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Chemistry

THE (1*H*-TETRAZOL-1-YL)ARENEDIAZONIUM SALTS AS CONVENIENT REAGENTS FOR QUINONES ARYLATION: SYNTHESIS OF 1,3-BENZOXATHIOL-2-ONES AND NAPHTHO [2,1-*d*][1,3]OXATHIOL-2-ONES BEARING (1*H*-TETRAZOL-1-YL)PHENYL MOTIF

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Abstract. A convenient two-step method for the synthesis of novel 1,3-benzoxathiol-2-ones and naphtho[2,1-*d*][1,3]oxathiol-2-ones bearing (1*H*-tetrazol-1-yl)phenyl motif was developed. As a key step of the synthesis, an arylation of quinones (1,4-benzoquinone, 1,4-naphthoquinones) with the (1*H*-tetrazol-1-yl)arenediazonium salts was studied and efficient protocols were elaborated to obtain a variety of substituted ((1*H*-tetrazol-1-yl)phenyl) benzo/naphtho-1,4-quinones in good to excellent yields. An alternative synthesis of ((1*H*-tetrazol-1-yl)phenyl) naphtho-1,4-quinones *via* Diels-Alder reaction of tetrazolylphenyl-1,4-benzoquinones was demonstrated. The prepared benzo/naphtho-1,4-quinones readily react with thiourea at room temperature in the presence of a strong mineral acid to form intermediate isothiuronium salts, which cyclize with high yields to condense 1,3-oxathiol-2-ones under heating.

Keywords: tetrazole, quinone, oxathiolone, Meerwein arylation, cyclization.

1. Introduction

Tetrazoles are an important class of polynitrogen-containing heterocyclic compounds with a wide range of practical applications. They are used as potential explosives, complexing agents, ligands, drugs, *etc.* In particular, their active use in drug discovery over the past 15 years has been acknowledged in recent reviews.[1,2] One of the reasons for tetrazole success in drug discovery is a commonly assumed bioisosterism of the metabolically stable tetrazole ring to cis-amide and carboxyl groups.[3] The compounds containing aryltetrazole fragments are privileged among the tetrazole drug candidates. As an example of scaffolds bearing (1*H*-tetrazol-1-yl)phenyl pharmacophore, several compounds demonstrated in Fig. should be noted. Thus, compound **A** is a potent ROMK channel inhibitor,[4] clinical candidate AZD-8165 (compound **B**) is a neutral thrombin inhibitor.[5] There is a number of promising tetrazole derivatives with a pronounced antifungal effect. For instance, compound **C** (TAK-456) bearing the 1,2,4-triazolyl and (tetrazol-1-yl)aryl moieties has shown a strong inhibitory effect on *Candida spp., A. fumigatus*, and *Cryptococcus neoformans*,[6] tetrazole-containing aminopyrimidines (compound **D**)[7] and 1-(4-(1*H*-tetrazole-1-yl)phenyl)-3-arylprop-2-en-1-one (compound **E**)[8] displayed high *in vitro* antifungal activity comparable to that of fluconazole, against *C. albicans, S. cerevisiae, A. niger*, and *A. fumigatus*. Several types of polynuclear heterocyclic compounds **F** and **G** containing tetrazolyl moieties are promising COX-1 and COX-2 inhibitors demonstrating anti-inflammatory activity comparable to that of the known drugs (diclofenac and indomethacin).[9]

Among other applications, it is worth mentioning the effectiveness of tetrazole derivatives as metal complexes, which are also used in biomedical research.[10,11] It is interesting to use them as a co-ligand for copper π-complexes.[12-14] Finally, 1*H*-tetrazoles were used for transannulation reaction to synthesize condensed pyrimidinones[15] for anticancer research.[16-18]

Quinoid compounds are widespread in nature. They are involved in many biological processes and are extremely important for almost every living organism.[19,20] At the same time, the features of the structure of quinones determine a wide range of their chemical reactions. They are active in many homolytic and heterolytic reactions, and capable of cycloaddition. The heterolytic reactions of

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quinones with nucleophilic reagents, in particular with S-, N-, and C-nucleophiles, are of special interest and importance. Due to such reactions, various derivatives are obtained, which are used as drugs, herbicides, fungicides, restrictive drugs, analytical reagents, polymer modifiers, catalysts, and reagents for fine organic synthesis.[21]

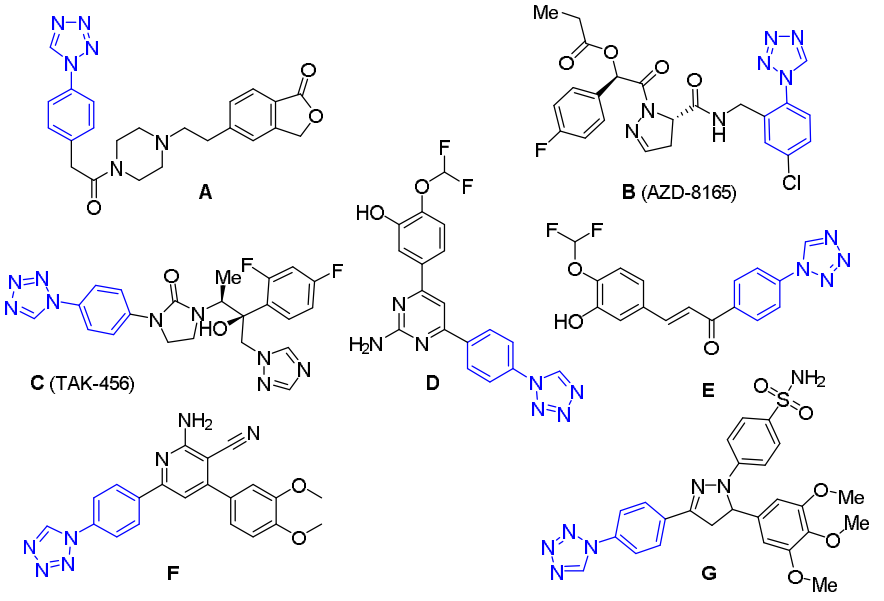


Fig. Biologically active compounds bearing (1*H*-tetrazol-1-yl)phenyl motif

Recently, there has been a growing interest in the chemical and biological properties of quinones, the structure of which includes aryl substituents. Increased interest in arylquinones is due to the fact that these compounds, on the one hand, are quite common in nature, and on the other hand, show a variety of biological and pharmacological activity.[22-24]

The reaction of some disubstituted 1,4-benzoquinone derivatives with arenediazonium salts (Meerwein reaction) is a rather convenient path to arylated 1,4-benzoquinones.[25-27] In the case of 1,4-naphthoquinones, Meerwein arylation requires the use of catalysts based on copper and its compounds, and still ends with the formation of arylnaphthoquinones but with yields lower than in the case of 1,4-benzoquinones.[25] This, obviously, has led to the search for new effective reagents and the development of favorable conditions for arylation reactions. The reactions, which are proven in the case of 1,4-naphthoquinones, include palladium-catalytic arylation according to Heck or Suzuki.[28-31]

In recent years, several more groups of methods for direct C–H functionalization of the quinone cycle with aryl fragments have been developed: arylation with arylboronic acids in the presence of transition metal-based catalysts,[24, 32-37] arylation with arylhydrazines,[38] benzamides,[39] diaryl iodonium salts,[40] and a number of others.[41] However, they usually require the use of expensive catalysts, specific reaction conditions, and, in some cases, hard-to-reach starting materials. Thus, the arylation of 1,4-quinones with arenediazonium salts remains an effective and affordable method for introducing aryl moieties into the quinone cycle.

2. Experimental

2.1. Materials and Methods

^{1}H and ^{13}C NMR spectra were recorded on Varian Unity Plus 400 (400 and 101 MHz, respectively) and Bruker 170 Avance 500 (500 and 126 MHz, respectively) spectrometers in DMSO-d_6 solutions using TMS or the deuterated solvenant as an internal reference. Mass spectral analyses were performed using an Agilent 1100 series LC/MSD with API-ES/APCI mode (200 eV). Elemental analyses were accomplished using a Carlo Erba 1106 instrument. Melting points were determined in open capillary tubes and were uncorrected.

2.1.1. General procedure, physical and spectral data

The starting tetrazolylanilines were obtained by known methods and their characteristics correspond to the literature data: 3-(1*H*-tetrazol-1-yl)aniline **1a**,[42] 3-(5-methyl-1*H*-tetrazol-1-yl)aniline **1b**,[43] 4-(1*H*-tetrazol-1-yl)aniline **1c**,[44] 4-(5-methyl-1*H*-tetrazol-1-yl)aniline **1d**,[45]

4-(5-(methylthio)-1*H*-tetrazol-1-yl)aniline **1e**,[46] 3-methyl-4-(1*H*-tetrazol-1-yl)aniline **1f**.[47]

2.1.1.1. General procedures for the preparation of 2-(1*H*-tetrazol-1-yl)arylbenzo-1,4-quinones (4a-f)

A solution of amine **1** (11 mmol) in 5 mL of concentrated hydrochloric acid was cooled to 273 K, and a cold solution of 0.76 g (11 mmol) of sodium nitrite in a minimal amount of water was added dropwise under stirring. The mixture was stirred at 273–278 K for 10 min, filtered (if necessary) to obtain a clear solution of (1*H*-tetrazol-1-yl)arenediazonium chloride **2**. Under constant stirring, the solution was added to a suspension of 1.3 g (12 mmol) of 1,4-benzoquinone **3**, and 3.7 g of sodium acetate trihydrate in 100 mL of water. After nitrogen evolution, the semisolid product was separated *via* decantation, washed with a small amount of water and dried. Then, the product was purified on flash column chromatography on Al_2O_3 using ethylacetate as eluent. Quinones **4a-f** were recrystallized from the dioxane-DMF mixture with a ratio of 2:1.

2-[3-(1*H*-Tetrazol-1-yl)phenyl]-1,4-benzoquinone (4a)
Yield 75 %; mp 434–435 K (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.10 (s, 1H), 8.12 (s, 1H), 8.08–8.00 (m, 1H), 7.74−7.66 (m, 2H), 7.11 (d, 1H, ^4J = 2.4 *Hz*), 6.98 (d, 1H, ^3J = 10.0 *Hz*), 6.93 (dd, 1H, ^3J = 10.0 *Hz*, ^4J = 2.4 *Hz*). Mass spectrum, *m/z*: 253 $[M+H]^+$. Found, %: C, 61.93; H, 3.27; N, 22.29. $C_{13}H_8N_4O_2$. Calculated, %: C, 61.90; H, 3.20; N, 22.21.

2-[3-(5-Methyl-1*H*-tetrazol-1-yl)phenyl]-1,4-benzoquinone (4b)
Yield 67 %; mp 443–444 K (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85−7.65 (m, 4H), 7.06 (d, 1H, ^4J = 2.4 *Hz*), 6.98 (d, 1H, ^3J = 10.0 *Hz*), 6.92 (dd, 1H, ^3J = 10.0 *Hz*, ^4J = 2.4 *Hz*), 2.63 (s, 3H). Mass spectrum, *m/z*: 267 $[M+H]^+$. Found, %: C, 63.17; H, 3.81; N, 20.91. $C_{14}H_{10}N_4O_2$. Calculated, %: C, 63.15; H, 3.79; N, 21.04.

2-[4-(1*H*-Tetrazol-1-yl)phenyl]-1,4-benzoquinone (4c)
Yield 64 %; mp 436–437 K (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.12 (s, 1H), 8.02 (d, 2H, *J* = 8.8 *Hz*), 7.77 (d, 2H, *J* = 8.8 *Hz*), 7.03 (d, 1H, ^4J = 2.4 *Hz*), 6.96 (d, 1H, ^3J = 10.0 *Hz*), 6.91 (dd, 1H, ^3J = 10.0 *Hz*, ^4J = 2.4 *Hz*). Mass spectrum, *m/z*: 253 $[M+H]^+$. Found, %: C, 61.79; H, 3.14; N, 22.34. $C_{13}H_8N_4O_2$. Calculated, %: C, 61.90; H, 3.20; N, 22.21.

2-[4-(5-Methyl-1*H*-tetrazol-1-yl)phenyl]-1,4-benzoquinone (4d)
Yield 56 %; mp 472–473 K (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.79 (d, 2H, *J* = 8.4 *Hz*), 7.75 (d, 2H, *J* = 8.4 *Hz*), 7.04 (d, 1H, ^4J = 1.6 *Hz*), 6.98 (d, 1H, ^3J = 10 *Hz*), 6.93 (dd, 1H, ^3J = 10 *Hz*, ^4J = 1.6 *Hz*), 2.64 (s, 3H). Mass spectrum, *m/z*: 267 $[M+H]^+$. Found, %: C, 63.06; H, 3.88; N, 21.09. $C_{14}H_{10}N_4O_2$. Calculated, %: C, 63.15; H, 3.79; N, 21.04.

2-{4-[5-(Methylthio)-1*H*-tetrazol-1-yl]phenyl}-1,4-benzoquinone (4e)
Yield 66 %; mp 485–486 K (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.80 (d, 2H, *J* = 8.2 *Hz*), 7.73 (d, 2H, *J* = 8.2 *Hz*), 7.05 (d, 1H, ^4J = 2.2 *Hz*), 6.96 (d, 1H, ^3J = 10 *Hz*), 6.91 (dd, 1H, ^3J = 10 *Hz*, ^4J = 2.2 *Hz*), 2.82 (s, 3H). Mass spectrum, *m/z*: 299 $[M+H]^+$. Found, %: C, 56.43; H, 3.34; N, 18.71. $C_{14}H_{10}N_4O_2S$. Calculated, %: C, 56.37; H, 3.38; N, 18.78.

2-[3-Methyl-4-(1*H*-tetrazol-1-yl)phenyl]-1,4-benzoquinone (4f)
Yield 73 %; mp 438–439 K (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 8.02–8.90 (m, 2H), 7.64 (s, 1H), 7.02 (d, 1H, ^4J = 2.4 *Hz*), 6.97 (d, 1H, ^3J =10.4 *Hz*), 6.90 (dd, 1H, ^3J = 10.4 *Hz*, ^4J = 2.4 *Hz*), 2.27 (s, 3H). Mass spectrum, *m/z*: 267 $[M+H]^+$. Found, %: C, 63.25; H, 3.72; N, 21.11. $C_{14}H_{10}N_4O_2$. Calculated, %: C, 63.15; H, 3.79; N, 21.04.

2.1.1.2. General procedures for the preparation of 6,7-R^3-2-(4-1H-tetrazol-1-yl)aryl-1,4-naphthoquinones (6a-f)

A solution of amine **1** (11 mmol) in 5 mL of concentrated hydrochloric acid was cooled to 273 K, and a cold solution of 0.76 g (11 mmol) of sodium nitrite in a minimal amount of water was added dropwise under stirring. The mixture was stirred at 273–278 K for 10 min, filtered (if necessary) to obtain a clear solution of (1*H*-tetrazol-1-yl)arenediazonium chloride **2**. Under constant stirring, this solution was added to a suspension of 1,4-naphthoquinones **5a**, **b** (12.4 mmol), 3.7 g of sodium acetate trihydrate, and 0.5 g of copper(I) oxide in 25 mL of acetone. The temperature of the reaction mixture was maintained in the range of 303–318 K. After nitrogen evolution, the mixture was left overnight. The formed precipitate was filtered off, washed with a small amount of water and dried. The 1,4-naphthoquinones **6a-f** were recrystallized from the DMF or ethanol-DMF mixture.

6,7-Dimethyl-2-[3-(5-methyl-1*H*-tetrazol-1-yl)phenyl]-1,4-naphthoquinone (6a)
Yield 36 %; mp 486–487 K (dec.) (EtOH–DMF, 1:3). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.92 (s, 1H), 7.90–7.75 (m, 5H), 7.21 (s, 1H), 2.64 (s, 3H), 2.42 (s, 6H). Mass spectrum, *m/z*: 345 $[M+H]^+$. Found, %: C, 69.70; H, 4.73; N, 16.34. $C_{20}H_{16}N_4O_2$. Calculated, %: C, 69.76; H, 4.68; N, 16.27.

2-[4-(1*H*-Tetrazol-1-yl)phenyl]-1,4-naphthoquinone (6b)
Yield 55 %; mp 477 K (dec.) (DMF); ^{1}H NMR (400 MHz, DMSO) δ 10.18 (s, 1H), 8.11–8.00 (m, 4H), 7.94–7.83 (m, 4H), 7.25 (s, 1H). ^{13}C NMR (126 MHz, DMSO) δ 184.58, 183.64, 146.09, 142.37, 135.31, 134.51, 134.46, 134.30, 134.22, 132.08, 131.64, 131.36 (2xC), 126.59,

125.51, 120.64 (2xC). Mass spectrum, *m/z*: 303 $[M+H]^+$. Found, %: C, 67.64; H, 3.21; N, 18.45. $C_{17}H_{10}N_4O_2$. Calculated, %: C, 67.55; H, 3.33; N, 18.53.

2-[4-(5-Methyl-1H-tetrazol-1-yl)phenyl]-1,4-naphthoquinone (6c)

Yield 43 %; mp 500 K (dec.) (EtOH–DMF, 2:1); ^{1}H NMR (400 MHz, DMSO) δ 8.12–8.04 (m, 2H), 7.81–7.98 (m, 6H), 7.31 (s, 1H), 2.65 (s, 3H). Mass spectrum, *m/z*: 317 $[M+H]^+$. Found, %: C, 68.29; H, 3.61; N, 17.83. $C_{18}H_{12}N_4O_2$. Calculated, %: C, 68.35; H, 3.82; N, 17.71.

2-{4-[5-(Methylthio)-1*H*-tetrazol-1-yl]phenyl}-1,4-naphthoquinone (6d)

Yield 54 %; mp 495 K (dec.) (EtOH–DMF, 1:1). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.15–8.05 (m, 2H), 8.00–7.85 (m, 4H), 7.81 (d, 2H, ^3J = 8.8 *Hz*), 7.28 (s, 1H), 2.83 (s, 3H). Mass spectrum, *m/z*: 349 $[M+H]^+$. Found, %: C, 62.11; H, 3.40; N, 16.12. $C_{18}H_{12}N_4O_2S$. Calculated, %: C, 62.06; H, 3.47; N, 16.08.

2-[3-Methyl-4-(1*H*-tetrazol-1-yl)phenyl]-1,4-naphthoquinone (6e)

Yield 32 %; mp 477–478 K (dec.) (EtOH–DMF, 1:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 8.16–8.04 (m, 2H), 8.00–7.90 (m, 2H), 7.78 (s, 1H), 7.74–7.64 (m, 2H), 7.28 (s, 1H), 2.24 (s, 3H). Mass spectrum, *m/z*: 317 $[M+H]^+$. Found, %: C, 68.46; H, 3.70; N, 17.77. $C_{18}H_{12}N_4O_2$. Calculated, %: C, 68.35; H, 3.82; N, 17.71.

6,7-Dimethyl-2-[4-(5-methyl-1*H*-tetrazol-1-yl)phenyl] -1,4-naphthoquinone (6f)

Yield 38 %; mp 494 K (dec.) (EtOH–DMF, 1:2). ^{1}H NMR (400 MHz, DMSO) δ 7.90–7.76 (m, 6H), 7.19 (s, 1H), 2.62 (s, 3H), 2.41 (s, 6H). ^{13}C NMR (126 MHz, DMSO) δ 184.64, 183.65, 152.26, 145.94, 143.96, 143.92, 135.53, 135.22, 134.40, 131.06 (2xC), 129.99, 129.69, 127.38, 126.33, 124.40 (2xC), 19.79, 19.75, 9.45. Mass spectrum, *m/z*: 345 $[M+H]^+$. Found, %: C, 69.84; H, 4.79; N, 16.19. $C_{20}H_{16}N_4O_2$. Calculated, %: C, 69.76; H, 4.68; N, 16.27.

2.1.1.3. General procedures for the preparation of 6,7-dimethyl-2-(4-1H-tetrazol-1-yl)aryl-1,4-naphthoquinones (6 g, h) (Diels-Alder reaction)

A suspension of appropriate compound **4** (4 mmol), 2,3-dimethyl-1,3-butadiene **7**[48] (0.45 mL, d = 0.726 g/mL) in 10 mL of glacial acetic acid was stirred for 48 h at room temperature. Then the reaction mixture was heated for 3-4 h, maintaining a slight boil and 1.1 g of chromium(VI) oxide in 3 mL of water was added. The mixture was refluxed for another 30 min and cooled to room temperature. Water (10 mL) was added and the precipitate was filtered off, washed with ethyl alcohol, and dried. The products were recrystallized from the ethanol-DMF mixture.

6,7-Dimethyl-2-[3-(1*H*-tetrazol-1-yl)phenyl]-1,4-naphthoquinone (6g)

Yield 76 %; mp 518 K (dec.) (EtOH–DMF, 1:3). ^{1}H NMR (400 MHz, DMSO) δ 10.18 (s, 1H), 8.18 (s, 1H), 8.07 (s, 1H), 8.00–7.77 (m, 4H), 7.29 (s, 1H), 2.45 (s, 6H). Mass spectrum, *m/z*: 331 $[M+H]^+$. Found, %: C, 69.00; H, 4.43; N, 16.91. $C_{19}H_{14}N_4O_2$. Calculated, %: C, 69.08; H, 4.27; N, 16.96.

6,7-Dimethyl-2-[4-(1*H*-tetrazol-1-yl)phenyl]-1,4-naphthoquinone (6h)

Yield 81 %; mp 484–485 K (dec.) (EtOH–DMF, 1:2). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.19 (s, 1H), 8.04 (d, 2H, ^3J = 8.6 *Hz*), 7.90 (d, 2H, ^3J = 8.6 *Hz*), 7.88 (s, 1H), 7.81 (s, 1H), 7.20 (s, 1H), 2.43 (s, 6H). Mass spectrum, *m/z*: 331 $[M+H]^+$. Found, %: C, 69.19; H, 4.13; N, 17.11. $C_{19}H_{14}N_4O_2$. Calculated, %: C, 69.08; H, 4.27; N, 16.96.

2.1.1.4. General procedures for the preparation of 5-hydroxy-7-[4-(1H-tetrazol-1-yl)aryl]-1,3-benzoxathiol-2-ones (8a-f) and 5-hydroxy-4-[4-(5-methyl-1*H*-tetrazol-1-yl)phenyl]naphtho[2,1-*d*][1,3]oxathiol-2-ones (10a, b)

The appropriate benzoquinone **4** or naphthoquinone **6** (2.78 mmol) was dissolved in 20 mL of glacial acetic acid (to achieve better homogeneity of the suspension, it was slightly heated). The solution of thiourea 0.3 g in 10 mL of 2N hydrochloric acid was added portion-wise for 30 min to a constantly stirred warm suspension of quinone. The solution was discolored. The reaction mixture was refluxed for 1 h, cooled and the precipitate was filtered off. The solid was washed on the filter with aqueous ethyl alcohol and dried.

5-Hydroxy-7-[3-(1*H*-tetrazol-1-yl)phenyl]-1,3-benzoxathiol-2-one (8a)

Yield 66 %; mp 526 K (dec.) (EtOH–H_2O, 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.13 (s, 1H), 9.81 (s, 1H), 8.17 (s, 1H), 7.97 (d, 1H, *J* = 8.0 *Hz*), 7.78–7.73 (m, 2H), 7.08 (d, 1H, *J* = 2.4 *Hz*), 6.95 (d, 1H, *J* = 2.4 *Hz*). Mass spectrum, *m/z*: 313 $[M+H]^+$. Found, %: C, 53.93; H, 2.47; N, 17.81. $C_{14}H_8N_4O_3S$. Calculated, %: C, 53.84; H, 2.58; N, 17.94.

5-Hydroxy-7-[3-(5-methyl-1*H*-tetrazol-1-yl)phenyl]-1,3-benzoxathiol-2-one (8b)

Yield 65 %; mp 526–527 K (dec.) (EtOH). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.80 (s, 1H), 7.90 (s, 1H), 7.84 (d, 1H, *J* = 8.0 *Hz*), 7.82–7.76 (m, 1H), 7.69 (d, 1H, *J* = 8.0 *Hz*), 7.10 (d, 1H, *J* = 2.4 *Hz*), 6.92 (d, 1H, *J* = 2.4 *Hz*), 2.66 (s, 3H). Mass spectrum, *m/z*: 327 $[M+H]^+$. Found, %: C, 55.41; H, 3.18; N, 17.01. $C_{15}H_{10}N_4O_3S$. Calculated, %: C, 55.21; H, 3.09; N, 17.17.

5-Hydroxy-7-[4-(1*H*-tetrazol-1-yl)phenyl]-1,3-benzoxathiol-2-one (8c)

Yield 73 %; mp 519 K (dec.) (EtOH–H_2O, 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 1H), 9.77 (s 1H), 8.04

(d, 2H, *J* = 8.6 *Hz*), 7.84 (d, 2H, *J* = 8.6 *Hz*), 7.06 (d, 1H, *J* = 2.4 *Hz*), 6.89 (d, 1H, *J* = 2.4 *Hz*). Mass spectrum, *m/z*: 313 $[M+H]^+$. Found, %: C, 53.76; H, 2.55; N, 17.99. $C_{14}H_8N_4O_3S$. Calculated, %: C, 53.84; H, 2.58; N, 17.94.

5-Hydroxy-7-[4-(5-methyl-1*H*-tetrazol-1-yl)phenyl]-1,3-benzoxathiol-2-one (8d)

Yield 61 %; mp 502–503 K (dec.) (EtOH). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.83 (s, 1H), 7.86 (d, 2H, *J* = 8.4 *Hz*), 7.78 (d, 2H, *J* = 8.4 *Hz*), 7.11 (d, 1H, *J* = 2.0 *Hz*), 6.92 (d, 1H, *J* = 2.0 *Hz*), 2.65 (s, 3H). Mass spectrum, *m/z*: 327 $[M+H]^+$. Found, %: C, 55.01; H, 3.11; N, 17.24. $C_{15}H_{10}N_4O_3S$. Calculated, %: C, 55.21; H, 3.09; N, 17.17.

5-Hydroxy-7-{4-[5-(methylthio)-1*H*-tetrazol-1-yl]phenyl}-1,3-benzoxathiol-2-one (8e)

Yield 95 %; mp 500–501 K (dec.) (EtOH–H_2O, 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.86 (s, 1H), 7.87 (d, 2H, *J* = 8.0 *Hz*), 7.76 (d, 2H, *J* = 8.4 *Hz*), 7.11 (d, 1H, *J* = = 2.0 *Hz*), 6.92 (d, 1H, *J* = 2.0 *Hz*), 2.83 (s, 3H). Mass spectrum, *m/z*: 359 $[M+H]^+$. Found, %: C, 50.21; H, 2.92; N, 15.75. $C_{15}H_{10}N_4O_3S_2$. Calculated, %: C, 50.27; H, 2.81; N, 15.63.

5-Hydroxy-7-[3-methyl-4-(1*H*-tetrazol-1-yl)phenyl]-1,3-benzoxathiol-2-one (8f)

Yield 91 %; mp 487–488 K (dec.) (EtOH–H_2O, 1:1). ^{1}H NMR (400 MHz, DMSO) δ 10.00 (s, 1H), 9.87 (s, 1H), 7.75 (s, 1H), 7.69–7.62 (m, 2H), 7.20 (s, 1H), 6.92 (s, 1H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 169.02, 154.89, 144.64, 137.95, 137.39, 133.77, 132.75, 131.47, 127.29, 126.54, 124.80, 124.29, 114.69, 109.49, 17.40. Mass spectrum, *m/z*: 327 $[M+H]^+$. Found, %: C, 55.32; H, 3.01; N, 17.08. $C_{15}H_{10}N_4O_3S$. Calculated, %: C, 55.21; H, 3.09; N, 17.17.

5-Hydroxy-4-[4-(5-methyl-1*H*-tetrazol-1-yl)phenyl]naphtho[2,1-*d*][1,3]oxathiol-2-one (10a)

Yield 85 %; mp 521–522 K (dec.) (EtOH–DMF, 2:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.91 (s, 1H), 8.41 (d, 1H, *J* = 8.4 *Hz*), 8.04 (d, 1H, *J* = 8.2 *Hz*), 7.89 (d, 2H, *J* = 8.4 *Hz*), 7.84 (d, 2H, *J* = 8.4 *Hz*), 7.76 (t, 1H, *J* = 7.6 *Hz*), 7.69 (t, 1H *J* = 7.6 *Hz*), 2.67 (s, 3H). Mass spectrum, *m/z*: 377 $[M+H]^+$. Found, %: C, 60.70; H, 3.38; N, 14.81. $C_{19}H_{12}N_4O_3S$. Calculated, %: C, 60.63; H, 3.21; N, 14.89.

5-Hydroxy-4-{4-[5-(methylthio)-1*H*-tetrazol-1-yl]phenyl}naphtho[2,1-*d*]-[1,3]oxathiol-2-one (10b)

Yield 73 %; mp >573 K (dec.) (EtOH–DMF, 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.95 (s, 1H), 8.40 (d, 1H, *J* = 7.7 *Hz*), 8.03 (d, 1H, *J* = 7.7 *Hz*), 7.86 (br.s, 4H), 7.75 (t, 1H, *J* = 7.6 *Hz*), 7.68 (t, 1H, *J* = 7.6 *Hz*), 2.84 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 168.51, 155.23, 147.35, 137.67, 136.10, 132.76, 131.12 (2xC), 128.40, 126.27, 125.02, 124.77 (2xC), 123.62, 120.41, 120.00, 118.90, 115.82, 15.27. Mass spectrum, *m/z*: 409 $[M+H]^+$. Found, %: C, 55.94; H, 2.90; N, 13.81. $C_{19}H_{12}N_4O_3S_2$. Calculated, %: C, 55.87; H, 2.96; N, 13.72.

2.1.1.5. General procedures for the preparation of 7-(1*H*-tetrazol-1-yl)phenyl-2-oxo-1,3-benzoxathiol-5-yl acetates (9a-c)

A drop of perchloric acid was added to the mixture of compound **8** (5 mmol) and acetic anhydride (5 mL). The mixture was stirred at room temperature for 4 h and then heated at 353 K for 1 h. The mixture was poured into water; the precipitate was filtered off, washed with water, and dried. The products were recrystallized from the ethanol-DMF (5:1).

7-[3-(5-Methyl-1*H*-tetrazol-1-yl)phenyl]-2-oxo-1,3-benzoxathiol-5-yl acetate (9a)

Yield 75 %; mp 423 K (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.01 (s, 1H), 7.93 (d, 1H, *J* = 6.1 Hz), 7.83–7.77 (m, 2H), 7.67 (s, 1H), 7.46 (s, 1H), 2.63 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 169.60, 169.03, 152.78, 147.76, 142.95, 136.21, 134.46, 130.82, 130.68, 125.41, 125.28, 125.00, 124.78, 121.93, 117.43, 21.18, 9.78. Mass spectrum, *m/z*: 369 $[M+H]^+$. Found, %: C, 55.54; H, 3.38; N, 15.22. $C_{17}H_{12}N_4O_4S$. Calculated, %: C, 55.43; H, 3.28; N, 15.21.

7-[4-(5-Methyl-1*H*-tetrazol-1-yl)phenyl]-2-oxo-1,3-benzoxathiol-5-yl acetate (9b)

Yield 75 %; mp 432–433 K (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.04 (t, 1H, *J* = 1.50 *Hz*), 7.97 (dt, 1H, *J* = 7.36, 1.50 *Hz*), 7.85 (t, 1H, *J* = 7.77 Hz), 7.81 (dt, 1H, *J* = 8.13, 1.50 *Hz*), 7.71 (d, 1H, *J* = 2.45 *Hz*), 7.49 (d, 1H, *J* = 2.47 *Hz*), 2.65 (s, 3H), 2.33 (s, 3H). Mass spectrum, *m/z*: 369 $[M+H]^+$. Found, %: C, 55.33; H, 3.31; N, 15.07. $C_{17}H_{12}N_4O_4S$. Calculated, %: C, 55.43; H, 3.28; N, 15.21.

7-{4-[5-(Methylthio)-1*H*-tetrazol-1-yl]phenyl}-2-oxo-1,3-benzoxathiol-5-yl acetate (9c)

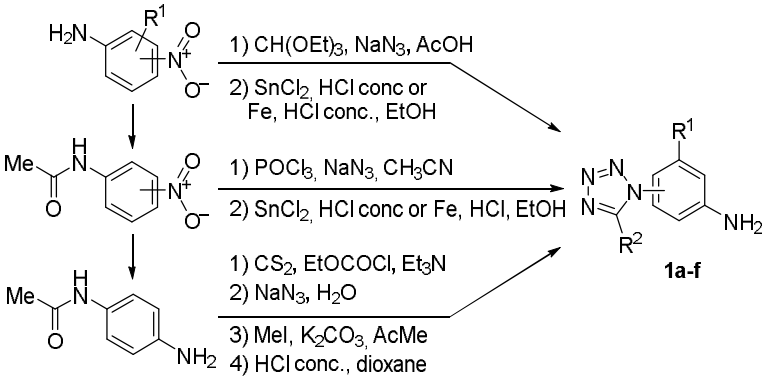
Yield 60 %; mp 462–463 K (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98 (d, 2H, *J* = 8.45 *Hz*), 7.86 (d, 2H, *J* = 8.35 Hz), 7.72 (d, 1H, *J* = 2.05 *Hz*), 7.49 (d, 1H, *J* = = 2.06 *Hz*), 2.82 (s, 3H), 2.34 (s, 3H). Mass spectrum, *m/z*: 401 $[M+H]^+$. Found, %: C, 50.93; H, 3.14; N, 13.91. $C_{17}H_{12}N_4O_4S_2$. Calculated, %: C, 50.99; H, 3.02; N, 13.99.

3. Results and Discussion

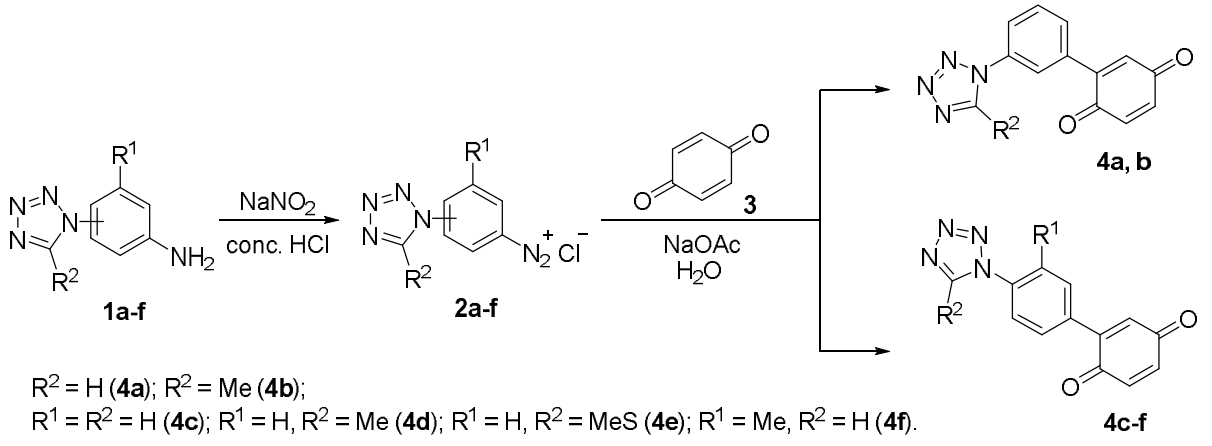
The starting (1*H*-tetrazol-1-yl)anilines were obtained from the available nitroanilines in several steps (Scheme 1). Thus, 5-unsubstituted tetrazoles were synthesized directly from nitroanilines by convenient reaction with ethyl orthoformate and sodium azide in acetic acid according to the previously described method.[49] Subsequent reduction of nitrotetrazoles led to the target compounds **1a-c**. At the same time, (5-methyl-1*H*-tetrazol-1-yl)anilines **1d**, **e** were obtained by pre-converting nitroanilines into acetyl derivatives following the annulation of

the tetrazole ring by a one-pot reaction with phosphorus oxychloride and sodium azide *via* the protocol developed by us recently.[50] Finally, the reduction of the nitro group in *N*-(4-nitrophenyl)acetamide led to the formation of monoacetylphenylenediamine, which was converted *via* the Kaluza reaction to *N*-(4-isothiocyanatophenyl)acetamide. The next 1,3-dipolar cycloaddition with sodium azide formed 5-mercapto-tetrazole, which gave the target (5-(methylthio)-1*H*-tetrazol-1-yl)aniline **1f** after alkylation with methyl iodide and removal of acetyl protection.

For the synthesis of 2-tetrazolylphenyl-1,4-benzoquinones **4a-f**, the arylation reaction of 1,4-benzoquinone **3** with diazonium salts **2a-f** obtained from amines **1a-f** was used. The reaction was carried out at room temperature in an aqueous medium in the acetate buffer. Compounds **4a-f** were prepared with high yields (Scheme 2).



Scheme 1. Synthetic routes to starting (1*H*-tetrazol-1-yl)anilines

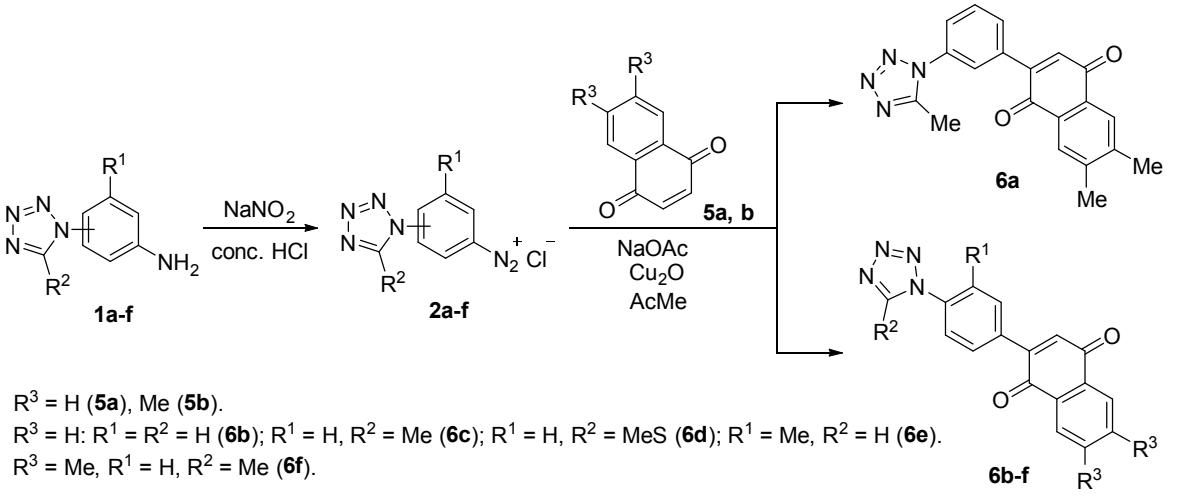


Scheme 2. Synthesis of 2-tetrazolylphenyl-1,4-benzoquinones **4a-f**

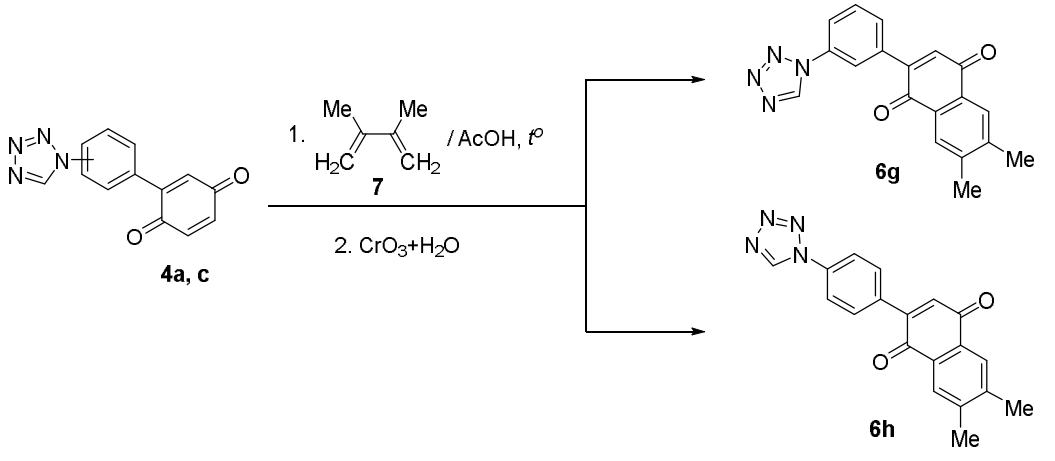
It is known that 1,4-naphthoquinones can also be arylated with arenediazonium salts under conditions of the catalytic action of copper or its salts.[51,52] However, it is noted that the yields of arylation products are low. Only when the anilines with a strong acceptor group, such as NO_2, were used, the yields of arylation reactions reached 50 %. Due to the fact that the tetrazolylphenyl moiety is an electron density acceptor, an increase in the reactivity of the arylation of naphthoquinones **5a**, **b** could be expected. It is established that in the aqueous-acetone solution in the presence of catalytic amounts of copper(I) oxide, tetrazolyl substituted naphthoquinones **6a-f** are formed with moderate yields (Scheme 3).

Since the yields in the arylation of naphthoquinones were slightly lower than in the arylation of 1,4-benzoquinones, we have proposed their alternative synthesis *via* the Diels-Alder reaction of tetrazolylphenyl-1,4-benzoquinones **4** with the following one-pot oxidation of the intermediate adduct with chromium(VI) oxide. 1,4-Benzoquinones have been previously shown as active dienophiles due to a significant activating effect of carbonyl groups. Butadiene and 2,3-dimethyl-1,3-butadiene reacted with quinone at room temperature or ~ 323 K in alcohol, acetic acid, or benzene in a solution forming the corresponding adducts with high yields. We found that the synthesized 2-tetrazolylphenyl-1,4-benzoquinones easily

reacted with diene, such as 2,3-dimethyl-1,3-butadiene **7**, *via* 2+4-cycloaddition leading to the corresponding products **6g**, **h** (Scheme 4). 2,3-Dimethyl-1,3-butadiene was obtained by dehydration of pinacol in hydrobromic acid.[48] Cycloadditions of 2-tetrazolylphenyl-1,4-benzoquinones with 2,3-dimethyl-1,3-butadiene were performed with an equimolar mixture of quinone with diene in glacial acetic acid at room temperature. 2+4-Cycloaddition *in situ* was easily converted to the corresponding naphthohydroquinones by heating for 3-4 h. The obtained 6,7-dimethyl-2-tetrazolylphenyl-1,4-hydro-naphthoquinones were oxidized to the corresponding 6,7-dimethyl-2-tetrazolylphenyl-1,4-naphthoquinones by the addition of chromium(VI) oxide.



Scheme 3. Synthesis of 2-tetrazolylphenyl-1,4-naphthoquinones **6a-f**



Scheme 4. Alternative synthesis of 2-tetrazolylphenyl-1,4-naphthoquinones *via* Diels-Alder reaction

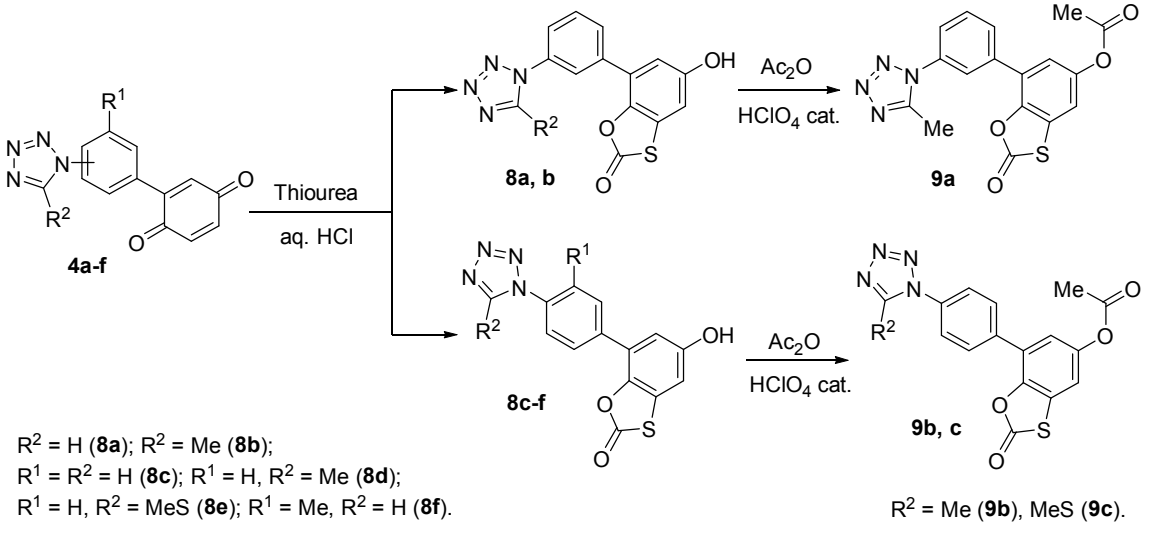
The method of obtaining naphthoquinone derivatives proved to be more effective than the two-step procedure with the extraction of intermediate adducts. The current approach allows to significantly simplify the experimental technique and improve the yields of the target products ((1*H*-tetrazol-1-yl)phenyl)-1,4-naphthoquinones **6**.

In order to further functionalize the obtained tetrazolylquinones, we studied their interaction with thiourea. The formation of a 1,3-benzoxathiol cycle based on 1,4-quinones was achieved mainly in several ways: by the interaction of quinones with thiocyanic acid or potassium ethyl xanthate,[53] with derivatives of dithiocarboxylic acids and dithiocarbamates of alkali metals,[54,55] arylthioamides or arylthioacetamides,[56] thiobenzoic and thioacetic acids.[57] It is also noteworthy that the reaction of 1,4-benzoquinone with thiosulfate anion leads to the formation of sulfothio-hydroquinone, which reacts with potassium cyanide and gives 5-hydroxy-2-imino-1,3-benzoxathiol.[53] However, in our opinion, the most convenient and quite promising one-stage method for obtaining 1,3-benzoxathiols is the reaction of quinones with thiourea.[58-60]

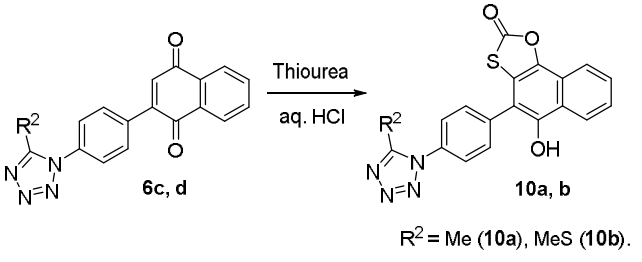
The substituted 1,4-quinones **4a-f** readily react with thiourea at room temperature in the presence of a strong mineral acid to form intermediate isothiuronium salts, which cyclize with high yields to 5-hydroxy-1,3-benzoxathiol-2-ones **8a-f** under heating (Scheme 5). It should be noted that the high reactivity of tetrazolylarylquinones indicates their synthetic potential, which can be realized in a number of transformations.[61,62]

Benzoxathiolones containing a phenolic group are known to react well with acylating and alkylating reagents.[59,60,63] 5-Hydroxy-7-tetrazolylphenyl-1,3-benzoxathiol-2-ones **8a-f** were readily acylated with acetic anhydride in the presence of hydrochloric acid by short heating of the reaction mixture. Compounds **9a-c** were prepared in good yields (Scheme 5).

Similarly to 2-tetrazolylphenyl-1,4-benzoquinones **4**, ((1*H*-tetrazol-1-yl)phenyl)naphtho-1,4-quinones **6** were also studied in the reactions with thiourea. It was found that the reaction of substituted 1,4-naphthoquinones **6c**, **d** with an excess of thiourea in a diluted hydrochloric acid occurred with the closure of the naphthooxathiolane cycle, and the formation of 5-hydroxy-4-[4-(5-methyl-1*H*-tetrazol-1-yl)phenyl]-naphtho[2,1-*d*][1,3]oxathiol-2-ones **10a**, **b**. It turned out that despite the possible steric hindrances of the aryl nucleus in position 3 of the naphthoquinone cycle, thiolanes **10a**, **b** were formed relatively easily with yields of 70–85 % (Scheme 6). The structure of compound **10** was confirmed by NMR spectroscopy.



Scheme 5. Synthesis of 1,3-benzoxathiol-2-one derivatives



Scheme 6. Synthesis of naphtho[2,1-*d*][1,3]oxathiol-2-ones

4. Conclusions

Thus, the arylation of quinones (1,4-benzoquinone, 1,4-naphthoquinones) with the (1*H*-tetrazol-1-yl)arenediazonium salts was studied and efficient protocols were elaborated to obtain a variety of substituted ((1*H*-tetrazol-1-yl)phenyl) benzo/naphtho-1,4-quinones in good to excellent yields. Alternative synthesis of ((1*H*-tetrazol-1-yl)phenyl)naphtho-1,4-quinones *via* Diels-Alder reaction of tetrazolylphenyl-1,4-benzoquinones was demonstrated. The obtained benzo/naphtho-1,4-quinones bearing (1*H*-tetrazol-1-yl)phenyl readily react with thiourea to form annulated 1,3-oxathiol-2-ones. The approach we have found is a novel, convenient and scalable method for the preparation of 1,3-benzoxathiol-2-ones and naphtho[2,1-*d*][1,3]oxathiol-2-ones bearing (1*H*-tetrazol-1-

yl)phenyl motif, which are potentially privileged scaffolds for medicinal chemistry.

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References

[1] Myznikov, L.V.; Vorona, S.V.; Zevatskii, Y.E. Biologically Active Compounds and Drugs in the Tetrazole Series. *Chem. Heterocycl. Compd. (N Y)* **2021**, *57*, 224-233. https://doi.org/10.1007/s10593-021-02897-4

[2] Wei, C.-X.; Bian, M.; Gong, G.-H. Tetrazolium Compounds: Synthesis and Applications in Medicine. *Molecules* **2015**, *20*, 5528-5553. https://doi.org/10.3390/molecules20045528

[3] Herr, R.J. 5-Substituted-1*H*-tetrazoles as Carboxylic Acid Isosteres: Medicinal Chemistry and Synthetic Methods. *Bioorg. Med. Chem*. **2002**, *10*, 3379-3393. https://doi.org/10.1016/S0968-0896(02)00239-0

[4] Tang, H.; de Jesus, R.K.; Walsh, S.P.; Zhu, Y.; Yan, Y.; Priest, B.T.; Swensen, A.M.; Alonso-Galicia, M.; Felix, J.P.; Brochu, R.M. et al. Discovery of a Novel Sub-Class of ROMK Channel Inhibitors Typified by 5-(2-(4-(2-(4-(1*H*-Tetrazol-1-yl)phenyl)acetyl)piperazin-1-yl)ethyl)isobenzofuran-1(3H)-one. *Bioorganic Med. Chem. Lett*. **2013**, *23*, 5829-5832. https://doi.org/10.1016/j.bmcl.2013.08.104

[5] Abrahamsson, K.; Andersson, P.; Bergman, J.; Bredberg, U.; Brånalt, J.; Egnell, A.-C.; Eriksson, U.; Gustafsson, D.; Hoffman, K.-J.; Nielsen, S. et.al. Discovery of AZD8165 – A Clinical Candidate from a Novel Series of Neutral Thrombin Inhibitors. *Med. Chem. Commun*. **2016**, *7*, 272-281. https://doi.org/10.1039/C5MD00479A

[6] Tsuchimori, N.; Hayashi, R.; Kitamoto, N.; Asai, K.; Kitazaki, T.; Iizawa, Y.; Itoh, K.; Okonogi, K. In Vitro and In Vivo Antifungal Activities of TAK-456, a Novel Oral Triazole with a Broad Antifungal Spectrum. *Antimicrob. Agents Chemother*. **2002**, *46*, 1388-1393. https://doi.org/10.1128/AAC.46.5.1388-1393.2002

[7] Vembu, S.; Parasuraman, P.; Gopalakrishnan, M. Synthesis, *in vitro* Antifungal and Antitubercular Evaluation of Novel Amino Pyrimidines Based Tetrazole Derivatives. *J. Pharm. Res*. **2014**, *8*, 1552-1558.

[8] Vembu, S.; Parasuraman, P.; Gopalakrishnan, M. Design, *in silico* Molecular Docking Studies, Synthesis, Spectral Characterization and *in vitro* Antifungal Evaluation of 1-(4-(1*H*-tetrazole-1-yl) phenyl)-3-arylprop-2-en-1-ones. *Der Pharma Chem*. **2014**, *6*, 35-44.

[9] Lamie, P.F.; Philoppes, J.N.; Azouz, A.A.; Safwat, N.M. Novel Tetrazole and Cyanamide Derivatives as Inhibitors of Cyclooxygenase-2 enzyme: Design, Synthesis, Anti-Inflammatory Evaluation, Ulcerogenic Liability and Docking Study. *J. Enzyme Inhib. Med. Chem*. **2017**, *32*, 805-820. https://doi.org/10.1080/14756366.2017.1326110

[10] Ismael, A.; Henriques, M.S.C.; Marques, C.; Rodrigues, M.; Barreira, L.; Paixao, J.A.; Fausto, R.; Cristiano, M.L.S. Exploring Saccharinate-Tetrazoles as Selective Cu(II) Ligands: Structure, Magnetic Properties and Cytotoxicity of Copper(II) Complexes Based on 5-(3-Aminosaccharyl)-tetrazoles. *RSC Adv*. **2016**, *6*, 71628-71637. https://doi.org/10.1039/C6RA15051A

[11] Reddy, S.R.K.; Surya, S.M.; Shaik, M.; Kanuparthy, P.R. Copper Complexes of Pyridyl–Tetrazole Ligands with Pendant Amide and Hydrazide Arms: Synthesis, Characterization, DNA-Binding and Antioxidant Properties. *Transit. Met. Chem*. **2016**, *41*, 517-523. https://doi.org/10.1007/s11243-016-0047-2

[12] Slyvka, Yu.I.; Fedorchuk, A.A.; Pokhodylo, N.T.; Lis, T.; Kityk, I.V.; Mys'kiv, M.G. A Novel Copper (I) Sulfamate π-Complex Based on the 5-(Allylthio)-1-(3,5-dimethylphenyl)-1*H*-tetrazole Ligand: Alternating-current Electrochemical Crystallization, DFT Calculations, Structural and NLO Properties Studies. *Polyhedron* **2018**, *147*, 86-93. https://doi.org/10.1016/j.poly.2018.03.015

[13] Slyvka, Y.; Goreshnik, E.; Pokhodylo, N.; Pavlyuk, O.; Mys'kiv, M. Two Related Copper(I) π-Complexes Based on 2-Allyl-5-(2-pyridyl)-2H-tetrazole Ligand: Synthesis and Structure of $[Cu(2\text{-apyt})NO_3]$ and $[Cu(2\text{-apyt})(H_2O)](BF_4)$ Compounds. *Acta Chim. Slov*. **2016**, *63*, 399-405. https://doi.org/10.17344/acsi.2016.2486

[14] Slyvka, Y.; Goreshnik, E.; Veryasov, G.; Morozov, D.; Fedorchuk, A.A.; Pokhodylo, N.; Kityk, I.; Mys'kiv, M. The Novel Copper(I) π,σ-Complexes with 1-(Aryl)-5-(allylthio)-1*H*-tetrazoles: Synthesis, Structure Characterization, DFT-Calculation and Third-Order Nonlinear Optics. *J. Coord. Chem*. **2019**, *72*, 1049-1063. https://doi.org/10.1080/00958972.2019.1580699

[15] Pokhodylo, N.T.; Shyyka, O.Y.; Matiychuk, V.S.; Obushak, M.D. New Convenient Strategy for Annulation of Pyrimidines to Thiophenes or Furans via the One-pot Multistep Cascade Reaction of 1H-Tetrazoles with Aliphatic Amines. *ACS Comb. Sci*. **2015**, *17*, 399-403. https://doi.org/10.1021/co5001376

[16] Shyyka, O.; Pokhodylo, N.; Finiuk, N.; Matiychuk, V.; Stoika, R.; Obushak, M. Anticancer Activity Evaluation of New Thieno[2,3-d]pyrimidin-4(3H)-ones and Thieno[3,2-d]pyrimidin-4(3H)-one Derivatives. *Sci. Pharm.* **2018**, *86*, 28. https://doi.org/10.3390/scipharm86030028

[17] Pokhodylo, N.T.; Shyyka, O.Y.; Slyvka, Y.I.; Goreshnik, E.A.; Obushak, M.D. Solvent-Free Synthesis of Cytisine-Thienopyrimidinone Conjugates via Transannulation of 1H-tetrazoles: Crystal and Molecular Structure, Docking Studies and Screening for Anticancer Activity. *J. Mol. Struct*. **2021**, *1240*, 130487. https://doi.org/10.1016/j.molstruc.2021.130487

[18] Shyyka, O.Y.; Pokhodylo, N.T.; Palchykov, V.A.; Finiuk, N.S.; Stoika, R.S.; Obushak, M.D. Cage-Like Amines in the Green Protocol of Transannular Thieno[2,3-d]Pyrimidinone Formation as Promising Anticancer Agents. *Chem. Heterocycl. Compd.* **2020**, *56*, 793-799. https://doi.org/10.1007/s10593-020-02732-2

[19] Burnett, A. R.; Thomson, R. H. Naturally Occurring Quinones. Part X. The Quinonoid Constituents of *Tabebuia avellanedae* (Bignoniaceae). *J. Chem. Soc. C* **1967**, 2100-2104. https://doi.org/10.1039/j39670002100

[20] Ma, W.; Long, Y.-T. Quinone/Hydroquinone-Functionalized Biointerfaces for Biological Applications from the Macro- to Nano-Scale. *Chem. Soc. Rev*. **2014**, *43*, 30-41. https://doi.org/10.1039/c3cs60174a

[21] Zhang, L.; Zhang, G.; Xu, S.; Song, Y. Recent Advances of Quinones as a Privileged Structure in Drug Discovery. *Eur. J. Med. Chem*. **2021**, *223*, 113632. https://doi.org/10.1016/j.ejmech.2021.113632

[22] Calì, V.; Tringali, C. Polyhydroxy-*P*-Terphenyls and Related *P*-Terphenylquinones from Fungi: Overview and Biological Properties. *Stud. Nat. Prod. Chem*. **2003**, *29*, 263-307. https://doi.org/10.1016/s1572-5995(03)80009-1

[23] Deb, A.; Agasti, S.; Saboo, T.; Maiti, D. Generation of Arylated Quinones by Iron-Catalyzed Oxidative Arylation of Phenols:

Formal Synthesis of Phellodonin, Sarcodonin ε, Leucomelone and Betulinan A. *Adv. Synth. Catal*. **2014**, *356*, 705-710. https://doi.org/10.1002/adsc.201301084
[24] Fujiwara, Y.; Domingo, V.; Seiple, I.B.; Gianatassio, R.; Del Bel, M.; Baran, P.S. Practical C−H Functionalization of Quinones with Boronic Acids. *J. Am. Chem. Soc*. **2011**, *133*, 3292-3295. https://doi.org/10.1021/ja111152z
[25] Rondestvedt Jr, C.S. Arylation of Unsaturated Compounds by Diazonium Salts (The Meerwein Arylation Reaction). *Org. React*. **2011**. https://doi.org/10.1002/0471264180.or024.03
[26] Honraedt, A.; Le Callonnec, F.; Le Grognec, E.; Fernandez, V.; Felpin, F.-X. C–H Arylation of Benzoquinone in Water through Aniline Activation: Synergistic Effect of Graphite-Supported Copper Oxide Nanoparticles. *J. Org. Chem*. **2013**, *78*, 4604-4609. https://doi.org/10.1021/jo4004426
[27] Lamblin, M.; Naturale, G.; Dessolin, J.; Felpin, F.-X. Direct C-H Arylation of Quinones with Anilines. *Synlett* **2012**, *23*, 1621-1624. https://doi.org/10.1055/s-0031-1291163
[28] Itahara, T. Oxidative Coupling of Quinones and Aromatic Compounds by Palladium(II) Acetate. *J. Org. Chem*. **1985**, *50*, 5546-5550. https://doi.org/10.1021/jo00350a023
[29] Singh, P.K.; Rohtagi, B.K.; Khanna, R.N. Arylation of Quintones with Aryl Mercuryl Chloride Catalyzed by Lithium Palladium Chloride. *Synth. Commun*. **1992**, *22*, 987-993. https://doi.org/10.1080/00397919208019287
[30] Best, W.M.; Sims, C.G.; Winslade, M. Palladium-Catalysed Cross Coupling of Arylboronic Acids with 2-Chloro-1,4-naphthoquinones: the Synthesis of 2-Aryl- and 2,3-Bisaryl-1,4-naphthoquinones. *Aust. J. Chem*. **2001**, *54*, 401-403. https://doi.org/10.1071/CH01024
[31] Gan, X.; Jiang, W.; Wang, W.; Hu, L. An Approach to 3,6-Disubstituted 2,5-Dioxybenzoquinones via Two Sequential Suzuki Couplings. Three-Step Synthesis of Leucomelone. *Org. Lett*. **2009**, *11*, 589-592. https://doi.org/10.1021/ol802645f
[32] Wang, J.; Wang, S.; Wang, G.; Zhang, J.; Yu, X.-Q. Iron-Mediated Direct Arylation with Arylboronic Acids Through an Aryl Radical Transfer Pathway. *Chem. Commun*. **2012**, *48*, 11769-11771. https://doi.org/10.1039/C2CC35468C
[33] Komeyama, K.; Kashihara, T.; Takaki, K. $FeSO_4$-promoted Direct Arylation of Benzoquinones with $ArB(OH)_2$ or $ArBF_3K$. *Tetrahedron Lett*. **2013**, *54*, 1084-1086. https://doi.org/10.1016/j.tetlet.2012.12.031
[34] Singh, P.P.; Aithagani, S.K.; Yadav, M.; Singh, V.P.; Vishwakarma, R.A. Iron-catalyzed Cross-Coupling of Electron-Deficient Heterocycles and Quinone with Organoboron Species via Innate C–H Functionalization: Application in Total Synthesis of Pyrazine Alkaloid Botryllazine A. *J. Org. Chem*. **2013**, *78*, 2639-2648. https://doi.org/10.1021/jo302797r
[35] Deb, A.; Manna, S.; Maji, A.; Dutta, U.; Maiti, D. Iron-Catalyzed Direct C-H Arylation of Heterocycles and Quinones with Arylboronic Acids. Eur. *J. Org. Chem*. **2013**, *2013*, 5251-5256. https://doi.org/10.1002/ejoc.201300743
[36] Ashok, P.; Ilangovan, A. Transition Metal Mediated Selective C vs N Arylation of 2-Aminonaphthoquinone and its Application Toward the Synthesis of Benzocarbazoledione. *Tetrahedron Lett*. **2018**, *59*, 438-441. https://doi.org/10.1016/j.tetlet.2017.10.075
[37] Molina, M.T.; Navarro, C.; Moreno, A.; Csákÿ, A.G. Arylation of Benzo-Fused 1,4-Quinones by the Addition of Boronic Acids under Dicationic Pd(II)-Catalysis. *Org. Lett*. **2009**, *11*, 4938-4941. https://doi.org/10.1021/ol902084g
[38] Patil, P.; Nimonkar, A.; Akamanchi, K.G. Aryl-Free Radical-Mediated Oxidative Arylation of Naphthoquinones Using o-Iodoxybenzoic Acid and Phenylhydrazines and Its Application toward the Synthesis of Benzocarbazoledione. *J. Org. Chem*. **2014**, *79*, 2331-2336. https://doi.org/10.1021/jo500131h
[39] Moon, Y.; Jeong, Y.; Kook, D.; Hong, S. Rh(III)-catalyzed Direct C–H/C–H Cross-Coupling of Quinones with Arenes Assisted by a Directing Group: Identification of Carbazole Quinones as GSKβ Inhibitors. *Org. Biomol. Chem*. **2015**, *13*, 3918-3923. https://doi.org/10.1039/C4OB02624A
[40] Wang, D.; Ge, B.; Li, L.; Shan, J.; Ding, Y. Transition Metal-Free Direct C–H Functionalization of Quinones and Naphthoquinones with Diaryliodonium Salts: Synthesis of Aryl Naphthoquinones as β-Secretase Inhibitors. *J. Org. Chem*. **2014**, *79*, 8607-8613. https://doi.org/10.1021/jo501467v
[41] Wang, Y.; Zhu, S.; Zou, L.-H. Recent Advances in Direct Functionalization of Quinones. *Eur. J. Org. Chem*. **2019**, *2019*, 2179-2201. https://doi.org/10.1002/ejoc.201900028
[42] Gaponik, P.N.; Karavai, V.P.; Davshko, I.E.; Degtyarik, M.M.; Bogatikov, A.N. Synthesis and Properties of Phenylenebis-1H-tetrazoles. *Chem. Heterocycl. Compd*. **1990**, *26*, 1274-1278. https://doi.org/10.1007/BF00476984
[43] Herbst, R.M.; Roberts, C.W.; Givens, H.T.F.; Harvill, E.K. The Synthesis of Nitro- and Amino-Phenyltetrazoles. *J. Org. Chem*. **1952**, *17*, 262-271. https://doi.org/10.1021/jo01136a014
[44] Zuo, Z.; Chen, M.; Shao, X.; Qian, X.; Liu, X.; Zhou, X.; Xiang, J.; Deng, P.; Li, Y.; Jie, H. *et al.* Design and Biological Evaluation of Tetrahydropyridine Derivatives as Novel Human GPR119 Agonists. *Bioorg. Med. Chem. Lett*. **2020**, *30*, 126855. https://doi.org/10.1016/j.bmcl.2019.126855
[45] Shurukhin, Y.V.; Klyuev, N.A.; Grandberg, I.I.; Konchits, V.A. Thermal Reactions of 1-Aryl-5-methyltetrazoles. *Chem. Heterocycl. Compd*. **1984**, *20*, 1177-1182. https://doi.org/10.1007/BF00503616
[46] Scott, F.; Britten, F.; Reilly, J. Notes - Polynitrogen Systems from the Hydrazinocarbonic Acids. Part VII. Some Reactions of 1-Phenyl-5-methylmercaptotetrazole. *J. Org. Chem*. **1956**, *21*, 1191-1193. https://doi.org/10.1021/jo01116a615
[47] Neamati, N.; Petasis, N.; Yamada, R. Propynoic acid carbamoyl methyl-almides and pharmaceutical compositions and methods based thereon. WO2012129452A2, 2012.
[48] Allen, C.F.H.; Bell, A. 2,3-Dimethyl-1,3-butadiene. *Organic Synth*. **1942**, *22*, 39. https://doi.org/10.15227/orgsyn.022.0039
[49] Pokhodylo, N.T.; Matiychuk, V.S.; Obushak, M.D. Synthesis of Isothiocoumarin Derivatives. *Chem. Heterocycl. Compd*. **2010**, *46*, 140-145. https://doi.org/10.1007/s10593-010-0484-3
[50] Pokhodylo, N.; Finiuk, N.; Klyuchivska, O.; Stoika, R.; Matiychuk, V.; Obushak, M. Bioisosteric Replacement of 1*H*-1,2,3-Triazole with 1*H*-Tetrazole Ring Enhances Anti-Leukemic Activity of (5-Benzylthiazol-2-yl)benzamides. *Eur. J. Med. Chem*. **2023**, *250*, 115126. https://doi.org/10.1016/j.ejmech.2023.115126
[51] Marini-Bettòlo, G.B.; Rossi, C. Action of Diazo Compounds on Quinones. II. Reaction between Diazocompounds and Naphthoquinones; Preparation of Phenylnaphthalenes. *Gazz. chim. ital*. **1942**, *72*, 208-215. (*Chem. Abstr*. **1943**, *37*, 4386–4387).
[52] Wurm, G.; Gurka, H.-J. Phenyl-1,4-naphthochinonderivate mit Hydroxylierungsmustern von Bioflavonoiden. *Pharmazie* **1997**, *52*, 739-743.
[53] Fiedler, H. Darstellung von Hydroxy-2-oxo- bzw.−2-thion-1.3-benzoxathiolen. *Chemische Berichte* **1962**, *95*, 1771-1785. https://doi.org/10.1002/cber.19620950731
[54] Klemm, K.; Geiger, B. Addition von Dithiocarbonsäure-Derivaten an *p*-Chinone. *Justus Liebigs Ann. Chem*. **1969**, *726*, 103-109. https://doi.org/10.1002/jlac.19697260116

[55] Harris, R.L.N.; Oswald, L.T. The Addition of Dithiocarbamic Acids to *p*-Benzoquinone. *Aust. J. Chem*. **1974**, *27*, 1309-1316. https://doi.org/10.1071/CH9741309
[56] Hartmann, H.; Mohn, F. Kationische Farbstoffe und Vorstufen. XVI. Styrylcyanine der 1,3-Oxathiolium-Reihe. *J. Prakt. Chem*. **1972**, *314*, 419-427. https://doi.org/10.1002/prac.19723140305
[57] Fabian, K.; Hartmann, H. Kationische Farbstoffe und Vorstufen. VI. Versuche zur Cyclisierung von S-Ketomethylen-sowie o-Hydroxyphenyl-thiolester-Derivaten zu 1,3-Oxathiolium- bzw. 1,3-Dithiolium-Salzen. *J. Prakt. Chem*.**1971**, *313*, 722-729. https://doi.org/10.1002/prac.19713130420
[58] Shadyro, O.I.; Timoshchuk, V.A.; Polozov, G.I.; Povalishev, V.N.; Andreeva, O.T.; Zhelobkovich, V.E. Synthesis and Antiviral Activity of Spatially-Screened Phenols: 1,3-Benzoxathiolan-2-one Derivatives. *Pharm. Chem. J*. **1999**, *33*, 366-369. https://doi.org/10.1007/BF02508708
[59] Obushak, N.D.; Matiichuk, V.S.; Martyak, R.L. Synthesis of Heterocycles Based on Products of Anion Arylation of Unsaturated Compounds. 5. Reaction of 2-Aryl-1,4-benzoquinones with Thiourea. *Chem. Heterocycl. Compd.* **2001**, *37*, 909-915. https://doi.org/10.1023/A:1012420128922
[60] Vellasco, W.T.; Gomes, C.R.B.; Vasconcelos, T.R.A. Chemistry and Biological Activities of 1,3-Benzoxathiol-2-ones. *Mini-Rev. Org. Chem.* **2011**, *8*, 103-109. https://doi.org/10.2174/157019311793979882
[61] Musyanovych, R. Reactions of Sulfenyl Chlorides of Substituted 1,4-Naphthoquinone. *Chem. Chem. Technol*. **2011**, *5*, 367-372. https://doi.org/10.23939/chcht05.04.367
[62] Shakh, Y.; Slesarchuk, M.; Syngaevsky, V.; Bolibrukh, K.; Karkhut, A.; Polovkovych, S.; Shevchuk, L.; Novikov, V. Interaction of 5-Substituted 1,4-Naphthoquinones and Amino Thiotriazoles: Reaction Ways and Regioselectivity. *Chem. Chem. Technol*. **2018**, *12*, 167-175. https://doi.org/10.23939/chcht12.02.167
[63] Thurman, D.E.; Stollings, H.W. Synthesis of Some 5-Hydroxynaphth[2,1-d]-1,3-oxathiol-2-ones. *J. Heterocycl. Chem*. **1973**, *10*, 117-119. https://doi.org/10.1002/jhet.5570100130

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(1*H*-ТЕТРАЗОЛ-1-ІЛ)АРЕНДІАЗОНІЄВІ СОЛІ ЯК ЗРУЧНІ РЕАГЕНТИ ДЛЯ АРИЛУВАННЯ ХІНОНІВ: СИНТЕЗ 1,3-БЕНЗОКСАТІОЛ-2-ОНІВ ТА НАФТО[2,1-*d*][1,3]ОКСАТІОЛ-2-ОНІВ, ЩО МІСТЯТЬ (1*H*-ТЕТРАЗОЛ-1-ІЛ)ФЕНІЛОВИЙ ФРАГМЕНТ

Анотація. *Розроблено зручний двостадійний метод синтезу нових 1,3-бензоксатіол-2-онів і нафто[2,1-d][1,3]оксатіол-2-онів, що містять (1Н-тетразол-1-іл)феніловий фрагмент. Як ключовий етап синтезу вивчено арилування хінонів (1,4-бензохінонів, 1,4-нафтохінонів) солями (1Н-тетразол-1-іл)арендіазонію та розроблено ефективні методики для отримання різноманітних заміщених ((1Н-тетразол-1-іл)феніл) бензо/нафто-1,4-хінонів з хорошими або високими виходами. Продемонстровано альтернативний синтез ((1Н-тетразол-1-іл)феніл)нафто-1,4-хінонів за допомогою реакції Дільса–Альдера тетразолілфеніл-1,4-бензохінонів. Отримані бензо/нафто-1,4-хінони легко реагують з тіосечовиною за кімнатної температури в присутності сильних мінеральних кислот з утворенням проміжних ізотіуронієвих солей, які циклізуються під час нагрівання, утворюючи 1,3-оксатіол-2-они з високим виходом.*

Ключові слова: *тетразол, хінон, оксатіолон, арилування Меервейна, циклізація.*