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ADLUMIDICEINE AND ADLUMICEINE: NEW ALKALOIDS OF NARCEINE TYPE*

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Key Word Index—*Papaver rhoeas*; *Corydalis sempervirens*; Papaveraceae; keto acids; enol lactone; quaternary salts of phthalideisoquinoline alkaloids.

Abstract—The structures of new alkaloids of narceine type, adlumidiceine (II), adlumiceine (III), and enol lactone of adlumidiceine (IV), isolated from *Papaver rhoeas* L. and *Corydalis sempervirens* (L.) Pers. (Papaveraceae), were determined by PMR, MS and IR spectra.

WHILE carrying out a systematic investigation of the alkaloids of the plant family Papaveraceae, we have studied the plants *Papaver rhoeas* L. and *Corydalis sempervirens* (L.) Pers. Column chromatography on alumina ($CHCl_3$–MeOH, 21:4) of the extract from the species *P. rhoeas* L. afforded a new alkaloid called adlumidiceine, m.p. 244–246° (from MeOH), [λ_{max}^{EtOH} nm (log ϵ) 232sh (4·14), 294 (3·87) and 306sh (3·75); $\lambda_{max}^{0\cdot05\text{ M ethanolic HCl}}$ 222sh (4·21), 295 (3·73), 316 (3·74); $\lambda_{max}^{0\cdot05\text{ M ethanolic NaOH}}$ 230 (4·08), 289 (3·82), 307sh (3·72)] besides rhoeadine, rhoeagenine, isorhoeagenine, isorhoeagenine-glucoside, the papaverrubines-*A* and -*E*, (—)-*N*-methylstylopine and coptisine. The PMR spectrum of adlumidiceine in CD_3COOD exhibited a six proton singlet at δ 2·88 which was assigned to the $N(Me)_2$ group and a multiplet at δ 2·8–3·5 (4H) attributable to the $Ar–CH_2–CH_2–N$ fragment. The broad singlet at δ 4·00 (2H) can be assigned to an $Ar–CH_2–CO$ fragment, the two singlets at δ 5·83 (2H) and 6·03 (2H) correspond to the OCH_2O groups on rings A and D. The singlets at δ 6·57 (1H), 6·70 (1H) and the doublets at δ 6·88 (1H), 7·21 (1H) (J_{ortho} 8·5 Hz) are attributable to the C5, C8, C5′ and C6′ aromatic protons. The IR spectrum in KBr showed the carbonyl frequency of a carboxylic group at 1691 cm^{-1} (dimer) and aromatic double bond peaks at 1609 and 1585 cm^{-1}; the spectrum resembled that of narceine (I) (Ref. 1). In the MS of adlumidiceine, the molecular ion is absent. The peak of the highest mass at 381·1211 arises from the ionized molecule by loss of water and corresponds to the respective enol lactone $C_{21}H_{19}NO_6$ (th. 381·1212). The MS with fragments at *m/e* 336 [$C_{19}H_{12}O_6$; M-(H_2O + $NHMe_2$)], 204 ($C_{12}H_{14}NO_2$; *a*: $R_1 + R_2 = O_2CH_2$),‡ 177 ($C_9H_5O_4$; *b*) and

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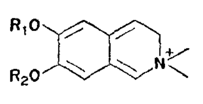
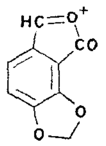
‡ The mechanism of the formation of this ion is discussed in Ref.3.

[1] HOLUBEK, J. and ŠTROUF, O. (1966) *Spectral Data and Physical Constants of Alkaloids*, Vol. II/370. Czechoslovak Academy of Sciences, Prague.

58 ($CH_2{=}NMe_2$) bears analogy to the MS of narceine[2] and to those of the recently studied[3] stilbene type methines of benzylisoquinoline alkaloids. On the basis of these data, adlumidiceine is attributable the structure II.



a



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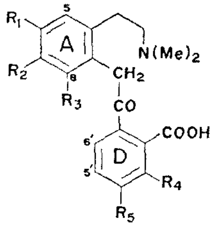
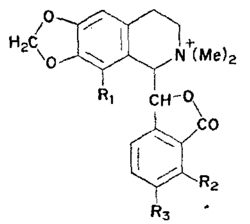
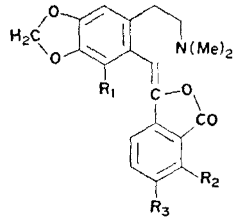


(I) $R_1 + R_2 = OCH_2O$; $R_3 = R_4 = R_5 = OMe$
(II) $R_1 + R_2 = R_4 + R_5 = OCH_2O$; $R_3 = H$
(III) $R_1 = R_2 = OMe$; $R_3 = H$; $R_4 + R_5 = OCH_2O$



(V) $R_1 = H$; $R_2 + R_3 = OCH_2O$
(VI) $R_1 = R_2 = R_3 = OMe$



(IV) $R_1 = H$; $R_2 + R_3 = OCH_2O$
(VII) $R_1 = R_2 = R_3 = OMe$

Adlumidiceine (II) was also isolated from *C. sempervirens* along with (—)-adlumine, bicuculine, capnoidine, protopine, oxysanguinarine and coptisine. Furthermore, a crystalline product of m.p. 222–228° (from MeOH) was obtained (column chromatography on alumina; $CHCl_3$–MeOH, 21:4) which on PC and TLC (silica gel, alumina, different solvent systems) gave only one spot. The PMR and MS spectra showed that it is a mixture in the ratio of about 1:1 of adlumidiceine (II) with substance III which we named adlumiceine. In the PMR spectrum of the mixture in CD_3COOD, the chemical shifts of the signals assigned to the N-$(Me)_2$, Ar–CH_2–CH_2–N, Ar–CH_2–CO, OCH_2O (ring D) groups and to C5′, C6′ aromatic protons were in agreement with those of II. The two singlets at δ 3·66 and 3·75 related to the methoxyl groups (ring A); the singlets at δ 6·60 and 6·77 are attributable to the C5 and C8 aromatic protons. The MS of the mixture showed besides the peaks of II the peaks of adlumiceine (III) at 397·1526 ($C_{22}H_{23}NO_6$, th. 397·1526; M-18), 352 [M-($H_2O + NHMe_2$)] and 220 ($C_{13}H_{18}NO_2$; *a*: $R_1 = R_2 = Me$). The fragments of mass 177 ($C_9H_5O_4$; *b*) and 58 ($CH_2{=}NMe_2$) are assumed to belong to both II and III. In the UV spectra of the compounds II and III, the position of the longest wavelength band corresponds to those of the similarly substituted benzoic or phthalic acids.[4]

Besides the alkaloids II and III, the plant *C. sempervirens* yielded a substance (column chromatography on alumina; $CHCl_3$) of m.p. 200–203° (from Et_2O), λ_{max}^{EtOH} nm ($\log \epsilon$) 224 (4·45), 238sh (4·39), 306 (4·14) and 388 (4·26)). The IR spectrum in KBr showed a strong band at 1785 cm^{-1} which is typical of the carbonyl frequency of a 5-membered lactone grouping.[5] In the PMR spectrum in $CDCl_3$, the singlet at δ 2·20 (6H) is assigned to the $N(Me)_2$ group and the multiplet at δ 2·6–3·0 (4H) to the Ar–CH_2–CH_2–N fragment. The two singlets at δ 6·00 (2H) and 6·20 (2H) are attributable to the methylenedioxy groups

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[2] DOLEJŠ, L. and PREININGER, V. unpublished results.

[3] DOLEJŠ, L. and SLAVÍK, J. (1973) *Org. Mass Spectros.* in press.

[4] ŠANTAVÝ, F., HRUBAN, L., ŠIMÁNEK, V. and WALTEROVÁ, D. (1970) *Coll. Czech. Chem. Commun.* **35,** 2418.

[5] BELLAMY, L. J. (1968) *Advances in Infrared Group Frequencies*, p. 166, Methuen, London.

on rings A and D. The singlets at δ 6·66 (1H), 6·83 (2H) and two doublets with J_{ortho} 8·0 Hz at δ 6·70 (1H) and 6·93 (1H) are ascribed to the four aromatic and one olefinic protons. The MS of this compound parallels that of II. On the basis of these data, structure IV has been assigned to the isolated enol lactone of adlumidiceine. This enol lactone IV has also not been known as yet. A compound identical with IV (from PMR, UV and IR spectra) has been prepared by alkalinization of the aqueous solution of capnoidine methiodide (V) with sodium hydroxide to pH ~14.

From the alkaloids of narceine type, only narceine (I) was found[6] in nature. The Hofmann degradation of narcotine methiodide (VI) affords[7] narceine (I) via the enol lactone VII. The present enol lactone IV and the keto acids II and III indicate that the plants contain quaternary phthalideisoquinoline alkaloids. From the experiments it is to be seen that in alkaline medium these alkaloids pass very easily into the corresponding enol lactones which can be converted into the keto acids of the narceine type.

Quaternary bases of alkaloids of the isoquinoline type have been frequently found in plants of the Papaveraceae; in recent years, Slavík *et al.*[8–10] have isolated the alkaloid californidine, a quaternary base of the pavine type and numerous *N*-methyltetrahydroprotoberberinium alkaloids.

EXPERIMENTAL

For the isolation of alkaloids see Ref. 11. The m.ps have been determined on the Kofler block and are uncorrected. The UV spectra were measured on a Unicam SP. 700, the IR spectra on an Infrascan H-900, the PMR spectra on a Varian T-60 (tetramethylsilane as internal standard), and the MS on an AEI MS 902 instrument.

Capnoidine methiodide (V). Capnoidine (60 mg) was refluxed in a mixture of ACCN and MeI (1:1) for 12 hr. After removal of the solvent by distillation, the compound V, m.p. 200–202° (from MeOH) was obtained in quantitative yield. λ_{max}^{EtOH} nm (log ε) 222sh (4·42), 237sh (3·93), 295 (3·68), 326 (3·68); IR (KBr) 1765 cm^{-1} (5-membered lactone grouping).

The enol lactone of capnoidine. The methiodide V (33 mg) was dissolved in 4 ml of H_2O, made alkaline with 20% NaOH to pH ~14 and extracted with Et_2O; yield 8·5 mg. The IR and PMR spectra showed that this substance of m.p. 200–203° (from Et_2O) is identical with the enol lactone of adlumidiceine (IV).

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[6] Pelletier, P. J. (1832) *Ann. Chim. Phys.* **50**, 240, 262.
[7] Freund, M. and Frankforter, G. B. (1893) *Ann. Chem.* **277**, 20.
[8] Slavík, J., Slavíková, L. and Haisová, K. (1967) *Coll. Czech. Chem. Commun.* **32**, 4420.
[9] Slavík, J., Dolejš, L. and Sedmera, P. (1970) *Coll. Czech. Chem. Commun.* **35**, 2597.
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[11] Preininger, V., Tošnarová, V. and Šantavý, F. (1971) *Planta Med.* **20**, 70.