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Microwave-Assisted Tandem Transformation on an Ionic-Liquid Support: Efficient Synthesis of Pyrrolo/Pyridobenzimidazolones and Isoindolinone-Fused Benzimidazoles

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Abstract: A tandem transformation that involves the formation of three bonds and two heterocyclic rings in a one-pot fashion through amino-alkylation of an ionic-liquid-immobilized diamine with keto acids followed by successive double intramolecular cyclizations to afford a tricyclic framework has been explored. This tandem cyclization has been utilized to develop a rapid and efficient method to synthesize various pyrrolo[1,2-*a*]benzimidazolones and pyrido[1,2-*a*]benzimidazolones on an ionic-liquid support by using focused microwave irradiation. The application of this tandem cyclization was further extended to the aromatic keto acids to provide isoindolinone-fused benzimidazoles, a structurally heterogeneous library with skeletal diversity. The outcome of the cascade reaction was confirmed by the X-ray crystallographic study of the product directly attached to the ionic-liquid support. Use of the ionic liquid as a soluble support facilitates purification by simple precipitation along with advantages like high loading capacity, homogeneous reaction conditions, and monitoring of the reaction progress by regular conventional spectroscopic methods, whereas application of microwave irradiation greatly accelerates the rate of the reactions.

Keywords: heterocycles · ionic liquids · microwave chemistry · supported synthesis · tandem reactions

Introduction

To enhance the traditional paradigm of small-molecule discovery, diversity-oriented synthesis has evolved into the systematic generation of a large number of druglike molecules that are available for screening and to identify lead compounds for pharmaceutical research and drug development.[1] To meet the growing demand for new, small molecules in high-throughput screening for drug discovery, substantial effort has been dedicated to develop solid-phase and solution-phase chemistries.[2] Highly successful and readily automated insoluble-solid-supported synthesis has been applied in numerous areas.[3] However, the problems associated with heterogeneous reaction conditions such as unequal distribution of the reaction sites and inefficient coupling rates have led to alternative soluble-support methodologies with the aim of restoring homogeneous reaction conditions and easily separating the desired compound from the support. The successful implementation of soluble polyethylene glycol (PEG), polyvinyl alcohol, and other soluble polymers in small-molecule synthesis retains more advantages over conventional solution-phase chemistry.[4] However, the use of soluble polymer supports suffers from the drawbacks of low loading capacity and low aqueous solubility. The drawbacks associated with solid- and soluble-polymer-supported synthesis urge chemists to search for alternative tools in their arsenal to restore facile, convenient, and nonpolluting synthetic protocols. The recently emergent ionic liquids (ILs) and their intriguing properties as environmentally benign reaction media have attracted considerable interest in numerous chemical reactions and biomedical applications.[5] Depending on the choice of anions and cations, the solubility of the ILs can be tuned readily to control the phase trafficking in organic and aqueous phases. These attractive features—together with high loading capacity and high thermal as well as chemical stability—make ionic liquids attractive for use as soluble supports in organic synthe-

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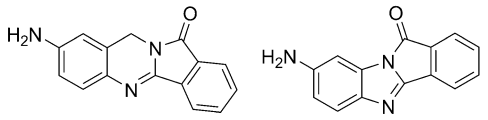
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/asia.201100277. It includes detailed experimental procedures as well as ^{1}H and ^{13}C NMR, mass, IR, and HPLC spectra of compounds **10**, **11**, **14**, **16**, **18**, and **9**.

sis. The substrate anchored on ILs is suitable for monitoring the reaction progress by conventional spectroscopic analysis. Moreover, for the reactions conducted in the homogeneous phase, the excess amounts of reagents and byproducts are removed by simple washing with a low-polar organic solvent. The recovered IL can be recycled in the synthetic process. This liquid-phase strategy has been demonstrated by several groups to synthesize small molecules and peptides in combinatorial fashion.[6]

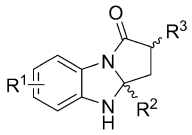
Diversity-oriented synthesis together with combinatorial parallel synthesis has been significantly affected by the introduction of microwave synthesis.[7] The use of microwaves in ionic-liquid-supported reactions has attracted the attention of many researchers in recent days. Ionic liquids absorb the microwave energy efficiently, through which the reaction rate can be accelerated remarkably. The synergies that arise from the combined use of microwaves and IL is certainly effective in meeting the increasing demand for environmentally benign chemical processes.[8]

To illustrate the rapid and efficient synthetic methodology on an ionic-liquid support, structurally fused benzimidazole with 2-pyrrolodinones, 2-pyridinones, and isoindolones were examined as the target compounds that occupy an important place in current therapeutic agents.[9] Irrespective of the target, the growing existence of imidazole-fused heterocycles in many drug entities has proven the remarkable ability of imidazole nuclei to serve both as biomimetics and reactive pharmacophores.[10] Batracyclin (**I**) and isoindolo[2,1-*a*]benzimidazoles (**II**) as topoisomerase II inhibitors have shown in vivo antitumor activity against murine leukemia P-388 and colon adenocarcinoma 38 cell lines.[11] Similarly, pyrroloimidazolones exhibited properties as cognition-enhancing pharmaceuticals,[12] whereas the expanded series of pyrrolobenzimidazolone derivatives (**III**) were evaluated for their anticonvulsant properties.[13] Substituted pyrimidobenzimidazole (**IV**) derivatives have been investigated to treat disorders of the central nervous system.[14]

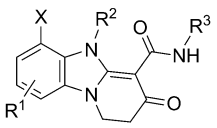


I

II



III



IV

Abstract in Chinese:

我們探究了一個可同時形成三個鍵及兩個雜環的一鍋化連續反應，此連續反應是由固定在離子溶液上的雙胺為起始物，此雙胺與酮酸進行胺基烷化反應接著再進行分子內雙重環化反應形成具有三環骨架結構的化合物。此連續環化反應能應用於發展快速及有效率的合成方法，也就是以離子液體為載體搭配上聚焦式微波反應器來合成具有不同取代基的 pyrrolo[1,2-a]benzimidazolones 及 pyrido[1,2-a]benzimidazolones。此連續環化反應能更近一步應用於芳香環酮酸，固定在離子溶液上的雙胺與芳香環酮酸反應可以得到具有異吲哚啉酮融合苯並咪唑骨架結構的多樣性分子庫。此連續反應的結果是直接由固定在離子溶液上產物的 X 射線晶體學研究所證實。利用離子溶液作為可溶載體只須以簡單的沉澱就可純化產物，還有其他的優點像是產物負載率較高、可用傳統的光譜分析方法監測反應的進行以及可利用微波輻射來大幅提高反應的速率。

Results and Discussions

3-Hydroxyethyl(1-methylimidazolium)tetrafluoroborate (**1**), readily available from the reaction of 1-methylimidazole and 2-bromoethanol,[16] was used as a suitable ionic-liquid (IL) support for an intended multistep synthetic sequence. The synthetic strategy to develop a distinct molecular framework commenced with the loading of 4-fluoro-3-nitrobenzoic acid (**2**) onto IL **1** through esterification, in which the IL acts as a soluble support for growing molecules. The esterification reaction was carried out in the presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC) and a catalytic amount of *N*,*N*′-dimethylaminopyridine (DMAP) in acetonitrile for 20 minutes in the microwave cavity at 80 °C to furnish IL-immobilized fluronitrobenzoate **3** (Scheme 1). The same esterification reaction under conventional heating required 48 hours. By taking advantage of the distinct solubility feature of the IL-anchored substrate, the excess amounts of reagents and the reaction byproducts can easily be removed by using less-polar organic solvents in which the IL conjugate substrate is insoluble. Accordingly, IL conjugate **3** was purified and obtained in good yields after washing with diethyl ether.

The immobilized fluoronitrobenzoate **3** was treated with various primary amines to substitute the fluorine atom through an *ipso*-fluoro nucleophilic substitution reaction under focused microwave irradiation. The *ipso*-fluoro displacement reaction was carried out in acetonitrile at 80 °C for about 10 minutes to obtain the IL-supported nitroamine **4**. In contrast, this reaction took 4 hours under reflux conditions. Various amines were used to create the substitutional diversity in the targeted framework. It is worth mentioning that that IL-linked ester functionality is stable under the microwave heating conditions and not cleaved by various amines. The *ipso*-fluoro displacement was monitored and confirmed by conventional proton NMR spectroscopy. To reduce the nitro functional group, IL-anchored substrate **4** was treated with zinc and ammonium formate in methanol for 30 minutes under reflux conditions. This metal reduction also smoothly occurred on the IL support to afford IL–diamine conjugate **5** with good yields in 5 minutes at 80 °C. The

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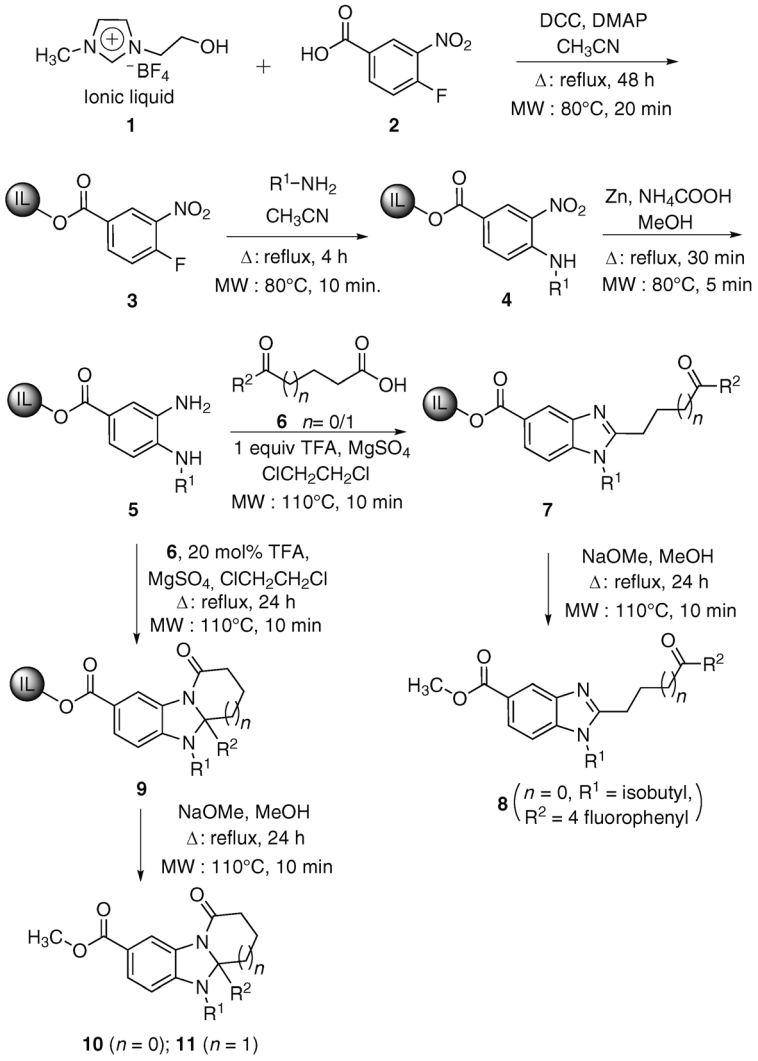
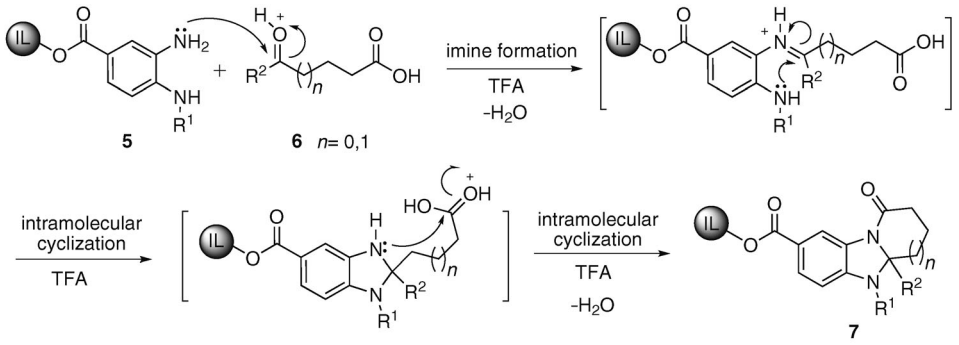


Scheme 1. Ionic-liquid-supported synthesis of pyrrolo/pyridobenzimidazolones.

reduction was confirmed by the upfield shifting of aromatic protons in the proton NMR spectrum of compound **5**.

The next challenge was the synthesis of pyrrolo/pyridobenzimidazolone derivatives from IL conjugate **5** through one-pot tandem transformations. Aliphatic γ-keto acids as well as δ-keto acids were used to produce structurally diverse heterocyclic skeletons along with substitutional diversity depending on the groups present on the keto acids. The γ-keto acids can provide a five-membered ring, whereas δ-keto acids undergo elaborate cyclization to a six-membered ring to provide a skeletally different tricyclic framework. Accordingly, IL diamine conjugate **5** was treated with various γ- and δ-keto acids **6** in the presence of trifluoroacetic acid (TFA) under microwave irradiation. During the optimization of conditions for the intended cascade cyclization, it was observed that the coupling of keto acid with *ortho*-phenylenediamine is dependent on the amount of acid used. We observed the coupling of the acid moiety with diamine functionality with a stoichiometric amount of TFA afforded 2-alkyl-substituted benzimidazoles **7**. The formation of compound **7** was attributed to the activation of acid functionality in the presence of a stoichiometric amount of TFA. The structure was confirmed to be compound **8** after removing the IL support in sodium methoxide solution. On the other hand, the coupling of keto acid with IL diamine conjugate **5** and successive intramolecular cyclizations were successfully achieved by using 20 mol% TFA with magnesium sulfate in dichloroethane under focused microwave irradiation at 110°C over 10 minutes (Scheme 1). The reaction mixture was purified again by precipitation in diethyl ether and separated by filtration to offer IL-supported pyrrolo/pyridobenzimidazolone derivatives **9** in good yields (72–85%). For comparison, the same reaction was carried out under conventional reflux conditions, which took 24 hours to furnish the same product in dichloroethane. In the particular case of R^2 as the alkyl group, this tandem reaction affords cyclized benzimidazolone derivatives **9** even with stoichiometric amounts of TFA. The formation of pyrrolo/pyridobenzimidazolone derivatives **9** was detected directly with the IL support by means of spectroscopic analysis. In the ^{1}H NMR spectrum of compound **9**, the absence of peaks that correspond to amine and acid protons together with the emergence of peaks due to alkyl protons present on the keto acid moiety suggested the successful cyclization of IL diamine conjugate **5** with keto acid **6**. Additionally, the stereogenic quaternary carbon appeared at $\delta = 89.5$ ppm in the C^{13} NMR spectrum of compound **9** along with the amide carbonyl carbon absorbance peak at $\delta = 175$ ppm. The formation of an amide bond was further confirmed by IR spectroscopy, which depicts the amide frequency band around 1720 cm^{-1}. Due to the ketonic nature of *tert*-amide carbonyl functionality, it may be a little higher.

The synthetic pathway that leads to pyrrolo/pyridobenzimidazolones through cascade reactions includes amino-alkylation and a subsequent double intramolecular cyclization process. The important mechanistic steps involved in the tandem transformation pathway for the formation of the tricyclic skeleton are depicted in Scheme 2. The tandem reaction is supposed to start from the acid-catalyzed imine for-



Scheme 2. Plausible mechanistic steps involved in the synthesis of pyrrolo/pyridobenzimidazolones.

mation through condensation of conjugate diamine **5** with keto acids **6** by excluding water molecules. The formation of an amide bond by amine–acid coupling was less likely in the presence of the comparatively more reactive ketone functionality, which readily reacts with amine to form an imine bond. The subsequent tandem transformation led to intramolecular cyclization through the attack of a secondary amine on an electrophilic imine carbon towards pentacyclic aza-ring formation to afford a benzimidazole derivative. The resulting benzimidic secondary amine and acid functionality present in one skeleton are in a more favorable position for cyclization to form a more stable five- or six-membered cyclic lactic ring. The intramolecular cyclization to form an amide was assisted by the liberation of a water molecule by the dehydrating agent magnesium sulfate, thereby resulting in pyrrolo/pyridobenzimidazolones **9**.

Finally, the removal of the ionic-liquid support from **9** was carried out in sodium methoxide/methanol solution under microwave irradiation at 110 °C over 10 minutes to furnish pyrrolo/pyridobenzimidazolone derivatives **10** and **11**. The cleaved IL was precipitated from the reaction mixtures by the addition of diethyl ether; the desired products were separated by filtration. The recovered IL was recycled in the synthetic process. The filtrate was concentrated and the crude final compounds were subjected to HPLC analysis. Further column chromatography purification furnished pyrrolo[1,2-*a*]benzimidazolones **10** and pyrido[1,2-*a*]benzimidazolones **11** in good yields (Table 1). A variety of 4-keto acids and 5-keto acids were used in combination with the *N*-alkyl substitution on the diamine moiety for this tandem transformation to furnish pyrrolo/pyridobenzimidazoles with substitutional diversity, as depicted in Table 1. In addition to the spectroscopic analysis, the final structure and outcome of the tandem transformation was unambiguously confirmed by the X-ray crystallographic study of compound **10 f**. Figure 1 depicts the ORTEP diagram of compound **10 f** (X-ray crystallographic data are specified in the Supporting Information). The crystal structure of compound **10 f** indicates that the phenyl group is present at the C26 carbon of the pyridobenzimidazole skeleton, which further proved its structure.

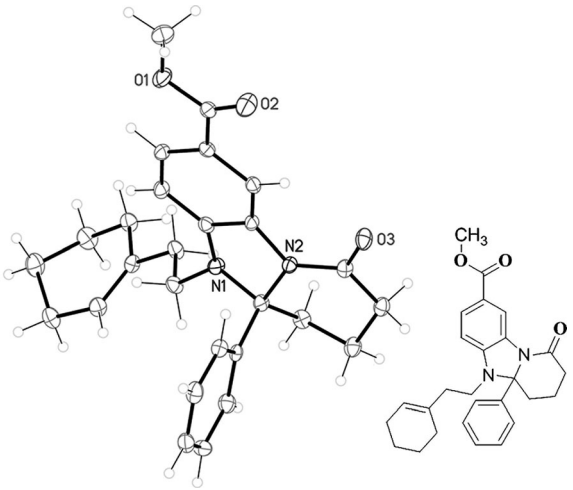
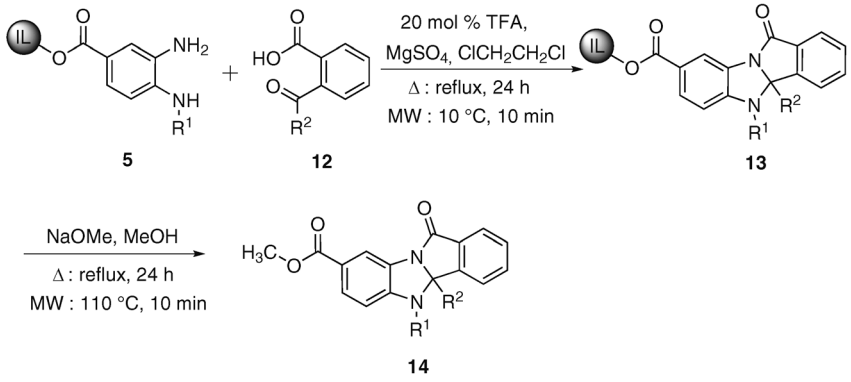


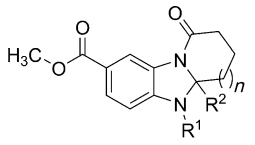
Figure 1. ORTEP diagram of compound **10 f**.

To extend the scope of the present cascade process, selective ionic-liquid-conjugated diamines were planned to react with α-ketobenzoic acids under the same reaction conditions to offer scaffold diversity and to provide a structurally distinct library. Accordingly, IL-supported diamine **5** was treated with 2-acylbenzoic acid **12** with 20 mol% TFA in dichloroethane under microwave irradiation at 110 °C (Scheme 3). IL-supported isoindolobenzimidazolones **13**



Scheme 3. Synthesis of isoindolinone-fused benzimidazole derivatives.

Table 1. Pyrrolo/pyridobenzimidazolone derivatives.



10 (n = 0); **11** (n = 1)

Compound	R^1	R^2	Mass[a]	LRMS[b]	Yield [%][c]
10a		$-CH_3$	302	97	85
10b		$-CH_3$	350	79	80
10c	Ph, Ph	$-CH_3$	440	96	83
10d			364	94	75
10e	O		366	98	72
10f			416	74	74
10g			412	95	75
10h		Et	392	86	72
10i	O	Et	394	93	75
10j		F	382	68	77
10k		F	396	85	75
11a		$-CH_3$	288	94	84
11b		$-CH_3$	316	84	82
11c	O	$-CH_3$	318	99	80
11d		$-CH_3$	364	94	83
11e	S	$-CH_3$	356	85	86
11f			378	95	75
11g			430	85	77
11h			432	70	70

[a] Mass (low-resolution (LR) MS) was detected as $[M]^+$. [b] HPLC purity of unpurified samples. [c] Yields were determined from the weight of purified samples [%].

were obtained in good yields within 10 minutes; they were purified by a simple precipitation method. The same reaction took 24 hours under reflux conditions for compete cyclization.

The confirmation of the structure of compound **13** and the outcome of the tandem transformation on aromatic ketobenzoic acid is feasible directly on the ionic-liquid support. The absence of peaks that correspond to amine and acid protons together with the emergence of the new peaks due to aromatic protons of the 2-acetyl benzoic acid moiety in the ^{1}H NMR spectrum of compound **13** along with the amide frequency band around 1720 cm^{-1} in the IR spectra suggested the cyclization of diamine conjugate **5** with 2-acetylbenzoic acid **12** on the ionic tag. Moreover, the structure of isoindolobenzimidazolone was unambiguously confirmed by the X-ray crystallographic study of compound **13a** directly with the ionic-liquid support. Figure 2 depicts the ORTEP diagram of compound **13a** (X-ray crystallographic data is specified in the Supporting Information). To the best of our knowledge, this is the first report of an X-ray crystallographic study on molecules linked with an ionic-liquid support.

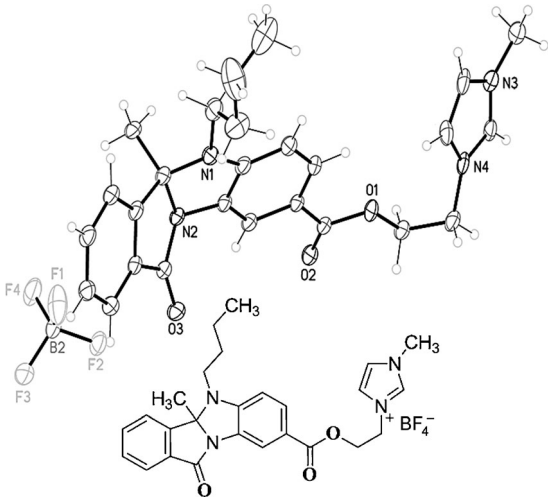


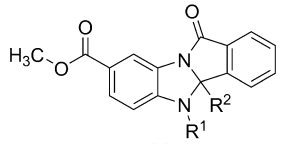
Figure 2. ORTEP diagram of isoindolobenzimidazolone **13a**.

The subsequent removal of the ionic-liquid support from **13** furnished isoindolobenzimidazolones **14** in good yield over two steps (Table 2).

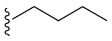
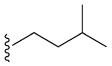
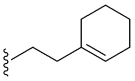
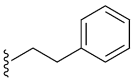
The scope of this method was further broadened by incorporation of the additional sulfur element in the scaffold. The IL-supported pyrrolobenzimidazolone **9f** and pyrrolobenzimidazolone **9e** were treated with Lawsson's reagent in toluene under focused microwave conditions at 150 °C. The thio derivative of the IL-supported pyrido- and pyrrolobenzimidazolones (**15** and **17**) were obtained in good yields over 10 minutes, whereas the same reaction took 24 hours under reflux conditions in toluene (Scheme 4). Further removal of the polymer support afforded thiopyrrolobenzimidazolone **16** and thiopyridobenzimidazolone **18**. The structures of thio compounds **16** and **18** were confirmed by proton NMR spectroscopy along with mass and IR analysis.

It is worth mentioning that the time taken to attain the desired reaction temperatures for all the reactions under microwave exposure is substantially shortened on account of

Table 2. Synthesis of isoindolobenzimidazolones.



14

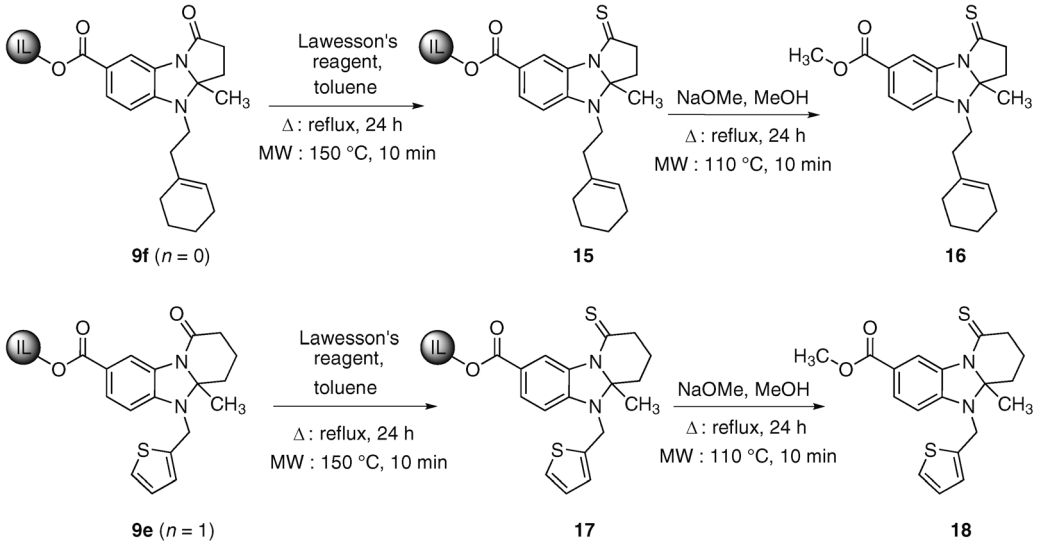
Compound	R^1	R^2	Mass[a]	LRMS[b]	Yield [%][c]
14a			350	78	85
14b			364	93	82
14c			402	85	80
14d			398	71	78

[a] Mass (LRMS) was detected as $[M]^+$. [b] HPLC purity of unpurified samples. [c] Yields were determined from the weight of purified samples [%].

the high-polar microwave absorbance medium created by the ionic-liquid support. The solubility of the ionic-liquid support throughout the sequence of reactions was not influenced by the growing chain. Thus separation and purification procedures become greatly simplified so that the general procedure involved precipitation and washing with low-polar organic solvents. Moreover, the ionic-liquid support is stable under microwave heating conditions. The reaction progress was monitored through regular proton NMR spectroscopy without releasing the intermediates from the support. The previous syntheses of pyrrolo/pyridobenzimidazolone derivatives are a time-consuming and tedious process in moderate overall yields and the R^1 group is limited to hydrogen.[17] In our current synthetic approach, we have successfully integrated the advantages of IL with microwave synthesis to afford a rapid synthesis of pyrrolo/pyridobenzimidazolones with high purity and yields. In addition, the total in-pot reaction time for the multistep synthesis was drastically reduced to around 1.2 hours under microwave irradiation conditions. For classical thermal reaction conditions, the total in-pot reaction time is around 125 hours. There was also a significant decrease in total reloading time by using IL as a support, which facilitates the purification in each step.

Conclusion

In summary, we have developed a rapid and efficient solution-phase approach to synthesize pyrrolo[1,2-*a*]benzimidazolones, pyrido[1,2-*a*]benzimidazolones, and isoindolinone-fused benzimidazoles with two points of diversity on an ionic-liquid support under microwave conditions. Here we have demonstrated a novel tandem reaction that efficiently affords different-sized fused heterocyclic skeletons. This cascade transformation mainly consists of three sequential steps: condensation of an amine functionality with keto carbonyl to afford imine, intramolecular cyclization through the imine bond to form an imidazole ring, and a second intramolecular cyclization to form various-sized fused lactam rings. Ionic liquid was explored as a high-loading liquid support for multistep organic synthesis in a homogeneous phase under microwave conditions. It is noteworthy that a synergy arises from the combined use of microwave heating with the ionic-liquid support and can be very effectively used to speed up the multistep synthesis of biologically interesting heterocycles.



Scheme 4. Synthesis of thio analogues of pyrido/pyrrolobenzimidazolone.

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Experimental Section

General Methods

Dichloroethane was distilled from calcium hydride before use. All reactions were performed under an inert atmosphere with unpurified reagents and dry solvents. Analytical thin-layer chromatography (TLC) was performed with 0.25 mm silica gel-coated Kieselgel 60 F254 plates. Flash column chromatography was performed using the indicated solvent and silica gel 60 (Merck, 230–400 mesh). ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded with a Bruker DX-300 spectrometer. Chemical shifts are reported in parts per million (ppm) on the δ scale from an internal standard. High-resolution mass spectra (HRMS) were recorded with a JEOL TMS-HX 110 mass spectrometer. Microwave experiments were performed with a CEM Discover microwave system in a closed vessel. The temperature for reaction was set by instrument.

General Procedure for the Synthesis of the Pyrrolo/Pyrido/Isoindolobenzimidazolones

Ionic liquid **1** (0.5 g, 2.3 mmol) in acetonitrile (5 mL) was added to the solution of **2** (0.51 g, 2.7 mmol, 1.2 equiv) in acetonitrile (5 mL), followed by the addition of DCC (0.57 g, 2.7 mmol, 1.2 equiv) and a catalytic amount of DMAP (0.002 g). The reaction mixture was irradiated with microwaves at 80 °C for 20 min. The precipitated dicyclohexyl urea (DCU) was filtered through a fritted Celite plug. The Celite plug was rinsed with acetonitrile, and the combined organic phase was concentrated under vacuum. The crude reaction mixtures were precipitated by slow addition of an excess amount of diethyl ether (100 mL). The precipitated ester conjugate was then filtered and washed to obtain IL-supported compound **3** in good yield. Various primary amines (6.7 mmol, 3.0 equiv) in acetonitrile (5 mL) were added to a solution of **3** in acetonitrile (5 mL), and the reaction mixtures were irradiated in a microwave cavity at 80 °C for 10 min to afford IL-immobilized nitroamines **4**. Upon concentration under reduced pressure, the crude residue was precipitated by addition of ether (100 mL). The precipitated IL conjugate **4** was then filtered through a fritted funnel and washed several times to remove the byproducts and dried. Zinc (7.0 equiv) and ammonium formate (NH_4COOH) (15.0 equiv) were added to the solution of nitroamine **4** in methanol and irradiated in a microwave cavity at 80 °C for 5 min. The insoluble zinc was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was purified by crystallization in ether to afford ionic-liquid-supported dimaine **5**. Various aliphatic γ- or δ-keto acids **6** (1.5 equiv) were added together with dry $MgSO_4$ and 20 mol% trifluoroacetic acid to the solution of **5** in ethylenedichloride (9 mL). The reaction mixture was subjected to microwave irradiation for 10 min at 110 °C to offer the IL-supported conjugates **9**. The crude reaction mixture was filtered through the fritted funnel, and the reaction mixture was precipitated by slow addition of cold ether (60 mL). The precipitated ionic-liquid conjugate was then filtered through a fritted funnel and washed several times with ether to get the ionic-liquid-supported pyrrolo/pyridobenzimidazoles **9**. The solution of 0.1 M NaOMe in MeOH (10 mL) was added to the solution of IL-supported conjugates **9** in methanol. The reaction mixture was subjected to microwave irradiation for 10 min at 110 °C. The reaction mixture was precipitated by addition of ether. The precipitate of IL was separated by filtration. The filtrates were concentrated under reduced pressure, and the crude pyrrolo/pyridobenzimidazoles were subjected to HPLC purification (68–99%). The residue was further purified by column chromatography over silica gel with ethylacetate/*n*-hexane (1:1) as an eluent to obtain the pure pyrrolo/pyridobenzimidazoles **10** and **11** in good yields (72–85%).

*Methyl 4-Butyl-3a-methyl-1-oxo-2,3,3a,4-tetrahydro-1H-benzo[d]pyrrolo[1,2-a]imidazole-7-carboxylate (**10a**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90 (d, J = 1.8 Hz, 1H), 7.72 (dd, J = 8.4, 1.8 Hz, 1H), 6.34 (d, J = 8.4 Hz, 1H), 3.8 (s, 3H), 3.29–3.08 (m, 2H), 2.84–2.71 (m, 2H), 2.39–2.33 (m, 2H), 1.65–1.53 (quint, J = 7.3 Hz, 2H), 1.4 (s, 3H), 1.37 (sext, J = 7.2 Hz, 2H), 0.93 ppm (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.6, 166.7, 147.5, 129.1, 127.5, 118.7, 115.5, 104.4, 88.9, 51.5, 42.6, 36.4, 33.0, 30.6, 22.2, 20.3, 13.6 ppm; MS (ESI): m/z: 302 [M^+]; HRMS (ESI): m/z: calcd for $C_{17}H_{22}N_2O_3$: 302.1630; found: 302.1625 [M^+]; IR (neat): $\tilde{\nu}$ = 2360, 1720, 1614 cm^{-1}; HPLC: 97%.

*Methyl 3a-Methyl-1-oxo-4-phenethyl-2,3,3a,4-tetrahydro-1H-benzo[d]pyrrolo[1,2-a]imidazole-7-carboxylate (**10b**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98 (d, J = 1.8, 1H), 7.81 (dd, J = 8.1, 1.8 Hz, 1H), 7.35–7.17 (m, 5H), 6.4 (d, J = 8.1 Hz, 1H), 3.89 (s, 3H), 3.63–3.54 (m, 1H), 3.38 (m, 1H), 3.03–2.89 (m, 2H), 2.73 (m, 1H), 2.41 (dd, J = 16.9, 8.5 Hz, 1H), 2.18 (dd, J = 16.9, 8.5 Hz, 1H), 1.90 (m, 1H), 1.44 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.8, 166.9, 147.0, 138.5, 129.1, 128.7, 128.6 (3C), 127.6, 126.7, 119.0, 115.7, 104.4, 88.9, 51.5, 44.9, 35.5, 34.7, 32.9, 22.5 ppm; IR (neat): $\tilde{\nu}$ = 2360, 1697, 1616 cm^{-1}; MS (ESI): m/z: 350 [M^+]; HRMS (ESI): m/z: calcd for $C_{21}H_{22}N_2O_3$: 350.1630; found: 350.1619 [M^+]; HPLC: 79%.

*Methyl 4-(3,3-Diphenylpropyl)-3a-methyl-1-oxo-2,3,3a,4-tetrahydro-1H-benzo[d]pyrrolo[1,2-a]imidazole-7-carboxylate (**10c**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96 (d, J = 1.8 Hz, 1H), 7.72 (dd, J = 8.1, 1.8 Hz, 1H), 7.22–7.32 (m, 10H), 6.12 (d, J = 7.8 Hz, 1H), 3.84 (t, J = 7.4 Hz, 1H), 3.84 (s, 3H), 3.30–3.10 (m, 2H), 2.79 (m, 1H), 2.56–2.24 (m, 5H), 1.41 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.5, 166.9, 147.3, 143.7, 143.6, 128.9, 128.7 (4C), 127.6 (3C), 127.5 (3C), 126.6, 119.1, 115.6, 104.7, 88.9, 51.6, 48.6, 41.3, 36.5, 34.2, 33.1, 22.3 ppm; IR (neat): $\tilde{\nu}$ = 2360, 1718, 1612 cm^{-1}; MS (ESI): m/z: 440 [M^+]; HRMS (ESI): m/z: calcd for $C_{28}H_{28}N_2O_3$: 440.2100; found: 440.2095 [M^+]; HPLC: 96%

*Methyl 4-Isobutyl-1-oxo-3a-phenyl-2,3,3a,4-tetrahydro-1H-benzo[d]pyrrolo[1,2-a]imidazole-7-carboxylate (**10d**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, J = 1.8 Hz, 1H), 7.76 (dd, J = 8.4, 1.8 Hz, 1H), 7.37–7.36 (m, 5H), 6.35 (d, J = 8.4 Hz, 1H), 3.83 (s, 3H), 3.18 (m, 1H), 2.89–2.53 (m, 5H), 1.95 (m, 1H), 1.25 ppm (t, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.9, 166.9, 148.0, 137.6, 129.3, 129.2, 128.8 (2C), 128.5, 125.4 (2C), 119.1, 114.7, 104.4, 91.4, 51.6, 51.5, 36.5, 33.6, 27.9, 20.5, 20.3 ppm; IR (neat): $\tilde{\nu}$ = 2360, 1720, 1612 cm^{-1}; MS (ESI): m/z: 364 [M^+]; HRMS (ESI): m/z: calcd for $C_{22}H_{24}N_2O_3$: 364.1787; found: 364.1782 [M^+]; HPLC: 94%.

*Methyl 4-(2-Methoxyethyl)-1-oxo-3a-phenyl-2,3,3a,4-tetrahydro-1H-benzo[d]pyrrolo[1,2-a]imidazole-7-carboxylate (**10e**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, J = 1.5 Hz, 1H), 7.78 (dd, J = 8.1, 1.5 Hz, 1H), 7.41–7.31 (m, 5H), 6.39 (d, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.44–3.36 (m, 2H), 3.34–3.25 (m, 5H), 3.21 (m, 1H), 2.80–2.49 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.5, 166.8, 146.8, 138.2, 129.1, 129.0, 128.8 (2C), 128.3, 125.2 (2C), 118.9, 114.8, 103.8, 90.9, 70.1, 58.7, 51.5, 42.3, 36.4, 33.2 ppm; IR (neat): $\tilde{\nu}$ = 2362, 1718, 1610 cm^{-1}; MS (ESI): m/z: 366 [M^+]; HRMS (ESI): m/z: calcd for $C_{21}H_{22}N_2O_4$: 366.1580; found: 366.1584 [M^+]; HPLC: 98%.

*Methyl 4-[2-(Cyclohex-1-en-1-yl)ethyl]-1-oxo-3a-phenyl-2,3,3a,4-tetrahydro-1H-pyrrolo[1,2-a]benzimidazole-7-carboxylate (**10f**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, J = 1.8 Hz, 1H), 7.79 (dd, J = 8.1, 1.8 Hz, 1H), 7.41–7.34 (m, 5H), 6.34 (d, J = 8.1 Hz, 1H), 5.39 (s, 1H), 3.86 (s, 3H), 3.31–3.06 (m, 3H), 2.68–2.52 (m, 3H), 1.95–1.84 (m, 6H), 1.64–1.48 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.9, 167.4, 147.1, 138.9, 134.8, 129.8, 129.7, 128.9 (2C), 128.6, 125.7 (2C), 124.2, 119.3, 115.3, 104.4, 91.4, 52.1, 42.7, 36.9, 36.7, 33.8, 28.8, 25.6, 23.2, 22.6 ppm; IR (neat): $\tilde{\nu}$ = 2360, 1720, 1612 cm^{-1}; MS (ESI): m/z: 416 [M^+]; HRMS (ESI): m/z: calcd for $C_{26}H_{28}N_2O_3$: 416.2100; found: 416.2097 [M^+]; HPLC: 74%.

*Methyl 4-Phenethyl-3a-phenyl-1-oxo-2,3,3a,4-tetrahydro-1H-benzo[d]pyrrolo[1,2-a]imidazole-7-carboxylate (**10g**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (d, J = 1.5 Hz, 1H), 7.83 (dd, J = 1.5, 8.1 Hz, 1H), 7.40–7.37 (m, 5H), 7.31–7.24 (m, 3H), 7.13–7.10 (m, 2H), 6.39 (d, J = 8.1 Hz, 1H), 3.9 (s, 3H), 3.46 (m, 1H), 3.32 (m, 1H), 3.01 (m, 1H), 2.87 (m, 1H), 2.66–2.52 (m, 2H), 2.45 (m, 1H), 2.20 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.4, 166.9, 146.4, 138.5,

138.5, 129.3, 129.2, 128.9 (2C), 128.6 (3C), 128.5 (2C), 126.6, 125.1, 119.1, 114.9, 104.0, 90.9, 51.6, 45.3, 35.6, 34.0, 33.2 ppm; IR (neat): $\tilde{\nu}$=2360, 1716, 1612 cm^{-1}; MS (ESI): *m/z*: 412 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{26}H_{24}N_2O_3$: 412.1787; found: 412.1794 [M^+]; HPLC: 95%.

*Methyl 4-Butyl-3a-(4-ethylphenyl)-1-oxo-2,3,3a,4-tetrahydro-1H-benzo[d]pyrrolo[1,2-a]imidazole-7-carboxylate (**10h**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.04 (d, *J*=1.8 Hz, 1H), 7.77 (dd, *J*=1.8, 8.1 Hz, 1H), 7.27 (d, *J*=8.4 Hz, 2H), 7.16 (d, *J*=8.4 Hz, 2H), 6.32 (d, *J*=8.1 Hz, 1H), 3.85 (s, 3H), 3.22–3.09 (m, 2H), 3.01 (m, 1H), 2.97–2.57 (m, 4H), 1.54 (m, 1H), 1.37–1.24 (m, 4H), 1.20 (t, *J*=7.6 Hz, 3H), 0.89 ppm (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=174.3, 167.0, 147.1, 145.4, 135.5, 129.3, 128.5, 128.3 (2C), 125.3 (2C), 118.7, 114.8, 103.8, 91.0, 51.6, 42.9, 36.6, 33.5, 30.4, 28.3, 20.3, 15.3, 13.8 ppm; IR (neat): $\tilde{\nu}$=2360, 1720, 1612 cm^{-1}; MS (ESI): *m/z*: 392 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{24}H_{28}N_2O_3$: 392.2100; found: 392.2091 [M^+]; HPLC: 86%.

*Methyl 3a-(4-Ethylphenyl)-4-(2-methoxyethyl)-1-oxo-2,3,3a,4-tetrahydro-1H-benzo[d]pyrrolo[1,2-a]imidazole-7-carboxylate (**10i**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.05 (d, *J*=1.5 Hz, 1H), 7.77 (dd, *J*=8.1, 1.5 Hz, 1H), 7.29 (d, *J*=8.4 Hz, 2H), 7.16 (d, *J*=8.4 Hz, 2H), 6.37 (d, *J*=8.1 Hz, 1H), 3.85 (s, 3H), 3.48–3.32 (m, 4H), 3.30 (s, 3H), 3.29–3.14 (m, 2H), 2.77–2.51 (m, 4H), 1.19 ppm (t, *J*=7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=174.5, 166.9, 146.9, 145.4, 135.6, 129.2, 128.5, 128.3 (2C), 125.4 (2C), 119.0, 114.9, 103.8, 91.0, 70.2, 58.8, 51.6, 43.1, 36.4, 33.3, 28.3, 15.3 ppm; IR (neat): $\tilde{\nu}$=2360, 1720, 1612 cm^{-1}; MS (ESI): *m/z*: 394 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{23}H_{26}N_2O_4$: 394.1893; found: 394.1884 [M^+]; HPLC: 93%.

*Methyl 3a-(4-Fluorophenyl)-4-isobutyl-1-oxo-2,3,3a,4-tetrahydro-1H-benzo[d]pyrrolo [1,2-a]imidazole-7-carboxylate (**10j**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.05 (d, *J*=1.5 Hz, 1H), 7.8 (dd, *J*=8.4, 1.5 Hz, 1H), 7.33 (dd, *J*=7.8, 0.9 Hz, 2H), 7.04 (t, *J*=7.8 Hz, 2H), 6.4 (d, *J*=8.4 Hz, 1H), 3.84 (s, 3H), 3.14 (m, 1H), 2.85 (dd, *J*=14.4, 8.4 Hz, 1H), 2.72 (dd, *J*=14.4, 8.4 Hz, 1H), 2.70–2.53 (m, 3H), 2.93 (m, 1H), 0.92 (d, *J*=6.8 Hz, 3H), 0.90 ppm (d, *J*=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=173.8, 166.8, 147.7, 133.8, 133.7, 129.3, 128.3, 127.5, 127.3 119.3, 115.9, 115.6, 114.8, 104.5, 90.8, 51.6, 51.5, 36.5, 33.4, 27.8, 20.5, 20.2 ppm; IR (neat): $\tilde{\nu}$=2360, 1720, 1612 cm^{-1}; MS (ESI): *m/z*: 382 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{22}H_{23}FN_2O_3$: 382.1693; found: 382.1700 [M^+]; HPLC: 68%.

*Methyl 3a-(4-Fluorophenyl)-4-(3-methylbutyl)-1-oxo-2,3,3a,4-tetrahydro-1H-pyrrolo[1,2-a]benzimidazole-7-carboxylate (**10k**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.06 (d, *J*=1.5 Hz, 1H), 7.79 (dd, *J*=8.4, 1.5 Hz, 1H), 7.4 (dd, *J*=8.6, 1.1 Hz, 2H), 7.04 (t, *J*=8.6 Hz, 2H), 6.32 (d, 8.4 Hz, 1H), 3.86 (s, 3H), 3.24–3.13 (m, 2H), 3.01 (m, 1H), 2.67–2.53 (m, 3H), 1.57 (m, 1H), 1.42 (m, 1H), 1.26 (m, 1H), 0.92 (d, *J*=6.8 Hz, 3H), 0.90 ppm (d, *J*=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=174.3, 166.9, 164.6, 161.3, 146.6, 134.3, 129.5, 127.3, 127.2, 119.0, 115.9, 115.7, 114.9, 104.0, 90.5, 51.7, 41.5, 36.9, 36.7, 33.3, 26.1, 22.7, 22.4 ppm; IR (neat): $\tilde{\nu}$=2360, 1718, 1610 cm^{-1}; MS (ESI): *m/z*: 396 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{23}H_{25}FN_2O_3$: 396.1849; found: 396.1841 [M^+]; HPLC: 85%.

*Methyl 5-Ethyl-4a-methyl-1-oxo-1,2,3,4,4a,5-hexahydrobenzo[4,5]imidazo[1,2-a]pyridine-8-carboxylate (**11a**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.39 (d, *J*=1.8 Hz, 1H), 7.76 (dd, *J*=8.4, 1.8 Hz, 1H), 6.39 (d, *J*=8.4 Hz, 1H), 3.86 (s, 3H), 3.32–3.18 (m, 2H), 2.68–2.47 (m, 2H), 2.26 (m, 1H), 2.08–1.81 (m, 3H), 1.40 (s, 3H), 1.26 ppm (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.3, 166.4, 144.5, 129.9, 128.8, 119.0, 117.2, 103.7, 83.9, 51.6, 37.0, 32.8, 30.6, 22.5, 16.9, 14.5 ppm; IR (neat): $\tilde{\nu}$=2362, 1714, 1654 cm^{-1}; MS (ESI): *m/z*: 288 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{16}H_{20}N_2O_3$: 288.1474; found: 288.1465 [M^+]; HPLC: 94%.

*Methyl 5-Butyl-4a-methyl-1-oxo-1,2,3,4,4a,5-hexahydrobenzo[4,5]imidazo[1,2-a]pyridine-8-carboxylate (**11b**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.38 (d, *J*=1.5 Hz, 1H), 7.74 (dd, *J*=8.1, 1.5 Hz, 1H), 6.37 (d, *J*=8.1 Hz, 1H), 3.85 (s, 3H), 3.23–3.02 (m, 2H), 2.67–2.46 (m, 2H), 2.20 (m, 1H), 2.06–1.79 (m, 3H), 1.60 (quintet, *J*=7.5 Hz, 2H), 1.43–1.35 (m, 2H), 1.37 (s, 3H), 0.95 ppm (t, *J*=7.3, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.2, 166.3, 145.1, 129.9, 128.9, 119.1, 117.2, 104.0, 84.0, 51.5, 42.7, 32.8, 31.1, 30.6, 22.0, 20.4, 16.9, 13.8 ppm; IR (neat): $\tilde{\nu}$=2358, 1708, 1658 cm^{-1}; MS (ESI): *m/z*: 316 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{18}H_{24}N_2O_3$: 316.1787; found: 316.1784 [M^+]; HPLC: 84%

*Methyl 5-(2-Methoxyethyl)-4a-methyl-1-oxo-1,2,3,4,4a,5-hexahydrobenzo[4,5]imidazo[1,2-a]pyridine-8-carboxylate (**11c**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.36 (d, *J*=1.5 Hz, 1H), 7.72 (dd, *J*=8.1, 1.5 Hz, 1H), 6.42 (d, *J*=8.1 Hz, 1H), 3.81 (s, 3H), 3.52–3.46 (m, 2H), 3.36–3.31 (m, 3H), 3.33 (s, 3H), 2.62–2.43 (m, 2H), 2.21 (m, 1H), 2.01–1.78 (m, 3H), 1.36 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.1, 166.4, 144.8, 129.8, 128.6, 119.4, 117.2, 104.0, 83.9, 70.6, 58.9, 51.5, 42.8, 32.7, 30.6, 22.0, 16.9 ppm; IR (neat): $\tilde{\nu}$=2360, 1702, 1654 cm^{-1}; MS (ESI): *m/z*: 318 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{17}H_{22}N_2O_4$: 318.1580; found: 318.1579 [M^+]; HPLC: 99%.

*Methyl 4a-Methyl-1-oxo-5-phenethyl-1,2,3,4,4a,5-hexahydrobenzo[4,5]Imidazo[1,2-a]pyridine-8-carboxylate (**11d**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.42 (d, *J*=1.8 Hz, 1H), 7.78 (dd, *J*=8.1, 1.8 Hz, 1H), 7.31–7.17 (m, 5H), 6.44 (d, *J*=8.1 Hz, 1H), 3.83 (s, 3H), 3.45 (m, 1H), 3.30 (m, 1H), 2.95–2.88 (m, 2H), 2.60–2.34 (m, 2H), 1.98–1.71 (m, 3H), 1.50 (m, 1H), 1.35 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.1, 166.4, 144.7, 138.6, 129.9, 128.9 (2C), 128.7, 128.5 (2C), 126.6, 119.4, 117.1, 103.9, 83.9, 51.5, 45.0, 35.1, 32.2, 30.5, 22.0, 16.8 ppm; IR (neat): $\tilde{\nu}$=2360, 1706, 1654 cm^{-1}; MS (ESI): *m/z*: 364 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{22}H_{24}N_2O_3$: 364.1787; found: 364.1795 [M^+]; HPLC: 94%.

*Methyl 4a-Methyl-1-oxo-5-(thiophen-2-ylmethyl)-1,2,3,4,4a,5-hexahydropyrido[1,2-a]benzimidazole-8-carboxylate (**11e**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.41 (d, *J*=1.5 Hz, 1H), 7.66 (dd, *J*=8.4, 1.5 Hz, 1H), 7.21 (d, *J*=4.8 Hz, 1H), 7.01 (d, *J*=3.6 Hz, 1H), 6.95 (dd, *J*=4.8, 3.6 Hz, 1H), 6.36 (d, *J*=8.4 Hz, 1H), 4.52 (s, 2H), 3.84 (s, 3H), 2.68–2.47 (m, 2H), 2.25–2.18 (m, 2H), 2.12–1.83 (m, 2H), 1.75 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.0, 166.4, 144.5, 141.1, 130.2, 128.4, 126.9, 125.1, 124.9, 120.3, 117.3, 105.4, 84.2, 51.6, 42.3, 32.7, 30.6, 21.9, 16.9 ppm; IR (neat): $\tilde{\nu}$=2360, 1706, 1656 cm^{-1}; MS (ESI): *m/z*: 356 [M]$^+$; HRMS (ESI): *m/z*: calcd for $C_{19}H_{20}N_2O_3S$: 356.1195; found: 356.1193 [M+1]$^+$; HPLC: 85%.

*Methyl 5-Butyl-1-oxo-4a-phenyl-1,2,3,4,4a,5-hexahydrobenzo[4,5]imidazo[1,2-a]pyridine-8-carboxylate (**11f**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.3 (d, *J*=1.5 Hz, 1H), 7.71 (dd, *J*=8.1, 1.5 Hz, 1H), 7.34–7.26 (m, 5H), 6.22 (d, *J*=8.1 Hz, 1H), 3.85 (s, 3H), 3.13–2.89 (m, 3H), 2.43 (m, 1H), 2.18–2.05 (m, 2H), 1.88 (m, 1H), 1.64 (m, 1H), 1.42 (m, 1H), 1.29–1.15 (m, 3H), 0.84 ppm (t, *J*=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.5, 167.2, 143.7, 138.6, 130.9, 129.0 (2C), 128.9, 128.7, 124.9 (2C), 118.6, 115.4, 103.3, 86.5, 51.4, 42.3, 30.8, 30.2, 29.9, 20.2, 14.7, 13.6 ppm; IR (neat): $\tilde{\nu}$=2360, 1708, 1664 cm^{-1}; MS (ESI): *m/z*: 378 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{23}H_{26}N_2O_3$: 378.1943; found: 378.1940 [M^+]; HPLC: 95%.

*Methyl 5-[2-(1-Cyclohexenyl)ethyl]-1-oxo-4a-phenyl-1,2,3,4,4a,5-hexahydrobenzo[4,5]imidazo[1,2-a]pyridine-8-carboxylate (**11g**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ=8.54 (d, *J*=1.5 Hz, 1H), 7.74 (dd, *J*=8.1, 1.5 Hz, 1H), 7.38–7.32 (m, 5H), 6.26 (d, *J*=8.1 Hz, 1H), 5.34 (s, 1H), 3.86 (s, 3H), 3.20 (m, 1H), 3.10–3.99 (m, 2H), 2.46 (m, 1H), 2.19–2.02 (m, 3H), 1.95–1.86 (m, 5H), 1.69–1.47 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=168.1, 167.7, 143.9, 139.2, 134.9, 131.5, 129.6 (2C), 129.5, 129.4, 125.5 (2C), 124.1, 119.2, 115.9, 103.8, 86.9, 52.0, 42.2, 36.4, 31.3,

30.7, 28.9, 25.6, 23.2, 22.6, 15.2 ppm; IR (neat): $\tilde{\nu}$ = 2360, 1708, 1664 cm^{-1}; MS (ESI): *m/z*: 430 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{27}H_{30}N_2O_3$: 430.2256; found: 430.2259 [M^+]; HPLC: 85%.

*Methyl 5-Cyclooctyl-1-oxo-4a-phenyl-1,2,3,4,4a,5-hexahydropyrido[1,2-a]benzimidazole-8-carboxylate (**11h**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.55 (d, *J* = 1.8 Hz, 1H), 7.67 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.42–7.34 (m, 5H), 6.29 (d, *J* = 8.1 Hz, 1H), 3.84 (s, 3H), 3.45 (t, *J* = 9.0 Hz, 1H), 3.08 (m, 1H), 2.44 (m, 1H), 2.17–1.98 (m, 2H), 1.95–1.52 (m, 12H), 1.39–1.25 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.6, 167.4, 141.3, 139.4, 131.5, 129.1 (3C), 128.4, 125.1 (2C), 117.7, 115.4, 105.0, 86.4, 53.3, 51.5, 33.1, 30.3, 30.7, 30.4, 30.3, 26.7, 26.4, 25.5, 24.8, 14.2 ppm; IR (neat): $\tilde{\nu}$ = 2360, 1706, 1666 cm^{-1}; MS (ESI): *m/z*: 432 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{27}H_{32}N_2O_3$: 432.2413; found: 432.2409 [M^+]; HPLC: 70%.

*Methyl 5-Butyl-4b-methyl-11-oxo-4b,11-dihydro-5H-benzo[4,5]imidazo[2,1-a]isoindole-8-carboxylate (**14a**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 1.5 Hz, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.78 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.67–7.75 (m, 3H), 6.38 (d, *J* = 8.4 Hz, 1H), 3.84 (s, 3H), 3.39 (t, *J* = 7.6 Hz, 2H), 1.72 (s, 3H), 1.50 (quint, *J* = 7.5 Hz, 2H), 1.24 (sext, *J* = 7.5 Hz, 2H), 0.87 ppm (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.4, 167. 4, 150.1, 147.9, 133.7, 132.9, 130.4, 129.9, 129.6, 125.8, 122.4, 119.7, 118.2, 105.1, 89.4, 52.1, 43.8, 31.1, 23.4, 20.7, 14.2 ppm; IR (neat): $\tilde{\nu}$ = 2360, 1720, 1612 cm^{-1}; MS (ESI): *m/z*: 350 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{21}H_{22}N_2O_3$: 350.1630; found: 350.1624 [M^+]; HPLC: 78%.

*Methyl 4b-Methyl-5-(3-methylbutyl)-11-oxo-4b,11-dihydro-5H-isoindolo[2,1-a]benzimidazole-8-carboxylate (**14b**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 1.5 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.79 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.65–7.60 (m, 2H), 6.36 (d, *J* = 8.4 Hz, 1H), 3.84 (s, 3H), 3.41 (t, *J* = 7.8 Hz, 2H), 1.73 (s, 3H), 1.59–1.24 (m, 3H), 0.9 ppm (d, *J* = 13.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9, 166.9, 149.4, 147.4, 133.3, 132.1, 129.9, 129.4, 129.2, 125.4, 121.9, 119.2, 117.7, 104.5, 88.9, 51.6, 41.9, 37.2, 26.1, 23.1, 22.5, 22.4 ppm; IR (neat): $\tilde{\nu}$ = 2360, 1720, 1614 cm^{-1}; MS (ESI): *m/z*: 364 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{22}H_{24}N_2O_3$: 364.1787; found: 364.1791 [M^+]; HPLC: 93%.

*Methyl 5-[2-(Cyclohex-1-en-1-yl)ethyl]-4b-methyl-11-oxo-4b,11-dihydro-5H-isoindolo[2,1-a]benzimidazole-8-carboxylate (**14c**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 1.5 Hz, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.81 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.59–7.53 (m, 2H), 6.38 (d, *J* = 8.1 Hz, 1H), 5.48 (s, 1H), 3.89 (s, 3H), 3.48 (t, *J* = 7.8 Hz, 2H), 2.19–1.9 (m, 2H), 1.89–1.85 (m, 4H), 1.72 (s, 3H), 1.55–1.37 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9, 166.9, 149.2, 147.5, 134.3, 133.3, 132.0, 129.9, 129.4, 129.1, 125.3, 123.7, 121.9, 119.2, 117.7, 104.5, 88.8, 51.6, 42.9, 36.5, 28.7, 25.0, 23.1, 22.6, 21.9 ppm; IR (neat): $\tilde{\nu}$ = 2358, 1720, 1612 cm^{-1}; MS (ESI): *m/z*: 402 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{25}H_{26}N_2O_3$: 402.1943; found: 402.1953 [M+1]$^+$; HPLC: 85%.

*Methyl 4b-Methyl-11-oxo-5-phenethyl-4b,11-dihydro-5H-benzo[4,5]imidazo[2,1-a]isoindole-8-carboxylate (**14d**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.1 (d, *J* = 1.5 Hz, 1H), 7.87–7.79 (m, 2H), 7.54–7.50 (m, 2H), 7.40 (m, 1H), 7.20–7.10 (m, 3H), 7.06–7.03 (m, 2H), 6.39 (d, *J* = 8.4, 1H), 3.90 (s, 3H), 3.68–3.62 (m, 2H), 2.87–2.70 (m, 2H), 1.71 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9, 166.9, 149.1, 147.3, 138.2, 133.4, 131.8, 129.7, 129.4, 129.3, 128.7 (2C), 128.5 (2C), 126.6, 125.3, 121.7, 119.6, 117.9, 104.6, 88.8, 51.7, 45.6, 34.9, 22.9 ppm; IR (neat): $\tilde{\nu}$ = 2362, 1712, 1619 cm^{-1}; MS (ESI): *m/z*: 398 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{25}H_{22}N_2O_3$: 398.1630; found: 398.1629 [M^+]; HPLC: 70%.

*Methyl 4-[2-(1-Cyclohexenyl)ethyl]-3a-methyl-1-thioxo-2,3,3a,4-tetrahydro-1H-benzo[d]pyrrolo[1,2-a]imidazole-7-carboxylate (**16**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.73 (d, *J* = 1.7 Hz, 1H), 7.87 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.50 (d, *J* = 8.4 Hz, 1H), 5.48 (s, 1H), 3.84 (s, 3H), 3.41 (m, 1H), 3.26–3.16 (m, 3H), 2.50–2.34 (m, 2H), 2.25 (t, *J* = 7.6 Hz, 2H), 1.99–1.97 (m, 4H), 1.67–1.51 (m, 4H), 1.47 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.8, 166.8, 148.7, 134.0, 130.6, 127.5, 123.9, 119.1, 117.2, 105.5, 95.7, 51.8, 47.3, 42.3, 38.0, 36.7, 25.4, 25.1, 22.7, 22.1, 20.3 ppm; IR (neat): $\tilde{\nu}$ = 2360, 1708, 1610 cm^{-1}; MS (ESI): *m/z*: 370 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{21}H_{26}N_2O_2S$: 370.1715; found: 370.1711 [M^+]; HPLC: 51%.

*Methyl 4a-Methyl-5-(thiophen-2-ylmethyl)-1-thioxo-1,2,3,4,4a,5-hexahydropyrido[1,2-a]benzimidazole-8-carboxylate (**18**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.69 (d, *J* = 1.5 Hz, 1H), 7.80 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.03 (d, *J* = 3.9 Hz, 1H), 7.23 (d, *J* = 4.8 Hz, 1H), 6.96 (dd, *J* = 4.8, 3.9 Hz, 1H), 6.46 (d, *J* = 8.4 Hz, 1H), 4.56 (s, 2H), 3.84 (s, 3H), 3.22–3.15 (m, 2H), 2.33 (m, 1H), 2.20 (m, 1H), 1.97–1.79 (m, 2H), 1.46 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.5, 166.8, 145.8, 140.6, 131.4, 130.4, 127.0, 125.3, 125.0, 120.4, 119.5, 105.9, 86.9, 51.8, 42.5, 41.8, 32.2, 21.8, 16.6 ppm; IR (neat): $\tilde{\nu}$ = 2360, 1706, 1602 cm^{-1}; MS (ESI): *m/z*: 372 [M+H]$^+$; HRMS (ESI): *m/z*: calcd for $C_{19}H_{20}N_2O_2S_2$: 372.0966; found: 372.0971 [M+1]$^+$; HPLC: 90%.

*Methyl 2-[3-(4-Fluorophenyl)-3-oxopropyl]-1-isobutyl-1H-benzimidazole-5-carboxylate (**9**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.39 (d, *J* = 1.2 Hz, 1H), 8.10–8.05 (m, 2H), 7.96 (dd, *J* = 8.7, 1.2 Hz, 1H), 7.31 (d, *J* = 8.7 Hz, 1H), 7.13 (t, *J* = 8.5 Hz, 2H), 4.03 (d, *J* = 7.8, 2H), 3.94 (s, 3H), 3.75 (t, *J* = 7.2 Hz, 2H), 3.2 (t, *J* = 7.2 Hz, 2H), 2.3 (septet, *J* = 6.8 Hz, 1H), 0.99 ppm (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.9, 167.7, 164.2, 155.9, 141.9, 138.8, 132.9, 130.8, 130.7, 123.9, 123.7, 121.3, 115.9, 115.6, 109.3, 51.9, 51.2, 35.7, 29.3, 21.5, 20.2 ppm (2C); IR (neat): $\tilde{\nu}$ = 2368, 1714, 1679 cm^{-1}; MS (ESI): *m/z*: 382 [M^+]; HRMS (ESI): *m/z*: calcd for $C_{22}H_{23}FN_2O_3$: 382.1693; found: 382.1697 [M^+]; HPLC: 92%.

Crystallographic Data

CCDC 817573 (**10f**) and 817574 (**13a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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