61076-71-9; **13**, 26407-92-1; **14**, 13431-10-2; **15**, 5391-52-6; **16**, 59863-98-8; **17**, 13461-16-0; **18**, 60546-76-1; **19**, 60546-78-3; **20**, 5391-53-7; **21**, 61076-72-0; **22**, 61076-73-1; **23**, 28118-54-9; **24**, 61076-74-2; **25**, 61076-75-3; **26**, 61076-76-4; **27**, 61076-77-5; **28**, 61076-78-6; **29**, 61076-79-7; **30**, 20112-79-2; **31**, 52839-23-3; **32**, 60546-75-0; **33**, 61076-80-0; **34**, 61076-81-1; **35**, 61076-82-2; **36**, 60498-94-4; **37**, 60546-77-2; **38**, 61076-83-3; **39**, 61076-84-4; **40**, 61076-85-5; **41**, 61076-86-6; **42**, 61076-87-7; **43**, 59863-93-3; methyl chloroformate, 79-22-1; ethyl chloroformate, 541-41-3; acetyl chloride, 75-36-5; imidazolidone, 120-93-4; imidazolidinethione, 96-45-7; *N*-methyl-2-methylthioimidazolinium HI, 61076-89-9; *N*-acetyl-2-methylthioimidazolinium HI, 61076-88-8; MeI, 74-88-4; allyl bromide, 106-95-6; 4-fluorobenzyl chloride, 352-11-4; ethyl chloroacetate, 105-39-5; chloroacetone, 78-95-5; *N*-methylethylenediamine, 109-81-9; ethyl carbonate, 105-58-8.

Supplementary Material Available. The complete experimental procedures employed for the preparation of all new compounds, the physical and spectral properties observed for all compounds, as well as two histograms summarizing extensive ^{13}C NMR data for the compounds reported herein (18 pages). Ordering information is given on any current masthead page.

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A Short Synthesis of Aromatic Analogues of the Aranotins

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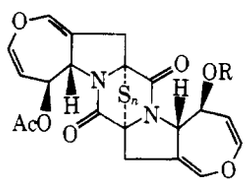
Received September 17, 1976

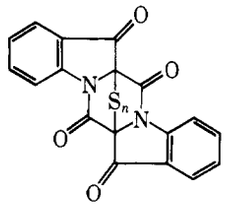
Various pyrazino[1,2-*a*:4,5'-*a'*]diindoles have been synthesized corresponding in structure to the diketopiperazine type dimers of indole- and indoline-2-carboxylic acids. 7,14-Dihydroxy-6*H*,13*H*-pyrazino[1,2-*a*:4,5-*a'*]diindole-6,13-dione reacted with sulfur monochloride and pyridine to give epidithio and epitrithio derivatives. These are aromatic analogues of the aranotins. The structure of the epitrithio derivative was verified by single-crystal x-ray crystallography. The space group is $P_{2_1}P_{2_1}P_{2_1}$ with pertinent cell data as follows: a = 9.199 (4), b = 13.846 (4), c = 13.248 (3) Å, and Z = 4.

The aranotins are a small group of sulfur-bridged diketopiperazines produced by the fungal species *Arachniotus aureus* and *Aspergillus terreus*.[1] The compounds have elicited attention from chemotherapists because of their antiviral activity which is observed in both in vivo and in vitro testing.[2]

Aranotin (**1**) and acetylaranotin (**2**, also known as LL-S88$_{(1)}$) are naturally occurring members of the group. Compounds **3** and **4** are partially synthetic members obtained by chemical modifications of acetylaranotin.[3] Since the dihydrooxepin rings may not be crucial to the biological activity of this series,[4] a synthesis of some aromatic analogues was initiated and led



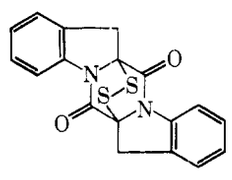
1, n = 2; R = H (aranotin)
2, n = 2; R = Ac (acetylaranotin)
3, n = 3; R = Ac
4, n = 4; R = Ac



5, n = 2
6, n = 3

to a short and easy synthesis of the analogues **5** and **6**.

The simplest aromatic analogue would be structure **7** and the bisindolodiketopiperazines **8**, **9**, and **10** were prepared as potential synthetic precursors to **7**.



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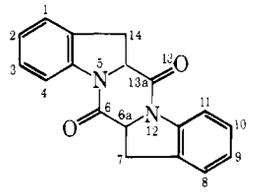

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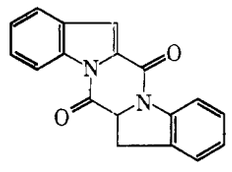

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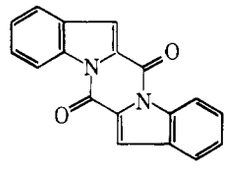
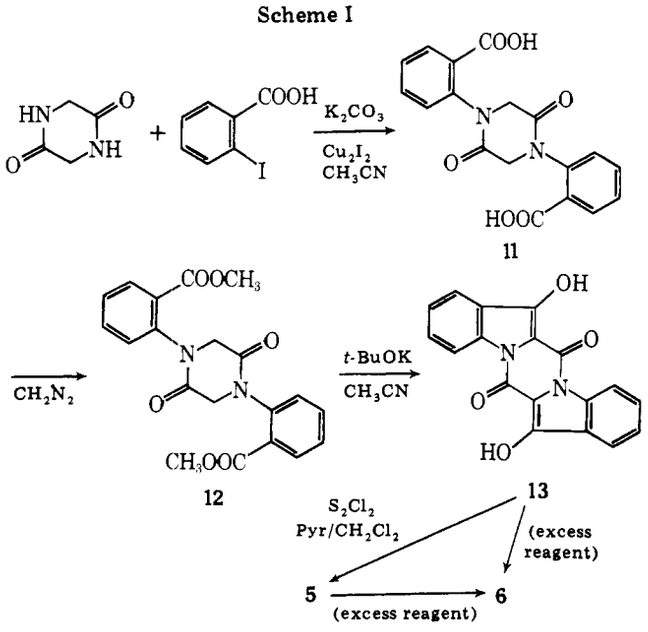


10

We were unable to obtain **7** from any of these three compounds[5] and proceeded to a synthesis of the slightly more complex analogues **5** and **6** as shown in Scheme I. The methods used to obtain **8**, **9**, and **10** are outlined in Scheme II.

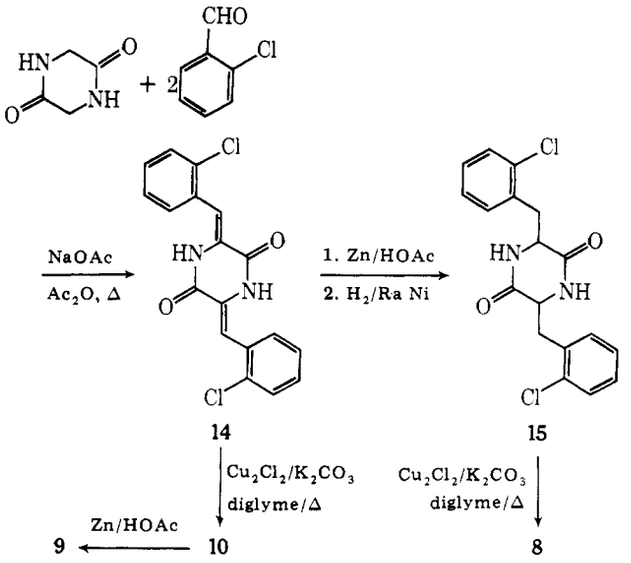
Scheme I



The syntheses described in Schemes I and II take advantage of the C_2 symmetry property of the products. By selecting the central diketopiperazine ring as the starting material, the synthetic steps proceed as dual transformations.

The copper-catalyzed nucleophilic substitution reaction leading to compound **11** has a precedent in the synthesis of dehydrogliotoxin reported by Kishi and co-workers.[6] Although the yield in this step was only 32%, substantial quantities of **11** could be prepared quite conveniently. The yields in the subsequent steps were quite good. The diacetate of **13** could be obtained directly from **11** by heating it with sodium acetate

Scheme II



and acetic anhydride, but the yield of **13** from hydrolysis of its diacetate was very poor compared with that obtained from the Dieckmann route shown.

The direct introduction of a disulfide bridge into a diketopiperazine using sulfur monochloride was reported for a simpler case.[7] The yield was only 17% and a mixture of di- and tetrasulfides was obtained. In the present case, the conversion of **13** to **5** proceeded in 65% yield and pure product was obtained by a simple recrystallization. When a large excess of sulfur monochloride was used, the trisulfide **6** was obtained in slightly lower yield. The intermediacy of the disulfide in the formation of the trisulfide can be inferred from the fact that **5** gave **6** when treated with more sulfur monochloride. Both compounds were tested for antiviral activity in mice using influenza-A2, coxsacki, and Semliki forest viruses but no activity was observed.

The structures of **5** and **6** were in agreement with the spectral and analytical data. In particular the mass spectra of both compounds contained M^+ peaks. Their NMR spectra, however, contained only aromatic proton signals and provide no proof for the assigned structures. In order to remove any equivocation about these structural assignments, we decided to take advantage of the propensity which compound **6** showed to produce well-formed crystals and carried out an x-ray crystallographic structure determination. The results are presented in Figure 1 and Tables I and II.

Two ancillary results of the x-ray crystallographic investigation of **6** deserve comment. One is that the crystal examined consisted of a single enantiomer as would be expected for space group $P_{2_12_12_1}$ indicating that the individual crystals had resolved spontaneously during crystallization. The second, possibly related result is that the sulfur bridge is unsymmetrical, not only in conformation but in C–S and S–S distances. The differences in these bond lengths (Table II) are well outside the 3σ error associated with them. The origin of this distortion may be either a crystal lattice effect or the result of an interaction between the central sulfur atom and the proximal benzene ring.

Syntheses of Compounds 8, 9, and 10. The Sasaki procedure[8] for condensing benzaldehydes with glycine anhydride was used to prepare compound **14**. Contrary to Sasaki's report, however, we found that these bisbenzylidenediketopiperazines were only *partially* reduced with zinc in boiling acetic acid. The resulting dihydro compound from **14** was further reduced to **15** with hydrogen and Raney nickel in acetic acid. This two-step reduction sequence was superior to direct catalytic reduction of **14** because of its very poor solubility.

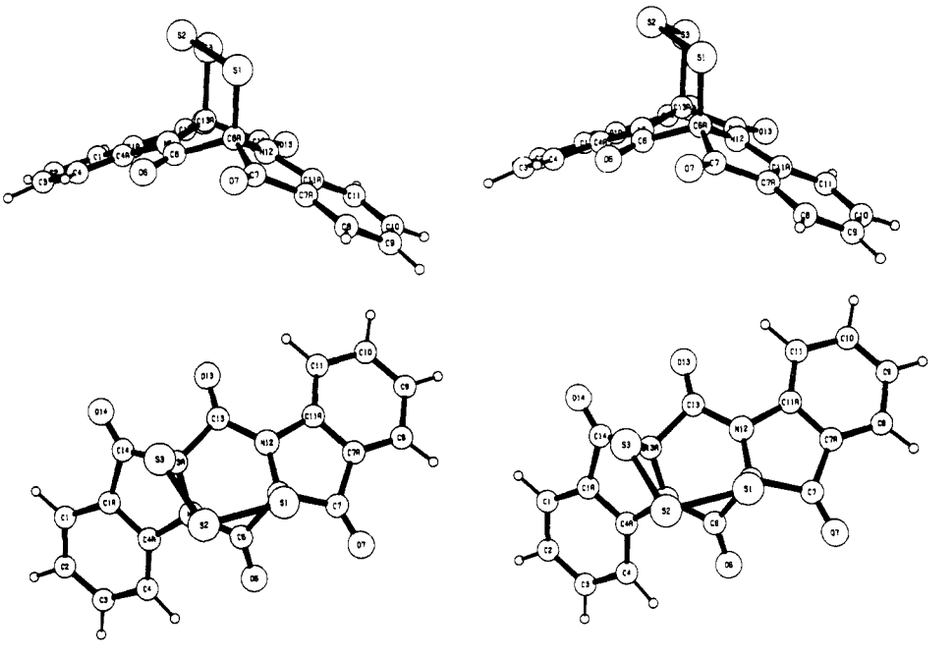


Figure 1. Stereoscopic drawings of compound **6**. The thermal ellipsoids for all nonhydrogen atoms are scaled to the 50% inclusion level. The hydrogen atoms are shown as spheres.

Table I. Crystal Data for 6

Space group	$P2_12_12_1$
a	9.199 (4)
b	13.846 (4)
c	13.248 (3)
Z	4
d_{calcd}	1.611
μ(Cu Kα), cm^{-1}	40.06

Table II. Bridge Bond Lengths and Angles for 6

S_1–C_{6A}	1.806 Å
S_3–C_{13A}	1.916 Å
S_1–S_2	2.069 Å
S_2–S_3	2.018 Å
S_2–S_1–C_{6A}	101°
S_1–S_2–S_3	105°
S_2–S_3–C_{13A}	101°

Double cyclizations via copper-catalyzed intramolecular substitution reactions were carried out on both **14** and **15** giving **10** and **8**, respectively, as shown in Scheme II. As with the bisbenzylidenediketopiperazines, the bisindolo compound **10** was reduced only to the dihydro level with zinc in acetic acid, giving compound **9**.

Compound **8** has been prepared previously by dimerization of ethyl indoline-2-carboxylate[5] and the reported melting point and NMR data are similar to those obtained from a sample prepared according to Scheme II. Neither route permits an assignment of stereochemistry. Nor can a distinction between the cis (with C_2 symmetry) and trans (with S_2 symmetry) isomers be made on the basis of the NMR spectra.

Experimental Section[9]

1,4-Bis(*o*-carboxyphenyl)-2,5-piperazinedione (11). A mixture of glycine anhydride (11.4 g, 0.1 mol), *o*-iodobenzoic acid (51 g, 0.205 mol), cuprous iodide (10 g, 0.052 mol), potassium carbonate (50 g, 0.36 mol), and acetonitrile (500 ml) was stirred at reflux under argon for 16 h. After cooling, the mixture was poured into water and filtered through Celite. The filtrate was acidified with dilute aqueous HCl, causing a gummy precipitate to form. Ether was added and the mixture stirred to give a cleaner precipitate. This was filtered, washed with water and ether, then air dried to give 11.5 g (32.5%) of crude compound **11** (single spot on TLC). A sample for analysis was recrystallized from ethanol/ether, giving colorless crystals with mp 279–281 °C; IR (Nujol) 3400, 2600, 2500, 1725, 1645, 1610, 1585 cm^{-1}; NMR (Me_2SO-d_6) 4.4 (s, broad, 4 H), 6.6 (s, broad, exchanged with D_2O), 7.6 ppm (aromatic H); mass spectrum *m/e* 336 and 354 (M^+, 100%).

Anal. Calcd for $C_{18}H_{14}N_2O_6$: C, 61.02; H, 3.98; N, 7.91. Found: C, 61.03; H, 4.17; N, 8.01.

1,4-Bis(*o*-carbomethoxyphenyl)-2,5-piperazinedione (12). The diacid **11** (4.0 g) gradually dissolved in reagent grade methanol (300 ml) during 45 min of boiling. After cooling, freshly prepared diazomethane in ether was added in portions until the yellow color persisted and TLC analysis showed that esterification was complete. The solution was filtered through Celite and stripped of solvent under reduced pressure. The crystalline residue was triturated with ether, collected, and air dried to give 3.95 g (91.5%) of colorless crystals. An analytical sample from methylene chloride/ether had mp 166–168 °C: IR (Nujol) 1715, 1660, 1590, and 1570 cm^{-1}; NMR ($CDCl_3$) 3.94 (s, 6 H), 4.47 (s, 4 H), and 7.3–8.3 ppm (m, 8 H); mass spectrum *m/e* 350 and 382 (M^+, 100%).

Anal. Calcd for $C_{20}H_{18}N_2O_6$: C, 62.82; H, 4.75; N, 7.33. Found : C, 62.56; H, 4.90; N, 7.48.

7,14-Dihydroxy-6*H*,13*H*-pyrazino[1,2-*a*:4,5-*a'*]diindole-6,-13-dione (13). Compound **12** (3.75 g, 0.0098 mol) in acetonitrile (100 ml) was stirred at reflux while potassium *tert*-butoxide (3.75 g, 0.033 mol) was added in portions. The resulting orange slurry was heated at reflux for an additional 1.5 h and then poured into water. The resulting clear solution was acidified with 3 N HCl and the fine yellow precipitate was collected on Whatman no. 42 filter paper. After washing with water and ether and then air drying, 2.87 g (92%) of pale yellow powder was obtained. A sample for analysis prepared by vacuum sublimation changed to fine needles above 250 °C but did not melt up to 320 °C. The sample had IR (Nujol) 3300, 1685, 1670, 1625, 1600 and 1575 cm^{-1}; mass spectrum *m/e* 318 (M^+, 100%). An NMR spectrum was precluded by poor solubility.

Anal. Calcd for $C_{18}H_{10}N_2O_4$: C, 67.93; H, 3.17; N, 8.80. Found: C, 67.82; H, 3.33; N, 8.75.

6a,13a-Epidithio-6a,7,13a,14-tetrahydro-6*H*,13*H*-pyrazino-[1,2-*a*:4,5-*a'*]diindole-6,7,13,14-tetraone (5). A suspension of compound **13** (2.0 g, 0.0063 mol) in methylene chloride (160 ml) was stirred vigorously while pyridine (4 ml, 0.05 mol) was added. Sulfur monochloride (1.2 ml, 2 g, 0.015 mol) was added slowly dropwise giving a clear yellow solution. After 10 min of stirring, the solution was washed with 0.6 N HCl (200 ml), dried, filtered, and concentrated under reduced pressure using a water bath at 35 °C. Crystals began to form when the volume was reduced to ca. 100 ml. Further concentration to ca. 50 ml by boiling was followed by storage in the freezer for 2 h. The crude product (1.68 g) was collected, washed with cold methylene chloride, and dried. Recrystallization from methylene

chloride gave 70 mg of insoluble starting material and 1.56 g (65%) of pure product in two crops of tiny, pale yellow needles. The recrystallized product decomposed without melting above 300 °C: IR (Nujol) 1730 and 1600 cm^{-1} (1745 and 1600 cm^{-1} in $CHCl_3$); NMR ($CDCl_3$) 7.3–8.4 ppm (m, aromatic H); mass spectrum *m/e* 64 (100%), 316, 318, and 380 (M^+).

Anal. Calcd for $C_{18}H_8N_2O_4S_2$: C, 56.83; H, 2.12; N, 7.36, S, 16.86. Found: C, 56.86; H, 2.29; N, 7.39; S, 16.57.

6a,13a-Epitrithio-6a,7,13a,14-tetrahydro-6*H*,13*H*-pyrazino-[1,2-*a*:4,5-*a'*]diindole-6,7,13,14-tetraone (6). A suspension of compound **13** (500 mg, 1.57 mmol) in methylene chloride (40 ml) was treated with pyridine (1 ml) and stirred for 10 min. Sulfur monochloride (0.9 ml, 1.5 g, 0.011 mol) was added all at once and the resulting solution was boiled gently for 15 min. It was then washed with 0.6 N HCl, dried, filtered, and concentrated to ca. 20 ml by boiling. After scratching with a seed crystal and chilling, the product which separated was collected, washed with cold methylene chloride, and air dried to give 380 mg (58%) of the epitrisulfide as a light yellow solid. Recrystallization from methylene chloride with charcoal treatment while in solution gave pale yellow crystals which decomposed without melting at 255 °C. The product had IR (KBr) 1747, 1700, and 1595 cm^{-1} (the neat solid has strong Raman bands at 1760, 1710, 1610, 630, and 490 cm^{-1}); NMR ($CDCl_3$/Me_2SO-d_6) 7.3–8.8 ppm (m, aromatic H); mass spectrum *m/e* 64, 96, 316 (100%), 318, and 412 (M^+).

Anal. Calcd for $C_{18}H_8N_2O_4S_3$: C, 52.42; H, 1.96; N, 6.79; S, 23.32. Found: C, 52.13; H, 2.00; N, 6.65; S, 23.20.

3,6-Bis(*o*-chlorobenzylidine)-2,5-piperazinedione (14). A mixture of glycine anhydride (114 g, 1 mol), *o*-chlorobenzaldehyde (310 g, 2.2 mol), sodium acetate (330 g, 4 mol), and acetic anhydride (520 g, 5.1 mol) was stirred and heated in an oil bath at 140–145 °C for 5 h. The reaction mixture was left to cool with stirring overnight and water was then added in 50-ml portions causing a vigorous reaction. After dilution to ca. 2 l., the black precipitate was collected and washed with water. This material was suspended in ethanol and heated on the steam bath with occasional swirling. It was then filtered and washed repeatedly with methylene chloride until a light yellow filter cake remained. After drying, the product weighed 176 g (49%). A sample recrystallized from CH_2Cl_2/EtOH decomposed without melting above 300 °C: IR (Nujol) 3250, 1700, and 1650 cm^{-1}; mass spectrum *m/e* 323 (100%) and 358 (M^+). Poor solubility precluded an NMR spectrum.

Anal. Calcd for $C_{18}H_{12}Cl_2N_2O_2$: C, 60.19; H, 3.37, Cl, 19.73; N, 7.80. Found: C, 60.57; H, 3 55; Cl, 19.93; N, 7.88.

3,6-Bis(*o*-chlorobenzyl)-2,5-piperazinedione (15). A mixture of compound **14** (25 g) and zinc dust (60 g) in glacial acetic acid (1 l.) was stirred at reflux for 16 h, during which the yellow starting material disappeared. A small amount of water was added carefully to the hot mixture to dissolve the precipitated zinc salts. The excess zinc was filtered and the filtrate concentrated by evaporation under reduced pressure. The colorless product was obtained in quantitative yield by precipitation with cold water followed by collecting, washing with water, and air drying. The product has IR (Nujol) 3200, 1690 and 1640 cm^{-1}. The NMR ($CDCl_3$/Me_2SO-d_6) spectrum has vinyl H singlets at 4.70 and 6.61 ppm showing the product to be a mixture (ca. 1:1) of cis and trans geometrical isomers:[10] mass spectrum *m/e* 325 (100%) and 360 (M^+, very weak). Without further characterization, this dihydro isomer mixture (5 g) was dissolved in hot glacial acetic acid (150 ml), treated with ca. 2 g of Raney nickel, and shaken under 60 psi of H_2 for 50 h. The catalyst was filtered and the filtrate diluted with water. The product was collected, washed with water, and air dried to give 4.3 g (85%) of colorless crystals. A sample recrystallized from acetic acid/ether had mp 220–222 °C; IR (Nujol) 3200, 3050, and 1680 cm^{-1}; NMR ($CDCl_3$/Me_2SO-d_6/D_2O) 2.61 (dd, H_A), 3.17 (dd, H_B), 4.10 (dd, H_X), J_{AB} = 14, J_{AX} = 8, J_{BX} = 5 Hz, 7.30 (aromatic H), and 7.90 (NH, seen before adding D_2O); mass spectrum *m/e* 327 (M − Cl, 100%).

Anal. Calcd for $C_{18}H_{16}Cl_2N_2O_2$: C, 59.52; H, 4.44; Cl, 19.52; N, 7.71. Found: C, 59.77; H, 4.65; Cl, 19.26; N, 7.70.

6a,7,13a,14-Tetrahydro-6*H*,13*H*-pyrazino[1,2-*a*:4,5-*a'*]diindole-6,13-dione (8). A mixture of compound **15** (5 g), cuprous chloride (5 g), and anhydrous potassium carbonate (5 g) in diglyme (100 ml) was stirred and heated at reflux under argon for 20 h. The mixture was then diluted with chloroform and filtered through Celite, the solid being washed several times with hot chloroform. The filtrate was concentrated to a small volume under reduced pressure during which the product began to crystallize. After chilling, the product was collected, washed with ether, and air dried to give 1.85 g (46%) of **8** as a light tan solid. A sample for analysis was vacuum sublimed giving colorless crystals. A recrystallized sample had mp 258–260 °C (lit.[5] mp 263–265 °C): IR (Nujol) 1670 and 1605 cm^{-1}; NMR ($CDCl_3$/Me_2SO-d_6) 3.37 (dd, H_A), 3.55 (dd, H_B), 5.19 (dd, H_X), J_{AB} = 17, J_{AX} = 10, J_{BX} = 8 Hz, 7.20 (m, 6 H, aromatic), and 8.0 (m, 2 H, aromatic); mass spectrum *m/e* 90, 117 (100%), and 290 (M^+).

Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.60; H, 4.80; N, 9.75.

6*H*,13*H*-Pyrazino[1,2-*a*:4,5-*a'*]diindole-6,13-dione (10).[11] A mixture of 60 g each of compound **14**, cuprous chloride, and anhydrous potassium carbonate in diglyme (2 l.) was stirred at reflux under argon for 18 h. After cooling, the mixture was diluted with water and the solid material filtered out. This solid was washed with water and with ether and then air dried. It was then extracted with boiling *o*-dichlorobenzene (500 ml) for ca. 1 h. The mixture was filtered through a preheated fine sintered glass funnel, the liquid in the funnel being kept at >150 °C during the filtration. Additional boiling *o*-dichlorobenzene was used as needed to keep the product in solution and to wash the filter cake of copper salts. The filtrate was cooled and the product collected. The product was then suspended in methylene chloride (500 ml), filtered again, and air dried to give 35.9 g (75%) of **10** as a pale yellow powder. A sample for analysis was vacuum sublimed giving fine yellow crystals with mp 326–328 °C: IR (Nujol) 1705, 1695, 1620, 1585, and 1570 cm^{-1}; mass spectrum *m/e* 286 (M^+, 100%). An NMR spectrum was precluded by poor solubility.

Anal. Calcd for $C_{18}H_{10}N_2O_2$: C, 75.52; H, 3.52; N, 9.78. Found: C, 75.42; H, 3.60; N, 9.88.

6a,7-Dihydro-6*H*,13*H*-pyrazino[1,2-*a*:4,5-*a'*]diindole-6,13-dione (9). A mixture of compound **10** (10 g) and zinc dust (20 g) in glacial acetic acid (250 ml) was stirred at reflux for 18 h. After cooling the mixture was diluted to 1 l. with water and the suspension of the product carefully decanted from the unreacted zinc. The product was collected by filtration, washed with water and with ether, then air dried to give a quantitative yield of **9** as pale yellow powder. Recrystallization from *o*-dichlorobenzene gave 8.4 g of pale yellow crystals with mp 303–306 °C: IR (Nujol) 1720, 1645, 1600, 1580, and 1560 cm^{-1}; NMR ($CDCl_3$/Me_2SO-d_6 spectrum is weak and poorly resolved owing to low solubility) 3.50 (m, 1 H), 4.30 (m, 1 H), 5.70 (m, 1 H), 7.40 (broad, aromatic H), and 8.03 ppm (s, 1 H); mass spectrum *m/e* 115, 143, 144, and 288 (M^+, 100%).

Anal. Calcd. for $C_{18}H_{12}N_2O_2$: C, 74.99; H, 4.20; N, 9.72. Found: C, 74.82; H, 4.26; N, 9.72.

Crystallographic Study of 6. Yellow crystals of **6** were grown from methylene chloride. A crystal approximately 0.11 × 0.06 × 0.05 mm was mounted on a glass capillary tube with epoxy resin. The space group was found to be $P2_12_12_1$ by a combination of film and counter methods. The cell constants were found using 14 reflections on a Hilger and Watts four circle diffractometer (Cu $K\alpha$,λ = 1.54178 Å, nickel filter) to be a = 9.199 (4), b = 13.846 (4), and c = 13.248 (3) Å. Additional crystal data appear in Table I. The crystal density was measured by flotation in aqueous KI as 1.62 g/ml, in good agreement with a calculated density of 1.611 g/ml assuming four molecules in the unit cell. Intensity data were collected using a scintillation counter with pulse-height discrimination, a θ–2θ scan technique, 1°/min scan rate with four background reflections measured every 100 reflections to monitor the extent of crystal decomposition and movement. Of 2015 independent reflections measured, with $\theta < 57°$, *1231* (with $I \geq 2.5\sigma_I$) were considered significantly greater than background.

Data were corrected for Lorentz, polarization, and absorption. The structure was solved by a multiple solution procedure.[12] Nearly all nonhydrogen atoms were located on the first E map. Inclusion of these atoms in an electron density calculation located all remaining atoms. Full-matrix least-squares refinement with first isotropic, then anisotropic refinement were utilized. The positions of all hydrogen atoms were calculated and placed with a C–H bond length of 1.0 Å. Further refinement using anisotropic temperature factors for nonhydrogen atoms and hydrogen atoms at fixed positions reduced R_u ($R = [(\Sigma w|F_o| - |F_c|)^2/\Sigma wF_o^2]^{1/2}$) to 0.087. A final difference Fourier map has no significant features.

Registry No.—**5**, 61193-59-7; **6**, 61193-60-0; **8**, 50501-06-9; **9**, 61193-61-1; **10**, 58881-41-7; **11**, 61193-62-2; **12**, 61193-63-3; **13**, 61193-64-4; **14**, 7670-67-9; *trans*-dihydro-**14**, 61193-65-5; *cis*-dihydro-**14**, 61193-66-6; **15**, 7763-25-9; glycine anhydride, 106-57-0; *o*-iodobenzoic acid, 88-67-5; sulfur monochloride, 10025-67-9; *o*-chlorobenzaldehyde, 89-98-5.

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Synthesis and Chemistry of Cyclic Sulfoximines[1]

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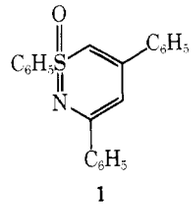
Received October 6, 1976

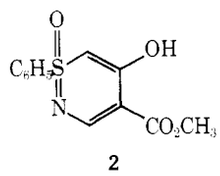
The synthesis of 1,2,4-thiadiazine 1-oxides, which are cyclic sulfoximines exemplified by **16, 19, 27,** and **30,** is reported. Alkylation of **16** with methyl iodide–NaH gives **20,** which in turn can be converted to **21; 16** on treatment with triethyloxonium tetrafluoroborate gives **27.** The unsaturated but nonaromatic 1,2,4-thiadiazine 1-oxide **30** can be prepared by the action of ethyl iodide on the silver salt of **27.** That **27** and **30** are ylidic in nature is shown by their ^1H and ^{13}C NMR spectra, which are discussed, and their ability to undergo electrophilic substitution in the same manner as thiabenzene 1-oxides. The mass spectra of the various thiadiazine 1-oxides show important fragmentation pathways involving phenyl migration from sulfur to the adjacent carbon. These migrations are not important in the spectra of the open-chain intermediates.

The chemistry of sulfoximines has been the focus of much attention in the past several years, and two reviews of this developing area of organosulfur chemistry have recently appeared.[3] Part of the interest in the chemistry of sulfoximines, which are capable of wide structural variations, has been concerned with the synthesis of heterocycles containing this functionality. Two arrangements are possible: (a) with the S=N moiety exocyclic to the ring, and (b) with the S=N moiety an integral part of the ring.[4] We report here the synthesis and chemistry of 1,2,4-thiadiazine 1-oxides, which are sulfoximine heterocycles that exemplify the second category.

Reported syntheses of sulfoximine heterocycles such as **1**[5] and **2**[6] have utilized an existing sulfoximine unit around which to construct a ring. Our initial synthetic goal which would provide access to the thiadiazine 1-oxide system was a diketo structure represented by **3.** The successful preparation of such



1



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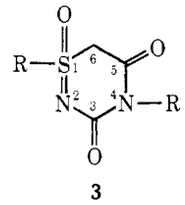

3

a dione was accomplished similarly by starting from an intact sulfoximine.

Scheme I depicts initial unsuccessful approaches. The carboxamidosulfoximine **5** was envisioned as a useful intermediate not only for the synthesis of the dione **3,** but also, by reaction with formic acid, nitrous acid, or reduction–carbonylation, for the generation of other heterocycles as well.

Attempted conversion of the corresponding sulfoxide **4**[7] to **5** by the standard reaction with hydrazoic acid[8] gave exclusively the Pummerer rearrangement product, diphenyl disulfide (**6**). Use of the versatile but unstable amino transfer reagent *O*-mesitylsulfonylhydroxylamine (MSH)[9] did provide the desired intermediate **5** but in less than acceptable yields.

Scheme I