Supporting Information

Synthesis and biological evaluation of potential bisubstrate inhibitors of protein farnesyltransferase. Design and synthesis of functionalized imidazoles.

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Experimental data of selected compounds

2-[2-(5-Hydroxymethyl-1-methyl-1*H*-imidazol-2-yl)-ethyl)-succinic acid 4-ethyl ester 1-methyl ester (21b).

Prepared according to general procedure A on compound **4b** (180 mg, 0.43 mmol) in THF (4 mL) with TBAF (0.57 mL, 0.57 mmol). After work-up and column chromatography (EtOAc/MeOH 9:1) **21b** (103 mg, 80%) was isolated as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.77 (s, 1H), 4.56 (s, 2H), 4.11 (q, J = 7.0 Hz, 2H), 3.69 (s, 3H), 3.58 (s, 3H), 2.91 (m, 1H), 2.79 (m, 2H), 2.69 (m, 2H), 2.51 (m, 1H), 2.04 (m, 2H), 1.23 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 171.6, 148.3, 131.4, 125.9, 60.7, 54.3, 52.0, 40.6, 36.2, 30.3, 29.3, 24.5, 14.1; IR (KBr) 1055, 1258, 1472, 1735 cm^{-1}; HRMS calcd for $C_{14}H_{23}N_2O_5$ $[M+H]^+$: 299.1607 found: 299.1613.

2-[3-(5-Hydroxymethyl-1-methyl-1*H*-imidazol-2-yl)-propyl)-succinic acid diethyl ester (21c).

Prepared according to general procedure A on compound **4c** (825 mg, 1.88 mmol) in THF (10 mL) with TBAF (2.80 mL, 2.80 mmol). After work-up and column chromatography (CH_2Cl_2/MeOH 9.5:0.5) **21c** (505 mg, 83%) was isolated as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.80 (s, 1H), 4.57 (s, 2H), 4.12 (m, 4H), 3.57 (s, 3H), 2.82 (m, 1H), 2.66 (m, 3H), 2.43 (dd, J = 5.0, 16.0 Hz, 1H), 2.01 (sl, 1H), 1.75 (m, 3H), 1.62 (m, 1H), 1.23 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 172.0, 149.0, 131.5, 125.8, 60.8, 60.7, 54.3, 41.1, 36.2, 31.5, 30.3, 26.8, 25.0, 14.3, 14.2; IR (KBr) 1493, 1732, 3193 cm^{-1}; MS (ESI+): m/z 327 $[M+H]^+$, 349 $[M+Na]^+$.

2-[2-(5-Formyl-1-methyl-1*H*-imidazol-2-yl)-ethyl)-succinic acid 4-ethyl ester 1-methyl ester (3b).

Prepared according to general procedure B on compound **21b** (95.0 g, 0.32 mmol) in $CHCl_3$ (7 mL) with MnO_2 (181 mg, 2.08 mmol). After refluxing for 32 h, filtration followed by column chromatography (EtOAc/MeOH 9.5:0.5) afforded **3b** (87.0 mg, 92%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.67 (s, 1H), 7.68 (s, 1H), 4.13 (q, J = 7.0 Hz, 2H), 3.88 (s, 3H), 3.71 (s, 3H), 2.96 (m, 1H), 2.77 (m, 3H), 2.53 (dd, J = 6.0, 16.5 Hz, 1H), 2.11 (m, 2H), 1.25 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.0, 174.5, 171.4, 154.7, 143.0, 132.0, 60.8, 52.1, 40.6, 36.2, 32.2, 28.7, 24.2, 14.2; IR (KBr) 1475, 1666, 1726 cm^{-1}; HRMS calcd for $C_{14}H_{20}N_2O_5Na$ $[M+Na]^+$: 319.1270 found: 319.1257.

2-[3-(5-Formyl-1-methyl-1*H*-imidazol-2-yl)-propyl)-succinic acid diethyl ester (3c).

Prepared according to general procedure B on compound **21c** (600 mg, 1.84 mmol) in $CHCl_3$ (40 mL) with MnO_2 (1.03 g, 12.0 mmol). After refluxing for 40 h, filtration followed by column chromatography (CH_2Cl_2/MeOH 9.7:0.3) afforded **3c** (580 mg, 97%) as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.69 (s, 1H), 4.14 (m, 4H), 3.87 (s, 3H), 2.86 (m, 1H), 2.72 (m, 3H), 2.45 (dd, J = 5.5, 16.0 Hz, 1H), 1.80 (m, 3H), 1.65 (m, 1H), 1.25 (m, 6H); ^{13}C NMR (75

MHz, $CDCl_3$) δ 179.1, 174.6, 171.7, 155.3, 143.1, 132.0, 60.8, 60.7, 40.9, 36.1, 32.2, 31.3, 26.3, 24.5, 14.2, 14.1; IR (KBr) 1475, 1669, 1728 cm^{-1}; HRMS calcd for $C_{16}H_{24}N_2O_5Na$ $[M+Na]^+$: 347.1583 found: 347.1578.

Compound 24b.

Prepared according to general procedure C. Deprotection: **22** (120 mg, 0.24 mmol) in a solution 75% TFA/CH_2Cl_2 (3 mL). Reductive amination: To a solution of the deprotected tripeptide in MeOH/CH_2Cl_2 1:1 (4 mL) were added: molecular sieves powder 4 Å (400 mg) and triethylamine (33.0 μL, 0.24 mmol), **3b** (70.0 mg, 0.24 mmol) and a solution of sodium cyanoborohydride (22.0 g, 0.35 mmol). After work-up the residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 9.5:0.5) to afford **24b** (125 mg, 77%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (bd, J = 7.0 Hz, 1H), 6.98–7.13 (m, 5H), 6.82 (bd, J = 7.0 Hz, 1H), 6.55 (s, 1H), 4.63 (m, 1H), 4.42 (m, 1H), 4.01 (q, J = 7.1 Hz, 2H), 3.52 (s, 3H), 3.51 (s, 3H), 3.41 (s, 3H), 3.38 (d, J = 15.0 Hz, 1H), 3.24 (d, J = 15.0 Hz, 1H), 2.97 (dd, J = 8.0, 14.0 Hz, 1H), 2.84 (dd, J = 8.0, 14.0 Hz, 1H), 2.54–2.74 (m, 6H), 2.38 (m, 2H), 2.26 (t, J = 7.5 Hz, 2H), 1.91 (m, 1H), 1.86 (s, 3H), 1.79 (m, 1H), 1.68 (m, 1H), 1.05 (t, J = 7.0 Hz, 3H), 0.64 (d, J = 7.0 Hz, 3H), 0.62 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5, 173.9, 171.9, 171.6, 171.1, 147.5, 136.6, 130.8, 129.3 (2C), 128.7 (2C), 127.0, 121.6, 67.7, 60.9, 54.0, 52.5, 52.2, 51.6, 42.1, 40.4, 38.0, 36.1, 31.6, 31.3, 31.0, 29.8, 28.8, 23.9, 19.4, 18.3, 15.3, 14.2; HRMS calcd for $C_{34}H_{52}N_5O_8S$ $[M+H]^+$: 690.3537 found: 690.3549.

Compound 24c.

Prepared according to general procedure C. Deprotection: **22** (160 mg, 0.31 mmol) in a solution 75% TFA/CH_2Cl_2 (3 mL). Reductive amination: To a solution of the deprotected tripeptide in MeOH/CH_2Cl_2 1:1 (4 mL) were added: molecular sieves powder 4 Å (400 mg) and triethylamine (40.0 μL, 0.31 mmol), **3c** (100 mg, 0.31 mmol) and a solution of sodium cyanoborohydride (30.0 mg, 0.47 mmol). After work-up the residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 9.5:0.5) to afford **24c** (175 mg, 79%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (bd, J = 6.5 Hz, 1H), 7.19–7.35 (m, 5H), 6.85 (bd, J = 6.5 Hz, 1H), 6.73 (s, 1H), 4.79 (q, J = 7.0 Hz, 1H), 4.63 (m, 1H), 4.14 (m, 4H), 3.73 (s, 3H), 3.59 (d, J = 14.0 Hz, 1H), 3.58 (s, 3H), 3.45 (d, J = 14.0 Hz, 1H), 3.16 (dd, J = 7.0, 14.0 Hz, 1H), 3.05 (dd, J = 6.5, 14.0 Hz, 1H), 2.64–2.88 (m, 5H), 2.47 (m, 3H), 2.12 (m, 1H), 2.06 (s, 3H), 1.94 (m, 2H), 1.74 (m, 4H), 1.25 (m, 6H), 0.85 (d, J = 7.0 Hz, 3H), 0.80 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5, 173.8, 171.9, 171.8, 171.0, 148.2, 130.4, 129.3 (2C), 128.7 (2C), 127.1, 122.2, 67.7, 60.9, 60.7, 54.0, 52.5, 52.2, 51.6, 42.3, 40.9, 37.9, 36.1, 31.6, 31.3, 31.0, 30.8, 29.8, 25.9, 24.6, 19.4, 18.2, 15.4, 14.2 (2C); HRMS calcd for $C_{36}H_{56}N_5O_8S$ $[M+H]^+$: 718.3850 found: 718.3856.

Compound 24d.

Prepared according to general procedure C. Deprotection: **23** (200 mg, 0.48 mmol) in a solution 75% TFA/CH_2Cl_2 (5 mL). Reductive amination: To a solution of the deprotected tripeptide in MeOH/CH_2Cl_2 1:1 (6 mL) were added: molecular sieves powder 4 Å (700 mg) and triethylamine (67.0 μL, 0.48 mmol), **3a** (143 mg, 0.48 mmol) and a solution of sodium cyanoborohydride (60.0 mg, 0.96 mmol). After work-up the residue was purified by column chromatography on silica gel (EtOAc/MeOH 9.6:0.4) to give **24d** (160 mg, 56%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (bd, J = 7.0 Hz, 1H), 7.10 (s, 1H), 7.03 (bd, J = 7.0 Hz, 1H), 4.43 (m, 2H), 4.13 (m, 4H), 3.84 (s, 3H), 3.81 (d, J = 14.0 Hz, 1H), 3.72 (s, 3H), 3.69 (d, J = 14.0 Hz, 1H), 3.37 (m, 2H), 3.13 (m, 1H), 2.95 (d, J = 6.0 Hz, 1H), 2.82 (m, 2H), 2.01 (m, 2H), 1.86 (m, 1H), 1.53 (m, 1H), 1.39 (d, J = 7.0 Hz, 3H), 1.23 (s, 6H), 0.93 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 173.0, 172.6, 171.4, 171.2, 146.3, 131.5, 120.0, 68.2, 61.2, 61.1, 57.6, 52.5, 48.3, 46.6, 42.2, 39.8, 37.3, 35.5, 31.8, 26.8, 25.1, 19.6, 18.5, 17.9, 15.5, 14.2, 14.1, 11.2; HRMS calcd for $C_{29}H_{50}N_5O_8$ $[M+H]^+$: 596.3659 found: 596.3652.

Compound 24e.

Prepared according to general procedure C. Deprotection: **23** (84.0 mg, 0.20 mmol) in a solution 75% TFA/CH_2Cl_2 (1.5 mL). Reductive amination: To a solution of the deprotected tripeptide in MeOH/CH_2Cl_2 1:1 (3 mL) were added: molecular sieves powder 4 Å (350 g) and triethylamine

(28.0 μL, 0.202 mmol), **3b** (60.0 mg, 0.20 mmol) and a solution of sodium cyanoborohydride (20.0 g, 0.30 mmol). After work-up the residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 9.5:0.5) to give **24e** (98.0 mg, 80%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (bs, 1H), 6.94 (s, 1H), 6.76 (bs, 1H), 4.50 (m, 1H), 4.34 (m, 1H), 4.13 (q, J = 7.0 Hz, 2H), 3.75 (d, J = 13.5 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 6H), 3.65 (d, J = 13.5 Hz, 1H), 2.94 (d, J = 5.5 Hz, 1H), 2.57–2.90 (m, 5H), 2.04 (m, 3H), 1.86 (m, 1H), 1.53 (m, 1H), 1.39 (d, J = 7.0 Hz, 3H), 1.24 (t, J = 7.0 Hz, 3H), 1.17 (m, 1H), 0.93 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5, 173.5, 173.0, 171.6, 170.9, 147.8, 130.6, 122.7, 68.2, 60.8, 57.3, 52.4, 52.1, 48.1, 42.6, 40.5, 37.3, 36.1, 31.6, 30.9, 28.9, 25.0, 24.0, 19.5, 18.3, 18.0, 15.4, 14.1, 11.1; HRMS calcd for $C_{29}H_{50}N_5O_8$ $[M+H]^+$: 596.3659 found: 596.3666.

Compound 24f.

Prepared according to general procedure C. Deprotection: **23** (258 mg, 0.62 mmol) in a solution 75% TFA/CH_2Cl_2 (5 mL). Reductive amination: To a solution of the deprotected tripeptide in MeOH/CH_2Cl_2 1:1 (6 mL) were added: molecular sieves powder 4 Å (700 mg) and triethylamine (90.0 μL, 0.62 mmol), **3c** (200 mg, 0.62 mmol) and a solution of sodium cyanoborohydride (58.0 mg, 0.93 mmol). After work-up the residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 9.5:0.5) to give **24f** (275 mg, 72%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (bd, J = 7.0 Hz, 1H), 7.12 (s, 1H), 6.71 (bd, J = 7.0 Hz, 1H), 4.49 (m, 1H), 4.33 (m, 1H), 4.15 (m, 4H), 3.81 (s, 3H), 3.80 (d, J = 14.0 Hz, 1H), 3.74 (s, 3H), 3.70 (d, J = 14.0 Hz, 1H), 2.96 (m, 3H), 2.85 (m, 1H), 2.71 (dd, J = 6.0, 16.0 Hz, 1H), 2.02 (m, 1H), 2.50 (dd, J = 6.0, 16.0 Hz, 1H), 1.62–1.91 (m, 6H), 1.53 (m, 1H), 1.41 (d, J = 7.0 Hz, 3H), 1.26 (m, 6H), 0.95 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 173.3, 173.0, 171.8, 171.0, 147.9, 131.6, 118.5, 68.4, 61.0, 60.8, 57.5, 52.5, 48.2, 42.3, 40.7, 37.3, 36.1, 31.8, 31.6, 30.8, 25.1, 25.0, 24.3, 19.5, 18.4, 18.0, 15.5, 14.2 (2C), 11.2; HRMS calcd for $C_{31}H_{54}N_5O_8$ $[M+H]^+$: 624.3972 found: 624.3983.

Compound 2b.

Prepared according to general procedure D. **24b** (18.9 mg, 0.03 mmol) in THF/MeOH/H_2O 1:1:1 (0.6 mL) and lithium hydroxide monohydrate (4.20 mg, 0.10 mmol) at 0 °C for 2 h and room temperature for 14 h. After work-up, **2b** (14.0 mg, 82%) was isolated as a white powder. ^{1}H NMR (300 MHz, CD_3OD) δ 6.90–7.11 (m, 5H), 6.48 (s, 1H), 4.61 (dd, J = 4.5, 11.0 Hz, 1H), 4.08 (dd, J = 5.0, 7.5 Hz, 1H), 3.37 (s, 3H), 2.93–3.17 (m, 3H), 2.60–2.74 (m, 4H), 2.36–2.51 (m, 4H), 2.21 (m, 3H), 1.90 (m, 1H), 1.82 (s, 3H), 1.72 (m, 1H), 1.51 (m, 1H), 0.63 (d, J = 7.0 Hz, 3H), 0.60 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 181.7, 179.7, 177.7, 176.4, 172.2, 149.8, 138.8, 132.6, 130.4, 129.6 (2C), 127.9 (2C), 121.4, 68.7, 55.7, 55.5, 44.9, 42.0, 40.5, 38.6, 34.0, 32.7, 31.4, 31.1, 30.2, 25.1, 20.1, 19.2, 15.3; HRMS calcd for $C_{30}H_{44}N_5O_8S$ $[M+H]^+$: 634.2911 found: 634.2949.

Compound 2c.

Prepared according to general procedure D. **24c** (18.9 mg, 0.03 mmol) in THF/MeOH/H_2O 1:1:1 (0.6 mL) and lithium hydroxide monohydrate (4.20 mg, 0.10 mmol) at 0 °C for 2 h and room temperature for 16 h. After work-up, **2c** (14.0 mg, 82%) was isolated as a colorless oil. ^{1}H NMR (300 MHz, CD_3OD) δ 7.18–7.41 (m, 5H), 6.71 (s, 1H), 4.89 (m, 1H), 4.36 (dd, J = 4.5, 7.0 Hz, 1H), 3.63 (s, 3H), 3.10 (m, 2H), 2.98 (m, 1H), 2.72–2.89 (m, 4H), 2.38–2.68 (m, 5H), 2.19 (m, 1H), 2.11 (s, 3H), 2.02 (m, 1H), 1.79 (m, 5H), 0.88 (d, J = 7.0 Hz, 3H), 0.84 (d, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 182.5, 179.7, 177.7, 176.5, 172.7, 150.0, 138.8, 132.1, 130.4, 129.6 (2C), 127.9 (2C), 122.8, 68.6, 55.8, 55.6, 45.1, 42.2, 40.6, 38.7, 34.0, 32.8, 32.6, 31.3, 31.2, 26.9, 26.2, 20.1, 19.2, 15.3; HRMS calcd for $C_{31}H_{44}N_5O_8S$ $[M-H]^+$: 646.2911 found: 646.2944.

Compound 2d.

Prepared according to general procedure D. **24d** (46.0 mg, 0.08 mmol) in THF/MeOH/H_2O 1:1:1 (1 mL) and lithium hydroxide monohydrate (12.0 mg, 0.28 mmol) at 0 °C for 1 h and room temperature for 1 h. After work-up, **2d** (36.4 mg, 89%) was isolated as a colorless foam. ^{1}H NMR (250 MHz, CD_3OD) δ 7.05 (s, 1H), 4.28 (m, 1H), 4.18 (m, 1H), 3.82 (d, J = 14.5 Hz, 1H), 3.80 (s, 3H), 3.61 (d, J = 14.5 Hz, 1H), 2.96–3.22 (m, 3H), 2.92 (dd, J= 1 .5, 6.5 Hz, 1H), 2.69 (m, 1H), 2.36 (m, 1H), 1.90 (m, 2H), 1.57 (m, 1H), 1.33 (d, J = 7.0 Hz, 3H), 1.24 (m, 1H), 0.94 (m, 12H); ^{13}C NMR (62.5 MHz, CD_3OD) δ 180.4, 178.9, 178.8, 176.3, 172.0, 148.9, 132.6, 121.0,

68.6, 59.0, 51.6, 44.4, 42.4, 40.2, 37.7, 32.8, 31.7, 28.9, 25.9, 19.9, 19.3, 19.0, 15.9, 11.2; HRMS calcd for $C_{24}H_{40}N_5O_8$ $[M+H]^+$: 526.2877 found: 526.2869.

Compound 2e.

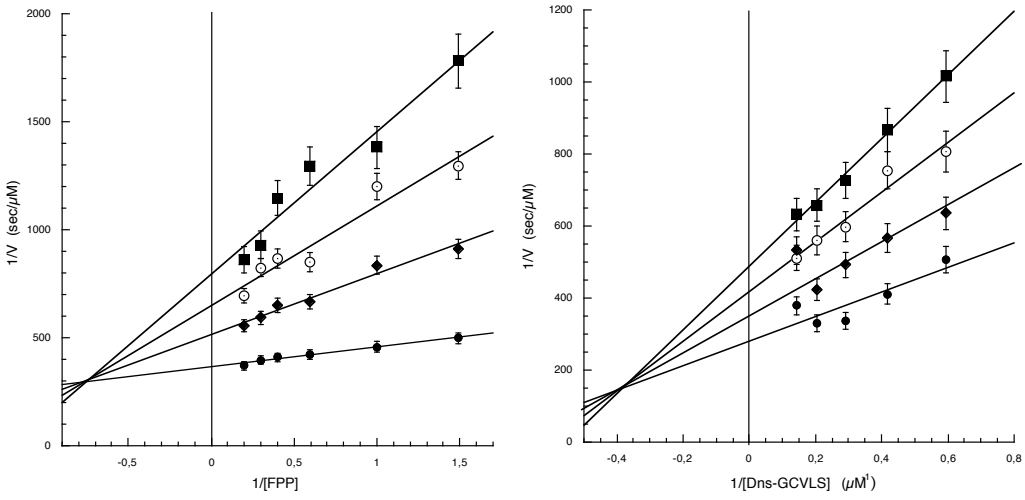
Prepared according to general procedure D. **24e** (27.7 mg, 0.05 mmol) in THF/MeOH/H_2O 1:1:1 (1.05 mL) and lithium hydroxide monohydrate (7.10 mg, 0.16 mmol) at 0 °C for 2 h and room temperature for 14 h. After work-up, **2e** (19.0 mg, 75%) was isolated as a white powder. ^{1}H NMR (300 MHz, CD_3OD) δ 6.96 (s, 1H), 4.19 (d, J = 7.0 Hz, 1H), 4.10 (q, J = 7.0 Hz, 1H), 3.72 (d, J = 14.0 Hz, 1H), 3.65 (s, 3H), 3.54 (d, J = 14.0 Hz, 1H), 2.83 (m, 3H), 2.57 (m, 2H), 2.33 (m, 1H), 1.74–2.00 (m, 4H), 1.47 (m, 1H), 1.24 (d, J = 7.0 Hz, 3H), 1.11 (m, 1H), 0.85 (m, 12H); ^{13}C NMR (75 MHz, CD_3OD) δ 181.2, 179.1, 178.9, 176.4, 172.2, 149.8, 133.0, 120.9, 68.7, 59.1, 51.7, 44.4, 42.5, 40.0, 37.9, 32.9, 31.6, 30.1, 26.0, 25.0, 20.0, 19.3, 19.1, 16.1, 11.3; HRMS calcd for $C_{25}H_{42}N_5O_8$ $[M+H]^+$: 540.3033 found: 540.3027.

Compound 2f.

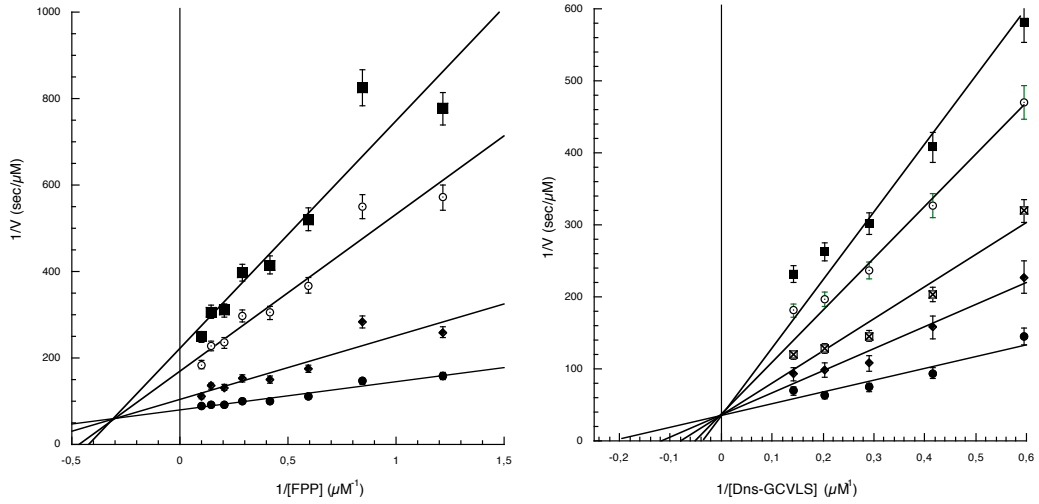
Prepared according to general procedure D. **24f** (51.5 mg, 0.08 mmol) in THF/MeOH/H_2O 1:1:1 (1.5 mL) and lithium hydroxide monohydrate (12.5 mg, 0.30 mmol) at 0 °C for 2 h and room temperature for 2 h. After work-up, **2f** (39.0 mg, 85%) was isolated as a colorless foam. ^{1}H NMR (300 MHz, CD_3OD) δ 6.90 (s, 1H), 4.30 (d, J = 7.5 Hz, 1H), 4.19 (q, J = 7.0 Hz, 1H), 3.80 (d, J = 14.0 Hz, 1H), 3.71 (s, 3H), 3.61 (d, J = 14.0 Hz, 1H), 2.94 (d, J = 6.5 Hz, 1H), 2.83 (m, 2H), 2.70 (m, 1H), 2.56 (dd, J = 7.0, 15.0 Hz, 1H), 2.34 (dd, J = 7.0, 15.0 Hz, 1H), 1.91 (m, 2H), 1.51–1.83 (m, 5H), 1.35 (d, J = 7.0 Hz, 3H), 1.23 (m, 1H), 0.95 (m, 12H); ^{13}C NMR (75 MHz, CD_3OD) δ 181.6, 178.8, 177.8, 175.2, 170.8, 148.9, 130.6, 122.0, 67.1, 57.8, 50.5, 44.2, 41.2, 39.8, 36.4, 31.5, 31.4, 29.9, 25.7, 25.0, 24.7, 18.7, 18.1, 17.7, 14.7, 9.9; HRMS calcd for $C_{26}H_{42}N_5O_8$ $[M-H]^+$: 552.3033 found: 552.3058.

<u>Inhibition of yeast FTase by **24c**, **2c**, **2e**. Lineweaver-Burk plots.</u>

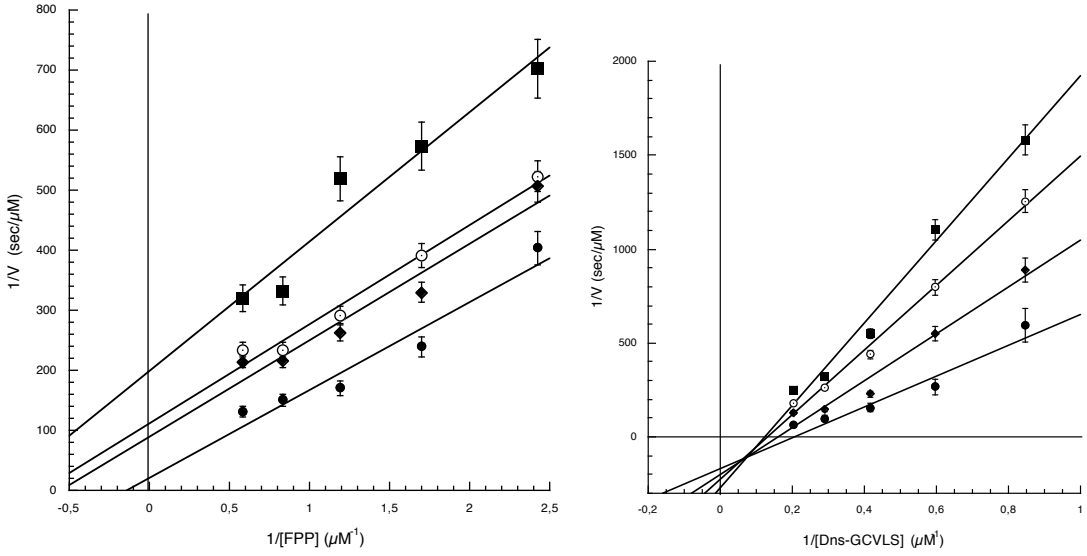
The kinetic experiments have been realized as described in the experimental section either with FPP as varied substrate with constant concentration of Dns-GCVLS of 2 µM or with Dns-GCVLS as varied substrate with constant concentration of FPP of 5 µM. The straight lines were calculated by linear regression using KaleidaGraph 3.6 software.



Compound **24c**. 0 (●), 25 (◆) 50 (⊙) 100 (■) µM



Compound **2c**. Concentration 0 (●), 36 (◆), 60 (☒) 120 (⊙) 200 (■) µM



Compound **2e**. Concentration 0 (●), 70 (◆) 140 (⊙) 200 (■) µM

Calculation of the K_i value for compound **2c**.