

aminoketone⁷. Applying a similar line of reasoning to the aromatization process, the reaction may be visualized as proceeding through a similar intermediate with the double bond participating in place of the migrating group. The subsequent steps in the aromatization process are best described as the simultaneous ejection of a proton, followed by collapse of the azacyclopropene intermediate through the attack of the reagents on the unsaturated reaction intermediate to yield a cyclohexadienone-imine as the initial reaction product. Tautomerization to the aromatic amine analog in each case adequately describes the final step in the aromatization process. The applicability to a system bearing geminal dimethyl groups through concurrent methyl migrations is apparent in the Figure, equation B. Further, this process should be dependent as in all Beckmann type rearrangements upon the configuration of the departing oxime-hydroxyl group. Competing with this mechanism in the case of oximes capable of isomerization will be participation of the α -carbanion in those cases in which its formation is possible (Figure, equation C).

Utilizing this mechanism, the aromatization of certain 2-tetralone^{9a} can be described and as well the formation of amino-thiophenes¹⁰ and dehydrogenation of 2-benzyl-1-tetralone¹¹ by partial oxime aromatization. The details of each of these processes can accurately be predicted on

the basis of a mechanism of this type. The dependency of the process upon the catalyst and solvent system adds additional support to a mechanism in which multidirectional collapse of the transition state controlled by the solvent catalyst environment most adequately describes the aromatization process. The mechanism presented here also has the advantage that it describes the reaction in terms of the closely related and in some cases competing Beckmann processes.

Zusammenfassung. Es wird ein Mechanismus für die sauer-katalysierende Aromatisierung der Oxime (Wolff-Aromatisierung) vorgeschlagen, der es erlaubt, z.B. die Beckmann-Umlagerungsprozesse und Fragmentierungen entsprechend den heutigen Erkenntnissen aufzufassen. Die einschlägige moderne Literatur wird im Sinn dieser neuen Beziehungen interpretiert.

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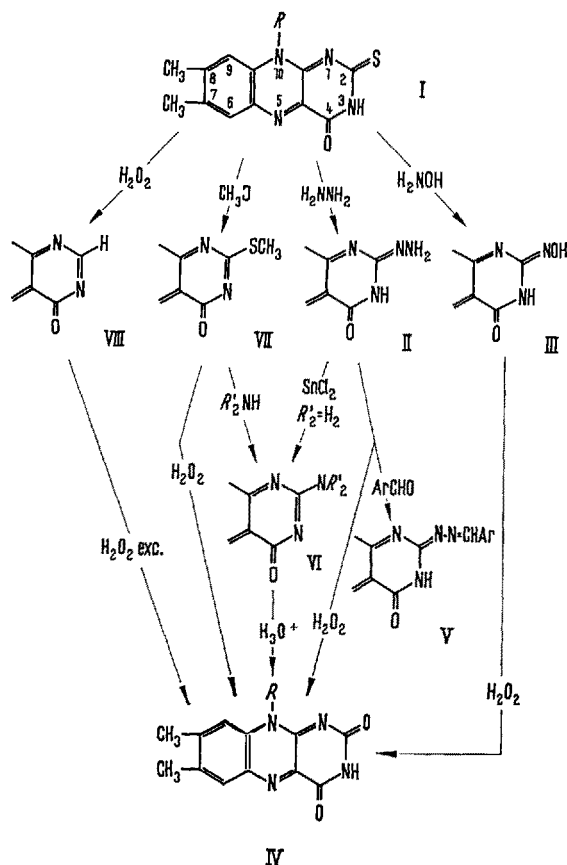
Department of Chemistry, Seton Hall University, South Orange (New Jersey, U.S.A.), May 9, 1962.

¹⁰ L. C. CHENEY and J. R. PIENING, J. Amer. chem. Soc. **67**, 729 (1945).

¹¹ H. LEUCHS and H. RAUCH, Ber. dtsch. chem. Ges. **48**, 1531 (1915).

Neue funktionelle Derivate des Riboflavins: Substitutionsreaktionen am Isoalloxazin-Kern

Im Rahmen unserer Studien zur Koordinationschemie der Flavocoenzyme^{1,2} benötigten wir Derivate des Iso-



alloxazins mit abgewandelten Substituenten im Pyrimidin-Teilkern. Im Gegensatz zu der Mannigfaltigkeit bekannter Derivate dieses Typs in den verwandten Reihen der Pteridine und Purine sind seit unserer ersten Synthese³ des 2-Thioisolumiflavins und des 2-Lumiflavims in jüngster Zeit nur noch die analogen Ribitylderivate 2-Thioriboflavin⁴ und 2-Riboflavimin⁵ beschrieben worden.

Ausgehend von 2-Thioisoalloxazinen I ($R = \text{CH}_3$ bzw. $R = \text{Ribityl}$) konnten wir eine grössere Zahl der gesuchten Derivate auf folgenden Wegen erhalten:

1. Die sehr reaktiven Thione I geben mit Hydrazin und Hydroxylamin in wasserfreiem Milieu (Dimethylformamid) direkt die Flavohydrazone II und die Flavoxime III. Beide Verbindungstypen sind nur in kationischer Form gegen O_2 und H_2O stabil, mit Peroxiden reagieren sie besonders leicht unter Rückbildung der unsubstituierten Flavine IV. Die Hydrazone II lassen sich weiter stabilisieren als unsymmetrische Azine V.

2. Die Thione I reagieren nur unbefriedigend mit anderen wasserfreien Basen zu den Aminen VI, lassen sich aber leicht (ohne Basenkatalyse!) alkylieren zu den S-Alkylderivaten VII, welche wir früher irrtümlich als N(3)-Alkylisomere angesehen haben⁶ und welche nun leicht mit wasserfreien Basen zu den gewünschten Aminen VI reagieren. Die Grundkörper VI, $R' = \text{H}$, erhält man jedoch noch einfacher durch Reduktion der Hydrazone II mit SnCl_2 .

¹ P. HEMMERICH und S. FALLAB, Helv. chim. Acta **41**, 498 (1958).

² P. BAMBERG und P. HEMMERICH, Helv. chim. Acta **44**, 1001 (1961).

³ P. HEMMERICH, S. FALLAB und H. ERLÉNMEYER, Helv. chim. Acta **39**, 1242 (1956).

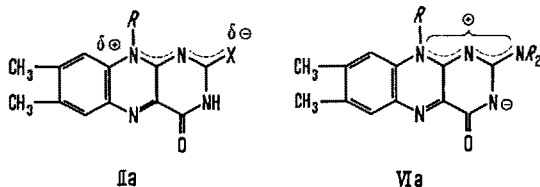
⁴ V. M. BEREZOVSKIJ und L. M. MEL'NIKOVA, Zurnal obscej chimii. **31**, 3827 (1961).

⁵ R. M. CRESSWELL, A. C. HILL und H. C. S. WOOD, J. chem. Soc. **1959**, 698.

⁶ P. HEMMERICH und H. ERLÉNMEYER, Helv. chim. Acta **40**, 180 (1957).

3. Die Thione I, welche durch Einwirkung von überschüssigem H_2O_2 schon bei Raumtemperatur zu IV entschweifelt werden, lassen sich bei Behandlung mit nur 2–3 Äquivalenten stark verdünnter Peroxyessigsäure in die Desoxyflavine VIII überführen. Diese sehr empfindlichen Körper⁷ lassen sich auf diesem Wege rein erhalten, sie autoxydieren jedoch in wässrig-alkalischer Lösung augenblicklich unter Bildung von IV.

Der Vergleich der Spektren zeigt, dass Flavoxime III (λ_{max} : 294 m μ , 526 m μ), Flavohydrazone II (λ_{max} : 296 m μ , 512 m μ) als echte (Aza)Chinon-Derivate in der Form IIa vorliegen, während für die Amine VI (λ_{max} : 276 m μ , 366 m μ , 452 m μ) die dipolare Form VIa am wahrscheinlichsten ist.



Arachnoidal Cell Clusters in the Lizard *Lacerta lepida*

Arachnoidal cell clusters were first described as post-mortem findings in the meninges of patients suffering from mental disease¹. In general these cell clusters have been accepted as a manifestation of advancing age. CUSHING, WEED and ESSICK observed that the arachnoidal cell clusters occurred not only in man but also in various laboratory animals². The association of the cell clusters with advancing age can be attributed largely to the work of WEED³, who in a series of cats of different ages found that in very young animals the cell clusters were never present, while they were always observed in very old animals. According to WATT⁴, in man arachnoidal cell clusters can be observed even in the unborn foetus and consequently factors other than those of old age must be considered in the aetiology.

We observed arachnoidal cell proliferations in a series of very young and adult specimens of the lizard *Lacerta lepida*. These proliferations appeared to be present in nearly 70% of all very young lizards. As in man⁴ the histological features varied from typical arachnoidal cell clusters to a more fibrous structure, which often showed degenerative changes and sometimes contained capillaries. The significance of the arachnoidal cell clusters is

Die Amine VI, $R = \text{CH}_3$, sind dementsprechend als einzige Derivate dieser Reihe in CHCl_3 unlöslich.

Experimentelle Details, physikochemische, koordinationschemische und biologische Eigenschaften sollen demnächst an anderer Stelle näher beschrieben werden.

Summary. Starting from 2-thioisalloxazines, a synthetic route to the formerly inaccessible 2-(alkyl)imino, 2-oximino, 2-hydrazono and 2-azino derivatives of vitamin B_2 was developed.

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Institut für Anorganische Chemie der Universität Basel (Schweiz), 18. Juni 1962.

⁷ Vgl. P. HEMMERICH und H. ERLÉNMEYER, *Helv. chim. Acta* **40**, 180 (1957); P. HEMMERICH, *Helv. chim. Acta* **41**, 514 (1958).

⁸ λ_{max} bezieht sich auf die Neutalmoleküle in CHCl_3 (II, III) resp. Äthanol (VI).

uncertain. CHORNYAK⁵ demonstrated that under conditions of anoxaemia the cells of the arachnoid do proliferate and form typical cell clusters as well as freely wandering macrophages. Such a mechanism could certainly operate *in utero*, but on the strength of the occurrence of arachnoidal cell clusters in *Lacerta lepida* it is likely that other factors are also involved. As our results in *Lacerta lepida* are in good agreement with those obtained in man⁴, a general significance should be attached to these structures.

Zusammenfassung. Beschreibung von Zellanhäufungen in der Arachnoidea bei der Eidechse *Lacerta lepida*.

A. STOLK

Department of Histology, Free University, Amsterdam (The Netherlands), July 3, 1962.

¹ L. MEYER, *Virchows Arch.* **17**, 209 (1859).

² H. CUSHING and L. H. WEED, *Johns Hopkins Hosp. Bull.* **26**, 297 (1915). – C. R. ESSICK, *Contr. Embryol.* **110**, Pub. 394, 377 (Carnegie Inst., Washington 1920).

³ L. H. WEED, *Johns Hopkins Bull.* **31**, 343 (1920).

⁴ J. WATT, *Nature (London)* **194**, 880 (1962).

⁵ J. CHORNYAK, *Bull. U.S. Army Med. Dept.* **8**, 695 (1948).

On the Specific Inhibition of Adrenal Steroid Biosynthesis

Since the discovery that amphenone¹ inhibits adrenal steroidogenesis, steadily growing interest in this special type of action resulted in the elaboration of a large number of substances^{2–5} with similar activity. Some of these were found to produce quite specific inhibitions of steroidal 11β -hydroxylation, such as e.g. Su-4885 (Metopirone®)^{6,7}, or of 17α -hydroxylation, e.g. Su-8000, Su-9055 and Su-10'603^{7,8}; these properties are of

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² W. L. BENCZE and M. J. ALLEN, *J. med. pharm. Chem.* **1**, 395 (1959).

³ J. J. CHART and H. SHEPPARD, *J. med. pharm. Chem.* **1**, 407 (1959).

⁴ J. H. U. BROWN, *Nature* **187**, 985 (1960).

⁵ R. GAUNT, J. J. CHART, and A. A. RENZI, *Science* **133**, 613 (1961).

⁶ J. J. CHART, H. SHEPPARD, M. J. ALLEN, W. L. BENCZE, and R. GAUNT, *Exper.* **14**, 151 (1958).

⁷ J. J. CHART, H. SHEPPARD, T. MOWLES, and N. HOWIE, *Endocrinology* **71**, 479 (1962).

⁸ H. SHEPPARD and J. J. CHART, *Biochem. Pharmacol.* **8**, 128 (1961).