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SYNTHESIS, CHARACTERIZATION AND ANTICONVULSANT ACTIVITY EVALUATION OF SOME 1,4-DIHYDROPYRIDINES AND 3,5-(SUBSTITUTED)OXYCARBONYL-1,4-DIHYDRO-2,6-DIMETHYL-N-[2-(4-SULFAMOYLPHENYLAMINO)-ACETYL]-4-(SUBSTITUTED)PYRIDINES

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Abstract: A series of 3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-4-(substituted)pyridines (**1a**-**j**) were synthesized by Hantzsch method for pyridine synthesis. Treatment with chloroacetyl chloride produced N-(2-chloroacetyl)-3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-4-(substituted)pyridines (**2a**-**e**), which on further treatment with sulfanilamide resulted in 3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-N-[2-(4-sulfamoylphenylamino)-acetyl]-4-(substituted)pyridines (**3a**-**e**). The structures has been established on the basis of spectral (IR, ^{1}H-NMR, mass) and elemental analysis. Compounds 1a-j and **3a**-**e** (5 mg/kg and 10 mg/kg) were evaluated for their anticonvulsant effect against pentylenetetrazole-induced convulsions with diazepam (4 mg/kg) as the reference. Compounds **3a**-**e** exhibited significant ($p < 0.01$) anticonvulsant activity compared to the control.

Keywords: 1,4-dihydropyridines, sulfanilamide, amides, anticonvulsant activity

Calcium channel blockers (1,4-dihydropyridines) are reported to be effective against the whole range of convulsive procedures including electro- and pentylenetetrazole convulsions and sound and high pressure-induced seizures (1-3). The sulfonamide carbonic anhydrase inhibitors (sulfanilamide) are believed to exhibit anticonvulsant effects by hyperpolarization of neurons as well as enhancement of GABA-ergic transmission (4-6). Further, the anticonvulsant activity of several amide derivatives is attributed to the allosteric modulation of the GABA and affinity to the voltage-sensitive calcium channel receptors (7). In the present work we attempted to investigate some 1,4-dihydropyridines and their molecular hybrids with carbonic anhydrase inhibitor (sulfanilamide) linked by amide moiety, which were expected to reveal higher anticonvulsant activity. Synthesis according to the Hantzsch method (8) involved the reaction of ethyl acetoacetate with aromatic aldehyde in the presence of ammonium hydroxide to yield the substituted 1,4-dihydropyridines **(1a-e)**, which on treatment with chloroacetyl chloride under alkaline condition (9) gave the corresponding N-(2-chloroacetyl)-3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-4-(substituted)pyridines **(2a-e)**. These on further reaction (10) with sulfanilamide afforded the formation of 3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-N-[2-(4-sulfamoylphenylamino)-acetyl]-4-(substituted)pyridines **(3a-e).** In the present investigation, the synthesized substituted 1,4-dihydropyridines and 3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-N-[2-(4-sulfamoylphenylamino)-acetyl]-4-(substituted)pyridines **(3a-e)** were evaluated for their anticonvulsant activity (11, 12).

EXPERIMENTAL

The purity of the compounds was checked by TLC on silica gel-G coated plates with 0.5% sodium chloride : ammonia : acetonitrile (50:20:30, v/v/v) and toluene : methanol : ammonia (75:20:5, v/v/v) as solvent systems and using iodine as visualizing agent. Melting points (Sisco, India) were determined in open capillary tubes and were uncorrected. IR spectra were recorded on FTIR-8400S (Shimadzu,

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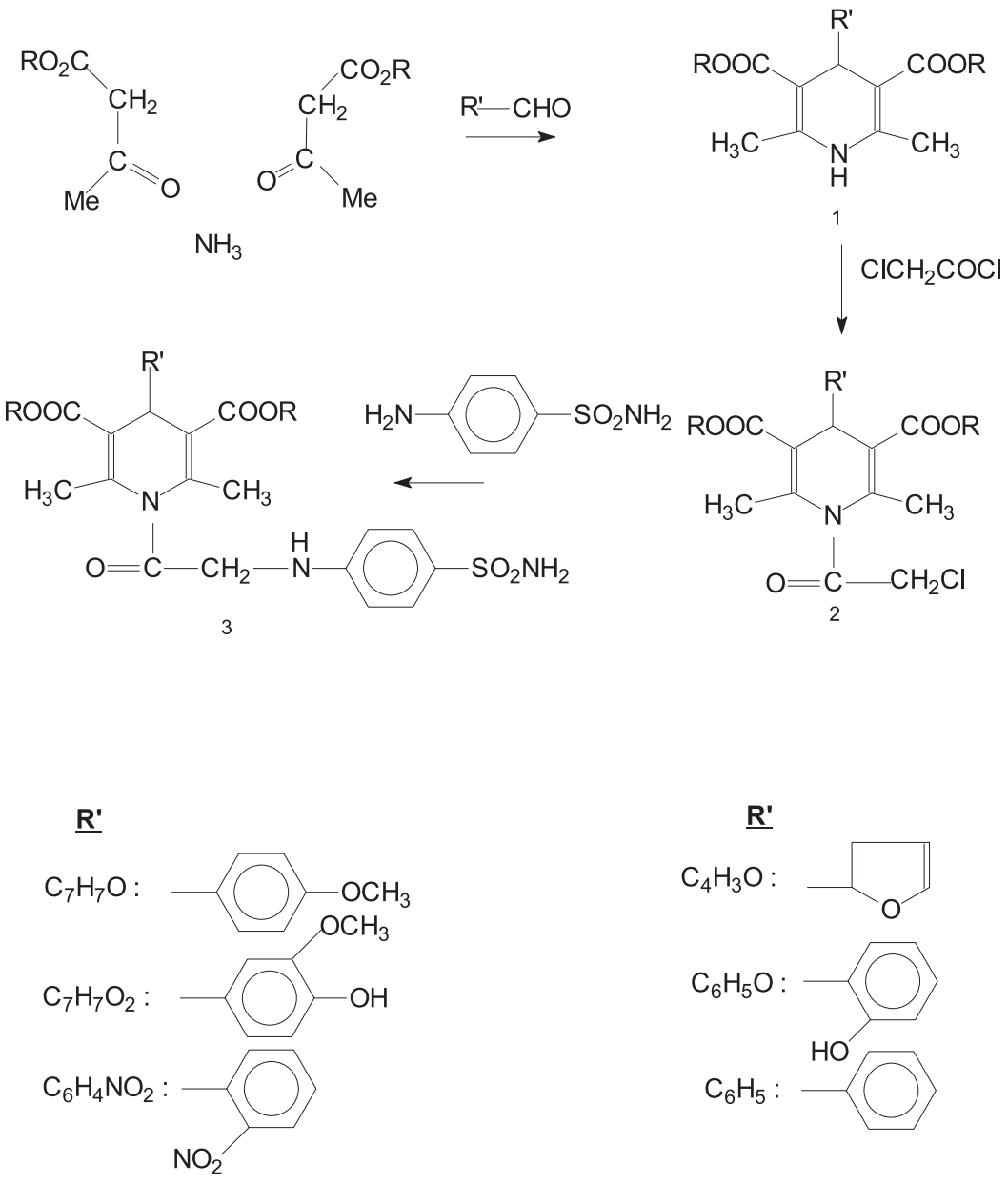

Scheme 1. Route of synthesis

Japan) spectrophotometer using KBr powder with diffuse reflectance attachment. ^{1}H-NMR spectra were recorded in $CDCl_3$ on a DRX-300 NMR (Bruker, USA) spectrophotometer (300 MHz) using TMS as an internal standard. Mass spectra of representative compounds were recorded on mass spectrometer API-4000 (MDS-SCIEX, Singapore). The CHN elemental analysis was carried out with Perkin Elmer-2400 (Italy) analyzer. Molecular masses of the compounds were determined by Rast's procedure (13).

The animal experiments were carried out following the protocols of animal ethical committee at Pharmacology Laboratory of University Department

of Pharmaceutical Sciences, Utkal University (Registration no-990/c/06/CPCSEA).

Synthesis of 3,5-diethoxycarbonyl-1,4-dihydro-2,6-dimethyl-4-(o-hydroxyphenyl)-pyridine (1f)

In a 250-mL round-bottomed flask, a solution of salicylaldehyde (0.2 mol), ethyl acetoacetate (0.2 mol), and conc. ammonium hydroxide (8 mL) in ethanol (60 mL) was heated under reflux for 3 h. To the resulting mixture, warm water (40 mL) was added and then allowed to cool. The separated product was filtered off, washed with 60% aqueous ethanol (10 mL) and recrystallized from ethanol. Other compounds of the series **(1a-j)** were synthesized in the above manner.

1a: IR (KBr, cm^{-1}): 3342.75 (N-H str.), 1689.7 (C=O str.), 1213.27 [C(=O)-O str.)], 2956.97 [C-H str. (aliphatic)], 3063.06 (C-H aromatic), 1450-1651.12 (C=C str.), 1253.77 (C-O-C asymmetric str.), 1031.95 (C-O-C.symmetric str.). ^{1}H-NMR ($CDCl_3$, δ ppm): 5.5 (1H, s, NH), 2.6 (6H, s, CH_3), 3.1-3.3 (6H, m, CH_3), 3.9 (3H, s, OCH_3) 7.2-7.4 (4H, m, Ar-H)

1b: IR (KBr, cm^{-1}): 3425.18 (O-H str.), 1681.98 (C=O str.), 1219.05 [C(=O)-O str.], 2937.68 [C-H str. (aliphatic)], 3061.13 (C-H aromatic), 788.91 (C-H-out of plane bend.), 1273.06 (C-O-C asymmetric str.), 1033.88 (C-O-C symmetric str.). ^{1}H-NMR ($CDCl_3$, δ ppm): 10.6 (1H, s, OH), 5.5 (1H, s, NH), 2.4 (6H, s, CH_3), 3.1-3.4 (6H, m, CH_3), 4.1 (3H, s, OCH_3), 6.8-7.3 (3H, m, Ar-H). MS (m/e, relative intensity): 374.1 (M^+, 100).

1c: IR (KBr, cm^{-1}): 3331.18 (N-H str.), 1681.98 (C=O str.), 1228.70 [C(=O)-O str.], 2953.12 [C-H str. (aliphatic)], 2995.55 (C-H aromatic), 744.55 [C-H-out of plane bend. (1,2-substituted benzene)], 1529.60 (Ar-NO_2 asymmetric str.), 1340.57 (Ar-NO_2 symmetric str.), 858.35 (C-N str. for Ar-NO_2). ^{1}H-NMR ($CDCl_3$, δ ppm): 5.7 (1H, s, NH), 2.3 (6H, s, CH_3), 3.6 (6H, s, CH_3), 7.2-7.7 (4H, m, Ar-H). MS (m/e, relative intensity): 345 (M^+, 100).

1d: IR (KBr, cm^{-1}): 3350 (N-H str.), 1704.41 (C=O str.), 2951.19 [C-H str. (aliphatic)], 3010 (C-H aromatic). ^{1}H-NMR ($CDCl_3$, δ ppm): 2.3 (6H, s, CH_3), 5.6 (1H, s, NH), 3.2-3.6 (6H, m, CH_3), 7.4-7.7 (4H, m, Ar-H).

1e: IR (KBr, cm^{-1}): 3342.75 (N-H str.), 1697.41 (C=O str.), 1220.98 [C (=O)-O str.], 2951.19 [C-H str. (aliphatic)], 3001.34 (C-H aromatic), 1435 (C=C str.). ^{1}H-NMR ($CDCl_3$, δ ppm): 3.1-3.3 (6H, m, CH_3), 5.6 (1H, s, NH), 2.3 (6H, s, CH_3), 6.8-7.2 (3H, m, Ar-H).

1f: IR (KBr; n, cm^{-1}): 3469.25 (O-H str.), 1693.56 (C=O str.), 1211.34 [C(=O)-O str.], 2976.26 [C-H str. (aliphatic)], 3053.42 (C-H aromatic), 786.98 [C-H-out of plane bend. (1,4-substituted benzene)]. ^{1}H-NMR ($CDCl_3$, δ ppm): 2.5 (6H, s, CH_3), 3.1-3.3 (6H, m, CH_3) 10.8 (1H, s, OH), 5.3 (1H, s, NH), 7.4-7.8 (4H, m, Ar-H).

1g: IR (KBr, cm^{-1}): 3406.18 (O-H str.), 1685.84 (C=O str.), 1222.91 [C(=O)-O str.], 2955.04 [C-H str. (aliphatic)], 3020.63 (C-H aromatic), 1433.16 (C=C str.), 754.19 [C-H-out of plane bend. (1,2-substituted benzene], 1249.91 (C-O-C asymmetric str.), 1053.17 (C-O-C symmetric str.). ^{1}H-NMR ($CDCl_3$, δ ppm): 10.6 (1H, s, OH), 3.3 (6H, s, CH_3), 5.3 (1H, s, NH), 3.6 (3H, s, OCH_3), 2.4 (6H, s, CH_3), 6.5-7.3 (3H, m, Ar-H).

1h: IR (KBr, cm^{-1}): 3342.75 (N-H str.), 1697.41 (C=O str.), 1220.98 (C(=O)-O str.), 2951.19 [C-H str. (aliphatic)], 3001.34 (C-H aromatic), 1435 (C=C str.).). ^{1}H-NMR ($CDCl_3$, δ ppm): 3.3 (6H, s, CH_3), 5.6 (1H, s, NH), 2.4 (6H, s, CH_3), 6.8-7.1 (3H, m, Ar-H).

1i: IR (KBr, cm^{-1}): 3350.46 (N-H str.), 1697.41 (C=O str.), 1213.27 [C(=O)-O str.], 2949.26 [C-H str. (aliphatic)], 2999.41 (C-H aromatic), 856.42 [C-H-out of plane bend. (1,4-substituted benzene)], 1236.41 (C-O-C asymmetric str.), 1028.09 (C-O-C symmetric str.). ^{1}H-NMR ($CDCl_3$, δ ppm): 5.7 (1H, s, NH), 2.5 (6H, s, CH_3), 6.4-6.8 (4H, m, Ar-H), 3.3 (6H, s, CH_3), 3.8 (3H, s, OCH_3).

1j: IR (KBr, cm^{-1}): 3344.68 (N-H str.), 1699.34 (C=O str.), 1220.98 [C(=O)-O str.], 2951.19 [C-H-str. (aliphatic)], 3026.41 (C-H aromatic), 1433.16-1651.12 (C=C str.), 700.18 [C-H-out of plane bend. (substituted benzene)]. ^{1}H-NMR ($CDCl_3$, δ ppm): 5.2 (1H, s, NH), 2.8 (6H, s, CH_3), 3.3 (6H, s, CH_3), 6.9-7.4 (5H, m, Ar-H).

Synthesis of 3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-N-[2-(4-sulfamoylphenylamino)-acetyl]-4-(substituted)pyridines (3a-e)

The synthesis of the title compounds was carried out using compounds **1a-j** as starting material in two steps. In the first step, 3,5-methoxycarbonyl-1,4-dihydro-2,6-dimethyl-4-(*o*-nitrophenyl)-pyridine (0.02 mol) was dissolved in 50 mL of 10% NaOH solution contained in conical flask. Then chloroacetyl chloride (0.02 mol) was added dropwise intermittently while stirring continuously with a magnetic stirrer. The stirring was continued for 2 h to complete the reaction. The obtained product, N-(2-chloroacetyl)-3,5-methoxycarbonyl-1,4-dihydro-2,6-dimethyl-4-(*o*-nitrophenyl)pyridine, was washed with water, filtered, dried and recrystallized from aqueous ethanol. Other compounds **(2a-e)** were synthesized in a similar manner.

Table 1. Physicochemical data of the synthesized compounds.

Comp. no.	R	R'	Molecular formula*	Molecular weight**	M.p (°C)	Yield (%)
1a	C_2H_5	C_7H_7O	$C_{20}H_{25}NO_5$	361	169	62
1b	C_2H_5	$C_7H_7O_2$	$C_{20}H_{24}NO_6$	374.5	172	70
1c	CH_3	$C_6H_4NO_2$	$C_{17}H_{17}N_2O_6$	346.4	160	76
1d	C_2H_5	C_6H_5	$C_{19}H_{22}NO_4$	326.5	175	70
1e	C_2H_5	C_4H_3O	$C_{17}H_{20}NO_5$	320	165	64
1f	C_2H_5	C_6H_5O	$C_{19}H_{22}NO_5$	342.4	122	72
1g	CH_3	$C_7H_7O_2$	$C_{18}H_{20}NO_6$	346.7	193	68
1h	CH_3	C_4H_3O	$C_{15}H_{16}NO_5$	289.85	190	65
1i	CH_3	C_7H_7O	$C_{18}H_{21}NO_5$	330	201	70
1j	CH_3	C_6H_5	$C_{17}H_{18}NO_4$	299	197	75
2a	C_2H_5	C_7H_7O	$C_{22}H_{25}0_6NCl$	434.5	160	62
2b	C_2H_5	$C_7H_7O_2$	$C_{22}H_{25}0_7NCl$	450.5	154	65
2c	CH_3	$C_6H_4NO_2$	$C_{19}H_{18}0_7N_2Cl$	421.5	170	65
2d	C_2H_5	C_6H_5	$C_{21}H_{23}0_5NCl$	404.5	140	65
2e	C_2H_5	C_4H_3O	$C_{19}H_{21}0_6NCl$	378.5	120	55
3a	C_2H_5	C_7H_7O	$C_{28}H_{32}O_8N_3$	535.62	164	48
3b	C_2H_5	$C_7H_7O_2$	$C_{28}H_{32}O_9N_3$	556.1	260	52
3c	CH_3	$C_6H_4NO_2$	$C_{25}H_{26}O_9N_4$	526.3	188	58
3d	C_2H_5	C_6H_5	$C_{27}H_{29}O_7N_3$	508.7	168	52
3e	C_2H_5	C_4H_3O	$C_{25}H_{28}O_8N_3$	496.7	129	46

* All compounds gave satisfactory elemental analysis (± 0.4% of theoretical values).
**Molecular weights of all compounds determined by Rast's procedure were satisfactory (± 0.5% of theoretical values).

In the second step, compound **2** (0.02 mol) and sulfanilamide (0.02 mol) in dry ethanol (50 mL) were refluxed for 8 h. The reaction mixture was cooled and poured onto crushed ice with continuous stirring. The resulted solid was filtered, washed with cold water, dried and recrystallized from aqueous ethanol to yield 3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-N-[2-(4-sulfamoylphenylamino)-acetyl]-4-(substituted)pyridines **(3a-e)**.

3a: IR (KBr, cm^{-1}): 3342.75 (N-H asymmetric str.), 3240.52 (N-H symmetric str.), 3061.13 (C-H aromatic str.), 1689.17 [C=O str. (*tert*. amide)], 1373.36 [$S(=O)_2$ asymmetric str.], 1174.69 [$S(=O)_2$ symmetric str.], 682.82 (C-S str.), 1456.30 (C=C str.) 1253.77 (C-O-C asymmetric str.). ^{1}H-NMR ($CDCl_3$, δ ppm): 3.3 (2H, s,-CH_2-) 2.4 (6H, s, CH_3), 3.8 (3H, s, OCH_3), 6.2 (1H, s, NH), 6.8-7.4 (4H, m, Ar-H). MS (m/e, relative intensity): 359 (M^+, 100), 538.

3b: IR (KBr, cm^{-1}): 3354.32 (N-H asymmetric str. broadened with overlapping of O-H str.), 3242.45 (N-H symmetric str. broadened), 2929.97 (C-H str.), 1693.56 [C=O str. (*tert*. amide)], 1371.43 [$S(=O)_2$ asymmetric str.], 1153.47 [$S(=O)_2$ symmetric str.], 678.97 (C-S str.), 1494.88 (C=C str.), 1238.34 (C-O-C asymmetric str.). ^{1}H-NMR ($CDCl_3$, δ ppm): 9.7 (1H, s, OH), 5.3 (1H, s, NH), 2.2 (6H, s, CH_3), 6.4-7.1 (3H, m, Ar-H), 3.8 (2H, s, -CH_2-), 4.1 (3H, s, OCH_3).

3c: IR (KBr, cm^{-1}): 3333.10 (N-H asymmetric str.), 3236.66 (N-H symmetric str.), 2955.04 (C-H aliphatic str.), 1687.77 [C=O str. *(tert*. amide)], 1379.15 [$S(=O)_2$ asymmetric str.], 1190.12 [$S(=O)_2$ symmetric str.], 686.68 (C-S str.), 1433.16 (C=C str.), 1529.60 [$(N=O)_2$ asymmetric str.], 1350.22 [$(N=O)_2$ symmetric str.], 858.35 (C-N str.). ^{1}H-NMR ($CDCl_3$, δ ppm): 2.8 (6H, s, CH_3), 3.3 (6H, s, CH_3), 3.7 (2H, s, -CH_2-), 5.6 (1H, s, NH), 7.2-7.5 (4H, m, Ar-H). MS (m/e, relative intensity): 344 (M^+, 100), 526.

3d: IR (KBr, cm^{-1}): 3342.75 (N-H asymmetric str.), 3238.59 (N-H symmetric str.), 3059.20 (C-H aromatic str.), 1687.77 [C=O str. (*tert*. amide)], 1373.36 [S $(=O)_2$ asymmetric str.], 704.04 (C-S str.),

Table 2. Anticonvulsant action of compounds **1a-j** and **3a-e.**

Compound	Dose (mg/kg)	Onset of convulsion(s)	Incidence of convulsion (%)
Control (vehicle)	-	165.3 ± 3.345	100
Diazepam	4	A	0
1a	5 10	197.0 ± 6.086 [b] 266.6 ± 6.396 [a]	66.4 49.8
1b	5 10	183.2 ± 4.415 [c] 240.1 ± 8.643 [b]	83.2 66.4
1c	5 10	189.5 ± 2.884 [b] 281.0 ± 4.747 [a]	66.4 49.8
1d	5 10	176.0 ± 4.389 [c] 264.3 ± 4.863 [a]	83.2 66.6
1e	5 10	198.8 ± 2.33 [b] 246.3 ± 5.78 [a]	83.2 66.6
1f	5 10	170.5± 3.214 [c] 182.1 ± 4.204 [c]	100 100
1g	5 10	171.5 ± 2.412 [c] 205.4 ± 7.542 [b]	100 83.2
1h	5 10	168.3 ± 2.556 [c] 181.0 ± 4.728 [c]	100 100
1i	5 10	179.0 ± 6.386 [c] 212 ± 4.752 [b]	100 83.2
1j	5 10	196.2 ± 3.321 [b] 216.3 ± 4.587 [b]	83.2 83.2
3a	5 10	294.0 ± 2.45 [a] 375.0 ±7.106 [a]	66.4 33.2
3b	5 10	284.5 ± 8.4 [a] 331.4 ± 8.124 [a]	66.4 33.2
3c	5 10	334.4 ± 2.53 [a] 418.2 ± 22.665 [a]	33.2 16.6
3d	5 10	249.0 ± 7.25 [b] 275.4 ± 5.225 [a]	83.2 66.4
3e	5 10	289.2 ± 3.65 [a] 359.8 ± 4.324 [a]	66.4 16.6
One way ANOVA	F p	81.594 < 0.01	-

Values are expressed as the mean ± standard error of the mean. n = 6 in each group. df = 15, 80.[a] $p < 0.01$, [b] $p < 0.05$, [c] $p > 0.05$.

1454.38 (C=C str.). ^{1}H-NMR ($CDCl_3$, δ ppm): 2.4 (6H, s, CH_3), 5.6 (1H, s, NH), 3-3.2 (6H, m, CH_3), 3.7 (2H, s, -CH_2-), 7.4-7.9 (4H, m, Ar-H).

3e: IR (KBr, cm^{-1}): 3346.61 (N-H asymmetric str.), 3221.23 (N-H symmetric str.), 3090.07 (C-H aromatic str.), 1651.12 [C=O str. (*tert*. amide)], 1371.43 [$S(=O)_2$ asymmetric str.], 1149.61 [$S(=O)_2$ symmetric str.], 682.82 (C-S str.), 1446.66 (C=C str.), 825.56 (C-H out of plane bend.). ^{1}H-NMR ($CDCl_3$, δ ppm): 2.2 (6H, s, CH_3), 5.6 (1H, s, NH), 3.7 (2H, s, -CH_2), 3.1-3.3 (6H, m, CH_3), 6.1-6.3 (3H, m, Ar-H).

Anticonvulsant activity

Swiss albino male mice, weighing 20–25 g, were obtained from an animal facility. Mice were housed in stainless steel wire-floored cages without any stressful stimuli. Room temperature was kept at 23 ± 2°C. Animals were fed standard laboratory chow and tap water *ad libitum*. Mice were randomly arranged in different groups, 6 in each. Test compounds were suspended in Tween 80 (0.2%) (Sigma, USA) and were given *i.p.* in doses of 5 mg/kg and 10 mg/kg. Dosing volume was 0.2 mL per 20 g. Diazepam (4 mg/kg) was dissolved in water in 2%

concentration and used as a reference standard. Pentylenetetrazole (PTZ, Sigma) was dissolved in water in 2% concentration and was given *i.p.* in a dose of 80 mg/kg 30 min after the test compounds or diazepam. The animals were observed for convulsions. Animals that showed no convulsions within one hour after PTZ injection were considered to be protected.

RESULTS

A series of 3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-4-(substituted)-pyridine **(1a-j)** were prepared with good yield following the standard method (8). The N-(2-chloroacetyl)-3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-4-(substituted)pyridines **(2a-e)** were synthesized with 50-60% yield by the reaction with chloroacetyl chloride. Compounds **2a-e** on treatment with sulfanilamide afforded 3,5-(substituted) oxycarbonyl-1,4-dihydro-2,6-dimethyl-N-[2-(4-sulfamoylphenylamino)-acetyl]-4-(substituted)pyridines **(3a-e)** in good yield (50-55 %). The physicochemical (Table 1) and spectral data support the proposed structure of the synthesized compounds. The results of anticonvulsant activity estimation were expressed as the mean ± standard error of the mean of six determinations. An onset of convulsion in seconds and incidence (%) of convulsions are reported in Table 2. The differences between the groups were determined using the one way analysis of variance (ANOVA) followed by Dunnett's test with 5% significance level ($p < 0.05$).

DISCUSSION AND CONCLUSION

The mechanism of formation of compounds **2a-e** could be rationalized in terms of electrophilic attack on nucleophilic center on the acyl group of chloroacetyl chloride by the lone pair of electrons on nitrogen of pyridine derivative accompanied by the loss of chloride ion and the proton to afford N-(2-chloroacetyl)-3,5-(substituted)oxycarbonyl-1,4-dihydro-2,6-dimethyl-4-(substituted)pyridines. Further, nucleophilic substitution reaction with amino group of sulfanilamide is believed to produce 3,5-(substituted) oxycarbonyl-1,4-dihydro-2,6-dimethyl-N-[2-(4-sulfamoylphenylamino)-acetyl]-4-(substituted)pyridines **(3a-e)**.

All the compounds delayed the onset of convulsions in a dose dependent manner (Table 2). All animals, which had showed convulsions died within 40 min. Among the compounds, **3c** showed the highest anticonvulsant activity. Compounds **3a-e** exhibited much better activity ($p < 0.01$) compared to compounds **1a-e**, suggesting enhancement of anticonvulsant effect of 1,4-dihydropyridines by molecular hybridization with sulfanilamide through the amide linkage. Compound **1f** and **1h** did not show significant ($p > 0.05$) anticonvulsant action at 10 mg/kg compared to the control. Compound **1f** and **1h** did not provide any protection against convulsions. The analysis of structural features reveals that substitution of nitro group and methoxy group enhance anticonvulsant potential of the compounds. In conclusion, some of the 1,4-dihydropyridines showed good anticonvulsant activity, which was enhanced by conjunction to sulfanilamide through the amide linkage. Substitution of aromatic ring with nitro group and methoxy group seems to increase the anticonvulsant action. Even though most of the synthesized compounds did not provide protection against convulsions, the data reported in this article may be a helpful guide for the medicinal chemists who are working in this area.

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