



Research Article

ANTIOXIDANT ACTIVITY OF NOVEL 4-OXO-AZETIDINE DERIVATIVES SYNTHESIZED FROM SCHIFF BASES

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ABSTRACT

The synthesized 4-Oxo-Azetidines which are established by spectral and analytical data are evaluated for their antioxidant activity. The activity of all compounds is identified by using nitricoxide and superoxide radical scavenging methods against Alkaline Dimethyl Sulphoxide (DMSO). The derivatives with chlorine substituent either at ortho or para on phenyl ring exhibited maximum activity in both methods. Least activity is shown by the compound having ortho nitro group on benzene ring.

Keywords: 4-Oxo- Azetidine, Schiff base, Antioxidant activity.

INTRODUCTION

4-oxo-Azetidines are 4-membered cyclic amides derived from Schiff bases which contain β -lactam unit as an essential structural feature of its molecule¹. Monocyclic Azetidinones are usually referred to as Azetidin-2-ones or 2-oxo azetidine, based on the nomenclature of parent heterocycle, Azetidine. The utility of 4-oxo-Azetidines as synthons for various biologically active compounds, as well as their recognition as cholesterol absorption inhibitors and enzyme inhibitors has given in various studies^{2,3}.

Free radicals are types of Reactive Oxygen Species (ROS), which include all highly reactive oxygen containing molecules^{4,5}. They are capable of attacking the healthy cells of the body, causing them to lose their structure and function. Cell damage caused by the free radicals appears to be a major contribution to aging and degenerative disease of aging such as cancer, cardiovascular diseases, cataract,

immune system decline, liver disease, diabetes mellitus, inflammation, renal failure and brain dysfunction^{6,7}.

EXPERIMENTAL WORK:

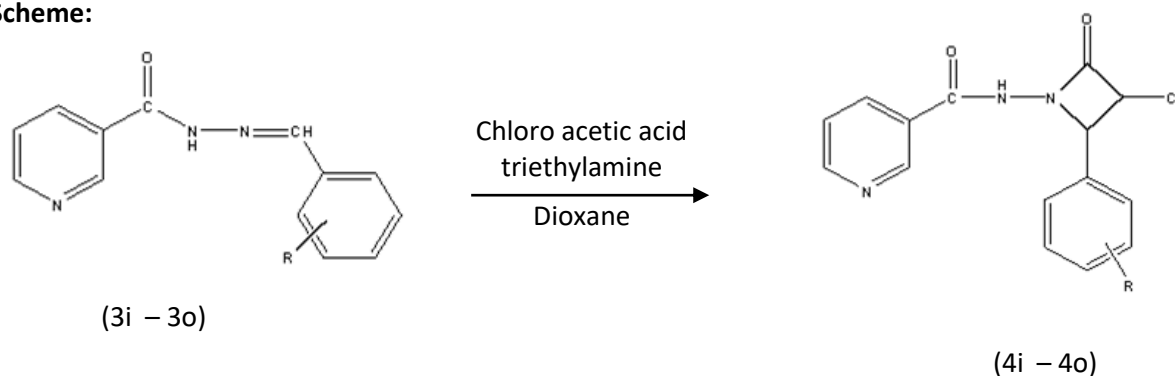
A new series of 4-Oxo-Azetidine derivatives (**4i-4o**) from Schiff bases are synthesized^{8,9}. The Schiff base derivatives on treatment with dioxane and triethylamine afforded targeted compounds (**4i-4o**). The structure of all synthesized compounds has been established on the basis of their spectral (IR, H^1 & C^{13} NMR and Mass) and analytical data. The purity of the compounds was confirmed by TLC. All the synthesized compounds were evaluated for their antioxidant activity.

SCHEME

The list of synthesized compounds (4i– 4o).

4i) N- (3-chloro - 2(4¹-chloro phenyl) -4-oxo-azetidine-1-yl) nicotinamide.

Scheme:



Where R = p-chloro (4i), m-bromo(4j),o-chloro (4k),o-methoxy(4l),o,p-dimethoxy(4m),3¹,4¹,5¹ trimethoxy(4n), o-nitro (4o).

4j) N- (3-chloro -2 (3¹-bromo phenyl) -4-oxo-azetidine-1-yl) nicotinamide

4k) N- (3-chloro -2 (2¹-chloro phenyl) -4-oxo-azetidine-1-yl) nicotinamide

4l) N- (3-chloro -2 (2¹-methoxy phenyl) -4-oxo-azetidine-1-yl) nicotinamide

4m) N- (3-chloro -2 (2¹, 4¹ - dimethoxy phenyl) -4-oxo-azetidine-1-yl) nicotinamide

4n) N- (3-chloro -2 (3¹, 4¹, 5¹ - trimethoxy phenyl) -4-oxo-azetidine-1-yl) nicotinamide

4o) N- (3-chloro -2 (2¹-nitro phenyl) -4-oxo-azetidine-1-yl) nicotinamide

Where R = p-chloro (4i), m-bromo(4j),o-chloro (4k),o-methoxy(4l),o,p-dimethoxy(4m),3¹,4¹,5¹ trimethoxy(4n), o-nitro (4o).

Antioxidant Activity ¹⁰⁻¹³:

All the synthesized compounds (4i-4o) were tested for their in vitro free radical scavenging Nitric oxide (NO) and scavenging of Superoxide radical with the alkaline DMSO method.

Assay of nitric oxide radical scavenging activity¹⁴:

Nitric oxide radical scavenging activity was assayed by using Griess reagent. The reaction mixture contained 5 ml of sample solution and ascorbic acid (standard) of different concentrations (25-200 µg / ml) in standard phosphate buffer solution (pH 7.4) , 5ml of sodium nitroprusside solution (5mM) in standard phosphate buffer (pH 7.4) and incubated for 5 hours at 25°C.

Control was prepared without compound but with an equivalent amount of buffer. Then 0.5ml of the incubation mixture was mixed with 0.5 ml of Griess reagent (Sulphanilamide 1%, o-phosphoric acid 2% and naphthyl ethylene diamine dihydro chloride 0.1%) and the absorbance was measured at 546 nm against blank (DMSO). The experiments were performed in triplicate. From the absorbance the percent of scavenging activity was calculated as follows and the results were shown in **Table 1**.

Scavenging activity (%) =

$$\frac{[(A_{546} (\text{control}) - A_{546} (\text{sample}))]}{A_{546} (\text{control})} \times 100$$

Assay of Superoxide Radical Scavenging Activity¹⁵:

Superoxide radical scavenging activity was assayed by nitro blue tetrazolium system. The reaction mixture containing 0.1ml of nitro blue tetrazolium (1mg/ml in DMSO) and 0.3ml of synthesized compounds (4i-4o) or standard in DMSO was added (1ml of DMSO containing sodium hydroxide 5mM in 0.1 ml of water) to give a final volume of 1.4ml and the absorbance was measured at 560nm against blank (DMSO). The percentage scavenging of superoxide radical was calculated by using above formula. The results were shown in **Table 2**.

RESULTS AND DISCUSSION:

The nitric oxide assay has been widely used to evaluate the free radical scavenging effectiveness of various antioxidant substances.

Table 1: Nitric oxide Radical Scavenging activity for 4-oxo- Azeti

S.No	Conc. (µg/ml)	STD.	CTRL.	4i	4j
1.	25	23.08	6.01	10.86	07.42
2.	50	34.64	6.01	21.67	07.42

Nitric oxide generated as a result of decomposition of sodium nitroprusside in aqueous medium, interacts with oxygen at physiological pH to produce nitrite ions, which are measured by using Griess reagent. The nitrite ions were subjected to diazotization followed by azo coupling reaction

to yield an azo dye, measured by an absorption band at 546nm. The scavenging ability of the synthesized compounds was compared with ascorbic acid as a standard. Compounds **4k** & **4m** produced better scavenging ability (Table-1). Compounds **4i**, **4j**, **4l** and **4m** showed moderate radical scavenging activity and **4o** compound showed least activity when compared to standard.

Even though superoxide radical is a weak oxidant, it gives rise to the generation of powerful and dangerous hydroxyl radical along with single oxygen, both of them lead to oxidative stress.

The experimental results suggest that **4k** showed better scavenging activity whereas **4i**, **4j** & **4n** exhibited moderate activity. Least activity is identified for the compounds **4l**, **4m** & **4o**.

CONCLUSIONS

4-Oxo- Azetidines exhibited significant to moderate activity when compared with standard ascorbic acid. Strong antioxidant activity was observed for N- (3-chloro -2 (2'-chloro phenyl) -4-oxo-azetidine-1-yl) nicotinamide (**4k**) in both methods. The antioxidant capacity of the compounds were found to be 8.02 to 90.12 for different concentrations (25-200 µg/ml).

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