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Dramatic Enhancement of Catalytic Activity in Ionic Liquid: Highly Practical Metal Triflates-Catalyzed Friedel-Crafts Alkenylation of Arenes with Alkynes in an Ionic Liquid

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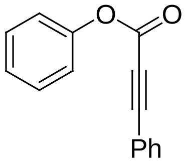
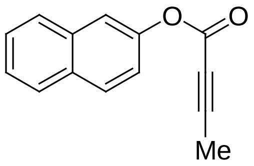
General. All reactions were performed in nitrogen atmosphere using standard schlenk techniques. Chromatographic purification of products was carried out by flash chromatography using Merck silica gel 60 (230-400 mesh). Thin layer chromatography was carried out on Merck silica gel 60F plates. ^{1}H NMR (300 MHz) and ^{13}C NMR (75.0 MHz) spectra were recorded on a Brucker-Spectrospin 300 spectrometer using TMS as an internal standard. GC-MS analysis were performed using GC/MSD; HP 5890.

Materials. All metal triflates used in this study were purchased from Aldrich. Ionic liquids used in this study were nearly chloride-free (<10 ppm) and their water content was ca. 200-300 ppm (determined by Karl-Fisher titration). Other organic solvent (methylcyclohexane) was distilled prior to used. All chemicals were obtained from commercial sources and used without further purification. Aryl 3-substituted propiolates and alkynalides were prepared according to the following procedure.

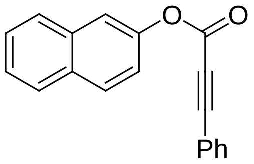
Representative procedure for the synthesis of 3-substituted propiolic acid aryl esters: $Me_3N{\cdot}HCl$ (258 mg, 2.7 mmol) was added to a stirred solution of phenylpropiolic acid (204.6 mg. 1.4 mmol), phenol (131.7 mg, 1.4 mmol), Et_3N (414.9 mg, 4.1 mmol), and DMAP (12,2 mg, 0.1 mmol) in CH_3CN (1.0 mL) at 0-5 ^oC under an N_2 atmosphere, and the mixture was stirred for 10 min. Me_2NSO_2Cl (387.7 mg, 2.7 mmol) in MeCN (1.0 mL) was added to the mixture at 0-5 ^oC, and the mixture was stirred at that temperature for 3 h. Water was added to the mixture, which was extracted with ether. The organic phase was washed with water, dried over anhydrous Na_2SO_4, and concentrated. The obtained crude product was purified by flash column chromatography (hexane : ether = 1:1) to give 270 mg (87 %) of pure phenyl 3-phenylpropiolate as a white solid.



^{1}H NMR (300 MHz. CDCl$_3$): δ 7.1-7.7 (m, 10H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 80.63, 89.08, 119.68, 121.85, 126.78. 129.05, 129.97, 131.41, 133.57, 150.57.



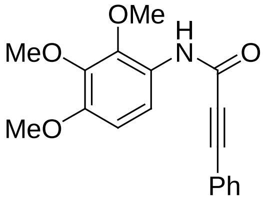
^{1}H NMR (300 MHz. CDCl$_3$): δ 2.09 (s, 3H), 7.26-7.28 (m, 1H), 7.48-7.50 (m, 2H), 7.61 (s, 1H), 7.80-7.88 (m, 3H);. ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 4.42, 72.58, 88.72, 118.99, 121.16, 126.42, 127.15, 128.19, 128.23, 130.02, 132.07, 134.09, 148.13, 152.52.



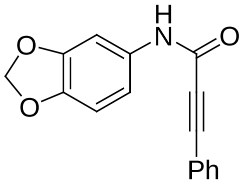
^{1}H NMR (300 MHz. CDCl$_3$): δ 7.35 –7.91 (m, 12H);. ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 80.78, 89.29, 119.11, 119.72, 121.20, 126.51, 127.23, 128.26, 128.29, 129.16, 130.12, 131.55, 132.16, 133.70, 134.15, 148.22, 152.96.

Representative procedure for the synthesis of phenylpropiolic acid arylamides:

$Me_3N \cdot HCl$ (258 mg, 2.7 mmol) was added to a stirred solution of phenylpropiolic acid (204.6 mg. 1.4 mmol), 3,4,5-trimethoxyaniline (256.5 mg, 1.4 mmol), Et_3N (414.9 mg, 4.1 mmol), and DMAP (12.2 mg, 0.1 mmol) in CH_3CN (1.0 mL) at 0-5 °C under an N_2 atmosphere, and the mixture was stirred for 10 min. Me_2NSO_2Cl (387.7 mg, 2.7 mmol) in MeCN (1.0 mL) was added to the mixture at 0-5 °C, and the mixture was stirred at that temperature for 3 h. Water was added to the mixture, which was extracted with ethyl acetate. The organic phase was washed with water, dried over anhydrous Na_2SO_4, and concentrated. The obtained crude product was purified by flash column chromatography (hexane : ethyl acetate = 1: 2) to give 366 mg (84%) of pure of phenyl propiolic acid 3,4,5-trimethoxyphenylamide as a yellow solid.

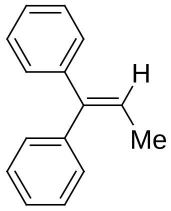


^{1}H NMR (300 MHz. CDCl$_3$): δ 3.75-3.78 (br s, 9H), 6.81-6.83 (br s, 2H), 7.20-7.48 (m, 5H), 7.76 (br s, 1H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 56.65, 61.48, 83.87, 86.23, 98.17, 120.37, 129.10, 130.86, 133.08, 133.93, 135.61, 151.39, 153.86.

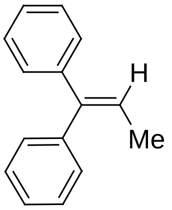


^{1}H NMR (300 MHz. CDCl$_3$): δ 5.95 (s, 2H), 6.75 (d, *J* = 8.3 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 7.26-7.54 (m, 6H), 7.88 (s, 1H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 83.85, 86.23, 101.83, 103.27, 108.59, 113.77, 120.42, 129.00, 130.71, 132.01, 133.05, 145.16, 148.29, 151.50.

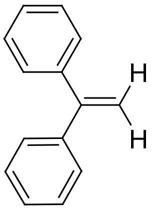
Typical procedure for Intermolecular Friedel-Crafts alkenylations in ionic liquid : Under a nitrogen atmosphere, a mixture of Sc(OTf)$_3$ (49.2 mg, 0.1 mmol), 1-phenyl-1-propyne (116.1 mg, 1 mmol), benzene (6 mL) and [bmim][SbF$_6$] (1 mL) was refluxed for 4 h. After completion of the reaction, the reaction mixture was cooled to room temperature. All the volatiles were then removed under reduced pressure and the residue was purified by flash column chromatography on silica (hexane) to give 177 mg (91 %) of pure 1,1-diphenyl-1-propene as a pale yellow solid.



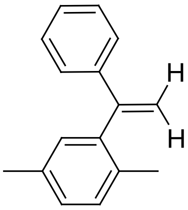
^{1}H NMR (300 MHz, CDCl$_3$) δ 1.76 (d, *J* = 7.0 Hz, 3H), 6.17 (q, *J* = 7.0 Hz, 1H), 7.17-7.40 (m, 10H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 16.21, 124.65, 127.19, 127.31, 127.68, 128.54, 128.62, 130.54, 140.48, 142.92, 143.44.



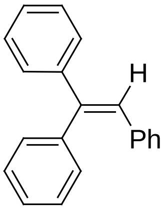
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.57-1.64 (d, *J* = 6.9 Hz, 3H), 2.08 (s, 3H), 2.36 (s, 3H), 6.32 (q, *J* = 6.9 Hz, 1H), 6.93 (s, 1H), 7.09-7.29 (m, 7H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 15.91, 19.49, 21.46, 124.09, 126.56, 127.04, 128.28, 128.32, 128.66, 130.35, 131.08, 133.86, 135.52, 139.57, 142.00.



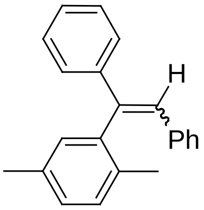
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.45 (s, 2H), 7.29-7.35 (m, 10H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 114.76, 128.16, 128.61, 128.72, 141.92, 150.48.



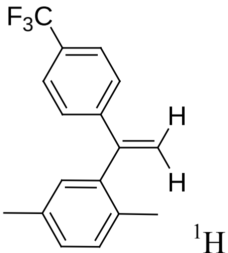
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.99 (s, 3H), 2.30 (s, 3H), 5.16 (d, *J* = 1.4 Hz, 1H), 5.73 (d, *J* = 1.4 Hz, 1H), 7.04-7.28 (m, 8H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.12, 21.42, 115.13, 127.00, 128.01, 128.71, 128.81, 130.49, 131.17, 133.43, 135.53, 141.16, 141.97, 150.09.



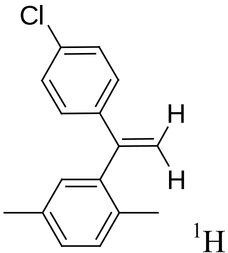
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.94-7.33 (m, 16H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 53.76, 126.94, 127.62, 127.72, 128.14, 128.27, 128.39, 128.83, 129.69, 130.48, 137.48, 140.47, 142.70, 143.51.



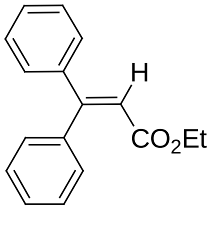
^{1}H NMR (300 MHz, CDCl$_3$): δ 1.99 (s, 3H), 2.27 (s, 3H), 6.94-7.32 (m, 14H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 19.51, 21.38, 127.02, 127.25, 127.70, 128.39, 128.50, 128.73, 128.78, 129.39, 130.78, 130.90, 133.70, 136.18, 137.79, 139.87, 141.79, 142.88.



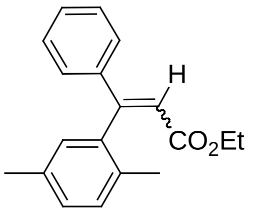
^{1}H NMR (300 MHz, CDCl$_3$): δ 1.98 (s, 3H), 2.34, (s, 3H), 5.38 (d, J= 1.1 Hz, 1H), 5.80 (d, J = 1.1 Hz, 1H), 7.02 – 7.58 (m, 7H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 20.10, 21.38, 116.82, 123.50 (q, ^3J(C-C-C-F) = 3.8 Hz), 124.65 (q, ^1J(C-F) = 272.4 Hz), 124.67 (q, ^3J(C-C-C-F) = 3.8 Hz), 129.12, 129.28, 130.39, 130.69, 131.16, 131.31 (q, ^2J(C-C-F) = 32.0 Hz), 133.26, 135.83, 140.96, 142.05, 149.00.



^{1}H NMR (300 MHz, CDCl$_3$): δ 1.99 (s, 3H), 2.33 (s, 3H), 5.19 (d, J = 1.2 Hz, 1H), 5.71 (d, J = 1.2 Hz, 1H), 7.01 – 7.25 (m, 7H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 19.99, 21.31, 115.52, 128.22, 128.83, 128.88, 130.50, 131.02, 133.25, 133.78, 135.62, 139.60, 141.35, 148.94.

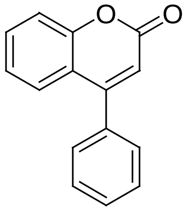


^{1}H NMR (300 MHz, CDCl$_3$): δ 1.11 (t, J = 7.1 Hz, 3H), 4.05 (q, J = 7.1 Hz, 2H), 6.36 (s, 1H), 7.21 – 7.39 (m, 10H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 14.37, 60.42, 117.92, 128.24, 128.47, 128.67, 128.95, 129.52, 129.75, 139.41, 141.22, 156.82, 166.51.

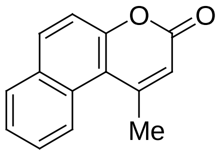


^{1}H NMR (300 MHz, CDCl$_3$): δ 1.07 (t, J = 7.1 Hz, 3H), 2.04 (s, 3H), 2.31 (s, 3H), 4.01 (q, J = 7.1 Hz, 2H), 6.49 (s, 1H), 6.85 (s, 1H), 7.03 – 7.13 (m, 2H), 7.25- 7.32 (m, 5H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 14.33, 19.34, 21.36, 60.27, 117.95, 127.82, 128.86, 128.90, 129.31, 129.74, 130.03, 132.62, 135.08, 138.87, 139.85, 156.31, 166.25.

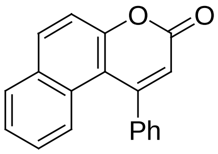
Typical procedure for Intramolecular Friedel-Crafts alkenylations in ionic liquid: Under a nitrogen atmosphere, a mixture of Hf(OTf)$_4$ (77.4 mg, 0.1 mmol), 3-phenylpropiolate (222.1 mg, 1 mmol), methylcyclohexane (6 mL) and [bmim][SbF$_6$] (1 mL) was refluxed for 9 h. After completion of the reaction, the reaction mixture was cooled to room temperature. All the volatiles were then removed under reduced pressure and the residue was purified by flash column chromatography on silica (hexane:diethyl ether) to give 113 mg (51 %) of pure 4-phenylcoumarin as a pale yellow solid.



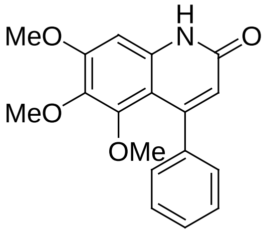
^{1}H NMR (300 MHz, CDCl$_3$): δ 6.38 (s, 1H), 7.20–7.59 (m, 9H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 115.59, 117.73, 124.56, 127.41, 128.84, 129.27, 130.08, 132.32, 135.61, 154.60, 156.09, 161.17.



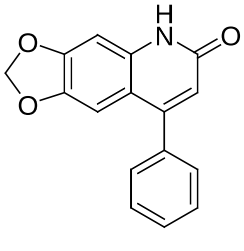
^{1}H NMR (300 MHz, CDCl$_3$): δ 2.95 (s, 3H), 6.40(s, 1H), 7.48 (d, J = 8.9 Hz, 1H), 7.56 (t, J = 7.3 Hz, 1H), 7.65 (t, J = 8.1, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H), 8.60 (d, J = 8.7 Hz, 1H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 26.92, 114.95, 117.01, 118.29, 125.46, 125.86, 128.32, 130.17, 130.70, 131.81, 134.12, 154.59, 155.13, 160.84.



^{1}H NMR (300 MHz. CDCl$_3$): δ 6.32 (s, 1H), 7.00-7.50 (m, 9H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 113.56, 117.34, 118.01, 125.87, 126.42, 127.21, 127.97, 129.51, 129.65, 129.72, 129.86, 131.82, 134.46, 140.09, 155.29, 156.99, 160.85.



^{1}H NMR (300 MHz. CDCl$_3$): δ 3.25 (s, 3H), 3.79 (s, 3H), 3.98 (s, 3H), 6.39 (s, 1H), 6.77 (s, 1H), 7.2-7.5 (m, 7H), 13.03 (s, 1H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 56.22, 60.74, 61.05, 94.36, 108.52, 119.86, 127.22, 127.53, 136.98, 138.61, 141.04, 150.94, 152.50, 156.59, 163.89.



^{1}H NMR (300 MHz. CDCl$_3$): δ 6.01 (s, 2H), 6.56 (s, 1H), 6.90 (s, 1H), 7.00 (s, 1H), 7.4-7.5 (m, 5H), 12.71 (s, 1H); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 96.84, 102.04, 104.00, 114.82, 128.65, 128.71, 128.95, 135.83, 137.30, 145.09, 151.24, 154.27.