heute durch das immer weiter in die Beobachtungspraxis eindringende Zenitteleskop gewiesen. Wenn jedoch nicht einmal die Mathematik als eine Formalwissenschaft einen Königsweg kennt, wie sollte dann der Astronomie als einer Realwissenschaft ein Prinzenpfad geschenkt sein, der *per aspera* des Gestrüpps geophysikalischer Effekte, wie das feine Wackeln der Erdachse und das Schlottern ihrer Rotation, mühelos *ad astra* des absoluten Fundamentalsystems führt?

Summary

About 300 years ago NEWTON estimated quantitatively the effect of the precession of the earth-top; 200 years ago BRADLEY discovered aberration and nutation; and 100 years ago BESSEL determined the parallax of a fixed star for the first time. Each of these discoveries set a new problem for position astronomy, for the astronomer relates his observations to an earth rotating on its own axis, so that the newly discovered effect always demands an improvement of the position of the stars. The whole of astronomy, as LAPLACE formulates it, depends upon the invariability of the earth's axis.

For more than 50 years it has been known that the earth moves irregularly (0″.6 in 1⅔2) owing to the non-coincidence of the axis of inertia and the axis of rotation. To account for this variation of latitude, the International Latitude Service has been set up to improve the star co-ordinates inspite of this axis effect. The Latitude Service set up by the International Astronomy Union together with the Union Internationale de Géophysique et Géodésie includes 6 permanent stations on the 39th latitude. For about 7 years it has been known definitely that the speed of rotation of the earth round its axis is variable (0⅔1 *per annum*) so that the star co-ordinates have to be corrected by an international latitude service. While the variation of latitude can be determined with a micrometer screw (precision 10^{-7}) the variations in rotation require a crystal clock (precision 10^{-8}). The finest effect of the mechanics, the variations of rotation of the earth-top, can only be demonstrated by the aid of electronics.

Although these variations of the earth-top really fall into the field of geophysics, where they lead to the interesting problem of secular variations of the earth-pole and continental drift, they are also very important for position astronomy. For the short period of time of observations in meridian, these effects have to be controlled by the finest technique known to science, which is the electronic. The fundamental star catalogues calculated by the mechanical techniques of the last century (pendulum clock and divided circle) have to be corrected today by "electronics".

None of the present star position catalogues, which are deduced by finer effects of the methods of middling and smoothing the calculus of least squares, surpass the exactitude of 0″.1, although 0″.01 is required for the stellar astronomic and geophysical theories. We are now forced to reject the models of a rigid body for the earth-top and to regard it as a fluid body, while the electronic precision of modern position astronomy also enforces a reform of the theories of classical stellar mechanics and classical geophysics.

Brèves communications - Kurze Mitteilungen
Brevi comunicazioni - Brief Reports

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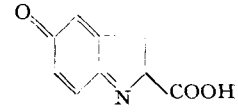
The Biogenesis of the Ergot Alkaloids

The unique moiety common to all known ergot alkaloids is the lysergic (or isolysergic) acid residue, the structure (I) of which has been demonstrated by JACOBS[1] and STOLL[2]. It is of some interest as well as possible significance that this molecule can be derived in a natural fashion from reasonable precursors by application of generally accepted biogenetic steps and plausible, slight modifications thereof.

Recently HARLEY-MASON[3] has presented convincing evidence that 5-hydroxyindoles[4] may well arise in natural systems from tyrosine, *via* 2,5-dihydroxyphenylalanine. Since it is known that indole may be biochemically converted to tryptophan, ROBINSON[1], on the basis of HARLEY-MASON's observations, has made the reasonable suggestion that the hydroxyindoles are the progenitors of hydroxytryptophans and that tyrosine may actually be the parent of both hydroxyindoles and indole itself. Since tyrosine is found associated with the



III*a*

alkaloids of ergot[2], the possibility that 5-hydroxytryptophan (II)[3] (or an equivalent) be available for the biosynthesis of lysergic acid is more than a remote one. II

[1] W. A. JACOBS and L. C. CRAIG, J. Amer. Chem. Soc. *60*, 1701 (1938).

[2] A. STOLL, A. HOFMANN, and F. TROXLER, Helv. chim. Acta *32*, 506 (1949).

[3] J. HARLEY-MASON, Chem. and Ind. *1952*, 173.

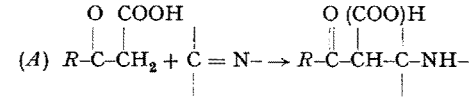
[4] R. J. S. BEER, K. CLARKE, H. G. KHORANA, and A. ROBERTSON, J. Chem. Soc. *1949*, 885. – M. M. RAPPORT, J. Biol. Chem. *180*, 961 (1949). – E. STEDMAN and G. BARGER, J. Chem. Soc. *1925*, 247. – H. WIELAND and F. VOCKE, Ann. Chem. *481*, 215 (1930).

[1] R. ROBINSON, Chem. and Ind. *1952*, 358.

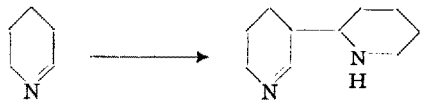
[2] S. FRÄNKEL and J. RAINER, Biochem. Z. *74*, 167 (1916).

[3] A. EK and B. WITKOP, J. Amer. Chem. Soc. *75*, 501 (1953).

is closely analogous to *p*-aminophenol, which can be oxidized easily to *p*-quinonimine. A similar process in the present case leads to III, which bears a close resemblance to the quinonimine III*a*, a probable[3] intermediate in the physiological-type synthesis of 5-hydroxyindole. III, like many quinones, should be susceptible to 1,4-addition. Furthermore, III is in reality a Shiff base, which type, along with *β*-ketoacids, can be a participant in the physiological-type synthesis of alkaloids[1]:



At this point there is introduced the second of the two hypothetical building blocks, dihydronicotinic acid (or a closely related species) (IV). The presence of this entity in the reduced forms of the coenzymes diphospho- and triphosphopyridine nucleotide (DPN and TPN) provides the precedent for its availability in biosynthesis. The molecule IV may be considered in the free form ($X = -OH$ and $R = H$) or in a temporarily combined form ($X = -NH_2$; $-CH_3$, *cf.* trigonelline; or



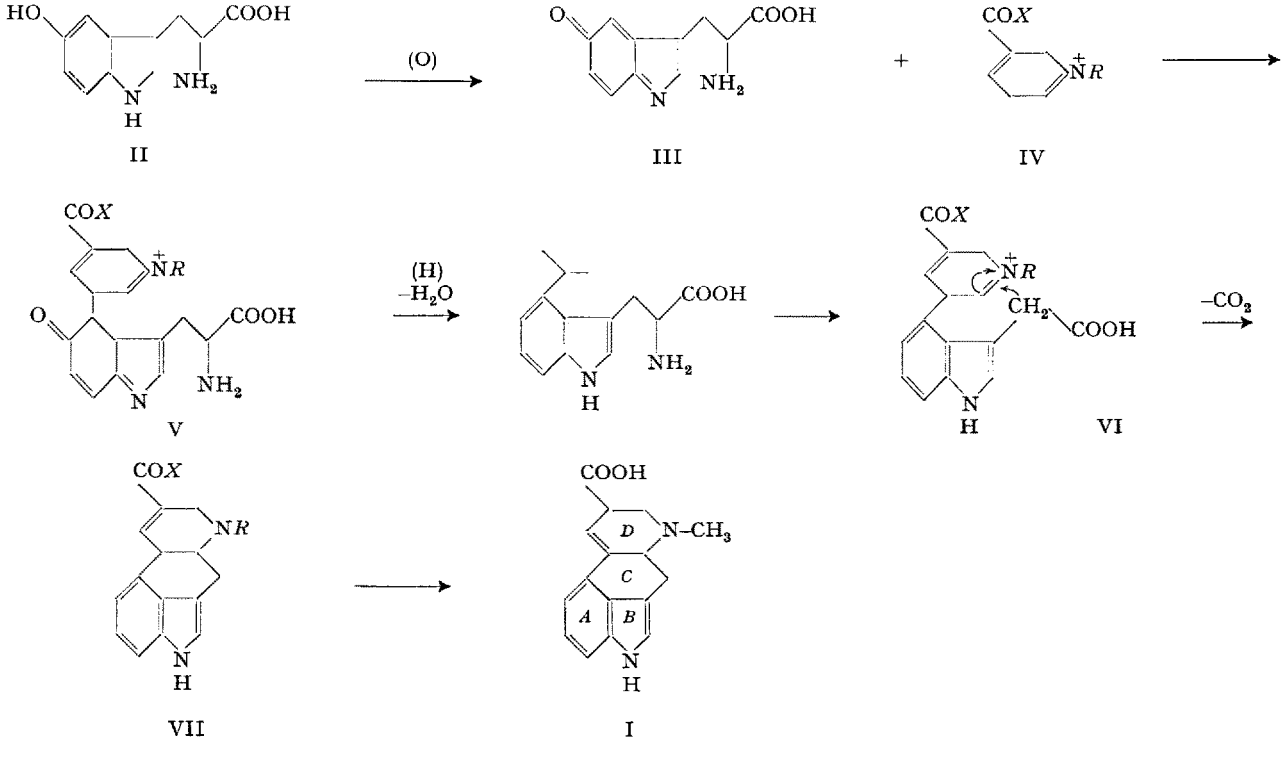
the remainder of the DPN or TPN molecule), and the mobile double bond system may be most fruitfully regarded as represented in IV. It should be noted that IV then bears a striking structural resemblance to a *β*-keto acid, the component required in a step such as represented in (*A*) above. The hydrogen on carbon-5 is activated by the group $-COX$ and especially by the imine function; the dimerization of 1-piperidein to decahydro-2,3-dipyridyl[1] demonstrates the effect of the latter in a reaction similar to those under present consideration. Furthermore, the quaternary form of IV should lend an added activation to the C-5 hydrogen, just as a quaternary salt of *α*- or *γ*-picoline loses a proton more easily than the picoline itself. The condensation of III and IV to give V is thus regarded as a logical extension of the simple model (*A*), and the skeleton required for the lysergic acid molecule is built up in a single step.

Removal of oxygen from, and aromatization of, the carbocyclic ring must be accomplished; this can be visualized as enzymatic reduction of the carbonyl group followed by dehydration. The process is also a requirement in ROBINSON's[2] scheme for the biochemical conversion of tyrosine to indole. While the molecule V would appear to be susceptible to isomerization to the 5-hydroxyindole, ALDER and STEIN[3] and others[4] have demonstrated that 2,3-dihydro-1,4-quinones are surprisingly stable so far as enolization is concerned. In fact members of this class have been chemically reduced[3] in acetic acid solution to the corresponding 4,5-dihydro compounds without evidence of aromatization. Thus, reaction outlets other than enolization may well be open to V, which is similar in structure to a dihydroquinone.

The remaining transformations leading to I are commonplace. Oxidation and transamination on the pyrrole side chain lead to VI, which now possesses an activated methylene group in favorable proximity to the imine function, and therefore undergoes ring closure[5].

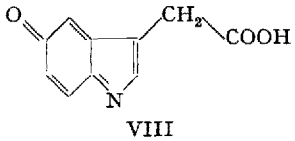
[1] E. HERZOG, Chimia *2*, 206 (1948). – C. SCHÖPF and H. STENER, Ann. Chem. *558*, 124 (1947). – C. SCHÖPF, A. KOMZAK, F. BRAUN, and E. JACOBI, Ann. Chem. *559*, 1 (1948).

[1] C. SCHÖPF, A. KOMZAK, F. BRAUN, and E. JACOBI, Ann. Chem. *559*, 1 (1948).
[2] R. ROBINSON, Chem. and Ind. 1952, *358*.
[3] K. ALDER and G. STEIN, Ann. Chem. *501*, 247 (1933).
[4] L. H. SARETT *et al.*, J. Amer. Chem. Soc. *74*, 1393 (1952).
[5] E. HERZOG, Chimia *2*, 206 (1948).



Decarboxylation (a facile process for indole-3-acetic acid itself); migration of the remaining double bond in ring *D*; and, if necessary, conversion of —*X* to —OH and *R* to $-CH_3$ complete the biosynthesis of lysergic acid.

Obviously the order of steps is not rigid, and several plausible variations of the above scheme can be easily visualized. For example, VIII is a possible parent molecule; it might be expected to condense with IV such that an essentially simultaneous formation of the bonds necessary for



VIII

ring *C* would take place. Thus the 4-position, rather than the 6-position, on the indole portion would be the expected point of juncture of the *A* and *D* rings.

Finally it is revealing to note in this connection that nicotinic acid has definitely been shown to arise in biological systems from tryptophan (the latter can also be isolated from ergots[1]). This observation supplies, in view of all the foregoing, the last link in a hypothetical reaction chain starting with tyrosine *only* and leading ultimately to lysergic acid.

E. E. VAN TAMELEN

Department of Chemistry, University of Wisconsin, Madison, Wis., July 11, 1953.

Zusammenfassung

Es wird ein biogenetischer Weg vorgeschlagen, der zu Lysergsäure, dem gemeinsamen Teilstück aller Mutterkornalkaloide, führt. Der grundlegende Schritt der Biogenese besteht nach unserem Vorschlag in der Kondensation von Dihydro-Nikotinsäure (oder einem Derivat derselben) mit dem Chinon III, das aus 5-Oxytryptophan (oder einer gleichwertigen Verbindung) sich bilden sollte.

[1] S. FRÄNKEL and J. RAINER, Biochem. Z. *74*, 167 (1916).

Darstellung von Polyasparaginsäuren (Polyaspartsäuren) aus dem thermischen Autokondensationsprodukt der Asparaginsäure

Mit dem Sammelnamen «Polyaspartsäuren» wurden von SCHIFF[1] die kristalline «Tetraaspartsäure» und die amorphe «Oktaaspartsäure» bezeichnet, die durch eine verhältnismässig schonende Hydrolyse aus ihren anhydridartigen Muttersubstanzen (Tetraaspartid bzw. Oktaaspartid) zugänglich waren. Das Gemisch der Aspartide entstand beim andauernden Erhitzen (180°) von Asparagin bzw. Asparaginsäure-Hydrochlorid in einem Strom von Salzsäuregas bzw. Kohlendioxyd[1], weiterhin noch besser aus freier Asparaginsäure durch unmittelbares Erhitzen (180–200°).

Wir haben die Untersuchungen von SCHIFF und anderen[2] wieder aufgenommen, mit dem Ziel, eine Polyaspartsäure möglichst hoher Gliederzahl zu gewinnen und ihre Struktur zu untersuchen. Zu diesem Zwecke wurde das thermische Autokondensationsprodukt der DL-Asparaginsäure in 0,1 *n* Natronlauge gelöst und aus dieser Lösung das Gemisch der freien Polyaspartsäuren über ihre schwerlöslichen Cu-II-Salze herausgewonnen. Ihre wässerige Lösung wurde nun solange dialysiert, bis mit Hilfe der papierchromatographischen Kontrolle in der rückständigen Lösung keine leicht beweglichen, ninhydrinpositiven Bestandteile mehr nachweisbar waren. Durch Lyophilisierung dieser Lösung wurde eine fast farblose Substanz gewonnen, die in Wasser äusserst leicht löslich ist. Ihre positive Biuret- und Ninhydrinreaktion, weiterhin ihre Analysendaten deuten an, dass es sich um eine *Polyasparaginsäure* handelt, die ein typisches, monotones Polypeptid darstellt. Auf Grund von Aminostickstoff-Bestimmungen (VAN SLYKE) lässt sich ein durchschnittliches Molgewicht von rund 8200 berechnen; dies würde einer Gliederzahl von 71 entsprechen.

Wir glauben annehmen zu dürfen, dass das thermische Autokondensationsprodukt der Asparaginsäure aus ihrem primär entstandenen Anhydrid (I) gebildet wird und die Struktur II besitzt (I—IV).

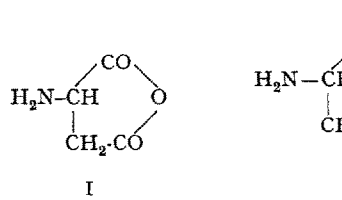
So wird es leicht verständlich, dass eine schonende Hydrolyse des Produktes II zu Polyasparaginsäure führt. Es lässt sich im voraus nicht sagen, ob dabei α-Polyasparaginsäure (III), β-Polyasparaginsäure (IV), eine aus α- *und* β-Asparagylresten in regelmässiger oder unregelmässiger Reihenfolge aufgebaute Polyasparaginsäure oder sogar ein Gemisch entsteht, das sämtliche Vertreter dieser möglichen Typen enthält.

Da die gewonnene Polyasparaginsäure in kaltem Wasser äusserst leicht löslich ist, kann die Struktur III

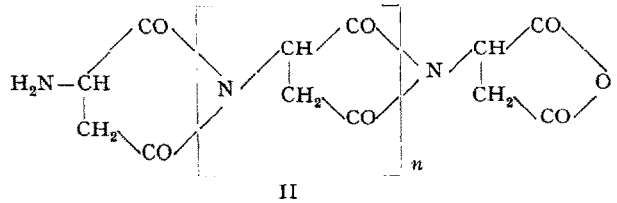
[1] H. SCHIFF, Ber. dtsch. chem. Ges. *30*, 2449 (1897).

[1] E. SCHAAL, Ann. Chem. *157*, 24 (1871).

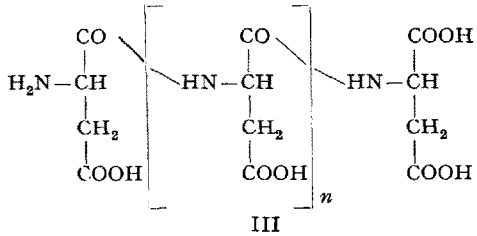
[2] H. SCHIFF, Ber. dtsch. chem. Ges. *30*, 2449 (1897). – E. SCHAAL, Ann. Chem. *157*, 24 (1871). – E. GRIMAUX, Bull. Soc. Chim. *38*, 64 (1882). – J. GUARESCHI, Gazz. Chim. *6*, 390 (1876). – H. SCHIFF, Ann. Chem. *303*, 183 (1898); *307*, 231 (1899); *310*, 301 (1900).



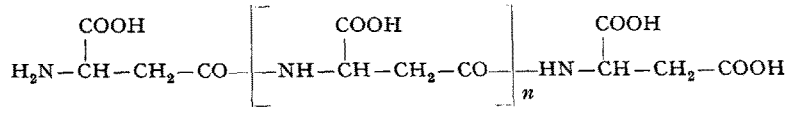
I



II



III



IV