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$POCl_3$ MEDIATED STAUDINGER REACTION OF IMINES WITH KETENES: SYNTHESIS OF MONOCYCLIC β-LACTAM AND 1, 3-OXAZINONE DERIVATIVES

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ABSTRACT

Monocyclic β-lactams commonly referred to as azetidin-2-ones and their derivatives have been extensively explored for their wide biological applications. The present study demonstrates a simple and efficient synthesis of monocyclic β-lactam derivatives via Staudinger reaction, well characterized by FT-IR, ^{1}H, ^{13}C-NMR, mass spectral data and elemental analysis. We also confirmed the formation of highly substituted 1,3-oxazin-4-ones under the same reaction conditions.

Keywords: β-lactams, 1,3-oxazin-4-ones, Staudinger reaction, Cycloaddition.

INTRODUCTION

Numerous methods have been developed for the synthesis of β-lactams which are extensively reviewed in the literature [1,2]. Among them, most commonly used are ketene-imine cyclization [3] (the Staudinger reaction) and ester enolate-imine condensation (the Gilman-Speeter reaction) [4]. The Staudinger reaction which involves [2+2] cycloaddition of ketenes with imines is the most preferred and convenient method for β-lactam synthesis [5-7]. Recently we have reported the synthesis of monocyclic β-lactam and unexpected oxazinones as antibacterial agents [8]. The docking studies of the most active compound with modeled penicillin binding protein-5 (PBP-5) revealed critical H-bond interactions with the active site residues showing the pharmacophoric features of these compounds. Prompted by these findings and in extension to our efforts to synthesize novel biologically active scaffolds [9,10] we employed this flexible and inexpensive approach for the synthesis of *N*-benzyl-3,4-diaryl substituted 2-azitidinone (β-lactam) derivatives and also confirmed the formation of 1,3-oxazin-4-ones (**3q**, **3r**).

EXPERIMENTAL

Chemicals and instruments

All the analytical grade chemicals and solvents were purchased from commercial sources and used without further purification. The IR spectra of compounds were obtained on Agilent Cary 630 FT-IR spectrometer and only major peaks are reported in cm^{-1}. ^{1}H and ^{13}C-NMR spectra were measured in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard on Bruker Spectrospin DPX-300 spectrometer at 300 MHz and 75 MHz, respectively and on Bruker Avance-II 400 spectrometer at 400 MHz. Mass spectra were obtained on AB-Sciex 2000 (Applied Biosystems) electron spray ionization mass spectrometer and on Agilent Ion trap- 63020 LC/MS spectrometer. Melting points were determined on digital Buchi melting point apparatus (M-560) and are uncorrected.

General procedure for the synthesis of imines (2a-2t)

A mixture of aryl aldehyde (1.0 mmol) and substituted benzylamine (1.0 mmol) in anhydrous ethanol was stirred at r.t. for 1-2 h. After completion of the reaction, the compound was extracted with ethyl acetate, washed with brine and dried over anhydrous sodium sulphate to yield the desired compound in good to excellent yield [8]. The R_f values of all the compounds were determined by using (Ethyl

acetate/n-Hexane, 30:70) as solvent system. The characterization of compounds **2a-d**, **2i-j**, **2n**, **2p**, **2r**, **2t** is previously reported [11-17].

(4-Methylbenzylidene)(phenyl)methylamine (2a): Yield: 95%.

(4-Methoxybenzylidene)(phenyl)methylamine (2b): Yield: 97%.

(3,4-Dimethoxybenzylidene)(phenyl)methylamine (2c): Yield: 76%.

((1H-Indol-3-yl)methylene)(phenyl)methylamine (2d): Yield: 94%.

(4-Methylbenzylidene)(4-chlorophenyl)methylamine (2e): White crystalline powder; M.p. 57-59 °C; yield: 89%; R_f = 0.84; IR (neat): ν (cm^{-1}) 1648 (C=N); 773 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.37 (s, 1H, C*H*); 7.69 (d, 2H, *J* = 7.8 Hz, Ar-*H*); 7.32-7.24 (m, 6H, Ar-*H*); 4.78 (s, 2H, CH_2); 2.41 (s, 3H, CH_3); ESI-MS (*m/z*): 244.2 $[M+H]^+$. Anal. calcd. for $C_{15}H_{14}ClN$: C, 73.92; H, 5.79; N, 5.75; found: C, 73.89; H, 5.75; N 5.70%.

(4-Methoxybenzylidene)(4-chlorophenyl)methylamine (2f): Light brown solid; M.p. 49-51 °C; yield: 98%; R_f = 0.78; IR (neat): ν (cm^{-1}) 1641 (C=N); 741 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.34 (s, 1H, C*H*); 7.76 (d, 2H, *J* = 8.2 Hz, Ar-*H*); 7.35-7.15 (m, 4H, Ar-*H*); 6.90 (d, 2H, *J* = 6.42 Hz, Ar-*H*); 4.81 (s, 2H, CH_2); 3.91 (s, 3H, OCH_3); ESI-MS (*m/z*): 260.5 $[M+H]^+$; Anal. calcd. for $C_{15}H_{14}ClNO$: C, 69.36; H, 5.43; N, 5.39; found: C, 69.33 H, 5.40; N, 5.32%.

(3,4-Dimethoxybenzylidene)(4-chlorophenyl)methylamine (2g): Light yellow oil; yield: 78%; R_f = 0.50; IR (neat): ν (cm^{-1}) 1644 (C=N); 810 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.31 (s, 1H, C*H*); 7.48 (s, 1H, Ar-*H*); 7.35- 7.27 (m, 4H, Ar-*H*); 7.21 (d, 2H, *J* = 9.0 Hz, Ar-*H);* 6.91 (d, 1H, *J* = 8.4 Hz, Ar-*H*); 4.77 (s, 2H, CH_2); 3.95 (s, 3H, OCH_3); 3.94 (s, 3H, OCH_3); ESI-MS (*m/z*): 290.5 $[M+H]^+$; Anal. calcd. for $C_{16}H_{16}ClNO_2$: C, 66.32; H, 5.57; N, 4.83; found: C, 66.28; H, 5.52; N, 4.80%.

((1H-Indol-3-yl)methylene)(4-chlorophenyl)methylamine (2h): Reddish brown oil; yield: 95%; R_f = 0.40; IR (neat): ν (cm^{-1}) 3058 (N-H); 1644 (C=N); 747 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 10.07 (s, 1H, N*H*); 8.55 (s, 1H, C*H*), 8.29 (d, 2H, *J* = 8.4 Hz, Ar-*H*), 7.76-7.72 (m, 1H, Ar-*H*), 7.53-7.26 (m, 11H, Ar-*H*), 4.81 (s, 2H, CH_2); ESI-MS (*m/z*): 275.6 $[M+H]^+$; Anal. calcd. for $C_{16}H_{13}ClN_2$: C, 71.51; H, 4.88; N, 10.42; found: C 61.47 H 4.86 N 10.40%.

(4-Methylbenzylidene)(4-methylphenyl)methylamine (2i): Yield: 97%.

(4-Methoxybenzylidene)(4-methylphenyl)methylamine (2j): Yield: 93%.

(3,4-Dimethoxybenzylidene)(4-methylphenyl)methylamine (2k): Yellow oil; yield: 92%; R_f = 0.57; IR (neat): ν (cm^{-1}) 1644 (C=N); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.29 (s, 1H, C*H*); 7.49 (s, 1H, Ar-*H*); 7.26-7.15 (m, 5H, Ar-*H*); 6.89 (d, 2H, *J* = 8.1 Hz, Ar-*H*); 4.77 (s, 2H, CH_2); 3.93 (s, 3H, OCH_3); 3.92 (s, 3H, OCH_3); 2.39 (s, 3H, CH_3); ESI-MS (*m/z*): 270.2 $[M+H]^+$; Anal. calcd. for $C_{17}H_{19}NO_2$): C, 75.81; H, 7.11; N, 5.20; found: C, 75.78; H, 7.08; N, 5.15%.

((1H-Indol-3-yl)methylene)(4-methylphenyl)methylamine (2l): Brown solid; M.p.: 56-58 °C; yield: 89%; R_f = 0.31; IR (neat): ν (cm^{-1}) 3156 (N-H); 1633(C=N); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.60 (s, 1H, N-*H*); 8.37 (s, 1H, C*H*); 7.51 (s, 1H, Ar-*H*); 7.38-7.17 (m, 8H, Ar-*H*); 4.82 (s, 2H, CH_2); 2.37 (s, 3H, CH_3); ESI-MS (*m/z*): 248.9 $[M+H]^+$; Anal. calcd. for $C_{17}H_{16}N_2$: C, 82.22 H, 6.49; N, 11.28; found: C, 82.19; H, 6.45; N, 11.24%.

(4-Methylbenzylidene)(4-methoxyphenyl)methylamine (2m): Yellow solid; M.p.: 62-64 °C; yield: 91%; R_f = 0.31; IR (neat): ν (cm^{-1}) 1611(C=N); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.31 (s, 1H, C*H*); 7.73 (d, 2H, *J* = 8.7 Hz, Ar-*H*); 7.28-7.18 (m, 6H, Ar-*H*); 4.78 (s, 2H, CH_2); 3.95 (s, 3H, OCH_3);

2.40 (s, 3H, C*H*$_3$); ESI-MS (*m/z*): 240.9 $[M+H]^+$; Anal. calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85; found: C 80.26 H 7.12 N 5.82%.

(4-Methoxybenzylidene)(4-methoxyphenyl)methylamine (2n): Yield: 91%.

(3,4-Dimethoxybenzylidene)(4-methoxyphenyl)methylamine (2o): Yellow solid; M.p: 44-45 °C; yield: 97%; R_f = 0.40; IR (neat): ν (cm^{-1}) 1603 (C=N); ^{1}H NMR (300 MHz, $CDCl_3$) (*δ*, ppm): 8.29 (s, 1H, C*H*); 7.49 (s, 1H, Ar-*H*); 7.27 (d, 2H, *J* = 7.8 Hz, Ar-*H*); 7.20 (d, *J* = 8.1 Hz, 3H, Ar-*H*); 7.18 (d, 1H, *J* = 8.7 Hz, Ar-*H*); 4.76 (s, 2H, C*H*$_2$); 3.95 (s, 3H, OC*H*$_3$); 3.94 (s, 3H, OC*H*$_3$); 3.82 (s, 3H, OC*H*$_3$); ESI-MS (*m/z*): 286.6 $[M+H]^+$; Anal. calcd. for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91; found: C, 71.52; H, 6.68; N, 4.86%.

((1H-Indol-3-yl) methylene) (4-methoxyphenyl)methylamine (2p): Yield: 89%.

(4-Methylbenzylidene)(4-fluorophenyl)methylamine (2q): Yellow oil; yield: 93%; R_f = 0.68; IR (neat): ν (cm^{-1}) 1603 (C=N); 1220 (C-F); ^{1}H NMR (300 MHz, $CDCl_3$) (*δ*, ppm): 8.37 (s, 1H, C*H*); 7.69 (d, 2H, *J* = 7.8 Hz, Ar-*H*); 7.37-7.24 (m, 4H, Ar-*H*); 7.07-7.02 (m, 2H, Ar-*H*); 4.78 (s, 2H, C*H*$_2$); 2.41 (s, 3H, C*H*$_3$); ESI-MS (*m/z*): 228.1 $[M+H]^+$; Anal. calcd. for. $C_{15}H_{14}FN$: C, 79.27; H, 6.21; N, 6.16; found: C, 79.23; H, 6.17; N, 6.12%.

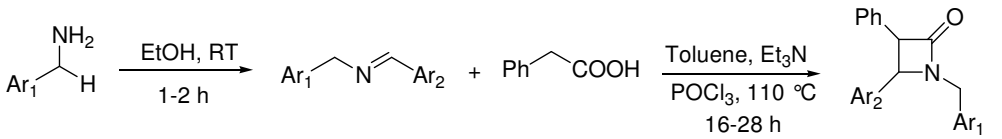
(4-Methoxybenzylidene)(4-fluorophenyl)methylamine (2r): Yield: 90%.

(3,4-Dimethoxybenzylidene)(4-fluorophenyl)methylamine (2s): Yellow oil; yield: 85%; R_f = 0.46; IR (neat): ν (cm^{-1}) 1644 (C=N), 1058 (C-F); ^{1}H NMR (300 MHz, $CDCl_3$) (*δ*, ppm): 8.31 (s, 1H, C*H*); 7.48 (s, 1H, Ar-*H*); 7.33-7.19 (m, 3H, Ar-*H*); 7.07-7.00 (m, 2H, Ar-*H*); 6.90 (d, 1H, *J* = 8.4 Hz, Ar-*H*); 4.77 (s, 2H, C*H*$_2$); 3.95 (s, 3H, OC*H*$_3$); 3.94 (s, 3H, OC*H*$_3$); ESI-MS (*m/z*): 274.5 $[M+H]^+$; Anal. calcd. for $C_{16}H_{16}FNO_2$: C ,70.31; H, 5.90; N, 5.12, found: C, 70.25; H, 5.86; N, 5.07%.

((1H-Indol-3-yl)methylene)(4-fluorophenyl)methylamine (2t): Yield: 89%.

General procedure for the synthesis of β-lactams and 1,3-oxazin-4-one derivatives

To a stirred solution of imine (1.0 mmol), phenylacetic acid (1.5 mmol) and triethylamine (4.0 mmol) in toluene (10 ml) maintained at 110 °C under inert atmosphere, a solution of phosphorous oxychloride (1.1 mmol) in toluene was added dropwise. After overnight refluxing, the mixture was extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The crude residue was purified by silica-gel chromatography (230-400 mesh) using 30-40% ethyl acetate in hexane to yield the title compounds in low to good yield [8]. The 1,3-oxazin-4-one derivatives were also obtained under the same reaction conditions in low to moderate yields ranging from 28-65%. The R_f values of all the compounds were determined by using (Ethyl acetate/n-Hexane 30:70) as solvent system.



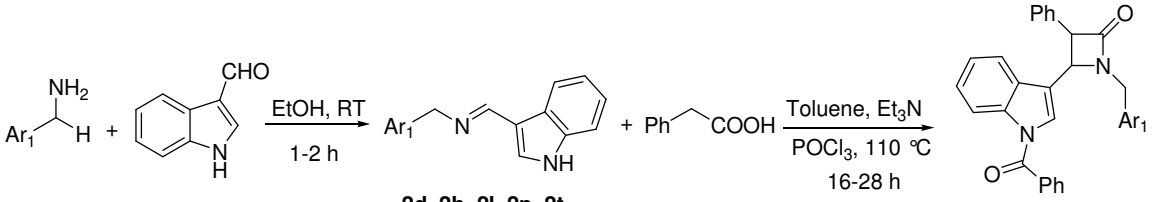
Ar_1 = Ph, *p*-F-Ph, *p*-Me-Ph, *p*-OMe-Ph
Ar_2 = 3,4-diOMe-Ph, *p*-Me-Ph

Scheme-1

1-Benzyl-3-phenyl-4-(4-methylphenyl)azetidin-2-one (3a): Reddish brown oil; yield: 24%; R_f = 0.42; IR (neat): ν (cm^{-1}) 1752 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) (*δ*, ppm): 7.41-7.04 (m, 14H, Ar-*H*); 4.71 (d, 1H, *J* = 14.0 Hz, azetidinone ring-H_a); 4.55 (d, 1H, *J* = 14.2 Hz, azetidinone ring-H_b); 4.14 (s, 1H, C*H*$_2$); 4.0 (s, 1H, C*H*$_2$); 2.45 (s, 3H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) (*δ*, ppm): 166.47,

164.71. 163.46, 163.13, 162.52, 134.46, 132.85, 129.83, 128.29, 127.35, 127.10, 119.50, 117.53, 115.33, 111.22, 55.47, 44.65; ESI-MS (*m/z*): 328.7 $[M+H]^+$; Anal. calcd. for $C_{23}H_{21}NO$: C, 84.37; H, 6.46; N, 4.28; found: C, 84.35; H, 6.42; N, 4.22%.

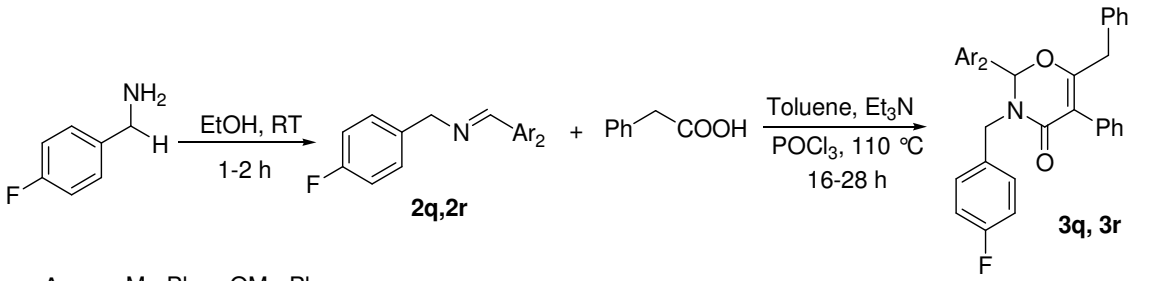
1-Benzyl-4-(4-methoxyphenyl)-3-phenylazetidin-2-one (3b): Light brown oil; yield: 40%; R_f = 0.54; IR (neat): ν (cm^{-1}) 1748 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) (*δ*, ppm): 7.33-7.06 (m, 12H, Ar-*H*); 6.72 (d, 2H, *J* = 7.1 Hz, Ar-*H*); 4.45 (d, 1H, *J* = 13.7 Hz, azetidinone ring-H_a); 4.15 (d, 1H, *J* = 14.2 Hz, azetidinone ring-H_b); 4.24 (s, 1H, CH_2); 4.10 (s, 1H, CH_2) 3.95 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) (*δ*, ppm): 172.40, 164.71, 163.15, 162.51, 134.43, 132.82, 129.85, 129.66, 129.14, 128.94, 128.52, 127.71, 127.24, 127.0, 118.57, 117.55, 115.33, 111.25, 59.96, 55.43, 44.61; ESI-MS (*m/z*): 344.2 $[M+H]^+$; Anal. calcd. for $C_{23}H_{21}NO_2$: C, 80.44; H, 6.16; N, 4.08; found: C, 80.40; H, 6.11; N, 4.04%.



2d, 2h, 2l, 2p, 2t **3d, 3h, 3l, 3p, 3t**

Ar_1 = Ph, *p*-F-Ph, *p*-Me-Ph, *p*-OMe-Ph, *p*-Cl-Ph

Scheme-2



2q,2r **3q, 3r**

Ar_2 = *p*-Me-Ph, *p*-OMe-Ph

Scheme-3

1-Benzyl-4-(3,4-dimethoxyphenyl)-3-phenylazetidin-2-one (3c): White crystalline solid; M.p. 127-129 °C; yield: 38%; R_f = 0.51; IR (neat): ν (cm^{-1}) 1752 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 7.34-7.29 (m, 6H, Ar-*H*); 7.21 (d, 4H, *J* = 7.0 Hz, Ar-*H*); 6.88-6.81 (m, 2H, Ar-*H*); 6.73 (s, 1H, Ar-*H*); 4.88 (d, 1H, *J* = 14.9 Hz, azetidinone ring-H_a); 4.29 (s, 1H, CH_2); 4.19 (s, 1H, CH_2); 3.91-3.88 (m, 4H, azetidinone ring-H_b, OCH_3); 3.83 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) (*δ*, ppm): 168.38, 149.62, 149.36, 135.76, 135.09, 129.51, 128.92, 128.81, 128.64, 127.79, 127.63, 127.38, 119.35, 111.39, 108.93, 77.49, 77.06, 76.64, 65.10, 63.35, 55.98, 44.72. ESI-MS (*m/z*): 374.3 $[M+H]^+$. Anal. calcd. for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75; found: C, 77.14; H 6.16; N, 3.71%.

1-Benzyl-3-phenyl-4-(1-(2-phenylacetyl)-1H-indol-3-yl)azetidin-2-one (3d): White crystalline solid; M.p. 110-112 °C; yield: 65 %; R_f = 0.77; IR (neat): ν (cm^{-1}) 1756 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 8.54 (d, 1H, *J* = 8.2 Hz, Ar-*H*); 7.52-7.28 (m, 14H, Ar-*H*); 7.26-7.09 (m, 5H, Ar-*H*); 4.88 (d, 1H, *J* = 16.0 Hz, azetidinone ring-H_a); 4.54 (s, 1H, CH_2); 4.46 (s, 1H, CH_2); 4.14 (s, 2H, CH_2); 3.87 (d, 1H, *J* = 14.9 Hz, azetidinone ring-H_b); ^{13}C NMR (75 MHz, $CDCl_3$) (*δ*, ppm): 169.03, 168.00, 136.72, 135.67, 134.92, 133.18, 129.04, 128.85, 128.54, 127.89, 127.85, 127.58, 127.42, 126.16, 124.40,123.36, 119.24, 119.13, 117.30, 77.46, 77.03, 76.61, 63.05, 57.25, 45.10, 43.03; ESI-MS (*m/z*): 471.0 $[M+H]^+$; Anal. calcd. for $C_{32}H_{26}N_2O_2$: C, 81.33; H, 5.97; N, 5.93; found: C, 81.30; H, 5.94; N, 5.90%.

1-(4-Chlorobenzyl)-3-phenyl-4-(4-methylphenyl)azetidin-2-one (3e): Light brown oil; yield: 25%; R_f = 0.62; IR (neat): ν (cm^{-1}) 1752 (C=O); 770 (C-Cl); ^{1}H NMR (400 MHz, $CDCl_3$) (*δ*, ppm): 7.34-

7.27 (m, 7H, Ar-*H*); 7.22-7.18 (m, 6H, Ar-*H*); 4.85 (d, 1H, *J* = 15.3 Hz, azetidinone ring-H_a); 4.16 (s, 1H, C*H*$_2$); 4.04 (s, 1H, C*H*$_2$); 3.84 (d, 1H, *J* = 14.7 Hz, azetidinone ring-H_b); 2.25 (s, 3H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 168.07, 164.51, 160.24, 135.35, 134.69, 134.54, 130.96, 129.36, 128.98, 128.89, 128.60, 127.92, 127.88, 127.78, 127.34, 65.29, 62.51, 44.77; ESI-MS (*m/z*): 362.3 $[M+H]^+$; Anal. calcd. for $C_{23}H_{20}ClNO$: C, 76.34; H, 5.57; N, 3.87; found: C, 76.29; H, 5.52; N, 3.83%

1-(4-Chlorobenzyl)-4-(4-methoxyphenyl)-3-phenylazetidin-2-one (3f): Yellow oil, yield: 22%; R_f = 0.50; IR (neat): ν (cm^{-1}) 1742 (C=O); 773 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.20-7.00 (m, 11H, Ar-*H*); 6.72 (d, 2H, *J* = 8.0, Ar-*H*); 4.37 (d, 1H, *J* = 14.2 Hz, azetidinone ring-H_a); 4.19 (d, 1H, *J* = 12.6 Hz, azetidinone ring-H_b); 4.10 (s, 1H, C*H*$_2$); 4.00 (s, 1H, C*H*$_2$); 3.85 (s, 3H, OC*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 171.98, 168.56, 164.39, 144.43, 144.0, 137.92, 136.54, 134.75, 132.62, 131.81, 129.51, 129.11, 128.86, 128.37, 128.19, 126.56, 117.39, 62.76, 57.42, 45.78; ESI-MS (*m/z*): 378.6 $[M+H]^+$; Anal. calcd. for $C_{23}H_{20}ClNO_2$: C, 73.11; H, 5.33; N, 3.71; found: C, 73.07; H, 5.30 N, 3.67%.

1-(4-Chlorobenzyl)-4-(3,4-dimethoxyphenyl)-3-phenylazetidin-2-one (3g): Brown oil; yield: 48%; R_f = 0.33; IR (neat): ν (cm^{-1}) 1665 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.42-7.04 (m, 9H, Ar-*H*); 6.61-6.52 (m, 3H, Ar-*H*); 4.75 (d, 1H, *J* = 14.9 Hz, azetidinone ring-H_a); 4.37 (d, 1H, *J* = 14.2 Hz, azetidinone ring-H_b); 4.23 (s, 1H, C*H*$_2$); 4.14 (s, 1H, C*H*$_2$); 3.73 (s, 6H, OC*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 170.63, 168.94, 166.34, 159.72, 146.41, 134.92, 133.91, 133.27, 132.62, 131.98, 129.71, 129.01, 128.56, 128.30, 128.09, 127.56, 125.39, 62.87, 57.49, 45.78; ESI-MS (*m/z*): 408.7 $[M+H]^+$; Anal. calcd. for $C_{24}H_{22}ClN_2O_3$: C, 70.67; H, 5.44; N, 3.43; found: C, 70.62; H, 5.40; N, 3.40%.

1-(4-Chlorobenzyl)-3-phenyl-4-(1-(2-phenylacetyl)-1H-indol-3-yl)azetidin-2-one (3h): White crystalline solid; M.p. 116-118 °C yield: 35%; R_f = 0.51; IR (neat): ν (cm^{-1}) 1756 (C=O); ^{1}H NMR (400 MHz, DMSO) (δ, ppm): 8.37 (d, 1H, *J* = 8.2 Hz, Ar-*H*); 8.23 (s, 1H, Ar-*H*); 7.44-7.22 (m, 15H, Ar-*H*); 7.23 (d, 2H, *J* = 8.3 Hz, Ar-*H*); 4.82 (s, 1H, C*H*$_2$); 4.72 (d, 1H, *J* = 15.6 Hz, azetidinone ring-H_a); 4.63 (s, 1H, C*H*$_2$); 4.38(s, 2H, C*H*$_2$); 4.02 (d, 1H, *J* = 15.6 Hz, azetidinone ring-H_b); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 169.01, 167.92, 136.74, 134.75, 134.05, 133.84, 133.18, 129.90, 129.10, 129.07, 129.01, 127.94, 127.76, 127.34, 126.26, 124.47, 123.51, 119.21, 118.78, 117.35, 77.48, 77.06, 76.03, 62.93, 57.26, 44.35, 43.11; ESI-MS (*m/z*): 505.4 $[M+H]^+$; Anal. calcd. for $C_{32}H_{25}ClN_2O_2$: C, 76.11; H, 4.99; N, 5.58; found: C, 76.05; H, 4.96; N, 5.56%.

1-(4-Methylbenzyl)-3-phenyl-4-(4-methylphenyl)azetidin-2-one (3i): White crystalline solid; M.p. 123-125 °C; yield: 65%, R_f = 0.65; IR (neat): ν (cm^{-1}) 1757 (C=O), ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.37-7.19 (m, 9H, Ar-*H*); 7.16-7.09 (m, 4H, Ar-*H*); 4.96 (d, 1H, *J* = 15.0, Hz, azetidinone ring-H_a); 4.33 (s, 1H, C*H*$_2$); 4.20 (s, 1H, C*H*$_2$); 3.77 (d, 1H, *J* = 14.7 Hz, azetidinone ring-H_b); 2.41 (s, 3H, C*H*$_3$); 2.35 (s, 3H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 168.26, 138.51, 137.45, 135.20, 134.27, 132.65, 129.79, 129.46, 128.85, 128.53, 128.01, 127.53, 127.39, 126.53, 77.46, 77.24, 77.03, 76.61, 65.09, 62.80, 44.19, 21.20, 21.11; ESI-MS (*m/z*): 683.4 $[2M+H]^+$; Anal. calcd. for $C_{22}H_{17}Cl_2NO$: C,84.42; H, 6.79; N, 4.10; found: C, 84.38; H, 6.75; N 4.06%.

1-(4-Methylbenzyl)-4-(4-methoxyphenyl)-3-phenylazetidin-2-one (3j): Yellow solid; M.p. 122-124 °C; yield: 36%; R_f = 0.53; IR (neat): ν (cm^{-1}) 1752 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.52 (t, 3H, *J* = 7.1 Hz, Ar-*H*); 7.28- 7.02 (m, 10H, Ar-*H*); 4.54 (d, 1H, *J* = 14.7 Hz, azetidinone ring-H_a); 4.22 (d, 1H, *J* = 14.2 Hz, azetidinone ring-H_b); 4.28 (s, 1H, C*H*$_2$); 4.09 (s, 1H, C*H*$_2$); 3.83 (s, 3H, OC*H*$_3$); 2.21 (s, 3H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 168.22, 166.32, 164.57, 147.79, 142.10, 136.71, 134.94, 133.20, 129.91, 129.42, 128.91, 128.53, 127.56, 121.91, 115.12, 110.91, 107.89, 59.43, 51.50, 43.30. ESI-MS (*m/z*): 358.7 $[M+H]^+$; Anal. calcd. for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.49; N, 3.92; found: C, 80.60; H, 6.45; N 3.87%.

1-(4-Methoxybenzyl)-4-(3,4-dimethoxyphenyl)-3-phenylazetidin-2-one (3k): Brown oil; yield: 48%; R_f = 0.41; IR (neat): ν (cm^{-1}) 1744 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.42 (d, 2H, *J* = 6.8 Hz, Ar-*H*); 7.27-6.93 (m, 7H, Ar-*H*); 6.61-6.52 (m, 3H, Ar-*H*); 4.79 (d, 1H, *J* = 14.9 Hz,

azetidinone ring-H_a); 4.57 (s, 1H, CH_2); 4.26 (s, 1H, CH_2); 4.22 (d, 1H, *J* = 14.4 Hz, azetidinone ring-H_b); 3.93 (s, 3H, OCH_3); 3.89 (s, 3H, OCH_3); 2.35 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 169.56, 168.34, 148.09, 144.14, 139.76, 136.42, 134.6, 129.72, 129.49, 129.26, 128.61, 127.58, 126.87, 123.32, 119.83, 116.89, 56.23, 50.62, 44.42; ESI-MS (*m/z*): 388.2 $[M+H]^+$; Anal. calcd. for $C_{25}H_{25}NO_3$: C , 77.49; H, 6.50; N, 3.61;, found: C, 77.45; H, 6.45; N 3.57%.

1-(4-Methylbenzyl)-3-phenyl-4-(1-(2-phenylacetyl)-1H-indol-3-yl)azetidin-2-one (3l): Yellow solid; M.p. 119-121 °C; yield: 48%, R_f = 0.61; IR (neat): ν (cm^{-1}) 1745 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.22 (s, 1H, Ar-*H*); 7.44-7.22 (m, 18H, Ar-*H*); 4.72 (d, 1H, *J* = 15.0 Hz, azetidinone ring-H_a); 4.02 (d, 1H, *J* = 14.4 Hz, azetidinone ring-H_b); 4.38 (s, 1H, CH_2); 4.11 (s, 1H, CH_2); 3.38 (s, 2H, CH_2); 2.38 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 169.01, 167.92, 136.74, 134.75, 134.05, 133.84, 133.18, 129.90, 129.10, 129.07, 129.01, 127.94, 127.76, 127.34, 126.26, 124.47, 123.51, 119.21, 118.78, 117.35, 77.48, 77.06, 76.03, 62.93, 57.26, 44.35, 43.11;. ESI-MS (*m/z*): 485.4 $[M+H]^+$; Anal. calcd. for $C_{33}H_{28}N_2O_2$: ,C 81.79; H, 5.82; N 5.78; found: C 81.74; H, 5.78; N, 5.74%.

1-(4-Methoxybenzyl)-3-phenyl-4-(4-methylphenyl)azetidin-2-one (3m): Brown oil; yield: 37%; R_f = 0.60; IR (neat): ν (cm^{-1}) 1758 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.54 (d, 2H, *J* = 8.1 Hz, Ar-*H*); 7.29-7.02 (m, 9H, Ar-*H*); 6.96 (d, 2H, *J* = 7.8 Hz, Ar-*H*); 4.91 (d, 1H, *J* = 16.0 Hz, azetidinone ring-H_a); 4.48 (d, 1H, *J* = 15.6 Hz, azetidinone ring-H_b); 4.16 (s, 1H, CH_2); 4.04 (s, 1H, CH_2); 3.88 (s, 3H, OCH_3); 2.28 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 169.78, 166.91, 164.25, 144.41, 136.53, 133.34, 129.73, 129.31, 128.56, 127.79, 127.46, 126.93, 124.91, 115.67, 110.87, 107.76, 59.56, 54.61, 44.70; ESI-MS (*m/z*): 358.8 $[M+H]^+$; Anal. calcd. for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.49; N, 3.92; found: C, 80.60; H, 6.764; N, 3.88%.

1-(4-Methoxybenzyl)-4-(4-methoxyphenyl)-3-phenylazetidin-2-one (3n)*:* Light brown oil; yield: 41%; R_f = 0.43; IR (neat): ν (cm^{-1}) 1756 (C=O), 737 (C-Cl) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.38-7.15 (m, 7H, Ar-*H*); 7.06 (d, 2H, *J* = 8.3 Hz, Ar-*H*); 6.95-6.72 (m, 4H, Ar-*H*); 4.73 (d, 1H, *J* = 14.7 Hz, azetidinone ring-H_a); 4.33 (s, 1H, CH_2); 4.20 (s, 1H, CH_2); 4.16 (d, 1H, *J* = 12.7 Hz, azetidinone ring-H_b); 3.96 (s, 3H, OCH_3); 3.93 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 166.14, 158.70, 148.79, 144.25, 134.99, 132.34, 129.1, 128.90, 128.43, 128.77, 127.50, 127.36, 126.62, 115.56, 115.12, 65.49, 63.37, 37.59 . ESI-MS (*m/z*): 374.3 $[M+H]^+$. Anal. calcd. for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75; found: C, 77.14; H, 6.17; N, 43.71%.

1-(4-Methoxybenzyl)-4-(3,4-dimethoxyphenyl)-3-phenylazetidin-2-one (3o): Yellow solid; M.p. 111-113 °C; yield: 72%; R_f = 0.28; IR (neat): ν (cm^{-1}) 1756 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.35-7.13 (m, 7H, Ar-*H*); 6.91-6.77 (m, 5H, Ar-*H*); 4.86 (d, 1H, *J* = 8.4 Hz, azetidinone ring-H_a); 4.30-4.20 (m, 2H, azetidinone ring-H_b, CH_2); 3.92 (s, 3H, OCH_3); 3.88 (s, 3H, OCH_3); 3.57 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 168.26, 159.20, 149.68, 149.38, 135.16, 129.94, 129.69, 128.89, 127.83, 127.57, 127.37, 119.32, 114.16, 111.48, 109.04, 77.47, 77.05, 76.63, 64.97, 63.12, 64.97, 55.99, 55.28, 44.10; ESI-MS (*m/z*): 404.0 $[M+H]^+$; Anal. calcd. for $C_{25}H_{25}NO_4$: C, 74.42; H, 6.25; N, 3.47; found: C, 74.38; H, 6.21; N, 3.43%.

1-(4-Methoxybenzyl)-3-phenyl-4-(1-(2-phenylacetyl)-1H-indol-3-yl)azetidin-2-one (3p): White crystalline solid; M.p. 117-119 °C; yield: 53%; R_f = 0.48; IR (neat): ν (cm^{-1}) 1750 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.54 (d, 1H, *J* = 8.2 Hz, Ar-*H*); 7.56-7.06 (m, 14H, Ar-*H*); 6.95-6.90 (m, 4H, Ar-*H*); 4.88 (d, 1H, *J* = 16.0 Hz, azetidinone ring-H_a); 4.54 (s, 1H, CH_2); 4.43 (s, 1H, CH_2); 4.24 (s, 2H, CH_2); 3.87 (d, 1H, *J* = 14.3 Hz, azetidinone ring-H_b); 3.63 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 169.03, 168.00, 136.72, 135.67, 134.92, 133.18, 129.04, 128.85, 128.54, 127.89, 127.85, 127.58, 127.42, 126.16, 124.40,123.36, 119.24, 119.13, 117.30, 77.46, 77.03, 76.61, 63.05, 57.25, 45.10, 43.03; ESI-MS (*m/z*): 501.4 $[M+H]^+$; Anal. calcd. for $C_{33}H_{28}N_2O_3$: C, 79.18; H, 5.64; N, 5.60; found: C, 79.14; H, 5.61; N 5.55%.

3-(4-Fluorobenzyl)-6-benzyl-5-phenyl-2-(4-methylphenyl)-2,3-dihydro-1,3-oxazin-4-one (3q): Brown oil; yield: 34%; R_f = 0.64; IR (neat): ν (cm^{-1}) 1767 (C=O); 1160 (C-F); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.49-7.33 (m, 7H, Ar-*H*); 7.27-7.21 (m, 9H, Ar-*H*); 6.98 (d, 2H, *J* = 8.7 Hz, Ar-*H*);

6.11 (s, 1H, C*H*); 5.32 (d, 1H, *J* = 14.8 Hz, C*H*); 3.92 (d, 1H, *J* = 15.0 Hz, C*H*); 3.57 (s, 2H,CH_2); 3.41 (s, 2H, CH_2); 2.4 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 166.78, 163.87, 163.39, 161.26, 160.62, 139.49, 138.77, 137.09, 128.20, 127.62, 123.38, 116.11, 115.82, 61.58, 59.14, 44.61; ESI-MS (*m/z*): 464.2 $[M+H]^+$; Anal. calcd. for $C_{31}H_{26}FNO_2$ C, 80.32; H, 5.65; N, 3.02; found: C 80.28; H 5.62; N, 2.98%.

3-(4-Fluorobenzyl)-6-benzyl-2-(4-methoxyphenyl)-5-phenyl-2,3-dihydro-1,3-oxazin-4-one (3r)*:* Reddish brown oil; yield: 45%; R_f = 0.61; IR (neat): ν (cm^{-1}) 1655 (C=O); 1160 (C-F); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.36-6.70 (m, 18H, Ar-*H*); 6.07 (s, 1H, C*H*); 5.20 (d, 1H, *J* = 15.0 Hz, C*H*); 3.91 (d, 1H, *J* = 15.3 Hz, C*H*); 3.84 (s, 2H, CH_2); 3.82 (s, 3H, OCH_3); 3.66 (m, 2H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 163.43, 161.29, 160.50, 160.22, 135.92, 133.28, 132.77, 131.59, 130.59, 130.49, 129.90, 129.79, 129.38, 128.75, 128.32, 128.15, 127.75, 126.51, 115.50, 113.89, 77.46, 44.07; ESI-MS (*m/z*): 480.2 $[M+H]^+$; Anal. calcd. for $C_{31}H_{26}FNO_3$: C, 77.64; H, 5.46; N, 2.92; found: C, 77.60; H, 5.42; N, 2.87% .

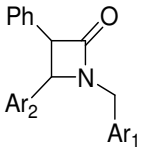
1-(4-Fluorobenzyl)-4-(3,4-dimethoxyphenyl)-3-phenylazetidin-2-one (3s): Light brown oil; yield: 28%; R_f =0.38; IR (neat): ν (cm^{-1}) 1748 (C=O); 1158 (C-F); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.37-7.17 (m, 7H, Ar-*H*); 7.02 (t, 2H, *J* = 8.4 Hz, Ar-*H*); 6.91-6.83 (m, 2H, Ar-*H*); 6.76 (s, 1H, Ar-*H*); 4.85 (d, 1H, *J* = 15.0 Hz, azetidinone ring-H_a); 4.30 (s, 1H, CH_2); 4.22 (s, 1H, CH_2); 3.92-3.86 (m, 7H, azetidinone ring-H_b, 2×OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 168.30, 163.96, 160.69, 149.74, 149.48, 134.99, 131.60, 130.40, 130.29, 129.41, 128.94, 127.66, 127.30, 119.35, 115.84, 115.55, 111.50, 108.97, 77.46, 76.62, 65.09, 63.34, 56.0, 43.98; ESI-MS (*m/z*): 392.0 $[M+H]^+$; Anal. calcd. for $C_{24}H_{22}FNO_3$: C, 73.64; H, 5.66; N, 3.58; found: C, 73.60; H, 5.62; N, 3.53%.

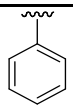
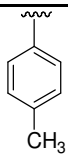
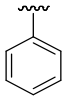
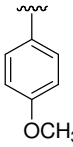
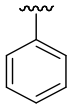
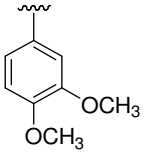
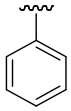
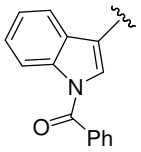
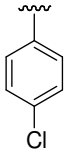
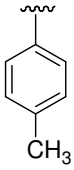
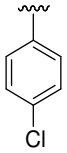
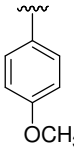
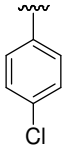
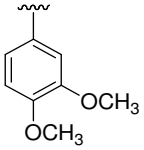
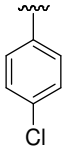
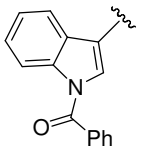
1-(4-Fluorobenzyl)-3-phenyl-4-(1-(2-phenylacetyl)-1H-indol-3-yl) azetidin-2-one (3t): Light yellow solid; M.p. 119-121 °C; yield: 62%, R_f = 0.44; IR (neat): ν (cm^{-1}) 1742 (C=O), 1148 (C-F); ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 7.36 (s, 1H, Ar-*H*); 7.21-6.95 (m, 18H, Ar-*H*); 4.72 (d, 1H, *J* = 14.9 Hz, azetidinone ring-H_a); 4.02 (d, 1H, *J* = 14.8 Hz, azetidinone ring-H_b); 4.38 (s, 1H, CH_2); 4.24 (s, 1H, CH_2); 3.38 (s, 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 168.02, 160.93, 135.53, 134.56, 130.95, 129.84, 129.42, 129.01, 128.80, 128.53, 128.26, 127.26, 126.66, 115.64, 86.64, 65.28, 46.69, 44.04. ESI-MS (*m/z*): 489.2 $[M+H]^+$; Anal. calcd. for $C_{32}H_{25}FN_2O_2$: C, 78.67; H, 5.16; N, 5.73; found: C, 78.61; H, 5.12; N, 5.70%.

RESULTS AND DISCUSSION

The reaction sequences to obtain title compounds (**3a-t**) and their intermediates (**2a-t**) are shown in Schemes-1, 2, and 3. Briefly, Imines (**2a-t**) were prepared by the condensation of commercially available benzylamines and aromatic aldehydes in quantitative yields. Imines were cyclized to yield β-lactams and highly substituted 1,3-oxazinone derivatives by treating with phenyl acetic acid and phosphorous oxychloride using triethylamine as a base. The cycloaddition reaction of imines resulted in exclusive formation of monocyclic β-lactams (**3a-c, 3e-g, 3i-k, 3m-o, 3s**) (Scheme-1). Indole substituted imines when treated with phenylacetic acid gave *N*-phenylacetylindole substituted β-lactam derivatives (**3d, 3h, 3l, 3p, 3t**) in low to moderate yields (Scheme-2). On the other hand, highly substituted 1,3-oxazinones (**3q**, **3r)** were obtained as exclusive product under similar conditions when imines (**2q, 2r**) were treated with phenylacetic acid (Scheme-3). The possible mechanism for the synthesis of β-lactams and 1,3-oxazinones has been reported earlier [8]**.** The structures of all the β-lactams (Table-1) and 1,3-oxazinones (Table-2) were established on the basis of their IR, ^{1}H, ^{13}C-NMR and mass spectral data. The IR spectrum of compound **3i** indicated the presence of β-lactam carbonyl (1752 cm^{-1}) in it. The ^{1}H-NMR spectral analysis showed the C3 proton resonating upfield at 3.77 ppm while the other C4 proton near the ring nitrogen exhibited resonance at 4.96 ppm. The positions of remaining proton resonances appeared at usual chemical shift values. The ^{13}C-NMR spectrum also showed similar chemical shifts exhibiting resonance of C3 and C4 at 62.80 and 65.09 ppm, respectively. The compound **3i** exhibited dimeric ion peaks as the base peak thus further confirming the formation of β-lactam ring.

Table-1: Structural data of β-lactam derivatives



Compound	Ar_1	Ar_2	Mol. Formula	Mol. Wt.
3a			$C_{23}H_{21}NO$	327.4
3b			$C_{23}H_{21}NO_2$	343.4
3c			$C_{24}H_{23}NO_3$	373.3
3d			$C_{31}H_{24}N_2O_2$	470.6
3e			$C_{23}H_{20}ClNO$	361.9
3f			$C_{23}H_{20}ClNO_2$	377.9
3g			$C_{24}H_{22}ClNO_3$	407.9
3h			$C_{31}H_{23}ClN_2O_2$	505.0

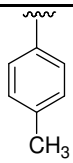
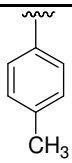
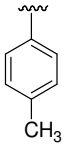
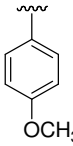
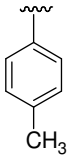
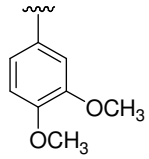
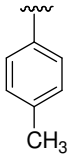
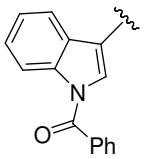
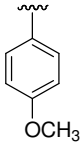
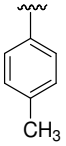
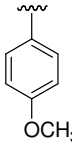
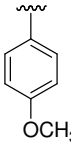
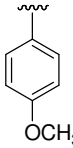
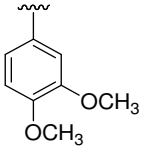
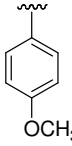
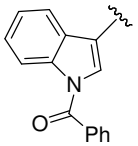
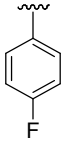
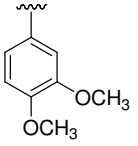
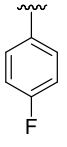
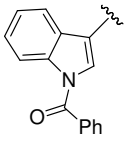
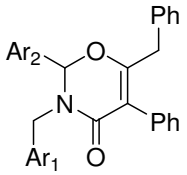
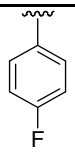
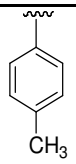
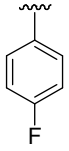
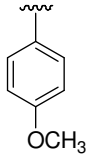
3i			$C_{24}H_{23}NO$	341.4
3j			$C_{24}H_{23}NO_2$	357.4
3k			$C_{25}H_{25}NO_3$	387.5
3l			$C_{32}H_{26}N_2O_2$	484.6
3m			$C_{24}H_{23}NO_2$	357.4
3n			$C_{24}H_{23}NO_3$	373.4
3o			$C_{25}H_{25}NO_4$	403.5
3p			$C_{32}H_{26}N_2O_3$	501.4
3s			$C_{24}H_{22}FNO_3$	391.4
3t			$C_{32}H_{25}FN_2O_2$	489.2

Table-2: Structural data of 1,3-oxazin-4-one derivatives



Compound	Ar_1	Ar_2	Mol.Formula	Mol.Wt.
3q			$C_{31}H_{26}FNO_2$	463.5
3r			$C_{31}H_{26}FNO_3$	479.5

CONCLUSION

In conclusion, Staudinger reaction was adopted to synthesize monocyclic β-lactams (**3a-p**, **3s-t**) from their corresponding imines and phenylacetic acid under the reaction conditions in low to good yield. We also confirmed the formation of highly substituted 1,3-oxazinones (**3q-r**) under the same reaction conditions. The evaluation of biological potential of these derivatives is under progress and will be reported in near future.

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REFERENCES

1. G. A. Koppel, In Small Ring Heterocycles, A. Hassner, (Ed.), Wiley, New York, p.223, 2 (1983).
2. N. De Kimpe, In Comprehensive Heterocyclic Chemistry II, A. R. Katritzky, C. W. Rees, E. F. V. Scriven and A. Padwa, (Eds.) Pergamon:Oxford, p.507, 1B (1996).
3. C. Palomo, J. M. Aizpurua, I. Ganboa and M. Oiarbide, *Eur. J. Org. Chem.*, 3223 (1999).
4. H. Gilman and M. Speeter, *J. Am. Chem. Soc.,* **65**, 2255 (1943).
5. H. Staudinger, *Liebigs Ann. Chem.* **356,** 51 (1907).
6. T. Tidwell, *Eur. J. Org. Chem.,* 563, (2006).
7. M. Benaglia, M. Cinquini and F. Cozzi, *Eur. J. Org. Chem.,* 563 (2000).
8. B. Aneja, M. Irfan, M. I. Hassan, A. Prakash, U. Yadava, C. G. Daniliuc, M. Zafaryab, M. M. A. Rizvi, A. Azam and M. Abid, *J. Enzyme Inhib. Med. Chem.*,1 (2015).
9. M. Irfan, B. Aneja, U. Yadava, S. I. Khan, N. Manzoor, C. G. Daniliuc and M. Abid, *Eur. J. Med. Chem.,* **93,** 246 (2015).
10. M. M. Masood, V. K. Pillalamarri, M. Irfan, B. Aneja, M. A. Jairajpuri, M. Zafaryab, M. M. A. Rizvi, U. Yadava, A. Addlagatta and M. Abid, *RSC Adv.* **5,** 34173 (2015).
11. F. Schaufelberger, L. Hu and O. Ramström, *Chem. Euro. J.,* **21**, 9776 (2015).
12. D. Dar'in, O. Bakulina, M. Chizhova and M. Krasavin, *Org. Lett.,* **17**, 3930 (2015).
13. N. J. Curtin, H. C. Barlow, K. J. Bowman, A. H. Calvert, R. Davison, B. T. Golding, B. Huang, P. J. Loughlin, D. R. Newell, P. G. Smith and R. J. Griffin, *J. Med. Chem.,* **47**, 4905 (2004).
14. C. V. Stevens, E. V Meenen, Y. Eeckhout, B. Vanderhoydonck and W. Hooghe, *Chem. Commun.,*

Cambridge U.K. **38,** 4827 (2005).
15. S. Zhao, C. Liu, Y. Guo, J. C. Xiao and Q. Y. Chen, *J. Org. Chem.,* **79**, 8926 (2014).
16. B. Saha, S. M. Rahaman, P. Daw, G. Sengupta and J. K. Bera, *Chem. Eur. J.,* **20**, 6542 (2014).
17. C. Catusse, R. Catusse, A. Gaset and J. P. Gorrichon, *J. Soc. Chim. Tunis.* **2,** 11 (1985).

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