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New thiourea organocatalysts and their application for the synthesis of 5-(1*H*-indol-3-yl)methyl-2,2-dimethyl-1,3-dioxane-4,6-diones a source of chiral 3-indoylmethyl ketenes

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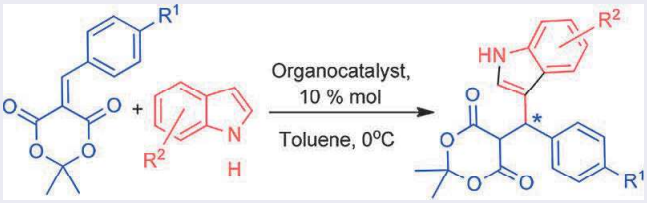
ABSTRACT

The stereoselective properties of modified thiourea organocatalysts were tested in the Friedel–Crafts alkylation of indole with 5-arylidene-2,2-dimethyl-1,3-dioxane-4,6-diones, which produces chiral 5-((1*H*-indol-3-yl)(aryl)methyl)-2,2-dimethyl-1,3-dioxane-4,6-diones. Based on a tentative reaction mechanism for ((S)-*N*-benzyl-2-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)-*N*,3,3-trimethylbutanamide organocatalysts, modifications were applied in four selected regions. Systematic structure-stereoselectivity relationship study allowed designing the best efficient organocatalyst for the investigated Friedel–Crafts alkylation of indole with 5-arylidene-2,2-dimethyl-1,3-dioxane-4,6-diones.

GRAPHICAL ABSTRACT



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Introduction

Indole derivatives are biologically active compounds. The structural pattern of indole can be found in an impressive variety of molecules, such as phytohormones,[1] neuro transmitters,[2] anti-inflammatory agents,[3] and anticancer medicine.[4] From the perspective of modern pharmacology, manipulation with serotonin and 5-HT receptors by stimulating with indole derivatives could be a key in solving problems related to mood, depression, and anxiety disorders. Therefore, synthesis of serotonin agonists, particularly targeted as selective serotonin reuptake inhibitors (SSRI), can be the center of interest in medicinal chemistry. The derivatives of homotryptamine[5] and tetrahydrocarbazoles[6] are an interesting group of SSRIs with indole moiety in molecules. Tetrahydrocarbazole derivatives are also useful for the treatment of human papillomaviruses.[7] The

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