Supporting Information

Supramolecular emulsifiers in biphasic catalysis: the substrate drives its own transformation

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Materials and methods

All chemicals were purchased from Acros, Strem or Aldrich Chemicals in their highest purity. Olive oil was purchased from Aldrich while Very High Oleic Sunflower Oil (VHOSO) was provided by Oleon. Roquette Frères (Lestrem, France) was gratefully acknowledged for generous gifts of β-CD, RAME-β-CD and CRYSMEB. Deionized water was used in all experiments. NMR spectra were recorded on a Bruker DRX300 spectrometer operating at 300 MHz for ^{1}H nuclei and 75 MHz for ^{13}C nuclei. $CDCl_3$ (99.50% isotopic purity), D_2O (99.50% isotopic purity) were purchased from Eurisotop.

Triolein was used as model triglyceride. Compared to technical grade triglycerides, its purity and symmetrical structure derived from glycerol and oleic acid has the significant advantage of facilitating the analysis of the reaction products. The phase diagrams were elaborated by mixing a well-known quantity of CDs, triolein and water in a test tube. The solution was stirred at the appropriate temperature using an oil bath for 20 min at 1400 rpm. The stirring was then switched off and the system is allowed to stand for a given period at a given temperature. The phase diagrams of CD/triolein/water systems were obtained by visual and microscopic observations. The benchmark chromophore Red 1 has been used to help visualizing the multiphase systems and determining the type of emulsion.

Optical microscopy of the different phases were realized using a Microscope Olympus BH-2 in transmission mode, with the following objectives: x10(MDPlan), X50 (ULWD MSplan). GCFID analysis were performed with a Perkin Elmer Clarus 500 chromatograph, using a Varian capillary column (length 30 m, internal diameter 0.025 μm).

GC-MS analysis were performed using a Shimadzu GC-17A gas chromatograph using a Varian capillary column (length 30 m, internal diameter 0.025 μm) and a Shimadzu GCMS-QP500 mass spectrometer. The product were analyzed using a temperature gradient from 250 °C to 300 °C at 1.5 °C/min.

Tensiometric measurements were performed using the hanging drop technic (drop of the CD solution in oil) with a Dataphysics OCA 15 instrument.

All the hydroformylation experiments were carried out in laboratory reactors from Parr Instrument Company (USA). To prevent oxidation of the catalyst precursors, the reaction mixture was transferred into the reactor using the standard Schlenk technique.

Formation of CD/T supramolecular complexes

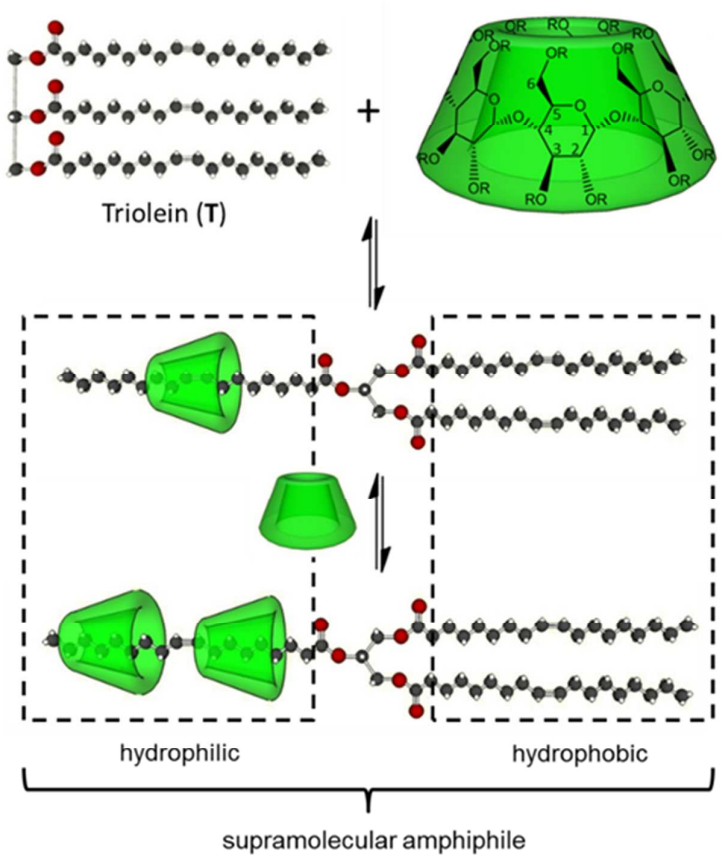

Figure S1. Equilibriums existing between free CD and triolein (**T**) and their 1:1 and 2:1 CD/**T** supramolecular complexes.

Gibbs equations

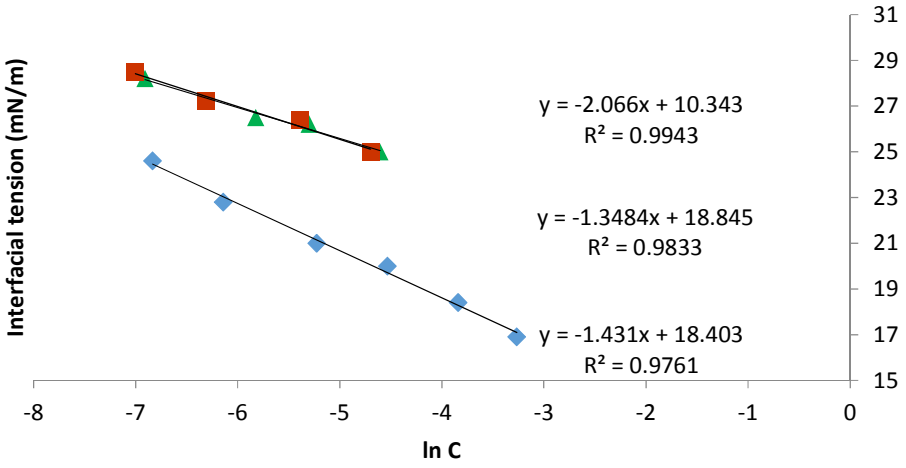

Figure S2. Linearization of the Gibbs equation calculated from the variation of the interfacial tension at the triolein/water interface. Only data recorded at low CD concentrations were considered to ensure a monomolecular adsorption of the CDs at the triolein/water interface. RAME-β-CD (◆), HP-β-CD (■) and CRYSMEB (▲) at RT.

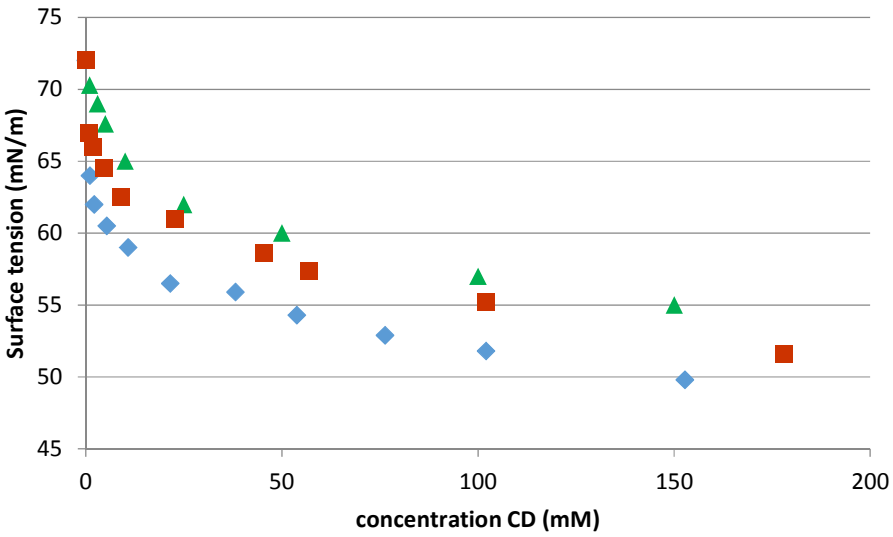

Figure S3. Surface tension variation at the air/water interface for RAME-β-CD (◆), HP-β-CD (■) and CRYSMEB (▲) at RT. Only data recorded at low CD concentrations were considered to ensure a monomolecular adsorption of the CDs at the air/water interface.

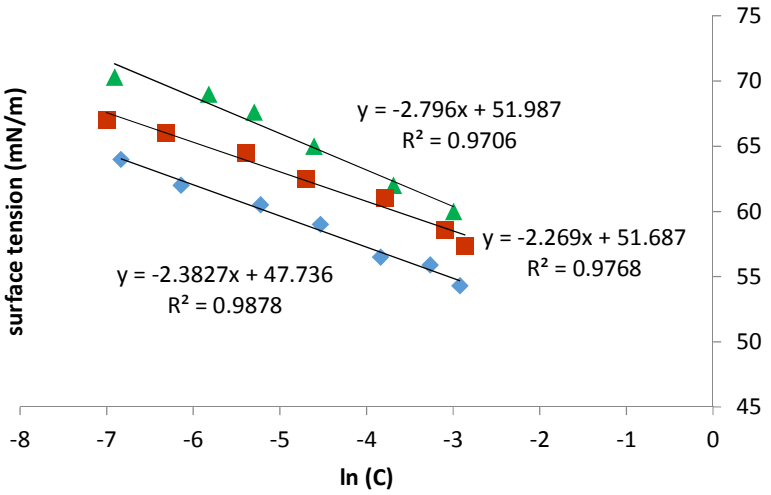

Figure S4. Linearization of the Gibbs equation calculated from the variation of the surface tension at the air/water interface for RAME-β-CD (◆), HP-β-CD (■) and CRYSMEB (▲) at RT. Only data recorded at low CD concentrations were considered to ensure a monomolecular adsorption of the CDs at the air/water interface.

Interfacial excess, interfacial area and CD/T stoichiometry

The surface concentration of the modified CD/**T** complexes at the interface of a two-phase system could be expressed as:

$$\Gamma_{T\subset CD} = \frac{-1}{RT}\frac{\partial\gamma}{\partial ln C_{CD}} \quad (1)$$

where $\Gamma_{\mathbf{T}\subset CD}$ is defined as the interfacial excess of the CD (mol.cm^{-2}) and γ the surface tension (mN.m^{-1}). From $\Gamma_{\mathbf{T}\subset CD}$, the interfacial area (surface occupied by the modified CD or the supramolecular CD/triglyceride complex) could be expressed as:

$$A_{T\subset CD} = \frac{10^{16}}{\Gamma_{T\subset CD} N_A} \left(\text{Å}^2\right) \quad (2)$$

where N_A is the Avogadro constant.

Both $\Gamma_{\mathbf{T}\subset CD}$ and $A_{\mathbf{T}\subset CD}$ were calculated from the above γ variations (Figure 3). Low concentrations of CDs were considered to ensure a monomolecular adsorption of the CDs at the interface, in line with the curve profiles depicted in Figure 3. Upon addition of **T** to the CD solutions, $\Gamma_{\mathbf{T}\subset CD}$ were calculated to be 8.3 .10^{-11}, 5.9 .10^{-11} and 5.4 .10^{-11} mol.cm^{-2} for RAME-β-CD, HP-β-CD and CRYSMEB, respectively. To the interfacial excesses corresponded interfacial areas of 199, 280 and 305 Å^2, respectively.

The CD/**T** stoichiometry was determined from the following equation (3):

$$N_{\mathbf{T}\subset CD} = \frac{A_{\mathbf{T}\subset CD}}{A_{CD,ref}} \quad (3)$$

Surfacic areas of CDs (in the absence of **T**) were determined using the same equations at the air/water interface in the presence of various CDs concentration. $A_{CD,ref}$ were 197 Å^2, 183 Å^2, 147 Å^2 for RAME-β-CD, HP-β-CD and CRYSMEB, respectively. These values are coherent with the surfacic area measured for the native β-CD (183 Å^2). The $A_{\mathbf{T}\subset CD}$ values were higher than the maximum surface occupied by the CD alone and corroborated the existence of **T**⊂CD supramolecular complexes at the aqueous/organic interface.

Conversely, the $N_{\mathbf{T}\subset CD}$ stoichiometry was 1, 1.5 and 2 for RAME-β-CD, HP-β-CD and CRYSMEB, respectively. A high CD/**T** molar ratio of 3 was found for native CDs, thus explaining the rapid precipitation of the native CD/**T** supramolecular complexes when the CD concentration raised.

Interfacial tension of **T**+CRYSMEB and **A**+CRYSMEB (**A** = hydroformylated products) mixtures were also measured. Using **T**, a significant decrease in γ was observed for increasing amounts of CRYSMEB, while a small variation was noticed using **A**. Thus, interactions between **A** and the CD cavity were negligible**.**

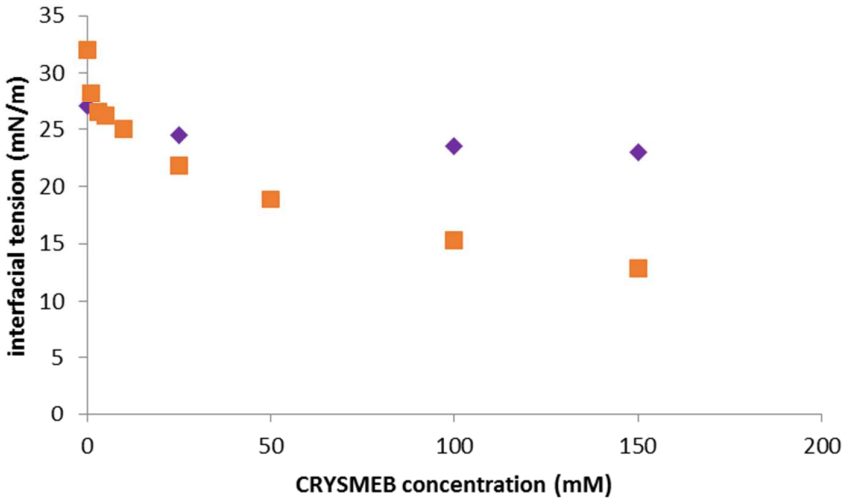

Figure S5. Surface tension variation at the interface between an aqueous solution of CRYSMEB and triolein (**T**) (■) or the hydroformylated products (**A**) (◆) at RT.

Catalytic experiments

In a typical experiment, $Rh(CO)_2(acac)$ (39 mg, 0.015 mmol, 1 eq) TPPTS (42 mg, 0.075 mmol, 5 eq) and CRYSMEB (2.3 g, 2 mmol) were degassed by vacuum-N_2 cycles three times and were dissolved in degassed deionized water (3.4 mL). The resting solution was stirred at room temperature until all the rhodium complex was dissolved (4 h). 1 mL of triolein (0.91 g, 1 mmol) was poured into the autoclave and N_2-purged. The catalytic solution was then cannulated under nitrogen into the autoclave. Once a temperature of 80 °C has been reached, the autoclave was pressurized under CO/H_2 pressure (80 bar) and the solution was vigorously stirred (1500 rpm). When the reaction was over, the apparatus was allowed to cool to room temperature and depressurized. The organic phase was extracted directly after opening the autoclave thank to products decantation. The products were analyzed by ^{1}H and ^{13}C NMR experiments. All runs have been performed at least twice in order to ensure reproducibility. Additionally, no trace of TPPTS could be detected in the organic phase by ^{1}H and ^{31}P NMR measurements.

^{1}H NMR spectra of reactant and product

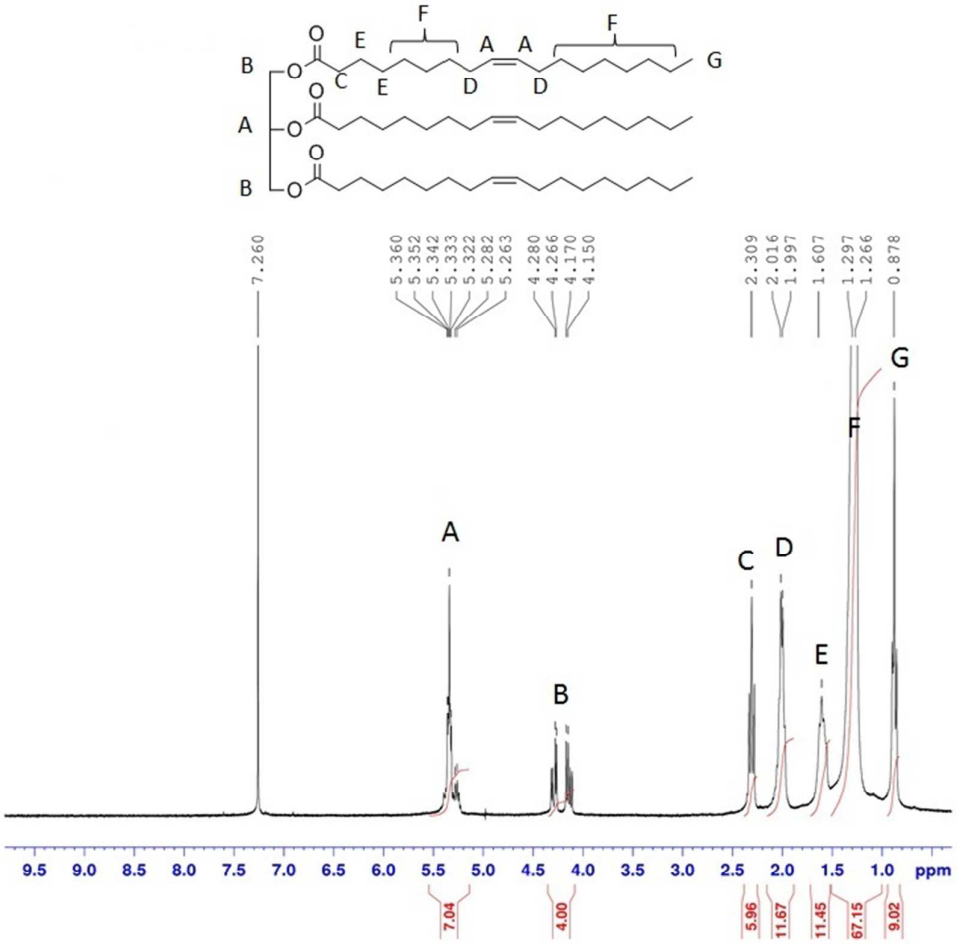

Figure S6. ^{1}H NMR spectrum of triolein (**T**) in $CDCl_3$ at 25 °C.

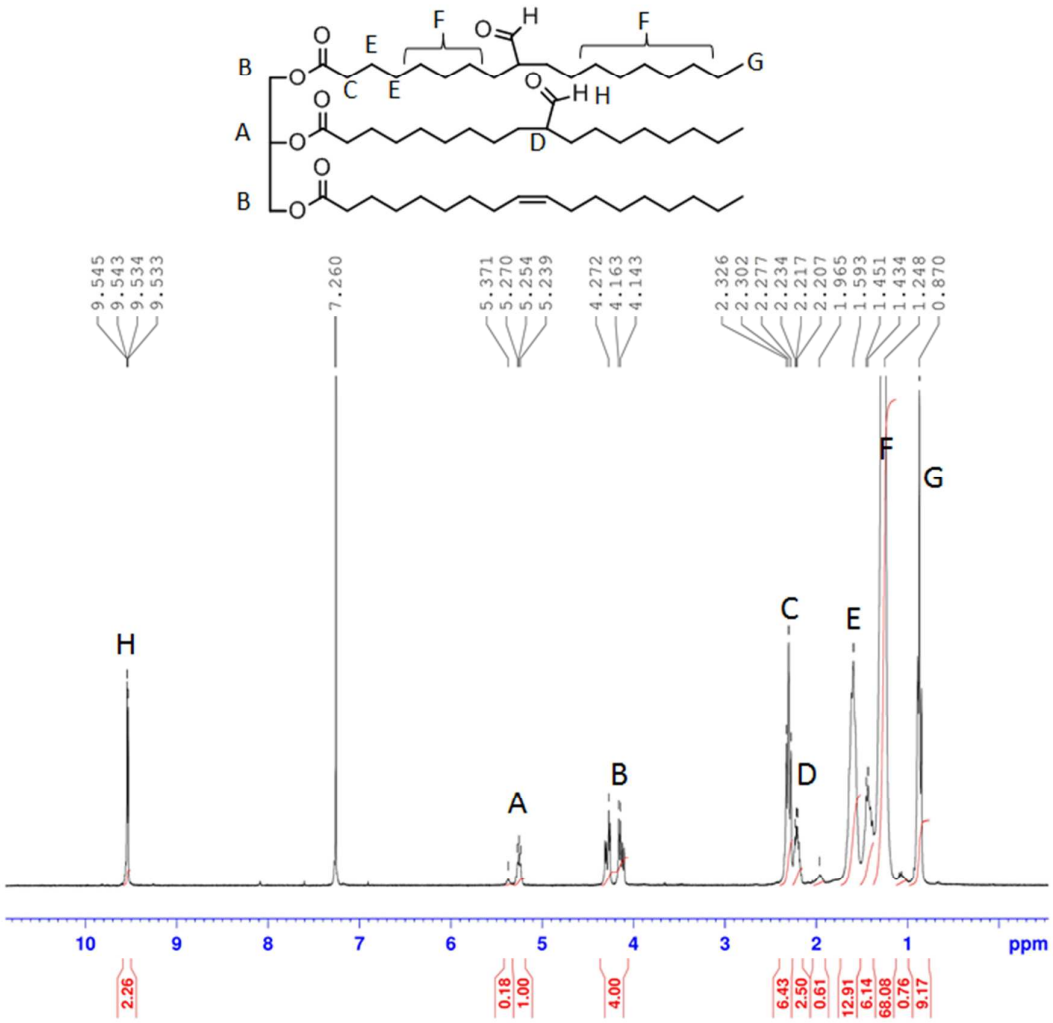

Figure S7. ^{1}H NMR spectrum of hydroformylated triolein (**T**) in $CDCl_3$ at 25 °C.

Conversion calculations

The normalization integration factor is given by $FN = \frac{B}{4}$. The B signal represents four protons of the glycerol moiety of the triglyceride. They are not involved in the hydroformylation reaction and can be used as a reference signal. The number of initial C=C double bonds (DB_i) is calculated from the pure initial substrate:

$$DB_i = \frac{A - FN}{2}$$

with A the peak integration of oléfinic proton added to one of glycerol moiety.

For example, $DB_i = 3$ for triolein.

Once the reaction is complete, the conversion is given by:

$$Conv.(\%) = \frac{DB_i - DB_f}{DB_i} \times 100 = \frac{A_i - A_f}{A_i - FN} \times 100$$

where A_i and A_f represent the integration values of the A signal before and after reaction, respectively.

The aldehyde selectivity is given by:

$$HF\ selec.(\%) = \frac{H/_{NF}}{DB_i - DB_f} \times 100$$

where H is the integration value of the H signal attributed to the formyl proton.

The hydrogenation selectivity is determined from the hydroformylation selectivity by:

$$hydrogenation\ selec.(\%) = 100 - selec.HF(\%)$$

Catalytic results

Table S1. Rh-catalyzed hydroformylation of **T**.[a]

Entry	CD	CD init. conc. ($mol.L^{-1}$)	Conv. (%)[b]	Aldehyde sel.(%)[b]	Hydrogenated products sel. (%)[b]
1	RAME-β-CD	0.13	9	57	43
2	RAME-β-CD	0.26	29	83	17
3	RAME-β-CD	0.52	53	86	14
4	RAME-β-CD	0.67	52	81	19
5	HP-β-CD	0.060	23	59	41
6	HP-β-CD	0.12	43	70	30
7	HP-β-CD	0.22	61	84	16
8	HP-β-CD	0.46	91	90	10
9	HP-β-CD	0.69	87	89	11
10	CRYSMEB[c]	0.030	41	82	18
11	CRYSMEB[c]	0.060	61	85	15
12	CRYSMEB[c]	0.12	79	97	3
13	CRYSMEB[c]	0.22	96	94	6
14	CRYSMEB[c]	0.31	94	94	6
15[d]	CRYSMEB[c]	0.22	94	94	6
16[e]	CRYSMEB[c]	0.22	94	93	7
17[f]	CRYSMEB[c]	0.22	93	93	7
18[g]	CRYSMEB[c]	0.22	95	86	14
19[h]	CRYSMEB[c]	0.22	96	74	26

[a] Conditions: **T** (1 mL, 1 mmol), $Rh(CO)_2(acac)$ (3.9 mg, 0.015 mmol), TPPTS (42 mg, 0.075 mmol), water (3.4 mL), 18 h, 80 °C, 80 bar CO/H_2 (1:1). [b] conversions and selectivities were determined by ^1H NMR. [c] water (8.2 mL), 6 h. [d] performed with the aqueous catalytic phase recovered from entry 13. [e] performed with the aqueous catalytic phase recovered from entry 15. [f] performed with the aqueous catalytic phase recovered from entry 16. [g] 80 bar CO/H_2 (1:2). [h] 80 bar CO/H_2 (2:1).

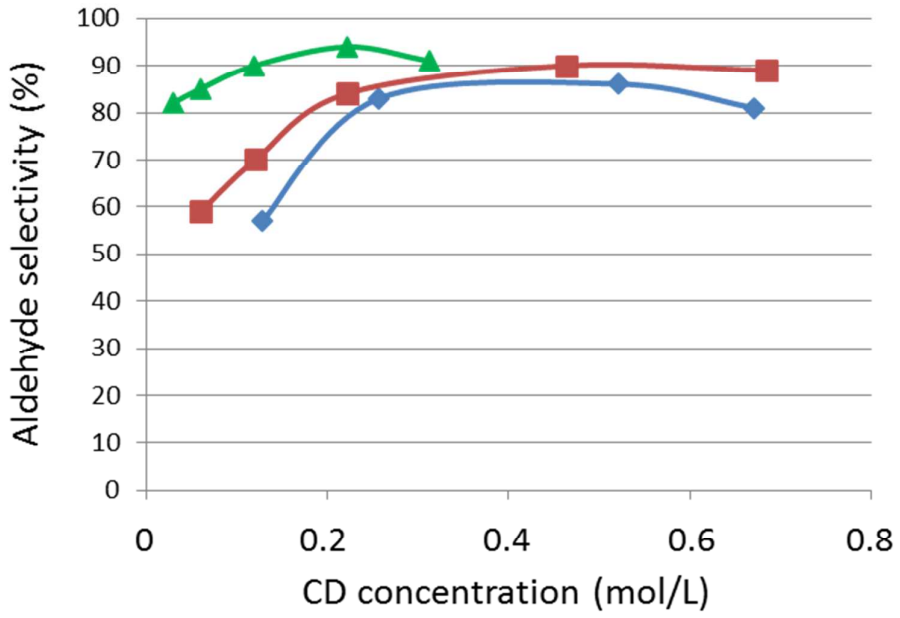

Figure S8. Aldehyde selectivity of the Rh-catalyzed hydroformylation of **T** as a function of the CD molar concentration for RAME-β-CD (◆), HP-β-CD (■) and CRYSMEB (▲).Conditions: **T** (1 mL, 1 mmol), $Rh(CO)_2(acac)$ (3.9 mg, 0.015 mmol), TPPTS (42 mg, 0.075 mmol), water (3.4 mL for ◆ and ■, 8.2 mL for ▲), 6 h, 80 °C, 80 bar CO/H_2.

Table S2. Fatty acids distributions of the studied naturally occurring vegetable oils.

The distributions were determined after a 36-h transesterification in methanol using 1 mol% of MeONa as catalyst. The resulting mixtures consisting of fatty acids methyl ester were analyzed by GC and GC-MS.

Entry	Fatty acids (mol%)	Formula	Olive oil	VHOSO
1	Palmitic	$C_{16:0}$	11	3.4
2	Palmitoleic	$C_{16:1}$	0.7	0.1
3	Stearic	$C_{18:0}$	4.2	3.2
4	Oleic	$C_{18:1}$	77	84
5	Linoleic	$C_{18:2}$	3.2	7.3
6	Linolenic	$C_{18:3}$	0.7	0.1
7	Arachidic	$C_{20:0}$	2.5	0.3
8	Eicosenoïc	$C_{20:1}$	nd	0.3
9	Behenic	$C_{22:0}$	0.6	1.1
10	Erucic	$C_{22:1}$	nd	nd

Table S3. Rh-catalyzed hydroformylation of commercial oils.[a]

Entry	CD	Oil	Average number of C=C[b]	Conv.(%)[b]	Aldehyde sel.(%)[b]	Conj. sel. (%)[b]
1	RAME-β-CD	Olive	2.78	48	71	-
2	RAME-β-CD	VHOSO	2.75	39	72	6
3	HP-β-CD	Olive	2.78	78	85	-
4	HP-β-CD	VHOSO	2.75	51	80	6
5	CRYSMEB[c]	Olive	2.78	86	86	-
6	CRYSMEB[c]	VHOSO	2.75	54	80	7

[a] Conditions: oil (1 mmol), $Rh(CO)_2(acac)$ (3.9 mg, 0.015 mmol), TPPTS (42 mg, 0.075 mmol), water (3.4 mL), 18 h, 80 °C, 80 bar CO/H_2. [b] Initial average number of C=C double bonds, conversions and selectivities were determined by ^1H NMR. [c] water (8 mL), 6 h.

Kinetics of the hydroformylation reaction

The following equation summarizes the equilibriums existing between **T**, the **T**⊂CD_n supramolecular complexes and the hydroformylated products (**A**).

(G = CO/H_2, Cat = Rh-catalyst)

Assuming a rapid decomplexation of **A** regarding the CD cavity (hypothesis in line with the interfacial tension measurements), the speed rate can be expressed as:

$$V = \frac{d[A]}{dt} = k_2[T \subset CD_x][G][Cat]$$

with [G] the CO/H_2 concentration and [Cat] the catalyst concentration.

The first step of the catalytic process is a complexation/decomplexation equilibrium where the thermodynamic constant can be expressed as:

$$K_1 = \frac{[T \subset CD_x]}{[T][CD]^x}$$

The speed rate can then be expressed as:

$$V = \frac{d[A]}{dt} = k_2 K_1 [CD]^x [T][G][Cat]$$

At any moment, the initial concentration of triglycerides is equal to the concentration of triglycerides plus the hydroformylated triglycerides:

$$[T]_0 = [T] + [A]$$

which can be expressed in terms of conversion as: $1 = (1 - X) + X$ where X is the conversion in triglycerides C=C double bonds at any moment.

The expression of the speed rate becomes:

$$V = \frac{dX}{dt} = k_2 K_1 [CD]^x (1 - X)[G][Cat]$$

$$\frac{dX}{(1-X)} = k_2 K_1 [CD]^x [G][Cat]dt$$

After integrating the equation, we obtain:

$$-\ln(1-X) + c = k_2 K_1 [CD]^x [G][Cat]t$$

where C is a constant.

At t=0, X=0 which means that C=0. Consequently:

$$\ln(1-X) = -k_2 K_1 [CD]^x [G][Cat]t$$

The amounts of catalyst is constant over time. Moreover, the interfacial excess calculated by tensiometric measurements is roughly 10^{-11} mol.cm^{-2} which is negligible with respect to the bulk CD concentration. As a consequence, the CD concentration is constant over time. Eventually, the CO/H_2 concentration (80 bar, 35 mmol of each gas) can also be considered constant as the consumption of CO/H_2 is negligible with respect to the substrate (1 mmol triolein).

Taking into account the above assumptions, the speed rate can be expressed as:

$$\ln(1-X) = -k_{app} [CD]_0{}^x t$$

where : $$k_{app} = k_2 K_1 [G][Cat]$$

Plotting ln(1-X) as a function of the CD initial concentration at a given time gives straight lines with slopes of $-K_{app}t$, thus confirming the first-order variation of the conversion with the CD initial concentration. This unambiguously indicates that a 1/1 **T**⊂CD supramolecular is at work during the hydroformylation reaction, whatever the nature of the CD. For **T**⊂CD_2 complexes (two CDs per alkenyl chain), straight lines would have been obtained plotting ln(1-X) as a function of $[CD]_0^2$.

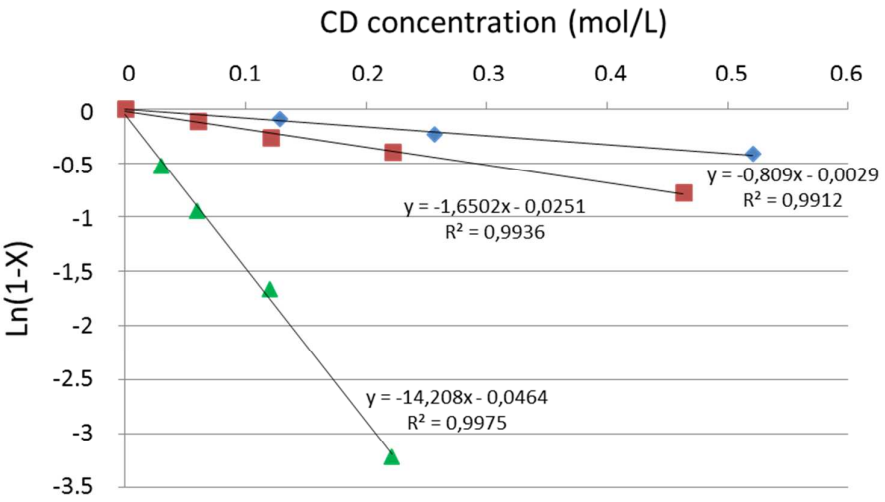

Figure S9. Variation of ln(1-X) (X = conversion) as a function of the concentration in RAME-β-CD (◆), HP-β-CD (■) and CRYSMEB (▲) at RT.

The only **T**⊂CD_n complex at the aqueous/organic interface in these conditions in a 1/1 complex for which the C=C double bonds of the triglyceride immediately undergo a hydroformylation reaction. In fact, under those dynamic conditions, the second complexation leading to the **T**⊂CD_2 is never reached due to the very short lifetime of the first complex at the interface. It was calculated that the formation of a **T**⊂CRYSMEB complex was 10-fold and 20-fold faster than the formation of a **T**⊂HP-β-CD complex and a **T**⊂RAME-β-CD complex, respectively (SI). Indeed, the k_{app} values have been estimated for each CD:

CD	**RAME-β-CD**	**HP-β-CD**	**CRYSMEB®**
k_{app}**(L.mol^{-1}.h^{-1})**	0.134	0.274	2.36