A mild and efficient synthesis of 2-oxazolines via transmidation –cyclodehydrosulfurisation of thioamides / aminoethanol

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Contents

1. General details ........................................... P2

2. Experimental procedure .............................. P3-P4

3. Selected copies of $^1$H, $^{13}$C NMR and Mass spectra P5-P12
1. General details

Reagents were obtained from commercial supplier, and used without further purification. Thioamides for Entry No. 2-6 and 8–11 (Table 1) were prepared by thionation of corresponding amide by reported method.¹ Melting point were measured by scientific-MP-DS melting point apparatus. Column chromatographic purification of products was performed on silica gel (60-120 mesh). ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AVANCE II 400 MHz. Chemical shifts were expressed in parts per millions (δ) downfield from the internal standard tetramethylsilane and were reported as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), td (triplet of doublet), br.s (broad singlet) and m (multiplet). Mass spectra was obtained in Agilent 5975C GC-MS and Elemental analysis was performed on Elementar vario MICRO cube CHNS analyser.

References:

2. Experimental procedures

(A) Procedure for the preparation of 2-(n-alkyl)-2-Oxazolines from n-alkyl thioamides (entry 11, 12 Table 1):

A homogenous mixture of thioamide (1 mmol), aminoethanol (0.0672 g, 1.1 mmol), was heated at 70°C. Progress of the reaction was monitored by TLC and GC-MS. Upon complete disappearance of thioamides, 0.5 ml of ethanol and K$_2$CO$_3$ (0.276 g, 2 mmol) were added. Reaction was continued further at the same temperature for 3.5-4 hrs. Reaction mixture was cooled to room temperature, 2.5 ml of water was added and extracted with n-hexane (15 ml). Organic layer is dried over anhydrous Na$_2$SO$_4$ and removal of solvent afforded pure products. For 2-Methyl-2-oxazoline after extraction with hexane it was treated with gaseous HCl until the solution is acidic. 3 ml of water is added to it and the organic layer is decanted off. The water layer was neutralized by NaHCO$_3$ and extracted by diethyl ether, dried over anhydrous Na$_2$SO$_4$. Solvent removal yielded the pure 2-Methyl-2-oxazoline.

(B) Procedure for the preparation of 2-(4-hydroxyphenyl)-2-Oxazoline from 4-hydroxythiobenzamide (entry 4, Table 1): 4-hydroxythiobenzamide (0.153 g, 1 mmol), aminoethanol (0.153 g, 2.5 mmol) and K$_2$CO$_3$ (0.276 g, 2 mmol) were taken in 0.5 ml of water. The reaction mixture was heated at 90°C and monitored by GC-MS for its progress. On completion of the reaction, reaction mixture was cooled to room temperature, neutralized by dil HCl. The pH of the contents was increased to 7.5-8 with NaHCO$_3$, and then extracted by Ethyl
acetate. After solvent removal the compound was purified by column chromatography.

(C) Procedure for the preparation of 2-(cyclohexyl)-2-Oxazoline from cyclohexyl thioamide (entry 9 Table 1): A mixture of cyclohexylthioamide (0.143g, 1 mmol), aminoethanol (0.092g, 1.5mmol) and K$_2$CO$_3$ (0.414g, 3mmol) in water (0.5ml) was heated to 80°C for 16 hrs. After completion of the reaction, the product was isolated and purified as mentioned in the general experimental procedure.
4. Selected copies of $^1$H, $^{13}$C NMR and Mass spectra

(i) $^1$H NMR spectra of 2-Phenyloxazoline

(ii) $^1$H NMR spectra of 2-(4-Bromophenyl)oxazoline

(iii) $^1$H NMR spectra of 2-(4-Methoxyphenyl)oxazoline

(iv) $^1$H NMR spectra of 2-(4-Hydroxyphenyl)oxazoline

(v) $^1$H NMR spectra of 2-(2, 4-Dichlorophenyl)-2-oxazoline

(vi) $^1$H NMR spectra of 2-(2, 5-Dichlorophenyl)oxazoline

(vii) $^1$H NMR spectra of 2-(3-Pyridyl)-2-oxazoline

(viii) $^1$H NMR spectra of 2-(2-Thienyl)-2-oxazoline

(ix) $^1$H NMR spectra of 2-(cyclohexyl)-2-oxazoline

(x) $^1$H NMR spectra of 2-(4-Methoxybenzyl)-2-oxazoline

(xi) $^{13}$C NMR spectra of 2-(4-Methoxybenzyl)-2-oxazoline

(xii) Mass spectra of 2-(4-Methoxybenzyl)-2-oxazoline

(xiii) $^1$H NMR spectra of 2-(n-Butyl)-2-oxazoline

(xiv) $^1$H NMR spectra of 2-Methyl-2-oxazoline
(i) $^1$H NMR spectra of 2-Phenyl oxazoline

(ii) $^1$H NMR spectra of 2-(4-Bromophenyl) oxazoline
(iii) $^1$H NMR spectra of 2-(4-Methoxyphenyl)oxazoline

(iv) $^1$H NMR spectra of 2-(4-Hydroxyphenyl)oxazoline
(v) $^1$H NMR spectra of 2-(2, 4-Dichlorophenyl)-2-oxazoline

(vi) $^1$H NMR spectra of 2-(2, 5-Dichlorophenyl)-2-oxazoline
(vii) $^1$H NMR spectra of 2-(3-Pyridyloxazoline

(viii) $^1$H NMR spectra of 2-(2-Thienyloxazoline
(ix) $^1$H NMR spectra of 2-(cyclohexyl)oxazoline

(x) $^1$H NMR spectra of 2-(4-methoxybenzyl)-2-oxazoline
(xi) $^{13}$C NMR spectra of 2-(4-methoxybenzyl)-2-oxazoline

(xii) Mass spectra of 2-(4-methoxybenzyl)-2-oxazoline
(xiii) $^1$H NMR spectra of 2-(n-Butyl)-2-oxazoline

(xiv) $^1$H NMR spectra of 2-Methyl-2-oxazoline