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Chemistry & Drug Discovery

Supporting Information

Supplementary Material

The stereochemical descriptors (R or S) were assigned according to the Cahn-Ingold-Prelog system (*Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 567) following the path of the higher priority atom (e.g. -NC=O higher than $–NHCR_2R_3$).

The following abbreviations are used throughout the text:

Me: methyl
Et: ethyl
t-Bu: *tert*-butyl
Ar: aryl
Ph: phenyl
Bn: benzyl
Cbz: benzyloxy carbonyl
EDC : 1-Ethyl-3-(3-dimethylaminopropyl)-carbodiimide
EtOAc: Ethyl Acetate
BOP: benzotriazol-l-yl-oxy-tris-(dimethylamino)phosphonium hexa-fluorophosphate
HOAT: 1-hydroxy-7-azabenzotriazole
HRMS (FT-ICR): high resolution mass spectrometry, Fourier Transform Ion Cyclotron Resonance
THF: tetrahydrofuran
DMSO: dimethylsulfoxide
Boc: tert-butyloxy carbonyl
ES MS Electrospray mass spectrum
TFA: trifluoracetic acid
DMF: N,N-dimethylformamide
rt: room temperature
HPLC: high performance liquid chromatography
LDA: lithium diisopropyamide

Scheme 2 Experimental Details

A solution of N-(*tert*-butoxycarbonyl)glycine **10** (20.0 g, 114 mmol), benzylamine (24.9 mL, 228 mmol), HOAT (15.5 g, 114 mmol), and EDC (43.8 g, 228 mmol) in DMF (75 mL) was stirred at room temperature for 2h. The solution was concentrated *in vacuo* and the residue partitioned between EtOAc (200 mL) and saturated aqueous $NaHCO_3$ (200 mL). The basic aqueous layer was removed and the organic layer washed with water (100 mL), 10% $KHSO_4$ (100 mL), water (100mL) and brine (100 mL). The organic extract was dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give 29.3 g (97% yield) of *tert*-butyl [2-(benzylamino)-2-oxoethyl]carbamate as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.26 (m, 5H), 6.44 (br s, 1H), 5.14 (br s, 1H), 4.46 (d, *J* = 5.9Hz, 2H), 3.82 (d, *J* = 5.9Hz, 2H), 1.43 (s, 9H), ES MS (M+Na) = 287.1.

Hydrogen chloride gas was bubbled into a solution of *tert*-butyl [2-(benzylamino)-2-oxoethyl]carbamate (28.3 g, 107 mmol) in EtOAc (100 mL) at 0 °C until saturated. Stirred reaction 1h, then purged with nitrogen gas and filtered to give 20.8 g (97% yield) of the HCl salt of N-1-benzylglycinamide as a white solid. ^{1}H NMR (400 MHz, CD_3OD) δ 7.34-7.31 (m, 4H), 7.29-7.24 (br m, 1H), 4.86 (s, 2H), 3.71 (s, 2H), ES MS (M+Na) = 165.1.

To a solution of N-1-benzylglycinamide hydrochloride salt (5.0 g, 24.9 mmol) in MeOH (42 mL) were added acetaldehyde (7.1 mL, 125 mmol) and trietyhylamine (2.8 mL, 19.9 mmol). The mixture was heated to reflux over night. The reaction was concentrated *in vacuo* and the crude brown oil treated with CH_2Cl_2. Filtration of the precipitate resulted in the recovery of 740 mg of N-1-benzylglycinamide starting material. The filtrate was purified by flash column chromatography on silica gel using a gradient elution of 0-7% MeOH in CH_2Cl_2. Collection and concentration *in vacuo* of the appropriate fractions afforded 740 mg (16% yield) of 3-benzyl-2-methylimidazolidin-4-one as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.24 (m, 5H), 4.82 (d, *J* = 15.1 Hz, 1H), 4.45 (q, *J* = 5.8 Hz, 1H), 4.12 (d, *J* = 15.1 Hz, 1H), 3.60 (d, *J* = 16.2 Hz, 1H), 3.46 (d, *J* = 16.2 Hz, 1H), 1.29 (d, *J* = 5.8 Hz, 3H), ES MS (M+H) = 191.1.

To a solution of 3-benzyl-2-methylimidazolidin-4-one (740 mg, 3.89 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added benzyl chloroformate (0.33 mL, 2.34 mL) followed by 4-dimethylaminopyridine (0.59 gm, 4.86 mmol) and a second portion of benzyl chloroformate (0.33 mL, 3.89 mmol). After stirring 1h, the reaction was partitioned between aqueous 10% $KHSO_4$ (50 mL) and CH_2Cl_2 (40 mL). The acidic aqueous phase was removed and the organic phase was washed with water (50 mL), brine (50 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to give a crude orange oil. Purification by flash column chromatography on silica gel using a gradient elution of 0-50% EtOAc in hexane and concentration *in vacuo* of the appropriate fractions afforded 745 mg (59% yield) of benzyl 3-benzyl-2-methyl-4-oxoimidazolidine-1-carboxylate as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.30 (m, 9H), 7.24-7.26 (m,

1H), 5.19-5.02 (m, 4H), 4.18-4.12 (m, 1H), 4.03-3.97 (m, 2H), 1.39-1.46 (m, 3H), ES MS (M+H) = 325.1.

Racemic benzyl 3-benzyl-2-methyl-4-oxoimidazolidine-1-carboxylate (700 mg) was resolved using a ChiralPak AS column (5 cm x 50 cm, 20u) with 100% MeOH at 50 mL/m. Concentration *in vacuo* gave the individual enantiomers **11a** and **11b** of benzyl 3-benzyl-2-methyl-4-oxoimidazolidine-1-carboxylate as peak 1 (319 mg) and peak 2 (321 mg) respectively. Peak 1 (**11a**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.30 (m, 9H), 7.24-7.26 (m, 1H), 5.19-5.02 (m, 4H), 4.18-4.12 (m, 1H), 4.03-3.97 (m, 2H), 1.39-1.46 (m, 3H), ES MS (M+H) = 325.1, [a] = +67.0° (Conc. 3.7 mg/mL CH_2Cl_2). Peak 2 (**11b**) : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.30 (m, 9H), 7.24-7.26 (m, 1H), 5.19-5.02 (m, 4H), 4.18-4.12 (m, 1H), 4.03-3.97 (m, 2H), 1.39-1.46 (m, 3H), ES MS (M+H) = 325.1, [a] = -69.2° (Conc. 3.54 mg/mL CH_2Cl_2).

Scheme 3 Experimental Details

A solution of (*S*)-(-)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanal **14** (6.87 g, 27.56 mmol) and (carbethoxymethylene)triphenylphosphine (9.60 g, 27.56 mmol) in toluene (150 mL) was stirred and heated to 80 °C for 70 min. The product was isolated by flash column chromatography on silica gel using a gradient elution of 5-25% EtOAc/hexanes. Collection and concentration of the appropriate fractions yielded the compound as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.22 (m, 3H), 7.19-7.17 (m, 2H), 6.92 (dd, *J* = 4.8, 15.6 Hz, 1H), 5.86 (dd, *J* = 1.6, 15.6 Hz, 1H), 4.62 (br s, 1H), 4.52 (br s, 1H), 4.19 (q, *J* = 7.2, 14.0 Hz, 2H), 2.95-2.90 (m, 2H), 1.40 (s, 9H), 1.30-1.25 (m, 3H); ES MS [M-100 (loss of Boc)+1] = 220.

To a mixture of methanesulfonamide (3.27 g, 34.41 mmol), potassium ferricyanide (III) (33.99 g, 103.23 mmol), potassium osmate (IV) dihydrate (127 mg, 0.34 mmol), and potassium carbonate (14.27 g, 103.23 mmol) in *tert*-butanol (150 mL) and water (75 mL) was added a sonicated solution of hydroquinine 2,5-diphenyl-4,6-pyrimidinediyl diether (DHQ-PYR, 606 mg, 0.69 mmol) in water (75 mL). The mixture was treated with solid ethyl (2*E*,4*S*)-4-[(*tert*-butoxycarbonyl)amino]-5-phenylpent-2-enoate **15** (11.00 g, 34.41 mmol) and stirred at rt overnight. The reaction was cooled to 0 °C and treated with sodium sulfite (50 g). Following stirring for 30 min at 0 °C and 1.5 h at rt, the mixture was extracted with EtOAc (3 x 200 mL). The combined organic layers were washed with brine (200 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford **16** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.23 (m, 5H), 4.81 (d, *J* = 9.2 Hz, 1H), 4.35 (s, 1H), 4.31-4.24 (m, 2H), 4.02-3.94 (m, 2H), 3.79 (br s, 1H), 3.09-3.04 (m, 1H), 2.95-2.90 (m, 1H), 2.66 (br s, 1H), 1.37 (s, 9H), 1.32-1.21 (m, 3H); ES MS (2M+23) = 729.

A solution of Ethyl (2*R*, 3*S*,4*S*)-4-[(*tert*-butoxycarbonyl)amino]-2,3-dihydroxy -5-phenylpentanoate **16** (6.69 g, 18.94 mmol) in CH_2Cl_2 (300 mL) was treated with triethylamine (3.43 mL, 24.62 mmol) and 4-nitrobenzenesulfonyl chloride (4.62 g, 20.84 mmol) and stirred at rt overnight. The reaction mixture was diluted with CH_2Cl_2 (200 mL) and washed with aqueous 1N HCl solution (150 mL) and brine (150 mL). The organic extract was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting residue was purified three times by flash column chromatography on silica gel using gradient elutions of 10-50% EtOAc/hexanes, 20-50% EtOAc/hexanes, and 0-30% EtOAc/hexanes. Collection and concentration of the appropriate fractions yielded Ethyl (2*R*, 3*S*,4*S*)-4-[(*tert*-butoxycarbonyl)amino]-2- *O*-[(4-nitrophenyl)sulfonyl]-3-hydroxy -5-phenylpentanoate as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (dd, *J* = 2.4, 9.2 Hz, 2H), 8.20 (d, *J* = 8.4 Hz, 2H), 7.33-7.19 (m, 5H), 5.28 (s, 1H), 4.67 (d, *J* = 8.0 Hz, 2H), 4.21-4.09 (m, 3H), 3.92-3.85 (m, 1H), 3.00 (d, *J* = 6.0 Hz, 2H), 1.38 (s, 9H), 1.28-1.21 (m, 3H); ES MS (M+23) = 561.

A suspension of sodium azide (2.33 g, 35.89 mmol) in DMF (50 mL) was heated to 50 °C for 20 min. The mixture was treated with a solution of Ethyl (2*R*, 3*S*,4*S*)-4-[(*tert*-butoxycarbonyl)amino]-2- *O*-[(4-nitrophenyl)sulfonyl]-3-hydroxy -5-phenylpentanoate (1.93 g, 3.59 mmol) in DMF (5 mL) and was stirred and heated to 50 °C overnight. The reaction was diluted with EtOAc (80 mL) and washed with water (40 mL) and brine (40 mL). The organic extract was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting residue was purified twice by flash column chromatography on silica gel using a gradient elution of 0-60% EtOAc/hexanes each time. Collection and concentration of the appropriate fractions yielded **17** as a yellow residue. ^{1}H NMR (400 MHz, CD_3OD) δ 7.32-7.27 (m, 2H), 7.24-7.21 (m, 3H), 4.71 (d, *J* = 7.2 Hz, 1H), 4.29 (q, *J* = 7.2, 14.4 Hz, 2H), 4.08-3.94 (m, 4H), 2.99 (dd, *J* = 4.0, 14.0 Hz, 1H), 2.90-2.85 (m, 1H), 1.51-1.31 (m, 12H); ES MS (M+23) = 401.

To a solution of **17** (0.8g, 2.1 mmol) in THF (10 mL) was added aqueous 1N LiOH (2.3mL, 2.3 mmol). The reaction was stirred at 0 °C 10 minutes then quenched by addition of a mixture of 75mL EtOAc and 25 mL 1N HCl. The layers were mixed and separated and the organic layer washed with brine (15 mL), and the organic extract was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford (2*S*, 3*S*,4*S*)-2-azido-4-[(*tert*-butoxycarbonyl)amino]-3-hydroxy -5-phenylpentanoic acid as a yellow residue. ^{1}H NMR (400 MHz, CD_3OD) δ 7.23-7.15 (m, 5H), 4.23-3.87 (m, 3H), 3.21-3.08 (m, 1H), 2.66-2.57 (m, 1H), 1.29 (s, 9H); ES MS (M+23) = 373.

Through a 0 °C solution of (2*S*, 3*S*, ,4*S*)-2-azido-4-[(*tert*-butoxycarbonyl)amino]-3-hydroxy -5-phenylpentanoic acid (15 mg, 0.04 mmol) in 2 mL EtOAc was passed HCl gas for 2 minutes and then the reaction was allowed to stir at 0 °C for 30 minutes then concentrated and the residue dissolved in 1 mL DMF. To this was added Et_3N (5 μL, 0.04 mmol), HOAt (5mg,

0.04mmol), and EDC (11mg, 0.06 mmol). The mixture allowed to stir for 3 hours then concentrated, partitioned between EtOAc (20 mL) and 10% $KHSO_4$ (10 mL), water (10mL) and brine (10 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography (1.5x12cm silica gel 30-60% EtOAc/hexane) afforded 6 mg of **18**. ^{1}H NMR (400 MHz, CD_3OD) δ 7.37-7.28 (m, 3Ar**H**), 7.17 (app d, 2Ar**H**, *J*= 7.0 Hz); 5.72 (br s, N**H**); 4.20 (m, C**H**OH); 3.99 (d, *J*=5.49 Hz, C**H**N_3); 3.77 (m, C**H**CH_2Ph); 3.01 (dd, *J*=14 and 4.9 Hz, C**H**HPh); 2.66 (dd, *J*=14 and 9.0 Hz, C**H**HPh); 2.46 (d, *J*=2.4 Hz, O**H**).

A solution of (2*S*, 3*S*, ,4*S*)-2-azido-4-[(*tert*-butoxycarbonyl)amino]-3-hydroxy -5-phenylpentanoic acid (0.74 g, 2.1 mmol), benzylamine (254 μL, 2.3 mmol), HOAT (72 mg, 0.53 mmol), and EDC (526 g, 2.75 mmol) in DMF (2 mL) was stirred at room temperature overnight. The solution was diluted with EtOAc (200 mL) and washed with 10% $KHSO_4$ (100 mL), water (100mL) and brine (100 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography (90g silica gel 10-100% EtOAc/hexane) afforded 0.6g of (2*S*, 3*S*,4*S*)-2-azido-4-[(*tert*-butoxycarbonyl)amino]-3-hydroxy -*N*-(benzyl)-5-phenylpentanamide amide as a poorly solubly white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4-7.18 (m, 11H), 4.70 (br d, 1H, J=4.22 Hz), 4.54 (dd, 1H, *J*= 5.9 and 14.8 Hz); 4.46 (dd, 1H, *J*= 5.6 and 14.8 Hz); 4.17 (br s, 1H); 3.93 (br s, 2H); 3.00 (dd, 1H, *J*= 14 and 3.8Hz); 2.9 (br dd, 1H); 1.35 (m, 9H), ES MS (M+1) = 440.1.

To a solution of (2*S*, 3*S*,4*S*)-2-azido-4-[(*tert*-butoxycarbonyl)amino]-3-hydroxy -*N*-(benzyl)-5-phenylpentanamide (300 mg, 0.7 mmol) in MeOH (10 mL) which had been degassed and purged with nitrogen was added a small amount of 10% Pd on carbon. The mixture was flushed with hydrogen and stirred overnight under a balloon atmosphere of hydrogen. The reaction was filtered, rinsed with MeOH, and concentrated *in vacuo* to afford **19** as a white solid. ^{1}H NMR (400 MHz, $CDClD_3$) δ 8.01 (br s, 1H); 7.5-7.2 (m, 10H), 4.99 (br d, 1H, *J*=9.34 Hz), 4.82 (br s, 1H); 4.47 (dd, 1H, *J*= 6.0 and 14.8 Hz); 4.40 (dd, 1H, *J*= 5.86 and 14.7 Hz); 4.07 (br s, 1H); 3.77 (br s, 1H); 3.49(d, 1H, *J*=5.31); 3.24(d, 1H, J=6.96Hz); 3.05 (dd, 1H, *J*= 14 and 5.9Hz); 2.87 (dd, 1H, *J*= 14 and 7.7Hz); 1.36 (m, 9H), ES MS (M+1) = 414.1.

To a solution of **19** (100 mg, 0.24 mmol) in MeOH (1.5 mL) were added acetaldehyde (0.20 mL, 4.8 mmol) and *p*-toluene sulfonic acid monohydrate (2.3mg, 0.01mmol). The mixture was heated in a sealed vessel to 160 °C for 5 minutes in a microwave reactor. The reaction was concentrated, diluted with EtOAc (50 mL), washed with saturated aqueous $NaHCO_3$ solution (25mL) and brine (25mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting residue was purified by flash column chromatography on silica gel (1.5x10cm) using a gradient elution of 40-90% EtOAc/hexanes gave 50mg of a 2:1 mixture of **22a** and **13d**. Further purification by reverse-phase chromatography (Gemini C_{18} column, gradient elution of 40% MeOH (0.05% NH_4OH) /H_2O (0.05% NH_4OH)) was required to separate diastereomers. **22a** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.5-7.2 (m, 10H), 5.43 (d, *J* = 8.97 Hz, 1H), 4.84 (d, *J* = 15

Hz, 1H), 4.36 (br s, 1H), 4.18 (br s, 1H), 4.11 (d, *J* = 15 Hz, 1H), 3.85 (br m, 1H), 3.53 (d, *J* = 7.32 Hz, 1H), 2.98 (dd, *J* = 13 and 5.9 Hz 1H), 2.90 (dd, *J* = 13 and 8.1 Hz, 1H), 1.35 (s, 9H), 1.26 (d, *J* = 5.77 Hz, 3H); **13d**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 3H), 7.20 (m, 2H); 5.32 (d, *J* = 9.5 Hz, 1H), 4.79 (d, *J* = 15 Hz, 1H), 4.38 (br q, *J*=5.37 Hz, 1H), 4.15 (m, 2H), 4.06 (d, *J* = 15 Hz, 1H), 3.80 (br m, 1H), 3.60 (d, *J* = 8.3 Hz, 1H), 3.01 (dd, *J*=14 and 6.59 Hz, 1H), 2.90 (dd, *J*=13 and 7.08 Hz, 1H), 1.37 (s, 9H), 1.11 (d, *J* = 5.62 Hz, 3H); HRMS (FT-ICR) $C_{25}H_{33}N_3O_4$+H = 440.2588; calculated 440.2544

A suspension of **17** (280 mg, 0.64 mmol) in EtOAc (50 mL) was cooled to 0 °C and treated with HCl gas for 5 min. The resulting solution was stirred for 1 h at 0 °C and concentrated *in vacuo* to afford (2*S*, 3*S*,4*S*)-2-azido-4-amino-3-hydroxy -*N*-(benzyl)-5-phenylpentanamide amide as a white solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.89 (t, *J* = 5.6 Hz, 1H), 7.89 (br s, 3H), 7.38-7.20 (m, 10H), 6.28 (d, *J* = 6.4 Hz, 1H), 4.38 (dddd, *J* = 6.0, 15.2, 20.8, 28.0 Hz, 2H), 4.25-4.21 (m, 1H), 3.95 (d, *J* = 8.8 Hz, 1H), 3.02 (dd, *J* = 4.0, 14.4 Hz, 1H), 2.78 (dd, *J* = 9.2, 14.8 Hz, 1H); ES MS (M+1) = 340.

To a solution of (2*S*, 3*S*,4*S*)-2-azido-4-amino-3-hydroxy -*N*-(benzyl)-5-phenylpentanamide amide hydrochloride salt (240 mg, 0.6 mmol) in CH_2Cl_2 (100 mL) at 0 °C was added phenyl chloroformate (80 μL, 0.64 mmol) and triethylamine (220 μL, 1.6 mmol). The reaction was stirred for 30 min at and diluted with CH_2Cl_2 (200 mL). The resulting mixture was washed with 10% aqueous $KHSO_4$ solution and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford the product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.23 (m, 11H), 7.20-7.16 (m, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 5.35 (d, *J* = 8.4 Hz, 1H), 4.53 (dd, *J* = 6.0, 15.2 Hz, 1H), 4.43 (dd, *J* = 5.6, 14.8 Hz, 1H), 4.13-4.04 (m, 3H), 4.01 (d, *J* = 4.0 Hz, 1H), 3.11-2.99 (m, 2H); ES MS (M+1) = 460.

A suspension of (2*S*, 3*S*,4*S*)-2-azido-4-[(phenyloxycarbonyl)amino]-3-hydroxy -*N*-(benzyl)-5-phenylpentanamide (280 mg, 0.6 mmol) in MeOH (50mL) was flushed with nitrogen gas and treated with 50 mg of 10% palladium on carbon and bubbling hydrogen gas for 3 h. The mixture was filtered through celite, and the resulting filtrate was concentrated *in vacuo* to afford **21**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.34-7.18 (m, 13H), 7.00 (m, 2H), 5.63 (d, *J* = 9.2 Hz, 1H), 4.45 (m, 3H), 4.21 (m, 1H); 3.91 (m, 1H), 3.30 (br d, J=7.5Hz, 1H); 3.13 (dd, *J* = 6.2, 14 Hz, 1H), 2.98 (dd, *J* = 7.5, 14 Hz, 1H), HRMS (FT-ICR) $C_{25}H_{27}N_3O_4$+H = 434.2051; calculated 434.2075.

To a solution of **21** (49 mg, 0.113 mmol) in MeOH were added isobutyraldehyde (82 mg, 1.130 mmol) and a small amount of *p*-toluene sulfonic acid. The mixture was heated to reflux overnight. The reaction was diluted with EtOAc (20 mL), washed with saturated aqueous $NaHCO_3$ solution, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting residue was purified by flash column chromatography on silica gel using a gradient elution of 15-50% EtOAc/hexanes.

Collection and concentration of the appropriate fractions afforded a white solid which was purified again by reverse phase chromatography on a C-18 column using a gradient elution of 95-5% H_2O (0.1% TFA)/CH_3CN (0.1% TFA) to give **22d** as the earlier eluting (minor) diastereomer which was partitioned between EtOAc and saturated $NaHCO_3$ solution. The organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford **22d** in free base form. ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.16 (m, 13H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.02 (d, *J* = 8.8 Hz, 1H), 4.92 (d, *J* = 15.2 Hz, 1H), 4.31-4.29 (m, 2H), 4.18 (t, *J* = 2.0 Hz, 1H), 3.92 (d, *J* = 15.2 Hz, 1H), 3.86 (dd, *J* = 3.6, 8.8 Hz, 1H), 3.54 (dd, *J* = 2.0, 8.8 Hz, 1H), 3.16 (dd, *J* = 8.0, 14.0 Hz, 1H), 3.00 (dd, *J* = 5.6, 14.0 Hz, 1H), 1.89-1.85 (m, 1H), 0.71 (d, *J* = 7.2 Hz, 3H), 0.52 (d, *J* = 6.8 Hz, 3H); HRMS (FT-ICR) $C_{29}H_{33}N_3O_4$+H = 488.2534; calculated 488.2544.