Suporting information (SI) for

Novel potent and selective thrombin inhibitors based on a central 1,4-benzoxazin-3(4*H*)-one scaffold

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Contents:

Synthetic procedures and spectral data:

*(E)-4-((4-Methyl-7-nitro-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-2-ylidene)methyl)benzonitrile (**2b**)*: Prepared as described in synthesis of *4-((4-Methyl-7-nitro-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-2-ylidene)methyl)benzonitrile (**2**).* Yield: 30 mg (3.2 %), m.p 209-211 °C. MS (EI): *m/z* (%) 321 (M^+, 100). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ = 3.45 (s, 3H, *N*-CH_3), 6.84 (s, 1H, C=CH), 7.44 (d, 1H, ^3J = 9.0 Hz, Ar-H^5), 7.86 (d, 2H, ^3J = 8.4 Hz, Ar-$H^{2'}$,$H^{6'}$), 8.04 (dd, 1H, ^4J = 2.5 Hz, ^3J = 9.0 Hz, Ar-H^6), 8.13 (d, 2H, ^3J = 8.4 Hz, Ar-$H^{3'}$,$H^{5'}$), 8.31 (d, 1H, ^4J = 2.5 Hz, Ar-H^8), ppm. ^{1}H-NMR (DMSO-d_6, 300 MHz): δ = 156.31 (C-3), 143.36 (C-8a), 143.04 (C-2), 141.28 (C-7), 138.33 (C-1'), 134.27 (C-4a), 133.31 (C-3', C-5'), 131.52 (C-2', C-6'), 120.34 (C-6), 119.75 (CN), 116.45 (C-5), 112.05 (C-8), 111.19, 111.10 (C-4', C=CH), 30.11 (*N*-Me) ppm. Anal. ($C_{17}H_{11}N_3O_4$) C, H, N.

*4-((7-Amino-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-2-yl)methyl)benzonitrile (**3**).* ^{13}C-NMR (DMSO-d_6, 75 MHz): δ = 163.48 (C-3), 145.40 (C-7), 143.95 (C-8a), 143.05 (C-1'), 131.82 (C-3', C-5'), 130.40 (C-2', C-6'), 118.85 (C-4a), 118.78 (CN), 115.68 (C-5), 109.21 (C-1'), 107.89 (C-6), 102.20 (C-8), 76.24 (CH), 35.75 (CH_2), 27.94 (*N*-Me) ppm.

*(E)-4-((7-Amino-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-2-ylidene)methyl)benzonitrile (**3a**).* ^{13}C-NMR (DMSO-d_6, 75 MHz): δ = 155.16 (C-3), 146.68 (C-7), 144.74 (C-2), 142.14 (C-8a), 139.24 (C-1'), 133.20 (C-3', C-5'), 130.68 (C-2', C-6'), 119.82 (CN), 117.13 (C-4a), 116.67 (C-5), 110.39, 110.21 (C-4', C-6), 109.19 (C=CH), 101.64 (C-8), 29.42 (*N*-Me) ppm.

*Methyl 3-(benzyl(2-(4-cyanobenzyl)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-yl)amino)-3-oxopropanoate (**5b**).* Prepared according to the *General procedure for the synthesis of N-acyl-4-((7-(benzylamino)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-2-yl)methyl)benzonitriles **5a**, **5b** and **5c***. Colorless hygroscopic oil, yield: 89.0 %. MS (FAB): *m/z* (%) = 484 (MH^+, 51), 57 (100). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 3.20 (dd, 1H, ^3J = 8.1 Hz, ^2J = 14.4 Hz, CH-$\underline{CH_2}$), 3.26 (s, 2H, CO-$\underline{CH_2}$-CO), 3.31-3.37 (m, 4H, *N*-CH_3, CH-$\underline{CH_2}$), 3.71 (s, 3H, COO$\underline{CH_3}$), 4.76-4.81 (m, 2H, 2-H, Ph-$\underline{CH_2}$-*N*), 5.02 (d, 1H, ^2J = 14.4 Hz, Ph-$\underline{CH_2}$-*N*), 6.64 (d, 1H, ^4J = 2.1 Hz, Ar-H^8), 6.71 (dd, 1H, ^4J = 2.1 Hz, ^3J = 8.7 Hz, Ar-H^6), 6.84 (d, 1H, ^3J = 8.7 Hz, Ar-H^5), 7.22-7.32 (m, 7H, Ph, Ar-$H^{2'}$,$H^{6'}$), 7.56 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{3'}$, $H^{5'}$) ppm. Anal. ($C_{28}H_{25}N_3O_5 \times 2/3\ H_2O$) C, H, N.

*Ethyl 4-(benzyl(2-(4-cyanobenzyl)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-yl)amino)-4-oxobutanoate (**5c**).* Prepared according to the *General procedure for the synthesis of N-acyl-4-((7-(benzylamino)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-2-yl)methyl)benzonitriles **5a**, **5b** and **5c***. Colorless oil, yield: 76.9 %. MS (EI): *m/z* (%) = 511 (M^+, 61), 383 (100). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 1.25 (t, 3H, ^3J = 7.2 Hz, -CH_2-$\underline{CH_3}$), 2.36 (t, 2H, ^3J = 6.6 Hz, *N*-CO-$\underline{CH_2}$-CH_2-COO), 2.65 (m, 2H, *N*-CO-CH_2-$\underline{CH_2}$-CO0), 3.17 (dd, 1H, ^3J = 8.4 Hz, ^2J = 14.4 Hz, CH-$\underline{CH_2}$), 3.29-3.35 (m, 4H, *N*-$\underline{CH_3}$, CH-$\underline{CH_2}$), 4.13 (q, 2H, *J* = 7.2 Hz, -$\underline{CH_2}$-CH_3), 4.75 (m, 2H, 2-H, Ph-$\underline{CH_2}$-*N*), 4.98 (d, 1H, ^2J = 14.4 Hz, Ph-$\underline{CH_2}$-*N*), 6.64 (d, 1H, ^4J = 1.8 Hz, Ar-H^8), 6.72 (dd, 1H, ^4J = 1.8 Hz, ^3J = 8.4 Hz, Ar-H^6), 6.83 (d, 1H, ^3J = 8.4 Hz, Ar-H_5), 7.17-7.28 (m, 5H, Ph), 7.29 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{2'}$,$H^{6'}$), 7.54 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{3'}$,$H^{5'}$) ppm. Anal. ($C_{30}H_{29}N_3O_5$) HRMS.

*Methyl 2-benzyl-3-(2-(4-cyanobenzyl)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-ylamino)-3-oxopropanoate (**5d**).* A solution of amine **3** (403 mg, 1.38 mmol), 2-benzyl-3-

methoxy-3-oxopropanoic acid (286 mg, 1.38 mmol) and HOBt (223 mg, 1.65 mmol) in DMF (40 mL) was prepared and pH was adjusted to 7 with *N*-methylmorpholine. EDC (343 mg, 1.79 mmol) was added and the reaction mixture was stirred overnight at room temperature. The solvent was evaporated in vacuo, and the oily residue was dissolved in ethyl acetate (100 mL) and washed successively with 10 % citric acid (2 × 50 mL), saturated $NaHCO_3$ solution (2 × 50 mL) and brine (1 × 50 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. The crude product was purified with column chromatography using petroleum ether/ethyl acetate (1:1) as eluant. Compound **5d** was obtained as yellow crystals. Yield: 457 mg (66.9 %), m.p. 64-66 °C. MS (EI): *m/z* (%) = 483 (M^+, 99), 91 (100). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ = 3.11-3.34 (m, 7H, Ph-$\underline{CH_2}$-CH-, *N*-$\underline{CH_3}$, 4-CN-Ar'-$\underline{CH_2}$), 3.64 (s, 3H, $\underline{CH_3}$-O-), 3.79 (t, 1H, ^3J = 7.6 Hz, -CO-$\underline{CH}$-CO-), 4.94 (m, 1H, 2-H), 7.05-7.29 (m, 8H, Ph, Ar-H^5, Ar-H^6, Ar-H^8), 7.48 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{2'}$,$H^{6'}$), 7.76 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{3'}$,$H^{5'}$), 10.1 (s, 1H, -CO-$\underline{NH}$-Ar) ppm. Anal. ($C_{28}H_{25}N_3O_5$) C, H, N.

*Methyl 3-(benzyl(2-(4-carbamimidoylbenzyl)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-yl)amino)-3-oxopropanoate trifluoroacetate (**6b**)*. Prepared according to the *General procedure for the synthesis of N-acyl-4-((7-(benzylamino)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-2-yl)methyl)benzimidamides **6a-6d***. White powder, yield: 42.1 %, m.p. 198-200 °C. MS (FAB): *m/z* (%) = 501 (MH^+, 54), 73 (100). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ = 3.11 (dd, 1H, ^3J = 8.4 Hz, ^2J = 14.4 Hz, CH-$\underline{CH_2}$), 3.26-3.39 (m, 6H, *N*-$\underline{CH_3}$, CO-$\underline{CH_2}$-CO, CH-$\underline{CH_2}$), 3.56 (s, 3H, COO$\underline{CH_3}$), 4.80 (d, 1H, ^2J = 15.0 Hz, Ph-$\underline{CH_2}$-*N*), 4.90 (d, 1H, ^2J = 15 Hz, Ph-$\underline{CH_2}$-*N*), 5.00 (dd, 1H, ^4J = 3.9 Hz, ^3J = 8.4 Hz, 2-H), 6.74 (d, 1H, ^4J = 2.1 Hz, Ar-H^8), 6.90 (dd, 1H, ^4J = 2.1 Hz, ^3J = 8.4 Hz, Ar-H^6), 7.13 (d, 1H, ^3J = 8.4 Hz, Ar-H^5), 7.20-7.33 (m, 5H, Ph), 7.44 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{2'}$,$H^{6'}$), 7.73 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{3'}$,$H^{5'}$), 9.13 (br

s, 2H, amidino-H), 9.28 (br s, 2H, amidino-H) ppm. HPLC: 98.7 %, t_r = 16.90 min. Anal. ($C_{28}H_{28}N_4O_5\times CF_3COOH$) C, H, N.

*Ethyl 4-(benzyl(2-(4-carbamimidoylbenzyl)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-yl)amino)-4-oxobutanoate trifluoroacetate (**6c**).* Prepared according to the *General procedure for the synthesis of N-acyl-4-((7-(benzylamino)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-2-yl)methyl)benzimidamides **6a-6d**.* Gray thick oil, yield: 49.8 %. MS (FAB): *m/z* (%) = 528 (M^+, 83), 69 (100). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ = 1.16 (t, 3H, ^3J = 6.9 Hz, -CH_2-$\underline{CH_3}$), 2.34 (m, 2H, *N*-CO-$\underline{CH_2}$-CH_2-COO), 2.50 (m, 2H, *N*-CO-$\underline{CH_2}$-CH_2-COO, signal overlapped with signal of DMSO), 3.12 (dd, 1H, ^3J = 8.7 Hz, ^2J = 14.1 Hz, CH-$\underline{CH_2}$), 3.30-3.40 (m, 4H, *N*-$\underline{CH_3}$, CH-$\underline{CH_2}$), 4.03 (q, 2H, ^3J = 6.9Hz, -$\underline{CH_2}$-CH_3), 4.77 (d, 1H, ^2J = 15.0 Hz, Ph-$\underline{CH_2}$-*N*), 4.87 (d, 1H, ^2J = 15.0 Hz, Ph-$\underline{CH_2}$-*N*), 5.01 (m, 1H, 2-H), 6.73 (d, 1H, ^4J = 1.5 Hz, Ar-H^8), 6.90 (dd, 1H, ^4J = 1.5 Hz, ^3J = 8.4 Hz, Ar-H^6), 7.13-7.31 (m, 6H, Ar-H^5, Ph), 7.44 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{2'}$,$H^{6'}$), 7.72 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{3'}$,$H^{5'}$), 9.06 (br s, 2H, amidino-H), 9.26 (br s, 2H, amidino-H) ppm. HPLC: 96.3 %, t_r = 18.51 min. Anal. ($C_{30}H_{32}N_4O_5$) HRMS.

*Methyl 2-benzyl-3-(2-(4-carbamimidoylbenzyl)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-ylamino)-3-oxopropanoate trifluoroacetate (**6d**).* Prepared according to the *General procedure for the synthesis of N-acyl-4-((7-(benzylamino)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-2-yl)methyl)benzimidamides **6a-6d**.* White powder, yield: 35.8 %, m.p. 149-152°C. MS (FAB): *m/z* (%) = 501 (MH^+, 49), 55 (100). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ = 3.12-3.20 (m, 3H, Ph-$\underline{CH_2}$-CH-, 4-CN-Ar'-$\underline{CH_2}$), 3.26 (s, 3H, *N*-CH_3), 3.34 (1H, s, 4-CN-Ar'-$\underline{CH_2}$, signal overlapped with water), 3.63 (s, 3H, $\underline{CH_3}$-O-), 3.84 (t, 1H, ^3J = 7.5 Hz, -CO-$\underline{CH}$-CO-), 4.95 (dd, 1H, ^4J = 4.3 Hz, ^3J = 8.8 Hz, 2-H), 7.02-7.11 (m, 2H, Ar-H^5, Ar-H^8),

7.17-7.32 (m, 6H, Ph, Ar-H^6), 7.54 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{2'}$,$H^{6'}$), 7.76 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{3'}$,$H^{5'}$), 9.03 (br s, 2H, amidino-H), 9.29 (br s, 2H, amidino-H), 10.26 (s, 1H, -CO-NH-Ar) ppm. HPLC: 95.0 %, t_r = 17.84 min. Anal. ($C_{28}H_{28}N_4O_5 \times CF_3COOH$) C, H, N.

*3-(Benzyl(2-(4-carbamimidoylbenzyl)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-yl)amino)-3-oxopropanoic acid (**7b**).* Prepared according to the *General procedure for alkaline hydrolysis of alkyl esters **6a-d**.* Gray hygroscopic oil, yield: 40.3 %. MS (ESI): *m/z* (%) = 487.20 (MH^+, 20), 469.33 (60), 457.27 (100). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ = 3.01 (s, 3H, *N*-CH_3) 3.15-3.23 (m, 4H, CH-CH_2, CO-CH_2-CO), 4.78-4.97 (m, 3H, Ph-CH_2-*N*, H-2), 6.82 (d, 1H, ^4J = 2.1 Hz, Ar-H^8), 7.03 (d, 1H, ^3J = 8.7 Hz, Ar-H^5), 7.19-7.34 (m, 8H, Ph, Ar-$H^{2'}$,$H^{6'}$, Ar-H^6), 7.77 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{3'}$,$H^{5'}$), 9.13 (br s, 2H, amidino-H), 9.28 (br s, 2H, amidino-H) ppm. HPLC: 98.4 %, t_r = 18.78 min. Anal. ($C_{27}H_{26}N_4O_5$) HRMS.

*4-(Benzyl(2-(4-carbamimidoylbenzyl)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-yl)amino)-4-oxobutanoic acid (**7c**).* Prepared according to the *General procedure for alkaline hydrolysis of alkyl esters **6a-d**.* White powder, yield: 82.3 %, m.p. > 300 °C. MS (ESI): *m/z* (%) = 501.2 (MH^+, 100). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ = 2.34 (m, 2H, *N*-CO-CH_2-CH_2-COOH), 2.51 (m, 2H, *N*-CO-CH_2-CH_2-COOH, signal overlapped with signal of DMSO), 3.05-3.40 (m, 5H, *N*-CH_3, CH-CH_2-), 4.77 (d, 1H, ^2J = 15.0 Hz, Ph-CH_2-*N*), 4.83 (d, 1H, ^2J = 15.0 Hz, Ph-CH_2-*N*), 5.01 (dd, 1H, *J* = 3.4 Hz, *J* = 8.4 Hz, 2-H), 6.80 (d, 1H, ^4J = 1.8 Hz, Ar-H^8), 6.90 (dd, 1H, ^4J = 1.8 Hz, ^3J = 8.7 Hz, Ar-H^6), 7.10 (d, 1H, ^3J = 8.7 Hz, Ar-H^5), 7.19-7.32 (m, 5H, Ph), 7.39 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{2'}$,$H^{6'}$), 7.77 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{3'}$,$H^{5'}$), 9.28 (br s, 2H, amidino-H), 10.78 (s, 2H, amidino-H) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz): δ = 176.39 (NH-CO-CH_2-CH_2-COOH), 171.82 (NH-CO-CH_2-CH_2-COOH), 165.69 (C=NH(NH_2)), 164.35 (C-3), 143.02 (C-8a), 142.21 (C-1'), 137.72 (C-7), 137.62 (Ph), 129.88

(C-2', C-6'), 128.18 (C-4a), 127.65 (Ph), 127.57 (Ph, C-4'), 126.88 (C-3', C-5'), 126.81 (Ph), 122.43 (C-6), 116.51 (C-5), 115.56 (C-8), 76.37 (C-2), 51.74 (Ph-$\underline{C}H_2$-), 35.80 (2-$\underline{C}H_2$), 31.65 (NH-CO-CH_2-$\underline{C}H_2$-COOH), 29.83 (NH-CO-$\underline{C}H_2$-CH_2-COOH), 28.07 (*N*-Me) ppm. HPLC: 96.2 %, t_r = 16.95 min. Anal. ($C_{28}H_{29}N_4O_5$) HRMS.

*2-Benzyl-3-(2-(4-carbamimidoylbenzyl)-4-methyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazin-7-ylamino)-3-oxopropanoic acid (**7d**).* Prepared according to the *General procedure for alkaline hydrolysis of alkyl esters **6a-d**.* White powder, yield: 74.3 %. MS (FAB): *m/z* (%) = 487 (MH^+, 43), 154 (100). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ = 3.06-3.10 (m, 2H, Ph-$\underline{CH_2}$-CH), 3.16 (d, 1H, ^2J = 13.5 Hz, Ph-$\underline{CH_2}$-), 3.20 (d, 1H, ^2J = 13.5 Hz, Ph-$\underline{CH_2}$-), 3.27 (3.28) (s, 3H, *N*-CH_3), 3.36 (d, 1H, ^2J = 13.5 Hz, Ph-$\underline{CH_2}$-), 3.40 (4.11) (dd, 1H, ^3J = 5.1 Hz, ^2J = 10.2 Hz, -CO-$\underline{CH}$-CO-), 4.87 (5.00) (dd, 1H, ^4J = 3.3 Hz, ^3J = 8.7 Hz, 2-H), 7.03-7.07 (m, 2H, Ar-H^5, Ar-H^8), 7.11-7.21 (m 5H, Ph), 7.29-7.35 (m, 1H, Ar-H^6), 7.53 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{2'}$,$H^{6'}$), 7.76 (d, 2H, ^3J = 8.1 Hz, Ar-$H^{3'}$,$H^{5'}$), 8.99 (br s, 2H, amidino-H), 10.16 (s, 1H, -CO-$\underline{NH}$-Ar), 11.26 (br s, 2H, amidino-H) ppm. HPLC: 98.7 %, t_r = 16.15 min. Anal. ($C_{27}H_{26}N_4O_5 \times 2\ H_2O$) C, H, N.

Molecular docking: Automated docking was used to determine the orientation of inhibitors bound in the active site of thrombin. A genetic algorithm method, implemented in the program AutoDock 3.0, was employed.[1] The structures of inhibitors were prepared with HyperChem 7.5, using the semi-empirical method MNDO.[2] All amide bonds were *trans* and were marked as non-rotatable. Compounds were protonated on the basic centre (amidino group) and assigned planar structure and marked as non-rotatable. Compounds **7a-d** were assigned a negative charge on the acidic centre (carboxylic group). The crystal structure of thrombin was obtained from the RCSB protein database (PDB entry: **1KTS**)[3] and the

inhibitor and all water molecules were removed. Polar hydrogen atoms were added and Kollman charges,[4] atomic solvation parameters and fragmental volumes were assigned to the protein using AutoDock Tools (ADT). For docking calculations, Gasteiger-Marsili partial charges[5] were assigned to the ligands and nonpolar hydrogen atoms were merged. The grid map, which was centred on the enzyme active site, was generated with AutoGrid. The grid dimensions were large enough (22 × 22 × 22 Å) to cover the inhibitors and the enzyme active site. Lennard-Jones parameters 12-10 and 12-6, supplied with the program, were used for modelling H-bonds and van der Waals interactions, respectively. The distance-dependent dielectric permittivity of Mehler and Solmajer[6] was used to calculate the electrostatic grid maps. Random starting points, orientations, and torsions were used for all ligands. The translation, quaternion, and torsion steps were taken from default values in AutoDock. The Lamarckian genetic algorithm and the pseudo-Solis and Wets methods were applied for minimization, using default parameters. The number of docking runs was 250, the population in the genetic algorithm 250, the number of energy evaluations 500 000, and the maximum number of iterations 27 000. Ligands with RMSD less than 1 Å were joined in clusters. For the interpretation of docking results the ligand with the lowest docked energy was chosen.

References

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IR data for all compounds.

All IR spectra were recorded as KBr discs.

Compd	∂ (cm^{-1})
2a	3066, 2221, 1688, 1638, 1599, 1522, 1377, 1320,1172, 877, 740
2b	2220, 1684, 1638, 1529, 1386, 1328, 1160, 1076, 871, 817, 740
3	3453, 3340, 2230, 1662, 1516, 1423, 1304, 1185, 1058, 795, 600
3a	3356, 2220, 1663, 1600, 1518, 1393, 1310, 1202, 870, 797, 602
4	3248, 2221, 1668, 1630, 1522, 1395, 1202, 1050, 825, 735
5a	3444, 2228, 1741, 1670, 1512, 1388, 1190, 1018, 700
5b	3471, 2950, 2227, 1744, 1657, 1512, 1386, 1182, 817, 700
5c	3414, 1635, 1616, 1512, 1387, 1174, 619
5d	3317, 2227, 1744, 1678, 1514, 1392, 1051, 808, 700
6a	3441, 1740, 1668, 1514, 1368, 1203, 1120, 578
6b	3310, 3084, 1746, 1695, 1645, 1512, 1393, 1205, 1135, 831, 723
6c	3108, 1665, 1512, 1392, 1292, 1179, 800
6d	3371, 1743, 1677, 1612, 1513, 1394, 1196, 698
7a	3414, 1652, 1616, 1511, 1419, 1419, 1393, 1352, 1290, 1184, 1141, 1056, 696
7b	3441, 1982, 1532, 1489, 1211, 1122, 802, 726
7c	3872, 2921, 2844, 1633, 1552, 1540, 1384, 1124, 1027, 988, 723
7d	3368, 1667, 1514, 1392, 1147, 1055, 700

Elemental Analysis Data and HRMS data.

Compd	Formula	Composition (calculated)			Composition (found)		
		%C	%H	%N	%C	%H	%N
2a	$C_{17}H_{11}N_3O_4$	63.55	3.45	13.08	63.64	3.56	13.11
2b	$C_{17}H_{11}N_3O_4$	63.55	3.45	13.08	63.59	3.56	13.13
3	$C_{17}H_{15}N_3O_2$	69.61	5.15	14.33	69.78	5.17	14.06
3a	$C_{17}H_{13}N_3O_2$	70.09	4.50	14.42	70.00	4.59	14.72
4	$C_{24}H_{21}N_3O_2$	75.18	5.52	10.69	75.17	5.67	10.78
5a	$C_{28}H_{25}N_3O_5$	69.55	5.21	8.69	69.38	5.55	8.47
5b	$C_{28}H_{25}N_3O_5 \times 2/3\ H_2O$	67.81	5.31	8.48	68.21	5.41	8.08
5c	$C_{24}H_{21}N_3O_2$ (M^+)		511.2107			511.2119	
5d	$C_{28}H_{25}N_3O_5$	69.55	5.21	8.69	69.41	4.97	9.02
6a	$C_{28}H_{28}N_4O_5 \times CF_3COOH \times 5/2\ H_2O$	54.58	5.15	54.94	54.94	4.97	8.12
6b	$C_{28}H_{28}N_4O_5 \times CF_3COOH$	58.63	4.76	9.12	58.49	5.01	8.87
6c	$C_{30}H_{32}N_4O_5$ (M^+)		528.2385			528.2373	
6d	$C_{28}H_{28}N_4O_5 \times CF_3COOH$	58.63	4.76	9.12	58.59	4.86	8.83
7a	$C_{26}H_{25}N_4O_5$ (MH^+)		473.1825			473.1818	
7b	$C_{27}H_{26}N_4O_5$ (M^+)		487.1981			487.1993	
7c	$C_{26}H_{25}N_4O_5$ (MH^+)		501.2138			501.2134	
7d	$C_{27}H_{26}N_4O_5 \times 2\ H_2O$	54.72	4.87	8.81	54.86	4.72	8.78