Supporting Information for
Palladium-Catalyzed Cleavage of O/N-Propargyl Protecting Groups in
Aqueous media under copper free condition

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General methods

Unless stated otherwise, reactions were performed under nitrogen atmosphere. All the solvents used were commercially available and distilled before use. Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F254; Merck), visualizing with ultraviolet light or iodine spray. Flash chromatography was performed on silica gel (SRL 230-400 mesh) using distilled petroleum ether, ethyl acetate, dichloromethane, chloroform and methanol. ¹H NMR spectra were determined in CDCl₃, DMSO-d₆ or MeOH-d₄ solution on Varian Gemini 200 MHz spectrometers. Proton chemical shifts (δ) are relative to tetramethylsilane (TMS, δ = 0.00) as internal standard and expressed in ppm. Spin multiplicities are given as s (singlet), d (doublet), t (triplet) and m (multiplet) as well as b (broad). Coupling constants (J) are given in hertz. Infrared spectra were recorded on a Perkin-Elmer 1650 FT- IR spectrometer. Melting points were determined using Buchi melting point B-540 apparatus and are uncorrected. Thermal analysis data was generated with the help of Shimadzu DSC-50 detector. MS spectra were obtained on a HP-5989A mass spectrometer. All the reagents used were from commercial sources and no further purification was performed.

Preparation of I (General procedure): A mixture of appropriate phenol / aniline (7.188 mmol) and anhydrous potassium carbonate (2.98 g, 21.56 mmol) in dry DMF (15 mL) was heated to 55-60 °C for half an hour under inert atmosphere. The mixture was then cooled to room temperature and propargyl bromide (1.026 g, 8.62 mmol) was added through septum using syringe. The mixture was stirred for 4 hours at room temperature (for phenols) or for 5 hours at 60 °C (for anilines) and poured in the ice water with stirring. Stirring continued for 10 minutes, solid separated was filtered and dried under vacuum to afford the desired compound **I**.

Palladium catalyzed cleavage of O/N-propargyl protecting groups (general procedure): A mixture of aryl propargyl ether / amine (5.65 mmol), bis-triphenylphosphinepalladium (II) chloride (0.159 g, 0.22 mmol) and triethylamine (4.57g, 45.65 mmol) in 2:1 DMF-H₂O (5.5 mL) was heated to 80 °C under inert atmosphere for 2-3 hours with stirring. After completion of the reaction, the mixture was poured in to water (30 mL) with stirring, acidified with 3 N HCl (in the case of aryl propargyl amines 3N HCl was added drop wise until the pH ~ 7) and then extracted with ethyl acetate (3 x 150 mL). Organic layers collected, combined, washed with water (2 x 100 mL), dried over anhydrous sodium sulphate, filtered and concentrated under vacuum. The residue was purified by using flash chromatography to afford the desired compound **II**.

4-(2-Propynyloxy)benzaldehyde (Ia): white solid, yield 95 %; mp: 77-79 °C. ¹H NMR (CDCl₃): 9.88 (s, 1H, CHO), 7.86-7.81 (d, J = 8.79 Hz, 2H), 7.09-7.05 (d, J = 8.79 Hz, 2H), 4.76 (s, 2H, CH₂), 2.55 (s, 1H, HC≡C-); IR (KBr, cm⁻¹): 3224 (HC≡C-), 2924, 2121 (-C≡C-), 1661 (C=O); MS (CI, i-Butane): 161 (M⁺+1, 50).

4-Hydroxybenzaldehyde (IIa): yield 75 %; mp: 117-118 °C (lit^{1a} 117-119 °C); ¹H NMR (CDCl₃): 9.86 (s, 1H, CHO), 7.82 (d, J = 8.79 Hz, 2H), 6.99 (d, J = 8.79 Hz, 2H); IR (KBr, cm⁻¹): 3301 (bs, OH), 2924, 1686 (C=O); MS (CI, i-Butane): 123 (M⁺+1, 100).

1-[4-(2-Propynyloxy)phenyl]-1-ethanone (Ib): white solid, yield 95 %; mp: 74-75 °C. ¹H NMR (CDCl₃): 7.95 (d, J = 8.86 Hz, 2H), 7.02 (d, J = 8.86 Hz, 2H), 4.71 (d, J = 2.14

Hz, 2H, CH₂), 2.53 (s, 3H, CH₃), 2.53 (s, 1H, HC≡C-). IR (KBr, cm⁻¹): 3225 (HC≡C-), 2122 (-C≡C-), 1661 (C=O), 1602; MS (CI, i-Butane): 175 (M⁺+1, 100).

4-Hydroxyacetophenone (IIb): white solid; yield 78 %; mp: 110-111 °C (lit^{1b} 109-111 °C); ¹H NMR (CDCl₃): 10.35 (s, 1H, D₂O exch., OH), 7.83 (d, J = 8.59 Hz, 2H), 6.84 (d, J = 8.59 Hz, 2H), 2.47 (s, 3H, CH₃); IR (KBr, cm⁻¹): 3311 (bs, OH), 1663 (C=O); MS (CI, i-Butane): 137 (M⁺+1, 100).

1-[3-Chloro-4-(2-propynyloxy)phenyl]-1-butanone (Ic): white solid; yield 71%; mp: 89-90 °C. ¹H NMR (CDCl₃): 8.05-7.88 (m, 2H), 7.16 (d, J = 8.59 Hz, 1H), 4.89 (d, J = 2.15 Hz, 2H, OCH₂), 2.92 (t, J = 6.98 Hz, 2H, CH₂), 2.61 (t, J = 2.42 Hz, 1H, HC≡C-), 1.88-1.73 (m, 2H, CH₂), 1.07 (t, J = 7.25 Hz, 3H, CH₃); IR (KBr, cm⁻¹): 3302 (HC≡C-), 2966, 2123 (-C≡C-), 1668 (C=O); MS (CI, i-Butane): 237 (M⁺+1, 100).

1-(3-Chloro-4-hydroxyphenyl)-1-butanone (IIc): white solid; yield 65%; mp: 123.5 – 124 °C. ¹H NMR (CDCl₃): 7.99-7.802 (m, 2H), 7.07 (d, J = 8.59 Hz, 1H), 6.03 (s, 1H, D₂O exch., OH), 2.88 (t, J = 7.25 Hz, 2H, CH₂), 1.81-1.67 (m, 2H, CH₂), 1.00 (t, J = 7.52 Hz, 3H, CH₃); IR (KBr, cm⁻¹): 3172 (bs, OH), 2962, 1635 (C=O); MS (CI, i-Butane): 199 (M⁺+1, 100).

1-Nitro-4-(2-propynyloxy)benzene (Id): pale yellow solid; yield 97%; DSC: 113.49 – 114.68 °C. ¹H NMR (CDCl₃): 8.25-8.21 (m, 2H), 7.08-7.04 (m, 2H), 4.77 (d, J = 2.44 Hz, 2H, OCH₂), 2.58 (t, J = 2.44 Hz, 1H, HC≡C-); IR (KBr, cm⁻¹): 3261 (HC≡C-), 2128 (-C≡C-), 1608; MS (CI, i-Butane): 178 (M⁺+1, 100).

4-Nitrophenol (IIId): yellow solid, yield 74%; mp: 112-113 °C (lit^{1c} 112-115 °C); ¹H NMR (CDCl₃): 8.18 (d, J = 5.1 Hz, 2H), 6.95 (d, J = 5.1 Hz, 2H), 6.19 (bs, D₂O Exch, 1H, OH); IR (KBr, cm⁻¹): 3320 (bs, OH), 2923, 1614, 1590; MS (CI, i-Butane): 140 (M⁺+1, 100).

3-Bromo-5-methoxy-4-(2-propynyloxy)benzaldehyde (Ie): yellow solid, yield 73 %; mp: 102-103 °C. ¹H NMR (CDCl₃): 9.86 (s, 1H, CHO), 7.68 (s, 1H), 7.40 (s, 1H), 4.89 (d, J = 2.44 Hz, 2H, OCH₂), 3.95 (s, 3H, OCH₃), 2.51 (s, 1H, HC≡C-); IR (KBr, cm⁻¹): 3282 (HC≡C-), 2935, 2127 (-C≡C-), 1689 (C=O); MS (CI, i-Butane): 269 (M⁺+1, 100), 271 (M⁺+2, 100).

3-Bromo-4-hydroxy-5-methoxybenzaldehyde (IIe): brown solid, yield 68 %; mp: 165-166 °C (lit^{1d} 164-166 °C); ¹H NMR (CDCl₃): 9.79 (s, 1H, CHO), 7.65 (s, 1H), 7.37 (s, 1H), 3.99 (s, 3H, OCH₃); IR (KBr, cm⁻¹): 3291 (bs, OH), 2940, 2850, 1675 (CHO); MS (CI, i-Butane): 231 (M⁺, 100), 233 (M⁺+2, 100).

4-Methoxy-3-(2-propynyloxy)benzaldehyde (If): white solid, yield 78 %; DSC: 74.5-75 °C; ¹H NMR (CDCl₃): 9.85 (s, 1H, CHO), 7.53-7.49 (m, 2H), 6.99 (d, J = 8.3 Hz, 1H), 4.81 (d, J = 2.44 Hz, 2H, OCH₂), 3.95 (s, 3H, OCH₃), 2.53 (s, 1H, HC≡C-); IR (KBr, cm⁻¹): 3231 (HC≡C-), 2122 (-C≡C-), 1674 (C=O); MS (CI, i-Butane): 191 (M⁺+1, 100).

3-Hydroxy-4-methoxybenzaldehyde (IIIf): yellow solid, yield 55 %; mp: 113-114 °C (lit^{1e} 113-115 °C); ¹H NMR (CDCl₃): 9.84 (s, 1H, CHO), 7.45-7.42 (m, 2H), 6.97 (d, J = 8.79 Hz, 1H), 5.87 (s, 1H, D₂O exch., OH), 3.99 (s, 3H, CH₃); IR (KBr, cm⁻¹): 3213, 2934, 1673, 1578, 1512, 1445, 1277; MS (CI, i-Butane): 153 (M⁺+1, 100).

1-Methoxy-4-(2-propynyloxy)benzene (Ig): white solid, yield 81 %; ¹H NMR (CDCl₃): 6.95-6.77 (m, 4H), 4.63 (d, J = 2.42 Hz, 2H, OCH₂), 3.77 (t, J = 2.15 Hz, 3H, OCH₃), 2.5 (t, J = 2.15 Hz, 1H, HC≡C-); IR (KBr, cm⁻¹): 3289 (HC≡C-), 2955; MS (CI, i-Butane): 163 (M⁺+1, 100).

4-Methoxyphenol (IIg): white solid, yield 63 %; mp: 55-56 °C (lit^{1f} 55-57 °C); ¹H NMR (CDCl₃): 6.83-6.74 (m, 4H), 4.90 (s, 1H, D₂O exch., OH), 3.77 (s, 3H, OCH₃); IR (KBr, cm⁻¹): 3382 (bs, OH), 2951; MS (CI, i-Butane): 125 (M⁺+1, 100).

3-Chloro-1-nitro-4-(2-propynyloxy)benzene (IIh): pale yellow solid, yield 89 %; DSC: 106-107 °C; ^1H NMR (CDCl_3): 8.32-8.15 (m, 2H), 7.18 (d, $J = 9.13$ Hz, 2H), 4.9 (d, $J = 2.15$ Hz, 2H, OCH_2), 2.62 (s, 1H, $\text{HC}\equiv\text{C}-$); IR (KBr, cm^{-1}): 3280 ($\text{HC}\equiv\text{C}-$), 2121 ($-\text{C}\equiv\text{C}-$); MS (CI, i-Butane): 212 ($\text{M}^+ + 1$, 100).

2-Chloro-4-nitrophenol (IIh): yellow solid, yield 77 %; ^1H NMR (CDCl_3): 8.31-8.1 (m, 2H), 7.13 (d, $J = 9.13$ Hz, 1H), 6.24 (bs, D_2O exch., 1H, OH); IR (KBr, cm^{-1}): 3392 (bs, OH), 1583, 1511; MS (CI, i-Butane): 174 ($\text{M}^+ + 1$, 100).

1-Chloro-4-(2-propynyloxy)benzene (IIi): pale brown oil, yield 70 %; ^1H NMR (CDCl_3): 7.26 (d, $J = 1.95$ Hz, 2H), 6.91 (d, $J = 8.79$ Hz, 2H), 4.67 (d, $J = 1.95$ Hz, 2H, OCH_2), 2.53-2.51 (m, 1H, $\text{HC}\equiv\text{C}-$); IR (KBr, cm^{-1}): 3297 ($\text{HC}\equiv\text{C}-$), 2923, 2123 ($-\text{C}\equiv\text{C}-$); MS (CI, i-Butane): 167 ($\text{M}^+ + 1$, 100).

4-Chlorophenol (IIi): brown solid, yield 71%; mp 43-44 °C (lit^{lg} 43-45 °C); ^1H NMR (CDCl_3): 7.19 (d, $J = 8.59$ Hz, 2H), 6.86 (d, $J = 8.86$ Hz, 2H), 5.11-4.25 (bs, 1H, D_2O exch., OH), IR (KBr, cm^{-1}): 3384 (bs, OH), 2920, 1593; MS (CI, i-Butane): 129 ($\text{M}^+ + 1$, 100).

1-Fluoro-4-(2-propynyloxy)benzene (IIj): yellow liquid, yield 83 %; ^1H NMR (CDCl_3): 7.05-6.89 (m, 4H), 4.66 (d, $J = 1.88$, 2H, OCH_2), 2.53 (s, 1H, $\text{HC}\equiv\text{C}-$); IR (KBr, cm^{-1}): 3304 ($\text{HC}\equiv\text{C}-$), 3020, 2125 ($-\text{C}\equiv\text{C}-$); MS (CI, i-Butane): 151 ($\text{M}^+ + 1$, 60).

4-Fluorophenol (IIj): white solid, yield 67%; mp: 47-48 °C (lit^{lh} 46-48 °C).

1-(2-Propynyloxy)benzene (IIk): yellow liquid, yield 55%; ^1H NMR (CDCl_3): 7.37-7.26 (m, 2H), 7.05-6.98 (m, 3H), 4.71 (d, $J = 2.44$ Hz, 2H, OCH_2), 2.54 (t, $J = 2.44$ Hz, 1H, $\text{HC}\equiv\text{C}-$); IR (KBr, cm^{-1}): 3293 ($\text{HC}\equiv\text{C}-$), 2122 ($-\text{C}\equiv\text{C}-$); MS (CI, i-Butane): 133 ($\text{M}^+ + 1$, 20).

Phenol (IIk): yield 75 %.

1-Iodo-4-(2-propynyloxy)benzene (II): brown solid, yield 82 %; ^1H NMR (CDCl_3): 7.59 (d, $J = 8.79$ Hz, 2H), 6.77 (d, $J = 8.79$ Hz, 2H), 4.67 (d, $J = 1.95$ Hz, 2H, OCH_2), 2.54 (s, 1H, $\text{HC}\equiv\text{C}-$); IR (KBr, cm^{-1}): 3276 ($\text{HC}\equiv\text{C}-$), 2924, 2128 ($-\text{C}\equiv\text{C}-$), 1570; MS (CI, i-Butane): 259 ($\text{M}^+ + 1$, 30), 258 (M^+ , 50).

4-Iodophenol (II l): yield 51 %; mp: 92-93 °C (lit^{li} 93-95 °C).

2-Propynyl-2-(2-propynyloxy)benzoate (Im): white solid, yield 87 %; DSC: 44-45 °C. ^1H NMR (CDCl_3): 8.05 (d, $J = 8.79$ Hz, 2H), 7.01 (d, $J = 8.79$ Hz, 2H), 4.90 (d, $J = 1.95$ Hz, 2H, OCH_2), 4.76 (d, $J = 2.44$ Hz, 2H, OCH_2), 2.55 (s, 1H, $\text{HC}\equiv\text{C}-$), 2.51 (s, 1H, $\text{HC}\equiv\text{C}-$); IR (KBr, cm^{-1}): 3288 ($\text{HC}\equiv\text{C}-$), 3246 ($\text{HC}\equiv\text{C}-$), 2125 ($-\text{C}\equiv\text{C}-$), 1716 ($\text{C}=\text{O}$), 1607; MS (CI, i-Butane): 215 ($\text{M}^+ + 1$, 100).

2-Hydroxybenzoic acid (II m): yellow solid, yield 45%; mp: 157-158 °C (lit^{lj} 158-161 °C); ^1H NMR (CDCl_3): 9.54 (bs, 1H, D_2O exch., OH), 7.89 (d, $J = 9.09$ Hz, 2H), 6.85 (d, $J = 8.79$ Hz, 2H); IR (KBr, cm^{-1}): 3392 (bs, OH & COOH), 2924, 1675 ($\text{C}=\text{O}$); MS (CI, i-Butane): 139 ($\text{M}^+ + 1$, 100).

1-[4-(2-Propynylamino)phenyl]-1-ethanone (In): yellow solid, yield 24 %; mp: 93-95 °C; ^1H NMR (CDCl_3): 7.86 (d, $J = 8.59$ Hz, 2H), 6.65 (d, $J = 8.59$ Hz, 2H), 4.48-4.47 (bs, 1H, D_2O exch., NH), 4.02-4.01 (m, 2H, NCH_2), 2.51 (s, 3H, CH_3), 2.25 (s, 1H, $\text{HC}\equiv\text{C}-$); IR (KBr, cm^{-1}): 3356 (NH), 3267 ($\text{HC}\equiv\text{C}-$), 2926, 2360 ($-\text{C}\equiv\text{C}-$), 1649 ($\text{C}=\text{O}$); MS (CI, i-Butane): 174 ($\text{M}^+ + 1$, 100).

4-Aminoacetophenone (II n): brown solid, yield 57 %; mp: 106-107 °C (lit^{lk} 105-107 °C); ^1H NMR (CDCl_3): 7.81 (d, $J = 8.59$ Hz, 2H), 6.65 (d, $J = 8.32$ Hz, 2H), 4.15 (bs, 2H, D_2O exch. NH_2), 2.51 (s, 3H, CH_3); IR (KBr, cm^{-1}): 3333, 2924, 1642 ($\text{C}=\text{O}$); MS (CI, i-Butane): 136 ($\text{M}^+ + 1$, 100).

4-Nitrophenyl(2-propynyl)amine (Io): yellow solid, yield 25 %; mp:139-141°C; ¹H NMR (CDCl₃): 8.14 (d, J = 8.86 Hz, 2H), 6.65 (d, J = 8.86 Hz, 2H), 4.69 (bs, 1H, D₂O exch., NH), 4.06-4.02 (m, 2H, NCH₂), 2.29 (s, 1H, HC≡C-); IR (KBr, cm⁻¹): 3408 (NH), 3243 (HC≡C-); MS (CI, i-Butane): 177 (M⁺+1, 100).

4-Nitroaniline (IIo): yellow solid, yield 52 %; mp: 149-150 °C; (lit¹¹ 149-151 °C).

4-Bromophenyl(2-propynyl)amine (Ip): yellow oil, yield 30 %; ¹H NMR (CDCl₃): 7.30 (d, J = 8.86 Hz, 2H), 6.57 (d, J = 8.59 Hz, 2H), 3.92 (s, 2H, NCH₂), 2.23 (s, 1H, HC≡C-); IR (KBr, cm⁻¹): 3413 (NH), 3292 (HC≡C-), 2925, 2115 (-C≡C-); MS (CI, i-Butane): 210 (M⁺, 100), 212 (M⁺+2, 100).

4-Bromoaniline (IIp): brown solid, yield 53 %; mp: 62-63 °C (lit^{1m} 62-64 °C).

References

1. Cat. Handbook of Fine Chemicals 2003-2004; Aldrich, (a) p 1020; (b) p 1020; (c) p1353; (d) p 319; (e) p1034; (f) p1193; (g) p 459; (h) p 918; (i) p 1077; (j) p 1637; (k) p 68; (l) p 1341; (m) p 269.