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Reaction of Aliphatic Imines of Trimethylsilylpropinal with 8-Mercaptoadenine

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Abstract—*N*9-Alkyl-7-(trimethylsilyl)-9*H*-[1,3]-thiazino[3,2-*e*]purine-4,9-diamines were synthesized by reaction of 3-trimethylsilyl-2-propinal alkylimines with 8-mercaptoadenine in anhydrous DMF. DFT quantum-chemical calculations of isomeric forms of one of the reaction products were performed.

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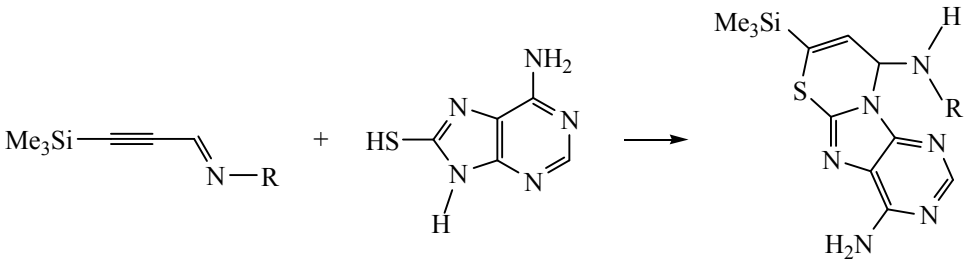
Presently chemistry of 1-aza-1,3-enynes is one of the intensively developing fields of organic chemistry since purposeful synthesis of heterocyclic compounds of different types is possible on their basis [1–5].

It was shown earlier that the reaction of 1-aza-1,3-enines with 2-mercaptobenzimidazole gives rise to polynuclear heterocyclic compounds, benzo[4,5]-imidazole[2,1-*b*][1,3]thiazin-4-ols [6]. Reaction of *tert*-butylimine of 3-trimethylsilyl-2-propinal with 2-mercaptobenzimidazole proceeds in methanol and is accompanied with desilylation [6]. In this work the reaction of alkylimines of 3-trimethylsilyl-2-propinal with 2-mercaptobenzimidazole, 8-mercaptoadenine, in DMF was studied.

Reaction of azaenynes with 8-mercaptoadenine proceeds in anhydrous DMF at room temperature with small exothermal effect over ~30 min to give desired products **I–III**.



I–III

R = *t*-Bu (**I**); cyclo-C_6H_{11} (**II**); Bn (**III**).

The obtained compounds **I–III** are crystalline substance with high melting points (>200ºC). Individuality of these compounds was proved by ^{1}H NMR spectroscopy.

The ^{1}H NMR spectrum of compound **I** (Fig. 1) contains a doublet at δ_H 6.43 ppm with the spin–spin coupling constant J_{HH} 5.08 Hz (H^1), a doublet at δ_H 2.34 ppm with J_{HH} 8.72 Hz (H^2), and a multiplet at δ_H 6.12–6.14 ppm (H^3, thiazine ring). The singlet signal at δ_H 0.29 ppm originates from nine trimethylsilyl protons. *tert*-Butyl protons appear as a singlet signal at δ_H 1.04 ppm. The singlet at δ_H 6.83 ppm belongs to two protons of aromatic amino group. The heterocyclic ring proton H^4 appears as a singlet signal at 8.06 ppm.

Compound **I** can exist as two possible isomers: *N*9-*tert*-butyl-7-(trimethylsilyl)-9*H*-[1,3]thiazino[3,2-*e*]-purine-4,9-diamine **Ia** and *N*6-*tert*-butyl-8-(trimethyl-silyl)-6*H*-[1,3]thiazino[3,2-*f*]purine-4,6-diamine **Ib** (Fig. 2). Analysis of ^{1}H NMR spectrum of compounds **I–III** testifies that all studied reactions afforded only

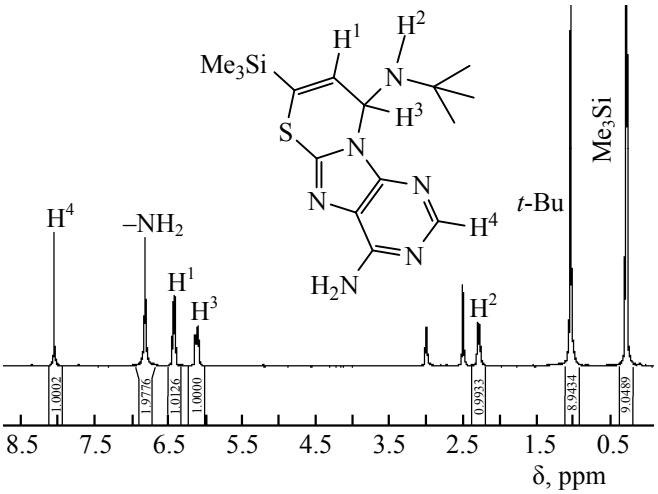


Fig. 1. [1]H NMR spectrum of compound **I**.

one isomer from two possible. However, it is impossible to conclude from these data, which isomer is the most probable product.

In order to establish, which of isomers **Ia** or **Ib** has most energetically advantageous structure, we made quantum-chemical calculations by DFT B3LYP method on 6-31G** basis using Jaguar 7.5 program package [7]. Analysis of normal vibration frequencies shows that geometries of isomer structures, obtained as a result of optimization, in gaseous phase correspond to minima on potential energy surface. Structural parameters of isomers **Ia** and **Ib** obtained as a result of the optimization of their geometry are represented in Fig. 2.

Calculated values of total energies of systems E_{tot} attest that at small difference in energies of zero vibration level the lesser value of E_{tot} (by –38.9 kJ mol^{-1}) is in isomer **Ia**, what allows a conclusion on its greater stability. The analysis of contributions in E_{tot} shows that its electron constituent, E_{el}, favors isomer **Ib** stabilization. However an overall decrease in E_{tot} in the case of isomer **Ia** is achieved by smaller energy contribution of the nuclear interaction energy E_{nuc}. Therefore, the increase in nuclear repulsion energy is one of the main factors, which destabilizes isomer **Ib**.

Based on quantum-chemical calculations for compound **I**, it is presumable that for similar compounds **II** and **III** the most energetically favorable isomers are those where the NH_2-groups are arranged similar to the structure of isomer **Ia**.

Therefore, the reaction of *N*-alkylimines of 3-trimethylsilyl-2-propinal with 8-mercaptoadenine in anhydrous DMF, unlike reaction of *N*-*tert*-butylimine of 3-trimethylsilyl-2-propinal with 2-mercaptobenzimidazole in methanol [6], leads to the retaining trimethylsilyl and amine moieties in compounds **I–III**. According to quantum-chemical DFT calculations, the most probable reaction product is the isomer, where the distance between aromatic and alkyl amino groups is maximal.

EXPERIMENTAL

Analytically pure reagents and solvents were used for the synthesis. The [1]H NMR spectra were registered on a Varian XL-300 instrument at operating frequency 300.13 MHz in DMSO-d_6. Elemental analysis was performed on a CHN-analyzer Perkin-Elmer 2400.

***N*9-*tret*-Butyl-7-(trimethylsilyl)-9*H*-[1,3]thiazino-[3,2-*e*]purine-4,9-diamine (I).** To 50 ml of 0.01 M

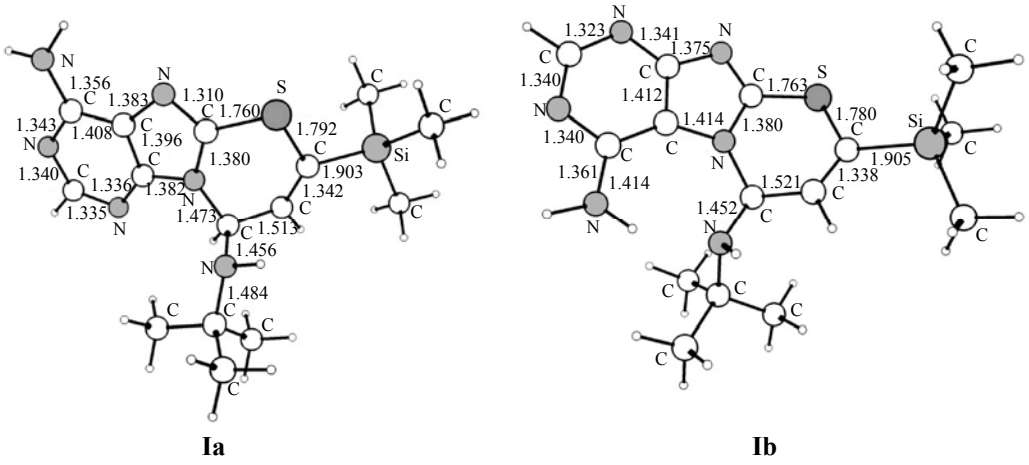


Fig. 2. Molecular structure and main bond lengths by DFT data for compound **I**.

solution of trimethylsilylpropinal imine in anhydrous DMF was added 0.01 mol of 8-mercaptoadenine at stirring to complete reagents dissolution. Then the mixture was filtered. After 30 min the end product begins to crystallize. Yellow crystals were filtered off and dried in air. Yield 60%, mp 282°C. Found, %: C 51.6; H 6.8; N 24.2. $C_{15}H_{24}N_6SSi$. Calculated, %: C 51.69; H 6.94; N 24.11. ^{1}H NMR spectrum, δ, ppm: 0.29 s (9H); 1.04 s (9H), 2.28 d (1H, $^3J_{HH}$ 8.72 Hz), 6.10–6.15 m (1H), 6.43 d (1H, $^3J_{HH}$ 5.08 Hz), 6.83 br.s (2H), 8.06 s (1H).

***N*9-Cyclohexyl-7-(trimethylsilyl)-9*H*-[1,3]thiazino-[3,2-*e*]purine-4,9-diamine (II)** was prepared similarly. Yield 55%, mp 242°C. Found, %: C 54.7; H 6.9; N 22.5. $C_{17}H_{26}N_6Ssi$. Calculated, %: C 54.51; H 7.00; N 22.44. ^{1}H NMR spectrum, δ, ppm: 0.29 s (9H), 0.81–1.08 m (5H), 1.48–1.58 m (5H), 2.39–2.51 m (2H), 6.12 t (1H, $^3J_{HH}$ 11.62 Hz), 6.24 d (1H, $^3J_{HH}$ 5.09 Hz), 7.70 s (2H), 8.04 s (1H).

***N*9-Benzyl-7-(trimethylsilyl)-9*H*-[1,3]thiazino-[3,2-*e*]purine-4,9-diamine (III)** was prepared similarly. Yield 60%, mp 220°C. Found, %: C 56.4; H 5.6; N 21.9. $C_{18}H_{22}N_6SSi$. Calculated, %: C 56.5; H 5.8; N 21.9. ^{1}H NMR spectrum, δ, ppm: 0.29 s (9H), 3.41–3.56 m (3H), 6.10 d (1H, $^3J_{HH}$ 4.36 Hz), 6.25 d (1H, $^3J_{HH}$ 4.36 Hz), 6.98 br. s (2H), 7.08–7.20 m (5H), 8.03 s (1H).

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