

## SYNTHESIS AND CHARACTERIZATION OF SOME NEW IMIDAZOLE-2-THIOLS AND ITS DERIVATIVES

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### ABSTRACT

3-chloro-2, 4-pentanedione on cyclisation with potassium thiocyanate and 4-chloroaniline gives 1-[1-(4-chlorophenyl)-2-mercapto-4-methyl-1H-imidazol-5-yl]-ethanone which on condensation with different aromatic aldehydes gives 1-[1-(4-chlorophenyl)-2-mercapto-4-methyl-1H-imidazol-5-yl]-3-(4-substituted phenyl)-prop-2-en-1-one (**2a-c**) which on react with hydrazine hydrate in the presence of ethanol and phenyl hydrazine, 2, 4-dinitrophenyl hydrazine in catalytic amount of sulphuric acid gives (**3a-c**), (**4a-c**), (**5a-c**) respectively and (**6a-c**) has been synthesized by the treatment of (**3a-c**) with benzoyl chloride in pyridine. All the synthesized compounds were confirmed on the basis of spectral data.

**Keywords:** Imidazole-2-thiols, 3-chloro-2,4-pentanedione, 4-chloroaniline, potassium thiocyanate, spectral data.

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### INTRODUCTION

Imidazole-2-thiols and its derivatives are potential bioactive agents due to their wide spectrum of pharmacological activities like antibacterial, fungicidal<sup>1</sup>, sympathomimetic activity<sup>2</sup>, anti-retrovirus activity and pharmaceutical compositions effective for the treatment of retrovirus infection such as human immunodeficiency syndromes<sup>3</sup>. Encouraged by diverse biological activities and in continuation of the research work on bioactive heterocycles. It was intended to design and synthesized some new imidazole-2-thiols and its derivatives.

The experimental work started from cyclisation of 3-chloro-2, 4-pentanedione with potassium thiocyanate and 4-chloroaniline gives 1-[1-(4-chlorophenyl)-2-mercapto-4-methyl-1H-imidazol-5-yl]-ethanone which on Claisen-Schmidt condensation with different aromatic aldehydes to give chalcones (**2a-c**). Chalcones (**2a-c**) on cyclisation with hydrazine hydrate, phenyl hydrazine, 2, 4-dinitrophenyl hydrazine and isoniazide in catalytic amount of sulphuric acid gives (**3a-c**), (**4a-c**), (**5a-c**) respectively and (**6a-c**) have been synthesized by the treatment of (**3a-c**) with benzoyl chloride in pyridine.

### EXPERIMENTAL

All melting points were determined in open capillaries and are uncorrected. The IR spectra were recorded in KBr using Perkin Elmer model 2000 spectrophotometer and reported wave numbers are given in  $\text{cm}^{-1}$ . <sup>1</sup>H NMR spectra were recorded in  $\text{CDCl}_3$  on a Bruker 400 MHz spectrophotometer using TMS as an internal standard (chemical shift in  $\delta$  ppm). The purity of all the synthesized compounds was checked by TLC on silica gel plates.

#### 1-[1-(4-chlorophenyl)-2-mercapto-4-methyl-1H-imidazol-5-yl]-ethanone (**1a**)

3-Chloro-2, 4-pentanedione (0.01mole) was added slowly in a drop wise fashion to the solution of 4-chloroaniline (0.01 mole) in ethanol (20 mL) with constant stirring for 1 h at 0-5 °C. After the addition the reaction mixture was stirred for 1 h at room temperature and kept the reaction mixture for 12 h. Then potassium thiocyanate (0.01 mole) was added to the reaction mixture which was reflux for 1 h, cooled and poured into crushed ice. The product separated out was filtered, washed with water, dried and recrystallized from ethanol to give (**1a**).

**1a:** IR (KBr,  $\text{cm}^{-1}$ ): 1611.4 (C=O), 1481.7 (C=N), 1444 (C=C), 1237 (C-O).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  ppm: 2.37 (s, 3H, -COCH<sub>3</sub>), 2.49 (s, 3H, Ar-CH<sub>3</sub>), 7.36-7.19(m, 4H, Ar-H).

**Preparation of 1-[2-mercapto-4-methyl-1-(4-chlorophenyl)-1H-imidazol-5-yl]-3-(4-methoxyphenyl)-prop-2-en-1-one (2a)**

Compound (**1a**) (0.01 mol) dissolved in ethanol (40 mL) and 4-methoxybenzaldehyde (0.01 mol) was added with constant stirring at room temperature. Then KOH solution (40%) was added to the reaction mixture with constant stirring, keeping the temperature of the reaction mixture below 10 °C through out the addition. The flask was corked and kept the reaction mixture for 48 hours at room temperature. Finally the reaction mixture was poured over crushed ice and neutralized with glacial acetic acid. The product separated out was filtered, washed with water, dried and recrystallized from ethanol to give (**2a**).

**2a:** IR (KBr,  $\text{cm}^{-1}$ ): 1642.1 (C=O), 1494.1 (C=N), 1453.4 (C=C), 1213.7 (C-O).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  ppm: 2.71 (s, 3H, -COCH<sub>3</sub>), 3.86 (s, 3H, Ar-CH<sub>3</sub>), 6.93-6.91 (m, 2H, Ar-H), 7.03-6.99 (d, 1H, -CO-CH=), 7.57-7.22 (m, 6H, Ar-H), 7.76-7.72 (d, 1H, Ar-CH=). Remaining compounds (**2b-c**) were synthesized by the same procedure.

**Preparation of 5-[5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4-methyl-1-(4-chlorophenyl)-1H-imidazole-2-thiol (3a)**

A mixture of (**2a**) (0.01 mol) and hydrazine hydrate (0.01 mol) in ethyl alcohol (30 mL) was refluxed for 8 hours. After cooling the reaction mixture was poured over crushed ice. The product separated out was filtered, washed with water, dried and recrystallized from ethanol to give (**3a**).

**3a:** IR (KBr,  $\text{cm}^{-1}$ ): 3311 (N-H), 1597.1 (C=N), 1509.7 (C=C), 1243.1 (C-O).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  ppm: 2.40 (s, 3H, Ar-CH<sub>3</sub>), 3.13-3.07 (dd, 1H, -CH<sub>2</sub>pyraz), 3.81 (s, 3H, OCH<sub>3</sub>), 4.27-4.21 (dd, 1H, -CH<sub>2</sub>pyraz), 5.25-5.20 (dd, 1H, -CHpyraz), 7.21-6.85 (m, 8H, Ar-H). Remaining compounds (**3b-c**) were synthesized by the same procedure.

**Preparation of 5-[5-(4-methoxyphenyl)-1-phenyl-4, 5-dihydro-1H-pyrazol-3-yl]-4-methyl-1-(4-chlorophenyl)-1H-imidazole-2-thiols (4a)**

A mixture of (**2a**) (0.01 mol) in ethyl alcohol (30 mL), phenyl hydrazine (0.01 mol) and 2-3 drops of sulphuric acid was refluxed for 12 hours. After cooling the reaction mixture was poured over crushed ice. The product separated out was filtered, washed with water, dried and recrystallized from ethanol to give (**4a**).

**4a:** IR (KBr,  $\text{cm}^{-1}$ ): 1592.7 (C=N), 1500 (C=C), 1245.2 (C-O).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  ppm: 2.40 (s, 3H, Ar-CH<sub>3</sub>), 3.13-3.07 (dd, 1H, -CH<sub>2</sub>pyraz), 3.84 (s, 3H, OCH<sub>3</sub>), 3.81-3.78 (dd, 1H, -CH<sub>2</sub>pyraz), 5.25-5.20 (dd, 1H, -CHpyraz), 7.22-6.81 (m, 13H, Ar-H). Remaining compounds (**4b-c**) were synthesized by the same procedure.

**Preparation of 5-[1-(2, 4-dinitrophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4-methyl-1-(4-chlorophenyl)-1H-imidazole-2-thiol (5a)**

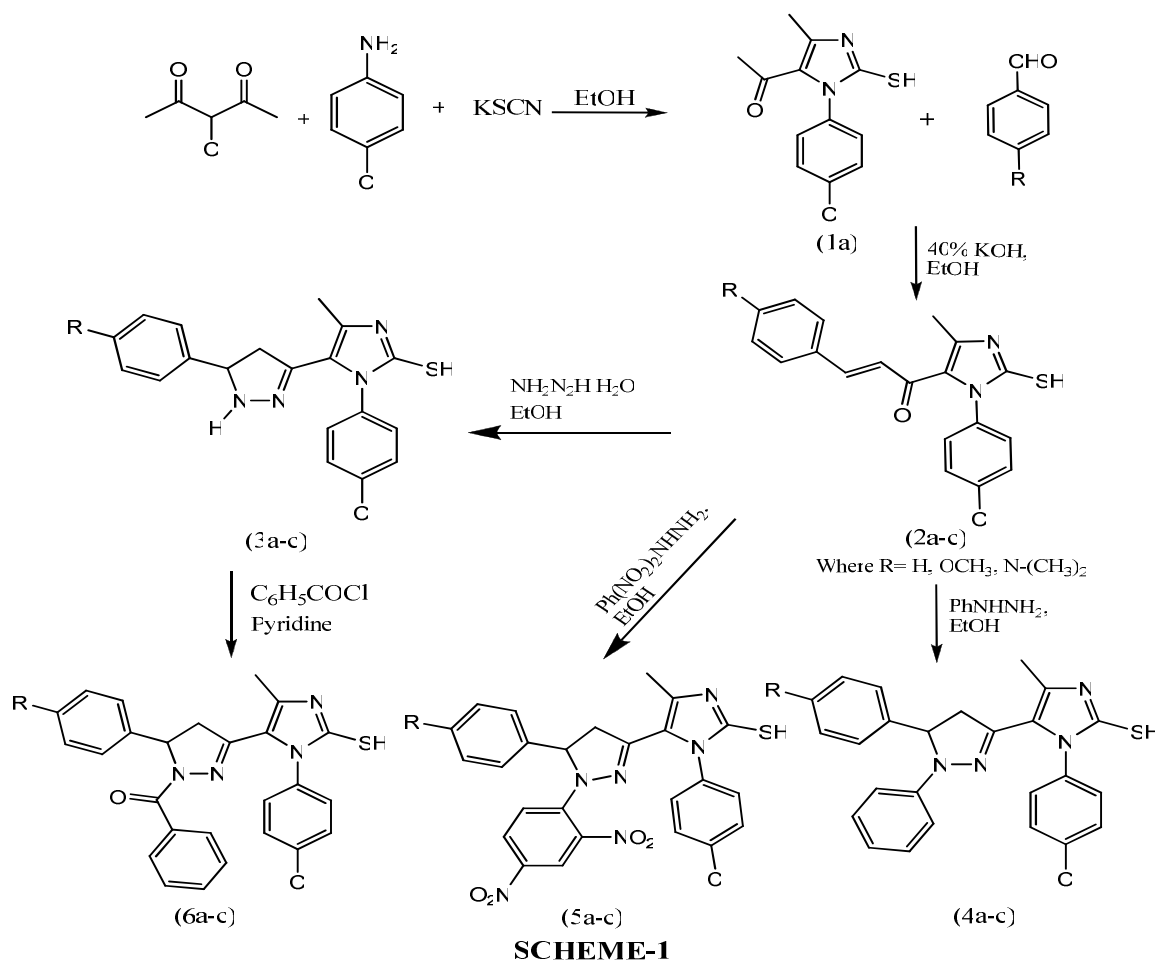
A mixture of (**2a**) (0.01 mol) in ethanol (30 mL), 2, 4-dinitrophenyl hydrazine (0.01 mol) and 2-3 drops of sulphuric acid was refluxed for 12 hours. After cooling the reaction mixture was poured over crushed ice. The product separated out was filtered, washed with water, dried and recrystallized from ethanol to give (**5a**).

**5a:** IR (KBr,  $\text{cm}^{-1}$ ): 1581.5 (C=N), 1507.3 (C=C), 1256 (Ar-O), 1171.1 (C-O).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  ppm: 2.30 (s, 3H, Ar-CH<sub>3</sub>), 3.88-3.85 (dd, 1H, -CH<sub>2</sub>pyraz), 3.87 (s, 3H, OCH<sub>3</sub>), 4.29-4.23 (dd, 2H, -CH<sub>2</sub> & -CHpyraz), 7.80-6.93 (m, 11H, Ar-H). Remaining compounds (**5b-c**) were synthesized by the same procedure.

**Preparation of 5-[1-(phenyl)-methanone-5-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol-3-yl]-4-methyl-1-(chlorophenyl)-1H-imidazole-2-thiol (6a)**

To the ice cold mixture of (**3a**) (0.01 mol) was dissolved in pyridine (30 mL). Then benzoylchloride (0.01 mol) was added dropwise to the reaction mixture with constant stirring at 0-5 °C. After completion of addition stirred the reaction mixture for 1 hour at room temperature. Finally the reaction mixture was poured over crushed ice and neutralized with HCl. The product separated out was filtered, washed with water, dried and recrystallized from ethanol to give (**6a**).

**6a:** IR (KBr,  $\text{cm}^{-1}$ ): 1604 (C=O), 1506 (C=N), 1447 (C=C), 1245.4 (Ar-O), 1176 (C-O).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  ppm: 2.40 (s, 3H, Ar- $\text{CH}_3$ ), 3.08-3.05 (dd, 1H,  $-\text{CH}_2\text{pyraz}$ ), 3.50-3.43 (dd, 1H,  $-\text{CH}_2\text{pyraz}$ ), 3.80 (s, 3H,  $\text{OCH}_3$ ), 4.90-4.85 (dd, 1H,  $-\text{CHpyraz}$ ), 7.41– 6.87 (m, 13H, Ar-H). Remaining compounds (**6b-c**) were synthesized by the same procedure and their physical data are given in Table-1.



## RESULT AND DISCUSSION

The structures of all the synthesized compounds were assigned on the basis of IR and  $^1\text{H}$  NMR. The IR spectrum of compound 2a shows the characteristic band at  $1642\text{ cm}^{-1}$  due to the  $-\text{C}=\text{O}$  group, the IR spectrum of compound 3a, 4a and 5a shows the characteristic band at  $1500\text{-}1600\text{ cm}^{-1}$  due to the  $-\text{C}=\text{N}$  group. There are no absorptions in the region of  $1600\text{-}1700\text{ cm}^{-1}$  indicating the absence of a  $-\text{C}=\text{O}$  group in these structure. The IR spectrum of compound 6a shows the characteristic band at  $1604\text{ cm}^{-1}$  due to the  $-\text{C}=\text{O}$  group and  $1561\text{ cm}^{-1}$  due to the  $-\text{C}=\text{N}$  group.

The  $^1\text{H}$  NMR spectrum of compound 2a showed doublet of  $-\text{CO}-\text{CH}=\text{}$  at  $\delta$  7.03-6.99ppm and Ar- $\text{CH}=\text{}$  at  $\delta$  7.76-7.72ppm, which confirmed the presence of chalcone moiety. The  $^1\text{H}$  NMR spectrum of compound 3a, 4a, 5a and 6a showed doublet of  $-\text{CH}_2$  near about  $\delta$  3.00-5.00ppm confirmed the cyclisation in pyrazoline.

Table-1: Physical data of the synthesized compounds

Compd	R	Molecular Formula	M.P. (°C)	Yield (%)
3a	OCH <sub>3</sub>	C <sub>20</sub> H <sub>19</sub> ClN <sub>4</sub> OS	157-160	63
3b	H	C <sub>19</sub> H <sub>17</sub> ClN <sub>4</sub> S	90-92	67
3c	N(CH <sub>3</sub> ) <sub>2</sub>	C <sub>21</sub> H <sub>22</sub> ClN <sub>5</sub> S	174-177	59
4a	OCH <sub>3</sub>	C <sub>26</sub> H <sub>23</sub> ClN <sub>4</sub> OS	127-130	68
4b	H	C <sub>25</sub> H <sub>21</sub> ClN <sub>4</sub> S	140-143	64
4c	N(CH <sub>3</sub> ) <sub>2</sub>	C <sub>27</sub> H <sub>26</sub> ClN <sub>5</sub> S	200-202	73
5a	OCH <sub>3</sub>	C <sub>26</sub> H <sub>21</sub> ClN <sub>6</sub> O <sub>5</sub> S	230-235	65
5b	H	C <sub>25</sub> H <sub>19</sub> ClN <sub>6</sub> O <sub>4</sub> S	217-220	69
5c	N(CH <sub>3</sub> ) <sub>2</sub>	C <sub>27</sub> H <sub>24</sub> ClN <sub>7</sub> O <sub>4</sub> S	208-210	70
6a	OCH <sub>3</sub>	C <sub>27</sub> H <sub>23</sub> ClN <sub>4</sub> O <sub>2</sub> S	170-172	67
6b	H	C <sub>26</sub> H <sub>21</sub> ClN <sub>4</sub> OS	140-143	65
6c	N(CH <sub>3</sub> ) <sub>2</sub>	C <sub>28</sub> H <sub>26</sub> ClN <sub>5</sub> OS	147-150	61

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