Functionalized Analogues of an Unnatural Amino Acid that Mimics a Tripeptide β-Strand

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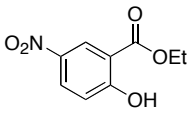
Supporting information

Synthetic Experimental Procedures.

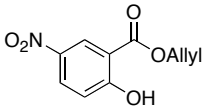
Commercial-grade reagents and solvents were used without further purification except as indicated. CH_2Cl_2 and THF were dried before use by percolation through anhydrous Al_2O_3 as described by Grubbs and coworkers.[1] DMF was dried in an analogous fashion by percolation through 3 Å molecular sieves.[2] All reactions were stirred magnetically; moisture-sensitive reactions were performed under nitrogen in flame-dried glassware. Reactions were monitored by thin-layer chromatography (TLC), usually using either EtOAc/hexanes or isopropanol/CH_2Cl_2 as the solvent system. Solvents were removed by rotary evaporation under moderate vacuum. Flash chromatography with silica gel was performed following the conditions described by Still and coworkers.[3] Before use, Amberlite IR-120 ion exchange resin was rinsed with H_2O and then washed with methanol and THF/H_2O (4:1) until the rinsing solution became neutral. After use, the resin was regenerated by washing with 1 M aq HCl and then rinsing with THF/H_2O (4:1) until the rinsing solution became neutral. High-resolution mass spectra were obtained by liquid secondary-ion ionization (LSI) of samples in an *m*-nitrobenzyl alcohol matrix bombarded with Cs^+ at 25 kV (instrumental variation = 2 mmu). Samples for elemental analysis were dried under vacuum (ca. 10^{-3} mmHg). Melting points were determined on a glass capillary melting point apparatus. Analytical reverse phase HPLC (RP-HPLC) was performed on a Beckman (Agilent Zorbax 80 SB C_{18} column, 50 x 4.6 mm; solvent A: H_2O/0.1% TFA, solvent B: CH_3CN/0.1% TFA), and preparative RP-HPLC was carried out on a Rainin machine (Agilent Zorbax 80 SB C_{18} column, 250 x 21.2 mm; solvent A: H_2O, solvent B: CH_3CN/0.2% AcOH). ^1H NMR spectra were acquired either on a Bruker DRX400 (400 MHz) spectrometer, on a Bruker DRX500 (500 MHz) spectrometer, or on a Bruker Cryoprobe (500 MHz) spectrometer. NMR data were processed by using Bruker XWINNMR

[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. A.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.
[2] Burfield, D. R. and Smithers, R. H. *J. Org. Chem.* **1978**, *43*, 3966–3968.
[3] Mitra, A.; Kahn, M.; Still, W. C. *J. Org. Chem.* **1978**, *43*, 2923–2925.

software. All samples were prepared as dilute solutions in either deuteriochloroform ($CDCl_3$) with v/v 0.05% tetramethylsilane (TMS) or d_6-dimethylsulfoxide (CD_3SOCD_3) with v/v 0.05% TMS. Chemical shifts are reported in parts per million (ppm) downfield from TMS (0.00 ppm). ^{13}C-NMR spectra chemical shifts are reported relative to $CDCl_3$ (77.0 ppm) or CD_3SOCD_3 (39.5 ppm).



Ethyl 2-hydroxy-5-nitrobenzoate. A solution of 2-hydroxy-5-nitrobenzoic acid (30.0 g, 163.8 mmol), absolute ethyl alcohol (200 mL), and H_2SO_4 (10 mL) was heated at reflux for 24 h. The reaction mixture was allowed to cool to room temperature, and the ethyl ester precipitated from the solution as long off-white needles. The crystals were isolated by filtration and washed with 20 mL of cold ethanol to yield 24.0 g (69%) of ethyl 2-hydroxy-5-nitrobenzoate: mp 95–97 °C (lit. 97 °C)[4]; IR (nujol) 3158, 1681, 1619, 1581, 1524 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 11.56 (s, 1 H), 8.79 (d, J = 2.8 Hz, 1 H), 8.33 (dd, J = 9.2, 2.8 Hz, 1 H), 7.09 (d, J = 9.2 Hz, 1 H), 4.49 (q, J = 7.1 Hz, 2 H), 1.47 (t, J = 7.1 Hz, 3 H); HRMS (CI) m/z for $C_9H_9NO_5$ $[M]^+$ calcd 211.0480, found 211.0479.

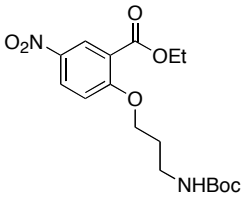


Allyl 2-hydroxy-5-nitrobenzoate. A solution of 2-hydroxy-5-nitrobenzoic acid (15.0 g, 81.9 mmol), allyl alcohol (40 mL), and H_2SO_4 (2 mL) was heated at reflux for 12 h. The reaction mixture was allowed to cool to room temperature, and excess allyl alcohol was removed under vacuum to give dark yellow crystals of the allyl ester. The crystals were dissolved in 50 mL of EtOAc/hexanes (1:3), and the solution was filtered through a silica gel plug (2 in diameter x 3 in height) using EtOAc/hexanes (1:3) as eluent. Removal of the solvent under vacuum afforded allyl 2-hydroxy-5-nitrobenzoate 9.5 g (52%) as pale yellow crystals: mp 62–63 °C; IR (nujol) 3181, 1685, 1623, 1584, 1527 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 11.44 (s, 1 H), 8.82 (d, J = 2.9 Hz, 1 H), 8.33 (dd, J = 9.2, 2.8 Hz, 1 H), 7.09 (d, J = 9.2 Hz, 1 H), 6.06 (ddt, J = 17.1, 10.4, 5.9 Hz, 1 H), 5.47 (appar dd, J = 17.2 Hz, 1.3 Hz, 1 H), 5.39 (appar dd, J = 10.4, 1.0 Hz, 1 H), 4.91 (appar dt, J = 6.0, 1.1 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 166.2, 139.9, 130.6, 130.5, 126.5, 120.1, 118.5, 112.1, 66.9; HRMS (CI) m/z for

[4] Tarbell, D. S.; Wystrach, V. P. *J. Am. Chem. Soc.* **1943**, *65*, 2146–2149.

$C_{10}H_9NO_5$ $[M]^+$ calcd 223.0480, found 223.0478. Anal. Calcd. for $C_{10}H_9NO_5$: C, 53.82; H, 4.06; N, 6.28. Found: C, 53.58; H, 4.07; N, 6.11.

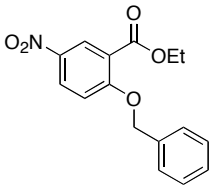
General procedure for preparation of ethers 2a, 2c, and 2d. A round-bottomed three-necked flask equipped with a thermometer, a reflux condenser, and a stopper was charged with ethyl 2-hydroxy-5-nitrobenzoate, finely ground K_2CO_3, and DMF. The mixture was heated to 70–100 °C, the appropriate alkylating agent was added all at once, and the reaction mixture was vigorously stirred. The progress of the reaction was monitored by TLC. Once the alkylation was complete, the reaction mixture was cooled to room temperature and partitioned between CH_2Cl_2 and water (ca. 10 times the volume of DMF, each). (For multi-gram scale reactions, DMF was first removed under vacuum to avoid large extraction volumes.) The layers were separated, and the aqueous phase was extracted with additional CH_2Cl_2. The combined organic layers were washed with $NaHCO_3$, water (twice), and satd aq NaCl solution. It was dried over Na_2SO_4, filtered, and concentrated under vacuum. Residual DMF was removed under high vacuum for 12 h.



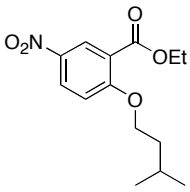
Ether 2a. Alkylation of ethyl 2-hydroxy-5-nitrobenzoate (2.1 g, 9.9 mmol) with 3-(*tert*-butoxycarbonylamino)propyl bromide[5] (4.8 g, 20.2 mmol) using K_2CO_3 (14.1 g, 102.0 mmol) in 70 mL DMF at 100 °C for 3 h, as described in the general procedure (above), generated 3.6 g (99%) of ether **2a** as a dark viscous oil of sufficient purity to use in the next step. An analytical sample was recrystallized from hexanes/EtOAc (9:1) to generate pure **2a** as white crystals: mp 52–53 °C; IR (nujol) 3367, 3338, 1731, 1699, 1612, 1584, 1528 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.75 (s, 1 H), 8.36 (dd, *J*

[5] Pearson, D. A.; Lister-James, J.; McBride, W. J.; Wilson, D. M.; Martel, L. J.; Civitello, E. R.; Dean, R. T. *J. Med. Chem.* **1996**, *39*, 1372–1382.

= 9.2, 2.9 Hz, 1 H), 7.05 (d, *J* = 9.2 Hz, 1 H), 5.64 (br s, 1 H), 4.41 (q, *J* = 7.2 Hz, 2 H), 4.24 (t, *J* = 5.7 Hz, 2 H), 3.41 (br q, *J* = 5.8 Hz, 2 H), 2.09 (br quintet, *J* = 5.9 Hz, 2 H), 1.44 (s, 9 H), 1.42 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 163.5, 156.7, 141.0, 129.4, 128.3, 120.7, 113.1, 79.3, 69.2, 62.0, 38.9, 29.5, 28.8, 14.7; HRMS (CI) *m/z* for $C_{17}H_{25}N_2O_7$ $[M + H]^+$ calcd 368.1661, found 368.1661. Anal. Calcd. for $C_{17}H_{24}N_2O_7$: C, 55.43; H, 6.57; N, 7.60. Found: C, 55.61; H, 6.46; N, 7.57.

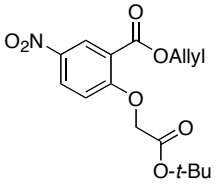


Ether 2c. Alkylation of ethyl 2-hydroxy-5-nitrobenzoate (4.3 g, 20.4 mmol) with benzyl bromide (7.2 mL, 10.4 g, 60.8 mmol) using K_2CO_3 (4.2 g, 30.4 mmol) in 20 mL DMF at 70 °C for 5 h, as described in the general procedure (above), generated 6.1 g (99%) of ether **2c** as a dark viscous oil of sufficient purity to use in the next step. An analytical sample was recrystallized from hexanes to generate pure **2c** as white crystals: mp 55–56 °C (lit. 75 °C)[4]; IR (nujol) 1697, 1613, 1587, 1522 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, *J* = 2.9 Hz, 1 H), 8.31 (dd, *J* = 9.2, 2.9 Hz, 1 H), 7.47 (d, *J* = 7.2 Hz, 2 H), 7.41 (appar t, *J* = 7.4 Hz, 2 H), 7.34 (appar t, *J* = 7.3 Hz, 1 H), 7.09 (d, *J* = 9.2 Hz, 1 H), 5.29 (s, 2 H), 4.39 (q, *J* = 7.2 Hz, 2 H), 1.37 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 163.0, 141.2, 135.6, 129.2, 129.1, 128.8, 128.2, 127.4, 121.9, 113.8, 71.7, 62.2, 14.7; HRMS (CI) *m/z* for $C_{16}H_{15}NO_5$ $[M]^+$ calcd 301.0950, found 301.0949. Anal. Calcd. for $C_{16}H_{15}NO_5$: C, 63.78; H, 5.02; N, 4.65. Found: C, 64.00; H, 5.03; N, 4.60.



Ether 2d. Alkylation of ethyl 2-hydroxy-5-nitrobenzoate (10.0 g, 47.3 mmol) with 1-bromo-3-methylbutane (17.0 mL, 21.4 g, 141.7 mmol) using K_2CO_3 (13.3 g, 96.2 mmol) and sodium iodide (14.2 g, 94.7 mmol) in 40 mL DMF at 100 °C for 4 h, as described in the general procedure

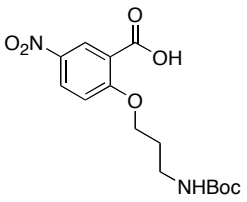
(above), generated 12.3 g (92%) of ether **2d** as a viscous oil of sufficient purity to use in the next step. An analytical sample was purified by column chromatography (EtOAc/hexanes 1:3) to generate pure **2d** as white crystals: mp 36–38 °C; IR (nujol) 1687, 1611, 1587, 1513 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, *J* = 2.9 Hz, 1 H), 8.32 (dd, *J* = 9.2, 2.9 Hz, 1 H), 7.03 (d, *J* = 9.2 Hz, 1 H), 4.39 (q, *J* = 7.2 Hz, 2 H), 4.18 (t, *J* = 6.6 Hz, 2 H), 1.93–1.87 (m, 1 H), 1.77 (q, *J* = 6.6 Hz, 2 H), 1.40 (t, *J* = 7.2 Hz, 3 H), 0.98 (d, *J* = 6.6 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 163.5, 140.8, 129.0, 128.1, 121.5, 113.1, 68.7, 61.9, 37.9, 25.3, 22.9, 14.7; HRMS (CI) *m/z* for $C_{14}H_{19}NO_5$ $[M]^+$ calcd 281.1263, found 281.1266. Anal. Calcd. for $C_{14}H_{19}NO_5$: C, 59.78; H, 6.81; N, 4.98. Found: C, 60.03; H, 6.82; N, 5.07.



Ether 4. A round-bottomed, one-necked flask equipped with a reflux condenser was charged with allyl 2-hydroxy-5-nitrobenzoate (8.3 g, 37.2 mmol), finely ground anhydrous K_2CO_3 (10.3 g, 74.5 mmol), and DMF (120 mL). The mixture was stirred at room temperature for 5 min, *t*-butyl bromoacetate (8.0 mL, 10.6 g, 54.3 mmol) was added all at once, and the stirring mixture was heated to 45 °C over 1.5 h. The mixture was stirred for 1.5 h at 45 °C and then was cooled to room temperature. The mixture was transferred to a separating funnel with 500 mL of EtOAc and was washed with satd aq NaCl solution (3 x 300 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under vacuum to generate 13.6 g of dark viscous oil. The oil was loaded on silica gel and subjected to chromatography on a silica gel column (3 in diameter x 7 in height, gradient elution with hexanes/EtOAc from 100:0 to 70:30) to provide 12.4 g of pure ether **4** (99 % yield) as light yellow oil. IR (nujol) 1744, 1649, 1614, 1588, 1524 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 2.9 Hz, 1 H), 8.33 (dd, *J* = 9.2, 2.9 Hz, 1 H), 6.91 (d, *J* = 9.2 Hz, 1 H), 6.04 (ddt, *J* = 17.2 Hz, 10.4 Hz, 5.8 Hz, 1 H), 5.43 (appar dq, *J* = 17.2, 1.4 Hz, 1 H), 5.31 (appar dq, *J* = 10.4, 1.2 Hz, 1 H), 4.85 (appar dt, *J* = 5.7, 1.3

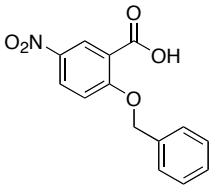
Hz, 2 H), 4.73 (appar s, 2 H), 1.47 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 163.5, 162.1, 141.3, 131.8, 128.6, 127.9, 121.2, 118.9, 113.3, 83.3, 66.5, 66.3, 28.1; HRMS (CI) *m/z* for $C_{16}H_{19}NO_7$ $[M]^+$ calcd 337.1161, found 337.1161. Anal. Calcd. for $C_{16}H_{19}NO_7$: C, 56.97; H, 5.68; N, 4.15. Found: C, 56.72; H, 5.77; N, 4.16.

General procedure for saponification of ethers 2a, 2c, and 2d to generate acids 3a, 3c, and 3d. A round-bottomed two-necked flask equipped with reflux condenser and thermometer was charged with ether **2** (**a**, **c**, or **d**). A sufficient quantity of a THF/water mixture (4:1) was added to make a clear solution. A 1 M aq NaOH solution was then added, and the mixture was stirred at 65 °C for 2–5 h, while monitoring the progress of the reaction by TLC. Once the saponification was complete, the reaction mixture was cooled to room temperature and then passed through a column of Amberlite IR-120 ion-exchange resin (1 in diameter x 4 in height, 1.9 mmol/mL). The resin was washed with additional THF/water mixture, and THF was removed from the combined solutions by rotary evaporation. The resulting opaque slurry was filtered to give a crystalline solid, which was rinsed with cold water to yield acid **3 (a**, **b**, or **c)**.

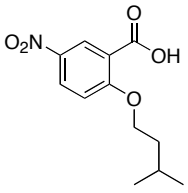


Acid 3a. Saponification of ether **2a** (3.6 g, 9.8 mmol) with 1 M aq NaOH solution (10.3 mL, 10.3 mmol) in a THF/water mixture (4:1, 80 mL) for 2.5 h as described in general procedure (above) produced 3.1 g (93%) of acid **3a** in sufficient purity for further use. An analytical sample was purified by dissolving a portion of this material in satd aq $NaHCO_3$, extracting twice with CH_2Cl_2, acidifying to pH 2 with 1 M aq HCl, isolating the resulting yellow crystals by filtration, and drying under vacuum: mp 124–125 °C; IR (nujol) 3320, 1714, 1647, 1610, 1581 cm^{-1}; ^{1}H NMR (500 MHz, CD_3SOCD_3) δ 13.43 (br s, 1 H), 8.46 (d, *J* = 2.8 Hz, 1 H), 8.36 (dd, *J* = 9.2, 2.9 Hz, 1 H), 7.33 (d, *J* =

9.1 Hz, 1 H), 6.91–6.88 (m, 1 H), 4.20 (t, J = 6.0 Hz, 2 H), 3.11 (q, J = 6.3 Hz, 2 H), 1.87 (quintet, J = 6.3 Hz, 2 H), 1.39 (s, 9 H); ^{13}C NMR (125 MHz, CD_3SOCD_3) δ 166.1, 163.2, 156.3, 140.5, 129.2, 127.1, 122.4, 114.6, 78.2, 67.9, 37.4, 29.5, 28.9; HRMS (CI) m/z for $C_{15}H_{20}N_2O_7$ $[M]^+$ calcd 340.1270, found 340.1265. Anal. Calcd. for $C_{15}H_{20}N_2O_7$: C, 52.94; H, 5.92; N, 8.23. Found: C, 52.82; H, 5.74; N, 8.05.

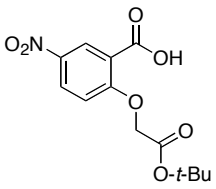


Acid 3c. Saponification of ether **2c** (6.1 g, 20.2 mmol) with 1 M aq NaOH solution (21.0 mL, 21.0 mmol) in a THF/water mixture (4:1, 40 mL) for 5 h as described in general procedure (above) produced 5.6 g of acid **3c**. Recrystallization from *i*-PrOH/water afforded 5.0 g (91%) of white crystals with a yellowish tinge: mp 165–166 °C (lit. 166 °C)[4]; IR (nujol) 1702, 1679, 1608, 1587, 1520 cm^{-1}; ^{1}H NMR (500 MHz, CD_3SOCD_3) δ 8.47 (d, J = 2.9 Hz, 1 H), 8.31 (dd, J = 9.2, 2.9 Hz, 1 H), 7.50 (d, J = 7.3 Hz, 2 H), 7.44 (d, J = 9.3 Hz, 1 H), 7.41 (t, J = 7.5 Hz, 2 H), 7.32 (t, J = 7.3 Hz, 1 H), 5.38 (s, 2 H); ^{13}C NMR (125 MHz, CD_3SOCD_3) δ 165.4, 161.9, 140.1, 135.9, 128.5, 128.4, 127.9, 127.2, 126.4, 122.1, 114.4, 70.5; HRMS (CI) m/z for $C_{14}H_{12}NO_5$ $[M + H]^+$ calcd 274.0715, found 274.0719. Anal. Calcd. for $C_{14}H_{11}NO_5$: C, 61.54; H, 4.06; N, 5.13. Found: C, 61.58; H, 4.19; N, 5.07.

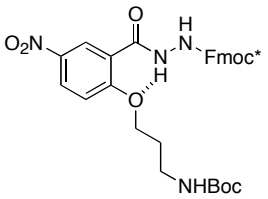


Acid 3d. Saponification of ether **2d** (12.3 g, 43.7 mmol) with 1 M aq NaOH solution (70 mL, 70 mmol) in a THF/water mixture (4:1, 100 mL) for 5 h as described in general procedure (above) produced 8.7 g (78%) of acid **3d**. Recrystallization of an analytical sample from *i*-PrOH/water afforded white crystals with a yellowish tinge: mp 134–135 °C; IR (nujol) 3122, 2651, 1708, 1681, 1612, 1582 cm^{-1}; ^{1}H NMR (500 MHz, CD_3SOCD_3) δ 8.43 (d, J = 2.9 Hz, 1 H), 8.35 (dd, J = 9.2, 2.9 Hz, 1 H), 7.37 (d, J = 9.3 Hz, 1 H), 4.22 (t, J = 6.5 Hz, 2 H), 1.85–1.80 (m, 1 H), 1.65 (q, J = 6.6 Hz, 2 H), 0.93 (d, J =

6.7 Hz, 6 H); ^{13}C NMR (125 MHz, CD_3SOCD_3) δ 166.2, 163.1, 140.4, 129.1, 126.9, 122.6, 114.6, 68.6, 37.7, 25.1, 22.9; HRMS (CI) *m/z* for $C_{12}H_{15}NO_5$ $[M]^+$ calcd 253.0950, found 253.0949. Anal. Calcd. for $C_{12}H_{15}NO_5$: C, 56.91; H, 5.97; N, 5.53. Found: C, 57.04; H, 6.10; N, 5.55.

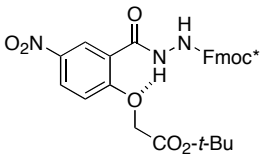


Acid 3b. Ether **4** (12.0 g, 35.6 mmol) was added to a mixture of *N*-methylmorpholine (24 mL), acetic acid (12 mL), and anhydrous THF (80 mL). Nitrogen was bubbled through the solution while it was stirred vigorously for 20 min. $Pd(PPh_3)_4$ (1.5 g, 1.3 mmol) was then added, and the reaction mixture was stirred under nitrogen and monitored periodically by TLC. After 20 h, the reaction appeared to be complete. The reaction mixture was concentrated by rotary evaporation, and the residue was partitioned in EtOAc (250 mL) and satd aq $NaHCO_3$ solution (600 mL), and dry $NaHCO_3$ was slowly added with stirring until no more gas was evolved. The aqueous phase along with a floating precipitate was separated and acidified to pH = 4.5 by addition of acetic acid. The white precipitate was isolated by filteration through a Büchner funnel and was washed with water and hexanes. The precipitate was suspended in DMF and was shaken with acidic Amberlite IR-120 resin. The resulting solution was separated from the resin and was concentrated by rotary evaporation. The residue was isolated by CH_2Cl_2/hexane (1:3) to give 9.2 g of acid **3b** (87% yield) as an off-white solid. An analytical sample was recrystallized from *i*-PrOH/water to give off-white crystals. mp 147–148 °C (dec); IR (nujol) 3229, 1737, 1727, 1618, 1536 cm^{-1}; ^{1}H NMR (500 MHz, CD_3SOCD_3) δ 13.3 (br s, 1 H), 8.46 (d, *J* = 3.0 Hz, 1 H), 8.34 (dd, *J* = 9.2, 3.0 Hz, 1 H), 7.22 (d, *J* = 9.3 Hz, 1 H), 4.97 (s, 2 H), 1.43 (s, 9 H); ^{13}C NMR (125 MHz, CD_3SOCD_3) δ 167.4, 165.9, 162.1, 141.1, 128.7, 127.1, 122.7, 114.8, 82.7, 66.5, 28.3; HRMS (CI) *m/z* for $C_{13}H_{15}NO_7$ $[M]^+$ calcd 297.0848, found 297.0851. Anal. Calcd. for $C_{13}H_{15}NO_7$: C, 52.53; H, 5.09; N, 4.71. Found: C, 52.82; H, 5.02; N, 4.68.

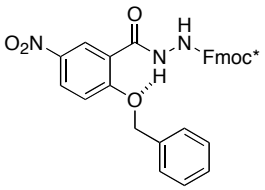


Fmoc*-hydrazide 5a. To an ice-cooled solution of acid **3a** (4.3 g, 12.6 mmol) in DMF (30 mL) were added *N*-ethyl-*N'*-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC, 2.6 g, 13.5 mmol) and 1-hydroxy-7-azabenzotriazole (HOAt, 1.8 g, 13.2 mmol). The solution was stirred for 20 min, and a solution of Fmoc*-$NHNH_2$[6] (4.4 g, 12.0 mmol) in DMF (30 mL) was added in one portion, and the reaction mixture was stirred for 3 h. The reaction mixture was transferred to a separating funnel with EtOAc (450 mL) and was washed with water (450 mL), satd aq $NaHCO_3$ solution (3 x 250 mL), and satd aq NaCl solution (250 mL). The solution was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to give pale yellow solid. Column chromatography on silica gel (gradient elution with hexanes/EtOAc from 100:0 to 55:45) afforded 8.0 g (97% yield based on Fmoc*-$NHNH_2$[6]) of Fmoc*-hydrazide **5a** as white crystals with a yellowish tinge. An analytical sample was recrystallized from EtOAc/hexanes (20:80) to give white crystals: mp 98–99 °C; IR (nujol) 3444, 3320, 3196, 1719, 1652, 1605, 1514 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.87 (br s, 1 H), 8.99 (br s, 1 H), 8.34 (dd, *J* = 9.1, 2.9 Hz, 1 H), 7.61 (br s, 4 H), 7.45 (br s, 1 H), 7.42 (d, *J* = 7.7 Hz, 2 H), 7.07 (d, J = 9.1 Hz, 1 H), 5.05 (br s, 1 H) 4.50 (d, *J* = 7.2 Hz, 2 H), 4.32 (s, 2 H), 4.23 (t, *J* = 6.9 Hz, 1 H), 3.41 (br s, 2 H), 2.09 (br s, 2 H), 1.37 (s, 18 H), 1.33 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) 161.1, 156.6, 156.0, 150.1, 143.8, 143.7, 141.8, 138.8, 128.6, 125.0, 122.1, 122.0, 121.2, 119.4, 112.6, 79.6, 68.7, 68.0, 47.1, 37.2, 35.0, 31.7, 29.6, 28.4; HRMS (ESI) *m/z* for $C_{38}H_{48}N_4O_8Na$ $[M + Na]^+$ calcd 711.3370, found 711.3354. Anal. Calcd. for $C_{38}H_{48}N_4O_8$: C, 66.26; H, 7.02; N, 8.13. Found: C, 66.11; H, 6.99; N, 8.15.

[6] (a) Stigers, K. D.; Koutroulis, M. R.; Chung, D. M.; Nowick, J. S. *J. Org. Chem.*, **2000**, *65*, 3858–3860. (b) Nowick, J. S.; Chung, D. M.; Maitra, K.; Maitra, S.; Stigers, K. D.; Sun, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7654–7661.

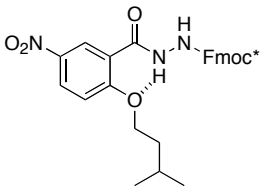


Fmoc*-hydrazide 5b. To an ice-cooled solution of acid **3b** (3.1 g, 10.4 mmol) in DMF (22 mL) were added *N*-ethyl-*N'*-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC, 2.1 g, 11.0 mmol) and 1-hydroxy-7-azabenzotriazole (HOAt, 1.5 g, 11.0 mmol). The solution was stirred for 20 min, and a solution of Fmoc*-$NHNH_2$[6] (3.6 g, 9.8 mmol) in DMF (22 mL) was added in one portion, and the reaction mixture was stirred for 3 h. The reaction mixture was transferred to a separating funnel with EtOAc (400 mL) and was washed with water (400 mL), satd aq $NaHCO_3$ solution (3 x 200 mL), and satd aq NaCl solution (200 mL). The solution was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to give pale yellow solid. Column chromatography on silica gel (gradient elution with hexanes/EtOAc from 100:0 to 70:30) afforded 6.1 g (96% yield based on Fmoc*-$NHNH_2$[6]) of Fmoc*-hydrazide **5b** as off-white crystals. An analytical sample was recrystallized from EtOAc/hexanes (1:9) to give white crystals: mp 158–159 °C; IR (nujol) 3386, 1736, 1677, 1613, 1530 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 10.13 (d, *J* = 3.0 Hz, 1 H), 9.14 (d, *J* = 2.8 Hz, 1 H), 8.38 (dd, *J* = 9.1, 2.9 Hz, 1 H), 7.63 (br s, 4 H), 7.42 (br s, 2 H), 6.98 (d, *J* = 9.1 Hz, 1 H), 6.97 (br s, 1 H), 4.74 (s, 2 H), 4.50 (d, *J* = 7.2 Hz, 2 H), 4.24 (br s, 1 H), 1.55 (s, 9 H), 1.37 (s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 163.2, 160.2, 156.9, 150.4, 144.1, 143.1, 139.1, 129.5, 129.2, 125.3, 122.4, 121.5, 119.6, 113.3, 84.9, 69.1, 67.1, 47.5, 35.3, 32.0, 28.5; HRMS (ESI) *m/z* for $C_{36}H_{43}N_3O_8Na$ $[M + Na]^+$ calcd 668.2948, found 668.2928. Anal. Calcd. for $C_{36}H_{43}N_3O_8$: C, 66.96; H, 6.71; N, 6.51. Found: C, 66.59; H, 6.70; N, 6.45.



Fmoc*-hydrazide 5c. A 250-mL two-necked round-bottomed flask, equipped with a rubber septum and a reflux condenser fitted with a nitrogen inlet adapter was charged with a solution of acid **3c** (2.0 g, 7.3 mmol) in CH_2Cl_2 (39 mL) and DMF (1 mL). A solution of oxalyl chloride

(2 M in CH_2Cl_2, 11.0 mL, 22.0 mmol) was added via syringe over 2 min. After gas and heat evolution subsided, the reaction mixture was stirred for 2.5 h. The reaction mixture was concentrated by rotary evaporation, and the crystalline residue was dissolved in CH_2Cl_2 (32 mL). The solution was cooled in an ice bath and transferred by syringe over 5 min into an ice-cooled solution of Fmoc*-$NHNH_2$[6] (2.6 g, 7.1 mmol) and pyridine (0.6 mL, 7.7 mmol) in 80 mL of CH_2Cl_2. The ice bath was allowed to melt and the reaction mixture was allowed to gradually warm to room temperature. After a total of 11 h, the reaction mixture was partitioned between CH_2Cl_2 (50 mL) and water (200 mL), and the aqueous phase was extracted with CH_2Cl_2 (100 mL). The organic fractions were combined and washed sequentially with satd aq $NaHCO_3$ (100 mL) and satd aq NH_4Cl (100 mL). It was dried over Na_2SO_4, filtered, and concentrated under vacuum to give 4.0 g of a white crystalline solid. Column chromatography on silica gel (application with CH_2Cl_2, gradient elution with hexanes/EtOAc) afforded 2.5 g (56% yield based on Fmoc*-$NHNH_2$[6]) of Fmoc*-hydrazide **5c** as off-white crystals. An analytical sample was recrystallized from EtOAc/hexanes (40:60): mp 195–196 °C; IR (nujol) 3222, 1736, 1708, 1667, 1523 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.40 (br s, 1 H), 9.11 (s, 1 H), 8.37 (dd, *J* = 9.1, 2.8 Hz, 1 H), 7.59–7.56 (m, 4 H), 7.39–7.29 (m, 7 H), 7.18 (d, *J* = 9.1 Hz, 1 H), 7.03 (br s, 1 H), 5.36 (s, 2 H), 4.49 (d, *J* = 6.9 Hz, 2 H), 4.21 (br s, 1 H), 1.35 (s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.9, 161.1, 156.4, 150.2, 143.8, 142.2, 138.9, 134.2, 129.5, 129.0, 128.0, 127.0, 125.1, 122.2, 121.9, 120.8, 119.4, 113.7, 72.7, 68.8, 47.2, 35.1, 31.7; HRMS (CI) *m/z* for $C_{37}H_{39}N_3O_6$ $[M]^+$ 621.2838, found 621.2851. Anal. Calcd. for $C_{37}H_{39}N_3O_6$: C, 71.48; H, 6.32; N, 6.76. Found: C, 71.53; H, 6.30; N, 6.80.



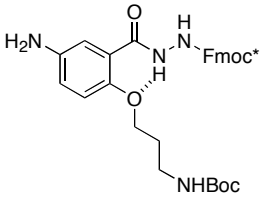
Fmoc*-hydrazide 5d. A 250-mL two-necked round-bottomed flask equipped with a rubber septum and a reflux condenser fitted with a nitrogen inlet adapter was charged with a

solution of acid **3d** (1.9 g, 7.5 mmol) in CH_2Cl_2 (39 mL) and DMF (1 mL). A solution of oxalyl chloride (2 M in CH_2Cl_2, 11.0 mL, 22.0 mmol) was added via syringe over 2 min. After gas and heat evolution subsided, the reaction mixture was stirred for 2 h. The reaction mixture was concentrated by rotary evaporation, and the crystalline residue was dissolved in CH_2Cl_2 (32 mL). The solution was cooled in an ice bath and transferred by syringe over 5 min into an ice-cooled solution of Fmoc*-$NHNH_2$[6] (2.6 g, 7.1 mmol) and pyridine (0.6 mL, 7.7 mmol) in CH_2Cl_2 (80 mL). The ice bath was allowed to melt, and the reaction mixture was allowed to gradually warm to room temperature. After a total of 7 h, the reaction mixture was partitioned between CH_2Cl_2 (50 mL) and water (200 mL), and the aqueous phase was extracted with CH_2Cl_2 (100 mL). The organic fractions were combined and washed sequentially with satd aq $NaHCO_3$ (100 mL) and satd aq NH_4Cl (100 mL). It was dried over Na_2SO_4, filtered, and concentrated under vacuum to give 3.9 g of a white crystalline solid. Column chromatography on silica gel (application with CH_2Cl_2, gradient elution with hexanes/EtOAc) afforded 2.7 g (63% yield based on Fmoc*-$NHNH_2$[6]) of Fmoc*-hydrazide **5d** as white crystals: mp 218–219 °C; IR (nujol, cm^{-1}) 3344, 3250, 1704, 1690, 1611, 1582, 1517; ^1H NMR (500 MHz, $CDCl_3$) δ 9.58 (br s, 1 H), 9.13 (br s, 1 H), 8.37 (dd, *J* = 9.1, 3.0 Hz, 1 H), 7.60 (br s, 4 H), 7.42 (br s, 2 H), 7.26 (br s, 1 H), 7.12 (d, *J* = 9.2 Hz, 1 H), 4.52 (d, *J* = 7.0 Hz, 2 H), 4.31–4.30 (m, 2 H), 4.27 (t, *J* = 7.0 Hz, 1 H), 1.86 (br s, 3 H), 1.37 (s, 18 H), 1.00 (appar d, *J* = 5.2 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 156.3, 150.4, 148.9, 144.0, 142.3, 139.1, 129.3, 129.1, 125.3, 122.4, 120.5, 119.7, 113.2, 69.9, 69.1, 47.4, 37.8, 35.3, 32.0, 25.7, 22.9; HRMS (CI) *m/z* for $C_{35}H_{43}N_3O_6$ $[M]^+$ calcd 601.3151, found 601.3151. Anal. Calcd. for $C_{35}H_{43}N_3O_6$: C, 69.86; H, 7.20; N, 6.98. Found: C, 69.97; H, 7.26; N, 7.01.

General procedure for hydrogen reduction on Pd/C catalyst.

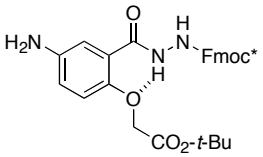
Fmoc*-hydrazide **5a, 5b,** or **5d** was dissolved in THF/MeOH (2:1) and placed in a three-necked round-bottomed flask equipped with magnetic stirring bar, a septum, a stopper, and an inlet with

stopcock. The inlet was connected to a 3-way adapter, attached to a hydrogen balloon and to a Schlenk manifold. Catalyst (10% Pd/C) was added to the reaction mixture, and the flask was evacuated, while stirring vigorously. [CAUTION: To reduce the risk of fire, the flask should be evacuated and filled with nitrogen before adding the catalyst, and the catalyst should be added with a gentle countercurrent of nitrogen.] The reaction vessel was then flushed with hydrogen and evacuated again. This cycle was repeated 3 times. Hydrogenation was conducted with *vigorous* stirring at room temperature for the specified amount of time. Typically, reaction was monitored by TLC every 20–30 min, and when starting material could no longer be observed, the reaction was *immediately* quenched by evacuating the reaction vessel and opening the flask to air. The reaction mixture was then filtered through a Celite bed on a glass filter, using generous amount of EtOAc as rinsing solvent. The solvent was removed under vacuum, and the resulting aniline was protected from light and dried 8–12 h under high vacuum. The product was used in the next step without further purification.

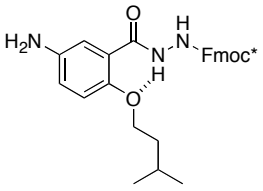


Aniline 6a. Using the general procedure described above, Fmoc*-hydrazide **5a** (3.9 g, 5.7 mmol) was reduced with 0.3 g of 10 % Pd/C catalyst in 85 mL of THF/MeOH (2:1). The reaction was monitored by TLC; the starting material could not be detected after 2.5 h. Upon workup, 3.8 g (102%) of crude aniline **6a** was isolated, which was used in the next step without further purification. A small sample of the crude product was purified by column chromatography on silica gel (gradient elution with hexanes/EtOAc from 2:1 to 1:4) to afford aniline **6a** as off-white crystals. mp 112–114 °C; IR (nujol, cm^{-1}) 3445, 3373, 3348, 3249, 1755, 1742, 1692, 1663, 1530; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.92 (br s, 1 H), 7.64–7.61 (m, 4 H), 7.50 (br s, 1 H), 7.49–7.48 (m, 1 H), 7.41 (d, *J* = 7.7 Hz, 2 H), 6.83–6.88 (m, 2 H), 5.09 (br s 1 H), 4.48 (d, *J* = 7.3 Hz, 2 H), 4.23 (t, *J* = 7.3 Hz, 1 H),

4.13 (t, J = 6.8 Hz, 2 H), 3.56 (br s, 2 H), 3.34–3.32 (m, 2 H), 2.05–2.03 (m, 2 H), 1.37 (br s, 27 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 158.9, 150.2, 150.0, 143.9, 141.0, 138.9, 125.1, 124.2, 122.2, 122.0, 120.3, 119.5, 118.3, 114.4, 68.7, 67.8, 53.7, 47.3, 37.9, 35.1, 31.9, 30.0, 28.6; HRMS (LSIMS) *m/z* for $C_{38}H_{50}N_4O_6Na$ $[M + Na]^+$ calcd 681.3628, found 681.3643. Anal. Calcd. for $C_{38}H_{50}N_4O_6$: C, 69.28; H, 7.65; N, 8.50. Found: C, 69.14; H, 7.78; N, 8.24.

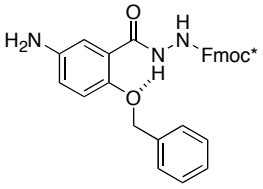


Aniline 6b. Using the general method described above, Fmoc*-hydrazide **5b** (2.1 g, 3.3 mmol) was reduced with 0.2 g of 10% Pd/C catalyst in 20 mL of THF/MeOH (2:1). TLC analysis indicated that the reaction was completed in 1.5 h. Removal of solvent afforded 2.0 g (97%) of crude aniline **6b**, which was sufficiently pure to be used in the next step. An analytical sample was purified by radial chromatography, using hexanes/EtOAc (1:1). mp 110–111 °C; IR (nujol, cm^{-1}) 3350, 1742, 1666, 1613; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.30 (br s, 1 H), 7.63–7.60 (m, 4 H), 7.49–7.48 (m, 1 H), 7.41 (d, J = 7.4 Hz, 2 H), 6.98 (br s, 1 H), 6.74–6.70 (m, 2 H), 4.57 (s, 2 H), 4.45 (d, J = 7.5 Hz, 2 H), 4.24 (t, J = 7.5 Hz, 1 H), 1.49 (s, 9 H), 1.37 (s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 168.0, 157.1, 150.4, 148.7, 144.3, 144.1, 139.1, 125.2, 122.6, 121.1, 119.6, 118.2, 116.7, 114.7, 83.7, 67.6, 63.0, 47.5, 35.3, 32.0, 28.5; HRMS (LSIMS) *m/z* for $C_{36}H_{46}N_3O_6$ $[M + H]^+$ calcd 616.3387, found 616.3376.



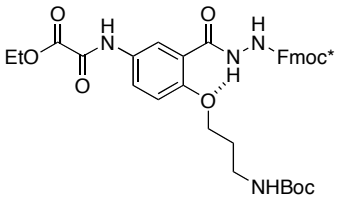
Aniline 6d. Using the general method described above, Fmoc*-hydrazide **5d** (2.7 g, 4.5 mmol) was reduced with 0.6 g of 10% Pd/C catalyst in 50 mL of THF/MeOH (2:1). TLC analysis indicated that the reaction was completed in 2.3 h. Removal of solvent afforded 2.6 g (100%) of crude aniline **6d**, which was used in the next step without further purification. An analytical sample was recrystallized from hexanes. mp 112–113 °C; IR (nujol, cm^{-1}) 3346, 1752, 1730, 1658, 1640, 1612,

1582; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (br s, 1 H), 7.70–7.68 (m, 4 H), 7.62 (br s, 1 H), 7.61 (d, *J* = 2.9 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 2 H), 6.88–6.81 (m, 2 H), 4.52 (d, *J* = 7.4 Hz, 2 H), 4.29 (t, *J* = 7.4 Hz, 1 H), 4.13 (t, *J* = 6.6 Hz, 2 H), 3.60 (br s, 2 H), 1.86–1.80 (m, 3 H), 1.43 (br s, 18 H), 1.01 (d, *J* = 7.6 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 156.2, 150.5, 150.2, 144.0, 140.8, 138.9, 125.0, 122.2, 120.4, 120.0, 119.4, 118.5, 114.3, 68.7, 53.6, 47.3, 38.2, 35.1, 31.8, 25.5, 21.3; HRMS (LSIMS) *m/z* for $C_{35}H_{45}N_3O_4$ $[M]^+$ calcd 571.3410, found 571.3417. Anal. Calcd. for $C_{35}H_{45}N_3O_4$ C, 73.52; H, 7.93; N, 7.35. Found: C, 73.56; H, 7.94; N, 7.25.



Aniline 6c through reduction by $SnCl_2$.[7] Fmoc*-hydrazide **5c** (2.5 g, 4.0 mmol) was dissolved in 100 mL absolute ethyl alcohol and placed in a three-necked round-bottomed flask equipped with a magnetic stirring bar, a reflux condenser with a nitrogen inlet, a thermometer, and a stopper. $SnCl_2$•$2H_2O$ (5.6 g, 24.8 mmol) was added, and the mixture was warmed to 67 ºC, while stirring vigorously. The reaction mixture was never allowed to boil, but the temperature was maintained at above 65ºC. The progress of the reduction was monitored by TLC. After 2.5 h, the reaction mixture was cooled to the room temperature and poured onto ice to form white emulsion. Saturated aq $NaHCO_3$ solution was then added to the emulsion to adjust the pH to 8.0. The aqueous solution was extracted with EtOAc three times. The combined organic layers were washed with satd aq NaCl solution, dried over Na_2SO_4, and concentrated to give 2.4 g (100%) of crude aniline **6c**, which was sufficiently pure to use in the next step. An analytical sample was purified by radial chromatography (gradient elution with hexanes/EtOAc from 3:1 to 1:1). mp 65–66 °C; IR (nujol, cm^{-1}) 3362, 1736, 1720, 1664, 1618, 1583; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.72 (br s, 1 H), 9.64–9.59 (m, 4 H), 7.64–7.59 (m, 4 H), 7.55–7.53 (m, 1 H),

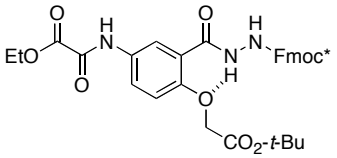
7.40–7.31 (m, 7 H), 7.15 (br s, 1 H), 6.86 (d, *J* = 8.8 Hz, 1 H), 6.80–6.76 (m, 1 H), 5.14 (s, 2 H), 4.44 (d, *J* = 7.3 Hz, 2 H), 4.24–4.22 (m, 1 H), 3.61 (br s, 2 H), 1.34 (br s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 164.9, 156.4, 150.2, 143.9, 141.3, 138.9, 136.1, 129.1, 128.8, 127.9, 125.0, 122.2, 120.6, 120.4, 119.4, 118.6, 115.3, 72.6, 68.7, 47.3, 35.1, 31.8; HRMS (LSIMS) *m/z* for $C_{37}H_{41}N_3O_4Na$ $[M + Na]^+$ calcd 614.2995, found 614.3002.



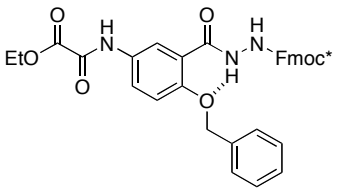
Oxamate ester 7a. To an ice-cooled solution of aniline **6a** (6.9 g, 10.5 mmol) in 80 mL of CH_2Cl_2 was added pyridine (1.4 mL, 16.7 mmol) via a syringe. Ethyl oxalyl chloride (1.3 mL, 1.6 g, 11.6 mmol) was then added via a syringe over 2 min, and the reaction mixture continued stirring at 0 °C. TLC analysis indicated that the reaction was completed in 30 min. The reaction mixture was then diluted with CH_2Cl_2 to a final volume of 250 mL and was washed with satd aq $NaHCO_3$ solution (2 x 250 mL), 5% aq citric acid solution (125 mL), water (250 mL), and satd aq NaCl solution (250 mL). The organic layer was dried over Na_2SO_4 and concentrated by rotary evaporation to give yellowish solid. Column chromatography on silica gel (gradient elution with hexanes/EtOAc from 80:20 to 40:60) afforded 5.5 g (70%) of oxamate ester **7a** as white solid. mp 114–115 °C; IR (nujol, cm^{-1}) 3381, 3222, 1758, 1741, 1708, 1686, 1661, 1546, 1500; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.93 (br s, 1 H), 9.03 (br s, 1 H), 8.24 (d, *J* = 7.1 Hz, 1 H), 8.05 (br s, 1 H), 7.63–7.61 (m, 5 H), 7.46–7.40 (m, 2 H), 7.04 (d, *J* = 9.1 Hz, 1 H), 5.06 (br s, 1 H), 4.48 (d, *J* = 7.3 Hz, 2 H), 4.42 (quartet, *J* = 7.2 Hz, 2 H), 4.23–4.20 (m, 3 H), 3.37–3.35 (m, 2 H), 2.09–2.06 (m, 2 H), 1.42 (t, *J* = 7.2 Hz, 3 H), 1.37 (br s, 27 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.3, 156.4, 155.9, 154.4, 154.1, 150.1, 143.7, 138.8, 131.0, 125.6, 125.1, 124.2, 123.6, 122.1, 119.9, 119.4, 113.2, 79.5, 68.7, 67.5, 64.0, 47.2, 37.7, 35.1, 31.8, 29.8, 28.5, 14.4; HRMS

[7] Bellamy, F. D.; Ou, K. *Tetrahedron Lett.* **1984**, *25*, 839–842.

(LSIMS) *m/z* for $C_{42}H_{54}N_4O_9Na$ [M + Na]$^+$ calcd 781.3788, found 781.3812. Anal. Calcd. for $C_{42}H_{54}N_4O_9$: C, 66.47; H, 7.17; N, 7.38. Found: C, 66.41; H, 7.23; N, 7.27.

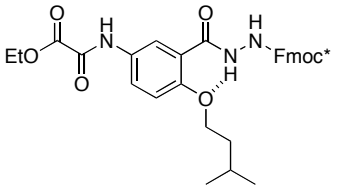


Oxamate ester 7b. To an ice-cooled solution of aniline **6b** (7.1 g, 11.5 mmol) in 150 mL of CH_2Cl_2 was added pyridine (1.2 mL, 15.2 mmol) via a syringe. Ethyl oxalyl chloride (1.4 mL, 1.7 g, 12.5 mmol) was then added via a syringe over 4 min, and the reaction mixture continued stirring at 0 °C. TLC analysis indicated that the reaction was completed in 30 min. Ethanol (0.5 mL) was added, and the reaction mixture was warmed to room temperature. The solvent was removed by rotary evaporation to give 10.3 g yellowish solid. Trituration with 60 mL of acetonitrile afforded 7.7 g (94%) of oxamate ester **7a**, sufficiently pure to be used in the next step. An analytical sample was purified by radial chromatography using hexanes/EtOAc (1:1). mp 213–214 °C (dec); IR (nujol, cm^{-1}) 3360, 1743, 1708, 1677, 1535; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 (br s, 1 H), 9.31 (br s, 1 H), 8.34 (d, *J* = 8.5 Hz, 1 H), 8.23 (d, *J* = 2.7 Hz, 1 H), 7.62 (br s, 4 H), 7.39 (d, *J* = 7.4 Hz, 1 H), 7.26 (br s, 1 H), 6.89 (d, *J* = 9.0 Hz, 1 H), 4.65 (s, 2 H), 4.47–4.40 (m, 4 H), 4.24–4.22 (m, 1 H), 1.52 (s, 9 H), 1.41 (t, *J* = 7.2 Hz, 3 H), 1.35 (s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 164.5, 161.2, 156.7, 154.5, 153.1, 150.1, 144.0, 138.9, 132.0, 125.5, 125.0, 124.8, 122.3, 120.6, 119.4, 113.5, 83.9, 68.7, 66.8, 64.0, 47.3, 35.1, 31.8, 28.3, 14.2; HRMS (LSIMS) *m/z* for $C_{40}H_{49}N_3O_9Na$ [M + Na]$^+$ calcd 738.3367, found 738.3349. Anal. Calcd. for $C_{40}H_{51}N_3O_{10}$: C, 65.47; H, 7.00; N, 5.73. Found: C, 65.29; H, 6.83; N, 5.76.



Oxamate ester 7c. To an ice-cooled solution of aniline **6c** (2.4 g, 4.1 mmol) in 40 mL of CH_2Cl_2 was added pyridine (0.4 mL, 5.0 mmol) via a syringe. Ethyl oxalyl chloride

(0.5 mL, 0.6 g, 4.4 mmol) was then added via a syringe over 5 min. The ice bath was removed, and the reaction mixture continued stirring at room temperature. TLC analysis indicated that the reaction was completed in 15 min. The reaction mixture was then diluted with CH_2Cl_2 and washed with water (twice) and satd aq NaCl solution (once). The organic layer was dried over Na_2SO_4 and was concentrated to give 2.5 g (88%) of crude oxamate ester **7c**, which was used in the next step without further purification. An analytical sample was recrystallized from hexanes/EtOAc (3:1). mp 171–172 °C; IR (nujol, cm^{-1}) 3341, 1742, 1702, 1657, 1548; ^1H NMR (500 MHz, $CDCl_3$) δ 9.68 (br s, 1 H), 9.17 (br s, 1 H), 8.31 (d, *J* = 8.2 Hz, 1 H), 8.16 (d, *J* = 2.8 Hz, 1 H), 7.61–7.58 (m, 4 H), 7.45–7.34 (m, 7 H), 7.24 (br s, 1 H), 7.10 (d, *J* = 9.1 Hz, 1 H), 5.26 (s, 2 H), 4.50–4.39 (m, 4 H), 4.22–4.20 (m, 1 H), 1.43 (t, *J* = 7.2 Hz, 3 H), 1.24 (s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 156.2, 154.4, 154.2, 150.1, 143.84, 143.80, 138.9, 135.3, 131.5, 129.3, 129.0, 127.9, 125.7, 125.0, 124.5, 122.2, 120.1, 119.4, 114.1, 72.1, 68.7, 64.0, 47.2, 35.1, 31.8, 14.2; HRMS (LSIMS) *m/z* for $C_{41}H_{46}N_3O_7$ $[M + H]^+$ calcd 692.3336, found 692.3331. Anal. Calcd. for $C_{41}H_{45}N_3O_7$: C, 71.18; H, 6.56; N, 6.07. Found: C, 70.92; H, 6.62; N, 6.05.

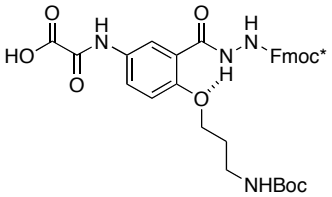


Oxamate ester 7d. To an ice-cooled solution of aniline **6d** (2.6 g, 4.5 mmol) in 35 mL of CH_2Cl_2 was added pyridine (0.4 mL, 5.0 mmol) via a syringe. Ethyl oxalyl chloride (0.6 mL, 0.7 g, 5.1 mmol) was then added via a syringe over 5 min, and the reaction continued stirring at 0 °C. TLC analysis indicated that the reaction was completed in 1 h. The reaction mixture was then diluted with CH_2Cl_2 and washed with water (twice) and satd aq NaCl solution (once). The organic layer was dried over Na_2SO_4 and was concentrated to afford 3.0 g (99%) of crude oxamate ester **7d**, which was used in the next step without further purification. An analytical sample was recrystallized from hexanes/EtOAc (9:1). mp 188–189 °C; IR (nujol, cm^{-1}) 3393, 3332, 1768, 1739, 1697, 1668, 1641,

1543; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (br s, 1 H), 9.28 (br s, 1 H), 8.32 (d, *J* = 8.2 Hz, 1 H), 8.17 (d, *J* = 2.7 Hz, 1 H), 7.62–7.59 (m, 5 H), 7.41–7.39 (m, 2 H), 7.04 (d, *J* = 9.1 Hz, 1 H), 4.48 (d, *J* = 7.2 Hz, 2 H), 4.41 (quartet, *J* = 7.2 Hz, 2 H), 4.22–4.20 (m, 3 H), 1.84–1.82 (m, 3 H), 1.40 (t, *J* = 7.2 Hz, 3 H), 1.35 (s, 18 H), 0.98 (d, *J* = 5.3 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 161.5, 155.9, 154.5, 154.4, 150.1, 143.8, 138.8, 131.2, 125.8, 124.9, 124.5, 122.1, 119.6, 119.4, 113.2, 68.6, 63.9, 47.2, 37.8, 35.0, 31.7, 28.5, 25.5, 22.7, 14.1; HRMS (LSIMS) *m/z* for $C_{39}H_{50}N_3O_7$ $[M + H]^+$ calcd 672.3649, found 672.3637. Anal. Calcd. for $C_{39}H_{49}N_3O_7$: C, 69.72; H, 7.35; N, 6.25. Found: C, 69.59; H, 7.39; N, 6.32.

General procedure for saponification of oxamate esters 7a–7d.

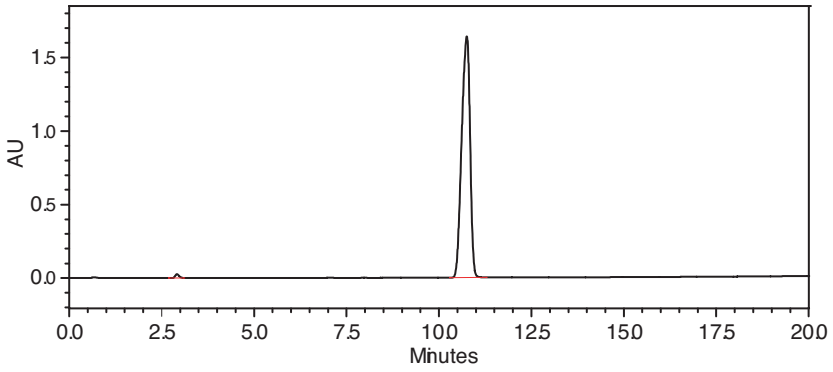
A 1 M aq NaOH solution was added to a solution of oxamate ester **7** (**a**, **b**, **c**, or **d**) in 4:1 THF/water mixture. The reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture was passed through a glass column fitted with a glass filter and packed with Amberlite 120-IR ino-exchange resin. The resin was then washed with fresh THF/water mixture, all THF/water fractions were combined, and THF was removed under vacuum to yield product **1** as a free acid.



Acid 1a. Using the general procedure described above, oxamate ester **7a** (5.5 g, 7.3 mmol) was saponified with 1 M aq NaOH solution (9.0 mL, 9.0 mmol) in 100 mL of THF/H_2O (4:1) solution. After 1 h, TLC analysis indicated the presence of starting material. To complete the reaction, 5.0 mL of 1 M aq NaOH solution (5.0 mmol) was added. TLC analysis indicated disappearance of the starting material in 20 min. Ion-exchange and removal of solvent resulted in precipitation of a white solid. The solid was dissolved in THF (100 mL) and concentrated under vacuum (x 3) to give 5.4 g (100%) of acid **1a**. The acid was of satisfactory purity for use in peptide synthesis. An analytical sample was purified either by recrystallization from *i*-PrOH/H_2O or by RP-HPLC. For

purification by RP-HPLC, 100 mg of **1a** was dissolved in 5 mL of acetonitrile/water (4:1) and was subjected to chromatography (gradient elution with acetonitrile/water 75:25 to 100:0, acetonitrile contained 0.25% AcOH). mp 224–225 °C; IR (nujol, cm^{-1}) 3342, 3240, 1710, 1693, 1666, 1530, 1500; ^1H NMR (500 MHz, CD_3SOCD_3) major rotamer: δ 14.16 (br s, 1 H), 10.78 (s, 1 H), 9.79 (s, 1 H), 9.62 (s, 1 H), 8.12 (s, 1 H), 7.86 (d, *J* = 8.5 Hz, 1 H), 7.76 (s, 2 H), 7.74 (d, *J* = 8.0 Hz, 2 H), 7.43 (d, *J* = 8.0 Hz, 2 H), 7.15 (d, *J* = 8.9 Hz, 1 H), 6.91 (br s, 1 H), 4.35 (d, *J* = 7.0 Hz, 2 H), 4.24 (t, *J* = 7.0 Hz, 1 H), 4.10 (br s, 2 H), 3.13 (appar q, *J* = 5.6 Hz, 2 H), 1.90-1.80 (m, 2 H), 1.36 (s, 18 H), 1.35 (s, 9 H); minor rotamer (partial data): δ 9.89, 9.74, 9.11, 8.23, 7.70–7.55, 7.37, 6.52, 4.31, 4.15, 1.23; ^{13}C NMR (125 MHz, CD_3SOCD_3) major rotamer: δ 165.2, 162.2, 156.8, 156.1, 155.8, 152.9, 149.5, 143.8, 138.1, 130.8, 124.6, 124.4, 122.5, 122.1, 119.3, 113.3, 77.6, 66.8, 65.9, 46.6, 36.3, 34.7, 31.5, 28.9, 28.2; minor rotamer (partial data): δ 31.3; HRMS (LSIMS) *m/z* for $C_{40}H_{50}N_4O_9Na$ $[M + Na]^+$ calcd 753.3475, found 753.3466. Anal. Calcd. for $C_{40}H_{50}N_4O_9$: C, 65.74; H, 6.90; N, 7.67; calcd. for $C_{40}H_{52}N_4O_{10}$: C, 64.16; H, 7.00; N, 7.48. Found: C, 64.17; H, 7.06; N, 7.42.

Analytical HPLC trace of acid **1a**
Zorbax 80sb column; Flow = 1 mL/min; λ = 254 nm
Gradient: solvent A/solvent B 50:50 to 0:100 over 20 min
Solvent A = water, 0.1% TFA; Solvent B = acetonitrile, 0.1% TFA



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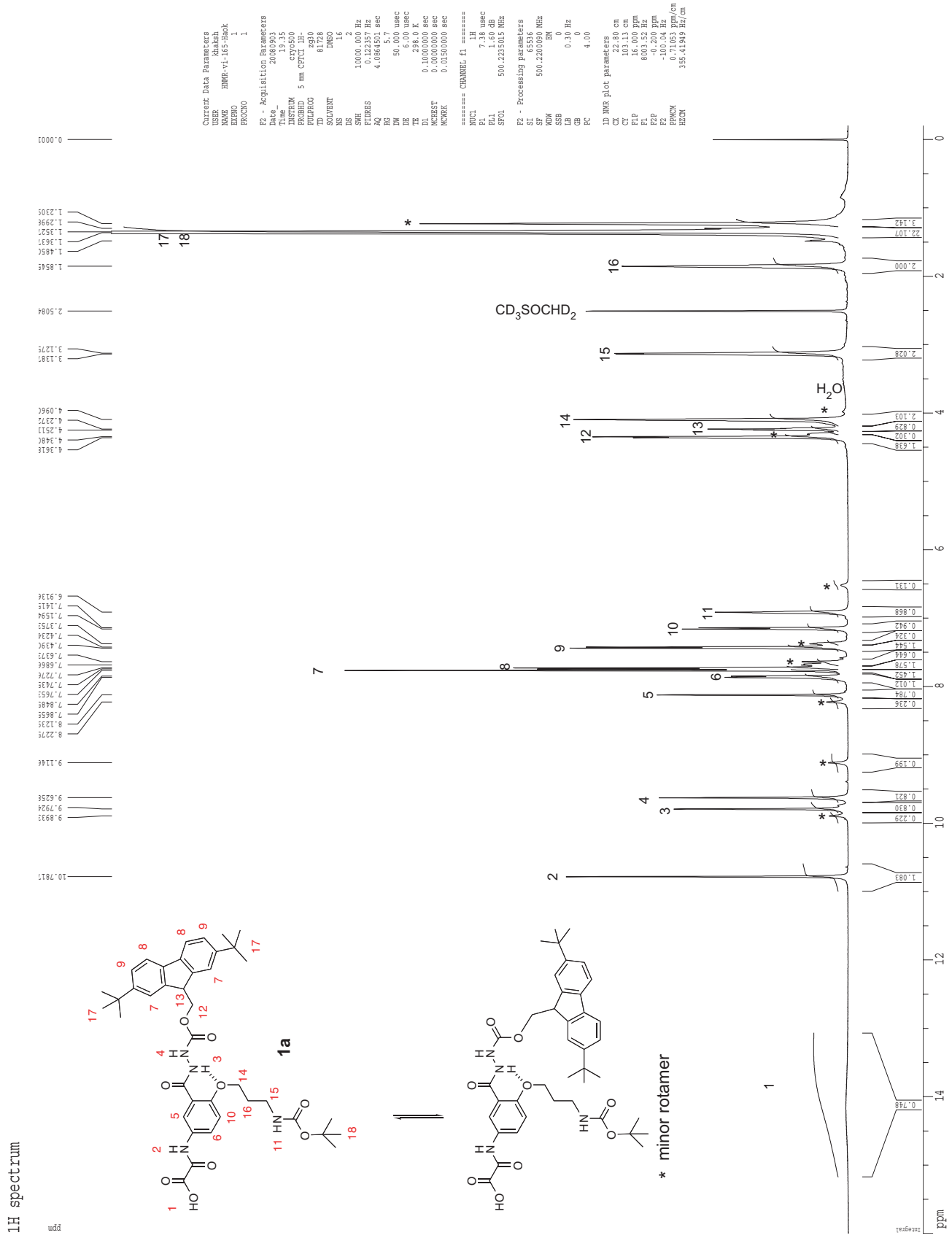
Totals	26024915	100.00	1666486	100.00


1H spectrum
1a
* minor rotamer
CD3SOCHD2
H2O


13C spectrum with 1H decoupling
ppm
28.23
28.90
31.29
31.46
34.69
36.34
39.01
39.17
39.34
39.51
39.67
39.76
39.84
40.01
46.59
65.92
66.79
77.57
113.29
119.31
122.13
122.47
124.41
124.59
130.84
138.11
143.79
149.54
152.87
155.79
156.13
156.75
162.16
165.17
1a
Current Data Parameters
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NAME HNMR-vi-165-Hack
EXPNO 102
PROCNO 1
F2 - Acquisition Parameters
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Time 19.45
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PROBHD 5 mm CPTCI 1H-
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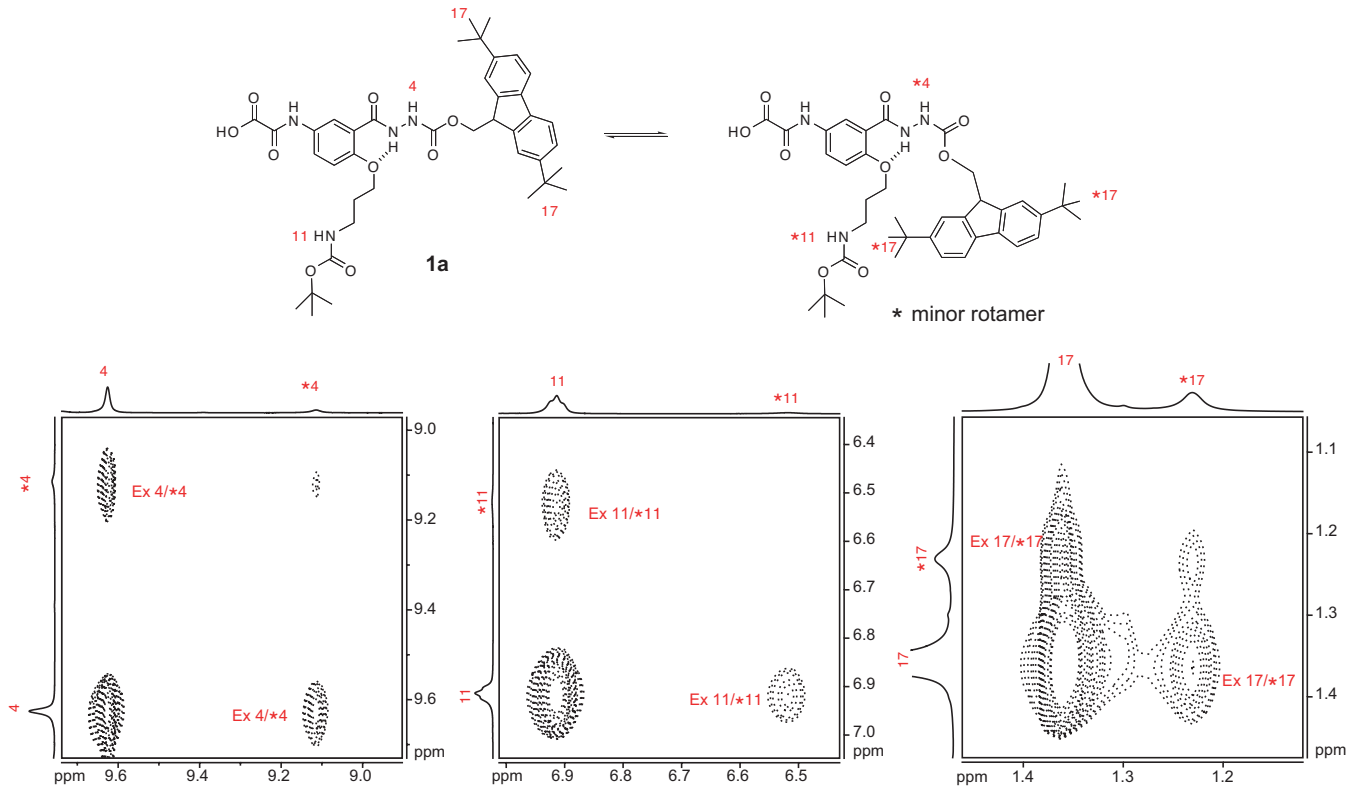
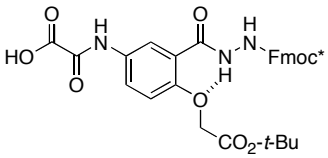
TD 65418
SOLVENT CDCl3
NS 256
DS 4
SWH 30303.031 Hz
FIDRES 0.463222 Hz
AQ 1.0794470 sec
RG 18390.4
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 14.75 usec
PL1 -1.00 dB
SFO1 125.7942548 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.80 dB
SFO2 500.2225011 MHz
F2 - Processing parameters
SI 65536
SF 125.7804777 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 26.50 cm
F1P 200.000 ppm
F1 25156.10 Hz
F2P -5.000 ppm
F2 -628.90 Hz
PPMCM 8.99123 ppm/cm
HZCM 1130.92102 Hz/cm
ppm
0
20
40
60
80
100
120
140
160
180

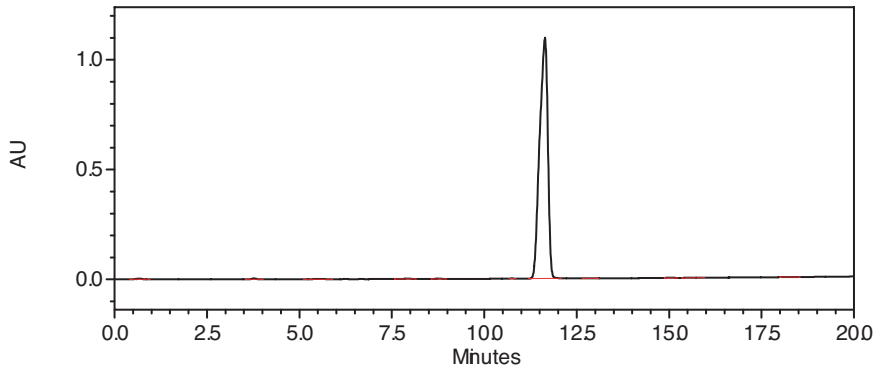
^{1}H EXSY studies of acid 1a. An EXSY experiment confirms the presence of a minor rotamer in equilibrium with the major rotamer in acids **1a**–**1d**. The 500 MHz EXSY study was performed at 298 K on a CD_3SOCD_3 solution of acid **1a**, as a representative of these compounds. The EXSY spectrum was acquired using the Tr-ROESY pulse sequence and 200-ms spin-lock mixing time. The data were recorded with 2048 data points in the f_2 domain and 128 data points in the f_1 domain and processed by zero-filling to a matrix of 1024 x 1024 real points. The EXSY cross-peaks have the same phase as the diagonal peaks, while the ROESY cross-peaks have the opposite phase.





Acid 1b. Using the general procedure described above, the oxamate ester **7b** (7.5 g, 10.5 mmol) was saponified with 1 M aq NaOH solution (10.5 mL, 10.5 mmol) in 100 mL of THF/H_2O (4:1) solution. After 1 h, TLC analysis indicated the presence of starting material. To complete the reaction, 10.0 mL of 1 M aq NaOH solution (10.0 mmol) was added. TLC analysis indicated disappearance of the starting material in 5 min. Ion-exchange and removal of solvent resulted in the precipitation of a white solid. The solid was dissolved in THF (100 mL) and concentrated under vacuum (x 2) to give 6.5 g (90%) of acid **1b**. The acid was of satisfactory purity for use in peptide synthesis. An analytical sample was purified either by recrystallization from *i*-PrOH/H_2O or by RP-HPLC. For purification by RP-HPLC, 100 mg of **1b** was dissolved in 7.5 mL of acetonitrile/water (4:1) and was subjected to chromatography by RP-HPLC (gradient elution with acetonitrile/water (75:25 to 100:0, acetonitrile contained 0.25% AcOH). mp 133–134 °C; IR (nujol, cm^{-1}) 3371, 2724, 1736, 1692, 1666, 1548; ^{1}H NMR (500 MHz, CD_3SOCD_3) major rotamer: δ 14.11 (br s, 1 H), 10.83 (s, 1 H), 10.00 (s, 1 H), 9.64 (s, 1 H), 8.36 (d, *J* = 2.0 Hz, 1 H), 7.88 (dd, *J* = 9.0, 2.0 Hz, 1 H), 7.77 (s, 2 H), 7.74 (d, *J* = 8.0 Hz, 2 H), 7.43 (d, *J* = 8.2 Hz, 1 H), 7.13 (d, *J* = 9.0 Hz, 1 H), 4.85 (s, 2 H), 4.37 (d, *J* = 7.0 Hz, 2 H), 4.24 (t, *J* = 7.2 Hz, 1 H), 1.45 (s, 9 H), 1.36 (s, 18 H); minor rotamer (partial data): δ 10.19, 9.19, 8.42, 7.70–7.56, 7.39-7.32, 7.17, 4.31, 4.10, 1.23; ^{13}C NMR (125 MHz, CD_3SOCD_3) major rotamer: δ 167.7, 164.3, 162.1, 156.8, 156.3, 152.2, 149.5, 143.8, 138.1, 131.7, 125.2, 124.6, 123.3, 122.1, 120.7, 119.3, 113.9, 82.2, 66.8, 66.1, 45.6, 34.7, 31.5, 27.7; minor rotamer (partial data): δ 31.3; HRMS (LSIMS) *m/z* for $C_{38}H_{45}N_3O_9Na$ $[M + Na]^+$ calcd 710.3054, found 710.3072. Anal. Calcd. for $C_{38}H_{45}N_3O_9$: C, 66.36; H, 6.59; N, 6.11; calcd. for $C_{38}H_{47}N_3O_{10}$: C, 64.67; H, 6.71; N, 5.95; Found: C, 64.97; H, 6.85; N, 5.67.

Analytical HPLC trace of acid **1b**
Zorbax 80sb column; Flow = 1 mL/min; λ = 254 nm
Gradient: solvent A/solvent B 50:50 to 0:100 over 20 min
Solvent A = water, 0.1% TFA; Solvent B = acetonitrile, 0.1% TFA



Time	Area	Area %	Height	Height %
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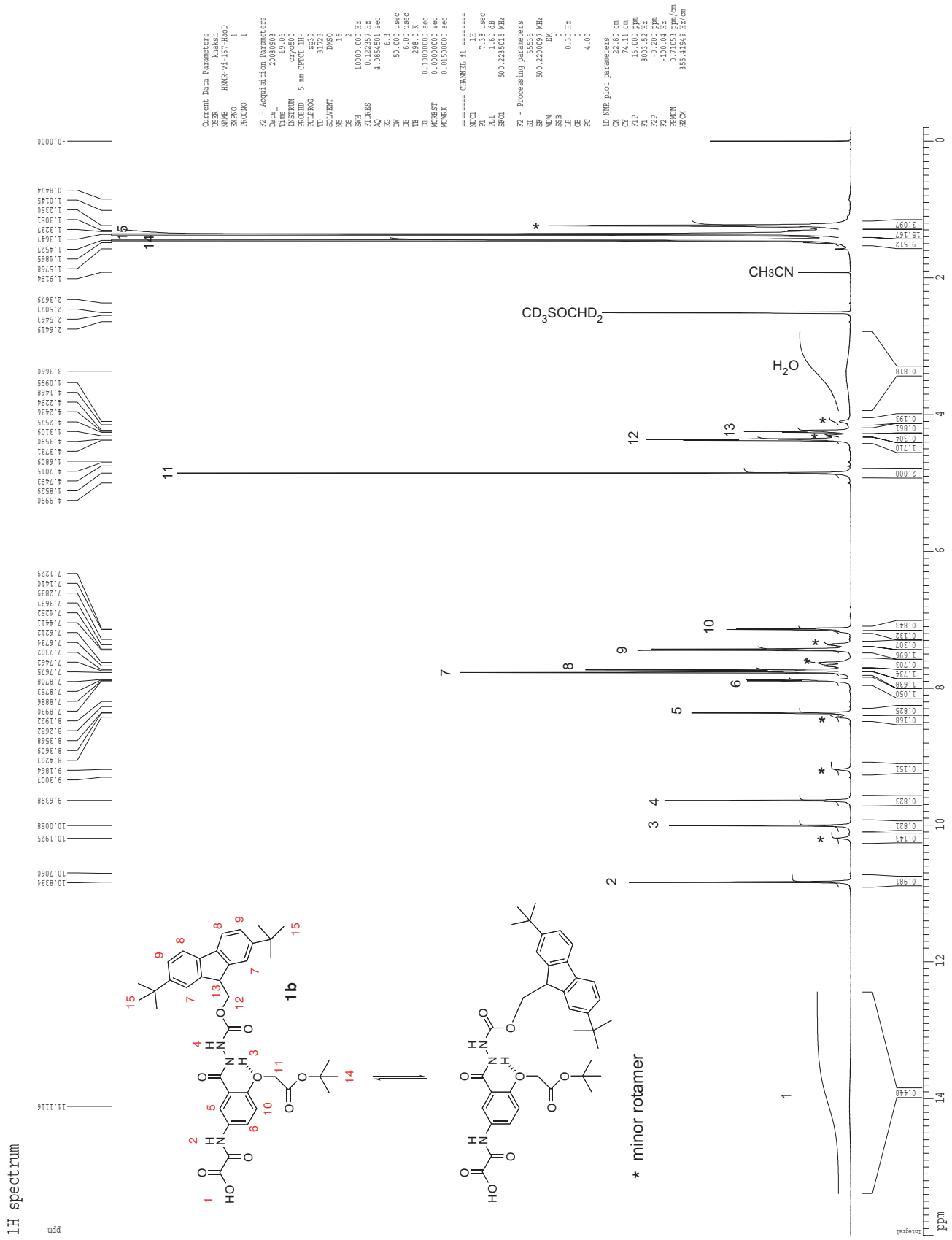
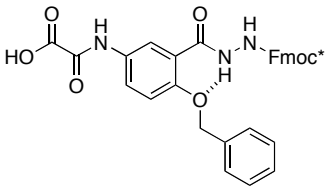
5.600	23039	0.14	1657	0.15
7.942	19998	0.12	1789	0.16
8.767	15282	0.09	1556	0.14
10.753	2663	0.02	440	0.04
11.642	16763150	99.07	1097380	98.64
12.975	2373	0.01	183	0.02
15.073	6512	0.04	643	0.06
15.812	4247	0.03	220	0.02
18.427	4294	0.03	223	0.02

Totals	16920695	100.00	1112506	100.00

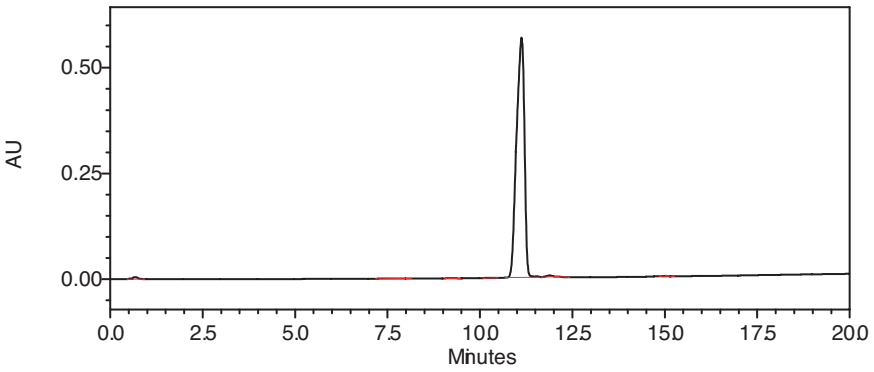

1H spectrum
1b
* minor rotamer
CH3CN
CD3SOCHD2
H2O


13C spectrum with 1H decoupling
ppm
1b



Acid 1c. Using the general procedure described above, the oxamate ester **7c** (2.5 g, 3.6 mmol) was saponified with 1 M aq NaOH solution (5.2 mL, 5.2 mmol) in 50 mL of THF/H_2O (4:1) solution. TLC analysis indicated that the reaction was completed in 10 min. Ion-exchange and removal of THF resulted in the precipitation of acid **1c** (2.4 g, 100%) as yellowish crystals. An analytical sample was purified either by recrystallization from *i*-PrOH/H_2O or by RP-HPLC. For purification by RP-HPLC, 100 mg of **1c** was dissolved in 5 mL of acetonitrile/water (4:1) and was subjected to chromatography by RP-HPLC (gradient elution with acetonitrile/water (75:25 to 100:0, acetonitrile contained 0.25% AcOH). mp 146–147 °C; IR (nujol, cm^{-1}) 3332, 2724, 1710, 1657, 1612, 1548; ^{1}H NMR (500 MHz, CD_3SOCD_3) major rotamer: δ 14.17 (br s, 1 H), 10.78 (s, 1 H), 9.91 (s, 1 H), 9.63 (s, 1 H), 8.12 (d, *J* = 1.7 Hz, 1 H), 7.80 (dd, *J* = 8.8, 1.7 Hz, 1 H), 7.76 (s, 2 H), 7.74 (d, *J* = 8.0 Hz, 2 H), 7.52 (d, *J* = 7.0 Hz, 2 H), 7.43 (d, *J* = 8.0 Hz, 2 H), 7.37 (t, *J* = 7.5 Hz, 2 H), 7.30 (t, *J* = 7.0 Hz, 1 H), 7.20 (d, *J* = 9.0 Hz, 1 H), 5.26 (s, 2 H), 4.35 (d, *J* = 7.5 Hz, 2 H), 4.23 (t, *J* = 7.0 Hz, 1 H), 1.35 (s, 18 H); minor rotamer (partial data): δ 9.99, 9.13, 8.18, 8.85, 7.70–7.57, 7.27–7.23, 4.27, 4.03, 1.22; ^{13}C NMR (125 MHz, CD_3SOCD_3) major rotamer: δ 165.2, 162.1, 156.8, 156.2, 152.5, 149.5, 143.8, 138.1, 136.7, 131.0, 128.4, 127.8, 127.4, 124.6, 124.2, 122.9, 122.4, 122.1, 119.3, 114.0, 70.0, 66.8, 46.6, 34.7; minor rotamer (partial data): δ 31.3; HRMS (LSIMS) *m/z* for $C_{39}H_{41}N_3O_7Na$ $[M + Na]^+$ calcd 686.2842, found 686.2820. Anal. Calcd. for $C_{39}H_{41}N_3O_7$: C, 70.57; H, 6.23; N, 6.33; calcd. for $C_{39}H_{43}N_3O_8$: C, 68.71; H, 6.36; N, 6.16. Found: C, 68.74; H, 6.42; N, 6.13.

Analytical HPLC trace of acid **1c**
Zorbax 80sb column; Flow = 1 mL/min; λ = 254 nm
Gradient: solvent A/solvent B 50:50 to 0:100 over 20 min
Solvent A = water, 0.1% TFA; Solvent B = acetonitrile, 0.1% TFA



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10.278	5929	0.07	487	0.08
11.127	8430715	98.58	567379	98.12
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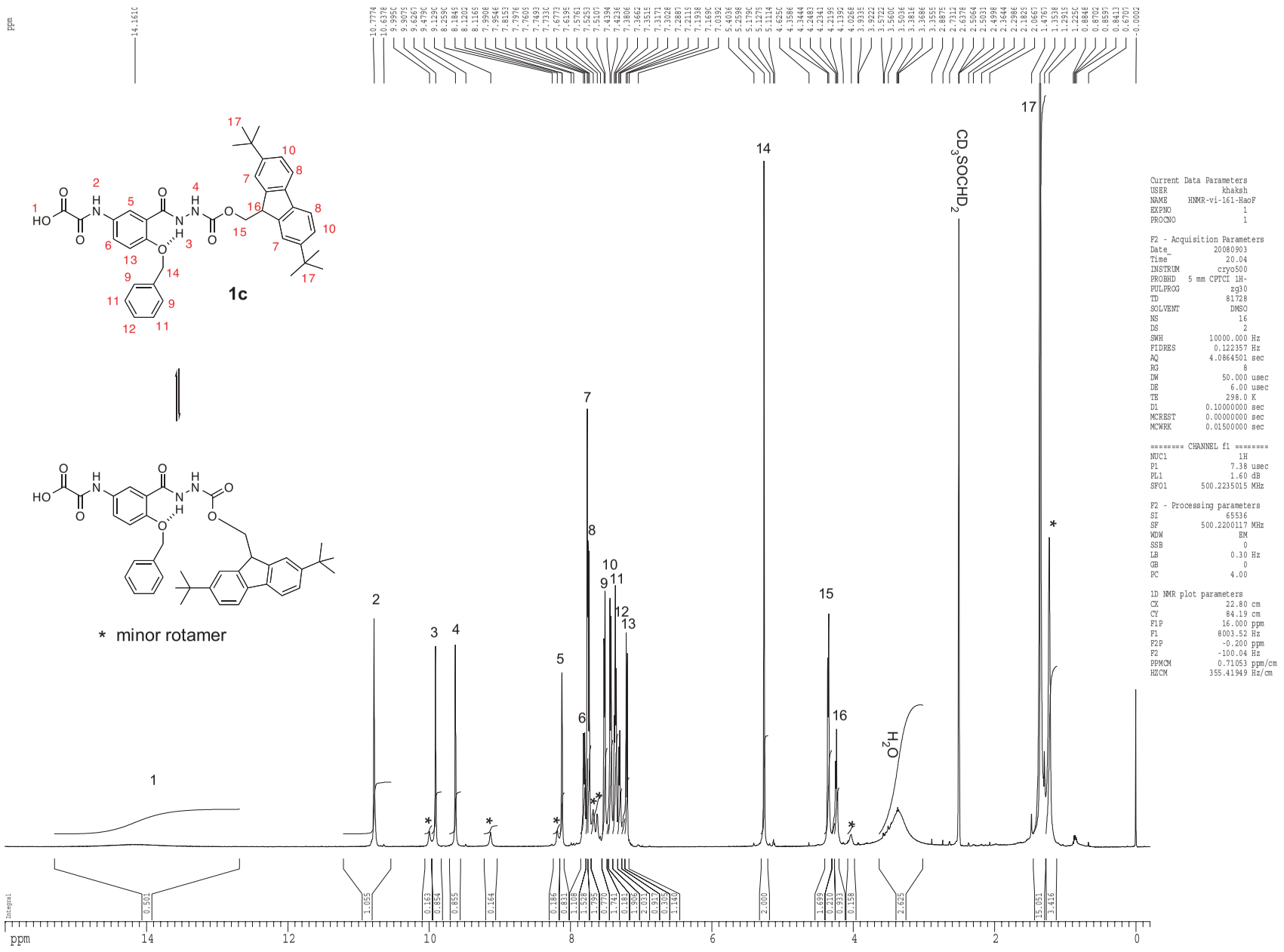
Totals	8552019	100.00	578229	100.00

1H spectrum


1c
* minor rotamer
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H2O
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NAME HNMR-vi-161-HaoF
EXPNO 1
PROCNO 1
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Time 20.04
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PROBHD 5 mm CPTCI 1H-
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TD 81728
SOLVENT DMSO
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DS 2
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RG 8
DW 50.000 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
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PL1 1.60 dB
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F2 - Processing parameters
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SF 500.2200117 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
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CY 84.19 cm
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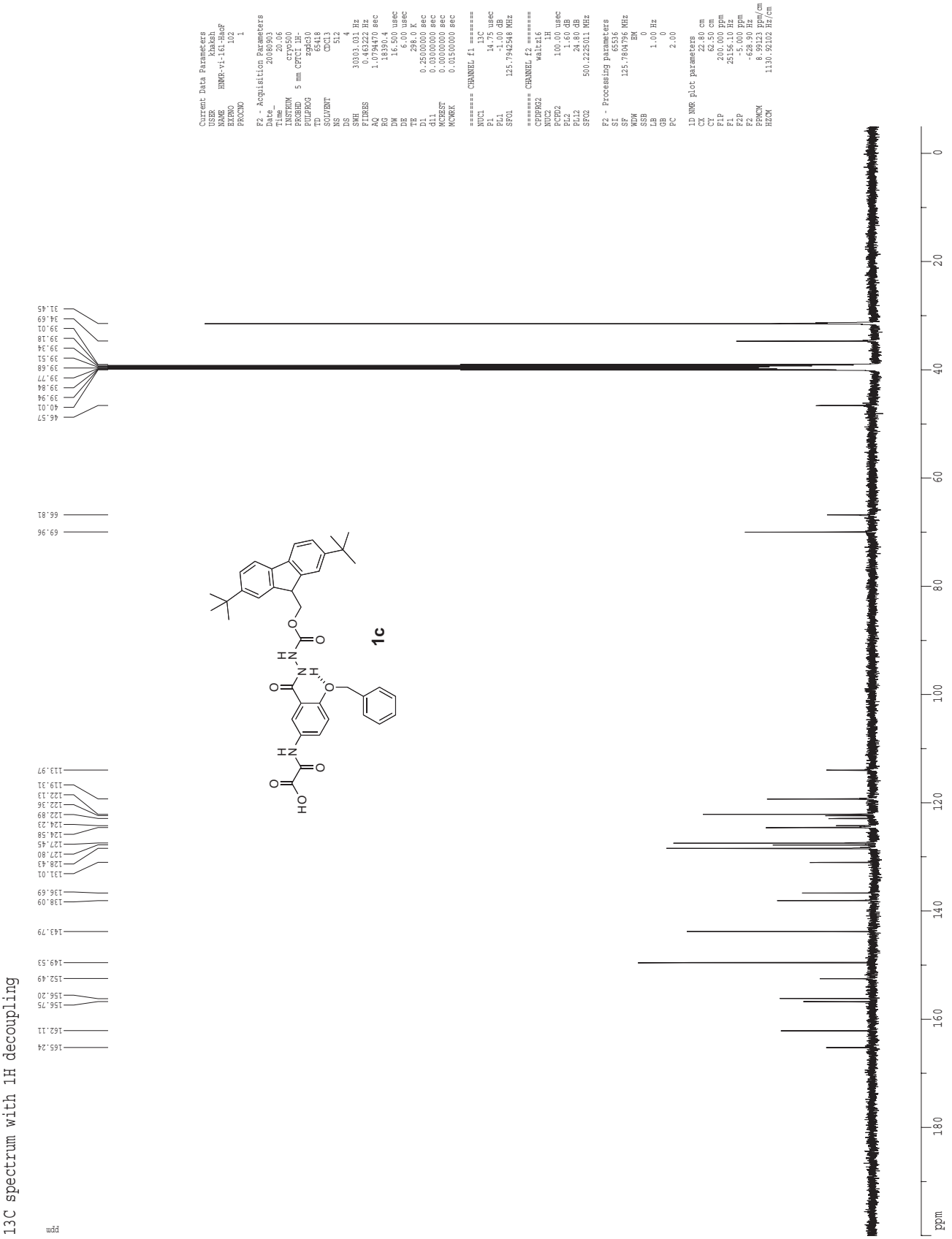
F1 8003.52 Hz
F2P -0.200 ppm
F2 -100.04 Hz
PPMCM 0.71053 ppm/cm
HZCM 355.41949 Hz/cm


13C spectrum with 1H decoupling
ppm
Current Data Parameters
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PROCNO 1
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TD 65418
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FIDRES 0.463222 Hz
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DE 6.00 usec
TE 298.0 K
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d11 0.03000000 sec
MCREST 0.00000000 sec
MCWREK 0.01500000 sec
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PL1 -1.00 dB
SFO1 125.7942548 MHz
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PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.80 dB
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F2 - Processing parameters
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GB 0
PC 2.00
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F2P -5.000 ppm
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HZCM 1130.92102 Hz/cm
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39.01
39.18
39.34
39.51
39.68
39.77
39.84
39.94
40.01
46.57
66.81
69.96
113.97
119.31
122.13
122.36
122.89
124.23
124.58
127.45
127.80
128.43
131.01
136.69
138.09
143.79
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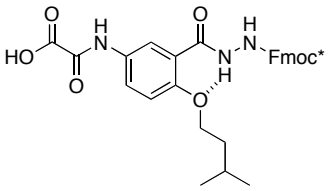
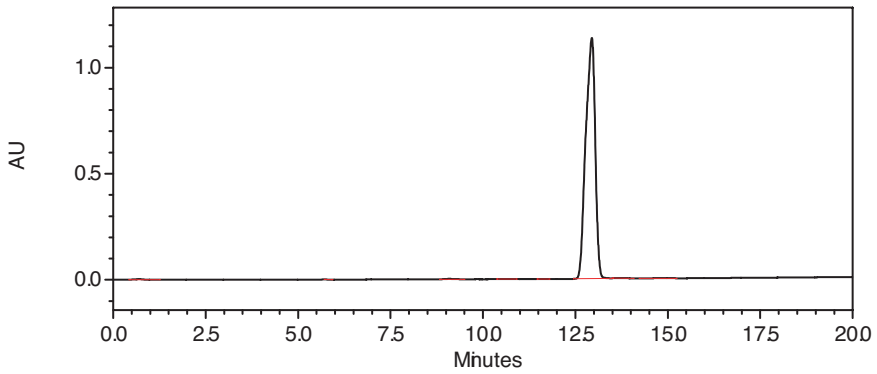
180
ppm



Acid 1d. Using the general procedure described above, the oxamate ester **7d** (2.1 g, 3.1 mmol) was saponified with 1 M aq NaOH solution (5.1 mL, 5.1 mmol) in 50 mL of THF/H_2O (4:1) solution. TLC analysis indicated that the reaction was completed in 10 min. Ion-exchange and removal of THF resulted in the precipitation of acid **1d** (2.0 g, 100%) as white crystals. An analytical sample was purified either by recrystallization from *i*-PrOH/H_2O or by RP-HPLC. For purification by RP-HPLC, 100 mg of **1d** was dissolved in 5 mL of acetonitrile/water (4:1) and was subjected to chromatography by RP-HPLC (gradient elution with acetonitrile/water (75:25 to 100:0, acetonitrile contained 0.25% AcOH). mp 208–210 °C; IR (nujol, cm^{-1}) 3357, 1724, 1690, 1677, 1664, 1649, 1529; ^{1}H NMR (500 MHz, CD_3SOCD_3) major rotamer: δ 14.17 (br s, 1 H), 10.80 (s, 1 H), 9.70 (s, 1 H), 9.65 (s, 1 H), 8.19 (br s, 1 H), 7.87 (dd, *J* = 9.0, 1.5 Hz, 1 H), 7.76 (s, 2 H), 7.73 (d, *J* = 8.0 Hz, 2 H), 7.43 (d, *J* = 8.0 Hz, 2 H), 7.19 (d, *J* = 9.0 Hz, 1 H), 4.37 (d, *J* = 7.0 Hz, 2 H), 4.25 (t, *J* = 6.8 Hz, 1 H), 4.12 (t, *J* = 6.5 Hz, 2 H), 1.84–1.71 (m, 1 H), 1.66 (app q, *J* = 6.5 Hz, 2 H), 1.36 (s, 18 H), 0.92 (d, *J* = 6.5 Hz, 6 H); minor rotamer (partial data): δ 9.77, 9.14, 8.23, 7.70–7.53, 7.36, 3.98, 1.24, 0.83; ^{13}C NMR (125 MHz, CD_3SOCD_3) major rotamer: δ 164.9, 162.2, 156.7, 156.1, 153.2, 149.5, 143.8, 138.1, 130.8, 124.7, 124.6, 122.6, 122.1, 121.9, 119.3, 113.5, 67.4, 66.7, 46.6, 37.2, 34.7, 31.4, 24.6, 22.5; minor rotamer (partial data): δ 31.3; HRMS (LSIMS) *m/z* for $C_{37}H_{45}N_3O_7Na$ $[M + Na]^+$ calcd 666.3155, found 666.3161.

Analytical HPLC trace of acid **1d**
Zorbax 80sb column; Flow = 1 mL/min; λ = 254 nm
Gradient: solvent A/solvent B 50:50 to 0:100 over 20 min
Solvent A = water, 0.1% TFA; Solvent B = acetonitrile, 0.1% TFA



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10.743	8900	0.04	608	0.05
11.262	9545	0.05	615	0.05
11.647	2417	0.01	246	0.02
12.943	20088376	99.02	1134823	99.06
13.693	29821	0.15	1586	0.14
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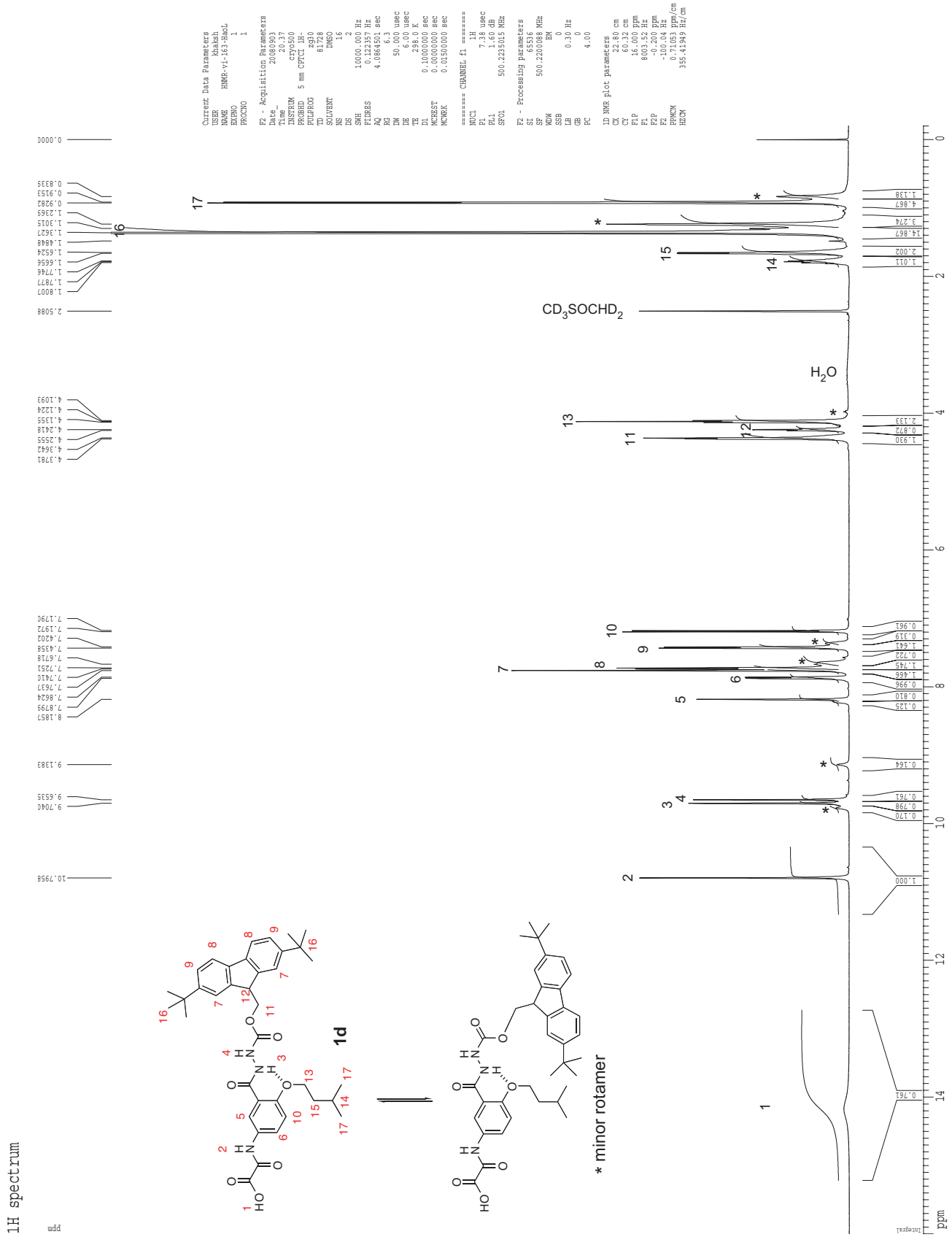
Totals	20286555	100.00	1145554	100.00


1H spectrum
1d
* minor rotamer
CD3SOCHD2
H2O
ppm


13C spectrum with 1H decoupling
ppm
1d
Current Data Parameters
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NAME NMR-vi-163-HaG
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PROCNO 1
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FIDRES 0.463222 Hz
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DE 6.00 usec
TE 298.0 K
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d11 0.03000000 sec
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GB 0
PC 2.00
1D NMR plot parameters
CX 22.80 cm
CY 27.72 cm
F1P 200.000 ppm
F1 25156.10 Hz
F2P -5.000 ppm
F2 -628.90 Hz
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