New transformation of α-acetylenic ketones under the action of 1,2-diaminoethane

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A reaction of 3-aryl-1-(3,4,5-trimethoxyphenyl)prop-2-yn-1-ones with 1,2-diaminoethane in boiling dioxane leads to 2-aryl-4,5-dihydro-1*H*-imidazoles and 1-(3,4,5-trimethoxyphenyl)ethanone.

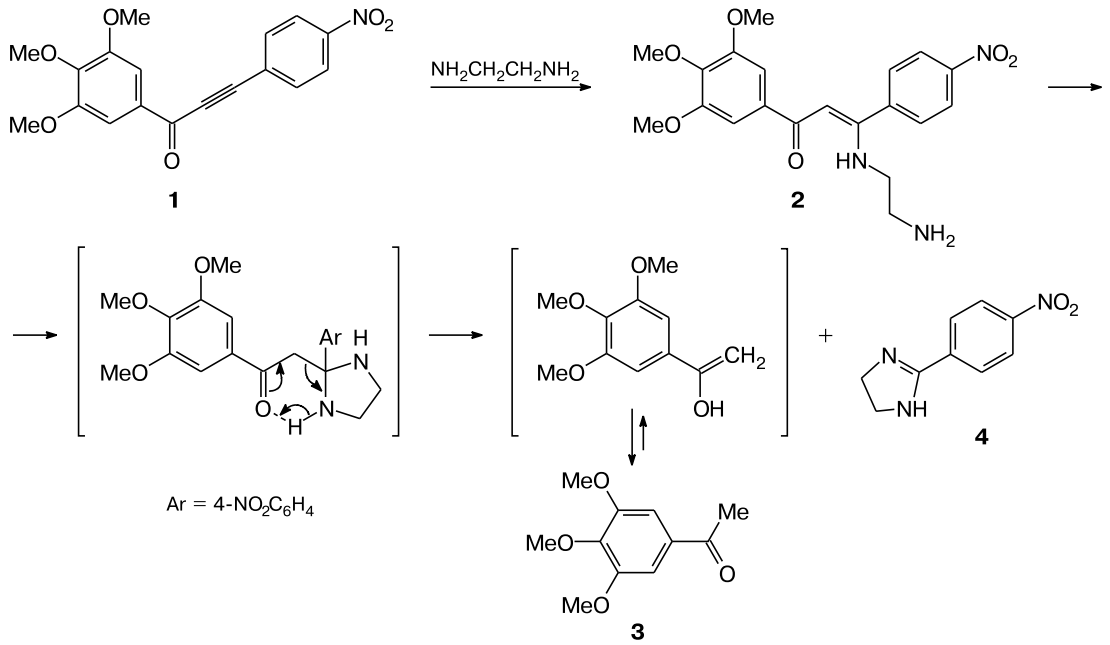
Key words: α-acetylenic ketones, heterocyclization, 1,2-diaminoethane, imidazolidines.

Earlier,[1] we have reported the data on the reaction of α-acetylenic ketone **1** with amino compounds (hydrazine hydrate, guanidine, hydroxylamine), which leads to heterocyclic derivatives, analogs of combretastatin A-4 (see Ref. 2). In continuation of our study of nucleophilic addition at the triple bond having in mind new analogs with a heterocyclic bridge, we studied a reaction of α-alkynylketones with 1,2-diaminoethane.

Herein we have found that reflux of 3-(4-nitrophenyl)-1-(3,4,5-trimethoxyphenyl)prop-2-yn-1-one (**1**) and 1,2-diaminoethane in dioxane (0.5 h) leads not only to the expected 3-(2-aminoethylamino)-3-(4-nitrophenyl)-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (**2**) (13%), but also to unexpected products of fragmentation at the triple bond, *i.e.*, 1-(3,4,5-trimethoxyphenyl)ethanone (**3**) (35%) and 2-(4-nitrophenyl)-4,5-dihydro-1*H*-imidazole (**4**) (34%) (Scheme 1).

To find whether this reaction takes place in the case of substrates having no additional electron-withdrawing substituent (NO_2), we carried out the reaction of 1,2-diami-

Scheme 1



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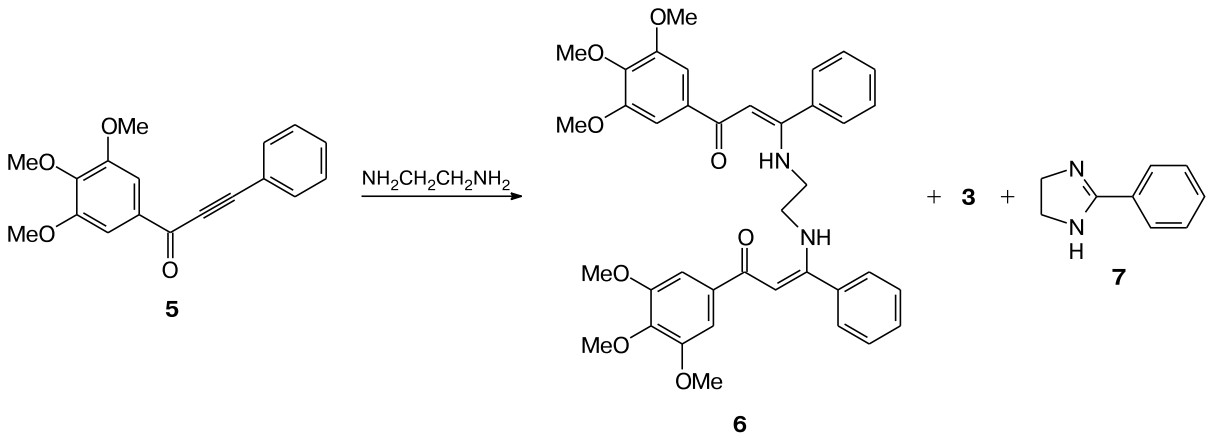
Scheme 2



noethane with phenylethynyl ketone **5** (Scheme 2). However, in this case formation of fragmentation products, ketone **3** and imidazole **7**, also took place, whose yields were 45 and 42%, respectively. In addition, instead of monosubstituted 1,2-diaminoethane, similar to compound **2**, a product of the double addition, symmetric diamine **6**, was formed (6%).

In conclusion, an unusually ready cleavage at the activated triple bond under the action of 1,2-diaminoethane was found, which leads to the corresponding aryl methyl ketones and 2-aryl-4,5-dihydro-1*H*-imidazoles.

Experimental

IR spectra were recorded on a Bruker Vector 22 spectrometer in KBr pellets. NMR spectra were recorded on a Bruker AV 400 spectrometer (400.13 MHz) in $CDCl_3$ or DMSO-d_6. Mass spectra were obtained on a Thermo Scientific DFS instrument (Double Focusing Sector Mass Spectrometer, Thermo Electron Corporation) with the direct inlet of the sample (the temperature of the ionization chamber was 220—270 °C, the ionization potential was 70 eV). Merck 60 (0.063—0.2 mm) silica gel was used for chromatography, TLC monitoring was performed on Silufol 60 F254 plates.

Reaction of 3-(4-nitrophenyl)-1-(3,4,5-trimethoxyphenyl)-prop-2-yn-1-one (1) with 1,2-diaminoethane. A mixture of ketone **1** (see Ref. 1) (0.682 g, 2 mmol) and 1,2-diaminoethane (0.12 g, 2 mmol) in dioxane (10 mL) was refluxed for 0.5 h. The reaction progress was monitored by TLC (Silufol, AcOEt). The reaction mixture was concentrated *in vacuo*, the residue was subjected to chromatography on silica gel (eluent: hexane, hexane—toluene (1 : 1), toluene, toluene—AcOEt (1 : 1), AcOEt).

3-(2-Aminoethylamino)-3-(4-nitrophenyl)-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (2). The yield was 0.11 g (13%), m.p. 258—260 °C (dioxane). ^{1}H NMR ($CDCl_3$), δ: 1.60 (br.s, 2 H, NH_2); 3.34 (m, 2 H, C(1)H_2); 3.76 (m, 2 H, C(2)H_2); 3.93 (s, 9 H, OMe); 5.73 (s, 1 H, =CH); 7.15 (s, 2 H, H(2′), H(6′)); 7.53 (d, 2 H, $H(2)_{Ph}$, $H(6)_{Ph}$, J = 8.6 Hz); 8.29 (d, 2 H, $H(3)_{Ph}$, $H(5)_{Ph}$, J = 8.6 Hz); 11.13 (s, 1 H, NH). ^{13}C NMR, δ: 45.25 (CH_2NH_2); 56.12 (2 OCH_3); 60.83 (OCH_3); 67.84 (CH_2NH); 94.03 (CH); 104.34 (C(2′), C(6′)); 124.02 (C(3), C(5)); 128.87 (C(2), C(6)); 134.40 (C(1′)); 140.85 (C(1)); 141.26 (C(4′)); 148.33 (C(4)); 153.03 (C(3′), C(5′)); 163.67 (CNH); 188.06 (CO). IR (KBr), ν/cm^{-1}: 3429 (NH). HRMS, found: m/z 384.1313 $[M - NH_3]^+$ ($C_{20}H_{20}O_6N_2$), 357.1084 $[M - CH_3CH{=}NH_2]^+$ ($C_{18}H_{17}O_6N_2$). Calculated: M = 401.1581 ($C_{20}H_{23}N_3O_6$).

The reaction also yielded **1-(3,4,5-trimethoxyphenyl)ethanone (3)** (0.15 g, 35%), m.p. 76—78 °C (benzene) (*cf.* Ref. 3: m.p. 77—79 °C) and **2-(4-nitrophenyl)-4,5-dihydro-1*H*-imidazole (4)** (0.13 g, 34%), m.p. 242—244 °C (dioxane) (*cf.* Ref. 4: m.p. 242—243 °C).

The reaction of 1-(3,4,5-trimethoxyphenyl)-3-phenylprop-2-yn-1-one (**5**)[5] with 1,2-diaminoethane was carried out similarly, the reaction time was 9 h. The reaction mixture was concentrated *in vacuo*, the residue was subjected to chromatography on silica gel (eluent hexane, hexane—toluene (1 : 1), toluene, toluene—AcOEt (1 : 1), AcOEt).

***N*,*N*′-Bis[3-oxo-1-phenyl-3-(3,4,5-trimethoxyphenyl)prop-1-en-1-yl]ethane-1,2-diamine (6).** The yield was 0.07 g (6%), m.p. 202—204 °C (benzene). ^{1}H NMR ($CDCl_3$), δ: 3.33 (m, 2 H, CH_2); 3.88 (s, 9 H, OMe); 5.68 (s, 1 H, =CH); 7.12 (s, 2 H, H(2′), H(6′)); 7.26 (m, 2 H, $H(2)_{Ph}$, $H(6)_{Ph}$); 7.44 (m, 3 H, $H(3)_{Ph}$—$H(5)_{Ph}$); 11.26 (s, 1 H, NH). ^{13}C NMR, δ: 44.97 (CH_2); 56.10 (2 OCH_3); 60.78 (OCH_3); 93.82 (CH); 104.22 (C(2′), C(6′)); 127.51 (C(2), C(6)); 128.63 (C(3′), C(5′)); 129.41 (C(4)); 134.99 (C(1′)); 135.35 (C(1)); 140.54 (C(4′)); 152.81 (C(3′), C(5′)); 166.48 (CNH); 187.67 (CO). IR (KBr), ν/cm^{-1}: 3437 (NH). Found (%): C, 69.94; H, 6.17; N, 4.35. $C_{38}H_{40}N_2O_8$. Calculated (%): C, 69.96; H, 6.18; N, 4.29.

The reaction also yielded **1-(3,4,5-trimethoxyphenyl)ethanone (3)** (0.35 g, 45%), m.p. 76—78 °C (benzene) (*cf.* Ref. 3: m.p. 77—79 °C) and **2-phenyl-4,5-dihydro-1*H*-imidazole (7)** (0.21 g, 42%), m.p. 93—95 °C (benzene) (*cf.* Ref. 6: m.p. 92—94 °C).

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