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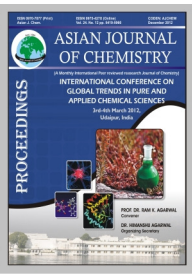

Synthesis of 2-Hydroxy-3-nitro/amino-5-methyl-α-substituted Thiocarbamidoacetophenones†

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The interactions of 2-hydroxy-3-nitro/amino-5-methyl-α-bromoacetophenone (**1**) with various thioureas (**5a-f**) in 1:1 molar proportion in acetone-ethanol medium on water bath for 6 h in round bottom flask to synthesis new series of 2-hydroxy-3-nitro/amino-5-methyl-α-substituted thiocarbamidoacetophenones (**6a-f**). The synthesized compounds in these reaction conditions have been characterized on the basis of conventional elemental analysis, chemical characteristic and IR, NMR spectral data.

Key Words: 2-Hydroxy-3-nitro/amino-5-methyl-α-bromoacetophenone, Thioureas, Acetone-ethanol medium.

INTRODUCTION

Acetophenone is important class of compound. Many of subtituted acetophenones are used as intermediate in the synthesis of heteroacycles. Substituted acetophenones are used as anti-mycobacterial agent, antibiotics or biocides[1]. They are also used as consumer fragrances and industrial solvent[2], herbicides[3] antimtagenic[4] and antimicrobial agents[5-11].

Substituted-α-bromoacetophenone is important precursor for synthesizing different organic compounds having medicinal, agricultural, pharmacological and biological importance[12-20]. As substituted-α-bromoacetophenone has bromine group, which is good leaving group, it was thought to replace this moiety with another suitable group with the substituted thiourea. Further, substituted α-bromoacetophenone is very reactive and sensitive towards substituted thioureas so, reaction was carried out in between substituted acetophenone and substituted thioureas into different solvents on water bath to form new series of substituted thiocarbamido acetophenones. These substituted thiocarbamidoacetophenones may have antiviral, antibacterial and antimicrobial activities[21-24].

For isolation of important nitrogen and sulphur containing heteroacycles having medicinal, agricultural, pharmacological and biological importance these compounds were also cyclized successfully into 1,2,5-thioxazines, which were then isomerized into 1,2,4-oxadiazines. These compounds may possess medicinal, biological and agricultural importance.

EXPERIMENTAL

The melting points of synthesized compounds were recorded using hot paraffin bath. The carbon and hydrogen analysis was carried out on Carlo-Ebra-1106 analyzer. Nitrogen estimation was carried out on Colman-*N*-analyzer-29. IR spectra were recorded on Perkin Elmer spectrometer in the range 4000-400 cm^{-1} in KBr pellets. PMR spectra were recorded on Bruker AC-300F spectrometer with TMS as an internal standard using $CDCl_3$ and DMSO-d_6 as a solvent. The purity of the compounds was checked on silica gel-G plates by TLC with layer thickness of 3 mm. All chemicals used were of AR grade (Indian make).

The reactions of 2-hydroxy-3-nitro/amino-5-methyl-α-bromoacetophenone (**1**) with different thioureas (**5**) were carried out in presence of acetone- ethanol medium to synthesis 2-hydroxy-3-nitro/amino-5-methyl-α-substituted thiocarbamido acetophenone (**6**).

RESULTS AND DISCUSSION

Synthesis of 2-hydroxy-3-nitro-5-methyl-α-thiocarbamidoacetophenone (6a): The 2-hydroxy-3-nitro-5-methyl-α-thiocarbamidoacetophenone (**6a**) was prepared by refluxing the mixture of 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (**1**) and thiourea (**5a**) in acetone-ethanol medium for 4 h on water bath. The remaining solvent was distilled off. Yellow crystals has been separated out which were washed with water and recrystallized with aqueous ethanol. Yield 80 %, m.p. 184 ºC, Colour-brilliant yellow.

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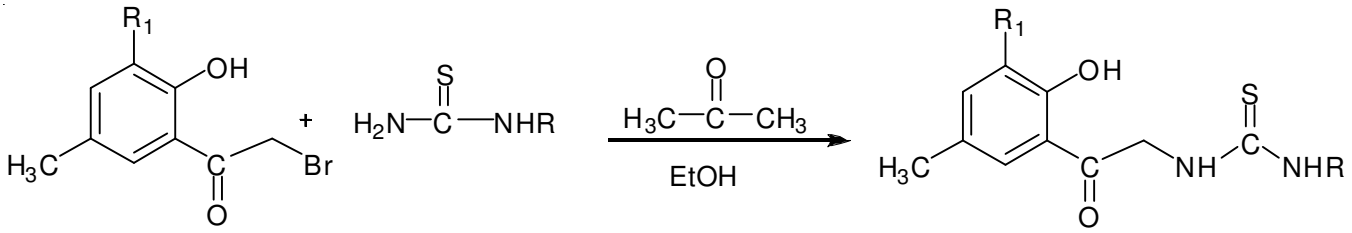

(1) (5) R = H, -Methyl, Ethyl -Allyl, Phenyl
R = NO_2 , NH_2 (6)

TABLE-1

S. No.	Expt. No.	Synthesis of 2-hydroxy-3-nitro-5-methyl- α-substituted thiocarbamidoacetophenones	Yield (%)	m.p. (ºC)	Colour
1	3	Methyl	70	196	Brilliant Yellow
2	4	Ethyl	72	217	Brilliant Yellow
3	5	Allyl	65	230	Brilliant Yellow

Elemental analysis: Element found (%) C 43.50, H 4.01, N 14.12, S 10.94. From analytical data the molecular formula was found to be $C_{10}H_{11}N_3O_4S$.

IR spectrum: IR spectrum of compounds was carried in KBr pellets and absorption absorbed cm^{-1} correlated as follows.

Absorption band (cm^{-1})	Assignment
3439	-OH stretching
3258	-NH stretching
3358 and 3335	$-NH_2$ stretching
1619	-C=O stretching
1529	-C=S stretching
1524	Ar-NO_2 asymmetric stretching
1355	Ar-NO_2 symmetric stretching
771	- NH_2 Wagging

PMR spectum: The PMR spectrum of compound was carried out in $CDCl_3$.

Chemical shift (ppm) observed	Assignment
12.7607	Ar-OH
7.4978-8.1456	Ar-H
2.6489-2.7117	$-CH_2NH$
2.3990	$-NH-CH_2$
2.3186	$-NH_2$
2.1763	Ar-CH_3
7.2685	$CDCl_3$

Synthesis of 2-hydroxy-3-nitro-5-methyl-α-phenylthiocarbamidoacetophenone (6e): 2-Hydroxy-3-nitro-5-methyl-α-phenylthiocarbamidoacetophenone (**6e**) was prepared by refluxing a mixture of 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (**1**) and phenylthiourea (**5e**) in acetone-ethanol medium for 4 h on water bath. The remaining solvent was distilled off. Yellow crystals has been separated out which were washed with water and recrystallized with aqueous ethanol. Yield 76%, m.p. 208 ºC.

Elemental analysis: Element found (%) C 55.11, H 4.23, N 11.11, S 8.23. From analytical data, the molecular formula was found to be $C_{16}H_{15}N_3O_4S$.

IR spectrum: The IR spectrum of a compound (**6e**) was carried out in KBr pellets and absorption absorbed (cm^{-1}) are given below in the table.

Absorption band (cm^{-1})	Assignment
3351	-OH stretching
3264	-NH stretching
3164	Ph-NH stretching
1638	-C=O stretching
1529	-C=S stretching
1449	Ar-NO_2 asymmetric stretching
1344	Ar-NO_2 symmetric stretching

PMR spectrum: The PMR spectrum of a compound (**6e**) was carried in $CDCl_3$ and chemical shift (ppm) reported.

Chemical shift (ppm) observed	Assignment
12.7623	Ar-OH
7.3338-8.2512	Ar-H and Ar-NH
2.6487-2.7112	$-CH_2NH$
2.4340	-NH-Ph
2.3983	CH_2-NH
2.1764	Ar-CH_3
7.2675	$CDCl_3$

Similarly, 2-hydroxy-3-nitro-5-methyl-α-methylthiocarbamidoacetophenone (**6b**), 2-hydroxy-3-nitro-5-methyl-α-ethylthiocarbamidoacetophenone (**6c**), 2-hydroxy-3-nitro-5-methyl-α-allylthiocarbamidoacetophenone (6d) were prepared by interaction of 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (**1**) with methylthiourea (**5b**), ethylthiourea (**5c**), allylthiourea (**5d**) in acetone-ethanol medium respectively by above mentioned method are listed in Table-1.

Synthesis of 2-hydroxy-3-amino-5-methyl-α-thiocarbamidoacetophenone (6f): 2-Hydroxy-3-amino-5-methyl-α-thiocarbamidoacetophenone (**6f**) was prepared by refluxing a mixture of 2-hydroxy-3-amino-5-methyl-α-bromoaceto-phenone (**1**) and thiourea (**5a**) in acetone-ethanol medium for 4 h on water bath. The remaining solvent was distilled off. Yellow crystals has been separated out which were washed with water and recrystallized with aqueous ethanol. Yield 83 % m.p. 175 ºC, colour - yellow.

Elemental analysis: Element found (%) - C 49.52, H 5.02, N 16.17, S 12.20.

TABLE-2

S. No.	Expt No.	Synthesis of 2-hydroxy-3-amino-5-methyl- α-substitutedthiocarbamidoacetophenones	Yield (%)	m.p. (ºC)	Colour
2	6	Methyl	79	184	Yellow
3	7	Ethyl	75	190	Yellow
4	8	Allyl	67	202	Yellow
5	9	Phenyl	60	240	Yellow

From analytical data, the molecular formula was found to be $C_{10}H_{13}N_3O_4$.

IR spectrum: The IR spectrum of a compound (**6f**) was carried out in KBr pellets and the important absorptions are given below in the table.

Absorption bands (cm^{-1})	Assignment
3431	-OH stretching
3408	$-NH_2$ stretching
3365	-NH stretching
3271	Ar-NH_2 stretching
1624	-C=O stretching
1521	-C=S stretching
723	- NH_2 Wagging

PMR spectrum: The PMR spectrum of compound (**6f**) was carried in $CDCl_3$ and chemical shift (ppm) reported.

Chemical Shift (ppm) observed	Assignment
12.7448	Ar-OH
7.4976-8.1409	Ar-H
4.6269	Ar-NH_2
2.6461-2.7115	$-CH_2$-NH
2.3979	-NH-CH_2
2.3144	$-NH_2$
2.1762	Ar-CH_3
7.287	$CDCl_3$

Similarly, 2-hydroxy-3-amino-5-methyl-α-methylthiocarbamidoacetophenone (**6g**), 2-hydroxy-3-amino-5-methyl-α-ethylthiocarbamidoacetophenone (**6h**), 2-hydroxy-3-amino-5-methyl-α-allylthiocarbamidoacetophenone (**6i**), 2-hydroxy-3-amino-5-methyl-α-phenylthio-carbamidoacetophenone (**6j**) were prepared by the interaction of 2-hydroxy-3-amino-5-methyl-α-bromoacetophenone (**2**) with methylthiourea (**5b**), ethylthiourea (**5c**), allylthiourea (**5d**), phenylthiourea (**5e**) in acetone-ethanol medium respectively by above mentioned method which are listed in Table-2.

Conclusions

Different derivatives of 2-hydroxy-3-nitro-5-substituted α-thiocarbamidoacetophenone and 2-hydroxy-3-amino-5-substituted α-thiocarbamidoacetophenone were synthesized by the use of novel method and reported correctly.

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