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ARTICLE

An Atom Economical Concise Green Synthetic Protocol for the Synthesis of 4-Substituted Benzylidene β-Lactams Easy Access by P_2O_5/SiO_2 Catalyzed Schiff Base

Neha Mishra, Takallum Khan, Himanshu Pandey, Kaushal Kumar, Pankaj Kosti, Mithun Kori and Ritu Yadav✉

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ABSTRACT

A simple and efficient protocol for the synthesis of Schiff bases *via* condensation reaction of electron rich heterocyclic amines with electrophilic carbon of the carbonyl compound. Recently an impressive and important area in catalysis involved organic synthesis is the best implementation of Lewis acids as a acid catalyst for Schiff base synthesis. The higher acidic property and proper loading of catalyst leads to proper participation in reaction as a catalyst. The reactions of these Lewis acids are enhanced by porous solid support as heterogeneous catalyst. We report herein an efficient concise green synthesis of a new kind of β-lactam derivatives of 2-amino-6-nitro-benzothiazole *via* SiO_2/P_2O_5 Lewis acid catalyzed Schiff bases. The reaction was carried out by the preparation of Schiff base through the condensation reaction of various aromatic aldehydes with substituted aromatic amines in the presence of P_2O_5/SiO_2 under green conditions by simple conventional methods. Further this Schiff base used for the green synthesis of β-lactams by the reaction with chloro-acetyl chloride. The advantage of this reaction is good dispersion of active reagent sites, associated selectivity and easier work up with reusable catalyst. These qualities combined together prove these processes as truly eco-friendly green protocol with high product yields and short reaction time.

KEYWORDS

Schiff bases, β-Lactams (2-azetidinone), Heterogeneous catalyst, Green synthesis.

INTRODUCTION

Heterocyclic compounds possess special reactivity especially nitrogen and sulphur atoms bearing congeners provide a unique and versatile approach for synthetic chemistry. The synthesis of heterocyclic compounds has become a cornerstone of synthetic organic chemistry. Among these the nitrogen and sulphur containing heterocyclic thiazole derivatives represents a pharmaceutical important class of compounds because of their diverse range of biological activities such as antifungal, antibacterial, antitumor, cytotoxic activities and therapeutic potentiality [1].

β-Lactams have a long and golden history in the field of antibacterial chemistry so these are still the main part of drug for treatment of infectious diseases caused by bacteria [2]. On

Author affiliations:

Synthetic Organic Chemistry Laboratory, Department of Chemistry, Dr. Hari Singh Gour Vishwavidyalaya, Sagar-470003, India

✉To whom correspondence to be addressed:

E-mail: nmishra1106@gmail.com

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the basis of other view of biological activities, the importance of β-lactams (2-azetidinone) as synthetic intermediates has been widely recognized in the preparation of various heterocyclic compounds of biological significance [3], for example, in the production or semi-synthesis of taxol and taxotere [4]. Nowadays β-lactams (azetidin-2-ones) have played a vital role in medicinal chemistry and many structural variants have been prepared and elaborated [5].

Heterocyclic Schiff bases have been the fascinating area of research due to their diverse chemical reactivity's and prominent antimicrobial properties. Moreover, *in vitro* antimicrobial behaviour of Schiff bases motivates the research investigations for enormous biological utilization. Various methodologies and routes have been developed for the synthesis of Schiff bases, but these have some limitations such as low yield and long reaction time [6,7]. In recent years environmentally benign synthetic methods have received considerable attention and some Lewis acid catalyzed protocols have been developed [8]. Organic reactions under the presence of heterogeneous catalyst have gained in popularity in last few decades.

In present work, we report the synthesis of new Schiff base in the presence of heterogeneous catalyst under the green aspect of carrying out environmentally benign processes with high yields. This process is far more superior to conventional methods. P_2O_5/SiO_2 has received considerable attention because of its own advantages, catalytic and storage property, inexpensive, highly reactive used in various organic transformations affording with the corresponding products in excellent yields and high selectivity [9,10]. P_2O_5/SiO_2 heterogeneous catalyst can be recycled and reused efficiently without much loss of its catalytic property [11]. Benzothiazole incorporated Schiff base exhibited prominent antimicrobial activity which we have published in our previous work [12].

Herein, we introduced phosphorus-pentoxide supported on silica gel as a heterogeneous catalyst for the first time for the synthesis of 2-oxo-4-substituted aryl-azetidine scaffold using our synthesized Schiff base under green solvent conditions (**Schemes I** and **II**). This heterogeneous catalysis allows the isolation of the catalytic sites, avoiding another interaction. So the heterogeneous catalyst can be easily separated and reused. These reactions are environmentally friendly. These methods represent a new, efficient and facile procedure for the synthesis of benzothiazole incorporated 2-oxo-4-substituted aryl-azetidine (β-lactams) compounds with high product yields which can be very significant. The structures of all the newly synthesized compounds were confirmed by elemental analysis, IR, ^{1}H NMR, ^{13}CNMR.

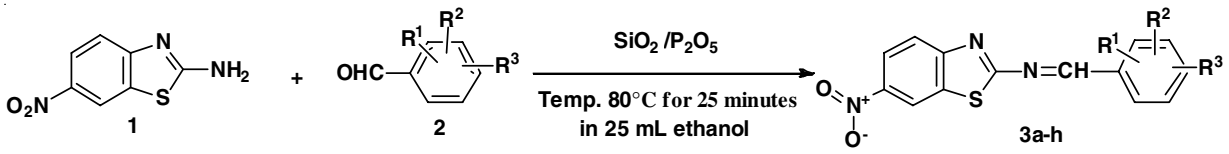
EXPERIMENTAL

All the melting points were determined in open capillaries and are uncorrected. The IR spectra were recorded on Shimadzu FT-IR 8300 spectrophotometer. Samples were prepared by finely dispersing powder material on a KBr disc. ^{1}H NMR and ^{13}C NMR spectra were measured on a Brucker DRX-300 spectrometer in DMSO-d_6 at 300 MHz and 100 MHz, respectively using TMS as an internal standard. Chemical shifts reported on δ scales. The purity of the compounds was checked by thin layer chromatography (TLC) on silica gel (G-60 mesh) using chloroform: methanol as an eluent. Synthesized sample were purified by column chromatography using silica gel (230-400 mesh). All other chemicals were purchased from Sigma-Aldrich and the reagent grade chemicals were purchased from commercial sources and further purified before use.

Preparation of silica-supported P_2O_5 catalyst: SiO_2/P_2O_5 was prepared by following the literature protocol [13]. All the catalysts were prepared by simple impregnation combination method of silica with phosphorous pentoxide. For this purpose, the mixture of 6 g support (silica) was impregnated with 1 g of P_2O_5 by simple stirring, mixing and grinding method then after the impregnated reagent was heated and dried in an oven at 120 °C, then the solid was calcined in a muffle furnace at designated temperatures for 3 h before use for the reaction. The obtained homogeneous mixture, free flowing, white powdery substance is sensitive towards moisture and thus should be stored in a sealed flask in a dedicator for later use. The exact loading of P_2O_5 at the surface of silica was identified by IR and SEM micrograph studies and prepared catalyst was then used for further catalytic studies [11].

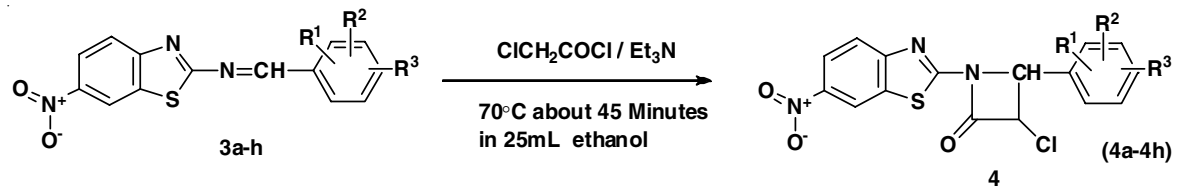
General procedure for the synthesis of Schiff base and 2-oxo-4–substituted aryl-azetidine derivatives

Step-1: SiO_2/P_2O_5 catalyzed method for the synthesis of Schiff base (3a-h): A mixture of the 2-amino-6-nitro-benzothiazole (0.01) and different aromatic benzaldehydes (0.01)



R^1 = 3-CH_3 = 4-CH_3' R^2= (2-OCH_3 = 4-OCH_3 = 3,4,5 tri OCH_3); R^3= X (2,4 Di Chlro = 2-Br = 3-Br)

Scheme-I: Synthetic route of SiO_2/P_2O_5 catalyzed Schiff base condensation in green conditions



R^1 = 3-CH_3 = 4-CH_3; R^2= (2-OCH_3 = 4-OCH_3 = 3,4,5 tri OCH_3); R^3= X (2,4 Di Chlro = 2-Br = 3-Br)

Scheme-II: Synthesis of benzothiazole incorporated β-lactams *via* synthesized Schiff base

and 0.025 g of (7% w/w) SiO_2/P_2O_5 were mixed thoroughly using a mortar and pestle. The reaction mixture was then transferred to an open Pyrex 100 mL round bottom flask and heated at 80 °C for 25 min in 25 mL ethanol After completion of the reaction (monitored by TLC using hexane and ethyl acetate (9:1 v/v) as eluent), the reaction mixture was cooled to room temperature and ethyl acetate was added (5 mL). The reaction mixture was filtered to remove the catalyst and concentrated to furnish products, the resulting product was purified by passing it through a chromatographic column packed with silica gel using chloroform/methanol (8:2 v/v) as eluant. After it purified product was recrystallized from chloroform, to give compound (**3a-h)** in excellent yield. The compounds (**3a-h)** was identified by spectrophotometric analysis.

[*N*-(2,4-Dichlorobenzylidene)-6-nitrobenzothiazole-2-amine (3a): m.f.: $C_{14}H_7N_3O_2SCl_2$, light yellow powder, the structure was established on the basis of spectral analysis. IR (KBr, ν_{max}, cm^{-1}): 1588 (C=N aromatic), 663 (C-S-C), 1616 (C=N *str.*, Schiff base), 827 (C-Cl). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.43 (s, 1H of azomethine), 7.32 (s, H, Ar-H of benzylidene), 7.41-7.42 (d, Ar-H, benzylidene), 8.92 (s for benzothiazole Ar), 8.74-8.73 (d for benzothiazole Ar). ^{13}C NMR ($CDCl_3$, 100 MHz): 119.3-154.9 (C of benzothiazole ring), 160.0 (N=CH, azomet), 174.6 (C of S-C=N of benzothiazole ring), 144.5 (C-NO_2 of benzothiazole), 127.1-129.1 (C of benzylidene ring) in the δ ppm ranges. All these fact collectively suggest the successful synthesis of compound **3a**.

[*N*-(2-Bromobenzylidene)-6-nitrobenzothiazole-2-amine (3b): m.f.: $C_{14}H_8N_3O_2SBr$, brownish crystals. IR (KBr, ν_{max}, cm^{-1}): 1584 (C=N aromatic), 610 (C-S-C) 1618 (C=N *str.*, Schiff base), 1368, 1512 (C-NO_2 sym., asym). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.46 (s, 1H of azomethine), 7.70-7.54 (m, H, Ar-H of benzylidene), 8.31 (s for benzothiazole Ar), 8.60 (d for benzothiazole aromatic ring). ^{13}C NMR ($CDCl_3$, 100 MHz): 121.4-154.6 (Ar), 160.02 (N=CH, azomet), 174.2 (C of S-C=N of benzothiazole ring), 144.2 (C-NO_2 of benzothiazole) in the δ ppm ranges.

[*N*-(3-Bromobenzylidene)-6-nitrobenzothiazole-2-amine (3c): m.f.: $C_{12}H_{12}N_5OSBr$, light red powder. IR (KBr, ν_{max}, cm^{-1}): 1582 (C=N aromatic), 1615 (C=N *str.*, Schiff base), 612 (C-S-C) 1365, 1510 (C-NO_2 sym., asym). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.46 (s, 1H of azomethine), 7.82-7.40 (m, H, Ar-H of benzylidene), 8.01 (s for benzothiazole Ar), 8.64 (d for benzothiazole aromatic ring). ^{13}C NMR ($CDCl_3$, 100 MHz): 121.4-154.4 (Ar), 160.01 (N=CH, azomet), 174.4 (C of S-C=N of benzothiazole ring), 144.0 (C-NO_2 of benzothiazole) in the δ ppm ranges.

[*N*-(4-Methylbenzylidene)-6-nitrobenzothiazole-2-amine (3d): m.f.: $C_{15}H_{11}N_3O_2S$, yellow powder.IR (KBr, ν_{max}, cm^{-1}): 1612 (C=N *str.*, Schiff base), 1580 (C=N aromatic), 609 (C-S-C) 1368, 1514 (C-NO_2 sym., asym). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.42 (s, 1H of azomethine), 7.68-7.26 (m, H, Ar-H of benzylidene), 2.32 (s, for 3H of 4-CH_3) 8.02 (s for benzothiazole Ar), 8.64 (d for benzothiazole aromatic ring). ^{13}C NMR ($CDCl_3$, 100 MHz): 21.20 (C of 4-CH_3) 121.2-154.6 (aromatic C), 160.0 (N=CH, azomet), 174.2 (C of S-C=N of benzothiazole ring), 144.2 (C-NO_2 of benzothiazole) in the δ ppm ranges.

[*N*-(3-Methylbenzylidene)-6-nitrobenzothiazole-2-amine (3e): m.f.: $C_{15}H_{11}N_3O_2S$, dark yellow powder.IR (KBr, ν_{max}, cm^{-1}): 1614 (C=N *str.*, Schiff base), 1581 (C=N aromatic), 609 (C-S-C) 1368, 1514 (C-NO_2 sym., asym). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.48 (s, 1H of azomethine), 7.68-7.27 (m, H, Ar-H of benzylidene), 2.34 (s, for 3H of 3-CH_3) 8.31 (s, for benzothiazole Ar), 8.62 (d, for benzothiazole aromatic ring). ^{13}C NMR ($CDCl_3$, 100 MHz): 21.4 (C of 4-CH_3) 121.3-154.8 (aromatic C), 160.0 (N=CH, azomet), 174.5 (C of S-C=N of benzothiazole ring), 144.2 (C-NO_2 of benzothiazole) in the δ ppm ranges.

[*N*-(2-Methoxybenzylidene)-6-nitrobenzothiazole-2-amine (3f): m.f.: $C_{15}H_{11}N_3O_3S$, amorphous yellow powder.IR (KBr, ν_{max}, cm^{-1}): 1615 (C=N *str.*, Schiff base), 1582 (C=N-aromatic), 609 (C-S-C) 1368, 1516 (C-NO_2 sym., asym). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.46 (s, 1H of azomethine), 7.75-7.06 (m, Ar-H of benzylidene), 3.84 (s, for 3H of 2-OCH_3) 8.32 (s, for benzothiazole Ar), 8.62 (d, for benzothiazole aromatic ring). ^{13}C NMR ($CDCl_3$, 100 MHz): 55.6 (C of 2-OCH_3) 111.3-157.8 (C, of aromatic ring), 161.0 (N=CH, azomet), 174.6 (C of S-C=N of benzothiazole ring), 144.2 (C-NO_2 of benzothiazole) in the δ ppm ranges.

[*N*-(4-Methoxybenzylidene)-6-nitrobenzothiazole-2-amine (3g): m.f.: $C_{15}H_{11}N_3O_3S$, light yellow powder. IR (KBr, ν_{max}, cm^{-1}): 1615 (C=N *str.*, Schiff base), 1582 (C=N aromatic), 607 (C-S-C) 1368, 1514 (C-NO_2 sym., asym). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.48 (s, 1H of azomethine), 7.85-7.08 (m, Ar-H of benzylidene), 3.82 (s, for H of 4-OCH_3) 8.32 (s, for benzothiazole Ar), 8.62 (d for benzothiazole aromatic ring). ^{13}C NMR ($CDCl_3$, 100 MHz): 55.8 (C of 4-OCH_3), 111.2-156.8 (C of aromatic ring), 160.2 (N=CH azomet), 174.6 (C of S-C=N of benzothiazole ring), 144.3 (C-NO_2 of benzothiazole) in the δ ppm ranges.

[*N*-(3,4,5-Trimethoxybenzylidene)-6-nitrobenzothiazole-2-amine (3h): m.f.: $C_{18}H_{16}N_2O_5S$, yellow crystalline powder. IR (KBr, ν_{max}, cm^{-1}): 1612 (C=N *str.*, Schiff base), 1580 (C=N aromatic), 609 (C-S-C) 1365, 1511 (C-NO_2 sym., asym). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.46 (s, 1H of azomethine), 7.14 (s, for Ar-H of benzylidene), 3.83 (s, for 9H of 3, 4, 5 tri-OCH_3), 8.52-8.31 (m for benzothiazole Ar), 8.92 (d for benzothiazole aromatic ring). ^{13}C NMR ($CDCl_3$, 100 MHz): 56.8-60.6 (C of 3,4,5,tri-OCH_3), 104.2-153.8 (C of aromatic ring), 160.01 (N=CH azomet), 98.8 (C of S-C=N of benzothiazole ring), 144.01 (C-NO_2 of benzothiazole) in the δ ppm ranges.

Step-2: Conventional method for the synthesis 2-oxo-4–substituted aryl-azetidine derivatives (4a-h) by using synthesized (3a-h) Schiff base: An equimolar mixture of compound **3a** (0.01) and triethylamine (0.01) in 25 mL ethanol then added chloroacetylchloride (0.01) drop-wise in ice bath then reaction mixture was carried out in 100 mL beaker and heated at 70 °C for about 45 min [14]. The progress of reaction was monitored by TLC using chloroform: methanol (9:1 v/v) as eluent. After that obtained resultant reactant mixture was washed with water filtered and dried to give a product, which was recrystallized from chloroform, to give compounds (**4a-h**). The synthesized compounds were identified by spectrophotometric analysis.

***N*-[{4-(2,4-Dichloro-benzylidene)-3-chloro-2-oxo-azetidine}]-6-nitrobenzothiazole-2-amine (4a):** m.f.:

$C_{16}H_8N_3O_3SCl_3$, m.p.190-195 °C, shiny light yellow crystals, the structure was established on the basis of spectral analysis, IR (KBr, ν_{max}, cm^{-1}): 3065 (Ar-C-H), 1030 (C-N), 1528 (C-NO_2), 1682 (C=O), 739 (C-Cl). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.62 (d, for benzothiazole ring H), 8.32-8.01 (d, for benzothiazole ring proton) 5.44 (s, 1H of CH-Cl), 5.08 (d, 1H, N–CH–Ar), 7.04-7.74 (m, 3H, Ar).^{13}C NMR ($CDCl_3$): 119.5-155.0 (C of aromatic ring), 162.4 (CO of β-lactam ring), 61.6 (CH-Cl of β-lactam ring), 62.5 (N-CH-Ar), 164.3 (S-C-N), 144.2 (C-NO_2 of benzothiazole) in the δ ppm ranges.

***N*-[{4-(2-Bromobenzylidene)-3-chloro-2-oxo-azetidine}]-6-nitrobenzothiazole-2-amine (4b):** m.f.: $C_{16}H_9N_3O_3SBrCl$, m.p. 195-198 °C, light yellow crystals, IR (KBr, ν_{max}, cm^{-1}): 3062 (Ar-C-H), 1031 (C-N), 1526 (C-NO_2 sym., asym), 1686 (C=O), 737 (C-Cl). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.64 (s, for benzothiazole ring H), 8.32-8.01 (m. for benzothiazole ring proton) 5.44 (s, 1H of CH-Cl), 5.08 (d, 1H, N–CH–Ar), 7.16-7.57 (m, 4H, Ar). ^{13}C NMR ($CDCl_3$): 122.2-135.5 (C of aromatic ring), 162.2 (CO of β-lactam ring), 61.2 (CH-Cl of β-lactam ring), 64.5 (N-CH-Ar), 164.5 (S-C-N), 144.4 (C-NO_2 of benzothiazole) in the δ ppm ranges.

***N*-[{4-(3-Bromobenzylidene)-3-chloro-2-oxo-azetidine}]-6-nitrobenzothiazole-2-amine (4c):** m.f.: $C_{16}H_9N_3O_3SBrCl$, m.p. 192-194 °C, yellow crystals. IR (KBr, ν_{max}, cm^{-1}): 3062 (Ar-C-H), 1030 (C-N), 1528 (C-NO_2 sym., asym), 1682 (C=O), 739 (C-Cl). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.62 (s, for benzothiazole ring H), 8.30-8.01 (m, for benzothiazole ring H) 5.43 (s, 1H of CH-Cl), 5.08 (d, 1H, N–CH–Ar), 7.26-7.45 (m, 4H, Ar). ^{13}C NMR ($CDCl_3$): 117.3-132.5 (C of aromatic ring), 162.2 (CO of β-lactam ring), 62.2 (CH-Cl of β-lactam ring), 67.5 (N-CH-Ar), 164.6 (S-C-N), 144.2 (C-NO_2 of benzothiazole) in the δ ppm ranges.

***N*-[{4-(4-Methylbenzylidene)-3-chloro-2-oxo-azetidine}]-6-nitrobenzothiazole-2-amine (4d):** m.f.: $C_{17}H_{12}N_3O_3SCl$, m.p. 185-188 °C, light brown crystals. IR (KBr, ν_{max}, cm^{-1}): 3060 (Ar-C-H), 1029 (C-N), 1523 (C-NO_2 sym., asym), 1682 (C=O), 738 (C-Cl). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.61 (s, for benzothiazole ring H), 8.32-8.01 (m. for benzothiazole ring proton) 5.42 (s, 1H of CH-Cl), 5.06 (d, 1H, N–CH–Ar), 7.14-7.47 (m, 4H, Ar) 2.30 (s, for 3H of 4-CH_3). ^{13}C NMR ($CDCl_3$): 123.2-145.5 (C of aromatic ring), 162.0 (CO of β-lactam ring), 62.2 (CH-Cl of β-lactam ring), 65.3 (N-CH-Ar), 165.3 (S-C-N), 144.2 (C-NO_2 of benzothiazole), 19.10 (C of 4-CH_3) in the δ ppm ranges.

***N*-[{4-(3-Methylbenzylidene)-3-chloro-2-oxo-azetidine}]-6-nitrobenzothiazole-2-amine (4e):** m.f.: $C_{17}H_{12}N_3O_3SCl$, m.p. 182-183 °C, red crystals. IR (KBr, ν_{max}, cm^{-1}): 3062 (Ar-C-H), 1031 (C-N), 1528 (C-NO_2 sym., asym), 1685 (C=O), 732 (C-Cl). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.62 (s, for benzothiazole ring H), 8.34-8.01 (m. for benzothiazole ring proton) 5.45 (s, 1H of CH-Cl), 5.07 (d, 1H, N–CH–Ar), 7.03-7.57 (m, 4H, Ar) 2.34 (s, for 3H of 3-CH_3). ^{13}C NMR ($CDCl_3$): 123.8-143.5 (C of aromatic ring), 162.1 (CO of β-lactam ring), 62.0 (CH-Cl of β-lactam ring), 69.3 (N-CH-Ar), 162.3 (S-C-N), 144.2 (C-NO_2 of benzothiazole), 22.06 (C of 3-CH_3) in the δ ppm ranges.

***N*-[{4-(2-Methoxybenzylidene)-3-chloro-2-oxo-azetidine}]-6-nitrobenzothiazole-2-amine (4f):** m.f.: $C_{17}H_{12}N_3O_4SCl$, m.p. 196-198 °C, red-orange crystals. IR (KBr, ν_{max}, cm^{-1}): 3060 (Ar-C-H), 1033 (C-N), 1528 (C-NO_2 sym., asym), 1682 (C=O), 738 (C-Cl). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.61 (s, for benzothiazole ring H), 8.33-8.01 (m. for benzothiazole ring proton) 5.44 (s, 1H of CH-Cl), 5.04 (d, 1H, N–CH–Ar), 7.13-6.97 (m, 4H, Ar) 3.72 (s, for 3H of 2-OCH_3). ^{13}C NMR ($CDCl_3$): 113.8-153.7 (C of aromatic ring), 162.2 (CO of β-lactam ring), 62.6 (CH-Cl of β-lactam ring), 61.3 (N-CH-Ar), 164.7 (S-C-N), 144.1 (C-NO_2 of benzothiazole), 56.3 (C of 2-OCH_3) in the δ ppm ranges.

***N*-[{4-(4-Methoxybenzylidene)-3-chloro-2-oxo-azetidine}]-6-nitrobenzothiazole-2-amine (4g):** m.f.: $C_{17}H_{12}N_3O_4SCl$, m.p. 195-197 °C, orange crystals. IR (KBr, ν_{max}, cm^{-1}): 3062 (Ar-C-H), 1030 (C-N), 1528 (C-NO_2 sym., asym), 1680 (C=O), 738 (C-Cl). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.62 (s, for benzothiazole ring H), 8.34-8.01 (m. for benzothiazole ring proton) 5.42 (s, 1H of CH-Cl), 4.92 (d, 1H, N–CH–Ar), 7.18-6.92 (m, 4H, Ar) 3.82 (s, for 3H of 4-OCH_3). ^{13}C NMR ($CDCl_3$): 114.8-159.7 (C of aromatic ring), 162.4 (CO of β-lactam ring), 62.1 (CH-Cl of β-lactam ring), 67.3 (N-CH-Ar), 164.8 (S-C-N), 144.2 (C-NO_2 of benzothiazole), 55.3 (C of 4-OCH_3) in the δ ppm ranges.

***N*-[{4-(3,4,5-Trimethoxybenzylidene)-3-chloro-2-oxo-azetidine}]-6-nitrobenzothiazole-2-amine (4h):** m.f.: $C_{19}H_{16}N_3O_6SCl$, m.p. 199-201 °C, light yellow amorphous. IR (KBr, ν_{max}, cm^{-1}): 3061 (Ar-C-H), 1030 (C-N), 1526 (C-NO_2 sym., asym), 1686 (C=O), 738 (C-Cl). ^{1}H NMR (300 MHz) (DMSO-d_6) δ ppm: 8.62 (s, for benzothiazole ring H), 8.34-8.01 (m. for benzothiazole ring proton) 5.42 (s, 1H of CH-Cl), 5.20 (d, 1H, N–CH–Ar), 6.53 (s, 2H, Ar) 3.85 (s, for 9H of 3,4,5,tri-OCH_3). ^{13}C NMR ($CDCl_3$): 104.8-152.7 (C of aromatic ring), 162.3 (CO of β-lactam ring), 62.3 (CH-Cl of β-lactam ring), 68.3 (N-CH-Ar), 164.7 (S-C-N), 144.4 (C-NO_2 of benzothiazole), 56.3- 60.5 (C of 3,4,5,tri-OCH_3) in the δ ppm ranges.

RESULTS AND DISCUSSION

In the present work, benzothiazole bearing azetidine-2-one (**4a-h**) moiety has been prepared (**Schemes I** and **II**). In **Scheme-I**, 2-amino-6-nitrobenzothiazole Schiff base was prepared by the simple condensation method catalyzed by SiO_2/P_2O_5 as a heterogeneous catalyst in green solvent and green condition, further in **Scheme-II**, these synthesized Schiff base **(3a-h)** cyclized to β-lactams (azetidinone) derivatives **(4a-h)** at normal green reaction conditions with quantitative yield (95%).

There is a possibility of formation of imine or azomethine *via* heterogeneous catalyst through Schiff base condensation reaction. It was confirmed by ^{1}H NMR, ^{13}C NMR and IR spectra that the Schiff base condensation reaction possibly done *via* using heterogeneous catalyst in green conditions and after that cyclization reaction takes place at azomethine position (-CH=N-) in high yield. In IR spectra (cm^{-1}) absorption bands at 1584 (C=N- aromatic), 610 (C-S-C), 1612-1618 (C=N *str.*, Schiff base), 1368, 1512 (C-NO_2 sym., asym). In ^{1}H NMR spectra common signals that appear are δ (ppm): a singlet at δ 8.42-8.48 corresponds to Schiff base (azomethine), 8.52-8.31 (m for benzothiazole Ar), 8.92 (d for benzothiazole aro-

matic ring). A multiplet at δ ppm 7.85-7.08 (m, Ar-H of benzylidene) corresponds to aromatic proton. The structures of compounds (**4a-h)** were supported by IR spectra as observed in (**3a-h)** with disappearance of 1612-1618 cm^{-1} for -N=CH- band with appearance of 1680-1686 cm^{-1} for >C=O of azetidinone. The ^1H NMR singlet signals of cyclised azetidinone were observed at δ 5.42 as a singlet, corresponding to -CH-Cl in the ring and δ 5.20 doublet, corresponding to 1H, N–CH–Ar. The other signals observed were same as (**3a-h**). ^{13}C NMR spectral data also supports the formation of compounds (**3a-h**) and (**4a-h**).

Considering the synthetic catalytic utilities of silica oxide supported phosphorous pentaoxide as a condensing catalyst and a dehydrating agent here it was therefore thought worthwhile to incorporate P_2O_5 on the surface of silica oxide with Schiff base condensation for obtaining the azomethine and synthesis of 2-azetidinones (**3a-h**) (Tables 1 and 2). To optimize the reaction conditions, several alternatives were performed.

TABLE-1
REACTION TIME AND YIELDS OF THE SYNTHESIZED SCHIFF BASE *via* SiO_2/P_2O_5 HETEROGENEOUS CATALYST AND BENZOTHIAZOLE

Compd.	6-Nitro-2-amino-benzothiazole + Benzaldehyde derivatives	Time (min)	Yield (%)
3a	2,4-Chlorobenzaldehyde	25	92
3b	2-Bromobenzaldehyde	25	93
3c	3-Bromobenzaldehyde	25	90
3d	4-Methylbenzaldehyde	25	92
3e	3-Methylbenzaldehyde	22	88
3f	2-Methoxybenzaldehyde	22	84
3g	4-Methoxybenzaldehyde	25	94
3h	3,4,5-Trimethoxybenzaldehyde	25	92

TABLE 2
REACTION TIME AND YIELDS OF THE SYNTHESIS OF 2-OXO-4-SUBSTITUTED ARYL-AZETIDINE DERIVATIVES BY USING SYNTHESIZED SCHIFF BASE

Compd.	Reactant Schiff base + Et_3N+ $ClCH_2COCl$	Time (min)	Yield (%)
4a	**3a**	45	87
4b	**3b**	40	85
4c	**3c**	42	92
4d	**3d**	40	80
4e	**3e**	45	87
4f	**3f**	41	95
4g	**3g**	40	92
4h	**3h**	40	94

A series of *N*-[{substituted-benzylidene)-3-chloro-2-oxo-azetidine}]-6-nitrobenzothiazole-2-amine (**4a-h**) (Table-2) were prepared *via* the 2-amino-6-nitro-benzothiazole Schiff base (**3a-h**) which was prepared by the simple heterogeneous catalyzed Schiff base condensation method with different aromatic aldehydes in the presence of SiO_2/P_2O_5 followed by green conditions. Moreover, the four-membered ring azetidinone was prepared by the cyclo-addition of equimolar amount of the azomethines, (**3a-h**) and chloro acetyl chloride in the presence of triethylamine catalyst to give *N*-[{4-(substituted-benzylidene)-3-chloro-2-oxo-azetidine}]-6-nitrobenzothiazole-2-amine. The overall reaction was monitored by thin layer chromatography (TLC) and was found to reach completion in 22-45 min giving 80-94 % yields of the Schiff base and corresponding 2-azetidinones. It was observed in another procedure that when the Schiff base condensation was carried under green condition using the mole proportions of the reactants and SiO_2/P_2O_5. The Schiff base condensation was completed within 25 min at 80 °C and gave 84-94% yields of the Schiff base. This was found to be the better alternative for obtaining Schiff bases as the time required for the completion of the reaction had been reduced. The highly feasible rate can be accounted for the Lewis acid behaviour of SiO_2/P_2O_5which might be helping to enhance the acidic property for reaction medium and also may be working as a dehydrating agent to remove the water formed in the reaction. Finally it is conceivable that further derivatization of such compounds will be of interest with hope to get more selective agents. The great importance of reusability of the catalyst is in the cost reduction of process chemistry. Therefore the reusability of the SiO_2/P_2O_5catalyst was investigated. For that, we performed the condensation of Schiff base using 1 mol of the substrate under the optimized reaction conditions. After the completion of the first cycle, the catalyst was filtered and washed with acetone followed by water and then allowed to evaporate the water in an oven overnight (100 °C) and was used for further reaction of synthesis of azomethine. Surprisingly, the catalyst remained efficient and the reaction afforded with excellent yields up to the 4th run (Table-3, entries 1-4).

TABLE-3
RESUABILITY OF SiO_2/P_2O_5 AS CATALYST IN THE SYNTHESIS OF SCHIFF BASES[a]

Entry	Run	Catalyst (mg)	Time (min)	Yield (%)[b]
1	1st	25	25	92
2	2nd	25	25	90
3	3rd	20	35	90
4	4th	20	45	85

[a]Reaction conditions: 2-Amino-6-nitro-benzothiazole (0.01 mol), different aromatic benzaldehydes (0.01), SiO_2/P_2O_5 , ethanol (25 mL). [b]Isolated yield.

Conclusion

In conclusion, we report a mild and efficient catalyst for the preparation of azomethine *via* Schiff base condensation from 2-amino-6-nitro-benzothiazole with corresponding aromatic aldehydes in presence of green solvent and further those converts into substituted 3-chloro-2-oxoazitidine in good yields with excellent reusability (Fig. 1) and short reaction times. This method is highly selective for the synthesis of azetidinones from catalyzed Schiff bases or azomethine by using green protocol. The use of an eco-friendly, inexpensive and

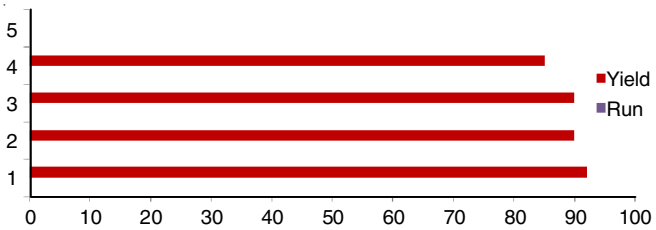


Fig. 1. Reusability of SiO_2/P_2O_5 as catalyst in the synthesis of Schiff base condensation reaction

relatively non-toxic catalyst and also green reagent is another advantage of this method. In contrast to other acid catalysts, storage and handling of this compound do not need special precautions and it can be stored on the bench top for weeks without losing its catalytic activity. Further investigation and new outcomes on the new application of SiO_2/P_2O_5 is on going in our research laboratory.

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