Tetrahedron Letters, Vol.31, No.13, pp 1865-1868, 1990
Printed in Great Britain

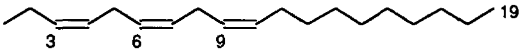
0040-4039/90 $3.00 + .00
Pergamon Press plc

SYNTHESIS OF A PHEROMONE OF *Boarmia selenaria VIA* A SILA-COPE ELIMINATION.STEREOCHEMICAL IMPLICATIONS§

Y. Langlois*, L. Konopski, N.V. Bac, A. Chiaroni and C. Riche
Institut de Chimie des Substances Naturelles, C.N.R.S., 91198 Gif-sur-Yvette, France

Summary. The use of a Sila-Cope elimination afforded a *Z,Z,Z* trienamine derivative, direct synthetic precursor of (3Z,6Z,9Z)-3,6,9-nonadecatriene **1**, one of the pheromone components of *Boarmia selenaria.* X-ray analysis of the tetrahydropyridinium salt **13** leading to the dienic vinyl silane **14** allowed the determination of the relative configurations of the tetrahydropyridine intermediates **7**, **8**, **9** and **12**.

Our continuing studies using 2-alkyl-1,2,5,6-tetrahydropyridines as precursors of dienic derivatives led to the syntheses of various dienic pheromones.[1] In particular, we have demonstrated that 1,4 *Z,E* and *Z,Z* dienes can be obtained with a good stereoselectivity via the Sila-Hofmann and the Sila-Cope eliminations.[2] Further scope of these reactions including the synthesis of (3Z, 6Z, 9Z)-3,6,9-nonadecatriene **1**, a component of the sex pheromonal system of the giant looper, *Boarmia selenaria*,[3] and also some study concerning the stereochemical implication of these eliminations are presented in this report.



1

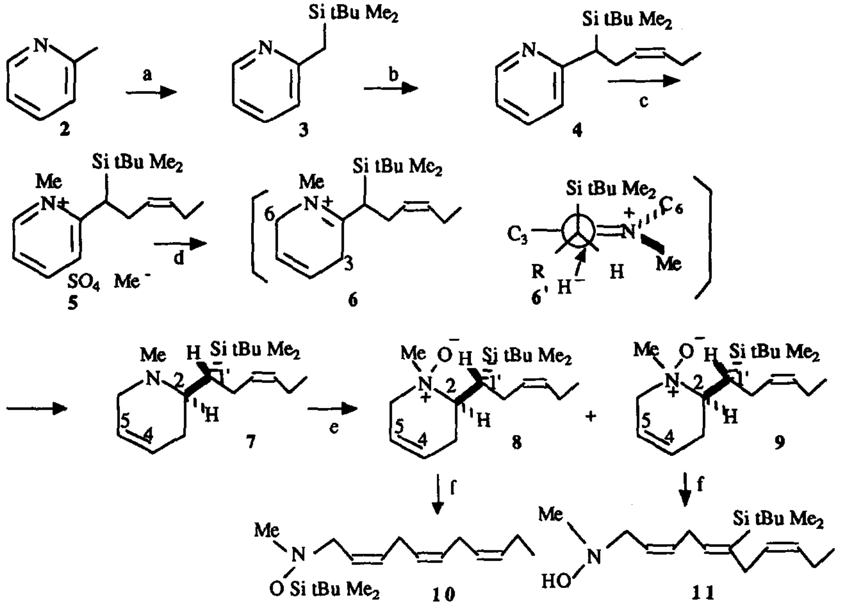
The synthesis of the pheromone **1** was initiated by transforming 2-methyl pyridine **2** into its silylated derivative **3** in 91% yield (Scheme I). This compound, after deprotonation and alkylation with (2Z)-1-bromo-2-pentene,[4] afforded the substituted pyridine **4** in 96% yield. The corresponding pyridinium salt **5** was quantitatively isolated after *N*-alkylation with an excess of dimethyl sulfate. This salt was reduced with sodium borohydride to furnish, after purification, the 1,2,3,6-tetrahydropyridine **7** in 67% yield as a single diastereomer. The stereochemical control during the reduction of the immonium salt intermediate **6** should be due to a peculiar conformation **6'** which differs from the models described by Cram and Felkin for the reduction of a carbonyl group.[5] Hydride attack by the less hindered face of this intermediate **6'** should give rise to the tetrahydropyridine derivative **7** in which the 2R* 1'S* relative configurations could be tentatively assigned (Scheme I).

Oxidation of **7** with MCPBA led quantitatively to a mixture of two diasteromeric *N*-oxides **8** and **9**. In contrast, with our previous work[2], theses *N*-oxides proved to be stable enough to be isolated by preparative thin layer chromatography with only partial spontaneous elimination. Each of the *N*-oxides **8** and **9** was subjected to the Sila-Cope elimination conditions (CH_3CN, 40°C, 2h). Thus the less polar *N*-oxide **8** gave rise to the less polar derivative **10** (SiO_2, eluent: CH_2Cl_2-MeOH-NH_4OH 85:14:1. Rf: 0.9) whereas the more polar *N*-oxide **9** provided the more polar derivative **11** (Rf: 0.6) (Scheme I). Careful examination of 400 MHz NMR spectra of compounds **10** and **11** showed, after double irradiation experiments, that the less polar compound **10** was the anticipated triene hydroxylamine derivative resulting from the expected Sila-Cope

---

§ Dedicated to the memory of the late Professor E. Lederer.

elimination whereas the more polar compound **11** was produced by a Cope elimination involving the proton on carbon α to the silicon group; this occurred at rather low temperature for this type of reactions,[6] probably as a consequence, in the transition state, of the stabilization effect due to the presence of silicon.



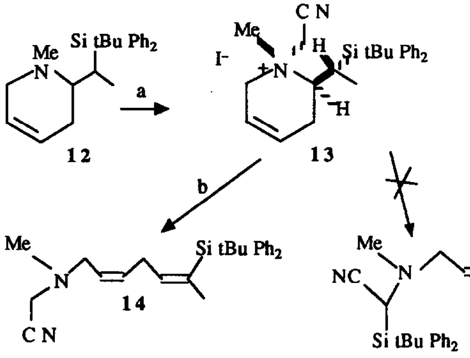
a: LDA (1.1 eq.), ClSitBuMe$_2$ (1.1 eq.), THF, -70°C, 1 h. b: LDA (1.2 eq.), (2Z)-1-bromo-2-pentene (1.2 eq.), THF, -60°C, 1h. c: Me$_2$SO$_4$ (10 eq.), 60°C, 16 h. d: NaBH$_4$ (10 eq.), MeOH, -5°C, 15 min. e : MCPBA (1.1 eq.), CH$_2$Cl$_2$, 0°C, 30 min. f: MeCN, 40°C, 2h.

To establish the relative configurations of the three asymmetric centers, including the nitrogen in *N*-oxide diastereomers **8** and **9**, these compounds or their salts were submitted to several attempts of crystallization in order to perform an X-ray analysis on a single crystal. Unfortunately these *N*-oxides spontaneously gave the previous elimination reactions. Thus we anticipated that a more stable quaternary ammonium salt which could give rise to the same intramolecular elimination reactions should be a good substrate for both X-ray analysis and further studies concerning the stereochemistry of such reactions.

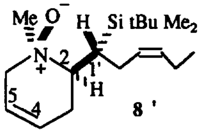
Thus the 1,2,3,6-tetrahydropyridine **12**, prepared as previously described,[2] afforded after *N*-alkylation with iodoacetonitrile, the crystalline tetrahydropyridinium salt **13**, the relative configuration of which was determined by X-ray analysis (Fig. 1);[7] it turned out that the relative configurations at C-2 and C-1' are in agreement with our preliminary hypothesis concerning the reduction of the pyridinium salt **5**.

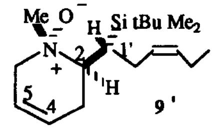
Furthermore, the tetrahydropyridinium salt **13** by treatment with potassium carbonate in dimethyl formamide afforded the diene hydroxylamine **14** in 91% yield by an intramolecular Hofmann elimination. No product **15** resulting from a Sila-Hofmann elimination was produced during this reaction. This observation enabled us to attribute the relative configuration **8'** at nitrogen for the *N*-oxide leading to a Sila-Cope elimination and the configuration **9'** for the *N*-oxide **9** leading to a Cope elimination . It is worthy of note that this intramolecular Hofmann elimination gave rise to a vinyl silane derivative **14** which could be of interest for further synthetic purpose.

Finally, the stereoselective synthesis of trienic pheromone **1** was achieved in five steps from the mixture of *N*-oxide diastereomers **8** and **9**. These compounds without separation were directly transformed into the trienic derivatives **10** (35%) and **11** (39%). After separation by chromatography, **10** was desilylated and alkylated in a single step to afford *N*-oxide **16** in 86% yield. This compound after reduction with zinc in acetic acid and *N*-alkylation led to the trienic ammonium salt **17** (two steps, 81%). Coupling of the ammonium salt **17** with the Grignard reagent **18** prepared from 1-bromo octane afforded, in addition to unreacted starting material (34%), a mixture of three products in a total yield of 62%. This mixture analysed by GC-MS[8] revealed the presence of three isomers having the molecular weight 262. After purification (SiO_2, $AgNO_3$ 15%, eluent: C_6H_{14}-CH_3CO_2Et 80:20), each compound was identified by careful study of its 400 MHz spectrum. The less polar compound **19** (20%) was identified as (3*Z*, 6*Z*, 8)-3,6,8 nonadecatriene formed by migration of the 9,10 double bond. The stereochemistry of the 8,9 double bond has not been determined. The second product (38%) was identified as (3*Z*, 6*Z*, 9*Z*)-3,6,9-nonadecatriene **1** by comparison of its mass and NMR spectra with those of a reference sample.[9] The third very minor product (1.4%) was identified as (3*Z*, 6*Z*, 9*E*)-3,6,9-nonadecatriene **20**.



a: ICH_2CN (46 eq.), 20°C, 18 h.
b: K_2CO_3 (1.5 eq.), DMF, 20°C, 50 h.





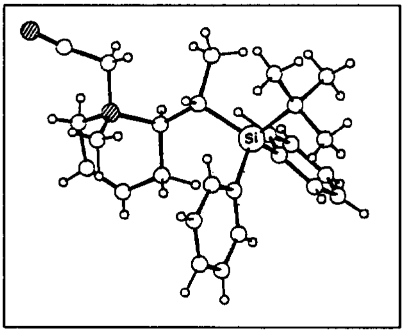
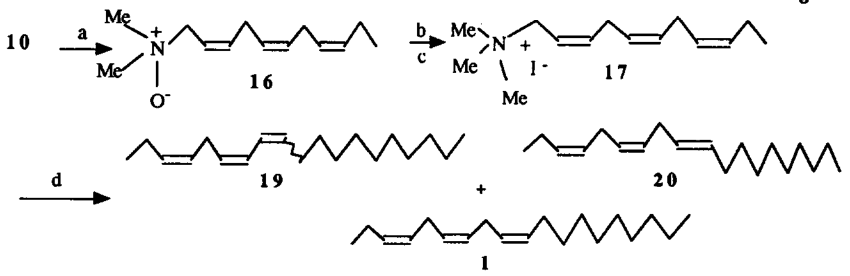


Fig. 1



a: MeI (20 eq.), CsF (5.7 eq.), MeOH, 20°C, 24 h. b: Zn (30 eq.), $AcOH/H_2O$ (50/50), 20°C, 30 min. c: MeI(2 eq.), MeOH, 20°C, 16 h. d: OctMgBr **1 8** (1.3 eq.), Li_2CuCl_4 (0.03 eq.), THF, -35°C, 20 h.

Achievement of the synthesis of the pheromone **1** led us to establish the relative configurations of the tetrahydropyridine intermediates **7**, **8**, **9** and **12** as well as a preparation of dienic vinyl silanes, useful intermediates for further syntheses.

Acknowledgements. We are grateful to Drs Andriamialisoa and Kouklovsky for ^1H 400 MHz and GC-MS spectra.

References and Note

1. a) Fall, Y.; Bac, N.V. and Langlois, Y. *Tetrahedron Lett.*, **1986**, *27*, 3611 and references therein.
   b) For a review concerning the synthesis of achiral pheromones see: R. Rossi, *Synthesis*, **1977**, 817.
   c) Baker, R. and Herbert, R.H., **1984**, "Insect Pheromones and Related Natural Products", *Natural Prod. Reps*, *1*, 299.
   d) Langlois, Y. *C.R. Acad. Sci., Ser. Gen.*, **1987**, *4(1)*, 39.
   e) For a review concerning the optically active pheromones see: K. Mori, *Tetrahedron*, **1989**, *45*, 3233.
2. Bac, N.V. and Langlois, Y. *J. Am. Chem. Soc.*, **1982**, *104*, 7666.
3. Becker, D.; Kimmel, T.; Cyjon, R.; Moore, I.; Wysoki, M.; Bestmann, H.J.; Platz, H.; Roth K. and Vostrowsky, O. *Tetrahedron Lett.*, **1983**, *24*, 5505.
4. Treatment of (2Z)-2-penten-1-ol (Lancaster) with PBr_3 in ether afforded (2Z)-1-bromo-2-pentene (geometrical purity >95%).
5. Eliel, E.L. *"Asymmetric Synthesis"*, J.D. Morrison Ed., Academic Press, 1984, vol. 2, chapter 5, 125.
6. Cope, A.C. and Le Bel, N.A. *J. Am. Chem. Soc.*, **1960**, *82*, 4656
7. Crystal data: $C_{26}H_{35}N_2\,Si^+$, I^-, monoclinic, $P2_1/a$, a = 13.994 (7), b = 12.118(6), c = 16.364 (10) Å, β = 112.5 (1); λ = 0.7107 (Mo Kα), 4992 intensities collected on a Philips diffractometer, 3610 observed reflexions $I > 3\sigma(I)$). Structure solved by Patterson-Fourier methods and refined by full matrix least-squares. Hydrogen atoms were refined with an isotropic thermal factor equivalent to that of the bonded atom (+20%). Final R factor : 0.041. Atomic coordinates, distances and angles were deposited with the Crystallographic Cambridge Data Bank.
8. Capillary column (25 m x 0.22 mm), CPSil.5CB, Chrompac, temperature 170°C to 250°C (2°C per min.).
9. We thank Prof. H.J. Bestmann and Dr. O. Vostrowsky for sending us copies of the mass and NMR spectra of pheromone **1**.

(Received in France 13 December 1989)