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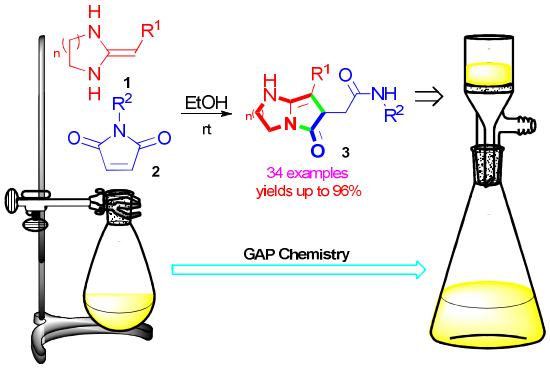

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An efficient synthesis of highly substituted bicyclic pyrrolidinone derivatives *via* a cascade reaction of heterocyclic ketene aminals (HKAs) and *N*-substituted maleimide in an environmentally friendly medium under catalyst-free conditions is described. This protocol uses group-assisted purification (GAP) chemistry in which purification *via* chromatography and recrystallization can be avoided, and the pure products were obtained simply by washing the crude products with 95% ethanol. The library of bicyclic pyrrolidinone derivatives has been constructed with moderate to excellent yields.

Introduction

The 2-Pyrrolidinone nucleus is one of the most represented structural motifs in naturally-occurring compounds and serves as a key synthetic intermediate or as a pharmacophore in drug discovery processes.[1] Among 2-pyrrolidinone derivatives, bicyclic pyrrolidinone derivatives as natural products have been widely researched, such as pyrrolams A–D (Fig. 1), which were isolated by Zeeck and co-workers in 1990 from the bacterial strain *Streptomyces olivaceus*. Bioassays revealed modest biological activity.[2a] Bicyclic pyrrolidinone derivatives have been used as anti-biotic agents (Carbapenem, Fig. 1),[2b] human NK_1 antagonists (Fig. 1),[3] proteasome inhibitors,[4] anti-seizure agents,[5] and transcription-factor inhibitors.[6]

Owing to the synthetic utilization and biological importance of the bicyclic pyrrolidinones, several methods for the construction of these kinds of compounds with diverse structural features and substitution patterns have been developed over the past decade. Synthetic approaches include radical or electrophilic cyclisations of unsaturated amides,[7] direct reaction of imines with cyclic anhydrides,[8] Au-catalysed cyclisations,[9] carbenoid C–H insertions cyclisations[10] and ring expansions.[11] However, many of these methods involve the use of expensive or toxic transition metals as catalysts (Rh, Au), extended reaction times, high temperatures, and also require tedious work-up procedures. Consequently, an efficient, concise and environmentally friendly approach for producing this class of bicyclic pyrrolidinones that tolerate a wide variety of functional groups is highly desirable.

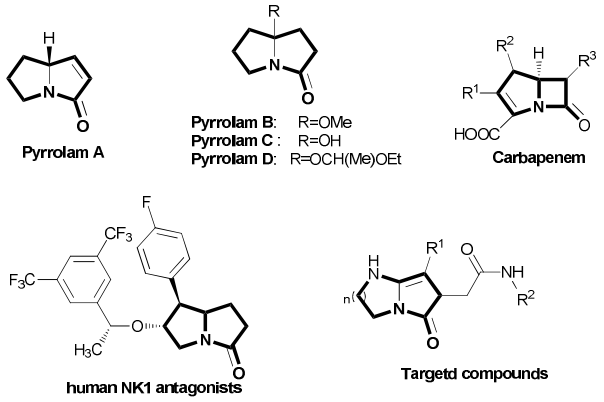
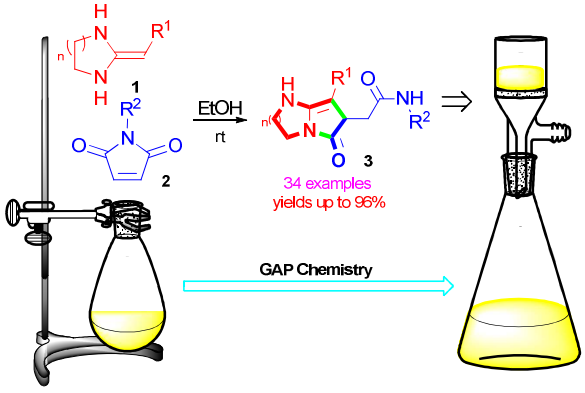


Fig. 1 Bicyclic pyrrolidinone derivatives and the target compounds.

In the past several years, our groups have demonstrated that heterocyclic ketene aminals (HKAs) are an emerging, more reactive class of functionalized synthons[12] through which a variety of biologically active heterocyclic[13] and fused heterocyclic compounds can be obtained, using easier and more efficient methodologies.[14-15] One concern of our group is synthesis of diverse compound libraries using green chemistry techniques under mild reaction conditions. The green synthesis can usually avoid tedious workup and purifications. In this paper we report a method for a concise synthesis of bicyclic pyrrolidinone derivatives. The pure products were obtained by relying on group-assisted purification (GAP) chemistry[16] to avoid traditional purification methods of column chromatography or recrystallization (Scheme 1).



Scheme 1 Synthesis of bicyclic pyrrolidinone derivatives.

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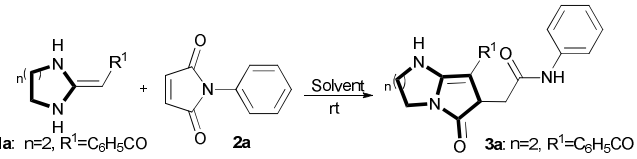
†Electronic supplementary information (ESI) available: CCDC 998644 (**3t**). For ESI and crystallographic data in CIF or other electronic format see DOI:

Results and discussion

Initially, HKA **1a** was reacted with the easily accessible material *N*-phenylmaleimide **2a** in acetone in the presence of Et_3N at room temperature. After 40 min, a light yellow solid was obtained with a 70% yield after separation by filtration (Table 1, entry 1). To establish the optimal reaction conditions, acid catalysts HOAc and a catalyst-free condition were involved (Table 1, entry 2–3). We found that the reactions could proceed in catalyst-free conditions, while the catalysts Et_3N and AcOH didn't obviously promote the reactions (Table 1, entries 1–2 *vs.* 3). Subsequently, we screened other solvents by still using a catalyst-free condition at room temperature (Table 1, entries 4–10). From the various entries, we believe that ethanol is a green solvent, and that room temperature is beneficial for reducing energy consumption and for convenient operation. Therefore, we propose that that the best reaction conditions for the synthesis of fused bicyclic pyrrolidinones are EtOH as a solvent, a catalyst-free condition, at ambient temperature for 20 min to obtain products with an 84% isolated yield (Table 1, entry 6).

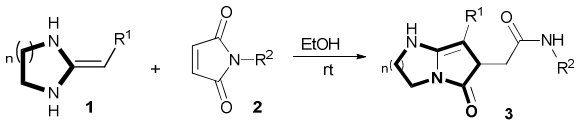
Table 1 Optimisation of reaction conditions[a]



Entry	Solvent	Catalyst	$t(^0C)$	Time/min	Yield[b] (%)
1	Acetone	Et_3N	r.t.	40	70
2	Acetone	AcOH	r.t.	40	67
3	Acetone	–	r.t.	40	72
4	CH_3CN	–	r.t.	120	25
5	AcOEt	–	r.t.	120	20
6	EtOH	–	r.t.	20	84
7	EtOH/H_2O=1:1	–	r.t.	30	77
8	MeOH	–	r.t.	10	35
9	CH_2Cl_2	–	r.t.	60	65
10	Dioxane	–	r.t.	120	34

[a] Reagents and conditions: HKA **1a** (0.50 mmol), *N*-phenylmaleimide **2a** (0.55mmol), solvent (15.0 mL). [b] Isolated yield based on HKA **1a**.

Table 2 Preparation of bicyclic pyrrolidinone derivatives[a]



Entry	n	R^1	R^2	3	Time/min	Yield[b] (%)
1	2	C_6H_5CO (**1a**)	C_6H_5 (**2a**)	**3a**	20	84
2	2	4-FC_6H_4CO (**1b**)	C_6H_5 (**2a**)	**3b**	20	70
3	2	4-ClC_6H_4CO (**1c**)	C_6H_5 (**2a**)	**3c**	20	85
4	2	2-ClC_6H_4CO (**1d**)	C_6H_5 (**2a**)	**3d**	20	83
5	2	4-MeC_6H_4CO (**1e**)	C_6H_5 (**2a**)	**3e**	20	92
6	2	4-$MeOC_6H_4CO$ (**1f**)	C_6H_5 (**2a**)	**3f**	20	73
7	2	C_6H_5CO (**1a**)	Benzyl (**2b**)	**3g**	20	95
8	2	4-FC_6H_4CO (**1b**)	Benzyl (**2b**)	**3h**	20	80
9	2	4-ClC_6H_4CO (**1c**)	Benzyl (**2b**)	**3i**	20	88
10	2	2-ClC_6H_4CO (**1d**)	Benzyl (**2b**)	**3j**	20	92
11	2	4-MeC_6H_4CO (**1e**)	Benzyl (**2b**)	**3k**	20	90
12	2	4-$MeOC_6H_4CO$ (**1f**)	Benzyl (**2b**)	**3l**	20	94
13	2	C_6H_5CO (**1a**)	4-FC_6H_4 (**2c**)	**3m**	60	72
14	2	4-FC_6H_4CO (**1b**)	4-FC_6H_5 (**2c**)	**3n**	60	85
15	2	4-$MeOC_6H_4CO$ (**1f**)	4-FC_6H_4 (**2c**)	**3o**	60	93
16	2	C_6H_5CO (**1a**)	4-$MeOC_6H_4$ (**2d**)	**3p**	120	94
17	2	4-FC_6H_4CO (**1b**)	4-$MeOC_6H_4$ (**2d**)	**3q**	60	84
18	2	4-$MeOC_6H_4CO$ (**1f**)	4-$MeOC_6H_4$ (**2d**)	**3r**	60	79
19	2	C_6H_5CO (**1a**)	Ethyl (**2e**)	**3s**	60	96
20	2	4-FC_6H_4CO (**1b**)	Ethyl (**2e**)	**3t**	60	85
21	2	C_6H_5CO (**1a**)	H (**2f**)	**3u**	60	79
22	3	4-FC_6H_4CO (**1b**)	C_6H_5 (**2a**)	**3v**	90	78
23	3	4-ClC_6H_4CO (**1c**)	C_6H_5 (**2a**)	**3w**	90	77
24	3	4-MeC_6H_4CO (**1e**)	C_6H_5 (**2a**)	**3x**	90	82
25	3	4-FC_6H_4CO (**1b**)	Benzyl (**2b**)	**3y**	90	90
26	3	4-MeC_6H_4CO (**1e**)	Benzyl (**2b**)	**3z**	90	92
27	1	C_6H_5CO (**1a**)	C_6H_5 (**2a**)	**3a′**	60	28[c]
28	1	4-$MeOC_6H_4CO$ (**1f**)	C_6H_5 (**2a**)	**3b′**	60	32[c]
29	1	C_6H_5CO (**1a**)	4-FC_6H_4 (**2c**)	**3c′**	60	71
30	1	C_6H_5CO (**1a**)	4-$MeOC_6H_4$ (**2d**)	**3d′**	60	76
31	1	4-$MeOC_6H_4CO$ (**1f**)	Benzyl (**2d**)	**3e′**	60	20[c]
32	1	C_6H_5CO (**1a**)	Ethyl (**2e**)	**3f′**	30	77
33	1	4-ClC_6H_4CO (**1c**)	Ethyl (**2e**)	**3g′**	30	78
34	1	4-$MeOC_6H_4CO$ (**1f**)	Ethyl (**2e**)	**3h′**	30	80

[a]Reagents and conditions: HKA **1a** (0.50 mmol), *N*-phenylmaleimide **2a** (0.55 mmol), solvent (15.0 mL). [b] Isolated yield based on HKA **1a**. [c] Isolated yields after column chromatography.

Based on the optimisation conditions, the scope and limitations of this protocol have been examined, and a number of six-membered ring HKAs **1b–1f** were used as substrates to react with *N*-phenylmaleimide **2a–2b**. The results demonstrated that the six-membered HKAs, with different substituents, were all good substrates for the cascade reaction at ambient temperature (Table 2, entries 1–12). The substituents of the HKAs **1** also had a slight influence on the reactivity and product yield. After that, *N*-(4-substituted phenyl) maleimides **2c–2d**, *N*-Ethylmaleimide **2e** and Maleimide **2f** were reacted with six-membered ring HKAs under the same conditions. In the long run, the reaction can provide the target compounds in good yields but the reaction times need to be extended (Table 2, entries 13–21).

Inspired by the obtained results, ring size was also investigated in our work. Thus, the seven-membered HKAs were reacted with *N*-phenylmaleimide **2a** and *N*-benzylmaleimide **2b**. The reactions proceeded smoothly under the same conditions and we attained a final product with good yields, albeit with prolonged reaction times (Table 2, entries 22–26). However, when the five-member HKAs were applied, the reaction produced a complicated mixture of products, and we obtained the final product by column chromatography with ethyl acetate as an eluent to afford bicyclic pyrrolidinones with low yields (Table 2, entries 27–28). More significantly, the five-member HKAs were reacted with *N*-(4-substituted phenyl) maleimides **2c–2d**, and *N*-Ethylmaleimide **2e** under the same conditions. The pure products were obtained by relying on GAP chemistry with moderate yields (Table 2, entries 32–34).

The ^{1}H, ^{13}C NMR spectra, IR spectra and high resolution mass spectra data have confirmed the structure of the target compound 3. In order to specifically test the structure, **3t** was characterised by X-ray crystallography as a representative compound, as shown in Figure 2.

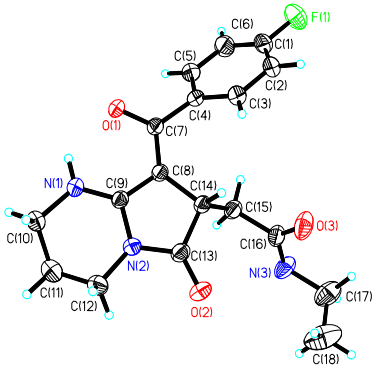
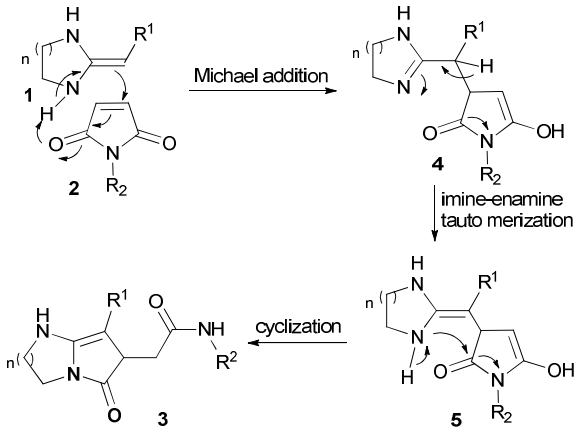


Fig. 2 ORTEP diagram of **3t**; ellipsoids are drawn at the 30% probability level.

A proposed mechanism for the synthesis of bicyclic pyrrolidinone derivatives **3** is shown in Scheme 2. Firstly, the *α-C* of HKAs **1** adds to the double bond of *N*-phenylmaleimide **2** and affords **4** *via* a Michael addition reaction. Secondly, the intermediate **4** is followed by imine-enamine tautomerization[17] to give compound **5**. Finally, the NH group of compound **5** attacks the amide carbonyl group *via* an intramolecular cyclisation reaction accompanied with ring-opening reaction to bicyclic pyrrolidinone **3**.



Scheme 2 Proposed mechanism for synthesis of bicyclic pyrrolidinone derivatives **3**.

Conclusions

In summary, a concise method for the synthesis of a series of bicyclic pyrrolidinones *via* HKAs and *N*-substituted maleimide at room temperature has been developed. The reaction showed that the synthetic route allowed the construction of fused bicyclic-pyrrolidinone derivatives with a wide range of substituents as important building blocks. Features of this strategy include some important aspects like convenient operation, short reaction times, green solvent, absence of catalysts and simple purification by washing the crude products with minimum amounts of common solvents, defined as GAP (group-assisted purification) chemistry. The library of bicyclic pyrrolidinones has been constructed with satisfactory yields.

Experimental Section

All compounds were fully characterized by spectroscopic data. The NMR spectra were recorded on a Bruker DRX500 (^{1}H: 500 MHz, ^{13}C: 125 MHz). Chemical shifts (δ) are expressed in ppm and *J* values are given in Hz. Deuterated DMSO-d_6 was used as solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using a KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF254. The melting points were determined on a XT-4A melting point apparatus and are uncorrected. HRMs were performed on an Agilent LC/Msd TOF instrument. All chemicals and solvents were used as received without further purification unless otherwise stated. Compounds **1** were prepared according to the literature.[18] Materials **2** were synthesized according with the literature.[19]

General Procedure: HKA derivatives **1** (0.50 mmol), *N*-substituted maleimides **2** (0.55 mmol) and ethanol (15 ml) were placed into a 25 mL round-bottom flask and the mixture was stirred at room temperature for 20–120 min. Completion of the reaction was monitored by TLC. The reaction mixture was then filtered to obtain the pure crude product, which was further washed with 95% EtOH to give pure product **3** with a yield of

20–96%. The products were further identified by FTIR, NMR and HRMS.

2-(8-Benzoyl-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)-*N*-phenylacetamide (3a). Light yellow solid: mp 191–193 °C; IR (KBr): 3424, 3244, 1740, 1632, 1526, 1434, 1158, 1082, 745 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.81 (br, 1H, NH), 9.54 (br, 1H, NH), 7.52–7.51 (m, 2H, ArH), 7.41–7.38 (m, 5H, ArH), 7.23–7.22 (m, 2H, ArH), 6.99–6.96 (m 1H, ArH), 4.03–3.95 (m, 1H, CH), 3.59–3.55 (m, 2H, NCH_2), 3.51–3.42 (m, 2H, CH_2N), 2.54–2.23 (m, 2H, CH_2CO), 1.95–1.89 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.8, 177.6, 168.4, 158.6, 142.3, 139.3, 129.6, 129.0, 128.5, 126.9, 123.3, 119.4, 88.5, 40.8, 38.7, 37.3, 36.9, 19.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{21}N_3NaO_3$ [(M+Na)$^+$], 398.1475; found, 398.1472.

2-(8-(4-Fluorobenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo-[1,2-*a*]pyrimidin-7-yl)-*N*-phenylacetamide (3b). Light yellow solid: mp 192–193 °C; IR (KBr):, 3313, 2933, 1733, 1619, 1537, 1441, 1149, 853, 760 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.80 (br, 1H, NH), 9.53 (br, 1H, NH), 7.59–7.56 (m, 2H, ArH), 7.40–7.39 (m, 2H, ArH), 7.24–7.19 (m, 4H, ArH), 6.99–6.96 (m, 1H, ArH), 4.00–3.96 (m, 1H, CH), 3.58–3.55 (m, 2H, NCH_2), 3.43–3.41 (m, 2H, CH_2N), 2.57–2.27 (m, 2H, CH_2CO), 1.94–1.92 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ =181.5, 177.1, 168.3, 161.9, 158.8, 139.2, 138.7, 129.3, 128.9, 123.4, 119.4, 115.4 (d, J = 21.3 Hz), 88.4, 40.8, 38.7, 37.3, 37.0, 19.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{20}FN_3NaO_3$ [(M+Na)$^+$], 416.1381; found, 416.1381.

2-(8-(4-Chlorobenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo-[1,2-*a*]pyrimidin-7-yl)-*N*-phenylacetamide (3c). Light yellow solid: mp 211.5–212.5 °C; IR (KBr): 3369, 3228, 1735, 1635, 1525, 1368, 1269, 1160, 1086, 772, 715 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.81 (br, 1H, NH), 9.55 (br, 1H, NH), 7.55–7.53 (m, 2H, ArH), 7.43–7.38 (m, 4H, ArH), 7.24–7.21 (m, 2H, ArH), 6.99–6.96 (m, 1H, ArH), 3.96–3.96 (m, 1H, CH), 3.59–3.55 (m, 2H, NCH_2), 3.43–3.42 (m, 2H, CH_2N), 2.60–2.29 (m, 2H, CH_2CO), 1.96–1.1.91 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ =181.2, 177.1, 168.3, 159.0, 141.0, 139.2, 134.1, 128.9, 128.9, 128.6, 123.4, 119.4, 88.6, 40.7, 38.7, 37.4, 37.1, 19.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{20}ClN_3NaO_3$ [(M+Na)$^+$], 432.1085; found, 432.1086.

2-(8-(2-Chlorobenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo-[1,2-*a*]pyrimidin-7-yl)-*N*-phenylacetamide (3d). Light yellow solid: mp 190-190.6 °C; IR (KBr): 3364, 3225, 1737, 1635, 1525, 1160, 1086, 772 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.62 (br, 1H, NH), 9.52 (br, 1H, NH), 7.45–7.42 (m, 3H, ArH), 7.35–7.32(m, 2H, ArH), 7.25–7.22 (m, 3H, ArH), 7.00–6.97 (m, 1H, ArH), 3.59–3.56 (m, 2H, CH_2N), 3.55–3.53 (m, 1H, CH), 3.49–3.43 (m, 2H, NCH_2), 2.44–2.03 (m, 2H, CH_2CO), 1.96–1.91 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 181.7, 177.4, 168.6, 158.6, 141.8, 139.8, 130.5, 130.5, 130.4, 129.4, 128.8, 128.0, 123.8, 120.0, 89.6, 40.7, 39.3, 37.8, 37.3, 20.3; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{20}ClN_3NaO_3$ [(M+Na)$^+$], 432.1085; found, 432.1086.

2-(8-(4-Methylbenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo-[1,2-*a*]pyrimidin-7-yl)-*N*-phenylacetamide (3e). Light yellow solid: mp 215–218 °C; IR (KBr): 3256, 3120, 1738, 1683, 1631, 1525, 1439, 1160, 1094, 837, 759 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.81 (br, 1H, NH), 9.52 (br, 1H, NH), 7.44–7.40 (m, 4H, ArH), 7.24–7.22 (m, 2H, ArH), 7.21–7.18 (m, 2H, ArH), 6.99–6.96 (m, 1H, ArH), 4.03–3.99 (m, 1H, CH), 3.57–3.54 (m, 2H, CH_2N), 3.42 (m, 2H, NCH_2), 2.53–2.28 (m, 2H, CH_2CO) 2.30 (s, 3H CH_3), 2.00–1.87 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ =183.3, 177.7, 168.9, 159.0, 139.8, 139.4, 129.8, 129.4, 127.6, 123.8, 124.6, 119.8, 88.9, 41.3, 40.0, 37.8, 37.6, 21.8, 20.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{24}N_3O_3$ [(M+H)$^+$], 390.1812; found, 390.1816.

2-(8-(4-Methoxybenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrro-lo[1,2-*a*]pyrimidin-7-yl)-*N*-phenylacetamide (3f). Light yellow solid: mp 207–209 °C; IR (KBr): 3334, 3244, 1731, 1638, 1526, 1438, 1161, 1090, 760 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.79 (br, 1H, NH), 9.54 (br, 1H, NH)), 7.51 (d, J = 8.5 Hz, 2H, ArH), 7.40 (d, J = 8.2 Hz, 2H, ArH), 7.23–7.20 (m, 2H, ArH), 6.99–6.96 (m, 1H, ArH), 6.91 (d, J = 8.6 Hz, 2H, ArH), 4.04–3.99 (m, 1H, CH), 3.76 (s, 3H, OCH_3), 3.61–3.49 (m, 4H, NCH_2CH_2N), 2.57–2.33 (m, 2H, CH_2CO), 1.96–1.89 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 187.5, 182.5, 175.1, 165.6, 163.8, 144.5, 139.8, 134.2, 134.2, 128.6, 124.6, 119.0, 95.5, 60.7, 46.2, 43.9, 42.6, 42.3, 25.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{24}N_3O_4$ [(M+H)$^+$], 406.1761; found, 406.1757.

2-(8-Benzoyl-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)-*N*-benzylacetamide (3g). Light yellow solid: mp 209–211.5 °C; IR (KBr): 3256, 3060, 2917, 1728, 1635, 1526, 1442, 1159, 907, 742 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.83 (br, 1H, NH), 7.92 (br 1H, NH–Bn), 7.55–7.50 (m, 2H, ArH), 7.42–7.36 (m, 3H, ArH), 7.30–7.27 (m, 2H, ArH), 7.22–7.21 (m, 1H, ArH), 7.11–7.09 (m, 2H, ArH), 4.19– 4.01 (m, 2H, CH_2Ph), 3.93–3.91 (m, 1H, CH), 3.62–3.45 (m, 2H, CH_2N), 3.40–3.39 (m, 2H, NCH_2), 2.39–2.11 (m, 2H, CH_2CO), 1.98–1.85 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 183.3, 177.7, 169.8, 159.2, 142.8, 140.25, 130.0, 129.0, 127.7, 127.5, 89.0, 42.6, 41.4, 39.6, 37.8, 36.4, 20.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{23}N_3NaO_3$ [(M+Na)$^+$], 412.1632; found, 412.1635.

***N*-Benzyl-2-(8-(4-fluorobenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)acetamide (3h).** Light yellow solid: mp 218–222 °C; IR (KBr): 3236, 3052, 1734, 1637, 1526, 1446, 1099, 845, 768 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.83 (br, 1H, NH), 7.94 (br 1H, NH–Bn), 7.60–7.58 (m, 2H,

ArH), 7.31–7.28 (m, 2H, ArH), 7.22–7.19 (m, 3H, ArH), 7.09–7.08 (m, 2H, ArH), 4.18–4.01 (m, 2H, CH_2Ph), 3.93–3.91 (m, 1H, CH), 3.62–3.45 (m, 4H, CH_2N), 2.44–2.15 (m, 2H, CH_2CO), 2.01–1.81 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 181.4, 177.2, 169.2, 163.8, 158.9, 139.7, 138.8, 129.4, 128.5, 127.2, 126.9, 115.3 (d, J = 21.3 Hz), 88.4, 42.1, 40.9, 38.7, 37.3, 35.9, 19.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{22}FN_3NaO_3$ [(M+Na)$^+$], 430.1537; found, 430.1537.

***N*-Benzyl-2-(8-(4-chlorobenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)acetamide (3i).** Light yellow solid: mp 232–234 °C; IR (KBr): 3366, 3227, 1736, 1635, 1525, 1086, 772 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.84 (br, 1H, NH), 7.95 (br 1H, NH–Bn), 7.56–7.54 (m, 2H, ArH), 7.44–7.42 (m, 2H, ArH) 7.31–7.28 (m, 2H, ArH), 7.21–7.19 (m, 1H, ArH)), 7.09–7.08 (m, 2H, ArH), 4.20–4.01 (m, 2H, CH_2Ph), 3.91 (m, 1H, CH), 3.63–3.49 (m, 2H, CH_2N), 3.40 (m, 2H, NCH_2), 2.55–2.16 (m, 2H, CH_2CO), 2.00–1.80 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 181.1, 177.1, 169.2, 159.1, 141.0, 139.7, 134.1, 129.0, 128.5, 128.5, 127.2, 126.9, 88.6, 42.1, 40.8, 38.7, 37.3, 35.9, 19.8; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{22}ClN_3NaO_3$ [(M+Na)$^+$], 446.1242; found, 446.1240.

***N*-Benzyl-2-(8-(2-chlorobenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)acetamide (3j).** Light yellow solid: mp 199–202°C; IR (KBr): 3363, 3226, 1738, 1635, 1525, 1086, 772 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.51 (br, 1H, NH), 8.02 (br 1H, NH–Bn), 7.46–7.42 (m, 1H, ArH), 7.36–7.30 (m, 4H, ArH), 7.23–7.18 (m, 4H, ArH), 4.18–7.07 (m, 2H, CH_2Ph), 3.56–3.52 (m, 1H, CH), 3.52–3.46 (m, 4H, NCH_2CH_2N), 2.28–1.93 (m, 2H, CH_2CO), 1.93–1.89 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 181.7, 177.5, 169.6, 158.6, 141.9, 140.3, 130.5, 130.4, 130.4, 129.0, 129.0, 127.9, 127.5, 89.7, 42.8, 40.5, 39.2, 37.7, 36.2, 20.3; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{22}ClN_3NaO_3$ [(M+Na)$^+$], 446.1242; found, 446.1241.

***N*-Benzyl-2-(8-(4-methylbenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)acetamide (3k).** Light yellow solid: mp 179–181 °C; IR (KBr): 3559, 3420, 3227, 1724, 1633, 1521, 1450, 1099, 756 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.85 (br, 1H, NH), 7.94 (br, 1H, NH-Bn), 7.47–7.45 (d, J = 7.9 Hz, 2H, ArH), 7.30–7.27 (m, 2H, ArH), 7.21–7.18 (m, 3H, ArH), 7.11–7.10 (d, J = 7.6 Hz, 2H, ArH), 4.19 –4.02 (m, 2H, CH_2Ph), 3.95–3.94 (m, 1H, CH), 3.61–3.44 (m, 2H, CH_2N), 3.47–3.45 (m, 2H, NCH_2), 2.40–2.16 (m, 2H, CH_2CO), 2.32 (s, 3H, CH_3), 1.94–1.85 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.7, 177.2, 169.4, 158.0, 139.7, 139.5, 139.0, 129.0, 128.5, 127.2, 127.1, 126.9, 88.4, 42.1, 41.0, 38.6, 37.3, 35.9, 21.4, 19.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{25}N_3NaO_3$ [(M+Na)$^+$], 426.1788; found, 426.1790.

***N*-Benzyl-2-(8-(4-methoxybenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)acetamide (3l).** Light yellow solid: mp 216–219 °C; IR (KBr): 3285, 3199, 2917, 1735, 1632, 1518, 1433, 1360, 1258, 1161, 1198, 1023, 849, 765, 613 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.83 (br, 1H, NH), 7.91 (br 1H, NH-Bn), 7.54–7.52 (d, J = 8.6 Hz, 2H, ArH), 7.31–7.25 (m, 1H, ArH), 7.21–7.20 (m, 1H, ArH), 7.10–7.09 (m, 2H, ArH), 6.91 (d, J =8.7 Hz, 2H, ArH), 4.18–4.02 (m, 2H, CH_2Ph), 3.95 (m, 1H, CH), 3.78 (s, 3H, OCH_3), 3.60–3.47 (m, 2H, CH_2N), 3.39–3.38 (m, 2H, NCH_2), 2.45–2.21 (m, 2H, CH_2CO), 1.97–1.81 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.1, 177.2, 169.4, 160.4, 158.6, 139.7, 134.7, 128.9, 128.5, 127.2, 126.9, 113.6, 88.1, 55.5, 42.1, 41.1, 38.6, 37.3, 35.9, 20.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{25}N_3NaO_4$ [(M+Na)$^+$], 442.1737; found, 442.1739.

2-(8-Benzoyl-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)-*N*-(4-fluorophenyl)acetamide (3m). Light yellow solid: mp 190.5–191.5 °C; IR (KBr): 3264, 3068, 1728, 1631, 1519, 1088, 837 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.81 (br, 1H, NH), 9.61 (br, 1H, NH), 7.52–7.50 (m, 2H, ArH), 7.47–7.35 (m, 5H, ArH), 7.07–7.04 (m, 2H, ArH), 4.04–3.94 (m, 1H, CH), 3.64–3.48 (m, 2H, CH_2N), 3.42–3.41 (m, 2H, NCH_2), 2.54–2.21 (m, 2H, CH_2CO), 1.97–1.89 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 183.3, 177.6, 168.8, 159.1, 157.7, 142.8, 136.2, 130.1, 129.0, 127.4, 121.5, 116.0 (d, J = 21.3 Hz), 88.9, 41.2, 39.2, 37.8, 37.3, 20.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{20}FN_3NaO_3$ [(M+Na)$^+$], 416.1381; found, 416.1380.

2-(8-(4-Fluorobenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo-[1,2-*a*]pyrimidin-7-yl)-*N*-(4-fluorophenyl)acetamide (3n). Light yellow solid: mp 129-132 °C; IR (KBr): 3267, 3076, 1733, 1636, 1515, 1440, 1267, 1224, 1158, 1082, 841, 772, 608, 510 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.80 (br, 1H, NH), 9.59(br, 1H, NH), 7.59–7.56 (m, 2H, ArH), 7.47–7.37 (m, 2H, ArH), 7.20–7.17 (m, 2H, ArH), 7.08–7.05 (m, 2H, ArH), 3.99–3.97 (m, 1H, CH), 3.62–3.50 (m, 2H, CH_2N), 3.43–3.42 (m, 2H, NCH_2), 2.57–2.25 (m, 2H, CH_2CO), 2.00–1.84 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 181.5, 177.1, 168.2, 162.9 (d, J = 245.0 Hz), 158.8, 158.2 (d, J = 238.8 Hz), 138.7, 135.6, 129.4, 121.1, 115.4 (d, J = 21.3 Hz), 115.3, 88.4, 40.8, 38.7, 37.3, 37.0, 19.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{19}F_2N_3NaO_3$ [(M+Na)$^+$], 434.1287; found, 3434.1287.

***N*-(4-Fluorophenyl)-2-(8-(4-methoxybenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)acetamide (3o).** Light yellow solid: mp 182–184.5 °C; IR (KBr): 3264, 3211, 3076, 1733, 1633 1512, 1428, 1255 1160, 1090, 1012 , 845, 767, 600, 498 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.81 (br, 1H, NH), 9.60 (br, 1H, NH), 7.53 (d, J =8.4 Hz, 2H, ArH), 7.45–7.42 (m, 2H, ArH), 7.09–7.05 (m, 2H, ArH), 6.93–6.91 (d, J= 8.4, 2H, ArH), 4.04–4.02 (m, 1H, CH), 3.77 (s, 3H, OCH_3), 3.55–3.54 (m,

2H, CH_2N), 3.43–3.42 (m, 2H, NCH_2), 2.58–2.33 (m, 2H, CH_2CO), 1.98–1.86 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.2, 177.2, 168.3, 160.4, 158.5, 135.7, 134.6, 128.8, 121.1, 115.5, 115.4, 113.7, 88.1, 55.4, 41.0, 38.6, 37.3, 37.0, 20.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{22}FN_3NaO_4$ [(M+Na)$^+$], 446.1487; found, 446.1485.

2-(8-Benzoyl-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)-*N*-(4-methoxyphenyl)acetamide (3p). Light yellow solid: mp 184.5–185.5 °C; IR (KBr): 3260, 3010, 1732, 1634, 1521, 14363, 1088, 828 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.84 (br, 1H, NH), 9.42 (br, 1H, NH), 7.55–7.54 (m, 2H, ArH), 7.45–7.38 (m, 3H, ArH), 7.35–7.33 (d, *J* = 9.0 Hz, 2H, ArH), 6.85–6.82 (d, *J* = 9.0 Hz, 2H, ArH), 4.01–3.99 (m, 1H, CH), 3.70 (s, 3H, OCH_3), 3.58–3.56 (m, 2H, CH_2N), 3.45–3.44 (m, 2H, NCH_2), 2.53–2.22 (m, 2H, CH_2CO), 2.02–1.88 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 183.3, 177.7, 168.3, 159.1, 155.8, 142.8, 133.0, 130.1, 129.0, 127.4, 121.4, 114.5, 89.0, 56.0, 41.3, 39.2, 37.8, 37.3, 20.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{23}N_3NaO_4$ [(M+Na)$^+$], 428.1581; found, 428.1579

2-(8-(4-Fluorobenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo-[1,2-*a*]pyrimidin-7-yl)-*N*-(4-methoxyphenyl)acetamide (3q). Light yellow solid: mp 225–226 °C; IR (KBr): 3260, 2937, 1732, 1655, 1521, 1088, 1033, 834 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.80 (br, 1H, NH), 9.37 (br, 1H, NH), 7.59–7.56 (m, 2H, ArH), 7.31–7.29 (d, *J*= 9.0 Hz, 2H, ArH), 7.21–7.19 (m, 2H, ArH), 6.81–6.79 (d, *J* = 9.0 Hz, 2H, ArH), 3.97–3.95 (m, 1H, CH), 3.68 (s, 3H, OCH_3), 3.57–3.53 (m, 2H, CH_2N), 3.42–3.41 (m, 2H, NCH_2), 2.54–2.23 (m, 2H, CH_2CO), 2.00–1.87 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.0, 177.7, 168.3, 163.4 (d, *J* = 245.0 Hz), 159.3, 155.9, 139.3, 133.0, 129.9, 121.4, 115.9 (d, *J* = 21.3 Hz), 114.5, 88.9, 56.0, 41.3, 39.2, 37.8, 37.4, 20.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{22}FN_3NaO_4$ [(M+Na)$^+$], 446.1487; found, 446.1484.

2-(8-(4-Methoxybenzoyl)-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)-*N*-(4-methoxyphenyl)acetamide (3r). Light yellow solid: mp 165–167 °C; IR (KBr): 3432, 3338, 1727, 1632, 1517, 1250, 1168, 1106, 1031, 841, 768, 616, 535, cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.82 (br, 1H, NH), 9.41 (br, 1H, NH), 7.54–7.52 (d, *J* = 8.7 Hz, 2H, ArH), 7.33–7.31 (d, *J* = 9.0 Hz, 2H, ArH), 6.93–6.91 (d, *J* = 8.7 Hz, 2H, ArH), 6.82–6.80 (d, *J* = 9.0 Hz, 2H, ArH), 4.03–4.01 (m, 1H, CH), 3.77 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.58–3.56 (m, 2H, CH_2N), 3.45–3.41 (m, 2H, NCH_2), 2.56–2.31 (m, 2H, CH_2CO), 1.98–1.86 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.2, 177.2, 167.9, 160.4, 158.5, 155.4, 134.7, 132.5, 128.8, 120.9, 114.0, 114.0, 113.7, 88.2, 55.5, 41.0, 38.7, 37.3, 36.9, 20.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{25}N_3NaO_5$ [(M+Na)$^+$], 458.1686; found, 458.1686.

2-(8-Benzoyl-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)-N-ethylacetamide (3s). Light yellow solid: mp 143.5–144.5 °C; IR (KBr): 3340, 3236, 1734, 1637, 1528, 1445, 1364, 1269, 1162, 1088, 744, 702, 635, 523 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.79 (br, 1H, NH), 7.53–7.47 (m, 2H, ArH), 7.40–7.35 (m, 2H, ArH), 7.33 (br, 1H, NH), 3.87–3.85 (m, 1H, CH), 3.59–3.44 (m, 4H, CH_2N), 2.92–2.82 (m, 2H, CH_2Me), 2.26–1.97 (m, 2H, CH_2CO), 1.94–1.86 (m, 2H, CH_2), 0.87–0.84 (m, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.8, 177.2, 168.9, 158.7, 142.3, 129.7, 128.4, 126.9, 88.6, 40.8, 38.7, 37.2, 36.0, 33.5, 19.9, 15.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{21}N_3NaO_3$ [(M+Na)$^+$], 350.1475; found, 350.1475.

***N*-Ethyl-2-(8-(4-fluorobenzoyl)-6-oxo-1,2,3,4,6,7-hexahydro-pyrrolo [1,2-*a*]pyrimidin-7-yl)acetamide (3t).** Light yellow solid: mp 199–200 °C; IR (KBr): 3324, 3072, 1729, 1631, 1538, 1446, 1372, 1102, 906, 857 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.78 (br, 1H, NH), 7.56–7.54 (m, 2H, ArH), 7.34 (br, 1H, NH), 7.20–7.16 (m, 2H, ArH), 3.85 (m, 1H, CH), 3.54–3.49 (m, 2H, CH_2N), 3.40 (m, 2H, NCH_2), 2.91–2.80 (m, 2H, CH_2Me), 2.30 –1.95 (m, 2H, CH_2CO), 1.96–1.83 (m, 2H, CH_2), 0.86–0.84 (m, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 181.4, 177.2, 168.8, 162.8 (d, *J* = 243.8 Hz), 158.8, 138.8, 129.4, 115.3 (d, *J* = 21.3 Hz), 88.5, 40.8, 38.7, 37.3, 36.0, 33.4, 19.9, 15.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{20}FN_3NaO_3$ [(M+Na)$^+$], 368.1381; found, 368.1379.

2-(8-Benzoyl-6-oxo-1,2,3,4,6,7-hexahydropyrrolo[1,2-*a*]pyrimidin-7-yl)acetamide (3u). Light yellow solid: mp 223–224 °C; IR (KBr): 3352, 3154, 1730, 1629, 1525, 1082, 890 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.80 (br, 1H, NH), 7.57–7.47 (m, 2H, ArH), 7.39 (m, 3H, ArH), 6.88 (br, 1H, NH), 6.52 (br, 1H, NH), 3.86–3.84 (m, 1H, CH), 3.55–3.46 (m, 4H, NCH_2), 2.25–1.97 (m, 2H, CH_2CO), 1.90–1.87 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.7, 177.3, 171.4, 158.7, 142.3, 129.5, 128.5, 127.0, 88.6, 40.7, 38.7, 37.3, 35.6, 19.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{16}H_{17}N_3NaO_3$ [(M+Na)$^+$], 322.1162; found, 322.1162.

2-(9-(4-Fluorobenzoyl)-7-oxo-2,3,4,5,7,8-hexahydro-1*H*-pyrrolo[1,2-*a*][1,3]diazepin-8-yl)-*N*-phenylacetamide (3v). Light yellow solid: mp 178–180 °C; IR (KBr): 3444, 3314, 1734, 1682, 1619, 1537, 1442, 1090, 853, 760 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.62 (br, 1H, NH), 9.54 (br, 1H, NH), 7.60–7.57 (m, 2H, ArH), 7.41–7.39 (m, 2H, ArH), 7.24–7.19 (m, 4H, ArH), 7.00–6.97 (m, 1H, ArH), 4.07–3.96 (m, 1H, CH), 3.96–3.69 (m, 2H, CH_2N), 3.64–3.60 (m, 2H, NCH_2), 2.62–2.23 (m, 2H, CH_2CO), 1.99–1.82 (m,4H, CH_2CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.0, 168.2, 165.1, 163.9, 162.0, 139.2, 138.6, 129.5, 129.0, 123.4, 119.3, 115.5 (d, *J* = 20.0 Hz), 90.2, 41.8, 40.9, 40.6, 37.2, 27.0, 24.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{22}FN_3NaO_3$ [(M+Na)$^+$], 430.1537; found, 430.1535.

2-(9-(4-Chlorobenzoyl)-7-oxo-2,3,4,5,7,8-hexahydro-1*H*-pyrrolo[1,2-*a*][1,3]diazepin-8-yl)-*N*-phenylacetamide (3w). Light yellow solid: mp 194.5–195.5 °C; IR (KBr): 3368, 3226, 1736, 1634, 1525, 1438, 1086, 1008, 772 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.62 (br, 1H, NH), 9.56 (br, 1H, NH), 7.55–7.53 (m, 2H, ArH), 7.45–7.43 (m, 2H, ArH), 7.39–7.38 (m, 2H, ArH), 7.24–7.21 (m, 2H, ArH), 6.99–6.9 (m, 2H, ArH), 4.00–3.98 (m, 1H, CH), 3.91–3.75 (m, 2H, CH_2N), 3.61–3.60 (m, 2H, NCH_2), 2.62–2.22 (m, 2H, CH_2CO), 1.92–1.90 (m,4H, CH_2CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 181.8, 178.4, 168.2, 165.2, 140.8, 139.2, 134.3, 129.0, 129.0, 128.7, 128.7, 123.4, 119.4, 90.4, 41.8, 40.7, 37.2, 27.0, 24.5; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{22}ClN_3NaO_3$ [$(M+Na)^+$], 446.1242; found, 446.1243.

2-(9-(4-Methylbenzoyl)-7-oxo-2,3,4,5,7,8-hexahydro-1*H*-pyrrolo[1,2-*a*][1,3]diazepin-8-yl)-*N*-phenylacetamide (3x). Light yellow solid: mp 197–198 °C; IR (KBr): 3248, 2917, 1737, 1683, 1619, 1536, 1440, 1053, 898, 756 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.64 (br, 1H, NH), 9.56 (br, 1H, NH), 7.45–7.40 (m, 4H, ArH), 7.24–7.19 (m, 4H, ArH), 6.99–6.96 (m, 1H, ArH), 4.05–4.03 (m, 1H, CH), 3.91–3.72 (m, 2H, CH_2N), 3.66–3.48 (m, 2H, NCH_2), 2.59–2.26 (m, 2H, CH_2CO), 2.32 (s, 3H, CH_3), 2.00–1.80 (m, 4H, CH_2CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 183.4, 178.5, 168.3, 164.9, 139.3, 129.1, 128.9, 128.9, 127.1, 123.3, 119.3, 119.3, 90.3, 41.9, 41.0, 40.7, 37.2, 27.1, 24.6, 21.4; HRMS (TOF ES^+): *m/z* calcd for $C_{24}H_{25}N_3NaO_3$ [$(M+Na)^+$], 426.1788; found, 426.1785.

***N*-Benzyl-2-(9-(4-fluorobenzoyl)-7-oxo-2,3,4,5,7,8-hexahydro-1*H*-pyrrolo[1,2-*a*][1,3]diazepin-8-yl)acetamide (3y).** Light yellow solid: mp 110-112 °C; IR (KBr): 3389, 3064, 1731, 1619, 1537, 1442, 1078, 837 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.67 (br, 1H, NH), 7.93 (br, 1H, NH), 7.60–7.68 (m, 2H, ArH), 7.31–7.28 (m, 2H, ArH), 7.22–7.18 (m, 3H, ArH), 7.09–7.07 (m, 2H, ArH), 4.21–3.91 (m, 2H, CH_2Ph), 3.94–3.91 (m, 1H, CH), 3.89–3.68 (m, 2H, CH_2N), 3.58–3.55 (m, 2H, NCH_2), 2.49–2.08 (m, 2H, CH_2CO), 1.97–1.79 (m, 4H, CH_2CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.0, 178.5, 169.2, 165.3, 162.4 (d, J = 245.0 Hz), 139.7, 138.6, 129.5, 128.5, 127.2, 126.9, 115.4 (d, J = 21.3 Hz), 90.2, 42.1, 41.9, 41.0, 36.1, 27.0, 24.5; HRMS (TOF ES^+): *m/z* calcd for $C_{24}H_{24}FN_3NaO_3$ [$(M+Na)^+$], 444.1693; found, 444.1694.

***N*-Benzyl-2-(9-(4-methylbenzoyl)-7-oxo-2,3,4,5,7,8-hexahydro-1*H*-pyrrolo[1,2-*a*][1,3]diazepin-8-yl)acetamide (3z).** Light yellow solid: mp 110.5–112 °C; IR (KBr): 3289, 2921, 1734, 1669, 1618, 1527, 1440, 1048, 738 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.68 (br, 1H, NH), 7.92 (br, 1H, NH), 7.45–7.44(m, 2H, ArH), 7.31–7.27 (m, 2H, ArH), 7.22–7.18 (m, 3H, ArH), 7.12–7.09 (m, 2H, ArH), 4.21–3.99 (m, 2H, CH_2Ph), 3.92–3.62 (m, 2H, CH_2N), 3.59–3.54 (m, 1H, CH), 3.44–2.55 (m, 2H, NCH_2), 2.45–2.11 (m, 2H, CH_2CO), 2.33 (s, 3H, CH_3), 1.88–1.784 (m,4H, CH_2CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 183.3, 178.5, 169.3, 165.1, 139.7, 139.4, 139.1, 129.0, 128.5, 127.2, 126.9, 90.3, 56.4, 42.1, 41.9, 40.7, 36.1, 27.1, 24.6, 21.4; HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{27}N_3NaO_3$ [$(M+Na)^+$], 440.1945; found, 440.1943.

2-(7-Benzoyl-5-oxo-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-a]-imidazol-6-yl)-*N*-phenylacetamide (3a´). Light yellow solid: mp 139–142.5 °C; IR (KBr): 3257, 3060, 1727, 1635, 1525, 1442, 1112, 742 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.55 (br, 1H, NH), 9.46 (br, 1H, NH), 7.45–7.43 (m, 2H, ArH), 7.39–7.32 (m, 3H, ArH), 7.28–7.24 (m, 4H, ArH), 7.04–7.01 (m, 1H, ArH), 3.92–3.88 (m, 1H, CH), 3.80–3.61 (m, 4H, CH_2CH_2), 2.97–2.50 (m, 2H, CH_2CO); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 189.7, 172.7, 166.4, 154.5, 142.4, 139.2, 129.1, 129.0, 128.5, 126.5, 123.7, 119.8, 84.7, 43.1, 41.9, 41.0, 36.5; HRMS (TOF ES^+): *m/z* calcd for $C_{21}H_{19}N_3NaO_3$ [$(M+Na)^+$], 384.1319; found, 384.1320.

2-(7-(4-Methoxybenzoyl)-5-oxo-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-6-yl)-*N*-phenylacetamide (3b´). Light yellow solid: mp 122–125 °C; IR (KBr): 3416, 3305, 1690, 1614, 1496, 1443, 1170, 1023, 841 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.66 (br, 1H, NH), 9.24 (br, 1H, NH), 7.47–7.45 (m, 2H, ArH), 7.29–7.26(m, 4H, ArH), 7.04–7.02 (m, 1H, ArH), 6.91–6.90 (m, 2H, ArH), 3.89–3.86 (m, 1H, CH), 3.76 (s, 3H, OCH_3), 3.71–3.70 (m, 4H, CH_2CH_2), 2.95–2.58 (m, 2H, CH_2CO); ^{13}C NMR (125 MHz, DMSO-d_6): δ =189.3, 172.7, 167.5, 160.2, 157.2, 139.3, 134.6, 129.1, 128.6, 123.7, 119.7, 113.7, 84.7, 55.6, 43.0, 41.9, 41.1, 36.3; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{21}N_3NaO_4$ [$(M+Na)^+$], 414.1424; found, 414.1427.

2-(7-Benzoyl-5-oxo-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]-imidazol-6-yl)-*N*-(4-fluorophenyl)acetamide (3c´). Light yellow solid: mp 131–132.5 °C; IR (KBr): 3499, 3400, 1686, 1620, 1508, 1102, 1013, 849 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.65 (br, 1H, NH), 9.48 (br, 1H, NH), 7.47–7.44 (m, 2H, ArH), 7.36–7.35 (m, 3H, ArH), 7.24–7.23 (m, 2H, ArH), 7.13–7.09 (m, 2H, ArH), 3.92–3.89 (m, 1H, CH), 3.77–3.57 (m, 4H, CH_2CH_2), 2.98–2.55 (m, 2H, CH_2CO); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 189.7, 172.6, 167.4, 159.4, 157.5, 142.4, 135.6, 129.1, 128.5, 126.4, 121.5, 115.6 (d, J = 21.3 Hz), 84.6, 43.1, 41.8, 40.9, 36.5; HRMS (TOF ES^+): *m/z* calcd for $C_{21}H_{18}FN_3NaO_3$ [$(M+Na)^+$], 402.1224; found, 402.1226.

2-(7-Benzoyl-5-oxo-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]-imidazol-6-yl)-*N*-(4-methoxyphenyl)acetamide (3d´). Light yellow solid: mp 181–182 °C; IR (KBr): 3264, 3072, 2958, 1689, 1624, 1504, 1025, 833, 702 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.49 (br, 1H, NH), 9.41 (br, 1H, NH), 7.36–7.33 (m, 5H, ArH), 7.25–7.22 (m, 2H, ArH), 6.85–6.83 (m, 2H, ArH), 3.92–

3.85 (m, 1H, CH), 3.78–3.71 (m, 2H, CH_2N), 3.70 (s, 3H, OCH_3), 3.68–3.53 (m, 2H, NCH_2), 2.95–2.54 (m, 2H, CH_2CO); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 189.7, 172.2, 167.5, 157.5, 155.6, 142.5, 132.3, 129.1, 128.4, 126.4, 121.3, 114.1, 84.8, 55.5, 43.1, 41.8, 40.8, 36.6; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{21}N_3NaO_4$ [(M+Na)$^+$], 414.1424; found, 414.1423.

***N*-Benzyl-2-(7-(4-methoxybenzoyl)-5-oxo-2,3,5,6-tetrahyd-ro-1*H*-pyrrolo[1,2-*a*]imidazol-6-yl)acetamide (3e´).** Light yellow solid: mp 191–193 °C; IR (KBr): 3309, 2925, 1691, 1625, 1498, 1450, 1021, 846, 702 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 9.44 (br, 1H, NH), 8.09 (br, 1H, NH-Bn), 7.32–7.31 (m, 2H, ArH), 7.25–7.23 (m, 3H, ArH), 7.21–7.20 (m, 2H, ArH), 6.82–6.80 (m, 2H, ArH), 4.26–4.11 (m, 2H, CH_2Ph), 3.92–3.82 (m, 1H, CH), 3.75 (s, 3H, OCH_3), 3.67–3.51 (m, 4H, CH_2CH_2), 2.86–2.55 (m, 2H, CH_2CO); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 189.1, 173.6, 167.8, 160.0, 139.8, 134.6, 128.6, 128.6, 127.5, 127.1, 113.5, 84.7, 55.5, 43.1, 42.6, 41.8, 40.1, 36.6; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{23}N_3NaO_4$ [(M+Na)$^+$], 428.1581; found, 428.1579.

2-(7-Benzoyl-5-oxo-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]-imidazol-6-yl)-*N*-ethylacetamide (3f´). Light yellow solid: mp 230.5–231.5 °C; IR (KBr): 3110, 2952, 1695, 1590, 1529, 1458, 1123, 984, 774 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.18 (br, 1H, NH), 7.29–7.25 (m, 3H, ArH), 7.18–7.14 (m, 2H, ArH), 6.82 (br, 1H, NH), 3.69–3.65 (m, 1H, CH), 3.53–3.47 (m, 4H, CH_2CH_2), 3.17–3.12 (m, 2H, CH_2Me), 2.84–2.41 (m, 2H, CH_2CO), 0.93–0.86 (m, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 189.0, 179.8, 176.4, 165.8, 144.4, 128.7, 127.2, 85.1, 43.7, 43.7, 40.0, 37.0, 33.7, 13.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{17}H_{20}N_3O_3$ [(M+H)$^+$], 314.1499; found, 314.1493.

2-(7-(4-Chlorobenzoyl)-5-oxo-2,3,5,6-tetrahydro-1*H*-pyrr-olo[1,2-*a*]imidazol-6-yl)-*N*-ethylacetamide (3g´). Light yellow solid: mp 221–223 °C; IR (KBr): 3395, 3273, 1690, 1589, 1523, 1401, 1127, 841 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.12 (br, 1H, NH), 7.35–7.33 (m, 2H, ArH), 7.21–7.17 (m, 2H, ArH), 6.86 (br, 1H, NH), 3.67–3.50 (m, 4H, CH_2CH_2), 3.17–3.14 (m, 1H, CH), 2.86–2.45 (m, 2H, CH_2CO), 2.52–2.48 (m, 2H, CH_2Me), 0.90–0.86 (m,3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ =187.1, 179.1, 175.9, 165.3, 142.6, 132.7, 128.8, 128.2, 84.8, 43.1, 43.1, 40.0, 36.5, 33.2, 12.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{17}H_{18}ClN_3NaO_3$ [(M+Na)$^+$], 370.0929; found, 370.0928.

***N*-Ethyl-2-(7-(4-methoxybenzoyl)-5-oxo-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-6-yl)acetamide (3h´).** Light yellow solid: mp 183–186 °C; IR (KBr): 3195, 2966, 1693, 1591, 1522, 1460, 1120, 1031, 825 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.19 (br, 1H, NH), 7.14 (d, *J*= 7.2 Hz, 2H, ArH), 6.84 (d, *J*= 8.1 Hz, 2H, ArH), 6.73 (br, 1H, NH), 3.85–3.81 (m, 1H, CH), 3.73 (s, 3H, OCH_3), 3.50–3.46 (m, 4H, CH_2CH_2), 3.23–3.19 (m, 2H, CH_2Me), 2.85–2.45 (m, 2H, CH_2CO), 0.94–0.89 (m, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 188.4, 179.4, 176.0, 165.2, 159.3, 136.3, 128.4, 113.5, 113.5, 84.8, 55.4, 43.1, 43.1, 36.5, 33.2, 13.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{22}N_3O_4$ [(M+H)$^+$], 344.1605; found, 344.1607.

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