Tetrahedron 67 (2011) 2760–2767

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

New pentacyclic ring systems: intramolecular cyclization of *o*,*o*′-disubstituted bibenzothiazoles

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ARTICLE INFO

Article history:
Received 18 November 2010
Received in revised form 21 January 2011
Accepted 14 February 2011
Available online 19 February 2011

Keywords:
Benzothiazole
Benzo[*c*]cinnoline
Carbazole
Reduction
Oxidation
Reductive cyclization mechanism

ABSTRACT

Efficient methods for the preparation of isomeric *o*,*o*′-diaminobibenzothiazoles (**8a** and **11a**) and *o*,*o*′-diamino-2,2′-dimethylbibenzothiazoles (**8b** and **11b**), potentially valuable building blocks for construction of hitherto unknown dithiazolo annulated pentacyclic heterocycles, have been developed. The dithiazolo annulated benzo[*c*]cinnolines **9a**, **9b**, and **12a** were prepared from the corresponding diamines by oxidation with $PhI(OAc)_2$ in good yield. The dithiazolo annulated carbazoles **13** and **14** were efficiently prepared from the corresponding diamines by thermal cyclization in H_3PO_4. The unusual course of reduction and product formation of *o*,*o*′-dinitrosubstituted bibenzothiazoles **6a** and **6b** with $SnCl_2$ under acidic conditions was rationalized by DFT quantum-mechanical calculations. It was suggested that cyclic products are formed from dinitroso derivatives and open-shell species immediately following on a - reduction path.

1. Introduction

Aryl- and heteroaryl-annulated nitrogen containing heterocycles are of considerable interest due to their various applications. In spite of a large variety of nitrogen fused pentacyclic ring systems and their remarkable biological activity, only a few such compounds with a benzothiazole moiety are known so far. Naturally occurring Dercitin and related alkaloids isolated from marine sponges *Dercitus* sp. and *Stelleta* sp. inhibit proliferation of P388 murine leukemia cells and exhibit immunosuppressive activity.[1] In the last decade some annulated benzothiazole pentacyclic heterocycles were synthesized and associated with antimicrobial,[2] antiprotozoal,[3] and antileishmanial[4] activity.

On the other hand, fused pentacyclic ring systems with a carbazole moiety, especially indolocarbazole derivatives, are well documented. A recent review[5] addresses their synthesis and wide range of applications, such as drug development, mechanistic biological studies, anion recognition, and the construction of new electronic devices. Some other pentacyclic carbazoles, such as Calothrixins and benzocyclobutacarbazole derivatives show antitumor activity.[6] Recently, a number of heteroaryl annulated[*a*]carbazoles were synthesized and photophysically evaluated showing interesting structure–property correlations.[7] Furthermore, pentacyclic benzo[*c*]cinnoline derivatives, such as dibenzo[*c*,*h*]cinnolines exhibit potent topoisomerase I-targeting activity and cytotoxicity.[8]

We have recently been interested in the synthesis of a series of substituted benzothiazoles,[9] condensed quinolones of benzo[*b*]thiophene,[10] and condensed benzo[*b*]thieno-naphthyridones,[11] which demonstrated excellent antitumor activity. A number of condensed quinolines from the benzimidazo[1,2-*a*]quinoline series[12] and diazacyclopenta[*c*]fluorene series[13] were also prepared, showing a prominent inhibitory effect. In connection with the above mentioned, and as a part of our continuous interest in the synthesis and biological evaluation of structurally different heterocycles, we decided to prepare several new pentacyclic polycondensed nitrogen containing heterocycles. In this paper we extend our previously described work[14] on the formation of *o*,*o*′-disubstituted bibenzothiazoles to the synthesis of two isomeric *o*,*o*′-diaminobibenzothiazoles and two *o*,*o*′-diamino-2,2′-dimethylbibenzothiazoles, as well as promote their intramolecular cyclization into the corresponding dithiazolo annulated carbazoles and benzo[*c*]cinnolines.

There are a number of cyclization methods for the construction of the core tricyclic nitrogen containing heterocycle from the appropriate substituted biphenyls,[15] and all of them could be prepared from *o*,*o*′-diaminosubstituted biphenyls. Surprisingly, when reduction of *o*,*o*′-dinitrosubstituted bibenzothiazoles was carried out with $SnCl_2$, a mixture of products was formed whose

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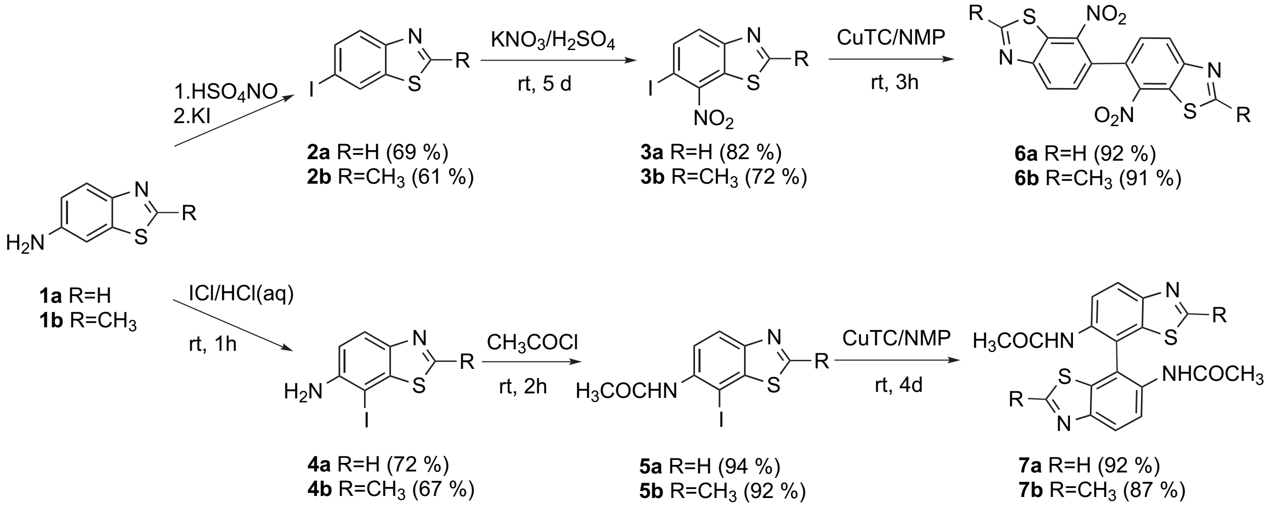
0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.02.037

distribution depends on amount of $SnCl_2$ used. The unusual course of the reduction of *o*,*o*′-dinitrosubstituted bibenzothiazoles is rationalized by quantum-mechanical calculations.

2. Results and discussions

2.1. Synthesis

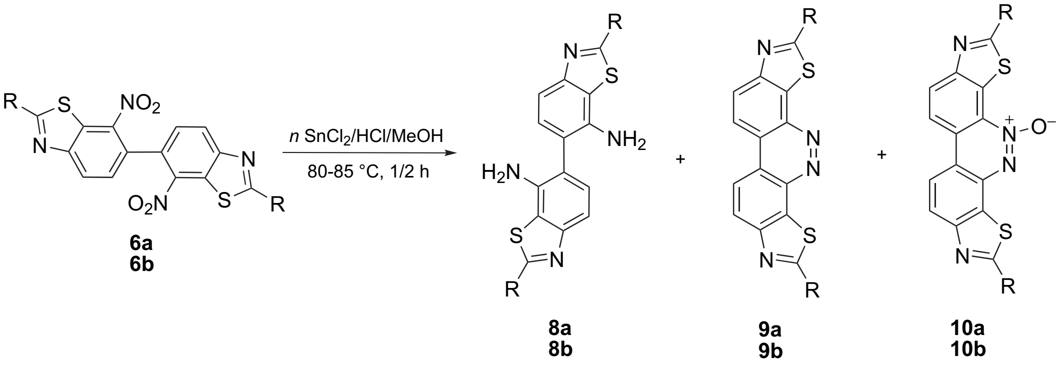
Our synthetic strategy was to prepare *o*,*o*′-diaminosubstituted bibenzothiazole derivatives as versatile building blocks for their conversion into the pentacyclic ring system. We have previously found that copper(I) thiophene-2-carboxylate (CuTC) efficiently mediated homocoupling of 6,7-disubstituted benzothiazoles.[14] Following such a methodology, in this paper we extended our work to 6,7-disubstituted-2-methylbenzothiazoles (Scheme 1).



Scheme 1.

Diazotation of readily accessible 6-aminobenzothiazole **1a** and 6-amino-2-methylbenzothiazole **1b** with nitrosylsulfate in acetic acid, followed by reaction of the formed diazonium salts with KI, produced the corresponding 6-iodo derivatives **2**. Their subsequent regioselective nitration at position 7 of the benzothiazole ring afforded **3**. The same regioselectivity was observed in electrophilic substitution of **1** with ICl in which 7-iodo derivatives **4** were formed. Derivatives **4** were converted into the corresponding aminoacetyl derivatives **5** by reaction with acetyl chloride in the presence of diisopropylethylamine as a base. All of the synthesized compounds **2**–**5** were obtained in very good yields. In the next step, using an efficient reductive homocoupling procedure with CuTC reported for a range of *ortho*-substituted aromatic halides,[16] reaction of nitro **3** and acetylamino **5** derivatives with 2.5 equiv of CuTC in *N*-methyl-2-pyrrolidone (NMP) gave *o*,*o*′-nitrodisubstituted **6** and *o*,*o*′-diacetylaminodisubstituted bibenzothiazoles **7** in excellent yields. Significant reaction time differences between nitro **3** and acetylamino **5** derivatives (3 h vs 4 days) can be attributed to activation by the nitro group in this Ullmann-like[16] reductive coupling.

Although there are many practical methods for the reduction of nitro to amino compounds, in our case they have limitations due to the possibility of the benzothiazole ring opening under basic conditions. Also, the formation of the benzo[*c*]cinnoline nucleus and its *N*-oxide from *o*,*o*′-dinitrosubstituted biaryls[17] is well described, but almost all efficient methods require basic conditions. We have recently found that the possibility of benzothiazole ring opening exists not only in strong alkaline conditions, but also in mild basic conditions if an electron withdrawing group is attached to the benzothiazole nucleus.[18] Therefore, we have decided to investigate the reduction in neutral or acidic conditions. Our previous attempts at reductive formation of benzo[*c*]cinnoline from dinitro derivatives **6a** by $Zn/AcOH/Ac_2O$[19] and $Zn/CaCl_2/EtOH$[20] were unsuccessful and only the starting dinitro compound **6a** was recovered. In this paper we applied an efficient literature method previously used for the preparation of triaminobiphenyl derivatives by the reduction of trinitrobiphenyl derivatives with 9 equiv of $SnCl_2$ in concd HCl ethanol solution (3 equiv per nitro group).[20] However, in our hands the reduction of dinitro derivatives **6** with 6 equiv of $SnCl_2$ (also 3 equiv per nitro group) gave a mixture of products (Scheme 2).



Scheme 2.

This unexpected result prompted us to investigate not only the preparation of targeted diamines **8**, but also the possibility of direct reductive formation of benzo[*c*]cinnolines **9** and the corresponding *N*-oxides **10**. The reductions were carried out by varying the amount of $SnCl_2$ (4–16 equiv) in MeOH/HCl (1:1, v/v) for 30 min at 80–85 °C. After pouring the reaction mixture into 2 M HCl, the diamines **8** were dissolved as water soluble dihydrochloride salts, and insoluble products **9** and **10** filtered off. By subsequent basification of the solution, crystallized diamines **8** were obtained in varying yields depending on the amount of $SnCl_2$ used (Table 1). Distribution of products **9** and **10** from the insoluble precipitate was obtained by LC–MS and ^{1}H NMR analysis.

Table 1
Reduction of *o*,*o*′-dinitro derivatives **6** with $SnCl_2$ (Scheme 2)

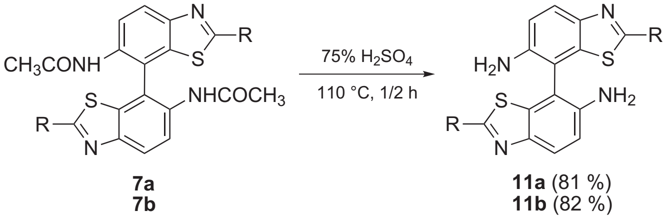
Entry	Substrate	$SnCl_2$	Product distribution	
			8	**9** and **10** (**9**:**10** ratio)[a]
1	**6a**	4	27%	45% (1:2)
2	**6a**	6	65%	11% (1:1)
3	**6a**	8	66%	13% (2:1)
4	**6a**	16	80%	5% (only **9a**)
5	**6b**	4	12%	76% (1:6)
6	**6b**	6	69%	21% (1:1)
7	**6b**	8	75%	6% (10:1)
8	**6b**	16	82%	4% (only **9b**)

The yields of products were calculated on the basis of full conversion.
[a] Determined by LC–MS and ^{1}H NMR.

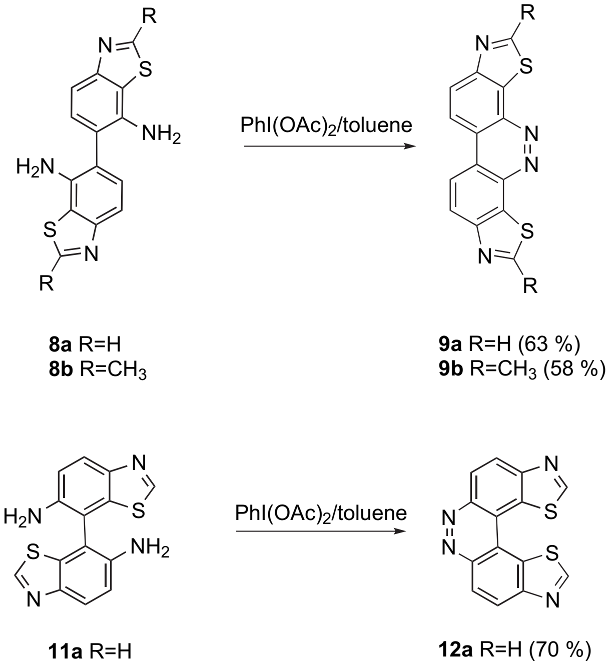
The conversion of dinitro derivatives **6** was complete except in entries 1 (90%) and 5 (95%). The diamines **8** were isolated by using 16 equiv of $SnCl_2$ in a very good yield of about 80%, while the same reactions afforded cinnolines **9** in a poor yield of about 5%. Attempts to isolate pure cinnoline derivatives **9** and the corresponding *N*-oxides **10** from their mixtures (entries 1–3 and 5–7), either by chromatography or crystallization, were unsuccessful. Only several crystallizations from toluene gave pure *N*-oxide **10b** in a low yield (26%). The likely reason is very low solubility of these compounds, also responsible for our failure to obtain their ^{13}C NMR spectra in any of standard deuterated solvents. The structures of benzo[*c*]cinnoline derivatives **9** and *N*-oxide **10b** were confirmed by ^{1}H NMR, IR, and MS spectroscopy as well as elemental analysis, while the structure of the corresponding *N*-oxide **10a** was only supported by LC–MS and ^{1}H NMR analysis of its mixture with benzo[*c*]cinnoline **9a**. The LC–MS data showed characteristic molecular ions at 295.1 for **9a**, 310.3 for **10a**, 323.1 for **9b**, and 339.1 for **10b**. The ^{1}H NMR spectrum of the corresponding mixtures taken in DMSO (**9a**/**10a**) and chloroform (**9b**/**10b**) showed the characteristic three peaks of benzo[*c*]cinnolines derivatives **9** (two aromatic doublets and a singlet at 9.74 ppm (**9a**), and 3.05 ppm (**9b**), respectively) while the corresponding *N*-oxides **10** showed six peaks. Withdrawal of the benzo[*c*]cinnoline chemical shifts from the ^{1}H NMR spectra of the corresponding mixture allowed us to assign the characteristic proton chemical shifts of *N*-oxides **10**, four aromatic doublets, and two close singlets (9.73, 9.68 ppm for **10a** and 3.02, 3.00 ppm for **10b**, respectively).

We now turned to our investigations to the preparation of benzo[*c*]cinnoline from the corresponding diamines by an oxidative method. The diamines **11** were easily obtained by hydrolysis of *N*-acetyl derivatives **7** with 75% H_2SO_4 in a very good yield (Scheme 3).

Only a few oxidative cyclizations of *o*,*o*′-diaminosubstituted biphenyl derivatives into the corresponding benzo[*c*]cinnolines have been described so far, using MnO_2[21] or $PhI(OAc)_2$.[20,22] We followed the $PhI(OAc)_2$ oxidative method of Barton,[22] and by modifying the reaction conditions successfully obtained the benzo[*c*]cinnoline skeleton from diamine **8a**, **8b**, and **11a** (Scheme 4).



Scheme 3.



Scheme 4.

The best yields of target products were obtained when oxidations were carried out in dry toluene with 1 equiv of $PhI(OAc)_2$ at 80 °C for 24 h. After separation of precipitated product, 1 equiv of $PhI(OAc)_2$ was added to the mother liquor and the reaction carried out for an additional 24 h at rt. Generally, the yields of products in NMP were for 20% lower than in toluene, while the reactions carried out in acetic acid gave only a complex mixture of products.

Since we have not been able to obtain **12b**, we resorted to quantum-mechanical calculations to find out whether the lack of formation of **12b** can be explained by some stereoelectronic factors introduced by the change of R=H to Me. At IEF-PCM/B3LYP/6-311++G(d,p) level of theory, cinnolines **12** are about 10 kcal/mol less stable than the corresponding cinnolines **9**, which are both planar. Since in the planar conformation of **12**, the sulfur atoms would be too close, minimum-energy geometry of **12** has C_2 symmetry with the dihedral angle between the benzothiazole rings around 30° (Fig. 1). As the energy change for the isodesmic reaction **9b**+**12a**→**9a**+**12b** is only −0.42 kcal/mol, it seems that the replacement of H with Me should actually help the cyclization. The lack of formation of **12b** is therefore a consequence of some other factors, perhaps differences in solubilities, or similar.

The thermal and acid stability of the benzothiazole nucleus gave us an opportunity to carry out the Täuber method of carbazole synthesis.[23] We efficiently converted diamines **8** and **11** into the corresponding, previously unknown, thiazolo annulated carbazole derivatives by heating the reaction mixture at 200 °C for 1.5 h in 85% H_3PO_4 (Scheme 5). The yields of carbazole derivatives **13** and **14** ranged from 59% for **13a** to 76% for **14b**.

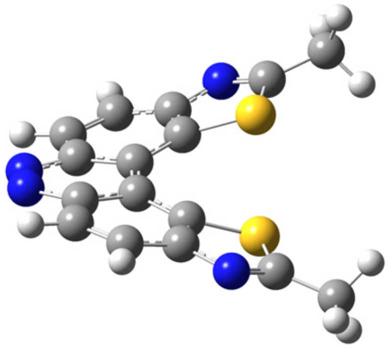
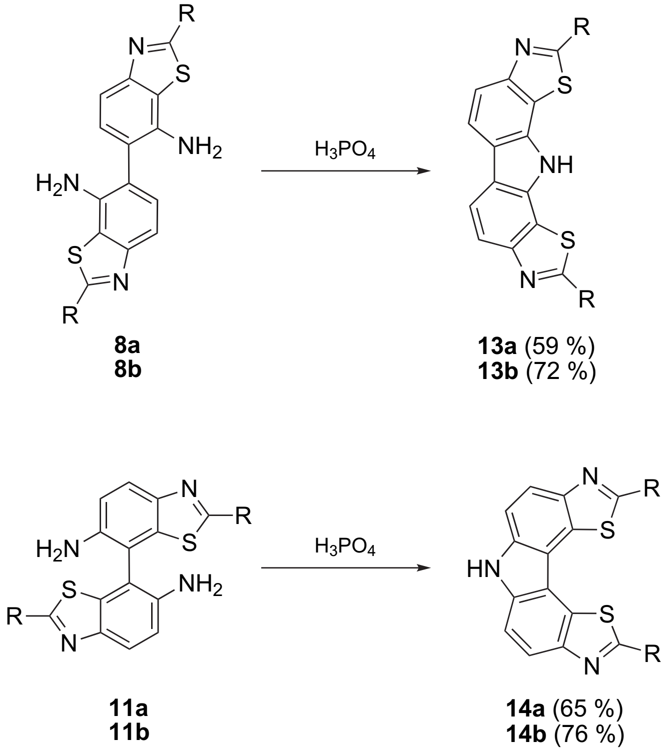


Fig. 1. Geometry of **12b** optimized on B3LYP/6-311++G(d,p) level of theory.



Scheme 5.

2.2. Mechanism of reductive cyclization

Although the reduction of aromatic nitro compounds is important not only for synthetic organic chemistry,[24] but also for environmental chemistry,[25] fine details of its reaction mechanism are still not known. Based on the available experimental data, one can assume that the acid-catalyzed reduction has three distinct steps, each consisting of two consecutive single-electron and proton transfer pairs of elementary reactions (Scheme 6).[26]

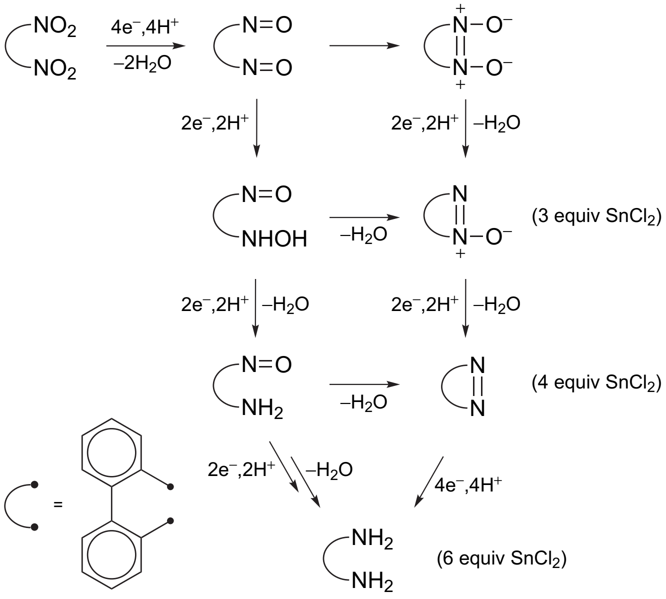
$$Ar{-}NO_2 \xrightarrow[-H_2O]{2e^-,2H^+} Ar{-}N{=}O \xrightarrow{2e^-,2H^+} Ar{-}NHOH \xrightarrow[-H_2O]{2e^-,2H^+} Ar{-}NH_2$$

Scheme 6. Mechanism of acid-catalyzed reduction of aromatic nitro compound to corresponding amine.

In some cases, depending on the substrates and reaction conditions, azoxy and azo byproducts are formed. Azoxy compounds are generally believed to originate from the coupling reaction between N=O and NHOH groups, and azo derivatives from the reaction between N=O and NH_2 groups.[24b,26] Reductive cyclization, observed in this paper, can be seen as an intramolecular counterpart of such bimolecular coupling reactions.

As a model compound for the computational study of the reductive cyclization mechanism, we selected *o*,*o*′-dinitrobiphenyl. Preliminary calculations have shown that its behavior in the studied reactions is very similar to the behavior of bibenzothiazoles **6**, suggesting that substituted thiazole rings have only a second-order effect on the course of these reactions.

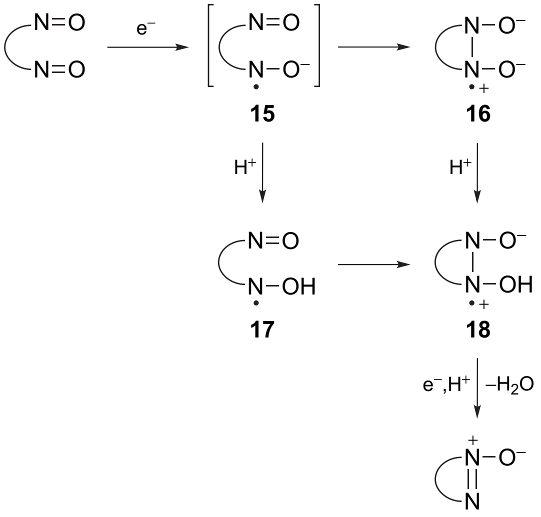
Based on our quantum-mechanical calculations, the general sequence of steps leading to the reduction and reductive cyclization of *o*,*o*′-dinitrobiphenyl can be concisely shown in Scheme 7.



Scheme 7. Main steps in acid-catalyzed reduction–cyclization of *o*,*o*′-dinitrobiphenyl.

We were not able to find any low-energy cyclization paths prior to the reduction of the nitro groups to at least the nitroso stage. The reaction of two nitroso groups, entropically favored in comparison to its bimolecular counterpart,[27] at B3LYP/6-311++G(d,p) level of theory has an activation energy of only 1.3 kcal/mol. Although under other reaction conditions the cyclization is possible through the reaction of the nitroso and hydroxylamino, or the nitroso and amino groups, in our case these two paths are negligible because both hydroxylamino and amino groups are protonated under the strongly acidic conditions. Once the nitro group gets reduced that far, the probability of cyclization is significantly diminished. However, the cyclic products can also be formed from several open-shell species immediately, following the reduction path (Scheme 8). Single-electron transfer to the dinitrosobiphenyl produces radical-anion **15**, which, when in a favorable conformation, in a barrierless process yields cyclic radical-anion **16**. On the other hand, if **15** survives long enough to get protonated to **17**, which is thermodynamically favorable ($\Delta_rG^o = -16.8$ kcal/mol), the cyclization barrier from **17** to **18** is only 4.5 kcal/mol. At MP2(fc)/6-311++G(d,p) level of theory cyclization barriers are generally several kcal/mol higher, but the trends are the same.

The claim that the low-energy cyclization produces the corresponding azodioxy compound is not inconsistent with our experimental observation that the reductive cyclization of **6** produces only azoxy and azo products. The calculations suggest that the azodioxy group can easily be reduced to the azoxy group. Protonation and single-electron transfer to the azodioxy compound



Scheme 8. Radical-anion mechanism of cyclization of dinitroso compounds.

produce the corresponding radical (Δ_rG^o=7.1 kcal/mol), which either directly releases a OH radical ($\Delta^{\neq}G^o$=4.0 kcal/mol) or concurrently with protonation releases a water molecule, producing the corresponding azoxy compound. As the loss of the second oxygen is more energy demanding, it is possible to isolate both azoxy and azo products.

Since our calculations show that the first step of the reductive cleavage of an azo to a diamino compound is comparably unfavorable, we suggest that the reduction of nitro to the diamino compound and cyclization are two parallel reactions.

3. Conclusion

In summary, preparation of isomeric *o,o′*-diaminobibenzothiazoles (**8a** and **11a**) and *o,o′*-diamino-2,2′-dimethylbibenzothiazoles (**8b** and **11b**), has been successfully achieved by a multistep synthesis. The dithiazolo annulated benzo[*c*]cinnolines **9a**, **9b**, and **12a** were prepared from the corresponding diamines by oxidation with $PhI(OAc)_2$ in a good yield. The dithiazolo annulated carbazoles **13** and **14** were prepared from the corresponding diamines by simple thermal cyclization in H_3PO_4 in a good yield. An unusual reduction of *o,o′*-dinitrosubstituted bibenzothiazoles **6a** and **6b** with $SnCl_2$ under acidic conditions was rationalized by quantum-mechanical calculations. It was suggested that cyclic products are formed from dinitroso derivatives and open-shell species immediately following a reduction path. Since our calculations show that the first step of reductive cleavage of an azo to a diamino compound is comparably unfavorable, we suggest that the reduction of a nitro to a diamino compound and cyclization are two parallel reactions. Full discussion of the reduction–cyclization mechanism will be published in a separate computational paper.

4. Experimental section

4.1. General

Melting points were determined on an Original Kofler Mikroheiztisch apparatus (Reichert, Wien). ^{1}H NMR and the ^{13}C NMR spectra were recorded with a Bruker Avance DPX-300 or Bruker AV-600, the deuterated solvents indicated were used. Chemical shifts are reported in parts per million (ppm) relative to TMS. IR spectra were recorded with a Bruker Vertex 70 FTIR spectrophotometer with an ATR sampling accessory and the signals are given in wave numbers (cm^{-1}). Mass spectra were recorded with an Agilent 1100 Series LC/MSD Trap SL spectrometer using electrospray ionization (ESI). Elemental analyses were performed at the microanalytical laboratories of the ‘Ruđer Bošković’ Institute. All chemicals and solvents were purchased from Aldrich Chemical or Acros Organics and dried by standard procedures. The 6-aminobenzothiazole **1a**[28] and 6-amino-2-methylbenzothiazole **1b**[29] were prepared according to the literature. The copper(I) thiophene-2-carboxilate (CuTC) was prepared according to the literature.[16]

4.2. Procedure for the preparation of 6-iodobenzothiazole derivatives 2a and 2b

To a mixture of concd H_2SO_4 (45 mL) and $NaNO_2$ (3.04 g, 44 mmol) warmed to 70 °C for 15 min then cooled to 40 °C, 6-aminobenzothiazole **1a** (6.0 g, 40 mmol) or 6-amino-2-methylbenzothiazole **1b** (6.57 g, 40 mmol) in acetic acid (80 mL) was added and stirred at rt for 30 min. A stirred solution of KI (7.32 g, 44 mmol) in water (70 mL) was heated to 70 °C, and the previously prepared diazonium salt was added. After 30 min the reaction mixture was poured onto ice and the obtained crude product was filtered off, washed with water, and dissolved in dichloromethane. The dichloromethane solution was treated with 10% $Na_2S_2O_3$, washed with water, and dried. The solvent was concentrated, and the residue purified by chromatography (silica gel/dichloromethane).

*4.2.1. 6-Iodobenzothiazole **2a**[14].* Yield of colorless solid was 7.15 g (68.5%), mp 80–81 °C (lit. 79–80 °C). ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ=7.87 (dd, 1H, *J*=1.8, 8.6 Hz, H-5), 7.87 (d, 1H, *J*=8.6 Hz, H-4), 8.60 (d, 1H, *J*=1.8 Hz, H-7), 9.34 (s, 1H, H-2).

*4.2.2. 6-Iodo-2-methylbenzothiazole **2b**[29].* Yield of colorless solid was 6.72 g (61.1%), mp 139–141 °C (lit. 140–141 °C). ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ=2.79 (s, 3H, H–CH_3), 7.70 (d, 1H, *J*=8.5 Hz, H-4), 7.77 (dd, 1H, *J*=1.6, 8.5 Hz, H-5), 8.46 (d, 1H, *J*=1.5 Hz, H-7).

4.3. Procedure for the preparation of 6-iodo-7-nitrobenzothiazole derivatives 3a and 3b

The 6-iodobenzothiazole **2a** (2.61 g, 10 mmol) or 6-iodo-2-methylbenzothiazole **2b** (2.75 g, 10 mmol) was added to a solution of KNO_3 (2.1 g, 20 mmol) in concd H_2SO_4 (12 mL), and the reaction mixture stirred at rt for 5 days. The reaction mixture was poured onto crushed ice, and neutralized with ammonia. The obtained crystals were filtered off, and washed with water. The crude product was purified by crystallization.

*4.3.1. 6-Iodo-7-nitrobenzothiazole **3a**[14].* Crystallization from toluene/cyclohexane (charcoal) gave 2.50 g (81.7%) of yellow crystals, mp 188–189 °C (lit. 188–189 °C). ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ=8.12 (d, 1H, *J*=8.5 Hz, H–Ar), 8.34 (d, 1H, *J*=8.5 Hz, H–Ar), 9.52 (s, 1H, H-2).

*4.3.2. 6-Iodo-2-methyl-7-nitrobenzothiazole **3b**.* Crystallization from toluene (charcoal) gave 2.31 g (72.2%) of yellow crystals, mp 172–173 °C. IR (ATR): υ=1587, 1504, 1412, 1319, 1265, 1161, 997, 817, 760 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ=2.79 (s, 3H, H–CH_3), 7.88 (d, 1H, *J*=8.4 Hz, H–Ar), 8.22 (d, 1H, *J*=8.4 Hz, H–Ar). ^{13}C NMR (151 MHz, DMSO-*d*$_6$): δ=19.2 (q), 87.0 (s), 127.8 (d), 132.6 (s), 140.0 (d), 144.1 (s), 154.2 (s), 171.5 (s). LC–MS (ESI): *m*/*z*=321.0 (MH$^+$). Anal. Calcd for $C_8H_5IN_2O_2S$ (320.11): C, 30.02; H, 1.57; N, 8.75. Found: C, 30.11; H, 1.52; N, 8.89.

4.4. Procedure for the preparation of 6-amino-7-iodobenzothiazole derivatives 4a and 4b

A solution of ICl (15.0 g, 0.1 mol) in diluted HCl (18 mL of concd HCl and 60 mL of water) was added to a solution of 6-

aminobenzothiazole **1a** (12.0 g, 80 mmol) or 6-amino-2-methylbenzothiazole **1b** (13.1 g, 80 mmol) in diluted HCl (9 mL of concd HCl and 120 mL of water). The reaction mixture was stirred at rt for 1 h and neutralized with a saturated solution of $NaHCO_3$. The crude product was purified by dry column chromatography[30] on silica gel with petrolether/ethyl acetate.

4.4.1. 6-Amino-7-iodobenzothiazole ***4a***[14]. Yield of colorless solid was 15.9 g (72.0%), mp 130–132 °C (lit. mp 130–132 °C). ^{1}H NMR (300 MHz, DMSO-d_6): δ=5.59 (s, 2H, H–NH_2), 6.96 (d, 1H, J=8.7 Hz, H-5), 7.76 (d, 1H, J=8.7 Hz, H-4), 9.00 (s 1H, H-2).

4.4.2. 6-Amino-7-iodo-2-methylbenzothiazole ***4b***. Yield of colorless solid was 15.6 g (67.2%), mp 119–121 °C. IR (ATR): υ=3389, 3285, 3188, 1601, 1591, 1520, 1452, 1391, 1173, 804, 725, 651 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.66 (s, 3H, H–CH_3), 5.41 (s, 2H, H–NH_2), 6.87 (d, 1H, J=8.6 Hz, H–Ar), 7.58 (d, 1H, J=8.6 Hz, H–Ar). ^{13}C NMR (75 MHz, DMSO-d_6): δ=20.0 (q), 70.3 (s), 114.0 (d), 122.6 (d), 142.4 (s), 144.8 (s), 147.4 (s), 159.6 (s). LC–MS (ESI): m/z=291.0 (MH$^+$). Anal. Calcd for $C_8H_7IN_2S$ (290.12): C, 33.12; H, 2.43; N, 9.66. Found: C, 33.21; H, 2.46; N, 9.78.

4.5. Procedure for the preparation of 6-acetylamino-7-iodobenzothiazole derivatives 5a and 5b

To a stirred solution of 6-amino-7-iodobenzothiazole **4a** (2.75 g, 10 mmol) or 6-amino-7-iodo-2-methylbenzothiazole **4b** (2.90 g, 10 mmol), and *N*,*N*-diisopropylethylamine (1.75 mL) in 1,2-dichloroethane (40 mL), acetyl chloride (1.42 mL, 20 mmol) was added dropwise. The reaction mixture was stirred at rt for 2 h, and left in a refrigerator overnight (5 °C). The crude product was filtered off, washed with 1,2-dichloroethane and water, and purified by crystallization.

4.5.1. 6-Acetylamino-7-iodobenzothiazole ***5a***[14]. Crystallization from EtOH/dichloromethane (charcoal) gave 2.88 g (93.6%) of colorless crystals, mp 243–244 °C (lit. mp 244 °C). ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.10 (s, 3H, H–OCCH_3), 7.53 (d, 1H, J=8.8 Hz, H–Ar), 8.06 (d, 1H, J=8.7 Hz, H–Ar), 9.47 (s, 1H, H–NHCO), 9.74 (s, 1H, H-2).

4.5.2. 6-Acetylamino-7-iodo-2-methylbenzothiazole ***5b***. Crystallization from EtOH/H_2O (charcoal) gave 3.06 g (92.1%) of colorless crystals, mp 235–236 °C. IR (ATR): υ=3265, 1647, 1587, 1504, 1363, 1267, 1091, 810, 653 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6, 60 °C): δ=2.07 (s, 3H, H–OCCH_3), 2.77 (s, 3H, H–CH_3), 7.44 (d, 1H, J=8.5 Hz, H–Ar), 7.85 (d, 1H, J=8.5 Hz, H–Ar), 9.45 (s, 1H, H–NHCO). ^{13}C NMR (75 MHz, DMSO-d_6, 60 °C): δ=19.8 (q), 23.0 (q), 88.2 (s), 121.5 (d), 125.3 (d), 137.5 (s), 144.0 (s), 147.9 (s), 165.6 (s), 168.6. LC–MS (ESI): m/z=333.0 (MH$^+$). Anal. Calcd for $C_{10}H_9IN_2OS$ (332.16): C, 36.16; H, 2.73; N, 8.43. Found: C, 36.02; H, 2.88; N, 8.54.

4.6. Procedure for the preparation of *o*,*o*′-dinitrosubstituted bibenzothiazole derivatives 6a and 6b

To a solution of 6-iodo-7-nitrobenzothiazole **3a** (3.02 g, 10 mmol) or 6-iodo-2-methyl-7-nitrobenzothiazole **3b** (3.20 g, 10 mmol) in NMP (40 mL), CuTC (4.7 g, 25 mmol) was added under nitrogen. The flask was stoppered, and the reaction mixture was stirred at rt for 3 h. The mixture was poured into ammonia (750 mL, 5% aq solution), and cooled overnight. The crude product was filtered off, washed with diluted ammonia, water, and purified by crystallization.

4.6.1. 7,7′*-Dinitro-6,6*′*-bibenzothiazole* ***6a***[14]. Crystallization from xylene (charcoal) gave 1.65 g (92.2%) of yellow crystals, mp>300 °C (lit. mp 312–313 °C). ^{1}H NMR (600 MHz, DMSO-d_6): δ=7.68 (d, 2H, J=8.2 Hz, H–Ar), 8.56 (d, 2H, J=8.2 Hz, H–Ar), 9.65 (s, 2H, H-2, H-2′).

4.6.2. 2,2′*-Dimethyl-7,7*′*-dinitro-6,6*′*-bibenzothiazole* ***6b***. Crystallization from xylene (charcoal) gave 1.76 g (91.3%) of yellow crystals, mp 278–280 °C. IR (ATR): υ=3043, 1603, 1542, 1508, 1425, 1321, 1296, 1267, 1178, 1001, 825, 650 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6, 50 °C): δ=2.91 (s, 6H, H–CH_3), 7.64 (d, 2H, J=8.2 Hz, H–Ar), 8.40 (d, 2H, J=8.2 Hz, H–Ar). ^{13}C NMR (151 MHz, DMSO-d_6, 50 °C): δ=19.3 (q), 127.9 (d), 129.1 (d), 131.8 (s), 132.8 (s), 139.8 (s), 154.4 (s), 172.3 (s). LC–MS (ESI): m/z=387.1 (MH$^+$). Anal. Calcd for $C_{16}H_{10}N_4O_4S_2$ (386.4): C, 49.73; H, 2.61; N, 14.50. Found: C, 49.70; H, 2.55; N, 14.41.

4.7. Procedure for the preparation of *o*,*o*′-diacetylaminosubstituted bibenzothiazole derivatives 7a and 7b

To a stirred solution of 6-acetylamino-7-iodobenzothiazole **5a** (3.18 g, 10 mmol) or 6-acetylamino-7-iodo-2-methylbenzothiazole **5b** (3.32 g, 10 mmol) in NMP (50 mL), CuTC (4.7 g, 25 mmol) was added under nitrogen. The flask was stoppered, and the reaction mixture was stirred at rt for 4 days. The mixture was poured in ammonia (750 mL, 5% aq solution), and left in a refrigerator for 3 days (5 °C). The obtained crude product was filtered off, washed with diluted ammonia, water, and purified by crystallization.

4.7.1. 6,6′*-Diacetylamino-7,7*′*-bibenzothiazole* ***7a***[14]. Crystallization from DMF gave 1.76 g (92.1%) of colorless crystals, mp>300 °C (lit. mp>300 °C). ^{1}H NMR (300 MHz, DMSO-d_6): δ=1.77 (s, 6H, H–OCCH_3), 7.88 (d, 2H, J=8.7 Hz, H–Ar), 8.15 (d, 2H, J=8.7 Hz, H–Ar), 9.16 (s, 2H, H–NHCO), 9.33 (s, 2H, H-2, H-2′).

4.7.2. 6,6′*-Diacetylamino-2,2*′*-dimethyl-7,7*′*-bibenzothiazole* ***7b***. Crystallization from EtOH gave 1.78 g (86.8%) of colorless crystals, mp 298–300 °C. IR (ATR): υ=3172, 3072, 2959, 1674, 1585, 1514, 1436, 1394, 1362, 1296, 1245, 1178, 1011, 818, 582 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ=1.79 (s, 6H, H–OCCH_3), 2.71 (s, 6H, H–CH_3), 7.78 (d, 2H, J=8.7 Hz, H–Ar), 9.07 (s, 2H, H–NHCO), 7.96 (d, 2H, J=8.7 Hz, H–Ar). ^{13}C NMR (75 MHz, DMSO-d_6): δ=20.1 (q), 23.5 (q), 122.4 (d), 124.6 (s), 124.9 (d), 133.5 (s), 136.9 (s), 150.6 (s), 167.0 (s), 169.4 (s). LC–MS (ESI): m/z=411.1 (MH$^+$). Anal. Calcd for $C_{20}H_{18}N_4O_2S_2$ (410.51): C, 58.52; H, 4.42; N, 13.65. Found: C, 58.41; H, 4.48; N, 13.71.

4.8. Procedure for the reduction of *o*,*o*′-dinitrobibenzothiazole derivatives 6a and 6b

To a solution of $SnCl_2 \times 2H_2O$ (3.61 g, 16 mmol) in MeOH (10 mL) and concd HCl (10 mL), 7,7′-dinitro-6,6′-bibenzothiazole **6a** (0.358 g, 1.0 mmol) or 2,2′-dimethyl-7,7′-dinitro-6,6′-bibenzothiazole **6b** (0.386 g, 1.0 mmol) was added. The reaction mixture was heated with stirring at 80–85 °C for 0.5 h, poured into 2 M HCl (40 mL), and the pale yellow solid was filtered immediately, washed with 2 M HCl, water, and dried giving the mixture of products **9a** and **10a** or **9b** and **10b**. The combined filtrates were cooled and made alkaline pH>12 with 20% NaOH. The corresponding diamine **8a** or **8b** was filtered off, washed with water, and purified by crystallization.

4.8.1. 7,7′*-Diamino-6,6*′*-bibenzothiazole* ***8a***. According to the above procedure using 16 mmol of $SnCl_2 \times 2H_2O$, and crystallization from toluene gave 0.247 g (82.9%) of pale yellow crystals, mp 203–205 °C. IR (ATR): υ=3373, 3262, 3149, 3080, 1629, 1544, 1456, 1401, 853 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6): δ=5.08 (s, 4H, H–NH_2), 7.14 (d, 2H, J=8.1 Hz, H–Ar), 7.40 (d, 2H, J=8.2 Hz, H–Ar), 9.24 (s, 2H, H-2, H-2′). ^{13}C NMR (151 MHz, DMSO-d_6): δ=111.8 (d), 118.0 (s), 120.4 (s), 129.7 (d), 140.1 (s), 154.0 (s), 155.0 (d). LC–MS (ESI):

m/z=299.1 (MH$^+$). Anal. Calcd for $C_{14}H_{10}N_4S_2$ (298.39): C, 56.35; H, 3.38; N, 18.78. Found: C, 56.12; H, 3.17; N, 18.42.

4.8.2. 2,2′-Dimethyl-7,7′-diamino-6,6′-bibenzothiazole ***8b***. According to the above procedure using 16 mmol of $SnCl_2{\times}2H_2O$, and crystallization from EtOH gave 0.268 g (82.2%) of pale yellow crystals, mp 219–221 °C. IR (ATR): υ=3327, 3217, 1623, 1518, 1462, 1412, 1180, 1099, 793, 644 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6): δ=2.60 (s, 6H, H–CH_3), 4.95 (s, 4H, H–NH_2), 7.13 (d, 2H, J=8.2 Hz, H–Ar), 7.29 (d, 2H, J=8.1 Hz, H–Ar). ^{13}C NMR (151 MHz, DMSO-d_6): δ=19.8 (q), 111.0 (d), 117.8 (s), 121.6 (s), 129.4 (d), 139.5 (s), 153.8 (s), 165.8 (s). LC–MS (ESI): m/z=327.2 (MH$^+$). Anal. Calcd for $C_{16}H_{14}N_4S_2$ (326.44): C, 58.87; H, 4.32; N, 17.16. Found: C, 58.78; H, 4.47; N, 17.08.

4.8.3. Benzothiazolo[7,6-c]thiazolo[4,5-h]cinnoline ***9a***. According to the above procedure using 16 mmol of $SnCl_2{\times}2H_2O$, and crystallization from DMF gave 0.016 g (5.4%) of colorless crystals, mp>300 °C. IR (ATR): υ=3076, 1599, 1546, 1444, 1377, 1296, 1128, 847, 808, 496 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6, 80 °C): δ=8.72 (d, 2H, J=8.9 Hz, H–Ar), 9.10 (d, 2H, J=8.9 Hz, H–Ar), 9.72 (s, 2H, H-2, H-2′). LC–MS (ESI): m/z=295.1 (MH$^+$). Anal. Calcd for $C_{14}H_6N_4S_2$ (294.35): C, 57.12; H, 2.05; N, 19.03. Found: C, 56.91; H, 2.12; N, 18.86.

4.8.4. 2,9-Dimethylbenzothiazolo[7,6-c]thiazolo[4,5-h]cinnoline ***9b***. According to the above procedure using 16 mmol of $SnCl_2{\times}2H_2O$, and crystallization from DMF gave 0.014 g (4.3%) of pale yellow crystals, mp>300 °C. IR (ATR): υ=3068, 2918, 1595, 1535, 1506, 1373, 1165, 1080, 814, 642, 611 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6, 80 °C): δ=2.99 (s, 6H, H–CH_3), 8.48 (d, 2H, J=8.9 Hz, H–Ar), 8.91 (d, 2H, J=8.9 Hz, H–Ar). ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.03 (s, 6H, H–CH_3), 8.45 (d, 2H, J=8.9 Hz, H–Ar), 8.65 (d, 2H, J=8.9 Hz, H–Ar). LC–MS (ESI): m/z=323.1 (MH$^+$). Anal. Calcd for $C_{16}H_{10}N_4S_2$ (322.41): C, 59.61; H, 3.13; N, 17.38. Found: C, 59.64; H, 3.12; N, 17.26.

4.8.5. 2,9-Dimethylbenzothiazolo[7,6-c]thiazolo[4,5-h]cinnoline-11-N-oxide ***10b***. According to the above procedure using 4 mmol of $SnCl_2{\times}2H_2O$, and several crystallization from toluene gave 0.088 g (25.9%) of yellow crystals, mp>300 °C. IR (ATR): υ=3097, 2920, 1593, 1506, 1473, 1431, 1340, 1286, 1092, 812, 651, 580 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.98 (s, 3H, H–CH_3), 3.00 (s, 3H, H–CH_3), 8.29 (d, 1H, J=8.9 Hz, H–Ar), 8.52 (d, 1H, J=8.9 Hz, H–Ar), 8.54 (d, 1H, J=8.9 Hz, H–Ar), 8.66 (d, 1H, J=8.9 Hz, H–Ar). LC–MS (ESI): m/z=339.1 (MH$^+$). Anal. Calcd for $C_{16}H_{10}N_4OS_2$ (338.41): C, 56.79; H, 2.98; N, 16.56. Found: C, 56.89; H, 3.02; N, 16.61.

4.9. Procedure for the preparation of *o,o′*-diaminosubstituted 7,7′-bibenzothiazole derivatives 11a and 11b

A solution of 6,6′-diacetylamino-7,7′-bibenzothiazole (**7a**) (1.15 g, 3 mmol) or 6,6′-diacetylamino-2,2′-dimethyl-7,7′-bibenzothiazole (**7b**) (1.23 g, 3 mmol) in 75% H_2SO_4 (15 mL) was stirred at 110 °C for 30 min. The reaction mixture was poured into water (300 mL), heated to boil (charcoal), filtered, and neutralized with concd ammonia. The obtained crude product was filtered off, washed with water, and purified by crystallization.

4.9.1. 6,6′-Diamino-7,7′-bibenzothiazole ***11a***. Crystallization from xylene gave 0.725 g (81.0%) of colorless crystals, mp 286–288 °C. IR (ATR): υ=3408, 3332, 3211, 3077, 1627, 1585, 1468, 870, 816 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ=4.96 (s, 4H, H–NH_2), 7.07 (d, 2H, J=8.7 Hz, H–Ar), 7.84 (d, 2H, J=8.7 Hz, H–Ar), 8.88 (s, 2H, H-2, H-2′). ^{13}C NMR (75 MHz, DMSO-d_6): δ=111.6 (s), 115.8 (d), 123.3 (d), 135.7 (s), 143.9 (s), 144.8 (s). LC–MS (ESI): m/z=299.1 (MH$^+$). Anal. Calcd for $C_{14}H_{10}N_4S_2$ (298.39): C, 56.35; H, 3.38; N, 18.78. Found: C, 56.21; H, 3.51; N, 18.91.

4.9.2. 6,6′-Diamino-2,2′-dimethyl-7,7′-bibenzothiazole ***11b***. Crystallization from DMF gave 0.804 g (82.1%) of colorless crystals, mp>300 °C. IR (ATR): υ=3412, 3317, 3207, 1620, 1587, 1463, 1406, 1172, 812, 651 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6, 80 °C): δ=2.60 (s, 6H, H–CH_3), 4.59 (s, 4H, H–NH_2), 6.99 (d, 2H, J=8.7 Hz, H–Ar), 7.64 (d, 2H, J=8.7 Hz, H–Ar). ^{13}C NMR (151 MHz, DMSO-d_6, 80 °C): δ=19.3 (q), 112.1 (s), 115.2 (d), 122.2 (d), 137.2 (s), 143.1 (s), 144.7 (s), 160.8 (s). LC–MS (ESI): m/z=327.2 (MH$^+$). Anal. Calcd for $C_{16}H_{14}N_4S_2$ (326.44): C, 58.87; H, 4.32; N, 17.16. Found: C, 58.98; H, 4.23; N, 17.00.

4.10. Procedure for the oxidative cyclization of *o,o′*-diaminosubstituted bibenzothiazole 8a, 8b, and 11a

To a stirred solution of *o,o′*-diaminobibenzothiazole (**8a**, **9a** or **9b**) (1 mmol) in dry toluene (180 mL) at 80 °C, diacetoxyiodobenzene (0.322 g, 1 mmol) was added. The reaction mixture was stirred at 80 °C for 24 h and the precipitated crude product filtered off. To the mother liquor, diacetoxyiodobenzene (0.322 g, 1 mmol) was added, and the reaction mixture stirred at rt for an additional 24 h. The precipitated crude product was filtered off, and the combined products were purified by crystallization.

4.10.1. Benzothiazolo[7,6-c]thiazolo[4,5-h]cinnoline ***9a***. Crystallization from DMF gave 0.186 g (63.3%) of colorless crystals, for which spectroscopic data are given in Section 4.8.3.

4.10.2. 2,9-Dimethylbenzothiazolo[7,6-c]thiazolo[4,5-h]cinnoline ***9b***. Crystallization from DMF gave 0.188 g (58.4%) of pale yellow crystals, for which spectroscopic data are given in Section 4.8.4.

4.10.3. Benzothiazolo[6,7-c]thiazolo[5,4-f]cinnoline ***12a***. Crystallization from DMF gave 0.207 g (70.4%) of colorless crystals, mp>300 °C. IR (ATR): υ=3067, 3039, 1450, 1354, 1101, 884, 858, 816 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6, 80 °C): δ=8.81 (d, 2H, J=9.0 Hz, H–Ar), 8.93 (d, 2H, J=9.0 Hz, H–Ar), 9.82 (s, 2H, H-2, H-11). LC–MS (ESI): m/z=295.1 (MH$^+$). Anal. Calcd for $C_{14}H_6N_4S_2$ (294.35): C, 57.12; H, 2.05; N, 19.03. Found: C, 57.08; H, 2.09; N, 18.93.

4.11. Procedure for the thermal cyclization of *o,o′*-diaminosubstituted bibenzothiazoles 8a, 8b, 11a, and 11b

A stirred solution of *o,o′*-diaminobibenzothiazoles (**8a**, **8b**, **11a** or **11b**) (1 mmol) in 85% H_3PO_4 (10 mL) equipped with a reflux condenser was heated at 200 °C for 1.5 h. The cooled reaction mixture was poured into water (150 mL), neutralized with ammonia, and the resulting precipitate filtered off, washed with water, and purified by crystallization.

4.11.1. 11H-Dithiazolo[5,4-a:4′,5′-i]carbazole ***13a***. Crystallization from EtOH/H_2O gave 0.166 g (59.0%) of colorless crystals, mp>300 °C. IR (ATR): υ=3155, 3084, 1620, 1552, 1410, 1228, 1007, 795, 598, 498 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.97 (d, 2H, J=8.5 Hz, H–Ar), 8.37 (d, 2H, J=8.5 Hz, H–Ar), 9.41 (s, 2H, H-2, H-9), 12.79 (s, 1H, H–NH). ^{13}C NMR (151 MHz, DMSO-d_6): δ=115.1 (d), 116.9 (s), 118.8 (s), 119.5 (d), 133.4 (s), 152.6 (s), 153.7 (d). LC–MS (ESI): m/z=282.0 (MH$^+$). Anal. Calcd for $C_{14}H_7N_3S_2$ (281.36): C, 59.76; H, 2.51; N, 14.93. Found: C, 59.84; H, 2.55; N, 14.79.

4.11.2. 2,9-Dimethyl-11H-dithiazolo[5,4-a:4′,5′-i]carbazole ***13b***. Crystallization from EtOH/H_2O gave 0.234 g (72.3%) of colorless crystals, mp 267–269 °C. IR (ATR): υ=3115, 3074, 3026, 2899, 2848, 1614, 1521, 1427, 1338, 1213, 1178, 786, 647, 596 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6): δ=2.88 (s, 6H, H–CH_3), 7.78 (d, 2H, J=8.4 Hz, H–Ar), 8.25 (d, 2H, J=8.4 Hz, H–Ar), 12.46 (s, 1H, H–NH). ^{13}C NMR (151 MHz, DMSO-d_6): δ=19.7 (q), 114.1 (d), 117.9 (s), 118.3 (d), 119.3 (s), 133.1 (s), 152.2 (s), 164.5 (s). LC–MS (ESI): m/z=310.1 (MH$^+$). Anal. Calcd for $C_{16}H_{11}N_3S_2$ (309.41): C, 62.11; H, 3.58; N, 13.58. Found: C, 62.22; H, 3.46; N, 13.71.

4.11.3. 6H-Dithiazolo[4,5-c:5′,4′-g]carbazole ***14a***. Crystallization from DMF/H_2O gave 0.184 g (65.4%) of colorless crystals, mp>300 °C. IR (ATR): υ=3184, 3116, 3022, 1587, 1458, 1390, 1306, 1227, 876, 785, 694 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6, 80 °C): δ=7.82 (d, 2H, J=8.8 Hz, H–Ar), 8.17 (d, 2H, J=8.8 Hz, H–Ar), 9.29 (s, 2H, H-2, H-10), 12.07 (s, 1H, H–NH). ^{13}C NMR (75 MHz, DMSO-d_6, 80 °C): δ=150.9 (d), 148.9 (s), 137.9 (s), 126.4 (s), 121.2 (d), 114.8 (s), 111.9 (d). LC–MS (ESI): m/z=282.0 (MH$^+$). Anal. Calcd for $C_{14}H_7N_3S_2$ (281.36): C, 59.76; H, 2.51; N, 14.93. Found: C, 59.93; H, 2.48; N, 14.77.

4.11.4. 2,10-Dimethyl-6H-dithiazolo[4,5-c:5′,4′-g]carbazole ***14b***. Crystallization from DMF/H_2O gave 0.234 g (75.7%) of colorless crystals, mp>300 °C. IR (ATR): υ=3188, 3138, 3037, 2937, 1618, 1585, 1520, 1425, 1402, 1308, 1176, 874, 800, 617 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.88 (s, 6H, H–CH_3), 7.71 (d, 2H, J=8.7 Hz, H–Ar), 7.98 (d, 2H, J=8.7 Hz, H–Ar), 12.13 (s, 1H, H–NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ=162.1 (s), 148.1 (s), 137.4 (s), 127.3 (s), 120.4 (d), 114.3 (s), 111.3 (d), 19.9 (q). LC–MS (ESI): m/z=310.1 (MH$^+$). Anal. Calcd for $C_{16}H_{11}N_3S_2$ (309.41): C, 62.11; H, 3.58; N, 13.58. Found: C, 62.01; H, 3.67; N, 13.66.

4.12. Computational details

All quantum-mechanical calculations were performed with the Gaussian 09 program.[31] Geometries of all reaction intermediates and cyclization transition structures of the acid-catalyzed reduction–cyclization mechanism were fully optimized at B3LYP/6-311++G(d,p) level of theory, previously established as adequate for this type of calculation.[32] Open-shell species were treated with a spin-unrestricted approach (UB3LYP). Nonspecific medium effects (in water) were modeled using IEF-PCM method as implemented in Gaussian 09. At each stationary point, a frequency calculation was performed at the same level of theory to characterize the geometry as a minimum or transition structure. Single-electron transfer reaction energies were calculated from the corresponding theoretical adiabatic electron affinities and experimental standard Sn^{4+}/Sn^{2+} one-electron reduction potential. Protonation reaction energies were calculated using the proton solvation value obtained from a cluster-continuum approach.[33] As a check of B3LYP results, IEF-PCM/MP2(fc)/6-311++G(d,p) single point calculations at B3LYP geometries were also performed. Results of these and other calculations, as well as full discussion of the reduction–cyclization mechanism, will be published in a separate computational paper.

Acknowledgements

This work was financially supported by Ministry of Science, Education, and Sports of The Republic of Croatia (grants nos. 117-0000000-3283, 119-1191342-1339, 125-0982464-1356). The authors would also like to thank The University Computing Centre of The University of Zagreb (SRCE) for the generous donation of computer time on the Isabella cluster.

References and notes

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