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A New Mn–Salen Micellar Nanoreactor for Enantioselective Epoxidation of Alkenes in Water

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Abstract: A new chiral Mn–salen catalyst, functionalized with a long aliphatic chain and a choline group, able to act as surfactant catalyst for green epoxidation in water, is here described. This catalyst was employed with a commercial surfactant (CTABr) leading to a nanoreactor for the enantioselective epoxidation of some selected alkenes in water, using NaClO as oxidant. This is the first example of a nanoreactor for enantioselective epoxidation of non-functionalized alkenes in water.

Keywords: epoxidation; water; enantioselectivity; nanoreactor; Mn-salen

1. Introduction

Water is an abundant molecule in nature and, due to its diffusion, cost, non-toxicity, and environmental compatibility, is probably one of the most desirable solvents for reactions. In fact, organic solvents are commonly used in the pharmaceutical and chemical industries as reaction media; however, for toxicological and environmental pollution reasons [1], industries aspire to reduce the number and amount of solvents applied in a drug or chemical production. However, the use of water as solvent for organic synthesis is limited by the low solubility of organic compounds and the facile decomposition of many active species in water. These drawbacks have recently been resolved by the use of nanocapsular systems [2] and micelles [3], which dissolve and stabilize organic substrates in water and, in some examples, act as molecular reactors for organic synthesis [4–8].

Olefin epoxidation is an important and useful reaction because it leads to a wide range of organic compounds with significant applications in several technological fields [9]. In particular, chiral Mn(III)-salen complexes have been used as catalysts to obtain chiral epoxides, which represent an essential target due to the importance of enantiomerically pure compounds in industry and pharmaceuticals [10–12]. In this context, many efforts have been addressed to leave behind the "poor eco-friendly conditions" (e.g., the use of organic solvent and reaction with strong conditions) and move toward more efficient and eco-compatible reactions, by using efficient heterogeneous catalysts [13–16] and/or reactions in aqueous media [3]. However, few examples of enantioselective epoxidation in water are reported in the literature [17–22]. A possible solution can be found by using a self-assembly process to obtain amphiphilic or self-assembled nanostructures [23–25], able to solubilize organic substrates in water.

Recently, our research group has developed new protocols to obtain epoxides with high enantioselectivity in water exploiting micelles, in which the surfactant act as co-ligand for a chiral Mn(III)-salen catalyst [17,18]. In these systems, the micellar catalyst acts as a nanoreactor for the epoxidation reaction.

Here we present the design, synthesis, and catalytic application of a new nanoreactor, in which chiral Mn(III)-salen catalyst **1-Mn** is itself a surfactant. Micellar nanoreactor consists in catalyst **1-Mn** and cetyltrimethylammonium bromide (CTABr), mixed in an appropriate ratio (see Figure 1). Epoxidation results obtained with selected alkenes confirm the ability of our system to act as enantioselective catalyst in water. To the best of our knowledge, this is the first example of chiral nanoreactor able to efficiently catalyze enantioselective epoxidation in pure water.

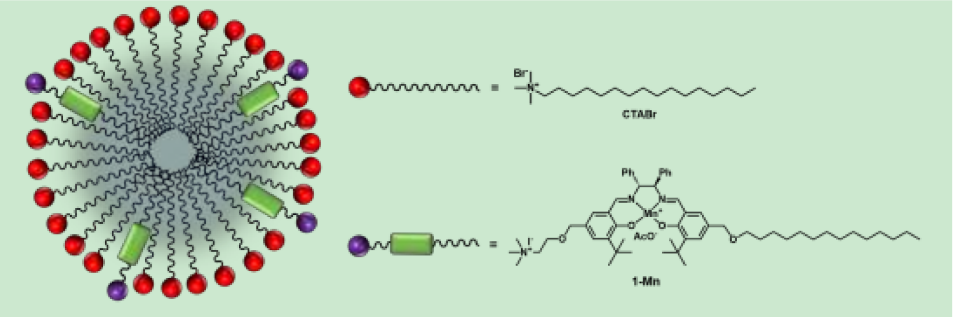


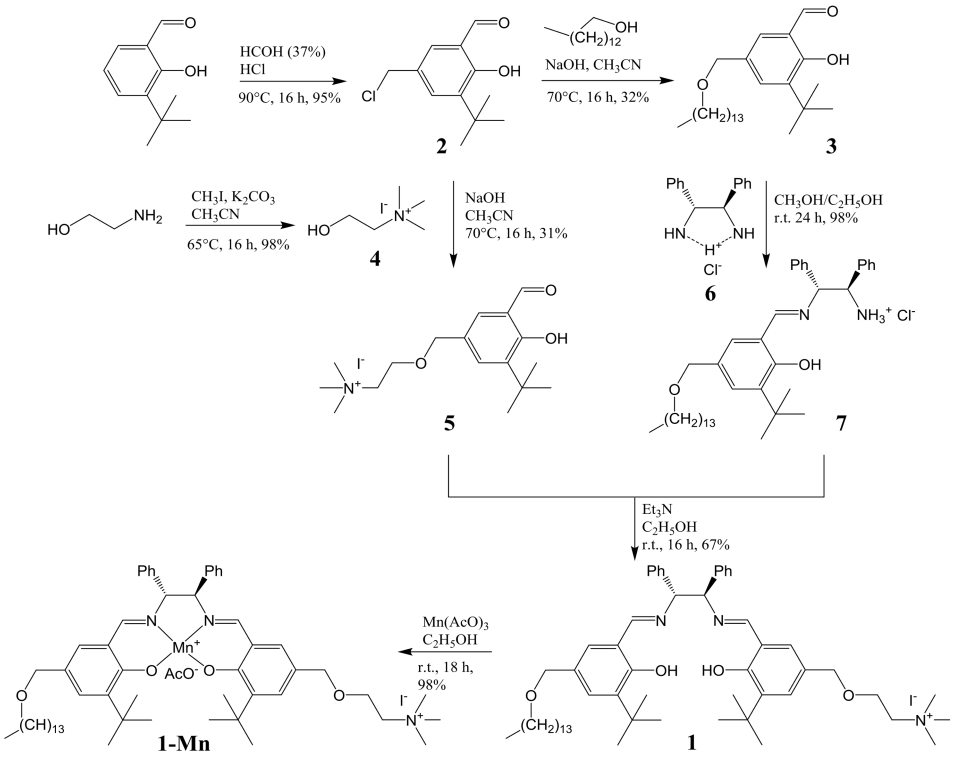
Figure 1. Schematic representation of the micellar nanoreactor and chemical structure of the catalyst **1-Mn** and CTABr.

2. Results and Discussion

Surfactant catalyst **1-Mn** was synthesized according the multi-step pathway shown in Scheme 1.

In the first step, 3-(*tert*-butyl)-2-hydroxybenzaldehyde was reacted with aqueous paraformaldehyde and HCl, leading to the 5-chloromethylated Compound **2** in high yield (95%) [26]. The reaction of **2** with a stoichiometric amount of tetradecanol in the presence of sodium hydroxide allowed for the selective introduction of the long aliphatic chain in 5-position, fundamental for the surfactant activity, (Compound **3**, yield 32%). Ethanolamine was hypermethylated by reaction with an excess of methyl iodide, in the presence of potassium carbonate, thus obtaining choline iodide **4** in almost quantitative yield. The choline derivative **4** was covalently bound to the aldehyde **2** following the same procedure used to prepare the aliphatic aldehyde **3**. Thus, using an equimolar ratio of **2** and **4** in basic conditions, the water-soluble choline-aldehyde **5** was synthesized in 31% yield. The salen moiety was assembled using the (*1R*,*2R*)-diphenyl-ethylendiamino-monochloride **6** [27,28], which, in the presence of the aldehyde **3**, afforded the mono-imino-amine-monochloride **7** in quantitative yield. Finally, surfactant chiral salen ligand **1** was obtained by condensation of **5** and **7**, in the presence of triethylamine (yield 67%). This strategy is the most viable way to obtain a "non-symmetrical salen ligand" in high yield [29–31]. The water-soluble manganese catalyst **1-Mn** was obtained in quantitative yield by addition of manganese acetate to the corresponding chiral ligand **1**. Compounds were fully characterized by NMR and ESI-MS (see Supplementary Materials).

The micellar nanoreactor was assembled using **1-Mn** and cetyltrimethylammonium bromide (CTABr) as co-surfactant in a different molar ratio (see Table 1). We selected a cationic surfactant to obtain a micellar surface fully covered by the same positive charges. In addition, catalyst was designed in order to confine the catalytic metal center inside the hydrophobic region of the nanoreactor (see Figure 1), in contrast with our previous works where it was located on the Stern layer [17,18]. We think the catalytic site sequestered in the interior of micelles should lead to higher reaction rates, due to a proximity effect with the alkene inside the core of a micelle.



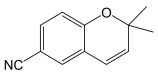
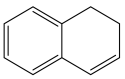
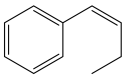
Scheme 1. Synthesis of catalyst **1-Mn**.

Micellar nanoreactor was characterized by DOSY measurements. In particular, diffusion coefficient data allowed us to calculate the hydrodynamic radius of the micelle [32–36]. The diffusion coefficient of a 0.03 M solution of CTABr in D_2O (the same concentration used in the epoxidation reaction) is 1.20×10^{-10} m^2 s^{-1}, corresponding to a hydrodynamic radius of ca. 2.15 nm (see Section 3) and thus in accordance with the formation of a micelle (the c.m.c. of CTABr is 8.6×10^{-4} M). The same measurements were performed with a 0.03 M solution of CTABr and 1 mM **1-Mn** in D_2O, and a diffusion coefficient of 1.17×10^{-10} m^2 s^{-1} was found (hydrodynamic radius of ca. 2.21 nm, see Section 3), thus confirming that the presence of our catalyst does not modify the dimension of the micelle.

Once the presence of micellar systems, with and without the addition of **1-Mn**, was confirmed, we tested our system as nanoreactor in the enantioselective epoxidation of some selected aromatic alkenes, in particular 6-cyano-2,2-dimethylchromene, 1,2-dihydronaphthalene, and *cis*-β-ethylstyrene in water, using NaClO as the oxidant. Results are summarized in Table 1. In fact, as reported by Corey et al., alkenes that are conjugated with a π-system are ideal substrates for enantioselective epoxidation by using a Jacobsen catalytic system [37].

Due to the high reactivity of 6-cyano-2,2-dimethylchromene in the oxidation reactions [38], using 0.03 M CTABr and 5% catalyst, total conversion in epoxide is complete in 3 h, with an enantiomeric excess of ca. 83% (Entries 1–2). The increase in concentration of CTABr from 0.03 to 0.06 M does not affect enantioselectivity and conversion values (Entries 3–4). Enantiomeric excess values with 1,2-dihydronaphthalene were also in the range of 80–84%, confirming the ability of the nanoreactor to achieve enantioselectivity. As shown in our previous works [17,18], 1,2-dihydronaphthalene presents lower reaction rates compared to 6-cyano-2,2-dimethylchromene.

Table 1. Enantioselective epoxidation of 6-CN-2,2-dimethylchromene, 1,2-dihydronaphthalene, and *cis*-β-ethylstyrene with NaClO catalyzed by micellar nanoreactor containing **1-Mn** and CTABr in H_2O at 25 °C [a].

Alkene	Entry	[CTABr] (M)	1-Mn (%) [b]	Time (h)	e.e. (%) [c]	Conv. (%) [c]
	1	0.03	5	1	83 [e]	85
	2	0.03	5	3	82 [e]	100
	3	0.06	5	1	83 [e]	87
	4	0.06	5	3	83 [e]	100
	5	0.03	5	1	83 [f]	17
	6	0.03	5	8	82 [f]	46
	7	0.03	10	8	84 [f]	64
	8	0.06	10	1	80 [f]	76
	9	0.06	10	3	83 [f]	100
	10	0.03	5	1	50 [g]	73
	11	0.03	5	2	51[g]	100
	12 [d]	0.015	10	1	56 [g]	88
	13 [d]	0.015	10	4	57 [g]	100
	14 [d]	0.03	10	1	56 [g]	86
	15 [d]	0.03	10	4	58 [g]	100
	16 [d]	0.06	10	1	58 [g]	85
	17 [d]	0.06	10	4	57 [g]	100

[a] In all experiments [alkene] = [NaClO] =1.17 × 10^{-2} M, buffered with 1 mL of 0.05 M Na_2HPO_4 at pH 11.2 in a total volume of 2 mL [39]. [b] referred to the alkene concentration. [c] Enantiomeric Excess (e.e.) and Conversion values (Conv.) were determined by Gas chromatographic (GC) analysis using a chiral column (see Section 3) and *n*-dodecane as internal standard. [d] NaClO was added dropwise in 1 h. [e] config. (*3R,4S*) determined by measuring the optical rotation. [f] config. (*1R,2S*) determined by measuring the optical rotation. [g] Enantiomeric excess (e.e.) value is referred to the to the major *cis* epoxide (*cis*/*trans* = 4).

In fact, under the same conditions, after 1 h of reaction, only a 17% conversion was obtained (Entry 1 vs. Entry 5). After 8 h of reaction, a 46% conversion value was observed (Entry 6). The increase in concentration of the catalyst **1-Mn** (10% respect to the substrate) was not sufficient to reach full conversion, affording a conversion of 64% (Entry 7). With 0.06 M CTABr, conversions increased to 76% after 1 h and 100% after 3 h (Entries 8 and 9, respectively). These results suggest strong contribution from the nature of the substrate to the reaction rate.

This hypothesis was confirmed considering *cis*-β-ethylstyrene: using 0.03 M CTABr and 5% catalyst, conversion reached 73% in 1 h and 100% after 2 h. However, the enantioselectivity value observed was 51% (Entries 10–11).

In order to increase enantioselectivity with this alkene, we evaluated the effect of CTABr surfactant concentration, performing epoxidation reactions at 0.015, 0.03, and 0.06 M CTABr, using 10% catalyst (Entries 12–17). We noted that the 10% catalyst amount led to a slight improvement in enantioselectivity (56–58%), while the reaction rates remained quite similar.

Noteworthy, the simple CTABr micelle containing selected alkenes in water, after the addition of NaClO, leads to a racemic mixture of epoxides; in the classic biphasic system (CH_2Cl_2/H_2O), this reaction has never been observed [10–12,40]. Thus, the presence of the chiral catalyst is essential to catalyze the enantioselective epoxidation of alkenes.

The recovery of the catalyst was also evaluated. In particular, after complete conversion of the starting alkene (we tested recovery using 1,2-dihydronaphthalene as substrate), **1-Mn** was extracted by an addition of dichlorometane. The organic phase was dried, and the resulting catalyst was reused in a new epoxidation, using the same conditions reported in Entry 9 of Table 1. Conversions and enantiomeric excess are reported in Figure 2. After five cycles, enantiomeric excess was constant, demonstrating the robustness of the catalyst.

Finally, we tested the sustainability of our protocol measuring the EcoScale of our process [41,42]. This scale takes into consideration the yield of the reaction, combined to several parameters, such as the price of reaction components, the safety of reagents, the technical setup, the temperature/time, the workup, and the purification. These parameters influence the quality of reaction conditions. After calculation of the appropriate "penalty points," the EcoScale value can be obtained. An ideal "green" reaction has an EcoScale of 100. In our case, an EcoScale value of 93 was calculated, thus confirming an excellent protocol.

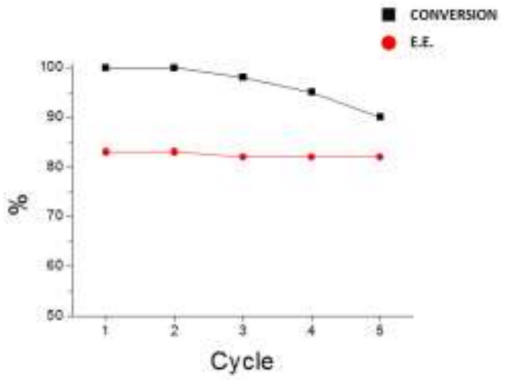


Figure 2. Enantiomeric excess (E.E.) variations and conversion values measured after 3 h by recycling **1-Mn** in the epoxidation of 1,2-dihydronaphthalene. Reaction conditions are reported in Entry 9 of Table 1.

3. Materials and Methods

3.1. General

The NMR experiments were carried out at 27 °C on a Varian UNITY Inova 500 MHz spectrometer (^{1}H at 499.88 MHz, ^{13}C-NMR at 125.7 MHz, Varian-Agilent, Santa Clara, CA, USA) equipped with pulse field gradient module (*Z* axis) and a tunable 5 mm Varian inverse detection probe (ID-PFG). ESI mass spectra were acquired on a API 2000™ AB Sciex (Milano, Italy) using MeOH (positive ion mode). All chemicals were reagent grade and were used without further purification. Enantiomeric excesses were determined by GC analysis with a Perkin Elmer Capillary (Perkin Elmer, Waltham, MA, USA) using a dimethylpentyl-beta (DIMEPEBETA-086) chiral column (25 m × 0.25 mm ID, 0.25 μm film) for 6-cyano-2,2-dimethylchromene; DiAcTBuSiliBETA-ov-1701 chiral column (25 m × 0.25 mm ID, 0.25 μm film) for *cis*-β-ethylstyrene and dimethyl-pentyl-beta (DMePeBETACDX) chiral column (25 m × 0.25 mm ID, 0.25 μm film) for 1,2-dihydronaphthalene. The absolute configuration of the obtained epoxides were determined by measuring the optical rotation with a polarimeter. Absolute configurations were assigned by comparison of the measured $[\alpha]_D^{20}$ values with those reported in the literature [43]. ^{1}H-NMR characterizations of Compounds **2** and **4** are according to those reported in the literature [15].

3.2. DOSY Measurements

The DOSY technique provides information about the size of the molecular aggregate in solution. In fact, by means of the Stokes–Einstein equation, the diffusion coefficient of the CTABr can be converted into its hydrodynamic radius R_h, and this value can be compared with the calculated radius obtained by the Hyperchem-minimized structure of the surfactant (in the maximum extension, CTABr is ca. 2 nm, leading a micellar aggregates of ca. 4 nm of diameter). Thus, combining the diffusion coefficient of the CTABr (D = 1.20 × 10^{-10} m^2 s^{-1}) with the viscosity of D_2O at 298 K in the Stokes–Einstein equation ($R = k_BT/6\pi\eta D$, where k_B is the Boltzmann constant, T is the absolute temperature, and η is the viscosity of D_2O at 298 K (0.85 cP)), a hydrodynamic radius R_h(exp) = 2.15 nm was obtained. The same treatment for the nanoreactor containing CTABr and **1-Mn** give a R_h(exp) = 2.21 nm.

3.3. Synthesis and Characterization

Synthesis of the aldehyde **2**. An amount of 0.720 mL (8.6 mmol) of aqueous formaldehyde and 9 mL of HCl conc. were added to 1 g (5.61 mmol) of the 3-*t*But-salicylaldehyde. The mixture was stirred at 90 °C for 16 h. The reaction was cooled to room temperature, obtaining a precipitate. Diethyl ether was added to the aqueous solution, extracted, and dried with Na_2SO_4. Evaporation of the solvent afforded Compound **2** (yield 95%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 11.85 (s, 1H, OH), 9.87 (s, 1H, CHO), 7.53 (d, *J* = 2.5 Hz, 1H, ArH), 7.44 (d, *J* = 2.5 Hz, 1H, ArH), 4.59 (s, 2H, –CH_2Cl), 1.43 (s, 9H, Ar–CH_3). Anal. Calcd. For $C_{12}H_{15}ClO_2$: C, 63.58; H, 6.67; Cl, 15.64. Found C, 63.51; H, 6.62; Cl, 15.58.

Synthesis of the aldehyde **3**. Tetradecanol (629 mg, 2.95 mmol) was dissolved in 25 mL of acetonitrile dry, and 118 mg (2.95 mmol) of NaOH was added. The mixture was heated at 70 °C for 4 h, and 700 mg (3.10 mmol) of the aldehyde **2**, dissolved in 15 mL of acetonitrile dry, were then added dropwise in 1 h. The reaction was stirred at 70 °C overnight under nitrogen. Then, the solvent was removed under reduced pressure, and the crude product was dissolved in CH_2Cl_2 and washed with water. The organic phase was dried with Na_2SO_4 and purified by column chromatography (*n*-hexane/EtOAc 98/2) affording the pure Compound **3** as oil (yield 32%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 11.76 (s, 1H, OH), 9.87 (s, 1H, CHO), 7.49 (d, *J* = 2.0 Hz, 1H, ArH), 7.37 (d, *J* = 2.0 Hz, 1H, ArH), 4.44 (s, 2H, Ar–CH_2–O), 3.48 (t, *J* = 6.5 Hz, 2H, O–*C*H_2–CH_2–), 1.62 (m, 2H, O–CH_2–*C*H_2–), 1.42 (s, 9H, Ar–CH_3), 1.25–1.30 (m, 22H, O–CH_2–CH_2–*(C*H_2*)*$_{11}$–CH_3), 0.88 (t, *J* = 7.5 Hz, 3H, O–CH_2–CH_2–$(CH_2)_{11}$–*C*H_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 197.0, 160.7, 138.3, 133.9, 130.9, 129.3, 120.3, 72.2, 70.7, 34.8, 31.9, 29.7, 29.66, 29.61, 29.47, 26.34, 29.2. ESI-MS *m*/*z* 405.3 $[M + H]^+$. Anal. Calcd. For $C_{26}H_{44}O_3$: C, 77.18; H, 10.96. Found C, 77.09; H, 10.89.

Synthesis of the choline iodide **4**. A suspension containing 2 g (32.7 mmol) of ethanolamine, 9 g (65.4 mmol) of K_2CO_3 anhydrous, and 23.11 g (163 mmol) of CH_3I in 25 mL of acetonitrile dry was stirred vigorously overnight at 65 °C under nitrogen. Then, reaction was filtered to remove the base, and solvent was removed under reduced pressure to yield pure hypermethylated Compound **4** (yield 98%).^{1}H-NMR (500 MHz, D_2O) δ 4.10 (m, 2H, OH–*C*H_2–), 3.56 (t, *J* = 5.0 Hz, 2H, –CH_2–N), 3.25 (s, 9H, N$(CH_3)_3$). Anal. Calcd. For $C_5H_{14}INO$: C, 25.99; H, 6.11; N, 6.06. Found C, 25.91; H, 6.03; N, 6.01.

Synthesis of the choline-aldehyde **5**. Choline iodide **4** (459 mg, 1.98 mmol) was dissolved under nitrogen in 40 mL of acetonitrile dry. Then, 79 mg (1.98 mmol) of NaOH was added, and the mixture was stirred at 70 °C for 3 h. Then, a solution of the aldehyde **2** (463 mg, 2.05 mmol, in 25 mL of acetonitrile dry) was added dropwise in 1 h. The reaction was stirred under nitrogen overnight at 70 °C. The reaction was monitored by TLC following the disappearance of the starting aldehyde **2**. The reaction was cooled to room temperature, the solvent was removed under reduced pressure, and Compound **5** (yield 31%) was purified by alumina column (from CH_2Cl_2 100% to CH_2Cl_2/CH_3OH 95/5). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 11.87 (s, 1H, OH), 9.91 (s, 1H, CHO), 7.45 (d, *J* = 2.0 Hz, 1H, ArH), 7.43 (d, *J* = 2.0 Hz, 1H, ArH), 4.56 (m, 2H, –*C*H_2–N$(CH_3)_3$), 4.00 (m, 4H, Ar–*C*H_2–O and O–*C*H_2–CH_2–), 3.44 (s, 9H, N$(CH_3)_3$), 1.42 (s, 9H, Ar-CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6) 109.81, 160.71, 136.95, 129.17, 128.80, 122.16, 117.74, 66.94, 55.14, 53.20, 45.71, 22.52, 14.39. ESI-MS *m*/*z* 294.2 $[M]^+$. Anal. Calcd. For $C_{17}H_{28}INO_3$: C, 48.46; H, 6.70; N, 3.32. Found C, 48.41; H, 6.62; N, 3.28.

Synthesis of the aldehyde **7**. To a solution of 190 mg (0.766 mmol) of (*1R,2R*)-diphenyl-ethylendiamino-monochloride **6** [27,28] dissolved in 20 mL of a mixture 50/50 of methanol/ethanol was added dropwise 299 mg (0.740 mmol) of aldehyde **3**, dissolved in 10 mL of the same solvent mixture. The reaction was stirred at room temperature for 24 h. Then, the solvent was removed under reduced pressure, and the crude product was washed with a few milliliters of water to remove the starting reagent **6** and filtered, yielding Compound **7** (yield 98%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 13.36 (s, 1H, OH), 8.74 (s, 1H, CHN), 8.55 (s br, 3H, NH_3), 7.36 (m, 2H, ArH), 7.19–7.29 (m, 10H, ArH), 5.03 (d, *J* = 10 Hz, 1H, CH methine), 4.88 (d, *J* = 10.0 Hz, 1H, CH methine), 4.35 (s, 2H, Ar–*C*H_2–O), 3.36 (t, *J* = 6.0 Hz, 2H, O–*C*H_2–CH_2–), 1.48 (m, 2H, O–CH_2–*C*H_2–), 1.38 (s, 9H, ArCH_3), 1.19–1.26 (m, 22H,

O–CH_2–CH_2–$(CH_2)_{11}$–CH_3), 0.82 (t, J = 6.5 Hz, 3H, O–CH_2–CH_2–$(CH_2)_{11}$–CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6) 156.83, 138.65, 133.68, 129.185, 128.98, 128.54, 128.48, 128.02, 126.74, 68.29, 60.73, 57.19, 36.55, 32.55, 31.29, 29.82, 29.01, 28.70, 25.71, 25.51, 22.10, 13.96. ESI-MS m/z 599.7 $[M]^+$. Anal. Calcd. For $C_{40}H_{59}ClN_2O_2$: C, 75.62; H, 9.36; N, 4.41. Found: C, 75.54; H, 9.27; N, 4.32.

Synthesis of ***1****.* To a solution of ethanol (30 mL) containing 270 mg (0.641 mmol) of **5** and 406 mg (0.641 mmol) of **7**, 190 µL of triethylamine were added slowly. The mixture was stirred at room temperature overnight. The solvent was then removed under reduced pressure. The salen (**1**) (yield 67%) was purified by a neutral alumina column (CH_2Cl_2 containing 5% CH_3OH). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 13.93 (s, 1H, OH), 13.75 (s, 1H, OH), 8.38 (s, 1H, CHN), 8.34 (s, 1H, CHN), 7.14–7.24 (m, 12H, ArH), 6.97 (m, 2H, ArH), 4.75 (m, 2H, CH methine), 4.39 (s, 2H, Ar–CH_2–O), 4.31 (s, 2H, Ar–CH_2–O), 3.93 (m, 2H, –CH_2–$N(CH_3)_3$, 3.86 (m, 2H, O–CH_2–CH_2–$N(CH_3)_3$), 3.43 (t, J = 6.5 Hz, 2H, O–CH_2–CH_2–), 3.38 (s, 9H, $N(CH_3)_3$), 1.60 (m, 2H, O–CH_2–CH_2–), 1.42 (s, 18H, Ar–CH_3), 1.25–1.30 (m, 22H, O–CH_2–CH_2–$(CH_2)_{11}$–CH_3), 0.88 (t, J = 7.5 Hz, 3H, O–CH_2–CH_2–$(CH_2)_{11}$–CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 166.73, 166.36, 139.30, 130.00, 129.81, 129.73, 129.62, 128.38, 127.96, 127.63, 79.99, 73.60, 72.69, 70.50, 63.50, 54.92, 45.87, 31.91, 29.67, 29.29, 26.21, 22.68, 15.49, 14.11, 8.60. ESI-MS m/z 874.7 $[M]^+$. Anal. Calcd. For $C_{57}H_{84}IN_3O_4$: C, 68.31; H, 8.45; N, 4.19. Found: C, 68.22; H, 8.36; N, 4.10.

Synthesis of ***1-Mn****.* In a round bottom flask containing 430 mg (0.430 mmol) of the salen **1** dissolved in 15 mL of absolute ethanol, 171 mg (0.643 mmol) of manganese (III) acetate dehydrate were added. The mixture was stirred at room temperature overnight. The solvent was then removed under reduced pressure, and the crude product was dissolved in CH_2Cl_2 and filtered to remove the excess of manganese (III) acetate. Evaporation of the solvent afforded **1-Mn** as a brown precipitate (yield 98%). ESI-MS m/z 927.5 $[M]^+$. Anal. Calcd. For $C_{59}H_{72}IMnN_3O_6$: C, 64.36; H, 6.59; N, 3.82. Found: C, 64.30 H, 6.51; N, 3.75.

Enantioselective epoxidation in the nanoreactor. In a typical run, alkene and *n*-dodecane (internal standard) were added to a stirred solution of surfactant and the catalyst **1-Mn** in distilled water (1 mL) and phosphate buffer (1 mL, 0.05 M Na_2HPO_4 at pH 11.2); after the complete solubilization, NaClO was added dropwise (5 µL/10 min) to the mixture and the reaction was kept in a round-bottom flask at 25 °C in a thermostatic bath. After a certain reaction time, the aqueous solution was extracted with 1 mL of CH_2Cl_2. Combined organic extracts were dried over anhydrous $MgSO_4$, reduced to a small volume, and analyzed by GC as described above.

4. Conclusions

A new surfactant catalyst, containing a chiral Mn–salen framework, able to catalyze in water enantioselective epoxidation of non-functionalized alkenes, is here presented. Epoxidation reactions were carried out into micellar systems, containing also a commercial surfactant (CTABr), thus forming the first nanoreactor able to achieve enantioselectivity in water. The epoxidation reactions with 6-CN-2,2-dimethylchromene and 1,2-dihydronaphthalene exhibited excellent results, with high conversions and enantioselectivity values. The structure of the surfactant catalyst likely plays a crucial role: in particular, the position of the catalytic metal center with respect to the micellar aggregate leads to different reactivities toward different alkenes. We are working on optimizing the nanoreactor structure: in particular, we believe that the length of the aliphatic moiety of the catalyst is crucial for improving the reactivity of aliphatic alkenes (e.g., *cis*-β-ethylstyrene).

Supplementary Materials: The following are available online at http://www.mdpi.com/2073-4344/8/4/129/s1: NMR, gCOSY, and ESI-MS spectra.

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40. We performed epoxidation of 6-CN-2,2-dimethylchromene without 1-Mn, with CTABr = [0.06], [alkene] = [NaClO] = 1.17×10^{-2} M, 0.05 M Na_2HPO_4 at pH 11.2, obtaining a conversion of 52% after 1 h, and 100% after 6 h; with 1,2-dihydronaphthalene, with the same conditions, conversion value was 38% after 1 h and 100% after 12 h while with *cis*-β-ethylstyrene we observed 47% of conversion after 1 h and 100 after 8 h.

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