Chemistry of L-Ascorbic and D-Isoascorbic Acids. 4. An Efficient Synthesis of 2-Deoxypentofuranoses[1]

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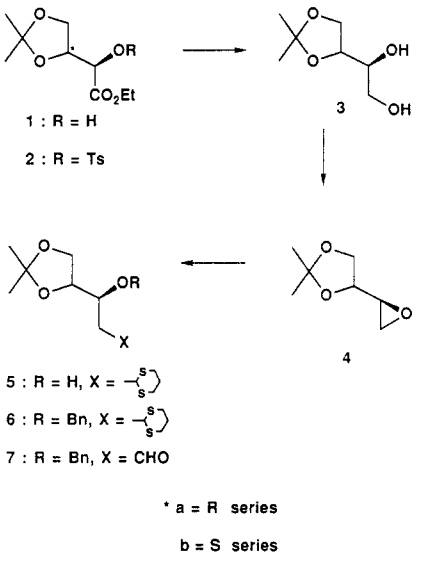
L-Ascorbic and D-isoascorbic acids have been converted to methyl 3-*O*-benzyl-2-deoxypentofuranosides. The synthetic routes are enantiospecific, efficient, and economic and proceed in high yields.

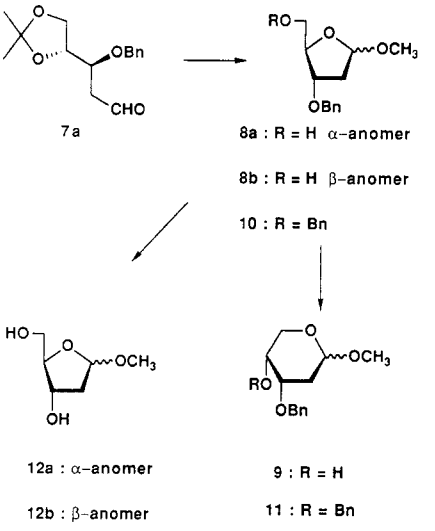
2-Deoxypentofuranoses, especially 2-deoxyribose, are attractive targets for the synthesis of nucleosides[2] and other molecules of biological interest.[3] Older reports on the synthesis of these compounds make use of other sugars such as D-arabinose,[4,5] D-erythrose,[6] D-glucose,[7] and D-xylose.[8,9] More recent approaches involve the preparation of 2-deoxypentonolactones, which can subsequently be reduced to the corresponding pentoses. Some of these approaches involve the nucleophilic addition of a two- or three-carbon fragment to 2,3-*O*-isopropylideneglyceraldehyde. Dichloro-[10] and difluoroacetate,[11] diallylzinc,[12] ketene silyl acetals,[13] and ester boron enolates[14] are examples of such nucleophiles.

Other methods using different starting materials have also been reported. Tartrates have been converted to a number of ribono- and xylonolactones.[15] An interesting 2+3 cycloaddition reaction between nitrile oxides and optically pure allyl ethers was reported to form a 2-deoxypentofuranose through an intermediate oxazoline.[16] Racemic 2-deoxypentofuranoses have been prepared via Reformatsky reaction of ethyl bromoacetate with acrolein.[17] More recently, a sequential one-carbon homologation involving the diastereoselective addition of 2-(trimethylsilyl)thiazole to (*R*)-2,3-*O*-isopropylideneglyceraldehyde was shown to furnish adducts convertible to D-ribose and 2-deoxy-D-ribose.[18]

Scheme I



Scheme II



The above syntheses suffer from either one of the two drawbacks: low yields[4-7] or the separation of enantiomers and/or diastereomers.[9-18] Furthermore, the non-carbohydrate approaches, which are centered around the aldol condensation, lead predominantly to erythro products. In this paper, a method in which all four stereoisomers of *erythro*- as well as *threo*-3,4-epoxy-1,2-*O*-isopropylidenebutane-1,2-diol are accessible is reported and their stereospecific conversion to other useful chirons is accomplished.

We have recently reported the synthesis of diastereomers **4a** and **4b** from D-isoascorbic and L-ascorbic acids, re-

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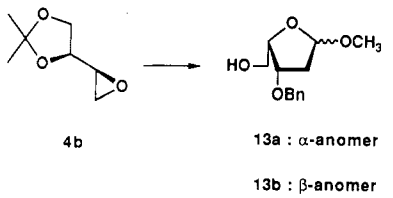
Scheme III



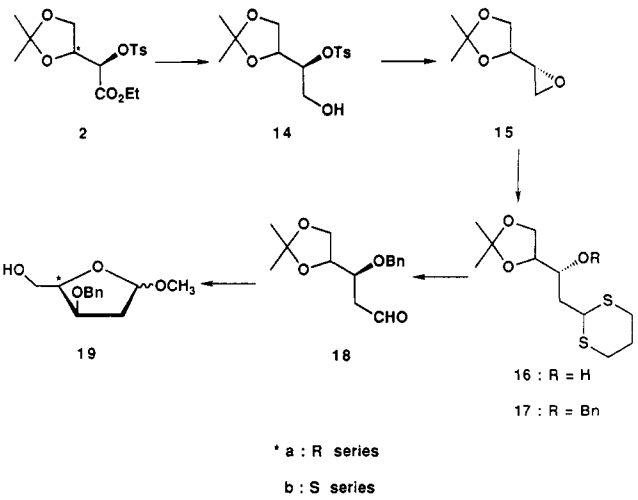
spectively.[19] These have now been converted to key aldehydes (Scheme I), which were cyclized to the title compounds.

Regiospecific ring opening of **4a** with the lithium salt of 1,3-dithiane[20] furnished **5a**, which was benzylated to give **6a**. Cleavage of the dithiane ring with methyl iodide and calcium carbonate[20] afforded aldehyde **7a**. This, upon treatment with 0.2% methanolic HCl at room temperature for 20 min, gave an α–β anomeric mixture (6:4) of methyl 2-deoxy-D-ribofuranosides (**8**) in 74.4% overall yield from epoxide **4a** (Scheme II). It should be emphasized that the duration of this reaction is critical for the exclusive formation of a pentofuranoside. As expected, longer reaction times led to the more thermodynamically favored pentopyranosides **9**.[21] Close monitoring of the hydrolytic reaction of **7a** with 0.2% methanolic HCl at room temperature by thin-layer chromatography and ^{1}H NMR spectroscopy clearly showed that initial pyranoside formation started after 40 min and continued to increase until an equilibrium mixture of **8** and **9** in the ratio 1:1 was attained after 4 h. This ratio was easily determined by integrating the well-separated anomeric proton resonances appearing at δ 4.88–5.13 (m) and 4.73 (t) for **8** and **9**, respectively.

Proof of the structural assignment was sought through conversion of these compounds to known derivatives. Methyl 3,5-di-*O*-benzyl-2-deoxy-D-ribofuranoside has been prepared by dibenzylation of the parent methyl furanoside.[22] When the mixture of **8** and **9** was subjected to benzylating conditions, the ^{1}H NMR data of the benzylated mixture **10** and **11** were identical to what was believed to be a mixture of anomeric furanosides **10**.[22] Therefore, alternate structural proof was sought and was derived from conversion of **8b** to **12b** whose ^{1}H NMR spectrum and optical rotation have been reported.[23] The anomeric mixture **8** was separated by column chromatography into the pure anomers **8a** and **8b**, which were debenzylated with use of sodium and liquid ammonia to the corresponding α- and β-methyl 2-deoxy-D-ribofuranosides (**12a** and **12b**, respectively). Attempts to debenzylate by hydrogenolysis were not successful. A high-resolution ^{1}H NMR spectrum and the optical rotation of **12b** were identical with those reported.[23] Furthermore, and in accordance with Hudson's rule,[24] the α-anomer **12a** was the more dextrortatory of the pair, providing additional evidence for structural assignment.

A series of identical reactions was applied to **4b** (Scheme III) to obtain an anomeric mixture of methyl 3-*O*-benzyl-2-deoxy-L-xylofuranoside, which were separated by column chromatography to afford **13a** and **13b**. The anomeric configurations of these compounds are also based on Hudson's rule for L-sugars where the more levorotatory isomer is assigned the α-configuration.

Scheme IV



The remaining diastereomers **19a** and **19b** could be obtained in a similar fashion from epoxides **15a** and **15b**, respectively (Scheme IV). Initial efforts to invert the stereochemistry at C-2 in **5** either by Mitsunobu reaction[25] or with cesium acetate[26] were not satisfactory. An alternate method to effect the inversion was sought by intramolecular S_N2 displacement of a secondary tosylate at C-3 with a primary hydroxyl group at C-4. This required selective reduction of the ester function in **2**. Aluminum hydride[27] appeared to be a well-suited reagent for the conversion of **2**[1] to **14**. Indeed, when a THF solution of aluminum hydride was added to **2** at 0 °C, hydroxy tosylate **14** was obtained in quantitative yield. Treatment of these compounds in ether with 1 equiv of methanolic sodium methylate furnished the corresponding epoxides **15a** and **15b**. Their conversions to targets **19a** and **19b** followed the procedure outlined earlier.

That no racemization took place throughout the synthetic routes is evidenced by the equal but opposite optical rotations of all enantiomeric pairs described, namely, **5a–16b**, **5b–16a**, **6a–17b**, **6b–17a**, **7a–18b**, and **7b–18a**.

In summary, an economical method for the preparation of 2-deoxypentofuranoses and other four- and five-carbon chirons was developed. Besides efficiency and high yields, it has the additional advantage of allowing direct and selective protection at O-3 with benzyl, allyl, and related groups without affecting O-5. The utility of this approach in the synthesis of other molecules is currently under investigation.

Experimental Section

Melting points were determined on a Buchi 535 melting point apparatus and are uncorrected. The ^{1}H NMR spectra were recorded at 90 or 300 MHz. Silica gel (Merck grade 60, 230–400 mesh, 60 Å) suitable for column chromatography was purchased from Aldrich. All solvent proportions are by volume unless otherwise stated. Elemental analyses were only obtained for one of two enantiomers.

2-[(2*S*,3*R*)-3,4-*O*-Isopropylidene-2,3,4-trihydroxybutyl-1]-1,3-dithiane (5a). To a stirred solution of 1,3-dithiane (10.25 g, 85.4 mmol) in dry THF (150 mL) at −30 °C under nitrogen was added *n*-butyllithium (58.7 mL, 1.6 M solution in hexane, 89.7 mmol). After the mixture was stirred for 2 h at −20 °C, epoxide **4a** (12.3 g, 85.4 mmol) in dry THF (25 mL) was added dropwise.

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The reaction mixture was stirred at 0 °C for an additional 3 h and then concentrated under reduced pressure on a rotary evaporator. Water (100 mL) was added to the reaction mixture, which was subsequently washed with ether (3 × 100 mL). The combined organic layers were washed with brine and dried ($MgSO_4$). The viscous material obtained after solvent removal at reduced pressure was chromatographed on a silica gel column with hexane–ethyl acetate (10:1) to give **5a**: 20.3 g, 98%; $[\alpha]^{25}_D$ −22.69° (*c* 3.05, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 3 H), 1.4 (s, 3 H) 1.53–2.23 (m, 4 H), 2.5 (br s, 1 H, D_2O exchangeable), 2.63–3.0 (m, 4 H), 3.76–4.1 (m, 4 H), 4.24 (dd, *J* = 9 and 4.5 Hz, 1 H).

Anal. Calcd for $C_{11}H_{20}O_3S_2$: C, 49.97; H, 7.62; S, 24.25. Found: C, 49.95; H, 7.72; S, 24.16.

2-[(2*S*,3*S*)-3,4-*O*-Isopropylidene-2,3,4-trihydroxybutyl-1]-1,3-dithiane (5b). This compound was prepared in 98.5% yield from **4b** by the procedure described for **5a**: $[\alpha]^{25}_D$ −25.88° (*c* 3.87, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 3 H), 1.43 (s, 3 H), 1.53–2.26 (m, 4 H), 2.36–2.33 (m, 5 H), 3.56–4.1 (m, 4 H), 4.3 (dd, *J* = 9 Hz, 1 H).

Anal. Calcd for $C_{11}H_{20}O_3S_2$: C, 49.97; H, 7.62; S, 24.25. Found: C, 50.03; H, 7.85; S, 24.03.

2-[(2*S*,3*R*)-2-*O*-Benzyl-3,4-*O*-isopropylidene-2,3,4-trihydroxybutyl-1]-1,3-dithiane (6a). Sodium hydride in mineral oil (60%, 1.110 g, 27.73 mmol) was washed with petroleum ether and suspended in anhydrous dimethylformamide (DMF, 25 mL). The stirred suspension was cooled to −10 °C, and a solution of alcohol **5a** (5.67 g, 21.5 mmol) in dry DMF (10 mL) was slowly added. After 30 min, a solution of benzyl bromide (3.3 mL, 27.75 mmol) in dry DMF (5 mL) was introduced dropwise. The mixture was stirred for 12 h at room temperature and was then poured into ice water (100 mL) and extracted with ether. The ether extract was repeatedly washed with water to remove residual DMF and dried ($MgSO_4$). The oily residue obtained after solvent removal was chromatographed with hexane–ethyl acetate (95:5) as eluent to give benzyl ether **6a** (7.3 g, 96%) as an oil: $[\alpha]^{25}_D$ −33.67° (*c* 1.4, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 3 H), 1.36 (s, 3 H), 1.5–2.33 (m, 4 H), 2.56–2.86 (m, 4 H), 3.66–4.2 (m, 5 H), 4.57, 4.66 (q_{AB}, *J* = 7.5 Hz, 2 H), 7.2 (s, 5 H).

Anal. Calcd for $C_{18}H_{26}O_3S_2$: C, 60.98; H, 7.39; S, 18.09. Found: C, 61.10; H, 7.57; S, 18.11.

2-[(2*S*,3*S*)-2-*O*-Benzyl-3,4-*O*-isopropylidene-2,3,4-trihydroxybutyl-1]-1,3-dithiane (6b). Benzyl ether **6b** was obtained from **5b**, according to the procedure described for the preparation of **6a**, in 96% yield: $[\alpha]^{25}_D$ −46.28° (*c* 2.59, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 3 H), 1.42 (s, 3 H), 1.53–2.23 (m, 4 H), 2.56–2.8 (m, 4 H), 3.53–4.3 (m, 5 H), 4.55, 4.71 (q_{AB}, *J* = 12 Hz, 2 H), 7.22 (s, 5 H).

Anal. Calcd for $C_{18}H_{26}O_3S_2$: C, 60.98; H, 7.39; S, 18.09. Found: C, 61.03; H, 7.55; S, 17.87.

(3*S*,4*R*)-3-*O*-Benzyl-4,5-*O*-isopropylidene-3,4,5-trihydroxypentanal (7a). Compound **6a** (0.934 g, 2.64 mmol) was placed in acetonitrile (44 mL), water (8 mL), $CaCO_3$ (0.792 g, 7.91 mmol) and methyl iodide (3.6 mL, 57.8 mmol), and the mixture was heated at 40 °C for 17 h. After being cooled to room temperature, the reaction mixture was diluted with ether (150 mL) and washed with 10% $Na_2S_2O_3$ (2 × 60 mL), water, and brine. The organic layer was dried ($MgSO_4$) and concentrated. The liquid obtained after solvent removal was chromatographed on a silica gel column with hexane–ethyl acetate (10:1) to give **7a**: 600 mg, 86%; $[\alpha]^{20}_D$ +5.23° (*c* 2.75, $CHCl_3$) (lit.[18] $[\alpha]^{20}_D$ +4.5° (*c* 2.75, $CHCl_3$)).

(3*S*,4*S*)-3-*O*-Benzyl-4,5-*O*-isopropylidene-3,4,5-trihydroxypentanal (7b). Aldehyde **7b** was prepared from **6b** following the procedure described for **7a**: $[\alpha]^{20}_D$ −34.28° (*c* 3.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 3 H), 1.36 (s, 3 H), 2.56 (dd, *J* = 3 and 0.75 Hz, 2 H), 3.43–4.4 (m, 4 H), 4.6 (s, 2 H), 7.23 (s, 5 H), 9.66 (t, *J* = 0.3 Hz, 1 H).

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.25; H, 7.78.

Methyl 3-*O*-Benzyl-2-deoxy-D-ribofuranoside (8). Aldehyde **7a** (0.5 g, 1.89 mmol) in dry methanol containing 0.2% HCl was stirred at room temperature for 20 min. Anhydrous Na_2CO_3 was added, and the mixture was filtered. The filtrate upon concentration afforded **8** (0.464 g, 92%) as a mixture of anomers, which were separated by column chromatography using hexane–ethyl acetate (4:1) as eluent.

Fraction 1. Methyl 3-*O*-benzyl-2-deoxy-β-D-ribofuranoside (8b): 0.184 g, 37%; $[\alpha]^{25}_D$ −52.59° (*c* 2.30, EtOH); ^{1}H NMR ($CDCl_3$) δ 2.03–2.33 (m, 2 H), 2.56 (s, 1 H, D_2O exchangeable), 3.33 (s, 3 H), 3.3–3.86 (m, 2 H), 4.06–4.33 (m, 2 H), 4.43 (s, 2 H), 5.03 (t, *J* = 3 Hz, 1 H), 7.26 (s, 5 H).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.42; H, 7.69.

Fraction 2. Methyl 3-*O*-benzyl-2-deoxy-α-D-ribofuranoside (8a): 0.28 g, 55%; $[\alpha]^{25}_D$ +26.64° (*c* 1.46, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.76–2.43 (m, 3 H), 3.37 (s, 3 H), 3.26–4.23 (m, 4 H), 4.52 (q, *J* = 7.5 Hz, 2 H), 5.0 (dd, *J* = 6 and 1.5 Hz, 1 H), 7.3 (s, 5 H).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.45; H, 7.72.

Methyl 2-Deoxy-α-D-ribofuranoside (12a). A solution of benzyl derivative **8a** (0.15 g, 0.63 mmol) in toluene (5 mL) was cooled in a dry ice–acetone bath, and ammonia (15 mL) was condensed into the reaction mixture. Sodium metal was added in portions with vigorous stirring until the mixture had an intense blue color. Stirring was continued for 40 min. The mixture was neutralized with NH_4Cl in methanol and evaporated to dryness. Diol **12a** was extracted from the residue with ethyl acetate. The organic extracts were dried ($MgSO_4$) and evaporated to dryness to give pure **12a** as an oil: 0.084 g, 90%; $[\alpha]^{25}_D$ +96.75° (*c* 1.17, H_2O); ^{1}H NMR (D_2O) δ 1.74–1.8 (m, 1 H), 2.16–2.25 (m, 1 H), 3.25 (s, 3 H), 3.46–3.61 (m, 2 H), 3.92–3.96 (m, 1 H), 4.09–4.14 (m, 1 H), 5.02–5.05 (dd, *J* = 5.3 and 1.3 Hz, 1 H).

Anal. Calcd for $C_6H_{12}O_4$: C, 48.64; H, 8.16. Found: C, 48.58; H, 8.23.

Methyl 2-Deoxy-β-D-ribofuranoside (12b). The product was obtained from benzyl ether **8b** by adapting the above-mentioned procedure: $[\alpha]^{25}_D$ −74.23° (*c* 0.815, H_2O) (lit.[23] $[\alpha]^{25}_D$ −72° (*c* 1.03, H_2O)).

Methyl 3-*O*-Benzyl-2-deoxy-L-xylofuranoside (13). Aldehyde **7b** was converted to **13** in 90% yield by following the procedure mentioned for the preparation of **8**.

Fraction 1. Methyl 3-*O*-benzyl-2-deoxy-α-L-xylofuranoside (13a): 0.18 g, 36%; $[\alpha]^{25}_D$ −75.97° (*c* 0.795, H_2O); ^{1}H NMR ($CDCl_3$) δ 1.33–1.73 (m, 1 H), 1.96–2.33 (m, 1 H), 2.65 (br s, 1 H, D_2O, exchangeable), 3.3 (s, 3 H), 3.33–3.84 (m, 4 H), 4.47, 4.57 (q_{AB}, *J* = 7.5 Hz, 2 H), 4.66 (t, *J* = 0.75 Hz, 1 H), 7.23 (s, 5 H).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.41; H, 7.67.

Fraction 2. Methyl 3-*O*-benzyl-2-deoxy-β-L-xylofuranoside (13b): 0.27 g, 54%; $[\alpha]^{25}_D$ −30.97° (*c* 0.875, H_2O); ^{1}H NMR ($CDCl_3$) δ 1.96–2.23 (m, 2 H), 2.4 (br s, 1 H, D_2O exchangeable), 3.27 (s, 3 H, 3.16–4.9 (m, 6 H), 5.08 (t, *J* = 2 Hz, 1 H), 7.23 (s, 5 H).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.48; H, 7.71.

(2*R*,3*S*)-1,2-*O*-Isopropylidene-3-*O*-(*p*-toluenesulfonyl)-1,2,3,4-butanetetrol (14a). A solution of aluminum hydride (60 mL, 30 mmol), prepared according to literature procedure,[27] was added to ester **2a** (30 g, 83.8 mmol) in dry THF (100 mL) at 0 °C. The mixture was stirred at that temperature for 1 h and decomposed slowly by the addition of water (25 mL), and the aqueous solution was extracted with ether (4 × 100 mL). The combined ether extracts were dried ($MgSO_4$) and concentrated to furnish **14a** (26 g, 99%). An analytical sample was obtained by silica gel column chromatography with hexane–ethyl acetate (4:1) as eluent: $[\alpha]^{25}_D$ +5.82° (*c* 1.975, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.26 (s, 3 H), 1.33 (s, 3 H), 1.93–2.26 (m, 1 H, D_2O exchangeable), 2.4 (s, 3 H), 3.53–4.66 (m, 6 H), 7.22, 7.68 (q_{AB}, *J* = 4.5 Hz, 4 H).

Anal. Calcd for $C_{14}H_{20}O_6S$: C, 53.15; H, 6.38; S, 10.13. Found: C, 53.35; H, 6.47; S, 10.17.

(2*S*,3*S*)-1,2-*O*-Isopropylidene-3-*O*-(*p*-toluenesulfonyl)-1,2,3,4-butanetetrol (14b). This compound was prepared from **2b** as above (for **14a**) in 99% yield. For analysis, a portion of the sample was purified by silica gel column chromatography with hexane–ethyl acetate (4:1) as eluent: $[\alpha]^{25}_D$ +10.58° (*c* 2.16, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.26 (s, 3 H) 1.33 (s, 3 H), 1.98–2.3 (m, 1 H, D_2O exchangeable), 2.42 (s, 3 H), 3.48–4.6 (m, 6 H), 7.16 7.61 (q_{AB}, *J* = 6 Hz, 4 H).

Anal. Calcd for $C_{14}H_{20}O_6S$: C, 53.15; H, 6.38; S, 10.13. Found: C, 53.38; H, 6.37; S, 10.15.

(2*R*,3*R*)-3,4-Epoxy-1,2-*O*-isopropylidenebutane-1,2-diol (15a). To a stirred solution of tosylate **14a** (25 g, 105.9 mmol) in dry ether (100 mL) was added a 2 M solution of freshly prepared

sodium methoxide in absolute methanol (53 mL, 105.9 mmol), and the mixture was stirred at room temperature for 1 h. The reaction mixture was filtered, and the filtrate was diluted with ether and washed with brine. The organic layer was dried ($MgSO_4$) and concentrated to afford epoxide **15a** (14 g, 91.5%). An analytical sample was obtained by short-path distillation: bp 42 °C (0.7 mmHg); $[\alpha]^{25}_D$ −0.69° (*c* 4.15, EtOH).

(2*S*,3*R*)-3,4-Epoxy-1,2-*O*-isopropylidenebutane-1,2-diol (15b). This compound was prepared in 92% yield from **14b** by using the procedure described for **15a**; $[\alpha]^{25}_D$ −10.96° (*c* 2.55, EtOH).

2-[(2*R*,3*R*)-3,4-*O*-Isopropylidene-2,3,4-trihydroxybutyl-1]-1,3-dithiane (16a). The procedure followed was identical with that described for the preparation of **5a**; $[\alpha]^{25}_D$ +24.96° (*c* 2.90, EtOH).

2-[(2*R*,3*S*)-3,4-*O*-Isopropylidene-2,3,4-trihydroxybutyl-1]-1,3-dithiane (16b). This was obtained from **15b** in 98% yield by following the method given for the synthesis of **5a**; $[\alpha]^{25}_D$ +22.62° (*c* 3.01, EtOH).

2-[(2*R*,3*R*)-2-*O*-Benzyl-3,4-*O*-isopropylidene-2,3,4-trihydroxybutyl-1]-1,3-dithiane (17a). Benzyl ether **17a** was obtained from **16a** according to the procedure described for the preparation of **6a**: 96% yield; $[\alpha]^{25}_D$ +46.97° (*c* 2.41, EtOH).

2-[(2*R*,3*S*)-2-*O*-Benzyl-3,4-*O*-isopropylidene-2,3,4-trihydroxybutyl-1]-1,3-dithiane (17b). Alcohol **16b** was benzylated to afford **17b** by following the method described for the preparation of **6a**; $[\alpha]^{25}_D$ +33.79° (*c* 1.53, EtOH).

(3*R*,4*R*)-3-*O*-Benzyl-4,5-*O*-isopropylidene-3,4,5-trihydroxypentanal (18a). Compound **17a** was converted to the product by using the method given for **7a**; $[\alpha]^{20}_D$ +34.55° (*c* 3.19, $CHCl_3$).

(3*R*,4*S*)-3-*O*-Benzyl-4,5-*O*-isopropylidene-3,4,5-trihydroxypentanal (18b). The procedure followed was identical with that described for the preparation of **7a**; $[\alpha]^{20}_D$ −5.0° (*c* 2.74, $CHCl_3$).

Methyl 3-*O*-Benzyl-2-deoxy-D-xylofuranoside (19a). Aldehyde **18a** was cyclized to give **19a** in 90% yield by following the procedure mentioned for the preparation of **8**: ^1H NMR ($CDCl_3$) δ 1.96–2.36 (m, 2 H), 2.43–2.86 (br s, 1 H, D_2O exchangeable), 3.33 (s, 3 H), 3.23–4.75 (m, 6.5 H), 5.13 (t, *J* = 1.5 Hz, 0.5 H), 7.23 (s, 5 H).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.59; H, 7.68.

Methyl 3-*O*-Benzyl-2-deoxy-L-ribofuranoside (19b). This compound was obtained from aldehyde **18b** according to the procedure described for the preparation of **8**: ^1H NMR ($CDCl_3$) δ 1.83–2.4 (m, 3 H), 3.31 (s, 3 H) 3.48–4.63 (m, 6 H), 4.86–5.13 (m, 1 H), 7.23 (s, 5 H).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.43; H, 7.72.

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Stereoselective Synthesis of (±)-Trichodiene

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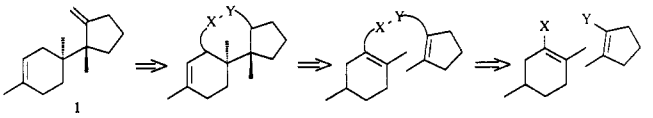
Details of a convergent stereoselective synthesis of trichodiene (1) from simple monocyclic starting materials are reported. Stereochemical control is effected by Nazarov cyclization of dienone **14** and C–C bond cleavage of the resulting tricyclic products **15** to form cyano dienes **20**.

Trichodiene (1) has attracted the attention of synthetic chemists both because it is the biogenetic precursor of the biologically active trichothecenes[1] and because it presents an interesting challenge for stereochemical control between the two adjacent quaternary carbons connected by an acyclic single bond. A variety of approaches to the synthesis of trichodiene have been reported.[2] We describe here the details of a cyclization–ring cleavage strategy, which makes use of a stereospecific electrocyclic reaction

Scheme I



to control stereochemistry.[3]

The conceptually appealing convergent approach (formation of the C–C bond between five- and six-membered rings) to the synthesis of trichodiene requires a method for synthesis of a C–C bond between two quaternary centers with control of stereochemistry. The problems of control in direct intermolecular coupling[4] led us to consider a strategy which makes the key bond-forming step an intramolecular reaction (Scheme I). We considered electrocyclic reactions[5] to be advantageous for this purpose because stereochemical control is assured by mechanistic

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(3) Portions of these results have been published in a preliminary communication: See ref 2e.

(4) The problems of a direct intermolecular convergent synthesis have been solved recently using the reaction of tin enolates with tricarbonylcyclohexadienyliumiron cations.[2j,k] The synthetically useful stereoselectivity (5:1) obtained by this method is, however, not an obvious consequence of the reaction used.

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