



## Synthesis of alkyloxy stilbenes by one-pot *O*-alkylation-Wittig and *O*-alkylation-Wittig–Heck reaction sequence

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### ARTICLE INFO

#### Article history:

Received 27 September 2012

Revised 20 October 2012

Accepted 23 October 2012

Available online 1 November 2012

#### Keywords:

One-pot reactions

*O*-Alkylation

Wittig reaction

Mizoroki–Heck reaction

Coupling reactions

Homogeneous catalysis

### ABSTRACT

A new route for the synthesis of alkyloxy stilbenes from hydroxy benzaldehydes is developed by a combination of one-pot reactions. Tandem one-pot *O*-alkylation-Wittig and *O*-alkylation-Wittig–Heck reactions offer a simple access to conjugated alkyloxy stilbenes. A highly conjugated tetra(*p*-alkyloxystyryl) benzene was synthesized from 1,2,4,5-tetrabromobenzene involving a series of one-pot operations following the *O*-alkylation-Wittig–Heck scheme.

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Conjugated molecules are important class of compounds due to their applications in the area of material chemistry. Molecules with  $\pi$ -conjugation are capable of allowing the mobility of electrons through continuous delocalization due to structural and orbital arrangements. Several such molecules are utilized as photovoltaic materials for solar cells, organic light emitting diodes, conducting materials, liquid crystals, optical brighteners, gels, pharmaceutical agents, DNA binding agents, sensors etc.<sup>1</sup> The nature of substitution and the length of conjugation of these molecules mainly influence their properties. Typically the mobility of electrons is controlled by choosing electron releasing or electron withdrawing groups placed at the appropriate positions of the organic molecule. In many studies the alkyloxy groups are selected as electron releasing groups due to the simplicity of their synthesis from corresponding phenols and the reasonable solubility of the resultant materials in routine solvents.<sup>2</sup> Generally the conjugation in the molecule is built by condensation reactions namely Wittig, Knoevenagel, Perkin etc., or by metal mediated coupling reactions such as Mizoroki–Heck or Sonogashira reactions.

Performing several chemical operations simultaneously in a single vessel, also referred as the one-pot or domino or tandem reactions has several distinct advantages. The compatible and complimentary synthetic procedures can reduce the purifications of the intermediate compounds, particularly important with unstable intermediates and may eventually save valuable resources.

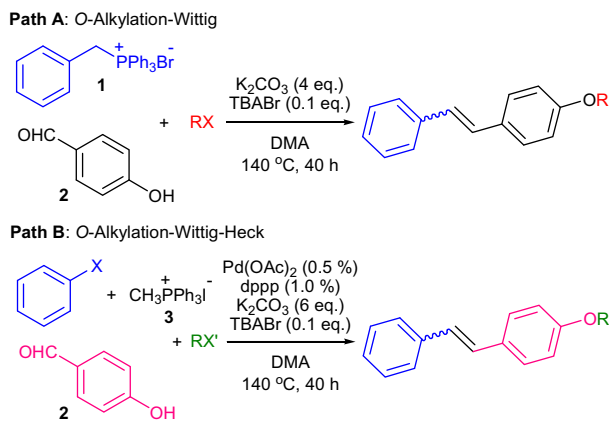
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Recently many attempts have been made to develop efficient protocols to achieve the one-pot synthesis of useful molecules.<sup>3</sup> As part of our interest in the synthesis of conjugated molecules from simple starting material we have developed one-pot dehydrohalogenation–Heck or Wittig–Heck,<sup>4</sup> Wittig–Suzuki,<sup>5</sup> and oxidation–Wittig–Heck<sup>6</sup> reaction schemes. In continuation of these efforts, in this communication we present a one-pot procedure for *O*-alkylation-Wittig and *O*-alkylation-Wittig–Heck reactions for the synthesis of alkyloxy conjugated molecules. The two different approaches developed for the synthesis of *O*-alkyloxystilbenes are outlined in Scheme 1.

In Path A, 4-hydroxybenzaldehyde **2** was subjected to two chemical transformations; firstly the aldehyde will undergo the Wittig reaction with a ylide generated from the phosphonium salt **1** of benzylhalide and secondly the *O*-alkylation of hydroxyl group with an appropriate alkylhalide. Since both the steps are taking place in the basic medium one can conduct them simultaneously. The availability of benzylhalide for the Wittig reaction can be a limiting factor of this approach. This may be addressed by adopting Path B, where the 4-hydroxybenzaldehyde may be converted into 4-alkyloxystyrene by the Wittig reaction with one carbon phosphonium salt **3** ( $\text{CH}_3\text{PPh}_3\text{I}$ ) and alkylation of hydroxyl group. The in situ generated 4-alkyloxystyrene can undergo the Pd catalyzed Mizoroki–Heck reaction with an appropriate aryl halide. This approach may have wider applications due to easy availability of functionalized aryl halides.

Synthesis of alkyloxystilbenes by Path A was investigated and the results are summarized in Table 1.



**Scheme 1.** Two one-pot paths for the synthesis of *O*-alkylstilbene.

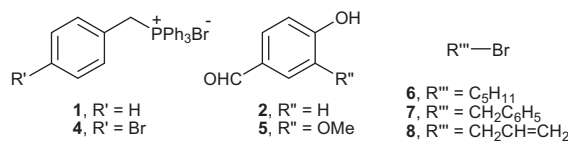
As expected for a typical Wittig reaction,<sup>7</sup> the stilbenes were formed in a mixture of isomers with *E* olefin formed in excess. The reaction conditions were not optimized and the products were isolated in moderate to good yields.

In the second approach the styrenes were synthesized by the in situ reaction with appropriate aldehyde and one carbon Wittig salt **3** and then subjected to the palladium catalyzed Mizoroki–Heck reaction.<sup>8</sup> This Path B was screened for a number of aldehydes and aryl halides under the homogeneous Pd(OAc)<sub>2</sub>-dppp catalyst system with good overall yields, see Table 2. In this protocol the Mizoroki–Heck step determines the stereochemistry of alkene and as expected the product was predominantly formed as *E* isomer.<sup>9</sup>

The development of tandem reactions involving Mizoroki–Heck reaction as one of the steps has also been investigated by others<sup>10</sup> and by us.<sup>4,6</sup> In Path B the in situ generated styrene by the reaction of ylide from one carbon phosphonium salt **3** and a variety of aldehydes, were trapped to build stilbenes by the catalytic coupling reaction. The approach involved an additional step in the one-pot sequence but still the conversions were comparable with the first process.

Certain small conjugated molecules also have significant applications in material chemistry due to their ability to transport electrons from one part to the other within their framework.<sup>2,11</sup> Some of the distyrylbenzenes with suitably placed alkyloxy substitutions have useful optical properties.<sup>2d</sup> The present method was

**Table 1**  
Synthesis of alkyloxystilbenes by Path A<sup>a</sup>



No	Phosphonium salt	Aldehyde/Alkyl halide	Alkyloxystilbene	Yield <sup>b</sup> (%) [ <i>E/Z</i> ] <sup>c</sup>
1	1	2/6		83 [69:31]
2	1	2/7		72 [76:24]
3	1	5/7		80 [57:43]
4	1	5/6		63 [72:28]
5	5	2/6		56 [65:35]
6	5	2/7		55 [57:43]
7	1	2/8		74 [71:29]
8	1	Salisaldehyde/6		84 [84:16]

<sup>a</sup> Conditions: phosphonium salt (1.2 equiv), aldehyde (1.0 equiv), alkyl halide (1.2 equiv), K<sub>2</sub>CO<sub>3</sub> (4 equiv), tetrabutylammonium bromide (TBAB) (10%), DMA, 140 °C, 40 h.

<sup>b</sup> Isolated yield.

<sup>c</sup> *E/Z* Ratio was determined by H NMR.

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