

Organometallic Reactions in Aqueous Medium. Conversion of Carbonyl Compounds to 1,3-Butadienes or Vinyloxiranes

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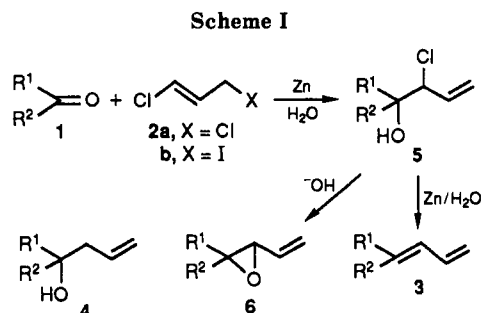
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Summary: Aldehydes and ketones can be converted by 1-chloro-3-iodopropene and zinc powder in aqueous medium to give 1,3-butadienes or vinyloxiranes in high yield.

The importance of organometallic reactions in organic synthesis requires no elaboration. A cardinal restriction in the use of many organometallic reagents is the strict exclusion of moisture. Extreme care must be exercised to ensure that the solvents and the reagents are anhydrous. The reaction often has to be conducted under an inert atmosphere, sometimes inside a drybox. A corollary to this moisture sensitivity is that organic substrates with functional groups containing acidic protons must be appropriately protected during the reaction.

Recently the possibility of conducting organometallic-type reactions in aqueous medium for the formation of carbon-carbon bonds has been considered.¹⁻³ Such reactions may offer the following advantages: (1) There is the practical convenience of not having to handle inflammable and anhydrous organic solvents. (2) The tedious task of protection-deprotection of certain functional groups may sometimes be avoided. (3) Water-soluble compounds such as carbohydrates can be reacted directly. So far, conditions have been developed for the synthesis of homoallylic alcohols in aqueous medium from carbonyl compounds and allyl halides² and for conjugate additions to α,β -unsaturated carbonyl compounds.³

As part of our program to study organic reactions in aqueous media,⁴ we report here a simple synthesis of 1,3-butadienes from carbonyl compounds in aqueous medium according to Scheme I. A typical experimental procedure (method A) is as follows: A mixture of the carbonyl compound 1 (1 mmol), 1,3-dichloropropene (2a, X = Cl; 1 mmol), and zinc powder (2 mmol) in 10 mL of water was heated to 35 °C with vigorous stirring for 3–4 h. The reaction mixture was cooled and quenched with ether. The organic product was isolated from the ether phase and purified by flash column chromatography to give the corresponding 1,3-butadiene 3 (Table I). The reaction has a number of interesting features. First, it is important to note that, in the reaction of benzaldehyde, the yield of 1-phenylbutadiene was quite satisfactory under these conditions in aqueous medium (entry 1) but failed to proceed at all in diethyl ether or other organic solvents normally used for organometallic reactions. Second, the



reaction seems to proceed with both aldehydes and ketones. With cinnamaldehyde, the corresponding triene was obtained (entry 13). Third, the butadienes were formed stereoselectively and, in the case of aldehydes, exclusively as the *E* isomers. Furthermore, unprotected hydroxy compounds such as glyceraldehyde (entry 24) and 5-hydroxypentanal (entry 23) underwent the diene conversion without difficulty. On the other hand, the yield of 3 was modest at best in all cases, in spite of efforts to vary the reaction temperature, time, amount of metal, etc. The poor yield was traced to the formation of the homoallylic alcohol 4, which must have been formed by the zinc-mediated reduction of the intermediate chlorohydrin 5.

The yield of the diene 3 can be substantially improved by using 1-chloro-3-iodopropene (2b, X = I) and the following experimental protocol (method B): A mixture of the carbonyl compound 1 (1 mmol), 2b (X = I; 1.5 mmol), and zinc powder (1.5 mmol) in 10 mL of water was stirred at room temperature until the zinc almost disappeared (in cases where the reaction did not start properly, 2–3 drops of hydrobromic acid (48%) or saturated NH_4Cl solution could be added to initiate the reaction). To the reaction mixture was then added 2 mL of hydrobromic acid (48%) and zinc powder (10 mmol) over a period of 5 h. The reaction mixture was then extracted with ether to give, after purification, the diene 3 in good to excellent yield (Table I). The simplicity and ease of the present diene synthesis should be compared with the Wittig reaction, which has been found to suffer from competing aldol condensation,⁵ lack of regiocontrol,⁶ low yield, and lack of stereoselectivity. The conventional organometallic reactions used for diene synthesis, mediated by silicon⁷ or tin,⁸ pose the usual restriction of moisture sensitivity. The present reaction offers the advantages of high yield, simple experimental operations, and in certain examples (entries 23 and 24) the elimination of the protection-deprotection sequence for the hydroxy function.

If the reaction was interrupted after the first stage of method B by extraction with ether, the intermediate chlorohydrin 5 could be isolated. Treatment of 5 in ethanolic NaOH (0.4 g/10 mL) gave the vinyloxirane 6 (me-

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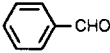
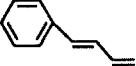
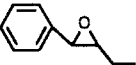
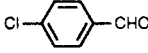
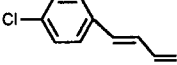
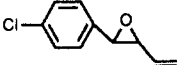

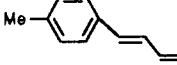
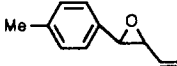
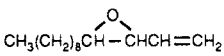
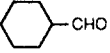
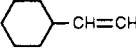
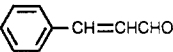
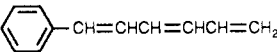

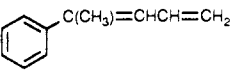
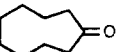
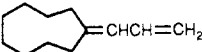

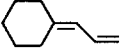

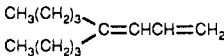
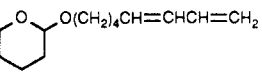

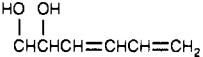
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Table I. Synthesis of 1,3-Dienes and Vinyloxiranes

entry no.	aldehyde	halide	product	% yield (method)	trans:cis ratio
1		$\text{ClCH}=\text{CHCH}_2\text{Cl}$		53 (A)	>98
2		$\text{ClCH}=\text{CHCH}_2\text{I}$		95 (B)	>98
3		$\text{ClCH}=\text{CHCH}_2\text{I}$		95 (C)	36:64
4		$\text{ClCH}=\text{CHCH}_2\text{I}$		97 (B)	>98
5		$\text{ClCH}=\text{CHCH}_2\text{I}$		95 (C)	36:64
6		$\text{ClCH}=\text{CHCH}_2\text{I}$		95 (B)	>98
7		$\text{ClCH}=\text{CHCH}_2\text{I}$		93 (C)	36:64
8	$\text{CH}_3(\text{CH}_2)_8\text{CHO}$	$\text{ClCH}=\text{CHCH}_2\text{Cl}$	$\text{CH}_3(\text{CH}_2)_8\text{CH}=\text{CHCH}=\text{CH}_2$	53 (A)	95:5
9		$\text{ClCH}=\text{CHCH}_2\text{I}$		92 (B)	95:5
10		$\text{ClCH}=\text{CHCH}_2\text{I}$		92 (C)	48:52
11		$\text{ClCH}=\text{CHCH}_2\text{Cl}$		48 (A)	>98
12		$\text{ClCH}=\text{CHCH}_2\text{I}$		93 (B)	>98
13		$\text{ClCH}=\text{CHCH}_2\text{Cl}$		38 (A)	>98
14		$\text{ClCH}=\text{CHCH}_2\text{I}$		86 (B)	>98
15		$\text{ClCH}=\text{CHCH}_2\text{Cl}$		53 (A)	85:15
16		$\text{ClCH}=\text{CHCH}_2\text{I}$		80 (B)	85:15
17		$\text{ClCH}=\text{CHCH}_2\text{Cl}$		36 (A)	
18		$\text{ClCH}=\text{CHCH}_2\text{I}$		95 (B)	
19		$\text{ClCH}=\text{CHCH}_2\text{I}$		93 (C)	
20	$\text{CH}_3(\text{CH}_2)_3\text{CO}(\text{CH}_2)_3\text{CH}_3$	$\text{ClCH}=\text{CHCH}_2\text{Cl}$		20 (A)	
21	$\text{CH}_3(\text{CH}_2)_8\text{COCH}_3$	$\text{ClCH}=\text{CHCH}_2\text{Cl}$	$\text{CH}_3(\text{CH}_2)_8\text{C}(\text{CH}_3)=\text{CHCH}=\text{CH}_2$	33 (A)	70:30
22		$\text{ClCH}=\text{CHCH}_2\text{I}$		75 (B)	68:32
23	$\text{HO}(\text{CH}_2)_4\text{CHO}$	$\text{ClCH}=\text{CHCH}_2\text{Cl}$		42 (A)	88:12
24		$\text{ClCH}=\text{CHCH}_2\text{Cl}$		33 (A)	>98

thod C) in quantitative yield (Table I). Alkenyloxiranes have become important structural units in natural products (e.g. the arachidonic acid cascade). A number of methods for the synthesis of alkenyloxiranes have been developed.^{8,9} It is interesting to note that, in the present reaction, the trans/cis ratio of **6** is in agreement with the diastereomeric ratio of the precursor chlorohydrin **5**, a result not unexpected for epoxide formation. On the other hand, the reduction of **5** to give **3** under the experimental conditions

is nonstereospecific but selective in giving the thermodynamically more stable *E* isomer. This is in contrast to the usual trans elimination under metal/dihalide reduction conditions.¹⁰ The reduction must therefore occur in two steps, likely involving a carbanion intermediate,¹¹ thus accounting for the formation of the side product **4** as well.

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