Triacetin enhances levels of acrolein, formaldehyde hemiacetals and acetaldehyde in electronic cigarette aerosols

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Supplementary Information

Synthesis and characterization of ^{13}C-labeled triacetin.

General procedure from glycerol. Glycerol (5 mmol, 1 equiv.) and acetic anhydride (20 mmol, 4 equiv.) were added to a 50 mL round bottom flask with a magnetic stir bar. Pyridine (20 mmol, 4 equiv.) was added and sealed with a closed cap. The solution was stirred for 24 hours. The mixture was added to a separatory funnel, and the ethyl acetate (EtOAc)/water layers separated. The water layer was extracted with EtOAc (3 × 50 mL). The combined EtOAc layers were dried over Na_2SO_4, filtered, and the solvent removed on the rotary evaporator. The crude residue was purified by flash column chromatography on silica gel with EtOAc/hexane 4/6 mixture as the eluent.

$^{13}C_3$-$C_6H_{14}O_6$ (4)

Prepared according to the general procedure on 1.6 mmol scale and obtained an isolated yield of 95% (0.3326 g) as a clear liquid. Spectral data is consistent with that of commercially obtained triacetin.

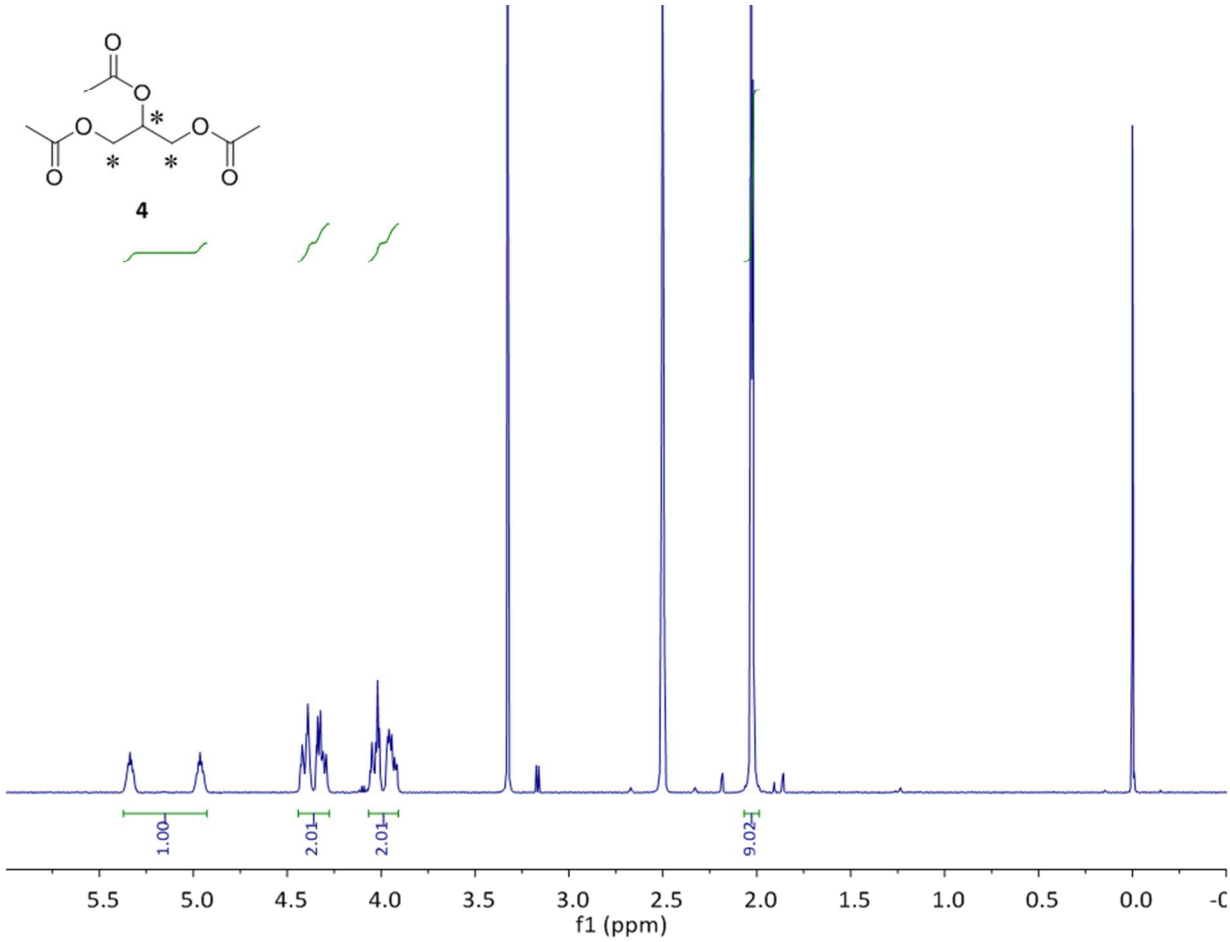

Figure S1. ^{1}H NMR spectra of compound **4** ($^{13}C_3$-TA). The asterisks represent the ^{13}C-labeling.

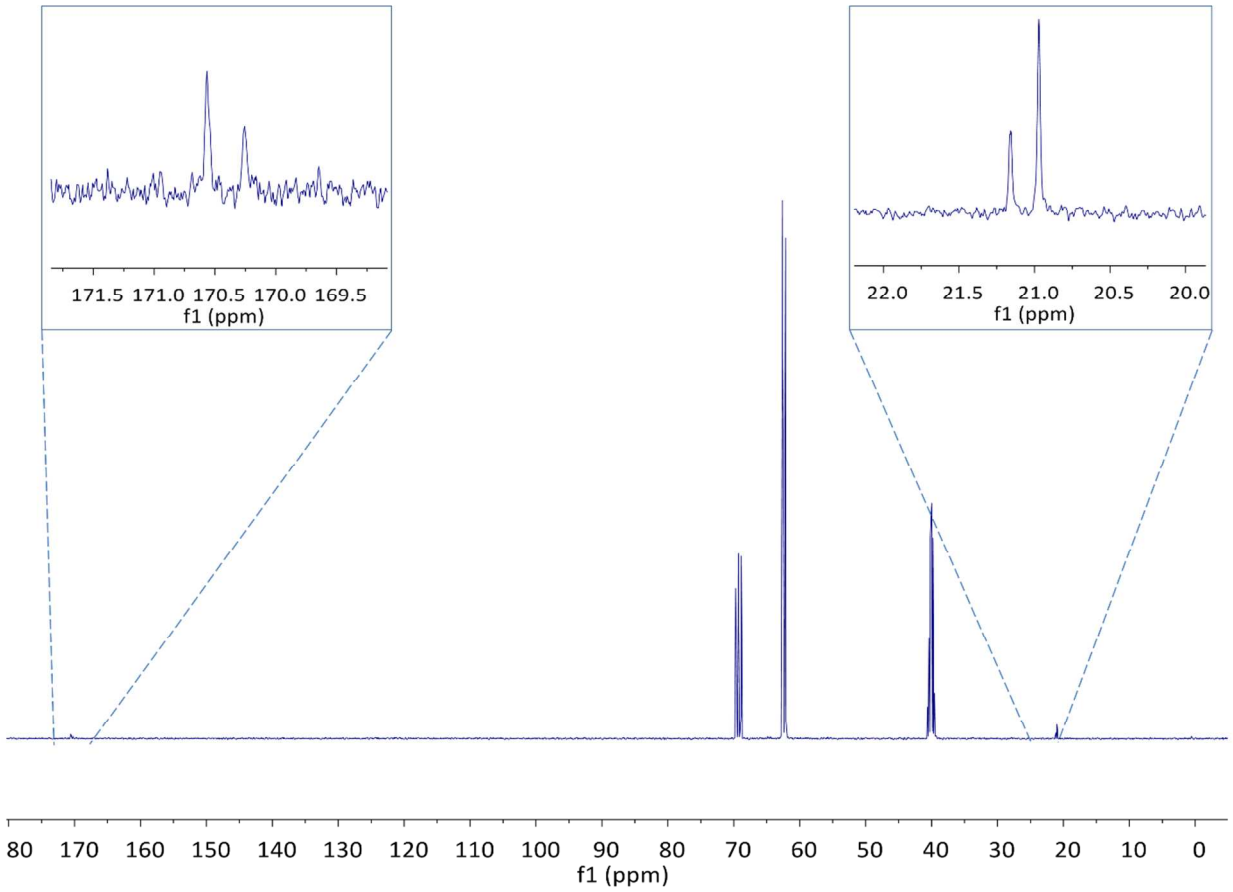

Figure S2. ^{13}C NMR spectra of compound **4** ($^{13}C_3$-TA). The insets display the carbon peaks which are at much lower relative intensities due to the ^{13}C-labeling.

$^{13}C_6$-$C_3H_{14}O_6$ (5)

Prepared according to the general procedure on 1.1 mmol scale and obtained an isolated yield of 95% (0.2333 g) as a clear liquid. Spectral data is consistent with that of commercially obtained triacetin.

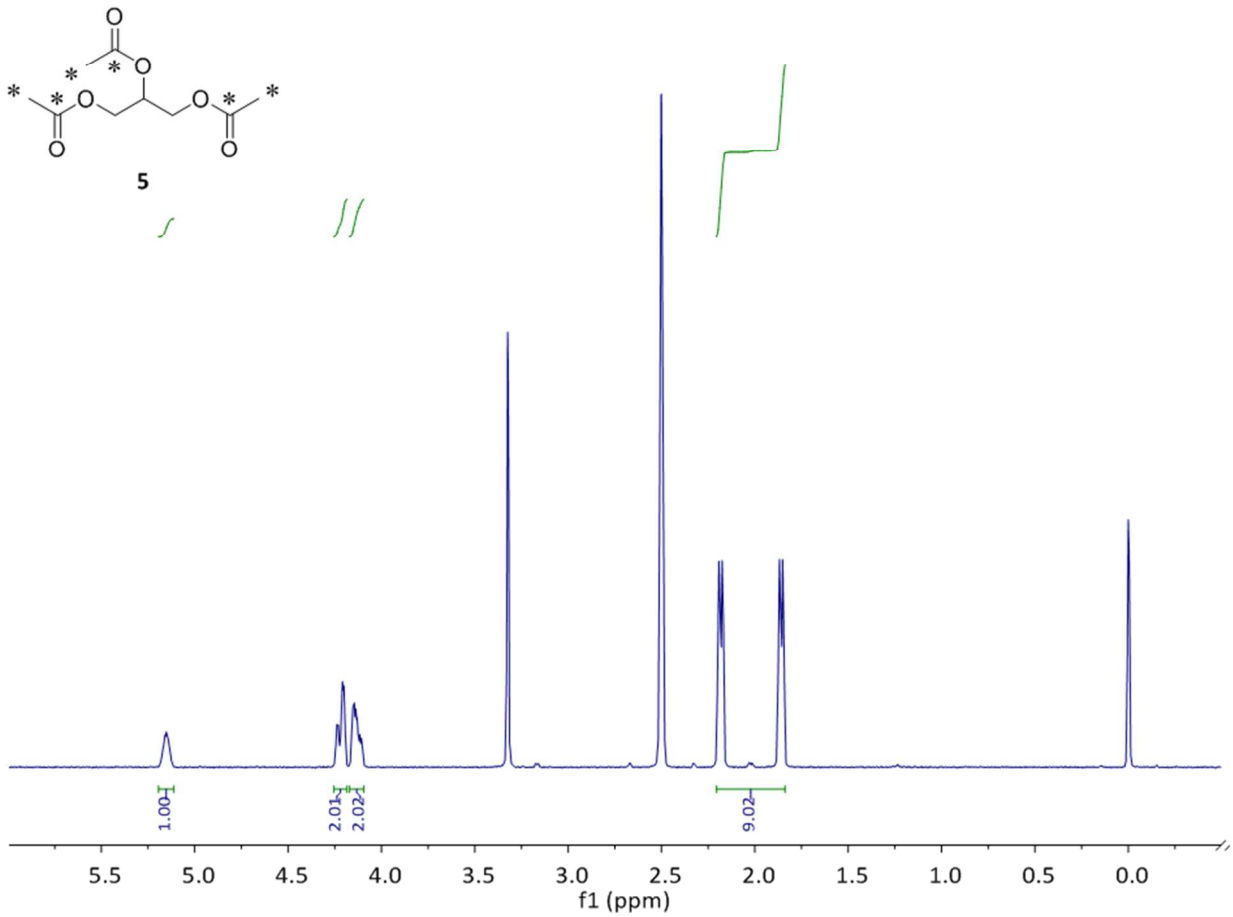

Figure S3. ^{1}H NMR spectra of compound **5** ($^{13}C_6$-TA). The asterisks represent the ^{13}C-labeling.

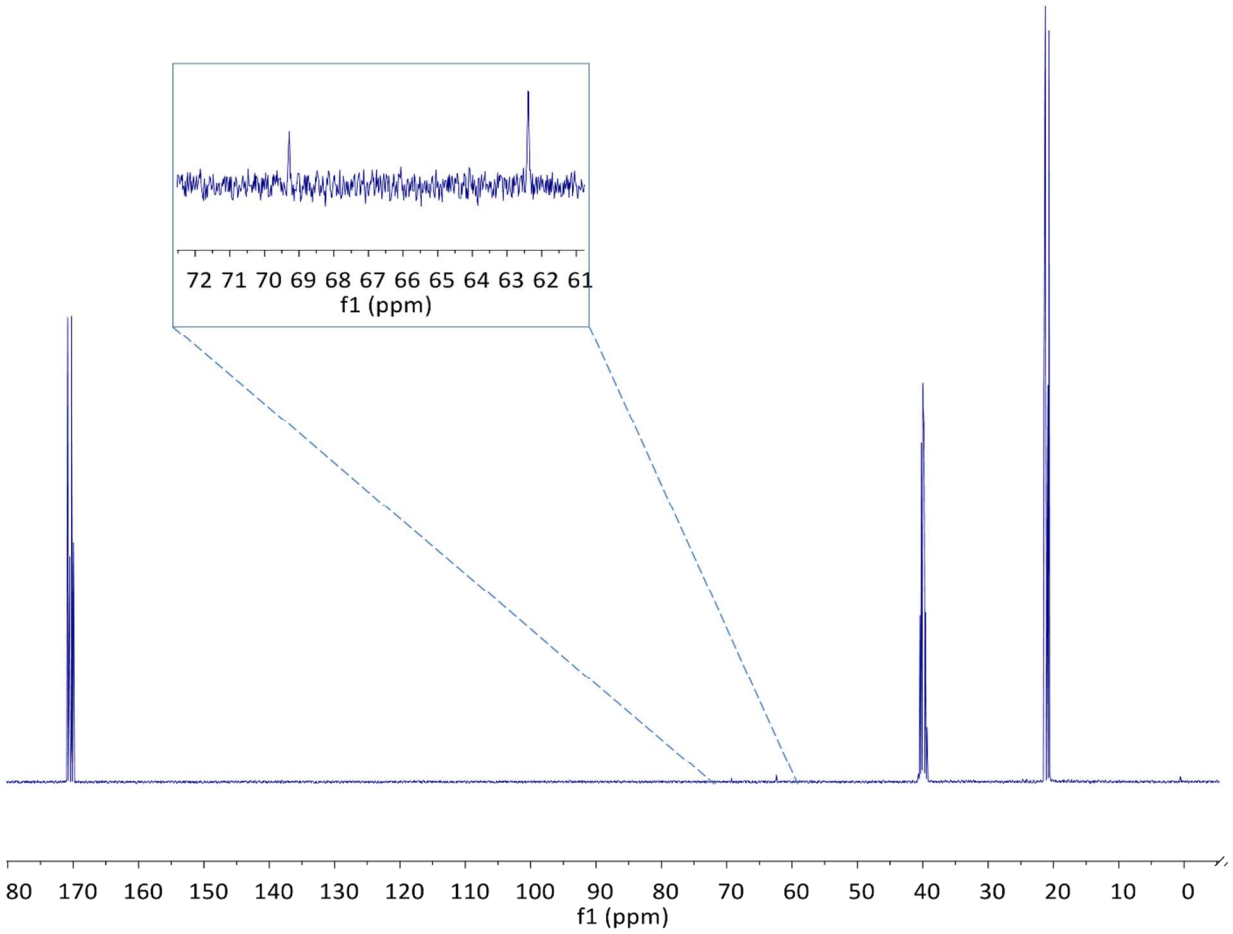

Figure S4. ^{13}C NMR spectra of compound **5** ($^{13}C_6$-TA). The inset displays the carbon peaks which are at much lower relative intensities due to the ^{13}C-labeling.

Quantification of 1a-3. Table S1 reports the quantification of formaldehyde hemiacetals (**1a-b**), acrolein (**2**), and acetaldehyde (**3**) by ^{1}H NMR using relative integrations against an internal standard. Values are presented as an average mg/g e-liquid consumed for each wattage tested. **1a**-**b** were integrated together due to their overlapping peaks. A p-value of <0.05 represents statistical significance. LOD was calculated to be 0.025mM using the International Union of Pure and Applied Chemistry method.[1] Table S2 reports the mass of e-liquid consumed for each sample, which were used to calculate the average mg/g.

Table S1. Quantification of compounds **1a**-**b**, **2** and **3** by ^{1}H NMR.

EC1: SMOK® Baby Q2						
Power setting	**Target compound**	**Concentration of solute in aerosol of PG/GLY e-liquid (mg/g)**	**Standard deviation**	**Concentration of solute in aerosol of 10% TA e-liquid (mg/g)**	**Standard deviation**	**p-value**
55W	**1a and b**	**0.00046**	**0.000656**	**0.00084**	**0.00070**	**0.611**
	2	**<LOD**	**-**	**0.00039**	**0.00055**	**-**
	3	**<LOD**	**-**	**<LOD**	**-**	**-**
65W	**1a and b**	**0.00062**	**0.000513**	**0.00162**	**0.00024**	**0.034**
	2	**<LOD**	**-**	**0.00043**	**0.00047**	**-**
	3	**<LOD**	**-**	**<LOD**	**-**	**-**
EC2: Kanger® Protank 2						
9W	**1a and b**	**<LOD**	**-**	**0.0937**	**0.0930**	**-**
	2	**<LOD**	**-**	**0.0047**	**0.0059**	**-**
	3	**<LOD**	**-**	**0.0030**	**0.0041**	**-**
11W	**1a and b**	**0.463**	**0.329**	**1.323**	**0.302**	**0.029**
	2	**0.208**	**0.119**	**0.519**	**0.134**	**0.044**
	3	**0.137**	**0.101**	**0.373**	**0.085**	**0.036**

Table S2. Mass of e-liquid consumed for each sample collected.

EC1: SMOK Baby Q2				
Power setting	**E-liquid solution**	**Initial mass of cartomizer (g)**	**Final mass of cartomizer (g)**	**Mass e-liquid consumed (g)**
55W	PG/GLY	49.5742	49.1751	0.3991
		49.5742	49.1751	0.3991
		49.5051	49.1576	0.3475
	TA/PG/GLY	49.7639	49.4324	0.3315
		49.6284	49.3175	0.3109
		49.4698	49.1166	0.3532
65W	PG/GLY	49.5416	49.1049	0.4367
		49.7651	49.3618	0.4033
		49.5471	49.1750	0.3721
	TA/PG/GLY	49.6309	49.2638	0.3671
		49.6385	49.2717	0.3668
		49.6965	49.3786	0.3179
		49.4190	49.0114	0.4076
EC2: Kanger Protank 2				
9 W	PG/GLY	42.8153	42.7423	0.0730
		42.9256	42.8630	0.0626
		43.0114	42.9397	0.0717
	TA/PG/GLY	43.0143	42.8431	0.1712
		42.8698	42.7840	0.0858
		42.7369	42.6343	0.1026
11 W	PG/GLY	43.1723	43.0388	0.1335
		42.7491	42.6496	0.0995
		42.7623	42.6592	0.1031
	TA/PG/GLY	42.8196	42.7098	0.1098
		42.6840	42.5752	0.1088
		42.7170	42.6214	0.0956
		42.3275	42.2355	0.0920

Reported concentration range of triacetin in e-liquid. Due to the current FDA regulations e-cigarette liquid manufactures do not need to report the full chemical composition of the e-liquid nor the chemical concentration. To determine the concentration that was used for this study, we compiled a list of the few manufacturers that report TA in their e-liquid, as well as one recent published report of TA concentration within e-liquid. Reported in Table S3 is the number of TA containing e-liquids that have a concentration level reported at or above 10% from each source. The 10% TA concentration used in this study represents a conservative and relevant concentration.

Table S3. Reported concentration range of triacetin in e-liquid*.*

	Number of TA-containing e-liquids reported with TA levels ≥ 10 %
Flavor Apprentice[2]	**7 of 19**
Simply Flavors[3]	**39 of 51**
Flavor West[4]	**13 of 24 (post-dilution)**
Behar, R. et al.[5]	**0 of 5**

Self-reported users' preferences for power output setting. To determine which battery power settings would be used for this study, we manually recorded users' self-reported preferences from Reddit. Two wattages were chosen for each e-cigarette device which would cover the range of reported preferences. Below is the list used; however, this is not an exhausted search due to the high volume of conversations and responses found on Reddit.

SMOK Baby, Q2 0.4 ohm coil

BeholderVee: "Tried a q2 coil on baby on 30-55w…"[6]
[deleted]: "I like to vape around 45-55 watts. (Q2)."[7]
Urano_Metria: "…I find the best flavor at 55W and notice I get the best vapor production and temp at around 65W, I have no problems sacrificing a tiny bit of flavor and vaping it at 60W."[8]
DeadRights: "I usually run it at about 65 - 70 watts."[9]
Rezingreenbowl: "…using the Q2 at 65w…"[10]
702jimboslice: "best through 55-65 and that's where it seems to have a sweet spot…"[11]

Protank 2, 2.2 ohm coil

Cravingvapor: "I am normally vaping at 8-10 watts."[12]
residualenvy. "…for my liking 2.2 at about 10W works great."[13]
kkeeiiggaann: "…don't need to be used above 8-9w to put out a decent vape."[14]
swancitysounds: "I like to stick around 9 watts."[15]
BikerKnight: "Would work great on your Protank 2 at 7-12W…"[16]
Okolo: "…depending on the juice I'm using, going up to 11 watts improves the taste…"[17]
NELyon: "I usually have my VV with the MPT2 at around 10.5 or 11 watts…"[18]

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