Tetrahedron Letters,Vol.23,No.5,pp 551-554,1982	0040-4039/82/050551-04$03.00/0
Printed in Great Britain

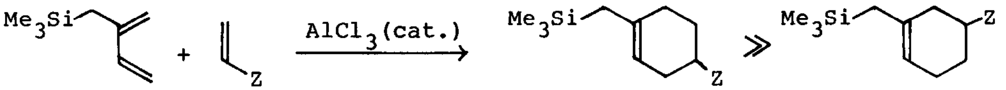
HIGHLY REGIOSELECTIVE DIELS-ALDER REACTIONS OF 2-TRIMETHYLSILYLMETHYL-1,3-BUTADIENE CATALYZED BY A LEWIS ACID AND APPLICATIONS TO SYNTHESES OF TERPENES[1]

Akira Hosomi, Hirokazu Iguchi, Jun-ichi Sasaki and Hideki Sakurai
Department of Chemistry, Tohoku University, Sendai 980 Japan

Summary: 2-Trimethylsilylmethyl-1,3-butadiene undergoes highly regioselective Diels-Alder reactions with dienophiles such as acrolein and methyl vinyl ketone catalyzed by aluminum chloride in which the "para" isomers are obtained almost exclusively. The adducts are converted readily to a variety of naturally occurring mono and sesquiterpenes.

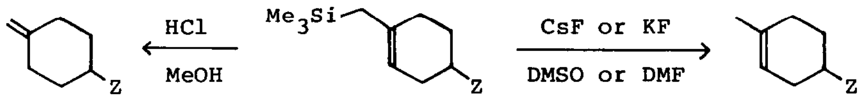
Previously we have described that 2-trimethylsilylmethyl-1,3-butadiene(**1**) is not only an efficient and convenient reagent for the regiospecific isoprenylation[2] but also an excellent diene for the highly regio- and stereoselective Diels-Alder reactions with unsymmetrical dienophiles.[3] We now report that the Lewis acid-catalyzed reaction of **1** with methyl vinyl ketone, acrolein and acrylic esters gives almost pure "para" adducts(**3**), and that the adducts are useful and convenient precursors for the synthesis of natural terpenes.

Table 1 lists the results of Lewis acid-catalyzed reactions of acrolein and acyclic and cyclic α,β-unsaturated ketones and esters, together with those of uncatalyzed reactions.[3] It is important to note that Lewis acid-catalyzed reactions[4] proceed not only faster but also more regioselectively than uncatalyzed reactions (eq. 1). Especially, acrolein and methyl vinyl ketone give almost pure "para" adducts in good yield.



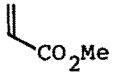
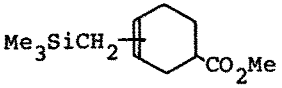
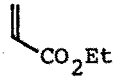
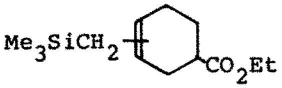
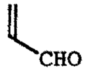
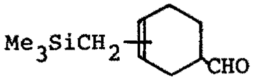
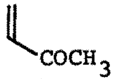
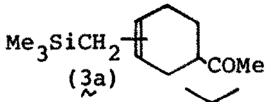
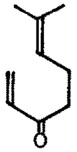
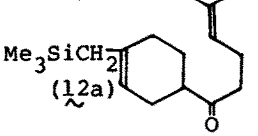
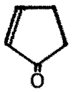
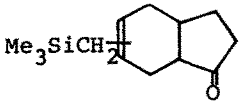
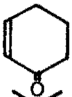
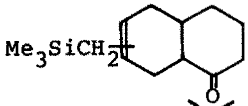
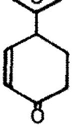
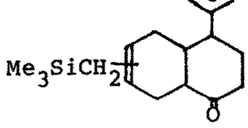
1　**2**　**3**(para)　**4**(meta)　(1)

The "para" adducts, thus obtained, are readily protodesilylated regioselectively by a Brønsted acid in methanol and cesium or potassium fluoride in aqueous dimethyl sulfoxide (DMSO) or dimethylformaldehyde (DMF) to give *exo*-methylenecyclohexanes and cyclohexenes, respectively. (eq. 2)



5　**3**　**6**　(2)

Table 1. Diels-Alder reactions of isoprenylsilane(1) with various dienophiles catalyzed by aluminum chloride

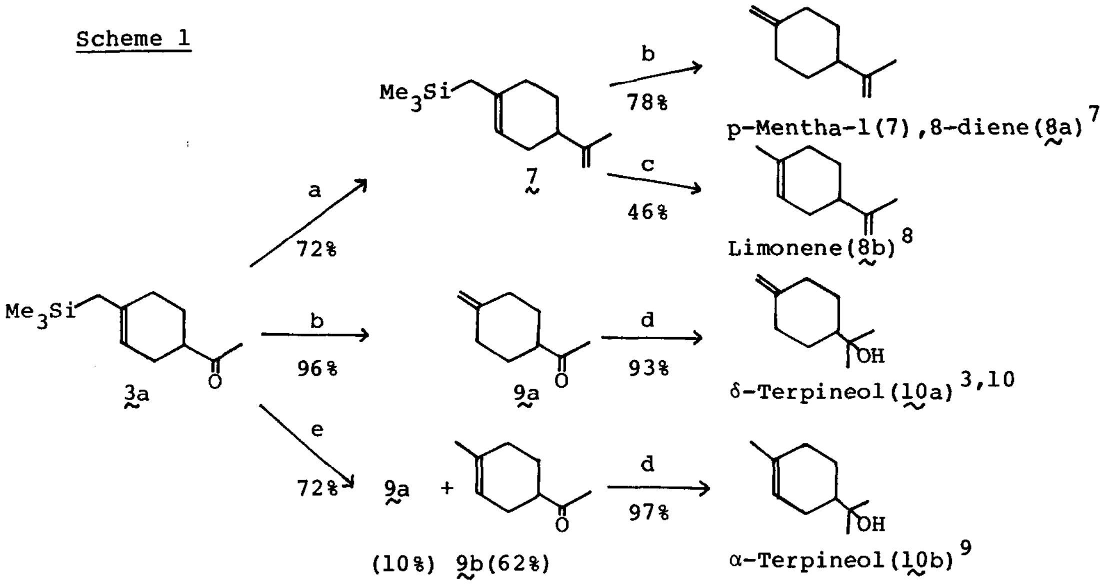
Entry	Dienophile	Reaction conditions[a] temp/°C, time/h	Products	% yield	Ratio of para : meta[c,d]
1		50-60, 2 (80, 46)[d]		75 (58)	99.5 : 0.5 (84 : 16)
2		50-60, 2 (80, 46)		72 (63)	99 : 1 (82 : 18)
3		15-20, 3.5 0, 6[e] (80, 34)		69 61 (69)	100 : 0 100 : 0 (97 : 3)
4		15-20, 3.5 0, 6[e] (80, 36)	 (3a)	64 58 (83)	100 : 0 100 : 0 (83 : 17)
5	 (11)	30, 6[e]	 (12a)	85	100 : 0
6		80, 2 (130, 15)		57 (43)	93 : 7 (89 : 11)
7		80, 2 (135, 20)		70 (17)	99 : 1 (84 : 16)
8		60, 13		56	95 : 5

---

[a] All reactions were carried out in the presence of 0.08-0.1 equiv. of $AlCl_3$ in benzene unless otherwise noted. [b] Yields after isolation by TLC.
[c] Determined by GLC. [d] Ratios as well as yields of uncatalyzed reactions are shown in parentheses. See ref. 3 except for entry 6 and 7. [e] Reactions were carried out in dichloromethane.

The adducts corresponding to an isoprene skeleton should serve as intermediates for the preparation of a variety of naturally occurring terpenes.[5] Indeed an adduct(3a) with methyl vinyl ketone can be converted to some monoterpenes as shown in Scheme 1.[6]

Scheme 1

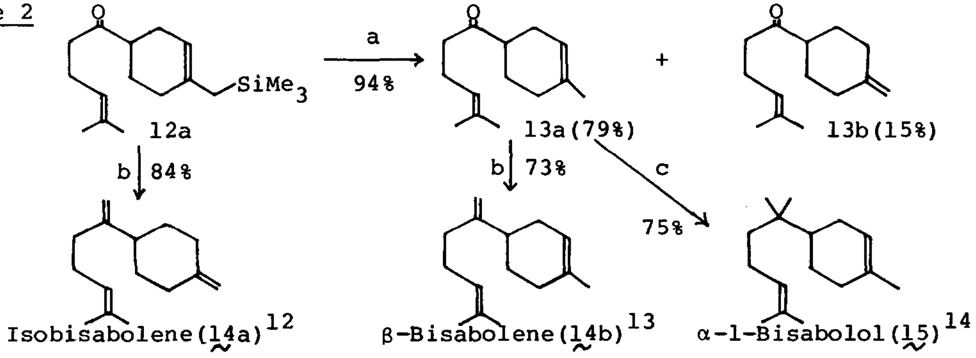


^{a} $MeSiCH_2MgCl/Et_2O$, reflux, 4h ^{b} HCl/MeOH, rt, 15 min. ^{c} CsF/DMSO, 100°, 30 min. ^{d} $MeMgBr/Et_2O$, rt, 30 min. ^{e} KF/DMSO, 120°, 12h

Methylenation[11] of the ketone(3a) followed by regioselective protodesilylation with hydrochloric acid in methanol or cesium fluoride in DMSO leads, *via* 7, to p-mentha-1(7),8-diene(8a) and limonene(8b), respectively. Desilylation followed by methylation with methylmagnesium bromide gave α- and δ-terpineol (10b and 10c), respectively. Preparation of terpineol involving an *exo*-methylene group is rather tedious,[10] but the present method provides a convenient route to the *exo*-methylene compounds.[3]

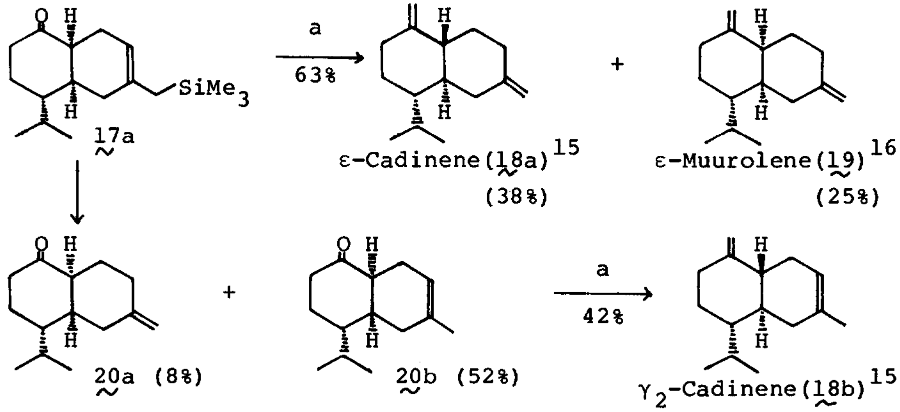
Similarly, some derivatives of bisabolanes and cadinanes have been prepared from the adducts, 12a and 17a, with 7-methylocta-1,6-dien-3-one(11) and cryptone (16), respectively, the results being shown in Scheme 2 and 3.

Scheme 2



^{a} CsF/DMSO, 100°, 1h ^{b}1) Me_3SiCH_2MgCl/Et_2O, reflux 3h; 2) 1M HCl/MeOH, rt, 15h ^{c} $MeMgBr/Et_2O$, reflux, 3h

Scheme 3



^{a}1) Me_3SiCH_2MgCl/Et_2O, reflux, 11h; 2) HCl/MeOH, rt, 15h
^{b} CsF/DMSO, 100°, 1h

This work demonstrates that 1 can be viewed as one of the isoprene synthon. The synthetic utility of the reaction was displayed by very high — almost perfect — regioselectivity of the Diels Alder reaction, ready accessibility of the starting materials and simple manipulation of the conversion.

Acknowledgement: We thank Toshiba Silicone Co., Ltd., and Denki Kagaku Kogyo Co., Ltd., for generous gifts of chlorosilanes and chloroprene, respectively. This research was supported by the Ministry of Education, Japan, for Grant-in-Aid for Scientific Research (No. 5654085).

References and Notes

1. Chemistry of Organosilicon Compounds 152.
2. A. Hosomi, M. Saito and H. Sakurai, Tetrahedron Lett., 429(1979).
3. A. Hosomi, M. Saito and H. Sakurai, Tetrahedron Lett., 21, 355(1980). See also S.R. Wilson, L.R. Philips and K.J. Natalie, Jr., J. Am. Chem. Soc., 101, 3340(1979).
4. a) T. Inukai and T. Kojima, J. Org. Chem., 31, 1121(1966); b) K.N. Houk and R.W. Strozier, J. Am. Chem. Soc., 95, 4094(1973); c) K.N. Houk, Accounts Chem. Res., 8, 361(1975).
5. All compounds obtained in this work gave correct elemental analysis and satisfactory spectral data. Yields are not always optimized.
6. References cited herein for terpenes are mostly recent ones.
7. R.L. Webb and J.P. Bain, J. Am. Chem. Soc., 75, 4279(1953).
8. O.P. Vig, K.L. Matta, G. Sigh and I. Raj, J. Indian Chem. Soc., 43, 7(1966).
9. K. Alser and W. Vogt, Ann., 564, 109(1949).
10. B.M. Mitzner and S. Lemberg, J. Org. Chem., 31, 2022(1966).
11. D.J. Peterson, J. Org. Chem., 33, 780(1968).
12. O.P. Vig, S.D. Sharma, K.L. Matta and J.M. Shegal, J. Indian Chem. Soc., 48, 993(1971).
13. O.P. Vig, J.P. Salota, B. Vig and R. Ram, Indian J. Chem., 5, 475(1967).
14. I. Iwashita, T. Kusumi and H. Kakizawa, Chem. Lett., 211(1970).
15. M.D. Soffer and L.A. Bur, Tetrahedron Lett., 211(1970), and references cited therein.
16. a) L. Westfelt, Acta Chem. Scand., 18, 572(1964); b) idem, ibid., 20, 2852(1966).

(Received in Japan 23 October 1981)