(2) E. J. Corey, T. K. Schaaf, W. Huber, U. Koelliker, and N. M. Weinshenker, *J. Amer. Chem. Soc.*, **92**, 397 (1970).
(3) J. E. Pike, F. H. Lincoln, and W. P. Schneider, *J. Org. Chem.*, **34**, 3552 (1969).
(4) J. H. Helberger and G. Manecke, German Patent 895,559.

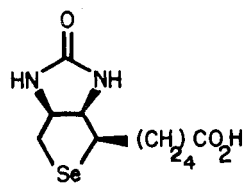
Preparation of *cis*-3,4-Ureyleneselenophane[1]

R. L. Martin and B. E. Norcross*

Department of Chemistry, State University of New York at Binghamton, Binghamton, New York 13901

Received September 3, 1974

In connection with our continuing study of the synthesis of selenobiotin we have prepared the parent fused biheter-



Selenobiotin

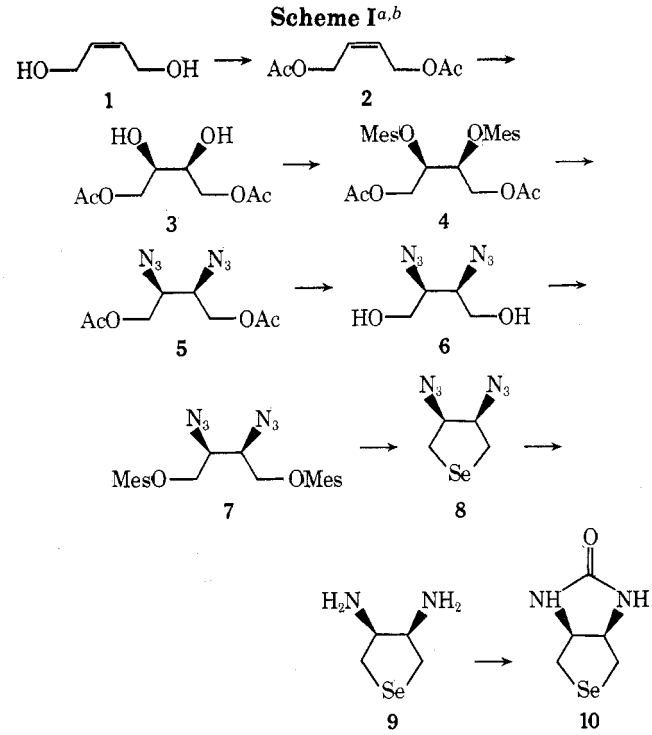
ocyclic system **10**. Effective synthetic entry is based on ring closure with divalent selenium after the cis, vicinal, azide functions, precursors of the needed amine groups, are positioned in a cis relationship on **7**. Approaches utilizing 3,4-disubstituted selenophanes or varied derivatives of *meso*-erythritol other than **4** failed to produce the desired diazidoselenophane (**8**) or diaminoselenophane (**9**), and are the subject of a future communication.

Proof of structure for the diazide **6** was realized by near-quantitative conversion to the known *meso*-2,3-diaminobutane-1,4-diol dihydrobromide[2] and dihydrochloride, by catalytic reduction and treatment with hydrogen halide.

This conversion further establishes the cis stereochemistry of the synthetic intermediates, and of the final product, since this cis arrangement of the nitrogen function is not affected by subsequent reactions. Supporting evidence for this cis, meso sterochemistry is found in the nmr spectra, which present complex multiplets resulting from the six-spin AA'BB'CC' system, the analyses of which are beyond the scope of this report. For instance, the spectra of the noncyclic meso compounds resemble that of meso-1,2,3,4-tetrachlorobutane, rather than *d*-1,2,3,4-tetrachlorobutane,[3] while the nmr spectra of the monocyclic compounds, and *cis*-3,4-ureyleneselenophane, are consistent with that reported for the similar system: *cis*-tetrahydro-2,2-dimethylthieno[3,4-*d*]-1,3-dioxole (the acetone ketal of *cis*-3,4-dihydroxythiophane).[4]

Of the vicinal diazides subsequently described, *meso*-2,3-diazidobutane-1,4-diol (**6**) slowly polymerizes on standing to an unidentified acetone-insoluble substance; in addition, the monomer is initially obtained as a supercooled liquid with such a high heat of fusion that efficient cooling is required at the onset of solidification to avoid detonation. The unexpected stability of some of the diazides was demonstrated by their melting point behavior: the acetate and methanesulfonate diesters, **5** and **7**, give sharp, reproducible melting points, and initially melt in an open flame before deflagrating mildly; under identical conditions, the liquid heterocyclic diazide **8** detonates violently. Most reactions outlined in Scheme I are easily performed within a relatively short period of time under reasonably mild conditions.

Scheme I[a,b]



[a] Compounds **5**–**10** are previously unreported. [b] For all new compounds, except **6** and **8**, analytically pure samples were obtained which gave either satisfactory elemental analyses or mass spectra consistent with the structure indicated.

Evaluation of the biological activity of **10** is underway, and will be separately reported.

Experimental Section

All temperature readings were uncorrected. Ir spectra were determined on a Perkin-Elmer Model 457 spectrophotometer. Nmr spectra were recorded on a Varian A-60 or HA-100D spectrophotometer. Mass spectra were determined at Cornell University, Ithaca, N.Y. Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Inc., Woodside, N.Y. Sodium selenide was purchased from Alfa Inorganics, Inc., Beverly, Mass.; *cis*-2-butene-1,4-diol was obtained from GAF Corp., Inc., Binghamton, N.Y. Those melting points taken in sealed evacuated capillaries are designated (SEC).

The diacetate **2** and the diol **3** were prepared according to literature procedures.[5]

***meso*-1,4-Di-*O*-acetyl-2,3-di-*O*-(methylsulfonyl)erythritol (4).** A solution of **3** (28.4 g; 0.140 mol) in pyridine (100 ml) is stirred at 0° and treated dropwise with methanesulfonyl chloride (34.4 g, 0.300 mol) over a 0.5-hr period. Stirring is continued 4 hr, and the mixture is then poured into 1 l. of ice water. The crystalline product which separates is collected by suction filtration, washed with several portions of cold water, and air dried to give 50.5 g (99.5%) of **4**: mp 138–140° (SEC) (lit.[7] mp 140–141°).

***meso*-1,4-Diacetyloxy-2,3-diazidobutane (5).** A solution of **4** (36.2 g, 0.100 mol) in DMSO (500 ml) is stirred and warmed to 60° in an oil bath. Finely powdered sodium azide (14.3 g, 0.220 mol) is added portionwise until solution is complete. The solution is then maintained at 90–100° for 24 hr before cooling to room temperature. The solution is poured into 1 l. of ice water. After addition of saturated sodium chloride solution (500 ml), the crystalline product is collected by suction filtration, washed with several portions of cold water, and air dried to give 24.7 g (96%) of **5**: mp (and remelt) 108.5–109.0° (SEC) (CCl_4); ir (KBr) 2180, 2120, 1730, 1320, 1240 cm^{-1}; nmr (pyridine) δ 2.04 (s, 6 H, CH_3), 4.12 (m, 2 H, CH), 4.52 (m, 4 H, CH_2).

Anal. Calcd for $C_8H_{12}N_6O_4$: C, 37.37; H, 5.02; N, 32.70. Found: C, 37.30; H, 4.68; N, 32.90.

***meso*-2,3-Diazidobutane-1,4-diol (6).** A solution of **5** (14.8 g, 0.058 mol) in 0.01% methanolic potassium hydroxide (200 ml) is stirred overnight in an open vessel. Removal of solvent and methyl acetate under reduced pressure and at room temperature produces a pale yellow, slightly opaque oil which is immediately redissolved

in methanol (100 ml). Treatment with charcoal (0.5 g), filtration, and solvent removal from the filtrate produce a clear, colorless oil which crystallizes exothermically (*caution:* vigorous cooling must be employed to avoid detonation) to give 10.0 g (99%) of **6**: mp (crude) 67–68° (SEC); ir (KBr) 3300, 2150, 2100, 1315, 1270, 1070 cm^{-1}; nmr (D_2O) δ 3.98 (m, 2 H, CH), 4.13 (m, 4 H, CH_2).

***meso*-2,3-Diaminobutane-1,4-diol.** A solution of **6** (7.4 g; 0.043 mol) in methanol (200 ml) containing 5% Pd/C catalyst (1.0 g) is shaken overnight under hydrogen (125 psi). The catalyst is removed by filtration, and the filtrate is stripped of solvent to give 5.2 g (100%) of the diaminediol, mp 126–127°. A solution of this compound (1.2 g, 0.010 mol) in acetone (50 ml) treated with 40% HBr (5 ml), produces a crystalline precipitate, which was collected by suction filtration, washed with several portions of acetone and air dried to give 2.4 g (85%) of the dihydrobromide: mp 212–213° (SEC) (lit.[2] mp 214–215°). A similar solution of the diaminediol treated with concentrated HCl (3 ml) gives, upon identical workup, 1.8 g (93%) of the dihydrochloride: mp 240–242° (SEC) (lit.[2] mp 241.5–242.5°).

***meso*-2,3-Diazido-1,4-dimesyloxybutane (7).** A solution of **6** (11.2 g; 0.065 mol) in pyridine (100 ml) is stirred at 0° and treated dropwise with methanesulfonyl chloride (16.4 g, 0.143 mol) over a 0.5-hr period. Stirring is continued 4 hr, and the mixture is then poured into 1.3 l. of ice water. The crystalline product which separates is collected by suction filtration, washed with several portions of cold water, and air dried to give 20.2 g (95%) of **7**: mp (and remelt) 92.0–92.5° (SEC) (EtOH); ir (KBr) 2125, 1360, 1290, 1175, 930, 820 cm^{-1}; nmr (acetone-d_6) δ 3.27 (s, 6 H, CH_3), 4.24 (m, 2 H, CH), 4.63 (m, 4 H, CH_2).

Anal. Calcd for $C_6H_{12}N_6O_6S_2$: C, 21.90; H, 3.92; N, 25.53; S, 19.48. Found: C, 22.20; H, 3.72; N, 25.15; S. 19.85.

***cis*-3,4-Diazidoselenophane (8).** Sodium selenide (10.0 g; 0.080 mol) is added portionwise to a stirred, degassed solution of **7** (19.7 g, 0.60 mol) in dimethyl sulfoxide (300 ml) under a nitrogen blanket. The reaction exotherm causes the temperature to rise to 45–50°. After stirring overnight, the mixture is poured into ice water (1.5 l.) and extracted with ethyl ether (4 × 400 ml). The ether extracts are combined, washed with water (4 × 500 ml) and saturated sodium chloride solution (2 × 200 ml), and dried ($MgSO_4$). After filtration the yellow ethereal solution is stripped of solvent to produce a yellow-orange oil. The liquid is dissolved in methanol (50 ml) and eluted (MeOH) from a 1-in. diameter column packed with neutral alumina (100 g). The eluent is stripped of solvent to yield a mobile yellow liquid with a marked offensive odor. The liquid is redissolved in methanol (50 ml), serially treated with charcoal (1.5 g), and filtered until a clear, colorless solution is obtained. This solution is stripped of solvent to give 6.2 (48%) of **8** as a colorless, mobile liquid, homogeneous by tlc: ir (neat) 2110, 1335, 1265 cm^{-1}; nmr (CCl_4) δ 3.00 (m, 4 H, CH_2), 412 (m, 2 H, CH).

***cis*-3,4-Diaminoselenophane (9).** A solution of **8** (6.2 g, 28.6 mol) in methanol (100 ml) containing Adams catalyst (0.5 g) is shaken overnight under hydrogen (125 psi). The catalyst is removed by filtration, and the filtrate is stripped of solvent to give 4.6 g (98%) of **9** as a colorless mobile liquid which readily absorbs carbon dioxide from the atmosphere. The diamine **9** is characterized as the dihydrochloride salt: mp 289–290° dec (SEC) (20% aqueous acetone); ir (KBr) 3100–2800, 1490 cm^{-1}; nmr (D_2O) δ 3.22 (m, 4 H, CH_2), 4.33 (m, 2 H, CH). Mass spectrum of the dihydrochloride gave a peak characteristic only of monoprotonated diamine **9** (70 eV), *m/e* 167 [(M + 1)$^+$].

***cis*-3,4-Ureyleneselenophane (10).** A solution of **9** (3.3 g, 0.020 mol) in benzene (50 ml) is treated with a 12.5% solution of phosgene (3.0 g, 0.030 mol) in benzene (24 ml) followed by pyridine (50 ml). After a 3-hr reflux, an additional 9 ml of phosgene solution (1.0 g; 0.010 mol) is added, and reflux is continued overnight. After removal of solvents under vacuum, water (200 ml) is added to the particulate residue, and the resulting slurry is vigorously stirred 0.5 hr. The solids are collected by suction filtration, washed with several portions of water, and air dried to give 2.0 g (53%) of **10**: mp 256–258° (SEC) (EtOH); 53%; ir (KBr) 3200, 1690, 1260 cm^{-1}; mass spectrum (70 eV) *m/e* 191 (M^+); nmr (DMSO-d_6) δ 3.2 (m, 4 H, CH_2), 4.64 (m, 2 H, CH).

Acknowledgment. Portions of this work were generously supported by the Joint Award Council of the Research Foundation of the State University of New York (JAC-40-259A, JAC-40-7123B).

Registry No.—**3**, 53431-90-6; **4**, 53431-91-7; **5**, 53431-92-8; **6**, 53431-93-9; **7**, 53431-94-0; **8**, 53431-95-1; **9**, 53431-96-2; **9** · 2HCl, 53431-97-3; **10**, 53431-98-4; methanesulfonyl chloride, 124-63-0; *meso*-2,3-diaminobutane-1,4-diol, 53431-99-5; sodium selenide, 1313-85-5.

References and Notes

(1) Taken in part from the Ph.D. Thesis of R. L. Martin, State University of New York at Binghamton, 1974.
(2) P. F. Feit and O. T. Nielsen, *J. Med. Chem.*, **10**, 927 (1967).
(3) W. W. Simmon and M. Zanger, "The Sadtler Guide to NMR Spectra," Sadtler Research Laboratories, Inc., Philadelphia, Pa., 1972, pp 105–106.
(4) R. Lett and A. Marguet, *Tetrahedron Lett.*, 2851, 2855 (1971).
(5) R. A. Raphael, *J. Chem. Soc.*, 401 (1952).
(6) N. A. Milas, S. Sussman, and H. S. Mason, *J. Amer. Chem. Soc.*, **61**, 1844 (1939).
(7) S. S. Brown and G. M. Timmis, *J. Chem. Soc.*, 3656 (1961).

A Convenient and Stereoselective Dithiol Synthesis

E. L. Eliel,[1a] V. S. Rao,[1a] S. Smith,[1b,2] and R. O. Hutchins*[1b]

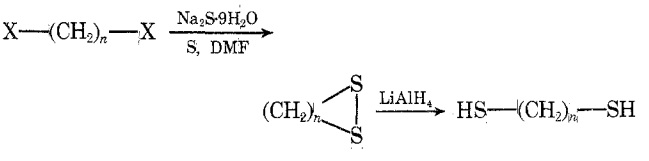
W. R. Kenan, Jr., Laboratories of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27514, and Department of Chemistry, Drexel University, Philadelphia, Pennsylvania 19104

Received September 19, 1974

Although several procedures are available for the preparation of dithiols,[3] our experience has been that the standard methods are often unreliable or give contaminated products, especially when tertiary or other hindered thiols are desired or where stereochemical control is required for the production of particular dithiol diastereomers. The need for relatively pure samples of such dithiols as precursors for various sulfur heterocycles[4] led us to investigate several approaches toward such systems. This Note describes a convenient dithiol synthesis which is particularly attractive for hindered systems and when a maximum of stereochemical control is essential.

The procedure involves initial conversion of a dihalide or disulfonate ester to a di- or polysulfide[5] by displacement with disulfide anion (prepared *in situ* from sodium sulfide and sulfur) and subsequent reduction to the dithiol with lithium aluminum hydride without prior isolation of intermediates. The pathway is illustrated in Scheme I and

Scheme I



or oligomers

Table I presents results for a variety of dithiols chosen to illustrate the versatility of the method with difficult to prepare compounds. For instance, entries 1 and 2 represent highly hindered systems, the former involving displacement of a bifunctional neopentyl system. Furthermore, minimal racemization of chiral centers occurs, thus allowing stereochemical control for the production of diastereomers (entries 3, 4, and 5). Finally, the secondary tertiary halide, 2-methyl-2,4-dibromopentane (entry 6), gave the otherwise difficult to obtain dithiol in respectable yield, presumably *via* initial displacement at the secondary carbon followed by internal substitution.

Experimental Section

Materials. Dimethylformamide was reagent grade from a freshly opened bottle, used without further purification. The sulfonate