

Stereochemistry of C-1 Hydrogen Exchange in the Interconversion of *trans,trans*- and *cis,trans*-Farnesols by Soluble Enzymes from Tissue Cultures of *Andrographis paniculata*

By KARL H. OVERTON* and FRANK M. ROBERTS

(Plant Tissue Culture Unit, Department of Chemistry, The University of Glasgow, Glasgow G12 8QQ)

Summary When a cell-free system from *A. paniculata* tissue cultures isomerises *trans,trans*-farnesol (*tt*-F) to *cis,trans*-farnesol (*ct*-F), the 1-*pro-R* hydrogen of *tt*-F is retained and the 1-*pro-S* hydrogen lost; by contrast, conversion of *ct*-F into *tt*-F proceeds with retention of the 1-*pro-S* and loss of the 1-*pro-R* hydrogen of *ct*-F.

We have previously shown¹ that a cell-free system from *Andrographis paniculata* tissue cultures transforms *tt*-F into *ct*-F with loss of one diastereotopic hydrogen from C-1. We now report on the stereochemistry of this loss in both the *tt*-F to *ct*-F and *ct*-F to *tt*-F conversions.

The farnesols (1*R*)-[1-³H₁]*tt*-F and (1*R*)-[1-³H₁]*ct*-F were obtained from commercial farnesol (*tt*-F : *ct*-F = 2 : 1) by

exchange in T₂O with horse liver ADH-NAD⁺-NADH-diaphorase according to the method of Simon² and separation of the isomers by multiple preparative t.l.c. Compounds (1*S*)-[1-³H₁]*tt*-F and (1*S*)-[1-³H₁]*ct*-F were obtained isotopically pure from [1-³H₂]*ct*-F and [1-³H₂]*tt*-F respectively, by the same method but using H₂O; LADH mediates isomerisation as well as exchange and proceeding from the other geometrical isomer ensures that the product cannot be contaminated with di-tritiated molecules that have failed to undergo exchange. Admixture of each tritiated specimen with the corresponding [4,8,12-¹⁴C₃]farnesol, biosynthesised by the cell-free system from [2-¹⁴C]mevalonate, and incubation with the enzyme system led to the results recorded in the Table.

TABLE

	$^3\text{H}/^{14}\text{C}$	% ^3H retained		$^3\text{H}/^{14}\text{C}$	% ^3H retained
(1R)-[1- ^3H]- + [4,8,12- $^{14}\text{C}_3$]- <i>tt</i> -F ..	11.22 ^b		(1S)-[1- ^3H]- + [4,8,12- $^{14}\text{C}_3$]- <i>tt</i> -F ..	6.92 ^b	
↓			↓		
<i>tt</i> -F-OAc ^a	10.64	95	<i>tt</i> -F-OAc	6.39	92
<i>tt</i> -F-OCH ₂ SiMe ₃ ^a	10.68	95	<i>tt</i> -F-OTCH ₂ SiMe ₃	6.26	90
<i>ct</i> -F-OAc	10.50	94	<i>ct</i> -F-OAc	0.18	3
<i>ct</i> -F-OCH ₂ SiMe ₃	10.74	96	<i>ct</i> -F-OCH ₂ SiMe ₃	0.23	3
(1R)-[1- ^3H]- + [4,8,12- $^{14}\text{C}_3$]- <i>ct</i> -F ..	4.51 ^b		(1S)-[1- ^3H]- + [4,8,12- $^{14}\text{C}_3$]- <i>ct</i> -F ..	6.30 ^b	
↓			↓		
<i>tt</i> -F-OAc	0.15	4	<i>tt</i> -F-OAc	6.55	104
<i>tt</i> -F-OCH ₂ SiMe ₃	0.23	5	<i>tt</i> -F-OCH ₂ SiMe ₃	6.05	96
<i>ct</i> -F-OAc	4.18	92	<i>ct</i> -F-OAc	6.14	97
<i>ct</i> -F-OCH ₂ SiMe ₃	4.22	94	<i>ct</i> -F-OCH ₂ SiMe ₃	6.20	98

^a Alcohols were converted into acetates and trimethylsilyl ethers for determination of radioactivity. ^b Average value for ROH, ROAc, and ROCH₂SiMe₃.

In a complementary experiment, the *ct*-F obtained from (1R)-[1- ^3H]-*tt*-F (tritium label retained), was exposed to LADH-diaphorase-NAD⁺-NADH. It retained its tritium label under these conditions also, as did the derived hexahydro-compound, suggesting that the label was in the non-exchangeable *pro-S* position, in accordance with the results of *ct*-F to *tt*-F exchange shown in the Table. However, the configurations of the monotritiated *cis*-farnesols, and hence

the conclusions based on them, depend on the unproven assumption that LADH exchanges the 1-*pro-R* hydrogen of *cis*-allylic alcohols, as it has been shown³ to exchange the 1-*pro-R* hydrogen of *trans*-allylic alcohols. This critical point is now receiving our attention.

We thank the S.R.C. for financial support.

(Received, 1st April 1974; Com. 361.)

¹ K. H. Overton and F. M. Roberts, *J.C.S. Chem. Comm.*, 1973, 378.

² H. Gunther, M. A. Alizade, M. Kellner, F. Biller, and H. Simon, *Z. Naturforsch.*, 1973, 28C, 241; H. Gunther, F. Biller, M. Kellner, and H. Simon *Angew. Chem. Internat. Edn.*, 1973, 12, 146.

³ D. Arigoni and E. L. Eliel in 'Topics in Stereochemistry,' vol. 4, ed. E. L. Eliel and N. A. Allinger, Wiley-Interscience, 1969, pp. 167, 217.