Synthesis And Identification 1-3 Diazepine From Ibuprofen

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ABSTRACT: The research was involved preparation of 1-3 diazepine from 2-(4-isobutylphenyl) propanoic acid (ibuprofen) by many steps including[Schiff bases,1-3 Oxazepine and 1-3deazepine] ibuprofen was used a basic substance to prepare of these compounds, via many steps: the first Step including prepared ester from Ibuprofen in absolute Ethanol solvent in the presence H_2SO_4 con so the following derivative was produced (M1). Step two including prepared hydrazid derivatives from reaction the ester with NH_2\cdot NH_2 H_2O.80% in the absolute Ethanol solvent were produced(M2). In the next step, a new Schiff bases compound prepared by a condensed reaction of(M2) with Acetophenone and 4-chloro Acetophenone was produced (K1,K2). The third step includes preparation of two Oxazepine ring by a reaction of tow Schiff bases produced by the first with maleic anhydride in dry benzene solvent to give the compound(H1, H2). In the end step includes the preparation of two deazepine ring by reaction 1-3 oxazepine ring with phenyl hydrazine to product the compound(1,2). These synthesized compound have been characterized by melting point, elemental analysis and FT-IR spectra.

Key word: Ibuprofen,Schiffs base,oxazepine,diazepin,anti-inflammatory,non-steroid,nonselective

1. Introduction
Ibuprofen is a non-steroid anti-inflammatory drug\(^\text{[1,2]}\). Ibuprofen work by inhibiting the enzyme cyclooxygenase(COX), which converts arachidonic acid into prostaglandin H2(PGH2). Ibuprofen is nonselective COX inhibitor, it inhibits tow isoforms of cyclooxygenase COX-1 and COX-2\(^\text{[3]}\) ibuprofen is used primarily as analgesic drug for fever, pain and inflammatory diseases such as osteoarthritis and rheumatoid arthritis\(^\text{[4]}\) butte the long use cause side effects such as peptic ulcer nausea, dyspepsia, gastrointestinal, Al zehyme\(^\text{[5]}\) and because it contains a set of (COOH) effective make us can addedketone group like acetophenon and 4-chloroacetophenon to convert ibuprofen into diazepine derivative including attending annular seven ring importance pharmaceutical and biological.

Experimental
All chemicals materials were supplied from Merck and BDH-chemical Company(uk). All measurements were carried out by:- Melting points: Electrothemal 9300, melting point Engineering LTD, U, K FT-IRspectra: Fourier transform infrared shimadzu (8300) (FI-IR), KBRdisc was performed by Co,S.Q.Iraq. Elemental Analysis (C.H.N): EA-017mth in center Lab of Babylon University H-NMR spectra: in center Lab of kashan university in Iran.

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1-B: preparation the compound 2- (4-isobutylphenyl) propanehydrazide
Taking the amount of (M1) 6gm ethyl 2- (4-isobutylphenyl) propanoate and dissolved in 30ml ethanol absolute and then add 9ml of NH$_2$NH$_2$H$_2$O80% gradually while stirring and then escalation for 16h and follow-up interaction mediated (TLC) and after the completion of the reaction we distilling the solvent and then we add cold water and let the mixture for a full day after that we filtration, washing with distilled water and let dry material then we re-crystallization .then we drain the material in the form of pure white crystals melting point 78°C (M2).

**TABLE(2). Physical properties of compound (M2).**

<table>
<thead>
<tr>
<th>Molecule Form</th>
<th>M.Wt</th>
<th>Color</th>
<th>M.p°C</th>
<th>Yield %</th>
<th>RF</th>
</tr>
</thead>
<tbody>
<tr>
<td>C13H20N2O</td>
<td>220.3</td>
<td>white</td>
<td>78°C</td>
<td>87.5</td>
<td>0.76</td>
</tr>
</tbody>
</table>

2-A: Preparation of the compound 2- (4-isobutylphenyl)-N’-(1-phenylethylidene) propanehydrazide
Taking (0.5) gm of the compound (M2) and melted in (30) ml of ethanol absolute and added (0.33) gm. of maleic anhydride than added 3 drop of G.A.A and refluxed for 8hr are monitored interact mediated by (TLC) produce 83%(K1)

**TABLE(3). Physical properties of compound (K1).**

<table>
<thead>
<tr>
<th>Molecule Form</th>
<th>M.Wt</th>
<th>Color</th>
<th>M.p°C</th>
<th>Yield%</th>
<th>RF</th>
</tr>
</thead>
<tbody>
<tr>
<td>C21H26N2O</td>
<td>322.44</td>
<td>yellow</td>
<td>80-83</td>
<td>83</td>
<td>0.61</td>
</tr>
</tbody>
</table>

2-B: Preparation of the compound N’-(1-(4-chlorophenyl) ethylidene)-2-(4-isobutylphenyl) propanehydrazide
Taking (0.5) gm. of the compound (M2) and melted in (30) ml of ethanol absolute and added (0.33) gm. 1-(4-chlorophenyl) ethanone than added 3 drop of G.A.A and refluxed for 8hr are monitored interact mediated by (TLC) produce 77%(K2)

**TABLE(4). Physical properties of compound (K2).**

<table>
<thead>
<tr>
<th>Molecule Form</th>
<th>M.Wt</th>
<th>Color</th>
<th>M.P°C</th>
<th>Yield %</th>
<th>RF</th>
</tr>
</thead>
<tbody>
<tr>
<td>C21H20SIN2O</td>
<td>356.89</td>
<td>white</td>
<td>85-88</td>
<td>77</td>
<td>0.52</td>
</tr>
</tbody>
</table>

3-A: Preparation of the compound (Z)-2-(4-isobutylphenyl)-N-(2-methyl-4,7-dioxo-2-phenyl-1,3-oxazepin-3(2H,4H,7H)-yl) propanamide
Mixture of equimolar amounts (0.5) gm. of (K1) and (0.14) gm. of maleic anhydride were dissolved in (30) ml of dry benzene and refluxed for (10) hr. After cooling a precipitate it re-crystallized from ethanol Consists Article of white color

**TABLE(5). Physical properties of compound (H1).**

<table>
<thead>
<tr>
<th>Molecule Form</th>
<th>M.Wt</th>
<th>Color</th>
<th>M.P°C</th>
<th>Yield%</th>
<th>RF</th>
</tr>
</thead>
<tbody>
<tr>
<td>C25H28N2O</td>
<td>420.50</td>
<td>yellow</td>
<td>79-83</td>
<td>67</td>
<td>0.53</td>
</tr>
</tbody>
</table>

3-B: Preparation of the compound (Z)-N-(2-(4-chlorophenyl)-2-methyl-4,7-dioxo-1,3-oxazepin-3(2H,4H,7H)-yl)-2-(4-isobutyl phenyl) propanamide
Mixture of equimolar amounts (0.5) gm. of (K2) and (0.14) gm. of maleic anhydride were dissolved in (30) ml of dry benzene and refluxed for (11) hr. After cooling a precipitate it re-crystallized from ethanol Consists Article of white color
### TABLE (6). Physical properties of compound (H2)

<table>
<thead>
<tr>
<th>Molecule Form</th>
<th>M.Wt</th>
<th>Color</th>
<th>M.P.ºc</th>
<th>Yield%</th>
<th>RF</th>
</tr>
</thead>
<tbody>
<tr>
<td>C25H27C1N20</td>
<td>454.92</td>
<td>white</td>
<td>96</td>
<td>76</td>
<td>0.58</td>
</tr>
</tbody>
</table>

4-A: Preparation of the compound (Z)-2-(4-isobutylphenyl)-N-(2-methyl-4,7-dioxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)propanamide

Take (0.16) gm from (H1) dissolved in (30) ml of dry benzene and added (0.02) from vinyl hydrazine and reflux (12) hr in 65ºc. After cooling a precipitate re-crystallized from ethanol.

### TABLE (7). Physical properties of compound (1)

<table>
<thead>
<tr>
<th>Molecule Form</th>
<th>M.Wt</th>
<th>Color</th>
<th>M.P.ºc</th>
<th>Yield%</th>
<th>RF</th>
</tr>
</thead>
<tbody>
<tr>
<td>C25H29N3O3</td>
<td>419.52</td>
<td>brown</td>
<td>125ºc</td>
<td>70</td>
<td>0.51</td>
</tr>
</tbody>
</table>

4-B: Preparation of the compound (Z)-N-(2-(4-chlorophenyl)-2-methyl-4,7-dioxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)-2-(4-isobutyl phenyl)propanamide

Take (0.16) gm from (H2) dissolved in (30) ml of dry benzene and added (0.02) from vinyl hydrazine and reflux (12) hr in 65ºc. After cooling a precipitate re-crystallized from ethanol.

### Results and Discussion

Diagnosed compounds prepared by FT-IR when comparing the spectrum FT-IR Shades of ibuprofen with other vehicles prepared. Notes the presence of a broad package in the composite primary Back to the group (OH) between (2500-3400) cm⁻¹ and also notes package back to the group C=O Carboxylic acid at (1724) cm⁻¹. The package is characteristic. When preparation (K1, K2) notes package back to the group C=N in the figure (2,3) shows consist Schiff's bases because the package related to C=N notes in (1676, 1668) cm⁻¹ and also notes in the figure (4,5) notes package back to the C=O ketone in the (1720, 1771) cm⁻¹ and notes package back to the C=O amid in the (1668, 1633) cm⁻¹ shows consist compounds 1-3 oxazipine. But in the figure (6,7) notes consist compounds diazipine because disappear C=O ketones and still C=O amid (1618, 1647) cm⁻¹. While Diagnosed compounds prepared in ¹H-NMR it notes single sign in the (2.5) ppm related to solvents' proton and notes poly single (7.9-7.7-7.6-7.5) ppm related to ring phenyls proton. And notes single sign 6.79 ppm related to ring oxazipine (CH=CH) while amid 's proton appear single sign in (8.066 ppm).

Figure (1) FT-IR Spectra of Ibuprofen.
Figure (2) FT-IR Spectra of compound (K1).

Figure (3) FT-IR Spectra of compound (K2).

Figure (4) FT-IR Spectra of compound (H1).

Figure (5) FT-IR Spectra of compound (1).

Figure (6) FT-IR Spectra of compound (H2).

Figure (7) FT-IR Spectra of compound (2).

Figure (8) H-NMR for compound (H2).

Reference

[2] Ioana Vasincu (Geangalau), Maria Apotroasezi, Grisztina Tuchilus. PHARMACY ORIGINALPAPERS REV. MEDCHIR. SOC. MED. Nat., Iasi-2013-Vol.11-7, no.2

[4] "Ibuprofen" Technical Information April 2010, Superseded issue dated January 2010 0.3-030720,- 10(page 1 of 14


I=EOH, G, A, A
A=Acetophenone
B=4-Chloro acetophenone
i= dry benzene
2=Maleic anhydride
3=Phenylhydrazine