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A novel, short and efficient synthesis of divinyl ethers

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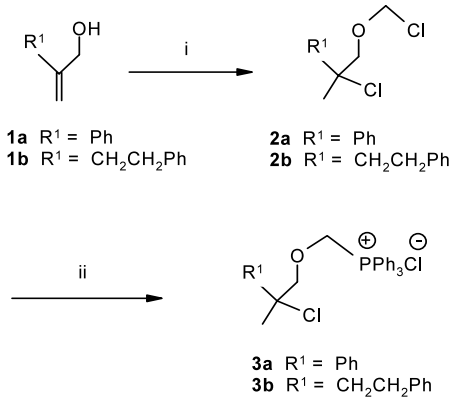
Abstract—An efficient one-step synthesis of divinyl ethers from aldehydes and ketones using Wittig olefination is described.

The special structure of divinyl ether has been of interest for many reasons. It displays rather unique thermodynamic[1] as well as spectroscopic[2] properties. It is an excellent substrate for investigating the photochemical oxa di-π methane rearrangement.[3] The parent compound was used as an anaesthetic.[4] The divinyl ether structural motif is a part of a group of compounds[5] known as 'oxylipins'. These serve as important signal molecules for the expression of defence gene against plant pathogens.[6] The oxylipins act as antimicrobial agents as well.[7] In spite of such diverse properties displayed by this simple structural unit there is no simple and general method for the synthesis of divinyl ethers, except for a few reports for the synthesis of specific compounds involving dehydrohalogenation of the corresponding β,β′-dihalo ethers at elevated temperature,[8] isomerisation of diallyl ethers using palladium on carbon[9] and using 5,5-disubstituted-3-nitrosooxazolidones.[10]

Recently, we have reported a novel protocol for the synthesis of allyl vinyl ethers.[11] This involves the preparation of allyl chloromethyl ether† which on treatment with triphenylphosphine, gave the corresponding Wittig salt. While attempting to extend this method to 2-phenyl-2-propen-1-ol **1a**, the dichloro compound **2a** was obtained when dry hydrogen chloride gas was bubbled through a mixture of **1a** and paraformaldehyde (Scheme 1). Apparently, concomitant addition of hydrogen chloride had taken place across the 1,1-disubstituted olefin in **1a** along with the chloromethylation of the alcohol. Reaction of the dichloro compound **2a** with triphenylphosphine gave the Wittig salt **3a** in good yield. Reaction of the salt **3a** with veratraldehyde (Table 1, entry 1), using excess base, gave the corresponding divinyl ether rather than the allyl vinyl ether. This constituted a novel protocol for the synthesis of divinyl ethers.

Reaction of various aldehydes and ketones with the salt **3a** gave the respective divinyl ethers in good yields (Table 1). A conjugated aldehyde also reacted with the salt **3a** as well to give the corresponding dienol vinyl ether in good yield (Table 1, entry 7). Unlike the olefin in allyl alcohol, the 1,1 disubstituted olefin in 2-phenyl -2-propen-1-ol **1a** is presumably sufficiently electron rich so that hydrogen chloride adds across it under the reaction conditions. As a result the dichloro compound **2a** is formed. From the Wittig salt **3a**, obtained from the chloro compound **2a**, the corresponding phosphorane is generated, in situ, on treatment with the base.



Scheme 1. *Reagents and conditions*: (i) $(HCHO)_n$, dry $HCl_{(g)}$, benzene, 5–10°C, stir, 6 h, (76%); (ii) PPh_3, benzene, rt, stir, 20 h, (78%).

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† **Caution**: Chloromethyl ethers are potent carcinogens and should be handled with due precautions.

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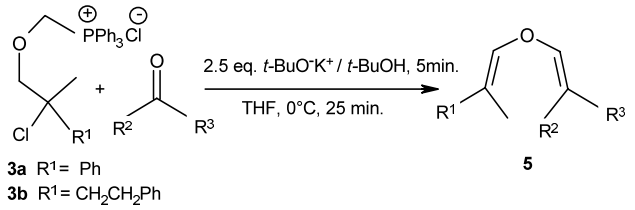
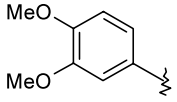
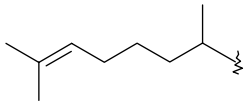
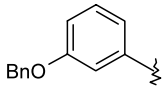
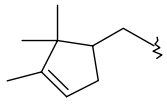
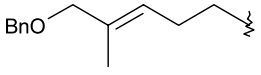
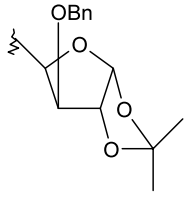
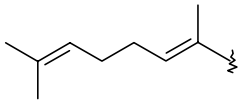
Table 1. Wittig olefination of aldehydes and ketones



3a R^1 = Ph
3b R^1 = CH_2CH_2Ph

Entry no.	Wittig salt	R^2	R^3	Yield (%)
1	**3a**		H	66
2	**3a**		H	74
3	**3a**		H	71
4	**3a**		H	73
5	**3a**		H	71
6	**3a**		H	78
7	**3a**		H	79
8	**3a**	Me	Me	67
9	**3b**	Me	Me	65

Simultaneously, the β proton of the methylene carrying ethereal oxygen, being more acidic, is preferentially abstracted by the excess base present to effect the dehydrochlorination and in the process the enolic olefin of the divinyl ether is produced.

Similarly, from 2-(2-phenylethyl)prop-2-en-1-ol **1b** the dichloro compound **2b** was obtained, which gave corresponding Wittig salt **3b**. Reaction of this Wittig salt **3b** with acetone furnished the divinyl ether (Table 1, entry 9) under the conditions mentioned above. This indicates that in general, the reaction of 2-substituted allylic alcohols yields divinyl ethers via the pathway discussed above.

In conclusion, the reaction sequence presented here constitutes a general, simple, efficient and convenient methodology for the synthesis of divinyl ethers.

General procedure for Wittig olefination: Potassium *t*-butoxide (2.5 equiv.) in *t*-butanol was added dropwise over 5 min to the stirred suspension of aldehyde or ketone (1 equiv.) and Wittig salt (**3a** or **3b**; 1.2 equiv.) in dry THF at 0°C under nitrogen. The reaction was further stirred for 25 min at 0°C. It was quenched using ice-cold water and extracted with ether. The organic layer was dried over anhydrous sodium sulphate and concentrated to give the crude product. Purification on a column of silica gel (100–200 mesh) using hexane: ethyl acetate, (98:2) as eluent gave the corresponding divinyl ether.

Acknowledgements

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