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SYNTHESIS OF SOME NEW SUBSTITUTED BENZOTHIAZOLES USING AMINOACRIDINE

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As a part of systematic investigation of synthesis, several new substituted acridin-9-yl-benzothiazol-2-yl amines were synthesized by oxidative cyclization of 1-acridinyl-3-aryl thiourea with bromine followed by basification with dilute ammonium hydroxide solution. Initially 1-acridinyl-3-aryl thiourea was prepared by the interaction of 9-aminoacridine hydrochloride with aryl isothiocyanate in alkaline medium. Constitutions of synthesized compounds have been established on the basis of elemental analysis, IR, PMR and ^{13}C NMR spectral studies.

A wide range of methods are available for synthesizing benzothiazole nucleus[1] but a real need exist for new procedure that support many kind of structural diversity and various substitution. It has been observed from the literature survey that, substituted benzothiazoles have been found to possess potential antimicrobial[2], anticancer[3] and antidiabetic[4] activities.

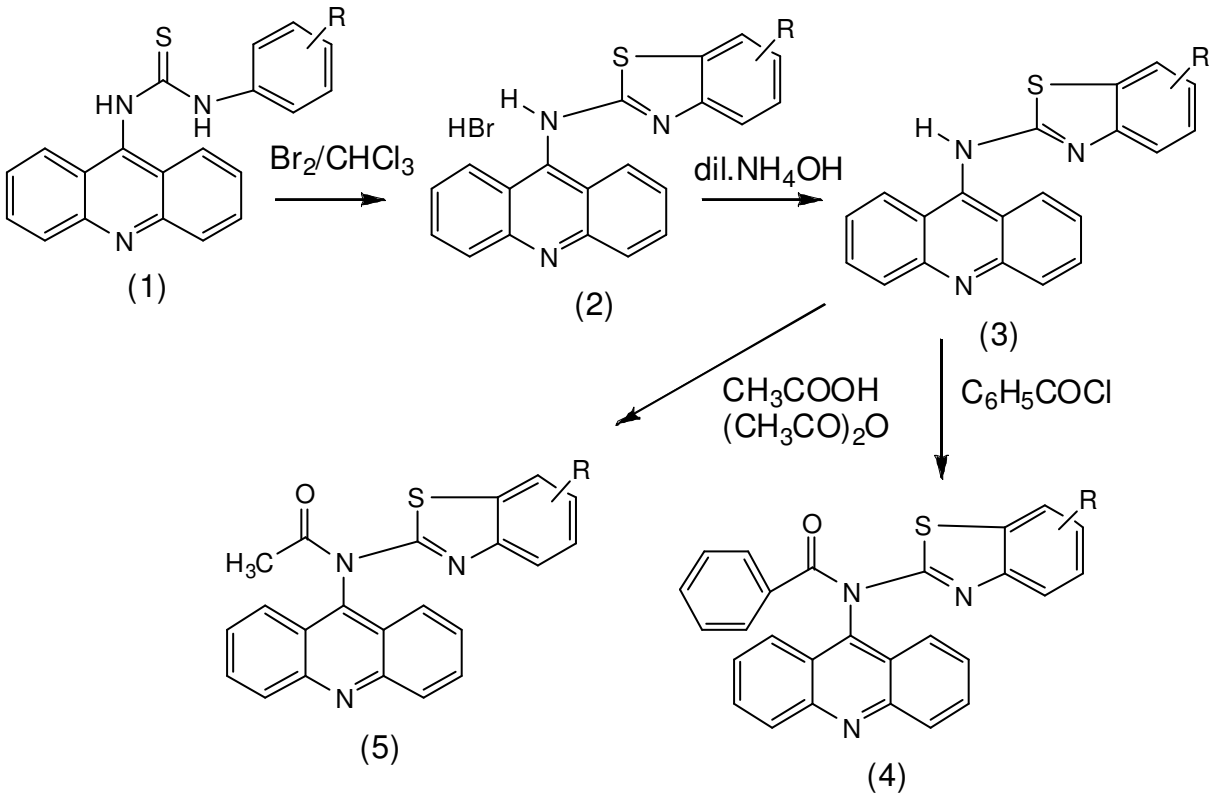
Synthetic applications of phenyl isothiocyanate have been investigated earlier and shown to have enough potentiality in the synthesis of nitrogen and sulphur containing 5 and 6 membered heterocyclic compounds. In view of the utility of these reagents in the synthesis of heterocyclic compounds and as a part of wider programme to provide alternative routes of synthesis, now the method for synthesis of substituted benzothiazole is reported.

Experimental

The melting points of all synthesized compounds were recorded using hot paraffin-bath and are uncorrected. ^1H NMR spectra were recorded with TMS as internal standard using $CDCl_3$ and DMSO-d_6 as solvents. IR spectra were recorded on a Perkin-Elmer spectrophotometer in the range 4000-400 cm^{-1} in nujol mull and as KBr pellet. Purity of the compounds was checked on silica gel-G plates by TLC.

Initially equimolar mixture of 9-aminoacridine hydrochloride[5] and phenyl isothiocyanate[6] in presence of sodium hydroxide was refluxed on a water bath for 2 hr using chloroform as a solvent, to afford 1-acridin-9-yl 3-phenyl thiourea[7] which was washed with water & recrystallized from ethanol.

1-Acridin-9-yl-3-phenyl thiourea in chloroform was taken in a two necked round bottom flask along with dropping funnel and equipped with mechanical stirrer. To this reaction mixture bromine in chloroform was added with stirring over a period of 2 hr. During the addition of bromine, temp of reaction mixture was maintained below 5^0. After completion of addition of bromine stirring was continued for a period of 1 hr. Chloroform was removed by filtration & resulting solid identified as a acridin-9-yl-benzothiazol-2-yl amine hydrobromide. It was neutralized with aqueous ammonia solution to afford free base, which was washed with water & recrystallized from ethanol to get compound **3**. **3** on acetylation with acetic anhydride and glacial acetic acid in 1:1 ratio yielded



SCHEME-1

Where

R=H,	2-CH_3,	3-CH_3,	4-CH_3,	2-Cl,	3-Cl,	4-Cl
a	b	c	d	e	f	g

acetyl derivative and on benzoylation with benzoyl chloride yielded benzoyl derivative.

1-Acridinyl-3-phenyl-thiourea 1a

Initially compound 1-acridinyl-3-phenyl-thiourea **1**a was prepared by refluxing the mixture of phenyl isothiocyanate (0.02 mol) and 9-amino acridine hydrochloride (0.02 mol) in sodium hydroxide in chloroform for 2 hr. The reaction mixture was cooled and the solid residue obtained was washed with water and recrystallized from ethanol and identified as a 1-acridinyl-3-phenyl-thiourea **1**a. This reaction was extended to synthesize other substituted thiourea i.e. 1-acridinyl-3-aryl-thiourea **1**b-**1**g.

Acridin-9-yl-benzothiazol-2-yl-amine 3a

The compound acridin-9-yl-benzothiazol-2-yl amine **3**a was prepared by oxidative cyclization of 1-acridinyl-3-phenyl thiourea **1**a in chloroform with bromine in chloroform. The bromine in chloroform was added in the reaction mixture taken in two naked round bottom flask till the persistence of brown colour, to give yellowish solid of hydrobromide salt **2** which on basification with ammonia afforded free base, which was recrystallized from ethanol and identified as a acridin-9-yl-benzothiazol-2-yl amine **3**a. This reaction was extended to synthesize other substituted benzothiazol-2-yl-amines **3**b-**3**g using 1-acridinyl-3-aryl-thioureas **3**.

3a: M.p. 218-220^0; IR (KBr) cm^{-1} : 3467, 3412, 3331 (NH), 1594 (C=N), 1487 (C=C), 1165 (C-N), 751 (C-S); PMR (DMSO-d_6), δ ppm : 8.7 (s, N-H proton exchangeable with D_2O), 7.88-7.99 (m, 4H, Ar), 7.44-7.51 (d, 4H, Ar); ^{13}C NMR (DMSO-d_6),δ ppm : 111, 128, 134, 140 (aromatic C-atoms), 156 (C-N). [Found : C, 73.60, H, 3.82, N, 13.02, S, 9.24 $C_{21}H_{13}N_3S$ requires C, 73.39, H, 3.97, N, 12.84, S, 9.78%].

3b : M.p. 234-236^0; IR (KBr): 3467, 3412, 3331 (NH), 3103 (C-H stretch), 1594 (C=N), 1487 (C=C), 1165 (C-N), 751 (C-S); PMR (DMSO-d_6): 8.7 (s, N-H proton exchangeable with D_2O), 7.88-7.99 (m, 4H, Ar), 7.44-7.51 (d, 4H, Ar), 1.3 (s, 3H); ^{13}C-NMR (DMSO-d_6): 20 (Ar-CH_3), 111, 128, 134, 140 (aromatic C-atoms), 156 (C-N). [Found : C, 73.98, H, 3.82, N, 12.66, S, 9.44, $C_{21}H_{15}N_3S$ requires C, 73.90, H, 4.39, N, 12.31, S, 9.38%].

3c: M.p. 196-198^0; IR (KBr) : 3467, 3412, 3331 (NH), 3103 (C-H strech), 1594 (C=N), 1487 (C=C), 1165 (C-N), 751 (C-S); PMR (DMSO-d_6): 8.7 (s, N-H proton exchangeable with D_2O), 7.88-7.99 (m, 4H, Ar), 7.44-7.51 (d, 4H, Ar), 1.3 (s, 3H); ^{13}C NMR (DMSO-d_6): 20, (Ar-CH_3), 111, 128, 140 (aromatic C-atoms), 156 (C-N). [Found : C, 74.03, H, 3.56, N, 13.02, S, 9.52 $C_{21}H_{15}N_3S$ requires C, 73.90, H, 4.39, N, 12.31, S, 9.38%].

3d: M.p. : 242-244^0; IR (KBr) : 3467, 3412, 3331 (NH), 3103 (C-H strech), 1594 (C=N), 1487 (C=C), 1165 (C-N), 751 (C-S); PMR (DMSO-d_6): 8.7 (s, N-H proton exchangeable with D_2O), 7.88-7.99 (m, 4H, Ar), 7.44-7.51 (d, 4H, Ar), 1.3 (s, 3H); ^{13}C NMR (DMSO-d_6): 20 (Ar-CH_3), 111, 128, 134, 140 (aromatic C-atoms), 156 (C-N). [Found : C, 74.02, H, 3.96, N, 13.06, S, 9.24 $C_{21}H_{15}N_3S$ requires C, 73.90, H, 4.39, N, 12.31, S, 9.38%].

3e: M.p. 250-252^0; IR (KBr): 3467, 3412, 3331 (NH), 1594 (C=N), 1487 (C=C), 1165 (C-N), 75 (C-S); PMR (DMSO-d_6): 111, 128, 134, 140 (aromatic C-atoms), 156 (C-N). [Found : C, 66.94, H, 3.02, N, 13.08, S, 8.22 $C_{20}H_{12}ClN_3S$ requires C, 66.48, H, 3.32, N, 11.63, S, 8.86%].

3f: M.p. 138-140^0; IR (KBr), 3467, 3412, 3331 (NH), 1594 (C=N), 12487 (C=C), 1165 (C-N), 751 (C-S); PMR (DMSO-d_6): 111, 128, 134, 140 (aromatic C-atoms), 156 (C-N). [Found : C, 66.94, H, 3.02, N, 13.08, S, 8.22 $C_{20}H_{12}ClN_3S$ requires C, 66.48, H, 3.32, N, 11.63, S, 8.86%].

3g: M.p. 156-160^0; IR (KBr): 3467, 3412, 3331 (NH), 1594 (C=N), 1487 (C=C), 1165 (C-N), 75 (C-S); PMR (DMSO-d_6): 8.7 (s, N-H proton exchangeable with D_2O), 7.88-7.99 (m, 4H, Ar), 7.44-7.51 (d, 3H, Ar); ^{13}C-NMR (DMSO-d_6): 111, 128, 134, 140 (aromatic C-atoms), 156 (C-N). [Found : C, 66.94, H, 3.02, N, 13.08, S, 8.22 $C_{20}H_{12}ClN_3S$ requires C, 66.48, H, 3.32, N, 11.63, S, 8.86%].

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