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Facile Synthesis of 4-Acylamino and 4-Sulphonamido β-lactams

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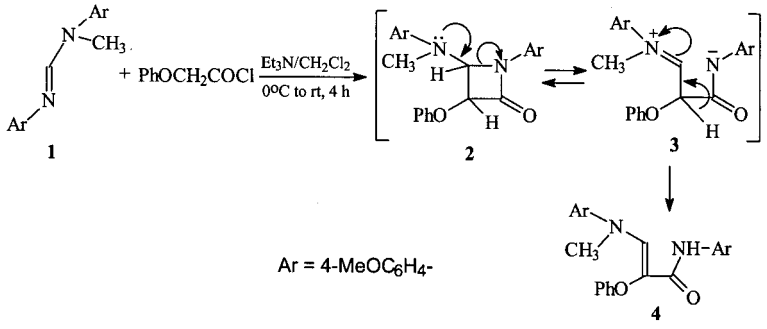
Abstract—The cycloaddition reaction of trisubstituted amidines (**7a**–**f**) with acid chlorides in presence of triethylamine gave 4-acylamino and 4-sulphonamido-*trans*-β-lactams (**9a**–**h**) in very good yields. Similarly *N*,*N*′-diarylamidines (**5a**–**d**) on reaction with 2 equiv. of acid chlorides (**8a**,**b**) gave 4-acylamino-*trans*-β-lactams (**10a**–**e**) via in situ generated acylamidines followed by cycloaddition reaction.

Introduction

In continuation of our efforts towards the synthesis of substituted β-lactams[1] and their utility as a synthon[2] for the synthesis of various biologically important compounds, we were interested in synthesis of 4-amino-β-lactams. Although, the first synthesis of 4-amino-β-lactams has been reported by the reaction of β,β-disubstituted enamines with arylisocyanate[3] as early as 1962 from Eli Lilly group, very few reports[4–7] have been appeared for the synthesis of these β-lactams. This is mainly due the fact that these β-lactams are highly susceptible towards moisture and undergo ring opening[3a] during aqueous work-up or on storage. Moreover, there is only one report wherein 4-substituted amino β-lactams have been prepared[8] by the reaction of highly reactive diphenylketene with various trisubstituted amidines. However, very few β-lactams could be isolated in the pure form as these compounds undergo ring cleavage mainly by the fission of C3–C4 bond leading to 2,2-diphenylacetanilides. Bicyclic β-lactams have been synthesized by the reaction of *N*-protected cyclic amidines either with ketenes[9] or carbene[10] chromium complexes.

It has also been shown that 4-(*N*,*N*-alkyl/aryl)-β-lactams with hydrogen on C3 (3-mono substituted β-lactams) undergo rapid ring opening via N1–C4 bond cleavage to give enamino amides.[3] We also made similar observation in the reaction of ketene derived from phenoxyacetyl chloride with *N*,*N*′-di-(*p*-anisyl)-*N*′-methylamidine (**1**) followed by aqueous work-up gave enamino amide (**4**) in 62% isolated yield instead of the expected β-lactam **2** (Scheme 1). The formation of enaminoamide (**4**) is presumably due to the N1,C4 cleavage of initially formed β-lactam (**2**) assisted by the participation of nitrogen lone pair of 4-amino group via intermediate **3**. We envisaged that this problem could be addressed by arresting the availability of lone pair with electron withdrawing group on amino nitrogen. We herein report an efficient synthesis of stable 4-substituted amino-β-lactams via cycloaddition reaction of



Scheme 1.

Keywords: cycloaddition reaction; azetidinones; Staudinger reaction.
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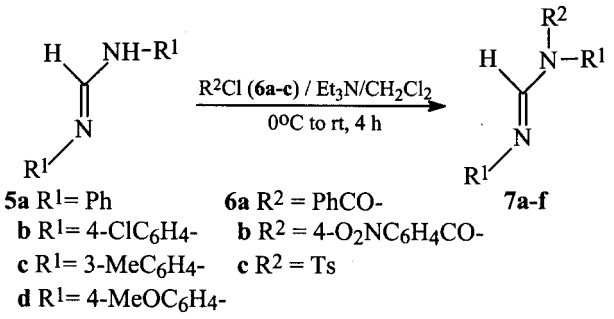
Table 1. Synthesis N-substituted amidines **7a–f**.

Sr.No.	Amidines **7**	R^1	R^2	Yield (%)	Mp (°C)
1.	**7a**	Ph	PhCO–	91	129–30
2.	**7b**	Ph	4–$NO_2C_6H_4CO$–	84	77–78
3.	**7c**	Ph	Ts	98	209–210
4.	**7d**	4-ClC_6H_4–	Ts	93	178–179
5.	**7e**	3-MeC_6H_4–	Ts	81	118–119
6.	**7f**	4-$MeOC_6H_4$–	Ts	93	100–101



Scheme 2.

ketenes with trisubstituted amidines bearing electron-withdrawing substituent on enamino nitrogen.

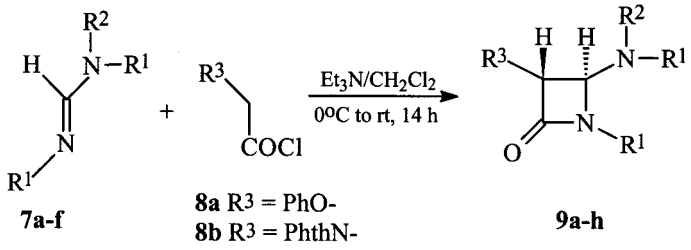
Results and Discussion

The starting trisubstituted amidines, *N′*-benzoyl-*N*,*N′*-diarylamidines (**7a**,**b**) and *N′*-sulphonyl-*N*,*N′*-diarylamidines (**7c–f**) were prepared by reacting *N*,*N′*-diarylamidines (**5a–d**) with aryloyl chloride (**6a,b**) or *p*-toluene sulphonyl chloride (**6c**) in presence of triethylamine (Scheme 2). The trisubstituted amidines **7a–f** on cycloaddition reaction with ketenes derived from acid chloride (**8a**,**b**) in presence of triethylamine afforded exclusively *trans*-β-lactams (**9a–h**) in very good yields (Scheme 3, Table 2). The assignment of *trans* stereochemistry for β-lactam protons is based on observed low vicinal coupling constant (~1–1.5 Hz). As anticipated these β-lactams (**9a–h**) were found to be very stable to aqueous work-up and did not undergo any decomposition even after keeping for several months at room temperature.

The reaction of two equivalents of substituted acetyl chloride with *N*,*N′*-diarylamidines (**5**) should also undergo cycloaddition reaction to give stable β-lactams via in situ generation of acylated amidines, structurally similar to amidines **7**. Thus, cycloaddition reaction of *N*,*N′*-diphenylamidine (**5a**) with two equivalent of phenoxyacetyl chloride (**8a**) in presence of triethylamine gave *trans*-β-lactam (**10a**) in very good yield. Similarly, other β-lactams (**10b–e**) were also prepared by the reaction of *N*,*N′*-diarylamidines (**5a–d**) with two equivalents acid chlorides (**8a,b**) in presence of triethylamine (Scheme 4, Table 3). The *trans* stereochemistry of β-lactam ring protons was further confirmed from single crystal X-ray analysis of compound **10a** (Fig. 1).

Conclusion

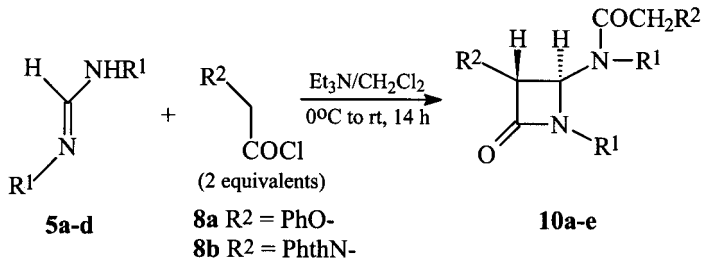
In summary, we have demonstrated that 4-substituted amino-β-lactams could be synthesized from trisubstituted amidines via cycloadditon reaction with ketenes. We have also shown that putting electron withdrawing substitutent on 4-amino group could increase the stability of β-lactams.



Scheme 3.

Table 2. Synthesis of 4-(*N*,*N*-disubstituted amino)azetidin-2-one (**9a-h**) from amidines **7**

Sr.No.	Compd **9**	R^1	R^2	R^3	Yield (%)	Mp (°C)
1	**9a**	Ph	PhCO-	PhO–	72	140–141
2	**9b**	Ph	4-$NO_2C_6H_4CO$-	PhO–	68	96–97
4	**9c**	Ph	Ts-	PhO–	80	179–180
5	**9d**	4-ClC_6H_4–	Ts-	PhO–	87	199–200
6	**9e**	3-MeC_6H_4–	Ts-	PhO–	86	161–162
7	**9f**	4-$MeOC_6H_4$–	Ts-	PhO–	82	191–192
8	**9g**	Ph	Ts-	PhthN–	82	239–240
9	**9h**	4-$MeOC_6H_4$–	Ts-	PhthN–	89	248–249



Scheme 4.

Table 3. Synthesis 4-(*N*-acyl-*N*-arylamino)azetidin-2-ones (**10a–e**) from amidines **5**

Sr. No.	Compd.**10**	R^1	R^2	Yield (%)	Mp (°C)
1	**10a**	Ph	PhO–	77	146–147
2	**10b**	4-ClC_6H_4–	PhO–	82	144–145
3	**10c**	3-MeC_6H_4–	PhO–	81	131–132
4	**10d**	4-$MeOC_6H_4$–	PhO–	73	142–143
5	**10e**	Ph	PhthN–	79	279–280

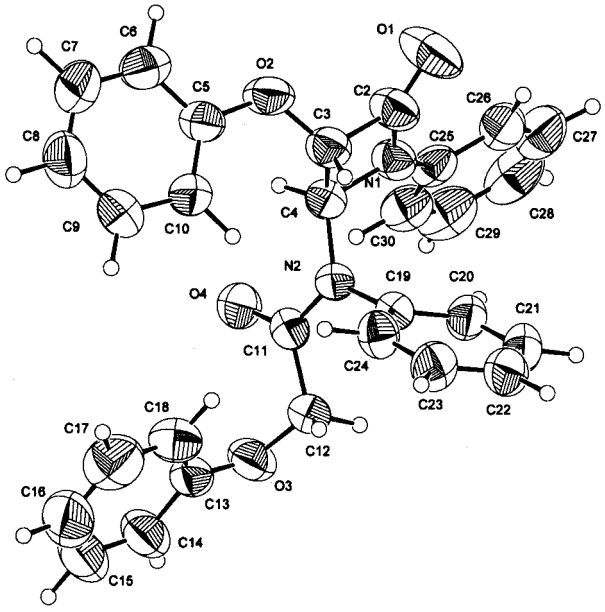


Figure 1. ORTEP diagram of **10a** without solvent.

Experimental

General

^1H NMR Spectra were recorded in $CDCl_3$ solution on a Bruker AC 200 spectrometer at 200 MHz and chemical shifts are reported in ppm downfield from tetramethylsilane. ^{13}C NMR spectra were recorded in $CDCl_3$ solution on a Bruker AC 200 instrument and chemical shifts are reported in ppm relative to the center line of $CDCl_3$ (77.0 ppm). Infrared spectra were recorded on a Perkin–Elmer Infracord Spectrophotometer Model 599-B using sodium chloride optics. Melting points were determined on a Thermonik Campbell melting point apparatus and were uncorrected. The microanalyses were performed on a Carlo-Erba, CHNS-O EA 1108 Elemental analyzer. Optical rotations were recorded on a JASCO-181 digital polarimeter under standard conditions. Methylene chloride was distilled over P_2O_5 under argon.

Preparation of *N,N′*-di-(*p*-anisyl)-*N′*-methylamidine 1. To a stirred mixture of *N,N′*-di-(*p*-anisyl)amidine (1.28 g, 0.005 mol), K_2CO_3 (1.38 g) and acetone (25 ml), iodomethane (1.06 g, 0.0074 mol) was added at room temperature and stirred further for 12 h. The reaction mixture was filtered and filtrate was distilled to remove acetone. The residue so obtained was crystallized from chloroform:pet. ether to give pure *title compound* **1** (1.24 g, 91.8%) as a yellow crystalline solid, mp 114–116°C [lit.,[11] mp 110–112°C]; [Found: C, 70.85; H, 6.86; N, 10.14. $C_{16}H_{18}N_2O_2$ requires C, 71.09; H, 6.71; N, 10.36]; ν_{max}(Nujol) 1620, 1500 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.45 (s, 3H), 3.75 (s, 3H), 3.80 (s, 3H), 6.70–7.15 (m, 8H), 7.95 (s, 1H); MS (*m/z*): 270 (M^+).

Enamino amide 4. To a mixture of *N,N′*-di-(*p*-anisyl)-*N′*-methylamidine (**1**, 1 g, 3.7 mmol), triethylamine (1.8 mL, 13 mmol), CH_2Cl_2 (20 mL), a solution of phenoxyacetyl chloride (**8a**, 0.75 g, 4.4 mmol) in CH_2Cl_2 (20 mL) was added over a period of 30 min at 0°C with stirring. The reaction mixture was allowed to warm-up to room temperature and stirred further for 12 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed successively with water (15 mL), satd. $NaHCO_3$ (20 mL), brine (10 mL) and dried over Na_2SO_4. The solution was passed through short column (silica gel, 60–120). The removal of solvent by distillation under reduced pressure gave crude product, which was purified by crystallization from methanol to give 0.926 g (61.8%) of pure enamino amide **4** as pale yellow crystalline solid, mp 137–139°C; [Found: C, 70.95; H, 6.18; N, 6.96. $C_{24}H_{24}N_2O_4$ requires C, 71.27; H, 5.98; N, 6.93]; ν_{max}(Nujol) 1650, 1580 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.30 (s, 3H), 3.75 (s, 3H), 3.80 (s, 3H), 6.75–6.85 (m, 4 H), 6.90–7.10 (m, 5 H), 7.25–7.45 (m, 4 H), 7.65 (s, 2H); MS (*m/z*): 404 (M^+).

General procedure for *N,N′*-diaryl-*N′*-benzoylamidine 7a,b

To a mixture of *N,N′*-diarylamidine (**5a**, 6 mol), triethylamine (2 ml, 15 mmol), CH_2Cl_2 (20 mL), a solution of benzoyl chloride (**6a,b,** 0.93 g, 6.6 mmol) in CH_2Cl_2 (20 mL) was added over a period of 10 min at 0°C. The reaction mixture was then allowed to warm-up to room temperature and stirred further for 4 h. The reaction mixture was then diluted with CH_2Cl_2 (20 mL) and washed successively with water (15 mL), satd. $NaHCO_3$ (10 mL), brine (10 mL) and dried over Na_2SO_4. It was then filtered and

filtrate on distillation under reduced pressure gave crude product (**7a**,**b**), which was purified by crystallization from chloroform:pet. ether.

***N*,*N*′-Diphenyl-*N*′-benzoylamidine 7a.** The *title compound* **7a** was obtained from *N*,*N*′-diphenylamidine (**5a**), as a white crystalline solid in 91% yield, mp 129–130°C [lit.,[12] mp 129–130°C]; [Found: C, 79.69; H, 5.46; N, 9.16. $C_{20}H_{16}N_2O$ requires C, 79.98; H, 5.37; N, 9.33]; ν_{max}(Nujol) 1630, 1570 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 6.90–7.50 (m, 15H), 9.00 (s, 1H); MS (*m*/*z*): 300 (M^+).

***N*,*N*′-Diphenyl-*N*′-(*p*-nitrobenzoyl)amidine 7b.** The *title compound* **7b** was obtained from *N*,*N*′-diphenylamidine (**5a**), as a pale yellow crystalline solid, yield 84%, mp 77–78°C; [Found: C, 69.38; H, 4.23; N, 12.05. $C_{20}H_{15}N_3O_3$ requires C, 69.56; H, 4.38; N, 12.17]; ν_{max}(Nujol) 1630, 1510 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.00–7.45 (m, 10H), 7.54 (d, *J*=9 Hz, 2H), 8.06 (d, *J*=9 Hz, 2H), 9.85 (s, 1H); MS (*m*/*z*): 345 (M^+).

General procedure for *N*,*N*′-diaryl-*N*′-(p-toluenesulphonyl)amidine 7c–f

To a mixture of *N*,*N*′-diarylamidine (2, 5 mol), triethylamine (2 ml, 15 mmol), CH_2Cl_2 (20 mL), a solution of *p*-toluenesulphonyl chloride (**6c**, 1.045 g, 5.5 mmol) in CH_2Cl_2 (20 mL) was added over a period of 10 min at 0°C. The reaction mixture was then allowed to warm-up to room temperature and stirred further for 4 h. The reaction mixture was then diluted with CH_2Cl_2 (20 mL) and washed successively with water (10 mL), satd. $NaHCO_3$ (10 mL), brine (10 mL) and dried over Na_2SO_4. It was then filtered and filtrate on distillation under reduced pressure gave crude product (**7c**–**f**), which was purified by crystallization from chloroform:pet. ether.

***N*,*N*′-Diphenyl-*N*′-(p- toluenesulphonyl)amidine 7c.** The *title compound* **7c** was obtained from *N*,*N*′-diphenylamidine (**5a**), as a white crystalline solid, yield 98%, mp 209–210°C [lit.,[13] mp 211°C]; [Found: C, 68.39; H, 5.36; N, 8.13; S, 9.26. $C_{20}H_{18}N_2O_2S$ requires C, 68.55; H, 5.18; N, 7.99; S, 9.15]; ν_{max}(Nujol) 1620, 1580, 1440 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.45 (s, 3H), 6.90–7.70 (m, 14 H), 8.72 (s, 1H); MS (*m*/*z*): 350 (M^+).

***N*,*N*′-Di-(4-chlorophenyl)-*N*′-(*p*-toluenesulphonyl)amidine 7d.** The *title compound* **7d** (93%) was obtained from *N*,*N*′-di-(4-chlorophenyl)amidine (**5b**) as a white crystalline solid, mp 178–179°C [lit.,[13] mp 181°C]; [Found: C, 57.39; H, 4.02; N, 6.53; S, 7.88. $C_{20}H_{16}$ $Cl_2N_2O_2S$ requires C, 57.29; H, 3.85; N, 6.68; S, 7.65]; ν_{max}(Nujol) 1620, 1550, 1440 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.45 (s, 3H), 6.90–7.80 (m, 12 H), 8.65 (s, 1H); MS (*m*/*z*): 419 (M^+).

***N*,*N*′-Di(3-methylphenyl)-*N*′-(*p*-toluenesulphonyl)amidine 7e.** The *title compound* **7e** was obtained from *N*,*N*′-di-(3-methylphenyl)amidine (**5c**) as a white crystalline solid in 81% yield, mp 118–119°C; [Found: C, 69.67; H, 5.99; N, 7.26; S, 8.31. $C_{22}H_{22}N_2O_2S$ requires C, 69.82; H, 5.86; N, 7.40; S, 8.47]; ν_{max}(Nujol) 1620, 1450 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.3 (s, 3H), 2.35 (s, 3H), 2.45 (s, 3H), 6.80–7.70 (m, 12 H), 8.70 (s, 1H); MS (*m*/*z*): 378 (M^+).

***N*,*N*′-Di(4-methoxyphenyl)-*N*′-(*p*-toluenesulphonyl)amidine 7f.** The *title compound* **7f** (93%) was obtained from *N*,*N*′-di-(4-methoxyphenyl)amidine (**5d**) as a white crystalline solid, mp 101–103°C [lit.,[13] mp 104°C]; Found: C, 64.62; H, 5.53; N, 7.02; S, 7.57. $C_{22}H_{22}N_2O_4S$ requires C, 64.37; H, 5.40; N, 6.82; S, 7.81; ν_{max}(Nujol) 1620, 1450, 1390 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.5 (s, 3H), 3.80 (s, 3H), 3.90 (s, 3H), 6.80–7.80 (m, 12 H), 8.70 (s, 1H); MS (*m*/*z*): 410 (M^+). (Table 1)

General procedure for the preparation of β-lactams 9a–h

To a mixture of trisubstituted amidine (**7a**–**f**, 3 mmol), triethylamine (1.7 mL, 12 mmol), CH_2Cl_2 (20 mL), a solution of acid chloride (**8a,b**, 4.5 mmol) in CH_2Cl_2 (20 mL) was added over a period of 20 min at 0°C with stirring. The reaction mixture was allowed to warm-up to room temperature and stirred further for 14 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed successively with water (15 mL), satd. $NaHCO_3$ (20 mL), brine (10 mL) and dried over Na_2SO_4. The solution was passed through short column (silica gel, 60–120). The removal of solvent by distillation under reduced pressure gave crude product, which was purified by crystallization from methanol to give pure β-lactams (**9a**–**h**) as white crystalline solids.

1-Phenyl-3-phenoxy-4-(*N*-phenyl-*N*-benzoylamino)azetidin-2-one 9a. The *title compound* **9a** was obtained from amidine **7a** and acid chloride **8a** by using above general procedure as a white crystalline solid, yield 72%, mp 140–141°C; [Found: C, 77.13; H, 5.21; N, 6.40. $C_{28}H_{22}N_2O_3$ requires C, 77.40; H, 5.10; N, 6.45]; ν_{max}(Nujol) 1750, 1630, 1510 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.05 (d, *J*=1.2 Hz, 1H), 6.80–8.00 (m, 21H). δ_c (50.3 MHz, $CDCl_3$) 68.12, 83.73, 116.41, 118.43, 123.15, 125.83, 128.26, 128.66, 129.10, 129.84, 130.09, 130.62, 135.38, 136.25, 137.93, 157.60, 161.50, 172.04; MS (*m*/*z*): 341 (M^+-93).

1-Phenyl-3-phenoxy-4-[*N*-phenyl-*N*-(4-nitrobenzoyl)-amino]azetidin-2-one 9b. The *title compound* **9b** was obtained from amidine **7b** and acid chloride **8a** by using above general procedure as a white crystalline solid, yield 68%, mp 96–97°C; [Found: C, 69.93; H, 4.34; N, 8.55. $C_{28}H_{21}N_3O_5$ requires C, 70.14; H, 4.41; N, 8.76]; ν_{max}(Nujol) 1760, 1640, 1580 cm^{-1}. δ_H (200 MHz, $CDCl_3$) 4.95 (d, *J*=1.1 Hz, 1H), 6.80–7.90 (m, 20H); δ_c (50.3 MHz, $CDCl_3$) 67.15, 82.90, 115.70, 117.70, 122.60, 122.80, 125.40, 128.80, 129.20, 129.40, 129.60, 129.80, 135.30, 136.10, 140.60, 148.00, 156.80, 160.60, 169.40; MS (*m*/*z*): 479 (M^+).

1-Phenyl-3-phenoxy-4-[*N*-phenyl-*N*-(*p*-toluenesulphonyl)-amino]azetidin-2-one 9c. The *title compound* **9c** was obtained from amidine **7c** and acid chloride **8a** by using above general procedure as a white crystalline solid, yield 80%, mp 179–180°C; [Found: C, 68.95, H, 4.84, N, 5.97, S, 6.47. $C_{28}H_{24}N_2O_4S$ requires C, 69.40; H, 4.99; N, 5.78; S, 6.62]; ν_{max}(Nujol) 1750, 1580, 1480 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.45 (s, 3H), 4.95 (d, *J*=1.1 Hz, 1H), 6.65 (d, *J*=1.1 Hz, 1H), 6.70–6.85 (m, 2H), 6.90–7.80 (m, 17H); δ_c (50.3 MHz, $CDCl_3$) 21.73, 71.61, 84.73, 116.41, 119.96, 123.31, 127.84, 129.90, 130.10, 130.29, 131.81,

133.21, 134.30, 136.67, 144.95, 157.29, 160.79; MS (*m/z*): 484 (M^+).

1-(4-Chlorophenyl)-3-phenoxy-4-[*N*-(4-chlorophenyl)-*N*-(*p*-toluenesulphonyl)amino]-azetidin-2-one 9d. The *title compound* **9d** was obtained from amidine **7d** and acid chloride **8a** by using above general procedure as a white crystalline solid, yield 87%, mp 199–200°C; [Found: C, 60.50; H, 3.87; N, 4.91. $C_{28}H_{22}N_2O_4Cl_2S$ requires C, 60.76; H, 4.00; N, 5.06]; ν_{max}(Nujol) 1750, 1580, 1475 cm^{-1}. δ_H (200 MHz, $CDCl_3$) 2.45 (s, 3H), 4.95 (d, *J*=1.2 Hz, 1H), 6.50 (d, *J*=1.2 Hz, 1H), 6.60–7.70 (m, 17H); δ_c (50.3 MHz, $CDCl_3$) 21.73, 71.62, 84.73, 116.41, 119.96, 123.31, 127.89, 129.91, 130.05, 130.29, 131.81, 133.26, 134.30, 136.68, 144.95, 157.34, 160.81; MS (*m/z*): 399 (M^+-153).

1-(3-Methylphenyl)-3-phenoxy-4-[*N*-(3-methylphenyl)-*N*-(*p*-toluenesulphonyl)amino]-azetidin-2-one 9e. The *title compound* **9e** was obtained from amidine **7e** and acid chloride **8a** by using above general procedure as a white crystalline solid, yield 86%, mp 161–162°C; [Found: C, 70.04; H, 5.38; N, 5.33; S, 5.99. $C_{30}H_{28}N_2O_4S$ requires C, 70.29; H, 5.51; N, 5.46; S, 6.25]; ν_{max}(Nujol) 1750, 1580 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.20 (s, 3H), 2.40 (s, 3H), 4.95 (d, *J*=1.2 Hz, 1H), 6.60 (d, *J*=1.2 Hz, 1H), 6.90–7.60 (m, 17H); δ_c (50.3 MHz, $CDCl_3$) 71.50, 84.34, 116.25, 120.00, 123.00, 126.80, 127.80, 128.20, 129.50, 130.00, 130.80, 132.50, 133.00, 135.50, 136.80, 139.00, 144.80, 157.20, 161.00; MS (*m/z*): 379 (M^+-133).

1-(4-Methoxylphenyl)-3-phenoxy-4-[*N*-(4-methoxylphenyl)-*N*-(*p*-toluenesulphonyl)amino]-azetidin-2-one 9f. The *title compound* **9f** was obtained from amidine **7f** and acid chloride **8a** by using above general procedure as a white crystalline solid, yield 82%, mp 192°C; [Found: C, 65.92; H, 5.27; N, 5.17. $C_{30}H_{29}N_2O_6S$ requires C, 66.04; H, 5.36; N, 5.13]; ν_{max}(Nujol) 1740, 1580, 1500 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.40 (s, 3H), 3.75 (s, 3H), 3.85 (s, 3H), 4.95 (d, *J*=1.2 Hz, 1H), 6.70 (d, *J*=1.2 Hz, 1H), 6.90–7.80 (m, 17H); δ_c (50.3 MHz, $CDCl_3$) 21.76, 55.66, 71.50, 84.30, 116.20, 120.40, 123.01, 125.10, 127.80, 128.90, 129.90, 132.90, 136.70, 144.40, 157.40, 157.50, 160.70; MS (*m/z*): 545 (M^+).

1-Phenyl-3-phthalimido-4-[*N*-phenyl-*N*-(*p*-toluenesulphonyl)amino]azetidin-2-one 9g. The *title compound* **9g** was obtained from amidine **7c** and acid chloride **8b** by using above general procedure as a white crystalline solid, yield 82%, mp 239–240°C; [Found: C, 66.82; H, 4.46; N, 7.63; S, 6.23. $C_{30}H_{23}N_3O_5S$ requires C, 67.03; H, 4.31; N, 7.82; S, 5.96]; ν_{max}(Nujol) 1750, 1680, 1480 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.30 (s, 3H), 5.20 (d, *J*=1.2 Hz, 1H), 6.75 (d, *J*=1.2 Hz, 1H), 6.90–8.20 (m, 18H); δ_c (50.3 MHz, $CDCl_3$) 21.47, 40.00, 57.70, 68.80, 78.70, 79.20, 79.60, 117.90, 123.60, 124.02, 125.80, 127.60, 128.90, 130.00, 130.40, 130.80, 131.30, 131.60, 135.00, 135.40, 144.70, 145.60, 166.30, 166.60, 167.09; MS (*m/z*): 537 (M^+).

1-(4-Methoxylphenyl)-3-phthalimido-4-[*N*-(4-methoxylphenyl)-*N*-(*p*-toluenesulphonyl)-amino]azetidin-2-one 9h. The *title compound* **9h** was obtained from amidine **7f** and acid chloride **8b** by using above general procedure as a white crystalline solid, yield 89%, mp 248–249°C. [Found: C, 64.47; H, 4.58; N, 6.93; S, 5.01. $C_{32}H_{27}N_3O_7S$ requires C, 64.31; H, 4.55; N, 7.03; S, 5.36]; ν_{max}(Nujol) 1750, 1580, 1480 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.35 (s, 3H), 3.80 (s, 3H), 3.90 (s, 3H), 5.15 (d, *J*=1.2 Hz, 1H), 6.65 (d, *J*=1.2 Hz, 1H), 6.80–8.00 (m, 16H); δ_c (50.3 MHz, $CDCl_3$) 21.27, 55.35, 55.44, 57.70, 69.00, 114.60, 114.80, 120.10, 123.60, 124.60, 127.30, 129.50, 131.50, 132.80, 134.60, 136.80, 144.00, 157.30, 159.20, 160.50, 166.30; MS (*m/z*): 448 (M^+-149).

General procedure for the preparation of β-lactams 10a–e

To a mixture of diarylamidine (**5**, 3 mmol), triethylamine (1.7 mL, 12 mmol), CH_2Cl_2 (20 mL), a solution of acid chloride (**8**, 6 mmol) in CH_2Cl_2 (20 mL) was added over a period of 30 min at 0°C with stirring. The reaction mixture was allowed to warm-up to room temperature and stirred further for 14 h. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed successively with water (15 mL), satd. $NaHCO_3$ (20 mL), brine (10 mL) and dried over Na_2SO_4. The solution was passed through short column (silica gel, 60–120). The removal of solvent by distillation under reduced pressure gave crude product, which was purified by crystallization from methanol to give pure β-lactams (**10a–e**) as white crystalline solids.

1-Phenyl-3-phenoxy-4-[*N*-phenyl-*N*-(phenoxyacetyl)-amino]azetidin-2-one 10a. The *title compound* **10a** was obtained from amidine **5a** and acid chloride **8a** by using above general procedure as a white crystalline solid, yield 77%, mp 146–147°C; [Found: C, 74.82; H, 5.45; N, 5.78. $C_{29}H_{24}N_2O_4$ requires C, 74.98; H, 5.21; N, 6.03]; ν_{max}(Nujol) 1766, 1693 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.25 (d, *J*=17.5 Hz, 1H), 4.50 (d, *J*=17.5 Hz, 1H), 4.95 (d, *J*=1.2 Hz, 1H), 6.70–7.20 (m, 21H); δ_c (50.3 MHz, $CDCl_3$) 66.25, 82.80, 114.40, 114.70, 115.90, 118.00, 121.10, 121.60, 122.80, 125.50, 128.70, 128.90, 129.40, 129.70, 130.40, 130.50, 134.00, 135.30, 157.00, 157.60, 160.80, 169.30. MS (*m/z*): 464 (M^+).

1-(4-Chlorophenyl)-3-phenoxy-4-[*N*-(4-chlorophenyl)-*N*-(phenoxyacetyl)amino]azetidin-2-one 10b. The *title compound* **10b** was obtained from amidine **5b** and acid chloride **8a** by using above general procedure as a white crystalline solid, yield 82%, mp 144–145°C; [Found: C, 65.21; H, 3.98; N, 4.98. $C_{29}H_{22}N_2O_4Cl_2$ requires C, 65.30; H, 4.16; N, 5.25]; ν_{max}(Nujol) 1760, 1680 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.30 (d, *J*=16.6 Hz, 1H), 4.50 (d, *J*=16.6 Hz, 1H), 4.95 (d, *J*=1.2 Hz, 1H), 6.70–7.70 (m, 19H); δ_c (50.3 MHz, $CDCl_3$) 66.25, 82.80, 114.40, 115.90, 118.00, 121.10, 121.60, 122.80, 125.50, 128.70, 128.90, 129.40, 129.70, 130.40, 130.50, 134.00, 135.30, 157.00, 157.60, 160.80, 169.30. MS (*m/z*): 286 (M^+-246).

1-(3-Methylphenyl)-3-phenoxy-4-[*N*-(3-methylphenyl)-*N*-(phenoxyacetyl)amino]azetidin-2-one 10c. The *title compound* **10c** was obtained from amidine **5c** and acid chloride **8a** by using above general procedure as a white crystalline solid, yield 81%, mp 131–132°C. [Found: C, 75.33; H, 5.49; N, 5.54. $C_{31}H_{28}N_2O_4$ requires C, 75.59; H,

5.73; N, 5.69]; ν_{max}(Nujol) 1750, 1670 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.2 (s, 3H), 2.4 (s, 3H), 4.25 (d, J=16.6 Hz, 1H), 4.55 (d, J=16.6 Hz, 1H), 4.95 (d, J=1.2 Hz, 1H), 6.75–7.50 (m, 19H); δ_c (50.3 MHz, $CDCl_3$) 20.70, 21.10, 82.40, 114.00, 114.70, 115.50, 118.50, 121.10, 122.30, 125.90, 129.00, 129.30, 129.60, 130.60, 133.70, 134.90, 139.30, 140.20, 156.70, 157.30, 160.40, 168.90; MS (*m*/*z*): 399 (M^+-93).

1-(4-Methoxyphenyl)-3-phenoxy-4-[*N*-(4-methoxyphenyl)-*N*-(phenoxyacetyl)amino]-azetidin-2-one 10d. The *title compound* **10d** was obtained from amidine **5d** and acid chloride **8a** by using above general procedure as a white crystalline solid, yield 73%, mp 142–143°C; [Found: C, 70.79; H, 5.28; N, 5.13. $C_{31}H_{28}N_2O_6$ requires C, 70.98; H, 5.38; N, 5.34]; ν_{max}(Nujol) 1768, 1685 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.85 (s, 3H), 3.88 (s, 3H), 4.25 (d, J=16 Hz, 1H), 4.50 (d, J=16 Hz, 1H), 5.00 (d, J=1.2 Hz, 1H), 6.60–7.50 (m, 19H); δ_c (50.3 MHz, $CDCl_3$) 55.50, 55.58, 66.30, 66.47, 82.80, 114.50, 115.00, 115.70, 115.90, 119.00, 121.60, 122.80, 126.20, 128.70, 129.50, 129.80, 130.60, 133.90, 157.20, 157.70, 160.40, 160.70, 169.80; MS (*m*/*z*): 524 (M^+).

1-Phenyl-3-phthalimido-4-[*N*-phenyl-*N*-(phthalimido-acetyl)amino]azetidin-2-one 10e. The *title compound* **10e** was obtained from amidine **5a** and acid chloride **8b** by using above general procedure as a white crystalline solid, yield 79%, mp 279–280°C; [Found: C, 69.22; H, 3.67; N, 9.58. $C_{33}H_{22}N_4O_6$ requires C, 69.47; H, 3.89; N, 9.82]; ν_{max}(Nujol) 1764, 1724, 1693 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.95 (d, J=16 Hz, 1H), 4.20 (d, J=16 Hz, 1H), 5.25 (d, J=1.2 Hz, 1H), 7.10 (d, J=1.2 Hz, 1H), 7.2–8.00 (m, 18H); δ_c (50.3 MHz, $CDCl_3$) 66.65, 117.97, 123.15, 123.65, 125.21, 129.75, 130.00, 130.50, 130.60, 131.00, 131.70, 132.00, 133.80, 134.10, 134.50, 134.79, 159.90, 166.80, 167.50, 168.00; MS (*m*/*z*): 451 (M^+-119).

X-Ray diffraction study. X-Ray structure determination of **10a** [$C_{29}H_{24}N_20_4.0.5(H_2O)$]: Colorless needles (0.74X0.2X0.12 mmgrown from methanol). M=473.51, monoclinic, space group $P2_1/C$, a=8.720(5) Å, b=16.606(7) Å, c=17.424(1) Å, β=16.606(1)°, V=2518.8(18) $Å^3$, Z=4, D=1.249 g cm^{-3}, μ=0.689 mm^{-1}, F(000)=996, T=293 K. Data were collected on Enaraf Nonius CAD-4 Single Crystal X-ray diffractometer using Cu–Kα radiation (λ=1.5406 Å) and $\omega-2\theta$ scan mode to a maximum θ range of 65°. The structure was solved by direct methods using MULTAN-80 (NRCVAX-program).[14] Least squares refinement of scale, positional and anisotropic thermal parameters for non hydrogen atom converged to R=0.0776. Rw=0.192 for 3340 unique observed reflections. Hydrogen atoms were geometrically fixed and confirmed by a difference fourier was held fixed during the refinement. The refinements were carried out using SHELXL-97.[15]

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