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SYNTHESIS OF A TRICYCLIC CIS-SELINANE-TYPE COMPOUND FROM GERMACRENE-D IN CONNECTION WITH PERSOONS' PERIPLANONE A

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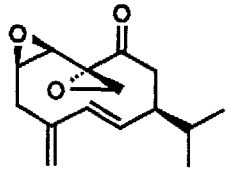
Summary: In connection with periplanone A, germacrene-D has been successfully converted into a tricyclic cis-selinane-type compound previously proposed to be Persoons' periplanone A. This synthetic compound did not show any biological activity against the male American cockroach.

Two sex pheromones of the American cockroach Periplaneta americana, periplanone A and periplanone B, which enter into the corresponding different receptors,[1,2] have been isolated by Persoons et al.[3] Of these two pheromones, the stereostructure of periplanone B was unambiguously determined as 1.[4] Furthermore, a tentative structure (2) of periplanone A has been alao proposed by the same authors.[5] However, our synthetic hydroazulenones (3, 4) are different from Persoons' periplanone A in their spectral data: particularly, the IR spectra of the synthetic compounds showed the CO absorption band at ca.1740 cm^{-1}, whereas the corresponding band in the latter was observed at 1710 cm^{-1}, indicating the presence of a six-membered ring ketone in Persoons' periplanone A.[6] Thus, the most plausible cis-selinane-type structure (5) was given to Persoons' periplanone A, on the basis of the ^1H NMR spectral data[6] coupled with molecular mechanics calculations.[7] On the other hand, Hauptmann et al. isolated a new sex pheromone (6) and named it periplanone A,[8] which is regarded as an



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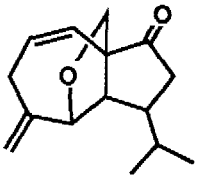

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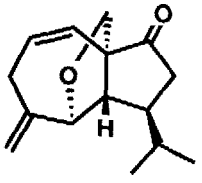

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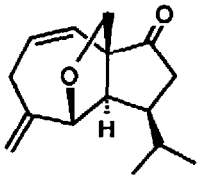

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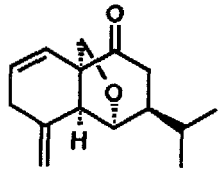

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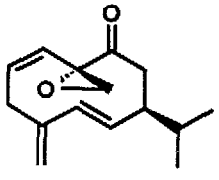

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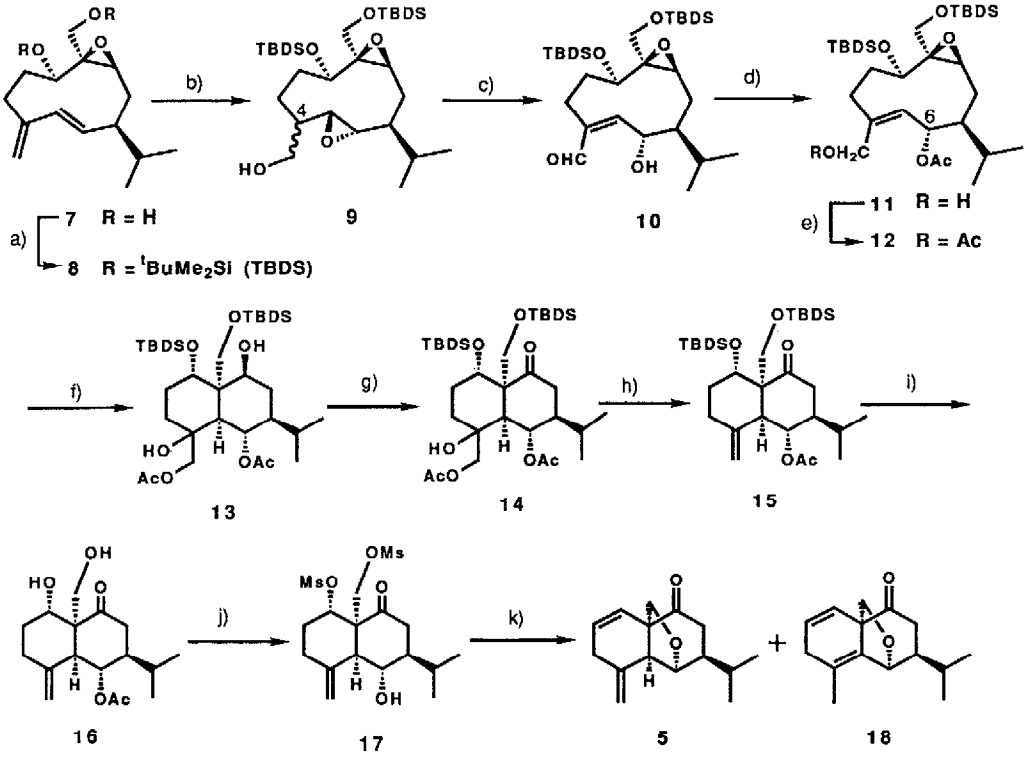
important precursor of periplanone B (**1**). This germacratrienone oxide (**6**) was also isolated from the American cockroach by Nishino et al.[9] In the previous paper,[10] we reported a short step synthesis of Hauptmann's periplanone A, which was proved to enter into the different receptor from that of periplanone B (**1**). As pointed out by Nishino et al.,[9] Persoons' periplanone A seems to be artifact. However, the structure must be elucidated before the definitive conclusion on this matter can be reached. We describe herein a synthesis of the tricyclic cis-selinane-type compound (**5**)[7] proposed as Persoons' periplanone A.

The known epoxide (**7**), which was readily derived from germacrene-D,[6,11] was converted into a disilyl ether (**8**),[12] in usual way, which was then subjected to hydroboration followed



a) $^tBuMe_2SiCl$ (2.2eq.) / Imidazole (3.6eq.) (room temp., overnight) (82%); b) 1. BH_3 (3eq.) / THF (-10°C, 5h), 2. 35%H_2O_2, 1N NaOH (0°C, 2h) (69% in 2steps), 3. mCPBA (8.6eq.) / Et_2O (room temp., 2.5days) (51%); c) $(COCl)_2$, DMSO / CH_2Cl_2 (-50°C, 15min) (89%); d) 1. Ac_2O / Pyridine (room temp., 4h) (99%), 2. DIBAL-H / THF (-75°C, 30min) (94%); e) Ac_2O / Pyridine (room temp., 1.5h) (92%); f) $AlCl_3$ (ca. 4eq.) / Et_2O (-30°C, 3.5h) (67%); g) PCC (ca. 11eq.),Celite / CH_2Cl_2 (room temp., 39h) (98%); h) 1. K_2CO_3 (0.92eq.) / MeOH (room temp., 1.3h) (83%), 2. $(Imd)_2CS$ (4.6eq) / toluene (refluxing temp., 5.3h) (100%), 3. $P(OMe)_3$ under Argon (refluxing temp., 19h) (99%); i) 80%AcOH (90°C, 30min) (100%); j) 1. MsCl / Pyridine under Argon (room temp., 4h) (100%), 2. K_2CO_3 (2.1eq) / MeOH (room temp., 21h) (100%); k) excess DBU / toluene under Argon (refluxing temp., 43.5h).

Scheme 1. Synthesis of tricyclic cis-selinane-type compound (**5**)

by oxidative hydroxylation and successive epoxidation with m-chloroperbenzoic acid to afford a diepoxide (**9**).[12] At this stage, the stereochemistry at the newly formed epoxide ring as well as at C_4-position remains undecided, but the molecular model suggests that its stereostructure is depicted as **9**, as proved later. On Swern oxidation, furthermore, **9** was readily converted into a desired α,β-unsaturated aldehyde (**10**),[12] in high yield, which was subjected to acetylation followed by careful reduction with DIBAL-H to afford an allyl alcohol (**11**),[12] wherein the trisubstituted double bond is in E-configuration as indicated by its ^{1}H NMR spectrum with the aid of NOE experiments [(HO)C$\underline{H}_a$H$_b$ - C_6-H (6.1%); (HO)CH$_a\underline{H}_b$ - C_6-H (5.7%)]. Acetylation of **11** afforded the corresponding acetate (**12**)[12] which was subjected to transannular reaction using $AlCl_3$ to afford in 67% yield the desired cis-selinane-type compound (**13**)[12] having functional groups suitable for the target molecule (**5**). This compound was successfully converted into **5**, as follows.

On PCC oxidation, **13** was readily converted into the corresponding ketone (**14**),[12] in almost quantitative yield, which was carefully hydrolyzed with K_2CO_3 (0.92 equiv) in MeOH and then converted into an olefin (**15**)[12] through a cyclic thiocarbonate intermediate in usual manner. Furthermore, **15** was desilylated with 80% aq AcOH to give a diol (**16**),[12] which was subjected to mesylation followed by hydrolysis with K_2CO_3 in MeOH to afford a desired compound (**17**) in quantitative yield. Finally, demesylation of **17** was effected with DBU in toluene to give two tricyclic compounds (**5** and **18**)[12] in 25 and 7.9% yields, respectively. Of them, the target compound (**5**) proposed as Persoons' periplanone A has the following spectral data: $C_{15}H_{20}O_2$ [m/z 232.1453 (M^+)]; IR (film) 1715, 1630 cm^{-1}; ^{1}H NMR (400 MHz, CS_2): δ 0.84(3H, d, J = 6.8 Hz), 1.12(3H, d, J = 6.8 Hz), 1.42(1H, m), 1.67(1H, m), 1.88(1H, br.d, J = 16.9 Hz), 1.90(1H, dd, J = 10.2, 16.6 Hz), 2.33(1H, dd, J = 7.3, 16.6 Hz), 2.95(1H, dd, J = 6.2, 16.9 Hz), 2.96(1H, br.s), 3.36(1H, d, J = 7.8 Hz), 3.61(1H, d, J = 7.8 Hz), 4.66(1H, d, J = 5.4 Hz), 4.89(1H, br.s), 5.01(1H, br.s), 5.73(1H, br.dd, J = 5.9, 9.3 Hz), 6.02(1H, dd, J = 2.4, 9.3 Hz). The synthetic tricyclic compound (**5**) so far obtained is not completely identical with Persoons' periplanone A in all respects of specteal data, although their spectral data are similar to each other. In the present study, therefore, we could not reach the final conclusion on Persoons' periplanone A,[13], but it should be noted that the tricyclic cis-selinane-type compound (**5**), which is expected to be derived from Hauptmann's periplanone A, shows no biological activity against the male American cockroach.

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11. The overall yield of **7** from germacrene-D has been considerablly improved.
12. The spectral data for the new compounds are in accord with the structures assigned, only selected data are cited: **8**: $C_{27}H_{52}O_3Si_2$ [m/z 480.3478(M^+)]; IR (film) 1608 cm^{-1}; ^1H NMR ($CDCl_3$): δ ca.0(12H, br.s), 0.7 - 1.0(24H, complex), 3.00(1H, dd, J = 3.6, 10.8 Hz), 3.47(1H, dd, J = 5.0, 9.0 Hz), 3.62(1H, d, J = 10.8 Hz), 3.85(1H, d, J = 10.8 Hz), 4.81(1H, br.s), 4.88(1H, br.s), 5.58(1H, dd, J = 8.6, 15.8 Hz), 6.02(1H, d, J = 15.8 Hz). **9**: IR (film) 3450 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.15(1H, br.d, J = 14.5 Hz), 2.61(1H, dd, J = 2.9, 8.7 Hz), 2.65(1H, dd, J = 2.9, 8.7 Hz), 3.14(1H, dd, J = 3.6, 10.9 Hz), 3.64(1H, m), 3.72(1H, d, J = 12.4 Hz), 3.72 - 3.81(2H, complex), 4.22(1H, d, J = 12.4 Hz). **10**: $C_{27}H_{52}O_5Si_2$ [m/z 512.3327(M^+)]; IR (film) 3450, 1685, 1640 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.85(18H, s), 0.8 - 2.4(15H, complex), 3.00(1H, br.d, J = 10.1 Hz), 3.1 - 4.0(3H, complex), 4.40(1H, br.t, J = 8.3 Hz), 6.30(1H, d, J = 8.3 Hz), 9.40(1H, br.s). **11**: $C_{28}H_{53}O_6Si_2$ [m/z 541.3353(M^+ - Me)]; IR (film) 3500, 1740 cm^{-1}; ^1H NMR (C_6D_6): δ 4.55(1H, d, J = 14.0 Hz), 4.72(1H, br.s)$^+$, 5.40(1H, br.s)$^+$, 5.69(1H, br.s)$^+$. $^+$ These signals became quite broad, because of its flexible conformation. **12**: $C_{31}H_{59}O_7Si_2$ [m/z 599.3797(M^+ + 1)]; IR (film) 1740 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.04(6H, s), 4.40(1H, d, J = 13.0 Hz), 4.70(1H, d, J = 13.0 Hz), 5.2 - 5.6(2H, complex). **13**: $C_{31}H_{59}O_8Si_2$ [m/z 615.3746(M^+ - 1)]; IR (film) 3400, 1735, 1720 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.89(3H, d, J = 6.8 Hz), 0.92(3H, d, J = 6.8 Hz), 0.94(9H, s), 1.4 - 1.9(10H, complex), 2.00(3H, s), 2.09(3H, s), 2.27(1H, d, J = 9.3 Hz), 3.68(1H, br.s), 3.75(1H, d, J = 11.2 Hz), 4.02(1H, d, J = 11.7 Hz), 4.23(1H, d, J = 11.2 Hz), 4.35(1H, m), 4.48(1H, d, J = 11.7 Hz), 5.22(1H, t, J = 9.3 Hz). **14**: mp 163 - 165 °C; $C_{31}H_{59}O_8Si_2$ [m/z 615.3751(M^+ + 1)]; IR (film) 3450, 1745, 1710 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.04(6H, s), 3.84(1H, d, J = 10.8 Hz), 4.01(1H, d, J = 10.8 Hz), 4.11(1H, d, J = 11.5 Hz), 4.30(1H, d, J = 11.5 Hz), 4.58(1H, m), 5.42(1H, d, J = 7.2 Hz). **15**: $C_{28}H_{51}O_5Si_2$ [m/z 523.3260 (M^+ - Me)]; IR (film) 1745, 1720, 1650 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.02(3H, s), 3.04(1H, br.d, J = 10.8 Hz), 3.40(1H, d, J = 9.0 Hz), 4.20(1H, dd, J = 5.4, 10.8 Hz), 4.28(1H, d, J = 9.0 Hz), 4.72(1H, t, J = 1.8 Hz), 4.84(1H, t, J = 1.8 Hz), 5.40(1H, t, J = 10.8 Hz). **16**: mp 148 - 150 °C; $C_{16}H_{23}O_4$ [m/z 279.1594(M^+ - CH_2OH)]; IR (film) 3400, 1740, 1700, 1650 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.00(3H, s), 2.70(1H, d, J = 10.8 Hz), 3.20(1H, m), 3.4 - 4.2(4H, complex), 4.66(1H, t, J = 1.7 Hz), 4.86(1H, t, J = 1.7 Hz), 5.42(1H, t, J = 10.8 Hz). **17**: IR (film) 3550, 1715, 1650 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.80(1H,d, J = 10.1 Hz), 2.98(3H, s), 3.08(3H, s), 3.92(1H, t, J = 10.1 Hz), 4.16(1H, d, J = 9.4 Hz), 4.70(1H, d, J = 9.4 Hz), 5.10(1H, br.s), 5.22(1H, br.s), 5.32(1H, dd, J = 5.8, 13.0 Hz). **18**: $C_{15}H_{20}O_2$ [m/z 232.1450(M^+)]; IR (film) 1715 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.88(3H, d, J = 6.1 Hz), 1.03(3H, d, J = 6.1 Hz), 1.45(1H, m), 1.79(3H, s), 2.01(1H, m), 2.29(1H, dd, J = 4.9, 16.5 Hz), 2.58(1H, dd, J = 4.6, 23.2 Hz), 2.66(1H, dd, J = 7.3, 16.5 Hz), 2.76(1H, br.d, J = 23.2 Hz), 3.46(1H, d, J = 6.7 Hz), 4.07(1H, d, J = 6.7 Hz), 4.98(1H, d, J = 3.7 Hz), 5.87(1H, br.d, J = 11.3 Hz), 5.93(1H, dt, J = 3.1, 11.3 Hz).
13. We could not directly compare our synthetic sample (**5**) with Persoons' periplanone A.

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