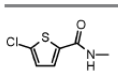
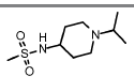
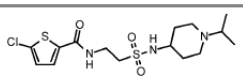
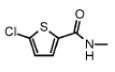
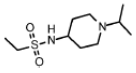
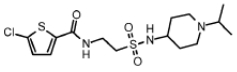
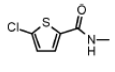
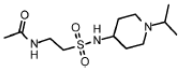
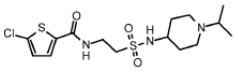
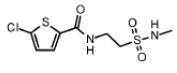
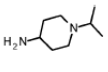
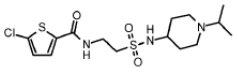
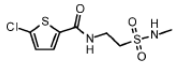
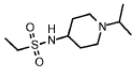
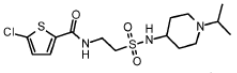
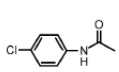
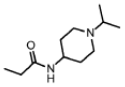
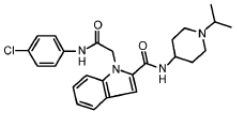
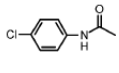
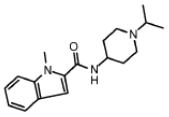
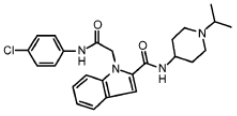
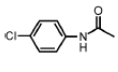
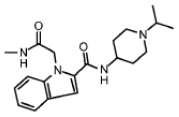
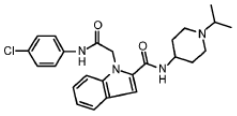
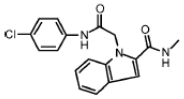
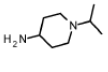
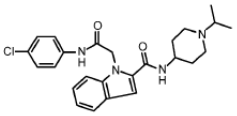
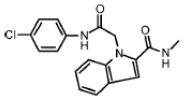
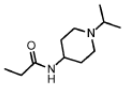
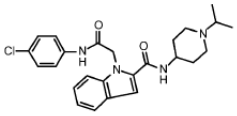
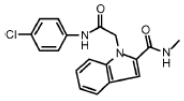
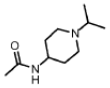
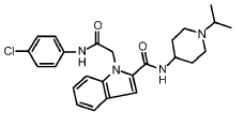
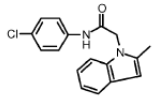
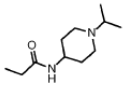
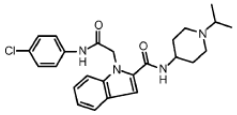
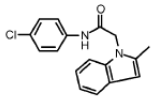
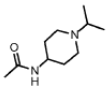
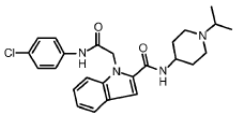
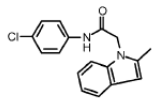
Table 2: Combination of fragments **1** and **2** with experimental free energy of binding ΔG to generate factor Xa inhibitors **1a** and **2a**.[a]

Fragment 1		Fragment 2		ΔG_{frag1}	ΔG_{frag2}	Final ligand		ΔG_{final}	ΔG_{link}[b]	Structural change
	**1g**		**1d**	−24.2	−11.4		**1a**	−49.6	−14.0	add single bond
	**1g**		**1c**	−24.2	−11.4		**1a**	−49.6	−14.0	remove methyl
	**1g**		**1b**	−24.2	−14.4		**1a**	−49.6	−11.0	remove amide group
	**1f**		**1e**	−24.0	−11.4		**1a**	−49.6	−14.2	remove *N*-methyl
	**1f**		**1c**	−24.0	−11.4		**1a**	−49.6	−14.2	remove ethylsulfonamide
	**2g**		**2c**	−20.0	−11.4		**2a**	−48.6	−17.2	add indole
	**2g**		**2h**	−20.0	−20.3		**2a**	−48.6	−8.3	remove methyl
	**2g**		**2b**	−20.0	−34.9		**2a**	−48.6	6.3	remove *N*-methylacetyl
	**2f**		**2e**	−25.8	−11.4		**2a**	−48.6	−11.4	remove *N*-methyl
	**2f**		**2c**	−25.8	−11.4		**2a**	−48.6	−11.4	remove propionamide
	**2f**		**2d**	−25.8	−11.4		**2a**	−48.6	−11.4	remove acetamide
	**2i**		**2c**	−15.4	−11.4		**2a**	−48.6	−21.8	remove 3 methyl groups
	**2i**		**2d**	−15.4	−11.4		**2a**	−48.6	−21.8	remove 2 methyl groups
	**2i**		**2e**	−15.4	−11.4		**2a**	−48.6	−21.8	add carbonyl

[a] Combination of fragments 1 and 2 results in a final ligand after minor structural changes as indicated. ΔG values are given in kJ mol^{-1}, they are calculated at 298 K. [b] The linker contributions are calculated using: $\Delta G_{link} = \Delta G_{final} - \Delta G_{frag1} - \Delta G_{frag2}$.