



## SYNTHESIS OF THIOCARBAMIDOACETOPHENONE AND CHARACTERIZATION

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### ABSTRACT

Acetophenone and thiocarbamides molecules have their own identity in pharmaceutical, medicinal, agricultural and industrial chemistry. Heterocycles containing oxygen are mostly abundant among the naturally occurring heterocyclic compounds and are important and interest of various scientist from inter-disciplinary sciences. In view of utility of acetophenones and thiocarbamides in various fields and a part of research work presently being undertaken in these laboratories in the synthesis of newer type of heterocycles, it was thought interesting to investigate the reaction of 2-hydroxy-3-nitro-5-methyl-alpha-bromoacetophenone with various thioureas in isopropanol medium to provide alternative or somewhat direct and easy route for the synthesis of 2-hydroxy-3-nitro-5-methyl- $\alpha$ -H/substituted thiocarbamidoacetophenone which are hitherto unknown. Structure determination and justification of newly synthesized compounds had been carried out on elemental analysis, chemical characteristics and through spectral data.

### INTRODUCTION

Organic chemistry of acetophenones, thiocarbamides with special reference to their significance in industrial, medicinal, pharmaceutical and biological sciences have been briefly studied by various scientists and chemists that when drug contain acetophenone or thiocarbamido group in it, those drug shows varieties of applications and having various medicinal properties so, it was thought interesting to synthesize such type of compounds which contain acetophenone as well as thiocarbamido moieties in the same compound. Considering all these facts into consideration it was thought interesting to interact 2-hydroxy-



3-nitro-5-methyl-bromoacetophenone with various thiocarbamides in isopropanol medium to synthesize a novel series of 2-hydroxy-3-nitro-5-methyl- $\alpha$ -H/substituted thiocarbamidoacetophenone which are hitherto unknown.

## **EXPERIMENTAL**

All the chemicals used to synthesize  $\alpha$ -bromoacetophenone and 2-hydroxy-3-nitro-5-methylacetophenones were of AR Grade (India make). The melting points of all the synthesize compounds were recorded by using hot paraffin bath and are uncorrected. Analysis of carbon and hydrogen was carried out on Carlo-Ebra-1106 analyser. Nitrogen estimation was carried out on Colman-N-analyzer 29. IR spectra were recorded on Perkin Elmer spectrophotometer in the range 4000-400  $\text{cm}^{-1}$  in KBr pellets. PMR spectra were recorded on Bruker AC-300F spectrometer using  $\text{CDCl}_3$  and DMSO- $d_6$  as solvent with TMS as internal standard. The purity of compounds was checked on Silica Gel-G plate by TLC with layer thickness of 0.30 mm.

### ***Preparation of 2-hydroxy-5-methyl- $\alpha$ -bromoacetophenone:***

A reaction mixture of 2-hydroxy-5-methylacetophenone (1) (0.1M, 15 g) and acetic acid (150 ml) was refluxed on gentle Bunsen burner directly. During refluxing a solution of bromine in acetic acid (70 ml, 25%, 6.4 ml bromine in acetic acid) was added drop wise to the reaction mixture. After complete addition of the brominating mixture, it was cooled and poured in ice cold water, brownish white crystals were separated out. It was washed several times with cold water and re-crystallized with aqueous acetic acid, yield 85%.



### **Properties of compound No.(1 )**

- It is brownish white crystalline solid, m.p. 53°C.
- It gave deep violet colorations with aqueous ferric chloride indicating the presence of phenolic -OH group
- The R<sub>f</sub> value was found to be 0.32 in dioxane solvent on Silica G-plate with layer thickness of 0.3 mm.
- It gave elemental analysis as carbon = 46.81% (calculated 47.16%), hydrogen = 3.82% (calculated 3.93%) and bromine = 34.77% (calculated 34.90%).
- **IR (cm<sup>-1</sup>):** spectrum of the compound was carried out in KBr pellets and important absorption can be correlated as 3422 H-bonded (-OH phenolic); 1636 (>C=O) bond stretching in o-hydroxy aryl ketone □ =669 aliphatic -Br stretching.
- **PMR:** The PMR spectrum was carried out in CDCl<sub>3</sub>+DMSO-D<sub>6</sub> with TMS as internal standard .The spectrum distinctly displays the signal due to Ar-OH protons at δ 11.50 ppm, Ar-H protons at 6.85-7.63ppm , -CH<sub>2</sub> protons at 2.35ppm.

### **Synthesis of 2-hydroxy -3-nitro-5-methyl-α-bromoacetophenone (4)**

Interaction of 2-hydroxy -5-methyl-acetophenone(1) and HNO<sub>3</sub> (Conc.) in presence of conc.H<sub>2</sub>SO<sub>4</sub>(2) was carried out at 0-4 degree to obtain 2-hydroxy-3-nitro-5-methyl-acetophenone which on further refluxing with bromine in acetic acid (3) yield 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (4) on pouring in ice cold water ,yield 82%, mp 88°C.



#### **Properties of compound No. (4)**

- It is golden brown color crystalline solid, m.p. 88°C.
- It gave deep violet colorations with aqueous ferric chloride indicating the presence of phenolic -OH group
- The R<sub>f</sub> value was found to be 0.32 in dioxane solvent on Silica G-plate with layer thickness of 0.3 mm
- It contains carbon, hydrogen, nitrogen and bromine elements.
- With aqueous ferric chloride it gives purple coloration, indicating the presence of phenolic -OH group.
- It gives diazotization test after reduction by Zn dust and HCl, indicating the presence of -NO<sub>2</sub> group.
- It gave elemental analysis as carbon = 39.25% (calculated 39.42%), hydrogen = 2.75% (calculated 2.92%), nitrogen = 4.87% (calculated 5.01%) and bromine = 29.01% (calculated 29.20%).
- **IR (cm<sup>-1</sup>):** spectrum of the compound was carried out in KBr pellets and important absorption can be correlated as  $\nu = 3404$ , H-bonded (-OH phenolic)  $\nu = 1652$ , =C=O bond stretching in o-hydroxy aryl ketone  $\nu = 663$  cm<sup>-1</sup> aliphatic C-Br stretching at  $\nu = 1530$ cm<sup>-1</sup>, Ar-NO<sub>2</sub> asymmetric stretching,  $\nu = 1356$  cm<sup>-1</sup>, Ar-NO<sub>2</sub> symmetric stretching.
- **PMR:** The PMR spectrum was carried out in CDCl<sub>3</sub>+DMSO-D<sub>6</sub> with TMS as internal standard. The spectrum distinctly displays the signal due to Ar-OH protons at  $\delta$  12.44 ppm, Ar-H protons at 7.25-8.09 ppm, -CH<sub>2</sub> protons at 4.55 ppm and -CH<sub>3</sub> protons at  $\delta = 2.40$  ppm.

#### **Preparation of 2-hydroxy -3-nitro-5-methyl- $\alpha$ -thiocarbamido acetophenone (6a)**

The reaction mixture of 2-hydroxy -3-nitro-5-methyl- $\alpha$ -bromoacetophenone was refluxed in isopropanol medium on water bath for 4 hours. During refluxing the suspended reactants went into the



solvent and new product was found to be gradually separated out. It was filtered in hot condition and re-crystallized with ethanol, shiny dark yellow colored crystals were isolated; yield 80%, mp 122°C.

**Properties of compound No. (6a)**

- It is dark yellow, crystalline solid, mp 122°C.
- It gave positive test for nitrogen and sulphur, while bromine is absent.
- It gives positive alkaline plumbite test indicating the presence of sulphur.
- It gives violet coloration with aqueous ferric chloride solution which clearly indicates that phenolic hydroxy group is present.
- The R<sub>f</sub> value was found to be 0.38.
- It gave elemental analysis as carbon = 43.01% (calculated 44.60%), hydrogen = 4.00% (calculated 4.08%), nitrogen = 15.42% (calculated 15.61%) and sulphur = 11.73% (calculated 11.90%).

**IR (cm<sup>-1</sup>)** : Spectrum of the compound was carried out in KBr pellets and important absorption can be correlated as H-bonded phenolic<sup>~</sup> OH stretching  $\nu = 3378 \text{ cm}^{-1}$ , >C=O stretching in o-hydroxy aryl ketone  $\nu = 1617 \text{ cm}^{-1}$ , >C=S stretching  $\nu = 1538 \text{ cm}^{-1}$ , Ar-NO<sub>2</sub> asymmetric stretching at  $\nu = 1466 \text{ cm}^{-1}$ , Ar-NO<sub>2</sub> symmetric stretching  $\nu = 1304 \text{ cm}^{-1}$ , -NH stretching  $\nu = 3273 \text{ cm}^{-1}$ , -NH bending (wagging) at  $\nu = 726 \text{ cm}^{-1}$ .

**PMR:** The PMR spectrum was carried out in CDCl<sub>3</sub>+ DMSO-*d*<sub>6</sub> solvent with TMS as an internal standard. This spectrum distinctly displayed the signals due to Ar<sup>~</sup> OH protons at  $\delta$  8.1 ppm, -NH<sub>2</sub> protons at  $\delta$  7.8 ppm, Ar<sup>~</sup> H protons at  $\delta$  6.8-7. ppm -CH<sub>2</sub> protons at  $\delta$  3.5ppm, and<sup>~</sup> CH<sub>3</sub> protons at  $\delta$  2.40 ppm. The signal at  $\delta$  1.2 is due to moisture in CDCl<sub>3</sub>/DMSO-*d*<sub>6</sub>. From all the above observations compound (6a) has

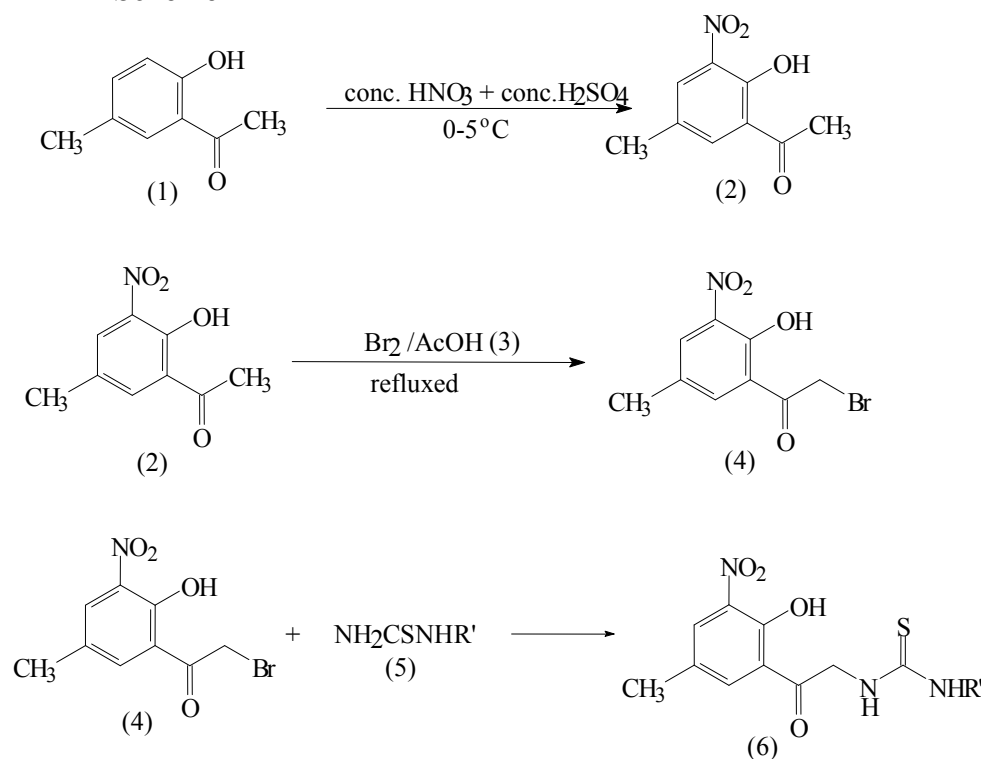
been assigned the structure as 2-hydroxy-3-nitro-5-methyl- $\alpha$ -thiocarbamidoacetophenone.

Similarly 6b to 6e were synthesized by the above mentioned method and are enlisted in Table -1.

**Table -1**

S. No.	Compound	2-Hydroxy-5-methyl- $\alpha$ -substituted thiocarbamidoacetophenones	Colour	Yield (%)	mp (°C)
1	(6a)	2-Hydroxy-5-methyl- $\alpha$ -thiocarbamidoacetophenone	Dark yellow	80	122
2	(6b)	2-Hydroxy-5-methyl- $\alpha$ - <b>methyl</b> thiocarbamidoacetophenone	Pale yellow	63	115
3	(6c)	2-Hydroxy-5-methyl- $\alpha$ - <b>ethyl</b> thiocarbamidoacetophenone	Lemmon Yellow	54	120
4	(6d)	2-Hydroxy-5-methyl- $\alpha$ - <b>phenyl</b> thiocarbamidoacetophenone	Orange Yellow	87	135
5	(6e)	2-Hydroxy-5-methyl- $\alpha$ - <b>allyl</b> thiocarbamidoacetophenone	Turmeric Yellow	68	128

**Scheme 1**





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