Tetrahedron Letters No. 19, pp 1687 - 1690, 1973. Pergamon Press. Printed in Great Britain.

BIOGENETIC-TYPE CYCLIZATION REACTIONS OF GERMACRONES IN THIOPHENOL

Masanobu Iguchi, Masatake Niwa and Shosuke Yamamura*

(Faculty of Pharmacy, Meijo University, Showa-ku, Nagoya, Japan)

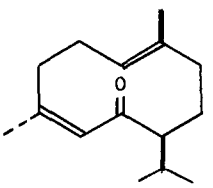
(Received in Japan 23 February 1973; received in UK for publication 29 March 1973)

Previously, we reported the biogenetic-type reactions of the germacrones.[1] We further examined the acid-catalysed cyclizations of the germacrones (I and II) in order to control the direction of the intramolecular cyclization reactions depending on conformations of the reactive intermediates of the germacrones. In fact, cyclization products varied with different kinds of acid (HCOOH, AcOH and H_2SO_4). Particularly, the formation of a guaiane-type compound (III) from I should be noted, as mentioned below.

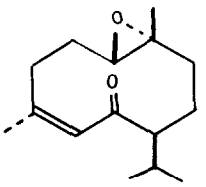
The acid-catalysed cyclization of the germacrone (I) with 80% aq.AcOH has been known to afford the cadinane-type compound.[1] On the other hand, when treated with AcOH in PhSH (room temp., 24hr) instead of 80% aq.AcOH, I was converted into a guaiane-type compound (III) in 50% yield, the structure of which was confirmed by its spectral data coupled with the following chemical evidences [m.p. 90-91°; $C_{21}H_{30}OS$; m/e 330(M^+) and 221; ν_{max}(KBr) 1700cm^{-1}; $\delta(C_6D_6)$ 0.87(6H, d, J= 6.7Hz), 1.06(3H, d, J= 6.3Hz), 1.21(3H, s), 2.75(1H, d, J= 8.5Hz) and 7.00-7.28ppm(5H, m)]. Its NMR spectrum indicates the presence of a secondary methyl group in addition to the isopropyl group. Furthermore, the doublet at δ2.75ppm can be assigned to a methine proton at C_5-position, which is coupled to an adjacent methine proton at C_1-position (J= 8.5Hz). Further treatment of III with Raney Ni in abs.EtOH under N_2 (under reflux, 6hr) gave a desulphurization product (IV) in 86% yield; m.p. 55-57°; $C_{15}H_{26}O$; m/e 222(M^+); ν_{max}(KBr) 1700cm^{-1}; $\delta(CDCl_3)$ 0.83(3H, d, J= 6.7Hz), 0.87(3H, d, J= 6.5Hz), 0.92(3H, d, J= 6.5Hz), 1.13(3H, d, J= 6.3Hz) and 2.86ppm(1H, q, J= 7.8 and 4.8Hz); ORD curve ($[\phi]^P_{321}$ +14° x 10^2; $[\phi]^T_{276}$ -39° x 10^2; A= +53). In particular, the appearance of a methine quartet at δ2.86ppm indicates that the PhS group

*To whom inquires should be addressed.

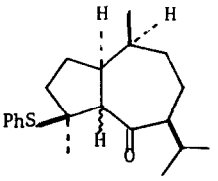
in III must be located at C_4-position. This was further confirmed by action of MeI in acetone (under reflux, 8hr) on III, leading to the formation of a fully substituted α,β-unsaturated ketone (V) in 66% yield: $C_{15}H_{24}O$; m/e 220(M^+); ν_{max}(film) 1670 and 1610cm^{-1}; λ_{max}(MeOH) 256nm (ε, 8270). From the above facts, the structure of the cyclization product should be represented by III except for its stereostructure. The relative configurations at the newly formed asymmetric carbon atoms in III remain unsettled. However, thiophenol



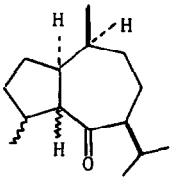
(I)



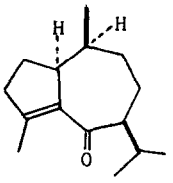
(II)



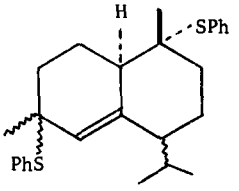
(III)



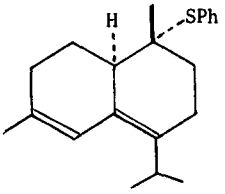
(IV)



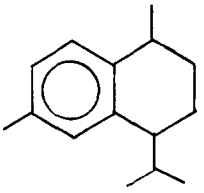
(V)



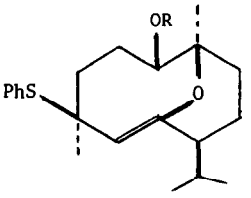
(VI and VI')



(VII)



(VIII)

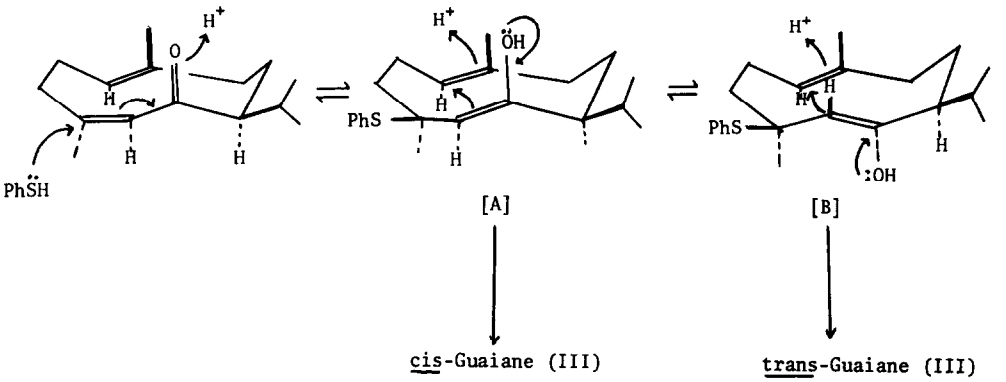


(IX) R = H

(X) R = Ac

attacks the conjugated double bond from a β-side in the known conformation of I,[1] and then the cyclization reaction must take place in a concerted manner leading to the formation of III, as described below. In this case, the cis-guaiane (III) may be formed from a possible intermediate [A]. On the other hand, if conformational change of [A] to

another intermediate [B] takes place, the trans-guaiane (III) must be formed.[2] Unfortunately, any complete evidences on the configuration at C_5-position have not yet been obtained.[3]



In the case of 100% HCOOH in PhSH-benzene (1 : 1) (room temp., 15hr) instead of AcOH, a mixture of four cyclization products (III, VI and VI', and VII) were obtained in 15, 12 and 5% yields, respectively. The inseparable mixture (VI and VI') can be easily converted into the conjugated diene (VII) as follows. When treated with MeI in acetone under N_2 (under reflux, 4hr), the mixture afforded the diene (VII) and calamenene (VIII), in 45 and 29% yields, respectively. On the other hand, action of conc.H_2SO_4 (0°, 30min) on VII gave the mixture (VI and VI') in 75% yield. The structure of the diene (VII) was confirmed by its spectral data: $C_{21}H_{28}S$ (m/e 312(M^+)); δ(CCl_4) 0.93(6H, d, J= 7.0Hz), 1.09(3H, s), 1.76(3H, br.s), 2.99(1H, m), 6.13(1H, br.s) and 7.30ppm(5H, m). Finally, the acid-catalysed cyclization reaction of I was effected with conc.H_2SO_4 in PhSH(0°, 30min) leading to the formation of the cadinane-type compounds (VI and VI', and VII) in 67 and 4% yields, respectively. In this case, any guaiane-type compound has not been isolated. Probably, these cadinanes are formed according to the same concerted mechanism as previously reported.[1]

The epoxy-germacrone (II) having the same conformation as that of I[1] was also treated with 100% HCOOH in PhSH (room temp., 40min) to give a hydroxy-olefin (IX) in 66% yield ($C_{21}H_{30}O_2S$; m/e 236(M^+- 110); ν_{max}(film) 3420br., 3050, 1665, 1580, 1040, 745 and 690cm^{-1}; δ ($CDCl_3$) 0.86(3H, d, J= 6.0Hz), 0.88(3H, d, J= 6.0Hz), 1.21(3H, s), 1.35(3H, s), 1.49 (1H, s; OH), 4.25(1H, t, J= 6.0Hz), 4.75(1H, s) and 7.30ppm(5H, complex)), which was converted into the corresponding acetate (X), in 86% yield, on acetylation with Ac_2O -

pyridine (0°, overnight). In the NMR spectrum of X, the triplet at δ4.25ppm in IX was observed at δ5.57ppm(1H, br.t, J=~6.8Hz). In the above reaction, any selinane-type compound has not been obtained.[1]

All compounds gave satisfactory physical data, and their structures were confirmed by IR, UV, NMR and mass spectrometric data.

The authors wish to thank Professor Yoshimasa Hirata (Nagoya University) for his invaluable suggestions.

REFERENCES

1. M. Iguchi, M. Niwa and S. Yamamura, Chem. Commun., 974 (1971); ibid., 689 (1972).

2. J. A. Marshall, W. F. Huffman and J. A. Ruth, J. Amer. Chem. Soc., 94, 4691 (1972).

3. Although the base-catalysed equilibrium experiment on IV has revealed that this compound was less stable than the newly formed isomer [$C_{15}H_{26}O$; m/e 222(M^+); ν_{max}(film) 1695cm^{-1}; δ($CDCl_3$) 0.84-1.06ppm(12H, complex); ORD curve ($[\phi]^T_{314}$ -46° x 10^2; $[\phi]^P_{272}$ +57° x 10^2; A= -103], further studies on this point have been required.