Supporting Information for

Reaction of Arynes with Amino Acid Esters

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Experimental

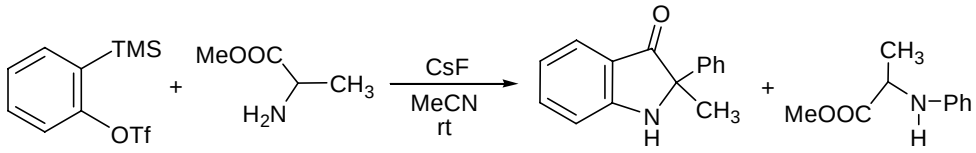
General

All chemicals were obtained from commercial suppliers and were used without further purification. Analytical TLC was carried out on precoated plates (Merck silica gel 60, F254) and flash column chromatography was performed with silica (Merck, 70-230 mesh). NMR spectra (^{1}H at 400 MHz; ^{13}C at 100 MHz) were recorded in $CDCl_3$, and chemical shifts are expressed in ppm relative to internal TMS for ^{1}H- and ^{13}C-NMR. Melting points were uncorrected.

Material

All reagents were purchased from TCI or Aldrich. Compound **1a, 1b, 1c** were prepared by the method reported by Kobayashi *et al*.[1] Amino acid esters were synthesized by the reaction of amino acids with MeOH in the presence of acid.[2]

Reaction of L-alanine methyl ester with triflate 1a in the presence of CsF

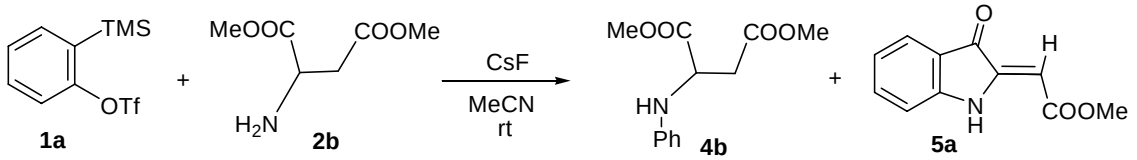


1a **2a** **3a** **4a**

To a suspension of CsF (0.31 g, 2.0 mmol) in acetonitrile (5 mL) was added a solution of L-alanine methyl ester **2a** (0.051 g, 0.50 mmol) and triflate **1a** (0.328 g, 1.1 mmol) in acetonitrile (1 mL). After stirring for 16h, the reaction mixture was poured into water (10 mL), extracted with ethyl acetate (7 mL x 3). The combined extract was dried over Na_2SO_4, filtered, and evaporated to give pale brown oil, which was chromatographed over SiO_2 by elution with hexane:ethyl acetate (10:1) to give 2-methyl-2-phenylindolin-3-one **3a** (0.073 g, 0.32 mmol) and *N*-phenylalanine methyl ester **4a** (0.009 g, 0.05 mmol). Compound **3a**: pale yellow oil.[3] ^{1}H NMR ($CDCl_3$) δ= 1.74 (s, 1H, CH_3), 4.97 (br, 1H, NH), 6.84 (dd, 1H, *J*= 8.4 and 8.0 Hz, Ar), 6.93 (d, 1H,

J= 8.4 Hz, Ar), 7.27-7.35 (m, 3H, Ar), 7.47-7.51 (m, 3H, Ar), 7.60(d, 1H, *J*= 7.6 Hz, Ar). ^{13}C NMR ($CDCl_3$) δ= 26.06 (CH_3), 70.08 (q-C), 113.79, 113.80, 120.47, 120.73, 127.12, 129.22, 130.22, 139.01, 141.82, 161.79 (Ar), 203.99 (C=O). $[\alpha]_D$= 0 (C= 0.85 EtOH). *N*-phenylalanine methyl ester (**4a**): colorless oil,[4] ^{1}H NMR ($CDCl_3$) δ= 1.47 (s, 1H, CH_3), 3.73 (s, 3H, OCH_3), 4.14 (br, 1H, NH), 4.21 (q, 1H, CH), 6.61 (d, 2H, *J*= 8.4 Hz, Ar), 6.74 (dd, 1H, *J*= 8.4 and 8.0 Hz, Ar), 7.18 (dd, 2H, *J*= 8.0 and 8.4 Hz, Ar).

Reaction of L-aspartic acid methyl ester with triflate 1a

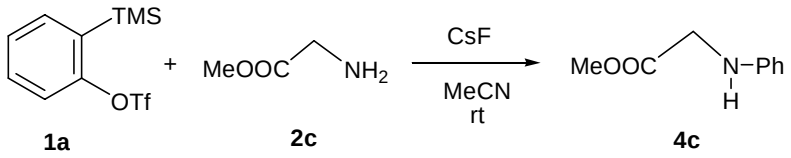


To a solution of L-aspartic acid methyl ester **2b** (0.081 g, 0.50 mmol) and CsF (0.30 g, 2.0 mmol) in acetonitrile (15 mL) was added triflate **1a** (0.36 g, 1.2 mmol). After stirring for 15h, the reaction mixture was poured into water (10 mL), extracted with dichloromethane (7 mL x 3). The combined extract was dried over Na_2SO_4, filtered, and evaporated to give pale brown oil, which was chromatographed over SiO_2 by elution with hexane:ethyl acetate (10:1) to give (*Z*)-methyl 2-(3-oxoindolin-2-ylidene)acetate (**5a**) (0.053 g, 0.26 mmol) and *N*-phenylaspartic acid methyl ester (**4b**) (0.012 g, 0.055 mmol).

Compound **5a**: orange prisms. mp 164-165^{o}C (lit.[5] mp 188^{o}C) ^{1}H NMR ($CDCl_3$)δ= 3.81 (s, 3H, OCH_3), 5.86 (s, 1H), 6.91 (d,1H, *J*= 8.0Hz, Ar), 6.82 (dd, 1H, *J*= 7.6 Hz, *J* = 7.6 Hz, Ar), 7.39 (dd, 1H, *J*= 8.0 and 7.6 Hz, Ar), 7.67 (d, 1H, *J*= 7.6 Hz, Ar), 8.82 (br, 1H, NH). ^{13}C NMR ($CDCl_3$) δ= 51.45 (O CH_3), 92.27 (=C), 111.28, 119.92, 121.28, 125.20, 137.11, 144.84, 152.50, 168.87 (C=O), 186.53 (C=O).

N-phenylaspartic acid methyl ester **4b**: colorless oil.[4]

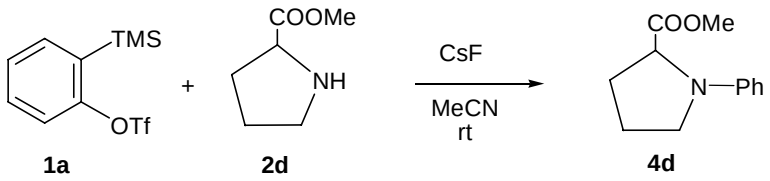
Reaction of glycine methyl ester 2c with triflate 1a



To a solution of glycine methyl ester **2c** (0.045 g, 0.50 mmol) and CsF (0.65 g, 4.0 mmol) in acetonitrile (5 mL) was added triflate **1a** (0.33 g, 1.1 mmol) in acetonitrile (3 mL). After stirring for 13h, the reaction mixture was poured into water (10 mL), extracted with dichloromethane (7 mL x 3). The combined extract was dried over Na_2SO_4, filtered, and evaporated to give pale brown oil, which was chromatographed

over SiO_2 by elution with hexane:ethyl acetate (10:1) to give *N*-phenylglycine methyl ester **4c** (0.066 g, 0.40 mmol). Compound **4c**: colorless oil,[4] ^{1}H NMR ($CDCl_3$) δ= 3.71 (s, 1H, OCH_3), 3.85 (s, 2H, CH_2), 6.54 (d, 2H, *J*= 8.0Hz, Ar), 6.74 (dd, *J*= 8.0 and 8.4 Hz, 1H, Ar), 7.16 (dd, *J*= 8.0 and 8.4 Hz, 1H, Ar).

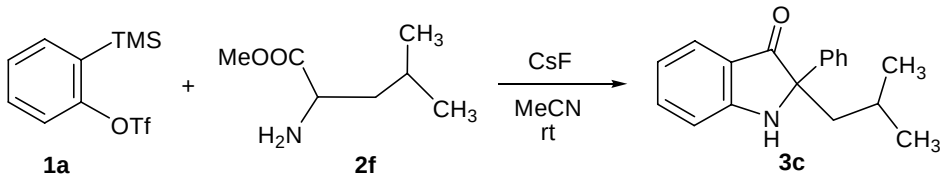
Reaction of L-proline methyl ester 2d with triflate 1a



1a **2d** **4d**

To a solution of L-proline methyl ester **2d** (0.065 g, 0.50 mmol) and CsF (0.30 g, 2.0 mmol) in acetonitrile (5 mL) was added triflate **1a** (0.33 g, 1.1 mmol) in acetonitrile (3 mL). After stirring for 16h, the reaction mixture was poured into water (10 mL), extracted with dichloromethane (7 mL x 3). The combined extract was dried over Na_2SO_4, filtered, and evaporated to give pale brown oil, which was chromatographed over SiO_2 by elution with hexane:ethyl acetate (10:1) to give *N*-pheny-L-proline methyl ester **4d** (0.022 g, 0.11 mmol). Compound **4d**: colorless crystals, mp 71-73^{o}C, $[\alpha]_D$ = -12.9 (c 0.55, $CHCl_3$). (lit.[6] mp 72-74^{o}C).

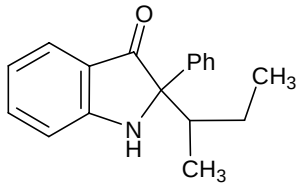
Reaction of L-Leucine methyl ester 2f with triflate 1a



1a **2f** **3c**

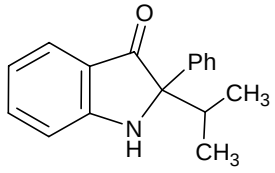
To a solution of L-leucine methyl ester **2f** (0.072 g, 0.50 mmol) and CsF (0.33 g, 2.2 mmol) in acetonitrile (5 mL) was added triflate **1a** (0.33 g, 1.1 mmol) in acetonitrile (1 mL). After stirring for 20 h, the reaction mixture was poured into water (10 mL), extracted with ethyl acetate (7 mL x 3). The combined extract was dried over Na_2SO_4, filtered, and evaporated to give pale brown oil, which was chromatographed over SiO_2 by elution with hexane:ethyl acetate (10:1) to give 2-isobutyl-2-phenylindolin-3-one **3c** (0.095 g, 0.36 mmol). **3c**: Yellow needles, mp 162-163^{o}C. ^{1}H NMR ($CDCl_3$) δ= 0.86 (d, 6H, *J*= 6.8 Hz, CH_3), 1.70 (sept, 1H, *J*= 6.8 Hz, CH), 1.99 (d, 1H, *J*=6.8 Hz, CH_2), 2.22 (d, 1H, CH_2), 5.80 (br,1H, NH), 6.80 (dd, 1H, *J*= 7.2 and 8.4 Hz, Ar), 6.96 (d, 1H, *J*= 8.4Hz, Ar), 7.24-7.37 (m, 3H, Ar), 7.47 (dd, 1H, *J*= 8.4 and 7.2 Hz, Ar), 7.56 (m, 3H, Ar). ^{13}C NMR ($CDCl_3$) δ= 22.27 (CH_3), 22.98 (CH_3), 23.63 (CH_2), 45.51 (CH), 70.67 (q-C), 110.45, 117.53, 118.01, 124.01, 124.19, 126.03, 127.16, 135.91, 138.36, 158.78 (Ar), 200.44 (C=O). Anal. Found: C, 81.47; H, 7.22; N, 5.28. Calcd for $C_{26}H_{18}O_3$: C, 81.37; H, 7.20; N, 5.29.

Other reaction was carried out in a similar manner.



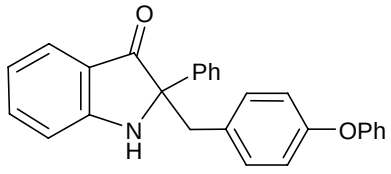
3d

Compound **3d**: yellow needles. mp 144-147^{o}C (diastereomeric mixture), ^{1}H NMR ($CDCl_3$) δ= 0.79 (d, 3H, *J*= 7.2 Hz, CH_3), 0.81-0.90 (m, 3H, CH_3), 0.92-1.40 (m, 2H, CH_2), 2.45-2.59 (m, 1H, CH), 5.15 (br s, 1H, NH), 6.77 (dd, 1H, *J*= 7.6 and 8,4 Hz, Ar), 6.95 (d, 1H, *J*= 8.4 Hz, Ar), 7.23-7.36 (m, 3H, Ph), 7.43 (dd, 1H, *J*= 7.6 and 8.4 Hz, Ar), 7.53 (d, 1H, *J*= 7.6 Hz, Ar), 7.59 (d, 2H, *J*= 8.0 Hz, Ph). ^{13}C NMR ($CDCl_3$) δ = 12.30 (CH_3), 12.42 (CH_3), 13.01 (CH_3), 13.87 (CH_3), 23.78 (CH_2), 24.44 (CH_2), 42.63 (CH), 43.02 (CH), 76.20 (q-C), 111.78, 118.90, 120.65, 125.24, 125.87, 127.64, 128.81, 137.43, 139.36, 160.95 (Ar), 202.51 (C=O). Anal. Found: C, 81.28; H, 7.48; N, 5.00. Calcd for $C_{26}H_{18}O_3$: C, 81.47; H, 7.22; N, 5.28.



3b

Compound **3b**: yellow needles, mp 132-134 ^{o}C (lit.[6] mp was not shown), ^{1}H NMR ($CDCl_3$) δ= 0.82 (d, 3H, *J*= 6.8 Hz, CH_3), 0.85 (d, 3H, *J*= 6.8 Hz, CH_3), 2.78 (septet, 1H, *J* = 6.8 Hz, CH), 6.77 (t, 1H, *J*= 8.2 Hz, Ar), 6.98 (d, 1H, *J*= 8.0 Hz, Ar), 7.22-7.35 (m, 3H, Ph), 7.45 (t, 1H, *J*= 7.6 Hz, Ar), 7.52 (d, 1H, *J*= 7.6 Hz, Ar), 7.60 (d, 2H, *J*= 8.0 Hz, Ph). ^{13}C NMR ($CDCl_3$) δ= 16.86 (CH_3), 17.77 (CH_3), 36.03 (CH), 75.60 (q-C), 111.77, 119.00, 122.05 (q-C), 125.32, 125.82, 127.65, 128.78, 137.43, 139.23 (q-C), 161.08 (Ar), 202.30 (C=O). IR ν (cm^{-1}): 3364 (N-H), 1667 (C=O).

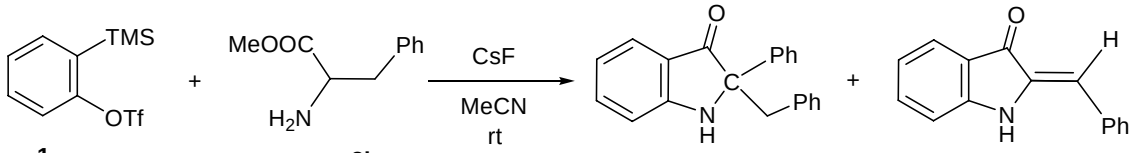


6

2-(4-phenoxybenzyl)-2-phenylindolin-3-one **6**: yellow needles, mp 51-52^{o}C. ^{1}H NMR ($CDCl_3$) δ= 3.26 (d, 1H, *J*= 13.8 Hz, CH_2), 3.45 (d, 1H, *J*= 13.8 Hz, CH_2), 4.96 (br, 1H, NH), 6.78 (dd, 2H, *J*= 6.0 Hz, 7.2 Hz, Ar), 6.85 (d, 2H, *J*= 5.6 Hz, Ar), 6.93(d, 2H, *J*= 8.0 Hz, Ar), 7.06 (dd, 1H, *J*= 8.0 and 6.8 Hz, Ar), 7.25-7.29 (m, 3H, Ar), 7.35 (dd, 2H, *J* = 7.4 and 7.4Hz, Ar), 7.42 (dd, 3H, *J*= 7.4 and 8.0 Hz, Ar), 7.52 (d, 1H, *J*= 7.4 Hz, Ar),

7.64 (d, 2H, *J*= 7.0 Hz, Ar). ^{13}C NMR ($CDCl_3$) δ= 44.10 (CH_2), 71.91 (q-C), 112.13, 118.84, 118,87, 119.30, 120.00, 123.36, 125.51, 126.28, 127.94, 128.77, 129.89, 130.67, 11.57, 137.50, 138.96, 157.39, 157.49, 160.12 (Ar), 202.43 (C=O). IR: $\nu_{C=O}$= 1678 cm^{-1}. Anal. Found: C, 82.63; H, 5.53; N, 3.59. Calcd for $C_{27}H_{21}NO_2$. C, 82.84; H, 5.41; N, 3.58.

Reaction of L-phenylalanine methyl ester 2i with triflate 1a in the presence of CsF



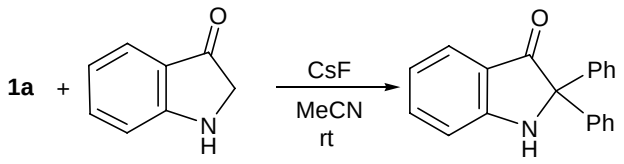
1 **2i** **3e** **5b**

To a solution of L-phenylalanine methyl ester **2i** (0.089 g, 0.5 mmol) and CsF (0.33 g, 2.2 mmol) in acetonitrile (5 mL) was added triflate **1a** (0.33 g, 1.1 mmol) in acetonitrile (1 mL). After stirring for 20h, the reaction mixture was poured into water (10 mL), extracted with ethyl acetate (7 mL x 3). The combined extract was dried over Na_2SO_4, filtered, and evaporated to give pale brown oil, which was chromatographed over SiO_2 by elution with hexane:ethyl acetate (10:1) to give 2-benzyl-2-phenylindolin-3-one **3e** (0.069 g, 0.13 mmol) and 2-benzylideneindolin-3-one **5b** (0.035 g, 0.16 mmol)

3e: yellow needles, mp 182-183 ^{o}C (lit.[7] mp was not shown). ^{1}H NMR ($CDCl_3$) δ= 3.23 (d, 1H, *J*= 13.6 Hz, CH_2), 3.51 (d, 1H, *J* = 13.6 Hz, CH_2), 4.95 (br, 1H, NH), 6.77 (dd, 1H, *J*= 7.8 and 7.1 Hz, Ar), 6.87 (d, 1H, *J*= 8.3 Hz, Ar), 6.95-6.98 (m, 2H, Ar), 7.15-7.18(m, 3H, Ar), 7.30-7.39 (m, 3H, Ar), 7.43(dd, *J*= 8.3 and 7.0 Hz, 1H, Ar);. ^{13}C NMR ($CDCl_3$). δ= 44.64 CH_2), 71.78 (q-C), 112.15, 119.29, 119.78, 125.58, 126.33, 127.21, 127.89, 128.38, 128.73, 130.28, 135.90, 137.56, 138.93, 160.08, 201.47. $[\alpha]_D$= 0.0 (c 0.60, EtOH).

5b: orange needless. mp 164-165 ^{o}C (lit.[8] mp 178 ^{o}C), ^{1}H NMR (CD_3CN) δ = 6.72 (s, 1H, CH), 6.98 (dd, 1H, *J* = 8.0 Hz, *J* = 8.0 Hz, Ar), 7.15 (d, 2H, *J* = 8.0 Hz, Ar), 7.40 (dd, 1H, *J* = 8.0 Hz, *J* = 8.0 Hz, Ar), 7.47-7.56 (m, 3H,, Ar), 7.68-7.63 (m, 3H, Ar), 8.10 (br, 1H, NH), ^{13}C NMR ($CDCl_3$). δ= 111.80, 112.21, 120.93, 121.99, 125.29, 128.77, 129.47, 129.74, 134.99, 135.59, 136.41, 153.40, 186.81 (C=O). Anal. Found: C, 84.04; H, 5.39; N, 4.71. Calcd for $C_{26}H_{18}O_3$: C, 84.25; H, 5.72; N, 4.68.

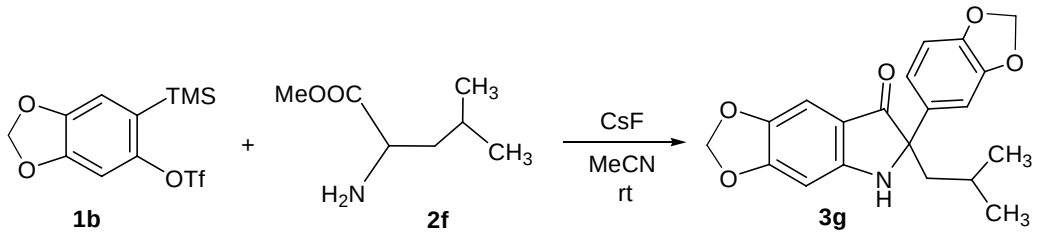
Reaction of indolin-3-one with trifrate 1a.



3f

To a solution of indolin-3-one (0.040 g, 0.30 mmol) and CsF (0.30 g, 2.0 mmol) in acetonitrile (8 mL) was added triflate **1a** (0.20 g, 0.66 mmol) in acetonitrile (1 mL). After stirring for 9 h, the reaction mixture was poured into water (10 mL), extracted with ethyl acetate (7 mL x 3). The combined extract was dried over Na_2SO_4, filtered, and evaporated to give pale brown oil, which was chromatographed over SiO_2 by elution with hexane:ethyl acetate (10:1) to give 2,2-dimethyllindolin-3-one **3f** (0.051 g, 0.18 mmol). **3f**: yellow needles, mp 116-120°C, (lit.[7] mp was not shown). ^{1}H NMR ($CDCl_3$) δ= 6.87 (t, 1H, *J*= 7.6 Hz, Ar), 6.94 (d, 1H, *J*= 8.4 Hz, Ar), 7.28-7.43 (m, 10H, Ph), 7.48 (dd, 1H, *J*= 8.4 and 7.6Hz, Ar), 7.65 (d, 1H, *J*= 8.4 Hz).

Reaction of 5-trimethylsilylbenzo[1,3]dioxol-6-yl trifluoromethanesulfonate 1b with L-leucine methyl ester.



1b **2f** **3g**

To a solution of L-leucine methyl ester **2f** (0.072 g, 0.50 mmol) and CsF (0.30 g, 2.0 mmol) in acetonitrile (10 mL) was added triflate **1b** (0.322 g, 1.2 mmol) in acetonitrile (1 mL). After stirring for 9 h, the reaction mixture was poured into water (10 mL), extracted with ethyl acetate (7 mL x 3). The combined extract was dried over Na_2SO_4, filtered, and evaporated to give pale brown oil, which was chromatographed over SiO_2 by elution with hexane:ethyl acetate (10:1) to give lindolin-3-one **3g** (0.134 g, 0.38 mmol). **3g**: yellow needles, mp 162-166°C. ^{1}H NMR ($CDCl_3$) δ = 0.86 (d, 6H, *J* = 6.4 Hz, 6H, CH_3), 1.66 (m, 1H, *J* = 6.4 and 5.2 Hz, CH), 1.86 (dd, 1H, *J* = 6.4 and 14.4 Hz, CHH), 2.12 (dd, 1H, *J* = 14.4 and 5.2 Hz, CHH), 4.90 (br, 1H, NH), 5.92 (br s, 2H, O-CH_2-O), 5.98 (br s, 2H, O-CH_2-O), 6.42 (s, 1H, Ar), 6.73 (d, 1H, *J* = 8.4 Hz, Ar), 6.89 (s, 1H, Ar), 7.01 (d, 1H, J =8.4 Hz, Ar), 7.08 (br s, 1H, Ar). ^{13}C NMR ($CDCl_3$) δ= 23.75 (CH_3), 24.52 (CH_3), 25.06 (CH_2), 46.97 (CH), 72.94 (q-C), 92.66 (OCH_2O), 101.18 (OCH_2O), 102.08, 102.42, 106.67, 108.14, 112.20, 118.72, 134.10, 142.62, 146.98, 147.98, 156.91, 159.43, (Ar), 199.68 (C=O). Anal. Found: C, 67.63; H, 5.48; N, 4.15. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96.

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