Synthesis of 8,8-R,R-8,9-dihydro[1,2,4]triazolo[1,5-*a*]quinazolin-6(7*H*)-ones

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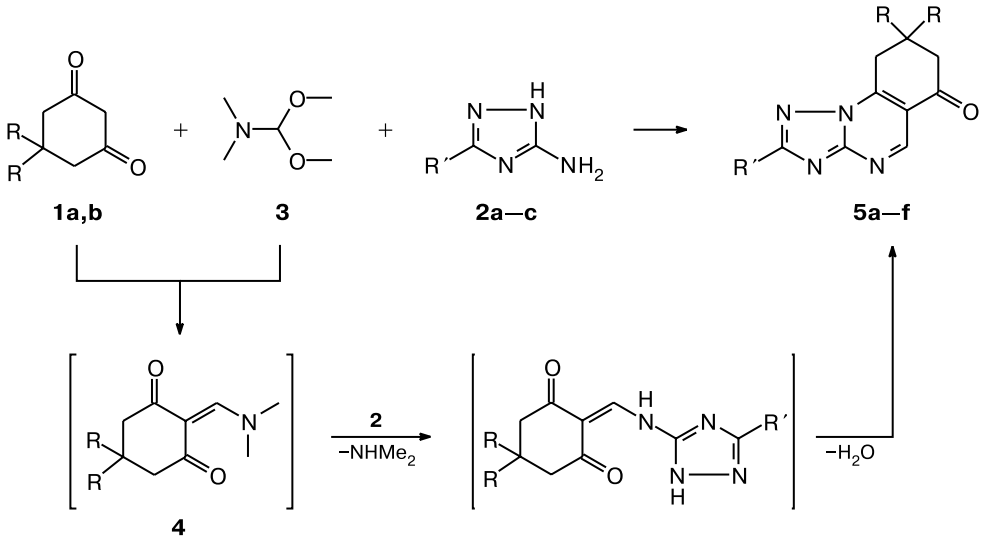
Three-component condensation of 3-amino-1,2,4-triazole (or its 5-methyl and 5-methylthio derivatives), dimedone (or cyclohexane-1,3-dione), and dimethylformamide dimethyl acetal afforded 8,8-R,R-8,9-dihydro[1,2,4]triazolo[1,5-*a*]quinazolin-6(7*H*)-ones.

Key words: 3-amino-1,2,4-triazole, dimedone, cyclohexane-1,3-dione, dimethylformamide dimethyl acetal, 8,8-dimethyl-8,9-dihydro[1,2,4]triazolo[1,5-*a*]quinazolin-6(7*H*)-one, three-component condensation.

Earlier,[1] we have found that hetarylguanidines of the formula $HetNHC(=NH)NH_2$ (Het is benzoxa(thia)zol-2-yl and 5-ethoxycarbonyl-4-methyl-1,3-thiazol-2-yl) enter into three-component condensation with triethyl orthoformate and dimedone (**1a**) to give the corresponding *N*-hetaryl-*N*-tetrahydrooxoquinazolylamines. Later,[2] we extended this reaction to 2-aminobenzimidazole, which also belongs to 1,3-azabinucleophiles; in the latter case, the tetrahydroquinazoline ring is annelated.

However, an attempt to employ 3-amino-1,2,4-triazole (**2a**) failed. Instead of the target product, which usually precipitates even from the hot reaction mixture, we obtained a multicomponent mixture that was difficult to separate (TLC). The synthesis was successful when orthoformate was replaced by dimethylformamide dimethyl acetal (**3**) used in such processes.[3,4] Apparently, the reaction proceeds through the *in situ* formation of enaminone **4** (Scheme 1). A reaction of the latter with aminotriazole, which is accompanied by elimination of the readily leaving dimethylamino group, gives rise to an intermediate whose intramolecular condensation yields the final product **5**. The reaction was extended to 3-amino-5-methyl- and 3-amino-5-methylthio-1,2,4-triazoles and cyclohexane-1,3-dione. The best results were obtained

Scheme 1



R = Me (**1a**, **5a—c**), H (**1b**, **5d—f**); R´ = H (**2a**, **5a,d**), Me (**2b**, **5b,e**), MeS (**2c**, **5c,f**)

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upon mixing of DMF dimethyl acetal with a dicarbonyl compound followed by addition of aminotriazole. This prevented possible side reactions of the latter with dimethyl acetal.

Experimental

The course of the reactions was monitored and the purity of the products was checked by TLC on Silufol UV-254 plates with chloroform—ethyl acetate (1 : 2) as an eluent. ^{1}H NMR spectra were recorded on a Bruker AC-300 instrument (300 MHz) in DMSO-d_6 with Me_4Si as the internal standard.

8,8-Dimethyl-8,9-dihydro[1,2,4]triazolo[1,5-*a*]quinazolin-6(7*H*)-one (5a). Dimedone **1** (1.4 g, 10 mmol) was added to dimethyl acetal **3** (1.44 g, 12 mmol) and the mixture was heated at 60 °C to complete homogenization, whereupon aminotriazole **2** (0.84 g, 10 mmol) was added. The reaction mixture was refluxed for 30 min. After cooling, it solidified and was diluted with propan-2-ol. The precipitate was filtered off and recrystallized from DMF. The yield of compound **5a** was 1.88 g (87%), m.p. 172—174 °C. Found (%): C, 61.26; H, 5.45; N, 25.74. $C_{11}H_{12}N_4O$. Calculated (%): C, 61.10; H, 5.59; N, 25.91. ^{1}H NMR, δ: 1.21 (s, 6 H, 2 Me); 2.65, 3.41 (both s, 2 H each, CH_2); 8.61 (s, 1 H, CH of triazole); 9.14 (s, 1 H, CH of quinazoline).

Compounds **5b—f** were obtained analogously.

2,8,8-Trimethyl-8,9-dihydro[1,2,4]triazolo[1,5-*a*]quinazolin-6(7*H*)-one (5b). The yield was 84%, m.p. 164—166 °C. Found (%): C, 62.61; H, 6.09; N, 24.42. $C_{12}H_{14}N_4O$. Calculated (%): C, 62.59; H, 6.13; N, 24.33. ^{1}H NMR, δ: 1.21 (s, 6 H, 2 Me); 2.60, 3.38 (both s, 2 H each, CH_2); 2.76 (s, 3 H, Me); 9.08 (s, 1 H, CH of quinazoline).

8,8-Dimethyl-2-methylthio-8,9-dihydro[1,2,4]triazolo[1,5-*a*]quinazolin-6(7*H*)-one (5c). The yield was 78%, m.p. 157—159 °C. Found (%): C, 60.11; H, 5.29; N, 21.44. $C_{12}H_{14}N_4OS$. Calculated (%): C, 54.94; H, 5.38; N, 21.36. ^{1}H NMR, δ: 1.20 (s, 6 H, 2 Me); 2.60, 3.32 (both s, 2 H each, CH_2); 2.71 (s, 3 H, MeS); 9.01 (s, 1 H, CH of quinazoline).

8,9-Dihydro[1,2,4]triazolo[1,5-*a*]quinazolin-6(7*H*)-one (5d). The yield was 73%, m.p. 211—213 °C. Found (%): C, 57.46; H, 4.29; N, 29.62. $C_9H_8N_4O$. Calculated (%): C, 57.44; H, 4.28; N, 29.77. ^{1}H NMR, δ: 2.32 (m, 2 H, C(8)H_2); 2.76 (t, 2 H, C(9)H_2, ^3J = 8.4 Hz); 3.51 (t, 2 H, C(7)H_2, ^3J = 8.4 Hz); 8.61 (s, 1 H, CH of triazole); 9.16 (s, 1 H, CH of quinazoline).

2-Methyl-8,9-dihydro[1,2,4]triazolo[1,5-*a*]quinazolin-6(7*H*)-one (5e). The yield was 75%, m.p. 280—282 °C. Found (%): C, 59.48; H, 4.79; N, 27.67. $C_{10}H_{10}N_4O$. Calculated (%): C, 59.40; H, 4.98; N, 27.71. ^{1}H NMR, δ: 2.32 (m, 2 H, C(8)H_2); 2.72 (t, 2 H, C(9)H_2, ^3J = 8.4 Hz); 2.89 (s, 3 H, Me); 3.46 (t, 2 H, C(7)H_2, ^3J = 8.4 Hz); 9.08 (s, 1 H, CH of quinazoline).

2-Methylthio-8,9-dihydro[1,2,4]triazolo[1,5-*a*]quinazolin-6(7*H*)-one (5f). The yield was 70%, m.p. 170—172 °C. Found (%): C, 51.24; H, 4.29; N, 23.97. $C_{10}H_{10}N_4OS$. Calculated (%): C, 51.27; H, 4.30; N, 23.91. ^{1}H NMR, δ: 2.32 (m, 2 H, C(8)H_2); 2.70 (t, 2 H, C(9)H_2, ^3J = 8.4 Hz); 2.78 (s, 3 H, MeS); 3.42 (t, 2 H, C(7)H_2, ^3J = 8.4 Hz); 9.03 (s, 1 H, CH of quinazoline).

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