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Synthesis and Characterization of 1, 3, 4-Oxadiazole Derivatives

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ABSTRACT

1,3,4-oxadiazole is a five member heterocyclic ring which is a very important compound for designing potent bioactive agents. This interesting group of compound has different biological activities such as anti-inflammatory, antimicrobial, anticancer, antitubercular, anticonvulsant, anti-HIV, hypogycemic and antioxidant etc. In the present research work, we have synthesized four newly 1,3,4-oxadiazole derive atives derived from existing NSAID Ibuprofen. The purity of compounds was checked by TLC and melting point. The melting point was determined by open capillary methods and uncorrected. Structure of all four newly synthesized compounds was confirmed by spectral analysis (FTIR, and ^{1}HNMR).

Keywords: Oxadiazole, 1, 3, 4-Oxadiazole derivatives, Heterocyclic, Ibuprofen, Cyclic compound.

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INTRODUCTION

Oxadiazole are widely used in pharmaceutical research to develop active drug substances. Among the all hetrocyclics, 1,3,4-oxadiazole is the very important class in synthetic medicinal chemistry having different biological activities such as anti-inflammatory[1], analgesic[2], antimicrobial[3], anti-HIV[4], anticancer[5], anthelmintic[6], anticonvulsant[7], antiviral[8], hypoglycemic[9], antitubercular[10]. Now we have synthesized some new 1,3,4-oxadiazole derivatives derived from Ibuprofen and characterized with spectral analysis.

MATERIAL AND METHODS

Synthetic studies

The title compounds were synthesized as given in the scheme 1. Ibuprofen was refluxed with absolute ethanol in presence of conc. Sulphuric acid to gave ester of Ibuprofen (I), this on reaction with hydrazine hydrate (99%) in absolute ethanol gave carbohydrazide of ibuprofen (II), this compound was refluxed with CS_2 in ethanol in the presence of KOH gave 1,3,4 - oxadiazole attached with Ibuprofen (III). The title compounds (IVa-d) were synthesized by reaction of III with various amines in presence of formaldehyde.

Spectral studies

The purity of compounds was checked by TLC and melting point. The melting point was determined by open capillary methods and uncorrected. Structure of all four newly synthesized compounds was confirmed by spectral analysis (FTIR, and ^{1}HNMR). The IR and 1H-NMR spectral data are given in the result and discussion part.

RESULT AND DISCUSSION

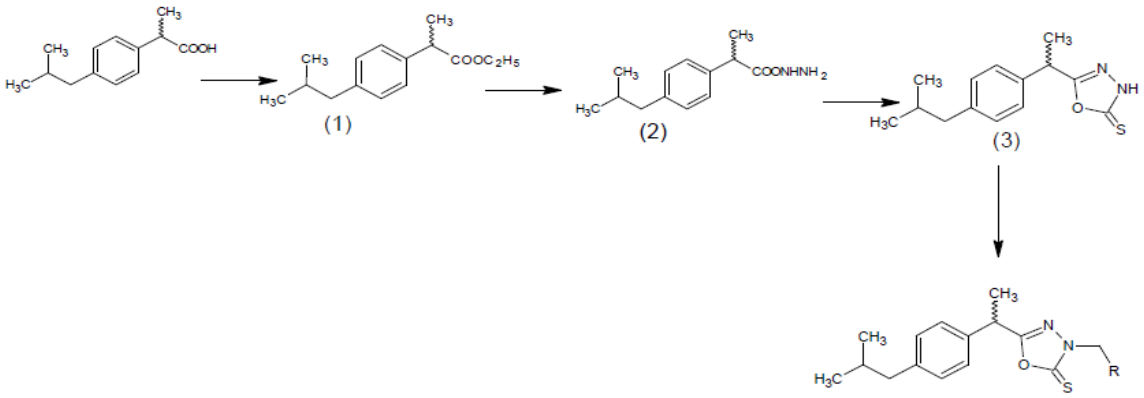
The sequence of the reaction employed for the synthesis of title compounds is outlined in Scheme 1. The physicochemical data and spectral data of the different synthesized compounds are given in Table I and Table II.

The Ibuprofen was converted to its ethyl esters (I) by esterification. The purity of the compound was confirmed by melting point, TLC and structure was confirmed by chemical test, IR and ^{1}HNMR spectral data. IR spectra showed the characteristic peak C-H stretching at 3082 cm^{-1}, C=O at 1730 cm^{-1}, C-O-C at 1238 cm^{-1}, C-Cl at 783 cm^{-1}. This was further supported by ^{1}H-NMR spectral data given in table II. This methyl ester was reacted with hydrazine hydrate, gave carbohydrazide (II). The purity of this compound was confirmed by melting point, TLC and structure was confirmed by IR and ^{1}HNMR spectral data. IR spectra showed the characterstic peak C-H stretching at 3022 cm^{-1}, C=O at 1637 cm^{-1}, C-Cl at 770 cm^{-1}. This was further supported by ^{1}H-NMR spectral data with δ value given in table II. This carbohydrazide was treated with CS_2/ KOH in ethanol gave 1,3,4- oxadiazole ring attached with Ibuprofen (III). The purity of the compound was confirmed by melting point, TLC

and structure was confirmed by IR and ^{1}HNMR spectral data. IR spectra showed the characterstic peak of C-H stretching at 3086 cm^{-1}, C=N at 1503 cm^{-1}, C=S at 1162 cm^{-1}, C-Cl at 777 cm^{-1}. This was further supported by ^{1}HNMR spectral data with δ value given in table II. Treatment of III with various amines in presence of formaldehyde gave the title compounds IVa-d. The purity of these compounds were assessed by melting point, TLC and Structure were confirmed by IR, and ^{1}HNMR data. Physicochemical data and spectral data of the different synthesized title compounds (IVa-d) are given in Table I and Table II.

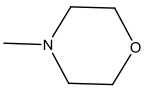
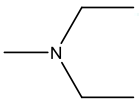
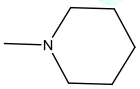
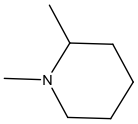
CONCLUSION

The four derivative of 1,3,4-oxadiazole were derived from Ibuprofen by different chemical reaction. All the synthesized compounds were characterized by physiochemical, chromatographically and spectral analysis. The melting point and thin-layer chromatography (TLC) were performed for check purity of the synthesized compounds. Spectral studies i.e. FTIR and ^{1}HNMR were performed for structure confirmation. All four compounds were synthesized with good yield.



Scheme 1

Table I: ***Physico-chemical data of title compounds (IVa-d)***

Compound	R	R	M.P. (°C)	Yield (%)	Rf *
IVa		Morpholine	132-134	74.5	0.30
IVb		Diethyl amine	216-218	69.9	0.41
IVc		Piperidine	102-104	70.7	0.29
IVd		2-Methyl Piperidine	184-186	70.7	0.44

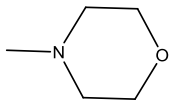
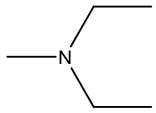
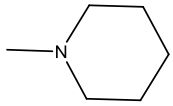
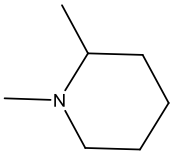
All compounds were recrystallized by methanol.

Stationary phase*- silica gel G.

Mobile phase- ethyl acetate: chloroform (4:1).

Visualizing agent- iodine vapours.

Table II: ***Spectral data of title compounds (IV a-d)***

Compound	R	IR spectra (KBr cm^{-1})	^1H NMR spectra (CDCl3,δ, ppm)
IV a		3068(C-H), 1576(C=N), 1511(C=C), 1312(C=S), 1249(C-O-C).	7.36-7.55(m, 4H, Ar-H), 3.05(s,1H, C-H), 1.93(s, 3H,CH_3), 4.17(s, 2H, CH_2), 2.12 (s, 2H, CH_2), 1.92 (s,1H, CH), 1.12 (t, 6H, CH_3, CH_3 of Ibuprofen), 3.68-3.65(t, 4H,morpholine), 2.79-2.76(t, 4H, morpholine).
IV b		2967(C-H), 1575(C=N), 1501(C=C), 1322(C=S), 1276(C-O-C).	7.66-7.85(m, 4H, Ar-H), 3.15(s,1H, C-H), 1.98(s, 3H,CH_3), 4.55(s, 2H, CH_2), 2.22 (s, 2H, CH_2), 1.97 (s,1H, CH), 1.22 (t, 6H, CH_3, CH_3 of Ibuprofen) , 3.02-2.60(m, 4H, CH_2, CH_2), 1.33-1.30(t, 6H, CH_3, CH_3).
IV c		2926(C-H), 1575(C=N), 1505(C=C), 1352(C=S), 1245(C-O-C).	7.76-7.45(m, 4H, Ar-H), 2.95(s,1H, C-H), 1.98(s, 3H,CH_3), 4.25(s, 2H, CH_2), 2.22 (s, 2H, CH_2), 1.96 (s,1H, CH), 1.12 (t, 6H, CH_3, CH_3 of Ibuprofen), 2.80-2.72(t, 4H, piperidine), 1.64(m, 2H, piperidine), 1.51-1.24(m, 4H,piperidine).
IV d		2942(C-H), 1578(C=N), 1507(C=C), 1299(C=S), 1237(C-O-C).	7.15-7.52(m, 4H, Ar-H), 3.25(s,1H, C-H), 1.96(s, 3H,CH_3), 4.25(s, 2H, CH_2), 2.18 (s, 2H, CH_2), 1.98 (s,1H, CH), 1.17 (t, 6H, CH_3, CH_3 of Ibuprofen), 2.80-2.72(m, 1H, piperidine), 1.74-1.55(m, 6H, piperidine), 1.37-1.35(d, 3H, 2-methyl piperidine), 1.25(m, 2H, piperidine).

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