Tetrahedron Letters, Vol.31, No.19, pp 2739-2742, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

SILA-PHEROMONES: SILICON ANALOGUES OF THE FEMALE SEX PHEROMONE OF THE PROCESSIONARY MOTH *Thaumetopoea pityocampa*

Gemma Arsequell, Francisco Camps*, Gemma Fabriàs and Angel Guerrero.
Department of Biological Organic Chemistry, C.I.D.(C.S.I.C.)
Jordi Girona 18-26, 08034 Barcelona-Spain.

Summary

The 15- and 10-dimethylsila-analogues of (Z)-13-hexadecen-11-ynyl acetate, the main component of the female sex pheromone of the processionary moth *Thaumetopoea pityocampa*, were synthesized to evaluate the influence of the silicon atom on the biological activity.

The increasing interest in bioactive organosilicon compounds[1] has led to the recent development of different sila-drugs such as sila-steroids[2a], sila-Vitamin A[2b] or Sila-procyclidine[2c], an analogue of the muscarinic drug Procyclidine, applied in antiparkinsonian therapy. Likewise, the bioisosteric replacement of carbon by silicon has also been investigated in sila-perfumes[2d]. However, from these studies an important drawback became evident, due to the reactivity of SiH_2 bonds that prevented the application of bioactive sila-analogues with these moieties under physiological conditions. In some cases, this problem has been circumvented by substituting $Si(CH_3)_2$ groups for stable CH_2 moieties.

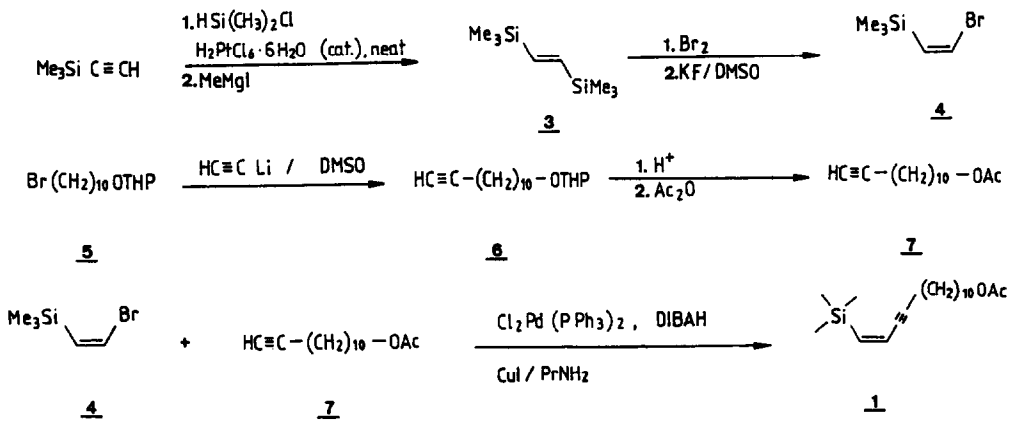
We anticipated that it might be worthwhile to apply this approach for preparation of unprecedented silapheromones. In the present communication, we report on the synthesis of acetates 1 and 2, the 15- and 10-dimethylsila-analogues of (Z)-13-hexadecen-11-ynyl acetate, the main component of the sex pheromone of the processionary moth *Thaumetopoea pityocampa*[3].

The synthesis of silapheromone 1, with one dimethylsilyl group in a vinylic position, was accomplished as depicted in Scheme I. As the most structural relevant feature of the natural pheromone is a conjugated (Z)-enyne moiety, a logical approach to compound 1 appeared to be the stereospecific coupling of the acetoxyalkyne 7 with (Z)-1-bromo-2-trimethylsilylethylene (4). For preparation of this vinylsilane we selected the hydrosilylation of alkynes as one of the most convenient routes. Regioselective *cis*-hydrosilylation[4] of commercially available 1-trimethylsilylacetylene with chlorodimethylsilane, at room temperature in the presence of the Speier's catalyst (hexachloroplatinic acid in isopropanol)[5], gave the corresponding chlorodimethylsilane. This compound was subsequently methylated with methyl magnesium iodide in Et_2O to yield the vinylsilane 3 in 71% yield.

Stereospecific *trans*-addition of bromine to vinylsilane 3 afforded a mixture of *meso*-1,2-dibromo-1,2-bis(trimethylsilyl)ethanes that underwent elimination of trimetilsilylbromide on treatment with potassium fluoride[6] in DMSO to give (Z)-1-bromo-2-trimethylsilylethylene (4).

The acetate 7 was obtained as we have reported[7] by treatment of the bromoalcohol derivative 5 with lithium acetylide in DMSO to afford the terminal alkyne that was succesively deprotected and acetylated with Ac_2O in pyridine.

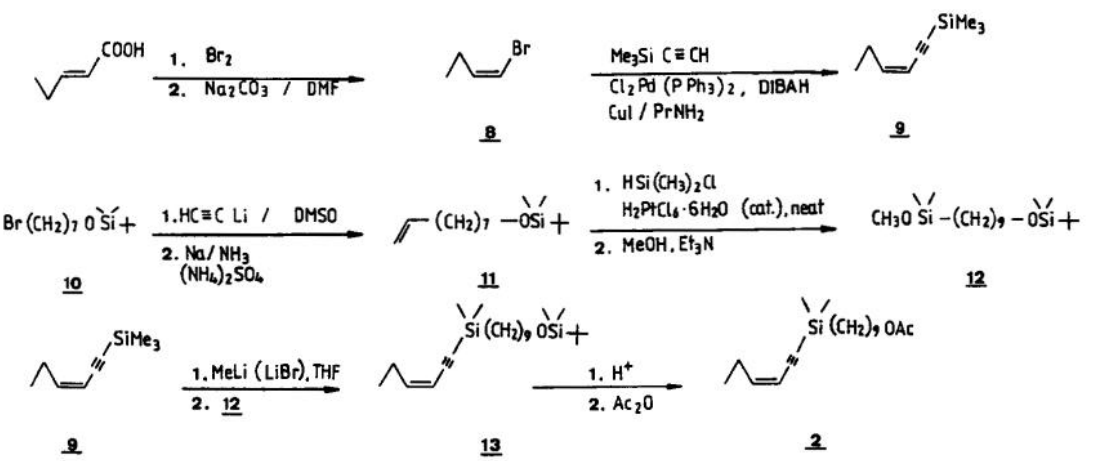
The planned stereospecific coupling of acetoxyalkyne 7 with derivative 4 was not as straightforward as anticipated. Recent examples of similar couplings with (Z) and (E) isomeric mixtures of 2-(bromovinyl)trimethylsilane revealed that the (E) isomer reacted very easily whereas the corresponding (Z) isomer was recovered unchanged under a variety of conditions[8]. After several unsuccessful attempts, cross-coupling reaction between the acetate 7 and a large molar excess (1:5) of bromoalkene 4 by a procedure developed in our laboratory[9], using a 10 mol% of "bis(triphenylphosphine)palladium (0)", generated *in situ* by reduction of $PdCl_2(PPh_3)_2$ with 2 equivalents of DIBAH in refluxing THF, and CuI(I) as catalysts, afforded the silicon analogue 1 in 60 % yield[15] .



SCHEME I

As depicted in Scheme II, the synthesis of 10-dimethylsila-analogue 2 was carried out by using the (Z)-enyne trimethylsilyl derivative 9, as protected acetylene. This compound was prepared in 89 % yield by stereospecific palladium cross-coupling reaction of commercially available trimethylsilylacetylene and (Z)-1-bromo-1-butene (8), under the above conditions[9]. The bromovinyl synthon 8 required for this coupling was easily prepared, in overall 59 % yield, by addition of bromine at -78°C to commercial *trans*-2-pentenoic acid, followed by bromodecarboxylation of the dibromoderivative obtained with Na_2CO_3 at 60°C in anhydrous DMF[10].

We anticipated that masked 9 alkyne could be reacted with an appropriate silyl derivative to incorporate the dimethylsilyl moiety at C10. For this purpose, we selected methoxysilane 12 since it is well established that methoxysilanes are suitable for the formation of C-Si bonds[11]. Preparation of compound 12 was carried out by the sequence outlined in Scheme II. Reaction of *tert*-butyldimethylsilyl ether of 7-bromoheptanol (10) with lithium acetylide in DMSO, followed by reduction of the terminal alkyne group with Na/NH_3 and $(NH_4)_2SO_4$[12] afforded alkene 11 in 81% yield. This alkene was hydrosilylated with chlorodimethylsilane at 80°C, under the above conditions[5], to give the corresponding terminal chlorosilane, that was converted into the required methoxysilane 12 by treatment with an excess of MeOH in Et_3N at r.t. Couplings of terminal 1-trimethylsilyl-1-alkynes in which the acetylide is generated with "naked fluoride" reagents, such as TASF or TBAF have been reported in the literature[13]. However, in our case we selected an alternative procedure to generate *in situ* the acetylide anion[14] that had been previously reported for quantitative monodesilylation of bis(trimethylsilyl) acetylenes and to our knowledge not previously used in the reactions with enyne derivatives. Treatment of protected enyne 9 with MeLi-LiBr complex at r.t. for 3.5 h in THF gave the corresponding acetylide that was reacted with a THF solution of methoxysilane 12 to afford derivative 13 in 44 % yield, after purification by column chromatography eluting with hexane. Finally, cleavage of the protecting group with a 1 % HCl (95:5) $EtOH/H_2O$ solution and acetylation with Ac_2O in pyridine afforded the silapheromone 2[15] with a 98 % stereomeric purity (GLC, NMR).



SCHEME II

Electroantenogram bioassays with 1 μg of sila-analogue 1 revealed an approximate 10% intensity of the antennal reponse of males of processionary moth when compared to that elicited by the same amount of natural pheromone. However, in field trials this compound neither showed any direct intrinsic

activity nor exhibited any synergistic or inhibitory action when mixed with natural pheromone at different ratios. Further work along this line is in progress in our laboratory.

Acknowledgements

Financial support from C.I.C.Y.T. Grants (AGR-89-532 and PB-87-0290) and a predoctoral fellowship from The Spanish Ministry of Education and Science to one of us (G.A.) are gratefully acknowledged. The authors also thank R. Montoya and R. Hernández (ICONA) for carrying out the field bioassays.

References and notes

1. a) R. Tacke and H. Linoh , *Bioorganosilicon chemistry* in *The Chemistry of Organosilicon Compounds*, Vol II, S.Patai, Z. Rappoport Ed., John Wiley and Sons, N.Y., 1989, p.1144-1206.
b) R. Tacke and U. Wannagat, *Synthesis and Properties of Bioactive Organo-Silicon Compounds in Bioactive Organo-Silicon Compounds*, Vol 84, *Topics in Current Chemistry*, F.L. Boschke ed., Springer-Verlag, N.Y., 1979, p. 1-75.
2. a) R.H. Peters, D.F. Crowe, M. Tanabe, M.A. Avery and W.K.M. Chong, *J.Med.Chem.* 1987,*30*,646. b) R. Münstedt and U. Wannagat, *J.Organomet.Chem.* 1987,*322*,11. c) R.Tacke, J. Pikies, H. Linoh, R. Rohr-Aehle and S. Gönne, *Liebigs Ann. Chem.* 1987,51. d) D. Wrobel and U. Wannagat, *Liebigs Ann.Chem.* 1982,734.
3. A.Guerrero, F. Camps, J. Coll, M.Riba, J.Einhorn, Ch. Descoins and J.Y. Lallemand, *Tetrahedron Lett.* 1981,2013.
4. C.Birkofer and T. Kühn, *Chem.Ber.* 1978,*111*,3119.
5. J.L.Speier, *Advances in Organometallic Chemistry*, Vol 17, F.G.A.Stone, R.West ed., Academic Press, N.Y., 1979, 407-447; J.L.Speier,J.A.Webster and G.H. Barnes, *J.Am.Chem.Soc.* 1957,*79*,974.
6. J.P.Pillot, J.Dunogués and R. Calas, *Synth. Commun.* 1979,*9*,395.
7. F. Camps, J. Coll, A. Guerrero and M. Riba, *J. Chem. Ecol*.1983,*9*,869.
8. a) B.P. Andreini, A. Carpita, R. Rossi and B. Scamuzzi, *Tetrahedron* 1989, *45*, 5621. b) V. Fiandenese, G. Marchese, G. Mascolo, F. Naso and L. Ronzini, *Tetrahedron Lett.* 1988, *29*, 3705.
9. F. Camps, E. Chamorro, V. Gasol and A. Guerrero, *Synth. Commun.* 1989, *19*, 3211.
10. W.P. Norris, *J.Org.Chem.* 1959,*24*,1579.
11. L. Birkkofer and O. Stuhl in reference 1a) p.655-761.
12. Henne and J. Greenle, *J.Am.Chem.Soc.* 1943,*65*,2020.
13. Y.Hatanaka and T.Hiyama, *J.Org.Chem.* 1988,*53*,918; Y. Hatanaka, K.Matsui and T. Hiyana, *Tetrahedron Lett.* 1989,*30*,2403; E.Nakamura and I.Kuwajima, *Angew.Chem.Int.Ed.Engl.* 1976,*15*,498.
14. A.B. Holmes, C.L.D. Jennings-White, A.H. Schulthess, B. Akinde and D.R.M. Walton, *J.Chem.Soc.,Chem.Comm.* 1979,840 ; A.B. Holmes and G.E. Jones, *Tetrahedron Lett.* 1980,*21*,3111.
15. Satisfactory analytical data were obtained for all the compounds reported herein. **1** : IR (Cl_4C) 2930, 2850, 1740, 1560, 1460, 1385, 1365, 1240, 910, 845 cm^{-1}. ^1H NMR (80 MHz, $CDCl_3$): δ 0.18,(s, 9H); 1.30 (br, 14H); 2.05 (s, 3H); 2.30 (m, 2H); 4.08 (t, J= 7 Hz, 2H); 5.97 (d, J_{AB} = 14.4 Hz, 1H); 6.29 (dt, J_{BA} = 14 Hz, J_{BC} = 4 Hz, 1H). ^{13}C NMR (20 MHz, $CDCl_3$): δ 171.1, 142.3, 125.3, 94.8, 80.7, 64.6, 28.6-30.9, 25.9, 21, 19.5, -1.0. Anal. calcd for $C_{19}H_{34}O_2Si$: C, 70.73; H, 10.64. Found. C, 70.53; H, 10.81. MS: 322 (M^+) (1), 307 (M^+-15)(12), 183 (2), 133 (10), 117 (100), 75 (24), 73 (20), 59 (12) and 43 (25). **2**: IR (Cl_4C): 2930, 2850, 2140, 1740, 1460, 1385, 1365, 1250, 1240, 840 cm^{-1}. ^1H NMR (80 MHz, $CDCl_3$): δ 0.18 (s, 6H); 0.60 (m, 2H); 1.00 (t, J = 7.8 Hz, 3H); 1.30 (br, 14H); 2.05, (s, 3H); 2.30 (m, 2H); 4.08 (t, J = 7 Hz); 5.40 (dt, J = 10.8 Hz, 1H); 5.90 (dt, J= 10.7 Hz and J = 7.0 Hz, 1H). ^{13}C NMR (20 MHz, $CDCl_3$): δ 171.2, 146.9, 108.6, 102.3, 97.0, 64.6, 26.5-33.2, 25.9, 23.8, 23.7, 20.9, 16.2, 13.2, -1.6. Anal. calcd for $C_{19}H_{34}O_2Si$: C, 70.73; H, 10.64. Found.: C, 70.67; H, 10.81. MS: 307 (M^+-15) (1), 243 (24), 183 (16), 137 (42), 117 (100), 59 (27) and 43 (55).

(Received in UK 5 March 1990)