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# An efficient two-step synthesis of 3-allylindoles

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**Abstract**—A two-step synthetic sequence for an efficient synthesis of 3-allylindoles is described.
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## 1. Introduction and discussion

Several methods have been developed for the synthesis of indoles and substituted indoles as they are a key feature of many natural products and pharmaceutical compounds.[1–20] However, there is still a need to develop newer methods for their synthesis. Alkylation of indoles or salts of indoles under drastic conditions yields a complex mixture of 1-substituted, 1,3-disubstituted, 3-substituted indoles[21–24] and/or indolenines.[25] The conversion of indoles to 3-allylindoles was effected via zinc-mediated Barbier reactions[26] or palladium catalysed allylation.[27] In yet another method, acid-catalysed Claisen rearrangement of 1-allylindole[28] furnished 3-allylindole. All the above methods utilise indoles as starting material.[28–32]

We herein describe an application of the Wittig olefination–Claisen rearrangement methodology[33] towards a short and efficient synthesis of 3-allylindoles in just two steps using simple starting materials viz. *o*-nitrobenzaldehydes. Wittig olefination of *o*-nitrobenzaldehyde **1a**, under standard conditions,[33] with allyloxymethylenetriphenylphosphorane furnished the corresponding allyl vinyl ether **2a**. The allyl vinyl ether **2a** was then subjected to a Claisen rearrangement by heating in refluxing diglyme–water solvent system (1:1) in the presence of excess $FeSO_4$ and $NH_3$ (Scheme 1). To our pleasant surprise, 3-allylindole **3a** was obtained from the reaction mixture.

This clearly indicated that the two reactions, namely, Claisen rearrangement of the allyl vinyl ether to the corresponding 4-pentenal and reduction of the nitro group with $FeSO_4$–$NH_3$ to the corresponding amine were effected simultaneously. The resulting amino aldehyde underwent in situ cyclisation to furnish 3-allylindole. Thus, the synthesis of 3-allylindole was achieved in only two steps. Reaction of substituted *o*-nitrobenzaldehydes also furnished, under the above reaction conditions, substituted 3-allylindoles in good yields.

Furthermore, reaction of the substituted *o*-nitrobenzaldehydes with potassium tertiary butoxide and another Wittig salt, namely, crotyloxymethylenetriphenylphosphonium chloride, gave the corresponding allyl vinyl ethers **4** in good yields (Scheme 2). These allyl vinyl ethers, under the above reaction conditions, furnished novel 3-(3-butenyl)indoles **5**. The present protocol offers a general method for the synthesis of 3-allylindoles in two simple steps. The utility of these 3-allylindoles in the synthesis of complex natural products is being actively investigated.

## 2. Experimental procedure for Claisen rearrangement/ring closure (3a)

To a stirred suspension of ferrous sulfate (16 g, 12 mmol) in diglyme–water (1:1, 5:5 ml), the allyl vinyl ether **2a** (mixture of *E* and *Z* isomers) (1 g, 1 mmol) was added. After refluxing the mixture for 15–20 min (TLC check), excess ammonia was added. The resulting solution was refluxed for 24 h (TLC check). The reaction mixture as such was purified by silica gel column

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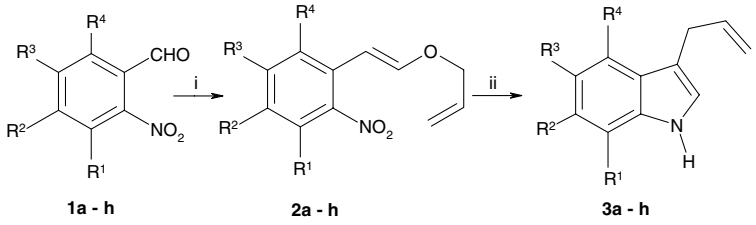
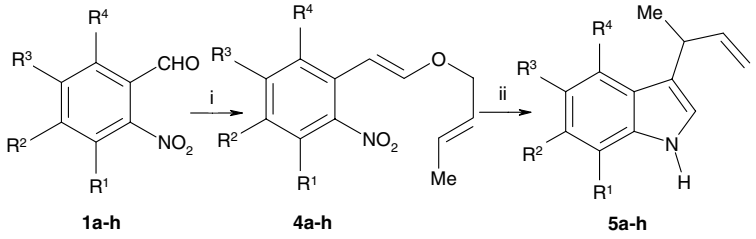



| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | % Yield[a] | |
|---|---|---|---|---|---|---|
| | | | | | **2** | **3** |
| **a** | H | H | H | H | 75 | 77 |
| **b** | OMe | H | H | H | 72 | 80 |
| **c** | H | H | H | Cl | 73 | 79 |
| **d** | H | H | Cl | H | 70 | 76 |
| **e** | H | OMe | OMe | H | 70 | 75 |
| **f** | Br | OMe | OMe | H | 71 | 74 |
| **g** | H | H | OH | H | 70 | 76 |
| **h** | H | -$OCH_2O$- | | H | 72 | 76 |

[a] Isolated yields

**Scheme 1.** Reagents and conditions: (i) $CH_2{=}CHCH_2OCH_2P^+Ph_3Cl^-$, *t*-$BuO^-K^+$, THF, 0 °C, 30 min; (ii) $FeSO_4$, $NH_3$, diglyme–water (1:1), reflux.




| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | % Yield[a] | |
|---|---|---|---|---|---|---|
| | | | | | **4** | **5** |
| **a** | H | H | H | H | 70 | 75 |
| **b** | OMe | H | H | H | 70 | 74 |
| **c** | H | H | H | Cl | 71 | 74 |
| **d** | H | H | Cl | H | 73 | 78 |
| **e** | H | OMe | OMe | H | 72 | 76 |
| **f** | Br | OMe | OMe | H | 73 | 79 |
| **g** | H | H | OH | H | 75 | 78 |
| **h** | H | -$OCH_2O$- | | H | 73 | 75 |

[a] Isolated yields

**Scheme 2.** Reagents and conditions: (i) $MeCH{=}CHCH_2OCH_2P^+Ph_3Cl^-$, *t*-$BuO^-K^+$, THF, 0 °C, 30 min; (ii) $FeSO_4$, $NH_3$, diglyme–water (1:1), reflux.

chromatography using the hexane–ethyl acetate (98:2) solvent system.

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