Supporting Information

Application of the Curtius rearrangement to the synthesis of 1'-aminoferrocene-1-carboxylic acid derivatives

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Substrates’ syntheses

Dimethyl ferrocene-1,1’-dicarboxylate – SI1. Under argon, BuLi (~1.6 M in hexanes, 78.1 mL, 125 mmol, 2.5 equiv) was added to a stirred solution of ferrocene (9.3 g, 50 mmol, 1.0 equiv) and TMEDA (18.7 mL, 14.5 g, 125 mmol, 2.5 equiv) in hexane (250 mL) and the reaction was stirred overnight at room temperature to give a deep red suspension. THF (100 mL) was added and the reaction mixture was cooled to -78 °C. Carbon dioxide was bubbled in the reaction mixture for 15 min and the reaction mixture was slowly warmed to room temperature upon bubbling. EtOAc (150 mL) was added and the organic phase was extracted with NaOH (10%, 3 x 100 mL). The combined aqueous layers were washed with EtOAc (2 x 100 mL) and acidified with HCl (12 M) until pH 1 was reached. The resulting solids were filtrated, washed with H2O and dried under high vacuum over P2O5 to give crude ferrocene-1,1’-dicarboxylic acid. The title product as an orange solid containing 3-5% of ferrocencarboxylic acid.

The crude product was dissolved in MeOH (150 mL), H2SO4 (96%, 1.0 mL) was added dropwise and the reaction mixture was heated at methanol reflux overnight. The reaction mixture was cooled to room temperature and volatiles were removed under vacuum. EtOAc (100 mL) and NaHCO3 (saturated, 100 mL) were added and the layers were separated. The aqueous layer was further extracted with EtOAc (2 x 100 mL). The combined organic layers were washed with MgSO4, filtrated and concentrated under vacuum to give the crude product. This was purified by column chromatography on silica, eluting with EtOAc/heptane (80:20 to 70:30) to give ferrocene-1,1’-dicarboxylate SI1 (16.6 g, 70.5%) and methyl ferrocene carboxylate SI2 (337.0 mg, 3%) as orange solids.

Dimethyl ferrocene-1,1’-dicarboxylate (SI1): mp 112-114 °C (lit.1 113.5-114.5 °C); IR (ATR): 3087, 2958, 1698, 1468, 1434, 1373, 1278, 1196, 1143, 1029, 964, 779 cm-1; 1H NMR (300 MHz, CDCl3) δ 4.78 (t, J = 2.0 Hz, 4H, 4 x FcCH), 4.36 (t, J = 2.0 Hz, 4H, 4 x FcCH) 3.78 (s, 6H, 2 x CH3); 13C NMR (75.4 MHz, CDCl3) δ 170.9 (2 x C=O), 73.1 (2 x FcC), 72.8 (4 x FcCH), 71.7 (4 x FcCH), 51.8 (2 x CH3). Methyl ferrocene carboxylate (SI2): mp 57-58 °C (lit.2 50-56 °C); IR (ATR): 2954, 1709, 1699, 1463, 1373, 1276, 1189, 1136, 1105, 1025, 961, 823 cm-1; 1H NMR (500 MHz, CDCl3) δ 4.78 (t, J = 1.7 Hz, 2H, 2 x FcCH), 4.37 (t, J = 1.7 Hz, 2H, 2 x FcCH), 4.18 (s, 5H, 5 x FcCH), 3.78 (s, 3H, CH3); 13C NMR (125.7 MHz, CDCl3) δ 172.4 (C=O), 71.4 (FcC), 71.2 (2 x FcCH), 70.3 (2 x FcCH), 69.9 (5 x FcCH), 51.7 (CH3).

Sodium ferrocene-1,1’-dicarboxylate (SI3). A solution of NaOH (2.17 g, 54.3 mmol, 8.2 equiv) in water (10 mL) was added to a solution of dimethyl ferrocene-1,1’-dicarboxylate (SI1, 2.0 g, 6.6 mmol, 1.0 equiv) in EtOH (10.0 mL) at 70 °C. After 2h at 75 °C, the reaction mixture was cooled to 0 °C and the resulting solids were filtrated, washed with cold EtOH (5 mL), Et2O (10 mL) and dried under vacuum to give the title product as a yellow solid (2.0 g, 95%). mp > 250 °C; IR (ATR): 3087, 1556, 1477, 1380, 1190, 1067, 1026, 806, 796 cm-1; 1H NMR (300 MHz, D2O) δ 4.75 (s, 4H, 4 x FcCH), 4.43 (s, 4H, x FcCH) 13C NMR (75.4 MHz, D2O) δ 179.4 (2 x C=O), 77.4 (2 x FcC), 73.1 (4 x FcCH), 71.0 (4 x FcCH).

(9H-Fluoren-9-yl)methanol (SI4). A modified procedure of Chong was followed:3 BuLi (~1.6 M in hexanes, 37.5 mL, 60.0 mmol, 1.0 equiv) was added to a solution of fluorene (10.0 g, 60.0 mmol, 1.0 equiv) in anhydrous THF (250 mL) at 0 °C over 5 min. After 3 min stirring at 0 °C, paraformaldehyde (2.0 g, 66.0 mmol, 1.1 equiv) was added in one portion. The reaction mixture was warmed to room temperature and stirred for 90 min. NaHCO3 sat. (150 mL) was added and the reaction mixture was extracted with Et2O (3 x 100 mL). The combined organic layers were dried over MgSO4, filtrated and concentrated under vacuum to give the crude product. This was purified by recrystallization in hexane/EtOH (600:8) to give the title product as a white solid (3.6 g, 30.5%). mp 100-102 °C (lit.1 100-101 °C); IR (ATR): 3252 (br), 1444, 1363, 1314, 1048, 1024, 754, 77, 725 cm-1; 1H NMR (300 MHz, CDCl3) δ 7.77 (d, J = 7.4 Hz, 2H, ArH), 7.60 (d, J = 7.4 Hz, 2H, 2 x ArH), 7.40 (dt, J = 7.4, 0.7 Hz, 2H, 2 x ArH), 7.32 (dt, J = 7.4, 1.1 Hz, 2H, 2 x ArCH), 4.10 (t, J = 6.0 Hz, 1H, CH), 4.01 (t, J = 6.0 Hz, 2H, CH2), 1.64 (t, J = 6.0 Hz, 1H, OH); 13C NMR (75.4 MHz, CDCl3) δ 144.5 (2 x ArC), 141.7 (2 x ArC), 127.7 (2 x ArCH), 127.3 (2 x ArCH), 124.9 (2 x ArCH), 120.2 (2 x ArCH), 65.3 (CH2), 50.6 (CH).

Ferrocene-1,1’-dicarboxylic acid (2). HCl (12 M) was added dropwise to a solution of sodium ferrocene-1,1’-dicarboxylate (SI3, 1.0 g, 3.1 mmol, 1.0 equiv) in water (20 mL) at 0 °C until pH 1 was...
reached. The resulting solids were filtrated, washed with water and dried under high vacuum over \( \text{P}_2\text{O}_5 \) to give the title product as an orange solid (800 mg, 93%). mp > 250 °C (decomp, lit. \(^4\) > 250 °C); IR (ATR): 2885 (br), 2557, 1668, 1488, 1404, 1297, 1168, 1032, 917, 840, 751 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d\(^6\)) \( \delta \) 12.32 (br s, 2H, 2 x CO\(^2\)H), 4.69 (s, 4H, 4 x FcCH), 4.44 (s, 4H, 4 x FcCH); \(^{13}\)C NMR (75.4 MHz, DMSO-d\(^6\)) \( \delta \) 171.1 (2 x C=O), 73.5 (2 x FcC); 72.6 (4 x FcCH); 71.3 (4 x FcCH).

IR spectra of the formation and consumption of 3 and 4

Formation of 3 and 4: top to bottom (1 min, 1 h, 2 h, 3 h, 4 h).

Formation of isocyanate from 4: top to bottom (1 min, 10 min, 20 min, 40 min, 60 min).
NMR spectra for compounds 1 – 15 and SI1-4

1'-(tert-Butoxycarbonyl)amino)ferrocene-1-carboxylic acid - 1
Ferrocene-1,1′-dicarboxylic acid - 2
1,1’-Diazidocarbonylferrocene - 3
1'-Azidocarbonylferrocene-1-carboxylic acid - 4
Triethylammonium 1'-carboxyferrocene-1-carboxylate - 5
$1'\text{-(Benzyloxycarbonyl)amino} \text{ferrocene-1-carboxylic acid - 7}$
1'-(Fluoren-9-yl) methoxycarbonyl)amino]ferrocene-1-carboxylic acid
1’-((Allyloxy carbonyl)amino)ferrocene-1-carboxylic acid - 9
2,5-Dioxopyrrolidin-1-yl 1'-\((\text{tert-}\text{butylcarbonylamino})\text{ferrocene-1-carboxylate - 10}}\)
2,5-Dioxopyrrolidin-1-yl 1’-((benzyloxy carbonyl)amino)ferrocene-1-carboxylate - 11
2,5-Dioxopyrrolidin-1-yl 1'-(fluoren-9-yl)methoxycarbonyl)amino)ferrocene-1-carboxylate - 12
2,5-Dioxopyrrolidin-1-yl 1′-((allyloxy carbonyl)amino)ferrocene -1-carboxylate - 13
1'-(tert-Butoxycarbonyl)amino)ferrocene-1-carboxylic anhydride - 14
$N$-methyl 1'-(tert-butoxycarbonyl)amino)ferrocene-1-carboxamide - 15
Dimethyl ferrocene-1,1'-dicarboxylate – SI1
Methyl ferrocene carboxylate – SI2
Sodium ferrocene-1,1'-dicarboxylate – SI3
(9H-Fluoren-9-yl)methanol – SI4