On the Photo-transformation of Ergot Alkaloids

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The photo-catalyzed transformation of ergot alkaloids has been investigated. The results conform with the conclusion of Stoll and Schlientz that in aqueous solutions the reaction is an addition of water to the double bond of ring D. It is shown here that a prerequisite for the reaction is that the solution contains suitable, strongly polar constituents in sufficient quantities. In water solution hydrogen ions, primary phosphate ions and to a less extent acetate ions are highly active.

Paper chromatography is suggested as a new means for the assignment of configurational relationships within the lumialkaloids. The order of migration on paper is the reverse of that on alumina within every pair of lumialkaloids investigated. Theoretically, identification of the lumilysergic acid obtained on cleavage of a lumialkaloid should be the best way of establishing the connexions between lumi-derivatives from different alkaloid series. Such identifications have been approached here by paper chromatography of the products of alkaline hydrolysis of lumialkaloids and have led to certain conclusions. The spots can be tentatively assigned to the four possible lumilysergic acids.

The fact that the pK_a -values of the lumi-derivatives of ergometrine and ergometrinine are considerably higher than those of the dihydroalkaloids may be explained by axial conformation of the hydroxyl group at C_{10} .

The preparation of lumi-derivatives of ergometrinine, ergocristine and ergocristinine is reported. Physical and chemical data of the new substances are given together with some supplementary findings on the lumi-derivatives of ergometrine, ergotamine and ergotaminine.

It is well known that ergot alkaloids are sensitive to light. This instability is of great importance in alkaloid chemistry and in pharmacy, but until recently it has not been studied in any detail. In this laboratory the subject had been treated for some time ¹, when Stoll and Schlientz ² gave an account of their work in that domain. They concluded that, on illuminating genuine ergot alkaloids in acid water solutions, a molecule of water is added to the double bond in ring D of the lysergic or isolysergic acid, forming new series of alkaloids analogous to the dihydroalkaloids. They distinguished the new derivatives with the prefix lumi-, and in order to indicate the stereoisomeric connexions with corresponding dihydroalkaloids they added the figure I or

II to the names. The preparation of lumi-derivatives of ergometrine, ergotamine and ergotaminine, was described and the usual physical and chemical data of the substances were given.

Genuine alkaloid

Lumialkaloid

The results obtained in this laboratory confirm and enlarge the work of Stoll and Schlientz. Moreover, to some extent the problem has been attacked by us in another way.

I. ON THE EXTERNAL PREREQUISITES FOR THE TRANSFORMATION

Having noticed by chance that transformation occurred very easily in phosphate buffers we studied the influence of different electrolytes on the velocity of the transformation. The results are reported in Figs. 1—4. Practically no transformation occurs in water or in solutions of neutral salts, *e. g.* sodium chloride (Figs. 1 and 3). In acid solutions, however, transformation takes place, and its considerable rate increase in the series of tartaric, phosphoric, hydrochloric acid solutions (Fig. 1) and in the series of phosphate buffers with decreasing pH (Fig. 2) shows that the hydrogen ion activity has an important effect. This conclusion conforms with the extensively accepted theories on the addition to double bonds of for instance hydrogen halides directly or of water by acid catalysis. The electrophilic hydronium ions are thought to be able to attack the electron excess of the double bond³.

However, certain anions, especially primary phosphate ions and to some extent acetate ions, promote the photo-transformation (Figs. 1, 2 and 4). On the other hand chloride, methanesulphonate and primary tartrate ions seem to have little or no effect. The rate variation in the series of phosphate buffers (Fig. 2) is interesting. The effect of the decreasing hydrogen ion concentration is compensated for by the increasing concentration of primary phosphate ions. Not until these begin to disappear above pH 6 does the transformation velocity diminish considerably. Moreover Fig. 3 shows that an increase of primary phosphate concentration enhances the transformation velocity appreciably. No satisfactory theoretical explanation of the influence of the anions has been found.

On irradiating glacial acetic acid solutions of ergot alkaloids we obtained rapid transformations with spectrophotometric characteristics similar to those in aqueous solutions. Judging from paper chromatography (see Section III A)

Fig. 1. Photo-transformation of ergotamine (tartrate) in water solutions of the composition stated in the figure. Irradiation with U.V.-light (max = 366 $m\mu$) at standard distance. Room temperature. The content of unchanged alkaloid was followed spectrophotometrically at 315 $m\mu$.

Fig. 2. Photo-transformation of ergometrine(maleate) in water solutions of the composition stated in the figure. Experimental conditions as in Fig. 1.

Fig. 3. Photo-transformation of ergometrine(maleate) in water solutions of the composition stated in the figure. Experimental conditions as in Fig. 1.

Fig. 4. Photo-transformation of ergometrine(maleate) in water solutions of the composition stated in the figure. Experimental conditions as in Fig. 1.

the transformation products were mainly the same as those obtained in water solutions *. Diluting the acetic acid with water or ether, respectively, we found that the transformation was much faster in the aqueous solution than in the ether solution.

From the above-mentioned facts it is possible to conclude that illumination is only one prerequisite for the transformation; another is that the solution contains suitable, strongly polar constituents in sufficient quantity. Thus in water solutions hydrogen ions, primary phosphate ions and to a less extent acetate ions are highly active.

* In the chromatographic process the transformation products came into contact with water.

II. ON THE PROPERTIES OF THE LUMIALKALOIDS

There are good theoretical and experimental reasons for the opinion that on the addition of water to the double bond of ring D the hydroxyl group goes to C₁₀, thus creating an asymmetric carbon atom. Like the dihydroalkaloids the lumialkaloids should exist in four series, deriving from four stereoisomeric lumilysergic acids, namely, according to Stoll's nomenclature, lumilysergic acid I, and II, lumi*isolysergic* acid I and II. The derivatives of lysergic acid differ from those of *isolysergic* acid by different configuration at C₈, and the substances designated I from those designated II by different configuration at C₁₀.

For the assignment of configurational relationships within the lumialkaloids as well as between the groups of dihydro- and lumialkaloids Stoll and Schlientz² used primarily the following indirect methods: 1) Comparison of the magnitude of the yields, 2) The order of adsorption on alumina, 3) Comparison of the specific optical rotations. In this work also paper chromatography of the lumialkaloids and of the lumilysergic acids obtained from them has been used for the same purposes.

From the beginning of our work we designated the lumialkaloids — regularly appearing in pairs — with the Greek letters α and β after their order of migration on paper chromatograms, the α -component moving more slowly than the β -component. This notation has been extensively used in this paper especially in the experimental part. However, the nomenclature of Stoll and Schlientz² seems more fundamental, and therefore later in this section a key will be given for the translation of our names into that nomenclature.

Already at the beginning of this work paper chromatography revealed that on illuminating a lysergic acid alkaloid only one transformation product appeared in quantities great enough to produce a spot while an *isolysergic* acid alkaloid always caused two spots¹. Working on a preparative scale with chromatography on alumina, however, new small fractions appeared as reported in the experimental section.

Comparing the R_F -values of Tables 2 and 3 with the order of migration on alumina (experimental part of this paper and Ref.²) it is found that the two lumi-derivatives of a certain alkaloid migrate on paper in an order which is the reverse of that on alumina. Paper chromatography seems to be an equally good method for classifying lumialkaloids as chromatography on alumina.

Experimental evidence obtained by Stoll and Schlientz supported the assumption that the substitution of the C₁₀-hydrogen of a pair of dihydroalkaloids for hydroxyl in the corresponding lumialkaloids did not affect the order of migration on alumina. It would have been interesting to investigate if this rule holds true also in paper chromatography but unfortunately the dihydroalkaloids necessary were not available. Stoll and his collaborators⁴ used the different adsorbability on alumina as an argument for assigning definite conformations at C₈ to the different dihydroalkaloids. The paper chromatography of the lumialkaloids shows, however, the uncertainty of such conclusions.

As is well known, epimerization at C₈ takes place easily in the genuine alkaloids but much more slowly after saturation of the double bond of ring D.

It was therefore hoped that alkaline hydrolysis of the lumialkaloids would give the corresponding lumilysergic acids in fairly pure form, serving as a new means for the study of the mutual configurative connexions between the lumialkaloids. Paper chromatography of the lumilysergic acids obtained by alkaline hydrolysis of pure lumialkaloids (see Section III A) showed, however, that matters were not so simple. Thus double spots were obtained from all lumialkaloids tried. As is seen from Fig. 5 the chromatograms were of two different types, β -lumi-ins and α -lumi-ins giving type I (two spots near each other) α -lumi-ins and β -lumi-ins type II (two spots more widely separated). The most reasonable explanation of the two spots is that after all an epimerization at C₈ takes place, this reaction having several parallels in the chemistry of alkaloids ^{6,7}. This prompts to caution in the interpretation of experiments in preparing lumilysergic acids from lumialkaloids by alkaline hydrolysis. The results, however, constitute a proof that the α -lumi-ins and the β -lumi-ins have the same configuration at C₁₀, while β -lumi-ins and α -lumi-ins have the other. Desiring to relate these two groups to the configuration of dihydro-alkaloids at C₁₀ we established that the criteria magnitude of yields, and order of migration on alumina lead to the same conclusion within the lumiergometrine series and lumiergocristine series as Stoll and Schlientz ² came to within the lumiergotamine series. Comparison of specific rotations lead to agreement with the other criteria in the ergocristine series, the ergometrine derivatives, however, giving inconsistent results; though of course this criterion is not to be trusted in the face of all other evidence.

The regularly recurring properties in each of the three series of lumialkaloids show the mutual connexions between the members, clearly reflected and confirmed also by the paper chromatograms, thus giving us a key to the configuration of the lumialkaloids hitherto investigated *.

α -lumi-in	= lumi-in II
β -lumi-in	= lumi-in I
α -lumi-inin	= lumi-inin I
β -lumi-inin	= lumi-inin II

In the light of this the paper chromatograms of the lumilysergic acids obtained on alkaline hydrolysis acquire renewed interest. In most cases the spots were unequal in magnitude, and if it is postulated that the bigger spot of a pair derives from the acid not rearranged at C₈ during hydrolysis it is possible to assign the spots to the four possible lumilysergic acids. This has been done at the bottom of Fig. 5, the perspicuousness of which is diminished by the fact that lumilysergic acid II and lumi~~is~~olysergic acid I do not separate on the paper chromatograms. The interpretation in Fig. 5 is still to be considered as hypothetical but it is supported by the fact that irradiated lysergic acid gives practically only one spot, namely, the one assigned to lumilysergic acid I.

* The key is probably valid also for the lumialkaloids not yet investigated.

In the discussion of the configurations and conformations of ergot alkaloids the pK_a -values have played a certain rôle. Therefore an approach to these constants was made for the fairly watersoluble lumi-derivatives of ergometrine and ergometrinine. In the course of the potentiometric titrations of the equivalent weights (molecular weights), more closely described in the experimental part, we noted the pH's, at which the alkaloids were half-neutralized. These pH-values can be regarded as relative pK_a -values for the acid in the equation $\text{HNCH}_3 \rightleftharpoons \text{H}^+ + \text{NCH}_3$. The figures obtained are recorded in Table 1 together with some values for comparison, partly taken from literature ^{8,9}.

Table 1. Estimated pK_a -values for ergometrine and derivatives. The figures obtained in this work refer to solutions containing 20 % ethanol.

	Obtained in this work	Obtained from literature	
Ergometrine	6.85	6.72 *	
Ergometrinine	7.40	7.26 **	7.38 **
Dihydroergometrine I		7.30 **	7.46 **
β -Lumiergometrine (I)	7.90		
α -Lumiergometrinine (I)	8.15		
β -Lumiergometrinine (II)	8.00		

* Ref.⁸; water solution.

** Ref.⁹; water solution.

Obviously the lumialkaloids are stronger bases than both genuine alkaloids and dihydroalkaloids. This is surprising at first sight because the inductive effect of an OH-group in C_{10} ought to be a weakening of the basicity of the nitrogen atom ³. However, Stenlake ¹⁰ has emphasized the purely electrostatic effect, which negative substituents under favourable steric conditions can exert on the amino-nitrogen of lysergic acid. Stoll and collaborators ⁴, accepting this opinion, have shown that 6-methyl-8-isohydroxyergoline I is a considerably stronger base than 6-methyl-8-hydroxyergoline I, concluding that the hydroxyl group is axial in the first-mentioned substance. C_8 and C_{10} are both equidistant from N_6 in ring D, and therefore the same substituent may have approximately the same influence on N_6 , whether it is situated at C_8 or at C_{10} . Now according to the theories on the conformation of the dihydroalkaloids developed by Cookson ⁵ and by Stoll and his collaborators ⁴ the hydrogen of C_{10} is axial in relation to ring D. Probably the hydroxyl of the lumialkaloids takes the same position, and that explains the comparatively strong basicity of these substances.

III. EXPERIMENTAL

A. Paper chromatography

We used the descending technique, performed at 20–22° C in glass tanks of 22 × 32 × 61 cm with Whatman No. 1 paper in pieces of 54 × 23 cm. Papers with four applications each were kept over-night in the atmosphere of the water-rich phase. To

facilitate equilibration a filter paper moistened with the liquid was fixed in the middle of the container. The pre-treatment of the papers and the development of the chromatograms are described below for the different groups of substances. To visualize the spots after the evaporation of the solvent we used a reagent described by Berg ¹¹, containing 0.5 g of *p*-dimethylaminobenzaldehyde in 5 ml of conc. HCl and 95 ml of ethanol. Fluorescent alkaloids could also be indicated by the U.V.-lamp.

Modifying the solvents suggested by Foster and collaborators ¹² for the separation of ergometrine and ergometrinine, we used benzene, butanol, acetic acid and water in the proportions 2.5:2.5:1:4 for the lumi-derivatives of ergometrine, ergometrinine, lysergic and isolysergic acid. At first considerable tailing was obtained. Shute ¹³ and Munier *et al.* ¹⁴, however, have suggested pretreatment of the papers with neutral salts. In our case a normalization of the spots was achieved by moistening the papers with 0.2 M NaCl and subsequent air-drying.

For paper chromatography of the peptide alkaloids of ergot many procedures have been suggested in recent years *e.g.* ^{11,12,15,16}. From our own investigations on counter current distribution ^{17,18} and from those of Berg on paper chromatography ¹¹ it was known that benzene displays good separating properties on peptide alkaloids. Starting from this fact we found the following combination of solvents useful for the lumi-derivatives of ergotamine, ergotaminine, ergocristine and ergocristinine: benzene, butanol, acetic acid and water (9:1:2:8). The papers were impregnated with sodium chloride as above. Some precautions were necessary because of the great volatility of the solvents. Thus one of the papers in the tank was always run empty, starting 1.5 h before the real chromatogram in order to keep the atmosphere saturated with the solvents.

In Tables 2 and 3 the results of the paper chromatography have been summarized and given as average R_F -values. The R_F -values were not very well reproducible probably because of the high volatility of the solvents. This disadvantage could as usual be overcome by running standard substances for comparison parallel to the test substances.

Alkaline hydrolysis of lumialkaloids was performed on the pattern given in Ref. ⁶. Protected from light about 1 mg of the substance was refluxed for 2 h with 1 ml of a 20 % solution of KOH in 50 % ethanol. After saturation with CO₂ (pH < 7) the solution was quickly evaporated to dryness on the water bath and the residue extracted with a few small portions of absolute ethanol. The filtered ethanol solution was directly applied to the chromatographic paper.

The chromatographic procedure was the same as for the lumiergometrins. Average R_F -values for the lumilysergic acids are given in Fig. 5.

B. The preparation of some lumialkaloids; their physical and chemical properties

For the preparation of lumialkaloids we had comparatively small quantities of genuine alkaloids at our disposal, and therefore some derivatives forming only in minor quantities have not been characterized completely.

Owing to experiences in the transformation velocity, reported in Section I of this paper, the alkaloids were illuminated in water solutions containing a strong acid (hydrochloric or methanesulphonic). For the separation of the reaction mixtures we applied chromatography on alumina, this method having been extensively used by Stoll and his collaborators ^{2,6}.

The elementary analyses have been performed under the direction of Dr. K. J. Karrman in the Analytical Department of the Chemical Institute, University of Lund. The paper chromatographic methods have been described in Section III A of this paper.

Transformation products of ergometrine

A solution of 0.25 g of ergometrine maleate in 10 ml of M/10 HCl was irradiated in a quartz flask under N₂ atmosphere, until the transformation had almost ceased as judged from spectrophotometric measurements of samples drawn; time: *ca.* 8 h; light-source: "Mineralight" U.V.-lamp, the radiation of which was limited to the region of 366 mμ. Some sodium phosphate and 2.5 g of NaCl were added to the liquid, and after adjusting

Table 2. *R_F*-values for ergometrine alkaloids and lumi-derivatives. The chromatographic procedure is described in the text (Section III A).

Ergometrine	0.57	Ergometrinine	0.68
α -Lumiergometrine	0.29	α -Lumiergometrinine	0.37
β -Lumiergometrine	0.36	β -Lumiergometrinine	0.54

Table 3. *R_F*-values for ergotamine and ergocristine alkaloids and lumi-derivatives. The chromatographic procedure is described in the text (Section III A).

Ergotamine	0.85	Ergocristine	>0.90
α -Lumiergotamine	0.25	α -Lumiergocristine	0.59
β -Lumiergotamine	0.54	β -Lumiergocristine	0.79
Ergotaminine	0.69	Ergocristinine	0.89
α -Lumiergotaminine	0.23	α -Lumiergocristinine	0.49
β -Lumiergotaminine	0.68	β -Lumiergocristinine	0.88

the pH to 9 it was extracted with 3×20 ml of a mixture of ethanol and ether (1:2). The extract was evaporated to dryness in a vacuum (N₂ atmosphere). The residue, dissolved in 1 ml of ethanol and 100 ml of absolute chloroform, was transferred to the top of a column of alumina (10–20 g), and gradually eluted with chloroform (ca. 500 ml) containing increasing amounts of ethanol (1–7 %). First a small fraction of unchanged ergometrine was obtained and then two fractions of transformed alkaloid, the first one very small, the second one strongly dominating. Their paper chromatographic properties showed them to be α -lumiergometrine and β -lumiergometrine, respectively.

α -Lumiergometrine was obtained in a quantity of only a few mg of raw product, which showed, however, a pure lumialkaloid absorption spectrum and gave a single spot on the paper chromatogram (Table 2).

β -Lumiergometrine. The dominating second fraction was dissolved in some absolute methanol and diluted with 5–7 volumes of ether. On scratching the walls of the vessel needle-shaped crystals were formed. Yield: 90 mg (air-dry). On the Kofler block the crystals gave off their solvent of crystallization at about 110° C, transforming into an apparently amorphous modification with a very diffuse melting point (about 146°–150° C). The material was uniform on paper chromatograms (Table 2).

After drying the substance in a high vacuum at 130° C the following constants were obtained: *Light absorption*: E (1 %, 1 cm) = 196 at 283 $m\mu$ (max.) in M/10 HCl. *Optical rotation*: $[\alpha]_D^{20} = -27^\circ$ (pyridine, $c = 1$). *Molecular weight*: acidimetric equiv.wt. = 347* (calc. for ergometrine + 1 H₂O: 343). *Elementary analysis*: Found: C 64.9; H 7.40; O 14.3; N 12.9. Calc. for C₁₅H₂₅O₃N₃ (343.4): C 66.45; H 7.34; O 13.98; N 12.24.

The properties of β -lumiergometrine are chiefly the same as reported by Stoll and Schlientz² for lumiergobasine.

Transformation products of ergometrinine

The same preparation procedure was used as for ergometrine. We obtained three fractions of non-fluorescent alkaloid, all with a maximum of light absorption at 283 $m\mu$. The first and the last of these were the main fractions and according to their paper-chromatographic properties they were called α -lumiergometrinine and β -lumiergometrinine, respectively. The very small intermediate fraction, which differed from the other two even paper chromatographically, was not examined any more.

α -Lumiergometrinine crystallized from absolute methanol as needles. Yield: 30 mg of air-dry crystals from 150 mg of ergometrinine. On the Kofler block the crystals were transformed into an apparently amorphous modification at about 135° C and melted diffusely and under decomposition at 193°–197° C. The material was uniform on the paper chromatogram (Table 2).

* Obtained by titrating potentiometrically ca. 2 mg of substance, dissolved in 0.15 ml of ethanol and 0.50 ml of water, with 0.02 N HCl.

1) For β -lumiergometrine the faster moving component dominated.

Fig. 5. Paper chromatography of lumiergometric acids obtained by alkaline hydrolysis of lumieralkaloids (idealized picture).

Fig. 6. Counter current distribution of β -lumiergocristine. Benzene/0.2 M phosphate buffer pH 5.9 (Photometric determination by *p*-dimethylaminobenzaldehyde).

After drying in a high vacuum at 130° C the substance showed the following properties: *Light absorption*: E (1 %, 1 cm) = 193 at 283 $m\mu$ (max.) in M/10 HCl. *Optical rotation*: $[\alpha]_D^{20} = +24^\circ$ (pyridine, $c = 1$). *Molecular weight*: acidimetric equiv.wt. = 341 (calc. for ergometrine + 1 H_2O : 343). *Elementary analysis*: Found: C 66.5; H 7.57; O 14.1; N 11.7. Calc. for $C_{19}H_{25}O_3N_3$ (343.4): C 66.45; H 7.34; O 13.98; N 12.24.

β -Lumiergometrine crystallized on evaporation of a solution in little ethanol and much chloroform. Yield: 55 mg of air-dry crystals from 150 mg of ergometrine. All attempts failed to crystallize the substance from solvents usually applied to ergot alkaloids as methanol, ethyl acetate or acetone. From warm benzene solutions it was precipitated as an apparently amorphous modification. On the Kofler block the crystalline β -lumiergometrine at 105° C gave off its solvent of crystallization, changing into an apparently amorphous modification, the melting point of which (ca. 125°–135° C) was very difficult to observe. The product was uniform on paper chromatogram (Table 2).

After drying the substance in a high vacuum at 120° C we obtained the following constants: *Light absorption*: E (1 %, 1 cm) = 188 at 283 $m\mu$ (max.) in M/10 HCl. *Optical rotation*:* $[\alpha]_D^{20} = +18^\circ$ (pyridine, $c = 1$). *Molecular weight*: acidimetric equiv.wt. = 356

* Based on one single experiment.

(calc. for ergometrine + 1 H₂O: 343). *Elementary analysis*: Found: C ...; H 7.30; O 14.2; N 12.0. Calc. for C₁₉H₂₆O₃N₃ (343.4): C 66.45; H 7.34; O 13.98; N 12.24.

Transformation products of ergocristine

0.25 g of ergocristine was dissolved in 50 ml of M/10 methanesulphonic acid. In order to give the same effect on the peptide alkaloids as on ergometrine the irradiation had to be more powerful and therefore a strong mercury-lamp without a filter was used in this case, completing the transformation in 1–2 h. The products were extracted with absolute chloroform after alkalinizing the reaction mixture with ammonia. The chloroform extract was dried over anhydrous sodium sulphate and poured onto a column of alumina (20–40 g). The elution was made step by step, first with chloroform containing 1 % ethanol until the small fraction of α -lumiergocristine had been obtained and then with chloroform containing 3 % ethanol until the dominating fraction of β -lumiergocristine had come out. The fractions were as soon as possible evaporated in a vacuum to dryness.

α -Lumiergocristine was formed only in minor quantities. The top fractions from several preparations — strongly contaminated with coloured substance — were collected and distributed between a large quantity of diluted hydrochloric acid (about M/20) and a small quantity of chloroform. The nearly colourless aqueous solution was alkalinized with ammonia and extracted with chloroform. From this solution a small quantity of substance (ca. 10 mg) could be obtained but we did not succeed in crystallizing it. However, it was uniform on paper chromatogram (Table 3).

β -Lumiergocristine was purified from colouring matter in the same way as the α -product and could be crystallized from methanol in short, thick prisms. Yield: 90 mg of air-dry crystals from 200 mg of ergocristine. Melt.p. on the Kofler block: 179°–181° (decomp.). It was uniform on the paper chromatogram (Table 3).

After drying in a high vacuum at 130° C the substance showed the following properties: *Light absorption*: E (1 %, 1 cm) = 109 at 283 m μ (max.) in M/10 HCl. *Optical rotation*: $[\alpha]_D^{20} = +17^\circ$ (pyridine; $c = 1$). *Molecular weight*: acidimetric equiv.wt.: 641 * (calc. for ergocristine + 1 H₂O: 628). *Elementary analysis*: Found: C 65.6; H 6.62; O 15.4; N 10.9. Calc. for C₃₅H₄₁O₆N₅ (627.7): C 66.96; H 6.58; O 15.29; N 11.16.

Transformation products of ergocristinine

The ergocristinine had to be dissolved in glacial acetic acid, the solution diluted with water to the strength of about 5 % acetic acid and finally made M/10 in respect of methanesulphonic acid. The irradiation and the extraction were made as described for ergocristine. For the separation gradient elution was used again. The transformation products were very sensitive to the ethanol percentage of the elutrient and therefore this was allowed to increase only slowly (0–1 % in 500 ml of elutrient). The main products were the α -lumiergocristinine and the β -lumiergocristinine. Between them small fractions with variable paper chromatographic properties appeared. These were not further examined.

α -Lumiergocristinine crystallized from methanol as needles. The yield was remarkably small. From 300 mg of ergocristinine only 33 mg of air-dried crystals were obtained. M.p. on the Kofler block: 234–236° C. It was uniform on paper chromatogram (Table 3).

Dried in a high vacuum at 130° C the α -lumiergocristinine showed the following properties: *Light absorption*: E (1 %, 1 cm) = 107 at 283 m μ (max.) in M/10 HCl. *Optical rotation* **: $[\alpha]_D^{20} = +116^\circ$ (pyridine, $c = 0.6$). *Molecular weight*: acidimetric equiv.wt.: 638 (calc. for ergocristinine + 1 H₂O: 628). *Elementary analysis*: Found: C 66.6; H 6.71; O 15.7; N 11.0. Calc. for C₃₅H₄₁O₆N₅ (627.7): C 66.96; H 6.58; O 15.29; N 11.16.

β -Lumiergocristinine. The raw product was purified from most of the coloured material as described for α -lumiergocristine. It was dissolved in much boiling benzene from which it precipitated on cooling in an apparently non-crystalline form. The yield of this product

* Obtained for the peptide alkaloids by titrating potentiometrically ca. 3 mg of substance, dissolved in 0.50 ml of glacial acetic acid, with 0.02 N perchloric acid.

** Based on one single experiment.

was 150–200 mg from 300 mg of ergocristinine. The material could not be brought to crystallization even after further chromatographic purifications. However, the substance obtained was uniform on paper chromatogram and gave a single top on counter current distribution (Fig. 6). On the Kofler block it had a reproducible and comparatively good melting point at 171–172° C (decomp.). Thus there are good reasons to believe that the substance was pure.

After drying in a high vacuum at 130° C the substance showed the following properties: *Light absorption*: E (1 %, 1 cm) = 107 at 283 $m\mu$ (max.) in M/10 HCl. *Optical rotation*: $[\alpha]_D^{20} = \pm 0^\circ$ (pyridine, $c = 1$). *Molecular weight*: acidimetric equiv.wt.: 650 (calc. for ergocristinine + 1 H₂O: 628). *Elementary analysis*: Found: C 66.5; H 6.57; O 15.6; N 11.0. Calc. for C₃₅H₄₁O₆N₅ (627.7): C 66.96; H 6.58; O 15.29; N 11.16.

Transformation products of ergotamine and ergotaminine

The lumi-derivatives from these alkaloids have been prepared and described by Stoll and Schlientz². The β -lumiergotamine had been made by us before we were aware of the Swiss paper. The main properties of our product were the following: It crystallized from methanol in short, thick prisms. M.p. on the Kofler block: 248° C (decomp.); $[\alpha]_D^{20} = +12^\circ$ (pyridine; $c = 1$) E (1 %, 1 cm) = 115 at 283 $m\mu$ (max.) in M/10 HCl. Acidimetric equiv. wt. (mol. wt.) = 605 (calc. for ergotamine + 1 H₂O: 600). Found: C 66.1; H 6.38; O 16.15; N 11.55. Calc. for C₃₃H₃₇O₆N₅ (599.7): C 66.09; H 6.22; O 16.01; N 11.68.

β -Lumiergotamine gave a slightly soluble hydrochloride and could be almost totally precipitated from its aqueous solution by an excess of hydrochloric acid. The paper chromatographic properties of the lumiergotamines and lumiergotaminines are reported in section III A of this paper (Table 3, Fig. 5).

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