Biosynthesis of the Lythraceae Alkaloids: Incorporation of Lysine

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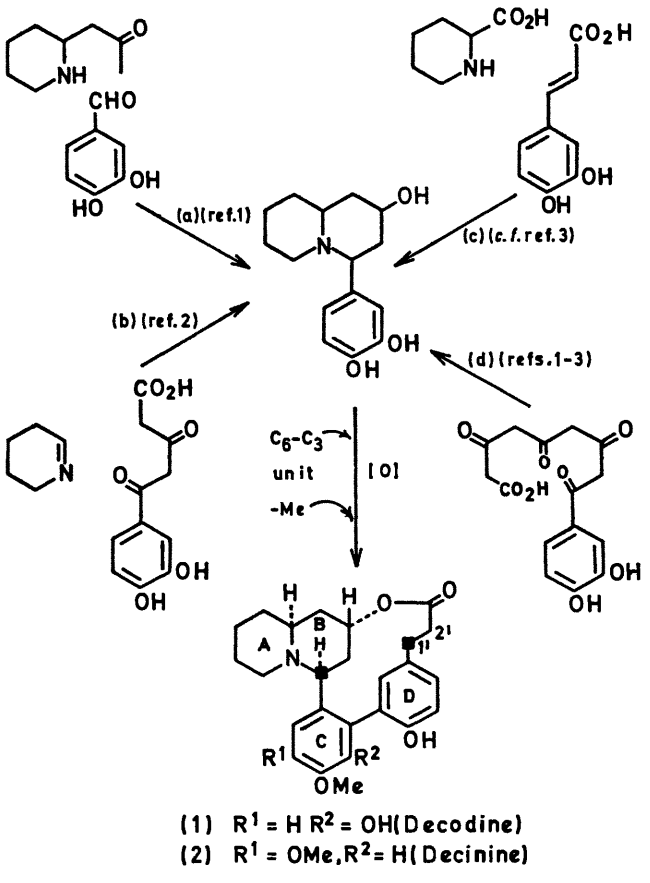
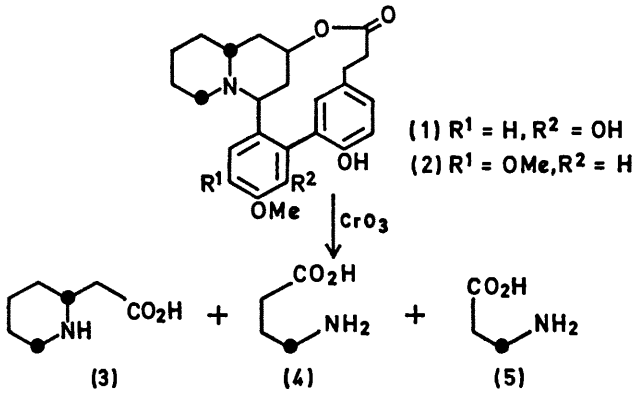
Summary Radioactivity from [2-^{14}C]- and from [6-^{14}C]-lysine enters the Lythraceae alkaloids decodine (**1**) and decinine (**2**); partial degradation of the alkaloids shows that incorporation is non-random and indicates that the C_5N moiety which constitutes ring A of the alkaloids is derived from lysine which is incorporated by way of a symmetrical intermediate.

SEVERAL biogenetic schemes have been suggested to account for the origin of the phenylquinolizidine system of the Lythraceae alkaloids. They are summarized in Scheme 1. A late step, included in all the hypotheses, is the introduction, by ester formation followed by a phenol coupling process, of a C_6–C_3 unit, derived from phenylalanine *via* cinnamic acid.[1–3] A similar C_6–C_3 precursor, or a C_6–C_1 unit derived from it by β-oxidation, is envisaged as the source of ring C and of one (or three) adjacent carbon atoms. Incorporation[3] of label from [3-^{14}C]phenylalanine into the predicted sites (■) of cryogenine [also known as vertine,[4] a diastereoisomer of 1′,2′-dehydrodecinine, *c.f.*, (**2**)] is consistent with these ideas, but does not discriminate among the four biogenetic suggestions. We have investigated the incorporation of activity from [2-^{14}C]-DL-lysine and [6-^{14}C]-DL-lysine into decodine and decinine in *Decodon verticillatus* (L.) Ell. Our results eliminate two of the biogenetic hypotheses.



SCHEME 1



SCHEME 2

Decodine and decinine, isolated[5] from plants of *D. verticillatus* to which [2-^{14}C]-DL-lysine (New England Nuclear) and [6-^{14}C]-DL-lysine (Commissariat à l'Energie Atomique, France) had been administered, were purified to constant radioactivity and partially degraded to locate the sites of labelling. Chromic acid oxidation yielded (Scheme 2) a mixture of products from which piperidine-α-acetic acid[6] (**3**), γ-aminobutyric acid (**4**), and β-alanine (**5**) were isolated and purified as *N*-dinitrophenyl derivatives. The relative specific activity of each of these degradation products is shown in the Table.

Since piperidine-α-acetic acid contained all activity of decodine and decinine derived from either [2-^{14}C]- or from [6-^{14}C]-lysine, incorporation of lysine into the alkaloids is

Relative specific activities of the partial degradation products of decodine and decinine

Precursor	Relative specific activity (%)			
	Decodine (**1**)	Piperidine-α- acetic acid (**3**)	γ-Aminobutyric acid (**4**)	β-Alanine (**5**)
[2-^{14}C]Lysine	100 ± 1	100 ± 1	50 ± 1	49 ± 1
[6-^{14}C]Lysine	100 ± 1	99 ± 3	51 ± 1	51 ± 1
	Decinine (**2**)			
[2-^{14}C]Lysine	100 ± 1	100 ± 2	57 ± 2	53 ± 1
[6-^{14}C]Lysine	100 ± 1	106 ± 2	52 ± 1	55 ± 2

non-random, and it is likely that an intact C_5N unit,† derived from lysine, is incorporated. Since γ-aminobutyric acid and β-alanine contained one half of the activity of the intact alkaloids, regardless of whether [2-^{14}C]- or [6-^{14}C]-lysine had been the precursor, the lysine-derived C_5N unit enters the alkaloids by way of a symmetrical intermediate.

Of the four biogenetic schemes only two, (a) and (b), (Scheme 1) are consistent with these results. To distinguish between them, incorporation into the alkaloids of labelled samples of Δ^1-piperideine[7] and pelletierine[7] must be examined. These experiments are in progress.

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† The carboxyl carbon of lysine does not enter the alkaloids; when [1-^{14}C]-DL-lysine (New England Nuclear) was administered to *D. verticillatus*, the alkaloid fraction was totally inactive.

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