Electronic Supporting Information (ESI) for: **Potent HIV-1 Protease Inhibitors Incorporating meso-Bicyclic Urethanes as P2-ligands: Structure-Based Design, Synthesis, Biological Evaluation and Protein-Ligand X-Ray Studies**

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HPLC (Table 1SI) and HRMS (Table 2SI) data of inhibitors **2,3, 26-30**. Crystallographic Data Collection and Refinement Statistics (Table 3SI).

Table 1. Purity of inhibitors **2,3, 26-30**

Inhibitor	Solvent system[a]	Retention Time (min)	Purity (%)	Column	Flow rate (mL/Min)
2	A	12.2	99%	XDB-C18 5 µM 4.6 x 150mm	2.0
	B	14.3	99%	XDB-C18 5 µM 4.6 x 150mm	2.0
3	A	12.1	99%	XDB-C18 5 µM 4.6 x 150mm	2.0
	C	12.8	99%	XDB-C18 5 µM 4.6 x 150mm	2.0
26	A	12.6	99%	XDB-C18 5 µM 4.6 x 150mm	2.0
	B	14.6	98%	XDB-C18 5 µM 4.6 x 150mm	2.0
27	A	12.1	96%	XDB-C18 5 µM 4.6 x 150mm	2.0
	C	12.7	97%	XDB-C18 5 µM 4.6 x 150mm	2.0
28	A	12.2	98%	XDB-C18 5 µM 4.6 x 150mm	2.0
	C	12.7	98%	XDB-C18 5 µM 4.6 x 150mm	2.0
29	A	12.3	98%	XDB-C18 5 µM 4.6 x 150mm	2.0
	C	12.9	99%	XDB-C18 5 µM 4.6 x 150mm	2.0
30	A	9.7	98%	XDB-C18 5 µM 4.6 x 150mm	2.0
	C	11.4	99%	XDB-C18 5 µM 4.6 x 150mm	2.0

[a]A= linear gradient from 20% acetonitrile, 80% water containing 0.05% trifluoroacetic acid to 80% acetonitrile, 20% water containing 0.05% trifluoroacetic acid in 20 min. B= linear gradient from 20% methanol, 80% water containing 0.05% trifluoroacetic acid to 80% MeOH in 20 min. C = linear gradient from 20% methanol, 80% water containing 0.05% trifluoroacetic acid to 100% MeOH in 20 min.

Table 2. HRMS for inhibitors **2,3, 26-30**

Inhibitor	HRMS
2	HRMS (*m/z*) calcd for $C_{28}H_{39}N_2O_8S$ $[M+H^+]$ 563.2427, found 563.2406
3	HRMS (*m/z*) calcd for $C_{29}H_{40}N_2NaO_8S$ $[M+Na]^+$ 599.2403, found 599.2394
26	HRMS (*m/z*) calcd for $C_{28}H_{38}N_2NaO_8S$ $[M+Na]^+$ 585.2247, found 585.2229
27	HRMS (*m/z*) calcd for $C_{29}H_{40}N_2NaO_9S$ $[M+Na]^+$ 615.2353, found 615.2361
28	HRMS (*m/z*) calcd for $C_{29}H_{40}N_2NaO_9S$ $[M+Na]^+$ 615.2353, found 615.2349
29	HRMS (*m/z*) calcd for $C_{29}H_{40}N_2NaO_8S$ $[M+Na]^+$ 599.2403, found 599.2421
30	HRMS (*m/z*) calcd for $C_{28}H_{38}N_2NaO_8S$ $[M+Na]^+$ 585.2247, found 585.2246

Table 3. Crystallographic Data Collection and Refinement Statistics

Space group	$P2_12_12$
Unit cell dimensions: (Å)	
a	58.00
b	86.34
c	45.83
Resolution range (Å)	50-1.07
Unique reflections	90,315
R_{merge} (%) overall (final shell)	7.0 (41.8)
I/σ(I) overall (final shell)	14.6(2.1)
Completeness (%) overall (final shell)	88.1 (51.3)
Data range for refinement (Å)	10-1.07
R (%)	15.2
R_{free} (%)	17.7
No. of solvent atoms (total occupancies)	162.9
RMS deviation from ideality	
Bonds (Å)	0.015
Angle distance (Å)	0.034
Average B-factors ($Å^2$)	
Main-chain atoms	13.1
Side-chain atoms	18.2
Inhibitor	12.5
Solvent	24.0
Residual density (max/min) ($eÅ^{-3}$)	0.38/-0.28