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PLATINUM-CATALYZED REGIOSELECTIVE HYDRATION OF 1-(2-PROPYNYL)-2-FORMYLPYRROLES

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Abstract – The hydration reaction of 1-(2-propynyl)-2-formylpyrroles with a platinum catalyst in aqueous media is described. Various 1-(2-oxopropyl)-2-formylpyrroles were regioselectively synthesized via the platinum-promoted intramolecular *6-exo-dig* cyclization pathway.

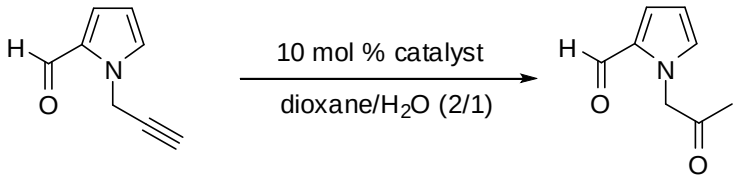
INTRODUCTION

Hydration of alkynes is a useful protocol for introduction of carbonyl component within the molecules, and various methodologies for the application in organic synthesis have been reported.[1,2] Among them, transition metal-catalyzed hydration of alkynes utilizing neighboring group participation is one of the useful protocol to obtain the desired product in high regioselectivity.[3] For example, Sahoo recently reported a gold-catalyzed hydration of propargyl acetates, in which α-acyloxy methyl ketones were regioselectively produced by assisting a neighboring carbonyl group.[3d] During the course of our studies on the platinum-catalyzed reactions using alkynyl compounds,[4] we focused on a regioselective hydration of 1-(2-propynyl)pyrroles utilizing neighboring group participation. We report herein a platinum-catalyzed hydration of 1-(2-propynyl)-2-formylpyrroles, in which various 1-(2-oxopropyl)-2-formylpyrroles can be synthesized in a regioselective manner.

RESULTS AND DISCUSSION

The initial attempts were carried out using 1-(2-propynyl)-2-formylpyrrole (**1a**) (Scheme 1). When the substrate **1a** was treated with 10 mol % of $PtCl_2$ in dioxane/H_2O (2/1) at 100 ºC for 10 min,[4a,b] the reaction successfully proceeded to afford 1-(2-oxopropyl)-2-formylpyrrole (**2a**) in 77% yield.[5] The reaction also proceeded when 10 mol % $AuCl_3$ was used as the catalyst, but the reaction time was prolonged to 10 h and the yield was decreased to 65%.

‡ This paper is dedicated to Prof. Ei-ichi Negishi on the occasion of his 77th birthday.

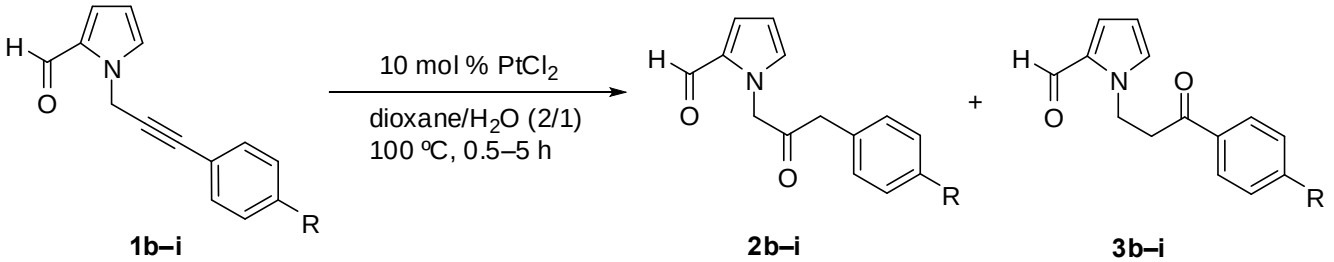


1a **2a**

catalyst	time	yield of **2a**
$PtCl_2$	10 min	77%
$AuCl_3$	10 h	65%

Scheme 1

We next attempted the reactions using various substrates **1b–1i** having an aryl group at the alkynyl position (Scheme 2). When phenyl-substituted substrate **1b** was subjected to the reaction with $PtCl_2$, the hydrated product **2b** was obtained in 82% yield together with the regioisomer **3b** in 12% yield (Table 1, entry 1). The tolyl- and *p*-methoxyphenyl-substituted substrates **1c** and **1d** were transformed to the ketones **2c** and **2d**, but considerable amount of the regioisomers **3c** and **3d** were also produced, respectively (entries 2 and 3). The reactions of **1e** and **1f**, having a fluoro and a chloro group on the aromatic ring, afforded the corresponding products **2e** and **2f** in moderate yields with good regioselectivity (entries 4 and 5). When the substrates **1g** and **1h** having an electron-withdrawing group were subjected to the reactions, the corresponding products **2g** and **2h** were obtained in low yields (entries 6 and 7). On the other hand, the reaction of the substrate **1i** which contains an ester moiety on the phenyl group successfully afforded the corresponding ketone **2i** and the regioisomer **3i** in 63% and 11% yields, respectively (entry 8). Interestingly, the observed regioselectivity for the production of **2** was contrary to the literature reports that *p*-Lewis acid-promoted hydrations of aryl-substituted alkynes prefer to add water at the RC≡*C*Ar carbon atom (R = alkyl).[6] These results imply that the reactions proceed by assisting a neighboring formyl group.



1b–i **2b–i** **3b–i**

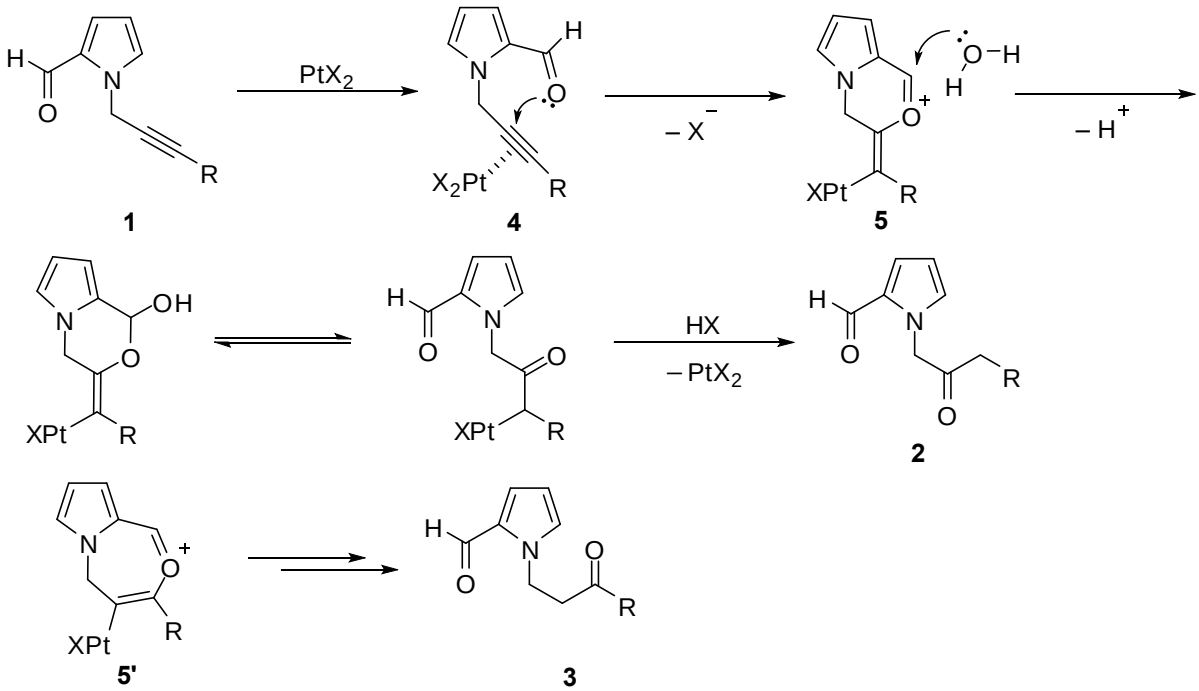
Scheme 2

Table 1. Platinum-catalyzed hydration of aryl-substituted substrates **1b–i**.

Entry	Substrate **1**	Time (h)	**2** (Yield /%)[a]	**3** (Yield /%)[a]
1	R = H (**1b**)	0.5	**2b** (82)	**3b** (12)
2	R = Me (**1c**)	2.5	**2c** (52)	**3c** (25)
3	R = OMe (**1d**)	5	**2d** (33)	**3d** (26)
4	R = F (**1e**)	1	**2e** (66)	**3e** (11)
5	R = Cl (**1f**)	2	**2f** (51)	**3f** (13)
6	R = Ac (**1g**)	1	**2g** (28)	**3g** (9)
7	R = CN (**1h**)	5	**2h** (28)	**3h** (6)
8	R = CO_2Me (**1i**)	1	**2i** (63)	**3i** (11)

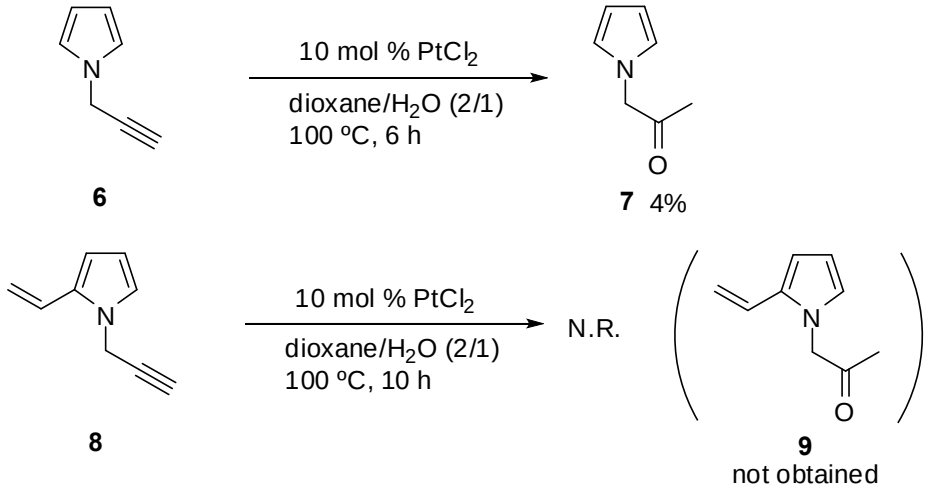
[a]Isolated yields.

A plausible mechanism for the hydration of the 1-(2-propynyl)-2-formylpyrroles **1** is shown in Scheme 3. The platinum catalyst activates the carbon-carbon triple bond in **1** by coordination as shown in **4**. Intramolecular *6-exo-dig* cyclization of the internal formyl oxygen occurs to form the cyclized intermediate **5**, which produces a ketone **2** upon hydrolysis followed by proto-demetallation process. It is expected that the regioisomers **3** are produced via the intermediate **5'**, derived from intramolecular *7-endo-dig* cyclization of **4**.



Scheme 3

Information on the reaction mechanism was gained by carrying out the reaction using formyl-free substrates (Scheme 4). When the 1-(2-propynyl)pyrrole (**6**) was subjected to the reaction, the yield of the hydrated product **7** was dramatically decreased to 4%. Furthermore, the reaction of vinyl-substituted substrate **8** did not give the corresponding product **9**. These results support the hypothesis that the reaction proceeds via the intramolecular *6-exo-dig* cyclization pathway by assisting a neighboring formyl group.



Scheme 4

In conclusion, we have developed a methodology for the synthesis of 1-(2-oxopropyl)-2-formylpyrroles by platinum-catalyzed hydration reactions. By introducing a formyl group on the pyrrole ring, regioselective hydration has been accomplished via the intramolecular *6-exo-dig* cyclization pathway. Functionalization of pyrroles is an important research area of heterocyclic chemistry for synthesizing a variety of biologically active natural products and industrially useful compounds in an efficient and selective manner.[7] Our reaction would provide a useful methodology for the selective functionalization of 1-(2-oxopropyl) pyrroles. Efforts to extend the scope of these reactions and their subsequent application to the syntheses of biologically active heterocyclic molecules are currently in progress.

EXPERIMENTAL

Solvents were dried and distilled according to standard protocols. The phrase 'residue upon workup' refers to the residue obtained when the organic layer was separated and dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure.

Starting Materials. 1-(2-Propynyl)-2-formylpyrroles **1a–1i** were prepared according to the procedures described in the literature.[8]

Typical Procedure for the Preparation of 1-(2-Propynyl)-2-formylpyrrole 1.

Synthesis of 1d: To a stirred solution of NaH (44.0 mg, 1.10 mmol) in DMF (20 mL) was added dropwise 2-formylpyrrole (95.1 mg, 1.00 mmol) in DMF (2 mL) at 0 °C and stirring was continued for 30 min at the same temperature. Then 1-(3-bromo-1-propyl)-4-methoxybenzene (247 mg, 1.10 mmol) in DMF (2 mL) was added to the solution at 0 °C. After stirring was continued for 20 min at the same temperature, the reaction mixture was quenched with water and extracted with Et_2O. The combined extracts were washed with 0.5 N HCl, and the residue upon workup was chromatographed on silica gel with hexane-AcOEt (90/10 v/v) as eluent to give 1-[3-(4-Methoxyphenyl)-2-propynyl]-2-formylpyrrole **1d** (218 mg, 91%) as a colorless solid.

1-(3-Phenyl-2-propynyl)-2-formylpyrrole (1b): Colorless plates; mp 54.2–56.3 °C (recrystallized from AcOEt-hexane); IR (KBr) 2977, 2808, 1660, 788, 754 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.43 (2H, s), 6.30 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.98 (1H, dd, *J* = 1.6 and 4.0 Hz), 7.30–7.34 (3H, m), 7.36–7.38 (1H, m), 7.44–7.47 (2H, m), 9.59 (1H, s); ^{13}C-NMR (100MHz, $CDCl_3$) δ 39.0 (CH_2), 82.7 (Cq), 86.1 (Cq), 110.0 (CH), 122.2 (Cq), 124.9 (CH), 128.3 (CH), 128.7 (CH), 130.4 (CH), 131.2 (Cq), 131.8 (CH), 179.5 (CH); HRMS (ESI) *m/z* calcd for $C_{14}H_{11}NNaO$ $[M+Na]^+$ 232.0738, found 232.0740.

1-[3-(4-Methylphenyl)-2-propynyl]-2-formylpyrrole (1c): Colorless needles; mp 44.7–45.6 °C (recrystallized from AcOEt-hexane); IR (KBr) 3133, 3039, 2933, 2812, 1660, 1509, 1405, 817, 744 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.35 (3H, s), 5.42 (2H, s), 6.29 (1H, dd, *J* = 2.8 and 4.0 Hz), 6.98 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.11–7.13 (2H, m), 7.32–7.35 (2H, m), 7.36–7.38 (1H, m), 9.58 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 21.4 (CH_3), 39.0 (CH_2), 81.9 (Cq), 86.3 (Cq), 109.9 (CH), 119.1 (Cq), 124.8 (CH), 129.1 (CH), 130.4 (CH), 131.1 (Cq), 131.7 (CH), 138.9 (CH), 179.5 (CH); HRMS (ESI) *m/z* calcd for $C_{15}H_{13}NNaO$ $[M+Na]^+$ 246.0895, found 246.0883.

1-[3-(4-Methoxyphenyl)-2-propynyl]-2-formylpyrrole (1d): Colorless needles; mp 42.4–44.6 °C (recrystallized from AcOEt-hexane); IR (KBr) 2963, 2845, 2228, 1662, 1249, 832 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.81 (3H, s), 5.41 (2H, s), 6.29 (1H, dd, *J* = 2.4 and 3.6 Hz), 6.82–6.86 (2H, m), 6.97 (1H, dd, *J* = 2.0 and 3.6 Hz), 7.37–7.40 (3H, m), 9.58 (1H, d, *J* = 0.4 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 39.1 (CH_2), 55.3 (CH_3), 81.3 (Cq), 86.1 (Cq), 109.9 (CH), 114.0 (CH), 114.3 (Cq), 124.9 (CH), 130.4 (CH), 131.2 (Cq), 133.3 (CH), 159.9 (Cq), 179.5 (CH); HRMS (ESI) *m/z* calcd for $C_{15}H_{13}NNaO_2$ $[M+Na]^+$ 262.0844, found 262.0844.

1-[3-(4-Fluorophenyl)-2-propynyl]-2-formylpyrrole (1e): Colorless needles; mp 62.4–64.1 °C (recrystallized from AcOEt-hexane); IR (KBr) 1661, 1507, 1406, 1220, 837, 746 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.41 (2H, s), 6.30 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.98 (1H, dd, *J* = 1.6 and 4.0 Hz), 6.99–7.04 (2H, m), 7.32–7.34 (1H, m), 7.40-7.45 (2H, m), 9.59 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 38.8 (CH_2), 82.5 (Cq), 84.8 (Cq), 110.0 (CH), 115.5 (CH, d, *J* = 21.4 Hz), 118.2 (Cq, d, *J* = 3.3

Hz), 124.8 (CH), 130.3 (CH), 131.1 (Cq), 133.7 (CH, d, *J* = 8.3 Hz), 162.6 (Cq, d, *J* = 248.7 Hz), 179.4 (CH); HRMS (ESI) *m/z* calcd for $C_{14}H_{10}FNNaO$ $[M+Na]^+$ 250.0644, found 250.0639.

1-[3-(4-Chlorophenyl)-2-propynyl]-2-formylpyrrole (1f): Colorless needles; mp 90.3–91.0 °C (recrystallized from AcOEt-hexane); IR (KBr) 3099, 2813, 2362, 1651, 1335, 1037, 792, 750 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.42 (2H, s), 6.30 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.98 (1H, dd, *J* = 1.6 and 4.0 Hz), 7.28–7.32 (3H, m), 7.35–7.38 (2H, m), 9.59 (1H, d, *J* = 0.8 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 38.9 (CH_2), 83.8 (Cq), 84.8 (Cq), 110.1 (CH), 120.7 (Cq), 124.9 (CH), 128.7 (CH), 130.4 (CH), 131.2 (Cq), 133.0 (CH), 134.8 (Cq), 179.6 (CH); HRMS (ESI) *m/z* calcd for $C_{14}H_{10}ClNNaO$ $[M+Na]^+$ 266.0349, found 266.0355.

1-[3-(4-Acetylphenyl)-2-propynyl]-2-formylpyrrole (1g): Thin yellow needles; mp 69.6–70.8 °C (recrystallized from AcOEt-hexane); IR (KBr) 3010, 2824, 2387, 2359, 1683, 1661, 1404, 838, 748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.60 (3H, s), 5.46 (2H, s), 6.32 (1H, dd, *J* = 2.0 and 4.0 Hz), 6.99 (1H, dd, *J* = 1.6 and 4.0 Hz), 7.30–7.32 (1H, m), 7.51–7.54 (2H, m), 7.89–7.92 (2H, m), 9.60 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 26.6 (CH_3), 38.8 (CH_2), 85.0 (Cq), 86.1 (Cq), 110.2 (CH), 124.9 (CH), 127.0 (Cq), 128.2 (CH), 130.4 (CH), 131.1 (Cq), 131.9 (CH), 136.7 (Cq), 179.6 (CH), 197.2 (Cq); HRMS (ESI) *m/z* calcd for $C_{16}H_{13}NNaO_2$ $[M+Na]^+$ 274.0844, found 274.0844.

1-[3-(4-Cyanophenyl)-2-propynyl]-2-formylpyrrole (1h): Colorless needles; mp 126.3–128.6 °C (recrystallized from AcOEt-hexane); IR (KBr) 2816, 2225, 1651, 1335, 840 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.46 (2H, s), 6.32 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.99 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.25–7.27 (1H, m), 7.51–7.53 (2H, m), 7.60–7.62 (2H, m), 9.59 (1H, d, *J* = 0.8 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 38.7 (CH_2), 84.0 (Cq), 87.4 (Cq), 110.3 (CH), 112.2 (Cq), 118.2 (Cq), 124.9 (CH), 127.1 (Cq), 130.4 (CH),131.1 (Cq), 132.0 (CH), 132.3 (CH), 179.6 (CH); HRMS (ESI) *m/z* calcd for $C_{15}H_{11}N_2O$ $[M+H]^+$ 235.0871, found 235.0865.

1-[3-(4-Methoxycarbonylphenyl)-2-propynyl]-2-formylpyrrole (1i): Colorless needles; mp 102.4–103.5 °C (recrystallized from AcOEt-hexane); IR (KBr) 2952, 2360, 1721, 1661, 1405, 1277, 1108, 786 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.92 (3H, s), 5.46 (2H, s), 6.31 (1H, dd, *J* = 2.8 and 4.0 Hz), 6.99 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.31–7.33 (1H, m), 7.49–7.52 (2H, m), 7.97–8.00 (2H, m), 9.59 (1H, d, *J* = 0.8 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 38.8 (CH_2), 52.1 (CH_3), 85.0 (Cq), 85.8 (Cq), 110.1 (CH), 124.8 (CH), 126.7 (Cq), 129.4 (CH), 129.9 (Cq), 130.3 (CH), 131.1 (Cq), 131.6 (CH), 166.2 (Cq), 179.5 (CH); HRMS (ESI) *m/z* calcd for $C_{16}H_{13}NNaO_3$ $[M+Na]^+$ 290.0793, found 290.0800.

General Procedure for Platinum–Catalyzed Hydration of 1: To a stirred solution of **1b** (50.0mg, 0.24 mmol) in dioxane/H_2O (2:1, 2 mL) was added $PtCl_2$ (6.4 mg, 0.024 mmol) at rt. After stirring was continued for 30 min at 100 °C, the resulting mixture was cooled to rt and diluted with minimum amount of Et_2O. The solution was dried over anhydrous $MgSO_4$ and filtered through a small amount of silica gel.

Concentration at reduced pressure gave the residue, which was chromatographed on silica gel with hexane-AcOEt (90/10 v/v) as eluent to give **2b** (44.5 mg, 82%) as a colorless solid and **3b** (6.7 mg, 12%) as a colorless solid.

1-(2-Oxopropyl)-2-formylpyrrole (2a): Yield 77%; colorless needles; mp 59.0–61.0 °C (recrystallized from AcOEt-hexane); IR (KBr) 1731, 1659, 1482, 1406, 762 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.23 (3H, s), 5.10 (2H, s), 6.32 (1H, dd, *J* = 2.4 and 4.4 Hz), 6.85–6.87 (1H, m), 7.00 (1H, dd, *J* = 2.0 and 4.4 Hz), 9.50 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 26.9 (CH_3), 57.9 (CH_2), 110.2 (CH), 124.6 (CH), 131.4 (Cq), 132.1 (CH), 179.7 (CH), 201.6 (Cq); HRMS (ESI) *m/z* calcd for $C_8H_9NNaO_2$ $[M+Na]^+$ 174.0531, found 174.0526.

1-(3-Phenyl-2-oxopropyl)-2-formylpyrrole (2b): Yield 82%; colorless needles; mp 66.6–69.4 °C (recrystallized from AcOEt-hexane); IR (KBr) 2929, 2807, 1734, 1659, 1405, 759 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.85 (2H, s), 5.09 (2H, s), 6.28 (1H, dd, *J* = 2.4 and 4.4 Hz), 6.77–6.79 (1H, m), 6.99 (1H, dd, *J* = 2.0 and 4.4 Hz), 7.25–7.31 (3H, m), 7.34–7.38 (2H, m), 9.49 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 47.4 (CH_2), 57.0 (CH_2), 110.2 (CH), 124.6 (CH), 127.3 (CH), 128.8 (CH), 129.6 (CH), 131.4 (Cq), 132.2 (CH), 133.0 (Cq), 179.7 (CH), 201.3 (Cq); HRMS (ESI) *m/z* calcd for $C_{14}H_{14}NO_2$ $[M+H]^+$ 228.1025, found 228.1026.

1-(3-Phenyl-3-oxopropyl)-2-formylpyrrole (3b): Yield 12%; colorless plates; mp 55.7–57.4 °C (recrystallized from AcOEt-hexane); IR (KBr) 2923, 2360, 1684, 1660, 1404, 743 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.50 (2H, t, *J* = 6.4 Hz), 4.73 (2H, t, *J* = 6.4 Hz), 6.19 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.94 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.14–7.16 (1H, m), 7.42–7.46 (2H, m), 7.54–7.58 (1H, m), 7.92–7.95 (2H, m), 9.54 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 39.7 (CH_2), 44.2 (CH_2), 109.6 (CH), 125.3 (CH), 128.1 (CH), 128.6 (CH), 131.1 (Cq), 132.9 (CH), 133.4 (CH), 136.5 (Cq), 179.2 (CH), 197.7 (Cq); HRMS (ESI) *m/z* calcd for $C_{14}H_{13}NNaO_2$ $[M+Na]^+$ 250.0844, found 250.0833.

1-[3-(4-Methylphenyl)-2-oxopropyl]-2-formylpyrrole (2c): Yield 52%; colorless needles; mp 69.9–70.8 °C (recrystallized from AcOEt-hexane); IR (KBr) 2929, 2820, 1733, 1659, 1405, 764 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.34 (3H, s), 3.80 (2H, s), 5.08 (2H, s), 6.27 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.76–6.78 (1H, m), 6.98 (1H, dd, *J* = 1.6 and 4.0 Hz), 7.13–7.16 (4H, m), 9.49 (1H, d, *J* = 0.8 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 21.0 (CH_3), 47.0 (CH_2), 56.9 (CH_2), 110.1 (CH), 124.6 (CH), 129.4 (CH), 129.5 (CH), 129.9 (Cq), 131.4 (Cq), 132.2 (CH), 137.0 (Cq), 179.7 (CH), 201.6 (Cq); HRMS (ESI) *m/z* calcd for $C_{15}H_{15}NNaO_2$ $[M+Na]^+$ 264.1000, found 264.0996.

1-[3-(4-Methylphenyl)-3-oxopropyl]-2-formylpyrrole (3c): Yield 25%; colorless needles; mp 40.5–42.7 °C (recrystallized from AcOEt-hexane); IR (KBr) 2922, 1660, 1404, 815, 759 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.39 (3H, s), 3.46 (2H, t, *J* = 6.4 Hz), 4.71 (2H, t, *J* = 6.4 Hz), 6.19 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.93 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.13–7.15 (1H, m), 7.22–7.24 (2H, m), 7.82–7.84 (2H, m),

9.54 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 21.6 (CH_3), 39.6 (CH_2), 44.3 (CH_2), 109.5 (CH), 125.3 (CH), 128.2 (CH), 129.3 (CH), 131.1 (Cq), 132.9 (CH), 134.1 (Cq), 144.2 (Cq), 179.2 (CH), 197.3 (Cq); HRMS (ESI) *m/z* calcd for $C_{15}H_{16}NO_2$ $[M+H]^+$ 242.1181, found 242.1180.

1-[3-(4-Methoxyphenyl)-2-oxopropyl]-2-formylpyrrole (2d): Yield 33%; colorless needles; mp 72.6–73.7 °C (recrystallized from AcOEt-hexane); IR (KBr) 2930, 2845, 1732, 1653, 1246, 1030, 831, 763 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.78 (2H, s), 3.80 (3H, s), 5.08 (2H, s), 6.28 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.77–6.79 (1H, m), 6.87–6.90 (2H, m), 6.98 (1H, dd, *J* = 1.6 and 4.0 Hz), 7.15–7.18 (2H, m), 9.49 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 46.5 (CH_2), 55.3 (CH_3), 56.9 (CH_2), 110.2 (CH), 114.3 (CH), 124.6 (CH), 125.0 (Cq), 130.6 (CH), 131.4 (Cq), 132.2 (CH), 158.9 (Cq), 179.7 (CH), 201.7 (Cq); HRMS (ESI) *m/z* calcd for $C_{15}H_{15}NNaO_3$ $[M+Na]^+$ 280.0950, found 280.0951.

1-[3-(4-Methoxyphenyl)-3-oxopropyl]-2-formylpyrrole (3d): Yield 26%; colorless needles; mp 71.1–72.6 °C (recrystallized from AcOEt-hexane); IR (KBr) 2966, 2926, 2852, 2816, 1660, 1600, 1256, 1170, 836, 761 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.43 (2H, t, *J* = 6.4 Hz), 3.86 (3H, s), 4.71 (2H, t, *J* = 6.4 Hz), 6.19 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.89–6.92 (2H, m), 6.93 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.13–7.15 (1H, m), 7.90–7.93 (2H, m), 9.54 (1H, d, *J* = 0.8 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 39.4 (CH_2), 44.4 (CH_2), 55.4 (CH_3), 109.5 (CH), 113.8 (CH), 125.3 (CH), 129.7 (Cq), 130.4 (CH), 131.1 (Cq), 132.9 (CH), 163.7 (Cq), 179.2 (CH), 196.2 (Cq); HRMS (ESI) *m/z* calcd for $C_{15}H_{15}NNaO_3$ $[M+Na]^+$ 280.0950, found 280.0950.

1-[3-(4-Fluorophenyl)-2-oxopropyl]-2-formylpyrrole (2e): Yield 66%: colorless needles; mp 63.8–65.6 °C (recrystallized from AcOEt-hexane); IR (KBr) 2931, 2809, 1735, 1659, 1407, 1223, 836, 765 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.82 (2H, s), 5.09 (2H, s), 6.29 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.80–6.82 (1H, m), 7.00 (1H, dd, *J* = 1.6 and 4.0 Hz), 7.01–7.06 (2H, m), 7.19–7.23 (2H, m), 9.49 (1H, d, *J* = 0.8 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 46.1 (CH_2), 57.1 (CH_2), 110.2 (CH), 115.6 (CH, d, *J* = 21.5 Hz), 124.6 (CH), 128.6 (Cq, d, *J* = 3.3 Hz), 131.2 (CH, d, *J* = 7.4 Hz), 131.3 (Cq), 132.2 (CH), 162.1 (Cq, d, *J* = 244.6 Hz), 179.7 (CH), 201.1 (Cq); HRMS (ESI) *m/z* calcd for $C_{14}H_{13}FNO_2$ $[M+H]^+$ 246.0930, found 246.0922.

1-[3-(4-Fluorophenyl)-3-oxopropyl]-2-formylpyrrole (3e): Yield 11%; colorless needles; mp 125.7–126.8 °C (recrystallized from AcOEt-hexane); IR (KBr) 2893, 2849, 1677, 1656, 1404, 1373, 852, 764 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.46 (2H, t, *J* = 6.4 Hz), 4.71 (2H, t, *J* = 6.4 Hz), 6.20 (1H, dd, *J* = 2.4 and 3.6 Hz), 6.94 (1H, dd, *J* = 2.0 and 3.6 Hz), 7.09–7.13 (3H, m), 7.95–7.98 (2H, m), 9.54 (1H, d, *J* = 0.8 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 39.7 (CH_2), 44.3 (CH_2), 109.6 (CH), 115.8 (CH, d, *J* = 22.3 Hz), 125.4 (CH), 130.7 (CH, d, *J* = 9.0 Hz), 131.1 (Cq), 132.9 (CH), 133.0 (Cq, d, *J* = 3.3 Hz), 165.9 (Cq, d, *J* = 254.4 Hz), 179.3 (CH), 196.1 (Cq); HRMS (ESI) *m/z* calcd for $C_{14}H_{13}FNO_2$ $[M+H]^+$ 246.0930, found 246.0930.

1-[3-(4-Chlorophenyl)-2-oxopropyl]-2-formylpyrrole (2f): Yield 51%; colorless needles; mp 84.5–87.3 °C (recrystallized from AcOEt-hexane); IR (KBr) 2927, 2807, 1734, 1656, 1492, 1481, 1323, 1092, 1066, 801, 760 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.81 (2H, s), 5.09 (2H, s), 6.30 (1H, dd, *J* = 2.8 and 4.4 Hz), 6.80–6.82 (1H, m), 7.00 (1H, dd, *J* = 2.0 and 4.4 Hz), 7.16–7.19 (2H, m), 7.31–7.33 (2H, m), 9.49 (1H, d, *J* = 0.8 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 46.3 (CH_2), 57.1 (CH_2), 110.3 (CH), 124.7 (CH), 128.9 (CH), 131.0 (CH), 131.3 (Cq), 131.4 (Cq), 132.2 (CH), 133.3 (Cq), 179.8 (CH), 200.8 (Cq); HRMS (ESI) *m/z* calcd for $C_{14}H_{13}ClNO_2$ $[M+H]^+$ 262.0635, found 262.0623.

1-[3-(4-Chlorophenyl)-3-oxopropyl]-2-formylpyrrole (3f): Yield 13%; colorless needles; mp 110.9–113.5 °C (recrystallized from AcOEt-hexane); IR (KBr) 2961, 2915, 1687, 1660, 1588, 1259, 1089, 1029, 801, 756 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.46 (2H, t, *J* = 6.4 Hz), 4.70 (2H, t, *J* = 6.4 Hz), 6.20 (1H, dd, *J* = 2.8 and 4.0 Hz), 6.94 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.12–7.14 (1H, m), 7.40–7.43 (2H, m), 7.85–7.89 (2H, m), 9.54 (1H, d, *J* = 0.8 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 39.7 (CH_2), 44.2 (CH_2), 109.7 (CH), 125.4 (CH), 129.0 (CH), 129.5 (CH), 131.1 (Cq), 132.9 (CH), 134.9 (Cq), 139.9 (Cq), 179.3 (CH), 196.5 (Cq); HRMS (ESI) *m/z* calcd for $C_{14}H_{13}ClNO_2$ $[M+H]^+$ 262.0635, found 262.0624.

1-[3-(4-Acetylphenyl)-2-oxopropyl]-2-formylpyrrole (2g): Yield 28%; colorless needles; mp 90.3–93.0 °C (recrystallized from AcOEt-hexane); IR (KBr) 1735, 1681, 1656, 1407, 1268, 761 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.60 (3H, s), 3.91 (2H, s), 5.11 (2H, s), 6.30 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.81–6.83 (1H, m), 7.01 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.33–7.35 (2H, m), 7.92–7.95 (2H, m), 9.50 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 26.6 (CH_3), 46.8 (CH_2), 57.3 (CH_2), 110.3 (CH), 124.7 (CH), 128.7 (CH), 129.9 (CH), 131.4 (Cq), 132.2 (CH), 136.2 (Cq), 138.3 (Cq), 179.8 (CH), 197.6 (Cq), 200.4 (Cq); HRMS (ESI) *m/z* calcd for $C_{16}H_{15}NNaO_3$ $[M+Na]^+$ 292.0950, found 292.0942.

1-[3-(4-Acetylphenyl)-3-oxopropyl]-2-formylpyrrole (3g): Yield 9%; colorless needles; mp 75.0–77.6 °C (recrystallized from AcOEt-hexane); IR (KBr) 1684, 1658, 1403, 1263, 792 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.63 (3H, s), 3.52 (2H, t, *J* = 6.4 Hz), 4.72 (2H, t, *J* = 6.4 Hz), 6.21 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.95 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.13–7.15 (1H, m), 8.01 (4H, s), 9.54 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 26.8 (CH_3), 40.1 (CH_2), 44.2 (CH_2), 109.7 (CH), 125.4 (CH), 128.3 (CH), 128.5 (CH), 131.2 (Cq), 132.9 (CH), 139.6 (Cq), 140.4 (Cq), 179.3 (CH), 197.2 (Cq), 197.3 (Cq); HRMS (ESI) *m/z* calcd for $C_{16}H_{15}NNaO_3$ $[M+Na]^+$ 292.0950, found 292.0950.

1-[3-(4-Cyanophenyl)-2-oxopropyl]-2-formylpyrrole (2h): Yield 28%; brown needles; mp 157.3–159.8 °C (recrystallized from AcOEt-hexane); IR (KBr) 2981, 2847, 2227, 1714, 1646, 1477, 839 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.92 (2H, s), 5.12 (2H, s), 6.32 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.84–6.86 (1H, m), 7.02 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.33–7.35 (2H, m), 7.62–7.64 (2H, m), 9.49 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 46.5 (CH_2), 57.4 (CH_2), 110.4 (CH), 111.3 (Cq), 118.6 (Cq), 124.8 (CH), 130.6 (CH), 131.3 (Cq), 132.2 (CH), 132.3 (CH), 138.3 (Cq), 179.8 (CH), 199.9 (Cq);

HRMS (ESI) *m/z* calcd for $C_{15}H_{13}N_2O_2$ $[M+H]^+$ 253.0977, found 253.0985.

1-[3-(4-Cyanophenyl)-3-oxopropyl]-2-formylpyrrole (3h): Yield 6%; colorless needles; mp 123.9–125.8 °C (recrystallized from AcOEt-hexane); IR (KBr) 3095, 2922, 2225, 1687, 1650, 1402, 765 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.51 (2H, t, *J* = 6.4 Hz), 4.71 (2H, t, *J* = 6.4 Hz), 6.21 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.96 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.11–7.13 (1H, m), 7.74–7.76 (2H, m), 8.01–8.03 (2H, m), 9.54 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 40.1 (CH_2), 44.1 (CH_2), 109.8 (CH), 116.8 (Cq), 117.8 (Cq), 125.5 (CH), 128.5 (CH), 131.2 (Cq), 132.6 (CH), 132.9 (CH), 139.4 (Cq), 179.4 (CH), 196.5 (Cq); HRMS (ESI) *m/z* calcd for $C_{15}H_{13}N_2O_2$ $[M+H]^+$ 253.0977, found 253.0981.

1-[3-(4-Methoxycarbonylphenyl)-2-oxopropyl]-2-formylpyrrole (2i): Yield 63%; colorless needles; mp 117.6–118.4 °C (recrystallized from AcOEt-hexane); IR (KBr) 2942, 1722, 1656, 1285, 851, 761, 746 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.90 (2H, s), 3.91 (3H, s), 5.10 (2H, s), 6.29 (1H, dd, *J* = 2.4 and 4.0 Hz), 6.79–6.81 (1H, m), 7.00 (1H, dd, *J* = 1.6 and 4.0 Hz), 7.30–7.32 (2H, m), 8.00–8.02 (2H, m), 9.50 (1H, d, *J* = 1.2 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 46.9 (CH_2), 52.0 (CH_3), 57.2 (CH_2), 110.3 (CH), 124.7 (CH), 129.2 (Cq), 129.7 (CH), 129.9 (CH), 131.3 (Cq), 132.2 (CH), 138.1 (Cq), 166.7 (Cq), 179.7 (CH), 200.3 (Cq); HRMS (ESI) *m/z* calcd for $C_{16}H_{16}NO_4$ $[M+H]^+$ 286.1079, found 286.1083.

1-[3-(4-Methoxycarbonylphenyl)-3-oxopropyl]-2-formylpyrrole (3i): Yield 11%; colorless needles; mp 94.1–95.8 °C (recrystallized from AcOEt-hexane); IR (KBr) 1720, 1682, 1657, 1404, 1280, 749 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.52 (2H, t, *J* = 6.4 Hz), 3.94 (3H, s), 4.72 (2H, t, *J* = 6.4 Hz), 6.20 (1H, dd, *J* = 2.0 and 4.0 Hz), 6.95 (1H, dd, *J* = 2.0 and 4.0 Hz), 7.12–7.14 (1H, m), 7.96–7.98 (2H, m), 8.08–8.11 (2H, m), 9.54 (1H, d, *J* = 0.8 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 40.1 (CH_2), 44.1 (CH_2), 52.4 (CH_3), 109.7 (CH), 125.4 (CH), 128.0 (CH), 129.9 (CH), 131.1 (Cq), 132.9 (CH), 134.2 (Cq), 139.6 (Cq), 166.1 (Cq), 179.3 (CH), 197.3 (Cq); HRMS (ESI) *m/z* calcd for $C_{16}H_{16}NO_4$ $[M+H]^+$ 286.1079, found 286.1082.

1-(2-Oxopropyl)-1*H*-pyrrole (7): Brown oil; IR (neat) 2925, 2854, 1732, 1463, 1377 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.06 (3H, s), 4.61 (2H, s), 6.24 (2H, t, *J* = 2.0 Hz), 6.61 (2H, t, *J* = 2.0 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 26.3 (CH_3), 59.1 (CH_2), 109.5 (CH), 121.6 (CH), 204.1 (Cq); HRMS (ESI) *m/z* calcd for C_7H_9NONa $[M+Na]^+$ 146.0582, found 146.0587.

1-(2-Propynyl)-2-vinyl-1*H*-pyrrole (8): According to the same procedure described for the synthesis of **1d**, **8** was prepared from 2-vinylpyrrole with propargyl bromide. Yellow oil; IR (neat) 2925, 2853, 2360, 1457 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.40 (1H, t, *J* = 2.4 Hz), 4.67 (2H, d, *J* = 2.4 Hz), 5.10 (1H, dd, *J* = 1.6 and 11.2 Hz), 5.52 (1H, dd, *J* = 1.2 and 17.2 Hz), 6.14 (1H, t, *J* = 3.2 Hz), 6.39 (1H, dd, *J* = 2.0 and 4.0 Hz), 6.64 (1H, dd, *J* = 11.2 and 17.2 Hz), 6.75–6.76 (1H, m); ^{13}C-NMR (100MHz, $CDCl_3$) δ 36.4 (CH_2), 73.5 (Cq), 78.1 (CH), 107.3 (CH), 108.6 (CH), 112.0 (CH_2), 122.0 (CH), 125.0 (CH), 131.6 (Cq); HRMS (ESI) *m/z* calcd for C_9H_9NNa $[M+Na]^+$ 154.0633, found 154.0629.

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