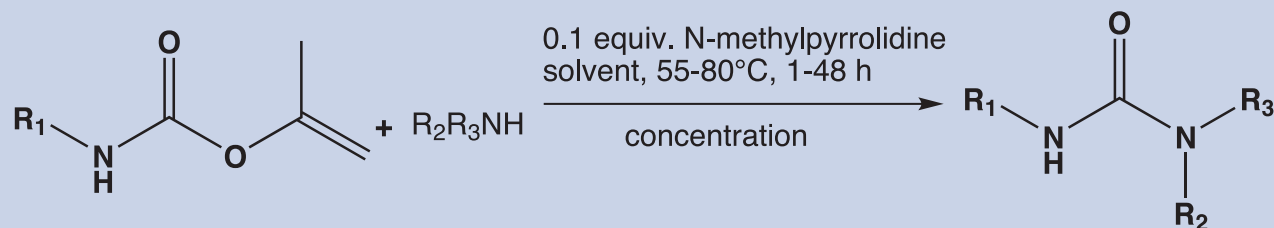


Isopropenyl Carbamates - Stable Isocyanate Replacements for the Practical Synthesis of Unsymmetrical Ureas

Ureas are common structural features present in drug molecules. Sorafenib (marketed as Nexavar by Bayer) is a multikinase inhibitor targeting a number of serine/threonine and receptor tyrosine kinases. It is a drug approved for the treatment of primary kidney cancer (advanced renal cell carcinoma) and advanced primary liver cancer (hepatocellular carcinoma). Tivozanib is a highly potent and selective oral inhibitor of vascular endothelial growth factor (VEGF) receptors 1, 2 and 3 currently in Phase 3 development. This method of inhibition has potential to treat a wide range of cancer types.

Traditional methods for urea synthesis, such as the use of phosgene or alkyl and aryl carbamates, are limited by the formation of symmetrical urea side products or reaction reversibility. Isopropenyl carbamates react with amines efficiently and irreversibly to give unsymmetrical ureas in high yield and purity. Upon reaction with an amine, isopropenyl carbamates liberate acetone enol, which rapidly tautomerises to acetone allowing irreversible urea formation.

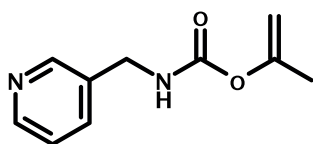
Ureas are most commonly formed by the reaction of an isocyanate with an amine. There is a limited number of commercially available isocyanates and these have minimal structural diversity. Furthermore, isocyanates are very susceptible to hydrolysis making them unsuitable for prolonged storage whereas isopropenyl carbamates are stable and can be stored indefinitely.



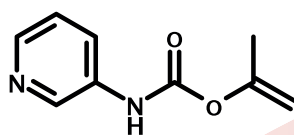
General Procedure for Urea Synthesis - Gallou et al , J.Org.Chem, 2005, 70, 6960-6963.

An equimolar solution of the isopropenyl carbamate and amine in THF is heated at 55°C (higher boiling solvents for 80°C) with a catalytic amount of base (0.1 eq of N-methylpyrrolidine or triethylamine) for up to 48 hours. The product is isolated by concentration under vacuum. Under these reaction conditions various functional groups are stable such as acetals and NBoc protected amines.

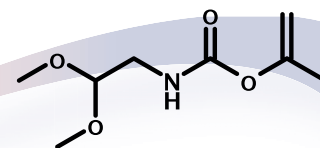
We have launched an exciting set of novel isopropenyl carbamates containing pharmacophoric features which can be used as scaffolds and isocyanate replacements. Formation of ureas by displacement of acetone enol is possible in the presence of masked aldehydes and NBoc groups. (Note - the corresponding isocyanates are not readily available). For accurate pricing and availability please check by substructure search "Isopropenyl carbamate" on our website: www.activate-scientific.com



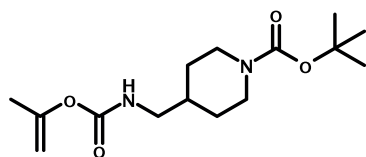
AS9000



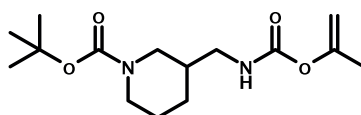
AS9009



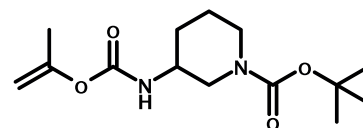
AS9008



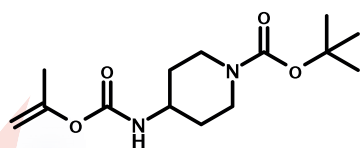
AS9001



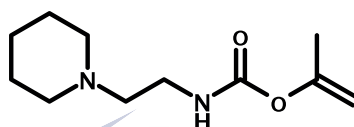
AS9002



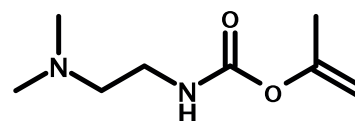
AS9004



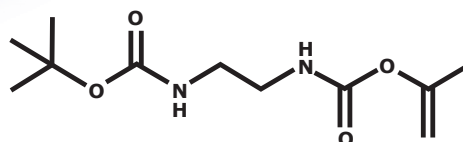
AS9003



AS9005



AS9006



AS9007

Standard Pack Sizes: 1-5-10-25g More compounds?
We would be happy to investigate the custom synthesis of any proprietary templates