# Rearrangements of Substituted 3-Azidoazetidines: Unexpected Formation of a Substituted Oxazole



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Thermolysis of neat *N*-carboethoxy-3-azido-3-ethylazetidine (**3**) at 200° under argon produced the corresponding cyclic imine **4** (68% yield). Prolonged refluxing of a mixture of *N*-triflylazetidin-3-one (**7**), sodium azide, and titanium tetrachloride in acetonitrile solvent afforded recovered **7** (25% yield) along with a colorless microcrystalline solid, **8**, mp 104-105° (20% yield), whose structure was established unequivocally *via* application of X-ray crystallographic methods.

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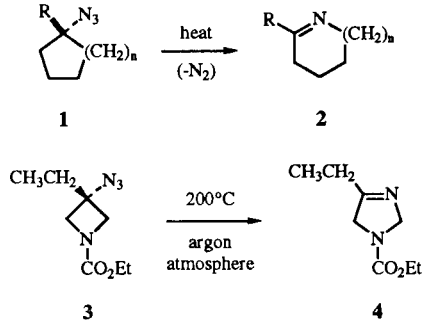
Electrophilic additions of reagents of the type $X^{\delta+}Y^{\delta-}$ across the highly strained N-C(3)σ-bond in substituted azabicyclo[1.1.0]butanes have been used to synthesize *N*,3-disubstituted azetidines [1,2]. Subsequently, these substituted azetidines have been converted into *N*-substituted azetidin-3-ones, which in turn have been utilized as intermediates in the synthesis of 1,3,3-trinitroazetidine, an important energetic material [1c,3].

We are interested in further exploring the chemistry of *N*,3-disubstituted azetidines and *N*-substituted azetidin-3-ones. In this connection, we sought to examine ring expansion reactions of 3-azidoazetidines as a means to synthesize new nitrogen-containing heterocyclic systems. As a first step toward accomplishing this objective, we focused our attention upon Schmidt-Curtius type rearrangements which proceed *via* intramolecular 1,2-shift of an alkyl or aryl group from a carbon terminus to an adjacent electron-deficient nitrogen terminus.

Thermolyses of alicyclic azides, *e.g.*, **1**, have been reported to afford the corresponding ring-expanded cyclic imines (*i.e.*, compounds of the type **2**, Scheme 1) [4]. In our hands, thermolysis of *N*-carboethoxy-3-azido-3-ethylazetidine (**3**) [1b] at 200° in an inert atmosphere produced the corresponding cyclic imine **4** (Scheme 1) in 68% yield. Compound **4** was characterized *via* analysis of its $^1H$ and $^{13}C$ nmr spectra (see Experimental).

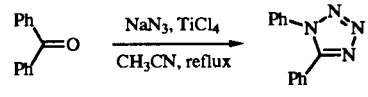
Recently, Suzuki and co-workers [5] utilized a sodium azide-titanium tetrachloride promoted Schmidt rearrangement of ketones **5** to synthesize 1,5-disubstituted 1*H*-tetrazoles **6** (Scheme 2). We now report the results obtained *via* an investigation of the corresponding reaction of *N*-triflylazetidin-3-one (**7**) [1a] with sodium azide-titanium tetrachloride-acetonitrile.

Scheme 1




**1** **2** **3** **4**

Scheme 2

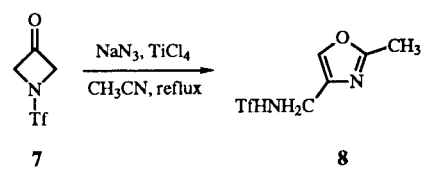



**5** **6**

Thus, a mixture of **7**, sodium azide and titanium tetrachloride in acetonitrile solvent was refluxed for 24 hours. Workup of the reaction afforded a mixture of products that could be separated *via* column chromatography on silica gel by using 10% ethyl acetate-hexane as eluent. Workup of the various chromatography fractions thereby obtained afforded recovered (unreacted) **7** (25% yield) along with a colorless microcrystalline solid, **8**, mp 104-105°, which was isolated in 20% yield. The structure of **8** (Scheme 3) was established unequivocally *via* application of X-ray crystallographic methods (see Experimental).

A control experiment was performed by repeating the reaction of **7** with titanium tetrachloride-acetonitrile in the absence of sodium azide. Under these conditions, **8** was not formed. Thus, we conclude (i) that sodium azide is necessary to the formation of **8** from **7** in this reaction and (ii) that it participates actively in the mechanism by which **8** is formed *via* reaction with sodium azide-titanium tetra-

Scheme 3




**7** **8**

Table 1

X-ray Structure Data for **8**

| Compound | **8** |
|---|---|
| Formula | $C_6H_7F_3N_2O_3S$ |
| Size (mm) | 0.25 x 0.31 x 0.36 |
| Space Group | $P2_1/c$ |
| a (Å) | 7.7494 (5) |
| b (Å) | 15.650 (1) |
| c (Å) | 8.4051 (8) |
| β (°) | 97.141 (7) |
| V (Å$^3$) | 1011.4 (1) |
| Z | 4 |
| $D_c$ (g-cm$^{-3}$) | 1.604 |
| μ (cm$^{-1}$) | 3.40 |
| $(2\theta_{max})$ | 44 |
| Total refl. | 1402 |
| Unique refl. | 1301 |
| $R_{int}$ | 0.020 |
| $I \geq 3\sigma(I)$ | 804 |
| Parameters | 136 |
| R, wR | 0.0497; 0.0497 |
| $(\Delta/\sigma)_{max}$ | <0.01 |
| $\rho_{min}$; $\rho_{max}$ | 0.25, -0.28 |

chloride-acetonitrile. Experiments which are designed to further clarify the mechanism of this unusual reaction are in progress.

## EXPERIMENTAL

Melting points are uncorrected. *N*-Carboethoxy-3-azido-3-ethylazetdine (**3**) [1b] and *N*-triflylazetidin-3-one (**7**) [1a] were prepared by using previously published procedures. Elemental microanalyses were performed by personnel at M-H-W Laboratories, Phoenix, AZ. High-resolution mass spectra were performed by personnel at the Midwest Laboratory for Mass Spectrometry, Department of Chemistry, University of Nebraska, Lincoln, NE.

1-Carboethoxy-4-ethyl-1,5-dihydro-1*H*-imidazole (**4**).

Thermal decomposition of azide **3** (400 mg, 1.94 mmoles) was performed by heating neat **3** at 200° under argon atmosphere for 0.5 hour. The resulting black syrup was purified *via* column chromatography on silica gel by eluting with 20% ethyl acetate-hexane. Workup of the chromatography fractions thereby obtained afforded pure **4** (220 mg, 68%) as a pale yellow oil; ir (film): 1700 cm$^{-1}$, ν C=O; $^1$H nmr (deuteriochloroform): δ 1.13 (t, J = 6.0 Hz, 3H, $CH_2CH_3$), 1.21 (t, J = 6.0 Hz, 3H, $CO_2CH_2CH_3$), 2.32 (q, J = 6.0 Hz, 2H, $CH_2CH_3$), 4.04-4.15 (m, 4H, ring $CH_2$ and $CO_2CH_2CH_3$), 5.14 (br s, 2H, ring $CH_2$); $^{13}$C nmr (deuteriochloroform): δ 9.88 (q), 14.7 (q), 25.1 (t), 54.7 (t), 55.0 (t), 61.2 (t), 153.6 (s), 173.9 (s).

*Anal.* Calcd. for $C_8H_{14}N_2O_2$: $M_r$+170.1055. Found (high-resolution mass spectrometry): $M_r$+170.1053.

2-Methyl-4-[*N*-(trifluoromethanesulfonyl)methyl]oxazole (**8**).

To a stirred suspension of sodium azide (520 mg, 8.0 mmoles) in acetonitrile (10 ml) under argon at room temperature was added titanium tetrachloride (378 mg, 2 mmoles) *via* syringe. To the resulting yellow solution was added **7** (205 mg, 1.0 mmole), and the reaction mixture was refluxed for 24 hours. The reaction mixture was diluted with 10% aqueous hydrochloric acid (25 ml), and the resulting suspension was concentrated *in vacuo* to remove most of the excess acetonitrile. The resulting aqueous suspension was extracted with ethyl acetate (3 x 20 ml). The combined organic layers were washed sequentially with water (50 ml) and brine (50 ml), dried (sodium sulfate) and filtered, and the filtrate was concentrated *in vacuo*. The yellow residue thereby obtained was purified by column chromatography on silica gel by eluting with 10% ethyl acetate-hexane. Workup of the initial chromatography fractions afforded unreacted **7** (51 mg, 25%). Continued elution of the chromatography column afforded pure **8** (49 mg, 20%) as a colorless microcrystalline solid, mp 104-105°; ir (potassium bromide): 3045 cm$^{-1}$, ν NH; $^1$H nmr (deuteriochloroform): δ 2.45 (s, 3H, $CH_3$), 4.31 (d, J = 6.0 Hz, 2H, $CH_2$), 7.52 (s, 1H, oxazole ring proton), 8.05 (br s, 1H, N*H*Tf); $^{13}$C nmr (deuteriochloroform): δ 13.6 (q), 38.7 (t), 110.0 (s), 116.4 (s), 122.8 (s), 129.1 (s), 135.4 (s), 136.0 (d), 163.3 (s).

*Anal.* Calcd. for $C_6H_7F_3N_2O_3S$: C, 29.51; H, 2.89; N, 11.47. Found: C, 29.77; H, 3.00; N, 11.53.

The structure of **8** was established unequivocally *via* application of X-ray crystallographic methods (*vide infra*).

X-ray Structure of 2-Methyl-4-[*N*-(trifluoromethanesulfonyl)-methyl]oxazole (**8**).

Data were collected on an Enraf-Nonius CAD-4 diffractometer by using the ω-2θ scan technique, MoKα radiation (λ = 0.71073 Å) and a graphite monochromator. Standard procedures in our laboratory that have been described previously were used for this purpose [6]. Pertinent details are presented in Table 1. Data were corrected for Lorentz and polarization effects but not for absorption. The structure of **8** was solved by direct methods (SIR [7]), and the model was refined by using full-matrix least-squares techniques. Due to the fact that **8** was an unexpected product of the reaction by which it was obtained, the atom assignments were examined very carefully. Final assignments are based upon thermal parameters, geometry, and hydrogen connectivities. All non-hydrogen atoms were treated with anisotropic thermal parameters. Hydrogen atoms were located on difference maps and then included in the model in idealized positions [U(H) = 1.3 Beq(C)]. All computations other than those specified were performed by using MolEN [8]. Scattering factors were taken from the usual sources [9].

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