Tetrahedron Vol. 35, pp. 2583 to 2589
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0040-4020/79/1101-2583/$02.00/0

ADDITION OF DIAZOMETHANE AND SULFUR YLIDES TO THE OXO-GROUP IN DERIVATIVES OF KETOSES AND ALDOSES

I. REACTIONS OF 2,3-O-ISOPROPYLIDENE-D-GLYCERALDEHYDE

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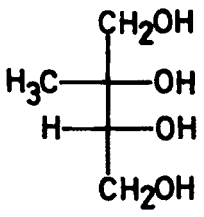
(*Received in U.K.* 14 *May* 1979)

Abstract—The reaction between 2,3-O-isopropylidene-D-glyceraldehyde and diazomethane, dimethylsulfonium methylide and dimethyloxosulfonium methylide has been studied. The sulfur ylides yield two epimeric epoxides, 1,2-anhydro-3,4-O-isopropylidene-D-erythritol and 1,2-anhydro-3,4-O-isopropylidene-D-threitol, with a slight preference for the *erythro* isomer.

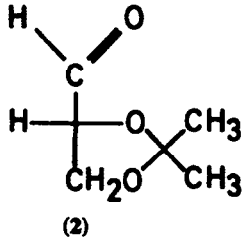
The reaction with diazomethane yields in addition to the epoxides a methyl ketone, 1-deoxy-3,4-O-isopropylidene-D-*glycero*-tetrulose. The relative yields of the three products have been discussed on the basis of mechanisms previously proposed for the reactions. The yield of methyl ketone was lowest when the reaction was carried out in pure diethyl ether solution. This solvent also gives the greatest preference for the *erythro* isomer of the two epoxides. Constitution and stereochemistry for the three products have been shown by synthesis.

Epoxidation of the CO group in ketoses is a useful technique for the synthesis of carbohydrates with a C-C-O-branching.[1] Our attention was drawn to this method during an attempt to synthesize 2-C-methyl-D-erythritol (**1**) which has been isolated



(**1**)

from *Convolvulus glomeratus*[2] and shown to have the absolute configuration as given.[3] Since epoxidations of pyranoses and furanoses are rather well studied we have undertaken a systematic study of the course of some epoxidation reactions of open chain carbohydrate derivatives. Although the products are not branched, we have started with 2,3-O-isopropylidene-D-glyceraldehyde (**2**) which was

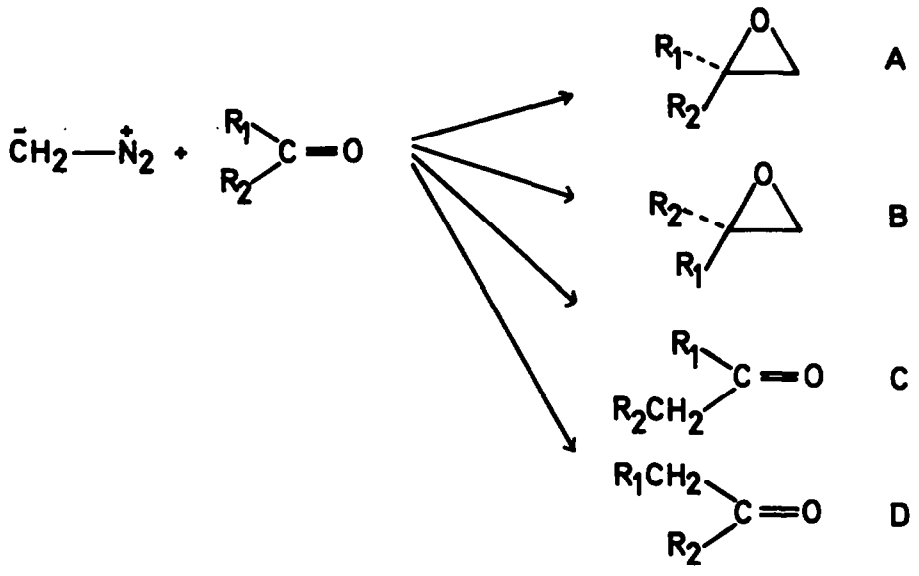


(**2**)

obtained from 1,2:5,6-di-O-isopropylidene-D-mannitol.[4] The reactions are additions of diazomethane, dimethylsulfonium methylide and dimethyloxosulfonium methylide, to the aldehyde group.

The addition of diazomethane to ketones and aldehydes is a well-known reaction.[5] The four primary products which are summarized in Scheme 1 are two epimeric epoxides (**A** and **B**) and two homologous ketones (**C** and **D**). Reaction with an aldehyde ($R_1 = H$) yields either the homologous aldehyde (**C**) or a methyl ketone (**D**) along with the epoxides. With excess of diazomethane the CO compounds are capable of reacting further. Since aldehydes are more reactive than ketones homologous aldehydes are rarely isolated.

For preparative purposes the point of interest is which of the four products will be the dominating in the particular case. A lot of work has been put into elucidation of the reaction mechanism.[6] It is established that in 1,3-dipoles with a central N, this atom is positively charged while the two others are negative. For diazomethane the charges are: CH_2 (−0.26) N (+0.31) N (−0.14).[7] Basically the problem is to decide whether it is a concerted or a two step mechanism. A two step mechanism which involves polar intermediates (Scheme 2) has seemed unlikely because of lack of any clearly defined dependency of reaction rate on solvent polarity.[6] A conserted 1,3-dipolar cycloaddition reaction is supposed to take either of the two courses *via* the cyclic intermediates I-IV as shown in Scheme 3.[6] Only the reaction passing through intermediate III and IV gives CO products. Whether the reaction will take the one or the other path is a matter of R_1 and R_2 and also of the medium in which the reaction is carried out. In a polar medium like methanol the lower process is favoured leading to a higher yield of CO compounds **C** and **D**. The reason for this may be formation of an H-bond between methanol and the CO oxygen, thus



Scheme 1

polarizing the bond and favouring an attack of CH_2^- at the CO carbon instead of N^-. More powerful co-ordination of the CO oxygen with Lewis acids completely eliminates the formation of epoxides.

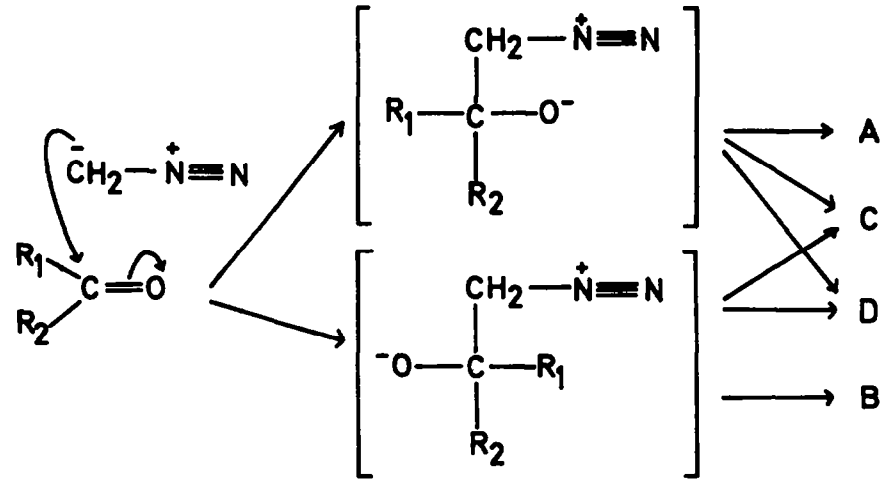
The dependency of R_1 and R_2 is best illustrated by the fact that electronegative groups favour epoxide formation. Thus 1,1,1-trichloro-2-propanone and chloral (trichloroacetal) yield almost exclusively epoxides.[6] However, the epoxide isolated from reaction with chloral is due to reaction of one mole of diazomethane with two moles of chloral.

A similar higher yield of epoxide was observed when going from acetone (R_1=R_2=Me) to 2-undecanone (R_1=Me, R_2=n—C_9H_{19}) which must be due to a steric effect.

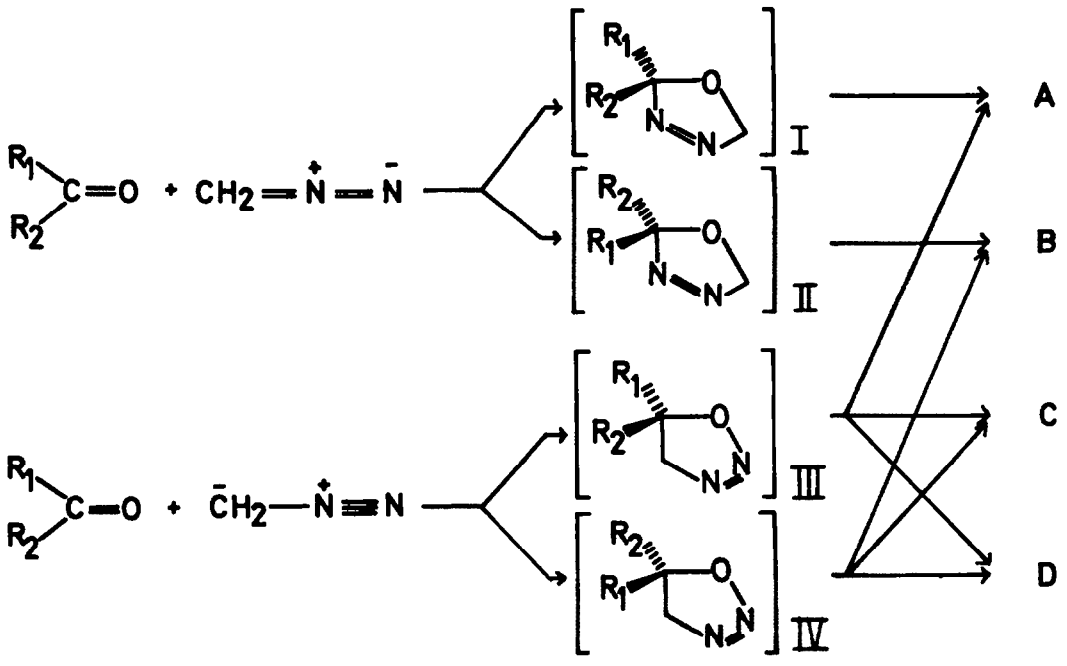
The reaction between 2,3-O-isopropylidene-D-glyceraldehyde and diazomethane was followed both by glc and ^{13}C NMR spectroscopy. The molar ratio of aldehyde to diazomethane at the start of the reaction was in all cases approximately 1:2.

The solvent systems that were used were diethyl ether with 0, 6, 12, 18 and 25% methanol corresponding to a molar ratio of methanol to **2** of 17, 34, 51 and 70.

Figure 1 shows the yield of methyl ketone **5** and the two epoxides **3** and **4** after 145 min reaction time



Scheme 2



Scheme 3

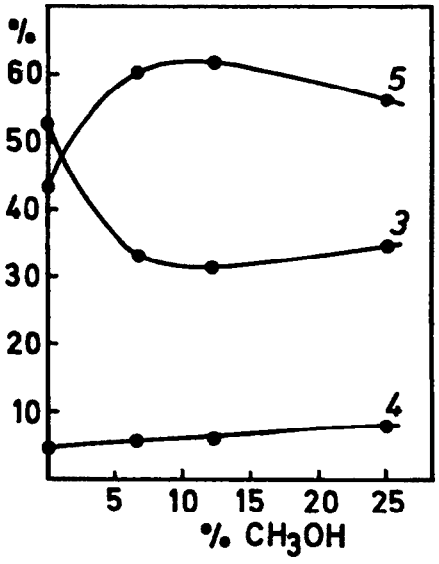
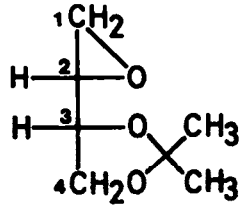


Fig. 1. The relative yields of 3, 4 and 5 after 145 min when 2 is reacted with diazomethane at various consentrations of methanol in diethyl ether.

with varying amounts of methanol. The data are based on the amount of aldehyde that had reacted. They were slightly lower when unreacted aldehyde was taken into account. It has been reported that polar solvents speed up the reaction[6] and also increase the ketone to epoxide ratio. It is seen from Fig. 1 that the maximum yield of methyl ketone in this case was obtained with 12% methanol. Higher percentage of methanol slightly decreased the methyl ketone to epoxide ratio. By methyl ketone



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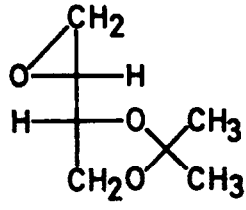
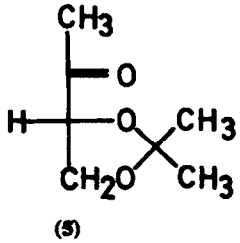


(4)

here is meant the sum of methyl ketone and products due to further reaction with another mole of diazomethane. The reaction of the methyl ketone 5 with diazomethane will be published in a coming paper.

It is also seen from Fig. 1 that the amount of the *threo* epoxide 4 was increasing slightly with increasing amount of methanol while the percentage of *erythro* epoxide 3 decreased on addition of methanol to reach a minimum at 12% methanol and then slightly increased again at higher methanol concentration. It seems reasonable to conclude that the methyl ketone 5 is formed at the cost of the *erythro* epoxide 3.

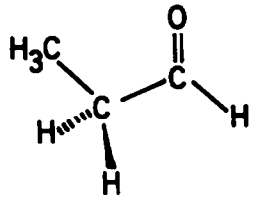
We feel that this result is best accounted for on the basis of the two step mechanism as shown in



(5)

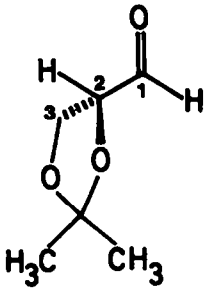
Schemes 2 and 4. All products may arise from an initial nucleophilic attack by $\overline{CH_2}$ at the CO carbon. The ratio of the two epoxides **3** and **4** is then primarily determined by the initial ratio of two epimeric intermediates V and VI.

It is well established that the most stable conformation of simple aliphatic aldehydes such as propanal is the conformation in which the Me group eclipses the CO group (**6**).[8] A study of vicinal



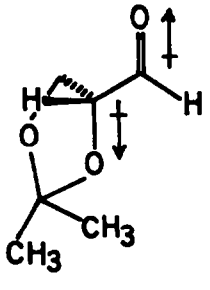
(6)

coupling constants in aldehydes[9] shows that the magnitude in most cases is 1-3 Hz, thus indicating dominance of the eclipsed comformation (**6**). In the ^{1}H NMR spectrum of 2,3-O-isopropylidene-D-glyceraldehyde the vicinal aldehyde coupling constant is of comparable size ($J_{1,2} \approx 1.5$ Hz) indicating only low population of the conformation in which H_1 and H_2 are in an anti-periplanar relationship (**7**).



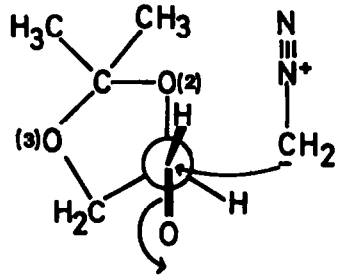
(7)

Analogous to electronegative α-substituents in ketones,[8] the closest ring oxygen (O_2), for dipol-dipol repulsion reasons, is supposed to be anti-periplanar to the aldehyde oxygen (**8**). A domi-



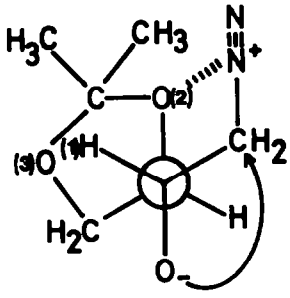
(8)

nance of this conformation which explains the observed vicinal coupling constant, will give best access to the CO carbon by the CH_2 group of diazomethane from the O_2-side as shown (**9**). This



(9)

leads to the intermediate V in Scheme 4. Now assuming a coordination due to electrostatic forces between the positive N atom and the ring oxygen O_2 as shown in **10** there is an ideal arrangement for



(10)

an epoxide to be formed by a back-side attack of the negatively charged O atom at the newly introduced CH_2 group (process b in Scheme 4).

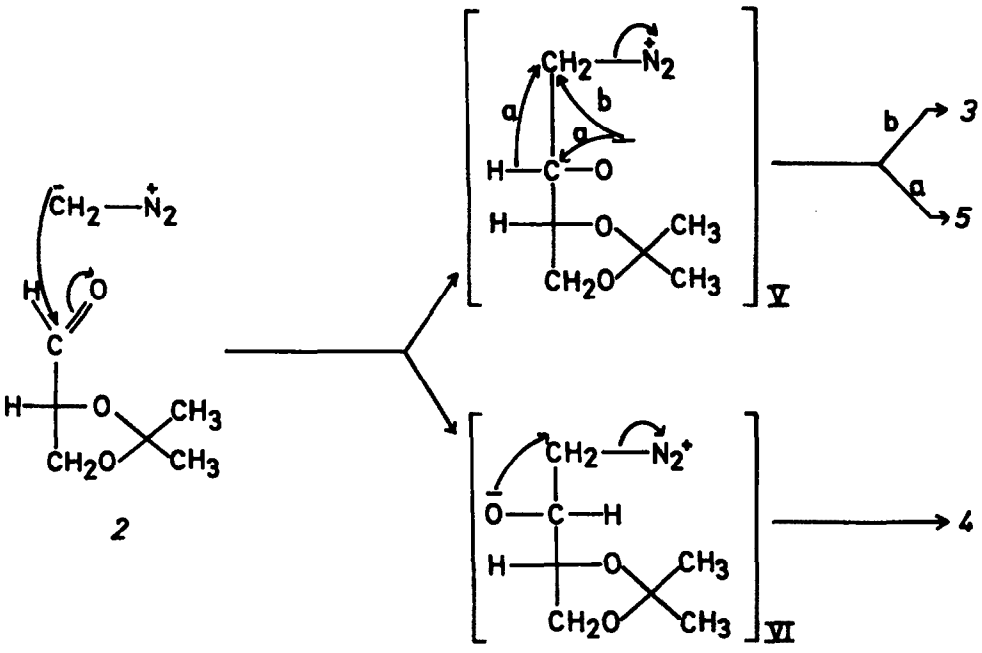
Addition of methanol weakens the attraction between O_2 and N_2^+ since the ring-oxygens now will also coordinate with the solvent molecules (large excess of methanol).

Then the CN_2—N_2^+-grouping will be more free to rotate around the C_1—CH_2-bond, thus forming among others, a conformer in which H_1 (the former aldehyde proton) occupies an anti-periplanar position to the N_2^+ group. This makes a hydrogen shift possible thus forming the methyl ketone **5** by process a in Scheme 4.

An attack of diazomethane from the opposite side of the one shown in **9** is sterically hindered explaining the low yield of **4**. Moreover, if this attack occurs, thus leading to intermediate VI in Scheme 4, then loss of N_2 yields exclusively epoxide. An arrangement in which H_1 is in an anti-periplanar relationship to the N_2^+ group in this case is for steric reasons unlikely.

The generally observed effect of loss of stereospecificity in epoxide formation on going from a non-polar to a polar medium is well understood on the basis of the mechanism given. The ratio of **3** to **4** changed from 12:1 in diethyl ether to approximately 5:1 when a large molar excess of methanol was added. The course of the reaction proposed in Scheme 4 includes that the initial stereoselectivity of this particular reaction in diethyl ether solution was 19:1.

As already mentioned, and which may be seen from Fig. 1, the amount of *threo* epoxide (**4**) increases slightly with increasing amount of



Scheme 4

methanol. This observation may be due to the lower preference for conformation **8**⇌**9** in a more polar medium. Thus other conformations which may allow an attack of diazomethane from the opposite side, may be slightly more probable than in unpolar medium.

The behaviour of 2-undecanone may also be explained on a stereochemical basis. In order to get homologation to the ethyl ketone it is necessary that the CH_2—N_2+ group be lined up along the n-C_9H_{19} chain which is not likely for steric reasons. The formation of epoxides does not require this arrangement.

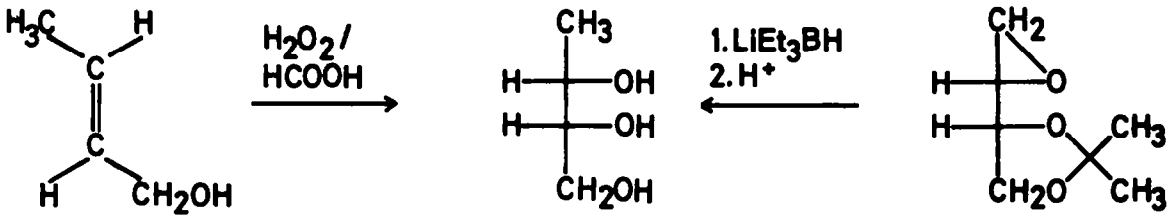
Epoxidation with the sulfur ylides such as dimethylsulfonium methylide and dimethyloxosulfonium methylide is known to yield only epoxides and no homologation. However, the relative yield of the epoxides formed on addition to unsymmetrical ketones seems to be somewhat unpredictable.[10]

The reactions in both cases seem to be simple nucleophilic additions similar to the one suggested in Scheme 2. For cyclic ketones there is a marked difference between the two ylides in the stereochemistry of their reactions. Dimethyloxosulfonium methylide is generally the most stereoselective one and it gives the epoxide with opposite stereochemistry from the epoxide formed with dimethylsulfonium methylide. This difference is suggested to have its origin in steric interactions and variation in the ability of the S atom to interact with the O atom of the CO group.

In agreement with this the reaction between 2,3-O-isopropylidene-D-glyceraldehyde and the two sulfur ylides gave no trace of the methyl ketone **5**. However, the formation of the epoxides **3** and **4** was not particularly stereoselective with either of the ylides. The oxo ylide gave **3** and **4** in the ratio 70:30 while the ratio with the other was approximately 60:40. This small difference may be due to reasons previously mentioned, but may just as well be attributed to the fact that the reactions were carried out in different solvents. The medium for the oxosulfur ylide reaction was dimethyl sulfoxide while the other reaction required the addition of tetrahydrofuran. This addition was necessary so that the reaction temperature could be kept at 0° which is below mp of pure DMSO.

The three primary products **3**, **4** and **5** formed in these addition reactions were separated and identified by synthesis. The two epoxides **3** and **4** of which one was always dominating, were separable on a silica column under medium pressure (30% ether in hexane, 1kg/cm^2). The ratio of the two epoxides was also very easily demonstrated in the ^{13}C NMR spectrum of the mixture. Particularly useful were the resonances of the two C_1 nuclei which appeared at 45.6 (**3**) and 43.7 (**4**) ppm. The assignments were made on the basis of the non-decoupled spectra. The $^1J_{13C^1H}$ coupling constants of the two methylene groups were approximately 177 Hz in the oxirane part (C_1) and 150 Hz in the dioxolane part (C_4). It was assumed that the spin-gitter relaxation times of the C_1-nuclei in **3** and **4** are of similar magnitude so that the relative intensities of their ^{13}C resonances give an adequate measure for their relative amounts.

However, in order to decide whether **3** or **4** was the dominating product we have synthesized the racemic mixture of dl-*erythro*butantriol via H_2O_2/formic acid *trans*-hydroxylation of crotyl alcohol **11** (Scheme 5).[11] The commercial crotyl alcohol that was used was approximately 90% *trans* isomer and in the mentioned synthesis it yielded

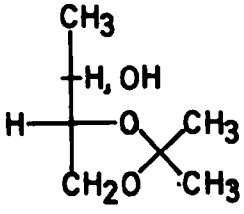


(11) (12) (13)

Scheme 5

erythro/threo butantriol **12/13** in the ratio 9:1. This mixture of butantriols was then compared (glc, ^{13}C NMR) with the product obtained when the epoxide mixture was reduced with lithiumtriethylborohydride and then hydrolyzed with diluted acetic acid.[12] It was then clear that the *erythro* isomer **3** was the dominating epoxide.

The methyl ketone **5** was synthesized from 2,3-O-isopropylidene-D-glyceraldehyde (**2**). The Grignard reaction with methylmagnesiumiodide gave a mixture of 70:30 of 1-deoxy-3,4-O-isopropylidene-D-erythritol (**14**) and -threitol (**15**). This mixture was oxidized with ruthenium tetroxide without



(14, 15)

separation of the two epimers to yield the methyl ketone **5**. This ketone showed identical chromatographic and spectroscopic properties with **5** formed in the diazomethane reaction.

EXPERIMENTAL

Chromatography. For glc was used a Perkin Elmer F-11 instrument with FI-detector and the temp was kept at 80°. The column was 5'×1/8" in size and packed with 5% TCEP [tri-1.2.3-(2-cyanoethoxy)-propane] on Chromosorb W 80/100. Tlc was performed on "Merck Fertigplatten" 0.25 mm Silicagel GF 254 and preparative separations on "Merck Fertigsäulen" Silicagel 60 size B applying a pressure of 1.0-1.2 kg/cm^2.

Spectroscopy. NMR spectra were recorded on Jeol FX-100, a Pulse-Fourier transform instrument, at 99, 6 MHz for ^1H and 25.1 MHz for ^{13}C. Solvent was $CDCl_3$ containing 1% TMS. Interpretations of both types of spectra were performed with extensive use of double irradiation. Mass spectra were recorded with AEI MS 902 and optical rotations with a Perkin Elmer 241 polarimeter.

Diazomethane. Was prepared in ether soln from N-methyl-N-nitroso-*p*-toluensulfonamid,[13] and the sulfur ylides as described by Corey and Chaykovsky.[14]

In this work there has been extensive use of space filling models of type "JUVO-Atommodelle", Karl Kurt Juchheim, Germany.

2,3-O-*Isopropylidene*-D-*glyceraldehyde* (**2**). To a vigorously stirred suspension of 1,2:5,6-di-O-isopropylidene-D-mannitol[4] (6 g) in dry benzene (170 ml) was gradually added $Pb(OAc)_4$ (10.2 g) which had been dried over KOH in vacuum.

After stirring for 9 hr at room temp, solid material was filtered off and solvent removed in vacuum. The remaining syrup was distilled (40-45°, 10 mm Hg) to yield **2** (2 g, 33%). ^1H NMR, δ ppm: 1.42 and 1.47 (both 3 H and *s*), 4.10 (2 H_3), 4.32 (H_2) and 9.72 (H_1, *d*, $J_{1,2}$ = 1.5 Hz). ^{13}C NMR: 20.7, 22.0 and 113.0 (isoprop), 64.5 (C_2), 79.8 (C_3) and 211.4 (C_1).

Reaction of **2** *with diazomethane.* To freshly prepared solns of **2** in diethyl ether with varying amounts of MeOH (0, 6, 12, 18, and 25% of total volume reaction mixture) was added ether solns of diazomethane (molar ratio **2**:diazomethane = 1:2). The mixtures were left in the dark at room temp and the reactions monitored by glc for 24 hr at intervals beginning immediately after the reactions were initiated. ^{13}C NMR spectra were also recorded from time to time as a double control. It was assumed that the relative intensities of the ^{13}C resonances gave an adequate measure for the relative amounts of **3** and **4** since the relaxation times of the carbons compared probably were of similar magnitude. Products due to further reactions with **5** were added to the values recorded for **5**. Fig. 1 gives the relative amounts of **3**, **4** and **5** for varying MeOH concentrations after 145 min reaction time. After this time the reactions had terminated.

Reaction of **2** *with dimethyloxosulfonium methylide.* To a vigorously stirred mixture of dimethyloxosulfonium methylide (2.1 g, 23 mmol) and dimethylsulfoxide (30 ml), **2** (2.7 g, 21 mmol) was added at room temp and under N_2. After stirring for 4 hr water (100 ml) was added and the mixture was extracted with ether (50 ml×3). The combined ether extracts were washed with water (60 ml×2), dried over $MgSO_4$ and concentrated in vacuum to yield a yellow oil (1.3 g, 9 mmol, 39%). Glc showed the two epoxides in the ratio **3**:**4** = 68:32 confirmed by ^{13}C NMR.

Reaction of **2** *with dimethylsulfonium methylide.* To a vigorously stirred mixture of dimethylsulfonium methylide (*ca* 3.5 g, 46 mmol), dimethyl sulfoxide (30 ml) and tetrahydrofuran (30 ml) was added at −13° (salt/ice) and under N_2 dropwise during 3 min **2** (7 g, 51 mmol) in THF (6 ml). The mixture was stirred for another 2 hr. The first 20 min at low temp, then at room temp. Water (300 ml) was added and after 5 min the mixture was extracted with ether (200 ml×3). The combined extracts were washed with water (200 ml×2), dried over K_2CO_3 and concentrated in vacuum to yield a brown oil (2.5 g, 34%). Glc of this oil showed the two epoxides in the ratio **3**:**4** = 62:38 which was confirmed by ^{13}C NMR.

Isolation of 1,2-*anhydro*-3,4-O-*isopropylidene*-D-*erythritol* (**3**) *and* 1,2-*anhydro*-3,4-O-*isopropylidene*-D-threitol (**4**). A mixture (0.95 g) of **3** and **4** resulting from the reaction of **2** with dimethyloxosulfonium methylide

was applied to a "Merck Fertigsäule" and eluted with 30% ether in hexane with a pressure of 1.0-1.2 kg/cm². Fractions were collected (20 ml × 35) and according to glc fractions 10 to 15 were identical and pure. These fractions were combined and concentrated in a stream of N_2 to yield the *erythro* epoxide **3** as an oil (0.23 g), $[\alpha]_D^{23} = +8.23°$ ($c = 0.41$, $CHCl_3$), $[\alpha]_{578}^{23} = 8.63°$, $[\alpha]_{546}^{23} = 9.60°$, $[\alpha]_{436}^{23} = 16.80°$, $[\alpha]_{365}^{23} = 25.86°$. MS: *m/e* 144 (0.1%, $M^{+\cdot}$), *m/e* 143 ($M-H^{\cdot}$), obs. 143.0710, calc. for $C_7H_{11}O_3$ 143.0708, *m/e* 129 (40%, $M-{}^{\cdot}CH_3$), *m/e* 101 (4%, $C_5H_9O_2^+$), *m/e*72 (13%, $C_4H_8O^{\cdot+}$), *m/e* 43 (100%, $C_2H_3O^+$). ^1H NMR δ ppm: 1.37 and 1.46 (both 3H and *s*), 2.64 (H_{1a}), 2.82 (H_{1b}) and 3.00 (H_2) ($J_{1a1b} \approx J_{1b2} = 4.9$ Hz = J_{cis}, $J_{1a2} = 2.9$ Hz = J_{trans}), 3.82 and 3.97 ($2H_4$) and 4.10 (H_3). ^{13}C NMR, δ ppm: 25.2 and 26.5 (both *q* and J = 127.4 Hz), 109.7 (*s*) (isopropylidene group), 45.6 (*t*, J = 176.4 Hz, C_1), 51.9 (*d*, J = 177.0 Hz, C_2), 66.8 (*t*, J = 148.9 Hz, C_4), 76.2 (*d*, J = 150.2 Hz, C_3).

Fractions 18-25 were combined and concentrated in a stream of N_2 to yield the oily *threo* epoxide **4** (85 mg), $[\alpha]_D^{23} = +3.84°$ ($c = 0.8$, $CHCl_3$), $[\alpha]_{578}^{23} = 4.08°$, $[\alpha]_{546}^{23} = 4.94°$, $[\alpha]_{436}^{23} = 11.38°$, $[\alpha]_{365}^{23} = 23.64°$. MS: obs. 143.0710, calc. for $C_7H_{11}O_3$ 143.0708, the spectrum was almost identical with the MS recorded for the *erythro* epoxide **3**. ^1H NMR, δ ppm: 1.36 and 1.44 (both 3H and *s*), 2.68 (H_{1a}), 2.79 (H_{1b}) and 3.01 (H_2) coupling constants as for **3** 3.95 ± 0.10 ($2H_4$ and H_3). ^{13}C NMR, δ ppm: 25.4, 26.4, 109.7, 43.7, 51.8, 65.8 and 76.1, coupling constants and assignments as for **3**.

Transformation of the epoxide mixture **3**+**4** *into a mixture of* 1-*deoxy*-D-*erythritol and* 1-*deoxy*-D-*threitol* (**12**+**13**). To a 1 molar soln of $LiEt_3BH$ in dry THF (5.25 ml) was added dropwise and under N_2 a soln in THF (2 ml) of the epoxide mixture (**3**+**4**) (0.5 g) resulting from the reaction of **2** with dimethyloxosulfonium methylide. The mixture was stirred for 2½ hr at room temp and a sat NH_4Cl soln (6 ml) was added. Dropwise a commercial (Merck p.a.) 30% H_2O_2 soln (4.2 ml) was added followed by K_2CO_3 (1 g). The mixture was filtered, and the organic layer was separated and the water layer extracted with diethyl ether (20 ml × 2). The combined extracts were saturated with K_2CO_3, washed with water (15 ml), dried over K_2CO_3 and concentrated in vacuum to yield a mixture of the oily **14**+**15** (0.44 g). From the ^{13}C NMR spectrum of this mixture the ratio of the erythritol: threitol was seen to be approximately 70:30. Resonances assignable to the erythritol were found at 18.2 (C_1), 64.5 (C_4) and 66.7 (C_2) while the corresponding peaks in the spectrum of the threitol were at 18.9, 66.0 and 68.7.

Separation of the two products were unsuccessful. To the mixture (0.51 g) was then added a 12% acetic acid solution (2.5 ml). After 30 min on a steam bath, water and AcOH were removed by azeotropic distillation with benzene (20 ml × 6). The residue (0.42 g) was washed with $CHCl_3$ and the remaining yellow syrup gave after evaporation in vacuum a mixture (0.37 g) of **12**+**13**. The epimeric ratio was shown by ^{13}C NMR to be **12**:**13** = 68:32. Resonances due to 1-deoxy-D-erythritol were found at: 25.3 (C_1), 70.5 (C_4), 75.6 (C_2) and 83.3 (C_3), and the corresponding resonances for the *threo* epimer at: 26.2, 70.7, 75.6 and 83.3.

1-*Deoxy*-D,L-*erythritol and* 1-*deoxy*-D,L-threitol (**12**+**13**) from crotylalcohol. To a mixture of commercial 30% H_2O_2 soln (28 ml, 0.78 mol) and formic acid (120 ml, 2.74 mol) was added dropwise crotylalcohol (15 g, 0.21 mol). Commercial crotylalcohol is a mixture of isomers, this one (Fluka) was shown by NMR to consist of *trans*:*cis* = 90:10. The temp of the mixture was during the addition kept below 30°. After 24 hr at room temp the mixture was evaporated to dryness in vacuum. A soln of NaOH in water (16 g in 30 ml) was added very slowly in order to keep the temp below 45°. After neutralization with 70% HCl and concentration, the mixture was extracted with boiling EtOAc. The filtered extract was concentrated in vacuum to yield a mixture of 1-deoxy-D, L-erythritol and -threitol (10 g, 45%) as a colourless syrup. The ^{13}C NMR spectrum showed resonances at the same positions as were found for the mixture of 1-deoxytetritols produced from the epoxide mixture, the signals due to the *erythro* isomer being the most prominent ones.

1-*Deoxy*-3,4-O-*isopropylidene*-D-*glycero*-*tetrulose* (**5**). A soln of **2** (17 g, 0.13 mol) in anhyd diethyl ether (100 ml) was added dropwise to MeMgI (prepared from 11 g Mg and 32 ml MeI) in anhyd ether (150 ml) at 0°. The mixture was stirred for 2 hr at room temp, neutralized with a sat NH_4Cl soln, extracted with ether (100 ml × 3), the combined extracts washed with water, dried over Na_2SO_4 and concentrated in vacuum. Distillation at 76°, 10 mm Hg, gave an oily mixture (12 g) of **14** and **15**. Glc and ^{13}C NMR showed the isomeric mixture to be *erythro*:*threo* = 70:30. The epimeric mixture (3 g, 0.02 mol) was dissolved in EtOH-free chloroform (50 ml) and water (50 ml), K_2CO_3 (0.7 g), potassium meta periodate (6 g, 0.026 mol) and ruthenium dioxide (0.16 g, 0.0015 mol) was added. The mixture was shaken for 4 hr at room temp and excess ruthenium tetroxide destroyed by addition of i-PrOH. The mixture was filtered, the water layer extracted with chloroform (50 ml × 3), the combined extracts washed with water and dried over $CaCl_2$. Distillation at 69°, 10 mm Hg gave **5** (1.93 g, 65%), $[\alpha]_D = +47.1°$ ($c = 1.87$, $CHCl_3$). MS: $M^{\cdot+}$ 144.0787 calc. for $C_7H_{12}O_3$ 144.0786, *m/e* 129 (13%, $M-{}^{\cdot}CH_3$), *m/e* 101 (58%, $C_5H_9O_2^+$), *m/e* 43 (100%, $C_2H_3O^+$). ^1H NMR δ, ppm: 1.38, 1.47 and 2.21 (all 3H and *s*), ABC-system: $\nu_A = 3.93$, $\nu_B = 4.12$ ($2H_4$), $\nu_C = 4.33$ (H_3), $J_{AB} = 9$ Hz, $J_{AC} = 6$ Hz, $J_{BC} = 9$ Hz. ^{13}C NMR: 25.0, 26.0 and 110.7 (isoprop), 26.1 (C_1), 66.3 (C_4) and 80.3 (C_3).

Acknowledgements—We are grateful to professor Vernon D. Parker for valuable discussions and for a fellowship to S. H. from UNIT.

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