2 as white crystals. For analytical purposes the HCl salt was prepared from ethanolic HCl: mp (HCl salt) 225–229 °C; ^{1}H NMR ($CDCl_3$, free base) δ 3.88 (2 H, t, J = 6.6), 3.87 (2 H, dt, J = 2.1, 6.6), 7.51 (2 H, m), 7.59 (1 H, s), 7.78 (1 H, s), 7.81 (1 H, d, J = 8.0), 7.90 (1 H, d,, J = 8.0), 8.56 (1 H, br s); MS, m/z (relative intensity) 181 (100), 152 (48), 89 (21). Anal. Calcd for $C_{13}H_{11}N$·HCl: C, 71.72; H, 5.56; N, 6.43. Found: C, 71.95; H, 5.72; N, 6.39.

3,4-Dihydrobenz[*f*]isoquinoline (5). To a three-necked 1-L round-bottomed flask with mechanical stirrer, reflux condenser, and addition funnel were added Celite (34 g), phosphorus pentoxide (68 g, 479 mmol), and benzene (360 mL). To this well stirred, refluxing mixture was added a solution of 1-(2-formamidoylethyl)naphthalene (18.15 g, 91 mmol) in chloroform (120 mL), dropwise over 1 h. The mixture was maintained at reflux for 24 h, cooled to room temperature, and diluted with water (1 L). This mixture was stirred for 4 h and was filtered through a pad of Celite. The filtrate was washed with chloroform, made basic with concentrated NH_4OH, and extracted with chloroform (3 × 250 mL). The combined chloroform extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product was chromatographed on 100 g of silica gel using ethyl acetate as eluant. There was obtained 5.60 g of **5** as the free base. For analytical purposes the HCl salt was prepared from ethanolic HCl: mp (HCl salt) 190–191 °C; ^{1}H NMR ($CDCl_3$, HCl salt) δ 3.65 (2 H, t, J = 8.8), 4.22 (2 H, t, J = 8.8), 7.73 (2 H, m), 7.92 (3 H, m), 8.13 (1 H, d, J = 7.8), 9.46 (1 H, s); ^{13}C NMR ($CDCl_3$, HCl salt) δ 21.2, 40.9, 121.1, 124.8, 127.1, 128.1, 129.1, 130.7, 137.3, 137.7, 165.6; MS, m/z (relative intensity) 181 (100), 152 (36), 139 (7), 84 (13), 76 (18). Anal. Calcd for $C_{13}H_{11}N$·HCl: C, 71.72; H, 5.56; N, 6.43. Found: C, 71.39; H, 5.89; N, 6.11.

Registry No. 2, 112576-38-2; 2·HCl, 112576-39-3; 4, 23950-49-4; 5, 23950-51-8; 5·HCl, 112576-40-6; 6, 20717-80-0; 7, 112576-41-7; 8, 112576-42-8; 9, 21628-46-6; 9·HCl, 112576-43-9; $AcCH_2CO_2Et$, 141-97-9; $(NH_2)_2CO$, 57-13-6.

An Attempted Synthesis of Biotin

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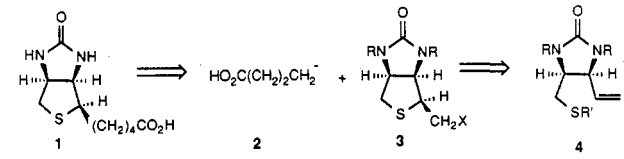
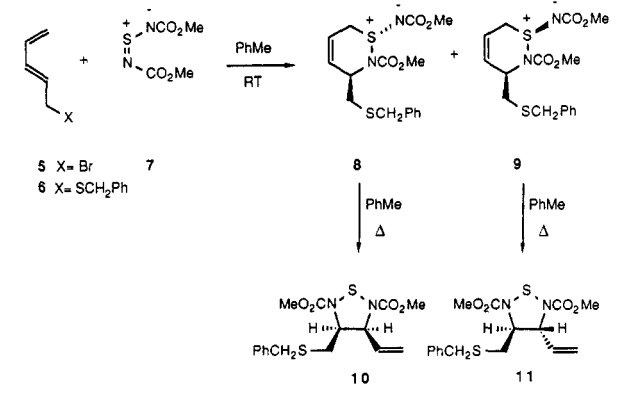
Renewed interest in the total synthesis of biotin (1)[1] has been spurred by recent findings[2] that emphasize the importance of this substance in the areas of nutrition and growth promotion. Despite efforts to develop new and efficient approaches to 1, the cofactor is still prepared commercially by the original Sternbach synthesis.[3] We have been attempting to effect a short, high yield, stereoselective total synthesis of biotin via the novel strategy outlined in Scheme I. It was our intention to prepare tetrahydrothiophene derivative 3, where X is an appropriate leaving group, and couple it with a synthetic equivalent for carbanion 2 to produce 1. We hoped that 3 could be synthesized from olefinic sulfide 4, which should

Scheme I



Scheme II



be available via our recently reported[4,5] methodology for stereoselective synthesis of unsaturated vicinal diamines. Clearly, in order for this route to be successful, the key cyclization of 4 to 3 must be achieved with the proper regiochemistry and stereochemistry at C-2.

The requisite erythro vicinal diamine derivative (cf. 4) was synthesized as outlined in Scheme II starting from the known (*E*)-pentadienyl bromide 5.[6] This compound upon treatment with the sodium salt of benzyl mercaptan was converted to sulfide 6 (97% yield). Diels–Alder cycloaddition of 6 with sulfur diimide 7 occurred in high yield in toluene at room temperature to produce a 7.7:1 mixture of epimeric dihydrothiazine imines 8 and 9. As anticipated from earlier work, no other regioisomeric adducts were detected.[5] Compounds 8 and 9 were not readily separable, so the mixture was used directly in the next step.

Heating the 7.7:1 mixture of adducts 8 and 9 in refluxing toluene induced a [2,3]-sigmatropic rearrangement, giving thiadiazolidines 10 and 11 in a 7.7:1 ratio in quantitative yield. We have previously shown that this type of rearrangement is stereospecific, with isomers having the stereochemistry shown in 8 affording 10 and 9 giving 11.[4,5] In fact, thermal rearrangement of a purified sample of major adduct 8 cleanly produced thiadiazolidine 10. The mixture of 10 and 11 could be readily separated at this stage by flash chromatography, and the desired major thiadiazolidine 10 was carried on.

Reduction of 10 with $NaBH_4$ gave the erythro dicarbamate 12 (91%). This compound was cyclized by using sodium hydride to urea 13 (89%).[4] Interestingly, the dibenzylated urea 14 could be prepared in a single step in 96% yield by a similar cyclization in the presence of benzyl bromide.

Treatment of olefinic sulfide 13 with bromine or NBS produced a new compound, which we believe is a cyclization product. However, the material was extremely insoluble and decomposed upon attempted chromatographic purification. On the other hand, sulfide 14 reacted cleanly

(1) For selected recent examples and further lead references, see: (a) Bory, S.; Luche, M. J.; Moreau, B.; Lavielle, S.; Marquet, A. *Tetrahedron Lett.* **1975**, 827. (b) Ohrui, H.; Emoto, S. *Tetrahedron Lett.* 1975, 2765. (c) Confalone, P. N.; Pizzolato, G.; Uskokovic, M. R. *Helv. Chim. Acta* **1976**, *59*, 1005. (d) Marx, M.; Marti, F.; Reisdorff, J.; Sandmeier, R.; Clark, S. *J. Am. Chem. Soc.* **1982**, *104*, 6460. (f) Bates, H. A.; Rosenblum, S. B. *Tetrahedron* **1985**, *41*, 2331. (g) Poetsch, E.; Casutt, M. *Chimia* **1987**, *41*, 148.

(2) (a) Blair, R.; Whitehead, C. *Feedstuffs* **1976**, *48*, 30. (b) McCormick, D. B. *Nutr. Rev.* **1973**, *33*, 97. (c) Bonjour, J. P. *Int. J. Vitam. Nutr. Res.* **1977**, *47*, 107. (d) Anderson, J. O.; Warnick, R. E. *Poultry Sci.* **1970**, *49*, 569.

(3) Goldberg, M. W.; Sternbach, L. H. U.S. Patents 489 232, 2 489 235, and 2 489 238, 1949.

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(6) Miginiac, P. *Ann. Chim.* **1962**, *7*, 445.

(7) Billimoria, J. D.; Maclagan, N. F. *J. Chem. Soc.* **1954**, 3257.

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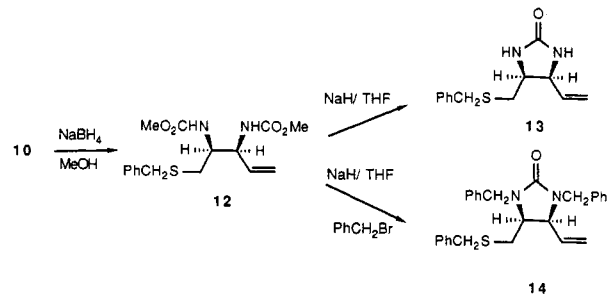
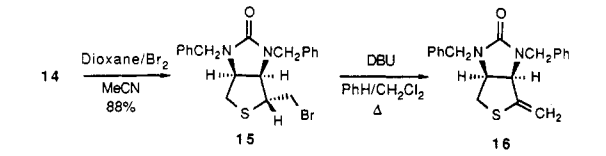


with bromine–dioxane complex[7] in acetonitrile to yield a single cyclization product eventually shown to be **15** (88%).



An attempt was made to characterize **15** by proton NMR comparison with closely related compounds.[1f] However, neither the regiochemistry nor stereochemistry of the cyclization product could be unambiguously established in this manner. A GASPE ^{13}C NMR[8] spectrum of **15** suggested that the compound did in fact have the desired [5,5]-bicyclic ring system. This assignment was supported by the elimination of HBr from **15** to furnish vinyl sulfide **16**, which clearly showed a terminal vinyl group in its ^1H NMR spectrum. Finally, the complete structure of **15** was firmly established by X-ray crystallography, indicating that the cyclization unfortunately had proceeded to give a tetrahydrothiophene epimeric at C-2 to that needed for biotin (cf. **3**).

Electrophilic cyclizations of olefinic alcohols and ethers to tetrahydrofurans have recently been investigated in detail with regard to their diastereofacial selectivity.[9] Similar studies have been performed on conversion of nitrogen-containing systems to pyrrolidines. Recently, Chamberlin et al. have attempted to unify these diverse results.[9] To our knowledge, diastereofacial selectivities in electrophilic cyclizations of olefinic sulfides to tetrahydrothiophenes have not been studied. Clearly conversion of **14** to **15** is a highly stereoselective process, but we are hesitant to draw mechanistic conclusions from a single example.[10] Since **15** has the incorrect stereochemistry for biotin, we have not pursued this route.

Experimental Section

(*E*)-2,4-Pentadienyl Benzyl Sulfide (6). A solution of (*E*)-2,4-pentadienyl bromide (**5**, 10.1 g, 68.7 mmol) in 100 mL of anhydrous CH_2Cl_2 was added dropwise to an ice-cold suspension of benzyl mercaptan (8.5 g, 69 mmol) and NaH (80% in mineral oil, 2.1 g, 70 mmol) in 150 mL of anhydrous CH_2Cl_2. After stirring the mixture for 2 h at 0 °C, water (250 mL) was added carefully, and the resulting layers were separated. The aqueous layer was back-extracted three times with 100-mL portions of CH_2Cl_2, and the combined organic layers were dried (Na_2SO_4). Rotary evaporation of the solution gave an oil, which was purified in three portions by dry column chromatography[11] (ethyl acetate–hexane) to give 12.6 g (97%) of diene **6** as a colorless oil: IR (film) 3035, 2910, 1010, 910, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 7.27 (5 H, s), 6.60–4.90 (5 H, m), 3.61 (2 H, s), 3.01 (2 H, d, J = 6.5 Hz); CI mass spectrum, m/z (relative intensity) 191 (22), 91 (100), 67 (100).

Reaction of (*E*)-2,4-Pentadienyl Benzyl Sulfide (6) with Sulfur Bis[(methoxycarbonyl)imide] (7). A solution of diene **6** (3.04 g, 16.3 mmol) in 150 mL of anhydrous toluene was cooled to 0 °C, and a solution of diimide **7** (3.39 g, 19.0 mmol) in 25 mL of anhydrous toluene was added dropwise. The ice bath was removed and the mixture was stirred for 10 h. Brine (100 mL) was added to the reaction mixture, the layers were separated, and the aqueous layer was extracted three times with 50-mL portions of ethyl acetate. The combined organic layers were dried ($MgSO_4$) and rotary evaporated. Purification of the oily residue by dry column chromatography (ethyl acetate–hexane) afforded 5.27 g (88%) of a white solid, which was judged by ^1H NMR (benzene-d_6, 200 MHz) to be a 7.7:1 mixture of epimeric adducts **8** and **9**. For characterization purposes, the major adduct **8** was purified by recrystallization (CH_2Cl_2–pentane). Otherwise, the mixture of adducts was used in the next step, with the minor product eventually being removed by flash chromatography (vide infra).

Data for major Diels–Alder adduct **8**: IR (film) 1730, 1640, 1440, 1295, 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.36 (5 H, m), 6.18 (1 H, ddd, J = 10.6, 4.4, 2.9 Hz), 5.97 (1 H, dddd, J = 10.3, 7.6, 2.2, 0.8 Hz), 4.60 (1 H, ddd, J = 5.2, 4.1, 1.2 Hz), 3.96 (3 H, s), 3.81 (1 H, dt, J = 15.6, 2.6 Hz), 3.76 (2 H, d, 1.2 Hz), 3.72 (3 H, s), 3.45 (1 H, ddd, J = 15.6, 7.3, 1.1 Hz), 3.09 (1 H, dd, J = 13.6, 6.6 Hz), 2.96 (1 H, dd, J = 13.6, 2.5 Hz); ^{13}C NMR ($CDCl_3$) δ 165.34, 154.97, 137.96, 130.40, 128.79, 128.51, 127.16, 116.13, 54.59, 52.97, 52.44, 42.81, 37.36, 35.60; CI mass spectrum, m/z (relative intensity) 369 (19), 138 (79), 76 (100).

Preparation of Thiadiazolidines 10 and 11. Diels–Alder adduct **8** (3.43 g, 9.32 mmol) in 150 mL of anhydrous toluene was refluxed for 1 h. The mixture was cooled to room temperature, the solvent was removed by distillation in vacuo, and the residual oil was purified by flash chromatography (50 mm column, 1:3 ethyl acetate/hexane) to give thiadiazolidine **10** (3.36 g, 98%) as a yellow oil: IR (film) 2960, 1720, 1440, 1340–1240, 705 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.26 (5 H, m), 5.71 (1 H, ddd, J = 17.0, 10.0, 7.1 Hz), 5.30 (1 H, d, J = 18.2 Hz), 5.23 (1 H, d, J = 10.4 Hz), 4.89 (1 H, d, J = 7.3 Hz), 4.79 (1 H, dd, J = 7.2, 5.3 Hz), 3.74 (3 H, s), 3.73 (2 H, s), 3.69 (3 H, s), 2.76 (1 H, dd, J = 14.0, 8.7 Hz), 2.50 (1 H, dd, J = 14.0, 5.3 Hz); CI mass spectrum, m/z (relative intensity) 369 (100, M + 1), 149 (100), 91 (100); EI mass spectrum, m/z (relative intensity) 368 (1), 84 (93), 49 (100); high-resolution mass spectrum calcd for $C_{16}H_{20}N_2O_4S_2$ 368.0864, found 368.0869.

In similar fashion, a 7.7:1 mixture of adducts **8** and **9** afforded a 7.7:1 mixture of thiadiazolidines **10** and **11** (100%), which was separated by flash chromatography.

Data for minor thiadiazolidine **11**: IR (film) 2960, 1720–1690, 1440, 1360–1260, 705 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.31 (5 H, m), 5.65 (1 H, ddd, J = 17.1, 10.3, 5.1 Hz), 5.25 (1 H, ddd, J = 16.9, 1.4, 1.0 Hz), 5.18 (1 H, ddd, J = 10.2, 1.4, 1.0 Hz), 4.86 (1 H, dd, J = 5.1, 0.7 Hz), 4.44 (1 H, ddd, J = 8.7, 6.3, 0.6 Hz), 3.77 (2 H, s), 3.74 (3 H, s), 3.73 (3 H, s), 2.77 (1 H, dd, J = 14.0, 6.3 Hz), 2.50 (1 H, dd, J = 14.0, 8.6 Hz); CI mass spectrum, m/z (relative intensity) 369 (85, M^+ + 1), 149 (100), 91 (100); EI mass spectrum, m/z (relative intensity) 368 (0.5), 84 (82), 49 (100); high-resolution mass spectrum calcd for $C_{16}H_{20}N_2O_4S_2$ 368.0864, found 368.0853.

Reduction of Thiadiazolidine 10. Thiadiazolidine **10** (3.36 g, 9.13 mmol) was dissolved in 150 mL of methanol and cooled to 0 °C. Sodium borohydride (175 mg, 4.61 mmol) was added, the ice bath was removed, and the mixture was stirred for 18 h, trapping the evolved H_2S in aqueous KOH solution. The mixture was purged with nitrogen for 10 min to remove residual H_2S and was rotary evaporated. The solid residue was taken up in 50 mL of ethyl acetate and was washed with 100 mL of brine, which was back-extracted with 50 mL of ethyl acetate. The combined organic layers were dried ($MgSO_4$) and evaporated. Purification of the residue by flash chromatography (50 mm column, 1:3 ethyl ace-

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(10) One possibility is that olefin–sulfide **14** does not cyclize via the usual "type A" conformation[9] leading to the desired all-cis isomer of **15** because both the stability and reactivity of this conformer is diminished: the stability via a steric interaction between the *N*-benzyl group and the *cis*-vinyl hydrogen; the reactivity since the nitrogen lone pair is orthogonal to the π bond reducing homoconjugation (cf. Kahn, S. D.; Hehre, W. J. *Tetrahedron Lett.* **1985**, *26*, 3647).

(11) Harwood, L. M. *Aldrichimica Acta* **1985**, *18*, 25.

tate/hexane) provided 2.81 g (91%) of erythro dicarbamate **12** as white crystals: mp 168–169 °C (recrystallized from ethyl acetate–hexane); IR (film) 3325, 2960, 1690, 1540, 1320, 1300, 1255, 1230, 1195, 1025, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.30 (5 H, m), 5.66 (1 H, ddd, J = 17.3, 10.1, 6.0 Hz), 5.36 (1 H, NH), 5.23 (1 H, dd, J = 17.4, 1.2 Hz), 5.13 (1 H, dd, J = 10.2, 1.2 Hz), 4.82 (1 H, NH), 4.39 (1 H, m), 3.96 (1 H, m), 3.73 (2 H, s), 3.69 (3 H, s), 3.67 (3 H, s), 2.47 (2 H, m); CI mass spectrum, m/z (relative intensity) 339 (40, $M^+ + 1$), 307 (73, $M^+ + 1 - CH_3OH$), 264 (28), 149 (43), 91 (100).

Cyclization of Erythro Dicarbamate 12 to Urea 13. Sodium hydride (80% in mineral oil, 400 mg, 13.3 mmol) was added to an ice-cold solution of erythro-dicarbamate **12** (3.60 g, 10.7 mmol) in 250 mL of anhydrous THF. The ice bath was removed and the suspension was stirred for 3 h. Aqueous NaOH solution (15%, 3 mL) was added, and the mixture was stirred for an additional 4 h and was evaporated. The solid residue was partitioned between 50 mL of ethyl acetate and 50 mL of a 1:1 brine/H_2O mixture. The aqueous layer was extracted three times with 50-mL portions of ethyl acetate, the combined extracts were dried ($MgSO_4$), and the solution was evaporated. Purification of the residual yellow oil by flash chromatography (50 mm column, ethyl acetate) provided 2.34 g (89%) of cyclic urea **13** as a colorless oil: IR (film) 2960, 1720, 1440, 1320, 1265, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.26 (5 H, m), 5.72 (1 H, ddd, J = 17.0, 10.1, 7.0 Hz), 5.70 (1 H, NH), 5.25 (1 H, dd, J = 17.1, 0.9 Hz), 5.18 (1 H, dd, J = 9.6, 0.9 Hz), 4.23 (1 H, dd, J = 8.0, 7.2 Hz), 3.75 (1 H, dt, J = 8.4, 5.5 Hz), 3.69 (2 H, s), 2.44 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 163.35, 137.63, 133.07, 128.61, 128.36, 126.97, 118.27, 57.83, 54.91, 36.22, 32.57; EI mass spectrum, m/z (relative intensity) 248 (3), 111 (41), 91 (32), 84 (100); high-resolution mass spectrum calcd for $C_{13}H_{16}N_2OS$ 248.0983, found 248.0975.

Preparation of Tribenzyl Cyclic Urea 14. Sodium hydride (80% in mineral oil, 65 mg, 2.2 mmol) was added to an ice-cold solution of dicarbamate **12** (270 mg, 0.80 mmol) and benzyl bromide (0.25 mL, 2.1 mmol). The ice bath was removed and the mixture was stirred for 12 h. Saturated NH_4Cl solution (1 mL) was added to the mixture and the solvent was evaporated. The solid residue was partitioned between 50 mL of ethyl acetate and 50 mL of water. The aqueous layer was extracted three times with 25-mL portions of ethyl acetate, and the combined extracts were dried ($MgSO_4$) and evaporated. Purification of the residual oil by flash chromatography (20 mm column, 1:3 ethyl acetate/hexane) gave 329 mg (96%) of **14** as a colorless oil: IR (film) 1700, 1440, 1420, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.27 (10 H, m), 7.13 (5 H, m), 5.65 (1 H, ddd, J = 17.0, 10.1, 8.9 Hz), 5.31 (1 H, dd, J = 10.2, 1.5 Hz), 5.17 (1 H, dd, J = 16.9, 1.3 Hz), 4.90 (1 H, d, J = 15.1 Hz), 4.62 (1 H, d, J = 15.5 Hz), 4.06 (1 H, d, J = 15.5 Hz), 3.82 (1 H, d, J = 15.0 Hz), 3.80 (1 H, t, J = 8.4 Hz), 3.49 (2 H, s), 3.41 (1 H, ddd, J = 8.5, 8.4, 4.5 Hz), 2.43 (2 H, m); EI mass spectrum, m/z (relative intensity) 428 (2), 291 (79), 91 (100); high-resolution mass spectrum calcd for $C_{27}H_{28}N_2OS$ 428.1922, found 428.1908.

Cyclization of Tribenzylurea 14 to Tetrahydrothiophene 15. Bromine–dioxane complex[7] was added in 20–30-mg portions to tribenzylurea **14** (55 mg, 0.13 mmol) in 15 mL of acetonitrile until starting material was consumed (TLC analysis). The yellow solution was stirred for 10 h, saturated sodium thiosulfate solution (5 mL) was added to the mixture, and the resulting solution was concentrated in vacuo. The residual material was partitioned between 20 mL of ethyl acetate and 20 mL of brine, and the aqueous layer was extracted three times with 20-mL portions of ethyl acetate. The combined extracts were dried ($MgSO_4$) and rotary evaporated to afford a yellow oil, which was purified by flash chromatography (10 mm column, 1:3 ethyl acetate/hexane) to give 47 mg (88%) of bromide **15** as a white solid: mp 128–129 °C (recrystallized from ethyl acetate–hexane); IR (film) 1695, 1455, 1450, 1240, 700 cm^{-1}; ^1H NMR (benzene-d_6, 360 MHz) δ 7.43 (2 H, m) 7.10 (8 H, m), 4.77 (1 H, d, J = 15.4 Hz), 4.75 (1 H, d, J = 15.4 Hz), 4.04 (1 H, d, J = 15.4 Hz), 3.79 (1 H, d, J = 15.4 Hz), 3.71 (1 H, d, J = 7.9 Hz), 3.34 (1 H, dd, J = 7.6, 4.4 Hz), 3.00 (1 H, dd, J = 11.9, 4.3 Hz), 2.88 (1 H, dd, J = 10.2, 4.3 Hz), 2.45 (1 H, dd, J = 11.9, 10.2 Hz), 2.27 (1 H, d, J = 12.9 Hz), 2.02 (1 H, dd, J = 13.0, 4.8 Hz); ^{13}C NMR ($CDCl_3$) δ 159.64, 137.50, 136.83, 128.71, 128.58, 128.23, 128.00, 127.64, 127.54, 65.45, 61.91, 53.84, 46.54, 46.27, 35.72, 34.26, 34.13; CI mass spectrum, m/z (relative intensity) 419 (93), 417 (100), 337 (68).

Preparation of Vinyl Sulfide 16. 1,8-Diazabicyclo[5.4.0]-undec-7-ene (DBU, 0.05 mL, 0.34 mmol) was added to a solution of bromide **15** (10 mg, 0.024 mmol) in 20 mL of a 2:1 mixture of benzene/CH_2Cl_2. The mixture was refluxed for 1 h and evaporated in vacuo to give an oil, which was purified by preparative TLC (1:2 ethyl acetate/hexane) to afford 6 mg (77%) of **16** as a colorless oil: IR (film) 2975, 2960, 1690, 1440, 1230, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.29 (10 H, m), 5.29 (1 H, s), 5.10 (1 H, s), 5.06 (1 H, d, J = 15.1 Hz), 4.81 (1 H, d, J = 15.3 Hz), 4.29–4.06 (2 H, m), 4.23 (1 H, d, J = 15.3 Hz), 4.02 (1 H, d, J = 15.6 Hz), 3.00 (2 H, m); CI mass spectrum, m/z (relative intensity) 337 (100).

Acknowledgment. This work was generously supported by the National Science Foundation (CHE 8402127). We thank Mr. A. Freyer for help in obtaining NMR spectra.

Supplementary Material Available: Tables of X-ray crystallographic data for tetrahydrothiophene **15** (9 pages). Ordering information is given on any current masthead page.

Syntheses of *ribo* and *arabino* Deoxy- and Deoxyaminoepoxybenzoxocin Sugar Analogues

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Previously, we have reported procedures to the epoxybenzoxocin ring system,[2,3] a structural fragment present in nogarol anthracyclines.[4] We have continued to explore the scope and limitations of various methods for functionalizing the pyranose ring in **1** and have now achieved brief, high-yield total syntheses of deoxy and deoxyamino sugar analogues with *ribo* and *arabino* configurations. Novel aspects of this work are our findings that the *erythro* acetamido ketobenzoxocin **7** can be equilibrated to the thermodynamically more stable *threo* isomer **8** and that the ketones **6** and **7** exist in the twist-boat conformation.

As indicated in Scheme I, catalytic hydrogenation of **1a**[2] gave the saturated ketone compound **1b** quantitatively. Addition of a solution of the ketone **1b** and isoamyl nitrite to a solution of sodium methoxide routinely furnished the α-oximino ketone **2** in 88% yield. These conditions were established only after considerable study; the use of other reagents or protocols gave little or no product. Sodium borohydride reduction of **2** to the alcohol **3a**, followed by catalytic reduction of the oxime functionality in **3a** and acetylation of the amino alcohol intermediate, furnished the diacetate **4a**. Ammonolysis of **4a** selectively cleaved the *O*-acetyl functionality and gave the acetamido hydroxyepoxybenzoxocin **4b** with the *ribo* configuration. The overall preparation of **4b** was stereospecific since both reduction steps occurred exclusively from the exo face due

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