[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE COLLEGE]

THE ACYLATION OF SOME 5-AMINOTETRAZOLE DERIVATIVES

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In connection with attempts to prepare 5-alkylacylaminotetrazoles from alkylacylcyanamides it was felt that knowledge of the properties of some acyl 5-alkylaminotetrazoles would be helpful in the isolation and identification of the products. For this purpose the acylation of several alkyl 5-aminotetrazoles was undertaken. 1-Benzyl-5-aminotetrazole (I) and 5-benzylaminotetrazole (II) were selected for initial studies because both compounds can be obtained easily by the benzylation of 5-aminotetrazole. Thiele and Ingle (1) had shown that several mono- and di-benzylaminotetrazoles are formed by interaction of benzyl chloride and 5-aminotetrazole under various conditions. When the reaction is done in aqueous alcoholic potassium carbonate solution, a mixture of benzylation products is formed from which 1-benzyl-5-aminotetrazole and 5-benzylaminotetrazole can be isolated rather easily. Furthermore, the structure of both compounds has been established through several independent syntheses; the former has been prepared from benzyl cyanide (2, 3) and from benzyl cyanamide (4), while the latter has been obtained by hydrolysis of 5-benzylcarbethoxyaminotetrazole and by the partial debenzylation of 5-dibenzylaminotetrazole (5).

Acetylation of 5-benzylaminotetrazole (II) with acetic anhydride in acetic acid solution gave a monoacetyl derivative which was soluble in aqueous potassium carbonate solution. Upon hydrolysis of the acetyl derivative with aqueous sodium hydroxide, potassium carbonate, or hydrochloric acid only 1-benzyl-5-aminotetrazole (I) was formed. The same acetyl derivative was formed on acetylation of 1-benzyl-5-aminotetrazole with boiling acetic anhydride. Hydrogenolysis of the benzyl group in alcoholic solution at room temperature using palladium-charcoal as catalyst gave 5-acetylaminotetrazole (V). Apparently rearrangement of the 5-benzylaminotetrazole took place during the acetylation reaction. On the basis of its properties the structure of 1-benzyl-5-acetylaminotetrazole (III) was assigned to the acetyl derivative.

It was known that 5-benzylaminotetrazole would rearrange at elevated temperature with the formation of 1-benzyl-5-aminotetrazole (6). The question arises whether rearrangement precedes acetylation or whether a labile acetyl derivative is first formed. Since no rearrangement occurred upon heating 5-benzylaminotetrazole in acetic acid or in 20% hydrochloric acid solution, it may be assumed that rearrangement of a labile acetyl derivative is involved.

Acetylation of 5-benzylaminotetrazole dissolved in aqueous potassium carbonate solution with acetic anhydride in the cold gave a second acetyl derivative (IV) which was insoluble in the aqueous potassium carbonate solution. This acetyl derivative dissolved slowly in cold dilute sodium hydroxide with elimi-

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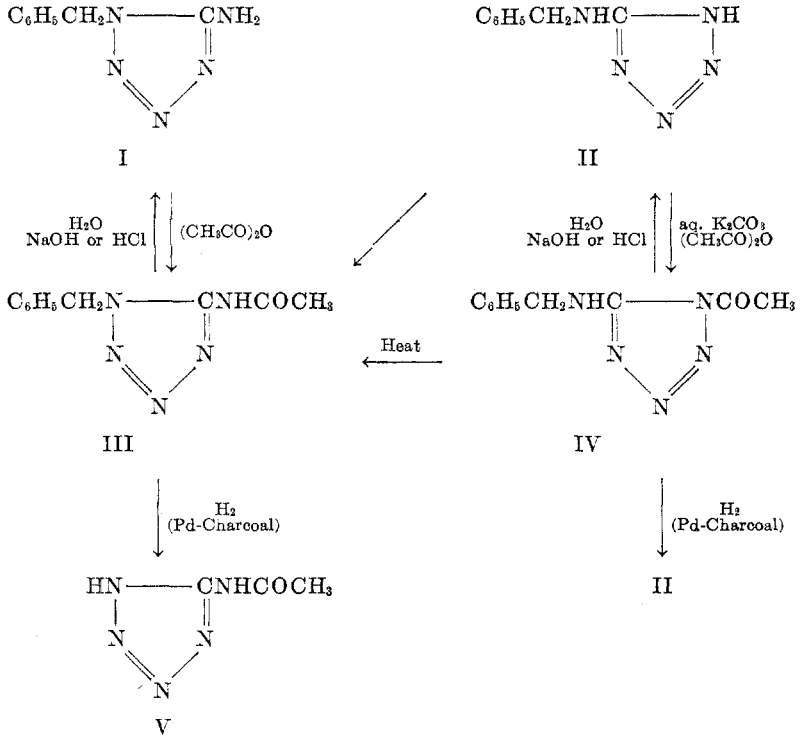
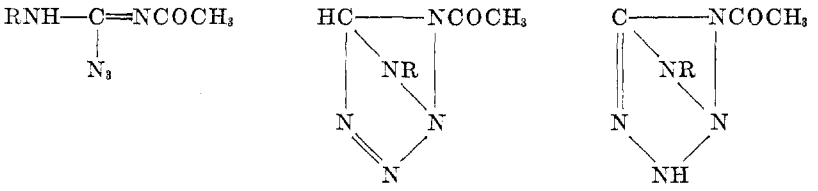
nation of the acetyl group and regeneration of 5-benzylaminotetrazole. Hydrolysis with warm 20% hydrochloric acid also regenerated 5-benzylaminotetrazole. On heating at 100° for about an hour the acetyl derivative (IV) was completely converted into the alkali-soluble acetyl derivative (III). Furthermore, after an attempted catalytic debenzylation of the acetyl derivative (IV) only 5-benzylaminotetrazole was recovered, apparently as the result of alcoholysis of the acetyl group. The absence of acidic properties in the acetyl derivative (IV) and the ease with which 5-benzylaminotetrazole could be regenerated suggested the structure of 1-acetyl-5-benzylaminotetrazole for the compound. The possibility that the product might be 2-acetyl-5-benzylaminotetrazole cannot be excluded. However, the ease of rearrangement to 1-benzyl-5-acetylaminotetrazole would be difficult to explain on this basis. The easy conversion of 1-aryl-5-aminotetrazoles to 5-arylaminotetrazoles and of the 5-alkylaminotetrazoles to 1-alkyl-5-aminotetrazoles (6) support the assumption of acetylation in the 1-position.



It is interesting to note that palladium-charcoal can effect selective hydrogenolysis of the benzylaminotetrazoles. The benzyl group on the ring at the 1-position is much more easily removed at room temperature than is the benzyl group substituted on the amino group (see also ref. 5).

Two mechanisms suggest themselves for the rearrangement, either the forma-

tion of a substituted guanyl azide (VI)[3] or the formation of a nitrogen bridge (VIIa or b) between positions 2 and 5 of the tetrazole ring. For reasons previously outlined (6) we are inclined to prefer the nitrogen bridge intermediate. In structure (VII) the bridge-nitrogen and the nitrogen in the 1-position of the original ring occupy equivalent positions; cleavage of the bond from the bridge-nitrogen to the 2-nitrogen of the original ring would reform structure IV, while cleavage of the bond between the 1 and 2 nitrogens of the original ring would result in structure III. The shift of a hydrogen accompanies both cleavages. The isomerizations may be equilibrium reactions, but in our experience the equilibrium appears to be well on the side of the 1-alkyl-5-acetylaminotetrazole structure. The greater negativity of the acetyl group as compared with the benzyl group should favor formation of the 5-acetylamino structure (6).



VI VIIa VIIb

R = $C_6H_5CH_2$, C_2H_5

5-Ethylaminotetrazole on acetylation with acetic anhydride in acetic acid solution gave the same acetyl derivative as was formed from 1-ethyl-5-aminotetrazole in boiling acetic anhydride. The acidic character of the acetyl derivative and its hydrolysis to 1-ethyl-5-aminotetrazole suggest that a similar rearrangement took place.

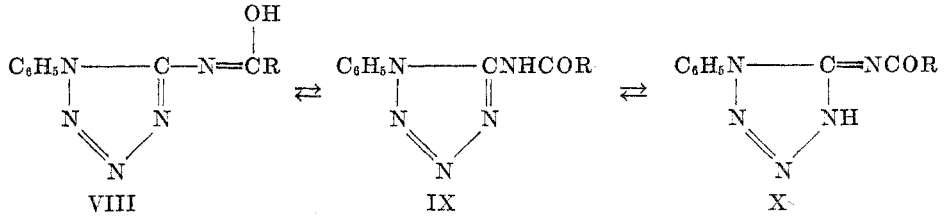
Benzoylation of 5-benzylaminotetrazole in pyridine solution in the cold with benzoyl chloride gave a product that appeared to be 1-benzyl-5-benzoylaminotetrazole. Assignment of structure was based on the solubility of the benzoyl derivative in aqueous alkali and its hydrolysis to 1-benzyl-5-aminotetrazole. It is possible that the initial benzoylation product was 1-benzoyl-5-benzylaminotetrazole and that rearrangement to the product isolated took place on crystallization from warm cyclohexane. Carbethoxylation of 5-benzylaminotetrazole dissolved in aqueous potassium carbonate solution gave a product that was insoluble in dilute aqueous acid or alkali and which differed from 5-benzylcarbethoxyaminotetrazole (5). The similarity of the properties of this product and those of 1-acetyl-5-benzylaminotetrazole suggest that 1-carbethoxy-5-benzylaminotetrazole was formed.

It seems likely that acylation of the 5-alkylaminotetrazoles takes place initially at the 1-position of the ring. Subsequently, depending upon conditions of the acylation, rearrangement to the 1-alkyl-5-acylaminotetrazoles takes place. Thus

[3] A guanyl azide structure has been suggested as an intermediate in the rearrangement of certain 1-aryl-5-aminotetrazoles to 5-arylaminotetrazoles by Dr. R. A. Henry in a private communication (See Ref. 13).

in hot acetic acid the initially formed 1-acetyl derivative rearranges rapidly to the more stable 5-acetylaminotetrazole configuration.

Both 1-ethyl- and 1-benzyl-5-acetylaminotetrazole titrate as very weak monobasic acids. 5-Acetylaminotetrazole also titrates as a weak monobasic acid but is about 10,000 times as strong as its 1-alkyl derivatives. In each case the titration curve had the form typical of a weak acid. The relatively great acidity of 5-acetylaminotetrazole is undoubtedly due to the hydrogen in position 1 (or 2) of the tetrazole ring. A second break in the titration curve due to the amidic hydrogen was not apparent when a second equivalent of base was added during the potentiometric titration of 5-acetylaminotetrazole. However, this observation has little significance due to the high *p*H of the medium. It is quite possible that 5-acetylaminotetrazole would behave as a dibasic acid in non-aqueous media. Stollé and Henke-Stark (7) noted that 1-phenyl-5-benzoylamino- and 1-phenyl-5-acetylamino-tetrazole (IX) were soluble in sodium carbonate solution and and could be titrated with sodium hydroxide. They suggested two tautomeric modifications (VIII and X) for the acylamino derivatives and concluded that the acidity was due to the structure (X) because neither benzanilide nor acetanilide are soluble in aqueous alkali. This comparison is not entirely valid. Just as the 5-alkyltetrazoles may be compared with the corresponding carboxylic acids in which the tetrazole residue replaces the carboxyl group (8), so it would seem more logical to compare 5-aminotetrazole and its derivatives to carbamic acid and its derivatives.



R = CH_3, C_6H_5

On this basis 1-ethyl- and 1-benzyl-5-acetylaminotetrazole should be compared with ethyl and benzyl N-acetylcarbamate, respectively. It is noteworthy in this connection that the acidic character of benzoylurethan has long been recognized (9, 10). This analogy suggests that the acidity of the 1-alkyl-5-acetylaminotetrazoles is due to the dissociation of a proton from the lactam (IX) or the lactim (VIII) form. Ethyl N-acetylcarbamate also forms a sodium salt (11).

The study of the acylation of 5-aminotetrazoles and the properties of the acyl derivatives is being continued.

EXPERIMENTAL[4, 5]

1-Benzyl-5-aminotetrazole and 5-benzylaminotetrazole. A suspension of 85 g. (1 mole) of anhydrous 5-aminotetrazole (12) in 400 ml. of water was treated with 69 g. (0.5 mole) of

[4] Micro-analyses were done on all compounds by Micro-Tech Laboratories, Skokie, Illinois.

[5] Melting points were done in open capillaries; temperatures are corrected.

anhydrous potassium carbonate. To the clear solution obtained by warming the mixture gently 126.5 g. (1 mole) of benzyl chloride and 250 ml. of 95% ethanol were added. The mixture was boiled under reflux for three hours, then diluted with an equal volume of water and chilled thoroughly. The mixture of benzylated aminotetrazoles that had separated was filtered by suction, washed with cold water, and air-dried. Extraction with three 150-ml. portions of benzene left about 60 g. of solid benzylation products. The benzene extracts contained a considerable quantity of low-melting benzylation products which have not been completely investigated. The mixture of solid products was suspended in 250 ml. of 10% sodium hydroxide and was shaken thoroughly before chilling and filtering off the insoluble portion. About 42 g. of alkali-insoluble material remained. The aqueous alkaline solution was heated to boiling and made just barely acid to Congo Red with hydrochloric acid. 5-Benzylaminotetrazole [Thiele and Ingle's β-monobenzylaminotetrazole (1)] crystallized from the hot solution as it was made acid. After chilling the product was filtered and recrystallized from 50% isopropyl alcohol. Yield 14 g., m.p. 186–187°,[6] no depression on admixture of an authentic sample (5).

Anal. Calc'd for $C_8H_9N_5$: N, 40.0. Found: N, 40.3.

The alkali-insoluble material was extracted with two portions of boiling water (1500 and 500 ml.). 1-Benzyl-5-aminotetrazole (Thiele and Ingle's α-monobenzylaminotetrazole) separated from the aqueous extracts and was recrystallized from 50% isopropyl alcohol. Yield 29 g., m.p. 190–191°, no depression on admixture of an authentic sample (3, 4).

Anal. Calc'd for $C_8H_9N_5$: N, 40.0. Found: N, 40.1.

The material insoluble in boiling water was recrystallized from 99% isopropyl alcohol from which it separated as needles. Yield 8.5 g., m.p. 170–171°. This material is insoluble in dilute aqueous sodium hydroxide or hydrochloric acid; it appears to be identical with the β-dibenzylaminotetrazole of Thiele and Ingle. Its structure remains to be established.

Anal. Calc'd for $C_{15}H_{15}N_5$: N, 26.3. Found: N, 26.4.

1-Benzyl-5-acetylaminotetrazole (III). *(A) By acetylation of 1-benzyl-5-aminotetrazole.* A solution of 2 g. of 1-benzyl-5-aminotetrazole in 10 ml. of acetic anhydride was boiled under reflux for two hours, was diluted with 20 ml. of glacial acetic acid and 2 ml. of water, and was evaporated to dryness on the steam-bath. The residue was twice recrystallized by dissolving in 20 ml. of hot ethyl acetate and diluting with an equal volume of petroleum ether. Needles, yield 2.2 g., m.p. 108–109°. This product was identical with the material obtained by acetylation of 5-benzylaminotetrazole with acetic anhydride in acetic acid solution.

Anal. Calc'd for $C_{10}H_{11}N_5O$: C, 55.3; H, 5.1; N, 32.2.
Found: C, 54.9; H, 5.0; N, 32.1.

The acetyl derivative is quite easily soluble in warm benzene, ethyl acetate, acetone, 95% ethanol, ethylene dichloride, and aqueous potassium hydroxide or potassium carbonate solution. It is only slightly soluble in ether, and insoluble in petroleum ether, water, and aqueous potassium bicarbonate solution. It is precipitated unchanged from its solution in cold potassium hydroxide or potassium carbonate.

Attempts to acetylate 1-benzyl-5-aminotetrazole in acetic acid solution with acetic anhydride gave a mixture from which most of the starting material could be recovered and only small amounts of impure acetyl derivative could be isolated.

(B) By acetylation of 5-benzylaminotetrazole. A solution of 1 g. of 5-benzylaminotetrazole in a mixture of 2 ml. of acetic anhydride and 4 ml. of acetic acid was heated on a boiling water-bath for 2½ hours. The solution was evaporated to dryness on a steam-bath and the residue was recrystallized from a mixture of equal volumes of ethyl acetate and ligroin. Yield 1.1 g., m.p. 109–110°, no depression on admixture of acetylated 1-benzyl-5-aminotetrazole.

Anal. Calc'd for $C_{10}H_{11}N_5O$: C, 55.3; H, 5.1; N, 32.2.
Found: C, 55.2; H, 5.2; N, 32.3.

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[6] The melting point of 5-benzylaminotetrazole varies from 180–193° depending on the rate of heating. The lower melting points are observed with very slow heating (5).

When 0.5 g. of 5-benzylaminotetrazole dissolved in 5 ml. of glacial acetic acid was heated as just described, the starting material was recovered quantitatively. After heating a solution of 5-benzylaminotetrazole in 20% hydrochloric acid under the same conditions, the starting material was recovered quantitatively. These observations indicate that the rearrangement followed acetylation.

Hydrolysis of 1-benzyl-5-acetylaminotetrazole in aqueous acid or alkaline solution gave 1-benzyl-5-aminotetrazole quantitatively. (*a*) A solution of 0.5 g. of 1-benzyl-5-acetylaminotetrazole in 20 ml. of boiling 20% hydrochloric acid was evaporated to dryness on the steam-bath. The residue was taken up in water, the solution neutralized with sodium hydroxide, and the precipitate recrystallized from boiling water. Yield 0.4 g., m.p. 190–191°, no depression observed on admixture of 1-benzyl-5-aminotetrazole. (*b*) A solution of 0.2 g. of the acetyl derivative in 10 ml. of 1% aqueous sodium hydroxide was boiled under reflux for two hours. On cooling 0.15 g. of 1-benzyl-5-aminotetrazole crystallized, m.p. 190–191°, no depression on admixture of an authentic sample. No 5-benzylaminotetrazole could be separated from the alkaline filtrate. (*c*) A suspension of 2.17 g. of acetyl derivative in 25 ml. of water was dissolved by addition of 15 ml. of 10% potassium carbonate solution. The solution was boiled under reflux for six hours, diluted with 75 ml. of water, and heated to boiling to redissolve solid that had separated. 1-Benzyl-5-aminotetrazole crystallized from the solution on cooling. Yield 1.6 g., m.p. 190–191°, no depression on admixture of an authentic sample. No 5-benzylaminotetrazole could be separated from the alkaline filtrate.

Debenzylation of 1-benzyl-5-acetylaminotetrazole. A solution of 5.4 g. (0.025 mole) of 1-benzyl-5-acetylaminotetrazole in 150 ml. of absolute ethanol was shaken at room temperature with 5 g. of 5% palladium-charcoal at an initial hydrogen pressure of 50 p.s.i. Hydrogenolysis was complete in two hours after which the catalyst was filtered off. Evaporation of the filtrate and recrystallization of the residue from water gave 0.4 g. of 5-acetylaminotetrazole, m.p. 268° with decomposition (1). The catalyst was extracted with boiling water (200, 50, and 50 ml.). From the aqueous extract 2.4 g. of 5-acetylaminotetrazole separated as typical glistening platelets, m.p. 268° with decomposition.

Acetylation of 5-benzylaminotetrazole in alkaline medium. 5-Benzylaminotetrazole (8.7 g., 0.05 mole) was dissolved in 100 ml. of water containing 20.7 g. (0.15 mole) of potassium carbonate. After addition of a few drops of capryl alcohol to control foaming 15.3 g. (0.15 mole) of acetic anhydride was added dropwise from a burette during 15 minutes with cooling in an ice-bath and manual agitation. The product began to precipitate from the solution almost immediately after addition of the acetic anhydride was started. The precipitate was filtered by suction, washed with cold 5% potassium carbonate solution, and then with water. The air-dried crude product (10.3 g.) was dissolved in 175 ml. of benzene at room temperature (warming the solution may cause partial rearrangement of the product). The clear benzene solution was evaporated in an air current to about 100 ml. and then diluted with 200 ml. of petroleum ether added at intervals in 50-ml. portions. 1-Acetyl-5-benzylaminotetrazole (IV) separated slowly as heavy prisms. Yield 9.0 g., m.p. 106–108°. Admixture of 1-benzyl-5-acetylaminotetrazole caused as much as 20° depression of the melting point. The product is insoluble in cold dilute sodium hydroxide (see also below) or hydrochloric acid, moderately soluble in cold benzene and ethyl acetate, sparingly soluble in ethanol, and insoluble in petroleum ether.

Anal. Calc'd for $C_{10}H_{11}N_5O$: C, 55.3; H, 5.1; N, 32.2.
Found: C, 55.5, 55.5; H, 5.2, 5.2; N, 32.2, 32.2.

Hydrolysis of 1-acetyl-5-benzylaminotetrazole. (*a*) A solution of 0.5 g. of 1-acetyl-5-benzylaminotetrazole in 10 ml. of warm 20% hydrochloric acid was evaporated to dryness on the steam-bath. The residue was dissolved in boiling water and the *p*H of the solution was adjusted with aqueous ammonia until just barely acid to Congo Red. On cooling 0.4 g. of 5-benzylaminotetrazole, m.p. and mixture m.p. 187–188°, was recovered. (*b*) 1-Acetyl-5-benzylaminotetrazole (0.4 g.) was stirred with 20 ml. of cold 2% aqueous sodium hydroxide. The solid dissolved completely in about 20 minutes. The clear, cold solution was carefully

made barely acid to Congo Red with hydrochloric acid. 5-Benzylaminotetrazole (0.3 g.), m.p. and mixture m.p. 187–188°, precipitated from the solution.

Thermal rearrangement of 1-acetyl-5-benzylaminotetrazole. 1-Acetyl-5-benzylaminotetrazole (0.5 g.) was heated in a boiling water-bath for about an hour. The solid gradually softened and melted to a clear liquid which became glassy on cooling but crystallized on contact with a little benzene. Recrystallization from cold benzene-petroleum ether mixture gave 0.3 g. of 1-benzyl-5-acetylaminotetrazole, m.p. and mixture m.p. 109–110°.

Attempted hydrogenolysis of 1-acetyl-5-benzylaminotetrazole. A suspension of 5.4 g. (0.025 mole) of finely powdered 1-acetyl-5-benzylaminotetrazole and 5 g. of 5% palladium-charcoal in 200 ml. of absolute ethanol was shaken at room temperature with hydrogen at an initial pressure of 50 p.s.i. for 42 hours. Only a negligible drop in hydrogen pressure was observed. The catalyst was removed and the alcoholic filtrate was evaporated to dryness at room temperature in an air stream. The residue was completely soluble in cold dilute potassium carbonate solution from which 5-benzylaminotetrazole separated on neutralization with hydrochloric acid. Yield 2.9 g. after recrystallization from 50% isopropyl alcohol, m.p. and mixture m.p. 187–188°. The catalyst was extracted repeatedly, first with cold benzene and finally with hot water. Evaporation of the extracts left only traces of materials not further identified.

Benzoylation of 5-benzylaminotetrazole. A solution of 1.8 g. of 5-benzylaminotetrazole in 20 ml. of pyridine was treated dropwise with an excess of benzoyl chloride with stirring and cooling in an ice-bath. The red solution was poured onto a mixture of ice and concentrated hydrochloric acid. The brown oil which separated was washed with water by decantation and then dissolved in warm cyclohexane from which it crystallized as fine needles, m.p. 108–109°. The product was insoluble in water and dilute hydrochloric acid but soluble in dilute sodium hydroxide and was probably 1-benzyl-5-benzoylaminotetrazole.

Anal. Calc'd for $C_{15}H_{13}N_5O$: C, 64.5; H, 4.7; N, 25.1.

Found: C, 64.7; H, 4.6; N, 25.2.

On heating 200 mg. of the benzoyl derivative with 10 ml. of 20% hydrochloric acid on the steam-bath for several hours a colorless solid was obtained which crystallized from water as fine needles, m.p. 190–191°. The hydrolysis product was identical with 1-benzyl-5-aminotetrazole. This observation supports the assumption that 1-benzyl-5-benzoylaminotetrazole was isolated after benzoylation of 5-benzylaminotetrazole.

Carbethoxylation of 5-benzylaminotetrazole. A solution of 1.8 g. of 5-benzylaminotetrazole in 10% aqueous potassium carbonate solution was treated at room temperature with an excess of ethyl chloroformate added dropwise with frequent vigorous shaking. The product precipitated as a granular solid that was dissolved in the minimum amount of cold ethyl acetate from which it crystallized as fine, colorless needles on addition of cyclohexane, yield 1.3 g., m.p. 59–61°. The product was insoluble in water, dilute hydrochloric acid, and dilute sodium hydroxide which suggested that 1-carbethoxy-5-benzylaminotetrazole had been formed.

Anal. Calc'd for $C_{11}H_{13}N_5O_2$: C, 53.4; H, 5.3; N, 28.3.

Found: C, 53.2, 53.3; H, 5.3, 5.4; N, 28.6, 28.3.

1-Ethyl-5-acetylaminotetrazole. (*a*) *From 1-ethyl-5-aminotetrazole.* A solution of 10 g. of 1-ethyl-5-aminotetrazole (4) in 75 ml. of acetic anhydride was boiled under reflux for six hours. After dilution with 100 ml. of 95% ethanol the solution was evaporated to dryness on the steam-bath. The residue was taken up in 100 ml. of warm benzene and the product was precipitated by the slow addition of an equal volume of petroleum ether. The crude product, 12.2 g., m.p. 82–90°, was contaminated with unacetylated material which could be separated only with difficulty. Acetylation was completed by boiling the crude material with 50 ml. of acetic anhydride for five hours. Excess acetic anhydride was evaporated as before and the residue was crystallized several times from ethylene dichloride-petroleum ether. Yield 9.4 g., m.p. 99–100°. The acetyl derivative is readily soluble in water and ethanol, moderately soluble in benzene and ethylene dichloride, and insoluble in petroleum ether.

Anal. Calc'd for $C_5H_9N_5O$: C, 38.7; H, 5.9; N, 45.1.
Found: C, 38.6, 38.6; H, 5.7, 5.8; N, 44.9, 44.9.

(*b*) *From 5-ethylaminotetrazole.* A solution of 1 g. of 5-ethylaminotetrazole (5) in a mixture of 3 ml. of acetic anhydride and 8 ml. of glacial acetic acid was boiled under reflux for 1½ hours. After dilution with an equal volume of 95% ethanol and evaporation of the solvent on a steam-bath, the residue was dissolved in 15 ml. of warm ethylene dichloride from which it crystallized on slow addition of an equal volume of petroleum ether. Yield 1.3 g., m.p. 99–100°. The product was identical with the material obtained by acetylation of 1-ethyl-5-aminotetrazole.

Anal. Calc'd for $C_5H_9N_5O$: C, 38.7; H, 5.9; N, 45.1.
Found: C, 38.5, 38.7; H, 5.9, 6.0; N, 45.0, 44.9.

Hydrolysis of 1-ethyl-5-acetylaminotetrazole. One gram of 1-ethyl-5-acetylaminotetrazole was dissolved in 10 ml. of water. After addition of 10 ml. of concentrated hydrochloric acid the solution was evaporated to dryness on the steam-bath. The residue was taken up in 5 ml. of water, and the solution was warmed and made just alkaline to Congo Red by addition of 20% sodium hydroxide. On cooling 1-ethyl-5-aminotetrazole crystallized, yield 0.6 g., m.p. and mixture m.p. 147–148°.

TABLE I

APPARENT ACIDIC DISSOCIATION CONSTANTS OF 5-ACETYLAMINOTETRAZOLE DERIVATIVES

COMPOUND	SOLVENT	APPARENT		NEUT. EQUIV.	
		pK_a	$K_a \times 10^3$	Calc'd	Found
5-Acetylaminotetrazole	Water	4.53	29500	127	127
1-Ethyl-5-acetylaminotetrazole	Water	8.38	4.17	155	156
1-Benzyl-5-acetylaminotetrazole	50% Methanol by volume	8.61	2.46	217	215

Potentiometric titrations. Solutions of 0.2224 g. of 5-acetylaminotetrazole (1) and 0.3502 g. of 1-ethyl-5-acetylaminotetrazole in 200 ml. of water, and 0.4282 g. of 1-benzyl-5-acetylaminotetrazole in 100 ml. of methanol diluted with 100 ml. of water were titrated with 0.1043 *N* aqueous potassium hydroxide using a Beckman *p*H Meter, Model G. The titration curves for all the compounds were of the weak acid type. Since it was thought that 5-acetylaminotetrazole might act as a dibasic acid, its titration was carried well beyond the addition of a second equivalent of base but a second break was not apparent. The apparent pK_a and K_a values, together with neutralization equivalents calculated from the titration data, are given in Table I.

SUMMARY

The rearrangement of several 5-alkylaminotetrazoles to 1-alkyl-5-acetylaminotetrazoles upon acetylation has been observed. Conditions for the formation of 1-acetyl-5-benzylaminotetrazole and its rearrangement to 1-benzyl-5-acetylaminotetrazole are described. A possible mechanism for the rearrangement is suggested. Apparent acidic dissociation constants of 5-acetylaminotetrazole and several of its 1-alkyl derivatives have been determined and structures contributing to the acidity of these compounds are discussed.

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