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Full Paper

Solventless Lactam Synthesis by Intramolecular Cyclizations of α-Iminoester Derivatives under Microwave Irradiation

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Abstract: We have previously reported a new synthesis of amides from esters and amines under microwave irradiation, offering much higher yields than those achieved with conventional heating [1]. We have now extended these studies to the ring closure of neat iminoesters **I2**, **I3** and **I4-I6** to give five- and six-membered ring lactams **L5**, **L6** and larger lactams **L7-L9** (where **I** means imine and **L** means lactam), respectively, under both classical heating conditions and microwave irradiation.

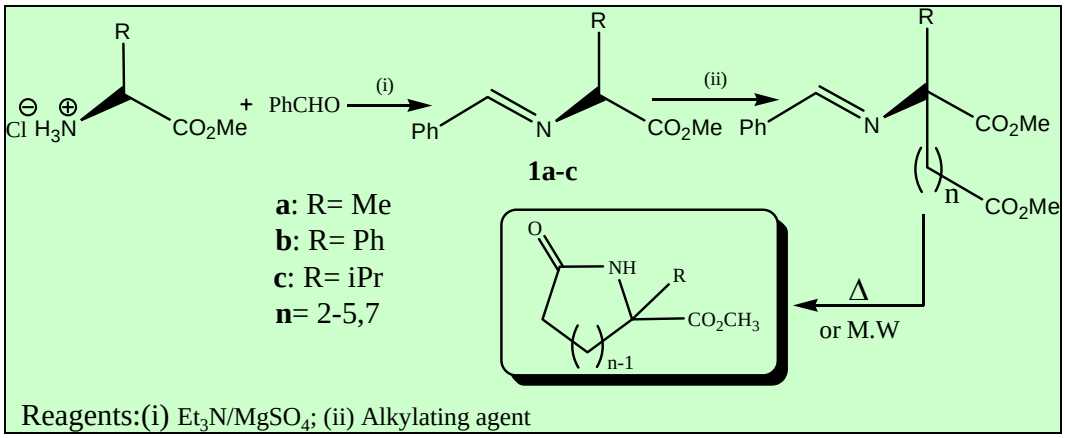
Keywords: Medium-sized ring lactams; imine alkylation; Schiff bases; microwave irradiation.

Introduction

Lactams are of considerable interest in a number of areas, ranging from drug discovery to the polymer industry, and consequently their synthesis has been, and still is, a topic of significant interest for organic chemists. Among the numerous methods developed radical strategies [2], especially intramolecular cyclizations of unsaturated α-carbamoyl radicals [3,4] or in our case imines, have been

shown to be some of the best tools for the construction of a variety of lactam skeletons ranging from β-lactams to medium- or larger sized ones. Encouraged by our recent results on the synthesis of amides under microwave irradiation [1], and by other publications in which this original synthetic method was used, we now report that neat imines can be utilised for lactam synthesis by simple cyclization either under classical heating conditions or under microwave irradiation (Scheme 1).

Scheme 1



Medium-sized (5 to 10-membered) ring lactams find widespread use in organic chemistry as key intermediates in the synthesis of more complex structures, or as core structures in natural products or pharmaceutically important compounds. Until now, the generation of such rings has been a challenge. During the past decade increasing interest has focused on the generation of cyclic and hairpin peptides and medium-sized rings were thought to represent suitable fragments. Furthermore, a range of complex natural products characterized by possessing such lactam structures and their total synthesis is a broad field for organic chemists to test new strategies and to develop new methods.

Microwave-assisted heating under controlled conditions has been shown to be an invaluable technology for medicinal chemistry and drug discovery applications, since it often dramatically reduces reaction times, typically from days or hours to minutes or even seconds. Compound libraries can then be rapidly synthesized using this new, enabling technology [5-9]. In our work we have used a monomode Synthewave® 402 type of microwave oven, with a maximum working volume under the microwave field of 40 mL and a maximum power of 300W. The samples are placed in a cylindrical quartz reactor (three available diameters: Ø = 1.8, 3 and 4 cm). This oven, formerly marketed by the Prolabo company, is controlled by means of the SYNSOFT® software package.

The aim of the present paper is to present and discuss a simple and new strategy for the formation of C-C bonds through a direct alkylation of α-iminoesters under solvent free conditions, using potassium tert-butoxide as base, and then, the cyclisation of the products under microwave irradiation to synthesize five- to ten-membered ring lactams. In particular, we present the results of our study on the intramolecular cyclization reactions of α-iminoesters derived from the aldimine **1**. Our results show that these cyclization reactions are highly effective and give access to useful heterocyclic ring systems.

Results and Discussion

The Michael reactions of imines have been used in numerous synthetic applications by our team [10] and by others and the method has facilitated the preparation of numerous compounds endowed with biological properties such as terpenes, steroids, and alkaloids. For our part, we have used the intramolecular cyclization of these imines for the formation of lactams with five to ten bonds.

Deprotonation of aldimine **I1** under solid-liquid PTC conditions using K_2CO_3 as a base [11] gives a highly active carbanion, whose reaction with methyl acrylate gives the alkylated product **I2** in good yield (70 to 85%) (Scheme 2). The reaction is carried out by simply stirring solid K_2CO_3, an aldimine **I1a-c**, methyl acrylate and *N*-benzylcinchonidinium bromide (N-BCB) as catalyst [11] in acetonitrile at room temperature for 4 to 5 hours. The results are summarized in Table 1. These Michael adducts then cyclize to provide five membered ring lactams **L5** (Scheme 2), either under classical heating or under microwave activation.

Scheme 2

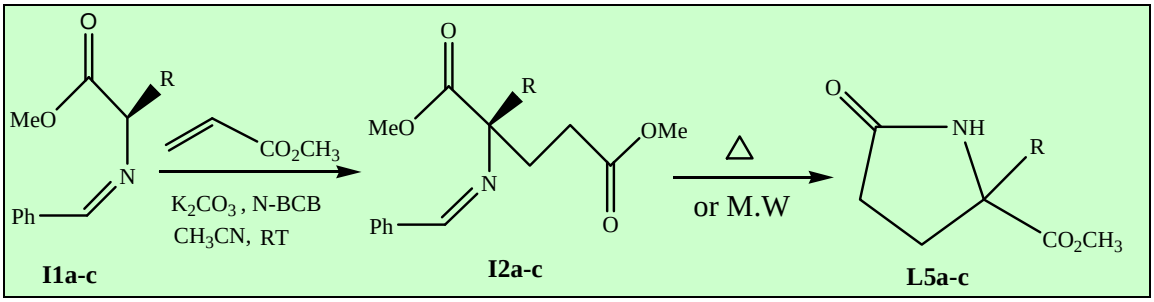
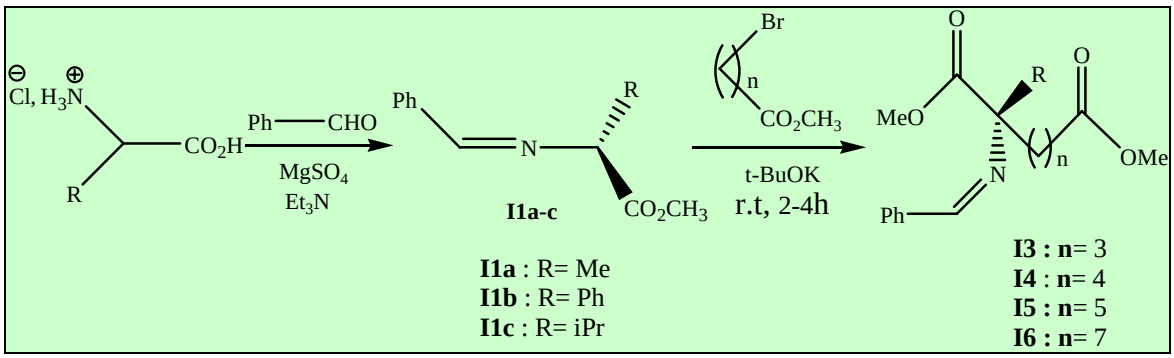


Table 1

I2	R	Time (h)	Yield (%)
a	Me	5	70
b	iPr	5	81
c	Phenyl	4	85

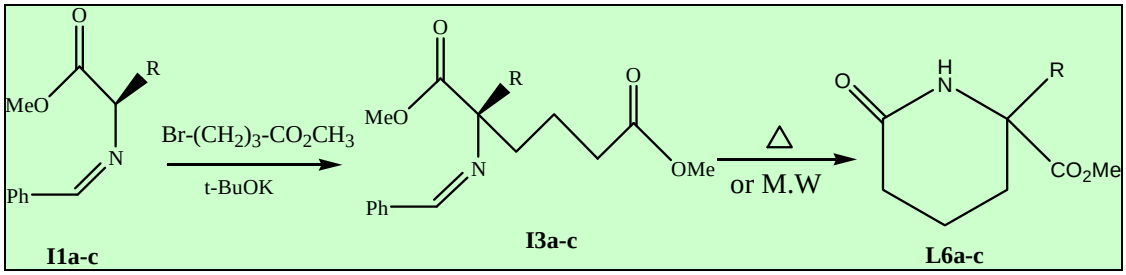
The α-alkylation of *N*-benzylidene imines **I1a-c** with longer chains is easily performed by the solventless treatment with bromoester derivatives catalysed by potassium tert-butoxide (t-BuOK) to give compounds **I3-I6**, which underwent cyclization to give six, seven-to ten-membered ring lactams **L6-L9** , in excellent yields under microwave irradiation (Schemes 3-4)

Scheme 3

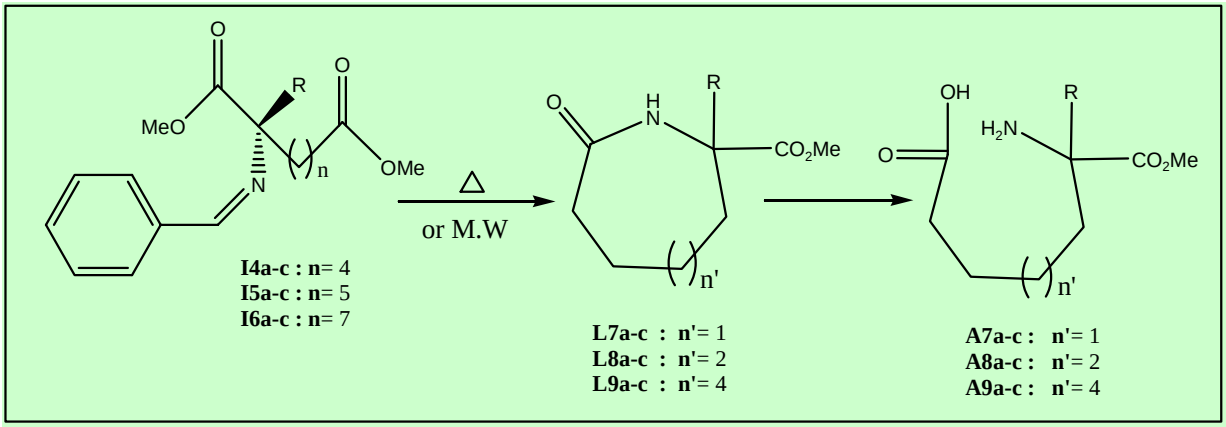


However, whereas the compounds **L6** are stable and isolable, the seven, eight and ten membered lactams **L7**-**L9** are somewhat unstable and readily open up to give the corresponding amino acids **A7**, **A8** and **A9** (Scheme **5**).

Scheme 4



Scheme 5



Previous work has shown that the alkylation of asymmetric imines can be effected under liquid–liquid [12], solid–liquid [13] and micellar phase-transfer conditions [14] and that homogeneous reaction conditions involving phosphazene bases [15] are also similarly effective. However, after a number of attempts to alkylate α-iminoesters using numerous and various conditions described in the literature [16-19], the results were rather poor. After several such attempts, we finally found a very simple and suitable way to alkylate imines in excellent yields under mild conditions with various bromoalkylesters **E** (where **E** represents esters) (Table 2). Medium-sized macrocyclic lactams of 8, 9 and 10 members have been traditionally harder to form than their smaller and larger-sized counterparts [20]. In fact and for our case, the five and six membered ring lactams are easily obtained, contrary to higher members cycles which open up to give the corresponding amino acids in the mass spectrometer.

Alkylation and intramolecular cyclization reactions of α-iminoester derivatives

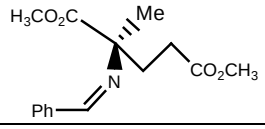
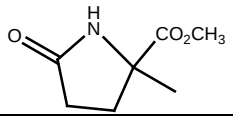
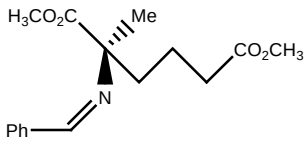
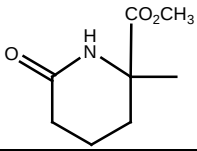
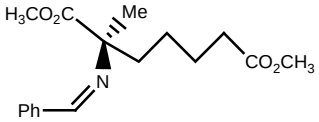
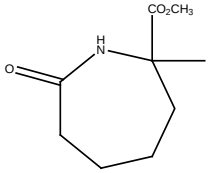
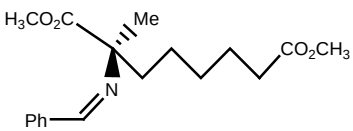
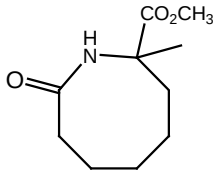
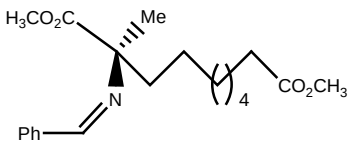
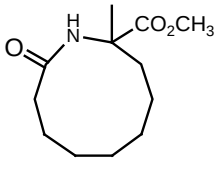
The α-iminoesters of type **1** were readily prepared by the condensation of the corresponding amino acids with benzaldehyde by standard procedures. *N*-Benzylcinchonidinium bromide (N-BCB) [11] catalysed the alkylation of compound **I1** with methyl acrylate, giving α-amino esters **I2** with 70–85% yield (Table **1**). These reactions were carried out under solid–liquid phase transfer conditions using solid potassium carbonate as the base. To prepare imines **I3** to **I6**, the aldimines **I1** were alkylated with bromoalkyl ester derivatives under solvent free conditions using potassium *tert*-butoxide (*t*-BuOK) as base (Table 2).

Table 2

Starting materials		Products	Time (h)	Yield (%)
I1a	Br-$(CH_2)_3$-CO_2Me (**E3**)	**I3a**	2	**91**
I1a	Br-$(CH_2)_4$-CO_2Me (**E4**)	**I4a**	3	**98**
I1a	Br-$(CH_2)_5$-CO_2Me (**E5**)	**I5a**	4	**97**
I1a	Br-$(CH_2)_7$-CO_2Me (**E6**)	**I6a**	4	**97**
I1b	Br-$(CH_2)_3$-CO_2Me (**E3**)	**I3b**	2	**85**
I1b	Br-$(CH_2)_4$-CO_2Me (**E4**)	**I4b**	3	**98**
I1b	Br-$(CH_2)_5$-CO_2Me (**E5**)	**I5b**	4	**97**
I1b	Br-$(CH_2)_7$-CO_2Me (**E6**)	**I6b**	5	**96**
I1c	Br-$(CH_2)_3$-CO_2Me (**E3**)	**I3c**	2.5	**89**
I1c	Br-$(CH_2)_4$-CO_2Me (**E4**)	**I4c**	3	**87**
I1c	Br-$(CH_2)_5$-CO_2Me (**E5**)	**I5c**	4	**86**
I1c	Br-$(CH_2)_7$-CO_2Me (**E6**)	**I6c**	6	**83**

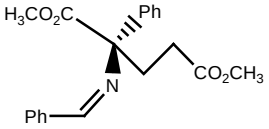
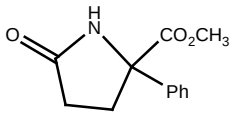
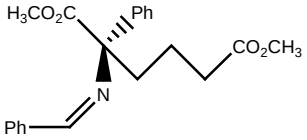
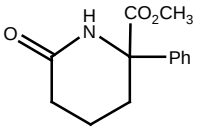
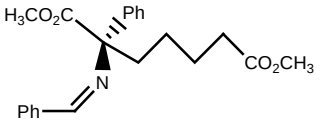
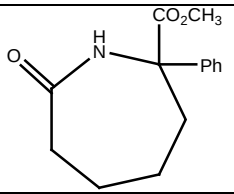
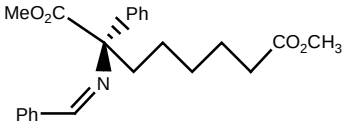
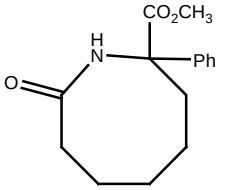
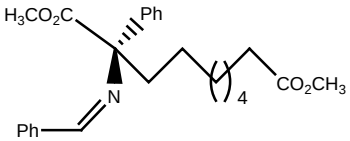
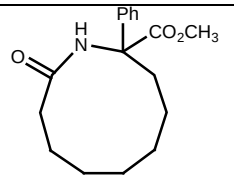
The resulting imines **I2-I6** were cyclized under either classical heating conditions or microwave irradiation to give the five to ten-membered ring lactams **L5-L9** (Tables 3-5) in good yields after washing with diethyl ether. Best yields were achieved with the latter technique. The isolated lactams were fully characterized by ^{1}H- and ^{13}C-NMR spectra and mass spectrometry.

Table 3: Intramolecular cyclization of imines **1** with R = Me

Substrate	Product	T°C △[a]	Time (days)	Yield (%)	T°C M.W	Time (min)	Yield (%)
		140	2	79	120	25	85
		150	3.5	78	130	20	81
		150	4	65	135	30	85
		160	5.5	55	135	30	85
		170	5	40	135	30	83

a) Oil bath temperature previously set before the experiment.

Table 4: Intramolecular cyclization of imines **1** with R = Ph

Substrate	Product	T°C △[a]	Time (days)	Yield (%)	T°C M.W	Time (min)	Yield (%)
		140	2	80	100	15	86
		145	3	69	115	20	88
		145	3.5	62	115	30	79
		150	3.5	56	120	30	78
		160	4	48	120	30	79

a) Oil bath temperature previously set before the experiment.

Table 5: Intramolecular cyclization of imines **1** with R = *i*-Pr

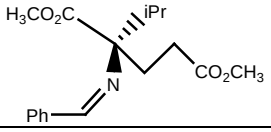
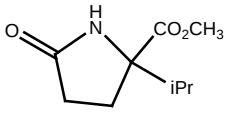
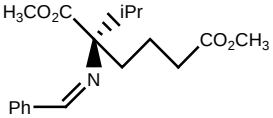
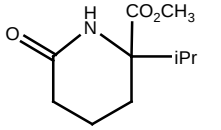
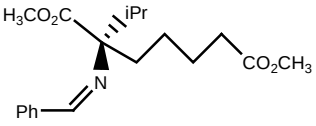
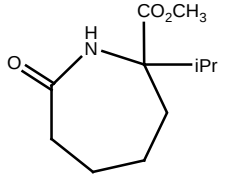
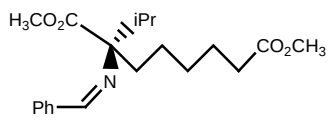
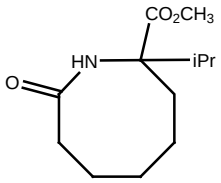
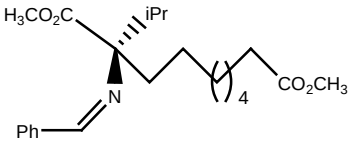
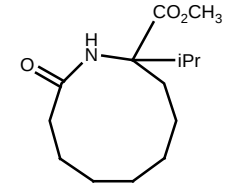
Substrate	Product	T°C △[a]	Time (days)	Yield (%)	T°C M.W	Time (min)	Yield (%)
		140	2	79	100	20	85
		140	3	70	110	25	82
		145	3.5	55	110	30	80

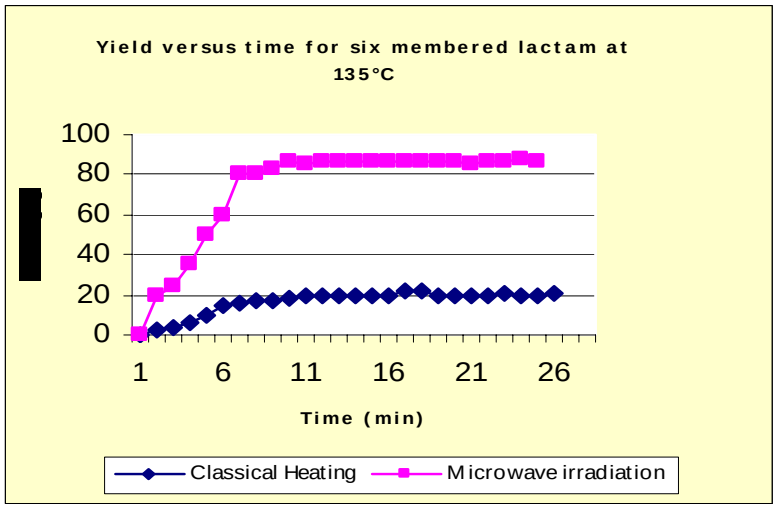
Table 5. Cont

		150	3.5	53	120	30	78
		155	4.5	46.7	120	30	76

a) Oil bath temperature previously set before the experiment.

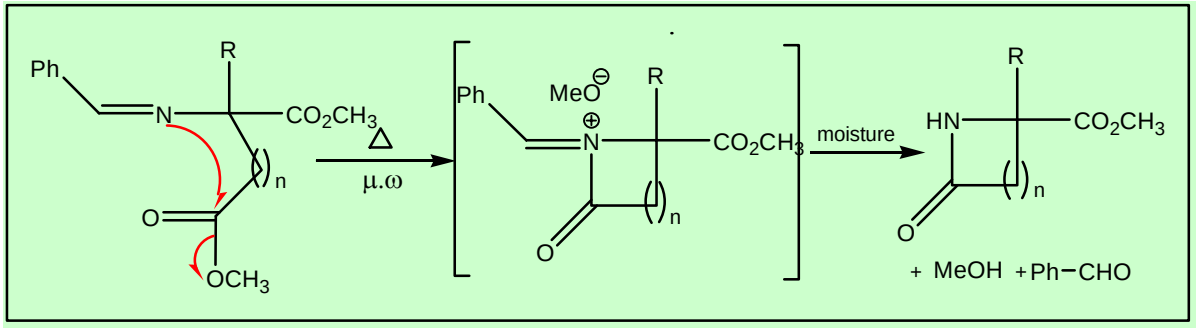
A high temperature (up to 135°C) was required for efficient cyclization of imines to give the five to ten-membered lactams. The cyclization was achieved either under classical heating or microwave irradiation, with the latter being a much more efficient procedure (Figure 1). No products could be isolated by classical heating with the same temperature conditions used under microwaves, but we did obtain them with lower yields after extended periods (2-5 days) at high temperatures.

Figure 1



Based on our results, we suggest the following mechanistic scenario for the intramolecular cyclization reactions of these iminoesters (Scheme 6).

Scheme 6



Conclusions

In summary, it is clear that intramolecular cyclization reaction of α-iminoesters under microwave irradiation is an efficient class of reaction. The cyclizations of α-iminoester derivatives of the type **1**, provide an easy access to a variety of lactam systems with different ring sizes in good yields.

Experimental

General

NMR spectra were measured on a Bruker AVANCE 300 spectrometer operating at 300 (^{1}H) and 75 (^{13}C) MHz, respectively, using $CDCl_3$ as solvent and TMS as internal standard and mass spectra Varian MAT 311 instrument. The masses recorded for the seven-, eight- and ten- membered ring lactams correspond to the peaks resulting from their hydrolysis followed by decarboxylation in the mass spectrometer. The alkylating agents methyl 4-bromobutyrate (**E3**) and methyl 5-bromovalerate (**E4**) were commercial products (from Acros), while methyl 6-bromohexanoate (**E5**) and methyl 8-bromooctanoate (**E6**) were obtained by esterification of their corresponding acid chlorides.

General procedure for the synthesis of α-iminoesters.

The α-iminoesters were prepared according to the procedure reported by Longmire *et al*. [21]. Triethylamine (l eq) and anhydrous magnesium sulphate (light excess) were added at 0°C to a stirred suspension of the appropriate amino acid methyl ester hydrochloride (alanine, phenylalanine or valine, 1 eq), in dry dichloromethane (10 mL) and the mixture was stirred for l h before the addition of the benzaldehyde (l eq). The reaction mixture was stirred overnight at room temperature after which it was filtered and the solvent removed *in vacuo*. The residue was taken up in diethyl ether (10 mL) and washed with brine (3×5 mL). The combined organic phases were then dried over $MgSO_4$ and evaporated to dryness to afford the desired products.

Representative procedure for the catalytic phase-transfer alkylation of **I1**.

To a mixture of aldimine **I1** (10 mmol) and catalyst (N-BCB, 1mmol) in acetonitrile (10 mL) solid potassium carbonate (2 mmol) and methyl acrylate (10 mmol) were added. The reaction mixture was stirred vigorously at room temperature (r.t) for 5 hours. Then, the mixture was filtered, washed with water and acetonitrile. The filtrate was concentrated under reduced pressure and the residue was taken up in ether. The ether solution was washed with saturated sodium chloride and dried over $MgSO_4$. After ether evaporation, the alkylated product **2** was obtained. The details of **I2a-c** have been given in Table 1.

General procedure for alkylation of α-iminoesters **I1**.

In a two-neck flask, provided with a refluxing condenser and equipped with a magnetic stirring bar was added an equimolar mixture of aldimine **1** and the alkylation agent (**E3-E6**). After 15 min of stirring, a slight excess (1.2 eq) of potassium tert-butoxide (t-BuOK) was added. The mixture was stirred for 2-6 h at room temperature (r.t), the product was then extracted with methylene chloride (CH_2Cl_2). The solvent was removed under reduced pressure and the alkylated imines were distilled on a Büchi apparatus. The details of the alkylated imines have been given in Table 2.

General Procedure for the preparation of lactams: Method A (MWI).

The typical procedure for the different size lactams synthesis is as follows: benzylidene imines **I2-I6** (1eq, 10^{-2} mol) are placed in the Ø: 2.5 cm reactor of a Synthewave ®402) focused microwave oven and irradiated for the specified temperature and time (see Tables 3-5). Upon completion of the reaction, the mixture was extracted with CH_2Cl_2 and washed with ether. After evaporation of the solvent, the resulting product was analyzed by ^{1}H-NMR, ^{13}C-NMR and mass spectra.

Method B (Conventional heating)

Reactions were performed under the same conditions using a previously heated oil bath, set at a temperature slightly higher (about 20°C) than the temperature measured in the microwave oven. As this study was done only for the comparison purposes and to see the influence of reaction times on the yields, the products were only analysed by ^{1}H-NMR.

Methyl 2-(benzylideneamino)propanoate (**I1a**): $C_{11}H_{13}NO_2$; Yield: 91%; Colorless oil, bp: 85°C/ 6.3x10^{-2}Torr (lit [23] mp 105-107 °C/2 Torr); ^{1}H-NMR δ: 1.52-1.54 (d, 3H, *J*= 3 Hz, C<u>H</u>$_3$), 3.74 (s, 3H, MeCO), 4.12-4.19 (q, 1H, *J*= 6.81 Hz, C<u>H</u>), 7.38-7.43 (m, 5H, Ph), 8.31 (s, 1H, C<u>H</u>=); ^{13}C-NMR δ: 19.45 (<u>C</u>H$_3$), 52.42 (O<u>C</u>H$_3$), 67.98 (<u>C</u>H), 128.35 (Ar<u>C</u>H), 128.51 (Ar<u>C</u>H), 131.13 (Ar<u>C</u>H), 135.69 (Ar<u>C</u>), 163.04 (H<u>C</u>=N), 176.99 (<u>C</u>=O); MS m/z: found [M-**.**CH$_3$]$^+$ 176.07115, requires 176.0711.

Dimethyl 2-(benzylideneamino)-2-methylpentanedioate (**I2a**) [23]: $C_{15}H_{19}NO_4$: Yield: 70%; yellow oil, bp: 90°C/6.3x10^{-2}Torr; ^{1}H-NMR δ: 1.50 (s, 3H, C<u>H</u>$_3$), 2.12-2.16 (t, 2H, *J*=7.75 Hz, C<u>H</u>$_2$), 2.43-2.54 (t, 2H, *J*= 8.21 Hz, C<u>H</u>$_2$), 3.62 (s, 3H, <u>Me</u>CO), 3.71 (s, 3H, <u>Me</u>CO), 7.27-7.41 (m, 5H, Ph), 8.26 (s, 1H, C<u>H</u>=); ^{13}C NMR δ: 25.88 (<u>C</u>H$_3$), 30.46 (<u>C</u>H$_2$), 32.67 (<u>C</u>H$_2$), 51.60 (O<u>C</u>H$_3$), 53.09 (O<u>C</u>H$_3$), 62.83 (<u>C</u>H), 127 (Ar<u>C</u>H), 128.59 (Ar<u>C</u>H), 128.85 (Ar<u>C</u>H), 135.69 (Ar<u>C</u>), 163.23 (H<u>C</u>=N), 174.92 (<u>C</u>=O), 178.17 (<u>C</u>=O); MS m/z: Found [M-.CH$_3$]$^+$ 262.1099, requires 262.1079; Found [M-.OCH$_3$]$^+$ 246.1153, requires 246.1130.

Dimethyl 2-(benzylideneamino)-2-methylhexanedioate (**I3a**): $C_{16}H_{21}NO_4$; Yield: 91%; yellow oil, bp: 90°C/6.3x10^{-2}Torr; ^{1}H-NMR δ: 1.60 (s, 3H, C<u>H</u>$_3$), 1.75-1.82 (qt, 2H, *J*= 7.8 Hz, C<u>H</u>$_2$), 1.98-2.06 (t, 2H, *J*=9 Hz, C<u>H</u>$_2$), 2.24-2.30 (t, 2H, *J*=8.2 Hz, C<u>H</u>$_2$), 3.61 (s, 3H, <u>Me</u>CO), 3.70 (s, 3H, <u>Me</u>CO), 7.15-7.81 (m, 5H, Ph), 8.33 (s, 1H, C<u>H</u>=); ^{13}C-NMR δ: 19.88 (<u>C</u>H$_2$), 24.76 (<u>C</u>H$_3$), 33.46 (<u>C</u>H$_2$), 35.67

(CH_2), 52.43 (OCH_3), 54.70 (OCH_3), 61.41 (CH), 126.68 (ArCH), 128.14 (ArCH), 130.85 (ArCH), 136.69 (ArC), 160.23 (HC=N), 174.42 (C=O), 176.27 (C=O); MS m/z: Found [M-.CO_2CH_3]$^+$ 232.3061, requires 232.3070.

Dimethyl 2-(benzylideneamino)-2-methylheptanedioate (**I4a**): $C_{17}H_{23}NO_4$; Yield: 98%; yellow oil, bp: 85°C/8x10^{-2}Torr; ^{1}H-NMR δ: 1.52 (s, 3H, CH_3), 1.37-1.77 (m, 4H, 2CH_2), 1.91-2.01 (t, 2H, *J*=6 Hz, CH_2), 2.32-2.40 (t, 2H, *J*=12 Hz, CH_2), 3.68 (s, 3H, MeCO), 3.78 (s, 3H, MeCO), 7.33-7.82 (m, 5H, Ph), 8.28 (s, 1H, CH=); ^{13}C-NMR δ: 23.10 (CH_2), 23.82 (CH_2), 25.22 (CH_3), 33.90 (CH_2), 39.74 (CH_2), 51.47 (OCH_3), 52.15 (OCH_3), 68.42 (CH),127.83 (ArCH), 128.79 (ArCH), 130.87 (ArCH), 136.36 (ArC), 159.26 (HC=N), 174.05 (C=O), 174.68 (C=O); MS m/z: Found [M-.OCH_3]$^+$ 274.1443, requires 274.1452; Found [M-.CO_2CH_3]$^+$ 246.1494, requires 246.1493.

Dimethyl 2-(benzylideneamino)-2-methyloctanedioate (**I5a**): $C_{18}H_{25}NO_4$; Yield: 97.3%; yellow oil, bp: 85°C/8x10^{-2}Torr; ^{1}H-NMR δ: 1.33-1.39 (qt, 2H, *J*= 6 Hz, CH_2), 1.50 (s, 3H, CH3), 1.61-1.69 (qt, 2H, *J*=5.46 Hz, CH_2), 1.90-1.98 (qt, 2H, *J*=5.2 Hz, CH_2), 2.29-2.34 (t, 2H, *J*=8 Hz, CH_2), 3.66 (s, 3H, MeCO), 3.75 (s, 3H, MeCO), 7.35-7.80 (m, 5H, Ph), 8.26 (s, 1H, CH=); ^{13}C-NMR δ: 23.11 (CH_2), 23.88 (CH_2), 24.78 (CH_2), 29.42 (CH_3), 34.00 (CH_2), 39.94 (CH_2), 51.48 (OCH_3), 52.14 (OCH_3), 68.51 (CH), 128.28 (ArCH), 128.56 (ArCH), 130.85 (ArCH), 136.06 (ArC), 159.18 (HC=N), 174.21 (C=O), 175.22 (C=O); MS m/z: Found [M-.CO_2CH_3]$^+$ 260.1650, requires 260.1646.

Dimethyl 2-(benzylideneamino)-2-methyldecanedioate (**I6a**): $C_{20}H_{29}NO_4$; Yield: 96.7%; yellow oil, bp: 80°C/9x10^{-2}Torr; ^{1}H-NMR δ: 1.22-1.46 (m, 6H, 3CH_2), 1.52 (s, 3H, CH_3), 1.60-1.73 (t, 2H, *J*=7.04 Hz, CH_2), 1.86-2.19 (m, 4H, 2CH_2), 2.29-2.33 (t, 2H, *J*=7.59 Hz, CH_2), 3.69 (s, 3H, MeCO), 3.78 (s, 3H, MeCO), 7.32-7.80 (m, 5H, Ph), 8.28 (s, 1H, CH=); ^{13}C-NMR δ: 22.78 (CH_2), 23.18 (CH_2), 23.31 (CH_2), 24.45 (CH_2), 28.57 (CH_2), 29.42 (CH_3), 34.01 (CH_2), 40.24 (CH_2), 51.38 (OCH_3), 51.80 (OCH_3), 63.50 (CH), 128.27 (ArCH), 128.54 (ArCH), 131.06 (ArCH), 137.06 (ArC), 162.26 (HC=N), 174.12 (C=O), 176.21 (C=O); MS m/z: Found [M-.CO_2CH_3]$^+$ 288.1963, requires 288.1980.

Methyl (benzylideneamino)(phenyl)acetate (**I1b**): $C_{16}H_{15}NO_2$; Yield:78%; pale yellow solid, mp: 63°C, (from EtOH); ^{1}H-NMR δ: 3.77 (s, 3H, MeCO), 5.23 (s, 1H, CH), 7.28-7.87 (m, 10H, 2Ph), 8.37 (s, 1H, CH=); ^{13}C-NMR δ: 52.52 (OCH_3), 69.78 (CH), 127.84 (ArCH), 128.12 (ArCH), 128.40 (ArCH), 128.68 (ArCH), 128.72 (ArCH), 131.28 (ArCH), 135.68 (ArC), 138.11 (ArC), 163.81 (HC=N); 171.58 (C=O); MS m/z: Found [M-.CO_2CH_3]$^+$ 194.0969, requires 194.0980.

Dimethyl 2-(benzylideneamino)-2-phenylpentanedioate (**I2b**): $C_{20}H_{21}NO_4$; Yield: 85%; yellow oil, bp: 85°C/8x10^{-2}Torr; ^{1}H-NMR δ: 2.32-2.44 (t, 2H, *J*=6.5 Hz, CH_2), 2.48-2.64 (t, 2H, *J*=7 Hz, CH_2), 3.63 (s, 3H, MeCO), 3.79 (s, 3H, MeCO), 7.24-7.74 (m, 10H, 2Ph), 8.39 (s, 1H, CH=); ^{13}C-NMR δ: 30.12 (CH_2), 31.05 (CH_2), 50.42 (OCH_3), 52.52 (OCH_3), 70.18 (CH), 126.74 (ArCH), 127.12 (ArCH), 128.39 (ArCH), 128.78 (ArCH), 129.52 (ArCH), 131.33 (ArCH), 135.58 (ArC), 137.21 (ArC), 163.78 (HC=N), 173.78 (C=O), 174.65 (C=O); MS m/z: Found M$^+$. 339.1470, requires 339.1502.

Dimethyl 2-(benzylideneamino)-2-phenylhexanedioate (**I3b**): $C_{21}H_{23}NO_4$; Yield: 85.6%; yellow oil, bp: 92°C/10^{-2}Torr; ^{1}H NMR δ: 1.52-1.80 (qt, 2H, *J*=5.16 Hz, C$\underline{H}_2$), 2.28-2.32 (t, 2H, *J*=6 Hz, C$\underline{H}_2$), 2.38-2.46 (t, 2H, *J*=6.7 Hz, C$\underline{H}_2$), 3.63 (s, 3H, Me$\underline{C}$O), 3.77 (s, 3H, Me$\underline{C}$O), 7.33-7.89 (m, 10H, 2Ph), 8.22 (s, 1H, C$\underline{H}$=); ^{13}C-NMR δ: 19.28 (C$\underline{H}_2$), 27.05 (C$\underline{H}_2$), 29.25 (C$\underline{H}_2$), 51.32 (O$\underline{C}$H$_3$), 52.29 (O$\underline{C}$H$_3$), 69.28 ($\underline{C}$H), 127.14 (Ar$\underline{C}$H), 127.21 (Ar$\underline{C}$H), 128.30 (Ar$\underline{C}$H), 128.88 (Ar$\underline{C}$H), 129 (Ar$\underline{C}$H), 131.13 (Ar$\underline{C}$H), 136.08 (Ar$\underline{C}$), 137.11 (Ar$\underline{C}$), 161.78 (H$\underline{C}$=N), 174.58 ($\underline{C}$=O), 175.15 ($\underline{C}$=O); MS m/z: Found [M-.CO_2CH_3]$^+$ 294.1494, requires 294.1489.

Dimethyl 2-(benzylideneamino)-2-phenylheptanedioate (**I4b**): $C_{22}H_{25}NO_4$; Yield: 98%; yellow oil, bp: 90°C/10^{-1}Torr; ^{1}H-NMR δ: 1.24-1.46 (m, 4H, 2C$\underline{H}_2$), 1.56-1.64 (t, 2H, *J*=9 Hz, C$\underline{H}_2$), 2.23-2.26 (t, 2H, *J*=4.23 Hz, C$\underline{H}_2$), 3.60 (s, 3H, Me$\underline{C}$O), 3.73 (s, 3H, Me$\underline{C}$O), 7.27-7.81 (m, 10H, 2Ph), 8.17 (s, 1H, C$\underline{H}$=); ^{13}C-NMR δ: 23.43 (C$\underline{H}_2$), 25.26 (C$\underline{H}_2$), 33.88 (C$\underline{H}_2$), 40.29 (C$\underline{H}_2$), 51.40 (O$\underline{C}$H$_3$), 52.35 (O$\underline{C}$H$_3$), 74.89 ($\underline{C}$H), 126.84 (Ar$\underline{C}$H), 127.40 (Ar$\underline{C}$H), 128.39 (Ar$\underline{C}$H), 128.49 (Ar$\underline{C}$H), 128.60 (Ar$\underline{C}$H), 131.11 (Ar$\underline{C}$H), 136.37 (Ar$\underline{C}$), 141.92 (Ar$\underline{C}$), 161.16 (H$\underline{C}$=N), 173.76 ($\underline{C}$=O), 176.15 ($\underline{C}$=O); MS m/z: Found [M-.CO_2CH_3]$^+$ 308.1650, requires 308.1657.

Dimethyl 2-(benzylideneamino)-2-phenyloctanedioate (**I5b**): $C_{23}H_{27}NO_4$; Yield: 97.11%; yellow oil, bp: 90°C/2x10^{-1}Torr; ^{1}H-NMR δ: 1.27-1.62 (m, 6H, 3C$\underline{H}_2$), 1.79-1.83 (t, 2H, *J*=7.5 Hz, C$\underline{H}_2$), 2.18-2.26 (t, 2H, *J*=4.4 Hz, C$\underline{H}_2$), 3.63 (s, 3H, Me$\underline{C}$O), 3.72 (s, 3H, Me$\underline{C}$O), 7.33-7.89 (m, 10H, 2Ph), 8.28 (s, 1H, C$\underline{H}$=); ^{13}C-NMR δ: 23.46 (C$\underline{H}_2$), 24.70 (C$\underline{H}_2$), 29.43 (C$\underline{H}_2$), 33.98 (C$\underline{H}_2$), 40.49 (C$\underline{H}_2$), 51.42 (O$\underline{C}$H$_3$), 52.32 (O$\underline{C}$H$_3$), 74.97 ($\underline{C}$H), 126.85 (Ar$\underline{C}$H), 127.35 (Ar$\underline{C}$H), 128.36 (Ar$\underline{C}$H), 128.48 (Ar$\underline{C}$H), 128.60 (Ar$\underline{C}$H), 131.07 (Ar$\underline{C}$H), 139.27 (Ar$\underline{C}$), 141.81 (Ar$\underline{C}$), 161.06 (H$\underline{C}$=N), 174.56 ($\underline{C}$=O), 175.75 ($\underline{C}$=O); MS m/z: Found [M-.CO_2CH_3]$^+$ 322.1807, requires 322.1805.

Dimethyl 2-(benzylideneamino)-2-phenyldecanedioate (**I6b**): $C_{25}H_{31}NO_4$; Yield: 96.5%; yellow oil, bp: 95°C/2x10^{-1}Torr; ^{1}H-NMR δ: 1.28-1.47 (t, 3H, *J*=13 Hz, C$\underline{H}_2$), 1.58-1.80 (m, 4H, 2C$\underline{H}_2$), 1.83-1.85 (t, 2H, *J*=11.5 Hz, C$\underline{H}_2$), 2.22-2.35 (m, 4H, 2C$\underline{H}_2$), 2.58-2.80 (t, 2H, *J*=11 Hz, C$\underline{H}_2$), 3.62 (s, 3H, Me$\underline{C}$O), 3.70 (s, 3H, Me$\underline{C}$O), 7.14-7.87 (m, 10H, 2Ph), 8.21 (s, 1H, C$\underline{H}$=); ^{13}C-NMR δ: 19.86 (C$\underline{H}_2$), 23.70 (C$\underline{H}_2$), 25.43 (C$\underline{H}_2$), 29.03 (C$\underline{H}_2$), 30.19 (C$\underline{H}_2$), 34.05 (C$\underline{H}_2$), 40.58 (C$\underline{H}_2$), 51.32 (O$\underline{C}$H$_3$), 52.12 (O$\underline{C}$H$_3$), 73.67 ($\underline{C}$H), 126.89 (Ar$\underline{C}$H), 128.34 (Ar$\underline{C}$H), 128.48 (Ar$\underline{C}$H), 128.59 (Ar$\underline{C}$H), 129.50 (Ar$\underline{C}$H), 130.06 (Ar$\underline{C}$H), 138.37 (Ar$\underline{C}$), 142.71 (Ar$\underline{C}$), 161.26 (H$\underline{C}$=N), 173.46 ($\underline{C}$=O), 174.75 ($\underline{C}$=O); MS m/z: Found [M-.CO_2CH_3]$^+$ 350.2120, requires 350.2117.

Methyl 2-(benzylideneamino)-3-methylbutanoate (**I1c**): $C_{13}H_{17}NO_2$; Yield: 94.5%; yellow oil, bp: 85°C/2x10^{-2}Torr; ^{1}H-NMR: δ: 0.99-0.94 (dd, 6H, *J*= 6.88 Hz, 2C$\underline{H}_3$), 2.37-2.43 (m, 1H, *J*= 6 Hz, C$\underline{H}$), 3.67-3.71 (d, 1H, *J*= 12 Hz, C$\underline{H}$), 3.75 (s, 3H, MeCO), 7.39-7.84 (m, 5H, Ph), 8.26 (s, 1H, C$\underline{H}$=); ^{13}C-NMR δ: 18.66 (C$\underline{H}_3$), 19.51 (C$\underline{H}_3$), 31.73 ($\underline{C}$H), 51.93 (O$\underline{C}$H$_3$), 80.39 ($\underline{C}$H), 128.32 (Ar$\underline{C}$H), 128.51 (Ar$\underline{C}$H), 131.07 (Ar$\underline{C}$H), 135.69 (Ar$\underline{C}$), 163.33 (H$\underline{C}$=N), 172.44 ($\underline{C}$=O); MS m/z: Found [M-**.**CO_2CH_3]+ 160.2434, requires 160.2441.

Dimethyl 2-(benzylideneamino)-2-isopropylpentanedioate (**I2c**): $C_{17}H_{23}NO_4$; Yield: 81.2%; yellow oil, bp: 90°C/10^{-2}Torr; ^{1}HNMR δ: 0.95-1.01 (dd, 6H, *J*= 9 Hz, 2C$\underline{H}_3$), 1.13-1.18 (t, 2H, *J*= 3 Hz, C$\underline{H}_2$),

2.34-2.43 (m, 1H, *J*= 9 Hz, CH), 2.70-2.96 (t, 2H, *J*= 9 Hz, CH_2), 3.78 (s, 3H, MeCO), 3.82 (s, 3H, MeCO), 7.44-7.80 (m, 5H, Ph), 8.28 (s, 1H, CH=); ^{13}C-NMR δ: 19.80 (CH_3), 20.17 (CH_3), 29.85 (CH_2), 30.25 (CH), 31.13 (CH_2), 50.91 (OCH_3), 52.06 (OCH_3), 68.20 (C), 128.59-136.8 (Ar), 162.23 (HC=N), 174.64 (C=O), 175.33 (C=O); MS m/z: Found [M-**.**CO_2CH_3]+ 246.1619, requires 246.1627.

Dimethyl 2-(benzylideneamino)-2-isopropylhexanedioate (**I3c**): $C_{18}H_{25}NO_4$; Yield: 89%; yellow oil, bp: 90°C/2x10^{-1}Torr; ^{1}H-NMR δ: 0.93-1.05 (dd, 6H, *J*= 9 Hz, $2CH_3$), 2.04-2.21 (qt, 2H, *J*= 2.3 Hz, CH_2), 2.37-2.44 (t, 2H, *J*= 10.7 Hz, CH_2), 2.51-2.57 (m, 1H, *J*= 12 Hz, CH), 3.37-3.43 (t, 2H, *J*= 3 Hz, CH_2), 3.69 (s, 3H, MeCO), 3.75 (s, 3H, MeCO), 7.34-7.82 (m, 5H, Ph), 8.25 (s, 1H, CH=); ^{13}C-NMR δ: 20.15 (CH_3), 20.57 (CH_3), 21.11 (CH_2), 29.95 (CH_2), 30.23 (CH), 31.03 (CH_2), 51.82 (OCH_3), 52.03 (OCH_3), 62.42 (C), 128.79-136.77 (Ar), 163.03 (HC=N), 175.34 (C=O), 175.69 (C=O); MS m/z: Found [M-**.**CO_2CH_3]+ 260.1778, requires 260.1784.

Dimethyl 2-(benzylideneamino)-2-isopropylheptanedioate (**I4c**): $C_{19}H_{27}NO_4$; Yield: 86.7%; yellow oil, bp: 96°C/ 6.3.10^{-4}Torr; ^{1}H-NMR δ: 0.93-1.05 (dd, 6H, *J*= 9 Hz, $2CH_3$),1.60-2.00 (m, 4H, *J*= 6.72 Hz, $2CH_2$), 2.22-2.43 (qt, 1H, *J*= 4.57 Hz, CH), 2.44-2.47 (t, 1H, *J*= 3 Hz, CH_2), 3.40-3.45 (t, 2H, *J*= 4.05 Hz, CH_2), 3.70 (s, 3H, MeCO), 3.77 (s, 3H, MeCO), 7.44-7.90 (m, 5H, Ph), 8.37 (s, 1H, CH=); ^{13}C-NMR δ: 19.76 (CH_3), 19.98 (CH_3), 20.15 (CH_2), 20.66 (CH_2), 30.17 (CH), 31.28 (CH_2), 32.07 (CH_2), 52.32 (OCH_3), 52.63 (OCH_3), 71.60 (C), 128.80-136.57 (Ar), 162.33 (HC=N), 173.84 (C=O), 174.29 (C=O); MS m/z: Found [M-**.**OCH_3]+ 302.1932, requires 302.1940.

Dimethyl 2-(benzylideneamino)-2-isopropyloctanedioate (**I5c**): $C_{20}H_{29}NO_4$\Yield: 86%; yellow oil, bp: 106°C/6x0^{-4}Torr; ^{1}H-NMR δ: 0.95-1.01 (dd, 6H, *J*= 9 Hz, $2CH_3$),1.45-1.87 (m, 6H, *J*= 9.87 Hz, $3CH_2$), 1.90-2.04 (qt, 1H, *J*= 4.57 Hz, CH), 2.33-2.40 (t, 1H, *J*= 10.6 Hz, CH_2), 3.39-3.47 (t, 2H, *J*= 4.71 Hz, CH_2), 3.70 (s, 3H, MeCO), 3.78 (s, 3H, MeCO), 7.32-7.91 (m, 5H, Ph), 8.29 (s, 1H, CH=); ^{13}C-NMR δ: 18.96 (CH_3), 19.07 (CH_3), 19.73 (CH_2), 19.98 (CH_2), 20.05 (CH_2), 31.07 (CH), 31.76 (CH_2), 32.01 (CH_2), 51.62 (OCH_3), 52.23 (OCH_3), 78.90 (C), 128.70-136.82 (Ar), 156.53 (HC=N), 175.18 (C=O), 176.08 (C=O); MS m/z: Found [M-**.**CO_2CH_3]+ 288.2089, requires 288.2097.

Dimethyl 2-(benzylideneamino)-2-isopropyldecanedioate (**I6c**): $C_{22}H_{33}NO_4$; Yield: 83.4%; yellow oil, bp: 110°C/10^{-3}Torr; ^{1}H-NMR δ: 0.93-1.00 (dd, 6H, *J*= 4.57 Hz, $2CH_3$),1.61-1.94 (m, 11H, CH, $5CH_2$), 2.33-2.40 (t, 1H, *J*= 10.44 Hz, CH_2), 3.39-3.45 (t, 2H, *J*= 8.37 Hz, CH_2), 3.69 (s, 3H, MeCO), 3.76 (s, 3H, MeCO), 7.37-7.82 (m, 5H, Ph), 8.26 (s, 1H, CH=); ^{13}C-NMR δ: 18.63 (CH_3), 19.48 (CH_3), 21.11 (CH_2), 23.40 (CH_2), 28.08 (CH_2), 31.59 (CH), 31.71 (CH_2), 31.95 (CH_2), 51.49 (CH_2), 51.91 (CH_2), 62.11 (OCH_3), 64.25 (OCH_3), 80.37 (C), 128.54-135.68 (Ar), 163.28 (HC=N), 172.41 (C=O), 173.52 (C=O); MS m/z: Found [M-**.**CO_2CH_3]+ 316.2406, requires 316.2410.

Methyl 2-methyl-5-oxopyrrolidine-2-carboxylate (**L5a**): $C_7H_{11}NO_3$; Yield: 85%, viscous and brown aspect; ^{1}H-NMR δ: 1.47 (s, 3H, CH_3), 1.92-2.02 (t, 2H, *J*= 8.32 Hz, CH_2), 2.32-2.48 (t, 2H, *J*= 5.87 Hz, CH_2), 3.70 (s, 3H, MeCO), 6.10 (large s, 1H, NH); ^{13}C-NMR δ: 25.88 (CH_3), 30.46 (CH_2), 32.67 (CH_2), 53.09 (CH_3CO), 62.83 (C), 174.91 (C=O), 178.17 (C=O); MS m/z: Found [M-**.**CO_2CH_3]+ 98.0608, requires 98.0605.

Methyl 2-methyl-6-oxopiperidine-2-carboxylate (**L6a**): $C_8H_{13}NO_3$; Yield: 81%, brown pasty solid; ^{1}H-NMR δ: 1.41 (s, 3H, C$\underline{H}_3$), 1.58-1.70 (qt, 2H, *J*= 7.56 Hz, C$\underline{H}_2$), 2.22-2.40 (t, 2H, *J*= 11.63 Hz, C$\underline{H}_2$), 3.40-3.53 (t, 2H, *J*= 10.43 (C$\underline{H}_2$), 3.75 (s, 3H, $\underline{Me}$CO), 6.59 (large s, 1H, N$\underline{H}$); ^{13}C-NMR δ: 20.55 ($\underline{C}H_3$), 22.39 ($\underline{C}H_2$), 30.60 ($\underline{C}H_2$), 32.04 ($\underline{C}H_2$), 51.12 ($\underline{C}H_3CO$), 59.71 ($\underline{C}$), 172.00 ($\underline{C}$=O), 174.35 ($\underline{C}$=O); MS m/z: Found [M-**.**CO_2CH_3]$^+$ 112.07624, requires 112.0769.

Methyl 2-methyl-7-oxoazepane-2-carboxylate (**L7a**): $C_9H_{15}NO_3$; Yield: 85%, brown paste; ^{1}H-NMR δ: 1.01-1.74 (m, 4H, 2C$\underline{H}_2$),1.46 (s, 3H, C$\underline{H}_3$), 2.35-2.42 (t, 2H, *J*= 9 Hz, C$\underline{H}_2$), 3.15-3.36 (t, 2H, *J*= 10.03 Hz, (C$\underline{H}_2$), 3.71 (s, 3H, $\underline{Me}$CO), 5.93 (large s, 1H, N$\underline{H}$); ^{13}C-NMR : δ: 23.10 ($\underline{C}H_2$), 23.74 ($\underline{C}H_2$), 23.81 ($\underline{C}H_3$), 29.69 ($\underline{C}H_2$), 33.89 ($\underline{C}H_2$), 52.12 ($\underline{C}H_3CO$), 68.41 ($\underline{C}$), 174.03 ($\underline{C}$=O), 174.66 ($\underline{C}$=O); MS m/z: Found [M-**.**OCH_3]+ 172.1047, requires 172.1052.

Methyl 2-methyl-8-oxoazocane-2-carboxylate (**L8a**): $C_{10}H_{17}NO_3$; Yield: 85%, brown paste; ^{1}H-NMR δ: 1.20-1.74 (m, 6H, 3C$\underline{H}_2$),1.53 (s, 3H, C$\underline{H}_3$), 2.27-2.35 (t, 2H, *J*= 10.13 Hz, C$\underline{H}_2$), 3.23-3.41 (t, 2H, *J*= 5.21 Hz, (C$\underline{H}_2$), 3.69 (s, 3H, $\underline{Me}$CO), 5.84 (large s, 1H, N$\underline{H}$); ^{13}C-NMR δ: 23.15 ($\underline{C}H_2$), 23.74 ($\underline{C}H_2$), 23.81 ($\underline{C}H_3$), 29.69 ($\underline{C}H_2$), 33.89 ($\underline{C}H_2$), 52.12 ($\underline{C}H_3CO$), 68.41 ($\underline{C}$), 174.03 ($\underline{C}$=O), 174.66 ($\underline{C}$=O); MS m/z: Found [M-**.C**O_2H]+ 172.1320, requires 172.1337.

Methyl 2-methyl-10-oxoazecane-2-carboxylate (**L9a**): $C_{12}H_{21}NO_3$; Yield: 83%, brown paste; ^{1}H-NMR δ: 1.03-1.29 (m, 10H, 5C$\underline{H}_2$),1.49 (s, 3H, C$\underline{H}_3$), 1.58-1.72 (t, 2H, *J*= 12.5 Hz, C$\underline{H}_2$), 2.26-2.36 (t, 2H, *J*= 11 Hz, (C$\underline{H}_2$), 3.66 (s, 3H, $\underline{Me}$CO), 5.56 (large s, 1H, N$\underline{H}$); ^{13}C-NMR δ: 18.85 ($\underline{C}H_2$), 19.25 ($\underline{C}H_2$), 20.35 ($\underline{C}H_2$), 24.25 ($\underline{C}H_2$), 25.37 ($\underline{C}H_2$), 29.69 ($\underline{C}H_3$), 34.57 ($\underline{C}H_2$), 35.79 ($\underline{C}H_2$), 51.46 ($\underline{C}H_3CO$), 66.31 ($\underline{C}$), 175.00 ($\underline{C}$=O), 175.75 ($\underline{C}$=O); MS m/z: Found [M-**.C**O_2H]+ 200.1642, requires 200.16505.

Methyl 5-oxo-2-phenylpyrrolidine-2-carboxylate (**L5b**): $C_{12}H_{13}NO_3$: Yield: 86%, brown dough, ^{1}H NMR (300 MHz, CDCl3): δ: 2.60-2.66 (t, 2H, J= 3.95 Hz, C$\underline{H}_2$),3.01-3.08 (t, 2H, J= 9 Hz, C$\underline{H}_2$), 3.79 (s, 3H, $\underline{Me}$CO), 5.78 (large s, 1H, N$\underline{H}$), 7.35-7.79 (m, 5H, Ph), ^{13}C NMR (75 MHz, $CDCl_3$): δ: 20.24 ($\underline{C}H_2$), 21.87 ($\underline{C}H_2$), 30.36 ($\underline{C}H_3CO$), 66.51 ($\underline{C}$), 126.74 (Ar$\underline{C}$H), 127.12 (Ar$\underline{C}$H), 128.39 (Ar$\underline{C}$H), 128.78 (Ar$\underline{C}$H), 129.52 (Ar$\underline{C}$H), 131.33 (Ar$\underline{C}$H), 135.58 (Ar$\underline{C}$), 137.21 (Ar$\underline{C}$), 176.70 ($\underline{C}$=O), 176.88 ($\underline{C}$=O); m/z: Found [M-**.C**O_2Me]+ 160.0758, requires 160.07624.

Methyl 6-oxo-2-phenylpiperidine-2-carboxylate (**L6b**): $C_{13}H_{15}NO_3$; Yield: 88%, brown paste; ^{1}H-NMR δ: 1.55-1.68 (qt, 2H, J= 6 Hz, C$\underline{H}_2$), 2.25-2.31 (t, 2H, J= 5 Hz, C$\underline{H}_2$), 2.40-2.49 (t, 2H, J= 4.35 Hz, C$\underline{H}_2$), 3.80 (s, 3H, $\underline{Me}$CO), 6.52 (large s, 1H, N$\underline{H}$), 7.33-7.90 (m, 5H, Ph); ^{13}C-NMR δ: 17.28 ($\underline{C}H_2$), 30.88 ($\underline{C}H_2$), 33.04 ($\underline{C}H_2$), 53.13 ($\underline{C}H_3CO$), 65.61 ($\underline{C}$), 125.05 (Ar$\underline{C}$H), 128.30 (Ar$\underline{C}$H), 129.00 (Ar$\underline{C}$H), 140.71 (Ar$\underline{C}$), 171.80 ($\underline{C}$=O), 171.99 ($\underline{C}$=O); MS m/z: Found [M+**.**] 233.1061, requires 233.10519.

Methyl 7-oxo-2-phenylazepane-2-carboxylate (**L7b**): $C_{14}H_{17}NO_3$; Yield: 79%, brown paste; ^{1}H-NMR δ: 1.37-1.59 (qt, 2H, J= 6 Hz, C$\underline{H}_2$), 1.63-1.76 (qt, 2H, J= 3.5 Hz, C$\underline{H}_2$), 2.23-2.41 (t, 2H, J= 11 Hz, C$\underline{H}_2$), 3.41-3.47 (t, 2H, J= 9 Hz, C$\underline{H}_2$), 3.70 (s, 3H, $\underline{Me}$CO), 6.02 (large s, 1H, N$\underline{H}$), 7.32-7.83 (m, 5H, Ph); ^{13}C-NMR δ: 22.94 ($\underline{C}H_2$), 24.82 ($\underline{C}H_2$), 36.14 ($\underline{C}H_2$), 37.64 ($\underline{C}H_2$), 52.81 ($\underline{C}H_3CO$), 65.19 ($\underline{C}$),

125.01-127.92 (ArH), 141.75 (ArC), 174.85 (C=O), 176.02 (C=O); MS m/z: Found [M-**.**COOH]$^+$ 220.1331, requires 220.13375.

Methyl 8-oxo-2-phenylazocane-2-carboxylate (**L8b**): $C_{15}H_{19}NO_3$; Yield: 78%, brown paste; ^{1}H-NMR δ: 1.10-1.84 (m, 6H, 3CH_2), 2.21-2.41 (t, 2H, J= 12 Hz, CH_2), 2.98-3.05 (t, 2H, J= 9 Hz, CH_2), 3.73 (s, 3H, MeCO), 6.32 (large s, 1H, NH), 7.33-7.86 (m, 5H, Ph); ^{13}C-NMR δ: 21.74 (CH_2), 22.22 (CH_2), 23.14 (CH_2), 36.36 (CH_2), 36.93 (CH_2), 52.86 (CH_3CO), 65.36 (C), 125.01-127.92 (ArH), 141.31 (ArC), 175.81 (C=O), 176.83 (C=O); MS m/z: Found [M-**.**COOH]$^+$ 234.1488, requires 234.1494.

Methyl 10-oxo-2-phenylazecane-2-carboxylate (**L9b**): $C_{17}H_{23}NO_3$; Yield: 79%, brown paste; ^{1}H-NMR δ: 0.92-1.36 (m, 10H, 5CH_2), 1.47-1.76 (t, 2H, J= 9.31 Hz, CH_2), 2.21-2.37 (t, 2H, J= 10.63 Hz, CH_2), 3.71 (s, 3H, MeCO), 6.36 (large s, 1H, NH), 7.34-8.06 (m, 5H, Ph), ^{13}C-NMR δ: 18.84 (CH_2), 19.04 (CH_2), 20.43 (CH_2), 22.42 (CH_2), 30.61 (CH_2), 36.73 (CH_2), 37.43 (CH_2), 52.81 (CH_3CO), 65.52 (C), 125.11-128.35 (ArH), 141.00 (ArC), 176.37 (C=O), 176.76 (C=O); MS m/z: Found [M-**.**COOH]$^+$ 262.1789, requires 262.1807.

Methyl 2-isopropyl-5-oxopyrrolidine-2-carboxylate (**L5c**): $C_9H_{15}NO_3$; Yield: 85%, brown paste; ^{1}H-NMR δ: 1.01-1.06 (dd, 6H, *J*= 9 Hz, 2CH_3), 1.08-1.30 (m, 1H, *J*= 6 Hz, CH), 2.93-3.00 (t, 2H, *J*= 9 Hz, CH_2), 3.58-3.65 (t, 2H, *J*= 9 Hz, CH_2), 3.77 (s, 3H, MeCO), 6.09 (large s, 1H, NH); ^{13}C-NMR δ: 18.56 (CH_3), 19.15 (CH_3), 28.25 (CH), 30.13 (CH_2), 30.3 (CH_2), 53.03 (OCH_3), 69.77 (C), 172.92 (C=O), 174.51 (C=O); MS m/z: Found [M-**.**CO_2CH_3]$^+$ 126.1030, requires 126.1052.

Methyl 2-isopropyl-6-oxopiperidine-2-carboxylate (**L6c**): $C_{10}H_{17}NO_3$; Yield: 82%, brown paste; ^{1}H-NMR δ: 1.04-1.29 (dd, 6H, *J*= 9 Hz, 2CH_3), 1.82-1.95 (qt, 2H, *J*= 6.5 Hz, CH_2), 2.03-2.09 (m, 1H, *J*= 6 Hz, CH), 2.18-2.24 (t, 2H, *J*= 9 Hz, CH_2), 2.36-2.42 (t, 2H, *J*= 9 Hz, CH_2), 3.71 (s, 3H, MeCO), 6.31 (large s, 1H, NH); ^{13}C-NMR δ: 18.60 (CH_3), 19.16 (CH_3), 20.13 (CH_2), 29.65 (CH), 31.14 (CH_2), 34.13 (CH_2), 53.28 (OCH_3), 65.43 (C), 172.55 (C=O), 173.58 (C=O); MS m/z: Found [M]$^+$ 199.1196, requires 199.1208.

Methyl 2-isopropyl-7-oxoazepane-2-carboxylate (**L7c**): $C_{11}H_{19}NO_3$; Yield: 80%, brown paste; ^{1}H-NMR δ: 1.04-1.27 (dd, 6H, *J*= 9 Hz, 2CH_3), 1.32-1.45 (m, 4H, 2CH_2), 1.66-1.84 (t, 2H, *J*= 6 Hz, CH_2), 2.06-2.17 (m, 1H, *J*= 6 Hz, CH), 2.35-2.45 (t, 2H, *J*= 9 Hz, CH_2), 3.70 (s, 3H, MeCO), 6.90 (large s, 1H, NH); ^{13}C-NMR δ: 20.12 (CH_3), 19.86 (CH_3), 21.24 (CH_2), 23.23 (CH_2), 25.92 (CH_2), 29.46 (CH), 34.67 (CH_2), 52.68 (OCH_3), 69.52 (C), 175.18 (C=O), 175.41 (C=O); MS m/z: Found [M-COOH]$^+$ 186.1356, requires 186.1365.

Methyl 2-isopropyl-8-oxoazocane-2-carboxylate (**L8c**): $C_{12}H_{21}NO_3$; Yield: 78%, black paste; ^{1}H-NMR δ: 0.80-1.01 (m, 6H, 3CH_2), 1.05-1.27 (dd, 6H, *J*= 9 Hz, 2CH_3), 1.89-1.95 (t, 2H, *J*= 6 Hz, CH_2), 2.01-2.07 (m, 1H, *J*= 6 Hz, CH), 2.38-2.44 (t, 2H, *J*= 9 Hz, CH_2), 3.69 (s, 3H, MeCO), 7.13 (large s, 1H, NH), ^{13}C-NMR δ: 19.43 (CH_2), 21.43 (CH_2), 21.89 (CH_2), 24.32 (CH_3), 25.46 (CH_3), 28.20 (CH_2), 31.27 (CH), 33.65 (CH_2), 52.78 (OCH_3), 68.72 (C), 174.98 (C=O), 176.38 (C=O); MS m/z: Found [M-COOH]$^+$ 200.1513, requires 200.1521.

Methyl 2-isopropyl-10-oxoazecane-2-carboxylate (**L9c**): $C_{14}H_{25}NO_3$; Yield: 76%, black paste; ^{1}H-NMR δ: 0.86-1.02 (dd, 6H, *J*= 6 Hz, 2C$\underline{H}_3$), 1.17-1.44 (m, 10H, 5C$\underline{H}_2$), 1.65-1.96 (m, 1H, *J*= 6 Hz, C$\underline{H}$), 2.21-2.34 (t, 2H, *J*= 9 Hz, C$\underline{H}_2$), 3.40-3.56 (t, 2H, *J*= 10.5 Hz, C$\underline{H}_2$), 3.70 (s, 3H, MeCO), 6.28 (large s, 1H, N$\underline{H}$); ^{13}C-NMR δ: 19.13 ($\underline{C}H_3$), 19.45 ($\underline{C}H_3$), 21.79 ($\underline{C}H_2$), 20.13 ($\underline{C}H_2$), 25.24 ($\underline{C}H_2$), 26.05 ($\underline{C}$H), 28.15 ($\underline{C}H_2$), 30.63 ($\underline{C}H_2$). 35.12 ($\underline{C}H_2$), 35.67 ($\underline{C}H_2$), 52.98 (O$\underline{C}H_3$), 68.83 ($\underline{C}$), 173.65 ($\underline{C}$=O), 176.68 ($\underline{C}$=O); MS m/z: Found $[M\text{-}COOH]^+$ 228.18151, requires 228.1834.

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