13.2 mL, 13.2 mmol), and Me_2NH (5–6 equiv) was obtained a brown residue which was purified by flash column chromatography on SiO_2 gel (2.5% MeOH/$CHCl_3$) to give the desired product. The product was recrystallized from ethyl acetate/hexane to give light yellow cubic crystals.

Yield: 1.20 g (40%).

R_f 0.39 (5% MeOH/$CHCl_3$).

mp 104°–106° C.

^{1}H NMR (DMSO-d_6) δ 1.91 (s, 3H), 2.11 (s, 6H), 4.22 (dd, J=5.2, 14.7 Hz, 1H), 4.34 (dd, J=6.1, 14.7 Hz, 1H), 5.11 (d, J=8.3 Hz, 1H), 7.23–7.31 (m, 5H), 8.18 (d, J=8.3 Hz, 1H), 8.55 (br s, 1H).

^{13}C NMR (DMSO-d_6) 22.43, 40.33 (2 C), 42.28, 69.42, 126.73, 127.27 (2 C), 128.21(2 C), 139.49, 168.49, 170.31 ppm.

IR (KBr) 3280, 1670 (br), 1500 (br), 1460, 760, 700 cm^{-1}.

Mass spectrum 250 (M^++1).

Elemental analysis Calculated for $C_{13}H_{19}N_3O_2$ 62.63% C; 7.68% H; 16.85% N. Found 62.82% C; 7.66% H; 16.69% N.

EXAMPLE 55

Synthesis of 2-Acetamido-N-benzyl-2-(N-hydroxyamino) acetamide.

Using 2-acetamido-N-benzyl-2-ethoxyacetamide (2.00 g, 8.0 mmol), BBr_3 (1M in CH_2Cl_2, 8.8 mL, 8.8 mmol), and anhydrous NH_2OH (5–6 equiv) gave an oily residue. The residue was separated into three components by flash chromatography on SiO_2 gel (7.5% MeOH/$CHCl_3$).

2-Acetamido-N-benzyl-2-(N-hydroxyamino)acetamide.

Yield: 0.14 g (7%).

R_f 0.30 (8% MeOH/$CHCl_3$).

mp 144°–146° C. (dec.) (recrystallized from EtOH)

^{1}H NMR (DMSO-d_6) δ 1.88 (s, 3H), 4.31 (d, J=5.7 Hz, 2H), 5.08 (dd, J=4.4, 8.1 Hz, 1H), 5.94 (dd, J=2.8, 4.4 Hz, 1H), 7.19–7.35 (m, 5H), 7.5 (d, J=2.8 Hz, 1H), 8.26 (d, J=8.1 Hz, 1H), 8.42 (t, J=5.7 Hz, 1H).

^{13}C NMR (DMSO-d_6) 22.69, 42.25, 67.86, 126.69, 127.14 (2 C), 128.18 (2 C), 139.08, 168.53, 169.67 ppm.

IR (KBr) 3320 (br), 1660 (br), 1540 (br), 1460, 750, 700 cm^{-1}.

Mass spectrum (FD) 238 (M^++1).

Elemental analysis Calculated for $C_{11}H_{15}N_3O_3$ 55.69% C; 6.37% H; 17.71% N. Found 55.86% C; 6.37% H; 17.38% N.

Dimer A.

Yield: 0.05 g (3%).

R_f 0.27 (8% MeOH/$CHCl_3$).

mp 177°–179° C. (recrystallized from EtOH).

^{1}H NMR (DMSO-d_6) δ 1.82 (s, 6H), 4.25–4.34 (m, 4H), 5.21 (d, J=9.3 Hz, 2H) 7.20–73.3 (m, 10H), 8.16 (d, J=9.3 Hz, 2H), 8.26 (t, J=5.8 Hz, 2H), 8.51 (s, 1H).

^{13}C NMR (DMSO-d_6) 22.54 (2 C), 42.30 (2 C), 67.55 (2 C), 126.63 (2 C), 127.13 (4 C), 128.11 (4 C), 139.02 (2 C), 168.24 (2 C), 169.33 (2 C) ppm.

IR (KBr) 3240 (br), 1640 (br), 1510 (br), 1450, 690 cm^{-1}.

Mass spectrum (FD) 442 (M^++1).

Elemental analysis Calculated for $C_{22}H_{27}N_5O_5$ 59.85% C; 6.16% H; 15.86% N. Found 59.56% C; 6.08% H; 15.64% N.

Dimer B.

Yield: 0.10 g (6%).

R_f 0.18 (8% MeOH/$CHCl_3$).

mp 184°–186° C. (recrystallized from MeOH).

^{1}H NMR (DMSO-d_6) δ 1.87 (6H), 4.20 (dd, J=5.3, 15.3 Hz, 2H), 4.44 (dd, J=6.2, 15.3 Hz, 2H), 5.28 (d, J=9.0 Hz, 2H), 7.15–7.31 (m, 10H), 8.00 (d, J=9.0 Hz, 2H), 8.39 (dd, J=5.3, 6.2 Hz, 2H), 8.51 (s, 1H).

^{13}C NMR (DMSO-d_6) 22.50 (2 C), 42.58 (2 C), 69.98 (2 C), 126.73 (2 C), 127.23 (4 C), 128.22 (4 C), 139.08 (2 C), 167.60 (2 C), 169.57 (2 C) ppm.

IR (KBr) 3300 (br), 1660 (br), 1530 (br), 1450, 740, 700 cm^{-1}.

Mass spectrum (FD) 442 (M^++1).

Elemental analysis Calculated for $C_{22}H_{27}N_5O_5$ 59.85% C; 6.16% H; 15.86% N. Found 60.09% C; 5.93% H; 15.76% N.

EXAMPLE 56

Improved Synthesis of 2-Acetamido-N-benzyl-2-(N-hydroxyamino)acetamide.

2-Acetamido-N-benzyl-2-bromoacetamide (prepared from 2-acetamido-N-benzyl-2-ethoxyacetamide (3.00 g, 12.0 mmol) and BBr_3 (1M in CH_2Cl_2, 17.2 mL, 17.2 mmol)) was dissolved in THF (250 mL), cooled (–10° C.), and then added dropwise (30 min) to a suspension of NH_2OH (5–6 equiv) in THF (50 mL) at –10° C. The reaction mixture was stirred (30 min) at this temperature and then allowed to warm to room temperature (1 h). The insoluble materials were filtered and the filtrate was concentrated in vacuo. The residue was separated into two components by flash column chromatography on SiO_2 gel (7.5% MeOH/$CHCl_3$).

2-Acetamido-N-benzyl-2-(N-hydroxyamino)acetamide.

Yield: 0.66 g (23%).

mp 144°–146° C. (dec.) (recrystallized from EtOH).

Dimer B.

Yield: 0.10 g (5%).

mp 184°–186° C. (recrystallized from MeOH).

Dimer A was not observed under these conditions.

EXAMPLE 57

Synthesis of 2-Acetamido-N-benzyl-2-(N^2-phenylhydrazino)acetamide.

Using 2-acetamido-N-benzyl-2-ethoxyacetamide (2.00 g, 8.0 mmol), BBr_3 (1M in CH_2Cl_2, 10.0 mL, 10.0 mmol), and phenylhydrazine (2.60 g, 24.0 mmol) gave a pale yellow oily residue which was purified by flash column chromatography on SiO_2 gel (2% MeOH/$CHCl_3$) to give the desired product. The product was recrystallized from chloroform/hexane as a light yellow solid.

Yield: 0.75 g (29%).

R_f 0.26 (2% MeOH/$CHCl_3$).

mp 132°–134° C.

^{1}H NMR (DMSO-d_6) δ 1.89 (s, 3H), 4.28 (d, J=5.8 Hz, 2H), 4.89 (d, J=5.2 Hz, 1H), 5.09 (dd, J=5.2, 7.4 Hz, 1H), 6.61 (t, J=7.4 Hz, 1H), 6.70–7.28 (m, 10H), 8.29 (d, J=7.4 Hz, 1H), 8.60 (t, J=5.8 Hz, 1H).

^{13}C NMR (DMSO-d_6) 22.88, 42.22, 66.22, 112.66 (2 C), 117.57, 126.65, 127.08 (2 C), 128.15 (2 C), 128.53 (2 C), 139.12, 149.90, 168.66, 170.04 ppm.

IR (KBr) 3300, 1640 (br), 1610, 1520 (br), 1460, 760, 700 cm^{-1}.

Mass spectra (FD) 313 (M^++1).

Elemental analysis Calculated for $C_{17}H_{20}N_4O_2$ 65.37% C; 6.45% H; 17.94% N. Found 65.15% C; 6.25% H; 17.71% N.

EXAMPLE 58

Synthesis of 2-Acetamido-N-benzyl-2-(N^2-benzyloxycarbonylhydrazino)acetamide.

Employing 2-acetamido-N-benzyl-2-ethoxyacetamide (3.00 g, 12.0 mmol), BBr_3 (1M in CH_2Cl_2, 15.0 mL, 15.0 mmol), and benzyl carbazate (4.58 g, 27.6 mmol), 0.95 g (21%) of the desired product was obtained. The product was recrystallized from chloroform/hexane to give a white amorphous solid.

R_f 0.32 (2% MeOH/$CHCl_3$).

mp 152°–154° C.

^{1}H NMR (DMSO-d_6) δ 1.85 (s, 3H), 4.27 (d, J=4.4 Hz, 2H), 5.00 (s, 2H), 5.14 (dd,J=3.1, 8.0 Hz, 1H), 5.23 (t, J=3.1 Hz, 1H), 7.25–7.35 (m, 10H), 8.26 (d, J=8.0 Hz, 1H), 8.56 (br s, 1H), 8.66 (br s, 1H).

^{13}C NMR (DMSO-d_6) 22.71, 42.23, 65.56, 65.97, 126.69, 127.16 (2 C), 127.61 (2 C), 127.77, 128.13 (2 C), 128.27 (2 C), 136.74, 138.87, 168.04, 169.95 ppm.

IR (KBr) 3325, 1620 (br), 1500 (br), 1440, 740, 680 cm^{-1}.

Mass spectrum (FD) 371 (M^++1).

Elemental analysis Calculated for $C_{19}H_{22}N_4O_4$ 61.61% C; 5.99% H; 15.13% N. Found 61.40% C; 6.21% H; 15.39% N.

EXAMPLE 59

Synthesis of 2-Acetamido-N-benzyl-2-phenoxyacetamide.

Using 2-acetamido-N-benzyl-2-ethoxyacetamide (3.00 g, 12.0 mmol), BBr_3 (1M in CH_2Cl_2, 15.0 mL, 15.0 mmol), and NaOPh (4.18 g, 30 mmol) gave a brown oily residue which was purified by flash column chromatography on SiO_2 gel using first $CHCl_3$ and then 2% MeOH/$CHCl_3$ as the eluents to give the desired product. The compound was recrystallized from chloroform/hexane.

Yield: 0.80 g (22%).

R_f 0.58 (3% MeOH/$CHCl_3$).

mp 125°–128° C. (softens at 122° C.).

^{1}H NMR (DMSO-d_6) δ 1.83 (s, 3H), 4.35 (d, J=5.7 Hz, 2H), 6.18 (d, J=9.4 Hz, 1H), 6.94–6.99 (m, 2H), 7.02–7.33 (m, 8H), 8.98 (t, J=5.7 Hz, 1H), 9.10 (d, J=9.4 Hz, 1H).

^{13}C NMR (DMSO-d_6) 22.54, 42.24, 76.44, 116.09 (2 C), 121.78, 126.84, 127.26 (2 C), 128.25 (2 C), 128.44 (2 C), 138.84, 155.97, 166.63, 170.73 ppm.

IR (KBr) 3300, 1650 (br), 1600, 1530 (br), 1490, 1450, 760, 700 cm^{-1}.

Mass spectrum (FD) 299 (M^++1).

Elemental analysis Calculated for $C_{17}H_{18}N_2O_3$.0.5 H_2O 66.43% C; 6.23% H; 9.11% N. Found 66.62% C; 6.23% H; 9.16% N.

EXAMPLE 60

Synthesis of 2-Acetamido-N-benzyl-2-(methylmercapto) acetamide.

A cooled (–78° C.) solution or Et_3N (4.85 g, 48.0 mmol) in THF (20 mL) was added to a cooled (–78° C.) solution of 2-acetamido-N-benzyl-2-bromoacetamide (prepared from 2-acetamido-N-benzyl-2-ethoxyacetamide (4.00 g, 16.0 mmol) and BBr_3 (1M in CH_2Cl_2, 20.0 mL, 20.0 mmol)) in THF (275 mL). A cooled (–78° C.) solution of excess MeSH (5–6 equiv) in THF (55 mL) was then added. The reaction mixture was stirred at this temperature (30 min) and then at room temperature (1 h). The insoluble materials were filtered and the filtrate was evaporated to dryness in vacuo. The oily residue obtained was purified by flash column chromatography on SiO_2 gel (2% MeOH/$CHCl_3$) to give 1.10 g (27%) of the desired product as a yellow orange oil. The product was purified by a second flash column chromatography on SiO_2 gel (2% MeOH/$CHCl_3$) to give 0.72 g of the pure product as a white solid.

R_f 0.65 (3% MeOH/$CHCl_3$).

mp 155°–157° C.

^{1}H NMR (CD_3NO_2) δ 1.98 (s, 3H), 2.08 (s, 3H), 4.39 (dd, J=6.1, 15.2 Hz, 1H), 4.49 (dd, J=6.1, 15.2 Hz, 1H), 5.51 (d, J=7.8 Hz, 1H), 7.15 (d, J=7.8 Hz, 1H), 7.17–7.41 (m, 6H).

^{13}C NMR (CD_3NO_2) 12.28, 22.94, 44.26, 56.03, 128.46, 128.60 (2 C), 129.77 (2 C), 140.17, 169.19, 171.06 ppm.

IR (KBr) 3320, 1650 (br), 1520 (br), 1460, 750 cm^{-1}.

Mass spectrum (FD) 253 (M^++1).

Elemental analysis Calculated for $C_{12}H_{16}N_2O_2S$ 57.12% C; 6.39% H; 11.10% N. Found 57.06% C; 6.57% H; 11.28% N.

EXAMPLE 61

Synthesis of 2-Acetamido-N-benzyl-2-(ethylmercapto) acetamide.

Using the procedure described for the synthesis of 2-acetamido-N-benzyl-2-(methylmercapto)acetamide, 2-acetamido-N-benzyl-2-ethoxyacetamide (2.00 g, 8.0 mmol) and EtSH (0.65 g, 10.4 mmol) were converted to 0.80 g (38%) of the desired product. The compound was further purified by recrystallization from chloroform/hexane to give a beige solid.

R_f 0.60 (4% MeOH/$CHCl_3$).

mp 146°–148° C.

^{1}H NMR (DMSO-d_6) δ 1.56 (t, J=7.4 Hz, 3H), 1.88 (s, 3H), 2.49–2.67 (m, 2H), 4.23 (dd, J=5.9, 15.2 Hz, 1H), 4.32 (dd, J=5.9, 15.2 Hz, 1H), 5.55 (d, J=9.1 Hz, 1H), 7.20–7.35 (m, 5H), 8.59 (d, J=9.1 Hz, 1H), 8.75 (t, J=5.9 Hz, 1H).

^{13}C NMR (DMSO-d_6) 14.73, 22.43, 23.73, 42.10, 53.70, 126.87, 127.14 (2 C), 128.32 (2 C), 139.01, 167.89, 169.02 ppm.

IR (KBr) 3240, 1620 (br), 1510 (br), 1415, 680, 640 cm^{-1}.

Mass spectrum (FD) 267 (M^++1).

Elemental analysis Calculated for $C_{13}H_{18}N_2O_2S$.0.25 H_2O 57.65% C; 6.88% H; 10.34% N. Found 57.48% C; 6.84% H; 10.28% N.

Preparation of Functionalized α-Heteroatom Substituted Amino Acids.

General Procedure.

A mixture of 2-acetamido-2-(N,N,N-trimethylammonium)acetamide tetrafluoroborate (1 equiv), and the nitrogen nucleophile (4–5 equiv) in MeOH (1 mmol/1 mL) was stirred at 55°–60° C. (3 h). The solvent was removed in vacuo and the residue was purified by flash column chromatography on SiO_2 gel using the indicated solvents as the eluent.

Using this procedure the following examples were prepared.

EXAMPLE 62

Synthesis of 2-Acetamido-N-benzyl-2-(N-methoxyamino) acetamide.

Using a MeOH solution of $MeONH_2$ (prepared from $MeONH_2$.HCl (2.83 g, 33.9 mmol) and NaOMe (1.41 g, 26.1 mmol)), and 2-acetamido-2-(N,N,N-trimethylammonium)acetamide tetrafluoroborate (2.70 g, 7.67 mmol) gave an oily residue which was purified by flash column chromatography on SiO_2 gel (2% MeOH/$CHCl_3$) to give the desired product. The product was recrystallized from chloroform/hexane.

Yield: 0.80 g (42%).

R_f 0.23 (2% MeOH/$CHCl_3$)

mp 95°–97° C.

^{1}H NMR (DMSO-d_6) δ 1.88 (s, 3H), 3.38 (s, 3H), 4.22–4.41 (m, 2H), 5.18 (dd, J=4.9, 7.8 Hz, 1H), 6.78 (d, J=4.9 Hz, 1H), 7.21–7.32 (m, 5H), 8.33 (d, J=7.8 Hz, 1H), 8.56 (br s, 1H).

^{13}C NMR (DMSO-d_6) 22.64, 42.28, 61.42, 66.25, 126.74, 127.19 (2 C), 128.19 (2 C), 139.11, 167.95, 169.66 ppm.

IR (KBr) 3300, 1650, 1620, 1510 (br), 1440, 750, 680 cm^{-1}.

Mass spectrum (FD) 252 (M^++1).

Elemental analysis Calculated for $C_{12}H_{17}N_3O_3$ 57.63% C; 6.82% H; 16.72% N. Found 57.06% C; 6.63% H; 16.65% N.

EXAMPLE 63

Synthesis of 2-Acetamido-N-benzyl-2-(N-(N-methylhydroxyamino))acetamide.

An MeOH solution (30 mL) of MeNHOH (21.74 mmol) (prepared from MeNHOH.HCl (2.36 g, 28.26 mmol) and NaOMe (1.17 g, 21.74 mmol)) and 2-acetamido-2-(N,N,N-trimethylammonium)acetamide tetrafluoroborate (2.20 g, 6.25 mmol) gave a residue which was purified by flash column chromatography on SiO_2 gel (6% MeOH/$CHCl_3$) to give the desired product as a white solid. The product was then purified by recrystallization from EtOH.

Yield: 0.95 g (61%).

R_f 0.32 (8% MeOH/$CHCl_3$).

mp 159°–161° C.

^{1}H NMR (DMSO-d_6) δ 1.95 (s, 3H), 2.43 (s, 3H), 4.26 (dd, J=5.7, 15.1 Hz, 1H), 4.35 (dd, J=5.7, 1.51 Hz, 1H), 5.09 (d, J=9.1 Hz, 1H), 7.21–7.29 (m, 5H), 8.05 (s, 1H), 8.18 (d, J=9.1 Hz, 1H), 8.23 (t, J=5.7 Hz, 1H).

^{13}C NMR (DMSO-d_6) 22.40, 42.34, 43.92, 71.49, 126.62, 127.12 (2 C), 128.12 (2 C), 139.14, 167.82, 170.28 ppm.

IR (KBr) 3440 (br), 3300, 1640, 1530, 1460, 750, 700 cm^{-1}.

Mass spectrum (FD) 252 (M^++1).

Elemental analysis Calculated for $C_{12}H_{17}N_3O_3$ 57.36% C; 6.82% H; 16.72% N. Found 57.65% C; 6.59% H; 16.66% N.

EXAMPLE 64

Synthesis of 2-Acetamido-N-benzyl-2-(N-(N,O-methylhydroxyamino))acetamide.

An MeOH solution (20 mL) of MeNHOMe (17.39 mmol) (prepared from MeNHOMe.HCl (2.20 g, 23.02 mmol) and NaOMe (0.94 g, 17.39 mmol)) and 2-acetamido-2-(N,N,N-trimethylammonium)acetamide tetrafluoroborate (2.10 g, 5.97 mmol) gave a solid residue. Flash column chromatography of the solid on SiO_2 gel (2% MeOH/$CHCl_3$) yielded pure desired product. The product was recrystallized from EtOH.

Yield: 1.30 g (82%).

R_f 0.39 (2% MeOH/$CHCl_3$).

mp 165°–167° C.

^{1}H NMR (DMSO-d_6) δ 1.93 (s, 3H), 2.43 (s, 3H), 3.32 (s, 3H), 4.25 (dd, J=5.9, 149 Hz, 1H), 4.37 (dd, J=5.9, 14.9 Hz, 1H), 5.19 (d, J=9.4 Hz, 1H), 7.21–7.35 (m, 5H), 8.31 (d, J=9.4 Hz, 1H), 8.56 (t, J=5.9 Hz, 1H).

^{13}C NMR (DMSO-d_6) 22.36, 39.68, 42.34, 59.16, 70.33, 126.74, 127.41 (2 C), 128.21 (2 C), 139.30, 167.38, 170.30 ppm.

IR (KBr) 3300, 1640 (br), 1540 (br), 1460, 750, 700 cm^{-1}.

Mass spectrum (FD) 266 (M^++1).

Elemental analysis Calculated for $C_{13}H_{19}N_3O_3$ 58.85% C; 7.22% H; 15.84% N. Found 59.05% C; 7.37% H; 15.75% N.

EXAMPLE 65

Synthesis of 2-Acetamido-N-benzyl-2-(N-isoxazolidino) acetamide.

Using 2-acetamido-2-(N,N,N-trimethylammonium) acetamide tetrafluoroborate (1.60 g, 4.55 mmol), isoxazolidine (prepared from isoxazolidine hydrobromide (2.41 g, 15.65 mmol) and NaOMe (0.70 g, 13.04 mmol)) gave the desired product. The product was recrystallized from chloroform/hexane to give a white amorphous solid.

Yield: 0.80 g (64%).

R_f 0.29 (4% MeOH/$CHCl_3$).

mp 149°–151° C.

^{1}H NMR (DMSO-d_6) δ 1.91 (s, 3H), 2.05–2.20 (m, 2H), 2.45–2.89 (m, 1H), 2.98–3.07 (m, 1H), 3.74–3.90 (m, 2H), 4.25 (dd, J=6.1, 15.3 Hz, 1H), 4.35 (dd, J=6.1, 15.3 Hz, 1H), 5.23 (d, J=9.2 Hz, 1H), 7.15–7.35 (m, 5H), 8.49 (d, J=9.2 Hz, 1H), 8.56 (br s, 1H).

^{13}C NMR (DMSO-d_6) 22.26, 28.26, 42.15, 48.94, 66.19, 68.77, 126.64, 127.02 (2 C), 128.13 (2 C), 139.22, 167.43, 170.27 ppm.

IR (KBr) 3400 (br), 3300, 1650, 1530, 1470, 740, 700, 610 cm^{-1}.

Mass Spectrum (FD) 278 (M^++1).

Elemental analysis Calculated for $C_{14}H_{19}N_3O_3$ 60.64% C; 6.91% H; 15.15% N. Found 60.16% C; 7.04% H; 15.07% N.

Preparation of Functionalized α-Heteroatom Substituted Amino Acids.

General Procedure.

2-Acetamido-N-benzyl-2-ethoxyacetamide (1 equiv) was suspended in Et_2O (100 mL/100 mmol), and then $BF_3.Et_2O$ (1.6–2.4 equiv) was rapidly added and the resulting solution was stirred (10 min). The nucleophile (H_2O or EtSH) (1.6–4.0 equiv) was then added and the reaction was stirred at room temperature (18–48 h). The reaction was then quenched by the addition of an aqueous $NaHCO_3$ (100 mL/10 mmol)/ice mixture. The experimental workup varied slightly for each compound and is described in the following examples along with the observed spectral properties.

EXAMPLE 66

Synthesis of 2-Acetamido-N-benzyl-2-hydroxyacetamide.

Reacting 2-acetamido-N-benzyl-2-ethoxyacetamide (1.00 g, 4.0 mmol), $BF_3.Et_2O$ (0.91 g, 6.4 mmol) and H_2O (0.12 g, 6.7 mmol) followed by aqueous $NaHCO_3$ workup gave an aqueous reaction mixture. The solution was then extracted with EtOAc (3×50 mL), and the combined EtOAc extracts were dried (Na_2SO_4), and concentrated in vacuo. The resi-

due was purified by flash column chromatography on SiO_2 gel (3% MeOH/$CHCl_3$) to give the desired product as a white solid.

Yield: 0.30 g (34%).

R_f 0.14 (3% MeOH/$CHCl_3$).

mp 136°–138° C.

^1H NMR (DMSO-d_6) δ 1.85 (s, 3H), 4.29 (d, J=5.9 Hz, 2H), 5.48 (dd, J=5.5, 8.6 Hz, 1H), 6.47 (d, J=5.5 Hz, 1H), 7.21–7.35 (m, 5H), 8.52 (t, J=5.9 Hz, 1H), 8.59 (d, J=8.6 Hz, 1H).

^{13}C NMR (DMSO-d_6) 22.66, 41.99, 71.42, 126.66, 127.22 (2 C), 128.13 (2 C), 139.20, 169.47, 169.62 ppm.

IR (KBr) 3300, 1620, 1530 (br), 1430 (br), 730, 690 cm^{-1}.

Mass spectrum, m/e (relative intensity) 223 (M^++1, 1), 163 (11), 134 (9), 106 (46), 91 (100), 77 (22), 65 (38).

Elemental analysis Calculated for $C_{11}H_{14}N_2O_3$ 59.45% C; 6.35% H; 12.61% N. Found 59.24% C; 6.36% H; 12.50% N.

EXAMPLE 67

Synthesis of 2-Acetamido-N-benzyl-2-(ethylmercapto) acetamido.

Using 2-acetamido-N-benzyl-2-ethoxyacetamide (2.00 g, 8.0 mmol), $BF_3.Et_2O$ (2.72 g, 19.2 mmol) and EtSH (2.38 g, 38.4 mmol) gave an aqueous reaction mixture. The solution was extracted with $CHCl_3$ (3×100 mL). The combined $CHCl_3$ layers were dried (Na_2SO_4), and then concentrated in vacuo to give the desired product as white solid.

Yield: 1.90 g (89%).

R_f 0.60 (4% MeOH/$CHCl_3$).

mp 148°–149° C. (mixed melting point with an authentic sample, of Example 61 was undepressed).

EXAMPLE 68

Synthesis of 2,2-Dicacetamido-N-benzylacetamide.

Ac_2O (1 mL) was added to a solution of 2-acetamido-N-benzyl-2-aminoacetamide (1.10 g, 4.98 mmol) in dry pyridine (10 mL) and then CH_2Cl_2 (20 mL) was added. The mixture was stirred at room temperature (4 h) and then the volatile materials were removed in vacuo. The residue was then treated with a saturated aqueous $NaHCO_3$ solution (50 mL). The white solid that remained was the desired product and-was filtered, dried (Na_2SO_4), and recrystallized from MeOH.

Yield: 1.20 g (92%).

mp 265°–267° C. (dec.).

^1H NMR (DMSO-d_6) δ 1.84 (s, 6H), 4.26 (d, J=5.8 Hz, 2H), 5.71 (t, J=7.6 Hz, 1H), 7.20–7.31 (m, 5H), 8.44 (d, J=7.6 Hz, 2H), 8.48 (t, J=5.8 Hz, 1H).

^{13}C (DMSO-d_6) 22.44 (2 C), 42.26, 56.99, 126.62, 127.02 (2 C), 128.12 (2 C), 139.15, 168.19, 169.39 (2 C) ppm.

IR (KBr) 3260, 1530, 1500, 740, 690 cm^{-1}.

Mass spectrum (FD) 264 (M^++1).

Elemental analysis Calculated for $C_{13}H_{17}N_3O_3$ 59.30% C; 6.51% H; 15.96% N. 59.16% C; 6.49% H; 15.86% N.

EXAMPLE 69

Synthesis of 2-Acetamido-N-benzyl-2-trifluoroacetamidoacetamide.

Ice cold trifluoroacetic anhydride (8 mL) was added in one portion to ice cold 2-acetamido-N-benzyl-2-aminoacetamide (1.00 g, 4.53 mmol). The reaction was accompanied by the evolution of heat. After stirring (5 min), the volatile materials were removed in vacuo. The residue was treated with a saturated aqueous $NaHCO_3$ solution (20 mL), and the solid that remained was filtered and washed with H_2O to give the desired product. The product was recrystallized from EtOH.

Yield: 1.00 g (70%).

R_f 0.34 (8% MeOH/$CHCl_3$).

mp 228°–230° C.

^1H NMR (DMSO-d_6) δ 1.90 (s, 3H), 4.30 (d, J=5.1 Hz, 2H), 5.85 (d, J=8.0 Hz, 1H), 7.21–7.35 (m, 5H), 8.64 (d, J=8.0 Hz, 1H), 8.75 (t, J=5.1 Hz, 1H), 10.04 (s, 1H).

^{13}C NMR(DMSO-d_6) 22.52, 42.52, 57.42, 117.4 (q, JCF= 288.3 Hz), 126.80, 127.16 (2 C), 128.21 (2 C), 138.93, 156.14 (q, JCF=35.3 Hz), 166.3.9, 169.88 ppm.

IR (KBr) 3300, 1720, 1660, 1520, 1380, 760, 700 cm^{-1}.

Mass spectrum (FD) 318 (M^++1).

Elemental analysis Calculated for $C_{13}H_{14}N_3O_3F_3$ 49.21% C; 4.45% H; 13.24% N. Found 49.48% C; 4.43% H; 13.10% N.

EXAMPLE 70

Synthesis of 2-Acetamido-N-benzyl-2-(N,N,N-trimethylammonium)acetamide Tetrafluoroborate.

A solution of 2-acetamido-N-benzyl-2-(N,N-dimethylamino)acetamide (1.93 g, 7.76 mmol) in nitromethane (7 mL) was added slowly to an ice cold solution of trimethyloxonium tetrafluoroborate (1.26 g, 8.54 mmol) in nitromethane (6 mL). The reaction mixture was stirred at this temperature (15 min) and then at room temperature (2 h). Anhydrous Et_2O (~50 mL) was added the reaction mixture and the white solid that separated was filtered, washed with Et_2O, and dried in vacuo.

Yield: 1.95 g (72%).

mp 171°–173° C. (dec.).

^1H NMR (CD_3NO_2) δ 2.14 (s, 3H), 3.18 (s, 9H), 4.50 (d, J=5.8 Hz, 2H), 5.70 (d, J=9.3 Hz, 1H), 7.30–7.41 (m, 5H), 7.57 (d, J=9.3 Hz, 1H), 7.70 (br s, 1H).

IR (KBr) 3300, 1680 (br), 1530, 1490, 710 cm^{-1}.

Mass spectrum (FD) 264 (M^+).

Elemental analysis Calculated for $C_{14}H_{22}N_3O_2BF_4$ 47.89% C; 6.31% H; 11.97% N. Found 47.80% C; 6.33% H; 12.00% N.

EXAMPLE 71

Synthesis of 2-Acetamido-N-benzyl-2-(ethylmercapto) acetamide-S-oxide.

A solution of m-chloroperbenzoic acid (1.00 g (~65%), 3.76 mmol) in CH_2Cl_2 (10 mL) was added dropwise into a stirred, cooled (–10° to –15° C.) CH_2Cl_2 solution (125 mL) of 2-acetamido-N-benzyl-2-(ethylmercapto)acetamide (1.00 g, 3.76 mmol) under N_2. The reaction was stirred (30 min) at this temperature and then, the m-chlorobenzoic acid was precipitated as its ammonium salt by passing NH_3 gas over the surface of the reaction solution. The excess NH_3 was removed by passing N_2 gas through the solution (20 min) at room temperature. The ammonium salt was filtered, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography on SiO_2 gel (2% MeOH/$CHCl_3$) to give the desired product. The product was recrystallized from chloroform/hexane as a white granular solid.

Yield: 0.55 g (52%).

R_f 0.23 (2% MeOH/$CHCl_3$).

mp 135°–137° C.

^{1}H NMR (DMSO-d_6) δ 1.15 (t, J=7.5 Hz, 3H), 1.99 (s, 3H), 2.49–2.56 (m, 1H), 2.65–2.72 (m, 1H), 4.34 (d, J=5.7 Hz, 2H), 5.55 (d, J=9.5 Hz, 1H), 7.23–7.34 (m, 5H), 8.74 (d, J=9.5 Hz, 1H), 8.77 (t, J=5.7 Hz, 1H).

^{13}C NMR (DMSO-d_6) 7.03, 22.34, 42.40, 42.47, 67.15, 126.89, 127.27 (2 C), 128.24 (2 C), 138.55, 164.66, 170.18 ppm.

IR (KBr) 3300 (br), 1640 (br), 1510 (br), 1370, 1230, 1100, 1020, 900 cm^{-1}.

Mass spectrum (FD) 283 (M^++1).

Elemental analysis Calculated for $C_{13}H_{18}N_2O_3S$ 55.30% C; 6.43% H; 9.92% N. Found 55.17% C; 6.38% H; 9.70% N.

EXAMPLE 72

Synthesis of 2-Acetamido-N-benzyl-2-(S-ethylmercapto) acetamide-S-oxide.

A solution of $NaIO_4$ (1.77 g, 8.27 mmol) in H_2O (20 mL) was added dropwise into a stirred solution of 2-acetamido-N-benzyl-2-(ethylmercapto)acetamide (2.00 g, 7.52 mmol) in MeOH (25 mL). A precipitate appeared rapidly. H_2O (~30 mL) was added to the mixture to dissolve most of the suspension, and the reaction was stirred (4 h) at room temperature. The reaction was concentrated in vacuo and the remaining aqueous mixture was extracted with $CHCl_3$ (3×100 mL). The combined $CHCl_3$ extracts were dried (Na_2SO_4) and the solvent was removed in vacuo. The oily residue (1.95 g, 92%) solidified on drying in vacuo. NMR analysis (DMSO-d_6) or the product showed that it was a 2:1 mixture of the two diastereomers of the desired product. The reaction was recrystallized from EtOAc to give nearly pure diastereomer A (1.20 g) that was obtained from the m-chloroperbenzoic acid reaction. The EtOAc mother liquor was concentrated and the remaining residue (0.75 g) was recrystallized from ethyl acetate/hexane to give a diastereomeric mixture (0.41 g) of the two diastereomers A and B in a 2:3 ratio, respectively.

R_f 0.60 (4% MeOH/$CHCl_3$).

mp 135°–137° C. (softens at 117° C.).

IR (KBr) 3300 (br), 1640 (br), 1510 (br), 1370, 1230, 1100, 1020, 900 cm^{-1}.

Mass spectrum (FD) 283 (M^++1).

Elemental analysis: Calculated for $C_{13}H_{18}N_2O_3S$: 55.30% C; 6.43% H; 9.92% N. Found: 55.58% C; 6.49% H; 9.97% N.

The following NMR spectral properties have been assigned to compounds A and B.

Diastereomer A.

^{1}H NMR (DMSO-d_6) δ 1.16 (t, J=7.5 Hz, 3H), 2.00 (s, 3H), 2.49–2.72 (m, 2H), 4.28–4.39 (m, 2H), 5.56 (d, J=9.7 Hz, 1H), 7.21–7.34 (m, 5H), 8.71–8.77 (m, 2H).

^{13}C NMR (DMSO-d_6) 7.10, 22.43, 42.48, 42.57, 67.23, 126.98, 127.36 (2 C), 128.33 (2 C), 138.63, 164.73, 170.25 ppm.

Diastereomer B.

^{1}H NMR (DMSO-d_6) δ 1.13 (t, J=7.6 Hz, 3H), 1.94 (s, 3H), 2.49–2.72 (m, 2H), 4.28–4.39 (m, 2H), 5.71 (d, J=9.9 Hz, 1H), 7.21–7.34 (m, 5H), 8.83 (d, J=9.9 Hz, 1H), 8.98 (t, J=5.6 Hz, 1H).

^{13}C NMR (DMSO-d_6) 6.47, 22.43, 41.53, 42.55, 67.90, 126.98, 127.36 (2 C), 128.33 (2 C), 138.39, 164.43, 169.82 ppm.

EXAMPLE 73

Synthesis of 2-Acetamido-N-benzyl-2-(ethanesulfonyl) acetamide.

An aqueous solution (20 mL) of $NaIO_4$ (3.00 g, 14.02 mmol) was added to a MeOH solution (20 mL) of 2-acetamido-N-benzyl-2-(ethylmercapto)acetamide (0.95 g, 3.57 mmol). The initial homogeneous solution rapidly became turbid. H_2O (~10 mL) was then added dropwise until the system became homogeneous. The solution was stirred (18 h) at 50°–60° C. MeOH (50 mL) was added to the reaction solution and the precipitated salt was filtered and washed with MeOH (10 mL). The filtrate was concentrated and the remaining solution was extracted with $CHCl_3$ (3×50 mL). The combined $CHCl_3$ extracts were dried (Na_2SO_4), and concentrated in vacuo. Time residue was purified by flash chromatography on SiO_2 gel (1% MeOH/$CHCl_3$) to give the desired product. The product was further purified by recrystallization from EtOH:.

Yield: 0.34 g (32%).

R_f 0.34 (3% MeOH/$CHCl_3$).

mp 161°–163° C.

^{1}H NMR (DMSO-d_6) δ 1.22 (t, J=7.4 Hz, 3H), 1.99 (s, 3H), 3.04–3.24 (m, 2H), 4.31 (dd, J=5.7, 15.3 Hz, 1H), 4.41 (dd, J=5.7, 15.3 Hz, 1H), 5.93 (d, J=9.8 Hz, 1H), 7.22–7.35 (m, 5H), 9.13 (t, J=5.7 Hz, 1H), 9.17 (d, J=9.8 Hz, 1H).

^{13}C NMR (DMSO-d_6) 5.72, 22.27, 42.63, 45.43, 69.14, 127.02, 127.28 (2 C), 128.33 (2 C), 138.16, 161.88, 169.83 ppm.

IR (KBr) 3300, 2940, 1660, 1520, 1310, 1230, 1120, 900 cm^{-1}.

Mass spectrum (FD) 298 (M^+).

Elemental analysis Calculated for $C_{13}H_{18}N_2O_4S$ 52.33% C; 6.08% H; 9.39% N. Found 52.52% C; 6.06% H; 9.53% N.

EXAMPLE 74

Synthesis of 2-Acetamido-N-benzyl-2-(N,N,N-trimethylammonium)acetamide Tetrafluoroborate.

A solution or 2-acetamido-N-benzyl-2-(N,N-dimethylamino)acetamide (1.93 g, 7.76 mmol) in nitromethane (7 mL) was added slowly to an ice cold solution of trimethyloxonium tetrafluoroborate (1.26 g, 8.54 mmol) in nitromethane (6 mL). The reaction mixture was stirred at this temperature (15 min) and then at room temperature (2 h). Anhydrous Et_2O (~50 mL) was added to the reaction mixture and the white solid that separated was filtered, washed with Et_2O, and dried in vacuo.

Yield: 1.95 g (72%).

mp 171°–173° C. (dec.).

^{1}H NMR (CD_3NO_2) δ 2.14 (s, 3H), 3.18 (s, 9H), 4.50 (d, J=5.8 Hz, 2H), 5.70 (d, J=9.3 Hz, 1H), 7.30–7.41 (m, 5H), 7.57 (d, J=9.3 Hz, 1H), 7.70 (br s, 1H).

IR (KBr) 3300, 1680 (br), 1530, 1490, 710 cm^{-1}.

Mass spectrum (FD) 264 (M^+).

Elemental analysis

Calculated for $C_{14}H_{22}N_3O_2BF_4$ 47.89% C; 6.31% H; 11.97% N. Found 47.80% C; 6.33% H; 12.00% N.

EXAMPLE 75

Synthesis of 2-Acetamido-N-benzyl-2-(1-pyrrole) acetamide.

A solution 2-acetamido-N-benzyl-2-bromoacetamide (prepared from 2-acetamido-N-benzyl-2-ethoxyacetamide

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