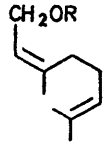
Geraniol and Nerol in Organic Synthesis. Useful Intermediates for the Synthesis of C_{17}-Juvenile Hormone

By PAUL A. GRIECO

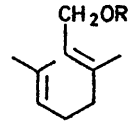
(*Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania* 15213)

Summary Nerol and geraniol have been utilized for the convenient preparation of 3-methyl-*cis*-pent-2-en-1-ol and 8-acetoxy-2,6-dimethyl-*trans,trans*-octa-2,6-dien-1-ol respectively, which represent useful intermediates for the construction of C_{17}-juvenile hormone.

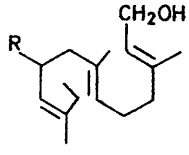
MANY naturally occurring systems have either *cis*- or *trans*-trisubstituted double bonds in which one of the substituents is a methyl group (*cf.* VI). The importance of these systems in the synthesis of polyisoprenoids has led to a number of new methods for the construction of trisubstituted olefins which exhibit very high stereoselectivity.[1]



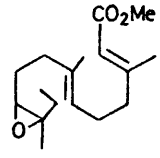
(I) a; R = H
b; R = Ac



(II) a; R = H
b; R = Ac

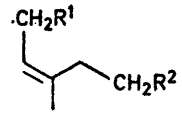


(V) R = H
(XII) R = SPh

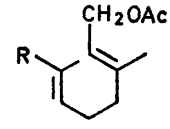


(VI)

Ozonolysis of neryl acetate (Ib) at −78° in CH_2Cl_2 followed by treatment with Me_2S gave (VII)[2] (*ca.* 60%) [b.p. 82° (0·5 mm); ν_{max} CO ($CHCl_3$) 1698 cm^{-1}; δ (CCl_4) 9·58 p.p.m. (t, 1H); R_f = 0·32 (hexane–ether, 2:1)]. When (VII) was treated with an equimolar amount of $(PPh_3)_3RhCl$,[3] in either C_6H_6 or CH_2Cl_2 at room temperature for 24 h, (IIIa) was produced (70%) [ν_{max} CO ($CHCl_3$) 1730 cm^{-1}; δ ($CHCl_3$) 1·00 p.p.m. (t, 3H)]. The acetate (IIIa) was further identified by comparison with an authentic sample prepared by a different route. The decarbonylation takes place under mild conditions in high yield with preservation of configuration about the olefinic bond and stoicheiometric formation of $(PPh_3)_2(CO)RhCl$. A convenient method[4] for the regeneration of $(PPh_3)_3RhCl$ has recently been reported making decarbonylations a more useful and attractive synthetic reaction. That the double bond present in (IIIa) did not undergo isomerization was demonstrated by treating the aldehyde[2] obtained by ozonolysis of geranyl acetate with $(PPh_3)_3RhCl$ and showing that the product obtained has a retention time on g.l.c. which was different than that observed for its geometrical isomer (IIIa). The alcohol (IIIb)



(III) a; R^1 = OAc, R^2 = H
b; R^1 = OH, R^2 = H
(VII) R^1 = OAc, R^2 = CHO
(X) R^1 = SPh, R^2 = H



(IX) R = CHO
(IV) R = CH_2OH
(XI) R = CH_2Br

which was obtained by methanolysis of its acetate in the presence of potassium carbonate, was converted into the thioether (X) (93%) by successive treatment of the alcohol (IIIb) in ether–hexamethylphosphoramide (4:1) with 1·0 equivalent of methyl-lithium, 1·05 equivalents of tosyl chloride,[5] and 1·05 equivalents of lithium thiophenoxide.[6]

Specific functionalisation of the isopropylidene terminus of geranyl acetate (IIb) was achieved by selenium dioxide oxidation[7] to the aldehyde (IX) [ν_{max} ($CHCl_3$) 1727 (OAc), 1681 (CHO), 1645 (C=C) cm^{-1}; δ (CCl_4) 9·28 p.p.m. (s, 1H); R_f = 0·70 (benzene–ether, 2:1)] followed by reduction with sodium borohydride in 95% ethanol at 0° to the desired all *trans* allylic alcohol (IV) [R_f = 0·44 (benzene–ether, 2:1)] in 40% overall yield from (IIb). Conversion of (IV) into the allylic bromide (XI) [δ (CCl_4) 3·90 (s, 2H), 5·30 (t, 1H),

5·52 (t, 1H); $R_f = 0·75$ (benzene–ether, 4:1)] was achieved in 90% yield using PBr_3 in ether at 0°.

The allylic bromide (XI) and the thioether (X) constitute respectively the right- and left-hand portions of the C_{17}-juvenile hormone molecule (VI).[6,8] These two fragments were combined by alkylation[6,9] of the anion of the thioether (X) at −78° in tetrahydrofuran with the bromide (XI), thus avoiding the use of any complex trisubstituted olefin synthesis and featuring positional and stereochemical control. Conversion of alcohol (XII) into C_{17}-juvenile hormone involving reductive cleavage of the thioether[6,9,10] function and oxidation to triene-carboxylic ester[11] followed by selective terminal epoxidation[12] have already been described.†

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† All new compounds had satisfactory analytical and/or spectral data.

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