Research Article

www.pharmaresearchlibrary.com/ijctpr ISSN: 2321-3760

International Journal of Current Trends in Pharmaceutical Research
IJCTPR, 2013: Vol. 1(3): 181-184

Synthesis and Characterization of new Thiazolidinone Derivatives and Screening for their Anti-Inflamatory activity

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Abstract

In the present study, a thiozolidinones derivatives were synthesized by the 1-actynaphthalene. 1-actynaphthalene on brominating with chloroform gives 1-bromoactynaphthalene which was reacted with substituted benzaldehyde thiosemicarbazone in ethanol as a solvent give 4-naphthalen-1-yl-2-{2-[(substituted phenyl) methylidene] hydrazino}-1,3-thiazole. This compound on addition reaction with thioglycolic acid in presence of zinc chloride as a catalyst and dioxane as a solvent gives the final compounds. Their structure has been well characterized by physical and spectral data. The new molecules have been evaluated for their potential anti-inflammatory and analgesic activity. Compound TB1 and TB2 were found to possess anti-inflammatory.

Key words: Thiazolidinones, Anti-inflammatory activity.

Introduction

4-Thiazolidinones are the derivative of thiazole which belongs to five member heterocyclic ring system with multiple applications.[1] 4-Thiazolidinone ring system contains sulphur and nitrogen heterogeneous at position 1 and 3 respectively and ketogroup at position 4.[2] Thiazolidinone derivatives are known to possess several promising pharmacological actions such as antimicrobial[3-5], anti-diabetic[6-8] anticonvulsant[9-10], anti-cancer[11-12] activities, anti-inflammatory[13-15], analgesic[16-17]. Therefore, the investigation of chemistry and biology of these compounds continue to appeal the synthetic and medicinal organic researches.

Chemistry

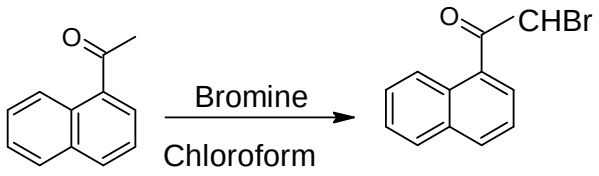
According to the reaction scheme1 two new Thiozolidinone compounds have synthesized and characterized. 1-actynaphthalene on brominating with chloroform gives 1-bromoactynaphthalene which was reacted with substituted benzaldehyde thiosemicarbazone in ethanol as a solvent give 4-naphthalen-1-yl-2-{2-[(substituted phenyl) methylidene] hydrazino}-1,3-thiazole(TA_1-TA_2).This compound on addition reaction with thioglycolic acid in presence of zinc chloride as a catalyst and dioxane as a solvent gives the final compounds.(TB_1-TB_2)

Experimental

Chemistry All the synthesized compounds were purified by recrystallization. Melting points were determined in open capillaries and all uncorrected. IR spectra (KBr pellet technique) were recorded using a Shimadzu spectrophoto meter.

Synthesis of 1-bromoacetyl naphthalene:

1-Acetylnaphthalene (0.02 moles) was taken in 20 mL of chloroform in a 250 mL conical flask. A solution of bromine (0.04 moles) in chloroform was prepared. The bromine solution was added to flask containing 1-acetylnaphthalene solution, drop wise with stirring. The chloroform mixture was distilled on a water bath. The solid obtained was washed with petroleum ether and then recrystallized from benzene yielding 1-bromoacetyl naphthalene.



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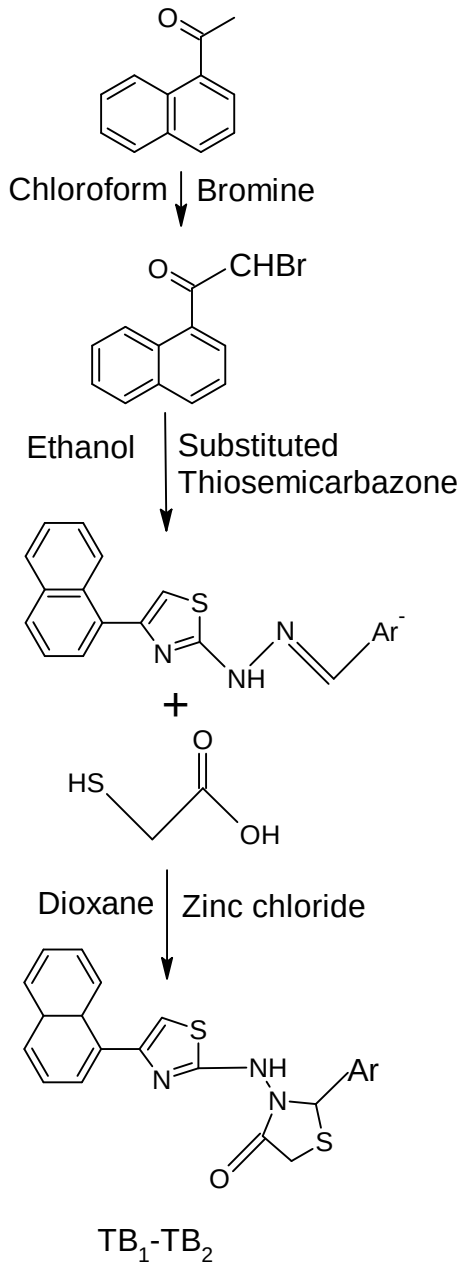
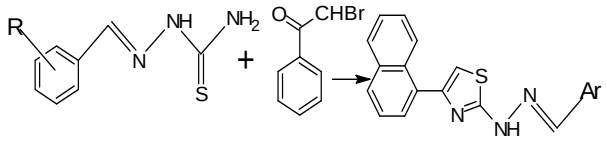
Sceme1:



Synthesis of 4-naphthalen-1-yl-2-{2-[(substituted phenyl) methylidene] hydrazino}-1,3-thiazole:

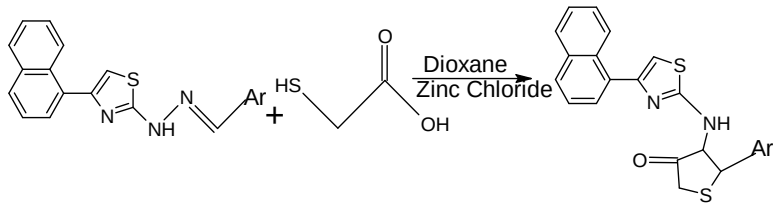
Equimolar quantities (0.01 mole) of 1-bromoacetylnaphthalene and substituted benzaldehyde thiosemicarbazones were dissolved in 50 mL of ethanol in a 100 mL round bottom flask. The reaction mixture was refluxed for 1-2 h. A solid was separated during refluxing which was hot filtered, dried and recrystallized from ethanol yielding 4-naphthalen-1-yl-2-{2-[(substituted phenyl)methylidene]hydrazino}-1,3-thiazole.



4-(naphthalen-1-yl)-2-[(2*E*)-2-(4-nitrobenzylidene)hydrazinyl]-1,3-thiazole(TA1) M.P.:224-225 % Yield :81; IR (KBr) cm-1: 1602(C=C- str),696(CH_2 -S- str),1341(CN str),1590(-C=N- str),1566(NH str),840(1,4-Disubstitution)(para),1512(NO_2 str).4-(naphthalen-1-yl)-2-[(2*E*)-2-(2-nitrobenzylidene)hydrazinyl]-1,3-thiazole (TA2) M.P.:215-216 % Yield :78; IR (KBr)cm-1:1614(C=C-str),696(CH_2-S-str),1338(CNstr),1590(-C=N-str),1554(NHstr),738(1,4 Disubstitution)(ortho),1518(NO_2 str)

General method for synthesis of 4-Thiazolidinone

A mixture of respective thiazole derivative (0.01 mole) and thiomalic acid (0.015 mole) in 25 mL of dioxane was taken in a 100 mL round bottom flask. To this solution 25 mg of $ZnCl_2$ was added and the reaction mixture was refluxed for 6-10 h. The mixture was then poured on crushed ice and solid so obtained was filtered, washed with water, dried and recrystallized from dioxane.



3-{[4-(naphthalen-1-yl)-1,3-thiazol-2-yl]amino}-2-(2-nitrophenyl)-1,3-thiazolidin-4-one (TB1) M.P.:233-234; % Yield :81; IR (KBr) cm-1: 1498(C=C- str),696(CH_2 -S- str),1338(CN str),1350(CN str),1590(-C=N- str),1566(NH str),738(1,4-Disubstitution) (ortho),1518(NO_2 str), 1665(C=O str). 3-{[4-(naphthalen-1-yl)-1,3-thiazol-2-yl]amino}-2-(4-nitrophenyl)-1,3-thiazolidin-4-one (TB2) M.P.: 219-220 % Yield :87; IR (KBr) cm-1: 1608 (C=C- str),690 (CH_2 -S- str),1284(CN str),1320(CN str),1560(NH str),1590(-C=N- str),843(1,4-Disubstitution)(para),1476(NO_2 str) 1716(C=O str)

Pharmacology

Two new compounds of thiozolidinone derivatives have been synthesized following scheme 1.The anti-inflammatory activity of the synthesized compounds were examined. Both the compounds (TB_1-TB_2) showed good anti-inflammatory activity by Carrageenan induced paw edema method.

Pharmacological Study

Anti-inflammatory Activity: The anti-inflammatory activity of new synthesized compound (TB_1-TB_2) revealed that both of the compound exhibited significant anti-inflammatory activity as compared to standard drug diclofinac sodium after ½,1,2hr (Table).

Compound	**Paw volume (ml) Time interval**			
	30min	1hr	2hr	%decrease in paw volume
Control	0.24	0.38	0.45	
Standard	0.23	0.34	0.24	76.33
TB_1	0.21	0.32	0.17	65.61
TB_2	0.22	0.30	0.15	62.61

Results and Discussion

Ant-inflammatory Activity:

The study was aimed at evaluating the anti-inflammatory effect of compounds on rats. Male Wister albino rats weighing between 200-250 gm, 3 per group were used for study. All the drugs, including the standard drug diclofinac sodium were administered i.p. at 50mgkg-1 doses. The anti-inflammatory screening is based upon a comparision of the activity produced by compound to be examined with that of activity produced by known concentration of a standard drug.

Conclusion

From the above result it has been concluded that thiazolidinones derivatives (TB1-TB2) may be used as lead compounds for anti-inflammatory activity and may further be evaluated for toxicological profile.

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