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Triphosgene: a versatile reagent for the synthesis of azetidin-2-ones

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Abstract—An efficient use of triphosgene, as an acid activator, for the synthesis of substituted azetidin-2-ones via ketene–imine cycloaddition reaction using various acids and imines have been described.

1. Introduction

Triphosgene [bis(trichloromethyl)carbonate] has emerged as a versatile synthetic auxiliary for the synthesis of some important class of organic compounds.[1] This white crystalline compound has proved to be safe and advantageous over its gaseous congener, phosgene. As a part of our on going program on synthesis[2] and development of methodologies for β-lactams,[3] we were interested in developing a mild and efficient acid activator for the construction of β-lactams by ketene–imine cycloaddition reaction (Staudinger reaction). In our recent communication[4] we have reported an efficient use of triphosgene as an acid activator in the construction of β-lactam ring by ketene–imine cycloaddition reaction. In this paper we wish to report the versatility of triphosgene as a reagent for the activation of various carboxylic acids and their utility for the synthesis of substituted azetidin-2-ones under very mild conditions.

Among the several methods for the synthesis of β-lactams, the cycloaddition reaction of ketenes with imines (Staudinger reaction) for the construction of β-lactam ring has found wide acceptance.[5] This is mainly because of its simplicity, predictability of stereochemical outcome and proven utility of this method for the synthesis of a large number of monocyclic, bicyclic, tricyclic, and spirocyclic β-lactams.[6] In the Staudinger reaction, the ketenes are generated in situ from acid halides by triethylamine or other tertiary amines[5] and reacted with imines to get β-lactams. In cases where the acid halides are either difficult to prepare or unstable, the acid activating reagents like ethyl chloroformate,[7] trifluoroacetic anhydride,[8] *p*-toluenesulfonyl chloride,[9] phosphorous derived reagents,[10] Mukaiyama reagent,[11] cyanuric chloride[12] and several others[5] have been used.

2. Results and discussion

We have successfully employed triphosgene for one-step cycloaddition reaction (Staudinger reaction) of acids (**1**) and imines (**2**) to get β-lactams (**3**). A solution of triphosgene (0.5 molar equivalent) in dichloromethane was slowly added to a cooled (−40°C) mixture of acids (**1**, 1 molar equivalent), imines (**2**, 1 molar equivalent), triethylamine (3 molar equivalent) in dichloromethane, and the reaction mixture was stirred at room temperature for 12 h. The reaction mixture was washed with water, saturated $NaHCO_3$, brine and passed through a short silica gel column to get pure β-lactams (**3**) in very good yields. We found this reaction to be very clean and various β-lactams were prepared in excellent yields (see Table 1). In fact this reagent was found to be better than other acid activators in terms of yields and simplicity of work-up procedure. Lower yields were obtained when one molar or 1/3 molar

Table 1. Synthesis of azetidin-2-ones (**3a**–**k**)

Entry No.	Compound	R^1	R^2	R^3	Yield[a] (%)
1	**3a**	PhO	Ph	Ph	89
2	**3b**	PhO	PMP[b]	Ph	95
3	**3c**	PhO	Ph	PMP	83
4	**3d**	PhO	PMP	PMP	82
5	**3e**	PhO	PMP	Styryl	93
6	**3f**	MeO	PMP	Ph	87
7	**3g**	MeO	Ph	PMP	86
8	**3h**	MeO	PMP	PMP	83
9	**3i**	Phth.	PMP	Styryl	78[c]
10	**3j**	2,4-Cl_2PhO	PMP	Ph	65
11	**3k**	2,4-Cl_2PhO	Ph	PMP	66

[a] Isolated yield.
[b] PMP=*p*-Methoxyphenyl.
[c] The reaction was carried out at 0°C.

Keywords: cycloaddition reaction; azetidinones; triphosgene; Staudinger reaction.

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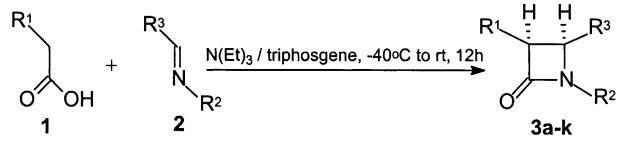


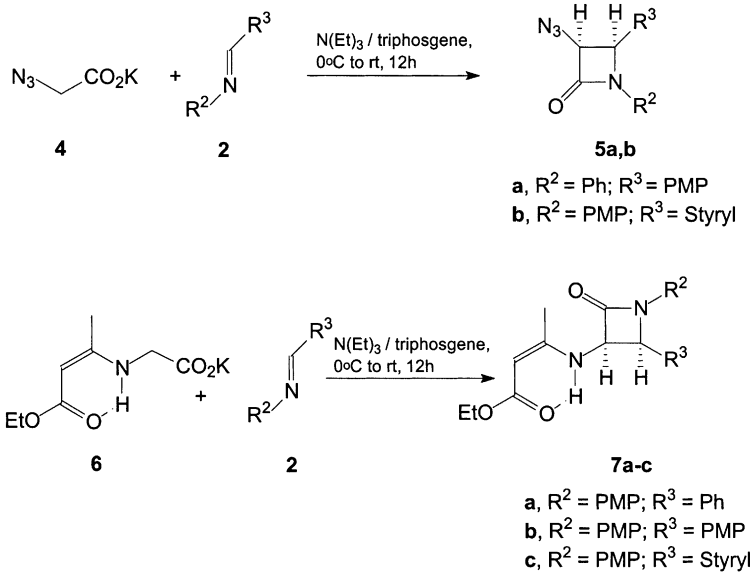
Scheme 1.

equivalent triphosgene and one molar equivalent acid (**1**) were used for the cycloaddition reaction.

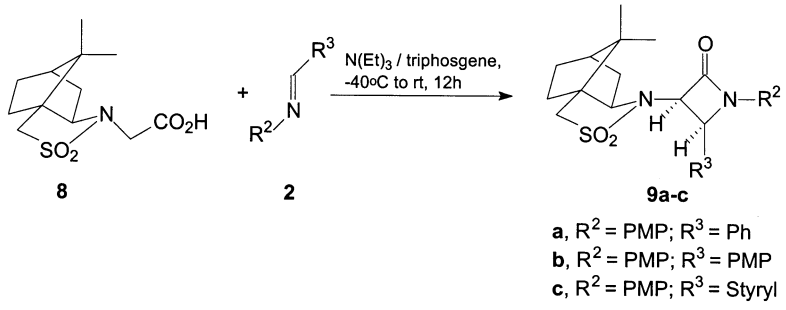
In all the cases the cycloaddition reaction was found to be stereoselective and only *cis*-β-lactam formation was observed (Scheme 1, Table 1). This method has also been applied for the synthesis of β-lactams derived from acids or imines, which are sensitive to mineral acids or thionyl chloride.

Triphosgene was also used as a reagent for the synthesis of β-lactams in good yields from the potassium salt of azidoacetic acid[12] or Dane's salt[13] and various imines (Scheme 2). These β-lactams are precursors for 3-aminoazetidin-2-ones, which are important synthons for a variety of β-lactam antibiotics.

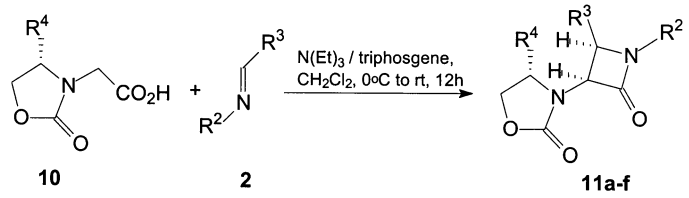
A solution of triphosgene in dichloromethane was added to the suspension of salt, imine and triethylamine in dichloromethane at 0°C. The reaction mixture was then stirred at room temperature for 12 h. Usual work-up of the reaction afforded β-lactams in very good yields. However, the reaction at lower temperature (−40°C) resulted in poor



Scheme 2.



Scheme 3.



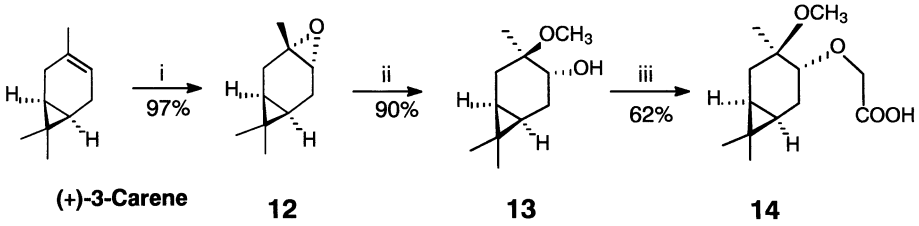
Scheme 4.

Table 2. Synthesis of azetidin-2-ones (**11a–f**) from oxazolidones (**10**) and imines (**2**)

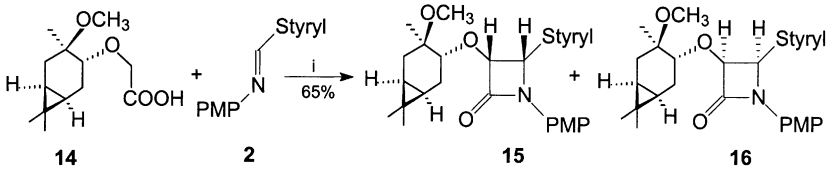
Entry No.	Compound	R^2	R^3	R^4	Yield (%)
1	**11a**	CH_2Ph	Ph	Ph	70
2	**11b**	PMP	Ph	CH_2Ph	67
3	**11c**	CH_2Ph	Ph	CH_2Ph	70
4	**11d**	PMP	Ph	*iso*-Propyl	71
5	**11e**	PMP	PMP	*iso*-Propyl	72
6	**11f**	CH_2Ph	Ph	*iso*-Propyl	70

yields of corresponding β-lactams. The formation of only *cis*-β-lactams was evident from the ^1H NMR spectra of the reaction product.

The acid activator, triphosgene, was also successfully employed for the synthesis of β-lactams from imines and chiral acids derived from camphorsultam, oxazolidinones, and carene. Camphorsultam derived acid (**8**) was obtained in good yield from Oppolzer's sultam in two steps using our earlier reported procedure.[14] The cycloaddition reaction of ketene derived from the acid (**8**) with imines in the presence of triethylamine and triphosgene, as an acid activator, was found to be stereospecific and gave β-lactams (**9a–c**) exclusively as a single diastereomer[14] (HPLC and ^1H NMR) (Scheme 3).



Scheme 5. *Reagents and conditions*: (i) $ClCO_2Et/H_2O_2/Na_3PO_4$, CH_2Cl_2; (ii) CH_3OH/PTSA, 2 h; (iii) $Na/ClCH_2CO_2H$, toluene.



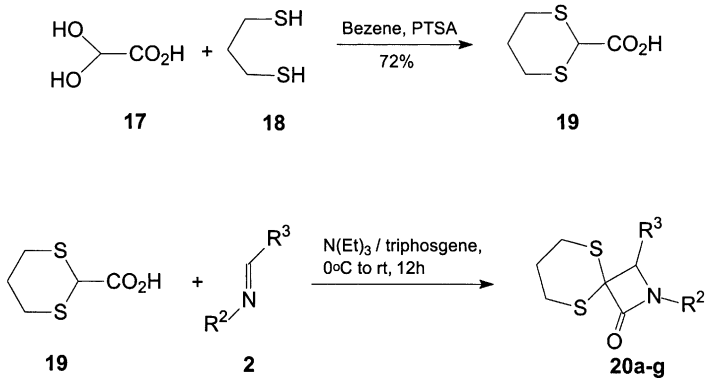
Scheme 6. *Reagents and conditions*: (i) Et_3N/triphosgene/dry CH_2Cl_2, −40°C to rt.

Table 3. Synthesis of azetidin-2-ones (**20a–g**) from dithioglyoxylic acid (**19**) and imines (**2**)

Entry No.	Compound	R^2	R^3	Yield (%)
1	**20a**	PMP	Ph	70
2	**20b**	Ph	PMP	71
3	**20c**	PMP	PMP	75
4	**20d**	PMP	Styryl	70
5	**20e**	Ph	Ph	72
6	**20f**	4-Cl-Ph	Styryl	69
7	**20g**	α-MeCHPh	Ph	69

Very high selectivity in the β-lactams (**11a–f**) formation was observed when triphosgene was used as an acid activator for cycloaddition reaction of chiral oxazolidinone derived acids (**10**) and imines (Scheme 4). The starting acids were prepared by N-alkylation of chiral oxazolidinone with ethyl bromoacetate followed by hydrolysis of the ester using the reported procedure.[15] The cycloaddition reaction was carried out at 0°C using the above acids and imine with triphosgene as an acid activator. HPLC and ^1H NMR analysis of the reaction mixture revealed the formation of only one diastereomer in excellent yield (Table 2).

The (+)-3-carene derived chiral acid (**14**) was prepared from naturally occurring monoterpene, (+)-3-carene by the reaction sequence as shown in Scheme 5. The carene epoxide, prepared by known method[16] from carene, was regio and stereospecifically opened with methanol under acidic conditions to get methoxy alcohol (**13**)[17] in quanti-



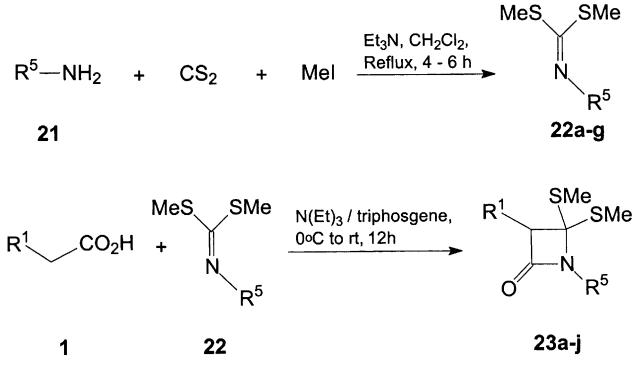
Scheme 7.

tative yield. The sodium salt of this alcohol was reacted with chloroacetic acid to get the required chiral acid (**14**). This (+)-3-carene derived chiral acid (**14**) also successfully underwent cycloaddition reaction with imines using triphosgene as an activator to give a diastereomeric mixture (60:40) of β-lactams (**15** and **16**) (Scheme 6). These diastereomers could not be separated by column chromatography. However, the major diasteromer could be separated by crystallization.

Spiro azetidin-2-ones (**20**) can also be easily obtained by the cycloaddition reaction of glyoxylic acid derivatives (**19**) with imines using triphosgene.

Dithioglyoxylic acid (**19**) was prepared by refluxing a mixture of glyoxylic acid and propanedithiol in benzene using PTSA[18] as a catalyst in very good yield. This dithioglyoxylic acid was reacted with various imines using triphosgene as an acid activator to afford spiro azetidin-2-ones (**20a–g**) in excellent yields (Table 3, Scheme 7). The cycloaddition reaction of dithioglyoxylic acid with chiral imine derived from *R* (+) α-phenylethylamine and benzaldehyde gave diastereomeric mixture (50:50) of β-lactams (see Table 3, entry 7). These diastereomers could not be separated either by column chromatography or crystallization.

This method was also extended for the preparation of protected 4-keto azetidin-2-ones (Scheme 8). The starting carbonimidodithioic acid dimethyl esters (**22a–g**, Table 4) were prepared by the reaction of various amines with carbon disulphide in presence of Et_3N, followed by methylation using methyl iodide.[19] The cycloaddition reaction of these dithioesters (**22**) with acids (**1**) using triphosgene as an activator gave good yields of 4,4-bismethylsulfanyl-azetidin-2-ones (**23a–j**, Table 5). The chiral imine was prepared from alanine methyl ester following the above



Scheme 8.

Table 4. Synthesis of carbonimidodithioic acid dimethyl esters (**22a–g**)

Entry No.	Compound	R^5	Yield (%)
1	**22a**	Ph	74
2	**22b**	CH_2Ph	79
3	**22c**	4-MeOPh	72
4	**22d**	$CH_2CH_2CH_3$	72
5	**22e**	CH_2CO_2Me	70
6	**22f**	CH_2CO_2Et	76
7	**22g**	$CH(Me)CO_2Me$	74

Table 5. Synthesis of azetidin-2-ones (**23a–j**) from acid (**1**) and imines (**22**)

Entry No.	Compound	R^1	R^5	Yield (%)
1	**23a**	PhO	Ph	68
2	**23b**	PhO	CH_2Ph	65
3	**23c**	PhO	4-OMePh	66
4	**23d**	PhO	CH_2CO_2Me	64
5	**23e**	PhO	CH_2CO_2Et	62
6	**23f**	PhO	$CH(Me)CO_2Me$	61
7	**23g**	MeO	CH_2CO_2Me	62
8	**23h**	MeO	CH_2CO_2Et	60
9	**23i**	Phth	$CH_2CH_2CH_3$	58
10	**23j**	Phth	CH_2CO_2Et	55

procedure. The reaction of this imine and phenoxyacetic acid using triphosgene in the presence of triethylamine gave diastereomeric mixture (70:30) of β-lactams in 60% yield (see Table 5, entry 6). Attempt to separate these diastereomers by column chromatography were unsuccessful.

3. Conclusion

In summary, we have shown the application and versatility of triphosgene as an acid activator for the synthesis of diversely substituted β-lactams under very mild reaction conditions *via* ketene–imine cycloaddition reaction.

4. Experimental

4.1. General

^1H NMR and ^{13}C NMR Spectra were recorded in $CDCl_3$ solution on a Brucker AC 200 or Bruker MSL 300 spectrometers and chemical shifts are reported in ppm downfield from tetramethylsilane for ^1H NMR. Infrared spectra were recorded on Perkin–Elmer Infrared Spectrophotometer, Model 599-B or Shimadzu FTIR-8400 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.

4.2. General procedure for synthesis of β-lactams (3a–k)

A solution of triphosgene (0.148 g, 0.5 mmol), in anhydrous CH_2Cl_2 (10 ml), was added slowly to a solution of acid (1 mmol), imine (1 mmol) and triethylamine (0.42 ml, 3 mmol) in anhydrous CH_2Cl_2 (10 ml), at −40°C. The reaction mixture was then allowed to warm up to room temperature and stirred further for 12 h. The reaction mixture was then washed with water (20 ml), saturated sodium bicarbonate solution (2×15 ml) and brine (10 ml). The organic layer was dried over anhydrous sodium sulphate and filtered through a short silica gel column to get pure β-lactams (**3a–k**), which were recrystallized from methanol.

4.2.1. 1-Phenyl-3-phenoxy-4-phenylazetidin-2-one (3a). White solid; yield 89%; mp 184°C; [found: C, 79.73; H,

5.20; N, 4.37. $C_{21}H_{17}NO_2$ requires C, 79.98; H, 5.43; N, 4.44]; ν_{max} ($CHCl_3$) 1755 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.45 (d, J=4.8 Hz, 1H), 5.60 (d, J=4.8 Hz, 1H), 6.75–7.50 (m, 15H); δ_C (50.3 MHz, $CDCl_3$+DMSO-d_6) 61.61, 80.76, 115.35, 117.26, 121.89, 124.32, 127.81, 128.07, 128.40, 128.88, 128.95, 132.26, 136.60, 156.55, 162.80; MS (*m*/*z*): 315 (M^+).

4.2.2. 1-(4-Methoxyphenyl)-3-phenoxy-4-phenylazetidin-2-one (3b). White solid; yield 95%; mp 186–188°C; [found: C, 76.41; H, 5.69; N, 3.93. $C_{22}H_{19}NO_3$ requires C, 76.52; H, 5.51; N, 4.06]; ν_{max} (Nujol) 1743 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.74 (s, 3H), 5.35 (d, J=4 Hz, 1H), 5.55 (d, J=4 Hz, 1H), 6.70–7.40 (m, 14H); δ_C (50.3 MHz, $CDCl_3$) 55.20, 61.90, 80.98, 114.16, 115.47, 118.67, 121.92, 127.92, 128.14, 128.48, 129.00, 132.43, 156.27, 156.50, 163.00; MS (*m*/*z*): 345 (M^+).

4.2.3. 4-(4-Methoxyphenyl)-1-phenyl-3-phenoxyazetidin-2-one (3c). White solid; yield 83%; mp 150°C (Lit.[20] mp 149–150°C); [found: C, 76.33; H, 5.61; N, 4.23. $C_{22}H_{19}NO_3$ requires C, 76.52; H, 5.51; N, 4.06]; ν_{max} ($CHCl_3$) 1739 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.75 (s, 3H), 5.4 (d, J=4.9 Hz, 1H), 5.60 (d, J=4.9 Hz, 1H), 6.70–7.40 (m, 14H,); δ_C (50.3 MHz, $CDCl_3$) 55.06, 61.64, 81.19, 113.87, 115.71, 117.54, 122.10, 124.42, 129.01, 129.16, 129.31, 136.99, 157.02, 159.85, 163.16; MS (*m*/*z*): 345 (M^+).

4.2.4. 1,4-Di(4-methoxyphenyl)-3-phenoxyazetidin-2-one (3d). White crystalline solid; yield 82%; mp 166–167°C; [found: C, 73.37; H, 5.81; N, 3.84. $C_{23}H_{21}NO_4$ requires C, 73.58; H, 5.68; N, 3.73]; ν_{max} (Nujol) 1740 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.80 (s, 6H), 5.40 (d, J=5.2 Hz, 1H), 5.50 (s, J=5.2 Hz, 1H), 6.70–7.50 (m, 13H); δ_C (50.3 MHz, $CDCl_3$) 54.95, 55.19, 61.59, 81.04, 113.63, 114.13, 115.48, 118.70, 121.87, 124.28, 129.01, 129.21, 130.27, 156.22, 156.81, 159.63, 162.33; MS (*m*/*z*): 375 (M^+).

4.2.5. 1-(4-Methoxyphenyl)-3-phenoxy-4-styrylazetidin-2-one (3e). White solid; yield 93%; mp 178–180°C; [found: C, 77.46; H, 5.82; N, 3.93 $C_{24}H_{21}NO_3$ requires C, 77.61; H, 5.70; N, 3.77]; ν_{max} ($CHCl_3$) 1749 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.75 (s, 3H), 5.00 (dd, J=4.4, 5.1 Hz, 1H), 5.50 (d, J=4.4 Hz, 1H), 6.35 (dd, J=5.1, 16.1 Hz, 1H), 6.75–7.50 (m, 15H); δ_C (50.3 MHz, $CDCl_3$) 57.68, 63.36, 83.72, 116.63, 117.96, 121.04, 124.55, 124.92, 128.90, 130.61, 130.83, 131.74, 133.00, 138.80, 139.17, 158.00, 159.63, 164.90; MS (*m*/*z*): 371 (M^+).

4.2.6. 1-(4-Methoxyphenyl)-3-methoxy-4-phenylazetidin-2-one (3f). White solid; yield 87%; mp 160–161°C; [found: C, 72.32; H, 6.12; N, 5.15. $C_{17}H_{17}NO_3$ requires C, 72.08; H, 6.01; N, 4.94]; ν_{max} (Nujol) 1741 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.15 (s, 3H), 3.75 (s, 3H), 4.80 (d, J=5 Hz, 1H), 5.20 (d, J=5 Hz, 1H), 6.75 (d, J=8.8 Hz, 2H), 7.20–7.40 (m, 7H); δ_C (50.3 MHz, $CDCl_3$) 57.63, 60.61, 64.04, 87.03, 116.53, 120.98, 130.16, 130.78, 132.81, 135.59, 158.54, 166.40; MS (*m*/*z*): 283 (M^+).

4.2.7. 1-Phenyl-3-methoxy-4-(4-methoxyphenyl)azetidin-2-one (3g). White solid; yield 86%; mp 129–130°C [found: C, 71.88; H, 5.80; N, 4.93. $C_{17}H_{17}NO_3$ requires C, 72.08; H, 6.00; N, 4.94]; ν_{max}(Nujol) 1751 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.20 (s, 3H), 3.80 (s, 3H), 4.80 (d, J=4.4 Hz, 1H), 5.20 (d, J=4.4 Hz, 1H), 6.80–7.40 (m, 9H); δ_C (50.3 MHz, $CDCl_3$) 54.98, 58.11, 61.05, 84.46, 113.83, 117.25, 124.09, 124.82, 128.83, 129.01, 136.95, 159.67, 164.23; MS (*m*/*z*): 283 (M^+).

4.2.8. 1,4-Di(4-methoxyphenyl)-3-methoxyazetidin-2-one (3h). White needles; yield 83%; mp 114–115°C [found: C, 68.84; H, 6.00; N, 4.64. $C_{18}H_{19}NO_4$ requires C, 68.99; H, 6.11; N, 4.47]; ν_{max} (Nujol) 1747 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.15 (s, 3H), 3.75 (s, 3H), 3.80 (s, 3H), 4.70 (d, J=4.4 Hz, 1H), 5.10 (d, J=4.4 Hz, 1H), 6.70 (d, J=10 Hz, 2H), 6.85 (d, J=10 Hz, 2H), 7.10–7.40 (m, 4H); δ_C (50.3 MHz, $CDCl_3$) 55.02, 55.20, 58.11, 61.19, 84.61, 113.83, 114.13, 118.61, 125.01, 129.09, 130.48, 156.10, 159.67, 163.64; MS (*m*/*z*): 313 (M^+).

4.2.9. 1-(4-Methoxyphenyl)-3-phthalimido-4-styrylazetidin-2-one (3i). White solid; yield 78%; mp 189–190°C (Lit.[21] mp 192–194°C); [found: C, 73.36; H, 4.92; N, 6.35. $C_{26}H_{20}N_2O_4$ requires C, 73.57; H, 4.75; N, 6.60]; ν_{max} (Nujol) 1728, 1743 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.75 (s, 3H), 5.00 (dd, J=5.8, 8.45 Hz, 1H), 5.70 (d, J=5.8 Hz, 1H), 6.4 (dd, J=8.45, 16.1 Hz, 1H), 6.80–7.90 (m, 14H); δ_C (50.3 MHz, $CDCl_3$) 55.52, 57.84, 61.11, 114.52, 118.67, 123.01, 123.78, 126.80, 128.71, 131.35, 131.57, 134.55, 135.54, 137.64, 156.57, 160.69, 167.34; MS (*m*/*z*): 424 (M^+).

4.2.10. 1-(4-Methoxyphenyl)-3-(2,4-dichlorophenoxy)-4-phenylazetidin-2-one (3j). White solid; yield 65%; mp 148–150°C; [found: C, 63.57; H, 4.06; N, 3.27; Cl, 17.31. $C_{22}H_{17}NO_3Cl_2$ requires C, 63.77; H, 4.11; N, 3.38; Cl, 17.16]; ν_{max} ($CHCl_3$) 1731 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.75 (s, 3H), 5.40 (d, J=4.9 Hz, 1H) 5.55 (d, J=4.9 Hz, 1H), 6.80–7.50 (m, 12H); δ_C (50.3 MHz, $CDCl_3$) 55.18, 61.28, 81.38, 114.21, 116.34, 118.69, 123.91, 127.15, 127.88, 128.25, 128.69, 129.68, 130.02, 132.04, 151.22, 156.41, 161.48; MS (*m*/*z*): 413 (M^+).

4.2.11. 1-Phenyl-3-(2,4-dichlorophenoxy)-4-(4-methoxyphenyl)azetidin-2-one (3k). White solid; yield 66%; mp 164–165°C; [found: C, 63.84; H, 4.39; N, 3.22; Cl, 17.31. $C_{22}H_{17}NO_3Cl_2$ requires C, 63.77; H, 4.11; N, 3.38; Cl, 17.16]; ν_{max} (Nujol) 1747 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.75 (s, 3H), 5.35 (d, J=4.4 Hz, 1H), 5.50 (d, J=4.4 Hz, 1H), 6.8–7.40 (m, 12H); δ_C (75.48 MHz, $CDCl_3$) 55.01, 60.93, 81.35, 113.79, 116.32, 117.21, 123.65, 123.95, 124.53, 127.19, 128.96, 129.23, 129.78, 136.59, 151.27, 159.84, 142.13; MS (*m*/*z*): 413 (M^+).

4.3. General procedure for synthesis of β-lactams (5a,b and 7a–c) from potassium salt 4 and 6

A solution of triphosgene (0.148 g, 0.5 mmol), in anhydrous CH_2Cl_2 (10 ml), was added slowly to a mixture of potassium salt (1 mmol), imine (1 mmol) and triethylamine (0.42 ml, 3 mmol) at 0°C. After the addition, the reaction mixture was allowed to warm up to room temperature and stirred for 12 h. The reaction mixture was then washed with water (20 ml), saturated sodium bicarbonate solution (2×15 ml) and brine (10 ml). The organic layer was dried over

anhydrous sodium sulphate and concentrated to get crude product, which was purified by column chromatography to give pure β-lactams (**5a**,**b** and **7a**–**c**).

4.3.1. 3-Azido-4-(4-methoxyphenyl)-1-phenylazetidin-2-one (5a). White solid; yield 68%; mp 120–122°C; [found: C, 68.42; H, 5.12; N, 15.10 $C_{16}H_{14}N_3O_2$ requires C, 68.56; H, 5.03; N, 14.99]; ν_{max} ($CHCl_3$) 1740 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.80 (s, 3H), 5.00 (d, J=5.4 Hz, 1H), 5.35 (d, J=5.4 Hz, 1H), 6.90–7.50 (m, 9H); δ_C (50.3 MHz, $CDCl_3$) 55.31, 60.61, 67.66, 114.57, 117.62, 124.45, 124.75, 128.94, 129.23, 136.99, 160.48, 161.84; MS (*m*/*z*): 413 (M^+).

4.3.2. 3-Azido-1-(4-methoxyphenyl)-4-styrylazetidin-2-one (5b). White solid; yield 83%; mp 115–116°C; [found: C, 67.72; H, 5.34; N, 17.66 $C_{18}H_{16}N_4O_2$ requires C, 67.48; H, 5.03; N, 17.49]; ν_{max} ($CHCl_3$) 1739 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.80 (s, 3H), 4.90 (dd, J=5.30, 8.30 Hz, 1H), 5.00 (d, J=5.30 Hz, 1H), 6.30 (dd, J=8.30, 15.95 Hz, 1H), 6.80–7.50 (m, 10H); δ_C (75.48 MHz, $CDCl_3$) 55.27, 59.75, 67.26, 114.26, 118.50, 122.40, 126.70, 128.59, 130.53, 135.27, 137.04, 156.47, 160.56; MS (*m*/*z*): 320 (M^+).

4.3.3. 1-(4-Methoxyphenyl)-3-(α-methyl-β-ethoxycarbonylamino)-4-phenyl-azetidin-2-one (7a). White solid; yield 70%; mp 140°C; [found: C, 69.50; H, 6.45; N, 7.20. $C_{22}H_{24}N_2O_4$ requires C, 69.46; H, 6.36; N, 7.36]; ν_{max} ($CHCl_3$) 1753 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.10 (t, J=7.1 Hz, 3H), 1.85 (s, 3H), 3.75 (s, 3H), 3.90 (q, J=7.1 Hz, 2H), 4.40 (s, 1H), 5.15 (dd, J=4.9, 8.8 Hz, 1H), 5.35 (d, J=4.9 Hz, 1H), 6.80 (d, J=9.3 Hz, 2H), 7.20–7.50 (m, 7H), 8.60 (d, J=8.8 Hz, 1H); δ_C (50.3 MHz, $CDCl_3$) 14.19, 19.45, 55.21, 58.23, 61.61, 63.30, 86.27, 114.21, 118.55, 127.00, 128.69, 128.91, 131.00, 132.77, 156.22, 158.21, 163.24, 169.13; MS (*m*/*z*): 380 (M^+).

4.3.4. 1-(4-Methoxyphenyl)-3-(α-methyl-β-ethoxycarbonylamino)-4-(4-methoxyphenyl)azetidin-2-one (7b). White solid; yield 65%; mp 118–120°C; [found: C, 67.60; H, 6.48; N, 6.59. $C_{23}H_{26}N_2O_5$ requires C, 67.30; H, 6.39; N, 6.83]; ν_{max} ($CHCl_3$) 1747 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.17 (t, J=7.1 Hz, 3H), 1.87 (s, 3H), 3.76 (s, 3H), 3.80 (s, 3H), 3.95 (q, J=7.1 Hz, 2H), 4.39 (s, 1H), 5.14 (dd, J=5.4, 8.8 Hz, 1H) 5.23 (d, J=5.4 Hz, 1H), 6.60–7.40 (m, 8H), 8.60 (d, J=8.8 Hz, 1H); δ_C (50.3 MHz, $CDCl_3$) 14.19, 19.41, 55.03, 55.18, 58.19, 61.20, 63.30, 86.16, 114.17, 114.47, 116.16, 118.58, 124.57, 128.36, 130.46, 156.19, 159.94, 163.32, 169.16; MS (*m*/*z*): 410 (M^+).

4.3.5. 1-(4-Methoxyphenyl)-3-(α-methyl-β-ethoxycarbonylamino)-4-styrylazetidin-2-one (7c). White solid; yield 73%; mp 115–116°C; [found: C, 71.10; H, 6.75; N, 7.03 $C_{24}H_{26}N_2O_4$ requires C, 70.92; H, 6.45; N, 6.89]; ν_{max} ($CHCl_3$) 1749 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.17 (t, J=7.1 Hz, 3H), 1.87 (s, 3H), 3.76 (s, 3H), 3.80 (s, 3H), 3.95 (q, J=7.1 Hz, 2H), 4.39 (s, 1H), 5.14 (dd, J=5.4, 8.8 Hz, 1H) 5.23 (d, J=5.4 Hz, 1H), 6.60–7.40 (m, 8H), 8.60 (d, J=8.8 Hz, 1H); δ_C (75.48 MHz, $CDCl_3$) 13.95, 19.17, 54.87, 58.03, 59.96, 62.53, 85.91, 113.83, 118.05, 122.38, 122.47, 126.38, 128.06, 134.41, 135.17, 136.69, 155.86, 158.97, 162.56, 169.41; MS (*m*/*z*): 405 (M^+-1).

4.4. General procedure for the synthesis of β-lactams (9a–c) from camphorsultam derived acid (8)

A similar general procedure, as for compounds **3a**–**k**, was employed for the synthesis of β-lactams (**9a**–**c**) from acid **8** and imines **2**.

4.4.1. (2*R*,3*S*,6*R*,3′*R*,4′*S*)-*N*-[1′-(*p*-Anisyl)-4′-phenylazetidin-2′-one-3′-yl]-2,10-camphorsultam (9a). White crystalline solid; yield 90%; mp 238–240°C (Lit.[15] mp 242–243°C); [found: C, 66.62; H, 6.19; N, 5.83; S, 6.70. $C_{26}H_{30}N_2O_4S$ requires C, 66.93; H, 6.48; N, 6.00; S, 6.87]; ν_{max} ($CHCl_3$) 1753 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.15 (s, 3H), 0.70 (s, 3H), 1.25–1.50 (m, 2H), 1.60–1.90 (m, 5H), 2.80 (d, J=13.7 Hz, 1H), 3.10 (d, J=13.7 Hz, 1H), 3.70 (t, J=7.5 Hz, 1H), 3.75 (s, 3H), 5.30 (m, 2H), 6.85 (d, J=10 Hz, 2H), 7.25–7.50 (m, 7H); δ_C (50.3 MHz, $CDCl_3$) 18.75, 19.78, 26.51, 32.35, 37.24, 44.74, 47.13, 48.19, 49.70, 55.21, 59.92, 61.09, 65.28, 114.17, 118.40, 127.48, 127.99, 128.36, 130.64, 133.47, 156.26, 160.34; MS (*m*/*z*): 466 (M^+); $[\alpha]^{25}_D$=+37.60 (*c* 1.0, CH_2Cl_2).

4.4.2. (2*R*,3*S*,6*R*,3′*R*,4′*S*)-*N*-[1′-(*p*-Anisyl)-4′-*p*-anisylazetidin-2′-one-3′-yl]-2,10-camphorsultam (9b). White crystalline solid; yield 90%; mp 210–212°C (Lit.[15] mp 215–216°C); [found: C, 65.42; H, 6.37; N, 5.86; S, 6.26. $C_{27}H_{32}N_2O_5S$ requires C, 65.30; H, 6.49; N, 5.64; S, 6.46]; ν_{max} ($CHCl_3$) 1753 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.20 (s, 3H), 0.75 (s, 3H), 1.20–1.50 (m, 2H), 1.60–1.85 (m, 5H), 2.90 (d, J=13.7 Hz, 1H), 3.10 (d, J=13.7 Hz, 1H), 3.70 (t, J=7.5 Hz, 1H), 3.80 (s, 6H), 5.25 (two merged doublets, 2H), 6.80–7.00 (m, 4H), 7.15–7.40 (m, 4H); δ_C (50.3 MHz, $CDCl_3$) 18.75, 19.74, 26.54, 32.35, 37.28, 44.74, 47.16, 48.23, 49.74, 55.21, 59.55, 60.98, 65.28, 113.88, 114.17, 118.40, 125.35, 128.66, 130.64, 156.22, 159.50, 160.41; MS (*m*/*z*): 496 (M^+); $[\alpha]^{25}_D$=+58.40 (*c* 1.0, CH_2Cl_2).

4.4.3. (2*R*,3*S*,6*R*,3′*R*,4′*S*)-*N*-[1′-(*p*-Anisyl)-4′-styrylazetidin-2′-one-3′-yl]-2,10-camphorsultam (9c). White crystalline solid; yield 82%; mp 204–206°C (Lit.[15] mp 208–210°C); [found: C, 68.23; H, 6.66; N, 5.97; S, 6.49. $C_{28}H_{32}N_2O_4S$ requires C, 68.27; H, 6.55; N, 5.69; S, 6.51]; ν_{max} ($CHCl_3$) 1751 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.90 (s, 3H), 1.00 (s, 3H), 1.30–1.65 (m, 2H), 1.75–2.00 (m, 5H), 3.20 (q, J=14 Hz, 2H), 3.70 (dd, J=4.9, 7.3 Hz, 1H), 3.80 (s, 3H), 4.90 (m, 1H), 5.10 (d, J=5.3 Hz, 1H), 6.35 (dd, J=5.3, 16.1 Hz, 1H), 6.60 (d, J=16.1 Hz, 1H), 6.90 (d, J=8.8 Hz, 2H), 7.25–7.50 (m, 7H); δ_C (50.3 MHz, $CDCl_3$) 19.73, 20.06, 26.49, 32.38, 38.00, 44.69, 47.37, 48.66, 50.13, 55.20, 58.18, 60.53, 65.90, 114.16, 118.28, 123.83, 126.44, 127.80, 128.24, 130.96, 133.61, 135.74, 156.25, 159.71; MS (*m*/*z*): 492 (M^+); $[\alpha]^{25}_D$=+59.0 (*c* 1.0, CH_2Cl_2).

4.5. General procedure for synthesis of β-lactams from acids derived from oxazolidinone

A similar general procedure, as for compounds **5a**,**b** and **7a**–**c**, was used for the synthesis of β-lactams (**11a**–**f**) starting from the acids **10** and imines **2**.

4.5.1. (4*R*,3′*R*,4′*R*)-3-[2′-Oxo-4′-(phenyl)-1′-(phenylmethyl)-3′-azetidinyl]-4-phenyl-2-oxazolidinone (11a).

White solid; yield 70%; mp 220–222°C (Lit.[16] mp 228–230°C); [found: C, 75.15; H, 5.45; N, 7.32. $C_{25}H_{22}N_2O_3$ requires C, 75.36; H, 5.56; N, 7.03]; ν_{max} (Nujol) 1750 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.87–4.02 (m, 2H), 4.10–4.38 (m, 2H), 4.42 (d, J=4.6 Hz, 1H), 4.55 (d, J=4.6 Hz, 1H), 4.95 (d, J=14.7 Hz, 1H), 7.00–7.50 (m, 15H); δ_C (50.3 MHz, $CDCl_3$) 44.96, 59.40, 60.43, 63.48, 69.92, 127.22, 127.52, 127.63, 128.36, 128.58, 129.17, 132.96, 134.65, 136.34, 156.63, 163.10; MS (*m*/*z*): (M^+−133); $[\alpha]^{30}_D$=−73.4 (*c* 1.0, $CHCl_3$).

4.5.2. (4*R*,3′*R*,4′*R*)-3-[2′-Oxo-4′-(phenyl)-1′-(4-methoxyphenyl)-3′-azetidinyl]-4-phenylmethyl-2-oxazolidinone (11b). White solid; yield 67%; mp 194°C; [found: C, 72.67; H, 5.63; N, 6.52. $C_{26}H_{24}N_2O_4$ requires C, 72.88; H, 5.65; N, 6.54]; γ_{max} ($CHCl_3$) 1753 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.80 (dd, J=13.2, 10.3 Hz 1H), 2.95 (dd, J=13.2, 3.9 Hz, 1H), 3.60–3.90 (m, 2H), 3.75 (s, 3H), 4.00–4.25 (m, 1H), 5.20 (d, J=4.9 Hz, 1H), 5.40 (d, J=4.9 Hz, 1H), 6.85–7.50 (m, 14H); δ_C (50.3 MHz, $CDCl_3$) 39.96, 55.29, 55.36, 60.58, 63.08, 67.60, 114.28, 118.40, 127.00, 127.30, 128.25, 128.40, 128.73, 130.82, 133.03, 135.09, 156.41, 157.47, 160.34; MS (*m*/*z*): 428 (M^+); $[\alpha]^{30}_D$=−80.20 (*c* 1.0, $CHCl_3$).

4.5.3. (4*R*,3′*R*,4′*R*)-3-[2′-Oxo-4′-(phenyl)-1′-(phenylmethyl)-3′-azetidinyl]-4-phenylmethyl-2-oxazolidinone (11c). White solid; yield 70%; mp 151°C; [found: C, 75.56; H, 5.81; N, 6.82. $C_{26}H_{24}N_2O_3$ requires C, 75.71; H, 5.87; N, 6.79]; ν_{max}(Nujol) 1745 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.90 (dd, J=13.1, 9.7 Hz, 1H), 2.95 (dd, J=13.1, 3.9 Hz, 1H), 3.60–3.80 (m, 2H), 3.80–4.10 (m, 1H), 4.25 (d, J=14.7 Hz, 1H), 4.80 (d, J=5.3 Hz, 1H), 5.00 (d, J=5.3 Hz, 1H), 5.10 (d, J=14.7 Hz, 1H), 7.00–7.50 (m, 15H); δ_C (50.3 MHz, $CDCl_3$) 39.87, 45.68, 55.53, 60.28, 64.10, 67.44, 127.03, 127.25, 127.95, 128.28, 128.46, 128.79, 133.75, 134.60, 135.11, 157.39, 163.71; MS (*m*/*z*): 412 (M^+); $[\alpha]^{30}_D$=−44 (*c* 1.0, $CHCl_3$).

4.5.4. (4*R*,3′*R*,4′*R*)-3-[2′-Oxo-4′-(phenyl)-1′-(4-methoxyphenyl)-3′-azetidinyl]-4-isopropyl-2-oxazolidinone (11d). White solid; yield 71%; mp 215–217°C; [found: C, 69.19; H, 6.13; N, 7.16. $C_{22}H_{24}N_2O_4$ requires C, 69.47; H, 6.36; N, 7.36]; ν_{max}($CHCl_3$) 1747 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.40 (d, J=6.8 Hz, 3H), 0.75 (d, J=6.8 Hz, 3H), 1.60–1.90 (m, 1H), 3.60–3.80 (m, 1H), 3.75 (s, 3H), 3.85–3.95 (m, 2H), 5.00 (d, J=5.4 Hz, 1H), 5.30 (d, J=5.4 Hz, 1H), 6.80–7.50 (m, 9H); δ_C (50.3 MHz, $CDCl_3$) 13.20, 17.72, 28.67, 55.18, 58.67, 61.09, 63.04, 63.19, 114.10, 118.33, 127.30, 128.21, 128.47, 130.82, 132.70, 156.19, 157.44, 160.27; MS (*m*/*z*): 380 (M^+); $[\alpha]^{30}_D$=−17.27 (*c* 1.0, $CHCl_3$).

4.5.5. (4*R*,3′*R*,4′*R*)-3-[2′-Oxo-4′-(4-methoxyphenyl)-1′-(4-methoxyphenyl)-3′-azetidinyl]-4-isopropyl-2-oxazolidinone (11e). White solid; yield 72%; mp 200–202°C; [found: C, 67.21; H, 6.42; N, 6.75; $C_{23}H_{26}N_2O_5$ requires C, 67.30; H, 6.39; N, 6.83]; ν_{max} ($CHCl_3$) 1753 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.50 (d, J=6.9 Hz, 3H), 0.75 (d, J=6.9 Hz, 3H), 1.60–1.90 (m, 1H), 3.60–3.80 (m, 1H), 3.75 (s, 3H), 3.80 (s, 3H), 3.85–3.95 (m, 2H), 5.00 (d, J=5.4 Hz, 1H), 5.30 (d, J=5.4 Hz, 1H), 6.80–7.50 (m, 8H); δ_C (50.3 MHz, $CDCl_3$) 13.42, 17.68, 28.45, 55.03, 55.18, 58.78, 60.84, 62.97, 63.19, 113.92, 114.06, 118.36, 124.39, 128.66, 130.86, 156.11, 157.36, 159.50, 160.38; MS (*m*/*z*): 410 (M^+); $[\alpha]^{30}_D$=−24.4 (*c* 1.0, $CHCl_3$).

4.5.6. (4*R*,3′*R*,4′*R*)-3-[2′-Oxo-4′-(phenyl)-1′-(phenylmethyl)-3′-azetidinyl]-4-isopropyl-2-oxazolidinone (11f). White solid; yield 70%; mp 185°C; [found: C, 72.33; H, 6.53; N, 7.76. $C_{22}H_{24}N_2O_3$ requires C, 72.51; H, 6.64; N, 7.69]; ν_{max} (Nujol) 1747 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.40 (d, J=6.8 Hz, 3H), 0.75 (d, J=6.8 Hz, 3H), 1.60–1.90 (m, 1H), 3.40–3.50 (m, 1H), 3.65–3.75 (dd, J=8.8, 11.5 Hz, 1H), 3.85–3.95 (dd, J=8.8, 4.4 Hz, 1H), 4.15 (d, J=14.7 Hz, 1H), 4.70 (d, J=4.9 Hz, 1H), 4.90 (d, J=4.9 Hz, 1H), 5.05 (d, J=14.7 Hz, 1H), 7.10–7.50 (m, 10H); δ_C (50.3 MHz, $CDCl_3$) 13.46, 17.57, 28.20, 45.14, 58.71, 60.54, 62.97, 63.92, 127.33, 127.70, 128.21, 128.32, 128.62, 133.29, 134.72, 157.22, 163.61; MS (*m*/*z*): 364 (M^+); $[\alpha]^{30}_D$=−40 (*c* 1.0, $CHCl_3$).

4.5.7. 4-Methoxy-4,7,7-trimethyl-bicyclo[4.1.0]heptan-3-ol (13). To a solution of (+)-3-carene oxide **12** (1.0 g, 6.5 mmol) in methanol (25 ml), a catalytic quantity of PTSA (30 mg) was added at 0°C and stirred for 2 h. The solvent was evaporated under reduced pressure and the residue was extracted with EtOAc (3×20 ml). The combined extracts were washed with brine (2×20 ml), dried over Na_2SO_4. It was filtered and the filtrate was concentrated to give the crude product **13** which on purification by column chromatography (silica gel, 60–120, 5% EtOAc in pet. ether) gave colourless oil (1.1 g, 90%) of pure methoxy alcohol (**13**); [found: C, 71.54; H, 11.16. $C_{11}H_{20}O_2$ requires C, 71.69; H, 10.93]; ν_{max} (Neat) 3461 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.60–0.70 (m, 2H); 0.95–1.25 (m, 1H), 0.96 (s, 3H), 0.99 (s, 3H), 1.16 (s, 3H), 1.62–1.80 (m, 1H), 2.00–2.20 (m, 2H), 2.50 (bs, 1H), 3.21 (s, 3H), 3.35–3.50 (m, 2H). MS (*m*/*z*): 184 (M^+); $[\alpha]^{28}_D$=−5.8 (*c* 1.5, $CHCl_3$).

4.5.8. (4-Methoxy-4,7,7-trimethyl-bicyclo[4.1.0]hept-3-yloxy)-acetic acid (14). To a solution of **13** (1.84 g, 10 mmol) in dry toluene (25 ml), clean sodium pieces (0.5 g) were added and gently refluxed for 15 h. The solution was cooled and the excess of sodium was removed by filtration through glass wool. The filtrate was heated to 85–90°C with stirring and a solution of chloroacetic acid (0.470 g, 5 mmol) in dry toluene (30 ml) was added in such a way that the refluxing should not be vigorous. A heavy precipitate of sodium chloroacetate was formed immediately. The reaction mixture was refluxed under stirring for an additional 48 h. The reaction mixture was diluted with toluene (30 ml) and extracted with water (3×25 ml) and the aqueous layer was acidified with 20% HCl. The crude product, which collects as brown oil on the top, was extracted with diethylether. The organic extract was dried over Na_2SO_4 and the solvent was removed under reduced pressure to give crude product as oil, which was purified by fractional distillation under reduced pressure to afford pale yellow oil (1.5 g, 62%) of the acid (**14**). Bp 90–95°C/5 mm; [found: C, 64.26; H, 9.26. $C_{13}H_{22}O_4$ requires C, 64.43; H, 9.15]; ν_{max} (Neat) 1731, 3600–2600 cm^{-1}; δ_H (200 MHz, $CDCl_3$), 0.95 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 3.38 (s, 3H, OCH_3), 1.20–2.40 (m, 7H, CH_2 and CH), 3.90 (d, J=17.6 Hz, 1H), 4.35 (d, J=17.6 Hz, 1H), 9.30 (bs, 1H). MS (*m*/*z*): 242 (M^+); $[\alpha]^{28}_D$=−58.48 (*c* 1.05, $CHCl_3$).

4.5.9. 3-(4-Methoxy-4,7,7-trimethyl-bicyclo[4.1.0]hept-3-yloxy)-4-styryl-1-(4-methoxyphenyl) azetidin-2-one (15 and 16). A solution of triphosgene (0.148 g, 0.5 mmol) in anhydrous CH_2Cl_2 (10 ml) was added slowly to a solution of the acid **14** (0.242 g, 1 mmol), imine **2** (0.237 g, 1 mmol) and triethylamine (0.42 ml, 3 mmol) in anhydrous CH_2Cl_2 (10 ml) at −40°C. The reaction mixture was allowed to warm up to room temperature and stirred for 12 h. It was then diluted with CH_2Cl_2 and washed successively with water (2×20 ml), saturated $NaHCO_3$ (2×20 ml), brine (20 ml), dried (anhyd. Na_2SO_4). The solvent was removed under reduced pressure and the residue was passed through a short silica-gel column to afford the β-lactams **15** and **16** (0.30 g, 65%) as the diastereomeric mixture (60:40). The major diastereomer was separated by crystallization from petroleum ether/acetone, which showed following spectral and analytical data. White solid; mp 232–234°C; [found: C, 75.72; H, 7.51; N, 3.14. $C_{29}H_{35}O_4N$ requires C, 75.46; H, 7.64; N, 3.03]; ν_{max} (Nujol) 1740 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.50–0.65 (m, 2H), 0.71 (s, 3H), 0.87 (s, 3H), 0.90–1.10 (m, 1H), 1.27 (s, 3H), 1.55–2.20 (m, 3H), 3.27 (s, 3H), 3.20–3.40 (m, 1H), 3.75 (s, 3H), 4.70 (dd, *J*=4.4, 8.7 Hz, 1H), 5.42 (d, *J*=4.4 Hz, 1H), 6.37 (dd, *J*=8.7, 16.0 Hz, 1H), 6.75–6.95 (m, 3H), 7.15–7.55 (m, 7H); δ_C (50.3 MHz, $CDCl_3$) 14.80, 15.50, 17.60, 19.10, 20.50, 26.20, 28.20, 29.70, 48.90, 55.40, 61.50, 78.20, 81.90, 84.20, 114.20, 118.50, 125.10, 126.50, 128.20, 128.60, 131.50, 135.50, 135.90, 156.10, 164.00; $[\alpha]^{23}_D$=−3.3 (*c* 1.2, CH_2Cl_2).

4.6. General procedure for synthesis of β-lactams (20a–g) from dithioglyoxylic acid (19)

A similar general procedure, as for compounds **5a**,**b** and **7a–c**, was used for the synthesis of β-lactams (**20a–g**) starting from the acid **19** and imines **2**.

4.6.1. 2-(4-Methoxyphenyl)-3-phenyl-5,9-dithia-2-aza-spiro[3,5]nonan-1-one (20a). White solid; yield 70%; mp 186°C; [found: C, 63.62; H, 5.50; N, 3.73; S, 18.04. $C_{19}H_{19}NO_2S_2$ requires C, 63.83; H, 5.36; N, 3.92; S, 17.94]; ν_{max} (Nujol) 1735 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.80–2.30 (m, 2H), 2.60–2.90 (m, 2H), 3.50–3.90 (m, 2H), 3.70 (s, 3H), 4.90 (s, 1H), 6.75–7.50 (m, 9H); δ_C (75.48 MHz, $CDCl_3$) 25.39, 28.18, 28.56, 55.63, 60.55, 66.86, 114.60, 118.75, 127.90, 128.54, 126.38, 130.89, 131.99, 156.47, 164.62; MS (*m/z*): 357 (M^+).

4.6.2. 2-Phenyl-3-(4-methoxyphenyl)-5,9-dithia-2-aza-spiro[3,5]nonan-1-one (20b). White solid; yield 71%; mp 155–156°C; [found: C, 63.65; H, 5.60; N, 4.10; S, 17.75. $C_{19}H_{19}NO_2S_2$ requires C, 63.83; H, 5.36; N, 3.92; S, 17.94]; ν_{max} (Nujol) 1737 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.80–2.30 (m, 2H), 2.60–2.90 (m, 2H), 3.50–3.90 (m, 2H), 3.70 (s, 3H), 4.90 (s, 1H), 6.75–7.50 (m, 9H); δ_C (50.3 MHz, $CDCl_3$) 25.33, 28.02, 28.42, 55.33, 60.66, 66.43, 113.92, 117.41, 123.55, 124.28, 129.17, 137.44, 160.42, 165.12; MS (*m/z*): 357 (M^+).

4.6.3. 2,3-Di(4-Methoxyphenyl)-5,9-dithia-2-aza-spiro[3,5]nonan-1-one (20c). White solid; yield 75%; mp 130°C; [found: C, 61.60; H, 5.72; N, 3.40; S, 16.54. $C_{20}H_{21}NO_3S_2$ requires C, 61.90; H, 5.46; N, 3.61; S, 16.40]; ν_{max} ($CHCl_3$) 1745 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.80–2.30 (m, 2H), 2.60–2.90 (m, 2H), 3.50–3.90 (m, 2H), 3.75 (s, 3H), 3.80 (s, 3H), 4.90 (s, 1H), 6.70–7.40 (m, 8H); δ_C (50.3 MHz, $CDCl_3$), 25.11, 27.76, 28.16, 55.03, 55.25, 60.58, 66.46, 113.66, 114.28, 118.47, 123.58, 128.91, 130.71, 156.19, 160.19, 164.38; MS (*m/z*): 387(M^+).

4.6.4. 2-(4-Methoxyphenyl)-3-styryl-5,9-dithia-2-aza-spiro[3,5]nonan-1-one (20d). White solid; yield 70%; mp 122–124°C; [found: C, 65.50; H, 5.68; N, 3.40; S, 16.64. $C_{21}H_{21}NO_2S_2$ requires C, 65.79; H, 5.48; N 3.65; S, 16.72]; ν_{max} ($CHCl_3$) 1745 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.80–2.30 (m, 2H), 2.60–2.90 (m, 2H), 3.50–3.90 (m, 2H), 3.75 (s, 3H), 4.50 (d, *J*=8.3 Hz, 1H), 6.40 (dd, *J*=8.3, 16 Hz, 1H), 6.75–7.50 (m, 10H); δ_C (75.48 MHz, $CDCl_3$) 25.27, 27.56, 28.11, 55.33, 60.58, 65.77, 114.26, 118.38, 121.96, 126.81, 128.36, 128.58, 130.93, 135.26, 137.46, 156.20, 163.98; MS (*m/z*): 383 (M^+).

4.6.5. 2,3-Diphenyl-5,9-dithia-2-aza-spiro[3,5]nonan-1-one (20e). White solid; yield 72%; mp 173–174°C (Lit.[22] mp 175–176°C); [found: C, 65.90; H, 5.43; N, 4.31; S, 19.73. $C_{18}H_{17}NOS_2$ requires C, 66.02; H, 5.23; N, 4.28; S, 19.58]; ν_{max} ($CHCl_3$) 1740 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.80–2.30 (m, 2H), 2.60–2.90 (m, 2H), 3.50–3.90 (m, 2H), 5.00 (s, 1H), 7.00–7.75 (m, 10H); δ_C (50.3 MHz, $CDCl_3$) 24.96, 27.72, 28.16, 60.07, 66.35, 117.04, 124.02, 127.44, 128.18, 128.91, 131.49, 137.11, 159.46, 164.68; MS (*m/z*): 357 (M^+).

4.6.6. 2-(4-Chlorophenyl)-3-styryl-5,9-dithia-2-aza-spiro-[3,5]nonan-1-one (20f). White solid; yield 69%; mp 154°C; [found: C, 62.19; H, 4.83; N, 3.39; S, 16.28. $C_{20}H_{18}NOS_2Cl$ requires C, 61.92; H, 4.68; N, 3.61; S, 16.53]; ν_{max} ($CHCl_3$) 1751 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.80–2.40 (m, 2H), 2.70–2.90 (m, 2H), 3.55–3.90 (m, 2H), 4.50 (d, *J*=8.3 Hz, 1H), 6.30 (dd, *J*=8.3, 16.1 Hz, 1H), 6.90 (d, *J*=16.1 Hz, 1H), 7.25–7.50 (m, 9H); δ_C (75.48 MHz, $CDCl_3$) 25.27, 27.65, 28.23, 60.89, 65.80, 118.29, 121.38, 126.90, 128.67, 129.16, 129.31, 135.17, 136.15, 137.86, 164.41; MS (*m/z*): 387 (M^+).

4.6.7. 2-(1′-Phenylethyl)-3-phenyl-2-aza-5,9-dithiaspiro-[3,5]nonan-1-one (20g). (Mixture of 2 diastereomers, 3*R*, 1′*R* and 3*S*, 1′*R*) Yellow oil; yield 69%; [found: C, 67.45; H, 5.86; N, 3.80; S, 17.91. $C_{20}H_{21}NOS_2$ requires C, 67.61; H, 5.92; N, 3.94; S, 18.03]; ν_{max} ($CHCl_3$) 1751 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.50 and 1.90 (2d, *J*=7.4, 6.9 Hz, 3H), 1.50–2.25 (m, 2H), 2.50–2.90 (m, 2H), 3.40–3.90 (m, 2H), 4.22 and 4.27 (2S, 1H), 4.35 and 5.00 (2 q, 1H), 7.00–7.50 (m, 9H); MS (*m/z*): 355 (M^+).

4.7. General procedure for the synthesis of carbonimidodithioic acid dimethyl esters (22a–g) from amines and aminoacid esters

To a solution of amine (10 mmol) and carbon disulfide (10 mmol) in dichloromethane (50 ml), triethylamine (10 mmol) was added slowly at 20°C and the reaction mixture was stirred for 30 min. Methyl iodide (12 mmol) was then added dropwise and the resulting mixture was refluxed for 2–3 h. The reaction mixture was then cooled

to room temperature and triethylamine (12 mmol), methyl iodide (12 mmol) were successively added dropwise. The reaction mixture was again refluxed for 2–3 h. After complete conversion of dithiocarbamate to carbonimidodithioate (TLC), the reaction mixture was washed with water (2×20 ml), brine (20 ml), dried (anhyd. Na_2SO_4) and concentrated under vacuum to get crude product, which was purified by column chromatography to get the desired product (**22a–g**) in 70–79% yield.

4.7.1. *N*-Phenyl carbonimidodithioic acid dimethyl ester (22a). Pale yellow oil; yield 74%; [found: C, 54.67; H, 5.44; N, 7.12; S, 32.23. $C_9H_{11}NS_2$ requires C, 54.78; H, 5.61; N, 7.09; S, 32.49]; ν_{max} ($CHCl_3$) 1587 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.34 (s, 3H), 2.45 (s, 3H), 7.00–7.30 (m, 5H); δ_C (50.3 MHz, $CDCl_3$) 14.44, 119.90, 123.35, 128.46, 149.50, 162.02; MS (*m/z*): 197 (M^+).

4.7.2. *N*-Benzyl carbonimidodithioic acid dimethyl ester (22b). Pale yellow oil; yield 79%; [found: C, 56.64; H, 6.08; N, 6.74; S, 30.56. $C_{10}H_{13}NS_2$ requires C, 56.83; H, 6.20; N, 6.62; S, 30.33]; ν_{max} ($CHCl_3$) 1590 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.40 (s, 3H), 2.55 (s, 3H), 4.60 (s, 2H), 7.00–7.30 (m, 5H); δ_C (50.3 MHz, $CDCl_3$) 14.52, 56.06, 126.45, 127.33, 128.14, 140.09, 158.76; MS (*m/z*): 211 (M^+).

4.7.3. *N*-(4-Methoxyphenyl) carbonimidodithioic acid dimethyl ester (22c). Pale yellow oil; yield 72%; [found: C, 52.68; H, 5.54; N, 6.32; S, 28.05. $C_{10}H_{13}NOS_2$ requires C, 52.83; H, 5.76; N, 6.16; S, 28.20]; ν_{max} (Neat) 1585 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.43 (s, 3H), 2.49 (s, 3H), 3.78 (s, 3H), 6.75–7.00 (m, 5H); δ_C (50.3 MHz, $CDCl_3$) 14.62, 55.02, 113.67, 121.22, 142.72, 155.99, 161.71; MS (*m/z*): 227 (M^+).

4.7.4. *N*-Propylcarbonimidodithioic acid dimethyl ester (22d). Pale yellow oil; yield 72%; [found: C, 43.98; H, 7.97; N, 8.69; S, 39.08. $C_6H_{13}NS_2$ requires C, 44.13; H, 8.02; N, 8.57; S, 39.26]; ν_{max} (Neat) 1590 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.00 (t, *J*=7.2 Hz, 3H), 1.65 (m, 2H), 2.35 (s, 3H), 2.55 (s, 3H), 3.40 (t, *J*=7.2 Hz, 2H); δ_C (50.3 MHz, $CDCl_3$) 11.53, 13.96, 14.07, 23.70, 54.25, 156.14; MS (*m/z*): 163 (M^+).

4.7.5. *N*-[Bis(methylthio) methylene] glycine methyl ester (22e). Pale yellow oil; yield 70%; [found: C, 37.58; H, 5.63; N, 7.51; S, 33.39. $C_6H_{11}NO_2S_2$ requires C, 37.28; H, 5.73; N, 7.24; S, 33.17]; ν_{max} (Neat) 1579, 1751 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.43 (s, 3H), 2.56 (s, 3H), 3.75 (s, 3H), 4.24 (s, 2H); δ_C (50.3 MHz, $CDCl_3$) 14.18, 14.51, 51.42, 53.73, 162.79, 170.07; MS (*m/z*): 193 (M^+).

4.7.6. *N*-[Bis(methylthio)methylene] glycine ethyl ester (22f). Pale yellow oil; yield 76%; [found: C, 40.26; H, 6.25; N, 6.87; S, 30.76. $C_7H_{13}NO_2S_2$ requires C, 40.55; H, 6.32; N, 6.75; S, 30.93]; ν_{max} (Neat) 1579, 1751 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.28 (t, *J*=7.3 Hz, 3H), 2.44 (s, 3H), 2.56 (s, 3H), 4.20 (q, *J* =7.3 Hz, 2H), 4.22 (s, 3H); δ_C (50.3 MHz, $CDCl_3$) 13.52, 13.85, 14.14, 53.51, 60.05, 162.24, 169.23; MS (*m/z*): 207 (M^+).

4.7.7. *N*-[Bis(methylthio)methylene] alanine methyl ester (22g). Pale yellow oil; yield 74%; [found: C, 40.31; H, 6.59; N, 6.78; S, 30.81. $C_7H_{13}NO_2S_2$ requires C, 40.55; H, 6.32; N, 6.75; S, 30.93]; ν_{max} (Neat) 1573, 1745 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.40 (d, *J*=6.8 Hz, 3H), 2.40 (s, 3H), 2.55 (s, 3H), 3.72 (s, 3H), 4.50 (q, *J*=6.8 Hz, 1H); δ_C (50.3 MHz, $CDCl_3$) 14.14, 14.36, 18.04, 51.38, 59.50, 160.70, 172.35; MS (*m/z*): 207 (M^+).

4.8. General procedure for the preparation of 4-keto protected β-lactams (23a–j)

A similar general procedure, as for compounds **5a**,**b** and **7a–c**, was used for the synthesis of β-lactams (**23a–j**) starting from the acids **1** and imines **22**.

4.8.1. 4,4-Bis-methylsufanyl-3-phenoxy-1-phenylazetidin-2-one (23a). White solid; yield 68%; mp 142°C; [found: C, 61.92; H, 5.40; N, 4.29; S, 19.10. $C_{17}H_{17}NO_2S_2$ requires C, 61.61; H, 5.17; N, 4.23; S, 19.35]; ν_{max} ($CHCl_3$) 1766 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.20 (s, 3H), 2.23 (s, 3H), 5.49 (s, 1H), 7.05–7.50 (m, 8H), 8.00 (d, *J*=8.3 Hz, 2H); δ_C (50.3 MHz, $CDCl_3$), 17.32, 18.23, 114.87, 119.72, 122.96, 124.28, 128.73, 129.83, 137.22, 140.60, 141.04, 156.0, 159.57; MS (*m/z*): 331(M^+).

4.8.2. 1-Benzyl-4,4-bis-methylsulfanyl-3-phenoxyazetidin-2-one (23b). White crystalline solid; yield 65%; mp 79–80°C (Lit.[23] mp 78–79°C); [found: C, 62.43; H, 5.60; N, 4.12; S, 18.36. $C_{18}H_{19}NO_2S_2$ requires C, 62.58; H, 5.54; N, 4.05; S, 18.56]; ν_{max} ($CHCl_3$) 1770 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.00 (s, 6H), 4.50 (q, *J*=15.2 Hz, 2H), 5.33 (s, 1H), 7.05–7.60 (m, 10H); δ_C (50.3 MHz, $CDCl_3$) 23.16, 24.13, 54.01, 91.16, 98.94, 126.37, 133.09, 138.31, 138.95, 139.32, 139.93, 145.69, 167.55, 173.65; MS (*m/z*): 330 (M^+-15).

4.8.3. 1-(4-Methoxyphenyl)-4,4-bis-methylsulfanyl-3-phenoxyazetidin-2-one (23c). White crystalline solid; yield 66%; mp 147–149°C (Lit.[23] mp 148–149°C); [found: C, 59.59; H, 5.56; N, 3.83; S, 17.53. $C_{18}H_{19}NO_3S_2$ requires C, 59.81; H, 5.30; N, 3.87; S, 17.74]; ν_{max} ($CHCl_3$) 1760 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.20 (s, 3H), 2.22 (s, 3H), 3.83 (s, 3H), 5.46 (s, 1H), 6.95–7.90 (m, 9H); δ_C (50.3 MHz, $CDCl_3$) 12.75, 14.18, 55.35, 79.61, 88.21, 114.38, 115.96, 120.23, 122.73, 128.83, 129.56, 157.13, 157.39, 160.59; MS (*m/z*): 361 (M^+).

4.8.4. (2,2-Bis-methylsulfanyl-4-oxo-3-phenoxy-1-yl)-acetic acid methyl ester (23d). White crystalline solid; yield 64%; mp 93–94°C; [found: C, 51.20; H, 5.34; N, 4.36; S, 19.36. $C_{14}H_{17}NO_4S_2$ requires C, 51.36; H, 5.23; N, 4.28; S, 19.58]; ν_{max} ($CHCl_3$) 1755, 1782 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.21 (s, 3H), 2.33 (s, 3H), 3.81 (s, 3H), 4.11 (dd, *J*=17.6 Hz, 2H), 5.41 (s, 1H), 7.05–7.40 (m, 5H); δ_C (50.3 MHz, $CDCl_3$) 12.72, 13.79, 40.25, 61.68, 80.25, 87.34, 115.61, 122.59, 129.43, 156.78, 162.95, 166.74; MS (*m/z*): 327 (M^+).

4.8.5. (2,2-Bis-methylsufanyl-4-oxo-3-phenoxy-1-yl)-acetic acid ethyl ester (23e). White crystalline solid; yield 62%; mp 99–100°C (Lit.[23] mp 100–101°C); [found: C, 52.53; H, 5.74; N, 4.05; S, 18.92. $C_{15}H_{19}NO_4S_2$ requires C, 52.77; H, 5.61; N, 4.10; S, 18.78]; ν_{max} ($CHCl_3$) 1749, 1780 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.32 (t, *J*=7.3 Hz, 3H),

2.20 (s, 3H), 2.33 (s, 3H), 4.00 (dd, J=17.6 Hz, 2H), 4.25 (q, J=7.3 Hz, 2H), 5.41 (s, 1H), 7.05–7.40 (m, 5H,); δ_C (50.3 MHz, $CDCl_3$) 12.76, 13.86, 40.29, 61.76, 80.28, 87.34, 115.61, 122.63, 129.46, 156.78, 162.95, 166.81; MS (m/z): 341 (M^+).

4.8.6. (2,2-Bis-methylsulfanyl-4-oxo-3-phenoxy-1-yl)-α-methylacetic acid methyl ester (23f). Pale yellow oil; yield 61%; [found: C, 52.90; H, 5.60; N, 4.10; S, 18.43 $C_{15}H_{19}NO_4S_2$ requires C, 52.76; H, 5.61; N, 4.10; S, 18.78]; ν_{max} ($CHCl_3$) 1747, 1776 cm^{-1}; δ_H (200 MHz, $CDCl_3$) (Mixture of two diastereomers) 1.75 and 1.80 (2 d, J=7.4, 7.8 Hz, 3H), 2.22, 2.31, 2.27 and 2.30 (4 s, 6H), 3.81 (s, 3H), 4.10 and 4.20 (2 q, J=7.4, 7.8 Hz, 2H), 5.32 and 5.36 (2 s, 1H), 7.05–7.40 (m, 5H); δ_C (50.3 MHz, $CDCl_3$) 13.79, 15.18, 17.91, 50.10, 52.46, 80.39, 88.22, 114.98, 115.79, 122.59, 129.39, 162.33, 169.9; MS (m/z): 341 (M^+).

4.8.7. (3-Methoxy-2,2-bis-methylsulfanyl-4-oxo-azetidin-1-yl)acetic acid methyl ester (23g). Pale yellow oil; yield 62%; [found: C, 40.60; H, 5.69; N, 5.28; S, 24.16. $C_9H_{15}NO_4S_2$ requires C, 40.74; H, 5.69; N, 5.28; S, 24.17]; ν_{max} (Neat) 1755, 1778 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.18 (s, 3H), 2.24 (s, 3H), 3.63 (s, 3H), 3.76 (s, 3H), 4.00 (dd, J=17.6 Hz, 2H), 4.67 (s, 1H); δ_C (50.3 MHz, $CDCl_3$) 16.10, 17.94, 40.66, 51.91, 58.48, 91.53, 149.09, 162.47, 169.82; MS (m/z): 265 (M^+).

4.8.8. (3-Methoxy-2,2-bis-methylsulfanyl-4-oxo-azetidin-1-yl)acetic acid ethyl ester (23h). Colourless oil; yield 60%; [found: C, 42.76; H, 6.32; N, 5.20; S, 23.11. $C_{10}H_{17}NO_4S_2$ requires C, 42.99; H, 6.13; N, 5.01; S, 22.95]; ν_{max} (Neat) 1747, 1782 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.28 (t, J=7.3 Hz, 3H), 2.18 (s, 3H), 2.25 (s, 3H), 3.64 (s, 3H), 4.00 (dd, J=17.5 Hz, 2H), 4.20 (q, J=7.3 Hz, 2H), 4.67 (s, 1H); δ_C (75.4 MHz, $CDCl_3$) 16.17, 18.04, 40.74, 51.94, 58.57, 80.08, 91.77, 149.03, 162.45, 169.81; MS (m/z): 279 (M^+).

4.8.9. 3-Phthalimido-4,4-bis-methylsulfanyl-1-propyl-azetidin-2-one (23i). White crystalline solid; yield 58%; mp 98–100°C; [found: C, 54.96; H, 5.05; N, 8.08; S, 18.01. $C_{16}H_{18}N_2O_3S_2$ requires C, 54.84; H, 5.18; N, 7.99; S, 18.29]; ν_{max} (Nujol) 1728, 1774 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.06 (t, J=7.4 Hz, 3H), 1.80 (m, 2H), 2.11 (s, 3H), 2.23 (s, 3H), 3.30 (m, 2H), 5.43 (s, 1H), 7.70–7.90 (m, 4H); δ_C (50.3 MHz, $CDCl_3$) 11.43, 13.30, 13.57, 21.62, 42.68, 65.84, 81.20, 123.58, 131.19, 134.35, 160.97, 166.30; MS (m/z): 335 (M^+-15).

4.8.10. [3-Phthalimido-2,2-bis-methylsulfanyl-4-oxo-azetidin-1-yl]-acetic acid ethyl ester (23j). White crystalline solid; yield 55%; mp 112–113°C; [found: C, 51.84; H, 4.91; N, 6.80; S, 15.93 $C_{17}H_{18}N_2O_5S_2$ requires C, 51.76; H, 4.60; N, 7.10; S, 16.26]; ν_{max} ($CHCl_3$) 1778, 1787 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.32 (t, J=7.3 Hz, 3H), 2.09 (s, 3H), 2.30 (s, 3H), 4.10 (dd, J=17.5 Hz, 2H), 4.25 (q, J=7.3 Hz, 2H), 5.57 (s, 1H), 7.70–8.00 (m, 4H); δ_C (50.3 MHz, $CDCl_3$) 12.68, 38.78, 40.51, 41.10, 41.50, 61.68, 65.21, 81.50, 123.14, 123.69, 131.15, 132.00, 133.76, 134.50, 160.86, 164.31, 166.22, 166.81, 167.80; MS (m/z): 394 (M^+).

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References

1. Cotarca, L.; Delogu, P.; Nardelli, A.; Sunjic, V. *Synthesis* **1996**, 553–576.
2. (a) Jayaraman, M.; Deshmukh, A. R. A. S.; Bhawal, B. M. *Synlett* **1992**, 749–750. (b) Jayaraman, M.; Nandi, M.; Sathe, K. M.; Deshmukh, A. R. A. S.; Bhawal, B. M. *Tetrahedron: Asymmetry* **1993**, *4*, 609–612. (c) Jayaraman, M.; Deshmukh, A. R. A. S.; Bhawal, B. M. *J. Org. Chem.* **1994**, *59*, 932–934. (d) Jayaraman, M.; Srirajan, V.; Deshmukh, A. R. A. S.; Bhawal, B. M. *Tetrahedron* **1996**, *52*, 3741–3756. (e) Karupaiyan, K.; Srirajan, V.; Deshmukh, A. R. A. S.; Bhawal, B. M. *Tetrahedron Lett.* **1997**, *38*, 4281–4284.
3. (a) Srirajan, V.; Deshmukh, A. R. A. S.; Bhawal, B. M. *Tetrahedron* **1996**, *52*, 5585–5590. (b) Jayaraman, M.; Puranik, V. G.; Bhawal, B. M. *Tetrahedron* **1996**, *52*, 9005–9016. (c) Jayaraman, M.; Deshmukh, A. R. A. S.; Bhawal, B. M. *Tetrahedron* **1996**, *52*, 8989–9004. (d) Srirajan, V.; Deshmukh, A. R. A. S.; Puranik, V. G.; Bhawal, B. M. *Tetrahedron: Asymmetry* **1996**, *7*, 2733–2738.
4. Krishnaswamy, D.; Bhawal, B. M.; Deshmukh, A. R. A. S. *Tetrahedron Lett.* **2000**, *41*, 417–419.
5. Georg, G. I.; Ravikumar, V. In *The Organic Chemistry of β-lactams*, Georg, G. I., Ed.; VCH: New York, 1993; p. 295 and references cited therein.
6. (a) Manhas, M. S.; Amin, S. G.; Bose, A. K. *Heterocycles* **1976**, *5*, 669. (b) Carroll, R. D.; Reed, L. L. *Tetrahedron Lett.* **1975**, 3435–3438. (c) Skiles, J. W.; McNeil, D. *Tetrahedron Lett.* **1990**, *31*, 7277–7280.
7. Bose, A. K.; Manhas, M. S.; Amin, S. G.; Kapur, J. C.; Kreder, J.; Mukkavilli, L.; Ram, B.; Vencent, J. E. *Tetrahedron Lett.* **1979**, 2771–2774.
8. Bose, A. K.; Kapur, J. C.; Sharma, S. D.; Manhas, M. S. *Tetrahedron Lett.* **1973**, 2319–2320.
9. Miyake, M.; Tokutake, N.; Kirisawa, M. *Synthesis* **1983**, 833–835.
10. (a) Cossio, F. P.; Lecea, B.; Palomo, C. *J. Chem. Soc., Chem. Commun.* **1987**, 1743–1744. (b) Arrieta, A.; Lecea, B.; Cossio, F. P.; Palomo, C. *J. Org. Chem.* **1988**, *53*, 3784–3791. (c) Manhas, M. S.; Lal, B.; Amin, S. G.; Bose, A. K. *Synth. Commun.* **1976**, *6*, 435–441. (d) Shridhar, D. R.; Ram, B.; Narayana, V. L. *Synthesis* **1982**, 63–65. (e) Cossio, F. P.; Ganboa, I.; Garcia, J. M.; Lecea, B.; Palomo, C. *Tetrahedron Lett.* **1987**, *28*, 1945–1948.
11. Georg, G. I.; Mashava, P. M.; Guan, X. *Tetrahedron Lett.* **1991**, *32*, 581–584.
12. Manhas, M. S.; Bose, A. K.; Khajavi, M. S. *Synthesis* **1981**, 209–211.
13. Dane, E.; Dress, F.; Konrad, P.; Dockner, T. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 658.
14. Srirajan, V.; Puranik, V. G.; Deshmukh, A. R. A. S.; Bhawal, B. M. *Tetrahedron* **1996**, *52*, 5579–5584.
15. Evans, D. A.; Sjogren, E. B. *Tetrahedron Lett.* **1985**, *26*, 3783–3786.
16. Shaha, S. C.; Joshi, G. D.; Pai, P. P.; Deshmukh, A. R. A. S.; Kulkarni, G. H. *Chem. Ind.* **1989**, *17*, 568.
17. Kropp, P. J. *J. Am. Chem. Soc.* **1966**, *88*, 4926–4934.

18. Bates, G. S.; Ramaswamy, S. *Can. J. Chem.* **1980**, *58*, 716–722.
19. Hoppe, D.; Beckmann, L. *Leibigs Ann. Chem.* **1979**, 2066–2075.
20. Ahluwalia, V. K.; Mallika, N.; Singh, R.; Mehta, V. D. *J. Indian Chem. Soc.* **1989**, *66*, 200–201.
21. Cossio, F. P.; Ganboa, I.; Garcia, J. M.; Lecea, B.; Palomo, C. *Tetrahedron Lett.* **1987**, *28*, 1945–1948.
22. Bellus, D. *Helv. Chim. Acta* **1975**, *58*, 2509–2511.
23. Bari, S. S.; Trehan, I. R.; Sharma, A. K.; Manhas, M. S. *Synthesis* **1992**, 439–442.