Synthesis of (±)-α-Chamigrene

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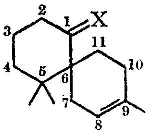
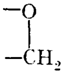
IN a previous Communication,[1] we reported the synthesis of 5,5,9-trimethylspiro[5,5]undec-8-en-1-one (I) and its transformation to (±)-chamigrene (II)[2] [now named (±)-β-chamigrene]. This communication deals with the synthesis, from (I), of the double bond isomer of (II), (—)-α-chamigrene (III), which has been very recently isolated from the seed oil of *Schizandra chinesis* Baillon.[3]

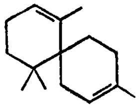
The spiro-ketone (I) was treated with an excess of dimethylsulphonium methylide under the standard conditions;[4] the product isolated was subjected to the same reaction four times, because a considerable amount of the starting ketone (I) remained unchanged after one operation. Thus, a single oxirane derivative (IV),† b.p. 90—93°% 0·2 mm, i.r. (CCl_4) 3030, 909, and 837 cm.$^{-1}$, n.m.r. (CCl_4, 60 Mc./sec., δ from internal Me_4Si) 0·90 (*gem*-Me_2), 1·58 (=C–Me), 2·10 (d, 1H, J = 5 c./sec.) and 2·63 (q, 1H, J = 5 and 1 c./sec.) (epoxymethylene), and 5·14 (m, =CH–), was obtained in 94% yield. Reduction of (IV) with lithium aluminum hydride gave quantitatively the tertiary alcohol (V), m.p. 25·5—27·0°, i.r. (CCl_4) 3630 cm.$^{-1}$, n.m.r. (CCl_4) 0·79, 1·15, 1·16 (*gem*-Me_2, $\text{HO–}\overset{|}{\underset{|}{\text{C}}}\text{–Me}$), 0·90 (OH), 1·62 (=C–Me), and 5·31 (=CH–).†‡ Treatment (generation of carbonium ion centre at C-1) of (V) with boron trifluoride etherate in ether at room temperature for 4·5 hr. afforded a hydrocarbon mixture; three major components [X, 42%; Y, 23%; (±)-β-chamigrene (II), 35%] of this mixture were separated by column chromatography on



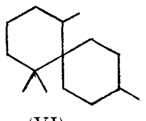
(I) X=O
(II) $X=CH_2$ (β-Chamigrene)

(IV) X=

$$X=\begin{array}{l}-O\\ \;|\\ -CH_2\end{array}$$

(V) X=OH,Me



(III) (α-Chamigrene)



(VI)

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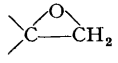
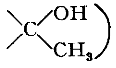
† The methylene group would presumably add to the ketone function in (I) from the less hindered side (C-7,8 side), however the configuration of  $\rangle\overset{O}{C{-}CH_2}$ (and  $\rangle C\begin{smallmatrix}OH\\ CH_3\end{smallmatrix}$) has not yet been established.

‡ The direct conversion of (I) into (V) by reaction with methyl-lithium or methylmagnesium iodide was unsuccessful, because of the unreactivity of (I) to these reagents even under drastic conditions.

silica gel–silver nitrate.[5] § The hydrocarbon X was identified to be (±)-α-chamigrene (III) from physical and chemical evidence: n.m.r. (CCl_4) 0·83, 0·88 (*gem*-Me_2), 1·63 (2 =C–Me) and 5·35 (2 =CH–) and the formation of chamigrane (VI), a mixture of epimers, also obtained from (II), by catalytic hydrogenation. The spectral data (i.r., n.m.r., mass) of both the synthetic and natural α-chamigrene are completely identical.¶[6] The tertiary alcohol (V) was also dehydrated by treatment with 80% aqueous phosphoric acid–acetic acid (r.t., 24 hr.) or iodine–benzene (boiling point, 30 min.), to give a mixture of the same three products, but in this case there was a small change in the relative ratio of (II), (III), and Y.

The spectral properties of hydrocarbon Y indicate that it was formed through skeletal rearrangement, and the elucidation of its structure is now in progress. The authors acknowledge support from the Ministry of Education of Japan and the Matsunaga Foundation.

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§ β-Chamigrene (II) was recovered unchanged by heating with boron trifluoride etherate–ether under reflux.

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[1] A. Tanaka, H. Uda, and A. Yoshikoshi, *Chem. Comm.*, 1967, 188.

[2] S. Itô, K. Endo, Y. Yoshida, M. Yatagai, and M. Kodama, *Chem. Comm.*, 1967, 186.

[3] Y. Ohta and Y. Hirose, Abstracts, 11th Symposium of Perfume, Terpenoid, and Essential Oil of the Chemical Society of Japan, Matsuyama, 1967, 157.

[4] E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 1965, **87**, 1353.

[5] N. P. Damodaran and Sukh Dev, *Tetrahedron Letters*, 1963, 1941.

[6] An alternative synthesis of (±)-α-chamigrene (III) has been recently reported, S. Kanno, T. Kato, and Y. Kitahara, *Chem. Comm.*, 1967, 1257.