Communications to the Editor

Chem. Pharm. Bull.
32(2) 815—817 (1984)

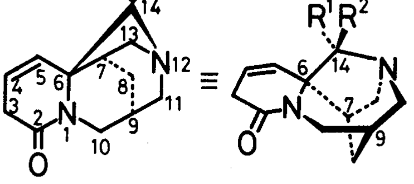
AN EFFECTIVE TRANSFORMATION OF (-)-CYTISINE-TYPE LUPIN ALKALOIDS INTO (-)-TSUKUSHINAMINE-TYPE ALKALOIDS

Shigeru Ohmiya,*,[a] Hirotaka Otomasu[a] and Isamu Murakoshi[b]
Faculty of Pharmaceutical Sciences, Hoshi University,[a] Ebara 2-4-41, Shinagawa-ku, Tokyo 142, Japan and Faculty of Pharmaceutical Sciences, Chiba University,[b] Yayoi-cho 1-33, Chiba 260, Japan

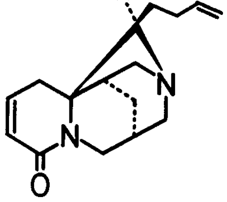
(-)-Tsukushinamine-A (1) and (-)-tsukushinamine-B (2), new cage-type lupin alkaloids from Sophora franchetiana Dunn (Leguminosae), were synthesized by means of intramolecular photocyclization from a common lupin alkaloid (-)-rhombifoline (7), coexisting in the same plant. The other (-)-cytisine-type alkaloids, (-)-N-methylcytisine (9) and (-)-N-ethylcytisine (8), were also transformed into the (-)-tsukushinamine-type alkaloids (4-6) in the same way.

KEYWORDS——lupin alkaloid; tsukushinamine-type alkaloid; (-)-tsukushinamine-A; (-)-tsukushinamine-B; (-)-rhombifoline; (-)-N-methylcytisine; (-)-N-ethylcytisine; photochemical synthesis; intramolecular photochemical 1,4-addition; Leguminosae

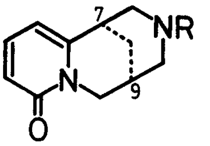
As a result of screening plants belonging to the Leguminosae for lupin alkaloids, a new cage-type lupin alkaloid, (-)-tsukushinamine-A (1), was isolated from the freshly harvested epigeal parts of Sophora franchetiana Dunn, a locally native and very rare shrub in Japan, together with the (-)-cytisine-type alkaloids (7 and 10) and the (-)-anagyrine-type lupin alkaloids (11 and 12).$^{1)}$ Its proposed structure has been confirmed by X-ray analysis as 1, including the absolute configuration (6R:7R:9S:14R).$^{2)}$ From the same sources, we have further isolated two new cage-type lupin alkaloids, (-)-tsukushinamine-B (2) and (-)-tsukushinamine-C (3), as the isomers of (-)-tsukushinamine-A (1).$^{3)}$



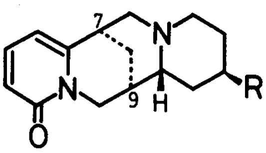
1; $R^1 = H$, $R^2 = CH_2CH=CH_2$
2; $R^1 = CH_2CH=CH_2$, $R^2 = H$
4; $R^1 = H$, $R^2 = CH_3$
5; $R^1 = CH_3$, $R^2 = H$
6; $R^1 = R^2 = H$



3



7; $R = CH_2CH_2CH=CH_2$
8; $R = CH_2CH_3$
9; $R = CH_3$
10; $R = H$



11; R = H
12; R = OH

The absolute configurations at positions 7 and 9 of (-)-tsukushinamine-A (1) are the same as those of (-)-cytisine (10, 7R:9S),[4,5] (-)-baptifoline (12, 7R:9R)[4,5] and (-)-rhombifoline (7, 7R:9S).[4,5] From the stereochemical point of view among the lupin alkaloids, we have proposed a biosynthetic pathway for the formation of the (-)-tsukushinamine-type alkaloids (1-3), in which it has been presumed that 1, 2, 3 and (-)-rhombifoline (7) might be metabolites of the anagyrine-type lupin alkaloid, such as (-)-baptifoline (12), coexisting in the same plant.[2,3]

This paper describes an effective method for the transformation of the (-)-cytisine-type lupin alkaloids (7-9) into the (-)-tsukushinamine-type alkaloids, such as 1, 2 and 3, by an intramolecular photocyclization reaction.

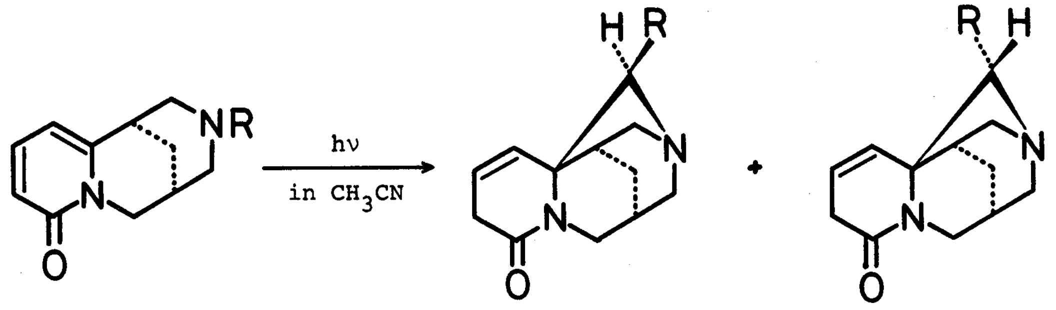
The photoreaction of tertiary aliphatic amines with aromatic hydrocarbons, such as benzene and naphthalene, have previously been reported to bring about 1,4-addition of an α-C-H bond in the amine to the aromatic ring.[6] It is also known that the photoaddition reaction causes an intramolecular cyclization of phenylalkylamines, such as 1-dimethylamino-3-phenylpropane and 1-dimethylamino-4-phenylbutane, to give *meta*-cyclization products.[7]

Our application of the intramolecular photoaddition reaction to (-)-N-alkylcytisines (7-9), which possess a pyridone ring as an aromatic group, resulted in formation of (-)-tsukushinamine-A (1), (-)-tsukushinamine-B (2) and their derivatives (4-6) in 90-95% yields: irradiation of a degassed solution of (-)-rhombifoline (7, 63 mg) in dry CH_3CN (30 ml) with a high pressure mercury lamp (400 W) through a Pyrex filter at 25-28°C for 6 h clearly gave a complete conversion of (-)- rhombifoline (7) to (-)-tsukushinamine-A (1) and (-)-tsukushinamine-B (2) in a ratio of approximately 1 : 3, respectively.

The identity of the reaction products as (-)-tsukushinamine-A (1) and (-)-tsukushinamine-B (2) was confirmed by comparing their ^1H-NMR, MS, $[\alpha]_D$ and co-TLC data with those of authentic samples, as described in previous papers.[1-3]

An analogous irradiation of (-)-N-methylcytisine (9) and (-)-N-ethylcytisine (8)[8] also gave new products 6 and two diastereomers 4 and 5, respectively. 6 is a new cage-type product having the fundamental skeleton of the (-)-tsukushinamine-type alkaloids (1-3).

This is the first report of chemical synthesis of the (-)-tsukushinamine-type alkaloids.



7; R = $CH_2CH_2CH=CH_2$
8; R = CH_2CH_3
9; R = CH_3

1; R = $CH_2CH=CH_2$
4; R = CH_3
6; R = H

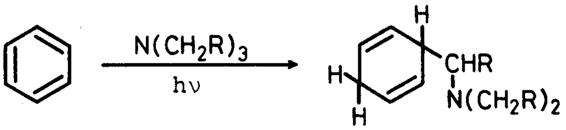
2; R = $CH_2CH=CH_2$
5; R = CH_3

Irradiation of the (-)-cytisine-type lupin alkaloids such as (-)-N-methylcytisine (9) and (-)-N-ethylcytisine (8) in H_2O did not cause any change in the starting materials. The (-)-tsukushinamines (1-6) have not been isolated so far from the other plant sources which contain (-)-N-alkylcytisine such as (-)-rhombifoline (7), (-)-N-ethylcytisine (8) and (-)-N-methylcytisine (9). These facts indicate that (-)-tsukushinamine-A (1) and (-)-tsukushinamine-B (2) are not artificial products formed from (-)-rhombifoline (7) during isolation of the alkaloids.

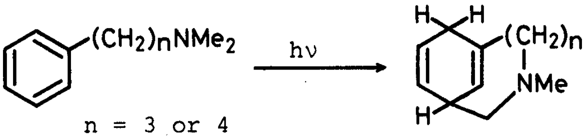
A more detailed investigation of these intra- and inter-molecular photoaddition reactions of amines to α-pyridones and of the biosynthetic pathway leading to the (-)-tsukushinamine-type alkaloids is in progress in our laboratories.

REFERENCES AND NOTES

1) S. Ohmiya, K. Higashiyama, H. Otomasu, J. Haginiwa and I. Murakoshi, Chem. Pharm. Bull., 27, 1055 (1979).
2) J. Bordner, S. Ohmiya, H. Otomasu, J. Haginiwa and I. Murakoshi, Chem. Pharm. Bull., 28, 1965 (1980).
3) S. Ohmiya, K. Higashiyama, H. Otomasu, J. Haginiwa and I. Murakoshi, Phytochemistry, 20, 1997 (1981).
4) S. Okuda, K. Tsuda and H. Kataoka, Chem. Ind. (London), 1961, 1115; S. Okuda, K. Tsuda and H. Kataoka, Chem. Ind. (London), 1961, 1751.
5) S. Okuda, K. Tsuda and H. Kataoka, Chem. Pharm. Bull., 13, 487 (1965); S. Okuda, K. Tsuda and H. Kataoka, Chem. Pharm. Bull., 13, 491 (1965).
6) M. Bellas, D. Bryce-Smith, M. T. Clarke, A. Gilbert, G. Klunklin, S. Krestonosich, C. Manning and S. Wilson, J. Chem. Soc., Perkin Trans. 1, 1977, 2571; D. Bryce-Smith and A. Gilbert, Tetrahedron, 33, 2459 (1977).



7) D. Bryce-Smith, A. Gilbert and G. Klunklin, J. Chem. Soc., Chem. Commun., 1973, 330.



8) I. Murakoshi, M. Watanabe, J. Haginiwa, S. Ohmiya and H. Otomasu, Phytochemistry, 21, 1470 (1982).

(Received December 17, 1983)