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Microwave-Assisted Synthesis of 2,5-Diarylthiazolo[5,4-*d*]thiazoles from Benzaldehydes and Dithiooxamide

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Abstract—One-pot condensation of dithiooxamide with aromatic aldehydes and subsequent oxidation of intermediate 2,5-dihydro[1,3]thiazolo[5,4-*d*][1,3]thiazoles with selenium dioxide afforded 2,6-diaryl[1,3]thiazolo[5,4-*d*][1,3]thiazoles which were characterized by ^{1}H and ^{13}C NMR, IR, and X-ray diffraction data.

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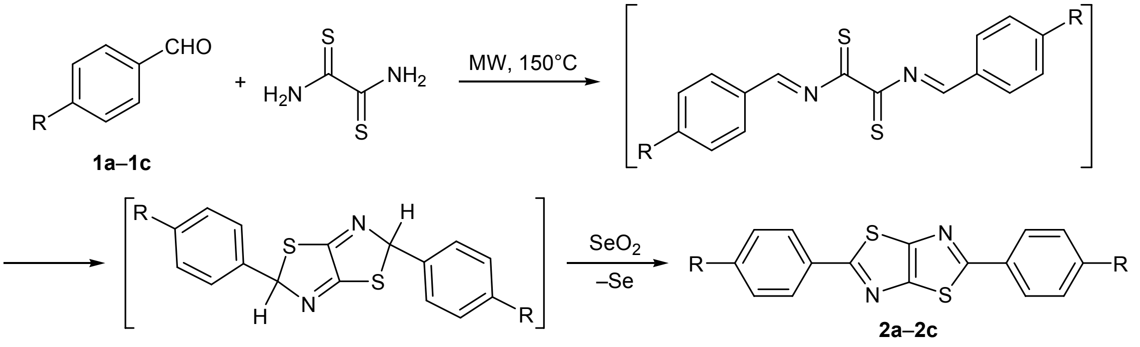
Thiazolo[5,4-*d*]thiazoles constitute an important class of bicyclic aromatic structures with two fused thiazole rings, which are characterized by a rigid planar skeleton and *p*-electron-deficient system capable of being involved in efficient intermolecular π–π interactions; therefore, these compounds possess attractive properties from the viewpoint of their use in electronics [1]. Fused thiazoles exhibit biological activity and are used in medicine [2–4]. They also found applications as components of photographic, semiconducting [2, 5–11], and optoelectronic materials [12, 13], ligands for coordination chemistry [10, 14], and liquid crystals [15]. Although the customer performance of materials based on thiazolothiazoles have been well documented, their synthetic chemistry has been studied to a lesser extent, and problems related to their synthesis remain topical.

The main procedure for the synthesis of thiazolo[5,4-*d*]thiazole derivatives was proposed for the first time in [16]; it was based on the condensation of dithiooxamide with excess aromatic aldehyde. The reactions are carried out in various solvents such as *o*-dichlorobenzene [17], phenol [18, 19], nitromethane [10], and DMF [10, 20] or under solvent-free conditions [4, 6, 16]. However, harsh reaction conditions (200°C) and long reaction time (24 h) favor tar formation and side processes, so that the yield of thiazolo[5,4-*d*]-thiazoles and their purity considerably decrease. The procedure requires 10–12 equiv of initial aldehyde, which hampers isolation and purification of the products. Alternative synthetic approaches to diarylthiazolo[5,4-*d*]thiazoles, e.g., treatment of 2,5-bis(acetylamino)thiazole with sodium thiocyanate in the presence of bromine and subsequent thermally induced cyclization [21] or acid-catalyzed reaction of 5-amino-2-aryl-4-sulfanylthiazole with an ortho ester [22], as well as other methods [1], have received only limited application.

Dessi et al. [23] have recently proposed a procedure for the synthesis of thiazolo[5,4-*d*]thiazoles via condensation of various aldehydes (aliphatic, aromatic, and some heterocyclic) with dithiooxamide at a ratio of 4 : 1 or 2 : 1 [23]. The first step leading to intermediate non-aromatic 2,5-dihydrothiazolo[5,4-*d*]thiazoles was activated by microwave irradiation. In the second step, the intermediate products were oxidized with chloranil or 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) on heating in nitrobenzene–THF. However, the necessity of two preparative steps and the use of expensive and toxic oxidants hampered the isolation and purification of the target products and increased the cost of the process.

In the present work we tried to carry out the synthesis of diarylthiazolo[5,4-*d*]thiazoles as a one-pot process under microwave irradiation at both steps (condensation of dithiooxamide with aromatic aldehydes and oxidative aromatization of intermediate 2,5-dihydrothiazolo[5,4-*d*]thiazoles). As oxidant in the

Scheme 1.

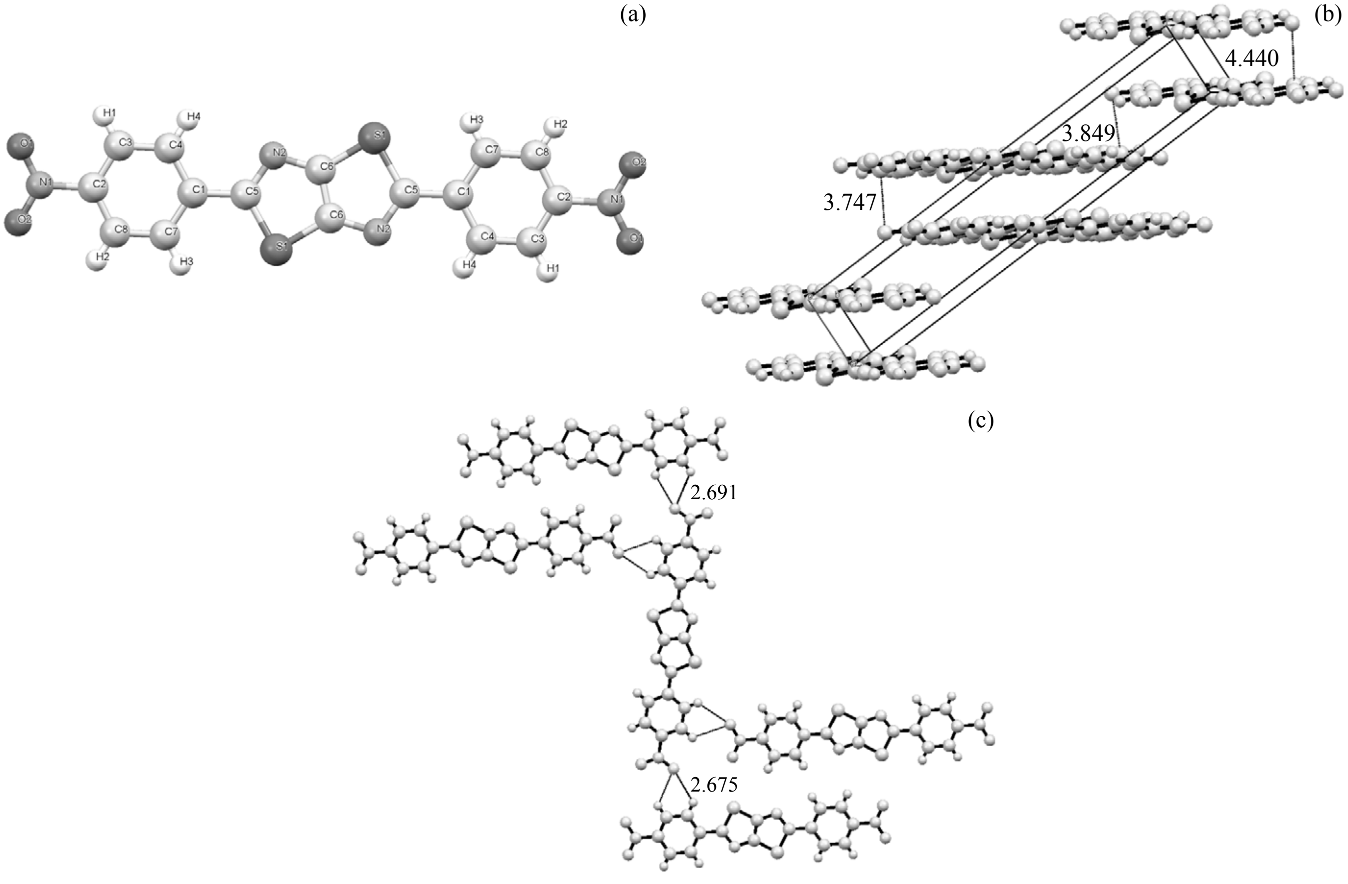


R = H (**a**), Cl (**b**), NO_2 (**c**).

second step we used selenium dioxide which, unlike chloranil and DDQ, is nontoxic and is converted into elemental selenium that can be readily separated from the reaction mixture.

The condensation of aromatic aldehydes **1a**–**1c** with dithiooxamide (150°C, 30 min) and subsequent oxidation with selenium dioxide (15 min) were carried out in dimethylformamide at a reactant ratio of 2 : 1 : 2 under microwave irradiation in the same reaction vessel (Scheme 1). After separation of elemental selenium, thiazolo[5,4-*d*]thiazoles **2a**–**2c** were isolated in a good yield. Unlike the procedure described in [23], the products required no additional purification by column chromatography.

Compounds **2a**–**2c** are high-melting colored crystalline substances sparingly soluble in organic sol-



(a) Structure of the molecule of 2,5-bis(4-nitrophenyl)[1,3]thiazolo[5,4-*d*][1,3]thiazole (**2c**), (b) layered crystal structure of compound **2c**, and (c) unit cell with short N–O···HC contacts according to the X-ray diffraction data.

Bond lengths and bond and torsion angles in the molecule of 2,5-bis(4-nitrophenyl)[1,3]thiazolo[5,4-*d*][1,3]thiazole (**2c**)

Bond	*d*, Å	Bond angle	ω, deg	Torsion angle	φ, deg
S^1–C^6	1.723(3)	$C^6S^1C^5$	88.16(13)	$O^1N^1C^2C^3$	–5.0(4)
O^1–N^1	1.202(4)	$C^4C^1C^5$	119.3(2)	$O^1N^1C^2C^8$	175.9(3)
C^1–C^4	1.397(4)	$C^5N^2C^6$	108.1(2)	$C^8C^2C^3C^4$	1.1(4)
C^1–C^5	1.467(4)	$O^1N^1C^2$	118.4(3)	$C^2C^3C^4C^1$	–1.2(4)
N^2–C^6	1.359(4)	$C^3C^2C^8$	122.5(3)	$C^5C^1C^4C^3$	–179.8(2)
C^2–C^3	1.366(4)	$C^8C^2N^1$	118.2(3)	$C^6N^2C^5S^1$	0.2(3)
C^3–C^4	1.383(4)	$C^3C^4C^1$	120.3(3)	$C^7C^1C^5N^2$	172.2(3)
C^6–$C^{6'}$	1.364(5)	$N^2C^5S^1$	116.2(2)	$C^7C^1C^5S^1$	–8.1(3)
S^1–C^5	1.750(3)	$N^2C^6C^{6'}$	118.4(3)	$C^6S^1C^5C^1$	179.7(2)
O^2–N^1	1.217(4)	$C^4C^1C^7$	119.0(2)	$C^5S^1C^6C^{6'}$	0.7(3)
C^1–C^7	1.398(4)	$C^7C^1C^5$	121.7(2)	$C^5C^1C^7C^8$	–180.0(2)
N^2–C^5	1.315(3)	$O^1N^1O^2$	123.9(3)	$C^3C^2C^8C^7$	–0.9(4)
N^1–C^2	1.476(3)	$O^2N^1C^2$	117.7(3)	$O^2N^1C^2C^3$	173.9(3)
C^2–C^8	1.379(4)	$C^3C^2N^1$	119.3(3)	$O^2N^1C^2C^8$	–5.1(4)
$C^{6'}$–$N^{2'}$	1.359(4)	$C^2C^3C^4$	118.9(3)	$N^1C^2C^3C^4$	–177.9(2)
C^7–C^8	1.378(4)	$N^2C^6S^1$	132.4(2)	$C^7C^1C^4C^3$	1.0(4)

vents. Their structure was confirmed by elemental analyses and ^{1}H and ^{13}C NMR and IR spectra. The IR spectra of **2a**–**2c** lacked carbonyl absorption bands typical of initial aldehydes **1a**–**1c**. The ^{1}H NMR spectra of **2a**–**2c** contained signals from aromatic protons but no signal from aldehyde proton. Carbons atoms of the thiazolo[5,4-*d*]thiazole fragment of **2a**–**2c** resonated in the ^{13}C NMR spectra at δ_C 150.9–151.41 (C^1, C^8) and 167.8–169.2 ppm (C^2, C^6).

The structure of **2c** was unambiguously determined by X-ray analysis (see figure and table). Molecule **2c** is planar (see figure, a), and the crystal structure of **2c** is layered with an interlayer distance of 3.74–4.44 Å (b). A unit cell comprises five molecules. Short intermolecular contacts are observed between hydrogen atoms of the benzene rings and one oxygen atom of the NO_2 group (2.68–2.69 Å; see figure, c). The principal bond lengths and bond and torsion angles in molecule **2c** are given in table.

In summary, we have developed a simple and efficient one-pot synthesis of thiazolo[5,4-*d*]thiazoles by reaction of dithiooxamide with aromatic aldehydes and subsequent oxidation of intermediate dihydrothiazolo[5,4-*d*]thiazoles. Selenium dioxide was used for the first time as oxidant in the second step. Both reaction steps are considerably accelerated by microwave irradiation. The procedure requires no excess aldehyde and is much less laborious than known methods for the preparation of thiazolo[5,4-*d*]thiazoles.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer at 400.61 and 100.13 MHz, respectively, using tetramethylsilane as internal standard. The IR spectra were recorded in KBr on a Bruker Vertex 70 spectrometer. The melting points were measured on a PolyTherm A hot stage microscope. The microwave-assisted reactions were carried out in an Anton Paar Monowave microwave reactor in an inert atmosphere at a constant temperature (control probe) and variable power (up to 400 W).

2,5-Diphenyl[1,3]thiazolo[5,4-*d*][1,3]thiazole (2a). A microwave reactor vial equipped with a magnetic stirrer was charged with 0.212 g (2.0 mmol) of aldehyde **1a**, 0.120 g (1.0 mmol) of dithiooxamide, and 4 mL of DMF. The mixture was heated for 30 min at 150°C under microwave irradiation and cooled to 55°C, 0.228 g (2.0 mmol) of selenium dioxide was added, and the mixture was stirred for 15 min at 200°C and cooled to room temperature. The precipitate was filtered off and recrystallized from THF. Yield 0.192 g (65%), fine light yellow lustrous crystals, mp 209–

212°C; published data: mp 209–210°C [16], 196–198°C [24]. IR spectrum, ν, cm^{-1}: 1499, 1456, 1428, 1319, 1221, 1032, 1007, 911, 887, 755, 684, 614. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.46–7.53 m (3H, *m*-H, *p*-H), 8.01–8.03 m (2H, *o*-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 126.49 (C^m), 129.21 (C^o), 130.77 (C^p), 134.03 (C^i), 150.98 (C^7, C^8), 169.26 (C^2, C^6). Found, %: C 64.90; H 3.38; N 9.32; S 21.49. $C_{16}H_{10}N_2S_2$. Calculated, %: C 65.28; H 3.42; N 9.52; S 21.78.

2,5-Bis(4-chlorophenyl)[1,3]thiazolo[5,4-*d*][1,3]-thiazole (2b) was synthesized in a similar way from 0.281 g (2.0 mmol) of 4-chlorobenzaldehyde (**1b**). Recrystallization from DMF gave fine light-yellow powder with metallic luster. Yield 0.193 g (53%), mp 291–293°C; published data [16]: mp 311–312°C. IR spectrum, ν, cm^{-1}: 1590, 1496, 1439, 1398, 1086, 1006, 841, 810, 659, 517, 499. ^{1}H NMR spectrum (C_6D_6), δ, ppm: 6.97–6.99 m (2H, *m*-H), 7.58–7.60 m (2H, *o*-H). ^{13}C NMR spectrum (C_6D_6), δ_C, ppm: 127.55 (C^m), 129.25 (C^o), 132.51 (C^i), 136.48 (C^p), 151.41 (C^7, C^8), 167.83 (C^2, C^6). Found, %: C 52.65; H 2.13; Cl 18.93; N 7.58; S 17.47. $C_{16}H_8Cl_2N_2S_2$. Calculated, %: C 52.90; H 2.22; Cl 19.52; N 7.71; S 17.65.

2,5-Bis(4-nitrophenyl)[1,3]thiazolo[5,4-*d*][1,3]-thiazole (2c) was synthesized in a similar way from 0.302 g (2.0 mmol) of 4-nitrobenzaldehyde (**1c**). The product was insoluble in disposable solvents and was purified by vacuum sublimation at 210–215°C. Yield 0.217 g (56%), bright red crystals, mp 398–402°C; published data [16]: mp 400–405°C. IR spectrum, ν, cm^{-1}: 1593, 1520, 1343, 1107, 849, 752, 687. Found, %: C 49.64; H 1.97; N 14.62; S 17.02. $C_{16}H_8N_4O_4S_2$. Calculated, %: C 49.99; H 2.10; N 14.58; S 16.68.

X-Ray analysis of compound 2c. The X-ray diffraction data were acquired at 296 K on a Bruker D8 Venture diffractometer (Photon 100 detector; MoK_α radiation, $\lambda = 0.71073$ Å; θ/2θ scanning in the range from 2.37 to 30.06°) from a 0.5 × 0.2 × 0.2-mm deep bronze singe crystal of **2c**. A correction for absorption by the crystal was applied by the multiscan technique. Monoclinic crystal system, space group $P2_1/c$; $C_8H_4N_2O_2S$; unit cell parameters: $a = 3.8459(4)$, $b = 9.3341(9)$, $c = 21.6500(18)$ Å; $\beta = 93.661(3)$°; $d_{calc} = 1.646$ g/cm^3; $\mu = 0.377$ mm^{-1}; $V = 775.61(13)$ Å^3; $Z = 4$. The structure was solved by the direct method using Bruker SAINT and SHELXS-13 [24] and was refined by the full-matrix least-squares procedure in anisotropic approximation for non-hydrogen atoms (isotropic approximation for hydrogen atoms); weight scheme $w = 1/[\sigma^2(F_0^2) + (0.0482P)^2 + 16.3125P]$, where $P = (F_0^2 + 2Fc^2)/3$. The positions of hydrogen atoms were determined from the difference electron density maps. The final divergence factor was $R = 0.0604$ [for 2744 reflections with $I > 2\sigma(I)$ of 9301 reflections]. The complete set of crystallographic data for compound **2c** was deposited as CIF file to the Cambridge Crystallographic Data Centre (entry no. CCDC 1 001 323) and is available at *www.ccdc.cam.ac.uk/data_request/cif.*

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