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Pd(II)-catalyzed intramolecular aminopalladation/direct C–H arylation under aerobic conditions: synthesis of pyrrolo[1,2-*a*]indoles

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ABSTRACT

Heating a DMA/pivalic acid (*v*/*v*=4/1) solution of diversely substituted 6-(phenylamino)hex-2-ynoates in the presence of a catalytic amount of $Pd(OAc)_2$ under oxygen atmosphere afforded pyrrolo[1,2-*a*]indoles in moderate to good yields. A domino sequence involving intramolecular aminopalladation followed by C–H activation and reductive elimination was proposed to account for the observed bis-cyclization.

1. Introduction

Pyrrolo[1,2-*a*]indole is an important structural motif found in many bioactive natural products and pharmaceuticals (Fig. 1).[1] Therefore, development of new synthetic methodologies allowing a rapid construction of this skeleton is highly desirable. Most of the existing methods required the pre-construction of functionalized indoles or pyrrolidines,[2,3] which were in turn prepared by multi-step processes.[4] Based on the Larock's indole synthesis,[5] Lu and co-workers at Boehringer-Ingelheim pharmaceuticals developed recently a one-step synthesis of polycyclic indoles by way of a Pd(0)-catalyzed intramolecular cyclization of 2-haloanilides bearing a properly tethered alkynyl function (Eq. 1, Scheme 1).[6] While the reaction is applicable to a wide range of substrates, it relied on the use of *ortho*-halogenated anilides as starting materials. In connection with our ongoing projects dealing with the development of palladium-catalyzed domino processes[7] involving C–H functionalization[8] as a key step,[9] we became interested in the development of a Pd(II)-catalyzed cyclization of **1** for the synthesis of pyrrolo[1,2-*a*]indoles **2** (Eq. 2, Scheme 1). If realized, this reaction would be more atom-economic and sustainable relative to Boehringer-Ingelheim Pharmaceuticals' protocol. Recent elegant work from Glorius[10] on the Pd(II)-catalyzed oxidative cyclization of *N*-aryl enaminones to indoles[11] and from Jiao[12] on the

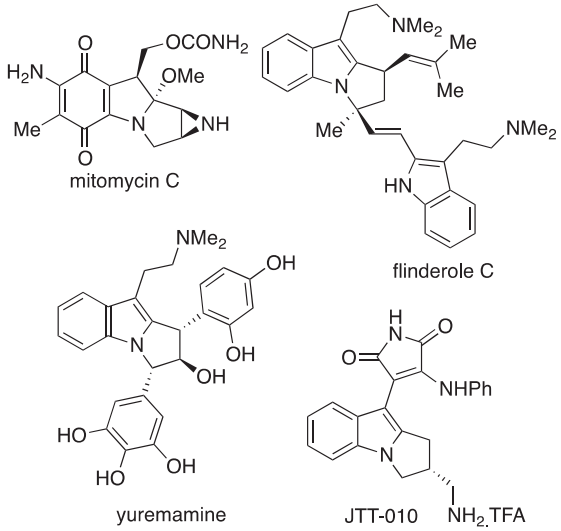

Fig. 1. Representative compounds containing pyrrolo[1,2-*a*]indole cores.

Pd(II)-catalyzed one pot synthesis of indoles from simple aniline and an activated alkyne provided hints to our reaction design.[13] Although aminometallation/C–C bond formation via C–H functionalization has been widely exploited in rhodium catalysis,[14] we noted that examples involving Pd(II)-catalyzed aminopalladation/C–H functionalization under oxidative conditions are scarce.[15,16]

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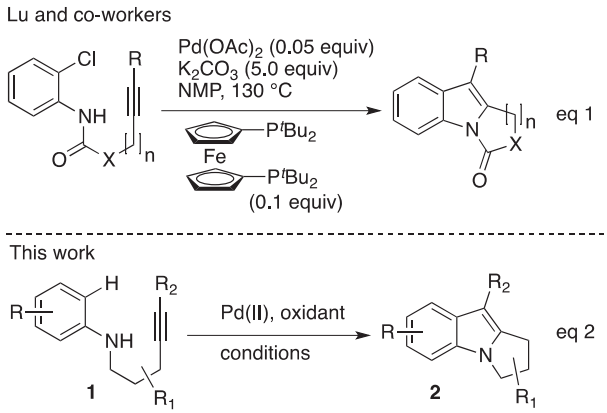
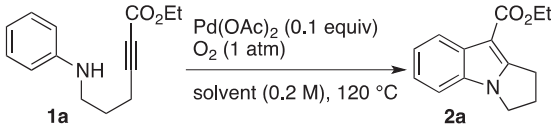


Scheme 1. Palladium-catalyzed synthesis of pyrrolo[1,2-*a*]indoles.

2. Results and discussions

We began our studies using the easily accessible ethyl 6-(phenylamino)hex-2-ynoate **1a**[17] as a model substrate for the survey of reaction conditions. As shown in Table 1, the double cyclization of **1a** proceeded in the presence of palladium acetate (0.1 equiv), pivalic acid[18] (1.0 equiv) under oxygen atmosphere[19] in DMA at 120 °C to afford the desired ethyl 2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-9-carboxylate (**2a**) in 34% yield (entry 1, Table 1). When the reaction was performed in a mixture of DMA/PivOH (*v*/*v*=4/1), we were pleased to isolate the expected pyrrolo[1,2-*a*]indole **2a** in 63% yield. Using palladium dichloride as catalyst instead of palladium acetate under the otherwise identical conditions led to complete degradation of the starting material (entry 10). Compound **2a** was isolated in lower yield when the reaction was performed in pure pivalic acid (entry 3) and other solvent mixtures (entries 4 and 5). Addition of a co-oxidant in the reaction in combination with molecular oxygen is detrimental to the reaction efficiency (entries 7–9). It should be mentioned that air was also a competent terminal oxidant to afford the desired product **2a** (entry 6).

Table 1
Pd-catalyzed bis-cyclization of ethyl 6-(phenylamino)hex-2-ynoate, survey of reaction conditions

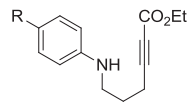
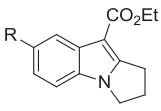
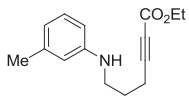
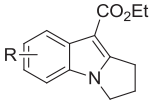
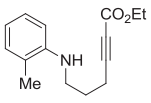
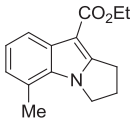
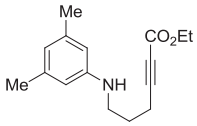
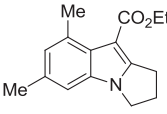
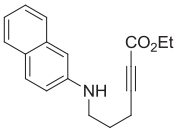
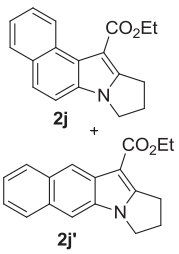
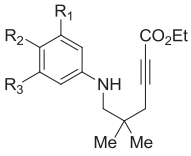
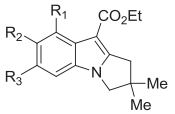
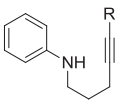
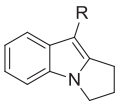


Entry	Co-oxidant[b]	Solvent	Yield[a] (%)
1	—	DMA[c]	34
2	—	DMA/PivOH (4/1)	63
3	—	PivOH	57
4	—	Xylene/PivOH (4/1)	50
5	—	DMSO/PivOH (4/1)	10
6	—[d]	DMA/PivOH (4/1)	52
7	BQ	DMA/PivOH (4/1)	35
8	$Cu(OAc)_2$	DMA/PivOH (4/1)	18
9	$PhI(OAc)_2$	DMA/PivOH (4/1)	34
10[e]	—	DMA/PivOH (4/1)	n. d.

[a] Isolated yield.
[b] Co-oxidant (2.0 equiv).
[c] PivOH (1.0 equiv).
[d] Under air atmosphere instead of O_2.
[e] $PdCl_2$ (0.1 equiv).

With the optimum conditions [$Pd(OAc)_2$ (0.1 equiv), O_2 (1.0 atm), DMA/PivOH=4/1, *c* 0.2 M at 120 °C] in hand, the scope of the domino process was next examined. The results are summarized in Table 2. Substrates with electron-withdrawing or -donating groups at *para*-position of aniline were tolerated furnishing the corresponding tricyclic indoles (**2b**–**f**) (entry 1, Table 2). When *N*-*meta*-tolyl-anilide was employed, a mixture of two separable regioisomers **2g** and **2g′** (1.2/1 ratio) was isolated in 83% overall yield in favor of the 6-substituted pyrrolo[1,2-*a*]indole **2g** (entry 2). However, the presence of a substituent *ortho* to anilide reduced dramatically the yield of the domino process (entry 3). Ethyl 6-((3,5-dimethylphenyl)amino)hex-2-ynoate **1i** underwent double cyclizations to produce the indole derivative **2i** in good yield (entry 4). Substrates containing *gem*-dimethyl group on the side chain reacted smoothly to provide the corresponding pyrrolo[1,2-*a*]indoles in good yields (entry 6). Cyclization of the β-naphthylaniline derivative **1j** furnished two separable regioisomers **2j** and **2j′** in 72% overall yield in favor of the 1,2-fused indole **2j** (ratio 3.2:1, entry 5). The presence of an electron-withdrawing group at the terminal position of alkyne is mandatory as the *N*-(5-phenylpent-4-yn-1-yl)

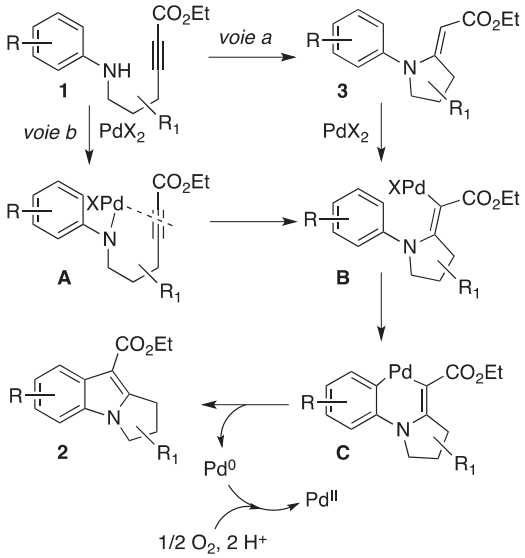
Table 2
Scope of the reaction[a]

Entry	Substrate **1**	Product **2**	Yield[b] (%)
1			**2b**, R=OMe, 41 **2c**, R=CO_2Et, 63 **2d**, R=CN, 46 **2e**, R=Me, 51 **2f**, R=Cl, 46
2			**2g**, R=6-Me and **2g′**, R=4-Me, 83 (1.2/1)
3			**2h**, 18
4			**2i**, 72
5			**2j**/**2j′**, 72 (3.2/1)
6			**2k**, R_1=R_2=R_3=H, 70 **2l**, R_1=R_3=H, R_2=CO_2Et, 69 **2m**, R_1=R_3=Me, R_2=H, 77
7			**2n**, R=CO_2Me, 51 **2o**, R=$CO_2{}^i$Pr, 47 **2p**, R=Ph, trace

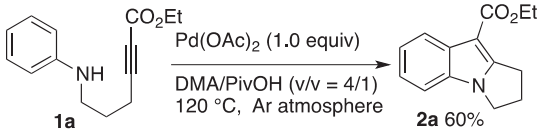
[a] Reactions were carried out under oxygen atmosphere using **1a** (1.0 equiv), $Pd(OAc)_2$ (0.1 equiv), and DMA/PivOH (*v*/*v*=4/1) at 120 °C, 4–8 h.
[b] Isolated yield.

aniline (**1p**) failed to produce the expected pyrrolo[1,2-*a*]indole **2p** (entry 7).

Treatment of **1a** in the presence of a stoichiometric amount of palladium acetate under an argon atmosphere afforded cyclization product **2a** in a similar yield (Scheme 3). This result is consistent with the Pd(II)/Pd(0) catalytic cycle. Mechanistically, either an intramolecular aza-Michael addition (*voie a*, Scheme 2) or an intramolecular aminopalladation (*voie b*, Scheme 2) could initiate the present domino process. To probe the reaction mechanism, (*E*)-ethyl-2-(1-phenylpyrrolidin-2-ylidene)acetate (**3a**) was synthesized.[20] Submitting **3a** to our standard conditions afforded **2a** in only 7% yield together with pyrrole (**5**, 8%)[21] and recovered starting material (Scheme 4). The result of this control experiment indicated that the *voie a* might not be the main pathway responsible for the conversion of **1a** to **2a**. It is interesting to note that Glorius has observed that *N*-methyl *N*-phenyl enaminone **6** failed to undergo the intramolecular dehydrogenative coupling to form indole under the conditions that were effective for the cyclization of secondary enaminone **7**.[10b] The deviation from the co-planarity between nitrogen atom and the double bond in tertiary enaminones **3a** and **6** could reduce the nucleophilicity of its β-carbon, impeding therefore the formation of the vinyl palladium intermediate of type B, hence the failure of the cyclization.

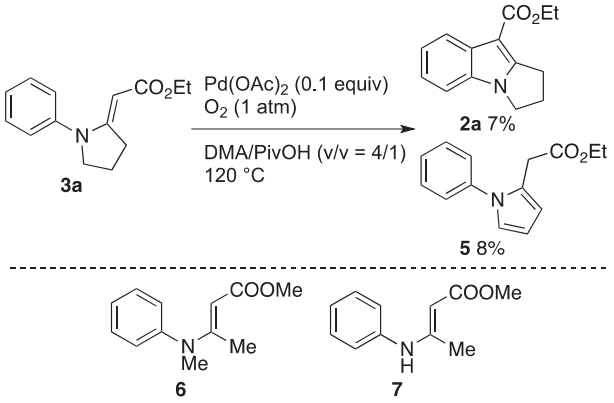


Scheme 2. Proposed mechanism for the domino process.



Scheme 3. Reaction of **1a** in the presence of a stoichiometric amount of palladium acetate under argon atmosphere.

On the basis of these preliminary results, we assumed that *voie b* (Scheme 2) would be operative to account for the formation of pyrrolo[1,2-*a*]indoles (**2**) from linear precursors **1**. Coordination of Pd(II) to the substrate **1** followed by *syn*-aminopalladation of alkyne via intermediate **A** would afford the vinyl-Pd(II) complex **B**.[22] Activation of the neighboring aromatic C–H bond would lead to the formation of a six-membered palladacycle **C**, which upon reductive elimination would provide the pyrrolo[1,2-*a*]indole **2** and Pd(0). Oxidation of Pd(0) to Pd(II) by O_2 completed then the catalytic cycle.



Scheme 4. Control experiment: attempted cyclization of enaminone **3a** under optimized conditions.

3. Conclusion

In summary, we disclosed a palladium-catalyzed one-step synthesis of pyrrolo[1,2-*a*]indoles (**2**) from diversely substituted ethyl 6-(phenylamino)hex-2-ynoates. A domino sequence involving intramolecular aminopalladation followed by direct C–H arylation was proposed to account for the bis-cyclization process.

4. Experimental part

4.1. General information

Melting points (mp) were recorded using Büchi B-540 melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer Spectrum BX FT-IR spectrometer. Proton NMR (^{1}H) spectra were recorded at 500 MHz on a Bruker AC-500 spectrometer or at 300 MHz on a Bruker AC-300 spectrometer. Carbon NMR (^{13}C) spectra were similarly recorded at 125 or 75 MHz. Proton NMR (^{1}H NMR) and carbon NMR (^{13}C NMR) chemical shifts (δ) are reported in parts per million (ppm) relative to residual proton signals in $CDCl_3$ (δ=7.26, 77.23). Coupling constants (J) are reported in Hertz (Hz) and refer to apparent multiplicities. The following abbreviations are used for the multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, quint: quintet, sex: sextet, sept: septet, m: multiplet. Mass spectra were obtained either from an AEI MS-50 (EI) or an AEI MS-9 using positive or negative electron spray (ES^+ or ES^-) for the high resolution mass spectra (HRMS). Flash chromatography was performed using SDS silicagel 60 (35–70 μm). Thin layer chromatography (TLC) was carried out on 5×20 cm plates with a layer thickness of 0.25 mm (SDS Silicagel 60 F254). Visualization was achieved under a UVP mineralight UVGL-58 lamp. All reagents were obtained from commercial suppliers unless otherwise stated. When necessary, organic solvents were routinely dried and/or distilled prior to use and stored over molecular sieves under argon. Procedures for the synthesis of substrates **1a**–**p** and **3a** are detailed in the Supplementary data.

4.2. General procedure for the pyrrolo[1,2-*a*]indoles formations

To a solution of **1** (1.0 equiv) in a mixture of DMA/PivOH (*v*/*v*=4/1, *c* 0.16 M) was added $Pd(OAc)_2$ (0.1 equiv). The reaction mixture was stirred under oxygen atmosphere at 120 °C until the complete disappearance of the starting material (monitored by TLC, usually 4 h). The solution was then cooled to rt, diluted with ethyl acetate, and washed with water, saturated aqueous $NaHCO_3$, successfully. The organic phase was dried over Na_2SO_4 and filtered. The filtrate

was concentrated under vacuum. The residue was purified by flash column chromatography on silica gel.

4.3. Characterization data

*4.3.1. Ethyl 2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2a**).* Yield=63%. Orange solid. Mp 87–89 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (dd, J=2.1, 6.0 Hz, 1H), 7.09–7.00 8 (m, 3H), 4.20 (q, J=7.0 Hz, 2H), 3.90 (t, J=7.2 Hz, 2H), 2.46 (quint, J=7.0 Hz, 2H), 1.26 (t, J=7.0 Hz, 3H). ^{1}H NMR spectroscopic data is identical to those reported in the literature.[3h]

*4.3.2. Ethyl 7-methoxy-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2b**).* Yield=41%. Orange solid. Mp 114–116 °C. R_f (heptane/EtOAc 9:1) 0.53. IR (neat, cm^{-1}) ν 2900, 1673, 1606, 1578, 1479, 1377, 1301, 1229, 1132, 1041, 805, 796, 713. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J=2.4 Hz, 1H), 7.12 (d, J=8.6 Hz, 1H), 6.83 (dd, J=2.4, 8.6 Hz, 1H), 4.35 (q, J=7.2 Hz, 2H), 4.07 (t, J=7.0 Hz, 2H), 3.89 (s, 3H), 3.27 (t, J=7.0 Hz, 2H), 2.63 (quint, J=7.0 Hz, 2H), 1.41 (t, J=7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 155.9, 153.1, 132.1, 128.0, 111.7, 110.7, 103.7, 99.3, 59.4, 56.0, 44.9, 26.8, 26.6, 14.9. HRMS m/z (ES+) calcd for $C_{15}H_{18}NO_3$: 260.1287, found 260.1300.

*4.3.3. Diethyl 2,3-dihydro-1H-pyrrolo[1,2-a]indole-7,9-dicarboxylate (**2c**).* Yield=63%. Yellow solid. Mp 130–131 °C. R_f (toluene/EtOAc 9:1) 0.41. IR (neat, cm^{-1}) ν 2980, 1706, 1685, 1424, 1269, 1198, 1109, 1024, 923, 835, 767, 677. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, J=1.2 Hz, 1H), 7.90 (dd, J=1.2, 8.3 Hz, 1H), 7.20 (d, J=8.3 Hz, 1H), 4.43-4.33 (m, 4H), 4.09 (t, J=7.2 Hz, 2H), 4.27 (t, J=7.2 Hz, 2H), 2.65 (quint, J=7.2 Hz, 2H), 1.42 (t, J=7.1 Hz, 3H), 1.41 (t, J=7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 167.8, 165.2, 154.3, 135.2, 130.6, 124.1, 124.0, 123.5, 109.6, 100.7, 60.8, 59.7, 44.7, 26.8, 26.3, 14.8, 14.6. HRMS m/z (ES+) calcd for $C_{17}H_{19}NO_4Na$: 324.1212, found 324.1227.

*4.3.4. Ethyl 7-cyano-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2d**).* Yield=46%. Orange solid. Mp 190–193 °C. R_f (toluene/EtOAc 8:2) 0.30. IR (neat, cm^{-1}) ν 2986, 2215, 1675, 1614, 1421, 1224, 1156, 1111, 888, 832, 783, 744. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (d, J=1.5 Hz, 1H), 7.40 (dd, J=1.5, 8.4 Hz, 1H), 7.26 (d, J=8.4 Hz, 1H), 4.38 (q, J=7.4 Hz, 2H), 4.15 (t, J=7.4 Hz, 2H), 3.31 (t, J=7.2 Hz, 2H), 2.71 (quint, J=7.2 Hz, 2H), 1.43 (t, J=7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 155.0, 134.3, 130.7, 126.8, 125.0, 120.7, 110.8, 104.7, 100.5, 60.0, 44.9, 26.8, 26.2, 14.8. HRMS m/z (ES+) calcd for $C_{15}H_{14}N_2O_2Na$: 277.0953, found 277.0951.

*4.3.5. Ethyl 7-methyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2e**).* Yield=51%. Orange solid. Mp 77–78 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J=1.4 Hz, 1H), 7.12 (d, J=8.0 Hz, 1H), 7.01 (dd, J=1.4, 8.0 Hz, 1H), 4.36 (q, J=7.2 Hz, 2H), 4.06 (t, J=7.0 Hz, 2H), 3.26 (t, J=7.0 Hz, 2H), 2.62 (quint, J=7.0 Hz, 2H), 2.48 (s, 3H), 1.41 (t, J=7.2 Hz, 3H). ^{1}H NMR spectroscopic data is identical to those reported in the literature.[3b]

*4.3.6. Ethyl 7-chloro-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2f**).* Yield=46%. Orange solid. Mp 141–142 °C. R_f (toluene/EtOAc 9:1) 0.65. IR (neat, cm^{-1}) ν 2978, 1682, 1544, 1448, 1425, 1376, 1317, 1202, 1103, 1037, 886, 778. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (m, 1H), 7.13 (m, 2H), 4.36 (q, J=7.0 Hz, 2H), 4.09 (t, J=7.4 Hz, 2H), 3.28 (t, J=7.4 Hz, 2H), 2.66 (quint, J=7.4 Hz, 2H), 1.41 (t, J=7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 154.1, 132.1, 131.3, 127.7, 122.2, 121.3, 110.9, 99.5, 59.7, 44.9, 26.8, 26.4, 14.9. HRMS m/z (ES+) calcd for $C_{14}H_{14}NO_2NaCl$: 286.0611, found 286.0617.

*4.3.7. Ethyl 6-methyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2g**).* Yield=45%. Orange solid. Mp 94–97 °C. R_f (toluene/EtOAc 9:1) 0.77. IR (neat, cm^{-1}) ν 2924, 1684, 1528, 1443, 1421, 1342, 1299, 1190, 1138, 1089, 762, 735. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.30–7.23 (m, 1H), 7.16 (d, J=7.6 Hz, 1H), 4.50 (q, J=7.2 Hz, 2H), 4.28 (t, J=7.0 Hz, 2H), 3.48 (t, J=7.0 Hz, 2H), 3.04 (s, 3H), 2.80 (quint, J=7.0 Hz, 2H), 1.57 (t, J=7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 153.3, 133.6, 132.6, 129.5, 124.1, 122.1, 107.7, 100.8, 59.6, 44.9, 27.6, 26.4, 22.9, 14.8. HRMS m/z (ES+) calcd for $C_{15}H_{18}NO_2$: 244.1338, found 244.1341.

*4.3.8. Ethyl 8-methyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2g'**).* Yield=38%. Orange solid. Mp 98–100 °C. R_f (toluene/EtOAc 9:1) 0.56. IR (neat, cm^{-1}) ν 2978, 1679, 1542, 1427, 1372, 1209, 1128, 1106, 1038, 811, 781, 744. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (dd, J=0.9, 7.78 Hz, 1H), 7.05 (m, 2H), 4.35 (q, J=7.1 Hz, 2H), 4.06 (t, J=7.0 Hz, 2H), 3.26 (t, J=7.0 Hz, 2H), 2.63 (quint, J=7.0 Hz, 2H), 2.47 (s, 3H), 1.41 (t, J=7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 152.5, 133.2, 131.7, 128.9, 123.3, 121.3, 110.1, 99.4, 59.4, 44.5, 26.8, 26.3, 21.8, 14.9. HRMS m/z (ES+) calcd for $C_{15}H_{17}NO_2Na$: 266.1157, found 266.1161.

*4.3.9. Ethyl 5-methyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2h**).* Yield=18%. Orange solid. Mp 117–118 °C. R_f (toluene/EtOAc 8:2) 0.55. IR (neat, cm^{-1}) ν 2996, 1668, 1618, 1551, 1469, 1383, 1231, 1161, 1047, 838, 742. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J=8.1 Hz, 1H), 7.11 (t, J=8.1 Hz, 1H), 6.94 (d, J=8.1 Hz, 1H), 4.42 (t, J=7.2 Hz, 2H), 4.37 (q, J=7.0 Hz, 2H), 3.26 (t, J=7.2 Hz, 2H), 2.66 (s, 3H), 2.63 (quint, J=7.2 Hz, 2H), 1.43 (t, J=7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 153.3, 132.5, 131.4, 123.6, 121.9, 120.9, 119.4, 99.5, 59.4, 47.8, 27.0, 25.8, 18.1, 14.9. HRMS m/z (ES+) calcd for $C_{15}H_{18}NO_2$: 244.1338, found 244.1339.

*4.3.10. Ethyl 6,8-dimethyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2i**).* Yield=72%. Yellow solid. Mp 155–158 °C. R_f (toluene/EtOAc 9:1) 0.67. IR (neat, cm^{-1}) ν 2978, 1681, 1525, 1420, 1370, 1202, 1176, 1093, 1034, 841, 783, 748. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (d, J=2.2 Hz, 2H), 4.31 (q, J=7.1 Hz, 2H), 4.00 (t, J=7.0 Hz, 2H), 3.24 (t, J=7.0 Hz, 2H), 2.83 (s, 3H), 2.56 (quint, J=7.0 Hz, 2H), 2.42 (s, 3H), 1.38 (t, J=7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 152.8, 133.9, 132.1, 131.8, 127.2, 125.7, 107.7, 100.4, 59.4, 44.6, 27.5, 26.2, 22.7, 21.5, 14.8. HRMS m/z (ES+) calcd for $C_{16}H_{19}NO_2Na$: 280.1313, found 280.1319.

*4.3.11. Ethyl 9,10-dihydro-8H-benzo[e]pyrrolo[1,2-a]indole-11-carboxylate (**2j**).* Yield=54%. Orange solid. Mp 169–172 °C. R_f (toluene/EtOAc 9:1) 0.65. IR (neat, cm^{-1}) ν 2987, 1706, 1682, 1453, 1379, 1264, 1139, 1027, 800, 768, 685. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.80 (d, J=8.7 Hz, 1H), 7.89 (d, J=7.9 Hz, 1H), 7.62–7.56 (m, 2H), 7.45 (t, J=7.9 Hz, 1H), 7.27 (d, J=7.9 Hz, 1H), 4.38 (q, J=7.2 Hz, 2H), 4.03 (t, J=7.1 Hz, 2H), 3.18 (t, J=7.1 Hz, 2H), 2.48 (quint, J=7.1 Hz, 2H), 1.43 (t, J=7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 151.4, 130.6, 129.8, 129.1, 128.5, 127.2, 125.7, 125.2, 123.9, 123.8, 111.2, 102.5, 59.7, 45.0, 28.0, 26.0, 14.8. HRMS m/z (ES+) calcd for $C_{18}H_{17}NO_2Na$: 302.1157, found 302.1167.

*4.3.12. Ethyl 2,3-dihydro-1H-benzo[f]pyrrolo[1,2-a]indole-11-carboxylate (**2j'**).* Yield=18%. Red solid. Mp 160–164 °C. R_f (heptane/EtOAc 9:1) 0.51. IR (neat, cm^{-1}) ν ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.02–7.99 (m, 1H), 7.91–7.88 (m, 1H), 7.64 (s, 1H), 7.40–7.37 (m, 2H), 4.42 (q, J=7.2 Hz, 2H), 4.19 (t, J=6.9 Hz, 2H), 3.38 (t, J=6.9 Hz, 2H), 2.72 (quint, J=6.9 Hz, 2H), 1.46 (t, J=7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 133.7, 132.0, 130.1, 129.9, 128.8, 127.5, 124.3, 123.5, 119.4, 105.7, 59.6, 44.7, 29.9, 26.8, 15.0. HRMS m/z (ES+) calcd for $C_{18}H_{17}NO_2Na$: 302.1157, found 302.1167.

*4.3.13. Ethyl 2,2-dimethyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2k**).* Yield=70%. White solid. Mp 83–84 °C. R_f (toluene/EtOAc 9:1) 0.58. IR (neat, cm^{-1}) ν 2954, 1674, 1543, 1431, 1208, 1102, 1042, 1012, 922, 784, 747, 736. ^{1}H NMR (500 MHz, $CDCl_3$)

δ 8.13 (d, *J*=7.6 Hz, 1H), 7.27–7.19 (m, 3H), 4.38 (q, *J*=7.1 Hz, 2H), 3.85 (s, 2H), 3.12 (s, 2H), 1.43 (t, *J*=7.1 Hz, 3H), 1.34 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 152.3, 133.2, 130.6, 121.9, 109.9, 100.2, 59.5, 57.8, 43.7, 41.7, 28.2, 14.9. HRMS *m*/*z* (ES+) calcd for $C_{16}H_{19}NO_2Na$: 280.1313, found 280.1321.

*4.3.14. Diethyl 2,2,6,8-tetramethyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole-7,9-dicarboxylate (**2l**).* Yield=69%. Yellow solid. Mp 100–102 °C. R_f (toluene/EtOAc 9:1) 0.80. IR (neat, cm^{-1}) ν 2960, 1698, 1536, 1415, 1339, 1168, 1086, 1038, 820, 782. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.84 (s, 2H), 4.32 (q, *J*=7.0 Hz, 2H), 3.78 (s, 2H), 3.09 (s, 2H), 2.84 (s, 3H), 2.43 (s, 3H), 1.39 (t, *J*=7.0 Hz, 3H), 1.32 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 152.0, 134.2, 132.1, 131.8, 126.7, 125.6, 107.6, 101.1, 59.5, 57.8, 42.9, 42.9, 28.2, 22.7, 21.5, 14.8. HRMS *m*/*z* (ES+) calcd for $C_{18}H_{24}NO_2$: 286.1807, found 286.1795.

*4.3.15. Ethyl 2,2,6,8-tetramethyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2m**).* Yield=77%. Yellow solid. Mp 100–102 °C. R_f (toluene/EtOAc 9:1) 0.80. IR (neat, cm^{-1}) ν 2960, 1698, 1536, 1415, 1339, 1168, 1086, 1038, 820, 782. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.84 (s, 2H), 4.32 (q, *J*=7.0 Hz, 2H), 3.78 (s, 2H), 3.09 (s, 2H), 2.84 (s, 3H), 2.43 (s, 3H), 1.39 (t, *J*=7.0 Hz, 3H), 1.32 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 152.0, 134.2, 132.1, 131.8, 126.7, 125.6, 107.6, 101.1, 59.5, 57.8, 42.9, 42.9, 28.2, 22.7, 21.5, 14.8. HRMS *m*/*z* (ES+) calcd for $C_{18}H_{24}NO_2$: 286.1807, found 286.1795.

*4.3.16. Methyl 2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2n**).* Yield=51%. White solid. Mp 75–78 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12–8.09 (m, 1H), 7.26–7.19 (m, 3H), 4.07 (t, *J*=7.2 Hz, 2H), 3.90 (s, 3H), 3.27 (t, *J*=7.2 Hz, 2H), 2.63 (quint, *J*=7.2 Hz, 2H). ^{1}H NMR spectroscopic data is identical to those reported in the literature.[3h]

*4.3.17. Isopropyl 2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate (**2o**).* Yield=47%. Orange solid. Mp 94–96 °C. R_f (toluene/EtOAc 9:1) 0.62. IR (neat, cm^{-1}) ν 2978, 1678, 1543, 1425, 1382, 1300, 1203, 1088, 1017, 783, 750. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (dd, *J*=1.9, 8.3 Hz, 1H), 7.12–7.04 (m, 3H), 5.13 (sept, *J*=6.2 Hz, 1H), 3.94 (t, *J*=7.1 Hz, 2H), 3.14 (t, *J*=7.1 Hz, 2H), 2.50 (quint, *J*=7.1 Hz, 2H), 1.25 (d, *J*=6.2 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 152.9, 132.9, 131.1, 121.8, 121.7, 121.6, 110.0, 99.9, 66.6, 44.6, 26.8, 26.3, 22.6. HRMS *m*/*z* (ES+) calcd for $C_5H_{17}NO_2Na$: 266.1157, found 266.1150.

*4.3.18. Ethyl 2-(1-phenyl-1H-pyrrol-2-yl)acetate (**5**).* Yield=8%. Orange oil. R_f (heptane/EtOAc 8:2) 0.51. IR (neat, cm^{-1}) ν 1732, 1598, 1460, 1368, 1324, 1324, 1257, 1178, 1141, 1031, 768, 697, 676. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (t, *J*=7.0 Hz, 2H), 7.37 (t, *J*=7.0 Hz, 1H), 7.32 (d, *J*=7.0 Hz, 2H), 6.80 (m, 1H), 6.26 (t, *J*=2.7 Hz, 1H), 6.24 (m, 1H), 4.06 (q, *J*=7.4 Hz, 2H), 3.59 (s, 2H), 1.17 (t, *J*=7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 140.1, 129.4, 127.6, 126.5, 125.7, 122.7, 110.0, 108.6, 61.1, 33.0 14.3. HRMS *m*/*z* (ES+) calcd for $C_{20}H_{12}NO_2$: 284.0837, found 284.0873.

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Supplementary data

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