Regioselective Direct C–H Alkylation of NH Indoles and Pyrroles by a Palladium/Norbornene-Cocatalyzed Process

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Received: 29.07.2013; Accepted: 03.08.2013

Abstract: Nitrogen-containing heterocycles, including 1H-indoles and electron-deficient 1H-pyrroles, undergo a palladium/norbornene-cocatalyzed regioselective alkylation at the C–H bond adjacent to the NH group. A primary alkyl halide is used as the electrophile and the reaction proceeds smoothly under mild conditions to give 2-alkyl-1H-indoles and 2-substituted or 2,3-disubstituted 5-alkyl-1H-pyrroles in good yields.

Key words: catalysis, alkylations, regioselectivity, heterocycles, palladium, indoles, pyrroles

1 Introduction

Indoles and pyrroles are two important classes of N-heterocycles that occur widely in natural products, drugs, and biologically active molecules.1 Alkyl-substituted indoles and pyrroles are of particular interest, because they form key structural elements of many structurally unique and biologically active natural products (Figure 1).2 However, few methods are available for constructing such structures by direct C–H substitution. Although considerable advances have been made in the direct C–H functionalization of indoles and pyrroles,3 the regioselective installation of an alkyl group onto these heterocyclic nuclei remains a challenge. Indoles undergo Friedel–Crafts alkylation selectively at the more electron-rich C3 position,4 but it is difficult to achieve direct C2 alkylation.5,6 In the case of pyrroles, Friedel–Crafts-type direct alkylation with alkyl electrophiles usually results in a mixture of regioisomers;7 other methods for regioselective alkylation of pyrroles are either circuitous or limited in substrate scope.8 Therefore, there remains a considerable need for efficient and regioselective methods for alkylation of indoles and pyrroles.

Figure 1 Natural products containing an alkylindole or alkylpyrrole structure

Inspired by the Catellani reaction,9 we developed a palladium(norbornene-cocatalyzed process that provides straightforward access to α-alkyl-substituted indole and
pyrrole derivatives from NH indoles\textsuperscript{10} and pyrroles\textsuperscript{11} (Scheme 1). In this reaction, the N-heterocycle interacts with palladium(II) and norbornene to give intermediate A, which then undergoes an intramolecular ortho-palladation to give palladaheterocycle B in the presence of a base (Scheme 2).\textsuperscript{10b,11} Subsequently, intermediate B reacts with the alkyl halide by oxidative addition, reductive elimination, norbornene expulsion, and protodepalladation to give the alkyl-substituted heterocycle. The role of norbornene in this process is to act as a transpositional cocatalyst that assists palladium in activating the $\alpha$-C–H bond of NH indoles and pyrroles, providing excellent regioselectivities for the alkylation reactions (C2-alkylation on indole and C5-alkylation on 2-substituted and 2,3-disubstituted pyrroles). This reaction adds to the toolbox of synthetic methods for direct C–H functionalization of N-heterocycles.

![Scheme 2](image)

**Scheme 2** The mechanism of the newly developed catalytic alkylation procedure

### 2 Scope and Limitations

The alkylation of 1H-indole (1a) with alkyl bromides 2a–j proceeded smoothly with the palladium(II)/norbornene cocatalytic system to give 2-alkyl-1H-indoles regioselectively (Procedure 1, variant a).\textsuperscript{10a} As shown in Table 1, a broad range of functionalized primary alkyl bromides are suitable as reaction partners. The reactions were conducted with bis(acetonitrile)dichloropalladium(II) as catalyst, norbornene as cocatalyst, and potassium carbonate as base in $N,N$-dimethylacetamide as solvent containing 0.5 M water as an additive. In general, the 2-alkylation products were obtained in moderate to good yields and, in certain cases, minor amounts of the 2,3-dialkyl-1H-indole (4–19%) were obtained as overalkylation byproducts. The steric effect of the alkyl bromide plays an important role in the alkylation reaction; primary alkyl bromides bearing a tertiary carbon center in the $\beta$-position reacted slowly (entries 2 and 6), whereas a secondary alkyl halide (2-iodopropane) failed to react. The reaction of 1H-indole with ethyl 3-bromopropionate failed to give the desired alkylation product as a result of elimination of hydrobromic acid under basic conditions to form ethyl acrylate. The use of an alkyl iodide instead of the corresponding alkyl bromide accelerated the reaction, but resulted in a considerable amount of the 2,3-dialkylation byproduct. Alkyl tosylates failed to react. Therefore, both reactivity and stability should be taken into account when choosing the alkyl coupling partners in this reaction.

1H-Indoles bearing electron-donating or electron-withdrawing substituents were superior substrates in this 2-alkylation reaction (Procedure 1, variant a).\textsuperscript{10a} Table 2 lists

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
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<td>14</td>
<td>3aa</td>
<td>67a</td>
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<td>2</td>
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<td>58c</td>
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<td>73</td>
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<tr>
<td>6</td>
<td>90</td>
<td>20</td>
<td>3af</td>
<td>65</td>
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<td>72</td>
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<td>14</td>
<td>3ah</td>
<td>56c</td>
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<td>65</td>
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<td>10</td>
<td>70</td>
<td>14</td>
<td>3aj</td>
<td>66c</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction conditions: indole 1 (1 mmol), primary alkyl bromide 2 (2 mmol), PdCl$_2$(MeCN)$_2$ (0.1 mmol), norbornene (2 mmol), K$_2$CO$_3$ (2 mmol), DMA + 0.5 M H$_2$O (5 mL), under argon.

\textsuperscript{b} Yield of isolated product.

\textsuperscript{c} A minor amount of the 2,3-dialkyl-1H-indole was isolated as a byproduct.
Table 2 Regioselective Direct Alkylation of Substituted 1H-Indoles 1b–k with Primary Alkyl Bromides 2 (Scheme 1, Procedure 1a)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base (equiv)</th>
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<th>Product</th>
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<td>K₂CO₃ (2)</td>
<td>14</td>
<td>3cg</td>
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<tr>
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<td>K₂CO₃ (2)</td>
<td>20</td>
<td>3dk</td>
<td>59</td>
</tr>
<tr>
<td>4</td>
<td>K₂CO₃ (2)</td>
<td>14</td>
<td>3ee</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>KHCO₃ (3)</td>
<td>15</td>
<td>3fk</td>
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<td>6</td>
<td>KHCO₃ (3)</td>
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<td>7</td>
<td>KHCO₃ (3)</td>
<td>38</td>
<td>3gl</td>
<td>56</td>
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<tr>
<td>8</td>
<td>KHCO₃ (4)</td>
<td>14</td>
<td>3hk</td>
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<tr>
<td>9</td>
<td>KHCO₃ (3)</td>
<td>14</td>
<td>3ij</td>
<td>87</td>
</tr>
<tr>
<td>10</td>
<td>KHCO₃ (3)</td>
<td>14</td>
<td>3jj</td>
<td>86</td>
</tr>
<tr>
<td>11</td>
<td>K₂HPO₄ (3)</td>
<td>17</td>
<td>3kk</td>
<td>90</td>
</tr>
</tbody>
</table>

* Reaction conditions: indole 1 (1 mmol), primary alkyl bromide 2 (2 mmol), PdCl₂(MeCN)₂ (0.1 mmol), norbornene (2 mmol), base, DMA + 0.5 M H₂O (5 mL), 70 ºC, under argon.

The same procedure also permits the 2-alkylation of 3-substituted 1H-indole derivatives (Scheme 3). The alkylation of 3-methyl-1H-indole (1m) with butyl bromide proceeded more slowly than the alkylation of 1H-indole and gave a moderate yield of the 2,3-dialkylated indole 3mk. Therefore, an optimization study was conducted to improve this type of reaction, especially for more complex substrates. A modified procedure (Procedure 1, variant b) using alkyl iodide 2n as the electrophile, palladium(II) chloride as the catalyst, and N,N-dimethylformamide–dimethyl sulfoxide as a solvent mixture in an atmosphere of air resulted in good conversion and high yield in the 2-alkylation of tryptophol derivative 1n (Scheme 3).

Because of the structural similarity between indole and pyrrole, our palladium(II)/norbornene-cocatalyzed alkylation process can also be applied to pyrrole derivatives.11 Interestingly, electron-deficient 1H-indoles usually afforded better yields of the 2-alkylindole products than did electron-rich 1H-indoles (compare entries 1–4 with entries 5–11), but a weaker base, such as potassium bicarbonate or dipotassium hydrogen phosphate had to be used to prevent generation of undesired N-alkylindole byproducts. Halogen-substituted 1H-indoles were suitable substrates and successfully gave the corresponding halogen-substituted 2-alkyl-1H-indoles (for example, entries 4–8), allowing access to more-complex heterocyclic compounds through cross-coupling reactions.

Conducted by using potassium bicarbonate as a mild base in dry N,N-dimethylacetamide at 90 ºC under air (Procedure 2). Table 3 shows some typical examples of 5-alkyl-
mination reactions of pyrrole-2-carboxylates 4a–c. The yields were generally good to excellent, and in all cases a single regioisomer was obtained. Although higher temperatures and longer reaction times were required for satisfactory conversion, this reaction, like the indole alkylation reaction, showed good tolerance to a range of functional groups. A limitation of this reaction is that it appears to be restricted to 1H-pyrrole-2-carboxylates as substrates; 2-cyano-, 2-(dimethylaminocarbonyl)−, 2-formyl−, and 2-acetyl-substituted 1H-pyrroles failed to give the desired products. Methyl 1H-pyrrole-3-carboxylate gave a mixture of 5-alkylation and 2,5-dialkylation products in low yield. Therefore, this procedure is best suited for the alkylation of alkyl 1H-pyrrole-2-carboxylates.

Procedure 2 can also be applied to a series of 2,3-disubstituted electron-deficient 1H-pyrroles 4d−i (Table 4).11 These substrates gave 5-alkylation products regioselectively, albeit in lower yields than pyrrole-2-carboxylates. Both alkoxycarbonyl and acyl groups can be used as electron-withdrawing substituents on either the C2- or the C3-position of pyrrole, although pyrrole carboxylates were found to be superior. A chlorinated pyrrole substrate 4i underwent smooth alkylation to give the chloro-substituted alkylpyrrole 5iq in high yield (entry 9). Because many methods have been reported for synthesizing 2,3-disubstituted electron-deficient pyroles,13 a combination of these methods and the present 5-alkylation procedure provides regioselective access to a range of advanced functionalized pyrrole derivatives.

The utility of the alkylation method for constructing α-alkylated N-heterocycles was showcased by its successful application in total syntheses of the Aspidosperma alkaloids aspidospermidine (6) and goniomitine (7).11 In the syntheses of aspidospermidine and goniomitine, the indole alkylation protocol permitted an unprecedented synthetic strategy in which the creation of the indole C2−alkyl bonds served as key steps in building the core structures of the two natural products. The syntheses were completed via the key intermediates 3ai and 3nm, respectively. In the synthesis of mycalazal 14, reduction of the pyrrole 5-tetradecylation product 5aa was carried out to afford the target molecule (Scheme 4).

![Scheme 4](image)

**Scheme 4** Natural products aspidospermidine (6), goniomitine (7), and mycalazal 14 (8) synthesized through regioselective direct α-alkylation of N-heterocycles

### 3 Summary

A straightforward and synthetically useful method for the regioselective α-alkylation of NH-indoles and pyroles has been developed that uses a palladium(II)/norbornene cocatalytic system. The method provides a one-step transformation of easily available N-heterocycles and alkyl halides into structurally diverse alkylation products not
Table 4  Regioselective Direct Alkylation of 2,3-Disubstituted Electron-Deficient 1H-Pyrroles 4d-1 with Primary Alkyl Bromides 2
(Scheme 1, Procedure 2)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Time (h)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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</tr>
<tr>
<td>2</td>
<td>23</td>
<td>5dp</td>
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</tr>
<tr>
<td>3</td>
<td>22</td>
<td>5ep</td>
<td>69</td>
</tr>
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<td>23</td>
<td>5fk</td>
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<td>23</td>
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<td>5gp</td>
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<tr>
<td>8</td>
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<td>59</td>
</tr>
<tr>
<td>9</td>
<td>22</td>
<td>5iq</td>
<td>91</td>
</tr>
</tbody>
</table>

a Reaction conditions: pyrrole 4 (1 equiv), primary alkyl bromide 2 (2 equiv), PdCl2(MeCN)2 (0.1 equiv), norbornene (2 equiv), KHCO3 (3 equiv), DMA (1 mL per mmol of pyrrole substrate 4, c = 1 M), 90 °C, under air.

b Yield based on recovered starting material.

c BuBr (4 equiv) and KHCO3 (5 equiv) were used.

d K2HPO4 (3 equiv) as base.

Procedures
Typical procedures for the various substrate classes shown in the schemes and in the tables are described below. Procedure 1 is subdivided into two variants (1a and 1b) that require modification of the catalyst and the solvent.

Procedure 1a (Tables 1 and 2)10a
A 50-mL Schlenk flask equipped with a magnetic stirring bar and a rubber septum was charged with 1H-indole substrate 1 (1.00 mmol), norbornene (188 mg, 2.00 mmol), the base [K2CO3 (276 mg, 2.00 mmol), KHCO3 (300 mg, 3.00 mmol), or K2HPO4 (522 mg, 3.00 mmol) as indicated], and PdCl2(MeCN)2 (25.9 mg, 0.100 mmol). A 0.5 M solution of H2O in DMA (5 mL) was added. The alkyl bromide 2 (2.00 mmol) was then added from a syringe, and the resulting mixture was degassed by three freeze–pump–thaw cycles with liquid nitrogen under high vacuum. The flask was then placed in an oil bath preheated to 70 °C or 90 °C, as indicated, and the mixture was stirred vigorously under balloon pressure of argon. Upon completion of the reaction (TLC), the mixture was cooled to r.t., diluted with Et2O (30 mL), and filtered. The filtrate was concentrated in a rotary evaporator (60 °C water bath, 8–10 mbar) to remove the Et2O and most of the DMA. The residue was purified directly by flash column chromatography [silica gel (dry loading)] to give the alkylation product 3.

Analytical data for representative 2-alkyl-1H-indole products 3aa, 3bd, 3ee, and 3ij are provided below. Data for other products can be found in the appropriate reference.10b

2-Tetradecyl-1H-indole (3aa)
White solid; yield: 213 mg (0.679 mmol, 67%); Rf = 0.64 (pentane–Et2O, 9:1, UV); mp 58–60 °C.

IR (ATR): 3413, 2916, 2847, 1616, 1584, 1551, 1457, 1408, 1290, 1231 cm–1.

δ1H NMR (500 MHz, CDCl3): δ = 0.88 (t, J = 7.0 Hz, 3 H), 1.23–1.34 (m, 20 H), 1.35–1.42 (m, 2 H), 1.71 (app quin, J ≈ 7.5 Hz, 2 H), 2.74 (t, J = 7.6 Hz, 2 H), 6.21 (br s, 1 H), 7.06 (app dt, J ≈ 0.9, J = 7.5 Hz, 1 H), 7.10 (app dt, J = 0.9, J = 7.5 Hz, 1 H), 7.29 (d, J = 7.9 Hz, 1 H), 7.52 (d, J = 7.2 Hz, 1 H), 7.83 (br s, 1 H).

δ13C NMR (90.6 MHz, CDCl3): δ = 14.3, 22.8, 28.5, 29.3, 29.49, 29.52, 29.6, 29.7, 29.81, 32.1, 99.6, 110.4, 119.7, 119.9, 121.1, 129.0, 136.0, 140.2.

MS (EI, 70 eV): m/z = 313 (45) [M+], 144 (45) [M – C12H25]+, 130 (100) [M – C12H25]+.

HRMS (EI, 70 eV): m/z (%) = 313.2759.

7-Methyl-2-[(tert-butyl(dimethyl)siloxy)ethyl]-1H-indole (3bd)
Pale-yellow oil; yield: 196 mg (0.679 mmol, 68%); Rf = 0.65 (pentane–Et2O, 9:1, UV).

IR (ATR): 3437, 2954, 2927, 2856, 1614, 1559, 1496, 1461, 1329, 1254 cm–1.

δ1H NMR (500 MHz, CDCl3): δ = 0.10 (s, 6 H), 0.97 (s, 9 H), 2.45 (s, 3 H), 2.98 (t, J = 5.6 Hz, 2 H), 3.94 (t, J = 5.6 Hz, 2 H), 6.22 (s, 1 H), 6.91 (d, J = 7.2 Hz, 1 H), 6.98 (app t, J ≈ 7.5 Hz, 1 H), 7.38 (d, J = 7.8 Hz, 1 H), 8.70 (br s, 1 H).

δ13C NMR (90.6 MHz, CDCl3): δ = 5.3, 16.9, 18.3, 26.1, 31.2, 63.3, 100.3, 117.7, 119.68, 120.7, 127.9, 135.7, 138.3.


HRMS (EI, 70 eV): m/z (%) calculated for C12H32NOSi: 289.1856; found: 289.1856.

Particulars of the reagents, substrates, and other chemicals that were used, together with analytical details, can be found in the appropriate references.10a,b,11

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Synthesis 2014, 46, 35–41

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6-Chloro-2-[2-(tetrahydro-2H-pyran-2-yloxy)ethyl]-1H-indole (3ce)
Pale-yellow oil; yield: 212 mg (0.758 mmol, 76%); Rf = 0.29 (pentane–Et2O, 2:1, UV).

IR (ATR): 3256, 2950, 2878, 1616, 1580, 1457, 1293, 1201 cm−1.

1H NMR (500 MHz, CDCl3): δ = 1.53–1.68 (m, 4 H), 1.75–1.81 (m, 1 H), 1.83–1.89 (m, 1 H), 3.02 (app t, J ≈ 5.9 Hz, 2 H), 3.48–3.53 (m, 1 H), 3.71 (app dt, J = 9.6, J ≈ 5.9 Hz, 1 H), 3.81–3.85 (m, 1 H), 4.05 (dt, J = 9.6, J ≈ 5.9 Hz, 1 H), 4.63 (dd, J = 4.8, 2.8 Hz, 1 H), 6.21–6.22 (m, 1 H), 7.02 (dd, J = 8.4, 1.9 Hz, 1 H), 7.26–7.29 (m, 1 H), 7.41 (d, J = 8.4 Hz, 1 H), 8.64 (br s, 1 H).

13C NMR (90.6 MHz, CDCl3): δ = 20.1, 25.4, 28.7, 31.0, 63.0, 67.3, 99.7, 100.1, 110.6, 120.2, 120.7, 126.9, 127.1, 136.5, 138.8. 

MS (EI, 70 eV): m/z (%) = 281 (11) [M+], 279 (25) [M+], 232 (6), 195 (73), 117 (31), 164 (85), 81 (61).

HRMS (EI, 70 eV): m/z [M+]: calcd for C15H13ClNO2: 279.0321; found: 279.1017.

Methyl 2-(4-Ethoxy-oxopent-5-enoyl)-1H-indole-5-carboxylate (3lj)
White solid; yield: 266 mg (0.877 mmol, 87%); Rf = 0.30 (pentane–Et2O, 9:1, UV); mp 91–92 °C.

IR (ATR): 3336, 2923, 2861, 1712, 1695, 1546, 1439, 1325, 1292, 1238 cm−1.

1H NMR (500 MHz, CDCl3): δ = 1.25 (t, J = 7.1 Hz, 3 H), 1.69–1.80 (m, 4 H), 2.35 (tt, J = 7.0 Hz, 2 H), 2.77 (tt, J = 7.0 Hz, 2 H), 3.92 (s, 3 H), 4.13 (q, J = 7.1 Hz, 2 H), 6.31 (m, 1 H), 7.28 (d, J = 8.5 Hz, 1 H), 7.83 (dd, J = 8.5, 1.7 Hz, 1 H), 8.28 (m, 1 H), 8.52 (br s, 1 H).

13C NMR (90.6 MHz, CDCl3): δ = 14.3, 14.5, 24.5, 27.9, 28.5, 34.0, 51.9, 60.5, 100.9, 110.2, 121.7, 127.2, 128.7, 128.5, 138.8, 141.0, 168.6, 173.8.

MS (EI, 70 eV): m/z (%) = 303 (56) [M+], 257 (34), 201 (100), 188 (68), 170 (26), 129 (21).

HRMS (EI, 70 eV): m/z [M+]: calcd for C17H15NO4: 303.1465; found: 303.1456.

Ethyl (2R,4S)-2-fluoro-4-[2-fluorobenzyl]morpholine (3mm): Procedure 1b (Scheme 3)106

A 250-mL round-bottom flask equipped with a magnetic stirring bar and a rubber septum was charged with indole 1n (1.55 g, 5.63 mmol), norbornene (1.06 g, 11.3 mmol), K2CO3 (3.12 g, 22.6 mmol), and alkyl iodide (1.55 g, 5.63 mmol). The reaction mixture was stirred until a single spot was observed on TLC. The reaction mixture was cooled to low temperature, and the organic layer was washed with brine. The inorganic salts were dissolved inorganic salts, and the resulting mixture was extracted with CH2Cl2 (5 × 25 mL). The extracts were combined, washed with brine (2 × 20 mL). The organic layers were combined, washed with brine (2 × 20 mL), dried (Na2SO4), filtered, and concentrated. The residue was purified by flash column chromatography (silica gel) to afford the desired product.

Analytical data for representative pyrrole alkylation products 5ap, 5fq, and 5iq are provided below. Data for other products can be found in the corresponding reference.11

Ethyl 5-(4-Ethoxy-4-oxobutyl)-1H-pyrrole-2-carboxylate (5ap)
Pale-yellow solid; yield: 228 mg (0.900 mmol, 90%); Rf = 0.15 (pentane–Et2O, 3:1, UV); mp 54–56 °C.

IR (ATR): 3224, 2978, 1719, 1683, 1201 cm−1.

1H NMR (500 MHz, CDCl3): δ = 1.25 (t, J = 7.1 Hz, 3 H), 1.35 (t, J = 7.1 Hz, 3 H), 1.97 (app quin, J = 7.4 Hz, 2 H), 2.33 (t, J = 7.3 Hz, 2 H), 2.69 (t, J = 7.5 Hz, 2 H), 4.13 (q, J = 7.1 Hz, 2 H), 4.30 (q, J = 7.1 Hz, 2 H), 5.98 (app t, J = 3.2 Hz, 1 H), 6.83 (dd, J = 3.7, 2.5 Hz, 1 H), 9.44 (br s, 1 H).

13C NMR (90.6 MHz, CDCl3): δ = 14.3, 14.6, 24.8, 27.1, 33.5, 60.2, 60.5, 108.5, 116.0, 121.7, 137.5, 161.5, 173.3.

MS (EI, 70 eV): m/z (%) = 253 (60) [M+], 207 (35), 165 (70), 152 (100), 106 (75).

HRMS (EI, 70 eV): m/z [M+]: calcd for C21H20NO3: 313.1309; found: 313.1305.

Ethyl 5-(3-[1,3-Dioxan-2-y]ethyl)-2-methyl-1H-pyrrole-3-carboxylate (5fq)
Pale-purple oil; yield: 165 mg (0.617 mmol, 61%); 71% based on recovered pyrrole substrate 4f; Rf = 0.29 (pentane–Et2O, 1:2, UV).

IR (ATR): 3278, 2926, 1655, 1458, 1232 cm−1.

1H NMR (500 MHz, CDCl3): δ = 1.32 (t, J = 7.1 Hz, 3 H), 1.34–1.38 (m, 1 H), 1.88 (dt, J = 5.0, 7.4 Hz, 2 H), 2.09 (app t, J = 5.0 Hz, J = 12.8 Hz, 1 H), 2.47 (t, J = 7.3 Hz, 2 H), 2.64 (J = 7.4 Hz, 2 H), 3.74–3.80 (m, 2 H), 4.12 (dd, J = 11.7, 5.0 Hz, 2 H), 4.24 (q, J = 7.1 Hz, 2 H), 4.57 (t, J = 5.0 Hz, 1 H), 6.21 (d, J = 2.9 Hz, 1 H), 8.69 (br s, 1 H).

13C NMR (90.6 MHz, CDCl3): δ = 13.3, 14.6, 21.5, 25.8, 34.5, 59.3, 66.9, 101.5, 106.8, 111.4, 130.0, 134.4, 166.0.

MS (EI, 70 eV): m/z (%) = 267 (60) [M+], 222 (33), 205 (100), 166 (49), 131 (76).

HRMS (EI, 70 eV): m/z [M+]: calcd for C15H18NO3: 267.1465; found: 267.1467.
Ethyl 3-Chloro-5-[2-(1,3-dioxan-2-yl)ethyl]-1H-pyrrrole-2-carboxylate (Siq)
White solid; yield: 257 mg (0.893 mmol, 91%); \( R_f = 0.13 \) (pentane–EtOAc 4:1, UV); mp 93–94 \( ^\circ \)C.

IR (ATR): 3276, 2969, 1673, 1491 cm\(^{-1}\).

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta = 1.37 \) (t, \( J = 7.2 \) Hz, 3 H), 1.37–1.40 (m, 1 H), 1.92 (app q, \( J = 6.3 \) Hz, 2 H), 2.06–2.16 (m, 1 H), 2.72 (t, \( J = 7.0 \) Hz, 2 H), 3.79 (app t, \( J \approx 7.0 \) Hz, 2 H), 4.16 (dd, \( J = 11.6, 4.9 \) Hz, 2 H), 4.34 (q, \( J = 7.2 \) Hz, 2 H), 4.59 (t, \( J = 4.7 \) Hz, 1 H), 5.96 (d, \( J = 2.9 \) Hz, 1 H), 9.62 (br s, 1 H).

\(^13\)C NMR (126 MHz, CDCl\(_3\)): \( \delta = 14.6, 21.9, 25.8, 33.8, 60.5, 67.1, 101.0, 109.8, 117.0, 119.2, 136.6, 160.4 \).

HRMS (EI, 70 eV): m/z 101.0, 109.8, 117.0, 119.2, 136.6, 160.4.

Acknowledgement
This project was supported by the Deutsche Forschungsgemeinschaft (Ba 1372/19-1). L.J. acknowledges the Alexander von Humboldt Foundation for a postdoctoral fellowship.

References


