ity measurements. Gliadin is stable even at *p*H 1.46, the lowest *p*H studied. Beyond *p*H 12 there is a drop in the sedimentation constant.

3. A number of measurements have been made in aqueous solution at low *p*H within the stability range. The results are in good agreement with those obtained in alcohol solution and corrected to a water basis.

4. The protein is inhomogeneous with respect to molecular weight. The sedimentation constant of the predominant constituent is 2.10×10^{-13}.

5. The molecular weight of the principal constituent was determined by measurement of the sedimentation equilibrium in aqueous solution. At *p*H 2.23 and above, when the temperature is 20° or lower, there is probably a mixture of whole and half molecules of weight 34,500 and 17,250. At higher temperatures and higher acidities dissociation into half molecules is complete.

6. The molecules are not spherical. The dissymmetry number is 1.21 for the half molecule, 1.92 for the whole molecule.

7. Purified gliadin was fractionated by the method used by Haugaard and Johnson. The least soluble fraction was found to contain a high concentration of heavy molecules, while the most soluble fraction consisted almost entirely of the constituent of lowest molecular weight.

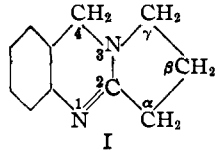
UPSALA, SWEDEN RECEIVED APRIL 5, 1935

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

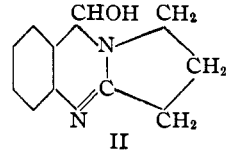
Structure of Vasicine. III. Position of the Hydroxyl Group[1]

R. C. MORRIS,[2] W. E. HANFORD AND ROGER ADAMS

With the structure of desoxyvasicine (I) definitely established through synthesis,[1,3] the position of the hydroxyl group in vasicine remains to be determined.



I

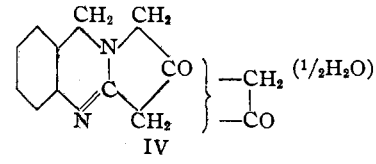


II

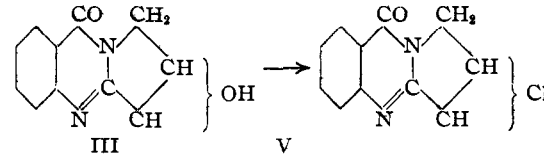
The reactions of vasicine previously described exclude the possibility of the hydroxyl group being in the γ position. It might be present, however, in the α-, β- or 4-position. The 4-position (II) would appear to be very unlikely since a molecule of this structure is a carbinol base and acid would very probably convert it into a quaternary ammonium salt with the elimination of water. The salts produced experimentally indicate no loss of water during formation.

Experimental evidence is presented in this communication in regard to the location of the hydroxyl group. Ghose[4] described the oxidation of vasicine by means of hydrogen peroxide. He reported two products (1) m. p. 213–214°, which involved the loss of two hydrogens and addition of one oxygen to vasicine, and (2) m. p. 168°, which involved the loss of two hydrogens with the retention of one-half molecule of water of crystallization. On the basis of the present established basic structure for vasicine, assuming the hydroxyl to be in the α- or β-position, these two oxidation products might possibly be represented by III and IV. Formula IV, for the compound m. p. 168°, however, would not coincide with Ghose's observation that it could be oxidized to III.

A restudy of the oxidation of vasicine by means of hydrogen peroxide has given results not identical with those of Ghose. Three per cent. hydrogen peroxide even on long heating left vasicine unchanged but with 30%, oxidation occurred. There was obtained by this procedure a mixture of unchanged vasicine and the product m. p. 213° reported by Ghose, which could be separated by fractional crystallization. The presence of the



IV



III V

(1) For the previous paper in this field see THIS JOURNAL, **57**, 921 (1935).

(2) Submitted as part of a thesis for the Degree of Doctor of Philosophy in Chemistry.

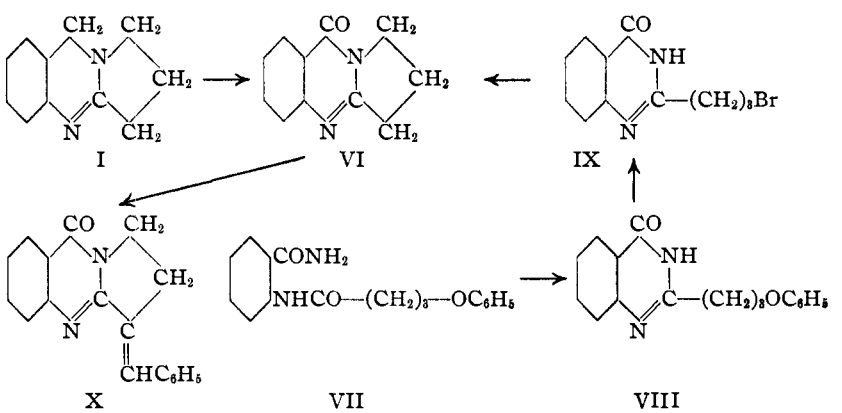
(3) Späth, Kuffner and Platzer, *Ber.*, **68**, 497 (1935).

(4) Ghose, Krishna, Narang and Rây, *J. Chem. Soc.*, 2740 (1932).

hydroxyl group in this product was demonstrated by the quantitative evolution of methane by means of methylmagnesium iodide and by replacement of the hydroxyl with chlorine V. The oxidation product of m. p. 213°, as well as the chlorine derivative prepared from it, readily undergo reduction by means of zinc and acid with the formation of desoxyvasicine.

The oxidation product of Ghose of m. p. 168° was never obtained. It is suggested that the reported product was probably a mixture of the oxidation product of m. p. 213° and of unchanged vasicine. A synthetic mixture of these two melts at 168° and, if in equal parts, the analysis would be identical with that reported by Ghose. A mixture would conform equally well to the observation of this investigator that the compound of m. p. 168° on oxidation resulted in the formation of the substance of m. p. 213°.

Desoxyvasicine (I) is more readily oxidized than vasicine. By 3% hydrogen peroxide, it is converted to a product with two hydrogens replaced by an oxygen which has the constitution (VI) as determined by synthesis. Phenoxybutyryl chloride reacts with *o*-aminobenzamide to yield the corresponding amide (VII); ring closure by heat (VIII); replacement of the phenoxyl group by bromine (IX); ring closure with alkali to give (VI).

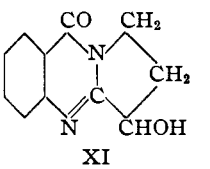


Compound (VI) shows the same ease of condensation with benzaldehyde as desoxyvasicine, to give a benzal derivative presumably of structure (X).

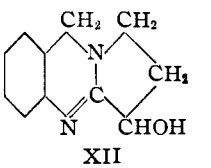
The 4-position in such dihydroquinazolines and quinazolones is apparently very susceptible to oxidation and reduction as demonstrated by the ease of oxidation of vasicine and desoxyvasicine and subsequent ease of reduction of these products.

Lead tetraacetate converts oxidized desoxyvasicine (VI) to an acetoxy derivative which on hydrolysis results in a molecule containing an hydroxyl group (XI).

As the α-methylene of VI is the one which, according to all analogous reactions, would be the point of attack by the lead tetracetate, the structure assigned to it (XI) is almost unquestionable. Compound XI, however, is identical with the hydrogen peroxide oxidation product of vasicine m. p. 213° (III). Thus by the synthesis of the oxidized vasicine (XI) from 2,3-trimethylene 4-quinazolone (VI), the structure of which is known and in which the carbonyl is in the 4-position, the 4-position for the hydroxyl group in oxidized vasicine, as well as in vasicine, is definitely excluded. At the same time it establishes with practical certainty that it is on the active methylene group which is the α-position. Since the hydroxyl group in vasicine is presumably in the same position as in its oxidation product, vasicine may be assigned formula (XII).



XI

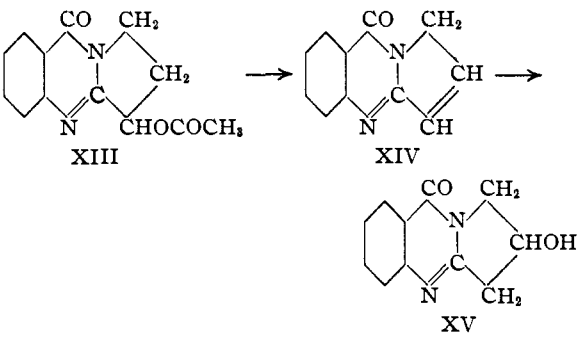


XII

The only possibility that the results of the lead tetraacetate reaction with 2,3-trimethylene 4-quinazolone may be misleading and that the hydroxyl might be in the β-position, lies in the unlikely assumption that in the mild alkaline hydrolysis of the acetoxy derivative (XIII), acetic acid is first eliminated (XIV) and water then adds to the resulting olefin linkage (XV).

Experimental

Oxidation of Vasicine; Formation of 2,3-(α-Hydroxytrimethylene)-4-quinazolone (III).—A suspension of 0.400 g. of vasicine in a mixture of 7 cc. of acetone (distilled over potassium permanganate) and 5 cc. of 30% hydrogen peroxide was heated under reflux at 60–70° for one and one-half hours. The solution was allowed to cool and evaporated to about 5 cc. A white crystalline product was formed which proved to be unchanged vasicine. The filtrate was evaporated to dryness, leaving a gummy residue, which crystallized upon the addition of 4–5 cc. of acetone. After several crystallizations from water, the pure material was obtained as microscopic crystals of m. p. 213–214°. A mixed melting with pure vasicine gave m. p. 168–170°; yield 0.151 g.



XIII XIV XV

Anal. Calcd. for $C_{11}H_{10}O_2N_2$: C, 65.34; H, 4.96; N, 13.86. Found: C, 65.22; H, 4.98; N, 13.74. Zerewitinoff: Sample 0.0480 g. gave 5.79 cc. of methane at 26° + 719 mm. Calcd. 6.1 cc. for one hydroxyl.

2,3-(α-Chlorotrimethylene)-4-quinazolone (V).—A mixture of 20 cc. of thionyl chloride and 0.200 g. of 2,3-(α-hydroxytrimethylene)-4-quinazolone was refluxed for one hour. The excess thionyl chloride was removed by distillation under reduced pressure and the residue dissolved in ice water. The aqueous solution was made slightly alkaline with aqueous ammonia and extracted with chloroform. The residue obtained by the evaporation of the chloroform was crystallized from petroleum ether (b. p. 60–110°); white needles of m. p. 109°; yield 0.113 g.

Anal. (Dried for 3 hrs. at 80° *in vacuo*) Calcd. for $C_{11}H_7ON_2Cl$: N, 12.72. Found: N, 12.53.

Reduction of 2,3-(α-Chlorotrimethylene)-4-quinazolone to Desoxyvasicine.—A mixture of 0.080 g. of the 2,3-(α-chlorotrimethylene)-4-quinazolone in 5 cc. of glacial acetic acid and 0.3 g. of zinc dust was stirred for one-half hour. Then 5 cc. of water was added and the solution stirred for another half hour. Finally 8 cc. of concentrated hydrochloric acid was introduced, the solution again stirred for one-half hour and then allowed to stand overnight. The mixture was made alkaline with aqueous ammonia and extracted with chloroform. The chloroform was evaporated and the residue was crystallized from petroleum ether (b. p. 60–110°), m. p. 88–89°; after drying for three hours over phosphorus pentoxide *in vacuo* at 56° it had a m. p. of 96–97°. Its picrate melted at 205° and a mixed melting point with the picrate of desoxyvasicine was 205–206°.

Anal. Calcd. for $C_{11}H_{12}N_2$: N, 16.28. Found: N, 16.05.

2,3-(α-Hydroxytrimethylene)-4-quinazolone was reduced in exactly the same manner with formation of desoxyvasicine.

Oxidation of Desoxyvasicine; Formation of 2,3-Trimethylene-4-quinazolone (VI).—The procedure in this preparation was almost identical to that described for the oxidation of vasicine. From 0.500 g. of desoxyvasicine, 8 cc. of acetone (distilled over potassium permanganate) and 6 cc. of 3% hydrogen peroxide, heated to 50–60° for one and one-half hours, after removal of unchanged desoxyvasicine, there was obtained a gummy residue. This was dried in a desiccator over sulfuric acid and purified by crystallization from petroleum ether (b. p. 60–110°) as white needles m. p. 110–110.5°; yield, 0.210 g.

Anal. Calcd. for $C_{11}H_{10}ON_2$: C, 71.0; H, 5.38; N, 15.04. Found: C, 71.12; H, 5.44; N, 15.01.

Benzal-2,3-trimethylene-4-quinazolone (X).—This was prepared in a manner similar to benzal-2,3-trimethylene-3,4-dihydroquinazoline.[1] It formed yellow crystals from petroleum ether (b. p. 60–110°), m. p. 137–139°.

Anal. Calcd. for $C_{18}H_{14}ON_2$: N, 10.60. Found: N, 10.69.

***o*-Aminobenzamide.**—The general method of Wojcik and Adkins was used.[5] A mixture of 100 g. of methyl anthranilate and approximately 50 cc. of liquid ammonia was placed in a high pressure bomb. The pressure was raised to 1200 lb. by the addition of hydrogen and the bomb heated for ten hours at 200°. The oil which was obtained after evaporation of the ammonia solidified on standing. After crystallization from water, white plates were obtained of m. p. 108° (melting point 108° reported by Kolbe (*J. prakt. Chem.*, **30**, 475 (1884)); yield 25 g.

***o*-(γ-Phenoxybutyrylamino)-benzamide (VII).**—To a solution of 8 g. of *o*-aminobenzamide in a mixture of 100 cc. of benzene and 100 cc. of ether was added 26 cc. of 10% aqueous sodium hydroxide. A solution of 13 g. of γ-phenoxybutyryl chloride[1] in 25 cc. of benzene was added slowly with shaking. A solid separated which was filtered and the benzene–ether layer was evaporated. The residue thus obtained and the filtered solid were combined and crystallized from benzene as white microscopic crystals of m. p. 150° in yield 13 g.

Anal. Calcd. for $C_{11}H_{18}O_3N_2$: N, 9.73. Found: N, 9.73.

2-(γ-Phenoxypropyl)-4-quinazolone (VIII).—A 50-cc. distilling flask containing 7 g. of *o*-(γ-phenoxybutyrylamino)-benzamide was placed in a Wood's metal bath and the temperature of the bath raised slowly to 230–235°. Water was eliminated and condensed on the side of the flask. After heating at this temperature for fifteen minutes the pressure was lowered to 20 mm. and the heating continued for ten minutes longer. On cooling the liquid solidified and was crystallized from benzene as light yellow plates of m. p. 181°; yield 6 g.

Anal. Calcd. for $C_{11}H_{16}O_2N_2$: N, 10.36. Found: N, 10.30.

2,3-Trimethylene-4-quinazolone (VI).—In an all-glass distilling apparatus was placed 6 g. of 2-(γ-phenoxypropyl)-4-quinazolone and 125 cc. of constant boiling hydrobromic acid. The mixture was heated to such a temperature that the hydrobromic acid distilled slowly. Before a negative test for phenol in the distillate was obtained it was necessary to add two 100-cc. portions of hydrobromic acid. The distillation was continued until about 5 cc. remained. The hydrobromide salt of 2-(γ-bromopropyl)-4-quinazolone IX was obtained by evaporation of the last few cc. of acid in a desiccator. The dried salt was dissolved in 100 cc. of absolute ethyl alcohol and a solution of 1.83 g. of potassium hydroxide in 20 cc. of absolute ethyl alcohol added. The solution was refluxed, on the steam-bath overnight, filtered and the alcohol evaporated. The oily residue crystallized on the addition of 5 cc. of ether. The solid was purified by crystallization

(5) Wojcik and Adkins, THIS JOURNAL, **56**, 2419 (1934).

from petroleum ether (b. p. 60–110°) as white needles of m. p. 110–110.5°. A mixed melting point with the compound obtained by the oxidation of desoxyvasicine melted at 110–110.5°, thus indicating the identity of the two products.

Anal. Calcd. for $C_{11}H_{10}O_2N_2$: C, 71.51; H, 5.38; N, 15.05. Found: C, 71.51; H, 5.62; N, 14.83.

Oxidation of 2,3-Trimethylene-4-quinazolone to 2,3-(α-Hydroxytrimethylene) - 4 - quinazolone (XI).—To a solution of 0.200 g. of 2,3-trimethylene-4-quinazolone in 15 cc. of thiophene-free, dry benzene was added 0.600 g. of freshly prepared lead tetraacetate. The mixture was well stirred and heated at 50–60° for twenty hours. After filtering, the solution was evaporated and the residue extracted with chloroform. Upon evaporation of the chloroform a light yellow oil remained. It was shaken with a 5% sodium carbonate solution until the two layers had disappeared. The product was then extracted with chloroform and the chloroform evaporated. The residue was extracted three times with 5-cc. portions of hot petroleum ether (b. p. 60–110°) to remove the starting material, over half of which was recovered. The residue was crystallized from a mixture of benzene and petroleum ether (b. p. 60–110°) as white microscopic needles, m. p. 211–212° (dec.); yield 15 mg. A mixed melting point with the oxidation product of vasicine melted at 212° (dec.), indicating the identity of these two products.

Anal. Calcd. for $C_{11}H_{10}O_2N_2$: C, 65.34; H, 4.96. Found: C, 65.52; H, 4.86.

Summary

1. Vasicine and desoxyvasicine have been oxidized to the corresponding 4-keto derivatives.

2. The structure of the oxidized desoxyvasicine was proven by synthesis.

3. Oxidized desoxyvasicine reacts with lead tetraacetate to give a hydroxy derivative identical with oxidized vasicine.

4. These facts indicate that the hydroxyl in vasicine is on the methylene attached to the 2-carbon atom.

URBANA, ILL. RECEIVED APRIL 22, 1935

NOTES

Note on the Construction of Glass Helices for Fractionating Column Packing

BY EDWIN E. ROPER, GEORGE F. WRIGHT, JOHN R. RUHOFF AND WALTER R. SMITH

In the past year we have prepared a large quantity (1600 cc.) of broken glass helices for fractionating column packing of the type first described by Wilson, Parker and Laughlin.[1] From this work we feel we have gained experience that may prove valuable in the fabrication, breaking and sorting of the helices.

We have followed, in general, the method outlined by Wilson, Parker and Laughlin for winding the helices. We use 75 cm. lengths of one-eighth inch diameter steel rod for the winding forms and wind the spiral coils from a 3-mm. Pyrex rod. This requires an oxygen flame about 4 cm. high, and precludes the use of brass as a winding form. The steel rods are drilled at one end (1 mm. diameter hole) and then made slightly conical toward this end by the use of emery paper. This facilitates the removal of the wound coil. The winding form is given a very thin coat of natural graphite by rubbing it with a cloth upon which the graphite has been sprinkled, together with a drop of light lubricating oil if necessary; this makes the removal of the finished spiral much easier, and also helps in the rotation of the form while the spiral is being wound. It is relatively simple to prepare spiral coils 40 cm. in length, which can be removed in one piece if desirable.

We use a simple bearing for the left end of the winding form, and the rotation is performed with the left hand, while the feeding of the Pyrex rod and the regulating of its angle to the long axis of the winding form are done with the right hand.

The long spiral coils obtained from the winding operation are threaded on to a convenient length (*ca.* 60 cm.) of bare No. 18 copper wire, and the blade of a thick knife is pressed down between each turn in order to break the fiber. The more closely the coil is wound, the easier is this step. Small helices of any desired number of turns or fractions of turn can be formed from the long coils by taking care to break off a definite number of turns from the end of the large helix. For instance, we wished to make single turns from our long coils; however, if we attempted to break off exactly one turn, a large number of the coils were less than three-quarters of a turn, but by attempting to break off one and a quarter turns, we obtained coils which were largely one turn, and only relatively small numbers of larger and smaller coils.

The broken coils of less than one turn fall off from the wire. The breaking is done over a black cloth, so that the material which falls off the wire can be collected and sorted more easily. The material which remains on the wire is sorted as it is removed. The coils that consist of more than the desired number of turns are best broken by hand over the black cloth and then this material is added to that which fell off the wire during the breaking operation. We have tried screening this combined lot and have found that a small (20-mesh) screen will take out the finer particles (one-quarter turn or less) and that an ordinary kitchen colander (circular holes about 4 mm. in diameter, spaced about 7 mm. between centers) will allow the half-turn size to drop through and retain the majority of the three-quarter turn size. An eight mesh wire screen does not do this nearly as satisfactorily, since the larger size

(1) (a) THIS JOURNAL, **55**, 2795 (1933); (b) **56**, 1396 (1934).