

반응방법에 따른 1-Benzofuran-2-yl thiadiazoles, Triazoles과 Oxadiazoles의 합성

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Synthesis and Characterization of 1-Benzofuran-2-yl thiadiazoles, Triazoles and Oxadiazoles by Conventional and Non-conventional Methods

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요약. Thiosemicarbazides의 cyclocondensation을 이용한 1,3,4-thiadiazoles, 1,3,4-triazoles과 1,3,4-oxadiazole계의 benzofuran의 합성을 좋은 수율로 합성하였다.

주제어: Thiosemicarbazide, Thiadiazoles, Triazoles, Oxadiazoles, Microwave와 Ultrasound irradiation

ABSTRACT. The synthesis of benzofuran based 1,3,4-thiadiazoles, 1,3,4-triazoles and 1,3,4-oxadiazole via cyclocondensation of thiosemicarbazides have been carried out by conventional and non-conventional methods in excellent yields of product.

Keywords: Thiosemicarbazide, Thiadiazoles, Triazoles, Oxadiazoles, Microwave and Ultrasound irradiation

INTRODUCTION

Benzofuran compounds are associated with various physiological and biological properties and thus find important use in various therapeutic areas in medicine. In nature's collection of biologically active heterocycles, benzo[*b*]furan derivatives¹⁻³ constitute a major group. They are usually important constituents of plant extracts used in traditional medicine.² Recently, a number of benzofuran analogues have been studied as potential inhibitors of 3-amylloid formation⁴ and HUVEC.⁵

Thiadiazole derivatives are highly potent inhibitors of HIV-1^{6a} and useful as anti-inflammatory^{6b} and anti-arrhythmic agents.^{6c} In addition, it is a common structural feature in many biologically active molecules which are used clinically in the treatment of some forms of epilepsy.^{6d} The complexes of thiadiazole derivatives are showing antifungal,^{7a} antibacterial^{7b} as well as carbonic anhydrase inhibitory activities.^{7c} In particular, 1,3,4-thiadiazole nucleus have been reported to possess CNS stimulant,^{8a} anticholinergic,^{8b} hypoglycemia,^{8c} anticonvulsant,^{8d} spasmolytic and anti-inflammatory activities.^{8e}

Triazoles are an important class of heterocyclic compounds. The derivatives of triazoles are exhibit important

biological properties such as, tranquilizer and sedative,^{9a} pesticidal,^{9b} antibacterial,^{9c} anxiolytic,^{9d} anticonvulsant,^{9e} antidepressants^{9f} and antifungal.^{9g}

The substituted oxadiazoles are heterocyclic compounds, which serve both as biomimetic and reactive pharmacophores and many are key elements with potential biological activities such as CNS stimulant, anti-inflammatory, hypotensive,^{10a} insecticidal,^{10b} bactericidal,^{10c} hypoglycemic,¹¹ analgesic, anticonvulsive, antiemetic, diuretic,¹² muscle relaxant¹³ and fungicidal¹⁴ activities.

The science of green chemistry was developed to meet the increasing demand for environmentally benign chemical processes. Microwave¹⁵ and ultrasonic¹⁶ irradiation techniques have an importance in the search for green synthesis because of their use as an efficient alternative heating source for organic reactions. The main advantage of microwave and ultrasonically assisted organic synthesis is the shorter reaction time, simple experimental procedure, very high yields and clean reaction of many microwave and ultrasonically induced transformations offers additional convenience in the field of organic synthesis.

Biological activities associated with 1-benzofuran, thiadiazoles, triazoles and oxadiazole moieties and advantages of microwave and ultrasound irradiation technique prompted

us to synthesize some oxadiazole, thiadiazoles and triazoles with 1-benzofuran.

EXPERIMENTAL

Ultrasound irradiation was carried out in ultrasonic cleaner model EN-20U-S manufactured by Entertech Electronics Pvt. Ltd, Mumbai, India having maximum power output of 100W and 33 KHz operating frequency. Microwave irradiation was carried out in Cem Discover Microwave oven - Maximum power-300-700w and model no. 908010, Maximum current-6.3 A with 50/60 MHz frequency (CEM-Matthews.NC. made in USA). All the melting points determined in open capillary tubes. I.R. spectra were recorded on Perkin-Elmer FTIR spectrophotometer using KBr disc. ^1H NMR spectra were recorded on Varian in DMSO at 300 MHz spectrophotometer and TMS as an internal standard. A mass spectrum was recorded on Finnigan mass spectrometer using electrospray Ionization technique. The elemental analysis was carried out on Flash EA-1112, 50/60 Hz, 1400-VA CHNS analyzer.

General Procedure

Ethyl 7-methoxy-3-methylbenzofuran-2-carboxyacid hydrazide (2).

To the stirred mixture of ethyl 7-methoxy-3-methylbenzofuran-2-carboxylate (0.01 mole) and hydrazine hydrate (0.015 mole) in ethanol (50 mL) at 78 °C. The progress of reaction was monitored on TLC. After completion of reaction (60 min.), reaction mass was poured over ice-water and solid compound was separated by filtration to obtain the product in 94% of yield. The crude solid product was crystallized from ethanol water (7:3 system) to get the desired product.

2-[(7-Methoxy-3-methyl-1-benzofuran-2-yl)carbonyl]-N-(2-methoxyphenyl) hydrazinecarbothioamide (4a).

Method (A) By conventional method: In RBF, mixture of equimolar amounts (0.01 mole) of acid hydrazide (2) and aryl isothiocyanates (3) (0.01 mole) with 15 mL ethanol was heated up to reflux on oil bath at 78 °C. Progress of the reaction was monitored on TLC. After completion of reaction (45 min.), reaction mass was poured over ice-water and solid compound was separated by filtration. The solid product was crystallized from ethanol water. This typical experimental procedure was followed to prepare other analogs of this series. The synthesized compounds by above procedures are listed in *Table 1* with their characterization data. Their structures have been confirmed by IR, ^1H NMR, mass spec-

tra and elemental analysis.

Method (B) By US method: In RBF, mixture of equimolar amount (0.01 mole) of acid hydrazide (2) and aryl isothiocyanates (3) (0.01 mole) with 15 mL ethanol was subjected for ultra sound irradiation for 20 minutes. Progress of reaction was monitored on TLC. After completion of reaction product obtained was poured over ice-water and separated by filtration. The solid product was crystallized from ethanol. This typical experimental procedure was followed to prepare other analogs of this series. The synthesized compounds by above method are characterized by IR, NMR, Mass spectra.

Method (C) By MW method: A mixture of equimolar amount of acid hydrazide (2) (0.01 mole), and aryl isothiocyanates (3) (0.01 mole) in ethanol (25 mL) was irradiated in a borosilicate glass tube (50 mL) inside a microwave oven for 90 - 120 sec at an output of 300 watts power, with short interruption of 15 sec to avoid excessive evaporation of solvent. Progress of reaction was monitored on TLC. The reaction mixture was cooled and poured in to ice water. Solid product was separated by filtration and crystallized with alcohol to afford the titled compound. The synthesized compounds by above method are characterized by IR, ^1H NMR, mass spectroscopy.

5-(7-Methoxy-3-methyl-1-benzofuran-2-yl)-N-phenyl-1,3,4-thiadiazol-2-amine (5a).

Method (A) By Conventional method: In 100 mL RBF, thiosemicarbazide (4a) (0.01mole) was taken with 5 mL conc. H_2SO_4 , the reaction mixture was well stirred at room temperature for 2 hours. After completion of reaction, as monitored by TLC, poured the mixture into crushed ice. The solid obtained was separated by filtration and crystallized from water:DMF (6:4) to get desired compounds. The synthesized compounds by above method are characterized by IR, ^1H NMR, mass spectroscopy.

Method (B) By US method: The solution of thiosemicarbazide (4a-i) (0.01 mole) was taken in 100 mL RBF with 5 mL conc. H_2SO_4 . And reaction mixture was subjected for ultrasound irradiation for 20 minutes. Progress of reaction was monitored on TLC. After completion of reaction contents was poured on crushed ice. Product obtained was separated by filtration, the product was crystallized from water: DMF (6:4) to get desired pure compound. This typical experimental procedure was followed to prepare other analogs of this series. The synthesized compounds by above method are characterized by IR, ^1H NMR, mass spectroscopy.

Method (C) By MW method: A solution of Thiosemicarbazide (4) (0.01mole) was taken in 50 mL borosilicate glass tube with 5 mL conc. H_2SO_4 . Reaction mixture was

Table 1. Characterization data of the synthesized compounds^a

Compd. No.	R	Conventional		US		MW		MP (°C)
		Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)	
4a	2-OMe	44	75	15	65	2	80	185
4b	3-OMe	35	72	20	95	2	85	164
4c	4-OMe	40	75	20	80	2	75	147
4d	H	45	85	20	85	2	75	195
4e	2-Me	45	70	20	87	2	78	177
4f	3-Me	40	83	20	80	2	75	165
4g	4-Me	45	77	20	89	2	75	188
4h	3-Cl	40	75	30	83	2	68	182
4i	2-Br	40	62	20	85	2	55	148
5a	2-OMe	120	70	20	84	3	78	255
5b	3-OMe	120	53	20	80	3	64	260
5c	4-OMe	120	70	20	77	3	87	240
5d	H	120	69	20	80	3	77	210
5e	2-Me	120	65	20	78	2	77	270
5f	3-Me	120	79	20	85	2	75	249
5g	4-Me	120	75	20	78	2	80	237
5h	3-Cl	120	67	20	71	2	68	300
5i	2-Br	120	77	20	83	3	75	267
6a	2-OMe	79	65	30	75	3	70	252
6b	3-OMe	90	67	35	75	3	70	245
6c	4-OMe	90	77	30	78	3	71	244
6d	H	90	63	30	68	2	67	250
6e	2-Me	90	66	30	70	2	63	247
6f	3-Me	90	67	35	70	3	68	244
7a	2-OMe	240	64	60	- ^b	3	- ^b	177
7b	3-OMe	240	66	60	- ^b	3	- ^b	197
7c	4-OMe	240	76	60	- ^b	3	- ^b	172
7d	H	240	77	60	- ^b	3	- ^b	195
7e	2-Me	240	70	60	- ^b	3	- ^b	194
7f	3-Me	240	67	60	- ^b	3	- ^b	165
7g	4-Me	240	65	60	- ^b	3	- ^b	170
7h	3-Cl	240	69	60	- ^b	3	- ^b	156

^aAll compounds were characterized by spectral analysis. ^bReaction not overcome.

irradiated inside a microwave oven for 2 min to 2.5 min at an output of 300 watts power, with short interruption of 15 second. Progress of the reaction was monitored by TLC. The reaction mixture was cooled and poured on crushed ice. Product was separated by filtration and crystallized from water:DMF (6:4) to get desired compound. The synthesized compounds by above method are characterized by IR, ¹H NMR, mass spectroscopy.

5-(7-Methoxy-3-methyl-1-benzofuran-2-yl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**6a**).

Method (A) By conventional method: A solution of thiourea (**4a-i**) (0.01mole) and 10 mL of 2N NaOH

was heated up to mild reflux for 1.5 hours. Progress of reaction was monitored on TLC. After completion of reaction, mixture was poured on crushed ice and acidified with dilute acetic acid. Product was separated by filtration and crystallized from water:DMF (6:4) to get desired compound. The synthesized compounds by above method are characterized by IR, ¹H NMR, Mass spectroscopy.

Method (B) By US method: A Solution of thiourea (**4a-i**) (0.01 mole) was taken in 100 mL RBF with 10 mL 2N NaOH solution. Reaction mixture was subjected for ultra sound irradiation for 30 minutes. Progress of reaction was monitored on TLC. After completion of reaction, mixture was poured on crushed ice and acidified with dilute

acetic acid. Product was separated by filtration and crystallized from water:DMF (6:4) to get desired compound. The Compounds synthesized by above method are characterized by IR, ¹H NMR, Mass spectroscopy.

Method (C) By MW method: Thiosemicarbazide (**4**) (0.01 mole) was taken in 50 mL borosilicate glass tube with 10 mL 2N NaOH solution. Reaction mixture was irradiated inside a microwave oven for 2 min to 2.5 min at an output of 300 watts power, with short interruption of 15 second. Progress of reaction was monitored on TLC. After compilation of reaction, mixture was poured on crushed ice and acidified with dilute acetic acid. Product was separated by filtration and crystallized from water:DMF (6:4) to get desired compound. The synthesized compounds by above method are characterized by IR, ¹H NMR, Mass spectroscopy.

5-(6-methoxy-3-methyl-1-benzofuran-2-yl)-N-(2-methoxyphenyl)-1,3,4-oxadiazol-2-amine (**7b**).

By conventional method: Thiosemicarbazide (**4a-h**) (0.01 mole) and 2 mL of 4N NaOH in ethanol was heated up to reflux temperature, than add a solution of Iodine (2.5 gm) and KI (3.2 gm) in 10 mL of ethanol at above temperature. The progress of reaction was monitored on TLC for 4 hrs at reflux temperature. Reaction mass was evaporated up to slurry and diluted with 10 mL of water and excess iodine was quenched with a 10% solution of sodium meta bisulphite. Solid product was filtered and crystallized from ethanol: water to get a desired compound. The synthesized compounds by above method are characterized by IR, ¹H NMR, Mass spectroscopy.

RESULTS AND DISCUSSION

In the present work, the commercially available benzofuran ester **1** was treated with hydrazine hydrate to give the acid hydrazide **2** in 94% yield. The synthesized acid hydrazide **2** was condensed with commercially available a series of aryl isothiocyanate **3a-i** in ethanol under reflux condition to obtain the corresponding hydrazine carbothiamide (**4a-i**) in 62 - 85% yield. The formation of the products has been confirmed by physical and spectroscopic data. The same condensation has also been achieved under microwave and ultrasound irradiation in good yields. Under ultrasound irradiation, it requires minimum time as compared to conventional heating method and yields are also good. Under microwave irradiation, it requires minimum time (2 min.) for the completion of the reaction. It suggests that the reactions under microwave irradiation condition are better for the synthesis of the titled compounds (**4a-i**). The intramolecular

cyclocondensation of hydrazine carbothiamide (**4a-i**) in the presence of Conc. H₂SO₄ at room temperature to form the corresponding thiadiazoles (**5a-i**) in 53 - 79% yields. The same products have been obtained under ultrasound irradiation in 20 min. and microwave irradiation in 2 min. with 71 - 85% and 64 - 87% yields respectively.

In this case, microwave irradiation method gives product formation in less time. The carbothiamides (**4a-i**) on cyclocondensation under basic condition by using NaOH gives the corresponding 1,2,4-triazoles (**6**) under conventional heating, ultrasound and microwave irradiation in good yields. All the synthesized triazoles (**6a-f**) were characterized by physical and spectroscopic data.

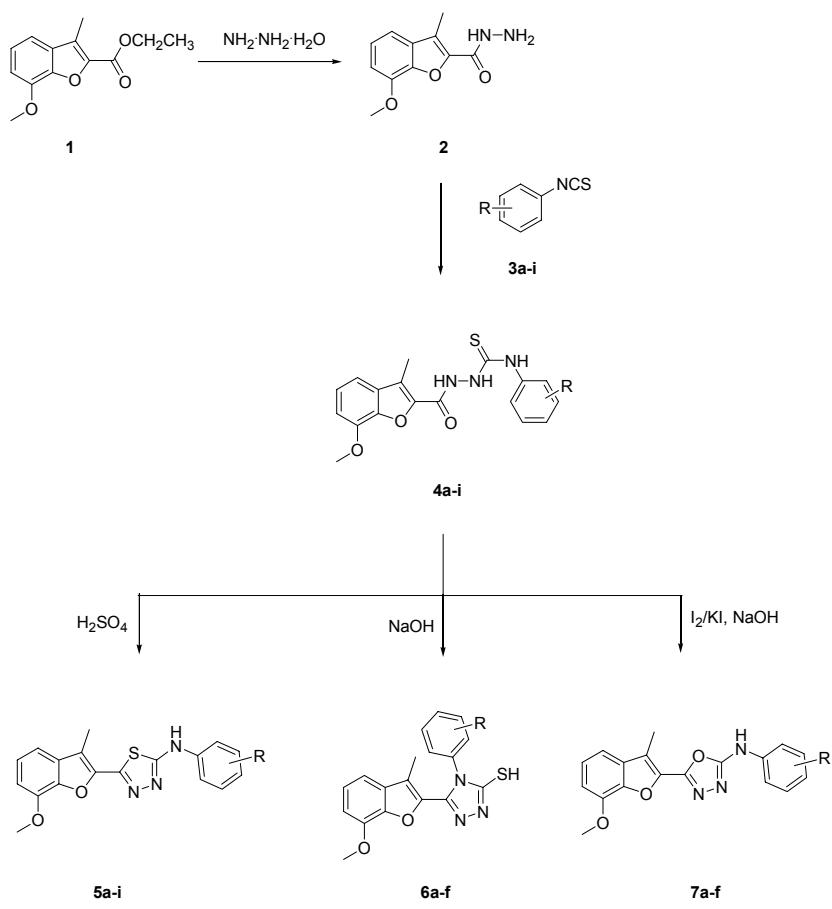
Again, the cyclocondensation of carbothiamide (**4a-i**) with I₂-KI and NaOH in ethanol give the corresponding 1,3,4-oxadiazoles (**7a-h**) in 1 h. with 64 - 77% yields. But, this cyclocondensation was not observed under ultrasound and microwave irradiation.

With these experimental procedures we have synthesized a new series of 1,3,4-thiadiazoles, 1,3,4-triazoles and 1,3,4-oxadiazoles (*Scheme 1*). The respective yields, times and physical data of synthesized compounds are summarized in (*Table 1*) and the formation of compounds was confirmed by spectroscopic analysis.

Compound **4a** shows the characteristic absorption peaks at 3138 cm⁻¹, 1678 cm⁻¹, 1192 cm⁻¹ due to N-H, -C=O and -C=S functionality respectively. ¹H NMR shows characteristic peaks due to -N-H protons at 9.6 δ (1H, s), 9.6 δ, (1H, s); and 10.52 δ, (1H, s); The structures of these compounds are also confirmed by their mass spectra. For compound **5** IR absorption peak at 3433 cm⁻¹ & 2910 cm⁻¹ due to -N-H functionality, ¹H NMR shows signal at 10.52 δ (1H, s) due to -N-H proton. The structures of these compounds are also confirmed by mass spectra. For compound **6** IR absorption peak at 1560 cm⁻¹ due to -C=N functionality. Compound **6** ¹H NMR shows signal at 14.3δ (1H, s). due to -SH proton. The structures of these compounds are also confirmed by mass spectra. For compound **7** IR absorption peak at 3238 cm⁻¹ and 1520 cm⁻¹ due to -N-H and -C=N functionality. The structures of these compounds are also confirmed by mass spectra.

Spectral Data.

(2) IR (KBr, cm⁻¹): 3460; 1680; 1610; 1202. ¹H NMR (300, MHz, DMSO-d₆, δ ppm): 2.94 (3H, s); 3.34 (3H, s); 6.57 (brs, 2H, NH2); 6.88 (1H, m); 7.22 (t, 1H, J = 1.2, 6.3 Hz); 8.10 (1H, d, J = 6.6 Hz); 9.47 (1H, s, NH). ES-MS: *m/z* (m+1): 221.2. Elemental Analysis:- Calc.: C-59.99%, H-5.49%, N-12.72; Found: C, 59.85; H, 5.24; N, 12.33.



(4a) **IR** (KBr, cm^{-1}): 3421; 3138; 1678; 1513; 1252. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.54 (3H, s); 3.73 (3H, s); 3.97 (3H, s); 6.88 (2H, d, J = 8.7 Hz); 7.10 (1H, d, J = 7.5 Hz); 7.28 (4H, m); 9.60 (1H, s); 9.69 (1H, s); 10.52 (1H, s). **ES-MS:** m/z (m+1): 385.9. **Elemental Analysis:-** Calc.: C-61.77%, H-5.18%, N-11.37%, S-8.68%; Found: C-61.42%, H-4.71%, N-11.11%, S-8.27%.

(4f) **IR** (KBr, cm^{-1}): 3423; 3145; 1682; 1520; 1258. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.28 (3H, s); 2.57 (3H, s); 3.98 (3H, s); 6.97 (1H, d, J = 8.7 Hz); 7.10 (1H, d, J = 7.5 Hz); 7.15-7.30 (5H, m); 9.67 (1H, s); 9.74 (1H, s); 10.54 (1H, s). **ES-MS:** m/z (m+ NH₃⁺) 386.43. **Elemental Analysis:-** Calc.: C-61.77%, H-5.18%, N-11.37%, S-8.68%; Found: C-61.33%, H-4.84%, N-11.05%, S-8.33%.

(5a) **IR** (KBr, cm^{-1}): 3433; 2910; 2777; 1631; 1609; 1580; 1493; 1233; 1182; 1028; 731; 587. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.55 (3H, s); 3.75 (3H, s); 3.96 (3H, s); 6.9-7.02 (2H, m); 7.26-7.52 (2H, m); 7.72 (1H, m); 7.90 (1H, t); 10.52 (1H, s). **ES-MS:** m/z (m+1): 385.9. **Elemental Analysis:-** C-64.94%, H-4.88%, N-11.96%, S-9.12%; Found: C-64.68%, H-4.53%, N-11.61%, S-8.65%.

(5e) **IR** (KBr, cm^{-1}): 3443; 29154; 2775; 1633; 1619; 1585; 1497; 1235; 1187; 1029; 737; 580. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.88 (3H, s); 3.95 (3H, s); 7.25-7.55 (4H, m); 7.34-7.64 (4H, m); 10.78 (1H, s). **ES-MS:** m/z (m+1): 337.39. **Elemental Analysis:-** Calc.: C-64.94%, H-4.88%, N-11.96%, S-9.12%; Found: C-64.75%, H-4.44%, N-11.69%, S-8.77%.

(6a) **IR** (KBr, cm^{-1}): 3098; 2939; 1514; 1248; 1172; 1036; 827; 731; 565. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.27 (3H, s); 3.70 (3H, s); 3.78 (3H, s); 6.98 (1H, d, J = 9.0 Hz); 7.20 (3H, m); 7.32 (1H, d, J = 9 Hz); 7.40-7.70 (2H, m); 14.45 (1H, s). **ES-MS:** m/z (m+1): 367.42. **Elemental Analysis:-** Calc.: C-64.94%, H-4.88%, N-11.96%, S-9.12%; Found: C-64.66%, H-4.54%, N-11.68%, S-8.71%.

(6b) **IR** (KBr, cm^{-1}): 3097; 2949; 1516; 1252; 1175; 1037; 837; 736; 575. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.28 (3H, s); 3.70 (3H, s); 3.79 (3H, s); 6.70-6.94 (2H, m); 7.00 (1H, d, J = 9.0 Hz); 7.21 (2H, m); 7.31 (2H, d, J = 9 Hz); 14.25 (1H, s). **ES-MS:** m/z (m+1): 367.42. **Elemental Analysis:-** Calc.: C-64.94%, H-4.88%, N-11.96%, S-9.12%; Found: C-64.67%, H-4.37%, N-11.58%, S-8.58%.

(6c) IR (KBr, cm^{-1}): 3096; 2946; 1517; 1242; 1165; 1035; 833; 732; 577. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.27 (3H, s); 3.70 (3H, s); 3.78 (3H, s); 6.75-6.93 (2H, m); 7.00 (1H, d, J =9.0 Hz); 7.20 (2H, m); 7.32 (2H, d, J =9 Hz); 14.35 (1H, s). **ES-MS:** m/z (m+1): 367.42. **Elemental Analysis:-** Calc.: C-64.94%, H-4.88%, N-11.96%, S-9.12%; Found: C-64.54%, H-4.49%, N-11.80%, S-8.79%.

(6d) IR (KBr, cm^{-1}): 3097; 2949; 1516; 1243; 1156; 1037; 839; 733; 577. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.30 (3H, s); 2.32 (3H, s); 3.66 (3H, s); 6.90 (1H, d, J =9 Hz); 7.18 (3H, m,); 7.30 (3H, m); 14.34 (1H, s). **ES-MS:** m/z (m+1): 351.42. **Elemental Analysis:-** C = 64.08%, H-4.48%, N-12.45%, S-9.50%; C = 63.74%, H-4.01%, N-12.15%, S-9.12%.

(6e) IR (KBr, cm^{-1}): 3092; 2941; 1513; 1239; 1160; 1031; 831; 729; 574. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.55 (3H, s); 3.75 (3H, s); 3.95 (3H, s); 7.02 (3H, m); 7.23 (2H, d, J =9.0 Hz); 7.72 (1H, d, J =9 Hz); 7.82 (1H, d, J =9 Hz); 10.50 (1H, s). **ES-MS:** m/z (m+1): 351.42. **Elemental Analysis:-** Calc.: C-64.94%, H-4.88%, N-11.96%, S-9.12%; Found: C-64.59%, H-4.38%, N-11.73%, S-8.66%.

(7a) IR (KBr, cm^{-1}): 3430; 3058; 2911; 1633; 1611; 1578; 1495; 1247; 1133; 1028; ; 722; 587. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.51 (3H, s); 3.73 (3H, s); 3.97 (3H, s); 6.89-7.31(5H, m); 7.55 (1H, d, J =8 Hz); 14.22 (1H, s). **ES-MS:** m/z (m+1): 351.35. **Elemental Analysis:-** Calc.: C-68.05%, H-5.11%, N-12.53%; Found: C-67.83%, H-4.92%, N-12.19%.

(7d) IR (KBr, cm^{-1}): 3430; 3066; 2915; 1631; 1611; 1587; 1495; 1247; 1133; 1025; 1011; 727; 681; 585. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.34 (3H, s); 3.66 (3H,s); 3.93 (3H, s); 6.9(1H, s); 7.05 (1H, s); 7.15-7.25 (5H, m,); 14.34 (1H, s). **ES-MS:** m/z (m+1): 335.31. **Elemental Analysis:-** Calc.: C-67.28%, H-4.71%, N-13.08%; Found: C-67.03%, H-4.32%, N-12.78%.

(7e) IR (KBr, cm^{-1}): 3433; 3068; 2910; 1631; 1609; 1580; 1493; 1245; 1135; 1028; 1014; 722; 684; 587. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.31 (3H, s); 2.32 (3H, s); 3.67 (3H, s); 6.93(1H, s); 7.21 (3H, m); 7.26-7.30 (4H, m,); 14.32 (1H, s). **ES-MS:** m/z (m+1): 335.35. **Elemental Analysis:-** Calc.: C-68.05%, H-5.11%, N-12.53%; Found: C-67.78%, H-4.81%, N-12.26%.

(7f) IR (KBr, cm^{-1}): 3443; 3038; 2917; 1631; 1607; 1585; 1494; 1243; 1139; 1029; 1017; 725; 683; 589. **$^1\text{H NMR}$** (300, MHz, DMSO-d⁶, δ ppm): 2.08 (3H, s); 2.36 (3H, s); 3.62 (3H, s); 6.88(1H, s); 7.18 (2H, m); 7.28 (2H, d, J =8 Hz); 7.28 (2H, d, J =8 Hz); 14.40 (1H, s). **ES-MS:** m/z (m+1): 335.33. **Elemental Analysis:-** Calc.: C-68.05%, H-5.11%, N-12.53%; Found: C-67.71%, H-4.83%, N-12.26%.

CONCLUSION

We have synthesized a new series of 1,3,4-thiadiazoles, 1,3,4-triazoles and 1,3,4-oxadiazole incorporation benzofuran ring by conventional and non-conventional methods. All the compounds were obtained in excellent yields.

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