

SUPPLEMENTARY MATERIALS

Bipiperidinyl Derivatives of Cannabidiol Enhance Its Antiproliferative Effects in Melanoma Cells

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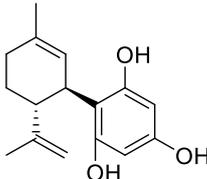
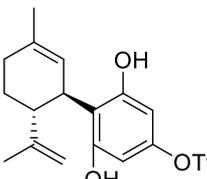
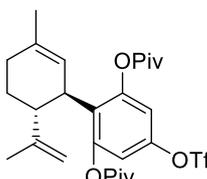
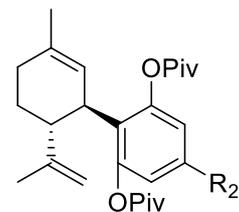
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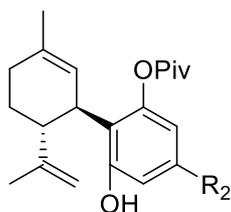
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Table S1. Inhibitory effects of the reaction intermediate **37-49** with a leaving group triflate (-OTf) or a protecting group pivaloyl (-Piv) on the growth of B16F10 cells at the concentration of 20 μ M.

Compound	MW (g/mol)	Functional group	Inhibition
37	260.33		n.a. ^a
38	392.39		n.a.
39	560.63		n.a.
			
Compound	MW(g/mol)	Functional group	Inhibition
40	426.60	R ₂ = 	n.a.
41	440.62	R ₂ = 	n.a.
42	452.64	R ₂ = 	n.a.
43	454.65	R ₂ = 	n.a.

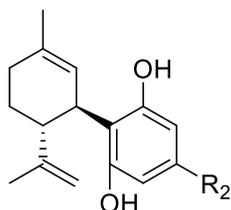
44	494.72	R ₂ =		n.a.
45	480.69	R ₂ =		n.a.
46	488.67	R ₂ =		n.a.



Compound	MW(g/mol)		Functional group	Inhibition
47	370.53	R ₂ =		n.a.
48	410.60	R ₂ =		32.3%
49	396.57	R ₂ =		49.0%

^an.a. = not active (no inhibition)

Table S2. Inhibitory effects of the synthetic cannabinoids **50-56** with various side chains on the growth of B16F10 cells at the concentration of 20 μM .



Compound	MW(g/mol)	R ₂ =	Functional group	Inhibition
50	258.36	R ₂ =	 CH ₃	n.a. ^a
51	272.39	R ₂ =		n.a.
52	284.40	R ₂ =		n.a.
53	286.42	R ₂ =		n.a.
54	326.48	R ₂ =		61.7%
55	312.45	R ₂ =		55.2%
56	320.43	R ₂ =		n.a.

^an.a. = not active (no inhibition)