[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY]

The Methylation of 5-Hydroxytetrazole[1a,1b]

BY KIYOSHI HATTORI, EUGENE LIEBER AND JEROME P. HORWITZ[2]

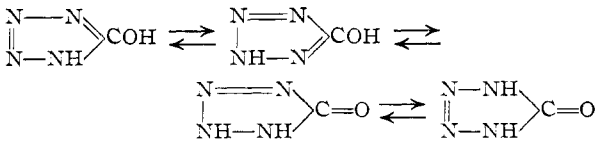
RECEIVED AUGUST 15, 1955

The methylation of 5-hydroxytetrazole with diazomethane affords a mixture of four dimethylated products, three of which have been established unequivocally. Though the fourth product is probably 1,3-dimethyl-5-tetrazolone, there is insufficient evidence to exclude 1,2-dimethyl-5-tetrazolone as a possibility.

While the alkylation of 5-aminotetrazole has been the subject of several investigations,[3-5] the corresponding study with 5-hydroxytetrazole has never been described. In fact, 1-methyl-5-hydroxytetrazole (V) and 5-methoxytetrazole are the only recorded derivatives of I. The methylation of I was undertaken as a concurrent phase of a study concerned with the elucidation of the crystallographic properties of this same tetrazole derivative.[6]

During the initial phase of the present investigation, several unsuccessful attempts were made to reproduce the 75% yield reported by Stolle[7] for the conversion of 5-aminotetrazole to I *via* tetrazolediazonium hydroxide. In our hands this procedure provided I in only 10% yield. The obvious importance of 5-hydroxytetrazole to the present study prompted a reinvestigation of Stolle's procedure which, after suitable modification, afforded the desired product in 45–55% yields. The salient features of the modified procedure are: (a) reduction of temperature from 60 to 0° and (b) the use of cupric sulfate as catalyst instead of cupric hydroxide.

The formation of a complex mixture of methylated products was anticipated from a consideration of the tautomeric forms of I. It therefore seemed



advisable to establish unequivocally the identity of at least two monomethylated derivatives of I as an aid in identifying some of the expected products.

1-Methyl-5-hydroxytetrazole (V).—The synthesis of V from methyl isothiocyanate was first described by Stolle and Henke-Stark.[8] However, the precursory tetrazole intermediates were also previously unknown and hence the synthesis cannot be considered unequivocal. The facile conversion of 5-aminotetrazole to 5-hydroxytetrazole[6] suggested the possibility of accomplishing a similar transformation with 1-methyl-5-aminotetrazole (III).

Previous attempts to alkylate 5-aminotetrazole (II) have resulted in a mixture of difficultly separable isomers.[9,10] However, the methylation of II with either methyl sulfate[11] or diazomethane affords a readily separable mixture of 1- and 2-methyl-5-aminotetrazole (III, IV).

Treatment of III with sodium nitrite in dilute mineral acid is reported to yield 1-methyl-5-nitrosoaminotetrazole.[9,12] In our hands this procedure afforded a pale yellow solid which, on two occasions, deflagrated in the filter funnel. The acute sensitivity of this material precluded a more detailed investigation.

It was found that, in fairly concentrated nitric acid, III could be smoothly converted into V on treatment with sodium nitrite. The addition of an equivalent quantity of cupric sulfate did not alter the yield. The product V showed the physical properties ascribed to it by the original investigators.[8]

2-Methyl-5-hydroxytetrazole (XII).—The interaction of 2-methyl-5-aminotetrazole (IV) and sodium nitrite in concentrated nitric acid failed to yield the expected 2-methyl-5-hydroxytetrazole (XII). Instead, a high melting white solid was isolated whose elementary analysis and chemical properties suggested the structure di-(2-methyl-5-tetrazolyl)-amine (VI).

The same reaction conducted in dilute nitric acid afforded a mixture of solids which resisted separation through fractional crystallization. Infrared measurements clearly indicated the presence of VI as one of the components. Confirmatory evidence for the latter observation was obtained when it was found that only VI remained after the mixture was subjected to acid hydrolysis.

It was noted that the initial mixture yielded an insoluble silver salt on treatment with aqueous silver nitrate whereas a pure sample of VI was not precipitated by this reagent. This information together with the apparent destruction, on acid hydrolysis, of the component affording a silver salt suggested the presence of a triazene derivative,[13]

(1) (a) Abstracted in part from a dissertation submitted by Kiyoshi Hattori to the Graduate School of Illinois Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Philosophy. (b) This work was supported by U. S. NOTS Inyokern, China Lake, Calif., Research Contract N123S-61517, Task Order No. 3.

(2) To whom all requests for reprints and additional information should be addressed.

(3) J. Thiele and H. Ingle, *Ann.*, **287**, 233 (1895).

(4) R. Stolle, E. Ehrmann, D. Rieder, H. Wille, H. Winter and R. Henke-Stark, *J. prakt. Chem.*, **134**, 282 (1932).

(5) R. A. Henry and W. G. Finnegan, THIS JOURNAL, **76**, 282 (1954).

(6) K. Hattori, J. P. Horwitz and E. Lieber, *Anal. Chem.*, **25**, 353 (1953).

(7) R. Stolle, *Ber.*, **62**, 1118 (1929).

(8) R. Stolle and F. Henke-Stark, *J. prakt. Chem.*, **124**, 261 (1930).

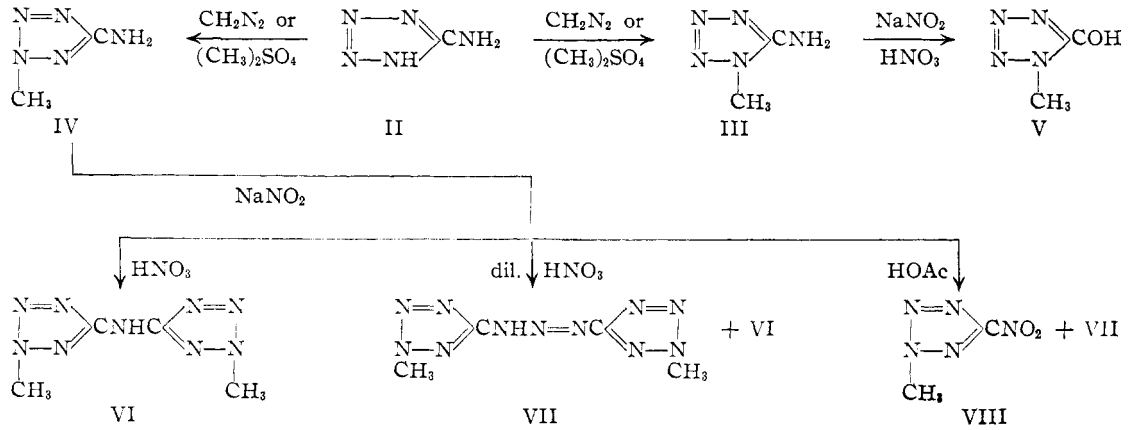
(9) J. Thiele and H. Ingle, *Ann.*, **287**, 249 (1895).

(10) R. M. Herbst, E. W. Roberts and E. J. Havrill, *J. Org. Chem.*, **16**, 139 (1951).

(11) While this work was in progress, R. A. Henry and W. G. Finnegan, THIS JOURNAL, **76**, 923 (1954), reported a similar study. We are happy to corroborate this prior publication.

(12) R. Stolle, *J. prakt. Chem.*, **134**, 286 (1932).

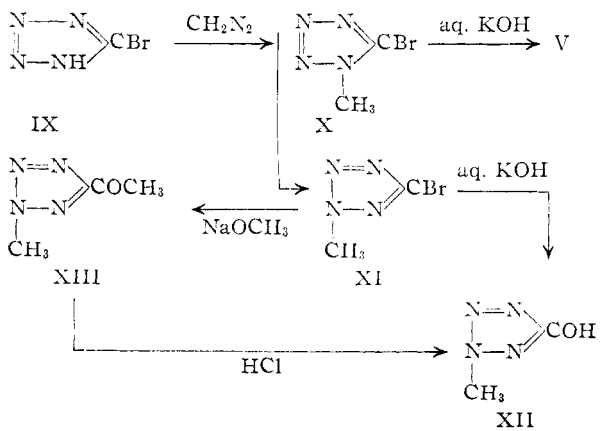
(13) The triazenes are decomposed by mineral acids, the nitrogen chain being broken and an amine splitting off. In addition, the hydrogen atom attached to the nitrogen atom of the triazene chain is replaceable by metals; see T. W. J. Taylor and W. Baker, "Sidgwick's Organic Chemistry of Nitrogen," Oxford University Press, London, 1949, p. 457.



which indeed proved to be the case. The separation was subsequently accomplished by extraction of the neutral component VI from the sodium salt of the triazene. The white crystalline material, liberated on acidification of an aqueous solution of the triazene salt, yielded an elementary analysis consistent with 1,3-di-(2′-methyl-5′-tetrazolyl)-triazene (VII). The latter was smoothly degraded to 2-methyl-5-aminotetrazole on treatment with aqueous hydrochloric acid. No other organic product was detected.

Apparently, the anomalous behavior of IV with respect to the attempted replacement of the corresponding diazonium salt is not confined to nitric acid alone. Thus, the diazotization of IV in aqueous acetic acid produced, in addition to VII, still another product, 2-methyl-5-nitrotetrazole (VIII). The latter was identified by reduction to starting material (IV).

The failure of IV to yield the desired 2-methyl-5-hydroxytetrazole (XII) prompted a study of the preparation and solvolysis of the monomethyl-5-bromotetrazoles. The interaction of 5-bromotetrazole (IX) and diazomethane afforded a mixture of methylated derivatives from which a solid X and a liquid XI were obtained as the major products on distillation. When X was hydrolyzed with aqueous potassium hydroxide, 1-methyl-5-hydroxytetrazole (V) was obtained in 60% yield. Thus the identity of the precursor X is established as 1-methyl-5-bromotetrazole. The hydrolysis of the liquid fraction XI, conducted in aqueous methanol, gave a new product whose elementary analysis



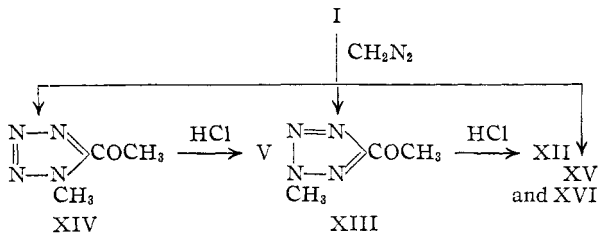
conformed to the requirements of a methylated derivative of 5-hydroxytetrazole. Since the starting material IX can give rise to only two monomethylated products, the latter must then be the desired 2-methyl-5-hydroxytetrazole (XII) and the precursory liquid XI is therefore 2-methyl-5-bromotetrazole. Confirmatory evidence for this conclusion was obtained from the observation that the liquid fraction XI on treatment with sodium methoxide in methanol yielded a low melting solid whose elementary analysis conformed with 2-methyl-5-methoxytetrazole (XIII). The latter, on acid hydrolysis, afforded a product identical with XII. These observations then establish the structure of both XII and XIII.

1-Methyl- and 2-Methyl-5-methoxytetrazole.—The addition of excess diazomethane to an ethereal solution of 5-hydroxytetrazole (I) produced a mixture of dimethylated products which were crudely separated into a liquid fraction (48%) and a solid (34%). Fractional distillation separated the liquid into two components, leaving a non-volatile residue in the still-pot. The higher boiling fraction, on acid hydrolysis, yielded a white solid which was identical with an authentic sample of 1-methyl-5-hydroxytetrazole (V). Thus, the precursor XIV is established as 1-methyl-5-methoxytetrazole. The lower boiling fraction exhibited an infrared spectrum essentially superimposable with that of 2-methyl-5-methoxytetrazole (XIII). Furthermore, when this same fraction was subjected to acid hydrolysis, the product was identified as 2-methyl-5-hydroxytetrazole (XII).

The solid isolated in the initial separation melted sharply and yielded an elementary analysis consistent with a dimethylated derivative of 5-hydroxytetrazole. However, the fact that this material proved inert toward hot, 20% hydrochloric acid, together with the detection of strong carbonyl absorption (1710 cm.$^{-1}$) in the infrared region of the spectrum, indicated that both methyl groups must be attached directly to the tetrazole ring. Therefore, this solid (XV) must be either 1,4- or 1,2-dimethyl-5-tetrazolone or possibly the *meso* ionic structure 1,3-dimethyl-5-tetrazolone. The latter would be analogous to the sydnone-like structure, 1,3-dimethyl-5-iminotetrazole, recently described by Bryden, *et al.*[14]

(14) J. H. Bryden, R. A. Henry, W. G. Finnegan, R. H. Boschan, W. S. McEwan and R. W. Van Dolah, THIS JOURNAL, **75**, 4863 (1953).

Infrared measurements on the non-volatile residue remaining in the still pot revealed the presence of still another carbonyl compound (1673 cm.$^{-1}$) in addition to a small amount of XIV. This carbonyl compound, while obviously different from solid XV, must also be a ring dimethylated product possessing one of the three possible structures mentioned above.



Methylation of 1-Methyl- and 2-Methyl-5-hydroxytetrazole.—Recently, Henry, Finnegan and Lieber[15] demonstrated that the principal product obtained from the benzylation of 1-methyl-5-aminotetrazole is 1-methyl-4-benzyl-5-iminotetrazole. A small amount of 1-methyl-3-benzyl-5-iminotetrazole was also shown to be present.

It was reasoned, by analogy, that the methylation of 1-methyl-5-hydroxytetrazole (V) might pursue a similar course, thus permitting the elucidation of one or possibly both of the ring-dimethylated products obtained from 5-hydroxytetrazole.

The methylation of V with diazomethane afforded a mixture of three dimethylated products. A preliminary separation was effected by washing the mixture of oily solids with carbon tetrachloride. Distillation of the carbon tetrachloride-soluble fraction gave a colorless liquid (10%) which was identified, from infrared measurements, as 1-methyl-5-methoxytetrazole (XIV). Additional confirmation was obtained from the observation that this liquid could be converted into starting material V on acid hydrolysis.

The carbon tetrachloride-insoluble material (83%) exhibited an infrared spectrum identical with that of the solid (XV) obtained in the methylation of 5-hydroxytetrazole. On the basis of the analogy with the work of Henry, *et al.*,[15] cited above, this product was tentatively assigned the structure 1,4-dimethyl-5-tetrazolone (XV).

When a sample of 1,4-dimethyl-5-iminotetrazole[16] was treated with nitrous acid,[17] the product, obtained in low yield, proved to be identical in every respect to that which we had tentatively assigned structure XV, 1,4-dimethyl-5-tetrazolone.

The methylation of 2-methyl-5-hydroxytetrazole (XII) with diazomethane yielded a mixture of two dimethylated products. Infrared measurements indicated the presence of a carbonyl compound (1673 cm.$^{-1}$) and hence established one of the components as a ring dimethylated derivative. It was further noted that this carbonyl absorption was identical with that observed in the case of the non-volatile residue (XVI) obtained in the methylation of 5-hydroxytetrazole.

The structurally isomeric dimethylated products were subjected to acid hydrolysis, which afforded a new mixture composed of an acidic material and a neutral component. The latter appeared to be the major product. The acidic substance was readily identified as 2-methyl-5-hydroxytetrazole (XII) and thus the corresponding dimethylated product must have been 2-methyl-5-methoxytetrazole (XIII).

A comparison of the infrared spectrum of the neutral component with the corresponding spectrum of the non-volatile residue (XVI) from the methylation of 5-hydroxytetrazole indicated that the compounds were identical, but at the same time quite different from 1,4-dimethyl-5-tetrazolone. It is evident, then, that XVI, a ring dimethylated product, must be either 1,2- or 1,3-dimethyl-5-tetrazolone.

It recently has been established that the methylation of 2-methyl-5-aminotetrazole affords 1,3-dimethyl-5-iminotetrazole as the major product. It therefore seemed reasonable to expect that XVI, the principal methylation product of 2-methyl-5-hydroxytetrazole, possessed the structure 1,3-dimethyl-5-tetrazolone. However, all attempts to convert 1,3-dimethyl-5-iminotetrazole by treatment with nitrous acid, into the corresponding 5-tetrazolone derivative, proved unsuccessful.

Henry, Finnegan and Lieber[18] reported that the 1,3-dialkyl-5-iminotetrazoles exhibit a characteristic absorption band between 254 and 258 mμ. The ultraviolet absorption spectrum of XVI is essentially the same as that reported for 1,3-dimethyl-5-iminotetrazole with a single well-defined maximum appearing at 256 mμ (ϵ 2030). This observation is used as indirect evidence to support the structure 1,3-dimethyl-5-tetrazolone for XVI since, in the absence of more conclusive chemical evidence, 1,2-dimethyl-5-tetrazolone cannot be excluded as a possible structure.

Experimental[19,20]

5-Hydroxytetrazole (I).—To a solution of 10.3 g. of 5-aminotetrazole monohydrate (0.1 mole) in a mixture of 200 ml. of water and 10 ml. of concentrated sulfuric acid was added 100 g. of ice. The mixture was cooled to 0° and a solution of 7.6 g. of sodium nitrite (0.11 mole) in 50 ml. of water was added dropwise with stirring. After the mixture had been stirred for one-half hour at ice-bath temperature, a previously cooled solution of 37 g. of cupric sulfate pentahydrate (0.15 mole) in 200 ml. of water was added. The mixture was then stirred for an additional one-half hour and finally placed in a refrigerator overnight at 5–10°. Occasionally, a copper salt would precipitate out on standing overnight. This was collected, dissolved in concentrated hydrochloric acid, treated with hydrogen sulfide and the filtrate combined with the original mother liquor.

Hydrogen sulfide was next passed into the blue-green solution and the cupric sulfide removed by filtration. The filtrate was then heated just to boiling and 81 g. of barium chloride dihydrate (0.33 mole) added to the clear, hot solution. The barium sulfate was removed by filtration and the filtrate evaporated to dryness on a steam-bath in a stream of air.

(15) R. A. Henry, W. G. Finnegan and E. Lieber, THIS JOURNAL, **76**, 2894 (1954).

(16) The authors are indebted to Dr. R. A. Henry, NOTS, Inyokern, China Lake, California, for a sample of this material.

(17) J. Thiele, *Ann.*, **287**, 253 (1895), first employed this reaction to convert a dibenzylated derivative of 5-aminotetrazole into the corresponding 5-hydroxy derivative. The exact position of the benzyl substituents still remains in question.

(18) R. A. Henry, W. G. Finnegan and E. Lieber, THIS JOURNAL, **76**, 2894 (1954).

(19) All melting points are uncorrected.

(20) Analyses are by the Micro-Tech Laboratories, Skokie, Ill.

The residue was placed in a Soxhlet extractor and refluxed with acetone for four hours. The acetone extract was evaporated to dryness and the residue recrystallized from water to give 4.3 g. (50% yield) of 5-hydroxytetrazole, m.p. 260° dec., lit.[7] 254° dec.

Anal. Calcd. for CH_2ON_4: C, 13.95; H, 2.34; N, 65.10. Found: C, 13.81; H, 2.42; N, 65.71.

Methylation of 5-Aminotetrazole (II). (a) **With Diazomethane.**—To an ethereal solution of diazomethane (0.029 mole) was added 2.0 g. of powdered 5-aminotetrazole monohydrate (0.019 mole). After the vigorous evolution of nitrogen had subsided, the reaction mixture was placed in a refrigerator for 24 hours. The solid, 1-methyl-5-aminotetrazole (III), which was deposited during this period was collected; yield 0.95 g. (50%), m.p. 215–225°. A single recrystallization from water gave a product melting at 227–228° (lit.[11] 226–228°).

The initial ether filtrate was evaporated to dryness to yield 0.9 g. (47%) of impure 2-methyl-5-aminotetrazole (IV), m.p. 80–85°. Recrystallization from benzene raised the melting point to 103–104° (lit.[11] 104.5–105.5°).

(b) **With Dimethyl Sulfate.**—To a suspension of 10.3 g. of 5-aminotetrazole monohydrate (0.1 mole) in 30 ml. of water, containing a drop of phenolphthalein, was added, dropwise and with stirring, a solution of 20% sodium hydroxide until the suspended material just dissolved and the solution became alkaline. With continued stirring, 20 ml. of dimethyl sulfate (0.11 mole) was introduced in small portions together with additional 20% sodium hydroxide to maintain an alkaline medium. The mixture was then refluxed for one hour, made alkaline to phenolphthalein once more and finally cooled. The solid III which was deposited was collected; wt. 2.85 g. (29% yield), m.p. 227–228°. An additional 0.3 g. (2%), m.p. 226–227°, was isolated upon concentrating the filtrate to approximately one-half the original volume.

The aqueous filtrate was then evaporated to dryness in a stream of air and the residue triturated with three 10-ml. portions of warm ether. The combined ether extracts were dried over anhydrous sodium sulfate and then evaporated to dryness to give 2.0 g. (20% yield) of IV, m.p. 95–100°. Three recrystallizations from ether raised the melting point to 103–104°.

1-Methyl-5-hydroxytetrazole (V).—In a mixture of 20 ml. of concentrated nitric acid and 10 ml. of water was dissolved 2.0 g. of 1-methyl-5-aminotetrazole (0.02 mole). The mixture was cooled to 10° and a solution of 1.45 g. of sodium nitrite (0.02 mole) in 5 ml. of water was added dropwise with stirring, maintaining a temperature of 10–20°. During the addition of sodium nitrite a vigorous evolution of gas occurred after which the mixture was stirred for an additional 20 minutes, then finally placed in a refrigerator for 24 hours. The mixture was next partially neutralized with *ca.* 20 ml. of aqueous 20% sodium hydroxide and then evaporated to dryness in a stream of air at room temperature. The residue was extracted for four hours with benzene in a Soxhlet apparatus. The solid obtained after evaporating the solvent was recrystallized from absolute ether to give 0.4 g. (20% yield) of V, m.p. 122–124° (lit.[8] 122°).

Anal. Calcd. for $C_2H_4ON_4$: C, 24.00; H, 4.00; N, 56.00. Found: C, 24.17; H, 3.98; N, 56.30.

Di-(2-methyl-5-tetrazolyl)-amine (VI).—To a mixture of 20 ml. of concentrated nitric acid and 10 ml. of water was added 2.0 g. of 2-methyl-5-aminotetrazole (0.02 mole). The solution was then cooled externally by an ice–salt mixture and a solution of 1.5 g. of sodium nitrite (0.02 mole) in 3 ml. of water was added dropwise with stirring. During this addition, a vigorous evolution of gas developed and a white solid was gradually deposited. The reaction mixture was next placed in a refrigerator for 24 hours following which it was concentrated to *ca.* one-fourth of the original volume by means of an air stream. The solid was collected and, when dry, amounted to 1.7 g., m.p. 260–261° dec. A single recrystallization from water provided 1.2 g. (66% yield) of white crystalline material, m.p. 267–268° dec.

Anal. Calcd. for $C_4H_7N_9$: C, 26.52; H, 3.87; N, 69.61. Found: C, 26.75; H, 3.90; N, 69.50.

1,3-Bis-(2-methyl-5-tetrazolyl)-triazene (VII).—A solution of 11.7 g. of 2-methyl-5-aminotetrazole (0.12 mole) in a mixture of 50 ml. of water and 12 ml. of concentrated nitric acid was cooled externally by an ice–salt-bath while a solution of 10.5 g. of sodium nitrite (0.15 mole) in 25 ml. of water was added dropwise with stirring. Immediately after the addition of sodium nitrite, the mixture was made basic with 20 ml. of 25% sodium hydroxide. The solution was heated to dissolve the solid product, filtered, then the red solution was evaporated to dryness in a stream of air. The solid residue was extracted with chloroform for six days in a Soxhlet apparatus. The remaining solid was dissolved in 200 ml. of water and slowly adjusted to a *p*H of approximately 6 with concentrated nitric acid. The white solid which deposited was immediately collected and washed with water, wt. 5.0 g. (20% yield), m.p. 204–207°. Six recrystallizations from water raised the melting point to 208–209°.

Anal. Calcd. for $C_4H_7N_{11}$: C, 22.96; H, 3.37; N, 73.66. Found; C, 22.91; H, 3.48; N, 73.88.

Acid Hydrolysis of VII.—A suspension of 2.59 g. of VII (0.012 mole) in 100 ml. of aqueous 20% hydrochloric acid was refluxed for one-half hour. The cooled solution was made basic with 150 ml. of aqueous 25% sodium hydroxide, then evaporated to dryness in a stream of air. The residue was next extracted with benzene in a Soxhlet apparatus. Evaporation of the solvent gave 0.78 g. (66% yield) of a white crystalline solid, m.p. 101–103° alone or with an authentic sample of 2-methyl-5-aminotetrazole.

The residue in the Soxhlet thimble was dissolved in 20 ml. of aqueous 20% hydrochloric acid and the clear solution evaporated to dryness. The dry solid was then extracted with benzene in a Soxhlet apparatus for 4 hours. Evaporation of the benzene failed to yield an organic product.

2-Methyl-5-nitrotetrazole (VIII) and VII.—A solution of 10.0 g. of 2-methyl-5-aminotetrazole (0.1 mole) in 35 ml. of 15% aqueous acetic acid was cooled to 0° by means of an ice–salt mixture. To the cold solution was added, dropwise with stirring, a solution of 7.6 g. of sodium nitrite (0.11 mole) in 15 ml. of water maintaining a temperature range of 0–10°. After 10 minutes the product was filtered from the pale yellow solution, wt. 7.8 g., m.p. 115–145°. The dry filter cake was then extracted for 6 hours in a Soxhlet apparatus with 50 ml. of a 1:1 mixture of petroleum ether (40–60°) and benzene. Evaporation of the mixed solvent gave 2.4 g. (18% yield) of a pale yellow solid, m.p. 80–83°. A single recrystallization from petroleum ether raised the melting point to 84–85°.

Anal. Calcd. for $C_2H_3N_5O_2$: C, 18.61; H, 2.34; N, 54.26. Found: C, 18.57; H, 2.43; N, 54.71.

The solid remaining in the Soxhlet thimble, 5.3 g. (41% yield), m.p. 204–207°, exhibited an infrared spectrum essentially superimposable with that of VII.

Reduction of VIII.—A solution of 1.03 g. of VIII, m.p. 80–83°, in 100 ml. of 95% ethanol, containing 5 mg. of Adams catalyst, was shaken with hydrogen for 2 hours at room temperature. The catalyst was collected and the solution, on evaporation of the solvent in a stream of air, gave 0.74 g. (94% yield) of 2-methyl-5-aminotetrazole, m.p. 92–101°. A single recrystallization from water raised the melting point to 102–104°.

1-Methyl- and 2-Methyl-5-bromotetrazole.—Into an ice-cold ether suspension of 38 g. of 5-bromotetrazole (0.255 mole) was distilled an ethereal solution of diazomethane until a yellow color persisted. Evaporation of the ether left an oil which, on distillation, gave 28 g. (68% yield) of 2-methyl-5-bromotetrazole (XI) (*vide infra*), b.p. 59–61° (4 mm.), $n^{25}D$ 1.501.

Anal. Calcd. for $C_2H_3N_4Br$: C, 14.73; H, 1.85; N, 34.40. Found: C. 14.93; H, 1.87; N, 34.24.

The residue in the still-pot crystallized to a yellow solid on cooling which, on recrystallization from ether, gave 5.5 g. (13% yield) of 1-methyl-5-bromotetrazole (X) (*vide infra*), m.p. 72–74°.

Anal. Calcd. for $C_2H_3N_4Br$: C, 14.73; H, 1.85; N, 34.40. Found: C, 15.08; H, 1.92; N, 34.00.

Hydrolysis of X.—A suspension of 0.8 g. of X (0.005 mole) in 10 ml. of 20% sodium hydroxide was refluxed for 10 hours. The clear solution was filtered, acidified with 3 ml. of concentrated nitric acid and then evaporated to dryness in a stream of air at room temperature. The solid residue was triturated with three 20-ml. portions of warm ether and the combined ether extracts evaporated to dryness. A white crystalline solid, wt. 0.3 g. (60% yield), m.p. 102–108°, remained. Recrystallization from ether raised the melting point to 118–120°. A mixed melting point with an au-

thentic sample of 1-methyl-5-hydroxytetrazole showed no depression.

2-Methyl-5-hydroxytetrazole.—A solution of 62.1 g. of XI (0.38 mole) in 150 ml. of water, 250 ml. of methanol and 67 g. of potassium hydroxide was refluxed for 48 hours. The solution was cooled, acidified with 100 ml. of concentrated hydrochloric acid and evaporated to dryness in a stream of air at room temperature. The solid residue was then extracted for 8 hours with ether in a Soxhlet apparatus. Evaporation of the solvent gave 23 g. (60% yield) of a white crystalline solid, m.p. 120–136°. Recrystallization from ether raised the melting point to 137–138°.

Anal. Calcd. for $C_2H_4ON_4$: C, 24.00; H, 4.00; N, 56.00. Found: C, 24.06; H, 3.91; N, 56.27.

2-Methyl-5-methoxytetrazole (XIII).—To a filtered solution of 2.3 g. of sodium (0.1 g. atom) in 30 ml. of methanol was added 1.9 g. of XI (0.032 mole). The mixture was refluxed for 24 hours and then evaporated to near dryness in a stream of air. The residue was triturated with three 20-ml. portions of warm ether and the combined ether extracts on evaporation afforded 1.0 g. of solid (27% yield), m.p. 37–42°. Recrystallization from ether gave a white crystalline material, m.p. 42–43°.

Anal. Calcd. for $C_3H_6ON_4$: C, 31.58; H, 5.30; N, 49.10. Found: C, 31.96; H, 5.43; N, 48.87.

A 1.14-g. sample of this product in 15 ml. of 20% aqueous hydrochloric acid was refluxed for 3 hours. The solution was evaporated to dryness in a stream of air and the residue, 0.98 g. (98% yield), m.p. 132–138°, was recrystallized from ether to give a crystalline solid, m.p. 137–138° alone or with an authentic sample of 2-methyl-5-hydroxytetrazole.

Methylation of 5-Hydroxytetrazole (I). (a) 1,4-Dimethyl-4-tetrazolone (XV).—Into an ice-cold suspension of 16.39 g. of I in 250 ml. of ether was distilled an ethereal solution of diazomethane until a yellow color persisted. After the vigorous evolution of nitrogen had subsided, the solution was placed in a refrigerator for 24 hours. On evaporation of the solvent, there remained a suspension of a white solid in a colorless liquid. The solid was filtered off and sucked dry; wt. 7.5 g., m.p. 110–117°. Recrystallization of this material from benzene gave 5 g. of a white crystalline solid, m.p. 116–117°.

Anal. Calcd. for $C_3H_6ON_4$: C, 31.58; H, 5.30; N, 49.10. Found: C, 32.07; H, 5.46; N, 49.60.

A 0.5-g. sample of this product, after a three-hour reflux period with 20% hydrochloric acid, was recovered unchanged, thus indicating that both methyl substituents must be attached to the tetrazole ring.

A solution of 3.2 g. of 1,4-dimethyl-5-iminotetrazole hydrochloride (0.021 mole) in 35 ml. of water was acidified with dilute hydrochloric acid. The mixture was cooled to 0° while a solution of 1.6 g. of sodium nitrite (0.023 mole) in 5 ml. of water was added dropwise with stirring. The reaction mixture was then placed in a refrigerator for 24 hours, then refluxed for 2 hours and finally evaporated to dryness in a stream of air at room temperature. The residue was crystallized from benzene to give 31 mg. of product, m.p. 116–117° alone or when mixed with the sample of XV obtained from the methylation of 5-hydroxytetrazole. Infrared measurements further demonstrated that the two compounds were identical with a strong absorption occurring at 1710 cm.$^{-1}$ in both cases.

(b) 2-Methyl-5-methoxytetrazole (XIII).—The filtrate remaining after the separation of XV afforded two distinct fractions on distillation, the first of which amounted to 1.79 g., b.p. 50–54° (3 mm.).

Anal. Calcd. for $C_3H_6ON_4$: C, 31.58; H, 5.30; N, 49.10. Found: C, 31.96; H, 5.43; N, 48.87.

This liquid crystallized on standing to a white solid, m.p. 42–43° alone or when mixed with an authentic sample of 2-methyl-5-methoxytetrazole (XIII). Furthermore, when a sample of product, m.p. 42–43°, was hydrolyzed in the previously described manner with 20% hydrochloric acid, the product was identified as 2-methyl-5-hydroxytetrazole.

(c) 1-Methyl-5-methoxytetrazole (XIV).—The second product of the fractional distillation, 1.60 g., $n^{25}D$ 1.456, was collected at 88–90° (2 mm.).

Anal. Calcd. for $C_3H_6ON_4$: C, 31.58; H, 5.30; N, 49.10. Found: C, 32.15; H, 5.22; N, 49.07.

A mixture of 0.5 g. (0.004 mole) of this fraction in 15 ml. of 20% aqueous hydrochloric acid was refluxed for 3 hours. The clear solution was evaporated to dryness and the residue recrystallized from ether to yield 0.22 g. of solid, m.p. 122–124°. A mixed melting point with an authentic sample of 1-methyl-5-hydroxytetrazole (V) was not depressed.

Infrared measurements performed upon the material remaining in the still pot following the fractional distillation revealed the presence of a small amount of XV with principal maxima occurring at 1581, 1495 and 1303 cm.$^{-1}$. In addition the presence of a new carbonyl compound (1673 cm.$^{-1}$) was detected in these same measurements.

Methylation of 2-Methyl-5-hydroxytetrazole (XII). (a) 1,3-Dimethyl-5-tetrazolone (XVI).—Into an ice-cold suspension of 18.25 g. of 2-methyl-5-hydroxytetrazole (0.18 mole) in 200 ml. of ether was distilled an ethereal solution of diazomethane until a yellow color persisted. Evaporation of the ether gave 18.7 g. of an oily solid which was refluxed for 3 hours with 25% hydrochloric acid. The reaction mixture was next made basic with 30 ml. of 25% sodium hydroxide and then evaporated to dryness with a stream of air at room temperature. The oily residue was extracted with 200 ml. of chloroform in a Soxhlet apparatus and the solvent concentrated under reduced pressure. The last traces of chloroform were removed at 5 mm. following which the residue suddenly solidified to a white crystalline mass, wt. 8.3 g. (40% yield), m.p. 58–62°. Two distillations of this material at 160° (3 mm.) gave 2.8 g. of a white crystalline solid, m.p. 64–65°. Infrared measurements indicated strong carbonyl absorption at 1673 cm.$^{-1}$ and, on the basis of the evidence to date, the product is assigned structure XVI.

Anal. Calcd. for $C_3H_6ON_4$: C, 31.58; H, 5.30; N, 49.10. Found: C, 31.76; H, 5.21; N, 49.16.

(b) 2-Methyl-5-hydroxytetrazole.—The solid remaining in the Soxhlet thimble was treated with 5 ml. of concentrated hydrochloric acid and the acidified solution evaporated to dryness in a stream of air at room temperature. The dry residue was next refluxed for 3 hours in a Soxhlet extractor and the solution evaporated to dryness. The residue, 3.1 g. (17% yield), m.p. 110–115°, was recrystallized from benzene to give 1.5 g. of a crystalline white solid, m.p. 136–137°. A mixed melting point with an authentic sample of 2-methyl-5-hydroxytetrazole showed no depression.

Methylation of 1-Methyl-5-hydroxytetrazole (V). (a) 1,4-Dimethyl-5-tetrazolone (XV).—Into an ice-cold suspension of 11.45 g. of 1-methyl-5-hydroxytetrazole (0.114 mole) in 250 ml. of ether was distilled an ethereal solution of diazomethane until a yellow color persisted. Evaporation of the ether left an oily solid, wt. 12.3 g., m.p. 102–108°. The residue was first washed with carbon tetrachloride and then recrystallized from ether to give 10.9 g. (83% yield) of XV, m.p. 116–117°.

(b) 1-Methyl-5-methoxytetrazole (XIV).—The carbon tetrachloride washings were combined and the solvent removed under reduced pressure. The liquid residue was then distilled affording 1.3 g. of XIV, b.p. 88° (2 mm.). When a sample of this material was hydrolyzed with aqueous hydrochloric acid in a manner essentially the same as that already described, 1-methyl-5-hydroxytetrazole was obtained in quantitative yield.

The residue in the still-pot was next submitted for infrared study from which it was estimated that the non-volatile material contained approximately 1% of XVI together with traces of XIV and XV.

DECATUR, ILLINOIS