

SYNTHESIS OF RACEMIC SESQUICARENE

Kenji Mori and Masanao Matsui

Department of Agricultural Chemistry, University of Tokyo

Bunkyo-ku, Tokyo 113, Japan

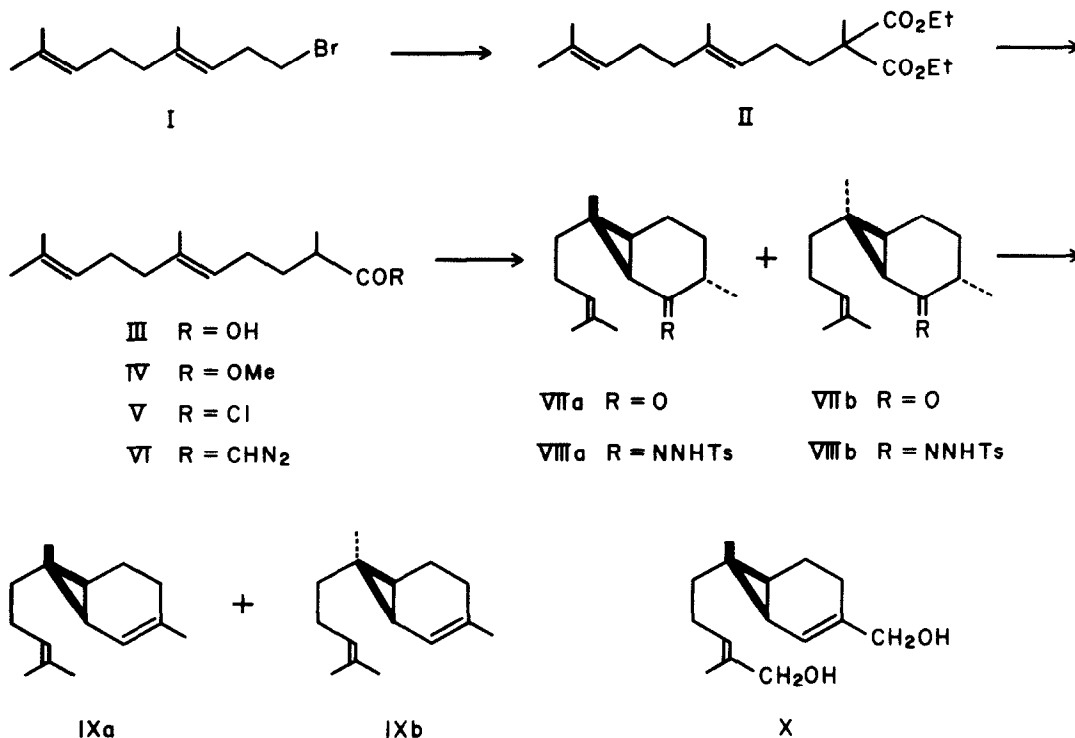
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SESQUICARENE (IXa) is a hydrocarbon isolated from the essential oil of fruits of Schisandra chinensis Baill. by Ohta and Hirose (1). In view of its structural similarity to sirenin (X), a plant sex hormone (2,3), we initiated our synthetic study on that novel sesquiterpene which has now been completed as described below.

4,8-Dimethylnona-3,7-dienyl bromide (I) (4) was condensed with diethyl methylmalonate to give a disubstituted malonic ester (II), b.p. 161-162°/4 mm,  $n_D^{18}$  1.4612 (5). This was hydrolyzed and decarboxylated to give an acid (III), b.p. 131-132°/0.15 mm,  $n_D^{17}$  1.4714, which consisted of  $\Delta^5$ -trans and cis isomers (3.5 : 1) judging from the g.l.c. analysis (6) of the corresponding methyl ester (IV)(15).

The sodium salt of the acid (III) was treated with oxalyl chloride to give an acyl chloride (V) which was converted into a diazoketone (VI) by treatment with ethereal diazomethane.

The desired bicyclo [4.1.0] heptane ring system was successfully constructed by the intramolecular  $\alpha$ -ketocarbene-olefin addition (7-10). Thus the diazoketone in cyclohexane was heated under reflux in the presence of powdered copper and cupric sulfate to give a crude product (VIIa + VIIb) in 59 % yield from the acid (III). This was chromatographed on silicic acid impregnated with silver nitrate (11) to give an analytically pure product (VIIa + VIIb), b.p. 130-131°/5 mm,  $n_D^{20}$  1.4898;  $\nu_{max}$  (film) 2950, 1676, 1450, 1380, 1350, 1330, 1240, 1220, 1185, 1110, 1050, 1030, 886  $cm^{-1}$ ;  $\delta$  0.98 (3H, d, J = 6Hz), 1.16 (3H, s), 1.58 (3H, s), 1.65 (3H, s), 5.03 (1H, broad t) ppm; (F<sub>und</sub> : C, 81.50; H, 10.92 %). This



was revealed to be a mixture of racemic sesquicaran-2-one (VIIa) and its C-7 epimer (VIIb) in the ratio of 2.4 : 1 by the g.l.c. analysis (6,12).

The introduction of the C-2,3 double bond was accomplished by the treatment of the corresponding oily tosylhydrazone (VIIIa + VIIIb) with n-butyllithium (13,14) to give a crude mixture of hydrocarbons (mainly IXa + IXb) in 22 % yield, b.p. 95-105°/ 6 mm. This was purified by preparative g.l.c. to give pure racemic sesquicarene (IXa), b.p. 102-103°/ 6 mm;  $n_D^{17}$  1.4920;  $\nu_{\max}$  (film) 2960, 2920, 2850, 2730, 1660, 1640, 1442, 1430, 1375, 1290, 1200, 1115, 1090, 1065, 990-945, 880, 850, 820  $\text{cm}^{-1}$ ;  $\delta$  0.83 (3H, s), 1.58 (3H, s), 1.64 (6H, s), 5.02 (1H, broad t), 5.45 (1H, broad s) ppm;  $M^+$  204; (Found: C, 88.24; H, 11.91 %). The above described spectral data are identical with those of the natural product. The identity was also proved by g.l.c (6).

The synthesis of racemic sirenin (X) is now actively pursued in this laboratory.

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#### REFERENCES AND FOOTNOTES

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Although the formulae depicted represent only one enantiomer, they are taken to mean a racemate in the case of synthetic products.
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5. The structures assigned to the intermediates were supported by satisfactory spectral and analytical data.
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12. The 7 $\beta$ -methyl isomer (VIIa) was assumed to exhibit a longer retention time because of its extending C<sub>6</sub> side chain. The assignment of the  $\alpha$ -configuration to the C-3

methyl group is based on our unpublished observation that 1-diazo-3,7-dimethyloct-6-en-2-one yields ( $\pm$ )-trans-caran-2-one upon cyclization.

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15. Since there is no synthetic operation in the sequence I to VI which may cause the cis-trans isomerization of the central double bond ( $\Delta^5$  in IV), each of the intermediates (I, II, III, V and VI) is probably a mixture of cis and trans isomers in the same ratio as IV (1 : 3.5). The discrepancy between this ratio (1 : 3.5) and the ratio of VIIb to VIIa (1 : 2.4) awaits further clarification. The preparation of pure  $\Delta^6$ -trans VI and its cyclization will remain to be an interesting problem.