Supporting Information for
Electrophilic Cyclization of 2-(1-Alkynyl)-2-alken-1-ones Using I₂/K₃PO₄ System: An
Efficient Synthesis of Highly Substituted Iodofurans

Yuanhong Liu* and Shaolin Zhou

State Key Laboratory of Organometallic Chemistry

Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences,

354 Fenglin Lu, Shanghai 200032, People's Republic of China

E-mail: yhliu@mail.sioc.ac.cn

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General Methods. ¹H and ¹³C NMR spectra were recorded at 300 and 75.4 MHz, respectively, in CDCl₃ (containing 1% TMS) solutions. Reactions were monitored by thin-layer chromatography. Column chromatography was performed on neutral silica gel (60N, 100-210 μm) and elution with a petroleum ether (60-90 °C)/AcOEt solvent system. The substrates of 2-(1-Alkynyl)-2-alken-1-ones **1a-1g** were prepared by the known procedures¹ from readily available alkenones and alkynes. CH₂Cl₂ was distilled from CaH₂. Other commercial reagents were used without further purification.

Representative procedure for the electrophilic cyclization reactions of 2-(1-Alkynyl)-2-alken-1-ones (1). To a solution of 2-(1-Alkynyl)-2-alken-1-ones **1** (0.2 mmol) in 2 mL CH₂Cl₂ was added MeOH (0.3 mmol), K₃PO₄ (0.22 mmol) and I₂ (0.22 mmol) at 0 °C. After 5 minutes, the above suspension was warmed up to room temperature and stirred for an appropriate time. The reaction mixture was then diluted with ethyl acetate, washed with saturated Na₂S₂O₃ solution, dried (Na₂SO₄), and filtered. The solvent was evaporated under reduced pressure, and the product was isolated by chromatography on a Al₂O₃ column.

3-Iodo-4-methoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (2a). ¹H NMR (CDCl₃, Me₄Si) δ 1.56(tt, *J*=10.5, 3.6 Hz, 1H), 1.83-1.90 (m, 1H), 1.94-2.05 (m, 1H), 2.12-2.20 (m, 1H), 2.49-2.61 (m, 1H), 2.68-2.76 (m, 1H), 3.48 (s, 3H), 4.11(t, *J* = 3.3 Hz, 1H), 7.24-7.42 (m, 3H), 7.94 (d, *J* = 7.8 Hz, 2H); ¹³C NMR (CDCl₃, Me₄Si) δ 18.2, 23.2, 26.7, 57.0, 65.0, 71.9, 123.4, 126.1, 127.7, 128.2, 130.5, 150.0, 153.8. HRMS(MALDI) for C₁₅H₁₆IO₂ [M+H]⁺: calcd 355.0195, found 355.0190.

3-Iodo-4-phenoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (2b) ^1H NMR (CDCl_3 , Me_4Si) δ , 1.69 (tt, $J = 13.8, 3.3$ Hz, 1H), 1.85-1.91 (m, 1H), 2.02-2.12 (m, 1H), 2.22-2.28 (m, 1H), 2.53-2.64 (m, 1H), 2.75-2.83 (m, 1H), 5.18 (s, 1H), 6.98 (t, $J = 7.5$ Hz, 1H), 7.08 (d, $J = 8.4$ Hz, 2H), 7.27-7.42 (m, 5H), 7.95 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (CDCl_3 , Me_4Si) δ 18.4, 23.1, 27.3, 64.6, 69.5, 116.5, 121.2, 122.3, 126.1, 127.9, 128.3, 129.5, 130.3, 150.2, 154.6, 157.8. HRMS(MALDI) for $\text{C}_{20}\text{H}_{17}\text{INaO}_2$ $[\text{M}+\text{Na}]^+$: calcd 439.0171, found 439.0165.

3-Iodo-2-phenyl-4-prop-2-ynyloxy-4,5,6,7-tetrahydrobenzofuran (2c) ^1H NMR (CDCl_3 , Me_4Si) δ 1.60 (tt, $J = 13.8, 3.0$ Hz, 1H), 1.86-1.91 (m, 1H), 2.02-2.09 (m, 1H), 2.21-2.27 (m, 1H), 2.46-2.61 (m, 2H), 2.68-2.77 (m, 1H), 4.36 (dd, $J = 4.5, 2.7$ Hz, 2H), 4.43 (t, $J = 2.4$ Hz, 1H), 7.24-7.32 (m, 1H), 7.37-7.42 (m, 2H), 7.91-7.94 (m, 2H); ^{13}C NMR (CDCl_3 , Me_4Si) δ 18.1, 23.1, 27.3, 56.7, 64.7, 70.2, 74.4, 80.3, 123.0, 126.1, 127.8, 128.2, 130.4, 150.0, 154.2. HRMS(MALDI) for $\text{C}_{17}\text{H}_{15}\text{INaO}_2$ $[\text{M}+\text{Na}]^+$: calcd 401.0014, found 401.0009.

4-Allyloxy-3-iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran (2d) ^1H NMR (CDCl_3 , Me_4Si) δ 1.57 (tt, $J = 13.5, 3.6$ Hz, 1H), 1.81-1.90 (m, 1H), 1.97-2.17 (m, 2H), 2.48-2.60 (m, 1H), 2.67-2.76 (m, 1H), 4.16-4.19 (m, 2H), 4.27 (t, $J = 2.7$ Hz, 1H), 5.18 (dd, $J = 10.2, 1.8$ Hz, 1H), 5.30-5.37 (m, 1H), 5.99-6.12 (m, 1H), 7.26-7.41 (m, 3H), 7.90-7.94 (m, 2H); ^{13}C NMR (CDCl_3 , Me_4Si) δ 18.2, 23.2, 27.4, 65.0, 70.3, 70.6, 116.9, 123.3, 126.1, 127.7, 128.2,

130.47, 135.2, 149.9, 153.9. HRMS(MALDI) for $C_{17}H_{18}IO_2$ $[M+H]^+$: calcd 381.0351, found 381.0346.

4-(7,7-Dimethylbicyclo[2.2.1]hept-2-yloxy)-3-iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran (2e) 1H NMR ($CDCl_3$, Me_4Si) δ (2 isomers in the ratio of 1:1) 0.79-0.88 (m, 9H), 1.03-1.29 (m, 2H), 1.37-1.53 (m, 2H), 1.56-1.69 (m, 2H), 1.72-1.84 (m, 1H), 1.97-2.17 (m, 4H), 2.49-2.76 (m, 2H), 3.81-3.90 (m, 1H), 4.25-4.26 (m, 1H), 7.21-7.30 (m, 1H), 7.36-7.41 (m, 2H), 7.92-7.96 (m, 2H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ (2 isomers in the ratio of 1:1) 13.7, 14.5, 17.8, 18.0, 18.9, 18.91, 19.76, 19.79, 23.39, 23.41, 26.6, 26.7, 28.1, 28.3, 29.1, 35.3, 38.3, 45.1, 45.2, 47.4, 47.8, 49.0, 49.7, 65.3, 65.5, 67.8, 71.1, 123.5, 124.4, 126.2, 127.6, 127.7, 128.2, 130.6, 149.77, 149.81, 153.8, 153.9. HRMS(MALDI) for $C_{24}H_{29}INaO_2$ $[M+Na]^+$: calcd 499.1110, found 499.1104.

3-Iodo-4-methoxy-2-p-tolyl-4,5,6,7-tetrahydrobenzofuran (2f) 1H NMR ($CDCl_3$, Me_4Si) δ 1.54 (tt, $J = 13.5, 3.3$ Hz, 1H), 1.82-1.88 (m, 1H), 1.94-2.04 (m, 1H), 2.11-2.19 (m, 1H), 2.35 (s, 3H), 2.48-2.59 (m, 1H), 2.66-2.75 (m, 1H), 7.19 (d, $J = 8.1$ Hz, 2H), 7.80 (d, $J = 8.1$ Hz, 2H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 18.2, 21.3, 23.2, 26.7, 57.0, 64.3, 71.9, 123.2, 126.1, 127.7, 128.9, 137.6, 150.3, 153.4. HRMS(MALDI) for $C_{16}H_{18}IO_2$ $[M+H]^+$: calcd

369.0351, found 369.0346.

2-Cyclohex-1-enyl-3-iodo-4-methoxy-4,5,6,7-tetrahydrobenzofuran (2g) ^1H NMR (CDCl_3 , Me_4Si) δ 1.51 (tt, $J = 13.5, 3.6$ Hz, 1H), 1.61-1.75 (m, 4H), 1.78-1.87 (m, 1H), 1.89-2.00 (m, 1H), 2.09-2.22 (m, 3H), 2.41-2.50 (m, 3H), 2.59-2.67 (m, 1H), 3.47 (s, 3H), 4.05 (t, $J = 2.7$ Hz, 1H), 6.42-6.46 (m, 1H); ^{13}C NMR (CDCl_3 , Me_4Si) δ 18.2, 21.8, 22.5, 23.1, 25.3, 26.4, 26.7, 57.0, 62.7, 71.9, 122.5, 127.6, 127.9, 152.1, 152.2. HRMS(MALDI) for $\text{C}_{15}\text{H}_{20}\text{IO}_2$ $[\text{M}+\text{H}]^+$: calcd 359.0508, found 359.0503.

2-(3-Iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran-4-yl)-1-phenylethanone (2h) ^1H NMR (CDCl_3 , Me_4Si) δ 2.07-2.19 (m, 4H), 2.89-2.98 (m, 2H), 3.36 (dd, $J = 16.8, 11.1$ Hz, 1H), 3.63-3.67 (m, 1H), 3.78 (dd, $J = 17.1, 2.4$ Hz, 1H), 7.54-7.62 (m, 1H), 7.68-7.77 (m, 4H), 7.85-7.89 (m, 1H), 8.24-8.37 (m, 4H); ^{13}C NMR (CDCl_3 , Me_4Si) δ 18.8, 23.1, 26.9, 28.5, 41.9, 65.1, 124.6, 126.0, 127.7, 128.2, 128.3, 128.6, 130.6, 133.1, 136.9, 149.6, 151.8, 198.9. HRMS(MALDI) for $\text{C}_{22}\text{H}_{19}\text{INaO}_2$ $[\text{M}+\text{Na}]^+$: calcd 465.0327, found 465.0322.

[4-(3-Iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran-4-yl)phenyl]dimethylamine (2i) ^1H NMR (CDCl_3 , Me_4Si) δ 1.71-1.86 (m, 3H), 1.97-2.06 (m, 1H), 2.62-2.78 (m, 2H), 2.90 (s, 3H), 2.92 (s, 3H), 3.81 (t, $J = 4.2$ Hz, 1H), 6.67 (d, $J = 8.7$ Hz, 2H), 6.99 (d, $J = 8.7$ Hz, 2H), 7.20-7.29 (m, 1H), 7.36-7.41 (m, 2H), 7.99-8.02 (m, 2H); ^{13}C NMR (CDCl_3 , Me_4Si) δ 19.0, 23.3, 32.9, 38.5, 40.6, 66.6, 112.3, 124.2, 125.8, 127.5, 128.2, 128.9, 130.8, 131.7, 148.9, 149.3, 152.5. HRMS(MALDI) for $\text{C}_{22}\text{H}_{23}\text{INO}$ $[\text{M}+\text{H}]^+$: calcd 444.0824, found 444.0805.

2,3-Diiodo-4-methoxy-4,5,6,7-tetrahydrobenzofuran (2j) ^1H NMR (CDCl_3 , Me_4Si) δ 1.54 (tt, $J = 13.2, 3.6$ Hz, 1H), 1.77-1.84 (m, 1H), 1.92-2.00 (m, 1H), 2.05-2.13 (m, 1H), 2.48-2.60 (m, 1H), 2.66-2.75 (m, 1H), 3.47 (s, 3H), 4.05 (t, $J = 3.0$ Hz, 1H); ^{13}C NMR (CDCl_3 , Me_4Si) δ 17.9, 23.4, 26.9, 57.2, 71.7, 82.9, 96.1, 123.9, 159.5. HRMS(EI) calcd for $\text{C}_9\text{H}_{10}\text{I}_2\text{O}_2$ 403.8770, found 403.8776.

3-Iodo-4-methoxy-4-methyl-2-phenyl-4,5,6,7-tetrahydrobenzofuran (2k) ^1H NMR (CDCl_3 , Me_4Si) δ 1.61 (s, 3H), 1.78-1.85 (m, 1H), 2.00-2.10 (m, 2H), 2.64-2.69 (m, 2H), 3.17 (s, 3H), 7.25-7.43 (m, 3H), 7.94 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (CDCl_3 , Me_4Si) δ 20.6,

23.3, 26.0, 33.8, 50.3, 60.9, 75.1, 122.9, 126.6, 127.9, 128.2, 130.5, 150.3, 152.9.
HRMS(MALDI) for C₁₆H₁₇INaO₂ [M+Na]⁺: calcd 391.0171, found 391.0165.

3-Iodo-4-methoxy-2-phenyl-5,6-dihydro-4H-cyclopenta[b]furan (2l) ¹H NMR (CDCl₃, Me₄Si) δ 2.36-2.43 (m, 1H), 2.63-2.78 (m, 2H), 2.96-3.03 (m, 1H), 3.43 (s, 3H), 4.65 (d, *J* = 6.6 Hz, 1H), 7.24-7.42 (m, 3H), 7.91 (d, *J* = 7.8 Hz, 2H); ¹³C NMR (CDCl₃, Me₄Si) δ 23.9, 34.8, 56.3, 59.7, 77.4, 126.1, 127.9, 128.3, 130.8, 132.8, 155.4, 161.9.
HRMS(MALDI) for C₁₄H₁₃INaO₂ [M+Na]⁺: calcd 362.9858, found 362.9852.

3-Iodo-4-(methoxy-phenylmethyl)-5-methyl-2-phenylfuran (2m) ¹H NMR (CDCl₃, Me₄Si) δ 2.22 (s, 3H), 3.44(s, 3H), 5.32 (s, 1H), 7.22-7.44 (m, 8H), 7.93-7.96 (m, 2H); ¹³C NMR (CDCl₃, Me₄Si) δ 12.8, 56.9, 67.7, 79.3, 123.0, 126.2, 126.7, 127.4, 127.8, 128.3, 130.3, 140.5, 149.8, 149.8. HRMS(MALDI) for C₁₆H₁₇INaO₂ [M+Na]⁺: calcd 391.0171, found 391.0165.

4-Methoxy-2-phenyl-3-phenylethynyl-4,5,6,7-tetrahydrobenzofuran (3). **2a** (355 mg, 1.0 mmol), PdCl₂(PPh₃)₂ (35 mg, 0.05 mmol), phenylacetylene (245 mg, 1.2 mmol) and CuI (38 mg, 0.1 mmol) were taken up in DMF (5 mL) at room temperature.

Diisopropylamine (0.42 mL, 3.0 mmol) was added, and the resulting mixture was stirred at 100 °C for 3 h. The mixture was diluted with ethyl acetate, washed with 1N HCl and brine. The organic layer was dried over MgSO₄, filtered and concentrated. The residue was isolated by chromatography on a Al₂O₃ column. ¹H NMR (CDCl₃, Me₄Si) δ 1.61-1.71 (m, 1H), 1.86-1.91 (m, 1H), 2.05-2.16 (m, 2H), 2.52-2.64 (m, 1H), 2.70-2.79 (m, 1H), 7.22-7.44 (m, 6H), 7.52-7.55 (m, 2H), 8.08 (d, *J* = 8.1 Hz, 2H); ¹³C NMR (CDCl₃, Me₄Si) δ 17.9, 23.1, 28.4, 57.2, 70.6, 82.5, 95.4, 103.2, 121.3, 123.6, 124.6, 127.6, 128.1, 128.4, 128.5, 130.7, 131.3, 152.7, 153.2. HRMS(MALDI) for C₂₃H₂₁O₂ [M+H]⁺: calcd 329.1542, found 329.1536.

References:

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