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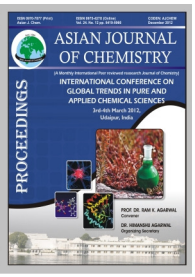

Synthesis of 2-Hydroxy-3-(3-substituted thiamido)amino-5-methyl-α-bromoacetophenones†

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2-Hydroxy-3-nitro-5-methyl-α-bromoacetophenone (**1**) firstly reduced to 2-hydroxy-3-amino-5-methyl-α-bromoacetophenone (**2**) with treatment of tin and hydrochloric acid. 2-Hydroxy-3-amino-5-methyl-α-bromoacetophenone (**2**) is further treated with various isothiocyanate (**3**) such as phenylisothiocyanate (**3a**), *p*-chloro-phenylisothiocyanate (**3b**), *p*-tolylisothiocyanate (**3c**), methylisothiocyanate (**3d**), ethylisothiocyanate (**3e**) and *t*-butylisothiocyanate (**3f**), in presence of acetone-ethanol medium to synthesize 2-hydroxy-3-(3-substituted thiamido)amino-5-methyl-α-bromoacetophenones (**4**). The products isolated in these reactions were characterized on the basis of conventional elemental analysis, chemical characteristrics and spectral data.

Key Words: 2-Hydroxy-3-amino-5-methyl-α-bromoacetophenone, Isothiocyanate, Acetone-ethanol.

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].

Acetophenones mainly occur in the heavy oil fraction of coal tar. It is generally used as solvent in the interactions of cellulose, ethers and esters in organic synthesis. It is also used as an intermediate in the synthesis of corrosion inhibitors pharmaceutical resins, flavouring agents, polymerization catalysts hypnotics under the name hypnone and perfume bases[12-19]. So, it appeared interesting to investigate the reactions of substituted α-bromoacetophenone (**2**) and different isothiocyanates (**3a-f**) to produce nitrogen and sulphur containing heterocycles having medicinal, agricultural, pharmacological and biological importance[20-30].

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). Substituted isothiocyanates were preapared by known literature method[9].

2-Hydroxy-3-amino-5-methyl-α-bromoacetophenone (**2**) and different isothiocyanates (**3a-f**) in acetone-ethanol medium were refluxed on water bath for 4 h in round bottom flask to produce 2-hydroxy-3-(3-substitued thiamido)amino-5-methyl-α-bromoacetophenones (**4a-f**). Substituted α-bromoacetophenone (**2**) has been prepared from 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (**1**) by reduction with tin and hydrochloric acid.

RESULTS AND DISCUSSION

Synthesis of 2-hydroxy3-(3-phenylthiamido)amino-5-methyl-α-bromoacetophenone (4a): Interaction of 2-hydroxy-3-amino-5-methyl-α-bromoacetophenone (**2**) was carried out with phenylisothiocyanate (**3a**) in acetone-ethanol (30 mL) medium on water bath for 4 h. It was filtered in hot conditions. The resultant filtrate was evaporated at room condition.

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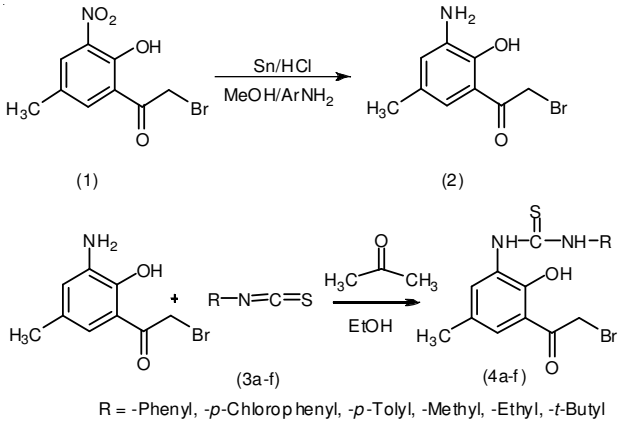
TABLE-1

S. No.	Expt. No.	2-Hydroxy-3-(substitutedthiamido)amino-5-methyl-α-bromoacetophenone	Yield (%)	m.p. (^{0}C)	Colour
1	2	*p*-Chlorophenyl	69	179	Dirty yellow
2	3	*p*-Tolyl	78	182	Dirty yellow
3	4	Methyl	77	178	Dirty yellow
4	5	Ethyl	81	147	Dirty yellow
5	6	*t*-Butyl	79	163	Dirty yellow

TABLE-2
REACTION-2-HYDROXY-3-AMINO-5-METHYL-α-BROMOACETOPHENONE+PHENYLISOTHIOCYANATE

S. No.	Medium	Quantity of medium (mL)	Time duration (h)	Yield (%)	m.p. (^{0}C)	Colour
1	Acetone	50	6	57	196	Dirty yellow
2	Ethanol	40	5	68	196	Dirty yellow
3	Ethanol-Acetone	30	4	82	195	Dirty yellow
4	Iso propyl alcohol	40	5	49	197	Dirty yellow



Needle shaped pale yellow crystals were isolated. Yield- 70 % m.p. - 196 ºC.

Elemental analysis: Elements found (%): C - 49.12, H 3.11, N 6.99, S 8.01. From analytical data molecules formula is found to be $C_{15}H_{15}N_2SO_2Br$.

IR spectrum: IR spectrum was carried out in KBr pellets and absorption observed in cm^{-1}

Absorption observed (cm^{-1})	Assignment
3456	-OH stretching
3346 and 3340	-NH stretching
1640	C=O stretching
1528	C=S stretching
1272 and 588	CH_2-Br stretching

PMR spectrum: The PMR spectrum was carried out in $CDCl_3$ and chemical shift in ppm.

Chemical shift (ppm) observed	Assignment
12.632	Ar-OH
7.420-8.060	Ar-H
7.065	-CH_2Br
2.675-2.690	-NH-Ph
2.330	Ar-CH_3
2.522	DMSO-d^6

Similarly, following compounds were prepared 2-hydroxy-3-(3-phenylthiamido)amino-5-methyl-α-bromoaceto-phenone (**4a**), 2-hydroxy-3-(3-*p*-chlorophenylthiamido)amino-5-methyl-α-bromoacetophenone (**4b**), 2-hydroxy-3-(3-*p*-tolyl-thiamido)amino-5-methyl-α-bromoacetophenone (**4c**), 2-hydroxy-3-(3-methyliamido)amino-5-methyl-α-bromoacetophenone (**4d**), 2-hydroxy-3-(3-ethylthiamido)amino-5-methyl-α-bromoacetophenone (**4e**), 2-hydroxy-3-(3-t-butyl-thiamido)amino-5-methyl-α-bromoacetophenone (**4f**) by the reduction of 2-hydroxy-3-nitro-5-methyl-α-bromoaceto-phenone (**1**) into 2-hydroxy-3-amino-5-methyl-α-bromoaceto-phenone (**2**) with tin and hydrochloric acid, which is further treated with, *p*-chlorophenylisothiocyanate (**3b**), *p*-tolylisothio-cyanate (**3c**), methylisothiocyanate (**3d**) ethylisothiocyanate (**3e**), *t*-butylisothiocyanate (**3f**) in acetone-ethanol medium respectively by above mentioned method in experiment No. 2 to 6 and listed in Table-1.

Interaction of 2-hydroxy-3-amino-5-methyl-α-bromo-acetophenone was carried out with phenylisothiocyanate in acetone medium and the time required for completion of reactions is in between 6 to 8 h. Reduce time duration of reaction and for maintaining green chemistry parameters and to develop new reaction conditions. The reactions were carried in various mediums and it was observed in som e medium the time span reduced as well as yield also increased as shown in Table-2.

From these results it was clear that the medium used for this reaction must be ethanol-acetone which reduced the time duration of this reaction, the quantity required is also less and yield is best among all the reaction conditions. If the reaction performed in this medium then green chemistry will be maintained. The authors are interested to reduce time span and quantity of solvent used as medium and also to increase yield and to maintain eco-friendly reaction. Physical study and mechanisms were not studied during reactions.

Conclusion

Different derivatives of 2-hydroxy-3-(3-substitued thiamido)amino-5-methyl-α-bromoacetophenones were synthesized by the use of novel method and reported correctly.

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