Tetrahedron Letters, Vol 32, No 42, pp 5995-5998 1991
Printed in Great Britain

0040-4039/91 $3 00 + 00
Pergamon Press plc

Assignment of (6*R**,10*R**)-Relative Stereochemistry to the Major Component of the Sex Pheromone of the Maritime Pine Scale, *Matsucoccus feytaudi*

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Summary (2*E*,4*E*,6*R*,10*S*)-4,6,10-Trimethyl-2,4-dodecadien-7-one **1** and its (6*S*,10*S*)-isomer were synthesized The ^{1}H NMR spectrum of (6*S*,10*S*)-**1** coincided with that reported for the major component of the sex pheromone of *Matsucoccus feytaudi*, which must therefore be either (6*S*,10*S*)- or (6*R*,10*R*)-**1**

In 1990 Einhorn *et al* isolated ca 200 µg of the major component of the sex pheromone of *Matsucoccus feytaudi*, an endemic pest of the maritime pine, from ca 35,000 females, and assigned its structure as depicted in **1** (Figure 1) with unknown stereochemistry at C-6 and C-10 [2] A pheromone **2** with its structure very similar to **1** had been isolated in 1989 by Lanier *et al* from *Matsucoccus matsumurae*, *M resinosae*, and *M thumbergianae* [3] A recent preliminary communication by Kallmerten and his co-workers on the assignment of relative stereochemistry of **2** as (6*R**,10*R**) or 6,10-*syn*[4] prompts us to report our result to propose 6,10-*anti* or (6*R**,10*R**)-relative stereochemistry to the natural **1** This work is an extension of our recent synthesis of **3**, the female specific compound of the woodroach, *Cryptocercus punctulatus* [5]

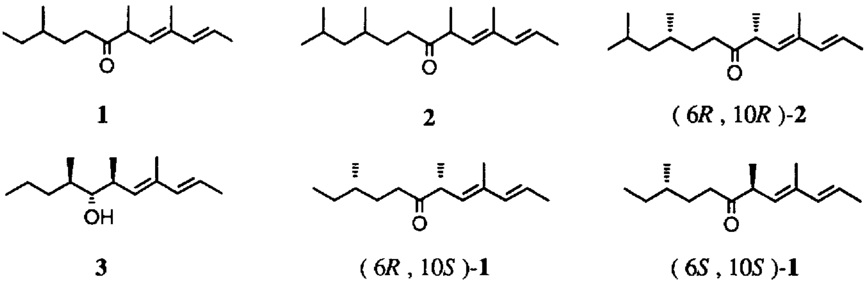
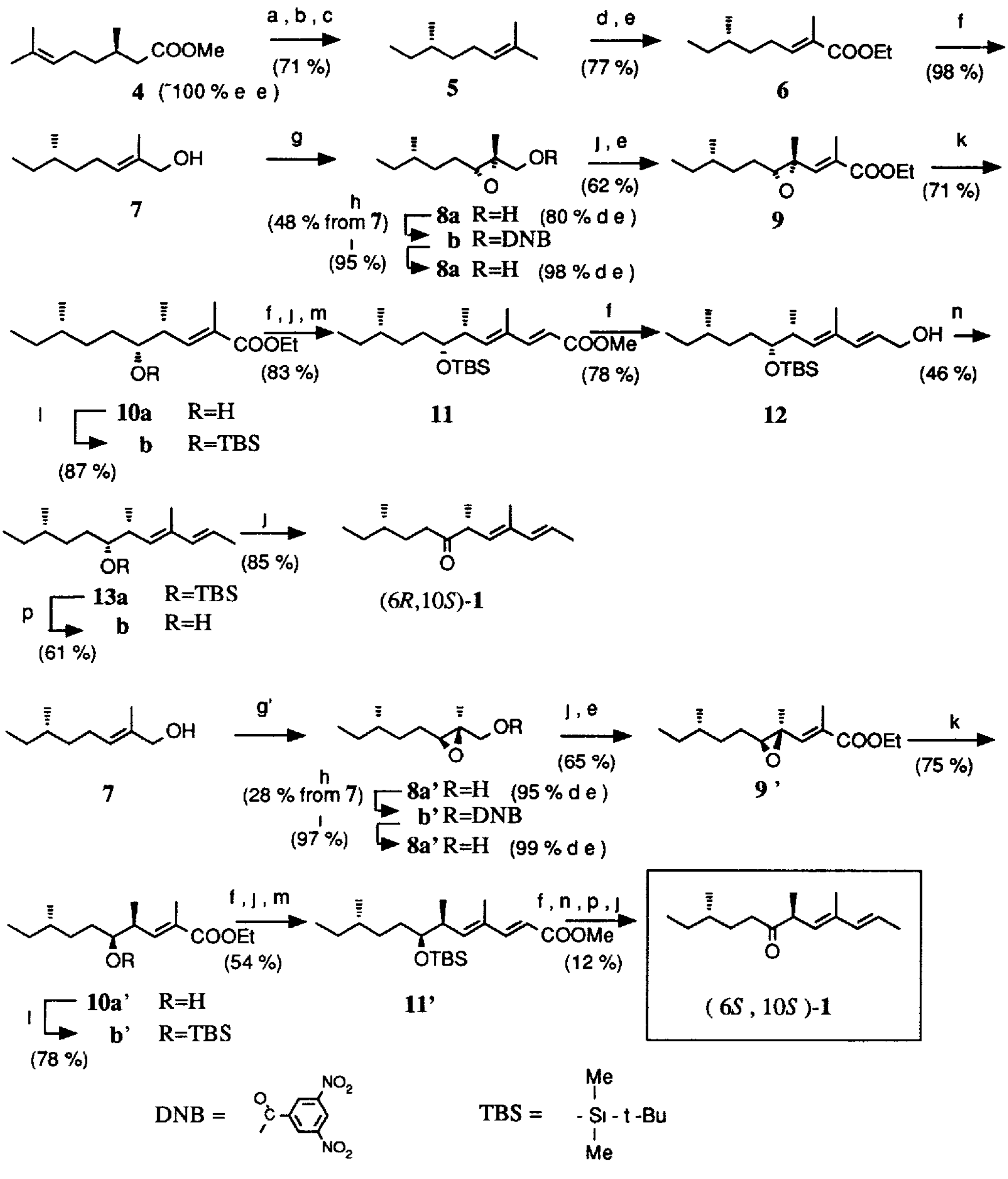


Figure 1 Structures of the pheromones

As shown in Figure 2, our synthesis started from methyl (*R*)-citronellate (**4**, ~100 % e e), and employed the Sharpless asymmetric epoxidation (**7** → **8a** and **7** → **8a'**) as the key step Preparation of **7**[6] from **4** was executed in the usual manner in six steps Epoxidation of **7** with (–)-diethyl D-tartrate as the chiral auxiliary afforded crude **8a** with 80% d e as analyzed by HPLC (stationary phase Daicel chiralcel OJ) The corresponding 3,5-dinitrobenzoate **8b** was crystalline (mp 48 5-49 5°C), and could be purified by recrystallization Mild alkaline hydrolysis of **8b** gave back pure **8a** with 98% d e Swern oxidation of **8a**



Reagents (a) $LiAlH_4$, Et_2O, 0-5°C, (b) TsCl, C_5H_5N, 0-5°C, (c) $LiAlH_4$, THF, 60-70°C, (d) O_3, $NaHCO_3$, MeOH-$CHCl_3$, -78°C, (e) $Ph_3P{=}C(Me)CO_2Et$, C_6H_6, 60-70°C, (f) (i-Bu)$_2$AlH, Et_2O, -78°C, (g) Ti(Oi-Pr)$_4$, D-(-)-DET, t-BuOOH, CH_2Cl_2, -23°C, (g') Ti(Oi-Pr)$_4$, L-(+)-DET, t-BuOOH, CH_2Cl_2, -23°C, (h) 3,5-DNBCl, C_5H_5N, Et_2O, 0-5°C, (i) N-NaOH aq, THF-MeOH, 0-5°C, (j) $(COCl)_2$, DMSO, CH_2Cl_2, -78°C then Et_3N, -78°C - r t , (k) $Pd_2(dba)_3CHCl_3$, Ph_3P, HCOOH, Et_3N, dioxane, r t , (l) TBSCl, imidazole, DMF, r t , (m) $(MeO)_2P(O)CH_2CO_2Me$, n-BuLi, THF, 0-5°C, (n) SO_3 C_5H_5N, THF, r t then 1 0 M $LiAlH_4$ in THF, r t , (p) (n-Bu)$_4$NF, THF, r t , prep-HPLC

Figure 2 Synthesis of (6*R*,10*S*)- and (6*S*,10*S*)-1 was followed by the Wittig reaction to furnish **9** Shimizu's palladium-catalyzed reductive cleavage[7] of the epoxide **9** smoothly yielded **10a** in 71% yield after chromatographic purification Subsequent to the protection of the hydroxy group as TBS ether to give **10b**, the diene part of the molecule was constructed to give **13a** *via* **11** and **12** according to the method used for the synthesis of **3**[5] Finally, the corresponding alcohol **13b** was purified by preparative HPLC (YMC-packed column, D-SIL-5-06, 20 x 250 mm), and oxidized under Swern condition to give (6*R*,10*S*)-**1**[8] The overall yield of (6*R*,10*S*)-**1** was 1 4% in twenty steps from **4** For the synthesis of (6*S*,10*S*)-**1**, the asymmetric epoxidation of **7** was executed by employing (+)-diethyl L-tartrate as the chiral auxiliary to give **8a'**, which could be purified by recrystallizing the corresponding 3,5-dinitrobenzoate **8b'**, mp 53 5 - 54 5°C The epoxy alcohol **8a'** was converted to (6*S*,10*S*)-**1**[9] in the same manner as in the case for the synthesis of (6*R*,10*S*)-**1** The overall yield of (6*S*,10*S*)-**1** from **4** was 0 37% in twenty steps

The 300 MHz ^{1}H NMR spectra of both (6*R*,10*S*)- and (6*S*,10*S*)-**1** were carefully compared with the published 400 MHz ^{1}H NMR spectrum of the naturally occurring pheromone[2] As shown in Figure 3, the two isomers showed distinctly different spectra, especially at the region of δ= 2 0-2 5 Signals assigned to the protons at C-8 of (6*S*,10*S*)-**1** appeared at δ= 2 14 (ddd, *J*= 16 9, 9 3, 5 9 Hz) and 2 28 (ddd, *J*= 16 9, 9 3, 5 9 Hz) in accordance with the signals reported for the natural pheromone, while the corresponding protons of (6*R*,10*S*)-**1** were observed at δ= 2 17(ddd, *J*= 16 7, 9 1, 5 9 Hz) and 2 26 (ddd, *J*= 16 7, 9 1, 5 9 Hz)

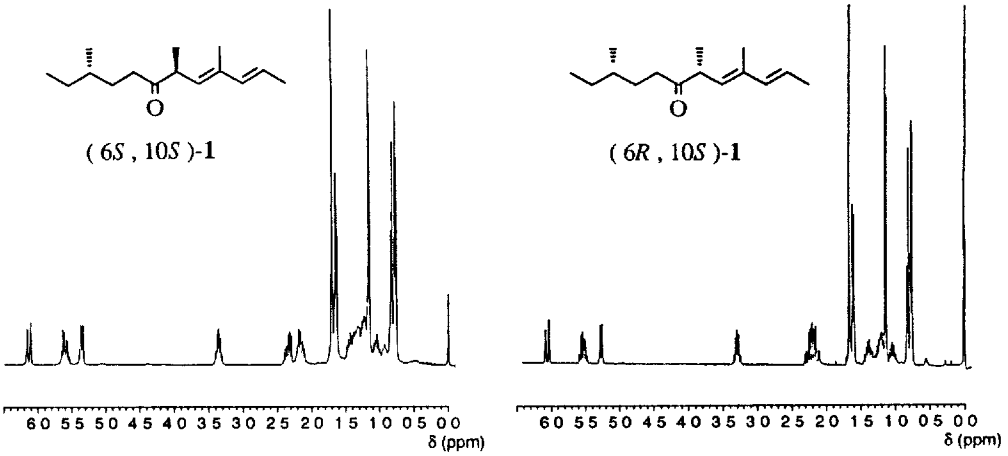


Figure 3 300 MHz ^{1}H NMR spectra of (6*R*,10*S*)- and (6*S*,10*S*)-**1** measured on Bruker AM 300 as C_6D_6 solutions with tetramethylsilane as an internal standard

The above described observation clearly indicates that the naturally occurring pheromone is either (6*R*,10*R*)- or (6*S*,10*S*)-**1** with 6,10-*anti* relative stereochemistry It should be noted that even in the same genus of *Matsucoccus*, *M feytaudi* employs 6,10-*anti*-**1** as the pheromone, while 6,10-*syn*-**2** is the pheromone of *M matsumurae* Synthesis of (6*R*,10*R*)-**1** is now under way to establish the absolute configuration of the naturally occurring pheromone

Acknowledgments. We thank Sankyo Co , Ltd for financial support (R)-Citronellic acid was kindly given to us by Takasago International Corporation, Ltd

References and Notes

1 Research Fellow on leave from Sankyo Co , Ltd (1990-1992)

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6 All the compounds described in this paper exhibited spectral (IR and NMR) and analytical (combustion or HRMS) data consistent with the given structures

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8 Spectral properties of (6R,10S)-**1** (1) IR (film) ν= 3040(m), 1725(s,sh), 1718(s), 1622(w), 1550(w), 968(s)cm^{-1} (2) ^{1}H NMR (300 MHz, C_6D_6) δ= 0 76 (d, 3H, J= 6 4 Hz), 0 81 (t, 3H, J= 7 3 Hz), 0 97 ~ 1 50 (m, 4H), 1 13 (d, 3H, J= 6 7 Hz), 1 61 (dm, 3H, J= 6 6 Hz), 1 63 ~ 1 72 (m, 1H), 1 67 (d, 3H, J= 1 1 Hz), 2 17 (ddd, 1H, J= 16 7, 9 1, 5 9 Hz), 2 26 (ddd, 1H, J= 16 7, 9 1, 6 5 Hz), 3 29 (dq, 1H, J= 9 8, 6 7 Hz), 5 24 (br d, 1H, J= 9 8 Hz), 5 50 (dq, 1H, J=15 5, 6 7 Hz), 6 01 (br d, 1H, J=15 5 Hz) (3) HRMS m/z= 222 1977 (Calc for $C_{15}H_{26}O$ 222 1984)

9 Spectral properties of (6S,10S)-**1** (1) IR (film) ν= 3040(m), 1725(s,sh), 1710(s), 1620(w), 1550(w), 965(s)cm^{-1} (2) ^{1}H NMR (300 MHz, C_6D_6) δ= 0 76 (d, 3H, J= 6 4 Hz), 0 81 (t, 3H, J= 7 2 Hz), 0 97 ~ 1 50 (m, 4H), 1 14 (d, 3H, J= 6 9 Hz), 1 62 (dm, 3H, J= 6 5 Hz), 1 63 ~ 1 72 (m, 1H), 1 67 (d, 3H, J= 1 2 Hz), 2 14 (ddd, 1H, J= 16 9, 9 3, 5 9 Hz), 2 28 (ddd, 1H, J= 16 9, 9 3, 5 9 Hz), 3 29 (dq, 1H, J= 9 9, 6 8 Hz), 5 25 (br d, 1H, J= 9 8 Hz), 5 49 (dq, 1H, J=15 4, 6 6 Hz), 6 01 (br d, 1H, J=15 9 Hz) (3) HRMS m/z= 222 1975 (Calc for $C_{15}H_{26}O$ 222 1984)

(Received in Japan 25 June 1991)