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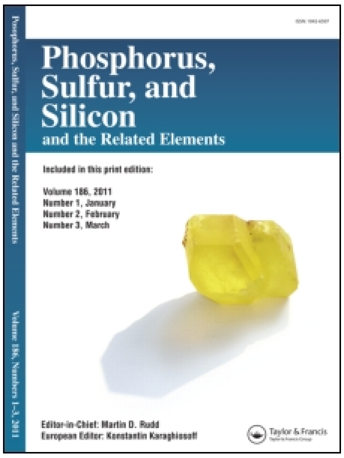

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Synthesis and Characterization of a New Class of Benzothiazolines

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Synthesis and Characterization of a New Class of Benzothiazolines

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A new class of benzothiazolines having the composition, $H\overline{NC_6H_4SC}(R)CH{:}C(OH)COOCH_3$ *[where* $R = C_6H_5$, $4\text{-}BrC_6H_4$, $4\text{-}ClC_6H_4$, $4\text{-}CH_3OC_6H_4$, $4\text{-}CH_3C_6H_4$*] have been synthesized by the equimolar condensation of aroyl pyruvates,* $RC(O)CH{:}C(OH)COOCH_3$ *with 2-aminothiophenol. These newly synthesized benzothiazolines have been characterized by elemental analyses and spectral [IR and NMR (*^1H *and* ^{13}C*)] studies.*

Keywords 2-Aminothiophenol; aroyl pyruvates; benzothiazoline and spectral studies

INTRODUCTION

Benzothiazolines and other compounds containing -NC_6H_4S- unit are reported to have biological activity.[1] A large number of benzothiazolines have been prepared by the reactions of aldehyde and ketones with 2-aminothiophenol.[2–4] Some benzothiazolines have also been prepared by the reactions of β-diketones and 2-aminothiophenol in 1:1 molar ratio.[5–7] However, reaction of β-diketone with 2-aminothiophenol in 1:2 molar ratio leads to formation of Schiff base.[8] Organoantimony(III) derivaties of these Schiff bases are found to have antifertility activity.[9] The aluminium derivatives of the benzothiazolines derived by the similar reaction of β-diketone with 2-aminothiophenol in 1:1 molar ratio, have also been reported to have considerable antifertility activity.[7] In view of the above, it has been considered worthwhile to prepare a new class of benzothiazolines by the reactions of aroyl pyruvates, a class of β-ketoesters with 2-aminothiophenol. Synthesis and characterization of these new benzothiazolines are described and discussed in this article.

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RESULT AND DISCUSSION

The condensation reactions of aroyl pyruvates with 2-aminothiophenol in equimolar ratio in refluxing benzene result the benzothiazolines, $H\overline{NC_6H_4SC}(R)CH{:}C(OH)COOCH_3$.

$$RC(O)CH{:}\ C(OH)COOCH_3 + H_2NC_6H_4SH \xrightarrow[\text{Reflux}]{C_6H_6} H\overline{NC_6H_4SC}RCH{:}\ C(OH)C(O)OCH_3 + H_2O$$

where $R = C_6H_5$, 4-BrC_6H_4, 4-ClC_6H_4, 4-$CH_3OC_6H_4$, 4-$CH_3C_6H_4$.

These colored compounds are found to be soluble in common organic solvents. They can be distilled under reduced pressure.

SPECTRAL STUDIES

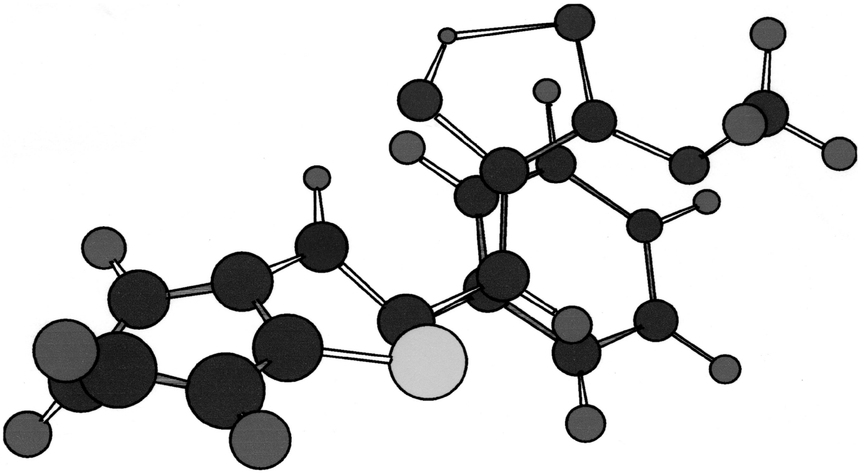
IR Spectra

IR spectra of these compounds show presence of νNH absorption band (3250–3425 cm^{-1}) and absence of νSH ($\sim$2540 cm^{-1}) absorption band. This indicates the presence of benzothiazoline ring in these compounds. A broad band observed in the range 3417–3638 cm^{-1} has been assigned to νOH vibrations. Appearance of this band shows enolization in these compounds. This is further supported by the appearance of νC=C—OH absorption band in the range at 1590–1606 cm^{-1} in these compounds.[10–11] It is important to note that this band is also observed at the same position in the spectra of corresponding aroylpyruvates. It appears that aromatic band is being overlapped with this band. The absorption band due to $\nu >$ C=O (ester) group has been observed at 1685–1692 cm^{-1}.

^{1}H NMR Spectra

^{1}H NMR spectra of these compounds show presence of NH proton signal in the range δ3.90–4.40 ppm, and absence of SH signal indicating the presence of benzothiazoline ring in these compounds. The CH_3 protons of ester group are observed as singlet at δ2.47–2.59 ppm in the spectra of these compounds. Unusual chemical shift of this group may be due to fall of this group in magnetic anisotropic zone of phenyl group. This has been confirmed by drawing a 3D model of the compound by a computer programme. The R group protons are observed as complex pattern in the range of δ6.91–8.16 ppm (Table I).

It is interesting to note that =CH signal is observed instead of CH_2 signal indicating the enolisation of these compounds. This is further supported by the appearance.5pc of a broad signal at δ15.1–15.35 ppm



MODEL 1 3D Diagram of benzothiazoline.

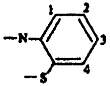
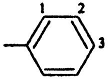
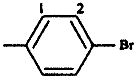
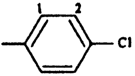
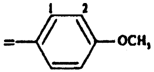
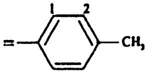
for OH group proton. The broadening of this signal may be due to the involvement of this OH group in hydrogen bonding. These results are in contrast to the results observed in case of benzothiazolines derived by the condensation of β-diketone with 2 aminothiophenol[12] where the enolisation of >C=O group does not take place.

^{13}C NMR Spectra

^{13}C NMR spectra of these compounds (Table II) exhibit a signal at δ158.68–160.07 ppm which has been assigned to C—N of benzothiazoline ring. Absence of —C=N signal and presence of C—N signal also supports the presence of benzothiazoline ring in these compounds. Appearance of >C—OH signal at δ161.88–163.1 ppm along with =CH carbon signal at δ 97.5–98.0 ppm indicate the enolisation in these organic compounds. The signal appearing at δ195.85–196.98 ppm has been assigned to >C=O (ester) group. Involvement >C=O group in hydrogen bonding is supported by the lowering of this signal as compared to its position (δ189.28–190.47 ppm) in corresponding pyruvates where this ester group remains free. The signal for CH_3 (ester) group appears in the region δ22.66–25.98 ppm. The signals for R group appear in the region δ125.22–135.59 ppm. The —NC_6H_4S— group signals appear in the range δ121.17–153.46 ppm in these compounds.

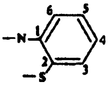
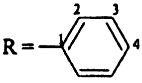
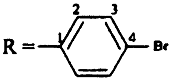
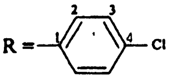
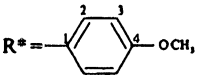
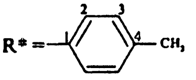
As discussed above, the spectral studies show the presence of benzothiazoline ring in these compounds. It may also be concluded that these compounds show enolisation and the OH group is involved in

TABLE I ^{1}H NMR Spectral Data (δ ppm) of the Benzothiozolines $H\overline{NC_6H_4SC}$(R)CH:C(OH)C(O)OCH$_3$

Compounds	R [J in MHz]	CH$_3$(ester)	=CH		NH	OH
R = 	7.94–7.96 (d) [7.75] 7.52 (t) [7.75] 7.54(t) [7.75]	2.59 (s)	8.99 (s)	7.94–7.96 (d) [7.75] 7.46 (t) [7.75] 7.47 (t) [7.75] 8.16–8.13 (d) [8.71]	4.01 (b)	15.1 (b)
R = 	7.51–7.53 (d) [7.80] 7.73–7.75(d) [7.80]	2.51(s)	8.99 (s)	7.89–7.92 (d) [7.80] 7.36–7.41 (t) [7.80] 7.45–7.51 (t) [7.80] 8.11–8.14 (d) [7.80]	4.12 (b)	15.27 (b)
R = 	7.80–7.83(d) [8.72] 7.34–7.36(d) [8.72]	2.51 (s)	8.97 (s)	7.89–7.91 (d) [8.72] 7.36–7.41 (t) [6.98] 7.45–7.50 (t) [6.98] 8.11–8.14(d) [8.72]	3.90(b)	15.27(b)
R = 	7.91–7.93 (d) [9.13] 6.91–6.94 (d) [8.22]	2.53 (s)	8.62 (s)	7.94–7.97 (d) [9.13] 7.41–7.46 (t) [7.30] 7.49–7.54 (t) [7.30] 8.12–8.15 (d) [8.22]	4.08 (b)	15.15 (b)
R = 	7.77–7.80 (d) [7.63] 7.12–7.15 (d) [7.63]	2.47 (s)	8.92 (s)	7.83–7.86(d) [7.63] 7.31–7.36 (t) [7.63] 7.40–7.45 (t) [7.63] 8.09–8.12 (d) [7.63]	4.40 (b)	15.35 (b)

*OCH$_3$ and —CH$_3$ group signals are observed as singlets at δ 3.86 and 2.29 ppm respectively.

TABLE II ^{13}C NMR Spectral Data (δ ppm) of Benzothiozolines $\mathrm{H\overline{NC_6H_4SC}(R)CH{:}C(OH)COOCH_3}$

Compound	R	=CH	CH3(ester)		=C—OH	C=O	CN
	133.03 132.22 127.48 125.35	97.50	25.70	153.37 136.28 127.74 124.73 122.78 121.17	163.0	196.98	158.68
	133.48 131.49 129.43 125.79	97.33	25.98	153.46 135.69 128.63 125.18 123.31 121.54	162.0	196.23	160.02
	133.59 131.73 129.85 125.22	97.21	25.87	153.42 135.31 127.93 125.17 123.47 121.44	161.88	195.59	160.07
	133.42 130.07 125.67 126.65	97.75	25.66	153.36 136.0 127.13 125.06 123.18 121.45	163.10	195.85	159.31
	133.01 131.54 129.42 125.60	96.30	25.71	153.26 135.92 127.39 125.23 123.39 121.57	162.12	195.94	159.95

*OCH_3 and —CH_3 group signals are observed as singlets at δ 54.92 and 27.06 ppm respectively.

hydrogen bonding. In view of the above facts these organic compounds may be assigned the structure described in (Figure 1).

EXPERIMENTAL

Material and Methods

All the chemicals used were of reagent grade. Solvents were dried by standard methods.[13] Aroyl pyruvates, $RC(O)CH{:}C(OH)COOCH_3$

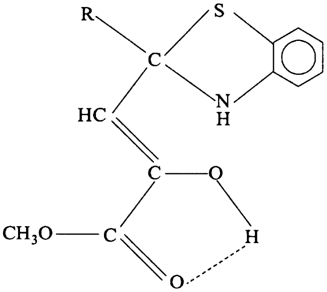
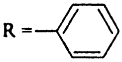
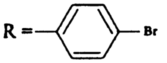
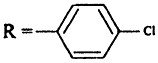
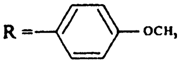
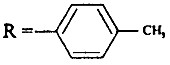


FIGURE 1 Structure of the benzothiazolines $H\overline{NC_6H_4SC}RCH{:}C(OH)C(O)\text{-}OCH_3$.

[where $R = C_6H_5$, 4-BrC_6H_4, 4-ClC_6H_4, 4-$CH_3OC_6H_4$, 4-$CH_3C_6H_4$] have been synthesized by literature method.[14] Nitrogen and sulphur were estimated by Kjeldhal and Messenger's methods respectively.[15] ^1H and ^{13}C NMR spectra were recorded on JEOL FX-90Q (90 MHz) or Brucker DPX 300 MHz in $CDCl_3$ solution using TMS as an internal (^1H NMR) or external (^{13}C NMR) reference respectively. IR spectra were recorded as neat film on Nicolet megna 550 spectrometer.

TABLE III Synthetic and Analytical Data of $H\overline{NC_6H_4SC}RCH{:}C(OH)COOCH_3$

Organic compounds	Reactants gm (mMol)		Molecular formula, color, physical state and yield% B.P. (−720 mm)	Elemental analyses found (calc.)	
	Aroyl pyruvate	2-ATP		%N	%S
	3.84 (18.62)	2.33 (18.61)	$C_{17}H_{15}O_3NS$, light yellow, liquid, 77 108–11	4.41 (4.47)	10.13 (10.23)
	5.83 (20.45)	2.56 (20.45)	$C_{17}H_{14}O_3NSBr$, brown, liquid, 79 70–2	3.52 (3.57)	8.07 (8.18)
	4.17 (17.33)	2.17 (17.33)	$C_{17}H_{14}O_3NSCl$, brown, liquid, 75 68–9	4.01 (4.03)	9.14 (9.22)
	4.66 (19.73)	2.47 (19.73)	$C_{18}H_{17}O_4NS$, brown, liquid, 81 142–5	4.02 (4.08)	9.22 (9.34)
	4.82 (21.89)	2.74 (21.89)	$C_{18}H_{17}O_3NS$, brown, liquid, 80 71–3	4.24 (4.28)	9.69 (9.80)

Since a similar method has been used for the synthesis of all these benzothiazolines and hence the synthesis of only one representative benzothiazoline is given in detail. Synthetic and analytical detail of the other analogous benzothiazolines are summarized in Table III.

Synthesis of $H\overline{NC_6H_4SC}(C_6H_5)CH{:}C(OH)C(O)OCH_3$

A benzene solution (~20 ml) of 2-aminothiophenol, $H_2NC_6H_4SH$ (2.33 gm, 18.61 mM) was added to the benzene solution (~20 ml) of aroyl pyruvate, $C_6H_5C(O)CH{:}C(OH)COOCH_3$ (3.84 gm, 18.62 mM). This reaction mixture was refluxed for ~4 h on a fractionating column. The water liberated during the condensation reaction was removed azeotropically. After completion of the reaction, the excess solvent was removed under reduced pressure. The light colored liquid product thus obtained was further purified by distilling it under reduced pressure. The compound was analyzed to give $N = 4.41$; $S = 10.13\%$, calc. for $C_{17}H_{15}NO_3S$; $N = 4.47$; $S = 10.23\%$.

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