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NEW STEREOCONTROLLED APPROACH TO SOME INSECT PHEROMONES VIA SILICON-DIRECTED BECKMANN FRAGMENTATION

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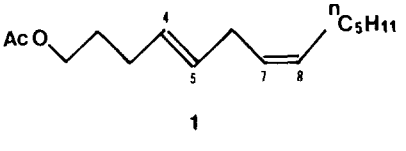
Abstract: The major components of sex pheromones of potato tuberworm moth and Douglas fir tussock moth have been synthesized via the regio- and stereo-controlled Beckmann fragmentation assisted by trimethylsilyl group.

Comprehensive works on the synthesis of insect pheromones have been reported in recent literatures to show biological activities and versatilities of synthetic methodology.[1] In terms of synthetic problem, regio- and stereo-selective construction of target olefins included in many insect pheromones has received much attention. We have recently reported that trimethylsilyl group can direct the regio- and stereo-chemistry of olefin formation in the Beckmann fragmentation of β-trimethylsilylketoximes.[2] We demonstrate herein the potent availability of the fragmentation in the synthetic sequences of some insect sex pheromones; (4E, 7Z)-4,7-tridecadienyl acetate 1 [a component of the sex pheromone of potato tuberworm moth (*Phthorimaea operculella*)][3] and (Z)- and (E)-6-heneicosen-11-one 2 and 3 [the major sex pheromone 2 and minor one 3 of Douglas fir tussock moth (*Orgyia pseudotsugata*)][4].



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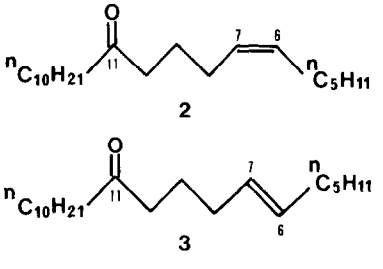

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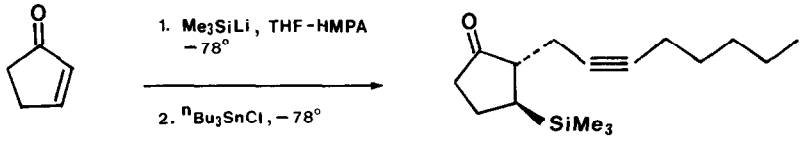
This new approach to stereospecific syntheses of the internal olefins of 1, 2, and 3 was started from the preparation of β-trimethylsilylketones by a sequencial 2,3-double alkylation of α,β-enone and a simple 1,4-addition to α,β-enone with trimethylsilyllithium, respectively.

Addition of 2-cyclopentenone (1.5 mmol) to an excess (2 mmol) of trimethylsilyllithiumn[5] in THF-HMPA (10:3, 13 mL) at -78°C generated the lithium enolate of 3-trimethylsilyl-cyclopentanone, which after treatment with tri-n-butyltin chloride (2 mmol)[6] at -78°C was alkylated with 1-bromo-2-octyne[7] (1.5 mmol) at -50~-40°C for 1 h to give the β-silylketone 4[8] in 67% yield.[9] The trapping of the enolate intermediate as the stannyl enolate (or stannyl ketone) is thought to lead good to excellent yield for the α-alkylation in the sequencial vicinal double alkylation. In spite of the prominent advantages of trialkylstannyl enolates for mono-alkylation of ketones, as already reported by Odic[10] and Tardella[11], there has been no adequate and remarkable application of the enolates in synthetic problems yet. We should, therefore, notify that the exquisite combination of trialkylstannyl enolate and alkynyl bromide gives smoothly the desired mono-alkylated product in the presence of HMPA at low temperature and provides a useful method for modification in cyclopentanoid chemistry.[12]



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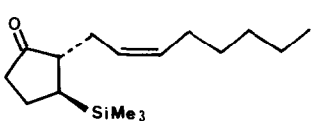
Hydrogenation of 4 with Pd-$BaSO_4$ and quinoline in methanol gave the cis-olefinic ketone 5[13] (84% yield). Oximation of 5 with hydroxylamine hydrochloride and sodium acetate in ethanol at room temperature followed by acetylation with acetic anhydride in pyridine gave the oxime acetate 6[14] (74%; total yield 91% from 5; syn-isomer, 17%). Treatment of 6 (0.34 mmol) with a catalytic amount of trimethylsilyl trifluoromethanesulfonate (ca. 10 mol%) in anhydrous dichloromethane (1 mL) at 0°C for 2.5 h afforded the (4E, 7Z)-dienonitrile 7[15] in 79% yield as a single stereoisomer. Reduction of 7 with diisobutylaluminum hydride at -78°C and then with sodium borohydride at 0°C followed by acetylation gave the desired compound 1[16], (4E, 7Z)-4,7-tridecadien-1-yl acetate, in 58% yield from 7.



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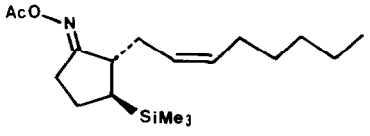

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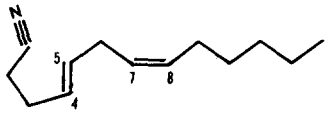

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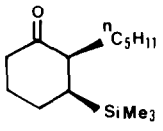
On the other hand, addition of 2-n-pentyl-2-hexenone 8[17] to a solution of trimethylsilyllithium at -78°C and subsequent quenching with methanol gave the corresponding silylated ketones which, after stirring at 0°C for 1 h, were isolated as a mixture of 2,3-cis and trans isomers (9:10 = 42:58, 94%).[18] After the separation by silica gel chromatography, 9 was converted to the oxime acetate 11[19] (61%; total yield 91% from 9, syn-isomer 30%) by oximation followed by acetylation in the same manner as described. Treatment of 11 with TMSOTf (10 mol%) at 0°C gave the (5Z)-5-undecenonitrile 12 in 88% yield.[20] Alkylation of 12 with decanyl Grignard reagent in ether at room temperature followed by hydrolysis with hydrochloric acid afforded the target ketone 2 as a colorless oil in 77% yield.[21]



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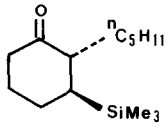

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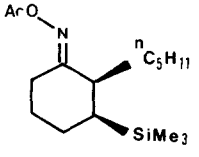

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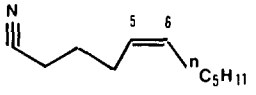

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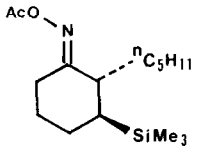
Alternatively, the trans isomer 3 was synthesized via the same procedure by employing the trans silylketone 10. Oximation and subsequent acetylation of 10 gave the corresponding oxime acetate 13[22] (87%, syn-isomer 9%), which was converted to 3 as a white solid via the fragmentation (14, 93%) and alkylation (71%).[23]



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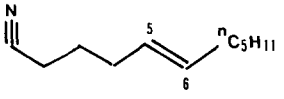


14

Thus these sequences allow a unique synthetic approach to internal olefins as included in some insect pheromones via the silicon-directed Beckmann fragmentation with high stereospecificity.

References and Notes:

(1) K. Mori, "The Total Synthesis of Natural Products", edited by J. ApSimon, Vol 4, (1981) John Wiely & Sons, Inc., New York, P 1-183.
(2) H. Nishiyama, K. Sakuta, N. Osaka, and K. Itoh, Tetrahedron Lett., 24, 4021 (1983).
(3) W.L. Roelofs, J.P. Kochansky, R.T. Carde, C.A. Henrick, J.N. Labovitz, and V.L. Corbin, Life Sci., 17, 699 (1975). A. Alexakis, G. Cahiez, and J.F. Normant, Tetrahedron Lett., 2027 (1978).
(4) R.G. Smith and G.D. Daves, Jr., J. Org. Chem., 40, 1593 (1975).
(5) W.C. Still, J. Org. Chem., 41, 3063 (1976).
(6) No addition of n-Bu$_3$SnCl gave a mixture of complicated products included a small amount of 4.
(7) 1-Bromo-2-octyne was prepared from propargyl alcohol in two steps;alkylation with LiNH$_2$ and n-C_5H_{11}Br in liquid NH$_3$ and bromination with PBr$_3$ and 2,6-lutidine in Et$_2$O.
(8) 4: IR (film)ν1740, 1250, 835 cm^{-1}; ^{1}H NMR (90 MHz, CHCl$_3$)δ 0.03 (CH$_3$Si), 0.84(t,CH$_3$), 1.1-1.5(m, 9H), 1.7-2.2(m, 5H), 2.3(m, 1H), 2.53 and 2.70 (m, 1H) ppm.

(9) Cis stereoisomer was obtained in 11% yield. Rf= 0.5 for trans and 0.6 for cis (hexane: ether = 3:1, SiO_2). Alkylation smoothly occurred at -50°C for about 30 min. There is no need to elevate the reaction temperature. cf. ref. (10) and (11).

(10) Y. Odic and M. Pereyre, J. Organomet. Chem., 55, 273 (1973).
(11) P.A. Tardella, Tetrahedron Lett., 1117 (1969).
(12) As reviews: M. Harre, P. Raddatz, R. Walenta, and E. Winterfeldt, Angew. Chem. Int. Ed. Engl., 21, 480 (1982); M. Demuth and K. Schaffner, Ibid., 21, 820 (1982); For example, Y. Kita, J. Segawa, J. Haruta, H. Yasuda, and Y. Tamura, J. Chem. Soc., Perkin I., 1099 (1982) and references cited therein; M. Suzuki, T. Kawagishi, T. Suzuki, and R. Noyori, Tetrahedron Lett., 23, 4057 (1982); M. Suzuki, T. Kawagishi, and R. Noyori, Ibid., 23, 5563 (1982).

(13) 5: IR (film)ν 1738 , 1250 cm^{-1}, no C-H band for E-disubstituted olefin.

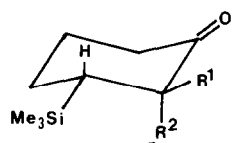
(14) 6: IR (film)ν 1765, 1650, 1245 cm^{-1}; ^1H NMR (90 MHz, $CHCl_3$)δ -0.06 (CH_3Si), 0.82 (t, CH_3), 2.05 (s, CH_3CO), 5.2-5.6 (m, 2H)ppm; ^{13}C (22.5 MHz, $CDCl_3$) -2.75 (CH_3Si), 13.9, 14.4, 19.6, 21.6, 22.5, 24.8, 27.3, 27.5, 29.3(2C), 30.1,30.5, 31.5, 44.7, 125.7, 132.2, 168.8, 177.5 ppm. Rf=0.5 for 6 (anti), 0.4 for syn (hexane-ether=1:1, SiO_2). The counpling constant $JC_\alpha H\text{-}C_\beta H$ of syn-isomer is ca. 1 Hz, which indicates 2,3-trans configuration. (C_2H, δ 2.9 ppm, m, 1 H , for syn-isomer)

(15) 7: IR (film)ν 2240, 965 cm^{-1}; ^1H NMR (90 MHz, TMS, $CDCl_3$)δ0.89 (t, CH_3), 1.1-1.5 (b, 6H), 1.8-2.1 (m, 4H), 2.34 and 2.36 (two singlets, 2H), 2.75 (broad t, 2 H), 5.2-5.8 (m, 4H); ^{13}C NMR (22.5 MHz, TMS, $CDCl_3$) 14.0, 17.7, 22.6, 27.2, 28.4, 29.3, 30.2, 31.5, 119.3(CN), 125.9, 126.6, 131.3, 132.2 ppm.

(16) 1: IR (film)ν 1740, 965 cm^{-1}; ^1H NMR (90 MHz, TMS, $CDCl_3$)δ 4.06 (t, 2H, CH_2OAc), 5.2-5.6 (m, 4H, olefinic) ppm; ^{13}C NMR (22.5 MHz, TMS, $CDCl_3$) 14.0, 20.9, 22.6, 27.1, 28.5, 28.9, 29.4, 30.4, 31.5, 64.0 (OCH_2), 127.4, 129.1, 129.6, 130.7, 171.0 (C=O) ppm. See, ref (3).

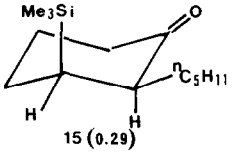
(17) D.F. Taber, B.P. Gunn, and I-C. Chiu, Organic Syntheses, Volume 61, 59 (1983).

(18) Quenching with MeOH at -78°C gave the different silylketone 15 from 9. 15 is thought to be a stereoisomer (axial-equatorial). Selective isomerization of 15 to 9 was unsuccessful under thermal (140°C, no reaction), acidic (p-TsOH, MeOH, decomposition), and basic (NaOMe, decomposition) conditions. Furthermore, oximation of 15 gave surprisingly only the syn-isomer 16, whose acetate did not cause the fragmentaion with TMSOTf at 0°C.



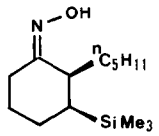
9 R^1=H,R^2=$^nC_5H_{11}$ (0.47)

10 R^1=$^nC_5H_{11}$,R^2=H (0.53)



15 (0.29)

(Rf, C_6H_{14} : Et_2O=10 : 1)



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After quenching with MeOH, stirring was continued at room temp. for 1 day to give 10 only.

(19) 11: IR (film)ν 1763, 1630 cm^{-1}; ^1H NMR (90 MHz, $CHCl_3$)δ -0.01 (CH_3Si), 2.12 (s, CH_3CO), 2.0 (m, 1H, HC_6-ax), 2.65 (dt, 1H, J=5.0, 5.0, 11.0 Hz, HC_2-ax), 3.10 (broad d, 1H, 14Hz, HC_6-eq)ppm.

(20) 12: IR (film)ν 2250, no C-H band for E-disubstituted olefin; ^1H NMR (90 MHz, TMS $CDCl_3$)δ 0.89 (CH_3), 1.1-1.95 (m, 8H), 1.7 (m, 2H), 2.1 (m, 2H), 2.34 (t, 2H, CH_2CN), 5.1-5.7 (m, 2H); ^{13}C NMR (22.5 MHz, TMS $CDCl_3$)14.1, 16.5, 22.6, 25.5, 26.0, 27.2, 29.4, 31.5, 119.8, 126.7, 132.6 ppm.

(21) 2: IR (film)ν 1710 cm^{-1}; ^1H NMR (90 MHz, TMS, $CDCl_3$)δ 0.88 (CH_3, 6H), 1.0-1.4 (m, 24H), 1.6 (m, 2H), 1.95 (m, 2H), 2.32 (broad t, 4H), 5.1-5.6 (m, 2H); ^{13}C NMR, 128.8,131.3 ppm; color less oil. See, ref (4).

(22) 13: IR (film)ν 1762, 1630 cm^{-1}; ^1H NMR (90 MHz, $CHCl_3$)δ0.0 (CH_3Si), 2.13 (s, CH_3CO), 1.9 (m, 1H, H_{C2}), 2.6 (broad t, 1H, H_{C6}), 2.9 (dt, 1H, H_{C6})ppm.

(23) 14: IR (film)ν 2245, 965 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$, TMS)δ 0.89 (CH_3), 1.1-1.5 (m, 8H), 1.7 (m, 2 H), 2.05 (m, 2H), 2.32 (t, 2H, CH_2CN), 5.1-5.7 (m, 2H) ppm; ^{13}C NMR (22.5 MHz, $CDCl_3$, TMS)14.1, 16.3, 22.6, 25.3, 29.2, 31.3 (2C), 32.6, 119.0, 127.3, 133.3 ppm.
3: IR (KBr disk)ν 1700, 960 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$, TMS)δ 0.87 (CH_3, 6H), 1.0-1.8 (m, 24H), 1.8-2.2 (m, 4H), 2.37 (t, 4H), 5.25-5.45 (m, 2H) ppm; ^{13}C NMR (22.5 MHz, $CDCl_3$, TMS) 129.3, 131.6 ppm; white solid, m.p. 34-35°C. See, ref (4), m.p. 36-38°C for the authentic compound.

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