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# Synthesis of Novel *N*-(4-Ethoxyphenyl) Azetidin-2-ones and Their Oxidative *N*-Deprotection by Ceric Ammonium Nitrate

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**Abstract:** It is shown that the *N*-(*p*-ethoxyphenyl) group on β-lactams can be oxidatively removed by ceric ammonium nitrate in good yield. Fourteen new *N*-(*p*-ethoxyphenyl)-2-azetidinones **8a-n** were synthesized through standard [2+2] ketene-imine cycloadditions (Staudinger reaction). Treatment of these compounds with ceric ammonium nitrate yielded the *N*-dearylated 2-azetidinones **9a-n** in good to excellent yields. The effects of solvent, molar equiv of CAN and different temperatures have been investigated and optimum conditions were established.

**Keywords:** 2-Azetidinones; *N*-insubstituted β-Lactam; ceric ammonium nitrate; Staudinger reaction; *p*-ethoxyphenyl (PEP) group.

## Introduction

Protection of the amide-NH is an area of protective group chemistry that has received little attention, and as a consequence, few good methods exist for amide-NH protection [1]. β-Lactam antibiotics can be synthesized by various routes, but the preparation of *N*-unsubstituted (NH) β-lactams is a common feature [2]. *N*-Unsubstituted β-lactams play a central role as key intermediates in the synthesis of several biologically active antibiotics [3]. The importance of these types of compounds for

the semi-synthesis of the novel anticancer agents Taxol and Taxotere is also well documented [4]. Benzyl [5], allyl [6], silyl [7], *p*-methoxyphenyl [8], 4-methoxybenzyl [9], (α-thiophenyl)benzyl [10], 4-(methoxymethoxy)phenyl [11], 2,4-dimethoxybenzyl [12], 3,4-dimethoxybenzyl [13], benzyloxy-aniline linker [14], Rink resin [15], methyl-*p*-tolyl-amine [16] and pyrrolidinomethyl [17] groups are often used for $N^1$-protection of β-lactams and can be deprotected using different methods to give *N*-unsubstituted β-lactams. With few exceptions the yields are poor. Furthermore, some methods require expensive or hard to find starting materials. Toxic and unsafe byproducts which are obtained in some cases and difficulties in the purification of the main products are other common problems. Among these methods, oxidative cleavage by ceric ammonium nitrate of a *p*-methoxyphenyl moiety attached to the β-lactam ring nitrogen offers the most direct synthesis of *N*-unsubstituted β-lactams [18]. This reaction involves oxidation of the aromatic ring to benzoquinone with the release of 1 mole equiv of MeOH and 1 mole equiv of product amide [19]. In this paper, we report the utility of the *p*-ethoxyphenyl (PEP) group as a new protecting group for the protection of $N^1$-2-azetidinones. The oxidative removal of this group by ceric ammonium nitrate (CAN) to yield *N*-unsubstituted β-lactams is also reported.

**Results and Discussion**

To test the feasibility of using the *p*-ethoxyphenyl (PEP) group, we first examined separately the reactions of hydroquinone diethyl ether (**5**) and *p*-ethoxyaniline (*p*-phenetidine, **6**) with CAN. Thus, compounds **5** and **6** were oxidatively transformed into *p*-benzoquinone at room temperature in 66% and 43% yield, respectively (Scheme 1).

**Scheme 1**. Reaction of hydroquinone diethyl ether **5** and *p*-ethoxyaniline **6** with CAN.
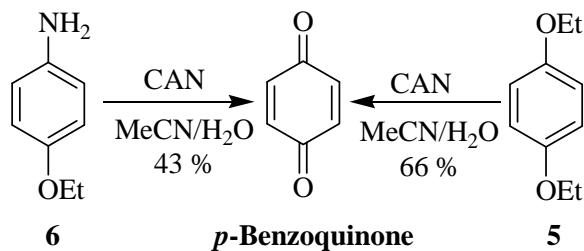


For our subsequent studies the starting Schiff bases **7a-f** were readily obtained in excellent yields by stirring a mixture of *p*-phenetidine and the corresponding aldehydes in refluxing ethanol. Cycloaddition reactions of imines **7a-f** with phthalimidioacetyl chloride and phenoxyacetyl chloride in the presence of triethylamine (Method A) or of imines **7a-b** with 2-naphthoxyacetic acid, 2,4-dichloro-phenoxyacetic acid and methoxyacetic acid in the presence of *p*-toluenesulfonyl chloride and triethylamine (Method B) gave *cis/trans* 2-azetidinones **8a-k** and **8l-n**, respectively, in good to excellent yields (Scheme 2, Table 1). The mechanism of the ketene-imine cycloaddition reaction involves initial nucleophilic attack of the imine nitrogen on the ketene carbonyl to form a zwitterionic intermediate, which cyclizes to form the β-lactam [21].

The FT-IR spectra of 2-azetidinones **8a-n** displayed the β-lactam carbonyl at 1743.5-1786.6 cm$^{-1}$. The indicated stereochemistry of 2-azetidinones **8a-n** was deduced from the coupling constant of H-3 and H-4, which was calculated to be $J_{3,4}$= 4.2-4-8 Hz for the *cis* and $J_{3,4}$= 2.5 Hz for the *trans* stereoisomers. The $^{13}$C-NMR showed the characteristic lactam carbonyl signal at 161.26-167.78 ppm.

**Scheme 2.** Synthesis of monocyclic 2-azetidinones **8a-n**.
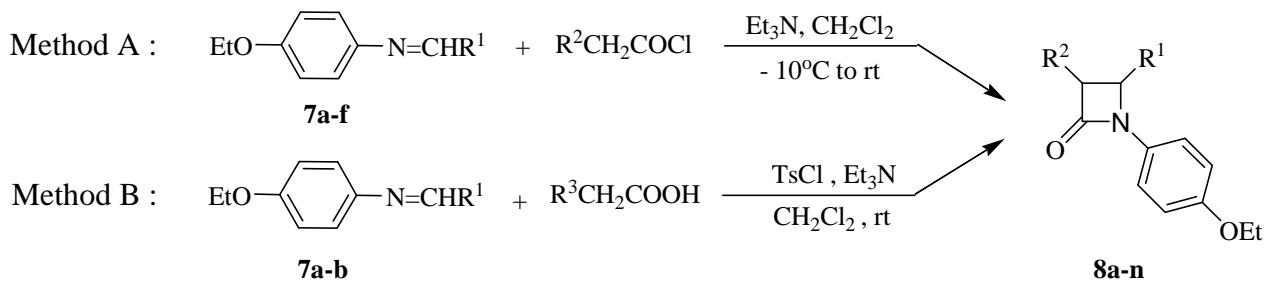


The phthalimido-2-azetidinones **8a-e** showed the C-3 signals at 63.03-63.68 and the C-4 signals at 61.03-62.68 ppm, whereas the alkoxy-2-azetidinones **8f-n** showed the corresponding signals at 81.09-84.74 and 63.59-63.23 ppm, respectively. Other spectroscopic and analytical data were consistent with the indicated structures.

**Table 1**. *N*-(*p*-Ethoxyphenyl)-2-azetidinones **8a-n**.

| Entry | Schiff base | Product | Method | R$^1$ | R$^2$ | *cis/trans* | Yield % |
|-------|-------------|---------|--------|-------|-------|-------------|---------|
| 1 | **7a** | **8a** | A | 4-NO$_2$Ph | PhthN | *trans* | 81 |
| 2 | **7b** | **8b** | A | 4-ClPh | PhthN | *trans* | 87 |
| 3 | **7c** | **8c** | A | 4-MeOPh | PhthN | *trans* | 80 |
| 4 | **7d** | **8d** | A | 4-MePh | PhthN | *trans* | 84 |
| 5 | **7e** | **8e** | A | C=CPh | PhthN | *cis* | 88 |
| 6 | **7a** | **8f** | A | 4-NO$_2$Ph | PhO | *cis* | 91 |
| 7 | **7b** | **8g** | A | 4-ClPh | PhO | *cis* | 88 |
| 8 | **7c** | **8h** | A | 4-MeOPh | PhO | *cis* | 90 |
| 9 | **7d** | **8i** | A | 4-MePh | PhO | *cis* | 94 |
| 10 | **7e** | **8j** | A | C=CPh | PhO | *cis* | 91 |
| 11 | **7f** | **8k** | A | 3,4-diMeOPh | PhO | *cis* | 95 |
| 12 | **7a** | **8l** | B | 4-NO$_2$Ph | 2-naphthO | *cis* | 84 |
| 13 | **7a** | **8m** | B | 4-NO$_2$Ph | 2,4-diClPhO | *cis* | 89 |
| 14 | **7d** | **8n** | B | 4-MePh | MeO | *cis* | 92 |

According to the reported procedure for *N*-dearylation of similar 2-azetidinones [8a], β-lactams **8a-n** were treated with ceric ammonium nitrate (3 eq.) in aqueous acetonitrile at 0°C for one hour (Scheme 3) to give NH-β-lactams **9a-n**.

**Scheme 3**. *N*-Dearylation of 2-azetidinones **8a-n** with 3 eq CAN at 0°C.
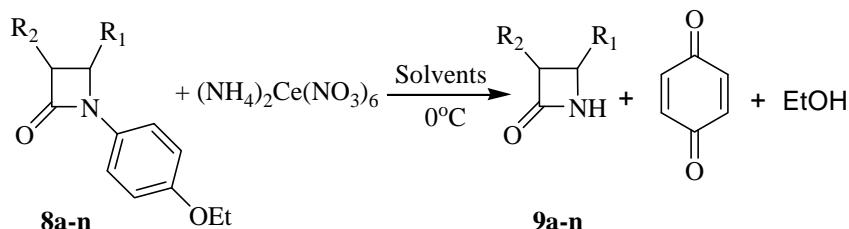


Next we decided to find the optimum condition for *N*-dearylation of the above 2-azetidinones. First, N-(*p*-ethoxyphenyl)-β-lactams **8a-n** were treated by CAN (3 eq.) in two different solvents (MeCN and THF) at 0°C for the times mentioned in Table 2. As shown in Table 2, acetonitrile was a better solvent than THF. Although the solubility of some substrates (especially 3-phthalimido-2-azetidinones **8a-e**) was not good, the yield was better. The optimum time for these reactions was 30 min, as seen from the table.

**Table 2**. Reaction of *N*-(*p*-ethoxyphenyl)-2-azetidinones **8a-n** with 3 eq. CAN at 0°C.

| Entry | Substrate | Product | Isolated yield (%) in CH₃CN/H₂O (3:1) | | | Isolated yield (%) in THF/H₂O (2:1) | | |
|---|---|---|---|---|---|---|---|---|
| | | | **15 min** | **30 min** | **1 hr** | **15 min** | **30 min** | **1 hr** |
| 1 | **8a** | **9a** | 51 | 77 | 76 | 35 | 63 | 62 |
| 2 | **8b** | **9b** | 33 | 74 | 75 | 56 | 70 | 70 |
| 3 | **8c** | **9c** | 60 | 81 | 81 | 40 | 55 | 56 |
| 4 | **8d** | **9d** | 53 | 78 | 77 | 38 | 68 | 69 |
| 5 | **8e** | **9e** | 65 | 82 | 83 | 48 | 62 | 60 |
| 6 | **8f** | **9f** | 63 | 80 | 77 | 43 | 53 | 52 |
| 7 | **8g** | **9g** | 48 | 82 | 82 | 30 | 58 | 60 |
| 8 | **8h** | **9h** | 62 | 86 | 79 | 42 | 71 | 72 |
| 9 | **8i** | **9i** | 57 | 84 | 83 | 50 | 65 | 65 |
| 10 | **8j** | **9j** | 54 | 76 | 78 | 39 | 64 | 65 |
| 11 | **8k** | **9k** | 53 | 84 | 81 | 58 | 76 | 73 |
| 12 | **8l** | **9l** | 66 | 80 | 80 | 45 | 59 | 61 |
| 13 | **8m** | **9m** | 49 | 76 | 79 | 37 | 54 | 50 |
| 14 | **8n** | **9n** | 69 | 83 | 82 | 47 | 66 | 63 |

TLC of the reaction mixtures confirmed the presence of *p*-benzoquinone, which was easily eliminated by forming the corresponding bisulfite adduct that could be washed out with water after workup with aqueous NaHSO₃ solution. Removal of the *p*-ethoxyphenyl (PEP) residue generally resulted in a shift at the β-lactam carbonyl function to a higher field and the appearance of NH peaks in the IR spectra (see the Experimental section). The formation of NH-β-lactams **9a-n** was also confirmed by mass spectra and elemental analyses. The ¹H-NMR spectra exhibited the NH signals at about 8.41-9.19 ppm as a broad peak in DMSO-*d*₆, which was eliminated by shaking vigorously with D₂O.

The mechanism of CAN deprotection of the *p*-ethoxyphenyl group from amides has not been fully studied. However experiments on the oxidation of 1,4-dimethoxybenzenes (similar to 1,4-diethoxy benzenes) to the corresponding quinones have shown that cleavage of the aryl-oxygen bonds requires two eq. of CAN [20]. Thus, it is found that at least two mol equiv of CAN are needed for the oxidation of *N*-(4-ethoxyphenyl)-2-azetidinones **8a-n** to *N*-unsubstituted-2-azetidinones **9a-n**. According to Table 3, it is shown that 2.8 mol eq. of CAN is sufficient for completing the oxidative *N*-dearylation of *N*-(4-ethoxyphenyl)-2-azetidinones **8a-n** (except for **8e**). Deprotection of compound **8e** needed three eq. of CAN to complete conversion to **9e** in 82% yield.

**Table 3**. Deprotection of 2-azetidinones **8a-n** by different molar of CAN in MeCN/$H_2O$ (3/1) at $0^{\circ}C$.

| Entry | Substrate | Product | Isolated yield (%) per molar equiv of CAN | | | | |
|:---:|:---:|:---:|:---:|:---:|:---:|:---:|:---:|
| | | | 2.0 | 2.5 | 2.8 | 3.0 | 3.5 |
| 1 | **8a** | **9a** | 22 | 48 | 78 | 77 | 75 |
| 2 | **8b** | **9b** | 18 | 42 | 74 | 74 | 75 |
| 3 | **8c** | **9c** | 31 | 51 | 82 | 81 | 82 |
| 4 | **8d** | **9d** | 17 | 37 | 77 | 78 | 75 |
| 5 | **8e** | **9e** | 14 | 32 | 73 | 82 | 81 |
| 6 | **8f** | **9f** | 24 | 44 | 80 | 80 | 79 |
| 7 | **8g** | **9g** | 34 | 53 | 84 | 82 | 76 |
| 8 | **8h** | **9h** | 30 | 49 | 85 | 86 | 85 |
| 9 | **8i** | **9i** | 29 | 40 | 85 | 84 | 83 |
| 10 | **8j** | **9j** | 19 | 31 | 76 | 76 | 76 |
| 11 | **8k** | **9k** | 27 | 49 | 84 | 84 | 82 |
| 12 | **8l** | **9l** | 22 | 47 | 80 | 80 | 80 |
| 13 | **8m** | **9m** | 18 | 40 | 76 | 76 | 76 |
| 14 | **8n** | **9n** | 33 | 53 | 83 | 83 | 84 |

The effect of different temperatures on this oxidation was studied next. 2-Azetidinones **8a**-**n** were treated separately with CAN for 30 min in aqueous acetonitrile at -10°C, 0°C and room temperature (RT). As shown in Table 4, nearly identical yields of NH-β-lactams **9a-n** were obtained at 0°C and RT. The lower yield of *N*-unsubstituted β-lactams in aqueous acetonitrile at -10°C may be attributed to the low solubility of 2-azetidinones **8a-n** at that temperature.

According to a reported mechanism for the cleavage of *p*-methoxyphenyl group [21], following mechanism shown in Scheme 4 is suggested for the oxidative cleavage of *p*-ethoxyphenyl moiety.

**Table 4**. Deprotection of β-lactams **8a-n** by 2.8 molar eq. of CAN for 30 min at different temperatures.

| Entry | Substrate | Product | Isolated yield (%) at low temperatures | | |
|---|---|---|---|---|---|
| | | | - 10 °C | 0 °C | RT |
| 1 | **8a** | **9a** | 31 | 78 | 75 |
| 2 | **8b** | **9b** | 34 | 74 | 76 |
| 3 | **8c** | **9c** | 38 | 82 | 81 |
| 4 | **8d** | **9d** | 30 | 77 | 77 |
| 5 | **8e** | **9e** | 43 | 73 | 71 |
| 6 | **8f** | **9f** | 42 | 80 | 81 |
| 7 | **8g** | **9g** | 48 | 84 | 83 |
| 8 | **8h** | **9h** | 50 | 85 | 85 |
| 9 | **8i** | **9i** | 43 | 85 | 86 |
| 10 | **8j** | **9j** | 44 | 76 | 78 |
| 11 | **8k** | **9k** | 43 | 84 | 83 |
| 12 | **8l** | **9l** | 47 | 79 | 80 |
| 13 | **8m** | **9m** | 39 | 78 | 74 |
| 14 | **8n** | **9n** | 49 | 83 | 85 |

**Scheme 4**
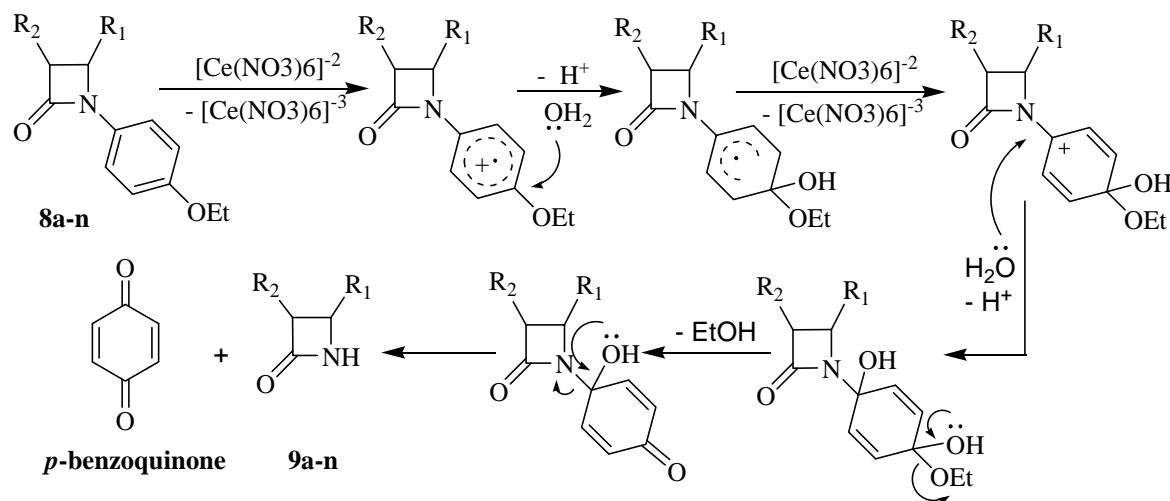


## Conclusions

In conclusion, in this study it was shown that the *p*-ethoxyphenyl group can be introduced onto the 2-azetidinone skeleton as a suitable *N*-protective group. Furthermore it can easily be removed by CAN under mild conditions. It should be noted that the $R^1$ and $R^2$ substitution on the β-lactam ring and the stereochemistry of the ring remain intact during the course of reaction. In addition to good to excellent yields of the products, ethanol is formed in this oxidation reaction, which is a less toxic and friendlier

byproduct for the environment than methanol. It is noteworthy that this oxidative cleavage is rapid and can be performed at room temperature.

## Experimental

*General*

All required chemicals were purchased from the Merck or Fluka chemical companies. Dichloromethane and triethylamine were dried by distillation over $CaH_2$ and then stored over 4Å molecular sieves. IR spectra were run on a Shimadzu FT-IR 8300 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded in DMSO-$d_6$ or $CDCl_3$ using a Bruker Avance DPX instrument (^{1}H-NMR at 250 MHz, ^{13}C-NMR at 62.9 MHz, respectively). Chemical shifts are reported in ppm (δ) downfield from TMS. All the coupling constants (*J*) are given in Hertz. The mass spectra were recorded on a Shimadzu GC-MS QP 1000 EX instrument. Elemental analyses were run on a Thermo Finnigan Flash EA-1112 series. Melting points were determined in open capillaries with a Buchi 510 melting point apparatus and are not corrected. Thin-layer chromatography was carried out on silica gel 254 analytical sheets obtained from Fluka. Column chromatography was performed on Merck Kieselguhr (230-270 mesh).

*General procedure for synthesis of Schiff bases* **7a-f**.

A mixture of *p*-ethoxyaniline (20.0 mmol) and corresponding aldehyde (20.0 mmol) was refluxed in EtOH for 2-4 hours. After cooling the solutions, the precipitate formed was filtered off and washed with ethanol to give pure Schiff bases **7a-f** as colored solid or crystals in excellent yields.

*(4-Nitrobenzylidene)-(4-ethoxyphenyl)amine* (**7a**). Brown solid (from *p*-phenetidine and 4-nitro-benzaldehyde); yield 97 %; m.p. 124-126 °C; IR (KBr) (cm$^{-1}$) 1620.1 (C=N); ^{1}H-NMR (CDCl$_3$) δ 1.33 (Me, t, 3H), 3.88 (OCH$_2$, q, 2H), 6.81-8.18 (ArH, m, 8H), 8.44 (HC=N, s, 1H); ^{13}C-NMR (CDCl$_3$) δ 14.82 (Me), 63.73 (OCH$_2$), 115.05-154.52 (aromatic carbons), 158.66 (C=N); GC-MS m/z = 270 [M$^+$]; Anal. calcd. for C$_{15}$H$_{14}$N$_2$O$_3$: C, 66.66; H, 5.22; N, 10.36. Found: C, 66.62; H, 5.39; N, 10.32.

*(4-Chlorobenzylidene)-(4-ethoxyphenyl)amine* (**7b**). Milky-coloured solid (from *p*-phenetidine and 4-chlorobenzaldehyde); yield 94 %; m.p. 92-94 °C; IR (KBr) (cm$^{-1}$) 1620.1 (C=N); ^{1}H-NMR (CDCl$_3$) δ 1.43 (Me, t, 3H), 4.00 (OCH$_2$, q, 2H), 6.87-7.80 (ArH, m, 8H), 8.39 (HC=N, s, 1H); ^{13}C-NMR (CDCl$_3$) δ 14.84 (Me), 63.63 (OCH$_2$), 114.94-156.43 (aromatic carbons), 157.85 (C=N); GC-MS m/z = 261 [M$^+$, $^{37}$Cl], 259 [M$^+$, $^{35}$Cl]; Anal. calcd. for C$_{15}$H$_{14}$ClNO: C, 69.36; H, 5.43; N, 5.39. Found: C, 69.29; H, 5.49; N, 5.44.

*(4-Methoxybenzylidene)-(4-ethoxyphenyl)amine* (**7c**). Milky-colour solid (from *p*-phenetidine and 4-methoxybenzaldehyde); yield 95 %; m.p. 128-130°C; IR (KBr) (cm$^{-1}$) 1612.4 (C=N); ^{1}H-NMR (CDCl$_3$) δ 1.41 (Me, t, 3H), 3.86 (OMe, s, 3H), 4.03 (OCH$_2$, q, 2H), 6.88-7.83 (ArH, m, 8H), 8.39 (HC=N, s, 1H); ^{13}C-NMR (CDCl$_3$) δ 14.88 (Me), 55.37 (OMe), 63.64 (OCH$_2$), 114.12-157.73

(aromatic carbons), 161.95 (C=N); GC-MS m/z = 255 [M$^+$]; Anal. calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.17; H, 6.80; N, 5.45.

*(4-Methylbenzylidene)-(4-ethoxyphenyl)amine* (**7d**). Yellow solid (from *p*-phenetidine and 4-methyl-benzaldehyde); yield 93 %; m.p. 87-89 °C; IR (KBr) (cm$^{-1}$) 1609.8 (C=N); $^1$H-NMR (CDCl$_3$) δ 1.31 (Me, t, 3H), 2.36 (Me, s, 3H), 4.00 (OCH$_2$, q, 2H), 6.85-7.76 (ArH, m, 8H), 8.39 (HC=N, s, 1H); $^{13}$C-NMR (CDCl$_3$) δ 14.84, 21.54 (2Me), 63.57 (OCH$_2$), 114.87-157.48 (aromatic carbons), 158.16 (C=N); GC-MS m/z = 239 [M$^+$]; Anal. calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85 Found: C, 80.35; H, 7.23; N, 5.89.

*(4-Cinnamylidene)-(4-ethoxyphenyl)amine* (**7e**). Light yellow solid (from *p*-phenetidine and cinnamaldehyde); yield 96 %; m.p. 76-78 °C; IR (KBr) (cm$^{-1}$) 1622.5 (C=N); $^1$H-NMR (CDCl$_3$) δ 1.40 (Me, t, 3H), 4.01 (OCH$_2$, q, 2H), 6.87-7.52 (ArH and CH=CH, m, 11H), 8.26 (HC=N, d, 1H); $^{13}$C-NMR (CDCl$_3$) δ 14.84 (Me), 63.61 (OCH$_2$), 114.94-157.78 (C=C and aromatic carbons), 159.29 (C=N); GC-MS m/z = 251 [M$^+$]; Anal. calcd. for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.19; H, 6.78; N, 5.52.

*(3,4-Dimethoxybenzylidene)-(4-ethoxyphenyl)amine* (**7f**). Green-yellow solid (from *p*-phenetidine and 3,4-dimethoxybenzaldehyde); yield 94 %; m.p. 82-84 °C. IR (KBr) (cm$^{-1}$) 1619.7 (C=N); $^1$H-NMR (CDCl$_3$) δ 1.39 (Me, t, 3H), 3.89, 3.95 (2OMe, 2s, 6H), 4.00 (OCH$_2$, q, 2H), 6.85-7.59 (ArH, m, 7H), 8.34 (HC=N, s, 1H); $^{13}$C-NMR (CDCl$_3$) δ 14.86 (Me), 55.91 (OMe), 63.57 (OCH$_2$), 108.73-157.35 (aromatic carbons), 157.78 (C=N); GC-MS m/z = 285 [M$^+$]; Anal. calcd. for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.60; H, 6.67; N, 4.94.

*Typical experimental procedure for the synthesis of 2-azetidinones* **8a-n**

*Method A*. A solution of the corresponding acyl chlorides (1.50 mmol) in dry CH$_2$Cl$_2$ (10 mL) was slowly added to a solution of Schiff bases **7a-f** (1.00 mmol) and triethylamine (3.00 mmol) in CH$_2$Cl$_2$ (15 mL) at –10 °C. The reaction mixture was then allowed to warm to room temperature, stirred overnight and then it was washed successively with saturated sodium bicarbonate solution (20 mL) and brine (20 mL), dried (Na$_2$SO$_4$) and the solvent was evaporated to give the crude product which was then purified by column chromatography or recrystalization from EtOAc.

*Method B*. A solution of Schiff base **7a-b** (1.0 eq.) was stirred with the corresponding substituted acetic acid (1.5 eq.), *p*-toluenesulfonyl chloride (1.5 eq.) and triethylamine (4-5 eq.) in dry CH$_2$Cl$_2$ at room temperature. After 8 to 10 h, the mixture was washed with saturated sodium bicarbonate solution and brine, dried over sodium sulfate and the solvent was evaporated to give the crude product which was then purified by recrystalization from EtOAc, unless stated otherwise.

*2-(1-(4-Ethoxyphenyl)-2-(4-nitrophenyl)-4-oxoazetidin-3-yl)isoindoline-1,3-dione* (**8a**). Yield: 81%; mp: 190-192 °C; IR (CHCl$_3$) cm$^{-1}$: 1738.0, 1776.2 (CO, phth); 1788.8 (CO, β-lactam); $^1$H-NMR (DMSO-*d*$_6$) δ 1.29 (Me, t, 3H), 3.92 (OCH$_2$, q, 2H), 5.32 (H-4, d, 1H, *J*=2.5), 5.70 (H-3, d, 1H, *J*=2.5),

6.92-8.27 (ArH, m, 12H); $^{13}$C-NMR (DMSO-$d_6$) δ 14.40 (Me), 58.33 (OCH$_2$), 61.52 (C-4), 63.26 (C-3), 115.00-155.38 (aromatic carbons), 161.11 (CO, phth), 166.63 (CO, β-lactam); GC-MS m/z = 457 [M$^+$]; Anal. calcd. for C$_{25}$H$_{19}$N$_3$O$_6$: C, 65.64; H, 4.19; N, 9.19. Found: C, 65.69; H, 4.13; N, 9.22.

*2-(2-(4-Chlorophenyl)-1-(4-ethoxyphenyl)-4-oxoazetidin-3-yl)isoindoline-1,3-dione* (**8b**). Yield: 87 %; mp: 211-213 °C IR (CHCl$_3$) cm$^{-1}$: 1720.4, 1758.9 (CO, phth), 1786.6 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.37 (Me, t, 3H), 3.97 (OCH$_2$, q, 2H), 5.22 (H-4, d, 1H, *J*=2.5), 5.32 (H-3, d, 1H, *J*=2.5), 6.78-7.76 (ArH, m, 12H); $^{13}$C-NMR (CDCl$_3$) δ 14.78 (Me), 60.68 (OCH$_2$), 62.68 (C-4), 63.68 (C-3), 115.02-156.01 (aromatic carbons), 161.23 (CO, phth), 166.78 (CO, β-lactam); GC-MS m/z = 448 [M$^+$, $^{37}$Cl], 446 [M$^+$, $^{35}$Cl]; Anal. Calcd for C$_{25}$H$_{19}$ClN$_2$O$_4$: C, 67.19; H, 4.29; N, 6.27. Found: C, 67.16; H, 4.27; N, 6.24.

*2-(1-(4-Ethoxyphenyl)-2-(4-methoxyphenyl)-4-oxoazetidin-3-yl)isoindoline-1,3-dione* (**8c**). Yield: 80 %; mp: 199-201 °C IR (CHCl$_3$) cm$^{-1}$: 1724.2, 1758.9 (CO, phth), 1778.0 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.09 (Me, t, 3H), 3.74 (OCH$_2$, q, 2H), 4.19 (OMe, s, 3H), 4.96 (H-4, d, 1H, *J*=2.5), 5.20 (H-3, d, 1H, *J*=2.5), 6.62-7.73 (ArH, m, 12H); $^{13}$C-NMR (CDCl$_3$) δ 14.50 (Me), 55.04 (OCH$_2$), 59.65 (OMe), 61.90 (C-4), 63.05 (C-3), 114.27-161.43 (aromatic carbons), 164.24 (CO, phth), 167.57 (CO, β-lactam); GC-MS m/z = 442 [M$^+$]; Anal. calcd. for C$_{26}$H$_{22}$N$_2$O$_5$: C, 70.58; H, 5.01; N, 6.33. Found: C, 70.63; H, 5.05; N, 6.28.

*2-(1-(4-Ethoxyphenyl)-2-oxo-4-p-tolylazetidin-3-yl)isoindoline-1,3-dione* (**8d**). Yield: 84 % mp: 202-204 °C; IR (KBr) cm$^{-1}$: 174.2, 1776.2 (CO, phth), 1788.7 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.35 (Me, t, 3H), 2.33 (Me, s, 3H), 3.94 (OCH$_2$, q, 2H), 5.25 (H-4, d, 1H, *J*=2.5), 5.32 (H-3, d, 1H, *J*=2.5), 6.68-7.85 (ArH, m, 12H); $^{13}$C-NMR (CDCl$_3$) δ 14.30, 20.73 (2Me), 60.70 (OCH$_2$), 62.27 (C-4), 63.13 (C-3), 114.41-155.32 (aromatic carbons), 161.11 (CO, phth), 166.35 (CO, β-lactam); GC-MS m/z = 426 [M$^+$]; Anal. calcd. for C$_{26}$H$_{22}$N$_2$O$_4$: C, 70.58; H, 5.01; N, 6.33. Found: C, 70.64; H, 5.05; N, 6.37.

*2-(1-(4-Ethoxyphenyl)-2-oxo-4-styrylazetidin-3-yl)isoindoline-1,3-dione* (**8e**). Yield: 88 %; mp: 161-163 °C; IR (CHCl$_3$) cm$^{-1}$: 1724.2, 1758.5 (CO, phth), 1774.7 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.37 (Me, t, 3H), 2.33 (Me, s, 3H), 3.97 (OCH$_2$, q, 2H), 5.03 (H-4, dd, 1H, *J*=5.5, 8.5), 5.68 (H-3, d, 1H, *J*=5.5), 6.32 (H-5, dd, *J*=8.5, 16.0), 6.85 (H-6, d, 1H, *J*=9.0), 7.19-7.82 (ArH, m, 13H); $^{13}$C-NMR (CDCl$_3$) δ 14.78 (Me), 57.69 (OCH$_2$), 61.04 (C-4), 63.67 (C-3), 114.99-155.82 (C=C, aromatic carbons), 160.56 (CO, phth), 167.28 (CO, β-lactam); GC-MS m/z = 438 [M$^+$]; Anal. calcd. for C$_{27}$H$_{22}$N$_2$O$_4$: C, 73.96; H, 5.06; N, 6.39. Found: C, 74.02; H, 5.09; N, 6.33.

*1-(4-Ethoxyphenyl)-4-(4-nitrophenyl)-3-phenoxyazetidin-2-one* (**8f**). Purified by column chromatography (eluent: 6:4 hexane-EtOAc); yield: 91 %; mp: 180-182 °C; IR (KBr) cm$^{-1}$: 1743.5 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.30 (Me, t, 3H), 3.89 (OCH$_2$, q, 2H), 5.39 (H-4, d, 1H, *J*=4.8), 5.55 (H-3, d, 1H, *J*=4.8), 6.68-8.08 (ArH, m, 13H); $^{13}$C-NMR (CDCl$_3$) δ 14.74 (Me), 61.11 (OCH$_2$), 63.72 (C-4), 81.24 (C-3), 115.17-156.49 (aromatic carbons), 161.82 (CO, β-lactam); GC-MS m/z = 404[M$^+$]; Anal. calcd. for C$_{23}$H$_{20}$N$_2$O$_5$: C, 68.31; H, 4.98; N, 6.93. Found: C, 68.28; H, 5.05; N, 6.88.

*4-(4-Chlorophenyl)-1-(4-ethoxyphenyl)-3-phenoxyazetidin-2-one* (**8g**). Yield: 88 %; mp: 164-166 °C; IR (KBr) cm$^{-1}$:1746.5 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.31 (Me, t, 3H), 3.87 (OCH$_2$, q, 2H), 5.24 (H-4, d, 1H, *J*=4.8), 5.45 (H-3, d, 1H, *J*=4.8), 6.68-7.23 (ArH, m, 13H); $^{13}$C-NMR (CDCl$_3$) δ 14.77 (Me), 61.41 (OCH$_2$), 63.68 (C-4), 81.09 (C-3), 115.03-156.78 (aromatic carbons), 162.26 (CO, β-lactam); GC-MS m/z = 395[M$^+$, $^{37}$Cl], 393 [M$^+$, $^{35}$Cl]; Anal. calcd. for C$_{23}$H$_{20}$ClNO$_3$: C, 70.14; H, 5.12; N, 3.56. Found: C, 70.24; H, 5.17; N, 3.50.

*1-(4-Ethoxyphenyl)-4-(4-methoxyphenyl)-3-phenoxyazetidin-2-one* (**8h**). Purified by column chromatography (eluent: 7:3 hexane-EtOAc); yield: 90 %; mp: 168-170 °C; IR (KBr) cm$^{-1}$:1753.5 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.30 (Me, t, 3H), 3.64 (OMe, s, 3H), 3.88 (OCH$_2$, q, 2H), 5.21 (H-4, d, 1H, *J*=4.7), 5.41 (H-3, d, 1H, *J*=4.7), 6.69-7.23 (ArH, m, 13H); $^{13}$C-NMR (CDCl$_3$) δ 14.79 (Me), 55.17 (OMe), 61.79 (OCH$_2$), 63.65 (C-4), 81.23 (C-3), 113.84-159.84 (aromatic carbons), 162.56 (CO, β-lactam); GC-MS m/z = 389 [M$^+$]; Anal. calcd. for C$_{24}$H$_{23}$NO$_4$: C, 74.02; H, 5.95; N, 3.60. Found: C, 73.97; H, 5.90; N, 3.64.

*1-(4-Ethoxyphenyl)-3-phenoxy-4-p-tolylazetidin-2-one* (**8i**). Yield: 94 %; mp: 165-167 °C; IR (CHCl$_3$) cm$^{-1}$: 1751.2 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.31 (Me, t, 3H), 2.25 (Me, s, 3H), 3.91 (OCH$_2$, q, 2H), 5.28 (H-4, d, 1H, *J*=4.8), 5.47 (H-3, d, 1H, *J*=4.8), 6.74-7.30 (ArH, m, 13H); $^{13}$C-NMR (CDCl$_3$) δ 14.76, 21.17 (2Me), 61.98 (OCH$_2$), 63.60 (C-4), 81.24 (C-3), 114.91-157.08 (aromatic carbons), 162.55 (CO, β-lactam); GC-MS m/z = 373 [M$^+$]; Anal. calcd. for C$_{24}$H$_{23}$NO$_3$: C, 77.19; H, 6.21; N, 3.75. Found: C, 77.25; H, 6.26; N, 3.73.

*1-(4-Ethoxyphenyl)-3-phenoxy-4-styrylazetidin-2-one* (**8j**). Yield: 91 %; mp: 171-173 °C; IR (CHCl$_3$) cm$^{-1}$: 1749.3 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.30 (Me, t, 3H), 3.90 (OCH$_2$, q, 2H), 4.90 (H-4, dd, 1H, *J*=4.9, 8.5), 5.37 (H-3, d, 1H, *J*=4.9), 6.23 (H-5, dd, *J*=8.5, 16.0), 6.75 (H-6, d, 1H, *J*=16.0), 6.87-7.38 (ArH, m, 14H); $^{13}$C-NMR (CDCl$_3$) δ 14.80 (Me), 61.12 (OCH$_2$), 63.70 (C-4), 81.48 (C-3), 115.01-157.42 (C=C, aromatic carbons), 162.23 (CO, β-lactam); GC-MS m/z = 385 [M$^+$]; Anal. calcd. for C$_{25}$H$_{23}$NO$_3$: C, 77.90; H, 6.01; N, 3.63. Found: C, 77.97; H, 6.06; N, 3.60.

*4-(3,4-Dimethoxyphenyl)-1-(4-ethoxyphenyl)-3-phenoxyazetidin-2-one* (**8k**). Yield: 95 %; mp: 186-188 °C; IR (KBr) cm$^{-1}$: 1758.2 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.36 (Me, t, 3H), 3.75, 3.81 (2OMe, 2s, 6H), 3.95 (OCH$_2$, q, 2H), 5.28 (H-4, d, 1H, *J*=4.2), 5.52 (H-3, d, 1H, *J*=4.2), 6.74-7.33 (ArH, m, 12H); $^{13}$C-NMR (CDCl$_3$) δ 14.77 (Me), 55.76, 55.94 (2OMe), 62.05 (OCH$_2$), 63.64 (C-4), 81.11 (C-3), 110.78-156.96 (aromatic carbons), 162.50 (CO, β-lactam); GC-MS m/z = 419 [M$^+$]; Anal. calcd. for C$_{25}$H$_{25}$NO$_5$: C, 71.58; H, 6.01; N, 3.34. Found: C, 71.63; H, 5,98; N, 3.38.

*1-(4-Ethoxyphenyl)-3-(naphthalen-2-yloxy)-4-(4-nitrophenyl)azetidin-2-one* (**8l**). Yield: 84 %; mp: 174-176 °C; IR (KBr) cm$^{-1}$: 1750.6 (CO, β-lactam); $^1$H-NMR (CDCl$_3$) δ 1.39 (Me, t, 3H), 3.95 (OCH$_2$, q, 2H), 5.51 (H-4, d, 1H, *J*=4.8), 5.74 (H-3, d, 1H, *J*=4.8), 6.79-8.11 (ArH, m, 15H); $^{13}$C-NMR (CDCl$_3$) δ 14.75 (Me), 61.08 (OCH$_2$), 63.73 (C-4), 81.16 (C-3), 108.98-156.28 (aromatic carbons), 161.70 (CO, β-lactam); GC-MS m/z = 454 [M$^+$]; Anal. calcd. for C$_{27}$H$_{22}$N$_2$O$_5$: C, 71.35; H, 4.88; N, 6.16. Found: C, 71.41; H, 4.92; N, 6.20.

*3-(2,4-Dichlorophenoxy)-1-(4-ethoxyphenyl)-4-(4-nitrophenyl)azetidin-2-one* (**8m**). Purified by column chromatography (eluent: 6:4 hexane-EtOAc); yield: 89 %; mp: 160-162 °C; IR (KBr) cm$^{-1}$: 1747.8 (CO, β-lactam); $^{1}$H-NMR (CDCl$_3$) δ 1.37 (Me, t, 3H), 3.96 (OCH$_2$, q, 2H), 5.52 (H-4, d, 1H, *J*=5.1), 5.56 (H-3, d, 1H, *J*=5.1), 6.78-8.22 (ArH, m, 11H); $^{13}$C-NMR (CDCl$_3$) δ 14.74 (Me), 60.44 (OCH$_2$), 63.73 (C-4), 81.84 (C-3), 115.19-156.38 (aromatic carbons), 161.26 (CO, β-lactam); GC-MS m/z = 476 [M$^+$, $^{37}$Cl], 474, 472 [M$^+$, $^{35}$Cl]; Anal. calcd. for C$_{23}$H$_{18}$Cl$_2$N$_2$O$_5$: C, 58.37; H, 3.83; N, 5.92. Found: C, 58.32; H, 3.88; N, 5.89.

*1-(4-Ethoxyphenyl)-3-methoxy-4-p-tolylazetidin-2-one* (**8n**). Yield: 92 %; mp: 133-135 °C; IR (KBr) cm$^{-1}$: 1744.5 (CO, β-lactam); $^{1}$H-NMR (CDCl$_3$) δ 1.34 (Me, t, 3H), 2.34 (Me, s, 3H), 3.94 (OCH$_2$, q, 2H), 4.76 (H-4, d, 1H, *J*=4.7), 5.12 (H-3, d, 1H, *J*=4.7), 6.73-7.28 (ArH, m, 15H); $^{13}$C-NMR (CDCl$_3$) δ 14.77, 21.24 (2Me), 61.61 (OCH$_2$), 63.59 (C-4), 84.74 (C-3), 114.85-155.64 (aromatic carbons), 163.78 (CO, β-lactam); GC-MS m/z = 311 [M$^+$]; Anal. calcd. for C$_{19}$H$_{21}$NO$_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.34; H, 6.85; N, 4.47.

*Typical experimental procedure for the synthesis of N-unsubstituted β-lactams* **9a-n**

A solution of (NH$_4$)$_2$Ce(NO$_3$)$_6$ (CAN, 2.0-3.5 mmol) in water (15 mL) was added dropwise to a solution of the β-lactam **8a-n** (1.00 mmol) in CH$_3$CN or THF (30 mL) at the temperature mentioned in Table 3. The mixture was stirred at corresponding temperature for the mentioned time, then water (30 mL) was added and the mixture was extracted with EtOAc (3×20 mL) and washed with 10 % aqueous NaHCO$_3$ (40 mL). The aqueous layer of NaHCO$_3$ was extracted again with EtOAc (15 mL) and all organic layers were combined and washed successively with 10 % NaHSO$_3$ (2×30 mL), 10 % NaHCO$_3$ (20 mL) and brine (20 mL) and then dried over sodium sulfate. After filtration and evaporation of the solvent *in vacuo*, the crude product was purified by column chromatography or recrystalization from diethyl ether, as indicated.

*2-(2-(4-Nitrophenyl)-4-oxoazetidin-3-yl)isoindoline-1,3-dione* (**9a**). Purified by recrystalization; yield: 77 %; mp: 210-212 °C; IR (CHCl$_3$) cm$^{-1}$: 1736.3, 1776.7 (CO, phth), 1785.5 (CO, β-lactam), 3373.5 (NH); $^{1}$H-NMR (DMSO-*d$_6$*) δ 4.99 (H-3, d, 1H, *J*=2.5), 5.70 (H-4, dd, 1H, *J*=1.3, 2.5), 7.38-8.27 (ArH, m, 8H), 9.11 (NH, brs, 1H); $^{13}$C-NMR (DMSO-*d$_6$*) δ 59.51 (C-4), 62.49 (C-3), 123.19-147.12 (aromatic carbons), 164.33 (CO, phth), 166.24 (CO, β-lactam); GC-MS m/z = 337 [M$^+$]; Anal. calcd. for C$_{17}$H$_{11}$N$_3$O$_5$: C, 60.54; H, 3.29; N, 12.46. Found: C, 60.60; H, 3.32; N, 12.51.

*2-(2-(4-Chlorophenyl)-4-oxoazetidin-3-yl)isoindoline-1,3-dione* (**9b**). Purified by recrystalization; yield: 74 %; mp: 196-198 °C; IR (CHCl$_3$) cm$^{-1}$: 1733.9, 1777.0 (CO, phth), 1785.0 (CO, β-lactam), 3373.5 (NH); $^{1}$H-NMR (DMSO-*d$_6$*) δ 4.92 (H-3, d, 1H, *J*=2.5), 5.04 (H-4, dd, 1H, *J*=2.5, 3.2), 7.41-7.92 (ArH, m, 8H), 9.01 (NH, brs, 1H); $^{13}$C-NMR (DMSO-*d$_6$*) δ 54.96 (C-4), 62.53 (C-3), 123.37-138.08 (aromatic carbons), 164.48 (CO, phth), 166.70 (CO, β-lactam); GC-MS m/z = 328 [M$^+$, $^{37}$Cl], 326 [M$^+$, $^{35}$Cl]; Anal. calcd. for C$_{17}$H$_{11}$ClN$_2$O$_3$: C, 62.49; H, 3.39; N, 8.57. Found: C, 62.55; H, 3.43; N, 8.54.

*2-(2-(4-Methoxyphenyl)-4-oxoazetidin-3-yl)isoindoline-1,3-dione* (**9c**). Purified by recristalization; yield: 81 %; mp: 190-192 °C; IR (KBr) cm$^{-1}$: 1735.7, 1775.6 (CO, phth), 1790.2 (CO, β-lactam), 3354.4 (NH); $^1$H-NMR (DMSO-$d_6$) δ 3.81 (OMe, s, 3H), 4.94 (H-3, d, 1H, *J*=2.5), 5.03 (H-4, dd, 1H, *J*=2.5, 3.1), 7.43-8.01 (ArH, m, 8H), 8.98 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 55.08 (OMe), 55.19 (C-4), 62.69 (C-3), 113.92-159.09 (aromatic carbons), 164.60 (CO, phth), 166.73 (CO, β-lactam); GC-MS m/z = 322 [M$^+$]; Anal. calcd. for $C_{18}H_{14}N_2O_4$: C, 67.07; H, 4.38; N, 8.69. Found: C, 67.11; H, 4.34; N, 8.65.

*2-(2-Oxo-4-p-tolylazetidin-3-yl)isoindoline-1,3-dione* (**9d**). Purified by recristalization; yield: 78 %; mp: 197-199 °C; IR (CHCl$_3$) cm$^{-1}$: 1740.0, 1775.0 (CO, phth), 1785.0 (CO, β-lactam), 3480.5 (NH); $^1$H-NMR (DMSO-$d_6$) δ 2.35 (Me, s, 3H), 4.94 (H-4, dd, 1H, *J*=2.5, 3.5), 5.04 (H-3, d, 1H, *J*=2.5), 7.23-8.03 (ArH, m, 8H), 9.02 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 20.68 (Me), 55.43 (C-4), 62.63 (C-3), 123.39-137.27 (aromatic carbons), 164.56 (CO, phth), 166.71 (CO, β-lactam); GC-MS m/z = 306 [M$^+$]; Anal. calcd. for $C_{18}H_{14}N_2O_3$: C, 70.58; H, 4.61; N, 9.15. Found: C, 70.62; H, 4.58; N, 9.21.

*2-(2-Oxo-4-styrylazetidin-3-yl)isoindoline-1,3-dione* (**9e**). Purified by recristalization; yield: 82 %; mp: 168-170 °C; IR (CHCl$_3$) cm$^{-1}$: 1726.2, 1768.6 (CO, phth), 1784.0 (CO, β-lactam), 3417.0 (NH); $^1$H-NMR (DMSO-$d_6$) δ 4.72 (H-4, m, 1H), 5.60 (H-3, d, 1H, *J*=5.2), 6.25 (H-5, dd, 1H, *J*=7.6, 16.0), 6.70 (H-6, d, 1H, *J*=16.0), 7.22-7.92 (ArH, m, 9H), 8.85 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 55.38 (C-4), 58.69 (C-3), 123.42-135.69 (C=C, aromatic carbons), 164.06 (CO, phth), 166.93 (CO, β-lactam); GC-MS m/z = 318 [M$^+$]; Anal. calcd. for $C_{19}H_{14}N_2O_3$: C, 71.69; H, 4.43; N, 8.80. Found: C, 71.74; H, 4.49; N, 8.78.

*4-(4-Nitrophenyl)-3-phenoxyazetidin-2-one* (**9f**). Purified by column chromatography (eluent: 4:6 hexane-EtOAc); yield: 80 %; mp: 160-162 °C; IR (KBr) cm$^{-1}$: 1774.4 (CO), 3247.9 (NH); $^1$H-NMR (DMSO-$d_6$) δ 5.33 (H-3, d, 1H, *J*=4.8), 5.77 (H-4, dd, 1H, *J*=2.2, 4.8), 6.77-8.20 (ArH, m, 9H), 9.10 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 56.01 (C-4), 82.71 (C-3), 115.04-156.24 (aromatic carbons), 165.78 (CO, β-lactam); GC-MS m/z = 284 [M$^+$]; Anal. calcd. for $C_{15}H_{12}N_2O_4$: C, 63.38; H, 4.25; N, 9.85. Found: C, 63.44; H, 4.30; N, 9.87.

*4-(4-Chlorophenyl)-3-phenoxyazetidin-2-one* (**9g**). Purified by recristalization; yield: 82 %; mp: 188-190 °C; IR (KBr) cm$^{-1}$: 1773.5 (CO), 3420.0 (NH); $^1$H-NMR (DMSO-$d_6$) δ 5.09 (H-3, d, 1H, *J*=4.5), 5.61 (H-4, dd, 1H, *J*=2.1, 4.5), 6.77-7.32 (ArH, m, 9H), 8.89 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 56.91 (C-4), 82.26 (C-3), 114.98-156.34 (aromatic carbons), 165.90 (CO, β-lactam); GC-MS m/z = 275 [M$^+$, $^{37}$Cl], 273 [M$^+$, $^{35}$Cl]; Anal. calcd. for $C_{15}H_{12}ClNO_2$: C, 65.82; H, 4.42; N, 5.12. Found: C, 65.78; H, 4.46; N, 5.08.

*4-(4-Methoxyphenyl)-3-phenoxyazetidin-2-one* (**9h**). Purified by recristalization; yield: 86 %; mp: 157-159 °C; IR (CHCl$_3$) cm$^{-1}$: 1776.3 (CO), 3409.9 (NH); $^1$H-NMR (DMSO-$d_6$) δ 3.66 (MeO, s, 3H), 5.02 (H-3, d, 1H, *J*=4.3), 5.52 (H-4, dd, 1H, *J*=1.8, 4.3), 6.55-7.35 (ArH, m, 9H), 9.08 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 54.83 (OMe), 56.45 (C-4), 81.76 (C-3), 113.19-158.68 (aromatic carbons),

166.84 (CO, β-lactam); GC-MS m/z = 269 [M$^+$]; Anal. calcd. for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.42; H, 5.66; N, 5.24.

*3-Phenoxy-4-p-tolylazetidin-2-one* (**9i**). Purified by recrystalization; yield: 84 %; mp: 180-182 °C; IR (KBr) cm$^{-1}$: 1773.9 (CO), 3300.0 (NH); $^1$H-NMR (DMSO-$d_6$) δ 1.95 (Me, s, 3H), 4.81 (H-3, d, 1H, *J*=4.4), 5.32 (H-4, dd, 1H, *J*=2.2, 4.4), 6.54-6.98 (ArH, m, 9H), 8.60 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 20.62 (Me), 56.52 (C-4), 82.34 (C-3), 115.07-156.66 (aromatic carbons), 166.14 (CO, β-lactam); GC-MS m/z = 253 [M$^+$]; Anal. calcd. for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.84; H, 6.03; N, 5.48.

*3-Phenoxy-4-styrylazetidin-2-one* (**9j**). Purified by column chromatography (eluent: 5:5 hexane-EtOAc); yield: 76 %; mp: 190-192 °C; IR (KBr) cm$^{-1}$: 1775.7 (CO), 3310.0 (NH); $^1$H-NMR (DMSO-$d_6$) δ 4.64 (H-4, m, 1H,), 5.51 (H-3, d, 1H, *J*= 4.3), 6.18 (H-5, dd, 1H, *J*= 7.4, 15.9), 6.65 (H-6, d, 1H, *J*= 15.9), 6.90-7.33 (ArH, m, 9H), 8.96 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 60.67 (C-4), 87.47 (C-3), 120.30-162.15 (C=C, aromatic carbons), 170.78 (CO, β-lactam); GC-MS m/z = 265 [M$^+$]; Anal. calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.92; H, 5.77; N, 5.24.

*4-(3,4-Dimethoxyphenyl)-3-phenoxyazetidin-2-one* (**9k**). Purified by recrystalization; yield: 86 %; mp: 140-142 °C; IR (KBr) cm$^{-1}$: 1777.7 (CO), 3418.9 (NH); $^1$H-NMR (DMSO-$d_6$) δ 3.58, 3.66 (2MeO, 2s, 6H), 5.03 (H-3, d, 1H, *J*=4.0), 5.58 (H-4, dd, 1H, *J*=2.2, 4.0), 6.64-7.26 (ArH, m, 8H), 8.83 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 55.23, 55.25 (2OMe), 56.40 (C-4), 81.13 (C-3), 111.02-156.59 (aromatic carbons), 165.98 (CO, β-lactam); GC-MS m/z = 299 [M$^+$]; Anal. calcd. for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.72; N, 4.68. Found: C, 68.31; H, 5.79; N, 4.73.

*3-(Naphthalen-2-yloxy)-4-(4-nitrophenyl)azetidin-2-one* (**9l**). Purified by column chromatography (eluent: 5:5 hexane-EtOAc); yield: 83 %; mp: 172-174 °C; IR IR (KBr) cm$^{-1}$: 1769.6 (CO), 3354.4 (NH); $^1$H-NMR (DMSO-$d_6$) δ 5.38 (H-3, d, 1H, *J*=4.5), 5.86 (H-4, dd, 1H, *J*=2.3, 4.5), 7.31-7.78 (ArH, m, 11H), 9.10 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 56.05 (C-4), 82.71 (C-3), 117.51-147.53 (aromatic carbons), 165.66 (CO, β-lactam); GC-MS m/z = 334 [M$^+$]; Anal. calcd. for $C_{19}H_{14}N_2O_4$: C, 68.26; H, 4.22; N, 8.38. Found: C, 68.23; H, 4.26; N, 8.42.

*3-(2,4-Dichlorophenoxy)-4-(4-nitrophenyl)azetidin-2-one* (**9m**). Purified by column chromatography (eluent: 5:5 hexane-EtOAc); yield: 78 %; mp: 160-162 °C; IR (KBr) cm$^{-1}$: 1775.5 (CO), 3320.5 (NH); $^1$H-NMR (DMSO-$d_6$) δ 5.34 (H-3, d, 1H, *J*=3.5), 5.77 (H-4, dd, 1H, *J*=2.4, 3.5), 7.32-8.22 (ArH, m, 7H), 9.20 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 55.49 (C-4), 82.99 (C-3), 116.31-150.69 (aromatic carbons), 165.00 (CO, β-lactam); GC-MS m/z = 356 [M$^+$, $^{37}$Cl], 354, 352 [M$^+$, $^{35}$Cl]; Anal. calcd. for $C_{15}H_{10}Cl_2N_2O_4$: C, 51.01; H, 2.85; N, 7.93. Found: C, 51.05; H, 2.92; N, 7.97.

*3-Methoxy-4-p-tolylazetidin-2-one* (**9n**). Purified by column chromatography (eluent: 4:6 hexane-EtOAc); yield: 77 %; mp: 92-94 °C; IR (KBr) cm$^{-1}$: 1765.8 (CO), 3414.0 (NH); $^1$H-NMR (DMSO-$d_6$) δ 2.11 (Me, s, 3H), 2.82 (OMe, s, 3H), 4.51 (H-4, dd, 1H, *J*=2.2, 4.4), 4.59 (H-3, d, 1H, *J*=4.4), 6.69-7.07 (ArH, m, 4H), 8.41 (NH, brs, 1H); $^{13}$C-NMR (DMSO-$d_6$) δ 20.65 (Me), 56.23 (OMe), 57.12 (C-

4), 86.26 (C-3), 127.35-136.75 (aromatic carbons), 167.48 (CO, β-lactam); GC-MS m/z = 191 [M$^+$]; Anal. calcd. for C$_{11}$H$_{13}$NO$_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.14; H, 6.92; N, 7.28.

## Acknowledgements

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