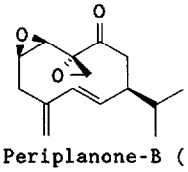
Tetrahedron Letters,Vol.30,No.38,pp 5145-5148,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

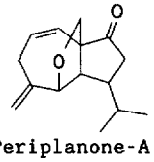
SYNTHETIC CONFIRMATION OF THE STRUCTURE OF THE REARRANGEMENT PRODUCT OF PERIPLANONE-A

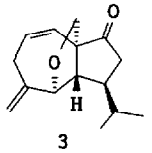
Kenji Mori* and Yasuhiro Igarashi
Department of Agricultural Chemistry, The University of Tokyo,
Yayoi 1-1-1, Bunkyo-ku, Tokyo 113, Japan

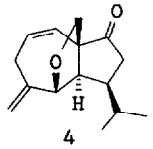
Summary: The stable and biologically inactive rearrangement product of Persoons's periplanone-A was shown to be **12** by the synthesis of (±)-**12**.

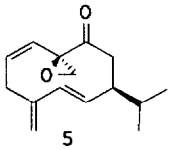
In 1974 Persoons *et al.* isolated two highly active sex pheromone components of the American cockroach(*Periplaneta americana*), and named them periplanone-A and periplanone-B.[1] Although the proposed structure of the latter[2,3] was confirmed by a number of its synthesis either as the racemate or as the naturally occurring enantiomer **1**,[4] the structure of the labile periplanone-A still remains obscure. The original structural proposal of periplanone-A as **2** by Persoons *et al.*[5,6] was challenged by Shizuri *et al.* who synthesized two hydroazulenones (±)-**3**[7] and (±)-**4**,[8] both of which showed the spectra different from those of the pheromone isolated by Persoons.[6]

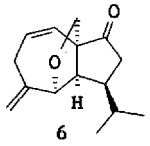

Periplanone-B (1)

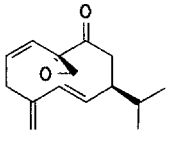

Periplanone-A (2)

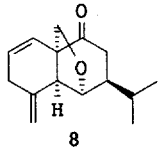

3

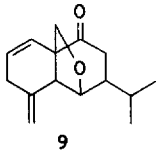

4

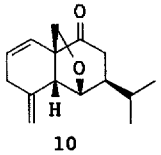

5

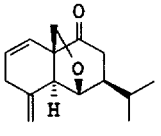

6

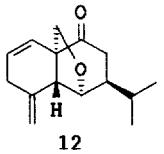

Hauptmann's periplanone-A (7)


8


9


10


11

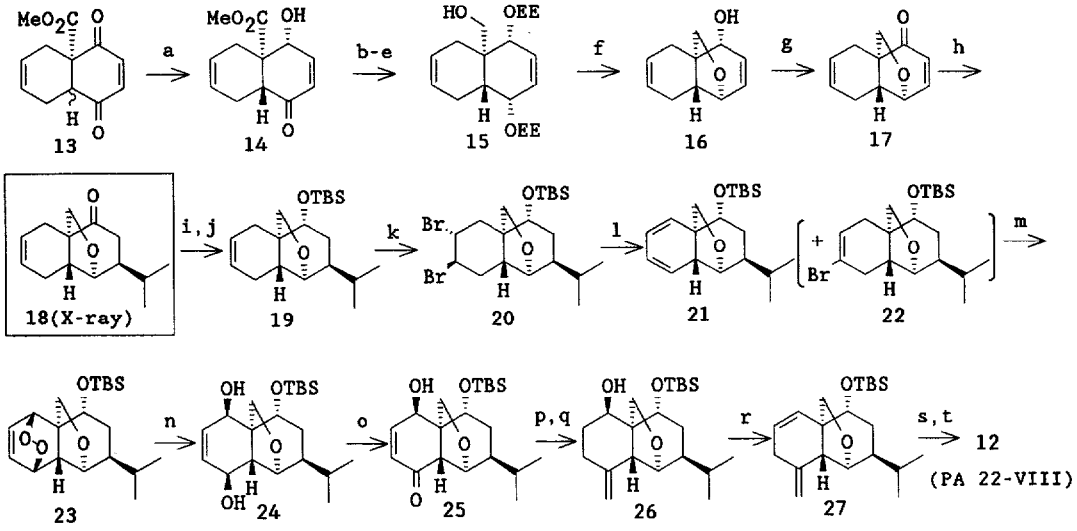

12
Rearrangement product(PA 22-VIII)

Macdonald *et al.* proposed **5** to be periplanone-A, basing on their synthesis of (±)-**5** which was thought to be bioactive.[9] The structure of the pheromone isolated by Persoons was postulated by them as **6**, the possible transannular cyclization product of **5**.[9] Syntheses of pure (±)-**5** later proved it to be only

weakly bioactive or inactive, and therefore 5 cannot be periplanone-A.[10,11] Meanwhile, Hauptmann *et al.* isolated 7 from the American cockroach, named it periplanone-A, synthesized (±)-7, and found it to be bioactive.[12] Subsequently the same compound 7 was also isolated by Nishino *et al.* together with periplanone-B(1), and 7 was again called periplanone-A.[13] Although synthetic (±)-7 was highly bioactive,[10,11] the spectral data of 7 were quite different from those reported for periplanone-A by Persoons.[6] Hauptmann's periplanone-A is therefore not identical with Persoons's periplanone-A. To account for the ^{1}H NMR spectral data of Persoons's periplanone-A and also on the basis of molecular mechanics calculations, Shizuri *et al.* proposed 8 as the plausible structure of Persoons's periplanone-A.[14] In short, there is no conclusive work to clarify the real structure of Persoons's periplanone-A.

We became interested in this problem from a differnt viewpoint. Persoons *et al.* noticed the labile nature of their periplanone-A to give a stable and biologically inactive rearrangement product with code name PA 22-VIII.[5,6] Indeed about 50% conversion was observed at 0°C in two weeks,[5] and even at -20°C the rearrangement took place.[6] The rearrangement product was thought to be 9,[5] to which the stereostructure was later assigned as depicted in 10.[6] Macdonald's synthesis of (±)-11 was followed by comparison of its ^{1}H NMR spectrum with those reported for the rearrangement product.[9] This enabled them to propose 12 as the structure of the rearrangement product.[9] The same conclusion was also announced by Shizuri *et al.*[14] Herein we report the first unambiguous synthesis of (±)-12, which shows spectral data identical with those reported by Persoons for the rearrangement product(PA 22-VIII).[5,6] This fact implies that Persoons's periplanone-A must be an unstable compound which readily furnishes 12.

Our synthesis started from the known Diels-Alder adduct (±)-13 (*cis*:*trans*=1:1.2).[15] Reduction of 13 with $LiAl(O^tBu)_3H$ yielded crystalline (±)-14, which was converted into (±)-15 as shown in the Scheme. Mesylation of 15 was followed by deprotection and base treatment to give (±)-16. The corresponding unsaturated ketone (±)-17 was submitted to the conjugate addition to furnish (±)-18, the structure of which was confirmed by an X-ray crystallographic analysis.[16] Reduction of 18 with Li/NH_3 was followed by silylation to give (±)-19, which was converted to the diene (±)-21(contaminated with (±)-22) via dibromide (±)-20. Photosensitized oxygenation of 21 gave (±)-23. LAH reduction of 23 yielded (±)-24, selective oxidation(MnO_2) of which afforded (±)-25. Hydrogenation of 25 was followed by its olefination to give (±)-26. Dehydration of 26 with Burgess reagent gave (±)-27. After its deprotection, the resulting alcohol was oxidized to give (±)-12 as needles, m.p. 115.5-117.0°C, whose spectral data[17] were identical with those reported for Persoons's rearrangement product. 300 MHz ^{1}H NMR spectrum of our (±)-12 is shown in Figure 1.



a)i)$LiAl(O^tBu)_3H$, THF, 0-5°C, ii)Chromatog. 39%. b)Ethyl vinyl ether, PPTS, CH_2Cl_2, r.t. quant. c)$NaBH_4$, $CeCl_3$, THF, 0-5°C, 71%. d)Ethyl vinyl ether, PPTS, CH_2Cl_2, r.t. 77%. e)$LiAlH_4$, Et_2O, 0°C-r.t. 87%. f)i)MsCl, Py, CH_2Cl_2, DMAP, 0-5°C, ii)MeOH, PPTS, r.t. iii)2.5% NaOMe in MeOH, r.t. 81% in 3 steps. g)$(COCl)_2$, DMSO, CH_2Cl_2, -78°C then Et_3N, -20°C, 92%. h)*i*-PrMgI, CuCN, Et_2O, -78-0°C, 75%. i)Li, NH_3, THF, *t*-BuOH, -78-0°C, 91%. j)TBSOTf, 2,6-Lutidine, CH_2Cl_2, 0-5°C, quant. k)$C_5H_5N{\cdot}HBr{\cdot}Br_2$, THF, r.t. quant. l)DBU, An, reflux. m)O_2, *hν*, Methylene Blue, MeOH, 5-10°C. n)$LiAlH_4$, THF, 0-5°C, 15% in 3 steps. o)MnO_2, $CHCl_3$, r.t. 72%. p)H_2, 10% Pd/C, EtOH, r.t. 92%. q)Ph_3PMeBr, *n*-BuLi, THF, r.t. 30%. r)$MeOCON^-SO_2N^+Et_3$, PhH, 75-80°C, 79%. s)TBAF, THF, r.t. t)PDC, CH_2Cl_2, MS 3A, r.t. 60% in 2 steps.

As we now possess a considerable amount of optically active Hauptmann's periplanone-A,[18] we shall hopefully obtain additional data to clarify the structure of Persoons's periplanone-A.[19]

REFERENCES AND NOTES

1. C. J. Persoons, F. J. Ritter, and W. J. Lichtendonk, *Proc. Kon. Ned. Akad. Wetensch.*, **C77**, 201 (1974).
2. C. J. Persoons, P. E. J. Verwiel, F. J. Ritter, E. Talman, P. J. F. Nooijen, and W. J. Nooijen, *Tetrahedron Lett.*, 2055 (1976).
3. C. J. Persoons, P. E. J. Verwiel, E. Talman, and F. J. Ritter, *J. Chem. Ecol.*, **5**, 221 (1979).
4. S. Kuwahara and K. Mori, *Heterocycles*, **28**, 167 (1989) and refs. therein.
5. E. Talman, P. E. J. Verwiel, F. J. Ritter, and C. J. Persoons, *Isr. J. Chem.*, **17**, 227 (1978).
6. C. J. Persoons, P. E. J. Verwiel, F. J. Ritter, and W. J. Nooyen, *J. Chem. Ecol.*, **8**, 439 (1982).
7. Y. Shizuri, S. Yamaguchi, Y. Terada, and S. Yamamura, *Tetrahedron Lett.*, **28**, 1791 (1987). The synthetic (±)-3 was biologically inactive.
8. Y. Shizuri, S. Yamaguchi, S. Yamamura, M. Ishihara, S. Ohba, Y. Saito, M. Niwa, Y. Terada, and M. Miyazaki, *Tetrahedron Lett.*, **28**, 3831 (1987). No description is available concerning the biological activity of (±)-**4**.
9. T. L. Macdonald, C. M. Delahunty, and J. S. Sawyer, *Heterocycles*, **25**, 305 (1987).

10. S. Takahashi, H. Takegawa, T. Takahashi, and T. Doi, *J. Pesticide Sci.*, 13, 501 (1988).
11. Y. Shizuri, K. Matsunaga, K. Tamaki, S. Yamaguchi, and S. Yamamura, *Tetrahedron Lett.*, **29**, 1971 (1988).
12. H. Hauptmann, G. Mühlbauer, and H. Sass, *Tetrahedron Lett.*, **27**, 6189 (1986).
13. C. Nishino, K. Kobayashi, M. Fukushima, M. Imanari, K. Nojima, and S. Kohno, *Chem. Lett.*, 517 (1988)
14. Y. Shizuri, S. Yamaguchi, Y. Terada, and S. Yamamura, *Tetrahedron Lett.*, **28**, 1795 (1987).
15. Y. Kojima and N. Kato, *Tetrahedron*, **37**, 2527 (1981). Attempts to increase the amount of the *trans*-13 by base-catalyzed equilibration were unsuccesful. Under a high-pressure condition, this Diels-Alder reaction gave an anomalous result. Our thanks are due to Prof. C. Kaneko and Dr. N. Katagiri, Tohoku University, for this experiment.
16. We thank Mr. H. Miura, Sumitomo Chemical Co., for this analysis.
17. ^{1}H NMR(300 MHz, CS_2) δ 0.94(3H, d, *J*=6.5 Hz), 0.96(3H, d, *J*=6.5 Hz), 1.40(1H, m), 1.82(1H, m), 2.15(1H, dd, *J*=3.5 and 16.5 Hz), 2.49(1H, dd, *J*=8.5 and 16.5 Hz), 2.63(1H, s), 2.73(1H, dd, *J*=5.0 and 18.5 Hz), 2.89(1H, d, *J*=18.5 Hz), 3.44(1H, d, *J*=8.0 Hz), 3.70(1H, d, *J*=8.0 Hz), 4.61(1H, d, *J*=3.0 Hz), 4.99 and 5.01(2H, each s), 5.70(1H, d, *J*=9.0 Hz), 5.82(1H, d, *J*=9.0 Hz); IR(KBr) ν_{max} 3060(m), 2990(s), 2940(s), 2910(s), 2890(m), 1710(s), 1655(m), 1470(w), 1420(w), 1390(w), 1370(w), 1270(w), 1260(m), 1240(w), 1185(m), 1160(m), 1080(w), 995(w), 930(m), 910(m), 895(m), 875(m), 805(w), 750(w), 720(m), 665(w); MS(70 eV) *m/z*(%) 232(M^+,6), 202(9), 189(11), 172(25), 159(74), 145(17), 141(18), 133(50), 127(100), 105(85), 104(75), 97(64), 91(80), 81(58), 79(43), 77(64), 69(48), 55(46), 43(74), 41(74).
18. S. Kuwahara and K. Mori, to be submitted.
19. The synthetic (±)-12 was confirmed to be biologically inactive.

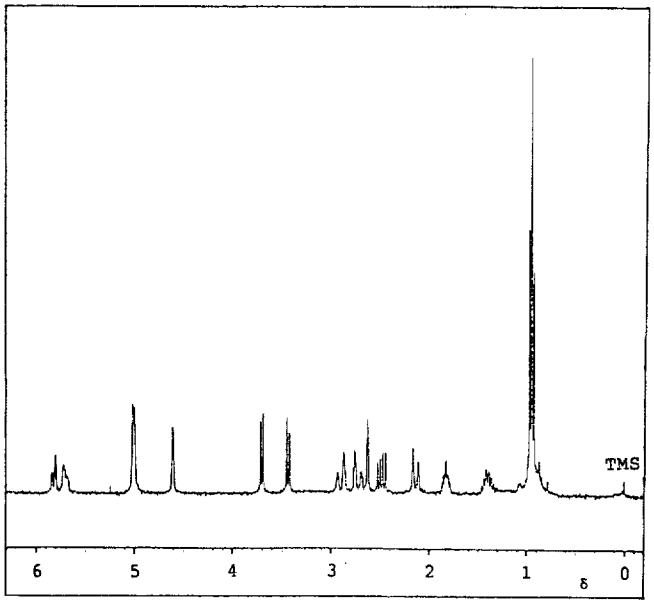


Figure 1. 300 MHz ^{1}H NMR Spectrum of (±)-12 in CS_2

(Received in Japan 13 June 1989)