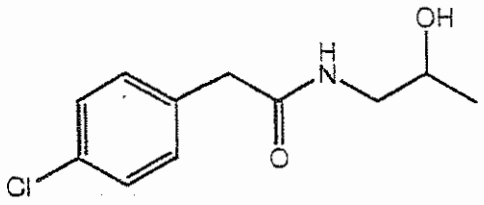
hydrochloride, its related salts, enantiomers, crystalline forms, and intermediates, have been reported in WO 2005/019179, WO 2006/069363, and U.S. Pat. No. 6,953,787.

In view of the growing demand for compounds for the treatment of disorders related to the 5-HT_{2C} receptor, new and more efficient routes to 3-benzazepines, including locaserin hydrochloride, are needed. The processes and compounds described herein help meet these and other needs.

SUMMARY ~~OF THE INVENTION~~

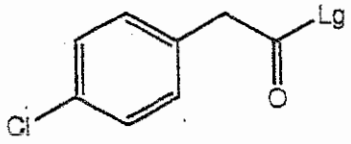
The present ~~invention~~disclosure provides intermediates, processes of preparing the same, and compositions containing the same, which are useful in the preparation of (R)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1H-3-benzazepine, and solid forms thereof, for the treatment or prophylaxis of 5-HT_{2C} associated disorders such as obesity and central nervous system diseases.

In one aspect, there is provided a process for preparing an amide compound of Formula 1-3:



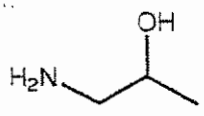
1-3

comprising reacting a phenylacetic acid derivative compound of Formula 1-1:



1-1

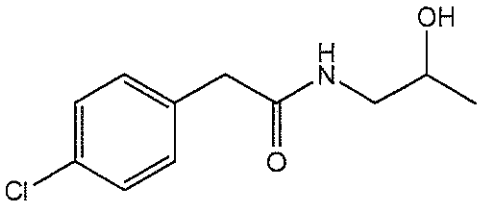
or salt thereof, wherein Lg is a leaving group,
with an amine compound of Formula 1-2:



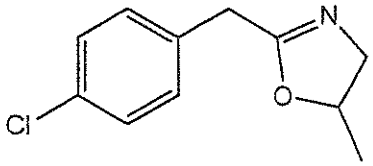
1-2

or salt thereof, in the presence of a coupling reagent to afford said amide compound of Formula 1-3.

The present ~~invention~~disclosure provides processes for preparing an amide compound of Formula 1-3 and optionally a dihydrooxazole compound of Formula 1-4, or salt thereof:

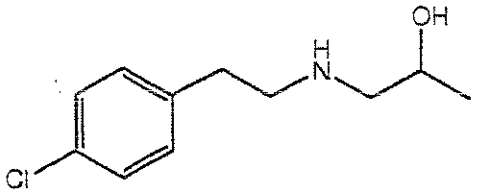


1-3



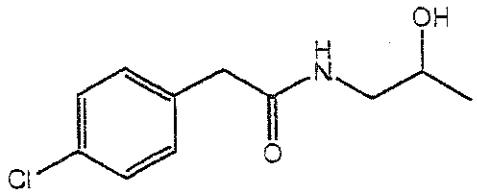
1-4.

In one aspect, there is provided a process for preparing an amino alcohol compound of Formula 2-1:



2-1

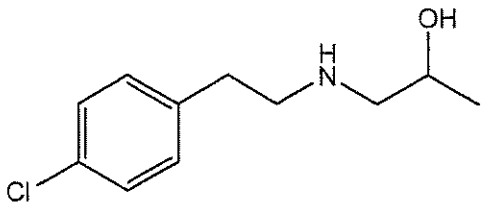
or salt thereof, comprising reacting an amide compound of Formula 1-3:



1-3

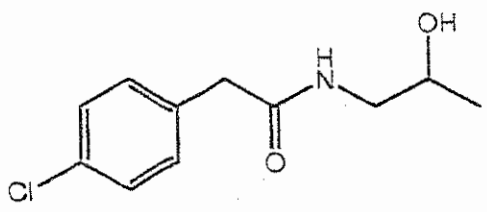
with a reducing agent to afford said amino alcohol compound of Formula 2-1, or salt thereof.

The present ~~invention~~disclosure further provides processes for preparing an amino alcohol compound of Formula 2-1, or salt thereof:



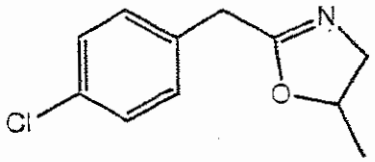
2-1.

In one aspect, there is provided a compound of Formula 1-3:



1-3.

In one aspect, there is provided a compound of Formula 1-4:



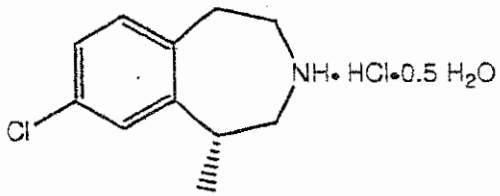
1-4

or salt thereof.

In one aspect, there is provided a composition comprising a compound as defined above, or salt thereof.

The present ~~invention~~disclosure further provides the amide compound of Formula 1-3, the dihydrooxazole compound of Formula 1-4, mixtures thereof, and compositions containing the same.

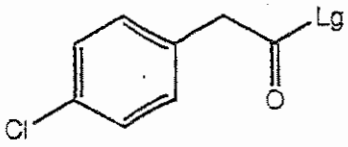
In one aspect, there is provided a process for preparing a compound of Formula 3-5:



3-5

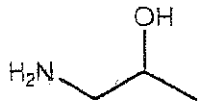
comprising:

a) reacting a phenylacetic acid derivative compound of Formula 1-1:



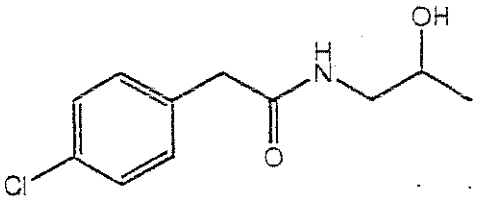
1-1

or salt thereof, wherein Lg is a leaving group, with an amine compound of Formula 1-2:

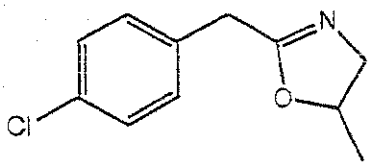


1-2

or salt thereof, in the presence of a coupling reagent to afford an amide compound of Formula 1-3 and optionally a dihydrooxazole compound of Formula 1-4, or salt thereof:

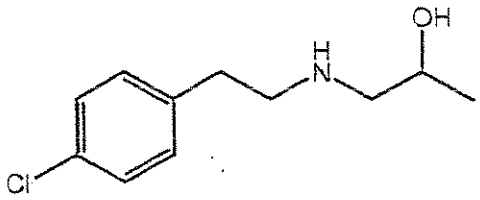


1-3



1-4

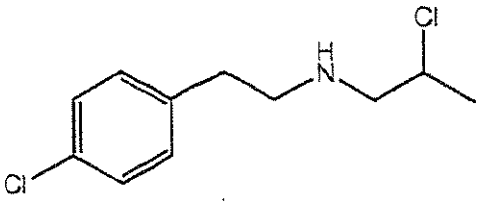
b) reacting said amide compound of Formula 1-3 and optionally said dihydrooxazole compound of Formula 1-4, or salt thereof, with a reducing agent to afford an amino alcohol compound of Formula 2-1:



2-1

or salt thereof;

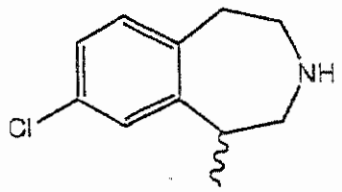
c) reacting said amino alcohol compound of Formula 2-1, or salt thereof, with a chlorinating reagent to afford a dichloro compound of Formula 3-1:



3-1

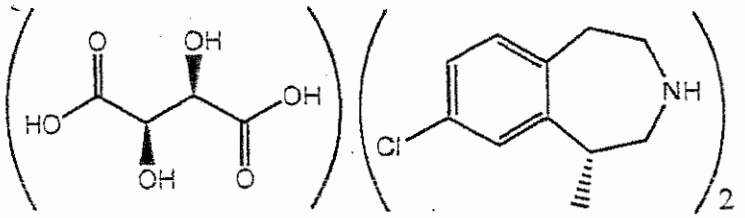
or salt thereof;

d) reacting said dichloro compound of Formula 3-1 with a cyclizing reagent to afford a 3-benzazepine compound of Formula 3-2:



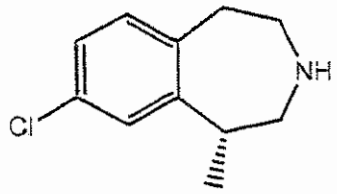
3-2

e) contacting said 3-benzazepine compound of Formula 3-2 with L-(+)-tartaric acid to afford a tartrate salt of Formula 3-3:



3-3

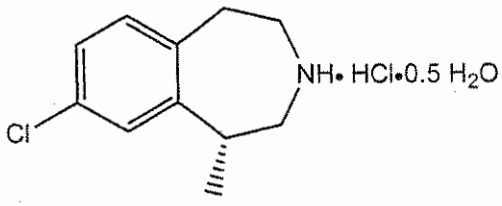
f) reacting said tartrate salt of Formula 3-3 with a base to afford the optically active compound of Formula 3-4:



and

g) reacting said optically active compound of Formula 3-4 with HCl to afford said compound of Formula 3-5.

The present ~~invention~~disclosure further provides processes for preparing a compound of Formula 3-5:



3-5