On the Photo-Transformation of Ergot Alkaloids

III. Two New Lumi-Ergot Alkaloids

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The preparation and properties of lumiergometrine II and lumiergocristine II have been described.

In work performed by Stoll and Schlientz¹ and by the present author² there has been reported the preparation of all the four lumialkaloids of the ergotamine series and three of the four possible lumialkaloids in each of the ergometrine and ergocristine series. However, the two missing alkaloids had been seen on chromatograms by this author² and now they have been prepared in a crystalline form.

The lumialkaloids in question are obtained in very minute yields on irradiation of the corresponding genuine alkaloids, and the methods of preparation therefore had to be refined. The new procedures are given under "Experimental". The main improvement in the case of ergometrine is the partition chromatographic procedure for the separation, taken from our work on lumisergic acids³. In the case of ergocristine the new method for removing coloured material from the alkaloids has turned out to be of general value in the peptide alkaloid group. Another improvement is here the decrease in ethanol content of the first elutrient in the chromatography. In that way the peak of lumiergocristine II is more completely separated from an impurity, making the substance more readily crystallizable.

EXPERIMENTAL

Lumiergometrine II (and I) from ergometrine

In a quartz flask under N₂ atmosphere a solution of 1 g of ergometrine maleate in 40 ml of M/5 HCl was irradiated by a mercury lamp (Hanovia S4) until the transformation ceased (c. 3 h) as judged from the quotient between the extinctions at 283 and 315 mμ. The blue solution was treated with 0.2 g of sodium phosphate and 10 g of sodium chloride

and the pH adjusted to 8–9 with sodium hydroxide. The alkaloids *etc.* were extracted with 5 × 50 ml of a mixture of ethanol and ether (1 + 2), the extract dried for several hours over desiccated sodium sulphate and finally evaporated to dryness in a vacuum (N₂ atmosphere). The residue was submitted to partition chromatography on celite. Column: 50 × 2.5 cm. Solvent: butanol, benzene and acetic acid 20 % (1 + 1 + 2). The water phase was used as a stationary phase and the organic phase as elutrient. The course of the elution was followed by the colour reaction with *p*-dimethylaminobenzaldehyde, performed as in paper chromatography ^{2,3} on spots of the eluate, which were applied to a sheet of filter paper. After a small fraction, containing, *i. a.*, untransformed ergometrine, two lumialkaloid fractions were obtained, the first one strongly dominating and containing lumiergometrine I, the second one containing lumiergometrine II. The two fractions were separately evaporated to dryness (vacuum, N₂ atmosphere), dissolved in a mixture of ethanol and chloroform (1 + 3) and filtered through a column of alumina, subsequently washed with the same solvent until no alkaloid appeared in the eluate. The solutions were evaporated to dryness again. The residue of lumiergometrine I was dissolved in 2 ml of methanol and treated with 12 ml of ether, when the substance crystallized. The lumiergometrine II was dissolved in 0.5 ml of methanol by heating. On cooling the material crystallized, and the crystallization was made more complete by adding 1 or 2 ml of ether.

The yield of lumiergometrine I was c. 65 % and of lumiergometrine II c. 1 %.

Lumiergometrine II, α -lumiergometrine of Ref², crystallized from methanol in thin needles. In accordance with the loss on drying (100°C, high vacuum) and acidimetric equivalent weight the crystals contained one mole of methanol of crystallization. They melted on the Kofler block very diffusely between 128–138°C under decomposition. The pK_a -value in 20 % ethanol obtained as in Ref² was 7.20. The following constants are given on a dry basis. *Light absorption*: E (1 %, 1 cm) = 189 at 285 $m\mu$ (max) in M/10 HCl. *Optical activity*: $[\alpha]_D^{20} = -19^\circ (\pm 5^\circ)$ in pyridine, $c = 0.4^*$. Sufficient material for elementary analysis was not available.

Lumiergocristine II (and I) from ergocristine

A solution of 1 g of ergocristine in 10 ml of concentrated acetic acid and 90 ml of water was illuminated as described for ergometrine in the previous paragraph. To the green solution was added 30 ml of 5 M sodium hydroxide and then 5 M ammonia to pH 9. The mixture was extracted with 3 × 15 ml of chloroform and the filtered solution evaporated to dryness (vacuum, N₂ atmosphere). The strongly discoloured residue was purified from most of the coloured material by the following procedure. It was weakly heated with 3 × 15 ml of 5 % tartaric acid solution. The liquid was centrifuged or filtered until clear and put into a separator together with 250 ml of ether. 10 ml of 5 M ammonia were added in one portion and the separator immediately rotated until the precipitate had mainly dissolved and only a small residue lay in the interphase. The remaining precipitate and the water solution in the separator were washed with a further 50 ml of ether, and then not only the ether but also as much as possible of the water phase was poured out. The rest was redissolved in 5 % tartaric acid solution and the treatment with ammonia and ether repeated on a smaller scale. The collected ether solutions were dried over desiccated sodium sulphate for several hours, and evaporated to dryness (vacuum, N₂ atmosphere). The residue, now only faintly coloured, was dissolved in 20 ml of methanol by gentle heating, and from this solution pure lumiergocristine I crystallized. The mother liquor was evaporated to dryness, dissolved in absolute chloroform and chromatographed on alumina (60 × 1 cm Al₂O₃). With 0.8 % ethanol in absolute chloroform as elutrient a small fraction of unchanged ergocristine came out first and then two small fractions of transformation products were obtained, the second one containing lumiergocristine II. On changing the elutrient to 5 % ethanol in chloroform another quantity of lumiergocristine I was obtained. The lumiergocristine II was crystallized from methanol.

* Based on one single determination.

The yield of lumiergocristine I was c. 70 % of lumiergocristine II c. 1 %.

Lumiergocristine II, α -lumiergocristine of Ref.², crystallized from methanol in short pillars. In accordance with the small loss on drying (1–2 % at 130°C, high vacuum) the crystals did not contain any solvent of crystallization. On the Kofler block they underwent some sort of transformation at about 70°C and melted at 171–174°C under decomposition. The following constants are calculated on a dry basis. *Light absorption*: E (1 %, 1 cm) = 104 at 285 m μ (max) in M/10 HCl. *Optical rotation*: $[\alpha]_D^{20} = 0^\circ (\pm 3^\circ)$ in pyridine, $c = 0.6$. *Elementary analysis*: Found: C 66.16; H 7.06; O 15.29; N 11.05. Calc. for $C_{31}H_{41}O_4N_5$ (627.7): C 66.96; H 6.58; O 15.29; N 11.16.

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