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Newer Applications of 1,5-Benzothiazepines and their anticonvulsant activity

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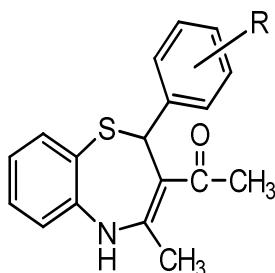
ABSTRACT

Benzothiazepines and its derivatives showed a wide spectrum of pharmacological activities such as anticonvulsant, antidepressant, antiviral, and antimicrobial activities. Therefore, some benzothiazepines substituted derivatives like Schiff bases and Mannich bases were prepared. These compounds were identified by m.p, R_f-value and spectral analysis. All the synthesized compounds were screened for anticonvulsant activities (chemoshock)

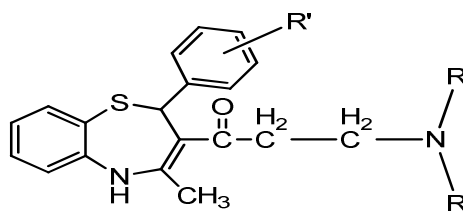
Keywords: Benzothiazepines, Schiff bases, Mannich bases, anticonvulsant activities.

INTRODUCTION

Benzothiazepines are the class of compounds having benzodiazepine type nucleus. The only difference between them is of S (sulphur) in place of N (nitrogen) atom in the heterocyclic ring system. The versatile application of benzothiazepines in the treatment of ailments of cardiovascular system such as coronary vasodilation, hypertension etc. Benzothiazepines are the versatile pharmacophore having various biological activities like cardiovascular activity, antipsychotic activity, anti-HIV activity, analgesic activity, antimicrobial activity etc. There are various benzothiazepines which have been synthesized and tested for their biological activities. Diltiazem S (DTZ) is a 1,5 benzothiazepine calcium channel blocker. Diltiazem is a non-dihydropyridine (DHP) member of the group of drugs known as benzothiazepine. The four different benzaldehydes yields 4 different benzothiazepines. The structure of 4 benzothiazepines can be given as below-



R = H, 2-Cl, 4-Cl, 2-NO₂



R'	R
H	CH ₃
H	C ₂ H ₅
4-Cl	CH ₃
4-Cl	C ₂ H ₅
2-Cl	CH ₃
2-Cl	C ₂ H ₅
2-NO ₂	CH ₃
2-NO ₂	C ₂ H ₅

PHYSICOCHEMICAL DATA OF COMPOUNDS-

compounds	Mol. formula	Mol. weight	M.p.	Rf value	% yield	¹ H-NMR	I.R	Elemental analysis
PBTP 1	C ₁₈ H ₁₆ NOSCl	329.06	135 ^o C	0.76	35%	.36-7.15(8H, -C ₆ H ₄), 1.71-2.30(6H, -CH ₃), 4.50(1H, -CH-), 4.0(1H, -NH-)	N-H - 3080, C=O - 1660, C=C - 1590	Standard value: C.65.54, H.4.82, N.4.25, Estimated value: C.65.50, H.4.82, N.4.22
PBTP 2	C ₂₃ H ₂₇ CN ₂ OS	414.99	100 ^o C	0.78	37%	6.36-7.15(8H, -C ₆ H ₄), 1.00-1.71(9H, -CH ₃), 2.40-3.04(8H, -CH ₂ -), 4.50(1H, -CH-), 4.0(1H, -NH-)	N-H - 3088, C=O - 1630, C=C - 1590, -CH ₂ -2960	Standard value: C.66.57, H.6.5, N.6.75 Estimated value: C.66.50, H.6.45, N.6.80
PBTP 3	C ₁₈ H ₁₈ CN ₃ S	343.87	55 ^o C	0.78	46%	6.36-7.15(8H, -C ₆ H ₄), 0.9-1.17(6H, -CH ₃), 4.50(1H, -CH-), 4.00(1H, -NH-), 7.0(2H, -NH ₂)	C=N - 1540, C=C - 1590, N-H - 3090	Standard value: C.62.87, H.5.28, N.12.22 Estimated value: C.62.90, H.5.33, N.12.30
PBTP 4	C ₂₁ H ₂₃ CN ₃ S	386.96	100 ^o C	0.78	37%	6.36-7.15 (8H, -C ₆ H ₄), 1.17-2.27 (9H, -CH ₃), 2.47-3.04 (4H, -CH ₂ -), 4.50(1H, -CH-), 4.00(1H, -NH-)	N-H - 3080, C=O - 1655, C=C - 1565	Standard value: C.65.18, H.5.99, N.7.24 Estimated value: C.65.34, H.4.74, N.4.22
PBTP5	C ₁₈ H ₁₉ N ₃ S	309.43	65 ^o C	0.81	49%	.36-6.93(4H, -C ₆ H ₄), 7.06-7.14(5H, -C ₆ H ₅), 0.9-1.71(6H, -CH ₃ -), 0.9-1.71(2H, -CH-), 4.00(1H, -NH-), 7.0(2H, -NH ₂)	N-H - 3060, C=C - 1575, C=N - 1530	Standard value: C.69.87, H.6.19, N.13.58 Estimated value: C.69.84, H.6.12, N.13.60
PBTP 6	C ₂₁ H ₂₃ CN ₂ OS	386.12	80 ^o C	0.85	37%	6.36-7.15 (8H, -C ₆ H ₄), 1.17-2.27(9H, -CH ₃), 2.47-3.04(4H, -CH ₂ -), 4.50(1H, -CH-), 4.0(1H, -NH-)	C=O - 1660, N-H - 3085, C=C - 1578, CH ₂ - 2935	Standard value: C.65.18, H.5.99, N.7.24 Estimated value: C.65.22, H.5.95, N.7.30
PBTP 7	C ₁₈ H ₁₈ CN ₃ S	343.78	90 ^o C	0.76	51%	6.36-7.15(8H, -C ₆ H ₄), 0.90-1.71(6H, -CH ₃), 4.50-(1H, -CH-), 4.00(1H, -NH-), 7.00(2H, -NH ₂)	N-H - 3080, C=C - 1590, C=N - 1540	Standard value: C.68.62, H.5.28, N.5.93 Estimated value: C.68.58, H.5.32, N.5.89
PBTP 8	C ₁₈ H ₁₆ N ₂ O ₃ S	340.09	125 ^o C	0.88	35%	6.36-8.07 (8H, -C ₆ H ₄), 1.17-2.30(6H, -CH ₃), 4.50(1H, -CH-), 4.00(1H, -NH-)	N-H - 3088, C=C - 1590, C=O - 1655, NO ₂ - 1500	Standard value: C.63.51, H.4.74, N.8.23 Estimated value: C.63.55, H.4.80, N.8.22
PBTP 9	C ₂₇ H ₂₃ ClN ₂ O ₄ S	506.11	89 ^o C	0.81	40%	6.33-8.27(12H, -C ₆ H ₄), 1.71-2.30(6H, -CH ₃), 2.78-3.25(4H, -CH ₂ -), 4.50(1H, -CH-)	C=O - 1650, C-N - 1535, C=C - 1590, CH ₂ - 2955	Standard value: C.63.96, H.4.57, N.5.33 Estimated value: C.66.99, H.4.49, N.5.32
PBTP 10	C ₂₃ H ₂₇ ClN ₂ OS	414.15	109 ^o C	0.92	39%	6.36-7.15 (8H, -C ₆ H ₄), 1.00-1.71(9H, -CH ₃), 2.40-3.04(8H, -CH ₂ -), 4.50(1H, -CH-), 4.00(1H, -NH-)	C=O - 1655, N-H - 3090, C=C - 1578, CH ₂ - 2980, NO ₂ - 1500	Standard value: C.66.57, H.6.56, N.6.75 Estimated value: C.66.52, H.6.52, N.6.80
PBTP 11	C ₂₇ H ₂₃ ClNO ₂ S	495.08	79 ^o C	0.96	35%	6.33-7.83(12H, -C ₆ H ₄), 1.71-2.30(6H, -CH ₃), 2.78-3.25(4H, -CH ₂ -), 4.50(1H, -CH-)	C=O - 1660, C=C - 1590, CH ₂ - 2950, C-N - 1465	Standard value: C.65.32, H.4.67, N.2.82 Estimated value: C.65.34, H.4.74, N.2.80
PBTP 12	C ₂₇ H ₂₃ ClN ₂ O ₄ S	506.11	89 ^o C	0.93	42%	.33-8.07(12H, -C ₆ H ₄), 1.71-2.30(6H, -CH ₃), 2.78-3.25(4H, -CH ₂ -), 4.50(1H, -CH-)	C=O - 1645, CH ₂ - 2935, C=C - 1580, C-N - 1455, NO ₂ - 1500	Standard value: C.63.96, H.4.57, N.5.53, Estimated value: C.65.34, H.4.74, N.4.22

PHARMACOLOGICAL EVALUATION
Anticonvulsant activity

Group	Isoniazid (30min)	Isoniazid (1 hr)	Isoniazid (2 hr)
PBTP1	30mg	30mg	NA
PBTP2	30mg	NA	NA
PBTP3	30mg	NA	NA
PBTP4	30mg	30mg	NA
PBTP5	30mg	NA	NA
PBTP6	30mg	NA	NA
PBTP7	NA	NA	NA
PBTP8	30mg	NA	NA
PBTP9	NA	NA	NA
PBTP10	30mg	NA	NA
PBTP11	30mg	30mg	NA
PBTP12	30mg	NA	NA
DIAZEPAM	10mg	10mg	10mg

RESULTS AND DISCUSSION

All the synthesized compounds were evaluated for their anticonvulsant activity using ISONIAZID, chemical induced convulsion models on male albino mice (20–25g). PEG-400 was used as vehicle & Diazepam 10mg/kg b.w. as a standard drug. All the synthesized derivatives were evaluated at the dose of 30mg/kg body weight & have shown good proconvulsant activity.

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