Towards a Greener Epoxidation Method: Use of Water-Surfactant Media and Catalyst Recycling in the Platinum-Catalyzed Asymmetric Epoxidation of Terminal Alkenes with Hydrogen Peroxide

Marco Colladon,[a] Alessandro Scarso,[a] and Giorgio Strukul[a],*

[a] Department of Chemistry, Università Ca' Foscari di Venezia, Dorsoduro 2137, 30123 Venice, Italy
Fax: (+39)-041-234-8517; e-mail: strukul@unive.it

Dedicated to Professor Mauro Graziani in occasion of his 70th birthday.

Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: Remarkable improvements in enantioselectivity as well as recycle were observed in the catalytic asymmetric epoxidation of terminal alkenes with a chiral, electron-poor platinum(II) catalyst with hydrogen peroxide as terminal oxidant in water-surfactant media.

Keywords: aqueous phase catalysis; asymmetric catalysis; epoxidation; hydrogen peroxide; platinum

Water as an alternative reaction medium[1] for organic reactions has been a well studied topic for several years, in particular for C−C coupling reactions[2] exploiting the peculiar properties of such solvent, *in primis* polarity and hydrophobic effect.[3] More recently, the employment of water as solvent is experiencing a sort of renaissance in the scientific community because of the growing stringent requirements concerning chemical production,[4] associated with possible catalyst recycling that is a common advantage of liquid water/organic biphasic reactions. To ensure the solubilization of metal catalysts in water, common transition metal-catalyzed organic transformations like hydrogenation[5] require ligand modification[6] with polar moieties that often turns out to involve tedious and time-consuming synthetic steps. Much more straightforward would be the employment of organometallic catalysts developed expressly for organic solvents and their solubilization in water with the aid of a surfactant, thus avoiding several synthetic steps and allowing the use of ordinary and/or commercially available ligands.

Surfactants play many roles at the same time,[7] firstly they improve the solubilization of organic reagents in water, secondly they favor compartmentalization of reagents thus improving local concentration and reactivity, thirdly in some cases they impart unique chemo- regio- and stereoselectivities.[8] While hydrogenation, hydroformylation and C−C coupling reactions have been already investigated in water and in micellar media,[7a,9] oxidation reactions still need to be thoroughly explored both in water[10] and in micellar media,[11] in particular stereoselective oxidation reactions in water or in micellar media are reported in only a few contributions to date.[12,13,14]

Oxidation processes are also experiencing a smooth but profound transformation from the employment of hazardous oxidants to greener ones, such as molecular oxygen and hydrogen peroxide.[15] Soft Lewis acids are intrinsically compatible with reactions in water as, at variance with early transition metal Lewis acid centers, they suffer neither from deactivation by water nor competition for substrate coordination.

Recently, we reported some interesting results observed in the asymmetric sulfoxidation of prochiral thioethers with a dimeric chiral Pt(II) complex in water-SDS medium (SDS=sodium dodecyl sulfate) with yields up to 99% and *ee*s up to 88%.[14] Exploiting the same fruitful approach, herein we present the employment of water-surfactant media in the catalytic asymmetric epoxidation of terminal alkenes[16] with the chiral Pt(II) complex {[(*S*,*S*)Chiraphos]Pt(C$_6$F$_5$)(H$_2$O)}(OTf)[17] (**1**) using hydrogen peroxide as the terminal oxidant (Scheme 1).

Initially a surfactant screening was performed (Table 1) to assess the degree of compatibility of the surfactant additives with the asymmetric epoxidation of 4-methyl-pentene as model substrate with one equivalent of hydrogen peroxide catalyzed by complex **1** (1% mol). The same reaction performed in 1,2-dichloroethane (DCE) showed 56% yield with 58% *ee*.[16] Conversely, in pure water without surfactant catalyst solubilization did not occur and no reac-
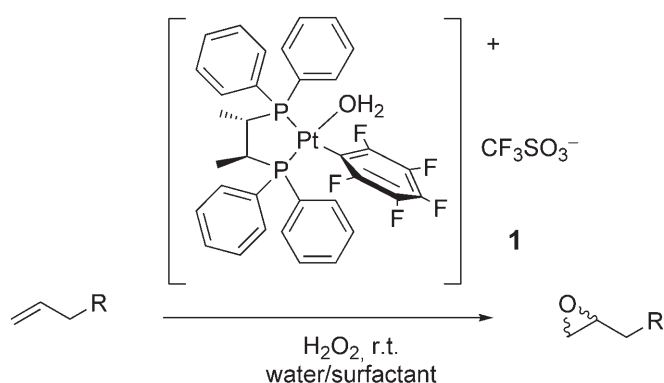
Scheme 1. {[(S,S)Chiraphos]Pt(C$_6$F$_5$)(H$_2$O)}(OTf) (**1**)-catalyzed asymmetric epoxidation of terminal alkenes with hydrogen peroxide in water with surfactants.

tion was observed (entry 2). Anionic as well as cationic micelles were not suitable for such reaction (entries 3 and 4), at variance with what is observed in sulfoxidation in the presence of a *bis*-cationic dimeric complex.[14] In the present case, a zwitterionic surfactant (*N*-dodecyl-*N,N*-dimethyl-3-ammonio-1-propane-

sulfonate) provided appreciable catalyst solubilization in water and the enantioenriched epoxide was produced in lower yield but with surprisingly enhanced *ee* (entries 1 and 5). Among neutral surfactants large differences were observed: while the sorbitane derivative SPAN60 showed no activity, alkyl polyoxyethylene derivative showed interesting results (entries 6 and 7).

A wide range of performance was observed with surfactants related to the Triton family, with large differences in activity related to the chemical structure and length of the surfactant itself (entries 8–10). The above observations suggest that the right balance of polarity, presence and size of functional groups in the micellar aggregate are all critical parameters to ensure good activity and selectivity. Moreover, the effect of surfactant concentration was investigated with Triton X100 (entries 10–13) observing a more pronounced effect on the activity, while enantioselectivity was little influenced but always above the values observed in the organic phase under identical experimental conditions.

Table 1. Catalytic enantioselective epoxidation of terminal 4-methylpentene with H$_2$O$_2$ mediated by **1** in micellar media. *General conditions:* 4-methylpentene:H$_2$O$_2$:**1** = 100:100:1; [4-methylpentene] = 0.83 mmol, [H$_2$O$_2$] = 0.83 mmol, [**1**] = 0.0083 mmol 1% mol, solvent water 0.5 mL, room temperature in air.

Entry	Time [h]	Yield [%][a]	*ee*[b] [%]	Abs. Conf.[c]	Solvent/Additive
1	4	56	58	*R*-(+)	DCE[d]
2	24	0	-	-	H$_2$O
3	24	0	-	-	H$_2$O/SDS[e]
4	24	0	-	-	H$_2$O/CTABr[f]
5	6	28	84	*R*-(+)	H$_2$O/Zwitterionic[g]
6	24	0	-	-	H$_2$O/SPAN60[h]
7	6	41	84	*R*-(+)	H$_2$O/POA[i]
8	24	0	-	-	H$_2$O/Triton-X405[j]
9	6	61	82	*R*-(+)	H$_2$O/Triton-X114[k]
10	6	34	78	*R*-(+)	H$_2$O/Triton-X100[l]
11	6	45	79	*R*-(+)	H$_2$O/Triton-X100[m]
12	6	51	82	*R*-(+)	H$_2$O/Triton-X100[n]
13	6	33	76	*R*-(+)	H$_2$O/Triton-X100[o]

[a] Yield in epoxide determined by extraction with hexane and GC analyses (column β-cyclodex).
[b] Enantiomeric excess determined by CSP-GC (column β-cyclodex).
[c] Absolute configuration determined by optical rotations and comparison of the retention orders with known literature data.
[d] Dichloroethane as solvent, [**1**] = 2% mol.
[e] Sodium dodecyl sulfate (75 mM, 1 mM in micelles).
[f] Cetyltrimethylammonium bromide (168 mM, 1 mM in micelles).
[g] *N*-Dodecyl-*N,N*-dimethyl-3-ammonio-1-propanesulfonate (150 mM, 1 mM in micelles).
[h] Sorbitane monostearate (150 mM, 1 mM in micelles).
[i] Polyoxyethylene alcohol (C$_{12}$H$_{25}$-C$_{18}$H$_{37}$)-(OCH$_2$CH$_2$)$_5$ (150 mM, 1 mM in micelles).
[j] Polyoxyethylene(40) isooctyl phenyl ether (150 mM, 1 mM in micelles).
[k] Polyoxyethylene(8) isooctyl cyclohexyl ether (150 mM, 1 mM in micelles).
[l] Polyoxyethylene(10) isooctyl phenyl ether (33 mM, 0.22 mM in micelles).
[m] Polyoxyethylene(10) isooctyl phenyl ether (75 mM, 0.5 mM in micelles).
[n] Polyoxyethylene(10) isooctyl phenyl ether (150 mM, 1 mM in micelles).
[o] Polyoxyethylene(10) isooctyl phenyl ether (230 mM, 1.5 mM in micelles).

The increment of enantiomeric excess observed between chlorinated solvent (58%) and water-non-ionic surfactant (84%) can be better expressed in terms of enantiomeric ratio[18] (organic 79:21; water-surfactant 92:8) and subsequently translated in terms of $\Delta\Delta G^{\neq}$ between the two transition states for the production of the enantiomeric epoxides. $\Delta\Delta G^{\neq}$ almost doubles from $-3.23 \text{ kJ mol}^{-1}$ to $-5.95 \text{ kJ mol}^{-1}$ by simply switching the reaction from DCE to water-non-ionic surfactant media, as a further evidence of the unique environmental conditions provided by micelles.

The synthetic scope of the enantioselective epoxidation reaction was investigated employing other terminal alkene substrates, as reported in Table 2.

From Table 2 it is clear that linear and γ-branched terminal alkenes are all suitable substrates with good conversions, comparable to those of reactions performed in the organic phase,[16] and with moderate to good *ee*s of the corresponding epoxides, even though in these cases no marked enhancement of enantioselectivity was observed between organic and water-non-ionic surfactant media, probably because of the lower steric hindrance of those alkenes with respect to 4-methylpentene. It seems conceivable that a fine tuning of the surfactant properties with respect to the individual substrate's steric properties is probably necessary to improve enantioselectivity. On the contrary, allylbenzene derivatives that are suitable substrates in organic solvent,[16] are not generally oxidized in the micellar medium because of insufficient solubilization. Only the more polar 3,4-dimethoxyallylbenzene reacted providing the corresponding enantioenriched epoxide with poor yield but interesting *ee*.

The use of biphasic catalysis opens the way to the possible recycling of the chiral catalyst by extracting the aqueous phase with a solvent in which **1** and the surfactant are both insoluble. To this end, we explored various experimental conditions characterized by different combinations of organic solvents for extraction and surfactants. We found that operating with Triton-X114 in a 2:1 substrate/oxidant excess, extracting the water phase with hexane and simply adding fresh substrate and 35% H_2O_2 for the next runs, makes it possible to perform up to three enantioselective epoxidation cycles with both constant yield and enantioselectivity (Table 3). The different experimental conditions employed were required to favor easier phase separation. This led to a slight decrease in *ee* and a more pronounced decrease in yield per individual cycle, but the total turnover number achieved was definitely higher. The major limitation to further recycling was

Table 3. Recycling experiments in the catalytic enantioselective epoxidation of 4-methylpentene with H_2O_2 in water/Triton-X114 solution mediated by **1**. *General conditions:* substrate:H_2O_2:**1** = 200:100:1; [substrate] = 6.6 mmol, [H_2O_2] = 3.3 mmol, [**1**] = 0.066 mmol, solvent water 4 mL, surfactant Triton-X114 (150 mM, 1 mM in micelles).
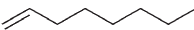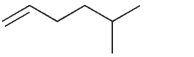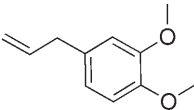
Cycle	Time [h]	Yield [%][a]	*ee* [%][b]	Abs. Conf.[c]
1	8	26	75	*R*-(+)
2	8	26	72	*R*-(+)
3	8	30	77	*R*-(+)

[a] Yield in epoxide determined by extraction with hexane and GC analyses (column β-cyclodex).
[b] Enantiomeric excess determined by CSP-GC (column β-cyclodex).
[c] Absolute configuration determined by optical rotations and comparison of the retention orders with known literature data.

Table 2. Catalytic enantioselective epoxidation of terminal alkenes with H_2O_2 in water/Triton-X100 solution mediated by **1**. *General conditions:* substrate:H_2O_2:**1** = 100:100:1; [substrate] = 0.83 mmol, [H_2O_2] = 0.83 mmol, [**1**] = 0.0083 mmol, solvent water 0.5 mL, surfactant Triton-X100 (150 mM, 1 mM in micelles), room temperature in air.

Entry	Substrate	Time [h]	Yield [%][a]	*ee* [%][b]	Abs. Conf.[c]
1		6	84	74	*R*
2		6	78	57	*R*
3		6	43	52	*R*
4		6	81	61	*R*
5		20	23	74[d]	*R*-(−)[e]

[a] Yield in epoxides determined by ^{1}H NMR.
[b] Enantiomeric excess determined by integration of the ^{1}H NMR spectrum in the presence of the chiral shift reagent europium tris-[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] Eu(hfc)$_3$ at room temperature in CDCl$_3$.
[c] Absolute configuration assigned by comparison to the deshielding effect in the presence of Eu(hfc)$_3$ at room temperature observed for other terminal epoxides.[16]
[d] Enantiomeric excess determined by chiral HPLC analysis on a Chiracel OD-H column.
[e] Absolute configuration determined by optical rotations and comparison with literature data.

not due to catalyst decomposition, but rather to the reaction medium losses that are unavoidably involved in carrying out the different operations manually on a small lab scale. Anyhow, the results of Table 3 prove the principle that catalyst separation and recycling without loss of activity and selectivity is indeed possible using the micellar medium.

In order to prove the solubilization of catalyst **1** in the micellar medium, as well as investigating its position in the micelles we carried out ^{31}P, ^{1}H NMR and 2D-NOESY spectra of **1** in H_2O-D_2O/Triton-X100 solution (see Supporting Information). The ^{31}P NMR spectrum shows the typical resonances of the Pt(II) complex **1** with chemical shifts similar to those found for **1** in chlorinated solvent but with a smaller $^{1}J_{P,Pt}$ for P *trans* to the catalytic site (3776 Hz instead of 4272 Hz). This observation might be consistent with the coordination of a hydroxy group instead of a neutral water molecule,[17] however, the unusual solvent (micellar) medium suggests these conclusions be taken very cautiously. In the ^{1}H NMR spectrum the signals of the aromatic rings of **1** close to the intense resonances of the surfactant are clearly visible. Insight into the position of catalyst **1** in the micelles is provided by a 2D-NOESY experiment where clear cross-peaks between the aromatic moieties of the complex and the terminal *tert*-butyl group of the surfactant are observed, indicating that the catalyst is located deeply in the apolar core of the micelles that behave as nanoreactors.

In conclusion, the methodology reported herein represents a viable way for carrying out asymmetric epoxidations in water with "ordinary" transition metal catalysts, thereby avoiding the need to modify the catalyst with hydrophilic functional groups. The extremely mild and environmentally friendly experimental conditions (room temperature, low catalyst loading, use of water as solvent, use of 35% H_2O_2 as oxidant) together with the easy isolation of the enantioenriched product by simple hexane two-phases extraction and the possibility to recycle the catalyst are all key features of the present system that demonstrate the viability of this "greener" synthetic method. Yields and enantioselectivities were from moderate to good, and in some cases the aqueous medium allowed a significant improvement in the asymmetric induction compared to the use of organic solvents. This is particularly interesting for a class of substrates that have been only sparingly investigated.[19] Enantioselectivity as well as yield and recyclability are all features that result from a critical balance between catalyst, substrate and surfactant properties and these relationships deserve further investigations that are currently underway.

Experimental Section

General Remarks

Water was purified according to the milliQ technique, 35% hydrogen peroxide as well as all the alkene substrates are commercial products (Aldrich) and were used without further purification. The chiral complex {[(*S*,*S*)Chiraphos]Pt-(C_6F_5)(H_2O)}(OTf) (**1**) was prepared following the procedure reported in the literature.[17]

Unless otherwise stated, ^{1}H NMR and $^{31}P\{^{1}H\}$ NMR spectra were recorded at 298 K on a Bruker AVANCE 300 spectrometer operating at 300.15 and 121.50 MHz, respectively. δ values in ppm are relative to $Si(CH_3)_4$ and 85% H_3PO_4, respectively. A 2D-NOESY experiment was acquired with a spectrum width of 10 ppm, a relaxation delay d_1 of 1 s, using 2 K data points in the t_2 dimension and 512 data points in the t_1 dimension, with subsequent weighting with the sine-bell function using 160 scans for each t_1 increment. The mixing time d_8 employed was 0.4 s.

GLC measurements were taken on a Hewlett–Packard 5890 A gas chromatograph equipped with an FID detector (carrier gas He). All reactions were monitored either by GC or ^{1}H NMR. The enantiomeric excess was determined as reported in Tables 1, 2 and 3.

Oxidation Reactions

These were carried out in a 2-mL vial equipped with a side-arm fitted with a screw-capped silicone septum to allow sampling. Stirring was performed by a Teflon-coated bar driven externally by a magnetic stirrer (700 rpm). A constant temperature (20 °C) was maintained by water circulation through an external jacket connected with a thermostat. The concentration of the commercial 35% H_2O_2 solution was checked iodometrically prior to use. Typically, the proper amount of surfactant was dissolved in deionized milliQ water (0.5 mL), followed by catalyst **1** (0.0083 mmol). After 10 min the substrate (0.83 mmol) was added and the mixture stirred for 10 min. To this 35% hydrogen peroxide was added in one portion (0.83 mmol) and the mixture stirred at room temperature. After a certain time, 1 mL of organic solvent (pentane or hexane) was added to extract the reagents and products and the organic phase was analyzed.

Recycling Procedures

These were carried as for normal oxidation reaction on a 4-mL volume, extracting the solution with an identical volume of hexane and leaving the system unstirred for 6 h to allow phase separation. The organic supernatant phase was then removed for analysis while the aqueous phase was recycled for a new catalytic run by addition of fresh substrate and oxidant.

Supporting Information

^{1}H and ^{31}P NMR spectra and 2D-NOESY spectrum of catalyst **1** in the micellar medium water/Triton-X100 solution.

Acknowledgements

References

[1] D. Adams, P. Dyson, S. Tavener, *Chemistry in Alternative Reaction Media*, John Wiley & Sons, London, **2004**.

[2] a) C. J. Li, *Chem. Rev.* **1993**, *93*, 2023; b) C. J. Li, *Chem. Rev.* **2005**, *105*, 3095.

[3] a) U. M. Lindström *Angew. Chem. Int. Ed.* **2006**, *45*, 548; b) M. C. Pirrung *Chem. Eur. J.* **2006**, *12*, 1312.

[4] a) P. T. Anastas, J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, New York **1998**; b) P. T. Anastas, M. M. Kirchhoff, *Acc. Chem. Res.* **2002**, *35*, 686; c) C. Bolm, O. Beckmann, O. G. A. Dabard, *Angew. Chem. Int. Ed.* **1999**, *37*, 1198; *Angew. Chem.* **1998**, *37*, 1198–1209.

[5] T. Dwars, G. Oehme, *Adv. Synth. Catal.* **2002**, *344*, 239.

[6] N. Pinault, D. W. Bruce, *Coord. Chem. Rev.* **2003**, *241*, 1.

[7] a) T. Dwars, E. Paetzold, G. Oehme, *Angew. Chem. Int. Ed.* **2005**, *44*, 7174; b) S. Taşcıoğlu, *Tetrahedron* **1996**, *52*, 11113; c) J. B. F. N. Engberts, *Pure Appl. Chem.* **1992**, *64*, 1653; d) K. Holmberg, *Eur. J. Org. Chem.* **2007**, 731.

[8] a) U. M. Lindstrom, *Chem. Rev.* **2002**, *102*, 2751; b) S. Otto, J. B. F. N. Engberts, *Org. Biomol. Chem.* **2003**, *1*, 2809; c) S. Kobayashi, K. Manabe, *Acc. Chem. Res.* **2002**, *35*, 209; d) D. Sinou, C. Rabeyrin, C. Nguefack, *Adv. Synth. Cat.* **2004**, *345*, 357.

[9] a) C.-J. Li, L. Chen, *Chem. Soc. Rev.* **2006**, *35*, 68; b) D. Sinoi, *Adv. Synth. Catal.* **2002**, *344*, 221.

[10] Examples of metal catalyzed oxidations: a) L. J. P. van den Broeke, V. G. de Bruijn, J. H. M. Heijnen, J. T. F. Keurentjes, *Ind. Eng. Chem. Res.* **2001**, *40*, 5240; b) Z. Bourhani, A. I. Malkov, *Chem. Commun.* **2005**, 4592; example of organocatalytic oxidations: R. Liu, C. Dong, X. Liang, X. Wang, X. Hu, *J. Org. Chem.* **2005**, *70*, 729.

[11] a) H. Yao, D. E. Richardson, *J. Am. Chem. Soc.* **2003**, *125*, 6211; b) A. Masuyama, K. Fukuoka, N. Katsuyama, M. Nojima, *Langmuir* **2004**, *20*, 82; c) A. Masuyama, T. Yamagichi, M. Abe, M. Nojima, *Tetrahedron. Lett.* **2005**, *46*, 213; d) A. Blaskó, C. A. Bunton, S. Wright, *J. Phys. Chem.* **1993**, *97*, 5435.

[12] M. Bonchio, T. Carofiglio, F. Di Furia; R. Fornasier, *J. Org. Chem.* **1995**, *60*, 5986.

[13] One example of stereoselective oxidation in reversed micelles in toluene is known: H. Tohma, S. Takizawa, H. Watanabe, Y. Fukuoka, T. Maegawa, Y. Kita, *J. Org. Chem.* **1999**, *64*, 3519.

[14] A. Scarso, G. Strukul, *Adv. Synth. Catal.* **2005**, *347*, 1227.

[15] a) B. S. Lane, K. Burgess, *Chem. Rev.* **2003**, *103*, 2457; b) G. Grigoropoulou, J. H. Clark, J. A. Elings, *Green Chem.* **2003**, *5*, 1; c) R. Noyori, M. Aoki, K. Sato, *Chem. Commun.* **2003**, 1977.

[16] M. Colladon, A. Scarso, P. Sgarbossa, R. A. Michelin, G. Strukul, *J. Am. Chem. Soc.* **2006**, *128*, 14006.

[17] E. Pizzo, P. Sgarbossa, A. Scarso, R. A. Michelin, G. Strukul, *Organometallics* **2006**, *25*, 3056.

[18] In order to better compare the enantioselectivity under different experimental conditions for asymmetric catalytic reactions, enantiomeric excess $ee = 100 \cdot \{([R]-[S])/([R]+[S])\}$ is replaced by enantiomeric ratio $er = [R]/[S]$ which more straightforwardly provides a direct measurement of selectivity as recently outlined: R. E. Gawley, *J. Org. Chem.* **2006**, *71*, 2411.

[19] I. W. C. E. Arends, *Angew. Chem. Int. Ed.* **2006**, *45*, 6250.