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THE SYNTHESIS OF CERTAIN 5-AMINOTETRAZOLE DERIVATIVES. I. THE ACTION OF HYDRAZOIC ACID ON SOME DIALKYLCYANAMIDES[1]

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Received February 17, 1953

While 5-aminotetrazole has been known for many years (1), its derivatives in which amino hydrogens are replaced by alkyl groups are not, in general, known. A study of this class of compounds, the 5-mono- and 5-di-alkylaminotetrazoles, is of interest for several reasons. Since the parent substance, 5-aminotetrazole, possesses both an acidic and a basic function, it would be interesting to know the effect of substituents on these functions. Furthermore, alkylation of 5-aminotetrazole leads to a mixture of products (2) and there is need for a direct, unequivocal synthesis of these derivatives. The possibility that this class of compounds might have useful pharmacological activity also seemed attractive.

The synthesis of 5-aminotetrazole and some of its substituted derivatives has been accomplished by a number of methods. The parent compound was first obtained by Thiele (1) through the action of nitrous acid on aminoguanidine. The reaction involved the initial formation of guanyl azide which readily cyclized to form 5-aminotetrazole. Busch and Bauer (3) have applied an analogous reaction to N,N′-diaryl-N″-aminoguanidines and have reported the formation of 1-aryl-5-arylaminotetrazoles. Recently a similar sequence of reactions has been applied to N-nitro-N′-aminoguanidine for the preparation of 5-nitraminotetrazole (4).

The direct formation of 5-aminotetrazole by the addition of hydrazoic acid to cyanamide was observed by Hantzsch and Vagt (5). It was suggested that the reaction involved the formation of guanyl azide through addition of hydrazoic acid to the cyanide group followed by immediate cyclization of the intermediate. Stollé (6) has applied the same type of reaction to several phenylalkylcyanamides and has described the formation of the corresponding 5-aminotetrazoles in which the amino hydrogens were replaced by a phenyl and an alkyl group.

The formation of 5-substituted tetrazoles by addition of hydrazoic acid to the cyano group of nitriles has become recognized as a general procedure through the studies of Dimroth and Fester with hydrocyanic acid (7), Oliveri-Mandalà with cyanogen, cyanogen bromide, and ethyl cyanoformate (8), and Mihina and Herbst with an extensive group of alkyl and aryl cyanides (9). In an attempt to prepare 5-alkyltetrazoles from nitriles by interaction with hydrazoic acid in the presence of concentrated sulfuric acid von Braun and Keller (10) observed the

[1] Based on a thesis submitted to the School of Graduate Studies at Michigan State College in 1952 by William L. Garbrecht in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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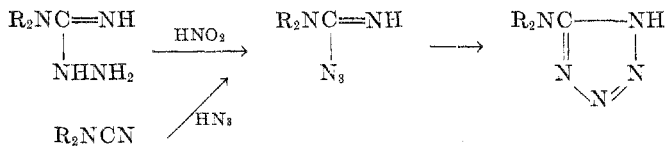
formation of 1-alkyl-5-aminotetrazoles. It has been suggested (11) that this reaction involves the intermediate formation of an imide azide which undergoes a Curtius type rearrangement to a carbodiimide derivative and that the latter adds a second molecule of hydrazoic acid to form a substituted guanyl azide which undergoes cyclization to the tetrazole.

Although the above reactions show that it is possible to arrive at the 5-aminotetrazole structure from several different starting points, it is interesting to observe that in each sequence of reactions a guanyl azide structure is proposed as the intermediate which undergoes cyclization to the tetrazole stage.

Of the several procedures available only two are suitable for the synthesis of 5-dialkylaminotetrazoles. Such compounds could conceivably be formed by action of nitrous acid on N,N-dialkyl-N′-aminoguanidines or by the addition of hydrazoic acid to dialkylcyanamides.



In view of the commercial availability of a number of dialkycyanamides the approach from this group of compounds was selected. Furthermore, the preparation of dialkylcyanamides in a single step from secondary amines by interaction with cyanogen bromide appeared to be much simpler than the preparation of the corresponding dialkylaminoguanidines.

The action of hydrazoic acid on the following dialkylcyanamides was studied: dimethyl-, diethyl-, diisopropyl-, di-*n*-butyl,- diisobutyl-, di-*n*-amyl-, diisoamyl-, dibenzyl-, benzylmethyl-, and benzylethyl-cyanamide; also included in this group were cyanomorpholine, cyanopyrrolidine, and cyanopiperidine. These materials were all known substances except di-*n*-amylcyanamide and cyanopyrrolidine and were prepared by the method of McKee (12) involving the action of potassium cyanide and bromine on an aqueous suspension of the appropriate secondary amine; or, preferably, by the direct addition of cyanogen bromide to solutions of the secondary amine in organic solvents.

$$2\ R_2NH + BrCN \rightarrow R_2NCN + R_2NH\cdot HBr$$

In Table I are summarized boiling point and refractive index data as well as literature references for the dialkylcyanamides. The secondary amines used in their preparation were all commercially available except benzylmethylamine and benzylethylamine. These were prepared by catalytic hydrogenation of the Schiff's bases resulting from the action of methylamine and ethylamine, respectively, on benzaldehyde (13).

The 5-dialkylaminotetrazoles were obtained in generally excellent yield by heating the appropriate cyanamide derivative with excess hydrazoic acid in either aqueous alcohol, benzene, xylene, or ethyl acetate solution for periods ranging from five to ninety hours. Since no effort was made to find optimum reaction conditions in each instance, the yields cited do not indicate maximum

possible yields and different yields obtained by changing solvent are not necessarily significant. The choice of solvent was dictated by the following considerations. In aqueous media, the cyanamide may undergo hydrolysis to a substituted urea and then to a secondary amine. This side reaction becomes more pronounced as the substituents become more bulky and hinder tetrazole formation. In the case of diisopropylcyanamide and, especially, diisoamylcyanamide non-aqueous media are indicated. Also, when the product is water-soluble, as is 5-(4-morpholinyl)tetrazole, the ease of isolation of the product is enhanced when the reaction is carried out in non-aqueous solution. In Table II are summarized the yields, reaction conditions, melting points, and analytical data for the 5-dialkylaminotetrazoles.

TABLE I

DIALKYLCYANAMIDES

COMPOUND	B.P., °C./MM.	n_D/°C.	REF.
Di-*n*-butylcyanamide[a]	147–151/35	1.4382/20	14
Diisobutylcyanamide[a]	123/25	1.4346/20	12
Di-*n*-amylcyanamide[a, b]	154–158/12	1.4422/20	—
Diisoamylcyanamide[c]	134/14	1.4405/20	12
Dibenzylcyanamide[c]	145–148/10 M.P. 54	—	15
Benzylmethylcyanamide[c]	139–142/12	1.5297/20	16
Benzylethylcyanamide[c]	160/12	1.5223/20	17
1-Cyanopiperidine[c]	102/11	1.4678/25	12
4-Cyanomorpholine[c]	117–119/15	1.4708/25	18
1-Cyanopyrrolidine[c, d]	107–110/17	1.4670/23	—

[a] Prepared by *Method A*. [b] *Anal.* Calc'd for $C_{11}H_{22}N_2$: N, 15.4. Found: N, 15.4. [c] Prepared by *Method B*. [d] *Anal.* Calc'd for $C_5H_8N_2$: C, 62.5; H, 8.4; N, 29.2. Found: C, 62.2, 62.1; H, 8.4, 8.2; N, 29.8, 29.9.

All of the 5-dialkylaminotetrazoles are acidic substances and dissolve readily in dilute, aqueous alkali. They are, in general, little soluble in cold water and readily soluble in ethanol. Their solubility in ether, while very limited with the lower members, becomes more pronounced as the size of the substituents increases. The basic function, while not comparable to the acidic function in strength, is sufficiently well expressed to lend acid solubility to most of the 5-dialkylaminotetrazoles studied; the exceptions are those with the largest substituents, *i.e.*, di-*n*-butyl-, di-*n*-amyl-, diisoamyl-, and dibenzyl-aminotetrazole.

All of the 5-dialkylaminotetrazoles form silver salts which are insoluble in water, alcohol, and cold dilute nitric acid. These salts do not appear to be light-sensitive or sensitive to shock, although they decompose with a flash when heated on a spatula. They may be decomposed by boiling in concentrated nitric acid and the silver content of the solution can subsequently be determined by the conventional Volhard technique. Silver salt formation by those tetrazoles which are not substituted on the ring nitrogens seems to be quite general (9) and could be adapted to a volumetric analytical scheme for these materials.

TABLE II

5-DIALKYLAMINOTETRAZOLES

5-SUBSTITUTED TETRAZOLES (Formula)	REACTION CONDITIONS[a]	YIELD, %	M.P., °C.[b]	CRYSTALLIZED FROM	ANALYSES		SILVER SALTS, ANALYSES		
					Calc'd	Found	Formula	Calc'd Ag	Found Ag
Dimethylamino ($C_3H_7N_5$)	A, 5.5	78	235–236	Water	N, 61.9	61.6	$C_3H_6AgN_5$	48.9	48.7
Diethylamino ($C_5H_{11}N_5$)	A, 6	43	124–125	Water	N, 49.6	49.2	$C_5H_{10}AgN_5$	43.4	43.1
Diisopropylamino ($C_7H_{15}N_5$)	A, 48 B, 64	47 77	184 dec.[c]	Ethyl acetate	C, 49.7 H, 8.9 N, 41.4	49.6 8.8 41.4	$C_7H_{14}AgN_5$	39.0	38.9
Diallylamino ($C_7H_{11}N_5$)	A, 17.5 B, 20	36 58	96–97	Ethylene dichloride	C, 50.9 H, 6.7 N, 42.4	50.9 6.7 42.3	$C_7H_{10}AgN_5$	39.6	39.4
Di-*n*-butylamino ($C_9H_{19}N_5$)	A, 15	85	132.5–133.5	Ethyl acetate	C, 54.8 H, 9.7 N, 35.5	54.6 10.2 35.4	$C_9H_{18}AgN_5$	35.4	35.6
Diisobutylamino ($C_9H_{19}N_5$)	A, 14	91	190–191	Aqueous ethanol	C, 54.8 H, 9.7 N, 35.5	54.5 10.1 35.5	$C_9H_{18}AgN_5$	35.4	35.8
Di-*n*-amylamino ($C_{11}H_{23}N_5$)	A, 24	87	91.5–92.5	Ethyl acetate	C, 58.6 H, 10.3 N, 31.1	58.7 10.4 31.0	$C_{11}H_{22}AgN_5$	32.4	32.1

Diisoamylamino ($C_{11}H_{23}N_5$)	C[d] D, 90	80 79	100–101	Diisopropyl ether	C, 58.6 H, 10.3 N, 31.1	58.4 10.6 31.2	$C_{11}H_{22}AgN_5$	32.4	32.1
Dibenzylamino ($C_{15}H_{15}N_5$)	A, 46	91	158–159	Ethyl acetate	C, 67.9 H, 5.7 N, 26.4	68.0 5.7 26.8	$C_{15}H_{14}AgN_5$	29.0	28.7
Benzylmethylamino[e] ($C_9H_{11}N_5$)	D, 22	89	135.5–136.5	Ethyl acetate	C, 57.1 H, 5.9 N, 37.0	56.9 5.9 37.1	$C_9H_{10}AgN_5$	36.4	36.2
Benzylethylamino[e] ($C_{10}H_{13}N_5$)	D, 57	88	134.5–135	Ethyl acetate	C, 59.1 H, 6.5 N, 34.5	58.9 6.6 34.7	$C_{10}H_{12}AgN_5$	34.8	34.4
1-Piperidyl ($C_6H_{11}N_5$)	A, 43 C, 25	79 85	199–199.5	Ethyl acetate	C, 47.0 H, 7.2 N, 45.7	46.7 7.0 45.9	$C_6H_{10}AgN_5$	41.4	41.2
4-Morpholinyl ($C_5H_9N_5O$)	C, 23	78	180.5–181	Ethyl acetate	C, 38.7 H, 5.8 N, 45.1	38.8 5.9 45.5	$C_5H_8AgN_5O$	41.1	40.7
1-Pyrrolidyl ($C_5H_9N_5$)	A, 26 C, 23	54 86	231 dec.	Absolute ethanol	C, 43.2 H, 6.5 N, 50.3	43.4 6.6 50.1	$C_5H_8AgN_5$	43.7	43.8

[a] Solvent is designated by capital letter: A, aqueous ethanol; B, ethyl acetate; C, benzene; D, xylene solutions of hydrazoic acid. The number indicates the hours of heating under reflux. [b] Melting points were taken in open capillaries and are corrected. [c] Exists also as a polymorphic modification, m.p. 162.5–163.5°. [d] Reaction carried out in a sealed tube at 100° for 55 hours. [e] Dr. R. A. Henry in a private communication has informed us of the preparation of these compounds from the appropriately substituted aminoguanidines.

Hydrochlorides may be prepared under anhydrous conditions but the resulting salts are of indefinite melting point. The potentiometric titration curves of these 5-dialkylaminotetrazole hydrochlorides, while clearly exhibiting two breaks corresponding roughly to the consumption of two equivalents of standard potassium hydroxide, were of little quantitative significance. A lack of good correspondence between the observed and calculated equivalence points reflected the difficulty in preparing pure hydrochlorides. The materials were either partially dissociated or, if crystallized in the presence of excess hydrogen chloride, they often contained occluded hydrogen chloride. The initial low *p*H of solutions of

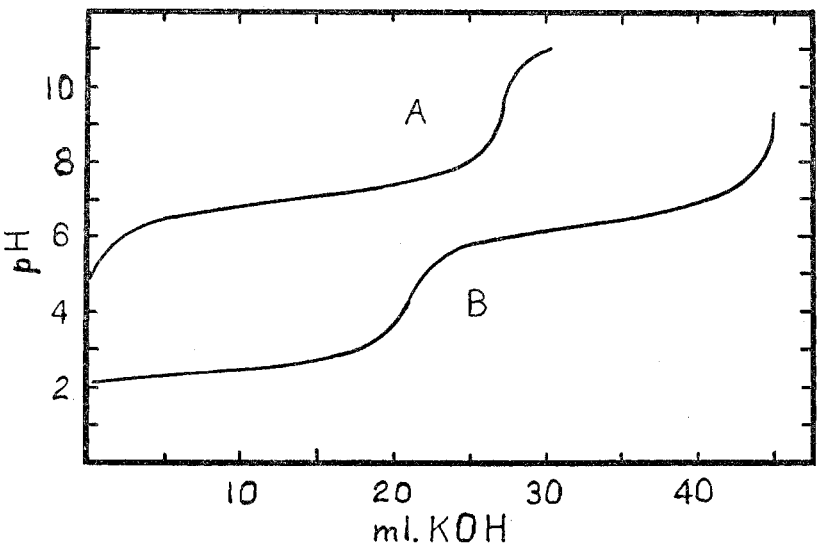


FIG. 1. TITRATION OF: A, 0.5590 g. of 5-di-*n*-butylaminotetrazole in 200 ml. of 50% methanol (by volume); B, 0.4272 g. of 5-diethylaminotetrazole hydrochloride in 200 ml. of water, both with 0.1043 *N* potassium hydroxide

the hydrochlorides indicated that they were largely dissociated in aqueous media. Potentiometric titration of the 5-dialkylaminotetrazoles with standard aqueous hydrochloric acid further substantiated this conclusion in that the *p*H observed was approximately that calculated for the corresponding hydrochloric acid concentration. The compounds were too weakly basic to permit determination of their basic dissociation constants by this technique.

Apparent acidic dissociation constants and equivalent weights of the 5-dialkylaminotetrazoles were determined potentiometrically in approximately 50 % aqueous methanol by volume of 25°. The titration curve for each compound was typical of that for a weak acid; no abnormalities were observed. The results are summarized in Table III. A representative titration curve is illustrated in Figure 1. A discussion of the acidic character of these materials and certain related compounds is deferred to a later paper.

Ultraviolet absorption spectra of 5-aminotetrazole and 5-dimethylamino-

tetrazole in aqueous solution were determined using a Beckman quartz spectrophotometer, Model DU. These compounds are essentially transparent throughout the range studied, 220–450 mμ., absorption beginning to occur near the lower limit of the instrument. The absorption data are represented graphically in Figure 2.

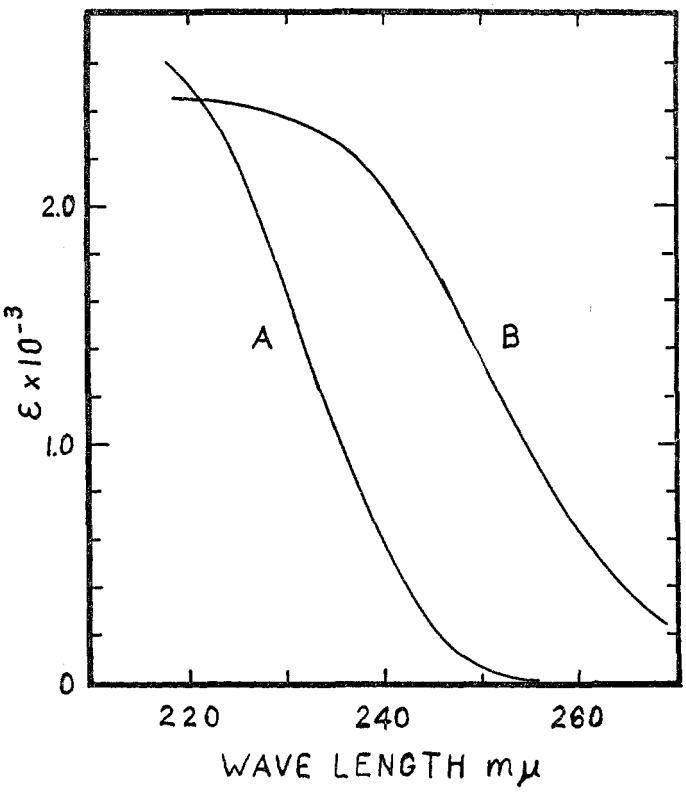


FIG. 2. ULTRAVIOLET ABSORPTION SPECTRA OF: A, 5-Aminotetrazole, 0.0186 g. per l.; B, 5-Dimethylaminotetrazole, 0.0072 g. per l., both in water

All the 5-dialkylaminotetrazoles described in the experimental part have been submitted to the Parke-Davis Laboratories for screening tests to ascertain whether they possess useful physiological and pharmacological properties.

EXPERIMENTAL[4, 5]

DIALKYLCYANAMIDES

Dimethyl-, diethyl, diallyl-, and diisopropyl-cyanamide were available through the courtesy of the American Cyanamide Company. The remainder of the dialkylcyanamides are listed in Table I and were prepared either by the method of McKee (12), *Method A*, or

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

[5] Melting points were taken in open capillaries unless otherwise noted and temperatures are corrected.

by the direct action of cyanogen bromide on the appropriate secondary amine, *Method B*. A typical example of each method is described.

Di-n-amylcyanamide (*Method A*). A mixture of 32 g. (0.2 mole) of di-*n*-amylamine, 59 g. (0.9 mole) of potassium cyanide, and 60 ml. of water was stirred vigorously and cooled while 12 ml. (0.45 mole) of bromine in 40 ml. of "Skellysolve B" was added dropwise. The addition required about an hour after which stirring and cooling in an ice-water bath were continued for an hour. The organic layer was separated, washed with dilute sodium hydroxide solution, then with water, and finally dried over sodium sulfate. After removal of the drying agent the solvent was evaporated and the dark red oily residue was distilled under reduced pressure. The product was obtained as a faintly yellow liquid, b.p. 154–158° at 12 mm., yield 31 g. (88%). A sample redistilled for analysis and refractive index determination was colorless.

1-Cyanopyrrolidine (*Method B*). An ethereal solution of 53 g. (0.5 mole) of cyanogen bromide was added dropwise to a stirred and cooled solution of 71 g. (1 mole) of pyrrolidine[6] over a period of two hours. After complete addition of the cyanogen bromide stirring was continued for several hours at room temperature. On removal of the solvent by evaporation a brown liquid remained from which the product was obtained as a faintly yellow oil by distillation under reduced pressure, b.p. 107–110° at 17 mm., yield 28 g. (58%). A sample redistilled for analysis and refractive index determination was colorless.

HYDRAZOIC ACID SOLUTIONS[7]

Aqueous and aqueous-alcoholic solutions of hydrazoic acid are easily prepared by addition of the calculated amount of hydrochloric acid to aqueous or aqueous-alcoholic solutions of sodium azide. Ethereal and ethyl acetate solutions of hydrazoic acid are best prepared by extraction of aqueous solutions of hydrazoic acid with the desired solvent.

Stock solutions of hydrazoic acid in benzene or xylene were prepared as follows: a sludge of 520 g. of sodium azide and 500 ml. of water is covered with 1500 ml. of benzene or xylene in a 5 l.-flask fitted with an efficient stirrer, a dropping-funnel with outlet below the liquid level, and a condenser. While cooling in an ice-water bath 250 ml. of concentrated sulfuric acid is added through the dropping-funnel during an hour and a half with vigorous stirring throughout. Stirring is continued for several hours after which the benzene layer is decanted into a tightly stoppered bottle containing sodium sulfate.

The concentration of the solutions of hydrazoic acid in organic solvents may be determined by titration of an aliquot with standard aqueous alkali using phenolphthalein as the indicator. The above procedure gives solutions in benzene or xylene of initial concentrations of 15–17 g. of hydrazoic acid per 100 ml. of solution.

5-DIALKYLAMINOTETRAZOLES

The 5-dialkylaminotetrazoles were prepared by heating the appropriate cyanamide under reflux in a solvent containing hydrazoic acid. Usually an excess of hydrazoic acid was used to provide for an appreciable loss through the condenser. The solvents used were aqueous ethanol, ethyl acetate, benzene, and xylene. In most instances the tetrazole could be obtained as a nearly pure crystalline solid by concentrating and chilling the reaction mixtures. Several typical examples are described in the following paragraphs. Reaction conditions and analytical data for all preparations are summarized in Table II.

5-Di-n-butylaminotetrazole. To a solution of 39 g. (0.25 mole) of di-*n*-butylcyanamide in 200 ml. of 95% ethanol was added an aqueous hydrazoic acid solution prepared by adding 40 ml. of concentrated hydrochloric acid to an ice-cold solution of 33 g. (0.5 mole) of sodium azide in 100 ml. of water. The reaction mixture was heated under reflux for 15 hours and then concentrated until turbid. Chilling precipitated 42 g. (85%) of fine, colorless needles which were recrystallized from ethyl acetate, yield 41 g., m.p. 132.5–133.5°.

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[6] Pyrrolidine was available through the courtesy of the Electrochemicals Division of E. I. DuPont de Nemours and Company.

[7] All operations involving hydrazoic acid should be carried out in a good hood.

5-Benzylmethylaminotetrazole. A solution of 80 g. (0.55 mole) of benzylmethylcyanamide in 200 ml. of xylene containing 32 g. of hydrazoic acid was heated under reflux for five hours. After addition of another 100 ml. of the xylene solution of hydrazoic acid heating was continued for 18 hours. Chilling precipitated a nearly colorless solid, yield 92 g. (89%), m.p. 134–136°. Recrystallization from ethylene dichloride gave fine, colorless needles, m.p. 135.5–136.5°.

5-Diisoamylaminotetrazole. A solution containing 10 g. (0.06 mole) of diisoamylcyanamide in 35 ml. of xylene containing 4.5 g. of hydrazoic acid was heated under reflux for 22 hours when another 35 ml. of the xylene-hydrazoic acid solution was added and heating was continued for 67 hours. Removal of the solvent under reduced pressure left a brown oil which, when treated with dilute aqueous potassium hydroxide, separated into three layers. The intermediate layer was separated and neutralized by the careful addition of hydrochloric acid. The sticky solid that separated was crystallized from diisopropyl ether, yield 9.8 g. of fine, colorless needles, m.p. 100–101°.

5-Diisopropylaminotetrazole. A solution containing 6.3 g. (0.05 mole) of diisopropylcyanamide, 4.2 g. (0.1 mole) of hydrazoic acid, 100 ml. of ethanol, and 50 ml. of water was heated under reflux for 65 hours. Most of the ethanol was removed by distillation and the residual solution was made alkaline with 10% potassium hydroxide. Unreacted cyanamide and amine were extracted with ether. On acidification of the alkaline solution a glistening, colorless solid precipitated, yield 3.3 g. (39%), m.p. 184° with decomposition. The tetrazole crystallized from ethyl acetate as fine, colorless needles with no change in melting point.

A subsequent repetition of the preparation gave a product, m.p. 162.5–163.5°. The low-melting form was gradually converted into the high-melting form on standing in a stoppered bottle for several months. Furthermore, solutions of the high-melting form in ethyl acetate deposited the high-melting form spontaneously but when seeded with the low-melting form that form deposited.

5-DIALKYLAMINOTETRAZOLE HYDROCHLORIDES

The hydrochlorides of the 5-dialkylaminotetrazoles were obtained by treating solutions of the tetrazoles in anhydrous ether or ethanolic ether with dry hydrogen chloride. The colorless, crystalline solids thus obtained were of indefinite melting point and were readily hydrolyzed in aqueous solution. Representative hydrochlorides are:

5-Di-n-butylaminotetrazole hydrochloride, colorless plates, decomposes in a sealed capillary at 183° after prior softening.

Anal. Calc'd for $C_9H_{12}ClN_5$: N, 30.0. Found: N, 30.3, 30.5.

5-Benzylmethylaminotetrazole hydrochloride, colorless needles, decomposes in a sealed capillary at 179° after prior softening.

Anal. Calc'd for $C_9H_{20}ClN_5$: N, 31.0. Found: N, 31.6, 31.5.

SILVER SALTS OF 5-DIALKYLAMINOTETRAZOLES

Small quantities (0.2–0.5 g.) of the tetrazoles dissolved in 10 ml. of ethanol were treated with a slight excess of aqueous silver nitrate solution. The white precipitate of silver salt was digested on the steam-bath for 15 minutes, filtered hot, washed with ethanol, and finally dried for several hours at 70°. Silver analyses were done by boiling weighed samples of the silver salts in about 30 ml. of concentrated nitric acid for half an hour, cooling, diluting with 15 ml. of water and titrating the silver ion with standard potassium thiocyanate solution using ferric alum indicator (20). The results are recorded in Table II.

The silver salts were insoluble in water, ethanol, and cold dilute nitric acid. They could not be detonated by sharp blows with a hammer on an anvil nor was any decomposition evident after several months exposure to daylight. On heating over a flame on a spatula all of them eventually decomposed with a flash.

POTENTIOMETRIC TITRATION OF 5-DIALKYLAMINOTETRAZOLES

The apparent acidic dissociation constants and equivalent weights of the 5-dialkylaminotetrazoles were determined by titration of weighed samples of the compounds in

approximately 0.01 *molar* aqueous or aqueous methanolic solution with 0.1043 *N* potassium hydroxide solution. The weighed samples were transferred to a 250 ml. volumetric flask and made up to volume with either water or methanol. Aliquots (100 ml.) diluted with 100 ml. of water were titrated in a thermostat at 25°. The *p*H was determined after each addition of alkali with a Beckman *p*H Meter, Model G. From these data the region of half neutralization was plotted on a large scale and the best straight line was drawn. The *p*H at half neutralization was taken from the plot and from it the apparent dissociation constant was calculated (21). The titration curves exhibited the normal form for a weak acid in each case. The data are summarized in Table III.

TABLE III

APPARENT ACIDIC DISSOCIATION CONSTANTS AND EQUIVALENT WEIGHTS OF SOME 5-DIALKYLAMINOTETRAZOLES IN APPROXIMATELY 50% AQUEOUS METHANOL BY VOLUME

5-SUBSTITUTED TETRAZOLE	APPARENT pK_a	APPARENT $K_a \times 10^8$	EQUIVALENT WEIGHT	
			Calc'd	Found
Amino	6.44	36	85	85
	(5.93)[a]	(120)[a, b]		(85)[a]
Dimethylamino	6.42	38	113	113
	(5.92)[a]	(120)[a]		(113)[a]
Diethylamino	6.96	11	141	140
	(6.33)[a]	(47)[a]		(142)[a]
Dibenzylamino	6.45	36	265	264
Benzylmethylamino	6.42	38	189	189
Benzylethylamino	6.61	25	203	203
Diallylamino	6.48	33	165	165
Diisopropylamino	7.24	5.8	169	168
Di-*n*-butylamino	7.00	10	197	196
Diisobutylamino	7.14	7.2	197	196
Di-*n*-amylamino	7.09	8.1	225	224
Diisoamylamino	7.16	6.9	225	222
4-Morpholinyl	5.80	160	155	154
1-Pyrrolidyl	6.88	13	139	138
1-Piperidyl	6.32	48	153	151

[a] Determination done in water.

[b] From conductimetric data the value 6.8×10^{-7} has been reported for K_a (19).

Potentiometric titrations of the 5-dialkylaminotetrazoles with standard hydrochloric acid solution were done in an analogous manner. The titration of several 5-dialkylaminotetrazole hydrochlorides with standard potassium hydroxide was similarly done. Because of the difficulty in obtaining hydrochlorides of reliable purity, these data were of little quantitative significance.

Typical potentiometric titration curves are illustrated in Figure 1.

ULTRAVIOLET ABSORPTION SPECTRA

The ultraviolet absorption spectra of 5-aminotetrazole (0.0186 g. per l.) and 5-dimethylaminotetrazole (0.0072 g. per l.) were examined in aqueous solution using a Beckman quartz spectrophotometer, Model DU, and a 10-mm. quartz cell. In the range examined, 220–450 mμ, both compounds were essentially transparent; absorption began near the lower limit of the instrument. The curves obtained are shown in Figure 2.

Similar results were obtained in this laboratory by Dr. J. S. Mihina who examine the absorption spectra of tetrazole, 5-methyltetrazole, 5-aminotetrazole, and 1-ethyl-5-aminotetrazole in aqueous solution and in the presence of equivalent amounts of hydrochloric acid or sodium hydroxide. The solutions were transparent throughout the range of the instrument except at the lowest range indicating that some resolution of the curve could be anticipated in the far ultraviolet.

SUMMARY

The interaction of dialkylcyanamides and hydrazoic acid in both polar and non-polar solvents has been shown to lead to 5-dialkylaminotetrazoles. This constitutes an excellent and simple method for the preparation of this group of compounds.

A group of fourteen new 5-dialkylaminotetrazoles has been prepared and characterized. The silver salts of all the compounds have been prepared and in several instances the hydrochlorides have been described.

Apparent acidic dissociation constants have been determined for all the 5-dialkylaminotetrazoles in 50% methanol solution and in several instances in aqueous solution.

The ultraviolet absorption spectra of 5-aminotetrazole, 5-dimethylaminotetrazole, and several related compounds have been described.

EAST LANSING, MICHIGAN

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