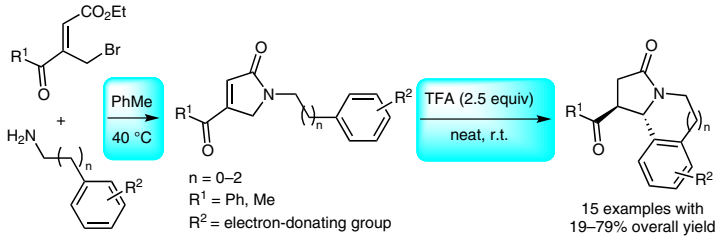
Synthesis K. Jebali et al. Paper

A Short and Efficient Approach to Pyrrolo[2,1-*a*]isoquinoline and Pyrrolo[2,1-*a*]benzazepine Derivatives

Khaoula Jebali[a,b]
Aurélien Planchat[a]
Hassen Amri[*b]
Monique Mathé-Allainmat[*a]
Jacques Lebreton[*a]

[a] Université de Nantes, CNRS, Laboratoire CEISAM-UMR CNRS 6230, Faculté des Sciences et des Techniques, 2 rue de la Houssinière, BP 92208, 44322 Nantes Cedex 3, France
jacques.lebreton@univ-nantes.fr
monique.mathe@univ-nantes.fr
[b] Département de Chimie, Université de Tunis El Manar, Faculté des Sciences, Campus, 2092 Tunis, Tunisia
hassen.amri@fst.rnu.tn



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Abstract A Brønsted acid promoted intramolecular Friedel–Crafts cyclization of β-benzoyl- and β-acetylpyrrol-2(5*H*)-one derivatives tethered via nitrogen to an electron-rich arene nucleus is developed. Using this efficient methodology, various pyrrolo[2,1-*a*]isoquinoline and pyrrolo[2,1-*a*]benzazepine derivatives are prepared in a two-step sequence starting from readily available ethyl (*Z*)-3-bromomethyl-4-oxo-4-phenylbut-2-enoate or ethyl (*Z*)-3-bromomethyl-4-oxopent-2-enoate.

Key words Friedel–Crafts reaction, nitrogen heterocycles, alkaloids, lactams, Brønsted acids

The 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline[1] ring system is present in many naturally occurring products, as either a simple tricyclic pyrroloisoquinoline core **A** or as more complex compounds bearing additional fused rings, as well as closed structures such as 1*H*-pyrrolo[2,1-*a*]benzazepine **B** (Figure 1).[2]

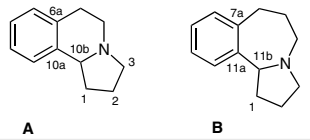


Figure 1 Frameworks of pyrrolo[2,1-*a*]isoquinoline **A** and pyrrolo[2,1-*a*]benzazepine **B**

The pyrroloisoquinoline ring system **A** is an important privileged core structure that forms the nucleus of numerous natural and synthetic biologically active compounds as depicted in Figure 2. For example, (*S*)-(–)-trolline,[3] an alkaloid isolated from the flowers of *Trollius chinensis* Bunge in 2004, exhibits antibacterial activity against respiratory bacteria[4] such as *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Klebsiella pneumoniae*, as well as moderate antiviral activity against influenza viruses A and B. Interestingly, (+)-oleracein E, the antipode of (–)-trolline isolated from *Portulaca oleracea* L., displays 1,1-diphenyl-2-picryl-hydrazyl (DPPH) radical scavenging activity[5] and can be regarded as an antioxidant. Lamellarin D,[6] isolated from the marine mollusk, *Lamellaria*, has been identified as a potent inhibitor of human topoisomerase I inducing apoptosis through a mitochondria-mediated pathway.[7] Jamtine, an antiglycemic alkaloid, is found in the aqueous extract of leaves of the climbing shrub, *Cocculus hirsutus*, which is commonly used in folk medicine, mainly in Pakistan.[8] Other alkaloids isolated from the *Erythrina* species, such as (+)-erysotramidine, present a large range of pharmacological effects including sedative, hypotensive, muscle-relaxant, anticonvulsant and CNS-depressant activities.[9] In the field of the potential treatment of inflammatory diseases, synthetic compound **1** inhibits PARP-1 (also known as Poly [ADP-ribose] polymerase 1) activity and protects cells against oxidative DNA damage.[10]

Numerous methodologies have been developed over the years enabling efficient access to a range of pyrrolo[2,1-*a*]isoquinoline- and pyrrolo[2,1-*a*]benzazepine-based natural products and related compounds.[11] Although many of these strategies have proved effective for the synthesis of these products, *N*-acyliminium chemistry has emerged as one of the most efficient methodologies. Since the pioneering work of Speckamp[12] and others,[13] the intramolecular acid-mediated cyclization of *N*-acyliminium ion intermediates,[14] or related species,[15] on electron-rich aromatic rings as π-nucleophile partners has been widely used for the synthesis of these N-heterocyclic compounds. In this context, it

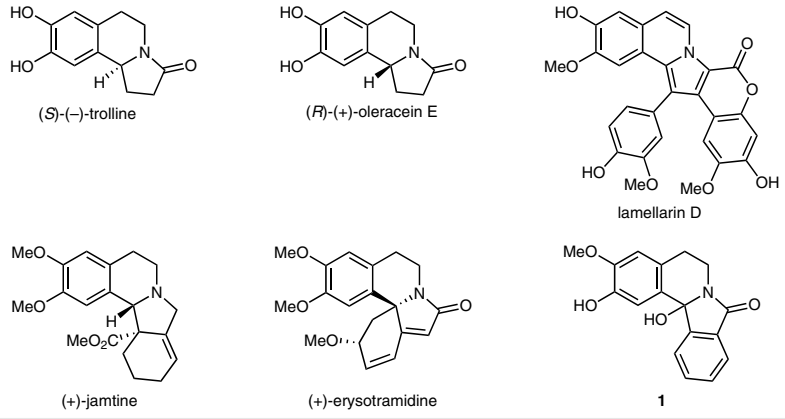


Figure 2 Selected pyrrolo[2,1-*a*]isoquinoline compounds

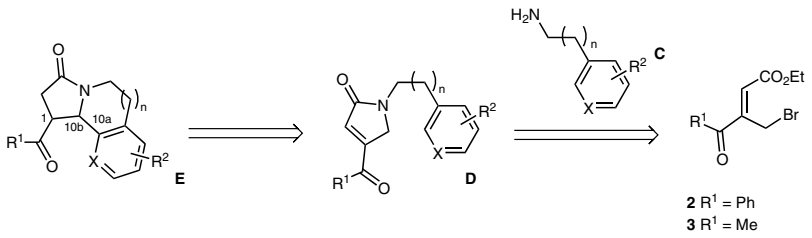
is important to mention the recent example of a Friedel–Crafts-type cyclization of hydroxylactam derivatives via *N*-acyliminium species catalyzed with tin(IV) triflimidate [$Sn(NTf_2)_4$] as a Lewis superacid, as published by Dalla, Duñach and co-workers.[16]

In continuation of our current investigations on the use of ethyl (*Z*)-3-bromomethyl-4-oxo-4-phenylbut-2-enoate (**2**) or ethyl (*Z*)-3-bromomethyl-4-oxopent-2-enoate (**3**) as versatile building blocks for the preparation of novel templates for drug discovery, as well as scaffolds for combinatorial libraries, we herein describe a practical and original synthetic route to the pyrrolo[2,1-*a*]isoquinoline and pyrrolo[2,1-*a*]benzazepine frameworks based on the retrosynthesis shown in Scheme 1.

Our goal was to develop a short sequence, in just two basic transformations, to prepare nitrogen polyheterocyclic compounds **E**. In this way, condensation of reactive bromide derivatives **2** or **3** with the appropriate amine N-tethered to an electron-rich arene nucleus **C** afforded the α,β-unsaturated γ-lactam intermediate **D**. The latter, by an intramolecular Friedel–Crafts cyclization,[17,18] via the formation of an *N*-acyliminium species, provided the C10a–C10b bond formation leading to the desired target derivatives **E**. It should be emphasized at this point that the presence of an acyl group at C-1 in compounds **E** affords an additional point of diversification by postsynthetic modification of these substituted tricyclic systems.

Our synthetic efforts started with the preparation of the required lactams for the intramolecular Friedel–Crafts cyclization. In previous work, we demonstrated that pyrrol-2(5*H*)-one derivatives **D** were easily accessible through a condensation reaction between ethyl (*Z*)-3-bromomethyl-4-oxopent-2-enoate (**3**) in the presence of two equivalents of amine in refluxing bromobenzene.[19] However, in order to use only one equivalent of amine, we investigated several sets of reaction conditions without success. For example, compound **5a** (see Table 1) was formed in low yield (<10%) when one equivalent of Et_3N was used to trap the HBr formed during the reaction (data not shown). Nevertheless, we were pleased to note that this condensation could be carried out in toluene at 40 °C with two equivalents of amine, instead of refluxing bromobenzene, with the same efficiency. In this manner, various β-benzoyl- and β-acetylpyrrol-2(5*H*)-one derivatives N-tethered to an electron-rich arene moiety, such as **4a**–**n**, were obtained in moderate to good yields (37–85%) (see Table 1).

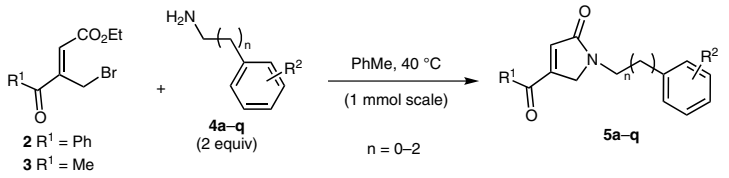
Having secured the preparation of a wide range of substrates, we next evaluated the intramolecular Friedel–Crafts-type Michael addition sequence. In order to identify the most efficient conditions, we performed a systematic optimization of this sequence using various Lewis and Brønsted acids. For a greater electron-donating effect for this cyclization step, we selected the substrate **5a**, which



Scheme 1 Retrosynthesis of the target heterocyclic compounds **E**

contains an aromatic ring bearing two methoxy groups with one located at the *para* position relative to the potential cyclization site.

Table 1 Synthesis of β-Benzoyl- or β-Acetyl-α,β-unsaturated γ-Lactams **5a–q**



R^2 = electron-donating group

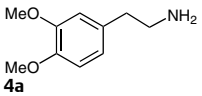
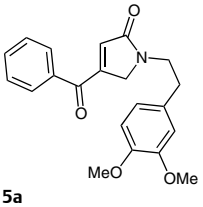
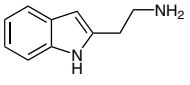
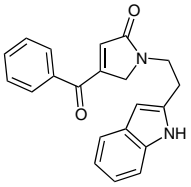
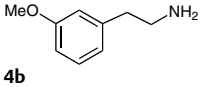
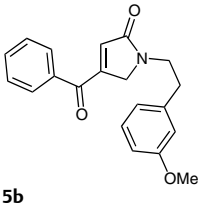
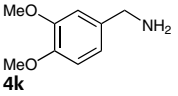
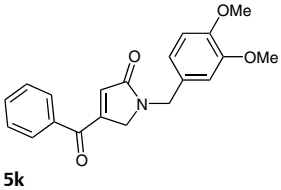
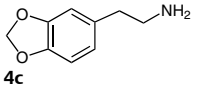
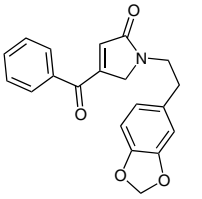
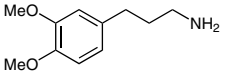
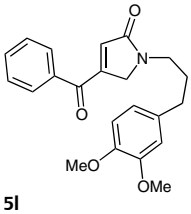
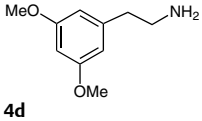
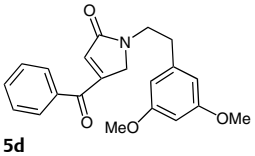
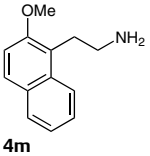
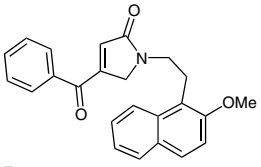
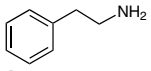
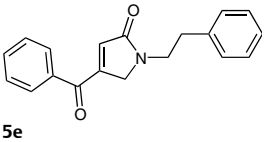
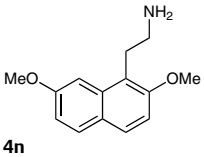
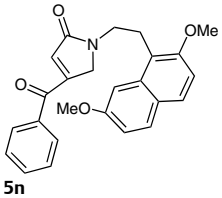
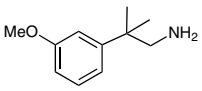
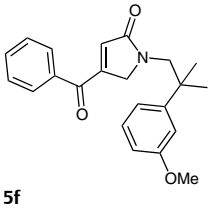
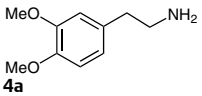
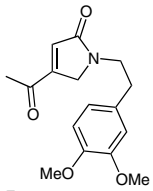
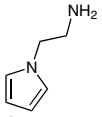
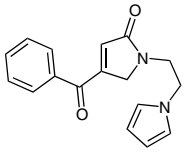
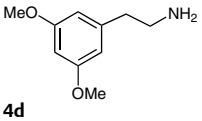
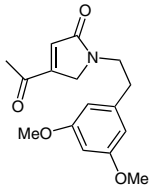
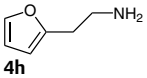
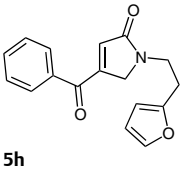
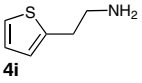
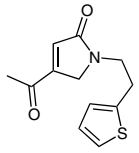
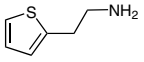
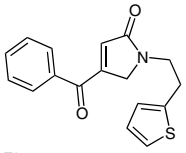
Amine	Time (h)	Pyrrol-2(5*H*)-one	Yield (%)[a]	Amine	Time (h)	Pyrrol-2(5*H*)-one	Yield (%)[a]
 **4a**	4	 **5a**	78	 **4j**	6	 **5j**	78
 **4b**	5	 **5b**	85	 **4k**	24	 **5k**	46
 **4c**	3	 **5c**	37	 **4l**	45	 **5l**	69
 **4d**	32	 **5d**	59	 **4m**	5	 **5m**	48
 **4e**	6	 **5e**	83	 **4n**	5	 **5n**	63

Table 1 (continued)

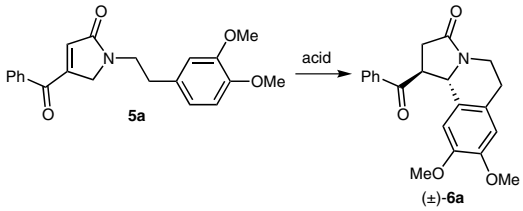
Amine	Time (h)	Pyrrol-2(5*H*)-one	Yield (%)[a]	Amine	Time (h)	Pyrrol-2(5*H*)-one	Yield (%)[a]
 **4f**	2	 **5f**	64	 **4a**	24	 **5o**	50
 **4g**	4	 **5g**	53	 **4d**	7	 **5p**	45
 **4h**	72	 **5h**	55	 **4i**	13	 **5q**	80
 **4i**	4	 **5i**	85				

[a] Yields refer to those of pure isolated products after chromatography.

Attempted intramolecular cyclization of this model substrate **5a** in the presence of 2.5 equivalents of different Lewis acids, such as $SnBr_4$, $TiCl_4$ or BCl_3, at room temperature in dichloromethane led to the recovery of unchanged starting material (Table 2, entries 1–3) or to decomposition with $FeCl_3$ (Table 2, entry 4). Under the same conditions with $BF_3{\cdot}Et_2O$, a trace amount of the desired cyclized adduct **6a** was isolated (<5% yield) (Table 2, entry 5), but in refluxing 1,2-dichloroethane the yield increased to around 25% (Table 2, entry 6). In this series, $AlCl_3$ gave the best yield with 40% of isolated cyclized compound **6a** (Table 2, entry 7). On the other hand, $AlBr_3$ was less efficient and only a trace amount (<10% yield) of the desired product **6a** was obtained (Table 2, entry 8). Among the tested Lewis acids, the best results were obtained with trimethylsilyl trifluoromethanesulfonate (TMSOTf) with a 62% yield of isolated cyclized compound **6a** being obtained (Table 2, entry 9). However, with this moisture-sensitive Lewis acid, the presence of trifluoromethanesulfonic acid (TfOH) is to be expected under these reaction conditions. So, to our delight, it transpired that TfOH promoted the desired intramolecular Friedel–Crafts-type Michael addition to afford compound **6a** in 78% yield by simple treatment at room temperature in dichloromethane (Table 2, entry 10). Moreover, when the cyclization reaction was performed with neat TFA (only 2.5 equivalents), the desired compound **6a** was also isolated in 78% yield (Table 2, entry 11). Finally, we attempted this cyclization using neat acetic acid at room temperature without success: most of the starting material was recovered unchanged (Table 2, entry 12). When heated at reflux temperature in a mixture of 1,2-dichloroethane and acetic acid, no cyclization occurred and significant decomposition of **5a** was noted (Table 2, entry 13).

It should be pointed out that the cyclized product **6a** was formed as a single diastereoisomer within the detection limits of ^1H and ^{13}C NMR spectroscopy of the crude mixture. The X-ray single-crystal diffraction analysis of pure (±)-**6a** confirmed the *trans*-stereochemical relationship between the benzoyl group at C-1 and the C10a–C10b bond, as illustrated in Figure 3. To complete this study, it is

Table 2 Optimization of the Cyclization Conditions[a]



Entry	Acid	Solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	$SnBr_4$	CH_2Cl_2	25	24	0[c]
2	$TiCl_4$	CH_2Cl_2	25	24	0[c]
3	BCl_3	CH_2Cl_2	25	48	0[c]
4	$FeCl_3$	CH_2Cl_2	25	7	0[d]
5	$BF_3{\cdot}Et_2O$	CH_2Cl_2	25	24	3
6	$BF_3{\cdot}Et_2O$	$ClCH_2CH_2Cl$	84	12	25
7	$AlCl_3$	CH_2Cl_2	25	48	40
8	$AlBr_3$	CH_2Cl_2	25	24	7
9	TMSOTf	CH_2Cl_2	25	16	62
10	TfOH	CH_2Cl_2	25	2	78
11	TFA	–[e]	25	6	78
12	AcOH	–[e]	25	4	0[c]
13	AcOH	$ClCH_2CH_2Cl$	84	48	0[d]

[a] Acid (2.5 equiv), **5a** (0.3 mmol), solvent (1.5 mL).
[b] Yield of isolated product.
[c] Quantitative recovery of the starting material.
[d] Starting material decomposed.
[e] Neat TFA or AcOH (2.5 equiv) was used.

worth noting that Dalla and co-workers recently reported an original and efficient methodology using 1,1,2,2-tetrachloroethane (TCE) as the solvent at reflux (146 °C) to generate a very small amount of HCl in situ.[20] This promoted the intramolecular Friedel–Crafts cyclization of *N*,*O*-acetals N-tethered to an electron-rich arene nucleus. Unfortunately, none of the expected compound **6a** was formed in refluxing TCE with our model substrate **5a**. The presence of a benzoyl group at C-4 seemed to have a significant effect on this cascade reaction and under our conditions (*vide infra*). In fact, an analogue of **6a** without a benzoyl group at C-4 was successfully obtained in 84% yield from the intramolecular cyclization of the corresponding *N*,*O*-acetal precursor by refluxing in TCE.[20] Although TfOH gave similar yields to TFA, the latter was chosen for investigation with other substrates as it is a cheaper reagent.

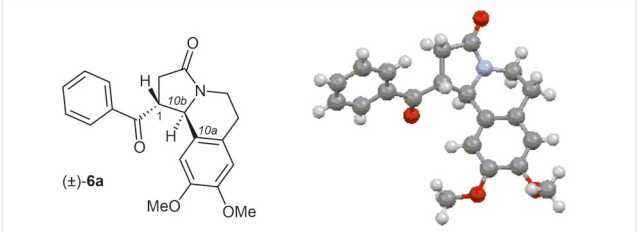
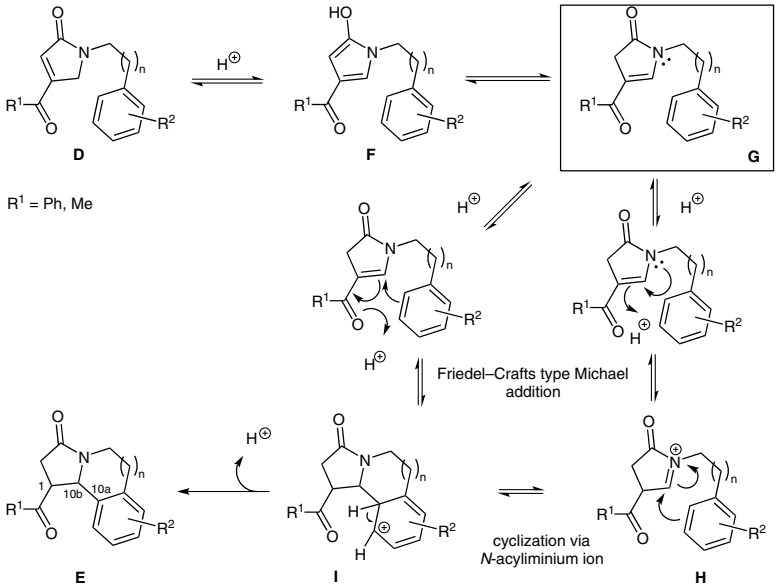


Figure 3 Single-crystal X-ray diffraction structure of (±)-**6a**

On the basis of the experimental results, a plausible mechanism for the formation of compound **E** is depicted in Scheme 2.

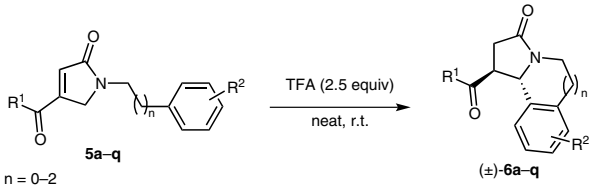
The process started with the isomerization of the double bond of the α,β-unsaturated γ-lactam derivative **D** *via* the intermediate **F** to give the corresponding key enamine intermediate **G**. Next, this latter intermediate **G**, in the pres-



Scheme 2 Proposed mechanism of the acid-promoted cyclization

ence of TFA, gave the reactive *N*-acyliminium species **H**, which subsequently underwent an aromatic π-cyclization reaction to provide the C10a–C10b bond formation followed by rearomatization affording the desired tricyclic pyrrolo derivative **E**.[21] It is interesting to note that the presence of an acyl moiety at C-4 in **D** could favor the isomerization of the double bond into the corresponding conjugated acylenamine **G** (*vide infra*). Moreover, in this context from intermediate **G**, an acid-promoted intramolecular Friedel–Crafts-type Michael addition process could also occur to afford the tricyclic pyrrolo derivative **E** via the intermediate **I**. With optimized experimental conditions in hand, we proceeded to investigate other α,β-unsaturated γ-lactams *N*-tethered to an electron-rich arene nucleus as π-nucleophiles. Therefore, all the subsequent cyclizations were carried out under these optimized conditions and the results are depicted in Table 3.

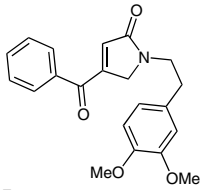
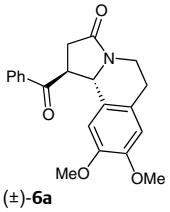
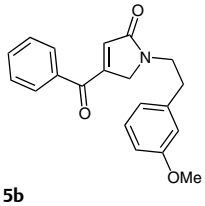
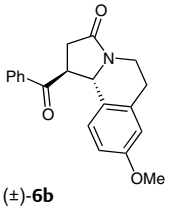
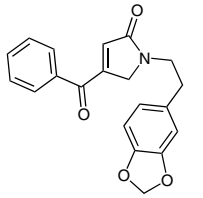
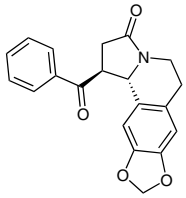
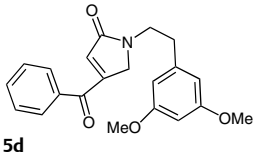
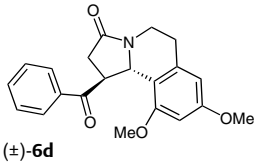
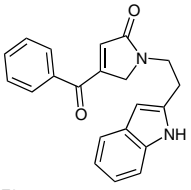
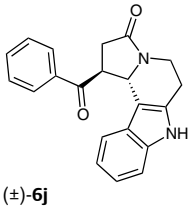
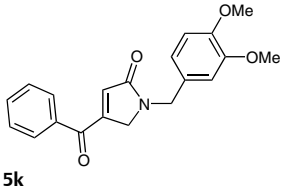
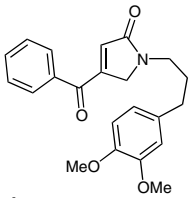
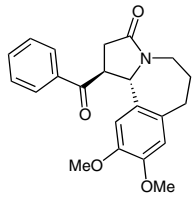
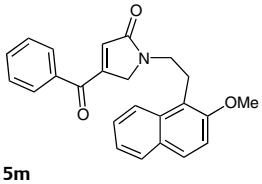
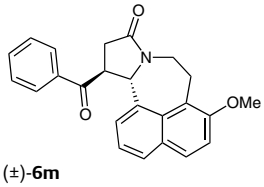
Table 3 Synthesis of β-Benzoyl- and β-Acetylpyrrol-2(5*H*)-one Derivatives **6a–q**



5a–q

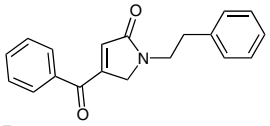
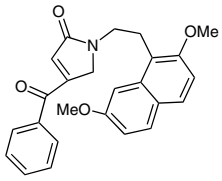
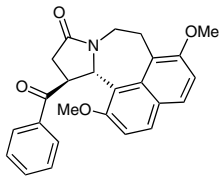
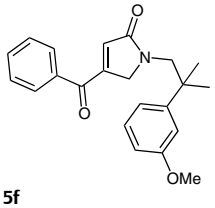
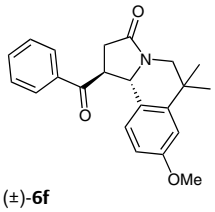
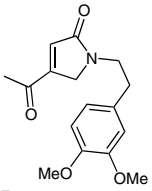
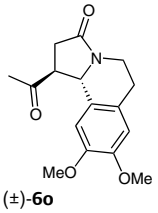
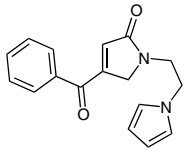
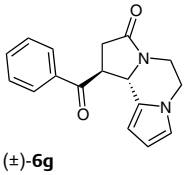
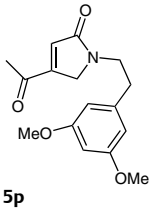
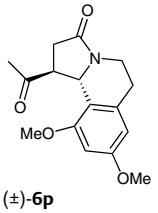
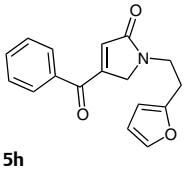
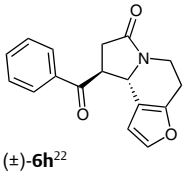
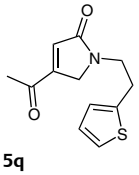
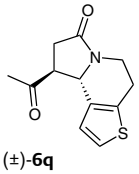
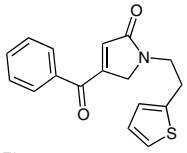
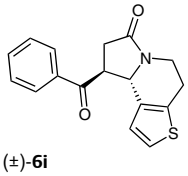
n = 0–2
R^1 = Ph, Me
R^2 = electron-donating group

(±)-**6a–q**

Entry	Substrate	Time (h)	Product	Yield (%)[a]
1	 **5a**	6	 (±)-**6a**	78
2	 **5b**	5	 (±)-**6b**	68
3	 **5c**	3	 (±)-**6c**	73
4	 **5d**	4	 (±)-**6d**	78
10	 **5j**	6	 (±)-**6j**	85
11	 **5k**	72	no cyclization (±)-**6k**	0
12	 **5l**	7	 (±)-**6l**	47
13	 **5m**	7	 (±)-**6m**	47

[a] Yield of isolated product.

Table 3 (continued)

Entry	Substrate	Time (h)	Product	Yield (%)[a]	Entry	Substrate	Time (h)	Product	Yield (%)[a]
5	 **5e**	96	no cyclization (±)-**6e**	0	14	 **5n**	6	 (±)-**6n**	88
6	 **5f**	4	 (±)-**6f**	67	15	 **5o**	24	 (±)-**6o**	54
7	 **5g**	5	 (±)-**6g**	86	16	 **5p**	12	 (±)-**6p**	43
8	 **5h**	7	 (±)-**6h**[22]	85	17	 **5q**	13	 (±)-**6q**	47
9	 **5i**	24	 (±)-**6i**	93					

[a] Yields refer to those of pure isolated products after chromatography.

A series of substrates with a phenyl ring bearing electron-donating substituents afforded the corresponding desired adducts **6a**–**d** in good yields (68–78%) (Table 3, entries 1–4). The position of the electron-donating groups apparently had no influence on the efficiency of the reaction.

However, with non-substituted phenyl ring compound **5e** (Table 3, entry 5), no reaction was observed. This clearly illustrates the electronic effect on this cyclization process. Interestingly, with substrates **5a**–**c** (Table 3, entries 1–3), no regioisomeric product resulting from cyclization at the *ortho* position was observed, which is probably due to steric reasons. We also examined the cyclization sequence with substrate **5f** having an *N*-ethyl chain with a *gem*-dimethyl carbon. The cyclized compound (±)-**6f** was isolated in 67% yield (Table 3, entry 6). Other substrates **5g**–**j**, containing electron-rich heteroaromatics such as pyrrole, furan, thiophene and indole, afforded the desired cyclized compounds **6g**–**j** in good to excellent 85–93% yields (Table 3, entries 7–10).

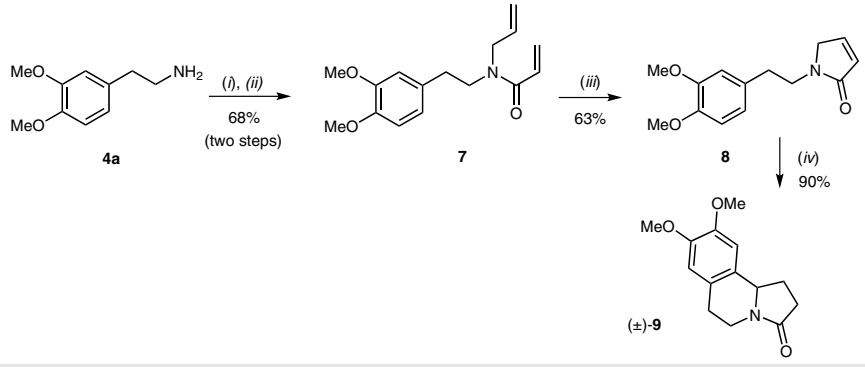
Next, to illustrate the synthetic viability of our methodology, we examined the effects of chain length with the *N*-methyl derivative **5k** and its corresponding *N*-propyl-tethered substrate **5l**, both with a phenyl ring bearing two methoxy groups, as in our model **5a**. In sharp contrast to the latter compound **5a**, no cyclization occurred with the *N*-methyl-tethered substrate **5k** (Table 3, entry 11). However,

on exposure of the *N*-propyl-tethered substrate **5l** to the optimized reaction conditions, the desired seven-membered annulated compound **6l** was obtained in a modest 47% yield (Table 3, entry 12) after purification by silica gel chromatography. This clearly indicated that the lactam-tethered aromatic ring with one carbon linker **5k** is too short to enable cyclization. To diversify the structural framework further, we examined in this sequence the reactivity of the naphthyl group as the π-electrophile. In this way, substrates **5m** and **5n** furnished the expected cyclized compounds **6m** and **6n** in 47% and 88% yields, respectively (Table 3, entries 13 and 14). The lower yield observed with pyrrol-2(5*H*)-one **5m** may result from the absence of the methoxy group at the C-7 position on the naphthyl ring compared to substrate **5n**. When the optimized conditions were applied to the acetyl pyrrol-2-one series, starting from the α,β-unsaturated γ-lactams **5o**–**q**, the expected cyclized products **6o**–**q** were isolated as well, although somewhat lower yields were obtained compared to their analogues in the benzoyl series (Table 3, entries 15–17, for **6a** and **6o**: 78% versus 54%, for **6d** and **6p**: 78% versus 43%, for **6i** and **6q**: 93% versus 47%). We assumed that the lower efficiency of these cyclization reactions is due to the sensitivity of the enolizable acetyl group to the strongly acidic reaction conditions.

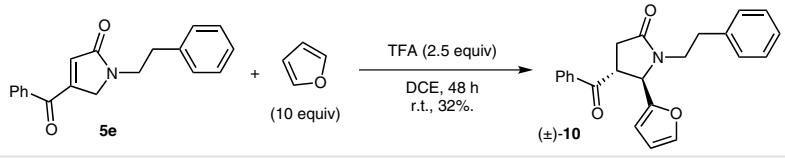
In addition, to evaluate whether an acyl residue at the C-4 position in compound **5a** could influence the reaction by favoring the formation of the expected conjugated enamine **G** (see Scheme 2), the derivative **8** was prepared as depicted in Scheme 3. It should be pointed out that in this case the intramolecular aromatic π-cyclization could only occur through an *N*-acyliminium ion (see Scheme 2). Under optimized cyclization conditions, a higher reaction temperature of 50 °C and a longer time were necessary to complete the conversion and afford the desired adduct (±)-**9** in 90% yield. This indicated that the rate of the cyclization of compound **8** was slightly decreased compared to the acyl parent **5a**.

After exploring different aspects of this intramolecular sequence with various substrates, we examined the bimolecular version with anisole and furan as electron-rich substrates under the optimized conditions. Unfortunately, all attempts failed with anisole, and only the formation of a complex mixture of compounds was observed. Thus, we turned our attention to furan. Despite screening various conditions, starting from the α,β-unsaturated γ-lactam **5e**, the desired adduct **10** was isolated in only 32% yield after purification on a silica gel column when the reaction was performed in DCE as the solvent with 10 equivalents of furan in the presence of 2.5 equivalents of TFA (Scheme 4).

In summary, we have successfully developed a simple, short and efficient stereoselective methodology for the construction of 1,2,3,5,6,7,10b-hexahydropyrrolo[2,1-*a*]isoquinoline and 1*H*-pyrrolo[2,1-*a*]benzazepine frameworks from the corresponding readily available ethyl (*Z*)-3-bromomethyl-4-oxo-4-phenylbut-2-enoate (**2**) or ethyl (*Z*)-3-bromomethyl-4-oxopent-2-enoate (**3**). The key step of this strategy involves a TFA-promoted intramolecular Friedel–Crafts cyclization on β-acyl-α,β-unsaturated γ-lactam intermediates N-tethered to a π-nucleophilic aryl or a heteroaromatic group, which are more suitable for the Friedel–Crafts reaction. Further improvements and applications in the field of medicinal chemistry are underway and the results will be reported in due course.



Scheme 3 *Reagents and conditions*: (i) allylbromide, K_2CO_3, THF; (ii) acryloyl chloride, Et_3N, CH_2Cl_2; (iii) Grubbs' second generation catalyst, toluene, 40 °C; (iv) TFA (2.5 equiv), 50 °C, 26 h.



Scheme 4 Synthesis of adduct **10** using an intermolecular process from **5e**

All solvents used were reagent grade. Non-commercial amines **4m** and **4n** were prepared as described in the literature.[23] TLC was performed on silica-covered aluminum (Kieselgel 60F_{254}, Merck). Eluted TLCs were revealed using UV radiation (λ = 254 nm) and molybdate solution. Flash column chromatography was performed on silica gel 60 (ACC 40–63 µm 5SDS-CarloErba). Infrared spectroscopic analyses were recorded on an IRTF Bruker Tensor, Spectrophotometer Specac Quest ATK system (samples were neat). NMR spectra were recorded on a Bruker AC300 (300 MHz for ^{1}H and 75 MHz for ^{13}C) and a Bruker 400 (400 MHz for ^{1}H and 100 MHz for ^{13}C) at room temperature, on samples dissolved in an appropriate deuterated solvent. Tetramethylsilane (TMS) for ^{1}H and the deuterated solvent signal for ^{13}C were used as references. Assignments of individual signals were carried out using COSY, HSQC, HMBC and DEPT experiments. Chemical shifts (δ) are expressed in parts per million (ppm), and coupling constants (*J*) in hertz (Hz). C_{IV} refers to quaternary carbons in the ^{13}C spectra. Low-resolution mass spectrometry (MS) were performed in the CEISAM laboratory on a Thermo-Finnigan DSQII quadripolar spectrometer using chemical ionization (CI) at 70 eV with NH_3 gas. High-resolution mass spectrometry (HRMS in Da units) was performed on an LC-Q-TOF (Synapt-G2 HDMS, Waters) instrument in the IRS-UN center (Mass Spectrometry platform, Nantes), or an LTQ-Orbitrap ThermoFisher Scientific instrument in the Oniris center (LABERCA laboratory, Nantes), or a MALDI-TOF apparatus (Autoflex III from Muker) in the INRA center (BIBS platform, Nantes).

Ethyl (*Z*)-3-(Bromomethyl)-4-oxo-4-phenylbut-2-enoate (2)

According to previous work,[19] to a stirred solution of ethyl 3-benzoylbut-3-enoate (10 g, 45 mmol) in CCl_4 (100 mL), Br_2 (55 mmol, 2.8 mL, 1.2 equiv) was added at –10 °C. The resulting mixture was left for 1 h at r.t. and then washed with sat. $Na_2S_2O_3$ solution, dried over $MgSO_4$ and filtered. Et_3N (100 mmol, 13.6 mL) was then added at –10 °C and stirring was continued for 10 h at r.t. The mixture was filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel (PE–Et_2O, 90:10) to give the desired product **2** as a yellow solid (10.2 g, 75%).

IR: 1716, 1664, 1270, 1208, 1154, 932, 713 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.82 (m, 2 H, H_{Ar}), 7.64–7.61 (m, 1 H, H_{Ar}), 7.52–7.48 (m, 2 H, H_{Ar}), 6.11 (s, 1 H, =C*H*), 4.91 (s, 2 H, CH_2Br), 4.28 (qd, *J* = 7.1 Hz, 2 H, CH_2CH$_3$), 1.32 (t, *J* = 7.1 Hz, 3 H, CH_3CH$_2$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5 (*C*OPh), 164.8 (*C*O$_2$Et), 149.4 (C_{IV}), 136.0 (C_{IV}), 133.7 (C_{Ar}), 130.0 (2 × C_{Ar}), 128.8 (2 × C_{Ar}), 126.2 (=CH), 61.5 (*C*H$_2$), 23.9 (*C*H$_2$Br), 14.2 (*C*H$_3$).

MS (CI$^+$): *m*/*z* = 296 [M]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{13}O_3BrNa$: 318.9940; found: 318.9937.

β-Benzoyl-α,β-unsaturated γ-Lactams 5a–n and β-Acetyl-α,β-unsaturated γ-Lactams 5o–q; General Procedure 1

Primary amine **4** (2.5 mmol, 2 equiv) was added dropwise to a solution of ethyl (*Z*)-3-(bromomethyl)-4-oxo-4-phenylbut-2-enoate (**2**) (300 mg, 1.00 mmol, 1 equiv) or ethyl (*Z*)-3-(bromomethyl)-4-oxopent-2-enoate (**3**) (300 mg, 1.20 mmol, 1 equiv) in toluene (7 mL) and the solution was heated at 40 °C until total consumption of the starting material. The solvent was removed in vacuo and the crude residue was purified by column chromatography on silica gel (CH_2Cl_2–Et_2O, 98:2 to 95:5).

4-Benzoyl-1-(3,4-dimethoxyphenethyl)-1,5-dihydro-2*H*-pyrrol-2-one (5a)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5a** was obtained as an orange oil in 78% yield (272 mg).

IR: 3060, 2935, 2835, 1717, 1514, 1260, 1235, 1154, 1141, 1026 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.38 (m, 5 H, H_{Ar}), 6.84–6.82 (m, 1 H, H_{Ar}), 6.72–6.69 (m, 3 H, H_{Ar}, =C*H*), 3.88 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.77 (t, *J* = 6.0 Hz, 2 H, CH_2CH$_2$), 3.46 (d, *J* = 3.0 Hz, 2 H, CH_2N), 2.87 (t, *J* = 6.0 Hz, 2 H, CH$_2$CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.9 (*C*OPh), 176.2 (*C*ON), 149.5 (C_{IV}), 148.3 (C_{IV}), 147.1 (=CH), 138.4 (C_{IV}), 131.7 (C_{Ar}), 130.3 (C_{IV}), 128.5 (2 × C_{Ar}), 128.3 (2 × C_{Ar}), 121.3 (C_{Ar}), 117.1 (C_{IV}), 112.1 (C_{Ar}), 111.7 (C_{Ar}), 56.1 (OCH$_3$), 56.0 (OCH$_3$), 44.5 (*C*H$_2$), 36.3 (*C*H$_2$), 35.0 (*C*H$_2$).

MS (CI$^+$): *m*/*z* = 352 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{21}O_4NNa$: 374.1362; found: 374.1359.

4-Benzoyl-1-(3-methoxyphenethyl)-1,5-dihydro-2*H*-pyrrol-2-one (5b)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5b** was obtained as a brown oil in 85% yield (272 mg).

IR: 2939, 2835, 1706, 1623, 1259, 1151 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.47 (m, 1 H, H_{Ar}), 7.40–7.37 (m, 4 H, H_{Ar}), 7.29–7.24 (m, 1 H, H_{Ar}), 6.87–6.83 (m, 1 H, H_{Ar}), 6.77–6.75 (m, 1 H, H_{Ar}), 6.72–6.70 (m, 2 H, = C*H*, H_{Ar}), 3.81–3.77 (m, 5 H, OCH_3, CH_2CH$_2$), 3.46 (d, *J* = 1.5 Hz, 2 H, CH_2N), 2.90 (t, *J* = 6.6 Hz, 2 H, CH$_2$CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.9 (*C*OPh), 176.2 (*C*ON), 160.2 (C_{IV}), 147.2 (=CH), 139.5 (C_{IV}), 138.4 (C_{IV}), 131.6 (C_{Ar}), 130.1 (C_{Ar}), 128.5 (2 × C_{Ar}), 128.3 (2 × C_{Ar}), 121.4 (C_{Ar}), 117.1 (C_{IV}), 114.9 (C_{Ar}), 112.3 (C_{Ar}), 55.3 (OCH$_3$), 44.3 (*C*H$_2$), 36.2 (*C*H$_2$), 35.4 (*C*H$_2$).

MS (CI$^+$): *m*/*z* = 322 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{20}O_3N$: 322.1438; found: 322.1441.

1-[2-(Benzo[*d*][1,3]dioxol-5-yl)ethyl]-4-benzoyl-1,5-dihydro-2*H*-pyrrol-2-one (5c)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5c** was obtained as a brown oil in 37% yield (123 mg).

IR: 2922, 2778, 1676, 1487, 1442, 1243, 1035 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.49 (m, 1 H, H_{Ar}), 7.46–7.38 (m, 4 H, H_{Ar}), 6.79 (d, *J* = 8.0 Hz, 1 H, H_{Ar}), 6.73 (t, *J* = 1.8 Hz, 1 H, =C*H*), 6.66–6.61 (m, 2 H, H_{Ar}), 5.95 (s, 2 H, CH_2), 3.74 (t, *J* = 6.4 Hz, 2 H, CH_2CH$_2$), 3.46 (d, *J* = 1.8 Hz, 2 H, CH_2N), 2.84 (t, *J* = 6.4 Hz, 2 H, CH$_2$CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.9 (*C*OPh), 176.2 (*C*ON), 148.2 (C_{IV}), 147.0 (=CH), 146.8 (C_{IV}), 138.5 (C_{IV}), 131.7 (C_{Ar}), 131.6 (C_{IV}), 128.5 (2 × C_{Ar}), 128.3 (2 × C_{Ar}), 122.2 (C_{Ar}), 117.3 (C_{IV}), 109.3 (C_{Ar}), 108.8 (C_{Ar}), 101.2 (*C*H$_2$), 44.5 (*C*H$_2$), 36.3 (*C*H$_2$), 35.1 (*C*H$_2$).

MS (CI$^+$): *m*/*z* = 336 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{18}O_4N$: 336.1230; found: 336.1230.

4-Benzoyl-1-(3,5-dimethoxyphenethyl)-1,5-dihydro-2*H*-pyrrol-2-one (5d)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5d** was obtained as a brown oil in 59% yield (206 mg).

IR: 2936, 2838, 2853, 1706, 1594, 1458, 1204, 1150 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.53–7.35 (m, 5 H, H_{Ar}), 6.74 (t, *J* = 1.8 Hz, 1 H, =C*H*), 6.40 (t, *J* = 2.1 Hz, 1 H, H_{Ar}), 6.32 (d, *J* = 2.1 Hz, 2 H, H_{Ar}), 3.78–3.74 (m, 8 H, CH_2CH_2, 2 × OCH_3), 3.46 (d, *J* = 1.8 Hz, 2 H, CH_2N), 2.86 (t, *J* = 6.6 Hz, 2 H, CH_2CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.9 (*C*OPh), 176.2 (*C*ON), 161.3 (2 × C_{IV}), 147.2 (=CH), 140.2 (C_{IV}), 138.4 (C_{IV}), 131.6 (C_{Ar}), 128.5 (2 × C_{Ar}), 128.2 (2 × C_{Ar}), 117.1 (C_{IV}), 107.1 (2 × C_{Ar}), 98.8 (C_{Ar}), 55.4 (2 × OCH_3), 44.2 (CH_2), 36.2 (CH_2), 35.6 (CH_2).

MS (CI^+): *m*/*z* = 352 $[M + H]^+$.

HRMS (ESI^+): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{22}O_4N$: 352.1543; found: 352.1545.

4-Benzoyl-1-phenethyl-1,5-dihydro-2*H*-pyrrol-2-one (5e)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5e** was obtained as a brown oil in 83% yield (241 mg).

IR: 1720, 1590, 1351, 1141, 697, 658 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.05 (m, 10 H, H_{Ar}), 6.57 (t, *J* = 2.0 Hz, 1 H, =C*H*), 3.68 (t, *J* = 6.8 Hz, 2 H, CH_2CH_2), 3.33 (d, *J* = 2.0 Hz, 2 H, CH_2N), 2.82 (t, *J* = 6.8 Hz, 2 H, CH_2CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.9 (*C*OPh), 176.1 (*C*ON), 147.0 (=CH), 138.4 (C_{IV}), 137.9 (C_{IV}), 131.6 (C_{Ar}), 129.1 (2 × C_{Ar}), 129.1 (2 × C_{Ar}), 128.4 (2 × C_{Ar}), 128.3 (2 × C_{Ar}), 127.1 (C_{Ar}), 117.1 (C_{IV}), 44.4 (CH_2), 36.2 (CH_2), 35.3 (CH_2).

MS (CI^+): *m*/*z* = 292 $[M + H]^+$.

HRMS (ESI^+): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{17}O_2NNa$: 314.1157; found: 314.1155.

4-Benzoyl-1-[2-(3-methoxyphenyl)-2-methylpropyl]-1,5-dihydro-2*H*-pyrrol-2-one (5f)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5f** was obtained as a yellow oil in 64% yield (223 mg).

IR: 2965, 1733, 1598, 1489, 1210 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.43 (m, 1 H, H_{Ar}), 7.35–7.22 (m, 5 H, H_{Ar}), 6.97–6.94 (m, 1 H, H_{Ar}), 6.89 (t, *J* = 1.8 Hz, 1 H, H_{Ar}), 6.84–6.81 (m, 1 H, H_{Ar}), 6.22 (t, *J* = 1.8 Hz, 1 H, =C*H*), 3.79 (s, 3 H, OCH_3), 3.66 (s, 2 H, CH_2), 3.42 (d, *J* = 1.8 Hz, 2 H, CH_2N), 1.37 (s, 6 H, 2 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.7 (*C*OPh), 176.8 (*C*ON), 160.0 (C_{IV}), 147.6 (C_{IV}), 147.2 (=CH), 138.5 (C_{IV}), 131.4 (C_{Ar}), 129.9 (C_{Ar}), 128.3 (2 × C_{Ar}), 128.2 (2 × C_{Ar}), 118.9 (C_{Ar}), 116.6 (C_{IV}), 113.3 (C_{Ar}), 111.2 (C_{Ar}), 55.4 (OCH_3), 54.4 (CH_2), 40.0 (C_{IV}), 35.7 (CH_2), 26.3 (2 × CH_3).

MS (CI^+): *m*/*z* = 350 $[M + H]^+$.

HRMS (ESI^+): *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{24}O_3N$: 350.1751; found: 350.1757.

1-[2-(1*H*-Pyrrol-1-yl)ethyl]-4-benzoyl-1,5-dihydro-2*H*-pyrrol-2-one (5g)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5g** was obtained as a brown oil in 53% yield (148 mg).

IR: 3056, 2936, 2872, 1717, 1684, 1264, 1157 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.36 (m, 5 H, H_{Ar}), 6.63 (t, *J* = 2.1 Hz, 2 H, =C*H*), 6.26–6.23 (m, 3 H, =C*H*), 4.12–4.09 (m, 2 H, CH_2CH_2), 3.84–3.81 (m, 2 H, CH_2CH_2), 3.47 (d, *J* = 1.8 Hz, 2 H, CH_2N).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.0 (*C*OPh), 176.1 (*C*ON), 146.2 (=CH), 138.0 (C_{IV}), 131.7 (C_{Ar}), 128.5 (2 × C_{Ar}), 128.4 (2 × C_{Ar}), 120.7 (2 × =CH), 117.9 (C_{IV}), 109.8 (2 × =CH), 48.4 (CH_2), 44.3 (CH_2), 36.0 (CH_2).

MS (CI^+): *m*/*z* = 281 $[M + H]^+$.

HRMS (ESI^+): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{17}O_2N_2$: 281.1285; found: 281.1285.

4-Benzoyl-1-[2-(furan-2-yl)ethyl]-1,5-dihydro-2*H*-pyrrol-2-one (5h)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5h** was obtained as a brown oil in 55% yield (155 mg).

IR: 2937, 1721, 1593, 1449, 1448, 695, 660 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.50 (m, 3 H, H_{Ar}), 7.43–7.39 (m, 2 H, H_{Ar}), 7.36 (d, *J* = 1.6 Hz, 1 H, =C*H*), 6.81 (t, *J* = 1.6 Hz, 1 H, =C*H*), 6.35–6.34 (m, 1 H, =C*H*), 6.12–6.11 (m, 1 H, =C*H*), 3.83 (t, *J* = 6.4 Hz, 2 H, CH_2CH_2), 3.47 (d, *J* = 1.6 Hz, 2 H, CH_2N), 2.96 (t, *J* = 6.4 Hz, 2 H, CH_2CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.0 (*C*OPh), 176.2 (*C*ON), 151.5 (C_{IV}), 146.7 (=CH), 142.0 (=CH), 138.5 (C_{IV}), 131.7 (C_{Ar}), 128.5 (2 × C_{Ar}), 128.4 (2 × C_{Ar}), 117.6 (C_{IV}), 110.7 (=CH), 108.0 (=CH), 41.5 (CH_2), 36.3 (CH_2), 27.8 (CH_2).

MS (CI^+): *m*/*z* = 282 $[M + H]^+$.

HRMS (ESI^+): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{16}O_3N$: 282.1130; found: 282.1135.

4-Benzoyl-1-[2-(thiophen-2-yl)ethyl]-1,5-dihydro-2*H*-pyrrol-2-one (5i)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5i** was obtained as a brown oil in 85% yield (253 mg).

IR: 3065, 2922, 2852, 1705, 1447, 1231, 1174 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.37 (m, 5 H, H_{Ar}), 7.26 (dd, *J* = 5.2 Hz, *J* = 1.6 Hz, 1 H, =C*H*), 7.00 (dd, *J* = 3.4 Hz, *J* = 1.6 Hz, 1 H, =C*H*), 6.86–6.84 (m, 1 H, =C*H*), 6.83 (t, *J* = 1.8 Hz, 1 H, =C*H*), 3.81 (t, *J* = 6.6 Hz, 2 H, CH_2CH_2), 3.48 (d, *J* = 1.8 Hz, 2 H, CH_2N), 3.17 (t, *J* = 6.6 Hz, 2 H, CH_2CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.0 (*C*OPh), 176.2 (*C*ON), 146.7 (=CH), 140.0 (C_{IV}), 138.5 (C_{IV}), 131.7 (C_{Ar}), 128.5 (2 × C_{Ar}), 128.4 (2 × C_{Ar}), 127.5 (=CH), 126.5 (=CH), 124.8 (=CH), 117.5 (C_{IV}), 44.8 (CH_2), 36.3 (CH_2), 29.5 (CH_2).

MS (CI^+): *m*/*z* = 298 $[M + H]^+$.

HRMS (ESI^+): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{16}O_2NS$: 298.0896; found: 298.0896.

1-[2-(1*H*-Indol-2-yl)ethyl]-4-benzoyl-1,5-dihydro-2*H*-pyrrol-2-one (5j)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5j** was obtained as a yellow oil in 78% yield (256 mg).

IR: 2921, 1703, 1591, 1143, 734, 659 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (br s, 1 H, NH), 7.56–7.54 (m, 1 H, H_{Ar}), 7.45–7.39 (m, 2 H, H_{Ar}), 7.27–7.23 (m, 2 H, H_{Ar}), 7.16–7.10 (m, 3 H, H_{Ar}), 7.02 (d, *J* = 3.2 Hz, 1 H, =C*H*), 6.59 (t, *J* = 1.6 Hz, 1 H, =C*H*), 3.87 (t, *J* = 6.4 Hz, 2 H, CH_2CH$_2$), 3.43 (d, *J* = 1.6 Hz, 2 H, CH_2N), 3.12 (t, *J* = 6.4 Hz, 2 H, CH$_2$CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.9 (*C*OPh), 176.3 (*C*ON), 147.5 (=*C*H), 138.4 (C_{IV}), 136.6 (C_{IV}), 131.4 (C_{Ar}), 128.4 (2 × C_{Ar}), 128.1 (2 × C_{Ar}), 127.1 (C_{IV}), 122.9 (C_{Ar}), 122.8 (C_{Ar}), 120.2 (C_{Ar}), 118.5 (C_{Ar}), 116.8 (C_{IV}), 112.2 (C_{IV}), 111.5 (C_{Ar}), 43.7 (*C*H$_2$CH$_2$), 36.3 (*C*H$_2$N), 25.0 (CH$_2$*C*H$_2$).

MS (CI$^+$): *m*/*z* = 331 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{18}N_2O_2Na$: 353.1266; found: 353.1266.

4-Benzoyl-1-(3,4-dimethoxybenzyl)-1,5-dihydro-2*H*-pyrrol-2-one (5k)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5k** was obtained as a brown oil in 46% yield (155 mg).

IR: 2930, 2840, 1717, 1520, 1247 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.59 (m, 2 H, H_{Ar}), 7.52–7.49 (m, 1 H, H_{Ar}), 7.45–7.39 (m, 2 H, H_{Ar}), 7.15 (t, *J* = 2.1 Hz, 1 H, =C*H*), 6.81–6.76 (m, 3 H, H_{Ar}), 4.64 (s, 2 H, CH_2Ar), 3.87 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.57 (d, *J* = 2.1 Hz, 2 H, CH_2N).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.0 (*C*OPh), 176.0 (*C*ON), 149.6 (C_{IV}), 149.3 (C_{IV}), 145.4 (=*C*H), 138.6 (C_{IV}), 131.8 (C_{Ar}), 128.6 (2 × C_{Ar}), 128.4 (C_{IV}), 128.3 (2 × C_{Ar}), 120.5 (C_{Ar}), 118.5 (C_{IV}), 111.5 (C_{Ar}), 111.3 (C_{Ar}), 56.1 (2 × OCH_3), 46.2 (*C*H$_2$), 36.6 (*C*H$_2$).

MS (CI$^+$): *m*/*z* = 338 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{19}O_4NNa$: 360.13628; found: 360.13593.

4-Benzoyl-1-[3-(3,4-dimethoxyphenyl)propyl]-1,5-dihydro-2*H*-pyrrol-2-one (5l)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5l** was obtained as a brown oil in 69% yield (250 mg).

IR: 3060, 2924, 2853, 1704, 1514, 1234, 1155 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.66–7.63 (m, 2 H, H_{Ar}), 7.57–7.52 (m, 1 H, H_{Ar}), 7.49–7.43 (m, 2 H, H_{Ar}), 7.16 (t, *J* = 1.8 Hz, 1 H, =C*H*), 6.78–6.75 (m, 1 H, H_{Ar}), 6.96–6.66 (m, 2 H, H_{Ar}), 3.84 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 3.56 (t, *J* = 7.2 Hz, 2 H, CH_2), 3.50 (d, *J* = 1.8 Hz, 2 H, CH_2), 2.59 (t, *J* = 7.5 Hz, 2 H, CH_2), 1.94 (qt, *J* = 7.5 Hz, *J* = 7.2 Hz, 2 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.9 (*C*OPh), 176.3 (*C*ON), 149.0 (C_{IV}), 147.6 (C_{IV}), 146.3 (C_{Ar}), 138.6 (C_{IV}), 133.0 (C_{IV}), 131.8 (C_{Ar}), 128.7 (2 × C_{Ar}), 128.2 (2 × C_{Ar}), 120.2 (C_{Ar}), 118.2 (C_{IV}), 111.6 (C_{Ar}), 111.4 (C_{Ar}), 56.0 (OCH_3), 55.9 (OCH_3), 42.4 (*C*H$_2$), 36.5 (*C*H$_2$), 32.5 (*C*H$_2$), 30.6 (*C*H$_2$).

MS (CI$^+$): *m*/*z* = 366 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{23}O_4NNa$: 388.1519; found: 388.1503.

4-Benzoyl-1-[2-(2-methoxynaphthalen-1-yl)ethyl]-1,5-dihydro-2*H*-pyrrol-2-one (5m)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5m** was obtained as a brown oil in 48% yield (177 mg).

IR: 3062, 2939, 2837, 1724, 1593, 1349, 1250 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89–7.83 (m, 3 H, H_{Ar}), 7.51–7.20 (m, 6 H, H_{Ar}), 6.95–6.91 (m, 2 H, H_{Ar}), 6.30 (t, *J* = 1.8 Hz, 1 H, =C*H*), 3.92 (s, 3 H, OCH_3), 3.88 (t, *J* = 6.6 Hz, 2 H, CH_2CH$_2$), 3.44 (t, *J* = 6.6 Hz, 2 H, CH$_2$CH_2), 3.36 (d, *J* = 1.8 Hz, 2 H, CH_2N).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.9 (*C*OPh), 176.6 (*C*ON), 155.1 (C_{IV}), 147.6 (=*C*H), 138.3 (C_{IV}), 133.3 (C_{IV}), 131.3 (C_{Ar}), 129.2 (C_{IV}), 128.9 (C_{Ar}), 128.8 (C_{Ar}), 128.2 (2 × C_{Ar}), 128.1 (2 × C_{Ar}), 127.3 (C_{Ar}), 123.9 (C_{Ar}), 122.4 (C_{Ar}), 118.9 (C_{IV}), 116.5 (C_{IV}), 112.8 (C_{Ar}), 56.3 (OCH_3), 42.8 (*C*H$_2$), 36.0 (*C*H$_2$), 24.2 (*C*H$_2$).

MS (CI$^+$): *m*/*z* = 372 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{22}O_3N$: 372.1594; found: 372.1598.

4-Benzoyl-1-[2-(2,7-dimethoxynaphthalen-1-yl)ethyl]-1,5-dihydro-2*H*-pyrrol-2-one (5n)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5n** was obtained as a brown oil in 63% yield (252 mg).

IR: 2938, 1681, 1262, 733, 661 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 9.0 Hz, 1 H, H_{Ar}), 7.72 (d, *J* = 9.0 Hz, 1 H, H_{Ar}), 7.46–7.40 (m, 1 H, H_{Ar}), 7.29–7.24 (m, 2 H, H_{Ar}), 7.18 (d, *J* = 2.7 Hz, 1 H, H_{Ar}), 7.13 (d, *J* = 9.0 Hz, 1 H, H_{Ar}), 7.04–6.99 (m, 3 H, H_{Ar}), 6.41 (t, *J* = 1.8 Hz, 1 H, =C*H*), 3.93 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 3.86 (t, *J* = 6.6 Hz, 2 H, CH_2CH$_2$), 3.40 (t, *J* = 6.6 Hz, 2 H, CH$_2$CH_2), 3.35 (d, *J* = 1.8 Hz, 2 H, CH_2N).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.9 (*C*OPh), 176.7 (*C*ON), 159.0 (C_{IV}), 155.6 (C_{IV}), 147.7 (=CH), 138.4 (C_{IV}), 134.8 (C_{IV}), 131.4 (C_{Ar}), 130.3 (C_{Ar}), 128.6 (C_{Ar}), 128.2 (2 × C_{Ar}), 128.1 (2 × C_{Ar}), 124.7 (C_{IV}), 117.5 (C_{IV}), 116.6 (C_{Ar}), 116.5 (C_{IV}), 110.0 (C_{Ar}), 100.9 (C_{Ar}), 56.2 (OCH_3), 55.4 (OCH_3), 42.5 (*C*H$_2$), 36.1 (*C*H$_2$), 24.3 (*C*H$_2$).

MS (CI$^+$): *m*/*z* = 402 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{24}O_4N$: 402.1700; found: 402.1704.

4-Acetyl-1-(3,4-dimethoxyphenethyl)-1,5-dihydro-2*H*-pyrrol-2-one (5o)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5o** was obtained as a yellow oil in 50% yield (144 mg).

IR: 2937, 1708, 1515, 1263, 1157 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.97 (t, *J* = 1.6 Hz, 1 H, =C*H*), 6.80–6.67 (m, 3 H, H_{Ar}), 3.84 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 3.74 (t, *J* = 6.8 Hz, 2 H, CH_2CH$_2$), 3.25 (d, *J* = 2.0 Hz, 2 H, CH_2N), 2.85 (t, *J* = 6.8 Hz, 2 H, CH$_2$CH_2), 2.12 (s, 3 H, COCH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.9 (*C*OCH$_3$), 176.1 (*C*ON), 149.3 (C_{IV}), 148.2 (C_{IV}), 144.0 (=*C*H), 130.1 (C_{IV}), 121.0 (C_{Ar}), 118.8 (C_{IV}), 112.1 (C_{Ar}), 111.6 (C_{Ar}), 56.0 (2 × OCH_3), 44.4 (*C*H$_2$), 35.6 (*C*H$_2$), 35.0 (*C*H$_2$), 25.0 (*C*OCH$_3$).

MS (CI$^+$): *m*/*z* = 290 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{20}O_4N$: 290.1387; found: 290.1384.

4-Acetyl-1-(3,5-dimethoxyphenethyl)-1,5-dihydro-2*H*-pyrrol-2-one (5p)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5p** was obtained as a brown oil in 45% yield (129 mg).

IR: 2941, 1718, 1646, 1596, 1204, 1151 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.96 (t, *J* = 1.6 Hz, 1 H, =C*H*), 6.35–6.34 (m, 1 H, H_{Ar}), 6.31–6.30 (m, 2 H, H_{Ar}), 3.78–3.75 (m, 8 H, 2 × OCH_3, CH_2CH_2), 3.27 (d, *J* = 1.6 Hz, 2 H, CH_2N), 2.85 (t, *J* = 6.8 Hz, 2 H, CH$_2$CH_2), 2.13 (s, 3 H, COCH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.0 (*C*OCH$_3$), 176.2 (*C*ON), 161.3 (2 × C_{IV}), 144.2 (=*C*H), 140.1 (C_{IV}), 118.8 (C_{IV}), 107.1 (2 × C_{Ar}), 98.9 (C_{Ar}), 55.5 (2 × O*C*H$_3$), 44.2 (*C*H$_2$), 35.7 (*C*H$_2$), 35.7 (*C*H$_2$), 25.1 (*C*H$_3$).

MS (CI$^+$): *m*/*z* = 290 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{19}O_4NNa$: 312.1206; found: 312.1196.

4-Acetyl-1-[2-(thiophen-2-yl)ethyl]-1,5-dihydro-2*H*-pyrrol-2-one (5q)

Following general procedure 1 and after purification by column chromatography on silica gel, compound **5q** was obtained as an orange oil in 80% yield (188 mg).

IR: 3070, 2979, 2923, 1717, 1368, 1230, 1175 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.19 (dd, *J* = 5.6 Hz, *J* = 0.9 Hz, 1 H, =C*H*), 6.97 (t, *J* = 1.8 Hz, 1 H, =C*H*), 6.96–6.93 (m, 1 H, =C*H*), 6.82–6.80 (m, 1 H, =C*H*), 3.80 (t, *J* = 6.6 Hz, 2 H, CH_2CH_2), 3.28 (d, *J* = 1.8 Hz, 2 H, CH_2N), 3.15 (t, *J* = 6.6 Hz, 2 H, CH$_2$CH_2), 2.14 (s, 3 H, COCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.2 (*C*OCH$_3$), 176.2 (*C*ON), 144.0 (=*C*H), 139.8 (C_{IV}), 127.4 (=*C*H), 126.4 (=*C*H), 124.7 (=*C*H), 118.9 (C_{IV}), 44.6 (*C*H$_2$), 35.6 (*C*H$_2$), 29.4 (*C*H$_2$), 25.1 (*C*H$_3$).

MS (CI$^+$): *m*/*z* = 236 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{13}O_2NSNa$: 258.0559; found: 258.0548.

1-Benzoylisoquinolinones 6a–n and 1-Acetylisoquinolinones 6o–q; General Procedure 2

TFA (2.5 equiv) was added under an Ar atm to compound **5** (0.3 mmol, 1 equiv) and the reaction mixture was stirred at r.t. until TLC indicated no remaining starting material. The reaction was then diluted with CH_2Cl_2 and washed with sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$ and the solvent was removed in vacuo. The crude product was purified by flash column chromatography on silica gel (CH_2Cl_2–Et_2O, 95:5) to give the desired product **6**.

1-Benzoyl-8,9-dimethoxy-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one [(±)-6a]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6a** was obtained as an orange solid in 78% yield (91 mg).

IR: 3059, 2935, 1718, 1684, 1514, 1263 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.97 (m, 2 H, H_{Ar}), 7.67–7.62 (m, 1 H, H_{Ar}), 7.54–7.50 (m, 2 H, H_{Ar}), 6.61 (s, 1 H, H_{Ar}), 6.28 (s, 1 H, H_{Ar}), 5.38 (d, *J* = 8.4 Hz, 1 H, C*H*N), 4.44–4.39 (m, 1 H, CH$_2$CH*H*′), 4.09–4.02 (m, 1 H, C*H*), 3.84 (s, 3 H, OCH_3), 3.45 (s, 3 H, OCH_3), 3.10–3.03 (m, 1 H, CH$_2$C*H*H′), 2.97–2.67 (m, 4 H, COCH_2, CH$_2$CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.0 (*C*OPh), 169.6 (*C*ON), 148.1 (2 × C_{IV}), 136.3 (C_{IV}), 134.2 (C_{Ar}), 129.2 (2 × C_{Ar}), 128.7 (2 × C_{Ar}), 128.0 (C_{IV}), 125.8 (C_{IV}), 111.9 (C_{Ar}), 107.9 (C_{Ar}), 58.6 (*C*H), 55.6 (OCH$_3$), 53.5 (OCH$_3$), 49.2 (*C*H), 37.9 (*C*H$_2$), 37.4 (*C*H$_2$N), 28.4 (*C*H$_2$CO).

MS (CI$^+$): *m*/*z* = 352 [M + H]$^+$.

HRMS (MALDI-DHB-PEG400): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{22}O_4N$: 352.1543; found: 352.1528.

1-Benzoyl-8-methoxy-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one [(±)-6b]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6b** was obtained as an orange oil in 68% yield (65 mg).

IR: 3056, 2935, 1676, 1679, 1581, 1205, 1181 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.00–7.95 [m, 4 H, (H_{Ar})$_p$, (H_{Ar})$_o$], 7.67–7.51 [m, 2 H, (H_{Ar})$_p$, (H_{Ar})$_o$], 7.50–7.47 [m, 4 H, (H_{Ar})$_p$, (H_{Ar})$_o$], 7.16 [t, *J* = 9.0 Hz, 1 H, (H_{Ar})$_o$], 6.69–6.62 [m, 3 H, (H_{Ar})$_p$, (2 × H_{Ar})$_o$], 6.60 [d, *J* = 9.0 Hz, 1 H, (H_{Ar})$_o$], 5.48 [d, *J* = 6.0 Hz, 1 H, (C*H*N)$_p$], 5.34 [d, *J* = 6.0 Hz, 1 H, (C*H*N)$_o$], 4.52–4.42 [m, 1 H, (CH*H*′N)$_o$], 4.39–4.32 [m, 1 H, (CH*H*′N)$_o$], 4.12–3.99 [m, 2 H, (*C*HCO)$_p$, (*C*HCO)$_o$], 3.76 [s, 3 H, (OCH_3)$_p$], 3.13 [s, 3 H, (OCH_3)$_o$], 3.12–2.61 [m, 10 H, (CH_2CH_2)$_{o,p}$, (*C*HH′N)$_{o,p}$, (*C*H_2CO)$_{o\ and\ p}$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.2 (*C*OPh)$_{o,p}$, 170.2 (*C*ON)$_o$, 169.4 (*C*ON)$_p$, 158.5 (C_{IV})$_p$, 155.9 (C_{IV})$_o$, 136.5 (C_{IV})$_o$, 136.0 (C_{IV})$_p$, 135.8 (C_{IV})$_o$, 135.2 (C_{IV})$_p$, 134.2 (C_{Ar})$_p$, 133.4 (C_{IV})$_p$, 129.1 (2 × C_{Ar})$_p$, 128.9 (2 × C_{Ar})$_o$, 128.7 (2 × C_{Ar})$_p$, 128.3 (2 × C_{Ar})$_o$, 128.0 (C_{Ar})$_o$, 126.2 (C_{Ar})$_p$, 125.4 (C_{IV})$_o$, 121.8 (C_{Ar})$_p$, 114.0 (C_{Ar})$_{o,p}$, 108.0 (C_{Ar})$_o$, 57.8 (*C*HN)$_o$, 57.5 (*C*HN)$_p$, 55.4 (OCH$_3$)$_p$, 54.2 (OCH$_3$)$_o$, 49.0 (*C*HCO)$_p$, 45.8 (*C*HCO)$_o$, 37.8 (*C*H$_2$)$_{o,p}$, 37.3 (*C*H$_2$)$_{o,p}$, 29.1 (*C*H$_2$)$_p$, 28.9 (*C*H$_2$)$_o$.

MS (CI$^+$): *m*/*z* = 322 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{20}O_3N$: 322.1438; found: 322.1440.

1-Benzoyl-1,5,6,11b-tetrahydro-[1,3]dioxolo[4,5-*g*]pyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one [(±)-6c]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6c** was obtained as a green oil in 73% yield (73 mg).

IR: 3062, 2902, 1682, 1485, 1247 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.97 (m, 2 H, H_{Ar}), 7.67–7.62 (m, 1 H, H_{Ar}), 7.55–7.51 (m, 2 H, H_{Ar}), 6.59 (s, 1 H, H_{Ar}), 6.35 (s, 1 H, H_{Ar}), 5.87 (dd, *J* = 5.9 Hz, *J* = 1.3 Hz, 2 H, CH_2), 5.49 (d, *J* = 8.0 Hz, 1 H, C*H*N), 4.36–4.31 (m, 1 H, CH$_2$CH*H*′), 4.05–3.97 (m, 1 H, C*H*), 3.12–3.05 (m, 1 H, CH$_2$C*H*H′), 2.95–2.86 (m, 2 H, CH*H*′CO, CH*H*′N), 2.72–2.60 (m, 2 H, C*H*H′CO, C*H*H′N).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.0 (*C*OPh), 169.2 (*C*ON), 146.9 (C_{IV}), 146.8 (C_{IV}), 135.9 (C_{IV}), 134.2 (C_{Ar}), 129.5 (C_{IV}), 129.2 (2 × C_{Ar}), 128.8 (2 × C_{Ar}), 127.1 (C_{IV}), 109.1 (C_{Ar}), 105.0 (C_{Ar}), 101.1 (*C*H$_2$), 57.7 (*C*HN), 49.1 (*C*H), 37.7 (*C*H$_2$), 37.5 (*C*H$_2$N), 28.9 (*C*H$_2$CO).

MS (CI$^+$): *m*/*z* = 336 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{18}O_4N$: 336.1230; found: 336.1231.

1-Benzoyl-8,10-dimethoxy-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one [(±)-6d]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6d** was obtained as a green oil in 78% yield (82 mg).

IR: 3057, 2925, 1679, 1592, 1246 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.94 (m, 2 H, H_{Ar}), 7.63–7.57 (m, 1 H, H_{Ar}), 7.52–7.46 (m, 2 H, H_{Ar}), 6.28 (d, *J* = 6.0 Hz, 1 H, H_{Ar}), 6.19 (d, *J* = 6.0 Hz, 1 H, H_{Ar}), 5.26 (d, *J* = 8.0 Hz, 1 H, C*H*N), 4.50–4.40 (m, 1 H, CH$_2$CH*H*′), 4.08–3.99 (m, 1 H, C*H*), 3.77 (s, 3 H, OCH_3), 3.11 (s, 3 H, OCH_3), 3.00–2.91 (m, 2H, CH$_2$C*H*H′, CH*H*′CO), 2.80–2.61 (m, 2 H, CH_2N, C*H*H′CO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.3 (*C*OPh), 170.2 (*C*ON), 159.7 (C_{IV}), 157.0 (C_{IV}), 136.6 (C_{IV}), 136.4 (C_{IV}), 133.4 (C_{Ar}), 128.9 (2 × C_{Ar}), 128.3 (2 × C_{Ar}), 118.0 (C_{IV}), 104.9 (C_{Ar}), 96.7 (C_{Ar}), 57.6 (*C*HN), 55.5 (OCH_3), 54.2 (OCH_3), 46.2 (*C*H), 37.4 (CH_2N), 37.4 (CH_2CO), 29.4 (CH_2).

MS (CI$^+$): *m*/*z* = 352 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{22}O_4N$: 352.1543; found: 352.1541.

1-Benzoyl-8-methoxy-6,6-dimethyl-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one [(±)-6f]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6f** was obtained as a green oil in 67% yield (70 mg).

IR: 3059, 2962, 1684, 1448, 1291 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00–7.96 (m, 2 H, H_{Ar}), 7.67–7.62 (m, 1 H, H_{Ar}), 7.55–7.50 (m, 2 H, H_{Ar}), 6.87–6.62 (m, 3 H, H_{Ar}), 5.52 (d, *J* = 8.1 Hz, 1 H, C*H*N), 4.12–3.66 [m, 3 H, C*H*, $CH_2C(CH_3)_2$], 3.76 (s, 3 H, OCH_3), 2.97–2.63 (m, 2 H, CH_2CO), 1.38 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.4 (*C*OPh), 169.6 (*C*ON), 158.9 (C_{IV}), 144.8 (C_{IV}), 136.1 (C_{IV}), 134.2 (C_{Ar}), 129.1 (2 × C_{Ar}), 128.9 (2 × C_{Ar}), 128.8 (C_{IV}), 128.3 (C_{IV}), 127.6 (C_{IV}), 126.1 (C_{Ar}), 112.4 (C_{Ar}), 111.7 (C_{Ar}), 58.2 (*C*HN), 55.4 (OCH_3), 49.5 (*C*H), 37.8 (CH_2CO), 35.5 (CH_2), 30.8 (CH_3), 26.4 (CH_3).

MS (CI$^+$): *m*/*z* = 350 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{24}O_3N$: 350.1751; found: 350.1752.

1-Benzoyl-1,5,6,10b-tetrahydrodipyrrolo[1,2-*a*:2′,1′-*c*]pyrazin-3(2*H*)-one [(±)-6g]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6g** was obtained as a brown oil in 86% yield (86 mg).

IR: 3061, 2923, 2853, 1679, 1296 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.97 (m, 2 H, H_{Ar}), 7.66–7.62 (m, 1 H, H_{Ar}), 7.55–7.50 (m, 2 H, H_{Ar}), 6.58–6.57 (m, 1 H, =C*H*), 6.12 (t, *J* = 2.8 Hz, 1 H, =C*H*), 5.75 (d, *J* = 8.0 Hz, 1 H, =C*H*), 5.42 (d, *J* = 7.6 Hz, 1 H, C*H*N), 4.46–4.41 (m, 1 H, C*H*), 4.20–4.14 (m, 1 H, C*H*), 4.06–3.95 (m, 2 H, CH_2CH_2), 3.37–3.29 (m, 1 H, CH_2CHH'), 2.89–2.68 (m, 2 H, CH_2CO).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.3 (*C*OPh), 170.2 (*C*ON), 136.0 (C_{IV}), 134.1 (C_{Ar}), 129.1 (2 × C_{Ar}), 128.8 (2 × C_{Ar}), 127.9 (C_{IV}), 119.8 (CH=*C*H), 108.8 (CH=*C*H), 103.7 (CH=*C*H), 55.4 (*C*HN), 48.2 (*C*H), 44.2 (CH_2CO), 37.5 (CH_2N), 36.7 (CH_2).

MS (CI$^+$): *m*/*z* = 281 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{17}N_2O_2$: 281.1205; found: 281.1209.

9-Benzoyl-4,8,9,9a-tetrahydrofuro[2,3-*g*]indolizin-7(5*H*)-one [(±)-6h]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6h** was obtained as a yellow solid in 85% yield (71 mg).

IR: 1676, 1418, 1256, 730, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.90 (m, 2 H, H_{Ar}), 7.62–7.58 (m, 1 H, H_{Ar}), 7.51–7.47 (m, 2 H, H_{Ar}), 6.99 (dd, *J* = 1.3 Hz, *J* = 0.7 Hz, 1 H, =C*H*O), 5.54 (d, *J* = 2.0 Hz, 1 H, CH=C*H*), 5.15 (dt, *J* = 7.0 Hz, *J* = 2.0 Hz, 1 H, C*H*N), 4.58–4.48 (m, 2 H, C*H*, CH*H*′CO), 2.98–2.87 (m, 2 H, C*H*H′CO, CH_2CHH'), 2.85–2.80 (m, 1 H, CH_2CHH′), 2.72–2.55 (m, 2 H, 2 × CH_2CHH').

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.9 (*C*OPh), 173.3 (*C*ON), 150.0 (C_{IV}), 141.3 (CH=*C*H), 137.3 (C_{IV}), 133.7 (C_{Ar}), 129.1 (2 × C_{Ar}), 128.4 (2 × C_{Ar}), 114.1 (C_{IV}), 107.7 (CH=*C*H), 57.3 (*C*HN), 42.2 (*C*H), 37.5 (CH_2N), 34.5 (CH_2CO), 23.1 (CH_2).

MS (CI$^+$): *m*/*z* = 282 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{16}O_3N$: 282.1125; found: 282.1127.

9-Benzoyl-4,8,9,9a-tetrahydrothieno[2,3-*g*]indolizin-7(5*H*)-one [(±)-6i]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6i** was obtained as a yellow oil in 93% yield (24 mg).

IR: 2925, 1733, 1456, 1255 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.95 (m, 2 H, H_{Ar}), 7.66–7.62 (m, 1 H, H_{Ar}), 7.54–7.50 (m, 2 H, H_{Ar}), 7.09 (d, *J* = 5.2 Hz, 1 H, =C*H*S), 6.57 (d, *J* = 5.2 Hz, 1 H, =C*H*), 5.40–5.37 (m, 1 H, C*H*N), 4.57–4.52 (m, 1 H, CH_2CHH'), 4.00–3.93 (m, 1 H, C*H*), 3.12–3.05 (m, 1 H, CH_2CHH'), 3.01–2.85 (m, 3 H, CH_2CH_2, CH*H*′CO), 2.73–2.66 (m, 1 H, C*H*H′CO).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.6 (*C*OPh), 169.7 (*C*ON), 136.0 (C_{IV}), 134.8 (C_{IV}), 134.1 (C_{Ar}), 133.7 (C_{IV}), 129.1 (2 × C_{Ar}), 128.7 (2 × C_{Ar}), 124.4 (CH=*C*H), 123.9 (CH=*C*H), 57.5 (*C*HN), 48.3 (*C*H), 37.5 (2 × CH_2), 24.9 (CH_2).

MS (CI$^+$): *m*/*z* = 298 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{16}O_2NS$: 298.0896; found: 298.0895.

1-Benzoyl-1,2,5,6,7,11c-hexahydro-3*H*-indolizino[7,8-*b*]indol-3-one [(±)-6j]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6j** was obtained as a yellow oil in 85% yield (84 mg).

IR: 3400, 1670, 1447, 1259, 730, 660 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.26 (m, 1 H, N*H*), 7.93–7.90 (m, 2 H, H_{Ar}), 7.68–7.62 (m, 1 H, H_{Ar}), 7.55–7.50 (m, 3 H, H_{Ar}), 7.30–7.27 (m, 1 H, H_{Ar}), 7.20–7.09 (m, 2 H, H_{Ar}), 5.46–5.43 (m, 1 H, C*H*N), 4.60–4.54 (m, 1 H, CH_2CHH'), 3.92–3.82 (m, 1 H, C*H*), 3.11–2.66 (m, 5 H, 2 × CH_2, CH_2CHH').

^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.1 (*C*OPh), 169.7 (*C*ON), 136.2 (C_{IV}), 135.7 (C_{IV}), 134.4 (C_{Ar}), 131.8 (C_{IV}), 129.2 (2 × C_{Ar}), 128.6 (2 × C_{Ar}), 126.8 (C_{IV}), 122.5 (C_{Ar}), 119.9 (C_{Ar}), 118.5 (C_{Ar}), 111.3 (C_{Ar}), 108.5 (C_{IV}), 55.0 (*C*HN), 50.3 (*C*H), 37.8 (CH_2), 37.2 (CH_2N), 21.3 (CH_2CO).

MS (CI$^+$): *m*/*z* = 331 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{18}N_2O_2Na$: 353.1266; found: 353.1268.

1-Benzoyl-9,10-dimethoxy-1,2,5,6,7,11b-hexahydro-3*H*-benzo[*c*]pyrrolo[1,2-*a*]azepin-3-one [(±)-6l]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6l** was obtained as a yellow oil in 47% yield (51 mg).

IR: 2936, 1678, 1516, 1260 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.82–7.79 (m, 2 H, H_{Ar}), 7.59–7.54 (m, 1 H, H_{Ar}), 7.45–7.40 (m, 2 H, H_{Ar}), 6.62 (s, 1 H, H_{Ar}), 6.49 (s, 1 H, H_{Ar}), 5.27 (d, *J* = 8.0 Hz, 1 H, C*H*N), 4.26–4.17 (m, 1 H, C*H*), 4.13–4.06 (m, 1 H, COCH*H*′), 3.85 (s, 3 H, OCH_3), 3.59 (s, 3 H, OCH_3), 3.08–2.87 (m, 2 H, CH_2CH*H*′, COCH*H*′), 2.84–2.81 (m, 2 H, CH_2), 2.55–2.48 (m, 1 H, CH_2CH*H*′), 2.29–2.15 (m, 1 H, CH_2CH*H*′), 1.77–1.64 (m, 1 H, CH_2CH*H*′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.6 (*C*OPh), 171.2 (*C*ON), 148.4 (C_{IV}), 147.4 (C_{IV}), 136.2 (C_{IV}), 134.0 (C_{Ar}), 130.2 (C_{IV}), 129.1 (C_{IV}), 128.9 (2 × C_{Ar}), 128.7 (2 × C_{Ar}), 114.1 (C_{Ar}), 111.5 (C_{Ar}), 66.4 (*C*H), 56.0 (O*C*H_3), 55.9 (O*C*H_3), 49.2 (*C*HN), 38.4 (CH_2N), 36.3 (CH_2CO), 30.0 (*C*H_2), 25.4 (*C*H_2).

MS (CI$^+$): *m*/*z* = 366 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{23}O_4NNa$: 388.1519; found: 388.1506.

12-Benzoyl-6-methoxy-7,8,12,12a-tetrahydronaphtho[1,8-*cd*]pyrrolo[1,2-*a*]azepin-10(11*H*)-one [(±)-6m]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6m** was obtained as a brown oil in 47% yield (55 mg).

IR: 3056, 2935, 1680, 1255 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05–8.02 (m, 2 H, H_{Ar}), 7.76–7.70 (m, 2 H, H_{Ar}), 7.67–7.61 (m, 1 H, H_{Ar}), 7.55–7.50 (m, 2 H, H_{Ar}), 7.33–7.18 (m, 3 H, H_{Ar}), 6.06 (d, *J* = 5.7 Hz, 1 H, C*H*N), 4.79–4.72 (m, 1 H, C*H*), 4.25–4.18 (m, 1 H, CH_2CH*H*′), 3.95 (s, 3 H, OCH_3), 3.93–3.86 (m, 1 H, CH_2C*H*H′), 3.41–3.17 (m, 2 H, 2 × CH_2CH*H*′), 3.03–2.73 (m, 2 H, CH_2CO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.7 (*C*OPh), 170.6 (*C*ON), 155.1 (C_{IV}), 135.3 (C_{IV}), 134.0 (C_{Ar}), 134.0 (C_{IV}), 132.9 (C_{IV}), 130.6 (C_{IV}), 129.8 (C_{Ar}), 129.2 (2 × C_{Ar}), 129.0 (C_{IV}), 128.6 (2 × C_{Ar}), 123.3 (C_{IV}), 123.3 (C_{Ar}), 122.8 (C_{Ar}), 113.4 (C_{Ar}), 59.8 (*C*HN), 56.8 (O*C*H_3), 43.5 (*C*H), 43.1 (*C*H_2), 35.7 (CH_2N), 23.8 (CH_2CO).

MS (CI$^+$): *m*/*z* = 372 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{22}O_3N$: 372.1594; found: 372.1596.

12-Benzoyl-1,6-dimethoxy-7,8,12,12a-tetrahydronaphtho[1,8-*cd*]pyrrolo[1,2-*a*]azepin-10(11*H*)-one [(±)-6n]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6n** was obtained as a brown oil in 88% yield (105 mg).

IR: 3059, 2959, 1680, 1256 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88–7.85 (m, 2 H, H_{Ar}), 7.68–7.65 (m, 2 H, H_{Ar}), 7.61–7.55 (m, 1 H, H_{Ar}), 7.49–7.43 (m, 2 H, H_{Ar}), 7.13 (d, *J* = 9.0 Hz, 1 H, H_{Ar}), 6.96 (d, *J* = 9.0 Hz, 1 H, H_{Ar}), 6.00 (d, *J* = 4.4 Hz, 1 H, C*H*N), 4.28–4.19 (m, 1 H, CH_2CH*H*′), 4.06–3.99 (m, 1 H, C*H*), 3.93 (s, 3 H, OCH_3), 3.70–3.50 (m, 2 H, 2 × CH_2CH*H*′), 3.44 (s, 3 H, OCH_3), 3.04–2.93 (m, 1 H, CH_2C*H*H′), 2.72–2.39 (AB system, 2 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.7 (*C*OPh), 172.1 (*C*ON), 155.9 (C_{IV}), 155.2 (C_{IV}), 135.8 (C_{IV}), 134.1 (C_{IV}), 133.3 (C_{Ar}), 129.9 (C_{Ar}), 128.9 (2 × C_{Ar}), 128.5 (C_{Ar}), 128.4 (2 × C_{Ar}), 125.5 (C_{IV}), 123.2 (C_{IV}), 119.8 (C_{IV}), 111.1 (C_{Ar}), 109.9 (C_{Ar}), 61.7 (*C*HN), 56.5 (O*C*H_3), 55.3 (O*C*H_3), 47.9 (*C*H), 41.7 (CH_2N), 35.0 (CH_2CO), 27.2 (*C*H_2).

MS (CI$^+$): *m*/*z* = 402 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{24}O_4N$: 402.1705; found: 402.1711.

1-Acetyl-8,9-dimethoxy-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one [(±)-6o]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6o** was obtained as an orange oil in 54% yield (46 mg).

IR: 1720, 1590, 1141, 697, 658 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.59 (s, 1 H, H_{Ar}), 6.51 (s, 1 H, H_{Ar}), 5.17 (d, *J* = 8.0 Hz, 1 H, C*H*N), 4.37–4.32 (m, 1 H, C*H*), 3.85 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 3.23–3.16 (m, 1 H, COCH*H*′), 3.03–2.96 (m, 1 H, CH_2CH*H*′), 2.92–2.57 (m, 4 H, CH_2C*H*H′, COC*H*H′, CH_2CH_2), 2.32 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.3 (*C*OCH$_3$), 169.3 (*C*ON), 148.4 (C_{IV}), 148.3 (C_{IV}), 128.3 (C_{IV}), 126.0 (C_{IV}), 112.0 (C_{Ar}), 108.1 (C_{Ar}), 56.9 (*C*HN), 56.1 (O*C*H_3), 56.0 (O*C*H_3), 54.2 (*C*H), 37.4 (*C*H_2N), 35.7 (CH_2CO), 29.8 (*C*H_3), 28.4 (*C*H_2).

MS (CI$^+$): *m*/*z* = 290 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{19}O_4N$: 290.1441; found: 290.1445.

1-Acetyl-8,10-dimethoxy-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one [(±)-6p]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6p** was obtained as a green oil in 43% yield (37 mg).

IR: 2936, 1683, 1606, 1437, 1170 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.31 (d, *J* = 2.3 Hz, 1 H, H_{Ar}), 6.26 (d, *J* = 2.3 Hz, 1 H, H_{Ar}), 5.06 (d, *J* = 7.5 Hz, 1 H, C*H*N), 4.42–4.32 (m, 1 H, CH_2CH*H*′), 3.78 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 3.21–3.12 (m, 1 H, C*H*), 2.98–2.81 (m, 2 H, 2 × CH_2CH*H*′), 2.73–2.59 (m, 2 H, CH_2CH*H*′, COCH*H*′), 2.56–2.46 (m, 1 H, COC*H*H′), 2.27 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.1 (*C*OCH$_3$), 170.1 (*C*ON), 159.7 (C_{IV}), 157.0 (C_{IV}), 136.4 (C_{IV}), 117.6 (C_{IV}), 105.1 (C_{Ar}), 97.0 (C_{Ar}), 56.7 (*C*HN), 55.5 (O*C*H_3), 54.6 (O*C*H_3), 51.8 (*C*H), 37.3 (*C*H_2N), 35.9 (CH_2CO), 29.7 (*C*H_3), 29.3 (*C*H_2).

MS (CI$^+$): *m*/*z* = 290 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{19}O_4NNa$: 312.1206; found: 312.1195.

9-Acetyl-4,8,9,9a-tetrahydrothieno[2,3-*g*]indolizin-7(5*H*)-one [(±)-6q]

Following general procedure 2 and after purification by column chromatography on silica gel, compound **6q** was obtained as a brown oil in 47% yield (51 mg).

IR: 2960, 1683, 1418, 1236, 1174 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.14 (d, *J* = 5.2 Hz, 1 H, =C*H*), 6.71 (d, *J* = 5.2 Hz, 1 H, =C*H*), 5.09 (dt, *J* = 8.0 Hz, *J* = 1.8 Hz, 1 H, C*H*N), 4.50–4.45 (m, 1 H, CH_2CH*H*′), 3.15–3.08 (m, 1 H, C*H*), 3.04–2.96 (m, 1 H, CH_2CH*H*′), 2.96–2.78 (m, 3 H, CH_2C*H*H′, CH_2CO), 2.64–2.57 (m, 1 H, CH_2C*H*H′), 2.29 (s, 3 H, COCH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.3 (*C*OCH$_3$), 169.6 (*C*ON), 134.8 (C_{IV}), 133.7 (C_{IV}), 124.3 (=*C*H), 124.0 (=*C*H), 56.6 (*C*HN), 53.0 (*C*H), 37.4 (*C*H_2N), 35.3 (CH_2CO), 29.6 (*C*H_3), 24.8 (*C*H_2).

MS (CI$^+$): *m*/*z* = 236 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{13}O_2NNaS$: 258.0559; found: 258.0550.

N-Allyl-N-(3,4-dimethoxyphenethyl)acrylamide (7)

To a solution of dimethoxyphenylethylamine **4a** (12 mmol, 3 equiv) in THF, K_2CO_3 (12 mmol, 3 equiv) and allylbromide (4 mmol, 1 equiv) were added at 0 °C. The mixture was then stirred at room temperature for 24 h. The reaction mixture was filtered through a pad of Celite®, the residue was washed with CH_2Cl_2 and the filtrate was then concentrated in vacuo. The crude product (2.8 mmol, 1 equiv) was diluted in CH_2Cl_2 and, under an N_2 atm at 0 °C, Et_3N (2.8 mmol, 1 equiv) and acryloyl chloride (2.8 mmol, 1 equiv) were added to the solution. The mixture was stirred at r.t. and complete conversion of the starting material was monitored by TLC. The solution was then quenched with H_2O. The aq phase was extracted with and the organic phase was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The crude residue was purified by column chromatography on silica gel (CH_2Cl_2–Et_2O, 90:10) to give compound **7** as a yellow oil (68%, 523 mg).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.87–6.57 (m, 4 H, 3 × H_{Ar}, =C*H*CO), 6.10 (ddd, *J* = 25.6 Hz, *J* = 16.8 Hz, *J* = 2.2 Hz, 1 H, COCH=CH*H*′), 5.88–5.70 (m, 1 H, CH_2=C*H*), 5.36 (ddd, *J* = 25.6 Hz, *J* = 16.8 Hz, *J* = 2.2 Hz, 1 H, COCH=C*H*H′), 5.18–5.05 (m, 2 H, =CH_2), 3.98–3.94 (m, 2 H, CH_2CH), 3.73 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 3.54–3.44 (m, 2 H, CH_2N), 2.76–2.69 (m, 2 H, CH_2CH_2).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 165.2/164.9 (C_{IV} rotamers), 148.6 (C_{IV} rotamers), 147.4/147.2 (C_{IV} rotamers), 134.5/133.9 (=CH rotamers), 131.5/130.8 (C_{IV} rotamers), 128.5/128.3 (=CH rotamers), 127.2/127.0 (=CH_2 rotamers), 120.8/120.4 (C_{Ar} rotamers), 116.8/115.9 (=CH_2 rotamers), 112.8/112.4 (C_{Ar} rotamers), 111.8 (C_{Ar} rotamers), 55.4/55.3 (2 × OCH_3 rotamers), 48.0 (CH_2 rotamers), 47.7 (CH_2 rotamers), 34.4/33.0 (CH_2 rotamers).

MS (CI$^+$): *m*/*z* = 276 [M + H]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{21}O_3NNa$: 298.1419; found: 298.1421.

1-(3,4-Dimethoxyphenethyl)-1,5-dihydro-2*H*-pyrrol-2-one (8)

Under an N_2 atm, compound **7** (275 mg, 1 mmol) was dissolved in toluene and Grubbs' 2nd generation catalyst (10 mol%) was added in small portions and the reaction was heated at 40 °C for 10 h. The reaction mixture was then concentrated in vacuo and the crude product was purified by column chromatography on silica gel (CH_2Cl_2–Et_2O, 90:10) to afford the lactam **8** as an orange oil (63%, 155 mg).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.97 (dt, *J* = 5.9 Hz, *J* = 1.7 Hz, 1 H, =C*H*CO), 6.80–6.71 (m, 3 H, H_{Ar}), 6.16 (dt, *J* = 5.9 Hz, *J* = 1.8 Hz, 1 H, HC=C*H*), 3.85 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.75 (dd, *J* = 2.3 Hz, *J* = 1.6 Hz, 2 H, CH_2), 3.67 (t, *J* = 7.2 Hz, 2 H, CH_2N), 2.84 (t, *J* = 7.2 Hz, 2 H, CH_2CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.5 (CON), 149.0 (C_{IV}), 147.7 (C_{IV}), 142.7 (=CH), 131.4 (C_{IV}), 128.3 (=CH), 120.7 (C_{Ar}), 111.9 (C_{Ar}), 111.4 (C_{Ar}), 56.0 (2 × OCH_3), 53.7 (CH_2N), 43.9 (CH_2CH_2), 34.6 (CH_2CH_2).

MS (CI$^+$): *m*/*z* = 248 [M + H]$^+$.

HRMS (MALDI-DHB-PEG400): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{18}O_3N$: 248.1281; found: 248.1276.

8,9-Dimethoxy-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3(2*H*)-one [(±)-9]

TFA (2.5 equiv) was added under an Ar atm to compound **8** (15 mg, 0.06 mmol) and the mixture was stirred at 50 °C until TLC indicated no remaining starting material. The reaction was then diluted with CH_2Cl_2 and washed with sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$ and the solvent was removed in vacuo. The crude residue was purified by flash column chromatography on silica gel (CH_2Cl_2–Et_2O, 90:10) to give the desired product as a brown oil (90%, 139 mg).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.61 (s, 1 H, H_{Ar}), 6.56 (s, 1 H, H_{Ar}), 4.72 (t, *J* = 7.4 Hz, 1 H, C*H*N), 4.30 (ddd, *J* = 12.4 Hz, *J* = 5.8 Hz, *J* = 2.5 Hz, 1 H, CHCH*H*′), 3.87 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.06–2.83 (m, 2 H, CH*H*′N, CHC*H*H′), 2.71–2.42 (m, 3 H, C*H*H′N, CH_2CH_2), 1.90–1.75 (m, 2 H, CH_2CO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.3 (CON), 148.2 (C_{IV}), 148.0 (C_{IV}), 129.4 (C_{IV}), 125.6 (C_{IV}), 111.8 (C_{Ar}), 107.7 (C_{Ar}), 56.7 (CH), 56.2 (OCH_3), 56.0 (OCH_3), 37.2 (CH_2N), 31.9 (CH_2CH_2), 28.2 (CH_2CO), 27.9 (CHCH_2).

MS (CI$^+$): *m*/*z* = 248 [M + H]$^+$.

HRMS (MALDI-DHB-PEG400): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{18}O_3N$: 248.1281; found: 248.1274.

4-Benzoyl-5-(furan-2-yl)-1-phenethylpyrrolidin-2-one [(±)-10]

To a solution of α,β-unsaturated lactam **5e** (0.4 mmol, 1 equiv) in DCE (10 mL), furan (10 equiv) and TFA (2.5 equiv) were added at r.t. The mixture was stirred until TLC indicated no remaining starting material. The mixture was then diluted with CH_2Cl_2 and the organic phase was washed with sat. $NaHCO_3$, dried over $MgSO_4$ and concentrated in vacuo. The desired product was obtained, after purification of the residue by column chromatography on silica gel (CH_2Cl_2–Et_2O, 95:5), as a yellow oil (32%, 21 mg).

IR: 1679, 1596, 1448, 1240, 746, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.82 (m, 2 H, H_{Ar}), 7.60–7.56 (m, 1 H, H_{Ar}), 7.47–7.43 (m, 3 H, 2 × H_{Ar}, =C*H*), 7.25–7.20 (m, 2 H, H_{Ar}), 7.17–7.10 (m, 3 H, H_{Ar}), 6.35 (dd, *J* = 3.2 Hz, *J* = 1.9 Hz, 1 H, =C*H*), 6.25 (dd, *J* = 3.2 Hz, *J* = 0.7 Hz, 1 H, =C*H*), 4.93 (d, *J* = 4.9 Hz, 1 H, C*H*N), 4.27–4.21 (m, 1 H, C*H*CO), 3.78–3.70 (m, 1 H, CHCH*H*′), 3.01–2.93 (m, 2 H, CHCH*H*′, CH_2CH*H*′N), 2.87–2.79 (m, 1 H, CH_2CH*H*′), 2.75 (dd, *J* = 16.8 Hz, *J* = 6.3 Hz, 1 H, CHCH*H*′), 2.61–2.54 (m, 1 H, CH_2CH*H*′).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.3 (COPh), 171.9 (CON), 151.1 (C_{IV}), 143.5 (C_{Ar}), 138.8 (C_{IV}), 135.1 (C_{IV}), 133.9 (C_{Ar}), 128.9 (2 × C_{Ar}), 128.8 (2 × C_{Ar}), 128.7 (2 × C_{Ar}), 128.6 (2 × C_{Ar}), 126.5 (=CH), 110.6 (=CH), 109.9 (=CH), 57.4 (CHN), 44.5 (CHCO), 42.8 (CH_2CON), 34.2 (CH_2CH_2), 33.8 (CH_2CH_2).

MS (CI$^+$): *m*/*z* = 382 [M + Na]$^+$.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{21}O_3NNa$: 382.1419; found: 382.1427.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1561398.

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