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SYNTHESIS OF GEIJERENE, AN ELEMENE-TYPE SESQUITERPENE

Kuniki Kato and Yoshimasa Hirata
(Chemical Institute, Nagoya University, Chikusa, Nagoya, Japan)
Shosuke Yamamura
(Faculty of Pharmacy, Meijo University, Showa-ku, Nagoya, Japan)

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Geijerene has been isolated from Geijera parviflora leaves and its structure been elucidated by two groups.[1] Finally, the stereo-structure of geijerene was established as I by X-ray analysis of racemic geijerene-silver nitrate adduct.[2] Recently, furthermore, dihydro-geijerene has been synthesized from germacrone.[3] Racemic geijerene (I),[1,4] which is regarded as an elemene-type sesquiterpene losing an isopropyl or isopropenyl group, is pretty interesting not only for its biosynthesis, but also for the thermal isomerization studies.[5] We describe here the synthesis of geijerene (I) from (-)-santonin.

Removal of an iodo-isopropyl group in II has been carried out as follows. Dehydrohalogenation of II with AgF - pyridine (room temp., 3 days) afforded in 72% yield an olefin (III), 132 - 133°, ν_{max} (Nujol) 3080, 1725, 1645 and 1250 cm^{-1}. Furthermore, ozonization of III in MeOH - $CHCl_3$ (2 : 1) at -78° followed by haloform reaction with NaOBr in dioxane (room temp., 4 hr.) gave a mixture of two acids, which were then heated in aq. AcOH (80°, 2 hr.) to afford in 43% yield a keto-acid (IV), m.p. 218 - 221° (in a sealed tube). IV was refluxed with Br_2- HgO in dichloro-ethane for 1 hr., and then treated with zinc powder in AcOH (under reflux, 1 hr.) to give in 40% yield a desired keto-olefin (V), m.p. 48 - 50°, ν_{max} (Nujol) 1710 and 1640 cm^{-1}.

A degradation of the cyclohexanone-ring of V and its conversion into geijerene (I) were carried out in high yields except for the final step.

When treated with HCOOEt - NaH in benzene under nitrogen (room temp., overnight), V afforded a condensation product (VI), m.p. 90 - 92°, which was oxidized with 30% H_2O_2 - aq. KOH (room temp., 4 hr.), and then esterified with diazomethane to give an oily diester (VII), m/e 254 (M^+), ν_{max} (film) 1735 and 1645 cm^{-1}. VII was further converted in three steps into a di-iodo-compound (IX): reduction of VII with $LiAlH_4$ in ether (room temp., 5 hr.) afforded the corresponding diol (VIII) which was treated with mesyl chloride - pyridine (0°, 1 hr. and then room temp., 30 min.), and then heated with a large excess of sodium iodide in acetone (under reflux, overnight) to afford an oily di-iodo-compound (IX), m/e 418 (M^+), δ0.92 (3H, s), 1.10 (3H, d, J= 7.5Hz), 3.0 - 3.5 (4H, m) and 5.2 - 6.0 (2H, m)(in $CDCl_3$). Finally, dehydrohalogenation of IX was effected with 1,5-diazobicyclo[5,4,0]undec-5-ene (80°, 6.5 hr.) to give a mixture of three compounds, which were carefully separated by preparative g.l.c.[SE-30 (20% on Chromosorb w); Injection temp. 140°, Column temp. 110°; He, 100 ml/min.] to afford in *ca.* 20% yield the desired hydrocarbon which was completely identical with an authentic sample of geijerene (I) (g.l.c. and IR spectrum). All compounds gave satisfactory physical data.

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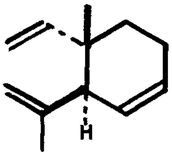
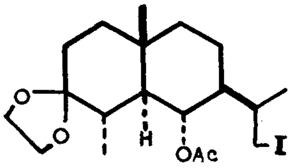


(I)



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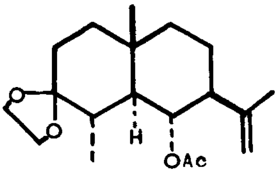

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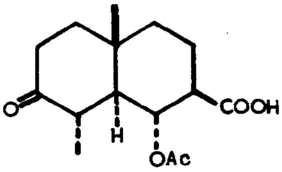

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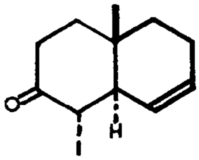

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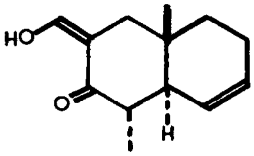

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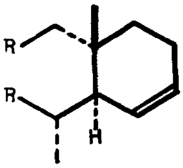

(VII) R = COOMe

(VIII) R = CH_2OH

(IX) R = CH_2I