*Phytochemistry*, Vol. 22, No. 2, pp. 627–628, 1983.
Printed in Great Britain.

0031-9422/83/020627-02$03.00/0


# PROTOPINE-*N*-OXIDE, AN ALKALOID FROM *BOCCONIA CORDATA*

K. IWASA, M. OKADA and N. TAKAO

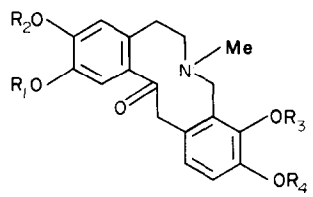
Kobe Women's College of Pharmacy, Motoyamakita-machi, Higashinada-ku, Kobe-shi 658, Japan

(*Revised received* 28 *June* 1982)

**Key Word Index**—*Bocconia cordata*; Papaveraceae; alkaloids; protopine-type *N*-oxide.

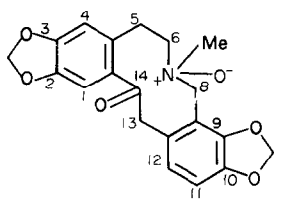
**Abstract**—The structure of a minor alkaloid of *Bocconia cordata* has been deduced as protopine-*N*-oxide by spectroscopic methods and confirmed by synthesis.

The protoberberines, protopines and benzophenanthridines have been isolated from *Bocconia cordata* [1]. A minor alkaloid was isolated from the whole plant in the vegetative stage, Kyoto prefecture, Japan. The new base, mp 145–146°, was isolated along with the known protopine (**1**) and allocryptopine (**2**) when the tertiary fraction was subjected to prep. TLC. The composition of the base, $C_{20}H_{19}NO_6$, was verified by high resolution mass spectrometry. The alkaloid has UV $\lambda_{max}^{EtOH}$ nm: 303 (3.96), 282 (sh, 3.80) and 230 (4.36) and IR $\nu_{max}$ $cm^{-1}$: 1680 and 3050–3500 absorptions. The mass spectrum of the base has a $M^+$ at *m/z* 369, a base peak at *m/z* 148 and fragment ions at *m/z* 352 $[M-17]^+$, 322, 310, 281, 267, 252, 206, 175, 163, 149 and 134. The fragment peak at *m/z* 352, due to an ion formed by a loss of a hydroxyl, is characteristic. The $^1H$ NMR spectrum showed the presence of one N–Me group, two methylenedioxy groups, and four aromatic protons.



**1** $R_1 + R_2 = R_3 + R_4 = CH_2$

**2** $R_1 + R_2 = CH_2$, $R_3 = R_4 = Me$



**3**

Spectroscopic examinations indicated that the new base is protopine *N*-oxide (**3**). This assumption was also supported by the 200 MHz $^1H$ NMR spectrum. In the aromatic region two singlets due to the *para* protons and an AB quartet attributed to the *ortho* protons were observed. The signal at $\delta$3.16 was assigned to the N–Me group. A quartet of the AX type centered at $\delta$3.45 and 4.76 with a coupling constant of 15.5 Hz was assigned to the protons at C-13. An AB quartet centered at $\delta$4.51 and 4.86 having a coupling constant of 14.0 Hz was attributed to the protons at C-8*. The new alkaloid was identical in all respects with the sample of protopine *N*-oxide (**3**) prepared by treatment of protopine (**1**) with *m*-chloroperbenzoic acid at room temperature. This is the first time the *N*-oxide of a protopine-type alkaloid has been isolated from a natural source.

It has been proved that the protopine-type alkaloids occupy a central position between the tetrahydroprotoberberine *N*-metho salts and the benzophenanthridines, and between the *N*-quaternary tetrahydroberberines and the rhoeadines in a biosynthetic pathway [2–6]. The mechanism of the biosynthetic conversion of the protopine intermediates to the benzophenanthridines is still unknown. That of protopine to rhoeadine has been suggested [5]. It may be expected that protopine *N*-oxide serves as a biosynthetic intermediate.

## EXPERIMENTAL

*Isolation of alkaloids.* Whole plants of *B. cordata* Wild. (21.8 g) were extracted with MeOH. The combined extracts were evaporated under red. pres. and the residue re-extracted with 3% aq. tartaric acid. The acidic soln was washed with $Et_2O$, made basic with $NH_4OH$ and extracted with $CHCl_3$. The alkaline $CHCl_3$ extract was separated into protopine- and allocryptopine-containing fractions by prep. Si gel TLC using MeOH–$CHCl_3$ (5:1). The allocryptopine-containing fraction was recrystallized from $CHCl_3$–MeOH to afford 57 mg of allocryptopine, mp 150–153°. The protopine-containing fraction was reseparated by prep. Si gel TLC in MeOH–$CHCl_3$ (5:1) to give protopine (50 mg), mp 210–213°, and a new base which was recrystallized from MeOH–$Me_2CO$ to afford the base *X* (8 mg), mp 144–145° (decomp.), EI–MS (probe) 75 eV, *m/z* (rel. int.): 369 $[M]^+$, (48), 352 (26), 322 (53), 310 (79), 281 (21), 267 (37), 252 (20), 206 (24), 175 (47), 163 (30), 149 (74), 148 (100), 134 (41). High resolution mass spectrometry, $C_{20}H_{19}O_6N$ $[M]^+$, calcd, 369.1210; found, 369.1168; UV $\lambda_{max}^{EtOH}$nm (log $\varepsilon$): 303 (3.96), 282 (sh, 3.80), 230 (4.36); IR $\nu_{max}^{nujol}$ $cm^{-1}$: 3500–3050 (*br*, $H_2O$ of

*Assignments for H-8 and H-13 were confirmed by comparison of the $^1H$ NMR spectrum with that of allocryptopine (**2**) *N*-oxide (a quartet centered at $\delta$4.73 and 4.76 and that centered at 3.44 and 4.78).

crystallization), 1680 (C = O); $^1$H NMR: $\delta$3.16 (3H, *s*, N–Me), 3.02 (1H, *m*), 3.25–3.70 (2H, *m*), 3.45 (1H, *d*, *J* = 15.5 Hz, H-13$_A$), 4.0 (1H, *m*), 4.51 (1H, *d*, *J* = 14.0 Hz, H-8$_A$), 4.76 (1H, *d*, *J* = 15.5 Hz, H-13$_B$), 4.86 (1H, *d*, *J* = 14.0 Hz, H-8$_B$), 6.02 (2H, *m*, $OCH_2O$), 6.07 (2H, *m*, $OCH_2O$), 6.77 (1H, *s*, H-4), 6.99 (1H, *d*, *J* = 7.9 Hz, H-11), 7.13 (1H, *s*, H-1), 7.23 (1H, *d*, *J* = 7.9 Hz, H-12).

*Preparation of protopine* N-*oxide.* Protopine (100 mg) was dissolved in $CHCl_3$ (20 ml) and *m*-chloroperbenzoic acid (65 mg) was then added over 30 min. The mixture was allowed to stand for 1.5 hr at room temp. The soln was washed with 5% $Na_2SO_3$, 5% $NaHCO_3$, and then satd NaCl soln. The $CHCl_3$ soln was dried and the solvent evaporated. The resulting crystals were recrystallized from MeOH–$Me_2CO$ to afford protopine *N*-oxide (98 mg), mp 145–146° (decomp.). The IR, $^1$H NMR and mass were identical with base *X*. Found: C, 62.04; H, 5.41; N, 3.38. Calc. for $C_{20}H_{19}O_6N.H_2O$: C, 62.01; H, 5.46; N, 3.63%.

## REFERENCES

1. Manske, R. H. F. (1979) in *The Alkaloids* Vol. 17, p. 391. Academic Press, New York.
2. Takao, N., Iwasa, K., Kamigauchi, M. and Sugiura, M. (1976) *Chem. Pharm. Bull.* **24**, 2859.
3. Takao, N., Kamigauchi, M., Iwasa, K. (1978) in Abstracts of the April Meeting of the Pharmaceutical Society of Japan, Okayama, p. 343.
4. Rönsch, H. (1972) *Eur. J. Biochem.* **28**, 123.
5. Tani, C. and Tagahara, K. (1977) *Yakugaku Zasshi* **97**, 93.
6. Iwasa, K. and Takao, N. (1982) *Phytochemistry* **21**, 611.