Supplementary Material

Synthesis of 2-Amino-3-fluoro-acrylic Acid Containing Peptides

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General Experimental

All NMR spectra were recorded on Varian U400, U500, or UI500NB spectrometers. ^{1}H spectra were referenced to $CHCl_3$ at 7.26 ppm and ^{13}C spectra were referenced to $CDCl_3$ at 77.23 ppm. ^{19}F spectra were referenced externally to 1% $C_6F_6/CDCl_3$ at –162.0 ppm. All spectra were taken in $CDCl_3$ unless otherwise indicated. Mass spectrometry (MS) experiments were carried out by the Mass Spectrometry Laboratory at the University of Illinois at Urbana-Champaign (UIUC). Elemental analysis was performed by the Microanalysis Laboratory at the UIUC. Infrared (IR) spectra were taken on a Mattson Galaxy Series FTIR 5000. Thin layer chromatography (TLC) was carried out on Merck silica gel 60 F_{254} plates. Compounds and solvents were obtained from Fisher, Aldrich, and Chem-Impex. Anhydrous $MgSO_4$ was used for drying organic solutions.

Synthesis of 2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-acrylic Acid Benzhydryl Ester (5). Compound **4**[1] (1.01 g, 2.06 mmol) was dissolved in 25 mL of anhydrous CH_2Cl_2. The solution was cooled to 0 ^{o}C. Methylsulfonyl chloride (MsCl) (0.26 g, 2.26 mmol) was added dropwise and the reaction was stirred for 10 min. Then triethylamine (0.46 g, 4.52 mmol) was added and the reaction was stirred for an additional 24 h at 0 ^{o}C. The solution was diluted with 80 mL of CH_2Cl_2 and washed with saturated aqueous NH_4Cl, $NaHCO_3$, and brine. The organic layer was dried and concentrated. Purification by silica gel chromatography (hexane: ethyl acetate / 5:1) provide 0.80 g of the desired product as a white powder (yield 82%). R_f: 0.38. mp 109-110 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.28 (t, J = 7.01 Hz, 1H, $CHCH_2$), 4.48 (d, J = 6.73 Hz, 2H, CH_2), 6.07 (s, 1H, CH_2), 6.40 (bs, 1H, CH_2), 7.07 (s, 1H, $CH(Ph)_2$), 7.33-7.45 (m, 15H, Ph, NH), 7.62 (d, J = 7.43 Hz, 2H, Ph), 7.80(d, J = 7.36 Hz, 2H, Ph); ^{13}C NMR (125 MHz, $CDCl_3$): δ 47.3 (CH/CH_3), 67.5 (C/CH_2), 79.3 (CH/CH_3), 106.9 (C/CH_2), 120.4 (CH/CH_3), 125.3 (CH/CH_3), 127.4 (CH/CH_3), 127.5 (CH/CH_3), 128.1 (CH/CH_3), 128.6 (CH/CH_3), 128.8 (CH/CH_3), 129.0 (CH/CH_3), 131.5 (C/CH_2), 139.7 (C/CH_2), 141.6 (C/CH_2), 143.9 (C/CH_2), 153.5 (C/CH_2), 163.4 (C/CH_2); IR: 3408, 3066, 3033, 1736, 1519, 1316, 1105, 981, 736 cm^{-1}. HRMS (FAB^{+}): calculated $C_{31}H_{25}NO_4$ 475.1784, found 475.1783. Anal. Calcd for $C_{31}H_{25}NO_4$: C, 78.30; H, 5.30; N, 2.95. Found: C, 78.25; H, 5.28; N, 3.11.

Synthesis of 2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-(4-methoxy-phenylsulfanyl)-propionic Acid Benzhydryl Ester (6). Compound **5** (0.143 g, 0.3 mmol) was placed in a 10 mL round bottom flask. The flask was flushed with N_2 and anhydrous THF (4 mL) was added. Triethylamine (0.061 g, 0.6 mmol) was added, followed by 4-methoxybenzenethiol (0.042 g, 0.3 mmol). The solution was stirred for 18 h, diluted with Et_2O (80 mL), washed with saturated $NaHCO_3$ (50 mL), 5% $KHSO_4$ (50 mL), dried, filtered and concentrated. The mixture was purified by flash chromatography (hexane: ethyl acetate / 5: 1) to give the product as a white powder (2 diastereomers, 0.129 g, 70%). R_f: 0.17. mp 107-108 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.31 (B of ABX, Jab = 14.2 Hz, Jbx = 5.5 Hz, 1H, CH_2), 3.46 (A of ABX, Jab = 14.2 Hz, Jax = 4.5 Hz, 1H, CH_2), 3.80 (s, 3H, OCH_3), 4.18 (t, J = 7.19 Hz, 1H, CH), 4.30-4.36 (m, 2H, CH_2), 4.76 (X of ABX, 1H, CH), 5.76 (d, J = 8.29 Hz, 1H, NH), 6.78 (d, J = 8.74 Hz), 2H, Ph), 6.88 (s, 1H, $CH(Ph)_2$), 7.31-7.38 (m, 20 H, Ph); ^{13}C NMR (125 MHz, $CDCl_3$): δ 38.9 (C/CH_2), 47.3 (CH/CH_3), 54.5 (CH/CH_3), 55.5 (CH/CH_3), 67.5 (C/CH_2), 78.8 (CH/CH_3), 114.9 (CH/CH_3), 120.2 (CH/CH_3), 125.0 (C/CH_2), 125.4 (CH/CH_3), 127.3 (CH/CH_3), 127.4

(CH/CH_3), 128.0 (CH/CH_3), 128.4 (CH/CH_3), 128.8 (CH/CH_3), 128.9 (CH/CH_3), 134.6 (CH/CH_3), 139.6 (C/CH_2), 140.0 (C/CH_2), 141.5 (C/CH_2), 144.0 (C/CH_2), 155.8 (C/CH_2), 159.7 (C/CH_2), 169.9 (C/CH_2); IR: 3425, 1720, 1500, 1235, 728 cm^{-1}. HRMS (FAB^+): calculated $C_{38}H_{33}NO_5S$ 615.2079, found 615.2075. Anal. Calcd for $C_{38}H_{33}NO_5S$: C, 74.12; H, 5.40; N, 2.27. Found: C, 73.91; H, 5.36; N, 2.38.

Synthesis of 2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-(4-methoxy-benzenesulfinyl)-propionic Acid Benzhydryl Ester (7). Compound **6** (0.391 g, 0.635 mmol) was dissolved in 25 mL of CH_2Cl_2 and the solution was cooled to –40 ^oC. A solution of *m*CPBA (Aldrich tech. grade, 57% peracid content determined by titration,[2] 0.160 g, 0.528 mmol) in CH_2Cl_2 (3 mL) was added dropwise. The solution was stirred at –40 ^oC and additional *m*CPBA (0.040 g, 0.132 mmol) was added to complete the reaction as determined by TLC. The mixture was diluted with 100 mL of CH_2Cl_2 in 2 h, washed with 10% aqueous $Na_2S_2O_3$ (30 mL), water (30 mL), and brine (30 mL). The organic layer was dried, filtered and concentrated. Purification by silica gel (hexane:ethyl acetate / 1: 1) gave the product as a white powder (0.381 g, 95%). R_f: 0.22. 2 diastereomers: mp 69-71 ^oC. ^1H NMR (500 MHz, $CDCl_3$): δ 3.25-3.33 (m, 2H, CH_2), 3.36-3.43 (m, 2H, CH_2), 3.81 (s, 3 H, OCH_3), 3.83 (s, 3H, OCH_3), 4.20 (t, J = 7.02 Hz, 2H, CH), 4.29-4.40 (m, 4H, CH_2), 4.73 (q, J = 6.04 Hz, 1H, CH), 4.85-4.89 (m, 1H, CH), 5.98 (bs, 1H, NH), 6.40 (t, J = 3.7 Hz, 1H, NH), 6.92 (s, 1H, $CH(Ph)_2$), 6.97-7.00 (m, 5H, Ph, $CH(Ph)_2$), 7.27-7.78 (m, 40H, Ph); ^{13}C NMR (125 MHz, $CDCl_3$): 50.7 (CH/CH_3), 51.6 (CH/CH_3), 55.7 (CH/CH_3), 55.8 (CH/CH_3), 67.7 (C/CH_2), 67.8 (C/CH_2), 79.1 (CH/CH_3), 79.3 (CH/CH_3), 115.2 (CH/CH_3), 125.5 (CH/CH_3), 126.6 (CH/CH_3), 127.3 (CH/CH_3), 128.0 (CH/CH_3), 128.5 (CH/CH_3), 139.4 (C/CH_2), 141.5 (C/CH_2), 143.9 (C/CH_2), 156.0 (C/CH_2), 162.6 (C/CH_2), 169.4 (C/CH_2). IR: 3270, 3063, 1723, 1594, 1496, 1450, 1304, 1260, 1173, 1087, 1030, 830, 759, 740, 700 cm^{-1}. HRMS (FAB^+): calculated $C_{38}H_{33}NO_6S$ 631.2029, found [M^++H] 632.2106. Anal. Calcd for $C_{38}H_{33}NO_6S$: C, 72.25; H, 5.27; N, 2.22. Found: C, 71.89; H, 5.28; N, 2.26.

Synthesis of 2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-fluoro-3-(4-methoxy-phenylsulfanyl)-propionic Acid Benzhydryl Ester (8). Compound **7** (0.238 g, 0.377 mmol) was dissolved in anhydrous CH_2Cl_2 (2 mL) in a 5 mL round-bottom flask under N_2. Diethylaminosulfur trifluoride (DAST) (0.091 g, 0.565 mmol) was added, followed by a solution of antimony trichloride ($SbCl_3$) (0.009 g, 0.04 mmol) in CH_2Cl_2 (0.3 mL). The solution was stirred at rt for 4 h until TLC showed complete consumption of starting material. An ice-cold $NaHCO_3$ solution was added and the mixture was stirred for 5-10 min. The mixture was diluted with CH_2Cl_2 80 (mL), and the organic layer was washed with brine (30 mL), dried, and concentrated. Purification over silica gel (hexane: ethyl acetate: 5:1) gave the product as 2 diastereomers (0.167 g, 70%). R_f: 0.18. ^1H NMR (400 MHz, $CDCl_3$): δ 3.80 (s, 3H, OCH_3), 4.26 (t, J = 7.4 Hz, 1H, CH), 4.40-4.48 (m, 2H, CH_2), 5.06-5.17 (m, 1H, CH), 5.76 (t, J = 9.7 Hz, 1H, NH), 6.05 (dd, J = 53.0 Hz, 3.3 Hz, CHF), 6.19 (dd, J = 54.0 Hz, 3.5 Hz, CHF), 6.86 (d, J = 8.5 Hz, 2H, Ph), 6.99 (s, 1H, $CH(Ph)_2$), 7.32-7.79 (m, 20H, Ph); ^{13}C NMR (125 MHz, $CDCl_3$): 47.2 (CH/CH_3), 55.6 (CH/CH_3), 58.3 (CH/CH_3), 58.5 (CH/CH_3), 67.8 (C/CH_2), 68.0 (C/CH_2), 79.6 (CH/CH_3), 79.7 (CH/CH_3), 102.8 (d, J = 224 Hz, CH/CH_3), 114.9 (CH/CH_3), 115.1 (CH/CH_3), 120.2 (CH/CH_3), 122.1(CH/CH_3), 125.4 (CH/CH_3), 127.4 (CH/CH_3), 127.6 (CH/CH_3), 128.6 (CH/CH_3), 128.9 (CH/CH_3), 135.8 (CH/CH_3), 135.9 (CH/CH_3), 139.2 (C/CH_2), 141.6 (C/CH_2), 143.9 (C/CH_2), 156.4 (C/CH_2), 160.8 (C/CH_2), 167.2 (C/CH_2); ^{19}F NMR (376 MHz, $CDCl_3$): (2 diastereomers) δ -156.0 (dd, J = 56.2 Hz, 15.3 Hz, CHF), -157.4 (dd, J = 56.5 Hz, 26.4 Hz, CHF). IR: 3318, 3065, 3033, 1727, 1592, 1494, 1450, 1249, 1178, 1030, 740, 699 cm^{-1}. HRMS (FAB^+): calculated $C_{38}H_{32}O_5NSF$ 633.1985, found 633.1984.

Synthesis of 2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-fluoro-acrylic Acid Benzhydryl Ester (10). Compound **8** (0.126 g, 0.199 mmol) was dissolved in CH_2Cl_2 (5 mL) and the solution was cooled to –20 ^oC. A solution of mCPBA (57 % peracid content, see **7**) (0.066 g, 0.219 mmol) in CH_2Cl_2 (2 mL) was added, and the reaction mixture was stirred at –20 to -5 ^oC for 1.5 h. The solution was diluted with CH_2Cl_2 (80 mL), washed with 10% aqueous $Na_2S_2O_3$, water (30 mL), and brine (30 mL). The organic layer was dried and concentrated to give product **9** as 4 diastereomers. Compound **9** was placed in a 10 mL flask without purification and anhydrous benzene (5 mL) was added. The solution was refluxed overnight. The solvent was removed under reduced pressure. Purification over silica gel (hexane:ethyl acetate / 5:1) gave product **10** as 2 diastereomers that were separable (0.046 g, 47%). (*E* isomer): R_f: 0.24. ^1H NMR (500 MHz, $CDCl_3$): δ 4.22 (t, J = 6.84 Hz, 1H, CH), 4.42 (d, J = 6.91 Hz, 2H, CH_2), 6.56 (s, 1H, NH), 7.02 (s, 1H, $CH(Ph)_2$), 7.30-7.43 (m, 14H, Ph), 7.56 (d, J = 7.30 Hz, 2H, Ph), 7.71 (d, J = 7.63 Hz, 2H, Ph), 8.18 (d, J = 77.3 Hz, 1H, CHF); ^{13}C NMR (125 MHz, $CDCl_3$): 47.1 (CH/CH_3), 67.8 (C/CH_2), 79.5 (CH/CH_3), 116.3 (d, $^2J_{CF}$ = 17.86 Hz, C/CH_2), 120.3 (C/CH_2), 125.2 (CH/CH_3), 127.2 (CH/CH_3), 127.4 (CH/CH_3), 128.1 (CH/CH_3), 128.4 (CH/CH_3), 128.9 (CH/CH_3), 139.7 (C/CH_2), 141.6 (C/CH_2), 143.7 (C/CH_2), 152.1 (d, $^1J_{CF}$ = 276.17 Hz, CH/CH_3), 153.5 (C/CH_2), 162.4 (C/CH_2); ^{19}F NMR (376 MHz, $CDCl_3$): δ -130.9 (d, J= 78.1 Hz, CHF). IR: 3403, 3065, 3023, 1709, 1519, 1495, 1450, 1384, 1365, 1277, 1216, 1143, 1045, 759, 740, 700 cm^{-1}. (*Z* isomer): R_f: 0.19. ^1H NMR (500 MHz, $CDCl_3$): δ 4.20 (t, J = 7.10 Hz, 1H, CH), 4.41 (d, J = 6.91 Hz, 2H, CH_2), 6.08 (s, 1H, NH), 6.98 (s, 1H, $CH(Ph)_2$), 7.28-7.42 (m, 14H, Ph), 7.57 (d, J = 7.51 Hz, 2H, Ph), 7.66 (d, J = 74.63 Hz, 1H, CHF), 7.77 (d, J = 7.59 Hz, 2H, Ph); ^{13}C NMR (125 MHz, $CDCl_3$): 47.1 (CH/CH_3), 68.2 (C/CH_2), 78.8 (CH/CH_3), 114.9 (d, $^2J_{CF}$ = 5.52 Hz, C/CH_2), 120.3 (C/CH_2), 125.3 (CH/CH_3), 127.3 (CH/CH_3), 128.0 (CH/CH_3), 128.5 (CH/CH_3), 128.6 (CH/CH_3), 128.9 (CH/CH_3), 139.4 (C/CH_2), 141.5 (C/CH_2), 143.8 (C/CH_2), 152.8 (d, $^1J_{CF}$ = 283 Hz, CH/CH_3), 153.4 (C/CH_2), 163.1 (d, $^1J_{CF}$ = 11.6 Hz, C/CH_2); ^{19}F NMR (376 MHz, $CDCl_3$): δ -117.2 (d, J = 72.6 Hz, CHF). IR: 3318, 3065, 3033, 1728, 1674, 1496, 1674, 1496, 1450, 1267, 1230, 1181, 1047, 910, 758, 740 cm^{-1}. HRMS (FAB^+): calculated $C_{31}H_{24}NO_4F$ 493.1689, found [M^++H] 494.1768.

Synthesis of 2-(9H-Fluoren-9-ylmethoxycarbonylamino)-3-(4-methoxy-phenylsulfanyl)-acrylic Acid Benzhydryl Ester (14). The same procedure was followed as given for compound **6**. (*E* isomer): yield: 76%; R_f: 0.34 (hexane:ethyl acetate / 5:2); ^1H NMR (500 MHz, $CDCl_3$): δ 3.79 (s, 3H, OCH_3), 4.22 (b, 1H, CH), 4.37 (d, J = 6.24 Hz, 2H, CH_2), 6.89 (d, J = 8.86 Hz, 2H, Ph), 7.00 (bs, 1H, NH), 7.10 (s, 1H, $CH(Ph)_2$), 7.27-7.56 (m, 18H, Ph), 7.75 (d, J = 7.61 Hz, 2H, Ph), 7.97 (bs, 1H, CHSAr); (*Z* isomer): yield: 88%; R_f: 0.29 (hexane:ethyl acetate / 5:2); ^1H NMR (500 MHz, $CDCl_3$): δ 3.83 (s, 3H, OCH_3), 4.24 (b, 1H, CH), 4.41 (b, 2H, CH_2), 6.44 (bs, 1H, NH), 6.91 (d, J = 8.70 Hz, 2H, Ph), 6.94 (s, 1H, $CH(Ph)_2$, 7.25-7.45 (m, 16H, Ph), 7.61 (d, J = 7.59 Hz, 2H, Ph), 7.66 (s, 1H, CHSAr), 7.77 (d, J = 7.70 Hz, 2H, Ph); ^{13}C NMR (125 MHz, $CDCl_3$): 47.1 (CH/CH_3), 55.7 (CH/CH_3), 68.0 (C/CH_2), 78.4 (CH/CH_3), 110.0 (C/CH_2), 115.3 (CH/CH_3), 120.2 (CH/CH_3), 121.0 (C/CH_2), 125.5 (CH/CH_3), 127.4 (CH/CH_3), 128.0 (CH/CH_3), 128.3 (CH/CH_3), 128.8 (CH/CH_3), 133.8 (CH/CH_3), 140.0 (C/CH_2), 141.5 (CH/CH_2), 143.9 (C/CH_2), 160.4 (C/CH_2), 162.4 (C/CH_2); HRMS (FAB^+), calculated $C_{38}H_{31}NO_5S$ 613.1923, found [M^+] 613.1923.

Synthesis of 2-(2-Acetylamino-acetylamino)-3-(4-methoxy-phenylsulfanyl)-propionic Acid Benzhydryl Ester (15). The procedure described by Hoeg-jensen et al was modified.[3] Compound **6** (0.633 g, 1.03 mmol) was dissolved in 10 mL of $CHCl_3$. 4-Aminomethylpiperidine (4-AMP, 3 mL) was added and the mixture was stirred for 30 min. The solution was diluted with $CHCl_3$ (80 mL), and extracted with 10% aqueous phosphate buffer, pH=5.5 (5 × 25 mL). The organic layer was dried and concentrated. The peptide coupling was started by adding Ac-Gly-OH (0.120 g, 1.03 mmol) and

PyBOP (0.535 g, 1.03 mmol) in $CHCl_3$ (10 mL), followed by DIEA (0.279 g, 2.16 mmol). After stirring for 30 min, the solution was diluted with $CHCl_3$ (120 mL), washed with 1N HCl (30 mL), saturated aqueous $NaHCO_3$ and brine. The organic layer was dried and concentrated. Purification over silica gel (CH_2Cl_2: MeOH / 20:1) provided the product as a white powder (0.386 g, 76%). R_f: 0.25. mp 169-171 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 1.96 (s, 3H, CH_3), 3.22 (B of ABX, Jab = 14.04 Hz, Jbx = 5.8, 6.2 Hz, 1H, CH_2), 3.39 (A of ABX, Jab =14.04 Hz, Jax = 4.6 Hz, 1H, CH_2), 3.75 (s, 3H, OCH_3), 3.82 (qd, J = 16.9 Hz, 5.12 Hz, 2H, CH_2), 4.85 (X of ABX, 1H, CH), 6.40 (t, J = 4.98 Hz, 1H, NH), 6.75 (d, J = 8.82 Hz, 2H, Ph), 6.78 (s, 1H, $CH(Ph)_2$), 7.04 (d, J = 7.52 Hz, 1H, NH), 7.25-7.35 (m, 12H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): 22.7 (CH/CH_3), 37.7 (C/CH_2), 42.8 (C/CH_2), 52.5 (CH/CH_3), 55.2 (CH/CH_3), 78.4 (CH/CH_3), 114.6 (CH/CH_3), 124.5 (C/CH_2), 126.9 (CH/CH_3), 127.9 (CH/CH_3), 128.0 (CH/CH_3), 128.4 (CH/CH_3), 134.1 (CH/CH_3), 139.1 (C/CH_2), 139.3 (C/CH_2), 139.5 (C/CH_2), 159.3 (C/CH_2), 168.9 (C/CH_2), 169.3 (C/CH_2), 170.6 (C/CH_2). IR: 3288, 3064, 1744, 1653, 1534, 1494, 1286, 1246, 1175, 1030, 827, 743, 670 cm^{-1}. HRMS (FAB^+): calculated $C_{27}H_{28}N_2O_5S$ 492.1719, found $[M^+ + H]$ 493.1796.

Synthesis of 2-(2-Acetylamino-acetylamino)-3-(4-methoxy-benzenesulfinyl)-propionic Acid Benzhydryl Ester (16). The same procedure was followed as given for compound **7** (93%, 2 diastereomers). mp 54-56 ^oC. ^1H NMR (500 MHz, $CDCl_3$): δ 2.01 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 3.16-3.23 (m, 2H, CH_2), 3.31-3.39 (m, 2H, CH_2), 3.84 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.88-4.03 (m, 4H, CH_2), 4.90 (q, J = 6.03 Hz, 1H, CH), 5.01-5.06 (m, 1H, CH), 6.28-6.31 (m, 2H, NH), 6.86 (s, 1H, $CH(Ph)_2$), 6.94-6.70 (m, 5H, Ph, $CH(Ph)_2$), 7.28-7.77 (m, 26H, Ph, NH); ^{13}C NMR (125 MHz, $CDCl_3$): 23.1 (CH/CH_3), 43.2 (C/CH_2), 49.4 (CH/CH_3), 55.8 (CH/CH_3), 58.0 (C/CH_2), 79.1 (CH/CH_3), 115.2 (CH/CH_3), 126.2 (CH/CH_3), 126.5 (CH/CH_3), 127.2 (CH/CH_3), 127.5 (CH/CH_3), 128.4 (CH/CH_3), 128.7 (CH/CH_3), 133.7 (C/CH_2), 139.3 (C/CH_2), 139.5 (C/CH_2), 162.5 (C/CH_2), 169.0 (C/CH_2), 169.8 (C/CH_2), 171.0 (C/CH_2). IR: 3294.9, 3054.8, 1746.8, 1668.0, 1496.7, 1265.5, 738.1, 703.4 cm^{-1}. HRMS (FAB^+): calculated $C_{27}H_{28}N_2O_6S$ 508.1746, found 508.1747.

Synthesis of 2-(2-Acetylamino-acetylamino)-3-fluoro-3-(4-methoxy-phenylsulfanyl)-propionic Acid Benzhydryl Ester (17). A similar procedure was followed as given for compound **8** (yield 62%). ^1H NMR (400 MHz, $CDCl_3$): δ 2.00 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 3.99 (dd, J = 5.1 Hz, 1.2 Hz, 1H, CH_2), 4.04 (d, J= 5.1 Hz, 1H, CH_2), 5.24-5.33 (m, 1H, CH), 5.94 (dd, J=52.8 Hz, 3.5 Hz, 0.5 H, CHF), 6.09 (dd, J=53.7 Hz, 2.6 Hz, 0.5 H, CHF), 6.17 (1H, NH), 6.80 (1H, NH), 6.84 (d, J=6.9 Hz, 2H, Ph), 6.97 (s, 1H, $CH(Ph)_2$), 7.27-7.44 (m, 12H, Ph);^{13}C NMR (125 MHz, $CDCl_3$): 23.1 (CH/CH_3), 43.4 (C/CH_2), 55.6 (CH/CH_3), 56.3 (CH/CH_3), 79.7 (CH/CH_3), 102.2 ($^1J_{C-F}$ = 229 Hz, CH/CH_3), 115.1 (CH/CH_3), 128.6 (CH/CH_3), 128.8 (CH/CH_3), 135.8 (CH/CH_3), 139.2 (C/CH_2), 160.8 (C/CH_2), 166.7 (C/CH_2), 166.9 (C/CH_2), 169.2 (C/CH_2), 169.6 (C/CH_2), 170.7 (C/CH_2); ^{19}F NMR (376 MHz, $CDCl_3$): (2 diastereomers) δ -155.6 (dd, J= 54.4 Hz, 14.2 Hz, CHF), -157.4 (dd, J= 54.7 Hz, 25.6 Hz, CHF). IR: 3416.6, 3054.9, 1750.1, 1671.2, 1495.7, 1265.6, 737.0, 704.4 cm^{-1}. HRMS (FAB^+): calculated $C_{27}H_{27}N_2O_5SF$ 510.1703, found $[M^+ + H]$ 511.1703.

Synthesis of 2-(2-Acetylamino-acetylamino)-3-fluoro-acrylic Acid Benzhydryl Ester (18). The same procedure was followed as given for compound **10** (yield 57%). (*E* isomer): ^1H NMR (400 MHz, $CDCl_3$): δ 2.03 (s, 3H, CH_3), 3.99 (d, J = 5.47 Hz, 2H, CH_2), 6.20 (bs, 1H, NH), 7.00 (s, 1H, $CH(Ph)_2$), 7.30-7.41 (m, 10H, Ph), 7.80 (s, 1H, NH), 8.50 (d, J = 78.4 Hz, 1H, CHF); ^{13}C NMR (125 MHz, $CDCl_3$): 23.1 (CH/CH_3), 44.1 (C/CH_2), 79.6 (CH/CH_3), 116.3 (d, $^2J_{CF}$ = 18.7 Hz, C/CH_2), 127.2 (CH/CH_3), 128.4 (CH/CH_3), 128.9 (CH/CH_3), 140.2 (d, $^1J_{CF}$ = 275 Hz, C/CH_2), 140.5 (C/CH_2), 162.2 (C/CH_2); 167.3 (C/CH_2), 171.1 (C/CH_2); ^{19}F NMR (376 MHz, $CDCl_3$): δ -127.0 (d, J= 78.4 Hz, CHF).

IR: 3283, 1659, 1527, 1374, 1269, 1225, 1183, 1144, 699 cm^{-1}. (*Z* isomer): ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.04 (s, 3H, CH_3), 4.05 (d, J = 5.28 Hz, 2H, CH_2), 6.43 (bs, 1H, NH), 6.93 (s, 1H, $CH(Ph)_2$), 7.30-7.37 (m, 10H, Ph), 7.60 (d, J = 74.50 Hz, 1H, CHF), 7.79 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): 23.1 (CH/CH_3), 43.9 (C/CH_2), 78.8 (CH/CH_3), 119.2 (d, $^{2}J_{CF}$ = 5.63 Hz, C/CH_2), 127.4 (CH/CH_3), 128.6 (CH/CH_3), 128.9 (CH/CH_3), 139.4 (C/CH_2), 157.0 (d, $^{1}J_{CF}$ = 330 Hz, CH/CH_3), 162.8 (d, $^{3}J_{CF}$ = 17.4 Hz, C/CH_2), 167.4 (C/CH_2), 171.2 (C/CH_2); ^{19}F NMR (376 MHz, $CDCl_3$): δ -113.9 (d, J= 76.09 Hz, CHF). IR: 3282, 1732, 1664, 1654, 1522, 1497, 1266, 1098, 699 cm^{-1}. HRMS (FAB^{+}), calculated $C_{20}H_{19}N_2O_4F$ 370.1329, found $[M^{+}+H]$ 371.1406.

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