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

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(-)-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⁾

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-alkylcytisinines (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 $^1\text{H-NMR}$, 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.

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.

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