for 3 hr. After cooling, 7.0 g. of XII, m.p. 189°, was obtained. A mixture of 3 g. of XI and 20 ml. of pyridine, heated on the steam bath for 1 hr., gave 2.8 g. of XII. The carbonyl absorption for XII occurred at 5.95 μ.

6b,11-Diazabenzo[*a*]fluorene-5,6-dione (XIV).—A mixture of 22.7 g. of I, 19 g. of *o*-aminopyridine in 100 ml. of ethoxyethanol was refluxed for 5 hr. To this was added 200 ml. of ethanol and the precipitate collected to give 26 g. of XIV, m.p. 298° (lit.,[10] m.p. 306°); carbonyl absorption at 5.97 μ.

Anal. Calcd. for $C_{15}H_8O_2N_2$: C, 72.6; H, 3.2; N, 11.3. Found: C, 72.6; H, 3.6; N, 11.1.

4a,9,14,15-Tetrazabenzo[*c*]indeno[2,1-*a*]anthracene (XV).—A mixture of 2.5 g. of XIV and 1.5 g. of *o*-phenylenediamine in 25 ml. of acetic acid was refluxed for 3 hr. The bright yellow precipitate which separated was collected and crystallized from trichlorobenzene to give 2.3 g. of XV, m.p. 285°, and no absorption in the carbonyl region of the infrared.

Anal. Calcd. for $C_{21}H_{12}N_4$: C, 78.8; H, 3.8; N, 17.5. Found: C, 78.6; H, 3.9; N, 17.4.

3-Phenyl-1,3a-diazaindene-2,2′-dicarboxylic Anhydride (XVI).—A suspension of 3.0 g. of XIV in 100 ml. of ethanol was treated with 5 ml. of 30% hydrogen peroxide, followed by 5 ml. of 50% sodium peroxide. After the mixture had been stirred at 25–30° for 1 hr., it was heated to 50° and 25 ml. of water and 5 ml. more of hydrogen peroxide were added. When solution was complete (10 min.), the solution was treated with Norit, filtered, and acidified with acetic acid. The white precipitate was crystallized from water to give 1.7 g. of white crystals of XVI, m.p. 195°. The anhydride absorption occurs at 5.48 and 5.72 μ.

Anal. Calcd. for $C_{15}H_8O_3N_2$: C, 68.3; H, 3.0; N, 10.6. Found: C, 68.6; H, 3.4; N, 10.6.

15,16-Dithia-5,10-diazanaphtho[2,3-*a*]benzo[*c*]anthracene (XVII).—Pyridine (50 ml.) containing 2.5 g. of VI and 3.0 ml. of *o*-aminobenzenethiol was heated to reflux for 2 hr., an equal volume of methanol was added, and the mixture chilled to give 2.5 g. of XVII, m.p. 291° (from dichlorobenzene), with no absorption in the NH or carbonyl region of the infrared spectrum.

Anal. Calcd. for $C_{22}H_{12}N_2S_2$: C, 71.5; H, 3.2; N, 7.6. Found: C, 71.5; H, 3.2; N, 7.3.

Other solvents, such as ethanol, ethoxyethanol, toluene, or dimethylformamide, gave XVII, but the yield was lower than in the example employing pyridine. A mixture of 3 g. of the enol betaine VI and 4 ml. of *o*-aminobenzenethiol refluxed for 2 hr. gave 3.2 g. of XVII.

Polynuclear Heterocycles. VII. The Properties of Azacarbons Containing the Enol Betaine Structure[1]

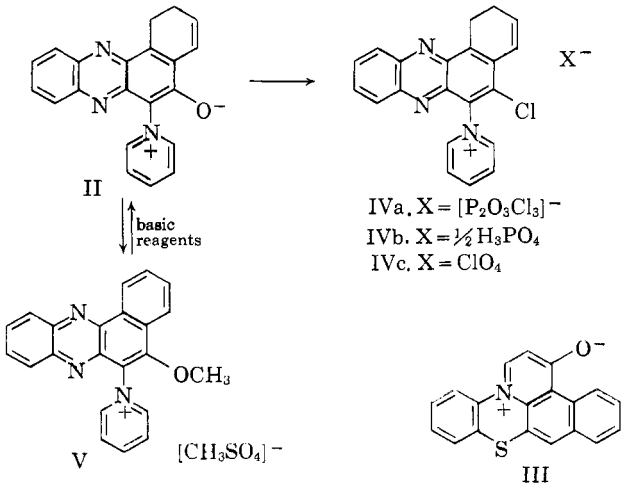
J. A. VANALLAN AND G. A. REYNOLDS

Research Laboratories, Eastman Kodak Company, Rochester, New York

Received July 26, 1962

The properties of 1*H*-benzo[*b*]pyrido[1,2,3-*mn*]phenothiazin-1-one (III) and quinolizone (XV), both of which appear to exist in highly polarized form, are compared with the enol betaines, 6-pyridiniumbenzo[*a*]phenazine 5-oxide (II), 1,4-dioxo-3-pyridinium 2-naphthoxide (VIII).

Initial studies dealing with the reaction of 2,3-dichloronaphtho-1,4-quinone (I) with *o*-phenylenediamine showed that these components react in the presence of pyridine to give 6-pyridiniumbenzo[*a*]phenazine 5-oxide (II).[2] The formal analogy of II to 1*H*-benzo[*b*]pyrido[1,2,3-*mn*]phenothiazin-1-one (III)[3] with respect to charge separation prompted us to compare the chemistry of these compounds. To this end, II was treated with phosphorus oxychloride to give the 5-chlorobenzo[*a*]phenazine pyridinium salt (IVa) which was successively converted to the phosphate salt (IVb) and to the perchlorate (IVc). Dimethyl sulfate reacts with II to give 5-methoxybenzo[*a*]phenazine-6-pyridinium methosulfate (V). The reaction of II with phosphorus oxychloride and dimethyl sulfate is therefore analogous to the corresponding reactions of III.[4]



Treatment of V with alcoholic piperidine, pyridine, sodium acetate, and potassium hydroxide gave the enol betaine II in over 90% yield. It has not been established whether the methoxy group is displaced by the base or the cleavage occurs between the oxygen atom and the methyl group. Attempts to replace the chlorine atom of IVc with piperidine resulted in the formation of 6-amino-5-chlorobenzo[*a*]phenazine (VI). The formation of an acetyl derivative (VIa) confirms the presence of an amino group and the infrared spectrum of VI shows that the amino group is primary. Oxidation of VI to benzo[*a*]phenazine-5,6-quinone (VII) demonstrates that VI still retains the benzo[*a*]-phenazine structure, *i.e.*, no rearrangement has occurred. The formation of VI from IVc is consistent with the concept that the initial reaction is the formation of the pseudo base A which undergoes subsequent ring opening to B which is then hydrolyzed to VI. This reaction has its counterpart in the hydrolysis of 2,4-dinitrobenzene pyridinium chloride to 2,4-dinitroaniline.[5]

We next turned our attention to the behavior of 1,4-dioxo-3-pyridinium 2-naphthoxide (VIII) which has an enol betaine structure similar to II. This material was recovered unchanged after three hours' boiling in phosphoryl chloride. If more vigorous conditions

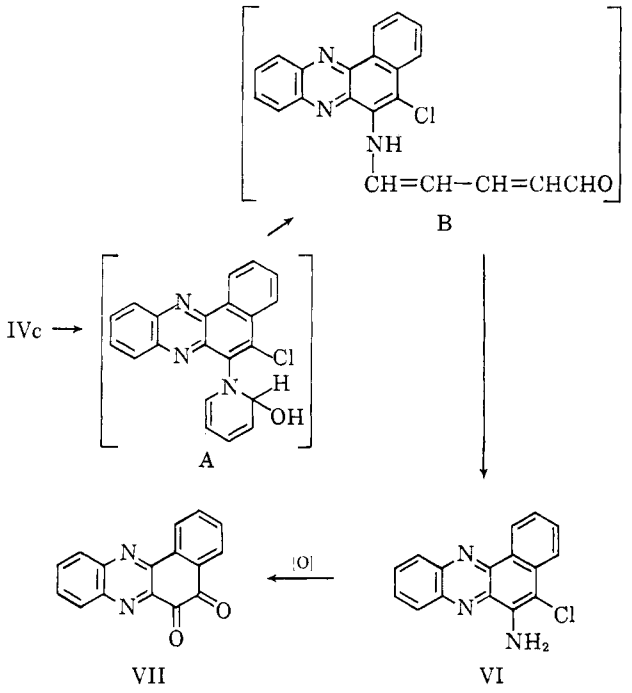
(1) Contribution no. 2310 from the Kodak Research Laboratories.

(2) Part VI, J. A. VanAllan and G. A. Reynolds, *J. Org. Chem.*, **28**, 1019 (1963).

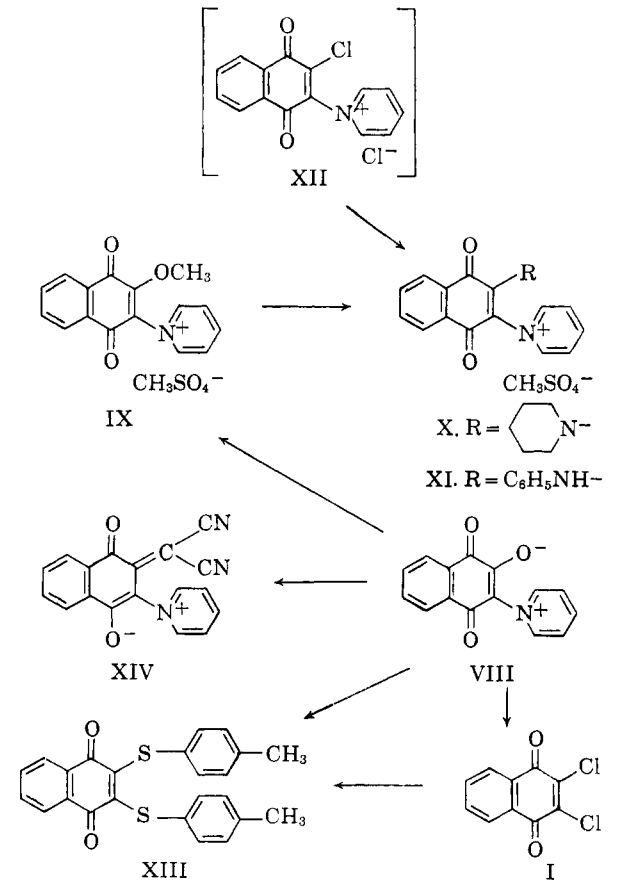
(3) J. A. VanAllan, G. A. Reynolds, and R. E. Adel, *ibid.*, **27**, 1659 (1962).

(4) Part V, G. A. Reynolds and J. A. VanAllan, *ibid.* **28**, 527 (1963).

(5) "Heterocyclic Compounds," Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 426.



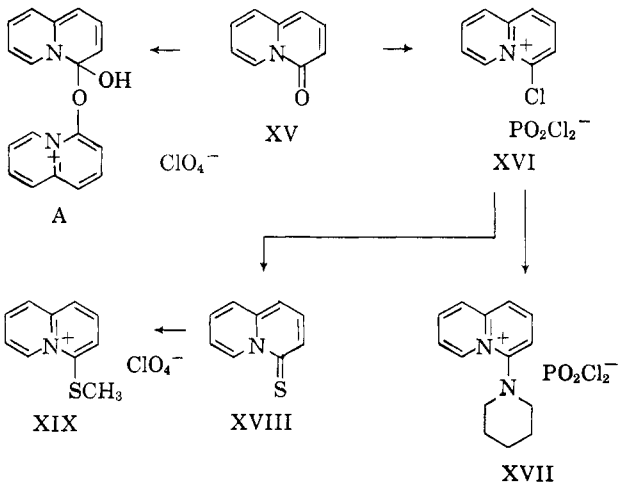
(phosphorus pentachloride in phosphoryl chloride) are used, the product is 2,3-dichloronaphtho-1,4-quinone (I). However, VIII reacts readily with dimethyl sulfate to give 1,4-dioxo-2-methoxynaphthyl-3-pyridinium methosulfate (IX) which, in turn, reacts with piperidine and aniline to give 1,4-dioxo-2-piperidino-3-pyridinium methosulfate (X) and 1,4-dioxo-2-anilino-3-pyridinium methosulfate (XI), respectively. Since XI may also be obtained if I is treated with aniline and pyridine in trichloropropane, there is little doubt that the assigned structures are the correct ones. The presumed intermediate, XII, was not isolated. With 4-methylbenzenethiol, both the methoxy group and the pyridine moiety are replaced to give 2,3-bis(4-methylphenylmercapto)-1,4-naphthoquinone (XIII), which is also obtained from I and 4-methylbenzenethiol in pyridine.



Malononitrile also reacts with VIII in acetic anhydride to give 3-dicyanomethylene-2-pyridinium-4-oxonaphthalene oxide (XIV) or an isomer thereof. The enol betaine II does not undergo this reaction.

It will be noted that compounds II and VIII contain two carbon atoms between the oxygen and the nitrogen atoms. The course of reaction of the types described in this paper was previously reported[4] for compounds in which the oxygen and the nitrogen atoms were separated by three carbon atoms (such as compound III) and one carbon atom (such as 4-quinolizone).

It has been shown previously[4] that XV forms a quaternary salt with dimethyl sulfate which reverts to XV on treatment with piperidine in the same fashion as compound V. With the intention of obtaining a quinolizinium compound which would react with piperidine, 4-quinolizone was converted to 4-chloroquinolizinium dichlorophosphate (XVI) in quantitative yield by means of phosphorus oxychloride. The chlorine atom in XVI is replaced by piperidine to give 4-piperidinoquinolizinium dichlorophosphate (XVII) in poor yield. Incidentally, attempts to form a perchlorate of XV led to the formation of a compound (A) whose analysis corresponds to the empirical composition, $C_{18}H_{14}ClN_2O_5$. We have assigned the tentative structure A solely on the basis of elemental analysis and the infrared spectrum which shows an absorption in the



hydroxyl region. Pursuant to a better synthesis of XVII, the perchlorate XVI was treated with sodium sulfide to give a 72% yield of thioquinolizone (XVIII) which has been prepared by Boekelheide and Lodge[6] in poor yield by fusion of XV with phosphorus pentasulfide. Thioquinolizone was also prepared in 40% yield from XVI and thiourea. The conversion of XVIII to 4-methylmercaptoquinolizinium perchlorate (XIX) is readily accomplished by treatment with dimethyl sulfate (an exothermic reaction), followed by treatment with perchloric acid. Piperidine reacts with XIX to give a product of unknown composition.

(6) V. Boekelheide and J. P. Lodge, Jr., *J. Am. Chem. Soc.*, **73**, 3681 (1951).

In summary: (a) The oxygen atom of III may be replaced by a dicyanomethylene group, a chlorine atom, or a methoxy group. These latter two substituents may then be replaced by a piperidino group.[4] In comparison, the oxygen of II may be replaced by a chlorine or a methoxy group. These derivatives react anomalously with piperidine to give, respectively, the amine VI and II. Malononitrile does not react with II. (b) The oxygen in the 2 position of VIII may be replaced by a dicyanomethylene group or a methoxyl group which, in turn, may be replaced by a piperidino group like III. (c) The oxygen atom of XV may be replaced by a chlorine atom or a methoxy group, and the chlorine atom is replaceable by piperidine. No reaction occurs between XV and malononitrile. Therefore, there is a diversity of chemical behavior between these compounds in spite of their formal similarity in respect to charge separation.

Experimental

The 2,3-dichloronaphthoquinone (I) was obtained from Eastman Kodak Co. 6-Pyridinium benzo[*a*]phenazine 5-oxide (II),[2] 1*H*-benzo[*b*]pyrido[1,2,3-*mn*]phenothiazin-1-one (III),[3] 1,4-dioxo-3-pyridinium 2-naphthoxide (VIII),[2] and quinolizone (XV)[5] were prepared according to the methods given in the literature cited.

5-Chlorobenzo[*a*]phenazine-6-pyridinium ($P_2O_3Cl_3$) (IVa).—A suspension of 30 g. of the betaine in 100 ml. of phosphorus oxychloride was heated at 95–100° for 5 hr. After cooling, the precipitate was collected on a sintered-glass funnel and crystallized from acetonitrile and ether to give 41 g. (78%) of IVa, m.p. 245°.

Anal. Calcd. for $C_{21}H_{13}O_3P_2Cl_4N_3$: C, 45.1; H, 2.3; Cl, 25.4. Found: C, 44.8; H, 2.6; Cl, 24.9.

Recrystallization of IVa from water gave the phosphate salt IVb, m.p. > 300°.

Anal. Calcd. for $[C_{21}H_{13}N_3Cl]_2H_3PO_4$: C, 64.5; H, 3.3; N, 10.7. Found: C, 64.4; H, 3.7; N, 10.7.

A solution of IVa (or IVb) in water, on treatment with 70% aqueous perchloric acid, gave IVc, m.p. 310° (from acetonitrile).

Anal. Calcd. for $C_{21}H_{13}O_4Cl_2N_3$: C, 57.1; H, 2.9; N, 9.5. Found: C, 56.9; H, 3.1; N, 9.2.

5-Methoxybenzo[*a*]phenazine-6-pyridinium Methosulfate (V).—A solution of 5 g. of II in 30 ml. of dimethyl sulfate was heated at 95–100° for 3 hr. and 90 ml. of acetone was added. The product which precipitated was collected and crystallized from a large volume of methanol to give 4.7 g. of V, m.p. 308°.

Anal. Calcd. for $C_{23}H_{19}O_5N_3S + H_2O$: C, 59.3; H, 4.0; N, 9.0; S, 6.9. Found: C, 59.6; H, 3.8; N, 9.2; S, 7.6.

6-Amino-5-chlorobenzo[*a*]phenazine (VI).—A suspension of 6 g. of IVc in 30 ml. of ethanol was treated with 6 ml. of piperidine and heated at 95–100°. Complete solution occurred in about 10–15 min., and bright red crystals soon separated. After 1 hr., the crystals were collected and recrystallized from butanol to give 3.4 g. of VI, m.p. 212°.

Anal. Calcd. for $C_{16}H_{10}N_3Cl$: C, 68.7; H, 3.6; N, 15.1; Cl, 12.6. Found: C, 69.0; H, 3.7; N, 14.8; Cl, 12.5.

The acetyl derivative had a m.p. 290° (from trichlorobenzene).

Anal. Calcd. for $C_{18}H_{12}ON_3Cl$: C, 67.3; H, 3.7; N, 13.1. Found: C, 67.2; H, 3.6; N, 13.0.

If IVc is replaced by V in the above reaction, the enol betaine II is formed in 93% yield. Other basic reagents, such as pyridine, sodium acetate, and potassium hydroxide, also react with V to give II, under the same conditions. Attempts to isolate *N*-methylpyridinium methosulfate from one run were unsuccessful.

Benzo[*a*]phenazine-5,6-quinone (VII).—To a suspension of 1 g. of VI in 10 ml. of acetic acid was added 3 ml. of nitric acid and 1 ml. of water. The mixture was heated at 100°; nitrous oxide fumes were given off; and the quinone VII precipitated. It was identified by comparison of its infrared spectrum with that of an authentic sample.

1,4-Dioxo-2-methoxynaphthyl-2-pyridinium Methosulfate (IX).—A mixture of 3 g. of the betaine VIII and 15 ml. of methyl sulfate was heated on the steam bath until complete solution resulted (2 hr). After cooling and dilution with ether, the solid was collected, washed with ether and recrystallized from methanol to yield 3.3 g. of IX, m.p. 165°.

Anal. Calcd. for $C_{17}H_{15}NO_7S$: C, 54.1; H, 4.0; N, 3.7. Found: C, 53.7; H, 4.1; N, 4.0.

The perchlorate salt had a m.p. 227°.

Anal. Calcd. for $C_{16}H_{12}ClNO_7$: C, 52.2; H, 3.3; N, 3.8. Found: C, 52.4; H, 3.4; N, 3.7.

1,4-Dioxo-2-piperidinonaphthyl-3-pyridinium Methosulfate (X).—A mixture of 0.75 g. of IX, 0.2 g. of piperidine and 25 ml. of ethanol was heated on the steam bath for 2 hr. After the mixture had been chilled in a deep freezer, a bright orange solid was collected and recrystallized from ethanol to yield 0.6 g. of X, m.p. 202°.

Anal. Calcd. for $C_{21}H_{22}N_2O_6S$: C, 58.5; H, 5.1; N, 6.5. Found: C, 58.8; H, 5.4; N, 6.2.

1,4-Dioxo-2-anilinonaphthyl-3-pyridinium Methosulfate (XI). Method A.—A mixture of 2 g. of IX and 1 g. of aniline in 50 ml. of ethanol was refluxed for 4 hr., chilled, and the light orange solid was collected and recrystallized from ethanol to yield 1.5 g. of XI, m.p. 251°.

Anal. Calcd. for $C_{22}H_{17}N_2O_6S$: C, 60.4; H, 3.9; N, 6.4. Found: C, 60.2; H, 4.1; N, 6.2.

The perchlorate had a m.p. 298° (see below).

Method B.—A suspension of 22.7 g. (0.1 mole) of I, 8 ml. of aniline and 200 ml. of trichloropropane was heated until solution was complete. Pyridine (12 ml.) was added and the mixture was heated for 12 hr. After cooling, the bright red crystals were collected and dried; yield, 20.9 g.; m.p., 244°. This material was dissolved in water and treated with 70% perchloric acid to give 19.8 g. of XI (m.p. 298°C) which was identical with the perchlorate obtained by method A.

Anal. Calcd. for $C_{21}H_{15}N_2O_6Cl$: C, 59.1; H, 3.5; Cl, 8.3. Found: C, 58.8; H, 3.7; Cl, 8.5.

2,3-Bis(4-methylphenylmercapto)-1,4-naphthoquinone (XIII).—A mixture of 4 g. of IX and 1.3 g. of *p*-toluenethiol in 50 ml. of ethanol was refluxed for 4 hr., chilled, and the orange solid collected. Two recrystallizations from ethanol gave 0.8 g. of XIII, m.p. 170°.

Anal. Calcd. for $C_{24}H_{18}S_2O_2$: C, 71.8; H, 4.5; S, 15.9. Found: C, 71.9; H, 4.3; N, 15.7.

3-Dicyanomethylene-2-pyridinium-4-oxonaphthalene 1-Oxide (XIV).—A solution of 5.0 g. of VIII and 4.0 g. of malononitrile in 40 ml. of acetic anhydride was heated at 95–100° for 2 hr. After cooling, the product was collected and crystallized from dimethylformamide to give 4.2 g. of blue-black crystals of XIV, m.p. 309°.

Anal. Calcd. for $C_{18}H_9O_2N_3$: C, 72.2; H, 3.0; N, 14.0. Found: C, 72.4; H, 3.1; N, 14.2.

The infrared spectrum of XIV shows typical nitrile band at 4.5 and at 5.95 μ for α,β-unsaturated ketones, both consistent with the formulation given.

4-Chloroquinolizinium Perchlorate (XVI).—Quinolizone (5.0 g.) was suspended in 10 ml. of phosphoryl chloride and heated to 90°. The quinolizone went into solution in about 5 min. and, within 10 min., the reaction mixture had solidified. The product was collected on a sintered-glass funnel, dissolved in water, and converted to the perchlorate by the addition of perchloric acid. The product (XVI) separated in long white needles; yield, 8.9 g.; m.p., 310°.

Anal. Calcd. for $C_9H_7NCl_2O_4$: C, 40.8; H, 2.6; Cl, 26.9. Found: C, 40.4; H, 2.9; Cl, 26.9.

4-Piperidinoquinolizinium Dichlorophosphate (XVII). Method A.—A mixture of 3 g. of 4-chloroquinolizinium dichlorophosphate and 0.9 g. of piperidine in 50 ml. of ethanol was refluxed for 2 hr., concentrated to 25 ml., and the white solid collected and recrystallized from methanol to yield 0.9 g. of XVII, m.p. 168°.

Anal. Calcd. for $C_{14}H_{17}Cl_2N_2O_2P$: C, 48.6; H, 4.9; N, 8.1. Found: C, 48.7; H, 4.5; N, 7.5.

Method B.—A mixture of 2.8 g. of 4-methylmercaptoquinolizinium perchlorate (XIX) and 0.9 g. of piperidine in 75 ml. of ethanol was refluxed for 3 hr. On cooling to room temperature, 0.2 g. of the starting material (XIX) was recovered. The mother liquors were evaporated to dryness and the sticky residue was digested with tetrahydrofuran to give a white solid which was recrystallized from a small volume of ethanol to yield 1.7 g. of a compound of unknown composition, m.p. 160°.

Anal. Found: C, 41.0; H, 7.0; N, 7.9.

4-Thioquinolizone (XVIII). Method A.—A solution of 60 g. of XVI in 300 ml. of water was treated with decolorizing charcoal and filtered. A solution of 60 g. of sodium sulfide nonahydrate in 300 ml. of water was added slowly, with constant stirring. After 3 hours' stirring, the bright yellow solid which formed was collected, washed with water, and dried to give 30.8 g. of XVIII, m.p. 104°.[5] Recrystallization from a mixture of toluene and ligroin did not change the melting point.

Method B.—A mixture of 6 g. of XVI, 1.5 g. of thiourea and 100 ml. of ethanol was refluxed for 1 hr. and then evaporated to dryness under vacuum. The residue was heated with 20 ml. of 10% sodium hydroxide solution for 15 min. on the steam bath, the solution saturated with sodium chloride, and the organic material extracted with chloroform. The chloroform was removed from the extract and the residue recrystallized from ligroin (b.p. 90–120°) to yield 2.8 g. of XVIII, m.p. 97–99°.

4-Methylmercaptoquinolizinium Perchlorate (XIX).—Thioquinolizone (29.3 g.) and 30 ml. of dimethyl sulfate were mixed. A vigorous exothermic reaction ensued and the reaction mixture solidified. The mixture was heated for 1 hr. at 90°, 200 ml. of water was added, and the heating was continued until solution was complete. To the solution was added 15 ml. of 70% perchloric acid. On cooling, 24 g. of XIX separated, m.p. 135° (from water).

Anal. Calcd. for $C_{10}H_{10}NSClO_4$: C, 43.6; H, 3.6; N, 5.1. Found: C, 42.9; H, 3.6; N, 5.0.

Attempt to Make the Perchlorate of Quinolizone.—A solution of 2.0 g. of XV in 15 ml. of water was treated with 1 ml. of 70% perchloric acid in 3 ml. of water. On cooling, a product separated which was crystallized from ethanol; yield, 1.2 g.; m.p., 155°.

Anal. Calcd. for $C_{18}H_{14}O_5N_2Cl$: C, 55.5; H, 3.6; N, 7.2. Found: C, 55.2; H, 3.9; N, 7.0.

A Novel Peptide Cleavage Reaction

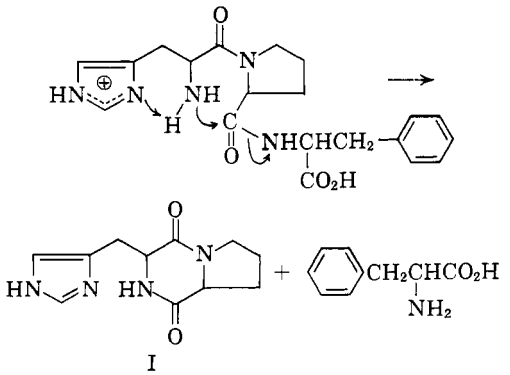
ROBERT H. MAZUR AND JAMES M. SCHLATTER

Division of Chemical Research, G. D. Searle & Company, Skokie, Illinois

Received October 9, 1962

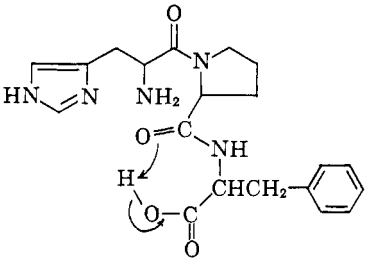
It has been observed that under mild acid treatment, the tripeptide His·Pro·Phe·OR is cleaved to yield histidylproline diketopiperazine (I) and Phe·OR. The reaction appears to be unusually rapid for the N-terminal sequence His·Pro but not completely specific.

We wish to report a reaction in which a peptide bond is cleaved under unexpectedly mild conditions. During some preliminary work on the synthesis of angiotensin II[1] the tripeptide ester His·Pro·Phe·OCH_3[2,3] and the unprotected tripeptide His·Pro·Phe were desired. Attempted preparation of the latter by detritylation with hot 50% acetic acid of Tr·Tr·His·Pro·Phe gave, surprisingly, phenylalanine and a second product which was ninhydrin negative and Pauly positive. The only other material obtained was triphenylcarbinol. We were able to identify the unexpected product as histidylproline diketopiperazine (I) (His·Pro). A plausible schematic mechanism for this reaction is shown.



I

In view of the potential utility of this reaction for protein degradation, we have attempted to determine what structural features are required. Our first observation was that there was a great difference in rate of cleavage between Tr·Tr·His·Pro·Phe· and Tr·Tr·His·Pro·Phe·OCH_3. The acid was completely hydrolyzed and cleaved in 50% acetic acid after 24 hours at room temperature while the ester was detritylated but otherwise unchanged under the same conditions. Heating the ester in 50% acetic acid on the steam bath caused the formation of His·Pro and Phe·OCH_3. The unexpected difference in reactivity between the acid and ester where the structural change is rather remote from the reaction center can be rationalized by hydrogen bonding between the carboxyl of phenylalanine and the amide carbonyl of proline. The effect is to produce a partial positive charge on the proline carbonyl facilitating nucleophilic attack by the histidine amino group. This rate enhancing mechanism, not available to the ester, follows.



Attempts to synthesize His·Pro·Phe were partially successful. Brief hydrolysis of Tr·Tr·His·Pro·Phe at 60° in 50% acetic acid gave predominantly His·Pro·Phe as indicated by paper chromatography. However, an absolutely pure material could not be isolated, and attempted crystallization from methanol resulted in complete cleavage.

An alternate approach was made through Tr·Tr·His·Pro·Phe·ONB, which behaved analogously to the methyl ester. Hydrolysis with 50% acetic acid at 90° yielded His·Pro and Phe·ONB while at 60° for ten minutes the principal product was His·Pro·Phe·ONB. Hydrogenolysis of Tr·Tr·His·Pro·Phe·ONB gave mixtures of His·Pro·Phe and cleavage products. Ad-

(1) R. H. Mazur, *Can. J. Chem.*, **40**, 1098 (1962).

(2) All amino acids (except glycine) have the L-configuration. The abbreviations are adapted from the proposal of Brand and Edsall.[4] Additional abbreviations are Tr = triphenylmethyl, Z = carbobenzoxy, ONB = *p*-nitrobenzyl ester, and ONP = *p*-nitrophenyl ester.