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SHORT COMMUNICATION

The biosynthesis of tigloyl esters in *Datura*

W. C. EVANS AND J. G. WOOLLEY

TIGLIC acid esters have been isolated from various *Datura* species and the translocation of 3,6-ditigloyloxytropane, 3,6-ditigloyloxytropan-7-ol and meteloidine from the roots to the leaves of *D. innoxia*, and the subsequent metabolism of these alkaloids, has already been described (Evans & Griffin, 1964). The origin of the tiglic acid moiety, however, does not appear to have been investigated.

It has been suggested that the tiglic acid could arise from acetoacetic acid by *C*-methylation followed by reduction and dehydration (Leete, 1963). In animal tissue homogenates, however, α-methylbutyryl-CoA and tigloyl- (or angeloyl-) CoA are intermediates in the degradation of isoleucine to acetate and propionate (Coon & Abrahamsen, 1952; Coon, Abrahamsen & Greene, 1952; Robinson, Bachhawat & Coon, 1956). It has also been proposed that isoleucine may be the precursor of α-methylbutyric acid in the α-methylbutyryl ester alkaloids of the *Duboisia* species (Barger, Martin & Mitchell, 1938), whilst in *Ascaris lumbricoides*, it has been shown that α-methylbutyric acid may arise by condensation of acetate and propionate (Saz & Weil, 1960).

In this work we have administered sodium acetate-2-^{14}C (0·025 mc), sodium propionate-1-^{14}C (0·025 mc), isoleucine-1-^{14}C (0·02 mc) and isoleucine-U-^{14}C (0·025 mc) via the roots to groups of 8-months old *Datura meteloides*. Other batches of *D. meteloides* were placed in an atmosphere containing $^{14}CO_2$ (0·025 mc). After 48 hr the roots and aerial parts of the plants were separately dried and the root alkaloids, without dilution with inactive carrier, were isolated by chromatography. The picrates of the separated alkaloids were recrystallised until a constant m.p. and a constant value for the specific activities were obtained. With the exception of the isoleucine-U-^{14}C experiments (Table 1), no labelling of the alkaloids could be detected.

TABLE 1. INCORPORATION OF ISOLEUCINE-U-^{14}C INTO THE ROOT ALKALOIDS OF *D. meteloides*

Alkaloid	Specific activity of picrate (dpm/mM)	Total activity of isolated picrate (dpm)	% Total activity of alkaloid in tigloyl moiety	% Total administered activity incorporated
3,6-Ditigloyloxytropane	$1·3 \times 10^6$	$3·3 \times 10^4$	100	0·06
3,6-Ditigloyloxytropan-7-ol	$4·4 \times 10^5$	$1·6 \times 10^4$	100	0·03
Meteloidine	$8·5 \times 10^5$	$4·5 \times 10^4$	100	0·08
Hyoscine		0		
Hyoscyamine		0		

From the Department of Pharmacy, University of Nottingham.

The results demonstrate a fairly rapid, and appreciable, incorporation of isoleucine-U-^{14}C into the tigloyl moiety of all the relevant alkaloids. Isoleucine-1-^{14}C is not incorporated and this is in accordance with the degradation of this amino-acid in animal tissue. Provided all the administered compounds gain equal access to the site of synthesis, it would appear that isoleucine is a more immediate precursor of the tigloyl moiety than either acetate or propionate. No significant labelling of the tropane ring was obtained in any instance, but in experiments of longer duration the incorporation of acetate has been adequately demonstrated by a number of workers.

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References

Barger, G., Martin, W. F. & Mitchell, W. (1938). *J. chem. Soc.*, 1685–1690.
Coon, M. J. & Abrahamsen, N. S. B. (1952). *J. biol. Chem.*, **195**, 805–812.
Coon, M. J., Abrahamsen, N. S. B. & Green, G. S. (1952). *Ibid.*, **199**, 75–83.
Evans, W. C. & Griffin, W. J. (1964). *Phytochemistry*, **3**, 503–511.
Leete, E. (1963). *Biogenesis of Natural Compounds*, 739, Oxford: Pergamon Press.
Robinson, W. G., Bachhawat, B. K. & Coon, M. J. (1956). *J. biol. Chem.*, **218**, 391–399.
Saz, H. J. & Weil, A. (1960). *J. biol. Chem.*, **235**, 914–918.