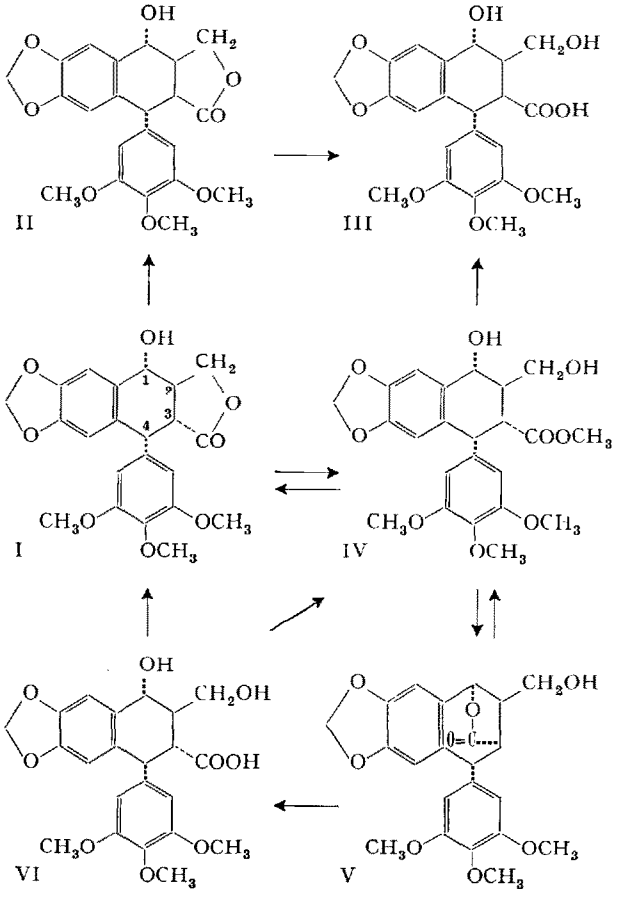
liefert V ein Monoacetylderivat, $C_{24}H_{24}O_9$, mit Smp. 184–186°; $[\alpha]_D^{20} = -60{,}2°$ (in Chloroform); IR-Banden bei 1777 und 1735 cm^{-1} in CH_2Cl_2. Die für Neopodophyllotoxin vorgeschlagene Formulierung als 1,3-Lacton[7,8] stützt sich unter anderem auf den Verlauf der alkalischen Hydrolyse. Mit NaOH entsteht nämlich aus Neopodophyllotoxin nicht die Pikrosäure III, sondern in guter Ausbeute die gesuchte Podophyllinsäure VI, $C_{22}H_{24}O_9$, (Smp. 160–167°; $[\alpha]_D^{20} = -286°$ in Pyridin und $-195{,}3°$ in Äthanol), deren Struktur durch folgende Korrelationen gesichert wird: Podophyllinsäure (VI) lactonisiert mit Di-cyclohexyl-carbodiimid leicht zu Podophyllotoxin. Durch Methylierung mit Diazomethan in Tetrahydrofuran entsteht aus VI ein Methylester $C_{23}H_{26}O_9$, der mit Podophyllinsäure-methylester (IV) identisch ist. Die molare Drehungsdifferenz zwischen Pikropodophyllinsäure (III) und Podophyllinsäure (VI) ($\Delta[M]_D = -410°$ in Äthanol) steht in guter Übereinstimmung mit dem Drehungsinkrement bei ähnlich gebauten Epimeren-Paaren (Tabelle).



Verbindungen	$[\alpha]_D$ (in Äthanol)	$[M]_D$	$\Delta[M]_D$
Pikropodophyllinsäure	−100°	−432°	−410°
Podophyllinsäure	−195°	−842°	
Pikropodophyllin	0°[a]	0°	−448°
Podophyllotoxin	−108°	−448°	
Pikropodophyllinsäure-hydrazid[5]	−106°	−473°	−447°
Podophyllinsäure-hydrazid[5]	−206°	−920°	

[a] c = 0,008, 2-dm-Rohr, Fehlergrenze ± 10°.

Die Gewinnung der Podophyllinsäure (VI) aus V bildet wie erwähnt den wichtigsten chemischen Hinweis für die dem Neopodophyllotoxin zugeschriebene Konstitution. Formel V erlaubt eine plausible Deutung für die Stereospezifität der Hydrolyse: durch die 1,3-Fixierung des Lactonrings im Neopodophyllotoxin wird aus räumlichen Gründen eine basenkatalysierte Epimerisierung an C-3 zu Pikroderivaten verunmöglicht.

Eine ausführliche Beschreibung der hier mitgeteilten Reaktionen wird in den Helvetica Chimica Acta erfolgen.

Summary. Methanolysis of podophyllotoxin (I) with $ZnCl_2$ as catalyst yields podophyllinic acid methyl ester (IV) and neopodophyllotoxin (V), a new isomer of podophyllotoxin. Neopodophyllotoxin which contains the lactone group in the 1,3-position is stereospecifically hydrolyzed by alkali to the hitherto unknown podophyllinic acid (VI).

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Pharmazeutisch-chemische Forschungslaboratorien, Sandoz AG, Basel (Schweiz), 4. Juni 1963.

[7] Die jetzt für Neopodophyllotoxin postulierte Struktur V wurde früher dem Podophyllotoxin (I) erteilt: BORSCHE und NIEMANN[3], E. SPÄTH, F. WESSELY und E. NADLER, Ber. dtsch. chem. Ges. *65*, 1773 (1932); vgl. [4].

[8] Eine ähnliche Cyclisation unter Ausbildung einer 1,3-Ätherbrücke stellt die Überführung von Podophyllol zu Anhydropodophyllol dar: D. C. AYERS und P. J. S. PAUWELS, J. chem. Soc. *1962*, 5025.

Application of Oscillographic Polarography in Photochemistry of Some Pyrimidines, Purines and Aminoacids

The majority of results from the branch of photochemistry of nucleic acids, proteins and their compounds was derived from the post-irradiational changes of their ultraviolet absorption spectra[1,2].

In the following communication some of the possibilities are quoted for the application of alternating-current oscillographic polarography[3] in the photochemistry of a number of pyrimidines, purines[4–6] and amino acids[7,8]. For our studies, we used a Polaroscope P 524 (Krizik, Prague), which allowed us to follow the functions dE/dt against E (Figure 1) and a dropping mercury electrode

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with the usual polarographic cells[3]. Oscillograms were registered on Isopan ISS 21/10 DIN cine film with an Exacta-Varex camera. The compounds studied were: uracil, 5-hydroxymethyluracil, thymine, cytosine, isocytosine, 5-hydroxymethylcytosine, adenine, hypoxanthine, phenylalanine, indole, tryptophan and histidine. The electrolytes used for the oscillopolarographic analyses were: sodium hydroxide, sulphuric acid and ammonium formate in molar concentrations. In our experiments we followed 0.001 M aqueous solutions of investigated compounds in an extent of pH 8.5–11.5. Solutions were irradiated by the UV germicide lamp Philips TUV, 30 W, at a distance of 20 cm. Solutions for the oscillopolarographic analyses were sampled 1, 5, 10, 15 and 20 h after the UV irradiation. Then was added 1 ml of a sample to 1 ml of a suitable electrolyte into the polarographic cell and immediately analysed.

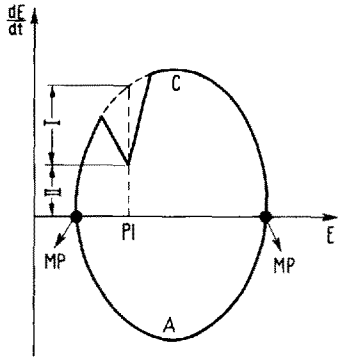
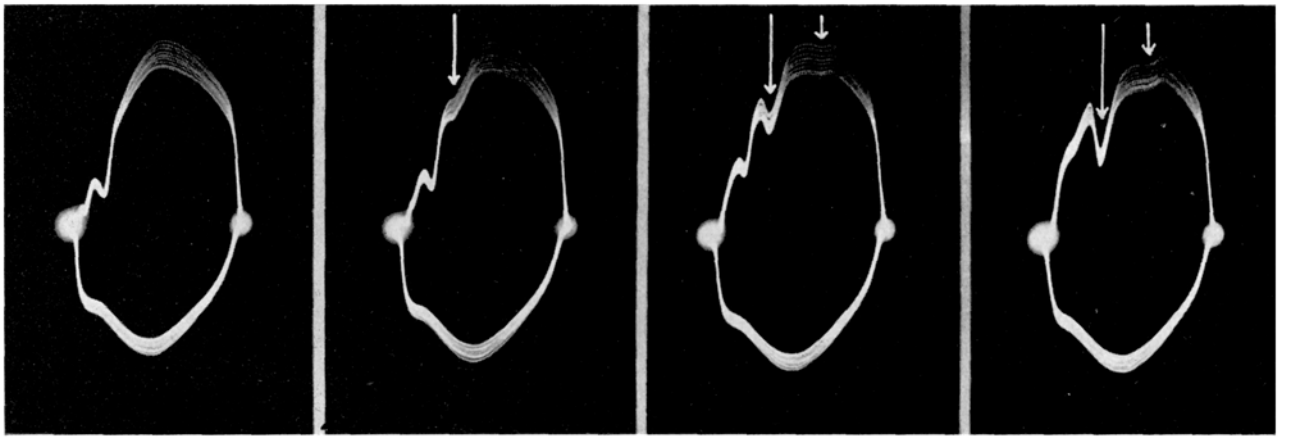


Fig. 1. Diagram dE/dt against E. The quality of the investigated compound is characterized by the potential of the indentation (PI), and quantity by the depth of the indentation. The position of the indentation is generally expressed by the quotient:

$$Q = \frac{\text{distance of indentation from the left marginal point}}{\text{distance between both marginal points}}$$

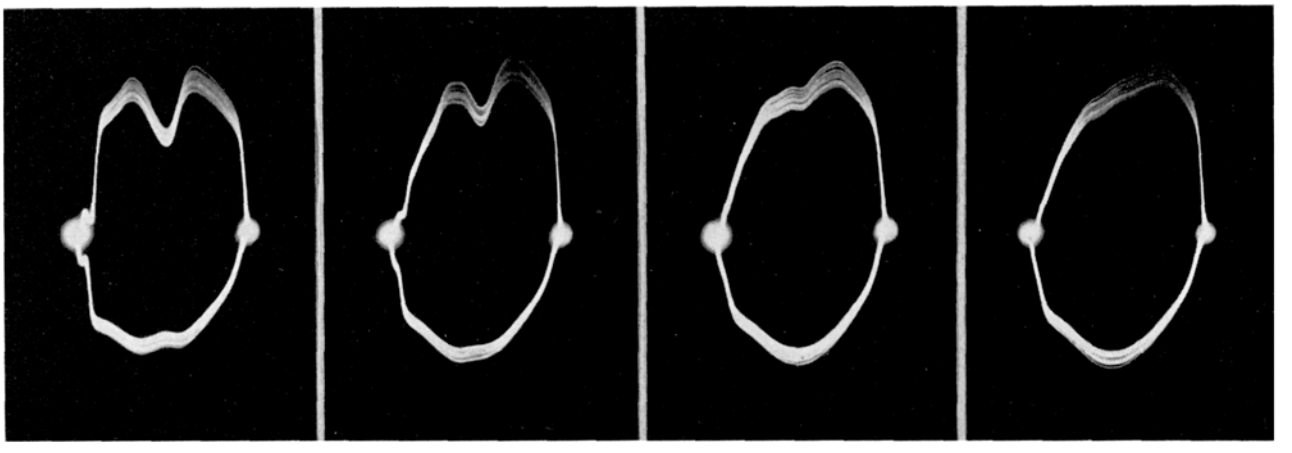
The distance *II* is more easily measured and in quantitative analysis is most often used. C, cathodic part; A, anodic part; MP, marginal point.

The changes passing in the solutions of investigated compounds under the influence of the UV irradiation manifested oscillopolarographically by the progressive decrease of the originally visible indentations up to their disappearance (Figures 2 a–d, 3 a–d). Some of the reaction products that arose, formed their own additional oscillopolarographic indentations (Figures 2 b-d, marked by arrows). In this way, it was possible to follow both qualitatively and quantitatively (see Figure 1) the time-course of photochemical reactions. Under the experimental conditions described, tryptophane[2,9] and isocytosine[10,11]



2a 2b 2c 2d

Fig. 2. (a) Oscillogram of isocytosine analysed in a sodium hydroxide medium, before the UV irradiation. (b) Sample analysed after 5 h of UV irradiation. (c) Sample analysed after 10 h of UV irradiation. (d) Sample analysed after 20 h of UV irradiation.



3a 3b 3c 3d

Fig. 3. (a) Oscillogram of tryptophan analysed in a sodium hydroxide medium, before the UV irradiation. (b) Sample analysed after 1 h of UV irradiation. (c) Sample analysed after 5 h of UV irradiation. (d) Sample analysed after 10 h of UV irradiation.

were most sensitive to the UV irradiation of their solutions.

The alternating-current oscillographic polarography means a new, very speedy and experimentally not very pretentious analytical method in the branch of photochemistry of biologically important substances and their closely related compounds. Besides decreases of investigated compounds caused by UV irradiation of their water solutions, this method permits the registration of some reaction products also in the photochemical reactions. It may therefore be assumed that it will be possible to extend in this way a knowledge of the course of some photochemical, and probably also radiation-chemical[10,12], reactions.

Zusammenfassung. Bei Anwendung der oszillographischen Polarographie mit Wechselstrom wurde der Einfluss der UV-Strahlung auf die wässrigen Lösungen einiger Bestandteile der Nukleinsäuren und Eiweißstoffe erforscht. Die oszillographischen Kurven der Funktion $dE/dt = f_1(E)$ wurden mit dem Polaroskop P 524 mit Hilfe der Quecksilbertropfelektrode verfolgt.

D. KALÁB

Research Department of Bioveta n.p., Ivanovice na Hané (Czechoslovakia), March 7, 1963.

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Totally Synthetic (±)-13-Alkyl-3-hydroxy and Methoxy-gona-1,3,5(10)-trien-17-ones and Related Compounds

The flexibility of our recently described total synthesis of estrone[1,2] readily permits the preparation of numerous gona-1,3,5(10)-triene derivatives in which, in particular, the substituent attached to the 13-position and the size of ring D are varied. Expressed generally, the key reaction in these syntheses is a Michael condensation of a vinyl ketone (I) (or the corresponding 6-aryl-1-diethylaminohexan-3-one, or a mixture of the two) to give the adduct (III). We now report that this reaction can be carried out for cases in which X = hydroxyl and methoxyl, R = ethyl, *n*- and iso-propyl, *n*- and iso-butyl, isoamyl, and *n*-hexadecyl, and n = 1 and 2. The adducts (III) undergo double cyclodehydration under acidic conditions[2] to (±)-13-alkyl-3-hydroxy and methoxy-gona-1,3,5(10),8,14 pentaen-17 and 17a-ones (IV), readily convertible by selective hydrogenation over a 2% palladized calcium carbonate catalyst in benzene[2] to the corresponding gona-1,3,5(10),8-tetraenes. D-Cyclopentano members of this series (i.e. n = 1) are isomerized in boiling methanolic hydrochloric acid to (±)-13-alkyl-3-hydroxy and methoxy-gona-1,3,5(10),9(11)-tetraen-17-ones, converted by catalytic hydrogenation over 10% palladized charcoal in ethanol to (±) 13-alkyl-3-hydroxy and methoxy-gona-1,3,5(10)-trien-17-ones[3]. The (±)-13-alkyl-3-methoxy-gona-1,3,5(10),8-tetraenones are converted by lithium in aniline-liquid ammonia[4], with or without preliminary reduction by sodium borohydride in methanol, to (±)-13-alkyl-3-methoxygona-1,3,5(10)-trien-17 and 17a-ols, which may be oxidized by the Jones reagent[5] to the corresponding gonatrien-17 and 17a-ones[3a]. The metal-ammonia reduction of the 8,9-double bond is impeded in the 3-hydroxy series, possibly because delocalization of phenoxide charge hinders electron addition to the styrenoid system. The end products are assigned the 'natural' type stereochemistry by analogy with stereochemical

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