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PAPER

Direct alkylation of indoles and amines by *tert*-enamides: facile access to pharmaceutically active 2-oxo-1-pyrrolidine analogues†

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Direct alkylation of indoles and amines by tertiary enamides for the synthesis of pharmaceutically active 2-oxo-1-pyrrolidine analogues was described. With only a 0.5 mol% catalyst loading, molecular iodine was demonstrated to be efficiently enough to promote the reaction under neat condition. Only Markovnikov addition product was obtained indicating that the reactions proceeded with excellent regioselectivity.

Introduction

2-Oxo-1-pyrrolidine fragment is featured in a wide variety of pharmacologically and biologically active compounds. For example, *N*-(2,6-dimethylphenyl)-2-(2-oxopyrrolidin-1-yl)acetamide, which is known as Nefiracetam, is a commonly used drug for the treatment of cerebrovascular disease; Levetiracetam, bearing a 2-oxo-1-pyrrolidine moiety, is also disclosed as a protective agent for the treatment and prevention of hypoxic and ischemic type aggressions of the central nervous system, as well as an effective compound in the treatment of epilepsy (the structures of two drugs were shown in Fig. 1).[1] The analogues of above pharmaceuticals, especially in which another biologically active alkaloid motif incorporated, has been discovered as well to exhibit good activities in the therapy of common diseases such as attention deficit hyperactivity disorder (ADHD), cardiac arrhythmia, asthmatic syndrome, and so on (typical structures can be depicted as A[1e] and B,[1d] Fig. 1). However, existing synthetic methods for these compounds significantly lack efficiency. Taking these facts into account, the development of a more convenient protocol for preparing compounds containing 2-oxo-1-pyrrolidine moiety as well as other alkaloid scaffolds such as indole and (heterocyclic) aromatic amine become highly desirable.

In recent years, enamide, as a good alternative in the family of electron-rich olefins, have attracted considerable attention in organic synthesis.[2] Despite extensive application of enamide as a nucleophile in organic synthesis,[3] the utilization of enamide as electrophile were relatively rare. Although electron-rich alkenes have been successfully employed in acid-catalyzed Friedel–Crafts (F–C) alkylation for industrial purpose, enamide has not been examined until chiral phosphoric acid-induced enantioselective F–C alkylations were reported.[4] Even so, organic transformation using enamide as alkylation reagent in the presence of Lewis acid catalysis was still unknown. More recently, we have described an efficient Fe(III)-catalyzed F–C alkylation between indoles and enamides in water.[5] Almost at the same time, Zhang and coworkers also reported the same reaction carried out in organic solvent.[6] Both cases provided efficient methods for the synthesis of pharmaceutical analogue of compound A. In view of the fact that compound A is an oral drug, if metallic catalysis is used during its preparation, metal residue will pose an inevitable problem for above processes. Thus, a metal-free approach to realize this transformation is highly anticipated. Quite recently, we fortunately found that molecular iodine,[7] which has been demonstrated to be a versatile catalyst in organic synthesis, could effectively promote the synthesis of pharmaceutical analogues of A and B under neat condition. Moderate to high yields of the desired products could be obtained with simple work-up. Herein, we report these results.

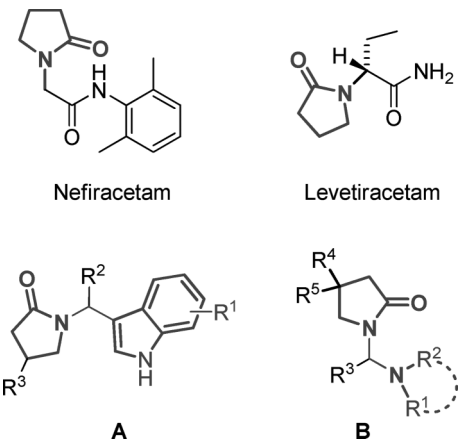

Fig. 1 Pharmaceuticals and their analogues containing 2-oxo-1-pyrrolidine fragment.

Results and discussion

Our initial attempt focused on the feasibility of reaction of indole (**2a**) with 1-vinylpyrrolidin-2-one (**1a**) under neat condition at

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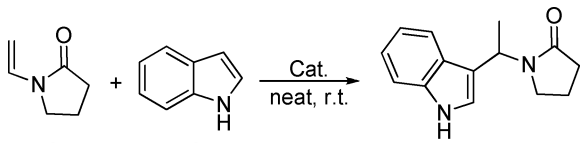
Table 1 Catalyst screening for the model reaction[a]



1a 2a 3aa

Entry	Catalyst (mol%)	Time (h)	Yield (%)[b]
1	—	24	0
2	I_2 (0.5)	2	91
3	$Fe(NO_3)_3 \cdot 9H_2O$ (0.5)	4	76
4	$In(OTf)_3$ (0.5)	4	74
5	$Cu(OTf)_2$ (0.5)	4	45
6	PTSA (0.5)	4	42
7	KI (0.5)	24	0
8	$PhI(OAc)_2$ (0.5)	24	0
9	I_2 (0.1)	4	54

[a] Reaction conditions: indole (0.5 mmol), 1-vinyl-2-pyrrolidinone (1.25 mmol), catalyst (0.0025 mmol). [b] Isolated yield based on indole as limiting reagent.

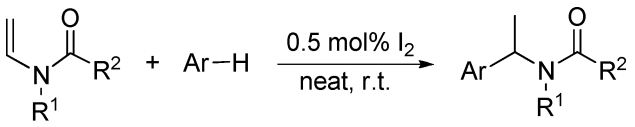
room temperature. As expected, the model reaction did not occur in the absence of catalyst under neat condition (Table 1, entry 1). But it was fortunately found that 0.5 mol% amount of iodine was sufficient to promote the reaction, high yield (91%) of product **3aa** was isolated after a short reaction time of 2 h. It should be noted that the reaction was regiospecific because only Markovnikov addition (from **1a**) and C3-alkylated (from **2a**) product was observed. Fe(III) catalyst, previously used in the similar system,[5] was also employed in the model reaction in order to compare its reactivity with iodine. The result apparently indicated that the catalytic activity of iodine was superior to that of Fe(III) catalyst (Table 1, entry 3). We also screened other commonly utilized Lewis or Brønsted acid catalysts, no better result was obtained in these cases (Table 1, entries 4–6). The effect of the source of iodine on the template reaction was subsequently examined. It seemed that both I^- and I^{3+} were inactive in mediating the reaction (Table 1, entries 7–8). Attempt to decrease the catalyst loading from 0.5 to 0.1 mol% was unsuccessful because the yield of desired product decreased even after a prolonged reaction time (Table 1, entry 9).

With the optimal reaction conditions in hand, we continued to examine the scope of the reaction by using various indoles and related electron-rich arenes. As illustrated in Table 2, the alkylation of indoles under neat condition could be accomplished with good generality. Indoles with electron-donating groups, such as methyl, phenyl, and benzyloxyl, provided the desired addition products within several hours in good to excellent yields (Table 2, entries 2–6, 9–10). Noteworthy, indoles with steric hindered substituents at 2-position has no detrimental effect on the reactions (Table 2, entries 3–4). Meanwhile, 5-nitro-1*H*-indole containing a strong electron-withdrawing group also worked well to furnish the desired product **3ah** in 65% yield (Table 2, entry 8). These results prompted us to investigate the use of other related electron-rich arenes. Pyrrole was firstly introduced and reacted with 1-vinylpyrrolidin-2-one (**2a**). Interestingly, a double alkylation of pyrrole by enamide was achieved giving rise to 2,5-dialkylated pyrrole **3ak** in 63% yield (Table 2, entry 11). Besides the heterocyclic arenes used above, other electron-rich arenes such as 1, 3, 5-trimethoxybenzene exhibited comparable reactivity with respect to that of indoles, leading to the adduct **3al** in 90% yield (Table 2, entry 12). Although pharmaceuticals containing azepan-2-one key structural unit has not been reported yet, the derivatives of structural-related fused ring 4,5-dihydro-1*H*-benzo[*b*]azepin-2(3*H*)-one have been discovered to be modulator of ghrelin receptor (GHSR) activity and often be used in treating and preventing conditions associated with obesity, obesity-related disorders or eating disorders.[8] Thus, 1-vinylazepan-2-one (**1b**) as another candidate of cyclic enamide was selected to synthesize the corresponding pharmaceutical analogous. It was observed that seven-membered cyclic enamide **1b** showed similar reactivity with that of **1a**, affording the desired products in moderate to high yields (Table 2, entries 13–16). Furthermore, acyclic enamide **1c** was also proven as a good candidate in undergoing alkylation with indole, and a 62% yield of the final product **3ca** was generated after workup (Table 2, entry 17).

Encouraged by the above successful access to the pharmaceutical analogous of compound A *via* alkylation of indoles by enamides, we were eager to know if the present protocol was general enough to construct the bio-active compounds with wider structural diversity. Thus, we turned our attention to the synthesis of compound B and its derivatives. The details of results were listed in Table 3. One of the pharmaceutical analogs containing a 1,2,3,4-tetrahydroquinoline skeleton was firstly considered to be the target for synthesis. It was a bit regret that the reaction of **1a** and **4a** was out of our expectation, and the yield of desired product was very poor, which probably due to the steric reason of 1,2,3,4-tetrahydroquinoline (Table 3, entry 1). Heterocyclic arene of 1*H*-benzo[*d*][1,2,3]triazole(**4b**) can be employed as a suitable substrate as well, affording the adduct in an acceptable yield of 53% (Table 3, entry 2). Especially noteworthy is that aniline was also active in the catalytic process (Table 3, entry 3), and hitherto few systematic studies have been achieved upon alkylation of anilines by enamides. Therefore, the scope and limitations of this alkylation reaction was next examined with a wide range of substituted anilines. As is shown, the presence of a strong electron-withdrawing group (CN, Ac, COOEt, and NO_2) at the *ortho*, *meta* and *para* position of aniline are well tolerated (Table 3, entries 4–9). The presence of a weak electron-withdrawing group such as halogens at the *para* or *ortho* position of aniline obviously reduced the reactivity presumably owing to the electronic effect and sometimes steric effect (Table 3, entries 10–11). Significant decrease of yield of desired adduct was also detected in the example of aniline with an electron-donating group (Me), albeit with a prolonged reaction time (Table 3, entry 12). What's more, aliphatic amine **4m**, which shows stronger basicity than anilines, was inert to the alkylation reaction (Table 3, entry 13). Nevertheless, sulfonamide **4n** demonstrated high efficiency to give the product **5an** in good yield (Table 3, entry 14). Based on these results, 1-vinylazepan-2-one (**1b**) was introduced to couple with active anilines, a comparable efficiency of **1b** was also observed, providing the target products in high yields (Table 3, entries 15–16). Furthermore, the structure of the representative compound **5aj** was confirmed by X-ray single crystal diffraction (Fig. 2).[9]

Further expansion of this protocol to thiol compound as nucleophile was also explored. It was found that the reaction of naphthalene-2-thiol with enamides **1a** and **1b** also proceeded smoothly to give *S*-alkylated products, majorly belonging to

Table 2 Alkylation of indoles and other electron-rich arenes with enamides[a]



1 2 3

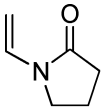
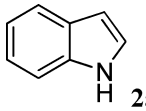
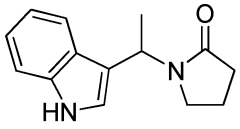
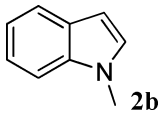
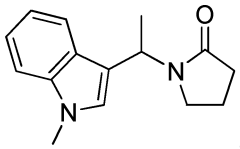
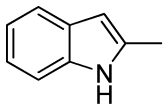
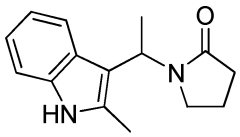
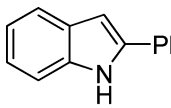
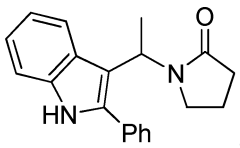
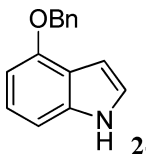
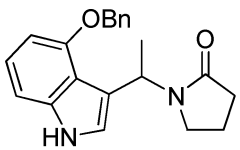
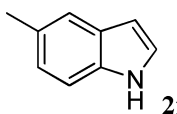
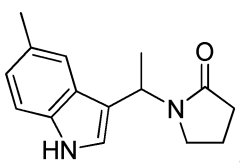
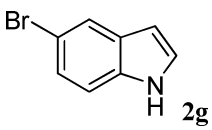
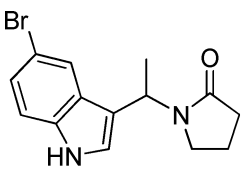
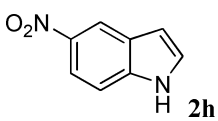
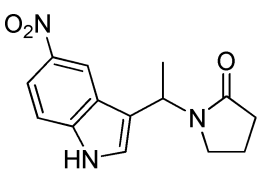
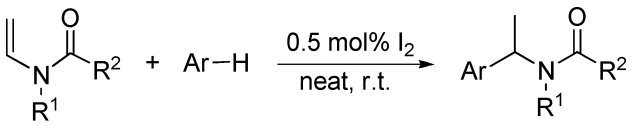
Entry	Enamide	ArH	Product	Time (h)	Yield (%)[b]
1	 1a	 2a	 3aa	2	91
2		 2b	 3ab	2	94
3		 2c	 3ac	1	94
4		 2d	 3ad	0.75	95
5		 2e	 3ae	0.5	89
6		 2f	 3af	1	92
7		 2g	 3ag	2	87
8		 2h	 3ah	1	65

Table 2 *(Contd.)*



1 **2** **3**

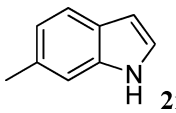
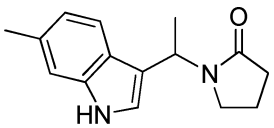
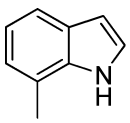
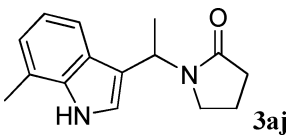
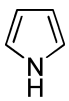
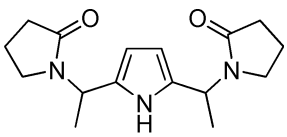
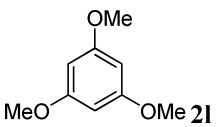
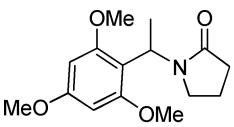
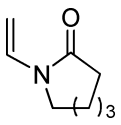
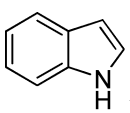
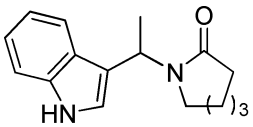
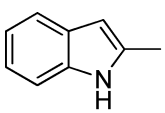
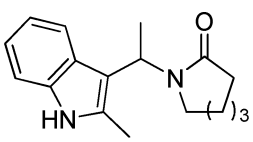
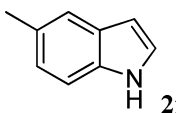
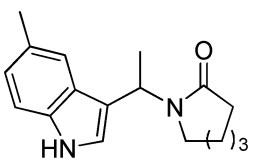
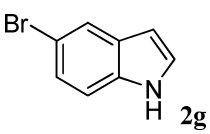
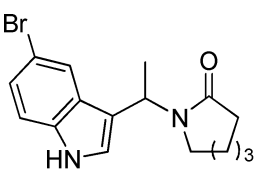
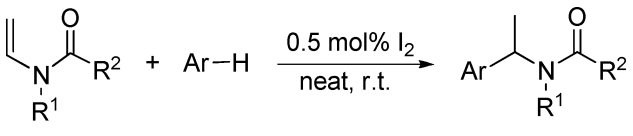
Entry	Enamide	ArH	Product	Time (h)	Yield (%)[b]
9		 **2i**	 **3ai**	3	96
10		 **2j**	 **3aj**	1	96
11		 **2k**	 **3ak**	1	63
12		 **2l**	 **3al**	5	90
13	 **1b**	 **2a**	 **3ba**	1.5	95
14		 **2c**	 **3bc**	1	66
15		 **2f**	 **3bf**	1	88
16		 **2g**	 **3bg**	5	65

Table 2 *(Contd.)*



Entry	Enamide	ArH	Product	Time (h)	Yield (%)[b]
17	**1c**	**2a**	**3ca**	1	62

[a] Reaction conditions: aromatic ring **2a–l** (1.0 mmol), enamide **1a–c** (2.5 mmol), iodine (0.5 mol%). [b] Isolated yield based on indole as limiting reagent.

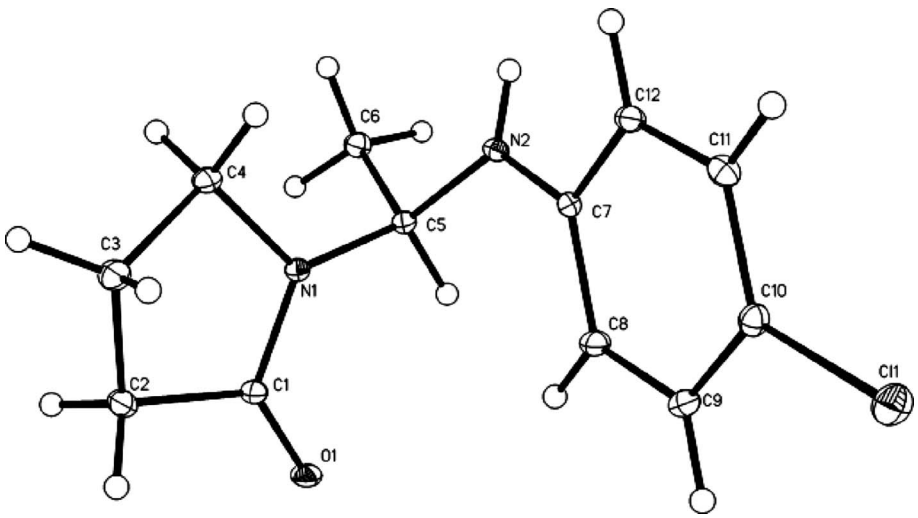
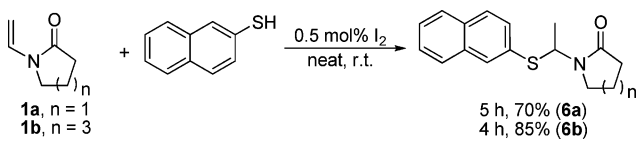


Fig. 2 Crystal structure of compound **5aj**.

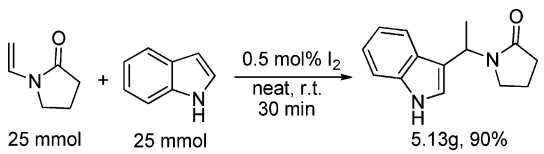
Markovnikov addition adducts, in 70% and 85% yields, respectively (Scheme 1).



Scheme 1

Considering the low catalyst loading, solvent-free conditions and a relatively wide generality of this protocol, it would be potentially useful in industrial process if the reactions could be scaled up. Thus, a large-scaled reaction of indole (25.0 mmol) with one equiv. of **1a** (25.0 mmol) was carried out under optimized conditions (Scheme 2). It was gratifying to find that the reaction was completed within 30 min and the pure product of **3a** could be obtained in 90% yield without need of excessive enamide and further purification by column chromatography.

Based on the reported results,[5] we suppose this iodine-catalyzed direct alkylation reaction would be carried out as follows (in Scheme 3): with the interaction of β-C (from C═C bond) and the molecular iodine, the polarized iodine atom with positive



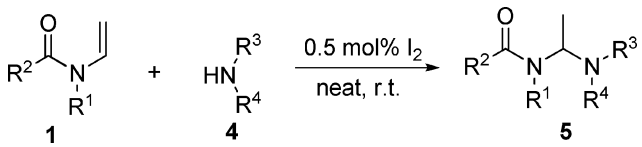
Scheme 2

charge was trapped and coordinated by the carbonyl group, thus a relatively stable six-membered intermediate was formed. Under this circumstance, the C═C bond, which was polarized simultaneously by iodine, was attacked by a nucleophile, after a hydrogen transfer step, as well as leaving of catalyst, the final product was thus produced.

Conclusion

In summary, we have developed a simple and highly efficient approach to synthesize pharmaceutically active 2-oxo-1-pyrrolidine analogues through Markonikov additions of indoles, anilines, and thiols to tertiary enamides. The reactions proceeded efficiently in the presence of 0.5 mol% molecular iodine to afford the desired 2-oxo-1-pyrrolidine derivatives in moderate to good yields. In

Table 3 Alkylation of amino compounds with enamides[a]



1 + 4 → 5

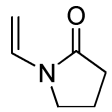
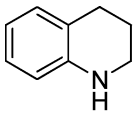
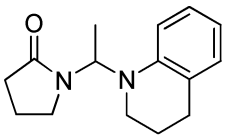
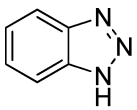
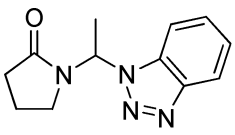
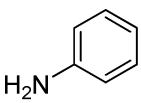
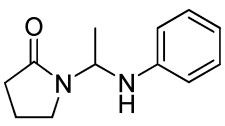
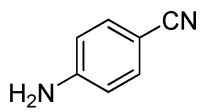
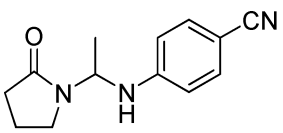
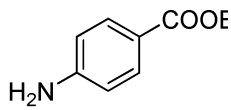
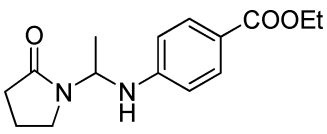
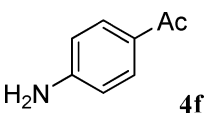
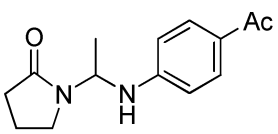
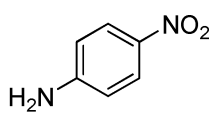
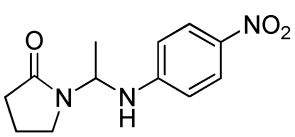
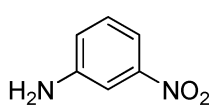
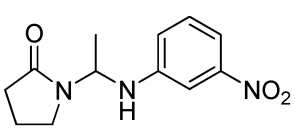
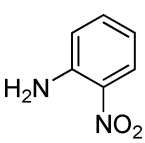
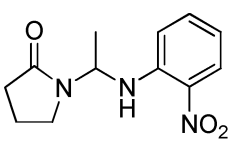
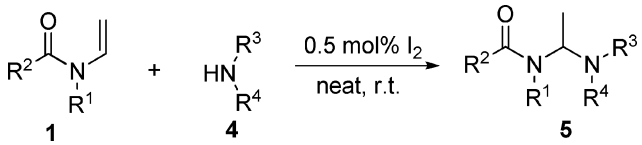
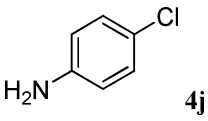
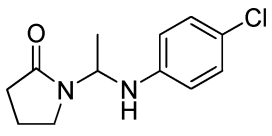
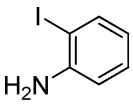
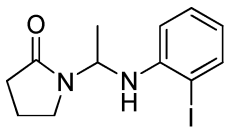
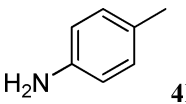
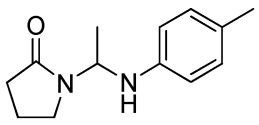
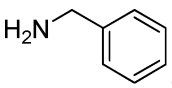
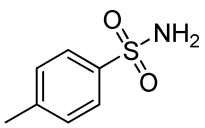
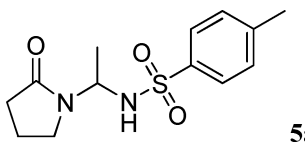
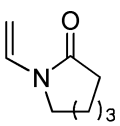
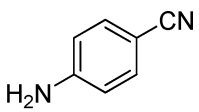
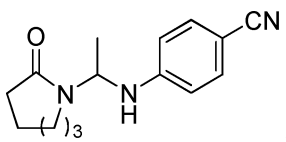
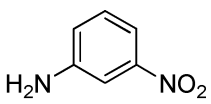
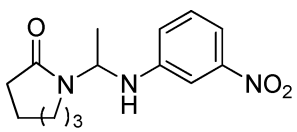
Entry	Enamide	Amine	Product	Time (h)	Yield (%)[b]
1	 **1a**	 **4a**	 **5aa**	12	21
2		 **4b**	 **5ab**	5	53
3		 **4c**	 **5ac**	10	44
4		 **4d**	 **5ad**	1	93
5		 **4e**	 **5ae**	6	87
6		 **4f**	 **5af**	12	95
7		 **4g**	 **5ag**	0.5	96
8		 **4h**	 **5ah**	1	81
9		 **4i**	 **5ai**	1	81

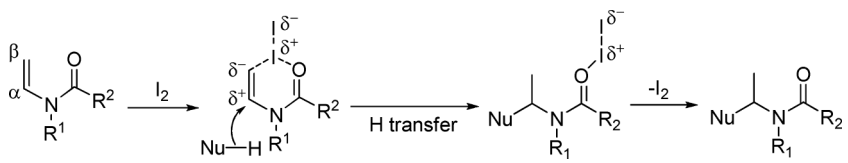
Table 3 *(Contd.)*



1 + 4 → 5

Entry	Enamide	Amine	Product	Time (h)	Yield (%)[b]
10		 **4j**	 **5aj**	12	65
11		 **4k**	 **5ak**	7	47
12		 **4l**	 **5al**	20	37
13		 **4m**	—	24	—
14		 **4n**	 **5an**	1	87
15	 **1b**	 **4d**	 **5bd**	1	95
16		 **4h**	 **5bh**	1	69

[a] Reaction conditions: amino compound **4** (1.0 mmol), enamide **1a–b** (2.5 mmol), iodine (0.5 mol%). [b] Isolated yield based on amino compound **4** as limiting reagent.



Scheme 3

addition, the reactions could be scaled up to gram level without the need of excessive substrate or any organic solvent, which would lead to a potential application in industrial process.

Experimental

General

Melting points were recorded on an Electrothermal digital melting point apparatus and were uncorrected. IR spectra were recorded on a Varian FT-1000 spectrophotometer using KBr optics. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian INOVA 300 or 400 MHz (^{1}H NMR) and 75 or 100 MHz (^{13}C NMR) spectrometer using $CDCl_3$ or DMSO-d_6 as solvent and TMS as internal standard. High resolution mass spectra were obtained using GCT-TOF instrument with EI or ESI source. X-ray diffraction data were recorded on a Rigaku Mercury CCD area detector with graphite monochromated Mo-Kα radiation.

General procedure for the alkylation of indoles, anilines and thiols with enamide. Nucleophile (1.0 mmol), I_2 (0.5 mol%) and enamide (2.5 mmol) were added into a flask. Then the mixture was vigorously stirred at room temperature, until nucleophile was completely consumed as indicated by TLC analysis. After the completion of reaction, the residue was directly purified by flash column chromatography with ethyl acetate and petroleum ether as eluents to afford pure product.

1-(1-(1*H*-Indol-3-yl)ethyl)pyrrolidin-2-one (3aa)[5]. (207 mg, 91%). White solid. m.p. 165–167 °C. IR (KBr): ν = 3243, 3165, 3107, 2972, 2876, 1659, 1490, 1440, 1288, 1198, 751 cm^{-1}. ^{1}H 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, 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) ppm. ^{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 ppm. HRMS: Calcd for $C_{14}H_{16}N_2O$: [M]$^+$ 228.1263; Found, 228.1266.

1-(1-(1-Methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ab)[5]. (227 mg, 94%). Yellow oil. IR (KBr): ν = 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), 1.78–193 (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) ppm. ^{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 ppm. HRMS: Calcd for $C_{15}H_{18}N_2O$: [M]$^+$ 242.1419; Found, 242.1418.

1-(1-(2-Methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ac)[5]. (227 mg, 94%). White solid. m.p. 176–177 °C. IR (KBr): ν = 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), 5.71–5.78 (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) ppm. ^{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 ppm. HRMS: Calcd for $C_{15}H_{18}N_2O$: [M]$^+$ 242.1419; Found, 242.1420.

1-(1-(2-Phenyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ad)[5]. (288 mg, 95%). White solid. m.p. 166–167 °C. IR (KBr): ν = 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), 5.68–5.75 (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) ppm. ^{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 ppm. HRMS: Calcd for $C_{20}H_{20}N_2O$: [M]$^+$ 304.1576; Found, 304.1577.

1-(1-(4-Phenoxy-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ae)[5]. (297 mg, 89%). White solid. m.p. 215–216 °C. IR (KBr): ν = 3160, 2930, 2870, 1650, 1510, 1443, 1352, 1288, 1230, 1099, 737 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58 (d, J = 6.9 Hz, 3H), 1.77–1.89 (m, 2H), 2.21–2.38 (m, 2H), 3.00–3.08 (m, 1H), 3.19–3.27 (m, 1H), 5.25 (s, 2H), 5.84–5.89 (q, J = 6.6 Hz, 1H), 6.45 (d, J = 7.5 Hz, 1H), 6.92–7.04 (m, 3H), 7.23–7.42 (m, 5H), 8.29 (br s, 1H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ = 173.4, 153.2, 138.9, 138.5, 129.0, 128.1, 127.8, 122.7, 122.4, 117.1, 116.0, 105.6, 101.2, 69.3, 44.8, 43.9, 32.0, 19.3, 18.3 ppm. HRMS: Calcd for $C_{21}H_{22}N_2O_2$: [M]$^+$ 334.1681; Found, 334.1678.

1-(1-(5-Methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3af)[5]. (222 mg, 92%). White solid. m.p. 173–174 °C. IR (KBr): ν = 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), 2.88–2.90 (m, 1H), 3.27–3.28 (m, 1H), 5.71–5.79 (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) ppm. ^{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 ppm. HRMS: Calcd for $C_{15}H_{18}N_2O$: [M]$^+$ 242.1419; Found, 242.1420.

1-(1-(5-Bromo-1*H*-indol-3-yl) ethyl)pyrrolidin-2-one (3ag)[5]. (266 mg, 87%). White solid. m.p. 154–156 °C. IR (KBr): ν = 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), 5.76–5.74 (q, J = 6.9 Hz, 1H), 7.14–7.31 (m, 3H), 7.74 (s, 1H), 8.25 (br s, 1H) ppm. ^{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 ppm. HRMS: Calcd for $C_{14}H_{15}BrN_2O$: [M]$^+$ 308.0347(^{81}Br); Found, 308.0343.

1-(1-(5-Nitro-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ah). (177 mg, 65%). Yellow solid. m.p. 241–242 °C. IR (KBr): ν = 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) ppm. ^{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 ppm. HRMS: Calcd for $C_{14}H_{15}N_3O_3$: [M]$^+$ 273.1113; Found, 273.1112.

1-(1-(6-Methyl-1*H*-indol-3-yl)ethyl)azepan-2-one (3ai). (232 mg, 96%). White solid. m.p. 135–136 °C. IR (KBr): ν = 3213,

3100, 2980, 2879, 1662,1610, 1493, 1440, 1289, 1119 cm^{-1}. ^1H 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) ppm. ^{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 ppm. HRMS: Calcd for $C_{15}H_{18}N_2O$: $[M]^+$ 242.1419; Found, 242.1416.

1-(1-(7-Methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3aj)[5]. (232 mg, 96%). White solid. m.p. 166–168 °C. IR (KBr): ν = 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), 5.74–5.80 (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) ppm. ^{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 ppm. HRMS: Calcd for $C_{15}H_{18}N_2O$: $[M]^+$ 242.1419; found, 242.1417.

1,1′-(1,1′-(1*H*-Pyrrole-2,5-diyl)bis(ethane-1,1-diyl))dipyrrolidin-2-one (3ak). (187 mg, 63%). Gray powder. m.p. 136–139 °C. IR (KBr): ν = 3197, 2975, 1689, 1664, 1439, 1289, 844 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ = 1.34 (d, J = 7.0 Hz, 6H), 1.79–1.88 (m, 4H), 2.22 (t, J = 8.0 Hz, 4H), 2.80–2.86 (m, 2H), 3.18–3.24 (m, 2H), 5.12 (q, J = 6.9 Hz, 2H), 5.83 (d, J = 2.2 Hz, 2H), 10.58 (br s, 1H, NH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 173.0, 131.0, 105.1, 43.5, 42.1, 31.1, 17.5, 16.6 ppm. HRMS: Calcd for $C_{16}H_{23}N_3O_2$: $[M]^+$ 289.1790; Found, 289.1795.

1-(1-(2,4,6-Trimethoxyphenyl)ethyl)pyrrolidin-2-one (3al)[5]. (251 mg, 90%). White solid. m.p. 94–96 °C. IR (KBr): ν = 3063, 2968, 2890, 1673, 1468, 1280, 1220, 1095 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.50 (d, J = 7.3 Hz, 3H), 1.84–1.96 (m, 2H), 2.30–2.35 (m, 2H), 3.23–3.28 (m, 1H), 3.51–3.56 (m, 1H), 3.81 (s, 9H), 5.84 (q, J = 7.3 Hz, 1H), 6.12 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.2, 160.5, 160.0, 109.8, 91.1, 55.9, 55.4, 44.6, 42.6, 31.7, 18.3, 17.4 ppm. HRMS: Calcd for $C_{15}H_{21}NO_4$: $[M]^+$ 279.1471; Found, 279.1476.

1-(1-(1*H*-Indol-3-yl)ethyl)azepan-2-one (3ba)[5]. (243 mg, 95%). White solid. m.p. 125–126 °C. IR (KBr): ν = 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), 6.26–6.33 (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) ppm. ^{13}C NMR (100 MHz, DMSO-*d6*): 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 ppm. HRMS: Calcd. for $C_{16}H_{20}N_2O$: $[M]^+$ 256.1576; Found, 256.1577.

1-(1-(2-Methyl-1*H*-indol-3-yl)ethyl)azepan-2-one (3bc)[5]. (178 mg, 66%). White solid. m.p. 151–153 °C. IR (KBr): ν = 3261, 2970, 2934, 2855, 1610, 1442, 1183, 745 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.05–1.41 (m, 4H), 1.58 (s, 2H), 1.70 (d, J = 7.2 Hz, 3H), 2.46 (s, 3H), 2.54–2.57 (m, 2H), 3.18–3.36 (m, 2H), 6.18–6.26 (q, J = 6.9 Hz, 1H), 7.05–7.14 (m, 2H), 7.29 (s, 1H), 7.70 (d, J = 7.5 Hz, 1H), 8.03 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 135.5, 134.2, 129.0, 121.2, 120.0, 119.4, 110.9, 110.9, 47.3, 44.6, 38.1, 30.4, 29.5, 24.0, 18.5, 13.3 ppm. HRMS: Calcd for $C_{17}H_{22}N_2O$: $[M]^+$ 270.1732; Found, 270.1732.

1-(1-(5-Methyl-1*H*-indol-3-yl)ethyl)azepan-2-one (3bf)[5]. (237 mg, 88%). White solid. m.p. 75–76 °C. IR (KBr): ν = 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), 6.21–6.28 (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) ppm. ^{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 ppm. HRMS: Calcd for $C_{17}H_{22}N_2O$; $[M]^+$ 270.1732: Found, 270.1732.

1-(1-(5-Bromo-1*H*-indol-3-yl)ethyl)azepan-2-one (3bg)[5]. (217 mg, 65%). White solid. m.p. 73–74 °C. IR (KBr): ν = 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), 6.19–6.26 (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) ppm. ^{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 ppm HRMS: Calcd for $C_{16}H_{19}BrN_2O$: $[M]^+$ 336.0660(^{81}Br); Found, 336.0645.

***N*-(1-(1*H*-Indol-3-yl)ethyl)-*N*-methylacetamide (3ca)[6].** (134 mg, 62%). White solid. m.p. 95–98 °C. IR (KBr): ν = 3243, 3050, 2957, 1650, 1497, 1456 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, including isomer): 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, including isomer): 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: Calcd for $C_{13}H_{16}N_2O$: $[M]^+$ 216.1263; Found, 216.1268.

1-(1-(3,4-Dihydroquinolin-1(2*H*)-yl)ethyl)pyrrolidin-2-one (5aa). (51 mg, 21%). Colorless oil. IR (KBr): ν = 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: Calcd for $C_{15}H_{21}N_2O$: $[M+H]^+$ 245.1654; Foud, 245.1660.

1-(1-(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)ethyl)pyrrolidin-2-one (5ab). (122 mg, 53%). White solid. m.p. 57–58 °C. IR (KBr): ν = 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: Calcd for $C_{12}H_{14}N_4O$: $[M]^+$ 230.1168; Found, 230.1168.

1-(1-(Phenylamino)ethyl)pyrrolidin-2-one (5ac). (90 mg, 44%). White solid; m.p.124–125 °C. IR (KBr): ν = 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: Calcd for $C_{12}H_{16}N_2O$: $[M]^+$ 204.1263; Found, 204.1262.

4-(1-(2-Oxopyrrolidin-1-yl)ethylamino)benzonitrile (5ad). (213 mg, 93%). White solid; m.p. 185–186 °C. IR (KBr): ν = 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: Calcd for $C_{13}H_{15}N_3O$: $[M]^+$ 229.1215; Found, 229.1213.

Ethyl 4-(1-(2-oxopyrrolidin-1-yl)ethylamino)benzoate (5ae). (240 mg, 87%). White solid; m.p. 91–92 °C. IR (KBr): ν = 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: Calcd for $C_{15}H_{20}N_2O_3$: $[M]^+$ 276.1474; Found, 276.1473.

1-(1-(4-Acetylphenylamino) ethyl)pyrrolidin-2-one (5af). (233 mg, 95%). White solid; m.p. 152–153 °C. IR (KBr): ν = 3221, 2968, 1746, 1678, 1445, 1162 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.48 (d, J = 6.4 Hz, 3H), 1.90–1.95 (m, 2H), 2.39–2.43 (m, 2H), 2.50 (s, 3H), 3.51–3.21(m, 1H), 3.30–3.36 (m, 1H), 4.49 (br s, 1H, NH), 5.75–5.78 (m, 1H), 6.65 (d, J = 8.7 Hz, 2H), 7.83 (d, J = 8.7 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.8, 175.1, 149.3, 131.0, 128.2, 112.6, 56.7, 41.0, 31.8, 26.3, 19.5, 18.0 ppm. HRMS: Calcd for $C_{14}H_{18}N_2O_2$: $[M]^+$ 246.1368; Found, 246.1385.

1-(1-(4-Nitrophenylamino)ethyl)pyrrolidin-2-one (5ag). (239 mg, 96%). Yellow solid; m.p. 204–205 °C. IR (KBr): ν = 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: Calcd for $C_{12}H_{15}N_3O_3$: $[M]^+$ 249.1113; Found, 249.1108.

1-(1-(3-Nitrophenylamino)ethyl)pyrrolidin-2-one (5ah). (201 mg, 81%). Yellow solid; m.p. 89–90 °C. IR (KBr): ν = 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: Calcd for $C_{12}H_{15}N_3O_3$: $[M]^+$ 249.1113; Found, 249.1108.

1-(1-(2-Nitrophenylamino)ethyl)pyrrolidin-2-one (5ai). (202 mg, 81%). Yellow solid; m.p. 89–91 °C. IR (KBr): ν = 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: Calcd for $C_{12}H_{15}N_3O_3$: $[M]^+$ 249.1113; Found, 249.1108.

1-(1-((4-Chlorophenyl)amino)ethyl)pyrrolidin-2-one (5aj). (155 mg, 65%). White solid; m. p. 162–164 °C. IR (KBr): ν = 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: Calcd for $C_{12}H_{15}ClN_2O$: $[M]^+$ 238.0873; Found, 238.0874.

1-(1-(2-Iodophenylamino)ethyl)pyrrolidin-2-one (5ak). (155 mg, 47%). Pale yellow oil. IR (KBr): ν = 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: Calcd for $C_{12}H_{15}IN_2O$: $[M]^+$ 330.0229; Found: 330.0232.

1-(1-(*p*-Tolylamino)ethyl)pyrrolidin-2-one (5al). (81 mg, 37%). White solid; m.p. 147–148 °C. IR (KBr): ν = 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: Calcd for $C_{13}H_{18}N_2O$: $[M]^+$ 218.1419; Found, 218.1417.

4-Methyl-*N*-(1-(2-oxopyrrolidin-1-yl)ethyl)benzenesulfonamide (5an). (245 mg, 87%). White solid. m.p. 113–115 °C. IR (KBr): ν = 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: Calcd for $C_{13}H_{18}N_2O_3S$: $[M]^+$ 282.1038; Found, 282.1039.

4-(1-(2-Oxoazepan-1-yl)ethylamino)benzonitrile (5bd). (244 mg, 95%). White solid; m.p. 196–197 °C. IR (KBr): ν = 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 = 176.1, 149.1, 133.9, 120.4, 113.3, 100.0, 58.4, 41.6, 38.0, 30.1, 29.0, 23.5,

19.5 ppm. HRMS: Calcd for $C_{15}H_{19}N_3O$: $[M]^+$ 257.1528; Found, 257.1512.

1-(1-(3-Nitrophenylamino)ethyl)azepan-2-one (5bh). (191 mg, 69%). Yellow solid; m.p. 115–117 °C. IR (KBr): ν = 3288, 3063, 2936, 1623, 1530, 1339, 1151, 982 cm^{-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: Calcd for $C_{14}H_{19}N_3O_3$: $[M]^+$ 277.1426; Found, 277.1426.

1-(1-(Naphthalen-2-ylthio)ethyl)pyrrolidin-2-one (6a). (190 mg, 70%). White solid. 62–63 °C. IR (KBr): ν = 2961, 1681, 1399, 1266, 1047, 644 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.54 (d, J = 6.9 Hz, 3H), 1.72–1.80 (m, 1H), 1.86–1.94 (m, 1H), 1.98–2.06 (m, 1H), 2.21–2.39 (m, 1H), 3.32–3.38 (m, 1H), 3,56–3.62 (m, 1H), 6.31 (q, J = 6.9 Hz, 1H), 7.44–7.49 (m, 3H), 7.74–7.79 (m, 3H), 7.85 (s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170, 129.1, 127.8, 126.0, 124.0, 123.0, 122.0, 121.7, 49.6, 37.0, 26.7, 17.7, 13.3 ppm. HRMS: Calcd for $C_{16}H_{17}NOS$: $[M]^+$ 271.1031; Found, 271.1029.

2-(1-(Naphthalen-2-ylthio)ethyl)cycloheptanone (6b). (254 mg, 85%). Colorless oil. IR (KBr): ν = 2854, 1640, 1448, 1131, 1023, 823, 739 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.35–1.40 (m, 1H), 1.47–1.58 (m, 8H), 2.33–2.43 (m, 2H), 3.32–3.36 (m, 1H), 3.44–3.50 (m, 1H), 6.65 (q, J = 6.8 Hz, 1H), 7.41–7.47 (m, 3H), 7.72–7.78 (m, 4H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.0, 133.8, 132.0, 131.9, 128.5, 128.3, 127.8, 127.7, 127.5, 126.6, 125.9, 55.8, 42.9, 37.6, 30.0, 29.2, 23.3, 19.4, 19.2 ppm. HRMS: Calcd for $C_{18}H_{21}NOS$: $[M]^+$ 299.1344; Found, 299.1344.

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9 Structural parameters for product **5aj**: data collection: Rigaku Mercury CCD area detector; crystal size: 0.10 × 0.60 × 0.15 mm^3; $C_{12}H_{15}ClN_2O$, Mr = 238.71, monoclinic, space group P 21/c, a = 11.180 (3), b = 9.4995 (18), c = 12.049(3) Å, α = 90.00, β = 111.894 (5), γ = 90.00, V = 1187.4(5) $Å^3$, Z = 4, D_c = 1.335 g cm^{-3}, R[$I > 2\sigma(I)$] = 0.0529, wR[$I > 2\sigma(I)$] = 0.1404.