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Reactions of β-Azolylenamines with Sulfonyl Azides as an Approach to *N*-Unsubstituted 1,2,3-Triazoles and Ethene-1,2-diamines

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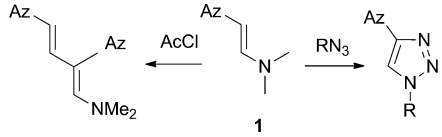
The reactions of β-azolylenamines **1** with sulfonyl azides **2** in acetonitrile furnished 1*H*-4-(azol-5-yl)-1,2,3-triazoles **3** in yields of 52–93 %. β-Benzoylenaminones and β-nitroenamine of type **1** also reacted with tosyl azide to form the same type of products **3**, proving the generality and efficiency of the method for the synthesis of *N*-unsubstituted 1,2,3-triazoles. On the other hand, the reactions of 3-(1-aryl-1,2,3-triazol-5-yl)enamines with tosyl azide in the absence of a solvent afforded a mixture of (*E*)-1-dimethylamino-2-tosylaminoethenes **5** and *N*,*N*-dimethyl-*N*′-tosylformamidine **6** in yields of 40–50 and 20 %, respectively. The formation of a variety of compounds from the reactions of enamines **1** with sulfonyl azides **2** is rationalized by the various possible transformations of the intermediate 5-dimethylamino-1,2,3-triazolines **7**.

Introduction

The chemistry of 1,2,3-triazoles has received increased interest after the copper-catalyzed alkyne to azides cyclization reaction was discovered, a reaction often associated with the concept of "click chemistry".[1] Many interesting 1,2,3-triazole derivatives that may act as bioconjugates,[2] chemosensors,[3] ligands,[4] or anion receptors[5] became easily available as a result of what is often called the "click reaction". In turn, it led to an increase in the use of 1,2,3-triazoles in medicine, materials chemistry, analytical chemistry, and organic synthesis. Cycloaddition reactions of enamines and 1,3-dicarbonyl compounds with azides present a promising but less studied approach to 1,2,3-triazoles.[6] We have turned our attention to the self-condensation of β-azolylenamines and their cycloaddition reactions with azides (Scheme 1). This methodology was unknown before our preliminary reports were published.[6e,7] The reactions of β-azolylenamines with aryl and alkyl azides were shown to be a convenient, regioselective, and general method for the preparation of 4-azolyl-1,2,3-triazoles in which these enamines are the synthetic equivalents of azolylalkynes.[6e] Therefore we can characterize this reaction as a "click" reaction. Although the reactions of enamines with alkynes are known from the theoretical work of Jones and Houk[6a] as HOMO (enamine)–LUMO (azide) controlled processes, reports of experimental cycloaddition reactions between enamines and azides bearing a strong electron-withdrawing substituent such as tosyl are not numerous[8] and totally lacking for β-azolylenamines. To expand our approach to 4-azolyl-1,2,3-triazoles and to evaluate the feasibility of using the cycloaddition reaction between β-azolylenamines and sulfonyl azides for the synthesis of 1-sulfonyl-4-azolyl-1,2,3-triazoles (potential precursors of azavinylcarbenes[9]), we have investigated the reactions of sulfonyl azides **2a**,**b** with a series of β-azolylenamines **1a**–**j**, enaminones **1k**,**l**, and *N*,*N*-dimethyl-2-nitroetheneamine **1m** (Scheme 2).



Scheme 1. Self-condensation and cycloaddition reactions of enamines **1**.

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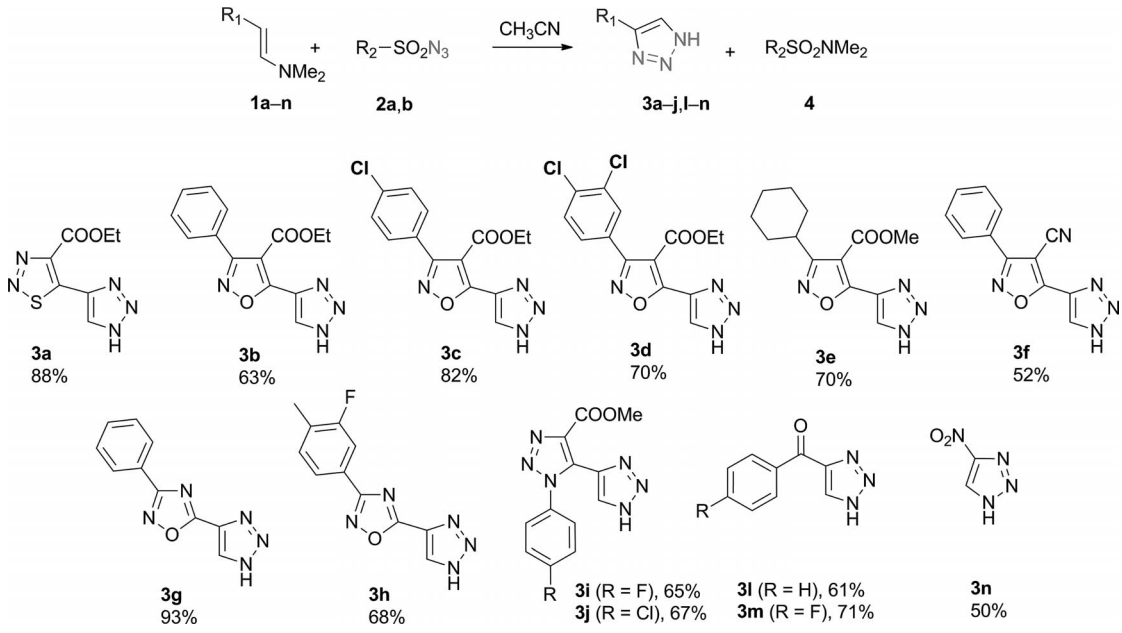


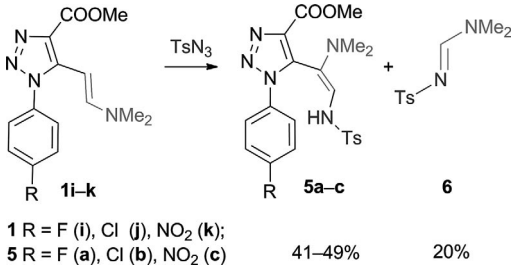
Scheme 2. Synthesis of 4-substituted 1*H*-1,2,3-triazoles.

Results and Discussion

We found that the reactions of β-azolylenamines **1a**–**j** with tosyl azide **2a** and of **1a**,**l** with mesyl azide **2b** in organic solvents such as acetonitrile afforded *N*-unsubstituted 4-azolyl-1,2,3-triazoles **3a**–**j** in yields of 52–93% instead of the expected 1-sulfonyl-1,2,3-triazoles. This reaction was accompanied by the formation of *N*,*N*-dimethylsulfonylamides **4**; tosylamide **4** (R^2 = Ts) was isolated and identified by ^{1}H NMR spectroscopy and by comparison of its melting point with data found in the literature.[10] The method of choice included the use of acetonitrile as solvent at room temperature followed by the extraction of triazoles **3a**–**j** with chloroform from the aqueous solutions of the reaction products. The use of other solvents and bases lowered the yields of the target products and resulted in the formation of tar-like mixtures. The structures of triazoles **3a**–**j** were confirmed by a combination of ^{1}H and ^{13}C NMR spectroscopy, including 2D HSQC and HMBC (^{1}H–^{13}C and ^{1}H–^{15}N), and mass spectrometry, which gave good agreement with the proposed structures. The ^{1}H and ^{13}C NMR spectra of compounds **3a**–**j** exhibit signals in the range 8.3–8.8 and 132.6–134.2 ppm corresponding to 5-H and C-4, respectively, confirming that all the products belong to the same class of compounds. The signals of C-4 and C-5 corresponding to the 1,2,3-thiadiazole ring of the product **3a** and those of C-4, C-3, and C-5 of the isoxazole ring of products **3b**–**f** in the ^{13}C NMR spectra are very similar to those observed for ethyl 5-[1-(4-chlorophenyl)-1*H*-1,2,3-triazol-4-yl]-1,2,3-thiadiazole-4-carboxylate and ethyl 5-[1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]-3-phenylisoxazole-4-carboxylate, respectively, described previously.[6e] Furthermore, the 2D HMBC ^{1}H–^{13}C and ^{1}H–^{15}N spectra of compound **3a** contain cross-peaks of 5-H with C-4 and with both β-nitrogen atoms, confirming unambiguously the presence of the 1,2,3-triazole fragment in **3a**.

N-Unsubstituted 1,2,3-triazoles **3** were obtained from reactions of enamines **1** bearing 1,2,3-thiadiazole, 1,2,3-triazole, isoxazole, and 1,2,4-oxadiazole rings. Moreover, enaminones **1l**,**m** and β-nitroenamine **1n** also reacted readily with tosyl azide to form the corresponding 1*H*-1,2,3-triazoles **3l**–**n** in yields of 50–71%. The NMR spectra and melting points of triazoles **3l**,**n** are very similar to the data reported for these compounds prepared by an independent method.[11] *N*-Unsubstituted 1,2,3-triazoles possess many interesting biological properties.[12] However, in contrast to 1,4-disubstituted 1,2,3-triazoles, access to 1*H*-1,2,3-triazoles is not well developed and includes the reactions of alkynes and haloalkenes with sodium azide, which has its limitations for the synthesis of azolyl-1*H*-1,2,3-triazoles because of the poor availability of azolylalkynes and -alkenes.[13] Probably for this reason, heterocyclic systems of 1*H*-1,2,3-triazoles conjugated to other azoles are very poorly represented in the literature,[14] and a general and efficient method for their preparation has not yet been developed. Although the formation of unsubstituted 1,2,3-triazoles from the reactions of enamines **1** with sulfonyl azides is a general process, we found that the use of a nonpolar solvent such as hexane or 1,4-dioxane or the absence of solvent dramatically changed the direction of the reactions of triazolylenamines **1i**–**k** with tosyl azide; the novel (*E*)-triazolylethene-1,2-diamines **5a**–**c** and amidine **6** were formed in yields of 40–50 and 20%, respectively (Scheme 3). The reaction of enamine **1i** with tosyl azide in dioxane was found to form, in addition to compounds **5a** and **6**, unsubstituted triazole **3i** in 5% yield. The study of the scope and limitation of the reactions of enamines with sulfonyl azides for

the synthesis of diaminoalkenes of type **5** is in progress. Diamines **5a**–**c** are less soluble in 1,4-dioxane and were easily separated from amidine **6** by filtration. Amidine **6** was separated from the remaining diamines **5a**–**c** and tar-like products by column chromatography on silica gel. The reactions of triazolylenamines **1i**–**k** with tosyl azide represent a rare example of an enamine transformation to diaminoalkenes, reported recently by Contini and Erba for the reactions of morpholinoenamines with sulfonyl azides.[8a] The structures of diamines **5a**–**c** were reliably confirmed by the combination of ^{1}H and ^{13}C NMR spectroscopy, HMBC (H–C, H–N), LCMS, and finally by X-ray diffraction analysis performed on a single crystal of **5c** (see Figure 1). In contrast to the results of Contini and Erba,[8a] diamines of type **5**, as shown by the X-ray analysis, exist in the *E* isomeric form. Amidine **6** has very similar NMR spectra to the reported compound prepared by the reaction of tosyl azide with DEAD in the presence of triethylamine.[15]



Scheme 3. Reactions of enamines **1i**–**k** with tosyl azide.

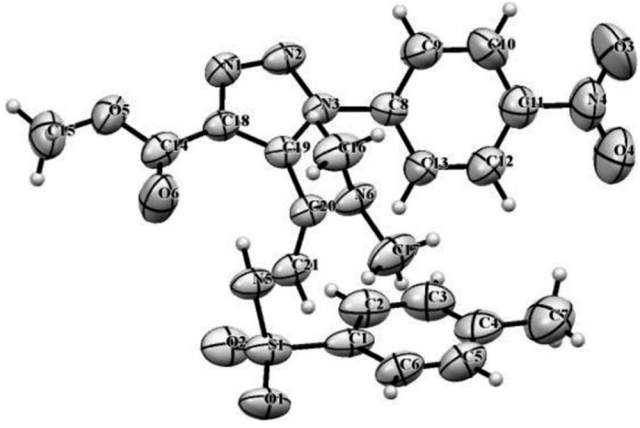
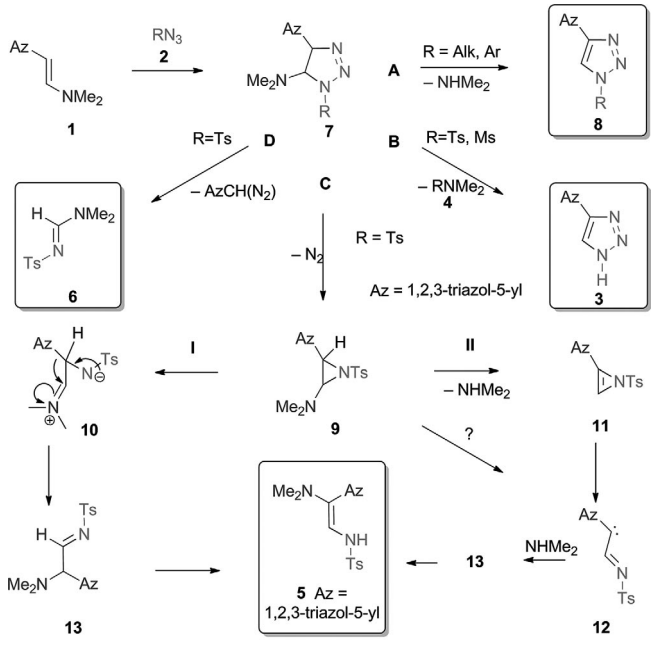


Figure 1. Structure of compound **5c**.

Discussion of the Reaction Mechanisms

The mechanism proposed for the reactions of enamines **1** with alkyl, aryl, benzyl, and sulfonyl azides **2** to yield compounds **3**–**5** and **8** are summarized in Scheme 4. Clearly, the first step in all the reactions is the formation of nonaromatic 4,5-dihydro-1,2,3-triazolines **7**. This type of process is well documented.[6c,16] Scheme 4 illustrates the formation of different kinds of follow-up products depending on the specific modes [**A**, **B**, **C** (**I**, **II**), and **D**] of stabilization of triazolines **7**. Thus, the elimination of dialkylamine leads to 1,4-disubstituted 1,2,3-triazole **8** as described by us recently.[6e] Somewhat similar eliminations of HCN, HHal, RSO_2H, and HNO_2 from intermediate triazolines to afford aromatic 1,2,3-triazoles are also known.[6f,17] The elimination of *N*,*N*-dimethyltosylamide **4** followed by a 1,5-hydrogen shift in the intermediate 4*H*-triazolines is an unknown mechanism for the formation of 1,2,3-triazoles of type **3**, described here for the reactions of enamines **1** with sulfonyl azides **2** (R = Ts, Ms). The formation of amidine **6** is proposed here to proceed as a retro 1,3-dipolar cycloaddition reaction of intermediate triazoline **7** by analogy with the work of Contini and Erba for the reaction of tosyl azide with β-alkylenamines.[8a] The second product, (5-ethyl-4-ethoxycarbonyl-1,2,3-triazol-5-yl)diazomethane, is not isolated probably because of its fast degradation. The pathway triazoline **7**→ acetamidine **6** was also recently used by Xu et al. to explain the formation of acetamidines in the reaction of tosyl azide with triethylamine and diethyl azodicarboxylate.[15] Because of the formation of a mixture of 1,2-diaminoethene **5** with amidine **6** in the reactions of β-(1,2,3-triazol-5-yl)enamines with TsN_3, we assume that the formation of **5** also started from intermediate triazoline **7**. The concerted mechanism proposed by Contini and Erba[8a] for the transformation of morpholino-dihydrotriazolines into azacycloalkenemonosulfonyl diamines looks hardly possible for the reactions of enamines of type **1** involving the shift of a dialkylamino group, which should have a higher activation barrier than



Az = 1,2,3-thiadiazol-, 1,2,3-triazol-, izoxazol-, 1,2,4-oxadiazol-5-yl

Scheme 4. Mechanisms for the reactions of enamines **1** with azides **2**.

the shift of an aromatic azolyl radical.[8b] Therefore we propose that the second step for the formation of compounds **5** involves the elimination of dinitrogen from triazolines **7** to form aziridines **9**. Precedents for this kind of reaction have been published elsewhere.[18] In its turn, aziridine **9** could undergo transformation to the final reaction products by the pathways **I** or **II** shown in Scheme 4. Both of them include aziridine ring-opening to form either zwitterion **10** or carbene **12**. Notably, a rearrangement is required for the formation of diamines **5** in which the dimethylamino group and triazolyl moiety are connected to the same carbon, in contrast to enamine **1** and aziridine **9** in which they are connected to adjacent carbon atoms. Mechanism **I** involves an azole1,2-shift whereas mechanism **II** involves three steps, 1) elimination of dimethylamine, 2) ring-opening of intermediate antiaromatic azirine **11** to form carbene **12** (the latter can also be formed directly from aziridine by concerted elimination of dimethylamine and rupture of the C–N bond), and 3) insertion of dimethylamine into the carbene. Both generate the same product (**13**), which in turn, through a 1,3-hydrogen shift, affords the final products **5**.

Conclusions

A general and efficient method for the synthesis of *N*-unsubstituted 1,2,3-triazoles based on the reactions of enamines with sulfonyl azides has been developed. The formation of various products from the reactions of enamines **1** with sulfonyl azides **2** led to the proposal of several pathways for the subsequent reactions of intermediates 5-amino-1,2,3-triazolines **7**. These reactions lead to 1*H*-1,2,3-triazoles **3** by elimination of *N*,*N*-dimethylsulfonylamides **4**, (*E*)-1-triazolyl-1-dimethylamino-2-tosylaminoethenes **5** by the elimination of dinitrogen, and *N*,*N*-dimethyl-*N*′-sulfonylamidoformamidine **6** by a retro 1,3-dipolar cycloaddition.

Experimental Section

The enamines **1a**–**l** were prepared by a method reported in the literature.[6e]

General Procedure for the Preparation of Methyl 5-(1*H*-1,2,3-Triazol-4-yl)-1,2,3-thiadiazole-4-carboxylate (3a): A mixture of enamine **1a** (0.228 g, 1.0 mmol) and tosyl azide **2b** (0.592 g, 3.0 mmol) in CH_3CN (5 mL) was stirred at room temperature for 12 h. The reaction mixture was then diluted with 5% aq. Na_2CO_3 (20 mL) and extracted with chloroform. Concentrated hydrochloric acid was added to the aqueous layer until pH 5 and the mixture extracted with EtOAc (2 × 20 mL). The combined organic layers were dried with Na_2SO_4 and solvent was removed under reduced pressure to furnish **3a** as a colorless solid, yield 0.200 g (88%); m.p. 186–188 °C; R_f = 0.43 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 832, 1201, 1297, 1502, 1724, 2869, 3169 cm^{-1}. ^1H NMR: δ = 4.01 (s, 3 H, OCH_3), 8.76 (s, 1 H, 5′-H), 15.81 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 52.4 (OCH_3), 127.4 (C-5′ is not decoupled), 134.0 (C-4′), 146.4 (C-5), 152.0 (C-4), 160.3 ppm. MS (ESI): *m*/*z* = 211.017 [M + H]$^+$. $C_7H_7N_5O_2S$: C 37.33, H 3.13, N 31.09, S 14.24; found C 37.41, H 3.08, N 31.01, S 14.29.

Compounds **3b**–**n** were obtained following the procedure for the preparation of **3a** from the corresponding enamines and tosyl azide.

Methyl 3-Phenyl-5-(1*H*-1,2,3-triazol-4-yl)isoxazole-4-carboxylate (3b): Colorless solid; yield 0.180 g (63%); m.p. 168–170 °C; R_f = 0.47 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 766, 1232, 1327, 1541, 1718 cm^{-1}. ^1H NMR: δ = 7.44–7.55 (m, 3 H, Ar-H), 7.61 (m, 2 H, Ar-H), 8.60 (br. s, 1 H, 5-H), 15.71 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 52.1 (OCH_3), 108.8 (br. s, C-4), 125.8 (br. s, C-5′), 127.5 (C-*i*, Ph), 128.3 (C-*m*, Ph), 128.8 (C-*o*, Ph), 130.1 (C-*p*, Ph), 133.7 (br. s, C-4′), 161.3 (C=O), 162.1 (C-3), 164.5 (C-5) ppm. MS (EI): *m*/*z* = 270 [M]$^+$. $C_{14}H_{12}N_4O_3$ (284.27): calcd. C 59.15, H 4.25, N 19.71; found C 59.09, H 4.29, N 19.77.

Ethyl 3-(4-Chlorophenyl)-5-(1*H*-1,2,3-triazol-4-yl)isoxazole-4-carboxylate (3c): Colorless solid; yield 0.262 g (82%); m.p. 180–182 °C; R_f = 0.41 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 832, 1132, 1313, 1416, 1719 cm^{-1}. ^1H NMR: δ = 1.11 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 4.22 (d, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 7.60 (m, 2 H, Ar-H), 7.70 (m, 2 H, Ar-H), 8.77 (s, 1 H, 5′-H), 15.96 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 13.5 (OCH_2CH_3), 61.2 (OCH_2CH_3), 108.1 (C-4), 126.6 (C-*i*, Ar), 128.3 (C-*m*, Ar), 129.7 (br. s, C-5′), 130.9 (C-*o*, Ar), 133.6 (br. s, C-4′), 134.0 (C-*p*, Ar), 160.6 (C=O), 161.4 (C-3), 164.8 (C-5) ppm. MS (EI): *m*/*z* = 318 [M]$^+$. $C_{14}H_{11}ClN_4O_3$ (318.72): calcd. C 52.76, H 3.48, N 17.58; found C 52.70, H 3.43, N 17.48.

Ethyl 3-(3,4-Dichlorophenyl)-5-(1*H*-1,2,3-triazol-4-yl)isoxazole-4-carboxylate (3d): Colorless solid; yield 0.247 g (70%); m.p. 188–190 °C; R_f = 0.51 (EtOAc/hexane, 1:1). ^1H NMR: δ = 1.11 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 4.21 (d, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 7.66 (dd, *J* = 8.4, 1.8 Hz, 1 H, Ar-H), 7.79 (d, *J* = 8.4 Hz, 1 H, Ar-H), 7.99 (d, *J* = 1.8 Hz, 1 H, Ar-H), 8.77 (s, 1 H, 5′-H), 15.94 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 13.9, 61.6, 108.5, 127.8, 128.9, 129.9, 130.9, 131.5, 131.8, 133.5, 134.0, 160.8, 161.0, 165.6 ppm. MS (EI): *m*/*z* = 352 [M]$^+$. $C_{14}H_{10}Cl_2N_4O_3$ (353.16): calcd. C 47.61, H 2.85, N 15.86; found C 47.69, H 2.78, N 15.80.

Methyl 3-Cyclohexyl-5-(1*H*-1,2,3-triazol-4-yl)isoxazole-4-carboxylate (3e): Colorless solid; yield 0.247 g (70%); m.p. 160–162 °C; R_f = 0.44 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 792, 1104, 1543, 1617, 1723, 2854, 2940 cm^{-1}. ^1H NMR: δ = 1.25–1.42 (m, 3 H, cyclohexyl-H), 1.43–1.53 (m, 2 H, cyclohexyl-H), 1.70 (d, *J* = 12.1 Hz, 1 H, cyclohexyl-H), 1.79 (d, *J* = 12.1 Hz, 2 H, cyclohexyl-H), 1.98 (d, *J* = 11.5 Hz, 2 H, cyclohexyl-H), 3.04–3.22 (m, 1 H, cyclohexyl-H), 3.84 (s, 3 H, OCH_3), 8.66 (s, 1 H, 5′-H); 15.86 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 25.5, 25.8, 31.0, 35.4, 52.0 (OCH_3), 107.1 (C-4), 133.9 (C-4′), 161.5 (C=O), 164.1 (C-3), 167.1 (C-5) ppm. MS (EI): *m*/*z* = 276 [M]$^+$. $C_{13}H_{16}N_4O_3$ (276.29): calcd. C 56.51, H 5.84, N 20.28; found C 56.58, H 5.81, N 20.22.

3-Phenyl-5-(1*H*-1,2,3-triazol-4-yl)isoxazole-4-carbonitrile (3f): Colorless solid; yield 0.120 g (52%); m.p. 189–190 °C; R_f = 0.48 (EtOAc/hexane, 1:1). ^1H NMR: δ = 7.63–7.64 (m, 3 H, Ar-H), 7.91–7.94 (m, 2 H, Ar-H), 8.49 (s, 1 H, 5-H) ppm. ^{13}C NMR: δ = 85.0 (C-4), 112.8 (CN), 126.6 (C-*i*, Ar), 127.8 (C-*o*, Ar), 129.9 (C-*m*, Ar), 130.6 (C-5′), 131.8 (C-*p*, Ar), 132.2 (C-4′), 161.7 (C-3), 171.2 (C-5) ppm. MS (EI): *m*/*z* = 237 [M]$^+$. $C_{12}H_7N_5O$ (237.22): calcd. C 60.87, H 3.05, N 29.60; found C 60.76, H 2.97, N 29.52.

3-Phenyl-5-(1*H*-1,2,3-triazol-4-yl)-1,2,4-oxadiazole (3g): Colorless solid; yield 0.198 g (93%); m.p. 210–212 °C; R_f = 0.40 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 1237, 1304, 1373, 1440, 1524, 1641, 2921, 3149 cm^{-1}. ^1H NMR: δ = 7.54–7.69 (m, 3 H, Ar-H), 8.00–8.17 (m, 2 H, Ar-H), 8.96 (br. s, 1 H, 5-H), 16.13 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 125.9 (C-*i*, Ph), 127.1 (C-*o*, Ph), 129.3 (C-*m*, Ph), 130.1 (C-5′), 131.7 (C-*p*, Ph), 132.6 (C-4′), 168.1 (C-3), 169.4 (C-5) ppm. MS (EI): *m*/*z* = 213 [M]$^+$. $C_{10}H_7N_5O$ (213.20): calcd. C 56.34, H 3.31, N 32.85; found C 56.39, H 3.26, N 32.80.

3-(3-Fluoro-4-methylphenyl)-5-(1*H*-1,2,3-triazol-4-yl)-1,2,4-oxadiazole (3h): Colorless solid; yield 0.167 g (68%); m.p. 258–259 °C; R_f = 0.49 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 814, 835, 1084, 1508, 1720, 3304 cm^{-1}. ^1H NMR: δ = 2.32–2.39 (m, 3 H, CH_3), 7.43 (s, 1 H, Ar-H), 7.72 (m, 1 H, Ar-H), 7.77–7.87 (m, 1 H, Ar-H), 8.66 (s, 1 H, 5-H), 15.93 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 14.7 (CH_3), 113.8, 123.4, 125.8, 128.9, 132.9, 133.1, 161.2, 167.6, 170.0 ppm. MS (EI): *m*/*z* = 245 $[M]^+$. $C_{11}H_8FN_5O$ (245.22): calcd. C 53.88, H 3.29, N 28.56; found C 53.78, H 3.23, N 28.51.

Methyl 3′-(4-Fluorophenyl)-1*H*,3′*H*-4,4′-bi-1,2,3-triazole-5′-carboxylate (3i): Compound **3i** was obtained following the procedure used for the preparation of **3a**, but MsN_3 was used instead of TsN_3. Colorless solid; yield 0.187 g (65%); m.p. 125–127 °C; R_f = 0.45 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 834, 1088, 1510, 1726, 2127, 3108 cm^{-1}. ^1H NMR: δ = 3.89 (s, 3 H, OCH_3), 7.30 (m, 2 H, Ar-H), 7.49 (m, 2 H, Ar-H), 8.22 (br. s, 1 H, 5-H), 15.33 (br. s, 1 H, NH) ppm. MS (EI): *m*/*z* = 288 $[M]^+$. $C_{12}H_9FN_6O_2$ (288.24): calcd. C 50.00, H 3.15, N 29.16; found C 50.10, H 3.10, N 29.21.

Methyl 3′-(4-Chlorophenyl)-1*H*,3′*H*-4,4′-bi-1,2,3-triazole-5′-carboxylate (3j): Colorless solid; yield 0.203 g (67%); m.p. 131–133 °C; R_f = 0.48 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 825, 1002, 1078, 1223, 1494, 1727, 2921, 3168 cm^{-1}. ^1H NMR: δ = 3.89 (s, 3 H, OCH_3), 7.40 (m, 2 H, Ar-H), 7.50 (m, 2 H, Ar-H), 8.25 (br. s, 1 H, 5-H), 15.35 (br. s, 1 H, NH) ppm. MS (EI): *m*/*z* = 304 $[M]^+$. $C_{12}H_9ClN_6O_2$ (304.70): calcd. C 47.30, H 2.98, N 27.58; found C 47.38, H 2.92, N 27.50.

4-Benzoyl-1*H*-1,2,3-triazole (3l): Colorless solid; yield 0.105 g (61%); m.p. 121–123 °C (ref.[11b] 122 °C). ^1H NMR: δ = 7.54 (m, 2 H, Ar-H), 7.64 (m, 1 H, Ar-H), 8.27 (m, 2 H, Ar-H), 8.44 (br. s, 1 H, 5-H), 15.58 (br. s, 1 H, NH) ppm. The NMR spectrum of **3k** is similar to that published previously.[11b]

(4-Fluorophenyl)(1*H*-1,2,3-triazol-4-yl)methanone (3m): Colorless solid; yield 0.140 g (71%); m.p. 179–181 °C. IR: $\tilde{\nu}$ = 768, 1241, 1598, 1659, 3120 cm^{-1}. ^1H NMR: δ = 7.43 (m, 2 H, Ar-H), 8.38 (m, 2 H, Ar-H), 8.69 (br. s, 1 H, 5-H), 13.81 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 115.7, 132.5, 133.4, 133.7, 145.9, 165.5, 184.4 ppm. MS (EI): *m*/*z* = 191 $[M]^+$. $C_9H_6FN_3O$ (191.16): calcd. C 56.55, H 3.16, N 21.98; found C 56.45, H 3.11, N 21.91.

4-Nitro-1*H*-1,2,3-triazole (3n): Colorless solid; yield 0.57 g (50%); m.p. 158–159 °C (ref.[19] 160–161 °C); R_f = 0.35 (EtOAc/C_2H_5OH, 10:1). IR: $\tilde{\nu}$ = 827, 1226, 1391, 1543, 3161, 3240 cm^{-1}. ^1H NMR: δ = 8.89 (s, 1 H, 5-H), 16.18 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 125.5, 153.5 ppm. The NMR spectra of **3n** are similar to those published previously.[20]

General Procedure for the Preparation of Methyl 5-[(*E*)-1-(Dimethylamino)-2-(4-methylphenylsulfonamido)ethenyl]-1-(4-fluorophenyl)-1*H*-1,2,3-triazole-4-carboxylate (5a): A mixture of enamine **1i** (0.290 g, 1.0 mmol) and TsN_3 (0.591 g, 3.0 mmol) was kept at room temperature for 1 h. CH_3CN was added to the reaction mixture and the precipitate was filtered off and washed with CH_3CN (2 mL). Triazole **5a** was obtained as a colorless solid. Yield 0.188 g (41%); m.p. 211–213 °C; R_f = 0.32 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 762, 1172, 1189, 1335, 1473, 1641, 3073, 3163, 3211 cm^{-1}. ^1H NMR: δ = 2.29 (s, 6 H, NMe_2), 2.44 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 5.49 (d, *J* = 9.1 Hz, 1 H, CH), 7.07 (m, 2 H, Ar-H), 7.21–7.46 (m, 4 H, Ar-H), 7.56 (m, 2 H, Ar-H), 9.08 (d, *J* = 9.1 Hz, 1 H, CH) ppm. ^{13}C NMR: δ = 20.9 (CH_3), 39.9 (NMe_2), 51.7 (OMe), 108.8 (C-2), 115.9 (C-*m*, Ar), 124.5 (C-1), 126.2 (C-*o*, Ar), 126.3 (C- *o*, Ts), 129.6 (C-*m*, Ts), 132.0 (C-*i*, Ar), 134.4 (C-5, triazol), 137.3 (C-*i*, Ts), 138.7 (C-4, triazol), 142.9 (*p*-C-Ts), 160.3 (C=O), 162.1 (C-*p*, Ar) ppm. MS (ESI): *m*/*z* = 460.144 $[M + H]^+$. $C_{21}H_{22}FN_5O_4S$ (459.49): calcd. C 54.89, H 4.83, N 15.24, S 6.98; found C 54.82, H 4.89, N 15.19, S 6.93.

Compounds **5b**,**c** were obtained following the procedure used for the preparation of **5a** from the corresponding enamines and TsN_3.

Methyl 1-(4-Chlorophenyl)-5-[(*E*)-1-(dimethylamino)-2-(4-methylphenylsulfonamido)ethenyl]-1*H*-1,2,3-triazole-4-carboxylate (5b): Colorless solid; yield 0.200 g (42%); m.p. 194–195 °C; R_f = 0.35 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 1057, 1122, 1225, 1341, 1729, 3236 cm^{-1}. ^1H NMR: δ = 2.31 (s, 6 H, NMe_2), 2.45 (s, 3 H, CH_3), 3.79 (s, 3 H, OCH_3), 5.49 (d, *J* = 9.1 Hz, 1 H, CH), 7.07 (m, 2 H, Ar-H), 7.27–7.37 (m, 6 H, Ar-H), 7.56 (m, 2 H, Ar-H), 9.09 (d, *J* = 9.1 Hz, 1 H, CH) ppm. ^{13}C NMR: δ = 21.5, 41.0, 52.2, 109.3, 124.9, 125.9, 126.8, 129.6, 130.1, 134.6, 134.7, 134.9, 137.8, 139.3, 143.3, 160.7 ppm. $C_{21}H_{22}ClN_5O_4S$ (475.95): calcd. C 52.99, H 4.66, N 14.71, S 6.74; found C 52.89, H 4.62, N 14.78, S 6.65.

Methyl 5-[(*E*)-1-(Dimethylamino)-2-(4-methylphenylsulfonamido)-ethenyl]-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylate (5c): Colorless solid; yield 0.238 g (49%); m.p. 219–221 °C; R_f = 0.28 (EtOAc/hexane, 1:1). IR: $\tilde{\nu}$ = 1082, 1144, 1279, 1622, 1731, 2853, 2923 cm^{-1}. ^1H NMR: δ = 2.31 (s, 6 H, NMe_2), 2.37 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 5.54 (d, *J* = 9.1 Hz, 1 H, CH), 7.33 (m, 2 H, Ar-H), 7.56 (m, 2 H, Ar-H), 7.59–7.67 (m, 2 H, Ar-H), 8.15–8.26 (m, 2 H, Ar-H), 9.16 (d, *J* = 9.1 Hz, 1 H, CH) ppm. ^{13}C NMR: δ = 20.8 (CH_3), 40.1 (NMe_2), 51.9 (OCH_3), 109.3 (C-2), 124.0 (C-1), 124.4 (C-*m*, Ar), 124.6 (C-*o*, Ar), 126.4 (C-*o*, Ts), 129.6 (C-*m*, Ts), 134.4 (C-5, triazole), 137.3 (C-*i*, Ts); 139.2 (C-4, triazole), 140.2 (C-*i*, Ar), 142.9 (C-*p*, Ts), 147.3 (C-*p*, Ar), 160.0 (C=O) ppm. MS (EI): *m*/*z* = 486 $[M]^+$. $C_{21}H_{22}N_6O_6S$ (486.50): calcd. C 51.84, H 4.56, N 17.27, S 6.59; found C 51.91, H 4.51, N 17.22, S 6.53.

***N*-[(*E*)-(Dimethylamino)methylidene]-4-methylphenylsulfonamide (6):** After isolation of **5a**, the residue was evaporated under vacuum and the crude mass was purified by column chromatography (AcOEt/hexane, 1:1) to afford sulfonamide **6** as a colorless solid, yield 0.045 g (20%), m.p. 134–135 °C (ref.[19] 134–136); R_f = 0.2 (AcOEt/hexane, 1:1). ^1H NMR: δ = 2.40 (s, 3 H, CH_3), 2.95 (s, 3 H, CH_3), 3.17 (s, 3 H, CH_3), 7.27 (m, 2 H, Ar-H), 7.62 (m, 2 H, Ar-H), 8.16 (s, 1 H, CH) ppm. MS (ESI): *m*/*z* = 227.085 $[M + H]^+$. The NMR spectrum of **6** is similar to that published previously.[21]

X-ray Crystallography: CCDC-979571 (for **5c**) 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.

Supporting Information (see footnote on the first page of this article): Experimental details, ^1H and ^{13}C NMR and HRMS spectra for all key intermediates and final products, X-ray crystal data for compound **5c**.

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[1] a) A. C. W. Tornoe, C. Christensen, M. Meldal, *J. Org. Chem.* **2002**, *67*, 3057–3064; V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2596–2599; *Angew. Chem.* **2002**, *114*, 2708; b) R. B. Buckley, H. Heaney, *Top. Heterocycl. Chem.* **2012**, *28*, 1–30.

[2] T. Zheng, S. H. Rouhanifard, A. S. Jallohand, P. Wu, *Top. Heterocycl. Chem.* **2012**, *28*, 163–184.
[3] M. Watkinson, *Top. Heterocycl. Chem.* **2012**, *28*, 109–136.
[4] J. D. Crowley, D. A. McMorran, *Top. Heterocycl. Chem.* **2012**, *28*, 31–84.
[5] S. Lee, A. H. Flood, *Top. Heterocycl. Chem.* **2012**, *28*, 85–108.
[6] a) G. O. Jones, K. N. Houk, *J. Org. Chem.* **2008**, *73*, 1333–1342; b) N. N. Mochul'skaya, E. N. Nagibina, Yu. S. Volchenkova, L. P. Sidorova, V. N. Charushin, *Russ. J. Org. Chem.* **2005**, *41*, 1694–1701; c) M. Brunner, G. Maas, F.-G. Klaerner, *Helv. Chim. Acta* **2005**, *88*, 1813–1825; d) P. K. Kadaba, *J. Org. Chem.* **1992**, *57*, 3075–3078; e) V. A. Bakulev, I. V. Efimov, N. A. Belyaev, Yu. A. Rozin, N. N. Volkova, O. S. El′tsov, *Chem. Heterocycl. Compds.* **2012**, *47*, 1593–1595; f) S. Mignani, Y. Zhou, T. Lecourt, L. Micouin, *Top. Heterocycl. Chem.* **2012**, *28*, 185–232; g) Yu. A. Rozin, J. Leban, W. Dehaen, V. G. Nenajdenko, V. M. Muzalevskiy, O. S. Eltsov, V. A. Bakulev, *Tetrahedron* **2012**, *68*, 614–618; h) N. T. Pokhodylo, V. S. Matiychuk, M. D. Obushak, *Synthesis* **2009**, *14*, 2321–2323.
[7] Yu. Shafran, Yu. Rozin, T. Beryozkina, S. Zhidovinov, O. Eltsov, J. Subbotina, J. Leban, R. Novikova, V. Bakulev, *Org. Biomol. Chem.* **2012**, *10*, 5795–5798.
[8] a) A. Contini, E. Erba, *RSC Adv.* **2012**, *2*, 10652–10660; b) M. Brunner, G. Maas, F. G. Klarner, *Helv. Chim. Acta* **2005**, *88*, 1813–1825; c) N. Kato, Y. Hamada, T. Shiori, *Chem. Pharm. Bull.* **1984**, *32*, 2496–2502.
[9] a) T. Miura, T. Biyajima, T. Fujii, M. Murakami, *J. Am. Chem. Soc.* **2012**, *1*, 194–196; b) B. Chattopadhyay, V. Gevorgyan, *Angew. Chem. Int. Ed.* **2012**, *51*, 862–872; *Angew. Chem.* **2012**, *124*, 886; c) N. Selander, B. T. Worrell, S. Chuprakov, S. Velaparthi, V. Fokin, *J. Am. Chem. Soc.* **2012**, *134*, 14670–14673; d) A. V. Gulevich, V. Gevorgyan, *Angew. Chem. Int. Ed.* **2013**, *52*, 1371–1373; *Angew. Chem.* **2013**, *125*, 1411.
[10] X. Tang, L. Huang, Ch. Qi, X. Wu, W. Wu, H. Jiang, *Chem. Commun.* **2013**, *49*, 6102–6104.
[11] a) G. Kh. Khisamutdinov, V. I. Slovetsky, Yu. M. Golub, S. A. Shevelev, A. A. Fainzil'berg, *Russ. Chem. Bull.* **1997**, *46*, 324–327; b) W. Holzer, K. Ruso, *J. Heterocycl. Chem.* **1992**, *29*, 1203–1207.
[12] a) M. Kume, T. Kubota, Y. Kimura, H. Nakashimizu, K. Motokawa, M. Nakano, *J. Antibiot.* **1993**, *46*, 177–192; b) G. Cristalli, A. Eleuteri, R. Volpini, S. Vittori, E. Camaioni, G. Lupidi, *J. Med. Chem.* **1994**, *37*, 201–205; c) M. J. Fray, D. J. Bull, C. L. Car, E. C. L. Gautier, C. E. Mowbray, A. Stobie, *J. Med. Chem.* **2001**, *44*, 1951–1962; d) S. Komeda, M. Lutz, A. L. Spek, Y. Yamanaka, T. Sato, M. Chikuma, J. Reedijk, *J. Am. Chem. Soc.* **2002**, *124*, 4738–4746; e) D. T. Gonzaga, D. R. Rocha, F. de C. da Silva, V. F. Ferreira, *Curr. Top. Med. Chem.* **2013**, *13*, 2850–2865.
[13] Y.-M. Wu, J. Deng, Q.-Y. Chen, *Synlett* **2006**, *4*, 645–647.
[14] P. A. Ferreira, V. L. M. Silva, J. Elguero, A. M. S. Silva, *Tetrahedron Lett.* **2013**, *39*, 5391–5394.
[15] X. Xu, X. Li, L. Ma, N. Ye, B. Wenig, *J. Am. Chem. Soc.* **2008**, *130*, 14048–14049.
[16] a) T. V. Lukina, S. I. Sviridov, S. V. Shorshnev, G. G. Alexandrov, A. E. Stepanov, *Tetrahedron Lett.* **2005**, *46*, 1205–1207; b) G. Bianchi, R. Gandolfi, *1,3-Dipolar Cycloaddition Chemistry* (Ed.: A. Padwa), Wiley, New York, **1984**, vol. 2, p. 495; c) D. Margeti, R. N. Warrener, D. N. Butler, Ch.-M. Jin, *Tetrahedron* **2012**, *68*, 3306–3318; d) N. N. Nagibina, V. N. Charushin, L. P. Sidorova, N. A. Klyuev, *Zh. Org. Khim.* **1988**, *34*, 461–474; e) V. P. Semenov, T. D. Andreeva, K. A. Oglobin, *Zh. Org. Khim.* **1988**, *24*, 217–220.
[17] a) M. Henriet, M. Houtekie, B. Techy, R. Touillaux, L. Ghosez, *Tetrahedron Lett.* **1980**, *21*, 223–226; b) A. Derdour, T. Benabdallah, B. Merah, F. Texier, *Bull. Soc. Chim. Fr.* **1990**, *1*, 69–78; c) S. Dey, T. Pathak, *RSC Adv.* **2014**, *4*, 9275–9278.
[18] a) Z. W. Lin, P. K. Kadaba, *J. Heterocycl. Chem.* **1997**, *34*, 1645–1650; b) R. Danion-Bougot, D. Danion, G. Francis, *Tetrahedron Lett.* **1990**, *31*, 3739–3742; c) G. Broggini, L. Garanti, G. Molteni, T. Pilati, *Tetrahedron: Asymmetry* **2001**, *12*, 1201–1206; d) G. Mloston, G. A. Bodziochi, Z. Gebulska, A. Linden, H. Heimgartner, *Pol. J. Chem.* **2007**, *81*, 631–641.
[19] T. E. Eagles, M. A. Khan, B. M. Lynch, *Org. Prep. Proced.* **1970**, *22*, 117–119.
[20] H. H. Licht, H. Ritter, H. R. Bircher, P. Bigler, *Magn. Reson. Chem.* **1998**, *36*, 343–350.
[21] Z. Niu, S. Lin, Z. Dong, H. Sun, F. Liang, J. Zhang, *Org. Biomol. Chem.* **2013**, *11*, 2460–2465.

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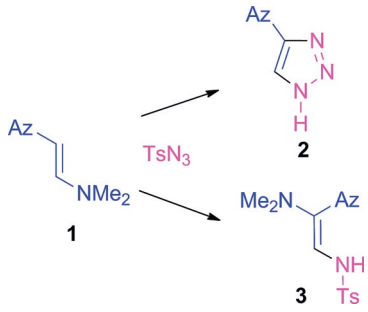
This paper deals with reactions of β-azolylenamines with sulfonyl azides. Variation of the reaction conditions leads to different products



Keywords: Nitrogen heterocycles / Enamines / Cycloaddition / Azides / Reaction mechanisms

