Accelerated Aging of Propylene Glycol and Glycerol

Juul Labs Science

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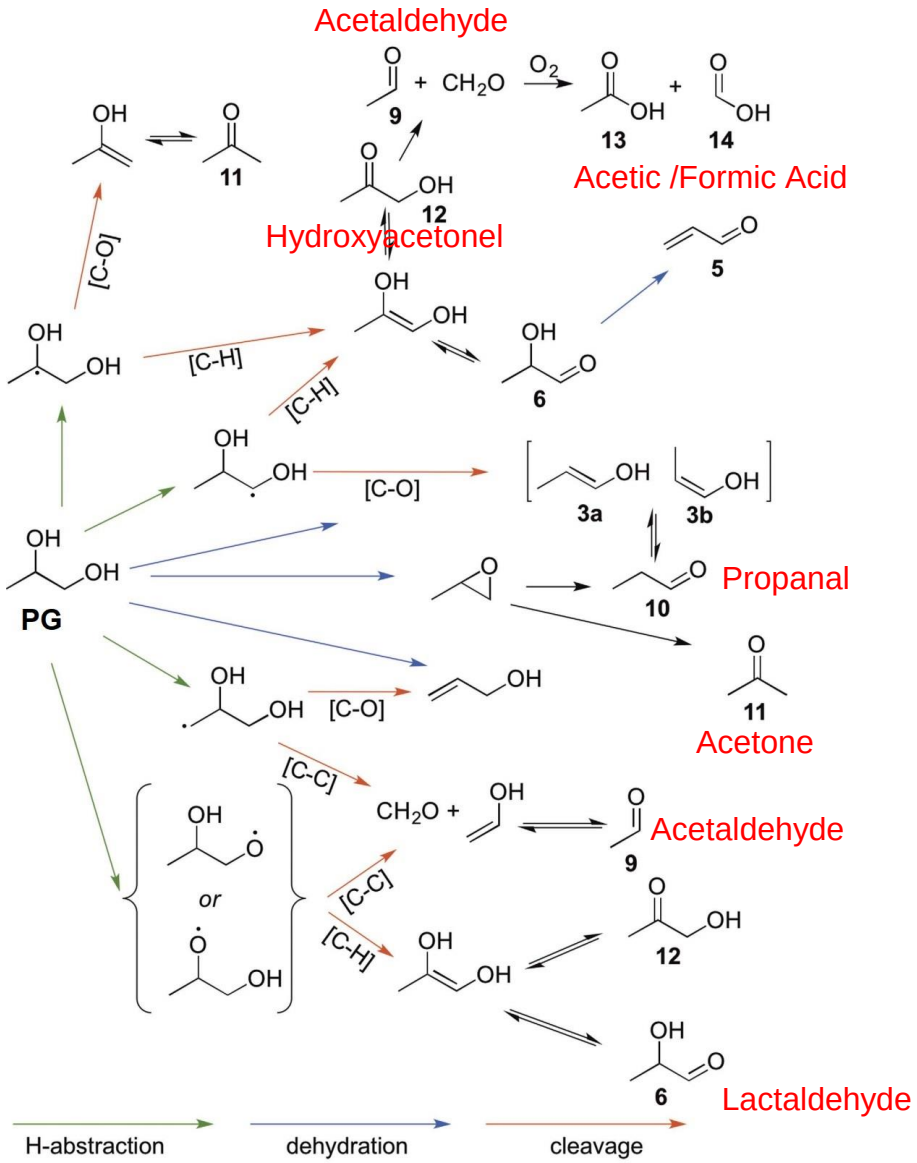
Introduction

- Because propylene glycol (PG) and glycerol (VG) are used as e-liquid carriers across the ENDS industry, a solid foundational knowledge of these materials is essential to fully characterize the e-liquid and aerosol.

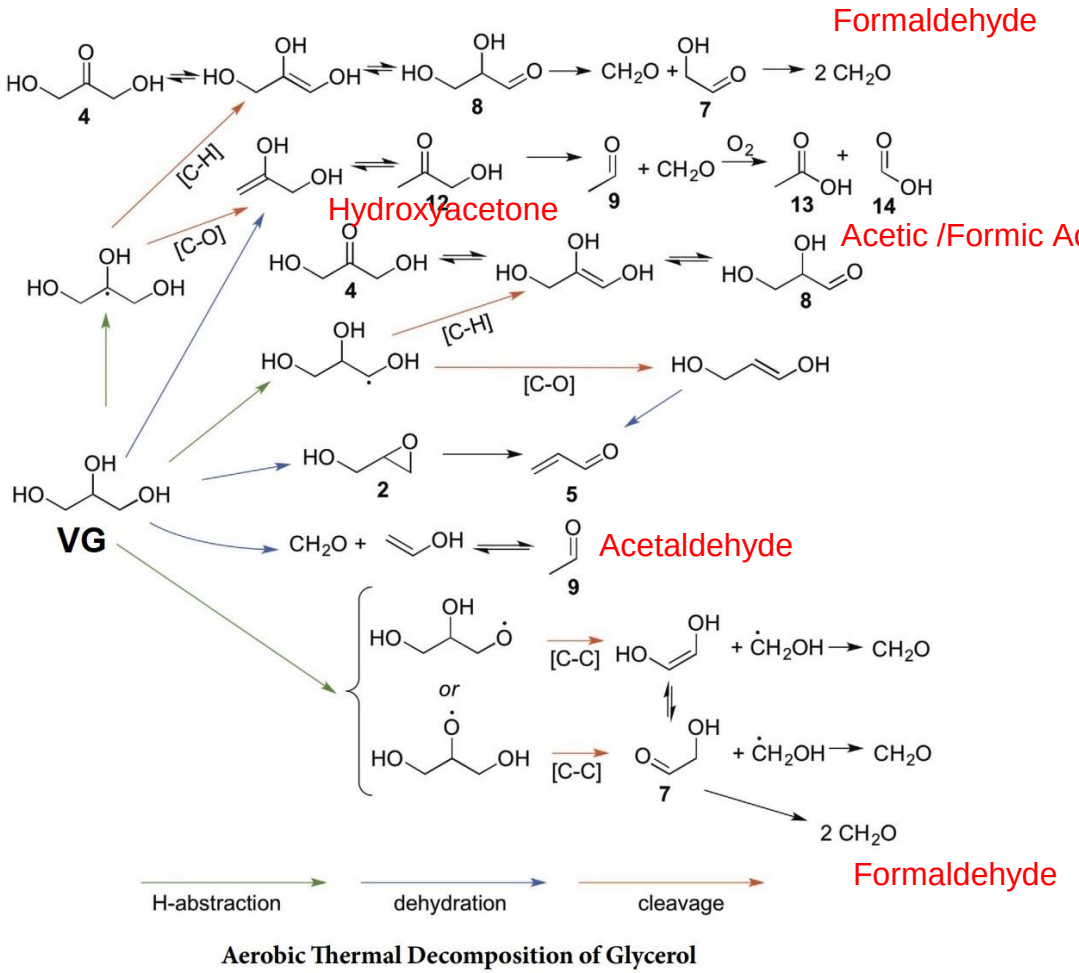
- These have the potential to degrade through oxidation, acidification, or radical processes during storage, resulting in new compounds.

- Because these new compounds may potentially transfer into the aerosol, resulting in consumer exposure, it is necessary to identify them as part of product characterization.

- Accelerated degradation under **exaggerated** conditions forces compound formation, allowing pre-emptive identification in case they appear in stability testing.



Aerobic Thermal Decomposition of Propylene Glycol.



Aerobic Thermal Decomposition of Glycerol

Do the decomposition products further react?

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Goals

- Examine the effect of moderate and exaggerated thermal degradation (45º & 90º C) on PG and VG.
- Determine the effect of water when present in the system.
- Identify compounds formed during exposure to elevated temperatures.
- Build a custom mass spectral database for improved compound identification.

Study Design - Propylene Glycol (PG), Glycerine (VG), Water (W)

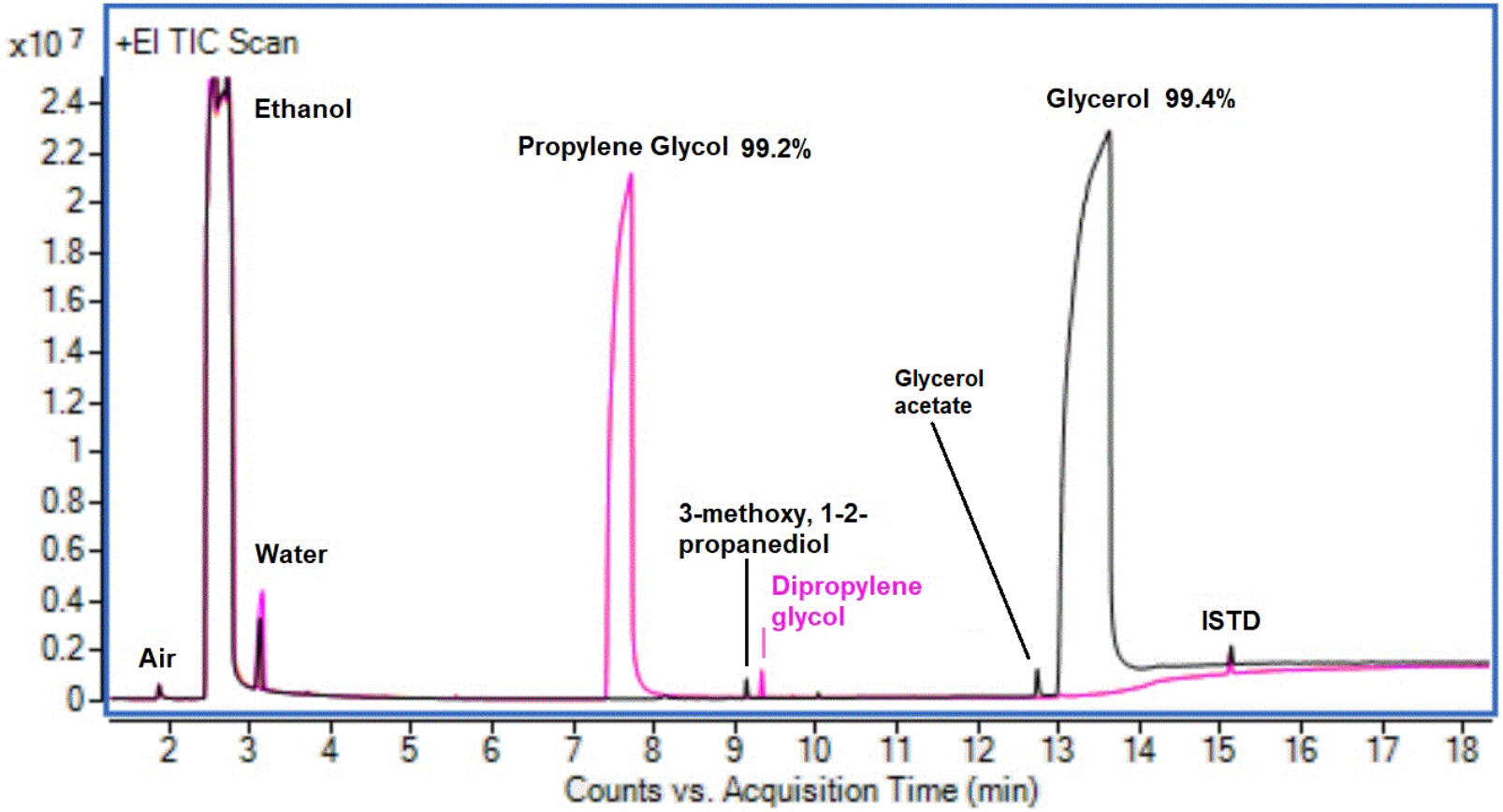
Sample	% PG	% VG	% Water	Temp ˚C
PG	100			45
VG		100		45
PG-VG	50	50		45
PG-W	93		7	45
VG-W		93	7	45
PG-VG-W	46.5	46.5	7	45
PG	100			90
VG		100		90
PG-VG	50	50		90
PG-W	93		7	90
VG-W		93	7	90
PG-VG-W	46.5	46.5	7	90
Reaction time = 0 to 25 days				

Experimental

- Reagents: ACS grade PG, VG, PG/VG (1:1)
- Storage: 2 mL glass vials with Teflon caps and headspace.
- Heating: Ovens set to 45 ºC and 90 ºC.
- Sampling: 50 µL aliquot diluted in 1 mL ethanol containing 10 mcg/mL 6-methylcoumarin as an internal standard for normalization.
- Analysis: Non-targeted GC-MS on a Stabilwax column, Agilent Unknowns Analyzer, Accurate mass Orbitrap. These data do not include LC compounds.
- Identification: Spectral using NIST 2017 and Wiley 11 spectral databases.

Time Zero – Initial Conditions

- Some impurities were identified in the non-USP, reagent grade PG and VG.



These were monitored for changes over time.
GC column degradation peaks were also seen over duration of the study.

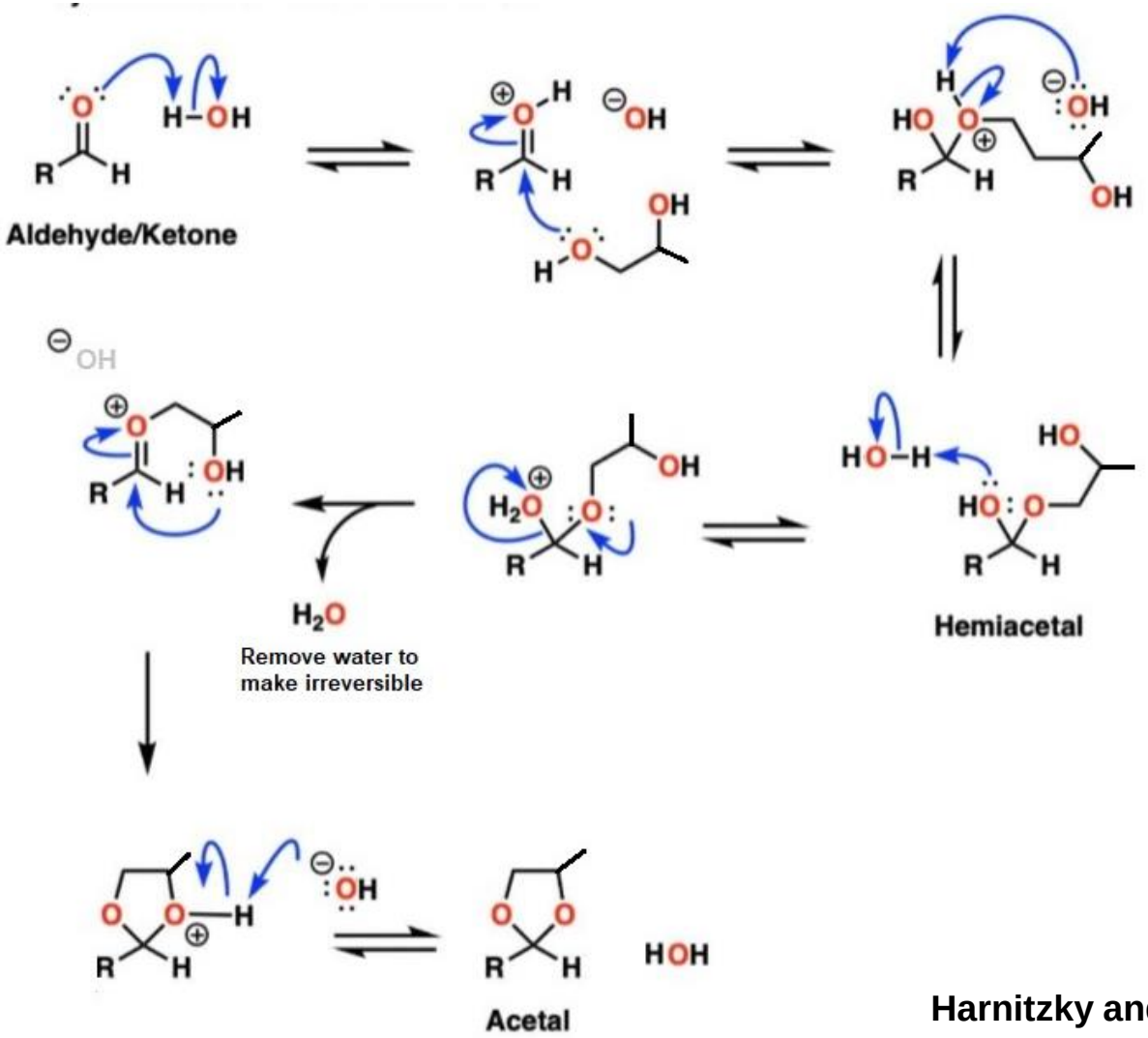
Results – Compound appearance with continuing growth 45˚C

Sample	Acetone	Hydroxyacetone	Hydroxypropanone	Dioxolanes	Diglycerols
PG-45˚C					
VG-45˚C					
PG-VG-45˚C		5 days			
PG-W-45˚C					
VG-W-45˚C					
PG-VG-W-45˚C					

Results – Compound appearance with continuing growth

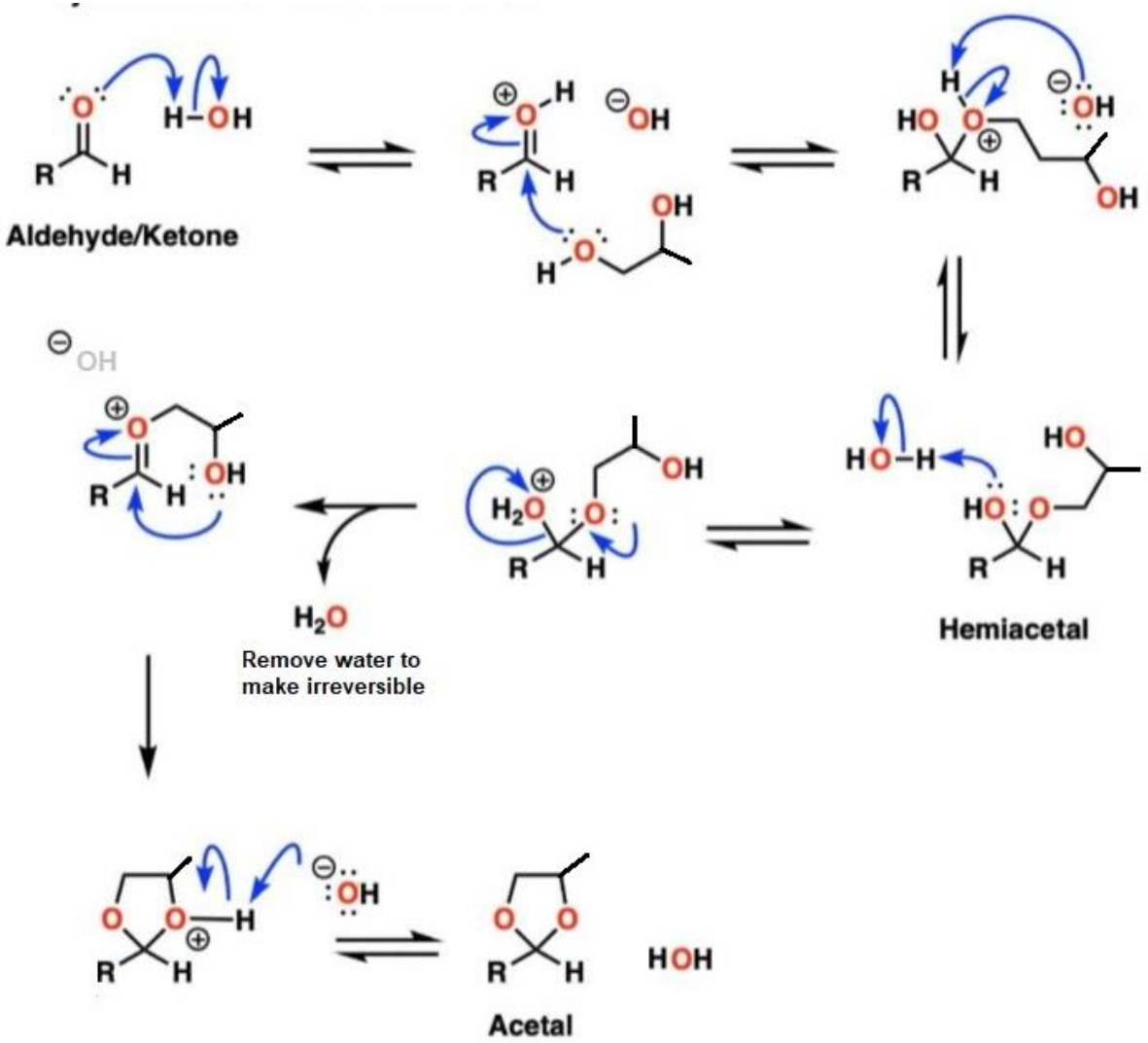
Sample	Acetone	Hydroxyacetone	Hydroxypropanone	Dioxolanes	Diglycerols
PG-45˚C					
VG-45˚C					
PG-VG-45˚C		5 days			
PG-W-45˚C					
VG-W-45˚C					
PG-VG-W-45˚C					
PG-90˚C		2 days		10 days	
VG-90˚C					
PG-VG-90˚C	14 days	2 days		5 days	
PG-W-90˚C	12 days	3 days	10 days	10 days	
VG-W-90˚C		7 days			19 days
PG-VG-W-90˚C	3 days	1 day		4 days	

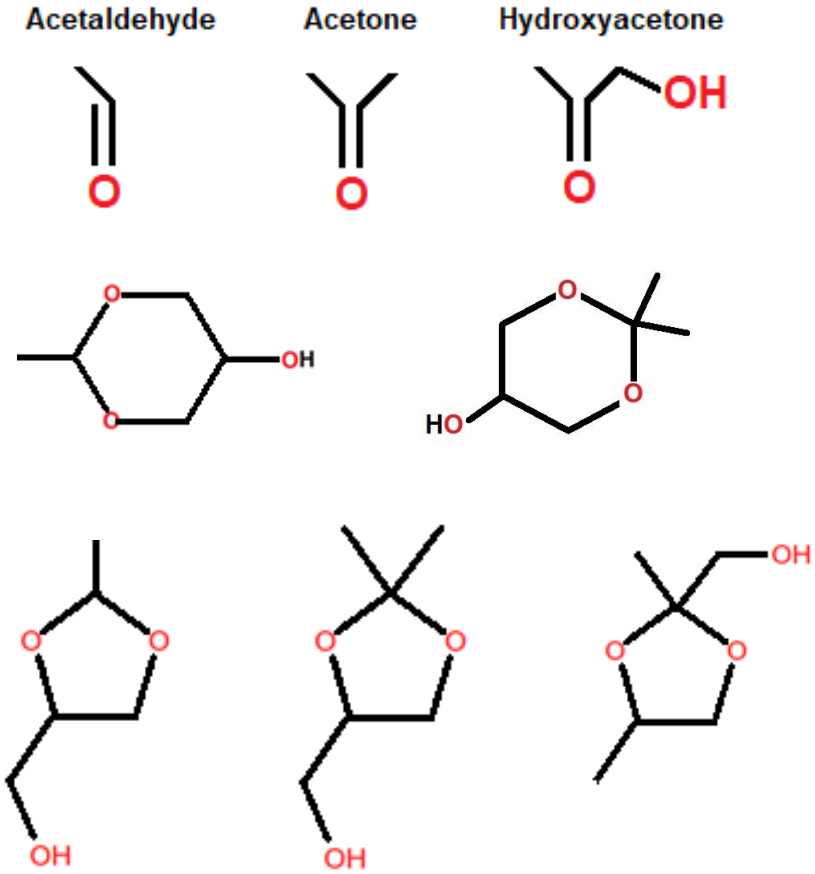
Cyclical Acetal Formation – mechanism



Harnitzky and Menschutkin , Melvin

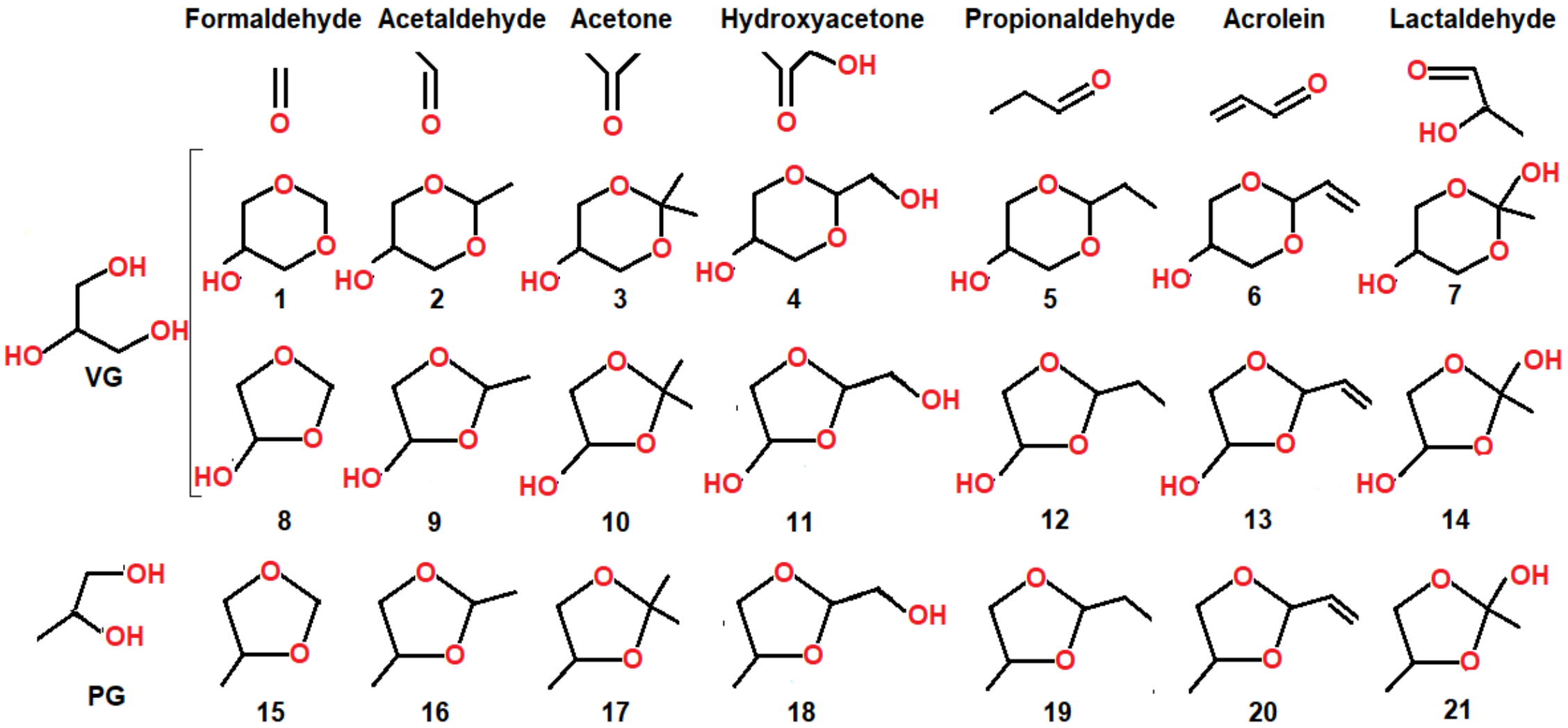
Cyclical Acetal Formation – mechanism



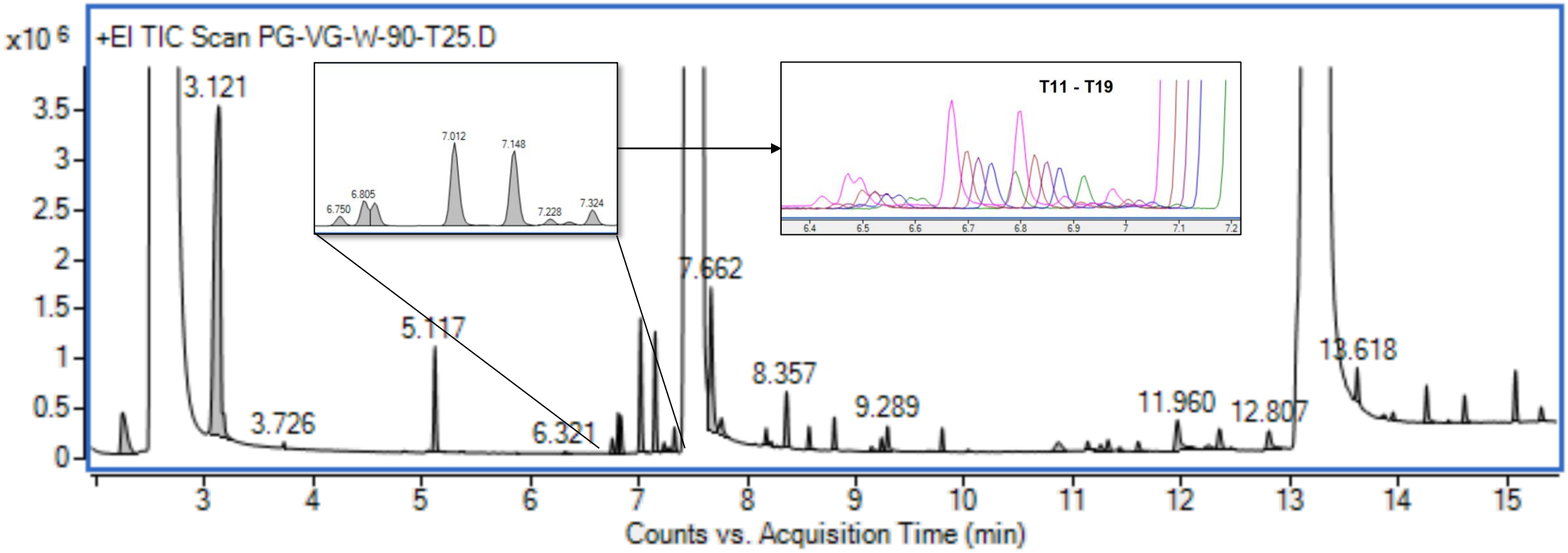


The decomposition products do indeed further react at 90 ˚C.

Cyclical Acetals from Simple Thermal Degradants

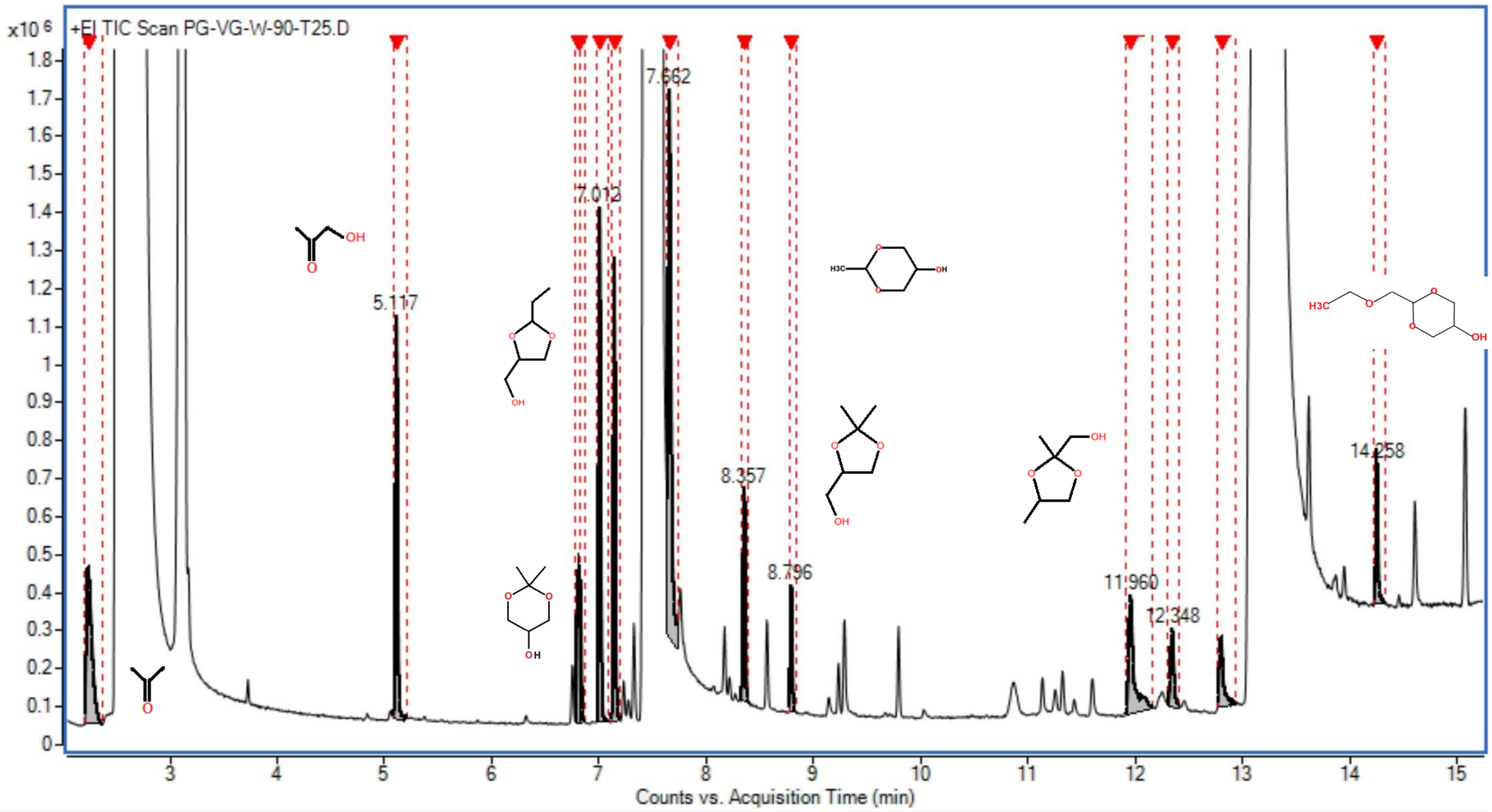


Sample Chromatography PG-VG-Water-90˚C for 25 days

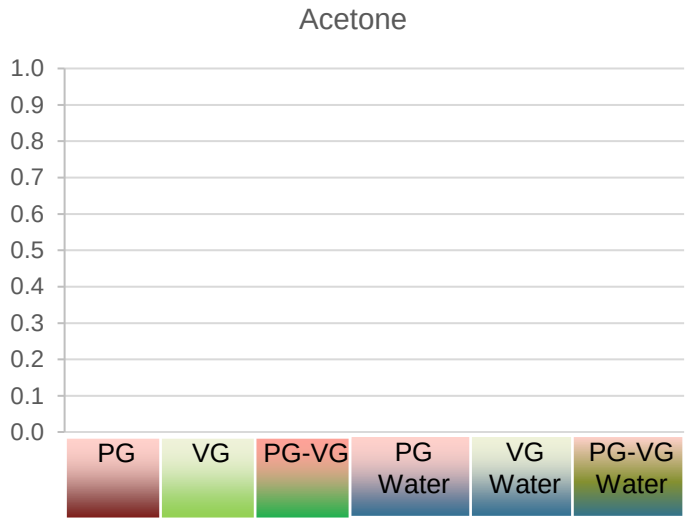


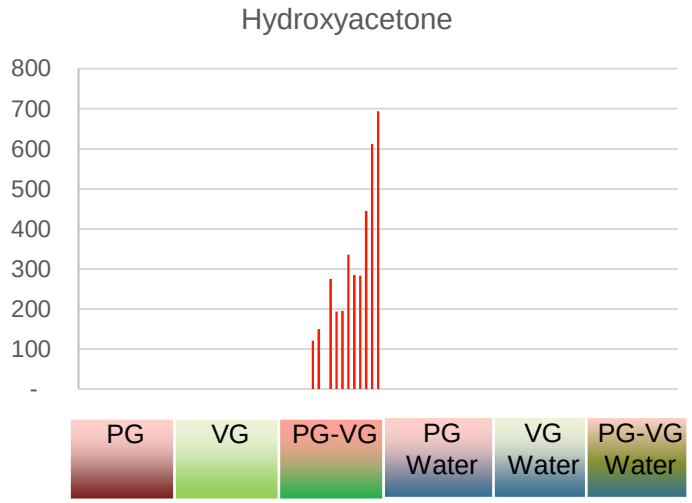
38 new compounds

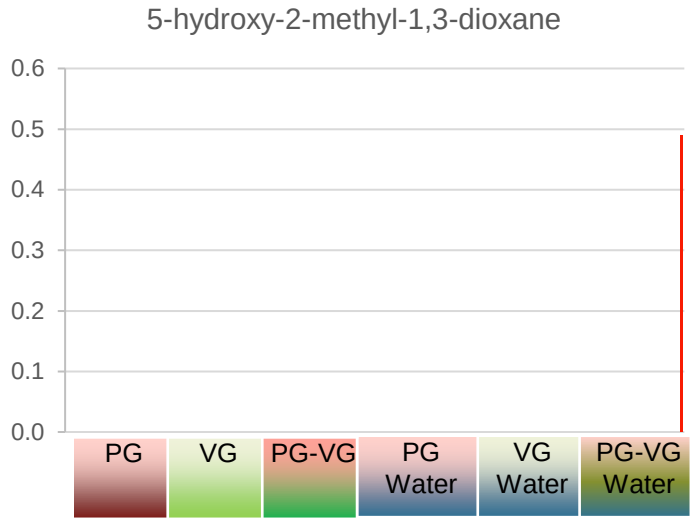
Top 10 Compounds PG-VG-Water-90 ˚C – Time 25 Days

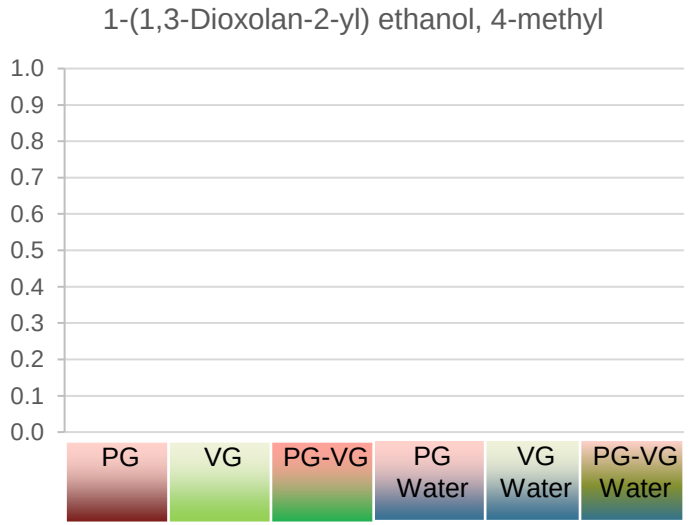


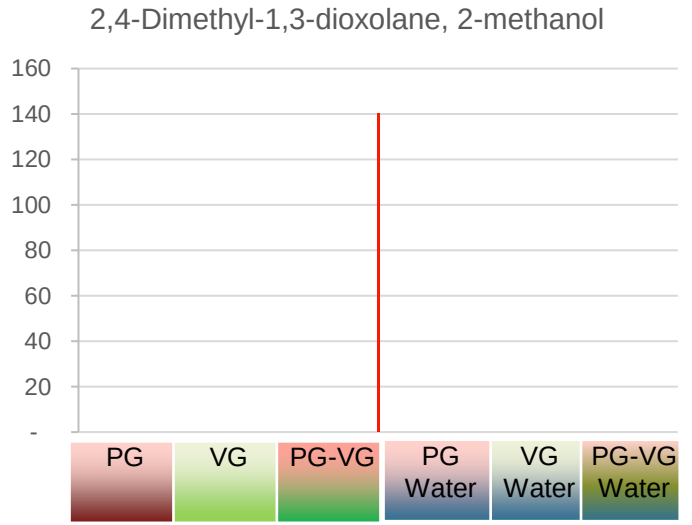
Thermal Degradation from 0 – 25 days at 45 ˚C (mcg/mL)

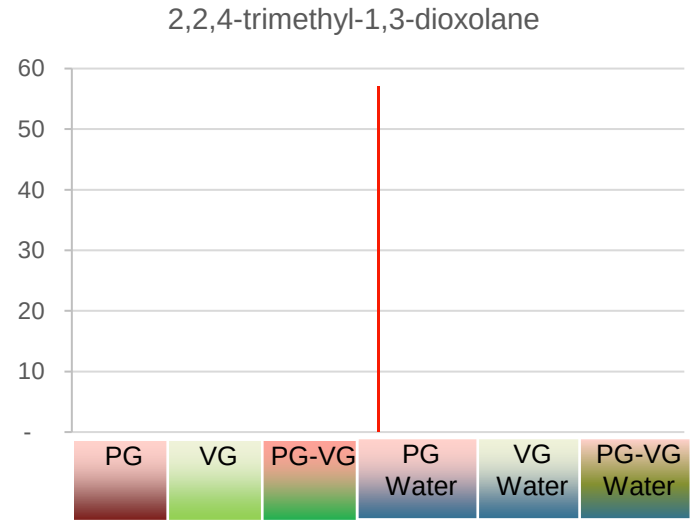




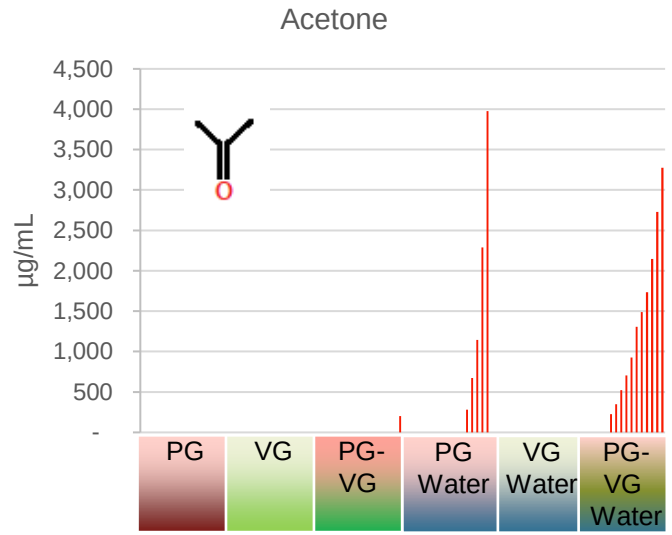


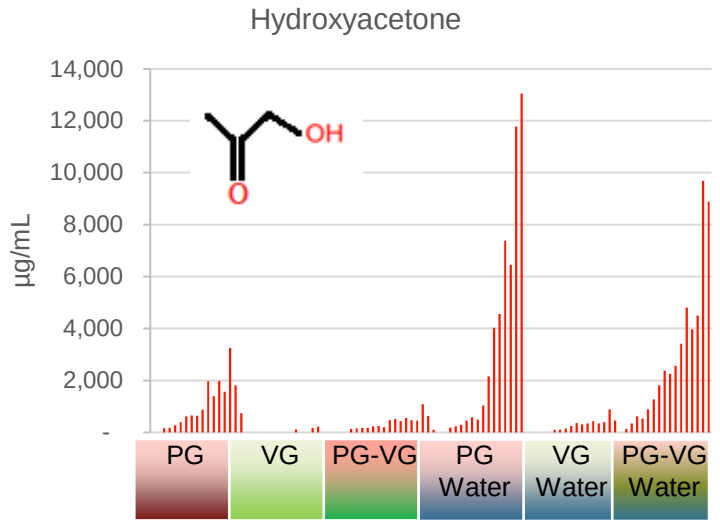


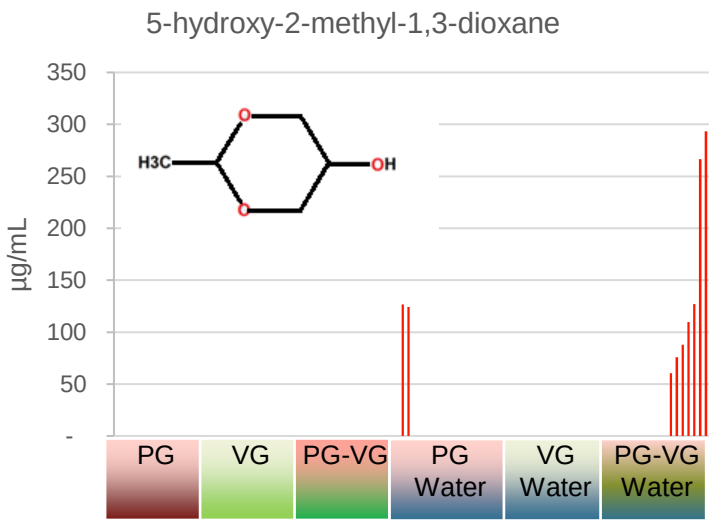


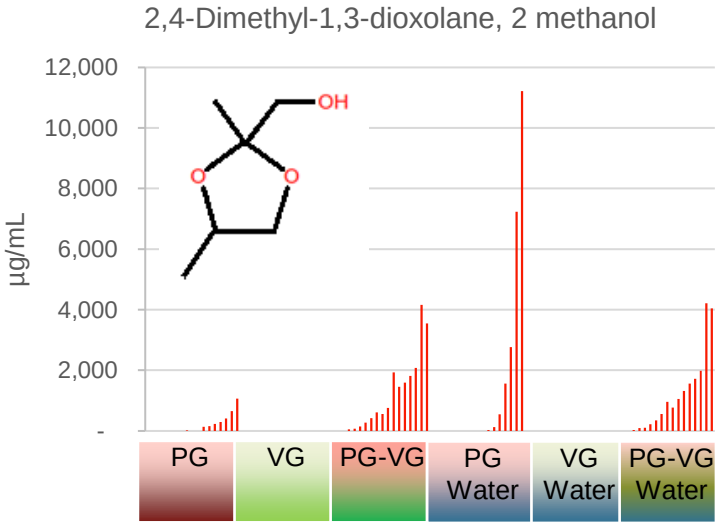


Thermal Degradation from 0 – 25 days at 90 ˚C



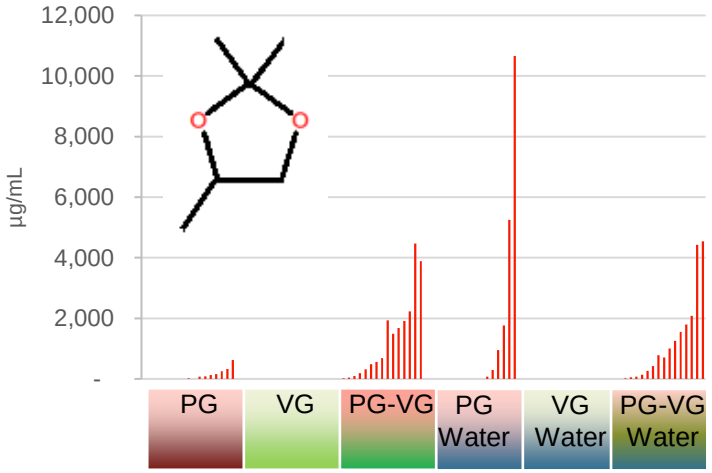




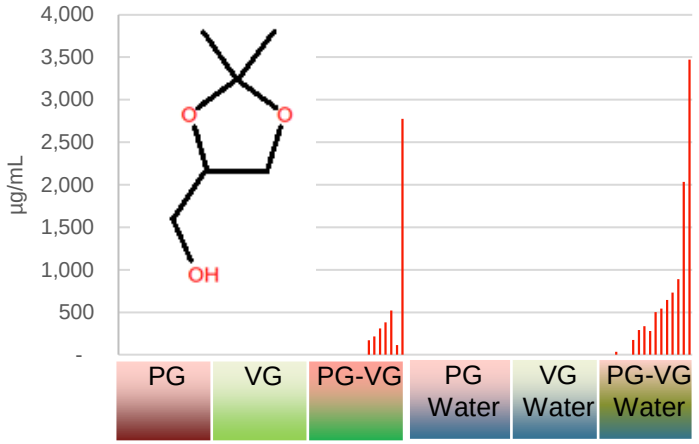


Thermal Degradation from 0 – 25 days at 90 ˚C

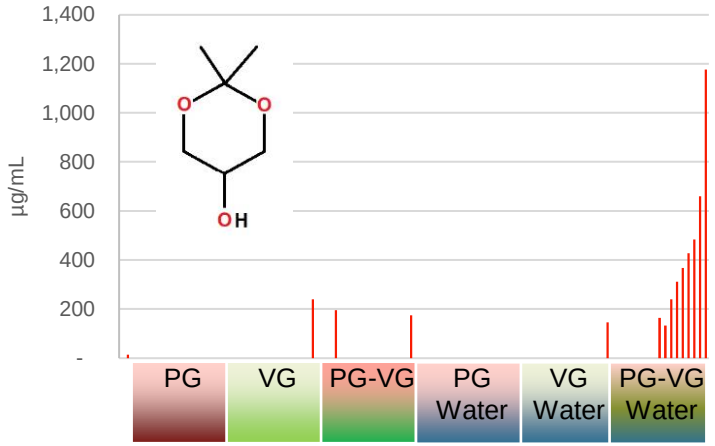
2,2,4-trimethyl-1,3-dioxolane



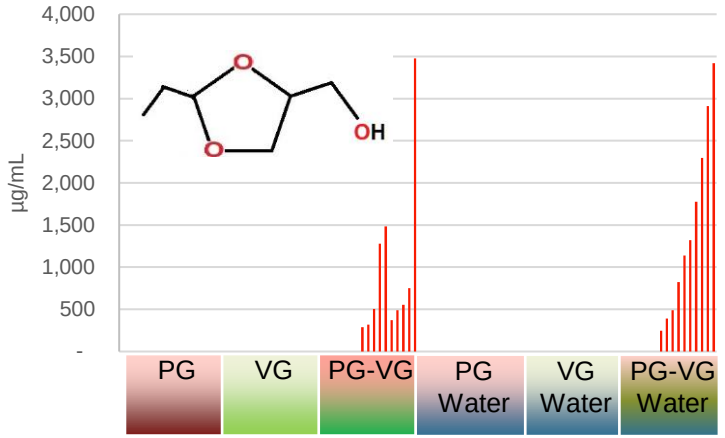
2,2-dimethyl-1,3-Dioxolane-4-methanol



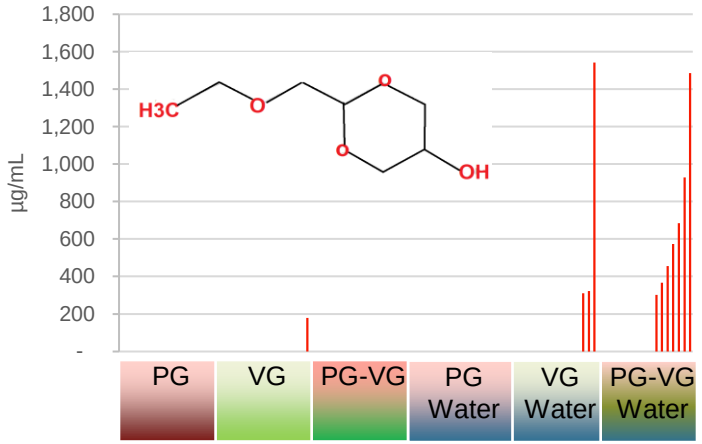
2,2-Dimethyl-1,3-dioxan-5-ol



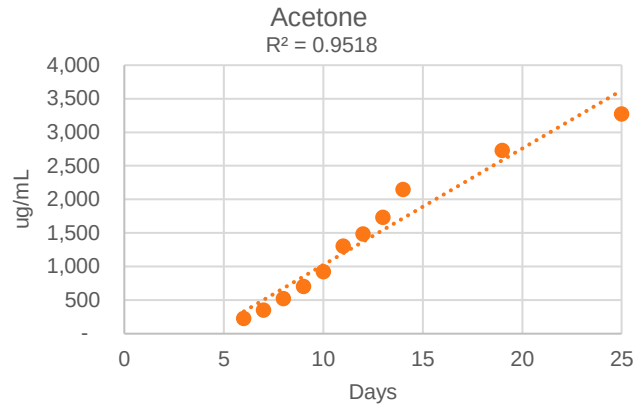
1,3-Dioxolane, 2-ethyl-4-methyl-

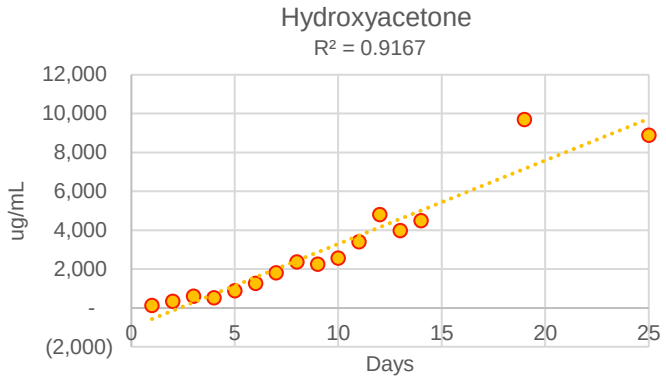


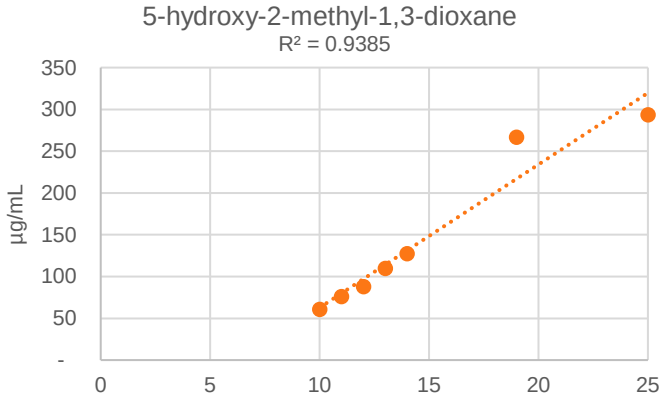
1,3-ethoxyethylideneglycerol

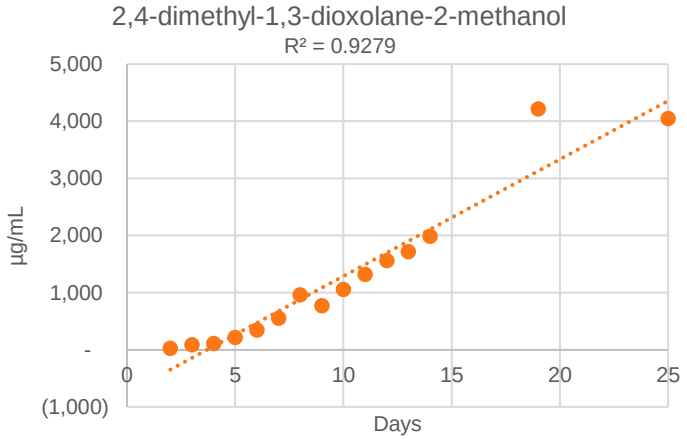


Thermal Degradation PG-VG-Water from 0 – 25 days at 90 ˚C

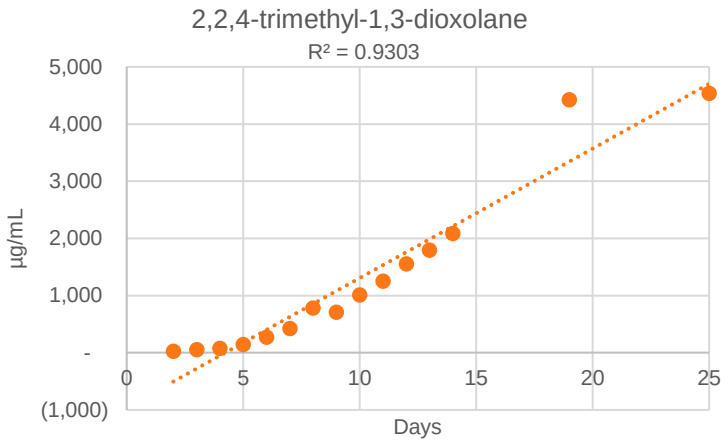


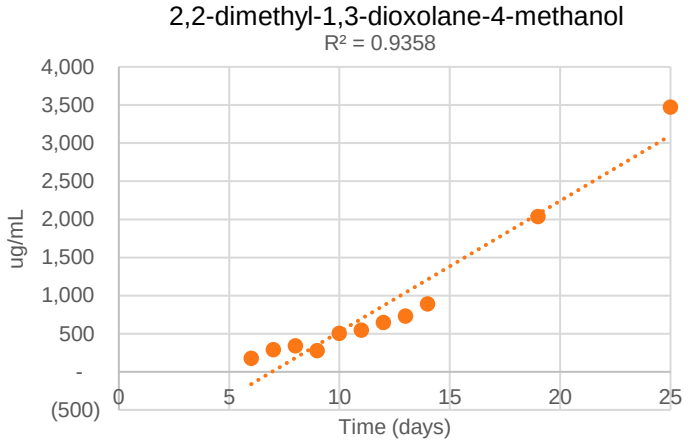


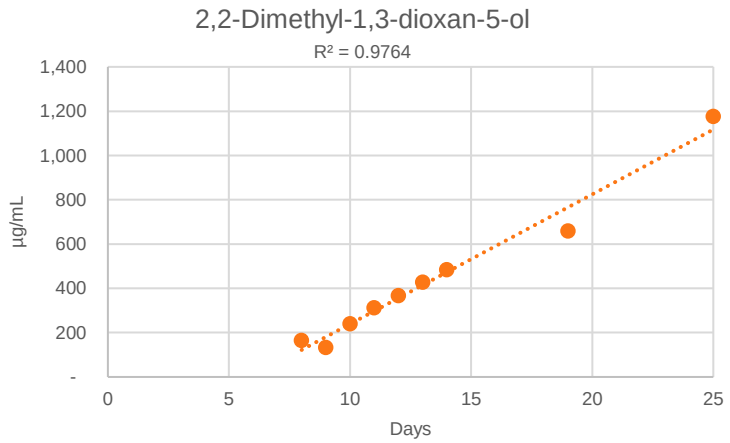


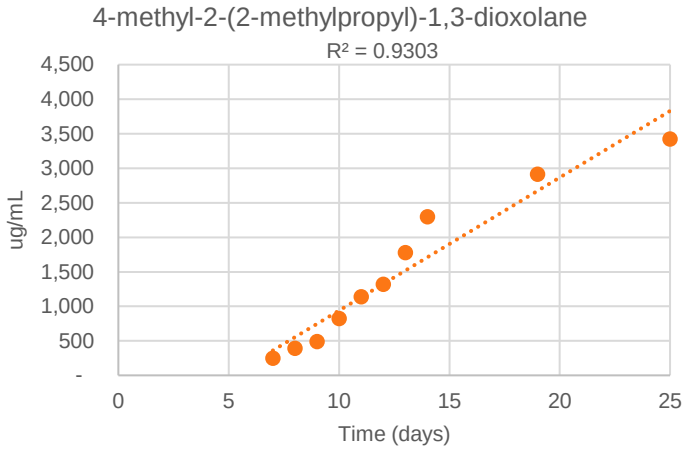


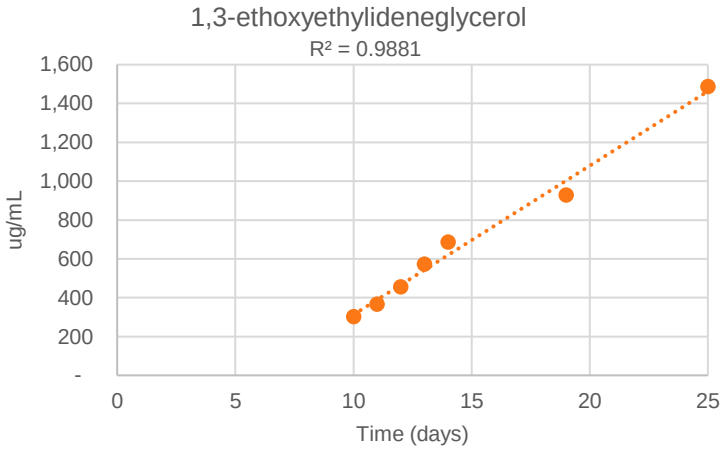
Thermal Degradation PG-VG-Water from 0 – 25 days at 90 ˚C



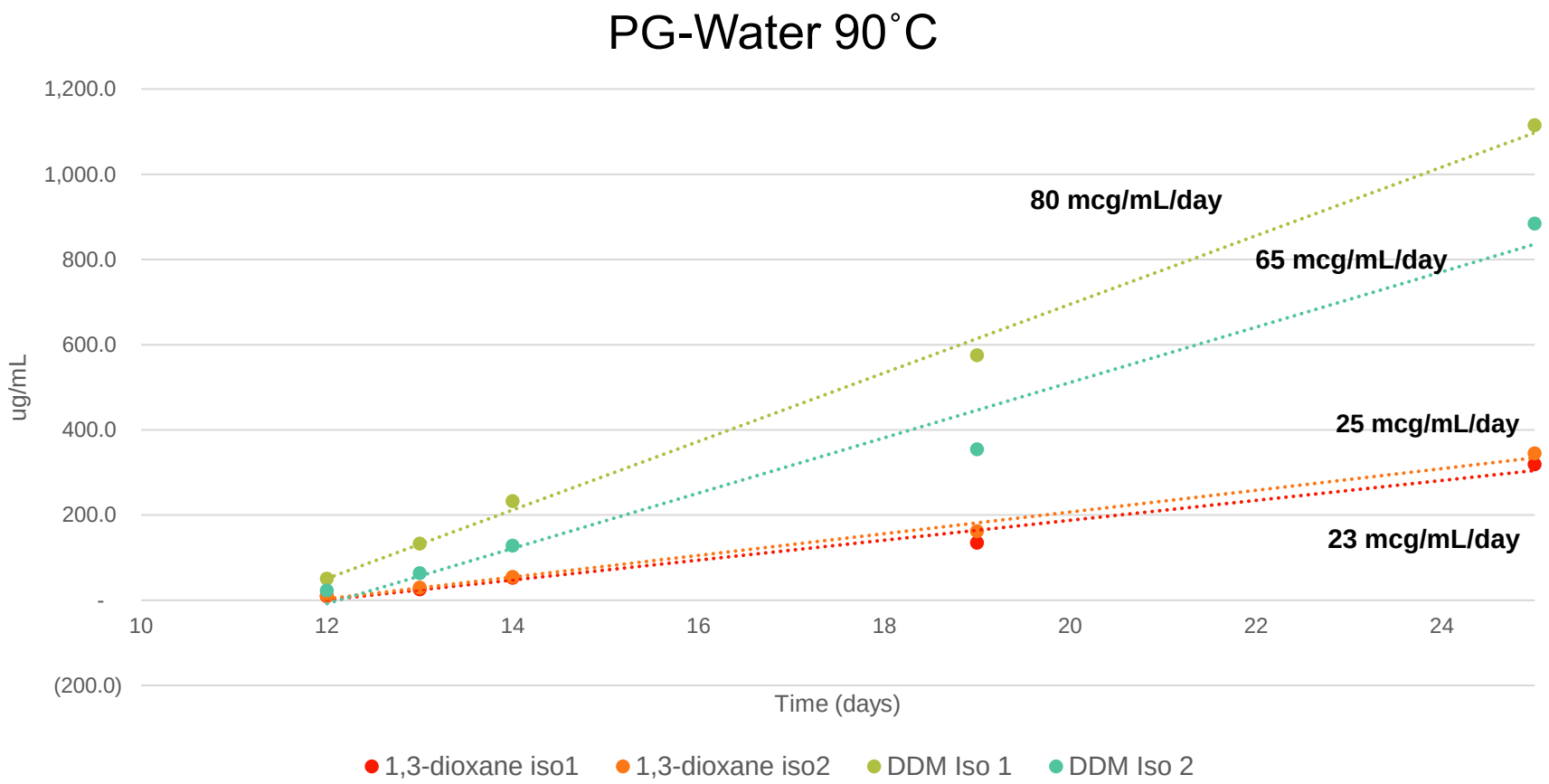








PG-W Product Formation



Constant reaction rate, with additional thermal data, degradation stability modeling may be possible.

Conclusions

- At 45 ˚C, only Hydroxyacetone was seen in significant concentrations by GCMS at these thresholds.
- In exaggerated thermal conditions, the formation of many low molecular weight decomposition molecules that are seen in aerosol, also appear in the e-liquid.
- These small molecules then combine with PG and VG to form dioxolanes.
- The formation of these compounds appears to follow a predictable rate, which may lead to the ability to model the long-term stability.
- If these compounds are seen in later NTA studies, we will know what they are and where they come from.

Acknowledgements

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Martha Garcia-Cervantes
- Foundational Science

Matthew Lyndon
- Non-targeted Analysis

Diane Wallace
- Non-targeted Analysis

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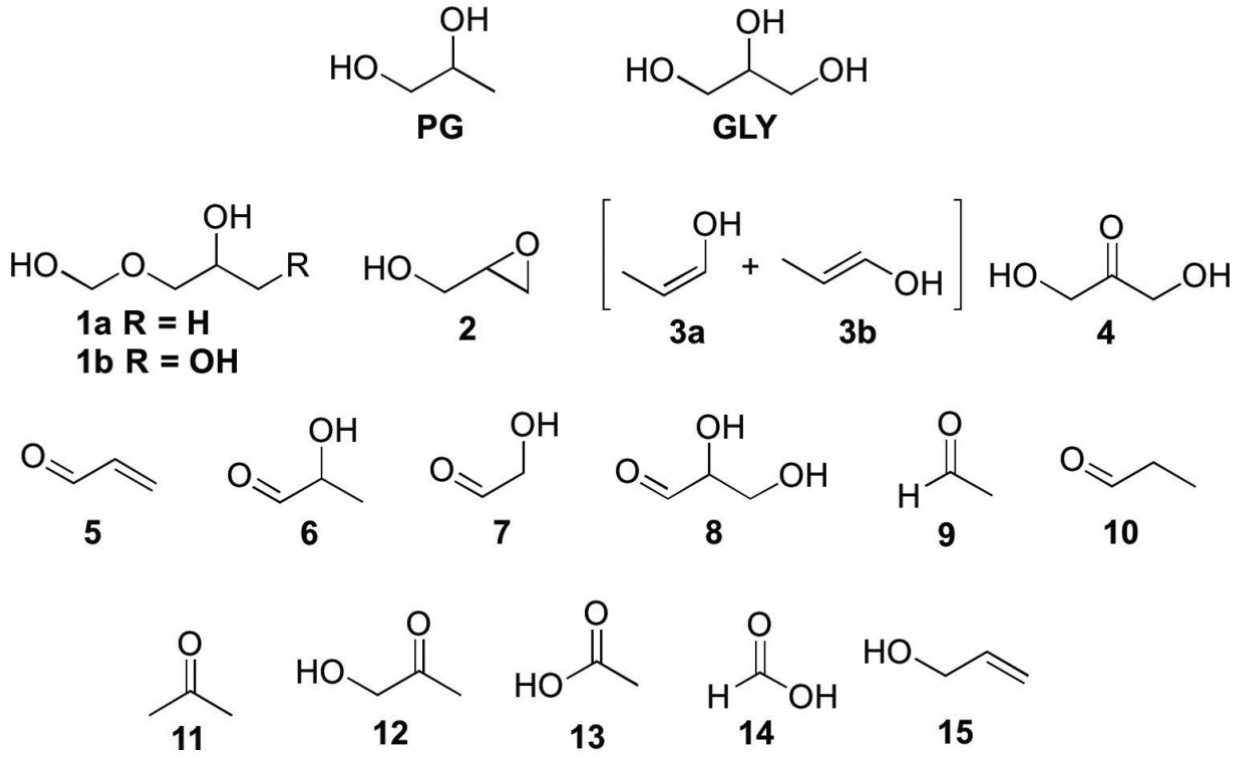

Figure 1. Compounds identified herein by ^{1}H NMR in e-cigarette aerosols derived from a single puff from an electronic cigarette. PG = propylene glycol; GLY = glycerol; **1a** = propylene glycol hemiformal (major isomer); **1b** = glycerol hemiformal (major isomer); **2** = glycidol; **3a** = (Z)-prop-1-en-1-ol; **3b** = (E)-prop-1-en-1-ol; **4** = dihydroxyacetone; **5** = acrolein; **6** = lactaldehyde; **7** = glycolaldehyde; **8** = glyceraldehyde; **9** = acetaldehyde; **10** = propanal; **11** = acetone; **12** = hydroxyacetone (acetol); **13** = acetic acid; **14** = formic acid; **15** = allyl alcohol.

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