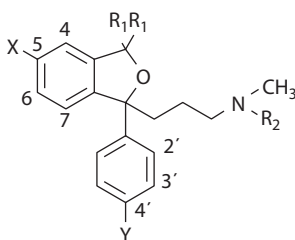


FIGURE 18.4 Discovery of phenylphthalane antidepressants.

TABLE 18.2

5-Hydroxytryptamine and Norepinephrine Reuptake Inhibition of Selected Talopram Derivatives



Compound	R ₁	R ₂	X	Y	5-HT Reuptake (In Vitro)	NE Reuptake (In Vivo)
					Rabbit Blood pl. IC ₅₀ (nM)	Mouse Heart ED ₅₀ (μmol/kg)
Talopram (18.28)	CH ₃	H	H	H	3,400	2.2
(18.30)	CH ₃	CH ₃	H	H	53,000	5
(18.31)	H	H	H	H	1,300	43
(18.32)	H	CH ₃	H	H	600	66
(18.33)	H	CH ₃	H	Cl	110	170
(18.34)	H	CH ₃	Cl	H	220	>200
(18.35)	H	CH ₃	Cl	Cl	24	>80
(18.36)	H	CH ₃	H	Br	310	N/A
(18.37)	H	CH ₃	H	CN	54	23
(18.38)	H	CH ₃	CN	Cl	10	>80
Citalopram (18.39)	H	CH ₃	CN	F	38	>40

Source: Data from Lundbeck Screening Database, H. Lundbeck A/S, Valby, Denmark.
N/A, not available.