Functionalization of α,β -Unsaturated Esters and ketons: A Facile and Highly Stereoselective One-Pot Approach to *N*-Protected α,β -Dehydroamino Acid Derivatives

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Contents

Experimental Section	S 2
NMR Data for Compound 4a-4l	S 2-5
X-ray Crystallography of 4a	S 6
¹ H NMR Spectra for Compound 4a-4l	S 7-18
¹³ C NMR Spectra for Compound 4a-4l	S 19-30

Experimental Section

General information NMR spectra were recorded at 500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR. CDCl_3 was the only solvent used for the NMR analysis, with TMS as the internal standard. Chemical shifts were reported downfield from TMS (0.00 ppm) for ^1H NMR and relative to CDCl_3 (77.0 ppm) for ^{13}C NMR. Column Chromatography was performed with silica gel Merck 60 (230-400 mesh).

Typical procedure of the one-pot synthesis of α,β -dehydroamino acids: Into a dry capped vial was added α,β -unsaturated substrate (1 mmol), copper (I) trifluoromethanesulfonate (CuOTf) benzene complex (50.3 mg, 0.1 mmol, 10 mol%), 4 Å molecular sieves (500 mg) and newly distilled CH_3CN 2 mL. 4-Ts NCl_2 (360 mg, 1.5 mmol) was dissolved in 4 mL newly distilled CH_3CN , then the resulting solution was introduced into the reaction vial *via* a syringe pump in a period of 30 minutes. The resulting solution was stirred at room temperature and monitored by TLC determination. Upon completion the reaction was quenched with 1.0 mL of saturated aqueous Na_2SO_3 solution followed by DABCO (5.0 mmol). The resulting system was stirred for 30 min at room temperature. The phase was separated, and the aqueous phase was extracted with EtOAc (3x10 mL). The combined organic phase was washed with brine, and dried with anhydrous sodium sulfate. Purification by flash chromatography (EtOAc/Hexane, v/v, 1/4) provided the pure product

4a ^1H NMR (500 MHz, CDCl_3) δ = 7.82-7.87 (m, 2H), 7.64-7.68 (m, 2H), 7.52 (s, 1H), 7.32-7.37 (m, 3H), 7.20-7.24 (m, 2H), 6.23 (s, 1H), 3.52 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 165.4, 143.9, 137.7, 136.3, 132.7, 131.0, 130.3, 129.3, 128.4, 127.5, 52.5, 21.5.

- 4b ^1H NMR (500 MHz, CDCl_3) δ = 7.86-7.92 (m, 2H), 7.65-7.69 (m, 2H), 7.47 (s, 1H), 7.34-7.39 (m, 3H), 7.20-7.24 (m, 2H), 6.27 (s, 1H), 4.81 (, J = 6.0 Hz, 1H), 2.38 (s, 3H), 1.09 (d, J = 6.0 Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ = 164.4, 143.9, 136.7, 136.3, 132.9, 131.1, 130.3, 129.4, 128.3, 127.7, 123.1, 69.8, 21.5.
- 4c ^1H NMR (500 MHz, CDCl_3) δ = 7.83-7.88 (m, 2H), 7.61-7.65 (m, 2H), 7.55 (s, 1H), 7.33-7.38 (m, 6H), 7.21-7.25 (m, 2H), 7.12-7.17 (m, 2H), 6.25 (s, 1H), 4.97 (s, 2H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 164.8, 143.8, 137.7, 136.3, 135.1, 132.7, 131.1, 130.4, 129.4, 128.6, 128.5, 128.4, 128.2, 127.5, 122.7, 67.5, 21.6.
- 4d ^1H NMR (500 MHz, CDCl_3) δ = 7.77-7.82 (m, 2H), 7.62-7.66 (m, 2H), 7.48 (s, 1H), 7.29 -7.33 (m, 2H), 7.22-7.26 (m, 2H), 6.22 (s, 1H), 3.54 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 165.2, 144.1, 136.3, 136.2, 132.3, 131.2, 129.4, 128.7, 127.5, 123.1, 52.7, 21.5.
- 4e ^1H NMR (500 MHz, CDCl_3) δ = 7.87-7.93 (m, 2H), 7.63-7.68 (m, 2H), 7.50 (s, 1H), 7.21-7.25 (m, 2H), 7.00-7.06 (m, 2H), 6.23 (s, 1H), 3.50 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 165.3, 164.7, 162.7, 144.0, 136.8, 136.2, 133.4, 133.3, 129.4, 129.0, 128.9, 127.5, 122.2, 122.1, 115.6, 115.4, 52.5, 21.5.
- 4f ^1H NMR (500 MHz, CDCl_3) δ = 7.75-7.81 (m, 2H), 7.64-7.69 (m, 2H), 7.51 (s, 1H), 7.20 -7.25 (m, 2H), 7.13-7.18 (m, 2H), 6.20 (s, 1H), 3.49 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 165.5, 143.8, 141.0, 138.1, 136.4, 131.2, 129.9, 129.3, 129.1, 127.5, 121.7, 52.4, 21.6, 21.5.

- 4g ^1H NMR (500 MHz, CDCl_3) δ = 8.14-8.20 (m, 2H), 7.94-7.99 (m, 2H), 7.58-7.64 (m, 2H), 7.52 (s, 1H), 7.21-7.26 (m, 2H), 6.39 (s, 1H), 3.60 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 164.6, 147.9, 144.5, 139.4, 136.0, 133.7, 131.4, 129.5, 127.4, 125.9, 123.5, 53.0, 21.5.
- 4h ^1H NMR (500 MHz, CDCl_3) δ = 7.84-7.89 (m, 2H), 7.77-7.82 (m, 2H), 7.54 (s, 1H), 7.53-7.58 (m, 1H), 7.43-7.48 (m, 2H), 7.34-7.38 (m, 3H), 6.20 (s, 1H), 3.51 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 165.3, 139.3, 137.9, 133.1, 132.6, 131.1, 130.5, 128.8, 128.5, 127.5, 122.5, 52.6.
- 4i ^1H NMR (500 MHz, CDCl_3) δ = 7.92-7.99 (m, 2H), 7.87-7.91 (m, 2H), 7.71-7.75 (m, 1H), 7.68 (s, 1H), 7.65-7.70 (m, 1H), 7.38-7.43 (m, 3H), 7.30 (s, 1H), 3.55 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 165.2, 147.5, 140.1, 134.5, 133.6, 132.9, 132.5, 131.1, 130.8, 130.6, 128.7, 125.6, 122.2, 52.5.
- 4j ^1H NMR (500 MHz, CDCl_3) δ = 7.79-7.85 (m, 2H), 7.58-7.63 (m, 2H), 7.37 (s, 1H), 7.34-7.39 (m, 2H), 7.19-7.24 (m, 2H), 6.73 (s, 1H), 2.39 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 195.1, 144.0, 136.4, 136.0, 132.9, 131.7, 130.9, 130.5, 129.4, 128.5, 127.5, 24.6, 21.6.
- 4k ^1H NMR (500 MHz, CDCl_3) δ = 7.77-7.82 (m, 2H), 7.69-7.74 (m, 2H), 7.52-7.58 (m, 3H), 7.40-7.45 (m, 2H), 7.35-7.40 (m, 3H), 7.17-7.22 (m, 2H), 7.03 (s, 1H), 6.88 (s, 1H), 2.32 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 193.6, 144.1, 139.1, 136.3, 136.2, 132.7, 132.3, 131.4, 130.8, 130.6, 129.5, 129.1, 128.6, 128.3, 127.5, 21.5.
- 4l ^1H NMR (500 MHz, CDCl_3) δ = 7.69-7.74 (m, 4H), 7.65-7.69 (m, 2H), 7.36-7.40 (m, 3H), 7.18-7.23 (m, 2H), 7.09-7.14 (m, 2H), 6.95 (s, 1H), 6.78 (s, 1H),

2.34 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ = 192.1, 166.3, 164.3, 144.2, 137.6, 136.2, 132.6, 132.5, 131.9, 131.8, 131.5, 130.6, 130.5, 129.5, 128.7, 127.5, 115.7, 115.5, 21.5.

04-051
in CDCl3
SW Probe
1gh080904.1
Pulse Sequence: szpu1

04-60
in CDCl3
SW Probe
1gh082404.1
Pulse Sequence: szpu1

04-064
in CDCl3
SW Probe
1gh083004.1
Pulse Sequence: s2pu1

04-055
in CDCl3
SW Probe
1gh082504.1

Pulse Sequence: szpul

No Title
in CDCl3
SW Probe
j1h073004

Pulse Seq

064
in CDCl3
SW Probe
j1h090104.1
Pulse Sequence:

065
in CDCl3
SW Probe
J1h090204.1
Pulse Sequence: szpu1

04-054
in CDCl3
SW Probe
1gh082004.1
Pulse Sequence: s2pu1

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160
140
120
100
80
60
40
20

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137.652

136.325

132.676

131.037

130.334

129.319

128.395

127.527

122.693

77.257

77.000

76.747

52.519

21.493

04-60
in CDCl3
SV Probe
1gc082404.1

Pulse Sequence: szpu1

180
160
140
120
100
80
60
40
20
ppm

164.838

143.808
137.734
136.293
135.104
132.739

131.120
130.405
129.366
128.572
128.493
128.395
128.245
127.526

122.656

77.253
77.000
76.747

67.486

21.573

-0.025