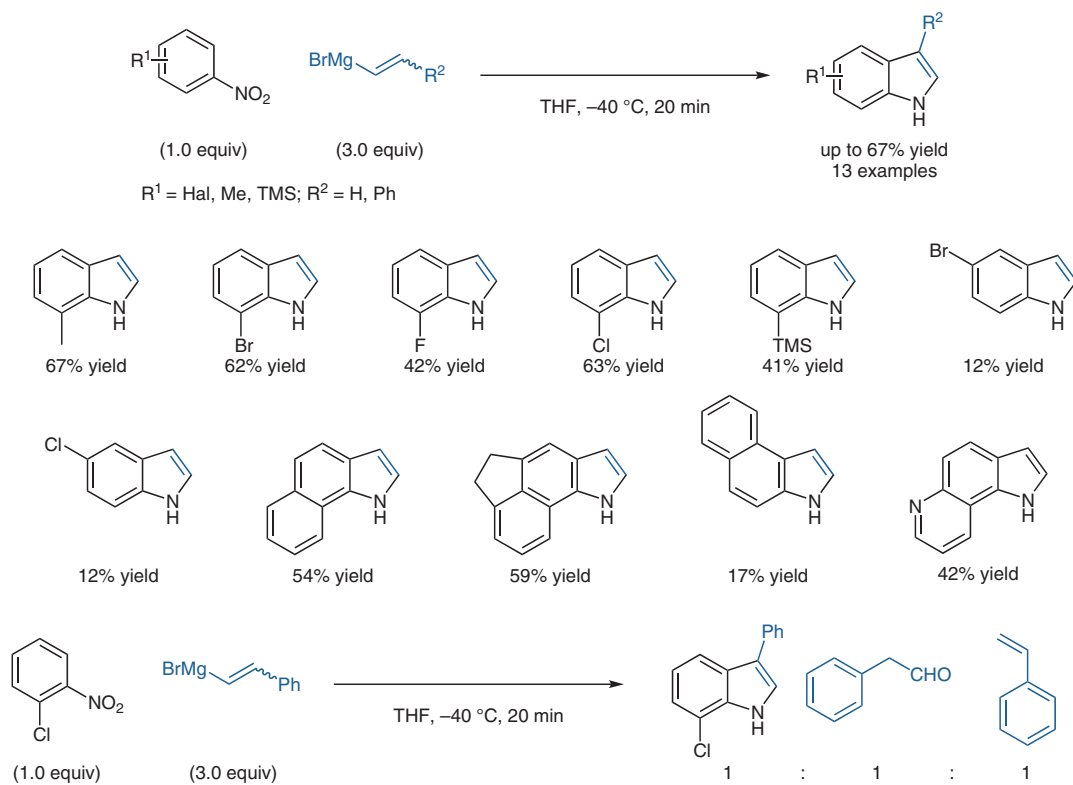


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The Reaction of Vinyl Grignard Reagents with 2-Substituted Nitroarenes: A New Approach to the Synthesis of 7-Substituted Indoles

Tetrahedron Lett. **1989**, *30*, 2129–2132, DOI: 10.1016/S0040-4039(01)93730-X.

The Bartoli Indole Synthesis



Significance: In 1989, Bartoli et al. reported an indole synthesis starting from substituted nitroarenes and vinyl Grignards. Satisfactory yields are obtained only for *ortho*-substituted nitroarenes; 4-substituted nitroarenes gave the corresponding anilines as major products. The versatile behavior of the vinyl Grignards is notable. The use of styryl magnesiumbromide in place of the vinyl magnesiumbromide leads to a mixture of desired indole, phenylacetaldehyde and styrene in a ratio of 1:1:1. The procedure allows for the efficient synthesis of 7-substituted indoles.

Review: For a review on the Bartoli indole synthesis and its applications, see: G. Bartoli, R. Dalpozzo, M. Nardi *Chem. Soc. Rev.* **2014**, *43*, 4728–4750.

Comment: The result of the styryl magnesiumbromide reaction is discussed in another publication of the same group concerning the mechanism of the reaction (*J. Chem. Soc., Perkin Trans. 2* **1991**, 657). According to the proposed mechanism, the first equivalent of Grignard reduces the nitro group to a nitroso functionality, ultimately leading to the phenylacetaldehyde shown in the scheme above. The second equivalent attacks the oxygen atom of the nitroso group in a SET-triggered reaction. The formed product undergoes [3,3]-sigmatropic rearrangement forming the *ortho*-substituted indole scaffold. The third equivalent deprotonates the nitrogen, which induces rearomatization of the six-membered ring and subsequent formation of the five-membered ring. In the reaction sequence shown in the scheme, this equivalent ends up as styrene. Quenching with NH_4Cl leads to dehydration and rearomatization of the five-membered ring.

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Synfacts 2021, 17(02), 0187 Published online: 20.01.2021
DOI: 10.1055/s-0040-1706673; Reg-No.: P17320SF

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Category

Metals in Synthesis

Key words

vinyl Grignard reagents

nitroarenes

indoles

Synfact Classic