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Research Article

10*H*-Pyrazino[2,3-b][1,4]benzotellurazine, a Novel Tellurium-Containing Heterocyclic System

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Condensation of 2,3-dichloropyrazine with 2-aminobenzenetellurole and 2-amino-5-methylbenzenetellurole, generated *in situ* by reduction of the corresponding ditellurides, resulted in the formation of novel 10*H*-pyrazino[2,3-b][1,4]benzotellurazine and its 7-methyl derivative. The products were purified *via* their well-crystallized 5,5-dibromo derivatives. X-ray crystallographic analysis of the title compound indicates that it has a pronounced V-shape and forms hydrogen-bonded dimers. Te, N-containing heterocycles have the potential of offering access to supramolecular assemblies.

1. Introduction

Organotellurium heterocycles have potential applications ranging from crystal engineering [1] to the synthesis of supramolecular assemblies, [2] the development of novel catalysts, [3] highly selective ligands [4], and photosensitizers for photodynamic therapy [5]. In the ongoing work, we aim to improve access to such compounds and investigate their physical and chemical properties, notably in light of the known tendency of Te, N-containing heterocycles to undergo self-assembly to ribbons, chains, and rings [6, 7]. While this behavior is well documented for telluradiazoles, tellurazoles, and isotellurazole-N-oxides, little is known about the properties of tellurazines. Our attempts to prepare 10*H*-pyrazino [2,3-b][1,4]benzotellurazine were based on the synthesis of 10*H*-pyrazino[2,3-b][1,4]benzothiazine, which was first reported in 1974 in the patent literature [8, 9] and noted for its strongly antibacterial effects. Further works extended the synthesis used to prepare the parent compound to several derivatives [10]. Only one reference exists for the preparation of a selenium analog [11]. All were prepared by the condensation of 2-aminothiophenol and 2-aminoselenophenol, respectively, with 2,3-dichloropyrazine or its derivatives under either basic or acidic conditions according to Figure 1.

The preparation of the analogous 10*H*-pyrazino[2,3-b] [1,4]benzotellurazine and its derivatives has remained unreported. In porting existing syntheses for sulfur compounds to tellurium congeners, several limitations have to be kept in mind. These include the propensity of 2-aminobenzenetellurole to undergo C-Te bond fission, notably under acidic conditions [12] and its extreme air sensitivity. [13] This necessitates the preparation of 2-aminobenzenetellurole and its derivatives *in situ*, by reduction of the corresponding ditellurides, as well as the use of neutral or basic conditions to achieve cyclization.

2. Materials and Methods

Bis(2-aminophenyl) ditelluride and bis(2-amino-5-methyl) ditelluride were prepared as previously reported [14]. All other chemicals were purchased from Fisher Scientific and used as received. Silica gel, neutral, 200 mesh, was used for flash chromatography. Melting points were recorded in open capillaries using an electrothermal SRS MPA160 apparatus and are not corrected. Nuclear magnetic resonance spectra were recorded on a Varian MR 400 MHz NMR spectrometer. High resolution mass spectra were recorded on an Agilent 6230 ESI TOF mass spectrometer. Peaks in the

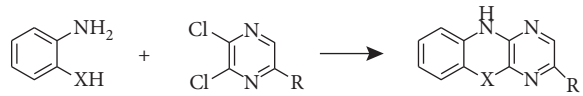

Figure 1: Previously published syntheses of 10*H*-pyrazino[2,3-b][1,4]benzothiazines (X = S, R = H or Cl) and 10*H*-pyrazino[2,3-b][1,4]benzoselenazine (X = S, Se; *R* = H, Cl).

$[M+H]^+$ cluster exceeding 10% of base are listed. Elemental analyses were obtained from Atlantic Microlab, Inc.

*2.1. 5,5-Dibromo-10H-pyrazino[2,3-b][1,4]benzotellurazine (**1**).* A mixture of bis(2-aminophenyl) ditelluride (175 mg, 0.4 mmol), 2,3-dichloropyrazine (119 mg, 0.8 mmol), sodium formaldehyde sulfoxylate (123 mg, 0.8 mmol), potassium hydroxide (90 mg, 1.6 mmol), and dimethyl sulfoxide (DMSO, 2.5 g) was heated to 120°C for 5 min and then to 165°C for 10 min. After cooling, the mixture was diluted with water (10 mL), and the resulting fine brownish-yellow precipitate was collected by centrifugation. It was dissolved in dichloromethane (DCM, 5 mL), insoluble material, and highly polar impurities were removed by flash chromatography (silica gel: DCM) and volatiles were allowed to evaporate in an open beaker under a hood. The residue was taken up in DCM (5 mL), and bromine was added until no further precipitate formed. The solvent and any remaining excess bromine were allowed to evaporate, and the residue was recrystallized twice from acetonitrile. Red crystals, mp 209–211°C; yield: 113 mg (31%). ^{1}H NMR (DMSO-d_6): δ = 7.13–7.17 (m, 1H), 7.53–7.58 (m, 2H), 8.26–8.30 (m, 2H), 8.53 (d, 1H). ^{13}C NMR (DMSO-d_6): δ = 113.14, 118.36, 122.66, 131.61, 132.64, 134.04, 138.00, 138.15, 144.71, 146.10. HRMS (*m*/*z*, %): $[M\text{-}Br]^+$ = 373.8847 (32.2), 375.8859 (77.0), 377.8872 (100), 379.8863 (46.7). Calculated for $C_{10}H_7Br_2N_3Te$: C, 26.31; H, 1.45; N, 9.20. Found: N, 26.48; H, 1.42; N, 8.98.

*2.2. 10H-Pyrazino[2,3-b][1,4]benzotellurazine (**2**).* A suspension of **1** (91 mg, 0.2 mmol) and in ethanol (2 mL) was reduced by adding excess hydrazine hydrate (10 mg, 0.2 mmol). The mixture was briefly heated to boiling and volatiles subsequently allowed to evaporate. The product was extracted with 3 × 10 mL of hot heptane and then recrystallized from acetonitrile. Brownish orange crystals, mp 96–97°C; yield: 46 mg (85%). ^{1}H NMR ($CDCl_3$): δ = 6.62 (d, 1H), 6.86 (t, 1H), 6.93 (s, broad, 1H), 7.06 (t, 1H), 7.64 (d, 1H), 7.90 (d, 1H). ^{13}C NMR ($CDCl_3$): δ = 96.03, 116.83, 124.36, 124.85, 128.83, 134.52, 139.96, 140.02, 141.36, 150.75. HRMS (*m*/*z*, %): $[M+H]^+$ = 293.9727 (11.3), 294.9744 (18.5), 295.9741 (52.5), 297.9755 (92.3), 299.9773 (100). Calculated for $C_{10}H_7N_3Te$: C, 40.47; H, 2.38; N, 14.16. Found: C, 40.64; H, 2.23; N, 14.11.

*2.3. 5,5-Dibromo-7-methyl-10H-pyrazino[2,3-b][1,4]benzotellurazine (**3**).* This compound was prepared in analogy to **1**, starting with bis(2-amino-5-methylphenyl) ditelluride (187 mg, 0.2 mmol) instead of bis(2-aminophenyl) ditelluride. Red crystals, mp 219–221°C; yield: 112 mg (30%). ^{1}H NMR (DMSO-d_6): δ = 2.32 (s, 3H), 7.35 (d, 1H), 7.49 (1H), 8.08 (1H), 8.27 (1H), 8.51 (d, 1H), 11.10 (s, 1H). ^{13}C NMR (DMSO-d_6): δ = 20.12, 112.70, 118.25, 131.43, 131.85, 133.40, 133.62, 135.70, 137.85, 144.70, 146.12. HRMS (*m*/*z*, %): $[M\text{-}Br]^+$ = 386.9008 (10.3), 387.8998 (31.9), 388.9000 (11.6), 389.9007 (74.4), 391.9021 (100), 392.9031 (10.0), 393.9013 (47.6). Calculated for $C_{11}H_9Br_2N_3Te$: C, 28.07; H, 1.93; N, 8.93. Found: C, 28.33; H, 1.81; N, 9.10.

*2.4. 7-Methyl-10H-pyrazino[2,3-b][1,4]benzotellurazine (**4**).* This compound was prepared in analogy to **2**, starting with **3** (94 mg, 0.2 mmol). Yellow solid, mp 122–123°C; yield: 58 mg (93%). ^{1}H NMR ($CDCl_3$): δ = 2.21 (s, 3H), 6.53 (d, 1H), 6.76 (s, N-H), 6.86 (d, 1H), 7.03 (s, 1H), 7.26 (d, 1H), 7.62 (d, 1H), 7.88 (d, 1H). ^{13}C NMR ($CDCl_3$): δ = 20.29, 95.85, 116.62, 124.83, 129.50, 133.94, 134.81, 138.85, 139.71, 139.93, 150.92. HRMS (*m*/*z*, %): $[M+H]^+$ = 307.9897 (11.1), 308.9916 (19.32), 309.9915 (55.4), 311.9928 (93.4), 312.9937 (10.3), 313.9947 (100), 314.9960 (10.4). Calculated for $C_{11}H_9N_3Te$: C, 42.51; H, 2.92; N, 13.52. Found: C, 42.51; H, 2.92; N, 13.68.

3. Results and Discussion

Few methods have been reported in the literature to prepare derivatives of benzo-1,4-tellurazine. These are primarily based on the treatment of 2,2′-dilithiodiphenylamine derivatives with tellurium or the mercuration of diphenylamine and its derivatives, followed by treatment with tellurium tetrachloride. [15, 16] The current work offers a novel approach to such compounds, starting with readily accessible bis(2-aminophenyl) ditelluride. Conceptually, the synthesis of **2** and **4**, based on that of 10*H*-pyrazino[2,3-b][1,4]benzothiazine [10], was straightforward. In practice, however, this reaction was difficult to implement. Several solvents were tested without success (ethanol, acetonitrile, dimethylformamide, and p-dioxane), but DMSO, under carefully controlled conditions, was suitable for ring closure. Much more drastic conditions were required than had been reported for the preparation of sulfur congeners [10, 17]. Below 160°C, ring closure remained incomplete, while at the boiling point of DMSO (189°C), decomposition was rapid. Even under optimized conditions, significant C-Te bond fission during synthesis was unavoidable. This is likely a consequence of a change in the balance between the strengths of bonds broken *vs*. bonds formed, which cannot be compensated for by the high nucleophilicity of the telluride anion. To further investigate this hypothesis, enthalpy changes associated with ring closure were calculated for the sulfur, selenium, and tellurium congeners using Gaussian 161. Minimum energy geometries of the reactant and product structures were optimized using Density Functional Theory. In all cases, the Becke-3-parameter-Lee-Yang-Parr functional, coupled to a DEF2TZVP basis set, was used [18]. Normal mode analysis was performed in order to check that optimized structure was at minimum energy geometries. The results, shown in Figure 2, are consistent with the observed decreased tendency of the tellurium precursor to undergo ring closure.

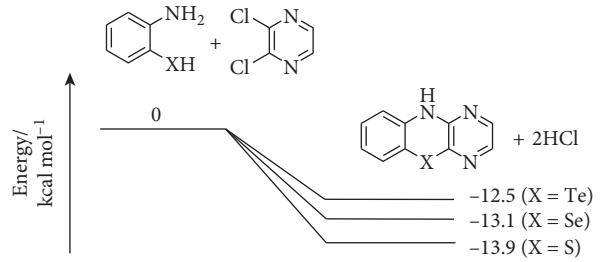

Figure 2: Comparison of free energy changes for the ring closure of 10*H*-pyrazino[2,3-b][1,4]benzotellurazine and its sulfur and selenium congeners.

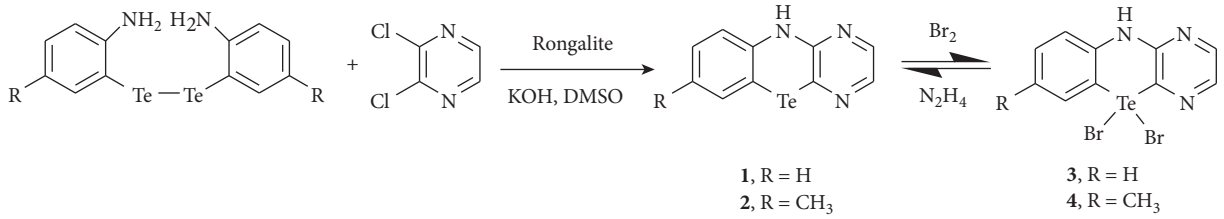

Figure 3: Preparation of 10*H*-pyrazino[2,3-b][1,4]benzotellurazine and its 7-methyl derivative.

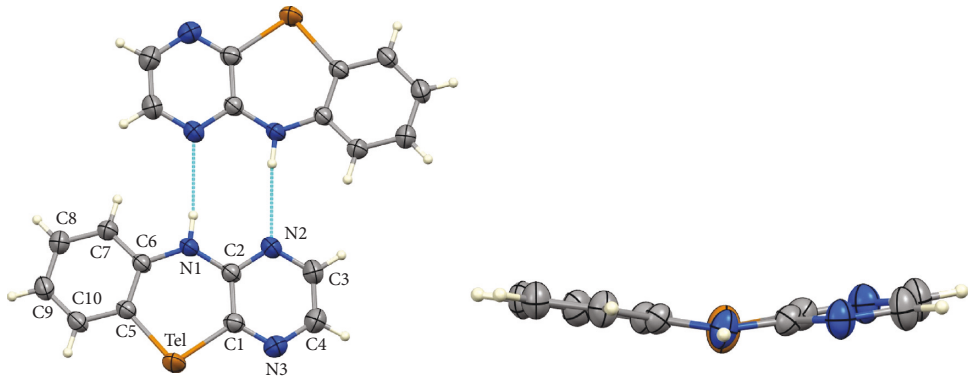

Figure 4: ORTEP plot of the hydrogen-bonded dimer of 10*H*-pyrazino [2,3-b][1,4]benzotellurazine and side view showing its V-shape.

Samples taken during the synthesis of **1** and analyzed by GC-MS indicate that cyclization proceeds in two distinct steps, namely, the formation of a monotelluride by nucleophilic displacement of one chlorine in 2,3-dichloropyrazine, followed by ring closure with formation of the secondary amine moiety. Monosubstitution was complete within one hour even at room temperature, which confirms the high nucleophilicity of aryltellurolate anions. The intermediate monotelluride was sensitive to air oxidation; consequently, no effort was made to purify it. In practice, an excess of potassium hydroxide was necessary to achieve reasonable yields. The crude products were contaminated with orange impurities of similar polarity (most likely ditellurides), which were removed by exploiting the fact that the target compounds can be brominated reversibly, as shown in Figure 3. The resulting 5,5-dibromo derivatives of compounds **2** and **4** were readily purified by recrystallization from acetonitrile and subsequently reduced to purified target products. It is noteworthy that the 5,5-dibromo derivatives did not generate molecular ions during mass spectrometric characterization. Instead, prominent $[M\text{-}Br]^+$ fragments were observed.

An ORTEP plot of **2** (Figure 4) shows the formation of hydrogen-bonded dimers in the solid state, as well as a V-shape of the molecule with a relative mean standard deviation from planarity for all nonhydrogen atoms of 0.185 Å.

By comparison, the only sulfur-containing congener for which crystallographic data are available, that is, 8-chloro-10*H*-pyrazino [2,3-b][1,4]benzothiazine, which is nearly planar with an relative means standard deviation from planarity of 0.041 Å for all carbon and nitrogen atoms [17]. This trend is reminiscent of that previously reported for the 9,10-dichalcogenaanthracenes, which adopt and increasingly V-shaped geometry as lighter chalcogen atoms are being replaced by heavier ones, [19] as well as that reported for phenotellurazine [20]. An ORTEP plot of **4**, the bromination product of **3**, is shown in Figure 5. In the crystalline state, this compound is characterized by the coordination of bromine to the N-H moieties of adjacent molecules and a ring structure that is essentially planar.

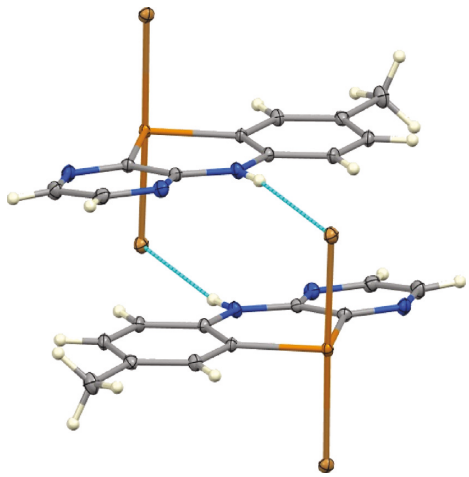

Figure 5: ORTEP plot of dimer of 5,5-dibromo-7-methyl-10*H*-pyrazino [2,3-b][1,4]benzotellurazine.

4. Conclusions

The preparation of novel 10*H*-pyrazino[2,3-b][1,4]benzotellurazine and selected derivatives extends the very limited range of reactions suited to prepare derivatives of benzo-1,4-tellurazine, which has permitted a study of their self-assembly behavior. 10*H*-pyrazino[2,3-b][1,4] benzotellurazine forms hydrogen-bonded dimers rather than the ribbon structurs typical of 1,2,5-telluradiazoles, apparently as a result of intermolecular hydrogen bonding between amino moieties outcompeting intermolecular Te-N coordination. In contrast, 5,5-dibromo-7-methyl-10*H*-pyrazino [2,3-b][1,4]benzotellurazine was found to form intermolecular assemblies characterized by the coordination of the N-H moieties to bromine atoms of adjacent molecules.

Data Availability

The structures of 1 and 4 were deposited with the Cambridge Crystallographic Data Centre (nos. 1963543 and 1963544).

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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References

[1] G. R. Desiraju, P. S. Ho, L. Kloo et al., "Definition of the halogen bond (IUPAC Recommendations 2013)," *Pure and Applied Chemistry*, vol. 85, no. 8, pp. 1711–1713, 2013.

[2] P. C. Ho, L. M. Lee, H. Jenkins, J. F. Britten, and I. Vargas-Baca, "Influence of acidic media on the supramolecular aggregation of iso-tellurazole N-oxides," *Canadian Journal of Chemistry*, vol. 94, no. 5, pp. 453–457, 2016.

[3] M. Abe, Y. You, and M. R. Detty, "21-Telluraporphyrins. 2. Catalysts for bromination reactions with hydrogen peroxide and sodium bromide," *Organometallics*, vol. 21, no. 21, pp. 4546–4551, 2002.

[4] S. Ahmad, K. K. Yadav, S. J. Singh, and S. M. S. Chauhan, "Synthesis of 5,10,15,20-meso-unsubstituted and 5,10,15,20-meso-substituted-21,23-ditellura/diselena core-modified porphyrinogens: oxidation and detection of mercury(II)," *RSC Advances*, vol. 4, no. 7, pp. 3171–3180, 2014.

[5] M. W. Kryman, T. M. McCormick, and M. R. Detty, "Longer-wavelength-absorbing, extended chalcogenorhodamine dyes," *Organometallics*, vol. 35, no. 11, pp. 1944–1955, 2016.

[6] A. Kremer, A. Fermi, N. Biot, J. Wouters, and D. Bonifazi, "Supramolecular wiring of benzo-1,3-chalcogenazoles through programmed chalcogen bonding interactions," *Chemistry—A European Journal*, vol. 22, no. 16, pp. 5665–5675, 2016.

[7] J. Kübel, P. J. W. Elder, H. A. Jenkins, and I. Vargas-Baca, "Structure and formation of the first (-O-Te-N-)4 ringfirst (–O–Te–N–)4 ring," *Dalton Transactions*, vol. 39, no. 46, pp. 11126–11128, 2010.

[8] Y. C. Tong, "Oxides of 10*H*-pyrazino(2,3-B)(1,4)benzothiazine," U.S. Patent 3821213, Dow Chemical Company, Midland, MI, USA, 1974.

[9] Y. C. Tong, "Aminoalkyl derivatives of 10*H*-pyrazino(2,3-b)(1,4)benzothiazine," U.S. Patent 3845044, Dow Chemical Company, Midland, MI, USA, 1974.

[10] C. O. Okafor, "Studies in the heterocyclic series. XIX. Synthesis of 1,4-diazaphenothiazine and its benzo derivatives," *Journal of Heterocyclic Chemistry*, vol. 18, no. 2, pp. 405–407, 1981.

[11] G. W. H. Cheeseman and G. Rishman, "The preparation and properties of 1,4-diazaphenoselenazine," *Tetrahedron*, vol. 36, no. 18, pp. 2681–2683, 1980.

[12] P. R. Mallikarachy, H. O. Brotherton, F. R. Fronczek, and T. Junk, "Facile access to organotellurium heterocycles by nitration of bis(3,5-dimethylphenyl) ditelluride," *Journal of Heterocyclic Chemistry*, vol. 42, no. 2, pp. 243–247, 2005.

[13] K. J. Irgolic, T. V. Georg, and D. Klamann, "Methoden der organischen Chemie," *Organotellurium Compounds*, vol. E12b, 1990.

[14] N. C. McMullen, F. R. Fronczek, and T. Junk, "Organotellurium Chemistry: remarkably facile preparation of benzo-1,3-tellurazoles," *Journal of Heterocyclic Chemistry*, vol. 50, no. 1, pp. 120–124, 2013.

[15] I. D. Sadekov, G. M. Abakarov, V. B. Panov, L. Yu Ukhin, A. D. Garnovskii, and V. I. Minkin, "Synthesis and reactivity of 10-alkylphenotellurazines," *Khimiya Geterotsiklicheskikh Soedinenii*, vol. 21, no. 6, pp. 757–768, 1985.

[16] K. J. Irgolic and T. Junk, "5-Aza-10-tellura-5,10-dihydroanthracenes (phenotellurazines)," *Heterocycles*, vol. 28, no. 2, pp. 1007–1013, 1989.

[17] W. S. Saari, D. W. Cochran, Y. C. Lee et al., "Preparation of some 10-[3-(dimethylamino)propyl]-10*H*-pyrazino[2,3-b][1,4]benzothiazines as potential neuroleptics," *Journal of Medicinal Chemistry*, vol. 26, no. 4, pp. 564–569, 1983.

[18] M. J. Frisch, G. W. Trucks, H. B. Schlegel et al., *Gaussian 09, Revision B.01*, Gaussian, Inc., Wallingford, UK, 2009.

[19] E. A. Meyers, K. J. Irgolic, R. A. Zingaro et al., "The crystal structures of 9,10-dichalcogenaanthracenes, C12H8XY, (X, Y) = (S, Se), (S, Te), (Se, Te), and (O, Se)," *Phosphorus and Sulfur and the Related Elements*, vol. 38, no. 3-4, pp. 257–269, 1988.

[20] T. Junk, K. J. Irgolic, J. H. Reibenspies, and E. A. Meyers, "Structure of phenotellurazine," *Acta Crystallographica Section C Crystal Structure Communications*, vol. 49, no. 5, pp. 938–940, 1993.