Supporting information for

A Mild Two-Step Propargylation of Aromatic Bioactive Small Molecules

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1. General procedure

All reactions were carried out under an argon atmosphere with dehydrated solvents under anhydrous conditions, unless otherwise noted. Dehydrated THF and CH$_2$Cl$_2$ were purchased from Kanto Chemical Co., Inc. Other solvents were dehydrated and distilled according to standard protocols. Reagents were obtained from commercial suppliers, unless otherwise noted. Reactions were monitored by thin-layer chromatography (TLC) carried out on Silica gel plates (Merck). Column chromatography was performed on Silica gel 60N (Kanto Chemical Co., Inc., spherical, neutral, 63-210 µm) or (Kanto Chemical Co., Inc., spherical, neutral, 40-50 µm). High performance column chromatography was performed on Mightysil Si60 250-20 mm (Kanto Chemical Co., Inc., spherical, neutral, 5 µm). IR spectra were recorded on a JASCO FT/IR-410 Fourier Transform Infrared Spectrophotometer. $^1$H-NMR (400 and 600 MHz) and $^{13}$C-NMR spectra (100 and 150 MHz) were recorded on JEOL JNM-AL-400 and JEOL JNM-ECA-600 spectrometers, respectively. For $^1$H-NMR spectra, chemical shifts (δ) are given from TMS (0.00 ppm) or CHCl$_3$ (7.26 ppm) in CDCl$_3$, CHD$_2$COCD$_3$ (2.05 ppm) in CD$_3$COCD$_3$ and CHD$_2$SOCD$_3$ (2.50 ppm) in CD$_3$SOCD$_3$ as internal standards. For $^{13}$C-NMR spectra, chemical shifts (δ) are given from CDCl$_3$ (77.0 ppm), CD$_3$COCD$_3$ (29.84 ppm and 206.26 ppm) and CD$_3$SOCD$_3$ (39.52 ppm) as internal standards. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd, = double doublet, ddt = double double triplet, m = multiplet, br = broad. EI mass spectra were recorded on JEOL JMS-DX303, JEOL JMS-700 and JEOL JMS-T 100 GC. FAB mass spectra were recorded on JEOL JMS-700. ESI mass spectra were recorded on Thermo Scientific Exactive Mass Spectrometer. HPLC was performed on Gilson Model 305 and 306 as pumps and Gilson Model 118 as a UV detector (254 nm) using Mightysil Si60 φ20-250 mm (Kanto Chemical Co., Inc., spherical, neutral, 5 µm).. Microwave irradiation was performed by using a Discover$^\text{TM}$ system (CEM Japan Inc).
2. Synthesis of complex 1a

Synthesis of (prop-2-yn-1-ol)dicobalt hexacarbonyl (S1)

A mixture of prop-2-yn-1-ol (0.90 mL, 15.6 mmol) and Co₂(CO)₈ (5.22 g, 15.6 mmol) in CH₂Cl₂ (38 mL) was stirred at room temperature for 5 h. The solution was concentrated in vacuo. Column chromatography of the residue on silica gel (EtOAc / Hexane = 1 / 4) yielded cobalt complex S₁ as a red solid (4.76 g, 13.9 mmol, 93%).

Synthesis of hexacarbonyl(2-propynylium)dicobalt tetrafluoroborate (1a)

To a solution of HBF₄•Et₂O (1.10 mL, 6.99 mmol) in Et₂O (6.0 mL) was added a solution of cobalt complex S₁ (798 mg, 2.33 mmol) in Et₂O (5.5 mL) dropwise over 15 min. The resulting mixture was stirred at room temperature for 2 h, causing precipitation of a red solid. The solid was filtered and rinsed three times with ether to remove fluoroboric acid. After vacuum drying, complex 1a was obtained as a fine red powder (828 mg, 2.01 mmol, 86%).

3. Synthesis of ammonium complex S2

To a suspension of complex 1a (100 mg, 0.243 mmol) in CH₂Cl₂ (4.0 mL) was added Et₃N (2.0 ml). The reaction mixture was stirred at room temperature for 1 h and then concentrated in vacuo. The residue was purified by silica gel column chromatography (MeOH : CHCl₃ = 1 : 4) to give complex S2 (74.5 mg, 0.145 mmol, 60%) as a red amorphous.

S2: red amorphous; IR (neat): 2055 cm⁻¹; ¹H-NMR (400 MHz, CD₃COCD₃): δ 7.06 (s, 1H), 5.22 (s, 2H), 3.69 (q, J = 7.1 Hz, 6H), 1.47 (t, J = 7.1 Hz, 9H); ¹³C-NMR (100 MHz, CD₃COCD₃): δ 199.7, 77.2, 75.7, 60.6, 53.6, 8.1; HRMS (ESI): calcd for C₁₅H₁₈NO₆Co₂ (M⁺): 425.9793, found: 425.9778.
4. Preparation of substrate 10

\[
\begin{align*}
\text{MeO} & \quad \text{H} & \quad \text{Cbz} \\
\text{MeO} & \quad \text{MeO} & \quad \text{S3} & \quad \text{H} & \quad \text{Cbz} \\
\text{MeO} & \quad \text{MeO} & \quad \text{MeO} & \quad \text{S3} & \quad \text{H} & \quad \text{Cbz} \\
\text{MeO} & \quad \text{MeO} & \quad \text{MeO} & \quad \text{MeO} & \quad \text{S3} & \quad \text{H} & \quad \text{Cbz}
\end{align*}
\]

To a solution of carbamate \( \text{S3}^2 \) (1.00 g, 3.17 mmol) in THF (16 mL) was added 60% NaH (387 mg, 9.68 mmol) at 0 °C and the resulting mixture was stirred for 30 min at room temperature. Then the reaction mixture was cooled at 0 °C and MeI (0.5 mL, 0.80 mmol) was added. The reaction mixture was allowed to warm to room temperature and stirred for 3.5 h. The reaction was quenched with sat. NH\(_4\)Cl (5 mL) and extracted with Et\(_2\)O (20 mL \times 2). The combined organic layers were washed with brine, dried over Mg\(_2\)SO\(_4\), filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt : Hexane = 1:1) to give \( \text{10} \) (998 mg, 3.03 mm, 95%) as a yellow oil.

10: yellow oil; IR (neat): 1701 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CD\(_3\)SOCD\(_3\)): \( \delta \) 7.37-7.29 (m, 5H), 6.84 (d, \( J = 8.0 \) Hz, 1H), 6.77 (d, \( J = 1.7 \) Hz, 1H), 6.79 (dd, \( J = 8.0 \) Hz, 1.7 Hz, 1H), 5.04 (s, 2H), 3.73 (s, 3H), 3.72 (s, 3H), 3.46 (t, \( J = 7.2 \) Hz, 2H), 2.83 (s, 3H), 2.73 (t, \( J = 7.2 \) Hz, 2H); \(^{13}\)C-NMR (100 MHz, CD\(_3\)SOCD\(_3\)): \( \delta \) 154.9, 148.8, 147.4, 136.7, 131.4, 127.7, 127.1, 126.8, 120.4, 113.3, 112.7, 65.6, 55.6, 55.5, 49.5, 33.7, 32.6; HRMS (ESI): calcd for C\(_{19}\)H\(_{23}\)NO\(_4\)Na ([M+Na]\(^+\)): 352.1519, found 352.1505.

5. Functionalization of aromatic bioactive small molecules

General procedure for the functionalization of aromatic bioactive small molecules

**Procedure A:** To a suspension of complex \( \text{1a} \) (0.150 mmol) and Cs\(_2\)CO\(_3\) (1.0 mmol) in CH\(_2\)Cl\(_2\) (1.0 mL) was added neat substrate (0.100 mmol) or a solution of substrate (0.100 mmol) in CH\(_2\)Cl\(_2\) (1.0 mL) at -20 °C or 0 °C. The solution was allowed to warm to 0 °C or room temperature and stirred until completion of the reaction as monitored by TLC. The reaction mixture was diluted with water (2.0 mL) and extracted with CH\(_2\)Cl\(_2\) (4.0 mL \times 2). The combined organic layers were dried over MgSO\(_4\), filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography or HPLC.

**Procedure B:** The suspension of complex \( \text{1a} \) (0.150 mmol), Cs\(_2\)CO\(_3\) (0.100 mmol) and substrate (0.100 mmol) in CH\(_2\)Cl\(_2\) (2.0 mL) was heated at 40 °C by microwave irradiation. After reaction was complete, the mixture was diluted with water (2.0 mL) and extracted with CH\(_2\)Cl\(_2\) (4.0 mL \times 2). The combined organic layers were dried over MgSO\(_4\), filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography.
Functionalization of estrone 3-methyl ether (2)

The procedure A was followed with a reaction time of 30 min at room temperature to provide a mixture (57.8 mg) of 3 (0.0451 mmol, 45%), 4 (0.0397 mmol, 40%) and 5 (6.60 µmol, 7%). The product ratio was determined by $^1$H-NMR. The analytical samples were obtained by HPLC separation (AcOEt : Hexane = 15 : 85, 9 mL/min).

3 (retention time: 13.5 min): red oil; IR (neat): 2018 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$): δ 7.07 (s, 1H), 6.57 (s, 1H), 6.00 (s, 1H), 4.07 (s, 2H), 3.79 (s, 3H), 2.89-2.86 (m, 2H), 2.50 (dd, $J = 19.1$ Hz, 8.5 Hz, 1H), 2.40-2.37 (m, 1H), 2.23-1.95 (m, 4H), 1.64-1.36 (m, 6H), 0.91 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$): δ 221.0, 199.9, 155.0, 136.4, 131.5, 127.6, 126.0, 110.6, 98.4, 73.7, 54.8, 50.4, 48.0, 43.8, 43.8, 35.9, 33.9, 31.6, 29.6, 26.6, 25.8, 21.6, 13.8; HRMS (ESI): calcd for C$_{28}$H$_{27}$O$_8$Co$_2$ ([M+H]$^+$): 609.0364, found: 609.0361.

4 (retention time: 14.3 min): red oil; IR (neat): 2014 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$): δ 7.19 (d, $J = 8.8$ Hz, 1H), 6.71 (d, $J = 8.8$ Hz, 1H), 5.94 (s, 1H), 4.26 (d, $J = 15.1$ Hz, 1H), 4.14 (d, $J = 15.1$ Hz, 1H), 3.81 (s, 3H), 3.06 (dd, $J = 16.7$ Hz, 5.8 Hz, 1H), 2.93-2.84 (m, 1H), 2.51 (dd, $J = 18.5$ Hz, 8.8 Hz, 1H), 2.39 (br s, 1H), 2.27 (br s, 1H), 2.20-2.05 (m, 4H), 1.66-1.40 (m, 6H), 0.90 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$): δ 220.9, 199.8, 155.0, 135.5, 132.5, 126.7, 124.8, 107.8, 95.9, 73.6, 54.7, 50.5, 47.9, 44.2, 37.7, 35.9, 31.6, 29.8, 27.0, 26.5, 26.1, 21.6, 13.8; HRMS (ESI): calcd for C$_{28}$H$_{26}$O$_8$Co$_2$Na ([M+Na]$^+$): 631.0184, found: 631.0184.

5 (retention time: 11.7 min): red oil; IR (neat): 2017 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$): δ 7.18 (s, 1H), 6.09 (s, 1H), 5.92 (s, 1H), 4.19 (s, 2H), 4.17 (s, 2H), 3.81 (s, 3H), 3.02 (dd, $J = 17.1$ Hz, 5.4 Hz, 1H), 2.90-2.81 (m, 1H), 2.51 (dd, $J = 18.4$ Hz, 8.6 Hz, 1H), 2.36 (br s, 1H), 2.21-2.04 (m, 4H), 1.97 (d, $J = 9.6$ Hz, 1H), 1.65-1.43 (m, 6H), 0.88 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$): δ 220.7, 199.7, 154.3, 136.4, 134.8, 131.9, 130.2, 126.5, 96.2, 95.2, 74.2, 61.4, 50.5, 47.9, 44.3, 37.4, 35.9, 34.7, 31.6, 31.2, 27.0, 26.4, 25.9, 21.6, 13.7; HRMS (ESI): calcd for C$_{37}$H$_{27}$O$_{14}$Co$_4$ ([M-H]$^-$): 930.8723, found: 930.8743.
Functionalization of mestranol (6) using 2,6-di-tert-butylpyridine as a base

The procedure A was followed, employing 2,6-di-tert-butylpyridine instead of Cs$_2$CO$_3$ as a base, with a reaction time of 30 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 20) to provide 7 (36.7 mg, 0.0579 mmol, 58%) and recovered 6 (11.2 mg, 0.0361 mmol, 36%).

7: red oil; IR (neat): 2033 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.21 (d, $J = 8.6$ Hz, 1H), 6.71 (dd, $J = 8.6$ Hz, 2.6 Hz, 1H), 6.63 (d, $J = 2.6$ Hz, 1H), 5.99 (s, 1H), 4.86 (d, $J = 13.0$ Hz, 1H), 4.72 (d, $J = 13.0$ Hz, 1H), 3.78 (s, 3H), 2.85-2.84 (m, 2H), 2.63 (s, 1H), 2.32-2.24 (m, 3H), 2.12-2.02 (m, 2H), 1.99-1.77 (m, 4H), 1.51-1.35 (m, 4H), 0.93 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 199.7, 157.4, 137.9, 132.6, 126.4, 113.8, 111.5, 93.3, 85.7, 84.8, 76.1, 70.8, 65.8, 55.2, 49.4, 47.8, 43.5, 39.2, 36.7, 33.9, 29.8, 27.3, 26.5, 22.9, 12.8; HRMS (FAB): calcd for C$_{30}$H$_{29}$O$_8$Co$_2$ ([M+H]$^+$): 635.0526, found: 635.0537.

Functionalization of mestranol (6) using Cs$_2$CO$_3$ as a base

The procedure A was followed with a reaction time of 30 min to provide a mixture (35.4 mg) of 8 (0.0260 mmol, 26%), 9 (0.0237 mmol, 24%) and recovered 6 (0.0148 mmol, 15%), and a mixture (4.50 mg) of 7 (<1.58 µmol, <2%), S4 (<0.689 µmol, <1%) and S5 (<0.896 µmol, <1%) containing unseparable and unknown byproduct. The ratio was determined by $^1$H-NMR. In this case, 1.2 equivalent of 1a was added.

The analytical samples were obtained by extensive silica gel column chromatography separation (AcOEt : hexane = 1 : 8 to 1 : 4).
8: red oil; IR (neat): 2018 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.07 (s, 1H), 6.56 (s, 1H), 5.99 (s, 1H), 4.07 (s, 2H), 3.79 (s, 3H), 2.83 (br s, 2H), 2.60 (s, 1H), 2.37-2.30 (m, 2H), 2.20 (br s, 1H), 2.04-1.99 (m, 1H), 1.95-1.67 (m, 5H), 1.53-1.33 (m, 4H), 0.88 (s, 3H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta\) 199.9, 154.9, 136.6, 132.0, 127.7, 125.9, 110.5, 98.5, 87.5, 79.9, 74.0, 73.7, 54.7, 49.4, 47.1, 43.4, 39.4, 39.0, 34.0, 32.8, 29.7, 27.3, 26.3, 22.8, 12.6; HRMS (ESI): calcd for C\(_{30}\)H\(_{27}\)O\(_8\)Co\(_2\) ([M-H]-): 633.0364, found: 633.0394.

9: red oil; IR (neat): 2018 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.20 (d, \(J\) = 8.7 Hz, 1H), 6.70 (d, \(J\) = 8.7 Hz, 1H), 5.93 (s, 1H), 4.24 (d, \(J\) = 15.0 Hz, 1H), 4.13 (d, \(J\) = 15.0 Hz, 1H), 3.80 (s, 3H), 3.01 (d, \(J\) = 16.8 Hz, 1H), 2.88-2.79 (m, 1H), 2.60 (br s, 1H), 2.35 (br s, 2H), 2.24 (br s, 1H), 2.06-1.67 (m, 6H), 1.53-1.29 (m, 4H), 0.87 (s, 3H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta\) 199.8, 154.9, 135.7, 132.9, 126.6, 124.8, 107.7, 96.0, 87.5, 79.9, 74.0, 73.7, 54.7, 49.5, 47.0, 43.8, 39.0, 38.7, 32.7, 29.8, 27.2, 27.1, 26.6, 22.8, 12.6; HRMS (ESI): calcd for C\(_{30}\)H\(_{27}\)O\(_8\)Co\(_2\) ([M-H]-): 633.0364, found: 633.0388.

A 1 : 1 mixture of S\(_4\) and S\(_5\): red oil; IR (neat): 2019 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.18 (d, \(J\) = 8.7 Hz, 0.5H), 7.07 (s, 0.5H), 6.70 (d, \(J\) = 8.7 Hz, 0.5H), 6.55 (s, 0.5H), 6.00 (s, 1.5H), 5.93 (s, 0.5H), 4.86 (d, \(J\) = 13.0 Hz, 1H), 4.72 (d, \(J\) = 13.0 Hz, 1H), 4.24 (d, \(J\) = 14.7 Hz, 0.5H), 4.13 (d, \(J\) = 14.7 Hz, 0.5H), 4.07 (s, 1H), 3.80 (s, 1.5H), 3.79 (s, 1.5H), 3.02-2.98 (m, 0.5H), 2.88-2.82 (m, 1.5H), 2.63 (s, 1H), 2.33-2.24 (m, 3H), 2.21-1.99 (m, 3H), 1.88-1.74 (m, 4H), 1.53-1.33 (m, 4H), 0.93 (s, 1.5H), 0.92 (s, 1.5H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta\) 199.9, 154.87, 154.86, 154.86, 135.7, 133.0, 132.1, 127.7, 126.6, 125.8, 124.8, 110.5, 107.7, 98.5, 96.0, 93.3, 85.70, 85.67, 84.9, 84.8, 76.1, 73.7, 70.8, 65.8, 54.75, 54.71, 49.48, 49.42, 47.8, 47.7, 43.8, 43.4, 39.2, 38.5, 36.7, 34.0, 29.7, 27.3, 27.2, 26.7, 26.4, 22.9, 12.8; HRMS (FAB): calcd for C\(_{36}\)H\(_{30}\)O\(_{11}\)Co\(_4\) ([M-3CO]+): 873.9116, found: 873.9118.

**Functionalization of benzyl (3,4-dimethoxyphenethyl)(methyl)carbamate (10)**

The procedure A was followed with a reaction time of 30 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 8 to 1 : 2) to provide \(10a\) (45.5 mg, 0.0697 mmol, 70%) and \(10b\) (3.09 mg, 4.73 \(\mu\)mol, 5%).

\(10a\) (a mixture of two rotamers): red oil; IR (neat): 2018 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.35-7.30 (m, 5H), 6.72 (s, 0.5H), 6.67 (s, 1H), 6.52 (s, 0.5H), 6.07 (s, 0.5H), 5.95 (s, 0.5H), 5.13 (s, 1H), 5.10 (s, 1H), 4.13 (s, 1H), 3.97 (s, 1H), 3.86 (s, 3H), 3.82 (s, 1.5H), 3.74 (s,
1.5H), 3.45 (br s, 2H), 2.93-2.84 (m, 5H); 13C-NMR (100 MHz, CDCl3): δ 199.8, 156.3, 148.5, 147.9, 137.1, 136.9, 131.2, 131.0, 128.8, 128.7, 128.2, 128.0, 113.7, 113.1, 97.4, 97.2, 73.6, 67.5, 67.2, 56.2, 56.0, 51.2, 50.8, 37.1, 36.8, 35.3, 34.8, 31.4, 30.9; HRMS (EI): calcd for C22H25NO4Co2 ([M-6CO]+): 485.0448, found: 485.0462.

10b (a mixture of two rotamers): red oil; IR (neat): 2019 cm⁻¹; 1H-NMR (600 MHz, CDCl3): δ 7.38-7.32 (m, 5H), 6.89 (d, J = 8.2 Hz, 0.5H), 6.79-6.73 (m, 1.5H), 5.98 (s, 0.5H), 5.88 (s, 0.5H), 5.12 (s, 1H), 5.11 (s, 1H), 4.23 (s, 1H), 4.06 (s, 1H), 3.85 (s, 2H), 3.82 (s, 4H), 3.44 (t, J = 7.6 Hz, 2H), 2.93 (s, 3H), 2.90-2.84 (m, 2H); 13C-NMR (150 MHz, CDCl3): δ 199.7, 156.0, 151.4, 147.4, 137.0, 136.8, 132.8, 132.5, 129.7, 129.6, 128.5, 128.0, 127.9, 127.8, 125.0, 111.5, 111.4, 95.9, 95.6, 73.8, 67.2, 67.0, 60.3, 55.8, 51.2, 50.6, 35.0, 34.5, 31.4, 30.9, 30.6; HRMS (ESI) C28H25Co2O10NNa ([M+Na]+) calcd for 676.0035, found: 676.0017.

Functionalization of indometacin methyl ester (11)

The procedure A was followed with a reaction time of 30 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 25) to provide 11a (35.6 mg, 0.0511 mmol, 51%) and 11b (10.2 mg, 0.0146 mmol, 15%).

11a: red oil; IR (neat): 2020 cm⁻¹; 1H-NMR (400 MHz, CDCl3): δ 7.63 (d, J = 7.8 Hz, 2H), 7.45 (d, J = 7.8 Hz, 2H), 6.90 (d, J = 9.0 Hz, 1H), 6.64 (d, J = 9.0 Hz, 1H), 5.91 (s, 1H), 4.55 (s, 2H), 3.90 (s, 3H), 3.83 (s, 3H), 3.70 (s, 3H), 2.37 (s, 3H); 13C-NMR (100 MHz, CDCl3): δ 199.9, 171.7, 168.3, 152.9, 139.5, 137.2, 133.9, 131.7, 131.3, 129.1, 128.2, 119.4, 113.3, 111.6, 106.9, 96.7, 73.2, 55.6, 52.2, 31.3, 29.5, 13.2; HRMS (ESI): calcd for C29H21NO10ClCo2 ([M+H]+): 695.9513, found: 695.9503.

11b: red oil; IR (neat): 2019 cm⁻¹; 1H-NMR (400 MHz, CDCl3): δ 7.66 (d, J = 8.3 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H), 6.91 (s, 1H), 6.90 (s, 1H), 5.89 (s, 1H), 4.03 (s, 2H), 3.88 (s, 3H), 3.68 (s, 3H), 3.67 (s, 2H), 2.33 (s, 3H); 13C-NMR (100 MHz, CDCl3): δ 199.7, 171.3, 168.4, 153.8, 139.3, 135.2, 131.1, 134.1, 130.3, 129.5, 129.1, 125.1, 116.0, 112.6, 99.1, 97.9, 73.7, 55.1, 52.1, 34.6, 30.3, 13.4; HRMS (ESI): calcd for C29H20NO10ClCo2Na ([M+Na]+): 717.9332, found: 717.9320.
Functionalization of naproxen methyl ester (12)

![Functionalization of naproxen methyl ester (12)](image)

The procedure A was followed with a reaction time of 30 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 12) to provide 12a (52.6 mg, 0.0925 mmol, 93%).

12a: red oil; IR (neat): 2019 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.90 (d, \(J = 8.9\) Hz, 1H), 7.75 (d, \(J = 9.9\) Hz, 1H), 7.68 (s, 1H), 7.48 (d, \(J = 8.9\) Hz, 1H), 7.24 (d, \(J = 9.9\) Hz, 1H), 5.91 (s, 1H), 4.61 (s, 2H), 3.96 (s, 3H), 3.87 (q, \(J = 7.1\) Hz, 1H), 3.68 (s, 3H), 1.59 (d, \(J = 7.1\) Hz, 3H); \(^13\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta\) 199.7, 175.1, 154.0, 135.3, 131.8, 129.1, 128.8, 126.8, 126.4, 123.7, 121.1, 112.7, 96.2, 73.5, 55.6, 52.0, 45.2, 29.0, 18.5; HRMS (EI): calcd for C\(_{19}\)H\(_{18}\)O\(_4\)Co\(_2\): [M-5CO]+: 427.9869, found: 427.9864.

Functionalization of compound 13

![Functionalization of compound 13](image)

The procedure A was followed with a reaction time of 30 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 2) to provide 13a (49.2 mg, 0.0758 mmol, 76%).

13a: red oil; IR (neat): 2018 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.18 (s, 1H), 7.76 (d, \(J = 8.7\) Hz, 1H), 7.35 (d, \(J = 8.7\) Hz, 1H), 7.08 (s, 2H), 7.06 (s, 1H), 6.04 (s, 1H), 4.29 (s, 2H), 3.94 (s, 3H), 3.89 (s, 6H), 3.82 (s, 3H); \(^13\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta\) 199.6, 196.4, 152.8, 141.4, 139.2, 134.2, 129.1, 128.6, 126.9, 124.3, 122.7, 116.0, 108.9, 107.6, 97.8, 73.5, 60.9, 56.3, 32.9, 29.9; HRMS (ESI): calcd for C\(_{28}\)H\(_{22}\)NO\(_{10}\)Co\(_2\): [M+H]+: 649.9902, found: 649.9902.

Functionalization of rotenone (14)

![Functionalization of rotenone (14)](image)

The procedure A was followed with a reaction time of 30 min. The crude product was...
purified by HPLC (AcOEt : hexane = 3 : 7, 9 mL/min) to provide 14a (18.9 mg, 0.0261 mmol, 26%) and 14b (2.11 mg, 2.02 µmol, 2%).

14a (retention time: 10.8 min): red oil; IR (neat): 2017 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ 7.83 (d, J = 8.4 Hz, 1H), 6.78 (s, 1H), 6.51 (d, J = 8.4 Hz, 1H), 6.00 (s, 1H), 5.28 (dd, J = 9.9 Hz, 8.0 Hz, 1H), 5.09 (s, 1H), 4.95-4.93 (m, 2H), 4.66 (dd, J = 11.9 Hz, 2.9 Hz, 1H), 4.17 (d, J = 11.9 Hz, 1H), 4.14 (s, 2H), 3.85 (d, J = 3.9 Hz, 1H), 3.83 (s, 3H), 3.74 (s, 3H), 3.32 (dd, J = 15.7 Hz, 9.9 Hz, 1H), 3.01 (dd, J = 15.7 Hz, 8.0 Hz, 1H), 1.78 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃): δ 199.9, 188.8, 167.3, 158.0, 147.7, 147.2, 145.1, 143.0, 130.0, 122.3, 113.4, 112.8, 112.6, 110.8, 109.0, 104.8, 96.6, 87.8, 73.6, 72.1, 65.9, 60.5, 56.4, 45.0, 31.3, 27.6, 17.1; HRMS (ESI): calcd for C₃₂H₂₅O₁₂Co₂ ([M+H]+): 719.0005, found: 718.9995.

14b (retention time: 8.8 min): red oil; IR (neat): 2018 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ 7.73 (s, 1H), 6.73 (s, 1H), 6.03 (s, 1H), 5.99 (s, 1H), 5.29 (t, J = 9.2 Hz, 1H), 5.11 (s, 1H), 4.98 (s, 1H), 4.91-4.89 (m, 1H), 4.64 (dd, J = 11.8 Hz, 3.1 Hz, 1H), 4.17 (d, J = 12.1 Hz, 1H), 4.14 (s, 2H), 4.07 (d, J = 15.5 Hz, 1H), 3.98 (d, J = 15.5 Hz, 1H), 3.83 (s, 4H), 3.72 (s, 3H), 3.32 (dd, J = 15.9 Hz, 9.7 Hz, 1H), 3.04 (dd, J = 15.8 Hz, 8.4 Hz, 1H), 1.81 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃): δ 199.8, 188.8, 165.3, 157.1, 147.7, 147.1, 145.1, 142.8, 129.8, 122.3, 117.5, 113.3, 113.03, 112.98, 110.8, 96.7, 96.2, 88.1, 73.67, 73.63, 72.2, 65.9, 60.6, 56.3, 45.1, 33.3, 31.6, 27.6, 17.3; HRMS (ESI): calcd for C₄₁H₂₇O₁₈Co₄ ([M+H]+): 1042.8520, found: 1042.8508.

**Functionalization of xanthotoxin (15)**

The procedure B was followed with a reaction time of 2 h. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 4) to provide 15a (15.1 mg, 0.0280 mmol, 28%) along with recovered 15 (14.5 mg, 0.0669 mmol, 67%)

15a: red oil; IR (neat): 2021 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ 8.03 (d, J = 9.8 Hz, 1H), 7.74 (d, J = 2.0 Hz, 1H), 6.91 (d, J = 2.0 Hz, 1H), 6.47 (d, J = 9.8 Hz, 1H), 5.95 (s, 1H), 4.50 (s, 2H), 4.24 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃): δ 199.1, 160.0, 147.3, 146.7, 143.9, 140.3, 132.3, 125.9, 123.5, 114.7, 114.1, 105.3, 94.2, 73.0, 61.5, 33.1; HRMS (ESI): calcd for C₂₁H₁₁O₁₀Co₂ ([M+H]+): 540.9011, found: 540.8994.
Functionalization of colchicine (16)

On 0.05 mmol scale, the procedure B was followed, employing 20 equiv. of Cs$_2$CO$_3$ instead of 10 equiv. with a reaction time of 1 h. The crude product was purified by silica gel column chromatography (MeOH : CHCl$_3$ = 1 : 40) to provide $16a$ (2.83 mg, 3.91 µmol, 8%) and recovered $16$ (15.7 mg, 0.0392 mmol, 79%).

$16a$: red oil; IR (neat): 2022 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.56 (br s, 1H), 7.54 (s, 1H), 7.21 (d, $J = 10.7$, 1H), 6.85 (d, $J = 10.7$ Hz, 1H), 5.93 (s, 1H), 4.66-4.60 (m, 1H), 4.32 (d, $J = 13.4$, 1H), 4.00 (s, 6H), 3.92 (d, $J = 13.4$ Hz, 1H), 3.91 (s, 3H), 3.61 (s, 3H), 2.90-2.88 (m, 1H), 2.27-2.25 (m, 2H), 2.00 (s, 3H), 1.90-1.87 (m, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 199.7, 179.6, 170.1, 164.2, 152.1, 151.6, 150.5, 145.5, 136.7, 135.6, 132.1, 130.2, 126.6, 112.7, 96.2, 96.1, 73.4, 61.4, 60.9, 60.7, 56.4, 52.5, 35.9, 30.3, 25.5, 22.9; HRMS (ESI): calcd for C$_{31}$H$_{27}$NO$_{12}$Co$_2$Na ([M+Na]$^+$): 746.0089, found: 746.0067.

Functionalization of estradiol (17)

The procedure A was followed with a reaction time of 30 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 8) to provide $17a$ (15.3 mg, 0.0166 mmol, 17%), $17b$ (8.88 mg, 0.0149 mmol, 15%), $17c$ (13.6 mg, 0.0227 mmol, 23%) and recovered $17$ (8.90 mg, 0.0327 mmol, 33%). In this case, starting material $17$ was dissolved in 5 ml of CH$_2$Cl$_2$ (0.02 M) and added.

$17a$: red oil; IR (neat): 2017 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.02 (s, 1H), 6.04 (s, 1H), 5.98 (s, 1H), 4.80 (s, 1H), 4.18 (s, 2H), 4.13 (d, $J = 16.1$ Hz, 1H), 4.06 (d, $J = 16.1$ Hz, 1H), 3.73 (br d, $J = 5.9$ Hz, 1H), 2.94 (br d, $J = 16.1$ Hz, 1H), 2.81 (dd, $J = 15.9$ Hz, 10.5 Hz, 1H), 2.28 (br d, $J = 11.2$ Hz, 1H), 2.15 (br s, 2H), 1.95 (br d, $J = 10.7$ Hz, 2H), 1.70 (br s, 1H), 1.49-1.19 (m, 10H), 0.76 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 199.5, 149.2, 134.7, 133.6, 126.3, 125.2, 123.8, 95.6, 94.1, 81.9, 73.6, 72.9, 50.0, 44.1, 43.2, 38.1, 36.7, 35.3, 30.6, 27.2, 26.4, 23.1, 11.0; HRMS (ESI): calcd for C$_{36}$H$_{27}$O$_{14}$Co$_4$ ([M-H]$^-$): 918.8723, found: 918.8710.
**17b**: red oil; IR (neat): 2017 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CD\(_3\)COCD\(_3\)): \(\delta\) 8.15 (s, 1H), 7.11 (s, 1H), 6.57 (s, 1H), 6.40 (s, 1H), 4.17 (d, \(J = 15.0\) Hz, 1H), 4.10 (d, \(J = 15.0\) Hz, 1H), 3.65 (br s, 1H), 3.58 (br s, 1H), 2.30 (br s, 1H), 2.12-1.95 (m, 3H), 1.83 (br s, 1H), 1.64 (br s, 1H), 1.46-1.19 (m, 10H), 0.76 (s, 3H); HRMS (ESI): calcd for C\(_{27}\)H\(_{25}\)O\(_8\)Co\(_2\) ([M-H])\(^{-}\): 595.0208, found: 595.0211.

**17c**: red oil; IR (neat): 2017 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CD\(_3\)COCD\(_3\)): \(\delta\) 8.25 (br s, 1H), 7.04 (d, \(J = 8.2\) Hz, 1H), 6.69 (d, \(J = 8.2\) Hz, 1H), 6.37 (s, 1H), 4.28 (d, \(J = 14.7\) Hz, 1H), 4.22 (d, \(J = 14.7\) Hz, 1H), 3.66 (br s, 1H), 3.57 (br s, 1H), 3.03 (br s, 1H), 2.25 (brs, 1H), 2.13 (br s, 1H), 1.95 (br s, 4H), 1.48-1.19 (m, 8H), 0.75 (s, 3H); HRMS (ESI): calcd for C\(_{27}\)H\(_{25}\)O\(_8\)Co\(_2\) ([M-H])\(^{-}\): 595.0208, found: 595.0224.

**Functionalization of podophyllotoxin (18)**

![Diagram of the functionalization of podophyllotoxin](image)

The procedure A was followed with a reaction time of 10 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 8) to provide 18a (20.4 mg, 0.0276 mmol, 28%).

**18a**: red oil; IR (neat): 2029 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.07 (s, 1H), 6.52 (s, 1H), 6.37 (s, 2H), 6.08 (s, 1H), 5.98 (d, \(J = 1.0\) Hz, 1H), 5.96 (d, \(J = 1.0\) Hz, 1H), 4.82 (d, \(J = 10.7\) Hz, 1H), 4.77 (d, \(J = 12.1\) Hz, 1H), 4.69 (d, \(J = 12.1\) Hz, 1H), 4.62-4.58 (m, 2H), 4.16 (t, \(J = 9.7\) Hz, 1H), 3.81 (s, 3H), 3.72 (s, 6H), 3.04-2.95 (m, 1H), 2.87 (dd, \(J = 14.2\) Hz, 4.6 Hz, 1H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta\) 199.3, 173.9, 152.6, 147.9, 147.7, 137.0, 135.3, 131.8, 130.3, 109.7, 107.9, 106.8, 101.5, 90.3, 78.0, 71.4, 71.2, 60.7, 60.7, 55.9, 45.5, 43.9, 37.8; HRMS (ESI): calcd for C\(_{31}\)H\(_{25}\)O\(_{14}\)Co\(_2\) ([M+H])\(^{+}\): 738.9903, found: 738.9888.

**Functionalization of eugenol (19)**

![Diagram of the functionalization of eugenol](image)

On 0.200 mmol scale, the procedure A was followed, employing K\(_2\)CO\(_3\) instead of Cs\(_2\)CO\(_3\) as a base, with a reaction time of 2 h. The crude product was purified by silica gel column...
chromatography (AcOEt : hexane = 1 : 20 to 1 : 8) to provide a mixture of **19a** (18.4 mg, 0.0369 mmol, 15%) and **19b** (7.23 mg, 14.5 µmol, 7%) and a single product of **19a** (15.1 mg, 0.0303 mmol, 18%). The mixture of **19b** and **19c** was separated by HPLC (AcOEt : hexane = 1 : 19, 9.4 mL/min).

**19a**: red oil; IR (neat): 2020 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ 6.81 (s, 1H), 6.65 (s, 1H), 6.04 (s, 1H), 5.97 (ddt, J = 17.0 Hz, 10.3 Hz, 6.4 Hz, 1H), 5.46 (s, 1H), 5.11 (dt, J = 10.3 Hz, 1.4 Hz, 1H), 5.04 (dt, J = 17.0 Hz, 1.4 Hz, 1H), 4.04 (s, 2H), 3.85 (s, 3H), 3.43 (dd, J = 6.4 Hz, 1.4 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ 199.6, 145.7, 144.1, 137.2, 131.6, 128.8, 116.1, 115.9, 112.2, 97.1, 73.5, 56.0, 36.82, 36.78; HRMS (ESI): calcd for C₁₀H₁₄O₈Co₂Na ([M+Na]+): 510.9245, found: 510.9238.

**19b** (retention time: 19.0 min): red oil; IR (neat): 2020 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ 6.61 (s, 1H), 6.60 (s, 1H), 6.03 (s, 1H), 5.92 (ddt, J = 16.8 Hz, 10.0 Hz, 6.5Hz, 1H), 5.60 (s, 1H), 5.09-5.04 (m 2H), 4.10 (s, 2H), 3.86 (s, 3H), 3.30 (d, J = 6.5 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ 199.7, 146.4, 141.9, 137.7, 131.3, 125.9, 122.7, 115.5, 109.9, 97.3, 73.7, 56.1, 39.9, 33.6; HRMS (EI): calcd for C₁₈H₁₄O₇Co₂ ([M-CO]+): 459.9404, found: 459.9400.

**19c** (retention time: 20.7 min): red oil; IR (neat): 2023 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ 6.88 (d, J = 9.0 Hz, 1H), 6.73 (s, 1H), 6.72 (d, J = 9.0 Hz, 1H), 6.03 (s, 1H), 6.01-5.91 (m, 1H), 5.25 (s, 2H), 5.10-5.06 (m, 2H), 3.81 (s, 3H), 3.34 (d, J = 6.8 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ 199.2, 150.2, 145.9, 137.6, 134.1, 120.3, 115.7, 115.1, 112.9, 89.6, 72.4, 69.7, 55.7, 39.9; HRMS (EI): calcd for C₁₂H₁₄O₂Co₂ ([M-6CO]+): 319.9658, found: 319.9637.

### 6. Decomplexation of dicobalt hexacarbonyl complexes

**Standard procedure**: To a solution of cobalt complex in MeCN (0.01 M) was added TEMPO⁺BF₄⁻ (0.5 equiv. × 8 or 9) every 5 min at - 40 °C. After completion of the reaction, the reaction was quenched with sat. NaHCO₃ (2 mL) and extracted with AcOEt (4 mL × 3). The combined organic layers were washed with brine, dried over MgSO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography.

#### Decomplexation of compound 19a

![Decomplexation Diagram](image-url)

On 11.7 mg (0.0234 mmol) scale, the standard procedure was followed with TEMPO⁺BF₄⁻.
(total 25.23 mg, 0.104 mmol) and a reaction time of 45 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 4) to provide 20 (4.05 mg, 0.0200 mmol, 86%).

**20**: colorless oil; IR (neat): 3294, 205w cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ 7.06 (s, 1H), 6.66 (s, 1H), 5.93 (ddt, J = 16.9 Hz, 10.2 Hz, 6.3 Hz, 1H), 5.46 (s, 1H), 5.06 (dd, J = 10.2 Hz, 1.4 Hz, 1H), 4.99 (dd, J = 16.9 Hz, 1.4 Hz, 1H), 3.87 (s, 3H), 3.46 (d, J = 2.4 Hz, 2H), 3.35 (d, J = 6.3 Hz, 2H), 2.15 (t, J = 2.4 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃): δ 145.4, 144.1, 136.6, 128.8, 127.2, 115.8, 115.1, 112.3, 82.1, 70.4, 56.0, 36.8, 21.7; HRMS (EI): calcd for C₁₃H₁₄O₂ (M⁺): 202.0994, found: 202.0986.

**Decomplexation of compound 10a**

On 44.6 mg (0.0683 mmol) scale, the standard procedure was followed with TEMPO⁺BF₄⁻ (total 74.5 mg, 0.306 mmol) and a reaction time of 45 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 1) to provide 21 (20.4 mg, 0.0555 mmol, 81%).

**21**: colorless oil; IR (neat): 3286 cm⁻¹; ¹H-NMR (400 MHz, CD₃SOCD₃): δ 7.36-7.30 (m, 5H), 6.97 (s, 1H), 6.72 (s, 1H), 5.06 (s, 2H), 3.74 (s, 1H), 3.70 (s, 3H), 3.49 (d, J = 2.5 Hz, 2H), 3.42 (t, J = 7.5 Hz, 2H), 2.86 (s, 3H), 2.78 (t, J = 7.5 Hz, 2H), 2.78 (t, J = 2.5 Hz, 1H); ¹³C-NMR (100 MHz, CD₃SOCD₃): δ 154.9, 147.7, 147.3, 136.6, 128.8, 127.8, 127.1, 126.9, 126.6, 114.5, 113.8, 82.2, 71.7, 65.7, 55.7, 48.8, 40.1, 33.8, 29.6, 20.7; HRMS (EI): calcd for C₂₂H₂₅NO₄ (M⁺): 367.1784, found: 367.1790.

**Decomplexation of compound 11b**

On 10.4 mg (0.0149 mmol) scale, the standard procedure was followed with TEMPO⁺BF₄⁻ (total 15.9 mg, 0.0656 mmol) and a reaction time of 40 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 12) to provide 22 (4.42 mg, 0.0108 mmol, 72%).
22: colorless oil; IR (neat): 3301 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.67 (d, $J = 8.7$ Hz, 2H), 7.48 (d, $J = 8.7$ Hz, 2H), 7.01 (s, 1H), 6.89 (s, 1H), 3.87 (s, 3H), 3.70 (s, 3H), 3.68 (s, 2H), 3.49 (d, $J = 2.6$ Hz, 2H), 2.46 (s, 3H), 1.97 (t, $J = 2.6$ Hz, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 171.4, 168.4, 153.4, 139.0, 135.5, 134.0, 131.1, 130.2, 129.14, 129.08, 120.7, 114.7, 112.5, 98.7, 81.5, 70.6, 55.7, 52.1, 30.2, 19.7, 13.3; HRMS (ESI): calcd for C$_{23}$H$_{21}$NO$_4$Cl ([M+H]$^+$): 410.1154, found: 410.1148.

Decomplexation of compound 12a

On 40.1 mg (0.0706 mmol) scale, the standard procedure was followed with TEMPO$^+$BF$_4^-$ (total 62.2 mg, 0.285 mmol) and a reaction time of 40 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 20) to provide 23 (18.2 mg, 0.0643 mmol, 91%).

23: colorless oil; IR (neat): 3290 cm$^{-1}$; $^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 8.02 (d, $J = 8.9$ Hz, 1H), 7.75 (d, $J = 7.9$ Hz, 1H), 7.69 (s, 1H), 7.50 (d, $J = 8.9$ Hz, 1H), 7.26 (d, $J = 7.9$ Hz, 1H), 3.97 (d, $J = 2.3$ Hz, 1H), 3.97 (s, 3H), 3.87 (q, $J = 7.0$ Hz, 1H), 3.67 (s, 3H), 1.97 (t, $J = 2.3$ Hz, 1H), 1.58 (d, $J = 7.0$ Hz, 3H); $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 175.0, 154.0, 135.6, 131.8, 129.3, 128.8, 126.7, 123.8, 117.5, 113.9, 82.8, 67.9, 56.8, 52.0, 45.2, 18.5, 14.4; HRMS (ESI): calcd for C$_{18}$H$_{19}$O$_3$ ([M+H]$^+$): 283.1329, found: 283.1324.

Decomplexation of compound 13a

On 49.2 mg (0.0758 mmol) scale, the standard procedure was followed with TEMPO$^+$BF$_4^-$ (total 84.1 mg, 0.346 mmol) and a reaction time of 45 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 20) to provide 24 (25.6 mg, 0.0704 mmol, 93%).

24: white amorphous; IR (neat): 3285 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 8.16 (d, $J = 1.4$ Hz, 1H), 7.80 (dd, $J = 8.7$ Hz, 1.4 Hz, 1H), 7.37 (d, $J = 8.7$ Hz, 1H), 7.13 (s, 1H), 7.10 (s, 2H), 3.95 (s, 3H), 3.88 (s, 6H), 3.82 (s, 3H), 3.70 (d, $J = 2.6$ Hz, 2H), 2.13 (t, 2.6 Hz, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 196.2, 152.8, 141.4, 139.4, 134.1, 129.0, 128.4, 126.3, 124.2, 122.9, 111.5, 109.1, 107.7, 82.0, 69.3, 61.0, 56.3, 32.9, 15.1; HRMS (EI): calcd for
C_{22}H_{21}NO_{4} (M^+): 363.1471, found 363.1485.

**Decomplexation of compound 17a**

On 19.0 mg (0.0318 mmol) scale, the standard procedure was followed with TEMPO^+BF_4^- (total 31.9 mg, 0.131 mmol) and a reaction time of 45 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 4 to 1 : 2) to provide 25 (7.13 mg, 0.0230 mmol, 72%).

25: colorless oil; IR (neat): 3305, 2115 cm^{-1}; ^1H-NMR (400 MHz, CDCl_3): δ 7.12 (d, J = 8.3 Hz, 1H), 6.67 (d, J = 8.3 Hz, 1H), 5.23 (br s, 1H), 3.74 (t, J = 8.3 Hz, 1H), 3.55 (d, J = 2.4 Hz, 1H), 2.99-2.93 (m, 1H), 2.85-2.81 (m, 1H), 2.33-2.27 (m, 1H), 2.23-2.10 (m, 2H), 2.02 (t, J = 2.4 Hz, 1H), 2.00-1.92 (m, 2H), 1.75-1.68 (m, 1H), 1.54-1.14 (m, 7H), 0.77 (s, 3H); ^13C-NMR (100 MHz, CDCl_3): δ 151.3, 136.2, 133.5, 125.1, 120.8, 113.3, 81.9, 81.8, 68.4, 50.0, 44.2, 43.2, 38.0, 36.7, 30.6, 27.3, 26.9, 26.6, 23.1, 15.2, 11.0; HRMS (ESI): calcd for C_{21}H_{25}O_{2} ([M-H]^-): 309.1849, found: 309.1863.

**Decomplexation of compound 9**

On 0.208 mmol scale, the standard procedure was followed with TEMPO^+BF_4^- (total 22.7 mg, 0.093 mmol) and a reaction time of 45 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 8 to 1 : 4) to provide 26 (6.83 mg, 0.0196 mmol, 94%).

26: colorless oil; IR (neat): 3301 cm^{-1}; ^1H-NMR (400 MHz, CDCl_3): δ 7.22 (d, J = 8.5 Hz, 1H), 6.76 (d, J = 8.5 Hz, 1H), 3.84 (s, 3H), 3.55 (s, 2H), 3.02 (dd, J = 17.4 Hz, 4.8 Hz, 1H), 2.89-2.80 (m, 1H), 2.61 (s, 1H), 2.39-2.23 (m, 3H), 2.04-1.66 (m, 8H), 1.56-1.33 (m, 5H), 0.88 (s, 3H); ^13C-NMR (100 MHz, CDCl_3): δ 154.8, 136.5, 133.2, 124.9, 122.9, 108.5, 87.6, 82.5, 79.9, 74.0, 67.0, 55.9, 49.5, 47.0, 43.8, 39.0, 38.6, 32.8, 27.3, 26.7, 26.6, 22.8, 14.9, 12.6; HRMS (ESI): calcd for C_{24}H_{29}O_{2} ([M+H]^+): 349.2162, found: 349.2160.
Decomplexation of compound 7

On 32.5 mg (0.0511 mmol) scale, the standard procedure was followed with TEMPO$^+\text{BF}_4^-$ (total 59.0 mg, 0.243 mmol) and a reaction time of 45 min. The crude product was purified by silica gel column chromatography (CH$_2$Cl$_2$) to provide 27 (15.1 mg, 0.0434 mmol, 85%).

27: colorless oil; IR (neat): 3288 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 7.20 (d, $J = $ 8.4 Hz, 1H), 6.71 (dd, $J = $ 8.4 Hz, 2.2 Hz, 1H), 6.63 (s, 1H), 4.34 (s, 2H), 3.77 (s, 3H), 2.87-2.84 (m, 2H), 2.67 (s, 1H), 2.43 (s, 1H), 2.35-2.25 (m, 3H), 2.22-2.09 (m, 1H), 2.02-1.94 (m, 1H), 1.88-1.71 (m, 4H), 1.54-1.30 (m, 4H), 0.92 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 157.4, 137.9, 132.5, 126.3, 113.8, 111.5, 86.1, 83.9, 80.8, 76.8, 73.5, 55.2, 53.9, 49.4, 47.7, 43.4, 39.2, 37.1, 33.9, 29.8, 27.2, 26.5, 22.8, 12.8; HRMS (ESI): calcd for C$_{24}$H$_{29}$O$_2$ ([M+H]$^+$): 349.2162, found: 349.2159.

Decomplexation of compound 19b

On 13.1 mg (0.0263 mmol) scale, the standard procedure was followed with TEMPO$^+\text{BF}_4^-$ (total 25.3 mg, 0.104 mmol) and a reaction time of 40 min. The crude product was purified by silica gel column chromatography (CH$_2$Cl$_2$ : hexane = 1 : 4) to provide 28 (3.01 mg, 0.0149 mmol, 58%) and recovered 19b (1.27 mg, 2.55 µmol, 10%).

28: colorless oil; IR (neat): 3307, 2120 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ 6.89 (d, $J = $ 3.0 Hz, 1H), 6.61 (d, $J = $ 3.0 Hz, 1H), 5.96 (ddt, $J = $ 16.8 Hz, 10.0 Hz, 6.5 Hz, 1H), 5.62 (s, 1H), 5.11-5.05 (m, 2H), 3.87 (s, 3H), 3.58 (d, $J = $ 2.8 Hz, 2H), 3.33 (d, $J = $ 6.5 Hz, 2H), 2.15 (t, $J = $ 2.8 Hz, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ 146.1, 141.3, 137.8, 131.4, 121.7, 121.1, 115.6, 109.7, 81.9, 69.9, 56.1, 40.0, 18.8; HRMS (ESI): calcd for C$_{13}$H$_{15}$O$_2$ ([M+H]$^+$): 203.1067, found: 203.1068.
Decomplexation of compound 17b

On 15.43 mg (0.0260 mmol) scale, the standard procedure was followed with TEMPO+BF₄⁻ (total 30.5 mg, 0.125 mmol) and a reaction time of 45 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 8 to 1 : 4) to provide 29 (2.68 mg, 8.63 µmol, 33%) and recovered 17b (4.03 mg, 6.76 µmol, 26%).

29: colorless oil; IR (neat): 3306 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ 7.22 (s, 1H), 6.54 (s, 1H), 5.12 (br s, 1H), 3.73 (t, J = 8.5 Hz, 1H), 3.54 (d, J = 2.8 Hz, 2H), 2.82-2.78 (m, 2H), 2.35-2.31 (m, 1H), 2.22 (t, J = 2.8 Hz, 1H), 2.17-2.07 (m, 2H), 1.98-1.93 (m, 1H), 1.88-1.84 (m, 1H), 1.73-1.66 (m, 1H), 1.52-1.15 (m, 8H), 0.78 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃): δ 151.3, 137.0, 133.0, 126.5, 119.5, 115.9, 81.9, 81.6, 70.9, 50.0, 44.0, 43.3, 38.8, 36.7, 30.6, 29.7, 29.2, 27.2, 26.4, 23.1, 19.8, 11.0; HRMS (ESI): calcd for C₂₁H₂₅O₂ ([M-H]⁻): 309.1849, found: 309.1860.

Decomplexation of compound 10b

On 8.73 mg (0.0133 mmol) scale, the standard procedure was followed with TEMPO (13.0 mg, 0.0535 mmol) and a reaction time of 40 min. The crude product was purified by silica gel column chromatography (AcOEt : hexane = 1 : 4 to 1 : 1) to provide S6 (3.86 mg, 0.0105 mmol, 79%).

S6: colorless oil; IR (neat): 3289 cm⁻¹; ¹H-NMR (400 MHz, CD₃SOCD₃): δ 7.36-7.30 (m, 5H), 7.36 (d, J = 8.6 Hz, 1H), 7.31 (d, J = 8.6 Hz, 1H), 5.07 (s, 2H), 3.79 (s, 3H), 3.77 (s, 3H), 3.51 (d, J = 2.7 Hz, 2H), 3.44 (t, J = 7.8 Hz, 2H), 2.86 (s, 3H), 2.84 (t, J = 7.8 Hz, 2H), 2.60 (t, J = 2.7 Hz, 1H); ¹³C-NMR (100 MHz, CD₃SOCD₃): δ 154.9, 150.6, 146.6, 136.7, 129.6, 128.7, 127.8, 127.1, 126.9, 124.4, 111.8, 82.6, 69.7, 65.7, 59.7, 55.5, 49.1, 33.8, 29.8, 14.6; HRMS (ESI) C₂₂H₂₆O₄N ([M+H]⁺) calcd for 368.1856, found 368.1852.
7. References
8. $^1$H-NMR Comparison of aromatic bioactive small molecules and their dicobalt hexacarbonyl complexes

Arrows indicate protons substituted by the propargyl dicobalt hexacarbonyl group.
9. NMR Spectra
Coupling b/w $H_a$ and $H_b$ not observed.
Coupling b/w $H_a$ and $H_b$ not observed.
auto
C:\Users\Gosei\Desktop\Valkyne functionalization\Mestranol\Mestranol2-13C.set.als

MeO

CO₂(CO)₆

9

DFILE: mestranol2-13C.set.als
COMNT: auto
DATIM: Sun Feb 07 18:34:36 2016
OBNUC: 13C
EXMOD: BCM
OBFREQ: 99.45 MHz
OBSET: 94.00 KHz
OBFIN: 10309.90 Hz
POINT: 22769
FREQU: 26845.64 Hz
SCANS: 2758
AC-QTM: 1.2200 sec
PD: 1.7790 sec
PW1: 5.50 usec
HNUC: IH
CTEMP: 23.1 c
SLVNT: CDCl₃
EXREF: 77.00 ppm
BF: 1.52 Hz
RGAIN: 22
Structure determined after decomplexation.
Structure determined after decomplexation.
single pulse decoupled gated NOE

C:\Users\Vgosn\Desktop\Valkyne functionalizationYN-CBZ-methyl homoveratrylamineYN-Cbz,MelHVA2--13C_set.xls

DFILE: N-Cbz,MelHVA2--13C_set.xls
COMNT: single pulse decoupled gated
DATIM: 2016-11-02 07:47:96
OWNUC: 13C
EXMOD: single_pulse_dec
OFREQQ: 150.92 MHz
OFSRT: 8.52 KHz
OBFIR: 1.74 Hz
PTT: 26214
FREQIR: 37878.21 Hz
SCANS: 13854
AC-QTM: 0.6921 sec
PD: 2.0000 sec
PW1: 4.90 usec
IRNUC: IH
CTEMP: 26.2 c
SLVNT: CDCL3
EXREF: 77.00 ppm
BF: 1.62 Hz
RGAIN: 38
Structure determined after decomplexation.
Structure determined after decomplexation.
The structure was determined by comparing NMR spectrum of 14 and 14a.
The structure was determined by comparing NMR spectrum of 14 and 14a. (rotenone’s NMR identification; R. Nunlist, J. Ralph, J. Heterocycl. Chem. 1988, 25, 351-352.)
Coupling b/w H_a and H_b not observed.
Coupling b/w $H_a$ and $H_b$ not observed.
Structure determined after decomplexation.
Coupling b/w $H_a$ and $H_b$ not observed.
Coupling b/w $H_a$ and $H_b$ not observed.
HMBC
single pulse decoupled gated NOE

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MeO

CO₂Me

23

PPI

210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0


DFILE: Dec-naproxen-13C_set.xls
COMNT: single pulse decoupled gated
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OBSET: 3.87 KHz
OBFIN: 9.09 Hz
POINT: 20214
FREQU: 37593.98 Hz
SCANS: 1024
AC-QTM: 0.6973 sec
PD: 2.0000 sec
PW1: 3.97 usec
RRNUC: 1H
CTEMP: 24.2 C
SLVNT: CDCl₃
EXREF: 77.00 ppm
BF: 1.02 Hz
RGAIN: 50
 FILE:  c:\users\vgose\desktop\alkyne functionalization\estradiol\estradiol2-1h_set.als

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DATIM  Fri Jul 15 18:03:07 2016
OBNUC  IH
EXMOD  NON
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OBSET  124.00 KHz
OBFIN  10050.00 Hz
POINT   1632
FREQU   7992.01 Hz
SCANS  32
ACQTM  2.0500 sec
PD   4.9500 sec
PW1    6.20 usec
IRNUC   IH
CTEMP  24.9 C
SLVNT  CDCl3
EXREF  0.00 ppm
BF   0.12 Hz
RGAIN  15

![Chemical Structure](image)
S6