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Recyclable $NaHSO_4$ catalyzed alkylation of *tert*-enamides with indoles or amines in water: facile construction of pharmaceutically analogous bis-alkaloid scaffolds †

Xue-Qiang Chu, Shun-Yi Wang* and Shun-Jun Ji*

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An efficient sodium hydrogen sulfate catalyzed alkylation of indoles or amines with tertiary enamides has been accomplished in water, affording the pharmacologically and biologically active 2-oxo-1-pyrrolidine derivatives in moderate to excellent yields. The key to our success is the use of $NaHSO_4$ as a low loading, inexpensive, green and recyclable catalyst and the reactions could be scaled up to gram level.

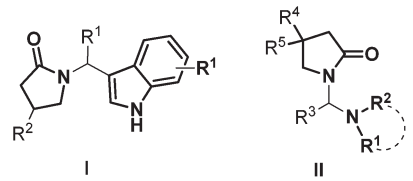
Introduction

The γ-butyrolactam ring is currently explored as a privileged structure for drug design and discovery due to the broad scope of numerous pharmacologically active agents and natural products.[1] For example, some of them are used as cerebrovascular disease drugs (Nefiracetam),[1a] protective agents of hypoxic and ischemic type aggressions of the central nervous system, as well as therapeutic compounds for epilepsy (Levetiracetam).[1b] Therefore, much attention has been paid to the synthesis and modification of above 2-oxo-1-pyrrolidine pharmaceutically derivatives. Other alkaloid scaffolds such as indole and (heterocyclic) aromatic amines are also implanted as subunit structures, and their typical structures can be depicted as **I**[1c] and **II**[1d] (Fig. 1).

Organic reactions in aqueous media are undergoing an unprecedented explosion of interest,[2] not only because water offers practical advantages over organic solvents from economical, environmental and safety standpoints, but also reactions in aqueous media display unique selectivity and reactivity, especially the alkylation reactions.[3] Despite various alkylation reagents (*e.g.*, alcohols, esters, and olefins) have been successfully employed in water,[4] most of these investigations focus on the electron-deficient alkenes.[5] Enamides, as good candidates in the realms of electron-rich olefins, are seldomly considered for the alkylation probably due to the poor electrophilicity.[6] Previously, Zhang *et al.*[7] and our group[8] have described an efficient Fe(III)-catalyzed alkylation of indoles with enamides. More recently, we also reported the use of iodine[9a] and AcOH[9b] in these transformations. However, catalytic amount of Brønsted acids delivered no or relatively low reactivity. What's more, existing methods for the synthesis of pharmaceutical analogues of compound **I** often suffer from limitations such as metal residue, medium detriment, narrow substrate scopes and catalyst non-recyclability. To the best of our knowledge, using enamide as alkylation reagent in the presence of inorganic salt catalysis in water is still unknown. As a continuation of our interests in green chemistry,[10] herein, we report the development of a simple procedure utilizing $NaHSO_4 \cdot H_2O$[11] as a transition metal-free, green, efficient and recyclable catalyst for alkylation of *tert*-enamides with indoles or amines in water.

Results and discussion

Initially, the reaction of indole **2a** with 1-vinylpyrrolidin-2-one **1a** was carried out under aqueous conditions without catalyst (Scheme 1). It was found that no desired product was formed (Table 1, entry 1). Then, the feasibility of Brønsted acid catalysis was investigated. Treatment of **1a** and **2a** with 5 mol% *p*-toluenesulfonic acid failed to give any product even with prolonged reaction time for 24 h (Table 1, entry 2). It should be



I II

Fig. 1 The typical structures of pharmaceutically active 2-oxo-1-pyrrolidine analogues.

Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou, 215123, P. R. China. E-mail: shunyi@suda.edu.cn; shunyi@suda.edu.cn; Fax: +86 512 65880307; Tel: +86-512-65880307

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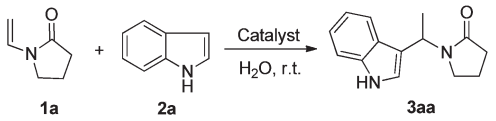


Scheme 1

noted that the desired product **3aa** was obtained in 81% yield when acetic acid was applied (Table 1, entry 3). This result is different with previous reports in organic medias.[7,9b] To our surprise, acidic-functionalized ionic liquid [PMIm]HSO_4[12] was sufficient to promote the reaction, and **3aa** could be obtained in 90% yield (Table 1, entry 4). When $NaHSO_4 \cdot H_2O$ and H_2SO_4 were applied to the reaction instead of [PMIm]HSO_4, similar results were found, respectively (Table 1, entries 5–6). This result suggested that the presence of HSO_4 groups was crucial to the high catalytic performance of the catalysts. To validate this hypothesis, other sodium salts such as $NaHSO_3$, Na_2HPO_4, Na_2SO_4 *etc.* were examined subsequently (Table 1, entries 7–11). As anticipated, no better results were obtained in these cases. Based on the above results, $NaHSO_4 \cdot H_2O$ is the preferred catalyst for this reaction. Further exploration led to a discovery that the yield of product could be increased to 97% then slowly decreased with the reaction time decreasing from 12 h to 3 h (Table 1, entries 5 and 12–13). Moreover, with an attempt to decrease the catalyst loading to 1 mol%, **3aa** also could be observed in 96% yield (Table 1, entry 14).

With the optimal reaction conditions in hand, we explored the scope of the reaction by using various indoles and the results are summarized in Table 2. Similar to the case of **2a**, the alkylation of indoles with electron-donating groups, such as methyl, phenyl, and methoxyl could be accomplished with good generality in water, provided the desired addition products in good to excellent yields (Table 2, entries 2–6 and 9–11). *N*-methylindole **2b** presented high efficiency in this system (Table 2, entry 2), although it failed under other Brønsted acid catalyzed conditions.[13] It was noteworthy that steric hindered **2d** with phenyl substituent at 2-position also could give the product **3ad** in 75% yield when 5 mol% $NaHSO_4 \cdot H_2O$ was used (Table 2, entry 4). Moreover, the yield decreased slightly with 4-methyl indole **2e**, possibly as a result of steric effects (Table 2, entry 5). Meanwhile, indoles with electron-withdrawing groups (Br and NO_2) also worked smoothly to furnish the corresponding alkylated products in 89% and 45% yields, respectively (Table 2, entries 7–8). Furthermore, 1-vinylazepan-2-one **1b**, the derivatives of structurally-related fused ring having important pharmacologically activities,[14] was selected to synthesize the corresponding pharmaceutical analogous. It was found that the reactivity of 1-vinylazepan-2-one **1b** was apparently lower than that of 1-vinylpyrrolidin-2-one **1a** (Table 2, entries 12–14), which may due to the steric hindrance arising from the bigger ring system. Another acyclic enamide **1c** was also proven as a good candidate in undergoing alkylation with indole, affording the desired products in 55% yield (Table 2, entry 15). Additionally, further expansion of this protocol to other *N*-vinyl compounds was limited, **1d** and *N*-vinylcarbazole **1e** were almost inert under the standard conditions, respectively (Table 2, entries 16–17).

Inspired by the above results, we were eager to know whether the present protocol was still general enough to construct the bio-active compound **II** with wider structural diversity under aqueous conditions. Thus, we turned our attention to investigate the scope and limitations of this alkylation reaction with a wide range of substituted anilines, moderate to good yields were achieved in the corresponding products, as shown in Table 3.

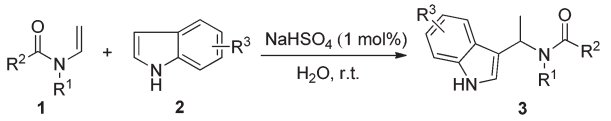
The substrates with strong electron-withdrawing groups on aryl ring, such as CN, COOEt, NO_2, exhibited good reactivity (Table 3, entries 1–3). In addition, the steric hindered 3-nitrophenylamine **4d** and 2-nitro-phenylamine **4e** were well tolerated (Table 3, entries 4–5). Notably, the presence of a weak electron-withdrawing group such as halogens at the *para* or *ortho* position of anilines obviously reduced the reactivity presumably owing to the electronic effect and sometimes steric effect (Table 3, entries 4–5). However, aniline **4h** and aniline with an electron-donating group (Me) **4i**, furnished the desired products **5ah** and **5ai** with yields of just 41% and 40% respectively, albeit with an elevated reaction temperature (Table 3, entries 8–9). Unfortunately, the reaction of **1a** with **4j** only afforded the product **5aj** in 35% yield (Table 3, entry 10). What's more, aliphatic amine **4k**, which shows stronger basicity than anilines, was inert to the alkylation reaction (Table 3, entry 11). Nevertheless, 1*H*-benzotriazole **4l** demonstrated high efficiency to give the target product in good yield (Table 3, entry 12). Another N-containing substrate, sulfonamide **4m** proceeded smoothly and 62% yield of addition product **5am** was obtained (Table 3, entry 13). When 1-vinylpyrrolidin-2-one **1a** was replaced with 1-vinylazepan-2-one **1b**, satisfying results were obtained (Table 3, entries 14–15).

Table 1 Optimization of reaction conditions[a]

Entry	Catalyst	Time (h)	Yield (%)[b]
1	—	12	0 (0[c])
2	PTSA[d]	24	0
3	HOAc	12	81
4	[PMIm]HSO_4[e]	12	90
5	$NaHSO_4 \cdot H_2O$	12	91
6[f]	H_2SO_4	12	90
7	$NaHSO_3$	12	Trace
8	Na_2HPO_4	12	Trace
9	Na_2SO_4	12	46
10	NaCl	12	<10%
11	NaOAc	12	0
12	$NaHSO_4 \cdot H_2O$	7	97
13	$NaHSO_4 \cdot H_2O$	3	88
14	1 mol% $NaHSO_4 \cdot H_2O$	7	96

[a] Reaction conditions: **2a** (0.5 mmol), **1a** (1.0 mmol), catalyst (5 mol%), H_2O (1.5 mL), at room temperature. [b] Isolated yield. [c] At 60 °C. [d] PTSA = *p*-toluenesulfonic acid. [e] [PMIm]HSO_4 = 3-methyl-1-pentyl-3*H*-imidazol-1-ium hydrogen sulfate. [f] Concentrated sulfuric acid (wt%: 98%) was used.

Table 2 Alkylation of indoles with enamides[a]



1 2 3

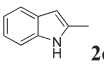
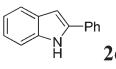
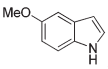
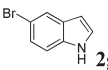
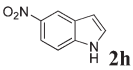
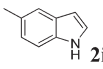
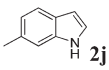
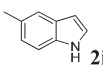
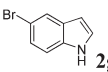
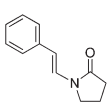
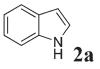
Entry	Enamide	Indole	Product	Time (h)	Yield (%)[b]
1	 1a	 2a	3aa	7	96
2		 2b	3ab	5	99
3		 2c	3ac	16	85
4		 2d	3ad	19	75[c]/80[d]
5[e]		 2e	3ae	15	56
6		 2f	3af	14	92
7		 2g	3ag	23	62/89[e]
8		 2h	3ah	19	32[c]/45[d]
9		 2i	3ai	19	95
10		 2j	3aj	23	90
11		 2k	3ak	15	87
12	 1b	 2a	3ba	25	87
13		 2i	3bi	23	91
14[e]		 2g	3bg	23	24
15	 1c	 2a	3ca	25	34/55[e]
16	 1d	 2a	3da	24	Trace

Table 2 (*Continued*)

Entry	Enamide	Indole	Product	Time (h)	Yield (%)[b]
17	 1e	 2a	—	24	NR[f]

[a] Reaction conditions: indoles **2a–k** (0.5 mmol), enamide **1a–e** (1.0 mmol), $NaHSO_4$ (1 mol%), H_2O (1.5 mL), at room temperature. [b] Isolated yield. [c] 5 mol% of catalyst was used, at 100 °C. [d] 3 equiv. **1a** was used at 60 °C for 24 h. [e] At 60 °C for 23 h. [f] NR = No reaction.

This mild and green methodology would be potentially useful for the synthesis of pharmaceutically active γ-butyrolactam analogues in industrial process. Therefore, a large-scaled reaction of indole **2a** (10.0 mmol) with 1.2 equiv. of **1a** (12.0 mmol) was carried out under little modified conditions (Scheme 2). To our delight, the reaction was completed in 5 h to give the pure product of **3aa** in 95% yield only after the removal of excessive **1a** under the reduced pressure without further purification and was washed with water.

In addition, to test the catalyst reusability, a series of relatively large-scaled experiments of **1a** and **2a** with 1 mol% $NaHSO_4 \cdot H_2O$ were carried out in water. The results are summarized in Fig. 2. The reaction could also give **3aa** in 60% yield after three cycles.

Conclusions

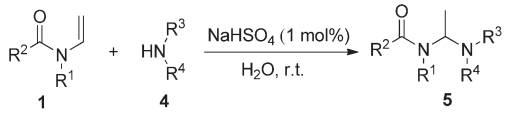
In summary, we have explored the efficient alkylation of indoles or amines with *tert*-enamides catalyzed by inexpensive $NaHSO_4$ with low loading under aqueous conditions, the desired product could up to 99% yield. The reactions could be scaled up to gram level and the catalyst was reusable for three times. Thus, this catalytic system serves as an environmentally benign tool for the efficient synthesis of pharmaceutically active 2-oxo-1-pyrrolidine derivatives and would lead to a potential application in industrial processes.

Experimental

General

Melting points were recorded on an Electrothermal digital melting point apparatus. IR spectra were recorded on a Varian FT-1000 spectrophotome-ter using KBr optics. ^{1}H NMR spectra were recorded on a Varian INOVA 400 and and ^{13}C NMR were recorded on a Varian INOVA 75 or 100 MHz spectrometer using $CDCl_3$ as solvent and TMS as internal standard. High resolution mass spectra were obtained using Micromа GCT-TOF instrument.

Table 3 Alkylation of amino compounds with enamides[a]



1 4 5

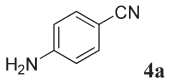
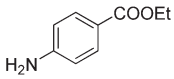
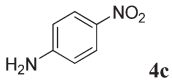
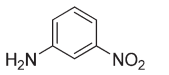
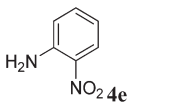
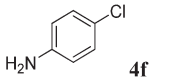
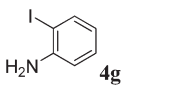
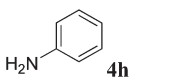
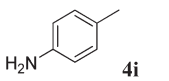
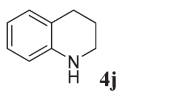
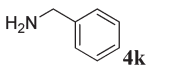
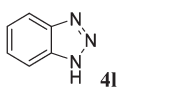
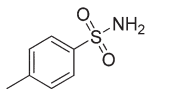
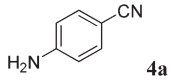
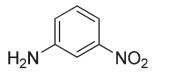
Entry	Enamide	Amine	Product	Time (h)	Yield (%)[b]
1	 1a	 4a	5aa	12	92
2		 4b	5ab	12	90
3		 4c	5ac	12	96
4		 4d	5ad	12	90
5		 4e	5ae	12	62
6		 4f	5af	24	73
7[c]		 4g	5ag	24	29
8		 4h	5ah	12	36/41[c]
9[c]		 4i	5ai	24	40
10[c]		 4j	5aj	24	35
11		 4k	—	24	NR[d]
12		 4l	5al	24	80
13		 4m	5am	24	63

Table 3 (*Continued*)

Entry	Enamide	Amine	Product	Time (h)	Yield (%)[b]
14	 1b	 4a	5ba	12	90
15		 4d	5bd	12	91

[a] Reaction conditions: enamide **1a–b** (1.0 mmol), amino compound **4** (0.5 mmol), $NaHSO_4$ (1 mol%), H_2O (1.5 mL), at room temperature. [b] Isolated yield. [c] At 100 °C for 24 h. [d] NR = No reaction.

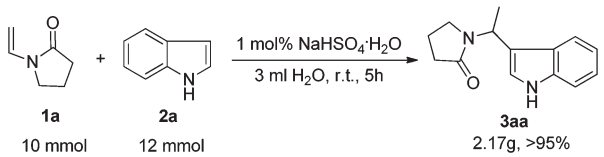
Typical procedure for the alkylation of indoles, anilines with enamides

Nucleophile (0.5 mmol), $NaHSO_4 \cdot H_2O$ (1 mol%), enamide (1 mmol) and water (1.5 mL) were added into a tube. Then the mixture was vigorously stirred at room temperature, until nucleophile was completely consumed as indicated by TLC analysis. Then the mixture was poured into H_2O and extracted with ethyl acetate (3 × 5 mL). The combined organic layer was washed with brine (2 × 3 mL), dried with anhydrous $MgSO_4$, and evaporated under the reduced pressure. Finally, the residue was purified by flash column chromatography with EtOAc and PE as eluents to afford pure product.

Typical procedure for reuse of $NaHSO_4$ in water

Indole **2a** (10 mmol), $NaHSO_4 \cdot H_2O$ (5 mol%), 1-vinylpyrrolidin-2-one **1a** (12 mmol) and water (3 mL) were added into a flask. Then the mixture was vigorously stirred at room temperature and and the progress of the reaction was monitored by TLC analysis. After completion of the reaction, 10 mL of deionized water was added into the reaction, the mixture was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layer washed with deionized water (3 × 5 mL), the water layer was collected. Organic layers were dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure and the residue was purified by flash column chromatography. $NaHSO_4$ left in water was concentrated to 1 mL under reduced pressure at 80 °C for another cycle.

1-(1-(1*H*-Indol-3-yl)ethyl)pyrrolidin-2-one (3aa). White solid; m.p. 165–167 °C. IR (KBr): 3243, 3165, 3107, 2972, 2876, 1659, 1490, 1440, 1288, 1198, 751 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ = 1.52 (d, J = 7.0 Hz, 3H), 1.62–1.73 (m, 1H), 1.78–1.88 (m,



1a 10 mmol + 2a 12 mmol → 3aa 2.17g, >95%

Scheme 2 A large-scaled reaction under neat conditions.

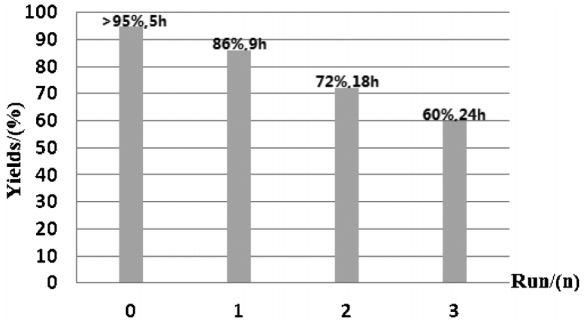


Fig. 2 Recyclability of catalyst.

1H), 2.18–2.34 (m, 2H), 2.67–2.73 (m, 1H), 3.22–3.27 (m, 1H), 5.53 (q, J = 6.9 Hz, 1H), 6.97 (t, J = 7.4 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 7.32 (s, 1H), 7.37 (d, J = 8.1 Hz, 1H), 7.42 (d, J = 7.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.8, 137.0, 126.9, 122.8, 122.6, 120.3, 119.9, 116.4, 111.6, 43.1, 42.7, 32.2, 18.2, 17.1. HRMS (EI): m/z calcd for $C_{14}H_{16}N_2O$: 228.1263; found: 228.1266.

1-(1-(1-Methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ab). Yellow oil. IR (KBr): 3056, 2971, 2890, 1673, 1468, 1280, 1213, 1095, 745 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58 (d, J = 7.2 Hz, 3H), 1.78–1.93 (m, 2H), 2.40–2.46 (m, 2H), 2.85–2.93 (m, 1H), 3.23–3.31 (m, 1H), 3.77 (s, 3H), 5.73–5.80 (q, J = 6.9 Hz, 1H, CH), 6.97 (s, 1H), 7.07–7.12 (m, 1H), 7.21–7.30 (m, 2H), 7.61 (d, J = 8.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.4, 137.4, 127.1, 127.0, 122.3, 119.9, 114.7, 109.5, 42.8, 42.5, 33.1, 32.0, 18.0, 17.0. HRMS (EI): m/z calcd for $C_{15}H_{18}N_2O$: 242.1419; found: 242.1418.

1-(1-(2-Methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ac). White solid; m.p. 176–177 °C. IR (KBr): 3317, 2974, 2933, 2876, 1656, 1491, 1435, 1287, 1198, 1051, 749 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.72 (d, J = 6.9 Hz, 3H), 1.82–2.00 (m, 2H), 2.32–2.41 (m, 2H), 2.48 (s, 3H), 3.11–3.19 (m, 1H), 3.53–3.61 (m, 1H), 5.75 (q, J = 7.2 Hz, 1H), 7.05–7.12 (m, 2H), 7.27 (t, J = 1.8 Hz, 1H), 7.70 (d, J = 7.5 Hz, 1H), 8.07 (br, s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.3, 135.6, 133.9, 128.3, 121.3, 119.9, 119.6, 111.0, 110.8, 44.0, 44.0, 31.9, 18.1, 18.0, 13.0. HRMS (EI): m/z calcd for $C_{15}H_{18}N_2O$: 242.1419; found: 242.1420.

1-(1-(2-Phenyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ad). White solid; m.p. 166–167 °C. IR (KBr): 3398, 3165, 2930, 2895, 1660, 1442, 1288, 1204, 778 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.62 (d, J = 6.9 Hz, 3H), 1.79–2.00 (m, 2H), 2.36–2.43 (m, 2H), 3.24–3.31 (m, 1H), 3.58–3.66 (m, 1H), 5.62 (q, J = 7.2 Hz, 1H), 7.16–7.23 (m, 2H), 7.39–7.49 (m, 6H), 7.84 (d, J = 7.8 Hz, 1H), 8.21 (br, s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.3, 737.3, 136.3, 133.0, 129.5, 129.1, 128.8, 128.3, 122.5, 121.0, 120.3, 111.7, 111.5, 45.3, 44.9, 32.0, 18.7, 18.3. HRMS (EI): m/z calcd for $C_{20}H_{20}N_2O$: 304.1576; found: 304.1577.

1-(1-(4-Methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ae). Yellow solid; m.p. 184–185 °C. IR (KBr): 3158, 3109, 3041, 2942, 2878, 1661, 1493, 1439, 1290, 750 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58 (d, J = 6.4 Hz, 3H), 1.82–1.93 (m, 2H), 2.43 (t, J = 7.9 Hz, 2H), 2.60 (s, 3H), 2.85–2.92 (m, 1H), 3.17–3.25 (m, 1H), 5.85 (q, J = 6.4 Hz, 1H), 6.86 (d, J = 6.8 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 7.21 (d, J = 12.7 Hz, 2H), 8.41 (br, s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.1, 137.2, 131.2, 125.5, 123.2, 122.4, 121.6, 115.9, 109.3, 44.4, 43.4, 32.4, 20.2, 17.9, 17.5. HRMS (EI): m/z calcd for $C_{15}H_{18}N_2O$: 242.1419; found: 242.1420.

1-(1-(5-Methoxy-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3af). White solid; m.p. 134.5–135.4 °C. IR (KBr): 3433, 3235, 3050, 2935, 2826, 1647, 1489, 1440, 1289, 1216, 1028, 926, 800, 666 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.57 (d, J = 6.9 Hz, 3H), 1.70–2.01 (m, 2H), 2.30–2.55 (m, 2H), 2.86 (dd, J = 8.9, 14.9 Hz, 1H), 3.26 (dd, J = 8.9, 14.5 Hz, 1H), 3.80 (s, 3H), 5.75 (q, J = 6.8 Hz, 1H), 6.84 (d, J = 8.7 Hz, 1H), 7.10 (s, 2H), 7.24 (d, J = 8.8 Hz, 1H), 8.61 (br, s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.5, 154.1, 146.4, 131.8, 126.9, 123.0, 115.5, 112.7, 112.2, 100.8, 55.9, 42.8, 42.3, 31.9, 17.8. HRMS (EI): m/z calcd for $C_{15}H_{18}N_2O_2$: 258.1368; found: 258.1364.

1-(1-(5-Bromo-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ag). White solid; m.p. 154–156 °C. IR (KBr): 3157, 3080, 2982, 1650, 1439, 1288, 1194, 885, 790 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58 (d, J = 7.2 Hz, 3H), 1.79–1.98 (m, 2H), 2.45 (t, J = 8.1 Hz, 2H), 2.82–2.90 (m, 1H), 3.24–3.31 (m, 1H), 5.70 (q, J = 6.9 Hz, 1H), 7.14–7.31 (m, 3H), 7.74 (s, 1H), 8.25 (br, s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9, 135.7, 128.6, 125.7, 123.9, 122.3, 116.1, 113.6, 113.2, 43.0, 42.7, 32.2, 18.2, 17.2. HRMS (EI): m/z calcd for $C_{14}H_{15}BrN_2O$: 308.0347(^{81}Br); found: 308.0343.

1-(1-(5-Nitro-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ah). Yellow solid; m.p. 241–242 °C. IR (KBr): 3379, 2968, 1660, 1522, 1295 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.54 (d, J = 6.8 Hz, 3H), 1.70–1.74 (m, 1H), 1.86–1.90 (m, 1H), 2.20–2.36 (m, 2H), 2.70–2.76 (m, 1H), 3.27–3.34 (m, 1H), 5.56–5.61 (m, 1H), 7.54 (d, J = 9.2 Hz, 1H), 7.64 (s, 1H), 8.00 (d, J = 8.4 Hz, 1H), 8.45 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 173.1, 140.5, 139.6, 127.2, 125.4, 117.6, 116.8, 115.7, 112.0, 41.4, 41.3, 31.0, 17.3, 16.7. HRMS (EI): m/z calcd for $C_{14}H_{15}N_3O_3$: 273.1113; found: 273.1112.

1-(1-(5-Methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ai). White solid; m.p. 173–174 °C. IR (KBr): 3154, 2928, 2890, 1652, 1490, 1441, 1290, 792 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58 (d, J = 6.9 Hz, 3H), 1.77–1.91 (m, 2H), 2.42–2.46 (m, 5H, CH_2), 2.88–2.90 (m, 1H), 3.27–3.28 (m, 1H), 5.75 (q, J = 6.6 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 7.09 (s, 1H), 7.24–7.27 (m, 1H), 7.39 (s, 1H), 8.26 (br, s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.7, 135.3, 129.5, 127.1, 124.4, 122.8, 119.3, 115.8, 111.3, 43.2, 42.8, 32.2, 22.0, 18.2, 17.2. HRMS (EI): m/z calcd for $C_{15}H_{18}N_2O$: 242.1419; found: 242.1420.

1-(1-(6-Methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3aj). White solid; m.p. 135–136 °C. IR (KBr): 3213, 3100, 2980, 2879, 1662, 1610, 1493, 1440, 1289, 1119 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.57 (d, J = 7.0 Hz, 3H), 1.74–1.81 (m, 1H), 1.87–1.93 (m, 1H), 2.41–2.46 (m, 5H), 2.84–2.89 (m, 1H), 3.23–3.29 (m, 1H), 5.73–5.78 (q, J = 7.0 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 7.04 (s, 1H), 7.16 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 8.36 (br, s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.50, 137.19, 132.19, 124.40, 121.84, 121.59, 119.07, 115.64, 111.38, 42.91, 42.39, 31.94, 21.80, 17.83, 16.80. HRMS (EI): m/z calcd for $C_{15}H_{18}N_2O$: 242.1419; found: 242.1416.

1-(1-(7-Methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ak). White solid; m.p. 166–168 °C. IR (KBr): 3222, 3113, 2971, 2933, 2873, 1650, 1614, 1498, 1444, 1298, 1201, 1123, 788 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.59 (d, J = 6.9 Hz, 3H), 1.78–1.91 (m, 2H), 2.40–2.46 (m, 2H), 2.49 (s, 3H), 2.83–2.91 (m, 1H), 3.23–3.31 (m, 1H), 5.77 (q, J = 6.6 Hz, 1H), 7.02–7.06 (m, 2H), 7.13(s, 1H), 7.46–7.49 (m, 1H), 8.11 (br, s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.7, 136.6, 126.4, 123.2, 122.4, 120.9, 120.4, 117.5, 116.7, 43.2, 42.7, 32.2, 18.2, 17.1, 17.1. HRMS (EI): m/z calcd for $C_{15}H_{18}N_2O$: 242.1419; found: 242.1417.

1-(1-(1*H*-Indol-3-yl)ethyl)azepan-2-one (3ba). White solid; m.p. 125–126 °C. IR (KBr): 3482, 3182, 2930, 1607, 1483, 1178, 744 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.12–1.32 (m, 3H), 1.52 (d, J = 6.9 Hz, 3H), 1.57–1.70 (m, 3H), 2.59–2.62 (m, 2H), 3.01–3.19 (m, 2H), 6.29 (q, J = 6.9 Hz, 1H), 7.07–7.22 (m, 3H), 7.36 (d, J = 8.1 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H), 8.26 (br, s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 173.8, 136.4, 126.4, 123.5, 121.2, 118.7, 118.5, 115.2, 111.4, 43.9, 41.8, 37.0, 29.2, 28.6, 23.0, 17.0. HRMS (EI): m/z calcd for $C_{16}H_{20}N_2O$: 256.1576; found: 256.1577.

1-(1-(5-Methyl-1*H*-indol-3-yl)ethyl)azepan-2-one (3bi). White solid; m.p. 75–76 °C. IR (KBr): 3464, 3184, 3159, 2932, 1585, 1486, 1446, 1174 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.12–1.30 (m, 3H), 1.50 (d, J = 6.9 Hz, 3H), 1.57–1.72 (m, 3H), 2.42 (s, 3H), 2.59–2.63 (m, 2H), 3.01–3.19 (m, 2H), 6.24 (q, J = 6.9 Hz, 1H), 7.01–7.10 (m, 2H), 7.23–7.26 (m, 1H), 7.35 (s, 1H), 8.13 (br, s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.0, 135.3, 129.2, 127.3, 124.3, 123.3, 119.6, 116.3, 111.2, 45.6, 43.3, 38.2, 30.5, 29.3, 23.8, 21.9, 17.6. HRMS (EI): m/z calcd for $C_{17}H_{22}N_2O$: 270.1732; found: 270.1732.

1-(1-(5-Bromo-1*H*-indol-3-yl)ethyl)azepan-2-one (3bg). White solid; m.p. 73–74 °C. IR (KBr): 3484, 3006, 2973, 2934, 1584, 1486, 1377, 1113 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.07–1.35 (m, 3H), 1.50 (d, J = 6.9 Hz, 3H), 1.57–1.71 (m, 3H), 2.60–2.64 (m, 2H), 3.00–3.17 (m, 2H), 6.22 (q, J = 6.9 Hz, 1H), 7.14 (s, 1H), 7.21–7.37 (m, 2H), 7.71 (s, 1H), 8.32 (br, s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.0, 136.9, 127.1, 123.1, 123.0, 122.7, 120.1, 117.1, 117.1, 111.6, 45.4, 43.4, 38.2, 30.5, 29.4, 23.9, 17.5. HRMS (EI): m/z calcd for $C_{16}H_{19}BrN_2O$: 336.0660 (^{81}Br); found: 336.0645.

***N*-(1-(1*H*-Indol-3-yl)ethyl)-*N*-methylacetamide (3ca).** White solid; m.p. 95–98 °C. IR (KBr): 3243, 3050, 2957, 1650, 1497, 1456 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, δ = 1.51 (d, J = 6.9 Hz, 3H), 1.65 (d, J = 6.5 Hz, 1H), 2.15 (s, 3H), 2.40 (s, 1H), 2.62 (s, 3H), 2.64 (s, 1H), 5.33 (q, J = 6.6 Hz, 0.35 H), 6.33 (q, J = 6.9 Hz, 1H), 7.05–7.19 (m, 4H), 7.35–7.44 (m, 1.7H), 7.57 (d, J = 7.9 Hz, 1H), 8.17 (s, 1H), 8.90 (s, 0.35H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ = 169.2, 169.0, 136.6, 136.5, 126.3, 126.0, 123.6, 123.6, 121.4, 121.3, 118.9, 118.7, 118.6, 118.4, 114.9, 114.6, 111.7, 111.5, 49.8, 43.5, 29.1, 26.7, 22.2, 21.8, 17.9, 16.5 ppm. HRMS (EI): m/z Calcd for $C_{13}H_{16}N_2O$: 216.1263; found, 216.1268.

1-(1-(1*H*-Indol-3-yl)-2-phenylethyl)pyrrolidin-2-one (3ad). White solid; m.p. 190.8–191.7 °C. IR (KBr): 3280, 2942, 2359, 1655, 1438, 1283, 741 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.82–1.72 (m, 2H), 2.29–2.19 (m, 2H), 2.97–2.91 (m, 1H), 3.39–3.27 (m, 2H), 3.44–3.40 (m, 1H), 6.02–5.98 (m, 1H), 7.11 (t, J = 7.4 Hz, 1H), 7.22–7.19 (m, 2H), 7.31–7.26 (m, 5H), 7.36 (d, J = 8.1 Hz, 1H), 7.71 (d, J = 7.9 Hz, 1H), 8.31 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.7, 138.2, 138.6, 129.1, 128.6, 126.7, 122.8, 122.6, 120.1, 119.8, 114.7, 111.5, 48.1, 42.8, 37.1, 31.7, 18.0 ppm. HRMS (EI): m/z calcd for $C_{20}H_{20}N_2ONa$: $[M+Na]^+$ 327.1473; found, 327.1468.

4-(1-(2-Oxopyrrolidin-1-yl)ethylamino)benzonitrile (5aa). White solid; m.p. 185–186 °C. IR (KBr): 3305, 2983, 2218, 1664, 1612, 1531, 1285, 1161 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.48 (d, J = 6.4 Hz, 3H), 1.88–2.05 (m, 2H), 2.39–2.44 (m, 2H), 3.15–3.21 (m, 1H), 3.30–3.36 (m, 1H), 4.51 (br s, 1H, NH), 5.70–5.75 (m, 1H), 6.67 (d, J = 8.6 Hz, 2H), 7.44 (d, J = 8.6 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.97, 148.93, 133.83, 120.30, 113.17, 99.97, 56.39, 40.86, 31.60, 19.08, 17.82 ppm. HRMS (EI): m/z Calcd for $C_{13}H_{15}N_3O$: 229.1215; found, 229.1213.

Ethyl 4-(1-(2-oxopyrrolidin-1-yl)ethylamino)benzoate (5ab). White solid; m.p. 91–92 °C. IR (KBr): 3503, 2977, 1708, 1439, 1281, 1103, 844, 770 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.36 (t, J = 7.1 Hz, 3H), 1.47 (d, J = 6.3 Hz, 3H), 1.86–1.99 (m, 2H), 2.40 (t, J = 8.0 Hz, 2H), 3.14–3.20 (m, 1H), 3.29–3.34 (m, 1H), 4.31 (q, J = 7.1 Hz, 2H), 5.75 (q, J = 6.2 Hz, 1H), 6.64 (d, J = 8.5 Hz, 2H), 7.88 (d, J = 8.5 Hz, 2H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ = 173.6, 165.7, 150.4, 130.9, 117.7, 111.8, 59.7, 55.6, 40.3, 18.5, 17.4, 14.3 ppm. HRMS (EI): m/z Calcd for $C_{15}H_{20}N_2O_3$: 276.1474; found, 276.1473.

1-(1-(4-Nitrophenylamino)ethyl)pyrrolidin-2-one (5ac). Yellow solid; m.p. 204–205 °C. IR (KBr): 3271, 3072, 2928, 1665, 1484, 1323, 1161, 832 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.51 (d, J = 6.4 Hz, 3H), 1.90–2.05 (m, 2H), 2.40–2.45 (m, 2H), 3.16–3.22 (m, 1H), 3.32–3.38 (m, 1H), 4.77 (d, J = 6.9 Hz, 1H), 5.75–5.81 (m, 1H, CH), 6.67 (d, J = 9.0 Hz, 2H), 8.09 (d, J = 9.0 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.15, 150.75, 126.53, 112.45, 56.69, 41.02, 31.62, 19.31, 17.98 ppm. HRMS (EI): m/z Calcd for $C_{12}H_{15}N_3O_3$: 249.1113; found, 249.1108.

1-(1-(3-Nitrophenylamino)ethyl)pyrrolidin-2-one (5ad). Yellow solid; m.p. 89–90 °C. IR (KBr): 3297, 3094, 2979, 1663, 1572, 1339, 1156, 735 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.50 (d, J = 6.3 Hz, 3H), 1.90–2.20 (m, 2H), 2.39–2.44 (m, 2H), 3.20–3.24 (m, 1H), 3.32–3.38 (m, 1H), 4.44 (br s, 1H), 5.74 (q, J = 6.2 Hz, 1H), 6.99 (d, J = 6.2 Hz, 1H), 7.31 (t, J = 8.1 Hz, 1H), 7.56 (s, 1H), 7.57 (d, J = 7.9 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.2, 149.3, 146.3, 130.3, 118.6, 112.8, 108.2, 56.9, 41.0, 31.7, 19.2, 17.9 ppm. HRMS (EI): m/z Calcd for $C_{12}H_{15}N_3O_3$: 249.1113; found, 249.1108.

1-(1-(2-Nitrophenylamino)ethyl)pyrrolidin-2-one (5ae). Yellow solid; m.p. 89–91 °C. IR (KBr): 3361, 3091, 2976, 1687, 1504, 1421, 1041, 753 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.57 (d, J = 6.3 Hz, 3H), 1.91–2.04 (m, 2H), 2.40–2.46 (m, 2H), 3.17–3.23 (m, 1H), 3.36–3.42 (m, 1H), 5.86–5.92 (m, 1H), 6.67 (t, J = 7.7 Hz, 1H), 7.04 (d, J = 8.6 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 8.09–8.19 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.8, 142.8, 136.7, 132.5, 126.6, 117.0, 115.3, 55.9, 40.7, 39.5, 19.3, 17.8 ppm. HRMS (EI): m/z Calcd for $C_{12}H_{15}N_3O_3$: 249.1113; found, 249.1108.

1-(1-((4-Chlorophenyl)amino)ethyl)pyrrolidin-2-one (5af). White solid; m.p. 162–164 °C. IR (KBr): 3302, 3105, 2981,

1602, 1493, 1428, 1258, 1160, 820 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.44 (d, J = 6.4 Hz, 3H), 1.85–2.06 (m, 2H), 2.39 (t, J = 8.2 Hz, 2H), 3.12–3.20 (m, 1H), 3.25–3.33 (m, 1H), 5.65 (q, J = 6.3 Hz, 1H), 6.57 (d, J = 8.8 Hz, 2H), 7.12 (d, J = 8.8 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.1, 143.7, 129.4, 123.2, 114.5, 57.1, 40.9, 31.8, 19.5, 17.9 ppm. HRMS (EI): m/z Calcd for $C_{12}H_{15}ClN_2O$: 238.0873; found, 238.0874.

1-(1-(2-Iodophenylamino)ethyl)pyrrolidin-2-one (5ag). Pale yellow oil. IR (KBr): 3231, 3067, 2978, 1680, 1498, 1418, 1121 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.51 (d, J = 6.4 Hz, 3H), 1.83–1.98 (m, 2H), 2.36–2.41 (m, 2H), 3.08–3.13 (m, 1H), 3.29–3.35 (m, 1H), 4.41 (br s, 1H), 5.75–5.79 (m, 1H, CH), 6.50 (t, J = 8.0 Hz, 1H), 6.70 (d, J = 8.2 Hz, 1H), 7.20 (t, J = 7.7 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.93, 144.24, 139.00, 129.90, 120.06, 112.43, 85.17, 56.96, 40.66, 31.69, 19.40, 17.78 ppm. HRMS (EI): m/z Calcd for $C_{12}H_{15}IN_2O$: 330.0229; found: 330.0232.

1-(1-(Phenylamino)ethyl)pyrrolidin-2-one (5ah). White solid; m.p.124–125 °C. IR (KBr): 3311, 3053, 2934, 1661, 1496, 1280, 1168 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.44 (d, J = 6.4 Hz, 3H), 1.84–1.91 (m, 2H), 2.39 (t, J = 8.1 Hz, 2H), 3.17–3.23 (m, 1H), 3.27–3.33 (m, 1H), 3.95 (s, 1H, NH), 5.69 (q, J = 6.0 Hz, 1H), 6.64 (d, J = 8.2 Hz, 2H), 6.76 (t, J = 7.3 Hz, 1H), 7.18 (d, J = 7.8 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.0, 145.1, 129.6, 118.5, 113.3, 57.1, 41.0, 31.9, 19.5, 17.9 ppm. HRMS (EI): m/z Calcd for $C_{12}H_{16}N_2O$: 204.1263; found, 204.1262.

1-(1-(*p*-Tolylamino)ethyl)pyrrolidin-2-one (5ai). White solid; m.p. 147–148 °C. IR (KBr): 3317, 3054, 2937, 1661, 1497, 1280, 1160 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.43 (d, J = 6.4 Hz, 3H), 1.82–1.96 (m, 2H), 2.23 (s, 3H), 2.38 (t, J = 8.0 Hz, 2H), 3.16–3.22 (m, 1H), 3.26–3.31 (m, 1H), 3.87 (br s, 1H), 5.66 (q, J = 6.4 Hz, 1H), 6.56 (d, J = 8.4 Hz, 2H), 6.98 (d, J = 8.4 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9, 142.8, 130.0, 127.6, 113.3, 57.3, 41.0, 31.9, 20.5, 19.5, 17.9 ppm. HRMS (EI): m/z Calcd for $C_{13}H_{18}N_2O$: 218.1419; found, 218.1417.

1-(1-(3, 4-Dihydroquinolin-1(2*H*)-yl)ethyl)pyrrolidin-2-one (5aj). Colorless oil; IR (KBr): 2981, 2939, 1677, 1499, 1316, 1186 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.49 (d, J = 6.7 Hz, 3H), 1.91–1.98 (m, 4H), 2.35–2.40 (m, 2H), 2.78 (t, J = 5.8 Hz, 2H), 3.13–3.18 (m, 1H), 3.34–3.38 (m, 2H), 3.44–3.47 (m, 1H), 6.87 (q, J = 6.6 Hz, 1H), 6.63–6.68 (m, 2H), 6.98 (d, J = 6.9 Hz, 1H), 7.08 (t, J = 7.7 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.5, 143.8, 129.3, 127.8, 122.7, 117.1, 111.6, 61.3, 43.2, 42.4, 31.2, 28.5, 22.4, 18.0, 16.8 ppm. HRMS (EI): m/z Calcd for $C_{15}H_{21}N_2O$: $[M+H]^+$ 245.1654; found, 245.1660.

1-(1-(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)ethyl)pyrrolidin-2-one (5al). White solid; m.p. 57–58 °C. IR (KBr): 3451, 2972, 1685, 1422, 1268, 1241, 1049, 752 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.84–1.87 (m, 1H), 1.99–2.04 (m, 1H), 2.12 (d, J = 6.7 Hz, 3H), 2.27–2.36 (m, 1H), 2.42–2.48 (m, 1H), 3.08–3.14 (m, 1H), 3.60–3.66 (m, 1H), 7.00 (q, J = 6.6 Hz, 1H), 7.39 (t, J = 7.3 Hz, 1H), 7.54–7.47 (m, 1H), 7.83 (d, J = 8.1 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.2, 145.9, 132.5, 127.9, 124.5, 119.7, 110.5, 60.0, 41.9, 31.0, 17.7, 17.1 ppm. HRMS (EI): m/z Calcd for $C_{12}H_{14}N_4O$: 230.1168; found, 230.1168.

4-Methyl-*N*-(1-(2-oxopyrrolidin-1-yl)ethyl)benzenesulfonamide (5am). White solid; m.p. 113–115 °C. IR (KBr): 3466, 3087, 1662, 1446, 1322, 1147, 1023, 878, 664 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ = 1.17 (d, J = 6.6 Hz, 3H), 1.59–2.03 (m, 2H), 1.95–2.03 (m, 1H), 2.38 (s, 3H), 2.74–2.78 (m, 1H), 2.97–3.03 (m, 1H), 3.34–3.37 (m, 1H), 5.39–5.42 (m, 1H), 7.37 (d, J = 7.8 Hz, 2H), 7.58 (d, J = 7.8 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 172.6, 142.8, 138.1, 129.3, 126.4, 56.4, 56.3, 30.4, 21.0, 18.9, 16.6 ppm. HRMS (EI): m/z Calcd for $C_{13}H_{18}N_2O_3S$: 282.1038; found, 282.1039.

4-(1-(2-Oxoazepan-1-yl)ethylamino)benzonitrile (5ba). White solid; m.p. 196–197 °C. IR (KBr): 3294, 3163, 2931, 2215, 1612, 1536, 1340, 1164, 1142, 817 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.40 (d, J = 6.4 Hz, 3H), 1.54–1.70 (m, 6H), 2.46–2.59 (m, 2H), 3.16–3.28 (m, 2H), 4.58 (br s, 1H), 6.15–6.20 (m, 1H), 6.63 (d, J = 8.7 Hz, 2H), 7.44 (d, J = 8.7 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.10, 149.14, 133.86, 120.39, 113.27, 99.98, 58.38, 41.57, 37.96, 30.07, 29.04, 23.47, 19.51 ppm. HRMS (EI): m/z Calcd for $C_{15}H_{19}N_3O$: 257.1528; found, 257.1512.

1-(1-(3-Nitrophenylamino)ethyl)azepan-2-one (5bd). Yellow solid; m.p. 115–117 °C. IR (KBr): 3288, 3063, 2936, 1623, 1530, 1339, 1151, 982cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.26 (m, 1H), 1.41 (d, J = 6.2 Hz, 3H), 1.54–1.68 (m, 5H), 2.49–2.56 (m, 2H), 3.20–3.30 (m, 2H), 4.64 (br s, 1H), 6.16–6.18 (m, 1H), 6.49 (d, J = 7.2 Hz, 1H), 7.30 (t, J = 8.2 Hz, 1H), 7.46 (s, 1H), 7.55 (d, J = 7.6 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.3, 149.3, 146.6, 130.2, 118.7, 112.7, 108.1, 59.0, 41.6, 38.0, 30.1, 29.1, 23.5, 19.6 ppm. HRMS (EI): m/z Calcd for $C_{14}H_{19}N_3O_3$: 277.1426; found, 277.1426.

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