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Stereoselective synthesis of 3-alkylidene/alkylazetidin-2-ones from azetidin-2,3-diones

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Abstract—Azetidin-2,3-diones have been used as synthons for the synthesis of C-3 alkylidene/alkylazetidin-2-ones. Some of the 3-alkylazetidin-2-ones are well known for their cholesterol absorption inhibitor activity. A regio and stereoselective Grignard reaction on a keto group followed by dehydration using PPh_3/CCl_4 reagent is a key step in this synthesis. Hydrogenation of the 3-alkylideneazetidin-2-ones provided stereoselectively *cis*-3-alkylazetidin-2-ones in very good yields.

1. Introduction

The β-lactam skeleton is the key structural unit of the most widely employed class of antibacterial agents, the β-lactam antibiotics.[1] The constant need for new drugs displaying broader antibacterial activity and the necessity for new β-lactam antibiotics to combat the microorganisms that have built up resistance against the most traditional drugs,[2] have maintained the interest of organic chemists in β-lactams for decades. The major cause of bacterial resistance to the antibiotics is a hydrolytic cleavage of the β-lactam ring by β-lactamase enzyme. As a consequence, several stable new β-lactams as well as β-lactamase inhibitors have been developed. Apart from the antibacterial agents,[1–3] β-lactams are also being increasingly used as synthons for the synthesis of a variety of pharmaceutically useful products.[4] An important class of compounds, which act as hydrolytic deactivators of β-lactamase enzyme, contains 3-alkylidene-β-lactam subunit (**1**). Also, the discovery of cholesterol absorption inhibition property associated with *trans*-3-alkylazetidin-2-ones[5] **2** and **3** (Fig. 1) renewed the interest in the synthesis of C-3-alkyl-substituted-β-lactams. Large number of β-lactams has been synthesized to study the structure activity relationship (SAR) in cholesterol absorption inhibitors.[6] In most of the synthesis, the azetidinone ring is constructed either by enolate–imine cyclocondensation[5a,b,6a,7] of appropriately substituted esters and imines or by a Staudinger ketene–imine cycloaddition reaction.[7i,8] The cholesterol absorption inhibitory property is normally associated with *trans*-azetidin-2-ones,[5] however, in some cases it has also been shown that C-3-alkyl-substituted *cis*-azetidin-2-ones are better cholesterol absorption inhibitors (Fig. 1).[9] Although several syntheses are described in literature,[7,8,10] there are very few reports wherein a suitably substituted azetidin-2-one itself has been used as a synthon[11] for the preparation of desired C-3-substituted-β-lactams.

2. Results and discussion

As a part of our ongoing research program on the application of azetidin-2-ones as synthons,[12] we herein report the synthesis of various 3-alkylidene/alkyl substituted azetidin-2-ones from azetidin-2,3-diones, a common starting material. In a recent publication[13] we have shown that Grignard reagent adds stereoselectively to a ketone in azetidin-2,3-dione (**4**) to give 3-alkyl-3-hydroxy-β-lactam. The approach of the Grignard reagent is controlled by the C-4 substituent on the ring, giving rise to trans stereochemistry in the product. The reductive removal of the corresponding xanthate has provided the *cis*-3-alkylazetidin-2-ones.

As a part of this project we were interested in developing a simple synthetic protocol to make large number of 3-alkylidene and 3-alkyl-β-lactams. Herein we report the syntheses of 3-alkylidene and 3-alkylazetidin-2-ones from the azetidin-2,3-diones **4**. The 3-alkyl-3-hydroxy-β-lactams (**5**), which are readily obtained from the Grignard reaction on azetidin-2,3-diones, could be easily converted to the corresponding 3-alkyl-3-chloro-β-lactams (**6**). Further transformation of chloro-β-lactams **6** to α-alkylidene-β-lactams **7** and **8** via dehydrohalogenation or direct reductive removal

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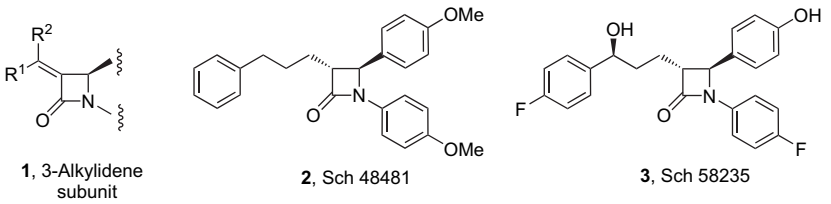


Figure 1. 3-Alkylidene/3-alkylazetidin-2-ones.

of the halogen would provide 3-alkyl-β-lactams **9**. Similarly catalytic hydrogenation of **7** and **8** would also provide 3-alkyl-β-lactams **9** (Scheme 1). With this idea in mind, we prepared 3-alkyl-3-hydroxy-β-lactams (**5**) from azetidin-2,3-diones **4**.

The starting azetidin-2,3-diones **4** could be easily obtained in very good yields by oxidation of the corresponding 3-hydroxy-β-lactam **13**, which in turn can be obtained from 3-acetoxy-β-lactams **12**. Since enantiomerically pure 3-hydroxy-β-lactams are also available,[14] the corresponding azetidindiones can also be prepared by oxidation of the hydroxyl group. However, to establish the synthetic protocol we have used racemic β-lactams for our work.

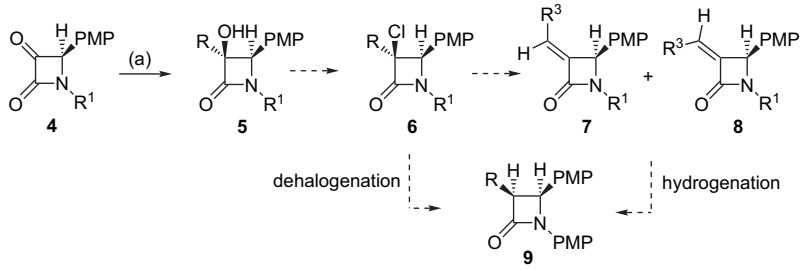
Staudinger cycloaddition of acetoxyacetyl chloride **10** with imines **11** gave 3-acetoxy-azetidin-2-ones **12** in 62–65% yields, which on careful hydrolysis with saturated sodium bicarbonate in methanol gave the corresponding 3-hydroxy-β-lactams **13** in quantitative yields. Oxidation of the hydroxyl group was carried out by a known procedure using phosphorous pentoxide and dimethyl sulfoxide[15] to give the desired azetidin-2,3-diones **4** (Scheme 2). The Grignard reagent, prepared from the corresponding alkyl or aryl halide, on reaction with diones **4** gave the addition products **5** in moderate to good yields (Table 1). A single isomer was formed indicating that the addition occurred exclusively from the side opposite to the C-4 substituent on the azetidinone ring. Slightly lower yields of the 3-isopropyl-3-hydroxy-β-lactams were obtained with the bulkier Grignard reagent *i*-PrMgBr.

Table 1. 3-Alkyl-3-hydroxyazetidin-2-ones **5a–m**

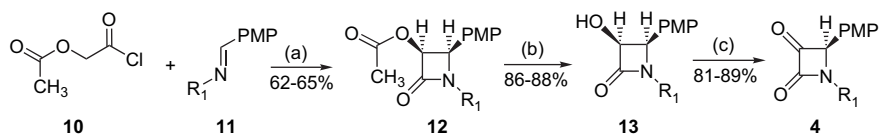
Entry	Compound	R	R^1	Yield[b] (%)
1	**5a**	*n*-Butyl	PMP[a]	55
2	**5b**	*n*-Butyl	Ph	60
3	**5c**	*n*-Octyl	PMP	57
4	**5d**	*n*-Octyl	Ph	62
5	**5e**	*n*-Heptyl	PMP	62
6	**5f**	*n*-Heptyl	Ph	58
7	**5g**	*n*-Propyl	PMP	69
8	**5h**	*n*-Propyl	Ph	62
9	**5i**	*iso*-Propyl	PMP	49
10	**5j**	*iso*-Propyl	Ph	52
11	**5k**	3-Phenylpropyl	PMP	61
12	**5l**	3-Phenylpropyl	Ph	62
13	**5m**	Ph	PMP	67

[a] PMP=4-methoxyphenyl.
[b] Isolated yields.

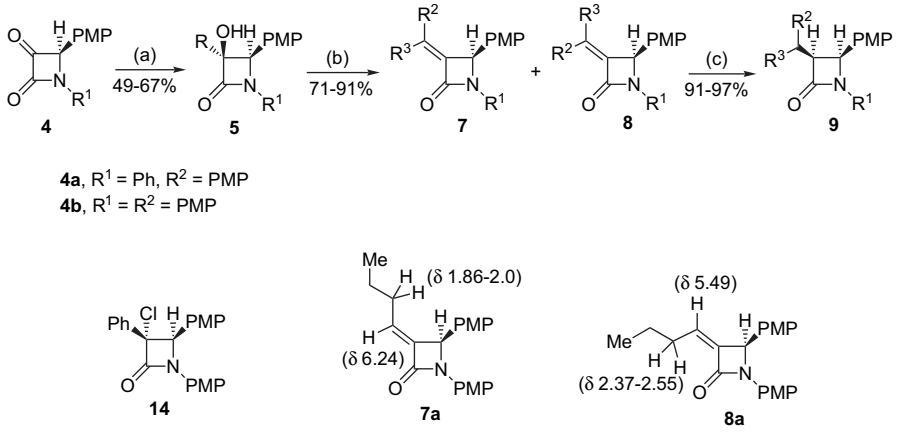
3-Butyl-3-hydroxyazetidin-2-one (**5a**) on reaction with PPh_3 in refluxing CCl_4 did not give the expected 3-chloro-β-lactam **6a**. However, the dehydration occurred and a mixture of *E* and *Z*-olefins **7a** and **8a** was obtained in very good yield (Scheme 3). Although, dehydration of oximes,[16] and other intermolecular dehydration with the PPh_3/CCl_4 reagent are well known,[17] there are some examples of olefin formation via an elimination of water from the corresponding hydroxy compounds.[18] The separation of both isomers from the mixture was achieved by flash column chromatography. The structure of the major compound was established as *E*-isomer (**7a**) on the basis of ^{1}H NMR spectrum. The downfield chemical shift of vinyl proton (δ 6.24, dt, J=1.4 and 7.3 Hz, 1H) compared to the corresponding *Z*-isomer (**8a**)



Scheme 1. Reagents and conditions: (a) RMgBr, THF, 0 °C to rt, 4 h.



Scheme 2. Reagents and conditions: (a) Et_3N, CH_2Cl_2, 0 °C to rt, 12 h; (b) $NaHCO_3$, Na_2CO_3, MeOH/H_2O, rt, 7 h; and (c) P_2O_5, DMSO, rt, 24 h.



Scheme 3. Reagents and conditions: (a) RMgBr, THF, 0 °C to rt, 4 h; (b) PPh_3/CCl_4, reflux, 12 h; and (c) H_2, Pt/C (10%), EtOAc, 12 h.

(δ 5.49, dt, J=1.0 and 7.8 Hz, 1H) was observed. This downfield shift of the vinyl proton is due to an anisotropic deshielding effect of the β-lactam carbonyl group. A similar deshielding effect was observed on the allylic methylene protons in *Z*-isomer **8b** (*Z*-isomer **8b**, δ 2.37–2.55, m, 2H; *E*-isomer **8a**, δ 1.86–2.0, m, 2H). The generality of the reaction was established by preparing several 3-alkylidene-β-lactams (Table 2). Both the isomers were separated by column chromatography and in all the cases *E*-isomer was found to be the predominant product. Single pure compounds (**7i** and **7j**) were obtained by the dehydration of 3-isopropyl-3-hydroxyazetidin-2-ones (**5i** and **5j**). 3-Phenyl-3-hydroxyazetidin-2-one **5m** under similar reaction conditions gave 3-phenyl-3-chloro azetidin-2-one **14** in 92% yield, as there was no β-H available in the side chain for elimination reaction.

A single product **9a** was expected from the catalytic hydrogenation of a mixture of olefins (**7a** and **8a**) using Pd/C. However, a partial isomerization of *cis*-β-lactam to a more stable trans-isomer was observed (cis/trans=70:30). The isomerization phenomenon was considerably suppressed (cis/trans=97:3) when Pt/C catalyst was used, and a single major *cis*-β-lactam **9a** was obtained by the hydrogenation of *E*/*Z*-mixture (**7a** and **8a**). Several 3-alkylidene-β-lactams were prepared (Table 2) and they were further hydrogenated to the corresponding *cis*-3-alkyl-β-lactams using Pt/C as the catalyst (Table 3). In most of the cases 3–5% of trans-isomer was detected from the ^{1}H NMR spectrum. The biological importance of both 3-alkylidene and 3-alkyl-β-lactams is well known. 3-Alkylidene-β-lactams are known for the β-lactamase inhibition activity, while 3-alkyl-β-lactams for their cholesterol absorption inhibition activity.

Table 2. 3-Alkylideneazetidin-2-ones **7a–l** and **8a–l**

Compounds **7** and **8**	R^1	R^2	R^3	Yield[a] (%)	*E*/*Z* (**7**:**8**)
a	PMP	*n*-Propyl	H	90	72:28
b	Ph	*n*-Propyl	H	90	71:29
c	PMP	*n*-Heptyl	H	89	71:29
d	Ph	*n*-Heptyl	H	88	66:34
e	PMP	*n*-Hexyl	H	94	71:29
f	Ph	*n*-Hexyl	H	89	69:31
g	PMP	Ethyl	H	85	72:28
h	Ph	Ethyl	H	86	69:31
i	PMP	Me	Me	71	—
j	Ph	Me	Me	70	—
k	PMP	2-Phenylethyl	H	91	70:30
l	Ph	2-Phenylethyl	H	89	70:30

[a] Total yield.

Table 3. 3-Alkylazetidin-2-ones **9a–l**

Compound	R^1	R^2	R^3	Yield[a] (%)	Cis/trans
9a	PMP	*n*-Propyl	H	92	98:2
9b	Ph	*n*-Propyl	H	95	96:4
9c	PMP	*n*-Heptyl	H	94	97:3
9d	Ph	*n*-Heptyl	H	91	97:3
9e	PMP	*n*-Hexyl	H	94	97:3
9f	Ph	*n*-Hexyl	H	95	98:2
9g	PMP	Ethyl	H	97	96:4
9h	Ph	Me	H	94	95:5
9i	PMP	Me	Me	92	95:5
9j	Ph	Me	Me	95	97:3
9k	PMP	2-Phenylethyl	H	94	97:3
9l	Ph	2-Phenylethyl	H	95	96:4

[a] Isolated yields.

3. Conclusion

In conclusion, a simple method for the synthesis of 3-alkylidene/alkylazetidin-2-ones from azetidin-2,3-dione is developed. One of the 3-alkylazetidin-2-ones, **9k** is well known as cholesterol absorption inhibitor. A mild and an efficient dehydration of 3-alkyl-3-hydroxyazetidin-2-ones by PPh_3/CCl_4 reagent is a key step in this synthesis.

4. Experimental

4.1. General

^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solutions on Brüker AC 200 and AV 400 spectrometers, and chemical shifts are reported in parts per million downfield from tetramethylsilane for ^{1}H 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 are uncorrected. The

microanalyses were performed on a Carlo-Erba, CHNS-O EA 1108 elemental analyzer. Mass spectra were recorded on API QSTAR PULSAR using electron spray ionization (ESI) method.

4.1.1. 3-Acetoxy-1,4-bis-(4-methoxyphenyl)azetidin-2-one (12a). A solution of acetoxyacetyl chloride (6.44 mL, 60 mmol) in anhydrous dichloromethane (20 mL) was added slowly to a mixture of imine (9.64 g, 40 mmol) and Et_3N (19.44 mL, 140 mmol) in anhydrous dichloromethane (60 mL) at 0 °C. After completion of the addition, the reaction mixture was allowed to warm up to room temperature and stirred for additional 18 h. The reaction mixture was then washed with water (3×75 mL), saturated $NaHCO_3$ (3×75 mL), and brine (75 mL). The organic layer was separated, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to give the crude product, which was purified by column chromatography (silica gel 60–120 mesh) using Pet ether/ethyl acetate (83:17) to afford compound **12a** (8.49 g, 62%) as a white solid, mp 152–154 °C [Found: C, 66.93; H, 5.75; N, 4.08; $C_{19}H_{19}NO_5$: requires C, 66.85; H, 5.61; N, 4.10%]; R_f (18% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$) 1753 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.73 (s, 3H, CO–CH_3), 3.75 (s, 3H, Ar–OCH_3), 3.80 (s, 3H, Ar–OCH_3), 5.27 (d, J=5.1 Hz, 1H, C4*H*), 5.87 (d, J=5.1 Hz, 1H, C3*H*), 6.77 (d, J=9.0 Hz, 2H, Ar), 6.86 (d, J=9.0 Hz, 1H, Ar), 7.22 (d, J=9.0 Hz, 2H, Ar), 7.25 (d, J=8.5 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 19.8, 55.2, 55.3, 61.01, 76.8, 113.8, 114.3, 118.8, 123.9, 129.2, 130.2, 156.5, 159.8, 161.3, 169.2; MS (*m*/*z*): 342 (M+1).

4.1.2. 3-Acetoxy-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (12b). Yield 65%; white solid, mp 164–166 °C [Found: C, 69.53; H, 5.45; N, 4.48; $C_{18}H_{17}NO_4$: requires C, 69.44; H, 5.50; N, 4.50%]; R_f (18% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1751 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.68 (s, 3H, COCH_3), 3.76 (s, 3H, Ar–OCH_3), 5.35 (d, J=5.1 Hz, 1H, C4*H*), 5.95 (d, J=5.1 Hz, 1H, C3*H*), 6.82 (d, J=9.00 Hz, 2H, Ar), 7.28–7.35 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 20.3, 55.9, 61.9, 76.3, 114.9, 119.3, 128.9, 129.3, 130.8, 132.8, 157.1, 161.8, 169.7; MS (*m*/*z*): 312 (M+1).

4.1.3. 3-Hydroxy-1,4-bis(4-methoxyphenyl)azetidin-2-one (13a). To a solution of 3-acetoxy-β-lactam **12a** (12.3 g, 36 mmol) in methanol (105 mL) was added a saturated solution of sodium bicarbonate (53 mL) followed by solid sodium carbonate (1.93 g, 18.25 mmol). The reaction mixture was stirred at room temperature for 12 h. After the reaction was complete (monitored by TLC), methanol was evaporated under reduced pressure and the residue was diluted with dichloromethane. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2 (3×50 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated in vacuo to furnish the crude reaction mixture, which on purification by silica gel column chromatography (60–120 mesh) using 30% ethyl acetate/Pet ether yielded 3-hydroxy-1-(4-methoxyphenyl)-4-phenylazetidin-2-one **13a** (10.6 g, 86%) as a white solid, mp 146–149 °C [Found: C, 68.32; H, 5.80; N, 4.61; $C_{17}H_{17}NO_4$: requires C, 68.22; H, 5.73; N, 4.68%]; R_f (40% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 3353, 1708 cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 2.15 (br s, 1H, –O*H*), 3.76 (s, 3H, Ar–OCH_3), 3.81 (s, 3H, Ar–OCH_3), 5.05 (d, J=5.7 Hz, 1H, –C4*H*), 5.13 (d, J=5.7 Hz, 1H, C3*H*), 6.70 (d, J=9.4 Hz, 2H, Ar), 6.84 (d, J=8.6 Hz, 2H, Ar), 7.15 (d, J=8.5 Hz, 2H, Ar), 7.24 (d, J=9.4 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 55, 55.2, 61.7, 76.7, 113.6, 114.4, 118.2, 126.5, 129.3, 130.8, 155.5, 159, 166.4; MS (*m*/*z*): 300 (M+1).

4.1.4. 3-Hydroxy-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (13b). Yield 88%; white solid, mp 215 °C [Found: C, 71.32; H, 5.80; N, 5.08; $C_{16}H_{15}NO_3$: requires C, 71.36; H, 5.61; N, 5.20%]; R_f (30% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$) 3353, 1708 cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 3.76 (s, 3H, Ar–OCH_3), 4.50 (br s, 1H, –O*H*), 5.09 (d, J=5.0 Hz, 1H, *C*4*H*), 5.12 (d, J=5.0 Hz, 1H, *C*3*H*), 6.71 (d, J=9.1 Hz, 2H, Ar), 7.19–7.39 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, DMSO-d_6): δ 55.4, 62.1, 77.8, 114.6, 118.2, 127.9, 128.2, 128.4, 131.0, 135.1, 155.8, 166.4; MS (*m*/*z*): 270 (M+1).

4.1.5. 1,4-Bis(4-methoxyphenyl)azetidin-2,3-dione (4a). To anhydrous P_2O_5 (0.98 g, 3.5 mmol calculated for P_4O_{10}) was added dry dimethyl sulfoxide (15 mL) at room temperature. The suspension was stirred for 5 min at the same temperature and then the corresponding 3-hydroxy-β-lactam (1.5 g, 5 mmol) was added in one portion with vigorous stirring. The reaction mixture was then stirred for additional 24 h. After the reaction was over, the mixture was slowly poured into cold aqueous $NaHCO_3$ (50 mL) and extracted with ethyl acetate. The organic layer was washed with brine (3×50 mL) and dried over sodium sulfate. Evaporation of the solvent under reduced pressure and then column chromatography (60–120 mesh silica gel, 20% ethyl acetate/Pet ether) provided the corresponding 3-keto-β-lactam (1.32 g, 89%); yellow solid, mp 144 °C [Found: C, 68.85; H, 5.13; N, 4.67; $C_{17}H_{15}NO_4$: requires C, 68.68; H, 5.08; N, 4.71%]; R_f (20% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1832, 1809, 1753 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 3.79 (s, 3H, Ar–OCH_3), 3.80 (s, 3H), 3.75 (s, 3H, Ar–OCH_3), 5.52 (s, 1H, C4*H*), 6.90 (d, J=9.0 Hz, 2H, Ar), 7.20 (d, J=8.6 Hz, 2H, Ar), 7.25 (d, J=8.6 Hz, 2H, Ar), 7.46 (d, J=9.0 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 55.3, 55.4, 74.4, 114.6, 114.9, 119.7, 123.5, 127.7, 129.8, 157.8, 160.1, 160.4, 191.2; MS (*m*/*z*): 298 (M+1).

4.1.6. 1-(4-Methoxyphenyl)-4-phenylazetidin-2,3-dione (4b). Yield 81%; yellow solid, mp 127 °C [Found: C, 71.86; H, 5.11; N, 5.27; $C_{16}H_{13}NO_3$: requires C, 71.90; H, 4.90; N, 5.24%]; R_f (40% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1832, 1809, 1753 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 3.75 (s, 3H, Ar–OCH_3), 5.52 (s, 1H, C4*H*), 6.90 (d, J=9.0 Hz, 2H, Ar), 7.24–7.38 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 55.3, 74.4, 114.6, 114.8, 119.7, 123.5, 127.8, 129.9, 157.8, 160.4, 191.2; MS (*m*/*z*): 268 (M+1).

4.1.7. 3-Butyl-3-hydroxy-1,4-bis(4-methoxyphenyl)azetidin-2-one (5a). To a solution of dione **4a** (0.891 g, 3 mmol) in dry THF (10 mL) was added a solution of *n*-butyl magnesium bromide (3.9 mmol) in dry THF at 0 °C. The mixture was stirred for 4 h at room temperature. Saturated aqueous NH_4Cl was then added and the reaction mixture was extracted with ethyl acetate (3×15 mL). The combined

organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by flash column chromatography (230–400 mesh silica gel) using 15% ethyl acetate/Pet ether to furnish compound **5a** (0.59 g, 55%) as brownish oil [Found: C, 70.98; H, 7.16; N, 3.89; $C_{21}H_{25}NO_4$: requires C, 70.96; H, 7.09; N, 3.94%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1728 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.96 (t, J=6.9 Hz, 3H, $CH_3(CH_2)_2CH_2$), 1.30–1.73 (m, 4H, $CH_3(CH_2)_2$–CH_2), 1.96–2.09 (m, 2H, $CH_3(CH_2)_2CH_2$), 3.76 (s, 3H, Ar–OCH_3), 3.81 (s, 3H, Ar–OCH_3), 4.98 (s, 1H, C4*H*), 6.79 (d, J=9.1 Hz, 2H, Ar), 6.82 (d, J=8.7 Hz, 2H, Ar), 7.22 (d, J=8.7 Hz, 2H, Ar), 7.29 (d, J=8.9 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.9, 22.9, 25.6, 35.1, 55.2, 55.4, 66.9, 85.9, 114.3, 114.5, 118.8, 125.7, 128.4, 130.6, 156.2, 159.9, 168; MS (*m*/*z*): 356 (M+1).

Following a similar procedure other 3-alkyl-3-Hydroxy-β-lactams **5b–m**, were synthesized.

4.1.8. 3-Butyl-3-hydroxy-1-(4-Methoxyphenyl)-4-phenylazetidin-2-one (5b). Yield 55%; brownish oil [Found: C, 73.50; H, 7.26; N, 4.45; $C_{20}H_{23}NO_3$: requires C, 73.82; H, 7.12; N, 4.30%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 3388, 1737 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.83 (t, J=6.9 Hz, 3H, $CH_3(CH_2)_2CH_2$), 1.25–1.76 (m, 4H, $CH_2(CH_2)_2CH_3$), 1.85–1.96 (m, 2H, $CH_3(CH_2)_2CH_2$), 3.63 (s, 3H, Ar–OCH_3), 4.90 (s, 1H, C4*H*), 6.79 (d, J=9.0 Hz, 2H, Ar), 7.22–7.37 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.9, 22.9, 25.6, 35.1, 55.2, 55.4, 66.9, 85.9, 114.3, 118.8, 127.2, 128.6, 129, 130.6, 134, 156.3, 167.9; MS (*m*/*z*): 326 (M+1).

4.1.9. 3-Octyl-3-hydroxy-1,4-bis(4-methoxyphenyl)azetidin-2-one (5c). Yield 57%; oil [Found: C, 72.96; H, 8.08; N, 3.40; requires: C, 72.98; H, 7.96; N, 3.78. $C_{25}H_{33}NO_4$: requires C, 72.96; H, 8.08; N, 3.40%]; R_f (15% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$) 3390, 1747, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.92 (t, J=6.4 Hz, 3H, $CH_3(CH_2)_6CH_2$), 1.31–1.46 (m, 12H, $CH_3(CH_2)_6$–CH_2), 2.01–2.08 (m, 2H, $CH_3(CH_2)_6CH_2$), 3.79 (s, 3H, Ar–OCH_3), 3.84 (s, 3H, Ar–OCH_3), 5.00 (s, 1H, C4*H*), 6.79 (d, J=9.1 Hz, 2H, Ar), 6.97 (d, J=8.9 Hz, 2H, Ar), 7.25 (d, J=8.7 Hz, 2H, Ar), 7.32 (d, J=9.0 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.0, 22.6, 23.6, 29.2, 29.8, 31.8, 35.3, 55.2, 55.4, 66.9, 85.9, 114.3, 114.5, 118.8, 125.7, 128.5, 130.7, 156.2, 159.8, 168.1; MS (*m*/*z*): 412 (M+1).

4.1.10. 3-Octyl-3-hydroxy-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (5d). Yield 62%; oil [Found: C, 75.62; H, 8.16; N, 3.75; $C_{24}H_{31}NO_3$: requires C, 75.56; H, 8.19; N, 3.67%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 3384, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.91 (t, J=6.7 Hz, 3H, $CH_3(CH_2)_6$–CH_2), 1.25–1.72 (m, 12H, $CH_3(CH_2)_6$–CH_2), 1.96–2.13 (m, 2H, $CH_3(CH_2)_6CH_2$), 3.78 (s, 3H, Ar–OCH_3), 5.04 (s, 1H, C4*H*), 6.81 (d, J=8.9 Hz, 2H, Ar), 7.28–7.45 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.1, 22.7, 23.7, 25.8, 29.3, 29.9, 31.9, 35.6, 55.4, 66.4, 86.2, 114.4, 118.9, 127.2, 128.7, 129.1, 130.7, 134.1, 156.4, 168; MS (*m*/*z*): 382 (M+1).

4.1.11. 3-Heptyl-3-hydroxy-1,4-bis(4-methoxyphenyl)-azetidin-2-one (5e). Yield 62%; colorless oil [Found: C, 72.78; H, 7.96; N, 3.68; $C_{24}H_{31}NO_4$: requires C, 72.52; H, 7.86; N, 3.52%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 3388, 1745, 1731 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.86 (t, J=6.4 Hz, 3H, $CH_3(CH_2)_5CH_2$), 1.20–1.54 (m, 10H, $CH_3(CH_2)_5$–CH_2), 1.89–2.02 (m, 2H, $CH_3(CH_2)_5CH_2$), 3.73 (s, 3H, Ar–OCH_3), 3.78 (s, 3H, Ar–OCH_3), 4.94 (s, 1H, C4*H*), 6.76 (d, J=9.1 Hz, 2H, Ar), 6.80 (d, J=8.9 Hz, 2H, Ar), 7.23 (d, J=8.6 Hz, 2H, Ar), 7.28 (d, J=9.0 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.0, 22.5, 28.7, 29.2, 29.7, 31.5, 35.3, 55.2, 55.3, 66.7, 85.8, 114.3, 114.5, 118.1, 125.7, 128.5, 130.7, 156.2, 159.8, 168.2; MS (*m*/*z*): 398 (M+1).

4.1.12. 3-Heptyl-3-hydroxy-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (5f). Yield 58%; thick oil [Found: C, 75.26; H, 7.56; N, 3.76; $C_{23}H_{29}NO_3$: requires C, 75.17; H, 7.95; N, 3.81%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 3390, 1747 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.89 (t, J=6.8 Hz, 3H, $CH_3(CH_2)_5CH_2$), 1.25–1.82 (m, 10H, $CH_3(CH_2)_5CH_2$), 1.87–2.03 (m, 2H, $CH_3(CH_2)_5CH_2$), 3.76 (s, 3H, Ar–OCH_3), 5.01 (s, 1H, C4*H*), 6.81 (d, J=9.1 Hz, 2H, Ar), 7.27–7.39 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.3, 22.9, 23.8, 29.3, 30.1, 31.9, 35.7, 55.6, 67.5, 86.4, 114.6, 119.1, 127.4, 129.3, 130.9, 134.3, 156.5, 168.1; MS (*m*/*z*): 368 (M+1).

4.1.13. 3-Propyl-3-hydroxy-1,4-bis(4-methoxyphenyl)-azetidin-2-one (5g). Yield 59%; thick oil [Found: C, 70.19; H, 6.87; N, 3.98; $C_{20}H_{23}NO_4$: requires C, 70.36; H, 6.79; N, 4.10%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1739 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.98 (t, J=7.2 Hz, 3H, $CH_3(CH_2)_2$), 1.53–1.62 (m, 2H, $CH_3(CH_2)$–CH_2), 1.90–1.98 (m, 2H, $CH_3CH_2CH_2$), 3.72 (s, 3H, Ar–OCH_3), 3.77 (s, 3H, Ar–OCH_3), 4.94 (s, 1H, C4*H*), 6.75 (d, J=9.1 Hz, 2H, Ar), 6.79 (d, J=8.7 Hz, 2H, Ar), 7.21 (d, J=8.7 Hz, 2H, Ar), 7.28 (d, J=9.1 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.3, 17.1, 37.5, 55.2, 55.4, 66.9, 85.9, 114.3, 114.5, 118.8, 125.7, 128.4, 130.6, 156.2, 159.9, 167.9; MS (*m*/*z*): 342 (M+1).

4.1.14. 3-Propyl-3-hydroxy-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (5h). Yield 62%; white solid, mp 144–146 °C [Found: C, 73.18; H, 6.76; N, 4.38; $C_{19}H_{21}NO_3$: requires C, 73.28; H, 6.85; N, 4.50%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$): 3461, 1739 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.03 (t, J=6.5 Hz, 3H, $CH_3(CH_2)_2$), 1.58–1.68 (m, 2H, $CH_3CH_2CH_2$), 1.96–2.07 (m, 2H, $CH_3CH_2CH_2$), 3.76 (s, 3H, Ar–OCH_3), 5.03 (s, 1H, C4*H*), 6.81 (d, J=9.1 Hz, 2H, Ar), 7.14–7.31 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.3, 17.1, 37.6, 55.4, 67.3, 86.2, 114.3, 118.8, 127.2, 128.6, 129, 130.6, 134, 156.3, 167.9; MS (*m*/*z*): 312 (M+1).

4.1.15. 3-Hydroxy-3-isopropyl-1,4-bis(4-methoxyphenyl)azetidin-2-one (5i). Yield 49%; thick oil [Found: C, 70.38; H, 6.86; N, 3.89; $C_{20}H_{23}NO_4$: requires C, 70.36; H, 6.79; N, 4.10%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 3488, 1735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.12 (d, J=7.0 Hz, 3H, $^aCH_3$–CH–$^bCH_3$), 1.20 (d, J=6.9 Hz, 3H, $^aCH_3$–CH–$^bCH_3$), 3.76 (s, 3H, Ar–OCH_3), 3.81 (s, 3H, Ar–OCH_3), 4.99 (s, 1H, C4*H*), 6.72 (d, J=9.1 Hz, 2H, Ar), 6.81 (d, J=8.9 Hz, 2H, Ar), 7.23 (d, J=8.6 Hz, 2H, Ar), 7.30 (d, J=9.2 Hz, 2H, Ar); ^{13}C NMR

(50.3 MHz, $CDCl_3$): δ 16.7, 17.1, 33.2, 55.3, 55.5, 64.9, 88.8, 114.3, 114.5, 118.8, 125.7, 128.4, 130.6, 156.2, 159.9, 167.8; MS (*m*/*z*): 342 (M+1).

4.1.16. 3-Hydroxy-3-isopropyl-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (5j). Yield 51%; white solid, mp 114–116 °C [Found: C, 73.18; H, 6.76; N, 4.38; $C_{19}H_{21}NO_3$: requires C, 73.33; H, 6.81; N, 4.50%]; R_f (35% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$): 3388, 1735 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.12 (d, *J*=7.0 Hz, 3H, $^aCH_3$–CH–$^bCH_3$), 1.20 (d, *J*=6.9 Hz, 3H, $^aCH_3$–CH–$^bCH_3$), 2.18–2.32 (m, 1H, $^aCH_3$–CH–$^bCH_3$), 3.81 (s, 3H, Ar–OCH_3), 5.01 (s, 1H, C4*H*), 6.72 (d, *J*=9.1 Hz, 2H, Ar), 7.19–7.56 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.3, 17.1, 37.6, 55.4, 67.3, 86.2, 114.3, 118.8, 127.2, 128.6, 129, 130.6, 134, 156.3, 167.9; MS (*m*/*z*): 312 (M+1).

4.1.17. 3-Hydroxy-1,4-bis-(4-methoxyphenyl)-3-(3-phenylpropyl)azetidin-2-one (5k). Yield 61%; thick oil [Found: C, 75.02; H, 6.32; N, 3.55; $C_{26}H_{27}NO_4$: requires C, 74.80; H, 6.52; N, 3.36%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 3384, 1731 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.97–2.14 (m, 4H, $PhCH_2(CH_2)_2$), 2.72 (t, *J*=6.9 Hz, 2H, $PhCH_2(CH_2)_2$), 3.80 (s, 3H, Ar–OCH_3), 3.85 (s, 3H, Ar–OCH_3), 4.98 (s, 1H, C4*H*), 6.81 (d, *J*=9.1 Hz, 2H, Ar), 6.94 (d, *J*=8.6 Hz, 2H, Ar), 7.17–7.37 (m, 9H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 25.2, 34.9, 35.9, 55.2, 55.3, 67, 85.8, 114.3, 114.5, 118.9, 125.6, 125.7, 128.3, 128.5, 130.6, 141.8, 156.3, 159.9, 168; MS (*m*/*z*): 418 (M+1).

4.1.18. 3-Hydroxy-1-(4-methoxyphenyl)-4-phenyl-3-(3-phenylpropyl)azetidin-2-one (5l). Yield 62%; thick oil [Found: C, 77.32; H, 6.52; N, 3.55; $C_{25}H_{25}NO_3$: requires C, 77.49; H, 6.50; N, 3.61%]; R_f (13% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$): 3369, 1731 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.81–2.01 (m, 4H, $PhCH_2(CH_2)_2$), 2.67 (t, *J*=7.1 Hz, 2H, $PhCH_2(CH_2)_2$), 3.71 (s, 3H, Ar–OCH_3), 4.93 (s, 1H, *C*4*H*), 6.75 (d, *J*=9.0 Hz, 2H, Ar), 7.18–7.40 (m, 12H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 25.2, 35, 35.7, 55.2, 66.99, 85.76, 114.3, 118.8, 127.2, 128.6, 129, 130.6, 134, 156.3, 167.9; MS (*m*/*z*): 388 (M+1).

4.1.19. 3-Hydroxy-1,4-bis-(4-methoxyphenyl)-3-phenylazetidin-2-one (5m). Yield 67%; white solid, mp 144–146 °C [Found: C, 73.69; H, 5.62; N, 3.85; $C_{23}H_{21}NO_4$: requires C, 73.58; H, 5.64; N, 3.73%]; R_f (14% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$) 1739 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.74 (br s, 1H, OH), 3.77 (s, 3H, Ar–OCH_3), 3.83 (s, 3H, Ar–OCH_3), 5.17 (s, 1H, C4*H*), 6.83 (d, *J*=8.7 Hz, 2H, Ar), 6.94 (d, *J*=8.6 Hz, 2H, Ar), 7.17–7.37 (m, 9H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 55.2, 55.3, 70.1, 86.6, 114.2, 114.4, 119.1, 124.9, 125.4, 128.4, 128.7, 128.8, 130.2, 138.8, 156.3, 160.0, 166.5; MS (*m*/*z*): 376 (M+1).

4.2. General procedure for dehydration of 3-butyl-3-hydroxy-1,4-bis(4-methoxyphenyl)azetidin-2-ones (7a and 8a)

A solution of alcohol **5a** (0.78 g, 2.19 mmol) and triphenylphosphine (1.14 g, 4.38 mmol) in anhydrous carbon tetrachloride (10 mL) was refluxed for 12 h. The reaction mixture was then filtered through a small pad of Celite and concentrated under reduced pressure to afford the crude product (0.67 g, 90%). The ^1H NMR of the crude product showed it to be a mixture of 3-alkylidene-β-lactams **7a** and **8a** (*E* and *Z* isomers 72:28), which were separated by flash column chromatography (Pet ether/ethyl acetate 9:1).

4.2.1. *E*-1,4-Bis-(4-methoxyphenyl)-3-butylideneazetidin-2-one (7a). Yield 72%; white solid, mp 88–89 °C [Found: C, 74.68; H, 6.88; N, 4.29; $C_{21}H_{23}NO_3$: requires C, 74.75; H, 6.87; N, 4.15%]; R_f (7% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1745 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.75 (t, *J*=7.3 Hz, 3H, =CH–$CH_2CH_2CH_3$), 1.24–1.37 (m, 2H, =CH–$CH_2CH_2CH_3$), 1.86–1.99 (m, 2H, =CH–$CH_2CH_2CH_3$), 3.77 (s, 3H, Ar–OCH_3), 3.84 (s, 3H, Ar–OCH_3), 5.38 (d, *J*=1.4 Hz, 1H, C4*H*), 6.25 (dt, *J*=1.4, 7.3 Hz, 1H, =$CH(CH_2)_2CH_3$), 6.83 (d, *J*=9.1 Hz, 2H, Ar), 6.93 (d, *J*=8.7 Hz, 2H, Ar), 7.29 (d, *J*=9.1 Hz, 2H, Ar), 7.40 (d, *J*=8.7 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.4, 21.6, 29.6, 55.3, 55.4, 62.6, 114.3, 114.4, 118.1, 127.6, 128.3, 128.8, 131.4, 142.3, 155.8, 159.8, 161.3; MS (*m*/*z*): 338 (M+1).

4.2.2. *Z*-1,4-Bis-(4-methoxyphenyl)-3-butylideneazetidin-2-one (8a). Yield 28%; yellow oil [Found: C, 74.65; H, 6.98; N, 4.19; $C_{21}H_{23}NO_3$: requires C, 74.75; H, 6.87; N, 4.15%]; R_f (7% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1734 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.96 (t, *J*=7.8 Hz, 3H, =CH–$CH_2CH_2CH_3$), 1.40–1.58 (m, 2H, =CH–$CH_2CH_2CH_3$), 2.44–2.66 (m, 2H, =CH–$CH_2CH_2CH_3$), 3.76 (s, 3H, Ar–OCH_3), 3.82 (s, 3H, Ar–OCH_3), 5.20 (d, *J*=1.0 Hz, 1H, C4*H*), 5.56 (t, *J*=1.0, 7.8 Hz, 1H, =$CH(CH_2)_2CH_3$), 6.82 (d, *J*=9.1 Hz, 2H, Ar), 6.92 (d, *J*=8.7 Hz, 2H, Ar), 7.28 (d, *J*=9.1 Hz, 2H, Ar), 7.32 (d, *J*=8.7 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.5, 22.4, 30.6, 55.2, 55.4, 62.5, 114.3, 114.4, 118.1, 128, 129.3, 131.3, 131.6, 142, 155.9, 159.7, 161.5; MS (*m*/*z*): 338 (M+1).

Following a similar procedure other 3-alkylidene-β-lactams **7b–l** and **8b–l** were also synthesized.

4.2.3. *E*-1-(Methoxyphenyl)-3-butylidene-4-phenylazetidin-2-one (7b). Yield 71%; white solid, mp 104–105 °C [Found: C, 78.34; H, 6.56; N, 4.63; $C_{20}H_{21}NO_2$: requires C, 78.15; H, 6.89; N, 4.56%]; R_f (8% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1732 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.73 (t, *J*=7.4 Hz, 3H, =CH–$CH_2CH_2CH_3$), 1.26–1.33 (m, 2H, =CH–$CH_2CH_2CH_3$), 1.81–1.99 (m, 2H, =CH–$CH_2CH_2CH_3$), 3.78 (s, 3H, Ar–OCH_3), 5.43 (d, *J*=1.4 Hz, 1H, C4*H*), 6.28 (dt, *J*=1.4, 7.6 Hz, 1H, =$CH(CH_2)_2CH_3$), 6.73 (d, *J*=9.1 Hz, 2H, Ar), 7.16–7.35 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.5, 22.4, 30.6, 55.3, 62.7, 114.3, 118.1, 126.5, 127.8, 128.4, 131.5, 137.4, 141.6, 155.8, 161.3; MS (*m*/*z*): 308 (M+1).

4.2.4. *Z*-1-(Methoxyphenyl)-3-butylidene-4-phenylazetidin-2-one (8b). Yield 29%; mp 106 °C [Found: C, 78.41; H, 6.99; N, 4.78; $C_{20}H_{21}NO_2$: requires C, 78.15; H, 6.89; N, 4.56%]; R_f (8% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.94 (t, *J*=7.5 Hz, 3H, =CH–$CH_2CH_2CH_3$), 1.41–1.52 (m, 2H, =$CHCH_2CH_2CH_3$), 2.41–2.64 (m, 2H, =CH–$CH_2CH_2CH_3$), 3.75 (s, 3H, Ar–OCH_3), 5.27 (d, *J*=1.2 Hz,

1H, C4*H*), 5.56 (dt, *J*=1.2, 7.9 Hz, 1H, =*CH*$(CH_2)_2CH_3$), 6.79 (d, *J*=9.1 Hz, 2H, Ar), 7.25–7.39 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.3, 21.6, 29.8, 55.4, 63, 114.3, 118.2, 127.1, 128.6, 128.9, 131.4, 137, 142.1, 155.9, 161.2; MS (*m*/*z*): 308 (M+1).

4.2.5. *E*-1,4-Bis-(4-methoxyphenyl)-3-octylideneazetidin-2-one (7c). Yield 71%; colorless oil [Found: C, 76.38; H, 7.96; N, 3.68; $C_{25}H_{31}NO_3$: requires C, 76.30; H, 7.94; N, 3.56%]; R_f (5% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1740, 1612 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.89 (t, *J*=6.7 Hz, 3H, =CH–$CH_2(CH_2)_5CH_3$), 1.13–1.28 (m, 10H, =CH–$CH_2(CH_2)_5CH_3$), 1.87–2.01 (m, 2H, =CH–$CH_2(CH_2)_5CH_3$), 3.77 (s, 3H, Ar–OCH_3), 3.83 (s, 3H, Ar–OCH_3), 5.37 (d, *J*=1.2 Hz, 1H, C4*H*), 6.24 (dt, *J*=1.2, 7.6 Hz, 1H, =*CH*$(CH_2)_6CH_3$), 6.81 (d, *J*=9.1 Hz, 2H, Ar), 6.92 (d, *J*=8.7 Hz, 2H, Ar), 7.31 (d, *J*=9.1 Hz, 2H, Ar), 7.28 (d, *J*=8.7 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.7, 22.2, 27.4, 28.0, 28.5, 31.3, 54.8, 55.0, 62.3, 114, 114.1, 117.8, 127.6, 128.3, 128.5, 131.1, 141.8, 155.5, 159.5, 161; MS (*m*/*z*): 394 (M+1).

4.2.6. *Z*-1,4-Bis-(4-methoxyphenyl)-3-octylideneazetidin-2-one (8c). Yield 29%; colorless oil [Found: C, 76.35; H, 7.89; N, 3.64; $C_{25}H_{31}NO_3$: requires C, 76.30; H, 7.94; N, 3.56%]; R_f (5% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1743 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.88 (t, *J*=6.5 Hz, 3H, =CH–$CH_2(CH_2)_5CH_3$), 1.14–1.62 (m, 10H, =CH–$CH_2(CH_2)_5CH_3$), 2.48–2.62 (m, 2H, =CH–$CH_2(CH_2)_5CH_3$), 3.75 (s, 3H, Ar–OCH_3), 3.80 (s, 3H, Ar–OCH_3), 5.22 (d, *J*=1.0 Hz, 1H, C4*H*), 5.54 (dt, *J*=1.0, 7.9 Hz, 1H, =*CH*$(CH_2)_6CH_3$), 6.79 (d, *J*=9.1 Hz, 2H, Ar), 6.89 (d, *J*=8.7 Hz, 2H, Ar), 7.26 (d, *J*=8.7 Hz, 2H, Ar), 7.28 (d, *J*=9.0 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.0, 22.5, 28.6, 28.9, 29.1, 31.7, 55.1, 55.3, 62.3, 114.2, 118.1, 127.9, 129.3, 131.5, 141.7, 155.8, 159.7, 161.5; MS (*m*/*z*): 394 (M+1).

4.2.7. *E*-1-(Methoxyphenyl)-3-octylidene-4-phenylazetidin-2-one (7d). Yield 71%; white solid, mp 74–76 °C [Found: C, 79.41; H, 7.99; N, 3.72; $C_{24}H_{29}NO_2$: requires C, 79.30; H, 8.04; N, 3.86%]; R_f (8% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1733 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.79 (t, *J*=6.8 Hz, 3H, =CH–$CH_2(CH_2)_5CH_3$), 1.03–1.20 (m, 10H, =CH–$CH_2(CH_2)_5CH_3$), 1.78–1.92 (m, 2H, =CH–$CH_2(CH_2)_5CH_3$), 3.67 (s, 3H, Ar–OCH_3), 5.31 (d, *J*=1.4 Hz, 1H, C4*H*), 6.16 (dt, *J*=1.4, 7.3 Hz, 1H, =*CH*$CH_2(CH_2)_5CH_3$), 6.76 (d, *J*=8.9 Hz, 2H, Ar), 7.16–7.36 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.7, 22.3, 27.5, 28.1, 28.5, 31.3, 55.1, 62.7, 114, 117.8, 126.7, 127.1, 127.8, 128.3, 128.7, 131.7, 141.6, 155.6, 161.9; MS (*m*/*z*): 364 (M+1).

4.2.8. *Z*-1-(Methoxyphenyl)-3-octylidene-4-phenylazetidin-2-one (8d). Yield 29%; colorless oil [Found: C, 79.41; H, 8.02; N, 3.82; $C_{24}H_{29}NO_2$: requires C, 79.30; H, 8.04; N, 3.86%]; R_f (8% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1733, 1616 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.77 (t, *J*=6.6 Hz, 3H, =CH–$CH_2(CH_2)_5CH_3$), 1.17–1.57 (m, 10H, =CH–$CH_2(CH_2)_5CH_3$), 2.34–2.56 (m, 2H, =CH–$CH_2(CH_2)_5CH_3$), 3.66 (s, 3H, Ar–OCH_3), 5.17 (d, *J*=1.0 Hz, 1H, C4*H*), 5.46 (dt, *J*=1.0, 7.8 Hz, 1H, =*CH*$(CH_2)_6CH_3$), 6.70 (d, *J*=8.9 Hz, 2H, Ar), 7.16–7.36 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.8, 22.2, 27.4, 28.1, 28.5, 31.3, 55.2, 62.4, 114, 117.8, 127.6, 128.1, 128.5, 129.5, 131.1, 141.8, 155.5, 161; MS (*m*/*z*): 364 (M+1).

4.2.9. *E*-1,4-Bis-(4-methoxyphenyl)-3-heptylideneazetidin-2-one (7e). Yield 71%; white solid, mp 65–66 °C [Found: C, 75.88; H, 7.88 N, 3.68; $C_{24}H_{29}NO_3$: requires C, 75.96; H, 7.70; N, 3.69%]; R_f (5% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1737 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.86 (t, *J*=6.7 Hz, 3H, =CH–$CH_2(CH_2)_4CH_3$), 1.22–1.38 (m, 8H, =CH–$CH_2(CH_2)_4CH_3$), 1.87–2.01 (m, 2H, =CH–$CH_2(CH_2)_4CH_3$), 3.76 (s, 3H, Ar–OCH_3), 3.83 (s, 3H, Ar–OCH_3), 5.37 (d, *J*=1.4 Hz, 1H, C4*H*), 5.24 (dt, *J*=1.4, 7.4 Hz, 1H, =*CH*$(CH_2)_5CH_3$), 6.81 (d, *J*=9.1 Hz, 2H, Ar), 6.92 (d, *J*=8.7 Hz, 2H, Ar), 7.31 (d, *J*=9.1 Hz, 2H, Ar), 7.38 (d, *J*=8.7 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.9, 22.4, 27.7, 28.3, 28.5, 31.3, 55.1, 55.3, 62.6, 114.3, 118.1, 127.9, 128.30, 128.8, 131.4, 142.1, 155.8, 159.8, 161.3; MS (*m*/*z*): 380 (M+1).

4.2.10. *Z*-1,4-Bis-(4-methoxyphenyl)-3-heptylideneazetidin-2-one (8e). Yield 29%; 107–108 °C [Found: C, 75.89; H, 7.76; N, 3.65; $C_{24}H_{29}NO_3$: requires C, 75.96; H, 7.70; N, 3.69%]; R_f (5% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1740 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.83 (t, *J*=6.6 Hz, 3H, =CH–$CH_2(CH_2)_4CH_3$), 1.19–1.39 (m, 8H, =CH–$CH_2(CH_2)_4CH_3$), 2.46–2.57 (m, 2H, =CH–$CH_2(CH_2)_4CH_3$), 3.70 (s, 3H, Ar–OCH_3), 3.76 (s, 3H, Ar–OCH_3), 5.17 (d, *J*=1.0 Hz, 1H, C4*H*), 5.49 (dt, *J*=1.0, 8.0 Hz, 1H, =*CH*–$CH_2(CH_2)_4CH_3$), 6.72 (d, *J*=9.1 Hz, 2H, Ar), 6.85 (d, *J*=8.7 Hz, 2H, Ar), 7.34 (d, *J*=9.1 Hz, 2H, Ar), 7.39 (d, *J*=8.7 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14, 22.5, 28.2, 28.7, 31.5, 55.2, 55.4, 62.4, 114.3, 114.4, 118.1, 128.1, 129.3, 131.6, 141.7, 155.8, 159.7, 161.5; MS (*m*/*z*): 380 (M+1).

4.2.11. *E*-1-(Methoxyphenyl)-3-heptylidene-4-phenylazetidin-2-one (7f). Yield 69%; white solid, mp 74 °C [Found: C, 79.41; H, 7.99; N, 3.73; $C_{23}H_{27}NO_2$: requires C, 79.05; H, 7.79; N, 4.01%]; R_f (5% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1731 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.78 (t, *J*=6.4 Hz, 3H, =CH–$CH_2(CH_2)_4CH_3$), 1.14–1.65 (m, 8H, =CH–$CH_2(CH_2)_4CH_3$), 2.34–2.53 (m, 2H, =CH–$CH_2(CH_2)_4CH_3$), 3.66 (s, 3H, Ar–OCH_3), 5.17 (d, *J*=1.2 Hz, 1H, C4*H*), 6.30 (dt, *J*=1.2, 7.3 Hz, 1H, =*CH*$(CH_2)_5CH_3$), 6.70 (d, *J*=9.1 Hz, 2H, Ar), 7.16–7.36 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.7, 22.3, 28.4, 29.4, 31.3, 55.1, 62.5, 114.1, 117.8, 126.3, 128.2, 128.7, 131.2, 131.6, 141.1, 155.6, 161.1; MS (*m*/*z*): 350 (M+1).

4.2.12. *Z*-1-(Methoxyphenyl)-3-heptylidene-4-phenylazetidin-2-one (8f). Yield 31%; white solid, mp 68–70 °C [Found: C, 79.31; H, 7.83; N, 3.71; $C_{23}H_{27}NO_2$: requires C, 79.05; H, 7.79; N, 4.01%]; R_f (5% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1731 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.78 (t, *J*=6.4 Hz, 3H, =CH–$CH_2(CH_2)_4CH_3$), 1.14–1.65 (m, 8H, =CH–$CH_2(CH_2)_4CH_3$), 2.34–2.53 (m, 2H, =CH–$CH_2(CH_2)_4CH_3$), 3.66 (s, 3H, Ar–OCH_3), 5.17 (d, *J*=1.0 Hz, 1H, C4*H*), 5.46 (dt, *J*=1.0, 7.9 Hz, 1H, =*CH*$(CH_2)_4CH_3$), 6.70 (d, *J*=9.1 Hz, 2H, Ar), 7.16–7.36 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.5, 22.6, 28.7, 29.1, 31.8, 55.2, 62.4, 114.2, 117.8, 126.5, 128.3,

128.7, 131.4, 131.9, 141.1, 155.6, 161.1; MS (*m*/*z*): 350 (M+1).

4.2.13. *E*-1,4-Bis-(4-methoxyphenyl)-3-propylideneazetidin-2-one (7g). Yield 72%; white solid, mp 88–90 °C [Found: C, 74.23; H, 6.68; N, 4.29; $C_{20}H_{21}NO_3$: requires C, 74.28; H, 6.55; N, 4.33%]; R_f (5% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.84 (t, J=7.5 Hz, 3H, =CH–CH_2CH_3), 1.67–2.05 (m, 2H, =CH–CH_2CH_3), 3.74 (s, 3H, Ar–OCH_3), 3.81 (s, 3H, Ar–OCH_3), 5.36 (d, J=1.4 Hz, 1H, C4*H*), 6.22 (dt, J=1.4, 7.3 Hz, 1H, =*CH*CH_2CH_3), 6.78 (d, J=9.1 Hz, 2H, Ar), 6.88 (d, J=8.7 Hz, 2H, Ar), 7.25 (d, J=9.1 Hz, 2H, Ar), 7.38 (d, J=8.7 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 12.9, 21.3, 55.2, 55.3, 62.5, 114.2, 114.3, 118.1, 128.3, 128.8, 129.l, 131.4, 141.5, 155.8, 159.8, 161.4; MS (*m*/*z*): 324 (M+1).

4.2.14. *Z*-1,4-Bis-(4-methoxyphenyl)-3-propylideneazetidin-2-one (8g). Yield 28%; white solid, mp 98–99 °C [Found: C, 74.23; H, 6.60; N, 4.37; $C_{20}H_{21}NO_3$: requires C, 74.28; H, 6.55; N, 4.33%]; R_f (5% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1728 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.96 (t, J=7.6 Hz, 3H, =CH–CH_2CH_3), 2.40–2.70 (m, 2H, =CH–CH_2CH_3), 3.75 (s, 3H, Ar–OCH_3), 3.80 (s, 3H, Ar–OCH_3), 5.22 (d, J=1.0 Hz, 1H, C4*H*), 5.54 (dt, J=1.0, 7.7 Hz, 1H, =*CH*CH_2CH_3), 6.79 (d, J=9.1 Hz, 2H, Ar), 6.89 (d, J=8.7 Hz, 2H, Ar), 7.26 (d, J=9.1 Hz, 2H, Ar), 7.29 (d, J=8.7 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.8, 22.3, 55.2, 55.4, 62.3, 114.3, 114.4, 118.1, 127.9, 129.3, 131.6, 132.9, 141.2, 155.9, 159.8, 161.4; MS (*m*/*z*): 324 (M+1).

4.2.15. *E*-1-(Methoxyphenyl)-3-propylidene-4-phenylazetidin-2-one (7h). Yield 69%; white solid, mp 153–154 °C [Found: C, 77.67; H, 6.49; N, 4.74; $C_{19}H_{19}NO_2$: requires C, 77.79; H, 6.53; N, 4.77%]; R_f (8% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1733 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.82 (t, J=7.4 Hz, 3H, =CH–CH_2CH_3), 1.81–2.06 (m, 2H, =CH–CH_2CH_3), 3.74 (s, 3H, Ar–OCH_3), 5.39 (d, J=1.4 Hz, 1H, C4*H*), 6.21 (dt, J=1.4, 7.7 Hz, 1H, =*CH*CH_2CH_3), 6.79 (d, J=9.1 Hz, 2H, Ar), 7.16–7.28 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 12.9, 21.3, 55.3, 62.9, 114.3, 118.1, 127, 128.6, 128.9, 129.2, 131.4, 137, 141.4, 155.9, 161.3; MS (*m*/*z*): 294 (M+1).

4.2.16. *Z*-1-(Methoxyphenyl)-3-propylidene-4-phenylazetidin-2-one (8h). Yield 31%; white solid, mp 125–126 °C [Found: C, 77.64; H, 6.56; N, 4.71; $C_{19}H_{19}NO_2$: requires C, 77.79; H, 6.53; N, 4.77%]; R_f (8% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1739, 1610 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.96 (t, J=7.2 Hz, 3H, =CH–CH_2CH_3), 2.33–2.61 (m, 2H, =CH–CH_2CH_3), 3.66 (s, 3H, Ar–OCH_3), 5.17 (d, J=1.1 Hz, 1H, C4*H*), 5.46 (dt, J=1.1, 8.1 Hz, 1H, =*CH*CH_2CH_3), 6.72 (d, J=9.1 Hz, 2H, Ar), 7.16–7.28 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.8, 22.3, 55.4, 62.7, 114.3, 118.1, 126.5, 128.4, 128.9, 131.5, 133.1, 137.4, 140.9, 155.9, 161.3; MS (*m*/*z*): 294 (M+1).

4.2.17. 3-Isopropylidene-1,4-bis-(4-methoxyphenyl)azetidin-2-one (7i). Yield 91%; white solid, mp 146–147 °C [Found: C, 74.12; H, 6.65; N, 4.02; $C_{20}H_{21}NO_3$: requires C, 74.28; H, 6.55; N, 4.33%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1731 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.54 (s, 3H, ^{a}*CH*$_3$–*C*=), 2.11 (s, 3H, ^{b}*CH*$_3$–C=), 3.73 (s, 3H, Ar–OCH_3), 3.80 (s, 3H, Ar–OCH_3), 5.22 (s, 1H, C4*H*), 6.76 (d, J=9.1 Hz, 2H, Ar), 6.89 (d, J=8.9 Hz, 2H, Ar), 7.25 (d, J=9.0 Hz, 2H, Ar), 7.32 (d, J=8.7 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 19.8, 20.2, 55.2, 55.4, 62.3, 114.3, 117.8, 128.4, 129.2, 131.8, 136.3, 137, 155.6, 159.6, 162; MS (*m*/*z*): 324 (M+1).

4.2.18. 3-Isopropylidene-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (7j). Yield 92%; white solid, mp 192–194 °C [Found: C, 77.65; H, 6.65; N, 4.52; $C_{19}H_{19}NO_2$: requires C, 77.79; H, 6.53; N, 4.77%]; R_f (10% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.55 (s, 3H, ^{a}*CH*$_3$–*C*=), 2.12 (s, 3H, ^{b}*CH*$_3$–C=), 3.73 (s, 3H, Ar–OCH_3), 5.28 (s, 1H, C4*H*), 6.78 (d, J=9.1 Hz, 2H, Ar), 7.33–7.43 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 16.7, 17.7, 33.2, 55.4, 65.2, 114.3, 118.8, 127.2, 128.6, 129.1, 130.5, 131, 156.3, 162; MS (*m*/*z*): 294 (M+1).

4.2.19. *E*-1,4-Bis-(4-methoxyphenyl)-3-(3-phenylpropylidene)azetidin-2-one (7k). Yield 70%; white solid, mp 91–92 °C [Found: C, 78.02; H, 6.32; N, 3.85; $C_{26}H_{25}NO_3$: requires C, 78.17; H, 6.31; N, 3.51%]; R_f (10% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1737 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.16–2.52 (m, 4H, =CH(CH_2)$_2$Ph), 3.79 (s, 3H, Ar–OCH_3), 3.83 (s, 3H, Ar–OCH_3), 5.11 (s, 1H, C4*H*), 6.24 (t, J=7.5 Hz, 1H, =CH(CH_2)$_2$Ph), 6.79 (d, J=9.1 Hz, 2H, Ar), 6.78 (d, J=9.0 Hz, 2H, Ar), 6.89 (d, J=8.7 Hz, 2H, Ar), 6.98–7.33 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 29.8, 34.6, 55.2, 55.4, 67.5, 114.3, 114.4, 118.2, 126.1, 126.3, 128.4, 128.7, 131.4, 140.6, 142.9, 155.9, 159.9, 161.1; MS (*m*/*z*): 400 (M+1).

4.2.20. *Z*-1,4-Bis-(4-methoxyphenyl)-3-(3-phenylpropylidene)azetidin-2-one (8k). Yield 30%; white solid, mp 103–105 °C [Found: C, 78.14; H, 6.15; N, 3.63; $C_{26}H_{25}NO_3$: requires C, 78.17; H, 6.31; N, 3.51%]; R_f (10% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1733 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.71–2.94 (m, 4H, =CH(CH_2)$_2$Ph), 3.73 (s, 3H, Ar–OCH_3), 3.79 (s, 3H, Ar–OCH_3), 5.18 (s, 1H, C4*H*), 5.51 (t, J=7.5 Hz, 1H, =*CH*(CH_2)$_2$Ph), 6.79 (d, J=9.1 Hz, 2H, Ar), 6.82 (d, J=8.6 Hz, 2H, Ar), 7.17–7.37 (m, 9H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 29.2, 34.4, 55.1, 55.3, 67.8, 114.1, 114.3, 118.2, 126.1, 126.3, 128.4, 128.7, 131.4, 140.6, 142.9, 155.9, 159.9, 161.2; MS (*m*/*z*): 400 (M+1).

4.2.21. *E*-1-(4-methoxyphenyl)-4-phenyl-3-(3-phenylpropylidene)azetidin-2-one (7l). Yield 70%; white solid, mp 102–103 °C [Found: C, 81.32; H, 6.38; N, 3.58; $C_{25}H_{23}NO_2$: requires C, 81.27; H, 6.27; N, 3.79%]; R_f (12% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$) 1736 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.19–2.56 (m, 4H, =CH(CH_2)$_2$Ph), 3.73 (s, 3H, Ar–OCH_3), 5.15 (s, 1H, *C4H*), 6.25 (t, J=7.7 Hz, 1H, =*CH*(CH_2)$_2$Ph), 6.78 (d, J=9.1 Hz, 2H, Ar), 6.95 (d, J=8.0 Hz, 2H, Ar), 7.21–7.38 (m, 10H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 29.8, 34.6, 55.3, 62.8, 114.3, 118.1, 126.1, 126.5, 127.1, 128.4, 128.7, 131.3, 136.8, 140.5, 142.7, 155.9, 161; MS (*m*/*z*): 370 (M+1).

4.2.22. *Z*-1-(4-Methoxyphenyl)-4-phenyl-3-(3-phenylpropylidene)azetidin-2-one (8l). Yield 30%; white solid,

mp 107–109 °C [Found: C, 81.37; H, 6.35; N, 3.63; $C_{25}H_{23}NO_2$: requires C, 81.27; H, 6.27; N, 3.79%]; R_f (8% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$): 1736 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.78–2.94 (m, 4H, =CH(CH_2)$_2$Ph), 3.78 (s, 3H, Ar–OCH_3), 5.25 (s, 1H, *C*4*H*), 5.83 (t, *J*=7.5 Hz, 1H, =*CH*(CH_2)$_2$Ph), 6.83 (d, *J*=8.9 Hz, 2H, Ar), 7.19–7.37 (m, 12H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 29.9, 35.4, 55.4, 62.7, 114.3, 118.1, 126, 126.3, 128.3, 128.5, 130.3, 137.2, 140.6, 142.1, 155.9, 161.1; MS (*m*/*z*): 370 (M+1).

4.2.23. 1,4-Bis-(4-methoxyphenyl)-3-butylazetidin-2-one (9a). To a mixture of 3-alkylidene-β-lactams **7a** and **8a** (0.168 g, 0.5 mmol) in 15 mL of ethyl acetate was added a catalytic amount of 10% Pt/C (30 mg). Hydrogenation was carried out under atmospheric pressure for 12 h. The catalyst was filtered through a pad of Celite and the solvent was removed under reduced pressure to give compound **9a** (0.155 g, 92%) as a white solid, mp 85–86 °C [Found: C, 74.27; H, 7.36; N, 4.02; $C_{21}H_{25}NO_3$: require C, 74.31; H, 7.42; N, 4.13%]; R_f (14% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 3359 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.97 (t, *J*=6.8 Hz, 3H, *CH*$_3$(CH_2)$_3$), 1.12–1.50 (m, 6H, CH_3(*CH*$_2$)$_3$), 3.47–3.57 (m, 1H, C3*H*), 3.74 (s, 3H, Ar–O*CH*$_3$), 3.80 (s, 3H, Ar–O*CH*$_3$), 5.11 (d, *J*=5.6 Hz, 1H, C4*H*), 6.79 (d, *J*=9.1 Hz, 2H, Ar), 6.82 (d, *J*=8.7 Hz, 2H, Ar), 7.22 (d, *J*=8.7 Hz, 2H, Ar), 7.29 (d, *J*=8.9 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.9, 22.9, 25.6, 35.1, 54.6, 55.4, 55.8, 59.9, 114.5, 114.8, 118.9, 125.9, 128.7, 130.6, 156.2, 159.9, 168.5; MS (*m*/*z*): 340 (M+1).

Following a similar procedure other 3-alkyl-β-lactams **9b–l** were synthesized.

4.2.24. 3-Butyl-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (9b). Yield 95%; white solid, mp 89–91 °C [Found: C, 73.98; H, 7.36; N, 3.98; $C_{20}H_{23}NO_2$: requires C, 73.82; H, 7.12; N, 4.30%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1737 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.72 (t, *J*=6.9 Hz, 3H, *CH*$_3$(CH_2)$_3$), 1.25–1.69 (m, 6H, CH_3(*CH*$_2$)$_3$), 3.46–3.57 (m, 1H, C3*H*), 3.76 (s, 3H, Ar–O*CH*$_3$), 5.11 (d, *J*=5.7 Hz, C4*H*), 6.73 (d, *J*=9.1 Hz, 2H, Ar), 7.20–7.36 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.7, 22.4, 25, 29.4, 54.7, 55.3, 58.4, 114.4, 118.7, 127.2, 128.6, 129.1, 130.6, 134, 156.3, 167.9; MS (*m*/*z*): 310 (M+1).

4.2.25. 3-Octyl-1,4-bis(4-methoxyphenyl)azetidin-2-one (9c). Yield 94%; thick oil [Found: C, 75.57; H, 8.32; N, 3.55; $C_{25}H_{33}NO_3$: requires C, 75.91; H, 8.41; N, 3.54%]; R_f (8% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$) 1742 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.86 (t, *J*=6.7 Hz, 3H, *CH*$_3$(CH_2)$_7$), 1.10–1.53 (m, 14H, CH_3(*CH*$_2$)$_7$), 3.44–3.54 (m, 1H, C4*H*), 3.75 (s, 3H, Ar–O*CH*$_3$), 3.81 (s, 3H, Ar–O*CH*$_3$), 5.37 (d, *J*=5.6 Hz, 1H, C4*H*), 6.79 (d, *J*=9.0 Hz, 2H, Ar), 6.88 (d, *J*=8.8 Hz, 2H, Ar), 7.19 (d, *J*=8.7 Hz, 2H, Ar), 7.26 (d, *J*=9.1 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.1, 22.6, 25.23, 27.2, 29.2, 29.3, 29.4, 31.8, 54.7, 55.2, 55.3, 57.9, 113.9, 114.2, 118.3, 118.4, 126.9, 128.4, 131.3, 155.7, 159.4, 167.7; MS (*m*/*z*): 396 (M+1).

4.2.26. 3-Octyl-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (9d). Yield 94%; thick oil [Found: C, 78.67; H, 8.39; N, 3.87; $C_{24}H_{31}NO_2$: requires C, 78.87; H, 8.55; N, 3.83%]; R_f (14% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1739 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 0.78 (t, *J*=7.0 Hz, 3H, *CH*$_3$(CH_2)$_6$$CH_2$), 1.09–1.40 (m, 12H, CH_3(*CH*$_2$)$_6$$CH_2$), 1.29–1.46 (m, 2H, CH_3(CH_2)$_6$*CH*$_2$), 3.42–3.56 (m, 1H, C3*H*), 3.69 (s, 3H, Ar–O*CH*$_3$), 5.09 (d, 1H, *J*=5.70 Hz, C4*H*), 6.73 (d, *J*=9.1 Hz, 2H, Ar), 7.14–7.28 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.9, 22.4, 25.2, 27.1, 28.7, 29.2, 29.4, 31.5, 54.7, 55.1, 55.3, 57.9, 113.9, 114.1, 118.3, 126.9, 131.3, 155.8, 167.7; MS (*m*/*z*): 366 (M+1).

4.2.27. 3-Heptyl-1,4-bis(4-methoxyphenyl)azetidin-2-one (9e). Yield 94%; thick oil [Found: C, 75.46; H, 8.34; N, 3.83; $C_{24}H_{31}NO_3$: requires C, 75.56; H, 8.19; N, 3.67%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1741 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.84 (t, *J*=6.9 Hz, 3H, *CH*$_3$(CH_2)$_5$$CH_2$), 1.11–1.53 (m, 12H, CH_3(*CH*$_2$)$_6$), 3.44–3.47 (m, 1H, C3*H*), 3.75 (s, 3H, Ar–O*CH*$_3$), 3.81(s, 3H, Ar–O*CH*$_3$), 5.11 (d, *J*=5.6 Hz, 1H, *C*4*H*), 6.77 (d, *J*=9.1 Hz, 2H, Ar), 6.85 (d, *J*=8.9 Hz, 2H, Ar), 7.19 (d, *J*=8.9 Hz, 2H, Ar), 7.24 (d, *J*=9.00 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.9, 22.4, 25.2, 27.1, 29.2, 31.5, 54.7, 55.1, 55.3, 57.9, 113.9, 114.1, 118.3, 126.9, 128.3, 131.3, 155.7, 159.7, 167.7; MS (*m*/*z*): 382 (M+1).

4.2.28. 3-Heptyl-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (9f). Yield 95%; white solid, mp 75–76 °C [Found: C, 78.45; H, 8.13; N, 3.87; $C_{23}H_{29}NO_2$: requires C, 78.60; H, 8.32; N, 3.99%]; R_f (15% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1739 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.89 (t, *J*=6.8 Hz, 3H, *CH*$_3$(CH_2)$_6$), 1.03–1.46 (m, 12H, CH_3(*CH*$_2$)$_6$), 3.40–3.51 (m, 1H, *C*3*H*), 3.69 (s, 3H, Ar–O*CH*$_3$), 5.14 (d, *J*=5.7 Hz, 1H, *C*4*H*), 6.81 (d, *J*=9.1 Hz, 2H, Ar), 7.27–7.39 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14, 22.5, 25.3, 27.1, 28.8, 29.2, 31.6, 54.7, 55.4, 58.4, 114.3, 118.4, 127.2, 128.3, 128.6, 131.3, 135.2, 156.5, 168.2; MS (*m*/*z*): 352 (M+1).

4.2.29. 3-Propyl-1,4-bis(4-methoxyphenyl)azetidin-2-one (9g). Yield 97%; white solid, mp 84–85 °C [Found: C, 73.76; H, 7.06; N, 4.25; $C_{20}H_{23}NO_3$: requires C, 73.82; H, 7.12; N, 4.30%]; R_f (9% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$): 1737 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.77 (t, *J*=6.5 Hz, 3H, *CH*$_3$(CH_2)$_2$), 1.14–1.45 (m, 4H, CH_3(*CH*$_2$)$_2$), 3.47–3.57 (m, 1H, C3*H*), 3.75 (s, 3H, Ar–O*CH*$_3$), 3.82 (s, 3H, Ar–O*CH*$_3$), 5.11 (d, *J*=5.4 Hz, 1H, C4*H*), 6.80 (d, *J*=9.00 Hz, 2H, Ar), 6.89–7.14 (d, *J*=8.9 Hz, 2H, –Ar), 7.22 (d, *J*=8.9 Hz, 2H, Ar), 7.29 (d, *J*=9.0 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.9, 20.5, 27.5, 54.5, 55.2, 55.4, 58, 113.9, 114.2, 118.3, 126.9, 127.1, 128.3, 131.3, 155.7, 159.4, 167.3; MS (*m*/*z*): 326 (M+1).

4.2.30. 3-Propyl-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (9h). Yield 94%; white solid, mp 111–112 °C [Found: C, 77.18; H, 7.06; N, 4.66; $C_{19}H_{21}NO_2$: requires C, 77.26; H, 7.17; N, 4.74%]; R_f (12% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$) 1739 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.75 (t, *J*=6.8 Hz, 3H, *CH*$_3$(CH_2)$_2$), 1.08–1.46 (m, 4H, CH_3(*CH*$_2$)$_2$), 3.51–3.61 (m, 1H, C3*H*), 3.75 (s, 3H, Ar–O*CH*$_3$), 5.16 (d, *J*=5.7 Hz, 1H, C4*H*), 6.81 (d, *J*=9.1 Hz, 2H, Ar), 7.14–7.31 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.8, 20.4, 27.9, 54.4, 55.3, 58.3, 114.2, 118.1,

118.3, 127.1, 128.1, 128.5, 131.3, 135.1, 155.4, 167.6; MS (*m*/*z*): 296 (M+1).

4.2.31. 3-Isopropyl-1,4-bis(4-methoxyphenyl)azetidin-2-one (9i). Yield 92%; white solid, mp 124–126 °C [Found: C, 73.79; H, 7.07; N, 4.27; $C_{20}H_{23}NO_3$: requires C, 73.82; H, 7.12; N, 4.30%]; R_f (14% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$) 1731 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.49 (d, J=6.3 Hz, 3H, $^aCH_3$–CH–$^bCH_3$), 1.15 (d, J=6.5 Hz, 3H, $^aCH_3$–CH–$^bCH_3$), 1.52–1.79 (m, 1H, $^aCH_3$–CH–$^bCH_3$), 3.17 (dd, J=5.5, 11.2 Hz, 1H, C3*H*), 3.73 (s, 3H, Ar–OCH_3), 3.80 (s, 3H, Ar–OCH_3), 5.06 (d, J=5.5 Hz, 1H, C4*H*), 6.74 (d, J=9.1 Hz, 2H, Ar), 6.81 (d, J=8.7 Hz, 2H, Ar), 7.23 (d, J=8.6 Hz, 2H, Ar), 7.30 (d, J=9.2 Hz, 2H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 20.6, 20.9, 25.7, 55.2, 55.4, 58.2, 62, 114, 114.2, 114.5, 127, 127.2, 128.4, 131.3, 155.7, 159.7, 167.2; MS (*m*/*z*): 326 (M+1).

4.2.32. 3-Isopropyl-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (9j). Yield 95%; white solid, mp 153–154 °C [Found: C, 77.21; H, 7.11; N, 4.76; $C_{19}H_{21}NO_2$: requires C, 77.26; H, 7.17; N, 4.74%]; R_f (16% EtOAc/Pet ether) 0.5; ν_{max} ($CHCl_3$) 1737 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.57 (d, J=6.6 Hz, 3H, $^aCH_3$–CH–$^bCH_3$), 1.12 (d, J=6.7 Hz, 3H, $^aCH_3$–CH–$^bCH_3$), 1.63–1.76 (m, 1H, $^aCH_3$–CH–$^bCH_3$), 3.17 (dd, J=5.7, 11.2 Hz, 1H, C3*H*), 3.67 (s, 3H, Ar–OCH_3), 5.01 (d, J=5.7 Hz, 1H, C4*H*), 6.74 (d, J=9.0 Hz, 2H, Ar), 6.81–7.30 (m, 7H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 20.4, 24.9, 25.4, 55.4, 58.7, 62, 114.2, 114.5, 127.3, 127.6, 128.4, 131.3, 159.7, 167.2; MS (*m*/*z*): 296 (M+1).

4.2.33. 1,4-Bis-(4-methoxyphenyl)-3-(3-phenylpropyl)-azetidin-2-one (9k). Yield 94%; white solid, mp 90–93 °C [Found: C, 77.57; H, 6.62; N, 3.49; $C_{26}H_{27}NO_3$: requires C, 77.78; H, 6.78; N, 3.49%]; R_f (10% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1741 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.18–1.66 (m, 4H, $PhCH_2(CH_2)_2$), 2.35–2.49 (m, 2H, $PhCH_2(CH_2)_2$), 3.46–3.57 (m, 1H, C3*H*), 3.75 (s, 3H, Ar–OCH_3), 3.83 (s, 3H, Ar–OCH_3), 5.11 (d, J=5.7 Hz, 1H, C4*H*), 6.78 (d, J=9.1 Hz, 2H, Ar), 6.90 (d, J=8.9 Hz, 2H, Ar), 7.00–7.27 (m, 9H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 24.9, 28.8, 35.6, 54.4, 55.2, 55.3, 57.9, 114.0, 114.1, 118.3, 125.6, 126.6, 127.1, 128.2, 131.2, 141.7, 155.7, 159.4, 167.4; MS (*m*/*z*): 402 (M+1).

4.2.34. 1-(4-Methoxyphenyl)-4-phenyl-3-(3-phenylpropyl)azetidin-2-one (9l). Yield 95%; white solid, mp 115–117 °C [Found: C, 80.58; H, 6.69; N, 3.49; $C_{25}H_{25}NO_2$: requires C, 80.83; H, 6.78; N, 3.77%]; R_f (10% EtOAc/Pet ether) 0.3; ν_{max} ($CHCl_3$) 1739 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.21–1.62 (m, 4H, $PhCH_2(CH_2)_2$), 2.36–2.45 (m, 2H, $PhCH_2(CH_2)_2$), 3.49–3.60 (m, 1H, C3*H*), 3.74 (s, 3H, Ar–OCH_3), 5.15 (d, J=5.8 Hz, 1H, C4*H*), 6.79 (d, J=9.1 Hz, 2H, Ar), 6.97 (d, J=8.9 Hz, 2H, Ar), 7.16–7.35 (m, 10H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 24.7, 28.9, 35.7, 54.5, 55.3, 57.9, 114.0, 114.1, 118.3, 125.6, 126.6, 127.1, 128.2, 129.5, 131.2, 141.7, 159.4, 167.4; MS (*m*/*z*): 372 (M+1).

4.2.35. 3-Chloro-1,4-bis-(4-methoxyphenyl)-3-phenylazetidin-2-one (14). Yield 92%; white solid, mp 58–60 °C [Found: C, 70.07; H, 5.07; Cl, 8.92; N, 3.46; $C_{23}H_{20}ClNO_3$: requires C, 70.14; H, 5.12; Cl, 9.00; N, 3.56%]; R_f (12% EtOAc/Pet ether) 0.4; ν_{max} ($CHCl_3$) 1757 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 3.70 (s, 3H, Ar–OCH_3), 3.76 (s, 3H, Ar–OCH_3), 5.50 (s, 1H, C4*H*), 6.65 (d, J=8.8 Hz, 2H, Ar), 6.82 (d, J=8.7 Hz, 2H, Ar), 7.12–7.34 (m, 9H, Ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 55.1, 55.4, 72.7, 113.9, 114.3, 119.3, 124.9, 125.1, 128.1, 128.6, 128.8, 130.2, 132, 156.6, 159.8, 161.7; MS (*m*/*z*): 394 (M+1).

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