it slowly decomposes upon standing in solution or neat. Kinetic studies on the cyclization of **5** (n = 2) (Scheme III) were carried out in the presence of 1,4-cyclohexadiene in benzene in order to determine its rate of cyclization to a benzenoid diradical at various temperatures and to define its energy of activation (E_a). As expected from Bergman's elegant studies,[3] under these conditions, **5** (n = 2) led to tetralin (**7**) and the two adducts **8a** and **8b** via benzenoid diradical **6** (Scheme III). At 37 °C the cyclization of **5** (n = 2) (Scheme III) proceeded with a half life ($t/2$) of 18 h and a rate constant (k_r) of 6.4 × 10^{-4}/min. The energy of activation (E_a) for this reaction was determined to be 23.8 kcal/mol.[15] Thus, it appears that structure **5** (n = 2) may serve as a useful "warhead" in damaging molecular or cellular structures such as DNA and tumor cells, without further activation.

Applications of the gathered knowledge to further studies in this area using computer design, synthesis, and biotechnology should be forthcoming and may prove therapeutically useful.

Acknowledgment. We thank Drs. May D. Lee, Ving J. Lee, and Robert Babine (Lederle Laboratories) and Professors Ralph Hirschmann and W. S. Dailey of this department for stimulating and helpful discussions. Our many thanks are also due to Drs. Patrick Carrol, George Furst, and John Dykins of this department for their superb assistance and helpful comments regarding X-ray crystallography, NMR, and mass spectroscopy, respectively. This work was financially supported by the National Science Foundation, Lederle Laboratories, Merck Sharp and Dohme, and the University of Pennsylvania.

Supplementary Material Available: ^{1}H NMR data for compounds **5** (n = 3-8), X-ray data for **5** (n = 3), kinetic data for **5** → **6**, and details for the synthesis of **5** (n = 2-8) (7 pages). Ordering information is given on any current masthead page.

(15) Calculations were made on the assumption of complete conversion of enediyne **5** (n = 2) to diradical **6** (at half life for the 37 °C run the material balance was ca. 95.5%). Reactions at 37, 50, 60, and 70 °C were carried out in degassed benzene solutions at 0.01 M concentrations of **5** (n = 2) and 100 mol equiv of 1,4-cyclohexadiene. The kinetics were followed by HPLC with diphenyl ether as internal standard. Further details can be found in the Supplementary Material.

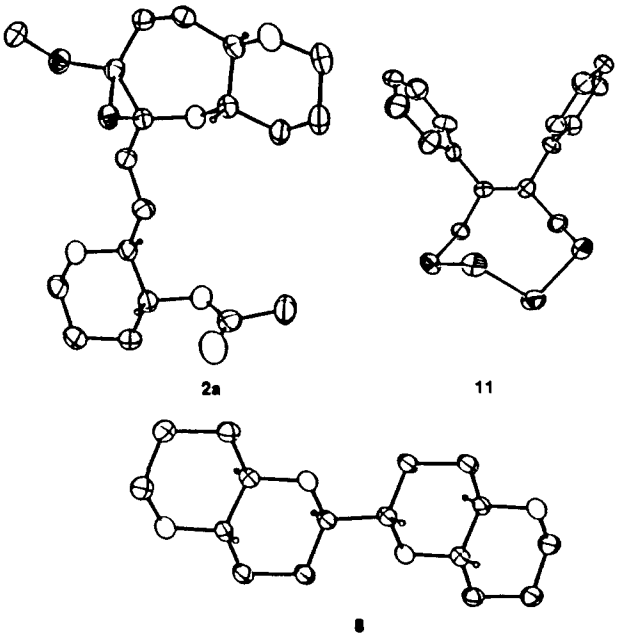
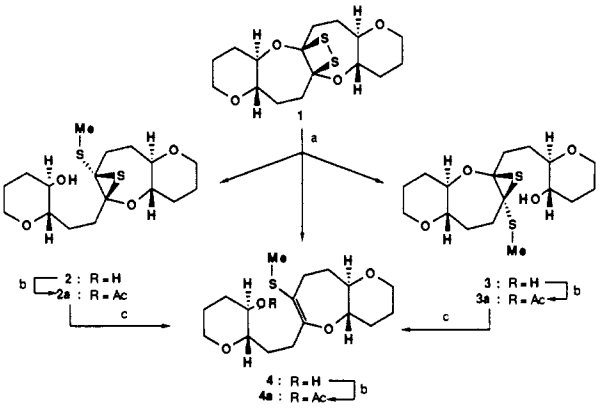


Figure 1. ORTEP drawings of **2a**, **8**, and **11**.

Scheme I[a]



[a] Reagents and conditions: (a) 2.0 equiv of $NaBH_4$, EtOH, 0 °C, 10 min, then 15.0 equiv of MeI, 30 min, **2** (35%), **3** (28%), **4** (12%); (b) 2.0 equiv of Ac_2O, 2.2 equiv of Et_3N, 0.1 equiv of DMAP, CH_2Cl_2, 0 °C, **2a** (85%), **3a** (80%), **4a** (81%); (c) 4.0 equiv of Ph_3P, CH_2Cl_2, 50 °C, 24 h, **2a**, **4a** (87%), **3a**, **4a** (80%).

Novel Chemistry of Dithiatopazine

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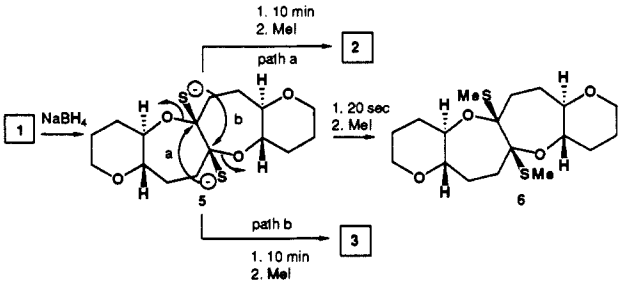
We have recently reported the synthesis of the first stable 1,2-dithietane compound, dithiatopazine (**1**).[1] In this communication, we wish to disclose some novel chemistry of this remarkable molecule including (i) a number of unique skeletal rearrangements, (ii) the synthesis of some unusual structures, and (iii) the transfer of sulfur atoms from dithiatopazine to suitable acceptors.

Scheme I depicts the transformations taking place when **1** is exposed to $NaBH_4$ in EtOH at 25 °C for 10 min, followed by quenching with excess MeI. The three products **2**, **3**, and **4** were isolated in 35, 28, and 12% yields, respectively, by preparative thin layer chromatography (R_f values, silica, 30% EtOAc in benzene, **2**: 0.27, **3**: 0.23, **4**: 0.20).[2] The structures of these novel compounds were based on spectroscopic and chemical data. Thus, these three compounds yielded, upon acetylation with excess

Scheme II[a]



[a] Presumed mechanism for the formation of **2** and **3** from **1**.

(1) Nicolaou, K. C.; Hwang, C.-K.; Duggan, M. E.; Carrol, P. J. *J. Am. Chem. Soc.* **1987**, *109*, 3801.

(2) All new compounds exhibited satisfactory spectral and analytical and/or exact mass data. Yields refer to spectroscopically and chromatographically homogeneous materials.

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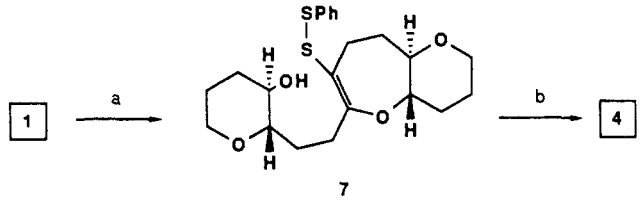
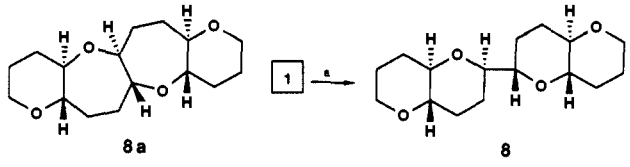
Scheme III[a]



[a] Reagents and conditions: (a) 1.2 equiv of NaH, 2.5 equiv of PhSH, THF, 0 °C, 24 h, 60%; (b) 1.2 equiv of Li–selectride, CH_2Cl_2, −78 °C, 15 min, then 5 equiv of MeI, −78 °C to 25 °C, 30 min, 60%.

Scheme IV[a]



[a] 2.0 equiv of $AgBF_4$, 15.0 equiv of Et_3SiH, CH_2Cl_2, 25 °C, 2 h, 90%.

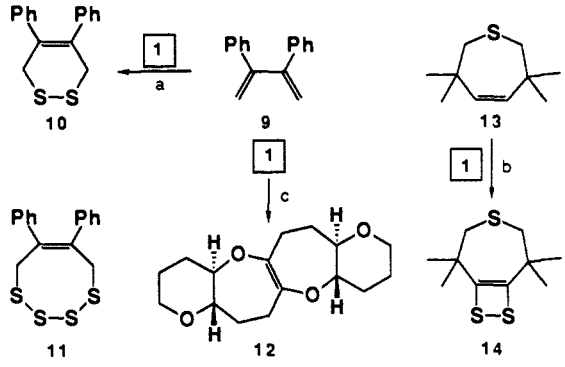
acetic anhydride, acetates **2a** (85%), **3a** (80%), and **4a** (81%), respectively. Furthermore, exposure of either acetate **2a** or **3a** to excess Ph_3P at 50 °C led to the unsaturated compound **4a** via desulfurization, suggesting the presence of the episulfide moiety and the diastereomeric relationship of these two episulfides.[3] Compound **2a** formed monoclinic colorless crystals from hexane, mp 119–120.5 °C. An X-ray crystallographic analysis of this compound confirmed the proposed structure and provided further support for the assigned structures of **3** and **4**. Figure 1 shows an ORTEP drawing of **2a**.

Mechanistically, **2** and **3** may arise from **1** as outlined in Scheme II. Thus, initial reductive cleavage of the S–S bond leads to the dianion **5** which may suffer rearrangement via path a leading to compound **2** or path b leading to the diastereomeric compound **3**. The intermediary of **5** was confirmed by its interception with MeI after 20-s exposure to $NaBH_4$, leading to the bis methylsulfide ether **6** (93% yield). Episulfides **2** and **3** carrying an additional sulfur and an oxygen atom in this particular arrangement are, to the best of our knowledge, the first examples of their class.[4]

The reaction of dithiatopazine (**1**) with sodium thiophenoxide also proved quite interesting, leading to the disulfide enol ether **7** in 60% yield (Scheme III).[5] The structure of **7** was supported by its spectral data and its chemistry. Particularly revealing were (i) the ^{13}C NMR (125 MHz, C_6D_6) showing signals at δ 164.20 and 117.19 for the two olefinic carbons and (ii) its conversion to compound **4** (Scheme I) by Li-selectride reduction followed by MeI quenching (60%).

A most remarkable and stereospecific rearrangement took place when dithiatopazine (**1**) was treated with excess Et_3SiH in the presence of $AgBF_4$ in CH_2Cl_2 (Scheme IV). The spectral data of the single product obtained in 90% yield indicated a symmetrical structure (eight ^{13}C NMR signals) but failed to distinguish between the 6,6-6,6 structure **8** and the initially suspected isomeric 6,7,7,6 structure **8a** corresponding to the dithiatopazine skeleton. Fortunately, the product of this reaction crystallized in colorless needles from ether–hexane, mp 155–156 °C. An X-ray crystallographic analysis revealed structure **8** for the product (see ORTEP drawing, Figure 1), providing that a skeletal rearrangement had indeed taken place.

Scheme V[a]



[a] Transfer of sulfur from dithlatopazine to acceptor molecules. Reagents and conditions: (a) 10.0 equiv of **9**, toluene, 100 °C, 12 h, **10** (25%), **11** (28%), **12** (90%); (b) 5.0 equiv of **13**, toluene, 100 °C, 12 h, **14** (66%), **12** (92%); (c) 2.0 equiv of $Fe(CO)_9$, $CHCl_3$, 25 °C, 2 h, 88%; 3.0 equiv of $Mo(CO)_6$, THF, 25 °C, 48 h, 90%.

Finally, we report on the ability of dithiatopazine (**1**) to donate its sulfur atoms to appropriate acceptors leading to novel polysulfides.[6] Scheme V summarizes some of these reactions. Thus, diene **9**, when heated in toluene at 100 °C with dithiatopazine (**1**), led to disulfide **10**[6b,c] (25%) and tetrasulfide **11**[7] (28%). In this reaction, dithiatopazine (**1**) was converted to olefin **12**[8] in high yield (90%). The structure of tetrasulfide **11** was confirmed by an X-ray crystallographic analysis (see ORTEP structure, Figure 1). Under similar conditions, the highly strained acetylenic compound **13**[9] was converted to dithietene **14**[10] (66%) and another, as yet, unidentified product, with olefin **12** again being formed in high yield (92%). Clean extrusion of both sulfur atoms from **1** was also observed upon treatment with $Fe_2(CO)_9$ (88%) or $Mo(CO)_6$ (90%).[11]

In conclusion, we have demonstrated that dithiatopazine (**1**) undergoes a series of unique and remarkable rearrangements leading to a number of novel structures. Further chemical, mechanistic and theoretical studies in this new area of sulfur chemistry are in progress.

Acknowledgment. We express our many thanks to Drs. George Furst, Patrick J. Carrol, and John Dykins for their superb NMR, X-ray, and mass spectroscopic assistance and helpful comments. This work was financially supported by the National Science Foundation and Merck Sharp and Dohme, U.S.A.

Supplementary Material Available: Selected spectral data for compounds **2**, **2a**, **3**, **3a**, **4**, **4a**, **7**, **8**, and **11** and X-ray crystallographic data for **2a**, **8**, and **11** (13 pages). Ordering information is given on any current masthead page.

(3) The ^{13}C NMR spectra of compounds **2a** and **3a** exhibited the expected signals for the episulfide carbons [125 MHz, C_6D_6, **2a**: δ 97.58 (S–C–O) 82.45 (S–C–S); **3a**: δ 94.07 (S–C–O), 81.98 (S–C–S)]. The ^{13}C NMR spectrum of **4a** exhibited signals at δ 118.29 and 161.77 suggesting a double bond of the type shown in this structure.

(4) Some related examples are mentioned in (a) Dittmer, D. C. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 7, p 131. (b) Fokin, A. V.; Kolomiets, A. F. *Russian Chem. Rev.* **1975**, *44*, 138.

(5) Mechanistic studies concerning the formation of this compound are currently in progress.

(6) For some leading references for the generation and trapping of diatomic sulfur, see: (a) Steliou, K.; Gareau, Y.; Harpp, D. N. *J. Am. Chem. Soc.* **1984**, *106*, 799. (b) Steliou, K.; Salama, P.; Brodeur, D.; Gareau, Y. *J. Am. Chem. Soc.* **1987**, *109*, 926. (c) Schmidt, M.; Gorl, V. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 887. (d) Ando, W.; Sonobe, J.; Akasaka, T. *Tetrahedron Lett.* **1987**, *28*, 6653.

(7) Dodson, R. M.; Srinivasan, V.; Sharma, K. S.; Sauers, R. F. *J. Org. Chem.* **1972**, *37*, 2367.

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(9) Krebs, A.; Kimling, H. *Liebigs Ann. Chem.* **1974**, 2074. We thank Professor Krebs for a generous gift of compounds **13** and **14**.

(10) Krebs, A.; Colberg, H.; Hopfner, U.; Kimling, H.; Odenthal, J. *Heterocycles* **1979**, *12*, 1153.

(11) Stimulating discussions with Professor D. H. Berry of this department concerning the organometallic chemistry of **1** are acknowledged.