Charnwood Molecular

Excellence in Chemistry

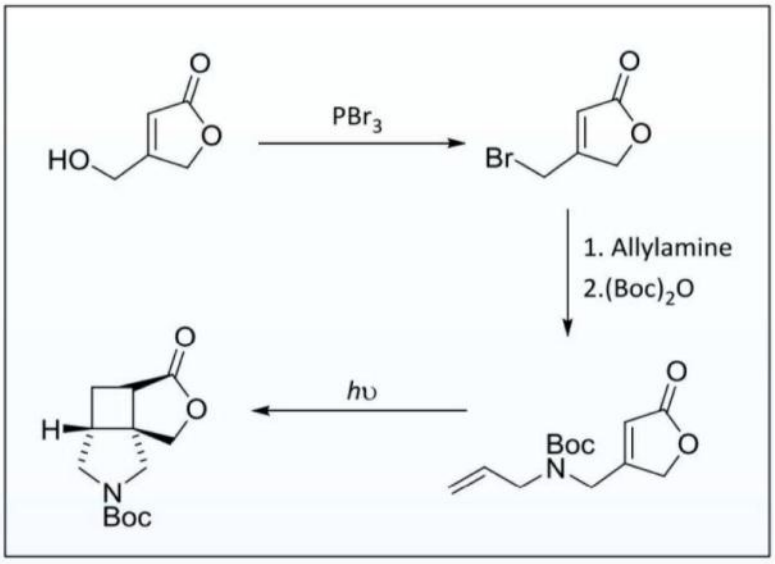
Photochemistry: Avoiding "The Flatlands"

Rapid Access to Complex 3D Medicinal Chemistry Scaffolds

Photochemistry is becoming increasingly utilised as a key enabling technology to provide discovery chemists with rapid access to complex, 3-dimensional molecular templates, covering new areas of chemical space.

Screening compounds generated from such novel scaffolds readily overcome the molecular 'flatness' (low sp^3 character) which has become prevalent in the industry in recent years,[i] driven by sp^2-sp^2 aryl couplings emerging as favoured synthetic steps. Low alkyl sp^3 character in compounds can have a negative effect on aqueous solubility and formulation, whilst increased aromaticity can increase undesired properties, such as CYP inhibition, plasma-protein binding & hERG binding, which negatively impact drug development.[ii]

3-Azacicyclo[3.2.0]heptanes have been identified as conformationally restricted analogues of pyrrolidine: the rigid cyclobutane allowing functional groups to be positioned in a spatially defined manner.[iii]



Using photochemical methods we have recently completed the synthesis of > 50g of the interesting 3D tricyclic core shown as an intermediate for a Medicinal Chemistry program.

The synthesis was performed using a state-of-the-art Rayonet RMR-200 photochemical reactor, which acts as an intense, safe source of ultraviolet light using 16 separate light sources. Various wavelengths from 254 nm to 570 nm are available from the reactor, which processes volumes of up to 2L without external cooling.

Charnwood Molecular can now offer photochemistry services for compounds including heterocycles, ketones, halide derivatives and olefins, providing our clients with key building blocks to enhance their Drug Discovery projects.

i. Lovering, F.; Bikker, J.; Humblet, C. *J. Med. Chem.*, **2009**, *52*, 6752

ii. Walters, W. P.; Green, J.; Weiss, J. R.; Murcko, M.A. *J. Med. Chem.*, **2011**, *54*, 6405 & references therein.

iii. Fort, D. A.; Woltering, T. J.; Alker, A. M.; Bach, T. *Chem. Commun.*, **2013**, *49*(29), 2989; Fort, D. A.; Woltering, T. J.; Alker, A. M.; Bach, T. *Heterocycles*, **2014**, *88*(2), 1079; Fort, D. A.; Woltering, T. J.; Alker, A. M.; Bach, T. J. *Org. Chem.*, **2014**, *79*(15), 7152.

Charnwood Molecular Ltd

The Heritage Building, 7 Beaumont Court,

Prince William Road, Loughborough, UK, LE11 5DA.

www.charnwood-molecular.com

+44 (0) 1509 232007 info@charnwood-molecular.com

#charnwoodmol charnwood-molecular