Synthesis Enabled Investigations into the Acidity and Stability of Atmospherically-relevant Isoprene-derived Organosulfates

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Abstract. Atmospheric organosulfates are a class of compounds present in secondary organic aerosols that are thought to serve as a marker of anthropogenic pollution. Organosulfates derived from isoprene epoxydiol (IEPOX) have been shown to be the most abundant and ubiquitous class of these compounds, but a lack of authentic standards that account for regiochemical and stereochemical derivatives has made the study of these compounds challenging. Herein we present a synthetic protocol to access the suite of the eight IEPOX-derived organosulfates that utilizes prenol as a common starting material and affords each compound as an ammonium salt. Our method generates either *syn* or *anti* stereochemical isomers with complete control over sulfate-ester regiochemistry. We present an evaluation of the inherent acidities of each compound by measuring aqueous pH of organosulfate solutions. The *syn* and *anti* tertiary organosulfate isomers demonstrated the lowest acidity (2.45 and 2.33, respectively) compared to the primary and secondary regioisomers of the suite. We also present preliminary stability data for each organosulfate compound utilizing aqueous time-point NMR spectroscopy. Primary and secondary organosulfates demonstrated no spectral change under both neutral and acidic conditions. The *syn* and *anti* tertiary organosulfates showed decomposition in approximately 30 days under aqueous conditions, and 10 and 12 days respectively under acidic conditions. The results presented provide new insights into the physical properties and atmospheric fate of IEPOX-derived organosulfates that should be valuable for climate modeling and future atmospheric studies.

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Introduction. The study of atmospheric aerosols and their relative influence on the climate system continues to be an area of intense scientific investigation in order to reduce the uncertainty concerning their formation, composition, and climate relevant effects.[1-5] It has been shown that secondary organic material (SOM) – formed by the atmospheric oxidation of biogenic and anthropogenic volatile organic compounds – represents a substantial fraction of organic matter in the atmosphere.[6] Although the constituents of biogenically-derived SOM have become an ongoing topic of interest within the atmospheric community, their climate relevant effects and physical properties remain poorly understood. Even more elusive are the interactions between SOM and the byproducts of anthropogenic pollution, such as nitrogen oxides and sulfur dioxide, which have been shown to serve as acidic seed particles in the atmosphere[2, 7-8] and thus enhance SOM formation.[9]

The volatile terpene isoprene (**1**, **Figure 1**) represents one of the most abundant biogenic volatile organic compounds (BVOCs) emitted into the atmosphere in amounts of over 500 Tg/year.[10-11] A significant fraction of SOM derived from isoprene is formed by photooxidation involving hydroxyl radicals, a process estimated to account for up to 50% of the global SOM budget.[12-15] The mechanism of isoprene photooxidation has been studied intensively,[16] suggesting that isomeric isoprene-derived epoxydiols (i.e., IEPOX isomers **2**–**4**) are the dominant isoprene-derived oxidation products under low NO_x conditions.

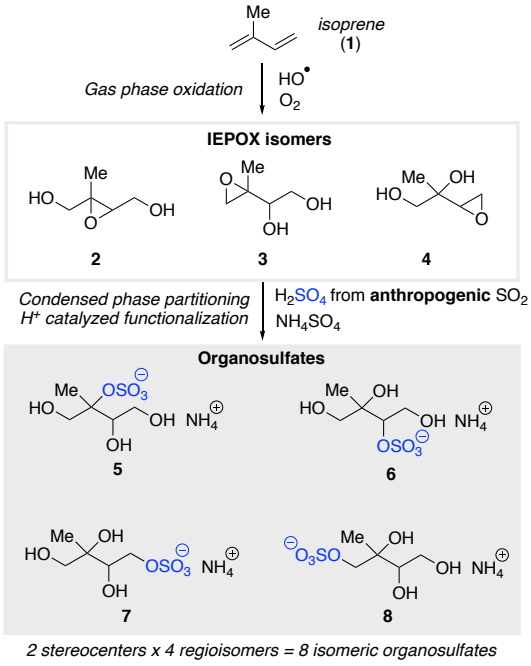

Figure 1. The gas-phase oxidation of isoprene **1** results in the formation of various isomers of isoprene epoxydiols (IEPOX) such as **2**, **3**, and **4**. The interaction of these oxidation products with acidic species and anthropogenic pollutants such as sulfuric acid and ammonium sulfate results in formation of a family of organosulfate compounds **5**, **6**, **7** and **8** as regiochemical and stereochemical isomers.

Gas-phase IEPOX isomers are thought to be key intermediates in the formation of low volatility products that form isoprene-derived SOM under low NO_x conditions.[16-20] Previously, we have demonstrated the surface activity of the various isomers of the IEPOX series, the most surface active being the long-lived and highly abundant *trans*-β-IEPOX (i.e., **2**).[21] It has been suggested that in the presence of acidic sulfate seed particles, gas phase IEPOX isomers partition into the condensed aerosol phase through an acid-catalyzed epoxide opening and subsequent nucleophilic attack of sulfate anion, resulting in the formation of sulfate ester-containing compounds known as organosulfates (i.e., **5**–**8**).[8, 16]

Organosulfates have become an area of focus within the atmospheric science community due to their frequency of detection and observed abundance in various laboratory and field studies.[22-25] The most abundant and ubiquitous organosulfates are considered to be those derived from isoprene, specifically from IEPOX.[26-30] The organosulfate derived from IEPOX and 2-methyltetraol oxidation products (m/z 215) was identified as one of the most abundant single organic compounds detected in atmospheric aerosols.[16, 31-32] In a recent study from Hettiyadura and co-workers analyzing organosulfates detected in Centreville, Alabama via hydrophilic interaction liquid chromatography coupled to triple quadrupole mass spectrometry, it was suggested that 2-methyltetraol sulfate, or IEPOX-derived organosulfate, accounted for 42–62% of detected bisulfate ion signal. Moreover, because the main source of sulfur dioxide in the atmosphere is emitted through fossil fuel combustion, the presence of atmospheric constituents bearing one or more sulfate ester group has been speculated to represent SOM that has been influenced by anthropogenic pollution. Consequently, the occurrence of organosulfates could likely serve as an effective molecular marker for anthropogenically-influenced SOM.

Although detection of the characteristic mass of the IEPOX-derived organosulfate has been demonstrated by a variety of laboratory and field studies,[32-34] both the position of the sulfate ester on the parent tetraol and the relative stereochemistry of the compounds remain unknown. While it has been suggested that the tertiary isomer of the IEPOX-derived organosulfate forms predominantly as a consequence of the proposed mechanism of nucleophilic attack,[16] the various organosulfate regiochemical isomers (**Figure 1**, **5**–**8**) may have different rates of hydrolysis and therefore different atmospheric lifetimes, properties and significance.[35-36] Analysis of homogenous forms of each IEPOX-derived sulfate isomer is essential for accurate comparison to field studies,[33] but such studies have been limited due to ineffective access to the desired compounds. Recently,

Surratt and co-workers disclosed a synthetic method to access two of the four regioisomeric IEPOX-derived organosulfates as diastereomeric potassium salts for use as standards.[37] While this work of preparing these standards has proven useful in the atmospheric community, preparation of a wider range of possible stereochemical and regiochemical of these compounds will be helpful in fostering more highly specific comparisons to field studies and beyond. As an initial step towards such integrated comparisons, we now report a synthetic strategy capable of accessing all eight isomers of the IEPOX-derived organosulfates as atmospherically-relevant ammonium salts (i.e., **5**–**8**). We also provide preliminary analytical data specific to each organosulfate concerning their lifetimes in both neutral and acidic media. In addition to this work, we believe these compounds will enable valuable quantitative insight into the presence of these compounds and their ultimate fate in the atmosphere.

Results and Discussion. ***Development of a Regioselective and Stereocontrolled Synthesis of IEPOX-derived Organosulfates.*** From a synthetic perspective, the targeted IEPOX-derived organosulfates presented several distinct challenges. Foremost of these challenges was to design a flexible route capable of installing the requisite sulfate group at any one of the four unique hydroxyl groups with complete regioselectivity. Compounding the complexity of the regiochemistry problem was that each sulfate ester can exist as one of two potential stereoisomers due to the relative configuration of the two stereocenters within the compounds. These considerations lead to eight potential organosulfate isomers comprising two sets of four regioisomeric *syn* or *anti* diastereomers. While conceivable, due to their mechanism of formation it is unlikely that these compounds exist in optically enriched form in the atmosphere; therefore, we limited our approach to accessing the eight possible racemates rather than the 16 possible enantiomerically pure isomers. If desired, however, the established approach could be readily

modified to achieve this outcome if such questions of chirality become important during future work.

Our initial synthetic considerations focused on determining the best method for installing the requisite sulfate groups. While the sulfate ester moiety can easily be installed by treating alcohols with dicyclohexylcarbodiimide and sulfuric acid, this method commonly leads to mixtures of products, and is typically only viable for the final step of a synthesis.[38] More recently, the use of protected sulfating reagents has become prevalent, since they allow for installation of a protected sulfate ester capable of surviving future chemical transformation prior to deprotection.[39] While highly versatile, these methods are often incompatible with more highly congested parent alcohols. On the other hand, SO_3•pyridine has been widely used for the direct and mild installation of sulfate esters onto a variety of alcohols. Consideration of these factors led us to design a synthesis wherein SO_3•pyridine would be used to sulfate an appropriately protected tetraol isoprene derivative. As well as employing appropriate sulfate ester installation strategies, we sought to devise a unified strategy to access both the *anti* and *syn* stereoisomers using prenol (**9**) as a common starting material, with stereocontrol arising from the mode of alkene dihydroxylation employed, and with regiocontrolled sulfation governed by a judicious choice of protecting groups.

Initially, we targeted the tertiary and secondary organosulfates sulfates possessing the *anti* stereochemistry (**Figure 2**). The synthesis commenced with a five-step sequence involving allylic oxidation and benzylation of prenol,[40] followed by epoxidation of the internal alkene using *m*CPBA to deliver epoxide **10** in 28% yield from **9**. Subjecting **10** to epoxide-opening under basic conditions using KOH:DMSO[41] yielded the desired *anti*-configured vicinal diol, which upon selective acetylation of the secondary hydroxyl group, delivered differentially protected tertiary alcohol **11** in high yield. With the free tertiary hydroxyl, alcohol **11** was uniquely poised to serve

as a divergent intermediate to access both the tertiary and secondary organosulfate isomers (i.e., *anti*-**5** and *anti*-**6**). Direct sulfation of **11** using SO_3•pyridine generated the fully protected sulfate **12** as a pyridine salt. To ensure our final product had the desired ammonium counterion, the pyridinium counterion was exchanged for ammonium by exposing **12** to 30% ammonium hydroxide, which also removed the acetyl group at the secondary position. The choice of the ammonium counterion was made due to the contention in the literature that the sulfate ester moiety found on atmospherically-relevant organosulfates is formed from the reaction of IEPOX with ammonium sulfate under acidic conditions.[8, 26, 42] Finally, global deprotection through hydrogenolysis afforded *anti*-**5** in good yield over 3 steps. To access the corresponding secondary species, alcohol **11** was converted into trisbenzyl derivative **13** by a triflic acid-catalyzed benzylation of the free tertiary alcohol using benzyl 2,2,2-trichloroacetimidate,[43] followed by removal of the acetyl group using potassium carbonate. As was the case for *anti*-**5**, a three-step procedure from **13** consisting of sulfation, installation of the desired ammonium counterion, and global hydrogenolysis afforded *anti*-**6** in reasonable yield. Due to the highly polar and hygroscopic nature of the organosulfate species, both the ammonium counterion installation and purification proved to be challenging when preparing these compounds as analytical standards. When using saturated sources of ammonium to install the ammonium counterion, such as ammonium chloride, carbonate, or sulfate, a substantial amount of ammonium impurity was seen via NMR spectroscopy. The aqueous solubility of the sulfate esters prevented purification by lyophilization and column chromatography once the ammonium counterion was installed. Faced with this logistical problem, we then attempted to install the ammonium counterion using volatile sources such as ammonium hydroxide, in which excess ammonium reagent would be removed under

vacuum. This idea proved successful, allowing clean installation of the sulfate group prior to global debenzylation as described above.

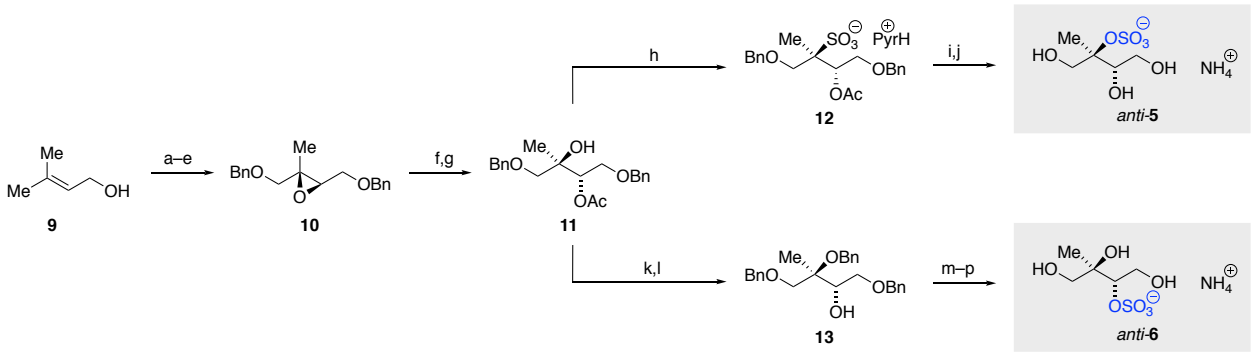

Figure 2. Synthesis of *anti*-configured tertiary and secondary organosulfates. Reagents and conditions: (a) BnBr (1.2 eq.), NaH (2 eq.), THF, 0 °C to room temp, 18 h; (b) SeO_2 (0.2 eq.), tBuOOH (2.0 eq.), salicylic acid (0.1 eq.), DCM, 19 h; (c) $NaBH_4$ (0.2 eq.), MeOH, 0 °C, 2h; 36% over 3 steps; (d) BnBr (1.2 eq.), NaH (2 eq.), THF, 0 °C to room temp, 18 h, 91%; (e) mCPBA (1.5 eq.), $NaHCO_3$ (5.0 eq.), DCM, 20 h, 85%; (f), KOH (50 eq.), DMSO, 120 °C, 24 hr, 64%; (g) DMAP (0.05 eq.), Ac_2O (1.05 eq.), DCM, 24 h, 85%; (h) SO_3Pyr (1.1 eq.), pyridine, 21 h; (i) NH_4OH (30% stock soln; 0.037 M wrt starting material); (j) Pd/C (0.15 eq.), H_2, MeOH, 24 h, 65% over 3 steps; (k) Benzyl 2,2,2-trichloroacetimidate (2.0 eq.), TfOH (0.5 eq.), DCM, 80%; (l) K_2CO_3 (1.5 eq.), MeOH, 21 h, 92%; (m) SO_3•Pyr (1.1 eq.), pyridine, 21 h; (n) NH_4OH (30% stock soln; 0.037 M wrt starting material); (o) Pd/C (0.15 eq.), H_2, MeOH, 24 h, 42% over 3 steps.

We next turned our attention to the two primary substituted *anti* organosulfate esters (i.e., *anti*-**7** and *anti*-**8**). In analogy to the prior synthesis of epoxide **10** (**Figure 2**), synthesis of *anti*-**7** began with a five-step protocol to covert prenol (**9**) into differentially protected epoxide **14** (**Figure 3**). Basic hydrolysis of the epoxide furnished the requisite *anti*-configured diol **15**, setting the stage for benzylidene formation and DDQ-mediated PMB ether cleavage to deliver primary alcohol **16** in 42% yield over the three steps. Sulfation using SO_3•Pyr, followed by counterion metathesis and exhaustive hydrogenolysis of benzyl and benzylidene groups gave *anti*-**7** in moderate yield over the three-steps from **16**. With respect to the remaining *anti*-**8**, modifying the aforementioned sequence by swapping the positions of the benzyl and PMB ethers to generate epoxide **17** (cf. epoxide **14**) enabled access to *anti*-**8** through an analogous sequence.

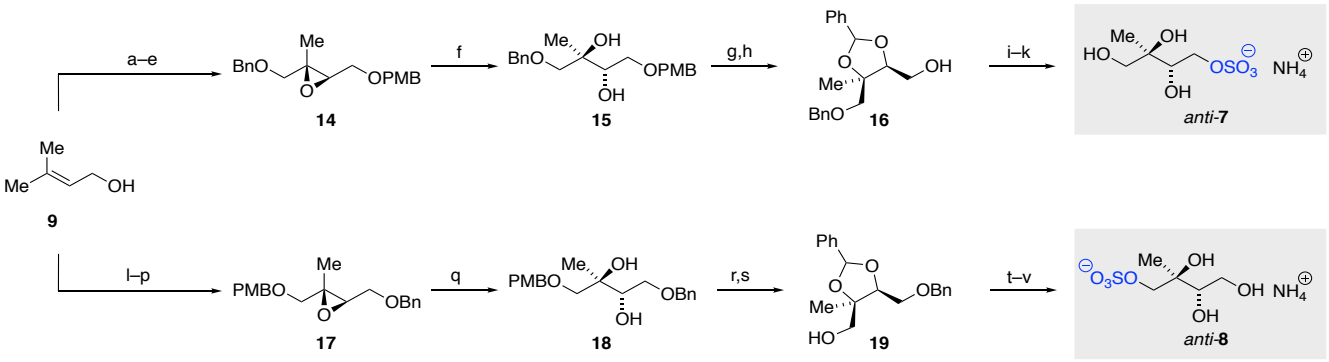

Figure 3. Synthesis of *anti*-configured primary organosulfates. Reagents and conditions: (a) PMBCl (1.2 eq.), NaH (2.0 eq.), THF, 0 °C then reflux, 18 h; (b) SeO_2 (0.2 eq.), tBuOOH (2.0 eq.), salicylic acid (0.1 eq.), DCM, 19 h; (c) $NaBH_4$ (0.2 eq.), MeOH, 0 °C, 2h; 36% over 3 steps; (d) BnBr (1.2 eq.), NaH (2 eq.), THF, 0 °C to room temp, 18 h, 78%; (e) mCPBA (1.5 eq.), $NaHCO_3$ (5.0 eq.), DCM, 20 h, 85%; (f), KOH (50 eq.), DMSO, 120 °C, 24 hr, 61%; (g) benzaldehyde (1.2 eq.), pTsOHH2O (0.02 eq.), $MgSO_4$ (1.4 eq.), DCM, 22 h; (h) DDQ (1.1 eq.), H_2O, DCM, 70% over 2 steps; (i) SO_3Pyr (1.1 eq.), pyridine, 21 h; (j) NH_4OH (30% stock soln; 0.037 M wrt starting material); (k) Pd/C (0.15 eq.), H_2, MeOH, 24 h, 51% over 3 steps; (l) BnBr (1.2 eq.), NaH (2 eq.), THF, 0 °C to room temp, 18 h; (m) SeO_2 (0.2 eq.), tBuOOH (2.0 eq.), salicylic acid (0.1 eq.), DCM, 19 h; (n) $NaBH_4$ (0.2 eq.), MeOH, 0 °C, 2h; 42% over 3 steps; (o) PMBCl (1.2 eq.), NaH (2.0 eq.), THF, 0 °C then reflux, 18 h, 66%; (p) mCPBA (1.5 eq.), $NaHCO_3$ (5.0 eq.), DCM, 20 h, 79%; (q) KOH (50 eq.), DMSO, 120 °C, 24 hr, 55%; %; (r) benzaldehyde (1.2

eq.), pTsOHH2O (0.02 eq.), $MgSO_4$ (1.4 eq.), DCM, 22 h; (s) DDQ (1.1 eq.), H_2O, DCM, 61% over 2 steps; (t) SO_3Pyr (1.1 eq.), pyridine, 21 h; (u) NH_4OH (30% stock soln; 0.037 M wrt starting material); (v) Pd/C (0.15 eq.), H_2, MeOH, 24 h, 55% over 3 steps.

Having established routes towards each of the four *anti*-disposed organosulfates, we wished to test the generality of our regioselective strategy by applying it to the synthesis of the corresponding *syn*-configured organosulfates (**Figures 4** and **5**). We envisioned that an analogous protecting group strategy to that used for accessing the *anti* compounds could be utilized for the desired *syn* species, with the only required modification being the method of alkene hydroxylation. To this end, *syn*-configured diol **20** was prepared from prenol (**9**) over five steps with the critical relationship between the two hydroxyl stereocenters deriving from a *syn*-specific OsO_4- catalyzed alkene dihydroxylation. Diol **20** was converted to tertiary alcohol **21** by selective acylation of the less hindered alcohol, establishing the common intermediate to access *syn*-**5** and *syn*-**6**. Preparation of each of these regioisomeric sulfates was accomplished without incident by employing the same series of transformations as detailed for the conversion of alcohol **11** into both *anti*-**5** and *anti*-**6** (cf. **Figure 2**). Finally, the remaining primary *syn*-regioisomers (i.e., *syn*-**7** and *syn*-**8**, **Figure 5**) were synthesized in a manner analogous to their *anti* counterparts (cf. **Figure 3**), with the only notable difference being the use of a TBS protecting group in place of a PMB group.

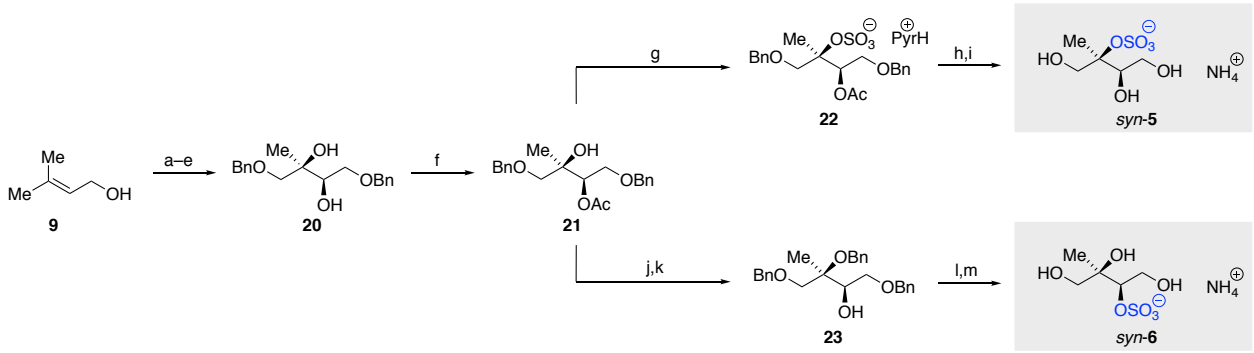

Figure 4. Synthesis of *syn*-configured tertiary and secondary organosulfates. Reagents and conditions: (a) BnBr (1.2 eq.), NaH (2 eq.), THF, 0 °C to room temp, 18 h; (b) SeO_2 (0.2 eq.), tBuOOH (2.0 eq.), salicylic acid (0.1 eq.), DCM, 19 h; (c) $NaBH_4$ (0.2 eq.), MeOH, 0 °C, 2h; 36% over 3 steps; (d) BnBr (1.2 eq.), NaH (2 eq.), THF, 0 °C to room temp, 18 h, 84%; (e) NMO (1.6 eq.), OsO_4 (2.5 w.t. % in *t*BuOH, 0.01 eq.), 1:1 THF:H_2O, 20 h, 92%; (f) DMAP (0.05 eq.), Ac_2O (1.05 eq.), DCM, 24 h, 94%; (g) SO_3•Pyr (1.1 eq.), pyridine, 21 h; (h) NH_4OH (30% stock soln; 0.037 M wrt starting material); (i) Pd/C (0.15 eq.), H_2, MeOH, 24 h, 84% over 3 steps; (j) Benzyl 2,2,2-trichloroacetimidate (2.0 eq.), TfOH (0.5 eq.), DCM, 80%; (k) K_2CO_3 (1.5 eq.), MeOH, 21 h, 88%; (l) SO_3Pyr (1.1 eq.), pyridine, 21 h; (m) NH_4OH (30% stock soln; 0.037 M wrt starting material); (n) Pd/C (0.15 eq.), H_2, MeOH, 24 h, 82% over 3 steps.

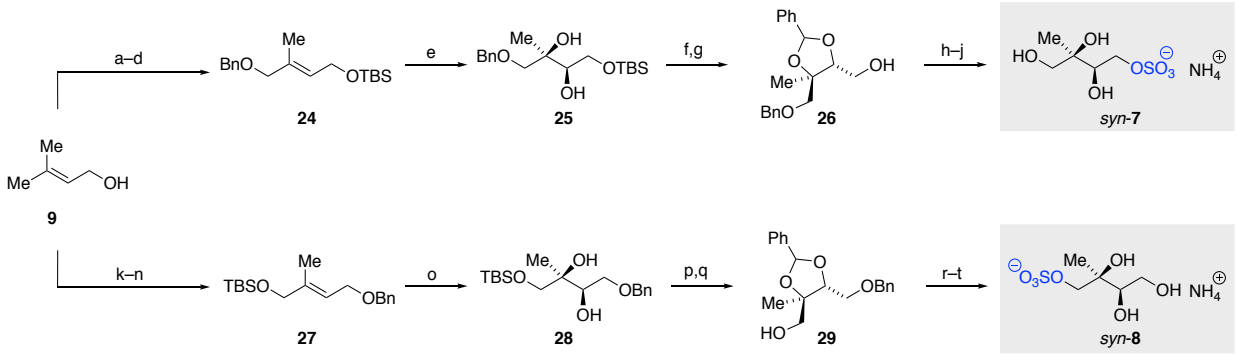

Figure 5. Synthesis of *syn*-configured primary organosulfates. Reagents and conditions: (a) TBSCl (1.1 eq.), DIPEA (1.8 eq.), DCM, 18 h; (b) SeO_2 (0.2 eq.), tBuOOH (2.0 eq.), salicylic acid (0.1 eq.), DCM, 19 h; (c) $NaBH_4$ (0.2 eq.), MeOH, 0 °C, 2h; 45% over 3 steps; (d) BnBr (1.2 eq.), NaH (2 eq.), THF, 0 °C to room temp, 18 h, 83%; (e) NMO (1.6 eq.), OsO_4 (2.5 w.t. % in *t*BuOH, 0.01 eq.), 1:1 THF:H_2O, 20 h, 78%; (f), benzaldehyde (1.2 eq.), pTsOHH2O (0.02 eq.), $MgSO_4$ (1.4 eq.), DCM, 22 h; (g) TBAF

(2.0 eq.), THF, 17 hours, 59% over 2 steps; (h) SO_3Pyr (1.1 eq.), pyridine, 21 h; (i) NH_4OH (30% stock soln; 0.037 M wrt starting material); (j) Pd/C (0.15 eq.), H_2, MeOH, 24 h, 64% over 3 steps; (k) BnBr (1.2 eq.), NaH (2 eq.), THF, 0 °C to room temp, 18 h; (l) SeO_2 (0.2 eq.), tBuOOH (2.0 eq.), salicylic acid (0.1 eq.), DCM, 19 h; (m) $NaBH_4$ (0.2 eq.), MeOH, 0 °C, 2h; 59% over 3 steps; (n) TBSCl (1.1 eq.), DIPEA (1.8 eq.), DCM, 18 h, 83%; (o) NMO (1.6 eq.), OsO_4 (2.5 w.t. % in *t*BuOH, 0.01 eq.), 1:1 THF:H_2O, 20 h, 77%; (p) benzaldehyde (1.2 eq.), pTsOHH2O (0.02 eq.), $MgSO_4$ (1.4 eq.), DCM, 22 h; (q) TBAF (2.0 eq.), THF, 17 hours, 64% over 2 steps; (r) SO_3Pyr (1.1 eq.), pyridine, 21 h; (s) NH_4OH (30% stock soln; 0.037 M wrt starting material); (t) Pd/C (0.15 eq.), H_2, MeOH, 24 h, 79% over 3 steps.

pH Dependence on Organosulfate Regiochemistry. With the newly synthesized IEPOX-derived organosulfates in hand (i.e., isomers **5**–**8**), we turned our attention to evaluating the intrinsic chemical properties of each discrete compound. Given that molecules functionalized with sulfate esters are often associated with higher potential acidity, as well as the postulated atmospheric transformation from IEPOX into relevant organosulfates occurring under acidic conditions, we first assessed the inherent acidity of our suite of organosulfates. Solutions of each organosulfate were prepared with concentrations of 0.1 M in deionized water and deuterium oxide, and acidity was measured for both sets of solutions using a pH meter (see SI for full table of measurements).

Shown in **Figure 6**, the specific regiochemical placement of the sulfate ester on each compound resulted in noticeable differences in measured pH, spanning a range from pH 3.1 to pH 2.0, equating to a 10-fold difference between the least and most acidic sulfates. Solutions of the primary sulfate esters (i.e., *syn*- and *anti*-**7** and **8**) were the least acidic, followed next by the secondary sulfates (i.e., *syn*- and *anti*-**6**) and then finally solutions of the tertiary sulfates afforded the most acidic solutions. Differences between the two diastereomeric series (*syn* vs. *anti*) were not significant, while all solutions of the organosulfates were markedly more acidic than solutions of ammonium sulfate and the corresponding non-sulfated tetraols (i.e., *syn* and *anti*-**30**). Given the importance of pH in governing various atmospheric processes such as heterogeneous reactions,

gas-to-particle partitioning, or physical changes to aerosol such as phase separation[44-47], the acidities of each discrete organosulfate solution may provide insight into their potential reactivities within the aerosol phase and postulated fate in the atmosphere. For example, it was shown by Riva and coworkers that the yield of SOA derived from isoprene was significantly enhanced in presence of acidic species, producing various isomeric organosulfates, with sulfates derived from 2-methyltetraols as the most abundant.[48]

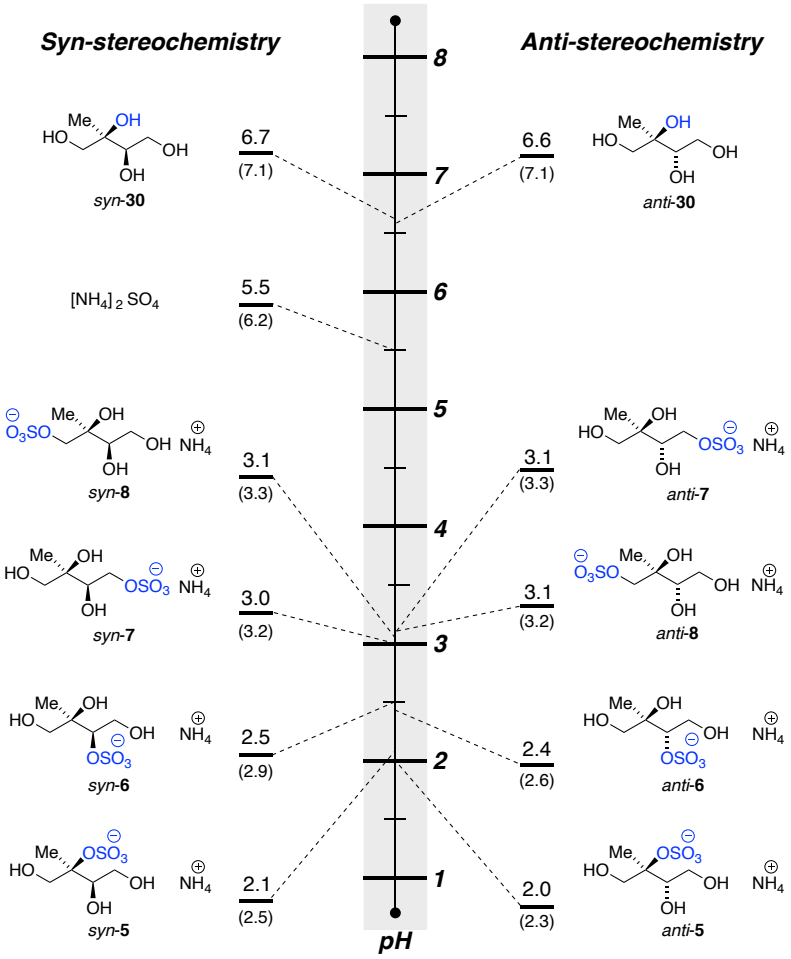

Figure 6. pH values for solutions of each synthesized organosulfate standard. Each solution was prepared as 0.1 M in deionized water; values shown in parentheses are pD values recorded from 0.1 M solutions in D_2O. The shown pH value is the average of three individual readings.

It is interesting that the most acidic solutions in the suite were derived from the tertiary sulfates (i.e., *syn*- and *anti*-**5**), which are thought to be the preeminent isoprene-derived sulfate ester containing species found in the atmosphere, and their presence likely influences the pH of the aerosol particles in which they are situated.

Evaluation of Organosulfate Stability using NMR Spectroscopy. The more sterically congested secondary and tertiary sulfates (i.e., **5** and **6**) are thought to be the dominant sulfate ester-bearing compounds in comparison to the corresponding primary sulfates due to the likely mechanism of epoxide opening under acidic conditions.[16, 35-36, 49] Given the importance of these species, investigations into their aqueous stability–whether an evaluation of decomposition rate or resultant product identification–are crucial for understanding the fate of these prevalent atmospheric species. Most of the work done to characterize and detect IEPOX-derived organosulfates and their fate in the atmosphere have relied on implementations of mass spectrometry. In 2010, Surratt and coworkers proposed a mechanistic rationale for the production of IEPOX-derived organosulfates as a function of acid-catalyzed uptake of IEPOX.[16] The authors utilized gas chromatography coupled with mass spectrometry and revealed several products as a result of epoxide opening under acidic conditions such as tetraols, hydroxylated ketones and sulfate esters, albeit without comparison to homogenous standards of the various tetraols and organosulfates. Further, this type of analysis precludes the direct identification of the corresponding regioisomers and stereoisomers of the IEPOX-derived organosulfates beyond identification of the canonical mass (m/z 215).

Beyond utilizing mass spectrometric methods, the use of nuclear magnetic resonance (NMR) spectroscopy has shown utility in detecting IEPOX-derived organosulfates. Elrod and coworkers disclosed a series of kinetic experiments utilizing various atmospherically relevant

IEPOX isomers in the presence of sulfate and nitrate and tracked the generation of the corresponding organosulfates and organonitrates.[35] These experiments elucidated the formation of primary and tertiary sulfate esters and their decomposition via NMR. Specifically, the primary organosulfates demonstrated relative inactivity after formation, while the tertiary species was subject to a slower acid-dependent hydrolysis reaction.

Though there have been several valuable studies concerning the stability of atmospheric compounds, such as organosulfates and other compounds influenced by anthropogenic pollution, many studies have been bound by use of model compounds or impure standards. Moreover, the decomposition products specific to each of the eight IEPOX-derived organosulfates has been challenging to study. With our unified approach to access these species in homogeneous form established, we set out to evaluate the stability of the IEPOX-derived organosulfates both in neutral and acidic conditions using NMR spectroscopy. To monitor the stability of each compound, each of the organosulfates synthesized in house were prepared as solutions in deuterium oxide (0.1 M) as well as 0.1 M d_2–sulfuric acid. The solutions were monitored by NMR in both hourly and daily time intervals dependent on the visibility of decomposition. All ^{1}H NMR spectra were collected on a Bruker 500 MHz spectrometer. **Figure 7** shows the overall lifetimes observed for each of the eight synthesized organosulfate isomers.

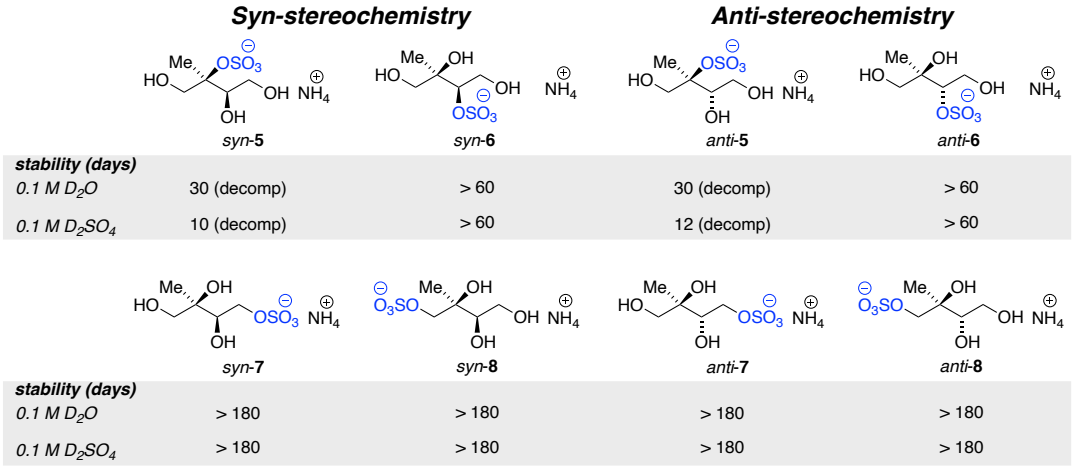

Figure 7. Comparison of estimated lifetimes of the suite of organosulfate isomers via ^{1}H NMR spectroscopy.

As expected in case of the primary organosulfates, both the *syn* and *anti* species (i.e., isomers **7** and **8**) were highly stable under neutral aqueous conditions for upwards of six months. Even when dissolved in d_2-sulfuric acid, the NMR spectra of the primary compounds were stagnant and not significantly changed. This is most likely due to the decreased steric hindrance experienced by the sulfate ester moiety, making the functional group resistant to hydrolysis or substitution. Surprisingly, the secondary species were also stable to both neutral and acidic conditions. Although these compounds are highly stable, their prevalence in the atmosphere is likely minimal due to the proposed epoxide opening mechanism, in which *trans*-β-IEPOX is protonated at the oxiryl oxygen, from which the intermediate could be subject to nucleophilic substitution.[16] Although attack at both the 2 and 3 position of the erythritol backbone is possible, the tertiary isomer is likely formed predominantly due to the more stable tertiary carbocation after the opening of the epoxide.

In the case of the tertiary organosulfates (i.e., *syn* and *anti* **5**), the stability was evaluated by monitoring the disappearance of the 3.63 ppm chemical shift of the methylene adjacent to the

sulfate ester group (see Supporting information). Under neutral conditions at 0.1 M in deuterium oxide, both compounds appear to be stable for approximately 28 days, which coincides with studies performed by Elrod and coworkers.[35] Under acidic conditions (0.1 M d_2–sulfuric acid), our results indicate that the rate of decomposition is moderately accelerated, as depression of the methylene signal occurs in approximately 10 days. Disclosed studies have historically suggested that the decomposition of the tertiary organosulfate likely proceeds with hydrolysis of the sulfate ester group, forming the parent tetraol after substitution.[35-36] However, the decomposition spectra of both tertiary species in neutral and acidic media do not match the spectra of the *syn* or *anti* 2-methyltetraols or show the tetraols as major decomposition products. When under vacuum, however, the spectra for both tertiary organosulfate samples perfectly match that of the corresponding tetraol after approximately three days (see Supporting information). These observations indicate that decomposition proceeds under vastly different pathways when comparing *in vacuo* and aqueous conditions, which may have implications for atmospheric processes.

The aqueous decomposition spectra of the tertiary organosulfates (i.e., *syn* and *anti* **5**) were quite similar, with decomposition generating a number of products as seen by multiple new peaks appearing within the NMR spectra. Unlike *syn*-**5**, however, whose decomposition spectrum provided no obvious diagnostic signals to aid interpretation, the *anti* sulfate generated clear signals at 9.28 ppm and 6.67 ppm characteristic of aldehyde and alkene groups, respectively (highlighted in blue within **Figure 8A**). Further analyses of ^{13}C NMR spectra of *anti*-**5** during decomposition revealed several additional peaks indicative of this putative structure. Inspection of the ^{13}C NMR spectra revealed a clear peak at 198.8 ppm, which corresponds to an aldehyde carbon resonance to pair with the observed aldehyde CH signal at 9.28 ppm within the ^{1}H NMR spectrum. The pair of

peaks at 6.67 ppm and 154.1 ppm in the ^{1}H and ^{13}C NMR spectra, respectively, suggest the presence of an olefinic proton and carbon atom respectively, which could be the result of tautomerization of the proposed aldehyde with the corresponding enol isomers (**Figure 8B**. See the Supporting Information for full proton and carbon spectra). We hypothesize that these signals could be due to the resultant product after ionization of the sulfate ester to carbocation **31** followed by a 1,2-hydride shift or elimination from the adjacent methylene group, generating aldehyde **32** and its enol tautomer **33** (**Figure 8C**). This aldehyde would generate the characteristic aldehydic proton seen at 9.28 ppm, while the alkene resonance at 6.67 ppm is consistent with the corresponding enol tautomer **33**.

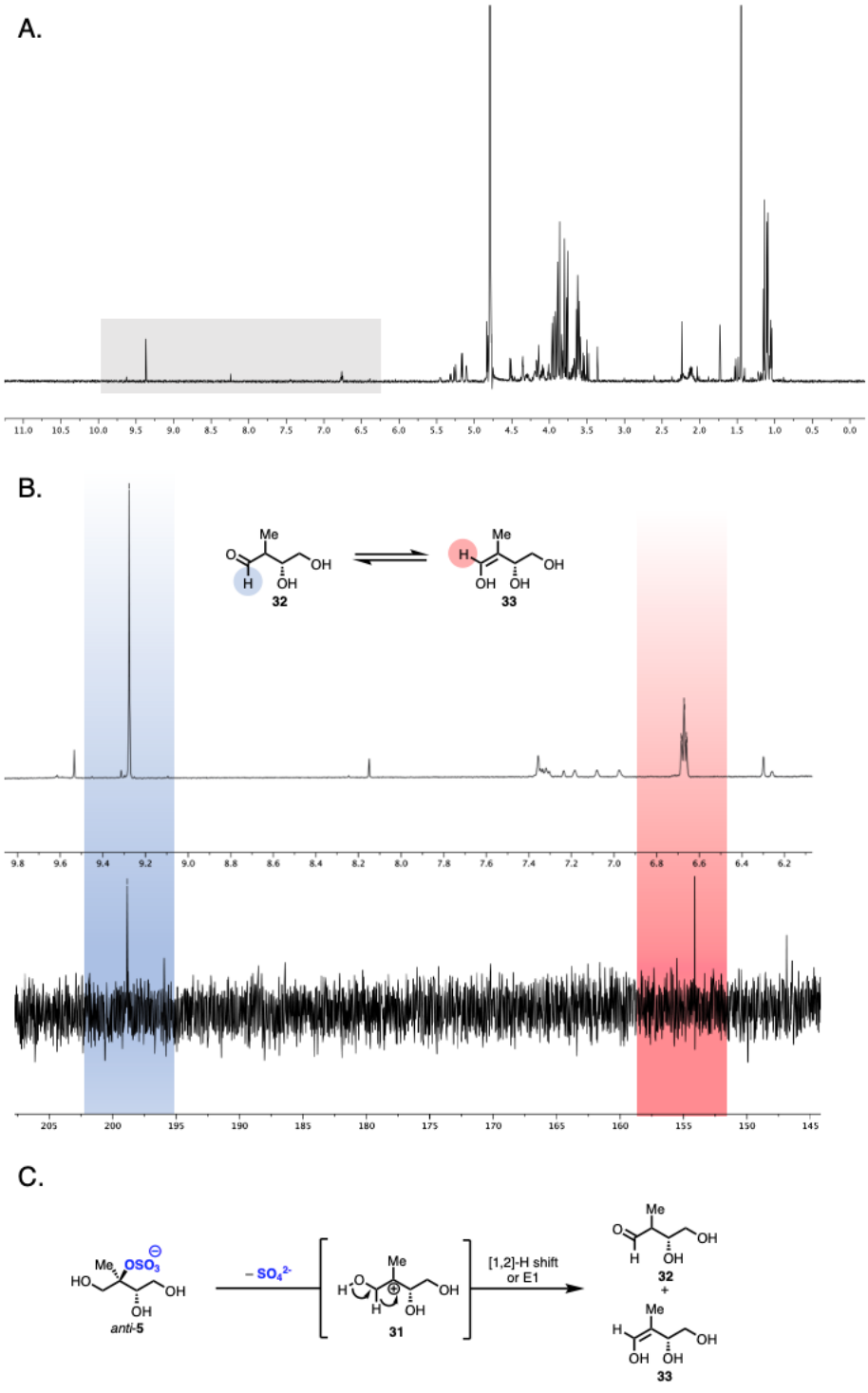

Figure 8. **A.** Decomposition spectrum of *anti*-**5** in deuterium oxide (0.1 M solution) after 28 days. **B.** Comparison of expanded regions of ^{1}H and ^{13}C decomposition spectra of *anti*-**5** showing key signals indicative of aldehyde **32** and enol tautomer **33**. The aldehydic resonances seen at δ 9.28 ppm and 198.8 ppm are highlighted in blue, and the olefinic peaks due to the relevant tautomer δ 6.67 and 154.1 ppm are highlighted in red. **C**. Proposed mechanistic pathway leading to the formation of **32** and **33** via carbocation intermediate **31** formed from ionization of the sulfate group within *anti*-**5**.

Tautomeric pair **31** and **32**, and related species, has previously been proposed as constituents of isoprene-derived SOA formed from the corresponding reaction of isoprene epoxydiols (i.e., IEPOX, see **Figure 1**) under acidic conditions.[16, 18] Laboratory investigations by Elrod and co-workers using IEPOX are particularly interesting as they showed the formation of species with ^{1}H NMR chemical shifts in CD_2Cl_2 closely matching those we observed from *anti*-**5** in D_2O.[50] Future work would be assisted by obtaining a homogenous standard of the supposed aldehyde decomposition product, although preliminary efforts within our lab along these lines were thwarted due to the inherent instability of the product which precluded isolation and characterization at this time.

Conclusions

In conclusion, we successfully synthesized the eight possible sulfate esters derived from IEPOX and report preliminary findings regarding the chemical properties of the suite of compounds, such as innate stability using NMR and inherent acidity via pH measurement. Our synthetic method is both stereo-controlled and regioselective, and we were able to generate the eight isomers in pure form. Access to these compounds enabled us to show that the acidity of IEPOX-derived organosulfate solutions is dependent upon the regiochemistry of the sulfate ester, with tertiary organosulfates leading to solutions that were ten times more acidic than the corresponding primary sulfates, with the secondary sulfates in the middle. Backbone stereochemistry, on the other hand, did not have a significant effect on pH. We also observed that the organosulfate solutions were significantly more acidic than either ammonium sulfate or the free tetraol alone, indicating a strong synergistic influence derived from mixing these biogenic and anthropogenic species.

The aqueous stability of the eight isomers was investigated under neutral and acidic conditions, and revealed that the primary sulfates were significantly more stable than the secondary and tertiary isomers. The relatively rapid decomposition of the tertiary organosulfates at low pH is noteworthy given the generally accepted notion that these isomers are the dominant forms found within isoprene-derived SOA particles.[16, 31-32] While decomposition of the tertiary sulfate under vacuum led to the expected free tetraol, aqueous decomposition was significantly more complex and led to mixtures that did not appear to contain appreciable quantities of the tetraol. We provided an analysis of the decomposition product of the *anti* tertiary sulfate as the result of a hypothesized 1,2-hydride shift and loss of the sulfate moiety leading to a proposed tautomeric mixture of an aldehyde/enol (i.e., **31**/**32**) that has also been proposed for acidic decomposition of isoprene epoxy diols.[50] The importance of these species on the properties of SOA has not been extensively investigated, but our results suggest such research may provide new insights. Along these lines, future work will involve the elucidation of the mechanism of organosulfate decomposition in order to provide insight that is relevant to the atmospheric fate of these compounds. Furthermore, we hope that access to the eight isomeric organosulfates by the synthetic routes reported here will assist in more highly specific analysis of these compounds in the laboratory and in the field.

Supporting Information.

Experimental procedures, NMR spectra, tabulated pH and pD data, organosulfate decomposition data, simulated NMR spectra.

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