

**PREPARATION OF (E)- α,β -UNSATURATED AROMATIC ALDEHYDES BY HIGH
STERESELECTIVE OLEFINFORMYLATION.**

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Abstract : Treatment of acetaldehyde *N*-ter-butylimine by two equivalents of LDA, followed by trimethylsilyl chloride trapping affords the α,α -disilylated imine; the latter reacts with aromatic aldehydes producing α,β -ethylenic aldehydes in excellent yields and with very high stereoselectivity in favour of the *E* isomer.

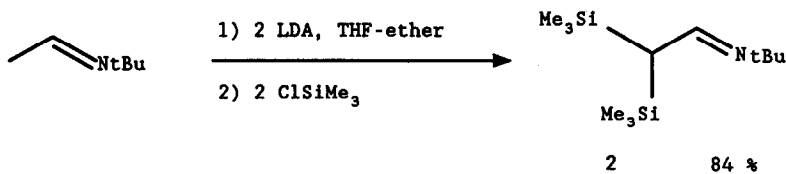
The conversion of an aldehyde into its vinylogue¹ is an important organic synthetic reaction since the α,β -unsaturated carbonyl compounds thus obtained are often used as intermediates in the preparation of natural compounds². The most known methods refer to the crotonisation, to the Wittig reaction or to its variations³.

During the last years, the authors have directed their efforts towards the utilization of silylated reagents in order to create a carbon-carbon double bond by the Peterson olefination⁴. Thus, Corey and Coll.⁵ employed the lithiated derivatives of α -silyl aldimines whereas Duhamel and Coll.⁶ carried out a similar process using α -silylated acetaldehyde.

Generally⁷, the authors obtain the aldehydes of *E* configuration whatever method applied. However, small quantities of the *Z* isomer contaminate the main product and chromatographic separation is necessary.

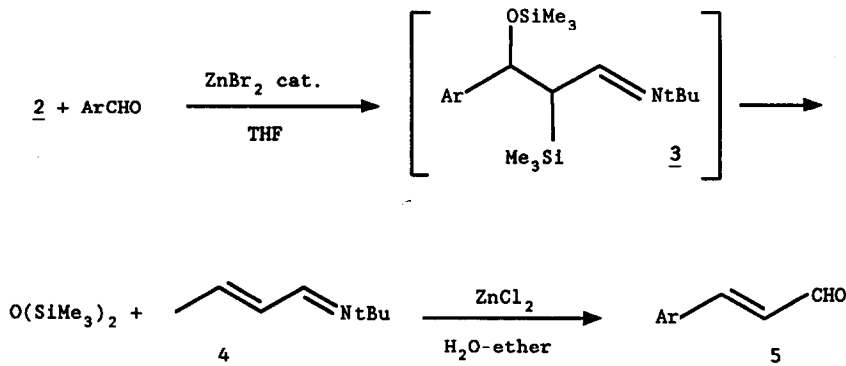
In connection⁸ with our work on silicon derivatives concerning a new preparation of Tigason^R and its analogues⁹, we describe in this report a new reagent permitting the transformation of an aromatic aldehyde into its vinylogue with very high stereoselectivity in favour of the *E* configuration.

This makes use of the disilylated imine 2, obtained as indicated below.



The NMR spectrum of 2 confirms the formula proposed and excludes an enamine structure. The intermediate 3 is not isolable. However, 4 has been easily isolated and characterised by NMR. The yields indicated are based on starting aldehydes without isolation of 4.

The E and Z isomers of α,β -unsaturated aldehydes are easily distinguished by the NMR signal of the formyl group¹⁰. In order to ensure the steric purity of our compounds, we prepared the 5aE/5aZ 96/4 mixture from authentic samples. 5aZ is easily revealed and quantified (¹H-RMN 60 MHz ; solution 30 %).

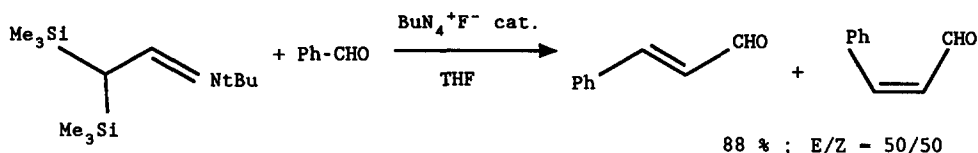


Ar	yield %*	E
<u>5a</u> Ph	86	~ 100 %
<u>5b</u> p(Me)C ₆ H ₄ -	85	> 98 %
<u>5c</u> p(MeO)C ₆ H ₄ -	90	~ 100 %

*The indicated yields refer to crude products obtained after evaporation of the solvent. The ¹H-NMR 60 MHz spectrum (concentrated solutions ~ 30 %) does not show any impurity.

The aliphatic aldehydes lead to the same reaction ; however we have not managed yet to optimize the yields. Ketones are enolised and do not react further.

If the C-Si bonds are activated by tetrabutylammonium fluoride, mixture (50/50) of the two isomers was obtained. Thus, this reaction could be used for the synthesis of α,β -unsaturated aromatic aldehydes of Z configuration.



EXPERIMENTAL ILLUSTRATION

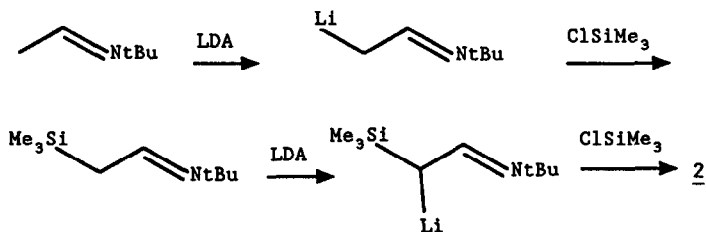
α,α -Bis(trimethylsilyl) ter-butylacetalimine 2. LDA is prepared by attack of the amine by lithium in the presence of an electron acceptor (α -methylstyrolene) in ether-THF 50/50. The imine is deprotonated¹¹ at $-70^{\circ}/-60^{\circ}\text{C}$ during 18 h. One equivalent of ClSiMe_3 is added and the mixture is stirred for 5 h at -60°C . Then a second equivalent of ClSiMe_3 is added at -60°C , the solution is kept at the same temperature for 1 h and then allowed to warm up to room temperature. The precipitate is filtered off, the solvent removed, the solid is filtered off again and the product distilled. $97-98^{\circ}\text{C}$, 12 torr.

¹H-NMR 60 MHz ; CCl_4 ; TMS ; δ (ppm) ; J(Hz) : 0.04, 18 H, s ; 1.10, 9 H, s ; 1.41, 1 H, d, 7.7 ; 7.89, 1 H, d, 7.7.

p-Methoxycinnamaldehyde 5c. Reagent 2 (0,02 mole), ZnBr_2 cat. (10 %) and *p*-methoxybenzaldehyde in deficient quantity (0,018 mole) are mixed in 20 ml THF and left aside for 6 h at 10°C , then overnight at 20°C . The imine 4 is extracted as a salt by a cooled dilute aqueous solution of H_2SO_4 , then freed by NaOH and extracted with ether. This ether solution is stirred with an aqueous solution of ZnCl_2 (5 %) for 6 h at 10°C , then left aside overnight at 20°C . The precipitate of $\text{Zn}(\text{OH})_2$ is filtered off, the organic layer washed by an aqueous diluted solution of H_2SO_4 , then by water and dried on MgSO_4 . By removing the solvent in vacuo, 5c crystallizes.

REFERENCES AND FOOTNOTES

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- 2 - P. Deshong et J.M. Leginus, *J. Org. Chem.*, 49, 3421, 1984 and references cited therein.
- 3 - Many references are cited in the following review and article : a) S.F. Martin, *Synthesis*, 633, 1979 ; b) H.J. Bestmann, K. Roth and M. Ettliger, *Chem. Ber.*, 115, 161, 1982.
- 4 - a) D. Peterson, *J. Org. Chem.*, 33, 780, 1968 ; b) P.F. Hudrlik and D. Peterson, *J. Am. Chem. Soc.*, 97, 1464, 1975.
- 5 - E.J. Corey, D. Enders and M.G. Bock, *Tetrahedron Lett.*, 7, 1976.
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- 7 - A modification of the structure of Wittig reagent allowed to obtain the Z aldehydes in good stereoselectivity ; see ref. 3b.
- 8 - a) M. Bellassoued, R. Ennigrou and M. Gaudemar, *J. Organometal. Chem.*, 338, 149, 1988; b) M. Bellassoued and M. Gaudemar, *Tetrahedron Lett.*, 29, 4551, 1988.
- 9 - These products are the most active medicines in the treatment of serious forms of acne.
- 10 - a) R. Olstein and E.F. Stephenson, *Aust. J. Chem.*, 32, 1595, 1979 ; b) K.C. Chan, R.A. Jewell, W.H. Nutting and H. Rapoport, *J. Org. Chem.*, 33, 3382, 1968, ; c) T. Nakai, H. Shiono and M. Okawara, *Tetrahedron Lett.*, 3625, 1974 ; see also ref. 3b.
- 11 - The sequence is probably as follows :



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