

A New Practical One-pot Conversion of Phenols to Anilines

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General information. Melting points were determined on a Yamato capillary melting point apparatus MP-21 and were uncorrected. Infrared spectra were recorded on a Horiba FT-210 spectrophotometer. NMR spectra were recorded on a Bruker DPX300 spectrometer. ¹H and ¹³C chemical shifts were referenced to the internal deuterated solvent or tetramethylsilane. HPLC was performed with a Shimadzu LC-6A, Shimadzu SPD-6A UV spectrophotometric detector on 254nm, and YMC ODS-A A-302 150mm × 4.6mm i.d. column. Mass spectra and elemental analyses were performed at Takeda Analytical Research Laboratories, Ltd.. All commercial chemicals and solvents used were reagent grade and were used without further purification. **2, 6, 9, 11, 13, 15** were compared with authentic samples and their analytical data were in perfect agreement with the authentic samples.

2-Bromo-2-methylpropanamide **2**

To a cooled solution of 500g (2.17mol) of 2-bromo-2-methylpropanoyl bromide in water (200mL) was added 400mL (ca.6.0mol) of 25% aqueous ammonium hydroxide in portions over a 2-hour period at 5-15°C. After an additional 1 hour of stirring at 0°C, the resulting white precipitate was collected, washed with 400mL of water twice to give 306.9g (85.0%) of **2** as white crystalline powder: HPLC(50mM KH₂PO₄-MeCN= 65:35) *t_R*: 2.7(**2**, area 98.8%); ¹H-NMR(300MHz, CDCl₃): 1.99(s, 6H), 5.87(brs, 1H), 6.59(brs, 1H).

6-Hydroxy-3,4-dihydro-1(2*H*)-naphthalenone **6**

A mixture of 100g (0.57mol) of 6-methoxy-3,4-dihydro-1(2*H*)-naphthalenone **17** and 340mL (500g) of 48% hydrobromic acid was heated at reflux for 8 hours. Water (200mL) was added to the solution and cooled slowly to room temperature. The precipitated crystalline powder were collected and washed with 200mL of water three times to give 87.9g (95.5%) of **6** as orange crystalline powder: HPLC(50mM KH₂PO₄-MeCN= 65:35) *t_R*: 11.3(**17**), 4.0(**6**, area 98.0%); ¹H-NMR(300MHz, DMSO-*d*₆): 1.98(quint, *J*=6.2Hz, 2H), 2.49(t, *J*=6.1Hz, 2H), 2.83(t, *J*=6.1Hz, 2H), 6.65(d, *J*=2.3Hz, 1H), 6.71(dd, *J*=8.6Hz, 2.4Hz, 1H), 7.74(d, *J*=8.5Hz, 1H), 10.30(s, 1H).

2-Methyl-2-[(5-oxo-5,6,7,8-tetrahydro-2-naphthalenyl)oxy]propanamide **7**

To a solution of 811mg (5mmol) of 6-hydroxy-3,4-dihydro-1(2*H*)-naphthalenone **6** in DMA (8mL) was added 600mg (15mmol) of sodium hydroxide. The mixture was stirred at room temperature for 1.5 hours, 2.490g (15mmol) of 2-bromo-2-methylpropanamide **2** was added and the mixture was stirred at room temperature for 3 hours. Water (16mL) was added to the solution and cooled slowly to room temperature. The precipitated crystalline powder were collected and washed with 8mL of water three times to give 576mg (46.6%) of **7** as white crystalline powder: HPLC(50mM KH₂PO₄-MeCN= 80:20) *t_R*: 4.5(**2**), 11.1(**6**), 20.5(**7**, area 99.4%); m.p. 117.5-119.5 ; IR(KBr): 3357.5, 3164.6, 1687.4, 1664.3, 1604.5cm⁻¹; ¹H-NMR(300MHz, CDCl₃): 1.61(s, 6H), 2.12(quint, *J*=6.1Hz, 2H), 2.61(t, *J*=6.2Hz, 2H), 2.91(t, *J*=6.1Hz, 2H), 5.65(brs, 1H), 6.41(brs, 1H), 6.75(d, *J*=2.3Hz, 1H), 6.84(dd, *J*=8.6Hz, 2.4Hz, 1H), 7.98(d, *J*=8.7Hz, 1H); ¹³C-NMR(75MHz, CDCl₃): 23.7, 25.5(2C), 30.4, 39.3, 81.8, 118.7, 119.0, 128.1, 129.6, 146.9, 159.2, 177.4, 197.6; MS(EI): *m/z* 247(M⁺); Anal. Calcd. for C₁₄H₁₇NO₃: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.71; H, 6.76; N, 5.71.

2-Hydroxy-2-methyl-*N*-(5-oxo-5,6,7,8-tetrahydro-2-naphthalenyl)propanamide **8**

To a solution of 4.87g (30mmol) of 6-hydroxy-3,4-dihydro-1(2*H*)-naphthalenone **6** in DMA (45mL) was added 3.60g (90mmol) of sodium hydroxide. The mixture was stirred at room temperature for 1 hour, 14.94g (90mmol) of 2-bromo-2-methylpropanamide **2** was added and the mixture was stirred at room temperature for 6 hours. After the reaction period, 3.60g (90mmol) of sodium hydroxide was added and the resulting mixture was stirred at 50°C for 3 hours. Water (90mL) was added to the solution and cooled slowly to room temperature. The precipitated crystalline powder were collected and washed with 45mL of water three times to give 5.60g (75.5%) of **8** as white crystalline powder: HPLC(50mM KH₂PO₄-MeCN= 80:20) *t_R*: 4.5(**2**), 11.1(**6**), 20.4(**7**), 17.7(**8**, area 99.6%); m.p. 162.5-163.0 ; IR(KBr): 3305.4, 1672.0, 1600.6, 1540.9cm⁻¹; ¹H-NMR(300MHz, CDCl₃): 1.58(s, 6H), 2.14(quint, *J*=6.2Hz, 2H), 2.65(t, *J*=6.2Hz, 2H), 2.73(s, 1H), 2.96(t, *J*=6.2Hz, 2H), 7.31(dd, *J*=8.5Hz, 2.1Hz, 1H), 7.78(d, *J*=1.6Hz, 1H), 8.01(d, *J*=8.5Hz, 1H), 8.90(brs, 1H); ¹³C-NMR(75MHz,

CDCl₃): 23.3, 27.8(2C), 30.0, 39.0, 74.2, 117.6, 118.4, 128.6, 128.7, 142.1, 146.4, 175.1, 197.8; MS(FAB): *m/z* 248(MH⁺); Anal. Calcd. for C₁₄H₁₇NO₃: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.19; H, 7.06; N, 5.64.

6-Amino-3,4-dihydro-1(2*H*)-naphthalenone **9** using **2**

To a solution of 487mg (3mmol) of 6-hydroxy-3,4-dihydro-1(2*H*)-naphthalenone **6** in DMA (4.5mL) was added 360mg (9mmol) of sodium hydroxide. The mixture was stirred at room temperature for 1 hour, 1.494g (9mmol) of 2-bromo-2-methylpropanamide **2** was added and the mixture was stirred at room temperature for 5 hours. After the reaction period, 1.080g (27mmol) of sodium hydroxide was added and the resulting mixture was stirred at 50°C for 1 hour. After the reaction period, 4.5mL of water was added and the mixture was heated at reflux for 1 hour. Water (9mL) was added to the solution and cooled slowly to room temperature. The precipitated crystalline powder were collected and washed with 4.5mL of water three times to give 287mg (59.3%) of **9** as off-white crystalline powder: HPLC(50mM KH₂PO₄-MeCN= 80:20) *t_R*: 4.6(**2**), 11.1(**6**), 20.4(**7**), 17.7(**8**), 8.6(**9**, area 99.6%); ¹H-NMR(300MHz, CDCl₃): 2.05(quint, *J*=6.1Hz, 2H), 2.55(t, *J*=6.2Hz, 2H), 2.81(t, *J*=6.2Hz, 2H), 4.11(brs, 2H), 6.40(d, *J*=2.2Hz, 1H), 6.52(dd, *J*=8.5Hz, 2.3Hz, 1H), 7.87(d, *J*=8.5Hz, 1H).

6-Amino-3,4-dihydro-1(2*H*)-naphthalenone **9** using **18**

To a solution of 811mg (5mmol) of 6-hydroxy-3,4-dihydro-1(2*H*)-naphthalenone **6** in DMA (8mL) was added 400mg (10mmol) of sodium hydroxide. The mixture was stirred at room temperature for 1 hour, 690mg (5mmol) of 2-bromoacetamide **18** was added and the mixture was stirred at room temperature for 1.5 hours. After the reaction period, 400mg (10mmol) of sodium hydroxide was added and the resulting mixture was stirred at 100°C for 3.5 hours. Water (24mL) was added to the solution and cooled slowly to room temperature. 3.200g (80mmol) of sodium hydroxide was added and the mixture was stirred at room temperature for one night. The precipitated crystalline powder were collected and washed with 8mL of water three times to give 262mg (32.5%) of **9** as off-white crystalline powder: HPLC(50mM KH₂PO₄-MeCN= 80:20) *t_R*: 11.1(**6**), 8.6(**9**, area 99.4%); ¹H-NMR(300MHz, CDCl₃): 2.05(quint, *J*=6.1Hz, 2H), 2.55(t, *J*=6.2Hz, 2H), 2.81(t, *J*=6.2Hz, 2H), 4.11(brs, 2H), 6.40(d, *J*=2.2Hz, 1H), 6.52(dd, *J*=8.5Hz, 2.3Hz, 1H), 7.87(d, *J*=8.5Hz, 1H).

1-(4-Aminophenyl)-1-propanone **11**

To a solution of 451mg (3mmol) of (4-hydroxyphenyl)-1-propanone **10** in DMF (4.5mL) was added 360mg (9mmol) of sodium hydroxide. The mixture was stirred at room temperature for 1 hour, 1.494g(9mmol) of 2-bromo-2-methylpropanamide **2** was added and the mixture was stirred at room temperature for 3 hours. After the reaction period, 1.080g (27mmol) of sodium hydroxide was added and the resulting mixture was stirred at 50°C for 1 hour. After the reaction period, 4.5mL of water and 720mg (18mmol) of sodium hydroxide were added and the mixture was heated at reflux for 1 hour. Water (9mL) was added to the solution and cooled slowly to room temperature. The precipitated crystalline powder were collected and washed with 4.5mL of water three times to give 387mg (86.4%) of **11** as white crystalline powder: HPLC(50mM KH₂PO₄-MeCN= 80:20) *t_R*: 4.5(**2**), 16.0(**10**), 12.5(**11**, area99.5%); ¹H-NMR(300MHz, CDCl₃): 1.24(t, *J*=7.3Hz, 3H), 2.94(q, *J*=7.3Hz, 2H), 4.15(brs, 2H), 6.68(d, *J*=8.8Hz, 2H), 7.86(d, *J*=8.7Hz, 2H).

(2-Aminophenyl)(phenyl)methanone **13**

To a solution of 595mg (3mmol) of (2-hydroxyphenyl)(phenyl)methanone **12** in DMF (6mL) was added 360mg (9mmol) of sodium hydroxide. The mixture was stirred at room temperature for 1 hour, 1.494g(9mmol) of 2-bromo-2-methylpropanamide **2** was added and the mixture was stirred at room temperature for over night. After the reaction period, 1.080g (27mmol) of sodium hydroxide was added and the resulting mixture was stirred at 50°C for 5 hour. After the reaction period, 4.5mL of water and 720mg (18mmol) of sodium hydroxide were added and the mixture was heated at reflux for 30 minutes. Water (12mL) was added to the solution and cooled slowly to room temperature. The precipitated crystalline powder were collected and washed with 6mL of water three times to give 453mg (76.5%) of **13** as yellow crystalline powder: HPLC(50mM KH₂PO₄-MeCN= 50:50) *t_R*: 2.2(**2**), 14.0(**12**), 9.0(**13**, area92.0%); ¹H-NMR(300MHz, CDCl₃): 6.09(brs, 2H), 6.61(dt, *J*=8.1Hz, 1.1Hz, 1H), 6.74(dd, *J*=8.3Hz, 0.8Hz, 1H), 7.30(dt, *J*=8.5Hz, 1.6Hz, 1H), 7.43-7.53(m, 4H), 7.63(d, *J*=1.7Hz, 1H), 7.66(d, *J*=1.3Hz, 1H).

4-Nitroaniline **15** from **14**

To a solution of 417mg (3mmol) of 4-nitrophenol **14** in DMF (4.5mL) was added 360mg (9mmol) of sodium hydroxide. The mixture was stirred at room temperature for 1 hour, 1.494g(9mmol) of 2-bromo-2-methylpropanamide **2** was added and the mixture was stirred at room temperature for three days. After the reaction period, 1.080g (27mmol) of sodium hydroxide was added and the resulting mixture was stirred at 50°C for 2 hours and at 100°C for 4 hours. After the reaction period, 4.5mL of water was added and the mixture was heated at reflux for 1 hour. Water (9mL) was added to the solution and cooled slowly to room temperature. The precipitated crystalline powder were collected and washed with 4.5mL of water

three times to give 156mg (37.7%) of **15** as yellow crystalline powder: HPLC(50mM KH₂PO₄-MeCN= 65:35) t_R: 2.8(**2**), 5.9(**14**), 5.6(**15**, area99.0%); ¹H-NMR(300MHz, CDCl₃): 4.38(brs, 2H), 6.61(d, *J*=9.1Hz, 2H), 8.05(d, *J*=9.1Hz, 2H).

4-Nitroaniline **15** from **16**

To a solution of 776mg (5mmol) of 4-nitrothiophenol **16** in DMA (5mL) was added 600mg (15mmol) of sodium hydroxide. The mixture was stirred at room temperature for 1 hour, 2.490g (15mmol) of 2-bromo-2-methylpropanamide **2** was added and the mixture was stirred at room temperature for 30 minutes and at 100°C for 1 hour. After the reaction period, 600mg (15mmol) of sodium hydroxide was added and the resulting mixture was stirred at 100°C for 1 hour. After the reaction period, 5mL of water and 2.400mg (60mmol) of sodium hydroxide were added and the mixture was heated at reflux for 1 hour. Water (10mL) was added to the solution and cooled slowly to room temperature. The precipitated crystalline powder were collected and washed with 5mL of water three times to give 338mg (48.9%) of **15** as yellow crystalline powder: HPLC(50mM KH₂PO₄-MeCN= 65:35) t_R: 2.7(**2**), 8.0(**16**), 5.5(**15**, area99.6%); ¹H-NMR(300MHz, CDCl₃): 4.39(brs, 2H), 6.62(d, *J*=9.1Hz, 2H), 8.07(d, *J*=9.0Hz, 2H).