Synthetic Methods

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Activation of the C–F Bond: Transformation of $CF_3N{=}N$- into 5-Azidotetrazoles**

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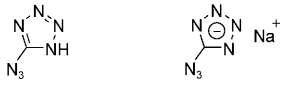
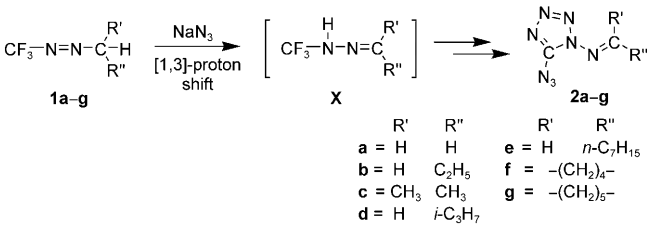
Considerable attention in recent years has been directed toward the synthesis of energetic heterocyclic compounds including the syntheses and applications of new energetic tetrazole derivatives. Recently, many kinds of energetic tetrazole compounds, some of which contained substituents such as azide groups, were reported.[1] The development of new synthetic routes towards energetic compounds continues to be a topic of significant interest in synthetic chemistry. Many papers have dealt with the preparation of 5-azidotetrazoles.[2] Nearly 70 years ago, 5-azidotetrazole and sodium 5-azidotetrazolate were prepared by the reaction of cyanogen halide (ClCN or BrCN) with sodium or barium azide and acid (Scheme 1).[3] Further detailed investigation on the syntheses and characterizations of 5-azidotetrazoles have been carried out.[4]



Scheme 1. 5-azidotetrazole and a 5-azidotetrazolium salt.

The reaction of trifluoronitrosomethane with organic amines forms the corresponding trifluoromethylazo compounds.[5] Several reactions of methyl(trifluoromethyl)diazene (**1a**, Scheme 2), including fluorination with metal fluorides (CoF_3, MnF_3) and chlorination with chlorine under UV irradiation, have been studied.[5g,6] With sodium azide, the sole product, formed in surprisingly good yield, from **1a** is the 5-azidotetrazole (**2a** Scheme 2).

Attempts to extend this methodology using other trifluoromethyldiazene compounds ($CF_3N{=}N$-alkyl), **1a–g**, revealed that the success of this reaction as a route to new energetic 5-azidotetrazoles, **2a–g**, is entirely a function of the alkyl group.



Scheme 2. Synthesis of several 5-azidotetrazoles, **2a–g**.

The presence of a hydrogen atom bonded to the α carbon of the substituent alkyl group of **1a–g** is crucial for this reaction to occur. For example, with groups such as *tert*-butyl or phenyl (that is, substituents with no α hydrogen atom), the reaction did not occur even under vigorous reaction conditions. However, in the presence of an α hydrogen atom, 5-azidotetrazoles, **2a–g**, were obtained in good yields from the corresponding trifluoromethylazoalkanes (**1a–g**), respectively (Scheme 2).[7]

5-Azidotetrazoles **2a–g**, with the exception of compound **2c**, were transparent, colorless or straw-colored viscous liquids which tended to form supercooled liquids rather than crystallizing. Compound **2c** solidified gradually after being allowed to stand at 25 °C for several weeks.

In the infrared spectra of the 5-azidotetrazoles, two characteristic strong bands at 1532–1545 and 2155–2160 cm^{-1} which are assigned to the asymmetric -N=C< and -N_3 stretching vibrations, respectively, are present. The ^{19}F NMR spectrum for the reaction mixture of **1c** contained signals at $\delta = -63.85$ and -63.94 ppm which are further downfield than that for the signal assigned to CF_3-N=N- ($\delta = -74.3$ ppm). All three of the resonances were significantly diminished by reaction completion. To obtain insight into the reaction intermediate, ^1H and ^{19}F NMR spectroscopic studies were used to monitor the behavior of **1c** in either CD_3CN or $[D_6]$DMSO as solvent in the presence or absence of a weak base, potassium fluoride (see Supporting Information). No change was observed in the ^1H and ^{19}F NMR spectra of **1c** when the reaction was carried out in CD_3CN for a week without base. In sharp contrast, a change was detected after five hours in the presence of a catalytic amount of potassium fluoride. The ^1H NMR spectrum (in CD_3CN solution) showed new peaks appearing at $\delta = 1.89$, 1.94, and 6.75 ppm with a concomitant decrease in the intensity of peaks at $\delta = 1.36$, 1.38 and 4.15 ppm, owing to the isopropyl group of **1c**. Similarly, the ^{19}F NMR spectrum showed a pair of new peaks at $\delta = -63.85$ and -63.94 ppm with a concomitant decrease in intensity of the peak at $\delta = -74.9$ ppm ($CF_3N{=}N$-). These newly formed peaks were identical with those detected in the

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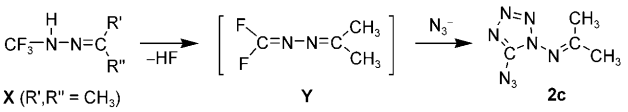
reaction mixture during the reaction. The ^{13}C NMR (CD_3CN) spectrum showed peaks ($\delta = 16.8$, 24.8, 120.9; q, $^1J(C,F) = 273$ Hz, and 155.6 ppm) for this intermediate (compared to **1c**, $\delta = 19.8$, 70.3, 120.9 ppm; q, $^1J(C,F) = 273$ Hz). This reaction proceeded rapidly in [D_6]DMSO to give the same product, even without addition of base. On the basis of these results, the intermediate obtained from azo compound **1c** was identified as the hydrazone compound **X** (Scheme 2, R′, R″ = CH_3) which was formed as the result of a base-catalyzed [1,3]-proton shift from the isopropylmethine group to the nitrogen of the CF_3N group (see Supporting Information).[8] The electron-withdrawing CF_3 group contributes to the acceleration of this isomerization.

To determine the difference between the Gibbs free energies (298 K) of **1c** and **X** (R′, R″ = CH_3), a computational study (MP2/6-311++G**) was performed on the [1,3]-proton shift, showing a difference of $-33\ kJ\,mol^{-1}$. The increased stability of the **X** (R′, R″ = CH_3) configuration in comparison with **1c** allows the facile [1,3]-proton shift from **1c** to **X** (R′,R″ = CH_3). Imidoyl halides (-N=CX_2; X = Cl, F) are very reactive toward N_3^-, and this is an important reaction for the synthesis of tetrazoles.[2a] In this reaction, different substitution products are obtained depending both on the reaction conditions (solvent, temperature, molar ratio of NaN_3) and the alkyl substrate linked to the imidoyl halide. In the case of the reaction of perfluoroalkylimino compounds with $(TMS)N_3$, only monoazido-substituted products are formed, without the formation of tetrazoles.[9] Secondary trifluoromethylamines were formed by reactions of imidoyl halides with hydrogen fluoride.[10]

Considering the facile transformation from a secondary trifluoromethylamine into a difluoroazomethine and the high reactivity of the imidoyl fluoride, it is likely that a difluoromethylidene hydrazone compound, CF_2=N-N=$C(CH_3)_2$ (**Y**), is formed as the reactive intermediate from **X** (R′, R″=CH_3) in the presence of NaN_3. The following reaction for the formation of **2c** from **1c** via **Y** is a probable reaction pathway (Scheme 3).



Scheme 3. Subsequent reaction of **X** (R′, R″ = CH_3) with NaN_3.

The intermediate **Y** was not detected by ^{19}F NMR spectral studies on the reaction mixture,[11] suggesting that the formation of **X** (R′, R″ = CH_3) is the rate-determining step and that the subsequent reaction of **Y** involving an addition-elimination reaction by N_3^- leading to **2c** occurs more rapidly. Therefore, in the present reaction, there are several favorable factors including the formation of **X** (R′, R″ = CH_3) [1,3]-proton shift, and the appropriate electron-donating substituent (-N=CR_1,R_2), which enables the tetrazole ring-closure to take place, forming carboimino-functionalized 5-azidotetrazole **2c**.

We also investigated the preparation of labeled **2c** from the reaction of **1c** with $Na^{15}N_3$.[12] In the ^{15}N NMR spectrum of **2c**, six signals are observed (Figure 1). The labeled azide nitrogen signals are at $\delta = -297.9$ (N_α), -143.5 (N_β) and -137.9 (N_γ), respectively. Three ^{15}N signals at $\delta = -75.5$ (N4), -16.5 (N2), and 4.3 (N3) are assigned to tetrazole by studying ^{15}N,^{15}N coupling.

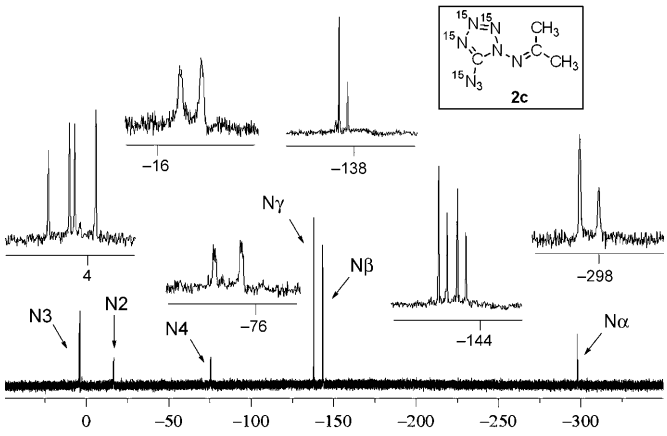


Figure 1. ^{15}N-labeled ^{15}N NMR spectrum of **2c**.

The structure of **2c** was determined by single-crystal X-ray diffraction.[13] A thermal ellipsoid plot of **2c** is given in Figure 2.

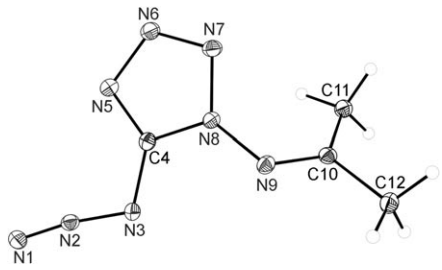


Figure 2. Molecular structure of **2c** with thermal ellipsoids set at 30% probability. Selected bond lengths [Å] and angles [°]: C4–N5 = 1.320(1), N5–N6 1.368(1), N6–N7 1.298(1), N7–N8 1.359(1), N8–C4 1.337(1), N8–N9 1.407(1), C4–N3 1.388(1), N3–N2 1.258(1), N2–N1 1.119(1); N5-C4-N8 = 109.80(8), C4-N8-N7 108.08(8), C4-N3-N2 112.89(8), N8-N9-C10 115.84(8); torsion angles [°]: N8-C4-N3-N2 172.77(8), C4-N8-N9-C10 136.88(9).

The melting, crystallization, and thermal decomposition points (decomposition onset) were determined for the 5-azidotetrazoles **2a**–**g** by differential scanning calorimetry (DSC, Table 1). These tetrazoles are thermally stable to approximately 150 °C. Owing to their tendency to form supercooled liquids in preference to crystalline solids, 5-azidotetrazoles **2d**, **2f**, and **2g** required time and patience to allow materials to crystallize. Crystallization was not successful for **2e**. However, in DSC studies, compounds **2d** and **2e** showed crystallization temperatures at −41 °C and −36 °C, respectively.[14]

The heats of formation for **2a**–**g** were calculated using Gaussian '03[15] and are also summarized in Table 1. These values were computed by using the method of isodesmic

Table 1: Thermal and physical properties of the 5-azidotetrazoles **2a**–**g**.[a]

Comp'd	Crystallization Temp.[a] [°C]	M.p.[a] [°C]	T_d[a] [°C]	Density[b] [g cm^{-3}]	$\Delta H°_f$[c] [kJ mol^{-1}]	$\Delta H°_f$ [kJ g^{-1}]	P[d] [GPa]	D[d] [m s^{-1}]
2a[e]	–	–	165	1.43	820.5	5.94	21.86	7635
2b	–	–	163	1.24	750.6	4.52	13.03	6691
2c[f]	–	67	149	1.36	730.3	4.39	16.45	7251
2d[g]	−41	15	166	1.20	719.4	3.99	11.83	6473
2e[g]	−36	−2	162	1.18	651.8	2.76	11.68	6429
2f[f]	–	42	153	1.39	752.7	3.65	15.99	7138
2g[f]	–	34	155	1.26	730.7	3.32	12.42	6523

[a] DSC under nitrogen gas 10 °C min^{-1}. [b] gas pycnometer. [c] calculated in Gaussian '03. [d] calculated using 83.68 kJ mol^{-1} for the enthalpy of sublimation for each compound in Cheetah 5.0. [e] Measured as viscous liquids for all compounds unless otherwise stated. [f] Solid sample obtained by recrystallization. [g] see Supporting Information.

reactions (see Supporting Information). The enthalpy of an isodesmic reaction (ΔH_{r298}) is obtained by combining the MP2(full)/6-311 + G** energy difference for the reaction, the scaled zero-point energies, and other thermal factors. All the 5-azidotetrazoles exhibit positive heats of formation with **2a** having the highest value (820.5 kJ mol^{-1}). By using the experimental values for the densities of the new substituted tetrazoles, **2a**–**g**, the detonation pressures (P) and velocities (D) were calculated based on traditional Chapman–Jouget thermodynamic detonation theory using Cheetah 5.0.[16] It can be seen that, with the exception of 2a, the new 5-azidotetrazoles exhibit lower detonation pressures than TNT ($P = 20$ GPa), attributed mainly to their lower densities.

Experimental Section

Caution: When handling these energetic materials, small scale and best safety practices (leather gloves, face shield) are strongly encouraged. We experienced an explosion in handling **2a** when the stopcock with a ground joint was opened after drying on the vacuum line. These 5-azidotetrazoles are very sensitive towards friction. Impact sensitivities for **2b**, **2c**, **2e** and **2f** were determined to be less than 1 J (BAM Fallhammer test).

2c: In a 50 mL Schlenk tube, **1c** (0.111 g, 0.79 mmol) and NaN_3 (0.127 g, 2.00 mmol) were taken up in CH_3CN (5 mL). The resultant solution was held at 55 °C for 10 h. The solvent was removed, and the residue was extracted with chloroform which when evaporated to leave a colorless liquid. Yield 99 %, 131 mg. Crystals suitable for single-crystal X-ray structure determination were obtained from chloroform/*n*-hexane.

IR (liq. film): $\tilde{\nu} = = 2159$ (s; $\nu_{as}(N_3)$), 1535 cm^{-1} (s; $\nu_{as}(N{=}C)$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.30$ (s, 3H), 2.13 ppm (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 21.5$ (q), 26.3 (q), 149.7 (s), 182.5 ppm (s); ^{15}N NMR (50.7 MHz, $CDCl_3$, 25 °C, CH_3NO_2): $\delta = -297.9$ (d, $^1J = 14.5$ Hz, N_α), −143.5 (dd, $^1J = 14.5$ Hz, $^1J = 6.5$ Hz, N_β), −137.9 (d, $^1J = 6.5$ Hz, N_γ), −75.5 (ddd, $^1J = 20.3$ Hz, $^2J = 1.6$ Hz, $^2J = 0.8$ Hz, N4), −16.5 (dd, $^1J = 16.3$ Hz, $^2J = 1.6$ Hz, N2), −4.3 ppm (dd, $^1J = 20.3$ Hz, $^1J = 16.3$ Hz, N3); MS (FAB; 3-nitrobenzyl alcohol matrix): $C_4H_6N_8$, 167.0320 (100) [$M^+ + H$], 333.0907 (9) [$2M^+ + H$].

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Keywords: azo compounds · C–F activation · hydrazones · nitrogen heterocycles · tetrazoles

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[7] **1a**–**g**:NaN_3 = 1:2–2.5 mmol and CH_3CN (5 mL) were used unless otherwise stated. Yield: **2a** (**1a**:NaN_3 = 1:1, 25 °C/24 h, 49 % yield, 63.8 mg), **2b** (60 °C/8 h, 78 %, 88.4 mg), **2c** (55 °C/10 h, 99 %, 131 mg), **2d** (60 °C/8 h, 98 %, 119 mg), **2e** (25 °C/24 h, 74 %, 125 mg), **2e** (**1e**:$(CH_3)_3SiN_3$ = 1:2, 25 °C/24 h, 75 %, 92.4 mg), **2f** (60 °C/8 h, 89 %, 110 mg), **2g** (60 °C/8 h, 93 %, 139 mg).

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[11] I. Ruppert, *Tetrahedron Lett.* **1980**, *21*, 4893 – 4896; The difluoroimino group (CF_2=N-) can be easily identified by ^{19}F NMR spectroscopy, as it gives rise to two doublets in the region of $\delta = -42$ to -49 and -56 to -58 ppm.

[12] Labeled **2c**, CF_3N=N*i*Pr (20.1 mg, 0.14 mmol), $Na^{15}N_3$ (21.9 mg, 0.32 mmol), CH_3CN (2.5 mL), 25 °C/24 h, 86 % Yield, 18.3 mg.

[13] Crystal Data: **2c**: ($C_4H_6N_8$): $M_r = 166.17$; crystal size $= 0.28 \times 0.20 \times 0.16$ mm^3; monoclinic, space group $P21/n$, $a = 8.8038(3)$, $b = 7.1821(2)$, $c = 11.8729(4)$ Å, $\beta = 96.665(1)°$, $V = 745.65(4$ Å^3, Z=4, $2\theta_{max} = 55°$, 1715 independent reflections, $R_1 = 0.309$ for 1161 reflections with $I > 2\sigma(I)$ and $wR_2 = 0.0790$, 134 parameters. CCDC 685655 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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