Amination of tetrazoles with hydroxylamine-*O*-sulfonic acid: 1- and 2-aminotetrazoles

R. RAAP
R and L Molecular Research Ltd., 8045 Argyll Road, Edmonton 82, Alberta

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1-Aminotetrazoles and 2-aminotetrazoles can be prepared by reacting tetrazoles with hydroxylamine-*O*-sulfonic acid in weakly alkaline aqueous solutions. The nuclear magnetic resonance spectra and some of the properties of these aminotetrazoles are described.

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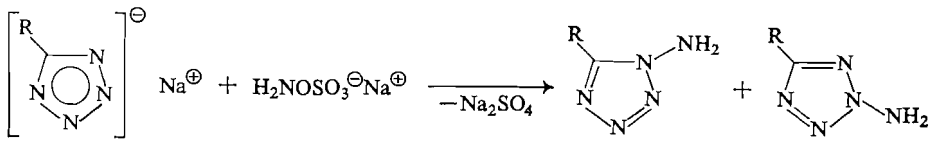
Of the aminotetrazoles, the 5-aminotetrazoles have received by far the most attention in the literature. The synthesis of 5-aminotetrazole itself was described as early as 1892 by Thiele (1). Only a few reports have been published on 1-aminotetrazoles. Stollé and co-workers (2) have prepared some 1-amino-5-aryltetrazoles and the hydrochlorides of 1,5-diaminotetrazole and 1-amino-5-hydrazinotetrazole. Recently Hagedorn and Winkelmann (3) described a synthesis of 1-aminotetrazole itself. As hydroxylamine-*O*-sulfonic acid had been successfully employed as a reagent for the amination of several substances, such as amines (4), alkylboranes (5), benzotriazoles (6), and benzoxazolin-2-one (7), we investigated its reaction with tetrazoles as a possible route to 1-aminotetrazoles and the (thus far) unknown 2-aminotetrazoles.

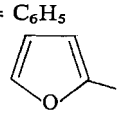
When a mixture of tetrazole and sodium carbonate in water was treated with hydroxylamine-*O*-sulfonic acid a 2:1 mixture of 1-aminotetrazole (**1***a*) and 2-aminotetrazole (**2***b*) could be isolated in a total yield of 38%. In the same manner were also prepared the compounds **2**–**5**. The isomers were separated by fractional distillation, fractional crystallization, or by elution chromatography on alumina or silica gel. The yields, some physical constants, and nuclear magnetic resonance (n.m.r.) data of the thus prepared *N*-aminotetrazoles are given in Table I.

The identity of **1***a* was confirmed by comparison with an authentic sample prepared by the procedure of Hagedorn and Winkelmann (3). The other isomer assignments are based on the difference in physical behavior and n.m.r. spectra of the isomer pairs. It has been shown that 2-substituted tetrazoles have lower boiling points and better solubilities in organic solvents than the corresponding 1-isomers (8–13) and with a few exceptions (10, 11, 13), the 2-isomers are also the lower melting ones. There have been several reports in the literature on the use of n.m.r. spectroscopy in assigning structural isomers (12–17, 23), and it has been clearly established that a *N*-substituent is more deshielded in the 2-isomer than in the corresponding 1-isomer. As Table I



a *b*

1 R = H
2 R = *n*-C_3H_7
3 R = C_6H_5
4 R =



5 R = NH_2

TABLE I

N-Aminotetrazoles

Compound	% Yield*	Melting point (recrystallizing solvent) or boiling point (mm Hg), (°C)	Nuclear magnetic resonance chemical shifts (τ)†		Formula	Analyses‡					
						% calculated			% found		
			N—NH_2	C^5—R		C	H	N	C	H	N
1-Aminotetrazole (1*a*)	25	137–142(0.7)§	2.90	0.88	CH_3N_5						
2-Aminotetrazole (1*b*)	13	89–91(0.3)	2.03	1.28	CH_3N_5						
1-Amino-5-*n*-propyltetrazole (2*a*)	35	134–139(0.1)	3.73		$C_4H_9N_5$						
2-Amino-5-*n*-propyltetrazole (2*b*)	26	98–100(0.1)	2.93		$C_4H_9N_5$	37.78	7.14	55.09	38.03	7.39	54.70
1-Amino-5-phenyltetrazole (3*a*)	15	156–158(EtOAc)‖	2.70		$C_7H_7N_5$	52.15	4.38	43.46	51.93	4.20	43.82
2-Amino-5-phenyltetrazole (3*b*)	32	109–111(C_6H_6-*n*-C_6H_{14})	1.73		$C_7H_7N_5$	52.15	4.38	43.46	52.14	4.38	43.02
1-Amino-5-(2′-furyl)tetrazole (4*a*)	28	165–167(MeOH)	2.70¶		$C_5H_5N_5O$	39.73	3.33	46.35	39.98	3.20	46.15
2-Amino-5-(2′-furyl)tetrazole (4*b*)	21	116–117(EtOAc-*n*-C_6H_{14})	1.75¶		$C_5H_5N_5O$	39.73	3.33	46.35	39.95	3.34	46.70
1,5-Diaminotetrazole (5*a*)	8.5	187–188 (decomp.)**(H_2O)	3.63	3.63	CH_4N_6	12.00	4.03	83.97	12.37	3.73	83.81
2,5-Diaminotetrazole (5*b*)	4.5	125–127 (decomp.)††(EtOAc)	2.62	4.21	CH_4N_6	12.00	4.03	83.97	12.49	4.31	83.28

*All the yields given refer to the actual isolated amount of pure isomer. The yields for compounds **2**, **3**, and **4** are based on unrecovered starting material (respectively 61, 67, and 71% of the starting materials were recovered). In the case of compounds **1** and **5** no attempt was made to recover starting material.

†The spectra were taken in DMSO-d_6, except for compounds 3*a* and 3*b* where $CDCl_3$ was used as solvent.

‡Some of the aminotetrazoles were analyzed in the form of a more stable derivative (Table II).

§Reported b.p. 118–120 (0.01 mm) (3).

‖Reported m.p. 155° (2*a*).

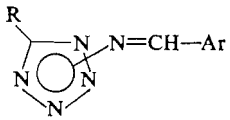
¶The furyl protons in 4*a* appeared as doublets at τ 1.92 (J = 2 c.p.s.) and 2.44 (J = 3.5 c.p.s.) and a quartet at τ 3.16; in 4*b* these τ values were 2.03, 2.81, and 3.25 respectively.

**The HCl salt decomposed at 175–176°; reported decomposition point 176° (2*b*).

††The HCl salt decomposed at 120°.

TABLE II

Some derivatives of *N*-aminotetrazoles with aldehydes



R	Ar	Melting point, (°C)	Recrystallizing solvent	Formula	Analyses					
					% calculated			% found		
					C	H	N	C	H	N
1-Isomers										
H	5-Nitro-2-furyl	158–159 (decomp.)	THF	$C_6H_4N_6O_3$	34.62	1.94	40.37	34.90	1.62	39.95
n-C_3H_7	p-$OCH_3C_6H_4$	91–93	C_6H_6 – n-C_6H_{14}	$C_{12}H_{15}N_5O$	58.75	6.16	28.55	58.87	6.42	29.00
n-C_3H_7	5-Nitro-2-furyl	115–117	EtOAc	$C_9H_{10}N_6O_3$	43.20	4.03	33.59	43.08	4.02	33.34
NH_2	C_6H_5	225–226 (decomp.)*	MeOH	$C_8H_8N_6$	51.05	4.29	44.66	50.46	4.18	44.50
NH_2	p-$OCH_3C_6H_4$	227–228 (decomp.)	DMF	$C_9H_{10}N_6O$	49.53	4.62	38.51	49.34	4.63	38.82
NH_2	5-Nitro-2-furyl	229 (decomp.)	DMF-EtOEt	$C_6H_5N_7O_3$	32.29	2.26	43.93	32.25	2.08	43.78
2-Isomers										
H	p-$OCH_3C_6H_4$	100–102	C_6H_6 – n-C_6H_{14}	$C_9H_9N_5O$	53.20	4.47	34.48	53.42	4.43	34.92
H	p-$O_2NC_6H_4$	161–162 (decomp.)	THF	$C_8H_6N_6O_2$	44.03	2.77		44.19	2.78	
H	5-Nitro-2-furyl	146–147 (decomp.)	THF	$C_6H_4N_6O_3$	34.62	1.94	40.37	34.84	2.21	40.08
n-C_3H_7	p-$OCH_3C_6H_4$	74–75	C_6H_6 – n-C_6H_{14}	$C_{12}H_{15}N_5O$	58.75	6.16	28.55	58.37	6.44	28.65
n-C_3H_7	5-Nitro-2-furyl	135–136 (decomp.)	C_6H_6	$C_9H_{10}N_6O_3$	43.20	4.03	33.59	43.34	4.06	33.78
C_6H_5	p-$O_2NC_6H_4$	169–170 (decomp.)	THF	$C_{14}H_{10}N_6O_2$	57.14	3.43	28.56	57.43	3.70	28.18
NH_2	C_6H_5	159–160 (decomp.)	MeOH	$C_8H_8N_6$	51.05	4.29	44.66	50.48	4.50	45.01
NH_2	p-$OCH_3C_6H_4$	176–177 (decomp.)	EtOH	$C_9H_{10}N_6O$	49.53	4.62	38.51	49.20	4.62	38.85
NH_2	5-Nitro-2-furyl	159 (decomp.)	THF	$C_6H_5N_7O_3$	32.29	2.26	43.93	32.82	2.19	43.45

*Reported m.p. 210° (decomp.) (2*b*).

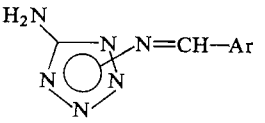
shows, there is indeed a substantial difference in chemical shift of the *N*-amino group between isomer pairs ($\Delta\tau$ 0.8–1.0). Compounds **1** and **5** also show the expected difference in chemical shift of the 5-hydrogen and the 5-amino group between two isomers (13, 14, 16).

Whereas heating 1-aminotetrazole with acetic anhydride results in ring opening and the formation of 2-acetylamino-1,3,4-oxadiazole (3), 1-amino-5-phenyltetrazole under these conditions gives 1-diacetylamino-5-phenyltetrazole (2*c*). 1,5-Diaminotetrazole upon heating with acetic anhydride gave a triacetyl derivative, believed to be 5-acetylamino-1-diacetylaminotetrazole as 5-amino-tetrazoles are reported to give only the monoacetylated derivatives under these conditions (17–19). Both the 1- and 2-aminotetrazoles could readily be condensed with aromatic aldehydes. The derivatives thus prepared are listed in Table II. In the case of the diaminotetrazoles the question arose which of the two amino groups reacted; from the position of the amino signals in the n.m.r. spectra (Table III) it could be concluded, however, that the 1- and 2-amino groups underwent reaction in preference to the 5-amino group.[1]

The explosive character of 1-aminotetrazole has already been mentioned (3). The 2-aminotetrazoles appear to be distinctively more explosive than their corresponding 1-isomers, and 2-aminotetrazole and 2,5-diaminotetrazole especially were able to produce devastating explosions.[2] Great care should therefore be exercised in handling the lower members of the *N*-aminotetrazoles. Aryl substitution, and to a lesser extent also alkyl substitution, appears to stabilize the *N*-aminotetrazoles considerably.

TABLE III

Nuclear magnetic resonance spectra of diaminotetrazole derivatives*



Ar		Chemical shifts (τ) NH_2	—N = CH—
C_6H_5	1-Isomer	2.76	0.80
	2-Isomer	3.43	0.90
O_2N	1-Isomer	2.64	0.86
	2-Isomer	3.27	0.96

*In DMSO-d_6.

Experimental

All melting points and boiling points are uncorrected. The n.m.r. spectra were measured using a Varian Associates model A-60 spectrometer with tetramethylsilane as a reference. Microanalyses were performed by Dr. G. Weiler and Dr. F. B. Strauss, Microanalytical Laboratory, Oxford, England.

Tetrazoles

The tetrazoles were prepared by literature procedures. Tetrazole itself was obtained by a reductive deamination of 5-aminotetrazole (9, 20) which in turn was obtained from dicyandiamide (21). 5-*n*-Propyltetrazole and 5-phenyltetrazole were prepared by the procedure of Finnegan *et al.* (22) from propionitrile and benzonitrile respectively. In the same manner 5-(2′-furyl)tetrazole, m.p. 198–200° (decomp.), could be prepared from 2-furylcyanide (92% yield).

Anal. Calcd. for $C_5H_4N_4O$: C, 44.12; H, 2.96; N, 41.16. Found: C, 44.26; H, 3.11; N, 40.98.

N-Aminotetrazoles

These were all prepared by essentially the same procedure, the only difference being in the work-up. The procedure is illustrated by the preparation of 1-aminotetrazole (**1***a*) and 2-aminotetrazole (**1***b*) as follows. Tetrazole (28.0 g, 0.40 mole) and sodium carbonate (46.4 g, 0.44 mole) were dissolved in 300 ml of water and the resulting mixture was heated to 75°. A solution of hydroxylamine-*O*-sulfonic acid (54.4 g, 0.48 mole) in 240 ml of water was added dropwise, with stirring, over a period of 20 min, the temperature of the reaction mixture being kept at 70–75°. Throughout the reaction a pH of 7–8 was maintained by the periodic addition of a saturated aqueous sodium bicarbonate solution. When the addition was completed the reaction mixture was heated under reflux for 20–30 min. After cooling the mixture was adjusted to pH 8 and then continuously extracted with ethyl acetate for 16 h. The ethyl acetate extract was dried and concentrated. The colorless residual oil was distilled *in vacuo* to give 4.3 g (13%) of 2-amino-

[1]Another indication of the higher reactivity of the 1-amino group over the 5-amino group was obtained when an equimolar mixture of 1-amino-5-*n*-propyltetrazole and 5-amino-1-*n*-propyltetrazole was allowed to react with only 0.5 equivalent of anisaldehyde (THF, room temperature). The only product isolated was 1-*p*-methoxybenzylideneamino-5-*n*-propyltetrazole (67% yield) whereas 76% of the 5-amino-1-*n*-propyltetrazole was recovered.

[2]Even a 4 mg sample of 2-aminotetrazole produced a very loud explosion when rapidly heated to 250–300°. 2,5-Diaminotetrazole not only detonated upon impact but when a small sample in a capillary tube was rapidly heated in a pre-heated Gallenkamp melting point apparatus, it detonated already at 210°, with sufficient force to break the bulb of the thermometer. With 1,5-diaminotetrazole on the other hand, no detonation could be affected.

tetrazole, b.p. 89–91° (0.3 mm). The distillation residue consisted of only 1-aminotetrazole (8.4 g, 25%) which could be distilled only in small quantities without appreciable decomposition, b.p. 137–142° (0.7 mm); reported b.p. 118–120° (0.01 mm) (3). The infrared and n.m.r. spectra of 1-aminotetrazole were superimposable with the corresponding spectra of an authentic sample (3).

The *N*-amino-5-*n*-propyltetrazoles **2***a* and **2***b* were prepared in the same manner. When after continuous extraction of the products with ethyl acetate the solution was acidified and again continuously extracted with ethyl acetate, 61% of 5-*n*-propyltetrazole being recovered. In the preparation of **3** and **4**, the products were extracted with 3–6 portions of ethyl acetate, then the reaction mixture was acidified to give respectively 67 and 71% of unreacted starting material. Isomers **3***a* and **3***b* were separated by elution chromatography on alumina; **3***b* was eluted with a 1:1 benzene – ether mixture, **3***a* was eluted with ether. Isomers **4***a* and **4***b* were separated by recrystallization of the crude mixture from ethyl acetate, which provided pure **4***a*; the residue obtained from the filtrate was then chromatographed on alumina and **4***b* eluted with a 1:1 ether – ethyl acetate mixture. The diaminotetrazoles **5***a* and **5***b* were isolated by continuous extraction with ethyl acetate. The extract was dried, concentrated, and cooled. The precipitated 1,5-diaminotetrazole was then recrystallized from water. The residue obtained from the filtrate was chromatographed on silica gel and 2,5-diaminotetrazole eluted with ethyl acetate. The yields, physical constants, n.m.r. spectra, and analytical data are listed in Table I.

1-Diacetylamino-5-phenyltetrazole

A mixture of 1-amino-5-phenyltetrazole (0.35 g, 2.17 mmole) and acetic anhydride (5 ml) was heated under reflux for 4 h. Removal of the excess acetic anhydride and recrystallization of the residue from methanol gave 0.42 g (79%) of product, m.p. 88–89°; reported m.p. 90° (2*c*). The n.m.r. spectrum ($CDCl_3$) contained a multiplet at τ 2.0–2.4 and a sharp singlet at τ 7.62 with an integrated area ratio of 5:6.

Anal. Calcd. for $C_{11}H_{11}N_5O_2$: C, 53.87; H, 4.52; N, 28.56. Found: C, 53.95; H, 4.53; N, 28.80.

5-Acetylamino-1-diacetylaminotetrazole

A mixture of 1,5-diaminotetrazole (0.40 g, 4.0 mmole) and acetic anhydride (6 ml) was heated under reflux for 2 h. The mixture was cooled and the white crystalline product, m.p. 186–188° (decomp.), collected by filtration. Yield, 0.48 g (53%). The n.m.r. spectrum (DMSO-d_6) contained singlets at τ 7.65 and 7.78 with an integrated area ratio of 2:1.

Anal. Calcd. for $C_7H_{10}N_6O_3$: C, 37.16; H, 4.46; N, 37.15. Found: C, 37.18; H, 4.36; N, 36.91.

Reaction of N-Aminotetrazoles with Aldehydes

Equimolar amounts of the aminotetrazole and the aldehyde were dissolved in benzene, tetrahydrofuran, or dimethylformamide, depending on the solubility of the aminotetrazole. A trace of *p*-toluenesulfonic acid was added and the reaction mixture was left at room temperature overnight. The product was isolated by removal of the solvent and recrystallization of the residue or by the addition of ether to the tetrahydrofuran or dimethylformamide solutions. In many instances the product crystallized from the reaction mixture. The yields amounted to 50–90%. The derivatives prepared are listed in Table II.

Acknowledgments

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