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SHORT COMMUNICATION

BIOSYNTHESIS OF LINALOOL IN HIGHER PLANTS

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Abstract—The labelling pattern of linalool biosynthesized from [2-^{14}C]mevalonic acid by *Cinnamomum camphora* was consistent with the pathway shown in the scheme. The activities at C-4 and C-8 (and/or C-10) were nearly equal, in opposition to the results[1,2] observed for the bicyclic terpene compounds.

INTRODUCTION

RECENTLY the thujane derivatives and camphor biosynthesized from [2-^{14}C]mevalonic acid (MVA) were shown[1,2] to contain their tracer mainly in one ring position suggesting they were derived from isopentenyl pyrophosphate (I) but not 3,3-dimethylallyl pyrophosphate (II). In order to clarify the generality of this unexpected result we have tested the labelling pattern in linalool (IV) biosynthesized from [2-^{14}C] MVA in *Cinnamomum camphora* Sieb. *var. linalooliferum* Fujita. No investigation has been made on (IV) which is an acyclic monoterpene which can be derived from geranyl pyrophosphate (III) in the early stages of monoterpenoid biosynthesis.

RESULTS AND DISCUSSION

The labelled precursor, [2-^{14}C]MVA, was fed into the cut stems of small twigs for one day. The twigs were then subjected to steam-distillation followed by column chromatography to isolate the pure specimen of linalool (IV). Incorporation of tracer was *ca.* 0·012%, which is comparable to that reported[1-3] for other monoterpenes.

Selective hydrogenation of (IV) over platinum oxide afforded 1,2-dihydrolinalool, which was degraded to acetone and 4-methyl-4-hexanolide (V) by permanganate-periodate oxidation.[4,5] Acetone was further degraded to iodoform and acetic acid, while the lactone (V) was subjected to Kuhn-Roth oxidation to give acetic acid. The degradation products and linalool were converted to barium carbonate by Van Slyke-Folch oxidation to determine their specific activities, shown in Table 1.

Acetone containing the tracer from C-8 and/or C-10 of (IV) had 46 per cent of the incorporated tracer. The residual activities, 54 per cent, were detected in the lactone (V) containing C-1 ~ C-6 and C-9. Acetic acid containing the tracer from C-1, C-2, C-3 and C-9 of (IV), obtained from (V), showed only a slight activity. This is probably due to random incorporation of labelled acetate which results from partial breakdown of the added MVA. The ^{14}C is thus mainly located at C-4 and C-8/10 in (IV).

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[4] R. U. LEMIEUX and E. VON RUDLOFF, *Can. J. Chem.* 33, 1701 (1955).
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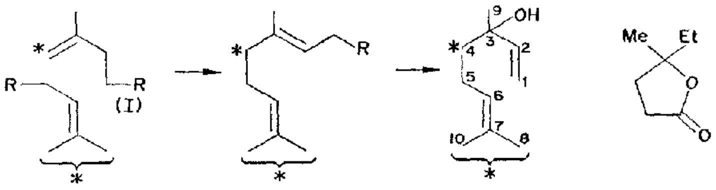
TABLE 1. SPECIFIC ACTIVITIES OF LINALOOL AND ITS DEGRADATION PRODUCTS

Compounds (Carbons originated from IV)	Specific activity dis/min/mM
Linalool (C-1$\sim$C-10)	607
Acetone (C-7, C-8 and C-10)	
Iodoform	124
Acetic acid	154
4-Methyl-4-hexanolide (C-1$\sim$C-6 and C-9)	331
Acetic acid (C-1$\sim$C-3 and C-9)	26

The resulted labelling pattern is consistent with the biosynthetic pathway shown in the scheme. The activities at C-4 and C-8 (and/or C-10), must have originated from (I) and (II) respectively, and are nearly equal. This is in contrast to the results[1,2] observed in the biosyntheses of the thujane derivatives and of camphor.



(II) (III) (IV) (V)

R = Pyrophosphate; * = ^{14}C

EXPERIMENTAL

Administration of labelled compound. A solution of [2-^{14}C]MVA (0·10 mc, 0·017 mM) and ATP (0·1 mM) was fed through a cut-stem into small twigs (*ca.* 400 g) which were maintained on phosphate buffer solution (pH 7·38) for 1 day before harvesting.

Isolation of radioactive linalool. The small twigs were subjected to steam-distillation. The oil obtained (6·7 g) was chromatographed on silica gel column. Elution with *n*-hexane–EtOAc afforded pure linalool (3·5 g).

Degradation of linalool. Linalool (598 mg) in MeOH (3 ml) was selectively hydrogenated on Adams PtO_2 (4 mg) to 1,2-dihydrolinalool (600 mg). The dihydrolinalool (200 mg) was oxidized with $KMnO_4$–KIO_4 reagent[4,5] for 24 hr. The excess oxidant was reduced with a minimum of $NaHSO_3$, and the weakly alkaline solution steam-distilled. Et_2O extraction of the acidified residual solution afforded 4-methyl-4-hexanolide (V) (98 mg; its S-benzylthiuronium salt, m.p. 132–133°, lit.[6] m.p. 132–132·5°). The aqueous distillate was subjected to hypoiodite oxidation. CHI_3 (369 mg) precipitated was filtered off and the usual treatment of the filtrate afforded HOAc as Na salt (38 mg). Kuhn–Roth oxidation of (V) (71 mg) gave HOAc as Na salt (94 mg).

Radioassay. Linalool and its degradation products were converted to $BaCO_3$ by Van Slyke-Folch oxidation and aliquots were counted on planchets at infinite thickness under a 2π-gas flow detector.

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