Supporting Information

I₂/CF₃CO₂Ag-mediated iodolactonization of various allenoic acids to

access versatile 6- to 9-membered ring vinylic iodolactones

Xiaobo Bao,[#] Guoli Wang,[#] Xu Dong,[#] Mengxiao Zhu, Lili Yang, Junjie Zhu,

Qingyuan Shi, Hongzhen Zhang, Dongyin Chen*

Table of contents

1. General methods of synthesis	2
2. General procedure for preparation of 1a-1j	2
3. General procedure for preparation of 4a-4k	6
4. General procedure for preparation of 6a-6i	11
5. Single crystal X-ray diffraction data of 2i	16
6. Copies of NMR spectra for 2a-2j, 3a, 3e, 3f, 5a-5k and 7a-7i	17
7. Copies of NMR spectra for 1a-1j, 4a-4k and 6a-6i	51
8. Copies of 2D NMR spectra for 2b, 5d and 7b	82

1. General methods of synthesis

All commercially available solvents and reagents were used without further purification unless otherwise specified. Reactions were monitored by thin layer chromatography (TLC) on Silica Gel 60 F254 plates. Purification was performed by flash column chromatography separations using silica gel (200-300 mesh). Melting points (mp) were measured on a X4 micro melting point apparatus. ¹H, ¹³C and ¹⁹F NMR spectra were recorded on a JEOL JNM-ECZS 400MHz NMR spectrometer with Me₄Si as the internal standard in DMSO- d_6 or CDCl₃. High resolution mass spectra (HRMS) were recorded on an Agilent 6500 Time-of-Flight (TOF) LC/MS system.

2. General procedure for preparation of 1a-1j

To a solution of tert-butyl 2-hydroxybenzoate (5 mmol) or tert-butyl 2-((4methylphenyl)sulfonamido)benzoate (5 mmol) in DMF (20 mL) was added K₂CO₃ (2.0 g, 15 mmol) and 3-bromoprop-1-yne (654 mg, 5.5 mmol). The resulting mixture was stirred at 80 °C until the TLC indicated the consumption of the starting material. The reaction system was quenched by H₂O and extracted with DCM. The combined organic phases were dried over anhydrous Na₂SO₄, filtered, and concentrated under vacuum. The residue was purified by a short silica gel column filtration (petroleum ether/DCM) to give intermediate I-1 in 51~99% yields.

To a solution of intermediate I-1 (3 mmol) in 1,4-dioxane (15 mL) was paraformaldehyde (540 mg, 6 mmol), CuBr (300 mg, 2.1 mmol) and dicyclohexylamide (1.1 g, 6 mmol) in sequence. The resulting mixture was stirred at 100 °C until the TLC indicated the consumption of the starting material. After cooling to room temperature, the solvent was removed under reduced pressure, and the residue was extracted with ethyl acetate. The combined organic phases were dried over anhydrous Na₂SO₄, filtered, and concentrated under vacuum. The residue was further purified by a short silica gel column filtration (petroleum ether/ethyl acetate) to give intermediate I-2 in 71~80% yields.

To a solution of intermediate **I-2** (2 mmol) in DCM (10 mL) was added TFA (1.0 mL). The resulting mixture was stirred at room temperature until the TLC indicated the consumption of the starting material. The solvent was removed under reduced pressure, and the residue was extracted with DCM. The combined organic phases were dried over anhydrous Na₂SO₄, filtered, and concentrated under vacuum. The residue was further purified by a short silica gel column filtration (DCM/MeOH) to give the desired products **1a-1g** in 95~99% yields.



Scheme S1. Synthesis of compounds 1a-1g.

A mixture of DIAD (1.4 g, 7 mmol) and PPh₃ (1.8 g, 7 mmol) in THF (5.0 mL) was stirred at room temperature for 0.5 h. Then, a solution of tert-butyl 2-hydroxybenzoate (5 mmol) or tert-butyl 2-((4-methylphenyl)sulfonamido)benzoate (5 mmol) and alkynol (5 mmol) in THF (25 mL) was slowly added into the mixture. The reaction mixture was stirred at room temperature until TLC indicated the consumption of starting material. The reaction system was quenched by H_2O and extracted with ethyl acetate. The combined organic phases were dried over anhydrous Na₂SO₄, filtered, and concentrated under vacuum. The residue was purified by a short silica gel column filtration (petroleum ether/ethyl acetate) to give intermediate **II-1** in 60~80% yields.

Following the similar procedure carried out for I-2, intermediate II-2 was prepared from II-1 in 75~83% yields.

Following the similar procedure carried out for 1a, the desired products 1h-1j were prepared form II-2 in 95~99% yields.



Scheme S2. Synthesis of compounds 1h-1j.



2-((Buta-2,3-dien-1-yl)oxy)benzoic acid (1a). White solid (732 mg, 77% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 8.16 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.53 (td, *J* = 7.9, 1.9 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 5.43 (p, *J* = 6.4 Hz, 1H), 4.97 (dt, *J* = 6.1, 2.7 Hz, 2H), 4.78 (dt, *J* = 6.0, 2.8 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 209.62, 165.49, 157.05, 135.05, 133.96, 122.50, 118.03, 113.07, 85.79, 78.39, 67.29. HRMS calcd for C₁₁H₁₁O₃ [M + H]⁺ *m/z* 191.07027, found 191.07051.



2-((Buta-2,3-dien-1-yl)oxy)-4-methylbenzoic acid (1b). White solid (735 mg, 72% yield over three steps). White solid. ¹H NMR (400 MHz, CDCl₃) δ 8.05 (d, *J* = 8.1 Hz, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.83 (s, 1H), 5.43 (p, *J* = 6.4 Hz, 1H), 4.98 (dt, *J* = 6.1, 2.7 Hz, 2H), 4.76 (dt, *J* = 5.8, 2.8 Hz, 2H), 2.40 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 209.68, 165.48, 156.96, 146.37, 133.88, 123.46, 115.32, 113.62, 85.80, 78.35, 67.20, 22.08. HRMS calcd for C₁₂H₁₃O₃ [M + H]⁺ *m/z* 205.08592, found 205.08620.



2-((Buta-2,3-dien-1-yl)oxy)-4-bromobenzoic acid (1c). Gray solid (887 mg, 66% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.21 (s, 1H), 5.42 (p, *J* = 6.5 Hz, 1H), 5.01 (dt, *J* = 6.2, 2.9 Hz, 2H), 4.78 (dt, *J* = 6.0, 2.8 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 209.90, 164.83, 157.21, 135.05, 129.20, 125.85, 117.08, 116.83, 85.39, 78.58, 67.79. HRMS calcd for C₁₁H₁₀BrO₃ [M + H]⁺ *m/z* 268.98078, found 268.98089.



2-((Buta-2,3-dien-1-yl)oxy)-5-formylbenzoic acid (1d). White solid (764 mg, 70% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 9.96 (s, 1H), 8.67 (d, *J* = 2.2 Hz, 1H), 8.11 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.19 (d, *J* = 8.6 Hz, 1H), 5.46 (p, *J* = 6.4 Hz, 1H), 5.01 (dd, *J* = 6.3, 3.0 Hz, 2H), 4.89 (dt, *J* = 6.0, 2.8 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 209.83, 189.98, 164.58, 161.32, 137.45, 134.55, 130.86, 118.71, 113.81,

85.37, 78.74, 67.88. HRMS calcd for $C_{12}H_{11}O_4 [M + H]^+ m/z$ 219.06573, found 219.06120.



2-((Buta-2,3-dien-1-yl)oxy)-4-nitrobenzoic acid (1e). White solid (799 mg, 68% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 8.29 (d, *J* = 9.0 Hz, 1H), 7.93 (d, *J* = 7.1 Hz, 2H), 5.44 (p, *J* = 6.5 Hz, 1H), 5.03 (dt, *J* = 6.3, 2.7 Hz, 2H), 4.90 (dt, *J* = 5.8, 2.7 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 210.12, 164.89, 157.53, 151.45, 134.81, 123.64, 116.50, 108.76, 85.23, 78.58, 68.27. HRMS calcd for C₁₁H₈NO₅ [M + H]⁺ *m/z* 234.04080, found 234.04034.



2-((Buta-2,3-dien-1-yl)oxy)-4-(trifluoromethyl)benzoic acid (**1f**). White solid (852 mg, 66% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 8.27 (d, *J* = 8.1 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.28 (s, 1H), 5.43 (p, *J* = 6.5 Hz, 1H), 4.99 (dd, *J* = 6.5, 2.8 Hz, 2H), 4.86 (dt, *J* = 5.9, 2.7 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 210.06, 164.76, 157.10, 136.28, 134.67, 123.14, 121.32, 118.87, 110.52, 85.33, 78.43, 67.89. ¹⁹F NMR (376 MHz, CDCl₃) δ -63.23. HRMS calcd for C₁₂H₈F₃O₃ [M -H]⁻ *m/z* 257.04310, found 257.04281.



2-((N-(buta-2,3-dien-1-yl)-4-methylphenyl)sulfonamido)benzoic acid (1g). White solid (130 mg, 38% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.99 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.50 – 7.38 (m, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 7.5 Hz, 1H), 5.22 (p, *J* = 7.0 Hz, 1H), 4.59 (d, *J* = 6.3 Hz, 2H), 4.29 (d, *J* = 7.2 Hz, 2H), 2.37 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 210.04, 170.17, 144.00, 138.17, 135.97, 132.97, 132.20, 131.55, 131.46, 129.67, 128.82, 127.90, 86.32, 76.18, 51.31, 21.65. HRMS calcd for C₁₈H₁₆NO₄S [M - H]⁻ *m/z* 342.08055, found 342.08001.



2-((Penta-3,4-dien-1-yl)oxy)benzoic acid (1h). White solid (602 mg, 59% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 10.92 (s, 1H), 8.18 (dt, *J* = 8.5, 2.7 Hz, 1H), 7.61 – 7.44 (m, 1H), 7.16 – 6.88 (m, 2H), 5.24 – 5.02 (m, 1H), 4.80 (dt, *J* = 6.5, 3.2 Hz, 2H), 4.32 (q, *J* = 6.2, 5.6 Hz, 2H), 2.60 (ddt, *J* = 9.4, 6.2, 3.3 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 209.27, 165.51, 157.42, 135.12, 134.00, 122.36, 117.75, 112.48, 85.50, 76.62, 68.72, 28.25. HRMS calcd for C₁₂H₁₃O₃ [M + H]⁺ *m/z* 205.08647, found 205.08625.



2-((4-Methyl-N-(penta-3,4-dien-1-yl)phenyl)sulfonamido)benzoic acid (1i). White solid (838 mg, 47% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 8.03 – 7.98 (m, 1H), 7.53 – 7.48 (m, 2H), 7.47 – 7.43 (m, 2H), 7.25 (s, 2H), 6.91 – 6.81 (m, 1H), 5.04 (p, *J* = 6.8 Hz, 1H), 4.64 (dt, *J* = 6.6, 3.2 Hz, 2H), 3.97 – 3.42 (m, 2H), 2.40 (s, 3H), 2.24 (d, *J* = 37.9 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 208.92, 168.99, 144.22, 138.14, 134.85, 132.94, 132.30, 132.25, 129.83, 129.71, 128.89, 128.13, 86.51, 75.87, 51.50, 27.47, 21.69. HRMS calcd for C₁₉H₂₀NO₄S [M + H]⁺ *m/z* 358.11130, found 358.11154.



2-((Hexa-4,5-dien-1-yl)oxy)benzoic acid (1j). White solid (630 mg, 58% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 8.17 (dd, J = 7.8, 1.9 Hz, 1H), 7.54 (td, J = 7.9, 1.9 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 7.04 (d, J = 8.5 Hz, 1H), 5.14 (p, J = 6.6 Hz, 1H), 4.71 (dt, J = 6.7, 3.3 Hz, 2H), 4.29 (t, J = 6.4 Hz, 2H), 2.20 (ddq, J = 10.1, 6.8, 3.3 Hz, 2H), 2.04 (p, J = 6.8 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 208.68, 165.50, 157.58, 135.14, 133.93, 122.33, 117.78, 112.67, 88.49, 76.08, 69.50, 28.01, 24.35. HRMS calcd for C₁₃H₁₅O₃ [M + H]⁺ m/z 219.10212, found 219.10201.

3. General procedure for preparation of 4a-4k

Following the similar procedure carried out for I-1, intermediate III-1 was prepared from methyl 4-bromo-1H-pyrrole-2-carboxylate in 92% yield.

Following the similar procedure carried out for I-2, intermediate III-2 was prepared from III-1 in 73% yield.

To a solution of **III-2** (2 mmol) in EtOH (10 mL) was added saturated KOH aqueous solution (2.5 mL). The reaction mixture was stirred at 25 °C until TLC indicated the consumption of starting material. The reaction system was adjusted to pH 2 by the addition of 10% HCl aqueous solution. The aqueous layer was extracted with DCM. The combined organic phases were dried over anhydrous Na₂SO₄, filtered, and

concentrated under vacuum. The residue was further purified by a short silica gel column filtration (DCM/MeOH) to give the desired product **4a** in 99% yield.



Scheme S3. Synthesis of compounds 4a.

Following the similar procedure carried out for **II-1**, intermediate **IV-1** was prepared from methyl 4-bromo-1H-pyrrole-2-carboxylate in 52% yield.

Following the similar procedure carried out for I-2, intermediate IV-2 was prepared from IV-1 in 78% yield.

Following the similar procedure carried out for 4a, the desired product 4b was prepared form IV-2 in 98% yield.



Scheme S4. Synthesis of compounds 4b.

Following the similar procedure carried out for I-1, intermediate V-1 was prepared from methyl 1H-indole-2-carboxylates in 89~95% yields.

Following the similar procedure carried out for I-2, intermediate V-2 was prepared from V-1 in 69~78% yields.

Following the similar procedure carried out for 4a, the desired products 4c-4g were prepared form V-2 in 95~99% yields.



Scheme S5. Synthesis of compounds 4c-4g.

Following the similar procedure carried out for **II-1**, intermediate **VI-1** was prepared from methyl 3-bromo-1H-indole-2-carboxylates in 45~64% yields.

Following the similar procedure carried out for I-2, intermediate VI-2 was prepared from VI-1 in 74~80% yields.

Following the similar procedure carried out for 4a, the desired products 4h-4k were prepared form VI-2 in 95~99% yields.



Scheme S6. Synthesis of compounds 4h-4k.



4-Bromo-1-(buta-2,3-dien-1-yl)-1H-pyrrole-2-carboxylic acid (4a). White solid (798 mg, 66% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.06 (d, J = 2.2 Hz, 1H), 6.94 (d, J = 2.0 Hz, 1H), 5.36 (p, J = 6.5 Hz, 1H), 4.92 – 4.85 (m, 2H), 4.85 – 4.79 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 209.15, 165.25, 129.08, 121.75, 121.43, 96.16, 87.86, 77.38, 48.11. HRMS calcd for C₉H₇BrNO₂ [M - H]⁻ m/z 239.96602, found 239.96643.



4-Bromo-1-(penta-3,4-dien-1-yl)-1H-pyrrole-2-carboxylic acid (4b). White solid (499 mg, 39% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.07 (d, *J* = 1.9 Hz, 1H), 6.88 (d, *J* = 1.9 Hz, 1H), 5.04 (p, *J* = 6.9 Hz, 1H), 4.67 (dt, *J* = 6.4, 3.0 Hz, 2H), 4.34 (t, *J* = 7.0 Hz, 2H), 2.49 – 2.37 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 209.15, 165.39, 129.75, 121.84, 121.35, 95.73, 85.99, 75.69, 49.12, 30.35. HRMS calcd for C₁₀H₁₀BrNNaO₂ [M + Na]⁺ *m/z* 277.97926, found 277.97965.



1-(Buta-2,3-dien-1-yl)-1H-indole-2-carboxylic acid (4c). White solid (499 mg, 39% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, *J* = 7.9 Hz, 1H), 7.45 (d, *J* = 14.9 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 5.38 (p, *J* = 6.5 Hz, 1H), 5.22 (dt, *J* = 6.2, 2.8 Hz, 2H), 4.76 (dt, *J* = 6.1, 2.8 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 208.92, 166.65, 139.78, 126.15, 126.05, 125.89, 123.06, 121.05, 113.09, 111.00, 87.92, 43.52, 32.53. HRMS calcd for C₁₃H₉NO₂ [M - H]⁻ *m*/*z* 212.07170, found 212.07140.



3-Bromo-1-(315-buta-2,3-dien-1-yl)-1H-indole-2-carboxylic acid (4d). White solid (1 g, 73% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 8.1 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.29 – 7.20 (m, 1H), 5.39 (p, *J* = 6.5 Hz, 1H), 5.20 (dt, *J* = 6.0, 2.7 Hz, 2H), 4.79 (dt, *J* = 6.2, 2.7 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 208.96, 166.55, 138.42, 127.21, 127.09, 123.50, 121.99, 121.86, 111.12, 102.31, 87.80, 44.63. HRMS calcd for C₁₃H₁₁BrNO₂ [M + H]⁺ *m/z* 291.99732, found 291.99778.



3-Bromo-1-(buta-2,3-dien-1-yl)-5-methoxy-1H-indole-2-carboxylic acid (4e). White solid (1.1 g, 72% yield over three steps). ¹H NMR (400 MHz, DMSO- d_6) δ 7.48

(d, J = 9.0 Hz, 1H), 7.01 (dd, J = 9.0, 2.4 Hz, 1H), 6.89 (d, J = 2.3 Hz, 1H), 5.36 (p, J = 6.3 Hz, 1H), 5.12 (dt, J = 6.0, 3.0 Hz, 2H), 4.74 (dd, J = 6.6, 3.2 Hz, 2H), 3.78 (s, 3H). ¹³C NMR (101 MHz, DMSO- d_6) δ 208.19, 162.36, 155.54, 132.83, 126.85, 126.33, 117.97, 113.34, 100.70, 97.13, 88.60, 78.02, 55.91, 43.86. HRMS calcd for C₁₄H₁₁BrNO₃ [M - H]⁻ m/z 319.99224, found 319.99234.



3,5-Dibromo-1-(buta-2,3-dien-1-yl)-1H-indole-2-carboxylic acid (4f). White solid (1.2 g, 63% yield over three steps). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.65 (d, *J* = 1.7 Hz, 1H), 7.57 (d, *J* = 8.8 Hz, 1H), 7.49 (dd, *J* = 8.9, 2.0 Hz, 1H), 5.39 (p, *J* = 6.1 Hz, 1H), 5.14 (dt, *J* = 6.0, 3.0 Hz, 2H), 4.73 (dt, *J* = 6.3, 3.0 Hz, 2H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 208.34, 162.32, 136.50, 129.29, 128.35, 128.01, 123.21, 114.75, 114.70, 96.68, 88.72, 78.51, 44.17. HRMS calcd for C₁₃H₈Br₂NO₂[M - H]⁻ *m/z* 367.89273, found 369.89002.



3-Bromo-1-(buta-2,3-dien-1-yl)-5-nitro-1H-indole-2-carboxylic acid (4g). White solid (977 mg, 58% yield over three steps). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.36 (d, J = 1.8 Hz, 1H), 8.19 (dd, J = 9.2, 2.3 Hz, 1H), 7.80 (d, J = 9.2 Hz, 1H), 5.45 (p, J = 6.1 Hz, 1H), 5.21 (dt, J = 6.0, 3.2 Hz, 2H), 4.73 (dt, J = 6.4, 3.1 Hz, 2H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 207.96, 161.74, 142.80, 140.04, 130.24, 125.79, 120.90, 117.87, 113.34, 99.38, 88.40, 78.58, 44.29, 32.51. HRMS calcd for C₁₃H₉BrN₂NaO₄ [M + Na]⁺ *m*/z 358.96434, found 358.96444.



3-Bromo-1-(penta-3,4-dien-1-yl)-1H-indole-2-carboxylic acid (4h). White solid (734 mg, 48% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.69 (dd, *J* = 15.3, 8.1 Hz, 1H), 7.45 – 7.33 (m, 2H), 7.27 – 7.16 (m, 1H), 5.10 (h, *J* = 7.1 Hz, 1H), 4.67 (td, *J* = 6.6, 5.9, 2.6 Hz, 3H), 4.64 – 4.57 (m, 1H), 3.98 (s, 1H), 2.61 – 2.32 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 209.18, 166.33, 138.37, 127.09, 126.32, 123.66, 122.00, 121.74, 121.48, 110.87, 102.01, 86.36, 75.58, 51.98, 45.37, 29.41. HRMS calcd for C₁₄H₁₂BrNNaO₂ [M + Na]⁺ *m/z* 327.99491, found 327.99493.



3,5-Dibromo-1-(penta-3,4-dien-1-yl)-1H-indole-2-carboxylic acid (4i). White solid (519 mg, 27% yield over three steps). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.66 – 7.60 (m, 2H), 7.47 (dd, *J* = 8.9, 2.0 Hz, 1H), 5.08 (p, *J* = 7.0 Hz, 1H), 4.64 – 4.50 (m, 4H), 2.31 (qt, *J* = 6.9, 2.8 Hz, 2H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 208.91, 162.19, 136.32, 128.91, 127.99, 127.83, 122.93, 114.46, 114.38, 96.30, 86.67, 75.80, 45.17, 29.71. HRMS calcd for C₁₄H₁₁Br₂NNaO₂[M + Na]⁺ *m/z* 405.90542, found 405.90587.



3-Bromo-1-(hexa-4,5-dien-1-yl)-1H-indole-2-carboxylic acid (4j). White solid (752 mg, 47% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 8.2 Hz, 1H), 7.42 (d, *J* = 3.8 Hz, 2H), 7.28 – 7.21 (m, 1H), 5.14 (p, *J* = 6.5 Hz, 1H), 4.73 (dt, *J* = 6.5, 3.2 Hz, 2H), 4.67 – 4.58 (m, 2H), 2.06 (dtt, *J* = 9.8, 6.5, 3.1 Hz, 2H), 2.01 – 1.91 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 208.64, 166.37, 138.43, 127.05, 126.94, 123.58, 122.01, 121.68, 110.89, 101.97, 89.14, 75.80, 45.35, 29.74, 25.40. HRMS calcd for C₁₅H₁₄BrNNaO₂ [M + Na]⁺ *m/z* 342.01056, found 342.01034.



3,5-Dibromo-1-(hexa-4,5-dien-1-yl)-1H-indole-2-carboxylic acid (4k). White solid (638 mg, 32% yield over three steps). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.65 – 7.60 (m, 2H), 7.46 (dd, *J* = 8.9, 2.0 Hz, 1H), 5.13 (p, *J* = 6.6 Hz, 1H), 4.70 (dt, *J* = 6.8, 3.5 Hz, 2H), 4.53 (t, *J* = 7.2 Hz, 2H), 1.88 (ddq, *J* = 10.2, 6.6, 3.3 Hz, 2H), 1.79 – 1.67 (m, 2H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 208.27, 162.13, 136.29, 128.92, 127.94, 127.74, 122.94, 114.37, 114.34, 96.22, 89.47, 76.42, 45.20, 30.00, 25.13. HRMS calcd for C₁₅H₁₃Br₂NNaO₂ [M + Na]⁺ *m/z* 419.92107, found 419.92087.

4. General procedure for preparation of 6a-6i

Following the similar procedure carried out for I-1, intermediate VII-1 was prepared from N-Ts amino acid methyl esters in 52~64% yields.

Following the similar procedure carried out for I-2, intermediate VII-2 was prepared from VII-1 in 68~77% yields.

Following the similar procedure carried out for 4a, the desired products 6a, 6c, 6e

and 6h-6i were prepared form VII-2 in 95~99% yields.



Scheme S7. Synthesis of compounds 6a, 6c, 6e and 6h-6i.

Following the similar procedure carried out for II-1, intermediate VIII-1 was prepared from N-Ts amino acid methyl esters in 35~44% yields.

Following the similar procedure carried out for I-2, intermediate VIII-2 was prepared from VIII-1 in 68~80% yields.

Following the similar procedure carried out for **4a**, the desired products **6b**, **6d** and **6f-6g** were prepared form **VIII-2** in 95~99% yields.



Scheme S8. Synthesis of compounds 6b, 6d and 6f-6g.



N-(buta-2,3-dien-1-yl)-N-tosylglycine (6a). Gray solid (647 mg, 46% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 4.94 (p, *J* = 6.9 Hz, 1H), 4.72 (dt, *J* = 6.5, 2.5 Hz, 2H), 4.06 (s, 2H), 3.89 (dt, *J* = 7.2, 2.6 Hz, 2H), 2.41 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 209.93, 174.63, 143.92,

136.63, 129.84, 127.42, 85.35, 76.77, 47.46, 46.94, 21.66. HRMS calcd for $C_{13}H_{14}NO_4S [M - H]^- m/z 280.06490$, found 280.06461.



N-(penta-3,4-dien-1-yl)-N-tosylglycine (6b). White solid (472 mg, 32% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.00 (p, J = 6.9 Hz, 1H), 4.66 (dt, J = 6.7, 3.2 Hz, 2H), 4.06 (s, 2H), 3.34 – 3.24 (m, 2H), 2.41 (s, 3H), 2.22 (tdd, J = 10.1, 6.7, 3.1 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 208.88, 174.44, 174.40, 143.85, 136.47, 129.78, 127.43, 86.40, 75.90, 48.37, 48.10, 27.12, 21.67. HRMS calcd for C₁₄H₁₇NaO₄S [M+ Na]⁺ *m/z* 318.07760, found 318.07751.



N-(buta-2,3-dien-1-yl)-N-tosylvaline (6c). Light yellow liquid (706 mg, 43% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 5.20 (dq, *J* = 8.3, 6.5 Hz, 1H), 4.74 – 4.66 (m, 2H), 4.10 (d, *J* = 10.0 Hz, 1H), 4.04 – 3.86 (m, 2H), 2.38 (s, 3H), 2.11 (ddt, *J* = 12.2, 9.4, 6.0 Hz, 1H), 0.96 (d, *J* = 6.4 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 208.86, 175.84, 143.72, 136.79, 129.56, 127.64, 88.20, 76.18, 65.34, 44.23, 28.36, 21.65, 19.73, 19.59. HRMS calcd for C₁₆H₂₁NNaO₄S [M + Na]⁺ *m/z* 346.10890, found 346.10868.



N-(penta-3,4-dien-1-yl)-N-tosylvaline (6d). Light yellow liquid (438 mg, 26% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 5.01 (p, *J* = 6.7 Hz, 1H), 4.67 (dt, *J* = 6.6, 3.1 Hz, 2H), 4.04 (d, *J* = 10.3 Hz, 1H), 3.40 (ddd, *J* = 16.3, 11.2, 5.4 Hz, 1H), 3.25 (ddd, *J* = 15.8, 11.3, 5.2 Hz, 1H), 2.44 (dtt, *J* = 11.3, 6.1, 2.8 Hz, 1H), 2.37 (s, 3H), 2.30 – 2.18 (m, 1H), 2.11 – 2.03 (m, 1H), 0.94 (t, *J* = 6.7 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 208.84, 175.96, 143.68, 136.72, 129.57, 127.57, 86.78, 75.66, 65.68, 44.92, 29.25, 28.61, 21.61, 19.82, 19.51. HRMS calcd for C₁₇H₂₁NO4S [M - H]⁻ *m/z* 336.12969, found 336.12919.



N-(buta-2,3-dien-1-yl)-N-tosylphenylalanine (6e). Light yellow liquid (687 mg, 37% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, J = 8.2 Hz, 2H), 7.32 – 7.09 (m, 7H), 5.05 (p, J = 6.9 Hz, 1H), 4.87 (dd, J = 8.6, 6.4 Hz, 1H), 4.74 (dq, J = 6.6, 2.2 Hz, 2H), 4.01 – 3.76 (m, 2H), 3.36 (dd, J = 14.4, 6.5 Hz, 1H), 3.00 (dd, J = 14.4, 8.6 Hz, 1H), 2.37 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 209.22, 176.31, 143.64, 136.86, 136.82, 129.59, 129.25, 128.74, 127.58, 126.98, 87.62, 76.54, 60.72, 45.01, 35.88, 21.62. HRMS calcd for C₂₀H₂₁NNaO₄S [M + Na]⁺ *m*/*z* 394.10890, found 394.10933.



N-(penta-3,4-dien-1-yl)-N-tosylphenylalanine (6f). Light yellow liquid (436 mg, 22% yield over three steps). ¹H NMR (400 MHz, DMSO- d_6) δ 7.62 (d, J = 8.1 Hz, 2H), 7.25 – 7.04 (m, 7H), 5.05 (p, J = 6.7 Hz, 1H), 4.69 (dt, J = 6.7, 3.2 Hz, 2H), 4.22 (t, J = 7.1 Hz, 1H), 3.35 – 2.99 (m, 3H), 2.55 (dd, J = 13.8, 6.9 Hz, 1H), 2.31 (s, 3H), 2.24 – 2.12 (m, 1H), 2.11 – 1.96 (m, 1H). ¹³C NMR (101 MHz, DMSO- d_6) δ 208.46, 171.31, 129.64, 129.57, 128.42, 127.65, 126.07, 87.76, 75.98, 65.43, 45.05, 38.91, 29.25, 21.47. HRMS calcd for C₂₁H₂₃NNaO₄S [M + Na]⁺ m/z 408.12455, found 408.12425.



N-(hexa-4,5-dien-1-yl)-N-tosylphenylalanine (6g). Light yellow liquid (470 mg, 23% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 10.61 (s, 1H), 7.59 – 7.50 (m, 2H), 7.30 – 7.07 (m, 7H), 5.02 (p, *J* = 6.6 Hz, 1H), 4.76 (t, *J* = 7.4 Hz, 1H), 4.66 (dt, *J* = 6.5, 3.2 Hz, 2H), 3.42 – 3.24 (m, 2H), 3.17 (ddd, *J* = 15.4, 10.5, 5.6 Hz, 1H), 2.95 (dd, *J* = 14.3, 7.9 Hz, 1H), 2.37 (d, *J* = 2.4 Hz, 3H), 1.92 (qq, *J* = 6.6, 3.3 Hz, 2H), 1.76 – 1.58 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 208.59, 176.06, 143.57, 136.90, 136.72, 129.57, 129.17, 128.72, 127.55, 126.99, 89.05, 75.56, 61.26, 45.66, 36.39, 29.13, 25.53, 21.60. HRMS calcd for C₂₂H₂₅NNaO₄S [M + Na]⁺ *m/z* 422.14020, found 422.13982.



3-((N-(buta-2,3-dien-1-yl)-4-methylphenyl)sulfonamido)propanoic acid (6h). White solid (664 mg, 45% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 7.70 – 7.66 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.91 (p, *J* = 6.9 Hz, 1H), 4.71 (dt, *J* = 6.5, 2.4 Hz, 2H), 3.84 (dt, *J* = 7.1, 2.6 Hz, 2H), 3.43 (dd, *J* = 8.4, 6.5 Hz, 2H), 2.73 – 2.67 (m, 2H), 2.41 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 209.60, 177.45, 143.73, 136.57, 129.92, 127.31, 85.90, 76.67, 47.72, 42.70, 34.05, 21.63. HRMS calcd for C₁₄H₁₆NO₄S [M - H]⁻ *m/z* 294.08055, found 294.07975.



4-((N-(buta-2,3-dien-1-yl)-4-methylphenyl)sulfonamido)butanoic acid (6i). White solid (648 mg, 42% yield over three steps). ¹H NMR (400 MHz, CDCl₃) δ 10.95 (s, 1H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 4.84 (p, *J* = 6.9 Hz, 1H), 4.67 (dt, *J* = 6.5, 2.5 Hz, 2H), 3.80 (dt, *J* = 7.3, 2.5 Hz, 2H), 3.18 (t, *J* = 6.9 Hz, 2H), 2.39 (d, *J* = 8.3 Hz, 5H), 1.84 (q, *J* = 7.2 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 209.56, 179.10, 143.53, 136.85, 129.86, 127.23, 85.78, 76.40, 46.99, 46.22, 30.90, 23.07, 21.60. HRMS calcd for C₁₅H₁₈NO₄S [M - H]⁻ *m/z* 308.09620, found 308.09541.

5. Single crystal X-ray diffraction data of 2i

Crystal of **2i** was grown by slow evaporation of tert-Butanol solution at room temperature (20 °C). X-ray diffraction data was collected at 293(2) K on a Bruker Kappa Apex Duo diffractometer with graded-multilayer focused CuK(alpha) X-rays.



Crystal data and structure refinement for 2i		
Identification code	2i	
CCDC number	2284212	
Bond precision	C-C = 0.0064 A	
Wavelength	1.54178	
Cell	a=9.5458(3) b=10.8218(3) c=18.6882(5)	
	alpha=102.663(1) beta=92.618(1) gamma=90.594(1)	
Temperature	150 K	
Volume	1881.21(9)	
Space group	P -1	
Hall group	-P 1	
Moiety formula	?	
Sum formula	C ₁₉ H ₁₈ I N O ₄ S	
Mr	483.30	
Dx,g.cm-3	1.706	
Ζ	4	
Mu (mm-1)	14.624	
F000	960.0	
h,k,lmax	11,13,23	
Nref	7613	
Tmin,Tmax	0.005,0.087	
Data completeness	0.985	
Theta(max)	74.712	
R(reflections)	0.0690(6825)	
wR2(reflections)	0.1889(7613)	
S	1.101	
Npar	545	

Figure S1. Crystal structure of 2i with thermal ellipsoids at 30% probability.



6. Copies of ¹H NMR and ¹³C NMR spectra for 2a-2j, 3a, 3e, 3f, 5a-5k and 7a-7i

¹H NMR spectrum of 2a



¹³C NMR spectrum of 2a





¹³C NMR spectrum of 3a





¹³C NMR spectrum of 2b

 $\begin{array}{c} 7.80\\ 7.78\\ 7.725\\ 7.255\\ 7.224\\ 7.224\\ 7.225\\ 7.224\\ 7.225\\ 7.224\\ 7.225\\ 7.225\\ 7.225\\ 7.225\\ 7.225\\ 7.225\\ 7.225\\ 7.225\\ 7.25$



¹H NMR spectrum of 2c



¹³C NMR spectrum of 2c



¹³C NMR spectrum of 2d







¹³C NMR spectrum of 2e



¹H NMR spectrum of 3e



¹³C NMR spectrum of 3e







¹³C NMR spectrum of 2f



¹⁹F NMR spectrum of 2f



¹H NMR spectrum of 3f



¹⁹F NMR spectrum of 3f







¹³C NMR spectrum of 2g







¹³C NMR spectrum of 2h







¹³C NMR spectrum of 2i







¹³C NMR spectrum of 2j







¹³C NMR spectrum of 5a

 7
 7
 7
 7
 7
 7
 8
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6
 6







¹³C NMR spectrum of 5b



¹H NMR spectrum of 5c



¹³C NMR spectrum of 5c



¹H NMR spectrum of 5d



¹³C NMR spectrum of 5d



¹H NMR spectrum of 5e



¹³C NMR spectrum of 5e





¹³C NMR spectrum of 5f






¹³C NMR spectrum of 5g



¹H NMR spectrum of 5h



¹³C NMR spectrum of 5h







¹³C NMR spectrum of 5i

7,756 7,756 7,756 7,756 7,756 7,756 6,64 7,728 6,64 7,228 6,222 2,22







¹³C NMR spectrum of 5j







¹³C NMR spectrum of 5k







¹³C NMR spectrum of 7a





190 180

50 40



¹H NMR spectrum of 7c



¹³C NMR spectrum of 7c







¹³C NMR spectrum of 7d



¹H NMR spectrum of 7e



¹³C NMR spectrum of 7e



¹³C NMR spectrum of 7f



¹H NMR spectrum of 7g



¹³C NMR spectrum of 7g



¹H NMR spectrum of 7h



¹³C NMR spectrum of 7h



¹H NMR spectrum of 7i



¹³C NMR spectrum of 7i



7. Copies of ¹H NMR and ¹³C NMR spectra for 1a-1j, 4a-4k and 6a-6i





¹³C NMR spectrum of 1a



¹³C NMR spectrum of 1b





¹³C NMR spectrum of 1c





¹³C NMR spectrum of 1d







¹³C NMR spectrum of 1e



¹³C NMR spectrum of 1f



80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 f1 (ppm)

¹⁹F NMR spectrum of 1f







¹³C NMR spectrum of 1g



¹H NMR spectrum of 1h



¹³C NMR spectrum of 1h



¹H NMR spectrum of 1i



¹³C NMR spectrum of 1i



¹³C NMR spectrum of 1j







¹³C NMR spectrum of 4a







¹³C NMR spectrum of 4b



¹H NMR spectrum of 4c



¹³C NMR spectrum of 4c



¹H NMR spectrum of 4d



¹³C NMR spectrum of 4d



220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 f1 (ppm)

¹³C NMR spectrum of 4e



¹H NMR spectrum of 4f



¹³C NMR spectrum of 4f



¹³C NMR spectrum of 4g



¹H NMR spectrum of 4h



¹³C NMR spectrum of 4h



¹³C NMR spectrum of 4i







¹³C NMR spectrum of 4j



¹³C NMR spectrum of 4k


¹³C NMR spectrum of 6a



¹H NMR spectrum of 6b



¹³C NMR spectrum of 6b



¹³C NMR spectrum of 6c



¹H NMR spectrum of 6d



¹³C NMR spectrum of 6d



¹H NMR spectrum of 6e



¹³C NMR spectrum of 6e



¹³C NMR spectrum of 6f



¹H NMR spectrum of 6g



¹³C NMR spectrum of 6g



¹H NMR spectrum of 6h



¹³C NMR spectrum of 6h



¹³C NMR spectrum of 6i









HMBC NMR spectrum of 2b



DEPT NMR spectrum of 2b













COSY NMR spectrum of 7b







