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Synthesis, Characterization And Evaluation For Anticonvulsant Activity Of Acetylnaphthalene and Substituted Acetylenaphthalene Derivative Of Heterocyclic Compounds

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A series of acetylnaphthalene and substituted acetylnaphtahlene have been prepared by mannich reaction with four different secondary amine compounds and formandehyde. In this reaction Acetyl gruoup of acetyl naphthalene and substituted acetylnaphthalene have been used as hydrogen active compound. The structures of new compounds have been confirmed by spectral data. The novel compounds were tested for anticonvulsant activity using pentylenetetrazole (scPTZ) test. Among the tested some acetylnaphthalene and substituted acetyl naphthalene derivatives of heterocyclic compounds were show significant anticonvulsant activity.

Keyword: Anticonvulsant activity, 1-acetylnaphthalene, 2-acetylnaphthalene, Acetic acid 1-amino-4-sulfo-naphthalen-2-yl ester

INTRODUCTION: Epilepsy is a physical condition that occurs when there is a sudden, brief change in how the brain works (Older words for seizures include convulsions and fits). When brain cells are not working properly, a person's consciousness, movement, or actions may be altered for a short time. Seizures are sudden alterations in behavior or motor function caused by an electrical discharge from the brain. Symptoms that may occur during a seizure can affect your muscles, sensations, behavior, emotions, consciousness or a combination of these. As WHO defines it, an 'epileptic seizure' is the result of transient dysfunction of part or all of the brain due to excessive discharge of a hyper-excitable population of neurons, causing sudden and transitory phenomena of motor, sensory, autonomic or psychic nature. Epilepsy is the second most common chronic neurological condition seen by neurologists. About two million Americans have epilepsy; of the 125,000 new cases that develop each year, up to 50% are in children and adolescents. Three percent will develop epilepsy by age 75. About 1 in 30 people in the UK develops epilepsy at some stage in their life. Epilepsy can begin at any age.

In general, seizures are well controlled by treatment in about 4 in 5 cases. It is estimated that there are 55, 00,000 persons with epilepsy in India and 3, 00,000 in UK[1,2]. It is estimated that in India, there will be 6-10 million people with epilepsy. In the BANGALOR URBAL RURAL NEUROEPIDEMIOLOGY SURVEY (a project report by Indian council for medical research), observed a prevalence rate of epilepsy 8.8 per 1000 population. [3] Nearly 95% of the clinically available drugs used to treat epilepsy were approved before 1985 and provide satisfactory seizure control in only 60%-70% of patients. These drugs, however, also cause notable adverse side effects, such as drowsiness, ataxia, gastrointestinal disturbance, hepatotoxicity, and megaloblastic anemia and even life-threatening conditions. The search for more effective and safer antiepileptic drugs, therefore an imperative challenge for medicinal chemistry [4]. In the past decade, several new drugs e.g., felbamate, lamotrigine, gabapentin, tiagabine, topiramate have been approved. Further compounds, e.g. Vigabatrine, nafimidone, nafimidone alcohol, levetiracetam, rufinamide, losigamone, remacemide, pregabalin, retiagabine, seretolide are presently in the clinical trials. [5]

The mechanism of action of currently available effective antiepileptics are: the induction of a prolonged inactivation of the Na^+ channel; the blockade of Ca^{2+} channel currents; the enhancement of the inhibitory GABAergic neurotransmission or the modulation of excitatory glutamatergic neurotransmission.[6].There for a need of new antiepileptic drug with novel novel therapeutic targets, enhanced efficacy and minimal side effects. Acetylnaphthalene and substituted acetylnaphthalene derivatives of heterocyclic compounds like imidazole and benzimidazole and piperidine showed an anticonvulsant activity. [7] A research article A. Karakurt *et al.* prepared oxime and oxime ether derivatives of anticonvulsant nafimidone (1-(2-naphthyl)-2-(imidozole-1-yl)ethanone), and benzoic acid -2-imidazole-1-yl-naphthalene-2yl-ethyl ester as potential anticonvulsant compounds. [8]

MATERIALS AND METHODS:

The chemicals used in the experiments were supplied by lobachemie (India) and s.d.fine Chem. Ltd. Melting points were determined by Visual melting point apparatus (Lab india) and are uncorrected. Purity of the compounds was checked on thin layer chromatography (TLC) plates (Silica gel G) in the solvent system Chloroform: Methanol (9:1, v/v) and Ethyl Acetate: Hexane (3:7,v/v), benzene: acetone (8:2, v/v) and Benzene : Ethylacetate : Methanol (8.5: 1.4 : 1v/v), the spots were located under iodine vapors and UV light. The IR spectra were obtained on a Perkin-Elmer 1720 FT-IR spectrometer (KBR pellets). The ^{1}H-NMR spectra were obtained on a Bruker AC 300 MHz spectrometer in DMSO-d6 using TMS as an internal standard.

Synthesis

General procedure for synthesis of 2-acetylnaphthalene derivative of heterocyclic compound . synthesis of compounds (A1-A4) :

In a 250ml three-necked flask was placed, 50 ml solution of 2-acetylnaphthalene 10.2 g (0.06 M) in ethyl alcohol and corresponding secondary amine (0.06M) and 6 ml formaldehyde solution. To the contents of the flask was then added slowly 2 ml conc. Hydrochloric acid from a dropping funnel. The flask then connected with the reflux condenser and gentle heating was applied to effect complete dissolution, after which the reaction mixture was stirred and refluxed for 4-6 hr at 100-110^{0}C. On cooling the contents of flask and pour the reaction mixture in 500 ml beaker containing approxi 100 ml of crushed ice. The product was filtered and washed with water to remove the traces of hydrochloric acid and dried. It was purified by recrystallization from ethyl alcohol. Practical Yield and m.p. was determined .

General procedure for Synthesis of 1-acetylnaphthalene derivative of heterocyclic compounds. Synthesis of compound. (B 1- B 4)

In a 250ml three-necked flask was placed, 50 ml solution of 1-acetylnapthalene 10.2 g (0.06 M) in ethyl alcohol and corresponding Secondary amine (0.06M) and 6 ml formaldehyde solution. To the contents of the flask was then added slowly 2 ml conc. Hydrochloric acid from a dropping funnel. The flask then connected with the reflux condenser and gentle heating was applied to effect complete dissolution, after which the reaction mixture was stirred and refluxed for 4-6 hr at 100-110^{0}C. On cooling the contents of flask and pour the reaction mixture in 500 ml beaker containing approxi 100 ml of crushed ice. The product was filtered and washed with water to remove the traces of hydrochloric acid and dried. It was purified by recrystallization from ethyl alcohol. Practical Yield and m.p. was determined.

Synthesis of Acetic acid 1- amino -4- Sulfo-napthalene-2-yl-ester. (Acetylation)

In a 250ml three-necked flask was placed, a solution containing 14.35 g (0.06 M) of 1-Amino-2-napthol-4- sulfonic acid in 50 ml of ethanol and 6.1 ml (0.06M) of Acetic anhydride and 6 ml of Glacial acetic acid in 50 ml of Ethanol. To the contents of the flask was then added slowly 2 ml conc. Sulphuric acid from a dropping funnel. The flask then connected with the reflux condenser and gentle heating was applied to effect complete dissolution, after which the reaction mixture was stirred and refluxed for 4-5 hr at 100-110^{0}C. On cooling the contents of flask solidified. The product was filtered and washed with water to remove the traces of hydrochloric acid and dried. It was purified by recrystallization from ethyl alcohol. Practical yield and melting point was determined.

General procedure for synthesis of heterocyclic derivative of acetic acid 1- amino -4- Sulfo-naphthalene-2-yl-ester. Synthesis of compound compounds (C1- C 3)

In a 250 ml three-necked flask was placed, 50 ml solution of Acetic acid-1-amino-4-sulfo naphthalene -2-yl-ester 16.87 g (0.06 M) in ethyl alcohol and corresponding Secondary amine (0.06M) and 6 ml Formaldehyde solution. To the contents of the flask was then added slowly 2 ml conc. Hydrochloric acid from a dropping funnel. The flask then connected with the reflux condenser and gentle heating was applied to effect complete dissolution, after which the reaction mixture was stirred and refluxed for 4-5 hr at 100-110^{0}C. On cooling the contents of flask and pour the reaction mixture in 500 ml beaker containing approxi 100 ml of crushed ice. The product was filtered and washed with water to remove the traces of hydrochloric acid and dried. It was purified by recrystallization from ethyl alcohol. Practical yield and m.p. was determined.

Spectral view of synthesized compounds:

- ***3-(1 H -Imidazol-1-yl)-1-(naphthalen-2-yl) propan-1-one*** **(A1).** The following spectral data were recorded for the compound **: IR** spectral data (γ cm $^{-1}$,KBr) : 3057 (C-H aromatic), 2994 (C-H aliphatic), 1673 C=O stretching, 1673 C=O stretch, 1365 C-N stretch. **^{1}H NMR** (DMSO D_6, 300 MHz): δ 2.5-2.7(s, 2H ,α methylene), 3.4 (s, 2H, β methylene), 7.6-8.6 (m, 7H, naphthalene H^1 H^3, H^4, H^5, H^6, H^7 , H^8), 7.61-7.68,(m, 3H, imidazole, H^2, H^4 , H^5). M.F.(C_{16} H_{14} N_2O).

- ***1-(2-Naphthyl)-3-(1-piperidinyl)-propan-1-one*** **(A2).** The following spectral data were recorded for the compound **: IR** spectral data (γ cm $^{-1}$, KBr), 3058 C-H stretching (aromatic), 2360 C-H stretching (aliphatic), 1465 C-H Bending (Aromatic),1625 (C=O) **^{1}H NMR** (DMSO D_6, 300 MHz): δ 2.5-2.7(s, 2H,α methylene), 3.4 (s, 2H, β methylene), 7.68(m, 2H, naphthalene H^4, H^5), 7.9-8.6 (s, 4H, naphthalene H^1, H^3 H^6,

H^7 , H^8), 2.53,(s, 2H, piperidine, , H^2 , H^6), M.F. ($C_{18}H_{21}NO$).

- ***1-(2-Naphthyl)-3-piperazin-1-yl-propan-1-one* (A3) .** The following spectral data were recorded for the compound **: IR** spectral data (γ cm $^{-1}$,KBr): 2940 C-H stretching (aromatic), 2860 C-H stretching (aliphatic), 3433 N-H str. (piperazine), 1644 N-H bending (piperazine), 1440 C-H Bending (Aromatic), 1260 C-N stretching, 1371 C-N amine. **^{1}H NMR** (DMSO D_6, 300 MHz): δ 2.5 (s, 2H ,α methylene), 2.7 (s, 2H, β methylene), 7.68-8.6 (m, 6H, naphthalene H^1, H^3, H^4, H^5 H^7 , H^8), 2.5,(s, 2H, piperazine, , H^2 , H^6), 2.7 (s, 2H, piperazine, , H^3 , H^5), 2.1 (s, piperazine NH), M.F. (C_{17} H_{20} N_2O).

- ***3-Benzoimidazol-1-yl-1-naphthalen-2-yl-propan-1-one* (A4).** The following spectral data were recorded for the compound **: IR** spectral data (γ cm $^{-1}$,KBr): 3100 N-H stretching *sec.* amine , 1616 C=C stretching, 2854 C-H stretching (aromatic), 2360 C-H stretching (aliphatic), 1673 C=O stretching, 1458 C-H Bending (Aromatic), 1272 C-N stretching, 1360 C-N amine. **^{1}H NMR** (DMSO D_6, 300 MHz): δ 2.7 (s, 2H,α methylene) 3.3 (s, 2H, β methylene), 7.7-8.2 (m, 6H, naphthalene H^1 ,H^3, H^4, H^5, H^7 , H^8), 8.1(s, H, benzimidazole, H^2), 7.25-7.7(m, 3H, benzimidazole, H^5, H^6, H^7), M.F. ($C_{20}H_{16}N_2O$)

- ***1-Naphthalen-1-yl-3-imidazol-1-yl-propan-1-one* (B1).** The following spectral data were recorded for the compound **: IR** spectral data (γ cm $^{-1}$,KBr) : 3086 (C-H aromatic), 2356 (C-H aliphatic), 1673 C=O stretching, 1678 C=O stretch, 1354 C-N stretch .**^{1}H NMR** (DMSO D_6, 300 MHz): δ 2.7(s, 2H, α methylene), 3.4 (s, 2H, β methylene), 7.5-8.7 (m,7H, naphthalene H^2, H^3 ,H^4, H^5, H^6, H^7, H^8), 7.5-7.6,(s, 3H, imidazole, H^2, H^4 , H^5), M.F. ($C_{16}H_{14}N_2O$)

- ***1-(1-Naphthyl)-3-(1-piperidinyl)-propan-1-one* (B2).** The following spectral data were recorded for the compound: **IR** spectral data (γ cm $^{-1}$, KBr) 3048 C-H stretching (aromatic), 2359 C-H stretching (aliphatic), 1619 C=O stretching , 1459 C-H Bending (Aromatic), 1355 C-N amine. **^{1}H NMR** (DMSO D_6, 300 MHz): δ 2.5-2.7(s,2H ,α methylene), 3.4 (s, 2H, β methylene), 7.6-8.7 (m, 7H, naphthalene H^2, H^3 ,H^4, H^5, H^6, H^7 , H^8), 2.3(s, 2H, piperidine, , H^2 , H^6), 1.1 (s, 3H, piperidine, , H^3 , H^4, H^5), M.F.($C_{18}H_{21}NO$)

- ***1-(1-Naphthyl)-3-(1-piperazinyl)-propan-1-one* (B3).** The following spectral data were recorded for the compound **: IR** spectral data (γ cm $^{-1}$,KBr): 2855 C-H stretching (aromatic), 2359 C-H stretching (aliphatic), 1455 C-H Bending (Aromatic), 3339 N-H str. (piperazine), 1677 (N-H bending of piperazine) 1161 C-N stretching, 1363 C-N amine, **^{1} H NMR** (DMSO D_6, 300 MHz): δ 2.4(s, 2H ,α methylene), 2.5 (s, 2H, β methylene), 7.6 (s, 2H, naphthalene H^2, H^5), 8.1-8.6 (m, 5H, naphthalene H^3 ,H^4,H^6, H^7 , H^8), 2.4,(s, 2H, piperazine, , H^2,H^6), 2.2 (s, 2H, piperazine, , H^3 , H^5), 1.1 (s, piperazine NH), M.F. (C_{17} H_{20} N_2O).

- ***3-Benzoimidazol-1-yl-1-naphthalen-1-yl-propan-1-one* (B4)**: The following spectral data were recorded for the compound **: IR** spectral data (γ cm $^{-1}$,KBr): 3054 N-H Stretching *sec.* amine , 1676 C=C stretching, 2856 C-H stretching (aromatic), 2358 C-H stretching (aliphatic), 1676 C=O stretching, 1457 C-H Bending (Aromatic), 1277 C-N stretching amine .**^{1} H NMR** (DMSO D_6, 300 MHz): δ 2.5 (s, 2H ,α methylene), 3.4 (s, 2H, β methylene), 7.25-8.6 (m, 7H, naphthalene H^3, H^2, H^4, H^5, H^6, H^7, H^8), 8.1(s, H, benzimidazole H^2), 7.6 (s, 2H, benzimidazole H^4 , H^7), 7.2 (s, 2H benzimidazole H^5, H^6), M.F. ($C_{20}H_{16}N_2O$).

- ***Imidazole-1-carboxylic acid 1-amino-4-sulfo-naphthalen-2-yl ester* (C1) :** The following spectral data were recorded for the compound **: IR** spectral data (γ cm $^{-1}$,KBr) : 3057 (C-H aromatic), 2994 (C-H aliphatic), 1673 C=O stretching, 1673 C=O stretch, 1365 C-N stretch, 1195 S=O stretch, 3418 N-H stretch, 1599 N-H bend. **^{1}H NMR** (DMSO D_6, 300 MHz): δ 2.7(s, 2H ,α methylene), 3.1(s, 2H, β methylene), 7.2-7.7 (m, 5H,

naphthalene H^3, H^5, H^6, H^7 , H^8), 7.1-7.6,(s, 3H, imidazole, H^2, H^4 , H^5), 4.6 (s, 2H, NH_2), 1.9 (s, H, sulphonic), M.F. ($C_{16}H_{15}N_3O_5S$)

- ***3-Piperidin-1-yl-propionic acid 1-amino-4-sulfo-naphthalen-2-yl ester* (C2)**: The following spectral data were recorded for the compound **: IR** spectral data (γ cm $^{-1}$, KBr) : 3057 (C-H aromatic), 2362 (C-H aliphatic), 1673 C=O stretching, 1673 C=O stretch, 1365 C-N stretch, 1194 S=O stretch, 3433 N-H stretch, 1598 N-H bend. **^{1}H NMR** (DMSO D_6,300 MHz): δ 2.5 (s, 2H ,α methylene), 2.7 (s, 2H, β methylene), 7.4-7.8 (m, 5H, naphthalene H^3, H^5, H^6, H^7, H^8), 2.5 (s, 2H, piperidine, , H^2 , H^6), 4.6 (s, 2H, NH_2), 1.9 (s, H, sulphonic), M.F. ($C_{18}H_{22}N_2O_5S$)

- ***3-Benzoimidazol-1-yl-propionic acid 1-amino-4-sulfo-naphthalen-2-yl ester* (C3) :** The following spectral data were recorded for the compound **: IR** spectral data (γ cm $^{-1}$, KBr) : 3057 (C-H aromatic), 2357 (C-H aliphatic), 1644 C=O stretch , 1347 C-N stretch, 1171 S=O stretch, 3398 N-H stretch, 1523 N-H bend. **^{1} H NMR** (DMSO D_6, 300 MHz): δ 2.5 (s, 2H ,α methylene), 3.2 (s, 2H, β methylene), 7.2-8.6 (m, 5H, naphthalene H^3, H^5, H^6, H^7, H^8), 8.1 (s, H, benzimidazole,H^2), 7.6 (s, 2H, benzimidazol H^4 , H^7), 7.2 (s, 2H, benzimidazole ,H^5, H^6), 4.6 (s, 2H, NH_2), 2.1 (s, H, sulphonic), M.F. ($C_{20}H_{17}N_3O_5S$)

Pharmacological activities:

Anticonvulsant activity:

Swiss albino mice of either sex weighing 25- 30 g was obtained from DIPSAR New Delhi. Animal were housed in a group of 6 mice per cage. experimental protocols were carried out with the permission from Institutional Animal Ethics Committee (IAEC) with protocol No. **IAEC/2011-I/Prot. No.14.** synthesized compounds were screened for their anticonvulsant activity by subcutaneous pentylenetetrazole (scPTZ) induce convulsion test. These methods claimed to detected compound possessing activity against absence seizures.

Pentylenetetrazole Induced Convulsion Test (sc PTZ)

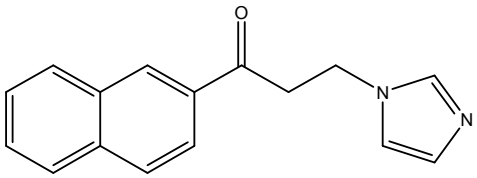
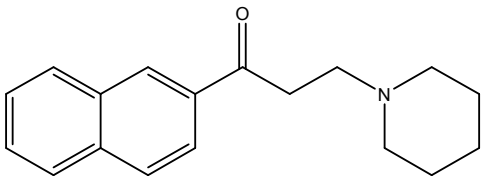
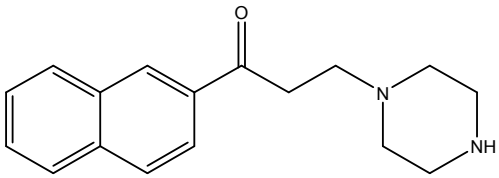
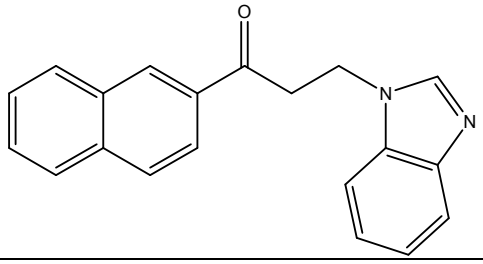
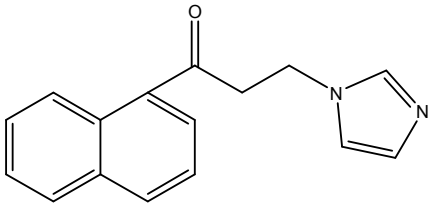
The convulsions were induced in mice by administering Pentylenetetrazole (PTZ) in the doses of 80 mg/kg intraperitoneally.
In the scPTZ test, adult male and female albino mice (Swiss albino mice) weighing 25-30 gm used. The animals were divided into three groups (control, standard and test) and each group comprising of six mice. Each animal was placed into an individual plastic cage for observation lasting 12 hour. The injections of test compounds (100mg/kg; i.p.) were prepared by suspending the compounds in 1% aq. CMC suspension. The test compounds were administered 30 min before PTZ challenge. Phenytoin was used as a standard anticonvulsant drug. The biological activity of these compounds was studied in 10 groups of six animals each as under:

Group 1:- Served as control group. These animals were treated with vehicle, 1% aq. CMC suspension, 1mL/100g body weight intraperitoneally. These animals also received PTZ (80 mg/kg) intraperitoneally after 30 min of injection of 1% aq. CMC suspension.

Group 2 to group 12: - Served as test groups. The animals of these groups were used for observing the influence of test compounds on PTZ induced convulsions or recovery or death. These animals were administered 1% aq. CMC suspension of test compounds 1 ml/100g by intraperitoneal route. Thirty minute later these animals were administered PTZ (80 mg/kg; i.p.) as a challenging agent. The animals were observed for a period of 30 min each (post-PTZ administration). The parameters noted were mean onset time of convulsions, recovery or death. Percentage recovery or Percentage survival after PTZ administration was recorded.

The structure, IUPAC name and physiochemical characteristics are given in the Table1 and Table 2

TABLE 1 : IUPAC Name

S. No.	Chemical Structure	I.U.P.A.C. Name
A1		3-(1 H -Imidazol-1-yl)-1-(naphthalen-2-yl) propan-1-one
A2		1-(2-Naphthyl)-3-(1-piperidinyl)-propan-1-one
A3		1-(2-Naphthyl)-3-piperazin-1-yl-propan-1-one
A4		3-Benzoimidazol-1-yl-1-naphthalen-2-yl-propan-1-one
B1		1-Naphthalen-1-yl-3-imidazol-1-yl-propan-1-one

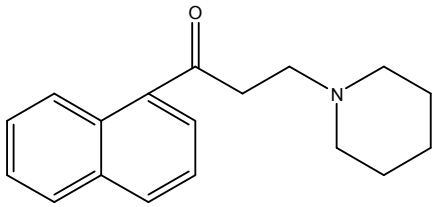
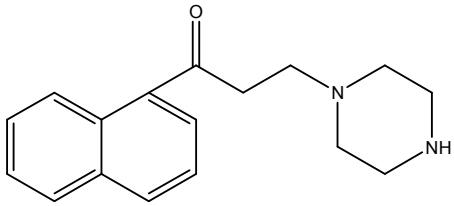
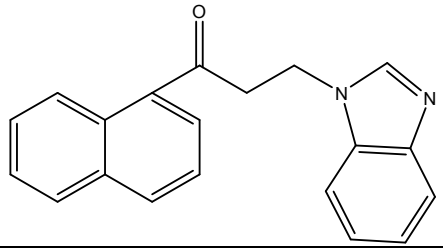
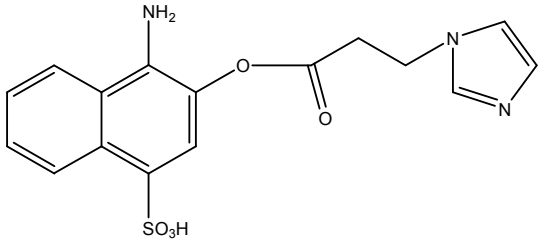
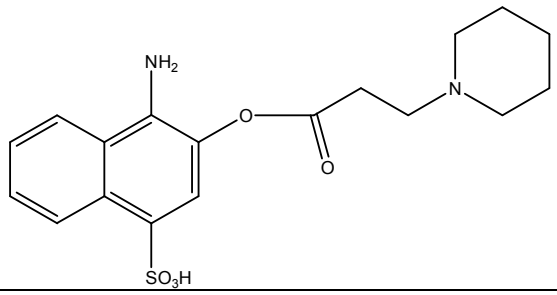
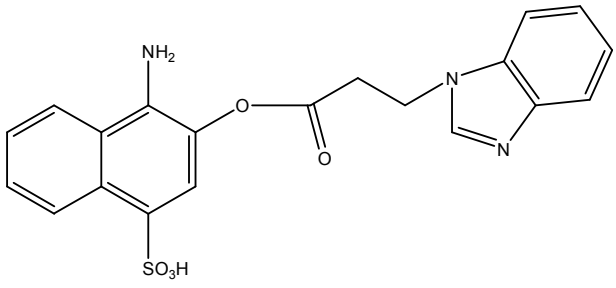
B2		1-(1-Naphthyl)-3-(1-piperidinyl)-propan-1-one
B 3		1-(1-Naphthyl)-3-(1-piperazinyl)-propan-1-one
B 4		3-Benzoimidazol-1-yl-1-naphthalen-1-yl-propan-1-one
C1		Imidazole-1-carboxylic acid 1-amino-4-sulfo-naphthalen-2-yl ester
C2		3-Piperidin-1-yl-propionic acid 1-amino-4-sulfo-naphthalen-2-yl ester
C3		3-Benzoimidazol-1-yl-propionic acid 1-amino-4-sulfo-naphthalen-2-yl ester

TABLE 2: Physiochemical Characteristics

Compound	Molecular Formula	Molecular Weight	Rf value	Melting Point (°C)	Yield (%)
A1	$C_{16}H_{14}N_2O$	250.29	0.7	501-03	82
A2	$C_{18}H_{21}NO$	267.36	0.65	452-54	80
A3	$C_{17}H_{20}N_2O$	268.35	0.8	458-60	75
A4	$C_{20}H_{16}N_2O$	300.49	0.62	478-80	70
B1	$C_{16}H_{14}N_2O$	250.29	0.72	490-92	72
B2	$C_{18}H_{21}NO$	267.36	0.58	435-37	65
B3	$C_{17}H_{20}N_2O$	268.35	0.72	454-56	62
B4	$C_{20}H_{16}N_2O$	300.49	0.78	462-64	70
C1	$C_{16}H_{15}N_3O_5S$	361.49	0.84	378-80	55
C2	$C_{18}H_{22}N_2O_5S$	378.48	0.65	426-28	60
C3	$C_{20}H_{17}N_3O_5S$	411.61	0.70	320-22	52

The increase in onset time of convulsions and percentage recovery was taken as parameter for anticonvulsant activity.

The animals of Group number 13 served as standard group received phenytoin (30 mg/kg; i.p.) 30 min before administration of PTZ (80 mg/kg; i.p.). These animals also were observed in above referred manner for onset-time of convulsions and percentage recovery or death.

All the compound exhibit mild to moderate activities. Aa values were expressed as mean ±SEM.

The data was analysed using student's t-test followed by Dunnett's test, the critriation for statistical significance was P<0.05. biological activity data of synthesized compounds is summarized in the following Table 3:

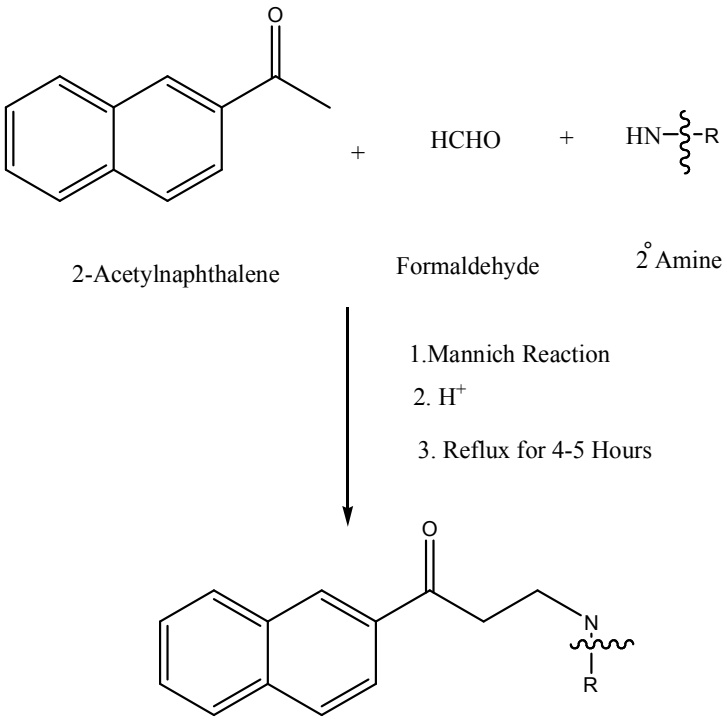
TABLE 3: Anticonvulsant activity of synthesized compound:-

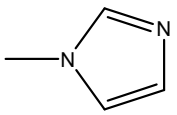
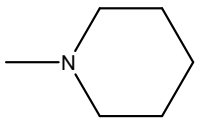
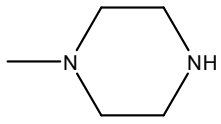
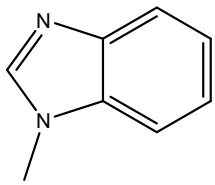
Group	Compound	Onset time of convulsion (S)	Recovery/death
1	Control (1% CMC)	39.3±0.8	Recovery
2	A1	148.8±2.4*	Recovery
3	A2	124.8±10	Recovery
4	A 3	43.7±2.5	Recovery
5	A4	123.1±1.1*	Recovery
6	B1	126.6±6.0*	Recovery
7	B2	133.5±4.3	Recovery
8	B3	39.0±4.6	Recovery
9	B4	134.8±2.0*	Recovery
10	C1	126.3±2.4*	Recovery
11	C2	131±4.9	Recovery
12	C3	143.5±2.8*	Recovery
13	Standard (Phenytoin)	152.5±1.5	Recovery

Phenytoin was used as standard drug. Values are expressed as Mean ± SEM.
* p<0.05 in comparison to control (n=6).

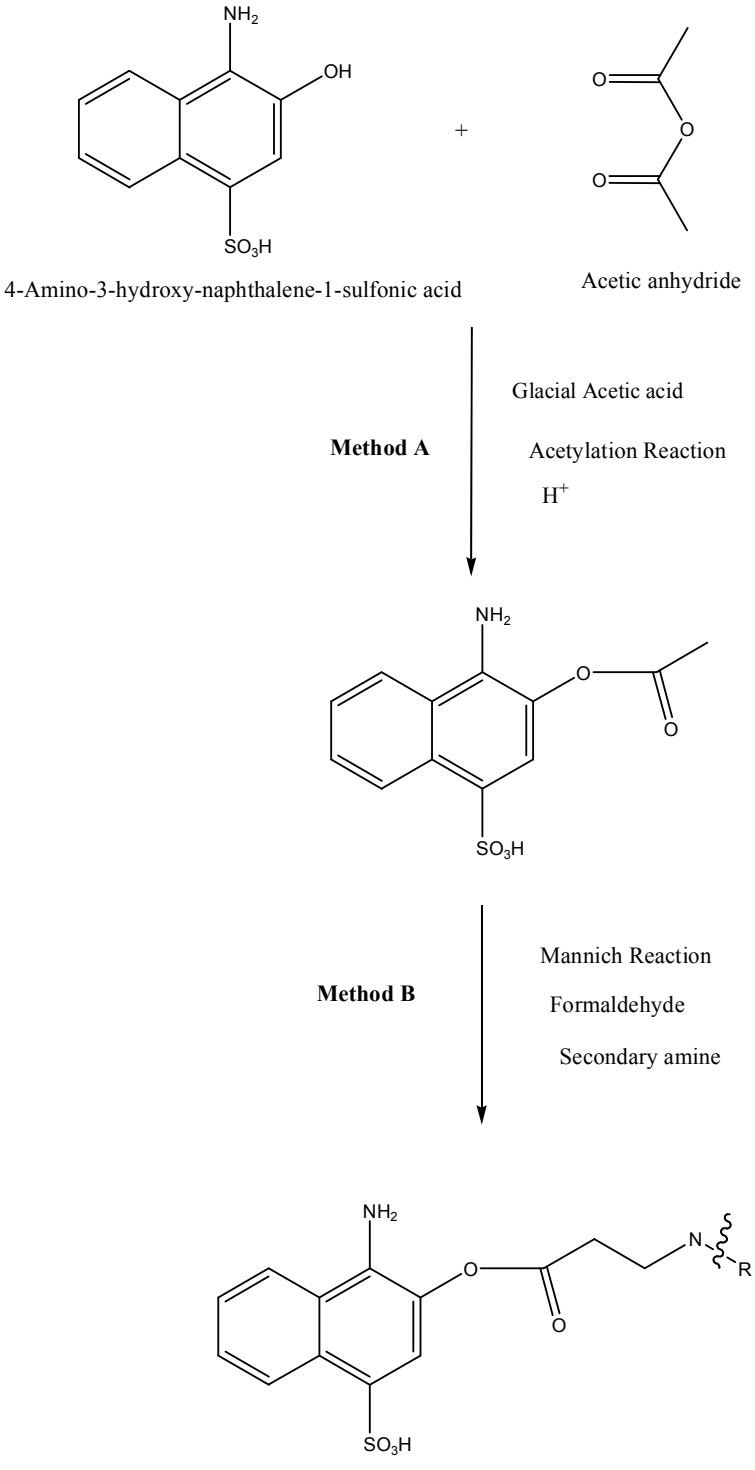
Reaction Scheme:

Scheme-I

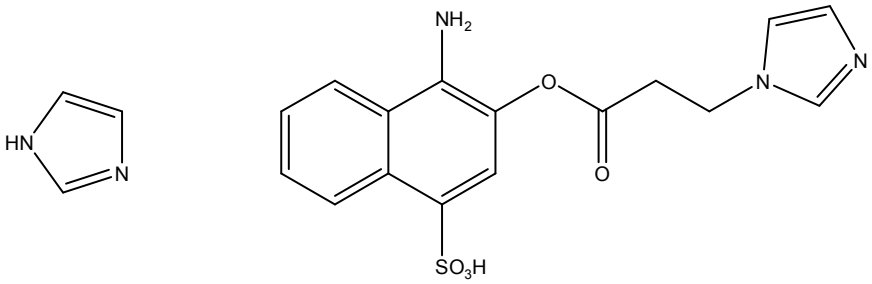


	R
A 1	
A 2	
A 3	
A 4	

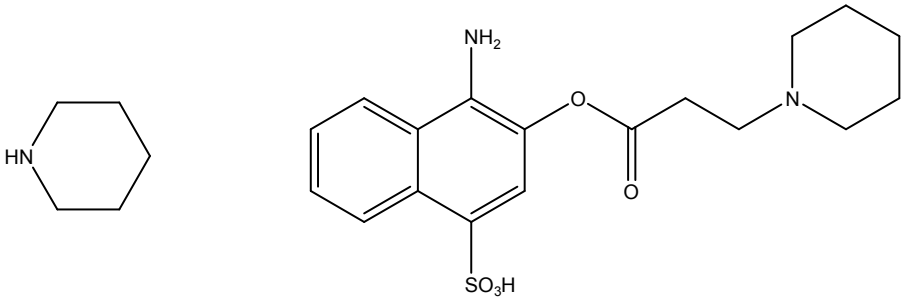
Scheme II


NH2
OH
SO3H
+
O
O
O
4-Amino-3-hydroxy-naphthalene-1-sulfonic acid
Acetic anhydride
Method A
Glacial Acetic acid
Acetylation Reaction
H+
NH2
O
O
SO3H
Method B
Mannich Reaction
Formaldehyde
Secondary amine
NH2
O
O
N
R
SO3H

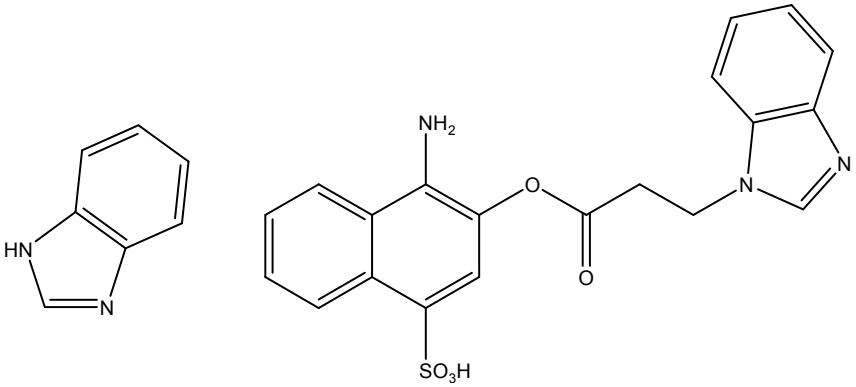
C 1



C 2



C 3



RESULT AND DISCUSSION:

The newly synthesized acetylnaphthalene derivative of heterocyclic compounds were done against seizure models, Chemical test subcutaneous pentylenetetrazole (scPTZ). In the present series of compounds, acetylnaphthalene derivatives were designed and synthesized to meet structural requirements like imidazole, piperidine and benzimidazole which is essential for anticonvulsant activity. The anticonvulsant data revealed that newly synthesized compounds **A1, A4, B1, B4, C1** and **C3** afforded significant protection at 100 mg/kg; i.p. in sc PTZ test. The anticonvulsant activity of the other tested compounds was found to be much moderately effective then phenytoin used as standard anticonvulsant.

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