

ENANTIOSELECTIVE ORGANOCATALYTIC SYNTHESIS OF *N*-ALKYLATED INDOLES

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The indole core **1** is present in a variety of biologically active natural products and pharmaceutical compounds [1]. The enantioselective functionalization of the *N*-position of indole ring system has been an active area of research [2, 3]. The aromaticity of the indole, low nucleophilicity of the nitrogen atom and weak acidity of *N*-*H* make the *N*-functionalization challenging.

The aim of this study is to find novel enantioselective organocatalytic methods for the *N*-alkylation of indole.

Previously, we demonstrated an enantioselective phase-transfer-catalyzed *N*-alkylation of nitroindoles with various Michael acceptors. The method provides products with high yields and moderate enantiomeric excess (Fig 1. **I** route) [4].

Here, we present the first organocatalytic method

where indole adducts **5** were implemented as electrophiles affording desired *N*-alkylated indoles with α -branched alkyl substituents **7** in high *ee*-values and in good yields (Fig 1. **II** route) [5]. Various nucleophiles **6** (nitroalkanes, malononitrile, malonic esters) can be used. The substitution pattern of the indole ring had no significant impact on the reaction outcome. Both electron-withdrawing and electron-donating substituents in any position of the heteroaromatic ring were well-tolerated.

References

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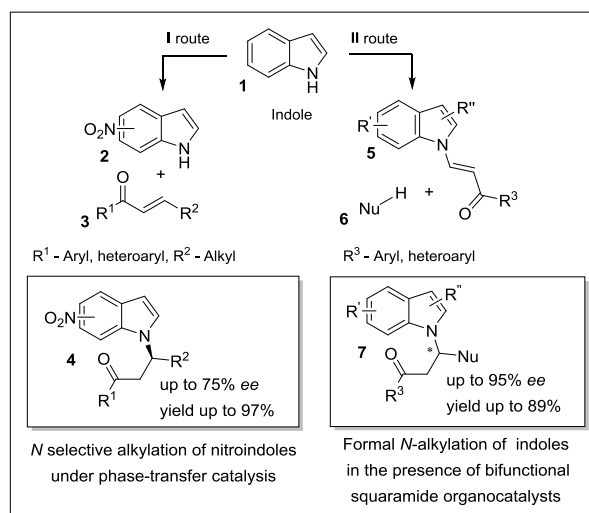


Fig. 1 Enantioselective *N*-functionalization of indole derivatives.