WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 4, 2015-2022. Research Article ISSN 2277– 7105

SYNTHESIS AND CHARACTERISATION OF SOME THIADIAZOLE DERIVATIVES

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Article Received on
22 Feb 2016,

Revised on 11 March 2016,
Accepted on 01 April 2016

DOI: 10.20959/wjpr20164-6047

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ABSTRACT

Synthesis of some thiadiazole derivatives were carried out by using dehydrative cyclisation reaction. Compounds were synthesized by reacting ethyl N-pyrrole acetate with thiosemicarbazide in the presence of sulphuric acid/ ammonia to form 2-amino-5-(N-pyrrole methyl) 1,3,4 thiadiazole. The obtained thiadiazole derivatives were reacted with substituted aromatic aldehydes in the presence of acetic acid to form N-substituted 1,3,4 thiadiazole derivatives. All the synthesized compounds were characterized by UV, IR, ^{1}H NMR, and MASS spectroscopy.

KEYWORDS: Pyrrole, 1,3,4-thiadiazole, Schiffs' base, Microwave synthesis.

INTRODUCTION

Pyrrole is a heterocyclic aromatic organic compound, having five- membered ring with the formula C_4H_5N. It is a colorless volatile liquid that darkens readily upon exposure to air. Porphobilinogen, a trisubstituted pyrrole, is the biosynthetic precursor to many natural products such as heme. Pyrroles are components of more complex macrocycles, including the porphyrins of heme, the chlorins, bacteriochlorins, chlorophyll, and porphyrinogens. Thiadiazoles constitute a class of heteroaromatic compound containing two heteroatoms (sulphur and nitrogen). This structural moiety is found in natural products and has been used as an essential skeleton in pharmaceutics and many medicinal compounds. Efficient and versatile synthetic methods for producing 1, 3, 4-Thiadiazole derivatives have been actively investigated. Many synthetic methods require an organized thiosemicarbazide derivative with functionalized N-alkynyl or aryl groups. Therefore, an alternative method having functional

group variations on 1, 3, 4- Thiadiazole nucleus is highly desirable for biological activity studies. Ecofriendly synthesis of 1,3,4 thiadiazole has not been reported in literature.[1]

MATERIAL AND METHODS

All the chemicals and reagents were procured from reputed firm. IR spectra (4000-400cm^{-1}) were recorded on Shimazdu FT-IR Spectrophotometer. ^{1}H-NMR spectra were recorded on Bruker Avance III HD Spectrometer in DMSO as a solvent; the chemical shifts (δ) are expressed in ppm using TMS as internal standard. MASS spectra were recorded on JEOL GC MATE-II, HR. TLC was carried out on a precoated plate and spots were visualized with Iodine vapour.

Procedure for synthesis

Step-1- Formation of ethyl N-pyrrole acetate

A mixture of pyrrole (0.1 mole) and ethylchloroacetate (0.1 mole) with potassium carbonate (6.168g) as subjected to microwave irradiation at 40°C for 3 minutes,which resulted in the formation of ethyl N-pyrrole acetate. It was recrystallized from benzene-chloroform (1:2) mixture.

Step-2- Formation of 1-N-pyrrole acetyl thiosemicarbazide

When a mixture of ethyl N-pyrrole acetate (0.03 mole) and thiosemicarbazide (0.03 mole) was subjected to microwave irradiation at 60°C for 5 min, the product 1-N-pyrrole acetyl thiosemicarbazide was formed. It was recrystallized from benzene-chloroform (1:2) mixture.

Step-3- Formation of 1,3,4 thiadiazole

1-N-pyrrole acetyl thiosemicarbazide (0.03 mole) was dissolved in chloroform and concentrated sulphuric acid (0.03 mole) and subjected to microwave irradiation at 40°C for 90 second, neutralized with strong ammonia, which resulted in the formation of 2-amino -5-N(pyrrole methyl)1,3,4 thiadiazole. It was recrystallized from benzene-chloroform (1:2) mixture.

Step-4- Formation of Schifs' base

When equimolar solution of 2-amino -5-N(pyrrole methyl)1,3,4 thiadiazole (0.02 mole) and substituted benzaldehyde derivatives (0.02 mole) in methanol (20 mL) with 4-5 drops of glacial acetic acid was subjected to microwave irradiation at 40°C for 90 seconds resulted in the formation of N-(5-((1H-Pyrrole-1-yl) methyl) -1, 3, 4-thiadiazole-2yl)-1-

phenylmethanimine. It was recrystallized from benzene-chloroform (1:2) mixture. Other compounds were synthesized similarly using various carbonyl compounds in place of benzaldehyde. Seven derivatives using different aromatic aldehyde were obtained RS1-RS7.[2-3]

Scheme of reaction

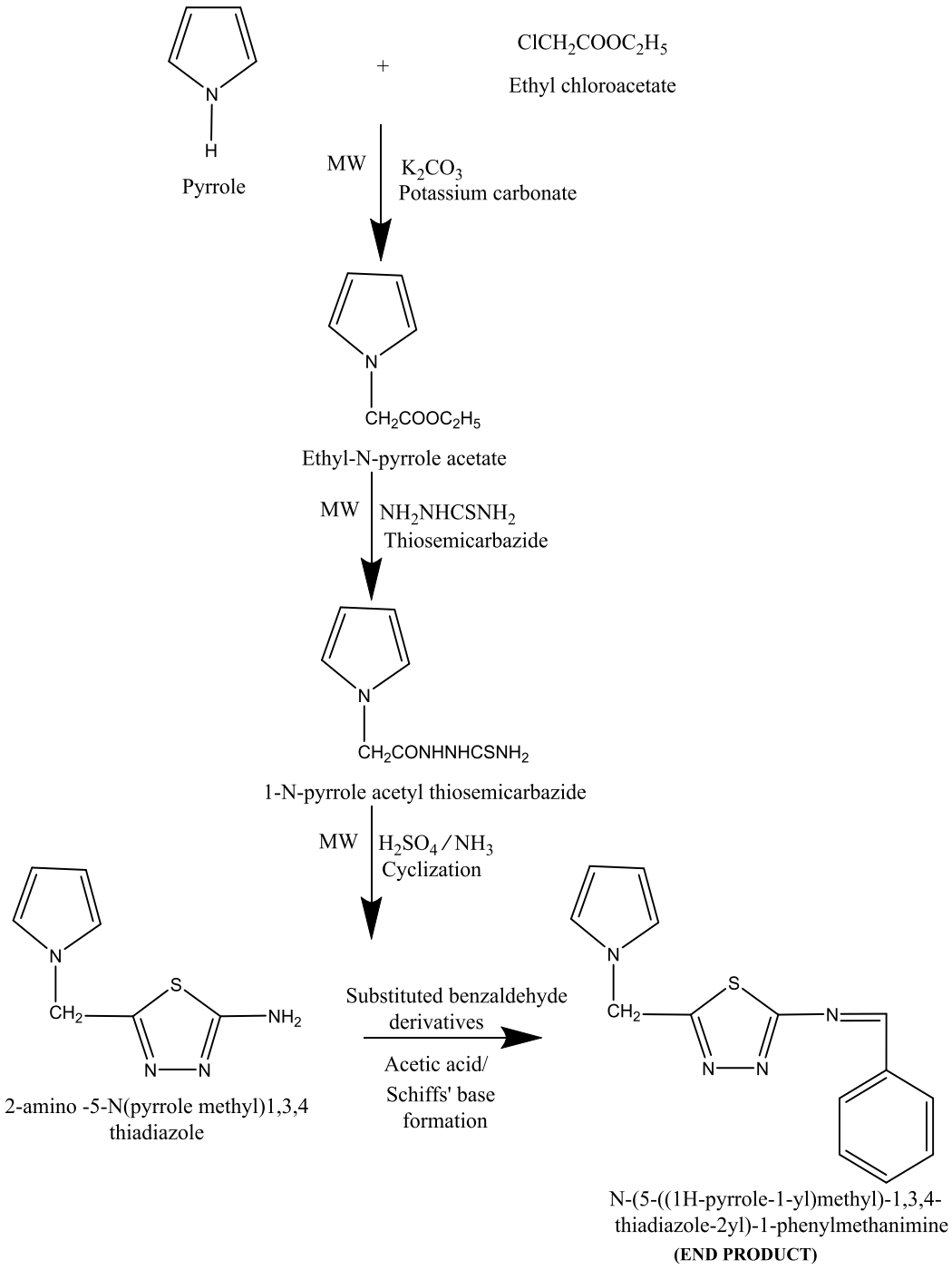


Table-1: Synthetic compounds with varied substituents

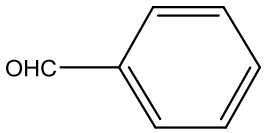
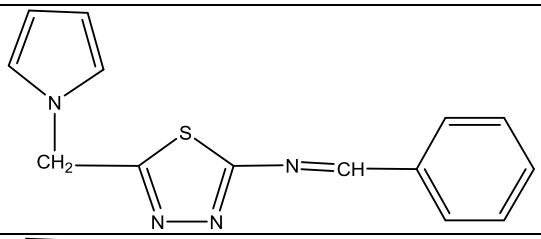
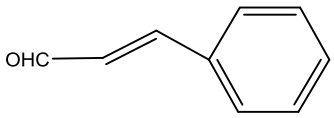
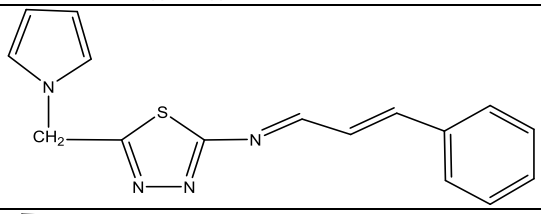
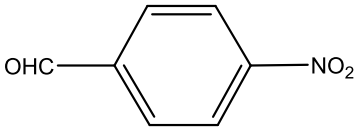
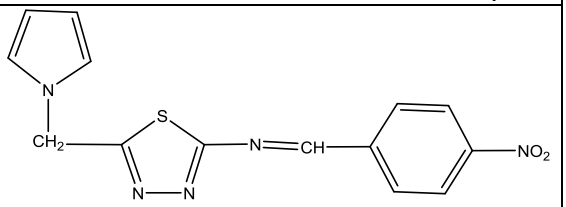
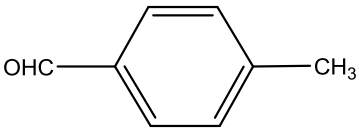
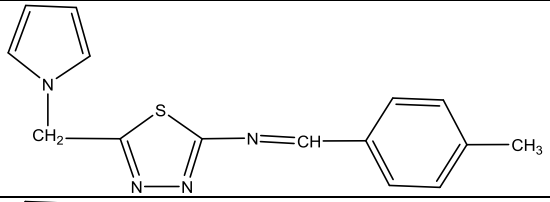
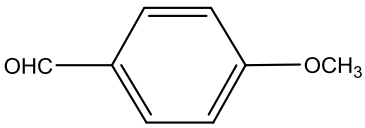
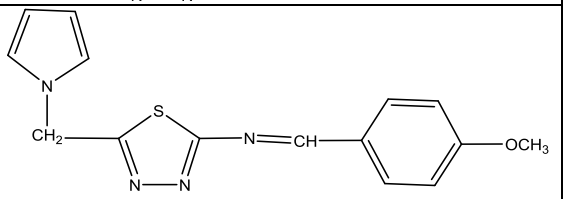
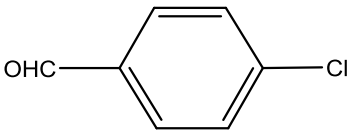
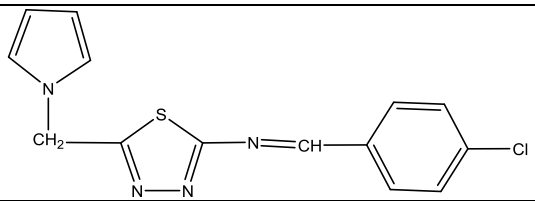
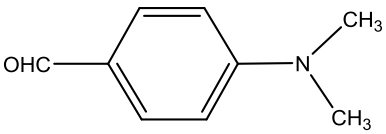
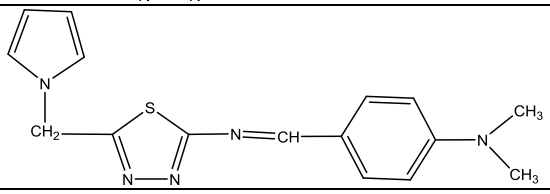
S.no	Compound	Ar	Final Product
1	RS 1		
2	RS 2		
3	RS 3		
4	RS4		
5	RS 5		
6	RS 6		
7	RS 7		

Table-2: Physical data of synthesized compounds.

S.no	Compound code	Molecular formula	Appearance/ Colour	Solubility	Melting point range (°c)	Rf - value	% Yield
1	RS1	$C_{14}H_{12}N_4S$	White crystalline solid	Dimethyl sulfoxide, chloroform	157-160	0.9736	50.48
2	RS2	$C_{16}H_{16}N_4S$	Dark brown crystalline solid	Dimethyl sulfoxide, chloroform	135-137	0.9428	86.07
3	RS3	$C_{14}H_{11}N_5O_2S$	Pale yellow crystalline solid	Dimethyl sulfoxide, chloroform	108-110	0.9750	51.49
4	RS4	$C_{15}H_{14}N_4S$	Ash crystalline solid	Dimethyl sulfoxide, chloroform	152-155	0.9230	66.66
5	RS5	$C_{15}H_{14}N_4OS$	Light brown crystalline solid	Dimethyl sulfoxide, chloroform	187-190	0.9000	48.86
6	RS6	$C_{14}H_{11}ClN_4S$	Black crystalline solid	Dimethyl sulfoxide, chloroform	140-142	0.7750	63.57
7	RS7	$C_{16}H_{17}N_5S$	Olive green crystalline solid	Dimethyl sulfoxide, chloroform	69-72	0.8461	86.95

RESULTS AND DISCUSSION

Purification

All the synthesized compounds purified by recrystallized from benzene: chloroform (1:2)mixture. The formation of product was confirmed by TLC using various mobile phases such as chloroform: methanol (2:8), hexane: ethyl acetate (7:1), hexane: acetone (6:4), benzene: acetone (9:1) mixture was used. The spots were identified by iodine vapour and UV chamber.[4]

CHARACTERIZATION

Physical Data

The physical data such as melting point, solubility were determined. The synthesized compounds were soluble in DMSO, chloroform. The melting points of synthesized compounds were determined by open tube capillary method with an aid of a melting point apparatus and are presented uncorrected.[5]

Analytical data of synthesized RS1-RS7 compound

RS1: N-(5-(1H-pyrrole-1-yl)methyl)-1,3,4-thiadiazole-2-yl)-1-phenylmethanimine

UV : The ethanolic solution of the compound exhibit maxima of 312.28nm when examined in the range of 200 to 400nm.

IR : (KBr υ cm^{-1}): 1533.41 (C=N Str), 1101.35 (C-N-C Str), 690.52 (C-S-C Str), 2995.45 (Ali-C-H Str), 3145.90 (Aro-C-H Str), 1600.92 (N=CH Str).

NMR : ^{1}H NMR δppm(DMSO): 1.66 (S,2H,CH_2), 9.91 (S,1H,N=CH), 6.48-7.43 (Aromatic & Hetero aromatic proton).

MASS : (m/z value): 268.0801 M^+ ion peak.

RS2: (1E,2E)-N-(5-((1H-pyrrole-1yl)methyl)-1,3,4-thiadiazole-2-yl-3- phenylprop-2-en-1-imine.

UV : The ethanolic solution of the compound exhibit maxima of 293.20nm when examined in the range of 200 to 400nm.

IR : (KBr υ cm^{-1}): 1544.98 (C=N Str), 1124.50 (C-N-C Str), 696.30 (C-S-CStr), 2926.01 (Ali-C-H Str), 3057.17 (Aro-C-H Str), 1597.06 (N=CH Str), 3024.38 (Ali-C=C Str).

NMR : ^{1}H NMR δppm (DMSO): 2.01 (S,2H,CH_2), 9.74 (S,1H,N=CH), 6.52-7.48 (Aromatic & hetero aromatic proton).

MASS : (m/z value): 296.3904 M^+ ion peak.

RS3: N-(5-((1H-Pyrrole-yl)methyl)-1,3,4-thiadiazole-2-yl)-1-(4 -nitrophenyl) methanimine

UV : The ethanolic solution of the compound exhibit maxima of 264.60nm when examined in the range of 200 to 400nm.

IR : (KBr υ cm^{-1}): 1533.41 (C=N Str), 1197.79 (C-N-C Str), 677.01 (C-S-C Str), 2848.86 (Ali-C-H Str), 3107.32 (Aro-C-H Str), 1606.70 (N=CH Str), 1346.31 (Aro-NO_2Str).

NMR : ^{1}H NMR δppm (DMSO): 2.72 (S,2H,CH_2), 10.19 (S,1H,N=CH), 7.35- 8.43 (Aromatic & hetero aromatic proton).

MASS : (m/z value): 313.3326 M^+ ion peak.

RS4: N-(5-((1H-Pyrrole-yl)methyl)-1,3,4-thiadiazole-2-yl)-1-(p-tolyl)methanimine

UV : The ethanolic solution of the compound exhibit maxima of 264.97nm when examined in the range of 200 to 400nm.

IR : (KBr υ cm^{-1}): 1543.05 (C=N Str), 1101.35 (C-N-C Str), 628.79 (C-S-C Str), 2920.23 (Ali-C-H Str), 3157.47 (Aro-C-H Str), 1597.06 (N=CH Str), 1460.11 (Aro-CH_3Str).

NMR : ^{1}H NMR δppm (DMSO): 1.75 (S,2H,CH_2), 9.98 (S,1H,N=CH), 6.72-7.77 (Aromatic & hetero aromatic proton), 2.38 (S,3H,CH_3).

MASS : (m/z value): 282.3748 M^+ ion peak.

RS5: N-(5-((1H-Pyrrole-yl)methyl)-1,3,4-thiadiazole-2-yl)-1-(4 methoxyphenyl) methanimine.

UV : The ethanolic solution of the compound exhibit maxima of 321.31nm when examined in the range of 200 to 400nm.

IR : (KBr υ cm^{-1}): 1544.98 (C=N Str), 1024.20 (C-N-C Str), 617.22 (C-S-C Str), 2933.73 (Ali-C-H Str), 3080.32 (Aro-C-H Str), 1597.06 (N=CH Str), 1249.87 (Aro-OCH_3 Str).

NMR : ^{1}H NMR δppm (DMSO): 1.32 (S,2H,CH_2), 9.89 (S,1H,N=CH), 6.92-7.63 (Aromatic & hetero aromatic proton), 3.85-3.91(d,3H,OCH_3).

MASS : (m/z value): 298.3609 M^+ ion peak.

RS6: N-(5-((1H-Pyrrole-yl)methyl)-1,3,4-thiadiazole-2-yl)-1-(4-chloro phenyl)methanimine

UV : The ethanolic solution of the compound exhibit maxima of 317.20nm when examined in the range of 200 to 400nm.

IR : (KBr υ cm^{-1}): 1527.62 (C=N Str), 1012.63 (C-N-C Str), 617.22 (C-S-C Str), 2922.16 (Ali-C-H Str), 3282.84 (Aro-C-H Str), 1598.99 (N=CH Str), 1089.78 (Aro-Cl Str).

NMR : ^{1}H NMR δppm (DMSO): 1.30 (S,2H,CH_2), 9.46 (S,1H,N=CH), 5.65-7.59 (Aromatic & hetero aromatic proton).

MASS : (m/z value): 302.7843 M^+ ion peak.

RS7: 4-((5-((1H-Pyrrole-yl-)methyl)-1,3,4-thiadiazole-2-yl)imino)methyl)-N,N-dimethyl Aniline

UV : The ethanolic solution of the compound exhibit maxima of 339.60nm when examined in the range of 200 to 400nm.

IR : (KBr υ cm^{-1}): 1550.77 (C=N Str), 1064.71 (C-N-C Str), 632.65 (C-S-C Str), 2916.37 (Ali-C-H Str), 3186.40 (Aro-C-H Str), 1597.06 (N=CH Str), 1373.32 (Aro-N-(CH_3) Str.

NMR : ^{1}H NMR δppm (DMSO): 1.50 (S,2H,CH_2), 9.74 (S,1H,N=CH), 6.69-7.76 (Aromatic & hetero aromatic proton), 3.09 (S,6H,$N(CH_3)_2$).

MASS : (m/z value): 311.4129 M^+ ion peak.[6]

CONCLUSION

A novel series of Schiffs' base containing 1, 3, 4-thiadiazole were synthesized by dehydrative cyclisation method. The synthesized compounds were identified by TLC and purified by recrystallization. The structures of synthesized compounds were confirmed by FT-IR, ^{1}H NMR and MASS Spectroscopy. The spectral data coincided with the assigned structure of the synthesized compounds.

ACKNOWLEDGEMENT

We express our sincere thanks to the Department of Pharmaceutical Chemistry, College of Pharmacy, Madurai Medical College, Madurai, for providing necessary facilities to carry out the work. We express our thanks to Mr. Murugesh, Indian Institute of Technology, Chennai, for helping with spectral study.

REFERENCES

1. Deepika Koti, U. Chandra Teja, G. Lakshmi Suneetha, K. Indira, B. Anupama, KN V Chenchu Lakshmi. Evaluation of Some Novel Synthesised 2-Amino-1,3,4-Thiadiazole Derivative. Sch. Acad. J. Pharm, 2014; 3(6): 432-437.
2. Anshul Chawla, Ramandeep Kaur and Anju Goyal. Importance of Microwave Reactions in the Synthesis of Novel Benzimidazole Derivatives: A Review. ***J***. Chem. Pharm. Res., 2011; 3(6): 925-944.
3. Srivastava S D, Rawat T.R. Synthesis of new benzotriazole derivatives: Antimicrobial and anticonvulsant agents. Indian journal of chemistry, 1999; 38(1): 623-627.
4. A.H.Beckett. Practical Pharmaceutical chemistry. 4th edition., 2007; 117-152.
5. Sharma Y.R. Elementry Organic Spectroscopy, Principles And Chemical Applications. 4th Edition., 2007; 90-200.
6. Robert M.Silverstein, G.Clayton Basster**.** Spectrophotometric Identification of Organic Compounds. 2nd Edition., 2007; 72-135.