SUPPLEMENTARY MATERIAL

Design, synthesis, and antimicrobial activities of new tanshinone IIA esters

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Sixteen new ester derivatives with various ClogP values of tanshinone IIA (TSIIA), a major lipophilic component of *Salvia miltiorrhiza*, were designed and synthesised, including 6 aliphatic esters (**3a-e**, **5a**), one phosphate ester (**4c**), and 9 aromatic esters (**5b-j**). Their antimicrobial activities against three Gram-positive bacteria strains, *Staphylococcus aureus*, *Bacillus subtilis*, and *Bacillus amyloliquefaciens*, and two Gram-negative bacteria strains, *Pseudomonas aeruginosa* and *Escherichia coli*, as well as two fungi species, *Candida albicans* and *Saccharomyces cerevisiae*, were evaluated *in vitro* by broth microdilution susceptibility tests. The results showed that keeping ClogP values in a certain range is necessary for their antimicrobial activities. For those compounds with ClogP values between 5 and 10, their MIC values showed positive correlations with ClogP values. In particular, compound **3e** exhibited fourfold and twofold higher potency than the standard drug amphotericin B against fungi *C. albicans* and *S. cerevisiae* with MIC values of 1.95 and 7.81 µg/mL, respectively.

Keywords: tanshinone IIA; ester derivatives; ClogP; synthesis; antimicrobial

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Part 1. Spectroscopic data of compounds **3a-e**, **4a-c**, and **5a-j**.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl-diacetate (**3a**): White amorphous solid; yield 84%; mp. 168 – 171 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 8.8 Hz, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.46 (q, *J* = 1.2 Hz, 1H), 3.40 – 3.09 (m, 2H), 2.40 (s, 3H), 2.39 (s, 3H), 2.26 (d, *J* = 1.2 Hz, 3H), 1.92 – 1.76 (m, 2H), 1.73 – 1.64 (m, 2H), 1.34 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 169.27, 168.78, 150.30, 144.26, 141.65, 134.86 (possibly overlapped signal), 131.43, 126.50, 124.24, 119.36, 118.39, 117.50, 115.50, 38.29, 34.90, 31.97 (possibly overlapped signal), 29.74, 21.11, 20.48, 20.15, 8.88. ESI MS (positive) *m/z* 783.0 [2M + Na]⁺.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl-dipropionate (**3b**): White amorphous solid; yield 82%; mp. 96 – 98 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 8.8 Hz, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.45 (q, *J* = 1.2 Hz, 1H), 3.34 – 2.98 (m, 2H), 2.69 (q, *J* = 7.6 Hz, 2H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.24 (d, *J* = 1.2 Hz, 3H), 1.86 – 1.77 (m, 2H), 1.72 – 1.65 (m, 2H), 1.36 – 1.31 (m, 12H); ¹³C NMR (125 MHz, CDCl₃) δ 172.61, 172.19, 150.26, 144.11, 141.58, 134.94 (possibly overlapped signal), 131.49, 126.38, 124.35, 119.32, 118.37, 117.59, 115.53, 38.30, 34.89, 31.98 (possibly overlapped signal), 29.89, 27.97, 27.42, 20.12, 9.20, 9.16, 9.00. ESI MS (positive) *m/z* 839.2 [2M + Na]⁺.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl dibutyrate (**3c**): White amorphous solid; yield 85%; mp. 101 – 102 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 8.8 Hz, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.45 (q, *J* = 1.2 Hz, 1H), 3.47 – 2.80 (m, 2H), 2.64 (t, *J* = 7.4 Hz, 2H), 2.62 (t, *J* = 7.4 Hz, 2H), 2.24 (d, *J* = 1.2 Hz, 3H), 1.90 – 1.77 (m, 6H), 1.71 – 1.65 (m, 2H), 1.35 (s, 6H), 1.10 (t, *J* = 7.4 Hz, 3H), 1.08 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 171.81, 171.41, 150.26, 144.07, 141.56, 134.97, 134.93, 131.49, 126.36, 124.38, 119.32, 118.37, 117.60, 115.53, 38.33, 36.37, 35.80, 34.90, 31.99 (possibly overlapped signal), 29.97, 20.11, 18.30, 18.21, 13.95, 13.88, 9.06. ESI MS (positive) *m/z* 895.3 [2M + Na]⁺.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl-dipentanoate (**3d**): White amorphous solid; yield 81%; mp. 101 – 103 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.09 (d, *J* = 8.8 Hz, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.45 (s, 1H), 3.49 – 2.89 (m, 2H), 2.66 (t, *J* = 7.4 Hz, 2H), 2.65 (t, *J* = 7.4 Hz, 2H), 2.25 (s, 3H), 1.86 – 1.75 (m, 6H), 1.72 – 1.65 (m, 2H), 1.54 – 1.44 (m, 4H), 1.35 (s, 6H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.99 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 171.97, 171.57, 150.26, 144.07, 141.55, 134.98, 134.94, 131.49, 126.35, 124.38, 119.31, 118.36, 117.60, 115.53, 38.32, 34.90, 34.22, 33.69, 31.98 (possibly overlapped signal), 29.97, 26.86, 26.81, 22.46, 22.43, 20.11, 13.81, 13.75, 9.06. ESI MS (positive) *m/z* 951.4 [2M + Na]⁺.

4-((11-hydroxy-1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10-yl)oxy)-4-oxo butanoic acid (**3e**): Light pink amorphous solid; yield 81%; mp. 140 – 143 °C; ¹H NMR (400 MHz, CD₃OD) δ 8.00 (d, *J* = 8.7 Hz, 1H), 7.56 (q, *J* = 1.2 Hz, 1H), 7.47 (d, *J* = 8.7 Hz, 1H), 3.24 (t, *J* = 6.0 Hz, 2H), 3.07 (d, *J* = 6.5 Hz, 2H), 2.82 (d, *J* = 6.5 Hz, 2H), 2.45 (d, *J* = 1.2 Hz, 3H), 1.91 – 1.84 (m, 2H), 1.77 – 1.72 (m, 2H), 1.39 (s, 6H); ¹H NMR (600 MHz, DMSO) δ 12.26 (s, 1H), 9.35 (s, 1H), 7.92 (d, *J* = 8.7 Hz, 1H), 7.77 (q, *J* = 1.2 Hz, 1H), 7.46 (d, *J* = 8.7 Hz, 1H), 3.14 (t, *J* = 5.4 Hz, 2H), 3.02 (t, *J* = 6.6 Hz, 2H), 2.61 (t, *J* = 6.6 Hz, 2H), 2.38 (d, *J* = 1.2 Hz, 3H), 1.78 – 1.74 (m, 2H), 1.65 – 1.62 (m, 2H), 1.30 (s, 6H); ¹³C NMR (150 MHz, DMSO) δ 174.04, 172.25, 149.82, 143.75, 143.05, 141.82, 130.21, 128.66, 125.27, 124.19, 118.05, 116.86, 116.31, 115.24, 38.52, 35.05, 32.28, 29.97, 29.66, 29.23, 29.06, 20.22, 9.88. ESI MS (positive) *m/z* 397.3 [M + H]⁺, 815.3 [2M + Na]⁺.

Tetraethyl (1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl) bis (phosphate) (**4a**): Light yellow oil; yield 65%; ¹H NMR (500 MHz, CDCl₃) δ 8.01 (d, *J* = 8.8 Hz, 1H), 7.53 (d, *J* = 8.8 Hz, 1H), 7.44 (q, *J* = 1.2 Hz, 1H), 4.32 – 4.24 (m, 4H), 4.14 – 4.06 (m, 4H), 3.41 (t, *J* = 5.6 Hz, 2H), 2.47 (d, *J* = 1.2 Hz, 3H), 1.79 – 1.72 (m, 4H), 1.36 (s, 6H), 1.34 (t, *J* = 7.0 Hz, 6H), 1.34 (t, *J* = 7.0 Hz, 6H), 1.18 (t, *J* = 7.0 Hz, 6H), 1.18 (t, *J* = 7.0 Hz, 6H); ³¹P NMR (202 MHz, CDCl₃): δ 3.26, 2.34. ESI MS (positive) *m/z* 569.2 [M + H]⁺.

Tetrabenzyl (1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl) bis (phosphate) (**4b**): Light yellow oil; yield 68%; ^1H NMR (400 MHz, CDCl_3) δ 8.00 (d, $J = 8.8$ Hz, 1H), 7.53 (d, $J = 8.8$ Hz, 1H), 7.42 (q, $J = 1.2$ Hz, 1H), 7.37 – 7.27 (m, 3H), 7.24 – 7.16 (m, 14H), 7.09 – 7.06 (m, 3H), 5.17 – 5.06 (m, 4H), 4.98 (s, 2H), 4.96 (s, 2H), 3.30 (t, $J = 6.4$ Hz, 2H), 2.39 (d, $J = 1.2$ Hz, 3H), 1.94 – 1.70 (m, 2H), 1.70 – 1.64 (m, 2H), 1.31 (s, 6H); ^{31}P NMR (202 MHz, CDCl_3): δ 6.90, 6.19. ESI MS (positive) m/z 817.3 $[\text{M} + \text{H}]^+$.

Sodium 1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl-bis (phosphate) (**4c**): White amorphous solid; yield 26%; mp. 181 – 183 °C; ^1H NMR (500 MHz, CD_3OD) δ 7.84 (d, $J = 8.7$ Hz, 1H), 7.39 (s, 1H), 7.38 (d, $J = 8.4$ Hz, 1H), 3.77 (t, $J = 5.4$ Hz, 2H), 2.56 (s, 3H), 1.82 – 1.75 (m, 2H), 1.76 – 1.67 (m, 2H), 1.31 (s, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 148.35, 142.05, 140.09, 137.87, 133.87 (possibly overlapped signal), 126.09, 124.39, 119.10, 117.72, 117.56, 116.71, 38.76, 34.47, 31.27 (possibly overlapped signal), 30.59, 19.46, 8.71; ^{31}P NMR (202 MHz, CD_3OD) δ 11.80, 10.43. ESI MS (positive) m/z 522.9 $[\text{M} - \text{Na} + 2\text{H}]^+$.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl bis(2-methylacrylate) (**5a**): White amorphous solid; yield 82%; mp. 154 – 156 °C; ^1H NMR (500 MHz, CDCl_3) δ 8.11 (d, $J = 8.8$ Hz, 1H), 7.58 (d, $J = 8.8$ Hz, 1H), 7.47 (s, 1H), 6.40 (d, $J = 0.8$ Hz, 1H), 6.38 (d, $J = 0.8$ Hz, 1H), 5.81 (d, $J = 0.9$ Hz, 1H), 5.79 (d, $J = 0.9$ Hz, 1H), 3.59 – 3.47 (m, 1H), 2.97 – 2.79 (m, 1H), 2.22 (s, 3H), 2.09 (d, $J = 0.6$ Hz, 3H), 2.07 (d, $J = 0.7$ Hz, 3H), 1.85 – 1.74 (m, 2H), 1.72 – 1.63 (m, 2H), 1.36 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.71, 165.32, 150.27, 144.04, 141.55, 135.73, 135.15 (possibly overlapped signal), 134.89, 131.67, 127.98 (possibly overlapped signal), 126.35, 124.52, 119.28, 118.33, 117.73, 115.65, 38.27, 34.89, 31.99, 31.98, 29.86, 20.11, 18.58, 18.45, 8.93. ESI MS (positive) m/z 887.3 $[2\text{M} + \text{Na}]^+$.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl dibenzoate (**5b**): White amorphous solid; yield 78%; mp. 234 – 236 °C; ^1H NMR (500 MHz, CDCl_3) δ 8.16 (d, $J = 8.8$ Hz, 1H), 8.13 (dd, $J = 8.4, 1.2$ Hz, 1H), 8.05 (dd, $J = 8.4, 1.2$ Hz, 1H),

7.60 (d, $J = 8.8$ Hz, 1H), 7.55 – 7.49 (m, 2H), 7.49 (q, $J = 1.2$ Hz, 1H), 7.38 (t, $J = 7.8$ Hz, 1H), 7.33 (t, $J = 7.8$ Hz, 1H), 3.65 – 3.53 (m, 1H), 2.97 – 2.81 (m, 1H), 2.18 (d, $J = 1.2$ Hz, 3H), 1.74 – 1.66 (m, 2H), 1.65 – 1.57 (m, 2H), 1.36 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.41, 164.96, 150.41, 144.18, 141.64, 135.38, 135.09, 133.68, 133.60, 131.84, 130.30 (possibly overlapped signal), 130.16 (possibly overlapped signal), 129.10, 128.54 (possibly overlapped signal), 128.47 (possibly overlapped signal), 128.41, 126.48, 124.67, 119.41, 118.38, 117.91, 115.80, 38.22, 34.90, 32.01, 31.96, 30.00, 20.02, 9.06. ESI MS (positive) m/z 505.5 $[\text{M} + \text{H}]^+$.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl-bis(4-methoxybenzoate) (**5c**): White amorphous solid; yield 79%; mp. 189 – 190 °C; ^1H NMR (500 MHz, CDCl_3) δ 8.14 (d, $J = 8.6$ Hz, 1H), 8.09 (d, $J = 8.8$ Hz, 2H), 8.02 (d, $J = 8.8$ Hz, 2H), 7.59 (d, $J = 8.8$ Hz, 1H), 7.48 (s, 1H), 6.86 (d, $J = 8.6$ Hz, 2H), 6.81 (d, $J = 8.8$ Hz, 2H), 3.83 (s, 3H), 3.82 (s, 3H), 3.63 – 3.49 (m, 1H), 2.98 – 2.83 (m, 1H), 2.18 (s, 3H), 1.74 – 1.67 (m, 2H), 1.66 – 1.60 (m, 2H), 1.35 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.11, 164.66, 163.88, 163.82, 150.31, 144.01, 141.51, 135.53, 135.28, 132.47 (possibly overlapped signal), 132.36 (possibly overlapped signal), 131.89, 126.30, 124.82, 121.59, 120.84, 119.33, 118.32, 118.05, 115.85, 113.81 (possibly overlapped signal), 113.75 (possibly overlapped signal), 55.44, 38.27, 34.88, 32.01, 31.95, 29.96, 20.05, 9.02. ESI MS (positive) m/z 587.8 $[\text{M} + \text{Na}]^+$.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl bis(benzo[d][1,3]dioxole-5-carboxylate) (**5d**): White amorphous solid; yield 45%; mp. 141 – 143 °C; ^1H NMR (500 MHz, CDCl_3) δ 8.13 (d, $J = 8.8$ Hz, 1H), 7.78 (dd, $J = 8.2, 1.7$ Hz, 1H), 7.72 (dd, $J = 8.2, 1.7$ Hz, 1H), 7.59 (d, $J = 8.8$ Hz, 1H), 7.56 (d, $J = 1.7$ Hz, 1H), 7.50 (d, $J = 1.7$ Hz, 1H), 7.48 (q, $J = 1.2$ Hz, 1H), 6.81 (d, $J = 8.2$ Hz, 1H), 6.77 (d, $J = 8.2$ Hz, 1H), 6.06 – 5.98 (m, 4H), 3.65 – 3.38 (m, 1H), 3.01 – 2.76 (m, 1H), 2.18 (d, $J = 1.2$ Hz, 3H), 1.76 – 1.68 (m, 2H), 1.67 – 1.58 (m, 2H), 1.35 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 164.63, 164.19, 152.25, 152.17, 150.30, 147.81, 147.78, 144.07, 141.55, 135.37, 135.10, 131.77, 126.51, 126.41, 126.37, 124.64, 123.05, 122.32, 119.31, 118.30, 117.87, 115.73, 109.99, 109.87, 108.16, 108.09, 101.94 (possibly

overlapped signal), 38.19, 34.86, 31.98, 31.90, 29.94, 20.01, 9.02. ESI MS (positive) m/z 615.7 $[M + Na]^+$.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl-bis(2-chlorobenzoate) (**5e**): White amorphous solid; yield 73%; mp. 186 – 187 °C; 1H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.8 Hz, 1H), 8.13 (dd, J = 8.0, 1.5 Hz, 1H), 8.06 (dd, J = 8.0, 1.5 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.51 (q, J = 1.2 Hz, 1H), 7.49 – 7.40 (m, 4H), 7.30 (td, J = 7.8, 1.5 Hz, 1H), 7.24 (td, J = 7.8, 1.5 Hz, 1H), 3.74 – 3.39 (m, 1H), 3.19 – 2.71 (m, 1H), 2.25 (d, J = 1.2 Hz, 3H), 1.81 – 1.69 (m, 2H), 1.67 – 1.59 (m, 2H), 1.36 (s, 6H); ^{13}C NMR (125 MHz, DMSO) δ 163.44, 162.93, 150.54, 144.31, 141.76, 135.29, 135.28, 135.04, 134.77, 133.74, 133.63, 132.63, 132.53, 131.69 (possibly overlapped signal), 131.64, 128.02, 127.36, 126.82, 126.74, 126.63, 124.51, 119.51, 118.42, 117.68, 115.69, 38.21, 34.93, 31.98 (possibly overlapped signal), 30.07, 20.00, 9.14. ESI MS (positive) m/z = 573.6 $[M + H]^+$.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl bis(3-chlorobenzoate) (**5f**): White amorphous solid; yield 76%; mp. 150 – 153 °C; 1H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.8 Hz, 1H), 8.09 (t, J = 1.7 Hz, 1H), 8.04 – 8.00 (m, 2H), 7.94 (dt, J = 7.8, 1.2 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.52 – 7.47 (m, 3H), 7.33 (t, J = 8.0 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 3.61 – 3.46 (m, 1H), 2.93 – 2.80 (m, 1H), 2.18 (d, J = 1.2 Hz, 3H), 1.79 – 1.68 (m, 2H), 1.69 – 1.60 (m, 2H), 1.35 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.16, 163.68, 150.45, 144.40, 141.79, 135.11, 134.83, 134.78, 134.74, 133.86, 133.78, 131.60 (possibly overlapped signal), 130.65, 130.17, 130.03, 129.96, 129.88, 128.27, 128.14, 126.66, 124.40, 119.42, 118.41, 117.67, 115.61, 38.12, 34.87, 31.92 (possibly overlapped signal), 29.93, 19.95, 9.00. ESI MS (negative) m/z 571.2 $[M - H]^-$, ESI MS (positive) m/z 595.5 $[M + H]^+$.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl bis(4-chlorobenzoate) (**5g**): White amorphous solid; yield 79%; mp. 145 – 146 °C; 1H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.8 Hz, 1H), 8.07 (d, J = 8.6 Hz, 2H), 7.99 (d, J = 8.6 Hz, 2H), 7.60 (d, J = 8.8 Hz, 1H), 7.49 (q, J = 1.2 Hz, 1H), 7.38 (d, J = 8.6 Hz, 2H), 7.34 (d, J = 8.6 Hz, 2H), 3.60 – 3.46 (m, 1H), 2.93 – 2.79 (m, 1H), 2.16 (d, J

= 1.2 Hz, 3H), 1.76 – 1.67 (m, 2H), 1.66 – 1.59 (m, 2H), 1.35 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 164.42, 163.98, 150.49, 144.40, 141.79, 140.55, 140.44, 135.12, 134.87, 131.64, 131.60 (possibly overlapped signal), 131.47 (possibly overlapped signal), 129.10 (possibly overlapped signal), 129.05 (possibly overlapped signal), 127.42, 126.75, 126.66, 124.49, 119.47, 118.45, 117.71, 115.63, 38.17, 34.92, 31.98 (possibly overlapped signal), 30.06, 20.01, 9.05. ESI MS (negative) m/z 571.3 $[\text{M} - \text{H}]^-$.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl-bis(4-fluorobenzoate) (**5h**): White amorphous solid; yield 74%; mp. 216 – 218 °C; ^1H NMR (500 MHz, CDCl_3) δ 8.19 – 8.13 (m, 3H), 8.11 – 8.05 (m, 2H), 7.61 (d, J = 8.8 Hz, 1H), 7.50 (q, J = 1.2 Hz, 1H), 7.07 (t, J = 8.6 Hz, 2H), 7.03 (t, J = 8.6 Hz, 2H), 3.61 – 3.49 (m, 1H), 2.97 – 2.82 (m, 1H), 2.18 (d, J = 1.2 Hz, 3H), 1.75 – 1.69 (m, 2H), 1.66 – 1.57 (m, 2H), 1.36 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 166.22 (d, J = 255.8 Hz), 166.18 (d, J = 255.8 Hz), 164.31, 163.84, 150.46, 144.33, 141.74, 135.21, 134.92, 132.87 (d, J = 14.8 Hz) (possibly overlapped signal), 132.79 (d, J = 14.8 Hz) (possibly overlapped signal), 131.68, 126.60, 125.29 (d, J = 2.4 Hz) (possibly overlapped signal), 124.58 (d, J = 2.4 Hz) (possibly overlapped signal), 124.55, 119.44, 118.43, 117.78, 115.90 (d, J = 22.0 Hz), 115.85 (d, J = 22.0 Hz), 115.67, 38.18, 34.91, 31.98, 31.93, 29.99, 20.01, 9.03. ESI MS (positive) m/z 541.0 $[\text{M} + \text{H}]^+$.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diylbis(4-(trifluoromethyl)benzoate) (**5i**): White amorphous solid; yield 71%; mp. 192 – 195 °C; ^1H NMR (500 MHz, CDCl_3) δ 8.25 (d, J = 8.2 Hz, 2H), 8.19 (d, J = 8.7 Hz, 1H), 8.17 (d, J = 8.2 Hz, 2H), 7.66 (d, J = 8.2 Hz, 2H), 7.64 (d, J = 8.7 Hz, 1H), 7.62 (d, J = 8.2 Hz, 2H), 7.52 (q, J = 1.2 Hz, 1H), 3.63 – 3.49 (m, 1H), 2.95 – 2.82 (m, 1H), 2.19 (d, J = 1.2 Hz, 3H), 1.79 – 1.68 (m, 2H), 1.68 – 1.59 (m, 2H), 1.37 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 164.01, 163.58, 150.59, 144.61, 141.95, 135.36 (q, J = 32.8 Hz), 135.26 (q, J = 32.8 Hz), 135.05, 134.75, 132.12, 131.56, 131.47, 130.62 (possibly overlapped signal), 130.48 (possibly overlapped signal), 126.84, 125.72 (q,

$J = 3.7$ Hz), 125.66 (q, $J = 3.7$ Hz), 124.38, 123.37 (q, $J = 272.9$ Hz), 123.32 (q, $J = 272.9$ Hz), 119.55, 118.52, 117.59, 115.57, 38.13, 34.94, 31.93 (possibly overlapped signal), 30.09, 19.97, 9.04. ESI MS (positive) m/z 663.6 $[M + Na]^+$.

1,6,6-trimethyl-6,7,8,9-tetrahydrophenanthro[1,2-b]furan-10,11-diyl-dipicolinate (**5j**): White amorphous solid; yield 85%; mp. 193 – 194 °C; 1H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, $J = 4.6$ Hz, 1H), 8.61 (d, $J = 4.6$ Hz, 1H), 8.20 (d, $J = 7.8$ Hz, 1H), 8.14 (d, $J = 8.8$ Hz, 1H), 8.13 (d, $J = 7.8$ Hz, 1H), 7.74 (td, $J = 7.8, 1.5$ Hz, 1H), 7.69 (td, $J = 7.8, 1.5$ Hz, 1H), 7.60 (d, $J = 8.8$ Hz, 1H), 7.48 (q, $J = 1.2$ Hz, 1H), 7.42 – 7.34 (m, 2H), 3.80 – 3.46 (m, 1H), 3.02 – 2.74 (m, 1H), 2.20 (d, $J = 1.2$ Hz, 3H), 1.74 – 1.65 (m, 2H), 1.64 – 1.57 (m, 2H), 1.33 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.51, 163.06, 150.51, 150.17, 150.15, 147.10, 146.49, 144.33, 141.75, 137.05, 137.01, 135.26, 134.95, 131.81, 127.29, 127.19, 126.65, 125.93, 125.78, 124.46, 119.51, 118.38, 117.74, 115.77, 38.20, 34.90, 31.96 (possibly overlapped signal), 29.89, 19.99, 8.99. ESI MS (positive) m/z 507.5 $[M + H]^+$.

Part 2. 1H NMR, ^{13}C NMR, and MS spectra of compounds **3a-e**, **4a-c**, and **5a-j**, as well as NOESY spectrum of **3e**.

Figure S1. 1H NMR, ^{13}C NMR, MS spectra of compound **3a**

TACE #9-18 RT: 0.29-0.54 AV: 5 NL: 1.36E8
F: + c ESI Full ms [50.00-1000.00]

Figure S2. ^1H NMR, ^{13}C NMR, MS spectra of compound **3b**

H1-ZZJU-172 (丙酯)
ZCIRI I-400
H1-ZZJU-172
TanP+2

TPRO #20-46 RT: 0.67-1.42 AV: 13 NL: 8.68E8
F: + c ESI Full ms [50.00-1000.00]

Figure S3. ^1H NMR, ^{13}C NMR, MS spectra of compound 3c

TBU

TBU #28-43 RT: 0.92-1.36 AV: 8 NL: 1.16E9
F: + c ESI Full ms [50.00-1000.00]

Figure S4. ^1H NMR, ^{13}C NMR, MS spectra of compound **3d**

H1-ZZJU-214 (戊酯)
 ZCIRI I-400
 H1-ZZJU-214
 TPEX-2

TPEN #10-17 RT: 0.34-0.53 AV: 4 NL: 1.13E9
F: + c ESI Full ms [50.00-1000.00]

Figure S5. ^1H NMR (CD_3OD), NOESY (CD_3OD), ^1H NMR (DMSO), ^{13}C NMR (DMSO), MS spectra of compound **3e**

H1-ZZJU-213 (虎单酯)
 ZCIRI I-400
 H1-ZZJU-213
 TSUC

Tasuc-3

Tasuc-3

琥珀酸衍生物TMSuc
C13-TmSuc

琥珀酸衍生物TMSuc
C13-TmSuc

琥珀酰衍生物TMSuc
C13-TmSuc

TMSUC_140710140040 #10-20 RT: 0.35-0.60 AV: 5 NL: 8.61E7
F: + c ESI Full ms [50.00-1000.00]

Figure S6. ^1H NMR, ^{31}P NMR, MS spectra of compound **4a**

ZCIRI I-400
P31-2ZJU-348
NDP2

Sample directory:
File: PHOSPHORUS
Pulse Sequence: s2pul
Solvent: CD3OD
Ambient temperature
INNOVA-400 "zc400"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 53981.1 Hz
256 repetitions
OBSERVE P31, 161.8972089 MHz
DECOUPLE H1, 399.9392257 MHz
Power 42 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
FT size 32768
Total time 8 min, 34 sec

Figure S7. ^1H NMR, ^{13}C NMR, MS spectra of compound **4b**

ZCIRI I-400
P31-2ZJU-346
NMP

Sample directory:
File: PHOSPHORUS

Pulse Sequence: s2pul

Solvent: CD3OD
Ambient temperature
INNOVA-400 "zc400"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 53981.1 Hz
256 repetitions
OBSERVE P31, 161.8972089 MHz
DECOUPLE H1, 399.9392257 MHz
Power 42 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
FT size 32768
Total time 8 min, 34 sec

Figure S8. ^1H NMR, ^{13}C NMR, MS spectra of compound **4c**

DPT-C¹³

DPT-C¹³

ZCIRI I-400
P31-ZZJU-349
NMP2

Sample directory:
File: PHOSPHORUS
Pulse Sequence: s2pul

Solvent: Acetone
Ambient temperature
INOVA-400 "zc400"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 53981.1 Hz
256 repetitions
OBSERVE P31, 161.8972089 MHz
DECOUPLE H1, 399.9397256 MHz
Power 42 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
FT size 32768
Total time 8 min, 34 sec

2012090701 #1-19 RT: 0.01-0.49 AV: 19 NL: 3.43E8
T: + c ESI Full ms [200.00-1300.00]

Figure S9. ^1H NMR, ^{13}C NMR, MS spectra of compound **5a**

T09_150318123049 #15-22 RT: 0.47-0.66 AV: 4 NL: 6.85E8
F: + c ESI Full ms [50.00-1000.00]

Figure S10. ^1H NMR, ^{13}C NMR, MS spectra of compound **5b**

T07 #6-21 RT: 0.22-0.67 Av: 8 NL: 5.62E7
F: + c ESI Full ms [50.00-1000.00]

Figure S11. ^1H NMR, ^{13}C NMR, MS spectra of compound **5c**

对甲氧基苯甲酸IIA

对甲氧基苯甲酸IIA

TDOM#9-14 RT: 0.28-0.41 AV: 3 NL: 9.14E7
F: + c ESI Full ms [50.00-1000.00]

Figure S12. ^1H NMR, ^{13}C NMR, MS spectra of compound **5d**

胡葱酰化IIA

胡葱酰化IIA

Figure S13. ^1H NMR, ^{13}C NMR, MS spectra of compound **5e**

邻氯苯甲酸IIA

邻氯苯甲酸IIB

T10 #13-31 RT: 0.41-1.00 AV: 10 NL: 1.57E7
F: + c ESI Full ms [50.00-1000.00]

Figure S14. ^1H NMR, ^{13}C NMR, MS spectra of compound **5f**

T11 #14-37 RT: 0.45-1.17 AV: 12 NL: 2.81E5
F: -c ESI Full ms [50.00-1000.00]

T11 #8-22 RT: 0.29-0.68 AV: 7 NL: 1.10E7
F: + c ESI Full ms [50.00-1000.00]

Figure S15. ^1H NMR, ^{13}C NMR, MS spectra of compound **5g**

对氯苯甲酰IIA

对氯苯甲酰IIA

T12 #9-16 RT: 0.32-0.51 Av: 4 NL: 4.59E5
F: -c ESI Full ms [50.00-1000.00]

Figure S16. ^1H NMR, ^{13}C NMR, MS spectra of compound **5h**

对氟苯甲酰IIA

对氟苯甲酰IIA

对氟苯甲酰IIA

T15 #7-11 RT: 0.21-0.34 Av: 3 NL: 6.43E7
F: + c ESI Full ms [50.00-1000.00]

Figure S17. ^1H NMR, ^{13}C NMR, MS spectra of compound **5i**

对三氟甲基苯甲酸IIA

对三氟甲基苯甲酸IIA

T13 #9-14 RT: 0.28-0.41 Av: 3 NL: 3.78E7
F: + c ESI Full ms [50.00-1000.00]

Figure S18. ^1H NMR, ^{13}C NMR, MS spectra of compound **5j**

2-苧烯甲酰IIA

2-苧烯甲酰IIA

T16 #35-43 RT: 1.12-1.37 AV: 5 NL: 3.18E8
F: + c ESI Full ms [50.00-1000.00]