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Catalytic Electronic Activation: Indirect “Wittig” Reaction of Alcohols

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1. General experimental detail

All reactions were performed under an atmosphere of dry argon using oven dried (150 ˚C) ACE pressure tubes. Toluene was distilled from sodium wire before use. Unless specified, all chemicals were purchased from Acros, Aldrich, Lancaster or Strem chemical companies and used as supplied. All phosphorane ylides were freshly prepared prior to use and used immediately. Although several of these are commercially available, superior results were obtained with freshly prepared ylides. Methyl (triphenylphosphoranylidene)acetate was prepared according to Lugtenburg,[1] methyl (triphenylphosphoranylidene)acetate according to Aitken,[2] *N*-methoxy-*N*-methyl-2-(triphenylphosphoranylidene)acetamide according to Evans[3] and (triphenylphopsphoranylidene)acetonitrile according to Willis.[4] Benzyl dimethylphosphonoacetate was prepared using the procedure of Büchi.[5]

2. General Procedures

(a) **General procedure for ester ylide reactions**:

To an argon purged pressure tube containing $[Ir(COD)Cl]_2$ (5 mol%), dppp (5 mol%), Cs_2CO_3 (5 mol%) and the phosphorane ylide (1.1 equiv.) was added benzyl alcohol (1 equiv.) followed by anhydrous toluene such that a reaction concentration of 0.333 M was achieved. The tube was sealed and then heated at 150 °C for 72 hours. The resulting reaction mixture was diluted with diethyl ether (20 mL) and then concentrated *in vacuo*. The crude residue was pre-adsorbed upon silica and purified by flash column chromatography (SiO_2, petroleum ether (bp 40-60 °C)/diethyl ether eluent system) to afford an inseparable mixture of the cinnamate and dihydrocinnamate esters. The cinnamate ester by-product was removed by oxidative workup following the method of von Rudloff.[6] The product mixture was dissolved in 50 mL of a 0.005 M potassium permanganate/0.25 M sodium metaperiodate/0.1 M potassium carbonate solution in 3:2 water/*tert*-butanol and stirred for 2 hours. The mixture was extracted with ether (3 x 25 mL) and the combined organic extracts washed with 1 M sodium hydroxide (2 x 50 mL), saturated brine (50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield the dihydrocinnamate ester product.

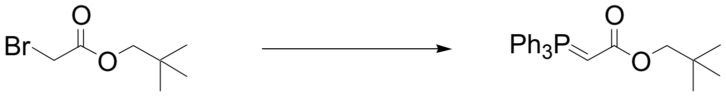
The following dihydrocinnamate ester products have been reported previously and displayed spectral data in agreement with that in the references cited: methyl dihydrocinnamate,[7] benzyl dihydrocinnamate[8] and *N*-methoxy-*N*-methyl 3-phenylpropionamide.[9]

(b) **General procedure for cyano ylide reactions**:

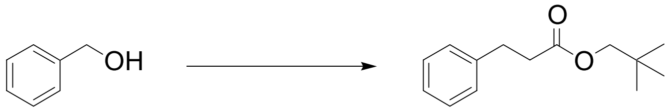
To an argon purged pressure tube containing $[Ir(COD)Cl]_2$ (5 mol%), dppp (5 mol%), Cs_2CO_3 (5 mol%) the necessary alcohol (1 equiv.) and (triphenylphosphoranylidene)acetonitrile (1.1 equiv.) was added anhydrous toluene such that a reaction concentration of 0.333 M was achieved. The tube was sealed and then heated at 150 °C for 72 hours. The resulting reaction mixture was diluted with diethyl ether (20 mL) and then concentrated *in vacuo*. The crude residue was pre-adsorbed upon silica and purified by flash column chromatography (SiO_2, petroleum ether (bp 40-60 °C)/diethyl ether eluent system) to afford the substituted propionitrile product.

The following substituted propionitriles products have been reported previously and displayed spectral data in agreement with that in the references cited: 3-(4-chlorophenyl)propionitrile,[10] 3-napthalene-2-yl-propionitrile[11] and 3-phenylbutyrolnitrile.[12]

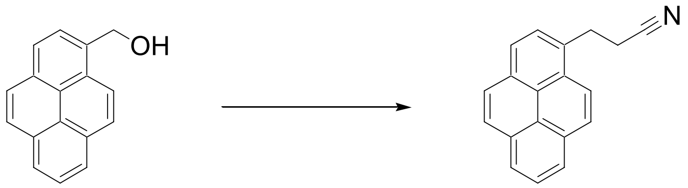
3. Specific Procedures



Neopentyl (triphenylphosphoranylidene)acetate. A solution of neopentyl bromoacetate (5.049 g, 24.15 mmol) and triphenylphosphine (6.334 g, 24.15 mmol) in toluene (80 mL) was stirred vigorously and heated at reflux for 16 hours. Concentration of the mixture *in vacuo* afforded the crude phosphonium salt, an orange gum that was used without further purification. A solution of the phosphonium salt in DCM (150 mL) was extracted with two portions of 2M potassium hydroxide (100 mL), washed with water (100 mL), saturated brine (100 mL), dried ($MgSO_4$), filtered and then concentrated *in vacuo* to afford the crude product, an orange foam. Recrystallisation from boiling petroleum ether (bp 40-60 °C) afforded pale yellow micro-crystals of the desired product. (6.97 g, 73% yield). NMR data clearly indicates the presence of the two isomeric (rotameric) forms of the ylide. Mp 94-98 °C (from petroleum ether (bp 40-60 °C). ^{1}H-NMR (300 MHz, d^6-DMSO, 298K) δ 0.36 (9H, s, 45%), 0.87 (9H, s, 55%), 2.35 (1H, d, *J* = 21.3 Hz, 54%), 2.78 (1H, d, *J* = 23.0 Hz, 46%), 3.36 (2H, s, 55%), 3.53 (2H, s, 45%), 7.51-7.66 (15H, m, Ph). ^{13}C-NMR (75.4 MHz, d^6-DMSO, 298K) δ 26.2 (s), 26.6 (s), 27.6 (s), 27.9 (s), 29.4 (d, *J* = 37.9 Hz), 31.1 (d, *J* = 72.3 Hz,), 70.6 (s), 71.0 (s), 127.1 (d, *J* = 30.8 Hz), 128.3 (d, *J* = 30.4 Hz), 128.8 (d, *J* = 11.9 Hz), 129.0 (d, *J* = 12.0 Hz), 131.5 (d, *J* = 9.8 Hz), 132.0 (d, *J* = 2.5 Hz), 132.2 (br. s), 132.5 (d, *J* = 10.0 Hz), 168.7 (d, *J* = 7.5 Hz), 170.7 (d, J = 14.5 Hz). $^{31}P\{^1H\}$-NMR (121.4 MHz, d^6-DMSO, 298K) δ 16.58 (br. s), 18.45 (br. s). IR (KBr) ν (cm^{-1}) 3055, 2949, 2863, 1614, 1475, 1437, 1374, 1330, 1113, 1060, 887, 749, 718, 693. MS (FAB$^+$, *m/z*) 391 [M+H]$^+$. HRMS (FAB$^+$) $C_{25}H_{28}O_2P$ [M+H]$^+$ requires 391.1827 found 391.1827. CHN analysis. $C_{25}H_{27}O_2P$ requires C 76.9 %, H 6.97 %; found C 77.0 %, H 6.77 %.



Neopentyl dihydrocinnamate. To an argon purged pressure tube containing $[Ir(COD)Cl]_2$ (0.067 g, 0.1 mmol), dppp (0.041 g, 0.1 mmol), Cs_2CO_3 (0.033 g, 0.1 mmol) and neopentyl (triphenylphosphoranylidene)acetate (0.859 g, 2.2 mmol) was added benzyl alcohol (0.212 g, 2.0 mmol, 197 μL) followed by anhydrous toluene (6 mL). The tube was sealed and then heated at 150 °C for 72 hours. The resulting reaction mixture was diluted with diethyl ether (20 mL) and then concentrated *in vacuo*. The crude residue was pre-adsorbed upon silica and purified by flash column chromatography (SiO_2, 100:1 petroleum ether (bp 40-60 °C)/diethyl ether) to afford an inseparable 3.47:1 mixture of neopentyl dihydrocinnamate and neopentyl cinnamate. The mixture was dissolved in 50 mL of a 0.005 M potassium permanganate/0.25 M sodium metaperiodate/0.1 M potassium carbonate solution in 3:2 water/*tert*-butanol and stirred for 2 hours. The mixture was extracted with ether (3 x 25 mL) and the combined organic extracts washed with 1 M sodium hydroxide (2 x 50 mL), saturated brine (50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford neopentyl dihydrocinnamate, a colourless liquid (0.237 g, 54% yield). R_f 0.76 (7:3 petroleum ether (bp 40-60 °C)/diethyl ether). ^1H-NMR (300 MHz, $CDCl_3$, 298K) δ 0.83 (9H, s), 2.58 (2H, t, J = 7.5 Hz), 2.89 (2H, t, J = 7.5 Hz), 3.69 (2H, s), 7.11-7.20 (5H, m). ^{13}C-NMR (75.4 MHz, $CDCl_3$, 298K) δ 26.5, 31.2, 31.4, 36.0, 73.9, 126.4, 128.4, 128.6, 140.7, 173.2. IR (liquid film) ν (cm^{-1}) 3028, 2959, 2869, 1732, 1604, 1497, 1478, 1456, 1377, 1366, 1291, 1244, 1160, 1078, 1014, 749. MS (EI$^+$, 70eV, *m/z*), 220 (57%, M$^{\cdot+}$), 150 (61), 133 (47), 105 (77), 104 (69), 91 (84), 71 (100), 57 (25), 43 (47). HRMS (EI$^+$) $C_{14}H_{20}O_2$ [M$^+$] requires 200.1463 found 220.1464.



3-pyren-1-yl-propionitrile. To an argon purged pressure tube containing $[Ir(COD)Cl]_2$ (0.05 g, 0.075 mmol), dppp (0.031 g, 0.075 mmol), Cs_2CO_3 (0.025 g, 0.075 mmol) and (triphenylphosphoranylidene)acetonitrile (0.497 g, 1.65 mmol) was added pyren-1-yl-methanol (0.345 g, 1.5 mmol) followed by anhydrous toluene (4.5 mL). The tube was sealed and then heated at 150 °C for 72 hours. The resulting reaction mixture was diluted with diethyl ether (20 mL) and then concentrated *in vacuo*. The crude residue was pre-adsorbed upon silica and purified by flash column chromatography (SiO_2, 30:1 to 7:3 petroleum ether (bp 40-60 °C)/diethyl ether) to afford a yellow solid, which was subsequently recrystallised from DCM/hexane to afford pale yellow micro-crystals. (0.237 g, 54% yield). R_f 0.23 (7:3 petroleum ether (bp 40-60 °C/diethyl ether). Mp 132-134 °C (from DCM/hexane). ^{1}H-NMR (400 MHz, $CDCl_3$, 298K) δ 2.80 (2H, t, *J* = 7.4 Hz), 3.64 (2H, t, *J* = 7.4 Hz), 7.85 (1H, d, *J* = 7.8 Hz), 7.98 (1H, d, *J* = 7.5 Hz), 8.01 (1H, s), 8.02 (1H, s), 8.10 (3H, m), 8.16 (2H, d, *J* = 7.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, 298K) δ 19.7, 29.6, 119.6, 122.4, 125.2, 125.4, 125.5, 125.6, 125.9, 126.5, 127.5, 127.7, 127.8, 128.6, 128.8, 131.1, 131.2, 131.7, 132.0. IR (KBr) ν (cm^{-1}) 3041, 2927, 2241, 1604, 1586, 1466, 1457, 1431, 1418, 1318, 1248, 1187, 1098, 841, 828, 820, 755, 712. MS (EI+, 70eV, *m/z*), 255 (27%, $M^{\cdot+}$), 220 (27), 215 (97), 213 (74), 205 (100), 105 (36), 71 (33), 57 (74), 43 (54). HRMS (EI^+) $C_{19}H_{13}N$ [M^+] requires 255.1048 found 255.1051.

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