$$3 \quad \log \frac{[LD_{50}]_{HH}}{[LD_{50}]_{XY}} = b_X + b_Y + e_X e_Y$$

$$4 \quad \log \frac{[LD_{50}]_{HH}}{[LD_{50}]_{XY}} = b_X + b_Y - e_X e_Y$$

combined models

Four sets of structural parameters, statistically elaborated with the help of the four equations, were used to work out the theoretical LD_{50} and these were plotted against the experimental results. The evaluation of these correlations by the correlation coefficient (r) proved, for the group under study, that only equation 3 is appropriate ($r = 0.981$). This model was then checked by the ψ^2-test. Although the ψ^2-test on a 5% significance level is not satisfactory for the whole group, it is satisfactory if hydroquinone is disregarded (Figure). The correlation coefficient equals 0.999. The values of the substituent constants b_i and e_i are as follows:

	NO_2	Cl	OH	CH_3	H	NH_2
b_i	0.565	0.328	0.318	0.217	0.005	−0.026
e_i	0.59	−0.07	0.53	0.04	−0.04	−0.87

We plan to investigate the meaning of constants b_i and e_i. It is possible that a relation can be found between the mathematical model mentioned and the L.F.E.R. constants[13,14]. The latter have already been applied to biological problems, especially in papers by ZAHRADNÍK[1-3] and lately HANSCH[8,9].

At present the *m*- and *o*-disubstituted derivates are being studied in the same way, and we are also working with additional substituents.

Zusammenfassung. Es wurden die i.v. LD_{50} einer Gruppe *p*-disubstituierter Benzolderivate, welche alle Kombinationen der erwähnten Substituenten enthielten, in Polyvinylpyrrolidonlösungen bestimmt. Der Zusammenhang zwischen der chemischen Struktur dieser Verbindungsklasse und ihrer biologischen Aktivität konnte mit einer vorgeschlagenen Gleichung beschrieben werden.

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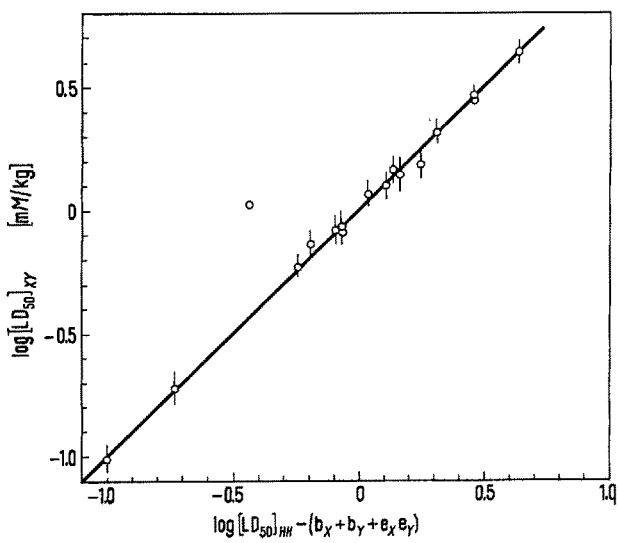
M. KRIVUCOVÁ, and D. VLACHOVÁ

Institute of Industrial Hygiene and Occupational Diseases, Prague (Czechoslovakia), July 21, 1964.



LD_{50}'s were determined on white mice with weight 20 ± 2 g by the Thompson method. The substances were administered intravenously in a 20% aqueous polyvinylpyrrolidone solution.

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Synthesis of Dehydroneotenone[1]

CROMBIE and WHITING have isolated (±)-neotenone (I) and dolineone (II) along with other compounds from the root of *Neorautanenia pseudopachyrrhiza* Harms[2]. This is the first plant in which both an isoflavanone and its corresponding rotenoid have been shown to occur together. They have also shown that (I) was easily dehydrogenated to dehydroneotenone (III) and the former could be reconstituted from the latter. We wish to report the synthesis of dehydrocompound (III) by a method used earlier[3]. Hoesch condensation of 6-hydroxy-2,3-

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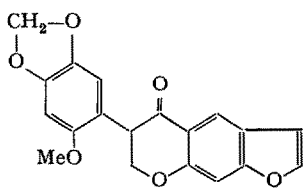
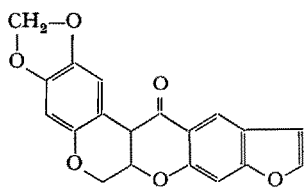
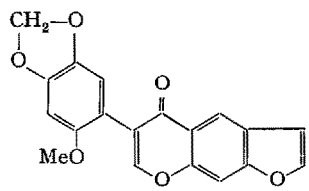


I

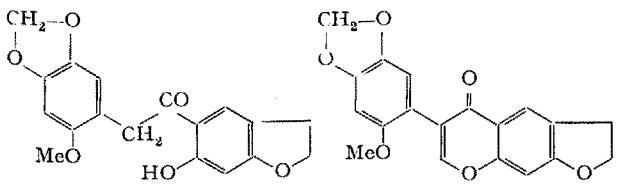


II



III

dihydrobenzo[b]furan[4] with 2-methoxy-4,5-methylenedioxybenzyl cyanide[5] yielded 6-hydroxy-5-(2-methoxy-4,5-methylenedioxyphenylacetyl)-2,3-dihydrobenzo[b]-furan (IV, m.p. 153°~154°, IR 1650 cm^{-1} (Nujol) (CO), UV λ_{max}^{EtOH} mμ (log ε); 239 (4.21), 284 (4.14), 330 (3.70). Found: C, 65.67; H, 4.95. $C_{18}H_{16}O_6$ requires: C, 65.85; H, 4.91%). Treatment of (IV) with ethyl *ortho*formate-pyridine-piperidine[6] gave the dihydrocompound (V, m.p. 247°~248°, IR 1644 cm^{-1} (Nujol) (γ-pyrone), UV λ_{max}^{EtOH} mμ (log ε); 241$_i$ (4.22), 251$_i$ (4.19), 310 (4.23). Found: C, 67.38; H, 4.47. $C_{19}H_{14}O_6$ requires: C, 67.45; H, 4.17%). On dehydrogenation with N-bromosuccinimide (V) afforded dehydroneotenone (III, m.p. 234°~235°, IR 1644, 1626, 1589, 1544, 1508 cm^{-1} (Nujol), UV λ_{max}^{EtOH} mμ (log ε); 238 (4.59), 309 (4.20). Found: C, 68.00; H, 3.84. $C_{19}H_{12}O_6$ requires: C, 67.85; H, 3.60%) (lit., m.p. 240°~241°[2], m.p. 242° (correct)[7], lit.[2], IR 1658, 1629, 1592, 1549, 1506 cm^{-1} (chloroform solution), UV λ_{max}^{EtOH} mμ (log ε); 239 (4.61), 308 (4.10)). (III) was readily converted into 6-hydroxy-5-(2-methoxy-4,5-methylenedioxyphenylacetyl)benzo[b]furan (m.p. 161°~162°) (lit.[2] m.p. 162°~163°) by alkaline hydrolysis, thus establishing the structure of (III).



IV V

Zusammenfassung. Aus 6-Hydroxy-5-(2-methoxy-4,5-methylendioxyphenylacetyl)-2,3-dihydrobenzo[b]furan (IV) wurde nach VENKATARAMAN Dihydrofurano-isoflavon (V) hergestellt und zu Dehydroneotenon (III) dehydriert.

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Department of Chemistry, Faculty of Science, University of Hiroshima (Japan), July 8, 1964.

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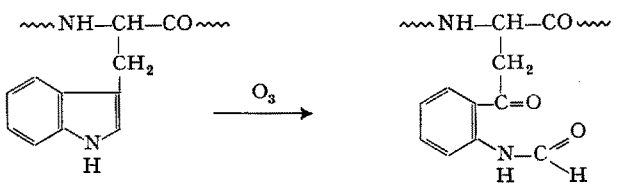
Inattivazione della gramicidina dovuta alla conversione triptofano → N'-Formilchinurenina

La gramicidina, isolata in forma cristallina da colture di *Bacillus brevis*, è costituita da una miscela di peptidi caratterizzati da un elevato contenuto in triptofano, dalla mancanza di residui N- e C-terminali, dalla notevole solubilità in alcool e dalla presenza di aminoacidi della serie D[1].

La composizione e la struttura primaria della frazione A, che costituisce la parte più cospicua della miscela peptidica (79%)[2], sono state recentemente determinate[3].

Con ricerche sistematiche sull'ozonizzazione di peptidi e proteine[4] è stato messo a punto un metodo per la modifica selettiva dei residui del triptofano a residui di N'-formilchinurenina, senza rottura di legami peptidici, come illustrato nello schema.



Alcune proteine biologicamente attive, hanno sopportato tale modifica conservando completamente la loro attività[5].

L'elevato contenuto in triptofano (40.2%) della gramicidina e l'alta resa di conversione triptofano-N'-formilchinurenina, ottenuta con la sua ozonizzazione[6] permettono di effettuare larghe e selettive variazioni sequenziali nei suoi peptidi costituenti, fornendo un'ottima occasione per lo studio di relazioni tra struttura ed attività biologica. Quest'ultima si esplica, come e noto, attraverso un'inibizione della crescita di numerosi organismi Gram positivi ed un effetto litico sui globuli rossi del sangue.

La gramicidina (N.B.C.) è stata ossidata in presenza di resorcinolo nelle condizioni già descritte[6]; nel prodotto finale di ossidazione la scomparsa del triptofano era completa.

La graduale conversione del triptofano ad N'-formilchinurenina è stata seguita per via spettrofotometrica a 315 mμ, come riportato in Figura 1.

Dalla soluzione di gramicidina in corso di ossidazione, sono stati opportunamente prelevati vari campioni, per le prove di attività antibatterica ed emolitica e per l'analisi del contenuto di chinurenina.

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