Biosynthesis of Rotenoids. The Origin of C-6a and the "Extra" Methylene at C-6

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RECENT work using *Derris elliptica* plants[1] has shown that the aryl ring of phenylalanine can provide ring A of rotenone (I) whilst C-1 of phenylalanine becomes C-12, and C-2 becomes C-12a. There is an aryl migration from the former C-3 of phenylalanine to the former C-2. Biosynthesis of amorphigenin (II) by germinating seeds of *Amorpha fruticosa* is similar.[1] This part of our investigation has been completed by showing that on feeding [3-^{14}C]-phenylalanine to *D. elliptica*, 87% of the rotenone label is located at C-6a. Degradation of the labelled rotenone was effected by dehydrogenation to 6a,12a-dehydrorotenone, followed by hydrolysis to derrisic acid. The latter was converted into its t-butyl perester[2] (III) and decarboxylated by heating in cumene at 130—140° to liberate the former C-6a of rotenone as carbon dioxide.

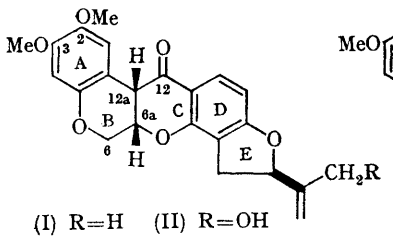
Attention has been turned to the origin of the "extra" carbon at C-6, necessary to convert an isoflavonoid into a rotenoid skeleton. It is found that it can be provided by methionine. [*Me*-^{14}C]-Methionine was wick-fed to *D. elliptica* plants and the [^{14}C]-labelled rotenone was isolated and demethylated by the Ziesel technique. The [^{14}C]methyl iodide was collected as triethylmethylammonium iodide,[3] combusted, and counted as barium carbonate. Another portion of the [^{14}C]rotenone was dehydrogenated, and the 6a,12a-dehydrorotenone was converted successively into rotenonone (IV) and rotenononic acid (VI). Decarboxylation of the latter (quinoline–copper bronze)[4] gave the former C-6 as carbon dioxide. The Table shows that [*Me*-^{14}C]methionine has, in these experiments, supplied C-6 of rotenone to the extent of 0·47—0·51 times that of the mean figure

TABLE

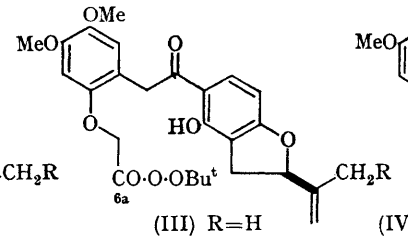
[^{14}C]*Methyl labelled methionine administration: label distribution in rotenoids*

	Incorp. %	2,3-OMe	C-6	2×C-6/2,3-OMe
Rotenone[a] (*D. elliptica* plants)	$0{\cdot}7 \times 10^{-2}$	0·77	0·18	0·47
	$12{\cdot}5 \times 10^{-2}$	0·74	0·19	0·51
Amorphigenin[a] (*A. fruticosa* seeds) ..	$0{\cdot}6 \times 10^{-2}$	0·77	0·19	0·50
	$11{\cdot}3 \times 10^{-2}$	0·77	0·26	0·68

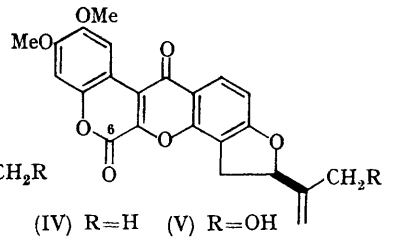
[a] Unit label.



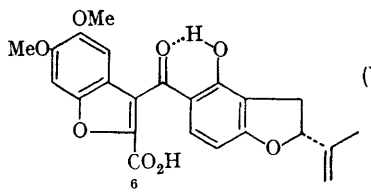
(I) R=H (II) R=OH



(III) R=H



(IV) R=H (V) R=OH



(VI) R=H
(VII) R=OH

for a ring A methoxy-group. Rather similar results (0·5—0·68) were obtained for amorphigenin using germinating *A. fruticosa* seeds: relative pool sizes may affect these figures. In both systems [*Me*-^{14}C]methionine appears to supply little labelled carbon to positions other than the methoxy-groups and C-6. It is concluded that methionine is a comparatively efficient source of the "extra" methylene carbon in rotenoids.

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[4] D. J. Adam, L. Crombie, and D. A. Whiting, *J. Chem. Soc.* (*C*), 1966, 550.