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Palladium-Catalyzed Cascade Process To Construct 1,2,5-Trisubstituted Pyrroles

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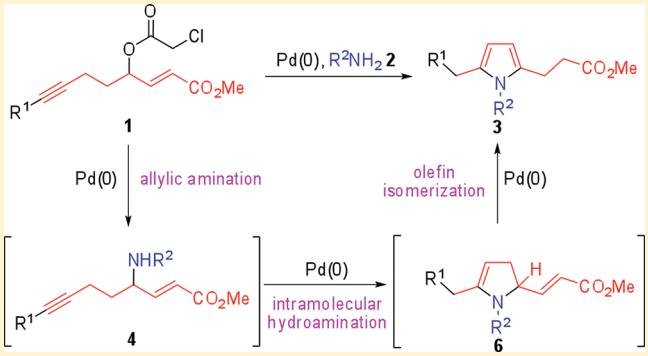
Supporting Information

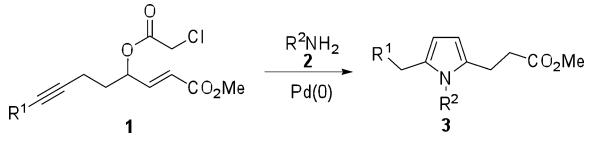
ABSTRACT: A novel palladium-catalyzed cascade allylic amination/intramolecular hydroamination/isomerization process of protected enynol **1** and primary amine **2** has been explored, which constructs the important 1,2,5-trisubstituted pyrroles. This transformation offers an alternative synthetic methodology capable of generating substituted pyrroles in a straightforward way.



Pyrroles have represented one of the more important heterocycles ever since their structure elucidation by von Bayer in the 1870s.[1−4] Substituted pyrroles are structural components of many naturally occurring bioactive compounds[5−9] and synthetic pharmaceuticals,[10] e.g., porphyrins and atorvastatin calcium. Also as key structural units, they are broadly used in organic conducting materials such as polypyrroles.[11−13] Consequently, development of methodologies for the synthesis of substituted-pyrrole derivatives is always an attractive research topic in the field of heterocycle chemistry. To date, many synthetic methods have been developed for the construction of pyrroles, including the classical Knorr reaction,[14,15] Hantzsch reaction,[16,17] and Paal−Knorr condensation reaction,[18−20] or transition-metal-catalyzed reactions.[21−27] Especially in the past several decades, transition-metal-catalyzed transformations have become increasingly important and popular because of their high efficiency in the construction of the complex molecules.[28−33] Accordingly, a variety of cycloisomerization reactions of acyclic precursors have been disclosed under the catalysis of palladium, platinum, copper, gold, rhodium, etc.[34−40]Among them, enyne cycloisomerizations, as typical atom-economic transformation processes, have been extensively applied in the synthesis of various cyclic compounds. However, the related methodologies for the synthesis of pyrrole remained underexplored.[3] Therefore, development of such synthetic approach using enynes as substrates is still of necessity.

During our continuous efforts on the transition-metal-catalyzed transformations of enynes,[41] we occasionally found that a protected enynol compound **1** could undergo a cyclization reaction with a primary amine **2** upon catalysis with palladium complex, which gave a synthetically useful 1,2,5-trisubstituted pyrrole **3** (Scheme 1). Herein, we wish to present this straightforward cascade protocol for the synthesis of pyrroles.

Scheme 1. Cyclization Reaction of Enynol 1 and Amine 2 To Form Pyrrole 3



Our optimization was initiated with compound **1a** and benzylamine **2a** as model substrates, and the results are summarized in Table 1. First with toluene as solvent, several Pd catalysts were screened toward their catalytic activity. Among them, $Pd_2(dba)_3$ (0.1 equiv) was found to be the best catalyst in the presence of PPh_3 (0.1 equiv) as additive at 80 °C, which gave pyrrole **3a** with a moderate yield of 48% (entry 1). While using $Pd(PPh_3)_4$, $Pd(CF_3CO_2)_2$, or $[PdCl(\eta^3\text{-}C_3H_5)]_2$ as catalyst, lower yields of **3a** were obtained (entries 2−4). When $Pd(PPh_3)_2Cl_2$ was used, no desired product was observed (entry 5). With THF as solvent, the reaction also did not give the desired product **3a** under the catalysis of $Pd_2(dba)_3/PPh_3$ at 60 °C (entry 6). Next, different amounts of PPh_3 as additive were applied in this model reaction (entries 7−9), which proved that 0.1 equiv of PPh_3 was the best choice.

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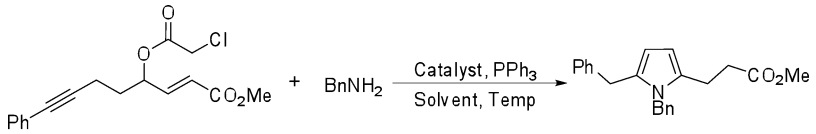
Table 1. Optimization of the Reaction Conditions[a]



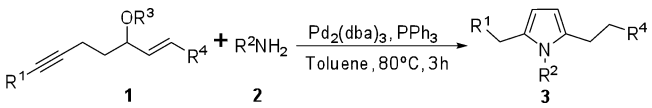
1a 2a 3a

entry	catalyst	PPh_3(equiv)	solution	T (°C)	yield[b] (%)
1	$Pd_2(dba)_3$	0.1	Tol	80	48
2	$Pd(PPh_3)_4$	0.1	Tol	80	29
3	$Pd(CF_3CO_2)_2$	0.1	Tol	80	23
4	$[PdCl(\eta^3\text{-}C_3H_5)]_2$	0.1	Tol	80	39
5	$Pd(PPh_3)_2Cl_2$	0.1	Tol	80	
6	$Pd_2(dba)_3$	0.1	THF	60	
7	$Pd_2(dba)_3$	0.05	Tol	80	18
8	$Pd_2(dba)_3$	0.5	Tol	80	31
9	$Pd_2(dba)_3$	1.0	Tol	80	18

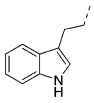
[a]Reaction conditions: protected enynol **1a** (0.5 mmol), primary amine **2a** (2.0 equiv, 1.0 mmol), catalyst (0.1 equiv, 0.05 mmol), and solvent (4.0 mL) at a corresponding temperature under Ar atmosphere. [b]Isolated yield.

To further probe the generality of this methodology, various primary amine substrates **2** were subjected to this reaction. As summarized in Table 2, all reactions went smoothly to afford

Table 2. Pd-Catalyzed Cyclization Reaction of Various Enynols and Amines[a]



1 2 3

entry	1	2	R^1	R^2	R^3	R^4	3	Yield(%)[b]
1	**1a**	**2a**	Ph	Bn	chloroacetyl	CO_2Me	**3a**	48
2	**1b**	**2a**	H	Bn	chloroacetyl	CO_2Me	**3b**	84
3	**1b**	**2b**	H	$PhCH_2CH_2$	chloroacetyl	CO_2Me	**3c**	41
4	**1b**	**2c**	H	allyl	chloroacetyl	CO_2Me	**3d**	58
5	**1b**	**2d**	H		chloroacetyl	CO_2Me	**3e**	50
6	**1b**	**2e**	H		chloroacetyl	CO_2Me	**3f**	83
7	**1b**	**2f**	H	Ph	chloroacetyl	CO_2Me	**3g**	50
8	**1b**	**2g**	H	2-naphthyl	chloroacetyl	CO_2Me	**3h**	42
9	**1b**	**2h**	H	*p*-methoxyphenyl	chloroacetyl	CO_2Me	**3i**	62
10	**1b**	**2i**	H	*p*-chlorophenyl	chloroacetyl	CO_2Me	**3j**	30
11	**1c**	**2a**	Ph	Bn	acetyl	CO_2Me		-
12	**1d**	**2a**	Ph	Bn	chloroacetyl	H		-

[a]Reaction conditions: protected enynol **1** (0.5 mmol), primary amine **2** (1.0 mmol), $Pd_2(dba)_3$ (10 mmol %), PPh_3 (10 mmol %), and solvent (4.0 mL) at 80 °C under Ar atmosphere. [b]Isolated yield.

the desired products in moderate to good yields (41−84%) within 3 h. Both aliphatic and aromatic amines afforded the expected pyrroles (entries 1−10). Additionally, we noticed that the yield of current cyclization reaction was correlated with the electron property of aromatic amines **2** to some degree. When substrate **2h** bearing the electron-donating methoxyl group was employed (entry 9), this reaction could give the expected product in moderate yield of 62%. However, in the presence of the chloro substituent (a weak electron-withdrawing group) in **2i**, the reaction gave slightly lower yield of 30% (entry 10). Furthermore, the scope of substrate **1** was also examined. We were pleased to find that not only substrates with aromatic alkyne moiety (entry 1) but also those with terminal alkynes reacted well (entries 2−10). To our surprise, when compound **1c** with an acetyl protecting group was subjected to the optimized reaction conditions, no expected product **3a** could be obtained (entry 11). It should be noted that no desired pyrrole product could be isolated using compound **1d** with a terminal olefin moiety, which indicated the presence of the CO_2Me group in substrate is necessary for this transformation (entry 12).

On the basis of the above experimental results, a plausible mechanism for this palladium-catalyzed cyclization reaction is proposed in Scheme 2. Initially, substrate **1** underwent a palladium-catalyzed Tsuji−Trost reaction, resulting in an allylic amination to afford alkynylamine compound **4**.[42] Next, an intramolecular addition of amine to alkyne took place and gave the hydroamination intermediate **5** with an exocyclic double bond.[43−45] Subsequent isomerization of the double bond in **5** led to dihydropyrrole intermediate **6**. Because of the slightly stronger acidity of γ-H in the α,β-unsaturated ester of the intermediate **6**, a palladium-catalyzed olefin isomerization proceeded smoothly and gave intermediate **7** with an exocyclic double bond, which further isomerized to afford the pyrrole product **3**.

In conclusion, we have developed a palladium-catalyzed intermolecular reaction of protected enynols for the first time, which involved a novel cascade allylic amination/intramolecular hydroamination/olefin−isomerization process and gave the 1,2,5-trisubstituted pyrroles in moderate to good yields. This work corroborates the application of the transition-metal catalyzed reaction of enyne compounds.

EXPERIMENTAL SECTION

Typical Procedure for the Cyclization Reaction. To a solution of $Pd_2(dba)_3$ (dba = dibenzylideneacetone) (0.1 equiv) and Ph_3P (0.1 equiv) in toluene (2.0 mL) at 80 °C with stirring under argon were added two solutions of protected enynol substrate **1** (0.5 mmol) and primary amine **2** (1.0 mmol, 2.0 equiv) in toluene (1.0 mL) concurrently with two syringes, respectively. Stirring was continued for 3 h at 80 °C. After being cooled to room temperature, the reaction mixture was directly purified by column chromatography (petroleum ether/acetone = 30/1) on silica gel to afford pyrrole **3**.

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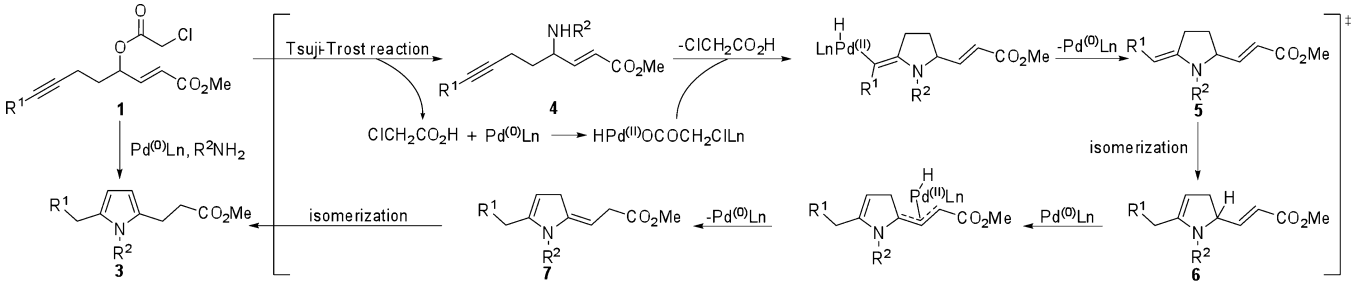
Scheme 2. Proposed Mechanism of the Cyclization Reaction To Form Pyrroles



*(E)-Methyl 4-(2-chloroacetoxy)-8-phenyloct-2-en-7-ynoate (**1a**):* R_f = 0.60 (25% EtOAc in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.39−7.38 (m, 2H), 7.28−7.26 (m, 3H), 6.89 (ddd, J = 7.9 Hz, 5.6 Hz, 0.8 Hz, 1H), 6.07−6.02 (m, 2H), 5.68−5.65 (m, 1H), 4.09 (s, 2H), 3.72 (s, 3H), 2.50 (t, J = 7.2 Hz, 2H), 2.04−1.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 166.2, 165.8, 143.5, 131.4, 128.1, 127.7, 123.2, 122.2, 87.5, 81.8, 73.1, 51.6, 40.6, 32.3, 15.1; IR (KBr) 3002w, 2952 m, 2233vw, 1726s, 1169s cm^{-1}; LRMS (ESI), m/z 321.2 [M + H]$^+$; HRMS (ESI) calcd for $C_{17}H_{17}ClNaO_4$ [M + Na]$^+$ 343.0708, found 343.0713.

*(E)-Methyl 4-(2-chloroacetoxy)oct-2-en-7-ynoate (**1b**):* R_f = 0.60 (35% EtOAc in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.82 (dd, J = 6.0 Hz, 15.8 Hz, 1H), 6.01 (dd, J = 15.8 Hz, 1.2 Hz, 1H), 4.10 (s, 2H), 3.73 (s, 3H),2.79−2.27 (m, 2H), 2.01 (t, J = 2.8 Hz, 1H), 1.95−1.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 166.2, 165.8, 143.3, 122.3, 82.0, 72.9, 69.7, 51.7, 40.6, 32.0, 14.2; IR (KBr) 3296s, 2944 m, 2119vw, 1726s, 1169s cm^{-1}; LRMS (ESI), m/z 262.2 [M + NH_4]$^+$; HRMS (ESI) calcd for $C_{11}H_{13}ClNaO_4$ [M + Na]$^+$ 267.0395, found 267.0397.

*(E)-Methyl 4-acetoxy-8-phenyloct-2-en-7-ynoate (**1c**):* R_f = 0.60 (25% EtOAc in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.40−7.37 (m, 2H), 7.29−7.26 (m, 3H), 6.90 (dd, J = 16.0 Hz, 5.6 Hz, 1H), 6.00 (dd, J = 15.6 Hz, 1.6 Hz, 1H), 5.62−5.57 (m, 1H), 3.74 (s, 3H), 2.50 (t, J = 6.8 Hz, 2H), 2.11 (s, 3H), 1.99 (q, J = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 169.9, 166.3, 144.9, 131.6, 128.2, 127.8, 123.5, 121.7, 88.0, 81.7, 71.4, 51.7, 32.7, 20.9, 15.4; IR (KBr) 2923s, 2853 m, 1728s, 1231s,758 m cm^{-1}; LRMS (ESI), m/z 304.2 [M + NH_4]$^+$; HRMS (ESI) calcd for $C_{17}H_{18}NaO_4$ [M + Na]$^+$ 309.1097, found 309.1096.

*7-Phenylhept-1-en-6-yn-3-yl 2-chloroacetate (**1d**):* R_f = 0.65 (25% EtOAc in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.40−7.38 (m, 2H), 7.29−7.25 (m, 3H), 5.85−5.78 (m, 1H), 5.50 (q, J = 6.8 Hz, 1H), 5.35 (d, J = 13.2 Hz, 1H), 5.26 (d, J = 10.4 Hz, 1H), 4.06 (s, 2H), 2.50−2.46 (m, 2H), 2.04−1.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 166.4, 134.8, 131.5, 128.2, 127.7, 123.5, 118.2, 88.2, 81.4, 75.7, 40.9, 32.8, 15.4; IR (KBr) 3081w, 2927 m, 2230w, 1756s, 1175s, 757 m cm^{-1}; LRMS (ESI), m/z 280.3 [M + NH_4]$^+$; HRMS (ESI) calcd for $C_{15}H_{15}ClNaO_2$ [M + Na]$^+$ 285.0653, found 285.0652.

*Methyl 3-(1,5-dibenzyl-1H-pyrrol-2-yl)propanoate (**3a**):* R_f = 0.28 (10% acetone in petroleum ether); Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.27−7.21 (m, 6H), 7.18 (d, J = 7.2 Hz, 2H), 6.81 (d, J = 7.2 Hz, 2H), 5.90 (d, J = 3.2 Hz, 1H), 5.87 (d, J = 3.2 Hz, 1H), 4.94 (s, 2H), 3.79 (s, 2H), 3.64 (s, 3H), 2.78 (t, J = 8.4 Hz, 2H), 2.60 (t, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 173.3, 139.4, 138.3, 131.5, 131.46, 128.7, 128.5, 128.4, 127.1, 126.2, 125.5, 107.3, 104.6, 51.6, 46.7, 33.2, 33.1, 21.9; IR (KBr) 3027w, 2923s, 1736s, 1164s cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{20}N_2O_4S$ [M + H]$^+$ 397.1217, found 397.1209.

*Methyl 3-(1-benzyl-5-methyl-1H-pyrrol-2-yl)propanoate (**3b**):* R_f = 0.25 (10% acetone in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.30−7.24 (m, 3H), 6.87 (d, J = 7.2 Hz, 2H), 5.89 (d, J = 7.2 Hz, 1H), 5.88 (d, J = 7.2 Hz, 1H), 5.06 (s, 2H), 3.66 (s, 3H), 2.80 (t, J = 8.0 Hz, 2H), 2.62−2.58 (m, 2H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 173.3, 138.3, 130.8, 128.8, 127.1, 125.6, 105.7, 104.4, 51.6, 46.6, 33.2, 22.0, 12.3; IR (KBr) 3029w, 2926s, 1736s, 1435s, 1155s, 730 m, 698 m cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{19}NO_2$ [M + H]$^+$ 258.1489, found 258.1496.

*Methyl 3-(5-methyl-1-phenethyl-1H-pyrrol-2-yl)propanoate (**3c**):* R_f = 0.30 (10% acetone in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.34−7.24 (m, 3H), 7.12 (d, J = 6.8 Hz, 2H), 5.80 (d, J = 6.8 Hz, 2H), 3.99 (t, J = 7.6 Hz, 2H), 3.72 (s, 3H), 2.89 (t, J = 7.6 Hz, 2H), 2.84−2.80 (m, 2H), 2.69−2.65 (m, 2H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 173.4, 138.3, 130.1, 128.8, 128.6, 127.9, 126.7, 105.5, 103.9, 51.7, 45.1, 37.6, 33.0, 21.8, 12.3; IR (KBr) 3026w, 2924s, 1734s, 1615s, 1435s, 1160s, 752 m, 700 m cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{21}NO_2$ [M + H]$^+$ 272.1645, found 272.1650.

*Methyl 3-(1-allyl-5-methyl-1H-pyrrol-2-yl)propanoate (**3d**):* R_f = 0.33 (10% acetone in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 5.94−5.85 (m, 1H), 5.83−5.81 (m, 1H), 5.12 (dd, J = 10.4 Hz, 1.2 Hz, 1H), 4.70 (dd, J = 17.2 Hz, 1.2 Hz, 1H), 4.41−4.39 (m, 2H), 3.70 (s, 3H), 2.86−2.82 (m, 2H), 2.68−2.64 (m, 2H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 173.4, 134.0, 130.4, 128.3, 115.7, 105.3, 104.0, 51.6, 45.4, 33.2, 21.8, 12.1; IR (KBr) 2924s, 2854 m, 1735s, 1616s, 1437s, 1159s cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{17}NO_2$ [M + H]$^+$ 208.1332, found 208.1329.

*Methyl 3-(1-(furan-2-ylmethyl)-5-methyl-1H-pyrrol-2-yl)-propanoate (**3e**):* R_f = 0.28 (10% acetone in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.34 (d, J = 1.2 Hz, 1H), 6.29 (dd, J = 3.2 Hz, 1.8 Hz, 1H), 6.03 (d, J = 3.2 Hz, 0.8 Hz, 1H), 5.83−5.82 (m, 2H), 4.95 (s, 2H), 3.70 (s, 3H), 2.96−2.92 (m, 2H), 2.68−2.64 (m, 2H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 173.4, 151.1, 142.2, 130.7, 128.5, 110.3, 107.0, 105.7, 104.3, 51.6, 40.5, 33.1, 21.9, 12.3; IR (KBr) 2923s, 2854 m, 1733s, 1616s, 1436s, 1167s, 747 m, 664 m cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{17}NO_3$ [M + H]$^+$ 248.1281, found 248.1282.

*Methyl 3-(1-(2-(1H-indol-3-yl)ethyl)-5-methyl-1H-pyrrol-2-yl)-propanoate (**3f**):* R_f = 0.20 (10% acetone in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.03 (brs, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.21 (td, J = 8.0 Hz, 0.8 Hz, 1H), 7.14 (td, J = 8.0 Hz, 0.8 Hz, 1H), 5.81 (d, J = 3.2 Hz, 1H), 5.79 (d, J = 3.2 Hz, 1H), 4.06−4.02 (m, 2H), 3.69 (s, 3H), 3.07−3.03 (m, 2H), 2.87 (t, J = 8.0 Hz, 2H), 2.67−2.64 (m, 2H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 173.5, 136.2, 130.2, 128.0, 127.2, 122.1, 122.0, 119.6, 118.5, 112.5, 111.2, 105.4, 103.9, 51.7, 44.2, 33.1, 27.0, 21.9, 12.4; IR (KBr) 3365s, 2923s, 2854 m, 1732s, 1614s, 1432s, 1160s, 744s cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{22}N_2O_2$ [M + H]$^+$ 311.1754, found 311.1747.

*Methyl 3-(5-methyl-1-phenyl-1H-pyrrol-2-yl)propanoate (**3g**):* R_f = 0.25 (10% acetone in petroleum ether); Viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.50−7.40 (m, 3H), 7.24−7.22 (m, 2H), 5.93 (s, 2H), 3.63 (s, 3H), 2.72−2.68 (m, 2H), 2.52−2.48 (m, 2H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 173.3, 138.5, 131.6, 129.4, 129.2, 128.3, 128.0, 105.7, 104.8, 51.6, 33.3, 22.4, 12.8; IR (KBr) 3061w, 2950s, 2923s, 2853 m, 1735s, 1618s, 1435s, 1162s, 771 m, 699 m cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{17}NO_2$ [M + H]$^+$ 244.1332, found 244.1335.

*Methyl 3-(5-methyl-1-(naphthalen-1-yl)-1H-pyrrol-2-yl)-propanoate (**3h**):* R_f = 0.22 (10% acetone in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.94 (dd, J = 8.0 Hz, 4.8 Hz, 2H), 7.59−7.51 (m, 2H), 7.48−7.42 (m, 2H), 7.10 (d, J = 8.4

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Hz, 1H), 6.03 (s, 2H), 3.57 (s, 3H), 2.57−2.41 (m, 4H), 1.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 173.2, 135.3, 134.2, 132.6, 131.9, 130.4, 128.8, 128.1, 127.3, 126.6, 126.4, 125.4, 123.1, 105.6, 104.8, 51.5, 33.5, 22.2, 12.4; IR (KBr) 3055w, 2923s, 2853 m, 1737s, 1419s, 1161s, 776 m cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}NO_2$ [M + H]$^+$ 294.1489, found 294.1483.

*Methyl 3-(1-(4-methoxyphenyl)-5-methyl-1H-pyrrol-2-yl)-propanoate (**3i**):* R_f = 0.21 (10% acetone in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.13 (d, J = 8.8 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 5.89 (s, 2H), 3.86 (s, 3H), 3.62 (s, 3H), 2.69−2.65 (m, 2H), 2.50−2.47 (m, 2H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 173.3, 159.0, 131.8, 131.3, 129.6, 129.3, 114.4, 105.4, 104.5, 55.4, 51.5, 33.4, 22.4, 12.8; IR (KBr) 2924 m, 2846 m, 1734 m, 1616s, 1513s, 1249s, 838 m cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{19}NO_3$ [M + H]$^+$ 274.1438, found 274.1433.

*Methyl 3-(1-(4-chlorophenyl)-5-methyl-1H-pyrrol-2-yl)-propanoate (**3j**):* R_f = 0.27 (10% acetone in petroleum ether); viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.45 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 5.91 (s, 2H), 3.63 (s, 3H), 2.69−2.65 (m, 2H), 2.51−2.47 (m, 2H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 173.2, 137.1, 133.9, 131.6, 129.6, 129.5, 129.3, 106.2, 105.2, 51.6, 33.3, 22.4, 12.8; IR (KBr) 2923s, 2853 m, 1735s, 1619s, 1492s, 1162s, 838 m cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{16}ClNO_2$ [M + H]$^+$ 278.0942, found 278.0945.

■ ASSOCIATED CONTENT

Supporting Information

[Experimental procedures for **1a−d** and copies of NMR spectra for compounds **1a−d** and **3a−j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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