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NOVEL METHOD FOR THE SYNTHESIS OF 4-(AZOL-5-YL)-1,2,3-TRIAZOLES

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We have proposed a novel, general, and efficient method for the synthesis of 4-(azol-5-yl)-1,2,3-triazoles by cycloaddition of azides to 2-azolylenamines. It was shown that the enamines **2, 5, 8** take part in [3+2] cycloaddition when fused with aromatic azides to give exclusively the bicyclic compounds **3, 6, 9** in high yields. The regiospecificity of the reaction is evidently due to the "push-pull" character of enamines, the reaction of which with zwitterionic azides gives one of two possible regioisomers. It should be noted that, in contrast to condensed 1,2,3-triazoles [1], the bicyclic groups of compounds of type **3, 6, 9** are poorly available [2]. The transformation described is the first example of cycloaddition of 3-hetarylenamines to azides [1, 3]. The structures of the compounds obtained were confirmed by ^{1}H and ^{13}C NMR spectroscopic data and elemental analysis. Assignments in the ^{13}C NMR spectra were made on the basis of 2D HMBC experimental data for compounds **3** and **8**.

The ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker Avance II 400 spectrometer (400, 100, and 376 MHz respectively) using DMSO-d_6 with TMS as internal standard. Elemental analysis for C, H, and N was performed on an automatic Perkin Elmer 2400 II analyzer. The analysis for sulfur was by titration of sulfate anion after combustion in oxygen.

Ethyl 5-[(*E*)-2-(dimethylamino)ethenyl]-1,2,3-thiadiazole-4-carboxylate (2). The Bredereck reagent [4] (0.553 g, 3 mmol) was added to compound **1** (0.172 g, 1 mmol) and heated for 2 h at 50ºC. The reaction product was cooled and hexane was added. The precipitate was filtered off, dried, and recrystallized from EtOH. Yield 0.184 g (81%); mp 114-115ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.32 (3H, t, *J* = 7.0, $CH_2C\underline{H}_3$); 2.99 (6H, s, $N(CH_3)_2$); 4.34 (2H, q, *J* = 7.0, $C\underline{H}_2CH_3$); 6.14 (1H, d, *J* = 13.0, =CH); 7.41 (1H, d, *J* = 13.0, =CH). ^{13}C NMR spectrum, δ, ppm: 14.2 ($CH_2\underline{C}H_3$); 39.5 ($N(CH_3)_2$, low intensity); 60.3 ($\underline{C}H_2CH_3$); 84.3 (=CH); 141.1 (C-5); 153.9 (=CH); 161.5 (C=O); 163.6 (C-4). Found, %: C 47.80; H 5.91; N 18.21; S 14.14. $C_9H_{13}N_3O_2S$. Calculated, %: C 47.56; H 5.77; N 18.49; S 14.11.

Methyl 5-[(*E*)-2-(Dimethylamino)ethenyl]-1-(4-fluorophenyl)-1*H*-1,2,3-triazole-4-carboxylate (5). Obtained similarly to compound **2**. Yield 0.249 g (86%); mp 145-146ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.77 (6H, s, $N(CH_3)_2$); 3.85 (3H, s, OCH_3); 4.82 (1H, d, ^{2}J = 13.4, =CH); 7.62-7.47 (4H, m, H Ar); 7.71 (1H, d, *J* = 13.4, =CH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 39.4 ($N(CH_3)_2$); 52.2 (OCH_3); 110.7 (=CH); 116.6 (d, $J_{C–F}$ = 23.2,

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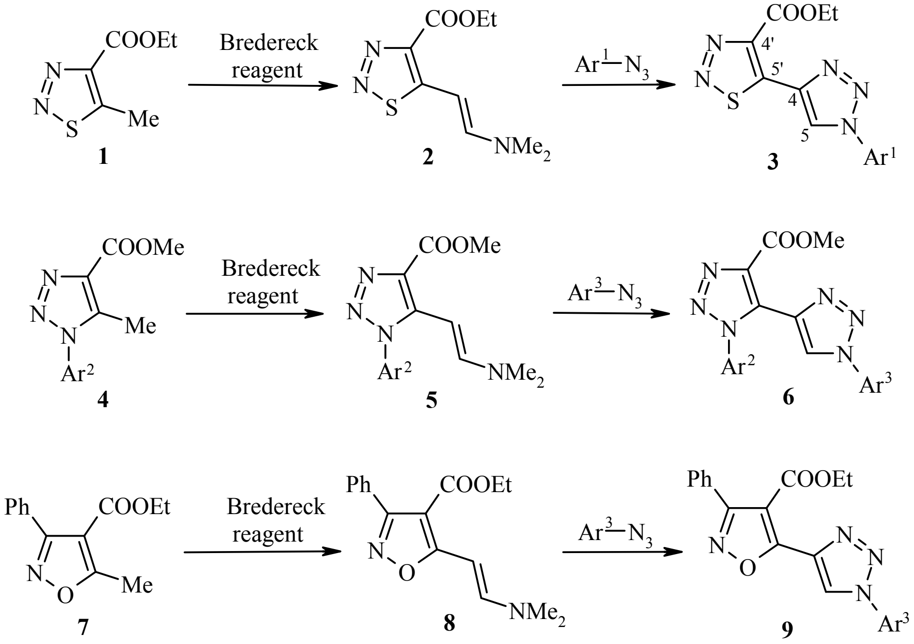
m-C Ar); 128.5 (d, $J_{C–F}$ = 9.6, *o*-C Ar); 129.1 (C-5); 132.6 (*i*-C Ar); 142.1 (=CH); 149.0 (C-4); 162.1 (d, $^1J_{C–F}$ = 247.4, *p* C Ar); 162.4 (C=O). ^{19}F NMR spectrum, δ, ppm: -111.1. Found, %: C 57.87; H 5.27; N 19.37. $C_{14}H_{15}FN_4O_2$. Calculated, %: C 57.93; H 5.21; N 19.30.



Ar^1 = 4-ClC$_6$H$_4$, Ar^2 = 4-FC$_6$H$_4$, Ar^3 = 4-O$_2$NC$_6$H$_4$
Bredereck reagent is 1-tert-butoxy-*N,N,N',N'*-tetramethylmethanediamine

Ethyl 5-[(*E*)-2-(Dimethylamino)ethenyl]-3-phenylisoxazole-4-carboxylate (8). Obtained similarly to compound **2**. Yield 0.238 g (83%); mp 85-87°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.13 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 3.01 (6H, br. s, $N(CH_3)_2$); 4.08 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 5.75 (1H, d, *J* = 13.5, =CH); 7.35-7.46 (2H, m, H Ph); 7.50 (1H, d, *J* = 13.5, =CH); 7.53-7.68 (3H, m, H Ph). Found, %: C 67.18; H 6.39; N 9.71. $C_{16}H_{18}N_2O_3$. Calculated, %: C 67.12; H 6.34; N 9.78.

Ethyl 5-[1-(4-Chlorophenyl)-1*H*-1,2,3-triazol-4-yl]-1,2,3-thiadiazole-4-carboxylate (3). 4-Chlorophenyl azide (0.153 g, 1 mmol) was added to compound **2** (0.227 g, 1 mmol) and heated for 1 h at 120-140°C. The reaction product was cooled and hexane was added. The precipitate was filtered off, dried, and crystallized from EtOH. Yield 0.291 g (87%); mp 227-228°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.42 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 4.52 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 7.59-7.76 (2H, m, H Ar); 7.90-8.09 (2H, m, H Ar); 9.37 (1H, s, H-5). ^{13}C NMR spectrum, δ, ppm: 14.3 ($CH_2\underline{C}H_3$); 62.5 ($\underline{C}H_2CH_3$); 122.0 (*m*-C Ar), 123.3 (C-5); 130.2 (*o*-C Ar); 134.9 (*p*-C Ar); 135.5 (*i*-C Ar); 137.0 (C-4); 146.5 (C-5'); 152.2 (C-4'); 161.4 (C=O). Found, %: C 46.03; H 2.98; N 20.84; S 9.62. $C_{13}H_{10}ClN_5O_2S$. Calculated, %: C 46.50; H 3.00; N 20.86; S 9.55.

Methyl 3'-(4-Fluorophenyl)-1-(4-nitrophenyl)-1*H*,3'*H*-4,4'-bi-1,2,3-triazole-5'-carboxylate (6). Obtained similarly to compound **3**. Yield 0.376 g (92%); mp 237-239°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.82 (3H, s, CH_3); 7.34 (2H, t, *J* = 8.6, H Ar); 7.59 (2H, dd, *J* = 8.8, *J* = 4.7, H Ar); 8.20 (2H, d, *J* = 9.0, H Ar); 8.42 (2H, d, *J* = 9.0, H Ar); 9.46 (1H, s, H-5). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 52.7 (OCH_3); 116.4 (d, $J_{C–F}$ = 23.2, *m*-C 3'-Ar); 121.0 (*m*-C 1-Ar); 125.6 (*o*-C 1-Ar); 126.5 (C-5); 128.4 (d, $J_{C–F}$ = 9.1, *o*-C 3'-Ar); 131.4 (*i*-C 3'-Ar); 132.2 (C-4); 133.7 (C-5'), 136.7 (*i*-C 1-Ar); 140.2 (C-4'); 147.1 (*p*-C 1-Ar); 160.6 (C=O); 162.6 (d, $J_{C–F}$ = 248.6, *p*-C 3'-Ar). Found, %: C 53.01; H 2.89; N 23.99. $C_{18}H_{12}FN_7O_4$. Calculated, %: C 52.82; H 2.95; N 23.95.

Ethyl 5-[1-(4-Nitrophenyl)-1*H*-1,2,3-triazol-4-yl]-3-phenylisoxazole-4-carboxylate (9). Prepared similarly to compound **3**. Yield 0.319 g (79%); mp 241-243°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.17 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 4.27 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 7.46-7.57 (3H, m, H Ar); 7.63-7.69 (2H, m, H Ar); 8.34-8.40

(2H, m, H Ar); 8.45-8.52 (2H, m, H Ar); 9.70 (1H, s, H-5). ^{13}C NMR spectrum, δ, ppm: 13.8 ($CH_2\underline{C}H_3$); 61.6 ($\underline{C}H_2CH_3$); 109.1 (C-4'); 121.1 (*o*-C Ar); 124.6 (C-5); 125.7 (*m*-C Ar); 128.2 (*o*-C Ph); 129.5 (*m*-C Ph); 130.1 (*p*-C Ph); 137.1 (*i*-C Ar); 140.5 (*i*-C Ph); 140.7 (C-4); 147.8 (*p*-C Ar); 162.0 (C=O); 162.9 (C-3'); 164.3 (C-5'). Found, %: C 59.55; H 3.59; N 17.24. $C_{20}H_{15}N_5O_5$. Calculated, %: C 59.26; H 3.73; N 17.28.

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