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Metal-free synthesis of sulfonamides via iodine-catalyzed oxidative coupling of sulfonyl hydrazides and amines

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ABSTRACT

A novel, rapid and environmentally-friendly protocol for the synthesis of sulfonamides using iodine as catalyst under solvent-free conditions is described. This method involves the oxidative coupling of sulfonyl hydrazides and amines in the presence of catalytic amount of iodine using TBHP as oxidant. This protocol does not require purification techniques such as column chromatography and recrystalization.

Sulfonamides have received significant relevance in modern organic chemistry and are very privileged class of compounds in synthetic and medicinal chemistry.[1] Sulfonamides are ubiquitous motif seen in many of natural products and pharmaceutically active compounds. Sulfonamide derivatives become popular ever since the discovery of their activity towards antibacterial, anticancer, antiviral, anticonvulsant, anti-inflamatory, antiviral, antitumor and HIV protease inhibitory[1,2] (Figure 1). Furthermore, sulfonamides can also be used as inhibitors for the enzymes carbonic anhydrase, potent COX-2 and caspase.[3] Azo dyes containing sulfonamide moiety are used for the improvement of fibre fixation and light-stability.[4] Because of the easy removal of sulfonamide group under mild conditions, these arylsulfonyls can be used as protecting groups for amino functionalities.[5] Due to their significance, over the last several years many endeavours have been made for the synthesis of sulfonamides. Most commonly, these sulfonamides can be synthesized by the reaction of sulfonyl chlorides with amines[6] and by the coupling of sulfonamides separately with organic alcohols or esters,[7] halides,[8] aryl boronic acids[9] and by aminosulfonation of hydrocarbons[10] under transition metal catalysis. Pan and his co-workers developed an oxygen-activated radical protocol for the synthesis of sulfonamides from aryl thiols under copper catalysis in the presence of stiochiometric amounts of $Cu(OAc)_2$ and cinnamic acid.[11] Chan-Lam coupling of sulfonyl azides and boronic acids under copper-catalysis is another alternative.[12] Though these methods are efficient for the synthesis of sulphonamides, most of them suffer from one or another drawback such as harsh and complex reaction conditions, slow reactivity, poor functional group tolerability, tedious purification procedures and usage of transition metals which may cause contamination in pharmaceutical industry. The title compounds can also be synthesized from the reactions of sodium sulfinates

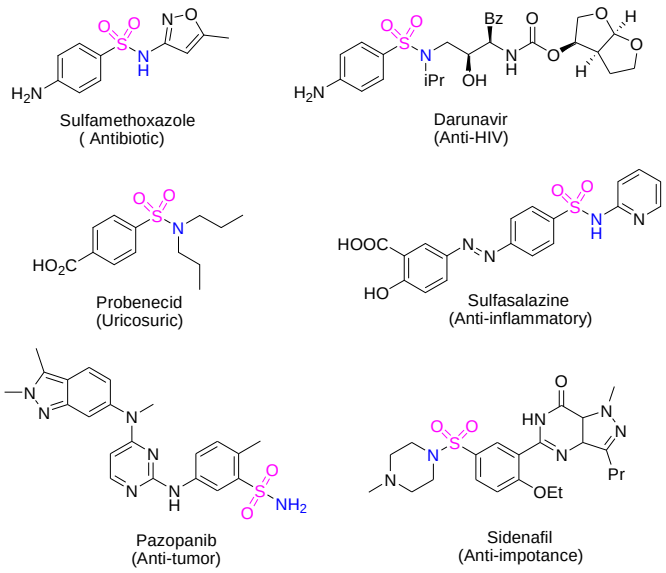

Figure 1. Drugs containing sulfonamide moiety.

with amines under metal and metal-free conditions.[13] Therefore, to overcome these problems it is highly desired to develop a novel, green and sustainable methods for the construction of sulfonamides.

In continuation of our work towards the development of green protocols,[14] herein, we report an efficient, rapid and green method for the construction of sulfonamides by iodine catalyzed[15] oxidative coupling reaction of sulfonyl hydrazides with amines under metal- and solvent-free conditions. The present metal- and solvent-free protocol has various advantages