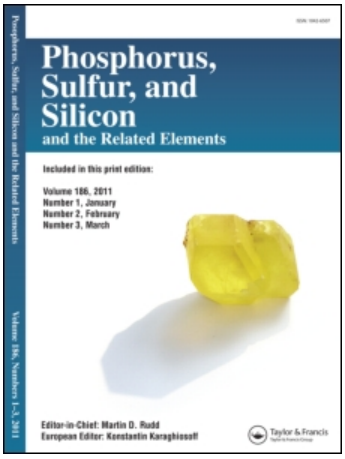

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Synthesis of Novel Derivatives of 1,5-Benzothiazepines (Part 1)

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SYNTHESIS OF NOVEL DERIVATIVES OF 1,5-BENZOTHIAZEPINES (PART 1)

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*Synthesis of 2,4-disubstituted 1,5-benzothiazepines **3a–3i** is reported by the condensation of 2-aminothiophenol **1** with 1,3-diones in pyridine. The structures of the compounds have been established by elemental, IR, ^{1}H NMR, ^{13}C NMR, and mass spectral analyses.*

Keywords: 1,5-Benzothiazepines; 1,3-diones; spectral studies

1,5-Benzothiazepines and its derivatives have attracted the attention of chemists mainly because of broad-spectrum biological activities exhibited by this class of compounds.[1–4] The 1,3-benzodioxole unit can be identified in some clinical antitumor agents like etoposide and teniposide.[5] Several heterocycles containing a dioxolane ring have been reported as possible anitfungal,[6] antiviral[7] agents. Unusual and manifold biological activities observed in 1,5-benzothiazepine class of compound stimulated our interest to synthesize some novel 1,5-benothiazepines bearing 1,3-benzodioxole moiety.

RESULT AND DISCUSSION

Propane-1-(1,3-benzodioxol-5-yl)-3-phenyl-1,3-dione **3a** and other compounds **3b–3i** having different substituent in phenyl ring, were treated with 2-amino thiophenol **1** in pyridine. Reaction is initiated by the nucleophilic attack of sulphydryl electrons on enolic carbon atom of the

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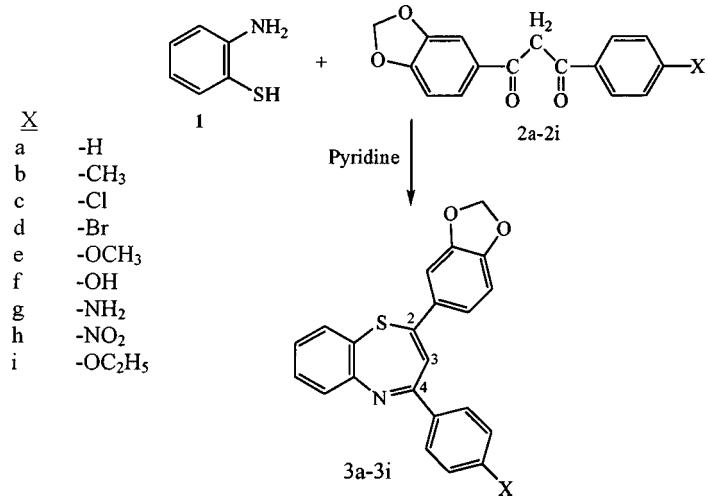

SCHEME 1

mentioned β-diketone followed by loss of water molecule. Now amino group comes in vicinity of carbonyl group, by dehydration resulting into cyclised product i.e. 1,5-benzothiazepines (Scheme 1). The spectroscopic studies and elemental analysis (Table I) of the synthesized compounds are consistent with the proposed structure.

Spectral Studies

IR Spectra

Absorption at 1612–1602 cm^{-1} have been assinged to ν(C=N) in seven-membered heterocyclic rings. The weak bands observed in the region 680–660 cm^{-1} may be assigned to C—S linkage.[8] The bands appearing in the region 1265–1235 cm^{-1} and 1060–1035 cm^{-1} are due to C—O—C asymmetric and symmetric vibrations respectively.

^{1}H NMR Spectra

The signals for methine and aromatic protons were indicated at δ 6.64–6.74 as a singlet and at δ 6.75–7.99 as a multiplet respectively. A singlet is obtained for dioxymethylene protons at δ 6.02–6.07. The ^{1}H NMR data for the compounds are given in Table II.

^{13}C NMR data for the compounds **3a–3i** presented in Table III and these data are in good agreement with their structures.

Mass spectra of compounds **3a–3i** gave the molecular ion peaks (m/z), which corresponded to their molecular weight. A cluster of ion peaks to $[M]^+$, $[M+2]^+$ at 391, 393 were observed in case of **3c**. The $[M+2]^+$

TABLE I Elemental Analysis Data of Title Compounds

Compd.	M.F.	M.W.	Elemental analysis calcd. and (found) C%	H%	N%	X%	m.p. (°C)
3a	$C_{22}H_{15}SO_2N$	357	73.95 (73.62)	4.20 (4.00)	3.92 (3.63)	—	178
3b	$C_{23}H_{17}SO_2N$	371	74.39 (74.11)	4.58 (4.36)	3.77 (3.45)	—	148
3c	$C_{22}H_{14}SO_2NCl$	391.5	67.43 (67.21)	3.58 (3.24)	3.58 (3.29)	9.07 (8.88)	156
3d	$C_{22}H_{14}SO_2NBr$	435	60.69 (60.16)	3.22 (3.06)	3.22 (3.00)	18.16 (17.91)	145
3e	$C_{23}H_{17}SO_3N$	387	71.32 (70.97)	4.39 (4.09)	3.62 (3.51)	—	138
3f	$C_{22}H_{15}SO_3N$	373	70.78 (70.37)	4.02 (3.78)	3.75 (3.49)	—	158
3g	$C_{22}H_{16}SO_2N_2$	372	70.97 (70.51)	4.30 (3.98)	7.53 (7.22)	—	160
3h	$C_{22}H_{14}SO_4N_2$	402	65.67 (65.23)	3.48 (3.16)	6.97 (6.76)	—	153
3i	$C_{24}H_{19}SO_3N$	401	72.32 (72.03)	4.74 (4.52)	3.49 (3.20)	—	147

peak was nearly one fourth of $[M]^+$ peak indicating the presence of isotopic Cl^{37}.

EXPERIMENTAL

All the melting points were uncorrected. The IR spectra were recorded on a Nicolet-Megna FT-IR 550 spectrophotometer in KBr pellets. The

TABLE II ^1H NMR Data of Title Compounds (in δ, ppm)

Compd.	X	Ar-X	OCH_2O (2H, s)	Methine (1H, s)	Aromatic protons (11H, m)
3a	—H	—	6.03	6.64	6.85–7.71 (12H, m)
3b	$-CH_3$	3H, 2.43 s	6.07	6.76	6.89–7.88
3c	—Cl	—	6.08	6.72	6.79–7.94
3d	—Br	—	6.02	6.67	6.83–7.94
3e	$-OCH_3$	3H, 3.85 s	6.02	6.66	6.81–7.99
3f	—OH	1H, 4.05, s	6.02	6.68	6.78–7.95
3g	$-NH_2$	2H, 4.41(b), s	6.03	6.71	6.81–7.98
3h	$-NO_2$	—	6.05	6.69	6.73–7.97
3i	$-OC_2H_5$	1.76 (3H, t, J = 6.9Hz) 3.92 (2H, q, J = 6.8Hz)	6.04	6.73	6.80-7.94

TABLE III ^{13}C NMR Data of Title Compounds (in δ ppm)

Compd.	Ar-X	O(C)O	C_2	C_3	C_4	Aromatic carbons
3a	—	101.7	137.3	92.0	151.0	148.6–106.9
3b	CH_3-20.6	101.3	135.9	91.5	150.8	147.6–106.5
3c	—	101.5	136.1	92.0	150.9	149.0–107.0
3d	—	101.9	138.4	92.4	151.6	148.3–107.2
3e	OCH_3-55.4	101.8	136.7	91.6	151.1	163.0–107.1
3f	—	101.4	136.4	92.2	151.7	161.8–106.4
3g	—	101.9	137.8	91.9	151.4	150.0–106.3
3h	—	101.5	138.6	91.7	150.7	154.3–106.8
3i	OCH_2-63.2, CH_3-14.7	101.7	137.0	92.0	151.3	162.3–107.1

^1H NMR and ^{13}C NMR spectra were scanned in $CDCl_3$ on an DRX 300 spectrometer at 300.13 and 75.48 MHz, respectively, using TMS as an internal standard. The mass spectra were recorded on a Jeol D-300 spectrometer. The purity of compounds was checked by TLC.

Generalized Preparation of Substituted 1,5-Benzothiazepines

2-Aminobenzene thiol (0.01 mmol) was added to the stirred suspension of β-diketone (0.01 mmol) in pyridine and the resulting mixture was refluxed for $\simeq$4 h. The mixture was cooled and poured onto crushed ice dropwise with vigorous stirring. The pale yellow precipitate formed was filtered, dried and crystallized from methanol. Purity of the compounds were checked by TLC using ($CHCl_3 : CH_3OH$, 2 : 8) as mobile phase.

REFERENCES

[1] F. Barzaghi, R. Fournex, and P. Mantegazze, *Arzneim-Forsch*, **23**(5), 683 (1973).
[2] Hamari Yokuhin Kogyo Co Ltd., Jap. Pat. 84106477 (1984) (Cl. Co 7D 281/10).
[3] Kawashima Co Lt., Kokai Jap. Pat. 85, 56, 972 (1985) (Cl. Co 7D 281/10).
[4] R. N. Brogden, R. C. Heel, T. M. Speight, and G. S. Avery, *Drugs*, **20**(3), 161 (1980).
[5] G. L. Chen, L. Yang, T. C. Rowe, B. D. Halligan, K. Tewey, and L. Liu, *J. Biol. Chem.*, **259,** 13560 (1984).
[6] B. Tal and D. J. Robeson, *Phytochemistry*, **25,** 77 (1986).
[7] S. Weitman, J. Marty, J. Jolivet, C. Locas, and D. D. Von Hoff, *Clin. Cancer Res.*, **6,** 1574 (2000).
[8] Charu Modwel, Ph.D. Thesis, University of Rajasthan, Jaipur (1991).