Synthesis of substituted-4, 6-diaryl-2-imino-diphenyl-6H-1, 3-thiazines

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ABSTRACT

Six different Chalcones I(a)-I(f ) were synthesized by condensing 2-hydroxy-3-iodo-5-methyl acetophenone with six different aromatic aldehydes in ethanol using NaOH. These chalcone were cyclized with diphenyl thiourea in ethanol yielding IIa – IIf. The synthesized compounds were characterized by I.R., NMR spectral analysis.

Key Words: - substituted 4, 6-diaryl-2-imino- diphenyl-6H-I, 3- Thiazines.

INTRODUCTION

M.Koketsu et al. have synthesized 1, 3 – thiazine derivatives a potential antimicrobial agents [1] M.Koketsu et al. have synthesized 2-alkythio-1, 3-thiazine derivatives from s- alkylthiocarbamate and a, b- unsaturated ketone [2]. Nicolas Leflemme et al. have synthesized dihydro and tetrahydro-1, 3- Thiazine derivatives from b aryl – b- amino acids [3]. X.F.Lin has synthesized methyl-2-amino-4-methyl-6-phenyl 6H-I, 3-Thazine-5-carboxylate [4]. Stefanie De Montis et al. have synthesized high yield 4H-l, 4- benzothiazine- dioxide derivative [5]. Fisyuk A.S. have synthesized with new approach for 1, 3 chloroisothiocynatoalkanes and synthesis of tetrahydro-1, 3-thiazine-2-thiones and 2- alkylamino -5, 6- dihydro-1, 3-thiazines [6]. Y.N.Yuskovets et al have synthesized new method for synthesis of 5-acyl-1, 3-Thiazines [7].

M.Koketsu synthesized 4-etyl-4-hydroxy-2-phenyl-5, 6-dihydro-4H-I, 3-thiazine [8]. Norbert G. De Kimpe have synthesized 5-Acetyl-2, 3- dihydro-1, 4- thiazine, avery intense roasty, popcornlike odorant [9]. M.Koketsu et al. have synthesized 4-hydroxy-4- methyl-2, 6-diphenyl-5, 6- dihydro-4-H-1, 3-thiazine [10].

Motomu muraoka et al. have studied reaction of 1, 3-Thiazines -2, 6-dithiones and synthesis of 2-alkythio-2, 3- dihydro-1, 3-Thizine-6-thiones by reductive alkylation of 1, 3- thiazine -2, 6- dithiones [11]. Motomu Muraoka synthesized 1, 3- thiazine derivatives from 2-iminocyclopentanedi thiocaboxilic acid [12]. N.Ingarsal have synthesized and antimicrobial activity of some amino-4-[1, 1'-biphenyl-4-y]-6-aryl-6H-I,3-thiazines [13].Dipti R.Patil et al. synthesized ecofriendly synthesis of benzoxazines and benzothiazines at ambient temperature without catalyst and their antibacterial and antifungal activity [14]. A.Nagrajan et al. have synthesized and studied biological activity of bis- Chalcones, bis-Thiazines, and bis-Pyrimidines [15].

Ujwala Sawarkar at al has studied synthesis, characterization and antimicrobial activity of some 2-(propen-1-one) aryl-3-substituted phenothiazine [16]. M.S.A.EL-Gaby have studied the synthesis of new cyclopenta [d] [1, 3] thiazine derivative and their use as antimicrobial agent [17]. Ibadur R.Siddigue et al have studied novel one-pot synthesis of 1, 3-dithiins and 1,3-thiazines under microwave irradiation [18]. Naresh Kumar et al have studied
synthesis of some new 10H-pyrido [3, 2-b] [1, 4] banzothiazine and their ribofuranosides as possible chemotherapeutic agents [19].

**MATERIALS AND METHODS**

Melting points of all synthesized compounds were determined in open capillary tube and are uncorrected. The purity of compounds were checked by TLC using silica G. I. R. spectra were recorded on Perkin-Climer-84 spectrometer (Cm⁻¹) in KBr disc and NMR (Brucker Avance II 400 NMR) using CDCl₃ as solvent.

**Synthesis of 2-hydroxy-3-iodo-5-methyl-acetophenone (Compound-1)**

By known method from p-cresol to p-cresyl-acetate prepared and then by fries migration-2-hydroxy-5-methyl acetophenone which on iodination gives 2-hydroxy-3-iodo-5-methyl acetophenone (Comp-1).

**Synthesis of substituted 2-hydroxy-3-iodo-5-methyl chalcones [Iₐ] – [I₇]**

Compound Iₐ to I₇ were synthesized from 2-hydroxy-3-iodo-5-methyl acetophenone by reacting with six different aromatic aldehydes by known method in solvent ethanol using 40% NaOH. The physical data of compound Iₐ to I₇ is given in table no. 1.

**Reaction scheme 1**

\[
\begin{align*}
\text{I} & \quad \text{OH} \\
\text{CH₃} & \quad \text{COCH₃} \\
\end{align*}
\]

\[+ \quad \text{RCHO} \quad \text{40%NaOH+ethanol} \]

\[
\begin{align*}
\text{I} & \quad \text{OH} \\
\text{CH₃} & \quad \text{C.CH=CH= R} \\
\end{align*}
\]

(I) \[\text{R} \quad \text{M.P.} \quad \; \text{Yield} \]

<table>
<thead>
<tr>
<th>S. N.</th>
<th>Compound No.</th>
<th>R</th>
<th>Molec. Formula</th>
<th>M.P. °C</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Iₐ</td>
<td></td>
<td>C₈H₆O₂I</td>
<td>110 °C</td>
<td>72%</td>
</tr>
<tr>
<td>2.</td>
<td>Iₙ</td>
<td></td>
<td>C₈H₆O₂I</td>
<td>142 °C</td>
<td>68%</td>
</tr>
<tr>
<td>3.</td>
<td>Iₖ</td>
<td></td>
<td>C₈H₆O₂I</td>
<td>160 °C</td>
<td>70%</td>
</tr>
<tr>
<td>4.</td>
<td>Iₖ</td>
<td></td>
<td>C₈H₆O₂I</td>
<td>80 °C</td>
<td>66%</td>
</tr>
<tr>
<td>5.</td>
<td>Iₖ</td>
<td></td>
<td>C₈H₆O₂I</td>
<td>130 °C</td>
<td>63%</td>
</tr>
<tr>
<td>6.</td>
<td>Iₖ</td>
<td></td>
<td>C₈H₆O₂I</td>
<td>80 °C</td>
<td>65%</td>
</tr>
</tbody>
</table>

The groups R are shown in Table no. 1

Table no.1
Synthesis of 4,6-diaryl-2-imino-2,3-diphenyl-6H-1,3-thiazine (IIa-III)

Compound (Ia to If) 0.01 M and diphenyl thiourea 0.01 M and 0.02 M KOH solution with a few drops of piperidine were refluxed in 25 ml ethanol for 2 to 2.5 hours. Dilute it with water and acidified with conc. HCL. The product crystallized from ethanol. Physical data are shown in table no. 2.

Reaction scheme no. 2

The groups R are shown in Table no.2.

<table>
<thead>
<tr>
<th>S. N.</th>
<th>Compound No.</th>
<th>R’</th>
<th>Mole. Formula</th>
<th>M.P.°C</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>IIa</td>
<td></td>
<td>C_{29}H_{23}ON_{2}S</td>
<td>116°C</td>
<td>65%</td>
</tr>
<tr>
<td>2.</td>
<td>IIb</td>
<td></td>
<td>C_{30}H_{25}O_{2}N_{2}S</td>
<td>138-142°C</td>
<td>60%</td>
</tr>
<tr>
<td>3.</td>
<td>IIc</td>
<td></td>
<td>C_{29}H_{23}O_{2}N_{2}S Cl</td>
<td>151°C</td>
<td>62%</td>
</tr>
<tr>
<td>4.</td>
<td>IIe</td>
<td></td>
<td>C_{30}H_{25}O_{2}N_{2}S Cl</td>
<td>108°C</td>
<td>63%</td>
</tr>
<tr>
<td>5.</td>
<td>IIf</td>
<td></td>
<td>C_{27}H_{21}O_{2}N_{2}S</td>
<td>140°C</td>
<td>58%</td>
</tr>
<tr>
<td>6.</td>
<td>IIg</td>
<td></td>
<td>C_{27}H_{21}O_{2}N_{2}S</td>
<td>128°C</td>
<td>60%</td>
</tr>
</tbody>
</table>

RESULTS AND DISCUSSION

Compound Ia – If and IIa – IIg were synthesized through the route as shown in general reactions R and R’ as shown in table no. 1 & 2. Similarly, physical data as shown in table no. 1 and 2. The synthesized compounds Ia (Ia) and IIa (IIa) were confirmed on the basis of IR, NMR spectral analysis.

Characterization data of compound 2-hydroxy-3-iodo-5-metyl acetophenone (1)

IR (KBr) v max cm⁻¹
3200 cm⁻¹ (s) – phenolic OH, 2919 cm⁻¹ (s) – Aromatic C-H stretching, 1635 cm⁻¹ C=O stretching, 1082 cm⁻¹ (S) Ar-CH₃ stretching, 1020 cm⁻¹ (S) CH₃ stretching, 642 cm⁻¹ C-I stretching.

H1 NMR: [δ CDCl₃]
2.3 δ (S, 3H, Ar-CH₃), 2.6 δ (S, 3H, COCH₃), 7.5 δ (S, 1H, Ar-H), 7.7 δ (S, 1H, Ar-H), 12.9 δ (S, 1H, Ar-OH).

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2-hydroxy-3-iodo-5-methyl–phenyl chalcone. (Ia)
IR (KBr) νmax cm⁻¹
3412 cm⁻¹ (br) – phenolic OH, 2917 cm⁻¹ (S) AR-C-H- Stretching, 1746 cm⁻¹ (S) C=O of O=C-CH=CH Stretching, 1358 cm⁻¹ (S) C-O stretching in Phenol, 1264-1230 cm⁻¹ (S) Ar-O stretching in ether, 563-548 cm⁻¹ (S) C-I stretching.

H1 NMR: [δ CDCl₃]
2.3-2.5 δ (S, 3H, Ar-CH₃), 7.4 δ (S, 2H, H-C=CH), 7.5-7.9 (m, 7H, Ar-H), 13.5 δ (br, 1H, Ar-OH).

2-hydroxy-3-iodo-5-methyl–phenyl-4-phenyl ethenyl chalcone. (Ie)
IR (KBr) νmax cm⁻¹
3400 cm⁻¹ (br) – phenolic OH, 2914 cm⁻¹ (S) AR-C-H- Stretching, 1631 cm⁻¹ (S) O=C-CH=C, 1353 cm⁻¹ (S) C-O stretching in Phenol, 1230 cm⁻¹ (S) Ar-O stretching in ether, 690.26 cm⁻¹ (S) C-I stretching.

H1 NMR: [δ CDCl₃]
2.1-2.3 δ (S, 3H, Ar-CH₃), 2.8-3 δ (S, 1H, O=C-CH), 5.2-5.3 δ (d, 2H, H-C=CH), 6.7-7.8 δ (m, 9H, Ar-H), 13.5-13.6 δ (br, 1H, Ar-OH).

-4- (2’-hydroxy -3-iodo-5-methyl phenyl) -6- (4- phenyl) -2, 3-diphenyl- imino- 6H- 1, 3-thiazine. (IIa)
IR (KBr) νmax cm⁻¹
3460 cm⁻¹ (br) – phenolic OH, 3206 cm⁻¹ (S) C=N- stretching, 3033-3010 cm⁻¹ (S) Ar-CH streching, Ar-CH₃ streching, 1449 cm⁻¹ (S) C=N streaching, C=C streaching vibration in aryl group., 1341 cm⁻¹ (S) C-N streaching, 818 cm⁻¹ (S) C-I streching.

H1 NMR: [δ CDCl₃]
2.1 δ (S, 3H, Ar-CH₃), 2.8-3.1 δ (d, 1H, CH₄), 3.8 δ (d, 1H, CH₆), 6.5-8.00 δ (m, 17H, Ar-H), 8.8-8.1 δ (br, 1H, Ar-OH).

CONCLUSION
Present study describes the synthesis of Chalcones and synthesis of 4,6 – diaryl-2-imino-2,3-diphenyl-6H-1,3-thiazines. Compounds were characterized by I.R.& N.M.R.

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