The Synthesis and Acid-catalysed Rearrangement of a Spiro[4,5]dec-6-en-2-one

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Summary The spiro[4,5]dec-6-en-2-one (**3**) has been synthesized and found to undergo rearrangement into the octalone (**4**) upon acid treatment.

IN an approach to the synthesis of sesquiterpenes such as hinesol (**1**)[1] and β-vetivone (**2**)[2] having a spiro[4,5]decane skeleton, we have prepared the spiro[4,5]dec-6-en-2-one (**3**). While exploring methods to introduce the three-carbon side-chain at C-2 of (**3**), we have found that this ketone readily undergoes acid-catalysed rearrangement into the dimethyloctalone (**4**).[3] Recently, Lawton and his co-workers[4] have reported that spiro[4,5]decenes such as (**5**) are converted into 6/6-fused products (**6**) on treatment with acidic reagents; we now report our observations on the behaviour of (**3**).

The product of rearrangement of (**3**), *i.e.* (**4**), was starting material for its synthesis. Treatment of (**4**) with $Pb(OAc)_4$ in HOAc–Ac_2O[5] gave the 2α-acetoxy-derivative, which on hydrolysis, air oxidation, and base-catalysed methylation according to the procedure of Rao and Axelrod[6] gave the 2-methoxydienone (**7**);† u.v. λ_{max} (EtOH) 251 nm (ε 11,300); i.r. ν_{max} ($CHCl_3$) 1655 (conjugated ketone), 1635 and 1610 cm^{-1} (conjugated double bonds); n.m.r. δ (CCl_4, Me_4Si as internal reference) 1·10 (d, *J* 6Hz, 3H, 5-Me), 1·25 (s, 3H, 9-Me), 3·57 (s, 3H, OCH_3), 5·74 (s, 1H, 1-H), and 5·90 p.p.m. (d, *J* 1 Hz, 1H, 4-H).

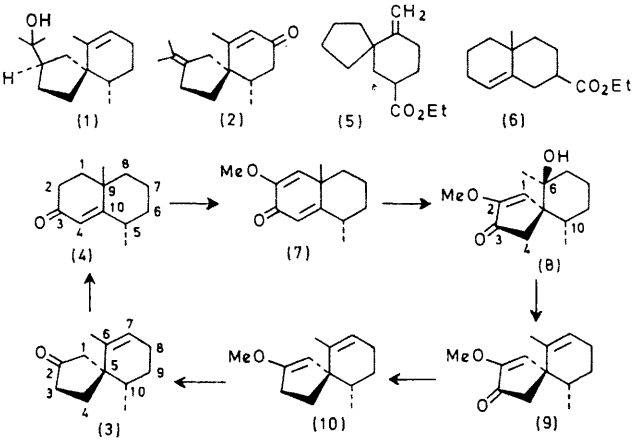
Irradiation of a *ca.* 1% solution of (**7**) in 45% aqueous HOAc at room temp. for 5 h using a 450 W high-pressure Hanovia lamp (quartz immersion well) gave the spiro-hydroxyketone (**8**) as the major photoproduct in *ca.* 30% yield. Compound (**8**) showed: u.v. λ_{max} (EtOH) 258 nm (ε 8300); i.r. ν_{max} ($CHCl_3$) 1711 (αβ-unsaturated cyclopentenone) and 1626 cm^{-1} (conjugated double bond); n.m.r. δ ($CDCl_3$, Me_4Si as internal reference) 0·72 (d, *J* 6 Hz, 3H, 10-Me), 1·05 (s, 3H, 6-Me), 2·16 and 2·72 (AB q, J_{AB} 19·5 Hz, 2H, 4-CH_2), 3·75 (s, 3H, OCH_3), and 6·33 p.p.m. (s, 1H, 1-H). The formation of (**8**) from (**7**) indicates that the C-2 methoxy-substituent exerts a similar influence to that of a C-2 methyl group on the course of the cyclohexadienone photochemical rearrangement.[7] In addition to (**8**), small amounts of other photoproducts were obtained from the aqueous HOAc irradiation of (**7**). The structures of these products as well as the results of irradiation of (**7**) in other solvents will be reported later.

Dehydration of (**8**) with thionyl chloride in pyridine gave (**9**) [u.v. λ_{max} (EtOH) 256 nm (ε 7900); i.r. ν_{max} ($CHCl_3$) 1712 (αβ-unsaturated cyclopentenone) and 1623 cm^{-1} (conjugated double bond); n.m.r. δ (CCl_4, Me_4Si as internal

† Correct elemental analyses or exact mass determinations have been obtained for all new compounds reported.

reference) 0·90 (d, J 6 Hz, 3H, 10-Me), 1·52 (m, 3H, 6-Me), 3·65 (s, 3H, OCH_3), 2·20 and 2·32 (AB q, J_{AB} 19 Hz, 2H, 4-CH_2), 5·52 (m, 1H, 7-H), and 6·22 p.p.m. (s, 1H, 1-H)] which was converted into a mixture of enol ethers containing mainly (**10**) (82% overall yield) by reduction of the carbonyl group with $LiAlH_4$ in ether (inverse addition), acetylation of the allylic hydroxy-group with Ac_2O in pyridine, and reductive cleavage of the allylic acetate with lithium in ethylamine,[8] again using the inverse addition technique. The enol ether (**10**) showed: i.r. ν_{max} ($CHCl_3$) 1645 cm^{-1} (enol ether); n.m.r. δ (CCl_4, Me_4Si as internal reference) 0·78 (d, J 6 Hz, 3H, 10-Me), 1·49 (d, J 5 Hz, 3H, 6-Me), 3·45 (s, 3H, OCH_3), 4·13 (t, J 1 Hz, 1H, 1-H), and 5·20 p.p.m. (m, 1H, 7-H). Treatment of (**10**) with oxalic acid in aqueous MeOH led to its quantitative hydrolysis to (**3**). Enone (**3**) showed i.r. absorption at 1740 cm^{-1} (thin film) for a cyclopentanone and lower frequency bands in locations similar to those reported by Marshall and Johnson[2] for the isomer of (**3**) having the C-1 methylene group and the C-10 methyl group *trans*. The n.m.r. spectrum of (**3**) (CCl_4) showed a doublet (J 6 Hz) at 0·93 p.p.m. for the C-10 methyl group, a doublet (J 1·5 Hz) at 1·65 for the C-6 methyl group, and a broad absorption ($W_{\frac{1}{2}}$ *ca.* 8 Hz) for the C-7 olefinic proton. The C-1 methylene protons of (**3**) appear to have almost identical chemical shifts for they give rise to a "singlet" at 2·15 p.p.m. at 60 MHz. This absorption appeared as two closely spaced peaks (*ca.* 1 Hz separation) at 100 MHz and could thus be attributed to peaks 2 and 3 of an AB quartet centred at 2·15 p.p.m. The C-1 methylene protons of the isomer of (**3**) (C-1 and C-10 methyl *trans*) appear as a well separated AB quartet.[2]

On heating of (**3**) with Dowex 50W-12X (H^+) resin in aqueous HOAc, it was converted into a mixture of products from which (**4**) was isolated in over 50% yield by preparative g.l.c. The conversion of (**3**) into (**4**) presumably involves formation of a carbonium ion at C-6, a 1,2-shift of C-4 to C-6, and loss of a proton to give initially the *cis*-isomer of (**4**). This compound would be expected to epimerize to the more stable *trans*-isomer (**4**) under the reaction conditions.



Under identical conditions to those used for the conversion of (**3**) into (**4**), β-vetivone (**2**) did not undergo a skeletal rearrangement, but was converted into a mixture of isomers resulting from isomerization of the isopropylidene double bond into the five-membered ring. Apparently, the allylic carbonium ion formed by protonation of (**2**) on the carbonyl oxygen atom is insufficiently reactive to undergo the ring-expansion reaction.

As has been pointed out by Lawton *et al.*,[4] the acid-catalysed conversions of spiro[4,5]decanes into 6/6-fused systems may be of importance in sesquiterpene biosynthesis as such rearrangements provide possible pathways for various skeletal interconversions, for example, eudesmanes into eremorphilanes.

We thank the National Institutes of Health for support of this work.

(*Received, July 28th*, 1970; *Com.* 1248.)

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