physiol. Chem.*, 1903, 38: 49.
 [2]. Amir M., Javed SA, Kumar H ;*Indian J. Pharm. Sciences*, 2007, 69(3): 337.
 [3]. Jain M. K., Sharnevas SC, *Organic Chem.* 2008, 3: 997.

- [4] . Sasada T, Kobayashi F, Sakai N, Konakahara T; *Org. Lett.*2009, 11, 2161.
- [5] . Zhichkin P, Fairfax D J, Eisenbein S A; *Synthesis*, 2002, 720.
- [6] . Ahmad O. K., Hill M D, Movassaghi M; *J. Org. Chem.*, 2009,74: 8460.
- [7] . Barthakur M. G., Borthakur M, Devi P, Saikia C J, Saikia A, Bora U; *Synlett*, 2007, 223.
- [8] . Karpov S. and Mulle T J J; *Synthesis*, 2003, 2815.
- [9] . Movassaghi M., Hill M. D.; *J. Am. Chem. Soc.*, 2006, 128: 14254.
- [10] . GhorabM. M., Heiba MI, Hassan AA; *JACS*.2011,7(1),1063.
- [11] . Kappe C. O.; *Eur J Med Chem*.2000, 35(12), 1043.
- [12] . Brown D. J. New York: Pergamon press, 1984. 57.
- [13] . Callery P., Gannett P.; Philadelphia Lippincott Williams and Wilkins, 2002. 934.
- [14] . Polak A., Scholer HJ. ;*Chemotherapy*. 1975, 21, 113.
- [15] . Cheng C., Roth B. In: Ellis GP; 8th ed. London: Butterworths, 1982. 267.
- [16] . Ghomi A. S., Ali M.; *Dig J Nanomater Biostruct* 2010,5(2):303.
- [17] . Lagoja I. M.; *Chem Biodivers*2005, 2(1):1.
- [18] . Brown D. J., Evans R. F., CowdenUK; Pergamon Press Oxford; 1984.15.
- [19] . Elderfield R. C. John Wiley & Sons New York; 1957. 6.
- [20] . Agarwal O. P. Krishna Prakashan Media (P) Ltd.; 2006. 735.
- [21] . Porter A. E. Pregamon Press, Elsevier Science BV Amsterdam; 1979. 14.
- [22] . Gavilan M. D., Gomez-Vidal J. A., Serrano F. R.;*Chem Lett*2008; 18, 1457.
- [23] . Ali M., Azad M., Siddiquia H. L., Nasim F. H.; *J Chinese Chem Soc*,2008; 55, 394.
- [24] . Siddiqui A. B., Trivedi A. R., Kataria V. B., Shah ;*Bioorg Med Chem Lett*,2014 15, 24, 1493.
- [25] . S. Cao, X. Qian, G. Song, B. Chai, and Z. Jiang; *Journal of Agricultural and Food Chemistry*,2003, 51, 152.
- [26] . K. Abouzid, M. Abdel Hakeem, O. Khalil, and Y. Maklad; *Bioorganic & Medicinal Chemistry*, 2008,16, 1, 382.
- [27] . W. Malinka, A. Redzicka, O. Lozach, ;*Il Farmaco*, 2004,59, 6, 457.
- [28] . Jain, K. S.; Chitre, T. S.; Miniyar, P. B.; Kathiravan, M. K.; Bendre, V. S.; Veer, V.S. *J. Curr. Sci.* 2006, 90, 793.
- [29] . Botta, M.; Corelli, F.; Maga, G.; Manetti, F.; Renzulli, M.; Spadari, S.; *Tetrahedron*2001, 57, 8357.
- [30] . Zanatta, N.; Flores, D. C.; Madruga, C. C.; Flores, A. F. C.; Bonacorso, H. ; *Tetrahedron Lett.*2006, 47, 573.