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Synthesis and biological evaluation of novel imidazol-1-ylacetic acid derivatives as non-brain penetrant bombesin receptor subtype-3 (BRS-3) agonists

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ABSTRACT

Novel compounds based on **1a** were synthesized with the focus of obtaining agonists acting upon peripheral BRS-3. To identify potent anti-obesity compounds without adverse effects on the central nervous system (CNS), a carboxylic acid moiety and a labile carboxylic ester with an antedrug functionality were introduced. Through the extensive synthetic exploration and the pharmacokinetic studies of intravenous administration in mice, the ester **2b** was selected owing to its most suitable pharmacological profile. In the evaluation of food intake suppression in C57BL/6N mice, **2b** showed significant *in vivo* efficacy and no clear adverse effects on blood pressure change in dogs administered the compound by intravenous infusion.

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