

The Reaction of Superoxide with Carbohydrate Sulphonates

Youngsook Shin and Jeong E. Nam Shin*

Department of Chemistry, Soong Sil University, Seoul 156-743

Received August 17, 1992

The reaction between methyl 2,3-di-O-benzyl-4,6-di-O-mesyl- α -D-glucopyranoside (**1b**) and potassium superoxide resulted in hydrolysis, and gave methyl 2,3-di-O-benzyl- α -D-glucopyranoside (**1**) as a sole product. When the reaction was performed with a vicinal dimesylate, methyl 4,6-O-benzylidene-2,3-di-O-mesyl- α -D-altropyranoside (**4b**), again the hydrolysis product, methyl 4,6-O-benzylidene- α -D-altropyranoside (**4**) was obtained. However, the reaction of potassium superoxide with another vicinal dimesylate, methyl 4,6-O-benzylidene-2,3-di-O-mesyl- α -D-glucopyranoside (**3b**), nucleophilic displacement took place to afford methyl 4,6-O-benzylidene- α -D-altropyranoside (**4**). Apparently different results from two trans vicinal dimesylates, **3b** and **4b** are explained by the transient formation of epoxides, methyl 2,3-anhydro-4,6-O-benzylidene- α -D-altropyranoside (**8**) and methyl 2,3-anhydro-4,6-O-benzylidene- α -D-mannopyranoside (**9**) by KO_2 . The reaction between the allo epoxide **8** and KO_2 gave altro **4**. The manno epoxide **9** also afforded altro **4** as the major product. Facile epoxide formation by the reaction of a vicinal dimesylate and superoxide was also observed with 3-O-benzyl-1,2-O-isopropylidene-5,6-di-O-mesyl- α -D-glucofuranose : 5,6-anhydro-3-O-benzyl-1,2-O-isopropylidene- β -L-idofuranose was obtained.

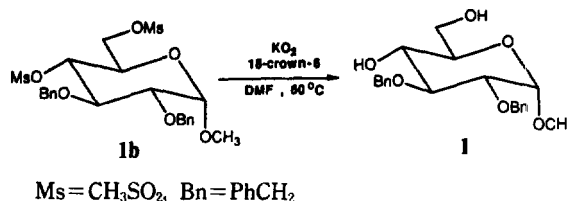
Introduction

Potassium superoxide (KO_2) and 18-crown-6 complex is reported to be an effective oxygen nucleophile compared with OH^- and RCOO^- .^{1,2} Development of a superior $\text{S}_{\text{N}}2$ delivery oxygen nucleophile to conventional reactants will allow for an easy access to valuable compounds of multiple chiral centers via stereoselective maneuver of abundant natural carbohydrates. In examining the possibility of $\text{S}_{\text{N}}2$ reaction between superoxide and carbohydrate sulphonates, methyl 2,3-di-O-benzyl-4,6-di-O-mesyl- α -D-glucopyranoside (**1b**) and methyl 4,6-O-benzylidene-2,3-di-O-mesyl- α -D-glucopyranoside (**3b**) were employed. Here, the former is known to be sensitive to $\text{S}_{\text{N}}2$ reactions while the latter is sluggish due to electronic and steric effects.³ It was anticipated that the use of superoxide to displace the mesyloxy substituents of the former (**1b**), by analogy with $\text{S}_{\text{N}}2$ displacement, would yield methyl 2,3-di-O-benzyl- α -D-galactopyranoside (**2**) easily, and that even superoxide would have difficulty with displacing the 2,3-mesyloxy groups of the latter (**3b**) and giving methyl 4,6-O-benzylidene- α -D-altropyranoside (**4**).^{3,4}

Instead, the reaction between the latter (**3b**) and superoxide produced the inverted product, methyl 4,6-O-benzylidene- α -D-altropyranoside (**4**), while the reaction of the former (**1b**) and superoxide gave the hydrolyzed, desulphonylated, retention product, methyl 2,3-di-O-benzyl- α -D-glucopyranoside (**1**). These, and related results will be discussed in this paper.

Results and Discussion

When methyl 2,3-di-O-benzyl-4,6-di-O-mesyl- α -D-glucopyranoside (**1b**) was subjected to reaction with potassium superoxide in DMF containing 18-crown-6 ether, a sole product was obtained and characterized as methyl 2,3-di-O-benzyl- α -D-glucopyranoside (**1**) (Scheme 1). The $^1\text{H-NMR}$ spectrum of **1** was identical to that of an authentic sample of **1**, while there was no indication that the $\text{S}_{\text{N}}2$ product, methyl 2,3-di-



Scheme 1.

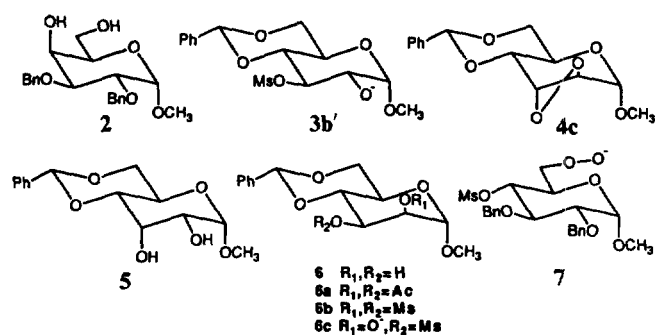


Figure 1.

O-benzyl- α -D-galactopyranoside (**2**) had been produced. With the retention of configuration at C-4, the hydrolysis product **1** is thought to be obtained from the attack of O_2^- on the sulfur atoms of mesyloxy groups of C-4 and C-6. This hydrolysis reaction appeared to be of value as a methodology of facile desulphonylation, since known methods to remove sulphonate groups often accompany other unwanted reactions such as elimination and reduction.^{6,7}

Interestingly, similar treatment of methyl 4,6-O-benzylidene-2,3-di-O-mesyl- α -D-glucopyranoside (**3b**) with superoxide produced methyl 4,6-O-benzylidene- α -D-altropyranoside (**4**) with inversion of configuration at C-2 and C-3. The present observation is contradictory to the comparative $\text{S}_{\text{N}}2$ reactivity of mesyloxy groups of **1b** and **3b** shown toward other nucleophiles.^{3,4} Possibility of the occurrence of concom-

itant hydrolysis and S_N2 reaction is excluded because of the absence of methyl 4,6-O-benzylidene- α -D-allopyranoside (**5**) or methyl 4,6-O-benzylidene- α -D-mannopyranoside (**6**) in the reaction mixture (Scheme 2, Figure 1).

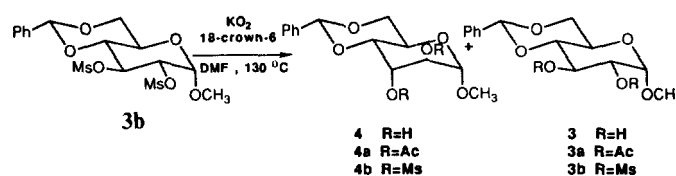
The substitution mechanism of superoxide with a monomesylate so far suggested is that the attack of O_2^- on an electrophilic carbon produces the inverted peroxide ion which is, then, reduced to the corresponding alcohol.^{1,2} The reaction of a dimesylate with superoxide is being believed to proceed to the formation of a monoperoxide ion by a preferential substitution of the more reactive mesyloxy group. The given peroxide ion then reacts intramolecularly with either the residual mesyloxy group, or a suitable hydrogen atom, resulting in the formation of a cyclic peroxide or a regiospecific elimination in each.^{2,3}

The same argument predicts the formation of monoperoxide ion **7** from the reaction of **1b** and superoxide. And **7** would give the inversion product **2** by possible intramolecular substitution at C-4. Furthermore, **3b** would give a peroxide ion (**6c**) of a rigid trans decalin system. **6c** would not allow for the formation of a new additional trans cyclic peroxide ring (**4c**) through an intramolecular substitution (Figure 1). As already mentioned, there was no indication of the formation of either **2** or **6c**. Hence the role of superoxide as a nucleophile may not be generalized in the reaction with carbohydrate sulphonates.

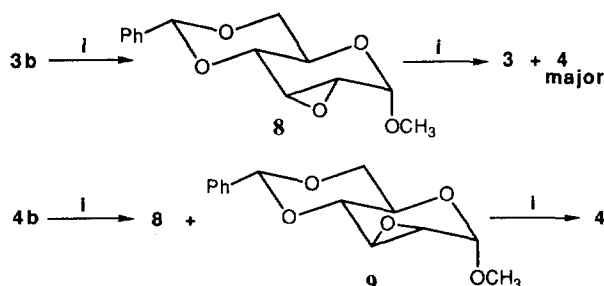
The reaction mixture of **3b** and superoxide was acetylated, purified, and then characterized by ^{13}C -NMR spectroscopy. The apparently pure product was found to be a mixture of two diastereomers, methyl 2,3-di-O-acetyl-4,6-O-benzylidene- α -D-allopyranoside (**4a**) and methyl 2,3-di-O-acetyl-4,6-O-benzylidene- α -D-glucopyranoside (**3a**) in about 3:1 ratio (Scheme 2). Their ^{13}C -NMR chemical shifts were identical to those of authentic samples of **4a** and **3a** (Table 1).⁵ This suggests the formation of an epoxide intermediate such as methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (**8**) and methyl 2,3-anhydro-4,6-O-benzylidene- α -D-mannopyranoside (**9**) by analogy with the conventional reaction of the 2,3-trans dimesylate **3b** with CH_3O^- .⁹ The epoxide, also **8** is thought to be formed by the intramolecular substitution of RO^- (**3b'**), which was liberated by the preferential attack of O_2^- on the 2-mesyloxy sulfur atom of **3b**. Close examination on tlc also exhibited the presence of allo epoxide intermediate **8** as the reaction of **3b** and superoxide proceeded. By analogy with epoxide ring opening by OH^- , nucleophilic attack of O_2^- on the epoxide **8** and the subsequent reduction provides the trans diaxial diol allo **4** as the major, and the trans diol gluco **3** as the minor in a 3:1 ratio.⁹ In fact, the same treatment of the authentic allo epoxide **8** with superoxide gave allo **4** and gluco **3** in a 3:1 ratio (Scheme 3).

More facile formation of epoxides was also observed in the reaction of superoxide with another trans dimesylate, methyl 4,6-O-benzylidene-2,3-di-O-mesyl- α -D-allopyranoside (**4b**). That is, methyl 2,3-anhydro-4,6-O-benzylidene- α -D-mannopyranoside (**9**) and methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (**8**) were obtained in a 3:1 ratio. When this mixture of anhydro sugars was further reacted with superoxide, allo **4** was obtained as the eventual major product (Scheme 3).

Support for the foregoing epoxide ring formation has also been furnished by the fact that 3-O-benzyl-1,2-O-isopropyl-

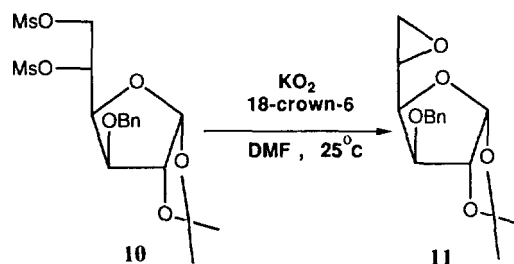


Scheme 2.



i. KO_2 -18-crown-6 in DMF, 130 °C

Scheme 3.



Scheme 4.

idene-5,6-di-O-mesyl- α -D-glucopyranoside (**10**), a terminal vicinal dimesylate, showed a facile reaction with superoxide and afforded a valuable synthetic intermediate, 5,6-anhydro-3-O-benzyl-1,2-O-isopropylidene- β -L-idofuranose (**11**) as the sole product (Scheme 4).¹⁰⁻¹² The 1H -NMR and ^{13}C -NMR spectra have been identical to those of the authentic sample synthesized by a known route (Table 1).

Although several products were formed in the reaction of superoxide with methyl 4,6-O-benzylidene-2,3-di-O-mesyl- α -D-mannopyranoside (**6b**), a rigid *cis*-vicinal dimesylate which can not give rise to epoxides **8** or **9**, allo **4** was not among those detected: the presence of hydrolysis products, methyl 4,6-O-benzylidene- α -D-mannopyranoside (**6**) and a monomesylate has been observed in 1H -NMR spectra.

In summary, superoxide and 18-crown-6 complex preferred to act as a base on carbohydrate sulphonates, and as an oxygen nucleophile on carbohydrate epoxides. The reagent hydrolyzed sulphonate **1b** and 1,2:5,6-di-O-isopropylidene-3-O-mesyl- α -D-glucopyranoside.¹³ Superoxide converted rigid vicinal trans 2,3-di-sulphonyloxy groups of **3b** and **4b** to trans 2,3-di-axial OHs of **4** through the formation of epoxide intermediates **8** and **9**. Superoxide also transformed a terminal vicinal dimesylate **10** to an inverted epoxide **11**. Thus, the reaction mechanism of superoxide varies with the electronic and steric environments of the sulphonyloxy groups of carbohydrate substrates. Superoxide and 18-crown-6 complex

Table 1. ^{13}C -NMR Data^a for the Compounds Obtained from the Reactions of Superoxide

Compound	C-1	C-2	C-3	C-4	C-5	C-6	CH ₃	AcetalC	CH ₂ Ph
3a	97.3	71.7	68.7	78.8	62.0	68.4	54.9	101.2	
4a	98.6	69.1	67.0	74.3	58.5	69.3	55.5	101.9	
8	96.9	50.5	53.8	74.8	61.6	69.4	55.7	102.4	
9	95.2	50.6	53.0	77.8	60.0	68.8	55.8	102.6	
11	105.4	82.7	82.4	82.0	50.1	43.1	26.3	71.9	111.9
							26.8		

^aIn CDCl₃. ^b ^{13}C data are assigned by the comparison with those in Ref 5. Assignments may be reversed.

Table 2. Reactions of Sulphonates with Superoxide and 18-Crown-6

Reactant	Product	KO ₂ (eq)	CE (eq)	Temp., °C	Reaction time, h	% Yield**
1b	1	8	2	60	24	30
3b	4, 3	7	1	130	24	39
8	4, 3	5	0.5	130	24	34
4b	9, 8	5	0.5	53	24	17
4b	9, 8, 4	5	0.5	130	48	39
6b	6+*	5	0.5	25	48	*
	monomesyl			130	5	*
10	11	6.5	0.5	25	72	35

*Unidentified. **Collection of pure fractions after column chromatography or crystalline product.

will provide for an efficient methodology in the carbohydrate syntheses through either the removal of sulphonyloxy groups or the formation of epoxide intermediates.

Experimental

Materials and Methods

Solutions were usually evaporated below 50°C under diminished pressure. DMF was dried and stored over molecular sieves (Type 4A). Potassium superoxide and 18-crown-6 were purchased from Sigma Chemical Co. Silica Gel for column chromatography (60, 70-230 mesh) was obtained from Merck (Art 7734). ^1H -NMR and ^{13}C -NMR spectra were recorded with a Bruker AW-80 or a Varian VXR-200 spectrometer, using CDCl₃ as the solvent. Chemical shifts (δ) are reported with reference to tetramethylsilane. IR spectra were recorded for films on KBr pellets with a Perkin-Elmer 1310 spectrometer. Tlc was conducted on plates coated with a 0.2 mm layer of Silica gel 60F₂₅₄ (Merck); the components were located by spraying the plate with 5% sulfuric acid and heating.

General Procedure

All the reactions were carried out under dry nitrogen atmosphere. A suspension of each carbohydrate sulphonate, potassium superoxide and 18-crown-6 in dry DMF was vigorously stirred under the given condition (Table 2). When the reaction was complete on tlcs, the reaction mixture was filtered on a sintered glass. The filtrate was stirred with a few drops of water to destroy the residual superoxide, and then evaporated to dryness under diminished pressure (50°C/30 mmHg). The solid was purified on a column of silica gel to remove crown ether and potassium salts by gradient elution starting from less polar solvents than those used on tlcs. Reactions were confirmed by the disappearance

of the peaks of 3.0 ppm for CH₃SO₂- in ^1H -NMR spectra, and 1350 cm⁻¹ for -SO₂CH₃ in IR spectra of the products. Characterization was done by the comparison of their ^1H -NMR and ^{13}C -NMR spectra with those of the authentic compounds. For compounds having OH groups, acetylated derivatives were used for the spectral characterization.

Methyl 2,3-di-O-benzyl- α -D-glucopyranoside (1)

(0.079 g) was obtained from 1b (0.41 g); R_f 0.52 for 1b and 0.17 for 1 (toluene : ethyl acetate, 5 : 3); mp. 89-90°C (lit¹⁴, mp. 79-80°C); ^1H -NMR (CDCl₃) δ 2.45 (br s, 2H, OH), 3.20-3.82 (m, 9H, OCH₃, H_{2,3,4,5,6}'), 4.50-5.10 (m, 3H, H₁, CH₂Ph), 7.20-7.45 (m, 10H, 2CH₂Ph).

Methyl 4,6-O-benzylidene- α -D-altropyranoside (4) and Methyl 4,6-O-benzylidene- α -D-glucopyranoside (3)

(0.085 g) were obtained from 3b (0.34 g); R_f 0.76 for 3b, 0.50 for 4 and 0.39 for 3 (toluene : ethyl acetate : ethanol, 5 : 5 : 2).

The same mixture of 4 and 3 (0.2 g) was also prepared from allo epoxide 8 (0.5 g); R_f 0.76 for 8, 0.51 for 4 and 0.41 for 3 (toluene : ethyl acetate : ethanol, 5 : 5 : 2); ^{13}C -NMR spectrum of the acetylated derivative showed the presence of 4a and 3a in a 3 : 1 ratio (Table 1).

Methyl 2,3-anhydro-4,6-O-benzylidene- α -D-mannopyranoside (9) and methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (8). 3 mg and 1 mg respectively, were obtained from 4b (37 mg) at 53°C; R_f 0.46 for 4b, 0.76 for 9, and 0.53 for 8 (toluene : ethyl acetate, 5 : 3). 4b (0.18 g) at 130°C gave 9 (30 mg), 8, and 4 (13 mg); mp. for 9 142-143°C (lit¹⁵, mp. 145-147°C); R_f 0.46 for 4b, 0.76 for 9, 0.53 for 8, and 0.11 for 4 (toluene : ethyl acetate, 5 : 3); ^1H -NMR and ^{13}C -NMR of 9 were identical to those of the authentic 9 which was synthesized by a known route (Table 2).

Reaction of methyl 4,6-O-benzylidene-2,3-di-O-me-

syl- α -D-mannopyranoside (6b) with superoxide was carried out in the same manner as described above. **6b** (0.13 g, 0.29 mmole) produced a mixture (0.033 g) of four compounds, which are not characterized yet; R_f 0.84 for **6b**, 0.66, 0.41 and 0.34 (toluene : ethyl acetate : ethanol, 5 : 5 : 2); $^1\text{H-NMR}$ of compounds having R_f 0.41 and 0.34 indicated hydrolysis had occurred.

5,6-anhydro-3-O-benzyl-1,2-O-isopropylidene- β -L-idofuranose (11) (0.046 g) was obtained from 3-O-benzyl-1,2-O-isopropylidene-5,6-di-O-mesyl- α -D-glucofuranose (**10**) (0.21 g, 0.46 mmole); R_f 0.42 for **10**, 0.59 for **11** (toluene : ethyl acetate, 5 : 3); $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ of **11** were identical to those of the authentic **11** that was synthesized by a known method.¹² (Table 2)

Acknowledgement. This work was supported by Research Center for New Bio-Materials in Agriculture, Seoul National University-KOSEF and Academic Foundation of Soong Sil University.

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Bonding of Electron Deficient Thallium-Metal Cluster Compound

Sungkwon Kang

Department of Chemistry, College of Natural Sciences, Chungnam National University,
Taejeon 305-764. Received September 8, 1992

Molecular orbital calculations at the extended Hückel level have been carried out for an electron deficient cluster, $\text{Ti}_3(\text{FeL}_3)_2(\text{FeL}_4)_3^{-3}$, where $\text{L}=\text{CO}$ or H^- . The LUMO, $2a_2''$, is destabilized by the secondary interaction of the LUMO with $1a_2''$ on $(\text{FeL}_3)_2$ fragment. This is one of six skeletal bonding orbitals which are associated with Ti- FeL_3 bonds. Overlap population analysis has been applied to account for two kinds of Ti-Fe bonds. Replacement of the terminal C_3FeL_4 by the C_2FeL_4 units in cluster results in slight energy stabilization of the cluster.

Introduction

A large number of clusters with both main group atoms and transition metals have been prepared and structurally determined.^{1,2} It is possible to predict the cage geometries of these cluster compounds through a set of electron counting rules.^{2,3} The chemical bonding of the cluster compound of $[\text{Et}_4\text{N}]_6[\text{Ti}_6\text{Fe}_{10}(\text{CO})_{36}]$ (**1**), however, has not been clearly understood yet. From our previous X-ray diffraction study⁴, the inter-Thallium distances were 3.71-3.77 Å, which are in the range of very weak Ti-Ti interactions.⁵ In the preliminary calculations the Ti-Ti overlap population was only 0.025.⁴ Ti^I-Ti^I interaction for the various molecular and solid-state structures was studied by C. Janiak and R. Hoffmann.⁶

In this paper we discuss the analysis of molecular orbital

calculations of compound **1** at the semiempirical extended Hückel level. The simple approach is to consider a dimer of a model system $\text{Ti}_3(\text{FeL}_3)_2(\text{FeL}_4)_3^{-3}$ (**2**), where $\text{L}=\text{Two}$ electron donor of CO or H^- .

