Syntheses of *C*-Amino- and *C*-Azido-1,2,4-triazoles

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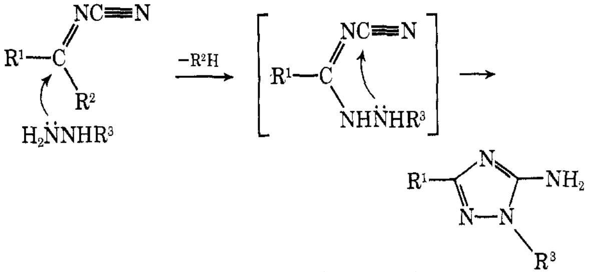
A series of *C*-amino-1,2,4-triazoles, substituted with methyl, dimethylamino, methoxy, and methylthio groups, was prepared from the appropriate *N*-cyanoazomethines and either hydrazine or methylhydrazine (eq 1). *C*-Azido-1,2,4-triazoles were prepared from the corresponding amines by diazotization followed by reaction with azide ion. When these diazotization reactions were carried out, the *C*-amino-1,2,4-triazoles derived from methylhydrazine, unlike those derived from hydrazine, yielded varying quantities of products depending on the acidity of the reaction media. Ir and proton nmr spectra of the *C*-azido-1,2,4-triazoles in various solvents indicated that none of them participates in imidoyl azide–tetrazole tautomerism, even at −82°.

C-Amino- and *C*-azido-1,2,4-triazoles were synthesized as part of an investigation of the possible imidoyl azide–tetrazole tautomerism of the azides. The *C*-amino-1,2,4-triazoles were prepared by the reaction of hydrazines with *N*-cyanoazomethines containing at least one good leaving group bonded to the azomethine carbon, an old but little-used method.[2-6] This reaction has been visualized as taking place by attack of the hydrazine, first on the azomethine carbon, and then on the carbon of the cyano group (eq 1).[2] We have used this method to obtain a series of *C*-amino-1,2,4-triazoles because it facilitates the preparation of 1,2,4-triazoles substituted with various groups, most of which have not been previously reported.


(1)

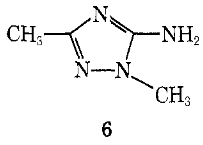
Results and Discussion

***C*-Amino-1,2,4-triazoles.** The reactants used and products formed when the method described above was implemented are listed in Table I.

Either the primary or secondary amino nitrogen atom of methylhydrazine can attack the azomethine carbon, giving rise to isomeric *C*-amino-1,2,4-triazoles. As indicated in Table I, both isomers (**6** and **7**) were isolated from the reaction of methylhydrazine with **1**. Only **11** was isolated from the reaction of methylhydrazine with **4**, although nmr spectra indicated the presence of two isomeric products.

Structures were assigned to isomers **6** and **7** on the basis of a previous preparation of **6**[14] and the assignments were confirmed when the nmr spectrum of **17** (prepared from **6**) proved to be identical with that of 1,3-dimethyl-1,2,4-triazole.[15]

Assignments of **6** and **11** to the major products formed in the reactions of methylhydrazine with **1** and **4**, respectively, mean that the less hindered primary amino nitrogen preferentially attacks the azomethine carbon (eq 1), consistent with the reactions of methylhydrazine with simpler acylating agents.[16-18]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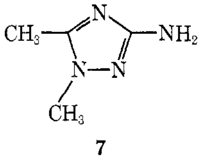
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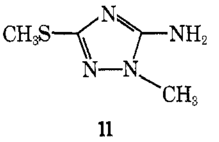
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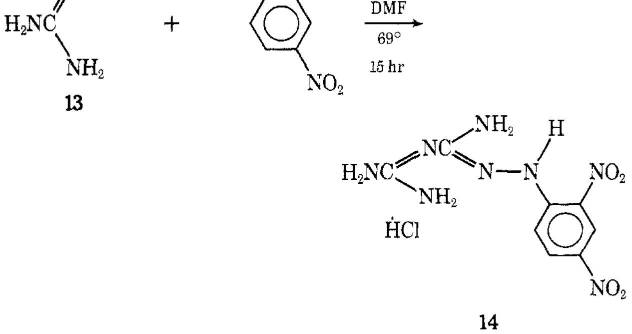
A change from polar to nonpolar solvents decreased the reaction rates of methylhydrazine with both **1** and **4**. Reactions of **4** in various solvents (acetonitrile, 95% ethanol, benzene) resulted in percentages of isomers which changed little (94–100% **11**); however, in reactions of **1** the per cent of **6** increased from 65 to 91% when the solvent was changed from 95% ethanol to benzene. We suggest that this increase in per cent of **6** may be due to a more selective attack by the least sterically hindered nitrogen atom of methylhydrazine with the decreased reaction rate.

Although the reactions of *N*-cyanoazomethines and hydrazines, indicated in Table I, proceeded readily, it is not a completely general method for preparing *C*-amino-1,2,4-triazoles. No reaction occurred when a solution of *N*-cyano-*S*-methylisothiourea (**12**), *p*-bromophenylhydrazine, and dimethylformamide (DMF) was refluxed for 12 hr.

When **12** and 2,4-dinitrophenylhydrazine were refluxed in DMF for 48 hr in an attempt to prepare 3,5-diamino-1-(2,4-dinitrophenyl)-1,2,4-triazole, the only compound that could be isolated from the reaction mixture was *m*-dinitrobenzene. It is probable that this transformation occurred by the action of atmospheric oxygen under the severe reaction conditions, since *m*-dinitrobenzene has been formed by the oxidation of 2,4-dinitrophenylhydrazine with manganese dioxide[19] and by the oxidation of 2,4-dinitrophenylhydrazones with ozone.[20]

Another method[21,22] was used in a second attempt to prepare 3,5-diamino-1-(2,4-dinitrophenyl)-1,2,4-triazole. When a suspension of cyanoguanidine (**13**), 2,4-dinitrophenylhydrazine hydrochloride, and DMF was heated, a solid precipitated which was formulated as **14** on the basis of its elemental analysis and nmr spectrum. The attack of amine salts on the cyano carbon of cyanoguanidine has been observed previously.[23,24]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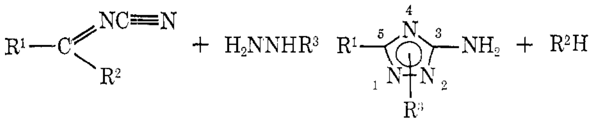
Unlike certain methylthio groups bonded to the 1,2,4-triazine nucleus,[25-27] the methylthio group of **10** could not be displaced by hydrazine. Hydrazine and **10** were refluxed in both 95% ethanol and acetonitrile for 22 hr without any reaction whatever.

Table I
C-Amino-1,2,4-triazoles Prepared from N-Cyanoazomethines



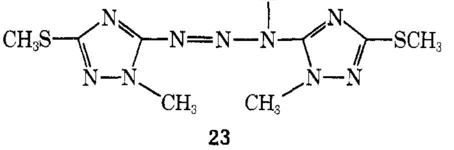
N-Cyanoazo-methine	R^1	R^2	R^3 (position on ring)	Triazole	Yield, %
1	CH_3	OC_2H_5	H[a]	**5**	59
1	CH_3	OC_2H_5	CH_3 (2)	**6**	83
1	CH_3	OC_2H_5	CH_3 (1)	**7**	
2	$(CH_3)_2N$	SCH_3	H[a]	**8**	95
3	CH_3O	OCH_3	H[a]	**9**	79
4	CH_3S	SCH_3	H[a]	**10**	92
4	CH_3S	SCH_3	CH_3 (2)	**11**	81

[a] 1,2,4-Triazoles of this type exist as tautomeric mixtures in which the hydrogen atom is bonded, primarily, to N-1 or N-2.[7-13]

C-**Azido-1,2,4-triazoles.** 5-Chloro-3-methylthio-1,2,4-triazole (**20**) was prepared by a method[28] in which the diazonium chloride formed from **10** was decomposed; however, the chloro group of **20**, like the methylthio group of **10**, proved to be unreactive toward nucleophilic substitution.[29] Compound **20** was refluxed together with equimolar quantities of sodium azide and ammonium chloride in DMF for 24 hr[30] and with equimolar quantities of hydrazine and triethylamine under the same conditions, but no reaction occurred in either case.

Reports of the preparation of five-membered heteroaromatic (pyrazole[31] and 1,3-thiazole[32]) azides by treating the diazonium salts with azide ion suggested that C-azido-1,2,4-triazoles could be obtained in the same way. Table II shows compounds, including the azides, that were prepared from C-amino-1,2,4-triazoles *via* the unisolated diazonium salts.

The diazotization reactions leading to **15** and **18–21** were relatively insensitive to the acidity of the media. In contrast, Table III illustrates how the percentages of products varied with the acidity of the aqueous solution when **11** was treated consecutively with nitrous acid and azide ion. In each reaction, in order to standardize conditions, the temperature was maintained below 1° while first a solution of sodium nitrite and then a solution of sodium azide was added; also, the second solution was added immediately following the first. The immediate addition of sodium azide solution was necessary since 1,3-bis(1-methyl-3-methylthio-1,2,4-triazol-5-yl)triazene (**23**) began precipitating during the addition of sodium nitrite solution in the reaction carried out at lowest acidity.



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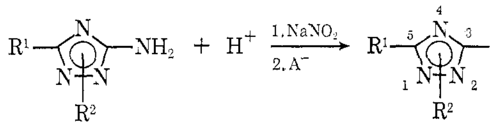
When the acidity of the reaction medium was greatest, the percentage of recovered amine starting material was greatest. Since the free base and not its conjugate acid is the species that is diazotized, at high concentrations of acid less amine is diazotized and, upon neutralization of the reaction mixture, most of it can be recovered.[33] On the other hand, when the acidity of the aqueous solution was lowest, the percentage of triazene formed was greatest. This is explained by the fact that the lower the hydrogen ion concentration, the greater the concentration of free base and the more likely it is to react with diazonium ion to form the triazene.

Table II
Compounds Prepared from the Diazonium Salts of C-Amino-1,2,4-triazoles



Product	R^1	R^2 (position on ring)	A	Normality[a]	Yield, %
15	CH_3	H[b]	N_3	2.0	76
16	CH_3	CH_3 (2)	N_3	0.72	10
17	CH_3	CH_3 (2)	H	0.41	36
18	$(CH_3)_2N$	H[b]	N_3	0.28	72
19	CH_3O	H[b]	N_3	0.54	80
20	CH_3S	H[b]	Cl	12	73
21	CH_3S	H[b]	N_3	0.81	70
22	CH_3S	CH_3 (2)	N_3	0.71	28

[a] Normality of the acidic solution before the addition of $NaNO_2$. [b] See footnote *a*, Table I.

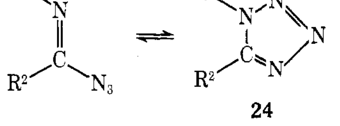
Table III
Variation of Product Percentages with Acidity of the Media in the Diazotization of 5-Amino-1-methyl-3-methylthio-1,2,4-triazole (11)

	Mol % of material recovered[a]		
Normality[b]	Amine **11**[c]	Azide **22**[c]	Triazene **23**[d]
10	70	30	
2.1	57	30	13
0.71		69	31

[a] At least 80% of the weight of **11** was accounted for. [b] Normality of the acidic solution before the addition of $NaNO_2$. [c] Percentages were determined by nmr spectroscopy. [d] Percentages were determined by weighing the isolated product.

Problems similar to those illustrated by Table III also arose when the preparations of **16**, **17**, and the isomer of **16**, 3-azido-1,5-dimethyl-1,2,4-triazole, were attempted. It should be noted that in all of these cases a methyl group, instead of hydrogen, is bonded to one of the ring nitrogen atoms. When 3-amino-5-alkyl-4-aryl-1,2,4-triazoles were diazotized, various products were formed depending on the acidity of the reaction medium;[34] however, other workers did not report differences in the diazotization reactions of N-substituted and unsubstituted C-amino-1,2,4-triazoles.[35]

The Absence of Imidoyl Azide–Tetrazole Tautomerism in *C*-Azido-1,2,4-triazoles. It has been found that the tetrazole tautomer (**24**) is favored when (1) R^1 and R^2 are electron donating; (2) the solvent is polar; and (3) the temperature is low.[36-39] It was reported that, when tetrazolyl hydrazine halides (**25**) were dissolved in 95% ethanol, an intramolecular displacement occurred which did not produce the expected triazolotetrazoles (**26**), but their valence tautomers, 3-aryl-5-azido-1,2,4-triazoles (**27**).[40] We have studied C-azido-1,2,4-triazoles with more varied substituents in various solvents and at low temperature.



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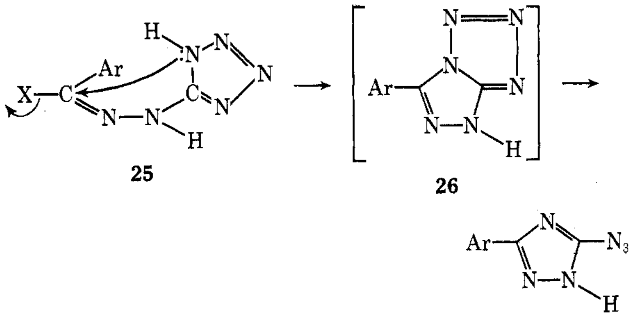
In addition to the sampling methods used to obtain the ir spectra reported in the Experimental Section, solutions of the C-azido-1,2,4-triazoles in $CHCl_3$ and DMSO-d_6 were examined by ir spectroscopy. Nmr spectra were obtained of solutions of C-azido-1,2,4-triazoles in $CDCl_3$ at 35°, acetone-d_6 at 25 and −82°,[41] and DMSO-d_6 at 35, 76, 125, and 175°. Since all the nmr spectra (except those of the samples in DMSO-d_6 at 175°) displayed the number of methyl group resonances (chemical shifts were constant for a given solvent regardless of temperature) expected for one of the tautomers, and all the ir spectra showed an azide band between 2120 and 2140 cm^{-1}, compounds **15, 16, 18, 19, 21,** and **22** all exist only as the azide tautomer.



25 **26** **27**

While the nmr samples were being heated to 175°, the Teflon caps were blown off the tubes, with the loss of sample, and the solutions became darker in color. The spectra taken after temperature equilibration showed peaks at the original chemical shifts along with a number of others of varying intensities. That these observations and spectra indicated decomposition of the azides, rather than a reversible change in the tautomerism, was proved since the spectra of the recooled samples were not identical with those taken before the sample had been heated.

The nonexistence of tetrazole tautomer in the case of *C*-azido-1,2,4-triazoles, regardless of the substituents, is probably due to the electron-withdrawing effect of the triazole ring itself. There are several instances in which the absence of tetrazole tautomer is attributed to the electron-withdrawing effect of a heteroaromatic ring fused to the ring bearing the azido group.[42-44]

Experimental Section

Melting points were determined on a Mel-Temp melting point apparatus and are uncorrected. Boiling points are also uncorrected. Uv spectra were recorded on a Bausch and Lomb Spectronic 505 spectrophotometer. Ir spectra were determined using Beckman IR-8 and Perkin-Elmer Model 137-B spectrophotometers.[45] Nmr spectra were obtained using Varian T-60 and HA-60-EL instruments employing tetramethylsilane as an internal standard. The mass spectra were determined with a Nuclide 12-90-G single-focusing instrument operating at 70 eV.[46] Both the solids and liquids were introduced *via* the direct inlet at the lowest temperature at which a spectrum could be obtained. The elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

Ethyl *N*-Cyanoacetimidate (1). A modification of the method reported by Huffman and Schaefer[5] was used to prepare this compound in 66% yield: bp 33° (0.1 Torr) [lit.[5] bp 95-96° (15 Torr)]; n_D 1.4512; uv max (95% EtOH) 232 nm (ϵ 1500); ir (capillary film) 3000 (m), 2205 (s), 1610 (s), 1410 (s), 1380 (s), 1320 (s), 1155 (m), 1040 (s), and 885 cm^{-1} (m); nmr ($CDCl_3$) δ 1.34 (t, 3, J = 7 Hz, CH_2CH_3), 2.40 (s, 3, CH_3), 4.30 (q, 2, J = 7 Hz, CH_2CH_3); mass spectrum (70 eV) m/e (rel intensity) 112 (13), 85 (15), 84 (12), 70 (18), 69 (15), 67 (17), 43 (100), 29 (18).

Dimethyl Cyanodithioimidocarbonate (4). A modification of the procedure by Hantzsch and Wolvekamp[47] was used to prepare this compound in 72% yield: mp 52.5-53.5° (lit.[47] mp 57°); ir (KBr) 2190 (s), 1470 (vs), 1310 (m), 1035 (s), and 945 cm^{-1} (s); nmr ($CDCl_3$) δ 2.66 (s, CH_3); mass spectrum (70 eV) m/e (rel intensity) 146 (91), 99 (100), 74 (73), 47 (48), 45 (64).

***N,N*-Dimethyl-*N'*-cyano-*S*-methylisothiourea (2).** This compound was prepared from **4** by the method of Wieland[48] in 100% yield, nmr ($CDCl_3$) δ 2.77 (s, 3, SCH_3), 3.27 [s, 6, $N(CH_3)_2$].

Dimethyl *N*-Cyanoimidocarbonate (3). A modification of the procedure of Wieland[48] was used to prepare this compound from **4** in 53% yield: mp 52-56° (lit.[48] mp 58-59°); ir ($CHCl_3$) 2220 (m), 1620 (s), 1485 (m), 1345 (s), 1035 (w), and 1000 cm^{-1} (w); nmr ($CDCl_3$) δ 4.00 (s, CH_3).

***N*-Cyano-*S*-methylisothiourea (12).** A procedure modeled after that of Davidson[49] was used to prepare this compound from **4** in 88% yield: mp 171-174° (lit.[50] mp 175°); uv max (H_2O) 244 nm (ϵ 9020); ir (fluorolube and Nujol mulls) 3310 (s), 3110 (s), 2200 (s), 2170 (s), 1660 (s), 1530 (s), 1480 (s), 1200 (s), and 985 cm^{-1} (s); nmr (DMSO-d_6) δ 2.46 (s, 3, CH_3), 8.50 (s, 2, NH_2); mass spectrum (70 eV) m/e (rel intensity) 115 (37), 68 (100), 60 (13), 48 (37), 47 (19), 45 (22), 43 (19).

Cyanoguanidine (13). A method similar to that described by Haag[51] was employed to prepare this compound in 88% yield: mp 209-211° (lit.[51] mp 205°); uv max (H_2O) 230 nm (ϵ 905); ir (fluorolube and Nujol mulls) 3440 (s), 3400 (s), 3340 (s), 3160 (s), 2210 (s), 2160 (s), 1640 (s), 1565 (s), 1500 (s), 1255 (s), 930 (m), 720 (m), and 665 cm^{-1} (m); nmr (DMSO-d_6) δ 6.60 (s, NH_2); mass spectrum (70 eV) m/e (rel intensity) 84 (100), 68 (50), 44 (13), 43 (54), 42 (25), 41 (12).

***C*-Amino-1,2,4-triazoles (Table I). General Procedure.** To a magnetically stirred solution of the *N*-cyanoazomethine (100 mmol) and acetonitrile (20 ml), surrounded by a cold water bath, was added the appropriate hydrazine (100 mmol). After the initial exothermic reaction, a precipitate formed, the water bath was removed, and the reaction mixture was stirred overnight. The precipitate was collected by suction filtration and washed with cold acetonitrile (10 ml) to give the following five compounds.

A. 3-Amino-5-methyl-1,2,4-triazole (5)[5] as white crystals: yield 59%; mp 149-150° (lit.[52] mp 148°); uv max (H_2O) 222 nm (ϵ 850); ir (fluorolube and Nujol mulls) 3420 (s), 3330 (s), 3220 (s), 3050 (s), 2700 (s, br), 1625 (s), 1595 (s), 1540 (s), 1475 (s), 1415 (s), and 1065 cm^{-1} (s); nmr (DMSO-d_6) δ 2.10 (s, 3, CH_3), 5.65 (s, 2, NH_2), 11.9 (s, 1, NH).

B. 3-Amino-5-dimethylamino-1,2,4-triazole (8) as white crystals in a yield of 95%, mp 187-189°. Sublimation (125°, 0.1 Torr) of this hygroscopic material gave an analytical sample: mp 189-191°; ir (fluorolube and Nujol mulls) 3200 (s, br), 1630 (s), 1555 (s), 1460 (s), 1405 (s), 1080 (m), 1050 (m), 930 (s), and 740 cm^{-1} (m); nmr (DMSO-d_6) δ 2.78 (s, 6, CH_3), 5.43 (s, 2, NH_2).

Anal. Calcd for $C_4H_9N_5$: C, 37.78; H, 7.13; N, 55.08. Found: C, 37.65; H, 7.07; N, 55.30.

C. 3-Amino-5-methoxy-1,2,4-triazole (9) as white crystals in a yield of 79%, mp 172-174°. Sublimation (110°, 0.1 Torr) of this hygroscopic material gave an analytical sample: mp 168-170°; ir (fluorolube and Nujol mulls) 3530 (m), 3350 (s), 3180 (s), 1660 (s), 1570 (s), 1490 (s), 1400 (s), 1345 (s), 1100 (m), 1040 (m), 1025 (m), and 980 cm^{-1} (m); nmr (DMSO-d_6) δ 3.75 (s, 3, CH_3), 5.90 (s, 2, NH_2), 11.15 (s, 1, NH).

Anal. Calcd for $C_3H_6N_4O$: C, 31.58; H, 5.30; N, 49.10. Found: C, 31.48; H, 5.29; N, 49.27.

D. 3-Amino-5-methylthio-1,2,4-triazole (10)[3] as white crystals in a yield of 92%, mp 138-139°. Recrystallization from acetonitrile gave an analytical sample: mp 139-140° (lit.[3] mp 135°); uv max (H_2O) 234 nm (ϵ 1740); ir (fluorolube and Nujol mulls) 3450 (s), 3320 (m), 3150 (s), 1645 (s), 1590 (s), 1500 (s), 1480 (m), 1465 (m), and 1280 cm^{-1} (s); nmr (DMSO-d_6) 2.43 (s, 3, CH_3) 5.98 (s, 2, NH_2), 11.94 (s, 1, NH).

Anal. Calcd for $C_3H_6N_4S$: C, 27.68; H, 4.65; S, 24.63. Found: C, 27.75; H, 4.76; S, 24.56.

E. 5-Amino-1-methyl-3-methylthio-1,2,4-triazole (11) as light yellow crystals in a yield of 81%, mp 103-106°. Recrystallization from acetonitrile gave an analytical sample: mp 105-106°; uv max (H_2O) 246 nm (ϵ 3200); ir (fluorolube and Nujol mulls) 3420 (s), 3340 (s), 3230 (s), 1620 (s), 1545 (s), 1475 (s), 1350 (s), 1310 (m), 1140 (m), and 745 cm^{-1} (m); nmr ($CDCl_3$) δ 2.60 (s, 3, SCH_3), 3.60 (s, 3, NCH_3), 4.48 (s, 2, NH_2).

Anal. Calcd for $C_4H_8N_4S$: C, 33.32; H, 5.59; N, 38.86. Found: C, 33.48; H, 5.74; N, 38.80.

The acetonitrile was evaporated from the original filtrate at reduced pressure to give 2.7 g of solid, the nmr ($CDCl_3$) spectrum of which showed the peaks due to **11**, listed above, as well as the following: δ 2.50 (s, 3), 3.57 (s, 3), 4.42 (s, 2). Assuming that the isomeric 3-amino-1-methyl-5-methylthio-1,2,4-triazole was responsible for these peaks, it comprised 30% of the solid or 6% of the total triazole produced in this reaction.

5-Amino-1,3-dimethyl-1,2,4-triazole (6). To a magnetically stirred solution of **1** (16.0 g, 143 mmol) and benzene (700 ml), surrounded by a cold water bath, was added methylhydrazine (8.0 ml, 153 mmol). The cooling bath was not replenished, and during continued stirring the solution became increasingly yellow and crystals precipitated. After 6 days, the reaction mixture was heated to boiling, the solution was decanted, and, upon recrystallization, the yellow crystals (8.4 g) were collected by suction filtration. Concentration of the filtrate produced a second crop (5.0 g) for a total yield of 83% triazole.

The first crop consisted of **6** which was recrystallized from benzene to give an analytical sample of white leaflets: mp 155–156° (lit.[14] mp 156°); uv max (H_2O) 222 nm (ϵ 1070); ir (fluorolube and Nujol mulls) 3320 (s), 3130 (s), 1650 (s), 1580 (s), 1535 (s), 1395 (s), 1350 (s), and 1115 cm^{-1} (m); nmr ($CDCl_3$) δ 2.20 (s, 3, CCH_3), 3.55 (s, 3, NCH_3), 5.23 (s, 2, NH_2).

Anal. Calcd for $C_4H_8N_4$: C, 42.84; H, 7.19; N, 49.97. Found: C, 42.82; H, 7.20; N, 50.01.

An nmr ($CDCl_3$) spectrum of the second crop showed that it consisted of 75% **6** and 25% **7**. Therefore, the minor component, **7**, comprised 9% of the total triazole obtained in this reaction.

Isolation of 3-Amino-1,5-dimethyl-1,2,4-triazole (7). A 2:1 mixture (9 g) of **6** and **7** was placed on a column of silica gel (300 g). The mixture was eluted with 40% acetone–60% trichloromethane. Fractions containing the first 1.5 g of triazole were combined and recrystallized from trichloromethane to give **7** (1.0 g). Recrystallization from benzene afforded an analytical sample of white crystals: mp 216–217° in a sealed tube; uv max (H_2O) 227 nm (ϵ 1350); ir (fluorolube and Nujol mulls) 3340 (s), 3190 (s), 1650 (s), 1560 (s), 1525 (s), 1425 (s), 1390 (s), and 655 cm^{-1} (s); nmr ($CDCl_3$) δ 2.32 (s, 3, CCH_3), 3.62 (s, 3, NCH_3), 4.10 (s, 2, NH_2).

Anal. Calcd for $C_4H_8N_4$: C, 42.84; H, 7.19; N, 49.97. Found: C, 43.08; H, 7.18; N, 50.07.

5-Methylamino-1,3-dimethyl-1,2,4-triazole Hydriodide (28). A magnetically stirred solution of **6** (100 mg, 0.834 mmol), iodomethane (1.0 ml, 16 mmol), and acetonitrile (5 ml) was heated at 87° for 22 hr. After the solution was allowed to cool, the crystallized white crystals were collected by suction filtration to yield **28** (45 mg, 21%): mp 229–230° dec; ir (KBr) 3260 (m), 3080 (m), 1670 (vs), 1600 (m), 1440 (m), 1165 (m), and 760 cm^{-1} (s); nmr (D_2O) δ 2.40 (s, 3, CCH_3), 3.54 (s, 3, NCH_3), 3.70 (s, 3, $^+NCH_3$), 4.64 (s, 2, $^+NH_2$); mass spectrum (70 eV) *m/e* (rel intensity) 128 (71), 127 (33), 126 (100), 125 (32), 69 (29), 57 (84), 42 (33).

Anal. Calcd for $C_5H_{11}IN_4$: C, 23.63; H, 4.36; N, 22.05. Found: C, 23.80; H, 4.30; N, 22.13.

Reaction of *N*-Cyano-*S*-methylisothiourea (12) with 2,4-Dinitrophenylhydrazine. A magnetically stirred solution of **12** (1.00 g, 8.70 mmol), 2,4-dinitrophenylhydrazine (1.72 g, 8.69 mmol), and DMF (10 ml) was refluxed for 48 hr. The reaction mixture was diluted with water (70 ml) and the dark precipitate (1 g) was collected by filtration. This material was boiled with acetonitrile and the insoluble portion (0.2 g) was removed by filtration. After the acetonitrile had been evaporated at reduced pressure, the residue was recrystallized from acetone–cyclohexane to yield *m*-dinitrobenzene (0.48 g, 33%). Recrystallization from ethanol–water gave a sample which melted at 87–88° (lit.[53] mp 89.5°). The ir and nmr spectra were identical with the published spectra[54] of *m*-dinitrobenzene.

Reaction of Cyanoguanidine (13) with 2,4-Dinitrophenylhydrazine Hydrochloride. A magnetically stirred mixture of **13** (1.00 g, 11.9 mmol), 50% aqueous 2,4-dinitrophenylhydrazine hydrochloride (5.58 g, 11.9 mmol), and DMF (10 ml) was heated at 69°. As the temperature increased, the reaction mixture became homogeneous, but within 1 hr a precipitate formed. After 17 hr, the precipitate was collected by suction filtration and washed thoroughly with acetone to give 1-(2,4-dinitroanilino)biguanide hydrochloride (**14**) as orange crystals (2.2 g, 58%), mp 246–247° dec. Recrystallization with DMF–95% EtOH afforded an analytical sample of fine orange needles, mp 250–251° dec. Silver chloride was precipitated when aqueous solutions of **14** and silver nitrate were combined. Compound **14** has the following spectral properties: ir (fluorolube and Nujol mulls) 3460 (m), 3420 (m), 3220 (m), 1680 (s), 1620 (s), 1575 (s), 1510 (s), 1490 (s), 1375 (s), and 1355 cm^{-1} (s); nmr (DMSO-d_6) δ 7.35 (d, 1, J = 10 Hz), 7.45 (s, 2), 7.95 (s, 5), 8.31 (q, 1, J = 10 Hz), 8.87 (d, 1, J = 3 Hz), 10.30 (s, 1); mass spectrum (70 eV) *m/e* (rel intensity) 265 (50), 183 (46), 38 (37), 36 (100).

Anal. Calcd for $C_8H_{11}ClN_8O_4$: C, 30.15; H, 3.48; N, 35.16; Cl, 11.13. Found: C, 30.34; H, 3.56; N, 34.99; Cl, 11.12.

***C*-Azido-1,2,4-triazoles (Table II). General Procedure.** A magnetically stirred solution of the amine (50 mmol), water (500 ml), and 96% sulfuric acid (quantity necessary to give the concentration indicated in Table II) was cooled to 0° by means of an ice-salt water bath. Then, in succession, solutions of sodium nitrite (55 mmol) in water (10 ml) and sodium azide (55 mmol) in water (10 ml) were added such that the temperature remained below 1°. After the second addition, the resulting solution was stirred overnight at 10°. The reaction mixture was neutralized with potassium bicarbonate, saturated with sodium chloride, and extracted with ethyl acetate (10 × 20 ml). The combined extracts were dried over anhydrous magnesium sulfate and the solvent was evaporated at reduced pressure.

A. 3-Azido-5-methyl-1,2,4-triazole (15). The solid residue was treated with activated charcoal and recrystallized from benzene to yield feathery, white crystals (76%): mp 144–145° (lit.[55] mp 143–145°); uv max (H_2O) 234 nm (ϵ 4470); ir (fluorolube and Nujol mulls) 3340 (w), 3170 (w), 3040 (m), 2930 (m), 2700 (m, br), 2430 (w), 2140 (s), 1500 (m), 1450 (m, br), 1420 (m), 1400 (m), 1375 (m), 1220 (w), and 1060 cm^{-1} (m); nmr ($CDCl_3$) δ 2.53 (s, 3, CH_3), 13.1 (s, 1, NH).

B. 5-Azido-1,3-dimethyl-1,2,4-triazole (16). The residual oil (0.7 g) was purified by molecular distillation (bath temperature 65–75°, pressure 0.13 Torr) to yield several drops of **16** as a yellow oil: ir (capillary film) 2140 (s), 1540 (s), 1505 (s), 1450 (s), 1410 (s), 1380 (s), 1340 (s), 1250 (s), 700 (m), and 690 cm^{-1} (m); nmr ($CDCl_3$) δ 2.30 (s, 3, CCH_3), 3.56 (s, 3, NCH_3).

Continuous extraction of the aqueous phase with trichloromethane gave 4.7 g of the amine starting material.

C. 3-Azido-5-dimethylamino-1,2,4-triazole (18). The solid residue (4.6 g, mp 153–154° dec) was treated with activated charcoal and recrystallized from benzene to give an analytical sample of yellow crystals: mp 153–154° dec; ir (fluorolube and Nujol mulls) 3330 (w), 2950 (m, br) 2410 (w), 2130 (s), 1640 (s), 1525 (s), 1430 (s), 1405 (s), 1350 (m), 1210 (m), 1045 (m), 930 (m), and 720 cm^{-1} (m); nmr ($CDCl_3$) δ 3.00 (s, 6, NCH_3), 11.7 (s, 1, NH).

Anal. Calcd for $C_4H_7N_7$: C, 31.37; H, 4.61; N, 64.03. Found: C, 31.40; H, 4.50; N, 64.12.

Continuous extraction of the aqueous phase with trichloromethane gave 1.1 g of amine starting material. The overall yield of azide was 72%.

D. 3-Azido-5-methoxy-1,2,4-triazole (19). The solid residue (80%, mp 106–108°) was treated with activated charcoal and recrystallized from benzene to afford an analytical sample of yellow crystals: mp 108–109°; ir (fluorolube and Nujol mulls) 3360 (w), 3200 (m), 3100 (m), 3020 (m), 2900 (m), 2850 (m), 2780 (m), 2720 (m), 2440 (w), 2130 (s), 1600 (s), 1535 (s), 1440 (s), 1395 (s), 1220 (m), and 1070 cm^{-1} (m); nmr ($CDCl_3$) δ 4.07 (s, 3, OCH_3), 11.70 (s, 1, NH).

Anal. Calcd for $C_3H_4N_6O$: C, 25.72; H, 2.88; N, 59.99. Found: C, 25.60; H, 2.87; N, 60.19.

E. 3-Azido-5-methylthio-1,2,4-triazole (21). The solid residue was treated with activated charcoal and recrystallized from benzene to yield an analytical sample of **21** (0.76 g, 70%) as light yellow crystals: mp 108–109°; uv max (H_2O) 238 nm (ϵ 6350); ir (fluorolube and Nujol mulls) 3360 (w), 3150 (m), 2940 (m), 2800 (m), 2440 (w), 2140 (s), 1490 (s), 1340 (m), 1315 (m), 1220 (m), and 1030 cm^{-1} (m); nmr ($CDCl_3$) δ 2.67 (s, 3, SCH_3), 12.50 (s, 1, NH).

Anal. Calcd for $C_3H_4N_6S$: C, 23.07; H, 2.58; N, 53.82. Found: C, 22.92; H, 2.57; N, 53.84.

F. 5-Azido-1-methyl-3-methylthio-1,2,4-triazole (22). After the reaction mixture was stirred overnight at 10°, a precipitate was collected by suction filtration and washed with water to yield 61% of 1,3-bis(1-methyl-3-methylthio-1,2,4-triazol-5-yl)triazene (**23**), mp 181–184° dec. This material was treated with activated charcoal and recrystallized from trichloromethane to afford an analytical sample of tan crystals: mp 191–192° dec; ir (fluorolube and Nujol mulls) 3210 (m), 3110 (m), 3040 (m), 2940 (m), 1590 (s), 1475 (s), 1385 (s), 1360 (s), 1345 (s), and 1215 cm^{-1} (s); nmr (DMSO-d_6) δ 2.74 (s, 6, SCH_3), 3.80 (s, 6, NCH_3), 12.8 (s, 1, NH); mass spectrum (70 eV) *m/e* (rel intensity) 299 (3), 271 (3), 156 (100), 128 (29), 82 (42), 43 (33), 15 (28).

Anal. Calcd for $C_8H_{13}N_9S_2$: C, 32.10; H, 4.38; N, 42.11. Found: C, 31.99; H, 4.43; N, 42.40.

The filtrate was neutralized, saturated, and extracted with trichloromethane (7 × 20 ml). The dark oil obtained by evaporation of the solvent from the dried, combined extracts was distilled to yield 28% of 5-azido-1-methyl-3-methylthio-1,2,4-triazole (**22**), bp 69–71° (0.12 Torr). Molecular distillation gave an analytical sample of yellow oil: ir (capillary film) 3340 (w), 2420 (w), 2120 (s), 1500 (s), 1425 (s), 1350 (s), and 1215 cm^{-1} (m); nmr ($CDCl_3$) δ 2.67 (s, 3, SCH_3), 3.67 (s, 3, NCH_3).

Anal. Calcd for $C_4H_6N_6S$: C, 28.23; H, 3.55; N, 49.38; S, 18.84. Found: C. 28.34; H, 3.62; N, 49.15; S, 18.68.

Consecutive Treatment of 3-Amino-1,5-dimethyl-1,2,4-triazole (7) with Nitrous Acid and Azide Ion. The general procedure for preparing the azides was employed using the following reagents: **7** (90 mg, 0.80 mmol); water (10 ml); 96% sulfuric acid

(78 mg, 0.76 mmol); sodium nitrite (97%, 65 mg, 0.91 mmol) in water (1 ml); and sodium azide (55 mg, 0.85 mmol) in water (1 ml). After the reaction mixture has been stirred overnight at 10°, a precipitate was collected by suction filtration and washed with water to yield 16 mg (17%) of 1,3-bis(1,5-dimethyl-1,2,4-triazol-3-yl)triazene (**29**): mp 226-228° dec; nmr (DMSO-d_6) δ 2.37 (s, 3, CCH_3), 3.74 (s, 3, NCH_3); mass spectrum (70 eV) m/e (rel intensity) 253 (3), 207 (5), 124 (100), 96 (48), 55 (55), 42 (52).

The filtrate was neutralized, saturated, and extracted with trichloromethane (6 × 5 ml). Evaporation of the solvents from the dried, combined extracts gave a yellow semisolid (60 mg). The nmr (DMSO-d_6) spectrum of this material showed peaks due to the triazene as well as the following: δ 2.51 (s, 3), 3.93 (s, 3). The appearance of a strong band at 2140 cm^{-1} in the ir ($CDCl_3$) spectrum indicated the presence of 3-azido-1,5-dimethyl-1,2,4-triazole.

1,3-Dimethyl-1,2,4-triazole (17). To a mechanically stirred solution of **6** (7.22 g, 64.5 mmol), 95% ethanol (400 ml), and 96% sulfuric acid (4.60 ml, 82.8 mmol) was added a solution of sodium nitrite (97%, 7.00 g, 98.5 mmol) and water (15 ml), whereupon a solid precipitated. The reaction mixture was heated at 65° for 15 hr and the resulting solution was concentrated to 30 ml at reduced pressure. The concentrate was diluted with water (150 ml), neutralized with potassium bicarbonate, saturated with sodium chloride, and extracted with trichloromethane (6 × 30 ml). After the combined extracts were dried over anhydrous magnesium sulfate and the solvent was evaporated at reduced pressure, the residual brown oil (5.5 g) was distilled to yield **17** (1.85 g, 36%), bp 25-27° (0.12 Torr) [lit.[15] bp 83° (20 Torr)]. Molecular distillation gave an analytical sample of colorless oil: ir (capillary film) 3120 (m), 2950 (m), 1525 (s), 1310 (s), 1195 (s), 740 (m), and 695 cm^{-1} (m); nmr ($CDCl_3$) δ 2.39 (s, 3, CCH_3), 3.86 (s, 3, NCH_3), 7.93 (s, 1, CH) [lit.[15] nmr ($CDCl_3$) δ 2.38 (s, 3, CCH_3), 3.84 (s, 3, NCH_3), 7.94 (s, 1, CH)].

Anal. Calcd for $C_4H_7N_3$: C, 49.47; H, 7.27; N, 43.27. Found: C, 49.26; H, 7.13; N, 43.17.

3-Chloro-5-methylthio-1,2,4-triazole (20). A procedure modeled after that of Reilly and Drumm[28] was used to convert **10** to **20** in 73% yield. Treatment with activated charcoal and recrystallization from ethyl acetate gave an analytical sample of white leaflets: mp 177-178°; uv max (H_2O) 228 nm (ϵ 2820); ir (fluorolube and Nujol mulls) 3090 (s), 2900 (s, br), 2750 (s), 1445 (s), 1305 (s), 1290 (s), 1030 (s), and 705 cm^{-1} (s); nmr (DMSO-d_6) δ 2.64 (s, 3, SCH_3), 14.30 (s, 1, NH).

Anal. Calcd for $C_3H_4ClN_3S$: C, 24.08; H, 2.70; N, 28.09; S, 21.43. Found: C, 24.40; H, 2.78; N, 28.36; S, 21.68.

Procedure for Variable-Temperature Nmr of *C*-Azido-1,2,4-triazoles. Nmr spectra were obtained on a Varian HA-60-EL instrument equipped with a variable-temperature probe. Sample temperatures above 35° were achieved by passing air over heating coils in the probe accessory. Temperatures below 35° were obtained by controlling the vaporization of liquid nitrogen from a Dewar flask by means of an immersed heater. Probe temperatures were monitored by measuring the difference in chemical shifts of the two signals of ethylene glycol for high temperatures (35-175°) and methanol for low temperatures (35 to −82°). For the high-temperature study, the azidotriazoles were dissolved in DMSO-d_6 (10% w/v); for the low-temperature study, solutions of acetone-d_6 (5% w/v) were used.

Registry No.—**1**, 1558-82-3; **2**, 51108-31-7; **3**, 24771-25-3; **4**, 10191-60-3; **5**, 4923-01-7; **6**, 51108-32-8; **7**, 34776-19-7; **8**, 51108-33-9; **9**, 51108-34-0; **10**, 45534-08-5; **11**, 51108-35-1; **12**, 51108-41-9; **13**, 51108-42-0; **14**, 51108-43-1; **15**, 15760-26-6; **16**, 461-58-5; **17**, 51108-36-2; **18**, 21041-86-1; **19**, 51108-37-3; **20**, 16778-76-0; **21**, 51108-38-4; **22**, 51108-39-5; **23**, 51108-40-8; **28**, 51108-44-2; **29**, 51108-45-3; H_2NNH_2, 302-01-2; H_2NNHMe, 60-34-4; 2,4-dinitrophenylhydrazine, 119-26-6.

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