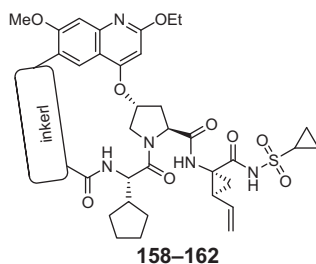


Table 7.25 2-Ethoxyquinoline carbamate constrained linkers.

Compound	Linker	3a K_i (nM)	1b replicon (nM)	1b mutants K_i (nM)			Rat [liver] @ 4 h (μ M)
				R155K	A156T	A156V	
157		2.2	11	1.3	41	–	35
158		4.6	17	0.5	0.8	15	10.2
159		4.1	38	0.9	49	–	–
160^a		18	–	2.2	52	–	–
161^b		7.7	16	2.4	4.8	16	–
162^b		1.0	11	0.2	2.8	14	27.0

^aMixture of stereoisomers.^bSingle isomer; absolute stereochemistry not established.

with a linear linker. Both **162** and **165** show sub-nanomolar to low-nanomolar potency across genotypes 1, 2 and 3, and also three different key mutation positions (R155, A156, D168).

In the 3-quinoline case, fusion of a cyclopentyl ring gave **168** and resulted in a broad activity profile against genotypes and key mutant enzymes (Table 7.28).