

BIOSYNTHESIS OF THE SECURINEGA ALKALOIDS-I.

SPECIFIC INCORPORATION OF TYROSINE.

Ronald J. Parry

Department of Chemistry, Brandeis University

Waltham, Massachusetts, U.S.A.

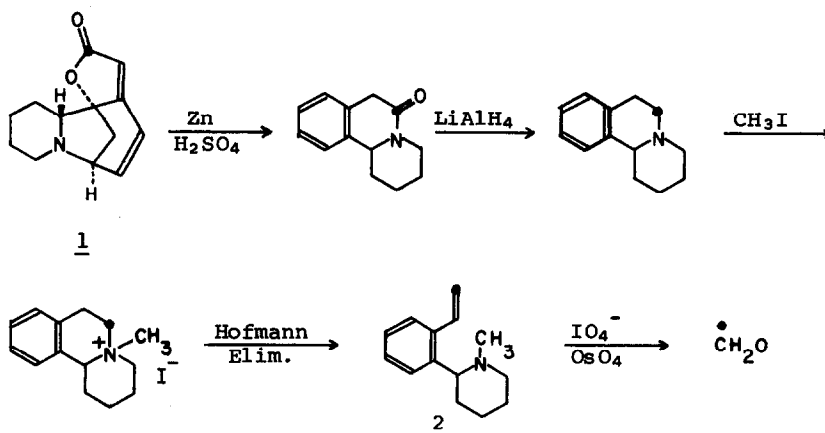
(Received in USA 2 November 1973; received in UK for publication 10 December 1973)

Plants of the genus Securinega (family Euphorbiaceae) elaborate a group of unique tetracyclic alkaloids of which securinine (1) is the most abundant.<sup>1</sup> We wish to report experiments indicating that these alkaloids are formed by a novel biosynthetic pathway.

Sufficient investigation of the biogenesis of piperidine alkaloids has been carried out to allow one to predict that the piperidine ring of 1 will be derived from L-lysine;<sup>2</sup> preliminary experiments in our laboratory support this prediction. Much greater interest surrounds the question of the origin of the remaining eight carbon atoms in the securinine skeleton. It occurred to us that this portion of the alkaloid might be derived from an aromatic amino-acid such as phenylalanine or tyrosine. This communication presents evidence that L-tyrosine, but not L-phenylalanine, serves as a specific precursor of securinine.

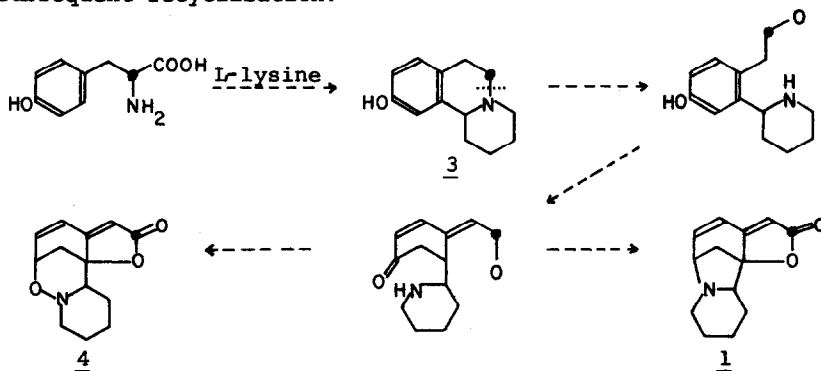
Administration of DL-2-<sup>14</sup>C-tyrosine to young Securinega suffruticosa (Pallas) Rehder plants by the cotton wick method gave after 14 days radioactive securinine (0.007% incorporation).<sup>3</sup> Administration of <sup>3</sup>H(G)-L-phenylalanine to S. suffruticosa under similar conditions yielded radioinactive securinine. This observation suggests that Securinega cannot convert L-phenylalanine into L-tyrosine by hydroxylation; this phenomenon has been observed in other Angiosperms.<sup>2</sup> The purified radioactive securinine obtained by

administration of 2-<sup>14</sup>C-DL-tyrosine was degraded to N-methyl-2-(o-vinylphenyl) piperidine (2) by means of the following reaction sequence:<sup>4,5</sup>



Cleavage of the vinyl group present in 2 with osmate-periodate and trapping of the liberated formaldehyde with dimedone<sup>6</sup> yielded radioactive dimedone-formaldehyde. The specific activity of the purified dimedone-formaldehyde corresponded to 92% of the activity of the piperidine derivative 2.

This result prompts us to suggest that the biosynthesis of securinine may proceed via a benzoquinolizine derivative (3) which undergoes ring-fission and subsequent recyclization:



Similar ring-fission processes are associated with the biosynthesis of benzo-phenanthridine alkaloids from protoberberine precursors<sup>7</sup> and with the biosynthesis of the quinoline alkaloids of Cinchona from indolic precursors.<sup>8,9</sup> In conjunction with the above proposal, the structure<sup>10</sup> of phyllantidine (4) which occurs in S. suffruticosa is of interest: it appears that the oxygen attached to the nitrogen atom of 4 may correspond to the phenolic hydroxyl oxygen of tyrosine. We are continuing to pursue these and other aspects of Securinega alkaloid biosynthesis.

#### Acknowledgements:

We wish to thank the Chemistry department for a starter grant. Special thanks are due to Prof. T. C. Huang for supplying us with S. suffruticosa seeds and to Dr. Seichi Saito for a generous gift of securinine.

#### References:

1. V. Snieckus, "The Securinega Alkaloids" in The Alkaloids, Vol. XIV, p. 425 ff, Ed. by R. H. F. Manske, Academic Press, New York, 1973.
2. I. D. Spenser, "The Biosynthesis of Alkaloids and of Other Nitrogenous Secondary Metabolites" in Comprehensive Biochemistry, Vol. 20, p. 231 ff, Ed. by M. Florkin and E. H. Stotz; Elsevier Publishing Co., Amsterdam, 1968.
3. Incorporation based on quantity of L-tyrosine administered.
4. Z. Horii, M. Ikeda, Y. Yamawaki, Y. Tamura, S. Saito, and K. Kodera, Tetrahedron, 19, 2101 (1963).
5. T. Nakano, T. H. Yang, and S. Terao, Tetrahedron, 19, 609 (1963).
6. A. R. Battersby, R. Binks, W. Laurie, G. V. Parry, and B. R. Webster, J. Chem. Soc., 7459 (1965).
7. A. R. Battersby, R. J. Francis, E. A. Ruveda, and J. Staunton, Chem. Commun., 89 (1965).

8. A. R. Battersby and R. J. Parry, Chem. Commun., 30 (1971).
9. A. R. Battersby and R. J. Parry, ibid., 31 (1971).
10. Z. Horii, T. Imanishi, M. Yamauchi, M. Hanaoka, J. Parello, and S. Munavalli, Tetrahedron Lett., 1877 (1972).