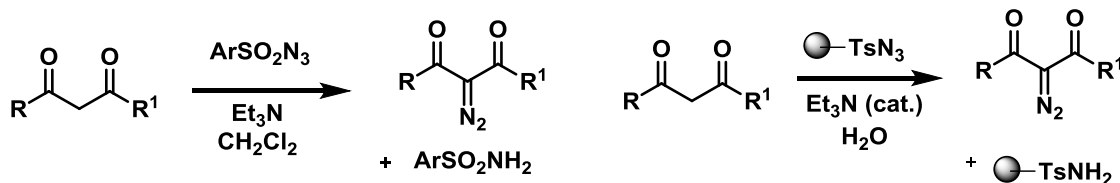


A Fresh Approach towards the Synthesis of α -Diazocarbonyl Compounds

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Abstract:

α -Diazocarbonyl compounds play a key role in organic synthesis due to the fact that they are easily prepared, and can undergo a wide range of chemical transformations *via* the initial loss of nitrogen. This is achieved under thermal, photochemical or catalytic conditions and generates reactive intermediates such as carbenes, carbenoids and carbonyl ylides.¹

There are a number of methods of synthesizing α -diazocarbonyl compounds², however the most common method for the introduction of the diazo group is by the methodology developed by Regitz.³ This involves reacting a substrate such as β -keto esters or β -diketones with tosyl azide in dry acetonitrile using triethylamine or potassium carbonate as a base,⁴ however tosyl azide is an extremely dangerous transfer reagent and care must be taken when handling it.^{5,6}

Despite their usefulness as intermediates and the range of chemical transformations which they can undergo, these compounds are not routinely used in industrial processes, due to the hazards that are associated with diazo-transfer reagents used such as tosyl azide, and also because they are carried out in harmful and non-environmentally friendly organic solvents such as dichloromethane/acetonitrile. Recently, diazo transfer has been reported in ionic liquids, utilizing sub-stoichiometric quantities of base.⁷ With this in mind, we decided to take a fresh look at the synthesis and methodology used to generate α -diazo- β -ketoesters, paying particular attention to doing the reactions in water, using a catalytic amount of base and utilising the safer polymer bound azide as highlighted above.⁸ In an extension of this work, using immobilised diazo transfer reagents and catalysts incorporated within a flow chemistry system can lead to these hazards being nullified through safer reactions and cleaner products (environmental aspect), faster reactions, quick reaction optimization and easy scale-up (to produce kilogram quantities).

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