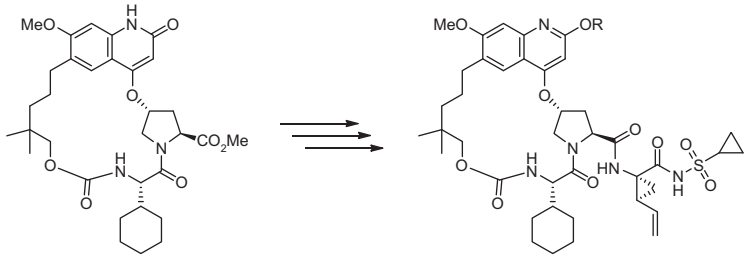
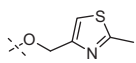
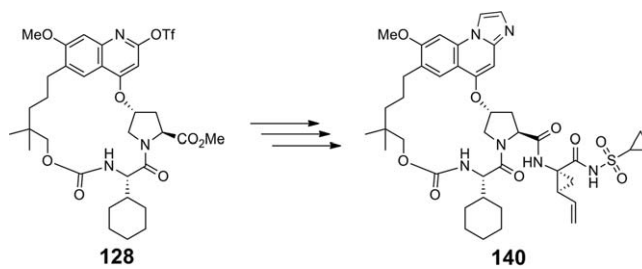
Table 7.21 2-Alkoxyquinoline SARs.



Compound	*OR*	*1b K_i (nM)*	*3a K_i (nM)*[a]	*1b replicon IC_{50} (nM)*		*Rat [liver] @ 4 h (μM)*
				10% FBS	*50% NHS*	
135		0.07	23	85	460	0.07
136		0.04	4.1	4	19	5.4
137		0.09	7.6	6	43	40
138		0.05	15	5	34	4.6
139		0.1	3.1	3.5	16	19



Scheme 7.8

subnanomolar regions, and methoxy analog **147** also provided a slight increase in rat liver exposure compared with unsubstituted **142**.

In addition to the methoxy analogs, unsubstituted tricycle **148** (Table 7.22) exhibited greatly improved gt3a enzyme activity ($K_i = 12$ nM) compared with P2 bicyclics. This represented a 16-fold increase in gt3a potency for **148** over bicyclic compound **114** and showed that simply a fused ring could give results similar to those seen with 2-quinoline substituents. This increase in potency was