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Notiz/Note

4*H*,5*H*-Benzo[1,2-*c*;3,4-*c'*]bis[1,2,5]thiadiazole-4,5-dione

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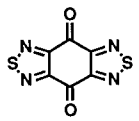
4*H*,5*H*-Benzo[1,2-*c*;3,4-*c'*]bis[1,2,5]thiadiazole-4,5-dione (**2**) was prepared by oxidation of 4-bromobenzobis[1,2,5]thiadiazole (**3d**) with nitric acid and subsequently converted into 5,6-dihydroxybenzenetetramine dihydrochloride (**10**) and the dimethoxy derivative **13**. Treatment of the 4-hydroxy derivative **3a** with chromium(VI) reagents led to cleavage of the benzene ring, giving dicarboxylic acid **4**.

4*H*,8*H*-Benzo[1,2-*c*;4,5-*c'*]bis[1,2,5]thiadiazole-4,8-dione (**1**) was prepared by the reaction of chloranil with ammonia followed by the ring closure of the obtained tetraamino-*p*-quinone with thionyl chloride[1]. As tetraamino-*o*-quinone seems to be hardly available, the above-mentioned method is obviously unapplied to the preparation of 4*H*,5*H*-benzo[1,2-*c*;3,4-*c'*]bis[1,2,5]thiadiazole-4,5-dione (**2**), which is an interesting building block for hetrocyclic analogues of triphenylene and also a precursor of benzenetetramine bearing an oxygen function each in the 5- and 6-positions. Since a series of 4-substituted benzo[1,2-*c*;3,4-*c'*]bis[1,2,5]thiadiazoles **3a**–**d** have become accessible[2], we investigated the oxidation of **3** as a preparative method of **2**.



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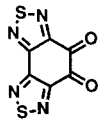
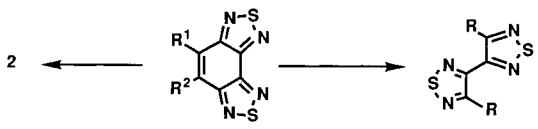


2

Due to the elcctron-withdrawing 1,2,5-thiadiazole ring, Fremy's salt[3] is ineffective for the oxidation of 4-hydroxybenzo[1,2-*c*;3,4-*c'*]bis[1,2,5]thiadiazole (**3a**), resulting in the recovery of **3a** in 70% yield. Treatment of **3a** with chromium(VI) oxide led to cleavage of the central benzene ring to afford dicarboxylic acid **4** in 60% yield. Compound **4** was converted into the diester **5** in 68% yield, which was reduced to the diol **6** in 68% yield. The desired quinone **2** was obtained as a stable yellow crystalline compound in the oxidation of **3a** with copper(II) nitrate; the yield was, however, poor (5%). The oxidation of **3a** with nitric acid furnished only a complex mixture of unidentified products.



3

	R^1	R^2
a	OH	H
b	OH	CH_2=CH-CH_2
c	MeO	H
d	Br	H

4-6

	R
4	CO_2H
5	CO_2Me
6	CH_2OH

Treatment of the 3-allyl-4-hydroxy derivative with chromium(VI) oxide gave **4**, albeit with a poor yield (6%), and unchanged **3b** was recovered in 34% yield. 4-Methoxybenzo[1,2-*c*;3,4-*c'*]bis[1,2,5]thiadiazole (**3c**) and its bromo derivative **3d** are inert towards chromium(VI) oxide and sodium dichromate; the starting materials were recovered in 60–90% yields.

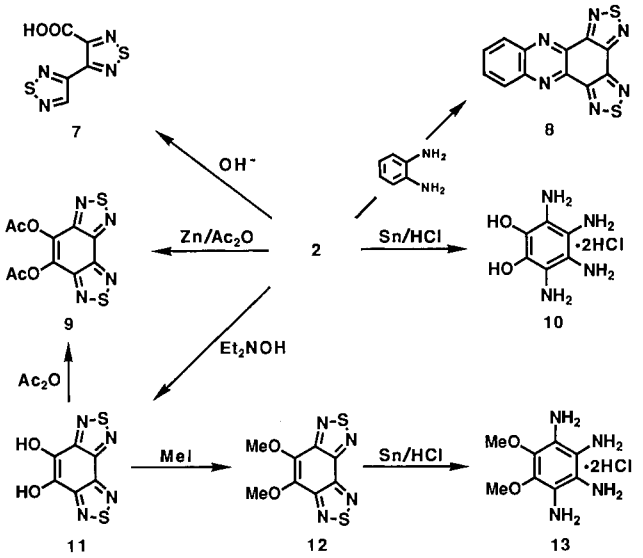
o-Quinone **2** was finally obtained in 74% yield, when **3d** was oxidized with nitric acid in sulfuric acid at 80–90°C for 4 h. The application of a higher reaction temperature (100–105°C) and a prolonged oxidation time (10 h) caused a decrease in the yield (33%).

In ^{13}C-NMR spectrum, **2** shows the signal of the carbonyl carbon atoms at $\delta = 169.9$, similar to the *p*-isomer **1** ($\delta = 168.7$)[1] but at ca. 10 ppm higher field than phenanthrene quinone, the dibenzo analogue of **2**. The electronic spectrum of **2** shows an absorption band at $\lambda = 309$ nm, which is red-shifted by 19 nm, as compared to **1** ($\lambda = 290$ nm)[1].

Under basic conditions, **2** is unstable; treatment of **2** with aqueous potassium hydroxide at 80–90°C for 2 h destroyed the quinone structure, giving monocarboxylic acid **7** in 44% yield. The reaction of **2** with *o*-phenylenediamine afforded phenazine **8**, as expected.

Stable 4,5-dihydroxybenzo[1,2-*c*;3,4-*c'*]bis[1,2,5]thiadiazole (**11**) was obtained by reduction of **2** with $NaBH_4$ (43%) and with *N*,*N*-diethylhydroxylamine[4] (94%). Compound **11** was easily *O*-methylated to **12** in 64% yield. Treatment of **11** with acetic anhydride furnished diacetate **9** in 67% yield, wich was also obtained directly by reduction of **2** with Zn in acetic anhydride, but the yield was poor (16%).

The preparation of benzenetetramines and naphthalenetetramines by the reduction of the corresponding aromatic bis[1,2,5]-thiadiazolo compounds with tin in concentrated hydrochloric acid has been reported[2,5,6]. A similar reduction of **2** and **12** gave the expected dihydrochlorides of 5,6-dihydroxybenzenetetramine **10** and the 5,6-dimethoxy derivative **13**, the first benzene-1,2,3,4-tetra-



mine derivative with two functional groups at the ring, in 53 and 37% yields, respectively.

Experimental

Melting points: uncorrected. — IR (KBr): Jasco IR-700. — ^{1}H and ^{13}C NMR: Jeol GSX-270; 270 MHz and 68 MHz, respectively; TMS as a reference unless stated otherwise. — MS: Jeol JMS-01SG-2; EI (75 eV). — Elemental analyses: Yanaco MT-5.

4H,5H-Benzo[1,2-c;3,4-c']bis[1,2,5]thiadiazole-4,5-dione (**2**): To a mixture of **3d** (136 mg, 0.50 mmol) and concentrated sulfuric acid (2.00 ml) cooled in an ice bath, a cold mixture of concentrated nitric acid ($d = 1.38$) (0.16 ml) and concentrated sulfuric acid (1.00 ml) was added dropwise at 0°C for 10 min. Then the mixture was heated at 85—90°C for 4 h, poured into ice-cold water, and continuously extracted with chloroform for ca. 12 h. The organic layer was separated, dried ($MgSO_4$), and the solvent evaporated in vacuo to leave **2** (83 mg, 74%) which was recrystallized from acetic acid to afford orange plates of m.p. 272°C (in a sealed tube). — IR: $\tilde{\nu} = 1710\ cm^{-1}$, 1550, 1415, 1360, 1090, 1050, 840, 825, 805. — ^{13}C NMR ([D$_6$]-DMSO): $\delta = 152.87$, 155.26, 169.94. — MS, *m/z*: 224 [M$^+$]. — $C_6N_4O_2S_2$ (224.2): calcd. C 32.14, N 24.99; found C 32.46, N 25.12.

4-Hydroxybenzo[1,2-c;3,4-c']bis[1,2,5]thiadiazole (**3a**)[2]: A mixture of **3d** (181 mg, 0.66 mmol), hydroxylammonium chloride (340 mg, 4.90 mmol), potassium hydroxide (760 mg, 14.0 mmol), *tert*-butyl alcohol (5 ml), and dioxane (10 ml) was heated under reflux for 5 h. After it had been cooled to room temp., the insoluble solid was filtered off and dissolved in water. The aqueous solution was acidified with concentrated hydrochloric acid to pH = 1, and the precipitated solid (70 mg) was filtered. This solid was extracted with hot chloroform, and the extract was concentrated in vacuo to give **3a** (62 mg, 45%). The filtrate was extracted with chloroform and the extract dried ($MgSO_4$), then the solvent was evaporated in vacuo to afford additional **3a** (35 mg, 35%).

3,3'-Di(1,2,5-thiadiazol-3-yl)-4,4'-dicarboxylic Acid (**4**): Concentrated sulfuric acid (3.5 ml) was added dropwise to a mixture of **3a** (529 mg, 2.52 mmol) and chromium(VI) oxide (1.00 g, 6.60 mmol) in water (6.0 ml) during 5 min with external cooling, and then additional chromium(VI) oxide (1.00 g, 6.60 mmol) in water (10 ml) was added to the mixture. After it had been stirred at room temp. for 4 h, it was continuously extracted with chloroform for ca. 12 h. The organic layer was separated, dried ($MgSO_4$), and the solvent evaporated in vacuo to leave a residue which, on recrystallization from benzene/acetone (5:1), gave **4** (389 mg, 60%) as colorless prisms, m.p. 203—206°C (decomp.). — IR: $\tilde{\nu} = 1715\ cm^{-1}$, 1481, 1315, 1271, 1238, 1125, 1000, 861, 845, 832, 818, 702. — ^{13}C NMR ([D$_6$]DMSO): $\delta = 152.50$, 155.24, 160.46. — MS, *m/z*: 258 [M$^+$]. — $C_6H_2N_4O_4S_2$ (258.2): calcd. C 27.91, H 0.78, N 21.70; found C 27.94, H 0.99, N 21.52.

Dimethyl 3,3'-Di(1,2,5-thiadiazol-3-yl)-4,4'-dicarboxylate (**5**): A mixture of **4** (387 mg, 1.50 mmol), *p*-toluenesulfonic acid (292 mg), methanol (5.0 ml), and benzene (15 ml) in a flask equipped with a Dean-Stark trap was heated under reflux for 24 h, and the reaction mixture was diluted with water. The organic layer was separated, washed with saturated aqueous NaCl, dried ($MgSO_4$), and the solvents were evaporated in vacuo to leave a residue which, on recrystallization from benzene/hexane (1:3), gave **5** (292 mg, 68%) as colorless prisms, m.p. 220—221°C (decomp.). — IR: $\tilde{\nu} = 2960\ cm^{-1}$, 1730, 1715, 1465, 1450, 1410, 1370, 1355, 1300, 1260, 1220, 1110, 1005, 950, 920, 850, 840, 810, 800. — ^{1}H NMR ($CDCl_3$): $\delta = 3.86$ (s). — MS, *m/z*: 286 [M$^+$]. — $C_8H_6N_4O_4S_2$ (286.3): calcd. C 33.56, H 2.11, N 19.57; found C 33.66, H 2.26, N 19.68.

4,4'-Di(hydroxymethyl)-3,3'-di(1,2,5-tiadiazol-3-yl) (**6**): A mixture of **5** (275 mg, 0.96 mmol), $NaBH_4$ (838 mg, 22.2 mmol), and triethylamine (0.5 ml) in ethanol (10 ml) was stirred at room temp. for 16 h. The mixture was poured into water and extracted with dichloromethane. The organic extract was dried ($MgSO_4$), and the solvent evaporated in vacuo to leave a residue which, on recrystallization from ethyl acetate, gave **6** (156 mg, 68%) as colorless needles, m.p. 160—162°C. — IR: $\tilde{\nu} = 3240\ cm^{-1}$, 2990, 1480, 1430, 1410, 1315, 1250, 1225, 1090, 1070, 1000, 980, 850, 830. — ^{1}H NMR ($CDCl_3$): $\delta = 5.04$ (4H, d, $J = 6$ Hz, became s when treated with D_2O), 5.56 (2H, t, $J = 6$ Hz, D_2O exchange). — MS, *m/z*: 230 [M$^+$]. — $C_6H_6N_4O_2S_2$ (230.3): calcd. C 31.30, H 2.63, N 24.33; found C 31.22, H 2.67, N 23.86.

3,3'-(1,2,5-Thiadiazol-3-yl)-4-carboxylic Acid (**7**): A mixture of **2** (238 mg, 1.06 mmol) and 8.5% aqueous potassium hydroxide (25 ml) was heated at 80—90°C for 2 h. After it had been cooled to room temp., insoluble materials were filtered off. The filtrate was acidified with 6 N hydrochloric acid to pH = 1 and extracted with dichloromethane. The extract was dried ($MgSO_4$) and the solvent evaporated in vacuo to leave a residue which was dissolved in chloroform and then precipitated from the solution by the addition of hexane. Recrystallization of the precipitates from benzene/hexane gave **7** (99 mg, 44%) as colorless needles, m.p. 128—131°C. — IR: $\tilde{\nu} = 1713\ cm^{-1}$, 1460, 1390, 1335, 1294, 1231, 1157, 1056, 935, 868, 841, 806, 793, 769, 707. — ^{1}H NMR ([D$_6$]DMSO): $\delta = 9.33$ (s). — ^{13}C NMR ([D$_6$]DMSO): $\delta = 151.52$, 152.72, 153.03, 153.62, 161.85. — MS, *m/z*: 214 [M$^+$]. — $C_5H_2N_4O_2S_2$ (214.2): calcd. C 28.03, H 0.94, N 26.15; found C 28.16, H 1.20, N 25.90.

Phenazino[1,2-c;3,4-c']bis[1,2,5]thiadiazole (**8**): A mixture of **2** (114 mg, 0.51 mmol) and *o*-phenylenediamine (265 mg, 1.24 mmol) in acetic acid (10 ml) was heated under reflux for 17 h. The precipitate formed was collected by filtration and recrystallized from chloroform/hexane (1:1) to give **8** (102 mg, 68%) as pale brown plates, m.p. 390—392°C (decomp.). — IR: $\tilde{\nu} = 1535\ cm^{-1}$, 1505, 1475, 1390, 1350, 1335, 1210, 1135, 1090, 835, 820, 790, 770. — ^{1}H NMR ($CDCl_3$): $\delta = 8.06$ (2H, m), 8.55 (2H, m). — MS, *m/z*: 296 [M$^+$]. — $C_{12}H_4N_6S_2$ (296.3): calcd. C 48.64, H 1.36, N 28.36; found C 48.45, H 1.73, N 28.29.

4,5-Diacetoxybenzo[1,2-c;3,4-c']bis[1,2,5]thiadiazole (**9**): A mixture of **11** (135 mg, 0.60 mmol), acetic anhydride (5 ml), and concentrated sulfuric acid (6 drops) was stirred at room temp. for 10 min and subsequently heated at 80—100°C for 15 min. The reaction

mixture was then poured into water, neutralized with $NaHCO_3$, and filtered to give **9**. The filtrate was extracted with dichloromethane (3 × 20 ml), the extract dried ($MgSO_4$), and the solvent evaporated to afford additional **9**. Recrystallization from benzene/cyclohexane (1:4) furnished **9** (127 mg, 67%) as colorless needles, m.p. 199–202°C (in a seales tube). – IR: $\tilde{\nu} = 1790$ cm^{-1}, 1200, 1070, 840. – ^{1}H NMR ($CDCl_3$): $\delta = 2.52$ (s). – MS, *m/z*: 310 [M$^+$]. – $C_{10}H_6N_4O_4S_2$ (310.3): calcd. C 38.71, H 1.95, N 18.05; found C 38.45, H 2.05, N 17.64.

Dihydrochloride **10** *of 5,6-Dihydroxybenzenetetramine:* To a mixture of **2** (158 mg, 0.705 mmol) and powdered tin (843 mg, 7.10 mmol) in degassed dioxane (10 ml), concentrated hydrochloric acid (5.0 ml) was added at room temp., and the mixture was then stirred for 4 h at room temp. The precipitate formed was filtered and dissolved in hot methanol. To this solution, hexane/ethanol (5:1) was added to afford **10** (70 mg, 53%) as a pale brown powder, m.p. 180–210°C (decomp.). – IR: $\tilde{\nu} = 3350-2576$ cm^{-1}, 1635, 1559, 1505, 1484, 1323, 1253, 1174, 1133, 1062, 763. – ^{1}H NMR ([D$_6$]DMSO, DSS as a reference): $\delta = 3.47$ (br. s), 9.10 (br. s). – MS, *m/z*: 170 [M$^+$]. – $C_6H_{10}N_4O_2 \cdot 2$ HCl (243.1): calcd. C 29.65, H 4.98, N 23.05; found C 29.86, H 4.71, N 23.11.

4,5-Dihydroxybenzo[1,2-c;3,4-c']bis[1,2,5]thiadiazole (**11**): A mixture of *N,N*-diethylhydroxylamine (220 mg, 2.50 mmol) in degassed ethyl acetate (2.0 ml) was added to a amixture of **2** (331 mg, 1.48 mmol) in degassed ethyl acetate (20 ml) at room temp. The mixture was stirred at room temp. for 50 min and poured into water to give **11** (314 mg, 94%) as orange needles, m.p. 316–319°C (decomp.) (in a sealed tube). – IR: $\tilde{\nu} = 3526$ cm^{-1}, 3350, 3216, 1619, 1519, 832. – ^{1}H NMR ([D$_6$]DMSO): $\delta = 10.37$ (s). – ^{13}C NMR ([D$_6$]DMSO): $\delta = 134.7$, 143.4, 153.1. – MS, *m/z*: 226 [M$^+$]. – $C_6H_2N_4O_2S_2 \cdot 0.25$ H_2O (230.7): calcd. C 31.23, H 1.09, N 24.28; found C 31.27, H 1.08, N 24.52.

4,5-Dimethoxybenzo[1,2-c;3,4-c']bis[1,2,5]thiadiazole (**12**): A mixture of **11** (299 mg, 1.18 mmol), methyl iodide (1.68 g, 11.2 mmol), and potassium carbonate (1.10 g, 8.00 mmol) in DMF (10 ml) was heated at 100–110°C for 3 h and poured into water. Then the mixture was acidified with 10% hydrochloric acid (pH = 1) and the precipitate formed was collected by filtration; recrystallized from cyclohexane yielded **12** (191 mg, 64%) as pale brown needles, m.p. 143–146°C. – IR: $\tilde{\nu} = 2946$ cm^{-1}, 1593, 1526, 1499, 1396, 1252, 1095, 1078, 938, 891, 837, 822, 802. – ^{1}H NMR ($CDCl_3$): $\delta = 4.32$ (s). – ^{13}C NMR ($CDCl_3$): $\delta = 61.68$, 142.11, 145.27, 153.52. – MS, *m/z*: 254 [M$^+$]. – $C_8H_6N_4O_4S_2$ (254.3): calcd. C 37.79, H 2.38, N 22.03; found C 37.37, H 2.43, N 22.03.

Dihydrochloride **13** *of 5,6-Dimethoxybenzenetetramine:* To a mixture of **12** (153 mg, 0.62 mmol) and powdered tin (764 mg, 6.44 mmol) in degassed dioxane (10 ml), concentrated hydrochloric acid (5.0 ml) was added at room temp., and the mixture was stirred for 4 h at room temp. The precipitate formed was filtered and dissolved in methanol. To this solution, hexane/ethanol (12:1) was added to yield **13** (61 mg, 37%) as colorless powder, m.p. 160–215°C (decomp.). – IR: $\tilde{\nu} = 3500-2500$ cm^{-1}, 1581, 1555, 1499, 1477, 1394, 1314, 1175, 1100, 1054, 997, 964, 849. – MS, *m/z*: 198 [M$^+$]. – $C_8H_{14}N_4O_2 \cdot 2$ HCl (271.2): calcd. C 35.44, H 5.95, N 20.67; found C 34.97, H 5.88, N 20.66.

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