

Supporting Information

Intermolecular Bromoesterification of Conjugated Enynes: An Efficient Synthesis of Bromoallenes

Hao-Yuan Wang,^a Wei Zhang,^a Casi M. Schienebeck,^a Scott R. Bennett,^a and Weiping Tang^{*a,b}

^a. School of Pharmacy, University of Wisconsin, Madison, WI, 53705 USA.

^b. Department of Chemistry, University of Wisconsin, Madison, WI, 53706 USA.

E-mail: wtang@pharmacy.wisc.edu

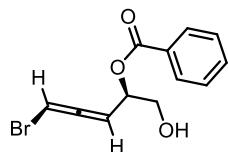
General remarks

All reactions in non-aqueous media were conducted under a positive pressure of dry argon in glassware that had been oven dried prior to use unless noted otherwise. Anhydrous solutions of reaction mixtures were transferred via an oven dried syringe or cannula. All solvents were dried prior to use unless noted otherwise. Thin layer chromatography was performed using precoated silica gel plates (EMD Chemical Inc. 60, F254). Flash column chromatography was performed with silica gel (Silicycle, 40-63 µm). Infrared spectra (IR) were obtained on a Bruker Equinox 55 Spectrophotometer. ¹H and ¹³C nuclear magnetic resonance spectra (NMR) were obtained on a Varian Unity-Inova 400 MHz or 500 MHz recorded in ppm (δ) downfield of TMS ($\delta = 0$) in CDCl₃ unless noted otherwise. Signal splitting patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), or multiplet (m), with coupling constants (J) in hertz. High resolution mass spectra (HRMS) were performed by Analytical Instrument Center at the School of Pharmacy or Department of Chemistry on an Electron Spray Injection (ESI) mass spectrometer.

General methods for the preparation of conjugated enynes:

Substrates **3a**, **3c**, **3e**, **3g**, **3h** were prepared according to our previously reported procedures¹ and their spectra are in accordance with literature.¹⁻⁴ Substrates **3b**,⁵ **3d**,⁶ and **3f**⁷ were prepared according to known procedures and their spectra are in accordance with literature.

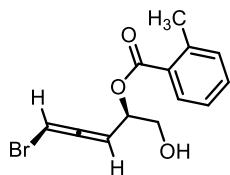
Characterization data for bromoesterification products:



2a: 5-bromo-1-hydroxypenta-3,4-dien-2-yl benzoate

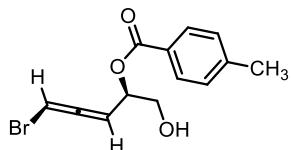
Colorless oil. 21.0 mg, 73% yield. (dr = 10:1, 68% yield for 1mmol scale) ¹H NMR (400 MHz, CDCl₃, TMS): δ 8.07 (d, $J = 7.2$ Hz, 2H), 7.59 (t, $J = 7.2$ Hz, 1H), 7.46 (t, $J = 7.6$ Hz, 2H), 6.18 – 6.08 (dd, $J = 5.6$,

2.0 Hz, 1H), 5.69 (qd, J = 5.2, 2.0 Hz, 1H), 5.58 (t, J = 5.6 Hz, 1H), 3.91 (br, s, 2H), 2.10 (br, s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 202.57, 166.03, 133.54, 129.92, 129.68, 128.61, 97.04, 75.28, 71.57, 64.22. IR (neat) ν 3454, 3061, 2934, 1719, 1265, 1069 cm^{-1} . HRMS (ESI) for $\text{C}_{12}\text{H}_{11}\text{BrO}_3$ ($\text{M}+\text{H}$), 282.9965 (Calc.), found 282.9967.



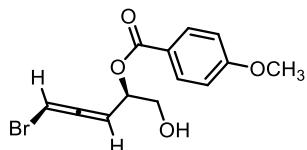
2b: 5-bromo-1-hydroxypenta-3,4-dien-2-yl 2-methylbenzoate

Colorless oil. 19.0 mg, 65% yield. ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.96 (d, J = 8.0 Hz, 1H), 7.43 (td, J = 7.5, 0.5 Hz, 1H), 7.29 – 7.23 (m, 2H), 6.14 (dd, J = 5.5, 2.0 Hz, 1H), 5.70 – 5.63 (m, 1H), 5.58 (t, J = 5.5 Hz, 1H), 3.98 – 3.86 (m, 2H), 2.61 (s, 3H), 2.03 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 202.63, 166.82, 140.67, 132.57, 131.93, 130.91, 129.02, 125.95, 97.12, 75.30, 71.36, 64.26, 21.95. IR (neat) ν 3425, 3060, 2927, 1719, 1250, 1073 cm^{-1} . HRMS (ESI) for $\text{C}_{13}\text{H}_{13}\text{BrO}_3$ ($\text{M}+\text{NH}_4$), 314.0387 (Calc.), found 314.0384.



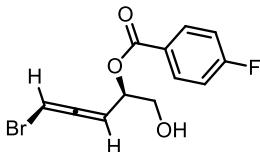
2c: 5-bromo-1-hydroxypenta-3,4-dien-2-yl 4-methylbenzoate

Colorless oil. 19.0 mg, 65% yield. ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.95 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 7.0 Hz, 2H), 6.12 (dd, J = 5.6, 2.0 Hz, 1H), 5.68 (m, 1H), 5.56 (t, J = 5.6 Hz, 1H), 3.98 – 3.85 (m, 2H), 2.42 (s, 3H), 1.25 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 202.56, 166.10, 144.37, 129.98, 129.34, 126.93, 97.17, 75.26, 71.41, 64.32, 21.86. IR (neat) ν 3440, 3060, 2924, 1719, 1268, 1105 cm^{-1} . HRMS (ESI) for $\text{C}_{13}\text{H}_{13}\text{BrO}_3$ ($\text{M}+\text{H}$), 297.0121 (Calc.), found 297.0123.



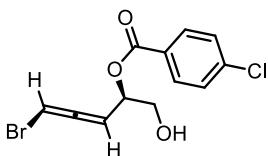
2d: 5-bromo-1-hydroxypenta-3,4-dien-2-yl 4-methoxybenzoate.

Colorless oil. 14.0 mg, 45% yield. ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.02 (d, J = 9.0 Hz, 2H), 6.93 (d, J = 8.5 Hz, 2H), 6.12 (d, J = 5.5 Hz, 1H), 5.67 (d, J = 5.0 Hz, 1H), 5.58 (t, J = 5.5 Hz, 1H), 3.92 (d, J = 4.5 Hz, 2H), 3.87 (s, 3H), 2.02 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 202.53, 165.77, 163.89, 132.04, 122.01, 113.89, 97.27, 75.23, 71.31, 64.38, 55.64. IR (neat) ν 3453, 3060, 2923, 1711, 1254, 1101 cm^{-1} . HRMS (ESI) for $\text{C}_{13}\text{H}_{13}\text{BrO}_4$ ($\text{M}+\text{H}$), 313.0070 (Calc.), found 313.0066.



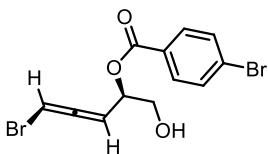
2e: 5-bromo-1-hydroxypenta-3,4-dien-2-yl 4-fluorobenzoate.

Colorless oil. 21.0 mg, 70% yield. ^1H NMR (400 MHz, CDCl_3 , TMS): δ 8.05 – 8.12 (m, 2H), 7.17 – 7.08 (t, J = 8.4 Hz, 2H), 6.13 (ddd, J = 5.6, 2.0, 0.4 Hz, 1H), 5.72 – 5.64 (m, 1H), 5.57 (td, J = 5.6, 0.4 Hz, 1H), 3.98 – 3.88 (m, 2H), 2.00 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 202.62, 166.17 (d, J = 253 Hz), 165.06, 132.54 (d, J = 9.3 Hz), 125.95, 115.84 (d, J = 21.9 Hz), 96.93, 75.33, 71.69, 64.22. IR (neat) ν 3440, 3061, 2927, 1720, 1265, 1113 cm^{-1} . HRMS (ESI) for $\text{C}_{12}\text{H}_{10}\text{BrFO}_3$ ($\text{M}+\text{Na}$), 322.9689 (Calc.), found 322.9690.



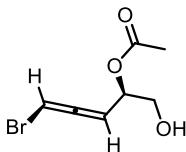
2f: 5-bromo-1-hydroxypenta-3,4-dien-2-yl 4-chlorobenzoate.

Colorless oil. 14.0 mg, 45% yield. ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.01 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 8.5 Hz, 2H), 6.13 (dd, J = 5.5, 2.0 Hz, 1H), 5.73 – 5.62 (m, 1H), 5.58 (t, J = 5.5 Hz, 1H), 3.99 – 3.85 (m, 2H), 2.00 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 202.65, 165.17, 140.09, 131.33, 129.01, 128.15, 96.85, 75.37, 71.79, 64.19. IR (neat) ν 3441, 3060, 2924, 1718, 1265, 1091 cm^{-1} . HRMS (ESI) for $\text{C}_{12}\text{H}_{10}\text{BrO}_3$ ($\text{M}+\text{Na}$), 338.9394 (Calc.), found 338.9392.



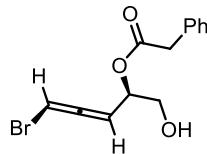
2g: 5-bromo-1-hydroxypenta-3,4-dien-2-yl 4-bromobenzoate.

Colorless oil. 16.0 mg, 44% yield. ^1H NMR (400 MHz, CDCl_3 , TMS): δ 7.93 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.4 Hz, 2H), 6.13 (dd, J = 6.0, 0.8 Hz, 1H), 5.72 – 5.65 (m, 1H), 5.57 (t, J = 6.0 Hz, 1H), 3.98 – 3.90 (m, 2H), 1.99 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 202.65, 165.31, 132.01, 131.44, 128.78, 128.61, 96.83, 75.38, 71.81, 64.18. IR (neat) ν 3424, 3060, 2923, 1720, 1265, 1116 cm^{-1} . HRMS (ESI) for $\text{C}_{12}\text{H}_{10}\text{Br}_2\text{O}_3$ ($\text{M}+\text{Na}$), 382.8888 (Calc.), found 382.8878.



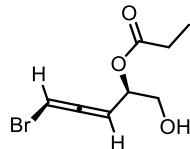
2h: 5-bromo-1-hydroxypenta-3,4-dien-2-yl acetate.

Colorless oil. 15.0 mg, 67% yield. ^1H NMR (500 MHz, CDCl_3 , TMS): δ 6.17 – 6.11 (m, 1H), 5.47 (t, $J = 5.5$ Hz, 1H), 5.45 – 5.39 (m, 1H), 3.88 – 3.72 (m, 2H), 2.18 – 2.08 (s, 3H), 1.86 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 202.59, 170.40, 96.84, 75.02, 71.14, 64.04, 21.12. IR (neat) v 3441, 3060, 2924, 1737, 1232, 1044 cm^{-1} . HRMS (ESI) for $\text{C}_7\text{H}_9\text{BrO}_3$ ($\text{M}+\text{NH}_4$), 238.0074 (Calc.), found 238.0078.



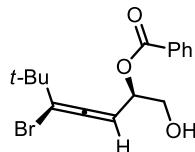
2i: 5-bromo-1-hydroxypenta-3,4-dien-2-yl 2-phenylacetate.

Colorless oil. 23.0 mg, 77% yield. ^1H NMR (400 MHz, CDCl_3 , TMS): δ 7.38 – 7.27 (m, 5H), 6.03 – 5.95 (m, 1H), 5.47 – 5.37 (m, 2H), 3.77 (m, 2H), 3.69 (s, 2H), 1.71 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 202.43, 170.97, 133.69, 129.37, 128.83, 127.44, 96.72, 75.23, 71.34, 63.98, 41.45. IR (neat) v 3454, 3060, 2922, 1734, 1245, 1146 cm^{-1} . HRMS (ESI) for $\text{C}_{13}\text{H}_{13}\text{BrO}_3$ ($\text{M}+\text{NH}_4$), 314.0387 (Calc.), found 314.0395.



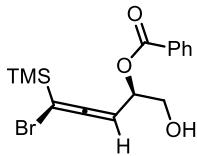
2j: 5-bromo-1-hydroxypenta-3,4-dien-2-yl propionate.

Colorless oil. 14.0 mg, 61% yield. ^1H NMR (400 MHz, CDCl_3 , TMS): δ 6.14 – 6.10 (m, 1H), 5.50 – 5.40 (m, 2H), 3.87 – 3.75 (m, 2H), 2.40 (q, $J = 7.6$ Hz, 2H), 1.26 (s, 1H), 1.21 – 1.13 (m, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 202.52, 173.88, 97.02, 75.05, 70.87, 64.13, 27.73, 9.26. IR (neat) v 3455, 3061, 2924, 1737, 1180, 1082 cm^{-1} . HRMS (ESI) for $\text{C}_8\text{H}_{11}\text{BrO}_3$ ($\text{M}+\text{NH}_4$), 252.0230 (Calc.), found 252.0234.



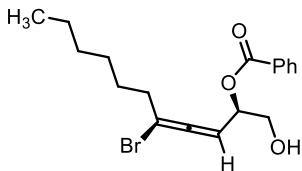
4a: 5-bromo-1-hydroxy-6,6-dimethylhepta-3,4-dien-2-yl benzoate.

Colorless oil. 24.0 mg, 71% yield. ^1H NMR (400 MHz, CDCl_3 , TMS): δ 8.07 (d, $J = 7.2$ Hz, 2H), 7.58 (td, $J = 8.0, 1.2$ Hz, 1H), 7.45 (t, $J = 7.6$ Hz, 2H), 5.70 – 5.62 (m, 1H), 5.45 (dd, $J = 5.2, 1.2$ Hz, 1H), 3.95 – 3.88 (m, 2H), 2.09 (s, 1H), 1.07 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3): δ 198.20, 166.16, 133.57, 130.03, 129.91, 128.66, 109.10, 94.74, 72.10, 64.40, 37.04, 31.17, 29.12, 28.99. IR (neat) v 3442, 3063, 2969, 1721, 1267, 1113 cm^{-1} . HRMS (ESI) for $\text{C}_{16}\text{H}_{19}\text{BrO}_3$ ($\text{M}+\text{Na}$), 361.0410 (Calc.), found 361.0414.



4b: 5-bromo-1-hydroxy-5-(trimethylsilyl)penta-3,4-dien-2-yl benzoate.

Colorless oil. 25.0 mg, 71% yield. ¹H NMR (400 MHz, CDCl₃, TMS): δ 8.06 (d, *J* = 8.8 Hz, 2H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 5.70 – 5.62 (m, 1H), 5.31 (d, *J* = 5.2 Hz, 1H), 3.97 – 3.83 (m, 2H), 2.04 (s, 1H), 0.09 (s, 9H). ¹³C NMR (100 MHz, CDCl₃): δ 203.76, 165.99, 133.49, 129.94, 129.83, 128.58, 91.75, 90.05, 71.65, 64.48, -2.05. IR (neat) v 3440, 3063, 2958, 1721, 1266, 1112 cm⁻¹. HRMS (ESI) for C₁₅H₁₉BrO₃Si (M+NH₄), 372.0626 (Calc.), found 372.0615.



4c: 5-bromo-1-hydroxy-undeca-3,4-dien-2-yl benzoate.

Colorless oil. 15.9 mg, 65% yield. ¹H NMR (400 MHz, CDCl₃, TMS): δ 8.07 (d, *J* = 8.1 Hz, 2H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 5.64 (dt, *J* = 6.1, 4.7 Hz, 1H), 5.46 (dt, *J* = 5.5, 3.0 Hz, 1H), 3.98 – 3.86 (m, 2H), 2.32 (td, *J* = 7.5, 2.9 Hz, 2H), 1.46 – 1.11 (m, 8H), 0.84 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 199.73, 166.18, 133.55, 130.00, 129.92, 128.66, 96.83, 94.69, 72.25, 64.42, 37.66, 31.61, 28.43, 27.97, 22.65, 14.24. IR (neat) v 3442, 3064, 2956, 2928, 2857, 1721, 1268, 1114, 909, 733, 711 cm⁻¹. HRMS (ESI) for C₁₈H₂₃BrO₃ (M+Na), 389.0722 (Calc.), found 389.0728.

References:

- (1) W. Zhang, H. Xu, H. Xu, W. Tang. *J. Am. Chem. Soc.* **2009**, *131*, 3832-3833.
- (2) B. M. Trost, J. L. Gunzner. *J. Am. Chem. Soc.* **2001**, *123*, 9449-9450.
- (3) W. Zhang, S. Zheng, N. Liu, J. B. Werness, I. A. Guzei, W. Tang. *J. Am. Chem. Soc.* **2010**, *132*, 3664-3665.
- (4) G. Kim, M. J. Seo. *Bull. Korean Chem. Soc.* **1995**, *16*, 1002-1003.
- (5) K. C. Nicolaou, C. A. Veale, S. E. Webber, H. Katerinopoulos. *J. Am. Chem. Soc.* **1985**, *107*, 7515-7518.
- (6) B. Seiller, C. Bruneau, P. H. Dixneuf. *Tetrahedron*, **1995**, *51*, 13089-13102.
- (7) J. K. Stile, J. H. Simpson. *J. Am. Chem. Soc.* **1987**, *109*, 2138-2152

