

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

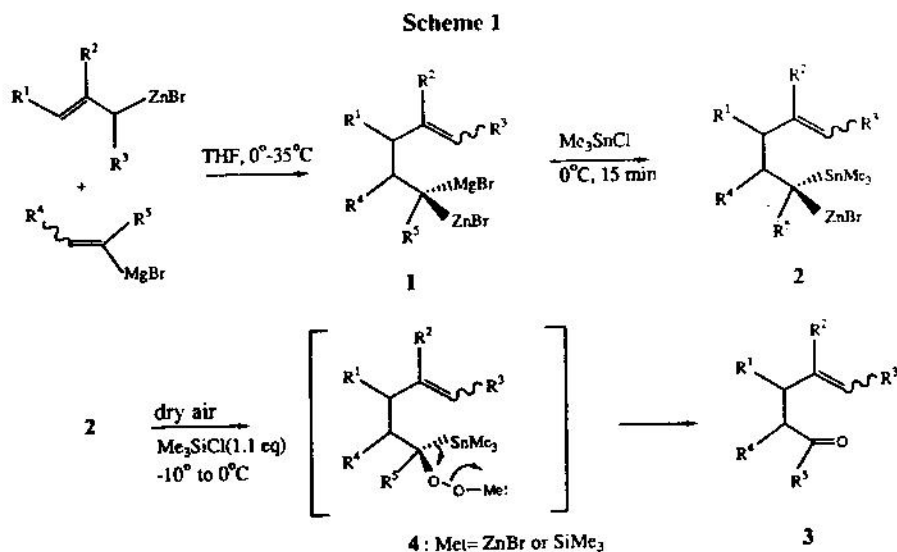
A New Stereoselective Approach to Aldol Products Part I

Paul Knochel*, Chaodong Xiao, Ming Chang P. Yeh

Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48109

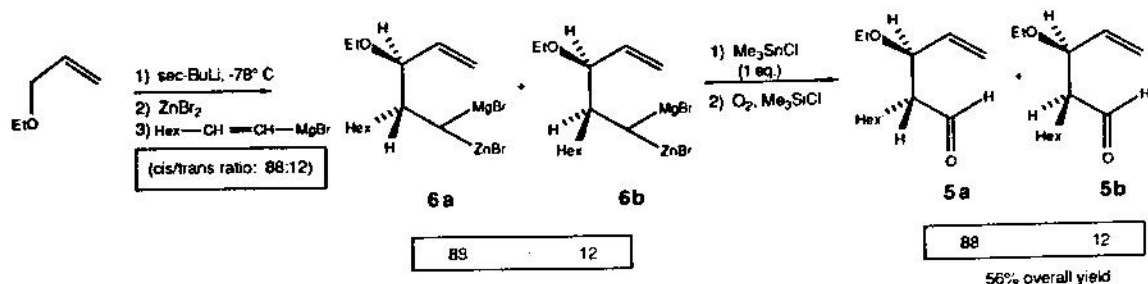
Summary: The 1,1-diorganometallics of magnesium and zinc **1** are converted by the reaction with Me_3SnCl to the 1,1-diorganometallics of tin and zinc **2** which are readily oxidized by dry air at -10° to 0°C to afford the corresponding aldehydes and ketones **3** in 57-91% yield. This mild oxidation 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 Me_3SnCl (1.1 eq.; 15 min.; 0°C) are oxidized under very mild conditions³ in the presence of Me_3SiCl 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**.

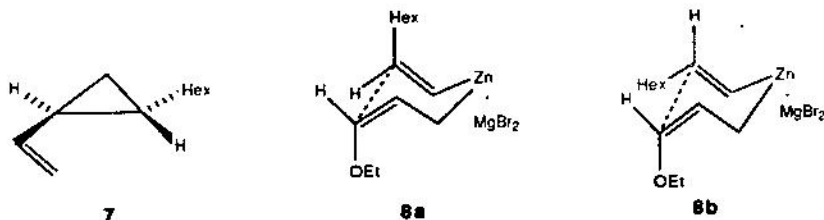


The oxidation to aryl ketones ($R^5 = \text{Ph}$) is especially fast (30 min. - 4hr.; 0°C) whereas the oxidation reaction to aldehydes requires longer reaction times (4 hr. - 10 hr., 0°C). The rate of the reaction is enhanced by the addition of Me_3SiCl (1.1-1.5 eq.) and retarded by the presence of co-solvents 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-ethoxyallylzinc bromide⁵ to 1-octenylmagnesium bromide (cis/trans ratio: 88:12) leads to a 88:12 mixture of two diastereomeric 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.



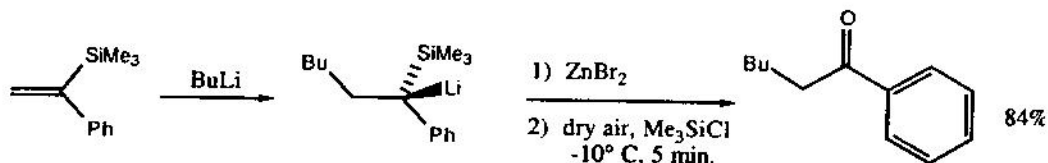
If we assume that 7 has been formed by an internal $\text{S}_{\text{N}}2$ substitution with inversion of configuration, we can assign the 2R^* , 3R^* configuration to 6a and consequently the 2S^* , 3R^* configuration to 6b. Thus the metaloclainen⁷ rearrangement leading to 6a and 6b seems to proceed via 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-trimethylsilylallylzinc bromide is regioselective, 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).

References

1. (a) Gaudemar, M., C.R. Acad. Sci. Paris, Ser. C, **1971**, 273, 1669. (b) Frangin, Y.; Gaudemar, M. C.R. Acad. Sci. Paris, Ser. C, **1974**, 278, 885. (c) Bellasoued, M.; Frangin, Y.; Gaudemar, M. Synthesis **1977**, 205. (d) Knochel, P.; Normant, J.F. Tetrahedron Lett. **1986**, 27, 1039.
2. Knochel, P.; Normant, J.F. Tetrahedron Lett. **1986**, 27, 1043, 4427, 4431, 5727.
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.
4. (a) Sosnovsky, G.; Brown, J.H. Chem. Rev. **1966**, 66, 529. (b) Czernecki, S.; Georgoulis, C.; Gross, B.; Prevost, C. C.R. Acad. Sci. Paris, Ser. C **1968**, 226, 1677.
5. (a) Evans, D.A.; Andrews, G.C.; Buckwalter, B. J. Am. Chem. Soc. **1974**, 96, 5560; (b) Still, W.C.; MacDonald, T.L. J. Am. Chem. Soc. **1974**, 96, 5561.
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.; König, J. Liebigs Ann Chem. **1965**, 688, 28.
7. Dewar, M.J.S.; Mertz, K.M. J. Am. Chem. Soc. **1987**, 109, 6553.
8. The more stable cis configuration of the metallated allylic ether is maintained during the [3,3]-sigmatropic shift; see ref. 5.
9. Retz, M.T.; Schinzer, D. Angew. Chem. **1977**, 89, 46.

(Received in USA 31 August 1988)