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Anodic formation of 3,6-diaryl-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazoles and 2(3-aryl-5-methyl-1*H*-[1,2,4]triazol-1-yl)-5-aryl-1,3,4-thiadiazoles

Belen Batanero *, Rebeca Saez, Fructuoso Barba

Department of Organic Chemistry, University of Alcala, Campus Universitario-Fac. Farmacia, N-II km. 33,6, 28871 Alcala de Henares, Madrid, Spain

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ABSTRACT

3,6-Disubstituted 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazoles together with the unknown systems 2-(3-aryl-5-methyl-1*H*-[1,2,4]triazol-1-yl)-5-aryl-1,3,4-thiadiazoles were obtained by anodic oxidation, under aprotic conditions, of aryl aldehyde *N*-(5-aryl-1,3,4-thiadiazol-2-yl) hydrazones. Mechanistic proposals are given.

1. Introduction

1,2,4-Triazolo[3,4-*b*][1,3,4]thiadiazole ring system was first made by *Kanaoka*.[1]

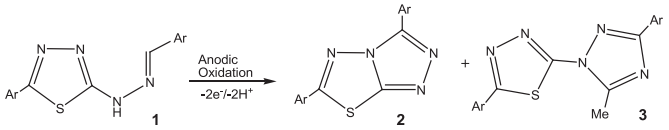
Because many of these 3,6-disubstituted derivatives possess interesting and various biological activity (antibacterial, analgesic, antiinflammatory, fungicidal, etc.)[2] much attention has been devoted to them.

There are two synthetic strategies for the preparation of these interesting 3,6-disubstituted derivatives depending on the starting material. In one case 5-substituted-4-amino-3-mercapto-1,2,4-triazoles were used,[3–7] while in the other case 5-substituted-2-hydrazino-1,3,4-thiadiazoles[3,8,9] were employed. The latter prepared by condensation of carbonothioic dihydrazide with appropriated aldehydes, followed by oxidative cyclization of the corresponding bis-hydrazones with iron(III) chloride in ethanol[8] or using silica-supported dichlorophosphate as a recoverable dehydrant, under microwave irradiations.[10]

To the best of our knowledge no reports have been published on the electrosynthesis of 3,6-disubstituted 1,2,4-triazolo[3,4-*b*][1,3,4] thiadiazole. However, electrochemical synthesis of 1,2,4-triazol-3-thione derivatives has been performed by anodic oxidation of *N*-thioamidohydrazones.[11]

2. Results and discussion

Herein, we report the electrochemical synthesis of several 3,6-disubstituted 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazoles (**2**) together with unknown 2-(3-aryl-5-methyl-1*H*-[1,2,4]triazol-1-yl)-5-aryl-1,3,4-thiadiazoles (**3**), by anodic oxidation in acetonitrile of 2-arylidene-1-(5-aryl-1,3,4-thiadiazol-2-yl)hydrazine (**1**) (Scheme 1), at a platinum electrode.



Scheme 1.

The obtained yields of **2** and the unexpected **3** (not previously described) are indicated in Table 1.

2-Arylidene-1-(5-aryl-1,3,4-thiadiazol-2-yl)hydrazine (**1**) were experimentally prepared by oxidation with iron(III) chloride of the corresponding bis-hydrazone, as already described by Shawali and Sayed.[8] However, together with the expected thiadiazoles (**1**), 4-(arylideneamino)-5-aryl-2*H*-1,2,4-triazole-3(4*H*)-thione (**4**) were also obtained. The formation of **4** can be explained by donation, to the benzyl cation, the electron pair from the nitrogen atom, instead of the electron pair of the sulfur atom, as it is showed in Scheme 2 (Table 2). Heterocycles **1** and **4** were isolated and characterized by

* Corresponding author. Tel.: +34 91 8852517; fax: +34 91 8854686; e-mail address: belen.batanero@uah.es (B. Batanero).

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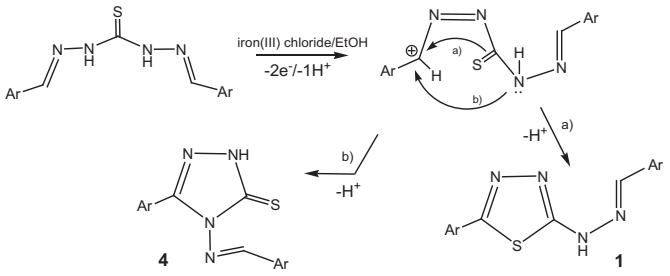
Table 1
Yields of **2** and **3** in the anodic oxidation of **1**

Ar	Yield of **2** (%)	Yield of **3** (%)
a: C_6H_5	60	22
b: 4-MeO–C_6H_4	58	31
c: 2-Me–C_6H_4	54	12
d: 4-Me–C_6H_4	55	11
e: 4-Cl–C_6H_4	64	16
f: 4-Br–C_6H_4	62	30



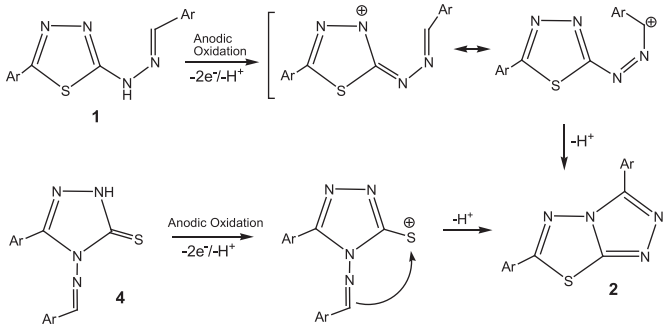
Scheme 2.

Table 2
Obtained yields of **1** and **4** in the oxidation of the corresponding bis-hydrazone with iron(III) chloride

Ar	Yield of **1** (%)	Yield of **4** (%)
a: C_6H_5	80	14
b: 4-MeO–C_6H_4	77	13
c: 2-Me–C_6H_4	82	10
d: 4-Me–C_6H_4	84	8
e: 4-Cl–C_6H_4	79	11
f: 4-Br–C_6H_4	77	12

their spectroscopical data, summarized in the experimental section of this paper.

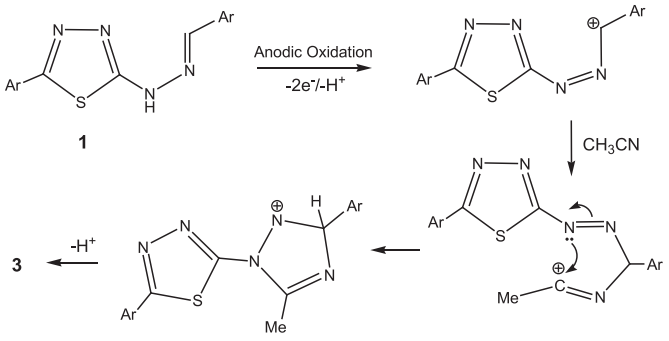
Cyclic voltammetry of **1** in acetonitrile/$LiClO_4$ as SSE (solvent-supporting-electrolyte system) at a platinum anode showed an irreversible anodic peak at +2.75 V (vs Ag/Ag^+). The anodic oxidation of thiadiazoles **1** or triazoles **4** under potentiostatic conditions (constant potential) led to the formation of same product **2**, through the proposed mechanism summarized in Scheme 3.



Scheme 3.

However, the electrolysis of **1** produced, together with **2**, the new compounds **3**, which formation involves an acetonitrile molecule. In this case, the oxidation of **1** to the benzyl cation is followed by a *Ritter* reaction with the solvent, to give (after subsequent intramolecular cyclization) the compound **3** (Scheme 4).

Surprisingly, when this reaction is performed under galvanostatic conditions (constant current of 200 mA) and at a graphite anode, the yield of **3** was increased to 49–64% at expense on the yield of **2**.



Scheme 4.

Finally, a direct anodic oxidation, starting from the initial bis-hydrazones, obtained by condensation of carbonothioic dihydrazide with the appropriated aldehyde, led to a mixture of **1**, **2**, and **3**, but in lower yields than the obtained in the anodic oxidation of **1**.

3. Conclusion

We can conclude:

(a) Unexpected 4-(benzylideneamino)-5-phenyl-2*H*-1,2,4-triazole-3(4*H*)-thione (**4**) together with expected 2-arylidene-1-(5-aryl-1,3,4-thiadiazol-2-yl)hydrazine (**1**) were obtained in the conventional oxidation of the corresponding bis-hydrazones with iron(III) chloride.
(b) The anodic oxidation of **1** or **4**, afforded 3,6-disubstituted 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazoles (**2**)
(c) A new family of 2-(3-aryl-5-methyl-1*H*-[1,2,4]triazol-1-yl)-5-aryl-1,3,4-thiadiazoles (**3**) were electrochemically obtained as secondary products when the reaction is carried out under controlled potential conditions. However **3** is the main product under galvanostatic conditions.
(d) The solvent, acetonitrile, plays an important roll in the synthesis of the new compounds **3**.

4. Experimental section

4.1. General

The electrolyses were carried out using an Amel potentiostat, Model 552, connected with an electronic coulombimeter integrator Amel, Model 721.

Mass spectra (EI, ionizing voltage 70 eV) were determined with a Hewlett–Packard Model 5988A mass-selective detector equipped with a Hewlett–Packard MS Chem Station. IR spectra were obtained, as dispersions in KBr, on a Perkin–Elmer Model 583 spectrophotometer.

^1H NMR and ^{13}C NMR (300 MHz & 75.4 MHz, respectively) spectra were recorded on a Varian Unity 300 apparatus with deuterochloroform as an internal standard. The chemical shifts are given in parts per million.

Melting points were determined on a Reichert Thermovar microhot stage apparatus, and are uncorrected. Elemental analyses were performed on a Leco CHNS Model 932 analyzer.

4.2. General procedure

Treatment of carbonothioic dihydrazide with appropriated aldehydes gave rise to the corresponding bis-hydrazones quantitatively. 1,2,4-Triazolo[3,4-*b*][1,3,4]thiadiazole (**1**) was obtained by conventional oxidation in EtOH of the bis-hydrazone with double

molecular amount of iron(III) chloride. After 30 min refluxing the mixture, it was stirred overnight, removed the solvent by vacuum and washed with water. Filtration of the crude product allowed the isolation of **1**, which was later crystallized in EtOH. The secondary product **4** was obtained from the EtOH filtrate after being chromatographed on silica gel 60 (35–70mesh) in a (24×2.5 cm) column, using mixtures hexane/EtOAc (7:3) as eluent.

*4.2.1. 2-Benzylidene-1-(5-phenyl-1,3,4-thiadiazol-2-yl)hydrazine (**1a**).* Compound **1a** (80% yield). Mp 241–243 °C [lit.[10] 242–244 °C]. ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 126.9, 127.3, 128.5, 128.9, 129.2, 130.2, 130.4, 130.8, 133.6, 147.1, 171.4.

*4.2.2. 2-(4-Methoxybenzylidene)-1-(5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl)hydrazine (**1b**).* Compound **1b** (77% yield). Mp 190–193 °C [lit.[10] 182–184 °C]. ^{1}H NMR (300 MHz, CD_3OD) δ: 3.75 (s, 3H), 3.77 (s, 3H), 6.82 (d, 2H, J=8.6 Hz), 6.88 (d, 2H, J=8.6 Hz), 7.52 (d, 2H, J=8.6 Hz), 7.64 (d, 2H, J=8.6 Hz), 7.97 (s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 55.3, 55.4, 114.2, 114.5, 126.4, 128.3, 128.6, 146.2, 161.3, 161.5, 170.0. MS *m*/*e* (relative intensity) EI: 341 (M^++1, 27), 340 (M^+, 97), 253 (10), 207 (74), 152 (38), 133 (81), 121 (91), 91 (100).

*4.2.3. 2-(2-Methylbenzylidene)-1-(5-(2-methylphenyl)-1,3,4-thiadiazol-2-yl)hydrazine (**1c**).* Compound **1c** (82% yield). Mp 210–212 °C. IR (KBr) ν(cm^{-1}): 3187, 3057, 2780, 1600, 1583, 1442, 1069, 751, 711. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.50 (s, 3H), 2.52 (s, 3H), 7.20–7.40 (m, 6H), 7.6 (d, 1H, J=6.8 Hz), 7.7 (d, 1H, J=6.8 Hz), 8.38 (s, 1H), 12.4 (br s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 19.1, 20.8, 22.1, 125.6, 125.7, 125.9, 128.7, 129.0, 129.1, 129.3, 130.4, 130.9, 131.4, 135.5, 135.6, 142.4, 169.3. MS *m*/*e* (relative intensity) EI: 309 (M^++1, 19), 308 (M^+, 35), 190 (25), 150 (100), 148 (76), 118 (46), 91 (15). Anal. Calcd for $C_{17}H_{16}N_4S$: C, 66.23; H, 5.19; N, 18.18; S, 10.39. Found: C, 65.99; H, 5.37; N, 17.88; S, 10.47.

*4.2.4. 2-(4-Methylbenzylidene)-1-(5-(4-methylphenyl)-1,3,4-thiadiazol-2-yl)hydrazine (**1d**).* Compound **1d** (84% yield). Mp 247–249 °C [lit.[12] 238–240 °C]. ^{1}H NMR (300 MHz, CD_3OD) δ: 2.39 (s, 3H), 2.41 (s, 3H), 7.22 (d, 2H, J=8.0 Hz), 7.27 (d, 2H, J=8.0 Hz), 7.6 (d, 2H, J=8.0 Hz), 7.75 (d, 2H, J=8.0 Hz), 8.1 (s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 21.2, 21.3, 126.6, 126.7, 127.7, 129.3, 129.6, 131.1, 140.0, 140.4, 145.1, 159.0, 170.4.

*4.2.5. 2-(4-Chlorobenzylidene)-1-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl)hydrazine (**1e**).* Compound **1e** (79% yield). Mp 222–224 °C [lit.[10] 218–220 °C]. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.45 (d, 2H, J=7.7 Hz), 7.51 (d, 2H, J=7.7 Hz), 7.64 (d, 2H, J=7.7 Hz), 7.72 (d, 2H, J=7.7 Hz), 8.07 (s, 1H), 12.6 (br s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 127.6, 127.7, 128.4, 128.8, 132.5, 133.6, 134.1, 142.1, 156.0, 169.4.

*4.2.6. 2-(4-Bromobenzylidene)-1-(5-(4-bromophenyl)-1,3,4-thiadiazol-2-yl)hydrazine (**1f**).* Compound **1f** (77% yield). Mp 217–220 °C. IR (KBr) ν(cm^{-1}): 3188, 3024, 2915, 1594, 1487, 1434, 1397, 1067, 1008, 816. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.6–7.8 (m, 8H), 8.1 (s, 1H), 12.4 (br s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 127.6, 127.7, 128.4, 128.8, 132.5, 133.6, 134.1, 142.1, 156.0, 169.4. MS *m*/*e* (relative intensity) EI: 440 (M^++4, 2), 438 (M^++2, 3), 436 (M^+, 1), 367 (8), 257 (12), 186 (86), 184 (100), 120 (38), 102 (28), 89 (76), 74 (52). Anal. Calcd for $C_{15}H_{10}Br_2N_4S$: C, 41.10; H, 2.28; N, 12.79; S, 7.31. Found: C, 40.84; H, 2.32; N, 12.67, S, 7.53.

*4.2.7. 4-(Benzylideneamino)-5-phenyl-2H-1,2,4-triazole-3(4H)-thione (**4a**).* Compound **4a** (14% yield). Mp 168–169 °C [lit.[13] 168–172 °C]. IR (KBr) ν(cm^{-1}): 3104, 2927, 1601, 1572, 1542, 1504, 1483, 1277, 759, 681. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.33–7.50 (m, 6H), 7.76–7.92 (m, 4H), 9.95 (s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 125.2, 128.5, 128.7, 129.0, 129.7, 130.8, 132.2, 132.7, 150.0, 162.7, 164.2. MS *m*/*e* (relative intensity) EI: 281 (M^++1, 23), 280 (M^+, 12), 178 (100), 120 (12), 118 (13), 104 (16), 91 (8).

*4.2.8. 4-(4-Methoxy-benzylideneamino)-5-(4-methoxyphenyl)-2H-1,2,4-triazole-3(4H)-thione (**4b**).* Compound **4b** (13% yield). Mp 170–172 °C. IR (KBr) ν(cm^{-1}): 3118, 2937, 1606, 1566, 1514, 1423, 1258, 1167, 1023, 827. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.84 (s, 3H), 3.87 (s, 3H), 6.95 (d, 2H, J=8.9 Hz), 6.97 (d, 2H, J=8.5 Hz), 7.83 (d, 2H, J=8.9 Hz), 7.90 (d, 2H, J=8.5 Hz), 9.75 (s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 55.4, 55.5, 114.0, 114.5, 117.7, 124.7, 130.2, 130.9, 149.7, 161.4, 162.5, 163.3, 164.4. MS *m*/*e* (relative intensity) EI: 341 (M^++1, 2), 340 (M^+, 5), 207 (55), 148 (8), 135 (79), 133 (100), 103 (3). Anal. Calcd for $C_{17}H_{16}N_4O_2S$: C, 60.00; H, 4.71; N, 16.47; S, 9.41. Found: C, 59.81; H, 4.99; N, 16.25; S, 9.70.

*4.2.9. 4-(2-Methyl-benzylideneamino)-5-(2-methylphenyl)-2H-1,2,4-triazole-3(4H)-thione (**4c**).* Compound **4c** (10% yield). Mp 194–196 °C. IR (KBr) ν(cm^{-1}): 3101, 2937, 1594, 1508, 1355, 1281, 969, 763. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.28 (s, 3H), 2.40 (s, 3H), 7.10–7.39 (m, 7H), 7.68 (d, 1H, J=7.6 Hz), 10.37 (s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 19.8, 20.3, 124.9, 125.7, 126.3, 127.6, 130.6, 130.9, 131.2, 132.2, 138.5, 139.9, 151.0, 161.7, 162.0. MS *m*/*e* (relative intensity) EI: 309 (M^++1, 11), 308 (M^+, 3), 233 (9), 192 (61), 158 (100), 131 (37), 116 (31), 90 (18). Anal. Calcd for $C_{17}H_{16}N_4S$: C, 66.23; H, 5.19; N, 18.18; S, 10.39. Found: C, 65.98; H, 4.95; N, 18.21; S, 10.23.

*4.2.10. 4-(4-Methyl-benzylideneamino)-5-(4-methylphenyl)-2H-1,2,4-triazole-3(4H)-thione (**4d**).* Compound **4d** (8% yield). Mp 230–231 °C. IR (KBr) ν(cm^{-1}): 3120, 2925, 1602, 1508, 1274, 825, 812, 727, 667. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.45 (s, 3H), 2.47 (s, 3H), 7.20–7.40 (m, 4H), 7.60–7.80 (m, 4H), 10.3 (s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 21.3, 127.6, 128.0, 128.6, 129.1, 129.5, 129.7, 142.2, 143.0, 144.1, 149.0, 164.5. MS *m*/*e* (relative intensity) EI: 309 (M^++1, 19), 308 (M^+, 19), 191 (100), 132 (39), 118 (71), 116 (19), 91 (47), 89 (22). Anal. Calcd for $C_{17}H_{16}N_4S$: C, 66.23; H, 5.19; N, 18.18; S, 10.39. Found: C, 66.21; H, 4.89; N, 17.88; S, 10.47.

*4.2.11. 4-(4-Chloro-benzylideneamino)-5-(4-chlorophenyl)-2H-1,2,4-triazole-3(4H)-thione (**4e**).* Compound **4e** (11% yield). Mp 208–210 °C. IR (KBr) ν(cm^{-1}): 3110, 2934, 1605, 1499, 1423, 1274, 1093, 827, 717. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.52–7.60 (m, 4H), 7.93 (d, 2H, J=8.0 Hz), 8.00 (d, 2H, J=8.0 Hz), 10.2 (s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 127.8, 128.4, 129.1, 129.2, 129.9, 130.3, 135.4, 137.3, 147.6, 161.4, 162.5. MS *m*/*e* (relative intensity) EI: 350 (M^++2, 6), 348 (M^+, 8), 213 (37), 211 (100), 153 (34), 151 (77), 139 (31), 137 (65), 124 (18), 102 (19), 76 (20). Anal. Calcd for $C_{15}H_{10}Cl_2N_4S$: C, 51.57; H, 2.87; N, 16.04; S, 9.17. Found: C, 51.41; H, 3.03; N, 16.17; S, 8.96.

*4.2.12. 4-(4-Bromo-benzylideneamino)-5-(4-bromophenyl)-2H-1,2,4-triazole-3(4H)-thione (**4f**).* Compound **4f** (12% yield). Mp 214–216 °C. IR (KBr) ν(cm^{-1}): 3104, 2930, 1590, 1497, 1421, 1272, 1072, 1012, 822, 714. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.70–7.80 (m, 4H), 7.80–7.87 (m, 4H), 9.87 (s, 1H). ^{13}C NMR (75.4 MHz, DMSO-d_6) δ: 124.3, 126.5, 130.1, 130.3, 131.1, 131.6, 131.8, 132.0, 147.9, 162.5, 164.6. MS *m*/*e* (relative intensity) EI: 440 (M^++4, 3), 438 (M^++2, 6), 436 (M^+, 3), 369 (10), 367 (18), 365 (10), 286 (10), 257 (100), 255 (72), 198 (22), 184 (60), 182 (60), 117 (22), 104 (50), 102 (75), 90 (31), 76 (36). Anal. Calcd for $C_{15}H_{10}Br_2N_4S$: C, 41.10; H, 2.28; N, 12.79; S, 7.31. Found: C, 40.89; H, 2.36; N, 12.82; S, 7.55.

4.3. General electrochemical procedure

The electrochemical oxidation of **1** (1 mmol, 60 ml SSE) was performed under potentiostatic conditions (a constant potential of

+2.7 V (vs Ag/Ag^+) was applied), or under galvanostatic conditions (constant current of 200 mA) in a concentric cell with two compartments separated by a low porosity (D4) glass frit diaphragm and equipped with a magnetic stirrer. The temperature was maintained constant at 20 °C. A platinum plate electrode (or a graphite electrode under galvanostatic conditions) was used as the anode. A platinum plate electrode as the cathode and a Ag/AgCl (sat) electrode as the reference. The SSE (solvent-supporting-electrolyte system) was dry acetonitrile containing 0.1 M lithium perchlorate. The initial current of 180 mA decreased to 40 mA after a charge consumption corresponding to a $2e^-$/substrate molecule process.

Once the reaction was finished the anodic solution was removed under reduced pressure. The residue was extracted with ether/H_2O. The organic phase was dried over $MgSO_4$ and concentrated by evaporation. The resulting solid, containing **2** and **3**, was chromatographed on silica gel 60 (35–70 mesh) in a (28×2.5 cm) column, using a mixture hexane/EtOAc (7:2) as eluent. The physical and spectroscopical properties of the new obtained products are summarized as follows:

*4.3.1. 3,6-Diphenyl-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (**2a**).* Compound **2a** (60% yield). Mp 202–204 °C [lit.[4] 204–205 °C].

*4.3.2. 3,6-Bis(4-methoxyphenyl)-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazole (**2b**).* Compound **2b** (58% yield). Mp 199–200 °C [lit.[8] 200–201 °C].

*4.3.3. 3,6-Bis(2-methylphenyl)-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazole (**2c**).* Compound **2c** (54% yield). Mp 116–118 °C [lit.[14] 120–122 °C].

*4.3.4. 3,6-Bis(4-methylphenyl)-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazole (**2d**).* Compound **2d** (55% yield). Mp 165–167 °C. IR (KBr) ν (cm^{-1}): 3060, 2918, 1609, 1478, 1185, 969, 947, 816. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.44 (s, 6H), 7.27–7.37 (m, 4H), 7.72–7.82 (m, 2H), 8.22–8.30 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 21.6, 21.7, 126.3, 127.0, 129.6, 130.1, 140.6, 142.2, 144.1, 143.7, 166.7. MS *m/e* (relative intensity) EI: 307 (M^++1, 9), 306 (M^+, 26), 162 (11), 136 (100), 118 (18), 89 (10). Anal. Calcd for $C_{17}H_{14}N_4S$: C, 66.67; H, 4.58; N, 18.30; S, 10.46. Found: C, 66.77; H, 4.81; N, 18.09; S, 10.49.

*4.3.5. 3,6-Bis(4-chlorophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (**2e**).* Compound **2e** (64% yield). Mp 233–235 °C [lit.[15] 235–236 °C].

*4.3.6. 3,6-Bis(4-bromophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (**2f**).* Compound **2f** (62% yield). Mp 227–230 °C. IR (KBr) ν(cm^{-1}): 3078, 1589, 1470, 1397, 1072, 1010, 980, 959, 828. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.6–7.7 (m, 4H), 7.75 (d, 2H, *J*=8.2 Hz), 8.20 (d, 2H, *J*=8.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 124.5, 125.0, 127.8, 127.9, 128.1, 128.6, 132.3, 132.9, 144.1, 146.7, 166.2. MS *m/e* (relative intensity) EI: 438 (M^++4, 12), 436 (M^++2, 24), 434 (M^+, 11), 227 (12), 225 (12), 201 (100), 183 (88), 181 (86), 146 (19), 120 (46), 102 (55), 75 (37). Anal. Calcd for $C_{15}H_8Br_2N_4S$: C, 41.28; H, 1.83; N, 12.84; S, 7.34. Found: C, 41.51; H, 1.99; N, 12.81; S, 7.22.

*4.3.7. 2-(5-Methyl-3-phenyl-1H-[1,2,4]triazol-1-yl)-5-phenyl-1,3,4-thiadiazoles (**3a**).* Compound **3a** (22% yield, 52% galvanost). Mp 180 °C. IR (KBr) ν(cm^{-1}): 3061, 2923, 1530, 1501, 1355, 1268, 761, 719, 688. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.0 (s, 3H), 7.38–7.44 (m, 3H), 7.44–7.50 (m, 3H), 7.88–7.94 (m, 2H), 8.07–8.12 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.0, 126.9, 127.6, 128.8, 129.4, 129.2, 129.6, 130.4, 131.6, 155.4, 160.7, 162.5, 167.2. MS *m/e* (relative intensity) EI: 320 (M^++1, 22), 319 (M^+, 65), 278 (21), 216 (27), 158 (53), 146 (20), 121 (100), 103 (12), 77 (11). Anal. Calcd for $C_{17}H_{13}N_5S$: C, 63.95; H, 4.07; N, 21.94; S, 10.03. Found: C, 64.37; H, 3.91; N, 21.77; S, 9.89.

*4.3.8. 2-(5-Methyl-3-(4-methoxyphenyl)-1H-[1,2,4]triazol-1-yl)-5-(4-methoxyphenyl)-1,3,4-thiadiazoles (**3b**).* Compound **3b** (31% yield, 64% galvanost). Mp 172–174 °C. IR (KBr) ν(cm^{-1}): 3040, 2925, 2853, 1606, 1505, 1384, 1252, 1175, 1030, 832, 753. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.0 (s, 3H), 3.85 (s, 3H), 3.87 (s, 3H), 6.98–7.02 (m, 4H), 7.90 (d, 2H, *J*=8.6 Hz), 8.07 (d, 2H, *J*=8.6 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 14.1, 55.3, 55.5, 114.1, 114.7, 121.9, 122.2, 128.3, 129.1, 155.0, 160.0, 161.2, 162.2, 166.7. MS *m/e* (relative intensity) EI: 380 (M^++1, 13), 379 (M^+, 49), 338 (10), 246 (5), 177 (38), 159 (41), 151 (100), 133 (55), 108 (7), 103 (6). Anal. Calcd for $C_{19}H_{17}N_5O_2S$: C, 60.16; H, 4.48; N, 18.47; S, 8.44. Found: C, 59.97; H, 4.62; N, 18.52; S, 8.65.

*4.3.9. 2-(5-Methyl-3-(2-methylphenyl)-1H-[1,2,4]triazol-1-yl)-5-(2-methylphenyl)-1,3,4-thiadiazoles (**3c**).* Compound **3c** (11% yield, 62% galvanost). Mp 130–132 °C. IR (KBr) ν(cm^{-1}): 3020, 2924, 2853, 1520, 1379, 1254, 1017, 765, 738. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.60 (s, 3H), 2.62 (s, 3H), 3.0 (s, 3H), 7.20–7.40 (m, 6H), 7.65 (d, 1H, *J*=8.0 Hz), 8.00 (d, 1H, *J*=8.0 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.0, 21.8, 22.1, 126.0, 126.5, 128.4, 128.5, 129.7, 129.8, 130.7, 130.8, 131.4, 131.9, 137.4, 137.6, 154.3, 161.4, 163.2, 166.6. MS *m/e* (relative intensity) EI: 348 (M^++1, 26), 347 (M^+, 34), 199 (100), 172 (13), 157 (47), 151 (34), 134 (17), 117 (38), 91 (26). Anal. Calcd for $C_{19}H_{17}N_5S$: C, 65.71; H, 4.90; N, 20.17; S, 9.22. Found: C, 65.88; H, 4.96; N, 20.41; S, 9.41.

*4.3.10. 2-(5-Methyl-3-(4-methylphenyl)-1H-[1,2,4]triazol-1-yl)-5-(4-methylphenyl)-1,3,4-thiadiazoles (**3d**).* Compound **3d** (11% yield, 49% galvanost). Mp 192–194 °C. IR (KBr) ν(cm^{-1}): 3041, 2924, 2853, 1505, 1378, 1265, 822, 746. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.33 (s, 3H), 2.35 (s, 3H), 2.97 (s, 3H), 7.15–7.30 (m, 4H), 7.80 (d, 2H, *J*=8.0 Hz), 7.97 (d, 2H, *J*=8.0 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.1, 21.5, 22.7, 126.8, 127.5, 129.4, 130.1, 140.5, 142.2, 155.2, 160.4, 162.6, 167.2. MS *m/e* (relative intensity) EI: 348 (M^++1, 13), 347 (M^+, 42), 306 (10), 230 (13), 173 (13), 161 (24), 143 (34), 135 (100), 117 (33), 91 (21). Anal. Calcd for $C_{19}H_{17}N_5S$: C, 65.71; H, 4.90; N, 20.17; S, 9.22. Found: C, 66.01; H, 4.87; N, 20.43; S, 9.24.

*4.3.11. 2-(5-Methyl-3-(4-chlorophenyl)-1H-[1,2,4]triazol-1-yl)-5-(4-chlorophenyl)-1,3,4-thiadiazoles (**3e**).* Compound **3e** (16% yield, 57% galvanost). Mp 230–233 °C. IR (KBr) ν(cm^{-1}): 3089, 2922, 2852, 1524, 1499, 1409, 1374, 1260, 1114, 1088, 1012, 841, 832, 747. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.1 (s, 3H), 7.49 (d, 2H, *J*=8.6 Hz), 7.56 (d, 2H, *J*=8.6 Hz), 7.95 (d, 2H, *J*=8.6 Hz), 8.13 (d, 2H, *J*=8.6 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.1, 127.8, 128.2, 128.8, 129.1, 129.4, 129.7, 136.4, 137.9, 155.6, 160.7, 161.8, 166.0. MS *m/e* (relative intensity) EI: 391 (M^++4, 5), 389 (M^++2, 23), 387 (M^+, 32), 348 (6), 346 (9), 252 (8), 250 (23), 183 (11), 181 (20), 165 (17), 163 (30), 157 (45), 155 (100), 139 (13), 138 (19), 102 (7). Anal. Calcd for $C_{17}H_{11}Cl_2N_5S$: C, 52.58; H, 2.83; N, 18.04; S, 8.25. Found: C, 52.77; H, 3.02; N, 18.23; S, 8.09.

*4.3.12. 2-(5-Methyl-3-(4-bromophenyl)-1H-[1,2,4]triazol-1-yl)-5-(4-bromophenyl)-1,3,4-thiadiazoles (**3f**).* Compound **3f** (30% yield, 60% galvanost). Mp 238–240 °C. IR (KBr) ν(cm^{-1}): 3060, 2924, 2853, 1588, 1526, 1497, 1406, 1264, 1114, 1069, 1009, 835, 818, 745. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.1 (s, 3H), 7.68 (d, 2H, *J*=8.6 Hz), 7.71 (d, 2H, *J*=8.6 Hz), 7.88 (d, 2H, *J*=8.6 Hz), 8.06 (d, 2H, *J*=8.6 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.1, 124.8, 126.2, 128.1, 128.4, 128.9, 132.0, 132.6, 132.7, 155.6, 160.8, 162.0, 166.1. MS *m/e* (relative intensity) EI: 479 (M^++4, 23), 477 (M^++2, 41), 475 (M^+, 22), 436 (10), 296 (100), 294 (98), 209 (33), 207 (31), 201 (67), 199 (69), 183 (97), 146 (32), 120 (94), 102 (60), 75 (28). Anal. Calcd for

$C_{17}H_{11}Br_2N_5S$: C, 42.77; H, 2.31; N, 14.67; S, 6.71. Found: C, 42.61; H, 2.52; N, 14.44; S, 6.89.

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