

N-Methyl-2,3,6-Trimethoxymorphinandien-7-one N-oxide: A Minor Alkaloid from *Alseodaphne perakensts*

Nordin H. Lajis, Zurina Mahmud, and Robert F. Toia

J. Nat. Prod., **1991**, 54 (2), 612-614 • DOI:

10.1021/np50074a046 • Publication Date (Web): 01 July 2004

Downloaded from <http://pubs.acs.org> on April 3, 2009

More About This Article

The permalink <http://dx.doi.org/10.1021/np50074a046> provides access to:

- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article



ACS Publications
High quality. High impact.

Journal of Natural Products is published by the American Chemical Society, 1155 Sixteenth Street N.W., Washington, DC 20036

N-METHYL-2,3,6-TRIMETHOXYMORPHINANDIEN-7-ONE N-OXIDE:
A MINOR ALKALOID FROM *ALSEODAPHNE PERAKENSIS*

NORDIN H. LAJIS,* ZURINA MAHMUD,

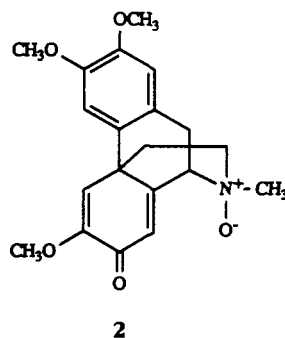
Department of Chemistry, Universiti Pertanian Malaysia, 43400 Serdang, Selangor, Malaysia

and ROBERT F. TOIA

Pesticide Chemistry and Toxicology Laboratory, Department of Entomological Sciences,
University of California, Berkeley, California 94720**ABSTRACT.**—The novel alkaloid *N*-methyl-2,3,6-trimethoxymorphinandien-7-one *N*-oxide [2] has been isolated as a minor constituent from *Alseodaphne perakensis*.

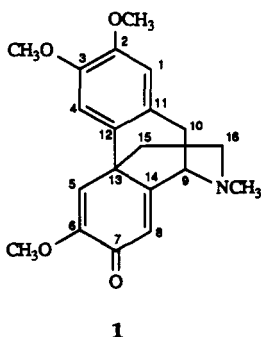
Alseodaphne perakensis (Gamb.) Kosterm. (Lauraceae) is a tree of moderate size that is widely distributed throughout peninsular Malaysia. Although there has been no reported use of this plant in traditional folk medicine practices (1), in field tests the leaves were found to be rich in alkaloids (2).¹ Initial chemical work on this species (3) led to the isolation of the major alkaloidal component, *N*-methyl-2,3,6-trimethoxymorphinandien-7-one [1], a compound noted previously in *Cocculus laurifolius* DC. (Menispermaceae) (4), *Rhigiocarya racemifera* Miens (Menispermaceae) (5), and *Litsea sebifera* Bl. (Lauraceae) (6).

In further work, we have now isolated a new polar, minor alkaloid, *N*-methyl-2,3,6-trimethoxymorphinandien-7-one *N*-oxide [2] present in the extract of the



leaves of *A. perakensis*. All attempts to crystallize the alkaloid, which is rather hygroscopic, proved fruitless, and after purification by multiple preparative tlc the compound was obtained as an amorphous, pale yellow solid.

The spectroscopic data were particularly useful in assigning structure. The uv spectrum is similar to that of 1 (7), suggesting close similarities in the respective chromophores, and the ir spectrum substantiated the presence of the conjugated carbonyl and aromatic functionalities. The general appearance of the ¹H-nmr spectrum of 2 was also similar to that of 1, with the exception of small chemical shift differences in comparable resonances. Three methoxy substituents and the *N*-methyl group were clearly present (δ 3.89, 3.85, 3.80, and 3.41, respectively), and four one-proton singlet signals were consistent with the two para oriented aromatic protons and the two cyclohexadienonyl protons. Other discrete structural elements recognizable, which were ac-



¹At the time of collection and preparation of this "Proceedings" the plant was tentatively assigned, incorrectly, as *Debaasia microcarpa*.

counted for in terms of the coupling patterns and the remaining resonances, were an isolated $-\text{CH}_2\text{CH}_2-$ and an isolated $-\text{CH}_2\text{CH} <$ spin system.

The mass spectrum of **2** afforded a molecular ion at m/z 357 consistent with a molecular formula of $\text{C}_{20}\text{H}_{23}\text{NO}_5$, indicating the presence of an additional 16 mass units with respect to **1**. Furthermore, a discrete loss of 16 amu to give an ion at m/z 341 was observed. These data, together with the considerations noted above, suggested **2** to be the *N*-oxide derivative of **1**. ^{13}C -nmr data supported this assignment. Again the spectrum showed close similarities to **1** (7) but with substantial downfield shifts for the carbon atoms attached to nitrogen (Table 1). This is consistent with either a deshielding or inductive effect of an *N*-oxide.

Proof for structure was achieved by peracid oxidation of **1** (8) to give the *N*-

oxide. Direct comparisons of this material with the naturally occurring compound showed them to be identical apart from small differences ($< 3\%$) in the calculated uv extinction coefficients. In addition, $\text{Zn}/\text{H}_2\text{SO}_4$ reduction of the naturally occurring *N*-oxide gave **1** as the major product, and this co-chromatographed with an authentic sample.

The presence of oxidation products in an extract raises the question as to whether or not the component is, in fact, an artifact. In this instance direct tlc examination of freshly collected and extracted leaf material indicated the *N*-oxide to be present.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were determined on a Kofler hot-stage and are uncorrected. Ir spectra were recorded on a Beckmann spectrophotometer and uv spectra on a Hitachi model 200-20 instrument. Eims were obtained on an AE1-MS 12 Instrument via a VG-display data acquisition system. ^1H - and ^{13}C -nmr spectra were recorded for CDCl_3 solutions on a Bruker Am 500 spectrometer at 500 and 125.7 MHz, respectively, or ^1H spectra on a Bruker WP 80 (80 MHz). Resonances are referenced to TMS.

PLANT MATERIAL.—Leaves from *A. perakensis* were collected from the Sungkai Forest Reserve, in Central Peninsula Malaysia, and air-dried. Voucher specimens designated as "B10" were prepared and deposited in the herbarium, Universiti Pertanian Malaysia. Air-dried leaves (4 kg) were ground to a fine powder and extracted as previously described (3) to give the crude alkaloids (10.7 g, 0.27%) as a brown gum. Preliminary fractionation of this gum by cc (Si gel 230-400 mesh, Merck) gave a polar fraction from which the title compound **2** was isolated by preparative tlc [Si gel, CHCl_3 -MeOH (9:1)] as an amorphous pale yellow solid: uv λ max nm (log ϵ) [EtOH] 236 (3.96), 282 (3.06); ir γ max cm^{-1} (CHCl_3) 1675 (C=O), 1650 (C=C), 1620, 1520 (aromatic), 1250, 1225, 1175, 1125, 750; ^1H nmr δ 6.84 (s, 1H), 6.63 (s, 1H), 6.59 (s, 1H), 6.51 (s, 1H), 4.36 (br s, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.80 (s, 3H), 3.48 (dd, $J=6, 19.1$ Hz, 1H), 3.41 (s, 3H), 3.32 (d, $J=19.1$ Hz, 1H), 3.20 (ddd, 2H), 2.75 (ddd, 1H), 1.85 (ddd, 1H); eims m/z (%) $[\text{M}]^+$ 357 (6), 341 (11), 326 (5), 298 (20), 285 (25), 284 (100), 283 (14), 269 (24), 256 (18), 255 (14), 241 (26).

TABLE 1. Comparison of ^{13}C nmr Data of *N*-Methyl-2,3,6-trimethoxymorphinandien-7-one [**1**] (7) and Its *N*-Oxide [**2**].

Assignment	Compound	
	1 (7)	2
C-1	110.39	110.99
C-2	148.00	149.57 ^a
C-3	148.35	149.58 ^a
C-4	108.63	109.50
C-5	118.81	117.58
C-6	151.39	152.50
C-7	180.80	180.34
C-8	122.15	124.38
C-9	60.89	76.30
C-10	32.63	36.01 ^b
C-11	128.76	127.46 ^c
C-12	129.99	130.65 ^c
C-13	42.29	41.08
C-14	161.75	155.94
C-15	41.18	37.30 ^b
C-16	45.68	60.52
N-Me	41.76	57.98
2-OMe ^d	56.33	56.98
3-OMe ^d	55.86	56.64
6-OMe	55.10	55.92

^{a-d}These assignments are not unambiguous and may be reversed.

THOXYMORPHINANDIEN-7-ONE [1].—*N*-Methyl-2,3,6-trimethoxymorphinandien-7-one (59 mg) in EtOH (4 ml) was oxidized with H₂O₂ (30%, 0.4 ml) at room temperature for 2 days. Excess H₂O₂ was destroyed by addition of a small amount of MnO₂ with intermittent shaking until the evolution of gas had ceased (8). The mixture was filtered and the filtrate evaporated under reduced pressure. The crude product (51 mg) was subjected to tlc [Si gel, CHCl₃-MeOH (9:1)] to give *N*-methyl-2,3,6-trimethoxymorphinandien-7-one *N*-oxide (32 mg, 52%). Comparison of the synthetic *N*-oxide with the naturally occurring material by tlc, nmr, ir, uv, and eims analyses showed them to be identical.

REDUCTION OF *N*-METHYL-2,3,6-TRIMETHOXYMORPHINANDIEN-7-ONE *N*-OXIDE [2].—A sample of the naturally occurring *N*-methyl-2,3,6-trimethoxymorphinandien-7-one *N*-oxide (37 mg) was dissolved in 2 N H₂SO₄ (5 ml), Zn powder (0.4 g) was added, and the mixture was stirred at room temperature for 5 h. The solution was filtered, diluted with H₂O, basified with anhydrous Na₂CO₃, and extracted with CHCl₃ (3 × 50 ml). After drying, the CHCl₃ was evaporated to give the crude product mixture (20 mg) which was examined by tlc [Si gel, CHCl₃-MeOH (9:1)]. The major component cochromatographed with *N*-methyl-2,3,6-trimethoxymorphinandien-7-one.

ACKNOWLEDGMENTS

The authors wish to thank the International Foundation for Science (IFS) for financial assistance (F/987-1) and The Network for the Chemis-

try of Biologically Important Natural Products, an activity of the International Development Program of Australian Universities and Colleges, for its support. We also thank Prof. J.R. Cannon and Dr. L. Byrne (University of Western Australia) for helpful discussions.

LITERATURE CITED

1. I.H. Burkill, "A Dictionary of the Economic Products of the Malay Peninsula," Ministry of Agriculture and Cooperatives, Kuala Lumpur, 1966.
2. N.H. Lajis, L.B. Din, M.W. Samsudin, A.L. Mohamed, R. Kiew, and R.F. Toia, "Aspects of Natural Product Chemistry—The Phytochemical Survey." Proceedings of a Workshop, 22-24 February 1985, Department of Chemistry, Universiti Pertanian Malaysia, Serdang, Selangor, Malaysia, 1985.
3. N.H. Lajis, Z. Mahmud, L.B. Din, and R.F. Toia, *Pertanika*, **12**, 421 (1989).
4. D.S. Bhakuni and S.C. Jain, *Tetrahedron*, **36**, 3107 (1980).
5. A.N. Tackie, D. Dwuma Badu, J.E. Knapp, D.J. Slatkin, and P.L. Schiff Jr., *Phytochemistry*, **13**, 2885 (1974).
6. M. Sivakumarm and K.W. Gopinath, *Indian J. Chem.*, **14B**, 150 (1976).
7. F. Roblot, R. Hocquemiller, and A. Cave, *Bull. Soc. Chim. Fr.*, **3-4** (Pt. 2), 139 (1984).
8. C.C.J. Culvenor, I.J. Drummond, and J.R. Price, *Aust. J. Chem.*, **7**, 277 (1954).

Received 23 July 1990