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1-Substituted 5-Aminotetrazoles: Syntheses from CNN_3 with Primary Amines

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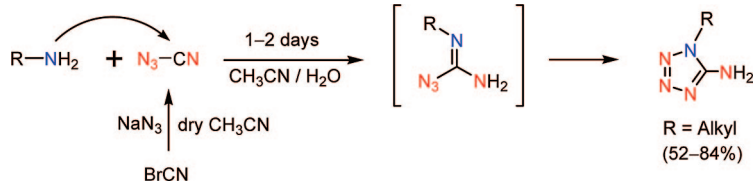
ABSTRACT



1-Substituted 5-aminotetrazoles were prepared in situ by an excellent reaction of cyanogen azide and primary amines to generate an imidoyl azide as an intermediate in acetonitrile/water. After cyclization, the intermediate gave 1-substituted aminotetrazole in good yield. This protocol also was utilized in the syntheses of bis- and tris(1-substituted 5-aminotetrazole) derivatives.

Aminotetrazoles are an interesting class of heterocycles that exhibit an unusually wide range of applications such as high energy density materials (HEDM),[1] useful ligands in coordination chemistry,[2] in bioorganic chemistry,[3] and as drugs in pharmaceuticals.[4] Additionally, aminotetrazoles have proven to be valuable for the preparation of their substituted analogues[5] and other nitrogen-containing heterocycles.[6]

More than 120 years ago, 1-substituted 5-aminotetrazole derivatives were prepared by the treatment of potassium aminotetrazolate with an alkyl halide.[7] In 1932, further investigation into the synthesis of methyl aminotetrazoles led to their generation through the high-temperature cycloaddition of sodium azide to monomethyl-thiourea in alcohol.[8] There are several reports in the literature describing the in situ generation of 1-substituted aminotetrazoles via the

(1) (a) Singh, R. P.; Verma, R. D.; Meshri, D. T.; Shreeve, J. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 3584–3601. (b) Steinhauser, G.; Klapötke, T. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3330–3347. (c) Singh, R. P.; Gao, H.; Meshri, D. T.; Shreeve, J. M. In *High Energy Density Materials*; Klapötke, T. M., Ed.; Springer: Berlin, Heidelberg, 2007; pp 35−83. (d) Klapötke, T. M. In *High Energy Density Materials*; Klapötke, T. M., Ed.; Springer: Berlin, Heidelberg, 2007; pp 85−122.

(2) (a) Tappan, B. C.; Huynh, M. H.; Hiskey, M. A.; Chavez, D. E.; Luther, E. P.; Mang, J. T.; Son, S. F. *J. Am. Chem. Soc.* **2006**, *128*, 6589–6594. (b) Huynh, M. H.; Hiskey, M. A.; Meyer, T. J.; Wetzler, M. *Proc. Natl. Acad. Sci.* **2006**, *103*, 5409–5412. (c) Hiskey, M. A.; Chavez, D. E.; Naud, D. L. 2001, US 6214139; *Chem. Abstr.* **2001**, *134*, 282929. (d) Hammerl, A.; Holl, G.; Kaiser, M.; Klapötke, T. M.; Mayer, P.; Nöth, H.; Piotrowski; Warchhold, H. M. *Eur. J. Inorg. Chem.* **2002**, 834–845. (e) Friedrich, M.; Galvez-Ruiz, J. C.; Klapötke, T. M.; Mayer, P.; Weber, B.; Weigand, J. *Inorg. Chem.* **2005**, *44*, 8044–8052.

(3) (a) Sureshbabu, V. V.; Venkataramanarao, R.; Naik, S. A.; Chennakrishnareddy, G. *Tetrahedron Lett.* **2007**, *48*, 7038–7041. (b) Purchase, C. F., II; White, A. D.; Anderson, M. K.; Bocan, T. M. A.; Bousley, R. F.; Hamelehle, K. L.; Homan, R.; Krause, B. R.; Lee, P.; Mueller, S. B.; Speyer, C.; Stanfield, R. L.; Reindel, J. F. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1753–1758. (c) Yamazaki, K.; Hasegawa, H.; Umekawa, Ueki, K.; Y.; Ohashi, N.; Kanaoka, M. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1275–1278. (d) Vieira, E.; Huwyler, J.; Jolidon, S.; Knoflach, F.; Mutelb, V.; Wichmann, J. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4628–4631.

(4) (a) White, A. D.; Creswell, M. W.; Chucholowski, A. W.; Blankley, C. J.; Wilson, M. W.; Bousley, R. F.; Essenburg, A. D.; Hamelehle, K. L.; Krause, B. R.; Stanfield, R. L.; Dominick, M. A.; Neub, M. *J. Med. Chem.* **1996**, *39*, 4382–4395. (b) Bavetsias, V.; Marriott, J. H.; Melin, C.; Kimbell, R.; Matusiak, Z. S.; Boyle, F. T.; Jackman, A. L. *J. Med. Chem.* **2000**, *43*, 1910–1926. (c) Upadhayaya, R. S.; Jain, S.; Sinha, N.; Kishore, N.; Chandra, R.; Arora, S. K. *Eur. J. Med. Chem.* **2004**, *39*, 579–592. (d) Castro, J. L.; Ball, R. G.; Broughton, H. B.; Russell, M. G. N.; Rathbone, D.; Watt, A. P.; Baker, R.; Chapman, K. L.; Fletcher, A. E.; Smith, S. J.; Marshall, G. R.; Ryecroft, W.; Matassa, V. G. *J. Med. Chem.* **1996**, *39*, 842–849.

(5) Katritzky, A. R.; Rogovoy, B. V.; Kovalenko, K. V. *J. Org. Chem.* **2003**, *68*, 4941–4943.

(6) (a) Klapötke, T. M.; Stierstorfer, J. *Helv. Chim. Acta* **2007**, *90*, 2132–2150. (b) Klapötke, T. M.; Radies, H.; Stierstorfer, J. *Z. Naturforsch.* **2007**, *62b*, 1343–1352. (c) Geisberger, G.; Klapötke, T. M.; Stierstorfer, J. *Eur. J. Inorg. Chem.* **2007**, 4743–4750. (d) Klapötke, T. M.; Sabate, C. M.; Welch, J. M. *Z. Anorg. Allg. Chem.* **2008**, *634*, 857–866.

(7) Thiele, J.; Ingle, H. *Liebigs Ann. Chem.* **1885**, *287*, 233–265.

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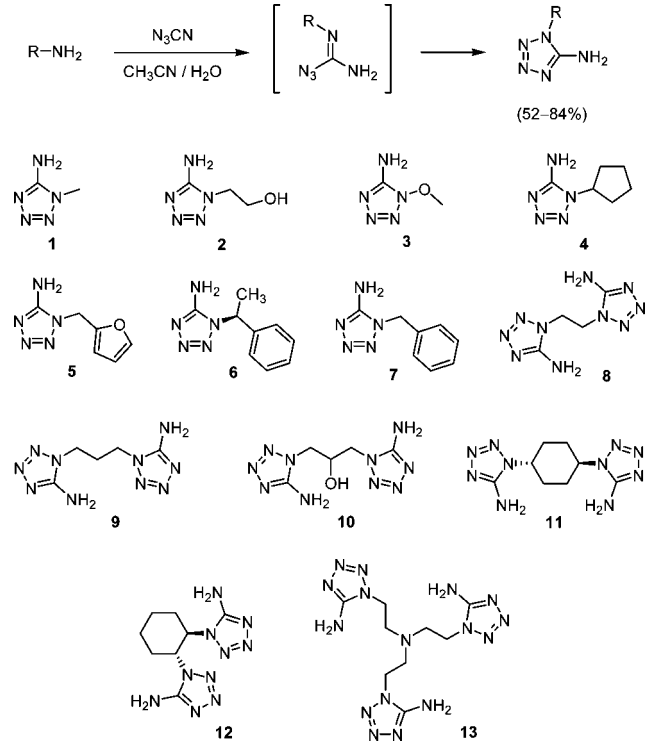
alkylation of 5-aminotetrazole with alkyl halides. However, selective alkylation of aminotetrazoles is not possible because of the competitive formation of 1- and 2-alkylated-5-aminotetrazoles.[4a,9] These isomers were separable by crystallization or column chromatography in very low yields. Another method for the synthesis of mono-, di-, and trisubstituted 5-aminotetrazoles is described using the mercury(II)-promoted attack of an azide anion on a thiourea.[10] The reaction proceeds through a guanyl azide intermediate which subsequently undergoes cyclization to the tetrazole. Di- and trisubstituted (benzotriazolyl)-carboximidamides from (benzotriazolyl)carboximidoyl chlorides (various substituents as alkyl, aryl, or heteroaryl) with sodium azide provide access to 1,*N*,*N*-trisubstituted 5-aminotetrazoles.[5] Reactions were performed at room temperature, and the aminotetrazole derivatives were obtained in 41−90% yield. Many methods for the synthesis of substituted aminotetrazoles are known,[11] but due to their importance, the development of new synthetic approaches using special reaction conditions continues as an active research area.

Recently, we have reported energetic nitrogen-rich derivatives of 1,5-diaminotetrazole generated in situ from cyanogen azide[12,13] and hydrazine derivatives.[14] However, amine derivatives are more suitable (commercial and inexpensive) and provide a variety of useful starting materials as possible replacements for 1,5-diaminotetrazoles. Our continuing interest in the development of 1-substituted 5-aminotetrazole compounds, which can be used for high-energy density materials or biologically active organic materials, has now been extended by the utilization of an excellent in situ method which involves reactions of cyanogen azide and primary amines (Scheme 1).

The commercially available amine compounds were reacted with 2−3 equiv of cyanogen azide dissolved in acetonitrile/water solution (4:1) to give initially the imidoyl azide as an intermediate. Subsequent cyclization of the intermediate led to the 1-substituted monoaminotetrazoles **1**−**7** in good yields [**1**[7] (61%), **2**[9b] (53%), **3** (70%), **4** (73%), **5** (74%), **6** (62%), **7** (52%)]. It is important to note that the synthesis of cyanogen azide from cyanogen bromide and sodium azide in dry acetonitrile should be performed with extreme care[12b,14] (see Supporting Information).

Scheme 1. Addition of a Primary Amine to Cyanogen Azide through the Intermediacy of an Imidoyl Azide and 1-Substituted 5-Aminotetrazoles



It is noteworthy that the current method can be efficiently applied to the preparation of bis(1-substituted-5-aminotetrazoles). Diamine compounds with 5−6 equiv of cyanogen bromide and excess sodium azide led to products in good yields [**8**[9c] (71%), **9**[9c] (84%), **10** (73%), **11** (72%), **12** (79%)] of bis(aminotetrazole) **8**−**12**. Removal of the acetonitrile/water solvent from the reaction mixture by air drying is followed by additional washing with acetonitrile and water (1:4). The structures of all aminotetrazole derivatives are supported by IR and ^{1}H, ^{13}C{^{1}H}, and ^{15}N NMR spectroscopic data as well as elemental analysis (see Supporting Information). The ^{1}H and ^{13}C{^{1}H} NMR spectra for **11** could not be recorded owing to its poor solubility in deuterated solvent. The three-substituted aminotetrazole **13** was obtained by reacting cyanogen azide with tris(aminoethyl)amine in water/acetonitrile using an analogous procedure (yield: 54%).

In Figure 1, the ^{15}N NMR spectra of **6** (top) at −333.89, −162.15, −89.60, −24.54, −7.32 ppm and **13** (bottom) with six signals at −351.98, −334.39, −173.92, −89.30, −20.52, and 6.87 are depicted. The signals of the primary amine appear as expected at high field in spectra with triplets (**6**: $^{1}J_{N,H}$ = 87 Hz; **13**: $^{1}J_{N,H}$ = 87 Hz). The

(8) Stolle, R.; Ehrmann, K.; Rieder, D.; Wille, H.; Winter, H.; Henke-Stark, F. *J. Prak. Chem.* **1932**, *134*, 282–309.

(9) (a) Henry, R. A.; Finnegan, W. G *J. Am. Chem. Soc.* **1954**, *76*, 926–928. (b) Finnegan, W. G.; Henry, R. A *J. Org. Chem.* **1959**, *24*, 1565–1567. (c) Barmin, M. I.; Gromova, S. A.; Mel'nikov, V. V. *Russ. J. Appl. Chem.* **2001**, *74*, 1156–1163.

(10) Batey, R. A.; Powell, D. A. *Org. Lett.* **2000**, *2*, 3237–3240.

(11) (a) Finnegan, W. G.; Henry, R. A.; Lieber, E. *J. Org. Chem.* **1953**, *18*, 779–791. (b) Percival, D. F.; Herbst, R. M *J. Org. Chem.* **1957**, *22*, 925–933. (c) Norris, W. P.; Henry, R. A. *J. Org. Chem.* **1964**, *29*, 650–660. (d) Demko, Z. P.; Sharpless, K. B. *J. Org. Chem.* **2001**, *66*, 7945–7950. (e) Himo, F.; Demko, Z. P.; Noodleman, L.; Sharpless, K. P. *J. Am. Chem. Soc.* **2003**, *125*, 9983–9987. (f) Butler, R. N.; Scott, F. L *J. Org. Chem.* **1966**, *31*, 3182–3187. (g) Peet, N. P *J. Heterocycl. Chem.* **1987**, *24*, 223–225.

(12) (a) Marsh, F. D.; Hermes, M. E. *J. Am. Chem. Soc.* **1964**, *86*, 4506–4507. (b) Marsh, F. D. *J. Org. Chem.* **1972**, *37*, 2966–2969. (c) McMurry, J. E.; Coppolino, A. P. *J. Org. Chem.* **1973**, *38*, 2821–2827. (d) Banert, K.; Joo, Y.-H.; Rüffer, T.; Walfort, B.; Lang, H. *Angew. Chem., Int. Ed.* **2007**, *46*, 1168–1171.

(13) Cyanogen azide, a colorless oil, was first isolated from the reaction of sodium azide and cyanogen chloride. The synthesis of cyanogen azide from sodium azide and cyanogen bromide and its reaction and characterization as well as handling were reported.[12a]

(14) Joo, Y.-H.; Twamley, B.; Garg, S.; Shreeve, J. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 6236–6239.

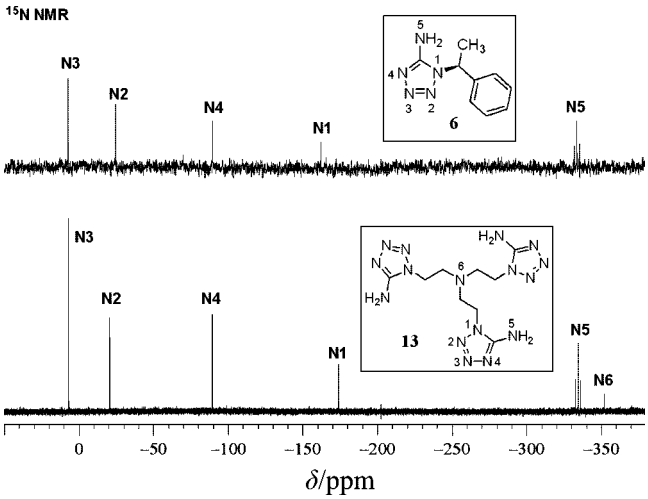


Figure 1. ^{15}N NMR spectra of **6** and **13** (delay of 10 s between pulses).

assignments are given based on the values of the chemical shifts of substituted aminotetrazole on comparison with the literature.[11e,14,15] For compound **13**, the N2 resonance (t, $^3J_{N,H} = 1.6$ Hz, N2) is split into triplets due to the coupling with the protons of $-CH_2-$. The N1 resonance was shown as slightly broadened by coupling with protons of ethylene. The signal for the N3 resonance was a singlet with no proton coupling observed.

The heats of formation for **2**−**13** were calculated with Gaussian 03[16] and are summarized in Table 1. These values were computed by using the method of isodesmic reactions. The enthalpy of an isodesmic reaction (ΔH_{r298}) is obtained by combining the MP2/6-311+G** energy difference for the reaction, the scaled zero points energies (B3LYP/6-31+G**), and other thermal factors (B3LYP/6-31+G**). All of the 1-substituted 5-aminotetrazoles exhibit positive heats of formation with **2**−**13** having values between 33.3 and 863.7 kJ•mol^{-1}. Density is one of the most important physical properties of energetic materials. The densities of most of the new aminotetrazoles range between 1.294 and 1.585 g•cm^{-3}. By using the experimental values for the densities of the 5-aminotetrazoles, **2**−**13**, the detonation pressures (P) and velocities (D) were calculated based on traditional Chapman−Jouget thermodynamic detonation theory using Cheetah 4.0 and 5.0 (see Supporting Information).[17] For compounds **8**−**13**, the calculated detonation pressures lie in the range between 14.61 and 19.88 GPa (comparable to TNT = 19.5 GPa and ADN = 23.7 GPa). Detonation velocities are found between 7177 and 7719 ms^{-1} (comparable to TNT = 6881 m•s^{-1} and ADN = 8074 m•s^{-1}). For initial safety testing, the impact sensitivity was tested according to BAM methods.[18] All compounds are insensitive toward impact with sensitivities >40 J (comparable to TNT = 15 J and TATB = 50 J).

Table 1. Physical Properties of 1-Substituted 5-Aminotetrazole Derivatives **2**−**13**

compd	yield [%]	T_m[a] [°C]	density[b] [g•cm^{-3}]	$\Delta_f H°_{298}$[c] [kJ•mol^{-1}]	$\Delta_f H°_{298}$ [kJ•g^{-1}]
2	53	160	1.511	33.3	0.258
3	70	166	1.503	226.7	1.97
4	73	202	1.294	213.8	1.40
5	74	159	1.432	226.7	1.37
6	62	193	1.398	260.2	1.38
7	52	194	1.382	300.7	1.72
8	71	274	1.567	536.6	2.74
9	84	287	1.567	513.9	2.44
10	73	256	1.585	323.2	1.43
11	72	346(dec.)	1.460	454.7	1.82
12	79	242	1.453	436.5	1.74
13	54	123	1.492	863.7	2.47

[a] Thermal decomposition temperature under nitrogen gas (DSC, 10 °C/min). [b] Gas pycnometer (25 °C). [c] Heat of formation (using 83.68 kJ•mol^{-1} for the enthalpy of sublimation for each compound; calculated via Gaussian 03).

In conclusion, we have developed a new method for the efficient preparation of 1-substituted 5-aminotetrazoles from cyanogen azide and amines. The reaction conditions for the formation of the final 1-substituted 5-aminotetrazoles are mild, and purification is simple. This synthesis of aminotetrazole derivatives could be utilized to prepare a variety of bioorganic compounds or organocatalysts as ligands. We are currently focusing our attention on efforts to discover compounds with high nitrogen content via this cyclization reaction and on application of the reaction for efficient syntheses of compounds that are useful for HEDM.

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Supporting Information Available: The experimental procedures, analytical data, and NMR spectra of products. This material is available free of charge via the Internet at http://pubs.acs.org.

OL8019742

(15) (a) Berger, S.; Braun, S.; Kalinowski, H.-O. *NMR-Spektroskopie von Nichtmetallen, Band 2*,^{15}N-NMR-Spektroskopie, Georg Thieme Verlag, Stuttgart: New York, 1992; pp 36−38. (b) Orendt, A. M.; Michl, J.; Reiter, J. *Magn. Reson. Chem.* **1989**, *27*, 1–3.

(16) Frisch, M. J., et al. *Gaussian 03*, revision D.01. See Supporting Information for full reference.

(17) (a) Fried, L. E.; Glaesemann, K. R.; Howard, W. M.; Souers, P. C. *CHEETAH 4.0 User's Manual*; Lawrence Livermore National Laboratory, 2004. (b) Bastea, S.; Fried, L. E.; Glaesemann, K. R.; Howard, W. M.; Souers, P. C.; Vitello, P. A. *CHEETAH 5.0 User's Manual*; Lawrence Livermore National Laboratory, 2007.

(18) (a) www.bam.de. (b) A portion of 20 mg of aminotetrazoles **2**−**13** was subjected to a drop-hammer test using a 10 kg weight dropped 40 cm height. A range in impact sensitivities from reference: Galvez-Ruiz, J. C.; Holl, G.; Karaghiosoff, K.; Klapötke, T. M.; Loehnwitz, K.; Mayer, P.; Noeth, H.; Polborn, K.; Rohbogner, C. J.; Suter, M.; Weigand, J. J. *Inorg. Chem.* **2005**, *44*, 4237−4253. (Insensitive > 40 J; less sensitive ≥ 35 J; sensitive ≥ 4 J; very sensitive ≤ 3 J).