DIMERIC PYRROLINE ALKALOIDS FROM *Lilium candium* L.

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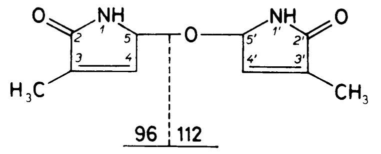
Dimeric compounds 5,5′-oxydi(3-methyl-3-pyrrolin-2-one) and 5-hydroxy-3-methyl-1-(3′-methyl-2′-oxo-3′-pyrrolin-5′-yl)-3-pyrrolin-2-one were isolated from bulbs of *Lilium candidum* L., family *Liliaceae*. Structure of these compounds has been confirmed by spectral measurements. The ether link between two substituted pyrroline rings represents a new type of dimeric alkaloids.

In our previous communications we described the isolation of organic acids[1,2], a flavone alkaloid[3], jatropham[4], several substituted dimeric γ-lactam compounds[5], the flavone kempherol, its derivative 8-(3-methylsuccinoyl)kempherol[6], (2-phenylethyl)-α-L-arabinopyranosyl-(1→6)-β-D-glucopyranoside, and 2-phenylethyl palmitate[7] from petals of *Lilium candidum* L. From the bulbs we further isolated and identified three pyrroline compounds (jatropham, ethyljatropham and citraconic acid imide)[8].

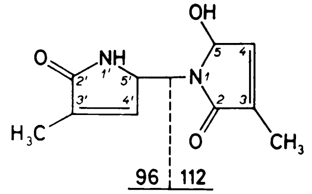
Our present paper concerns the isolation and identification of 5,5′-oxydi(3-methyl-3-pyrrolin-2-one) (*I*) and 5-hydroxy-3-methyl-1-(3′-methyl-2′-oxo-3′-pyrrolin-5′-yl)-3-pyrrolin-2-one (*II*).

The UV spectrum of compound *I* exhibits a maximum at 254 nm indicating the presence of a conjugated carbonyl group. This is confirmed also by the bands at 1 680 and 1 650 cm^{-1} in the IR spectrum. According to its mass spectrum, the compound *I* has a composition $C_{10}H_{12}N_2O_3$ ($M^{+\bullet}$ 208·0835). The main and characteristic fragmentation consists in the cleavage of the ether bond which gives rise to ions of m/z 96 (base peak) and m/z 112. The lability of the ether bond is manifested by the instability of molecular ions (the molecular peak is only tiny). The summary formula corresponds to a dimer which arose from two molecules of jatropham with elimination of water. The ^{13}C NMR spectrum of compound *I* exhibits only five signals, indicating that the molecule contains an element of symmetry. Comparison of ^{13}C chemical shifts of the C-5 atoms in jatropham[4] (δ 79·2) and compound *I* (δ 83·3) shows that both the jatropham units are bonded via the oxygen atom on C-5. An analogous change was observed[8] also with ethyljatropham (δ 85·5). The existence of the ether bond between the carbon atoms C-5 and C-5′ is further confirmed by the coupling constant J(H-5, C-5′) = J(H-5′, C-5) = 5·2 Hz.

The IR spectrum of compound *II* contains bands at 1 680 and 1 645 cm^{-1} which, together with the UV maximum at 254 nm, indicate the presence of a conjugated carbonyl group. The compound has a molecular ion $M^{+\bullet}$ 208·0842 corresponding to the composition $C_{10}H_{12}N_2O_3$. The two most abundant peaks in the mass spectrum (m/z 111 and 96) arise by cleavage of the C—N bond between both rings under elimination of hydrogen in position 5 of 5-hydroxy-2-methyl-3-pyrrolin-2-one, as proven by measurement of the deuterated compound.



I



II

The compound *II* is an isomer of compound *I*. Unlike the ^{1}H NMR spectrum of *I* and jatropham, the ^{1}H NMR spectrum of *II* exhibits signals of six protons or groups of protons and thus it does not contain any element of symmetry. Of these six signals three had chemical shifts very similar to those of jatropham[4]. Contrary to compound *I*, the jatropham units in compound *II* are bonded not via oxygen on C-5 but via the N-1 nitrogen atom and the C-5′ carbon atom. The three signals mentioned belong to the part of the molecule with free hydroxyl group. We have isolated analogous dimers from *Lilium candidum* L. already previously[5]. Characteristic for such dimers are four- or five-bond coupling constants of the protons H-5′ and H-5 or H-5′ and H-4. Both the mentioned interactions have been observed also in the case of compound *II*.

EXPERIMENTAL

The melting points were determined on a Kofler microblock. UV spectra were taken on a UV-VIS (Zeiss, Jena) instrument in methanol, IR spectra on a Perkin–Elmer 477 spectrophotometer by the KBr technique (wavenumbers in cm^{-1}). Mass spectra were obtained with a JEOL MS 100 D and a ZAB-EQ (VG Analytical, Manchester) spectrometers (electron energy 70 eV). NMR spectra were measured on a Bruker AM-300 instrument in CD_3OD, using tetramethylsilane as an internal standard. The chemical shifts are given in ppm (δ-scale), the coupling constants (J) in Hz. Column chromatography was performed on silica gel No 3 (Silpearl) which was modified according to the literature[9], thin-layer chromatography was carried out on Silufol UV 254, 366 nm.

The bulbs of *Lilium candidum* L. (20 000 g) were extracted with 96% and 70% ethanol (3 × 80 l) at room temperature. The obtained extracts were concentrated and freeze-dried at −40°C for 24 h. The obtained extract (1 042 g) was dissolved in 5% hydrochloric acid. The aqueous solution was extracted successively with light petroleum, ether and chloroform, made alkaline (pH 11) and extracted with chloroform and chloroform–ethanol (2 : 1). The compounds present in the chloroform extract (59·8 g) were separated by chromatography on a silica gel column (600 g) in benzene–acetone (8 : 2—7 : 3) and then in acetone. The fractions (à 150 ml) were analyzed by thin-layer chromatography in chloroform–methanol (9 : 1); spots were detected by UV light at 254 nm. Total 348 fractions were collected.

Fractions 104—108 afforded 10 mg of crystalline 5,5′-oxydi(3-methyl-3-pyrrolin-2-one) (*I*), m.p. 213—215°C, R_F 0·52 (chloroform–methanol 8 : 2). UV spectrum, λ_{max}, nm: 254. IR spectrum: 1 700, 1 680, 1 650. Mass spectrum, *m/z* (%): $M^{+\cdot}$ 208·0835 (4) $C_{10}H_{12}N_2O_3$ (calculated 208·0848), 96 (100), 97 (78), 112 (16), 41 (16), 68 (9), 69 (8), 78 (4). ^{1}H NMR spectrum: 6·69 dq, 2 H (H-4, H-4′, *J*(4, 5) = *J*(4′, 5′) = 1·75; *J*(4, 3-CH$_3$) = *J*(4′, 3′-CH$_3$) = 1·7); 5·50 dq, 2 H (H-5, H-5′, *J*(4, 5) = *J*(4′, 5′) = 1·75; *J*(5, 3-CH$_3$) = *J*(5′, 3′-CH$_3$) = 1·3); 1·82 dd, 6 H (3-CH$_3$, 3′-CH$_3$), *J*(5,3-CH$_3$) = *J*(5′, 3′-CH$_3$) = 1·3). ^{13}C NMR spectrum: 175·5 (C-2, C-2′); 140·8 (C-4, C-4′); 138·4 (C-3, C-3′); 83·3 (C-5, C-5′); 10·5 (3-CH$_3$, 3′-CH$_3$).

Fraction 334 gave 20·1 mg of 5-hydroxy-3-methyl-1-(3′-methyl-2′-oxo-3′-pyrrolin-5′-yl)-3-pyrrolin-2-one (*II*), m.p. 194—198°C, R_F 0·49 (chloroform–methanol 8 : 2). UV spectrum, λ_{max}, nm: 254. IR spectrum: 1 700, 1 680, 1 645, 1 450, 1 405, 1 380, 1 205. Mass spectrum, *m/z* (%): $M^{+\cdot}$ 208·0842 (26) $C_{10}H_{12}N_2O_3$ (calculated 208·0848), 111 (100), 97 (11), 96 (78), 69 (15), 68 (12), 41 (30), 39 (15). ^{1}H NMR spectrum: 6·76 dq, 1 H (H-4′, *J*(4′, 5′) = 2·0; *J*(4′, 3′-CH$_3$) = 1·7); 6·64 dqd, 1 H (H-4, *J*(4, 5) = 1·8; *J*(4, 3-CH$_3$) = 1·7; *J*(4, 5′) = 0·4); 5·96 dqdd, 1 H (H-5′, *J*(4′, 5′) = 2·0; *J*(5′, 3′-CH$_3$) = 1·7; *J*(5′, 4) = 0·4; *J*(5′, 5) = 0·3); 5·40 dqd, 1 H (H-5, *J*(4, 5) = 1·8; *J*(5, 3-CH$_3$) = 1·4; *J*(5, 5′) = 0·3); 1·91 dd, 3 H (3′-CH$_3$, *J*(5′, 3′-CH$_3$) = 1·7; *J*(4′, 3′-CH$_3$) = 1·7); 1·85 dd, 3 H (3-CH$_3$, *J*(5, 3-CH$_3$) = 1·4; *J*(4, 3-CH$_3$) = 1·7).

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