When sulfur meets oxidant

Transition-metal-catalyzed oxidative cross-coupling between boronic acids and heteroatom nucleophiles has been well known as the Chan?Lam reaction and emerged as a powerful protocol for the construction of carbon-nitrogen bonds or carbon-oxygen bonds, due to a variety of readily available boronic acids and their derivatives. However, direct cross-coupling between metallic nucleophile and sulfide has been less studied, despite its importance in the pharmaceutical industry, material science, and food chemistry in the race toward organosulfur compounds synthesis. There are three main reasons for this: a) strong coordination of the lone pair electrons on sulfur to the transition metal; b) preferential oxidization to disulfide when thiol meets oxidant; and c) unpleasant smell during the experimental process.

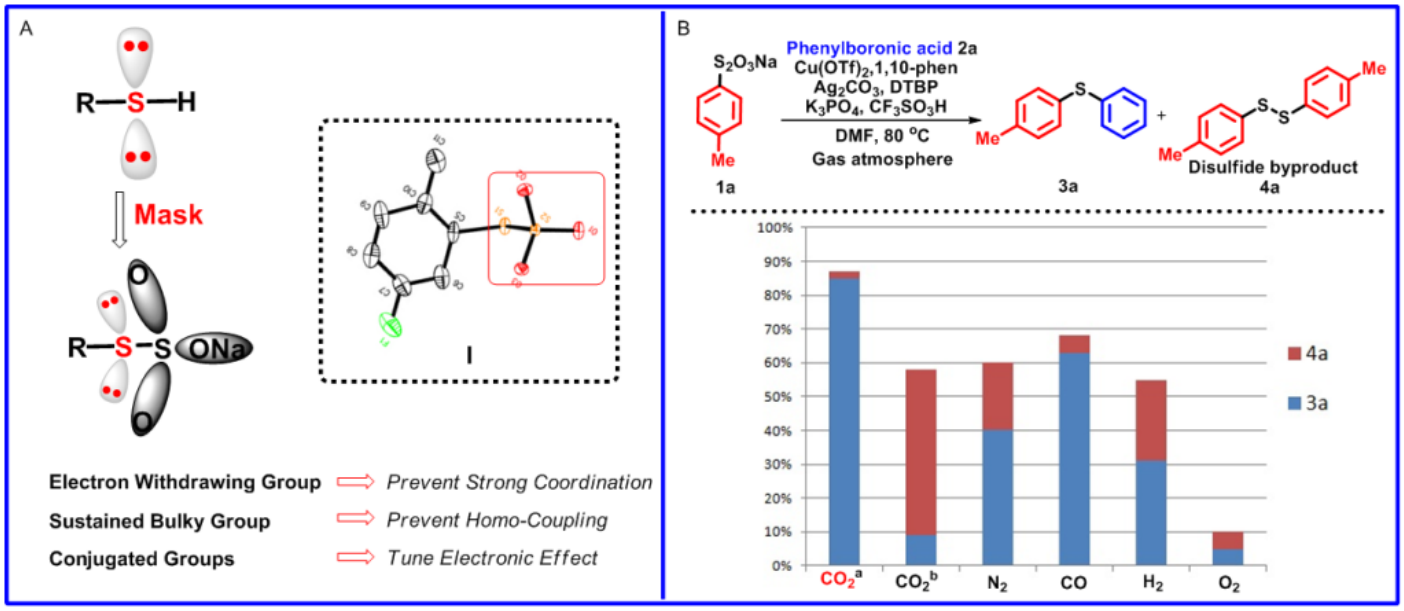

Fig. 1. (A) Masked Sulfide. (B) Dramatic Atmosphere Effect

Cu-catalyzed direct oxidative cross-coupling between boronic acids and masked sulfides delivering thioethers was described in this study, in which the SO_3^-, as a mask, has shown a distinctive effect on oxidative cross-coupling condition and its structure has been confirmed by X-ray diffraction analysis (Fig. 1A). SO_3^- should be the right candidate for the mask because of its unique properties: a) an electron withdrawing group preventing the strong coordination to metal; b) a sustained bulky group preventing homo-coupling; and c) a conjugated group tuning the electron effect on sulfur. In addition, by-product disulfide could be suppressed efficiently *via* masked strategy under CO_2 atmosphere (Fig. 1B). Current observations from the physical absorption phenomenon and control experiments demonstrated that the enabling atmosphere played the role of stabilization and slow release of the mask, perhaps by the formation of carbonate, bicarbonate,

or carbonic acid.

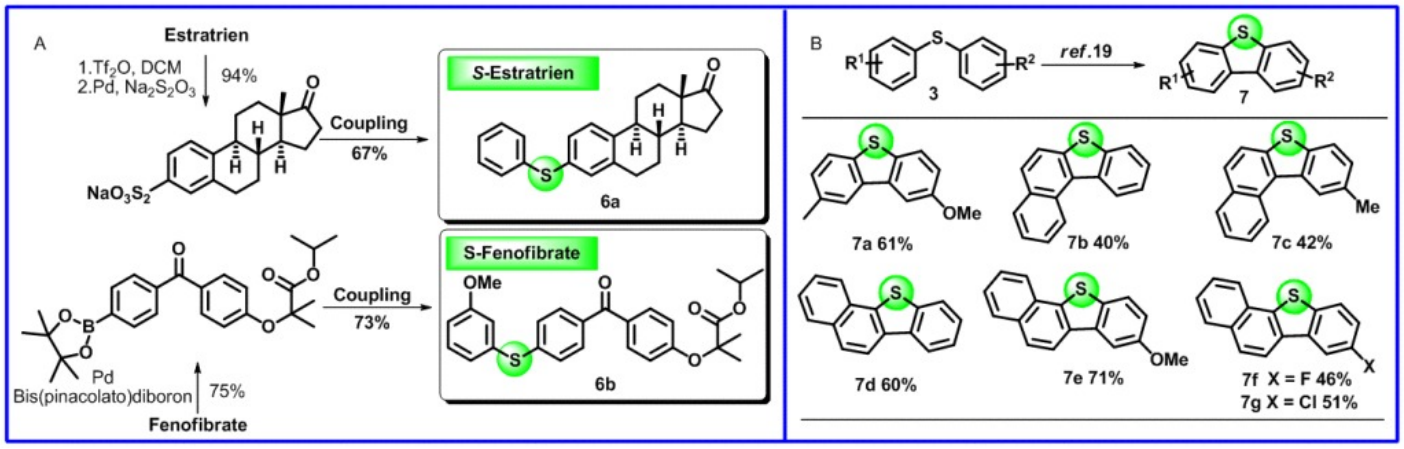

Fig. 2. Application in Parmaceutical and Material

Furthermore, a broad scope of aromatics and scalable processes indicates its practicality, which could be readily applied to drug late-stage diversi?cation (Fig. 2A). Estratrien, a kind of female hormone drug, could be easily transformed to the corresponding organic thiosulfate salt in 94% yield, to afford sulfur-modified estratrien followed by oxidative sulfurating cross-coupling. This method offers great potential for the generation of drug analogue libraries. From another aspect, this method could be carried out to establish unsymmetrical dibenzothiophenes (DBTs), which consititute a core framework in certain kinds of organic compounds including pharmaceuticals, photoactive compounds, dyes, liquid crystals, and conducting polymers (Fig. 2B).

Publication

CO2-promoted oxidative cross-coupling reaction for C-S bond formation via masked strategy in an odourless way.
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