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The Interaction of 3,6-dihydrazino-s-tetrazine with some aliphatic aldehydes

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Abstract

The condensation of 3,6-dihydrazino-s-tetrazine with a number of the substituted and unsubstituted aliphatic aldehydes has been studied; this reaction procedure conditions have been determined; the isomeric composition of the corresponding hydrazones has been identified. The addition of the unsubstituted aldehydes to the reaction has been shown to result in the selective formation of E-isomers while α- or β- substituted aldehydes form the mixture of Z,E-isomers of azomethynes. It has been found that 3,6-bis(allylidenehydrazino)-s-tetrazine in the solution of dimethylsulfoxide corresponds to the aromatic form (87.5%) and chinoid form (12.5%). The effect of pH medium on 3,6-Bis (allylidenehydrazino)-s-tetrazine in the solutions has been studied. The presence of the double bonds in the allylic fragment has been found out to promote deeper conjugation followed by the chinoid structure formations.

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Keywords: 3,6-dihydrazino-s-tetrazine, condensation, azomethynes, aldehydes, Z, E – isomers.

1. Introduction

The derivatives of s-tetrazine are being drawn many researchers attention due to the availability of a number of valuable properties because of their application in practice. They are distinguished by the increased crystalline density, high positive enthalpy of the formation, thermal stability and a pronounced proportion of nitrogen1, 2.

Thanks to the complex of these characteristics, the compounds based on s-tetrazine are promising to be used in
the high energy compositions\textsuperscript{3}, gas generating formulations\textsuperscript{4}, smokeless propellants\textsuperscript{5,6}, as starting substances to prepare nanomaterials on the base of carbon nitride\textsuperscript{7,8}.

The literature gives little informations on the reactions of 3,6-dihydrazino-s-tetrazine with the derivatives of the carbonyl compounds. The derivatives of 3,6-dihydrazino-s-tetrazine with acetaldehyde, benzaldehyde, salicylaldehyde and acetone\textsuperscript{9} have been described. However, the methods cited by some authors can be improved through the yield and purity of the end products. In addition, some spectral characteristics of the compounds should be revised to corroborate the compounds structure.

2. Result and Discussion

The thermodynamic calculations we have been performed for some substances in the row of the azomethynes derivatives of 3,6-dihydrazino-s-tetrazine showed their high probabilistic energy characteristics (Table 1).

Table 1. The calculated parameters of derivatives 3,6-dihydrazino-s-tetrazine.

| Compound | \(\Delta H\), kD/kg | \(\rho\), g/cm\(^3\) |
|----------|------------------|------------------|
| 3 | 4401.6 | 1.541 |
| 4a | 3181.9 | 1.325 |
| 4b | 2525.0 | 1.273 |
| 4c | 2015.0 | 1.232 |
| 4e | 4515.4 | 1.453 |
| 4f | 838.1 | 1.292 |
| 4g | 1663.0 | 1.494 |
| 4h | 3912.5 | 1.403 |
| 4i | 3461.8 | 1.336 |
| 4j | 6039.6 | 1.252 |

The compounds given have been synthesized via the condensation of 3,6-dihydrazino-s-tetrazine with the substituted and unsubstituted aliphatic aldehydes.

In using the acetals of aldehydes in the condensation reaction with 3,6-dihydrazino-s-tetrazine in the acidic medium as well as in the case of the preparation of the azomethynes derivatives of 1,5-diaminotetrazole shown earlier\textsuperscript{10} we haven’t obtained the results desired. We can explain this by a low stability of 3,6-dihydrazino-s-tetrazine in the acidic medium. The reaction has been successfully carried out in the neutral medium, 3,6-dihydrazino-s-tetrazine having nucleophilicity sufficient enough to interact with a number of aldehydes, so the presence of an acid needed to activate the carbonyl group isn’t required.

Taking the instability and hard isolation of certain aldehydes into the account we have developed and succeeded in using two-stages one pot method to obtain desired products.

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\begin{align*}
\begin{array}{c}
\text{R} \\
\text{OC}_2\text{H}_5
\end{array}
\quad \xrightarrow{\text{H}^+ / \text{HOH}}
\begin{array}{c}
\text{R} \\
\text{OC}_2\text{H}_5
\end{array}
\end{align*}
\]

\[
\begin{align*}
\begin{array}{c}
\text{H}_2\text{NN} \quad \text{N} \quad \text{N} \\
\text{N} \quad \text{N} \quad \text{N} \quad \text{NH} \quad \text{NH}_2
\end{array}
\quad \xrightarrow{\text{pH}=7}
\begin{array}{c}
\text{R} \\
\text{NN} \quad \text{N} \quad \text{N} \\
\text{N} \quad \text{N} \quad \text{NN} \quad \text{NH} \\
\text{NH}_2
\end{array}
\end{align*}
\]

Fig. 1. Scheme of condensations 3,6-dihydrazino-s-tetrazine with aldehydes.

At the first stage the hydrolysis of acetal and the neutralization of the reaction mixture up to pH=7 are to be carried out. At the second stage, into the solution obtained 3,6-dihydrazino-s-tetrazine is added, and the process is completed in the same reactor. Easily accessible and stable aldehydes can be added into the reaction in a free form. The condensation reaction proceeds in an aqueous medium the acryl aldehyde excluded the reaction of that with 3,6-dihydrazino-s-tetrazine in the aqueous medium yields polymeric products. We managed to synthesize the compound.
(4 i) in performing the reaction in methanol with the catalytic quantity of glacial acetic acid present. Thus, the following compounds given in the table 2 were obtained.

Table 2. Synthesized azomethyne derivatives of 3,6-dihydrazino-s-tetrazine

| Compounds 4 | R            | Yield, % | Reactions time, hrs |
|-------------|--------------|----------|---------------------|
| a           | CH₃          | 42.6     | 4.5                 |
| b           | CH₃CH₂       | 84.6     | 5.5                 |
| c           | i-Pr         | 93.8     | 3.5                 |
| d           | BrCH₂        | 51.6     | 6                   |
| e           | N₂CH₂        | 74.2     | 4                   |
| f           | CH₂CH₂OCH₂   | 61.6     | 3                   |
| g           | NO₂CH₂CH₂    | 93.5     | 4                   |
| h           | N₂CH₂CH₂     | 82.2     | 6                   |
| i           | CH₂=CH       | 50.2     | 1.5                 |
| j           | CH≡≡C        | 74.6     | 2.0                 |

All the hydrazones obtained (4 a–j) are bright-colored crystalline substances stable in keeping. The analysis of 1H NMR-spectrum of the products isolated shows that the addition of the non-substituted aldehydes into the reaction results in selective forming E-isomers in the condensation reaction. The condensation with the aldehydes substituted favors the increased fraction of Z-isomers in the reaction products.

Table 3. 1H NMR data of tetrazines (4 a–j).

| Compounds 4 | δ, ppm CH=N (Z-isomer) | δ, ppm CH=N (E-isomer) | Correlation of E:Z-isomers | δ, ppm of other protons |
|-------------|------------------------|------------------------|-----------------------------|------------------------|
| a           | -                      | 7.50 q                 | -                           | 1.92 d (6H, H²); 11.23 s (2H, NH). |
| b           | -                      | 7.51 t                 | -                           | 1.05 t (6H, H¹); 2.27 m (4H, H²); 11.21 s (2H, NH). |
| c           | -                      | 7.45 d                 | -                           | 1.07 d (12H, H¹); 2.53 m (2H, H²); 11.25 c (2H, NH). |
| d           | 7.01 t                 | 7.73 t                 | 19:1                        | 4.82 d (4H, H²); 11.78 s (2H, NH). |
| e           | 6.83 t                 | 7.56 t                 | 19:1                        | 4.12 d (4H, H²); 11.73 s (2H, NH). |
| f           | 6.85 t                 | 7.53 t                 | 17:3                        | 1.13 t (6H, H¹); 3.48 q (4H, H²); 4.08 d (4H, H³); 11.61 s (2H, NH). |
| g           | 6.77 t                 | 7.54 t                 | 19:1                        | 2.92 q (4H, H²); 4.81 t (4H, H³); 11.47 s (2H, NH). |
| h           | 6.75 t                 | 7.50 t                 | 19:1                        | 2.55 q (4H, H²); 3.57 t (4H, H³); 11.45 s (2H, NH). |
| i           | -                      | 7.87 d                 | -                           | 5.59 q (4H, H²); 6.53 m (2H, H³); 11.71 s (2H, NH). |
| j           | -                      | 8.11 s                 | -                           | 3.82 s (2H, H³); 7.69 s (2H, H³); 11.01 s (2H, NH). |

A high thermodynamic stability of E-isomers is exhibited in heating the compounds (4d–h) in dimethylformamide. For 4 hours, according to the loss of the signal of the azomethyne proton of Z-isomers in the 1H NMR-spectrum, the quantitative isomerization of Z- into E-isomers has been occurring. In neutral and basic media the limiting stage of the addition is commonly the stage of dehydration. The formation of the alternative geometric isomers is executed via the E-isomer predominance, where the tetrazine fragment is located on the same side with the hydrogen atom of the aldehyde group. The thermodynamics of the water eliminating out also favors to form E-isomers, and the experimental results on the isomerization of Z-isomers into E-form are verified.

The analysis of 1H NMR – spectrum for the compound (4 i) recorded in deuterated dimethylsulfoxide showed the presence of two singlet signals at 11.71 and 11.39 ppm in the region that is characteristic for NH-protons. The signal at 11.71 ppm corresponds to the structure of (4 i), and the signal at 11.39 ppm corresponds to tautomeric chinoid...
structure (4i-I) presented in the scheme 2.

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\text{4i-I}
\]

Fig. 2. Chinoid form of 3,6-Bis(allylidenehydrazino)-s-tetrazine.

The integral intensity of NH-protons (4i-4i-I) ratio is 7:1. The color of the compound obtained is specific, if the derivatives of 3,6-dihydrazino-s-tetrazine are of bright-red color, then the compound (4i) is visualized as dark-blue crystals. The basic medium bonding the mobile NH-proton is assumed to promote the tautomeric transition into the structure (4i-I). To elucidate this theory we have studied the influence of pH-medium on the equilibrium of the tautomeric structures (4i and 4i-I) in the solution of DMSO – H₂O (2:1). In adding the bases (aqueous solutions of alkali and ammonia) the color changes drastically from the orange-red to blue-green one. On the other hand, when acidifying the solution obtained up to pH=7, the original orange-red color is restored. More detailed investigation of pH-effect on the tautomeric transition (4i-4i-I) has been made on the UV- spectrophotometer in the visible rage. The curves of the absorption for the compound (4i) in the neutral (1), alkaline (2, pH=12) and acidic (3, pH=2) media are given the figure 3.

Fig. 3. The Curves of the absorption 3,6-Bis(allylidenehydrazino)-s-tetrazine under different values pH.

Due to the value of the bathochromic shift (38 nm), one can suppose the formation of the ionic structures (4i-II) (fig.4) followed by a deeper cycle conjugation with the external π – bonds.

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\text{4i-II}
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Fig. 4. Ionic form of 3,6-Bis(allylidenehydrazino)-s-tetrazine
The aggregation of the facts said above is a characteristic feature of chinoids. Thus, due to the ratio of the integral intensities of NH-protons in $^1$H NMR-spectrum one can conclude that the compound (4i) in the solution of the deuterated dimethylsulfoxide consists of an aromatic form of tetrazine (87.5 %) and a chinoid form (12.5 %).

Another products of the condensation 4 (4i excluded) do not demonstrate chinoid NH-proton in $^1$H NMR-spectra. We think this phenomenon is related to a larger nucleophilicity of the double-bond conjugated and a deeper overlapping of the double C-C bond of an external chain compared with a triple C-C bond.

3. Experiment

IR-spectra were recorded on Shimadzu FTIR-9600 spectrophotometer in the tablets of KBr. UV-spectra were registered on the spectrophotometer of Shimadzu UV-1800. The elementary analysis was performed on CHN-analyzer “Carlo Erba”, model 1106, NMR-spectra were registered on Bruker AM-400 instrument (operating frequencies 400,13 ($^1$H) and 100,78 MHz ($^{13}$C), in the solutions DMSO-$d_6$ internal standard TMS. Mass-spectra were recorded on Shimadzu LCMS-8030 instrument (survey mode ESI). The purity control of the compounds obtained was carried out by TLC on the plates Alufol (Merck), the visualization was performed in UV-light and iodine steams. The starting 3,6-dihydrazino-s-tetrazine was synthesized according to the procedure described in$^{12}$.

**General compound preparation procedure (4a-c, j):** To the suspension (3.5 mmol) of 3,6-dihydrazino-s-tetrazine in the water (30 ml) while stirring the corresponding aldehyde (10.0 mmol) is added. The reaction mixture is stirred at the ambient temperature, the precipitate is filtered off, washed and dried, recrystallized from the mixture MeOH-H$_2$O 1:1. The reaction time and yields are given in the table 2, $^1$H NMR spectra data are shown in the table 3.

**General compounds preparation procedure (4d – h):** The mixture of the corresponding aldehyde acetal (8.4 mmol), water (30 ml) and concentrated hydrochloric acid (2.0ml) is being stirred for 2 hours at 55-60 °C and then it is cooled to the room temperature. The mixture is neutralized with sodium bicarbonate to pH=7 and 3,6-dihydrazino-s-tetrazine (3.5 mmol) is added. Then it is stirred at the room temperature, the precipitate is filtered off, washed with water, alcohol and then dried. It is recrystallized from MeOH-DMFA 4:1. The reaction time and yields are given in the table 2, $^1$H NMR spectra data in the table 3.

**The preparation of 3,6-Bis(allylidenedehydrazano)-s-tetrazine (4i).** The mixture of 3,6-dihydrazino-s-tetrazine 0.5g (3.5 mmol), acryl aldehyde 0.78 g (14.0 mmol), 3 drops of glacial acetic acid in methanol (15 ml) is being boiled for 1.5 hour. Then it is cooled to 0 °C, the residue is filtered off, washed with methanol and air-dried. The yield is 0.38g (50.2 %).

3.6-Bis(Ethylidenedehydrazano)-s-tetrazine (4a): mp 175 °C (dec.). R$_f$=0.46 (CHCl$_3$-MeOH 1:1). Anal.calcd. for C$_9$H$_{10}$N$_8$: C 37.11; H 5.19; N 57.70. Found: C 36.53; H 5.02; N 57.15. IR, cm$^{-1}$: 3204 (NH); 2951 (CH); 1573; 1451 (C=N); 1047 (ring). $^{13}$C NMR, δ: 18.21 (C$_2$); 143.63 (C$_3$); 159.89 (C-tetrazine). MS, m/z: 193[M-H$^+$].

3.6-Bis(Propylidenedehydrazano)-s-tetrazine (4b): mp 176 °C (dec.). R$_f$=0.48 (CHCl$_3$-MeOH 1:1). Anal.calcd. for C$_{10}$H$_{14}$N$_8$: C 47.98; H 7.25; N 44.77. Found: C 47.72; H 7.04; N 44.08. IR, cm$^{-1}$: 3214 (NH); 2929 (CH); 1575; 1446 (C=N); 1046 (ring). $^{13}$C NMR, δ: 19.96 (C$_2$); 30.96 (C$_3$); 152.18 (C$_1$); 159.89 (C-tetrazine). MS, m/z: 223[M+H$^+$].

3.6-Bis(isobutilidenedehydrazano)-s-tetrazine (4c): mp 153-154 °C (dec.). R$_f$=0.57 (CHCl$_3$-MeOH 1:1). Anal.calcd. for C$_{12}$H$_{18}$N$_8$: C 47.98; H 7.25; N 44.77. Found: C 47.72; H 7.04; N 44.08. IR, cm$^{-1}$: 3210 (NH); 2929 (CH); 1575; 1446 (C=N); 1046 (ring). $^{13}$C NMR, δ: 19.66 (C$_2$); 30.96 (C$_3$); 152.18 (C$_1$); 159.89 (C-tetrazine). MS, m/z: 251[M+H$^+$].

3.6-Bis(2-bromethylidenedehydrazano)-s-tetrazine (4d): mp 153-154 °C (dec.). R$_f$=0.46 (CHCl$_3$-MeOH 5:1). Anal.calcd. for C$_{13}$H$_{14}$Br$_2$N$_8$: C 20.27; H 2.29; N 31.83. Found, %: C 19.73; H 2.05; N 31.33. IR, cm$^{-1}$: 3210 (NH); 2998 (CH); 1564; 1423 (C=N); 1045 (ring); 744 (C-Br). $^{13}$C NMR, δ: 61.94 (C$_2$); 143.24 (C$_1$); 159.98 (C-tetrazine). MS, m/z: 273[M-Br+H$^+$].

3.6-Bis(2-azidoethylidenedehydrazano)-s-tetrazine (4e): mp 356 °C (dec.). R$_f$=0.60 (CHCl$_3$-MeOH 1:1). Anal.calcd. for C$_{19}$H$_{26}$N$_{14}$: C 26.09; H 2.92; N 31.33. Found: C 25.61; H 2.69; N 30.22. IR, cm$^{-1}$: 3208 (NH); 2995 (CH); 2100 (N$_2$); 1574; 1440 (C=N); 1045 (ring). $^{13}$C NMR, δ: 50.90 (C$_2$); 140.47 (C$_1$); 159.85 (C-tetrazine). MS, m/z: 273[M-3H$^+$].

3.6-Bis(etoxyethylidenedehydrazano)-s-tetrazine (4f): mp 157-158 °C (dec.). R$_f$=0.35 (CHCl$_3$-MeOH 10:1). Anal.calcd. for C$_{10}$H$_{12}$N$_{10}$O$_{2}$: C 42.55; H 6.43; N 39.69. Found: C 41.98; H 6.24; N 39.02. IR, cm$^{-1}$: 3213 (NH); 2977 (CH); 1581; 1446 (C=N); 1108 (C-O-C); 1046 (ring). $^{13}$C NMR, δ: 15.03 (C$_2$); 65.28 (C$_3$); 69.21 (C$_4$); 143.63
3,6-Bis(3-nitropropylidenehydrazino)-s-tetrazine (4g): mp 166-167 °C (dec.). Rf=0.58 (CHCl₃-MeOH 5:1). Anal. calcd. for C₈H₁₂N₁₀O₄: C 30.77; H 3.87; N 44.86. Found: C 30.87; H 3.69; N 44.27. IR, ν, cm⁻¹: 3214 (NH); 2923 (CH); 1552 (NO₂); 1436 (C=N); 1045 (ring). ¹³C NMR, δ: 29.22 (C₂/); 71.91 (C₃/); 142.57 (C₁/); 159.75 (C-tetrazine). MS, m/z: 281 [M-H]-.

3,6-Bis(3-azidopropylidenehydrazino)-s-tetrazine (4h): mp 135-137 °C (dec.). Rf=0.44 (CHCl₃-MeOH 10:1). Anal. calcd. for C₈H₁₂N₁₄: C 31.58; H 3.98; N 64.45. Found: C 31.01; H 3.77; N 63.89. IR, ν, cm⁻¹: 3208 (NH); 2938 (CH); 2118 (N₃); 1574; 1446 (C=N); 1045 (ring). ¹³C NMR, δ: 31.73 (C₂/); 48.01 (C₃/); 144.15 (C₁/); 159.82 (C-tetrazine). MS, m/z: 305 [M+H]+.

3,6-Bis(allylidenehydrazino)-s-tetrazine (4i): mp 212 °C (dec.). Rf=0.65 (CHCl₃-MeOH 5:1). Anal. calcd. for C₈H₁₀N₈: C 44.03; H 4.62; N 51.35. Found: C 43.51; H 4.52; N 50.89. IR, ν, cm⁻¹: 3220 (NH); 2902 (CH); 1621 (C=CH); 1581 (C=N); 1048 (ring). ¹³C NMR, δ: 122.64 (C₃/); 134.26 (C₂/); 145.70 (C₁/); 159.77 (C-tetrazine). MS, m/z: 219 [M+H]+.

3,6-Bis(propynylidenehydrazino)-s-tetrazine (4j): mp 124 °C (dec.). Rf=0.64 (CHCl₃-MeOH 5:1). Anal. calcd. for C₈H₆N₈: C 44.86; H 2.82; N 52.32. Found: C 44.23; H 2.63; N 51.78. IR, ν, cm⁻¹: 3266 (NH₂); 3117 (C≡CH); 2105 (C≡C); 1572; 1448 (C≡N); 1046 (ring). ¹³C NMR, δ: 82.19 (C₃/); 84.23 (C₂/); 144.92 (C₁/); 158.44 (C-tetrazine). MS, m/z: 215 [M+H]+.

4. Conclusions

The number of azomethyne derivatives of 3,6-dihydrazino-s-tetrazine unknown earlier has been synthesized and characterized for the first time. The effect of the substituent in the molecule of aldehyde on the isomeric composition of the condensation products has been shown. Unsubstituted aldehydes react to form E-isomers while the aldehydes substituted give the mixtures Z- and E-isomers. The methods of NMR and UV-spectroscopy allowed to conclude that the allylic position of a double bond in a side chain of a tetrazine cycle promoted forming chinoid structure with a deeper conjugation in basic media.

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