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N-Heterocyclic olefin catalysis for the ring opening of cyclic amidine compounds: a pathway to the synthesis of ε-caprolactam and γ-lactam-derived amines

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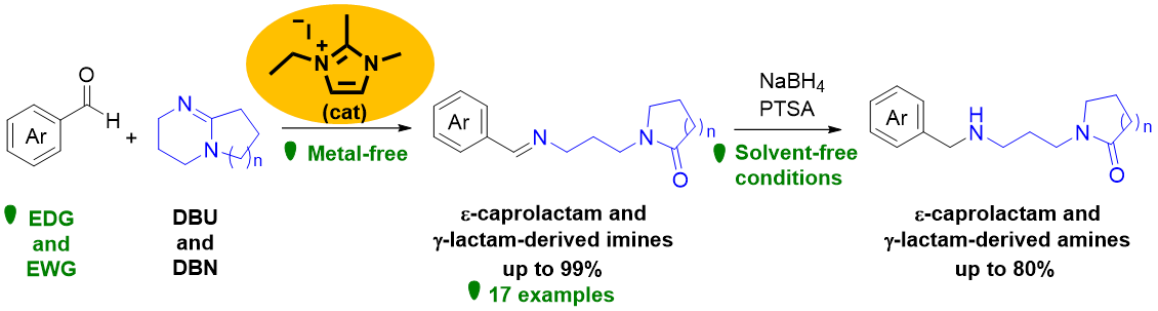
Supporting Information



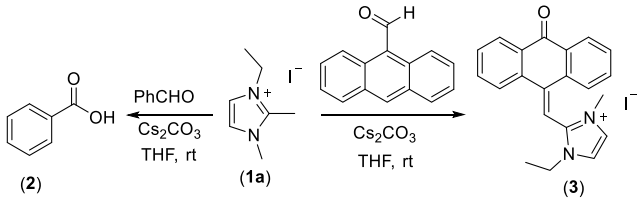
ABSTRACT: For the first time, 1,2-dimethyl-3-ethylimidazolium iodide (**1a**) catalyzes the ring opening of the bicyclic amidine system of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) or DBN (1,5-diazabicyclo[4.3.0]non-5-ene) on reaction with aldehydes. The mechanism here proposed involves a N-heterocyclic olefin (NHO) catalytic species that acts as a nucleophile to promote the cyclic amidine ring opening. The resulting ε-caprolactam and γ-lactam-derived imines were obtained in moderate to excellent yields (28-99%) and reduced to the corresponding amines by sodium borohydride. Confirmation of the imine product was achieved via single-crystal X-ray diffraction studies.

INTRODUCTION

N-heterocyclic olefins (NHO), the alkylidene derivatives of N-heterocyclic carbenes, emerged in the last years as promising organocatalysts with enhanced nucleophilicity and Brønsted basicity in result of its highly polarized C–C bond.[1,2] The exceptional donor capacity of such electron-rich olefin was explored by some authors in metal complexes[1,3-5] as a catalyst in polymerization of acrylic monomers[6,7] or lactone monomers[8] in transesterification reactions[9] or as captors and catalyst in reactions with CO_2.[10,11] As expected, alkylation of this 1,3-dipolar species is feasible and was used by Beller et al.[12] to prepare a phosphine ligand for a palladium catalyst. Notwithstanding the extensive work done with the frequently studied class of imidazolium-based ionic liquids (IL), very little has been published concerning the reactivity of these azolium salts when functionalized at the C2-position from where the NHO emerge on treatment with a base.[13] From our recent work we have observed an unusual reactivity associated to NHO derived from 1,2-dimethyl-3-ethylimidazolium iodide (**1a**), namely the oxidation of aromatic aldehydes to the corresponding carboxylic acids (**2**) in the presence of a mild base[14] or the synthesis of a new heteroarylidene-9(10*H*)-anthrone structure (**3**) (Scheme 1).[15] In both cases an oxidative role of 1,2-dimethyl-3-ethylimidazolium iodide (**1a**) was found with the isolation of a transient and unstable reduced species derived thereof.[14] The overlap between these two important fields, the azolium salts and the NHO species to which it can give rise, may provide access to unknown and unpredictable reactivity with great advance in both parts and with a new area to which one should be paying attention, the concept of NHOs from azolium-based salts.[16,17]

Diamines, specially 1,2-diamines or 1,4-diamines the majority of which display C2-symmetry have a special role in coordination chemistry.[18-20] The 1,3-diamine family has not been used so often in coordination chemistry[20-22] due to the limited methods documented for its synthesis. Furthermore, 1,3-diamines are important structural motifs existing in many natural products with an increasing importance in pharmaceutical chemistry.[23] They are also an important building block in synthetic organic chemistry namely as a substrate for the preparation of cyclic amidinium salts which are common synthetic precursors for the preparation of N-heterocyclic carbenes (NHC).[24] Even so, limited efforts have been devoted to the development of effective synthetic approach to 1,3-diamines.[25]

Scheme 1. Reactivity of 2-substituted imidazolium salt with aldehydes

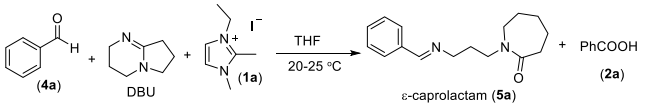


Rueping et al.[26] used enantiopure pyrazolidine and pyrazoline derivatives as precursors for the preparation of chiral 1,3-diamine derivatives through cleavage of the N-N bond of the pyrazolidine moiety in the presence of SmI_2.[26] Other methods described for the synthesis of 1,3-diamines involved the Michael addition of nitroalkanes to nitroalkenes [27] or the Mannich-type reaction between aldimines and nitriles[28,29] both requiring further hydrogenation. Other methods reported in the literature are more laborious involving the ring opening of the aziridine by nucleophiles.[30] Although scarcely reported in the literature, a way of achieving a 1,3-diamine propane chain involves the ring opening of cyclic amidine compounds such as DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) or DBN (1,5-diazabicyclo[4.3.0]non-5-ene). The role of DBN or DBU as a sterically hindered, weakly nucleophilic amidine type strong base and catalyst is well known,[31] especially in dehydrohalogenation reactions, but some reports in literature revealed their ability to act as nucleophiles.[32] Its capacity to act as nucleophile led to some unexpected results revealed by the ring opening of the bicyclic amidine reported the first time by Lambert in 1994[33] and followed by a few others involving as ultimate product, ε-caprolactam derivatives.[34-37] The nucleophilic character of DBU and DBN was observed on the reaction with carbonyl electrophilic species namely, methyl esters,[38] *p*-nitrophenyl carbonate,[39] imidazolides[40]) benzoxazinones,[37] on the hydrolysis of amide carbonyls[41] or even in palladium-catalyzed carbonylation reactions[42] in all cases towards lactams resulting from the ring opening of the cyclic amidine. [37,40]

RESULTS AND DISCUSSION

Here we disclose a new role of NHO species as catalysts for the ring opening of DBU or DBN on reaction with aldehydes to form the corresponding ε-caprolactam (**5**) and γ-lactam (**6**) derived imines. Initial reactions were performed with benzaldehyde (**4a**) and DBU in the presence of a mole equivalent of **1**, and unexpectedly a ring opening of the amidine system was observed with the formation of the ε-caprolactam derived imine **5a** in 85% yield (Table 1 entry 1). Opposite to what was previously observed by us [14] when using other bases on reactions of **4a** with **1**, the formation of benzoic acid (**2a**) was here detected in very small amount (9%). This could correlate with the oxidative ability of the 2-methylimidazolium salts as studied by cyclic voltammetry and presents a cathodic peak (Ep between -2.59 and -2.62 V a very small shift) (see supporting information). The work up of the reaction involved evaporation to dryness and wash of the crude residue with Et_2O to remove the product and unreacted aldehyde followed by acidification of the residue with HCl 1M and extraction with dichloromethane to remove the corresponding carboxylic acid **2a**.

Table 1. Ring opening of DBU on reaction with benzaldehydes to the corresponding ε-caprolactam derived imine by NHO catalysis[a]

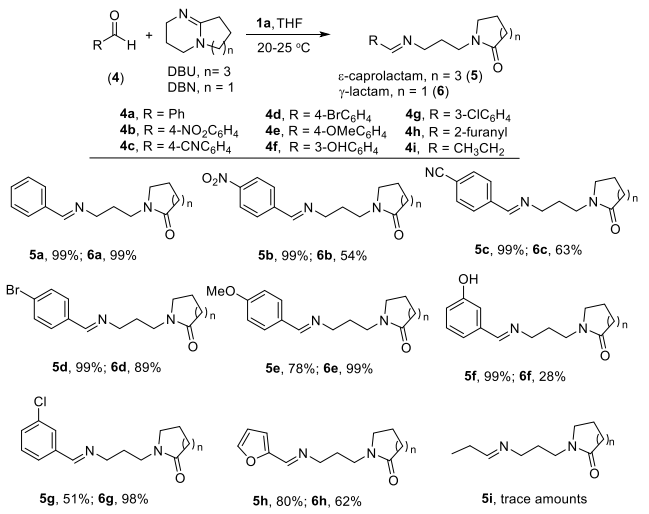


entry	**1** (equiv)	Time (h)	**4**[b] yield (%)	**2** yield (%)	**5**[c] yield (%)
1	1	24	6	9	85
2	1	48	4	10	80
3	1	72	10	9	70
4	1	192	40	9	41
5	0.1	24	7	40	50
6	0.25	24	22	17	60
8[d]	0.1	6	20	10	68
9[d]	0.2	6	0	0	80[e]
10[d]	0.2	8	14	11	74
11	0	24	>99	-	-

[a]Unless otherwise noted, the reaction was conducted on a scale of 0.2 mmol of **4a**, 1.2 equiv of **1a** and DBU (1.2 equiv) in 5 mL of THF at 20-25 °C; [b]recovered; [c]yield obtained by NMR integration of the Et_2O layer; [d]reaction performed with 1 equiv of DBU; [e]DBU was identified as 20% in the Et_2O layer.

The imidazolium salt remained in the aqueous phase. By thin layer chromatography it was possible to observe, during the course of the reaction, the presence of aldehyde which could be due to unreacted starting material or hydrolysis of the imine during the elution. Thus, we ran the reaction for several days (Table 1, entries 1 to 4) without taking particular conditions to exclude moisture from the reaction mixture. In these cases we observed an increase on the amount of recovered aldehyde which could be associated with hydrolysis of compound **5a**. Next, we turned our attention to a possible catalytic role of the imidazolium **1a**. The yields decreased slightly as the amount of acid increased (Table 1, entry 1 *vs* entries 5 and 6). Since we observed that the yield of the aldehyde recovered increased with time, we reduced the time of reaction (6 h) without the imine formation yield being affected (Table 1, entries 5 *vs* 8 and 9 *vs* 10). A blank assay was performed in the absence of **1a** and no formation of **5a** was observed (Table 1, entry 11). A similar study was performed with DBN which allowed us to achieve the γ-lactam derived imine (**6a**) in very good yield 99 %. Using benzaldehyde as substrate, the best reaction conditions found comprised the use of 10 mol% of **1a** on reaction with DBU and 20 mol% of **1a** in reaction with DBN. After optimization of the reaction conditions for both DBU and DBN, the substrate scope was explored (Scheme 2). With aliphatic aldehydes we have observed the GC-MS and on the NMR crude the presence of **5i** in trace amounts. The compound must be instable since the hydrolysis compound **8** (Scheme 3) was the major compound identified by GC-MS together with unreacted DBU. Fortunately, a crystal was obtained for compound **6b** which allowed us to confirm by X-ray crystallography the structure of the γ-lactam derived imine (SI, Figure S1).

Scheme 2. Scope of substrates[a]



[a]Unless otherwise noted, the reaction was conducted on a scale of 0.66 mmol DBU and **4** (1 equiv) or 0.8 mmol of DBN and **4** (1 equiv) in 5 mL of THF at 30 °C for 6h. For the ε-caprolactam (**5**) 20 mol% of **1a** were used and for the γ-lactam (**6**) 10 mol% of **1a** were used.

Then, we turned our attention to other imidazolium salts as **1b** and **1c**. We have observed that the amount of benzoic acid increased in relation to **1a** (Table 2, entries 1 and 7 vs Table 1, entry 9).

Taking in attention the results, a mechanism proposal is presented in scheme 3. After the attack of the NHO to the activated intermediate of DBU-aldehyde (**7**), a ring opening of the amidine ring occurs in which, after water addition, the ε-caprolactam (**5**) is obtained and the NHO is recovered. The formation of the ε-caprolactam ring opening product of DBU (**8**) was also identified in mixtures of imine and DBU. Although initially we though that **8** could have origin on the hydrolysis of **5**, the absence of aldehyde on these samples led us to propose a catalytic role for DBU on the hydrolysis reaction (Scheme 3) assisted by the presence of water (no measures for the exclusion of moisture were taken for the samples stored). To exclude the possible formation of **8** by catalysis of **1a**, an assay was performed between the imidazolium salt **1a** and DBU in the absence of aldehyde. After 6h and 24h no formation of **8** was observed. Also, resting samples of mixtures of DBU and **5a** shows with time the formation of compound **8** justifying the mechanism presented.

To extend the applicability of the methodology, the compounds were further reduced with $NaBH_4$/PTSA to get the corresponding ε-caprolactam (**9**) γ-lactam (**10**) derived amines using a very simple procedure[43] (Scheme 4).

Scheme 3. Proposed mechanism for the ring opening of cyclic amidine by NHO catalysis

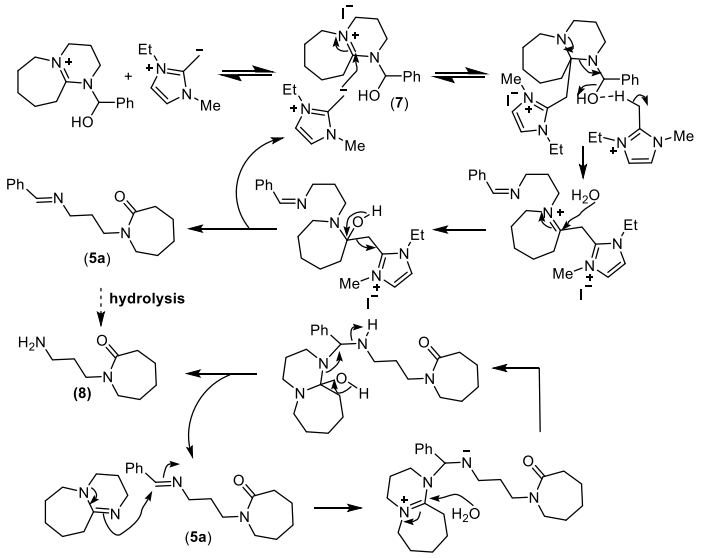
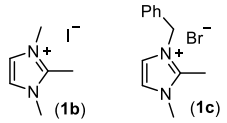


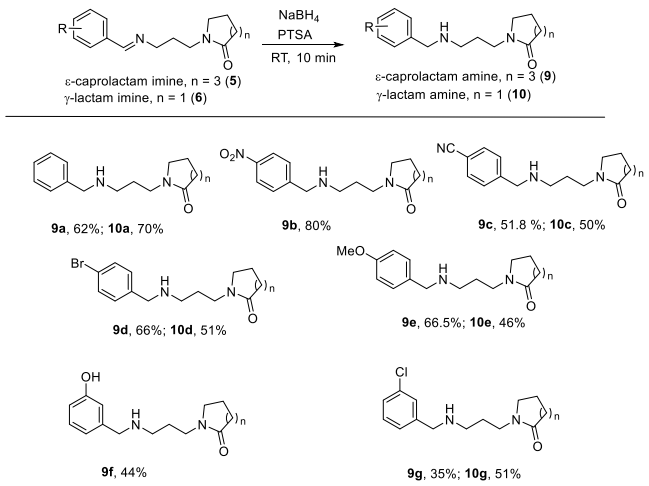
Table 2. Screening with other imidazolium salts[a]



entry	**4**	DBN or DBU	**1**	**2** yield (%)	**5** yield (%)	**6** yield (%)
1	**4a**	DBU[a]	**1b**	22	22	
2	**4b**	DBU[a]	**1b**		32	
3	**4e**	DBU[a]	**1b**		73	
4	**4a**	DBN[b]	**1b**			72
5	**4b**	DBN[b]	**1b**			72
6	**4e**	DBN[b]	**1b**			38
7	**4a**	DBU[a]	**1c**	13	65	
8	**4b**	DBU[a]	**1c**		10	
9	**4e**	DBU[a]	**1c**		29	
10	**4a**	DBN[b]	**1c**			78
11	**4b**	DBN[b]	**1c**			59
12	**4e**	DBN[b]	**1c**			66

[a]Reaction conducted on a scale of 0.66 mmol of 4 in 5 mL of THF at 20-25 °C with 20 mol% of 1 for the reaction conducted with DBU (1 equiv); [b]Reaction conducted on a scale of 0.80 mmol of 4 in 5 mL of THF at 20-25 °C 10 mol% of 1 for the reaction conducted with DBN (1 equiv). Scheme 4. Reduction of imines substrates[a]

Scheme 4. Reduction of imines substrates[a]



[a]Unless otherwise noted, the reaction was conducted on a scale of 0.15 to 0.20 mmol of imines **5** or **6**.

CONCLUSIONS

In summary, new families of ε-caprolactam and γ-lactam derived imines were obtained in excellent yields by catalysis with 2-methylimidazolium salt derived NHO. The reactivity of 1,2-dimethyl-3-alkyl imidazolium iodide (**1**) highlighted by these unexpected results as well as by previous work from the group underlines the broad potential of these compounds, easily prepared and easy to handle, as non-passive species in effecting a wide range of synthetic applications. The work here presented is an interesting approach to 1,3-diamines privileged structures. This is an important motif in natural products, but also an important building block in synthetic organic chemistry with limited efforts devoted effectively to its synthetic approach in literature.

EXPERIMENTAL SECTION

General methods and materials. All the reagents and solvents were obtained commercially and these were used without further purification. The solvents used were dried using current laboratory techniques. Thin layer chromatography (TLC) was carried out on aluminium-backed Kieselgel 60 F254 silica gel plates (Merck). Plates were visualized either by UV light (254 and/or 366nm). Preparative layer chromatography (PLC) was performed on Merck Kieselgel GF 254 silica gel plates with a thickness of 0.5 mm or 1 mm. Column chromatography was carried out using silica gel Kieselgel 60 (Merck), 70 - 230 mesh particle size as stationary phase, in normal phase chromatography. Ultraviolet (UV) spectroscopy spectra were recorded on a Thermo Corporation spectrophotometer, Helius γ, on quartz cell support. Absorption spectrum measurements were made in the range of 220 to 400 nm. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX400 at 400 and 100 MHz, respectively. Mass spectra (MS) using the ESI-TOF or APCI technique were obtained from Unidade de Masas e Proteómica, the University of Santiago de Compostela, Spain.

Crystallographic details: Crystals of **6b** suitable for single-crystal X-ray analysis grew from the oil obtained from the evaporation of a diethyl ether solution of **6b**. Selected crystals were covered with Fomblin (polyfluoroether oil) and mounted on a nylon loop. The X-ray diffraction data were collected at 296(2) K on a Bruker D8 Venture diffractometer equipped with a Photon 100 CMOS detector, using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). Data were processed using APEX2 suite software package, which includes integration and scaling (SAINT), absorption corrections (SADABS) and space group determination (XPREP). Structure solution and refinement were done using direct methods with the programs SHELXS-16 inbuilt in APEX and WinGX-Version 2014.1[44] software packages. All non-hydrogen atoms were refined anisotropically and the hydrogen atoms were inserted in idealized positions and allowed to refine riding on the parent carbon atom, except for the hydrogen atoms of the water molecule that were located in the electron density map and refined isotropically. The molecular diagrams were drawn with Mercury,[45] included in the software package. Table S1 contains crystallographic experimental data and structure refinement parameters. Selected structural parameters are listed in Table S2. CCDC 1876034 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

General procedure for the synthesis of ε-caprolactam and γ-lactam derived imines (5 and 6): In a round bottom flask equipped with a magnetic stirrer, dry THF (C = 0.01M), DBU or DBN (1 equiv.) and 1,2-dimethyl-3-ethylimidazolium iodide (**1**) (20 mol % for DBU or 10 mol % for DBN) were stirred at rt for 15 min. Then, the aldehyde derivative (**4**) (1 equiv.) was added to the reaction mixture. The reaction was stirred at 30ºC for 6h. The reaction was followed by TLC, eluting with a mixture of CH_2Cl_2/ MeOH (95/5). The reaction mixture was evaporated to dryness and the crude was washed with ethyl ether (20 to 30 mL). The ethyl phase was evaporated under reduced pressure to dryness to give the following products.

1-(3-(Benzylideneamino)propyl)azepan-2-one (5a): From DBU (0.05 mL, 0.34 mmol), compound **1** (16.9 mg, 0.07 mmol) and compound **4a (**34 mmL, 0.34 mmol), compound **5a** was obtained as a colorless oil (85.7 mg, 0.33 mmol); η = 99% ; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.28 (s, 1H, N=CH), 7.72-7.69 (m, 2H, ArH), 7.40-7.38 (m, 3H, ArH), 3.62 (t, *J* = 7.2 Hz, 2H, CH_2), 3.46 (t, *J* = 7.2 Hz, 2H, CH_2), 3.37-3.34 (m, 2H, CH_2), 2.50-2.47 (m, 2H, CH_2), 1.92 (t, *J* = 7.2 Hz, 2H, CH_2), 1.70-1.62 (m, 6H, CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.9 (C=O), 161.6 (HC=N), 136.3 (C), 130.7(CH), 128.7 (2xCH), 128.3(2xCH), 59.2 (CH_2), 49.5 (CH_2), 46.5 (CH_2), 37.4 (CH_2), 30.1 (CH_2), 29.4 (CH_2), 28.8 (CH_2), 23.6 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M]^+$ Calcd for $C_{16}H_{22}N_2O$ 258.1732; Found 258.1723.

1-(3-((4-Nitrobenzylidene)amino)propyl)azepan-2-one (5b): From DBU (0.05 mL, 0.34 mmol), compound **1** (16.9 mg, 0.067 mmol) and compound **4b (**50.6 mg, 0.34 mmol), compound **5b** was obtained as a yellow oil (100.7 mg, 0.33 mmol); η = 99%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.38 (s, 1H,N=CH), 8.26 (d, *J* = 8.4 Hz, 2H, ArH), 7.53 (d, *J* = 8.4 Hz, 2H, ArH), 3.61 (t, *J* = 7.2 Hz, 2H, CH_2), 3.45 (t, *J* = 7.2 Hz, 2H, CH_2), 3.37-3.35 (m, 2H, CH_2), 2.51-2.48 (m, 2H, CH_2) 1.91 (t, *J* = 7.2 Hz, 2H, CH_2), 1.72-1.63 (m, 6H, 3x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.9 (C=O), 159.4 (HC=N), 149.1 (C), 141.8 (C), 128.9 (2xCH), 124.0 (2xCH), 59.4 (CH_2), 49.7 (CH_2), 46.2 (CH_2), 37.4 (CH_2), 30.1 (CH_2), 29.2 (CH_2), 28.9 (CH_2), 23.6

(CH_2) ppm. GC-MS: tr 25.89, m/z 303. HRMS (APCI) m/z: [M + H]$^+$ Calcd for $C_{16}H_{22}N_3O_3$ 304.1656; Found 304.1654.

4-(((3-(2-Oxoazepan-1-yl)propyl)imino)methyl)benzonitrile (5c): From DBU (0.05 mL, 0.34 mmol), compound **1** (16.9 mg, 0.067 mmol) and compound **4c (**43.9 mg, 0.34 mmol), compound **5c** was obtained as a yellow oil (94 mg, 0.33 mmol); η = 99%;^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.32 (s, 1H,N=CH), 7.83 (d, *J* = 8.0 Hz, 2H, ArH), 7.69 (d, *J* = 8.0 Hz, 2H, ArH), 3.66 (t, *J* = 6.8 Hz, 2H, CH_2), 3.46 (t, *J* = 6.8 Hz, 2H, CH_2), 3.37-3.35 (m, 2H, CH_2), 2.51-2.48 (m, 2H, CH_2) 1.94 (t, *J* = 6.8 Hz, 2H, CH_2), 1.72-1.64 (m, 6H, 3x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.9 (C=O), 159.8 (HC=N), 140.2 (C), 132.5 (2xCH), 128.6 (2xCH), 118.7 (C), 113.9 (C), 59.3 (CH_2), 49.7 (CH_2), 46.3 (CH_2), 37.4 (CH_2), 30.1 (CH_2), 29.3 (CH_2), 28.9 (CH_2), 23.6 (CH_2) ppm. GC-MS: tr 24.82, m/z 283. HRMS (APCI) m/z: [M + H]$^+$ Calcd for $C_{17}H_{22}N_3O$ 284.1754 Found 284.1757.

1-(3-((4-Bromobenzylidene)amino)propyl)azepan-2-one (5d): From DBU (0.05 mL, 0.34 mmol), compound **1** (16.9 mg, 0.067 mmol) and compound **4d (**61.9 mg, 0.34 mmol), compound **5d** was obtained as a yellow oil (112 mg, 0.33 mmol); η = 99%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.24 (s, 1H,N=CH), 7.59 (d, *J* = 8.4 Hz, 2H, ArH), 7.53 (d, *J* = 8.4 Hz, 2H, ArH), 3.68 (t, *J* = 7.2 Hz, 2H, CH_2), 3.47 (t, *J* = 7.2 Hz, 2H, CH_2), 3.38-3.36 (m, 2H, CH_2), 2.51-2.48 (m, 2H, CH_2) 1.95 (t, *J* = 6.8 Hz, 2H, CH_2), 1.72-1.64 (m, 6H, 3x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.9 (C=O), 160.4 (HC=N), 135.2 (C), 131.9 (2xCH), 129.6 (2xCH), 125.1 (C), 59.2 (CH_2), 49.8 (CH_2), 46.4 (CH_2), 37.4 (CH_2), 30.1 (CH_2), 29.4 (CH_2), 28.9 (CH_2), 23.6 (CH_2) ppm. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{22}BrN_2O$ 337.0911; Found 337.0910.

*1-(3-((4-Methoxybenzylidene)amino)propyl)azepan-2-one (5e):*From DBU (0.050 mL, 0.34 mmol), compound **1** (16.9mg, 0.067 mmol) and compound **4e (**40.7 mmL, 0.33 mmol), compound **5e** was obtained as a yellow oil (75.5 mg, 0.26 mmol); η = 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.21 (s, 1H,N=CH), 7.66 (d, *J* = 8.4 Hz, 2H, ArH), 6.91 (d, *J* = 8.4 Hz, 2H, ArH), 3.84 (s, 3H, OMe), 3.58 (t, *J* = 7.2 Hz, 2H, CH_2), 3.45 (t, *J* = 7.2 Hz, 2H, CH_2), 3.37-3.35 (m, 2H, CH_2), 2.51-2.48 (m, 2H, CH_2) 1.91 (t, *J* = 7.2 Hz, 2H, CH_2), 1.71-1.63 (m, 6H, 3x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.9 (C=O), 161.7 (C), 160.9 (HC=N), 129.7 (2xCH), 129.3 (C), 114.1 (2xCH), 59.2 (CH_2), 55.5 (OMe), 49.8 (CH_2), 46.5 (CH_2), 37.5 (CH_2), 30.1 (CH_2), 29.5 (CH_2), 28.9 (CH_2), 23.6 (CH_2) ppm. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{25}N_2O_2$ 289.1913; Found 289.1911.

1-(3-((3-Hydroxybenzylidene)amino)propyl)azepan-2-one (5f):; From DBU (0.05 mL, 0.34 mmol), compound **1** (16.9 mg, 0.067 mmol) and compound **4f (**40.9 mg, 0.34 mmol), compound **5f** was obtained as a yellow oil (91 mg, 0.33 mmol); η = 99%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.19 (s, 1H, N=CH), 7.22 (s, 1H, ArH), 7.17 (t, *J* = 8.0 Hz, 1H, ArH), 7.08 (d, *J* = 7.2 Hz, 1H, ArH), 6.90 (d, J = 7.2 Hz, 1H, ArH), 3.60 (t, *J* = 6.8 Hz, 2H, CH_2), 3.47 (t, *J* = 6.4 Hz, 2H, CH_2), 3.37-3.31 (m, 2H, CH_2), 2.54-2.49 (m, 2H, CH_2) 1.92 (t, *J* = 7.2 Hz, 2H, CH_2), 1.71-1.63 (m, 6H, 3x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 176.2 (C=O), 162.5 (HC=N), 158.8 (C), 137.2 (C), 129.7 (CH), 119.2 (CH), 118.9 (CH), 115.0 (CH), 58.9 (CH_2), 49.8 (CH_2), 46.6 (CH_2), 37.3 (CH_2), 30.0 (CH_2), 29.2 (CH_2), 28.7 (CH_2), 23.4 (CH_2) ppm. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{23}N_2O_2$ 275.1756; Found 275.1754.

1-(3-((3-Chlorobenzylidene)amino)propyl)azepan-2-one (5g): From DBU (0.05 mL, 0.34 mmol), compound **1** (16.9mg, 0.067 mmol) and compound **4g** (0.039mL, 0.34 mmol), compound **5g** was obtained as a yellow oil (50 mg, 0.17 mmol); η = 51%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.24 (s, 1H, N=CH), 7.75 (s, 1H, ArH), 7.56 (d, *J* = 7.6 Hz, 1H, ArH), 7.37-7.40 (m, 2H, ArH), 3.62 (t, *J* = 6.8 Hz, 2H, CH_2), 3.46 (t, *J* = 6.4 Hz, 2H, CH_2), 3.37-3.35 (m, 2H, CH_2), 2.51-2.49 (m, 2H, CH_2) 1.92 (t, *J* = 7.2 Hz, 2H, CH_2), 1.73-1.64 (m, 6H, 3x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.9 (C=O), 160.2 (HC=N), 138.1 (C), 134.9 (C), 130.7 (CH), 130.0 (CH), 127.8 (CH), 126.6 (CH), 59.2 (CH_2), 49.8 (CH_2), 46.4 (CH_2), 37.5 (CH_2), 30.1 (CH_2), 29.4 (CH_2), 28.9 (CH_2), 23.6 (CH_2) ppm. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{22}ClN_2O$ 293.1415; Found 293.1415.

1-(3-((Furan-2-ylmethylene)amino)propyl)azepan-2-one (5h): From DBU (0.05 mL, 0.34 mmol), compound **1** (16.9 mg, 0.067 mmol) and compound **4h** (0.028 mL, 0.34 mmol), compound **5h** was obtained as a yellow oil (67 mg, 0.27 mmol); η = 80%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.10 (s, 1H, N=CH), 7.50 (d, *J* = 2.0 Hz, 1H, HetArH), 6.72 (d, *J* = 3.6 Hz, 1H, HetArH), 6.47 (dd, *J* = 3.6 and 2.0 Hz, 1H, HetArH), 3.59 (t, *J* = 6.8 Hz, 2H, CH_2), 3.44 (t, *J* = 7.2 Hz, 2H, CH_2), 3.36-3.34 (m, 2H, CH_2), 2.51-2.48 (m, 2H, CH_2) 1.94 (t, *J* = 7.2 Hz, 2H, CH_2), 1.71-1.61 (m, 6H, 3x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.9 (C=O), 151.6(C), 150.2 (HC=N), 144.8 (CH), 114.3 (CH), 111.7 (CH), 59.4 (CH_2), 49.7 (CH_2), 46.3 (CH_2), 37.5 (CH_2), 30.1 (CH_2), 29.4 (CH_2), 28.9 (CH_2), 23.6 (CH_2) ppm. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{21}N_2O_2$ 249.1597; Found 249.1598*1-(3-(Benzylidene-amino)propyl)pyrrolidin-2-one (6a):* From DBN (0.05 mL, 0.40 mmol), compound **1** (16.9 mg, 0.067 mmol) and compound **4a** (0.041 mL, 0.40 mmol), compound **6a** was obtained as a colourless oil (103.5 mg, 0.40 mmol); η = 99%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.29 (s, 1H, N=CH), 7.72-7.71 (m, 2H, ArH), 7.41-7.39 (m, 3H, ArH), 3.64-3.61 (m, 2H, CH_2), 3.43-3.37 (m, 4H, 2xCH_2), 2.32 (t, *J* = 8.4 Hz, 2H, CH_2), 2.00-1.93 (m, 4H, 2xCH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.1 (C=O), 161.7 (HC=N), 136.3 (C), 130.7 (CH), 128.7 (2xCH), 128.2 (2xCH), 59.3 (CH_2), 47.3 (CH_2), 40.9 (CH_2), 31.2 (CH_2), 28.5 (CH_2), 18.0 (CH_2) ppm. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{19}N_2O$ 231.1492; Found 231.1492.

1-(3-((4-Nitrobenzylidene)amino)propyl)pyrrolidin-2-one (6b): From DBN (0.05 mL, 0.40 mmol), compound **1** (16.9mg, 0.067 mmol) and compound **4b (**61 mg, 0.40 mmol), compound **6b** was obtained as a yellow solid (66.5 mg, 0.22 mmol)**;** η = 54%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.37 (s, 1H, N=CH), 8.26 (d, *J* = 8.4 Hz, 2H, ArH), 7.89 (d, *J* = 8.4 Hz, 2H, ArH), 3.68 (t, *J* = 6.8 Hz, 2H, CH_2), 3.44-3.36 (m, 4H, 2x CH_2), 2.33 (t, *J* = 8.0 Hz, 2H, CH_2), 2.04- 1.94 (m, 4H, 2x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.2 (C=O), 159.7 (HC=N), 149.1 (C), 141.8 (C), 128.9 (2xCH), 124.0 (2xCH), 59.3 (CH_2), 47.2 (CH_2), 40.7 (CH_2), 31.2 (CH_2), 28.2 (CH_2), 18.0 (CH_2) ppm. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{18}N_3O_3$ 276.1343; Found 276.1346.

4-(((3-(2-Oxopyrrolidin-1-yl)propyl)imino)methyl)benzonitrile (6c): From DBN (0.05 mL, 0.40 mmol), compound **1** (16.9mg, 67,00µmol) and compound **4c (**53 mg, 0.40 mmol), compound **6c** was obtained as a yellow solid (73 mg, 0.26 mmol); η = 63%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.31 (s, 1H, N=CH), 7.83 (d, *J* = 8.0 Hz, 2H, ArH), 7.69 (d, *J* = 8.4 Hz, 2H, ArH), 3.65 (t, *J* = 6.8 Hz, 2H, CH_2), 3.43-3.35 (m, 4H, 2x CH_2), 2.33 (t, *J* = 8.0 Hz, 2H, CH_2), 2.03- 1.92 (m, 4H, 2x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.1 (C=O), 160.0 (HC=N), 140.1 (C), 132.6 (2xCH), 128.6 (2xCH), 118.7 (C), 114.0 (C), 59.2 (CH_2), 47.2 (CH_2), 40.7 (CH_2), 31.2 (CH_2), 28.2 (CH_2), 18.0 (CH_2)

ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}N_3O$ 256.1444; Found 256.1446.

1-(3-((4-Bromobenzylidene)amino)propyl)pyrrolidin-2-one (6d): From DBN (0.05 mL, 0.40 mmol), compound **1** (16.9 mg, 0.067 mmol) and compound **4d (**74.9 mg, 0.40 mmol), compound **6d** was obtained as a brown oil (121.6 mg, 0.36 mmol); η = 89%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.23 (s, 1H, N=CH), 7.59 (d, *J* = 8.4 Hz, 2H, ArH), 7.52 (d, *J* = 8.4 Hz, 2H, ArH), 3.60 (t, *J* = 6.8 Hz, 2H, CH_2), 3.42-3.35 (m, 4H, 2x CH_2), 2.32 (t, *J* = 8.0 Hz, 2H, CH_2), 2.02- 1.90 (m, 4H, 2x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.1 (C=O), 160.6 (HC=N), 153.1 (C), 132.0 (2xCH), 129.6 (2xCH), 125.1 (C), 59.2 (CH_2), 47.2 (CH_2), 40.8 (CH_2), 31.2 (CH_2), 28.3 (CH_2), 18.0 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}BrN_2O$ 309.0594; Found 309.0597.

1-(3-((4-Methoxybenzylidene)amino)propyl)pyrrolidin-2-one (6e): From DBN (0.05 mL, 0.40 mmol), compound **1** (16.9mg, 0.067 mmol) and compound **4e** (0.049 mL, 0.40 mmol), compound **6e** was obtained as a brown oil (115.7 mg, 0.40 mmol); η = 99%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.20 (s, 1H, N=CH), 7.64 (d, *J* = 8.4 Hz, 2H, ArH), 6.90 (d, *J* = 8.4 Hz, 2H, ArH), 3.83 (s, 3H, OMe), 3.58 (t, *J* = 6.8 Hz, 2H, CH_2), 3.42-3.35 (m, 4H, 2x CH_2), 2.31 (t, *J* = 8.0 Hz, 2H, CH_2), 2.01- 1.84 (m, 4H, 2x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.1 (C=O), 161.7 (C-OMe), 161.1 (HC=N), 129.7 (2xCH), 129.2 (C), 114.1 (2xCH), 59.2 (CH_2), 55.5 (OMe), 47.2 (CH_2), 40.9 (CH_2), 31.2 (CH_2), 28.5 (CH_2), 18.0 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{21}N_2O_2$ 261.1600; Found 261.1598.

1-(3-((3-Chlorobenzylidene)amino)propyl)pyrrolidin-2-one (6g): From DBN (0.05 mL, 0.40 mmol), compound **1** (16.9mg, 0.067 mmol) and compound **4g** (0.048 mL, 0.40 mmol), compound **6g** was obtained as a colourless oil (116.5 mg, 0.39 mmol); η = 98%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.23 (s, 1H, N=CH), 7.74 (s, 1H, ArH), 7.56 (d, *J* = 7.2 Hz, 1H, ArH), 7.38-7.30 (m, 2H, ArH), 3.62 (t, *J* = 6.8 Hz, 2H, CH_2), 3.43-3.35 (m, 4H, 2x CH_2), 2.33 (t, *J* = 8.0 Hz, 2H, CH_2), 2.03-1.90 (m, 4H, 2x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.1 (C=O), 160.3 (HC=N), 138.0 (C), 134.9 (C), 130.7 (CH), 130.0 (CH), 127.8 (CH), 126.6 (CH), 59.2 (CH_2), 47.3 (CH_2), 40.8 (CH_2), 31.2 (CH_2), 28.4 (CH_2), 18.0 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}ClN_2O$ 265.1102; Found 265.1102.

1-(3-((Furan-2-ylmethylene)amino)propyl)pyrrolidin-2-one (6h): From DBN (0.05 mL, 0.40 mmol), compound **1** (16.9 mg, 0.067 mmol) and compound **4h (0.0**34 mL, 0.40 mmol), compound **6h** was obtained as a colourless oil (24.6mg, 0.099 mmol); η = 28%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.09 (s, 1H, N=CH), 7.49 (br s, 1H, HetArH), 6.72 (br s, 1H, HetArH), 6.46 (br s, 1H, HetArH), 3.58 (t, *J* = 6.8 Hz, 2H, CH_2), 3.42-3.34 (m, 4H, 2x CH_2), 2.33 (t, *J* = 8.0 Hz, 2H, CH_2), 2.01-1.94 (m, 4H, 2x CH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 175.1 (C=O), 151.5 (C), 150.4 (HC=N), 144.9 (CH), 114.4 (CH), 111.7 (CH), 59.4 (CH_2), 47.2 (CH_2), 40.8 (CH_2), 31.2 (CH_2), 28.4 (CH_2), 18.0 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{17}N_2O_2$ 221.1282; Found 221.1285.

General procedure for the synthesis of ε-caprolactam and γ-lactam derived amines (9 and 10):[43] The sodium borohydride (1 equiv.) and p-toluenesulfonic acid monohydrate (1 equiv.) were added to ε-caprolactam (**5**) or γ-lactam compound (**6**) (1 equiv.) in glass vails for 10–15 min at room temperature under solvent-free conditions. The reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ (10 ml) and extracted with CH_2Cl_2 (3x10 mL). The combined extract was dried over anhydrous Na_2SO_4, filtered and concentrated to give the following products.

1-(3-(Benzylamino)propyl)azepan-2-one (9a): From compound **5a** (50 mg, 0.19 mmol), sodium borohydride (7.3 mg, 0.19 mmol) and p-toluenesulfonic acid monohydrate (36.8 mg, 0.19 mmol), compound **9a** was obtained as a colourless oil (31.4 mg, 0.12 mmol); η = 62%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.16-7.28 (m, 5H, ArH), 3.70 (s, 2H, CH_2), 3.34 (t, *J* = 6.8 Hz, 2H, CH_2), 3.23-3.20 (m, 2H, CH_2), 2.53 (t, *J* = 6.8 Hz, 2H, CH_2), 2.42-2.39 (m, 2H, CH_2), 1.67-1.50 (m, 8H, 4xCH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 176.2 (C=O), 139.4 (C), 128.4(2xCH), 128.4 (2xCH), 127.1(CH), 53.8 (CH_2), 49.6 (CH_2), 45.9 (CH_2), 45.7 (CH_2), 37.2 (CH_2), 30.0 (CH_2), 28.5 (CH_2), 27.9 (CH_2), 23.4 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{25}N_2O$ 261.1961; Found 261.1963.

4-(((3-(2-Oxoazepan-1-yl)propyl)amino)methyl)benzonitrile (9c): From compound **5c** (50 mg, 0.18 mmol), sodium borohydride (6.7 mg, 0.18 mmol) and p-toluenesulfonic acid monohydrate (33.6 mg, 0.18 mmol), compound **9c** was obtained as a yellow oil (40.3 mg, 0.14 mmol); η = 80%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.56 (d, *J* = 7.6 Hz, 2H, ArH), 7.42 (d, *J* = 7.6 Hz, 2H, ArH), 3.78 (s, 2H, CH_2), 3.41 (br s, 2H, CH_2), 3.26 (br s, 2H, CH_2), 2.53 (br s, 2H, CH_2), 2.45 (br s, 2H, CH_2), 1.67 (br s, 4H, 2xCH_2), 1.59 (br s, 4H, 2xCH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 176.1 (C=O), 146.1 (C), 132.1 (2xCH), 128.7 (2xCH), 119.0 (CN), 110.5 (C), 53.4 (CH_2), 49.4 (CH_2), 45.8 (CH_2), 45.4 (CH_2), 37.1 (CH_2), 29.9 (CH_2), 28.5 (CH_2), 28.0 (CH_2), 23.4 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{24}N_3O$ 286.1916; Found 286.1916.

1-(3-((4-Bromobenzyl)amino)propyl)azepan-2-one (9d): From compound **5d** (50 mg, 0.15 mmol), sodium borohydride (5.6 mg, 0.048 mmol) and p-toluenesulfonic acid monohydrate (28.2 mg, 0.15 mol), compound **9d** was obtained as a light brown oil (26.4 mg, 0.078 mmol); η = 52%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.42 (d, *J* = 7.6 Hz, 2H, ArH), 7.19 (d, *J* = 7.6 Hz, 2H, ArH), 3.70 (s, 2H, CH_2), 3.41 (br s, 2H, CH_2), 3.28-3.26 (m, 2H, CH_2), 2.55 (br s, 2H, CH_2), 2.49-2.46 (m, 2H, CH_2), 1.66-1.67 (m, 4H, 2xCH_2), 1.63-1.60 (m, 4H, 4xCH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 176.2 (C=O), 139.1 (C), 131.5 (2xCH), 130.1 (2xCH), 120.8 (C), 53.3 (CH_2), 49.6 (CH_2), 45.9 (CH_2), 45.6 (CH_2), 37.2 (CH_2), 30.0 (CH_2), 28.6 (CH_2), 28.1 (CH_2), 23.5 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{24}BrN_2O$ 339.1068; Found 339.1067.

1-(3-((4-Methoxybenzyl)amino)propyl)azepan-2-one (9e): From compound **5e** (50 mg, 0.17 mmol), sodium borohydride (6.6mg, 0.17 mmol) and p-toluenesulfonic acid monohydrate (32.9 mg, 0.17 mmol), compound **9e** was obtained as a brown oil (33.8 mg, 0.12 mmol); η = 67%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.22 (d, *J* = 8.4 Hz, 2H, ArH), 6.82 (d, *J* = 8.4 Hz, 2H, ArH), 3.76 (s, 3H, OMe), 3.70 (s, 2H, CH_2), 3.40 (br s, 2H, CH_2), 3.27 (br s, 2H, CH_2), 2.58 (br s, 2H, CH_2), 2.46 (br s, 2H, CH_2), 1.70-1.68 (m, 4H, 2xCH_2), 1.60 (br s, 4H, 4xCH_2) ppm. ^{13}C{1H} NMR ($CDCl_3$, 100 MHz) δ: 176.2 (C=O), 158.7 (C-OMe), 131.8 (C), 129.6 (2xCH), 113.8 (2xCH), 55.3 (OMe), 53.2 (CH_2), 49.6 (CH_2), 45.8 (CH_2), 45.7 (CH_2), 37.2 (CH_2), 30.0 (CH_2), 28.6 (CH_2), 27.9 (CH_2), 23.5 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{27}N_2O_2$ 291.2067; Found 291.2067.

1-(3-((3-Hydroxybenzyl)amino)propyl)azepan-2-one (9f): From compound **5f** (50 mg, 0.18 mol), sodium borohydride (6.9 mg, 0.18 mmol) and p-toluenesulfonic acid monohydrate (34.7 mg, 0.18 mmol), compound **9f** was obtained as a colourless oil (22.3 mg, 0.080 mmol); η = 44%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.32 (br s, 1H, ArH), 7.24 – 7.20 (m, 3H, ArH),4.65 (s, 1H,

NH), 3.74 (s, 2H, CH_2), 3.42 (t, *J* = 6.8 Hz, 2H, CH_2), 3.30 – 3.27 (m, 2H, CH_2), 2.56 (t, J = 6.8 Hz, 2H, CH_2), 2.50 – 2.47 (m, 2H, CH_2), 1.73-1.67 (m, 4H, 2xCH_2), 1.64 – 1.58 (m, 4H, 4xCH_2) ppm. $^{13}C\{1H\}$ NMR ($CDCl_3$, 100 MHz) δ: 176.9 (C=O), 157.5 (C), 139.8 (C), 129.7 (CH), 119.8 (CH), 115.7 (CH), 115.0 (CH), 53.4 (CH_2), 49.6 (CH_2), 45.7 (CH_2), 45.6 (CH_2), 37.1 (CH_2), 30.0 (CH_2), 28.5 (CH_2), 27.4 (CH_2), 23.4 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{25}N_2O_2$ 277.1914; Found 277.1911.

1-(3-((3-Chlorobenzyl)amino)propyl)azepan-2-one (9g): From compound **5g** (50 mg, 0.17 mmol), sodium borohydride (6.5 mg, 0.17 mmol) and p-toluenesulfonic acid monohydrate (32.5 mg, 0.17 mmol), compound **9g** was obtained as a colourless oil (17.8 mg, 0.06 mmol); η = 35%; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.10 (t, *J* = 7.6 Hz, 1H, ArH), 6.88 (br s, 1H, ArH), 6.74 (t, *J* =8.4 Hz, 2H, ArH), 3.71 (s, 2H, CH_2), 3.44 (t, *J* = 7.2 Hz, 2H, CH_2), 3.29 – 3.27 (m, 2H, CH_2), 2.61 (t, J = 6.4 Hz, 2H, CH_2), 2.51 – 2.48 (m, 2H, CH_2), 1.69-1.67 (m, 4H, 2xCH_2), 1.61 – 1.58 (m, 4H, 4xCH_2) ppm. $^{13}C\{1H\}$ NMR ($CDCl_3$, 100 MHz) δ: 176.4 (C=O), 134.3 (C), 128.5 (CH), 127.5 (C), 127.3 (CH), 127.0 (CH), 126.6 (CH), 53.3 (CH_2), 49.7 (CH_2), 45.8 (CH_2), 45.7 (CH_2), 37.2 (CH_2), 30.1 (CH_2), 28.6 (CH_2), 27.9 (CH_2), 23.5 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{24}ClN_2O$ 295.1572; Found 295.1570.

1-(3-(Benzylamino)propyl)pyrrolidin-2-one (10a): From compound **6a** (50 mg, 0.22 mmol)**,** sodium borohydride (8.2 mg, 0.22 mmol) and p-toluenesulfonic acid monohydrate (41.3 mg, 0.22 mmol), compound **10a** was obtained as a colourless oil (38 mg, 0.16 mmol); η = 70%; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.34-7.29 (m, 5H, ArH), 4.65 (s, 1H, NH), 3.75 (s, 2H, CH_2), 3.38 – 3.29 (m, 4H, 2xCH_2), 2.58 (t, *J* = 6.8 Hz, 2H, CH_2), 2.33 (t, *J* = 8.0 Hz, 2H, CH_2), 2.00-1.92 (m, 2H, CH_2), 1.75-1.68 (m, 2H, CH_2) ppm. $^{13}C\{1H\}$ NMR ($CDCl_3$, 100 MHz) δ: 175.3 (C=O), 139.5 (C), 128.5 (2xCH), 128.4 (2xCH), 127.0 (CH), 53.9 (CH_2), 47.2 (CH_2), 46.0 (CH_2), 40.2 (CH_2), 31.0 (CH_2), 27.2 (CH_2), 17.9 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{21}N_2O$ 233.1648; Found 233.1648.

4-(((3-(2-Oxopyrrolidin-1-yl)propyl)amino)methyl)benzonitrile (10c): From compound **6c** (50 mg, 0.20 mmol), sodium borohydride (7.4 mg, 0.20 mmol) and p-toluenesulfonic acid monohydrate (37.3 mg, 0.20 mmol), compound **10c** was obtained as a colourless oil (25.7 mg, 0.10 mmol); η = 50%; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.62 (d, *J* = 8.0 Hz, 2H, ArH), 7.54 (d, *J* = 8.0 Hz, 2H, ArH), 4.77 (s, 1H, NH), 3.90 (s, 2H, CH_2), 3.40 – 3.25 (m, 4H, 2xCH_2), 2.66 (t, *J* = 6.8 Hz, 2H, CH_2), 2.40 (t, *J* = 8.0 Hz, 2H, CH_2), 2.07-1.99 (m, 2H, CH_2), 1.87-1.82 (m, 2H, CH_2) ppm. $^{13}C\{1H\}$ NMR ($CDCl_3$, 100 MHz) δ: 176.9 (C=O), 146.4 (C), 132.7 (2xCH), 128.1 (C), 127.2 (2xCH), 118.6 (CN), 52.3 (CH_2), 48.0 (CH_2), 45.4 (CH_2), 39.9 (CH_2), 30.9 (CH_2), 25.6 (CH_2), 18.1 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}N_3O$ 258.1597; Found 258.601.

1-(3-((4-Bromobenzyl)amino)propyl)pyrrolidin-2-one (10d): From compound **6d** (50 mg, 0.16 mmol), sodium borohydride (6.1 mg, 0.16 mmol) and p-toluenesulfonic acid monohydrate (30.8 mg, 0.16 mmol), compound **10d** was obtained as a light brown oil (25.7 mg, 0.083 mmol); η = 51%; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.41 (d, *J* = 8.8 Hz, 2H, ArH), 7.20 (d, *J* = 8.8 Hz, 2H, ArH), 3.72 (s, 2H, CH_2), 3.35 – 3.32 (m, 4H, 2xCH_2), 2.57 (t, *J* = 6.8 Hz, 2H, CH_2), 2.35 (t, *J* = 8.0 Hz, 2H, CH_2), 2.02-1.90 (m, 2H, CH_2), 1.98-1.71 (m, 2H, CH_2) ppm. $^{13}C\{1H\}$ NMR ($CDCl_3$, 100 MHz) δ: 175.8 (C=O), 131.8 (2xCH), 131.1 (C), 130.5 (2xCH), 128.7 (C), 52.9 (CH_2), 47.5 (CH_2), 45.7 (CH_2), 40.1 (CH_2), 31.0 (CH_2), 26.7 (CH_2), 18.0 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{20}BrN_2O$ 311.0752; Found 311.0754.

1-(3-((4-Methoxybenzyl)amino)propyl)pyrrolidin-2-one (10e): From compound **6e** (50 mg, 0.19 mmol), sodium borohydride (7.3 mg, 0.19 mmol) and p-toluenesulfonic acid monohydrate (36.5 mg, 0.19 mmol), compound **10e** was obtained as a brown oil (23.3 mg, 0.089 mmol); η = 46%; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.25 (d, *J* = 8.4 Hz, 2H, ArH), 6.84 (d, *J* = 8.4 Hz, 2H, ArH), 3.78 (s, 3H, OMe), 3.75 (s, 2H, CH_2), 3.37 – 3.31 (m, 4H, 2xCH_2), 2.64 (t, *J* = 6.8 Hz, 2H, CH_2), 2.36 (t, *J* = 8.0 Hz, 2H, CH_2), 2.03-1.964 (m, 2H, CH_2), 1.81-1.76 (m, 2H, CH_2) ppm. $^{13}C\{1H\}$ NMR ($CDCl_3$, 100 MHz) δ: 175.7 (C=O), 159.1 (C-OMe), 131.7 (C), 130.0 (2xCH), 114.0 (2xCH), 55.4 (OMe), 53.0 (CH_2), 47.5 (CH_2), 45.7 (CH_2), 40.2 (CH_2), 31.0 (CH_2), 26.8 (CH_2), 18.0 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{23}N_2O_2$ 263.1758; Found 263.1754.

1-(3-((3-Chlorobenzyl)amino)propyl)pyrrolidin-2-one (10g): From compound **6g** (50 mg, 0.19 mmol), sodium borohydride (7.1 mg, 0.19 mmol) and p-toluenesulfonic acid monohydrate (35.9 mg, 0.19mol), compound **10g** was obtained as a colourless oil (25.8 mg, 0.097 mmol); η = 51%; ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.37 – 7.28 (m, 4H, ArH), 3.86 (m, 2H, CH_2), 3.37 – 3.31 (m, 4H, 2xCH_2), 2.65 (t, *J* = 6.8 Hz, 2H, CH_2), 2.36 (t, *J* = 8.0 Hz, 2H, CH_2), 2.02 - 1.95 (m, 2H, CH_2), 1.86 - 1.79 (m, 2H, CH_2) ppm. $^{13}C\{1H\}$ NMR ($CDCl_3$, 100 MHz) δ: 175.6 (C=O), 141.0 (C), 134.4 (C), 129.9 (CH), 128.6 (CH), 127.6 (CH), 126.7 (C), 53.1 (CH_2), 47.4 (CH_2), 45.9 (CH_2), 40.1 (CH_2), 31.0 (CH_2), 27.0 (CH_2), 18.0 (CH_2) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{20}ClN_2O$ 267.1260; Found 267.1259.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Crystallographic data, voltamograms, NMR and mass spectra for compounds (PDF)

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Notes

The authors declare no competing financial interest.

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