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# A SIMPLE SYNTHESIS OF α,β-UNSATURATED ALDEHYDES BY THE REACTION OF VINYLSILANES WITH DICHLOROMETHYL METHYL ETHER PROMOTED BY TITANIUM(IV) CHLORIDE. APPLICATION TO THE SYNTHESIS OF ETHYL 12-OXO-10(*E*)-DODECENOATE AND NUCIFERAL

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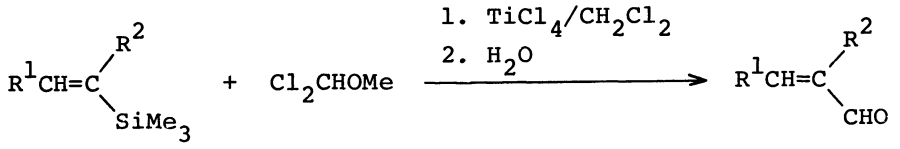
1,2-Disubstituted vinyltrimethylsilanes (1) readily underwent formylation with replacement of the silyl group when treated with dichloromethyl methyl ether and titanium(IV) chloride. This reaction provides a simple procedure for the selective preparation of (*E*)-2-alkenals (2) and was conveniently applied to the synthesis of ethyl 12-oxo-10(*E*)-dodecenoate and nuciferal.

We have reported a simple procedure for the synthesis of α,β-unsaturated aldehydes (2-alkenals) (2, $R^2$ = H) which involves a facile 1-chloromethoxymethylation of vinylsilanes (1, $R^2$ = H) with dichloromethyl methyl ether promoted by titanium(IV) chloride (eq 1).[1]




1 2 (1)

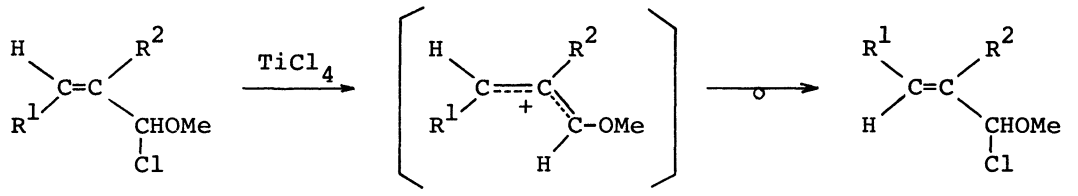
A recent publication dealing with stereochemistry of electrophilic substitution of 1,2-disubstituted vinyltrimethylsilanes,[2] prompts us to report briefly our own results which relate closely to this report. Also, a synthetic application of the facile formylation of vinylsilanes to two naturally occurring substances is presented.

1,2-Disubstituted vinyltrimethylsilanes undergo the reaction as smoothly as monosubstituted ones. In Table 1 was summarized the preparation of disubstituted 2-alkenals (2a-d). All 2-alkenals obtained had (*E*)-configuration. This was the case even when 2-trimethylsilyl-2(*Z*)-octene (1d) as well as (*Z*)-1-trimethylsilyl-1-heptene[1] was used as a starting material under the standard reaction conditions.[3] The fact that 2d has (*E*)-configuration solely is best explained in terms of titanium(IV) chloride-catalyzed isomerization of a (*Z*)-α-chloroallyl ether (3) initially formed with retention of configuration to a sterically more stable (*E*)-isomer (4),[4] which, in turn, gives (*E*)-2-alkenal by hydrolysis (eq 2).

Table 1. Preparation of Disubstituted 2-Alkenals (2)

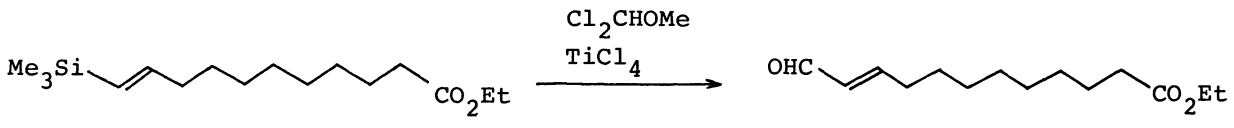
| | Vinylsilane (1) | 2-Alkenal (2) | Yield[a] (%) | NMR, CHO[b] δ (ppm) |
|---|---|---|---|---|
| a | (*E*)-EtCH=C(Et)SiMe$_3$ | (*E*)-EtCH=C(Et)CHO | 73 | 9.21 |
| b | (*E*)-PrCH=C(Pr)SiMe$_3$ | (*E*)-PrCH=C(Pr)CHO | 79[c] | 9.28 |
| c | (*E*)-PhCH=C(Me)SiMe$_3$ | (*E*)-PhCH=C(Me)CHO | 80 | 9.37 |
| d | (*Z*)-AmCH=C(Me)SiMe$_3$[d] | (*E*)-AmCH=C(Me)CHO | 71 | 9.26 |

a) Determined by GLC (*n*-undecane as an internal standard).
b) Diagnosis of (*E*)-configuration, see ref. 5).
c) Isolated yield.
d) Preparation of (*Z*)-*n*-$C_6H_{13}$CH=C(Me)SiMe$_3$, see ref. 6).




3 4 (2)

Giving only (*E*)-2-alkenals regardless of the stereochemistry of starting vinylsilanes, the present reaction provides a simple procedure for the synthesis of ethyl 12-oxo-10(*E*)-dodecenoate (6), a useful intermediate to bombykol, and (±)-nuciferal (9), as illustrated in the following schemes.



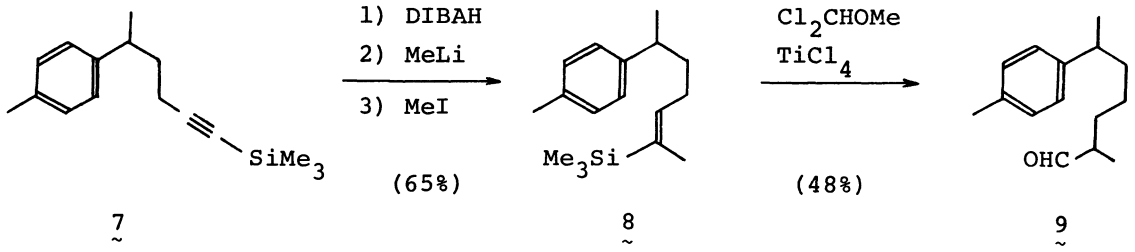

5 6

Scheme 1

Bombykol,[7] 10(*E*),12(*Z*)-hexadecadien-1-ol, is a pheromone specifically found in glands of female silkworm moth, *Bombyx mori*. Bestmann *et al.*[8] have recently prepared a methyl homolog of 6 as a key intermediate in their synthesis of bombykol. The ester, which was obtained from methyl 10-undecenoate by ozonolysis followed by the Wittig reaction (34% overall yield), was treated with *n*-butylidene triphenylphosphorane to afford methyl 10(*E*),12(*Z*)-hexadecadienoate, an immediate precursor of bombykol.

In the present work, ethyl 11-trimethylsilyl-10(*E*)-undecenoate (5) was prepared by a chloroplatinic acid-catalyzed hydrosilylation of ethyl 10-undecynoate with trimethylsilane in 72% yield. The vinylsilane (5) (0.28 g, 1.0 mmol) was allowed to react with dichloromethyl methyl ether (0.13 ml, 1.5 mmol), and titanium(IV) chloride (0.17 ml, 1.5 mmol) at -60°C for 4 h. Hydrolysis of the reaction mixture and column chromatographic purification (silica gel, *n*-hexane-ether as eluent) of the crude product afforded 6 (0.20 g, 83% yield); IR (film) 2930, 2720, 1735, 1690, 1640, and 1180 $cm^{-1}$. NMR ($CCl_4$, TMS) δ 1.22 (t, *J* = 7.0 Hz, 3H), 1.35 (bs, 12H), 2.05-2.55 (m, 4H), 4.04 (q, *J* = 7.0 Hz, 2H), 5.97 (dd, *J* = 16 Hz, 1H), 6.72 (dt, *J* = 6.5, 16 Hz, 1H), and 9.04 ppm (d, *J* = 7.8 Hz, 1H).

Nuciferal,[9] a sesquiterpene aldehyde obtained from the leaves of *Torreya nucifera*, was prepared as outlined in scheme 2.




7 8 9

Scheme 2

The preparation of 1-trimethylsilyl-5-*p*-tolyl-1-hexyne (7) was carried out by using known 1-bromo-3-*p*-tolyl-butane[10] in two steps (70% overall yield). 7 (5.67 g, 23.2 mmol) was subjected to the reductive alkylation[6] by sequential treatment with diisobutylaluminum hydride (DIBAH) (2.45 M in *n*-heptane; 11.3 ml, 27.6 mmol) at 30°C for 24 h, methyllithium (1.8 M in ether; 17.0 ml, 31 mmol) at 0°C for 20 min, and a large excess of methyl iodide (10 g) at room temperature overnight to give, after usual workup, 5.9 g of a 1 : 2 mixture (by GLC) of 1-trimethylsilyl-5-*p*-tolyl-1(*E*)-hexene and desired 2-trimethylsilyl-6-*p*-tolyl-2(*E*)-heptene (8). 8 was purified by fractional distillation, bp 103-106°/3 Torr, 3.9 g (65%).[11] The disubstituted vinylsilane (8) (0.26 g, 1.0 mmol) was formylated in a similar manner to that described above to give 2-methyl-6-*p*-tolyl-2(*E*)-hepten-1-al (9, nuciferal)[12] (0.10 g, 48% yield): IR (film) 2950, 2720, 1690, and 1640 $cm^{-1}$. NMR ($CCl_4$, TMS) δ 1.24 (d, *J* = 7.0 Hz, 3H), 1.58 (s, 3H), 1.7-2.2 (m, 4H), 2.28 (s, 3H), 2.45-2.95 (m, 1H), 6.26 (t, *J* = 7.0 Hz, 1H), 6.96 (s, 4H), and 9.22 ppm (s, 1H).

Acknowledgments

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## References and Notes

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2) T. H. Chan, P. W. K. Lau, and W. Myhajlowskij, Tetrahedron Lett., 3317 (1977).
3) To a mixture of 1 (5 mmol) and dichloromethyl methyl ether (5 mmol) in dichloromethane (5 ml) at -78°C is added dropwise titanium(IV) chloride (0.56 ml, 5 mmol) in dichloromethane (5 ml) and the mixture is stirred for 1 h.
4) We have observed similar activation by titanium(IV) chloride of an α-chlorohomoallyl ether, which was formed by the reaction of allyltrimethylsilane with dichloromethyl methyl ether and was found to be even more reactive than the dichloromethyl ether. For related discussion, see C. F. Garvers, H. S. C. Spies, and H. E. Visagie, Tetrahedron Lett., 81 (1978), and A. Hosomi, M. Endo, and H. Sakurai, Chem. Lett., 499 (1978).
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10) D. A. Evans, G. C. Andrews, T. T. Fujimoto, and D. Well, Tetrahedron Lett., 1389 (1973).
11) NMR ($CCl_4$, TMS) δ 0.04 (s, 9H), 1.24 (d, $J$ = 6.8 Hz, 3H), 1.58 (s, 3H), 1.8-2.1 (m, 4H), 2.31 (s, 3H), 2.68 (bs, 1H), 5.64 (t, $J$ = 6.5 Hz, 1H), and 7.01 ppm (s, 4H).
12) In complete accordance with the reported NMR data: T. Sakai and K. Nishimura, Bull. Chem. Soc. Jpn., 38, 381 (1965).

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