Synthesis of substituted 2λ4δ2-[1,2,3]thiadiazolo[3,4-c]benzimidazoles and 2λ4δ2-[1,2,3,5]thiatriazolo[3,4-c]benzimidazoles

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Abstract

Electrophilic substitution reactions in [1,2,3]thiadiazolo[3,4-c]benzimidazoles and [1,2,3,5]thiatriazolo[3,4-c]benzimidazoles and the cyclisation reactions of 5(6)-substituted N-aminobenzimidazol-2-ylmethanols were investigated. Bromo-, dibromo-, nitro-, dinitro-, and methoxy-substituted [1,2,3]thiadiazolo[3,4-c]benzimidazole and [1,2,3,5]thiatriazolo[3,4-c]benzimidazole derivatives were synthesized.

Keywords: [1,2,3]Thiadiazolo[3,4-c]benzimidazole, [1,2,3,5]thiatriazolo[3,4-c]benzimidazole, electrophilic substitution, cyclisation

Introduction

1,2,3-Thiadiazoles are of substantial interest in medicinal chemistry for treatment of thromboses,1 as antibacterials,2-4 platelet-activating factors,5 in agricultural chemistry as plant growth activators, and inducers of systemic acquired resistance (SAR) in plants.6,7 1,2,3-Thiadiazoles are also valuable as synthetic intermediates for substituted acetylenes,8-10 thioamides,11 5-aryloxy(thio)-1,2,3-thiadiazoles12 and other heterocyclic systems.13 We have reported previously the synthesis of the first representatives of a fused heterocyclic system containing the 1,2,3-thiadiazole moiety – [1,2,3]thiadiazolo[3,4-c]benzimidazole.14 The aim of this study is to investigate the synthesis and reactivity of 3-chloro[1,2,3]thiadiazolo[3,4-c]benzimidazole (1) and its aza-analog, [1,2,3,5]thiatriazolo[3,4-c]benzimidazole15 (2), with substituents on the benzene ring.
Results and Discussion

It is known that compound 1 is unstable in basic medium and nucleophilic substitution often leads to decomposition of the thiadiazole ring. To determine the properties of compounds 1 and 2, and to investigate possibilities for the introduction of substituents into the benzene ring, electrophilic substitution reactions of 3-chloro[1,2,3]thiadiazolo[3,4-c]benzimidazole (1) and its [1,2,3,5]thiatriazole analog (2) have been studied.

We have found that nitration of compounds 1 and 2 (Scheme 1) at -4 °C in a mixture of fuming nitric acid and sulfuric acid afforded mononitro derivatives 3 and 4 in 42 and 48% yields, respectively (Method A).

Scheme 1

However, 3-chloro-7-nitro[1,2,3]thiadiazolo[3,4-c]benzimidazole (3) was obtained in better yield (83%) when the reaction was performed at 70-80 °C in a mixture of fuming nitric acid and trifluoroacetic acid (Method B). The nitration of 1 and 2 performed in a mixture of fuming nitric acid and sulfuric acid at 60-70 °C gave the 5,7-dinitro derivatives 5 and 6 as the sole products of the reaction in 71 and 67% yields, respectively.

Bromination reactions of compounds 1 and 2 were studied under different conditions (Table 1). The bromination reaction performed with bromine in acetic acid or in dilute sulfuric acid at 60 °C gave similar results: in both reactions, the 7-monobromo derivative 7 was formed in ca. 75% yield. The use of bromine in dioxane at room temperature afforded 7-bromo-3-chloro[1,2,3]thiadiazolo[3,4-c]benzimidazole (7) in 86% yield. 1,2,3,5-Thiatriazole 2 under the same bromination conditions gave the analogous 7-bromo derivative 8 in 69% yield. Reaction of compound 1 with bromine without solvent at room temperature led to a mixture of the monobromo derivative 7 and the 5,7-dibromo compound 9 in a ratio of 2:1 (according to the ¹H NMR spectra). All attempts to separate 7 from 9 using fractional crystallization or column
chromatography failed. The 5,7-dibromo derivative 9 was formed as the sole reaction product when compound 1 was refluxed in an excess of bromine for 16 h. Thus the method of choice for the synthesis of the monobromo derivatives appears to be the reaction of compounds 1 and 2 with bromine in dioxane at room temperature.

Table 1. Data of the bromination reactions of 3-chloro[1,2,3]thiadiazolo[3,4-c]benzimidazole (1) and [1,2,3,5]thiatriazolo[3,4-c]benzimidazole (2)

<table>
<thead>
<tr>
<th>Initial compd.</th>
<th>Method (bromination conditions)</th>
<th>Reaction temperature (°C)</th>
<th>Reaction time (h)</th>
<th>Product yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Method A (Br₂/AcOH)</td>
<td>60</td>
<td>6</td>
<td>7 (72)</td>
</tr>
<tr>
<td>1</td>
<td>Method B (Br₂/H₂SO₄, H₂O)</td>
<td>60</td>
<td>4</td>
<td>7 (75)</td>
</tr>
<tr>
<td>1</td>
<td>Method C (Br₂/dioxane)</td>
<td>rt</td>
<td>4</td>
<td>7 (86)</td>
</tr>
<tr>
<td>1</td>
<td>Method D (Br₂)</td>
<td>rt</td>
<td>10</td>
<td>7 and 9; 2/1</td>
</tr>
<tr>
<td>1</td>
<td>Method D (Br₂)</td>
<td>reflux</td>
<td>16</td>
<td>9 (40)</td>
</tr>
<tr>
<td>2</td>
<td>Method C (Br₂/dioxane)</td>
<td>rt</td>
<td>16</td>
<td>8 (69)</td>
</tr>
</tbody>
</table>

It should be noted that under mild conditions of nitration and bromination the electrophilic substitution took place only at position 7 of compounds 1 and 2. The formation of other isomers was not observed. Compounds 1 and 2 did not undergo Friedel-Crafts acetylation because of the formation of practically insoluble complexes with aluminium chloride or tin tetrachloride.

It was also necessary to find synthetic methods for the preparation of [1,2,3]thiadiazolo[3,4-c]benzimidazoles and [1,2,3,5]thiatriazolo[3,4-c]benzimidazoles carrying substituents at other positions of the benzene ring. For this purpose, [5(6)-nitrobenzimidazol-2-yl]methanol (10), 5(6)-nitrobenzimidazol-2-ylamine (11), [5(6)-bromobenzimidazol-2-yl]methanol (12), and [5(6)-methoxybenzimidazol-2-yl]methanol (13) were used as starting materials (Scheme 2). Amination of compounds 10-13 with hydroxylamine-O-sulfonic acid at 40-50 °C afforded mixtures of the corresponding 1H-benzimidazolamines 14-21. The substituent in the benzene ring had no influence on the site of N-amination. According to the ¹H NMR spectra the ratio of isomers 14 and 18, 15 and 19, 16 and 20, 17 and 21 was always close to 1:1. The mixtures of 1-amino derivatives (14 and 18, 15 and 19, 16 and 20, 17 and 21) appeared to be inseparable, either by column chromatography or fractional crystallization. Therefore, expecting that the cyclic products will have more distinct difference in physical properties, the pairs of isomers 14-21 were used in the reaction with thionyl chloride without prior separation. Thus, the 1-amino derivatives 14 and 18 reacted with thionyl chloride to give a 1:1 mixture of 3-chloro-7-nitro[1,2,3]thiadiazolo[3,4-c]benzimidazole (3) and 3-chloro-6-nitro[1,2,3]thiadiazolo[3,4-c]benzimidazole (23), which was fractionated by chromatography. Similarly, compounds 15 and 19 reacted with thionyl chloride to give a mixture of 7-nitro- and 6-nitro-[1,2,3,5]thiatriazolo[3,4-c]benzimidazoles (4 and 24), but these were inseparable by column chromatography or fractional crystallisation.
The bromo derivatives 16 and 20 reacted with thionyl chloride, giving a mixture of 7-bromo-3-chloro- and 6-bromo-3-chloro[1,2,3]thiadiazolo[3,4-c]benzimidazoles (7 and 25) which were separated chromatographically. Analytical data of compounds 7 and 25 were in agreement with those in ref. 18. The yield of compound 7 was significantly improved (86 vs 25% in ref. 18) by direct bromination of thiadiazole 1, but we were unable to obtain a better yield of compound 25.

The methoxy derivatives 17 and 21 gave the corresponding 3-chloro-7-methoxy- and 3-chloro-6-methoxy[1,2,3]thiadiazolo[3,4-c]benzimidazoles (22 and 26) and, in an unexpected reaction, the product of benzene ring chlorination – 3,8-dichloro-7-methoxy[1,2,3]thiadiazolo-[3,4-c]benzimidazole 27. The usual yields of compounds 22, 26, and 27 were low because of their significant instability under the reaction conditions and the slow reaction of compounds 17 and 21 with thionyl chloride.

Scheme 2

**Experimental Section**

**General.** Melting points were determined in open capillaries. IR spectra were recorded in KBr on a Perkin-Elmer spectrophotometer model FT-IR Spectrum BX II. NMR spectra were recorded on Varian Unity Inova (300 MHz for $^1$H NMR and 75 MHz for $^{13}$C NMR). HRMS spectra were obtained on a mass spectrometer Dual-ESI Q-TOF 6520 (Agilent Technologies). The purity of compounds was monitored by TLC using silica gel 60 F$_{254}$ aluminium plates (Merck).
3-Chloro-7-nitro-2i4δ2-[1,2,3]thiadiazolo[3,4-c]benzimidazole (3) and 7-nitro-2i4δ2-[1,2,3,5]thiatriazolo[3,4-c]benzimidazole (4)

**Method A.** A mixture of conc. H2SO4 (0.9 g, 9.2 mmol) and 100% HNO3 (0.4 g, 6.3 mmol) was cooled to −4 °C. Compound 1 (0.02 g, 0.095 mmol) or compound 2 (0.025 g, 0.14 mmol) was added and the reaction mixture was kept at −4 °C for 0.5 h, then poured onto ice and extracted (EtOAc). The organic layer was washed with H2O and evaporated to dryness under reduced pressure. The obtained solid was crystallized to give compound 3 as fine yellow orange crystals (0.01 g, 42%), mp 207-208 °C (EtOAc) or compound 4 as fine red brown crystals (0.015 g, 48%), mp 246-247 °C (EtOAc).

**Method B.** Compound 1, (0.1 g, 0.47 mmol) was added to a mixture of CF3CO2H (3 mL) and 100% HNO3 (0.46 g, 7.3 mmol) and stirred at 70-80 °C for 8 h. CF3CO2H was evaporated under reduced pressure. H2O (4 mL) was added to the residue. The obtained solid was filtered off and crystallized to give compound 3 as fine yellow orange crystals (0.1 g, 83%), mp 207-208 °C (EtOAc).

**Compound 3.** 1H NMR (DMSO-d6): δ 7.96 (d, 1H, J = 9 Hz, 5-H), 8.42 (dd, 1H, J = 2 and 9 Hz, 6-H), 9.13 (d, 1H, J = 2 Hz, 8-H). 13C NMR (DMSO-d6): 106.8, 121.1, 121.9, 136.2, 140.2, 141.7, 155.7, 158.4. IR (υ, cm−1): 1521, 1350 (NO2). Anal. Calcd. for C8H7ClN4O2S (254.654): C, 37.91; H, 1.13; N, 22.26%. HRMS: Calcd for C8H7ClN4O2S: 254.9744. Found: 254.9736.

**Compound 4.** 1H NMR (DMSO-d6): δ 8.03 (d, 1H, J = 9 Hz, 8-H), 8.47 (dd, 1H, J = 2 and 9 Hz, 7-H), 9.23 (d, 1H, J = 2 Hz, 5-H). 13C NMR (DMSO-d6): δ 111.2, 120.4, 123.0, 123.8, 139.9, 158.2, 165.8. IR (υ, cm−1): 1542, 1347 (NO2). Anal. Calcd. for C7H3N3O2S (221.197): C, 38.01; H, 1.37; N, 31.66. Found: C, 38.36; H, 1.4; N, 31.86%. HRMS: Calcd for C7H3N3O2S: 222.0086. Found: 222.0088.

3-Chloro-5,7-dinitro-2i4δ2-[1,2,3]thiadiazolo[3,4-c]benzimidazole (5) and 5,7-dinitro-2i4δ2-[1,2,3,5]thiatriazolo[3,4-c]benzimidazole (6)

Compound 1 (0.12 g, 0.57 mmol) or compound 2 (0.12 g, 0.68 mmol) was dissolved in a mixture of conc. H2SO4 (4.5 g) and 100% HNO3 (2.0 g) and stirred at 60-70 °C for 6 h, then cooled to rt and poured onto ice. The obtained precipitate was filtered off and crystallized to give the nitro-compounds 5 or 6.

**Compound 5.** Fine yellow crystals (0.12 g, 71%), mp 245-246 °C (DMF). 1H NMR (DMSO-d6): δ 9.16 (d, J = 2 Hz, 6-H), 9.52 (d, J = 2 Hz 8-H). 13C NMR (DMSO-d6): 109.5, 112.8, 139.4, 140.2, 145.1, 146.6, 153.2, 159.4. IR (υ, cm−1): 1529, 1318 (NO2). Anal. Calcd. for C8H3ClN5O3S (299.651): C, 32.07; H, 0.67; N, 23.37. Found: C, 32.27; H, 0.57; N, 23.26%. HRMS: Calcd for C8H3ClN5O3S: 299.9594. Found: 299.9589.

**Compound 6.** Fine red brown crystals (0.12 g, 67%) mp 254-226 °C (DMF). 1H NMR (DMSO-d6): δ 9.19 (d, 1H, J = 2.4 Hz, H-7), 9.66 (d, 1H, J = 2.4 Hz, H-5). 13C NMR (DMSO-d6): 108.3, 112.4, 137.7, 138.6, 139.6, 146.9, 149.5. IR (υ, cm−1): 1540, 1329 (NO2). Anal. Calcd. for
C₂H₂N₆O₄S: C, 31.59; H, 0.76; N, 31.57. Found: C, 31.36; H, 0.8; N, 31.46% HRMS: Calcd for C₂H₃N₆O₄S: 266.9937. Found: 266.9938.

7-Bromo-3-chloro[1,2,3]thiadiazolo[3,4-c]benzimidazole (7)

**Method A.** Compound 1 (0.08 g, 0.38 mmol) and bromine (0.06 g 0.38 mmol) in AcOH (3 mL) were heated at 60 °C for 6 h and then cooled. The precipitate that formed was filtered off, washed with H₂O, aqueous Na₂CO₃ and Na₂SO₃ solutions, and crystallized to give compound 7 (0.08 g, 72%).

**Method B.** Compound 1 (0.03 g, 0.14 mmol) and bromine (0.02 g, 0.38 mmol) in H₂SO₄ (0.6 mL) and H₂O (0.8 mL) were heated at 60 °C for 6 h and then cooled. The obtained precipitate was filtered off, washed with H₂O, aqueous Na₂CO₃ and Na₂SO₃ solutions and crystallized to give compound 7 (0.03 g, 75%).

**Method C.** Solutions of compound 1 (0.2 g, 0.95 mmol) in dioxane (5 mL) and bromine (0.15 g, 0.95 mmol) in dioxane (3 mL) were combined and stirred at rt for 4 h. The precipitate was filtered off, washed with H₂O, aqueous Na₂CO₃ and Na₂SO₃ solutions and crystallized to give compound 7 (0.24 g, 86%).

**Method D.** A mixture of bromine (3 mL) and compound 1 (0.04 g, 0.19 mmol) was kept at rt for 10 h and evaporated under reduced pressure. The solid residue was washed with H₂O, aqueous Na₂CO₃ and Na₂SO₃ solutions to give a mixture of compounds 7 and 9 (2:1).

Compound 7: fine orange brown crystals mp 193-194 °C (MeOH). ¹H NMR (DMSO-d₆): δ 7.71 (dd, 1H, J = 2 and 9 Hz, 6-H), 7.81 (dd, 1H, J = 0.3 Hz, and 9 Hz, 5-H), 8.47 (dd, 1H, J = 1 Hz and 2 Hz, 8-H). ¹³C NMR (DMSO-d₆): δ 112.8, 116.2, 123.0, 126.6, 129.4, 131.7, 151.7, 152.5. IR (v, cm⁻¹): 3042, 3030 (CH). Anal. Calcd. for C₈H₃BrClN₃S (288.552): C, 33.30; H, 1.05; N, 14.56. Found: C, 33.56; H, 1.15; N, 14.63%. HRMS: Calcd for C₈H₃BrClN₃S: 287.8998. Found: 287.9001.

7-Bromo-2⁻⁴δ⁻²-[1,2,3,5]thiatriazolo[3,4-c]benzimidazole (8). Compound 2 (0.04 g) was treated with bromine according to the method C used for compound 7 for 16 h to give compound 8 as fine red brown crystals (0.04 g, 69%), mp 145-146 °C (MeOH). ¹H NMR (DMSO-d₆): 7.79 (dd, 1H, J = 2 Hz, J = 9 Hz, 7-H), 7.89 (dd, 1H, J = 1 and Hz, 8-H), 8.42 (dd, 1H, J = 1 and 2 Hz, 5-H). ¹³C NMR (DMSO-d₆): δ 113.0, 117.4, 122.9, 126.4, 132.05, 154.55, 163.4. IR (v, cm⁻¹): 3045, 3038 (CH). Anal. Calcd. for C₈H₃BrN₄S (255.096): C, 32.96; H, 1.19; N, 21.96. Found: C, 33.11; H, 1.29; N, 21.68%. HRMS: Calcd for C₈H₃BrN₄S: 254.9340. Found: 254.9346.

5,7-Dibromo-3-chloro-2⁻⁴δ⁻²-[1,2,3]thiadiazolo[3,4-c]benzimidazole (9). A mixture of compound 1 (0.2 g, 0.95 mmol) and bromine (3 mL) was refluxed for 16 h. An excess of bromine was evaporated at reduced pressure, the precipitate was filtered off, washed with H₂O, aqueous Na₂CO₃ and Na₂SO₃ solutions and crystallized from DMF to give compound 9 as fine orange brown crystals (0.07 g, 40%), mp 235-237 °C. ¹H NMR (DMSO-d₆): δ 8.05 (d, 1H, J = 2 Hz, ArH), 8.54 (d, 1H, J = 2 Hz, ArH). ¹³C NMR (DMSO-d₆): 117.2, 122.5, 124.4, 135.0, 137.1, 138.2, 155.3, 166.0. IR (v, cm⁻¹): 3051, 3034 (CH). Anal. Calcd. for C₈H₂Br₂ClN₃S (367.448):
C, 26.15; H, 0.55; N, 11.44. Found: C, 26.20; H, 0.53; N, 11.65%. HRMS: Calcd for C₈H₃Br₂ClN₃S: 367.8083. Found: 367.8076.

**1-Amino-6-nitrobenzimidazol-2-ylmethanol (14) and (1-amino-5-nitrobenzimidazol-2-yl)methanol (18).** [5(6)Nitro-1H-benzimidazol-2-yl]methanol (10) (4.4 g, 23 mmol) and KOH (4.8 g) in water (40 mL) was treated with hydroxylamine-O-sulfonic acid (6.0 g, 53 mmol) in water (15 mL), neutralized with NaHCO₃ immediately before reaction. The reaction temperature was kept within 35-40 °C. After the exothermic reaction had ceased, the reaction mixture was heated to 40-50 °C for 0.5 h, then left overnight at rt. The obtained crystals were filtered off, washed with cold H₂O and recrystallized (EtOH) to give a mixture (1.6 g, 34%) of compounds 14 and 18 in 1:1 ratio. ¹H NMR (DMSO-d₆): δ 4.82 (2H, s, CH₂), 5.62 (1H, br. s, OH), 6.23 (2H, s, NH₂), 6.26 (2H, s, NH₂), 8.49 - 8.52 (2H, m, ArH), 7.6 - 8.3 (2H, m, ArH). ¹³C NMR (DMSO-d₆): δ 55.3, 55.4, 106.9, 110.3, 115.2, 117.0, 117.8, 119.2, 135.2, 138.8, 140.3, 142.4, 142.6, 144.4, 158.8, 159.9. IR (v, cm⁻¹): 3135, 3099, 3034, 1537, 1348 (OH, NH₂, NO₂). Anal. Calcd. for C₈H₈N₄O₃ (208.174): C 46.16; H 3.87; N 26.91. Found: C 46.07; H 3.81; N 27.15. HRMS: Calcd for C₈H₈N₄O₃: 209.0674. Found: 209.0674.

**3-Chloro-7-nitro-2,4-diazirino-[1,2,3]thiadiazolo[3,4-c]benzimidazole (3) and 3-chloro-6-nitro-2,4-diazirino-[1,2,3]thiadiazolo[3,4-c]benzimidazole (23).** The mixture of compounds 14 and 18 (0.5 g, 2.4 mmol), obtained as above, was refluxed with SOCl₂ (5 mL) for 10 min. Excess of SOCl₂ was evaporated under reduced pressure, and the residue was treated with aqueous NaHCO₃. The resulting solid mixture (0.53 g, 86%) of 3 and 23 was filtered off and fractionated by chromatography. Compound 3 was identical with a sample synthesized by nitration of compound 1.

**Compound 23.** Fine orange yellow crystals m. p. 227-228 °C (DMF). ¹H NMR (DMSO-d₆): δ 8.10 (dd, 1H, J = 2 and 9 Hz, 7-H), 8.43 (d, 1H, J = 9 Hz, 8-H), 8.65 (d, 1H, J = 2 Hz, 5-H). ¹³C NMR (DMSO-d₆): 114.4, 117.9, 123.8, 136.6, 142.5, 146.9, 151.4, 157.9. IR (v, cm⁻¹): 1535, 1353 (NO₂). Anal. Calcd. for C₈H₃ClN₄O₂S (254.654): C, 37.73; H, 1.19; N, 22.00. Found: C 37.44; H 1.55; N 22.28%. HRMS: Calcd for C₈H₃ClN₄O₂S: 254.9744. Found: 254.9738.

**5-Nitro-1H-benzimidazole-1,2-diamine (15) and 6-nitro-1H-benzimidazole-1,2-diamine (19).** A solution of 5(6)-nitro-1H-benzimidazol-2-amine (11) (7.12 g, 40 mmol) and KOH (5 g) in H₂O (50 mL) was treated with hydroxylamine-O-sulfonic acid (8 g) in H₂O (15 mL) neutralized with NaHCO₃ immediately before reaction. The reaction temperature was kept within 40-50 °C. After the exothermic reaction had ceased, the mixture was heated to 40-50 °C for 3 h, then cooled to rt and left overnight. Crystals that separated were filtered off, washed with cold H₂O and recrystallized (EtOH) to give a 1:1 mixture (6.7 g, 87%) of compounds 15 and 19. ¹H NMR (DMSO-d₆): δ 6.83 (4H, s, NH₂), 7.07 (4H, s, NH₂), 7.17 (1H, d, J = 9 Hz, ArH) 7.22 (1H, d, J = 9 Hz, ArH), 7.80-8.00 (4H, m, ArH). ¹³C NMR (DMSO-d₆): δ 103.0, 106.6, 109.71, 113.7, 114.8, 117.7, 134.6, 138.6, 140.1, 140.3, 141.7, 147.2, 158.0, 159.4. IR (v, cm⁻¹): 3109, 3120, 3085, 3031 (NH₂). Anal. Calcd. for C₇H₇N₃O₂ (193.163): C 43.53, H 3.65, N 36.26. Found: C 43.37, H 3.81, N 36.15%. HRMS: Calcd for C₇H₇N₃O₂: 194.0678. Found: 194.0682.
7-Nitro-2i,4iδ2-[1,2,3,5]thiatriazolo[3,4-c]benzimidazole (4) and 6-nitro-2i,4iδ2-[1,2,3,5]thiatriazolo[3,4-c]benzimidazole (24). The mixture (0.1 g, 0.52 mmol) of 5- and 6-nitro-1H-benzimidazole-1,2-diamines obtained as above was refluxed in SOCl2 (10 mL) for 10 h. Excess SOCl2 was evaporated in vacuo, and the residual crystalline solid was treated with Na2CO3 solution, extracted (EtOAc) and fractionated by column chromatography. The usual yield of the mixture of compounds 4 and 24 (1:1) obtained in this way was 0.03 g (30%). Compound 4: 1H NMR (DMSO-d6): δ 8.02 (1H, d, J = 9 Hz, 5-H), 8.47 (1H, dd, J = 2 and 9 Hz, 6-H), 9.21 (1H, d, J = 2 Hz, 8-H). 13C NMR (DMSO-d6): δ 111.3, 120.4, 123.0, 123.8, 140.0, 158.2, 165.8. Compound 24: 1H NMR (DMSO-d6): δ 8.54 (1H, d, J = 9 Hz, 8-H), 8.10 (1H, dd, J = 2 and 9 Hz, 7-H), 8.74 (1H, d, J = 2 Hz, 5-H), 13C NMR (DMSO-d6): δ 114.9, 115.0, 116.2, 128.1, 146.5, 153.3, 164.6. IR (ν, cm⁻¹): 1552, 1545, 1351, 1329 (NO2). Anal. Calcd. for C17H14N2S: 222.0086. Found: C 39.88, H 3.52, N 17.46. HRMS: Calcd for C17H14N2S: 222.0086. Found: 222.0081.

(1-Amino-6-bromo-1H-benzimidazol-2-yl)methanol (16) and (1-amino-5-bromo-1H-benzimidazol-2-yl)methanol (20). A solution of [5(6)-bromo-1H-benzimidazol-2-yl]methanol (12) (5.2 g, 22.7 mmol) and KOH (5 g) in H2O (40 mL) was treated with hydroxylamine-O-sulfonic acid (6 g) in H2O (15 mL) neutralized with NaHCO3 immediately before reaction. The reaction temperature was kept below 40 °C. After the exothermic reaction had ceased, the reaction mixture was heated to 40-50 °C for 0.5 h and then cooled to rt. The obtained crystals were filtered off, washed with cold H2O and crystallized from H2O to give a 1:1 mixture (3.7 g, 67%) of compounds 16 and 20. IR (ν, cm⁻¹): 3350, 3313, 3184, 3120 (NH2). 1H NMR (DMSO-d6): δ 4.73 (4H, s, CH2), 5.43 (1H, s, OH), 5.45 (1H, s, OH), 6.01 (2H, s, NH2), 6.03 (2H, s, NH2), 7.31 (1H, d, J = 9 Hz, ArH), 7.39 (1H, d, J = 9 Hz, ArH), 7.46 (1H, d, J = 9 Hz, ArH), 7.53 (1H, d, J = 9 Hz, ArH), 7.67 (1H, s, ArH), 7.73 (1H, s, ArH). 13C NMR (DMSO-d6): δ 55.8, 112.5, 113.5, 114.2, 115.0, 121.5, 122.0, 124.9, 125.4, 135.7, 137.8, 139.6, 141.9, 156.2, 156.5. IR (ν, cm⁻¹): 3350, 3313, 3184, 3120 (OH, NH2). Anal. Calcd. for C5H8BrN3O (242.073): C 39.67, H 3.31, N 17.36. Found: C 39.88, H 3.52, N 17.46%. HRMS: Calcd for C5H8BrN3O: 241.9929. Found: 241.9926.

(1-Amino-6-methoxy-1H-benzimidazol-2-yl)methanol (17) and (1-amino-5-methoxy-1H-benzimidazol-2-yl)methanol (21). [5(6)-Methoxy-1H-benzimidazol-2-yl]methanol (13) (5 g, 28 mmol) was treated with a neutralized solution of hydroxylamine-O-sulfonic acid as described above for compound 12. The obtained solid was crystallized from H2O to give a 1:1 mixture (3.7 g, 65%) of compounds 17 and 21. 1H NMR (DMSO-d6): δ 3.78 (3H, s, OCH3), 3.81 (3H, s, OCH3), 4.68 (4H, d, J = 6 Hz, CH2), 5.36 (2H, t, J = 6 Hz, OH), 5.91 (4H, s, NH2), 6.6-7.54 (6H, m, ArH). 13C NMR (DMSO-d6): δ 52.6, 55.2, 55.2, 57.7, 93.1, 101.4, 110.2, 110.9, 111.6, 119.5, 130.4, 134.0, 136.5, 140.4, 153.5, 154.4, 155.3, 155.8. IR (ν, cm⁻¹): 3358, 3322, 3191, 3131 (OH, NH2). Anal. Calcd. for C5H12N3O2 (193.203): C 55.74, H 5.74, N 21.75. Found: C 55.82, H 5.64, N 21.86%. HRMS: Calcd for C5H12N3O2: 194.0930. Found: 194.0927.

3-Chloro-7-methoxy-2i,4iδ2-[1,2,3]thiadiazolo[3,4-c]benzimidazole (22), 3-chloro-6-methoxy-2i,4iδ2-[1,2,3]thiadiazolo[3,4-c]benzimidazole (26) and 3,8-dichloro-7-methoxy-2i,4iδ2-[1,2,3]-
thiadiazolo[3,4-c]benzimidazole (27). The mixture of compounds 17 and 21 (0.2 g, 1.04 mmol) was refluxed with SOCl₂ (5 mL) for 0.5 h, and then evaporated under reduced pressure. The residue was treated with aqueous NaHCO₃ solution and fractionated by column chromatography [Rf (toluene/EtOAc, 2:1) for compounds 26, 22 and 27 are 0.2, 0.26 and 0.35, respectively].

**Compound 22.** Fine orange crystals 0.04 g (16%), dec. >147 °C. ¹H NMR (CDCl₃): δ 3.93 (3H, s, OCH₃), 7.26 (1H, dd, J = 2 and 9Hz, 6-H), 7.44 (1H, d, J = 2Hz, 8-H), 7.81 (1H, d, J = 9Hz, 5-H). ¹³C NMR (CDCl₃): δ 56.2, 93.4, 121.2, 122.4, 125.3, 128.8, 150.0, 150.2, 155.3. IR (υ, cm⁻¹): 1265 (C-O). Anal. Calcd. for C₉H₆ClN₃OS (239.682): C 45.10, H 2.52, N 17.53. Found: C 45.35, H 2.64, N 17.59%. HRMS: Calcd for C₉H₇ClN₃OS: 239.9998. Found: 240.0003.

**Compound 26.** Fine orange crystals 0.02 g (8%), dec. >180 °C, ¹H NMR (CDCl₃): δ 3.95 (3H, s, OCH₃), 6.97 (1H, dd, J = 2 and 9 Hz, 7-H), 7.24 (1H, d, J = 2 Hz, 5-H), 8.00 (1H, d, J = 9 Hz, 8-H). ¹³C NMR (CDCl₃): δ 55.9, 100.6, 113.7, 113.8, 123.4, 124.2, 151.1, 156.4, 161.1. IR (υ, cm⁻¹): 1257 (C-O). Anal. Calcd. for C₉H₆ClN₃OS (239.682): C 45.10, H 2.52, N 17.53. Found: C 45.21, H 2.49, N 17.68%. HRMS: Calcd for C₉H₇ClN₃OS: 239.9998. Found: 240.0001.

**Compound 27.** Fine orange crystals 0.04 g (14%), m. p. 195-197 °C. ¹H NMR (CDCl₃): δ 4.07 (3H, s, OCH₃), 7.08 (1H, d, J = 9 Hz, 7-H), 8.02 (1H, d, J = 9 Hz, 8-H). ¹³C NMR (CDCl₃): δ 57.5, 107.9, 111.1, 111.7, 123.4, 124.2, 151.1, 156.4, 161.1. IR (υ, cm⁻¹): 1268 (C-O). Anal. Calcd. for C₉H₅Cl₂N₃OS (274.127): C 39.43, H 1.84, N 15.33. Found: C 39.58, H 2.07, N 15.65%. HRMS: Calcd for C₉H₅Cl₂N₃OS: 273.9609. Found: 273.9603.

**References**