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# A Mild Pummerer-Like Reaction of Carbohydrate-Based Selenoethers and Thioethers Involving Linear Ozonide Acetates as Putative Intermediates

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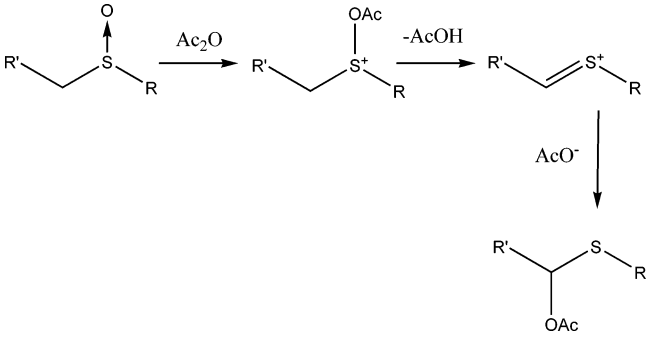
***Abstract:*** Pummerer-like rearrangements of carbohydrate-based heterocycles containing selenium and sulfur were investigated. To the best of our knowledge, this is the first report on the Pummerer rearrangement in selenoheterocycles. Ozonization of 1,4-anhydro-D-galactitol or 1,5-anhydroxylitol derivatives containing sulfur or selenium as the ring heteroatom gave unstable intermediates that were attributed to ozonides. These intermediates decomposed upon warming to give selenoxides or sulfoxides. Significantly, addition of acetic anhydride at low temperature to the ozonization reaction mixtures gave Pummerer-rearrangement products after warming to ambient temperature. However, when the isolated selenoxides or sulfoxides were treated with acetic anhydride, Pummerer rearrangement occurred but the sulfoxides required much higher reaction temperatures. The latter results are at variance with the former and are interpreted in terms of the rearrangement of the ozonide acetate intermediates in the former cases. To probe whether the rearrangement proceeded heterolytically via extrusion of singlet oxygen or homolytically via the generation of radical species, trapping experiments with rubrene and electron paramagnetic resonance (EPR) studies with the radical trap DMPO were performed. The results of these experiments are consistent with the intermediacy of radical species and suggest a new and milder synthetic method to generate Pummerer-type products.

## Introduction

The Pummerer reaction[1] represents an excellent strategy for introducing functionality α to heteroatoms. This reaction has been used extensively in the synthesis of functionalized heterocycles, and there are a plethora of natural products whose syntheses involve one or more Pummerer reactions (reviewed in ref 2). Also, in recent years, the "Pummerer reaction" has been extended to the syntheses of heterocycles containing silicon or nitrogen.[3] Nevertheless, the rearrangements of selenoxides have been elusive. The facile elimination of selenoxides adds to the difficulty of their study, thereby explaining the paucity of examples in the literature of Pummerer reactions involving selenoxides.[4]

Mechanistically, the Pummerer reaction[1] is traditionally known as the reaction of a sulfoxide with an acid anhydride[1,5]

***Scheme 1***




that results in oxidation at the α-carbon and yields an α-substituted sulfide (e.g., Scheme 1). This reaction is proposed to follow an elimination/addition mechanism.[6]

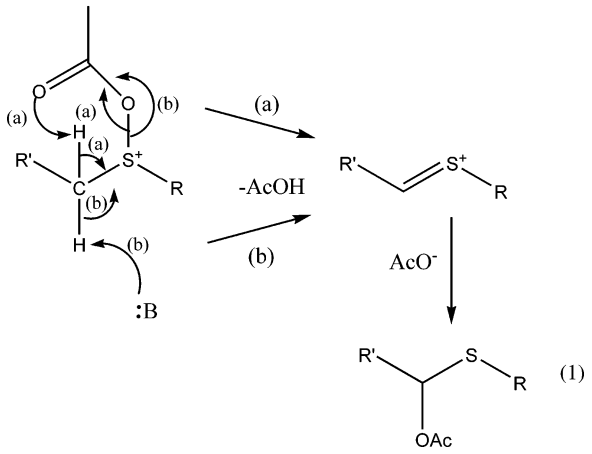
Whether the elimination proceeds in a concerted manner to form the thiacarbenium ion (eq 1) or in a stepwise fashion to first generate the ylide (eq 2) has not been firmly established. In addition, it is not known whether the elimination is intramolecular (pathway a) or intermolecular (pathway b) in both eqs 1 and 2.[6] However, labeling experiments have shown that internal transfer of the acetoxy group to the α- carbon is not the major reaction pathway.[6]

One way to address the aforementioned issue would be to study the regioselectivity of α-acetoxylation in asymmetric

(1) Pummerer, R. *Ber*. **1909**, *42*, 2275−2282.
(2) Bur, S. K.; Padwa, A. *Chem. Rev*. **2004**, *104*, 2401−2432.
(3) (a) Padwa, A. *Phosphorus, Sulfur Silicon Relat. Elem*. **1999**, *153*−*154*, 23−40. (b) Padwa, A.; Danca, D. M.; Ginn, J. D.; Lynch, S. M. *J. Braz. Chem. Soc*. **2001**, *12*, 571−585. (c) Padwa, A.; Bur, S. K.; Danca, D. M.; Ginn, J. D.; Lynch, S. M. *Synlett* **2002**, *6*, 851−862.
(4) (a) Hagiwara, H.; Kafuku, K.; Sakai, H.; Kirita, M.; Hoshi, T.; Suzuki, T.; Ando, M. *J. Chem. Soc., Perkin Trans. 1* **2000**, *16*, 2577−2578. (b) Okuma, K.; Kojima, K.; Koga, Y.; Shioji, K. *Heterocycles*. **2000**, *52*, 1021−1024. (c) Uneyama, K.; Maeda, K.; Tokunaga, Y.; Itano, N. *J. Org. Chem*. **1995**, *60*, 370−375. (d) Laitalainen, T.; Simonen, T.; Kivekas, R.; Klinga, M. *J. Chem. Soc., Perkin Trans. 1* **1983**, *2*, 33−40. (e) Nagao, Y.; Ochiai, M.; Kaneko, K.; Maeda, A.; Watanabe, K.; Fujita, E. *Tetrahedron Lett*. **1977**, *15*, 1345−1348. (f) Reich, H. J.; Shah, S. K. *J. Org. Chem*. **1977**, *42*, 1773−1776.
(5) Horner, L.; Kaiser, P. *Ann*. **1959**, *626*, 19−25.
(6) Johnson, C. R.; Phillips, W. G. *J. Am. Chem. Soc*. **1969**, *91*, 682−687.

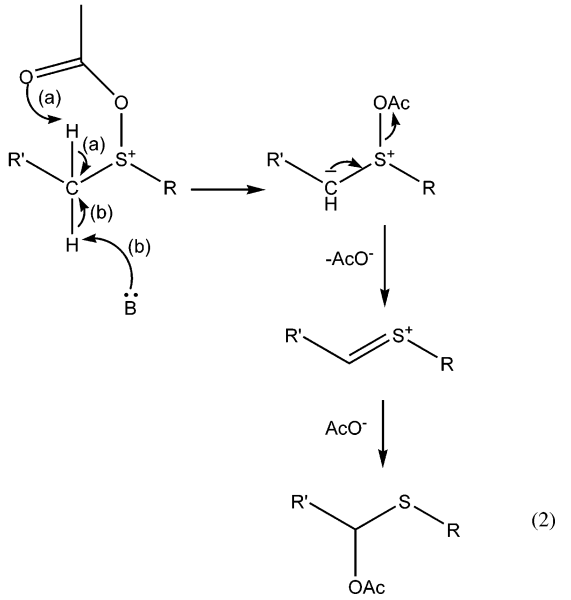
10.1021/ja0557029 CCC: $33.50 

**Concerted elimination**




(1)

**Formation of an ylide intermediate**




(2)

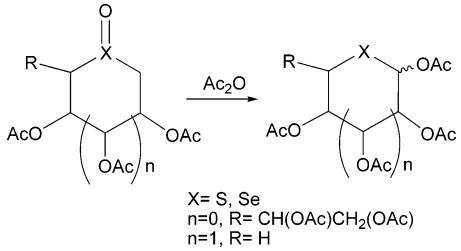
substrates. It is expected that in such substrates, proton removal from the more substituted α-carbon will lead to the more stable thiacarbenium ion **B**, while the more stable ylide **A** would be generated if the proton was abstracted from the least substituted α-carbon (Scheme 2).[6] The products resulting from either intermediate are different and can therefore be an indicator of the mechanism of the reaction.

Some studies have also suggested that the rate-determining step might be the abstraction of the α-proton,[7,8] and hence the acidity of this proton is also expected to play a crucial role in directing the regiochemistry of such rearrangement reactions.

A modified Pummerer reaction which makes use of trifluoroacetic anhydride (TFAA) instead of acetic anhydride has been reported to be milder,[9] the rearrangements of the sulfoxides proceeding at lower temperature and generally in higher yield.[9] TFAA has been shown to be particularly effective when relatively acidic α-protons are present.[6]

The carbohydrate community's interest in heteroatom analogues of sugars in which the ring oxygen has been replaced with sulfur or selenium is increasing. Such heteroanalogues could find interesting application in the synthesis of hydrolytically stable oligosaccharide and nucleoside mimics. Compounds containing thiosugars have been shown to exhibit a variety of properties ranging from glycosidase inhibitory activities[10] to antiviral and antitumor activities.[11] Many thiosugars with sulfur in the ring and bearing a functional group at C-1 have been synthesized,[12] but their seleno counterparts, on the other hand, are so rare that they are almost nonexistent.[13] Furthermore, the syntheses of some of the thio sugars are tedious and sometimes low-yielding, and alternative synthetic routes are therefore desirable.

***Scheme 3***




We envisioned that a possible strategy for a versatile synthesis of heterosugars might be the functionalization of anhydroalditols via the Pummerer rearrangement (Scheme 3). We note that the Pummerer reactions of carbohydrate sulfoxides,[14,15] including its application in the synthesis of thionucleosides,[16] have been reported. Most recently, Fujita et al.[16] have described their findings on the Pummerer reaction of thioanhydroalditols. However, the Pummerer rearrangement of selenoethers, particularly anhydroselenosugars, remains unprecedented. We thus embarked on such a study and describe herein our findings on the Pummerer rearrangement of anhydroseleno sugars and also describe a novel rearrangement of the corresponding ozonide acetates of seleno- and thioethers that furnishes the same

***Scheme 2***

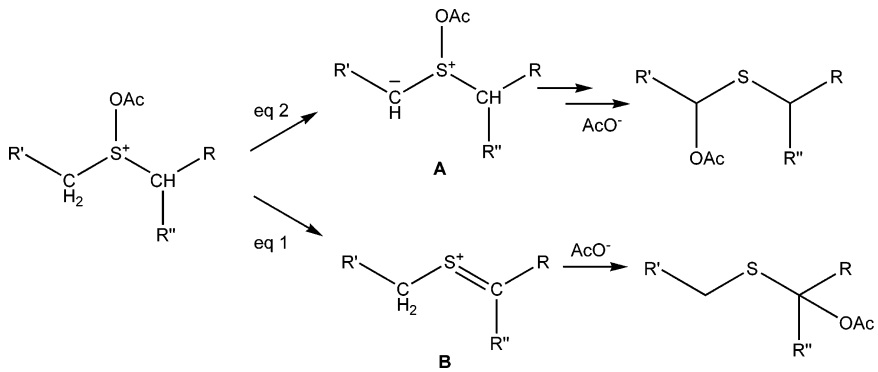
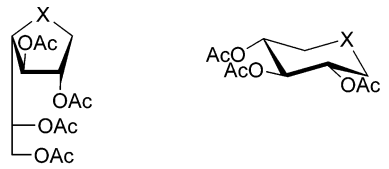


***Chart 1***



**1** X=S
**2** X=Se

**3** X=S
**4** X=Se

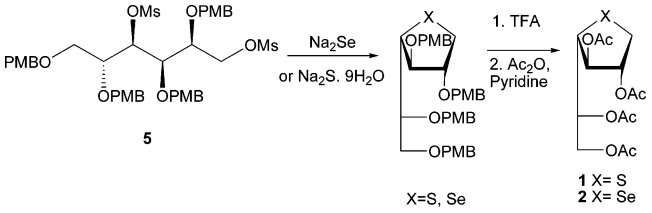
products by a milder and more facile route that might find general utility in the area of organic synthesis.

## Results and Discussion

While the focus of this paper is the study of the Pummerer rearrangement in selenoheterocycles, two other issues are also addressed, namely (a) the comparison in reactivity between the sulfoxides and selenoxides and (b) the regioselectivity of α-substitution in asymmetric substrates in the Pummerer rearrangement. The regiochemistry of substitution in asymmetric thioheterocycles has been investigated recently,[16] but the reactivity of the analogous selenoheterocycles has not been investigated to date. Compounds **1**−**4** (Chart 1) were chosen for study. We were motivated in our choice by two factors. The symmetric xylitol derivatives **3** and **4** were chosen because the regiochemistry of substitution at the α-carbon is not an issue, and they should therefore provide an opportunity to study the difference in reactivity between the corresponding sulfoxide and the selenoxide, while compounds **1** and **2** were chosen because they possess an α-substituent. Thus, the reactions of these four compounds should shed light on both the difference in reactivity between thio and seleno heterocycles and also the regioselectivity of the rearrangement in asymmetric compounds.

Compounds **3**[17] and **4**[18] were available from previous work in our laboratory. Compound **2** was obtained from the *p*-methoxybenzyl (PMB)-protected selenogalactitol,[19] while compound **1**[20] was synthesized in a similar fashion (Scheme 4) from the dimesylated intermediate **5** in good yields.

***Scheme 4***



**5**

X=S, Se

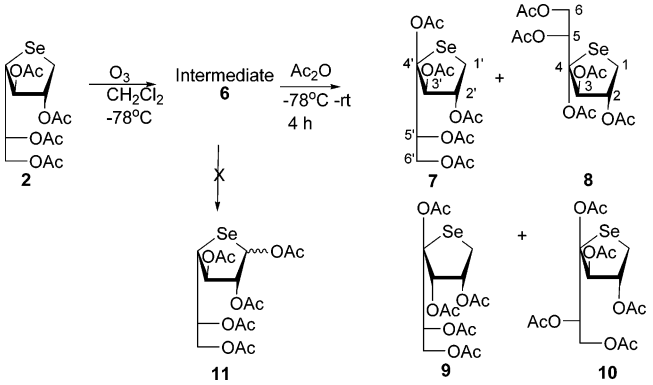
**1** X= S
**2** X= Se

Various methods of oxidation can be used to generate sulfoxides and selenoxides. In the present study our choice of oxidant was ozone, since ozonization of the respective sulfides and selenides proceeded with excellent yields and also because of the ease of processing of the reaction mixtures. During the course of our study, we discovered some very interesting behavior of the ozonization reaction mixtures when subjected to different conditions. Accordingly, we report these results in a separate section.

**Ozonization Followed by Direct Treatment with Acetic Anhydride.** Compounds **1**−**4** were oxidized by bubbling ozone through a solution of the anhydro sugars in $CH_2Cl_2$ at −78 °C until the solutions turned light blue. Nitrogen gas was then passed through the solutions for a few minutes to displace any residual ozone. The reaction mixtures of **1**−**4** were then treated directly with acetic anhydride at −78 °C and then allowed to warm to room temperature over a period of 3 to 4 h. The rearrangements of the selenosugars **2** and **4** were examined first.

Because the exact nature of the immediate oxidized products resulting from ozonization at −78 °C is still unresolved at this stage, we will refer to them as intermediates, appropriately numbered. Thus, reaction of the selenogalactitol intermediate **6** with acetic anhydride gave four products, after processing and purification by column chromatography (Scheme 5).

***Scheme 5***



**2**

**11**

**7**

**8**

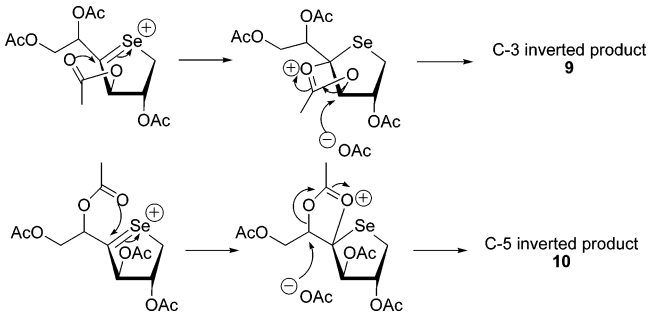
**9**

**10**

Compounds **7**−**10** were obtained in a 1:1:1:1 ratio. The 1-*O*-acetate, corresponding to the selenogalactofuranose compound **11** was not isolated. Instead, both isomers of the 4-*O*-acetate, compounds **7** and **8**, were formed along with two other isomerized products, **9** and **10**. The least polar fraction was found to be a mixture of two compounds, namely compounds **7** and **9**. The structures of compound **7** and **9** were assigned by means of a 1D-NOE experiment (Figure S1, Supporting Information; the resonances of compound **7** are designated as primed descriptors). For compound **7**, when the resonance corresponding to H-3′ was irradiated, an enhancement in the resonance corresponding to H-5′ was observed, and vice-versa. In addition, an enhancement in the resonance corresponding to H-1b′ was observed, showing that H-3′ was on the α-face and confirming that the side chain at C-4 was also on the α-face. For compound **9**, separate irradiation of the H-2 and H-3

(7) Tuleen, D. L.; Stephens, T. *J. Org. Chem.* **1969**, *34*, 31−35.
(8) Wolfe, S.; Kazmaier, P. M. *Can. J. Chem.* **1979**, 57, 2388−2396.
(9) Sharma, A. K.; Ku, T.; Dawson, A. D.; Swern, D. *J. Org. Chem.* **1975**, *40*, 2758−2764.
(10) Gunaga, P.; Moon, H. R.; Choi, W. J.; Shin, D. H.; Park, J. G.; Jeong, L. S. *Curr. Med. Chem.* **2004**, *11*, 2585−2637.
(11) Robina, I.; Vogel, P. *Curr. Org. Chem.* **2002**, *6*, 471−491.
(12) Fernandez-Bolanos, J. G.; Al-Masoudi, N. A. L.; Maya, I. *Adv. Carbohydr. Chem. Biochem*. **2001**, *57*, 21−98.
(13) Schiesser, C. H.; Zheng, S. L. *Tetrahedron Lett.* **1999**, *40*, 5095−5098.
(14) Skelton, B. W.; Stick, R. V.; Tilbrook, D. M. G.; White, A. H.; Williams, S. J. *Aust. J. Chem*. **2000**, *53*, 389−397.
(15) Naka, T.; Nishizono, N.; Minakawa, N.; Matsuda, A. *Tetrahedron Lett*. **1999**, *40*, 6297−6300.
(16) Fujita, J.; Matsuda, H.; Yamamoto, K.; Morii, Y.; Hashimoto, M.; Okuno, T.; Hashimoto, K. *Tetrahedron* **2004**, *60*, 6829−6851.
(17) Halila, S.; Benazza, M.; Demailly, G. *Tetrahedron Lett.* **2001**, *42*, 3307−3310.
(18) Szczepina, M. G.; Johnston, B. D.; Yuan, Y.; Svensson, B.; Pinto, B. M. *J. Am. Chem. Soc*. **2004**, *126*, 12458−12469.
(19) Veerapen, N.; Yuan, Y.; Sanders, D. A. R.; Pinto, B. M. *Carbohydr. Res.* **2004**, *339*, 2205−2217.
(20) Ghavami, A.; Chen, J. J.; Pinto, B. M. *Carbohydr. Res*. **2004**, *339*, 401−407.

***Scheme 6***



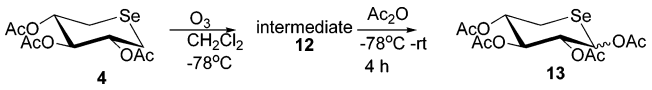

resonances showed corresponding enhancements of the H-3 and H-2 resonances, respectively, indicating that these hydrogens both are on the same side of the ring. Furthermore, no enhancements of the resonances corresponding to H-5, H-6a, or H-6b were observed when H-3 was irradiated, confirming that the configuration at C-3 had been inverted.

Pure fractions of the other two products were obtained by chromatography. The fraction of intermediate polarity was assigned to compound **8** with the help of 1D-NOE experiments (Figure S2). The stereochemistry of the side chain at C-4 was assigned by irradiation of the H-3, H-5, and H-2 resonances. No NOE correlation was observed between H-3 and H-5, while a NOE correlation was observed between H-2 and H-6a and H-6b, thereby confirming that the side chain at C-4 is on the $\beta$-face. The most polar fraction was assigned to compound **10**. In this case, a small NOE correlation was observed between H-3 and H-5, and no NOE correlation was observed between H-2 and H-6 (Figure S3), indicating that the side chain at C-4 is on the $\alpha$-face. Strong NOE correlations between H-3 and both H-6 hydrogens were also observed, corroborating this conclusion. Compounds **10** and **7** are indistinguishable diastereomers with different stereochemistry at C-5, and **10** was arbitrarily assigned as the isomer in which C-5 is inverted.

We suggest that the rearranged products **9** and **10** result from stabilization of an intermediate selena-carbenium ion by neighboring group participation by the 3- or 5-*O*-acetate groups, with subsequent opening of the acetoxonium ions by acetate ion to give the inverted products at C-3 or C-5 (Scheme 6).

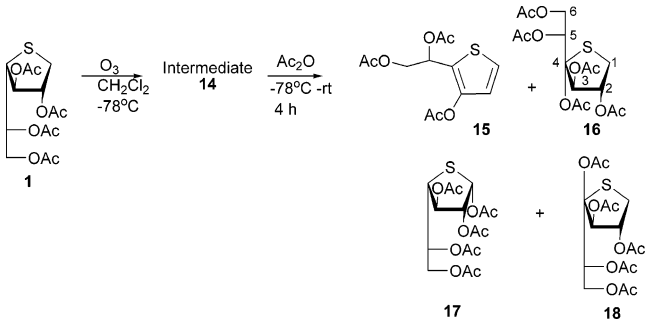
When the selenoxylitol **4** was reacted under the same reaction conditions as those described previously, the rearranged product **13** was obtained as a mixture of diastereomers in 97% yield (Scheme 7). The equatorial $\beta$-isomer was formed as the major product ($\alpha$:$\beta$ = 1:6.5) as judged by the large diaxial coupling between H-1 and H-2 in the $^1$H NMR spectrum.

***Scheme 7***




We next turned our attention to the reactions of the thiosugars **1** and **3**, for purposes of comparison. Reaction of the thiogalactitol intermediate **14** with acetic anhydride gave four products after processing and purification by column chromatography, together with some recovered starting material (Scheme 8). The starting material **1** was recovered in 16% yield, the thiophene derivative **15** was formed in 11% yield, while the combined yield of compounds **16**, **17**, and **18** was 62%, with compounds **17** and **18** exhibiting identical chromatographic mobility. Compound **16** was also very close in polarity, hence difficult to separate. The compounds **16**, **17**, and **18** were obtained in a ratio of 2.2:1:2.2, respectively, as estimated by $^1$H NMR spectroscopy.

***Scheme 8***




The stereochemistry at C-4 in compounds **16** and **18** was confirmed by means of 1D-transient NOE experiments, while the NMR data for compound **17** matched those reported by Ledekremer et al.[21] A relatively pure fraction of compound **16** was subjected to 1D-NOE experiments (Figure S4) which showed that when either H-3 or H-5 was irradiated, no NOE enhancements between H-3 and H-5 were observed, thus indicating that H-3 and H-5 were distant and most likely on opposite faces of the five-membered ring. On the other hand, when H-2 was irradiated, an enhancement of the resonance corresponding to H-6a was observed, indicating that the side chain at C-4 is on the $\beta$-face in compound **16**.

Compounds **17** and **18** could not be separated, but the resonances in the $^1$H NMR spectrum of the mixture were well separated (Figure S5), and the resonances corresponding to compound **18** could be differentiated from those of the known compound **17**. The major isomer was thereby assigned to be compound **18**, while the minor isomer was assigned to be compound **17**. The resonances corresponding to H-3 and H-5 were each saturated separately, and enhancements in the H-5 and H-3 resonances, respectively, were observed. Furthermore, enhancements in the resonances corresponding to H-6a and H-6b were also observed upon saturation of the H-3 resonance. Such enhancements in the resonances of H-6 were not observed when H-2 was saturated, confirming that the side chain is on the $\alpha$-face in compound **18**.

We next turned our attention to the thioxylitol derivative **3**. It should be noted that compound **3** is highly crystalline and tended to precipitate out of solution at −78 °C. Therefore, the latter was dissolved in an excess of solvent (Table 1). Unexpectedly, the thioxylitol derivative **3** did not undergo rearrangement under the same reaction conditions used previously (Scheme 9). Instead, the sulfoxide **20** was isolated, after processing. Even prolonged reaction times at room temperature or at 40 °C did not lead to the formation of any new product.

***Scheme 9***

***Table 1.*** Summary of outcomes of Reactions of the Seleno- and Thioanhydro Sugars

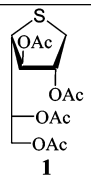
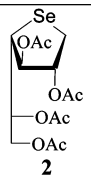
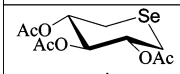
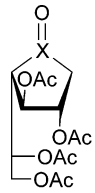
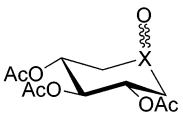
| Substrate | Reaction conditions for ozonization | Product isolated after addition of acetic anhydride (5 eq) at -78 °C to the reaction mixture after ozonization |
|---|---|---|
|  **1** | 1. $8.6\times10^{-3}$ M, $CH_2Cl_2$, -78 °C.<br>2. $1.4\times10^{-3}$ M, $CH_2Cl_2$, -78 °C. | 1. Pummerer-type products<br>2. Pummerer-type products |
|  **2** | $1.0\times10^{-2}$ M, $CH_2Cl_2$, -78 °C. | Pummerer-type products |
|  **3** | $1.5\times10^{-3}$ M, $CH_2Cl_2$, -78 °C. | Sulfoxide |
|  **4** | $9.2\times10^{-3}$ M, $CH_2Cl_2$, -78 °C. | Pummerer-type products |

***Chart 2***



**21** X=S
**22** X=Se



**20** X=S
**23** X=Se

We do not believe that the concentration of the reaction mixture plays a determinant role in the rearrangement because the thiogalactitol **1** also underwent rearrangement at this lower concentration (Table 1). We attribute these observations to a lower reactivity of the thioxylitol **3** compared to the thiogalactitol **1** under the reaction conditions.

**Pummerer Rearrangement of the Oxides.** The difference in behavior between the two thiosugar derivatives **1** and **3** prompted us to investigate the reactions in more detail. We first isolated the sulfoxides **20** and **21** and the selenoxides **22** and **23** (Chart 2), before subjecting them to separate reactions with acetic anhydride.

Thus, ozonization of compounds **1**−**4** followed by evaporation of the solvent at 20 °C gave the desired oxides that were characterized by IR and $^1$H NMR spectroscopy. It should be noted that the oxides **21** and **22** were obtained almost exclusively as one isomer at the stereogenic heteroatom centers, while **20** and **23** were each obtained as a mixture of diastereomers in an 8:1 ratio (axial/equatorial). The selenoxides started to decompose when kept at room temperature, while the sulfoxides were stable for days at room temperature. The selenoxides were thus only characterized by $^1$H NMR and IR spectroscopy. Strong absorbance peaks in the IR spectrum in the region 1020−1050 $cm^{-1}$, characteristic of S═O and Se═O stretching vibrations were observed. The $^1$H NMR spectra also showed a downfield shift in the H-1 resonances, consistent with the formation of the oxides (Table S2, Supporting Information).

Each oxide was then dissolved in $CH_2Cl_2$ and treated with 5 equiv of acetic anhydride at room temperature for 5 h. Interestingly, the reactions of the selenoxides **22** and **23** proceeded smoothly to give the same products as before, but the sulfoxides **20** and **21** were unreactive at room temperature. Since we had previously observed that the thiogalactitol derivative **1** did undergo rearrangement to give four compounds when treated with ozone, followed by acetic anhydride at −78 °C (Scheme 8), we were forced to reconsider our assumption that all of the previous reactions had proceeded through the sulfoxide or selenoxide intermediates.

We then closely monitored by TLC the reactions of the intermediates **6**, **12**, **14**, and **19** formed at −78 °C upon ozonization. These intermediates were more polar than the corresponding oxides on TLC. After addition of acetic anhydride at −78 °C, there seemed to be little change in the polarity of these intermediates. As the reaction mixtures warmed in the following half hour, TLC analysis indicated the presence of less polar compounds. We were unable to ascertain by TLC analysis whether the intermediate compounds **6**, **12,** and **14** reacted to give rearranged products via the selenoxides **22**, **23**, or the sulfoxide **21**, respectively. However, intermediate **19** did eventually give the stable sulfoxide **20**.

It is interesting to note, however, that when the sulfoxides **20** and **21** were refluxed in toluene containing 5 equiv of acetic anhydride for 48 h in the presence of NaOAc, they underwent rearrangement. Previous attempts to achieve the Pummerer rearrangement by heating the mixtures of the sulfoxides **20** and **21** and acetic anhydride (5 equiv) in toluene, in the absence of

(21) Varela, O.; Cicero, D.; De Lederkremer, R. M. *J. Org. Chem.* **1989**, *54*, 1884−1890.

**Scheme 10**

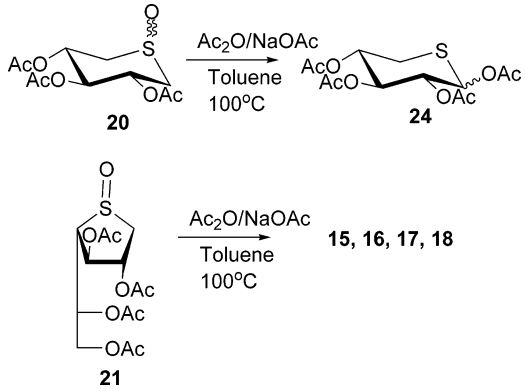
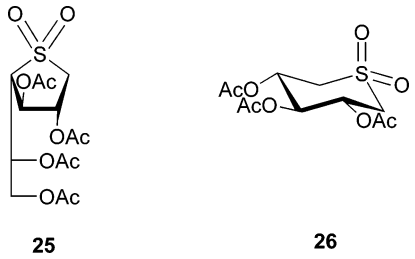



**Chart 3**




NaOAc, for 12 h were unsuccessful. In the case of the thiogalactitol sulfoxide **21**, the same products as those observed before were obtained in very comparable ratios. As for the thioxylitol sulfoxide **20**, the $\beta$-*O*-acetate was formed as the major product in an $\alpha$:$\beta$ ratio of 1:4 (Scheme 10).

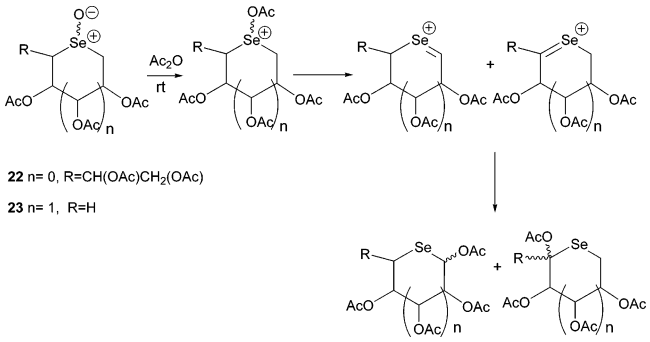
To confirm that the sulfoxides **20** and **21** were indeed the products formed as a result of ozonization, these species were generated using a different oxidizing agent, namely sodium metaperiodate.[22] These sulfoxides were obtained as a mixture of diastereomers. However, the $^1$H and $^{13}$C NMR spectra of the major isomers as well as the microanalysis data of these oxides corresponded to those generated by ozonization. The lack of stereoselectivity in the periodate oxidation may be explained by the fact that the procedure was carried out at a higher temperature of 0 °C as opposed to −78 °C in the ozonization procedure. These sulfoxides were then treated with acetic anhydride and NaOAc in refluxing toluene, as with compounds **20** and **21**. Pummerer rearrangement products were obtained as before; however, the product distribution ratio for the thiogalactitol sulfoxide derivatives differed, **15**, **16**, **17**, and **18** being formed in a 1:6:1:2 ratio, respectively.

To completely eliminate any speculation that the sulfoxides might be contaminated with sulfones, hence explaining their relative low reactivity, we synthesized the respective sulfones **25** and **26** by oxidation of the sulfides with MCPBA (Chart 3). The sulfones were obtained in high yields, and comparison of their spectroscopic data to those of the sulfoxides allowed us to discount this possibility (Figures S8, S9).

The fact that the selenoxides **22** and **23**, unlike the sulfoxides **20** and **21**, undergo Pummerer rearrangement at room temperature (Scheme 11) suggests that it may be due to their higher reactivities.

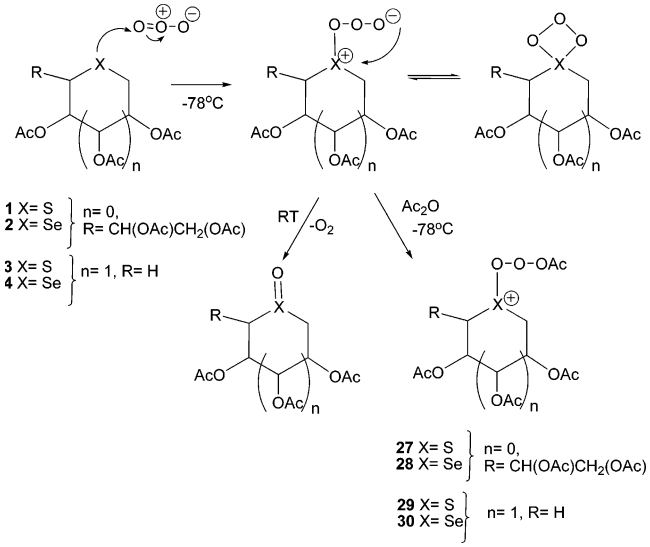
**Formation of an Intermediate in the Ozonization Reaction?** To account for these surprising results, we invoke the

**Scheme 11**




initial formation of a thioether ozone adduct at −78 °C. This adduct could exist as a linear ozonide[23] in equilibrium with the cyclic form (Scheme 12). Linear ozonide formation has been proposed previously in the ozone-mediated oxidation of sulfides to sulfoxides,[23] while other experimental data have supported the formation of phosphite-ozone cyclic adducts in the oxidation of phosphites.[24] We propose that, once formed, the linear ozonides[25] could be trapped by acetic anhydride to give acetylated ozonide intermediates which rearrange upon warming to room temperature to give the $\alpha$-acetoxy products (Scheme 12).

**Scheme 12**




Little is known about the stability of ozonides of sulfides and selenides and the subsequent elimination of molecular oxygen to form the corresponding sulfoxides or selenoxides. Mechanistic studies have been performed on the ozonization of sulfur-containing compounds since early 1900.[26] Several reaction pathways[23,26,27] have been proposed for the oxidation of the sulfur atom by ozone, and each of these proposed pathways has some experimental support. For example, it has been proposed that the linear ozonides can decompose in different ways, including internal abstraction of $\alpha$-protons by

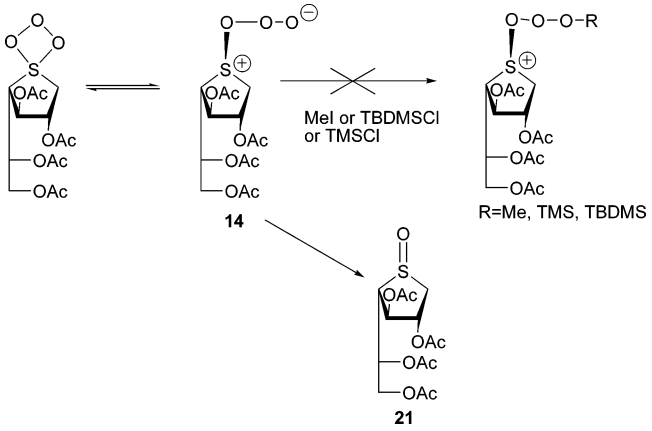
(22) Leonard, N. J.; Johnson, C. R. *J. Org. Chem.* **1962**, *27*, 282−284.

(23) Bailey, P. S.; Khasab, A. Y. *J. Org. Chem.* **1978**, *43*, 675−678.
(24) Murray, R. W.; Kaplan, M. L. *J. Am. Chem. Soc.* **1969**, *91*, 5358−5364.
(25) (a) Horner, L.; Schaefer, H.; Ludwig, W. *Chem. Ber.* **1958**, *91*, 75−81. (b) Thompson, Q. E. *J. Am. Chem. Soc.* **1961**, *83*, 845−851. (c) Maggiolo, A.; Blair, E. A. *Adv. Chem. Ser.* **1959**, *21*, 200−201.
(26) Razumovskii, S. D.; Shatokhina, E. I.; Malievskii, A. D.; Zaikov, G. E. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1975**, *3*, 543−546.
(27) Corey, E. J.; Ouannès, C. *Tetrahedron Lett.* **1976**, 4263−4266.

the negatively charged oxygen in the ozonide, resulting in oxidation of the α-carbon.[23] In the present study, however, only sulfoxides and selenoxides were isolated upon warming to room temperature (Scheme 12).

**Attempts to Isolate and Characterize the Intermediates.** Because of the incongruity in the reactions of the thiogalactitol derivative **1** and its oxide **21**, these two compounds were chosen for further studies in an attempt to characterize the proposed intermediate **14**. However, our efforts to trap the more polar intermediates, which we propose above as being the thioether ozone adduct, were not successful. Addition of MeI, TMSCl, or TBDMSCl to the ozonized reaction mixture of **1** at −78 °C (Scheme 13) resulted in isolation of the sulfoxide **21** after warming to room temperature over 2 h.

***Scheme 13***

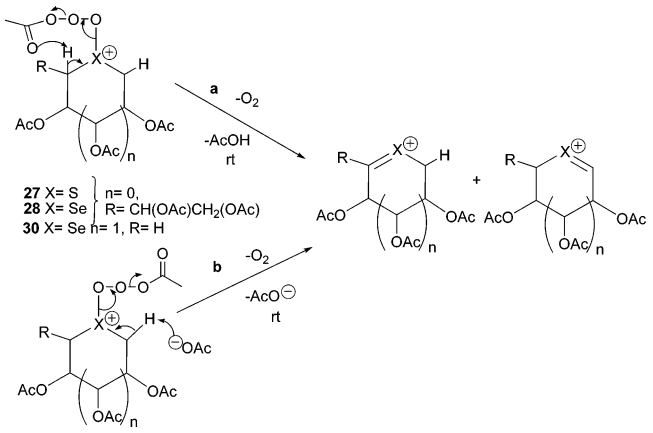



To the best of our knowledge, the ozonides are not stable at room temperature. A study performed on silyl hydrotrioxides[28] (RSiOOOH) showed that they decompose in the temperature range −70 to −40 °C. This prompted us to perform a low-temperature NMR experiment on the reaction of the thiogalactitol **1** at −80 °C. The reaction was performed in $CD_2Cl_2$ at −78 °C, and the reaction mixture was pipetted, using a precooled pipet, into a cooled NMR tube, which was maintained at −78 °C with the help of a dry ice/acetone bath until it was transferred to the cooled probe of the spectrometer. The temperature was allowed to stabilize for about 5 min before the spectra were acquired. Curiously, both the $^1$H and $^{13}$C NMR spectra of the ozonized thiogalactitol at −80 °C were identical to those of the sulfoxide **21** at the same temperature. We also failed to observe any difference in the $^1$H NMR spectra at −60, −40, and 0 °C between the sulfoxide and the ozonized sample when we allowed the latter to warm.

**Rearrangement Pathways.** We propose that the acetylated ozonides can rearrange via either a heterolytic or a homolytic mechanism to generate the Pummerer-type products. In the heterolytic pathway, the highly reactive, acetylated ozonides **27**, **28**, and **30** rearrange via abstraction of an α-proton, either intramolecularly (a) or intermolecularly (b), to give the thia- or selena-carbenium ions (Scheme 14), while the ozonide acetate **29** decomposes to give the sulfoxide **20** (Scheme 15).

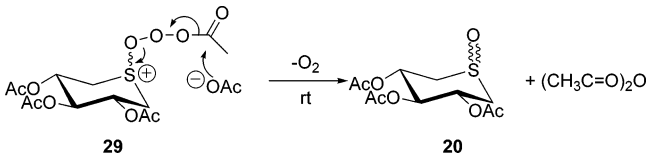
In the case of the thioxylitol derivative **3**, presumably the α-protons are not acidic enough to be abstracted by the acetate anion or the peracetate oxygen, but because the ozonide acetate

***Scheme 14***




**29** is unstable at room temperature, molecular oxygen is eventually extruded. A possible extrusion mechanism to give the sulfoxide **20** is depicted in Scheme 15.

***Scheme 15***




In the heterolytic rearrangements of both the thioether-ozone adduct and the acetylated ozonide described above (Schemes 12, 14, and 15) to generate the oxides and Pummerer products, respectively, one of the expected byproducts is singlet oxygen ($^1O_2$). Because of the visible evidence of reaction, indicated by the disappearance of its bright orange color upon oxidation, rubrene can be used as an acceptor to trap active singlet oxygen.[29] Hence, when rubrene was added to a solution of the ozonized reaction mixture of thiogalactitol **1** at −78 °C and the solution was allowed to warm to room temperature, the intense orange color disappeared, indicating that $^1O_2$ was indeed released upon decomposition of the ozonide adduct to generate the sulfoxide **21**. This result is similar to that previously observed with the decomposition of phosphite-ozone cyclic adducts in the oxidation of phosphites.[24] In contrast, no loss of color was detected when rubrene was added to the ozonized reaction mixture, to which acetic anhydride had been previously added. In this case, presumably no singlet oxygen was generated, or it represented a minor pathway.

The homolytic pathway for the rearrangement of the acetylated ozonide was then considered, and electron paramagnetic resonance (EPR) experiments were carried out to probe this hypothesis. To determine the presence of transient radical species we added the nitrone spin trap, 5,5-dimethy-1-pyrroline *N*-oxide **31** (DMPO),[30] which reacts with short-lived radicals to yield stable paramagnetic spin adducts. The adducts are formed by addition to C-1 of DMPO, giving a stable nitroxide radical species that is readily detectable with EPR, and whose EPR spectrum displays $^1$H and $^{14}$N hyperfine couplings that are distinctive for a particular addition product. Interestingly, DMPO can also be used to trap singlet oxygen.[31] Hence, when the

(28) Plesnicar, B.; Cerkovnik, J.; Koller, J.; Kovac, F. *J. Am. Chem. Soc*. **1991**, *113*, 4946−4953.

(29) Wilson, T. *J. Am. Chem. Soc*. **1966**, *88*, 2898−2902.

(30) Janzen, E. G. In *Free Radicals in Biology*; Pryor, W. A., Ed.; Academic Press: New York, 1980; Vol IV, and references therein.

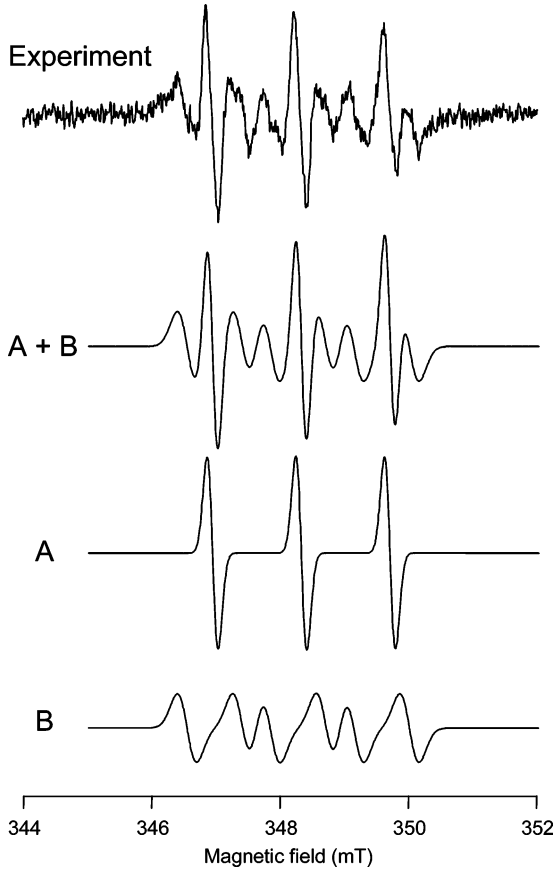
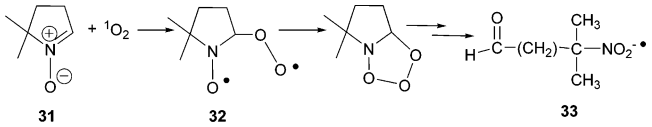



***Figure 1.*** Experimental EPR spectrum observed from a sample which contained the ozonized thiogalactitol **1** and DMPO, and simulated spectra shown in traces (A) and (B). (*Experimental parameters*) microwave frequency 9.86 GHz, Modulation amplitude 0.1 mT, microwave power 0.64 mW, receiver gain $1 \times 10^5$, time constant 5.12 ms, scan time 10 s, average of 100 scans. (*Simulation parameters*) Spectrum A: $a(^{14}N)$ 1.38 mT, line width 0.19 mT. Spectrum B: $a(^{1}H)$ 0.86 mT, $a(^{14}N)$ 1.34 mT, line width 0.3 mT.

***Scheme 16***




ozonized reaction mixture of thiogalactitol **1** was trapped with an excess of DMPO at −78 °C, an EPR spectrum consisting of two distinct species, one of which was comprised of six equal intensity lines and the other of three, was observed (Figure 1).

The six-line spectrum in Figure 1 was well simulated using parameters $a(^{1}H) = 0.86$ mT, $a(^{14}N) = 1.34$ mT, line width = 0.3 mT. These parameters are typical for alkoxyl or dioxyl adducts of DMPO where the hyperfine couplings are derived from unpaired electron spin density at the nitroxide nitrogen and the $^{1}H$ at C-1.[32] The three-line spectrum was simulated with parameters $a(^{14}N) = 1.38$ mT, line width = 0.19 mT. The absence of resolved $^{1}H$ hyperfine splitting implies a ring-opened product formed via cleavage of the N—C-1 bond; the $^{14}N$ coupling is typical for a terminal nitroxide radical.[33] A similar three-line spectrum was observed by Bilski et al.[31] and was attributed to the nitro radical anion **33** (Scheme 16), resulting from oxidative ring opening of DMPO by $^{1}O_2$. The authors proposed the initial formation of biradical **32** via the addition of $^{1}O_2$ to the carbon atom in the C=N bond.[31] This intermediate could then undergo various rearrangements to give **33**, among other products.[31] Alternatively, a 1,3-dipolar cycloaddition reaction of singlet oxygen to give a trioxazolidine, followed by reaction with additional singlet oxygen, should yield **33**. Compound **32** consists of an aminoxyl and an alkyl dioxyl radical. While a six-line pattern generated by the aminoxyl radical was observed, the expected doublet or broad singlet generated by the dioxyl radical was not. Literature reports of the spectra of such species in solution are relatively rare and mostly poorly characterized. However, the spectra of ROO• that have been reported are generally described as broad and featureless,[32−34] and the authors have commented on the broadening effect of dissolved oxygen in the solutions, which will also be a factor in our experiments. Fessenden et al.[33] assign broad featureless spectra centered at ∼20 G below the free electron *g* value (at X-band), which they assign to ROO•, for various alkyl R groups. We were not able to observe such spectra in our experiments, but this is very likely because of the broadness of the lines. We note that this situation will actually be exacerbated if there is a significant proton hyperfine coupling to the $^{1}H$ on C-1, since this will lead to additional broadening, further inhibiting resolution of the spectrum from the baseline. Nonetheless, the EPR experiment, which corroborates the findings obtained in the trapping experiment with rubrene, provides support for the formation of singlet oxygen and, hence, the thioether-ozone adduct.

On the other hand, when the ozonized reaction mixture of the thiogalactitol **1**, formerly treated with acetic anhydride, was trapped with an excess of DMPO, a different EPR spectrum was observed. In this case, a well-resolved seven-line spectrum with intensity ratios of 1:2:2:2:2:2:1 was produced on top of a broader spectrum, the outer two lines of which were clearly visible (Figure 2). Through simulation we were able to determine that the seven-line spectrum was described by two equivalent protons with $a(^{1}H) = 0.36$ mT, $a(^{14}N) = 0.67$ mT, line width = 0.12 mT. This hyperfine pattern is distinctive for formation of a ketone at C-1 giving the adduct often referred to as DMPOX **35** (5,5-dimethyl-2-oxopyrroline-1-oxyl).[35,37] Through analysis of the variation of the actual line intensities of the DMPOX signal from the ideal, we were able to estimate the structure of the underlying broad spectrum and found this to be very similar to that of the six-line spectrum found in the reaction described above for the formation of the sulfoxide in dichloromethane. To account for the formation of DMPOX without the generation of $^{1}O_2$, we propose the fragmentation of the ozonide acetate to yield an acetate radical and a dioxyl radical (Scheme 17). This fragmentation is somewhat similar to the thermal decomposition of peroxyesters[38] and the $Cu^{2+}$/ $Cu^{+}$ catalyzed α-acetoxylation of cyclic sulfides by *tert*-butyl peroxyesters.[39] Subsequent abstraction of the α-H then generates a hydroperoxide radical, which is then trapped by DMPO (Scheme 17).

(31) Bilski, P.; Reszka, K.; Bilska, M.; Chignell, C. F. *J. Am. Chem. Soc.* **1996**, *118*, 1330−1338.
(32) Livingston, R.; Zeldes, H. *J. Chem. Phys.* **1966**, *44*, 1245−1259.
(33) Fessenden, R. W.; Schuler, R. H. *J. Chem. Phys.* **1963**, *39*, 2147−2195.
(34) Mulcahy, M. F. R.; Steven, J. R.; Ward, J. C. *Aust. J. Chem.* **1965**, *18*, 1177−1181.
(35) Beuttner, G. R. *Free Radical Biol. Med.* **1987**, *3*, 259−303.
(36) Berliner, L. J. *Spin Labeling: Theory and Applications*. Academic Press: New York, 1976.
(37) Aurich, H. G.; Troesken, J. *Liebigs Ann. Chem.* **1971**, *745*, 159−163.
(38) Kharasch, M. S.; Sosnovsky, G.; Yang, N. C. *J. Am. Chem. Soc.* **1959**, *81*, 5819−5824.
(39) Sosnovsky, G.; Lawesson, S. O. *Angew. Chem., Int. Ed.* **1964**, *76*, 218−225.

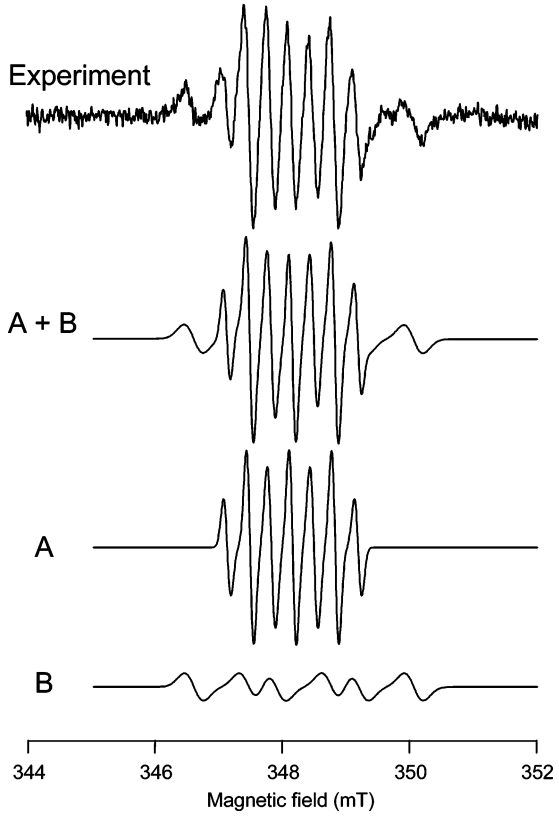
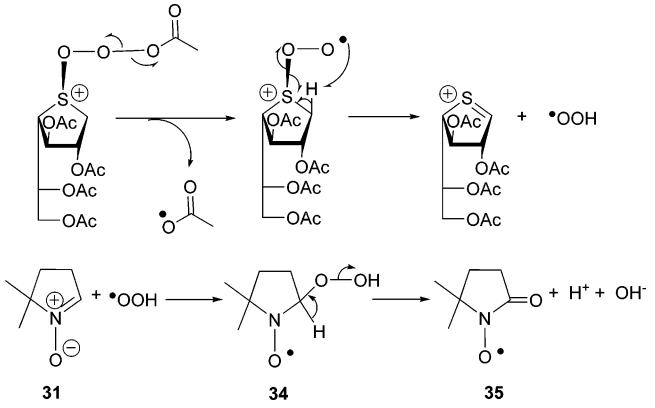



***Figure 2.*** Experimental EPR spectrum observed from a sample which contained the ozonization reaction mixture of thiogalactitol **1**, 5 equiv of acetic anhydride and DMPO, and simulated spectra shown in traces (A) and (B). (*Experimental parameters*) microwave frequency 9.85 GHz, Modulation amplitude 0.2 mT, microwave power 0.64 mW, receiver gain $2 \times 10^4$, time constant 5.12 ms, scan time 10 s, average of 16 scans. (*Simulation parameters*) Spectrum A: $a(^1H \times 2)$ 0.36 mT, $a(^{14}N)$ 0.67 mT, line width 0.12 mT. Spectrum B: $a(^1H)$ 0.86 mT, $a(^{14}N)$ 1.34 mT, line width 0.3 mT.

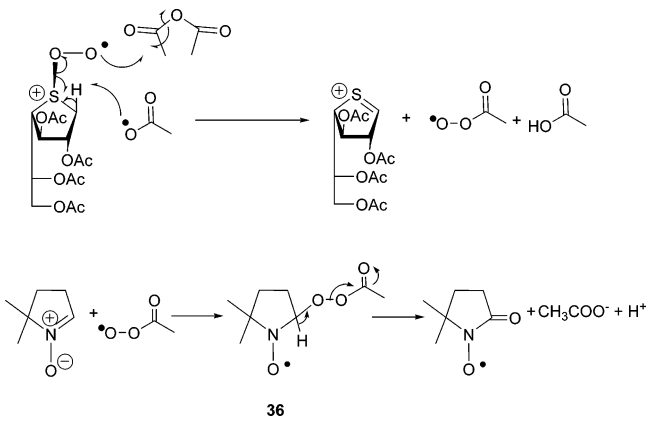
***Scheme 17***




Alternatively, intermolecular α-H abstraction would generate a peracetate radical, which could also be trapped with DMPO and eventually yield DMPOX (Scheme 18). Our experiments do not allow us to differentiate between these two possibilities.

We attribute the broad, likely six-line spectrum to the dioxyl DMPO adducts **34** and **36**, which are initially formed before degradation to DMPOX. One would expect the pattern of the dioxyl adducts (**34** and **36**) and the biradical **32** to be somewhat similar, but the coincidence of $a(^1H)$ and $a(^{14}N)$ values is striking; we do note, however, that four of the likely six lines are obscured by the DMPOX signal, making determination of

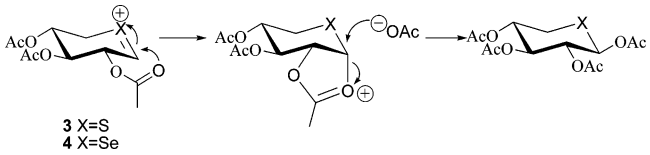
***Scheme 18***




the hyperfine parameters inaccurate and that these two spectra were recorded in different media, owing to the additional presence of acetic anhydride in the second EPR experiment (Figure 2).

**Regioselectivity of the Pummerer Rearrangement.** The asymmetric substrates **1** and **2** yielded rearrangement products at the more substituted α-carbon, suggesting that the rearrangements proceed via a heterocarbenium ion intermediate rather than the ylides (Schemes 2, 14) in both the usual Pummerer rearrangement and the rearrangement of the ozonides. However, our experiments do not permit comment on whether the proton abstraction to form the heterocarbenium ion is intramolecular or intermolecular.

***Scheme 19***




On a similar note, the preferred formation of the $\beta$-isomer in both anhydroxylitol derivatives **3** and **4** (Schemes 7, 10) can be accounted for by stabilization of the intermediate heterocarbenium ion by the acetoxy group at C-2 or C-4 (Scheme 19), the incoming acetate nucleophile being directed to the $\beta$-face.

## Conclusions

Pummerer rearrangement of selenoheterocycles yielded stable α-acetoxylated derivatives. Overall, the selenoheterocycles are more reactive than their sulfur congeners under the reaction conditions described in this paper. In the conventional Pummerer reaction, the selenoxides underwent rearrangement at room temperature, while the sulfoxides required harsher conditions to afford rearranged products. In addition, the ozonide acetate intermediates of both seleno derivatives underwent rearrangement to give the α-acetoxylated products, while only the ozonide acetate intermediate of the thiogalactitol derivative did so; the thioxylitol derivative, on the other hand afforded the sulfoxide.

Trapping experiments and EPR studies allowed us to conclude that the thioether-ozone adduct decomposed to the sulfoxide with the release of singlet oxygen, whereas the ozonide acetate rearrangement in the thio derivative **1** proceeded via a radical mechanism.

It can be concluded that the presumed intermediates, acetylated ozonides, are reactive species that can rearrange under milder conditions than the corresponding sulfoxides or selenoxides to give the α-acetoxylated selenoethers and thioethers. This milder method should be of general utility in organic synthesis. Finally, the products obtained indicate that the reactions proceed preferentially through the formation of the more stable thia- or selena-carbenium ion, thereby favoring a concerted elimination mechanism (eq 1).

## Experimental Section

**General.** Optical rotations were measured with a Rudolph Research Autopol II automatic polarimeter. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Varian 500 NMR spectrometer at 500 and 125 MHz, for $^1$H and $^{13}$C, respectively. Low temperature $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker AMX-400 NMR spectrometer at 400.13 and 100.6 MHz, for $^1$H and $^{13}$C, respectively. Chemical shifts are given in ppm downfield from TMS for those spectra measured in $CDCl_3$. Chemical shifts and coupling constants were obtained from a first-order analysis of the spectra. All assignments were confirmed with the aid of two-dimensional $^1$H/$^1$H COSY, $^1$H/$^{13}$C HMQC. 1D NOE experiments were recorded at 295 K on the Varian 500 NMR spectrometer. For each 1D NOE spectrum, 64 or 128 scans were acquired. A mixing time of 500 ms was used in all the 1D NOE experiments. Infrared spectra (IR) were recorded as evaporated films (ef) using a Perkin-Elmer 599B IR spectrophotometer. Analytical thin-layer chromatography (TLC) was performed on aluminum plates precoated with Merck silica gel 60F-254 as the adsorbent. The developed plates were air-dried, exposed to UV light and/or sprayed with a solution containing 1% $Ce(SO_4)_2$ and 1.5% molybdic acid in 10% aqueous $H_2SO_4$, and heated. Compounds were purified by flash chromatography on Kieselgel 60 (230−400 mesh). Solvents were distilled before use and were dried, as necessary, according to literature procedures. Solvents were evaporated under reduced pressure and below 50 °C. High-resolution mass spectra were liquid secondary ionization fast atom bombardment (LSIMS(FAB)) or ES run on a Kratos Concept H double focusing mass spectrometer at 10000 RP.

**EPR Measurements.** EPR spectra were collected on a Bruker ECS-106 X-band spectrometer. Measurements were made at room temperature with samples contained in flame-sealed Pasteur pipets. Small sample volumes were required due to the relatively high dielectric constants of the solvents, which meant that larger volumes made it impossible to tune the instrument. Individual spectra were simulated using Bruker's WINEPR simfonia software and later summed by importing these data into a spreadsheet.

**General Procedure (a) for Ozonization.** A solution of each of the peracetylated alditols **1**, **2**, and **4** in $CH_2Cl_2$ (50 mL) and **3** in $CH_2Cl_2$ (100 mL) was cooled to −78 °C. Ozone gas was then bubbled through the solution until the latter turned light blue. Formation of the ozonides was confirmed by TLC analysis (EtOAc/MeOH, 7:1), which showed the formation of more polar compounds. $R_f$ values for intermediates **6**, **12**, **14**, and **19** were 0.22, 0.35, 0.20, and 0.31, respectively. Subsequently, $N_2$ gas was bubbled through the solution for approximately 5 min while the temperature was maintained at −78 °C.

**WARNING:** Although we have not experienced any accidents in handling solutions of the ozonized reaction mixtures, care should be taken in handling concentrated solutions of these potentially hazardous compounds. We also note that the subsequent decompositions/degradations of the ozonized products proceeded smoothly and that the experiments were carried out on a small scale.

**General Procedure (b) for the Rearrangement of the Ozonides.** To the reaction mixture at −78 °C was added acetic anhyride (5 equiv). The reaction was allowed to warm to rt over a period of 2 to 3 h. The reaction was followed by TLC analysis (hexanes/EtOAc, 1:1). When the reaction was complete, as indicated by formation of less polar products, the reaction mixture was diluted with $CH_2Cl_2$ and quenched with cold saturated $NaHCO_3$ solution. The organic extract was then washed with saturated NaCl solution (2 × 10 mL), dried over anhydrous $Na_2SO_4$, and concentrated in vacuo. The residue was then purified by column chromatography.

**General Procedure (c) for the Pummerer Rearrangement.** The reaction mixtures of **1**, **2**, and **4** from general procedure (a) were concentrated in vacuo at 20 °C. Compound **3** was dissolved in a mixture of $CH_2Cl_2$ and MeOH (45 mL, 2:1) (because of precipitation of the salt at −78 °C), cooled to −78 °C, and treated with ozone gas. The solvents were then removed in vacuo at 20 °C. $R_f$ values (hexanes/EtOAc, 1:2) for oxides **21**, **22**, **20**, and **23** were 0.26, 0.28, 0.44, and 0.44, respectively. In the case of the selenoxides, the residues were then redissolved in $CH_2Cl_2$ (25 mL), acetic anhyride (5 equiv) was added, and the reaction mixtures were stirred at room temperature for 5 h. The reaction was followed by TLC analysis (hexanes/EtOAc, 1:1). In the case of the sulfoxides, the residues were also initially dissolved in $CH_2Cl_2$ (25 mL). Acetic anhydride (5 equiv) was added, and the reaction mixtures were stirred at room temperature for 24 h. Since TLC analysis revealed no formation of any new product, the reaction mixtures were heated at 40 °C for another 24 h. However the starting materials remained intact. The $CH_2Cl_2$ was then evaporated, and toluene (25 mL) was added. When the reaction mixtures were refluxed in toluene for 12 h, no new product was formed; but when NaOAc (2 equiv) was added and the reaction mixtures were stirred at 100 °C for 48 h, TLC analysis indicated the formation of less polar products (EtOAc/hexanes, 1:1). The reaction mixtures were diluted with $CH_2Cl_2$ (20 mL) and quenched with cold saturated $NaHCO_3$ solution. The organic extracts were then washed with saturated NaCl solution (2 × 10 mL), dried over anhydrous $Na_2SO_4$, and concentrated in vacuo. The residues were then purified by column chromatography.

**2,3,5,6-Tetra-*O*-acetyl-1,4-anhydro-4-seleno-D-galactitol (2).** 1,4-Anhydro-2,3,5,6-tetra-*O*-*p*-methoxybenzyl-4-seleno-D-galactitol[19] (1.00 g, 1.42 mmol) was dissolved in TFA (5 mL) and stirred at rt for 1 h, after which the TFA was removed in vacuo. The residue was washed with $CH_2Cl_2$ (3 × 10 mL), the organic washings were discarded, and the solid was dissolved in pyridine (20 mL). Acetic anhydride (20 mL) was then added, and the reaction mixture stirred at rt overnight, after which the solvents were evaporated and the residue was taken up in $CH_2Cl_2$ (50 mL). This solution was washed with saturated $NaHCO_3$ solution (3 × 10 mL) and saturated NaCl (2 × 10 mL), dried over anhydrous $Na_2SO_4$, and concentrated under vacuo. The residue was then passed through a short silica column (hexanes/EtOAc, 1:1, $R_f$ = 0.50) to give **2** as a white solid (0.51 g, 92%). $[\alpha]_D$ +18° (*c* 0.28, $CHCl_3$); $^1$H NMR ($CDCl_3$): $\delta$ 5.36−5.33 (2H, m, H-2, H-3), 5.27 (1H, ddd, $J_{5,4}$ = 7.6, $J_{5,6a}$ = 3.5, $J_{5,6b}$ = 5.9 Hz, H-5), 4.43 (1H, dd, (1H, dd, $J_{6a,6b}$ = 12.1 Hz, H-6a), 4.04 (1H, dd, H-6b), 3.72 (1H, dd, $J_{4,3}$ = 5.7 Hz, H-4), 3.21 (1H, dd, $J_{1a,1b}$ = 10.4, $J_{1a,2}$ = 4.7 Hz, H-1a), 2.95 (1H, dd, $J_{1b,2}$ = 6.1 Hz, H-1b), 3.11, 2.09, 2.07, 2.06 (12H, 4s, 4 × OCOC*H*$_3$). $^{13}$C NMR ($CDCl_3$): $\delta$ 170.71, 170.20, 170.17, 169.81 (4 × O*C*=OCH$_3$), 78.30 (C-3), 77.55 (C-2), 70.80 (C-5), 64.44 (C-6), 42.16 (C-4), 22.68 (C-1), 21.15, 21.10, 21.08, 20.97 (4 × OCO*C*H$_3$). Anal. Calcd for $C_{14}H_{20}O_8Se$: C, 42.54; H, 5.10. Found: C, 42.50; H, 5.30.

**Rearrangement of 1,4-Anhydro-2,3,5,6-tetra-*O*-acetyl-4-seleno-D-galactitol (2).** Compound **2** (200 mg, 0.51 mmol) was subjected to the reaction conditions described in general procedures (a) and (b). TLC analysis of the reaction mixture showed 3 components. Elution of the least polar component after column chromatography (hexanes/EtOAc, 1:1, $R_f$ = 0.48) gave compounds **7** and **9** as a colorless oil in a 1:1 mixture (100 mg, 44%).$^1$H NMR ($CDCl_3$) data for **7**: $\delta$ 5.68 (1H, d, $J_{3,2}$ = 9.7 Hz, H-3), 5.57 (1H, ddd, $J_{2,1a}$ = 7.8, $J_{2,1b}$ = 8.3 Hz, H-2), 5.16 (1H, dd, $J_{5,6b}$ = 2.4, $J_{5,6a}$ = 4.7 Hz, H-5), 4.68 (1H, dd, $J_{6a,6b}$ = 12.4 Hz, H-6a), 4.30 (1H, dd, H-6b), 3.51 (1H, dd, $J_{1a,1b}$ = 9.8 Hz, H-1a), 2.86 (1H, dd, H-1b), 2.14−2.04 (15H, 5s, 5 × OCOC*H*$_3$).$^{13}$C NMR ($CDCl_3$): $\delta$ 170.50−168.74 (5 × O*C*=OCH$_3$), 76.80 (C-4), 76.77

(C-3), 75.17 (C-2), 71.66 (C-5), 62.68 (C-6), 21.2−20.56 (5 × OCO*C*H$_3$), 19.84 (C-1). $^1$H NMR ($CDCl_3$) data for **9**: $\delta$ 5.88 (1H, d, $J_{3,2}$ = 1.9 Hz, H-3), 5.69 (1H, dd, $J_{5,6b}$ = 2.4, $J_{5,6a}$ = 4.8 Hz, H-5), 5.36 (1H, ddd, $J_{2,1a}$ = 5.5, $J_{2,1b}$ = 2.4 Hz, H-2), 4.45 (1H, dd, $J_{6a,6b}$ = 11.6 Hz, H-6a), 4.34 (1H, dd, H-6b), 3.69 (1H, dd, $J_{1a,1b}$ = 11.4 Hz, H-1a), 3.42 (1H, dd, H-1b), 2.14−2.04 (15H, 5s, 5 × OCOC*H*$_3$).$^{13}$C NMR ($CDCl_3$): $\delta$ 170.50−168.74 (5 × O*C*═OCH$_3$), 83.75 (C-4), 83.73 (C-3), 79.39 (C-2), 73.07 (C-5), 64.18 (C-6), 31.63 (C-1), 21.2−20.56 (5 × OCO*C*H$_3$). Anal. Calcd for $C_{16}H_{22}O_{10}Se$ (isomers **7**and **9**): C, 42.39; H, 4.89. Found: C, 42.19; H, 5.01.

Further elution (hexanes/EtOAc, 1:1, $R_f$ = 0.46) provided compound **8** as a colorless oil (53 mg, 23%). $[\alpha]_D$ −13° (*c* 0.23, $CHCl_3$);$^1$H NMR ($CDCl_3$): $\delta$ 5.87 (1H, d, $J_{3,2}$ = 8.9 Hz, H-3), 5.74 (1H, dd, $J_{5,6b}$ = 8.2, $J_{5,6a}$ = 2.2 Hz, H-5), 5.46 (1H, ddd, $J_{2,1a}$ = 6.6, $J_{2,1b}$ = 8.5 Hz, H-2), 4.54 (1H, dd, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.22 (1H, dd, H-6b), 3.18 (1H, dd, $J_{1a,1b}$ = 9.8 Hz, H-1a), 2.94 (1H, dd, H-1b), 2.15, 2.14, 2.12, 2.05, 2.01 (15H, 5s, 5 × OCOC*H*$_3$). $^{13}$C NMR ($CDCl_3$): $\delta$ 170.87, 170.21, 169.80, 169.38, 169.19 (5 × O*C*═OCH3), 86.01 (C-4), 80.48 (C-3), 74.98 (C-2), 73.66 (C-5), 64.26 (C-6), 21.76 (C-1), 21.68, 21.13, 21.06, 20.92 (5 × OCO*C*H$_3$).

Elution (hexanes/EtOAc, 1:1, $R_f$ = 0.44) of the more polar component provided compound **10** as pale yellow oil (49 mg, 21%). $[\alpha]_D$ +92° (*c* 1.1, $CHCl_3$); $^1$H NMR ($CDCl_3$): $\delta$ 5.90 (1H, dd, $J_{5,6b}$ = 7.4, $J_{5,\ 6a}$ = 2.6 Hz, H-5), 5.65 (1H, d, $J_{3,2}$ = 9.5 Hz, H-3), 5.43 (1H, ddd, $J_{2,1b}$ = 9.4, $J_{2,1a}$ = 6.5 Hz, H-2), 4.82 (1H, dd, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.29 (1H, dd, H-6b), 3.18 (1H, dd, $J_{1a,1b}$ = 9.4 Hz, H-1a), 2.77 (1H, dd, H-1b), 2.12, 2.07, 2.06, 2.04 (15H, 5s, 5 × OCOC*H*$_3$). $^{13}$C NMR ($CDCl_3$): $\delta$ 170.68, 170.32, 169.67, 169.45, 169.28 (5 × O*C*═OCH3), 82.48 (C-4), 76.06 (C-3), 75.84 (C-2), 72.71 (C-5), 63.96 (C-6), 21.94 (C-1), 21.05, 21.01, 20.98, 20.83, 20.46 (5 × OCO*C*H$_3$). Anal. Calcd for $C_{16}H_{22}O_{10}Se$ (isomers **8** and **10**): C, 42.39; H, 4.89. Found: C, 42.59; H, 5.06.

**Pummerer Rearrangement of 1,4-Anhydro-2,3,5,6-tetra-*O*-acetyl-4-seleno-D-galactitol (2).** Compound **2** (110 mg, 0.28 mmol) was subjected to the reaction conditions described in general procedures (a) and (c). TLC analysis and $^1$H NMR showed that the same products reported above were obtained.

**Rearrangement of 1,5-Anhydro-2,3,4-tri-*O*-acetyl-4-seleno-D-xylitol (4).** Compound **4** (150 mg, 0.46 mmol) was subjected to the reaction conditions described in general procedures (a) and (b). The residue was purified by column chromatography (hexanes/EtOAc, 1:1, $R_f$ = 0.47) to give the product **13** as a colorless oil (163 mg, 92%) in an $\alpha$:$\beta$ ratio of 1:6.5. $^1$H NMR ($CDCl_3$) data for $\beta$-**13**: $\delta$ 6.06 (1H, d, $J_{1,2}$ = 9.3 Hz, H-1), 5.47 (1H, t, $J_{3,2}$ = $J_{3,4}$ = 9.2 Hz, H-3), 5.20 (1H, ddd, $J_{4,5a}$ = 9.8, $J_{4,5b}$ = 4.8 Hz, H-4), 5.05 (1H, t, H-2), 2.88−2.76 (2H, m, H-5a, H-5b), 2.06, 2.03, 2.02, 2.01 (12H, 4s, 4 × OCOC*H*$_3$).$^{13}$C NMR ($CDCl_3$): $\delta$ 169.97, 169.69, 169.46, 169.06 (4 × O*C*═OCH$_3$), 74.27 (C-1), 73.15 (C-3), 72.81 (C-2), 64.74 (C-4), 21.07, 20.89, 20.74 (4 × OCO*C*H$_3$), 19.89 (C-5). Anal. Calcd for $C_{13}H_{18}O_8Se$: C, 40.96; H, 4.76. Found: C, 40.66; H, 4.80.

**Pummerer Rearrangement of 1,5-Anhydro-2,3,4-tri-*O*-acetyl-4-seleno-D-xylitol (4).** Compound **4** (100 mg, 0.31 mmol) was subjected to the reaction conditions described in general procedures (a) and (c). TLC analysis and $^1$H NMR showed that the same products as reported above were obtained.

**Rearrangement of 1,4-Anhydro-2,3,5,6-tetra-*O*-acetyl-4-thio-D-galactitol (1).** Compound **1** (150 mg, 0.43 mmol) was subjected to the reaction conditions described in general procedures (a) and (b). TLC analysis of the reaction mixture showed four components. Elution of the least polar component after column chromatography (hexanes/EtOAc, 1:1, $R_f$ = 0.62) gave compound **15** as a colorless oil. $[\alpha]_D$ −44° (c 0.18, $CHCl_3$); $^1$H NMR ($CDCl_3$) data for **15** (13.5 mg, 11%): $\delta$ 7.27 (1H, d, H-1), 6.89 (1H, d, $J_{2,1}$ = 5.5 Hz, H-2), 6.32 (1H, dd, $J_{5,6a}$ = 3.9, $J_{5,6b}$ = 7.5 Hz, H-5), 4.39 (1H, dd, $J_{6a,6b}$ = 11.8 Hz, H-6a), 4.30 (1H, dd, H-6b), 2.33, 2.09, 2.07 (9H, 3s, 3 × OCOC*H*$_3$). $^{13}$C NMR ($CDCl_3$): $\delta$ 170.72, 169.96, 169.01 (3 × *C*═O), 145.187 (C-3), 124.69 (C-1), 123.94 (C-4), 122.34 (C-2), 65.74 (C-5), 65.17 (C-6), 21.10, 21.00, 20.95 (3 × *C*H$_3$). EI−HRMS Calcd for $C_{12}H_{14}O_6S$ (M+): *m*/*z* 286.0511. Found: *m*/*z* 286.0515.

The second component ($R_f$ = 0.48) was found to be recovered starting material **1** (24 mg, 16%).

The third and most polar fourth component ($R_f$ values ranging from 0.4 to 0.42 in hexanes/EtOAc, 1:1) containing compounds **16**, **17**, and **18** were difficult to separate completely; hence, their combined yield of 62% (108 mg) is reported rather than their individual yields. Almost pure fractions of the third component were combined to yield mainly compound **16** as a colorless oil. $^1$H NMR data for compound **16** ($CDCl_3$): $\delta$ 6.00 (1H, d, $J_{3,2}$ = 7.6 Hz, H-3), 5.64 (1H, dd, $J_{5,6b}$ = 8.6, $J_{5,6a}$ = 2.3 Hz, H-5), 5.27 (1H, ddd, $J_{2,1a}$ = 6.3, $J_{2,1b}$ = 7.5 Hz, H-2), 4.61 (1H, dd, $J_{6a,6b}$ = 11.9 Hz, H-6a), 4.23 (1H, dd, H-6b), 3.21 (1H, dd, $J_{1a,1b}$ =10.8 Hz, H-1a), 3.12 (1H, dd, H-1b), 2.16, 2.12, 2.09, 2.06, 2.02 (15H, 5s, 5 × OCOC*H*$_3$). $^{13}$C NMR ($CDCl_3$): $\delta$ 170.81, 170.26, 169.74, 169.44, 169.38 (5 × *C*═O), 93.73 (C-4), 79.11 (C-3), 75.70 (C-2), 73.17 (C-5), 64.15 (C-6), 31.63 (C-1), 22.02, 21.08, 21.04, 21.03, 20.95 (5 × *C*H$_3$).

Almost pure fractions of the fourth component after column chromatography (hexanes/EtOAc, 1:1) gave a mixture of compounds **17** and **18** in a 1:2.2 ratio.$^1$H NMR and $^{13}$C NMR ($CDCl_3$) data for **17** were consistent with the literature.[21]

$^1$H NMR ($CDCl_3$) data for **18**: $\delta$ 5.85 (1H, dd, $J_{5,6a}$ = 2.7, $J_{5,6b}$ = 7.1 Hz, H-5), 5.72 (1H, d, $J_{3,2}$ = 8.7 Hz, H-3), 5.48 (1H, ddd, $J_{2,1a}$ = 7.2, $J_{2,1b}$ = 8.2 Hz, H-2), 4.72 (1H, dd, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.28 (1H, dd, H-6b), 3.31 (1H, dd, $J_{1a,1b}$ = 10.5 Hz, H-1a), 2.72 (1H, dd, H-1b), 2.12, 2.07 (15H, 5s, 5 × OCOC*H*$_3$).$^{13}$C NMR ($CDCl_3$): $\delta$ 170.73, 170.45, 169.63, 169.35, 168.95 (5 × *C*═O), 89.64 (C-4), 76.01 (C-3), 75.84 (C-2), 72.23 (C-5), 63.35 (C-6), 29.52 (C-1), 22.00, 21.04, 21.00, 20.98, 20.88 (5 × *C*H$_3$). Anal. Calcd for $C_{16}H_{22}O_{10}S$ (as a mixture of isomers **16**, **17**, and **18**): C, 47.29; H, 5.46. Found: C, 46.90; H, 5.16.

**Pummerer Rearrangement of 1,4-Anhydro-2,3,5,6-tetra-*O*-acetyl-4-thio-D-galactitol (1).** Compound **1** (100 mg, 0.38 mmol) was subjected to the reaction conditions described in general procedures (a) and (c). TLC analysis and $^1$H NMR showed that the same products reported above were obtained.

**Pummerer Rearrangement of 1,5-Anhydro-2,3,4-tri-*O*-acetyl-5-thio-D-xylitol (3).** Compound **3** (150 mg, 0.54 mmol) was subjected to the reaction conditions described in general procedures (a) and (c). The residue was purified by column chromatography (hexanes/EtOAc, 1:1, $R_f$ = 0.46) to give **24** as a white solid (148 mg, 82%) in an $\alpha$:$\beta$ ratio of 1:4. $^1$H NMR ($CDCl_3$) data for $\beta$-**24**: $\delta$ 5.83 (1H, d, $J_{1,2}$ = 8.8 Hz, H-1), 5.33 (1H, t, $J_{3,2}$ = $J_{3,4}$ = 8.6 Hz, H-3), 5.11−5.03 (2H, m, H-2, H-4), 2.95 (1H, dd, $J_{5a,5b}$ = 13.8, $J_{5a,4}$ = 3.9 Hz, H-5a), 2.72 (1H, dd, $J_{5a,4}$ = 9.5 Hz, H-5b), 2.07, 2.04, 2.03, 2.02 (12H, 4s, 4 × OCOC*H*$_3$).$^{13}$C NMR ($CDCl_3$): $\delta$ 170.02, 169.73, 169.51, 160.04 (4 × O*C*═OCH$_3$), 73.21 (C-1), 72.43 (C-3), 72.02 (C-2), 71.98 (C-4), 27.82 (C-5), 21.03, 20.86, 20.77, 20.75 (4 × OCO*C*H$_3$). Anal. Calcd for $C_{13}H_{18}O_8S$: C, 46.70; H, 5.43. Found: C, 46.59; H, 5.32.

**1,5-Anhydro-2,3,4-tri-*O*-acetyl-5-thio-D-xylitol-*S*-oxide (20).** To a solution of the thioxylitol **3** (180 mg, 0.65 mmol) in MeOH (20 mL) at 0 °C was added a solution of $NaIO_4$ (210 mg, 0.98 mmol, 1.5 equiv) in water (10 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and then allowed to warm to rt for 2 h. The mixture was then diluted with water (50 mL) and extracted with $CHCl_3$ (3 × 20 mL). The organic extracts were combined, dried over anhydrous $Na_2SO_4$, and concentrated to give a white solid that was purified by flash chromatography (EtOAc) to give the sulfoxide as an inseparable mixture of diastereomers as a white powder (172 mg, 90%). $^{13}$C NMR ($CDCl_3$) for major isomer (*ax*)-1,5-anhydro-2,3,4-tri-*O*-acetyl-5-thio-D-xylitol-*S*-oxide (**20**): $\delta$ 170.15, 169.34 (3 × O*C*═OCH3), 72.84 (C-3), 66.01 (C-2, C-4), 48.59 (C-1, C-5), 20.96, 20.88 (3 × OCO*C*H$_3$). Anal. Calcd for $C_{11}H_{16}O_7S$: C, 45.20; H, 5.52. Found: C, 45.28; H, 5.44. The $^1$H

NMR and IR spectroscopic data were identical to those of the sulfoxide isolated after ozonization (Table S2).

**1,4-Anhydro-2,3,5,6-tetra-*O*-acetyl-4-thio-D-galactitol-(*R*,*S*)-*S*-oxide (21).** To a solution of the thiogalactitol **1** (240 mg, 0.68 mmol) in MeOH (20 mL) at 0 °C was added a solution of $NaIO_4$ (220 mg, 1.02 mmol, 1.5 equiv) in water (10 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and then allowed to warm to rt for 2 h. The mixture was then diluted with water (50 mL) and extracted with $CHCl_3$ (3 × 20 mL). The organic extracts were combined, dried over anhydrous $Na_2SO_4$, and concentrated to give a white solid that was purified by flash chromatography (EtOAc) to give the sulfoxide as an inseparable mixture of diastereomers as a white powder (230 mg, 92%). $^{13}C$ NMR ($CD_2Cl_2$) for major isomer 1,4-anhydro-2,3,5,6-tetra-*O*-acetyl-4-thio-D-galactitol-(*S*)-*S*-oxide (**21**): $\delta$ 172.13, 171.76, 171.48, 171.30 (4 × O*C*═OCH3), 77.87 (C-5), 77.71 (C-3), 75.01 (C-2), 70.06 (C-4), 65.08 (C-6), 55.59 (C-1), 22.45, 22.40, 22.29 (4 × OCO*C*H$_3$). Anal. Calcd for $C_{14}H_{20}O_9S$: C, 46.15; H, 5.53. Found: C, 46.34; H, 5.67. The $^1H$ NMR and IR spectroscopic data were identical to those of the sulfoxide isolated after ozonization (Table S2).

**Pummerer Rearrangement of 1,5-Anhydro-2,3,4-tri-*O*-acetyl-5-thio-D-xylitol-*S*-oxide (20).** Treatment of the mixture of sulfoxides **20** under the reaction conditions described in general procedure (c) gave compound **24** as a white solid in an $\alpha$:$\beta$ ratio of 1:4, the same ratio as observed before.

**Pummerer Rearrangement of 1,4-Anhydro-2,3,5,6-tetra-*O*-acetyl-4-thio-D-galactitol-(*R*,*S*)-*S*-oxide (21).** Treatment of the mixture of sulfoxides **21** under the reaction conditions described in general procedure (c) gave compounds **15**, **16**, **17**, and **18** in a 1:6:1:2 ratio.

**1,4-Anhydro-2,3,5,6-tetra-*O*-acetyl-4-thio-D-galactitol-*S*-sulfone (25).** A mixture of the thiogalactitol **1** (200 mg, 0.58 mmol) and MCPBA (68% purity, 250 mg, 2.5 equiv) was dissolved in dry $CH_2Cl_2$ (40 mL) and stirred at room temperature for 2 h. The reaction mixture was then quenched with sodium thiosulfate solution and extracted with $CH_2Cl_2$ (3 × 20 mL).The organic extracts were washed with saturated $NaHCO_3$ solution (3 × 20 mL), combined, dried over anhydrous $Na_2SO_4$, and concentrated to give a white solid that was purified by flash chromatography (EtOAc) to give the sulfone as a white solid (210 mg, 95%). $^1H$ NMR ($CDCl_3$): $\delta$ 5.51 (1H, ddd, H-5), 5.40 (1H, dd, $J_{3,2} = J_{3,4} = 4.2$ Hz, H-3), 5.35 (1H, ddd, H-2), 4.53 (1H, dd, $J_{6a,6b} = 12.6$, $J_{6a,5} = 3.4$ Hz, H-6a), 4.17 (1H, dd, $J_{6b,5} = 4.7$ Hz, H-6b), 3.67 (1H, dd, $J_{1a,1b} = 14.1$, $J_{1a,2} = 6.1$ Hz, H-1a), 3.61 (1H, dd, $J_{4,5} = 9.9$ Hz, H-4), 3.35 (1H, dd, $J_{1b,2} = 3.8$ Hz, H-1b), 2.15, 2.12, 2.08 (12H, 4s, 4 × OCOC*H*$_3$).$^{13}C$ NMR ($CDCl_3$): $\delta$ 170.29, 169.53, 169.40, 169.05 (4 × *C*═O), 72.84 (C-5), 70.39 (C-3), 68.22 (C-2), 65.57 (C-4), 62.85 (C-6), 55.10 (C-1), 20.76, 20.69, 20.62, 20.59 (4 × *C*H$_3$). IR ($CH_2Cl_2$ film): 1265 cm$^{-1}$(S═O asymm. str.), 1136 cm$^{-1}$ (S═O sym. str.). Anal. Calcd for $C_{14}H_{20}O_{10}S$: C, 44.21; H, 5.30. Found: C, 44.41; H, 5.26.

**1,5-Anhydro-2,3,4-tri-*O*-acetyl-5-thio-D-xylitol-*S*-sulfone (26).** A mixture of the thioxylitol **3** (150 mg, 0.54 mmol) and MCPBA (68% purity, 235 mg, 2.5 equiv) was dissolved in dry $CH_2Cl_2$ (40 mL) and stirred at rt for 2 h. The reaction mixture was then quenched with sodium thiosulfate solution and extracted with $CH_2Cl_2$ (3 × 20 mL). The organic extracts were washed with saturated $NaHCO_3$ solution (3 × 20 mL), combined, dried over anhydrous $Na_2SO_4$, and concentrated to give a white solid that was purified by flash chromatography (EtOAc) to give the sulfone **26** as a white solid (165 mg, 98%). $^1H$ NMR ($CDCl_3$): $\delta$ 5.35−5.29 (3H, m, H-2, H-3, H-4), 3.60−3.53 (2H, m, H-1a, H-5a), 3.25−3.16 (2H, m, H-1b, H-5b), 2.08, 2.06 (9H, 2s, 3 × OCOC*H*$_3$). $^{13}C$ NMR ($CDCl_3$): $\delta$ 169.56, 169.01 (3 × *C*═O), 72.05 (C-3), 66.74 (C-2, C-4), 52.78 (C-1, C-5), 20.57, 20.49 (3 × *C*H$_3$). IR ($CH_2Cl_2$ film): 1265 cm$^{-1}$ (S═O asymm. str.), 1215 cm$^{-1}$ (S═O sym. str.). Anal. Calcd for $C_{11}H_{16}O_8S$: C, 42.85; H, 5.23. Found: C, 42.92; H, 5.16.

**Preparation of Stock Solutions for the Chemiluminescence Reactions.** A stock solution of the thiogalactitol **1** (670 mg, 1.9 mmol) in $CH_2Cl_2$ (200 mL) was prepared, and 20 mL portions (0.19 mmol) of this solution were used for the chemiluminescence reactions. Similarly a stock solution of rubrene (10 mg, 0.02 mmol) in $CH_2Cl_2$ (100 mL) was prepared, and 5 mL portions (0.001 mmol, 0.005 equiv) were used in the following experiments. The rubrene stock solution was kept cold in dry ice.

**General Procedure (d) for the Chemiluminescence Reactions.** Ozone was bubbled through a solution of the thiogalactitol **1** in $CH_2Cl_2$, placed in a flask fitted with a thermometer, and cooled to −78 °C, until the latter turned blue. This solution was then purged by passing a stream of nitrogen through it for 20 min. The blue color of the solution disappeared after around 5 min of nitrogen purging.

**Control Experiment 1.** To verify the efficiency of the nitrogen purging, ozone was bubbled through $CH_2Cl_2$ (20 mL) at −78 °C until the latter turned blue. The solvent was then purged for 20 min, after which a portion of rubrene was added. The intense orange color of rubrene persisted but disappeared when ozone was bubbled through the solution again.

Control experiments 2 and 3 were performed to ensure that neither the starting material **1** nor the resulting product **21** caused any discoloration of rubrene.

**Control Experiment 2.** To a portion of thiogalactitol **1** at −78 °C and under a nitrogen atmosphere was added a portion of rubrene. The mixture was kept at −78 °C for 10 min, after which the cooling bath was removed and the mixture was allowed to warm to room temperature. The orange color of the solution persisted throughout the process.

**Control Experiment 3.** To a portion of the sulfoxide **21** at −78 °C and under a nitrogen atmosphere was added a portion of rubrene. The mixture was kept at −78 °C for 10 min, after which the cooling bath was removed and the mixture was allowed to warm to room temperature. The orange color of the solution persisted throughout the process.

**Control Experiment 4.** Ozone was bubbled through a portion of the stock solution of rubrene (20 mL) at −78 °C, and the intense orange color immediately started to fade until the solution turned colorless and eventually light blue, indicating an excess of ozone.

**Chemiluminescence Reaction 1.** The thiogalactitol **1** was subjected to the reaction conditions described in general procedure (d). A portion of the cold rubrene solution was then added, and the mixture was stirred at −75 °C and under nitrogen for 10 min, after which the intense orange color was still present. The cooling bath was then removed, and the mixture slowly was allowed to warm. The color started to fade at −55 °C and completely disappeared at −45 °C.

**Chemiluminescence Reaction 2.** The thiogalactitol **1** was subjected to the reaction conditions described in general procedure (d). Acetic anhydride (5 equiv), previously precooled in dry ice, was added, and the mixture was stirred at −75 °C for 5 min, after which a portion of the cold rubrene solution was added and the mixture stirred at −75 °C for another 10 min. The intense orange color persisted even when the cooling bath was removed and the mixture was slowly allowed to warm to room temperature over 2 h. The reaction proceeded to give rearranged products as judged by TLC analysis and $^1H$ NMR of the crude mixture obtained after workup.

**Spin Trapping Experiments.** Ozone was bubbled through a solution of the thiogalactitol **1** in $CH_2Cl_2$ (10 mL, 10 mM), cooled to −78 °C, until the latter turned blue. This solution was then purged by passing a stream of nitrogen through it for 20 min. DMPO (0.5 mmol) was then added, and the dry ice/acetone bath was removed. The reaction mixture was allowed to stir for 5 min before some of it was transferred to a flame-sealed 9" Pasteur pipet, fitted into the cavity of the EPR spectrometer.

In the second experiment, acetic anhydride (5 equiv) was added at −78 °C to the purged ozonized reaction mixture of thiogalactitol **1** (10 mL, 10 mM) and the reaction mixture stirred at −78 °C for approximately 3 min before the addition of DMPO. The dry ice/acetone bath was then removed, and the reaction mixture was allowed to stir

for 5 min. The same procedure as that above was then used for acquisition of the EPR spectrum.

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**Supporting Information Available:** Selected NMR spectra illustrating typical $^1$H NMR and 1D-transient NOE experiments for compounds **7**−**10**, **16**−**18**, low temperature $^1$H NMR and $^{13}$C NMR spectra for the thiogalactitol derivatives study, as well as $^1$H NMR spectra for compounds **20**, **21**, **25**, and **26**, data table consisting of $^1$H NMR chemical shifts, coupling constants and IR data of the oxides **20**−**23** (12 pages). This material is available free of charge via the Internet at http://pubs.acs.org.

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