The American Journal of Applied Sciences
(ISSN – 2689-0992)
Published: September 29, 2020 | **Pages:** 143-153
Doi: https://doi.org/10.37547/tajas/Volume02Issue09-23

IMPACT FACTOR
2020: 5. 276

Journal Website: http://usajournalshub.com/index,php/tajas

Synthesis Of 2,5-Dimersapto-1,3,4-Thiadiazol Products

Jololiddinov Fazliddin Yuldashali Ugli
Trainee-Researcher Of Academic Institute Of Bioorganic Chemistry Named After O.S Sodikov Laboratory Of Low Molecular Weight Biologically Active Compounds, Uzbekistan

Xaitboev Xamid
Senior Researcher, Candidate Of Chemical Sciences Of Academic Institute Of Bioorganic Chemistry Named After Os Sodikov Laboratory Of Low Molecular Biologically Active Compounds, Uzbekistan

Boboev Baxrom Nurillaevich
Doctor Of Chemical Sciences, Professor, Head Of The Department Of Chemistry Of Natural Compounds, Faculty Of Chemistry, National University Of Uzbekistan

ABSTRACT

Potentially bioactive 2,5-bis derivatives of 1,3,4-thiadiazole with alkaloid moieties were synthesized byreaction of 1,3,4-thiadiazol-2,5-dithiol with N-acryloyl-substituted derivatives of the alkaloids anabasine,cytisine, and D-pseudoephedrine.1,3,4-Thiadiazole-2,5-disulfonic acid was synthesized by oxidation of 2,5-dimercapto-1,3,4-thiadiazole,and onium salts of this acid were prepared by its reactions with selected alkaloids and secondaryamines.

KEYWORDS

Synthesis 1,3,4-thiadiazol-2,5-dithiol, alkaloids, N-alkaloid-substituted acrylamides,1,3,4-Thiadiazole-2,5-disulfonic acid

INTRODUCTION

One of the main tasks of organic chemistry is the synthesis and production of substances with new therapeutic properties. Today, chemists are interested in heterocyclic compounds and their applications in pharmaceuticals and chemistry.1,3,4-thiadiazole is a common heterocyclic compound containing two nitrogen and sulfur atoms. There are several isomers of 1,3,4-thiadiazole, including 1,2,3-thiadiazole, 1,2,4-

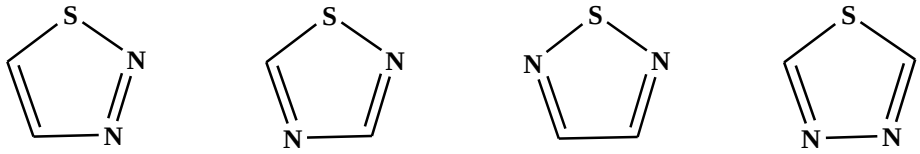
The American Journal of Applied Sciences
(ISSN – 2689-0992)
Published: September 29, 2020 | **Pages:** 143-153
Doi: https://doi.org/10.37547/tajas/Volume02Issue09-23

IMPACT FACTOR
2020: 5. 276

thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole [1]. Scheme 1

1,3,4-Thiadiazole was first described in 1882 by Fischer and further developed by Busch and his coworkers .The advent of sulfur drugs and the later discovery of mesoionic compounds greatly accelerated the rate of progress in this field[2].

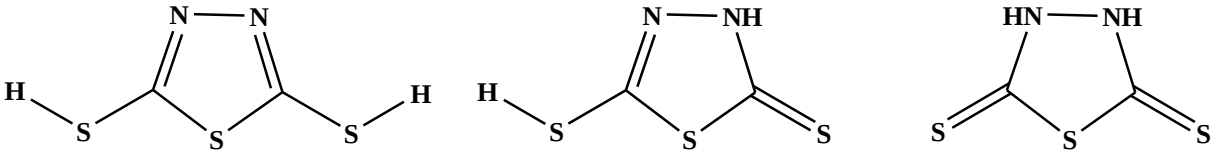
Scheme 1. Isomers of thiadiazole.



1,2,3 thiadiazole 1,2,4 thiadiazole 1,2,5 thiadiazole 1,3,4 thiadiazole

Thiadiazole is found in the live form of ditiolvadition tautome in the literature preserved in gold gugut. In fact, the first of the three tautomeric structures recorded in the literature is the most common.

Scheme2. Three tautomer shapes



-dithiol from 5-mercapto-1,3,4-thiadiazole-2(3H)-thione -dithione from

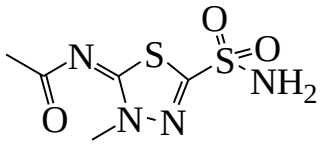
1,3,4-thiadiazole derivatives are widely used in medicine, pharmaceuticals and agriculture [1]. New derivatives of 1,3,4-thiadiazole are gaining popularity because they are widely used in various directions [4]. They are used against fungi [5-8], antibacterial [9-12], anti-inflammatory [13-15], analgesic [16-17], anti-leishmaniasis [18-19], anti-cancer [20-22], anti-oxidant [23-26], molluscicidal [27 -28], antidiabetic [29], central nervous system (CNS) depressant [30], anticonvulsant [31-32], anti-tuberculosis [33-34], anti-depressant [35], antitumor [36] and others, therefore, this study is important in the synthesis of new derivatives of 2,5-dimersapto-1,3,4-thiadiazole.

1,3,4-thiadiazole derivatives have high potential in agrochemistry as herbicides, fungicides, insecticides [37], pesticides, bactericides and plant growth regulators [1]. Drugs containing 1,3,4-thiadiazole nuclei, such as metazolamide, megazol, acetazolamide, and cefazolins, are known [38,39]

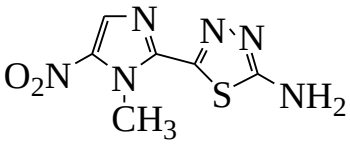
The American Journal of Applied Sciences
(ISSN – 2689-0992)
Published: September 29, 2020 | **Pages:** 143-153
Doi: https://doi.org/10.37547/tajas/Volume02Issue09-23

IMPACT FACTOR
2020: 5. 276

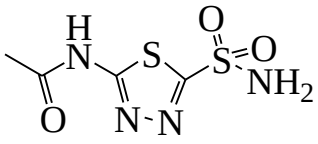
Scheme 3



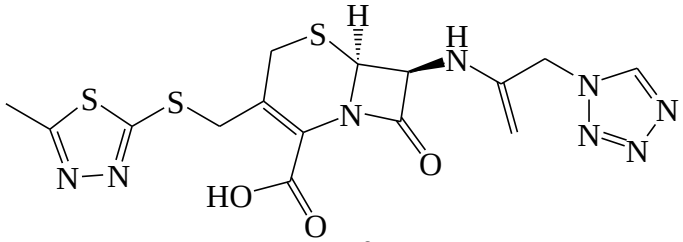
Metazolamide



Megazol



Acetazolamide



Cefazolin

MATERIALS AND METHODS

Experimental

The course of reactions and purity of 2–4were monitored using TLC on Silufol UV-254 standard plates with elutionby propan-2-ol:NH4OH:H2O (7:2:1) and detection by iodine vapor. Elemental analyses of all compounds agreed with thosecalculated. Melting points were determined on a Boetius apparatus. IR spectra in KBr disks were recorded on an Avatar-320spectrometer; PMR spectra in DMSO-d6, on a Bruker AC-300 spectrometer at operating frequency 300 MHz relative to TMS internal standard (compound 2,3,4).

The IR spectra of the compounds were recorded onan Avatar-320 spectrometer in KBr pellets and mullsin mineral oil, and the 1H and 13C NMR spectra, ona Mercury-300 spectrometer with a working frequencyof 300 MHz, solvent DMSO-d6.(compound5-12).

Synthesis of 2,5-dimercapto-1,3,4-thiadiazole (1) [40]:

A mixture of (99%) hydrazine hydrate (5 mL, 0.02 mol) and carbon disulfide (15 mL, 0.02 mol) with drypyridine (50 mL) was refluxed for (5 h). Then the excess solvent was then distilled off, and the resulting solid was separated out by adding (25 mL) of water and (5 mL) of hydrochloric acid. The mixture was then filteredand the solid was recrystalized from ethanol.

2,5-Bis(1-(anabasin-1-yl)propan-1-on-3-thio)-1,3,4-thiadiazole (2)[41].

A solution of anabasine (1.62 g, 0.01 mol) inbenzene was cooled, stirred vigorously in the presence of triethylamine (1.01 g, 0.01 mol), treated dropwise with acryloylchloride(0.91 g, 0.01 mol) over an hour, and stirred at room temperature for 2 h. The resulting precipitate of triethylammoniumhydrochloride was filtered off. The filtrate was cooled, stirred, treated dropwise with a solution of 1,3,4-thiadiazol-

The American Journal of Applied Sciences
(ISSN – 2689-0992)
Published: September 29, 2020 | **Pages:** 143-153
Doi: https://doi.org/10.37547/tajas/Volume02Issue09-23

IMPACT FACTOR
2020: 5. 276

2,5-dithiol (0.75 g, 0.005 mol) in anhydrous EtOH over an hour, and stirred at room temperature for 2 h. The resulting precipitatewas filtered off to afford a white powdery compound (1.3 g, 44%), mp 89–90°C (EtOH), Rfo.82, C28H34N6O2S3. PMRspectrum (300 MHz, DMSO-d6, δ, ppm, J/Hz): 1.81 (4H, m, H-9,9′), 2.08 (4H, m, H-8,8′), 2.50 (4H, m, H-10,10′), 2.81(4H, t, J14,15 = 6.0, H-14,14′), 3.27 (2H, m, H-7,7′), 3.32 (4H, t, J15,14 = 6.0, H-15,15′), 3.71 (4H, m, H-11,11′), 7.15 (2H, q,H-3,3′), 7.58 (2H, q, H-4,4′), 8.31 (2H, d, H-6,6′), 8.50 (2H, d, H-2,2′).

2,5-Bis(1-(cytisin-1-yl)propan-1-on-3-thio)-1,3,4-thiadiazole (3) [41].

Was synthesized analogously to 1 from cytosine (1.9 g, 0.01 mol) to afford a white powdery compound (2.4g, 75%),mp 121–122°C (EtOH), Rfo.53, C30H34N6O4S3. PMRspectrum (300 MHz, DMSO-d6, δ, ppm, J/Hz): 1.92 (4H, m, H-8,8′), 2.81 (4H, t, J14,15 = 6.0, H-14,14′), 2.90 (4H, m,H-11,11′), 2.98 (2H, m, H-9,9′), 3.10 (2H, m, H-7,7′), 3.30 (4H, t, J15,14 = 6.0, H-15,15′), 3.36 (4H, m, H-13,13′), 3.80 (2H, m,Hax-10,10′), 4.36 (2H, m, Heq-10,10′), 5.98 (2H, dd, H-5,5′), 6.33 (2H, dd, H-3,3′), 7.23 (2H, dd, H-4,4′).

2,5-Bis(1-(D-pseudoephedrin-1-yl)propan-1-on-3-thio)-1,3,4-thiadiazole (4) [41].

Was synthesized analogously to 1from D-pseudoephedrine (1.65 g, 0.01 mol) to afford an oily compound that was purified by column chromatography over silica gel with elution by benzene:EtOH (2:1), Rf 0.78, C28H36N4O4S3. PMR spectrum (300 MHz, DMSO-d6, δ, ppm, J/Hz):0.98 (6H, d, 2CH–CH3), 2.48 (2H, m, 2CH–N), 2.65 (6H, s, 2N–CH3), 2.80 (4H, t, J14,15= 6.0, H-14,14′), 3.40 (4H, t, J15,14= 6.0, H-15,15′), 4.68 (2H, d, CH–OH), 5.35 (2H, s, 2OH), 6.28, 7.34 (10H, m, 2ArH).

Synthesis of 1,3,4-Thiadiazole-2,5-disulfonic acid(5) [42]:

A 2.5% aqueous solution of 6.32 g (0.04 mol) of KMnO4 was added dropwise with stirring at room temperature over a period of 3 h to an aqueous solution of 1.5 g (0.01 mol) of 2,5-dimercapto-1,3,4-thiadiazole. The mixture was heated with stirring on a water bath until its complete decolorization. The precipitate of manganese dioxide was filtered off, the filtrate was evaporated, and the dry residue was washed with alcohol. 1,3,4-Thiadiazole-2,5-disulfonic acid 4was recrystallized from ethanol-water, 10 : 1.

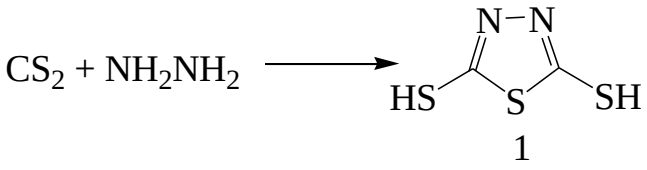
Synthesis of alkaloid- and amine-containing salts of 1,3,4-thiadiazole-2,5-disulfonic acid, (6-12) [42].

An aqueous solution of 0.02 mol of appropriate secondary amine or alkaloid was added dropwise with stirring over a period of 1 h to an aqueous solution of 2.46 g (0.01 mol) of 1,3,4-thiadiazole-2,5-disulfonic acid 6. The mixture was stirred at room temperature for 12 h and left in a vacuum desiccator to remove the solvent. The solid residue was washed with alcohol, filtered off, and recrystallized from ethanol-water, 10 : 1.

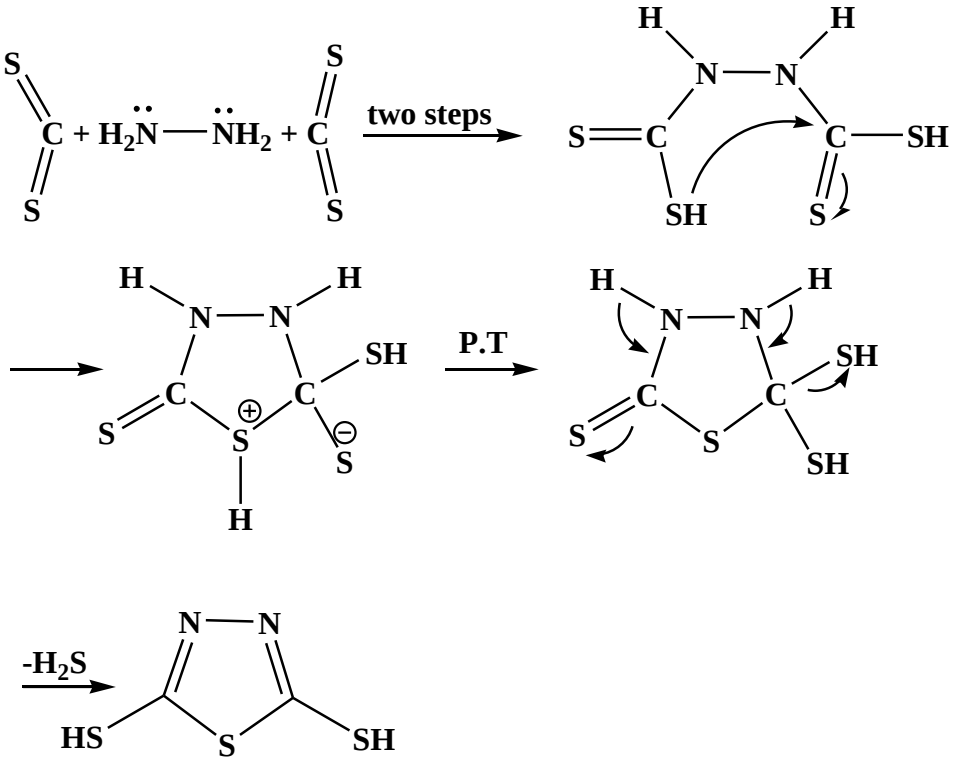
The American Journal of Applied Sciences
(ISSN – 2689-0992)
Published: September 29, 2020 | **Pages:** 143-153
Doi: https://doi.org/10.37547/tajas/Volume02Issue09-23

IMPACT FACTOR
2020: 5. 276

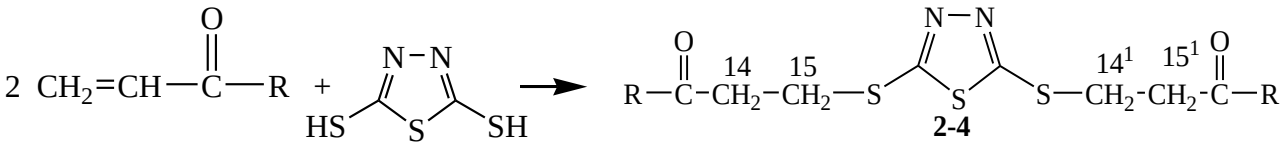
RESULTS AND DISCUSSION



The mechanism for the formation of 2,5-dimercapto-1,3,4-thiadiazole (1) is shown in **Scheme :4**



Scheme 4.Reaction mechanism for the preparation of compound 1.



The American Journal of Applied Sciences
(ISSN – 2689-0992)
Published: September 29, 2020 | **Pages:** 143-153
Doi: https://doi.org/10.37547/tajas/Volume02Issue09-23

IMPACT FACTOR
2020: 5. 276

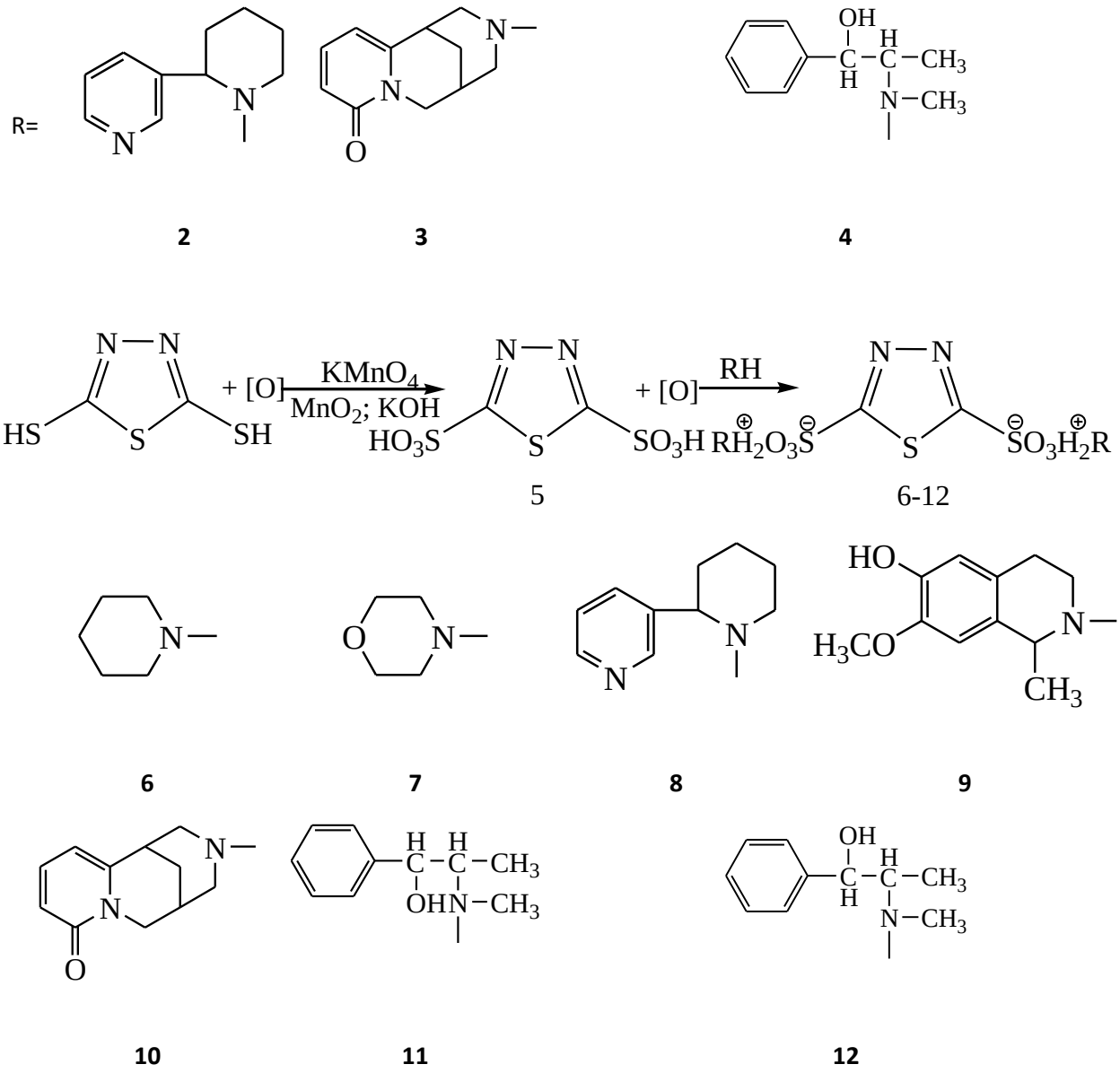


Table 1: Elemental analysis and physical properties of prepared compounds5-12**[42]**.

№	Formula	%Yield	m.p(C)	Elemental analysis calc. (found)		
				%C	%H	%N
5	$C_2H_2N_2O_6S_3$	98.0	>350	9.67 (9.76)	0.90(0.81)	11.30(11.38)
6	$C_{12}H_{24}N_4O_6S_3$	76.9	>350	34.7(34.62)	5.72(5.77)	13.35(13.46)
7	$C_{10}H_{20}N_4O_8S_3$	66.9	>350	28.5(28.57)	4.64(4.76)	13.25(13.33)

The American Journal of Applied Sciences
(ISSN – 2689-0992)
Published: September 29, 2020 | **Pages:** 143-153
Doi: https://doi.org/10.37547/tajas/Volume02Issue09-23

IMPACT FACTOR
2020: 5. 276

8	$C_{22}H_{30}O_6S_3$	42.8	>350	46.39(46.32)	5.20(5.26)	14.84(14.74)
9	$C_{24}H_{30}N_4O_6S_3$	52.6	>350	50.81(50.88)	5.38(5.30)	9.81(9.89)
10	$C_{24}H_{30}N_6O_8S_3$	70.0	>350	46.00(46.01)	4.70(4.79)	13.51(13.42)
11	$C_{22}H_{32}N_4O_8S_3$	50.1	>350	45.89(45.83)	5.50(5.56)	9.82(9.72)
12	$C_{22}H_{32}N_4O_8S_3$	56.1	>350	45.77(45.83)	5.44(5.56)	9.70(9.72)

The yields of final products 2–4 were 36–75% and depended not so much on the electron-donating properties of thealkaloid moiety in the amide as on the conformational rigidity of the rings in the starting alkaloids that prevented the β-C atomof the double bond from being shielded. Compound 3 was obtained in the highest yield. This was explained by the conformationalrigidity of the cytisine rings compared with the conformational flexibility of anabasine and D-pseudoephedrine. Products 2–4 were powdery and oily compounds that were soluble in EtOH and CHCl3 with heating. Their structuresand compositions were proved using IR and PMR spectroscopy and elemental analysis.IR spectra of 2–4 contained absorption bands at 780–730 cm–1 (C–SH), 1060–1040, 1160–1120, 1270–1250 (S–C–S,N=C–S, N–N), and 1460–1390 (N=C) that were identified as absorption bands of the thiadaizole ring [43, 44]. Other functionalgroups of 2–4 appeared in characteristic regions of the spectrum at 1695–1624 (C=O), 1480–1440 (–CH2–), and 705–680(C–S–) [45].

The structure and composition of 5-12wereconfirmed by IR, 1H NMR, and 13C NMR spectroscopy,and also by elemental analysis.The IR spectra of all the onium salts synthesizedcontain characteristic absorption bands of the thiadiazolering at 680, 730, 1400, and 1500 cm-1,bands in the range 656-649 cm-1 assigned to -SO3-vibrations, and absorption bands at 3501-3421 cm-1characteristic of secondary ammonium salts [45].

In the 1H NMR spectra of 6-12, recorded inDMSO-d6, protons of the ammonium group appearas an ill-resolved multiplet centered at 14.6 ppm.The chemical shifts of signals from protons of alkaloidand secondary amine fragments have typicalvalues[46].

In the 13C NMR spectrum of 1,3,4-thiadiazole-2,5-disulfonic acid 5, the heterocyclic carbon atom appearsas a singlet at 168.0 ppm. In the 13C NMR spectrumof piperidinium salt of 1,3,4-thiadiazole-2,5-disulfonicacid 6, the heterocyclic carbon atom appears asa singlet at 158.4 ppm, and carbon atoms of the piperidinefragment give signals at 23.1, 25.5, 26.0, 42.5,and 45.5 ppm[47].

CONCLUSION

2.5-dimercapto-1,3,4-thiadiazole derivatives were synthesized. Oxidation of 2,5-dimercapto-1,3,4-thiadiazolewith an aqueous solution of KMnO4 yielded 1,3,4-thiadiazole-2,5-disulfonic acid. Its reactions with selectedalkaloids and cyclic secondary amines gavethe corresponding salts.

The American Journal of Applied Sciences
(ISSN – 2689-0992)
Published: September 29, 2020 | **Pages:** 143-153
Doi: https://doi.org/10.37547/tajas/Volume02Issue09-23

IMPACT FACTOR
2020: 5. 276

REFERENCES

1. Yang Hu,Cui-Yun Li,Xiao-Ming Wang,Yong-Hua Yang, and Hai-Liang Zhu.,1,3,4-Thiadiazole: Synthesis, Reactions, and Applications in Medicinal,Agricultural, and Materials Chemistry.,Chem. Rev.2014, 114, 10, 5572–5610.
2. KratikaShrivastava, Suresh Purohit and SaritaSinghal. Studies On Nitrogen And Sulphur Containing Heterocyclic Compound: 1,3,4 – thiadiazole. Asian Journal of Biomedical and Pharmaceutical Sciences 3(21) 2013, 6-23.
3. Jigar K. Mistry, Richard Dawes, AmitavaChoudhury, and Michael R. Van De Mark., 5-Mercapto-1,3,4-thiadiazole-2(3H)-thione: Synthesis and Structure of Alkylated Derivatives., 2014 May Journal of Heterocyclic Chemistry 51(3):747 – 754.
4. Shaker Awad Abdul Hussein and Ammar Abdul Razzak M. Kubba.,Synthesis, characterization and antimicrobial activity of new 2,5-disubstituted-1,3,4-thiadiazole derivatives., Der PharmaChemica, 2015, 7 (9):250-260.
5. Liu, F., Luo, X.-Q., Song, B.-A., Bhadury, P. S., Yang, S., Jin, L.-H.,Hu, D.-Y. Synthesis and antifungal activity of novel sulfoxide derivatives containing trimethoxyphenyl substituted 1,3,4-thiadiazole and 1,3,4-oxadiazole moiety. Bioorganic & Medicinal Chemistry, (2008).16(7), 3632–3640.
6. Chen, C.-J., Song, B.-A., Yang, S., Xu, G.-F., Bhadury, P. S., Jin, L.-H., Chen, Z.Synthesis and antifungal activities of 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-thiadiazole and 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-oxadiazole derivatives. Bioorganic & Medicinal Chemistry, (2007)15(12), 3981–3989
7. Zoumpoulakis, P., Camoutsis, C., Pairas, G., Soković, M., Glamočlija, J., Potamitis, C., &Pitsas, A.Synthesis of novel sulfonamide-1,2,4-triazoles, 1,3,4-thiadiazoles and 1,3,4-oxadiazoles, as potential antibacterial and antifungal agents. Biological evaluation and conformational analysis studies.Bioorganic & Medicinal Chemistry, (2012)20(4)
8. Alwan, W. S., Karpoormath, R., Palkar, M. B., Patel, H. M., Rane, R. A., Shaikh, M. S., … Mlisana, K. P. Novel imidazo[2,1-b]-1,3,4-thiadiazoles as promising antifungal agents against clinical isolate of Cryptococcus neoformans. European Journal of Medicinal Chemistry, (2015).95, 514–525.
9. Wu, Q., Cai, H., Yuan, T., Li, S., Gan, X., & Song, B. Novel vanillin derivatives containing a 1,3,4-thiadiazole moiety as potential antibacterial agents. Bioorganic & Medicinal Chemistry Letters, (2020).127113.
10. Chen, J., Yi, C., Wang, S., Wu, S., Li, S., Hu, D., & Song, B. Novel amide derivatives containing 1,3,4-thiadiazole moiety: Design, synthesis, nematocidal and antibacterial activities. Bioorganic & Medicinal Chemistry Letters. 29 (2019) 1203–1210.
11. Li, P., Shi, L., Yang, X., Yang, L., Chen, X.-W., Wu, F., … Song, B.-A. Design, synthesis, and antibacterial activity against rice bacterial leaf blight and leaf streak of 2,5-substituted-1,3,4-oxadiazole/thiadiazolesulfone derivative. Bioorganic & Medicinal Chemistry Letters, (2014). 24(7), 1677–1680.
12. Li, P., Shi, L., Gao, M.-N., Yang, X., Xue, W., Jin, L.-H., Song, B.-A. Antibacterial activities against rice bacterial leaf blight and tomato bacterial wilt of 2-mercapto-

5-substituted-1,3,4-oxadiazole/thiadiazole derivatives. Bioorganic & Medicinal Chemistry Letters, (2015).25(3), 481–484

13. Ragab, F. A., Heiba, H. I., El-Gazzar, M. G., Abou-Seri, S. M., El-Sabbagh, W. A., & El-Hazek, R. M. Anti-inflammatory, analgesic and COX-2 inhibitory activity of novel thiadiazoles in irradiated rats. Journal of Photochemistry and Photobiology B: Biology, (2017).166, 285–300.
14. Omar, Y. M., Abdu-Allah, H. H. M., & Abdel-Moty, S. G.. Synthesis, biological evaluation and docking study of 1,3,4-thiadiazole-thiazolidinone hybrids as anti-inflammatory agents with dual inhibition of COX-2 and 15-LOX. Bioorganic Chemistry, (2018), 80, 461–471.
15. Maddila, S., Gorle, S., Sampath, C., &Lavanya, P. Synthesis and anti-inflammatory activity of some new 1,3,4-thiadiazoles containing pyrazole and pyrrole nucleus. Journal of Saudi Chemical Society, (2016).20, S306–S312.
16. Hafez, H. N., Hegab, M. I., Ahmed-Farag, I. S., & El-Gazzar, A. B. A.A facile regioselective synthesis of novel spiro-thioxanthene and spiro-xanthene-9′,2-[1,3,4]thiadiazole derivatives as potential analgesic and anti-inflammatory agents. Bioorganic & Medicinal Chemistry Letters, (2008).18(16), 4538–4543
17. Salgın-Gökşen, U., Gökhan-Kelekçi, N., Göktaş, Ö.,Köysal, Y., Kılıç, E., Işık, Ş.,Özalp, M. 1-Acylthiosemicarbazides, 1,2,4-triazole-5(4H)-thiones, 1,3,4-thiadiazoles and hydrazones containing 5-methyl-2-benzoxazolinones: Synthesis, analgesic-anti-inflammatory and antimicrobial activities. Bioorganic & Medicinal Chemistry, (2007).15(17), 5738–5751.
18. Almandil, N. B., Taha, M., Rahim, F., Wadood, A., Imran, S., Alqahtani, M. A.,Gollapalli, M. Synthesis of novel quinoline-based thiadiazole, evaluation of their antileishmanial potential and molecular docking studies. Bioorganic Chemistry, (2019).85, 109–116.
19. Tahghighi, A., Marznaki, F. R., Kobarfard, F., Dastmalchi, S., Mojarrad, J. S., Razmi, S., …Foroumadi, A. Synthesis and antileishmanial activity of novel 5-(5-nitrofuran-2-yl)-1,3,4-thiadiazoles with piperazinyl-linked benzamidine substituents. European Journal of Medicinal Chemistry, (2011).46(6), 2602–2608.
20. Wei, M.-X., Feng, L., Li, X.-Q., Zhou, X.-Z., & Shao, Z.-H. Synthesis of new chiral 2,5-disubstituted 1,3,4-thiadiazoles possessing γ-butenolide moiety and preliminary evaluation of in vitro anticancer activity. European Journal of Medicinal Chemistry, (2009).44(8), 3340–3344.
21. Kumar, D., Maruthi Kumar, N., Chang, K.-H., & Shah, K. Synthesis and anticancer activity of 5-(3-indolyl)-1,3,4-thiadiazoles. European Journal of Medicinal Chemistry, (2010).45(10), 4664–4668.
22. Kumar, D., Kumar, N. M., Chang, K.-H., Gupta, R., & Shah, K..Synthesis and in-vitro anticancer activity of 3,5-bis(indolyl)-1,2,4-thiadiazoles. Bioorganic & Medicinal Chemistry Letters, (2011) 21(19), 5897–5900.
23. Jakovljević, K., Matić, I. Z., Stanojković, T., Krivokuća, A., Marković, V., Joksović, M. D., Joksović, L. Synthesis, antioxidant and antiproliferative activities of 1,3,4-thiadiazoles derived from phenolic acids. Bioorganic & Medicinal Chemistry Letters, (2017).27(16), 3709–3715.
24. Jakovljević, K., Joksović, M. D., Botta, B., Jovanović, L. S., Avdović, E., Marković, Z., Marković, V. Novel 1,3,4-thiadiazole

conjugates derived from protocatechuic acid: Synthesis, antioxidant activity, and computational and electrochemical studies. ComptesRendus. (2019). 22 585-598.

25. Djukic, M., Fesatidou, M., Xenikakis, I., Geronikaki, A., Angelova, V. T., Savic, V.,Saso, L.In vitro antioxidant activity of thiazolidinone derivatives of 1,3-thiazole and 1,3,4-thiadiazole. Chemico-Biological Interactions, (2018).286, 119–131
26. Sauer, A. C., Leal, J. G., Stefanello, S. T., Leite, M. T. B., Souza, M. B., Soares, F. A. A., Dornelles, L.. Synthesis and antioxidant properties of organosulfur and organoselenium compounds derived from 5-substituted-1,3,4-oxadiazole/thiadiazole-2-thiols. Tetrahedron Letters, (2017)58(1), 87–91.
27. Fadda, A. A., Abdel-Latif, E., & El-Mekawy, R. E. Synthesis and molluscicidal activity of some new thiophene, thiadiazole and pyrazole derivatives. European Journal of Medicinal Chemistry, (2009).44(3), 1250–1256.
28. El Shehry, M. F., Abu-Hashem, A. A., & El-Telbani, E. M. Synthesis of 3-((2,4-dichlorophenoxy)methyl)-1,2,4-triazolo(thiadiazoles and thiadiazines) as anti-inflammatory and molluscicidal agents. European Journal of Medicinal Chemistry, (2010).45(5), 1906–1911.
29. Lee, J., Lee, S.-H., Seo, H. J., Son, E.-J., Lee, S. H., Jung, M. E., Lee, J.Novel C-aryl glucoside SGLT2 inhibitors as potential antidiabetic agents: 1,3,4-Thiadiazolylmethylphenyl glucoside congeners. Bioorganic & Medicinal Chemistry, (2010)18(6), 2178–2194.
30. Jatav, V., Mishra, P., Kashaw, S., & Stables, J. P. Synthesis and CNS depressant activity of some novel 3-[5-substituted 1,3,4-thiadiazole-2-yl]-2-styryl quinazoline-4(3H)-ones. European Journal of Medicinal Chemistry, (2008). 43(1), 135–141.
31. Harish, K. P., Mohana, K. N., &Mallesha, L. Synthesis of indazole substituted-1,3,4-thiadiazoles and their anticonvulsant activity. Drug Invention Today, (2013).5(2), 92–99.
32. Rajak, H., Behera, C. K., Pawar, R. S., Singour, P. K., &Kharya, M. D. A novel series of 2,5-disubstituted 1,3,4-thiadiazoles as potential anticonvulsant agent. Chinese Chemical Letters, (2010).21(10), 1149–1152.
33. Quintana, C., Klahn, A. H., Artigas, V., Fuentealba, M., Biot, C., Halloum, I., Arancibia, R. Cyrhetrenyl and ferrocenyl 1,3,4-thiadiazole derivatives: Synthesis, characterization, crystal structures and in vitro antitubercular activity. Inorganic Chemistry Communications, (2015). 55, 48–50
34. Alegaon, S. G., Alagawadi, K. R., Sonkusare, P. V., Chaudhary, S. M., Dadwe, D. H., & Shah, A. S. Novel imidazo[2,1-b][1,3,4]thiadiazole carrying rhodanine-3-acetic acid as potential antitubercular agents. Bioorganic & Medicinal Chemistry Letters, (2012).22(5), 1917–1921.
35. Yusuf, M., Khan, R. A., & Ahmed, B.. Syntheses and anti-depressant activity of 5-amino-1, 3, 4-thiadiazole-2-thiol imines and thiobenzyl derivatives.Bioorganic & Medicinal Chemistry, (2008) 16(17), 8029–8034.
36. Zhang, K., Wang, P., Xuan, L.-N., Fu, X.-Y., Jing, F., Li, S., Chen, B.-Q. Synthesis and antitumor activities of novel hybrid molecules containing 1,3,4-oxadiazole and 1,3,4-thiadiazole bearing Schiff base moiety. Bioorganic & Medicinal Chemistry Letters, (2014) 24(22), 5154–5156.

Published: September 29, 2020 | **Pages:** 143-153
Doi: https://doi.org/10.37547/tajas/Volume02Issue09-23

37. Lv, M., Liu, G., Jia, M., &Xu, H.Synthesis of matrinic amide derivatives containing 1,3,4-thiadiazole scaffold as insecticidal/acaricidal agents. Bioorganic Chemistry, (2018).81, 88–92

38. Gomha, S., Edrees, M., Muhammad, Z., & El-Reedy, A.5-(Thiophen-2-yl)-1,3,4-thiadiazole derivatives: synthesis, molecular docking and in vitro cytotoxicity evaluation as potential anticancer agents. Drug Design, Development and Therapy, (2018)Volume 12, 1511–1523.

39. Karolina Jasiak, AgnieszkaKudelko, Monika Wróblowska, Anna Biernasiuk, Anna Malm, and Maria Krawczyk. Convenient Synthesis and Biological Activity of Mono and Diacyl 2,5-Dimercapto-1,3,4-thiadiazole Derivatives. Journal of Heterocyclic Chemistry.2017.54(6) 3241-3249.

40. JumatSalimon,NadiaSalih, EmadYousif, AyadHameed and HibaIbraheem. Synthesis, Characterization and Biological Activity of Schiff Bases of 2, 5-Dimercapto-1,3,4-thiadiazole . Australian Journal of Basic and Applied Sciences, 4(7): 2016-2021, 2010

41. T. S. Zhivotova. Reaction of 1,3,4-thiadiazol-2,5-dithiolwith n-acryloyl-substitutedderivatives of several alkaloids. Chemistry of Natural Compounds, Vol. 45, No. 6, 2009.

42. T. S. Zhivotova, A. M. Gazaliev, O. V. Dryuk, and A. Zh. Seitembetova. Synthesis and Antioxidant Activity of Alkaloid- andAmine-containing Salts of 1,3,4-Thiadiazole-2,5-disulfonic Acid. Russian Journal of Applied Chemistry, 2008, Vol. 81, No. 2, pp. 259-262.

43. T. E. Glotova, A. S. Nakhmanovich, and T. N. Komarova, Khim. Geterotsikl.Soedin., 8, 1144 (1988).

44. A. A. Katritskii, Physicochemical Methods in Chemistry of Heterocyclic Compounds [in Russian], Khimiya,Moscow, 1966, p. 59.

45. L. J. Bellamy, Advances in Infrared Group Frequencies, Methuen, London, 1968.

46. Gazaliev, A.M., Zhurinov, M.Zh., and Fazylov, S.D.,Novyebioaktivnyeproizvodnyealkaloidov(NewBioactive Alkaloid Derivatives), Alma-Ata: Gylym,1992.

47. Levy, G.C,.and Nelson, G.L., Carbon-13 NuclearMagnetic Resonance for Organic Chemists, NewYork: Wiley, 1972.