crystallizing from hot water as clusters of fine needles (calcd. for $C_3H_7O_6PBa$: P, 10.1; Ba, 44.7; found: P, 9.8; Ba, 44.3).

The radioactivity of the various samples was measured by means of a sensitive Geiger–Müller counter; the substances, in aqueous solution, being contained in a standardized glass cell. This technique, in contrast to the usual method of ignition and measurement of the activity of the ash, makes it possible subsequently to manipulate the radioactive substances unchanged. It leads, however, to considerably lower activity counts than those obtained with the ashed residues. Representative solutions of sodium glycerophosphate and of phosphoric acid (from the phosphorus oxychloride originally employed), containing 84.8 and 70.9 mg. of phosphorus, respectively, yielded respective counts of 0.797 and 0.815 impulses per minute per mg. of phosphorus when examined under strictly comparable conditions. As was to be expected, the ratio $^{32}_{15}P$: $^{31}_{15}P$ was constant in all compounds prepared, after allowance had been made for the natural decay of the unstable isotope.

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DEPARTMENT OF BIOLOGICAL CHEMISTRY
COLUMBIA UNIVERSITY ERWIN CHARGAFF
NEW YORK, N. Y.

RECEIVED JUNE 4, 1938

THE TRANSIENT INHIBITION OF THE THERMAL DECOMPOSITION OF BUTANE BY NITRIC OXIDE

Sir:

It has been shown by the writers [Echols and Pease, THIS JOURNAL, **59,** 766 (1937)] that the decomposition of butane is inhibited by nitric oxide. Subsequent study of the reaction has clearly indicated that the inhibition by nitric oxide is a *transient effect*. Careful analysis of the reacted gases has shown that this is not the result of removal of the nitric oxide by reaction.

For example, with 200 mm. of butane and 20 mm. of nitric oxide at 520° it is found that the initial slope of the reaction curve is nearly zero, but that the slope slowly rises with time until at 20% reaction it is very nearly that of the uninhibited reaction at the same percentage decomposition. Under these conditions less than 10% of the nitric oxide has reacted.

It has been found that these facts, together with all of the data so far obtained on the phenomenon, may be very nearly quantitatively explained by the assumption that the nitric oxide forms an unstable compound with chain carriers leading to an equilibrium of the form:

$$R + NO \rightleftarrows NOR$$

where R is the chain carrier, presumably a free radical.

This equilibrium is slowly established in the initial stages of the reaction and as the equilibrium is approached the "feed-back" of radicals neutralizes the inhibition, producing a normal rate of the butane decomposition. A detailed discussion of the facts will be presented shortly.

FRICK CHEMICAL LABORATORY L. S. ECHOLS
PRINCETON UNIVERSITY R. N. PEASE
PRINCETON, N. J.

RECEIVED JUNE 20, 1938

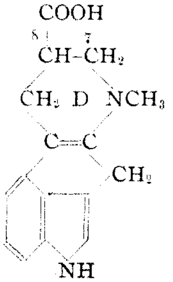
THE POSITION OF THE CARBOXYL GROUP IN LYSERGIC ACID

Sir:

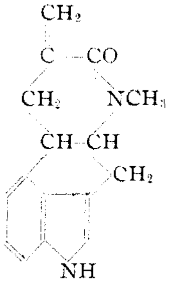
We have reported previously [*J. Biol. Chem.*, **113,** 760 (1936)] that dihydrolysergic acid, contrary to lysergic acid which loses carbon dioxide and methylamine somewhat above 200°, can be sublimed at 25 mm. from a bath heated at 300°. *Anal.* Calcd. for $C_{16}H_{18}O_2N_2$: C, 71.06; H, 6.72. Found: C, 71.3; H, 6.61.] However, more recent investigation of the sublimation of α-dihydrolysergic acid has shown that a chemical change accompanies such sublimation which is accentuated by raising the temperature to 350°. A neutral substance was isolated from the chloroform solution of the sublimate after extraction of dihydrolysergic acid with dilute potash. After recrystallization from methyl alcohol, the substance was obtained in a yield of 33% (m. p. 305–307° with decomposition) $[\alpha]^{25}\mathrm{D} -219°$ (*c*, 0.48 in pyridine). Analysis showed that its formation involved loss of water. [*Anal.* Calcd. for $C_{16}H_{16}ON_2$: C, 76.15; H, 6.40; N, 11.11; (N)CH_3, 5.96. Found: C, 76.10; H, 6.58; N, 11.02; CH_3, 5.04.] Contrary to dihydrolysergic acid, it no longer dissolved in dilute acid or alkali, but it still gave the characteristic Keller color reaction unimpaired. Also contrary to the dihydro acid, it was found to be unsaturated since on catalytic hydrogenation it absorbed 1 mole of hydrogen with the formation of a neutral dihydro derivative which melted with decomposition at 336°. [*Anal.* Calcd. for $C_{16}H_{18}ON_2$: C, 75.54; H, 7.14. Found: C, 75.50; H, 7.12.]

In a communication by L. C. Craig, T. Shedlovsky, R. G. Gould, Jr., and W. A. Jacobs which is now in press, an investigation of the dissociation constants of lysergic acid and its derivatives has been reported, which has made it necesssary to revise our previous tentative conclusion that the COOH group of lysergic acid is in position 7, *i. e.*, on the carbon atom adjoining the N atom of Ring D. Such an arrangement would place it in the category of a substituted α-amino acid like proline. Instead, the evidence indicates a β-amino acid derivative and that the point of attachment of the COOH group is the carbon atom β to the N atom or position 8 as shown in formula I.

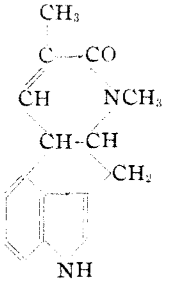
The formation of the above neutral pyrolysis product from dihydrolysergic acid fits in well with such β-substitution of the COOH group and must be interpreted as an unsaturated cyclic amide possessing either formula II or III.



I



II



III

It is well known that β-amino acids, in contradistinction to the α-acids, decompose readily into unsaturated acids and ammonia. For instance, β-alanine gives readily ammonia and acrylic acid. In accordance with this property, dihydrolysergic acid should cleave between the N atom and carbon atom 7 to give an unsaturated complex secondary amino acid which would at once lactamize. Model experiments with the various piperidine carboxylic acids are now in progress to verify the nature and formation of this pyrolysis product of dihydrolysergic acid.

THE LABORATORIES OF
THE ROCKEFELLER INSTITUTE
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NEW YORK, N. Y.

WALTER A. JACOBS
LYMAN C. CRAIG

RECEIVED JUNE 21, 1938

ENOL ETHERS OF STEROID KETONES

Sir:

The following is a report of the synthesis of enolic ethers of unsaturated ketonic sterols. For the preparation of these compounds the modification of Arbuzov and Mikhailova [*J. Gen. Chem.* (*U. S. S. R.*), **6,** 390 (1936)] of the classical Claisen method was used. Instead of obtaining the expected ketal, the reaction yielded directly the enol ether, one molecule of alcohol having been split out.

As a class, these compounds are stable in a solid state, but quite unstable in solution. From Table I it may be seen that in chloroform solution at room temperature the rotation changes rapidly from a negative to a positive one, the final rotation in each case being that of the free ketone. Very probably the traces of hydrochloric acid in the chloroform are the cause of the rapid splitting of the ethoxyl group, since in pyridine solution the rotation remained practically unchanged. By hydrolyzing the testosterone enol ether propionate with alcoholic potash it was possible to remove the propionic acid group without splitting the ethoxyl out of the molecule.

TABLE I

Time, hours	Specific rotation of enol ethyl ethers Cholestenone[a]	 Testosterone benzoate[b]	 Testosterone propionate[c]
0	−102.3	− 42.5	−140
0.5	− 33.8	+130	−114
1	+ 18.2	+142	
2	+ 67.6	+143	+60
24	+ 87.7		+88 (48 hours)

[a] 1.1% in chloroform. [b] 1.01% in chloroform. [c] 1.2% in chloroform.

In pyridine solution the specific rotations were −96.0° for cholestenone enol ethyl ether, and −67.5° for testosterone benzoate enol ethyl ether. These values changed only slightly after standing for several hours.

The fact that all the new substances show initially a negative rotation would indicate that one of the double bonds is in ring A, the other in ring B [Ulrich Westphal, *Ber.*, **70**, 2128 (1937)].

These substances are prepared by dissolving 5 g. of the ketone in 10 cc. of ethyl orthoformate and 1 cc. of formic acid. The solution is cooled to 20° and one drop of concentrated sulfuric acid added. The mixture is warmed on the waterbath to 50° with constant stirring, held at this temperature for ten minutes. After standing overnight at room temperature, ether is added and the solution washed with water, soda and finally with water until neutral. After drying, the ether is evaporated and the residue recrystallized from acetone or ligroin.

Table II gives the physical constants of these compounds as well as the substances isolated from