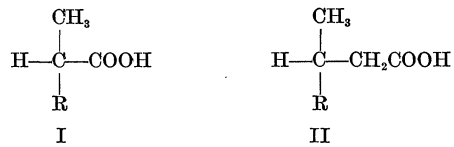
SPECIAL ARTICLES

ON THE EXTENT OF THE VALIDITY OF THE "RULE OF SHIFT"

THE members of two configurationally related homologous series of substances of the general structure



are characterized by the following properties:

In type I the partial rotations of the COOH group and of the rest of the molecule are of the same sign. In type II they are of opposite sign. If the carboxyl group in the first series of substances is levorotatory, it is dextrorotatory in the second. The question arose as to the effect of the substitution of the hydrogen atom of the carboxyl group by a nitrophenyl group on the rotations in the visible region of the spectrum of the members of each group and on the partial rotations of the respective groups attached to the asymmetric carbon atom. This inquiry is of significance in connection with the question of the extent of the validity of the so-called "Rule of Shift," which postulates that in configurationally related substances an identical substitution brings about a shift of rotation in the same direction.

In order to obtain the desired information the rotatory dispersion of several substances of types I and II were studied. The results are summarized in the table.

A scrutiny of the table reveals that in the first group of substances, measured either in homogeneous state or in heptane, the substitution causes a shift of the rotations to the left in all members, but in the second group of substances measured in heptane, the lower members on substitution respond with a shift of the rotation to the left, whereas the higher members show, under the same circumstances, a shift to the right. From the study of the rotatory dispersion curves of the members of II, it becomes evident that in the lower members the substitution affects principally the second contribution, whereas in the higher members the first contribution is enhanced to a higher degree.

Thus, caution has to be exercised when the "Rule of Shift" is made use of for correlating the configura-

MAXIMUM MOLECULAR ROTATIONS OF CORRELATED p-NITROPHENYL ESTERS OF α-SUBSTITUTED ACETIC AND PROPIONIC ACIDS

Acids	Free acid	p-Nitrophenyl esters of the acids				
	$[M]^{25}_{5892.6}$		$[M]^{25}_{5892.6}$	Sign of contribution first	Sign of contribution second	Character of dispersion curve
2-Methylbutyric acid (1)	−18	in heptane	−45.2			
		homogeneous	−41.8			
2-Methylcaproic acid (1)	−24.3	in heptane	−66.3	−	−	normal
		homogeneous	−57.8	−	−	"
3-Methylvaleric acid (1)	−10.4	in heptane	−18.0	+	−	abnormal
		homogeneous	−20.1	+	−	"
3-Methylcaproic acid (1)	+ 3.6	in heptane	+ 0.86	+	−	normal
		homogeneous	− 5.11*	+	−	abnormal
3-Methylheptylic acid (1)	+ 6.1	in heptane	+ 6.1			
		homogeneous	+ 0.85			
3-Methylcaprylic acid (1)	+ 8.1	in heptane	+10.8	+	−	normal
		homogeneous	+ 4.2*	+		"

* In a short note published by Levene and Meyer this value was reported with incorrect sign and the value reported for 3-methylcaprylic acid in homogeneous state was erroneous. (See P. Stevens, *Jour. Am. Chem. Soc.*, 56: 997, 1934). This error is unaccountable in view of the fact that the polariscopic readings were made by two observers, G. M. Meyer and R. E. Marker.

tions of substances whose two component partial rotations are of opposite sign.

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PSEUDORABIES AS A CONTAGIOUS DISEASE IN SWINE

PSEUDORABIES is recognized as an acute, infectious, highly fatal disease of cattle, cats and dogs. The causative virus is readily transmissible by inoculation to rabbits, guinea-pigs, rats and mice as well as to other animals less commonly used for experimental purposes. Pruritus and rapid death after a relatively short incubation period are salient features of the disease. Pseudorabies has not been found to be contagious among any of the common laboratory animals nor among cattle, cats or dogs, and its method of spread under natural conditions is unknown.

The susceptibility of domestic swine to pseudorabies was not extensively investigated by earlier workers; Schmiedhoffer[1] was unable to infect pigs experimentally. On the other hand, von Ratz[2] observed the disease occurring naturally in wild swine. The writer[3,4] has found that the virus administered subcutaneously produced in swine a mild disease in marked contrast to the uniformly fatal form which it produces in other species. The susceptibility of domestic swine to pseudorabies has since been observed by other workers[5,6,7] and the disease has been found to occur naturally in this species in Holland and Hungary as a rather mild ailment. The clinical features of swine pseudorabies induced by subcutaneous inoculation are malaise, decreased appetite and a 4 to 6 day febrile reaction; rarely, indefinite symptoms of central nervous system involvement were observed.

Further work has shown that the virus when administered intranasally produces a similar disease. In one instance intranasal inoculation was followed by a pneumonia. The mild disease described above may follow the repeated feeding of large amounts of virus or the intramuscular injection of small amounts. In the latter case a weakness or paresis of the inoculated leg may be detected. Injected intracerebrally under ether anesthesia into swine the virus produces marked central nervous system symptoms and death in from 36 to 96 hours.

In addition it has been observed that pseudorabies in swine is contagious. In a series of 9 experiments normal swine were placed in the same isolation pen with pigs experimentally infected either subcutaneously or intramuscularly with pseudorabies virus. In 8 of these experiments the exposed swine developed pseudorabies. In the single negative experiment it is believed, from what is known now, that the infected pig was removed before it had reached the stage at which the disease was communicable. Although the Hungarian virus was used in most of these experiments, the Iowa strain (mad itch) was also found capable of transferring from swine to swine by contact.

Pseudorabies in swine infected by pen exposure closely resembled the disease seen in pigs inoculated subcutaneously. None of the experimental animals died and none appeared dangerously ill. The nature of the illness contracted by exposure was proven in every case either by the demonstration of virus during the course of the disease or of specific virucidal antibodies in the blood serum following recovery. The latent period between the time of first exposure and the onset of symptoms varied from 4 to 11 days, probably depending upon the stage of the disease in the inoculated animal when the normal animal was placed in the pen.

In studying the mode of transmission of pseudorabies in swine it was found that hog lice played no rôle. Neither could virus be demonstrated in the urine, feces or salivary glands of infected pigs, indicating that the saliva and the excreta were unimportant as regards the transmission of the disease. Study of the distribution of the virus in swine killed early in an illness contracted by exposure finally suggested its portal of entrance. In such animals virus could be demonstrated only in the nasal washings. To test the possibility that virus spread from pig to pig by way of the nose, experiments were conducted in which the nasal passages of intramuscularly inoculated swine, as well as of those being exposed, were washed out daily with sterile physiological saline. By means of the inoculation of small amounts of these washings subcutaneously into rabbits it was found that virus was present in the nasal passages of inoculated swine on the sixth day, which is usually the last day of temperature elevation, and that it might persist for a day or two longer. It was not present

[1] J. Schmiedhoffer, *Z. Infektionskrankh., Haustiere,* 8: 383, 1910.
[2] S. von Ratz, *Z. Infektionskrankh., Haustiere,* 15: 99, 1914.
[3] R. E. Shope, *Jour. Exp. Med.,* 54: 233, 1931.
[4] R. E. Shope, *Proc. Soc. Exp. Biol. and Med.,* 30: 308, 1932.
[5] A. Burggraaf and L. F. D. E. Lourens, *Tijdschr. Diergeneesk.,* 59: 981, 1932.
[6] A. Braga and A. Faria, *Revista de Vet. e Zootech.,* 18: Nos. 3–4, 1932, referred to in *Bol. Instit. Vital Brazil,* No. 16, 1934.
[7] P. Remlinger and J. Bailly, *Bull. L'Acad. Vet. France,* 6: 169, 1933.