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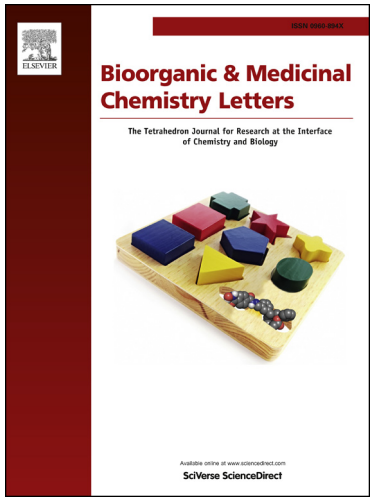

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Imidazole - Derived Agonists for the Neurotensin 1 Receptor

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Abstract— A scaffold-hop program seeking full agonists of the neurotensin-1 (NTR1) receptor identified the probe molecule **ML301** (**1**) and associated analogs, including its naphthyl analog (**14**) which exhibited similar properties. Compound **1** showed full agonist behavior (79 - 93%) with an EC_{50} of 2.0 – 4.1 μM against NTR1. Compound **1** also showed good activity in a Ca mobilization FLIPR assay (93% efficacy at 298 nM), consistent with it functioning via the G_q coupled pathway, and good selectivity relative to NTR2 and GPR35. In further profiling, **1** showed low potential for promiscuity and good overall pharmacological data. This report describes the discovery, synthesis, and SAR of **1** and associated analogs. Initial *in vitro* pharmacologic characterization is also presented.

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