Synthesis and Spectroscopic Properties of New Azo Dyes Derived from 3-Ethylthio-5-cyanomethyl-4-phenyl-1,2,4-triazole

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Abstract: New 1,2,4-triazole colorants were obtained, in high yields, by coupling 3-ethylthio-5-cyanomethyl-4-phenyl-1,2,4-triazole (1) with diazotized aniline derivatives 2, 4 and 6. The azo dyes prepared in this work may exist in three tautomeric forms. We found that the tautomerism is influenced mainly by the nature of substituent at the para position of the aniline coupling component. This tautomerisation was observed in the NMR spectra of the dyes. The dyes were characterized by IR, 1H-NMR, 13C-NMR and MS spectroscopic techniques.

Keywords: synthesis; azo-hydrazone tautomerism; coupling reaction; diazotization

1. Introduction

Azo-functionalized dyes bearing aromatic heterocyclic components [1] have attracted ever increasing attention in recent years due to their wide range of color, brightness, simplicity and ease of manufacturing and good dyeing performance [2–5]. They are used in high tech applications such as lasers and non-linear optical systems [6], thermal transfer printing and fuel cells [7], dye sensitized solar cells [8], photodynamic therapy [9], and metallochromic indicators [10]. They are also used in dyeing textiles, leather, paper, food and cosmetic products [11]. Furthermore, azo dye compounds are known for their medicinal importance [12–15] and are also known to be involved in a number of biological
reactions such as inhibition of DNA, RNA and protein synthesis, carcinogenesis and nitrogen fixation [16]. In a broader sense, the azo dyes constitute the largest diverse group of all the synthetic colorants [17]. In addition, hydrazones are the well known class of biologically and pharmacologically active compounds in the field of synthetic chemistry [18–20]. Some hydrazones have been introduced as potent drugs such as gyromitrin [21] used as a toxin and dihydralazine [22] used as a hypertensive drug. Moreover, hydrazones are an important class of chemical intermediates, which can act as electrophiles and as nucleophiles in chemical reactions [23–27]. 1,2,4-Triazoles and their derivatives play an important role in modern drug discovery and have attracted attention from both industrial and academic groups. These systems are important pharmaceuticals due to their interesting biological activities [28–31]. Several compounds containing 1,2,4-triazole rings are well known as drugs. For example, vorozole, letrozole, and anastrozole are non-steroidal drugs used for the treatment of cancer [32], while loreclezole is used as anticonvulsant [33] and fluconazole is used as an antimicrobial drug [34]. In the light of the above report and in continuation to our previous work on the synthesis of heterocyclic systems containing 1,2,4-triazole moiety [35–37], the present work focuses on the synthesis, spectroscopic properties of some novel azo dyes derived from 3-ethylthio-5-cyanomethyl-4-phenyl-1,2,4-triazole [35]. Furthermore, we also examined the effect of substituent at the para position of the aniline coupling component on the nature of the resulting products.

In solution, the azo dyes theoretically may be involved in azo-hydrazone tautomerism. Since the tautomeric ratio is important for the industrial application of azo dyes, determination of azo-hydrazone tautomerism (AHT) in the solid state and in solution is of interest both from a theoretical and practical aspects because the two tautomers have different technical properties and dyeing performance [38]. Therefore, it was considered worthwhile to determine the tautomeric structure of the products prior to exploring their applications.

2. Results and discussions

As a starting point for our investigation, we first examined the coupling reaction of compound 1 with benzenediazonium chloride (2). Thus, coupling of diazonium salt 2 with compound 1 in aqueous ethanol in the presence of a buffered sodium acetate solution gave 5-ethylthio-\(N'\),4-diphenyl-4\(H\)-1,2,4-triazole-3-carbohydrazonoyl cyanide (3B), as the only isolable product, in excellent yield (Scheme 1).

**Scheme 1.** Coupling reaction of 1 with benzene diazonium chloride.

![Scheme 1](image)

The prepared dye may exist in three possible tautomeric forms, namely the azo form A, the hydrazone form B and the azo-enamine form C, as depicted in Figure 1. The IR spectrum (in KBr)
revealed the presence of absorption bands at $\nu = 3236$ and $2213 \text{ cm}^{-1}$ due to the NH and cyano groups, respectively. On the other hand, the other $\nu_{\text{max}}$ value at $1231 \text{ cm}^{-1}$ was assigned to the N-N stretching mode [39].

**Figure 1.** Three tautomeric structures of diazonium coupling product of 1.

Kostyuchenko et al. reported that the molecular ion of tautomeric monoazo dyes cleaves preferentially at the N-N bond in the hydrazone and at one of the C-N bonds in the azo tautomer, yielding high abundance fragments with corresponding metastable ions [40]. In the mass spectrum of 3B, the respective molecular ion peak (M+) and the (M+ + 1) peak were observed. In addition, the spectrum showed characteristic peaks at $m/z$ values corresponding to C$_8$H$_5$NH (resulting from cleavage at the N-N bond), C$_8$H$_5$N$_3$ and C$_{10}$H$_{10}$N$_3$S ion fragments. The latter two fragments correspond to 4-phenyl-1,2,4-triazole and 3-ethylthio-4-phenyl-1,2,4-triazole residues, respectively. Moreover, the base peak that appeared at $m/z$ 77 with relative intensity of 100% is due to cleavage of the phenylium cation (Ph$^+$) from M$.^+$ Taken together the data is in good agreement with the proposed hydrazone structure. The $^1$H-NMR spectral data shows that two tautomeric forms 3B (hydrazone form) and 3C (azo-enamine form) are present in CDCl$_3$ solution with relative intensities of 1:3 (Scheme 1, Table 1).

**Table 1.** Tautomer ratios in the solid state and in CDCl$_3$ solution.

| Product | In Solid State | In CDCl$_3$ Solution |
|---------|---------------|----------------------|
|         | Azo Hydrazone | Hydrazine:Azo-enamine |
| 3       | 100           | 3B:3C (25:75)        |
| 5       | 100           | 5B:5C (20:80)        |
| 7       | 100           | 7B:7C (60:40)        |
| 8       | 100           | 8B:8C (17:83)        |

In the $^1$H-NMR spectrum a singlet at $\delta = 8.83 \text{ ppm}$ [41] is due to N-H proton of hydrazone form 3B (25%) and the other downfield singlet at $\delta = 13.71 \text{ ppm}$ [42] was assigned to the triazole N-H in the azo-enamine form 3C (75%). Tautomeric ratios were calculated from their $^1$H-NMR integrals by comparison of the NH signal of the hydrazone form 3B and NH signal of the azo-enamine form 3C. Therefore, $^1$H-NMR chemical shift data can readily be employed to study the tautomeric equilibria quantitatively. Also, the $^{13}$C-NMR spectrum of this product in CDCl$_3$ displayed signals in agreement with the mixture of two tautomers, hydrazone form 3B and azo-enamine form 3C. The spectrum showed besides the signals due to aromatic, ethyl, cyano and triazole carbones, two characteristic signals at $\delta = 99.05$ and 140.75 ppm attributable to the carbon atom at position 6 in both tautomeric forms 3C and 3B, respectively (see Experimental). Due to the novelty of this product, the $^{13}$C-NMR chemical shifts values were assigned for these carbon atoms by comparing the experimental data in the
Next, we examined the effect of substitution at the para-position of the diazonium salt benzene ring on the equilibrium between the three forms A–C (Figure 1). Recently, Pavlović and his co-workers [44] have been reported that the electron-releasing substituents at the para position of the diazonium salt benzene ring increase the azo form content, while electron-withdrawing groups increase the content of the hydrazone form. In accordance with these results, it was found that the coupling reaction of 1 with diazotized 4-methylaniline (4), under similar reaction conditions as above, afforded 5-ethyl-thio-3-(1-(4-methylphenylazo)-4-phenyl-acetonitrile)-4H-1,2,4-triazole (5A), in 82% yield (Scheme 2).

Scheme 2. Coupling reaction of 1 with diazotized 4-methylaniline.

The structure of this azo dye was verified by elemental analyses and spectroscopic methods (IR, MS, 1H- and 13C-NMR). Structure 5A seemed to be logical according to the IR spectrum (in KBr) which disclosed no amino group (NH) absorption band and the presence of intense cyano and azo (-N=N-) [45] bands at 2217 and 1547 cm\(^{-1}\), respectively. The mass spectral data of azo dye 5A showed a molecular ion peak (M\(^+\)) at \(m/z\) 362 (40%) which was in concordance with the molecular mass (362) of the product (C\(_{19}\)H\(_{18}\)N\(_6\)S). In addition, cleavage at one of the C-N bonds in the azo tautomer 5A led to the appearance of the base peak at \(m/z\) 91 (CH\(_3\)-C\(_6\)H\(_4\)) with relative intensity of 100%. Moreover, the spectrum showed characteristic peaks at \(m/z\) 119 (14%), 143 (6%), 156 (11%) and 243 (4%) corresponding to CH\(_3\)-C\(_6\)H\(_4\)-N=N (resulting from cleavage at the CN bond), C\(_3\)H\(_8\)N\(_3\) (4-phenyl-1,2,4-triazole), C\(_8\)H\(_5\)N\(_3\)-CH (4-phenyl-1,2,4-triazole with CH group at C-3), and C\(_{10}\)H\(_{10}\)N\(_3\)-CH-CN (3-ethylthio-4-phenyl-1,2,4-triazole with CH-CN group at C-5) residues, respectively. This would suggest that compound 5A exist almost exclusively in the azo form. Interestingly, the 1H-NMR spectral data shows that the hydrazone form 5B and azo-enamine tautomeric form 5C are present in CDCl\(_3\) solution with relative intensities of 1:4 (Scheme 2, Table 1). The 1H-NMR spectrum revealed a similar pattern as observed for 3B and 3C (see Experimental). Also, the spectrum do not show any more signals around 4.5 ppm which is usually reported for the methine proton of azo form 5A of the annulated similar compounds [46]. In addition, the 13C-NMR spectrum of this product in CDCl\(_3\) showed signals in accordance with the mixture of two tautomers, hydrazone form 5B and azo-enamine form 5C. The spectrum showed besides the signals due to aromatic, ethyl, methyl, cyano and triazole carbones, two characteristic signals at \(\delta = 98.34\) and 139.57 ppm attributable to carbon atom at position 6 in both tautomeric forms 5C and 5B, respectively (see Experimental).
Attention was next turned to investigate the coupling reaction of the diazonium salts having electron withdrawing substituents at para position of benzene ring with compound 1. Surprisingly, when compound 1 was coupled with diazotized 4-chloroaniline (6), under the same reaction conditions as above, it afforded two tautomers, 7A (major product) and 8B (minor product) (Scheme 3), which readily separated by preparative TLC (PLC) using silica gel.

**Scheme 3.** Coupling reaction of 1 with diazotized 4-chloroaniline.

To the best of our knowledge, this is the first reported isolation of two isomers in solid state in such reactions. The identity of major product 7A was supported by spectroscopic data. For example, its mass spectrum showed a molecular formula C_{18}H_{15}ClN_{6}S (M+ 382) and peaks at 139 (Cl-C_{6}H_{4}-N=N-, 17%) and 111 (Cl-C_{6}H_{4}, base peak, 100%) confirming its presumed structure (see Experimental). The IR spectrum showed no amino group (NH) absorption, but absorption bands for CN and -N=N- groups were observed at $\nu = 2217$ and 1547 cm$^{-1}$, respectively. Interestingly, the $^1$H-NMR spectral data shows that the azo-enamine tautomeric form 7C and hydrazone form 7B are present in CDCl$_3$ solution with relative intensities of 1:1.5 (Scheme 3, Table 1). The $^1$H-NMR spectrum disclosed, besides the characteristic signals for the ethyl and aromatic protons, only two singlet signals at $\delta = 8.91$ and 13.74 ppm attributable to N-H proton of the hydrazone form 7B and triazole N-H in the azo-enamine form 7C, respectively. Also, the $^{13}$C-NMR spectrum of this product in CDCl$_3$ displayed signals in agreement with the mixture of two tautomers, the hydrazone form 7B and azo-enamine form 7C (see Experimental). The structure of the minor product 8B was fully confirmed with the help of analytical and spectroscopic data. Particularly, the IR spectrum showed an amino group (NH) absorption band. Moreover, its structure is supported by its mass spectrum which showed the molecular ion peak at m/z 382 (29%), which is consistent with its structural formula. Other prominent peaks that observed at m/z 126 (Cl-C$_6$H$_4$-NH, 12%) and 111 (Cl-C$_6$H$_4$, base peak, 100%) confirming its presumed structure (see Experimental). However, the $^1$H-NMR spectrum revealed two singlet
signals for the N-H proton of the hydrazone form 8B and the triazole N-H in the azo-enamine form 8C with relative intensities of 1:5 (Table 1). This may be interpreted by assuming that the product 8B exists in CDCl₃ as a mixture of the two tautomeric forms 8B and 8C (cf. Scheme 3). Also, the ¹³C-NMR spectrum of this product in CDCl₃ displayed signals in agreement with the mixture of two tautomers, the hydrazone form 8B and the azo-enamine form 8C (see Experimental). Unfortunately, we did not succeed in growing the single crystal of compounds 3, 5, 7 and 8 suitable for X-ray crystallographic analysis.

3. Experimental

3.1. General

Melting points were measured on a Gallenkamp apparatus and are not corrected. IR spectra (KBr) were recorded with a Nicolet Magna 520FT IR spectrophotometer. Peaks are reported in cm⁻¹. ¹H and ¹³C-NMR spectra were recorded on a Bruker DPX (600 MHz for ¹H-NMR and 150 MHz for ¹³C-NMR) spectrometer in CDCl₃ using TMS as an internal standard; the chemical shifts are given in δ units (ppm). Mass spectra were performed on a Shimadzu GCMS-QP 1000 EX mass spectrometer at 70 eV. Analytical thin-layer chromatography (TLC) was performed on aluminum sheets precoated with silica gel (Merck, Kieselgel 60 PF₂₅₄). Visualization was accomplished by UV light. Microanalytical data were obtained from the Microanalytical Data Unit at Cairo University, Egypt.

3.2. General Procedure for the Synthesis of Arylhydrazone (or Arylazo) Compounds 3, 5, 7 and 8

A cold solution of aryl diazonium salt (4 mmol) was prepared by adding a sodium nitrite solution (0.4 g, 6 mmol, dissolved in 2 mL water) to a pre-cooled solution of arylamine hydrochloride (4 mmol of either of the appropriate aniline derivatives 2 and 4 in 2 mL of 6 M hydrochloric acid) with continuous stirring. The resulting solution of the aryl diazonium salt was then added carefully to a cold solution of 1,2,4-triazole derivative 1 (4 mmol) in ethanol (40 mL) containing sodium acetate (0.66 g in 2 mL H₂O). The reaction mixture was stirred at room temperature for 24 h and the resulting solid product was collected by filtration, washed well with H₂O and dried to afford compounds 3B and 5A, respectively, which were purified by preparative TLC using silica gel plates (toluene/acetone, 10:2), followed by recrystallization from EtOH. In the case of the reaction of 1 with 6, the resulting solid product was chromatographed on a preparative TLC plate using 10:3 toluene/acetone as eluent to give two zones. Extraction with acetone followed by recrystallization from EtOH gave compounds 7A and 8B, respectively.

2-(5-Ethylthio-4-phenyl-4H-[1,2,4]triazol-3-yl)-2-(phenylhydrazono)acetonitrile (3B). Yellow crystals. Yield (1.28 g, 90%); m.p.: 172–174 °C. IR (KBr): ν = 3236 (NH), 2937 (aliph. CH), 2213 (CN), 1594 (C=N), 1231 (N-N) cm⁻¹. ¹H-NMR: δ = 1.44 (t, 3H, J = 7.2 Hz, CH₃), 1.48 (t, 3H, J = 7.2 Hz, CH₃), 3.28–3.34 (m, 4H, 2 CH₂), 6.38 (d, 2H, J = 8.4 Hz, ArH), 6.99 (t, 1H, J = 8.4 Hz, ArH), 7.12–7.15 (m, 5H, ArH), 7.31–7.32 (m, 2H, ArH), 7.35–7.42 (m, 6H, ArH), 7.59–7.63 (m, 3H, ArH), 7.65–7.68 (m, 1H, ArH), 8.83 (s, 0.25H, hydrazone NH), 13.71 (s, 0.75H, triazole NH); ¹³C-NMR: δ = 14.65 (CH₃), 14.67 (CH₃), 26.61 (CH₂), 26.75 (CH₂), 99.05 (=C-CN in azo-enamine form), 114.27 (CN), 114.30 (CN),...
2-(5-Ethylthio-4-phenyl-4H-1,2,4-triazol-3-yl)-2-(4-methylphenyldiazenyl)acetonitrile (5A). Yellow crystals. Yield (1.22 g, 82%); m.p.: 169–170 °C. IR (KBr): \( \nu = 2980, 2920 \) (aliph. CH), 2217 (CN), 1594 (C=N), 1547 (-N=N-) cm\(^{-1}\); \(^1\)H-NMR: \( \delta = 1.43 \) (t, 3H, \( J = 7.2 \) Hz, CH\(_3\)), 1.47 (t, 3H, \( J = 7.2 \) Hz, CH\(_3\)), 2.26 (s, 3H, CH\(_3\)), 2.34 (s, 3H, CH\(_3\)), 3.28-3.34 (m, 4H, 2 CH\(_2\)), 6.27 (d, 2H, \( J = 8.4 \) Hz, ArH), 6.94 (d, 2H, \( J = 8.4 \) Hz, ArH), 7.18 (d, 2H, \( J = 8.4 \) Hz, ArH), 7.30-3.32 (m, 5H, ArH), 7.35–7.37 (m, 3H, ArH), 7.59–7.63 (m, 3H, ArH), 7.65–7.67 (m, 1H, Ar H), 8.78 (s, 0.20H, hydrazone NH); 13C-NMR: \( \delta = 14.66 \) (CH\(_3\)), 14.68 (CH\(_3\)), 20.70 (CH\(_3\)), 20.92 (CH\(_3\)), 26.60 (CH\(_2\)), 26.76 (CH\(_2\)), 98.34 (=C-CN in azo-enamine form), 114.21 (CN), 114.50 (CN), 115.48 (4 Ar-C), 127.37 (1 Ar-C), 128.22 (3 Ar-C), 129.78 (2 Ar-C), 130.04 (2 Ar-C), 130.07 (4 Ar-C), 131.50 (2 Ar-C), 131.64 (1 Ar-C), 133.75 (1 Ar-C), 134.58 (1 Ar-C), 134.64 (2 Ar-C), 134.88 (1 Ar-C), 139.57 (CN-C=N-NH in hydrazone form), 148.55 (triazole C-3), 148.73 (triazole C-3), 153.97 (triazole C-5), 154.75 (triazole C-5); MS \( m/z \) (rel. int. %) 363 (M\(^+\) + 1, 11), 362 (M\(^+\), 40), 361 (21), 348 (5), 347 (6), 346 (8), 345 (6), 335 (6), 334 (16), 333 (10), 306 (9), 305 (11), 274 (2), 273 (5), 257 (5), 243 (4), 242 (6), 231 (4), 230 (5), 215 (14), 188 (4), 157 (8), 156 (11), 149 (11), 148 (7), 144 (6), 143 (6), 128 (8), 119 (14), 118 (13), 117 (9), 106 (8), 105 (22), 104 (13), 103 (11), 97 (6), 92 (14), 91 (100), 90 (26), 77 (49), 76 (17), 66 (6), 65 (27), 64 (21), 63 (12), 61 (6), 60 (9), 59 (13), 56 (9), 51 (26); Anal. Calcd. for C\(_{19}\)H\(_{18}\)N\(_{6}\)S (362.45): C, 62.96; H, 5.01; N, 19.60; S, 12.43. Found: C, 63.14; H, 4.87; N, 19.38; S, 12.52.

2-(4-Chlorophenyldiazenyl)-2-(5-ethylthio-4-phenyl-4H-1,2,4-triazol-3-yl)acetonitrile (7A). Yellow crystals. Yield (0.785 g, 50%); m.p.: 118–120 °C. IR (KBr): \( \nu = 2925 \) (aliph. CH), 2217 (CN), 1597 (C=N), 1547 (-N=N-) cm\(^{-1}\); \(^1\)H-NMR: \( \delta = 1.43 \) (t, 3H, \( J = 7.2 \) Hz, CH\(_3\)), 1.48 (t, 3H, \( J = 7.2 \) Hz, CH\(_3\)), 3.27–3.35 (m, 4H, 2 CH\(_2\)), 6.30 (d, 2H, \( J = 9 \) Hz, ArH), 7.10 (d, 2H, \( J = 9 \) Hz, ArH), 7.30–7.36 (m, 8H, ArH), 7.57–7.68 (m, 6H, ArH), 8.91 (s, 0.60H, hydrazone NH), 13.74 (s, 0.40H, triazole NH); \(^1\)C-NMR: \( \delta = 14.65 \) (2 CH\(_3\)), 26.62 (CH\(_2\)), 26.76 (CH\(_2\)), 99.68 (=C-CN in azo-enamine form), 108.93 (CN), 114.02 (CN), 114.56 (2 Ar-C), 116.65 (2 Ar-C), 127.33 (3 Ar-C), 128.17 (2 Ar-C), 128.99 (1 Ar-C), 129.28 (4 Ar-C), 129.61 (1 Ar-C), 129.85 (1 Ar-C), 130.12 (4 Ar-C), 131.48 (1 Ar-C), 131.61 (1 Ar-C), 134.54 (1 Ar-C), 139.48 (1 Ar-C), 140.44 (CN-C=N-NH in hydrazone form), 148.30 (triazole C-3), 148.49 (triazole C-3), 154.37 (triazole C-5), 155.11 (triazole C-5); MS \( m/z \) (rel. int. %) 384 (M\(^+\), 27), 382 (M\(^+\), 78), 381 (20), 356 (4), 355 (7), 354 (13), 353 (15), 352 (5), 328 (7), 327 (10), 326 (13), 325 (17), 324 (7), 293 (7), 244 (4), 243 (9), 242 (15), 241 (7), 232 (3), 231 (3), 215 (15), 214 (10), 213 (7), 192 (3), 191 (8), 183 (4), 182 (6), 181 (7), 167 (5), 157 (10), 156 (25), 155 (13), 149 (12), 148 (5), 143 (3), 142 (6), 141 (9), 140 (4), 139 (17), 138 (11), 129 (13), 128 (12), 127 (10), 126 (11), 125 (9), 119 (5), 118 (17), 113 (32), 112 (17), 111 (100), 110 (78), 105 (23), 104 (15), 103 (12), 102 (13), 100 (6), 99 (16), 92 (8), 88 (4), 87 (5), 86 (11), 85 (7), 84 (13), 83 (10), 82 (6), 81 (17), 80 (100), 79 (78), 78 (21), 77 (6), 76 (100), 75 (77), 74 (13), 73 (10), 72 (6), 71 (100), 70 (73), 69 (17), 68 (100), 67 (21), 66 (6), 65 (9), 64 (13), 63 (7), 62 (6), 61 (5), 60 (5), 59 (17), 58 (9), 57 (13), 56 (9), 55 (17), 54 (7), 53 (13), 52 (6), 51 (5), 50 (14); Anal. Calcd. for C\(_{19}\)H\(_{16}\)N\(_{6}\)S (348.42): C, 62.05; H, 4.63; N, 24.16; S, 9.20. Found: C, 61.91; H, 4.78; N, 24.35; S, 9.06.
2-(4-Chlorophenylhydrazono)-2-(5-ethylthio-4-phenyl-4H-[1,2,4]triazol-3-yl)acetonitrile (8B).

Reddish crystals. Yield (0.60 g, 38%); m.p.: 219–221 °C. IR (KBr): $\nu$ = 3240 (NH), 2924 (aliph. CH), 2220 (CN), 1595 (C=N), 1233 (N-N) cm$^{-1}$; $^1$H-NMR: $\delta$ = 1.44 (t, 3H, $J$ = 7.2 Hz, CH$_3$), 1.48 (t, 3H, $J$ = 7.2 Hz, CH$_3$), 3.28–3.37 (m, 4H, 2 CH$_2$), 6.29 (d, 2H, $J$ = 9 Hz, ArH), 7.10 (d, 2H, $J$ = 9 Hz, ArH), 7.31–7.38 (m, 8H, ArH), 7.57–7.69 (m, 6H, ArH), 8.79 (s, 0.17H, hydrazone NH), 13.74 (s, 0.83H, triazole NH); $^{13}$C-NMR: $\delta$ = 14.69 (2 CH$_3$), 26.65 (CH$_2$), 26.78 (CH$_2$), 99.71 (=C-CN in azo-enamine form), 114.05 (CN), 115.45 (CN), 116.68 (3 Ar-C), 127.36 (1 Ar-C), 128.20 (4 Ar-C), 129.02 (1 Ar-C), 129.34 (1 Ar-C), 129.65 (4 Ar-C), 129.87 (1 Ar-C), 129.93 (1 Ar-C), 130.16 (4 Ar-C), 131.52 (1 Ar-C), 131.64 (2 Ar-C), 139.44 (1 Ar-C), 140.47 (CN-C=N-NH in hydrazone form), 148.30 (triazole C-3), 148.52 (triazole C-3), 154.40 (triazole C-5), 155.05 (triazole C-5); MS m/z (rel. int. %) 384 (M$^+$, 10), 382 (M$^+$, 29), 381 (11), 362 (3), 356 (3), 355 (3), 354 (5), 353 (4), 352 (2), 348 (3), 328 (3), 327 (4), 326 (4), 325 (7), 324 (2), 319 (6), 317 (8), 316 (5), 293 (3), 244 (2), 243 (3), 242 (7), 241 (3), 231 (2), 215 (7), 214 (4), 213 (2), 157 (4), 156 (9), 155 (6), 149 (4), 143 (2), 142 (4), 141 (9), 140 (4), 139 (29), 129 (5), 128 (8), 127 (5), 126 (12), 125 (7), 119 (2), 118 (6), 113 (31), 112 (20), 111 (100), 110 (27), 105 (8), 104 (4), 103 (4), 102 (5), 101 (8), 100 (3), 99 (17), 91 (13), 90 (12), 87 (3), 78 (4), 77 (31), 76 (17), 75 (36), 74 (13), 66 (2), 65 (9), 64 (12), 63 (17), 62 (6), 61 (7), 60 (4), 52 (5), 51 (23), 50 (17); Anal. Calcd. for C$_{18}$H$_{15}$ClN$_6$S (382.87): C, 56.47; H, 3.95; Cl, 9.26; N, 21.95; S, 8.37. Found: C, 56.66; H, 3.83; Cl, 9.40; N, 22.04; S, 8.54.

4. Conclusions

In conclusion, we have synthesized new azo dyes utilizing 3-ethylthio-5-cyanomethyl-4-phenyl-1,2,4-triazole as a coupling component. The experimental results show that the substituents at the para-position of the diazonium salt benzene ring have some effect on the ratio of the resulting tautomers. 5-ethylthio-N',4-diphenyl-4H-1,2,4-triazole-3-carbohydrazonoyl cyanide (3B) (hydrazone form) was obtained by coupling 1 with benzenediazonium salt 2, while the azo dye 5A was obtained by coupling 1 with diazotized 4-methylaniline (4). Interestingly, coupling of 1 with diazotized 4-chloroaniline (6) afforded two isomeric products, 7A (azo form) and 8B (hydrazone form). To the best of our knowledge, this is the first reported isolation of two isomers in the solid state in such reactions. Analysis of the $^1$H-NMR data shows that the hydrazone and azo-enamine forms are the only two tautomers present in CDCl$_3$ solution and the ratio of these tautomers depends on the electron-donating and electron-withdrawing properties of the substituent present at the para-position of the aryldiazonium salt.

Conflicts of Interest

The authors declare no conflict of interest.
References

1. Towns, A.D. Developments in azo disperse dyes derived from heterocyclic diazo components. *Dyes Pigm.* 1999, 42, 3–28.
2. Venkataraman, K. *The Chemistry of Synthetic Dyes*; Academic Press: New York, NY, USA and London, UK, 1970; Volume III, pp. 303–369.
3. Zhang, Y.; Hou, W.; Tan, Y. Structure and dyeing properties of some anthraquinone violet acid dyes. *Dyes Pigm.* 1997, 34, 25–35.
4. Hallas, G.; Towns, A.D. Dyes derived from aminothiophenes. Part 7: Synthesis and properties of some benzo[b]thiophene-based azo disperse dyes. *Dyes Pigm.* 1997, 35, 219–237.
5. Faustino, H.; El-Shishtawy, R.M.; Reis, L.V.; Santos, P.F.; Almeida, P. 2-Nitroso-benzo-thiazoles: Useful synthons for new azobenzothiazole dyes. *Tetrahedron Lett.* 2008, 49, 6907–6909.
6. Sternberg, E.; Dolphin, D.; Matsuoka, M. *Infrared Absorbing Dyes*; Plenum: New York, NY, USA, 1990; pp. 193–212.
7. Gregory, P. *High-Technology Applications of Organic Colorants*; Springer-Verlag: Berlin, Germany, 1993; pp. 7–281.
8. Mekkawi, D.E.; Abdel-Mottaleb, M.S.A. The interaction and photo stability of some xanthenes and selected azo sensitizing dyes with TiO2 nanoparticles. *Int. J. Photo. Energy* 2005, 7, 95–101.
9. Gregory, P. Modern reprographics. *Rev. Prog. Coloration* 1994, 24, 1–16.
10. Marchevsky, E.; Olsina, R.; Marone, C. 2-[2-(5-Chloropyridyl)azo]-5-(dimethylamino)phenol as indicator for the complexometric determination of zinc. *Talanta* 1985, 32, 54–56.
11. Zhi-Gang, Y.; Chun-Xia, Z.; De-Feng, Z.; Freeman, H.S.; Pei-Tong, C.; Jie, H. Monoazo dyes based on 5,10-dihydrophenophosphazine, Part 2: Azo acid dyes. *Dyes Pigm.* 2009, 81, 137–143.
12. Garg, H.G.; Praksh, C. Preparation of 4-arylazo-3,5-disubstituted-(2H)-1,2,6-thiadiazine-1,1-dioxides. *J. Med. Chem.* 1972, 15, 435–436.
13. Khalid, A.; Arshad, M.; Crowley, D.E. Accelerated decolorization of structurally different azo dyes by newly isolated bacterial strains. *Appl. Microbiol. Biotech.* 2008, 78, 361–369.
14. Farghaly, Th.A.; Abdallah, Z.A. Synthesis, azo-hydrazone tautomerism and antitumor screening of N-(3-ethoxycarbonyl-4,5,6,7-tetrahydro-benzo[b]thien-2-yl)-2-aryl-hydrazone-3-oxobutanamide derivatives. *ARKIVOC* 2008, 17, 295–305.
15. Avci, G.A.; Ozkinali, S.; Ozluk, A.; Avci, E.; Kocaokutgen, H. Antimicrobial activities, absorption characteristics and tautomeric structures of o,o’-hydroxyazo dyes containing an acryloyloxy group and their chromium complexes. *Hacettepe J. Biol. Chem.* 2012, 40, 119–126.
16. Park, Ch.; Lim, J.; Lee, Y.; Lee, B.; Kim, S.; Lee, J.; Kim, S. Optimization and morphology for decolorization of reactive black 5 by Funalia trogii. *Enzyme Microb. Tech.* 2007, 40, 1758–1764.
17. Pandey, A.; Singh, P.; Iyengar, L. Bacterial decolorization and degradation of azo dyes. *Inter. Biodet. Biodeg.* 2007, 59, 73–84.
18. Moldovan, C.M.; Oniga, O.; Parvu, A.; Tiperciuc, B.; Verite, P.; Pirnau, A.; Crisan, O.; Bojita, M.; Pop, R. Synthesis and anti-inflammatory evaluation of some new acylhydrazones bearing 2-arylthiazole. *Eur. J. Med. Chem.* 2011, 46, 526–534.
19. Yogeeswari, P.; Menon, N.; Semwal, A.; Arjun, M.; Sriram, D. Discovery of molecules for the treatment of neuropathic pain: Synthesis, antiallodynic and antihyperalgesic activities of 5-(4-nitrophenyl)furoic-2-acid hydrazones. *Eur. J. Med. Chem.* 2011, 46, 2964–2970.

20. Vavrikova, E.; Polanc, S.; Kocevar, M.; Horvati, K.; Bosze, S.; Stolarikova, J.; Vavrova, K.; Vinsova, J. New fluorine-containing hydrazones active against MDR-tuberculosis. *Eur. J. Med. Chem.* 2011, 46, 4937–4945.

21. Dart, R.C. Mushrooms. In *Medical Toxicology*; Williams & Wilkins: Philadelphia, PA, USA, 2004; pp. 1719–1735.

22. Stern, H.C.; Matthews, J.H.; Belz, G.G. Influence of dihydralazine induced afterload reduction on systolic time intervals and echocardiography in healthy subjects. *Br. Heart J.* 1984, 52, 435–439.

23. Manabe, K.; Oyamada, H.; Sugita, K.; Kobayashi, S. Use of acylhydrazones as stable surrogates of unstable imines in allylation, mannich-type, and cyanide addition reactions. *J. Org. Chem.* 1999, 64, 8054–8057.

24. Keith, J.M.; Gomez, L. Exploration of the mitsunobu reaction with tosyl- and boc-hydrazones as nucleophilic agents. *J. Org. Chem.* 2006, 71, 7113–7116.

25. Keith, J.M.; Jacobsen, E.N. Asymmetric hydrocyanation of hydrazones catalyzed by lanthanide-PYBOX complexes. *Org. Lett.* 2004, 6, 153–155.

26. Tan, K.L.; Jacobsen, E.N. Indium-mediated asymmetric allylation of acylhydrazones using a chiral urea catalyst. *Angew. Chem. Int. Ed.* 2007, 46, 1315–1317.

27. Lazny, R.; Nodzewska, A. N,N-Dialkylhydrazones in organic synthesis. From simple N,N-dimethylhydrazones to supported chiral auxiliaries. *Chem. Rev.* 2010, 110, 1386–1434.

28. Rollas, S.; Kalyoncuoglu, N.; Sur-Altiner, D.; Yegenoglu, Y. Usubstituted-2,4-dihydro-3H-1,2,4-triazole-3-thiones. Synthesis and antibacterial and antifungal activities. *Pharmazie* 1993, 48, 308–309.

29. Sugane, T.; Tobe, T.; Hamaguchi, W.; Shimada, I.; Maeno, K.; Miyata, J.; Suzuki, T.; Kimizuka, T.; Kohara, A.; Morita, T.; et al. Synthesis and biological evaluation of 3-biphenyl-4-yl-4-phenyl-4H-1,2,4-triazoles as novel glycine transporter 1 inhibitors. *J. Med. Chem.* 2011, 54, 387–391.

30. Demange, L.; Boeglin, D.; Moulin, A.; Mousseaux, D.; Ryan, J.; Berge, G.; Gagne, D.; Heitz, A.; Perrissoud, D.; Locatelli, V.; et al. Synthesis and Pharmacological in vitro and in vivo. evaluations of novel triazole derivatives as ligands of the Ghrelin receptor 1. *J. Med. Chem.* 2007, 50, 1939–1957.

31. Zhang, Q.; Keenan, S.M.; Peng, Y.; Nair, A.C.; Yu, S.J.; Howells, R.D.; Welsh, W.J. Discovery of novel triazole-based opioid receptor antagonists. *J. Med. Chem.* 2006, 49, 4044–4047.

32. Clemons, M.; Coleman, E.R.; Verma, S. Aromatase inhibitors in the adjuvant setting: Bringing the gold to a standard? *Cancer Treat. Rev.* 2004, 30, 325–332.

33. Johnston, G.A. Medicinal chemistry and molecular pharmacology of GABA(C) receptors. *Curr. Top. Med. Chem.* 2002, 2, 903–913.

34. Shujuan, S.; Hongxiang, L.; Gao, Y.; Fan, P.; Ma, B.; Ge, W.; Wang, X. Liquid chromatography-tandem mass spectrometric method for the analysis of fluconazole and evaluation of the impact of phenolic compounds on the concentration of fluconazole in *Candida albicans*. *J. Pharm. Biomed. Anal.* 2004, 34, 1117–1124.

35. Mekheimer, R.; Shaker, R.M. Synthesis and reactivity of 3-alkylthio-5-cyanomethyl-4-phenyl-1,2,4-triazoles. *J. Chem. Res. (S)* 1999, 1999, 76–77.
36. Mekheimer, R.A.; Ibrahim, Y.R.; Ahmed, E.A.; Frey, W. Naphthyridines. Part 3: First example of the polyfunctionally substituted 1,2,4-triazolo[1,5-g][1,6]naphthyridines ring system. *Tetrahedron* **2009**, *65*, 9843–9849.

37. Mekheimer, R.A.; Sayed, A.A.R.; Ahmed, E.A. Novel 1,2,4-triazolo[1,5-a]pyridines and their fused ring systems attenuate oxidative stress and prolong lifespan of *Caenorhabditis Elegans*. *J. Med. Chem.* **2012**, *55*, 4169–4177.

38. Gregory, P. Azo dyes: Structure-carcinogenicity relationships. *Dyes Pigments* **1986**, *7*, 45–56.

39. Kelemen, J.; Moss, S.; Sauter, H.; Winkler, T. Azo-hydrazone tautomerism in azo dyes. II. Raman, NMR and mass spectrometric investigations of 1-phenylazo-2-naphthylamine and 1-phenylazo-2-naphthol derivatives. *Dyes Pigm.* **1982**, *3*, 27–47.

40. Kostyuchenko, E.E.; Traven, V.F.; Stepanov, B.I. Tautomeric transformations and color of monoazo dyes. *Zh. Obshch. Khim.* **1978**, *48*, 3797.

41. Karci, F.; Demircali, A. Synthesis of 4-amino-1H-benzo[4,5]imidazo[1,2-a]pyrimidin-2-one and its disperse azo dyes. Part 2: Hetarylazo derivatives. *Dyes Pigm.* **2006**, *71*, 97–102.

42. Colanceska-Ragenovic, K.; Dimova, V.; Kakurinov, V.; Molnar, D.G.; Buzarova, A. Synthesis, antibacterial and antifungal activity of 4-substituted-5-aryl-1,2,4-triazoles. *Molecules* **2001**, *6*, 815–824.

43. Khan, Z.F. ChemBioDraw Ultra 12.0. The Islamic University, Gaza, Palestine, issue: 20.2, 2013.

44. Pavlović, G.; Racané, L.; Ćičak, H.; Tralić-Kulenović, V. The synthesis and structural study of two benzothiazolyazo dyes: X-ray crystallographic and computational study of azo-hydrazo tautomerism. *Dyes Pigm.* **2009**, *83*, 354–362.

45. Satam, M.A.; Raut, R.K.; Telore, R.D.; Sekar, N. Fluorescent acid azo dyes from 3-(1,3-benzothiazol-2-yl)naphthalen-2-ol and comparison with 2-naphthol analogs. *Dyes Pigm.* **2013**, *97*, 32–42.

46. Loghmani-Khouzani, H.; Mehrabi, H.; Sadeghi, M.M.M.; Gawinecki, R. Study of hydrazo-hydrazoimine tautomerism in α-azo-6-ketomethylphenanthridines. *J. Iran. Chem. Soc.* **2009**, *6*, 129–137.

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