

## The Biosynthesis (+)- and (-)-Camphor

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RECENTLY it was shown that thujane derivatives [*e.g.* thujone (VI)] biosynthesised from [2-<sup>14</sup>C]mevalonic acid (MVA), contained the bulk of their tracer at one ring position such that isopentenyl pyrophosphate [IPP, (I)], but not 3,3-dimethylallyl pyrophosphate [DMAPP, (II)], was the tracer-containing precursor.<sup>1</sup> In order to test the generality of this unexpected result we have determined the labelling pattern in optical isomers of camphor biosynthesised from [2-<sup>14</sup>C]MVA in *Artemisia californica*, *Salvia leucophylla* L., and *Chrysanthemum balsamita* L. Our specimens produced material of 80—93% optical purity with  $[\alpha]_{546}^{25}$  +42°, +52°, and -44° (*c* 5, ethanol) respectively.

A solution of MVA (0.075 mc, 0.015 mmole) and ATP (0.1 mmole) was stem-fed into leaves (*ca.* 150 g.) which were maintained on nutrient solution for 4 to 5 days before harvesting. The extracted oils were diluted with carrier and pure samples of camphor were obtained by preparative g.l.c. Incorporations of tracer, *ca.* 0.02%, were typical of those reported for other monoterpenes.<sup>2</sup>

Degradation was accomplished (a) by oxidation to camphoric acid followed by Schmidt reaction to liberate carbon dioxide [containing the tracer from C(2) and C(3), in (VII)] and a diamine; (b) by conversion into  $\alpha$ -bromoborneol and thence into bornene, which underwent a retro-Diels-Alder reaction to yield ethylene [containing tracer from C(5) and C(6)] and a mixture of isomeric trimethylcyclopentadienes; (c) by conversion into isobornyl

xanthate, which on pyrolysis gave camphene with complete retention of optical activity,<sup>3</sup> followed by ozonolysis to give formaldehyde [containing tracer from C(10)] together with a lactone; and (d) by the above route to camphene followed by racemisation *via* Nametkin rearrangement to equilibrate C(8), C(9), and C(10) to the bridgehead methylene, followed by ozonolysis to liberate tracer from this position. The specific activities in counts per min. per millimole (corrected for quenching) for the highly purified degradation products or their functional derivatives were:

### *A. californica*

- (a) Camphoric acid 166; carbon dioxide 22; diamine 140.
- (b) Bornene 886; ethylene 740; dienes 110  $\pm$  40.
- (c) (+)-Camphene 527; formaldehyde 33; lactone 512.
- (d) ( $\pm$ )-Camphene 147; formaldehyde 20; lactone 120.

### *S. leucophylla*

- (a) Camphoric acid 642; carbon dioxide 45; diamine 627.
- (b) Bornene 618; ethylene 454; dienes 120  $\pm$  40.

### *C. balsamita*

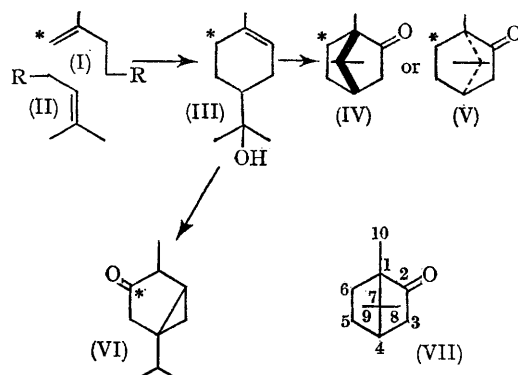
- (a) Camphoric acid 866; carbon dioxide 41; diamine 737.
- (b) Bornene 1505; ethylene 1200  $\pm$  200; dienes 130  $\pm$  40.

The standard deviations were  $\pm 0.5\%$  except where volatility or scarcity of product caused the errors recorded.

The C(5) and C(6) positions of camphor from all three sources contained 73—83% of the incorporated tracer. This is consistent with the predominant adoption of the appended biosynthetic route in which each optical isomer [(IV) and (V)] is derived from the corresponding isomer of  $\alpha$ -terpineol (III) and the situation is completely analogous to that found for the thujanes. The balance of tracer is fairly evenly distributed to the other carbon atoms, presumably as a result of degradation of MVA to smaller units and incorporation of these. In support of this mechanism, feeding  $[2-^3\text{H}]$ MVA to *C. balsamita* L. led to camphor with a specific activity of 1840, which fell to 238 on heating with base under conditions<sup>4</sup> which are known to remove both tracer atoms located on C(6) *via* homoenolisation.

It thus appears that the biosynthesis of monoterpenes in higher plants from MVA under these

conditions involves condensation of IPP derived from the additive with DMAPP that is mainly present in a metabolic pool.



R = Pyrophosphate; \* = <sup>14</sup>C

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<sup>1</sup> D. V. Banthorpe and K. W. Turnbull, *Chem. Comm.*, 1966, 177.

<sup>2</sup> W. D. Loomis, in "Terpenoids in Plants", ed. J. B. Pridlam, Academic Press, London, 1967, p. 59.

<sup>3</sup> C. A. Bunton, D. Whitaker, and K. Khaleeluddin, *Nature*, 1961, **190**, 715.

<sup>4</sup> A. Nickon and J. A. Lambert, *J. Amer. Chem. Soc.*, 1966, **88**, 1905.