Organogels from trehalose difatty esters amphiphiles

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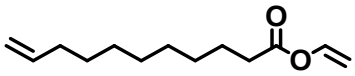
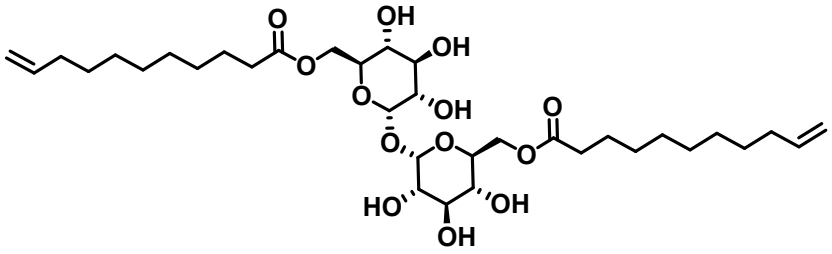
Experimental and Supporting Information

Experimental Methods

Synthesis



Vinyl undecenoate (1) (transvinylation of undecenoic acid): Undecenoic acid (1 eq) and a 15 eq. excess of vinyl acetate (VAc) was poured in a vial for the microwave reactor. Then, palladium acetate (0.05 eq.), and potassium hydroxide (0.10 eq.) were added and the resulting reaction mixture was stirred under microwave at 60 °C for 2 h. The reaction mixture was diluted in DCM and then filtrated over celite to remove the palladium acetate, before removing the solvent with a rotary evaporator. The resulting residue was purified by silica gel flash chromatography using an elution gradient of 2-5% MeOH in DCM to give the vinyl undecenoate. Yield: 95 %. ^{1}H NMR (DMSO-d_6, 400MHz, δ (ppm)): 7.29 (m, 1H, =C<u>H</u>-OCO-), 5.81 (m, 1H, -C<u>H</u>=CH_2), 4.97 (m, 2H, C<u>H</u>$_2$=CH-), 4.88 (d, 1H, CH_2=C<u>H</u>-OCO-), 4.56 (d, 1H, CH_2=C<u>H</u>-OCO-), 2.37 (t, 4H, -C<u>H</u>$_2$-COO-), 2.04 (m, 4H, -C<u>H</u>$_2$-CH=CH-), 1.67 (m, 4H, -C<u>H</u>$_2$-CH_2-COO-), 1.30 (m, 20H, aliphatic -C<u>H</u>$_2$-).



Trehalose diundecenoate (2) (enzymatic esterification of trehalose): The lipase (2.8 g) was added to a mixture of trehalose (3 g, 9 mmol), vinyl ester (6.8 g, 22 mmol, 2.5 eq) in dry acetone (40 mL). The reaction mixture was stirred at 45 °C for 72 hr. After the reaction time, THF was added to well dissolve the diesters of trehalose, then the reaction mixture was filtered and the solvent was removed with the rotary evaporator. The obtained crude product was purified by silica gel flash chromatography using an elution gradient of 5-25% methanol in EtOAc-DCM (1:1) to give pure trehalose diesters as white solids. Yield: 50 %. ^{1}H NMR (DMSO-d_6, 400MHz, δ (ppm)): 5.78 (m, 2H, -CH=CH2), 5.04 (d, 2H, -OH, H4), 4.94 (m, 4H, CH2=CH-), 4.89 (d, 2H, -OH, H3), 4.82 (d, 2H, -CH-, H1), 4.76 (d, 2H, -OH, H2), 4.21 (d, 2H, -CH-, H6), 4.04 (m, 2H, -CH-, H6), 3.89 (m, 2H, -CH-, H5), 3.55 (m, 2H, -CH-, H3), 3.26 (m, 2H, -CH-, H2), 3.13 (m, 2H, -CH-, H4), 2.27 (t, 4H, -CH2-COO-), 2.01 (m, 4H, -CH2-CH=CH-), 1.51 (m, 4H, -CH2-CH2-COO-), 1.33-1.25 (m, 20H, aliphatic -CH2-)).

The same two-step procedure was employed for the synthesis of the five following trehalose diesters

Trehalose dioleate

^{1}H NMR (DMSO-d6, 400MHz, δ (ppm)): 5.31 (m, 4H, -CH=CH-), 5.04 (m, 2H, -OH, H4), 4.87 (d, 2H, -OH, H3), 4.83 (d, 2H, -CH-, H1), 4.74 (d, 2H, -OH, H2), , 4.24 (d, 2H, -CH-, H6), 4.03 (m, 2H, -CH-, H6), 3.88 (m, 2H, -CH-, H5), 3.54 (m, 2H, -CH-, H3), 3.25 (m, 2H, -CH-, H2), 3.12 (m, 2H, -CH-, H4), 2.26 (t, 4H, -CH_2-COO-CH_3), 1.98 (m, 4H, -CH=CH2-), 1.50-1.24 (m, 44H, aliphatic -CH_2-), 0.85 (t, 6H, aliphatic -CH_3). Tm = 135°C.

Trehalose distearate

^{1}H NMR (DMSO-d6, 400MHz, δ (ppm)): 5.05 (m, 2H, -OH, H4), 4.90 (d, 2H, -OH, H3), 4.82 (d, 2H, -CH-, H1), 4.75 (d, 2H, -OH, H2), , 4.21 (d, 2H, -CH-, H6), 4.03 (m, 2H, -CH-, H6), 3.89 (m, 2H, -CH-, H5), 3.55 (m, 2H, -CH-, H3), 3.25 (m, 2H, -CH-, H2), 3.12 (m, 2H, -CH-, H4), 2.26 (t, 4H, -CH_2-COO-CH_3), 1.50-1.23 (m, 60H, aliphatic -CH_2-), 0.85 (t, 6H, aliphatic -CH_3).

Trehalose diundecenoate

^{1}H NMR (DMSO-d6, 400MHz, δ (ppm)): 5.78 (m, 2H, -CH=CH_2), 5.05 (d, 2H, -OH, H4), 4.97 (m, 4H, CH_2=CH-), 4.87 (d, 2H, -OH, H3), 4.82 (d, 2H, -CH-, H1), 4.74 (d, 2H, -OH, H2), 4.24 (d, 2H, -CH-, H6), 4.02 (m, 2H, -CH-, H6), 3.89 (m, 2H, -CH-, H5), 3.54 (m, 2H, -CH-, H3), 3.28 (m, 2H, -CH-, H2), 3.13 (m, 2H, -CH-, H4), 2.27 (t, 4H, -CH_2-COO-), 2.01 (m, 4H, -CH_2-CH=CH-), 1.51-1.25 (m, 28H, aliphatic -CH_2-).

Trehalose dierucate

^{1}H NMR (DMSO-d6, 400MHz, δ (ppm)): 5.32 (m, 4H, -CH=CH-), 5.04 (m, 2H, -OH, H4), 4.88 (d, 2H, -OH, H3), 4.82 (d, 2H, -CH-, H1), 4.75 (d, 2H, -OH, H2), , 4.25 (d, 2H, -CH-, H6), 4.02 (m, 2H, -CH-, H6), 3.87 (m, 2H, -CH-, H5), 3.55 (m, 2H, -CH-, H3), 3.25 (m, 2H, -CH-, H2), 3.11 (m, 2H, -CH-, H4), 2.26 (t, 4H, -CH_2-COO-CH_3), 1.98 (m, 8H, -CH=CH_2-), 1.50-1.24 (m, 60H, aliphatic -CH_2-), 0.85 (t, 6H, aliphatic -CH_3). Tm = 151 °C.

Trehalose dilinoleate

^{1}H NMR (DMSO-d6, 400MHz, δ (ppm)): 5.32 (m, 8H, -CH=CH-), 5.03 (m, 2H, -OH, H4), 4.87 (d, 2H, -OH, H3), 4.82 (d, 2H, -CH-, H1), 4.73 (d, 2H, -OH, H2), , 4.24 (d, 2H, -CH-, H6), 4.04 (m, 2H, -CH-, H6), 3.90 (m, 2H, -CH-, H5), 3.55 (m, 2H, -CH-, H3), 3.26 (m, 2H, -CH-, H2), 3.11 (m, 2H, -CH-, H4), 2.73 (t, 4H, -CH=CH-CH2-CH=CH-), 2.26 (t, 4H, -CH_2-COO-CH_3), 2.02 (m, 8H, -CH=CH_2-), 1.50-1.25 (m, 32H, aliphatic -CH_2-), 0.86 (t, 6H, aliphatic -CH_3). Tm = 138 °C.

Trehalose dielaidate

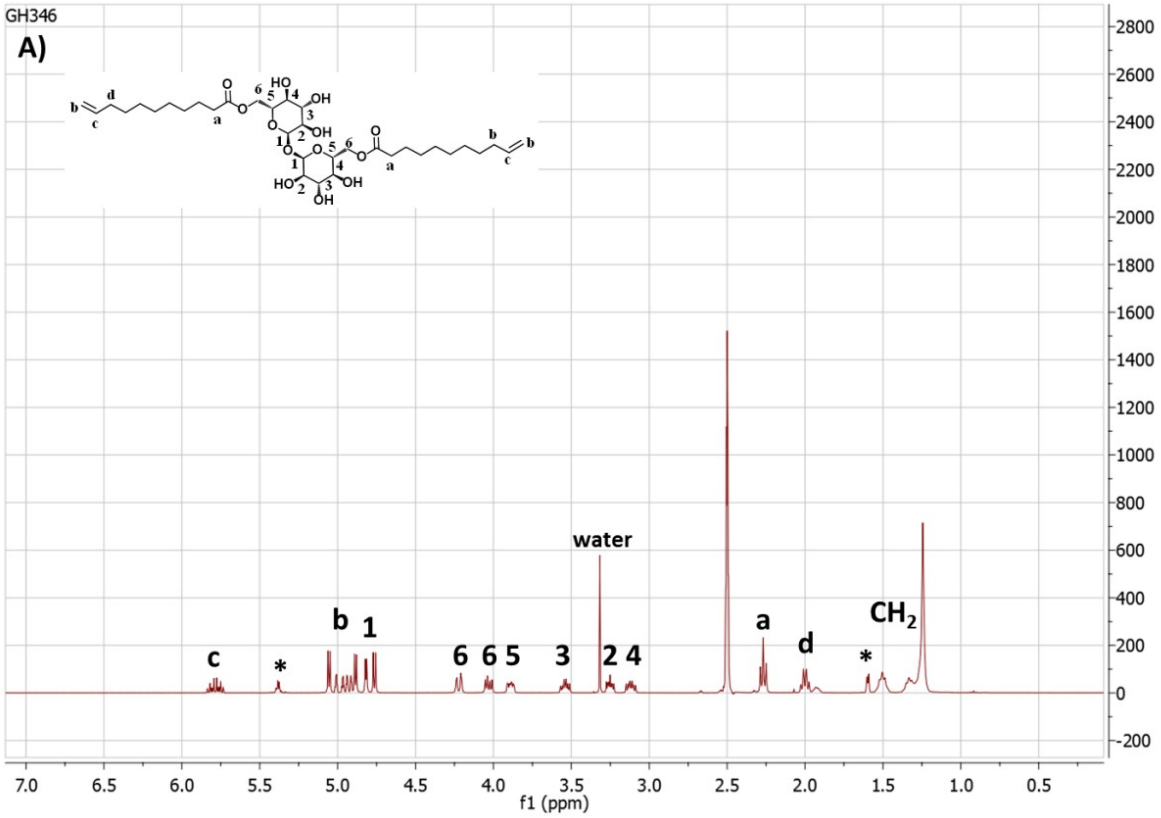
^{1}H NMR (DMSO-d6, 400MHz, δ (ppm)): 5.35 (m, 4H, -CH=CH-), 5.04 (m, 2H, -OH, H4), 4.88 (d, 2H, -OH, H3), 4.82 (d, 2H, -CH-, H1), 4.75 (d, 2H, -OH, H2), , 4.24 (d, 2H, -CH-, H6), 4.03 (m, 2H, -CH-, H6), 3.89 (m, 2H, -CH-, H5), 3.54 (m, 2H, -CH-, H3), 3.27 (m, 2H, -CH-, H2), 3.11 (m, 2H, -CH-, H4), 2.26 (t, 4H, -CH_2-COO-CH_3), 1.93 (m, 4H, -CH=CH_2-), 1.50-1.24 (m, 44H, aliphatic -CH_2-), 0.85 (t, 6H, aliphatic -CH_3). Tm = 148 °C.

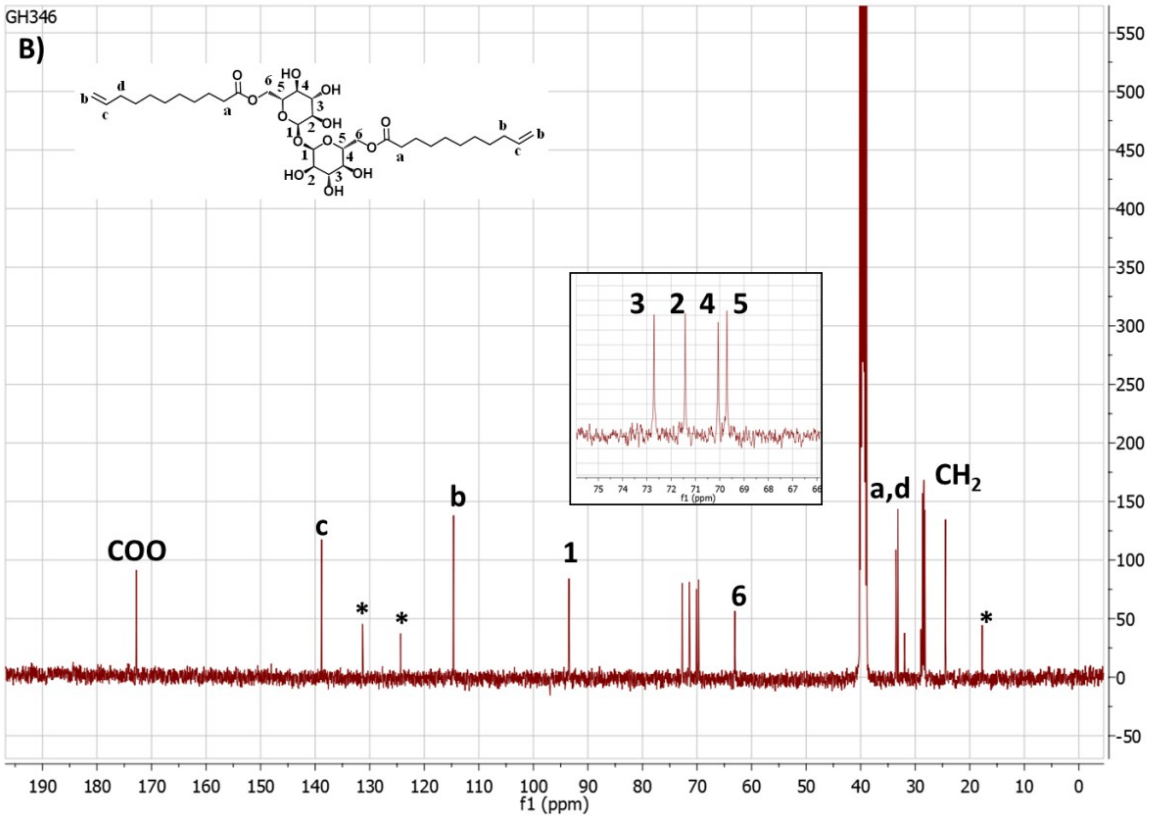
Gel preparation and gelation test

Gel samples were prepared by adding a precise quantity of trehalose diesters to a desired solvent (vegetable oils and pharmaceutical grade oils), followed by heating and stirring until complete dissolution of the diesters in the vegetable oils. After getting a homogeneous solution, the mixture was cooled down to room temperature. The sample vials were inverted to confirm the gel formation.

To evaluate the efficiency of these trehalose diesters as gelators, the MGC of each diester was determined. The minimal gelation concentration (MGC) was determined by diluting the gel until getting a solution after the gelation procedure (homogenization by heating and shaking, and then cooling).

Supporting Information





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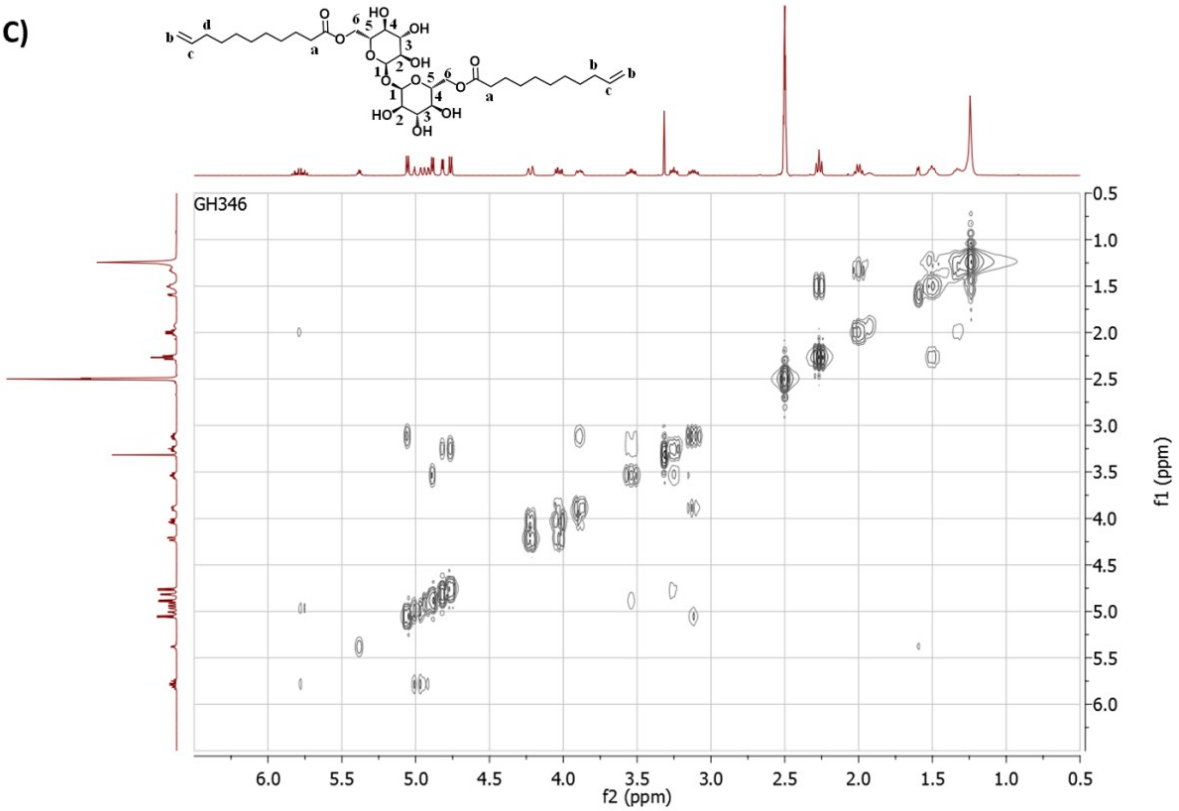

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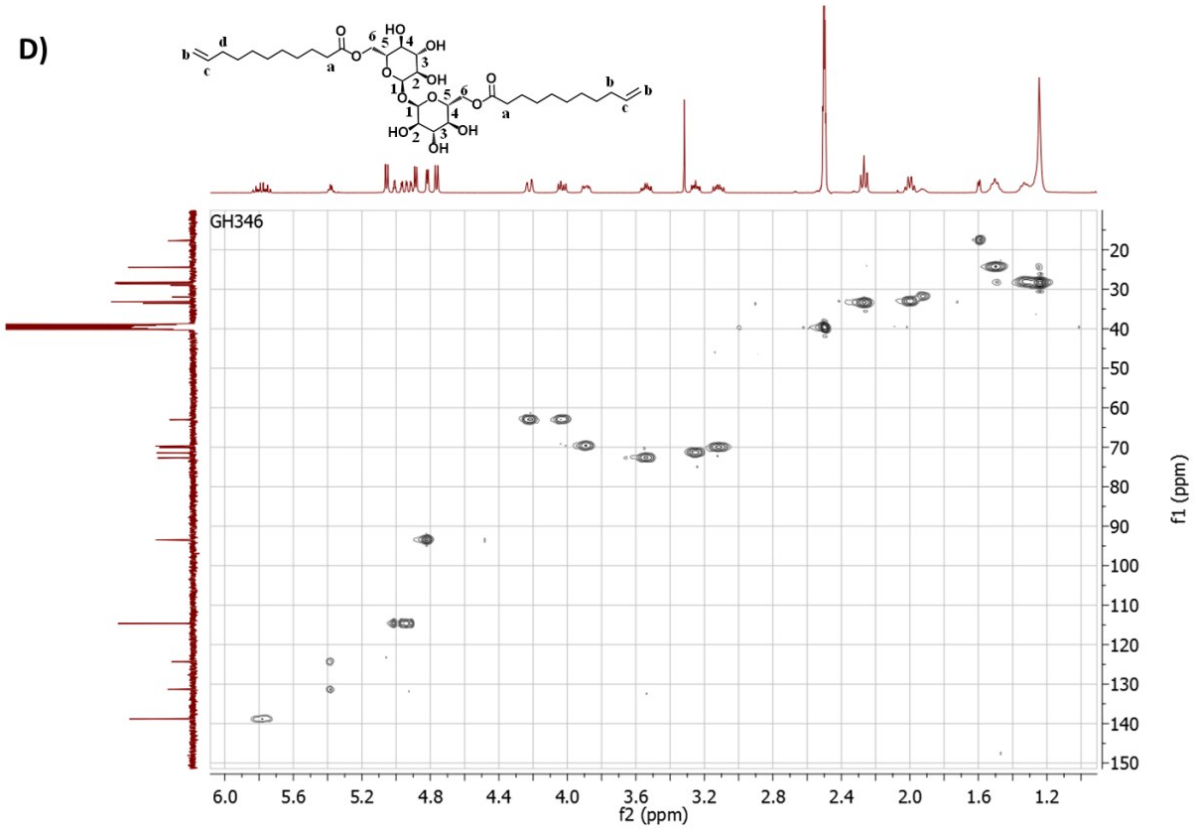

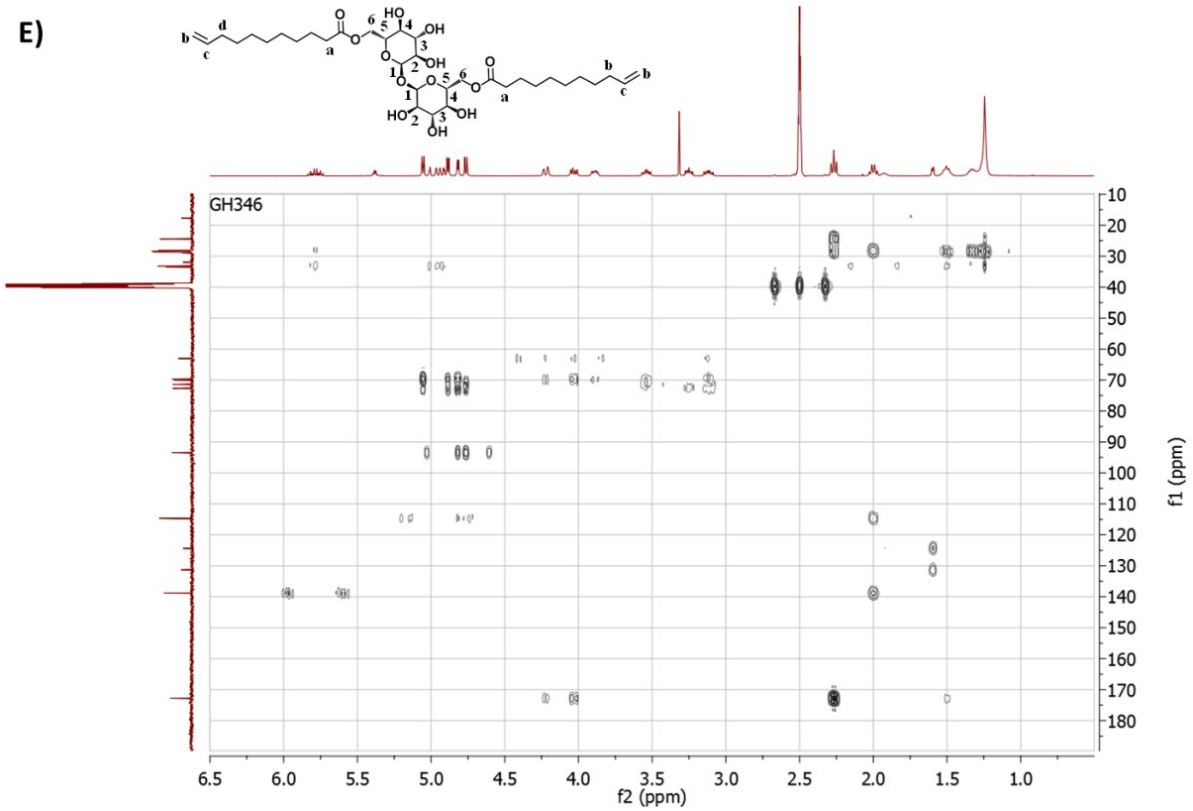

Figure S1: NMR spectra of trehalose diundecenoate performed in DMSO-d_6. A) ^{1}H NMR, B) ^{13}C NMR, C) ^{1}H-^{1}H COSY NMR, D) ^{1}H-^{13}C HSQC NMR, E) ^{1}H-^{13}C HMBC NMR. *correspond to isomerized double bonds of trehalose diundecenoate

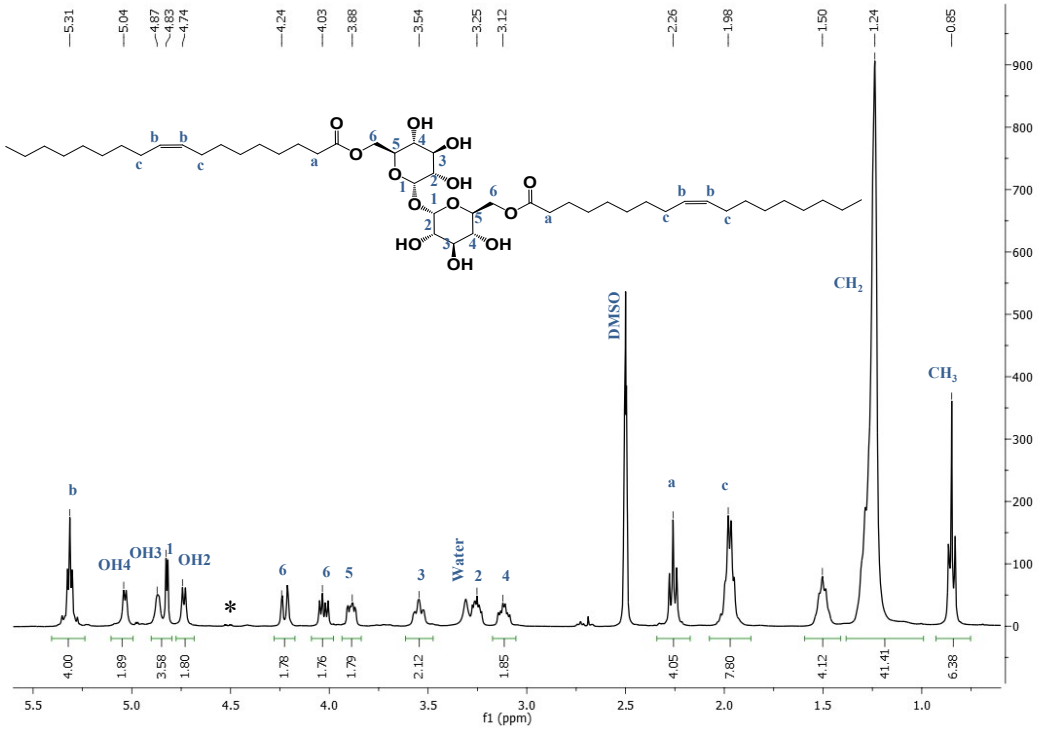

Figure S2: ^{1}H NMR spectrum of trehalose dioleate performed in DMSO-d6 *correspond to trehalose monooleate impurity

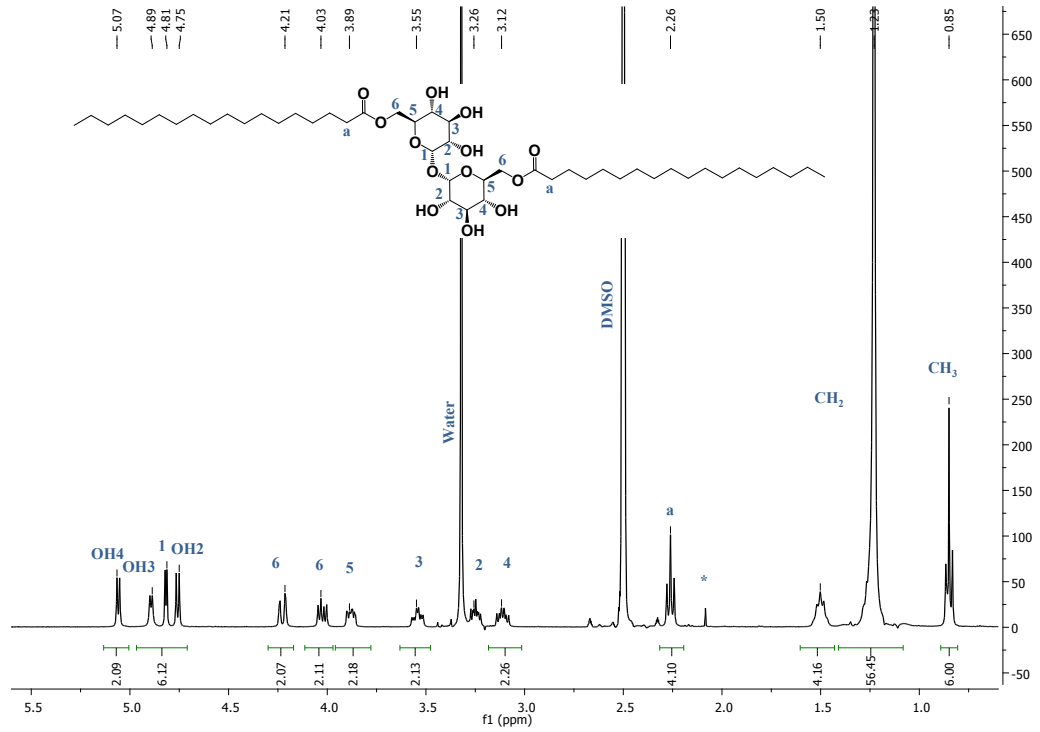

Figure S3: ^{1}H NMR spectrum of trehalose distearate performed in DMSO-d6

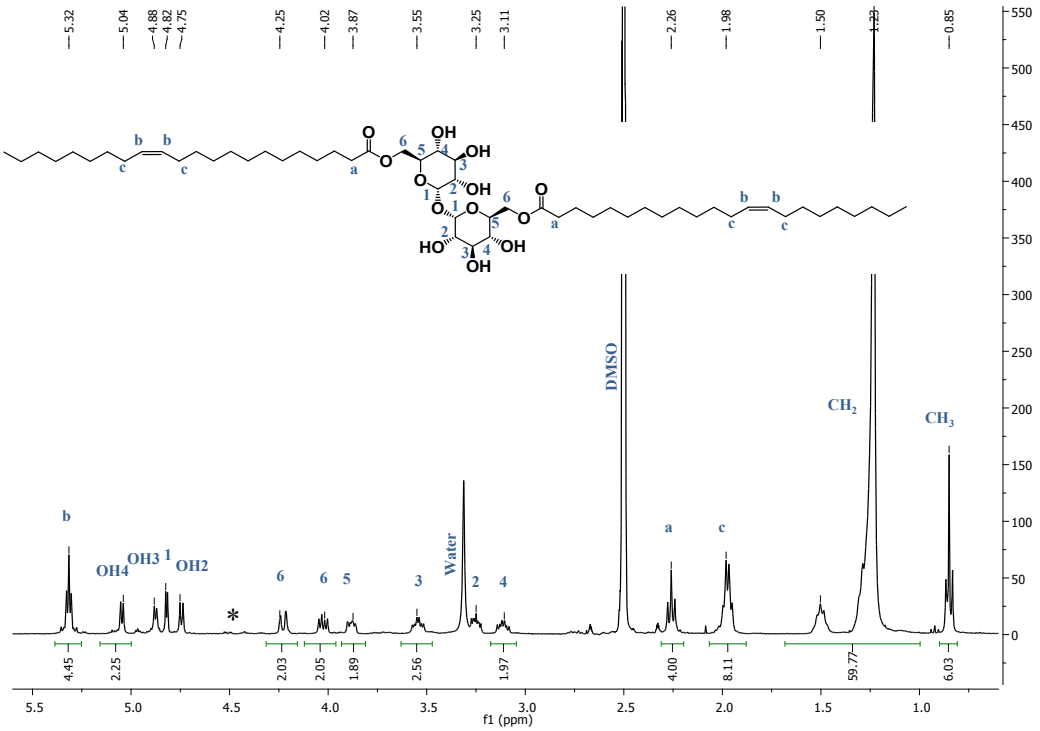

Figure S4: ^{1}H NMR spectrum of trehalose dierucate performed in DMSO-d6 *correspond to trehalose monoerucate impurity

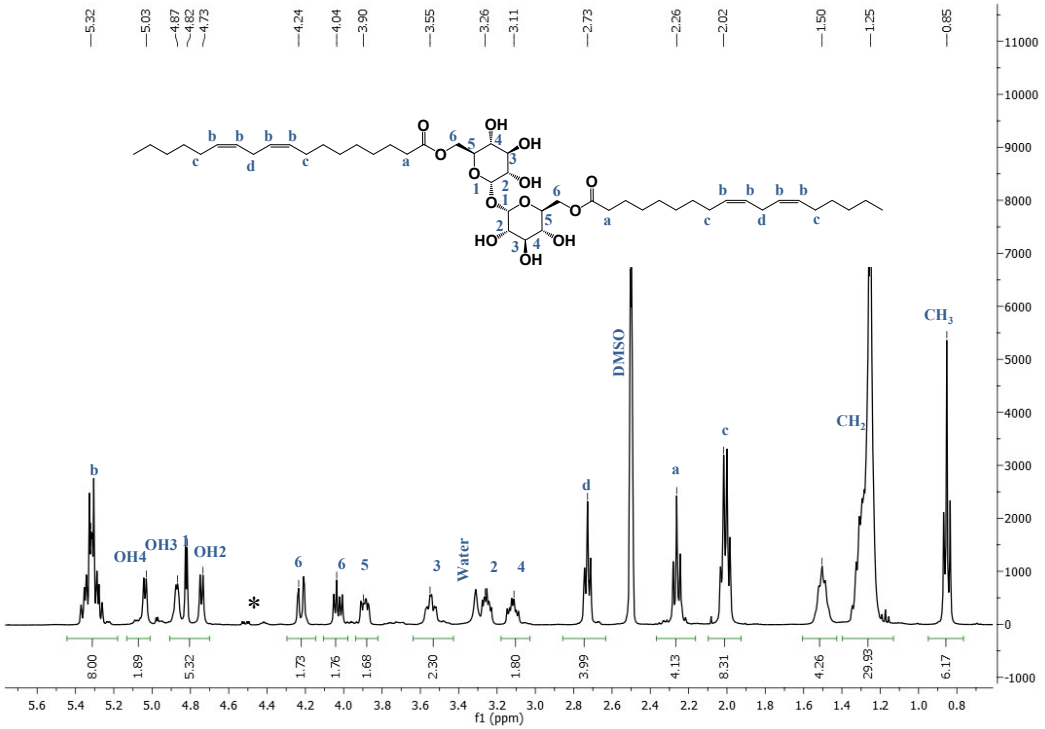

Figure S5: ^{1}H NMR spectrum of trehalose dilinoleate performed in DMSO-d6 *correspond to trehalose monolinoleate impurity

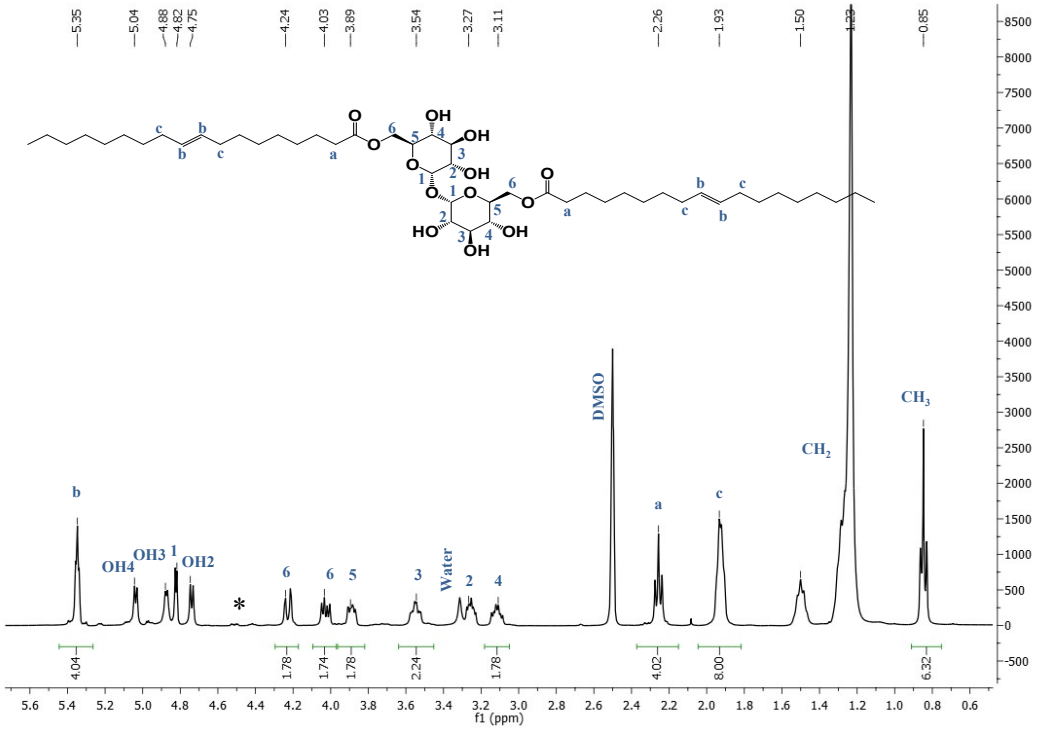

Figure S6: ^{1}H NMR spectrum of trehalose dielaidate performed in DMSO-d6 *correspond to trehalose monoelaidate impurity

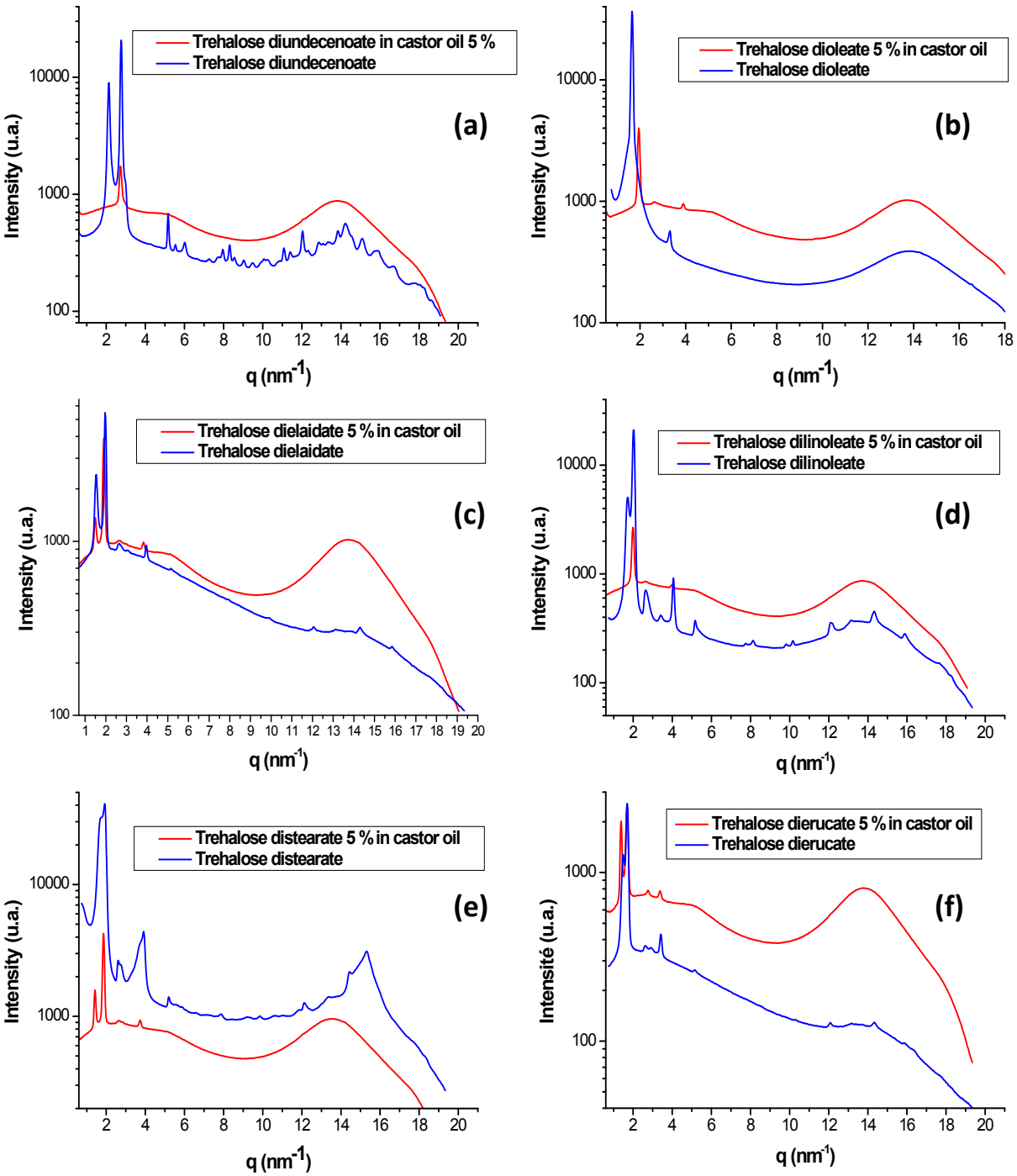

Figure S7: X-ray scattering patterns of pure trehalose diesters and of the gel in castor oil at 5 wt%/v

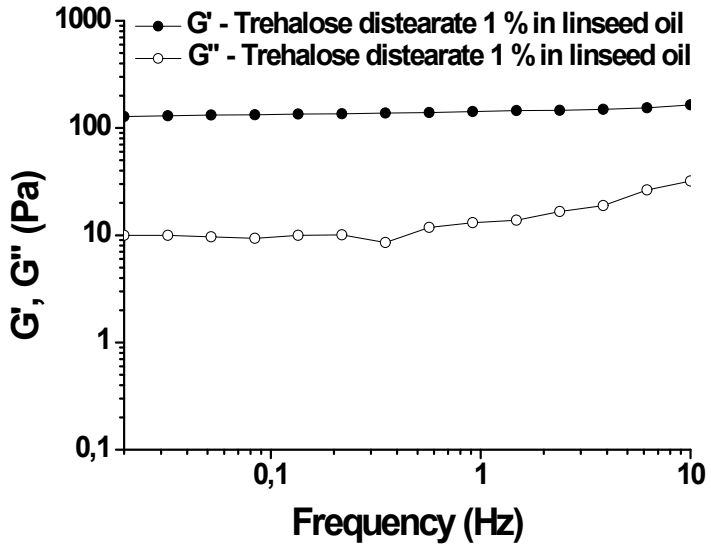

Figure S8: Oscillatory frequency sweep measurement of gel prepared with trehalose distearate in linseed oil at 1 wt.%/v

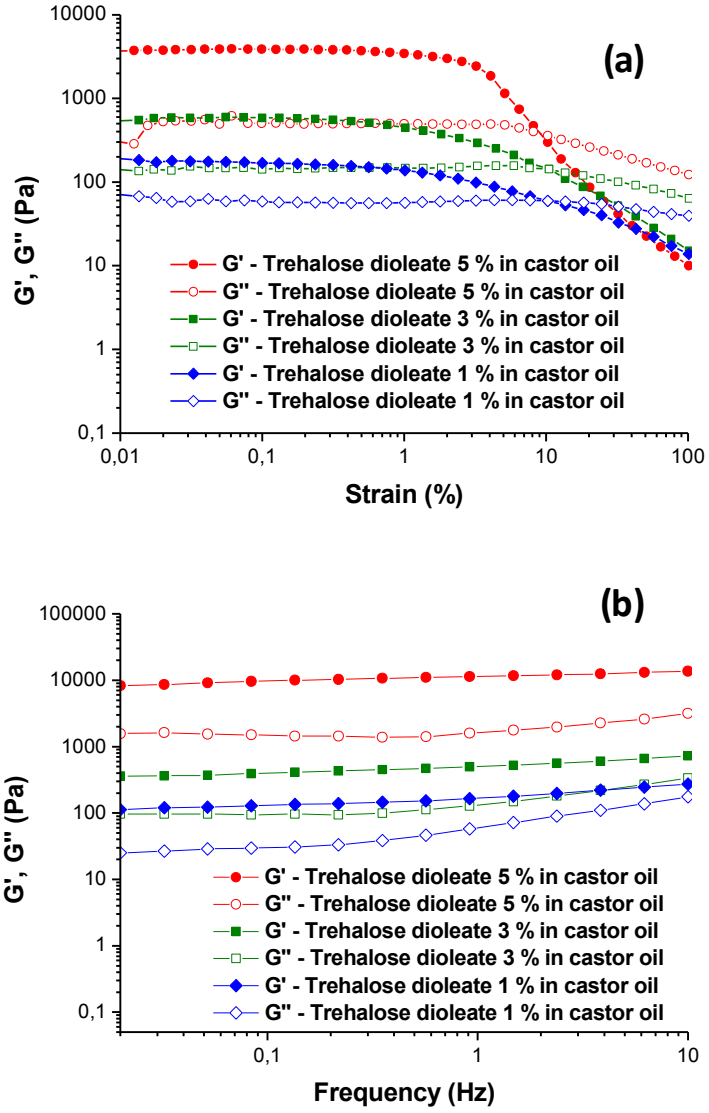

Figure S9: Concentration-dependent rheology measurement (strain sweep (a) and oscillatory frequency sweep (b)) of trehalose dioleate in castor oil

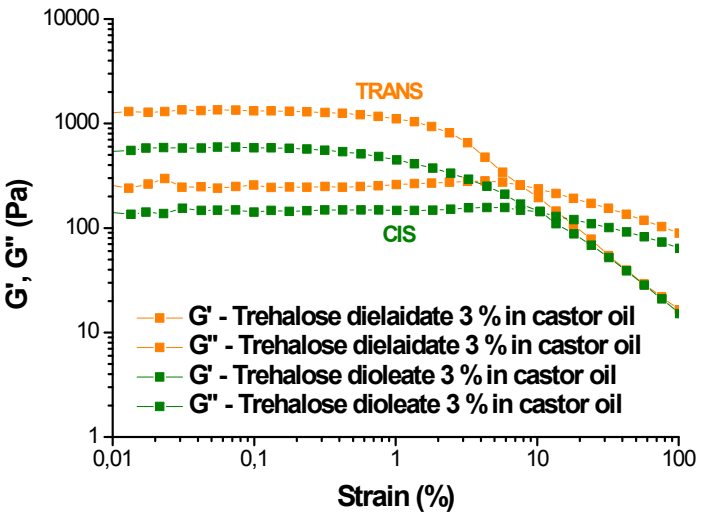

Figure S10: Effect of the cis-trans configuration on the rheological properties of gel in castor oil. Oscillatory strain sweep performed on gel made from trehalose dioleate (CIS) and trehalose dielaidate (TRANS) at 3 wt.%/v

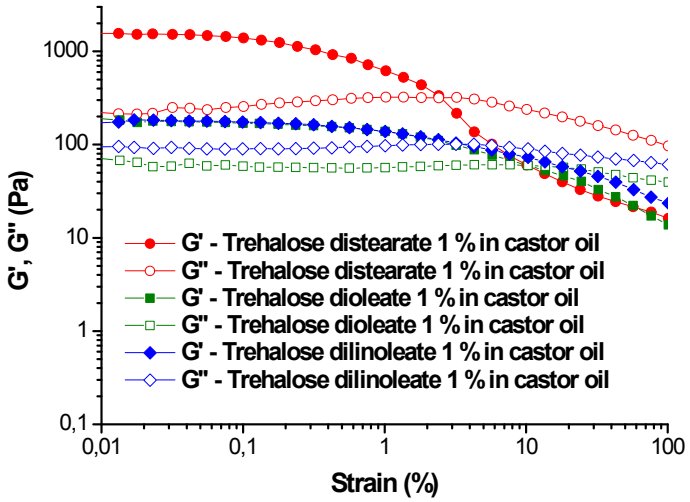

Figure S11: Effect of the unsaturation number of the alkyl chain on rheological properties of gel. Oscillatory strain sweep performed on gels made from trehalose distearate (red curve), trehalose dioleate (green curve) and trehalose dilinoleate (blue curve) in castor oil at 1 wt.%

Glycolipids	Vegetable oil	wt.%	Tgel-to-sol (°C)	γ_y (%)	G' (Pa)	G'' (Pa)
Trehalose Distearate (C18:0)	Olive oil	1	133	0,6	300	20
		2	133	2,9	2600	300
		3	136	3,3	2800	360
	Linseed oil	1	131	0,4	200	20
		2	131	1,2	600	60
		3	134	1,6	2100	160
	Castor oil	1	nd	1,8	1500	200
		2	nd	33,5	12700	240
		3	124	12,5	16000	1700
Trehalose Dioleate (C18:1)	Olive oil	1	119	0,3	20	10
		2	132	1,5	500	70
		3	124	1,8	600	90
	Linseed oil	1	122	0,5	30	10
		2	126	0,7	500	40
		3	125	0,9	700	100
	Castor oil	1	nd	1,6	200	50
		2	114	1,8	600	70
		3	111	20,2	4200	500
Trehalose Dilinoleate (C18:2)	Olive oil	1	nd	0,2	60	20
		2	112	4,8	2500	400
		3	120	5	1900	200
	Linseed oil	1	121	0,5	50	20
		2	115	2,3	2300	300
		3	123			
	Castor oil	1	97	1	300	100
		2	104	1,7	600	200
		3	104	5,1	2400	400
Trehalose Dielaidate (C18:1 trans)	Olive oil	1	nd	0,3	60	15
		2	126	1,5	400	60
		3	124	3,1	1100	100
	Linseed oil	1	nd	1,2	100	10

		2	126	2,5	900	100
		3	127	2,7		
	Castor oil	1	94	0,9	200	70
		2	105	3,1	1400	260
		3	120	18,4	4700	600
Trehalose Diundecenoate (C11:1)	Olive oil	1	134		32400	3500
		2	136	44	76500	15000
		3	140			
	Linseed oil	1	nd	11	12000	1400
		2	131	140	76500	15000
		3	140			
	Castor oil	1	102	4,5	3900	1000
		2	118	22,8	57000	24000
		3	119			
Trehalose Dierucate (C22:1)	Olive oil	1	nd	0,2	200	30
		2	103	0,5	400	90
		3	103	2,6	2700	500
	Linseed oil	1	nd	0,2	100	30
		2	114	1	800	250
		3	118	5,1	3100	600
	Castor oil	1	nd	1	200	70
		2	106	3,3	1500	300
		3	nd	4,8	3900	1000

Table S1: Gel-to-sol temperature and rheological data of the gels.