Chemoselective Radical Cleavage of Cbz-Protected Nitrogen Compounds

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Supporting Information

N-Cbz derivatives **4**, **8-12** and **14-16** were prepared from commercially available azoles, amides or amines by treatment with Cbz-Cl, under standard basic conditions. For **4**, **9** and **12**: NaH, THF; for **8** and **11**: Et₃N, THF; for **10**, **15** and **16** (KOH, acetone).

The corresponding deprotected products were compared with authentic samples and their data were in full agreement.

Methyl 4-[1-(benzyloxycarbonyl)-3-indolyl]-4-oxobutanoate (**2**).

n-Bu₃SnH (0.21 mL, 0.8 mmol) in C₆H₆ (3 mL) was added over a period of 1 h (syringe pump) to a heated (reflux) solution of **1** (0.28 g, 0.64 mmol), methyl acrylate (0.27 g, 3.2 mmol) and AIBN (10 mg, 0.06 mmol) in C₆H₆ (6 mL). After additional 2-3 h at reflux, the solution was concentrated under reduced pressure, and the residue was partitioned between hexanes (5 mL) and acetonitrile (5 mL), and the polar layer was washed with hexanes (3 x 5 mL) to remove tin compounds. The solvent was removed and the crude product was chromatographed (SiO₂, flash, 75:25 hexanes-AcOEt) to give **2**: 0.11 g (47%); ¹H NMR (CDCl₃, 300 MHz) 2.78 (t, *J* = 6.8 Hz, 2H), 3.24 (t, *J* = 6.8 Hz, 2H), 3.70 (s, 3H), 5.50 (s, 2H), 7.43 (m, 7H), 8.20 (m, 1H), 8.30 (m, 1H), 8.32 (s, 1H); HRMS calcd for C₂₁H₁₉NO₅ 365.1257, found 365.1250.

Representative Deprotection Procedure: *Trans*-3-(benzyloxycarbonyl)-4-(1-methyl-3-indolylcarbonyl)-2-piperidone.

A solution of 2-piperidone **13**¹ (210 mg, 0.4 mmol), *n*-Bu₃SnH (0.16 mL, 0.6 mmol), and AIBN (7 mg, 0.04 mmol) in ethylbenzene (4 mL) was heated at reflux temperature. After the mixture was stirred for 0.5 h, a second portion of AIBN (7 mg, 0.04 mmol) was added. The mixture was stirred at reflux temperature for an additional 0.5 h and then concentrated under reduced pressure. The residue was partitioned between hexanes (10 mL) and acetonitrile (10 mL), and the polar layer was washed with hexanes (3 x 10 mL) to remove tin compounds. The solvent was removed, and the crude product was chromatographed (SiO₂, flash, 99:1 AcOEt-MeOH) to give the secondary amide: 140 mg (90%); ¹H NMR (CDCl₃, 300 MHz,) 2.13 (m, 2H), 3.44 (m, 2H), 3.68 (s, 3H), 3.92 (dt, *J* = 4.4, 9.6, 10 Hz, 1H), 4.03 (d, *J* = 10.2 Hz, 1H), 5.13 (s, 2H), 6.57 (br s, 1H), 7.10-7.40 (m, 8H), 7.74 (s, 1H), 8.38 (m, 1H); ¹³C NMR (CDCl₃, 50.3 MHz) 26.1 (CH₂), 33.6 (CH₃), 41.0 (CH₂), 44.6 (CH), 50.6 (CH), 67.1 (CH₂), 109.7 (CH), 114.7 (C), 122.6 (CH), 122.9 (CH), 123.7 (CH), 126.4 (C), 127.6 (CH), 127.7 (CH), 128.1 (CH), 135.5 (C),

136.2 (CH), 137.6 (C), 168.1 (C), 170.1 (C), 193.3 (C). Anal. Calcd for C₂₃H₂₂N₂O₄: C, 70.71; H, 5.67; N, 7.17. Found: C, 70.64; H, 5.86; N, 7.06.

¹Bennasar, M.-L.; Roca, T.; Grier, R.; Bosch, J. *J. Org. Chem.* **2002**, 67, 6268-6271.

Methyl (3-indolyl)-4-oxobutanoate (3).

Prepared as above from **2**: 95%; ¹H NMR (CDCl₃, 400 MHz) 2.81 (t, *J* = 6.8 Hz, 2H), 3.25 (t, *J* = 6.8 Hz, 2H), 3.71 (s, 3H), 7.28 (m, 2H), 7.41 (m, 1H), 7.93 (d, *J* = 3.2 Hz), 8.37 (m, 1H), 8.65 (br s, 1H); ¹³C NMR (CDCl₃, 50.3 MHz) 28.2 (CH₂), 34.3 (CH₂), 51.8 (CH₃), 111.3 (CH), 117.8 (C), 122.4 (CH), 122.7 (CH), 123.8 (CH), 125.4 (C), 130.9 (CH), 136.2 (C), 173.8 (C), 193.5 (C); HRMS calcd for C₁₃H₁₃NO₃ 231.0894, found 231.0899.