(23S,25R)-calcidiol lactone (4)[5] by reduction with diisobutyl alminium hydride (DIBAL) (toluene, -70 °C) in high yield (93%). It is interesting to note that only one anomer at C-26 was obtained as verified by the ^{1}H NMR spectrum ($CDCl_3$): δ 1.34 (3 H, s, H-27) 3.8-4.20 (2 H, m, H-3 and H-23), 4.83 (2 H, br s, H-19 and H-26), 5.07 (1 H, br s, H-19), 6.14 (2 H, AB q, J = 11 Hz, H-6 and H-7).

Experimental Section

The melting point was determined with a Yanaco micro melting point apparatus and was not corrected. ^{1}H NMR spectra were obtained with a Varian XL-100 instrument. Chemical shifts are reported in parts per million relative to tetramethylsilane. Mass spectra were obtained with a JEOL JMS-D300 spectrometer. Infrared spectra were obtained with a JASCO A-302 spectrometer. UV spectra were recorded on a Union Giken SM 401 spectrometer.

Iodolactonization of 4-Phenyl-1,2,4-triazoline-3,5-dione Adducts of (25*R*)- and (25*S*)-3β,25-Dihydroxy-5,7,22-cholestatrien-26-oic Acids (7a,b). Method A. Iodine (25 mg, 9.8 × 10^{-2} mmol) was added to a solution of carboxylic acid **7** (20 mg, 3.3 × 10^{-2} mmol) in CH_3CN (1 mL) at 0 °C, and the solution was stirred at that temperature for 5 h. After addition of aqueous $Na_2S_2O_3$, the mixture was extracted with $CHCl_3$, washed with brine, dried over Na_2SO_4, and evaporated. The product ratio was analyzed by HPLC [column, μ-Porasil; solvent, 2-propanol-hexane (15:85) for the analysis of the products from **7b** and ethyl acetate-hexane (7:3) for those from **7a**].

Method B. Carboxylic acid **7** (20 mg) was dissolved in Et_2O-THF (1:1 2 mL) and combined with aqueous saturated $NaHCO_3$ (2 mL). The solution was stirred for 30 min at room temperature and cooled to 0 °C, and then iodine (25 mg) was added. After 5 h, the reaction mixture was worked up as above, and the products were analyzed by HPLC.

Method C. A solution of carboxylic acid **7** (20 mg) and pyridine (20 μL, 2.5 × 10^{-1} mmol) in CH_3CN or CH_2Cl_2 (1 mL) was stirred at room temperature for 30 min and cooled to 0 °C, and then iodine (25 mg) was added. The mixture was stirred at that temperature for 5 h and then worked up as above. The products were analyzed by HPLC.

The results of the iodolactonization are shown in Table I.

4-Phenyl-1,2,4-triazoline-3,5-dione Adducts of (23*S*,25*R*)- and (23*R*,25*R*)-3β,25-Dihydroxy-22-iodo-5,7-cholestadiene 26,23-Lactone (8a,a′). A solution of **7a** (105 mg, 1.74 × 10^{-1} mmol) and pyridine (105 μL, 1.3 mmol) in CH_2Cl_2 (6 mL) was stirred at room temperature for 30 min and cooled to 0 °C, and then iodine (133 mg, 5.24 × 10^{-1} mmol) was added. After 2.5 h, iodine (133 mg) and pyridine (105 μL) were added, and the resultant solution was stirred for a further 7.5 h at 0 °C. Aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with $CHCl_3$, washed with brine, dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel (6 g) by using hexane-ethyl acetate (2:8) as the eluent to give a 1:4 mixture of **8a** and **8a′** (95 mg). The mixture was subjected to the next reaction without separation.

4-Phenyl-1,2,4-triazoline-3,5-dione Adducts of (23*R*,25*R*)- and (23*S*,25*R*)-3β,25-Dihydroxy-5,7-cholestadiene 26,23-Lactone (9a,a′). To a solution of the iodolactone (**8a** and **8a′**, 1:4; 100 mg, 1.37 × 10^{-1} mmol) in DME (4 mL) was added n-Bu_3SnH (300 μL, 1.14 mmol), and the mixture was stirred at 60 °C for 1.5 h. After evaporation of the solvent, the residue was dissolved in CH_3CN and washed with hexane to remove organic tin compounds, and the CH_3CN was evaporated. The residue was chromatographed on silica gel (10 g) with hexane-ethyl acetate (2:8) as the eluent to yield **9a** (16 mg) and **9a′** (62 mg) in that order. **9a**: MS, m/e 428 (M^+ - triazoline), 395. **9a′**: MS, m/e 428 (M^+ - triazoline), 395; IR ($CHCl_3$) 1685, 1785, 1770; ^{1}H NMR ($CDCl_3$) δ 0.80 (3 H, s, H-18), 0.94 (3 H, s, H-19), 1.44 (3 H, s, H-27), 4.15-4.65 (2 H, m, H-3 and H-23).

(23*S*,25*R*)-5,7-Cholestadiene-3β,23,25,26-tetrol (10). To a suspension of $LiAlH_4$ (10 mg, 0.26 mmol) in THF (1 mL) was added a solution of **9a′** (28 mg, 4.6 × 10^{-2} mmol) in THF (1 mL), and the mixture was refluxed for 50 min. After the excess of the reagent was quenched with aqueous THF, the mixture was filtered and washed with THF and $CHCl_3$-MeOH (2:1), and the combined filtrate and washings were dried over Na_2SO_4 and evaporated. The residue was chromatographed on Sephadex LH-20 (10 g) with hexane-$CHCl_3$-MeOH (25:75:2) as the eluent to yield **10**: 18 mg; mp 225-228 °C; MS, m/e 432 (M^+), 414, 399, 383; ^{1}H NMR (Me_2SO-d_6) δ 0.58 (3 H, s, H-18), 0.86 (3 H, s, H-19), 1.07 (3 H, s, H-27), 3.6-4.0 (2 H, m, H-3 and H-23), 5.37 and 5.52 (2 H, m, H-6 and H-7); UV (95% EtOH) 272, 282, 293 nm.

(23*S*,25*R*)-23,25,26-Trihydroxyvitamin D_3 (2). A solution of **10** (6 mg) in 95% EtOH (200 mL) was irradiated by a high-pressure mercury lamp (200 W) through a Vycor filter for 5 min under an argon atmosphere, the temperature being maintained below 5 °C. The solvent was evaporated, and the residue was chromatographed on Sephadex LH-20 (25 g) and eluted with hexane-$CHCl_3$-MeOH (25:75:2.5) to yield previtamin D: 2.6 mg; UV (95% EtOH) 260 nm. The previtamin D was dissolved in 95% EtOH (2 mL), heated for 7 h at 60-63 °C, and then allowed to stand at room temperature for 8 h. After evaporation of the solvent, the residue was chromatographed on Sephadex LH-20 (25 g) and eluted with hexane-$CHCl_3$-MeOH (25:75:2.5) to give vitamin D **2**: 1.9 mg; high-resolution MS, $C_{27}H_{44}O_4$ requires m/e 432.3239, found m/e 432.3256; ^{1}H NMR ($CDCl_3$) δ 0.56 (3 H, s, H-18), 1.22 (3 H, s, H-27), 3.57 (2 H, AB q, J = 11 Hz, H-26), 3.8-4.2 (2 H, m, H-3 and H-23), 4.82 (1 H, br s, H-19), 5.04 (1 H, br s, H-19), 6.13 (2 H, AB q, J = 11 Hz, H-6 and -7); UV (95% EtOH) 265 nm.

(23*S*,25*R*)-25-Hydroxyvitamin D_3 26,23-Lactol (3). A solution of (23S,25R)-calcidiol lactone (**4**;[5] 1.8 mg, 4.2 × 10^{-3} mmol) in toluene (300 μL) was cooled to -70 °C under argon, diisobutyl aluminium hydride (25% hexane solution, 26.5 μL, 4.7 × 10^{-2} mmol) was added, and the mixture was stirred for 2 h at that temperature. The reaction was quenched with cold ethanol (150 μL) at -70 °C, stirred for 20 min at that temperature, and then allowed to warm to room temperature. The mixture was diluted with $CHCl_3$, washed with 5% HCl and water, dried over Na_2SO_4, and evaporated. The residue was chromatographed on Sephadex LH-20 (10 g) with hexane-$CHCl_3$-MeOH (35:65:2) as the eluent to give lactol **3**: 1.67 mg; MS, m/e 430 (M^+), 412, 394, 379, 356, 342; IR ($CHCl_3$) 3400 cm^{-1}; UV (95% EtOH) 265 nm.

Registry No. **2**, 83198-41-8; **3**, 83136-06-5; **4**, 77714-47-7; **7a**, 81495-58-1; **7b**, 80320-87-2; **8a**, 80320-88-3; **9a**, 78109-10-1; **9a′**, 78183-86-5; **10**, 83136-07-6; (23S,25R)-23,25,26-trihydroxyprevitamin D_3, 83136-08-7.

Reaction between 2-Amino-2-deoxy-D-glucose Derivatives and Sulfite. 2. Synthesis of 2-(D-*arabino*-Tetrahydroxybutyl)-5-(3,4-dihydroxy-2-sulfobutyl)pyrazine

Shoji Fujii* and Yasuzo Kosaka

Department of Agricultural Chemistry, Kyoto Prefectural University, Shimogamo, Kyoto 606, Japan

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In continuation of our studies of the reaction of 2-amino-2-deoxy-D-glucose (**1**) derivatives in sodium bisulfite solution we recently reported the condensation of 2-amino-2-deoxy-D-glucose oxime with glyoxal-sodium bisulfite.[1] We now report the condensation of 2 mol of **1** in heated sodium bisulfite solution. The principal product is a pyrazine derivative with two polyhydroxyalkyl side chains one of which is sulfonated. The reaction constitutes a new route to sulfonated polyhydroxyalkylpyrazine derivatives.

The formation of the two pyrazine derivatives "fructosazine" (**2**) and "deoxyfructosazine" (**3**) from **1** has been reported.[2,3] Excessive side reactions of **1** in alkaline media resulted, however, in a low yield of **2**. Ingles[4,5] found

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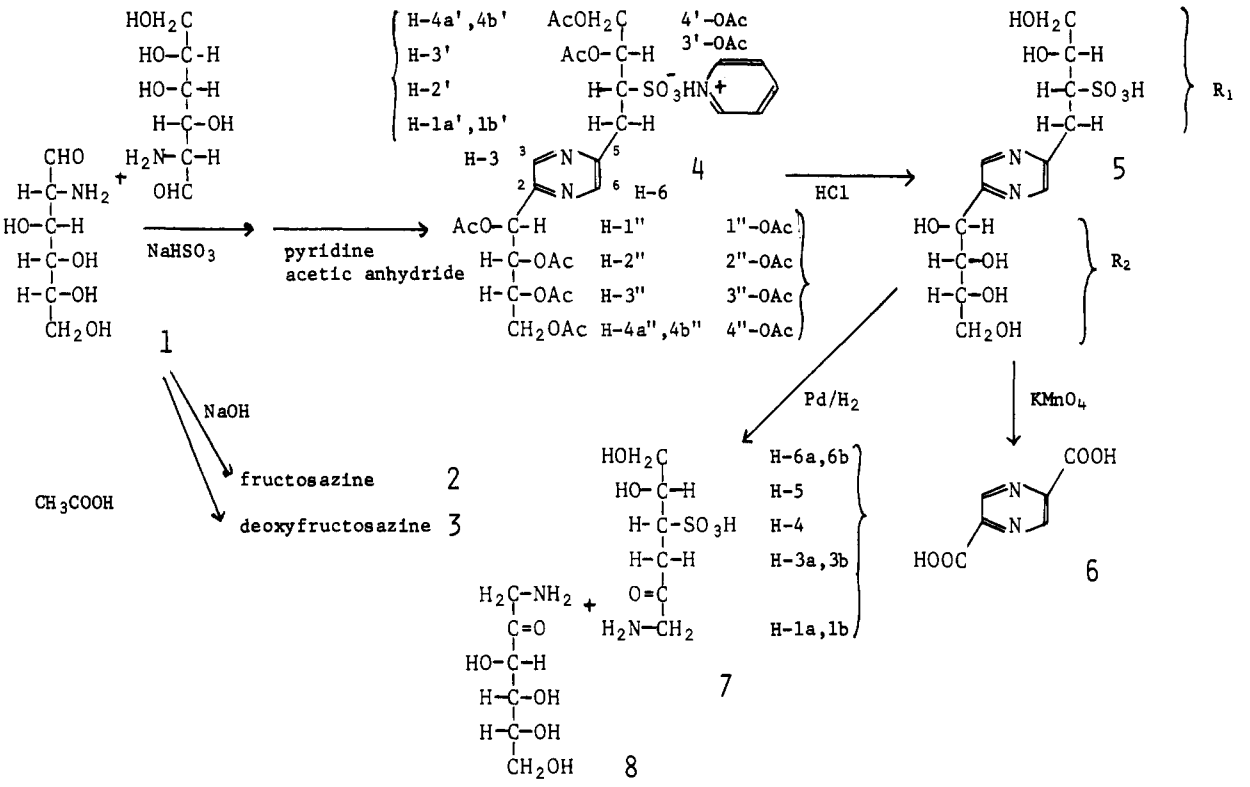
Scheme I



that side reactions of amino sugars could be minimized by conducting the reactions in sulfurous acid, which formed bisulfite addition compounds. Our attempts to increase the yield of **2** from **1** by using a bisulfite reaction medium led unexpectedly to the formation of a sulfonated polyhydroxyalkylpyrazine.

Equimolar amounts of **1** and sodium bisulfite in aqueous solution were heated under oxidative conditions by passing air through the reaction mixture. The reaction mixture was treated with cation-exchange resin (H^+). Condensation of the effluent and addition of methanol gave a precipitate. Acetylation of this precipitate with excess acetic anhydride and pyridine produced crystals (**4**), which gave **5** by deacetylation with ethanolic hydrogen chloride (Scheme I).

Compound **5** gave pyrazine-2,5-dicarboxylic acid (**6**) on permanganate oxidation, and its filtrate was positive to barium chloride. The polyhydroxyalkyl side chain is oxidized easily with potassium permanganate,[1,2] and the sulfo group on the pyrazine ring is stable and is not released during the oxidation, as shown previously.[1] We thus concluded that the compound **5** is a 2,5-disubstituted pyrazine derivative with a sulfo group in its side chain.

Hydrogenolysis of **5** according to the method of Kuhn et al.[3] gave two compounds, **7** (which corresponds to the side chain R_1) and **8** (side chain R_2), one of which (**8**) had ^1H NMR and IR spectra and an R_f value identical with those of authentic 1-amino-1-deoxy-D-fructose hydrochloride.

Ingles obtained[6] 3,4-dideoxy-4-sulfo-D-2-hexosulose from D-glucose and sodium bisulfite, and Kuhn et al.[3] obtained 1-amino-3-deoxy-D-2-hexulose by hydrogenolysis of deoxyfructosazine. The mechanisms of these reactions suggested that 1-amino-1,3,4-trideoxy-4-sulfo-D-2-hexulose was the most probable structure for **7**. Nothing can be said about the configuration at C-4 of **7**, but the configuration at C-5 is probably retained, as this center does not take part in the reaction.

Table I. ^1H NMR (60 MHz) Data for **4** in $CDCl_3$

chemical shift,[a] δ	proton	coupling constant, Hz
8.95 (2 H, m)	α-protons of pyridine	
8.42 (1 H, m)	γ-proton of pyridine	
8.80 (2 H, m)	β-protons of pyridine	
8.50 (2 H, s)	H-3 and H-6 of pyrazine ring	
	Side Chain R_2	
6.15 (1 H, d)	H-1″	$J_{1'',2''} = 3.2$
5.70 (1 H, q)	H-2″	$J_{2'',3''} = 8.1$
5.30 (1 H, m)	H-3″	$J_{3'',4a''} = 2.0$, $J_{3'',4b''} = 5.3$
4.25 (2 H, m)	H-4a″, H-4b″	$J_{4a'',4b''} = 12.5$
	Side Chain R_1	
5.84 (1 H, m)	H-3′	
4.25 (2 H, m)	H-4a′, H-4b′	
3.85 (1 H, m)	H-2′	
3.48 (2 H, m)	H-1a′, H-1b′	
2.20 (3 H, s)	1″-OAc	side chain R_2
2.19 (3 H, s)	2″-OAc	
2.05 (3 H, s)	3″-OAc	
2.03 (3 H, s)	4″-OAc	
1.99 (3 H, s)	3′-OAc	side chain R_1
1.93 (3 H, s)	4′-OAc	

[a] The number of hydrogens and the multiplicity are given in parentheses.

Final proof would probably depend on the synthesis of **7**, but decoupling of the ^1H NMR spectrum of **4** gave additional proof for the structure of side chain R_1. Two methylene signals (H-3a,3b and H-6a,6b of **7**) and two methine signals (H-4 and H-5 of **7**) were accompanied by the typical pattern of a D-*arabino*-tetraacetoxybutyl side chain (R_2, Table I). Five signals at low field indicated the presence of one pyridine unit. The low-field proton pattern (δ 8.50, s, 2 H) was similar to the patterns of 2-(D-

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arabino-tetraacetoxybutyl)-5-methylpyrazine[7] (δ 8.38, s, 2 H) and fructosazine octaacetate[2] (δ 8.53, s, 2 H).

Thus, the most probable structure for the acetylated compound **4** is the 2-(D-*arabino*-tetraacetoxybutyl)-5-(3,4-diacetoxy-2-sulfobutyl)pyrazine pyridinium salt, and the structure of the principal product of this condensation reaction is the hydroxy derivative of **4** (**5**).

Experimental Section

^{1}H NMR spectra were recorded at 60 MHz with a Hitachi R-24 spectrometer. Measurements were made in $CDCl_3$ solution containing tetramethylsilane as an internal standard and in D_2O with the sodium salt of 3-(trimethylsilyl)propanesulfonic acid (DSS) as the internal standard. IR spectra were measured as KBr pellets and recorded on an IR-27 Shimadzu spectrophotometer. UV spectra were measured with Hitachi spectrometer, Model 124. Analytical paper chromatography was performed with the solvent systems (A) pyridine/isoamyl alcohol/water (40:35:30) and (B) ethyl acetate/pyridine/acetic acid/water (5:5:1:3). Spots on the paper chromatogram were developed with $FeSO_4$ solution[8] and permanganate–periodate solution.[9] All melting points were determined with a Yanaco micro melting point apparatus and are uncorrected.

Condensation Products of 2-Amino-2-deoxy-D-glucose in the Presence of Sodium Bisulfite. 2-Amino-2-deoxy-D-glucose hydrochloride (17.2 g) was dissolved in 80 mL of water containing 0.08 mol of sodium bisulfite (8.32 g) and sodium hydroxide (3.2 g, 0.08 mol). The mixture was heated at 80 °C for 5 h, and during the reaction air was bubbled through the mixture. After the reaction mixture had been passed through a column of Amberlite IR-120 (H^+), its acidic effluent was concentrated to syrup in vacuo. Paper chromatography (system A) of this syrup showed that it contained four components: the main product (**5**, R_f 0.34) and small amount of other three components (R_f 0.43, 0.21, 0.10). Methanol was added to produce a precipitate which, after filtration and a washing with methanol, gave a hygroscopic solid weighing 3 g.

2-(D-*arabino*-Tetraacetoxybutyl)-5-(3,4-diacetoxy-2-sulfobutyl)pyrazine (4). Acetylation was carried out according to the method of Taha.[10] A mixture of 6 g of the hygroscopic solid, 300 mL of acetic anhydride, and 300 mL of pyridine was stirred overnight at room temperature. This reaction mixture was poured into ice–water and treated with chloroform. The chloroform layer formed was washed successively with 0.3 N hydrogen chloride solution and water, dried with anhydrous sodium sulfate, and concentrated in vacuo to give crystals. After three recrystallizations from methanol, the yield was 252 mg of **4**: mp 179 °C; $[\alpha]^{15}_D$ 0° (*c* 0.1, MeOH); UV (MeOH) λ_{max} 206, 256, 263, 269, 275 nm; IR (KBr) ν_{max} 3030 (CH_2), 1750 (C=O), 1640 (C=N), 1380, 1230 (SO_3H) cm^{-1}; NMR ($CDCl_3$), Table I. Anal. Calcd for $C_{29}H_{37}N_3O_{15}S$: C, 49.78; H, 5.33; N, 6.01; S, 4.58. Found: C, 49.82; H, 5.30; N, 5.90; S, 4.20.

2-(D-*arabino*-Tetrahydroxybutyl)-5-(3,4-dihydroxy-2-sulfobutyl)pyrazine (5). Ten grams of **4** was suspended in 400 mL of ethanol after which hydrogenchloride gas was passed through it to produce the gelatinous precipitate. After filtration, the precipitate was washed several times with ethanol and then reprecipitated from water and ethanol which gave an amorphous mass: 4.1 g; mp 115 °C; $[\alpha]^{15}_D$ −53.6° (*c* 1.0, H_2O); UV (H_2O) λ_{max} 276 nm (ε 7360); IR (KBr) ν_{max} 1620 (C=N), 1170 (SO_3H), 1030 cm^{-1}. Anal. Calcd for $C_{12}H_{20}N_2O_9S$: C, 39.13; H, 5.47; N, 7.60; S, 8.70. Found: C, 39.32; H, 5.14; N, 7.16; S, 8.37.

Pyrazine-2,5-dicarboxylic Acid (6). One gram of **5** in 150 mL of water was neutralized with 2 N potassium hydroxide solution. Another 0.7 g of potassium hydroxide was added to bring the pH to 11.6. Enough potassium permanganate was added to this solution in portions under continuous stirring to oxidize compound **6**. The slight excess of potassium permanganate was digested with ethanol. The precipitated manganese oxide was filtered and its filtrate passed through a column of Amberlite IR-120 (H^+). Condensation in vacuo of this solution gave white crystals. Recrystallization from water produced 130 mg of the product, yield 28%. This crystal had an IR spectrum, R_f value and color development in solvent system A and $FeSO_4$ identical with those found for **6** derived from **3**.

Hydrogenolysis of Compound 5 and 1-Amino-1,3,4-trideoxy-4-sulfo-2-hexulose (7). Hydrogenolysis of **5** was performed according to the method of Kuhn et al.[3] A 674.4-mg sample of **5** was dissolved in 10 mL of 2 N hydrochloric acid, and then palladium oxide (50 mg) was added to this solution. This solution was treated for 16 h under a slightly increased atmosphere of hydrogen. After sufficient hydrogen had been consumed, the reaction mixture was filtered, and its filtrate was concentrated in vacuo to give the crystals. After recrystallization from water, the yield was 38 mg of **7**: mp 151 °C; IR (KBr) 3400 (OH), 2900 (CH_2), 1620 (NH_2), 1520 cm^{-1}; NMR (D_2O) δ 3.28 (2 H, s, H-1a and H-1b), 2.48 (2 H, m, H-3a and H-3b), 3.4–3.9 (4 H, m, H-4, H-5, H-6a, and H-6b). Anal. Calcd for $C_6H_{13}NO_6S\cdot0.25H_2O$: C, 31.10; H, 5.87; N, 6.04; S, 13.84. Found: C, 31.05; H, 5.82; N, 6.01; S, 13.78.

The filtrate also was concentrated to give 7.5 mg of other crystals (**8**). These crystals had an IR spectrum and an R_f value (0.28 in solvent system B) identical with those for the 1-amino-1-deoxy-D-fructose hydrochloride prepared from deoxyfructosazine (**3**).

Registry No. **1**, 3416-24-8; **4**, 82995-49-1; **5**, 82995-50-4; **6**, 122-05-4; **7**, 82995-51-5; **8**, 4429-04-3; $NaHSO_3$, 7631-90-5.

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Preparation and Diels–Alder Reaction of (1*E*)-1,3-Dimethoxybutadiene

Paul Dowd* and William Weber

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

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A high degree of synthetic utility has been demonstrated for the 1,3-dioxygenated butadienes by Danishefsky and his collegues.[1] Their synthesis and development of 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (I), as well as other electron-rich dienes, has made possible wide-ranging synthetic advanes.[1]

We recently encountered an innstance in which the (trimethylsilyl)oxy group of I suffered intermolecular transfer to the oxygen atom of thiolen-2-one in preference to the anticipated Diels–Alder reaction.[2] Accordingly, it appeared that a 1,3-dialkoxybutadiene might provide a useful alternative for those rare instances in which intramolecular silyloxy group transfer intervenes in the Diels–Alder reaction of I.

The literature contains one report[3] of 1,3-diethoxy-1,3-butadiene. Other 1,3-dialkoxybutadienes, including 1,3-dimethoxybutadiene, are unknown.

We intended to prepare 1,3-dimethoxy-1,3-butadiene (II) by pyrolysis of the acetal 1,1,3-trimethoxybut-2-ene (III). The latter is ordinarily prepared by addition of sodium methoxide in methanol[4] to 1,1-dimethoxybut-2-yne (IV) (the prepartion of IV is described in the Experimental Section) at 150 °C in a sealed tube.

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