Process for the Preparation of ClC-1 Chloride Channel Inhibitors

Technical field

The present disclosure relates to novel chemical processes for the synthesis of ClC-1 chloride channel inhibitors.

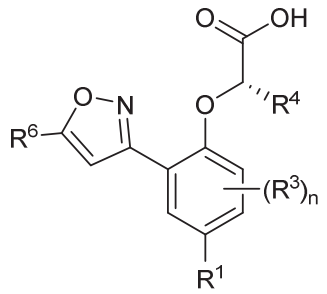
Background

This disclosure relates to chemical processes for making compounds which are ClC-1 chloride channel inhibitors. As described in WO 2016/202341, ClC-1 chloride channel inhibitors may be useful in the treatment of neuromuscular disorders, such as myasthenia gravis and ALS, or in reversing and/or ameliorating a neuromuscular blockade.

Summary

In order to develop treatments of neuromuscular disorders, there is a need for ClC-1 chloride channel inhibitors. The present disclosure provides a novel industrially applicable process for the preparation of compounds of Formula I. The compounds of Formula I inhibit ClC-1 ion channels and are capable of restoring neuromuscular transmission, as evidenced by the data generated by investigation of the compound set in biological models described herein. These compounds can thus be used to treat or ameliorate muscle weakness and muscle fatigue in neuromuscular junction disorders caused by disease or by neuromuscular blocking agents.

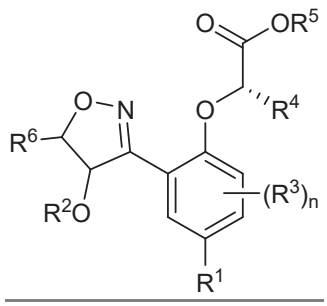
In one aspect, the present disclosure refers to a process for the preparation of compounds of Formula I



Formula I

comprising step a) wherein

i) a compound of Formula II is reacted with an acid or base



Formula II

and

ii) a compound of Formula I is isolated from the reaction mixture,

wherein

- R^1 is selected from the group consisting of H, F, Cl, Br and I;
- R^2 is selected from the group consisting of C_{1-5} alkyl and C_{3-5} cycloalkyl
- R^3 is selected from the group consisting of deuterium, F, Cl, Br and I;
- R^4 is selected from the group consisting of H, deuterium, C_{1-5} alkyl, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-5} cycloalkyl and C_5 cycloalkenyl, each of which may be optionally substituted with one or more, identical or different, substituents R^7;
- R^5 is selected from the group consisting of C_{1-5} alkyl optionally substituted with one or more, identical or different, substituents R^8, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl optionally substituted with one or more, identical or different, substituents R^8, phenyl optionally substituted with one or more, identical or different, substituents R^9 and benzyl optionally substituted with one or more, identical or different, substituents R^9;
- R^6 is selected from the group consisting of H, deuterium C_{1-5} alkyl and C_{3-5} cycloalkyl;
- R^7 is independently selected from the group consisting of deuterium, tritium, F, Cl, Br, I, CN, isocyanide, C_{3-5} cycloalkyl optionally substituted with one or more, identical or different, substituents R^8, O-C_{1-3} alkyl optionally substituted with one or more, identical or different, substituents R^8, S-C_{1-3} alkyl optionally substituted with one or more, identical or different, substituents R^8, CH_2-O-C_{1-3} alkyl optionally substituted with one or more,

identical or different, substituents R^8 and CH_2-S-C_{1-3} alkyl optionally substituted with one or more, identical or different, substituents R^8;

- R^8 is independently selected from the group consisting of deuterium and F;
- R^9 is independently selected from the group consisting of deuterium, methoxy, nitro, cyano, Cl, Br, I and F; and
- n is an integer 0, 1, 2 or 3.

In another aspect, the present disclosure refers to a A compound of formula (II) as disclosed herein, selected from the group consisting of:

methyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

ethyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

tert-butyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

methyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

ethyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

tert-butyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

methyl (2*S*)-2-[4-chloro-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

methyl (2*S*)-2-[4-bromo-2-(5-methyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

methyl (2*S*)-2-[4-bromo-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

ethyl (2*S*)-2-[4-chloro-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

ethyl (2*S*)-2-[4-bromo-2-(5-methyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

ethyl (2*S*)-2-[4-bromo-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

tert-butyl (2*S*)-2-[4-chloro-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

tert-butyl (2*S*)-2-[4-bromo-2-(5-methyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-bromo-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-chloro-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-bromo-2-(5-methyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-bromo-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-chloro-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-bromo-2-(5-methyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-bromo-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-chloro-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-bromo-2-(5-methyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-bromo-2-(5-cyclopropyl-4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-2-cyclopropylacetate;
methyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclobutylpropanoate;
methyl 2-[4-bromo-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
methyl 2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
methyl (2*S*)-2-[4,5-dichloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-chloro-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

methyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
methyl (2*S*)-2-[4-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;
methyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;
methyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
methyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;
methyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;
methyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-2-cyclopropylacetate;
ethyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclobutylpropanoate;
ethyl 2-[4-bromo-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
ethyl 2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
ethyl (2*S*)-2-[4,5-dichloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-chloro-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
ethyl (2*S*)-2-[4-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;

ethyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;
ethyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;
ethyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
ethyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;
ethyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;
ethyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-2-cyclopropylacetate;
tert-butyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclobutylpropanoate;
tert-butyl 2-[4-bromo-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
tert-butyl 2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
tert-butyl (2*S*)-2-[4,5-dichloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-chloro-5-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
tert-butyl (2*S*)-2-[4-fluoro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;
tert-butyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;

tert-butyl (2*S*)-2-[4-chloro-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
tert-butyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;
tert-butyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;
tert-butyl (2*S*)-2-[4-bromo-2-(4-butoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-2-cyclopropylacetate;
methyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclobutylpropanoate;
methyl 2-[4-bromo-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
methyl 2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
methyl (2*S*)-2-[4,5-dichloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-chloro-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
methyl (2*S*)-2-[4-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;
methyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;
methyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
methyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;

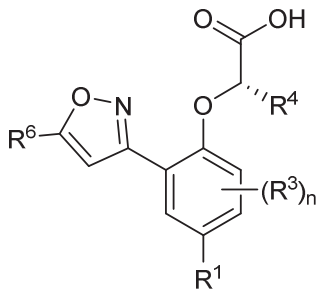
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methyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;
methyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-2-cyclopropylacetate;
ethyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclobutylpropanoate;
ethyl 2-[4-bromo-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
ethyl 2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
ethyl (2*S*)-2-[4,5-dichloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-chloro-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
ethyl (2*S*)-2-[4-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;
ethyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;
ethyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
ethyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
ethyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;
ethyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;

ethyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-2-cyclopropylacetate;
tert-butyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclobutylpropanoate;
tert-butyl 2-[4-bromo-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
tert-butyl 2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]acetate;
tert-butyl (2*S*)-2-[4,5-dichloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-bromo-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-chloro-5-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
tert-butyl (2*S*)-2-[4-fluoro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate;
tert-butyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;
tert-butyl (2*S*)-2-[4-chloro-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate;
tert-butyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-cyclopropylpropanoate;
tert-butyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]butanoate;
tert-butyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]-3-methylbutanoate; and
tert-butyl (2*S*)-2-[4-bromo-2-(4-ethoxy-4,5-dihydroisoxazol-3-yl)phenoxy]propanoate.

In another aspect, the present disclosure refers to a process for the preparation of a pharmaceutical composition comprising the steps of

i) preparing a compound selected from the group consisting of
(2S)-2-[4-bromo-5-fluoro-2-(1,2-oxazol-3-yl)phenoxy]-2-cyclopropylacetic acid;
(2S)-2-[4-bromo-2-(1,2-oxazol-3-yl)phenoxy]-3-cyclobutylpropanoic acid;
2-[4-bromo-5-fluoro-2-(1,2-oxazol-3-yl)phenoxy]acetic acid;
2-[4-bromo-2-(1,2-oxazol-3-yl)phenoxy]acetic acid;
(2S)-2-[4,5-dichloro-2-(1,2-oxazol-3-yl)phenoxy]propanoic acid;
(2S)-2-[4-bromo-5-fluoro-2-(1,2-oxazol-3-yl)phenoxy]propanoic acid;
(2S)-2-[4-chloro-5-fluoro-2-(1,2-oxazol-3-yl)phenoxy]propanoic acid;
(2S)-2-[4-chloro-2-(1,2-oxazol-3-yl)phenoxy]-3-cyclopropylpropanoic acid;
(2S)-2-[4-fluoro-2-(1,2-oxazol-3-yl)phenoxy]propanoic acid;
(2S)-2-[4-chloro-2-(5-cyclopropyl-1,2-oxazol-3-yl)phenoxy]propanoic acid;
(2S)-2-[4-chloro-2-(1,2-oxazol-3-yl)phenoxy]-3-methylbutanoic acid;
(2S)-2-[4-chloro-2-(1,2-oxazol-3-yl)phenoxy]butanoic acid;
(2S)-2-[4-chloro-2-(1,2-oxazol-3-yl)phenoxy]propanoic acid;
(2S)-2-[4-bromo-2-(1,2-oxazol-3-yl)phenoxy]-3-cyclopropylpropanoic acid;
(2S)-2-[4-bromo-2-(1,2-oxazol-3-yl)phenoxy]butanoic acid;
(2S)-2-[4-bromo-2-(1,2-oxazol-3-yl)phenoxy]-3-methylbutanoic acid;
(2S)-2-[4-bromo-2-(5-methyl-1,2-oxazol-3-yl)phenoxy]propanoic acid;
(2S)-2-[4-bromo-2-(5-cyclopropyl-1,2-oxazol-3-yl)phenoxy]propanoic acid; and
(2S)-2-[4-bromo-2-(1,2-oxazol-3-yl)phenoxy]propanoic acid
as disclosed herein and
ii) formulating said compound into a pharmaceutical composition.

In one ~~aspect~~example, the disclosure provides a process for the preparation of compounds of Formula I



Formula I