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SYNTHESIS OF SOME NOVEL THIAZOLIDINE DERIVATIVES WITH BENZOTHIAZOLE MOIETY.

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ABSTRACT

As a part of systematic investigation of synthesis of N-[2-(2-chloroquinolin-3-yl)-4-oxo-1, 3-thiazolidin-3-yl]-1, 3-benzothiazole-2-carboxamide V (a-g) was achieved by corresponding manich bases IV (a-g) by reaction with thioglycolic acid. Manich base IV (a-g) was prepared by corresponding quinolene derivative III (a-g) and 1, 3-benzothiazole-2-carbohydrazide II. The synthesized compounds have been characterized by physico-chemical and spectral analysis.

KEYWORDS: Thiazolidine, Benzothiazole, Mannich bases, Zeolite.

INTRODUCTION

Heterocyclic chemistry comprises at least half of all organic chemistry research worldwide. The large numbers of biologically active molecules that contain heterocyclic rings has played important roles in the drug discovery process and exhibit various biological activities. A literature survey identified several thiazolidine derivatives in the development phase as potential new drugs. The versatility of the thiazolidine skeleton, in addition to its relative chemical simplicity and accessibility, makes these chemicals amongst the most promising sources of bioactive compounds. Numerous reports have appeared in the literature highlighting thiozolidine chemistry and its use. Thiazolidine possesses wide range of pharmacological activities viz.antibacterial[1], cytotoxic[2], anti-HIV[3], antiviral[4], anti-inflammatory[5], anti-fungal[6], anticonvulsant[7], antioxidant[8], antitumor[9], antidiabetic[10], antidepressant[11] etc.

Looking at the importance of these heterocyclic nuclei, it is thought of interest to accommodate thiazolidine and 2-aminobenzothiazole moieties in single molecular

framework. In continuation to our research work on thiazolidine derivatives we are reporting the synthesis N-[2-(2-chloroquinolin-3-yl)-4-oxo-1,3-thiazolidin-3-yl]-1,3-benzothiazole-2-carboxamide.

MATERIALS AND METHODS

Melting points of the synthesized compounds were determined by open capillary and are uncorrected. The purity of the compounds was checked using pre-coated TLC plates (MERCK). The developed chromatographic plates were visualized under UV at 254 nm. IR spectra were recorded using KBr on Shimadzu FTIR model 8400 spectrophotometer, ^{1}HNMR spectra was recorded in $CDCl_3$ on a Bruker Topspin-400 MHz instrument using TMS as internal standard.

EXPERIMENTALS

General procedure for synthesis of ethyl-2-benzthiozole carboxylate (I)

The mixture of o-aminothiophenol (0.1 mol) and diethyl oxalate (0.2 mol) reflux for four hour gives ethyl-2-benzthiozole carboxylate (I). The compound was recrystallized with ethanol.

General procedure for synthesis of 1,3-benzothiazole-2-carbohydrazide(II)

To a stirred solution of (I) (0.01 mol) in ethanol, hydrazine hydrate (0.05 mol) added drop wise with constant stirring. This solution is refluxed for six hours. After completion of reaction mixture was cooled, filtered washed with water & compound (II) was collected.

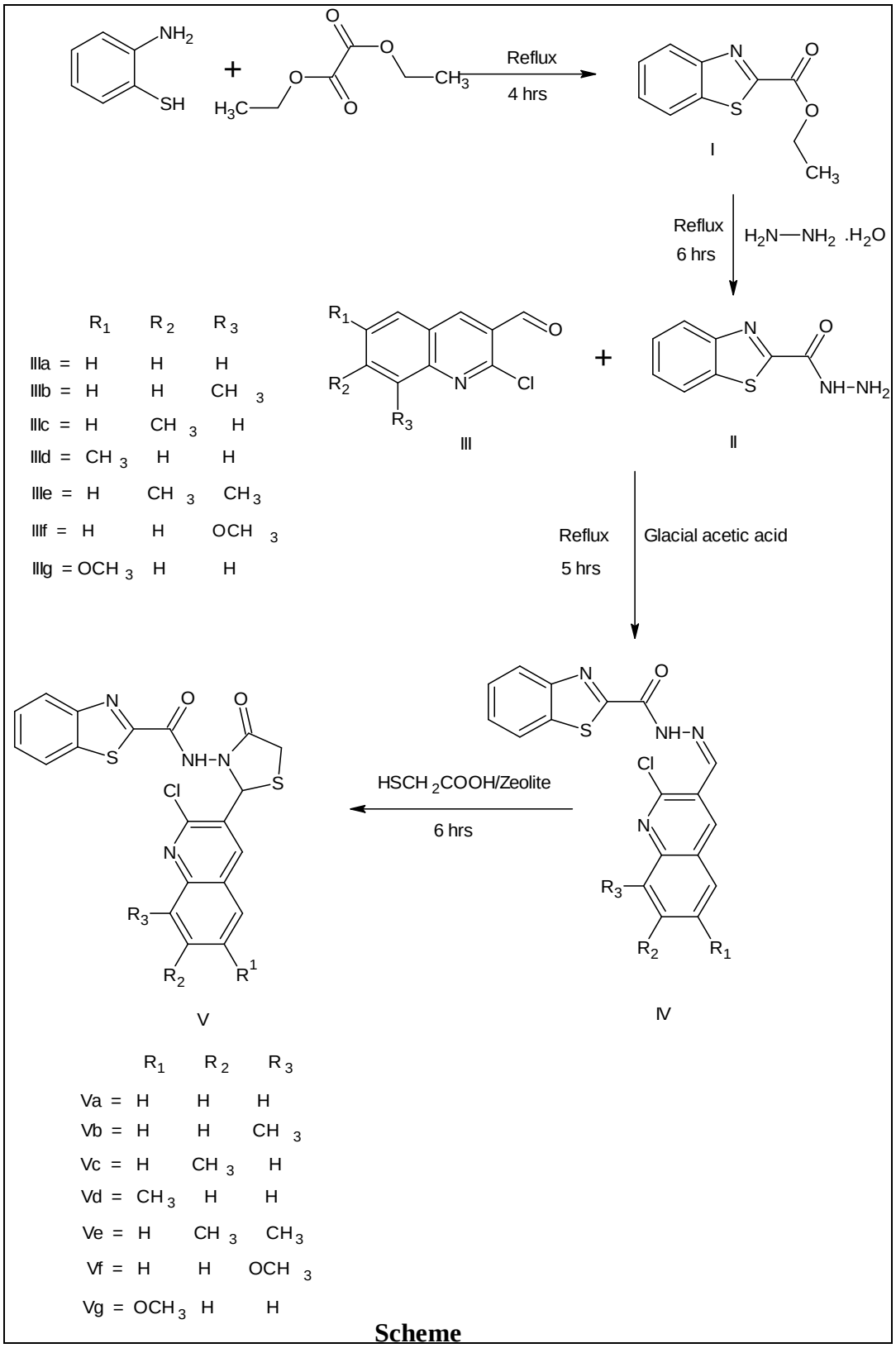
General procedure for synthesis of N'-[(1E)-(3-chloroisoquinolin-4-yl) methylene-1, 3-benzothiazole-2-carbohydrazide IV (a-g)

A mixture of compound (II) (0.01 mol) and 2-methylquinoline-3-carbaldehyde III (a-g) (0.01 mol) in methanol (25 ml) in the presence of catalytic amount of glacial acetic acid was refluxed for 5 hrs. The solvent was removed under reduced pressure and the resulting crude product was purified by passing it through a chromatographic column packed with silica gel using chloroform: methanol (8:2 v/v) as eluant.

General procedure for synthesis of N-[2-(2-chloroquinolin-3-yl)-4-oxo-1, 3-thiazolidin-3-yl]-1, 3-benzothiazole-2-carboxamide V(a-g)

The mixture of compound IV (a-g), (0.01 mol) and thioglycolic acid (0.01 mol) were refluxed in ethanol (25ml) for 6hrs. The solvent was evaporated and the reaction mixture was

neutralized with cold dilute sodium bicarbonate solution, the product formed was filtered off and recrystallized by chloroform to get product V (a-g).



Scheme

Spectral Characterization and elemental analysis of synthesized compounds V(a-g).

N-[2-(2-chloroquinolin-3-yl)-4-oxo-1,3-thiazolidin-3-yl]-1,3-benzothiazole-2-carboxamide [V-a]

IR (cm^{-1}): 3330 (-NH), 3055 (Ar-H), 1665(>C=O, amido), 1650(>C=C<), 754 (Ar-Cl)

^{1}H-NMR (δ, ppm): 4.06-4.34 (2H, s, -CH_2); 5.78 (1H, s, N-CH-S); 7.21-7.84 (5H,m, Ar-H); 7.57-7.90 (4H, m, Ar-H); 9.59 (1H, s, -NH); **Mass**: m/z:-441 (M+), 443 (M++) **MF**:- $C_{20}H_{13}ClN_4O_2S_2$; **Calculated**: C,54.48; H,2.97; Cl,8.04; N,12.71; O,7.26; S,14.54 **Found**: C, 54.34; H, 3.04; N,12.58.

***N*-[2-(2-chloro-8-methylquinolin-3-yl)-4-oxo-1, 3-thiazolidin-3-yl]-1, 3-benzothiazole-2-carboxamide [V-b]**

IR (cm^{-1}): 3334 (-NH), 3059 (Ar-H), 1667(>C=O, amido), 1648(>C=C<). 754 (Ar-Cl)

^{1}H-NMR (δ, ppm):- 2.67 (3H, s, -CH_3); 4.06-4.34(2H, s, -CH_2); 5.78 (1H, s, N-CH-S) 7.53-7.77 (4H, m, Ar-H); 7.21-7.84 (4H, m, Ar-H); 9.59 (1H, m, -NH). **Mass**: m/z:-455 (M+); (457 M++) MF:$C_{21}H_{15}ClN_4O_2S_2$; **Calculated**: C,55.44; H,3.32; N,12.31 **Found**: C, 55.54; H, 3.26; N, 12.49.

***N*-[2-(2-chloro-7-methylquinolin-3-yl)-4-oxo-1, 3-thiazolidin-3-yl]-1, 3-benzothiazole-2-carboxamide [V-c]**

IR (cm^{-1}): 3334 (-NH), 3059 (Ar-H), 1665(>C=O, amido), 1648(>C=C<), 754 (Ar-Cl)

^{1}H-NMR (δ, ppm):- 2.55 (3H, s, -CH_3); 4.06-4.34(2H, s, -CH_2); 5.78 (1H, s, N-CH-S) 7.15-7.79 (4H, m, Ar-H); 7.21-7.84 (4H, m, Ar-H); 9.59 (1H, m, -NH). Mass: m/z:-455 (M+); (457 M++) **MF**: $C_{21}H_{15}ClN_4O_2S_2$; **Calculated**: C, 55.44; H, 3.32; N, 12.31 **Found**: C, 55.58; H, 3.22; N, 12.54.

***N*-[2-(2-chloro-6-methylquinolin-3-yl)-4-oxo-1,3-thiazolidin-3-yl]-1,3-benzothiazole-2-carboxamide [V-d]**

IR (cm^{-1}): 3330 (-NH), 3055 (Ar-H), 1665(>C=O, amido), 1650(>C=C<), 754 (Ar-Cl)

^{1}H-NMR (δ, ppm):- 2.51 (3H, s, -CH_3); 4.06-4.34(2H, s, -CH_2); 5.78 (1H, s, N-CH-S) 7.46-7.72 (4H, m, Ar-H); 7.21-7.84 (4H, m, Ar-H); 9.59 (1H, m, -NH). Mass: m/z:-455 (M+); (457 M++) MF: $C_{21}H_{15}ClN_4O_2S_2$; **Calculated**: C, 55.44; H, 3.32; N, 12.31 **Found**: C, 55.55; H, 3.27; N, 12.44.

***N*-[2-(2-chloro-7,8-dimethylquinolin-3-yl)-4-oxo-1,3-thiazolidin-3-yl]-1,3-benzothiazole-2-carboxamide [V-e]**

IR (cm^{-1}): 3330 (-NH), 3055 (Ar-H), 1665(>C=O, amido), 1650(>C=C<), 754 (Ar-Cl)

^{1}H-NMR (δ, ppm):- 2.58 (3H, s, -CH_3); 3.27 (3H, s, -CH_3) 4.06-4.34(2H, s, -CH_2); 5.78 (1H, s, N-CH-S); 7.21-7.84 (4H, m, Ar-H); 7.25 (1H, d, Ar-H); 7.45 (1H, d, Ar-H); 7.72 (1H, s, Ar-H); 9.59 (1H, m, -NH). **Mass**: m/z:- 455 (M+); (457 M++) **MF**: $C_{22}H_{17}ClN_4O_2S_2$; **Calculated**: C,56.34; H,3.65; N,11.95 **Found**: C, 56.44; H, 3.52; N, 12.14.

***N*-[2-(2-chloro-8-methoxyquinolin-3-yl)-4-oxo-1,3-thiazolidin-3-yl]-1,3-benzothiazole-2-carboxamide [V-f]**

IR (cm^{-1}): 3330 (-NH), 3055 (Ar-H), 1665(>C=O, amido), 1650(>C=C<), 754 (Ar-Cl)

^{1}H-NMR (δ, ppm):- 3.93 (3H, s, -OCH_3); 4.06-4.34(2H, s, -CH_2); 5.78 (1H, s, N-CH-S); 7.10-7.72 (4H, m, Ar-H); 7.21-7.34 (4H, m, Ar-H); 9.31 (1H, m, -NH). **Mass**: m/z:- 471 (M+); (473 M++). **MF**: $C_{21}H_{17}ClN_4O_3S_2$; **Calculated**: C, 53.56; H, 3.21; N, 11.90 Found: C, 53.44; H, 3.12; N, 11.86.

***N*-[2-(2-chloro-6-methoxyquinolin-3-yl)-4-oxo-1, 3-thiazolidin-3-yl]-1,3-benzothiazole-2-carboxamide [V-g]**

IR (cm^{-1}): 3330 (-NH), 3055 (Ar-H), 1665(>C=O, amido), 1650(>C=C<), 754 (Ar-Cl)

^{1}H-NMR (δ, ppm):- 3.90 (3H, s, -OCH_3); 4.06-4.34(2H, s, -CH_2); 5.78 (1H, s, N-CH-S); 6.99-7.72 (4H, m, Ar-H); 7.21-7.34 (4H, m, Ar-H); 9.31 (1H, m, -NH). **Mass**: m/z: - 471 (M+); (473 M++) MF: $C_{21}H_{17}ClN_4O_3S_2$; **Calculated**: C, 53.56; H, 3.21; N, 11.90 **Found**: C, 53.54; H, 3.27; N, 11.94.

Table No.-I: Physical data of synthesized compounds IV (a-g) -V (a-g).

Compound No.	R_1	R_2	R_3	M.P. ^{0}C	Yeild %	MW
IVa	H	H	H	180	62	441
IVb	H	H	CH_3	210	58	455
IVc	H	CH_3	H	209	56	455
IVd	CH_3	H	H	189	64	455
IVe	H	CH_3	CH_3	202	68	469
IVf	H	H	OCH_3	187	57	471
IVg	OCH_3	H	H	178	59	471
Va	H	H	H	201	70	441
Vb	H	H	CH_3	189	65	455
Vc	H	CH_3	H	188	64	455
Vd	CH_3	H	H	180	69	455
Ve	H	CH_3	CH_3	209	63	469
Vf	H	H	OCH_3	201	69	471
Vg	OCH_3	H	H	183	75	471

RESULT AND DISCUSSION

I synthesized new thiazolidene derivatives from quinolene derivative and 1, 3-benzothiazole-2-carbohydrazide. The mixture of o-aminothiophenol reflux with diethyl oxalate gives ethyl-2-benzthiozole carboxylate. This compound reacts with hydrazine hydrate gives 1, 3-benzothiazole-2-carbohydrazide. 2-methylquinoline-3-carbaldehyde reflux with 1,3-benzothiazole-2-carbohydrazide gives N'-[(1E)-(3-chloroisoquinolin-4-yl) methylene-1, 3-benzothiazole-2-carbohydrazide. This compound on reacting with thioglycolic acid formed product N-[2-(2-chloroquinolin-3-yl)-4-oxo-1, 3-thiazolidin-3-yl]-1, 3-benzothiazole-2-carboxamide. The yield of compounds found to be in the range of 60-80%. The products were characterized by elemental analysis, IR, NMR and mass spectroscopy.

CONCLUSION

In conclusion, I have demonstrated a simple and efficient protocol for the synthesis of thiazolidene derivatives with benzothiazole moiety. The method is very simple, clean and yield of the products are good.

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