

SUPPLEMENTARY MATERIALS

Properly Substituted Benzimidazoles as a New Promising Class of Nicotinate Phosphoribosyltransferase (NAPRT) Modulators

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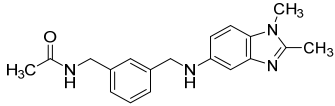
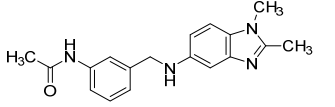
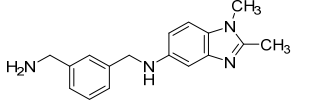
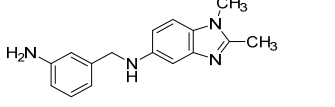
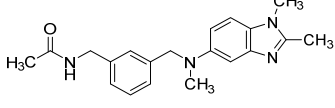
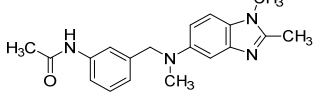
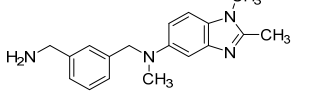
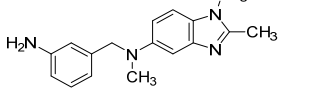
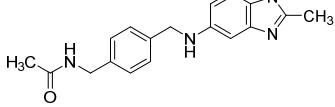
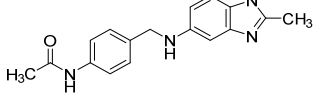
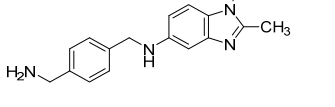
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Table S1. NAPRT inhibition/activation effect of tested compounds

Compound	Structure	% Inhibition	-Fold stimulation
17		30.3 ± 6.0	-
18		46.1 ± 8.1	-
19		0.6 ± 0.9	-
20		-	1.25 ± 0.05
21		0	0
22		5.0 ± 1.2	-
23		-	1.14 ± 0.05
24		-	1.44 ± 0.04
25		13.0 ± 3.1	-
26		1.3 ± 0	-
27		1.9 ± 0.9	-

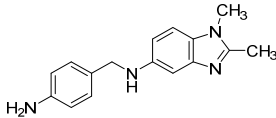
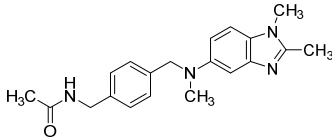
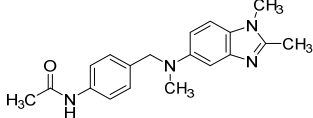
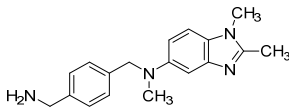
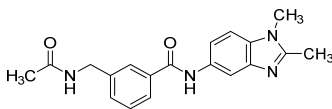
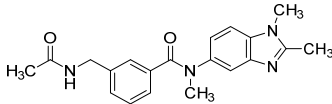
28		0	0
29		12.0 ± 2.2	-
30		0	0
31		-	1.58 ± 0.07
32		-	1.47 ± 0.07
33		-	1.08 ± 0.03

Table S2. Elemental analysis results for compounds **17-33**.

Compd	Formula	Calcd			Found		
		C%	H%	N%	C%	H%	N%
17	C ₁₉ H ₂₂ N ₄ O.2HCl	57.73	6.12	14.17	57.99	5.98	13.90
18	C ₁₈ H ₂₀ N ₄ O.2HCl	56.70	5.82	14.69	56.42	5.99	14.39
19	C ₁₇ H ₂₀ N ₄ .2HCl	57.80	6.28	15.86	57.65	6.13	15.91
20	C ₁₆ H ₁₈ N ₄ .2H ₂ C ₂ O ₄	53.81	4.97	12.55	54.03	4.77	12.68
21	C ₂₀ H ₂₄ N ₄ O.H ₂ C ₂ O ₄	61.96	6.15	13.14	62.15	6.00	13.37
22	C ₁₉ H ₂₂ N ₄ O.2HCl	57.73	6.12	14.17	58.01	6.23	13.94
23	C ₁₈ H ₂₂ N ₄ .2H ₂ C ₂ O ₄	55.69	5.52	11.81	55.91	5.70	12.02
24	C ₁₇ H ₂₀ N ₄ .H ₂ C ₂ O ₄	61.61	5.99	15.13	61.84	6.11	15.33
25	C ₁₉ H ₂₂ N ₄ O.2HCl	57.73	6.12	14.17	57.96	6.21	14.02
26	C ₁₈ H ₂₀ N ₄ O.2H ₂ C ₂ O ₄	54.10	4.95	11.47	54.23	5.02	11.25
27	C ₁₇ H ₂₀ N ₄ .2H ₂ C ₂ O ₄	54.78	5.25	12.17	54.90	5.16	12.33
28	C ₁₆ H ₁₈ N ₄	72.15	6.81	21.04	72.39	6.95	20.82
29	C ₂₀ H ₂₄ N ₄ O.2HCl	58.68	6.40	13.69	58.38	6.23	13.60
30	C ₁₉ H ₂₂ N ₄ O.HCl	63.59	6.46	15.61	63.76	6.34	15.84
31	C ₁₈ H ₂₂ N ₄ .2H ₂ C ₂ O ₄	57.73	6.12	14.17	57.79	6.01	14.01
32	C ₁₉ H ₂₀ N ₄ O ₂ .H ₂ C ₂ O ₄	59.15	5.20	13.14	59.44	5.30	13.03
33	C ₂₀ H ₂₂ N ₄ O ₂ .HCl	62.09	5.99	14.48	62.35	5.87	14.69

Materials and general methods for the synthesis and chemical characterization of the final compounds and intermediates.

All the reagents have been purchased and used without further purification. Melting points were taken in glass capillary tubes on a Büchi SMP-20 apparatus. Elemental analyses (C, H, N, and S) were recorded on FLASH 2000 instrument (ThermoFisher Scientific). The elemental composition of the compounds agreed to within $\pm 0.4\%$ of the calculated value. ^1H -NMR spectra were recorded either with a Bruker 500 Ascend (Bruker BioSpin Corporation, Billerica, MA, USA) and Varian Mercury AS400 instruments, and chemical shifts (ppm) are reported relative to tetramethylsilane. Spin multiplicities are given as s (singlet), d (doublet), dd (double doublet), t (triplet), or m (multiplet). IR spectra were recorded on PerkinElmer 297 instrument and spectral data (not shown because of the lack of unusual features) were obtained for all compounds reported and are consistent with the assigned structures. ESI-MS spectra were recorded in the positive- [ESI-MS(+)] or negative-ion [ESIMS(-)] mode on a Waters Micromass ZQ spectrometer equipped with a single quadrupole (Waters Corporation, Milford, MA, USA), using a methanol mobile phase. The compounds were added to reagent grade methanol to give approximately 0.1 mM solutions. These solutions were injected (1 μL) into the spectrometer fitted with an autosampler. The pump delivered the solutions to the mass spectrometer source at a flow rate of 200 $\mu\text{L}/\text{min}$, and nitrogen was employed both as a drying gas and as a nebulizing gas. Capillary voltage was typically 2500 V. The temperature of the source was 100 $^{\circ}\text{C}$, while the temperature of the desolvation was 400 $^{\circ}\text{C}$. All reactions were monitored by thin-layer chromatography using silica gel plates (60 F254; Merck), visualizing with ultraviolet light. Chromatographic separations were performed on silica gel columns (Kieselgel 40, 0.040–0.063 mm, Merck) by flash chromatography. Compounds were named following IUPAC rules as applied by ChemBioDraw Ultra (version 12.0) software for systematically naming organic chemicals. The purity of the novel compounds was determined by combustion analysis and was $\geq 95\%$.