Synthesis of the Anti-Prostate Cancer Drug Abiraterone Acetate

Supporting Information

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General Experimental Methods

All glassware’s were over-dried at 120°C and all reactions were conducted under a nitrogen atmosphere. Solvents: methanol and CH$_3$CN, for chromatography were distilled before use. THF, toluene, DME and 1,4-dioxane were pre-dry over Na wire. Reflux the pre-dried solvent over Na(1% w/v) and Benzophenone (0.2% w/v) under a nitrogen atmosphere until the blue colour of the benzophenone ketyl radical anion persists.

Instruments.

Reagents were used as such without purification. $^1$H NMR (600 MHz) and $^{13}$C NMR (150 MHz) were recorded using a Bruker spectrometer. The chemical shift data are reported as δ (ppm) using tetramethylsilane as internal standard. Mass spectra were recorded using an Agilent 1200-6320 Ion Trap XCT instrument.

Typical Procedure for Pd-Catalyzed Coupling reaction

A stirred solution of 7(4mmol) in 1,4-dioxane(50mL) in a 100 mL round-bottomed flask was purged with nitrogen and Pd-Catalyst (0.04mmol) and ligand(0.07mmol) were added. After stirring for 10 minutes, to the resultant refous solution was added base (3 mmol) base, then stirring for 5 minutes and 6 (5 mmol) was added. The flask was fitted with a reflux condenser and these were purged with nitrogen. The mixture was heated to the refluxing temperature in an oil bath pan with stirring for 24 hours. The reaction was completed and the solution turned to orange from dark brown.

light green solid(91.6%, yield) m.p.: 176-178°C; Rf= 0.47(1/40 CH$_2$Cl$_2$/methanol ). $^1$H NMR (600MHz, CDCl$_3$): δ 1.05(s, 3H, 19-CH$_3$), 1.07(s, 3H, 18-CH$_3$), 2.26-2.30(m, 2H, 16-2H ), 2.42(s, 24-CH$_3$), 3.51-3.58(m, 1H, 3α-H), 5.39(d, 1H, J=4.8Hz, 6-H), 7.29(d, 2H, Ts2-H, Ts6-H), 7.82(d, 2H, Ts3-H, Ts4-H).
$^{13}$C NMR ($^{150}$MHz, CDCl$_3$): $\delta$ 16.56, 19.37, 20.47, 21.58, 23.39, 25.98, 31.22, 31.30, 31.58, 33.69, 36.62, 37.20, 42.21, 44.74, 50.29, 53.60, 71.62, 120.92, 128.01, 128.28, 129.31, 129.94, 135.56, 141.07, 143.75, 171.63.

![Image](pale yellow solid(58.9%, yield) m.p.: 213-215°C, lit.$^{[1]}$ 212-215°C; Rf= 0.24(1/40 CH$_2$Cl$_2$/methanol). $^1$H-NMR (600MHz,CDCl$_3$): $\delta$ 0.95(s, 3H, 19-CH$_3$), 0.97(s, 3H, 18-CH$_3$), 3.41-3.63(m, 1H, 3α-H), 5.32(d,1H, J=4.8Hz, 6-H), 5.90(s,1H, 16-H), 7.12-7.18(m, 1H, Py5-H), 7.58(d, 1H, J=8.0Hz, Py4-H), 8.37(d,1H,J=4.4Hz, Py6-H), 8.54(s, 1H, Py2-H). $^{13}$C NMR (150MHz, CDCl$_3$): $\delta$ 16.56, 19.33, 19.41, 20.37, 30.47, 31.46, 31.62, 31.80, 35.28, 36.66, 37.22, 42.30, 47.35, 51.80, 57.57, 71.50, 121.24, 123.05, 129.28, 133.05, 133.78, 141.13, 147.67, 151.67.

![Image](white solid(44.3%, yield). m.p.: 143-145°C, lit.$^{[2]}$ 144-145°C; Rf= 0.36(1/40 CH$_2$Cl$_2$/methanol). $^1$H-NMR (600MHz,CDCl$_3$): $\delta$ 1.05(s, 3H, 19-CH$_3$), 1.08(s,3H, 18-CH$_3$), 2.04(s, 3H, CH$_3$CO$_2$), 4.58-4.66(m, 1H, 3α-H), 5.42(d, 1H, J=4.76Hz, 6-H), 5.99(s, 1H, 16-H), 7.22(dd, 1H, J$_1$=4.8Hz, J$_2$=7.8Hz, Py5-H), 7.64(d, 1H, J=7.9Hz, Py4-H), 8.46(d, 1H, J=4.6Hz, Py6-H), 8.63(s, 1H, Py2-H). $^{13}$C NMR (150MHz, CDCl$_3$): $\delta$ 16.56, 19.29, 20.48, 21.44, 27.72, 30.37, 31.78, 35.27, 36.64, 37.02, 38.17, 47.35, 50.34, 57.46, 73.82, 122.16, 122.89, 132.87, 133.64, 140.62, 147.82,147.96, 151.66, 170.38.

yellow solid(8.4%, yield). m.p. 154-156°C; Rf= 0.28(1/40 CH$_2$Cl$_2$/ methanol). $^1$H-NMR (600MHz,CDCl$_3$): $\delta$ 0.95(s, 3H, 19-CH$_3$), 0.97(s, 3H, 18-CH$_3$), 5.32(d,1H, J=4.8Hz, 6-H), 5.90(s,1H, 16-H), 7.12-7.18(m, 1H, Py5-H), 7.20-7.25(m,1H, Py’5-H), 7.58(d, 1H, J=8.0Hz, Py4-H), 7.69(d,1H,J=6.8Hz, Py’4-H), 8.21(d,1H,J=4.2Hz, Py6-H), 8.31(d,1H,J=3.2Hz, Py’6-H), 8.42(s, 1H, Py’2-H), 8.54(s, 1H, Py2-H). $^{13}$C NMR (150MHz, CDCl$_3$): $\delta$ 16.56, 19.32, 19.41, 20.37, 30.46, 31.46, 31.61, 31.80, 35.28, 36.70, 37.21, 42.30, 47.53, 51.80, 57.57, 71.50, 120.83, 121.24,
1H, 13C - NMR spectra

Figure 1S. 1H NMR Spectrum (600 MHz, CDCl₃) of abiraterone acetate(compound 1)
Figure 2S. $^{13}$C NMR Spectrum (150 MHz, CDCl$_3$) of abiraterone acetate (compound 1)

Figure 3S. $^1$H NMR Spectrum (600 MHz, CDCl$_3$) of abiraterone(compound 2)
Figure 4S. $^{13}$C NMR Spectrum (150 MHz, CDCl$_3$) of abiraterone (compound 2)

Figure 5S. 1H NMR Spectrum (600 MHz, CDCl3) of Dehydroepiandrosterone-17 N-tosylhydrazones (compound 7)
Figure 6S. $^{13}$C NMR Spectrum (150 MHz, CDCl$_3$) of Dehydroepiandrosterone-17 N-tosylhydrazones (compound 7)

Figure 7S. 1H NMR Spectrum (600 MHz, CDCl$_3$) of compound 9
Figure 8S. $^{13}$C NMR Spectrum (150 MHz, CDCl$_3$) of compound 9
References
