*ejpmr, 2016,3(6), 538-540*

**SJIF Impact Factor 3.628**

**EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH**

www.ejpmr.com

**Review Article**

**ISSN 2394-3211**

**EJPMR**

# SYNTHESIS OF 8-SUBSTITUTEDTHIOCARBAMIDO-1-METHYL-6-PHENYL-4H-[1,2,4] TRIAZOLO[4,3-a][1,4]BENZODIAZEPINES

**D. T. Tayade[a*] and P. R. Kale[b]**

[a]Department of Chemistry, Government Vidarbha Institute of Science and Humanities, Amravati 444604.
[b]Department of Chemistry, S.R.R.Lahoti Science College, Morshi 444905.

***Corresponding Author: D. T. Tayade**

Department of Chemistry, Government Vidarbha Institute of Science and Humanities, Amravati 444604.

**Article Received on 21/04/2016** **Article Revised on 12/05/2016** **Article Accepted on 31/05/2016**

**ABSTRACT**

Recently in this laboratory a novel series of 8-substitutedthiocarbamido-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepines **[IIIA(a-e)]** was successfully synthesized by the interactions of 8-choloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo [4,3-a] [1,4] benozodiazepine **(IA)** with various thioureas **(IIa-e)** in isopropanol medium. The structure determination and justification of the synthesized compounds were done on the basis of chemical characteristics, elemental analysis and spectral studies.

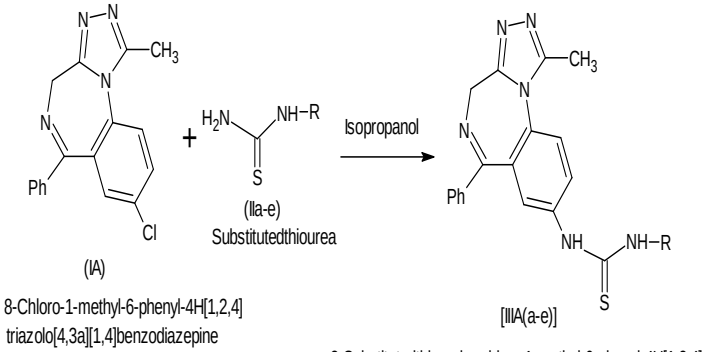
**KEYWORDS:** Various isothiocyanate, 8-choloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo [4,3-a] [1,4] benozodiazepine and isopropanol.

## INTRODUCTION

Benzodiazepine nucleus is useful nucleus in the case of liposome in a potent carrier for targeted doxorubicin having high affinity for sigma receptor and used for the treatment of human malignancies including human prostate cancer cells. 1,4-Benzodiazepinedione has been reported as potent antagonist's interaction in vitro and in cell-based assays and also proved that they possess anti-consultant, anxiolytic, anti-tumor properties.[1] It is effective against cholecystokinin receptor (CCK), opiate receptor and platelet glycoprotein antagonists.[2-3] Many derivatives of benzodiazepines are widely used as sedative, anti-depressive, anti-inflammatory and hypnotic agents.[4-5] It is also used as dyes for acrylic fibers.[6] Recently new series of 1,2,4-thiadiazoles, 1,3,5-thiadiazines and 1,3,5-dithiazines were synthesized by exploring the synthetic applications of -thiocarbamido, -amino, -halo, -cyano, etc. and their antimicrobial, antifungal, antibacterial, analgesic physiochemical parameters[7-10] were studied.

8-Chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a] [1,4] benozodiazepine **(IA)** and their derivatives showed agricultural, medicinal, biological, pharmaceutical, industrial significances and applications. By considering all these facts this research scheme was designed.

The main objective of the work is to synthesize a novel series of 8-substituted -thiocarbamido-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine **[III(a-e)].** This was synthesized by the interactions of 8-choloro-1-methyl-6-phenyl-4H-[1,2,4]-triazolo [4,3-a][1,4] benozodiazepine **(IA)** with various thioureas **(IIa-e)** in isopropanol medium **Scheme-I.**




(IA)
8-Chloro-1-methyl-6-phenyl-4H[1,2,4] triazolo[4,3a][1,4]benzodiazepine

(IIa-e)
Substitutedthiourea

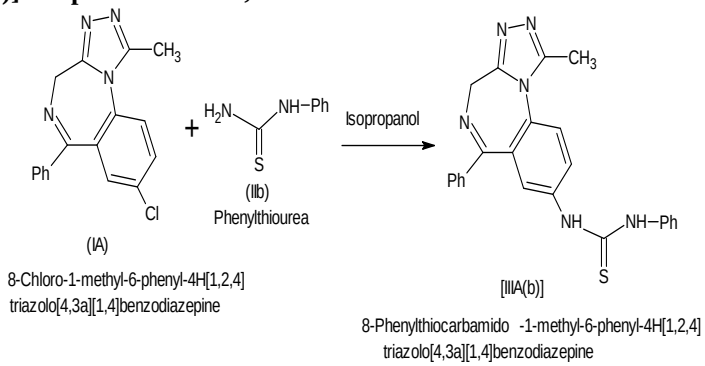
[IIIA(a-e)]
8-Substitutedthiocarbamido -1-methyl-6-phenyl-4H[1,2,4] triazolo[4,3a][1,4]benzodiazepine

Where, R= -H, -phenyl, -methyl, -ethyl, -allyl

**Scheme-I**

**Synthesis of 8-phenylthiocarbamido-1-methyl-6-phenyl-4H-[1,2,4] triazolo[4,3-a] [1,4] benzodiazepine**
8-Phenylthiocarbamido-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a[1,4]benzodi- azepine was synthesized by refluxing 8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo [4,3-a] [1,4] benozodiazepine **(IA)** and phenylthiourea **[IIA]** in isopropanol medium for 4 hours on water bath, lemon crystals were separated out at room conditions, filtered and dried. Recrystlised from aqueous ethanol. Yield 93 %, m.p. 215 $^0$C.

**The formation of [IIIA(b)]is depicted as below,**




**[IIIA(b)]**

**Properties of [IIIA(b)]**
It is lemon colour crystalline solid having melting point 215$^0$C. It gave positive test for nitrogen and sulphur. It was desulphurized by alkaline plumbite solution which clearly indicate the presence of C=S group. It was soluble in water, ethanol, DMSO-$d_6$ while insoluble in carbon tetrachloride, chloroform, benzene, petroleum ether.

It formed picrate having melting point 180$^0$C. Elemental analysis: [C: 66.70% (found), 67.92% (calculated), H: 03.74% (found), 04.71% (calculated), N: 19.80% (found), 19.81% (calculated), S: 06.50% (found), 07.54 % (calculated)]. IR Spectrum: The IR spectrum was carried out in KBr-pellets The important absorptions are correlated as (cm$^{-1}$) 3423.65 -N–H stretching, 2889.33 C-H stretching, 1722.43 N=C-N stretching, 1514.12 N-C=S stretching, 1155.36 C-N stretching. NMR Spectrum: The NMR spectrum was carried out in DMSO-$d_6$ and $CDCl_3$ This spectrum distinctly displayed the signals due to Ar-H protons at δ 9.6438-7.1048 ppm, –NH proton at δ 3.3378 ppm, -$CH_2$ protons at δ 2.5628-2.5537 ppm, -$CH_3$ protons at δ 1.1221 ppm.

Similarly, 8-thiocarbamido-1-methyl-6-phenyl-4H-[1,2,4] triazolo [4,3-a] [1,4] benzodi- azepine [IIIA(a)], 8-methylthiocarbamido-1-methyl-6-phenyl-4H-[1,2,4]triazolo [4,3-a] [1,4] benzodiazepine [IIIA(d)], 8-allylthiocarbamido-1-methyl-6-phenyl-4H-[1,2,4] triazolo[4,3-a] [1,4] benzodiazepine [IIIA(e)] were synthesized by the interactions of 8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4] benozodiazepine (IA) with thiourea (IIc), methyl- thiourea (IId) and allylthiourea (IIe) respectively by the above mentioned method and enlisted in Table No. II-5

**Table No. II-5**

| Sr.No. | **8-Substitutedthiocarbamido-1-methyl-6-phenyl-4H-[1,2,4]triazolo [4,3-a] [1,4] benzodiazepines (IIIc-e)** | **Yield (%)** | **M.P. ˚C** |
|---|---|---|---|
| 1. | 8-Thiocarbamido-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4] benzodiazepine **(IIIAa)** | 96 | 237 |
| 2. | 8-**Ethyl**-------benzodiazepine **[IIIA(c)]** | 94 | 203 |
| 3. | 8-**Methyl**------benzodiazepine **[IIIA(d)]** | 82 | 190 |
| 4. | 8-**Allyl**---------benzodiazepine [**(IIIA(e)]** | 91 | 178 |

**REFERENCES**

1. Hulme C., Peng J., Tang S. Y., Burns C. J., Morize I., Labaudiniere R. J., Org. Chem. 1998; 63: 8021.
2. Keating T. A., Armstrong R. W., J. Org. Chem., 1996; 61: 8935.
3. Kalinski C., Umkehrer M., Ross G., Kolb J., Burdacka, C., Hiller W., Tetrahedron Lett., 2006; 47: 3423.
4. Aversa M. C., Ferazzo A., Giannetto P., Kohnke F. H., Synthesis, 1986; 230.
5. Chimirri A., Grasso S., Ottana R., Romeo G., Zappala M., J. Heterocyclic Chem., 1990; 27: 371.

6. Herbert J. A. L., Suschitzky H. J. Chem. Soc., Perkin Trans, 1974; 1 2657.
7. Bansal R.K., J.Heterocycyclic Chemistry, 2012; 8; 12-24.
8. Fernandes P.S and Sonar T.M., J.Ind.Chem. Soc, 1986; 53(4): 427.
9. Saleem F., Eur. Pat., CHAPPL 87/1 APR, 1987; 13: 3600009, Chem Abstr, 1989; 110: 114893.
10. Hedge J.C., Satheesha Rai N. and Balkrishna K., J.Chem.Sci.,III, 2007; 9(4): 299-302.