g. of 1-(β-aminoethyl)benzimidazole dihydrochloride, m.p. 271–277° dec.[9]

In a similar manner the β-aminoalkylbenzimidazoles in Table II were prepared. One was isolated as the free base, the others as the dihydrochlorides. Even after several recrystallizations, these salts decomposed over a rather wide range at the melting point. In order to obtain material for preliminary pharmacological testing, the mixtures of isomeric 5- and 6-substituted amides (Table I, R″ ≠ H) were treated as above with hypobromite. No attempt other than ordinary recrystallization was made to separate the mixtures of products.

Acknowledgment. The authors wish to acknowledge the continued interest of Dr. Lee C. Cheney throughout this work. Microanalyses were performed by Richard M. Downing.

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(9) This compound has also been prepared by a different synthesis, starting with *N*-(2-phthalimidoethyl)-*o*-phenylenediamine [P. Mamalis, V. Petrow, and B. Sturgeon, *J. Chem. Soc.*, 1600 (1950).

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

Alkylated 5-Aminotetrazoles, Their Preparation and Properties[1]

DOUGLAS F. PERCIVAL[2] AND ROBERT M. HERBST

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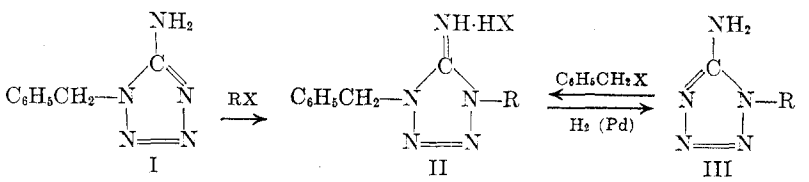
A group of 1,4-benzylalkyl-5-iminotetrazolines was prepared both by alkylation of 1-benzyl-5-aminotetrazole and by benzylation of 1-alkyl-5-aminotetrazoles. In each instance both processes gave identical pairs of compounds. Furthermore, catalytic hydrogenolysis removed the benzyl group from both products and in each case a 1-alkyl-5-aminotetrazole was recovered. These observations confirm the conclusion that the alkylation of 1-alkyl-5-aminotetrazoles takes place in the 4-position. A group of 1,4-dialkyl-5-iminotetrazolines in which both alkyl groups were the same was prepared by similar procedures. A comparable group of 1-alkyl-5-alkylaminotetrazoles was prepared both by addition of hydrazoic acid to the appropriate carbodiimides and from suitable aminoguanidines. The marked differences between comparably substituted 1,4-dialkyl-5-iminotetrazolines and 1-alkyl-5-alkylaminotetrazoles further substantiates the conclusion that alkylation of 1-alkyl-5-aminotetrazoles leads primarily to the 1,4-dialkyl-5-iminotetrazolines with the alkylating agents and conditions employed. An attempt has been made to correlate the physical and chemical properties of the alkylated 5-aminotetrazoles with the tautomeric and resonance possibilities inherent in the several groups.

Many years ago Thiele and Ingle[3] showed that benzylation of 5-aminotetrazole led to several mono- and dibenzylated products whose structures were not established at that time. More recently the alkylation of a number of 1-alkyl-5-aminotetrazoles was studied[4] and it was noted that the introduction of a second alkyl group caused marked changes in the physical and chemical properties of the compounds. Although structures were assigned to the dialkylated aminotetrazoles, it was recognized that further work was required to establish the true structure of these compounds. Subsequently, based on a comparison of the physical properties of several dialkylated aminotetrazoles and their derivatives in which the same pair of alkyl groups had been introduced in different order, it was suggested that the compounds were actually 1,4-dialkyl-5-iminotetrazolines.[5] This conclusion was supported by the ethylation of 1-benzyl-5-aminotetrazole (I) with ethyl sulfate followed by removal of the benzyl group by hydrogenolysis and isolation of 1-ethyl-5-aminotetrazole (III, R = ethyl).[5] A similar conclusion was reached by Henry *et al.*, as the result of methylation of I and isolation of 1-methyl-5-aminotetrazole (III, R = methyl) after hydrogenolytic removal of the benzyl group.[6] In both cases the conclusions were further supported by the fact that the benzylethyl(or methyl-)iminotetrazolines (II, R = ethyl or methyl, were identical whether prepared by ethylation (or methylation) of I or by benzylation of III (R = ethyl or methyl).



In this report further studies of the alkylation of 1-substituted 5-aminotetrazoles with a variety of alkylating agents are described from which it may

(1) Based on a thesis submitted to the School for Advanced Graduate Studies at Michigan State University in 1955 by Douglas F. Percival in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Present address: California Research Corp., Richmond, Calif.

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

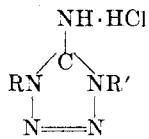
(4) R. M. Herbst, C. W. Roberts, and E. J. Harvill, *J. Org. Chem.*, **16**, 139 (1951).

(5) R. M. Herbst and D. F. Percival, *J. Org. Chem.*, **19**, 439 (1954).

(6) R. A. Henry, W. G. Finnegan, and E. Lieber, *J. Am. Chem. Soc.*, **76**, 2894 (1954).

TABLE I

1,4-DIALKYL-5-IMINOTETRAZOLINE HYDROCHLORIDES



R	R′[a]	Yield %	M.P.° C.[b]	Formula	Analyses Calculated C	H	N	Found C	H	N
Methyl	Benzyl[c]	47	216	$C_9H_{12}ClN_5$	47.9	5.4	31.0	48.1	5.5	30.4
Benzyl	Methyl	50	216	$C_9H_{12}ClN_5$	47.9	5.4	31.0	48.2	5.5	30.9
Ethyl	Benzyl[c]	55	225	$C_{10}H_{14}ClN_5$	50.1	5.9	29.2			29.2
Benzyl	Ethyl	49	224	$C_{10}H_{14}ClN_5$	50.1	5.9	29.2			29.2
n-Propyl	Benzyl	74	199	$C_{11}H_{16}ClN_5$	52.1	6.3	27.6	52.2	6.1	27.5
Benzyl	*n*-Propyl	58	198	$C_{11}H_{16}ClN_5$	52.1	6.3	27.6	52.0	6.7	27.5
n-Butyl	Benzyl	79	196	$C_{12}H_{18}ClN_5$	53.8	6.8	26.2	53.8	6.9	26.0
Benzyl	*n*-Butyl	62	195	$C_{12}H_{18}ClN_5$	53.8	6.8	26.2	54.3	6.7	26.0
β-Phenylethyl	Benzyl	80	221	$C_{16}H_{18}ClN_5$	60.9	5.7	22.2	61.0	6.0	22.0
Benzyl	β-Phenylethyl	49	220	$C_{16}H_{18}ClN_5$	60.9	5.7	22.2	60.7	5.6	22.5
Methyl	Methyl[d]	56	241	$C_3H_8ClN_5$	24.1	5.4	46.8	24.0	5.5	47.1
Ethyl	Ethyl[d]	45	228	$C_5H_{12}ClN_5$	33.8	6.8	39.4	34.0	6.9	39.1
n-Propyl	*n*-Propyl	54	193	$C_7H_{16}ClN_5$	40.9	7.8	34.0	41.0	8.0	33.6
n-Butyl	*n*-Butyl	46	203	$C_9H_{20}ClN_5$	46.2	8.6	30.0	46.2	8.5	29.9
Benzyl	Benzyl[d]	65	214	$C_{15}H_{16}ClN_5$	59.7	5.3	23.2	59.9	5.5	23.1

[a] R′ is the group introduced by alkylation. [b] All compounds melted with decomposition; mixtures of the respective pairs showed no depression of the melting points. [c] Ref. 4. [d] Ref. 3.

be concluded that the nature of the alkylated products is not greatly influenced by the character of the alkylating agents. For this purpose I was alkylated with alkyl sulfates, alkyl benzene- and toluenesulfonates, and a number of alkyl halides. Furthermore, the corresponding 1-alkyl-5-aminotetrazoles (III) were prepared from alkylcyanamides[7] and benzylated with benzyl chloride. In each instance identical 1,4-benzylalkyl-5-iminotetrazolines (II) were formed by both routes as evidenced by comparison of the melting points and mixture melting points of their hydrochlorides, phenylthioureas, and benzenesulfonyl derivatives (Tables I and III) and infrared absorption spectra of their hydrochlorides. Identity of the products was also substantiated by removal of the benzyl group by hydrogenolysis and isolation of the anticipated 1-alkyl-5-aminotetrazole (III).

In addition, a series of 1,4-dialkyl-5-iminotetrazolines with identical alkyl groups in both positions was prepared by interaction of the 1-alkyl-5-aminotetrazoles with similar alkyl benzene- or toluenesulfonates. The properties of the 1,4-dialkyl-5-iminotetrazolines obtained in this way were similar to those of the benzyl alkyl compounds. They were characterized as hydrochlorides, phenylthioureas, and benzenesulfonyl derivatives (Tables I and III). As a result it is now possible to identify the dimethyl, diethyl, and *alpha* dibenzyl 5-aminotetrazoles of Thiele and Ingle[3] as the 1,4-dialkyl-5-iminotetrazolines. Furthermore, all of the compounds described by Herbst, Harvill, and Roberts[4] as 1-alkyl-5-alkylaminotetrazoles should be formulated as 1,4-dialkyl-5-iminotetrazolines.

For comparative purposes a group of 1-alkyl-5-alkylaminotetrazoles (VI) with identical alkyl substituents in both positions was prepared (Table II). Two procedures were used for the synthesis of these compounds. Symmetrically substituted dialkylthioureas (IV) were converted into dialkylcarbodiimides (V) by treatment with mercuric oxide,[8] followed by interaction of the carbodiimides with hydrazoic acid in benzene or xylene solution to form the tetrazoles (VI). Although it is likely that the procedures developed by Stollé[9] for the preparation of 1-aryl-5-arylaminotetrazoles from symmetrical diarylthioureas by interaction with sodium azide in the presence of lead carbonate or oxide involve the transitory formation of diarylcarbodiimides, we have found no record of the synthesis of tetrazoles from previously formed carbodiimides. To support the identity of the products formed in this reaction sequence the same group of 1-alkyl-5-alkylaminotetrazoles was prepared from appropriately substituted aminoguanidines (VIII) by the procedure developed by Finnegan *et al.*[10] The compounds prepared by both procedures were identical in every respect (Table II) and differed markedly from the correspondingly substituted 1,4-dialkyl-5-iminotetrazolines. The

(7) W. L. Garbrecht and R. M. Herbst, *J. Org. Chem.*, **18**, 1014 (1953).

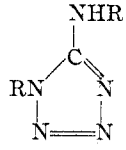
(8) E. Schmidt, F. Hitzler, and E. Lahde, *Ber.*, **71**, 1933 (1938). E. Schmidt and W. Striewsky, *Ber.*, **73**, 286 (1940); *Ber.*, **74**, 1285 (1941).

(9) R. Stollé, *Ber.*, **55**, 1289 (1922); *Ber.*, **62**, 1118 (1929); *J. prakt. Chem.*, **134**, 282 (1932).

(10) W. G. Finnegan, R. A. Henry, and E. Lieber, *J. Org. Chem.*, **18**, 779 (1953).

TABLE II

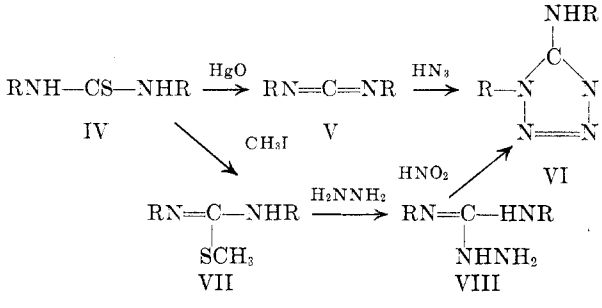
1-ALKYL-5-ALKYLAMINOTETRAZOLES



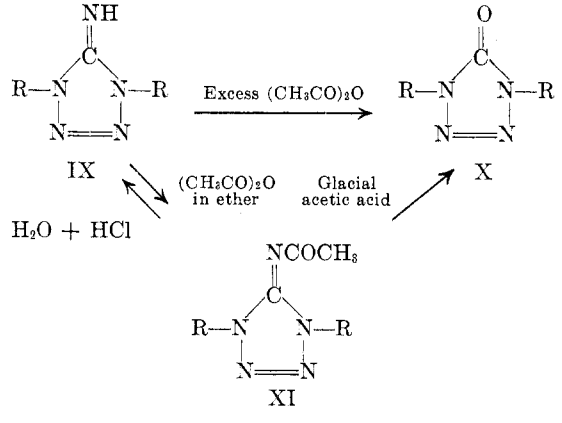
R	M.P., °C.[a]	Method	Yield, %[b]	Formula	Analyses Calculated C	H	N	Found C	H	N
Methyl	171–172	A-1	32	$C_3H_7N_5$	31.9	6.2	61.9	32.0	6.3	62.2
Ethyl[c]	92–93	A-1	57	$C_5H_{11}N_5$	42.5	7.9	49.6	42.9	7.8	49.1
	92–93	B	59							
n-Propyl	70–71	A-1	69	$C_7H_{15}N_5$	49.7	8.9	41.4	50.1	9.1	41.0
	71–72	B	50							
Isopropyl	160–161	A-2	78	$C_7H_{15}N_5$	49.7	8.9	41.4	49.5	8.9	41.5
	160–161	B	62					49.8	8.7	41.3
n-Butyl	73–74	A-1	61	$C_9H_{19}N_5$	54.8	9.7	35.5	54.9	9.6	35.1
	72–73	A-2	73							
	73–74	B	48							
Benzyl[d]	167–168	A-1	50	$C_{15}H_{15}N_5$	67.9	5.7	26.4	68.1	5.9	26.3
	167–168	A-2	68							

[a] Mixture melting points of products made by different methods showed no depression. [b] Yields are based on amount of thiourea employed in methods A-1 and A-2, or aminoguanidine hydriodide in method B. [c] Ref. 10. [d] Ref. 3.

beta dibenzyl 5-aminotetrazole of Thiele and Ingle[3] is identical with VI (R = benzyl) prepared by either of these methods.



During attempts to prepare an acetyl derivative of 1,4-dibenzyl-5-iminotetrazoline (IX, R = benzyl) by treatment with excess hot acetic anhydride, a compound was obtained in which the imino group had apparently been replaced by oxygen, possibly by acetolysis. The product, 1,4-dibenzyl-4-ketotetrazoline (X, R = benzyl), was identical with the material obtained according to Thiele and Ingle[3] from the nitroso derivative of IX (R = benzyl) upon warming with glacial acetic acid. It is interesting to note that Thiele's nitroso derivative can be hydrolyzed to the iminotetrazoline (IX) with hot, dilute hydrochloric acid. In order to determine whether these reactions involved acetolysis, IX (R = benzyl) was acetylated with acetic anhydride in ether solution. Under these conditions the hydrate of an acetyl derivative, XI (R = benzyl) was obtained which on hydrogenolysis over palladium oxide gave 5-acetylaminotetrazole. Whether the water was chemically bound by addition to the C=N linkage, or whether by complex formation has not been determined. However, heating the acetyl derivative with glacial acetic acid caused conversion to X (R = benzyl), while heating with dilute hydrochloric acid led back to IX (R = benzyl).



In extending these observations to other iminotetrazolines it was found that 1,4-diethyl-5-iminotetrazoline (IX, R = ethyl) on heating with excess acetic anhydride gave a mixture of the acetyl derivative, XI (R = ethyl), and the ketotetrazoline, X (R = ethyl). The acetyl derivative, which was not hydrated, gave X (R = ethyl) and acetamide on boiling with glacial acetic acid, and was hydrolyzed to IX (R = ethyl) with boiling, dilute hydrochloric acid. The acetolysis apparently requires the intermediate formation of the acetyl derivatives of the 1,4-dialkyl-5-iminotetrazolines; IX (R = benzyl) was recovered unchanged after boiling with glacial acetic acid for 0.5 hr. and the hydrochloride of IX (R = benzyl) showed no change upon boiling with either glacial acetic acid or acetic anhydride. Attempts to acetolyze the benzoyl or benzenesulfonyl derivatives of IX (R = benzyl)

with acetic acid or anhydride were unsuccessful, although the former could be hydrolyzed easily with boiling hydrochloric acid. 5-Acetylaminotetrazole, although it can be hydrolyzed easily with concentrated hydrochloric acid, was recovered unchanged after boiling for several hours with glacial acetic acid. Similarly, the acetyl derivatives of 1-alkyl- and 1-aryl-5-aminotetrazoles are easily hydrolyzed with hydrochloric acid but stable toward glacial acetic acid.[11] Apparently the 1,4-dialkyl-5-iminotetrazoline structure, IX, is essential and acetolysis under the conditions studied is limited to the acetyl and nitroso derivatives of IX.

The marked increase in basicity of the 1,4-dialkyl-5-iminotetrazolines as compared with the 1-alkyl-5-aminotetrazoles is striking. Although the 1-alkyl-5-alkylaminotetrazoles also exhibit distinctly basic character, the increase does not seem to be as marked. It has long been recognized that the 1-alkyl-5-aminotetrazoles do not exhibit the characteristics usually associated with primary amines; even those of low molecular weight have rather high melting points and their basic properties are apparent only under anhydrous conditions in the presence of strong proton donors, as recently confirmed by titrations with perchloric acid in glacial acetic acid.[12a] Murphy and Picard[12b] have suggested, on the basis of spectrographic studies, that the 1-alkyl-5-aminotetrazoles have polymolecular structures involving intermolecular hydrogen bonding. We would suggest that a resonance hybrid derived from a series of dipolar contributing forms could explain not only the high melting points but the lack of basic character as well. In such structures (Figure 1*a*), the immonium ion state would deprive the amino group of its ability to donate a pair of electrons to the reagents with which it usually reacts. The dipolar character of the resonance hybrid could also account for the preferential alkylation in the 4 position.

The marked increase in basic properties of the 1,4-dialkyl-5-iminotetrazolines appears to be associated with the change from tetrazole to tetrazoline ring system where formation of dipolar structures of the type postulated in Figure 1 is unlikely. Furthermore, the 5-iminotetrazolines present structural features closely analogous to the guanidine structure which may account for their

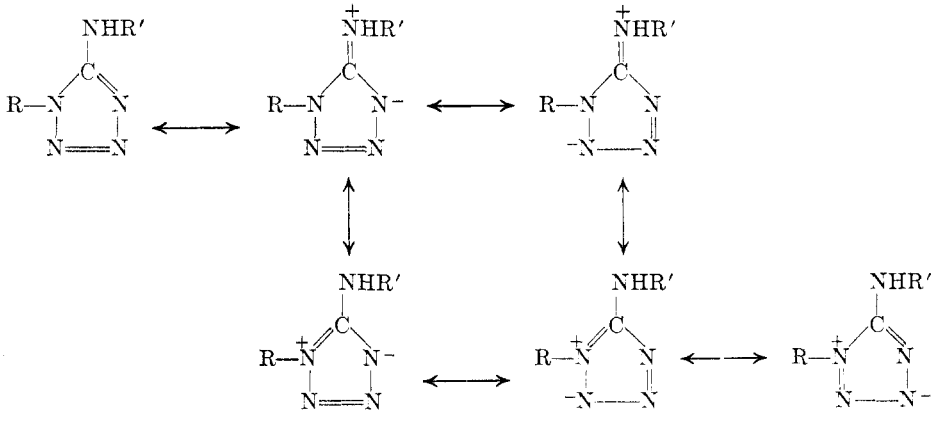


FIG. 1. (a), R = ALKYL, R′ = H; (b), R, R′ = ALKYL

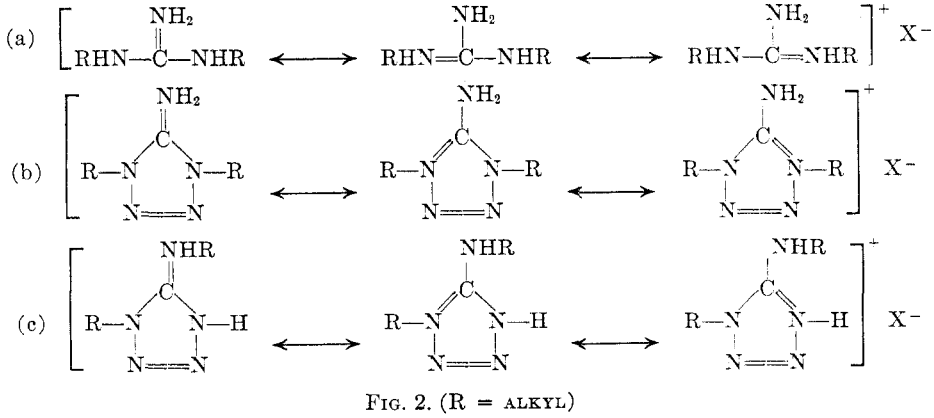


FIG. 2. (R = ALKYL)

physical and chemical characteristics. Thus, the imino group retains its ability to donate a pair of electrons so that stable salts can be formed with acids in which the cation (Fig. 2b) is stabilized by resonance of the guanidinium ion type (Fig. 2a).

(11) R. M. Herbst and W. L. Garbrecht, *J. Org. Chem.*, 18, 1283 (1953).

(12) (*a*) P. Rochlin, D. B. Murphy, and S. Helf, *J. Am. Chem. Soc.*, 76, 1451 (1954). (*b*) D. B. Murphy and J. P. Picard, *J. Org. Chem.*, 19, 1807 (1954).

The 1-alkyl-5-alkylaminotetrazoles are generally solids with melting points intermediate between those of the isomeric 1,4-dialkyl-5-iminotetrazolines (usually liquids) and the related 1-alkyl-5-aminotetrazoles. The solid character of the 1-alkyl-5-alkylaminotetrazoles may also be attributed to the possibility of a resonance hybrid involving dipolar contributing forms (Fig. 1b) while their basicity could derive from guanidinium type resonance of the cation formed by reaction with acids (Fig. 2c). Since ring substitution in the 1,4- positions produces a somewhat greater degree of symmetry in the structure than alkylation of the amino group, it should not be surprising to find appreciable differences in the basicity of the two isomeric dialkylated 5-aminotetrazoles.

Infrared spectra of a series of 1-alkyl-5-aminotetrazoles, 5-alkylaminotetrazoles, 5-dialkylaminotetrazoles, 1,4-dialkyl-5-iminotetrazoline hydrochlorides, and 1-alkyl-5-alkylaminotetrazoles and their hydrochlorides have been recorded.[13]

EXPERIMENTAL[14]

1-Alkyl-5-aminotetrazoles. 1-Methyl-,[4] 1-ethyl-,[7] 1-*n*-propyl-,[4] 1-isopropyl-,[4] 1-*n*-butyl-,[4] 1-benzyl-,[7] and 1-*β*-phenylethyl-5-aminotetrazole[4] were prepared by a slight modification of the method of Garbrecht and Herbst.[7]

1,4-Dialkyl-5-iminotetrazolines. These compounds were prepared by heating a mixture of the 1-alkyl-5-aminotetrazole and the alkylating agent without diluent in an oil bath until an exothermic reaction was initiated.[4] The temperature of the oil bath was kept constant for 0.5–1.0 hr. after cessation of the exothermic reaction. The products remained as thick viscous masses in the case of the benzene- or toluenesulfonates, and solidified during the reaction period or on cooling in the case of the hydrochlorides. The alkylating agents employed were either alkyl halides, alkyl sulfates, alkyl benzene- or toluenesulfonates. The 1,4-dialkyl-5-iminotetrazolines were isolated as hydrochlorides (Table I) and characterized as phenylthioureas and as benzenesulfonyl derivatives (Table III). Several typical preparations are described.

1-Benzyl-4-n-propyl-5-iminotetrazoline hydrochloride. Method A, from 1-n-propyl-5-aminotetrazole. A mixture of 25.4 g. (0.2 mole) of 1-*n*-propyl-5-aminotetrazole and 25.4 g. (0.2 mole) of benzyl chloride was heated in an oil bath. At a bath temperature of 135° a homogeneous melt formed, followed by an exothermic reaction and resolidification of the mixture. Heating was continued at 145° for 0.5 hr. The product was crystallized first from 95%, then from 90% isopropyl alcohol; colorless lustrous needles, m.p. 199–200° with decomposition, yield 37.6 g.

Method B, from 1-benzyl-5-aminotetrazole. A mixture of 8.75 g. (0.05 mole) of 1-benzyl-5-aminotetrazole and 10.8 g. (0.05 mole) of *n*-propyl *p*-toluenesulfonate was heated to 160–165° in an oil bath. A homogeneous melt formed and the bath was maintained at this temperature 0.5 hr. After cooling, the reaction mixture was dissolved in 20 ml. of isopropyl alcohol and treated with 20 ml. of 5*N* sodium hydroxide. The organic base was extracted with ether, the ethereal solution was dried over sodium carbonate, and then treated with 10 ml. of concentrated hydrochloric acid to pre-

TABLE III

1,4-DIALKYL-5-IMINOTETRAZOLINE DERIVATIVES

R	R′[a]	Phenylthioureas						Benzenesulfonyl Derivatives					
		M.P., °C.	Formula	Analyses				M.P., °C.	Formula	Analyses			
				Calcd.		Found				Calcd.		Found	
				N	S	N	S			N	S	N	S
Methyl	Benzyl	124–125	$C_{16}H_{16}N_6S$	25.9		26.1		82–84	$C_{15}H_{15}N_5O_2S$	21.3		21.2	
Benzyl	Methyl	123–124	$C_{16}H_{16}N_6S$	25.9		25.8		82–84	$C_{15}H_{15}N_5O_2S$	21.3		20.7	
Ethyl	Benzyl	117–118	Ref. 4										
Benzyl	Ethyl	117–118	Ref. 4										
n-Propyl	Benzyl	134–135	$C_{18}H_{20}N_6S$	23.9		24.0		80–82[b]	$C_{18}H_{21}N_5O_2S$	18.9		18.9	
Benzyl	*n*-Propyl	134–135	$C_{18}H_{20}N_6S$	23.9		23.8		80–81[b]	$C_{18}H_{21}N_5O_2S$	18.9		18.9	
n-Butyl	Benzyl	114–115	$C_{19}H_{22}N_6S$	22.9		23.0		67–68	$C_{18}H_{21}N_5O_2S$	18.9		18.8	
Benzyl	*n*-Butyl	113–114	$C_{19}H_{22}N_6S$	22.9		22.7		67–68	$C_{18}H_{21}N_5O_2S$	18.9		18.8	
β-Phenylethyl	Benzyl	125–126	$C_{23}H_{22}N_6S$	20.3		20.5		98–99	$C_{22}H_{21}N_5O_2S$	16.7		16.9	
Benzyl	*β*-Phenylethyl	123–124	$C_{23}H_{22}N_6S$	20.3		20.7		97–98	$C_{22}H_{21}N_5O_2S$	16.7		16.9	
Methyl	Methyl	210–211	$C_{10}H_{12}N_6S$	33.8	12.9	33.7	13.3	125–126	$C_9H_{11}N_5O_2S$	27.7	12.9	27.7	13.2
Ethyl	Ethyl	108–109	$C_{12}H_{16}N_6S$	30.4	11.6	30.6	11.8	67–68	$C_{11}H_{15}N_5O_2S$	24.9	11.4	24.4	11.4
n-Propyl	*n*-Propyl	95–96	$C_{14}H_{20}N_6S$	27.6	10.5	27.1	10.6	46–47	$C_{13}H_{19}N_5O_2S$	22.6	10.5	22.7	10.5
n-Butyl	*n*-Butyl	92–93	$C_{16}H_{24}N_6S$	25.3	9.6	25.6	9.6	41–42	$C_{15}H_{23}N_5O_2S$	20.8	9.6	20.9	9.7
Benzyl	Benzyl	140–141	$C_{22}H_{20}N_6S$	21.0	8.0	21.2	8.3	89–90	$C_{21}H_{19}N_5O_2S$	17.3	7.9	17.3	8.1

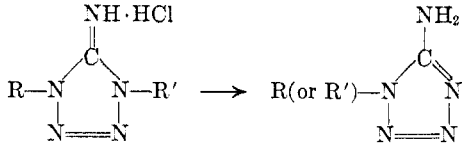
[a] R′ is the group introduced by alkylation. [b] Toluenesulfonyl derivatives.

(13) D. F. Percival, *Alkylated 5-Aminotetrazoles, Their Preparation and Properties.* Ph.D. Thesis, Michigan State University, 1955.

(14) Analyses were done by Micro-Tech Laboratories, Skokie, Ill.

TABLE IV

DEBENZYLATION OF 1,4-ALKYLBENZYL-5-IMINOTETRAZOLINES



1,4-Alkyl-benzyl-5-imino-tetrazoline hydrochloride		1-Alkyl-5-aminotetrazole		
R	R′[a]	R or R′	M.P.°C.	Yield, %
Methyl	Benzyl	Methyl	227–228	82
Benzyl	Methyl	Methyl	226–227	86
n-Propyl	Benzyl	*n*-Propyl	150–152	76
Benzyl	*n*-Propyl	*n*-Propyl	151–152	87
n-Butyl	Benzyl	*n*-Butyl	148–149.5	77
Benzyl	*n*-Butyl	*n*-Butyl	148–149	75
β-Phenylethyl	Benzyl	β-Phenylethyl	175–177	81
Benzyl	β-Phenylethyl	β-Phenylethyl	176–177	79

[a] R′ is the group introduced by alkylation.

cipitate the hydrochloride which was recrystallized from isopropyl alcohol, yield 7.3 g., m.p. 198–199° with decomposition.

1,4-Di-n-butyl-5-iminotetrazoline hydrochloride. A mixture of 7.1 g. (0.05 mole) of 1-*n*-butyl-5-aminotetrazole and 11.4 g. (0.05 mole) of *n*-butyl *p*-toluenesulfonate was heated in an oil bath. At 155–160° a homogeneous melt had formed and the bath was kept at this temperature for 0.5 hr. The solid which formed on cooling the reaction mixture was dissolved in 20 ml. of isopropyl alcohol, treated with 20 ml. of 5*N* sodium hydroxide and the organic base extracted with ether. The ethereal solution was dried over sodium carbonate and treated with 10 ml. of concentrated hydrochloric acid. On evaporation of the solvent the hydrochloride remained as a solid and was crystallized from isopropyl alcohol–ether mixture, yield 5.4 g., m.p. 203–204° with decomposition.

Phenylthioureas derived from the 1,4-dialkyl-5-iminotetrazolines. The base was liberated by treatment of the 1,4-dialkyl-5-iminotetrazoline hydrochloride with 5*N* sodium hydroxide and extracted with ether. After drying the ethereal solution over sodium carbonate and evaporating the solvent, the residual base was warmed with phenyl isothiocyanate. The phenylthioureas so formed were washed with petroleum ether and 50% isopropyl alcohol and crystallized, usually from aqueous isopropyl alcohol or ligroin. Physical constants and analytical data are collected in Table III.

Benzenesulfonyl derivatives. Approximately 0.5 g. of the 1,4-dialkyl-5-iminotetrazoline hydrochloride and 0.5 ml. of benzenesulfonyl chloride were suspended in 10 ml. of 10% sodium hydroxide and shaken. The benzenesulfonyl derivatives solidified on cooling the mixture and were crystallized from aqueous isopropyl alcohol. In one instance, 1,4-benzyl-*n*-propyl-5-iminotetrazoline, the *p*-toluenesulfonyl derivative was prepared in the same manner because the benzenesulfonyl derivative could not be induced to crystallize. Physical constants and analytical data are collected in Table III.

Hydrogenolysis of 1,4-alkylbenzyl-5-iminotetrazolines. A solution of about 0.01 mole of the 1,4-alkylbenzyl-5-iminotetrazoline hydrochloride in 80 ml. of 75% isopropyl alcohol was shaken with 0.1 g. of palladium oxide catalyst at 50 p.s.i. hydrogen pressure. The calculated amount of hydrogen was taken up in about 2 hr. The catalyst was filtered off, washed with hot isopropyl alcohol and the combined filtrate and washings neutralized with sodium carbonate. After concentration of the solution the 1-alkyl-5-aminotetrazole crystallized. All the 1,4-alkylbenzyl-5-iminotetrazolines were debenzylated in this way and in each instance the anticipated 1-alkyl-5-aminotetrazole could be isolated in yields of 70–90%. Identity of the products was established by melting point and mixture melting point. Pertinent data are collected in Table IV.

Acetolysis of 1,4-dialkyl-5-iminotetrazolines. 1,4-Dibenzyl-5-ketotetrazoline (X, R = benzyl). *A.* Two grams of 1,4-dibenzyl-5-iminotetrazoline, obtained from the hydrochloride by treatment with sodium hydroxide and extraction with ether, was heated under reflux with 10 ml. of acetic anhydride for 0.5 hr. The solution was diluted with 20 ml. of isopropyl alcohol, evaporated to a small volume, treated with water until permanent turbidity developed, and chilled. The product separated and was recrystallized from cyclohexane; colorless needles, yield 1.6 g. (79%), m.p. 105–106°.

Anal. Calcd. for $C_{15}H_{14}N_4O$: C, 67.4; H, 5.3; N, 21.1. Found: C, 67.7; H, 5.3; N, 20.8.

B. One gram of 1,4-dibenzyl-5-iminotetrazoline hydrochloride was suspended in 10 ml. of water and treated with 10 ml. of 5*M* sodium nitrite. The mixture was warmed and water added until a clear solution formed. On cooling the nitrite separated as needles, m.p. 109° with decomposition[3] after recrystallization from ether. The nitrite was dissolved in glacial acetic acid and diluted with water to turbidity. On cooling the nitroso derivative separated, m.p. 105° with decomposition.[3] The nitroso derivative was dissolved in 3 ml. of glacial acetic acid and heated for 40 min. on a steam bath. During the first 10 min. the yellow color disappeared. The hot solution was diluted with 40 ml. of 50% isopropyl alcohol and the product that separated on cooling was recrystallized from cyclohexane; colorless needles, m.p. 104–106°, no depression on admixture of the material prepared in *A*. The same product was also obtained by heating the nitrite in glacial acetic acid for 0.5 hr.

1,4-Dibenzyl-5-acetyliminotetrazoline hydrate. The base from 9 g. (0.03 mole) of 1,4-dibenzyl-5-iminotetrazoline hydrochloride was treated in ether solution with 5.4 g. (0.05 mole) of acetic anhydride. The residue left on evaporation of the ether was suspended in 20 ml. of water and treated with small portions of sodium carbonate until gas evolution ceased. The solid obtained by cooling the mixture was crystallized from 50% isopropyl alcohol; yield 7.1 g., m.p. 61–62°. No water lost on drying in a vacuum at 40°.

Anal. Calcd. for $C_{17}H_{17}N_5O.H_2O$: C, 62.8; H, 5.9; N, 21.5. Found: C, 62.8; H, 5.8; N, 21.3.

Acetolysis of 1,4-dibenzyl-5-acetyliminotetrazoline hydrate. A solution of 2 g. of the acetyliminotetrazoline in 10 ml. of glacial acetic acid was boiled under reflux for 0.5 hr. Dilution of the hot solution with water to turbidity and cooling gave a product which was crystallized from cyclohexane; yield 1.5 g., m.p. 105–106°, no depression on admixture of 1,4-dibenzyl-5-ketotetrazoline.

Hydrolysis of 1,4-dibenzyl-5-acetyliminotetrazoline hydrate.

About 1 g. of the acetyliminotetrazoline was boiled under reflux with 10 ml. of concentrated hydrochloric acid for about 3 min. The product which separated from the hot solution was filtered and washed with 50% isopropyl alcohol; yield quantitative, m.p. 213–214° with decomposition, no depression on admixture of 1,4-dibenzyl-5-iminotetrazoline hydrochloride. The nitroso derivative of 1,4-dibenzyl-5-iminotetrazoline likewise was hydrolyzed to the iminotetrazoline on boiling with concentrated hydrochloric acid.

Hydrogenolysis of 1,4-dibenzyl-5-acetyliminotetrazoline hydrate. A solution of 6.1 g. (0.02 mole) of the acetyliminotetrazoline in 150 ml. of absolute ethanol was shaken at room temperature with hydrogen at 50 p.s.i. in the presence of 0.1 g. of palladium oxide catalyst. After 3.5 hr. the reaction was interrupted, the mixture filtered, and the residue washed with 20 ml. of boiling water. The colorless solid that separated from the aqueous washings on cooling was recrystallized from water, yield 1.65 g., m.p. 263° with decomposition, no depression on admixture of 5-acetylaminotetrazole.[11]

1,4-Diethyl-5-acetyliminotetrazoline (XI, R = ethyl). A solution of 20 g. of 1,4-diethyl-5-iminotetrazoline, obtained from the hydrochloride by treatment with sodium hydroxide, extraction with ether and distillation under reduced pressure (b.p. 121–122° at 20 mm.), in 40 g. of acetic anhydride was distilled slowly at atmospheric pressure until most of the acetic anhydride had been removed. After removing from the residual liquid the forerun of acetic acid and anhydride the following fractions were collected at 2 mm.: (*a*) 3.4 g., b.p. 94–95°, n_D^{25} 1.45857; (*b*) 15.2 g., b.p. 95°, n_D^{25} 1.4896; (*c*) 5.7 g., b.p. 95–97°, n_D^{25} 1.4850. Fraction *b* was redistilled at 2 mm. and fractions were collected as follows: (*i*) 2.1 g., b.p. 94–95°, n_D^{25} 1.4901; (*ii*) 2.3 g., b.p. 95°, n_D^{25} 1.4909; (*iii*) 3.2 g., b.p. 95°, n_D^{25} 1.4910; (*iv*) 1.9 g., b.p. 95°, n_D^{25} 1.4910; *v* 3.5 g., b.p. 95–96°, n_D^{25} 1.4916. Fractions *ii–iv* were apparently identical; a sample of fraction *iii* was submitted for elemental analysis.

Anal. Calcd. for $C_7H_{13}N_5O$: C, 46.0; H, 7.1; N, 38.2. Found: C, 45.9; H, 7.2; N, 38.1.

Acetolysis of 1,4-diethyl-5-acetyliminotetrazoline. A solution of 15 g. of the crude acetyl derivative in 20 ml. of glacial acetic acid was boiled under reflux for 2 hr., after which the solution was distilled under reduced pressure. The forerun of acetic acid was discarded and the following fractions were collected at 2 mm.: (*a*) 4.3 g., b.p. 55–60°, n_D^{25} 1.4514; (*b*) 5.2 g., b.p. 60–61°, n_D^{25} 1.4586; (*c*) 2.4 g., b.p. 62°, n_D^{25} 1.4606; (*d*) 1.7 g., b.p. 62–64°, n_D^{25} 1.4634. Fraction *d* solidified at room temperature and could be shown to be acetamide; recrystallized from isopropyl alcohol–cyclohexane, m.p. 81–82°, mixture m.p. with acetamide not depressed. The other fractions were recombined and dissolved in cyclohexane. After filtering off a small amount of acetamide that separated slowly, the material was again fractionated at 12 mm. A fraction, b.p. 94°, n_D^{25} 1.4531, was submitted for analysis.

Anal. Calcd. for $C_5H_{10}N_4O$: C, 42.2; H, 7.1; N, 39.4. Found: C, 42.3, 42.2; H, 7.2, 7.0; N, 38.1, 38.0.

The low nitrogen values could be due to a trace of acetamide which would not affect the carbon-hydrogen values greatly, or they might be due to an idiosyncrasy of the compound. A similar fraction was heated with 1*N* sodium hydroxide to hydrolyze any acetamide present. Distillation gave a product, b.p. 94° at 12 mm., n_D^{25} 1.4530, but the nitrogen analysis was not improved.

Hydrolysis of 1,4-diethyl-5-acetyliminotetrazoline. One gram of the acetyliminotetrazoline was boiled for 2 hr. with 5 ml. of concentrated hydrochloric acid. The solution was diluted with 15 ml. of acetone and treated with ether until turbid. 1,4-Diethyl-5-iminotetrazoline hydrochloride crystallized on cooling, m.p. and mixture m.p. 227–228° with decomposition.

1,4-Dibenzyl-5-benzoyliminotetrazoline. 1,4-Dibenzyl-5-iminotetrazoline hydrochloride (1 g.) was shaken with 1 ml. of benzoyl chloride and 20 ml. of 10% sodium hydroxide. The benzoyl derivative was crystallized from isopropyl alcohol, m.p. 85–86°.

Anal. Calcd. for $C_{22}H_{19}N_5O$: C, 71.5; H, 5.2; N, 19.0. Found: C, 71.4; H, 5.3; N, 18.8.

Hydrolysis of the benzoyl derivative was accomplished by boiling under reflux for 0.5 hr. with a mixture of concentrated hydrochloric and glacial acetic acids. On diluting with water and cooling 1,4-dibenzyl-5-iminotetrazoline hydrochloride crystallized, m.p. and mixture m.p. 213–214° with decomposition.

Acetolysis of the benzoyl derivative was attempted by boiling in glacial acetic acid for 0.5 hr. and by boiling with acetic anhydride for 0.5 hr. In both instances only unchanged benzoyl derivative was recovered.

1,4-Dibenzyl-5-benzenesulfonyliminotetrazoline was refluxed in separate experiments with 3*N* and 6*N* hydrochloric acid, glacial acetic acid, and 10% aqueous potassium hydroxide. In each instance the benzenesulfonyl derivative was recovered. There was no evidence of hydrolysis or acetolysis.

1,4-Dibenzyl-5-iminotetrazoline was boiled under reflux in glacial acetic acid for 0.5 hr.; the hydrochloride was subjected to similar treatment with both glacial acetic acid and acetic anhydride. In all cases the starting material was recovered unchanged as hydrochloride.

5-Acetylaminotetrazole[11] (2 g.) was recovered unchanged after boiling for 2.5 hr. in 10 ml. of glacial acetic acid; hydrolysis was accomplished easily by evaporating a mixture of 1 g. of 5-acetylaminotetrazole and 5 ml. of concentrated hydrochloric acid on the steam bath. The residue of 5-aminotetrazole crystallized from water, m.p. and mixture m.p. 203–204°.[9]

N,N′-Dialkylthioureas. *N,N′*-Diethyl-, diisopropyl-, di-*n*-butyl, and diphenylthiourea were commercial products. *N,N′*-Di-*n*-propylthiourea, m.p. 71–72°,[15] yield 94%, and *N,N′*-dibenzylthiourea, m.p. 146–147°,[16] yield 97%, were prepared from the primary amine and carbon bisulfide in toluene solution according to Strakosch.[17] *N,N′*-Dimethylthiourea was prepared by interaction of methyl isothiocyanate and methylamine,[18] yield 85%, m.p. 52–53°.

S-Methyl-N,N′-dialkylisothiuronium iodides were prepared by interaction of the *N,N′*-dialkylthioureas and methyl iodide in isopropyl alcohol solution, an adaptation of the procedure of Braun and Randall.[19] Only *S*-methyl-*N,N′*-di-*n*-butylisothiuronium iodide failed to crystallize. Physical constants and analytical data for the remaining compounds are given in Table V.

TABLE V

S-METHYL-*N,N′*-DIALKYLISOTHIURONIUM IODIDES

RHN—C(SCH$_3$)=NR·HI

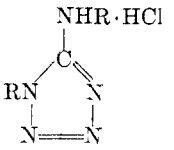
R	M.P., °C.	Yield, %	Analysis			
			Calculated		Found	
			N	S	N	S
Ethyl	75–76	91	10.2	11.7	9.8	12.0
n-Propyl	61.5–63	94	9.3	10.6	8.7	11.0
Isopropyl	122–123	98	9.3	10.6	9.1	10.7
Benzyl	119.5–120.5	98	7.0	8.1	7.2	8.5

N,N′-Dialkyl-N″-aminoguanidine hydriodides were prepared by an adaptation of the procedure of Kerstin and Smith[20] involving interaction of the *S*-methyl isothiuro-

(15) O. Hecht, *Ber.*, **23**, 281 (1890).
(16) E. A. Werner, *J. Chem. Soc.*, **59**, 406 (1891).
(17) J. Strakosch, *Ber.*, **5**, 692 (1872).
(18) A. E. Dixon, *J. Chem. Soc.*, **63**, 328 (1893).
(19) C. E. Braun and W. M. Randall, *J. Am. Chem. Soc.*, **56**, 2134 (1934).
(20) G. W. Kerstin and G. B. L. Smith, *J. Am. Chem. Soc.*, **58**, 800 (1936).

TABLE VI

1-ALKYL-5-ALKYLAMINOTETRAZOLE HYDROCHLORIDES



R	M.P., °C.[a]	Method	Formula	Analyses Calculated C	H	N	Found C	H	N
Methyl	209 dec.	A-1	$C_3H_8ClN_5$	[b]		46.8			46.5
Ethyl	162–163	A-1	$C_5H_{12}ClN_5$	33.8	6.8	39.4	34.1	6.7	39.6
	161–163	B					33.7	6.8	39.5
n-Propyl	141–142	A-1	$C_7H_{16}ClN_5$	40.9	7.3	34.1	41.1	7.6	34.1
	141–142	B					40.9	7.8	34.0
Isopropyl	192–193	A-2	$C_7H_{16}ClN_5$						
	193–194	B		[c]		34.1			34.0
n-Butyl	156–157	A-1	$C_9H_{20}ClN_5$	46.2	8.6	30.0	46.0	8.5	30.1
	156–157	A-2							
	156–157	B					46.1	8.7	30.1
Benzyl	160–161	A-1	$C_{15}H_{16}ClN_5$	[d]		23.2			23.5

[a] Mixture melting points of the respective pairs showed no depression. [b] Calcd. Cl, 23.7. Found: Cl, 23.9. [c] Calcd. Cl, 17.2. Found: Cl, 17.0. [d] Calcd. Cl, 11.8. Found: Cl, 11.9.

nium iodides and hydrazine in isopropyl alcohol solution. Difficulty in crystallizing the hydriodides made it necessary to purify samples of the products for analysis as benzal derivatives or as picrates.

Benzal N,N'-diethyl-N"-aminoguanidine hydriodide, m.p. 204–206°, crystallized from isopropyl alcohol.

Anal. Calcd. for $C_{12}H_{19}IN_4$: I, 36.7; N, 16.2. Found: I, 36.6; N, 16.2.

N,N'-Di-n-propyl-N"-aminoguanidine picrate, yellow crystals from water, m.p. 105–106°.

Anal. Calcd. for $C_{13}H_{21}N_7O_7$: C, 40.4; H, 5.4; N, 25.3. Found: C, 40.5; H, 5.6; N, 25.5.

N,N'-Di-isopropyl-N"-aminoguanidine picrate, yellow crystals from water, m.p. 93–94°.

Anal. Calcd. for $C_{13}H_{21}N_7O_7$: C, 40.4; H, 5.4; N, 25.3. Found: C, 40.6; H, 5.7; N, 25.7.

Benzal N,N'-di-n-butyl-N"-aminoguanidine hydriodide, crystallized from ethylene chloride, m.p. 123–124°.

Anal. Calcd. for $C_{16}H_{27}IN_4$: I, 31.5; N, 14.0. Found: I, 31.3; N, 14.0.

1-Alkyl-5-alkylaminotetrazoles (VI) *from carbodiimides.* The method involved conversion of *N,N'*-dialkylthioureas into *N,N'*-dialkylcarbodiimides according to Schmidt *et al.*,[8] and subsequent interaction of the carbodiimides with hydrazoic acid. Two techniques were used: *Method A-1* using ether-water mixtures as solvents, and *Method A-2* using benzene-chloroform mixtures as solvents for the reactants. The preparation of 1-*n*-butyl-5-*n*-butylaminotetrazole affords an example of both techniques.

Method A-1. A mixture of 37.6 g. (0.2 mole) of *N,N'*-di-*n*-butylthiourea, 300 ml. of ether, and 400 ml. of water was stirred vigorously while 54 g. (0.25 mole) of yellow mercuric oxide was added slowly during 10 min. The mercuric oxide turned black as fast as it was added. Stirring was continued for 5 min. before the mixture was filtered by suction. The mercuric sulfide was washed with ether and the ether layers were separated and dried for 10–15 min. over calcium chloride. The ether solution was decanted from the drying agent, 100 ml. of a benzene solution containing 15 g. of hydrazoic acid[21] was added and the resulting solution boiled under reflux for 1.5 hr. The solvents and excess hydrazoic acid were removed by distillation. The oily residue solidified when washed with petroleum ether. The 1-*n*-butyl-5-*n*-butylaminotetrazole was recrystallized from ether–petroleum ether, m.p. 73–74°, yield 61% based on thiourea. The hydrochloride was prepared in ether with dry hydrogen chloride and recrystallized from ether–isopropyl alcohol, m.p. 156–157°.

Method A-2. A mixture of 18.8 g. (0.1 mole) of *N,N'*-di-*n*-butylthiourea, 43.2 g. (0.2 mole) of yellow mercuric oxide, 100 ml. of benzene, 100 ml. of chloroform and 15 g. of anhydrous calcium chloride was heated under reflux for an hour. The mercuric sulfide was filtered by suction and washed with 50 ml. of hot chloroform. To the combined filtrate and washings 50 ml. of a xylene solution containing 8 g. of hydrazoic acid[21] were added and the mixture boiled under reflux for 1.5 hr. The volume of the reaction mixture was reduced to 100 ml. by distillation, the residual solution cooled, diluted with 100 ml. of ether and treated with dry hydrogen chloride until precipitation of the hydrochloride was complete. The hydrochloride was recrystallized from ether–isopropyl alcohol, m.p. 156–157°, yield 73% based on the thiourea.

Other 1-alkyl-5-alkylaminotetrazoles prepared by these techniques and their hydrochlorides are listed in Tables II and VI, respectively. 1-Phenyl-5-phenylaminotetrazole was prepared by method A-1; recrystallized from isopropyl alcohol, m.p. 161–162°,[9] yield 67%.

Anal. Calcd. for $C_{13}H_{11}N_5$: N, 29.6. Found: N, 30.0.

1-Alkyl-5-alkylaminotetrazoles (VI) *from aminoguanidines. Method B.* The procedure of Finnegan *et al.*,[10] was used. The preparation of 1-*n*-butyl-5-*n*-butylaminotetrazole serves as an example. A solution of 0.1 mole of crude *N,N'*-di-*n*-butyl-*N"*-aminoguanidine hydriodide in 100 ml. of water was acidified with 1.3 ml. of concentrated nitric acid. Silver nitrate (17.2 g., 0.1 mole) dissolved in 22 ml. of water was added with continued stirring. After 0.5 hr. any excess of silver ion was precipitated by addition of 1.2 ml. of concentrated hydrochloric acid, the silver halide was filtered off and washed with two 20-ml. portions of hot water. The combined filtrate and washings were cooled in an ice bath, 7.3 ml. of concentrated hydrochloric acid were added followed by a solution of 0.1 mole of sodium nitrite in 22 ml. of water, the latter dropwise with stirring and cooling so that the temperature remained below 10° until a faint starch-iodide test was obtained. Careful addition of 12.1 g. (0.11 mole) of sodium carbonate caused an oil to separate which solidified on standing overnight. The 1-*n*-butyl-5-*n*-butylaminotetra-

(21) All operations involving hydrazoic acid must be done in a well ventilated hood.

zole was recrystallized from ether-petroleum ether, m.p. 73–74°. Admixture of the same product prepared by method A-1 or A-2 caused no depression of the melting point; yield 48% based on crude aminoguanidine hydriodide.

The hydrochloride was prepared in ether solution with dry hydrogen chloride and recrystallized from ether–isopropyl alcohol, m.p. and mixture m.p. 156–157°.

All the 1-alkyl-5-alkylaminotetrazoles and their hydrochlorides prepared by this procedure are listed in Tables II and VI, respectively. In all cases the products were identical with the materials prepared by Method A-1 or A-2.

EAST LANSING, MICH.

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

Synthesis of 1-Substituted Tetrazoles[1]

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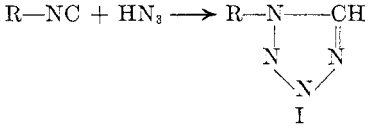
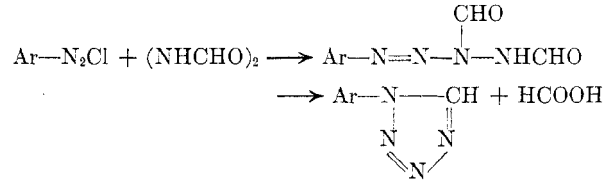
A group of seven 1-alkyltetrazoles was prepared by interaction of alkyl isocyanides and hydrazoic acid in benzene solution. The same method was applied to the synthesis of 1-phenyltetrazole but the yield was very poor. The Dimroth procedure for preparation of 1-aryltetrazoles by coupling diformyl hydrazide and diazonium salts also gave very poor yields of 1-phenyltetrazole. A new procedure involving an adaptation of the von Braun synthesis of 1,5-disubstituted tetrazoles was developed. Interaction of formanilides successively with phosphorus pentachloride and hydrazoic acid in toluene gave fair yields of the desired 1-aryltetrazoles. A group of eight 1-aryltetrazoles was prepared in this way. Their ultraviolet absorption spectra were determined and compared with those of comparable 5-aryltetrazoles.

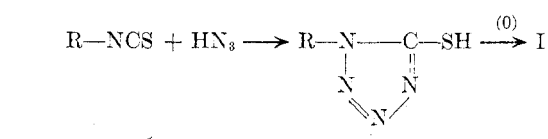
Although many 5-substituted tetrazoles are known, only very few 1-substituted tetrazoles have been described. Benson,[3] in his review of tetrazole chemistry, listed only seven examples including the questionable 1-hydroxytetrazole. It was the purpose of this study to investigate the preparation and properties of a larger group of 1-substituted tetrazoles.

Of the known methods for synthesis of 1-substituted tetrazoles three appeared to offer possibilities of rather general application. Oliveri-Mandalà and Alagna[4] obtained 1-methyl-, 1-ethyl-, and 1-phenyltetrazole by addition of hydrazoic acid to the appropriate isocyanide in ether solution. 1-Aryltetrazoles were prepared by Dimroth and de



Montmollin[5] by coupling aryl diazonium salts with diformyl hydrazide in aqueous alkaline medium and cyclizing the resulting diazohydrazide with warm aqueous alkali. Freund and Paradies[6] and later Stollé and Henke-Stark[7] oxidized 1-substituted-5-mercaptotetrazoles which had been prepared by interaction of isothiocyanates and hydrazoic acid or sodium azide. Although only 1-methyl- and 1-phenyltetrazole have been prepared this way, a variety of 1-substituted 5-mercaptotetrazoles have been described.[3]





For the preparation of 1-alkyltetrazoles the addition of hydrazoic acid to alkyl isocyanides[4] appeared to be the most generally applicable procedure. A series of seven 1-alkyltetrazoles was prepared in this way (Table I) but the method leaves much to be desired because of the disagreeable character of the requisite alkyl isocyanides. The latter were best prepared by the technique of Guillemard[8] by interaction of alkyl iodides and silver cyanide at steam bath temperature under reflux. Crude yields of the isocyanides were generally satisfactory, although the products were probably contaminated with dimerized or polymerized material in increasing quantity on standing which necessitated immediate use of the crude products in the next step of the synthesis. An attempt to estimate the isocyanide content of the crude products by a bromide-bromate titration in-

(1) Based on a thesis submitted by Frances G. Fallon to the School for Advanced Graduate Studies at Michigan State University in 1956, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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