APOLLO SCIENTIFIC

BICYCLOPENTANES

Bicyclo[x.y.z]alkanes are recognised in chemistry as two saturated rings fused by two common atoms.

Bicyclo[x.y.z]alkanes are known for their use as rigid spacer units within larger molecular structures, in head groups of liquid crystals(1) and as termini in some molecular wires(2). More recently, due to their potential as bioisosteres for aromatic groups, interest in these functional groups has grown. Replacement of a fluorophenyl group in the γ-Secretase inhibitor BMS-708,163 with bicyclo[1.1.1]pentane (Fig. 1) was found to improve solubility and passive permeability without compromising the inhibitor properties(3). BMS-708,163 is currently being investigated as a potential drug which could be used to treat Alzheimer's disease.

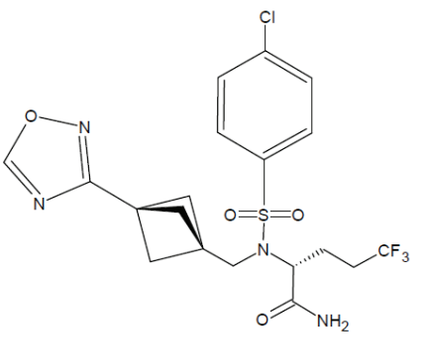
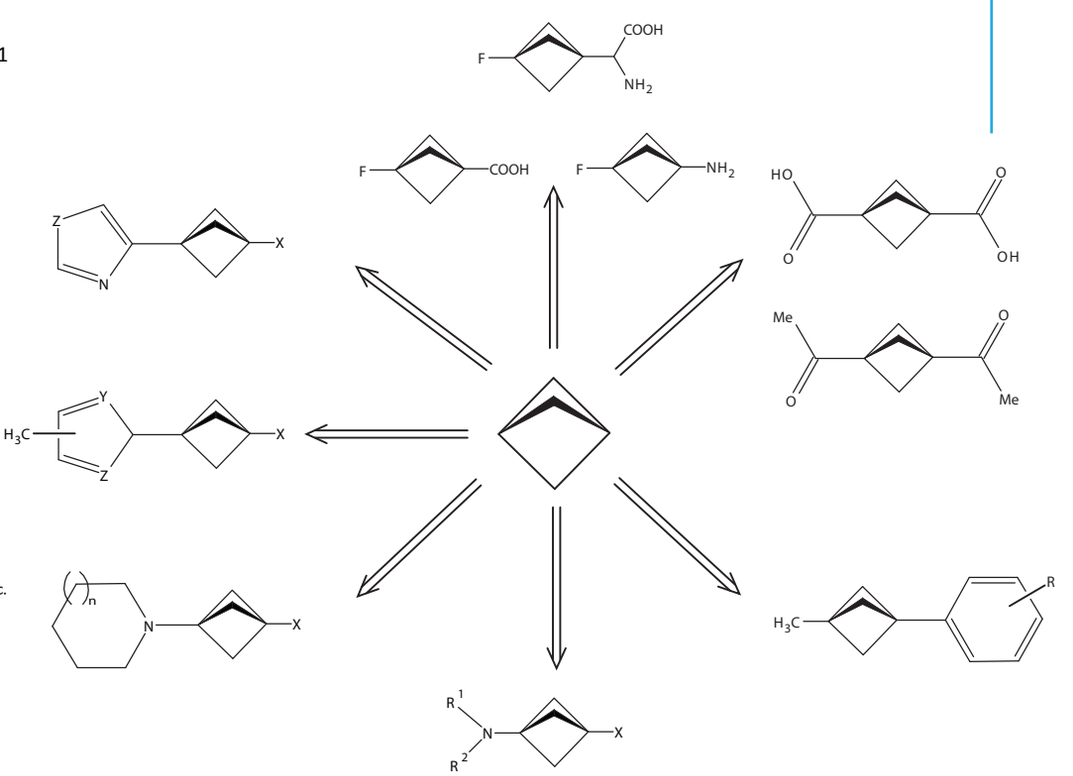


Fig. 1: BMS-708,163 substitute

The wide variation of bicyclo[x.y.z]alkane structures which are available can be utilised to mimic various aromatic groups as a result of their bond lengths, the angles between exit vectors and their rigidity. As such, in addition to phenyl groups they offer potential as substitutes for furan, thiophene, pyrrole, pyridine and other heteroaromatics. Alternatively, replacement of a cycloalkane, with bicyclo[1.1.1]pentane can be used to retain stereochemistry of the molecule which can be lost through ring flipping. It is also thought that bicyclo[1.1.1]pentane could also be used as an isostere for –^{t}Bu and alkyne groups(4).

We have a wide range of bicyclo[1.1.1]pentane compounds which have recently been developed and are now available, derivatives of which can be made on demand. A selection of possible structures is highlighted below.

(1) *Molecular Crystals and Liquid Crystals*., 1991, **209**, 201
(2) *J. Phys. Chem*., 2003, **107**, 3970
(3) *J. Med. Chem*., 2012, **55**, 3414
(4) *Chem. Med. Chem*., **2015**, *10*, 461



X= NHR, CO_2R, CN, CH_2OH, CH_2NH_2, F, Cl, Br, I, etc.

R, R^1, R^2 = Alkyl, Aryl

n = 0, 1, 2

Y = N, CH

Z = O, NR, S

Tel: +44 (0)161 406 0505
Fax: +44(0)161 406 0506
Email: sales@apolloscientific.co.uk
Website: www.apolloscientific.co.uk
@ ApolloSciUK

Apollo Scientific Ltd
Whitefield Rd
Stockport, Bredbury
Cheshire
SK6 2QR