We would like to thank the five reviewers for their helpful comments. We are pleased that all five acknowledged the importance of our work and have carefully edited our manuscript based on their suggestions. Our specific answers to reviewer comments are in bullet points below the original referee comments in **bold**, changes to the manuscript are in *italics*.

Response to Referee #1

This manuscript describes the synthesis and characterization of a number of hydroxy nitrate esters of monoterpene compounds. Specifically, the work refines a previously identified route to hydroxy nitrate esters – reaction of epoxide precursors with bismuth nitrate – and shows that it is a general pathway to a variety of potentially important nitrate esters. Because of the need for analytical standards for organic nitrates, this work will be of interest to readers of Atmospheric Chemistry and Physics. I recommend publication after the authors consider the following suggestions for improvement of the manuscript.

Thank you for the acknowledgement of the importance of our work.

1. **p. 2 line 24: The cited work was not controversial - it was a case of scientific fraud. I would change this last clause to "and has been subject of a retracted study."**
    - We were unaware of the specific circumstances of the retraction and have corrected the last sentence to read *"and has been subject of a retracted study."*
2. **p. 3 line 7: It seems as if the column chromatography method is critical to the success of this work (intractable mixtures turn out to be tractable). Is this particular system critical to this success? I'm not familiar with it.**
    - Automated chromatography systems have become common in both academic and industrial organic laboratories. Teldyne Isco and Biotage are two of the major companies that manufacture such systems. Typically the chromatography systems can handle higher pressures and also finer grades of silica. The increased pressure, finer grades of silica, coupled with the accuracy of pumps for gradient elutions leads to better separations than standard glass column chromatography. We have not tested the purification of these compounds by methods other than the CombiFlash Isco. We have tested other lower grades (40-63 μm irregular) of silica and have found that the finer grade (25 μm spherical silica) gives optimal separation.
3. **p. 3 line 25: 13C NMR data is very useful when using reference data to analyze com- plex mixtures. I see that some species have 13C characterization, and some don't (like this species). It would strengthen the utility of this work if as much 13C characterization were included.**
    - We have included full characterization (^{1}H & ^{13}C NMR, IR, HRMS, melting point, R_f) for all new compounds. Known compounds, such as *trans*-carene oxide, have been described by their ^{1}H NMR and a literature reference, as is standard practice.
4. **p. 7 line 1: There should be a reference to the numbering system here (or preceding this section) and the information given that the structures are given later in the paper. I also think the name should include monoterpene precursor to help keep track of the various species.**
    - We have appended structures for each experimental procedure to clarify the numbers and structures.
5. **p. 19 line 18: The authors should expand on how their results bear on previous work. Generally, it would be valuable to point out that these reactions generally lead to ring opening of the bicyclic backbone of the monoterpene. The atmospheric chemistry literature contains a number of proposed monoterpene epoxide reaction products in which the bicyclic backbone is retained (for example, see Duporte, G et al. Experimental Study of the Formation of Organosulfates from α-Pinene Oxidation. Part I: Product Identification, Formation Mechanisms and Effect of Relative Humidity. The Journal of Physical Chemistry A 2016, 120**

(40), 7909–7923) even though the synthetic literature shows that this is not usually the case. Specifically, it should be pointed out that Rindelaub's compounds 1 and 2 are the present work's compounds 17 and 22, and some comparison of the two methods should be given. The authors should also summarize the species for which they were not able to isolate compounds (such as several tertiary nitrates, which have previously been shown to highly susceptible to hydrolysis) since this is valuable information concerning the potential stability of these compounds in the atmosphere.
   - We have added the following to the conclusions section "*Interestingly, we did not observe the formation of a-pinene oxide and b-pinene oxide products that retained their bicyclic ring structures. This is consistent with the solution phase synthetic literature (Kaminska et al., 1992) but in contrast to many atmospheric reports (For example, see: Rindelaub, 2016b; Duporte, G., et al., 2016).*"
   - The reports of compounds 1 & 2 lacked reference to relative stereochemistry. Due to the potential presence of diastereomers, we prefer to keep our compounds (that are single diastereomers and indicated relative stereochemistry) labeled separately.

6. **p. 2 line 10: typo (incomplete citation)**
   - citation corrected to *(Nozière et al., 2015)*
7. **p. 11 line 1: type: add "oxide" to heading name**
   - name corrected to *"β-pinene oxide"*
8. **Figure 7, Compounds 23 and 24: It is very difficult to see the dashed line bonds to the nitrate groups.**
   - Decreased the hatch spacing/increased the number of hatches for dashed bonds
9. **p. 16 line 3: typo: slashed "o" should be lower case**
   - corrected to "Brønsted"
10. **p. 16 line 12: typo: author name is currently in all capital letters**
    - corrected capitalization of author names in reference.

Response to Referee #2
Thank you for the valuable comments and suggestions. Our answers are in bullet points below the original referee comments in **bold**, changes to the manuscript are in *italics*.

In the manuscript titled "Preparation and purification of atmospherically relevant a-hydroxynitrate esters of monoterpenes", McKnight et al described the synthesis of a series of nitrate esters. Currently there is large uncertainties in secondary organic aerosol formation especially from organic nitrate esters derived from biogenic volatile organic compounds, in part hindered by the availability of standards. Thus, availability of nitrate ester standard would bridge the critical knowledge gap exists in our further understanding of the mechanism of aerosol formation. This would be of interest to the reader of ACP.

Thank you for this positive assessment. We also hope that the availability of these compounds will help fill this critical knowledge gap.

1. **First of all, since this is a journal on atmospheric science and the title stated "Preparation and purification of atmospherically relevant a-hydroxynitrate esters of monoterpenes", the reviewer feels that it is worthwhile to more specifically spell out the relevance of the synthetic targets with atmospheric chemistry mechanistically. The way the authors frame the whole set of compounds as a general class "nitrate ester of monoterpenes" is good in a general way with the synthesis of variously nitrate esters as the general aim, a little bit more detailed account on the relevance of all the targeted compounds with atmospheric chemistry would be appropriate for majority of the reader of this journal. The author did an extensive investigation on the reaction**

of nitrate with epoxide, if that were to be emphasized for its relevance, it would be better to spell out clearly.

- We have clearly delineated the importance of these compounds in terms of atmospheric chemistry in the introduction section. As a technical note, we believe that the introduction is sufficient background information to convey the importance of our work and will leave descriptions of the detailed and complicated mechanistic fates to the references sited therein.

2. **As the author presented in the manuscript, IR would provide characteristic peaks for NO2 group, supporting the existence of nitro group in the analyzed molecule. As the indicated in table 1 of this manuscript, compared to the corresponding alcohols, the nitrate esters likely would have very similar NMR spectral profile with only the proton and carbon at the alpha position to the nitrate ester group to likely exhibit significant chemical shift difference. On the other hand, mass spectroscopy would be very important in such characterization if a good spectrum is feasible. The absence of such data from many nitrate ester target compounds in this manuscript would be better to be explained since only the HRMS of a few of them are provided.**
   - HRMS data have been added for all previously unreported nitrate esters.
3. **The opening of the cis and trans-1,2-limonene oxide with Bi(NO2)3 under the same conditions led to different nitrate ester with nitro group attached to different positions to afford different constitutional isomer, instead of stereoisomer. The reason behind it might be the same as the kinetic resolution of the cis and trans-1,2-limonene oxide. This fact merits more discussion and more detailed 2-D NMR spectroscopy evidence in addition to those original 1-D NMR spectrum provided by the author would be very helpful to go with the description text.**
   - Added clarifying text and updated figure 5. *"The nitration of the cis isomer was predicted to produce the tertiary nitrate ester via stereoelectronic effects. The dominant conformation of cis-1,2-limonene oxide is expected to be a pseudo-half chair (Figure 5). Nucelophilic substitution at the less substituted position would proceed through a lower energy chair-like transition state, whereas attack at the more substituted carbon leads to a very unstable twist-boat. The nitration of cis-1,2-limonene oxide (**cis-12**) proceeded smoothly in both dioxane (53%) and dichloromethane (63%). Respectively, the trans isomer was expected to produce the secondary nitrate ester."*
   - HSQC data have been added to the supplement document
4. **The characterization of limonene-diol doesn't seem to match with other report (J. Am. Chem. Soc. 2018, 140, 1502−1507). Since the other report provided the original NMR spectrum, it would be feasible for the author to provide an explanation of the discrepancy. Furthermore, in figure 4, the author attributed the transformation of compound 10 to 11 and back an interchange equilibrium. That interpretation is better to be explained further since it is not obvious.**
   - Thank you for bringing this to our attention. We revisited the reaction of **9** in acetonitrile & dioxane. Upon further characterization (^{13}C NMR, gHSQC) we determined that the product formed in acetonitrile is actually a 1:1 diastereomeric mixture of oxazolidine **10a**. Of note were ^{13}C signals at: 162.62, 162.55 ppm (carbonyl carbon), 72.77, 72.62 ppm (tetrasubstituted C), 13.87, 13.86 ppm ($\underline{C}H_3C$). The structure was further confirmed by an IR stretch at 1674 cm^{-1} and an *m/z* 193.8 (M+). This type of reactivity with bismuth nitrate and acetonitrile opening epoxides was also observed by Pinto, et al., 2007.
   - The interchange of either limonene-diol or nitrate **10** can be rationalized by an intramolecular elimination and tautomerization.
5. **There are other suggestions**

Page 1 Line 21. The abbreviation "ON" is not necessary as it is used only once.

- Amended the text to utilize the abbreviation for organonitrate.

Page 2 Figure 1. Compound 1 is basically compound 13 without stereo isomer indication.

- The reports of compounds 1 & 2 lacked reference to relative stereochemistry. Due to the possible presence of two diastereomers, we prefer to keep our compounds (that are single diastereomers and indicated relative stereochemistry) labeled separately.

Page 3 Line 17. "0.86 mL, 1 g" incorrect.

- Corrected to "0.86 g, 1 mL"

Page 3 Line 25. Citation year incorrect.

- Corrected to 2009

Page 3 Line 27. Citation better to be placed at the first mention.

- Amended to "Crocker and Grayson, 1969" at first mention.

Page 4 line 10. "(9 am – 11 am)" relevant?

- deleted

Page 5 line 7. Citation better to be placed at the first mention

- Amended to "Steiner, et al., 2002" at first mention.

Response to Referee #3

Thank you for the valuable comments and suggestions. Our answers are in bullet points below the original referee comments in **bold**, changes to the manuscript are in *italics*.

This review is submitted with the benefit of having read reviews of anonymous Re- viewers 1 and 2. As stated in the previous reviews, this work contributes procedures for synthesis of a number of vicinal hydroxynitrate esters derived from a monoterpene. The esters can serve as much needed authentic standards for characterizing components of SOA and therefore the work should be published. There are a number of comments that the authors need to address prior to publication.

Thank you for acknowledging the critical need for these standards. We hope that our work will help fill this gap in the literature.

Most important: the authors should include 1H and 13C NMR traces for all compounds that have not been previously reported, and should also include HSQC and HMBC spectra where this is critical for structural elucidation. In particular, the assignment of quaternary carbons is readily evident from the absence of C–H cross peaks in the HSQC spectra.

Since the authors had access to high-resolution mass spectrometry, exact mass mea- surements and fragmentation patterns should be provided either in the experimental section of the text or the SI for all compounds not previously reported.

- We have included all ^{1}H, ^{13}C NMR and HSQC spectra in the SI for all compounds not previously reported. We have also added HRMS data in the experimental section for all compounds not previously reported.

Globally, there is considerable carelessness with regard to the presentation of this manuscript. Conventionally, solvent names do not begin with upper case letters and in the case of deuterated solvents, the notation "d" is italicized (e.g., chloroform-[italics]d). This convention is adhered to randomly throughout.

The use of abbreviations for solvents is also not consistent (e.g. EtOAc:Hex and ethyl acetate:hexanes (solvent and compound names are inappropriately capitalized in the text)).

- We have fixed the minor typos and inconsistent abbreviations.

Several citations are only partially given in the text (e.g. Cocker, 1969 on p. 4, l. 8) and in one case, a citation in the text is missing from the bibliography (Charbonneau, 2018; Charbonneau was misspelled).

- We have amended the partial citations to full citations at first instance.

- Charbonneau, 2018 has been added to the bibliography.

There are mistakes in nomenclature: trans-3-carene (not trans-(3)-carene). Synthetic targets are referred to as "title" compounds. However, "target compound" would be preferable, since compounds do not appear in titles.
- Corrected instances of extraneous parentheses.
- Replaced "title compound" with the names compounds and compound numbers.

Reaction/synthetic schemes should be separated from tables and figures and appropriately designated.
- Sometimes it may be appropriate to separate a table from a reaction scheme, we do not believe that it is appropriate in this case. The tables are communicating different reaction conditions of the connected reaction scheme and would be meaningless if separated.

1. **The authors might note that products having two or more asymmetric carbons were isolated and characterized as mixtures of diastereomers. Visual inspection of the NMR spectra does not appear to how any resolution of the mixture by NMR. Did the authors look for any such result?**
- We have indicated in the text and by using line bonds (not wedged or dashed) the cases where we generated mixtures of diastereomers. For example, the perillic alcohol epoxides **15**, 8,9-limonene oxide (**9**), nitrate ester **10**, oxazoline **10a**, and aldehyde **11** are the only mixtures of diastereomers. All other compounds are drawn, characterized and reported as single diastereomers.
2. **For the preparation of trans-carene oxide (p. 3, starting with l. 17), did the authors start with optically pure (+)-carene or a racemic mixture? This is important, since epox- idation with mCPBA will give an enantiomerically pure epoxide from enantiomerically pure starting material. The synthesis of the cis oxide described below apparently starts with (+)-carene.**
    - The starting material was corrected to (+)-carene.
3. **Preferred nomenclature for cpd 20 would be 2-methyl-5-(propan-2-ylidine)cyclohex- 2-en-1-ol.**
    - Amended to "5-isopropylidene-2-methyl-2-cyclohexen-1-ol"
4. **Visual inspection of the 1H NMR trace of cpd 24 appears to be consistent with the signal at 5.31 ppm as a poorly resolved doublet-of-doublets. It is not clear how the authors interpreted this signal as a doublet-of-doublets-of-doublets.**
    - The expansion of the NMR trace clearly shows the reported doublet-of-doublets-of-doublets. This is corroborated by gCOSY correlation to the adjacent methylene as well as long-range, 4-bond coupling to the methyne (-C*H*OH). This type of 4-bond coupling (*J* = 1-2 Hz) is quite common in substituted cyclohexane derivatives (see: Crews, P., et al. *Organic Structure Analysis,* Oxford University Press, 1998, pages 142-143).
5. **5. p. 7, l. 16 and following; p. 13, l. 3 and following: As pointed out by Reviewer 1, there is a problem with the structural assignment of limonene 8,9-dihydrodiol (10) to the crude product of Bi(NO3)3 treatment of limonene 8,9-oxide (9). This is true as well for the rearrangement product 2-(4-methylcyclohex-3-en-1-yl)propanal (preferred nomenclature) (11). The 1H NMR data provided do not match published data for either proposed structure (diol: J. Am. Chem. Soc. 2018, 140, 1502−1507; aldehyde: Phytochemistry 2017, 144, 208 – 215). This reviewer notes that the reported 1H NMR of the diol was acquired at a spectrometer frequency of 600 MHz, although the only expected difference would be improved resolution of the proton splittings.**
    - Thank you for bringing this to our attention. We revisited the reaction of **9** in acetonitrile & dioxane. Upon full characterization we determined that the product formed in acetonitrile is actually a 1:1 diastereomeric mixture of oxazolidine **10a**. Of note were ^{13}C signals at: 162.62, 162.55 ppm (carbonyl carbon), 72.77, 72.62 ppm (tetrasubstituted C), 13.87, 13.86 ppm ($\underline{C}H_3C$). The structure was further confirmed by an IR stretch at 1674 cm^{-1} and an *m/z* 193.8 (M+). This

type of reactivity with bismuth nitrate and acetonitrile opening epoxides was also observed by Pinto, et al., 2007.

- We have added tabulated ^{1}H and ^{13}C NMR for aldehyde 11 in the supplemental information to show the comparison to both Uehara, et al., 2017 and a second reference, Reid and Watson, 2018. The data are in agreement within expected error.

6. **On p. 11, starting with line 12: The authors should provide additional discussion justifying the structural assignments of cpds 27 and 29. Neither of these compounds appears to have been structurally characterized by NMR in the literature. In the 1H NMR spectrum of 27, the signal at ~5.6 ppm appears to be a broad doublet. It is unclear why the authors have used the designation "multiplet". In the 1H NMR spectrum of 29, which is a racemic mixture, the lowest field signal (H attached to the nitrate-substituted C) should be a singlet, as it appears to be. Why is it described as a doublet?**
    - The structural assignments of **27** and **29** are in the body of the text (after figure 8) and bear distinct similarities to the related nitrate esters **23** and **24**. The signal at 5.6 appears as a poorly resolved doublet-of-doublet-of doublets, i.e. multiplet. As with **24**, this is due to long-range, 4-bond coupling.
    - For **29**, the ^{1}H NMR signal is a doublet with the reported 1.6 Hz coupling constant. Again, this is due to apparent long-range, 4-bond coupling and is corroborated by gCOSY data.
7. **Figure 2: The authors should add the diol and aldehyde structures to this scheme. There is sufficient space and this gives the true picture of reaction products.**
    - Included diol and aldehyde structures in figure 2.
8. **p. 12. l. 15: The phrase, ". . .assigned to the methyne adjacent to the alcohol..." should be rewritten as ". . .assigned to the alcohol methyne carbon..." As written, the statement "adjacent to" is confusing. Where heteronuclear correlations are important in verifying structure, the 2D spectra should be added to the SI. As pointed out above, it would be helpful if all the NMR data were included in SI.**
    - Phrase was amended to *"assigned to the alcohol methyne carbon"*
    - gHSQC spectra for all compounds not previously characterized have been added to the SI.
9. **p. 12, l. 17: The rationale for assigning the quaternary carbon would be better explained by stating that no C–H cross peak was observed for the 13C signal at 95.6 ppm in the HSQC experiment.**
    - Amended to "A tetrasubstituted carbon, with no correlations in the gHSQC, at 95.6 ppm was consistent with the tertiary nitrate ester."
10. **p. 16, l. 12: "Epimer" is misused here. Platydiol (the name "platydiol" automatically designates the the di-endo geometry of the diol) has a plane of symmetry, and there are no optical isomers.**
    - Replaced "its epimer" with "its *trans* diastereomer." We note that the *trans*-diastereomer is epimeric at one stereocenter from platydiol.
11. **p.17, l. 14: In discussing the structural verification of nitrate ester 27, it would be helpful to include the HSQC spectrum. As presented in the text, there is not enough data to be convincing regarding the structural assignment.**
    - gHSQC spectra for all compounds not previously characterized have been added to the SI.
12. **12. p. 17, bottom: The table of spectral data should have the heading at the top.**
    - table heading moved to the top.

Response to Referee #4

Thank you for the valuable comments and suggestions. Our answers are in bullet points below the original referee comments in **bold**, changes to the manuscript are in *italics*.

The manuscript presents synthesis methods for nitrate esters with relevance to terpene oxidation products in the atmosphere. The authors report preparation and purification of nine nitrate esters

and additionally provide some details on unsuccessful methods. The information contained in this manuscript will be of interest to atmospheric chemists looking into nitrate radical oxidation products and I recommend acceptance after the following comments are addressed.

Thank you for the general comments on the importance of our work.

1. **Was the HPLC listed on page 3 line 12 used on the Orbitrap? If so, what conditions were used (solvents, gradient, spray conditions, etc.). Were both positive and negative ion mode used? How was the instrument mass calibrated?**
   - The HRMS data was generated by direct infusion, bypassing the HPLC. The ion mode is indicated as either "ESI+" or "ESI-" as well as in the charge of the masses observed. The facility technician loaded the most recent tune files (for both positive and negative modes) and checked the calibration with a standard sample (reserpine).
2. **Acronyms I noticed that should be added to the list: CV, TLC, br, dq and qd, vs, Rf etc.**
   - abbreviations have been added to section 2.1.
3. **Exact mass measurements were only provided for a subset of the samples. Why is this the case? Also, the expected exact masses for the anions are incorrect, check to make sure the mass of the electron has been added. The expected exact mass for C10H16O4N- is 214.10848. (page 9 line 6 and page 10 line 16)**
   - HRMS data has been added for all previously unreported compounds.
   - exact mass for C10H16O4N- was corrected to 214.10848.
4. **Methanolysis products were observed when methanol was used as the analysis solvent (page 18). Were these the only products observed or were the desired products also observed? Did this occur for all the nitrate esters? Also, please clarify what M+ is for each of the masses. I can see how m/z 185.1 is formed but I do not see where m/z 223.13 is coming from. Also, are these exact mass measurements? If so, providing more numbers after the decimal is a good idea.**
   - These were low resolution GC-MS data. The *m/z* 223.1 is consistent with M+K (it was incorrectly indicated as M+Na).
5. **Figure 7 is very crowded, especially at the far right side on top. I recommend providing a little more space between compounds 22, 23 and 24 so that they are easier to see.**
   - added spacing to figure 7 as allowed by document margins.
6. **Incomplete citation on page 2, line 10**
   - replaced with "Nozière et al., 2015"
7. **m/z should be italic throughout**
   - corrected to italicized *m/z*.
8. **Formatting on the citations looks a little odd, especially the spacing between the comma and the dates**
   - Deleted extra spacing in citations.

Response to Referee #5

Thank you for the valuable comments and suggestions. Our answers are in bullet points below the original referee comments in **bold**, changes to the manuscript are in *italics*.

The paper by McKnight et al. presents successful synthetic routes to the preparation of the hydroxy nitrates that are produced in nature by the atmospheric oxidation of monoterpenes. In recent years it has been shown that formation of these organic nitrates are an important sink for NOx in the atmosphere, as well as an important mechanism for the production of atmospheric aerosol. Such aerosol results from an interaction between anthropogenic NOx, and biogenic monoterpenes. Thus, interestingly, control of NOx emissions (from combustion) can influence the role of production of atmospheric aerosol from biogenic emissions. There is thus considerable interest in these

compounds, and their atmospheric chemistry, and, e.g. the ability to study their hydrolysis rates. However, the atmospheric chemistry community has not had much success in making these compounds, and that is a major stumbling block to progress. Here is a paper that connects the organic synthesis community to the atmospheric chemistry community in a useful way, and the atmospheric chemistry community increasingly needs this connection, in more general terms. This paper is technically important, and will stimulate a great deal of badly needed research, likely to start with atmospheric chemists at Reed. So, this paper should be published, and I think can be done with only editorial changes. That said, the authors need to be aware that the audience here is indeed atmospheric chemists, who are not versed in the editorial jargon of synthetic organic chemists. So, the paper could be made more readable and useful if the authors shed the notion that they are writing to organic chemists. They are, at best, writing to organic chemists existing with the labs of atmospheric chemistry professors.

Thank you for the assessment of the need for this work. In addition to filling the need for nitrate ester standards, we hope that our work will help bridge the gap between the synthetic and atmospheric communities. We attempted to mitigate the use of jargon and tried to write to a more general audience. We appreciate your input and comments for improving the manuscript.

1. **The last sentence of the Introduction is unclear – 30-40% of MT emissions are at night, or the nitrate radical consumes 30-40% of the emitted MTs at night? Please note that the OH radical oxidation pathway is still an important source of MT-nitrates, e.g. as discussed in Pratt et al., 2012.**
    - Clarified page 1, line 20: Replaced "This nitrate oxidation pathway has been shown to be important with 30-40% of monoterpene emissions occurring at night (Pye et al., 2010)."
    - "*Nitrate oxidation pathways have been shown to be important particularly during nighttime. A large portion (30-40%) of monoterpene emissions occur at night (Pye et al., 2010). These emissions can then react with NO_3 radicals, formed from the oxidation of NO_2 emissions by O_3, (Pye et al., 2010).*"
2. **Line 21, page 2 – is there a better reference for this quite general organic chemistry laboratory hazard?**
    - Despite the well-known hazards of nitric acids, explosions and other accidents occur nearly every year. I believe that it is important to reference examples of recent accidents, such as the incident at UC Berkeley.
    - A second reference (Parker, 1995) was also added.
3. **The Ma et al. paper should not be cited. If you go to the ACP web site, it says "This paper has been retracted."**
    - The reference to the original Ma paper was removed. The citation for the retraction remains.
4. **Page 3, line 17 – what is CPBA? (Good example of my comment above; most organic chemists will know that it doesn't stand for Certified Professional Behavioral Analyst).**
    - We added meta-chloroperoxybenzoic acid (m-CPBA) to the list of abbreviations.
5. **Page 3, line 27 – should the reference be Crocker and Grayson, 1969? And on Page 4, line 8.**
    - Reference for trans-carene oxide (page 3, line 27) is correct.
    - Page 4 line 8 was corrected from Croker, 1969 to Crocker and Grayson, 1969.
6. **Page 5, line 8 should be Steiner et al., 2002. And line 16.**
    - replaced "Steiner" with *"Steiner et al., 2002"*
7. **Page 7, at 2.3.1 title, refer the Table 1 for structures. The reader needs to see the structures. Line 2 – do you mean the trans-3-carene epoxide? Also on line 10, the epoxide?**
    - Inserted structures for each experimental procedure.
    - Corrected "trans-3-carene" to *"trans-3-carene oxide"*
8. **Page 8, line 4, those percentages are the yields? Please try to avoid organic synthetic chemists shorthand. Also line 13. For structures 16 and 17, line 22, are there yields?**

- Replaced "(53% in dioxane; 62% in DCM)" with *"(53% yield in dioxane; 62% yield in DCM)"*
- The yields for 16 & 17 were reported in their individual descriptions. Added %yields in the summary description.

9. **Page 8, line 24, what is "the title compound"? Also page 9, lines 4, 17, and 23. There is sloppy shorthand on this page, e.g. line 13 – "the following". What following?**
    - This nomenclature and formatting is standard for organic chemistry experimental procedures.
    - Deleted "the following" and replaced the title compound with "nitrate ester," where indicated.
10. **Line 11 – you mean the a-pinene oxide? Line 17 – by "title compound" you mean the aldehyde? Similarly, I find line 23 confusing. You synthesized the alcohol?**
    - Page 9, line 11, replaced with a-pinene oxide.
    - Clarified by replacing the title compound with the appropriate nitrate ester.
11. **Page 10, lines 13 and 14 – "The title compound", when the title compound is "Nitrate ester 23" does not make for great/easy reading. Perhaps it would be helpful that in each case, the structure should be shown next to the name, as a graphic? That would really make the paper more readable.**
    - Clarified by replacing the title compound with the appropriate nitrate ester and added a graphic with the structure of the compound
12. **Page 14, line 8 – provide a reference for the fast hydrolysis rates.**
    - Added citations to Boyd et al., 2015; Darer et al., 2011; Liu et al., 2012.
13. **Page 19, line 6, re decomposition of ester 14 – does this depend on water content in the solvent? Do you know what the decomposition products are? The corresponding diol?**
    - Nitrate ester **14** was stored as a neat (i.e. water and solvent-free) liquid.
    - Decomposition produces a complex mixture of products that have not been identified.
    - Rephrased to clarify *"For example, tertiary nitrate ester **4** is particularly stable stored as a solid at 0 ºC. In contrast, when secondary nitrate ester **14** was stored as a neat oil at 0 ºC, it decomposed to a complex mixture within a few weeks."*
14. **Page 19, line 9 – the "the" methods, but "successful methods".**
    - corrected to *"successful methods"*
15. **Line 17 – insert "for" after "important".**

- corrected to *"is important for"*

Technical Note: Preparation and purification of atmospherically relevant α-hydroxynitrate esters of monoterpenes

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Abstract. Organic nitrate esters are key products of terpene oxidation in the atmosphere. We report here the preparation and purification of nine nitrate esters derived from (+)-3-carene, limonene, α-pinene, β-pinene and perillic alcohol. The availability of these compounds will enable detailed investigations into the structure reactivity relationships of aerosol formation and processing and will allow individual investigations into aqueous phase reactions of organic nitrate esters.

1 Introduction

Biogenic volatile organic compound (BVOC) emissions account for ~88% of non-methane VOC emissions. Of the total BVOC estimated by the Model of Emission of Gases and Aerosols from Nature version 2.1 (MEGAN2.1), isoprene is estimated to comprise half, and methanol, ethanol, acetaldehyde, acetone, α-pinene, β-pinene, limonene, ethene and propene together encompass another 30%. Of the terpenoids, α-pinene alone is estimated to generate ~66 Tg year $^{-1}$ (Guenther et al., 2012). These monoterpenes can be oxidized by nitrate radicals that are projected to account for more than half of the monoterpene-derived secondary organic aerosol (SOA) in the US (Pye et al., 2010). Nitrate oxidation pathways have been shown to be important particularly during nighttime. A large portion (30-40%) of monoterpene emissions occur at night (Pye et al., 2010). These emissions can then react with NO_3 radicals, formed from the oxidation of NO_2 emissions by O_3, (Pye et al., 2010).

The full role of organic nitrates (ON) is complicated with many different sources and sinks (Perring et al., 2013). Fully deconvoluting the atmospheric processing of terpene-derived ON is difficult particularly due to partitioning into the aerosol phase in which hydrolysis and other reactivity can occur (Bleier and Elrod, 2013;

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Rindelaub et al., 2014; 2015; Romonosky et al., 2015; Thomas et al., 2016). Hydrolysis reactions of nitrate esters of isoprene have been studied directly (Jacobs et al., 2014) and the hydrolysis of ON have been studied in bulk (Baker and Easty, 1950). These and other studies have shown that the hydrolysis of ON is dependent on structure (Darer et al., 2011). For example, primary and secondary ON are thought to be relatively stable (Hu et al., 2011). In contrast, tertiary nitrates have been shown to hydrolyze on the order of hours (Boyd et al., 2015; Liu et al., 2012) to minutes (Darer et al., 2011). To the best of our knowledge there is only one study of the hydrolysis of an isolated terpene-derived hydroxynitrate (**2**) (Rindelaub et al., 2016).

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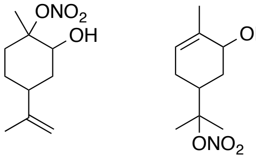

1 **2**

Figure 1: Two hydroxynitrate esters with available spectral data. Relative stereochemistry is undefined.

Furthermore, fully understanding the atmospheric processes of organic molecules is restricted by the ability to identify these species (Nozière et al., 2015). Part of this challenge is, of course, related to the lack of available standards. While one certainly cannot synthesize all of the atmospherically relevant ON, having access to representative compounds from monoterpenes would enable key studies. With these molecules in hand, the atmospheric chemistry community could directly study the ON reactivity, such as hydrolysis, and deconvolute the structure-reactivity relationships. Additionally, novel method development would be enabled and validated (Rindelaub et al., 2016b). For example, Nozière and co-authors called attention to “the lack of NMR spectra libraries for atmospheric markers” as a barrier for utilizing NMR spectroscopy in atmospheric science. While the preparation of α-hydroxynitrates of terpenes has been alluded to in a handful of reports, we have only been able to identify NMR data for two species (Figure 1). Two main methods appear to have been attempted, treating an epoxide with either fuming nitric acid (Rollins et al., 2010) or bismuth nitrate (Rindelaub et al., 2016b; Romonosky et al., 2015). The utility of the former is limited by the extreme hazards involved with mixing fuming nitric acid with organic materials (Parker, 1995; Univ. of Calif., Berkeley, 2018) and only provides characterization data for a single compound. On the surface the latter appears to be a usable method but on closer inspection lacks spectral data, perhaps due to intractable and inseparable mixtures (Romonosky et al., 2015) and has been subject of a retracted study (Pöschl et al., 2011).

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2 Experimental

2.1 Instrumentation and materials

All starting materials and reagents were purchased from commercial sources and used without further purification unless otherwise noted. Bismuth nitrate (98%) was purchased from Strem Chemicals and ground to a fine powder prior to use. Isoprene, MVK, (+)-3-carene, β-pinene, α-pinene oxide and 1,2-limonene oxide were purchased from Aldrich. Silica gel chromatography was performed on a TeldyneIsco CombiFlash+ Lumen using 25 µm SiliCycle spherical silica gel. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV400 spectrometer with chloroform (7.26 ppm) or benzene (7.28 ppm) as internal standards. IR spectra were recorded on a ThermoNicolet IR100 spectrometer using a Thunderdome Attenuated Total Reflectance (ATR) sample accessory. Melting points were collected on a DigiMelt 160 melting point apparatus. Exact masses were collected at the BioAnalytical Mass Spectrometry facility at Portland State University using a ThermoElectron LTQ-Orbitrap Discovery high resolution mass spectrometer with a dedicated Accela HPLC system. Low resolution masses were collected on a Varian Saturn 2000 GC-MS with a Restek Crossbind Rxi-5ms column. Abbreviations include: *meta*-chloroperoxybenzoic acid (m-CPBA), hexanes (Hex), ethyl acetate (EtOAc), column volume (CV), thin layer chromatography (TLC), retention factor (R_f), diastereomeric ratio (d.r.), broad (br), singlet (s), doublet (d), doublet of doublets (dd), doublet of doublets of doublets (ddd), doublet of quartet (dq), triplet (t), multiplet (m), broad (b), weak (w), medium (m), strong (s), very strong (vs).

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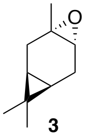
2.2 Preparation of epoxides



2.2.1 *trans*-Carene oxide (3)

3

To a solution of (+)-3-carene (0.86 g, 1 mL, 7.34 mmol) in dichloromethane (25 mL) at 0 ºC was added *meta*-chloroperoxybenzoic acid (m-CPBA) (1.85 g, 8.1 mmol, 1.1 equiv). The solution was warmed to 23 ºC over 1 hour. The solution was poured onto sat. aq sodium bicarbonate (30 mL) and extracted with dichloromethane (3 x 30 mL). The combined organics were washed with sat. aq sodium bicarbonate (2 x 30 mL), dried ($MgSO_4$) and concentrated to yield a crude clear, colorless oil (1.17 g). The crude oil was purified by column chromatography (SiO_2; 0 – 25% EtOAc/Hex over 10 column volumes) to yield clear colorless oil (685 mg, 4.5 mmol; 61%

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yield): ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.82 (s, 1H), 2.28 (ddd, *J* = 16.4, 9.0, 1.9 Hz, 1H), 2.13 (dd, *J* = 16.2, 9.1 Hz, 1H), 1.63 (dt, *J* = 16.4, 2.3 Hz, 1H), 1.48 (dd, *J* = 16.1, 2.3 Hz, 1H), 1.24 (s, 3H), 1.00 (s, 3H), 0.72 (s, 3H), 0.52 (td, *J* = 9.1, 2.3 Hz, 1H), 0.44 (td, *J* = 9.1, 2.3 Hz, 1H) ppm. Spectral data is consistent with literature reports (Cabaj et al., 2009).

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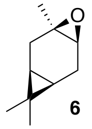

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2.2.2 *cis*-Carene oxide (6)

According to the methods of Crocker and Grayson, 1969, a round bottom flask was charged with a solution of (+)-3-carene (2.7 g, 20 mmol) in dioxane (20 mL) and water (10 mL). Calcium carbonate (2 g, 20 mmol) and N-bromosuccinimide (7 g, 40 mmol) were added to the solution. The internal temperature rose to 50 ºC after the initial addition. The mixture was stirred for 2 h then poured onto water (50 mL), filtered, and washed with diethyl ether. The filtrate was extracted with ether (2 x 100 mL). The combined extract was washed with water (3 x 100 mL), sodium thiosulfate (5% aq, 20 mL), dried (Na_2SO_4) and concentrated to yield a crude pale yellow oil. Purification by column chromatography (SiO_2; 0 – 50% EtOAc/Hex) yielded the bromohydrin as a white crystalline solid (4.6 g, 99% yield): ^{1}H NMR (400 MHz, chloroform-*d*) δ 4.07 (dd, *J* = 11.1, 7.6 Hz, 1H), 2.50 – 2.36 (m, 2H), 2.21 (dd, *J* = 14.6, 10.1 Hz, 1H), 1.41 (dd, *J* = 4.9, 1.2 Hz, 1H), 1.38 (s, 3H), 1.03 (s, 3H), 1.00 (s, 3H), 0.91 – 0.80 (m, 1H), 0.70 (m, 1H). Spectral data is consistent with literature reports (Cocker & Grayson 1969). Bromohydrin (2.44 g, 10.5 mmol) was dissolved in 100 mL tBuOH (warmed with a water bath). Potassium *tert*-butoxide (2.44 g, 21.8 mmol, 2.08 equiv) was added and the solution was stirred at rt for 2 hours. The solution was poured onto water (50 mL), extracted with diethyl ether (3 x 75 mL), washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated to yield 2.5 g crude clear oil. Purification by column chromatography (40 g SiO_2; 0 – 25% EtOAc/Hex over 10 CVs) yielded a clear colorless oil (1.31 g, 63% yield): ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.89 (d, *J* = 5.6 Hz, 1H), 2.30 (ddd, *J* = 16.7, 9.0, 5.6 Hz, 1H), 2.08 (dd, *J* = 16.4, 8.9 Hz, 1H), 1.82 (s, 1H), 1.78 (s, 1H), 1.32 (s, 3H), 0.98 (s, 3H), 0.94 (s, 3H), 0.63 – 0.49 (m, 2H). Spectral data is consistent with literature reports (Cocker and Grayson, 1969).

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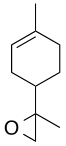

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2.2.3 8,9-Limonene oxide (9)

Methyl vinyl ketone (10 mL, 90 mmol), isoprene (10 mL, 75 mmol), and DCM (90 mL) were added to a round bottom flask with stir bar. The flask was purged with inert atmosphere and chilled to 0°C with stirring. AlCl$_3$ (1.2 g, 9 mmol) was added in three portions over 10 minutes. The ice bath was removed and the reaction mixture was stirred for 1.5 hours. The crude reaction mixture was filtered through a 1.5 inch silica gel pad (350 mL, 9 cm diameter) washed with 8% EtOAc:Hex (4 x 160 mL). The filtrate was concentrated to yield 1-(4-methyl-3-cyclohexene) ethenone (**8**) as a clear yellow liquid (9.68 g, 88% yield): ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.44 – 5.38 (m, 1H), 2.59 – 2.49 (m, 1H), 2.15 – 2.20 (s, 4H), 2.06 – 1.95 (m, 3H), 1.67 (s, 3H), 1.61 (m, 2H). Spectral data is consistent with literature reports (Buss et al., 1987). Sodium hydride (1.766 g, 44.16 mmol) was suspended in dry DMSO (25 mL). A solution of trimethylsulfonium iodide (10.356 g, 47.06 mmol) in DMSO (50 mL) was added via cannula. The solution was stirred at rt for 30 minutes then heated to 50 ºC until gas evolution ceased (1 h). To this solution was added 1-(4-methyl-3-cyclohexen-1-yl) ethenone **8** (5 g, 36 mmol) and heated to 70 ºC for 2 hours. The reaction mixture was cooled to room temperature and poured onto sat. aq. NH$_4$Cl (100 mL), extracted with MTBE (4 x 100 mL). The combined organics were washed with water (4 x 50 mL), dried (MgSO$_4$) and concentrated to yield 5.1 g crude oil. Purification by column chromatography (80 g SiO$_2$; 0-20% EtOAc/Hex over 10 CV) yielded 8,9-limonene oxide (1:1 d.r.) as a clear, colorless oil (3.76 g, 68% yield): ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.43 – 5.33 (br s, 1H), 2.67 (t, *J* = 5.3 Hz, 1H), 2.58 (dd, *J* = 10.9, 4.8 Hz, 1H), 2.17 – 1.73 (m, 5H), 1.66 (s, 3H), 1.44 (m, 2H), 1.29 (d, *J* = 4.5 Hz, 3H). Spectral data is consistent with literature reports (Almeida and Jr., 2005)

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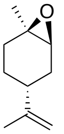

2.2.4 *cis*-1,2-Limonene oxide (12-*cis*) ***12-cis***

According to the methods of Steiner, et al., 2002, a 20 mL scintillation vial was charged with 1,2-limonene oxide, pyrrolidine & water. The vial was sealed with a Teflon lined cap and heated to 88 ºC for 24 h. The vial was cooled to rt, transferred to a separatory funnel with 100 mL pentane, washed with sat. aq. ammonium chloride (3 x 30 mL) and water (1 x 50 mL). The organics were dried ($MgSO_4$) and concentrated to yield a light yellow oil. Purification by column chromatography (80 g spherical SiO_2; 0-15% EtOAc/Hex over 10 CV's) yielded *cis*-1,2-limonene oxide as a clear, colorless oil. (1.52 g, 64%): ^{1}H NMR (400 MHz, chloroform-*d*) δ 4.77 – 4.71 (m, 1H), 4.69 (s, 1H), 3.07 (s, 1H), 2.22 – 2.07 (m, 2H), 1.90 – 1.84 (m, 2H), 1.75 – 1.64 (m, 5H), 1.33 (s, 3H), 1.28 – 1.15 (m, 1H) ppm. Spectral data is consistent with literature reports (Steiner et al., 2002).

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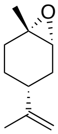

2.2.5 *trans*-1,2-Limonene oxide (12-*trans*) ***12-trans***

According to the methods of Steiner, et al., 2002, a 50 mL flask was charged with 1,2-limonene oxide (4.57 g, 30 mmol), pyrazole (0.34 g, 5 mmol) and water (16.2 mL). The reaction was heated to reflux for 5 hours. The reaction mixture was cooled to 80 ºC and transferred to a separatory funnel. Warm water (80 ºC; 60 mL) was added. The emulsion was extracted with pentane (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to yield 1.481 g crude oil. Purification by column chromatography (80 g spherical SiO_2; 0 – 20% EtOAc/Hex over 13.5 CV) yielded *trans*-1,2-limonene oxide (485 mg, 20% yield): ^{1}H NMR (400 MHz, chloroform-*d*) δ 4.68 (s, 2H), 3.01 (d, *J* = 5.3 Hz, 1H), 2.11 – 2.00 (m, 2H), 1.96 – 1.82 (m, 1H), 1.75 – 1.64 (m, 5H), 1.45 – 1.36 (m, 2H), 1.34 (s, 3H) ppm. Spectral data is consistent with literature reports (Steiner et al., 2002).

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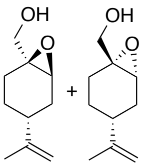

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2.2.6 Perillic alcohol epoxide (15)

Perillic alcohol (5 mL, 31.46 mmol) was combined with dichloromethane (62 mL) in a round bottom flask with stir bar and cooled to 0 ºC under inert atmosphere. m-CPBA (5.97 g, 34.61 mmol) was added in 5 portions over the course of 10 minutes. After 30 minutes the reaction was warmed back up to room temperature and allowed to stir for an hour at room temperature. The reaction mixture was filtered through celite, washed with DCM (3 x 30 mL), then transferred to a separatory funnel where it was washed with sodium bicarbonate (50 mL) and brine (50 mL). The organic layer was dried (Na_2SO_4) and concentrated to yield a crude oil (5.1 g) Purification by column chromatography (80 g spherical SiO_2; 0 – 100% EtOAc/Hex over 15 CV's) yielded the epoxide **15** as a clear, colorless oil (3.363 g, 19.8 % yield): ^{1}H NMR (400 MHz, chloroform-*d*) δ 4.77 – 4.66 (m, 2H), 3.78 – 3.59 (m, 2H), 3.41 – 3.31 (m, 1H), 2.26 – 2.14 (m, 1H), 2.09 (dtd, *J* = 14.9, 5.6, 1.8 Hz, 1H), 1.88 – 1.83 (m, 1H), 1.80 – 1.59 (m, 7H), 1.56 – 1.38 (m, 1H), 1.32 – 1.16 (m, 1H). Spectral data is consistent with literature reports (Thomas et al., 2016).

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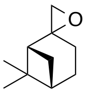
2.2.7 β -pinene oxide



Potassium peroxide monosulfate (4.750 g, 31.20 mmol) was dissolved in deionized water (60 mL). Sodium bicarbonate (4.019 g, 47.84 mmol) was placed into a 125 mL erlenmeyer flask and acetone (40 mL) was added, followed by β-pinene (1.59 mL, 9.974 mmol). The solution of potassium peroxide monosulfate mixture was slowly added into the β-pinene mixture over the course of three minutes via syringe while the mixture was stirring at 800 rpm. The reaction mixture was stirred for exactly 30 minutes while stirring at 800 rpm at room temperature. The reaction mixture was transferred to a separatory funnel and extracted with dichloromethane (2 x 40 mL), dried ($MgSO_4$) and concentrated to produce a clear oil (1.500 g, 96% yield). ^{1}H NMR (400 MHz, chloroform-*d*) δ 2.79 (d, *J* = 4.8 Hz, 1H), 2.62 (d, *J* = 4.8 Hz, 1H), 2.30 (dtd, *J* = 10.3, 5.9, 1.5 Hz, 1H), 2.19

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(ddd, *J* = 15.1, 10.7, 8.1 Hz, 1H), 2.06 – 1.97 (m, 1H), 1.97 – 1.79 (m, 2H), 1.75 – 1.65 (m, 2H), 1.53 (t, *J* = 5.4 Hz, 1H), 1.27 (s, 3H), 0.94 (s, 3H). Spectral data is consistent with literature reports (Charbonneau et al. 2018).

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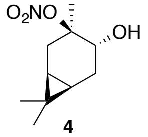
2.3 General nitration method

A round bottom flask was charged with a solution of epoxide (2 mmol) in toluene, dioxane or dichloromethane (10 mL, 0.2 M). Bismuth nitrate (1.164 g, 2.4 mmol, 1.2 equiv) was added to the reaction mixture. The reaction mixture was stired for 30 – 60 minutes. When TLC indicated complete consumption of starting material the reaction was filtered through a 1 inch celite pad and washed with DCM (2 x 15 mL). The filtrate was transferred to a separatory funnel and washed with sodium bicarbonate (3 x 15 mL). The organic layer was dried with sodium sulfate, filtered and concentrated to yield a crude liquid. Desired products were isolated via column chromatography.



4

2.3.1 Nitrate ester 4

Nitration of *trans*-3-carene oxide (3 mmol) was carried out according to the general method with dioxane. Purification of the crude oil by column chromatography(12 g SiO_2, 0-30% EtOAc/Hex) yielded nitrate ester **4** as a white crystalline solid (345 mg, 53% yield): mp = 52.2-54.0 °C; IR (ATR) cm^{-1} 3412 (br w, OH), 2944 (w), 2360 (w), 1616 (vs, NO_2), 1291 (m, NO_2), 868 (m, NO_2); HRMS ESI+ *m/z* calc'd for $[C_{10}H_{18}O_4N]^+$ (216.1230, observed; 216.1236, expected) ^{1}H NMR (400 MHz, chloroform-*d*) δ 3.70 (dd, *J* = 9.6, 7.6 Hz, 1H), 2.86 – 2.78 (m, 1H), 2.16 (dd, *J* = 14.8, 7.5 Hz, 1H), 1.83 (ddd, *J* = 14.8, 9.6, 7.9 Hz, 1H), 1.65 (s, 3H), 1.47 (dd, *J* = 14.3, 4.1 Hz, 1H), 1.03 (s, 3H), 1.01 (s, 3H), 0.83 – 0.73 (m, 2H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 95.68, 71.03, 28.37, 28.34, 27.02, 19.95, 18.98, 17.95, 15.70, 14.39 ppm.

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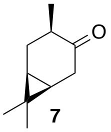
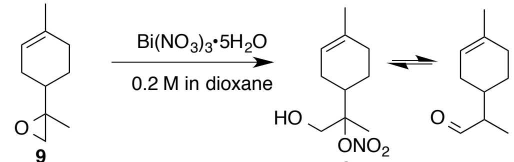


2.3.2 *cis*-4-caranone (7)

Nitration of *cis*-3-carene oxide was attempted according to the general method with dioxane or dichloromethane. Purification of the crude oil by column chromatography (12 g SiO_2, 0-40% EtOAc/Hex) yielded *cis*-4-caranone as a clear, colorless oil (53% yield): R_f 0.51 (5% EtOAc:Hex; anisaldehyde); ^1H NMR (400 MHz, chloroform-*d*) δ 2.54 (ddd, *J* = 18.0, 8.4, 1.0 Hz, 1H), 2.44 – 2.25 (m, 3H), 1.33 – 1.20 (m, 1H), 1.14 – 0.99 (m, 5H), 0.97 (d, *J* = 6.4 Hz, 3H), 0.86 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 216.79, 41.99, 36.84, 29.77, 27.91, 22.83, 20.34, 19.47, 14.89, 14.11 ppm. Spectral data is consistent with literature reports (Kolehmainen et al., 1993).



9 **10** **11**

2.3.3 Reaction of 8,9-limonene oxide (9)

Nitration of 8,9-limonene oxide (**9**) was attempted according to the general method with acetonitrile or dioxane. Dioxane yielded a mixture of putative nitrate ester **10** and aldehyde **11** (1:0.25) as a crude oil. Nitrate **10** (1:1 d.r.): R_f 0.25 (15% EtOAc:Hex; anisaldehyde); IR (ATR) cm^{-1} 3417 (br), 2913 (w), 1613 (vs, NO_2), 1439 (w), 1289 (m, NO_2), 865 (s, NO_2); ^1H NMR (400 MHz, chloroform-*d*) δ 5.39 – 5.35 (m, 1H), 4.06 – 3.86 (m, 2H), 2.41 – 2.26 (m, 1H), 2.09 – 1.82 (m, 5H), 1.66 (s, 3H), 1.49 (s, 1.5H), 1.48 (s, 1.5H), 1.43 – 1.31 (m, 2H) ppm; ^{13}C NMR (101 MHz, chloroform-*d*) δ 134.31, 134.01, 119.57, 119.31, 97.40, 97.17, 64.62, 64.27, 38.24, 38.19, 30.58, 30.47, 26.42, 25.87, 24.19, 23.32, 23.25, 23.22, 17.17, 16.78 ppm. Purification by column chromatography (12 g SiO_2 gold column, 0-50% EtOAc/Hex over 30 CV) yielded acetaldehyde **11** (1:1 d.r) as a clear, colorless oil (105 mg, 35% yield): ^1H NMR (400 MHz, chloroform-*d*) δ 9.69 (d, *J* = 2.4 Hz, 0.5H), 9.68 (d, *J* = 2.7 Hz, 0.5H), 5.42 – 5.35 (m, 1H), 2.35 – 2.25 (m, 1H), 2.10 – 1.73 (m, 6H), 1.68 – 1.62 (br s, 3H), 1.46 – 1.32 (m, 1H), 1.10 (s, 1.5H), 1.08 (s, 1.5H) ppm; ^{13}C NMR (101 MHz, chloroform-*d*) δ 205.55, 205.47,

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134.09, 134.05, 119.95, 119.88, 51.00, 50.68, 34.32, 34.25, 30.15, 29.99, 29.67, 28.05, 27.31, 25.43, 23.43, 10.34, 10.24 ppm. Spectral data is consistent with literature reports (Uehara et al., 2017; Reid & Watson, 2018).

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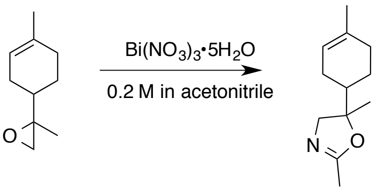
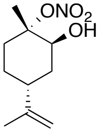


9 **10a**

Acetonitrile yielded oxazoline **10a** (1:1 d.r.) as a clear, colorless oil (76% yield): R_f 0.46 (75% EtOAc:Hex; anisaldehyde); IR (ATR) cm^{-1} 3323 (br), 2963 (m), 2913 (m), 1674 (vs), 1437 (m), 1384 (m), 1265 (m), 991 (vs), 915 (m); ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.38 (s, 1H), 4.10 (d, *J* = 6.2 Hz, 0.5H), 4.08 (d, *J* = 6.1 Hz, 0.5H), 3.82 (d, *J* = 8.3 Hz, 0.5H), 3.79 (d, *J* = 8.3 Hz, 0.5H), 2.16 – 1.91 (m, 6H), 1.89 – 1.75 (m, 1H), 1.73 – 1.56 (m, 5H), 1.29 – 1.14 (m, 4H); ^{13}C NMR (101 MHz, chloroform-*d*) 162.73, 162.64, 134.23, 133.89, 120.28, 120.23, 77.22, 76.08, 75.39, 72.75, 72.60, 42.55, 42.28, 30.65, 30.57, 26.75, 26.39, 25.03, 24.58, 23.79, 23.75, 23.37, 13.88, 13.87 ppm; GC-MS (100 – 275 ºC; 15 ºC/min): 6.691 min, *m/z* 193.8 (M+, 100%), 135.0 (M - [C_2H_3NO], 10%).



13

2.3.4 Nitrate ester 13

Nitration of *cis*-1,2-limonene oxide was carried out according to the general method with dioxane or dichloromethane. Purification by column chromatography (12 g SiO_2 gold column, 0-50% EtOAc/Hex over 30 CV) yielded nitrate ester **13** as a clear, colorless oil (53% yield in dioxane; 62% yield in DCM): IR (ATR) cm^{-1} 3660 (w, alcoholic OH), 3340 (bd w, alcoholic OH), 2980 (m), 1618 (s, NO_2), 1291 (m, NO_2), 860 (vs, NO_2);

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HRMS ESI+ *m/z* calc'd for $[C_{10}H_{17}O_4NNa]^+$ (238.1052, observed; 238.1055, expected); ^{1}H NMR (400 MHz, chloroform-*d*) δ 4.76 (dd, *J* = 8.1, 1.5 Hz, 2H), 4.13 (s, 1H), 2.35 (ddt, *J* = 11.6, 8.4, 4.1 Hz, 1H), 2.24 (dtd, *J* = 14.8, 3.7, 1.4 Hz, 1H), 1.98 – 1.78 (m, 3H), 1.76 – 1.73 (m, 4H), 1.68 – 1.58 (m, 4H), 1.49 (tdd, *J* = 13.3, 11.6, 3.6 Hz, 1H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 148.49, 109.48, 91.34, 69.22, 36.84, 33.86, 29.90, 25.77, 20.98, 20.93 ppm.

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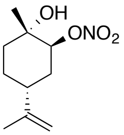

14

2.3.5 Nitrate ester 14

Nitration of *trans*-1,2-limonene oxide was carried out according to the general method with dioxane or dichloromethane. Purification by column chromatography (12 g SiO_2, 0-50% EtOAc/Hex over 30 CV) yielded nitrate ester **14** as a clear, colorless oil (63% in dioxane; 54% in DCM): R_f 0.39 (15% EtOAc:Hex; anisaldehyde); IR (ATR) cm^{-1} 3414 (bd w, alcoholic OH), 2940 (w), 1627 (s, NO_2), 1279 (m, NO_2), 876(m, NO_2), 851 (m, NO_2); HRMS ESI+ *m/z* calc'd for $[C_{10}H_{17}O_4NNa]^+$ (238.1048, observed; 238.1055, expected); ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.01 (s, 1H), 4.76 (d, *J* = 6.6 Hz, 2H), 2.19 (tt, *J* = 10.9, 3.1 Hz, 1H), 2.03 (ddd, *J* = 14.7, 12.1, 2.6 Hz, 1H), 1.92 (dq, *J* = 14.4, 3.5, 2.7 Hz, 1H), 1.74 (s, 3H), 1.69 – 1.56 (m, 4H), 1.32 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 148.27, 109.57, 84.43, 69.55, 37.96, 34.78, 29.91, 26.96, 20.89 ppm.

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2.3.6 Nitration of perillic alcohol epoxide (15)

Nitration of 4-(1-methylethenyl)-7-oxabicyclo[4.1.0]heptane-1-methanol (**15**) was carried out according to the general method with dichloromethane. Purification by column chromatography (12 g SiO_2, 0-40% EtOAc/Hex over 30 CV) yielded two regioisomers, nitrate esters **16** and **17** in 23% and 32% yield, respectively.

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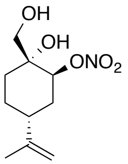

2.3.6.1 Nitrate ester 16

16

Nitrate ester **16** was isolated as a white, crystalline solid (106 mg, 23% yield): mp = 72-75°C; R_f 0.31 (30% EtOAc:Hex; anisaldehyde); IR (ATR) cm^{-1} 3285 (bd w, alcoholic OH), 2941 (w), 1627 (vs, NO_2), 1280 (s, NO_2), 880 (s, NO_2), 850 (s, NO_2); HRMS ESI+ *m/z* calc'd for $[C_{10}H_{17}O_4NNa]^+$ (238.1054, observed; 238.1055, expected); ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.23 (s, 1H), 4.80 – 4.73 (m, 2H), 3.74 (dd, *J* = 10.9, 5.0 Hz, 1H), 3.44 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.59 (d, *J* = 1.0 Hz, 1H), 2.27 – 2.16 (m, 1H), 2.03 – 1.97 (m, 2H), 1.79 (t, *J* = 5.2 Hz, 1H), 1.71 – 1.61 (m, 3H), 1.58 (d, *J* = 0.8 Hz, 4H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 148.24, 109.58, 79.89, 70.98, 66.45, 38.47, 29.70, 29.55, 25.10, 20.77 ppm.

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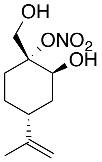

2.3.6.2 Nitrate ester 17

17

Nitrate ester **17** was isolated as a clear, colorless oil (149 mg, 32% yield): R_f 0.20 (30% EtOAc:Hex; anisaldehyde); IR (ATR) cm^{-1} 3286 (bd w, alcoholic OH), 2941 (w), 1623 (vs, NO_2), 1288 (s, NO_2), 863 (vs, NO_2); HRMS ESI- *m/z* calc'd for $[C_{10}H_{16}O_4N]^-$ (214.10813, observed; 214.10848, expected); ^{1}H NMR (400 MHz, chloroform-*d*) δ 4.76 (d, *J* = 8.5 Hz, 2H), 4.31 (s, 1H), 4.27 (d, *J* = 13.0 Hz, 1H), 3.99 (d, *J* = 13.0 Hz, 1H), 2.41 (tt, *J* = 12.1, 3.6 Hz, 1H), 2.27 – 2.19 (m, 1H), 1.98 – 1.78 (m, 3H), 1.75 (s, 3H), 1.72 – 1.65 (m, 1H), 1.51 – 1.38 (m, 1H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 148.58, 109.43, 92.51, 65.67, 62.91, 37.47, 33.53, 25.33, 25.26, 20.86 ppm.

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2.3.7 Nitration of α-pinene oxide

Nitration of α-pinene oxide was carried out according to the general method. Crude oil from a 10 mmol reaction was purified by column chromatography (40 g SiO_2, 0-40% EtOAc/Hex over 30 CV) yielded the following isomerization products and nitrate esters.

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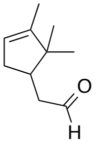

19

2.3.7.1 α-campholenic aldehyde (19)

α-Campholenic aldehyde **19** was isolated as a clear, colorless oil: R_f 0.59 (10% EtOAc:Hex; anisaldehyde); ^{1}H NMR (400 MHz, benzene-d_6) δ 9.51 (t, J = 2.1 Hz, 1H), 5.23 (s, 1H), 2.41 (dddt, J = 13.8, 6.0, 2.7, 1.6 Hz, 1H), 2.25 – 2.16 (m, 1H), 2.11 (ddd, J = 15.9, 4.4, 1.8 Hz, 1H), 2.00 (ddd, J = 15.9, 10.3, 2.3 Hz, 1H), 1.80 (ddp, J = 15.8, 9.2, 2.5 Hz, 1H), 1.58 (dt, J = 3.0, 1.6 Hz, 3H), 0.90 (s, 3H), 0.68 (s, 3H). Spectral data is consistent with literature reports (Thomas et al., 2016).

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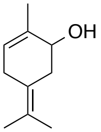

20

2.3.7.2 5-isopropylidene-2-methyl-2-cyclohexen-1-ol (20)

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Compound **20** was isolated as a white, crystalline solid: R_f 0.47 (20% EtOAc:Hex; anisaldehyde); ^{1}H NMR (400 MHz, chloroform-d) δ 5.49 (ddd, J = 4.4, 3.2, 1.5 Hz, 1H), 3.99 (t, J = 4.2 Hz, 1H), 2.86 (d, J = 19.6 Hz, 1H), 2.69 – 2.56 (m, 2H), 2.35 (d, J = 15.5 Hz, 1H), 1.78 – 1.75 (m, 3H), 1.74 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (101 MHz, chloroform-d) δ 135.94, 125.57, 124.23, 123.29, 70.34, 35.92, 29.83, 20.31, 20.14, 19.91 ppm. Spectral data is consistent with literature reports (Motherwell et al., 2004).

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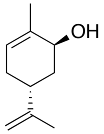

21

2.3.7.3 *trans*-Carveol (21)

trans-Carveol was isolated as a clear, colorless oil: R_f 0.37 (20% EtOAc:Hex; anisaldehyde); ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.62 (dd, *J* = 5.2, 1.5 Hz, 1H), 4.78 – 4.73 (m, 2H), 4.06 – 4.03 (m, 1H), 2.34 (ddd, *J* = 13.7, 9.8, 2.9 Hz, 1H), 2.21 – 2.12 (m, 1H), 1.96 (dq, *J* = 13.6, 2.3 Hz, 1H), 1.93 – 1.85 (m, 1H), 1.85 – 1.81 (m, 3H), 1.77 (s, 3H), 1.64 (dd, *J* = 13.2, 4.0 Hz, 1H), 1.61 – 1.57 (m, 1H) ppm. Spectral data is consistent with literature reports). (Motherwell et al., 2004).

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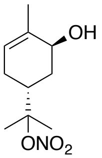

22

2.3.7.4 *trans*-Carveol nitrate ester 22

Nitrate ester **22** was isolated as a clear, colorless oil: IR (ATR) cm^{-1} 3353 (bd w, alcoholic OH), 2917 (w), 1614 (vs, NO_2), 1293 (s, NO_2), 868 (m, NO_2); ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.32 (ddd, *J* = 9.9, 3.5, 2.1 Hz, 1H), 4.12 (ddd, *J* = 10.6, 4.6, 1.9 Hz, 1H), 2.68 – 2.49 (m, 2H), 1.88 (t, *J* = 4.8 Hz, 1H), 1.43 (dd, *J* = 14.1, 3.7 Hz, 1H), 1.24 (dd, *J* = 13.8, 4.8 Hz, 1H), 1.11 (s, 3H), 0.97 (s, 3H), 0.94 (s, 3H) ppm. Spectral data is consistent with literature reports (Rindelaub et al., 2016b).

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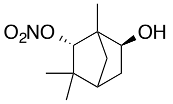

23

2.3.7.5 Nitrate ester 23

Nitrate ester **23** was isolated as a white, crystalline solid: mp = 132-134 °C; R_f 0.29 (25% EtOAc:Hex; anisaldehyde); IR (ATR) cm^{-1} 3294 (bd w, alcoholic OH), 2961 (w), 2360 (w), 1624 (m, NO_2), 1282 (m, NO_2),

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862 (m, NO_2); HRMS ESI- *m/z* calc'd for $[C_{10}H_{16}O_4N]^-$ (214.10797, observed; 214.10848, expected); ^{1}H NMR (400 MHz, chloroform-*d*) δ 4.64 (s, 1H), 4.00 (ddd, *J* = 7.1, 3.3, 0.9 Hz, 1H), 2.37 (ddd, *J* = 13.8, 7.1, 2.5 Hz, 1H), 1.81 (d, *J* = 4.3 Hz, 1H), 1.60 – 1.51 (m, 3H), 1.32 (dt, *J* = 13.8, 4.0 Hz, 1H), 1.23 (s, 3H), 1.22 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 94.13, 68.52, 53.01, 47.34, 40.49, 37.76, 37.10, 29.24, 19.12, 14.75 ppm.

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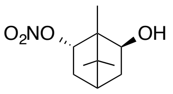

24

2.3.7.6 Nitrate ester 24

Nitrate ester **24** was isolated as a white, crystalline solid: mp = 62-64 °C; R_f 0.24 (15% EtOAc:Hex; anisaldehyde); HRMS ESI+ *m/z* calc'd for $[C_{10}H_{17}O_4NNa]^+$ (238.10459, observed; 238.10498, expected); IR (ATR) cm^{-1} 3434 (w, alcoholic OH), 2959 (w), 1622 (s, NO_2), 1284 (vs, NO_2), 856 (m, NO_2); ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.31 (ddd, *J* = 9.9, 3.8, 2.1 Hz, 1H), 4.12 (m, 1H), 2.69 – 2.48 (m, 2H), 1.87 (t, *J* = 4.9 Hz, 1H), 1.43 (dd, *J* = 14.0, 3.7 Hz, 1H), 1.24 (dd, *J* = 13.7, 4.7 Hz, 1H), 1.11 (s, 3H), 0.97 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 91.04, 78.09, 52.58, 49.53, 42.73, 39.05, 36.71, 20.20, 19.70, 11.79 ppm.

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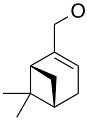
2.3.8 Nitration of β-pinene oxide

Nitration of β-pinene oxide (11.1 mmol) was carried out according to the general procedure in toluene. Purification by column chromatography (80 g SiO_2, 0-30% EtOAc/Hex over 20 CV) yielded a 1:1 mix of myrtenol (**26**) and nitrate **29** (344 mg, 9 % combined yield), perillic alcohol (**28**, 600 mg, 36% yield) and nitrate **27** (71 mg, 3% yield). The combined myrtenol and nitrate **29** were separated by column chromatography (40 g SiO_2; 5-20% EtOAc/Hex over 25 CV).



26

2.3.8.1 Myrtenol (26)

Myrtenol was isolated as a clear, colorless oil: R_f 0.25 (15% EtOAc:Hex; anisaldehyde); ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.49 (dt, *J* = 3.0, 1.5 Hz, 1H), 4.00 (t, *J* = 1.8 Hz, 2H), 2.42 (dt, *J* = 8.6, 5.6 Hz, 1H), 2.37 –

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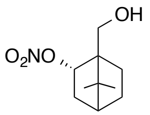
2.20 (m, 2H), 2.19 – 2.09 (m, 2H), 1.61 – 1.45 (m, 1H), 1.31 (s, 3H), 1.19 (d, *J* = 8.6 Hz, 1H), 0.85 (s, 3H) ppm. Spectral data is consistent with literature reports (Motherwell et al., 2004)



27

2.3.8.2 Nitrate ester 27

Nitrate ester **27** was isolated as a clear colorless oil: IR (ATR) cm^{-1} 3362 (bd w, alcoholic OH), 2947 (w), 1624 (s, NO_2), 1281 (vs, NO_2), 864 (m, NO_2); HRMS ESI- *m/z* calc'd for $[C_{10}H_{16}O_4N]^-$ (214.10813, observed; 214.10848, expected); ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.57 – 5.49 (m, 1H), 3.71 (q, *J* = 11.5, 8.5 Hz, 2H), 2.55 (ddt, *J* = 14.1, 9.8, 3.9 Hz, 1H), 1.95 – 1.83 (m, 2H), 1.76 (t, *J* = 4.5 Hz, 1H), 1.52 – 1.22 (m, 5H), 1.10 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 85.30, 62.08, 53.45, 48.62, 45.59, 35.78, 27.53, 22.88, 20.20, 20.02 ppm.

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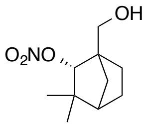

29

2.3.8.3 Nitrate ester 29

Nitrate ester **29** was isolated as a white, crystalline solid: mp = 59-61 °C; R_f 0.55 (15% EtOAc:Hex; anisaldehyde); IR (ATR) cm^{-1} 3374 (bd w, alcoholic OH), 2915 (w), 1625 (s, NO_2), 1281 (vs, NO_2), 863 (m, NO_2); HRMS ESI+ *m/z* calc'd for $[C_{10}H_{17}O_4NNa]^+$ (238.10474, observed; 238.10498, expected); ^{1}H NMR (400 MHz, chloroform-*d*) δ 4.92 (d, *J* = 1.6 Hz, 1H), 3.75 (d, *J* = 11.3 Hz, 1H), 3.65 (d, *J* = 11.3 Hz, 1H), 1.90 – 1.80 (m, 3H), 1.72 – 1.63 (m, 1H), 1.56 – 1.50 (m, 1H), 1.24 – 1.20 (m, 4H), 0.96 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 89.49, 63.82, 54.38, 48.25, 40.28, 37.03, 29.26, 24.74, 22.11, 19.46 ppm.

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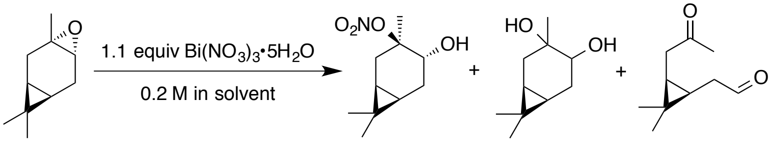
3 Results and discussion

3.1 Synthesis



3 **4** **caronaldehyde**

entry	solvent	%**4**	%diol	%caronaldehyde
1	CH_2Cl_2	14	18	3
2	CH_3CN	6	15	7
3	dioxane	53	16	3

Figure 2: Effect of solvent on nitration of *trans*-(3)-carene oxide.

Previous reports have described the opening of epoxides and aziridines using bismuth nitrate in acetonitrile (Das et al., 2007). Others report optimal conditions in dichloromethane (Rindelaub et al., 2016b), or 1,4-dioxane with undesired side reactions in acetonitrile (Pinto et al., 2007). Thus, we began our investigations into the nitration of *trans*-carene oxide (**3**) using bismuth nitrate in various solvents (Figure 2). In our hands, dioxane clearly outperformed dichloromethane, yielding 53% of the desired product after 45 minutes (entry 3). A diol was isolated as a major (16%) byproduct. Attempts to mitigate hydrolysis by the use of base or molecular sieves were ineffective. Acetonitrile produced a complex intractable mixture with a high amount of diol and caronaldehyde (entry 2). Other solvents, such as THF and nitromethane, also produced complex mixtures with no trace of desired nitrate. Methanol, interestingly, only produced an undesired methyl ether. It is unclear if this product was generated through methanolysis of the nitrate ester or direct substitution of the epoxide. The regiochemistry of the nitration was easily elucidated with gHSQC NMR data. A doublet of doublets at 3.69 ppm correlated with a carbon shift at 71.1 ppm and was thus assigned to the alcohol methyne carbon. A tetrasubstituted carbon, with no correlations in the gHSQC, at 95.6 ppm was consistent with the tertiary nitrate ester. Finally, the IR of compound **4** displayed the expected strong absorbances at 1616, 1291, and 868 cm^{-1}.

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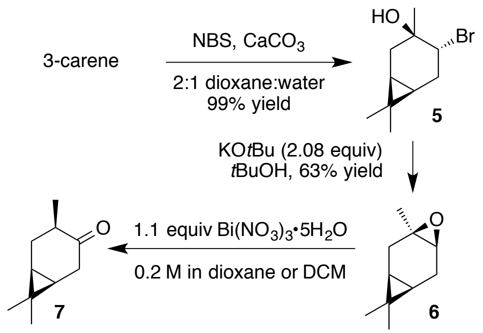

Figure 3: Preparation of *cis*-3-carene oxide and attempted nitration.

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Next, we aimed to investigate the impact of relative stereochemistry on the nitration. We hypothesized that the secondary nitrate would predominate due to classical stereoelectronic effects. (+)-3-Carene was treated with N-bromosuccinimide and calcium carbonate to produce a bromohydrin which subsequently cyclized under basic conditions to produce *cis*-carene oxide (Cocker and Grayson, 1969). Interestingly, we never observed the desired nitrate ester. Instead a 1,2-hydrogen shift generated *cis*-4-caranone (7) in 53% yield.

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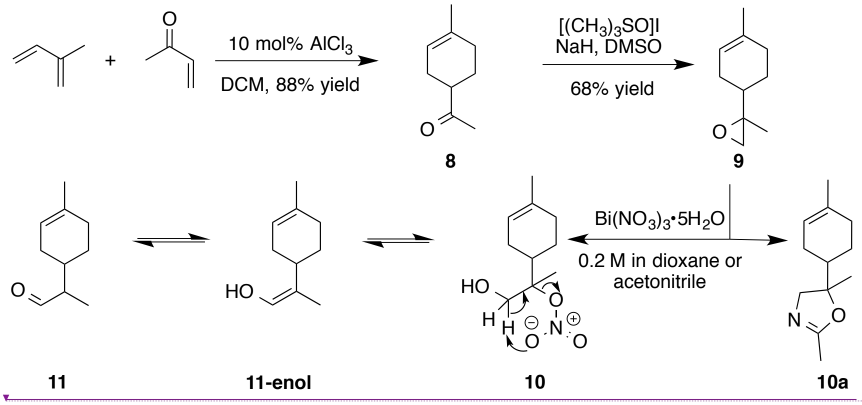

Figure 4: Preparation of 8.9-limonene oxide and attempted nitration.

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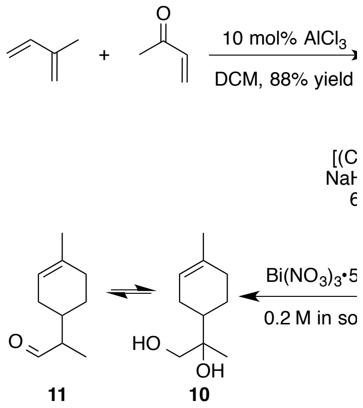

The preparation of 8,9-limonene oxide (**9**) began with a Diels-Alder reaction to form 1-(4-methyl-3-cyclohexene) ethenone (**8**) in 88% yield. Corey-Chaykovsky addition of a sulfur ylide cleanly produced 8,9-limonene oxide (**9**). Nitration of **9** was attempted in a variety of solvents (DCM, benzene, dioxane, acetonitrile, nitromethane). In acetonitrile, oxazoline **10a** (1:1 d.r.) was cleanly produced presumably via nucleophilic addition of acetonitrile and subsequent cyclization to the oxazoline. Pinto, et al. 2007 observed a similar bismuth nitrate mediated epoxide opening with acetonitrile. In dioxane, aldehyde **11** (1:1 d.r.) was observed along with a product consistent with a tertiary nitrate ester **10** (1:1 d.r.) in a 0.25:1 mixture. Formation of **11-enol** presumably proceeds via a facile intramolecular elimination of nitric acid. The IR of the crude mixture showed the expected strong absorbances at 1613, 1288 and 865 cm^{-1}. A set of signals in the ^{13}C NMR at 97.40 & 97.17 ppm, with no gHSQC correlations, are consistent with a tertiary nitrate. Attempts to purify this mixture on silica gel gave small amounts of **11** and unidentifiable decomposition products. Furthermore, the fast hydrolysis rates of tertiary nitrate esters hinder the ability to isolate these products (Boyd et al., 2015; Darer et al., 2011; Liu et al., 2012). No reaction was observed when non-polar solvents such as DCM and benzene were employed. We hypothesize that the steric hindrance at the β-carbon severely limits reactivity.

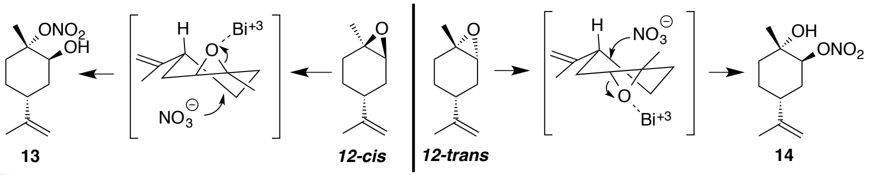

Figure 5: Nitration of *cis*- and *trans*-1,2-limonene oxide.

Commercially available 1,2-limonene oxide was resolved into pure samples of *cis*- and *trans*-1,2-limonene oxide by treating with cyclic amine bases (Steiner et al., 2002). The nitration of the *cis* isomer was predicted to produce the tertiary nitrate ester via stereoelectronic effects. The dominant conformation of *cis*-1,2-limonene oxide is expected to be a pseudo-half chair (Figure 5). Nucelophilic substitution at the less substituted position would proceed through a lower energy chair-like transition state, whereas attack at the more substituted carbon leads to a very unstable twist-boat. The nitration of *cis*-1,2-limonene oxide (***cis*-12**) proceeded smoothly in both dioxane (53%) and dichloromethane (63%). Respectively, the *trans* isomer was expected to produce the secondary nitrate ester. The nitration of *trans*-1,2-limonene oxide (***trans*-12**) also proceeded smoothly in both dioxane (63%) and dichloromethane (61%). Contrary to previous reports (Romonosky et al., 2015), we did not observe the desired nitrate esters in acetonitrile. gHSQC NMR data was used to verify nitrate ester **13** was

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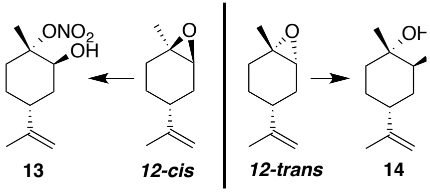

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tertiary and **14** was secondary. For **13**, a broad singlet at 4.12 ppm correlated with a carbon shift at 69.2 ppm and was thus assigned to the methyne adjacent to the alcohol. A tetrasubstituted carbon at 91.4 ppm was consistent with the tetrasubstituted nitrate ester. Similarly for **14**, a broad triplet at 5.00 ppm correlated with a carbon shift at 84.45 ppm and was thus assigned to the methyne adjacent to the nitrate ester. A tetrasubstituted carbon at 69.5 ppm was consistent with the tertiary alcohol.

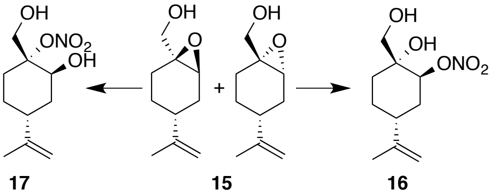
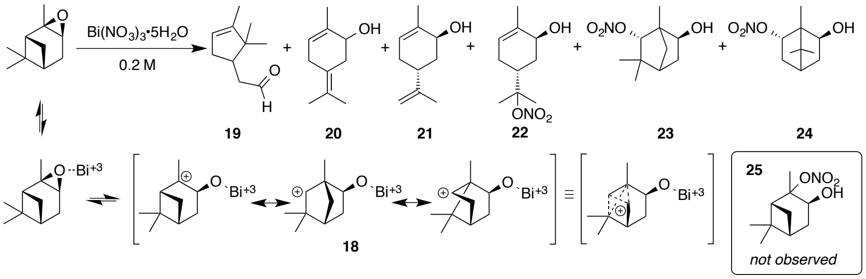


Figure 6: Nitration of perillic alcohol oxide.

Under acidic conditions, β-pinene oxide undergoes facile rearrangement to form perillic alcohol. Accordingly, we prepared the epoxide **15** by treating perillic alcohol with 1 equivalent of m-CPBA. The inseparable mixture of diastereomers were treated with bismuth nitrate under the standard reaction conditions. Nitrate esters **16** and **17** were easily separated by column chromatography and assigned to the secondary and tertiary nitrate esters, respectively. These isomers were formed from the *cis*- and *trans*-epoxide diastereomers in an analogous fashion to the limonene isomers. For **16**, a broad singlet at 5.21 ppm correlated with a carbon shift at 80.1 ppm and was thus assigned to the methyne adjacent to the nitrate ester. A tetrasubstituted carbon at 70.9 ppm was consistent with the tertiary alcohol. Similarly for **15**, a broad singlet at 4.22 ppm correlated with a carbon shift at 65.6 ppm and was thus assigned to the methyne adjacent to the alcohol. A tetrasubstituted carbon at 92.8 ppm was consistent with the tertiary nitrate ester.



entry	solvent	temp (ºC)	additive	%**19**	%**20**	%**21**	%**22**	%**23**	%**24**
1	CH_2Cl_2	23	--	21	2	5	2	1	4
2	CH_2Cl_2	-78	--	--	--	--	--	--	--
3	CH_2Cl_2	-78	1 equiv TBAN	20	--	6	13	3	--
4	dioxane	23	--	25	--	--	5	5	2
5	Toluene	23	--	22	1	4	4	8	--
6	Toluene	23	1 equiv TBAN	28	8	13	6	4	2

Figure 7: Nitration of α-pinene oxide.

The facile rearrangements of α-pinene with both Brønsted and Lewis Acids (Kaminska et al., 1992) can be thought to proceed via a non-classical isobornyl cation (**18**) (Kong et al., 2010). We expected the reaction with bismuth nitrate to generate a complex mixture of products due to the many reactive sites. As shown in Figure 7, three rearrangement products (campholenic aldehyde **19**, diene **20**, and *trans*-carveol **21**) and three nitrate esters (**22**, **23**, **24**) were observed. The structure of nitrate ester **23** was identified by a clear singlet at 4.64 ppm (s, 1H). 2D-NMR data (gCOSY, gHSQC and gHMBC) along with comparison to 6-exo-hydroxyfenchol, the analogous diol confirmed the structural assignment (Miyazawa and Miyamoto, 2004). Correspondingly, nitrate ester **24** displayed a distinct doublet of doublets of doublets at 5.31 ppm that correlated to the methyne adjacent to the nitrate ester. Again, 2D NMR data (gCOSY, gHSQC and gHMBC) was used in conjunction with the literature spectra for platydiol and its *trans* diastereomer to verify the assignment (Kuo et al., 1989).

Under all conditions campholenic aldehyde was the major product (20-28% yield). First generation nitrate ester **25** was not found under all conditions. All six components were isolated in small amounts when the reaction was run in dichloromethane (Figure 7, entry 1). Cooling the reaction to -78 ºC completely shut down all

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reactivity (entry 2). Interestingly, adding one equivalent of tetrabutylammonium nitrate (TBAN) as an external nitrate source in addition to bismuth nitrate at -78 ºC generated mostly nitrate **22** (entry 3). More polar solvents, like dioxane (entry 4), generated slightly higher amounts of nitrates at room temperature. Aromatic solvents, such as benzene and toluene provided the best yield of **23.** Interestingly, adding TBAN to the nitration in toluene dramatically increased the amounts of diene **20** and *trans*-carveol **21**. Using acetonitrile as a solvent generated a complex mixture that appeared to be mainly diols. Zirconium nitrate produced a similar distribution of products (Das et al., 2006), but other metal nitrate complexes ($Y(NO_3)_3 \bullet 6H_2O$, $Co(NO_3)_2 \bullet 6H_2O$) resulted in no observable reaction.

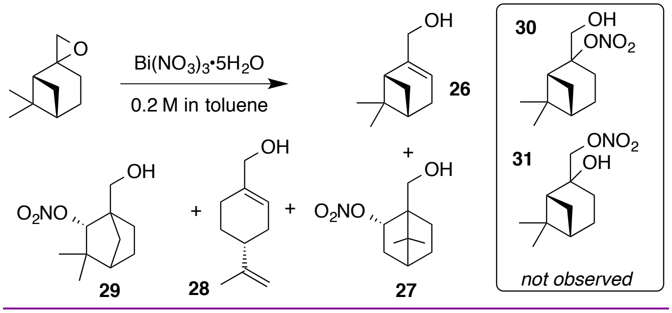

Figure 8: Nitration of β-pinene oxide.

The nitration of β-pinene was similarly complicated by isomerization pathways through the corresponding non-classical carbocation. Nitrate **27** initially co-eluted with myrtenol (**26**) but was separable upon a second purification by column chromatography. The methyne proton of **27** at 5.51 ppm is correlated with a carbon at 85.3 ppm in the gHSQC NMR. This data is consistent with the secondary nitrate ester. Similarly, the methyne proton in nitrate **29** is a doublet at 4.91 ppm (J^4 = 1.6 Hz; W-coupling). This signal correlates with a carbon at 89.5 ppm. Interestingly, nitrates **30** and **31** were not observed.

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3.2 Spectral data

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Table 1. Collated ^{1}H and ^{13}C NMR data with IR absorbances for nitrate esters.

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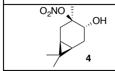
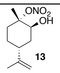
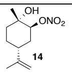
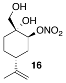
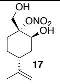
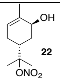
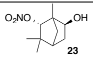
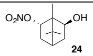
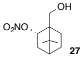
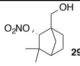
compound	C**H**ONO$_2$ (ppm)	**C**HONO$_2$ (ppm)	IR (cm^{-1})		
 4	--	95.6	1616	1291	868

 13	--	91.4	1618	1291	860
 14	5.00 (s, 1H)	84.4	1627	1279	876
 16	5.21 (s, 1H)	80.1	1627	1280	880
 17	--	92.5	1623	1288	863
 22	--	94.2	1614	1293	868
 23	4.64 (s, 1H)	94.13	1624	1282	862
 24	5.31 (ddd, *J* = 9.9, 3.8, 2.1 Hz, 1H)	91.04	1622	1284	856
 27	5.51 (m, 1H)	85.3	1624	1281	864
 29	4.91 (s, 1H)	89.5	1625	1281	863

As shown in table 1, all nitrate esters displayed the expected strong nitrate ester absorbances at ~1600, 1300, and 900 cm^{-1}. Methyne protons next to the secondary nitrate esters appeared between 4.64 ppm and 5.51 ppm. Carbon chemical shifts were found over a broader range than anticipated from 80.1 to 95.6 ppm. Finally, we observed masses consistent with methanolysis products (185.1 *m/z* M+; 223.1 *m/z* M+K) when nitrate esters were analysed (GC-MS) as solutions in methanol. Further experimentation is necessary to evaluate the implications of methanolysis.

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3.3 Stability and storage

We were surprised to find that five of the nitrate esters (**4**, **16**, **23**, **24**, and **29**) are solids. We have stored these compounds at 0 ºC for up to 9 months with no noticeable decline in purity. The remaining nitrate esters are stable at 0 ºC for 2-4 weeks. Interestingly, some of these compounds appear to deviate from the expected stability patterns (*vide supra*). For example, tertiary nitrate ester **4** is particularly stable stored as a solid at 0 ºC. In contrast, when secondary nitrate ester **14** was stored as a neat oil at 0 ºC, it decomposed to a complex mixture within a few weeks. Freezing the samples as a solution in benzene is recommended for longer term (~6 month) storage.

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4 Conclusions

We have clearly delineated successful methods required to synthesize and purify nine nitrate esters derived from mono-terpenes. Seven of these compounds are undescribed in the literature and the remaining two had gaps in their characterization. Interestingly, we did not observe the formation of α-pinene oxide and β-pinene oxide products that retained their bicyclic ring structures. This is consistent with the solution phase synthetic literature (Kaminska et al., 1992) but in contrast to many atmospheric reports (For example, see: Rindelaub, 2016b; Duporte, G., et al., 2016). We believe that the availability of these compounds will enable further study of the structure-reactivity relationships. For example, comparing the specific hydrolysis rates for tertiary versus secondary nitrate esters in **13** and **14** as well as **17** and **16** could help deconvolute the fates of each terpene in the atmosphere. We also believe that these compounds will assist in confirming the identities of organic nitrates that have previously been limited to detection by MS based methods (Rindelaub, 2016b). Using our methods it is possible to cleanly isolate 50-100 mg even of the least prevalent isomers from the nitration reactions of α-pinene and β-pinene. The availability of these compounds is important for further studies into the influence of terpene structure on the fate and roles of organic nitrates in SOA formation.

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Supplementary material related to this article is available online at:

Author contributions. RL designed the experiments and prepared the manuscript with contributions from all co-authors. All co-authors carried out experiments and contributed to reviewing and editing the manuscript.

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compounds. We are particularly grateful to Drew Gingerich, Nick Till, Stewart Green, Alyssa Harrison, Carlo Berti for preliminary experiments and to the 2014 and 2015 Chem 343 students for their assistance in this research.

References

Almeida, Q. A. and Jr., J.: Chemoselective Formation of 8,9-Epoxy-limonene, Synthetic Commun, 35(10), 1285–1290, doi:10.1081/scc-200057232, 2005.

Bleier, D. B. and Elrod, M. J.: Kinetics and Thermodynamics of Atmospherically Relevant Aqueous Phase Reactions of α-Pinene Oxide, J Phys Chem, 117(20), 4223–4232, doi:10.1021/jp402093x, 2013.

Boyd, C., Sanchez, J., Xu, L., Eugene, A., Nah, T., Tuet, W., Guzman, M. and Ng, N.: Secondary organic aerosol formation from the β-pinene+NO_3 system: effect of humidity and peroxy radical fate, Atmos Chem Phys, 15(13), 7497–7522, doi:10.5194/acp-15-7497-2015, 2015.

Buss, A. D., Greeves, N., Mason, R. and Warren, S.: Applications of the stereochemically-controlled Horner-Wittig reaction: synthesis of feniculin, (*E*)-non-6-en-1-ol, a pheromone of the mediterranean fruit fly, (*E*)- and (*Z*)-dec-5-en-1-ol, tri-substituted alkenes, and (*Z*)-α-bisabolene, J Chem Soc Perkin Transactions 1, 2569–2577, doi:10.1039/p19870002569, 1987.

Cabaj, J.E., Lukesh, J.M., Pariza, R.J., and Zizelman, P.M.: Large-Scale Preparation of (+)-p-Menth-2-ene-1,8-diol, a Key Intermediate in the Synthesis of Δ-9-Tetrahydrocannabinol, Org Process Res Dev, 2009, 1323, 58-361 doi: 10.1021/op8002272

Charbonneau, L., Foster, X. and Kaliaguine, S.: Ultrasonic and Catalyst-Free Epoxidation of Limonene and Other Terpenes Using Dimethyl Dioxirane in Semibatch Conditions, ACS Sustain Chem Eng, 6(9), 12224–12231, doi:10.1021/acssuschemeng.8b02578, 2018.

Cocker, W. and Grayson, D. H.: A convenient preparation of (−)-β-3,4-epoxycarane, Tetrahedron Lett, 10(51), 4451–4452, doi:10.1016/s0040-4039(01)88721-9, 1969.

Darer, A. I., Cole-Filipiak, N. C., O'Connor, A. E. and Elrod, M. J.: Formation and Stability of Atmospherically Relevant Isoprene-Derived Organosulfates and Organonitrates, Environ Sci Technol, 45(5), 1895–1902, doi:10.1021/es103797z, 2011.

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Das, B., Krishnaiah, M. and Venkateswarlu, K.: Zirconyl nitrate mediated regioselective ring opening of epoxides and aziridines: an easy synthesis of β-nitrato-alcohols and -sulfonamides, Tetrahedron Lett, 47(34), 6027–6029, doi:10.1016/j.tetlet.2006.06.114, 2006.

Das, B., Krishnaiah, M., Venkateswarlu, K. and Reddy, V.: Efficient Regio- and Stereoselective Conversions of Oxiranes and Aziridines into β-(Nitrooxy)-Substituted Alcohols and Amines by Using Bismuth Nitrate, Helv Chim Acta, 90(1), 110–113, doi:10.1002/hlca.200790002, 2007.

Duporte, G., Flaud, P.-M., Geneste, E., Augagneur, S., Panui, E., Lamkaddam, H., Gratien, A., Doussin, J.-F., Budzinski, H., Villenave, E. and Perraudin, E.: Experimental Study of the Formation of Organosulfates from α-Pinene Oxidation. Part I: Product Identification, Formation Mechanisms and Effect of Relative Humidity. J Phys Chem A, 120 (40), 7909–7923, doi:10.1021/acs.jpca.6b08504, 2016.

Guenther, A., Jiang, X., Heald, C., Sakulyanontvittaya, T., Duhl, T., Emmons, L. and Wang, X.: The Model of Emissions of Gases and Aerosols from Nature version 2.1 (MEGAN2.1): an extended and updated framework for modeling biogenic emissions, Geosci Model Dev, 5(6), 1471–1492, doi:10.5194/gmd-5-1471-2012, 2012.

Hu, K., Darer, A. and Elrod, M.: Thermodynamics and kinetics of the hydrolysis of atmospherically relevant organonitrates and organosulfates, Atmos Chem Phys, 11(16), 8307–8320, doi:10.5194/acp-11-8307-2011, 2011.

Jacobs, M., Burke, W. and Elrod, M.: Kinetics of the reactions of isoprene-derived hydroxynitrates: gas phase epoxide formation and solution phase hydrolysis, Atmos Chem Phys, 14(17), 8933–8946, doi:10.5194/acp-14-8933-2014, 2014.

Kaminska, J., Schwegler, M., Hoefnagel, A. and van Bekkum, H.: The isomerization of α-pinene oxide with Brønsted and Lewis acids, Recl Trav Chim Pay-B, 111(10), 432–437, doi:10.1002/recl.19921111004, 1992.

Kolehmainen, E., Laihia, K., Heinänen, M., Rissanen, K., Fröhlich, R., Korvola, J., Mänttäri, P. and Kauppinen, R.: Oxygen-containing bicyclic monoterpenes. ^{1}H, ^{13}C and ^{17}O NMR Spectroscopic and X-ray diffraction studies of seven oxidation products of (+)-3-carene, J Chem Soc Perkin Transactions 2, 0(4), 641–648, doi:10.1039/p29930000641, 1993.

Kong, J., Schleyer, P. v. R. and Rzepa, H. S.: Successful Computational Modeling of Isobornyl Chloride Ion-Pair Mechanisms, J Org Chem, 75(15), 5164–5169, doi:10.1021/jo100920e, 2010.

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Kuo, Y. -H., Chen, W. -C. and Shih, K. -S.: ChemInform Abstract: Platydiol, a New Monoterpene from the Pericarp of Platycladus orientalis, Cheminform, 20(46), doi:10.1002/chin.198946296, 1989.

Liu, S., Shilling, J. E., Song, C., Hiranuma, N., Zaveri, R. A. and Russell, L. M.: Hydrolysis of Organonitrate Functional Groups in Aerosol Particles, Aerosol Sci Tech, 46(12), 1359–1369, doi:10.1080/02786826.2012.716175, 2012.

Miyazawa, M. and Miyamoto, Y.: Biotransformation of (+)-(1R,2S)-fenchol by the larvae of common cutworm (Spodoptera litura), Tetrahedron, 60(13), 3091–3096, doi:10.1016/j.tet.2004.01.076, 2004.

Motherwell, W. B., Bingham, M. J., Pothier, J. and Six, Y.: A study of some molecularly imprinted polymers as protic catalysts for the isomerisation of α-pinene oxide to *trans*-carveol, Tetrahedron, 60(14), 3231–3241, doi:10.1016/j.tet.2004.02.016, 2004.

Nozière, B., Kalberer, M., Claeys, M., Allan, J., D'Anna, B., Decesari, S., Finessi, E., Glasius, M., Grgić, I., Hamilton, J. F., Hoffmann, T., Iinuma, Y., Jaoui, M., Kahnt, A., Kampf, C. J., Kourtchev, I., Maenhaut, W., Marsden, N., Saarikoski, S., Schnelle-Kreis, J., Surratt, J. D., Szidat, S., Szmigielski, R. and Wisthaler, A.: The Molecular Identification of Organic Compounds in the Atmosphere: State of the Art and Challenges, Chem Rev, 115(10), 3919–3983, doi:10.1021/cr5003485, 2015.

Parker, K. A., Ledeboer, M. W. and Pettigrew, J. D.: Nitric Acid, Encyclopedia of Reagents for Organic Synthesis, doi:10.1002/047084289x.rn022.pub2, 1995.

Perring, A., Pusede, S. and Cohen, R.: An Observational Perspective on the Atmospheric Impacts of Alkyl and Multifunctional Nitrates on Ozone and Secondary Organic Aerosol, Chem Rev, 113(8), 5848–5870, doi:10.1021/cr300520x, 2013.

Pinto, R., Salvador, J. and Roux, C.: Bismuth(III) salts mediated regioselective ring opening of epoxides: an easy route to halohydrins and β-hydroxy nitrates, Tetrahedron, 63(37), 9221–9228, doi:10.1016/j.tet.2007.06.054, 2007.

Pöschl, U., Carslaw, K., Koop, T., Sander, R. and Sturges, W.: Editorial Note "α -Pinene nitrates: synthesis, yields and atmospheric chemistry''' published in Atmos. Chem. Phys., 11, 6337-6347, 2011," Atmos Chem Phys, 11(23), 12065–12065, doi:10.5194/acp-11-12065-2011, 2011.

Pye, H., Chan, A., Barkley, M. and Seinfeld, J.: Global modelling of organic aerosol: the importance of reactive nitrogen

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Ma, S., Rindelaub, J., McAvey, K., Gagare, P., Nault, B., Ramachandran, P. and Shepson, P.: α-Pinene nitrates: synthesis, yields and atmospheric chemistry, Atmos Chem Phys, 11(13), 6337–6347, doi:10.5194/acp-11-6337-2011 , 2011., 2012.

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(NOx and NO_3), Atmos Chem Phys, 10(22), 11261–11276, doi:10.5194/acp-10-11261-2010, 2010.

Reid, W. B. and Watson, D. A.: Synthesis of Trisubstituted Alkenyl Boronic Esters from Alkenes Using the Boryl-Heck Reaction, Org Lett, 20(21), 6832–6835, doi:10.1021/acs.orglett.8b02949, 2018.

Rindelaub, J., McAvey, K. and Shepson, P.: Determination of α-pinene-derived organic nitrate yields: particle phase partitioning and hydrolysis, Atmospheric Chem Phys Discuss, 14(3), 3301–3335, doi:10.5194/acpd-14-3301-2014, 2014.

Rindelaub, J. D., McAvey, K. M. and Shepson, P. B.: The photochemical production of organic nitrates from α-pinene and loss via acid-dependent particle phase hydrolysis, Atmos Environ, 100, 193–201, doi:10.1016/j.atmosenv.2014.11.010, 2015.

Rindelaub, J. D., Wiley, J. S., Cooper, B. R. and Shepson, P. B.: Chemical characterization of α-pinene secondary organic aerosol constituents using gas chromatography, liquid chromatography, and paper spray-based mass spectrometry techniques, Rapid Commun Mass Sp, 30(13), 1627–1638, doi:10.1002/rcm.7602, 2016a.

Rindelaub, J. D., Borca, C. H., Hostetler, M. A., Slade, J. H., Lipton, M. A., Slipchenko, L. V. and Shepson, P. B.: The acid-catalyzed hydrolysis of an α-pinene-derived organic nitrate: kinetics, products, reaction mechanisms, and atmospheric impact, Atmos Chem Phys, 16(23), 15425–15432, doi:10.5194/acp-16-15425-2016, 2016b.

Rollins, A., Fry, J., Hunter, J., Kroll, J., Worsnop, D., Singaram, S. and Cohen, R.: Elemental analysis of aerosol organic nitrates with electron ionization high-resolution mass spectrometry, Atmos Meas Tech, 3(1), 301–310, doi:10.5194/amt-3-301-2010, 2010.

Romonosky, D. E., Nguyen, L. Q., Shemesh, D., Nguyen, T. B., Epstein, S. A., Martin, D., Vanderwal, C. D., Gerber, B. R. and Nizkorodov, S. A.: Absorption spectra and aqueous photochemistry of β-hydroxyalkyl nitrates of atmospheric interest, Mol Phys, 113(15–16), 2179–2190, doi:10.1080/00268976.2015.1017020, 2015.

Steiner, D., Ivison, L., Goralski, C. T., Appell, R. B., Gojkovic, J. R. and Singaram, B.: A facile and efficient method for the kinetic separation of commercially available *cis*- and *trans*-limonene epoxide, Tetrahedron Asymmetry, 13(21), 2359–2363, doi:10.1016/s0957-4166(02)00646-8, 2002.

Thomas, W. C., Dresser, W. D., Cortes, D. A. and Elrod, M. J.: Gas Phase Oxidation of Campholenic Aldehyde and Solution Phase Reactivity of its Epoxide Derivative, J Phys Chem, doi:10.1021/acs.jpca.6b08642, 2016.

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Uehara, A., Tommis, B., Belhassen, E., Satrani, B., Ghanmi, M. and Baldovini, N.: Odor-active constituents of Cedrus atlantica wood essential oil, Phytochemistry, 144 (J. Essent. Oil Res. 16 2004), 208–215, doi:10.1016/j.phytochem.2017.09.017, 2017.

Univ. of California, Berkeley: Lesson Learned – Nitric Acid Waste Over-pressurization Event. https://ehs.berkeley.edu/lessons-learned/lesson-learned-nitric-acid-waste-over-pressurization-event , last access: 1 July, 2019.

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