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# CONVERSION OF BERBERINE INTO BERBERRUBINE BY SELECTIVE DEMETHYLATION UNDER MICROWAVE IRRADIATION

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SYNTHETIC COMMUNICATIONS Vol. 32, No. 19, pp. 3027–3029, 2002

### CONVERSION OF BERBERINE INTO BERBERRUBINE BY SELECTIVE DEMETHYLATION UNDER MICROWAVE IRRADIATION<sup>[1]</sup>

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#### ABSTRACT

Berberine, a natural alkaloid, underwent selective demethylation under microwave irradiation to form an important bioactive compound, berberrubine in excellent yield.

Berberine (1),<sup>[2]</sup> a quaternary alkaloid of *Tinospora cardifolia*, is an important bioactive compound possessing antianaemic and antineoplastic properties. The compound also exhibits various other pharmacological effects including respiratory stimulation, transient hypotension and convulsion. In connection to our recent work<sup>[3–6]</sup> on the chemical modifications of natural bioactive molecules we desired to prepare various analogues of berberine (1) which will be evaluated for their biological properties.

Berberine (1) was irradiated under microwave irradiation for 5 min. The product (yield 98%) was identified as a naturally occurring alkaloid,

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#### DAS AND SRINIVAS

berberrubine (2).<sup>[7,8]</sup> The structure of the latter was established from its physical and spectral (<sup>1</sup>H NMR and MS) properties. Berberine (1) contains two methoxy groups in its D-ring at C-9 and C-10. Under microwave irradiation the selective demethylation of the C-9 methoxy group resulted in the formation of berberrubine (2).



Berberrubine (2) is reported<sup>[7]</sup> to exhibit antimicrobial activity against *Mycobacterium smegmatis* while berberine (1) was found to be inactive under similar experimental conditions. The method developed here is very simple and efficient for the preparation of 2 in excellent yield from the naturally abundant 1. Compound 2 can be utilized for its known biological activity and can also be employed for evaluation of its new biological properties.

#### **EXPERIMENTAL**

**Microwave irradiation of berberine (1):** Berberine (1, 100 mg) was taken in an erlenmeyer flask and the flask was placed in an alumina bath inside a commercial microwave oven (BPL BMO 700T). The compound was irradiated for 5 min and taken out from the oven. The product was shaken with CHCl<sub>3</sub> (10 mL) and filtered. The solvent was evaporated from the filtrate to yield berberrubine (2, 94 mg, yield 98%) as red amorphous solid, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta$  9.18 (1H, s, H-8), 7.55 (1H, s, H-13), 7.24 (1H, s, H-1), 7.22 (1H, d, J = 8.0 Hz, H-11), 6.71 (1H, s, H-4), 6.42 (1H, d, J = 8.0 Hz, H-12), 6.06 (2H, s, -OCH<sub>2</sub>O-), 4.40 (2H, t, J = 6.0 Hz, H<sub>2</sub>-6), 3.91 (3H, s, -OMe), 3.10 (2H, t, J = 6.0 Hz, H<sub>2</sub>-5); <sup>1</sup>H NMR (TFA + CDCl<sub>3</sub>):  $\delta$  9.64 (1H, s, H-8), 8.22 (1H, s, H-13), 7.85 (1H, d, J = 8.0 Hz, H-11), 7.64 (1H, d, J = 8.0 Hz, H-12), 7.28 (1H, s, H-1), 6.82 (1H, s, H-4), 6.12 (2H, s, -OCH<sub>2</sub>O-), 4.94–4.82 (2H, m, H<sub>2</sub>-6), 4.06 (3H, s, -OMe), 3.32–3.20 (2H, m, H<sub>2</sub>-5); FAB MS: m/z 322 (M<sup>+</sup> + 1, 22%); Anal. Calcd. for C<sub>19</sub>H<sub>15</sub>NO<sub>4</sub>: C, 71.03; H, 4.67; N, 4.36. Found: C, 71.14; H, 4.58; N, 4.27.

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#### **CONVERSION OF BERBERINE INTO BERBERRUBINE**

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