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# Synthesis and Spectral Studies of Benzothiazolo-(2,3-c)-5-Chloro-2,3-Dihydro-1,2,4-Triazepine

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2-Hydrazinobenzothiazole (I), on treatment with acrylonitrile, gave β-(2-hydrazinobenzothiazolyl)-propiononitrile (II) which was hydrolysed to corresponding acid (III). The corresponding acid chloride, on heating in the presence of pyridine, gave benzothiazolo-(2,3-*c*)-2,3-dihydro-1,2,4-triazepin-5-one (IV). This seven-membered keto product on treatment with phosphoryl chloride gave benzothiazolo-(2,3-*c*)-5-chloro-2,3-dihydro-1,2,4-triazepine (V) which was also obtained directly by heating β-(2-hydrazinobenzothiazolyl)-propanoic acid (III) with phosphoryl chloride. Structures of the compounds have been established by elemental analysis and spectral data.

## INTRODUCTION

The benzothiazole derivatives[1–3] are well known anti-inflammatoric agents. On the other hand, some of the derivatives of 1,4-benzodiazepines[4–6] are psychotropic agents possessing also weak analgesic activity. Synthesis of some thiazolo-triazepines have been reported[7, 8] which were found to possess central nervous depressant activity, psychosedative and tranquillising properties. Hence, a new route was sought to combine these systems to visualise whether the new synthesized benzothiazolo-(2,3-*c*)-5-chloro-2,3-dihydro-1,2,4-triazepine (V) would exert analgo-antipyretic and psychotropic properties. Since the compound (V) prepared presently has a reactive chlorine and could be replaced by biologically active substituted amino groups, the possibility of encountered interesting biological properties in this type exists.

A survey of literature reveals that cyanoethylation of 2-hydrazinobenzothiazole is not reported so far. 2-Hydrazinobenzothiazole (I) in ethanol was refluxed with acrylonitrile in the presence of triethylamine. The product obtained after the removal of ethanol was shown to be β-(2-hydrazinobenzothiazolyl)-propiononitrile (II) (Fig. 1) on the basis of elemental analysis and mass spectrum which shows the molecular ion at 218.

β-(2-Hydrazinobenzothiazolyl)-propiononitrile on boiling with hydrochloric acid was hydrolysed to β-(2-hydrazinobenzothiazolyl)-propanoic acid (III). This structure was arrived at on the basis of elemental analysis and spectral data. The

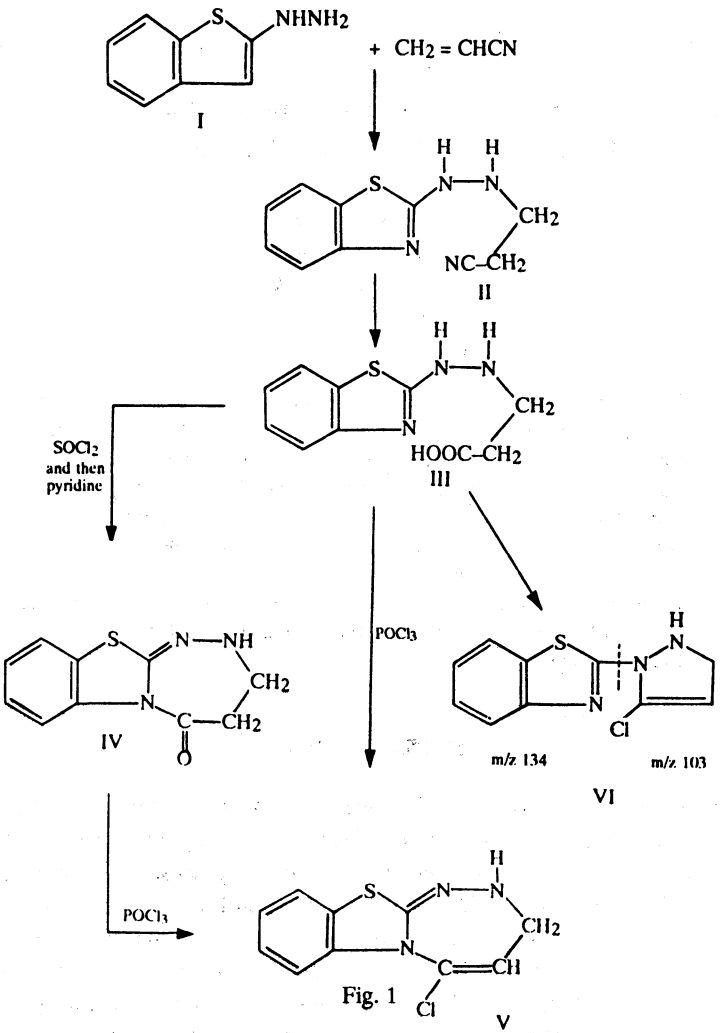
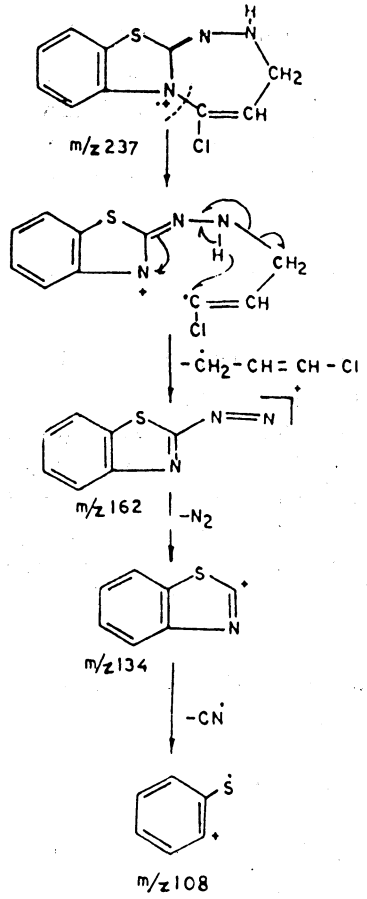



Fig. 1

i.r. spectrum shows an intense peak at 1700 $cm^{-1}$ corresponding to the carbonyl group of –COOH. The mass spectrum shows a molecular ion at 237.

β-(2-Hydrazinobenzothiazolyl)-propanoic acid on heating with thionyl chloride was converted to its acid chloride derivative. After removing excess of thionyl chloride under reduced pressure, the acid chloride was heated in the presence of pyridine. The product obtained was shown to be benzothiazolo-(2,3-*c*)-2,3-dihydro-1,2,3-triazepin-5-one (IV) on the basis of elemental analysis. This compound was then heated with phosphoryl chloride for 2 hrs, to obtain benzothiazolo-(2,3-*c*)-5-chloro-2,3-dihydro-1,2,4-triazepine (V). The same compound (V) was also obtained directly by heating β-(2-hydrazinobenzothiazolyl)-propanoic acid (III) with phosphoryl chloride for 3 hrs. Its mixed melting point with the compound obtained from (IV) was not depressed. The authentication of

the structure was done with the help of elemental analysis and spectral data. The compound (V) shows presence of chlorine. In i.r. spectrum, there is absence of carbonyl peak but shows the additional peak 755 $cm^{-1}$ due to C–Cl. The PMR was scanned in trifluoroacetic acid because of its poor solubility in other solvents. The proton value of multiplet in the region 7.4 to 7.9 ppm is due to aromatic protons. The methine proton and methylene protons appeared at 4.5 ppm and 3.65 ppm respectively. In addition to above, a weak peak at 9.9 ppm is assigned to N–H proton. Mass spectrum of compound (V) does not show peak at m/z 103 which would have been formed due to possible five membered pyrazolidine structure (VI). Bansal and coworkers[9] have observed that there was an intial fragmentation of the pyrazolone ring with expulsion of $N_2R$(R = H, $C_6H_5$) and also resulting in the formation of phenyldiazonium cation (m/z 105) in the mass spectra of some 3-(2-benzothiazolyl)-5-pyrazolones. As such fragmentation is not observed in the mass spectrum of compound (V), the study of mass fragmentation of compound (V) certainly helps in arriving at the fused seven-membered triazepine structure (V) and does not favour the structure (VI).



The mass spectrum shows molecular ion base peak at 237 which is 100% and M+2 peak at 239 which is approximately one-third the intensity of the molecular ion base peak. This shows presence of chlorine atom in the compound. Molecular ion undergoes homolytic cleavage of N–C bond, followed by the loss of $\dot{C}H_2$–CH=CH–Cl radical giving ion at m/z 162 which then loses $N_2$ forming species at m/z 134. It then fragments with the loss of $\dot{C}N$ yielding ion at m/z 108.

## EXPERIMENTAL

Melting points were taken in a paraffin-bath and are uncorrected. IR spectra were recorded on a Perkin-Elmer spectrophotometer model 337 ($\nu_{max}$ in $cm^{-1}$), PMR spectra in $CF_3COOH$ on an EM-360 60MHz NMR spectrometer (chemical shifts in δ, ppm) and mass spectra on a Jeol-300 mass spectrophotometer. Purity of the compounds was checked by TLC on silica gel plates and spots were located by iodine vapours.

### β-(2-Hydrazinobenzothiazolyl)-propiononitrile (II)

2-Hydrazinobenzothiazole (1.65 gm 0.01 mol) in ethanol (15 ml) was mixed with acrylonitrile (3 ml) in the presence of triethylamine (0.5 ml.). The reaction mixture was refluxed on a water bath for 5 hrs. It was cooled and distilled to remove ethanol. The reaction mixture was poured over ice. The solid obtained was filtered and crystallised from 50% ethanol. yield 1.3 gm (60%); m.pt. 104°C (Found: C, 55.1; H, 4.4; N, 25.5%. $C_{10}H_{10}N_4S$ requires C, 55.0; H, 4.5; N, 25.7%); IR (nujol): 1620, 1515, 1455 (aromatic C=C), 2240 (C≡N), 3320 (–NH); MS: m/z 218 ($M^+$), 192 (M–CN).

### β-(2-Hydrazinobenzothiazolyl)-propanoic acid (III)

β-(2-Hydrazinobenzothiazolyl)-propiononitrile (1 gm) was refluxed with conc. HCl (10 ml) for 2 hrs. On cooling, the separated solid was filtered and washed with water. It was dissolved in $NaHCO_3$ solution and filtered. Filtrate on treatment with decolourising charcoal and on acidification with dil. HCl afforded a white product which was recrystallised from ethanol. Yield 0.65 gm (59%); m.pt. 192°C (Found: C, 50.4; H, 4.5; N, 17.5%; $C_{10}H_{11}N_3O_2S$ requires C, 50.6; H, 4.6; N, 17.7%); IR (nujol): 1620, 1520, 1450 (aromatic C=C); 1700 (C=O); 3325 (–NH); MS: m/z 237 ($M^+$)

### Benzothiazolo-(2,3-c)-2,3-dihydro-1,2,4-triazepin-5-one (IV)

β-(2-Hydrazinobenzothiazolyl)-propanoic acid (1 gm) was heated with thionyl chloride (3 ml) on a water bath for 1 hr. It was cooled and thionyl chloride was removed under reduced pressure. Pyridine (2 ml) was then added to the reaction mixture and heated on the water bath for 1 hr. It was cooled and poured in water. The solid that separated was filtered and washed with dil. HCl and water. It was

recrystallised from dioxane. Yield 0.5 gm (52%); m.pt. 301°C (Found: C, 54.6; H, 4.0; N, 18.9%, $C_{10}H_9N_3OS$ requires C, 54.8; H, 4.1; N, 19.2%); IR (nujol): 1610, 1500, 1460 (aromatic C=C), 1710 (C=O), 3330 (–NH); MS: m/z 219 ($M^+$).

**Benzothiazolo-(2,3-*c*)-5-chloro-2,3-dihydro-1,2,4-triazepine (V)—from compound (IV).**

A mixture of benzothiazolo-(2,3-*c*)-2,3-dihydro-1,2,4-triazepin-5-one (1 g) and phosphoryl chloride (10 ml) was refluxed over an oil bath at 160°C for two hours. The flask was cooled and the contents were poured on to crushed ice. Excess of $NH_3$ solution was added to it. The pale brownish solid was filtered and recrystallised from ethanol. Yield 0.54 gm (50%), m.pt. 188°C.

**Compound (V) from compound (III)**

A mixture of β-(2-hydrazinobenzothiazolyl)-propanoic acid (1 gm) and phosphoryl chloride (10 ml) was refluxed over an oil bath at 160°C for 3 hrs. The flask was cooled. The contents were poured on the crushed ice and basified with $NH_3$ solution. The pale brownish product was filtered and recrystallised from ethanol. Yield 0.55 gm (55%), m.pt. 188°C. The mixed m.pt. with the compound obtained from compound (IV) was not depressed. (Found: C, 50.4; H, 3.1; N, 17.5; Cl, 14.5%, $C_{10}H_8N_3ClS$ requires C, 50.6; H, 3.4; N, 17.7; Cl, 14.8%); IR (nujol): 1560, 1450, 1390 (aromatic C=C), 610 (C=N), 1280 (C–N), 755 (C–Cl); PMR ($CF_3COOH$) : 9.9 (N–H, s); 7.4–7.9 (4H, m, Ar–H); 4.5 (CH, t); 3.65 ($CH_2$, t); MS: m/z 239 (M+2 33%), 237 ($M^+$ 100%), 162, 135, 134, 108, 96, 89, 78.

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