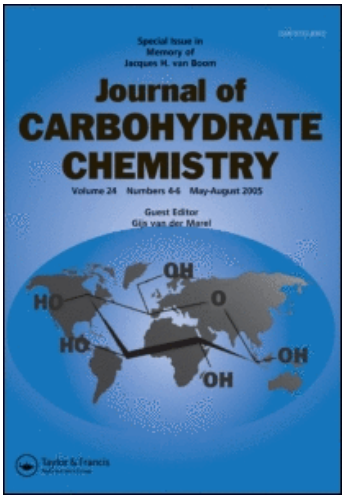


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Unsaturated, Branched, Six-Membered Carbocycles from 2,6-Diuloses

Donald E. Kiely[a]; Charles C. Cantrell[a]; James M. Riordan[a]; Gerald J. Abruscato[a]
[a] Department of Chemistry, University of Alabama in Birmingham, Birmingham, Alabama

To cite this Article Kiely, Donald E. , Cantrell, Charles C. , Riordan, James M. and Abruscato, Gerald J.(1982) 'Unsaturated, Branched, Six-Membered Carbocycles from 2,6-Diuloses', Journal of Carbohydrate Chemistry, 1: 1, 49 — 69
To link to this Article: DOI: 10.1080/07328308208085078
URL: http://dx.doi.org/10.1080/07328308208085078

J. CARBOHYDRATE CHEMISTRY, 1(1), 49-69 (1982)

UNSATURATED, BRANCHED, SIX-MEMBERED CARBOCYCLES FROM 2,6-DIULOSES[1,2]

Donald E. Kiely,* Charles C. Cantrell, James M. Riordan
and Gerald J. Abruscato

Department of Chemistry
University of Alabama in Birmingham
Birmingham, Alabama 35294

Received March 3, 1982

ABSTRACT

Mild treatment of 3,4,5-tri-O-acetyl-1,7-dibromo-1,7-dideoxy-xylo-2,6-heptodiulose (2) with acetate ion in several solvents produced unsaturated, branched, six-membered carbocyclic compounds. 4S(R),5R(S),6R(S)-6-acetoxy-4-bromomethyl-4,5-epoxy-6-ethoxy-2-cyclohexenone (3) was the predominant cyclization product in ethanol solution, and the 6-methoxy analog (4) was the major product in methanol solution. Cyclization of 2 in acetone cleanly produced the cross-conjugated ketone 4S(R)-2-acetoxy-3-bromo-4-bromomethyl-4-hydroxy-2,5-cyclohexadien-1-one (5), and cyclization of the 1,7-dichloro analog of 2, compound 9, gave the corresponding dichlorocyclohexadien-1-one 11. Compound 8, the 4-O-acetyl derivative of 5, and 2,3,4,6-tetraacetoxybenzyl acetate (7) were derived from 2 in an acetic anhydride-potassium acetate mixture while the deoxycyclose D,L-(3,4,6/5)-4,5,6-tri-O-acetyl-3-C(iodomethyl)-3,4,5,6-tetrahydroxycyclohexanone (12) was the reductive cyclization product from treatment of an acetone solution of 2 with sodium iodide. The mechanisms of the cyclization reactions are considered.

INTRODUCTION

Previous reports from this laboratory[2d,3] described a novel synthesis of branched-chain epi-configuration deoxyhalogeno- and deoxyaminocyclitols resulting from the base induced cyclization of the tri-O-acetyl-1,7-dibromo, dichloro, and diazido-1,7-dideoxy-xylo-2,6-heptodiuloses. During the course of these investigations it was observed that controlled, but prolonged treatment of the

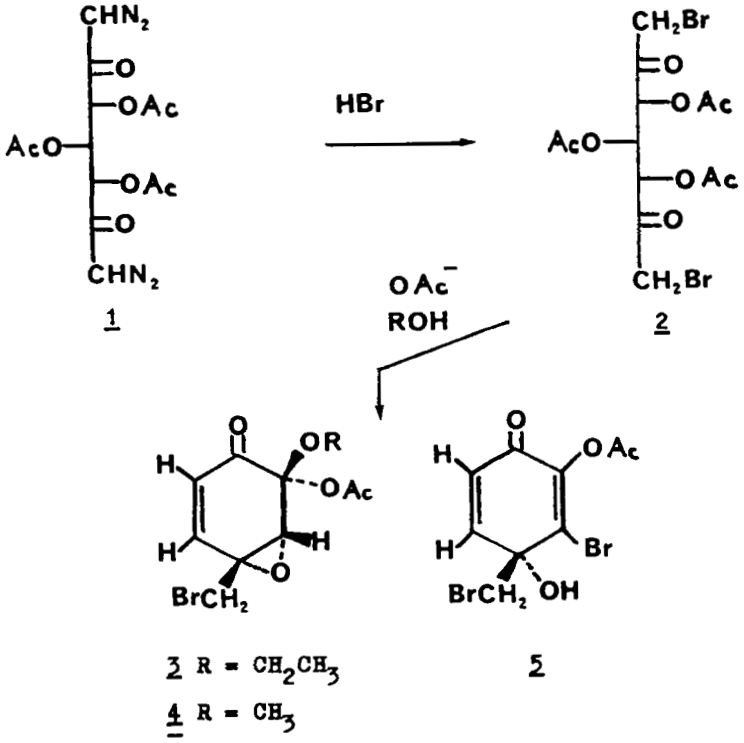
reaction mixtures with base produced some unusual, highly functionalized, and unsaturated six-membered carbocyclic compounds, the subjects of this paper.

RESULTS AND DISCUSSION

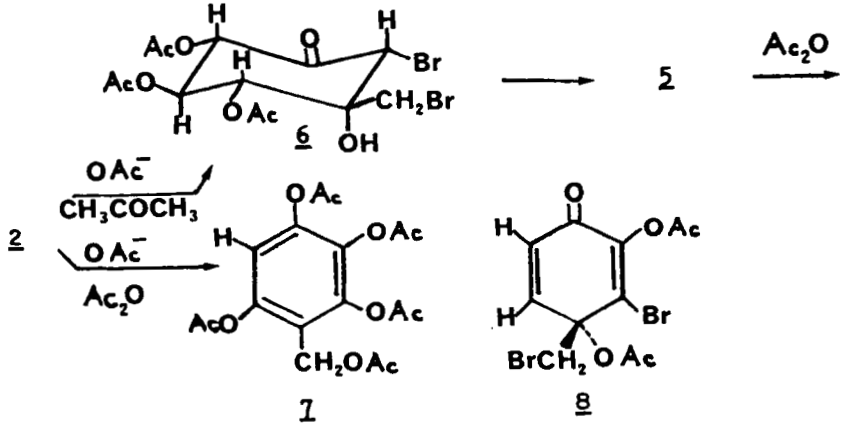
It is well known that a halogen, such as chlorine or bromine, when substituted on a carbon alpha to a carbonyl function is readily displaced by a nucleophile.[4] This premise was the basis for an experiment in which the alpha-haloketone tri-O-acetyl-1,7-dibromo-1,7-dideoxy-xylo-2,6-heptodiulose (2), in ethanol solution, was stirred with solid sodium acetate. The expected product was penta-O-acetyl-xylo-2,6-heptodiulose.[5] The reaction did not produce any of the desired acyclic diketone but rather gave a mixture of two carbocyclic ketones; the epoxycyclohexenone 3, as the major product, and the cross-conjugated cyclohexadienone 5, as the minor product (Scheme 1). The structure of 3 was ultimately determined by an X-ray crystallographic study.[2c] It has now been shown that the same reaction produces the C-6 methoxy compound (4) when methanol is used as the solvent in place of ethanol. Clearly, the alcohol solvent is the source of the alkoxy substituent on both 3 and 4.

An anhydrous acetone solution of 2 was then stirred at room temperature with solid anhydrous sodium acetate in order to promote S_N2 displacement of bromide ion and to avoid direct solvent participation in the reaction. However, after several hours 2 was completely converted to a single cyclic product, the dibromocyclose 6.[2d,4] Continued stirring of the reaction mixture (24 hours) produced the unsaturated ketone 4S(R)-2-acetoxy-3-bromo-4-bromomethyl-4-hydroxy-2,5-cyclohexadien-1-one (5) as the sole organic product from the reaction (Scheme 2). The course of the stepwise conversion of 2 to 5 was monitored by ^{1}H NMR.[1d] During the formation of 5 the two downfield doublets due to H-5 and H-6 gradually replaced the ring proton signals from 6. A downfield shift in the position of the signals from the bromomethyl protons also occurred as 5 was formed from 2. Complete conversion of 2 to 5 in one hour was also achieved by substituting sodium acetate trihydrate for anhydrous sodium acetate as the base in the reaction. However, in using the hydrated form of the base the reaction proceeded too rapidly to allow isolation of 6, the direct precursor of 5.

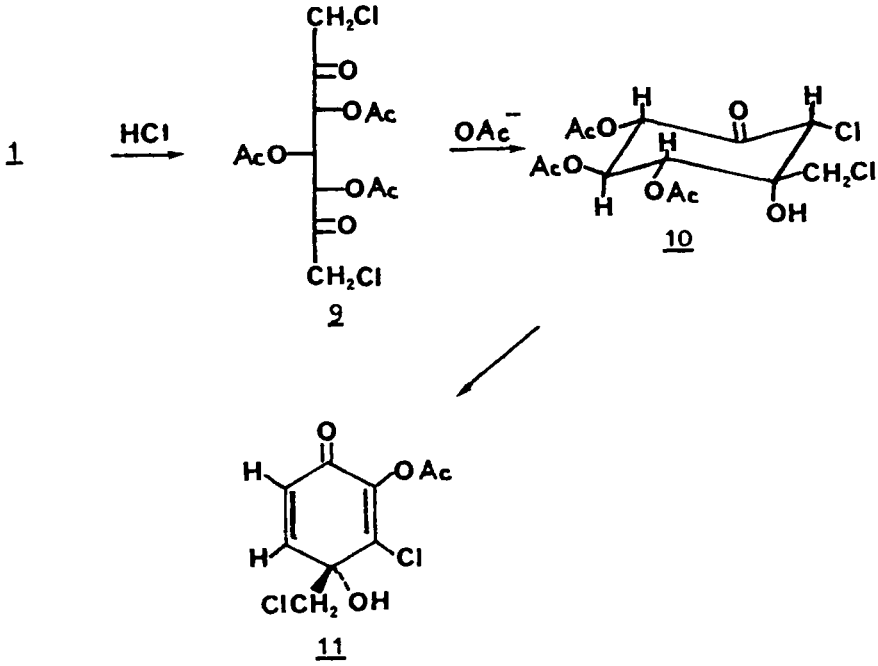
SCHEME 1



SCHEME 2



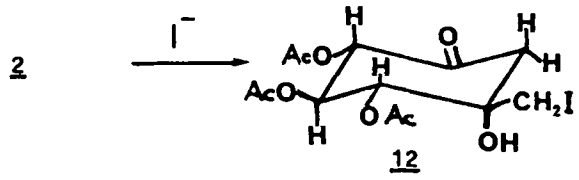
SCHEME 3



The dichlorocyclohexadienone derivative 11 was prepared in a similar manner by treating an acetone solution of 3,4,5-tri-O-acetyl-1,7-dichloro-xylo-2,6-heptodiulose (9) with anhydrous sodium acetate. Under these reaction conditions, as with 2, cyclization was rapid relative to the elimination-rearrangement sequence that produced 11 (Scheme 3). Limiting the reaction time resulted in a convenient high yield conversion of 9 to 10.[3]

Direct displacement of bromide with acetate from a bromomethyl sugar ketone was demonstrated by Wolfrom and co-workers forty years ago.[6] Specifically, these workers described the conversion of penta-O-acetyl-1-bromo-1-deoxy-D-gluco-2-heptulose to hexa-O-acetyl-D-gluco-2-heptulose with potassium acetate using acetic anhydride as the solvent. However, when an acetic anhydride solution of 2 was stirred with potassium acetate for several hours, no acyclic product was

SCHEME 4



12

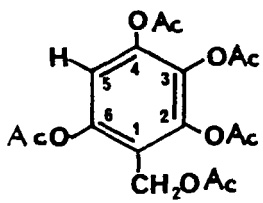
observed. Rather, the starting diulose was converted to the carbocycles 2,3,4,6-tetraacetoxybenzyl acetate (7), and the 4-O-acetyl derivative of 5, compound 8 (Scheme 2). This latter compound was also prepared by direct acetylation of 5.

The argument that the aromatic product obtained by treating 2 with potassium acetate/acetic anhydride is the tetraacetoxybenzyl acetate 7 is based on a consideration of both the ^{1}H and ^{13}C NMR spectra of the product. The ^{1}H NMR spectrum of the product contains a single aromatic proton resonance (δ 7.10), two overlapping (δ 2.36) and two separated (δ 2.30 and 2.28) aromatic acetoxy singlets, as well as two and three-proton singlets (δ 5.09 and 2.0) from the benzyl acetate portion of the molecule. Symmetrical isomer 7b was ruled out as the product since the ring acetoxy protons would be seen as two six proton singlets. The overlap of the signals from two ring acetoxy groups suggested a comparable structural environment for these two functions possibly the C-3 and C-4 acetoxy groups of 7a,[2a,2b] since each of these groups is flanked by two of the same (acetoxy) substituents. However, it can also be argued that the coincidence of these signals may result from a subtle combination of electronic and structural factors operating within the molecule and that the product is in fact 7.

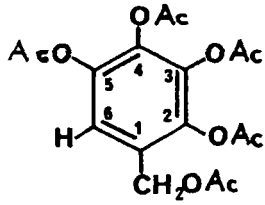
The correct assignment of the product as structure 7 came only after evaluation of the product's ^{13}C NMR spectrum.

Chemical shift values for ring carbons of polysubstituted aromatic compounds are reasonably predictable by application of the principle of substituent additivity[7] and can be calculated by using the following expression.

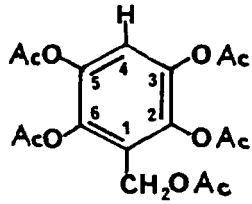
$$\delta_{calcd} = 128.5 + S_{ipso} + S_{ortho} + S_{meta} + S_{para}$$



7



7a



7b

δ_{calcd}	calculated ring carbon chemical shift (ppm)
128.5	^{13}C chemical shift value of the parent benzene carbons (ppm)
S terms	substituent chemical shift (SCS) values (ppm) at ipso, ortho, meta and para ring positions

The SCS values employed were taken from the paper of Ewing[8] and are given in Table 1.

The results from comparing the calculated ^{13}C chemical shift values for the ring carbons of 7 and 7a with those actually found is summarized in Table 2. Since the $\delta_{calcd} - \delta_{found}$ values for five of the six ring carbons of 7 are considerably smaller than those calculated for 7a, we have assigned 7 as the aromatic product obtained by treating 2 with potassium acetate/acetic anhydride.

It is clear from our results that acetate is not a good enough nucleophile to readily accomplish the desired halide displacement from 2 or 9. However, it is possible to displace bromide from 2 with azide ion prior to cyclization, an observation consistent with the high nucleophilic character of azide ion.[3] Thus, it also seemed reasonable that treatment of the dibromodiulose 2 in an aprotic solvent, with a good nucleophile that was also a weak base, should lead to an acyclic diketone rather than a cyclic product. When an acetone solution of 2 was stirred with sodium iodide, the product from the reaction (79%) was the iododeoxycyclose 12 (Scheme 4). The mild conditions required for this conversion underscored even more than the reactions previously discussed the driving force that these activated xylo-configuration diuloses have for cyclization to the carbocyclic ring system.

Table 1. Selected ^{13}C Substituent Chemical Shift Values (ppm) of Monosubstituted Benzenes

Substituent	S_{ipso}	S_{ortho}	S_{meta}	S_{para}
H	0.0	0.0	0.0	0.0
OAc	22.4	-7.1	0.4	-3.2
CH_2OAc	7.8	0.0	-0.2	-0.2

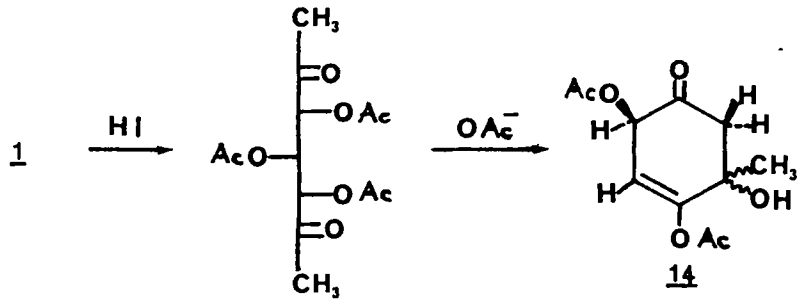
Table 2. Comparison of Calculated (δ_{calcd}) with Found (δ_{found}) Ring Carbon Chemical Shifts

Compound 7	C-1	C-2	C-3	C-4	C-5	C-6
δ_{calcd} (ppm)	119.3	144.6	133.3	144.4	111.3	148.5
δ_{found} (ppm)	120.2	143.5	133.1	143.3	115.8	147.0
$\delta_{calcd} - \delta_{found}$ (ppm)	-0.9	1.1	0.2	1.1	-4.5	1.5

Compound 7a	C-1	C-2	C-3	C-4	C-5	C-6
δ_{calcd} (ppm)	126.8	141.0	136.9	137.0	140.8	119.0
δ_{found} (ppm)	120.2	147.0	133.1	143.3	143.5	115.8
$\delta_{calcd} - \delta_{found}$ (ppm)	6.6	-6.0	3.8	-6.3	-2.7	3.2

When 3,4,5-tri-O-acetyl-1,7-dideoxy-xylo-2,6-heptodiulose (13), prepared by hydrogen iodide reduction of 1, was stirred in benzene-ethanol solution with sodium acetate for five days a major and two minor products were formed with a small amount of starting material remaining. The major product was purified by preparative TLC and obtained as a crystalline solid. On the basis of elemental, ^1H NMR and IR spectroscopic analyses, the structure of the product has been assigned to that of the non-conjugated cyclohexenone derivative 14 (Scheme 5). As expected, 13, lacking halogens on the terminal carbons, was less reactive toward ring closure than either 2 or 9. However, it is not clear what driving force gives rise to the non-conjugated system found in 14.

SCHEME 5

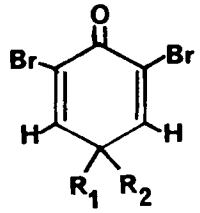


13 14

Examination of the chemical literature has revealed that the dihalocyclohexadienones 5 and 11 are structurally related to a number of interesting previously reported compounds, compounds not synthetically prepared from carbohydrates. For example, the 2,6-dibromo-2,5-cyclohexadien-1-one derivatives 15, 16 and 17 were prepared by a halogenation-oxidation sequence from phenolic precursors.[9] These compounds have been shown to be effective as insecticides against the tobacco budworm, with 16 also showing activity against the boll weevil.[10] The synthetically derived halo-imino compounds 18 and 19 were recently reported as members of a series of compounds used in formulating a new index for antitumor activity.[11] Among brominated compounds that have been isolated from sponges are the cyclohexadienone 20,[12,13] the phenol 21, and the quinone 22, the latter two compounds showing antibacterial activity.[14]

Mechanistic Considerations

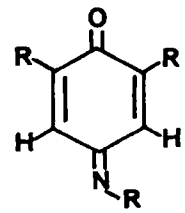
The intramolecular condensation of 2 and 9 proceed under mildly basic conditions with a high degree of stereoselectivity in forming the cycloses 6 and 10.[3] It is these cycloses which then undergo loss of acetic acid with accompanying rearrangement to produce the unsaturated six-membered carbocycles described. Conversion of 2 to 5 through the cyclose 6 can be considered to occur in a stepwise manner. In basic solution 6 equilibrates with the enolates 23 and 24 (Scheme 6). The latter enolate can lose acetate by a 1,4-



15 $R_1 = R_2 = CH_3$

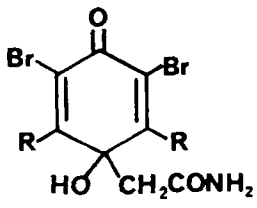
16 $R_1 = CH_3$ $R_2 = OH$

17 $R_1 = CH_3$ $R_2 = OAc$

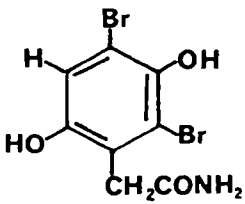


18 R = Br

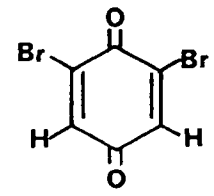
19 R = Cl



20



21

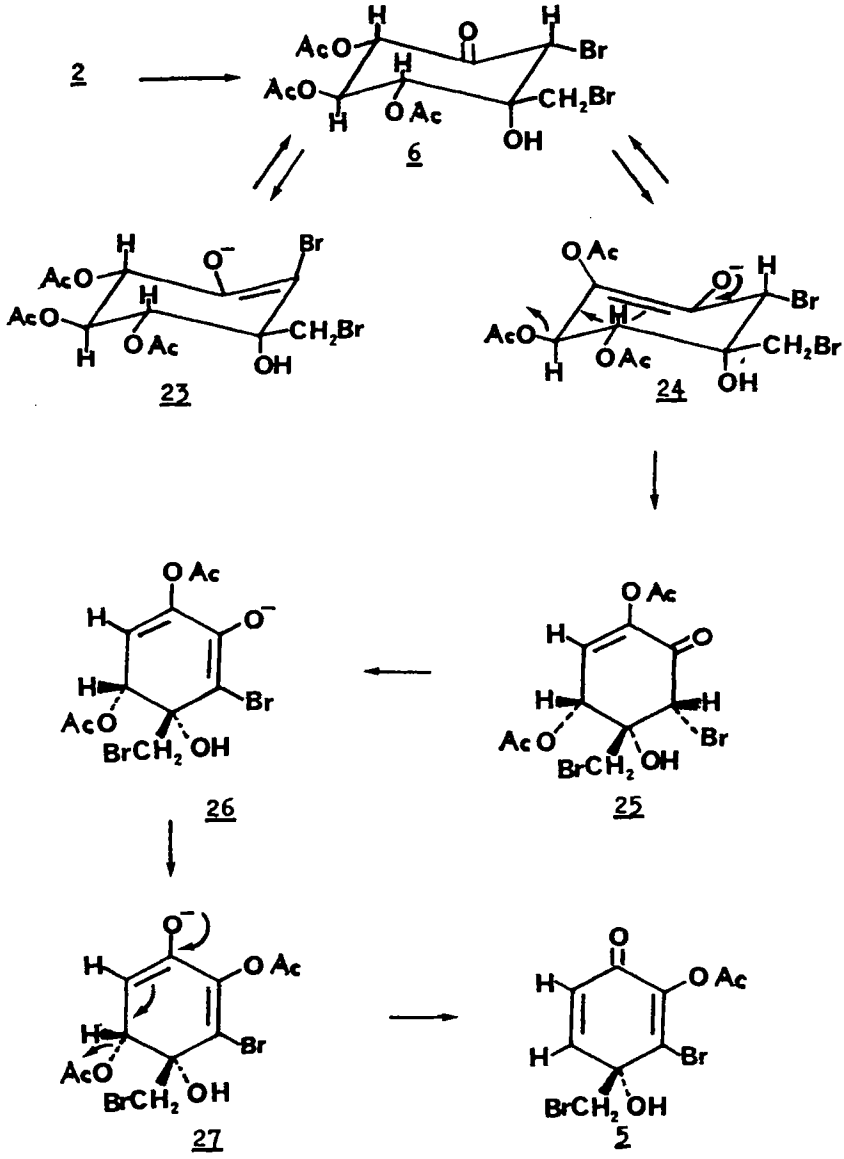


22

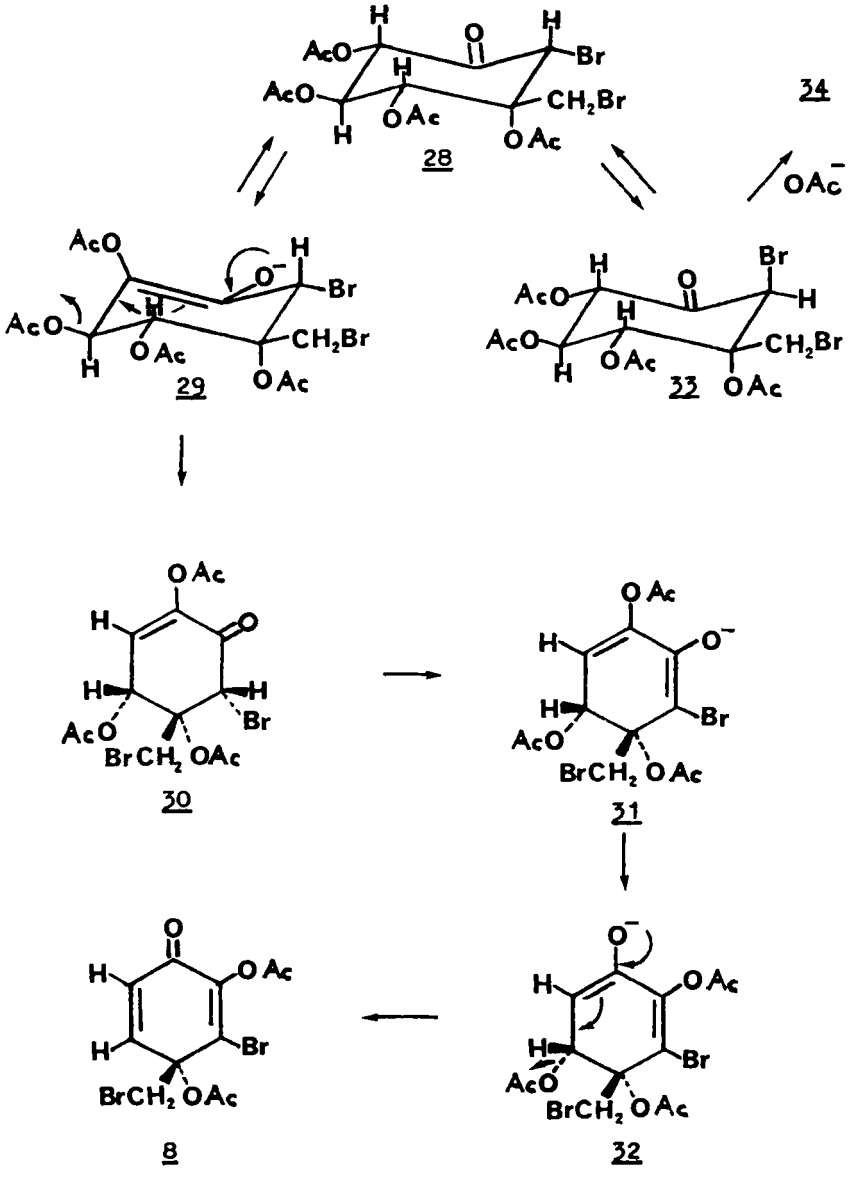
elimination in forming 25, which itself enolizes to the cyclic diene 26. The enolate 27, formed by an acetyl migration on 26, also undergoes a 1,4-elimination of acetate, producing the final product 5. Aromatization of cyclose pentaacetates and pentabenzoates with base to acylated benzenetetrols has been known for some time,[15,16,17] and key intermediates in these transformations include α,β-unsaturated ketones structurally similar to 25.

The mechanistic sequence leading from 2 to 8 in acetic anhydride (Scheme 7) is depicted as being similar to that which produces 5. However, acetylation of the tertiary hydroxyl group on the cyclose ring occurs, probably right after ring formation, giving 28. This intermediate can serve as the starting point for the production of 8 and the aromatic compound 7 (Scheme 8). Epimerization at C-2 of 28 can generate the ketone 33 with an axial bromine. The axial bromine of 23 is labile to nucleophilic displacement and with acetate may be converted to the cyclose pentaacetate 34. Conversion of 34 to 7 can be envisioned as occurring in a number of steps, with one possible route outlined in Scheme 8.

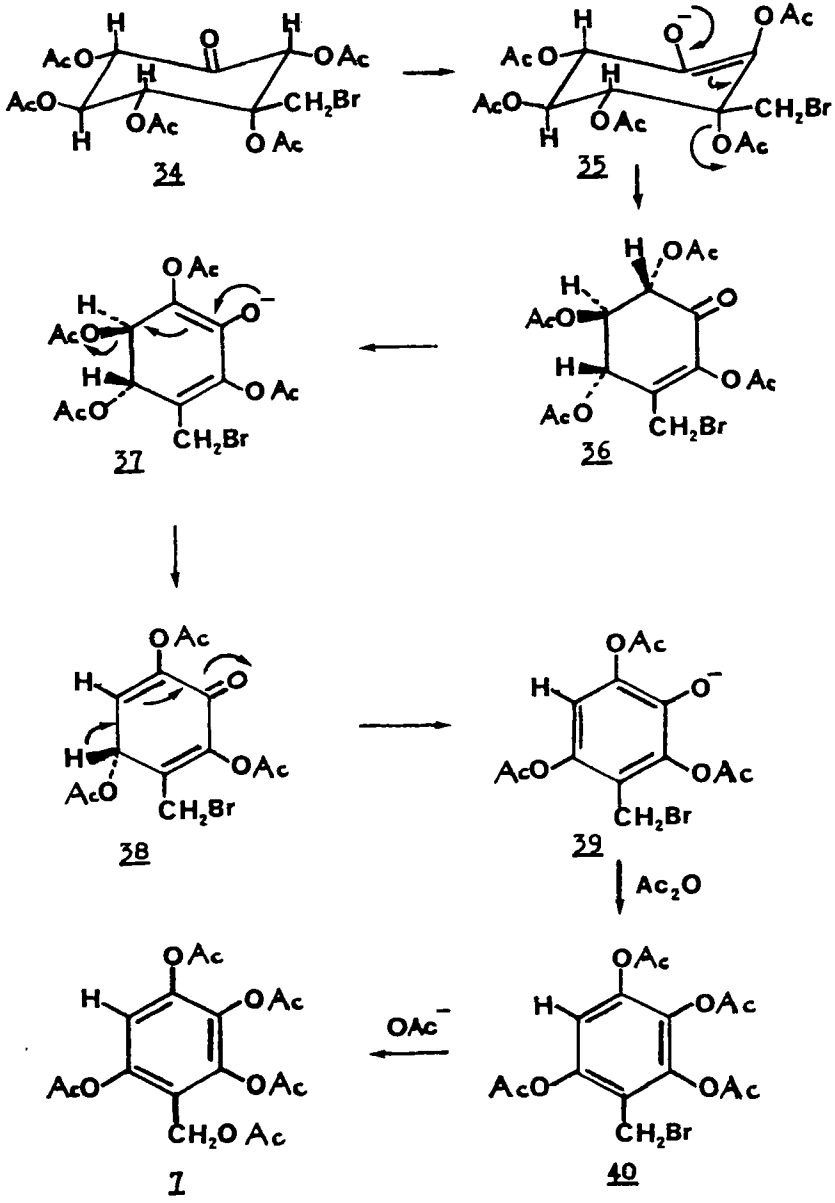
SCHEME 6



SCHEME 7

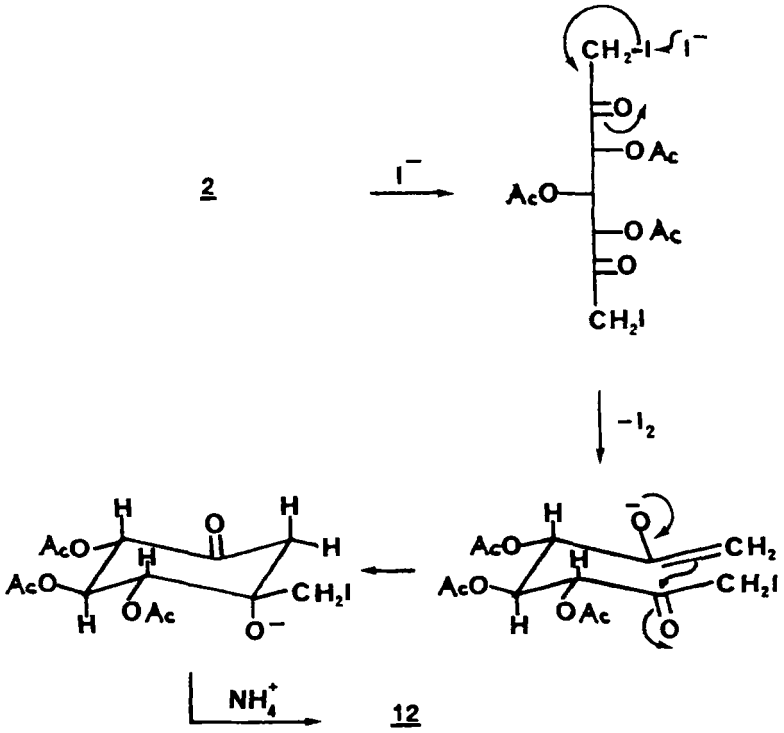


SCHEME 8

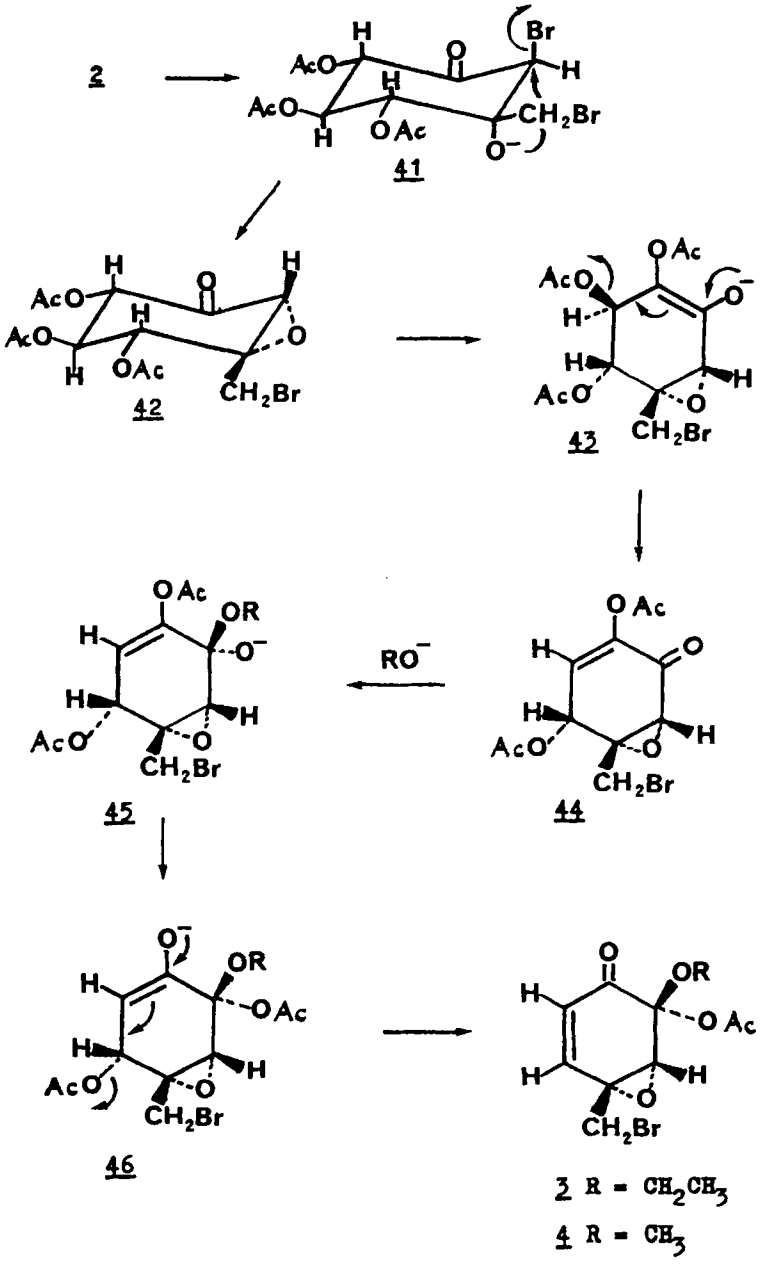


Conversion of 2 to the deoxyiodocyclose 12 is probably initiated by a rapid displacement of terminal bromides with sodium iodide, giving the reactive diiodoketone 41 (Scheme 9). This displacement hypothesis is in keeping with the finding that azide displaces bromide from 2 before ring closure occurs.[3] The reduction step that produces iodine follows quickly after the initial displacement since the color of iodine was observed even at the early stages of the reaction. The enolate (42), produced by the reduction of 41 with iodide, can cyclize in standard aldol condensation fashion giving the alkoxide 43 and then the product 12. Ammonium sulfate served as the protonating agent in the final step and as a product stabilizing acidic buffer. If the ammonium sulfate was excluded

SCHEME 9



SCHEME 10



during the reaction, the product yield went down due to product decomposition.

A number of mechanistic pathways for the conversion of 2 to the oxiranes 3 and 4 can be envisioned, and one such mechanism for the formation of 3 was proposed.[2c] An alternate mechanism for the generation of 3 (and 4) is now offered (Scheme 10). The revised mechanism is in keeping with the mechanisms suggested for the formation of the unsaturated compounds 5, 7, 8 and 11 in that loss of acetic acid from the ring is due to a 1,4-type elimination. The epoxide 42 arises by displacement of the axial ring bromide of 41, with 41 being the kinetically controlled cyclization product in alcohol or simply the product of base-catalyzed epimerization. An intriguing aspect of the formation of 3 and 4 is the stereoselective addition of alcohol to the ring at some point in the mechanism. What we propose is that ethanol or methanol as ethoxide or methoxide adds to the ring carbonyl of 44 on the less sterically hindered face of the ring, opposite to the face bearing the epoxide. Acetyl migration on 45 is followed by final acetate elimination to give 3 or 4.

EXPERIMENTAL

General Methods. Melting points were obtained with a Fisher-Johns melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded at 60 MHz with a Varian Model HA-60IL spectrometer or at 90 MHz with a Varian Model 390 spectrometer, tetramethylsilane serving as an internal standard. The ^{1}H spectrum of 12 was recorded using a Bruker 400 MHz instrument; 32K Fourier Transform spectra were obtained from 236 transients using a spectral width of 20 KHz and a pulse delay of 3 seconds. The ^{13}C spectrum of 7 was recorded at 100.6 MHz using the same instrument. IR spectra were obtained using a Perkin-Elmer 337 or 283 grating infrared spectrophotometer. Mass spectra were recorded with a Hitachi-Perkin-Elmer RMU-7 double-focusing mass spectrometer. Thin-layer chromatography was carried out on plates coated with silica gel GF-254 (E. Merck, Darmstadt) and components detected by spraying with 20% sulfuric acid. Chromatographic solvent systems are given as volume-to-volume ratios. Solutions were concentrated under reduced pressure. The acid-form

cation-exchange resin generally used was Dowex AG 50W-X2. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, GA, or Galbraith Laboratories, Inc., Knoxville, TN.

4S(R),5R(S),6R(S)-6-Acetoxy-4-bromomethyl-4,5-epoxy-6-ethoxy-2-cyclohexenone (3). A suspension of 2 (1.1 g) and sodium acetate trihydrate (0.45 g) in ethanol (5 mL) was stirred at room temperature for 1 h. The resultant brown colored suspension was concentrated and the residue extracted with chloroform (25mL). The mixture was filtered, the filtrate was treated with decolorizing carbon and concentrated to give a reddish-brown oil. A TLC analysis (benzene-ether, 1:1) showed that the oil was composed of a major product, Rf 0.80, and a minor product, Rf 0.62. The mixture was chromatographed on silica gel (45 g in a 20 mm x 370 mm column) with benzene-ether (1:1). The major product was obtained as a white solid which was recrystallized from ethanol giving 3 as colorless needles, 0.33 g (45%): mp 78-80°C. ^{1}H NMR and IR data for 3 have been reported.[2c]

Anal. Calcd for $C_{11}H_{13}BrO_5$ (305.10): C, 43.27; H, 4.29; Br, 26.22. Found: C, 43.77; H, 4.54; Br, 25.64.

The minor product (0.04 g) was identified as 5 by comparison of its IR and ^{1}H NMR spectra with the spectra of material prepared by treating 2 with sodium acetate in acetone.

4S(R),4R(S),6(R)S-6-Acetoxy-4-bromomethyl-4,5-epoxy-6-methoxy-2-cyclohexenone (4). A solution of 2 (0.40 g) and sodium acetate trihydrate (0.25 g) in methanol was stirred at room temperature for 1 h. The solution was concentrated, the residue extracted with chloroform (20 mL), and the chloroform solution decolorized with carbon. The orange, oily product (0.30 g), which TLC (benzene-ether, 1:1) showed was composed of a major component (Rf 0.80) and a minor component (Rf 0.62), was chromatographed on silica gel (20 g in a 15 mm x 370 mm column) with benzene-ether (1:1). The major component was obtained as a colorless oil which crystallized from ethanol to give 4, 0.10 g (40%): mp 106-108°C; IR (KBr) 1725 (ester C=O) and 1675 cm^{-1} (α,β-unsaturated C=O); ^{1}H NMR ($CDCl_3$, 60 MHz) δ7.20 (d, 1, H-3, $J_{H-2,H-3}$ = 10.0 Hz), 6.15 (d, 1, H-2), 4.25 (s, 1, H-5), 3.55 (s, 2, CH_2Br), 3.40 (s, 3, OCH_3) and 2.20 (s, 3, CH_3CO_2).

Anal. Calcd for $C_{10}H_{11}BrO_5$ (291.11): C, 41.23; H, 3.78; Br, 27.45. Found: C, 41.30; H, 3.83; Br, 26.90.

The minor component (0.03 g) was identified as 5.

4S(R)-2-Acetoxy-3-bromo-4-bromomethyl-4-hydroxy-2,5-cyclohexadien-1-one (5). Method a.[1b] A solution of 2 (0.40 g) in acetone (10 mL) was stirred for 2 h at room temperature with suspended sodium acetate trihydrate. The mixture was concentrated, the residue extracted with chloroform (20 mL), and the filtrate decolorized with charcoal. The oily product, predominantly a single component as shown by TLC (benzene-ether 2:1), was further purified by silica gel column chromatography with benzene-ether (1:1). The chromatographically homogeneous product (5, 0.20 g, 68%) had a mp 78-80°C: IR (KBr) 3450 (OH), 1770 (enol ester C=O) and 1675 cm^{-1} (α,β-unsaturated ketone C=O); UV max (95% ethanol) 276 (ε 3700), 242 (ε 9500), and 220 nm (ε 5000); ^1H NMR ($CDCl_3$, 60 MHz) δ 7.00 (d, 1, H-5, $J_{H-5,H-6}$ = 10.0 Hz), 6.40 (d, 1, H-6), 3.60 (d of d, 2, CH_2Br, J_{gem} = 11.0 Hz), 3.80 (s, 1, OH) and 2.35 (s, 3, CH_3CO_2); mass spectrum (70 eV) m/e (relative intensity) dibromo isotopic clusters corresponding to (M+2), (M), (M-2) at 342 (4), 340 (8), 338 (4) and loss of $CH_2=C=O$ at 300 (56), 298 (100), 296 (56).

Anal. Calcd for $C_9H_8Br_2O_4$ (339.98): C, 31.79; H, 2.37; Br, 47.00. Found: C, 31.92; H, 2.51; Br, 46.86.

Method b. The cyclization of 2 to the cyclose 6 in anhydrous acetone with anhydrous sodium acetate as previously described[3] was complete after 3 h. When the reaction mixture was stirred for an additional 20-24 h, conversion of 6 to 5 was achieved. The crystalline product was obtained without chromatographic purification.

4S(R)-2-Acetoxy-3-chloro-4-chloromethyl-4-hydroxy-2,5-cyclohexadien-1-one (11). Fused sodium acetate (0.50 g) was suspended in a solution of anhydrous acetone (10 mL) containing 9 (0.95 g). The reaction mixture was stirred at room temperature until TLC (toluene-ether, 1:1) showed that the starting material was gone and a much faster moving component was the predominant product. The reaction mixture was filtered, the filtrate was concentrated at room temperature, and the syrupy residue was purified by silica gel column chromatography (ether-toluene, 1:2) giving 11 (0.47 g, 73%); mp 86-90°C. Recrystallization from toluene gave an analytical sample: mp 93-95°C; IR (KBr) 3380 (OH), 1740 (ester C=O), 1680 (α,β-unsaturated ketone C=O), 1660 and 1625 cm^{-1} (C=C); ^1H NMR (Me_2CO-d_6, 90 MHz) δ 7.08 (d, 1, H-5, $J_{H-5,H-6}$ = 9.8 Hz), 6.34 (d, 1, H-6), 6.10 (s, 1, OH), 3.87 (d of d, 2, CH_2Cl, J = 12 Hz), and 2.25 ppm (s, 3, CH_3CO_2).

Anal. Calcd for $C_9H_8Cl_2O_4$ (251.07): C, 43.06; H, 3.21; Cl, 28.24. Found: C, 43.00; H, 3.24; Cl, 28.21.

4(S)R-2,4-Diacetoxy-3-bromo-4-bromomethyl-2,5-cyclohexadien-1-one (8). A solution of 2 (0.21 g) in acetic anhydride (5 mL) and pyridine (0.10 mL) was stirred at room temperature for 6 h. The solution was concentrated to a light brown oil which was dissolved in ether and the ether-solution treated with decolorizing carbon. The resultant colorless oil was chromatographed on a column of silica gel (20 g in a 14 x 460 mm column) with benzene-ether (1:1) to give 8 as a homogeneous, colorless oil: 0.16 g (68%); IR (neat) 1780 (enol ester C=O) and 1675 cm^{-1} (α,β-unsaturated ketone C=C); UV max (95% ethanol) 276 (ε4430), 246 (ε10,000) and 220 nm (ε6430); ^1H NMR ($CDCl_3$, 60 MHz) δ 7.0 (d, 1, H-5, $J_{H-5,H-6}$ = 10.0 Hz), 6.50 (d, 1, H-6), 3.7 and 3.6 (each d, each 1, CH_2-Br, J_{gem} = 11.0 Hz), 2.35 and 2.10 (each s, each 3, CH_3CO_2); mass spectrum (70 eV) m/e (relative intensity), dibromo isotopic cluster (M-42 at 342 (35), 340 (8), 338 (4) and (M-84) at 300 (38), 298 (78), 296 (38); monobromo doublets (M-Br,42) at 261 (78), 259 (78), and (M-Br, 84) at 219 (95), 217 (93). The presence of a peak at 301 (38) and the inordinately large peak at 342 (35), suggests that the sample, although chromatographically homogeneous, contained a small amount of nonbrominated contaminant.

Anal. Calcd for $C_{11}H_{10}Br_2O_5$ (382.02): C, 34.58; H, 2.64; Br, 41.84. Found: C, 34.59; H, 2.70; Br, 41.70.

2,3,4,6-Tetraacetoxybenzyl acetate (7) and 8, treatment of 2 with potassium acetate in acetic anhydride. Crystalline 2 (0.70 g) was added to a suspension of potassium acetate (3.0 g) in acetic anhydride (10 mL) and the mixture was stirred at room temperature for 3 h. Water (25 mL) was added to the brown suspension and the resultant aqueous solution extracted with two 25 mL portions of chloroform. The chloroform extract was dried ($MgSO_4$) and concentrated to yield an orange oil (0.50 g). TLC analysis (ether-benzene, 1:1) showed a major product (Rf 0.33) and a minor product (Rf 0.75). The oil was chromatographed on silica gel (30 g in a 15 mm x 460 mm column) with benzene-ether (1:1). The solid major component 7 (0.30 g, 52%) was recrystallized from ether-hexane as colorless needles: mp 93-95°C; IR (KBr) 1750 cm^{-1} (ester C=O); UV max (95% ethanol) 268 (ε 1000) and 218 nm (ε 13,400); ^1H NMR ($CDCl_3$, 60 MHz) δ 7.10 (s, 1, H-6), 5.09

(s, 2, $C\underline{H}_2OAc$), 2.36 (s, 6, $C\underline{H}_3CO_2$), 2.30 (s, 3, $C\underline{H}_3CO_2$), 2.28 (s, 3, $C\underline{H}_3CO_2$), and 2.0 (s, 3, $C\underline{H}_3CO_2$); mass spectrum (70 eV) m/e (relative intensity) (M) at 382 (3), (M-42) at 340 (16) and (M-84) at 298 (42); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.3, 168.4, 167.3, 167.2, 166.6 (each $CH_3\underline{C}O_2$), 1470 (C-6), 143.5 (C-2), 143.3 (C-4), 133.1 (C-3), 120.2 (C-1), 115.8 (C-5), 55.2 ($\underline{C}H_2$), 21.1, 20.7, 20.6, 20.2 and 20.1 (each $\underline{C}H_3CO_2$).

Anal. Calcd for $C_{17}H_{18}O_{10}$ (382.33): C, 53.41; H, 4.75. Found: C, 53.42; H, 4.83.

The minor component, isolated as a colorless oil (0.12 g), was found to be 8 by comparison of its IR and ^1H NMR spectra with those obtained from the acetylation product of 5.

3,4,5-Tri-O-acetyl-1,7-dideoxy-xylo-2,6-heptadiulose (13). A solution of 1[5] (2.0 g) in cold chloroform (50 mL) was charged to a separatory funnel. Cold, aqueous hydriodic acid (10 mL, 47-50%) was added to the solution and the reaction mixture gently shaken until gas evolution stopped (ca. 30 min.). The dark brown reaction mixture was washed with water (2 x 50 mL), with 10% aqueous sodium thiosulfate solution until free of iodine, and again with water (50 mL). The yellow colored chloroform solution was dried ($MgSO_4$) and concentrated to an orange solid which was recrystallized from ether to yield 13 (0.80 g, 47%): mp 68-90°C. Recrystallization from ether gave an analytical sample of 13: mp 68-90°C; IR (KBr) 1749 and 1733 (ester C=O), and 1723 cm^{-1} (ketone C=O); ^1H NMR (CCl_4, 60 MHz) δ 5.60 (t, 1, $\underline{H}$-4, $J_{H-3, H-4}$ and $H-4, H-5$ = 4.0 Hz), 5.17 (d, 2, $\underline{H}$-3 and $\underline{H}$-5), 2.19 (s, 6, two $C\underline{H}_3CO$), 2.14 (s, 6, two $C\underline{H}_3CO_2$) and 2.10 (s, 3, $C\underline{H}_3CO_2$).

Anal. Calcd for $C_{13}H_{18}O_8$ (302.27): C, 51.65; H, 6.00. Found: C, 51.89; H, 5.91.

Treatment of 13 with sodium acetate in benzene-ethanol. A solution of 13 (0.50 g) in benzene (75 mL) and absolute ethanol (25 mL) was stirred at room temperature with sodium acetate trihydrate (0.50 g) for five days. The reaction mixture was analyzed by TLC (benzene-ether, 1:1) and found to contain a small amount of unreacted starting material plus a major product and two minor products. The cloudy, orange colored solution was treated with acid form cation exchange (Amberlite IR-120, 5 mL) and stirred occasionally over 30 min. The

resin was removed by filtration, and the filtrate concentrated to a syrup. The syrup was preparatively chromatographed on two silica gel GF plates (1000μ x 20 cm x 20 cm) with benzene-ether (2:1). The major product, 2,4-di-O-acetyl-2,4,5-trihydroxy-5-methyl-3-cyclohexenone (14), which ran just above the origin, was obtained as a chromatographically homogeneous, crystalline compound: mp 94-96°C; IR (KBr) 3520 (OH), 1772 (enol ester C=O), 1744 (ester C=O), and 1710 cm^{-1} (ketone C=O); ^1H NMR ($CDCl_3$) δ6.28 (d, 1, H-3, $J_{H-2,H-3}$ = 3.0 Hz), 5.55 (d, 1, H-2), 3.68 (broad s, OH), 2.84 and 2.58 (both d, each 1, H-6, H-6', J_{gem} = 8.5 Hz), 2.16 and 2.12 (each s, each 3, CH_3CO_2), and 1.38 (s, 3, CH_3 at C-5).

Anal. Calcd for $C_{11}H_{14}O_6$ (242.23): C, 54.54; H, 5.83. Found: C, 54.50; H, 5.51.

The faster moving minor components were not isolated in sufficient quantity to enable their identification.

D,L-(3,4,6/5)-4,5,6-Tri-O-acetyl-3-C-(iodomethyl)-3,4,5,6-tetrahydroxycyclohexanone (12). To a suspension of finely divided, anhydrous ammonium sulfate in anhydrous acetone (20 mL) containing 2 (1.01 g) was added sodium iodide (1.25 g). The reaction mixture was stirred at room temperature for 24 h. The mixture was concentrated, the residue suspended in dichloromethane (50 mL), and the suspension washed twice with 10% aqueous sodium thiosulfate (50 mL) and once with water (50 mL). The dichloromethane solution was dried ($MgSO_4$) and concentrated. Purification of the crude product by silica gel column chromatography (toluene-ether, 1:1) gave 12 (0.81 g, 79%): mp 172-175°C. Recrystallization from toluene gave 0.45 g of 12: mp 179-181°C; IR (KBr) 3400 (OH), 1760 and 1740 cm^{-1} (ester and ketone C=O); ^1H NMR (Me_2CO-d_6) δ5.76 (d of d, 1, H-3, $J_{2,3}$ = 5.1 Hz, $J_{3,4}$ = 4.5 Hz), 5.60 (two d, 2, H-2 and H-4), 3.45 and 3.41 (d of d, 2, CH_2I, J = 10.7 Hz), 3.21 (d, 1, H-6a, $J_{6a,6e}$ = 14.6 Hz), 2.78 (s, 1, OH), 2.70 (d, 1, H-6e, $J_{6a,6e}$ = 14.6 Hz), 2.07 (s, 9, 3 CH_3CO_2).

Anal. Calcd for $C_{13}H_{17}IO_8$ (428.18): C, 36.47; H, 4.00; I, 29.64. Found: C, 36.49; H, 4.02; I, 29.64.

ACKNOWLEDGMENT

This work was supported by a grant from the National Institute of General Medical Sciences, National Institutes of Health, Bethesda,

MD 20014. We thank J. Glickson, UAB Cancer Center, for the use of the Fourier Transform NMR spectrometer.

REFERENCES AND FOOTNOTES

1. Paper 8 on Delta-Dicarbonyl Sugars.

2. For preliminary reports see a. G. J. Abruscato, C. E. Cantrell, D. E. Kiely, and L. Benzing-Nguyen, "Abstracts of Communications", VII International Symposium on Carbohydrate Chemistry, Bratislava, Czechoslovakia, August 1974; b. C. E. Cantrell, Ph.D. dissertation, University of Alabama in Birmingham, 1975; c. C. E. Cantrell, D. E. Kiely, R. A. Hearn, and C. E. Bugg, Tetrahedron Lett., 4379 (1973); and d. D. E. Kiely and J. M. Riordan in ACS Symposium Series, No. 125, "Aminocyclitol Antibiotics", K. L. Rinehart and T. Suami, Eds., American Chemical Society, 1980, p. 95.

3. J. M. Riordan, D. E. Kiely, L. J. DeLucas, H. M. Einspahr, and C. E. Bugg, Carbohydr. Res., 82, 303 (1980).

4. A. E. Streitwieser, Jr., Chem. Rev., 56, 571 (1956).

5. C. E. Cantrell, D. E. Kiely, G. J. Abruscato, and J. M. Riordan, J. Org. Chem., 42, 3562 (1977).

6. M. L. Wolfrom, S. W. Waisbrot, and R. L. Brown, J. Am. Chem. Soc., 64, 2329 (1942).

7. G. C. Levy, R. L. Lichter, and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists", 2nd ed.; Wiley, New York, 1980, p. 100.

8. D. F. Ewing, Org. Magn. Reson., 12, 499 (1979).

9. A. P. Leftwick and E. W. Parnell, Ger. Offen., 2,603,864, 1976; Chem. Abstr., 86, 29436h (1977).

10. A. A. Guerra, R. D. Garcia, and R. D. Wolfenbarger, Southwest Entomol., 5, 153 (1980).

11. E. M. Hodnett, J. Amirmoazzami, and G. Prakash, J. Biol. Phys., 5, 24 (1977).

12. E. Fattorusso, L. Minale, and G. Sodano, J. Chem. Soc., Perkin Trans. 1, 16 (1972).

13. G. M. Sharma and P. R. Burkholder, Tetrahedron Lett., 4147 (1967).

14. P. D. Shaw, Process Biochemistry, June/July 1981, 13, and references therein.

15. L. Anderson, in D. Horton and W. Pigman, Eds., "The Carbohydrates", Vol. 1A, Academic Press, New York, 1972, p. 519.

16. T. Posternak, "The Cyclitols", Holden-Day, San Francisco, 1965.

17. H. S. Isbell, Ann. Rev. Biochem., 12, 205 (1943).