

Unexpected course of Wittig reaction when using cinnamyl aldehyde as a substrate

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Abstract

When trans-cinnamyl aldehyde was used as a substrate of the Wittig reaction, instead of the olefination product, formation of four products with (E)-1,3-diphenylprop-2-en-1-ol and cinnamyl alcohol was observed being quite unexpected ones. The possible mechanism of this unusual reaction has been considered.

Keywords

trans-cinnamyl aldehyde; Wittig reaction; Wittig olefination

INTRODUCTION

The Wittig reaction has been one of the premier routes to obtain alkenes¹⁻³ according to the well-known and generally accepted mechanism shown in Scheme 1.⁴

In this paper an unusual and surprising course of this classical reaction has been observed when *trans*-cinnamyl aldehyde was used as substrate.

RESULTS AND DISCUSSION

Under the classical conditions of Wittig reaction between *trans*-cinnamyl aldehyde **1** and (methoxymethyl)triphenylphosphonium chloride **3** one may expect elongation of the carbon chain leading to the formation of a compound **2** (Path A, Scheme 2). The product **2** of this reaction was intended to be synthesized as a substrate suitable for further transformations. Surprisingly, quite unexpected results were obtained. When using strong base, upon typical procedure of Wittig reaction (entries 1 and 2, Table 1), starting material was completely consumed with the formation of four products as indicated by TLC analysis. Column chromatography enabled to separate compounds seen as first two spots as one fraction in a form of yellow oil, which provided rather complex spectra. However, the formation of crystalline product was observed upon storage and, after its separation, spectroscopic analysis revealed the formation of compound **7** (Path B, Scheme 2). Compounds seen as third and fourth spots turned out to be allylic alcohol **5** and cinnamyl alcohol **6** respectively. Neither the usual olefination product **2** nor any other products were observed. The use of a weaker base, such as DBU (1,8-diazabicyclo[5.4.0]undec-7-ene), did not lead to the formation of any product and only starting material **1** was recovered quantitatively (entry 3, Table 1).

Similar effective nucleophilic arylation of aldehydes and imines with tetrarylphosphonium salts upon action of weak bases has been recently proposed as a general synthetic procedure.⁵ In my case this reaction came out to be inefficient considering the very poor yields of product **5**. However, the unusual transfer of a phenyl group of Wittig reagent to cinnamyl aldehyde requires some explanation. A literature survey gave no answer here, although the loss of one phenyl group from triphenylphosphonium ylides **8** upon action of reducing agent, like lithium aluminum hydride, with the formation of phosphines **9** has been described (Scheme 3). This mechanism is not, however, well understood.^{6,7}

In our case the lack of reducing agent does not allow such an interpretation. Thus, another explanation is derived from the observation of Banejee *et al.*, who noticed the formation of phosphine **11** upon action of base on (methoxymethyl)triphenylphosphonium chloride **3**. This phosphine,⁶ in turn could be oxidized yielding compound **7** (Scheme 4). Similar loss of the aromatic fragment of the molecule was observed for cyclic α -phosphonium salts when using potassium *t*-butylate as a base.⁸ Once more, the mechanism of this reaction needs further studies. The formation of cinnamyl alcohol **6** may suggest that this compound, rather than air, serves as oxidizing agent in the case of this study.

On the other hand, the reaction of methyllithium with methyltriphenylphosphonium bromide **12** alongside with deprotonation of the α -hydrogen atom and formation of ylide **14** is accompanied with the release of benzene (Scheme 5).⁷

These data, although point out on possible non-typical consumption of (methoxymethyl)triphenylphosphonium chloride **3** and formation of some phenyl intermediate still did not allow to solve the mechanism of formation of compounds **5** and **6**.

CONCLUSIONS

Reaction between *trans*-cinnamyl aldehyde **1** and (methoxymethyl)triphenylphosphonium chloride **3** provided unexpected products. Mechanisms of their formation is still not understood and require further studies.

EXPERIMENTAL

All reagents were purchased from Sigma-Aldrich, were of analytical grade and used without further purification. ^1H , ^{31}P and ^{13}C NMR experiments were performed on a Bruker Avance III HD spectrometer operating at 400.13 MHz (^1H), 161.98 MHz (^{31}P) and 100.61 MHz (^{13}C).

(E)-1,3-Diphenylprop-2-en-1-ol (**5**) and (methoxymethyl)diphenylphosphine oxide (**7**).

In a 250-mL well-dried Schlenk flask, equipped with a magnetic stirrer bar, THF (87 mL) was introduced, followed by the addition of (methoxymethyl)triphenylphosphonium chloride **3** (4.8 g, 14 mmol, 1.5 equiv) under argon. The system was cooled to -78°C and *n*-BuLi was added *via* syringe (11.25 mL, 18 mmol, 1.6M in hexanes). The reaction was left for 1 h in 0°C . Then it was cooled to -78°C again and cinnamyl aldehyde **1** was added dropwise (1.1 mL, 9 mmol, 1 equiv). The reaction was left with stirring for 24 h at room temperature. Then, the reaction mixture was concentrated and extracted with Et_2O /water three times. The residue was concentrated and purified by column chromatography on silica gel using cyclohexane/ Et_2O as the eluent (100/0 \rightarrow 50/50) to give 231 mg of *(E)*-1,3-diphenylprop-2-en-1-ol **5** as a yellow oil (11% of yield). R_f (silica, cyclohexane/diethyl ether: 7/3) = 0.3 (UV). ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.22-7.44 (m, 10H, H_{Ar}), 6.69 (d, $J=15.9\text{Hz}$, 1H, H_8) 6.38 (dd, $J=6.5\text{Hz}$, $J=15.9\text{Hz}$, 1H, H_7) 5.38 (d, $J=6.5\text{Hz}$, 1H, H_9), 2.13 (s, 1H, H_{10}); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 142.6 (C_{11}), 136.4

(C₅), 131.4 (C₇), 130.4 (C₈), 128.5 (2C, C_{Ar}), 128.4 (2C, C_{Ar}), 127.7 (2C, C_{Ar}), 126.5 (2C, C_{Ar}), 126.2 (2C, C_{Ar}), 75.0 (C₉).

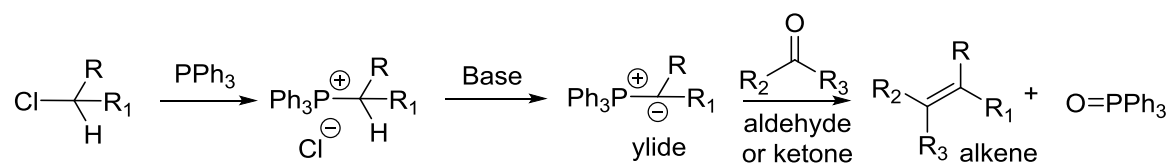
Product **7** was obtained in the same procedure. Purification by column chromatography led to the mixture of compounds. After 48h, white solid was formed in the flask. Isolation of a small amount of white solid allowed its identification as compound **7**. Spectroscopic characterization of this compound is in full agreement with literature data.⁶

FUNDING

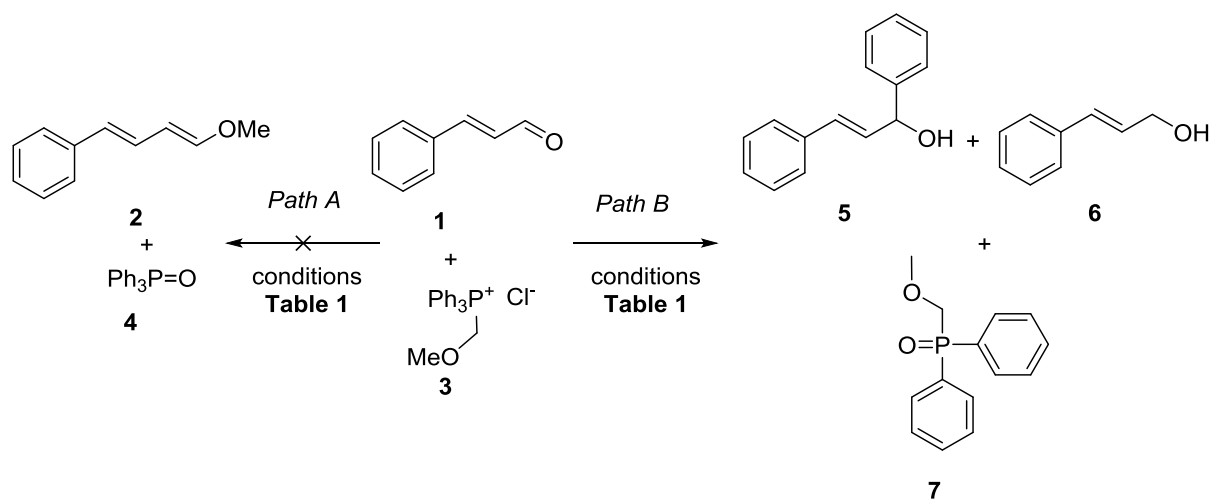
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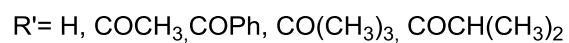
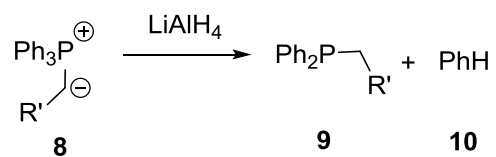
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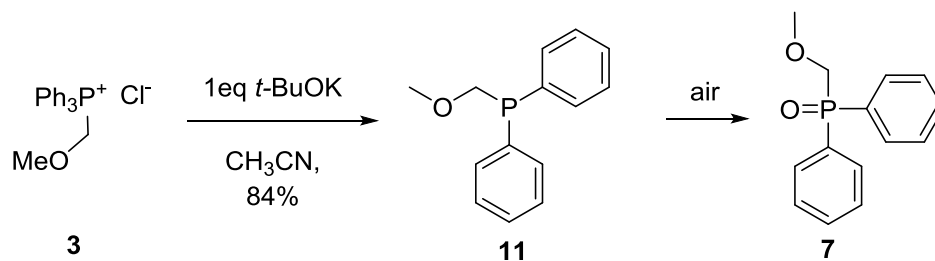
Scheme 1 General mechanism of the Wittig reaction



Scheme 2 Reaction of *trans*-cinnamyl aldehyde with (methoxymethyl)triphenylphosphonium chloride under typical conditions of Wittig reaction



Scheme 3 Reaction of some triphenylphosphonium ylides with lithium aluminium hydride.



Scheme 4 Decomposition of (methoxymethyl)triphenylphosphonium chloride in basic conditions

Table 1 Applied conditions of the studied reaction

Entry	Conditions (Solvent: THF) Base	Yield ^[a] of 5 ; 6 [%]
1	2 eq <i>n</i> -BuLi	11 %; 7%
2	2 eq NaH	10 %; 5%
3	1.1 eq DBU	NO ^[b]

^[a] isolated yield ^[b] NO, no reaction