Synthesis And Identification 1-3 Diazepine From Ibuprofen

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ABSTRACT: The research was involved preparation of 1-3 diazepin 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-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 FTIR and HMNR spectroscopy by their UN corrected melting points, elemental analysis and FT-IR spectra

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

1. Introduction

Ibuprofen Is a non-steroid anti-inflammatory drug[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[3] ibuprofen is used primarily as analgesic drug for fever, pain and inflammatory diseases such as osteoarthritis and rheumatoid arthritis [4] butthe long use cause side effects such as peptic ulcer nausea, dyspepsia, gastrointestinal, Al zehymer[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 derivativeincluding 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 UniversityH-NMR spectra: in center Lab of kashan university in Iran.

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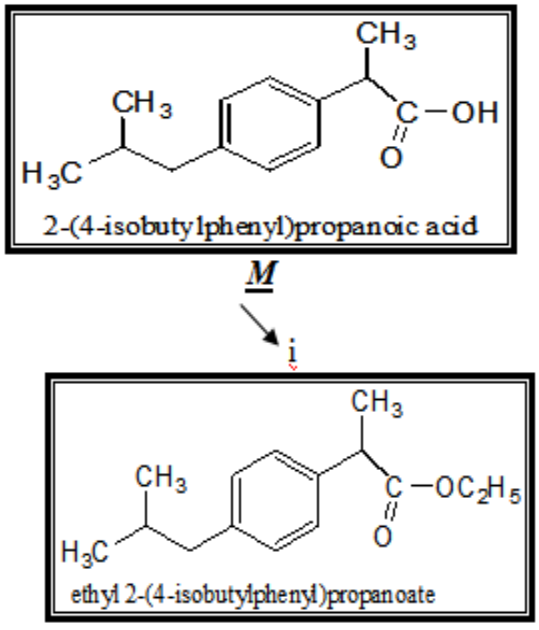
Synthesis methods

1-A: Preparation of the compound ethyl 2 -(4-isobutylphenyl) propanoate.

Been taking (10) gm. of (Ibuprofen) 2-(4-iso butylphenyl) propanoic acid. is dissolved in(40) ml of ethanol absolute. After the completion of solvent is added 4 drop of H_2SO_4concenter. Escalation for 16h. Follow-up interaction by (TLC). After the completion of the reaction we instillation the solvent .Then Added cold water. We conclude by CCl_4. washwater distilled water article Na_2CO_3 5% and then with distilled water until neutral drain the over Na_2SO_4

TABLE (1).Physical properties of **(M1)**

Molecular for	M.Wt	Color	M.pc	Yield%	R.F(3:2)(Tluene:ETOH
C15H22O2	234.33	Pale Yellow	L	78	0.68



i=ETOH abs,,H,,ref

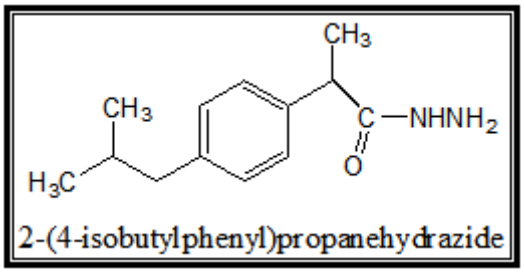
M1

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_2NH_2-H_2O80% 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 78ċ (M2).

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

Molecular For	M.Wt	Color	M.p°c	Yield %	R.f (2:3) (EtoH:Toluene)
C13H20N2O	220.3	white	78°c	87.5	0.76



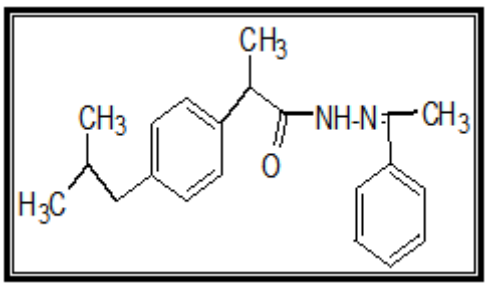
M2

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 (o.33)gm. (acetophenone) than added 3 drop of G.A.A and refluxed for 8hr are monitored interact mediated by(TLC) produse 83%(K1)

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

Moleculer For	M.Wt	Color	MP°c	Yield%	RF
C21H26N2O	322,44	yellow	80-83	83	0.61



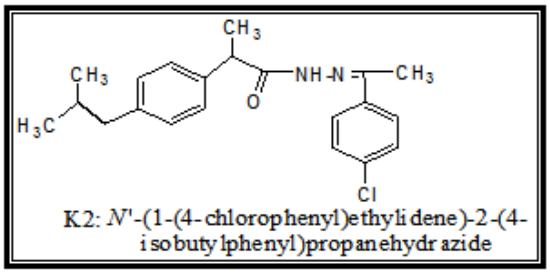
K1: 2-(4-isobutylphenyl)-*N*'-(1-phenylethylidene)propanehydrazide

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 (o.33)gm. 1-(4-chlorophenyl) ethanone than added 3 drop of G.A.A and refluxed for 8hr are monitored interact mediated by (TLC) produce77% (K2)

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

Moleculer For	M.Wt	Color	MP°c	Yield%	RF
C212H25ClN2O	356.89	white	85-88	77	0.52

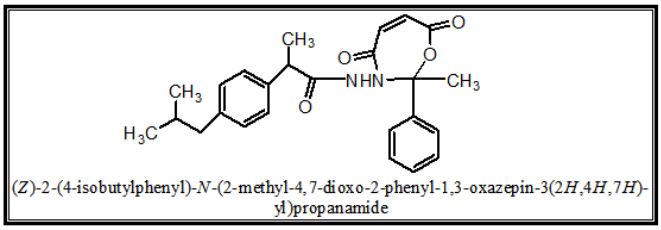


3-A: Preparation of the compound (Z)-2-(4-isobutylphenyl)-N-(2-methyl-4,7-dioxo-2-phenyl-1,3-oxazepin-3(2H,4H,7H)-yl) propanamide

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)**

Moleculer For	M.Wt	Color	MP°c	Yield%	RF
C25H28N2O4	420.50	yellow	79-83	67	0.53



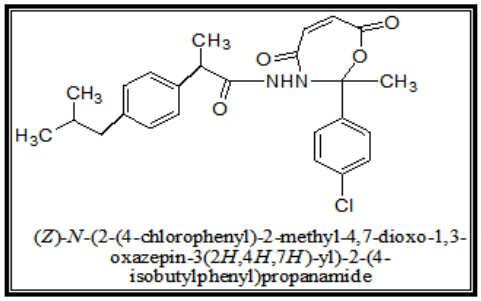
H1

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)**

Moleculer For	M.Wt	Color	MP°c	Yield%	RF
C25H27C1N20	454.92	white	96	78	0.58



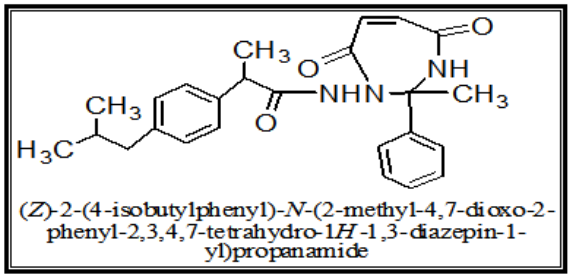
H2

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

Take (o.16)gm from(H1) dissolved in (30)ml of dry benzene and added (0.02) from vinyl hydrazine and rfalaks (12)hr in 65ºc After cooling a precipitate it re crystallized from ethanol consists Article ……..

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

Moleculer Fon:	M.Wt	Color	MP°c	Yield%	RF
C25H29N3O3	419.52	brown	125ċ	70	0.51



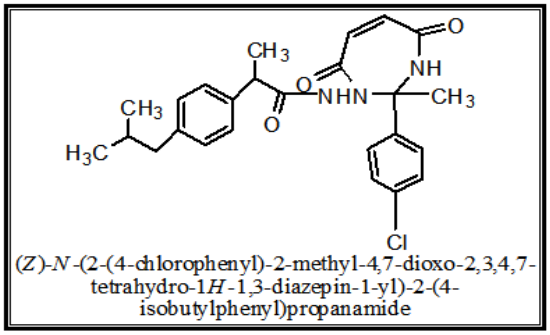
1

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 (o.16)gm.From(H2) dissolved in (30)ml of dry benzene and added (0.02) from vinyl hydrazine and reflex (12)hr. in 65ºc After cooling a precipitate it re-crystallized from ethanol consists Article ……..

TABLE (8). Physical properties of compound.(2)

Moleculer Fon:	M.Wt	Color	MP°c	Yield%	RF
C25H28ClN3O3	453.96	white	103ċ	69	0.48



2

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-¹The package, which is characteristic. When preparation (K1,K2)notes package back to the group C=N in the figure (2,3) shows consist schffe's bases because the package related to C=N notes in (1676,1668) cm-¹ andalso 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 shows consist compounds diazipine because disappear C=O ketones and still C=O amide (1618,1647) cm-¹.whileDiagnosed compounds preparedin ^{1}H-NMRwe notes single sign in the(2.5)ppmrelated to solvents' proton .and notes poly single (7.9-7.7-7.6-7.5) ppmrelated to ring phenyls proton. And notes single sign6. 79ppm related to ring oxazipine (CH=CH) .while amid 'sproton appear single sign in (8.066ppm).

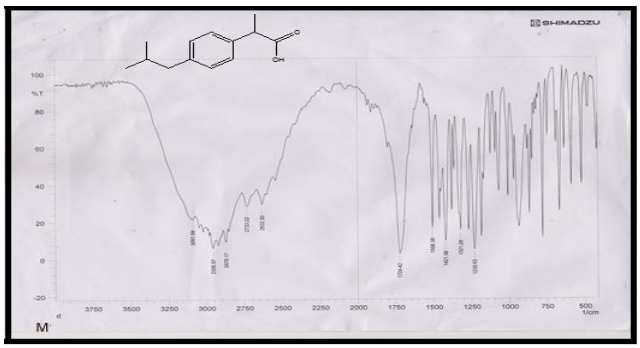


Figure (1) FT-IR Spectra of Ibuprofen.

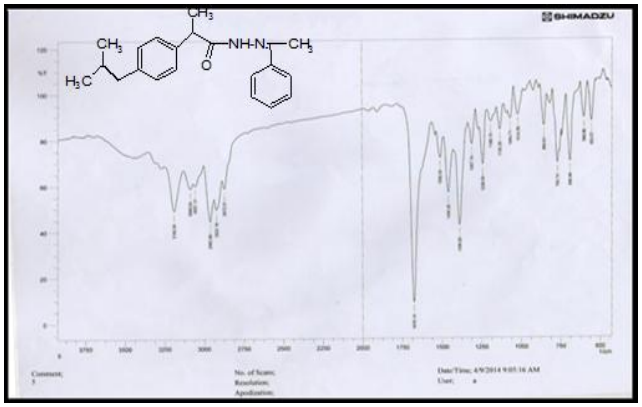


Figure (2) FT-IR Spectra of compound (K1).

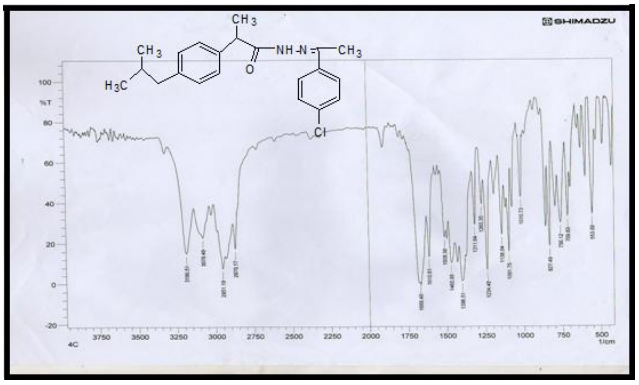


Figure (3) FT-IR Spectra of compound (K2).

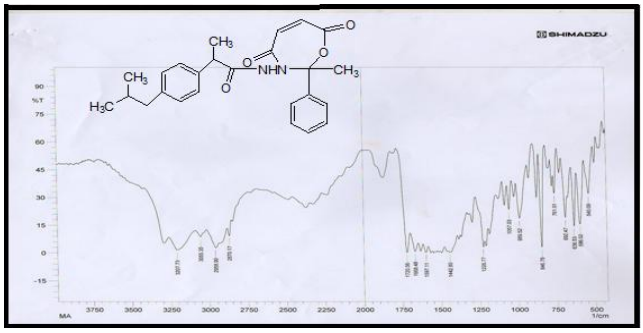


Figure (4) FT-IR Spectra of compound (H1).

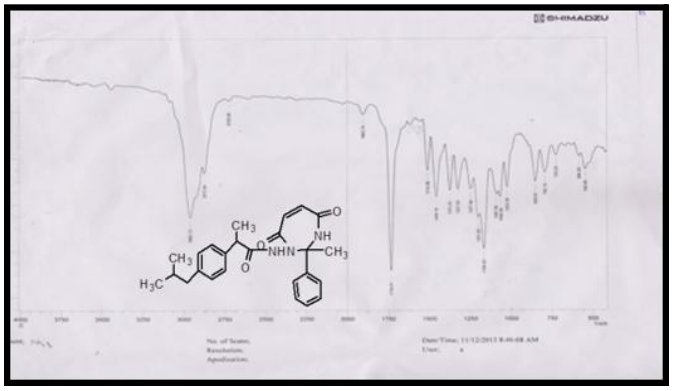


Figure (5) FT-IR Spectra of compound (1).

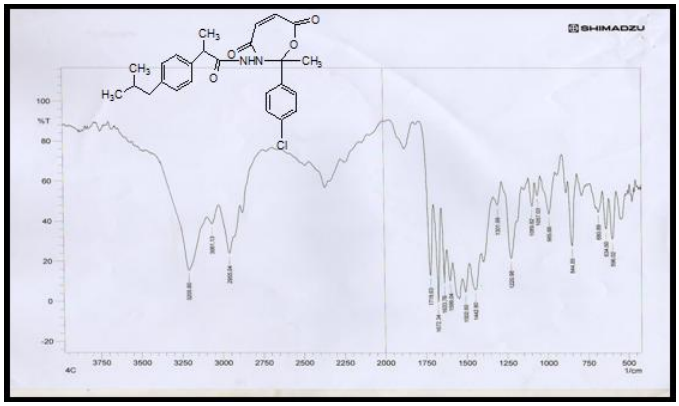


Figure (6) FT-IR Spectra of compound (H2).

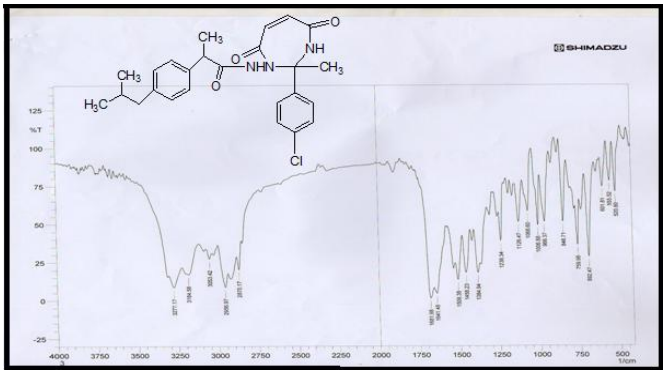


Figure (7) FT-IR Spectra of compound(2).

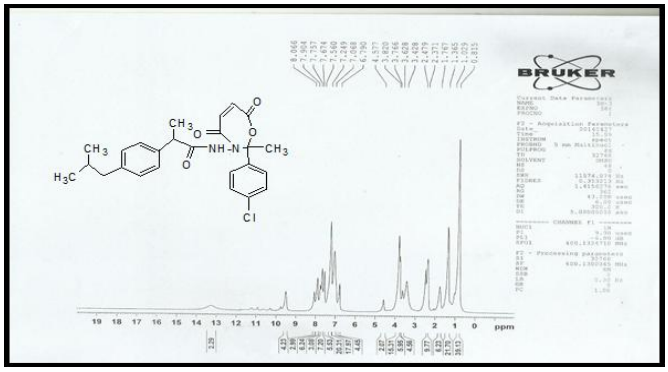


Figure (8) H-NMR for compound (H2).

Reference

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