

A Mild Oxidation of 1,1-Diorganometallics to Ketones and Aldehydes.

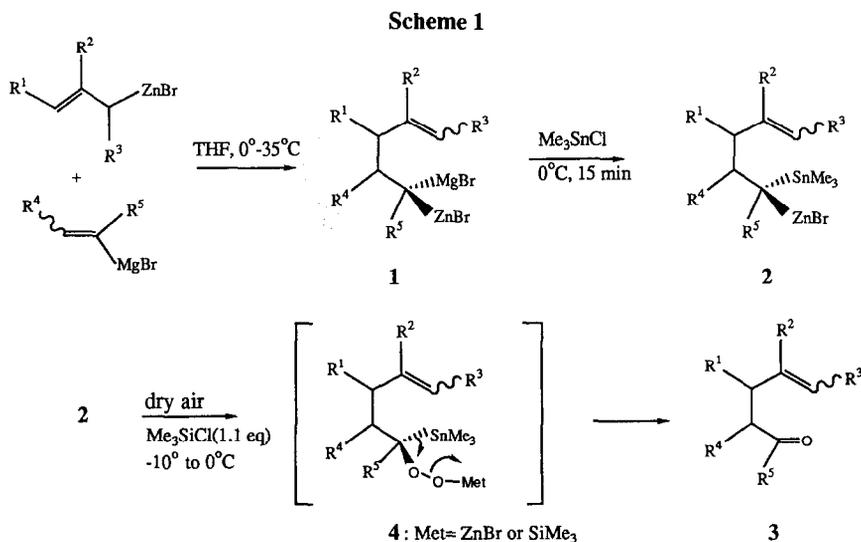
A New Stereoselective Approach to Aldol Products Part I

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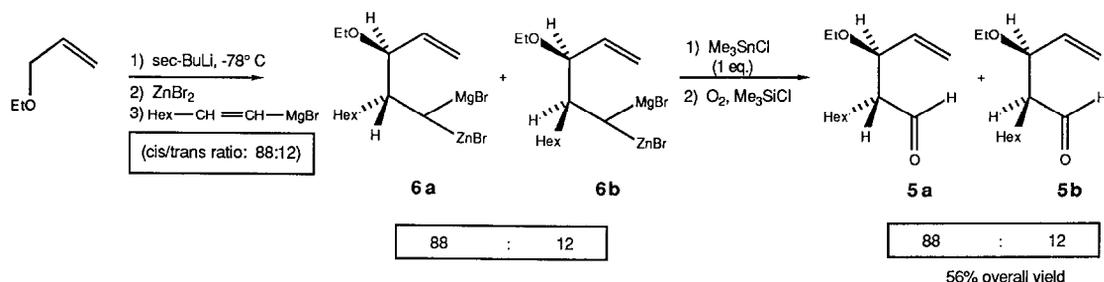
Summary: The 1,1-diorganometallics of magnesium and zinc **1** are converted by the reaction with Me₃SnCl to the 1,1-diorganometallics of tin and zinc **2** which are readily oxidized by dry air at -10° to 0°C to afford the corresponding aldehydes and ketones **3** in 57-91% yield. This mild oxidation reaction allows a new stereoselective approach to aldol products. An extension of the reaction to 1,1-diorganometallics of silicon and zinc is described.

The 1,1-diorganometallics of magnesium (or lithium) and zinc **1** are readily available by the carbometallation reaction¹ of alkenyl magnesium or -lithium derivatives with allylic zinc bromides and react with various electrophiles². We report now that the α -trimethylstannyl, zinc compounds **2** obtained by the reaction of the diorganometallics **1** with Me₃SnCl (1.1 eq.; 15 min.; 0°C) are oxidized under very mild conditions³ in the presence of Me₃SiCl by dry air to afford the corresponding ketones or aldehydes **3** in fair to good yields (see Scheme 1 and Table). The reaction proceeds by an insertion of oxygen into the carbon-zinc bond⁴ to afford the intermediate **4** which then decomposes to the carbonyl compound **3**.

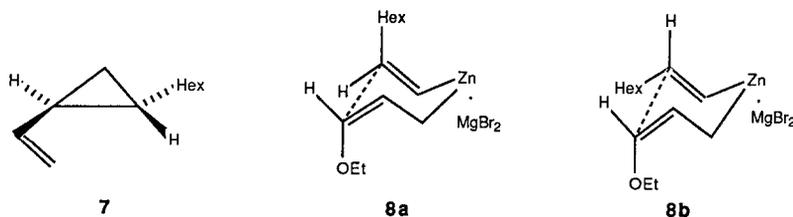


The oxidation to aryl ketones ($R^5 = \text{Ph}$) is especially fast (30 min. - 4hr.; 0°C) whereas the oxidation reaction to aldehydes requires longer reaction times (4 hr. - 10 hr., 0°C). The rate of the reaction is enhanced by the addition of Me_3SiCl (1.1-1.5 eq.) and retarded by the presence of co-solvents like DMF or Me_2S . This oxidation procedure can be used to prepare aldol compounds of type **5** with high stereoselectivity (see Scheme 2).

Scheme 2



Thus the addition of 3-ethoxyallyl zinc bromide⁵ to 1-octenylmagnesium bromide (cis/trans ratio: 88:12) leads to a 88:12 mixture of two diastereoisomeric diorganometallics **6a** and **6b** which was oxidized under our standard conditions (6 hrs.; -15°C) to furnish the two aldehydes **5a** and **5b** in a ratio of 88:12 and in 56% overall yield. This indicates an almost complete transfer of the stereochemistry of the alkenyl magnesium derivatives to the aldehydes **5**. The relative configuration of the diorganometallics **6a** and **6b** has been determined by heating a THF solution of **6a** and **6b** at 45°C which leads to the formation of trans-2-hexyl-1-vinylcyclopropane **7** in 48% yield (cis/trans ratio 5:95)⁶.



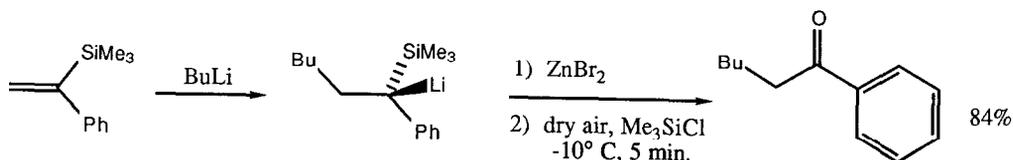
If we assume that **7** has been formed by an internal $\text{S}_{\text{N}}2$ substitution with inversion of configuration, we can assign the 2R^* , 3R^* configuration to **6a** and consequently the 2S^* , 3R^* configuration to **6b**. Thus the metalocyclization⁷ rearrangement leading to **6a** and **6b** seems to proceed via the chain transition state **8a** and **8b** respectively in which the configuration of both starting organometallics is maintained⁸. The oxidation reaction could furthermore be extended to α -trimethylsilyl, zinc diorganometallics. Thus the addition at -30°C of butyllithium (1.1 eq.) to a THF solution of 1-trimethylsilylstyrene⁹, followed by the addition of zinc bromide and a very fast oxidation (5 min.; -20°C) with dry air affords 1-phenyl hexanone in 84% yield (see Scheme 3).

Table. Aldehydes and Ketones **3** Formed by the Air Oxidation of the 1,1-Diorganometallics **1** (via **2**).

R ¹	R ²	Products of Type 3 R ³	R ⁴	R ⁵	Reaction Time of the oxidation	yield (%)
H	H	H	Ph		30 min.	89
H	Me	H	H	Ph	1 hr.	85
H	4-methylcyclohexen-3-yl-	H	H	Ph	3 hrs.	65
Me	H	H	H	Ph	4 hrs.	57
H	Bu	H	H	Ph	2 hrs.	91
H	Bu	H	Hex ^b	H	4 hrs.	66
H	4-methylcyclohexen-3-yl	H	Hex ^b	H	4 hrs.	60
H	H	H	Hex ^b	H	10 hrs.	81
H	Me	H	Hex ^b	H	5 hrs.	87
Me	H	H	Hex ^{b,c}	H	5 hrs.	78
H	H	Me ₃ Si	Hex ^{b,d}	H	5 hrs.	77

- a Isolated yield which includes the formation of the 1,1-diorganometallic, its stannylation and subsequent oxidation. Satisfactory spectral data (IR, ¹H, ¹³C-NMR, high resolution mass spectra) were obtained.
- b A 88:12 cis/trans mixture of 1-octenylmagnesium bromide has been used.
- c A 75:25 ratio of two diastereoisomers was obtained.
- d The addition of 1-trimethylsilyllallylzinc bromide is regiospecific, but leads to the formation of cis/trans isomers (cis/trans ratio: 88:12)

Scheme 3



Further extensions of this methodology are currently being investigated in our laboratory. (See also the following publication).

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References

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3. Typical procedure.
5.4 ml (8.5 mmol) of a THF solution of allylzinc bromide (1.57N) was added under argon to 12.5 ml (8 mmol) of a THF solution of 1-octenylmagnesium bromide (0.64N). The reaction mixture was stirred at 35°C for 45 minutes to complete the formation of the diorganometallic. After the addition of 15 ml of dry THF, the reaction mixture was cooled to -20°C and 1.79g (9 mmol) of Me₃SnCl in 5 ml of THF was added. After 15 minutes of stirring at 0°C, 10 ml of dry THF was added to the resulting milky solution which was cooled to -10°C. The argon inlet was replaced by a balloon filled with dry air. GC monitoring of the reaction indicated that the oxidation was complete after 10 hours at -5°C. After the usual work-up, the resulting residue was purified by flash-chromatography (solvent: hexane/ether (95:5)) to afford 1.09g (81%) of 2-allyl octanal.
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6. The diastereoisomer **6a** undergoes the ring closure far more readily than **6b**; this explains the high cis/trans ratio observed. If allyl tetrahydropyranyl ether is used instead of allyl ether, then both diastereoisomers cyclize readily at 25° C and afford the vinylcyclopropane **7** in 65%. The cis/trans ratio (12:88) is now identical with the cis/trans ratio of the starting octenylmagnesium bromide. The assignment of the stereochemistry of **7** is based ¹H-NMR data; see Roth, W.R.; Konig, J. *Liebigs Ann Chem.* **1965**, *688*, 28.
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