Biosynthesis of Montanine

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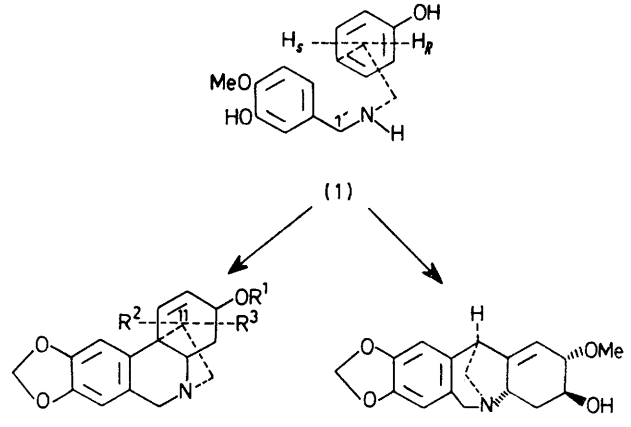
Summary It has been shown that *Rhodophiala bifida* converts *O*-methyl-(2*R*)-[2-$^{3}H_1$,1′-^{14}C]norbelladine (**1**) into both haemanthamine (**2**) and montanine (**4**) with the loss of the *pro-R* hydrogen of C-2 in (**1**).

WHILE chemical conversions from the haemanthamine into montanine ring systems have been observed,[1] the analogous biosynthetic route has provided contradictory results.[2,3]

O-Methyl-(2*R*)-[2-$^{3}H_1$]norbelladine[2] was mixed with *O*-methyl[1′-^{14}C]norbelladine (ratio $^{3}H_1:{}^{14}C$, 5·61 ± 0·18) which had been prepared from 3-benzyloxy-4-methoxybromobenzene by carbonation of the Grignard reagent with $^{14}CO_2$ and subsequent standard transformations. The doubly labelled (**1**) was injected as an aqueous solution into bulbs of growing *Rhodophiala bifida*. After a two-week period, the bulbs were processed and haemanthamine (**2**; $^{3}H_1:{}^{14}C$, 1·36 ± 0·02) and montanine (**4**; $^{3}H_1:{}^{14}C$, 1·31 ± 0·06) were isolated. This represents a loss of 76 and 77% of the tritium present at C-2 in (**1**) when transformed into haemanthamine and montanine, respectively. The residual tritium in both compounds is attributed to partial racemization which occurred during the synthesis[2] and was shown to be located at C-11 in (**2**) by oxidizing (**2**) with CrO_3–pyridine. The resulting oxohaemanthamine (**3**; $^{3}H_1:{}^{14}C$, 0·023) retained $<2\%$ of the tritium present in (**2**).



(1)

(2); R^1 = Me, R^2 = H, R^3 = OH

(3); R^1 = Me, R^2 = R^3 = O

(4)

The above data show that the biological conversion of *O*-methyl-(2*R*)-[2-$^{3}H_1$,1′-^{14}C]norbelladine into haemanthamine and montanine occurs with the loss of the *pro-R* hydrogen of C-2 in (**1**). These data are consistent with the reported biosynthesis of haemanthamine in various Amaryllidaceae.[2,3] This contradicts the reported biosynthesis of montanine in *Haemanthus coccineus*.[4]

(*Received, 22nd April* 1976; *Com.* 448.)

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