Synthesis of some Fused Heterocyclic Compounds from α-Bromo Tetralone and Indanone

Ahlam M.N. Yahya  
Department of Chemistry  
College of Science  
Mosul University

Akram N. Mohammad  
Department of Chemistry  
College of Education for Girls  
Mosul University

(Received 31 / 3 / 2010 ; Accepted 13 / 7 / 2010 )

ABSTRACT

A number of heterocyclic compounds (7-14) were prepared by the reaction of α-bromo ketones (3,4) with 2-amino-5-phenyl-1,3,4(thiadiazole or oxadiazole) and 5-phenyl-1,3,4-triazole-2-thiol. Moreover, on heating under reflux of α-bromo ketones (3,4) in the presence of ethanol with thiazole derivatives (5,6) (was prepared from the reaction of α-bromo ketone (3,4) with thiourea), compounds (7,8) were obtained. The structure of the synthesized compounds have been elucidated by their physical and spectral methods.

Keywords: oxadiazole, thiadiazole, triazole, tetralone, indanone, imidazole derivatives, α-halo ketone
INTRODUCTION

Tetralones and indanones are compounds which are very important as intermediate products for synthesizing various medicinal starting materials such as steroids (House et al., 1960; Brown et al., 1981), serotonin pre-synaptic inhibitor compounds with antidepressant activity (Johnson and Doub, 1999), non-steroidal anti-inflammatory (NSAID) drugs (Brunel et al., 1995) and for the treatment of Alzheimer's disease (Sayena et al., 2003). Substituted imidazoles have been extensively used in medicine and agriculture (Barger and Dale, 1910; Dale and Laidlaw, 1910). These compounds show antifungal activity (Dubini et al., 1992; Petersen et al., 1993; Rolth and Fenner, 1994; Werbrouks and Debergh, 1996; Wurbrouck et al., 1996; Furtado and Minami, 1997; Urbanik et al., 1998), anticonvulsant properties (Nardi et al., 1981; Graziani et al., 1983; Robertson et al., 1986; Catto et al., 1989; Hetzheim et al., 1990; Roth and Fenner, 1994); tumor-inhibiting (Keppler et al., 1987); inhibitors of p38 mitogen activated protein kinase (Liverton et al., 1999; Magnus et al., 2006); anti-inflammatory (Labanauskas et al., 2006). Therefore, many investigators reported the synthesis of this type of compounds (Magnus et al., 2006; Jasinski et al., 2006; Davood et al., 2007; Shieh and Mckenna, 2008). A series of derivatives of 1,3,4-oxadiazol has been prepared and were known to have a wide spectrum of biological activity (Yarvenko et al., 1993; Piatnitski chekler et al., 2008; Levins and Wan, 2008). On the other hand, 1,3,4-thiazole derivatives were synthesized and investigated their antimicrobial activity (Gong and Yang, 2006; Demirbas et al., 2008; Hadizadch and Vosooghi, 2008). Therefore, an attempt was made to prepare versatile fused heterocyclic compounds from tetralone and indanone owing to their practical significance.

EXPERIMENTAL

Melting points (M.P.) were measured on Electrothermal 9300 melting point apparatus and are uncorrected. Infrared (FT-IR) spectra were recorded on infrared spectrophotometer model tensor 27 Bruker Co., using KBr discs. Ultraviolet (UV) spectra were measured on Shimadzu UV-1650 PC ,UV-Visible spectrophotometer. 2-Amino-5-phenyl-1,3,4-thiadiazole (a), 5-phenyl-1,3,4-triazole-2-thiol (b) and 2-amino-5-phenyl-1,3,4-oxadiazole (c) were prepared using a previously reported method; (Al-Juboory, 2001; Eissa, 2006; Husain and Jamal, 1987).

**Synthesis of α-bromo ketones (3,4): (Kolsch, 1950; Rutherrford, 1955; House et al., 1960)**

To a solution of (0.3 mole, 40 gm) of 1-tetralone (1) or 1-indanone (2) in (40 ml) of ether, cooled to (0°C) with (0.3 mole, 48 gm) of bromine was added. The mixture was heated for fifteen minutes on a water-bath to expel most of the hydrogen bromide, then cooled and filtered. The solid product was washed with ether. The melting point and spectral data were shown in (Table 1).

**Synthesis of 2-Amino[1,2-d]tetralino or indano-1,3-thiazole (5,6): (Koelsch, 1950; King and Hlavacek, 1950; Arcus and Barrett, 1958)**

To a solution of (0.2 mole, 1.07gm) of thiourea in ethanol (5 ml) heated under reflux, 2-bromo-1-tetralone or indanone (3,4) (0.1 mole, 3 gm) in ethanol (15 ml) was added during (1.5 hrs), heating was continued for (15 min.). This crude reaction mixture was cooled and
extracted with ether to remove unreacted ketone. The residue was then dissolved in boiling water and filtered off. The solution was then cooled and made basic with ammonium hydroxide. The precipitate was filtered off and recrystallized from ethanol-water. The melting point and spectral data were shown in (Table 1).

**Synthesis of imidazole tetrahydro thiazole derivatives (7,8) :  (Arcus and Barrett, 1958)**

A mixture of α-bromo ketone (3,4) (0.01 mole) and compound (5) (0.01 mole, 2.26 gm) in (40 ml) ethanol was refluxed for (4 hrs.). The solution was then cooled and made basic with ammonium hydroxide and extracted with ether. After evaporation of ether, the precipitate was filtered off and recrystallized from ethanol-water. The physical constant and spectral data were illustrated in (Table 1).

**Synthesis of fused 1,3,4-thiadiazole derivatives (9,10) :  (King and Hlavacek, 1950)**

To a solution of α-bromo ketone (3,4) (0.01 mole) in ethanol (40 ml), 2-amino-5-phenyl-1,3,4-thiadiazole (a) (0.01 mole, 1.77 gm) was added. The reaction mixture was boiled for (3-4 hrs.). The precipitate was filtered off and recrystallized from ethanol. The physical constants and spectral data were illustrated in (Table 1).

**Synthesis of fused 1,3,4-triazole derivatives (11,12) :  (Wiley et. al, 1951)**

To a solution of α-bromo ketone (3,4) (0.01 mole) in (40 ml) of ethanol, (0.01 mole, 1.77 gm) of 2-amino-5-phenyl-1,3,4-triazole (b) was added. The mixture was refluxed for (3 hrs.). After cooling, cold water was added to the product mixture. The precipitated product was filtered off and recrystallized from ethanol. The physical constants and spectral data were illustrated in (Table 1).

**Synthesis of fused 1,3,4-oxadiazole derivatives (13,14) :  (Wiley et. al, 1951)**

A mixture of α-bromo ketone (3,4) (0.01 mole) and (0.01 mole, 1.77 gm) of 2-amino-5-phenyl-1,3,4-oxadiazole (c) in (40 ml) of ethanol was refluxed for (4 hrs.). The reaction mixture was cooled to room temperature then poured in ice-water (10 ml). The precipitated product was removed by filtration, washed with ice-water and ether then recrystallized from ethanol. The physical constants and spectral data were illustrated in (Table 1).
Table 1: Physical and spectral data for compounds (3-14).

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>M.P (°C)</th>
<th>Yield (%)</th>
<th>Colour</th>
<th>UV (EtOH) $\lambda_{max}$ (nm)</th>
<th>I.R (KBr) $\nu$ (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C-S</td>
</tr>
<tr>
<td>3</td>
<td>37-38</td>
<td>55</td>
<td>white</td>
<td>256,300</td>
<td>1718</td>
</tr>
<tr>
<td>4</td>
<td>37-39</td>
<td>50</td>
<td>white</td>
<td>254,293</td>
<td>1780</td>
</tr>
<tr>
<td>5</td>
<td>135-137</td>
<td>50</td>
<td>Yellow</td>
<td>246,320</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>209-211</td>
<td>80</td>
<td>Fat Brown</td>
<td>246,306</td>
<td>1780</td>
</tr>
<tr>
<td>7</td>
<td>223-225</td>
<td>45</td>
<td>Brown</td>
<td>252,316</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>167-169</td>
<td>35</td>
<td>Brown</td>
<td>280,336</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>198-200</td>
<td>35</td>
<td>Yellow</td>
<td>238,314</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>130-132</td>
<td>42</td>
<td>Yellow</td>
<td>248,300</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>158-160</td>
<td>40</td>
<td>Yellow</td>
<td>242,308</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>116-118</td>
<td>28</td>
<td>Yellow</td>
<td>250,302</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>199-203</td>
<td>30</td>
<td>Fat yellow</td>
<td>246,304</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>120-122</td>
<td>55</td>
<td>Yellow</td>
<td>248,316</td>
<td></td>
</tr>
</tbody>
</table>

* Reported melting points (°C) for compounds 3 and 4 were (37-38) and (37-38.5) respectively, (Rutherford and Stevens, 1955); and for compound 5 and 6 was (133-134) and (213-214) respectively, (King and Halavacek, 1950)

RESULTS AND DISCUSSION

$\alpha$- Tetralones and indanones are known for being particularly useful as synthesis intermediates for preparing different pharmaceutical starting materials (Repinskaya et al., 1982).

The Hantzsch's synthesis of thiazole (Wiley and Behr, 1951) involving reaction of the tautomeric form (II) (isothioamide) of thiourea with ($\overset{\text{C-BR}}{\text{C}}$) carbon of the $\alpha$-halo ketone to form 2-amino thiazole derivatives (scheme 1). The first step of the reaction of $\alpha$-bromo tetralone (3) with thiourea involves formation of a carbon-sulfur link with elimination of hydrogen bromide molecule. In the second step, ring closure takes place with elimination of water molecule to form 2-amino[1,2-d] tetralone or indano-1,3-tetrahydro thiazole (5,6) (King and Halavacek, 1950). The reaction mechanism could be illustrated as follow(scheme 1) (Wiley and Behr, 1951).
The structure of compounds (5,6) was confirmed on the base of IR and UV spectra. The IR spectra showed the presence of absorption band at (1624-1629 cm\(^{-1}\)) related to (C=N) bond stretching, (1600-1604 cm\(^{-1}\)) related to (C=C) bond stretching and (3240-3262 cm\(^{-1}\)) assigned to (NH) bonds stretching. While the UV spectra showed \(\lambda_{\text{max}}\) at (254-256 nm) related to \((\pi\rightarrow\pi^*)\) and (293-300 nm) related to \((n\rightarrow\pi^*)\) transition (Finar, 1977).

The compounds (7,8) were prepared by the condensation reaction of \(\alpha\)-bromo ketone (3,4) with compound (5) (scheme 3). This reaction proceeded through substitution–addition mechanism as shown in (scheme 2).

The IR spectral data of compounds (7,8) showed absorption bands at (646-648 cm\(^{-1}\)), (1348-1388 cm\(^{-1}\)); (1561-1623 cm\(^{-1}\)) and (1630-1687 cm\(^{-1}\)) which are related to bond stretching of (C-S), (C-N), (C=C) and (C=N) groups respectively (Nakanishi, 1962). The UV spectra of these compounds showed absorption band at \(\lambda_{\text{max}}\) (252-280 nm) and (316-336 nm) due to the \((\pi\rightarrow\pi^*)\) and \((n\rightarrow\pi^*)\) transition and ring system (Parikh, 1974; Finar, 1977).
α-Bromo ketones (3,4) was allowed to react with 2-amino-5-phenyl-1,3,4-thiadiazole (a) in alcoholic solution to afford the corresponding compounds (9,10) (Dodson and King, 1945; King and Hlavacek, 1950) (scheme 2 and 3). The obtained products (9,10) were identified by their IR data. There infrared spectra show the following bands (1336-1376 cm\(^{-1}\)), (1030-1034 cm\(^{-1}\)), (1604-1631 cm\(^{-1}\)) and (1630-1690 cm\(^{-1}\)) which related to (C-N), (N-N), (C=C) and (C=N) groups respectively (Phillips et al., 1998; Parikh, 1974; Nakanishi, 1962). The UV spectra showed lower wave length in \(\lambda_{\text{max}}\) at (238-248 nm) and (300-314 nm) due to the (\(\pi\rightarrow\pi^*\)) and (n→\(\pi^*\)) transition and steric effect (Finar, 1977; Katritzky and Rees, 1984).

Imidazo[2,3-b]1,3,4-tetrahydro triazole (10,11) were prepared by condensation of α-bromo ketone (3,4) and 5-phenyl-1,3,4-triazole-2-thiol (b) in the presence of alcohol as yellow crystalline products, (scheme 2 and 3). The structure formula of (11,12) were confirmed on the bases of their IR and UV spectra. The IR spectra showed the absorption band at (1029-1061 cm\(^{-1}\)) for (N-N) bond stretching, (C-S) absorption band at (649-683 cm\(^{-1}\)), (C-C) absorption band at (1577-1623 cm\(^{-1}\)) and (C=N) absorption band at (1630-1686 cm\(^{-1}\)) (Nakanishi, 1962; El-Rayyes and Al-Jawhary, 1986), while the UV spectra showed maximum absorption at \(\lambda_{\text{max}}\) (242-250 nm) and (302-308 nm) due to the (\(\pi\rightarrow\pi^*\)) and (n→\(\pi^*\)) transition and also to the steric effect (Parikh, 1974).

The final compounds (13,14) synthesized from the reaction of corresponding 2-amine-5-phenyl-1,3,4-oxadiazole (c) with α-bromo ketone (3,4) (Wiley, 1945) (scheme 2 and 3). The IR spectra for these compounds showed absorption bands at (1661-1682 cm\(^{-1}\)) assigned to (C=N) bond stretching, (1596-1616 cm\(^{-1}\)) assigned to (C=C) bond stretching, (1347-1386 cm\(^{-1}\)) for (C-N) bond stretching, sym. at (1118-1172 cm\(^{-1}\)) and asym. at (1213-1247 cm\(^{-1}\)) related to (C-O-C) bond stretching and (1070-1084 cm\(^{-1}\)) related to (N-N) bond stretching. The UV spectra of compounds (12,13) showed absorption band at \(\lambda_{\text{max}}\) (246-248 nm) and (304-316 nm) related to the electronic transition (\(\pi\rightarrow\pi^*\)) and (n→\(\pi^*\)) (Finar, 1977).


Ahlam M.N. Yahya and Akram N. Mohammad


Synthesis of some Fused Heterocyclic………


