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2-TRIMETHYLSILYLMETHYL-1,3-BUTADIENE AS A NOVEL REAGENT FOR ISOPRENYLATION. NEW ACCESS TO IPSENOL AND IPSDIENOL, PHEROMONES OF *Ips paraconfusus*[1]

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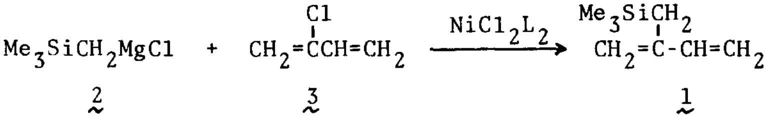
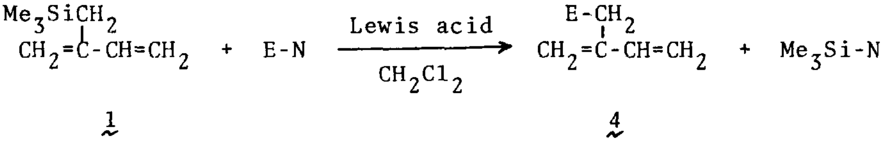
Isoprenylation is one of the important reactions to synthesis of various natural products, and 2-bromomethyl-1,3-butadiene has been used as a reagent of introducing an isoprenyl group in a single step.[2] However, the reagent is not always convenient because of its limitation in applications.[3] Preparation of the reagent is also tedious. We report here preparation of 2-trimethylsilylmethyl-1,3-butadiene (1), which can be used as a convenient reagent of introducing an isoprenyl group into electrophilic carbon centers in a single step, and its application to synthesis of two principal components of the aggregation pheromone of *Ips paraconfusus* Lanier, (*confusus*) a bark beetle (family Scolytidae).[2b,4]

In the course of studies on the introduction of a functionality in the allyl group of allylsilanes,[5] we have found that 2-trimethylsilylmethyl-1,3-butadiene (1)[6] was obtained by the coupling reaction of the Grignard reagent (2) of chloromethyltrimethylsilane and 2-chloro-1,3-butadiene (chloroprene, 3) in the presence of a catalytic amount of dihalodiphosphinenickel(II).[7] (eq. 1)



$$\underset{\mathbf{2}}{Me_3SiCH_2MgCl} + \underset{\mathbf{3}}{CH_2{=}\overset{Cl}{\overset{|}{C}}CH{=}CH_2} \xrightarrow{NiCl_2L_2} \underset{\mathbf{1}}{CH_2{=}\overset{Me_3SiCH_2}{\overset{|}{C}}{-}CH{=}CH_2} \qquad (1)$$

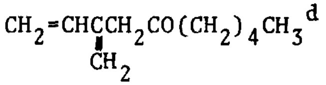
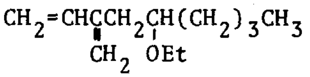
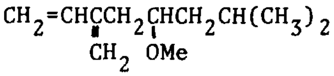
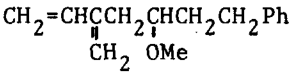
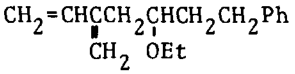
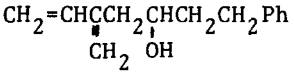
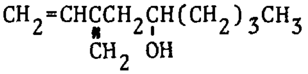
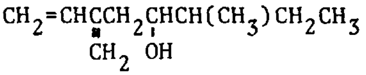
Like other allylic silanes,[5] the isoprenylsilane (1), thus obtained, can react with various electrophilic species such as acetals,[8] acid chlorides,[5a] and carbonyl compounds,[9,10] with an aid of a Lewis acid to give the corresponding isoprenylated products 4. (eq. 2) The results are listed in Table 1.



$$\underset{\mathbf{1}}{CH_2{=}\overset{Me_3SiCH_2}{\overset{|}{C}}{-}CH{=}CH_2} + E{-}N \xrightarrow[CH_2Cl_2]{\text{Lewis acid}} \underset{\mathbf{4}}{CH_2{=}\overset{E-CH_2}{\overset{|}{C}}{-}CH{=}CH_2} + Me_3Si{-}N \qquad (2)$$

Titanium tetrachloride is the most effective activator for the present reaction among various Lewis acids, although aluminum chloride is also an efficient

Table 1. Reactions of 2-trimethylsilylmethyl-1,3-butadiene (1) with electrophilic chemical species in the presence of a Lewis acid[a]

Entry	Electrophiles	Lewis acid	Reaction time	Product (% Yield)[b,c]	
1	$(CH_3)_2CHCH_2COCl$	$TiCl_4$	1 min.	7	(77)
2	$(CH_3)_2C{=}CHCOCl$	$TiCl_4$	10 min.	8	(71)
3	$CH_3(CH_2)_4COCl$	$TiCl_4$	1 min.	 $CH_2{=}CH\underset{\underset{CH_2}{\|}}{C}CH_2CO(CH_2)_4CH_3$[d]	(66)
4	$CH_3(CH_2)_3CH(OEt)_2$	$TiCl_4$	10 min.	 $CH_2{=}CH\underset{\underset{CH_2}{\|}}{C}CH_2\underset{\underset{OEt}{\mid}}{C}H(CH_2)_3CH_3$	(52)
5	$(CH_3)_2CHCH_2CH(OMe)_2$	$TiCl_4$	10 min.	 $CH_2{=}CH\underset{\underset{CH_2}{\|}}{C}CH_2\underset{\underset{OMe}{\mid}}{C}HCH_2CH(CH_3)_2$	(88)
6	$PhCH_2CH_2CH(OMe)_2$	$TiCl_4$	5 min.	 $CH_2{=}CH\underset{\underset{CH_2}{\|}}{C}CH_2\underset{\underset{OMe}{\mid}}{C}HCH_2CH_2Ph$	(81)
7	$PhCH_2CH_2CH(OEt)_2$	$TiCl_4$	7 min.	 $CH_2{=}CH\underset{\underset{CH_2}{\|}}{C}CH_2\underset{\underset{OEt}{\mid}}{C}HCH_2CH_2Ph$	(63)
8	$(CH_3)_2CHCH_2CHO$	$AlCl_3$	2 min.	5	(30)[e]
		$TiCl_4$	5 sec.		(22)
9	$PhCH_2CH_2CHO$	$AlCl_3$	2 min.	 $CH_2{=}CH\underset{\underset{CH_2}{\|}}{C}CH_2\underset{\underset{OH}{\mid}}{C}HCH_2CH_2Ph$	(43)[e]
		$TiCl_4$	1 sec.		(37)
10	$CH_3(CH_2)_3CHO$	$AlCl_3$	2 min.	 $CH_2{=}CH\underset{\underset{CH_2}{\|}}{C}CH_2\underset{\underset{OH}{\mid}}{C}H(CH_2)_3CH_3$	(25)[e]
11	$CH_3CH_2CH(CH_3)CHO$	$AlCl_3$	2 min.	 $CH_2{=}CH\underset{\underset{CH_2}{\|}}{C}CH_2\underset{\underset{OH}{\mid}}{C}HCH(CH_3)CH_2CH_3$	(44)[e]
		$TiCl_4$	1 sec.		(15)

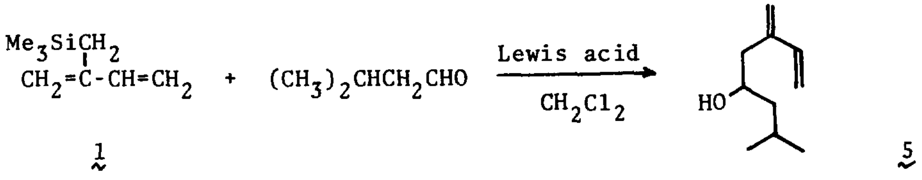
a. All reactions were carried out in dichloromethane at -78°C. b. Yields after isolation by tlc. c. Yields are not always optimized. d. The trimethylene dithioketal of this product is known as a precursor of PGE_1, PGA_1, $PGF_{1\beta}$. See ref. 2c. e. Yields after hydrolysis with MeOH-HCl.

activator for carbonyl compounds. Acetals and acid chlorides are generally more reactive as electrophilic species than carbonyl compounds such as ketones and aldehydes.

The following procedure illustrates the simplicity of the present reaction. To an electrophile (1.1 mmol) in dry dichloromethane (10 ml), a Lewis acid (1.0 mmol) was added at -78°C. After several seconds with stirring, 1 (1.1 mmol) in dichloromethane (5 ml) was added and the reaction mixture was stirred under a condition given in the table and hydrolyzed. After usual work-up, an isoprenylated product was isolated by the preparative tlc or glc.

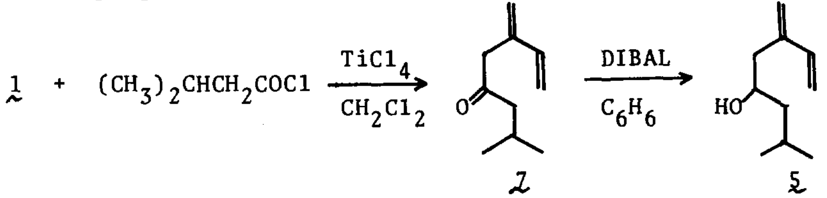
A new route to ipsenol (5) and ipsdienol (6), principal components of the aggregation pheromone of *Ips paraconfusus*, a bark beetle,[2b, 12] is a unique synthetic application of the present isoprenylation reaction.

The reaction of 1 with isovaleraldehyde in the presence of aluminum chloride or titanium tetrachloride directly afforded (±)-ipsenol (5), 2-methyl-6-methylene-oct-7-en-4-ol, although the yield was rather low. (entry 8)

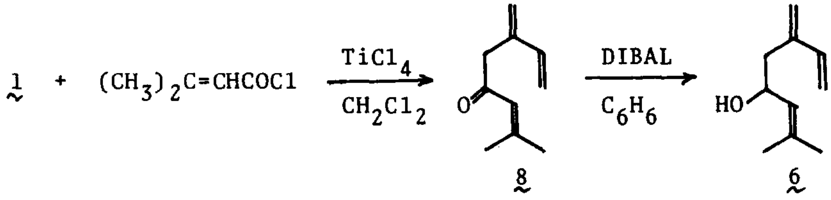


$$\underset{\textstyle 1}{\overset{\mathrm{Me_3SiCH_2}}{\mathrm{CH_2{=}\overset{|}{C}{-}CH{=}CH_2}}} + \mathrm{(CH_3)_2CHCH_2CHO} \xrightarrow[\mathrm{CH_2Cl_2}]{\text{Lewis acid}} \quad (3)$$

However, 5 was obtained in 62% overall yield by the reduction with diisobutylaluminum hydride (DIBAL) of a ketone 7,[13] which was prepared by the reaction of 1 with isovaleryl chloride in the presence of $TiCl_4$. Similarly, (±)-ipsdienol (6), 2-methyl-6-methylene-octa-2,7-diene-4-ol, was obtained by reduction of myrcenone (8),[13] prepared from 1 and 3,3-dimethylacryloyl chloride, in 75% yield. Related works are in progress.



(4)



(5)

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References and Notes

1. Chemistry of Organosilicon Compounds. 120
2. a) R. C. Krug and T. F. Yen, J. Org. Chem., **21**, 1083 (1956); b) R. G. Riley, R. M. Silverstein, J. A. Katzenellenbogen, and R. S. Lenox, ibid., **39**, 1957 (1974); c) E. J. Corey, N. H. Anderson, R. M. Carlson, J. Paust, E. Vedejs, I. Vlattas, and R. E. K. Winter, J. Am. Chem. Soc., **90**, 3245 (1968).
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4. R. M. Silverstein, J. O. Rodin, and D. L. Wood, Science, **154**, 509 (1966); J. Econ. Entmol., **60**, 944 (1967).
5. For recent reports in this area, see a) A. Hosomi, H. Hashimoto, and H.

Sakurai, J. Org. Chem., 43, 2551 (1978); b) A. Hosomi and H. Sakurai, Tetrahedron Lett., 2589 (1978), and references cited therein.

6. All new compounds obtained in this work gave correct elemental analysis and satisfactory spectral data.
7. 1 was obtained in excellent yield according to a similar procedure to the coupling reaction reported by K. Tamao, K. Sumitani, Y. Kiso, M. Zembayashi, A. Fujioka, S. Kodama, I. Nakajima, A. Minato, and M. Kumada, Bull. Chem. Soc. Japan, 49, 1958 (1976). The yield of 1 depends on the nickel complex used. Nickel complex used and % yield were: $Ni(Ph_2P(CH_2)_3PPh_2)Cl_2$, 91; $Ni(PPh_2(CH_2)_2PPh_2)Cl_2$, 35; $Ni(PPh_3)_2Cl_2$, 3.4. Experimental procedure is as follows. Chloromethyltrimethylsilane (18.7 g, 0.152 mol) was added slowly to magnesium (4.29 g, 0.176 g-atom) in dry ether at room temperature. The resulting Grignard reagent 2 was added dropwise to a solution of chloroprene (3) (16.6 g, 0.187 mol) in ether in the presence of $Ni(dppp)Cl_2$ (0.49 g, 8.6 mmol) and the reaction mixture was heated at reflux with stirring for 6 h. After hydrolysis and usual work-up, the solvent was removed by distillation. By distillation of the residue, 1 (19.3 g, 0.138 mol), boiled at 69-70°C/80 mmHg, was obtained in 91% yield. Nmr $\delta(CCl_4)$, 0.03 (9H, s, $Si\text{-}C\underline{H}_3$), 1.71 (2H, d, J=1 Hz, $Si\text{-}C\underline{H}_2$) 4.7-5.2 (4H, m, $=C\underline{H}_2$), 6.36 (1H, d of d, J=11 and 17 Hz, $=C\underline{H}\text{-}$); ir cm^{-1} (neat), 3090, 1635, 1595, 995, 905; uv λmax (hexane), 231.0 nm ($\varepsilon=1.17\times10^4$).
8. A. Hosomi, M. Endo, and H. Sakurai, Chem. Lett., 941 (1976).
9. A. Hosomi, H. Sakurai, Tetrahedron Lett., 1295 (1976).
10. Contrary our previous report on the conjugate addition of allylsilanes to α,β-enones,[11] 1 afforded [4+2] cycloadducts with α,β-enones. We will report the detail of the reaction later.
11. A. Hosomi and H. Sakurai, J. Am. Chem. Soc., 99, 1673 (1977).
12. Synthesis of 5 and 6 can be traced according to the following refernces: a) ref.3; b) O. P. Vig, R. C. Anand, G. L. Kad, and J. M. Sehgal, J. Indian Chem. Soc., 47, 999 (1970); c) J. A. Katzenellenbogen and R. S. Lenox, J. Org. Chem., 38, 326 (1973); d) K. Mori, Agric. Biol. Chem., 38, 2045 (1974); e) C. F. Garbers and F. Scott, Tetrahedron Lett., 1625 (1976); f) S. Karlsen, P. Frϕyen, and L. Skattebϕl, Acta Chem. Scand., B 30, 644 (1976); Chem. Abstract, 85, 192911x (1976); g) K. Mori, Tetrahedron Lett., 2187 (1975); h) Idem, ibid., 1609 (1976); i) G. Ohloff and W. Giersch, Helv. Chim. Acta, 60, 1496 (1977); j) M. Bertrand and J. Viala, Tetrahedron Lett., 2575 (1978).
13. Although ketones 7 and 8 can be purified by tlc, the crude ketones are pure enough to further reduction. Purification of the ketones by glc sometimes brings isomerization of olefinic bonds in the isoprenyl group to afford the corresponding conjugate enones.

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