

synapse is designed to transmit from the inhibitory to the excitatory axon.

The existence of inhibitory synapses on the motor nerve terminals clarifies the physiological observations. The minimum time of about 1 msec for the appearance of presynaptic inhibition following the arrival of the inhibitory impulse is consistent with a process involving a single chemically transmitting synapse, but too slow for typical electrical transmission⁸ and probably too fast for diffusion of transmitter from the inhibitory neuromuscular synapses. We suggest that axo-axonal synapses are the agents of presynaptic inhibition in crustacean muscle¹².

Zusammenfassung. Es ist anzunehmen, dass die präsynaptische Hemmung der Crustaceen-Muskeln durch Reaktion eines hemmenden Überträgerstoffs mit Rezep-

toren der Endigungen der motorischen Nervenfasern zustande kommt. Synaptische Kontakte des hemmenden Axons mit den Endigungen der motorischen Nervenfasern sind mit dem Elektronenmikroskop beobachtet worden. Wahrscheinlich vermitteln diese Strukturen den präsynaptischen Effekt.

H. L. ATWOOD and A. JONES

Zoology Department, University of Toronto, Toronto (Canada) 7 August 1967.

¹² We thank H. JOHNSTON for technical assistance. The study was supported by grants from the National Research Council of Canada and the Muscular Dystrophy Association of Canada.

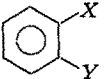
Chemical Structure and Biological Activity of *o*-Disubstituted Derivatives of Benzene

We suggested in previous reports^{1,2} the four-parameter equation (1) expressing a quantitative relation between the structure of *m*- and *p*-disubstituted benzene derivatives and the magnitude of their biological effect.

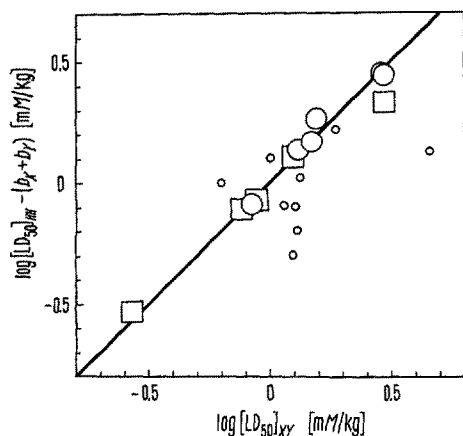
$$\log[\text{LD}_{50}]_{HH} - \log[\text{LD}_{50}]_{XY} = b_X + b_Y + e_X \times e_Y \quad (1)$$

The symbol $\log[\text{LD}_{50}]_{XY}$ means logarithm LD_{50} , expressed in mM/kg body weight of the benzene derivative with substituents *X* and *Y*; $\log[\text{LD}_{50}]_{HH}$ is the same quantity for benzene.

We wish to report here our results obtained with a

series of substances of type , where *X* and *Y*

represent H, CH₃, Cl, OH, NO₂, NH₂; the series of substances studied included all possible combinations of



The toxicity data (LD_{50}) were determined for white mice (weight 20 ± 2 g) by the Thompson method. The substances were administered i.v. in a 20% polyvinylpyrrolidone⁴ solution. $\square$ *o*-derivatives of benzene where *X* = *Y*; $\circ$ *X* $\neq$ *Y* respectively; $\circ$ mono-substituted derivatives.

X and *Y*. The statistical treatment of the experimental data proved that *o*-disubstituted benzenes do not fulfil (1) because no e_{o-X} exist, which satisfies the whole set of data. However, for *o*-disubstituted benzenes which satisfy the condition *X* = *Y*, interesting results were obtained. The data for these substances fit (2).

$$\log[\text{LD}_{50}]_{HH} - \log[\text{LD}_{50}]_{o-XX} = 2b_{o-X} \quad (2)$$

where $b_{o-X} = b_{m-X} = b_{p-X}$ (see ²). For substances where *X* $\neq$ *Y*, the toxicity is, in most cases, lower than that given by $b_X + b_Y$.

The data fitting (2) can be added to the series of *m*- and *p*-disubstituted benzene derivatives for calculating more precise b_X constants. These new data of b_X are summarized in the Table³.

<i>X</i>	NO ₂	Cl	OH	CH ₃	H	NH ₂
b_X	0.503	0.294	0.273	0.182	0.007	0.071

The correlation of measured toxicities with calculated values are shown in the Figure⁴.

Zusammenfassung. Es wurden die i.v. LD_{50} einer Gruppe *o*-disubstituierter Benzolderivate, welche alle Kombinationen der erwähnten Substituenten enthielt, bestimmt. Die quantitative Korrelation zwischen chemischer Struktur und biologischer Aktivität wird in einer Gleichung gefasst.

K. BOČEK, J. KOPECKÝ and M. KRIVUCOVÁ

Institute of Industrial Hygiene and Occupational Diseases, Praha (Czechoslovakia), 25 May 1967.

¹ K. BOČEK, J. KOPECKÝ, M. KRIVUCOVÁ and D. VLACHOVÁ, *Experientia* 20, 667 (1964).

² J. KOPECKÝ, K. BOČEK and D. VLACHOVÁ, *Nature* 207, 981 (1965).

³ Acknowledgment. We should like to thank Mr. Z. ROTH for the statistical evaluation of our results.

⁴ Acknowledgment. We should like to thank the Badische Anilin und Soda-Fabrik for a sample of polyvinyl-pyrrolidone (Kollidon® biologisch geprüft).