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REQUIREMENTS FOR THE ARTEMISYL, SANTOLINYL AND LAVANDULYL FISSIONS OF CHRYSANTHEMIC ACID RELATIVES UNDER CARBONIUM ION TYPE INITIATION

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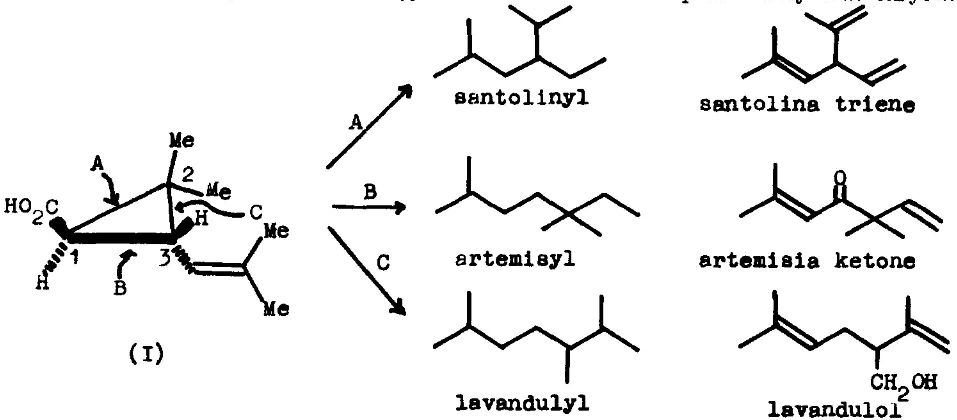
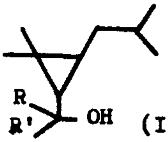
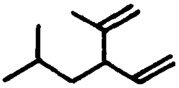
The monoterpenoid cyclopropane 1(*R*), 3(*R*)-(+)-*trans*-chrysanthemic acid (I), possessing a "middle to tail" isoprenoid fusion, occurs in Nature as esters (rethrins) with certain cyclopentenolones.[1] Cleavage of the ring in the three ways possible leads to three different monoterpene skeletal types as shown. The possibility that chrysanthemyl alcohol (V, R = OH) (as pyrophosphate) might give rise to a carbonium ion which could lead to artemisia compounds or santolina triene has recently received speculative attention,[2] and such compounds occur together in *Santolina chamaecyparissus* L.[3,4] In the present communication it is shown that by employing readily effected chemical alterations each of the three ring bonds A - C can be made to rupture by carbonium ion type reactions to give compounds with santolinyl, artemisyl and lavandulyl skeletons. These reactions are also of interest in connection with specific atom isolation for biosynthetic work, and since (±)-*cis*- and (±)-*trans*- chrysanthemic acid are readily available (and have been resolved)[5,6] have some general synthetic possibilities.

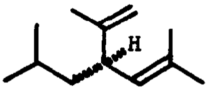


(I)

(±)-*trans*-Dihydrochrysanthemyl alcohol (II, R = R' = H) was resistant to heating with small amounts of toluene-*p*-sulphonic acid (PTSA) but on treating at 0° with thionyl chloride the santolina diene (III) (40%) was isolated (PGLC) from the mixture of five products formed.* In the generalised case (II, R = R' = Me), the tertiary alcohol made by Grignard reaction from (±)-*trans*-dihydrochrysanthemic ester decomposed on distillation giving the diene (±)-(IV) (63%) directly. By using methyl 1(*R*), 3(*R*)-(-)-*trans*-dihydrochrysanthemate the (*R*)-diene (IV)

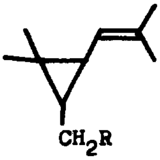

(II)

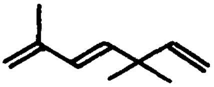

(III)


(IV)

$[\alpha]^{20}_{D}$ -33° (ethanol) was also obtained: this retains the original 3-configuration.

When the unsaturated isobutenyl side-chain of the chrysanthemyl series replaces the saturated side chain of the dihydro-series the relative energies of transition states formerly leading to rupture A (tertiary centre) as opposed to B (secondary) become drastically altered. Whether the matter is considered in terms of classical or non-classical carbonium ions it seems that involvement of the conjugated homoallylic system would be energetically preferred to the homoallylic, both having tertiary termini. Experimentally, it was found that fission at B rather than A now occurred with emergence of compounds of the artemisia series. Both *cis*- and *trans*- chrysanthemyl alcohol (V, R = OH) or the methyl ether (V, R = OMe) gave the *trans*-artemisia triene (VI) (approx. 55%) when heated with a small quantity of PTSA in benzene. The hydrocarbon (VI) was also formed (50%) when (V, R = OH) was treated with toluene-*p*-sulphonyl chloride in pyridine. Thionyl chloride gave a mixture of products, 40% of which was (VI) (PGLC), and phosphorus tribromide and pyridine[7] again gave a mixture from which (VI) was readily isolated.


(V)


(VI)

Functionalised *trans*-products from this type of artemisia cleavage are formed when the aldehyde (VII, R = H)[8] or the ketone (VII, R = Me)[9] are refluxed with PTSA in benzene: the

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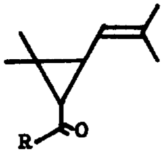
*Mixtures were separated by preparative gas-liquid chromatography (PGLC) or spinning band distillation. Satisfactory analytical data have been obtained for new compounds; structure assignments rest on N.M.R. and other spectroscopic information together with, in some cases, mass spectra and hydrogenation.

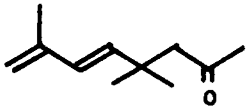
Consideration of compression in the transition states in this and analogous examples shows that the *trans*- olefin is heavily favoured.

products are (VIII) (65%) and (IX) (60%) respectively. The Reformatski product (X) from (VII, R = H) yields, under similar conditions, the triene ester (XI) and the possibilities as a block extension method [using (I) or (VII, R = H or Me etc.)] are shown by Grignard reaction on



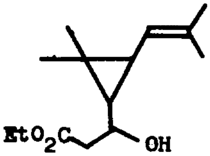
(VII)

(VIII)

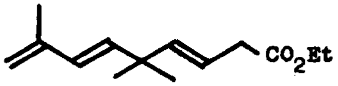


(IX)

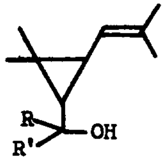
methyl (±)-*trans*-chrysanthemate. The tertiary alcohol formed (XII, R = R' = Me) dehydrates during work-up (ammonium chloride) and distillation to give (XIII, R = R' = Me) (70%). On



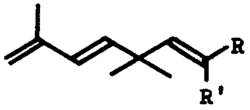
(X)



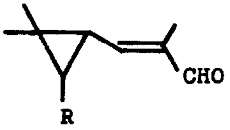
(XI)



(XII)



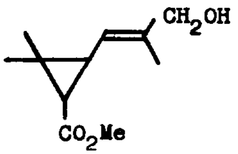
(XIII)



(XIV)

the other hand (XIV, R = CH$_2$OH and CHO) were resistant to ring cleavage with PTSA under conditions which did not cause extensive decomposition. In these cases the conjugated homoallylic carbonium ion system would be destabilised by the electron withdrawal of the aldehyde group.

The type of ring breakage, C, to give monoterpenoid types with a lavandulyl skeleton occurs under carbonium ion conditions when the isobutenyl side-chains of chrysanthemic acid derivatives are suitably functionalised. Thus, the 3'-alcohol (XV), or its *cis*- cyclopropane relative, on heating with PTSA gives the *trans*-triene ester (XVI)[10] (60%) which on standing as a petrol solution over alumina (Woelm basic, Grade 1) partially isomerises to (XVII) and (XVIII, R = Me), (42:27:31 after 30 min., by GLC analysis): base hydrolysis gives (XVIII, R = H).[10] Using the optically active alcohol (+)-(XV) derived from 1(R),3(R)-(+)-*trans*-chrysanthemic acid the ester (XVI), $[\alpha]_D^{20}$ -6.8 (ethanol), retaining the original configuration at C_1, and therefore (*R*) as shown, was isolated. The diol (XIX) similarly gives (XVI).[11] A further example of the lavandulyl type of cleavage occurs when the diol (XX) is heated with a little PTSA in benzene. Here cleavage A, B and C are possible. Five components have been detected in reaction products but under the conditions mentioned the major compound (47% of mixture, isolated by PGLC) is (XXI). A second substantial product (34%) appears to be (XXII) derived by internal trapping of the carbonium ion.



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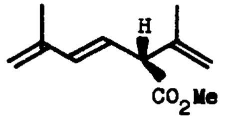
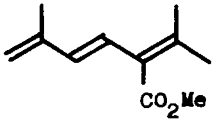
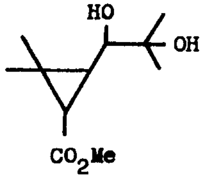


(XVI)



(XVII)



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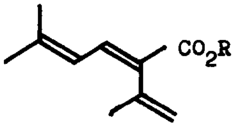

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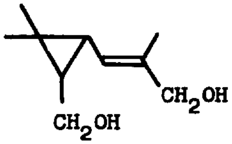

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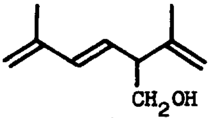
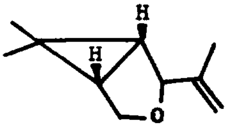


(XXI)



(XXII)

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