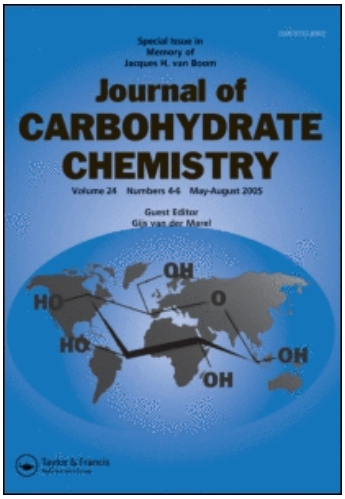


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Phase Transfer Promoted Ruthenium Oxide Oxidations of Carbohydrates II

Philip E. Morris Jr; Donald E. Kiely; Gerald S. Vigee; Pavol Kòváč

To cite this Article Morris Jr, Philip E. , Kiely, Donald E. , Vigee, Gerald S. and Kòváč, Pavol(1990) 'Phase Transfer Promoted Ruthenium Oxide Oxidations of Carbohydrates II', Journal of Carbohydrate Chemistry, 9: 5, 661 — 673
To link to this Article: DOI: 10.1080/07328309008543861
URL: http://dx.doi.org/10.1080/07328309008543861

J. CARBOHYDRATE CHEMISTRY, 9(5), 661-673 (1990)

PHASE TRANSFER PROMOTED RUTHENIUM OXIDE OXIDATIONS OF CARBOHYDRATES II

Philip E. Morris, Jr.,[1] Donald E. Kiely,* and Gerald S. Vigee

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

Pavol Kováč

NIDDK, National Institutes of Health, Bldg. 8
Bethesda, Maryland 20892

Received October 23, 1989 - Final form May 18, 1990

ABSTRACT

The use of a phase transfer catalyst, benzyltriethylammonium chloride (BTEAC), is described in conjunction with the ruthenium dioxide/periodate : water/chloroform system for the oxidation of carbohydrate alcohols to the corresponding ketone, aldehyde, or carboxylic acid. The method was found to be applicable to carbohydrates appropriately protected as acetals, ethers, or containing a benzoyloxy group not positioned to readily undergo β-elimination. While the method was very suitable for the oxidation of carbohydrate secondary alcohols to ketones, it was found to be less suitable for the oxidation of a carbohydrate primary alcohol to the corresponding aldehyde or carboxylic acid. Evidence presented suggests that under the mildly basic conditions of the reaction, ruthenium tetraoxide is converted to ruthenate and perruthenate ions in the aqueous solution and then the perruthenate ion is carried by the phase transfer catalyst into the organic layer where oxidation of the substrate occurs. A number of examples illustrating the scope of the method are presented.

INTRODUCTION

We recently reported the use of a phase transfer catalyst, benzyltriethylammonium chloride (BTEAC),[2] in promoting the oxidation of some secondary alcohols to ketones

using ruthenium tetraoxide generated *in situ* by reaction of "active" ruthenium dioxide and periodate. The reported oxidation procedure was applied very successfully to carbohydrates partially protected with ether and acetal groups but containing a free secondary alcohol group, and to some non-carbohydrate secondary alcohols. Furthermore, the oxidation procedure was applicable to both small and large scale reactions. The broad goals of the studies described here were to determine the scope and limitations of the use of a phase transfer catalyst in promoting ruthenium tetraoxide oxidations of carbohydrate alcohols in general, and to further elaborate the role the phase transfer catalyst plays in the oxidations.

RESULTS AND DISCUSSION

"Active" Ruthenium Dioxide - Preparation and Function. In our earlier report[2] we described the use of "active" ruthenium dioxide[3] to generate the higher oxidation state(s) of ruthenium. Although there are many examples in the literature using "active" ruthenium dioxide, to the best of our knowledge, this material has never been thoroughly characterized nor has its role as it applies in oxidations been well defined.[3-6] The preparation of "active" ruthenium dioxide, as reported by Stevens and Bryant,[3] was modeled after a procedure described by Cotton and Wilkinson,[7] in which lower oxides of ruthenium were oxidized under alkaline conditions to higher oxides which in turn were reduced by alcohol. The following redox reactions[7] describe the behavior of ruthenium tetraoxide in alkali hydroxide solutions.

$$4RuO_4 + 4OH^- \text{------>} 4RuO_4^- + O_2 + 2H_2O$$
$$4RuO_4^- + 4OH^- \text{------>} 4RuO_4^{=} + O_2 + 2H_2O$$

Ruthenium tetraoxide (Ru^{VIII}) is first reduced to peruthenate (Ru^{VII}) and then to ruthenate (Ru^{VI}). It has, however, been recently determined from X-ray crystal studies that the ruthenate (Ru^{VI}) is not the tetrahedral $RuO_4^{=}$ but rather the trigonal bipyramidal *trans* $[Ru^{(VI)}O_3(OH)_2]^{-2}$.[8] Following the Stevens and Bryant procedure,[3] commercial ruthenium dioxide was fused with sodium chlorate and sodium hydroxide and "active" ruthenium dioxide was then precipitated from an aqueous, basic alcohol solution. The ruthenium tetraoxide produced in the fusion reaction would presumably be converted by comparable reactions to sodium ruthenate which when treated with alcohol would render the insoluble black "active" ruthenium dioxide. Thus, the fusion procedure gave a material which had gone through one oxidation-reduction cycle. It is noteworthy that Benyon and co-workers in 1968 reported that their active form of ruthenium dioxide had

been through an oxidation reduction cycle and furthermore that only hydrated ruthenium dioxide ($2H_2O$) was satisfactory for oxidations of this type.[9]

The "active" ruthenium dioxide was treated with periodate at neutral pH in water to give a pale yellow solution. Ultraviolet (UV) analysis of this solution gave a spectrum that closely matched a published spectrum of ruthenium tetraoxide in water.[10,11] The sample was then treated with potassium carbonate to make the solution slightly basic since the alcohol oxidations are carried out at basic pH. On treatment with carbonate, the solution changed from a pale yellow to an intense yellow color. The fine structure of the ruthenium tetraoxide spectrum (λ_{max} 380 nm) disappeared and was replaced by a single strong absorption at λ_{max} 385 nm. The spectrum from the sample superimposed a reported spectrum for the perruthenate anion, RuO_4^-.[10,11]

Based on this information we propose that during the oxidation RuO_4^- is carried into the organic layer by the phase transfer catalyst, where oxidation of the substrate occurs. During oxidation of the substrate, RuO_4^- anion is reduced to a form(s) which has not yet been determined. This reduced form is then reoxidized by periodate and the cycle is continued. Interestingly, a quaternary ammonium perruthenate tetrapropylammonium perruthenate (TPAP),[12] has recently become commercially available[13] for similar alcohol oxidations. This preformed quaternary ammonium perruthenate is an oxidant of the form we are suggesting is generated *in situ* using our system.

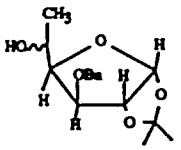
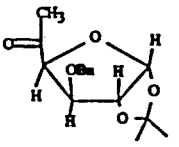
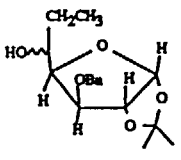
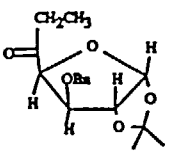
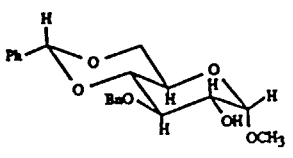
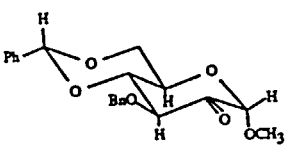
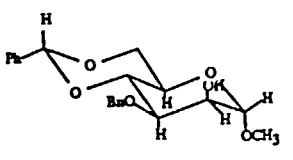
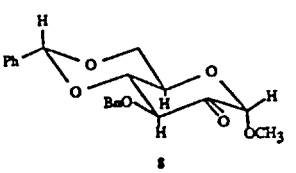
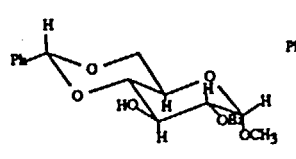
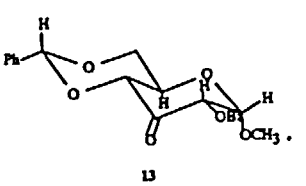
The role of the phase transfer catalyst now proposed differs from that which was suggested in our initial report.[2] There it was proposed that the increase in the rate of oxidation using a phase transfer catalyst might be due to the ease with which the lower oxidation state(s) of ruthenium was reoxidized by the quaternary ammonium periodate complex. This earlier proposed rational may at best play only a secondary role for oxidation rate enhancement in our system.

Oxidations of Carbohydrate Secondary Alcohols - The objective of this study was to further evaluate the oxidation procedure for carbohydrate secondary alcohol groups as found in both furanoid and pyranoid structures. The alcohol substrates, product ketones, reaction times, and product yields are given in the Table. Two epimeric mixtures of exocyclic secondary furanoid alcohols (**1,2** and **4,5**) and four cyclic secondary pyranoid alcohols (**7,9,10**, and **12**) were oxidation substrates.

The general oxidation procedure involved dissolving the alcohol in ethanol-free chloroform and stirring this solution at room temperature with an equal volume of water containing "active" ruthenium dioxide, a slight excess of sodium periodate, potassium carbonate, and 1-10 mol% of BTEAC. The reactions were quenched with 2-propanol.

Table

Oxidation of Carbohydrate 2° Alcohols

Substrate	Product	time, h	%yield
 1,2	 3	48 48	88 84
 4,5	 6	4	87
 7	 8	2	87
 9	 8	2	90
 12	 13	8	75

Potassium carbonate, employed to neutralize HCl formed from the hydrolysis of phosgene (produced in the air-oxidation of chloroform), also makes the aqueous solution basic enough for the formation of ruthenate and perruthenate ions.

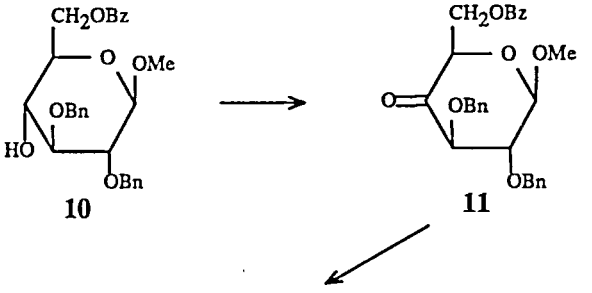
As an extension of our exocyclic furanoid secondary alcohol oxidations, mixtures of the deoxy sugars 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**1**) and 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**2**), were oxidized to 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (**3**) in high yield. Similarly, a mixture of 3-*O*-benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranose (**4**) and 3-*O*-benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-α-D-*gluco*-heptofuranose (**5**) was efficiently oxidized to the corresponding 5-ulose derivative, 3-*O*-benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-heptofuranos-5-ulose (**6**).

Oxidation of the mixture of **1** and **2** was carried out both on a large scale (24.5 g, 84% yield) and on a small scale (5.8 g, 88% yield). Oxidation of the mixture of **4** and **5** was carried out on a moderate scale (11.5 g, 87% yield). The alcohol mixtures (**1**,**2** and **4**,**5**) were prepared from an alkyl Grignard addition to 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose.[14]

Both equatorial and axial hydroxyl groups on pyranose rings were oxidized with comparable ease. Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-*arabino*-hexopyranos-2-ulose (**8**) was conveniently prepared from either methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**7**),[15] or from its C-2 epimer, methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**9**).[16] Surprisingly, oxidation of the *gluco* alcohol **7** gave the ketone **8** as the only product while the *manno* alcohol **9** gave a mixture of **8** and its hydrate. This latter mixture was clearly evident from its ^{1}H NMR spectrum which included two anomeric proton signals (5.68 and 5.61 ppm). The mixture was converted to the single ketone **8** by dehydration through azeotropic distillation with toluene, followed by drying *in vacuo*. These and previous results[2] clearly establish that the oxidation is generally applicable to carbohydrates containing a free secondary alcohol group but otherwise protected with ether and/or acetal groups.

Oxidation of a carbohydrate containing an ester group was found to be subject to side reactions which were in part dictated by the structure of the product ketone. Oxidation of methyl 6-*O*-benzoyl-2,3-di-*O*-benzyl-β-D-glucopyranoside (**10**)[17] was complete in 2 h giving a single component (TLC). However, workup of the reaction mixture gave an oil whose ^{1}H NMR spectrum showed more than one anomeric doublet. The TLC of the product after workup showed streaking beginning at the origin, suggesting that the product (**11**) was decomposing. The product upon standing decomposed to a dark colored material plus crystals that were readily separated and identified as benzoic acid. It

was concluded that the putative ketone **11** underwent β-elimination of the 6-*O*-benzoyloxy group to an α,β-unsaturated ketone which in turn gave further degradation products.



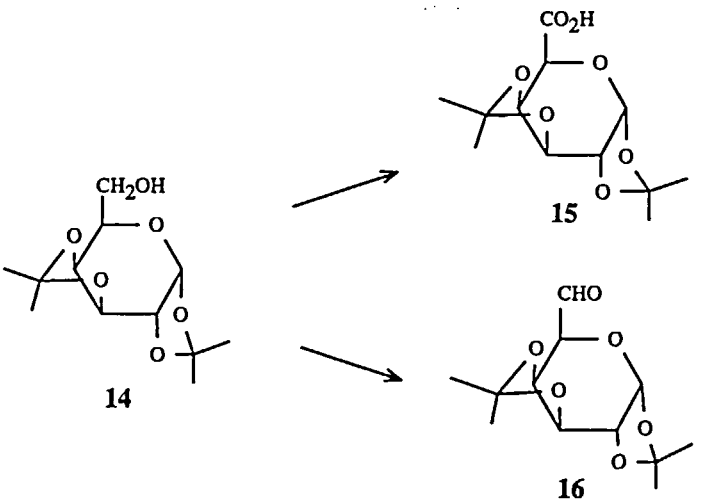
Since it was noted that prolonged exposure of the starting alcohol **10** to the alkaline reaction conditions of the oxidizing medium, even in the absence of oxidizing agent, served to hydrolyze the 6-*O*-benzoyl group, the oxidation was repeated with sodium hydrogen carbonate in place of the more strongly basic potassium carbonate. The results were essentially the same with both reactions, suggesting that the principal problem was in the instability of the product.

Facile elimination of a benzoyloxy group on a carbon beta to a carbonyl function has been observed. For example, methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside eliminated benzoic acid to give 2(S)-methoxy-4-benzoyloxy-6-(R)-benzoyloxymethyl-5,6-dihydro-2*H*-pyran-5-one when it was oxidized under standard conditions with DMSO-Ac_2O.[18]

Oxidation of partially ester protected pyranoside secondary alcohols should occur with minimal complication if the ester functions are not positioned to undergo β-elimination in the product ketone. Indeed, oxidation of methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**12**) using the phase transfer catalyst method gave methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-*ribo*-hexopyranosid-3-ulose (**13**) without complication (75 % yield).

Oxidation of a Carbohydrate Primary Alcohol- The goal of this part of the study was to determine if our oxidation system could be used for selective oxidation of a 1° alcohol group on a carbohydrate to either an aldehyde or carboxylic acid function. 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (**14**) was chosen as the model carbohydrate for this study.

Initial oxidations of **14** were designed to give the carboxylic acid 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranuronic acid (**15**).[19] Ultimately three different sets of reaction conditions were employed, the standard oxidation procedure and two modified procedures. Use of the standard oxidation procedure gave **15** in 75% yield after a reaction time of 70 h. However, when acetonitrile was included in the reaction mixture, oxidation was complete in 43 h with a 63% yield. The rationale to include acetonitrile in the oxidizing medium was based upon a report by Sharpless et al. that acetonitrile facilitates ruthenium tetraoxide oxidations that yield carboxylic acids.[20] When CH_2Cl_2 and acetonitrile were used in combination, a 78% yield of **15** was obtained after a reaction time of 40 h. Using these later conditions the oxidation was scaled up, (52.0 g **14**, 5 days, 65% yield) but required a silica gel column chromatography step to isolate the pure acid **15**. Although the conversion of **14** to **15** was optimized using CH_2Cl_2 as the solvent, we recommend $CHCl_3$ as the solvent of choice. We have found that



14 **15** **16**

reactions often occur in an uncontrolled manner in CH_2Cl_2 but do not occur in CCl_4. A recent Polish patent describes the phase-transfer oxidation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose to 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose hydrate with RuO_4 in CCl_4 in high yield in 20 min.[21] We have tried to reproduce this result several times, but without success.

Oxidation of **14** to the aldehyde 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**16**) was carried out using; a stoichiometric amount of IO_4^- (relative to the alcohol **14**), ethanol-free choloroform containing no acetonitrile, and a reaction time of 30 h. Aldehyde **16** was obtained in 57% yield after silica gel column chromatographic purification. Overall, the reaction is difficult to control since over-oxidation to the carboxylic acid **15** unavoidably occurs.

Conclusions and Recommendations

1. The method was found to be generally applicable for oxidation of secondary alcohols to ketones in appropriately protected furanoid and pyranoid molecules. Ether and acetal protecting groups are particularly well suited to the oxidation conditions.

2. Oxidation of a partially protected monosacccharide containing a single benzoate function not positioned to undergo facile β-elimination proceeded without complication.

3. Oxidation rate enhancement in the presence of a quaternary ammonium phase transfer catalyst is thought to result from transfer of perruthenate ion, formed under the basic reaction conditions, from the aqueous phase to the organic phase.

4. Alcohol free chloroform is a very good solvent for these oxidations. Use of methylene chloride as a solvent is not recommended since it is subject to oxidation.

5. Results from the oxidation of a primary alcohol (**14**) to either an aldehyde (**16**) or acid (**15**) were only moderately successful. Oxidation to the acid on a small scale (1-10 g) may provide a useful alternative to other available procedures.

6. Although only one phase transfer catalyst (BTEAC) was used in this study, other catalysts may offer specific advantages and can be easily incorporated into the experimental procedure.

7. The ruthenium oxide recovered after the workup procedure has good activity and can be used in further oxidations.

8. "Active" ruthenium dioxide is best stored in the presence of moisture in order to maintain its highly reactive state.

Experimental

General Procedures. All reagents were analytical grade and were used without further purification. RuO_2 is taken to mean "active" ruthenium dioxide as prepared according to the method of Stevens and Bryant.[3] Ethanol-free chloroform was prepared

by shaking with an equal volume of concd H_2SO_4, washing with H_2O, distilling from P_2O_5 and storing under N_2 until used. This reagent is best used immediately since in the absence of a stabilizer it decomposes on standing to give phosgene and HCl. All solvents were evaporated under diminished pressure (H_2O aspiration) at < 40 °C. Melting points (mp) were determined on a Fisher-Johns melting point apparatus and are reported uncorrected. Thin-layer chromatography (TLC) was performed on precoated 250-μm silica gel GF glass plates from Analtech, Inc. Chromatograms were visualized by spraying with a 0.1 M 2,4-dinitrophenylhydrazine solution in 1:1 95% EtOH-H_3PO_4 or concd H_2SO_4 followed by heating. Infrared (IR) spectra were recorded on a Beckman Aculab spectrometer and ^1H NMR spectra were recorded at 300 MHz (Nicolet Fourier Transform Spectrometer) in $CDCl_3$ with resonances reported downfield from Me_4Si. All reaction mixtures were stirred magnetically unless otherwise stated. Carbon and hydrogen elemental analyses were performed by Atlantic Microlabs, P. O. Box 80569, Atlanta, GA 30366.

3-*O*-Benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (3). A mixture of 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**1**) and 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**2**, 5.8 g, 20 mmol),[14] was dissolved in EtOH-free $CHCl_3$ (25 mL) and the solution stirred vigorously with H_2O (25 mL), BTEAC (6 mol%, 0.23 g, 1 mmol), $NaIO_4$ (5.3 g, 25 mmol), RuO_2 (50 mg), and K_2CO_3 (0.75 g). The reaction mixture was stirred for 48 h at which time TLC (1:1 Et_2O-tol) showed complete conversion of **1** and **2** to **3**. 2-Propanol (5 mL) was added to consume excess $NaIO_4$ and RuO_4 and the reaction mixture was filtered through celite. The organic layer was separated, dried ($MgSO_4$), and concentrated to give chromatographically pure **3** as an oil which crystallized on standing overnight: 5.1 g (17.5 mmol, 88% yield); mp 55-56 °C (lit.[14] 55-56 °C); IR 1700 cm^{-1} (C=O), no OH stretching band.

This reaction was then repeated on a larger scale: alcohols **1** and **2** (24.5 g, 83.6 mmol), BTEAC (5 mol%, 0.92 g), RuO_2 (200 mg), $NaIO_4$ (21.4 g 100 mmol), K_2CO_3 (3.0 g), and t = 48 h; yield = 84% (20.5 g, 70.4 mmol).

3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-heptofuranos-5-ulose (6). A mixture of the alcohols 3-*O*-benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranose (**4**) and 3-*O*-benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-α-D-*gluco*-heptofuranose (**5**, 11.5 g, 37.5 mmol)[14] was dissolved in EtOH-free $CHCl_3$ (50 mL) and the solution stirred vigorously with H_2O (50 mL), BTEAC (10 mol%, 0.855 g), RuO_2 (100 mg), $NaIO_4$ (10.7 g, 50 mmol) and K_2CO_3 (1.5 g). The reaction mixture was stirred for 4 h at which time TLC (1:1 Et_2O-tol) showed complete conversion of **4** and **5** to **6**. Workup as for **3** gave chromatographically pure **6** as a syrup: (11.5 g, 37.5 mmol, 87%); IR (neat)

1700 cm^{-1} (C=O), no OH stretching band. The ^1H NMR spectrum was consistent with the reported spectrum.[14]

Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-α-D-*arabino*-hexopyranos-2-ulose (8).

a. Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[15] (**7**, 300 mg) was dissolved in EtOH-free $CHCl_3$ (5 mL) and the solution stirred vigorously with H_2O (5 mL), BTEAC (50 mg), $NaIO_4$ (1 eq, 320 mg), and K_2CO_3 (50 mg). TLC (1:1 Et_2O-tol) showed complete conversion of **7** to **8** in 2 h. Usual workup gave white crystalline **8** after decolorization with Norit: (261 mg, 87%); mp 145-147 °C; IR 1720 cm^{-1} (C=O), no OH stretching band; $[\alpha]_D^{23}$ +11.5 (*c* 4.96, acetone); ^1H NMR ($CDCl_3$) δ 3.46 (s, 3H, OCH_3), 3.84 (dd, 1H, H-4), 4.20 (m, 1H, H-5), 4.38 (dd, 1H, H-6 eq), 4.53 (d, 1H, H-3, $J_{3,4}$ = 10.5 Hz), 4.75 (s, 1H, H-1), 4.93, 4.74 (AB quartet, 2H, CH_2Ph), 5.56 (s, 1H, PhCH), and 7.2-7.6 ppm (m, 10H, $PhCH_2$ and PhCH).

Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99. Found: C, 68.17; H, 6.04.

b. A solution of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside[16] (**9**, 1.5 g, 4.16 mmol) in EtOH-free $CHCl_3$ (15 mL) was stirred with H_2O (15 mL), $NaIO_4$ (963 mg, 4.5 mmol), BTEAC (50 mg), K_2CO_3 (50 mg), and RuO_2 (50 mg). Usual workup after 2 h followed by decolorization with Norit gave a crystalline mixture of **8** and its hydrate **8a** (1.34 g, 3.73 mmol, 90%). The mixture of **8** and **8a** was dissolved in toluene (10 mL) and concentrated to dryness at 50 °C three times. This procedure gave pure **8**; mmp with **8** prepared as above 143-145 °C. ^1H NMR spectrum was identical to that from a.

Methyl 6-*O*-Benzoyl-2,3-di-*O*-benzyl-β-D-*xylo*-hexopyranos-4-ulose (11) Attempted Preparation. Crystalline methyl 6-*O*-benzoyl-2,3-di-*O*-benzyl-β-D-glucopyranoside[17] (**10**, 480 mg, 1 mmol) was dissolved in EtOH-free $CHCl_3$ (10 mL) and the solution stirred vigorously with H_2O (10 mL), BTEAC (50 mg), $NaIO_4$ (235 mg, 1.1 mmol), RuO_2 (50 mg), and K_2CO_3 (50mg). Complete conversion of **10** to a higher running single product (considered to be **11**) in 2 h was shown by a single spot on TLC (1:1 Et_2O-tol). Usual workup followed by Norit decolorization yielded a syrup which gave multiple spots on TLC: (288 mg, 60%). No satisfactory analysis on the syrup could be obtained since the syrup underwent extensive decomposition during workup. When the syrup was left standing, a crystalline material formed which was identified as benzoic acid: mp 121-122 °C (lit.[22] mp 122.4 °C).

Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-α-D-*ribo*-hexopyranosid-3-ulose (13). Methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**12**, 358 mg, 1.0 mmol) prepared according to the procedure of Collins et al.,[23] was dissolved in EtOH-free $CHCl_3$ (15 mL). The solution was stirred vigorously 8 h with H_2O (5 mL), BTEAC (50

mg), $NaIO_4$ (423 mg, 2.0 mmol), RuO_2 (50 mg), and K_2CO_3 (10 mg). The mixture was continously stirred until TLC (1:1 Et_2O-tol) showed complete conversion of **12** to **13**. 2-Propanol was added to consume excess $NaIO_4$ and RuO_4 and the reaction mixture was filtered through celite. The organic layer was separated, dried ($MgSO_4$), and concentrated to give a solid product which was passed through a short column of silica gel (1:1 Et_2O-tol) yielding **13** (267 mg, 75 % yield): mp 193-195 °C (lit.[23] 198-199 °C); ^1H NMR ($CDCl_3$) δ 8.10 - 7.15 (10H, aromatic), 5.56 (dd, 1H, H-2, $J_{1,2}$ = 4.22 Hz, $J_{2,4}$ = 1.1 Hz), 5.53 (s, 1H, PHCH), 5.28 (d, 1H, H-1, $J_{1,2}$ = 4.22 Hz), 4.33-4.40 (m, 2H, overlapping H-6eq & H-4), 4.12 (m, 1H, H-5), 3.91 (ψt, 1H, H-6ax, $J_{6ax,6eq}$ = 10.3 Hz, $J_{6ax,5}$ = 10.2 Hz), and 3.43 ppm (s. 3H, OMe).

***1,2:3,4-Di-O-Isopropylidene-α-D-galactopyranuronic acid* (15).**

a. 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (**14**,[24] 424.4 mg, 1,63 mmol) was dissolved in EtOH-free $CHCl_3$ (10 mL) and the solution stirred vigorously with H_2O (10 mL), RuO_2 (50 mg), and BTEAC (50 mg). Stirring was continued for 70 h at which time TLC (1:1 acetone-tol) showed complete conversion of **14** to **15**. The reaction was quenched by the addition of 2-propanol and made slightly acidic with 6N H_2SO_4. The reaction mixture was filtered through celite and the organic layer was separated, dried ($MgSO_4$), and concentrated to give crystalline **15** (326.2 mg, 1.2 mmol, 75%): mp 155-157 °C (lit.[19] mp 157-159 °C); IR 3100 cm^{-1} (broad OH), 1750 cm^{-1} (C=O).

b. The preceding reaction was repeated on a larger scale and included acetonitrile: **14** (5.2 g, 20 mmol); $CHCl_3$ (50 mL), H_2O (50 mL), $NaIO_4$ (6.4 g, 30 mmol), BTEAC (50 mg), K_2CO_3 (750 mg), RuO_2 (100 mg) and CH_3CN (10 mL); t = 43 h, (3.5 g, 63% yield).

c. CH_2Cl_2 as the solvent: **14** (5.2 g, 20 mmol), CH_2Cl_2 (50 mL), H_2O (50 mL), $NaIO_4$ (6.4 g, 30 mmol), BTEAC (50 mg), K_2CO_3 (750 mg), RuO_2 (100 mg) and CH_3CN (10 mL); t = 40 h, (4.3 g, 78 % yield)

d. The reaction as described in c was repeated except on a larger scale: **14** (52 g, 0.2 mol), CH_2Cl_2 (350 mL), H_2O (350 mL), $NaIO_4$ (64 g, 0.3 mol), BTEAC (250 mg), K_2CO_3 (3.75 g), RuO_2 (250 mg), and CH_3CN (15 mL); t = 5 days, (35.5 g, 65% after column chromatography with silica gel 60, eluent 1:1 $CHCl_3$-Et_2O).

1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (16). A solution of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**14**,[24] 26.0 g, 0.1 mol) in EtOH-free $CHCl_3$ (250 mL) was mechanically stirred with H_2O (250 mL), $NaIO_4$ (25.7 g, 0.12 mmol), BTEAC (0.1 mmol, 22.8 mg, 15 mol%); K_2CO_3 (2.5 g) and RuO_2 (500 mg). TLC at 30 h showed conversion of **14** to **16** with some acid **15** appearing at the origin. Both of these compared favorably with authentic materials on TLC. Usual workup after

30 h gave crude **16** (16.4 g, 63%) containing some carboxylic acid **15**. Column chromatography over silica gel using $CHCl_3$-Et_2O (1:1) as the eluent gave syrupy **16** (14.8 g, 57%); IR 1725 cm^{-1} (C=O), small 3100 cm^{-1} (OH). The ^1H NMR spectrum was consistent with the reported spectrum.[25]

REFERENCES AND FOOTNOTES

1. Taken in part from the Ph.D. dissertation of P. E. Morris, Jr., University of Alabama at Birmingham, Birmingham, Alabama, 1988.
2. P. E. Morris, Jr. and D. E. Kiely, *J. Org. Chem.*, **52**, 1149 (1987).
3. C. L. Stevens and C. P. Bryant, *Methods Carbohydr. Chem.*, **6**, 337 (1972).
4. D. C. Baker, D. Horton, C. G. Tindall, Jr., *Methods Carbohydr. Chem.*, **6**, 337 (1972).
5. J. L Courtney in *Organic Syntheses by Oxidation With Metal Compounds*, W. J. Mijs and C. R. H. I de Jonge, Eds.; Plenum Press: New York and London, 1986, p 445.
6. J. L. Courtney and K. F. Swansbourough, *Rev. Pure Appl. Chem.*, **22**, 47 (1972).
7. F. A. Cotton and G. Wilkinson in *Advanced Inorganic Chemistry*, 2nd ed.; John Wiley and Sons, Inc.: New York, N. Y., 1966, p 915. See also the above 4th ed., 1980, p 1005; 5th ed., 1988, p 881.
8. M. O. Elout, W. G. Haijie and M. J. A. Masskant, *Inorg. Chem.*, **27**, 610 (1988).
9. P. J. Benyon, P. M. Collins, D. Gardiner, W. G. Overend, *Carbohydr. Res.*, *6*, 431 (1968).
10. E. A. Seddon and K. R. Seddon in *The Chemistry of Ruthenium*, R. J. H. Clark, Ed.; Elsevier Press: Amsterdam, 1984, p 58.
11. R. E. Connick and C. R. Hurley, *J. Am. Chem. Soc.*, **74**, 5012 (1952).
12. W. P. Griffith, S. V. Ley, G. P. Whitcombe, and A. D. White, *J. Chem. Soc., Chem. Comm.*, 1625 (1987).
13. Aldrich Chemical Company, Milwaukee, Wisconsin, U.S.A.
14. D. E. Kiely, H. Walls, Jr., and R. L. Black, *Carbohydr. Res.*, **31**, 387 (1973).
15. T. Ogawa and T. Kaburgi, *Carbohydr. Res.*, **103**, 53 (1982).
16. A Lipták, I. Czégény, J. Harangi, and P Nánási, *Carbohydr. Res.*, **73**, 327 (1970).
17. Y. Ittah and C. P. J. Glaudemans, *Carbohydr. Res.*, **95**, 189 (1981).
18. F. W. Lichtenthaler, *Methods Carbohydr. Chem.*, *6*, 348 (1972)

19. P. Kóvac, *J. Carbohydr., Nucleosides, Nucleotides*, **1**, 183 (1974) and references therein.

20. P. H. J. Carlson, T. Katsuki, V. S. Martin, and K. B. Sharpless, *J. Org. Chem.*, **46**, 3936 (1981).

21. T. Kiersznicki, B. Karuga, and W. Szeja, Pol. Pat. 121419 (1982), *Chem. Abs.*, **103**, 71612g (1985).

22. *Langes Handbook of Chemistry*, Twelfth ed.; J. A. Dean, Ed.; McGraw-Hill: New York, N.Y., 1979, p 7-96.

23. P. M. Collins, D. Gardiner, S. Kumar, and W. G. Overend, *J. Chem. Soc., Perkins Trans. 1*, 2597 (1972).

24. Syrupy **14** was purified via its crystalline 6-O-acetate according to the method of H. Ohle and G. Berend, *Ber.*, **58**, 2585 (1925).

25. D. Horton, M. Nakadate, and J. M. J. Tronchet, *Carbohydr. Res.*, **7**, 56 (1968).