

A Novel Traceless Resin-bound Guanidinyllating Reagent for Secondary Amines to Prepare *N,N*-Disubstituted Guanidines

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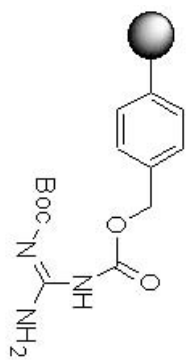
Experimental

Boc-guanidine (6) Guanidine hydrochloride **5** (7.5 g, 78.5 mmol) was dissolved in aqueous 4N NaOH (40 mL) and cooled to 0 °C. Di-*tert*-butyl dicarbonate (13.71 g, 62.8 mmol, 0.8 eq.) was dissolved in 1,4-dioxane (80 mL) and was added dropwise to the guanidine solution with vigorous stirring. The reaction was allowed to react for 15 h after which the solvents were removed under reduced pressure. The crude product was suspended in 20 mL H₂O, sonicated for 10 min and filtered. The white solid was then suspended in 20 mL diethyl ether, sonicated for 10 min, filtered and subsequently dried in a desiccator. The product was isolated as a white solid in 88% yield (8.80 g). $R_f = 0.1$ (CHCl₃:MeOH:AcOH 90:8:2). NMR (400 MHz, CDCl₃) δ 1.44 (s).

Resin (4) The *p*-nitrophenyl carbonate Wang resin **7** (5 g, 3 mmol) was first washed with 50 mL DMF and subsequently suspended in another 50 mL of DMF. Freshly distilled triethylamine (2.1 mL, 15 mmol, 5 eq.), Boc-guanidine **6** (2.39 g, 15 mmol, 5eq.) and 4-(dimethylamino)pyridine (37 mg, 0.3 mmol, 0.1 eq.) were added. The mixture was agitated for 24 h after which the resin was washed with DMF (2 x 50 mL), DCM (2 x 50 mL), MeOH (2 x 50 mL), DCM (2 x 50 mL), MeOH (2 x 50 mL), DCM (2 x 50 mL) and dried in a desiccator. FT-IR (KBr) 1944, 1873, 1804, 1732, 1657, 1623, 1602, 1583,

1543, 1513, 1493, 1452, 1422, 1370, 1285, 1267, 1244, 1153, 1120, 1070, 1041, 1028, 1011 cm^{-1} .

In an oven-dried 3-necked flask under argon atmosphere, resin **8** was suspended in dry DCM (50 mL) and cooled to $-78\text{ }^{\circ}\text{C}$. Freshly distilled triethylamine (2.1 mL, 15 mmol, 5 eq.) was added and the suspension stirred for 15 min. Triflic anhydride (2.52 mL, 15 mmol, 5 eq.) was added dropwise via a glass syringe over 15 min. The mixture was allowed to warm to $0\text{ }^{\circ}\text{C}$ and stirred for 1 h. The resin mixture was poured through a fritted filter, washed thoroughly with MeOH and DCM and dried in a desiccator. FT-IR (KBr) 1944, 1873, 1794, 1740, 1692, 1623, 1616, 1601, 1584, 1554, 1513, 1493, 1452, 1396, 1373, 1344, 1304, 1195, 1171, 1129, 1099, 1071, 1054, 1025, 1014 cm^{-1} .



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