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THEBAINE METHOCHLORIDE FROM *PAPAVER BRACTEATUM**

HASSO RÖNSCH† and WOLFGANG SCHADE‡

Academy of Sciences of the GDR, Research Centre of Molecular Biology and Medicine,† Institute for Plant Biochemistry, 402 Halle/S., Weinberg, GDR; ‡ Central Institute for Microbiology and Experimental Therapy, 69 Jena, Beuthenbergstr. 11, GDR

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Key Word Index—*Papaver bracteatum*; Papaveraceae; scarlet poppy; morphine alkaloids; thebaine methochloride; high resolution MS.

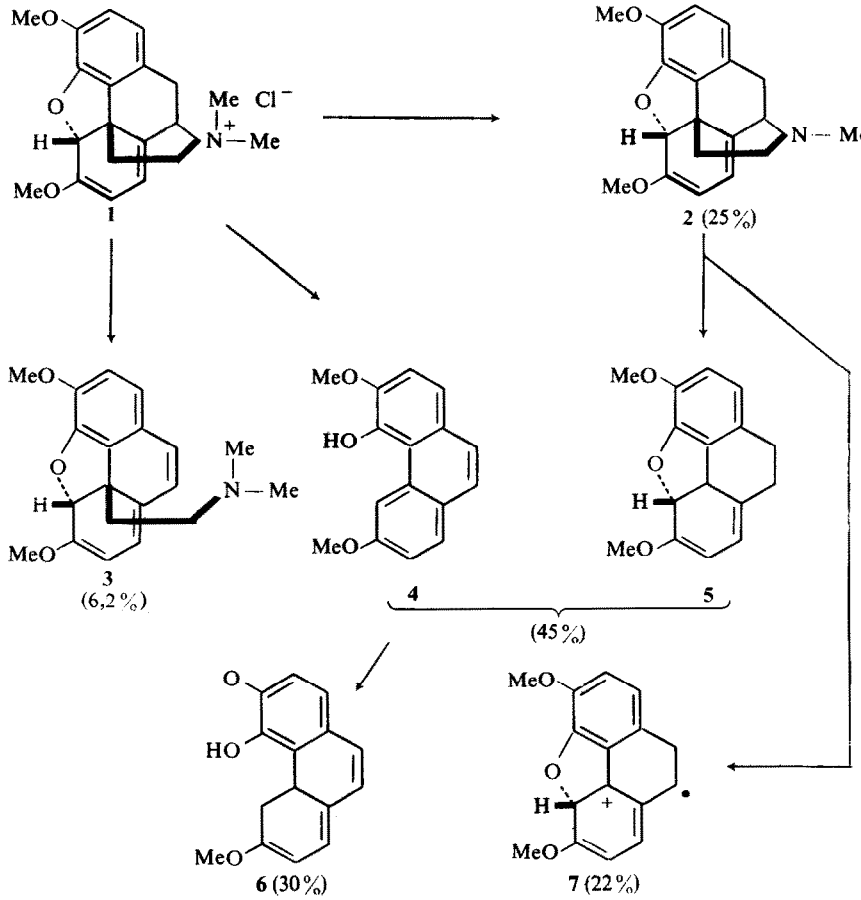
With regard to the continuing interest in thebaine readily available from *Papaver bracteatum* Lindl. [2–4], which a UNO working group [5] wants to substitute for *P. somniferum*, we wish to report that a quaternary thebaine derivative can accompany this morphine alkaloid.

A highly polar substance encountered in crude alkaloids during studies on the biosynthesis of alpinigenine [6], was separated from both thebaine and alpinigenine [1] using chromatography on low-activity alumina. After ion exchange, it was characterized as thebaine methochloride (**1**). Naturally occurring quaternary morphine alkaloids are for instance the thebaine *N*-oxides detected in *P. bracteatum* recently [7]. In the aerial plant material harvested when alkaloid synthesis is maximal, i.e. shortly after the end of flowering, the highest content of **1** was 0.14% dry wt. But the yield obtained from roots in autumn, where thebaine (**2**) is accumulated, did not exceed 0.04% dry wt, and only traces were detected in heads, leaves and stems at the time of seed harvest.

It should be noted that the plant material used was found to be remarkably uniform and to correspond in important details to the original botanical description given by Lindley. The alpinigenine as well as the thebaine strains, both of which contain **1**, distinctly differ from *P. orientale* L. [2, 4, 8, 9].

The mass spectrum of **1** is best rationalized by assuming the isolated natural product to be a quaternary derivative of thebaine (**2**) that simultaneously undergoes thermal degradation by two routes [10]. The cleaving of methyl chloride leads to thebaine (**2**) whereas thermal Hofmann degradation results in thebaimethine (**3**), both of which were identified by high resolution MS (see Scheme 1).

* Part XIII in the series "*Papaver bracteatum*". For part XII see ref. [1].



Scheme 1. MS of thebaine methochloride (**1**).

The rather complex spectrum of **1** shows the individual peaks also produced, if **2** and **3** were separately analysed [11, 12]. The appearance of the fragment ion **6** indicates that there must be an appreciable contribution of thermally formed thebenol (**4**) to the ion *m/e* 254.0957. The latter should also represent the species **5** formed from **2** which is, however, much less intense in the spectrum of thebaine [13]. The signal at *m/e* 255 is a narrow-distant doublet consisting of the ^{13}C-satellites of **4** and **5** in addition to a low-intensity fragment ion to be presumably visualized as **7**, which is among the main peaks in the mass spectrum of **2** [13]. Unfortunately, an exact mass determination was impossible.

Thebaine methochloride was prepared from thebaine and found to be identical with its natural counterpart (see Experimental).

EXPERIMENTAL

Isolation of thebaine methochloride (**1**). The plant material was the same as in earlier investigations [1, 2, 6]. Aerial parts of *P. bracteatum* plants (unripe heads, green leaves and upper halves of stems) were harvested shortly after the end of flowering (e.g. at the end of June), cut and dried at 80°. After sifting the seeds, the material was ground and subjected to usual work-up as described [1] to afford 7.2 g crude alkaloid. On TLC at Al_2O_3 using $CHCl_3$–MeOH (4:1 + 1% aq. NH_3) **1** showed R_f 0.49 whereas **2** + alpinigenine run with the front. A soln of crude alkaloid in $CHCl_3$–MeOH (19:1) was applied to a column prepared from 360 g Al_2O_3 (Merck, 10% H_2O) in the same solvent, which was also used to elute the tertiary bases (3.8 g in 600 ml). 1.5 l. $CHCl_3$–MeOH (9:1) gave 2.6 g **1** as a brownish powder, which was purified by Soxhlet extraction with Me_2CO. The crystalline product, not sharply melting (2.1 g; 0.14% dry wt), was dissolved in 100 ml H_2O and then passed through 25 ml Dowex 1 × 4 OH^--form. The filtrate was neutralized with dil. HCl, the solvent evapd to dryness and residue crystallized from Me_2CO–H_2O, needles, mp 188–190°, $[\alpha]_D^{20}$ −125.8° (MeOH; *c* 0.81): IR (dried at 136°/1 mm Hg), ν_{max}^{nujol} cm^{-1}: 1635, 1672 and 1708 (enol ether); 3380–3430 (H_2O); UV: λ_{max}^{EtOH} nm (log ε): 214(4.41), 226(4.42), 285(4.22); MS (probe) 75 eV *m/e* (rel. int.): 325.1675 [M^+ −HCl, **3**, calc. for $C_{20}H_{23}NO_3$: 325.1678] (6.0), 311.1532 [M^+ $-CH_3Cl$, **2**, calc. for $C_{19}H_{21}NO_3$: 311.1521] (23), 296.1305 [**2** $-CH_3$, calc. for $C_{18}H_{18}NO_3$: 296.1287] (7.0), 280.1113 [**3** $-HN(CH_3)_2$, calc. for $C_{18}H_{16}O_3$: 280.1099] (6.0), 254.0957 [**4** + **5**, calc. for $C_{16}H_{14}O_3$: 254.0943] (49), 255 [**7**] (10), 239.0701 [**6**, calc. for $C_{15}H_{11}O_3$: 239.0708] (31), 72.0817 [calc. for CH_3—CH=$N^+(CH_3)_2$: 72.0813] (23), 58.0673 [calc. for CH_2=N^+ $(CH_3)_2$: 58.0657] (100), 50.1130 [calc. for CH_3Cl: 50.1095] (80); ^1H NMR (60 MHz, D_2O, 2,2-dimethyl-2-silapentane-5-sulfonic acid): δ 7.00 (2H, *s*, aromat. H), 6.25 (1H, *d*, *J* = 7 Hz, C-7), 5.72 (1H, *s*, C-5), 5.41 (1H, *d*, *J* = 7 Hz, C-8), 3.95 (3H, *s*, CH_3OAr), 3.76 (3H, *s*, CH_3OC-6), 3.53 + 3.42 (6H, 2*s*, $N^+(CH_3)_2$), 2.91 (2H, *d*, *J* = 8 Hz, C-13), 1.41 (1H, *t*, *J* = 8 Hz, C-14). (Found: C, 60.6; H, 6.9; N, 3.5. $C_{26}H_{24}ClNO_3 + 2H_2O$ requires: C, 60.4; H, 7.1; N, 3.5%).

Preparation of **1** *from thebaine* (**2**). 1 *g* **2** in 15 ml MeOH and 3 ml CH_3I was heated under reflux for 2 hr. On evaporating the solvents an oily product was obtained which was transformed via Dowex (see above) into the methochloride **1**, needles from Me_2CO–H_2O: mp 190–192° $[\alpha]_D^{21}$ +124.9° (MeOH, *c* 0.85). There was no depression in the mmp performed with **1** obtained from plants. The identity of the two products was confirmed by the IR and MS spectra.

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