

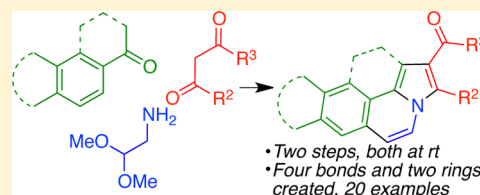
# Mild and General Synthesis of Pyrrolo[2,1-*a*]isoquinolines and Related Polyheterocyclic Frameworks from Pyrrole Precursors Derived from a Mechanochemical Multicomponent Reaction

Marco Leonardi, Mercedes Villacampa, and J. Carlos Menéndez\*<sup>1b</sup>

Departamento de Química Orgánica y Farmacéutica, Facultad de Farmacia, Universidad Complutense, 28040 Madrid, Spain

**S** Supporting Information

**ABSTRACT:** The combination of a three-component, solvent-free pyrrole synthesis performed under mechanochemical conditions with a TMSOTf-catalyzed oxonium-mediated cyclization gave general access to pyrrolo[2,1-*a*]isoquinoline derivatives under very mild conditions. The structural diversity generated by this method was extended by the preparation of six additional unusual polyheterocyclic frameworks.



## INTRODUCTION

Privileged structures, defined by Evans as “single molecular frameworks able to provide ligands for diverse receptors”,<sup>1</sup> have found a broad application in drug discovery, including traditional<sup>2</sup> and diversity-oriented<sup>3</sup> approaches. Known privileged structures include a variety of simple nitrogen heterocycles such as dihydropyridine, quinoline, tetrahydroquinoline, piperazine, benzodiazepine, and pyrrole. Polyheterocyclic scaffolds based on privileged structures are very attractive for drug discovery programs owing to their ability to direct the interaction of heteroatoms in the drug molecule with target proteins. For this reason, such scaffolds have received much attention as drug candidates<sup>4</sup> and there is, therefore, a need for synthetic methods allowing their rapid and efficient construction from simple starting materials.<sup>5</sup>

Among this class of compounds, heterocycles with a ring-fusion nitrogen atom are of considerable pharmaceutical relevance. More specifically, the pyrrolo[2,1-*a*]isoquinoline framework constitutes the structural core of a large family of alkaloids,<sup>6</sup> and many natural and unnatural derivatives of this heterocyclic system have shown interesting pharmacological properties such as antidepressant,<sup>7</sup> cardiotoxic<sup>8</sup> and serotonin uptake modulating activity.<sup>9</sup> Furthermore, the lamellarins, a family of anticancer marine alkaloids, contain a complex polycyclic core based on the pyrrolo[2,1-*a*]isoquinoline nucleus.<sup>10</sup>

A number of synthetic methodologies give access to the fully unsaturated pyrrolo[2,1-*a*]isoquinoline system, but they rely on multistep strategies and normally require harsh reaction conditions.<sup>11</sup> The most general method involves 1,3-dipolar cycloadditions, e.g., between isoquinolinium *N*-ylides and alkynes.<sup>12</sup> Domino processes generating two rings have also been developed, including silver-catalyzed domino cycloisomerization/dipolar cycloaddition processes<sup>13</sup> and Cu(OTf)<sub>2</sub>/chiral Pybox complex-catalyzed enantioselective cyclizations of tertiary enamides.<sup>14</sup> Other procedures that have allowed the preparation of specific pyrrolo[2,1-*a*]isoquinoline compounds include the reaction between chromone-3-carbaldehyde,

isoquinoline, and phenacyl bromide in aqueous micellar media<sup>15</sup> and a protocol based on the Pd(II)-catalyzed alkylation of the phenyl ring of 2-phenylpyrroles, followed by allylation and a “Pd-induced pyrrole addition”.<sup>16</sup> Lamellarin precursors derived from the pyrrolo[2,1-*a*]isoquinoline system have been prepared by multistep procedures starting from suitable methyl pyrrole-2-carboxylate derivatives, including *N*-alkylation/intramolecular Heck reaction/dehydrogenation<sup>17</sup> or *N*-alkylation/triflic acid-promoted Pomeranz–Fritsch<sup>18</sup> sequences. Generally speaking, these methods are not easily adapted to the preparation of fused derivatives of the pyrrolo[2,1-*a*]isoquinoline system. Although the indolo[2,1-*a*]isoquinoline and pyrido[1,2-*a*:4,3-*b'*]diindole systems can be accessed by a silver-catalyzed domino process starting from 2-alkynylbenzaldehydes or 3-alkynylindole-2-carbaldehydes, respectively,<sup>19</sup> at present there is not a unified strategy that allows the general preparation of these polyheterocyclic systems.

## RESULTS AND DISCUSSION

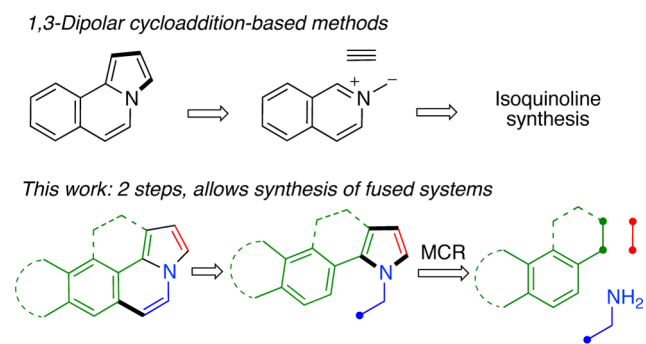
In this context, we report here the development of a new two-step protocol for the synthesis of the pyrrolo[2,1-*a*]isoquinoline ring system, which proceeds under very mild conditions and can be readily extended to the preparation of more complex, polyheterocyclic frameworks. Our method is based on the disconnections summarized in Scheme 1.

The preparation of the pyrrole derivatives required as precursors (compounds **6**) was carried out by an adaptation of a mechanochemical sequential three-component reaction related to the Hantzsch pyrrole synthesis.<sup>20</sup> Our protocol starts with the *in situ* generation of  $\alpha$ -iodoketones **2** from ketones **1**, *N*-iodosuccinimide, and toluenesulfonic acid under high-speed vibration milling conditions for 1 h (for compounds **1–o**, the  $\alpha$ -iodoketones had to be prepared in a separate step from the ketone and I<sub>2</sub> in the presence of CuO).<sup>20b,21</sup> Addition of active

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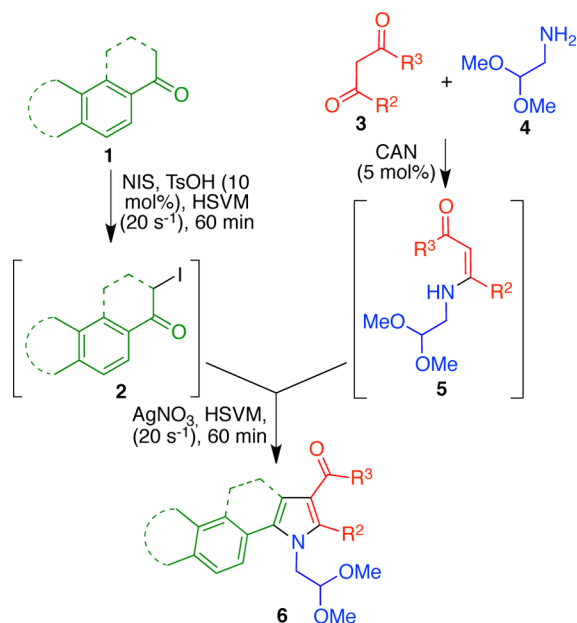
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### Scheme 1. Disconnection Scheme Planned in This Work, Compared with the Main Previous Method



methylene compounds **3**, 2,2-dimethoxyethylamine **4**, and 5% of Ce(IV) ammonium nitrate (CAN), premixed for 20 min to ensure the generation of the intermediate enaminone **5**, followed by silver nitrate and an additional 1 h mechanochemical reaction, afforded compounds **6** (Scheme 2). It is interesting to

### Scheme 2. Mechanochemical, Three-Component Synthesis of Pyrroles and Fused Pyrroles Bearing an *N*-(2,2-Dimethoxyethyl) Chain



note that the mildness of the reaction conditions and the absence of solvent prevented CAN-promoted side reactions at the acetal functional group, such as its hydrolysis.<sup>22</sup>

For the second step of our procedure, we needed to induce the cyclization of the acetal function onto the aromatic ring at the pyrrole C-5 position of compounds **6**. When carried out on benzylamine-derived substrates, this transformation is known as the classical Pomeranz–Fritsch isoquinoline synthesis,<sup>23</sup> which is normally performed under very harsh acidic conditions and often requires an extra step for aromatization. Owing to the potential low stability of pyrrole derivatives under such conditions, we sought to perform our transformation in the presence of Lewis acids. Thus, the preparation of model compound **7a** from the corresponding pyrrole **6a** was assayed in the presence of a large excess of aluminum trichloride in dichloroethane,<sup>24</sup> with modest yields (Table 1, entries 1 and 2).

Table 1. Optimization of the Synthesis of **7a**

entry	catalyst (%)	conditions	yield (%)
1	AlCl <sub>3</sub> (400)	DCE, rt, 8 h (Ar)	30
2	AlCl <sub>3</sub> (400)	DCE, rt, 24 h (Ar)	50
3	BF <sub>3</sub> ·Et <sub>2</sub> O (500)	dioxane, rt, 4 h (Ar)	0
4	BF <sub>3</sub> ·Et <sub>2</sub> O (500)	dioxane, 120 °C, 0.5 h (Ar)	69
5	TfOTMS (150)	DCM, rt, 5 min (Ar)	90
6	TfOTMS (100)	DCM, rt, 5 min (air)	89
7	TfOTMS (50)	DCM, rt, 5 min (air)	88
8	TfOTMS (15)	DCM, rt, 5 min (air)	89

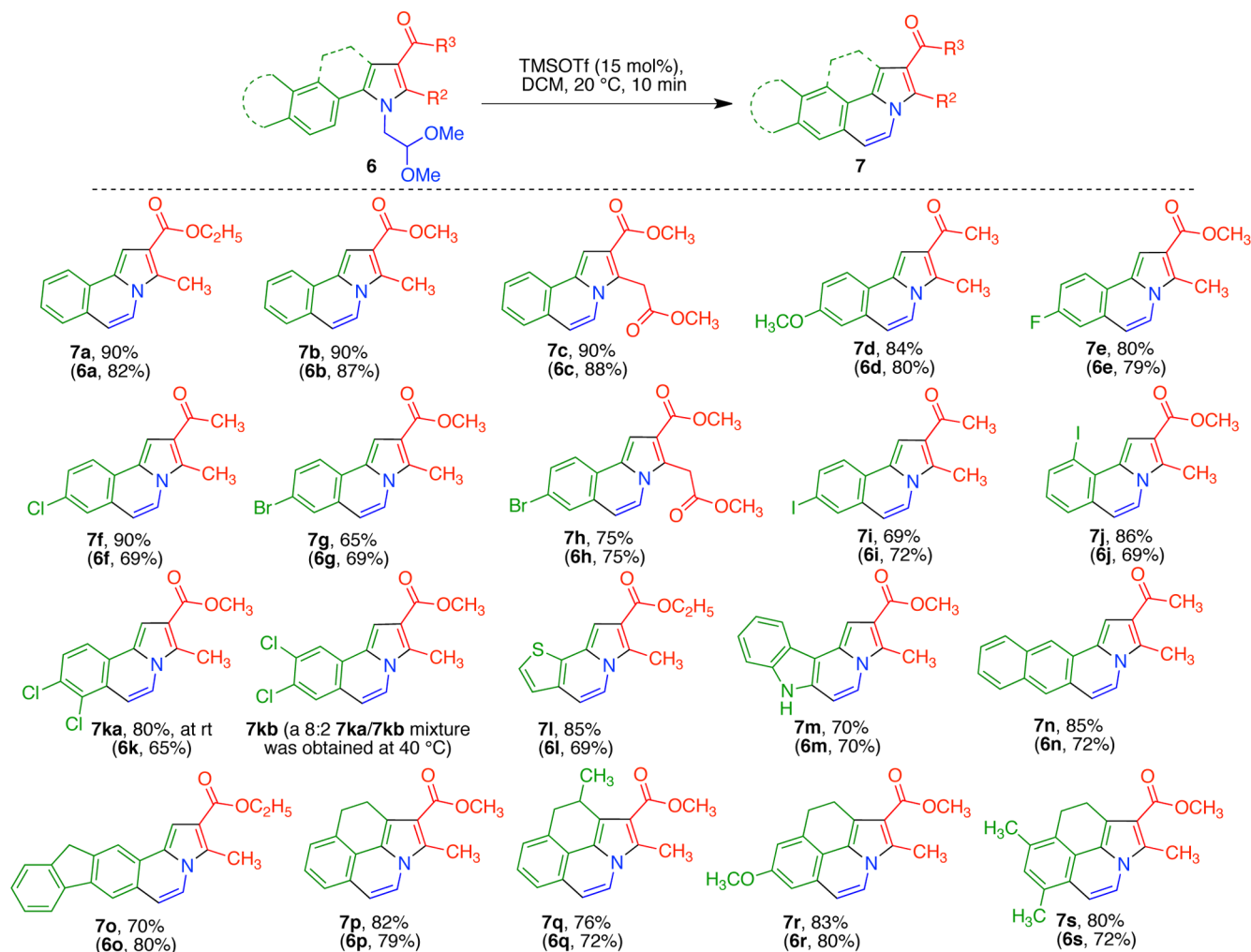
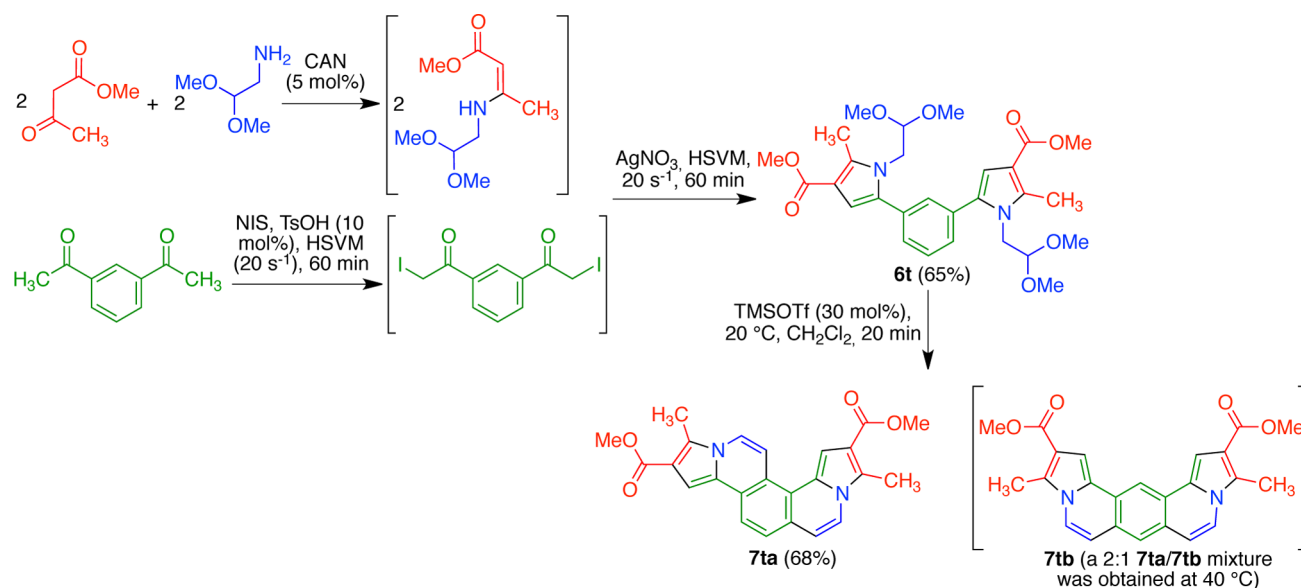
Using boron trifluoride etherate in 1,4-dioxane as the Lewis acid promoter,<sup>25</sup> the reaction failed at room temperature (entry 3) but afforded **7a** in 69% yield at 120 °C. In an effort to improve this result, we resorted to trimethylsilyl triflate, which is well-known to activate acetals via the formation of oxonium species<sup>26</sup> but which has received very little attention for cyclization reactions leading to heterocyclic systems, and not always acts as a catalyst in the few examples known.<sup>27</sup> In our initial experiment, **6a** was transformed into **7a** in an excellent 90% yield in the presence of TfOTMS (1.5 equiv) in dry dichloromethane under an argon atmosphere. The reaction was very fast and was complete in only 5 min at room temperature (entry 5). Subsequent experiments proved that the reaction could be carried out open to the air (entry 6) and in the presence of catalytic amounts of trimethylsilyl triflate (entry 7) without loss in yield. The optimal conditions involved the use of 15% of the catalyst (entry 8).

With these optimized conditions in hand, we studied the scope of the reaction, bringing different substitutions in most of the positions of the starting pyrrole in order to increase the structural complexity in the final products. As shown in Scheme 3, we studied the influence of the nature of the substituents on the C-5 aromatic ring on the electrophilic aromatic substitution step, finding that the reaction allowed a wide range of substitutions and worked well with unsubstituted phenyl derivatives (**7a–c**) and also when electron-releasing groups were present on the C-5 substituent (**7d**). Interestingly, the presence of electron-withdrawing groups did not hamper the reaction, allowing the preparation of fluoro- (**7e**), chloro- (**7f**), bromo- (**7g, 7h**), and iodo- (**7i, 7j**) derivatives. These substituents are potential synthetic handles for the additional functionalization of these compounds using cross-coupling chemistry. Interestingly, the presence of two Cl substituents in the starting material was also well tolerated in terms of reactivity. Under the usual conditions, this reaction afforded exclusively the 7,8-dichloro derivative **7ka**, while a higher temperature (40 °C) led to a 8:2 **7ka/7kb** mixture.

By replacing the 5-phenyl by other aromatic substituents, namely, 2-thienyl, 3-indolyl, 2-naphthyl, and 2-fluorenyl, four different heterocyclic frameworks, represented by compounds **7l, 7m, 7n**, and **7o**, respectively, were obtained. These skeletons are very scarcely (**7l, 7m**) or not at all (**7n, 7o**) represented in the literature. The use of 1-tetralone derivatives as the ketone component allowed the synthesis of compounds **7p–7s**, derived from the hitherto unknown benzo[*de*]pyrrolo[3,2,1-*ij*]quinoline framework.

In order to expand the scope of the method, we also examined double TMSOTf-promoted cyclizations. The required starting material **6t** was prepared via a multicomponent reaction starting from 1,3-diacetylbenzene, 2 equiv of aminoaceta-

Scheme 3. Scope of the Cyclization of Compounds 6 in the Presence of TMSOTf

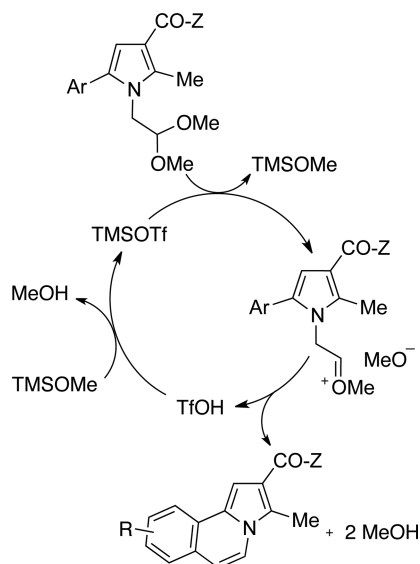
Scheme 4. Synthesis of the Pentacyclic Compound 7t by One-Pot Construction of Two Pyrrolo[2,1-*a*]isoquinoline Systems

aldehyde dimethyl acetal, and 2 equiv of methyl acetoacetate. The cyclization proceeded uneventfully and yielded the angular pentacyclic compound 7ta when the reaction was performed at

20 °C, and a 2:1 mixture of 7ta and its linear regioisomer 7tb at 40 °C (Scheme 4). Again, 7ta,b represent previously unknown frameworks.

The cyclization reaction is assumed to proceed by the mechanism summarized in Scheme 5.

**Scheme 5. Proposed Mechanism for TMSOTf-Promoted Cyclizations**



## CONCLUSION

We report a general, two-step preparation of pyrrolo[2,1-*a*]isoquinolines and representatives of six related complex polyheterocyclic frameworks from simple, commercially available starting materials under very mild conditions. This protocol generates four new bonds and two rings, the second of which arises from a new Pomeranz–Fritsch-type reaction catalyzed by trimethylsilyl triflate. The combination of a multicomponent reaction with a final cyclization step can be viewed as an application of the strategy involving the sequential use of multicomponent reactions and subsequent cyclization steps that has been variously described as MCR and subsequent “secondary reactions”,<sup>28</sup> MCR followed by postcondensation modifications<sup>29</sup> or as the build-couple-pair strategy,<sup>30</sup> and has been widely employed for the fast generation of molecular diversity and complexity.<sup>31</sup>

## EXPERIMENTAL SECTION

**General Experimental Details.** All reagents and solvents were of commercial quality and were used as received. Mechanochemical reactions were carried out in a vibratory mixer mill at a frequency of 20 Hz using a 25 mL zirconium oxide grinding jar and a single zirconium oxide ball 20 mm in diameter. Reactions were monitored by thin layer chromatography on aluminum plates coated with silica gel and fluorescent indicator. Separations by flash chromatography were performed on silica gel (40–63  $\mu\text{m}$  particle size). Melting points were determined either using an immersion apparatus and are uncorrected. Infrared spectra were recorded with an FTIR spectrophotometer working by attenuated total reflection (ATR), with a diamond accessory for solid and liquid samples. NMR spectroscopic data were recorded using a spectrometer operating at 250 MHz for  $^1\text{H}$  NMR and 63 MHz for  $^{13}\text{C}$  NMR; chemical shifts are given in ppm and coupling constants in hertz. High-resolution mass spectra (HRMS) were recorded on a TOF mass spectrometer fitted with an electrospray detector (ESI). Elemental analyses were determined using a microanalyzer based on the flash combustion technique.

**General Procedure for the Synthesis of Pyrrole Derivatives 6 under Solvent-Free High-Speed Vibration Milling (HSVM) Conditions.** The suitable ketone (0.5 mmol), *N*-iodosuccinimide

(NIS, 0.5 mmol), and *p*-toluenesulfonic acid (PTSA, 10 mol %) were added to a ball mill vessel, along with a zirconium oxide ball. The vessel was fitted to one of the horizontal vibratory arms of the ball mill, while the other arm was occupied with an empty vessel. The ball mill was set to vibrate at a frequency of 20  $\text{s}^{-1}$  for 60 min. Then, a mixture of aminoacetaldehyde dimethyl acetal (1.0 mmol), the suitable  $\beta$ -dicarbonyl compound (0.75 mmol) and cerium(IV) ammonium nitrate (CAN, 5 mol %), previously stirred at room temperature during 30 min, and silver nitrate (0.5 mmol) were added to the vessel. The reaction was subjected to the vibratory movement at the same frequency for 60 min. Then, the reaction vessel was cleansed with ethyl acetate and the suspension was filtered to remove the silver iodide precipitate. The organic layer was washed with water (2 mL) and dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel eluting with a gradient from petroleum ether to 8:2 petroleum ether–ethyl acetate afforded the desired pyrrole derivatives. Compounds **6l**–**6o** were prepared from isolated  $\alpha$ -iodoketones, obtained by treatment of the corresponding ketones with iodine in the presence of  $\text{CuO}$ .<sup>20b,21</sup>

**Ethyl 1-(2,2-Dimethoxyethyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylate (6a).** Prepared from acetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and ethyl acetoacetate (0.75 mmol); yield: 130 mg (82%); dark orange oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.59–7.35 (m, 5H), 6.59 (s, 1H), 4.31 (q,  $J$  = 7.1 Hz, 2H), 4.15 (t,  $J$  = 4.8 Hz, 1H), 4.07 (d,  $J$  = 4.8 Hz, 2H), 3.16 (s, 6H), 2.67 (s, 3H), 1.37 (t,  $J$  = 7.1 Hz, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.5, 137.7, 133.5, 132.9, 129.5, 128.4, 127.6, 112.0, 110.0, 104.1, 59.3, 55.1, 46.4, 14.4, 11.8; IR (neat)  $\nu$ : 3013, 2982, 2835 (C-H), 1687 (C=O), 1242, 1196 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{18}\text{H}_{23}\text{NO}_4$ : C, 68.12; H, 7.30; N, 4.41; found: C, 68.09; H, 7.25; N, 4.35.

**Methyl 1-(2,2-Dimethoxyethyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylate (6b).** Prepared from acetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and methyl acetoacetate (0.75 mmol); yield: 132 mg (87%); yellowish oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43–7.30 (m, 5H), 6.57 (s, 1H), 4.17–4.13 (m, 1H), 4.06 (d,  $J$  = 5.2 Hz, 2H), 3.82 (s, 3H), 3.15 (s, 6H), 2.67 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.8, 137.7, 133.6, 132.7, 129.4, 128.4, 127.5, 111.6, 109.9, 104.0, 55.0, 50.5, 46.4, 11.7; IR (neat)  $\nu$ : 2947 and 2835 (C-H), 1696 (C=O), 1244 and 1183 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{17}\text{H}_{21}\text{NO}_4$ : C, 67.31; H, 6.98; N, 4.62; found: C, 67.01; H, 6.75; N, 4.63.

**Methyl 1-(2,2-Dimethoxyethyl)-2-(2-methoxy-2-oxoethyl)-5-phenyl-1H-pyrrole-3-carboxylate (6c).** Prepared from acetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and dimethyl-1,3-acetonedicarboxylate (0.75 mmol); yield: 159 mg (88%); yellowish solid; mp: 78–80  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.48–7.37 (m, 5H), 6.61 (s, 1H), 4.31 (s, 2H), 4.10 (m, 3H), 3.83 (s, 3H), 3.76 (s, 3H), 3.15 (s, 6H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  170.7, 165.5, 134.6, 133.3, 132.6, 129.8, 128.6, 127.9, 113.4, 110.2, 104.3, 55.3, 52.2, 50.9, 47.0, 31.3; IR (neat)  $\nu$ : 2942, 2923, 2848 (C-H), 1749, 1696 (C=O), 1248, 1223, 1195, 1164 (C-O)  $\text{cm}^{-1}$ ; ESI-MS: ( $m/z$ ) 320.1 ( $\text{M}^+$  + Na); elemental analysis (%) calcd. for  $\text{C}_{19}\text{H}_{23}\text{NO}_6$ : C, 63.15; H, 6.42; N, 3.88; found: C, 63.41; H, 6.77; N, 3.63.

**1-(1-(2,2-Dimethoxyethyl)-5-(4-methoxyphenyl)-2-methyl-1H-pyrrol-3-yl)ethan-1-one (6d).** Prepared from 4'-methoxyacetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and acetylacetone (0.75 mmol); yield: 126 mg (80%); orange oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35–7.30 (m, 2H), 7.00–6.92 (m, 2H), 6.44 (s, 1H), 4.19 (t,  $J$  = 5.1 Hz, 1H), 4.01 (d,  $J$  = 5.1 Hz, 2H), 3.85 (s, 3H), 3.17 (s, 6H), 2.65 (s, 3H), 2.42 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  194.9, 159.1, 136.6, 133.1, 130.9, 124.9, 120.6, 113.8, 110.1, 103.8, 55.1, 54.9, 46.0, 28.4, 12.2; IR (neat)  $\nu$ : 3006, 2937, 2836 (C-H), 1648 (C=O), 1287, 1246 (C-O)  $\text{cm}^{-1}$ ; ESI-MS: ( $m/z$ ) 318.2 ( $\text{M}^+$  + H); elemental analysis (%) calcd. for  $\text{C}_{18}\text{H}_{23}\text{NO}_4$ : C, 68.12; H, 7.30; N, 4.41; found: C, 68.07; H, 7.27; N, 4.43.

**1-(1-(2,2-Dimethoxyethyl)-5-(4-fluorophenyl)-2-methyl-1H-pyrrol-3-yl)ethan-1-one (6e).** Prepared from 4'-fluoroacetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and

acetylacetone (0.75 mmol); yield: 127 mg (79%); orange solid; mp: 106–108 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46–7.33 (m, 2H), 7.23–7.05 (m, 2H), 6.53 (s, 1H), 4.17 (t,  $J = 5.3$  Hz, 1H), 4.02 (d,  $J = 5.3$  Hz, 2H), 3.82 (s, 3H), 3.18 (s, 6H), 2.65 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.8, 164.2–160.3 (d,  $J = 248.2$  Hz), 137.6, 132.6, 131.4–131.3 (d,  $J = 8.12$  Hz), 128.9–128.8 (d,  $J = 3.1$  Hz), 115.6–115.2 (d,  $J = 21.4$  Hz), 111.7, 110.1, 104.0, 55.2, 50.7, 46.4, 11.7; IR (neat)  $\nu$ : 2973, 2945, 2840 (C-H), 1691 (C=O), 1242, 1192 (C-O), 1129 (C-F)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{17}\text{H}_{20}\text{FNO}_4$ : C, 63.54; H, 6.27; N, 4.36; found: C, 63.32; H, 6.19; N, 4.29.

**1-(5-(4-Chlorophenyl)-1-(2,2-dimethoxyethyl)-2-methyl-1H-pyrrol-3-yl)ethan-1-one (6f)**. Prepared from 4'-chloroacetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and acetylacetone (0.75 mmol); yield: 111 mg (69%); yellowish oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44–7.33 (m, 4H), 6.50 (s, 1H), 4.23 (t,  $J = 5.3$  Hz, 1H), 4.03 (d,  $J = 5.3$  Hz, 2H), 3.19 (s, 6H), 2.67 (s, 3H), 2.43 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  194.9, 137.2, 133.6, 132.3, 131.2, 130.8, 128.7, 121.0, 110.9, 103.7, 55.1, 46.2, 28.5, 12.3; IR (neat)  $\nu$ : 2994, 2933, 2834 (C-H), 1653 (C=O), 1245 (C-O), 1012 (C-Cl)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{17}\text{H}_{20}\text{ClNO}_3$ : C, 63.45; H, 6.26; N, 4.35; found: C, 63.35; H, 6.20; N, 4.29.

**Methyl 5-(4-Bromophenyl)-1-(2,2-dimethoxyethyl)-2-methyl-1H-pyrrole-3-carboxylate (6g)**. Prepared from 4'-bromoacetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and methyl acetoacetate (0.75 mmol); yield: 131 mg (69%); white solid; mp: 91–93 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.61–7.53 (m, 2H), 7.33–7.26 (m, 2H), 6.56 (s, 1H), 4.19 (t,  $J = 5.3$  Hz, 1H), 4.04 (d,  $J = 5.3$  Hz, 2H), 3.83 (s, 3H), 3.20 (s, 6H), 2.66 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.7, 138.1, 132.5, 131.8, 131.7, 131.0, 121.8, 110.4, 103.9, 55.2, 50.8, 46.6, 11.8; IR (neat)  $\nu$ : 2999, 2948, 2839 (C-H), 1691 (C=O), 1242, 1212 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{17}\text{H}_{20}\text{BrNO}_4$ : C, 53.42; H, 5.27; N, 3.66; found: C, 53.35; H, 5.22; N, 3.56.

**Methyl 5-(4-Bromophenyl)-1-(2,2-dimethoxyethyl)-2-(2-methoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate (6h)**. Prepared from 4'-bromoacetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and dimethyl-1,3-acetonededicarboxylate (0.75 mmol); yield: 165 mg (75%); yellowish solid; mp: 59–61 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57–7.54 (m, 2H), 7.29–7.26 (m, 2H), 6.58 (s, 1H), 4.27 (s, 2H), 4.15 (t,  $J = 5.1$  Hz, 1H), 4.04 (d,  $J = 5.1$  Hz, 2H), 3.80 (s, 3H), 3.73 (s, 3H), 3.17 (s, 6H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  170.5, 165.1, 133.4, 133.3, 131.6, 131.4, 131.1, 122.0, 113.5, 110.5, 103.9, 55.1, 52.0, 50.8, 46.9, 31.1; IR (neat)  $\nu$ : 2982, 2953, 2906 (C-H), 1756, 1703 (C=O), 1245, 1226, 1182, 1149 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{19}\text{H}_{22}\text{BrNO}_6$ : C, 51.83; H, 5.04; N, 3.18; found: C, 51.79; H, 4.99; N, 3.18.

**1-(1-(2,2-Dimethoxyethyl)-5-(4-iodophenyl)-2-methyl-1H-pyrrol-3-yl)ethan-1-one (6i)**. Prepared from 4'-iodoacetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and acetylacetone (0.75 mmol); yield: 149 mg (72%); orange solid; mp: 121–123 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.81–7.70 (m, 2H), 7.23–7.11 (m, 2H), 6.50 (s, 1H), 4.23 (t,  $J = 5.3$  Hz, 1H), 4.04 (d,  $J = 5.3$  Hz, 2H), 3.20 (s, 6H), 2.66 (s, 3H), 2.43 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  194.9, 137.6, 137.3, 132.4, 132.2, 131.2, 121.0, 110.9, 103.7, 93.3, 55.1, 46.2, 28.5, 12.3; IR (neat)  $\nu$ : 2989, 2931, 2835 (C-H), 1649 (C=O), 1248, 1207 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{17}\text{H}_{20}\text{INO}_3$ : C, 49.41; H, 4.88; N, 3.39; found: C, 49.39; H, 4.80; N, 3.37.

**Methyl 1-(2,2-Dimethoxyethyl)-5-(2-iodophenyl)-2-methyl-1H-pyrrole-3-carboxylate (6j)**. Prepared from 2-iodoacetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and methyl acetoacetate (0.75 mmol); yield: 148 mg (69%); yellowish oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (dd,  $J = 8.0, 1.1$  Hz, 1H), 7.46–7.32 (m, 2H), 7.10 (m, 1H), 6.51 (s, 1H), 4.13 (t,  $J = 5.3$  Hz, 1H), 3.95–3.71 (m, 5H), 3.16 (s, 6H), 2.66 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.9, 139.1, 137.9, 137.2, 134.4, 132.4, 129.9, 127.9, 111.3, 110.4, 104.2, 102.7, 55.1, 50.6, 46.7, 11.6; IR (neat)  $\nu$ : 2992, 2947, 2835 (C-H), 1697 (C=O), 1235, 1197 (C-O), 1067 (C-I)  $\text{cm}^{-1}$ ; elemental

analysis (%) calcd. for  $\text{C}_{17}\text{H}_{20}\text{INO}_4$ : C, 47.57; H, 4.70; N, 3.26; found: C, 47.49; H, 4.65; N, 3.18.

**Methyl 5-(3,4-Dichlorophenyl)-1-(2,2-dimethoxyethyl)-2-methyl-1H-pyrrole-3-carboxylate (6k)**. Prepared from 3',4'-dichloroacetophenone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and methyl acetoacetate (0.75 mmol); yield: 120 mg (65%); yellowish oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.55 (d,  $J = 2.1$  Hz, 1H), 7.50 (d,  $J = 8.3$  Hz, 1H), 7.27 (dd,  $J = 8.3, 2.1$  Hz, 1H), 6.58 (s, 1H), 4.25 (t,  $J = 5.3$  Hz, 1H), 4.04 (d,  $J = 5.3$  Hz, 2H), 3.83 (s, 3H), 3.22 (s, 6H), 2.66 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.6, 138.3, 132.8, 132.5, 131.7, 131.4, 131.1, 130.4, 128.6, 112.2, 111.0, 103.8, 55.2, 50.8, 46.7, 11.8; IR (neat)  $\nu$ : 2993, 2848, 2836 (C-H), 1699 (C=O), 1241, 1196 (C-O)  $\text{cm}^{-1}$ ; ESI-MS: ( $m/z$ ) 394.1 ( $\text{M}^+ + \text{Na}$ ); elemental analysis (%) calcd. for  $\text{C}_{17}\text{H}_{19}\text{Cl}_2\text{NO}_4$ : C, 54.85; H, 5.15; N, 3.76; found: C, 54.73; H, 5.10; N, 3.75.

**Ethyl 1-(2,2-Dimethoxyethyl)-2-methyl-5-(thiophen-2-yl)-1H-pyrrole-3-carboxylate (6l)**. Prepared from 2-acetylthiophene (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and ethyl acetoacetate (0.75 mmol); yield: 111 mg (69%); yellowish oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36–7.34 (m, 1H), 7.14–7.08 (m, 2H), 6.72 (s, 1H), 4.38–4.25 (m, 3H), 4.12 (d,  $J = 5.4$  Hz, 2H), 3.27 (s, 6H), 2.66 (s, 3H), 1.37 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.3, 138.4, 133.7, 127.3, 127.1, 125.8, 125.5, 112.2, 111.9, 104.2, 59.4, 55.4, 46.8, 14.4, 11.8; IR (neat)  $\nu$ : 2934, 2834 (C-H), 1694 (C=O), 1287, 1246 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{16}\text{H}_{21}\text{NO}_4\text{S}$ : C, 59.42; H, 6.55; N, 4.33; found: C, 59.38; H, 6.49; N, 4.35.

**Methyl 1-(2,2-Dimethoxyethyl)-5-(1H-indol-3-yl)-2-methyl-1H-pyrrole-3-carboxylate (6m)**. Prepared from 3-acetylindole (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and methyl acetoacetate (0.75 mmol); yield: 120 mg (70%); dark yellow oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  8.59 (br s, 1H), 7.62 (d,  $J = 7.7$  Hz, 1H), 7.45 (d,  $J = 8.1$  Hz, 2H), 7.37 (d,  $J = 2.4$  Hz, 1H), 7.32–7.14 (m, 2H), 6.71 (s, 1H), 4.27 (t,  $J = 5.3$  Hz, 1H), 4.07 (d,  $J = 5.3$  Hz, 2H), 3.88 (s, 3H), 3.17 (s, 6H), 2.72 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.3, 137.3, 135.7, 127.6, 126.2, 124.1, 122.5, 120.2, 119.5, 111.6, 111.2, 110.6, 108.1, 104.3, 55.2, 50.7, 46.8, 11.9; IR (neat)  $\nu$ : 3323 (N-H), 2911, 2854 (C-H), 1680 (C=O), 1225, 1135 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_4$ : C, 66.65; H, 6.48; N, 8.18; found: C, 66.57; H, 6.39; N, 8.15.

**1-(1-(2,2-Dimethoxyethyl)-2-methyl-5-(naphthalen-2-yl)-1H-pyrrol-3-yl)ethan-1-one (6n)**. Prepared from 2-acetylnaphthalene (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and acetylacetone (0.75 mmol); yield: 121 mg (72%); white solid; mp: 97–99 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04–7.88 (m, 4H), 7.66–7.48 (m, 3H), 6.63 (s, 1H), 4.30–4.21 (m, 1H), 4.16 (m, 2H), 3.16 (s, 6H), 2.73 (s, 3H), 2.48 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  195.0, 137.3, 133.4, 133.2, 132.4, 130.1, 128.4, 128.1, 127.9, 127.6, 127.3, 126.4, 126.2, 121.0, 111.0, 103.8, 55.0, 46.3, 28.6, 12.3; IR (neat)  $\nu$ : 2999, 2836, 2836 (C-H), 1648 (C=O), 1200 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{21}\text{H}_{23}\text{NO}_3$ : C, 74.75; H, 6.87; N, 4.15; found: C, 74.71; H, 6.80; N, 4.10.

**Ethyl 1-(2,2-Dimethoxyethyl)-5-(9H-fluoren-2-yl)-2-methyl-1H-pyrrole-3-carboxylate (6o)**. Prepared from 2-acetylfluorene (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and ethyl acetoacetate (0.75 mmol); yield: 162 mg (80%); yellowish solid; mp: 89–91 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.84 (m, 3.3 Hz, 2H), 7.60 (m, 2H), 7.48–7.32 (m, 3H), 6.66 (s, 1H), 4.34 (q,  $J = 7.1$  Hz, 2H), 4.25–4.17 (m, 1H), 4.14 (m, 2H), 3.97 (s, 2H), 3.17 (s, 6H), 2.71 (s, 3H), 1.40 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.5, 143.4, 143.2, 141.1, 141.0, 137.7, 133.9, 131.2, 128.2, 126.9, 126.8, 126.0, 125.0, 119.9, 119.8, 112.0, 110.1, 104.1, 59.2, 55.1, 46.5, 36.8, 14.4, 11.8; IR (neat)  $\nu$ : 2962, 2918, 2838 (C-H), 1682 (C=O), 1246, 1194 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{25}\text{H}_{27}\text{NO}_4$ : C, 74.05; H, 6.71; N, 3.45; found: C, 73.98; H, 6.65; N, 3.38.

**Methyl 1-(2,2-Dimethoxyethyl)-2-methyl-4,5-dihydro-1H-benzog[j]indole-3-carboxylate (6p)**. Prepared from  $\alpha$ -tetralone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and methyl acetoacetate (0.75 mmol); yield: 130 mg (79%); orange solid; mp: 60–62 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57 (d,  $J = 7.6$  Hz, 1H), 7.27

(dd,  $J = 10.6, 4.7$  Hz, 2H), 7.13 (dd,  $J = 11.6, 4.2$  Hz, 1H), 4.61 (t,  $J = 5.2$  Hz, 1H), 4.36 (d,  $J = 5.2$  Hz, 2H), 3.86 (s, 3H), 3.36 (s, 6H), 3.02–2.90 (m, 2H), 2.90–2.79 (m, 2H), 2.68 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.5, 139.1, 136.7, 129.3, 128.5, 128.1, 126.6, 125.1, 123.9, 120.3, 109.8, 104.3, 55.4, 50.5, 48.1, 30.8, 21.6, 12.1; IR (neat)  $\nu$ : 2935, 2899, 2834 (C-H), 1696 (C=O), 1255, 1225, 1194 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{19}\text{H}_{23}\text{NO}_4$ : C, 69.28; H, 7.04; N, 4.25; found: C, 69.22; H, 6.98; N, 4.23.

**Methyl 1-(2,2-Dimethoxyethyl)-2,4-dimethyl-4,5-dihydro-1H-benzog[indole]-3-carboxylate (6q).** Prepared from 4-methyl-1-tetralone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and methyl acetoacetate (0.75 mmol); yield: 123 mg (72%); green oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57 (d,  $J = 7.7$  Hz, 1H), 7.22 (m, 3H), 4.58 (t,  $J = 5.1$  Hz, 1H), 4.37 (d,  $J = 5.1$  Hz, 2H), 3.85 (s, 3H), 3.35 (s, 3H), 3.33 (s, 3H), 3.10–2.80 (m, 3H), 2.67 (s, 3H), 1.26 (d,  $J = 7.5$  Hz, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.5, 141.3, 139.2, 128.4, 127.3, 127.1, 126.3, 125.3, 122.3, 120.5, 110.3, 104.3, 55.5, 55.4, 50.5, 48.0, 34.3, 29.1, 19.8, 12.1; IR (neat)  $\nu$ : 2948, 2836 (C-H), 1691 (C=O), 1272, 1248, 1217 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{20}\text{H}_{25}\text{NO}_4$ : C, 69.95; H, 7.34; N, 4.08; found: C, 69.89; H, 7.28; N, 4.04.

**Methyl 1-(2,2-Dimethoxyethyl)-7-methoxy-2-methyl-4,5-dihydro-1H-benzog[indole]-3-carboxylate (6r).** Prepared from 7-methoxy-1-tetralone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and methyl acetoacetate (0.75 mmol); yield: 144 mg (80%); dark orange oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.51 (d,  $J = 8.6$  Hz, 1H), 6.96–6.73 (m, 2H), 4.59 (d,  $J = 5.1$  Hz, 1H), 4.32 (d,  $J = 5.1$  Hz, 2H), 3.84 (s, 6H), 3.36 (s, 6H), 2.99–2.90 (m, 2H), 2.83 (m, 2H), 2.66 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.5, 157.0, 138.9, 138.1, 128.0, 122.5, 121.9, 121.5, 114.8, 110.9, 109.6, 104.3, 55.4, 55.1, 50.5, 48.0, 31.3, 21.6, 12.0; IR (neat)  $\nu$ : 2940, 2905, 2834 (C-H), 1694 (C=O), 1245, 1239, 1189 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{20}\text{H}_{25}\text{NO}_5$ : C, 66.84; H, 7.01; N, 3.90; found: C, 66.76; H, 6.97; N, 3.89.

**Methyl 1-(2,2-Dimethoxyethyl)-2,6,8-trimethyl-4,5-dihydro-1H-benzog[indole]-3-carboxylate (6s).** Prepared from 5,7-dimethyl-1-tetralone (0.5 mmol), aminoacetaldehyde dimethyl acetal (1 mmol), and methyl acetoacetate (0.75 mmol); yield: 129 mg (72%); yellowish oil;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30 (s, 1H), 6.88 (s, 1H), 4.63 (t,  $J = 5.0$  Hz, 1H), 4.37 (d,  $J = 5.0$  Hz, 2H), 3.88 (s, 3H), 3.39 (s, 6H), 2.95 (m, 2H), 2.81–2.78 (m, 2H), 2.70 (s, 3H), 2.37 (d,  $J = 2.5$  Hz, 6H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.4, 139.0, 135.3, 134.8, 131.7, 129.0, 128.3, 128.0, 123.5, 119.2, 109.4, 104.4, 55.2, 50.4, 48.0, 25.5, 21.4, 21.2, 20.3, 12.00; IR (neat)  $\nu$ : 2947, 2832 (C-H), 1695 (C=O), 1261, 1226, 1194 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{21}\text{H}_{27}\text{NO}_4$ : C, 70.56; H, 7.61; N, 3.92; found: C, 70.51; H, 7.55; N, 3.92.

**Dimethyl 5,5'-(1,3-Phenylene)bis(1-(2,2-dimethoxyethyl)-2-methyl-1H-pyrrole-3-carboxylate) (6t).** Prepared from 1,3-diacetylbenzene (0.5 mmol), aminoacetaldehyde dimethyl acetal (2 mmol), and methyl acetoacetate (1.5 mmol); yield: 171 mg (65%); yellowish solid; mp = 122–124 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49–7.39 (m, 2H), 6.60 (s, 1H), 4.20 (d,  $J = 5.0$  Hz, 1H), 4.11 (d,  $J = 5.0$  Hz, 2H), 3.84 (s, 3H), 3.18 (s, 6H), 2.68 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.8, 138.0, 133.2, 130.6, 128.7, 128.5, 111.9, 110.3, 104.1, 55.1, 50.7, 46.6, 11.8; IR (neat)  $\nu$ : 2920, 2843 (C-H), 1695 (C=O), 1246, 1213 (C-O)  $\text{cm}^{-1}$ ; HRMS calcd. for  $\text{C}_{28}\text{H}_{36}\text{N}_2\text{O}_8$  ( $\text{M}^+ + \text{Na}$ ): 551.2363, found: 551.2390; elemental analysis (%) calcd. for  $\text{C}_{28}\text{H}_{36}\text{N}_2\text{O}_8$ : C, 63.62; H, 6.86; N, 5.30; found: C, 63.56; H, 6.85; N, 5.25.

**General Procedures for the Synthesis of Pyrrolo[2,1-*a*]isoquinoline-Related Frameworks 7.** To a round-bottom flask was added the corresponding pyrrole derivative **6** (1.0 equiv), trimethylsilyl trifluoromethanesulfonate (0.15–0.3 equiv), and DCM as solvent (4 mL/mmol). The reaction was stirred at room temperature for 10–20 min and monitored for conversion by TLC. At the end of the reaction, the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with a gradient from petroleum ether to 8:2 petroleum ether–ethyl acetate.

**Ethyl 3-Methylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (7a).** Prepared from pyrrole **6a** (0.2 mmol); yield: 41.5 mg (82%); dark yellow solid; mp: 113–115 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  8.03 (d,  $J = 8$  Hz, 1H), 7.64–7.45 (m, 3H), 7.39 (dd,  $J = 7.5, 1.2$  Hz, 1H), 7.35 (m, 1H), 6.83 (d,  $J = 7.5$  Hz, 1H), 4.41 (q,  $J = 7.1$  Hz, 2H), 2.79 (s, 3H), 1.46 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.8, 128.4, 127.8, 127.7, 126.9, 126.4, 126.3, 126.0, 122.0, 120.9, 114.9, 112.7, 100.7, 59.9, 14.5, 10.4; IR (neat)  $\nu$ : 3053, 2980, 2938 (C-H), 1690 (C=O), 1296, 1227 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{16}\text{H}_{15}\text{NO}_2$ : C, 75.87; H, 5.97; N, 5.53; found: C, 75.80; H, 5.89; N, 5.50.

**Methyl 3-Methylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (7b).** Prepared from pyrrole **6b** (0.2 mmol); yield: 43 mg (90%); green solid; mp: 133–135 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (d,  $J = 7.8$  Hz, 1H), 7.60–7.44 (m, 3H), 7.39 (dd,  $J = 7.5, 1.3$  Hz, 1H), 7.35–7.29 (m, 1H), 6.81 (d,  $J = 7.6$  Hz, 1H), 3.94 (s, 3H), 2.78 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1, 128.5, 127.8, 127.8, 126.9, 126.4, 126.3, 126.0, 121.9, 120.8, 114.6, 112.8, 100.6, 51.1, 10.3; IR (neat)  $\nu$ : 2993, 2947 (C-H), 1697 (C=O), 1230 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{15}\text{H}_{13}\text{NO}_2$ : C, 75.30; H, 5.48; N, 5.85; found: C, 75.21; H, 5.47; N, 5.82.

**Methyl 3-(2-Methoxy-2-oxoethyl)pyrrolo[2,1-*a*]isoquinoline-2-carboxylate (7c).** Prepared from pyrrole **6c** (0.2 mmol); 53 mg (90%); yellowish solid; mp: 171–173 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (d,  $J = 7.9$  Hz, 1H), 7.66 (d,  $J = 7.5$  Hz, 1H), 7.61–7.46 (m, 2H), 7.43 (dd,  $J = 7.5, 1.2$  Hz, 1H), 7.38 (s, 1H), 6.88 (d,  $J = 7.5$  Hz, 1H), 4.47 (s, 2H), 3.94 (s, 3H), 3.73 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  170.0, 165.7, 129.5, 128.0, 127.0, 126.5, 126.4, 126.2, 123.3, 122.1, 121.0, 115.9, 113.4, 101.1, 52.4, 51.4, 30.4; IR (neat)  $\nu$ : 2994, 2949, 2843 (C-H), 1725, 1695 (C=O), 1240, 1197 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{17}\text{H}_{15}\text{NO}_4$ : C, 68.68; H, 5.09; N, 4.71; found: C, 68.59; H, 5.03; N, 4.63.

**1-(8-Methoxy-3-methylpyrrolo[2,1-*a*]isoquinolin-2-yl)ethan-1-one (7d).** Prepared from pyrrole **6d** (0.2 mmol); yield: 43 mg (84%); dark orange solid; mp: 126–128 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.93 (d,  $J = 8.8$  Hz, 1H), 7.60 (d,  $J = 7.6$  Hz, 1H), 7.16–7.09 (m, 2H), 7.00 (d,  $J = 2.6$  Hz, 1H), 6.78 (d,  $J = 7.6$  Hz, 1H), 3.92 (s, 3H), 2.78 (s, 3H), 2.61 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  196.5, 158.0, 128.6, 127.8, 126.3, 123.4, 122.8, 121.3, 120.3, 116.8, 113.0, 108.9, 99.1, 55.4, 29.1, 10.7; IR (neat)  $\nu$ : 2994, 2899, 2838 (C-H), 1656 (C=O), 1259, 1223 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{16}\text{H}_{15}\text{NO}_2$ : C, 75.87; H, 5.97; N, 5.53; found: C, 75.78; H, 5.91; N, 5.44.

**Methyl 8-Fluoro-3-methylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (7e).** Prepared from pyrrole **6e** (0.2 mmol); yield: 41 mg (80%); yellowish solid; mp: 82–84 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02–7.96 (m, 1H), 7.66 (d,  $J = 7.6$  Hz, 1H), 7.28–7.18 (m, 3H), 6.79 (d,  $J = 7.6$  Hz, 1H), 3.93 (s, 3H), 2.80 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1, 161.0 (d,  $J = 245.7$  Hz), 128.0 (d,  $J = 16.4$  Hz), 124.0 (d,  $J = 8.2$  Hz), 123.0, 122.1, 116.3, 115.9, 114.9, 112.3, 112.0, 111.9, 100.2, 51.2, 10.4;  $^{19}\text{F}$  NMR (235 MHz,  $\text{CDCl}_3$ )  $\delta$  –115.67, –115.72, –115.75, –115.78, –115.81; IR (neat)  $\nu$ : 2955, 2856 (C-H), 1709 (C=O), 1255 (C-O), 1140 (C-F)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{15}\text{H}_{12}\text{FNO}_2$ : C, 70.03; H, 4.70; N, 5.44; found: C, 69.91; H, 4.63; N, 5.39.

**1-(8-Chloro-3-methylpyrrolo[2,1-*a*]isoquinolin-2-yl)ethan-1-one (7f).** Prepared from pyrrole **6f** (0.2 mmol); yield: 46 mg (90%); yellowish solid; mp: 179–181 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.90 (d,  $J = 8.5$  Hz, 1H), 7.61 (d,  $J = 7.6$  Hz, 1H), 7.51 (d,  $J = 2.0$  Hz, 1H), 7.42 (dd,  $J = 8.5, 2.0$  Hz, 1H), 7.20 (s, 1H), 6.74 (d,  $J = 7.6$  Hz, 1H), 2.78 (s, 3H), 2.61 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  196.2, 131.5, 128.1, 127.6, 127.6, 127.2, 126.3, 124.8, 123.2, 123.1, 121.8, 112.1, 101.1, 29.1, 10.7; IR (neat)  $\nu$ : 3116, 3058, 3000 (C-H), 1653 (C=O), 1088 (C-Cl)  $\text{cm}^{-1}$ ; ESI-MS: ( $m/z$ ) 280.0 ( $\text{M}^+ + \text{Na}$ ); elemental analysis (%) calcd. for  $\text{C}_{15}\text{H}_{12}\text{ClNO}$ : C, 69.91; H, 4.69; N, 5.44; found: C, 69.88; H, 4.65; N, 5.38.

**Methyl 8-Bromo-3-methylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (7g).** Prepared from pyrrole **6g** (0.2 mmol); yield: 41 mg (65%); white solid; mp: 158–160 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.87 (d,  $J = 8.5$  Hz, 1H), 7.70 (d,  $J = 1.9$  Hz, 1H), 7.63 (d,  $J = 7.6$  Hz,

1H), 7.57 (dd,  $J = 8.5, 1.9$  Hz, 1H), 7.32 (s, 1H), 6.75 (d,  $J = 7.6$  Hz, 1H), 3.93 (s, 3H), 2.79 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.0, 130.9, 129.3, 128.2, 128.0, 127.9, 125.2, 123.6, 122.0, 119.4, 115.0, 111.6, 101.2, 51.3, 10.4; IR (neat)  $\nu$ : 2922, 2852 (C-H), 1705 (C=O), 1232 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{15}\text{H}_{12}\text{BrNO}_2$ : C, 56.63; H, 3.80; N, 4.40; found: C, 56.56; H, 3.71; N, 4.34.

**8-Bromo-3-(2-methoxy-2-oxoethyl)pyrrolo[2,1-*a*]isoquinoline-2-carboxylate (7h).** Prepared from pyrrole **6h** (0.2 mmol); yield: 56 mg (75%); white solid; mp: 199–201 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.90 (d,  $J = 8.5$  Hz, 1H), 7.73 (d,  $J = 1.8$  Hz, 1H), 7.69 (d,  $J = 7.6$  Hz, 1H), 7.60 (dd,  $J = 8.5, 1.8$  Hz, 1H), 7.38 (s, 1H), 6.80 (d,  $J = 7.6$  Hz, 1H), 4.47 (s, 2H), 3.94 (s, 3H), 3.74 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  169.9, 165.5, 131.0, 129.3, 128.9, 128.1, 125.0, 123.7, 123.7, 122.1, 119.9, 116.3, 112.2, 101.5, 52.5, 51.5, 30.4; IR (neat)  $\nu$ : 3060, 2952 (C-H), 1704 (C=O), 1229, 1198 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{17}\text{H}_{14}\text{BrNO}_4$ : C, 54.28; H, 3.75; N, 3.72; found: C, 54.15; H, 3.75; N, 3.71.

**1-(8-Iodo-3-methylpyrrolo[2,1-*a*]isoquinolin-2-yl)ethan-1-one (7i).** Prepared from pyrrole **6i** (0.2 mmol); yield: 48 mg (69%); yellowish solid; mp: 219–221 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.89 (s, 1H), 7.79–7.67 (m, 2H), 7.60 (d,  $J = 7.6$  Hz, 1H), 7.23 (s, 1H), 6.72 (d,  $J = 7.6$  Hz, 1H), 2.78 (s, 3H), 2.61 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  196.2, 136.4, 135.5, 128.2, 127.7, 127.4, 125.6, 123.4, 123.1, 121.6, 111.9, 101.4, 90.5, 29.1, 10.7; IR (neat)  $\nu$ : 3111, 3001 (C-H), 1656 (C=O), 1074 (C-I)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{15}\text{H}_{12}\text{INO}$ : C, 51.60; H, 3.46; N, 4.01; found: C, 51.55; H, 3.45; N, 4.00.

**Methyl 10-Iodo-3-methylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (7j).** Prepared from pyrrole **6j** (0.2 mmol); yield: 63 mg (86%); dark orange solid; mp: 155–157 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  8.67 (s, 1H), 8.11 (dd,  $J = 8, 1.3$  Hz, 1H), 7.52 (d,  $J = 7.5$  Hz, 1H), 7.45 (dd,  $J = 7.8, 1.3$  Hz, 1H), 6.95 (m, 1H), 6.67 (d,  $J = 7.5$  Hz, 1H), 3.94 (s, 3H), 2.74 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.0, 141.8, 128.9, 128.6, 128.1, 127.5, 127.3, 126.3, 121.2, 113.9, 113.1, 106.5, 89.6, 51.2, 10.5; IR (neat)  $\nu$ : 3079, 2946, 2910 (C-H), 1697 (C=O), 1231 (C-O), 1057 (C-I)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{15}\text{H}_{12}\text{INO}_2$ : C, 49.34; H, 3.31; N, 3.84; found: C, 49.32; H, 3.30; N, 3.81.

**Methyl 7,8-Dichloro-3-methylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (7ka).** Prepared from pyrrole **6k** (0.2 mmol); yield: 49 mg (80%); yellow solid; mp: 179–181 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.85 (d,  $J = 8.6$  Hz, 1H), 7.72 (d,  $J = 7.9$  Hz, 1H), 7.53 (d,  $J = 8.6$  Hz, 1H), 7.34 (s, 1H), 7.29 (m, 2H), 3.94 (s, 3H), 2.81 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  165.8, 130.2, 129.4, 129.1, 128.3, 127.3, 126.2, 125.7, 122.8, 121.3, 115.7, 108.8, 101.9, 51.3, 10.4; IR (neat)  $\nu$ : 2922, 2853 (C-H), 1695 (C=O), 1238 (C-O)  $\text{cm}^{-1}$ ; ESI-MS: ( $m/z$ ) 330.0 ( $\text{M}^+ + \text{Na}$ ); elemental analysis (%) calcd. for  $\text{C}_{15}\text{H}_{11}\text{Cl}_2\text{NO}_2$ : C, 58.47; H, 3.60; N, 4.55; found: C, 58.42; H, 3.54; N, 4.49.

When the reaction was carried out at 40 °C, a 8:2 mixture of **7ka** and a second regioisomer (**7kb**) was detected. Isomer **7kb** (methyl 8,9-dichloro-3-methylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate) could not be isolated in a pure state. Its NMR data, obtained from the mixture, are given below.

$^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 (s, 1H), 7.60–7.57 (m, 2H), 7.26 (s, 1H), 6.69 (d, 1H), 3.94 (s, 3H), 2.78 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.7, 131.7, 130.1, 129.6, 129.0, 128.7, 128.2, 128.0, 127.2, 126.6, 126.1, 125.9, 125.9, 125.6, 123.4, 122.1, 121.2, 115.3, 111.0, 109.8, 108.7, 101.9, 101.9, 51.3, 51.3, 10.4.

**Ethyl 7-Methylthieno[3,2-*g*]indolizine-8-carboxylate (7l).** Prepared from pyrrole **6l** (0.2 mmol); yield: 65 mg (85%); green solid; mp: 93–95 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 (d,  $J = 8$  Hz, 1H), 7.68–7.46 (m, 3H), 7.41 (dd,  $J = 7.5, 1.2$  Hz, 1H), 7.36 (s, 1H), 6.86 (d,  $J = 7.5$  Hz, 1H), 4.41 (q,  $J = 7.1$  Hz, 2H), 2.82 (s, 3H), 1.46 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.7, 130.5, 130.2, 126.5, 126.3, 124.3, 123.1, 119.6, 115.6, 108.2, 98.1, 59.9, 14.4, 10.6; IR (neat)  $\nu$ : 3112, 2971, 2910, 2858 (C-H), 1691 (C=O), 1228, 1204 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{14}\text{H}_{13}\text{NO}_2\text{S}$ : C, 64.84; H, 5.05; N, 5.40; S, 12.36; found: C, 64.80; H, 5.03; N, 5.39; S, 12.30.

**Methyl 3-Methyl-7H-indolizino[7,8-*b*]indole-2-carboxylate (7m).**

Prepared from pyrrole **6m** (0.2 mmol); yield: 39 mg (70%); green solid; mp: 237–239 °C;  $^1\text{H}$  NMR (250 MHz, acetone- $d_6$ )  $\delta$  10.70 (br s, 1H), 8.12 (dd,  $J = 7.9, 1.1$  Hz, 1H), 8.01 (d,  $J = 7.6$  Hz, 2H), 7.64–7.55 (m, 1H), 7.33–7.13 (m, 2H), 7.07 (s, 1H), 3.87 (s, 3H), 2.82 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz, acetone- $d_6$ )  $\delta$  166.9, 139.2, 132.4, 128.7, 125.8, 124.7, 123.3, 123.0, 121.3, 121.1, 116.2, 112.5, 109.2, 103.1, 96.4, 51.4, 10.9; IR (neat)  $\nu$ : 2962, 2916, 2839 (C-H), 1682 (C=O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_2$ : C, 73.37; H, 5.07; N, 10.07; found: C, 73.33; H, 5.06; N, 9.99.

**1-(3-Methylbenzo[*g*]pyrrolo[2,1-*a*]isoquinolin-2-yl)ethan-1-one (7n).** Prepared from pyrrole **6n** (0.2 mmol); yield: 46 mg (85%); yellowish solid; mp: 217–219 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  8.40 (d,  $J = 8.3$  Hz, 1H), 8.08 (d,  $J = 8.8$  Hz, 1H), 7.94–7.89 (m, 2H), 7.81 (d,  $J = 7.8$  Hz, 1H), 7.71–7.53 (m, 3H), 7.32 (s, 1H), 2.84 (s, 3H), 2.67 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  196.6, 131.9, 129.5, 129.2, 128.8, 128.7, 127.1, 126.1, 125.8, 124.4, 123.5, 122.4, 121.5, 120.9, 120.7, 108.3, 100.5, 29.2, 10.7; IR (neat)  $\nu$ : 2996, 2919, 2852 (C-H), 1654 (C=O), 1224 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{19}\text{H}_{15}\text{NO}$ : C, 83.49; H, 5.53; N, 5.12; found: C, 83.42; H, 5.51; N, 5.07.

**Ethyl 3-Methyl-12H-indeno[1,2-*g*]pyrrolo[2,1-*a*]isoquinoline-2-carboxylate (7o).** Prepared from pyrrole **6o** (0.2 mmol); yield: 41 mg (70%); dark yellow solid; mp: 189–191 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.59–7.55 (m, 2H), 7.33–7.28 (m, 2H), 6.57 (s, 1H), 4.20 (t,  $J = 5.3$  Hz, 1H), 4.05 (d,  $J = 5.3$  Hz, 2H), 3.84 (s, 3H), 3.20 (s, 6H), 2.66 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  165.8, 143.4, 143.3, 141.1, 140.2, 128.9, 127.6, 127.0, 126.9, 125.6, 125.5, 125.1, 120.4, 119.9, 118.1, 117.6, 114.9, 113.2, 100.5, 59.8, 36.8, 14.5, 10.5; IR (neat)  $\nu$ : 2924, 2854 (C-H), 1696 (C=O), 1232 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{23}\text{H}_{19}\text{NO}_2$ : C, 80.92; H, 5.61; N, 4.10; found: C, 80.84; H, 5.60; N, 4.07.

**Methyl 2-Methyl-9,10-dihydrobenzo[*de*]pyrrolo[3,2,1-*ijj*]quinoline-1-carboxylate (7p).** Prepared from pyrrole **6p** (0.2 mmol); yield: 43 mg (82%); red solid; mp: 73–75 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.53 (d,  $J = 7.6$  Hz, 1H), 7.38–7.29 (m, 3H), 6.78 (d,  $J = 7.6$  Hz, 1H), 3.95 (s, 3H), 3.33–3.27 (m, 4H), 2.80 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.9, 131.7, 127.7, 126.6, 126.1, 125.7, 124.4, 123.4, 123.0, 120.7, 112.5, 112.4, 112.1, 50.9, 27.9, 22.2, 10.4; IR (neat)  $\nu$ : 2913, 2853 (C-H), 1687 (C=O), 1252 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{17}\text{H}_{15}\text{NO}_2$ : C, 76.96; H, 5.70; N, 5.28; found: C, 76.91; H, 5.70; N, 5.27.

**Methyl 2,10-Dimethyl-9,10-dihydrobenzo[*de*]pyrrolo[3,2,1-*ijj*]quinoline-1-carboxylate (7q).** Prepared from pyrrole **6q** (0.2 mmol); yield: 42 mg (76%); dark yellow solid; mp: 77–79 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.50 (d,  $J = 7.6$  Hz, 1H), 7.40–7.30 (m, 3H), 6.75 (d,  $J = 7.6$  Hz, 1H), 3.93 (s, 3H), 3.51–3.33 (m, 2H), 3.03–2.95 (m, 1H), 2.77 (s, 3H), 1.47 (d,  $J = 6.7$  Hz, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.9, 136.7, 127.6, 126.1, 125.8, 124.8, 123.6, 123.3, 123.2, 120.6, 112.6, 111.5, 50.8, 33.1, 30.6, 21.0, 10.4; IR (neat)  $\nu$ : 3058, 2882, 2835 (C-H), 1690 (C=O), 1217 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{18}\text{H}_{17}\text{NO}_2$ : C, 77.40; H, 6.13; N, 5.01; found: C, 77.35; H, 6.08; N, 5.00.

**Methyl 7-Methoxy-2-methyl-9,10-dihydrobenzo[*de*]pyrrolo[3,2,1-*ijj*]quinoline-1-carboxylate (7r).** Prepared from pyrrole **6r** (0.2 mmol); yield: 49 mg (83%); dark yellow solid; mp: 114–116 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 (d,  $J = 7.6$  Hz, 1H), 6.97–6.86 (m, 1H), 6.79 (d,  $J = 2.1$  Hz, 1H), 6.65 (d,  $J = 7.6$  Hz, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 3.34–3.12 (m, 4H), 2.73 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.9, 158.3, 133.5, 126.8, 126.7, 123.9, 121.1, 118.5, 115.2, 112.3, 112.2, 109.6, 105.6, 55.4, 50.8, 28.0, 22.1, 10.3; IR (neat)  $\nu$ : 2936, 2885, 2844 (C-H), 1694 (C=O), 1255 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{18}\text{H}_{17}\text{NO}_3$ : C, 73.20; H, 5.80; N, 4.74; found: C, 73.19; H, 5.73; N, 4.76.

**Methyl 2,6,8-Trimethyl-9,10-dihydrobenzo[*de*]pyrrolo[3,2,1-*ijj*]quinoline-1-carboxylate (7s).** Prepared from pyrrole **6s** (0.2 mmol); yield: 47 mg (80%); dark orange solid; mp: 215–217 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.47 (d,  $J = 7.5$  Hz, 1H), 6.97 (s, 1H), 6.84 (d,  $J = 7.5$  Hz, 1H), 3.93 (s, 3H), 3.31 (m, 2H), 3.13 (m, 2H), 2.77 (s, 3H), 2.49 (s, 3H), 2.38 (s, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  167.0,

134.6, 130.7, 129.2, 127.1, 126.8, 124.2, 120.2, 119.3, 112.1, 111.9, 109.6, 50.8, 24.5, 21.9, 19.0, 18.1, 10.4; IR (neat)  $\nu$ : 2914, 2860 (C-H), 1688 (C=O), 1256 (C-O), 1057 (C-I)  $\text{cm}^{-1}$ ; ESI-MS: ( $m/z$ ) 316.1 ( $M^+ + \text{Na}$ ); elemental analysis (%) calcd. for  $\text{C}_{19}\text{H}_{19}\text{NO}_2$ : C, 77.79; H, 6.53; N, 4.77; found: C, 77.73; H, 6.49; N, 4.74.

**Dimethyl 4,10-Dimethyldipyrrolo[2,1-a:2',1'-i][2,8]phenanthroline-5,11-dicarboxylate (7ta).** Prepared from pyrrole **6t** (0.2 mmol); yield: 55 mg (68%); green solid; mp: 255–257 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  7.98 (t,  $J = 8.2$  Hz, 2H), 7.78 (d,  $J = 7.6$  Hz, 1H), 7.68 (m, 2H), 7.61 (d,  $J = 8.2$  Hz, 1H), 7.39 (s, 1H), 6.90 (d,  $J = 7.6$  Hz, 1H), 3.98 (s, 3H), 3.96 (s, 3H), 2.83 (s, 6H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1, 166.0, 128.9, 127.5, 127.3, 127.2, 126.6, 125.7, 122.6, 121.4, 120.9, 120.7, 120.4, 115.2, 115.2, 113.5, 110.2, 105.9, 101.1, 51.3, 51.3, 10.6, 10.4; IR (neat)  $\nu$ : 2929, 2919 (C-H), 1710 (C=O), 1237, 1231 (C-O)  $\text{cm}^{-1}$ ; elemental analysis (%) calcd. for  $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}_4$ : C, 71.99; H, 5.03; N, 7.00; found: C, 71.90; H, 4.97; N, 6.98.

When the reaction was carried out at 40 °C, a 2:1 mixture of **7ta** and a second regioisomer (**7tb**) was detected. Isomer **7tb** (dimethyl 3,11-dimethylindolizino[7,8-g]pyrrolo[2,1-a]isoquinoline-2,12-dicarboxylate) could not be isolated in pure state. Its NMR data, obtained from the mixture, are given below.

$^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  8.35 (s, 1H), 7.91 (dd,  $J = 12.4$ , 8.2 Hz, 1H), 7.73–7.45 (m, 2H), 7.33 (s, 2H), 6.80 (d, 7.5 Hz, 2H), 3.95 (s, 3H), 2.79–2.75 (d, 3H);  $^{13}\text{C}$  NMR (63 MHz,  $\text{CDCl}_3$ )  $\delta$  166.0, 128.8, 128.0, 127.5, 125.9, 124.9, 124.6, 114.6, 114.1, 112.4, 102.0, 51.2, 10.6.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02995.

Copies of spectra of all compounds (PDF)

## ■ AUTHOR INFORMATION

### Corresponding Author

\*E-mail: josecm@ucm.es.

### ORCID

J. Carlos Menéndez: 0000-0002-0560-8416

### Notes

The authors declare no competing financial interest.

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