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Synthesis and Pharmacological Evaluation of Novel 1-(2, 6-Difluorobenzyl)-1h-1, 2, 3-Triazole Derivatives for Cns Depressant and Anticonvulsant Profile

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ABSTRACT

A series of 1-(2, 6-difluorobenzyl)-1H-1, 2, 3-triazole (5a-d and 7a-d) were synthesized and evaluated for CNS depressant and anticonvulsant activities by photoactometer, rotarod and pentylene tetrazole induced convulsion method respectively in Swiss albino mice. Diazepam was used as a standard drug. Out of the 8 compounds tested, compounds (5b, 7a and 7b) were showed the CNS depressant activity comparable to that of diazepam at a dose of 5 mg/kg. The active members of the series (5b, 7a and 7b) were selected for anticonvulsant activity study.

Keywords: 1, 2, 3-triazole, CNS depressant, Pentylenetetrazole, Clonic convulsions.

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INTRODUCTION

Central nervous system (CNS) depressant agents are an important class of drugs, which are useful in the treatment of anxiety and related emotional disorders. Among the different class of CNS depressant agents, benzodiazepines were found to have good activity and well accepted by patients. They are acting through benzodiazepine receptors, which are adjacent to γ-amino butyric acid (GABA) receptors. GABA is the major inhibitory neurotransmitter in the brain. It controls excitability of many central nervous system pathways. Epilepsy is the third most frequent neurological disorder encountered in the elderly after cerebrovascular disease and dementia. Currently used anticonvulsant agents for treatment of epilepsy have certain disadvantages such as notable adverse effects and inefficient therapy in some seizure types, a clear need for safer and more effective antiepileptic drugs is well known. Therefore, the development of new antiepileptic drugs with approved therapeutic properties is an important challenge for medicinal chemists [1-4]. The 1, 2, 3-triazole system has widespread uses, and it has been considered as an interesting component in terms of biological activity [2-5]. Extensive literature review revealed that two structures among the compounds studied for anticonvulsant activity are carboxamide moiety and 1, 2, 3-triazole nucleus shows potent anticonvulsant activity. 4-pyridinecarboxamide[5], Ameltolide[6] and Ralitoline[7] are the examples of carboxamide analogs and acetazolamide, methazolamide are the examples of 2, 5-disubstituted-1, 3, 4-thiadiazole analogs[8, 9]. The literature survey reveals that triazoles were reported for analgesic, anti-inflammatory, anti allergic and CNS depressant activities. A large number of references[10-17] showed that triazoles are having excellent CNS depressant and anticonvulsant activities. Significant CNS depressant activity was reported for triazoles especially triazolopyrimidines[18], triazolothienopyrimidine[19,20], 1,3,4-thiadiazolotetrahydrobenzothienopyrimidine[21] and 1,3,4-thiadiazole-quinazoline[22] has given an impetus to synthesize some non-benzodiazepine ligands which are devoid of typical benzodiazepine mediated side effect such as physical dependence, amnesia, over sedation. In this paper, we report details of synthesis and evaluation of the CNS depressant and anticonvulsant profiles of these compounds.

MATERIAL AND METHOD

Thin-layer chromatography (TLC) was performed on silica gel analytical TLC plates (60 F_{254}, Merck, Darmstadt, Germany). Melting points (uncorrected) were determined on a Boetius apparatus. The IR spectra were recorded with Perkin–Elmer 597 Specord M-80 spectrometer (The Perkin–Elmer Corporation Ltd, Beaconsfield, Bucks, England). ^{1}HNMR spectra were recorded on

Aspect 3000, BrukerAC400 (400MHz) spectrometer and the chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane as internal standard. Electron ionization mass spectra were recorded on a VG-250 spectrometer (VG Labs., Tritech England) with ionization energy maintained at 70eV. Elemental analyses were obtained with an acceptable range (±0.4%) using a Perkin–Elmer 2400B CHN analyzer.

CHEMISTRY

Synthesis of 2-(azidomethyl)-1, 3-difluorobenzene (2*)*

A mixture of 2, 6-difluorobenzylchloride (5 g, 0.024 mol) sodium azide (1.72 g, 0.026 mol) and water (50 ml) were heated to 75° C. for 30 h and the progress of the reaction was monitored by TLC. After completion of the reaction, the contents were cooled to room temperature. Aq. layer was extracted with 3×100 ml ethyl acetate. Organic layers were combined and washed with brine. The organic layer was separated and dried over anhydrous Na_2SO_4, and solvents removed under reduced pressure to obtain of as an oily product.

Synthesis of methyl 1-(2, 6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxylic acid (3)

Methyl propiolate (2.1 ml, 0.0207 mol) was added drop wise at room temperature to a mixture of 2-(azidomethyl)-1, 3-difluorobenzene (3.0 g, 0.0207 mol) and water (50 ml) then heated to 65° C for 5 hours. The progress of the reaction was monitored by TLC. After the completion of reaction, the reaction mixture was cooled to room temperature. The solid obtained was filtered and then washed with water (10 ml). The product was dried under vacuum at 50° C to give methyl 1-(2, 6-difluorobenzyl)-1H-1, 2, 3-triazole-4-carboxylic acid as a white solid.

Synthesis of 1-[(2, 6-difluorophenyl) methyl]-1H-1, 2, 3-triazole-4- carboxylic acid (4)

A solution of lithium hydroxide monohydrate (0.49g, 0.0117 mol) in water (2 ml) is added toa stirred solution of the ester 3 (1g, 0.0039 mol) in methanol (4 ml) and THF (4 ml). The suspension is stirred overnight and concentrated under reduced pressure. The obtained residue was acidified to pH 3.5 with 2N hydrochloric acid. The aqueous layer was extracted with ethyl acetate (3 x 25 ml). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude products were crystallized from methanol and ether to get off-white solid 4.

General procedure for the synthesis of compounds (5a-d)

1-[(2, 6-difluorophenyl) methyl]-1H-1, 2, 3-triazole-4- carboxylic acid (1.0 mmol), EDC·HCl (1.3 mmol) and DMF (10 ml) were added to a round-bottom flask, then HOBt (1.0 mmol), amine (1.0 mmol) and triethylamine (2.0 mmol) were added to the above mixture. Reaction mixture was stirred at room temperature for 10 h. Reaction mixture is diluted with water. Solid precipitates

were filtered under suction on buchner funnel and then washed with water (20 ml). The crude products were crystallized from ethanol to get off-white solid.

1-(2, 6-difluorobenzyl)-1H-[1, 2, 3-triazole-4-carbohydrazide (6)

The ester 3 (1g, 0.0039 mol) was charged into 20 ml methanol and refluxed with 1 ml hydrazine hydrate for 4 hours. Reaction mixture was cooled to room temperature. Methanol was removed on rotavapour under reduced pressure. Solid precipitates were filtered under suction on buchner funnel. Product was washed with 10 ml diethyl ether.

General procedure for the synthesis of compounds (7a-d)

A mixture of 1.0 mmol of 1-(2, 6-difluorobenzyl)-1H-[1, 2, 3-triazole-4-carbohydrazide (6) and 1.0 mmol of the corresponding aldehyde derivative in 10 ml of absolute ethanol was stirred at room temperature for 0.5 to 2 h, in the presence of two drops of acetic acid as a catalyst. The end of the reaction was observed by TLC, and the hydrazones **7a-d** were isolated by concentration of the reaction mixture under reduced pressure, followed by neutralization with a 10% aqueous solution of sodium bicarbonate. The resulting precipitate was filtered, washed with 10 ml water.

***In Vivo* Pharmacological Evaluation**

CNS depressant activity by photoactometer method

The title compounds (5 a-d and 7a-d) were screened for their CNS depressant activity using photoactometer [23]at 30 min and 1 h after drug administration. The CNS depressant activity of animal inside the photometer chamber was recorded as a photoactometer counts. Decreased score suggest the CNS depressant activity. The Swiss albino mice of either sex weighing 25-30 g weight were used. They were divided into groups of six animals each and each group was allowed to get acquainted for 10 min. Thereafter the photoactometer counts were noted for a period of 10 min which was the initial reading (control). The test compounds were suspended in 1% CMC solution in distilled water and administered at a dose of 5 mg/kg *i.p.* of the body weight. Each group is served as its own control. One of the groups was treated with diazepam as the standard at a dose of 5 mg/kg. After twenty min of administration of test compound, the animals were kept into the photoactometer chamber and the counts were noted for 10 min after a 10 min rest in the chamber. The same procedure was repeated after 50 min. Decrease in the number of counts for each group was calculated and the %CNS depressant activity was determined by the following formula. %CNS depressant activity= (Control reading – Decrease in count/ Control reading) X 100. The observations are tabulated as Table 1.

Anticonvulsant activity (PTZ induced seizure test) [24]

Of the various compounds tested for CNS depressant activity, the most active four derivatives 5b, 7a and, 7b were evaluated for anticonvulsant activity. The dose required for protecting the animal from pentylenetetrazole (PTZ) induced clonic convulsions was determined for tested compound (Table 2). Aqueous solution of PTZ (dose 85 mg/kg) was administered orally to group of six mice, 30 min after the administration of the test compound as suspension in 1% CMC *i.p.* Mice were then observed for a period of 20min for the symptoms of clonic convulsions. Number of animals in each group, which were protected against PTZ induced clonic convulsions, was used as a percentage response parameter for calculating the effective anticonvulsant dose (ED_{50}) of the test compound. All the tested compounds offered good protection to the animals from the PTZ induced clonic convulsions at the dose levels 6.0-12.0 mg/kg, body weight. The compound 5l exhibited the best anticonvulsant activity by protecting 100 % animals at dose of 6.0 mg/kg body weight. ED_{50} of these compounds have also been calculated and tabulated in Table 3.

RESULTS AND DISCUSSION

Chemistry

2, 6-difluorobenzyl azide[25] (**2)** prepared by reacting the corresponding, commercially available 2, 6-difluorobenzyl chloride **(1)** with sodium azide. 2, 6-difluorobenzyl azide **(2)** undergoes cycloaddition with methyl propiolate to give methyl 1-(2, 6-difluorobenzyl)-1H-1, 2, 3-triazole-4-carboxylic acid[27] (**3)**. Ester **(3)** was hydrolyzed by lithium hydroxide to get 1-(2, 6-difluorobenzyl)-1H-1, 2, 3-triazole-4-carboxylic acid **(4)**. The 1-(2, 6-difluorobenzyl)-1H-1, 2, 3-triazole-4--carboxamide analogs **(5a-e)** were prepared by condensing the acid with cyclic amines under peptide bond formation chemistry using [1-(3-dimethylaminopropyl)-3-ethylcarbodiimide]hydrochloride and 1-hydroxybenzotriazole hydrate in the presence of triethylamine at 25–28°C. Aromatized ester **(3)** was converted into required hydrazide **(6)** by reacting with hydrazine hydrate in methanol. The hydrazide was used for preparation of arylhydrazone analogs **(7a-d)** with various heterocyclic aldehydes. The title compounds (5a-d) and (7a-d) were synthesized by the route depicted in figure 1. The formation of 6 was confirmed by the presence of NH and NH_2 signals around 3140 -3300 cm^{-1} in the IR spectra. It also showed a peak for carbonyl (C=O) at around 1675 cm^{-1}. The NMR spectrum of the compound 4 showed signals at δ 4.42 (bs, 2H, NHN*H*$_2$), and δ 9.66 (bs, 1H, N*H*NH_2). The formation of imine product is indicated by the disappearance of peaks due to NH_2 of the starting material at 3140-3300 cm^{-1} in IR spectra of all the compounds (7a–d). The NMR spectrum of (7a–d) showed the absence of NH_2 signals. The ^{1}H NMR spectra of compound (5a-d and 7a–d) showed singlet at δ 5-65-5.75 due to benzylic

proton and a multiplet at δ 7.50–7.25 integrating for one aromatic proton and at δ 7.00–6.90 integrating for two aromatic protons were observed in spectrum. The mass spectra of the synthesized final compounds gave molecular ion peak exactly at M+1 indicated that the data is in agreement with the predicted structures.

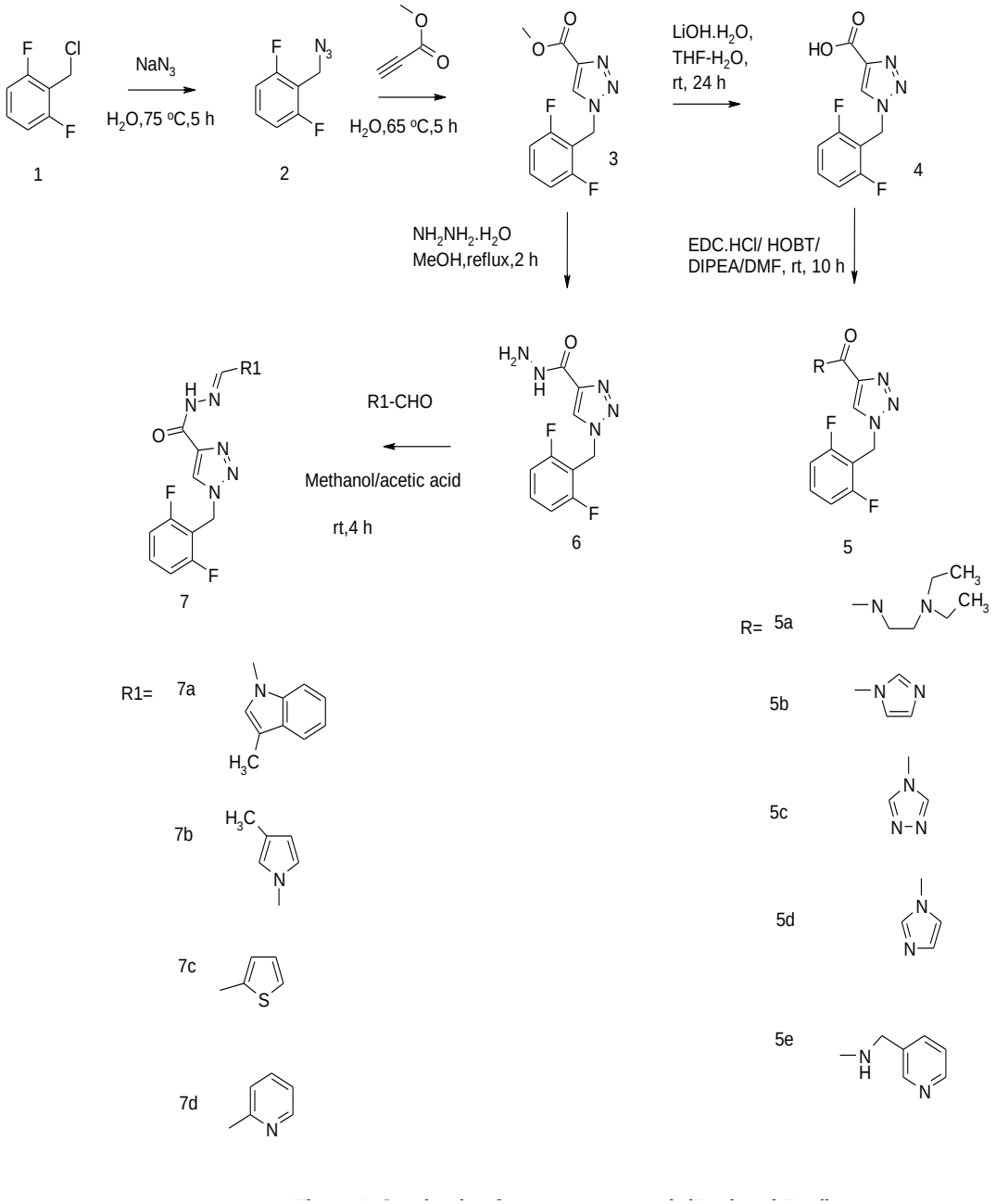

Figure 1: Synthesis of target compounds(5 a-d and 7 a-d)

Synthesis of 2-(azidomethyl)-1, 3-difluorobenzene (2*)*

Yield: 3.8 g (85%); **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 7.30-7.40 (m, 1H, Ar-H), 6.92-7.03 (m, 2H, Ar-H), 4.45 (s, 2H, CH2); **ESI-MS** (m/z): 170(M+1); **Molecular Weight**: - 169; **Molecular Formula**: - $C_7H_5F_2N_3$.

Synthesis of methyl 1-(2, 6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxylic acid (3)

Yield: 2.5 g (85%); **mp**.: 137-140 ^{o}C; **ESI-MS** (m/z): 254(M+1); **Molecular Weight**: - 253; **Molecular Formula**: - $C_{11}H_9F_2N_3O_2$.

Synthesis of 1-[(2, 6-difluorophenyl) methyl]-1H-1, 2, 3-triazole-4- carboxylic acid (4)

Yield: **0.74 g (80%)**; mp.: **200-203 ^{o}C**; 1H NMR (400 MHz, DMSO-d_6, δ ppm): **8.73 (s, 1 H, Ar-H), 7.47-7.57 (m, 1H, Ar-H), 7.18 (m, 2H, Ar-H), 5.73 (s, 2H, CH_2)**; ESI-MS (m/z): **240 (M+1)**; Molecular Weight:- **239**; Molecular Formula:- **$C_{10}H_7F_2N_3O_2$.**

[1-(2, 6-difluorobenzyl)-1H-[1, 2, 3]-triazol-4-yl (1H imidazol-1yl)]-methanone (5a)

Yield: 0.25 g (83%); **mp**.: 254-257 ^{o}C; **IR** (KBr, cm^{-1}): 1670 (C=O); **^{1}H NMR** (400 MHz, DMSO-*d*6, δ ppm): 8.85 (s, 1H, Ar-H), 8.55-8.54 (d, 1H, imidazol-H), 7.79 (s, 1H, imidazol-H), 7.43-36 (m, 1H, Ar-H), 7.01-6.97 (m, 2H, Ar-H), 6.51 (s, 1H, imidazol-H), 5.73 (s, 2H, CH_2) **ESI-MS** (*m*/*z*): 290 (M+1); **Molecular Weight**:-289; Molecular Formula:- $C_{13}H_9F_2N_5O$.

[1-(2, 6-difluorobenzyl)-1H-[1, 2, 3]-triazol-4-yl (1H-1,2,4- triazol-1yl)]-methanone (5b)

Yield: 0.28 g (93%); **mp**.: 225-228 ^{o}C; **IR** (KBr, cm^{-1}): 1678 (C=O); **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 8.92 (s, 1H, 1,2,4- triazol -H), 8.50 (s, 1H Ar-H), 8.12 (s, 1H, 1,2,4- triazol -H), 7.47-40 (m, 1H, Ar-H), 7.10-7.00 (m, 2H, Ar-H), 5.75 (s, 2H, CH_2); **ESI-MS** (*m*/*z*):291 (M+1); **Molecular Weight**:-290; **Molecular Formula**:- $C_{12}H_8F_2N_6O$.

[1-(2, 6-difluorobenzyl)-1H-[1, 2, 3]-triazol-4-yl (1H- pyrazol-1yl)]-methanone (5c)

Yield: 0.29 g (97%); **mp**.: 171-174 ^{o}C; **IR** (KBr, cm^{-1}): 1680 (C=O); **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 8.77 (d, 1H, pyrazol -H), 8.53 (s, 1H Ar-H), 8.13 (d, 1H, pyrazol -H), 7.62-7.56 (m, 1H, pyrazol -H), 7.45-39 (m, 1H, Ar-H), 7.12-7.04 (m, 2H, Ar-H), 5.71 (s, 2H, CH_2); **ESI-MS** (*m*/*z*): 290 (M+1); **Molecular weight**:-289; **Molecular Formula**:- $C_{13}H_9F_2N_5O$.

1-(2, 6-difluorobenzyl)-N-(pyridin3-ylmethyl)-1H-[1, 2, 3]-triazole-4-carboxamide (5d)

Yield: 0.29 g (79%); **mp**.: 205-208 ^{o}C; **IR** (KBr, cm^{-1}): 1685 (C=O); **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 8.22 (s, 1H, Ar-H), 7.36-7.46 (m, 1H, Ar-H), 6.92-6.98 (m, 2H, Ar-H), 5.75 (s, 2H, CH_2), 4.51 (bs, 1H, OH), 4.38 (m, 2H, CH_2-piperazine), 3.90-3.95 (m, 2H CH_2-piperazine), 3.85 (m, 4H, CH_2-piperazine), 3.50 (t, 2H, CH_2), 3.33 (t, 2H, CH_2); **ESI-MS** (*m*/*z*): 352 (M+1); **Molecular weight**:-351; **Molecular Formula**:- $C_{16}H_{19}F_2N_5O_2$.

1-(2, 6-difluorobenzyl)-1H-[1, 2, 3-triazole-4-carbohydrazide (6)

Yield: 0.8 g (80 %); mp.: 187-190 ^{o}C; **IR** (KBr, cm^{-1}) : 3300, 3225 (NH_2), 3140 (NH), 1675(C=O); **^{1}H NMR** (400MHz, DMSO-*d*6, δ ppm); 9.66 (bs, 1H, NH), 8.53 (s, 1H, Ar-H), 7.50 (m, 1H, Ar-H), 7.15-7.19 (m, 2H, Ar-H), 5.69 (s, 2H, CH_2), 4.42 (bs, 2H, NH_2); **ESI-MS** (*m*/*z*): 254 (M+1); **Molecular weight:**-253; **Molecular Formula**:- $C_{10}H_9F_2N_5O$.

E-1-(2, 6-difluorobenzyl)-N-((1-methy1-H-lindol-3-yl) methylene)-1H-[1, 2, 3]-triazole-4-carbohydrazide (7a)

Yield: 0.17 g (44 %); **mp**.: 122-125 ^{o}C; **IR** (KBr, cm^{-1}) : 3251 (NH), 1690 (C=O), 1552 (C=N); **^{1}H NMR** (400 MHz, DMSO-*d*6 ,δ ppm) 9.0 (bs, 1H, NH), 8.62 (s, 1H, Ar-H), 7.45-7.51 (m, 1H, Ar-H), 7.13-7.18 (m, 2H, Ar-H), 5.74 (s, 2H, CH_2); **ESI-MS** (*m*/*z*): 395(M+1); **Molecular weight**:-394; **Molecular Formula**:- $C_{20}H_{16}F_2N_6O$.

E-1-(2, 6-difluorobenzyl)-N-((1-methy1-H-pyrrol-3-yl) methylene)-1H-[1, 2, 3]-triazole-4-carbohydrazide (7b)

Yield: 0.2 g (59 %); **mp**.: 137-140 ^{o}C; **IR** (KBr, cm^{-1}): 3255 (NH), 1695(C=O), 1555 (C=N); **^{1}H NMR** (400 MHz, DMSO-*d*6 ,δ ppm) 9.0 (bs, 1H, NH), 8.64 (s, 1H, Ar-H), 7.47-7.53 (m, 1H, Ar-H), 7.15-7.19 (m, 2H, Ar-H), 5.72 (s, 2H, CH_2); **ESI-MS** (*m*/*z*): 345(M+1); **Molecular weight**:-344; **Molecular Formula**:- $C_{16}H_{14}F_2N_6O$.

E-1-(2,6-difluorobenzyl)-N-(thiophen-2-ylmethylene)-1H-[1,2,3]-triazole-4-carbohydrazide (7c)

Yield: 0.26 g (74 %): **mp**.: 157-160 ^{o}C; **IR** (KBr, cm^{-1}): 3258 (NH), 1700 (C=O), 1558 (C=N); **^{1}H NMR** (400 MHz, DMSO-d6,δ ppm) 8.62 (s, 1H, Ar-H), 7.39-7.43 (m, 1H, Ar-H), 7.05-7.12 (m, 2H, Ar-H), 5.22 (bs, 2H, NH_2), 5.70 (s, 2H, CH_2); **ESI-MS** (m/z): 348 (M+1); **Molecular weight**:-347 **Molecular Formula**:- $C_{15}H_{11}F_2N_5OS$.

E-1-(2, 6-difluorobenzyl)-N-(pyridin-2-ylmethylene)-1H-[1, 2, 3]-triazole-4-carbohydrazide (7d)

Yield: 0.30 g (89 %): **mp**.: 178-181 ^{o}C; **IR** (KBr, cm^{-1}): 3250 (NH), 1687 (C=O), 1560 (C=N); **^{1}H NMR** (400 MHz, DMSO-d6,δ ppm) 8.62 (s, 1H, Ar-H), 7.39-7.43 (m, 1H, Ar-H), 7.05-7.12 (m, 2H, Ar-H), 5.22 (bs, 2H, NH_2), 5.70 (s, 2H, CH_2); **ESI-MS** (m/z): 343 (M+1); **Molecular weight**:-342; **Molecular Formula**:- $C_{16}H_{12}F_2N_6O$.

Pharmacological Activity

The title derivatives (5a-d and 7a–d) were evaluated for CNS depressant activity (Motor coordination) at a dose of 5 mg/kg in Swiss albino mice. The activity was compared with diazepam as a standard drug. Of the various compounds tested for CNS depressant, the most active four derivatives 5b, 7a and 7b were evaluated for anticonvulsant activity at different dose level. The results of the various activities are presented in (Table 1, 2 and 3). All the derivatives tested for CNS depressant activity by photoactomer, shown decrease in locomotor activity between 60.09 to 83.20 % after 60 min. where 60.09% was the lowest and 8320% was the maximal decrease in locomotor activity when compared to diazepam as reported in (Table 1).The three derivatives (5b,

7a and 7b) showed comparable CNS depressant activity at a dose of 5 mg/kg *i.p*. after 60 min. of administration to that of standard drug diazepam (88.23 %) at a dose of 5 mg/kg. All the compounds except (5d and 7d) exhibited more than 70 % decrease in locomotor activity after 60 min. The most active four derivatives (5b, 7a and 7b) among the series were evaluated for anticonvulsant activity (Table 2). The dose required for protecting the animal from pentylenetetrazole (PTZ) induced clonic convulsions was determined. All the three compounds offered good protection to the animals from the PTZ induced clonic convulsions at the dose levels of 5.0-11.0 mg/kg body weight, while diazepam shown 100% protection at the dose of 2.5 mg/kg. Again the compound 7b exhibited the anticonvulsant activity by protecting 100% animal at dose of 7.0 mg/kg body weight. The ED_{50} values for anticonvulsant activity of four compounds have also been calculated and given in (Table 3). The ED_{50} values for these derivatives are in the range of 5.50 to 9.50 mg/kg while that of diazepam shown the ED_{50} 1.0. The pharmacological results indicated that the series of compounds exhibited comparable CNS depressant than anticonvulsant activities.1H-[1, 2, 3-triazole-4-carbohydrazide (7a-d) derivative show better activities than 1H-[1, 2, 3-triazole-4-carboxamide derivative (5a-d).

Table 1: CNS Depressant activity by Photoactometer (n =6 animals; dose 5 mg /kg *i.p.*)

Compound	Photoactometer counts[a]			%CNS depressant activity	
	Prior(control)	30min after	60 min after	After 30min	After 60min
		Administration of Test compound			
5a	98±1.74	30±1.28	27±1.28	69.38	72.24
5b	135±1.76	34±1.47	25±1.25	74.81	81.48
5c	105±1.78	37±1.44	30±1.25	64.76	71.42
5d	110±1.77	45±1.23	43±1.17	59.09	60.09
7a	125±1.71	30±1.34	21±1.30	76.00	83.20
7b	118±1.75	23±1.15	20±1.12	80.50	83.20
7c	100±1.76	32±1.47	29±1.25	68.00	71.00
7d	97±1.71	33±1.34	30±1.30	65.59	69.07
Diazepam	102±1.60	16±1.21	12±1.17	84.31	88.23

[a] Each score represents the means±SEMof six mice, significantly different from the control score at $p<0.05$ (Student's t-test).

Table 2: Anticonvulsant activity (n=6 animals, *orally)*

Compound	Dose (mg/kg)	% of Animal protected against PTZ induced clonic convulsions
5b	9.0	33.33
	10.0	83.33
	11.0	100.00
7a	8.0	33.33
	9.0	66.66
	10.0	100.00

7b	5.0	16.66
	6.0	83.33
	7.0	100.00
Diazepam	0.5	16.66
	1.0	50.00
	2.0	83.33
	2.5	100.00

Table 3- Effective dose (ED_{50}) protecting 50% population from pentylenetetrazole (85 mg/kg, orally) induced clonic convulsions (n=6 animals) in mice.

Compound	ED_{50} mg/kg
5b	9.50
7a	8.50
7b	5.50
Diazepam	1.00

CONCLUSION

In the present investigation, 8 new 1-(2, 6-difluorobenzyl)-1H-1, 2, 3-triazole derivatives were synthesized and characterized by spectral analysis. They were screened for CNS depressant, and anticonvulsant activities and compounds 5b, 7a and 7b exhibited promising activity.

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