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NARCEINONE, AN ALKALOID FROM *PAPAVER SOMNIFERUM**

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Key Word Index—*Papaver somniferum*; Papaveraceae; alkaloids; narceine; narceinone; biomimetic conversion.

Abstract—Besides narceine, a new secophthalideisoquinoline alkaloid, narceinone, has been identified in the unlanced dried capsules of *Papaver somniferum* as 14-oxonarceine from spectral analysis and by the biomimetic oxidation of narceine.

INTRODUCTION

Papaver somniferum which elaborates several alkaloids of medicinal importance [1] has been investigated by several workers with the isolation of more than 40 alkaloids [2]. Due to morphological, genetic and ecological variations, *P. somniferum* exists in several chemical races [3–5] which are potential sources of novel alkaloids. A new strain of *P. somniferum* with enhanced alkaloid content was developed by the Plant Breeding Section of this Institute. In continuation of the programme for screening medicinally important plants [6], the present authors undertook the chemical investigation of the unlanced husk of this new strain of *P. somniferum*, collected from the Institute farm, Lucknow, and the investigation led to the isolation of a new alkaloid narceinone (**2**) together with other known alkaloids including narceine. Narceinone is the fourth example of the occurrence of diketosecophthalideisoquinoline alkaloids in nature [7].

RESULTS AND DISCUSSION

By pH gradient and chromatographic methods narceinone (**2**) was isolated as crystalline compound (MeOH), mp 162°, $C_{23}H_{25}O_9N$ ($[M]^+$ *m/z* 459) and it gave a positive Dragendorff's test for alkaloids. Its IR spectrum showed a band at 1660 cm^{-1} (conjugated C=O) and the UV spectral data [234 (sh), 264, 270, 288 (sh) nm] are characteristic of secophthalideisoquinoline alkaloids. The ^{13}C chemical shift values of C-5, C-6, C-8, C-13 and C-14 of **2** at δ28.55, 57.32, 171.05, 199.20 and 199.22, respectively, were also indicative of the presence of a diketoacid possessing a secophthalideisoquinoline structure in **2**. The ^1H NMR spectrum of **2** showed clearly the presence of an *N*, *N*-dimethylaminoethyl group (δ2.75, *s*, 6H; δ2.9–3.25, *m*, 4H), a methylenedioxy group (δ5.80, *s*, 2H), three methoxyl groups (δ3.90, *s*, 3H; δ3.85, *s*, 3H; δ3.80, *s*, 3H) and aromatic protons (δ6.36, *s*, 1H; δ6.88, *d*, 1H, $J=9$ Hz; δ7.42, *d*, 1H, $J=9$ Hz) similar to those of narceine **1**. The above spectral data together with the absence of a signal at δ4.20 (^1H NMR) in narceinone corroborate structure **2** in which C-14 is oxidized to an oxo group ($CH_2 \rightarrow CO$).

Furthermore, narceinone was synthesized by oxidation of **2** in a biomimetic way using methanolic alkali according to the procedure of Shamma *et al.* [8]. Compound **2** is the first natural occurrence of the 13,14-diketosecophthalideisoquinolene class of alkaloids having oxygenation at C-1. Formation of this novel alkaloid **2** in *P. somniferum* could be visualized following the series narcotine · · · → narceine · · · → narceinone. *Papaver somniferum* was exracted with different solvents (e.g. MeOH, 2% HOAc–MeOH and EtOH) and narceinone (**2**) was found to be present in all extracts (TLC and ^1H NMR). Narceine (**1**) remained unchanged throughout the isolation procedure used for **2**. Thus, **2** is a secondary metabolite of *P. somniferum* and not an artefact.

EXPERIMENTAL

NMR: 80 MHz; δvalues; solvents DMSO-d_6, CD_3OD; mps uncorr. TLC was developed on silica gel and spots were visualized by spraying with Dragendorff's reagent. The plant material was collected from the CIMAP farm, Lucknow.

Extraction. Fresh powdered unlanced husks of *P. somniferum* (1.3 kg) were extracted in the cold with MeOH (7 × 2 l). After concn under red pres., the residue was acidified with 200 ml of 3% HOAc and filtered. The filtrate was defatted with *n*-hexane and then subjected to pH gradient extraction (pH 3–6.5) using $CHCl_3$ as solvent. The whole soln was then basified to pH 8.5 with 25% NH_3 soln and the basic soln extd with $CHCl_3$ and *n*-BuOH, successively.

Isolation. The *n*-BuOH extract was chromatographed over neutral Al_2O_3 and 100 fractions of 250 ml each were collected using solvent and solvent mixtures of increasing polarities. Fractions were mixed together according to their TLC composition.

Narceine **1**. The earlier $CHCl_3$–MeOH (9:1) fractions afforded a pale brown mass which on further purification by Al_2O_3 CC afforded **1**, crystallizing from $CHCl_3$–MeOH as needles

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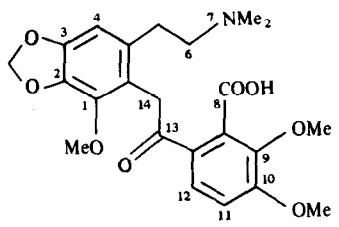

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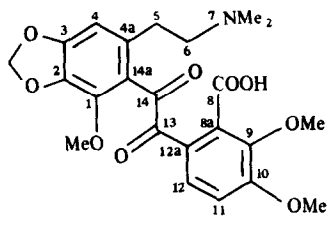

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(50 mg), mp 152°; TLC (silica gel): R_f 0.35 ($CHCl_3$–MeOH, 9:1); IR ν_{max}^{KBr} cm^{-1}: 1660, 1560, 1365, 1235, 1040, 980; UV λ_{max}^{MeOH} nm: 270; ^1H NMR (CD_3OD, 80 MHz): δ2.75 (6H, *s*, *N*-methyls), 2.85–3.30 (4H, *m*, H_2-5 and H_2-6), 3.78 (9H, *br s*, 3 × OMe), 4.20 (2H, *s*, H_2-14), 5.80 (2H, *s*, CH_2<O,O>), 6.35 (1H, *s*, H-4), 6.88 1H, *d*, *J* = 9 Hz, H-12) and 7.45 (1H, *d*, *J* = 9 Hz, H-11); ^{13}C NMR (CD_3OD, 20 MHz): δ199.44 (C-13), 170.45 (C-8), 155.00 (C-10), 147.74 (C-9), 143.78 (C-3), 141.94 (C-1), 135.50, 130.50, 130.04 (C-2, C-4a, C-12a & C-14a), 123.76 (C-12), 119.27 (C-8a), 110.45 (C-11), 103.97 (C-4), 100.60 (CH_2<O,O>), 60.70, 59.41, 55.84 (3 × OMe), 57.21 (C-6), 41.81 (N-Me) and 28.61 (C-5); MS: *m/z* (rel int.%), 445 $[M]^+$ (0.5), 427 (6.50), 58 (100).

Narceinone **2**. After the isolation of narceine, the later $CHCl_3$–MeOH (9:1) fractions yielded a brown crystalline mass which was purified by Al_2O_3 CC to afford a crystalline compound from MeOH (40 mg); TLC (silica gel): R_f 0.32 ($CHCl_3$–MeOH, 9:1); IR ν_{max}^{KBr} cm^{-1}: 3340, 1660, 1560, 1455, 1235, 1040, 980; UV λ_{max}^{MeOH} nm: 234(sh), 264, 270, 288(sh); ^{13}C NMR (CD_3OD, 20 MHz); δ199.20, 199.22 (C-13 and C-14), 171.05 (C-8), 155.26 (C-10), 148.02 (C-9), 144.02 (C-3), 142.01 (C-1), 135.86, 135.50, 130.50, 130.04 (C-2, C-4a, C-12a & C-14a), 124.06 (C-12), 119.33 (C-8a), 110.56 (C-11), 104.12 (C-4), 100.81 (CH_2<O⁻,O⁻>), 60.84, 59.63, 56.00 (3 × OMe), 57.32 (C-6), 41.92 (N-Me) and 28.55 (C-5); MS: *m/z* (rel. int. %): 459 $[M]^+$ (13.3), 58(100).

Elemental analysis: found C, 60.10; H, 5.33; N, 3.10; $C_{23}H_{25}O_9N$ requires C, 60.13; H, 5.45; N, 3.05%.

Oxidation of narceine to narceinone. Narceine (10 mg) was stirred with 10% NaOH soln (MeOH–H_2O, 1:1, 20 ml) for 24 hr, and after usual work-up, the product was found to be identical with narceinone (**2**) in all respects (mp, IR, ^1H NMR).

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