e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
Volume:05/Issue:03/March-2023 Impact Factor- 7.868 www.irjmets.com

A REVIEW ON SYNTHESIS AND PHARMACOLOGICAL ACTIVITY THIOSERMICARBAZIDE

Waghmare Rahul R.*1, Lokhande Rahul P.*2, Tarade Akshay D.*3

*1,3UG Student, Department Of Pharmaceutical Chemistry, Samarth Institute Of Pharmacy, Belhe, Pune (Maharashtra) India.

*2Assistant Professor, Department Of Pharmaceutical Chemistry, Samarth Institute Of Pharmacy, Belhe, Pune (Maharashtra) India.

ABSTRACT

Thiosemicarbazides are potent intermediates for the synthesis of pharmaceutical and bioactive materials and thus, they are used extensively in the field of medicinal chemistry. The imine bond (-N=CH-) in this compounds are useful in organic synthesis, in particular for the preparation of heterocycles and non-natural β-aminoacids. A synthesis of some new thiosemicarbazide like 1-(3-bromo-4-hydroxy-5- methoxybenzylidene)-4-(4-bromophenyl)thiosemicarbazide by condensation of 3-bromo-4- hydroxy-5-methoxybenzaldehyde with 4-(4-bromophenyl)thiosemicarbazide is carried out. Organic compounds have plays vital role in biological chemical activities and also use for increase people's quality of life. Semicarbazide and thiosemicarbazide are sulfur and nitrogencontaining organic compounds with diverse biological activities. They are Schiff's bases formed by the condensation product of aldehydes or ketones with different amines. These derivatives are urea and thiourea derivatives depend on the attached aldehydes or ketones moiety. Antibacterial, antifungal, anticonvulsant, antitubercular, antimalarial, anticancer, analgesic, antipyretic, anti-inflammatory, antioxidant, antiviral.

Keywords: Thiosemicarbazide, Semi Carbazides, Metal Complexes, Spectral Characterization.

I. INTRODUCTION

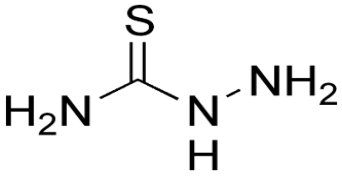
Thiosemicarbazides (TSC) having the -CO-NH-NHCS-NH- functional group are generally synthesized from reactions of hydrazides with isothiocyanates in different organic solvents [1]. TSC are used both as pharmacological active compound sand as starting compounds for the synthesis of diverse bioactiveheterocyclic compounds such as 1,2,4-triazole, 1,3,4- oxadiazole, 1,3,4-thiadiazole and thiazolinone [2-4]. They are also showed a wide range of various biological activities like antimicrobial [5], antiviral [6], anticancer [7], anti-inflammatory [8], anti-tubercular [9], topoisomerase IV and urease inhibitors [10,11]. Moreover, thiosemicarbazides can easily form metal complexes with different transition metals due to their donor groups such as nitrogen, oxygen, and sulfur

Thiosemicarbazides are convenient precursors which have been extensively utilized in heterocyclic synthesis. From the point of view of biological activity, thiosemicarbazide derivatives are useful intermediates and subunits for the development of molecules having pharmaceutical or biological interest. Within the last few years, an increased interest in the chemistry of thiosemicarbazides has developed. The results reported so far show that thiosemicarbazides undergo a wide variety of reactions that produced new chemical systems.

Thiosemicarbazide (NH2-NH-CSNH2) is the simplest hydrazine derivative of thiocarbamic acid [13]. The chemical behaviour of thiosemicarbazide is alike to its correspondent semicarbazide, however, is of superior chemical adaptability of the thione group as compared with that of keto group and is liable for more diverse behaviour of thiosemicarbazide [14].The utilization of these derivatives in organic synthesis has become a traditional approach for the preparation of a wide range of heterocyclic compounds [15].

e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
Volume:05/Issue:03/March-2023 Impact Factor- 7.868 www.irjmets.com

Drug Profile-

Thiosemicarbazide	
Drug Name -	Thiosemicarbazide
Synonym-	N-aminothiourea, thiocarbamylhydrazine, thiosemicarbazide, thiosemicarbazide, hydrochloride, thiosemicarbazide monohydrochloride
Structure-	
Odour	Odourless
Colour	White Crystalline Powder
Molecular Weight-	91.14
Molecular Formula-	CH_5N_3S
Uses-	used in photography, Anti-tubercular activity, Anti-viral.
Melting Point	ca 180° dec
Solubility	Soluble in water, ethanol, alcohols and hot methanol.
Storage & Sensitivity	Ambient temperatures.

II. SYNTHESIS OF THIOSEMICARBAZIDE

The synthesis of thiosemicarbazides may be carried out in several ways. The general method involves the preparation of thiosemicarbazides by nucleophilic additions of amines or carbohydrazides to isothiocyanates or carbon disulfide.

2.1. Preparation of Thiosemicarbazide compounds

A mixture of aromatic aldehyde [0.01 mole], thiosemicarbazide [0.01 mole] in 20 mL of ethanol, and four drops of glacial acetic acid were heated under reflux for 5 h. The product was cooled to room temperature, and the solid was filtered, dried, and purified to provide compounds via recrystallization with ethanol.

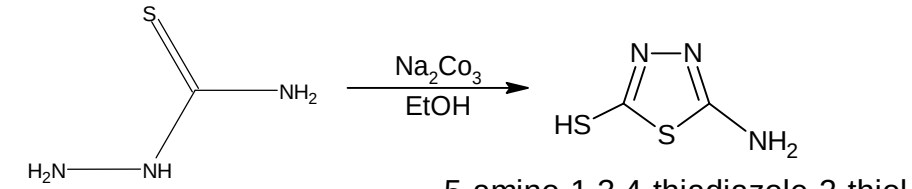
2.2. Synthesis of 2-(4-substituted-benzylidene hydrazono)-1, 3- thiazolidine-4-one compounds

A mixture of thiosemicarbazide derivatives compounds was prepared by heating and continuous stirring for 0.01 mole chloroacetic acid (0.01 mole), and- anhydrous sodium acetate (0.01 mole) in 20 mL glacial acetic acid under reflux for 8 h. The produced mixtures for compounds were left to cool via poured into ice cold water, and the separated solid was filtered off, washed with water, dried, and recrystallized by absolute ethanol.

2.3. Synthesis of 2-amino -1,3,4- thiadiazole -5- thiol compound

Exact 0.02 mole, 1.82 (g) from thiosemicarbazide suspended in 15 mL ethanol was added to anhydrous sodium carbonate (0.02 mole, 2.12 g) and 3 mL carbon disulphide, the produced mixture was warmed with stirring under reflux for 1 h., then heated on the steam bath for 4 h. The most solvent was removed, and the residue was dissolved in ice- water and acidified with concentrated hydrochloric acid

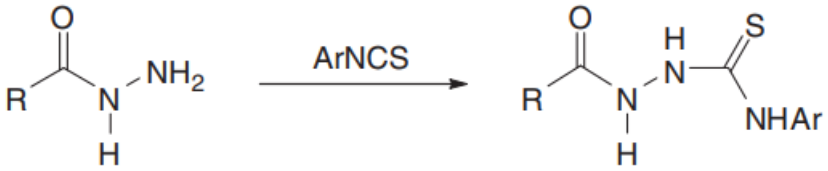
e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
Volume:05/Issue:03/March-2023 Impact Factor- 7.868 www.irjmets.com



hydrazinecarbothioamide 5-amino-1,3,4-thiadiazole-2-thiol

2.4. Using isothiocyanates

Treatment of carbohydrazides with aryl isothiocyantes under different reaction conditions (e.g., pyridine, NaOH, KOH and NaH) gave the 1,4-disubstituted thiosemicarbazide derivatives 1[13-22]

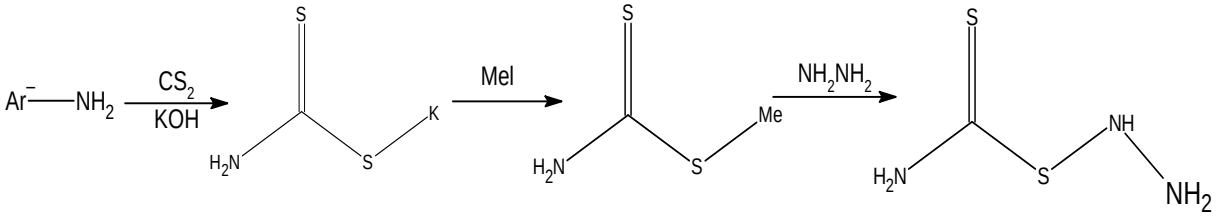


1

Reaction- Synthesis of 1,4 -Disubstituted Thiosemicarbazide

2.5. Using carbon disulfide

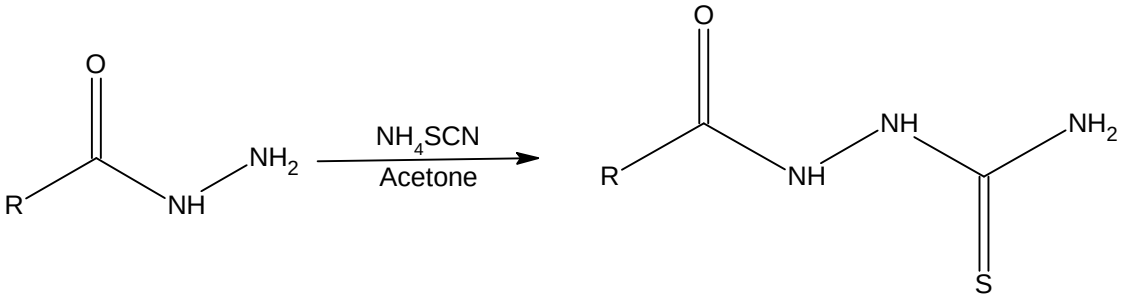
The base-catalysed nucleophilic addition of arylamines to carbon disulfide gives potassium aryl carbamodithioates which react with methyl iodide to afford N-aryl methyldithiocarbamates which on hydrazinolysis give 4-arylthiosemicarbazides



Reaction- Synthesis of 4-arylthiosemicarbazides

2.6. Using ammonium thiocyanate

Heating of carbohydrazides with ammonium thiocyanate in acetone afforded 1-acylthiosemicarbazides

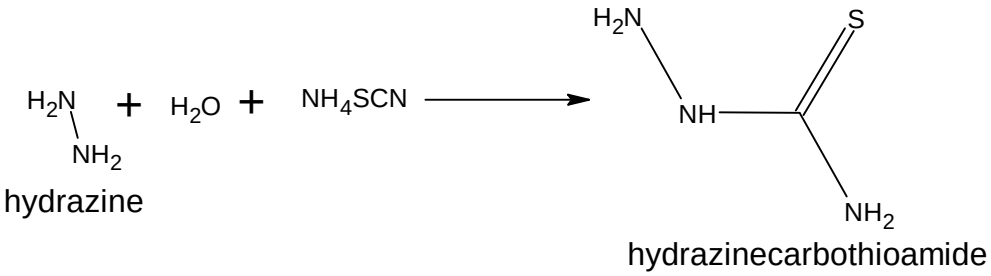


Reaction- Synthesis of 1-arylthiosemicarbazides

2.7. Preparation of Thiosemicarbazide compounds

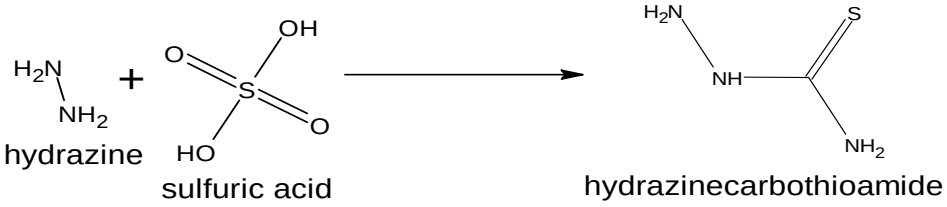
To a solution of 224 m. 25% hydrazine hydrate and 100 ml. water, 144 g. hydrazine sulfate were added at 40° C. while stirring; the pH was adjusted between 3 and 4. To this solution at a temperature of 40 C., were added 240 g. ammonium thiocyanate whereby a solution of hydrazonium thiocyanate resulted with simultaneous formation of ammonium sulfate. We then added 6 mi. acetone, and the mixture was heated to 95-110 C. for 8 hours. After the reaction was completed, the reaction mixture was cooled down to 8° C. and the crystallized thiosemicarbazide was drawn off, washed with water, and dried. Obtained were 178 g. thiosemicarbazide corresponding to 89% of the theoretical yield.

e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
Volume:05/Issue:03/March-2023 Impact Factor- 7.868 www.irjmets.com



2.8. Preparation of Thiosemicarbazide compounds

To a solution of 112 ml. 25% hydrazine hydrate, 72 g. hydrazinesulfate were added under stirring, and the solution was then adjusted to a pH of 3-4. To this solution, 120 g. ammonium thiocyanate were added at 40 C. Stirring was continued for another 10 minutes, whereafter 105 ml. methanol were added. After stirring for a short while, the precipitated ammonium sulfate was drawn off. After addition of 3 ml. acetone, the filtrate was boiled for 16 hours under reflux. After cooling down to 7 C., the crystallized thiosemicarbazide was drawn off, washed and dried. Obtained were 87 g., corresponding to 87% of the theoretical yield.

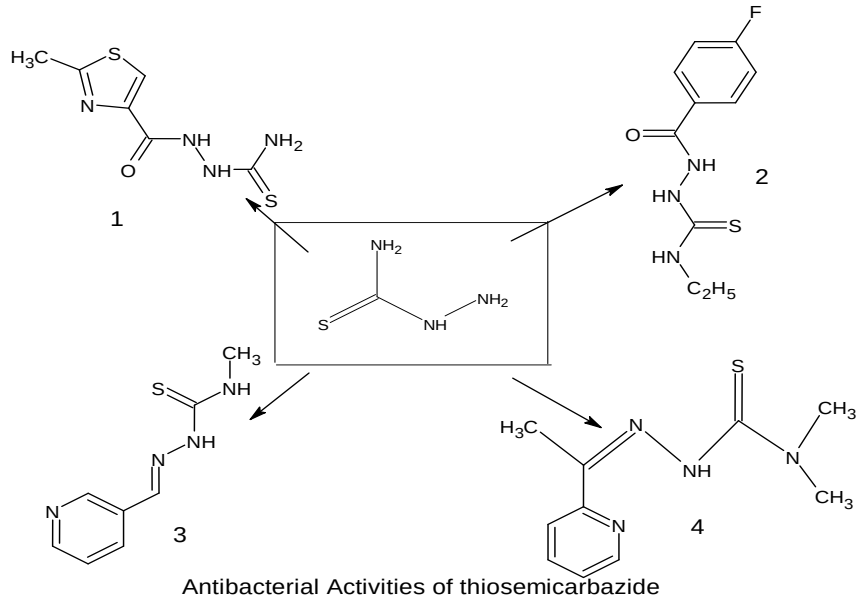


III. BIOLOGICAL ACTIVITIES OF THIOSEMICARBAZONE DERIVATIVES

The shortest hydrazine derivative of thiocarbamide acid is thiosemicarbazide (NH2- NH-CSNH2). The molecular thiosemicarbazide is similar to its semi carbazide analogs, but the thione group has greater chemical versatility than the keto group, resulting in more complex actions of thiosemicarbazide derivatives.

IV. ANTIBACTERIAL ACTIVITY

Thiosemicarbazide derivatives have shown to be effective antibacterial agents. Thiosemicarbazide derivatives have been possessing excellent antibacterial activities. Compounds 1-(2,4-dimethyl thiazole-5- carboxyl)-N-4-ethyl-thiosemicarbazide (1), 1-(4- fluoro benzoyl)-N-4-ethyl thiosemicarbazide (2), 2-pyridine-aldehyde-4-N-methyl thiosemicarbazone (3) and 2-acetyl pyridine-4-N, N'-dimethylthio-semicarbazone (4) were tested for their in vitro antibacterial activities against E. coli at 0.4-0.5µM concentration. Compound 2 has the greatest lipophilic capacity to affect the penetration of Gram-negative species such as E. coli. Compounds 3 and 4 have specific antibacterial effects on both E. coli and S. aureus at 0.1 mg/ml [28]



Antibacterial Activities of thiosemicarbazide

e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
Volume:05/Issue:03/March-2023 Impact Factor- 7.868 www.irjmets.com

V. ANTIVIRAL ACTIVITY

A virus particle, also known as a virion, is essentially a nucleic acid (DNA or RNA) enclosed in a protein shell or coat. Viruses are extremely small, approximately 15-25 nano meters in diameter. A virus is a small infectious agent that can replicate only inside the living cells of an organism. Viruses can infect all types of living organisms, such as animals and plants to bacteria. For many years virus diseases have been considered as intractable to selective antiviral drugs because the replicative cycle of the virus was assumed to be too closely interwoven with normal cell metabolism so that any attempt to suppress virus reproduction would be doomed to kill (or severely harm) the uninfected cell as well. With the elucidation of virus-specific events as targets for chemotherapeutic attack and the advent of a number of specific antiviral agents, it has become increasingly clear that a selective chemotherapy of virus infections can be achieved and that virus reproduction can be suppressed without deleterious effects on the host [29,30]

VI. APPLICATIONS OF THISEMICARBAZIDE

Thiosemicarbazides were formerly used to stimulate respiration or as antidotes to barbiturate overdose. They are now most commonly used as experimental tools. Thiosemicarbazide is used as a reagent to detect ketones and certain metals. It is used in photography. It is also an intermediate in forming a class of compounds that may be used as herbicides, It will dissolve in water. This material is used as a reagent for ketones and certain metals, for photography and as a rodenticide. It is also effective for control of bacterial leaf blight of rice.

VII. CONCLUSION

On the Basis of this Study we Conclude that the thiosemicarbazide is biological active in various ways which is very useful in pharmaceutical industry. Thiosemicarbazide is screened for their in vivo biological Activities such as Antibacterial activity and Antiviral activity with the help of different bacterial strains E.coli and S. Aureus Bacteria. the various applications of thiosemicarbazide are present.

VIII. REFERENCE

[1] B. F. Abdel-Wahab, S. F. Mohamed, A. E.-G. E. Amr, M. M. Abdalla, Synthesis and reactions of thiosemicarbazides, triazoles, and Schiff bases as antihypertensive α-blocking agents, Monatsh Chem, 139, 2008, 1083-1090.

[2] S. Singhal, S. Arora, S. Agarwal, R. Sharma, N. Singhal, A review on potential biological activities of thiosemicarbazides, World J Pharm Sci, 2013, 2, 4661-4681.

[3] A.G. Galina, N.K. Angelina, Thiosemicarbazides in the synthesis of five- and six membered heterocyclic compounds, Russ Chem Rev, 81, 2012, 494-523.

[4] A.A. Hassan, A.M. Shawky, Thiosemicarbazides in heterocyclization, J Heterocyclic Chem, 48, 2011, 495-516.

[5] S.G. Kücükgüzel, E.E. Oruc, S. Rollas, F. Sahin, A. Özbek, Synthesis, characterisation and biologicalactivity of novel 4- thiazolidinones, 1,3,4-oxadiazoles and some related compounds, Eur J Med Chem, 37, 2002, 197-206.

[6] T. Plech, M. Wujec, A. Siwek, U. Kosikowska, A. Malm, Synthesis and antimicrobial activity of thiosemicarbazides,s-triazoles and their Mannich bases bearing 3-chlorophenyl moiety, Eur J Med Chem, 46, 2011, 241-248.

[7] G. Cihan-Üstündag, E. Gürsoy, L. Naesens, N. UlusoyGüzeldemirci, G. Çapa, Synthesis and antiviral properties of novel indole-based thiosemicarbazides and 4-thiazolidinones, Bioorgan Med Chem, 24, 2016, 240-246.

[8] Y. Dadaş, G. P. Coşkun, O. Bingol-Akpinar, D. Ozsavci, Ş. G. Kucukguzel, Synthesis and anticancer activity of tolmetin thiosemicarbazides, Marmara Pharm J, 19, 2015, 259-267

[9] M. Amir, S. Kumar, Synthesis and evaluation of antinflammatory, analgesic, ulcerogenic and lipid peroxidation properties of ibuprofen derivatives, Acta Pharmaceut, 57, 2007, 31-45.

[10] K.D. Thomas, A.V. Adhikari, S. Telkar, I.H Chowdhury, R. Mahmood, N.K Pal, G. Row, E. Sumesh, Design, synthesis and docking studies of new quinoline-3-carbohydrazide derivatives as antitubercular agents, Eur J Med Chem, 46, 2011, 5283-5292.

[11] A. Siwek, P. Staczek, J. Stefanska, Synthesis and structureactivity relationship studies of 4-arylthiosemicarbazidesas topoisomerase IV inhibitors with Gram-positive antibacterial activity. Searchfor molecular basis of antibacterial activity of thiosemicarbazides, Eur J Med Chem, 46, 2011, 5717-5726.

[12] B. Ali, K.M. Kahan, A. Kanwal, S. Hussain, S. Hussain, M. Ashraf, M. Raiz, A. Waddood, S. Perveen, Synthetic nicotinic/isonicotinic thiosemicarbazides: In vitro urease inhibitory activities and molecular docking studies, Bioorg Chem, 79, 2018, 34-45.

[13] M.A. Bhat, A.A. Khan, H.A. Ghabbour, C.K. Quah, H.K. Fun, x-ray structure and antimicrobial activity of N-(4-chlorophenyl)-2-(pyridin-4-ylcarbonyl) hydrazinecarbothioamide, Trop. J. Pharm. Res. 15 (2016) 1751–1757. doi: 10. 4314/tjpr.v15i8.22.

[14] R.S. Keri, K. Chand, S. Budagumpi, S.B. Somappa, S.A. Patil, B.M. Nagaraja, An overview of benzo [b] thiophene-based medicinal chemistry, Eur. J. Med. Chem. 138 (2017) 1002–1033. doi: 10.1016/j.ejmech.2017.07.038.

[15] M.A. Metwally, S. Bondock, H. El-Azap, E.E. Kandeel, Thiosemicarbazides: synthesis and reactions, J. Sulfur Chem. 32 (2011) 489–519. doi: 10.1080/ 17415993.2011.601869.

[16] Nalan, T.K.; Gueltaze, C.; Aysel, G.; Meltem, U.; Dilek, S. J. Enzyme Inhib. Med. Chem. 2010, 25, 126–131.

[17] Hui-Cheng, W.; Rong-Shan, L.; Heng-Shan, D. Indian J. Heterocycl. Chem. 2009, 19, 99–100.

[18] Asif, H.; Md, A.; Afroz, S.; Yasmin, K. Indian J. Heterocycl. Chem. 2009, 19, 93–94.

[19] Mihaela, M.; Valeriu, S.; Lenuta, P.; Marcel, P.; Jacques, D.; Cristian, P. Molecules 2009, 14, 2621–2631.

[20] Shui-Sheng, C.; Song, Y.; Hui-Quan, L.; Si-Chang, S. Huaxue Shiji 2009, 31, 507–510; Chem. Abstr. 2009, 151, 508539.

[21] Horacio, C.; Gerald, B.; Dominique, S. J. Org. Chem. 2009, 74, 5553–5558. (8) Kunwar, A.; Pandey, A.K.; Singh, S.C.; Singh, S. Indian J. Appl. Pure Biol. 2009, 24, 155–160; Chem. Abstr. 2009, 152, 74971.

[22] Monazza, S.; Tashfeen, A.; Shahid, H.; Khalid, M.K. ARKIVOC 2009, 7, 210–221. (10) Ahmet, C.; Pelin, K.; Metin, K. Asian J. Chem. 2009, 21, 617–626.

[23] Prabhu, C.J.; Suresh, S.; Basavaraj, K. Orient. J. Chem. 2009, 25, 1023–1028.

[24] Basavaraja, K.M.; Somasekhar, B.; Appalaraju, S. Indian J. Heterocycl. Chem. 2008, 18, 69–72.

[25] Spali´nska, K.; Foks, H.; Ke¸dzia, A.; Wierbowska, M.; Kwapisz, E.; Ge¸bska, A.; ZiółKowska-Klinkosz, M. Phosphorus, Sulfur Silicon 2006, 181, 609–625.

[26] Pandeya, S.N.; Sriram, D.; Nath, G.; Declecq, E. Eur. J. Pharm. Sci. 1999, 9, 25–31.

[27] Yogeeswari, P.; Sriram, D.; Mehta, S.; Nigam, D.; Mohankumar, M.; Muougesan, S.; Stables, J.P. Farmaco 2005, 60, 1–5. (16) Demirbas, N. Turk. J. Chem. 2005, 29, 125–133.

[28] M. Sheikhy, A.R. Jalilian, A. Novinrooz, F. Motamedi-Sedeh. Synthesis and in vitro antibacterial evaluation of some thiosemicarbazides and thiosemicarbazones. J. Biomed. Sci. & Engineer., 5 (2012) 39-42.

[29] E. De Clarcq, J. Pharm. Exp. Therap., 197, 1 (2001).

[30] I.J. Kang, L.W. Wang, T.A. Hsu, A. Yueh, C.C. Lee, Y.-C. Lee, C.-Y. Lee, Y.-S. Chao, S.-R. Shih and J.-H. Chern, Bioorg. Med. Chem. Lett., 21, 1948 (2011).

[31] Sr R J L. Hawley's Condensed Chemical Dictionary, 15th Edition[J]. Wileys Scientific Technical & Medical Databases, 2007, 14(1):592-593.

[32] Greenstein G R. The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals (14th edition)[J]. Reference Reviews, 2006, 21(6):40-40.