Supporting Information

Design and Synthesis of Potent HIV-1 Protease Inhibitors Incorporating Hexahydrofuropyranol-Derived High-Affinity P_2 Ligands: Structure-Activity Studies and Biological Evaluations .

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Analytical Purity

Table 1. Analytical purity of inhibitors **35a-g**, **36** and **37** determined by HPLC.

Inhibitor	Method A		Method B	
	R_t (min)	Purity (area %)	R_t (min)	Purity (area %)
35a	12.9	98.2	15.8	97.7
35b	12.8	99.2	16.1	98.1
35c	14.4	95.2	17.6	97.5
35d	15.4	96.0	18.0	98.0
35e	19.4	99.5	20.4	99.3
35f	12.4	95.8	15.6	95.6
35g	13.1	97.2	16.0	98.6
36	10.6	96.2	13.4	97.9
37	10.0	97.1	13.8	97.4

HPLC conditions:

Method A = Agilent Eclipse XDB-C18 (4.6 x 150 mm, 5 µm); t = 0-1 min (MeCN:H_2O:TFA 20:80:0.05), t = 1-20 min (*gradient to* MeCN:H_2O:TFA 90:10:0.05), t = 20-25 min (MeCN:H_2O:TFA 90:10:0.05); Flow = 1.5 mL/min; single detection wavelength λ = 215 nm, T = 25 °C, injection volume 30 µL, 10 min equilibration time between run.

Method B = Agilent Eclipse XDB-C18 (4.6 x 150 mm, 5 µm); t = 0-1 min (MeOH:H_2O:TFA 25:75:0.05), t = 1-20 min (*gradient to* MeOH:H_2O:TFA 95:5:0.05), t = 20-25 min (MeOH:H_2O:TFA 95:5:0.05); Flow = 1.5 mL/min; single detection wavelength λ = 215 nm, T = 25 °C, injection volume 30 µL, 10 min equilibration time between run.

Table 2. High resolution mass spectrometry data for inhibitors **35a-g**, **36** and **37**.

Inhibitor	Molecular Formula	HRMS Technique	Ion	Calculated	Found
35a	$C_{29}H_{40}N_2O_8S$	ESI	$[M+Na^+]$	599.2403	599.2406
35b	$C_{29}H_{40}N_2O_8S$	ESI	$[M+Na^+]$	599.2403	599.2407
35c	$C_{30}H_{42}N_2O_7S$	ESI	$[M+Na^+]$	597.2610	597.2621
35d	$C_{30}H_{42}N_2O_7S$	ESI	$[M+Na^+]$	597.2610	597.2612
35e	$C_{31}H_{44}N_2O_6S$	ESI	$[M+Na^+]$	595.2818	595.2816
35f	$C_{29}H_{40}N_2O_8S$	ESI	$[M+Na^+]$	599.2403	599.2397
35g	$C_{29}H_{40}N_2O_8S$	ESI	$[M+Na^+]$	599.2403	599.2397
36	$C_{28}H_{39}N_3O_7S$	ESI	$[M+Na^+]$	584.2406	584.2402
37	$C_{29}H_{40}N_2O_8S$	ESI	$[M+Na^+]$	599.2403	599.2414