Supporting Information

A Remarkable Series of Vinblastine Analogues Displaying Enhanced Activity and an Unprecedented Tubulin Binding Steric Tolerance: C20' Urea Derivatives

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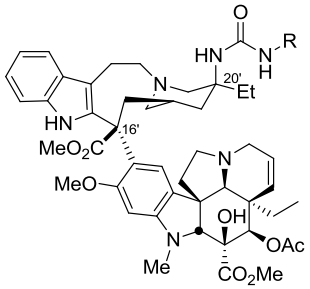
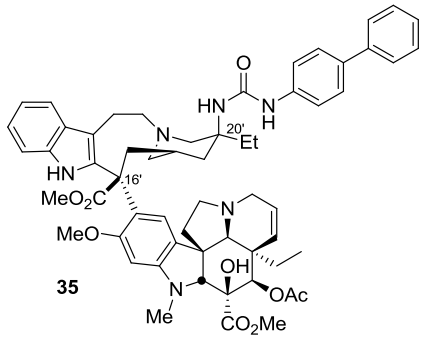
Figure S1.



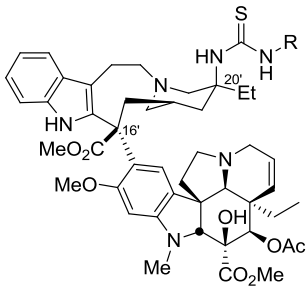
Compound	IC_{50} (nM) L1210	HCT116	HCT116/VM46
Vinblastine (**1**)	6.0	6.8	600
R = H (**11**)	40	7.5	4400
Alkyl			
R = methyl (**14**)	5.7	0.82	530
R = ethyl (**15**)	2.1	0.73	90
R = *n*-propyl (**16**)	6.0	2.7	221
R = *i*-propyl (**17**)	5.5	5.7	430
R = cyclopropyl (**18**)	3.9	0.73	85
R = *n*-butyl (**19**)	5.7	4.6	270
R = *t*-butyl (**20**)	40	20	670
R = cyclohexyl (**21**)	5.8	5.4	450
R = cyclohexyl (**22**)	48	8.8	>1000
Aryl			
R = C_6H_5 (**23**)	6.5	5.1	390
R = *p*-C_6H_4F (**24**)	5.7	3.9	400
R = *p*-C_6H_4Cl (**25**)	6.2	6.7	590
R = *p*-$C_6H_4CH_3$ (**26**)	4.5	4.8	330
R = *p*-$C_6H_4CF_3$ (**27**)	7.3	7.1	610
R = *p*-$C_6H_4OCH_3$ (**28**)	4.9	2.0	230
R = *m*-$C_6H_4OCH_3$ (**29**)	5.4	0.77	80
R = *o*-$C_6H_4OCH_3$ (**30**)	4.8	0.77	65
R = $CH_2C_6H_5$ (**31**)	6.4	7.3	740
R = $CH_2CH_2C_6H_5$ (**32**)	6.3	6.3	590
R = CH_2(2-pyridyl) (**33**)	24	5.6	670
R = CH_2(2-furyl) (**34**)	5.4	5.1	530

Figure S2.



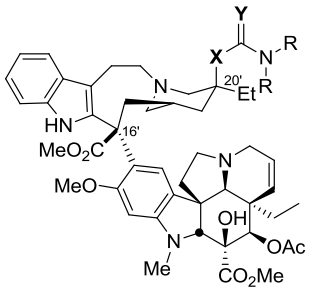
Compound	IC_{50} (nM)		
	L1210	HCT116	HCT116/VM46
1	6.0	6.8	600
35	6.4	6.9	470

Figure S3.



Compound	IC_{50} (nM)		
	L1210	HCT116	HCT116/VM46
Vinblastine (**1**)	6.0	6.8	600
R = H (**11**)	55	7.7	2000
R = C_6H_{11} (**36**)	30	20	520
R = C_6H_5 (**37**)	50	40	650
R = $CH_2CH_2(4\text{-}FC_6H_4)$ (**38**)	60	60	750

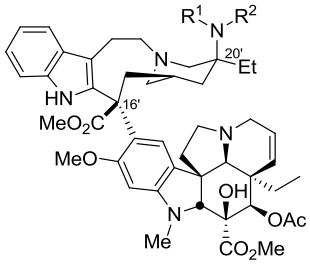
Figure S4.



X = O, NH
Y = O, S

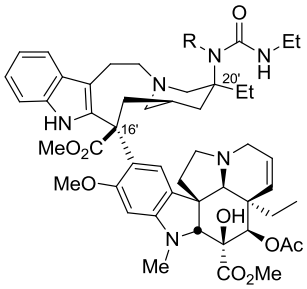
Compound	IC_{50} (nM) L1210	HCT116	HCT116/VM46
Vinblastine (**1**)	6.0	6.8	600
X = NH, Y = O			
R = H (**11**)	40	7.5	4400
R = CH_3 (**39**)	5.9	2.8	80
R = CH_2CH_3 (**40**)	8.3	7.2	550
R = Morpholine (**41**)	5.3	4.5	360
R = Piperidine (**42**)	5.5	3.9	50
X = NH, Y = S			
R = H	55	7.7	2000
R = CH_3 (**43**)	7.8	8.7	250
X = O, Y = O			
R = CH_3 (**44**)	5700	4700	9100

Figure S5.



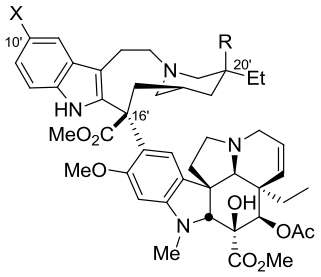
Compound	IC_{50} (nM) L1210	HCT116	HCT116/VM46
Vinblastine	6.0	6.8	600
R^1 and R^2 = H (**7**)	640	600	>10000
R^1 = H R^2 = CH_3 (**45**)	70	60	8500
R^1 and R^2 = CH_3 (**46**)	1300	980	>10000

Figure S6.



Compound	IC_{50} (nM)		
	L1210	HCT116	HCT116/VM46
R = H (**15**)	2.1	0.73	90
R = Me (**47**)	570	610	8500

Figure S7.



Compound	IC_{50} (nM)		
	L1210	HCT116	HCT116/VM46
R = OH, X = H (**1**)	6.0	6.8	600
R = NHCONHEt, X = H (**15**)	2.1	0.73	90
R = OH, X = F (**48**)	0.70	0.80	80
R = NHCONHEt, X = F (**49**)	0.70	0.62	70