Indian Journal of Chemistry
Vol. 37B, February 1998, pp. 161 - 162

Note

Synthesis of some new 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines and 2-aryl-4-(2′-hydroxy-3′/5′-chloro-5′/3′-hydroxymethylphenyl)-2,3-dihydro-1,5-benzothiazepines.

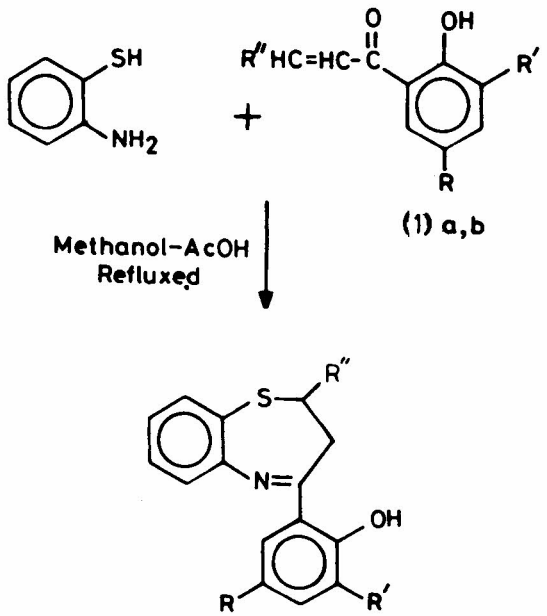
V M Gurav*
Post Graduate Department of Chemistry
Yeshwant Mahavidyalaya, Nanded-431 602, India
and
S V Agarkar
Department of Chemistry, Anuradha College of Engineering, Chikhali - 443 201. (Distt. Buldana), India.

Received 26 March 1997; accepted (revised)
17 November 1997

The title compounds **2a,b** have been synthesized from the corresponding, 1-(2′-hydroxy-3′/5′ -chloro-5′/3′-hydroxy methyl-phenyl)-3 - aryl-2-propen-1-ones (**1**) by condensation with *o*-aminothiophenol in ethanol containing a few drops of piperidine followed by cyclisation in the presence of acetic acid. Some of the representative members have been screened for their antifungal activity against *Penicillium notatum*. In general, the compounds have been found to be stimulatory against *Penicillium notatum*.

Benzothiazepine derivatives were found to possess neuroleptics[1], antiserotonin[2], psychotropic[3], antidepressant[4], coronary vasodilatory[5-6] and anticovulsant[7]. In view of the significant biological applicability of 1,5-benzothiazepines, it was thought worthwhile to synthesize 2,3- dihydro-4-(2′- hydroxy-3′/5′-chloro - 5′/3′-hydroxy-methylphenyl) - 2-(phenyl)-1,5 benzothiazepines. Although some benzothiazepines with monosubstituted phenyl group at 2 and 4 positions were reported[8], benzothiazepines with trisubstituted phenyl group at 4-position have not been studied so far. Therefore, attempts were made to synthesize 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines **2a,b**.

The starting chalcones **1a,b** were synthesized as described in literature[9]. Their reactions with *o*-aminothiophenol in ethanol containing a few drops



	R	R'	R"
(I) a)	CH_2OH,	Cl,	Substituted Aryl groups
(I) b)	Cl,	CH_2OH,	Substituted Aryl groups
(II) a)	CH_2OH,	Cl,	Substituted Aryl groups
(II) b)	Cl,	CH_2OH,	Substituted Aryl groups

Scheme I

of piperidin followed by cyclisation in the presence of acetic acid yielded the title benzothiazepines **2a,b**. Their IR spectra did not show any absorption bands in the region 3500-3311 cm^{-1}, indicating the absence of NH or OH group. The absence of -OH absorption band may be attributed to the strong intramolecular hydrogen bonding with the lone pair of electrons on nitrogen. Presence of C=N band in the region 1589-1609 cm^{-1}, supported the assigned structure **2a**. Further support for structure **2a,b** was gathered from the PMR spectrum of representative compound. The PMR spectrum of 2-Aryl-4-(2′-hydroxy-3′-chloro-5′-hydroxymethyl phenyl)-2,3-dihydro-1,5-benzothiazepine exhibited signals at δ 2.4 (s, 1H, CH_2OH),

Table 1—Characteristic data of 2-aryl-4-(2′-hydroxy-3′/5′-chloro-5′/3′-hydroxy-methyl-phenyl)-2,3-dihydro-1,5-benzothiazepines **2 a,b**

R″	m.p. (°C)	Yield %	Solvent forCrystal lisation	Analysis % *Found (Calcd)*
		2a, R = CH_2OH R′ = Cl		
Phenyl	132	70	EtOH AcOH Mixt.	7.65 (8.09)
o-Chloro phenyl	207	68	EtOH/AcOH	6.94 (7.44)
p-Chloro phenyl	157	66	EtOH/AcOH	7.84 (7.44)
o-Methyl phenyl	215	67	EtOH	7.45 (7.81)
p-Methoxy phenyl	201	63	EtOH/AcOH	7.42 (7.52)
o-Hydroxy phenyl	161	65	EtOH	7.62 (7.77)
m-Hydroxy phenyl	170	68	AcOH	7.41 (7.77)
p-Hydroxy phenyl	198	70	AcOH	7.53 (7.77)
a-Naphthyl	196	65	AcOH	6.90 (7.18)
		2b, R = Cl, R′ = CH_2OH		
Phenyl	125	65	EtOH	8.46 (8.09)
o-Chloro phenyl	198	60	AcOH	7.67 (7.44)
p-Chloro phenyl	145	65	AcOH	7.52 (7.44)
o-Methyl phenyl	201	60	EtOH	7.67 (7.81)
p-Methoxy phenyl	199	62	EtOH	7.42 (7.52)
α-Naphthyl	192	60	AcOH	7.32 (7.18)

2.6-3.3 (m, 2H, CH_2-CH), 4.5(s, 2H, CH_2OH), 4.95 (dd, 1H,CH_2-CH, J = 10.5 Hz), 6.6-7.6 (m, 10H, Ar-*H*) and 12.9 (s, 1H, O*H*, chelated OH, exchanged with D_2O.).

Antifungal screening

Antifungal screening of some of the representative members from this series was done by dry weight method. In general, the compounds were found to be stimulatory against *Penicillium notatum* at 100 and 250 ppm.

Experimental Section

Melting points are uncorrected. IR spectra were recorded on Perkin Elmer infrared spectrophotometer (vmax in cm^{-1}) and PMR (chemical shifts in δ-ppm) in $CDCl_3$ on a Varian T-60 instrument using TMS as internal standard. Purity of compounds was checked by TLC.

2,3-dihydro-4-(2′-hydroxy-3′/5′-chloro-5′/3′-hydroxymethylphenyl)-2-(phenyl)-1,5-benzothiazepines: General procedure. To a mixture of 1-(2′-hydroxy-3′/5′-chloro-5′/3′-hydroxymethyl phenyl)-3-aryl-2-propen-1-ones (0.01 mole) and *o*-aminothiophenol (0.01 mole) in ethanol (50 mL), a few drops of piperidine were added and the reaction mixture was refluxed for 2 hr on a steam bath. It was acidified with glacial acetic acid (10 mL) and further refluxed for two hours and cooled. The reaction mixture was left overnight at room temperature. Solid thus obtained was then filtered off and crystallized from proper solvents. Purity of the products was checked by TLC. The structures were confirmed by elemental analysis, IR and PMR data. The compounds thus synthesized, are recorded in Table-I along with their characterization data. Melting points, yields, elemental analysis and solvent for crystallization are listed in Table-I.

Acknowledgement

Thanks are due to Prof (Dr) D B Ingle, Department of Chemistry, Marathwada University, Aurangabad for his keen interest in the work. Thanks are also due to Dr B S Dhengle, Principal, Yeshwant Mahavidyalaya, Nanded for providing necessary laboratory facilities.

References

1 Niemegear CJE & Janssen PAI, *J Pharm Pharmacol*, 12, **1960**, 744.
2 Shaw E N & Willey D W, *J Pharm expt Therap*, 116, **1956**, 164.
3 Maki Y & Suzuki M *Chem Abstr*, 81, **1974**, 77984d.
4 Hunziker F, Kunzle F, Scindler O & Schumutz J Helv *Chim Acta*, 47, **1964**, 1163.
5 Kugita, Hiroshi *et. al, Chem Abstr*, 76, **1972**, 59674V.
6 Chikada, Mikhinko *et. al, Chem Abstr*, 76, **1972**, 85854 Y.
7 Inoue, Hirosumi *et al, Chem Abstr*, 90, **1979**, 137874 F.
8 Albert L & Rezsco B, *Chem Abstr*, 85, **1976**, 4331 b.
9 Gurav V M & D B Ingle, *Indian J Chem*, 25B, **1986**, 868.