Alessandro Scarso
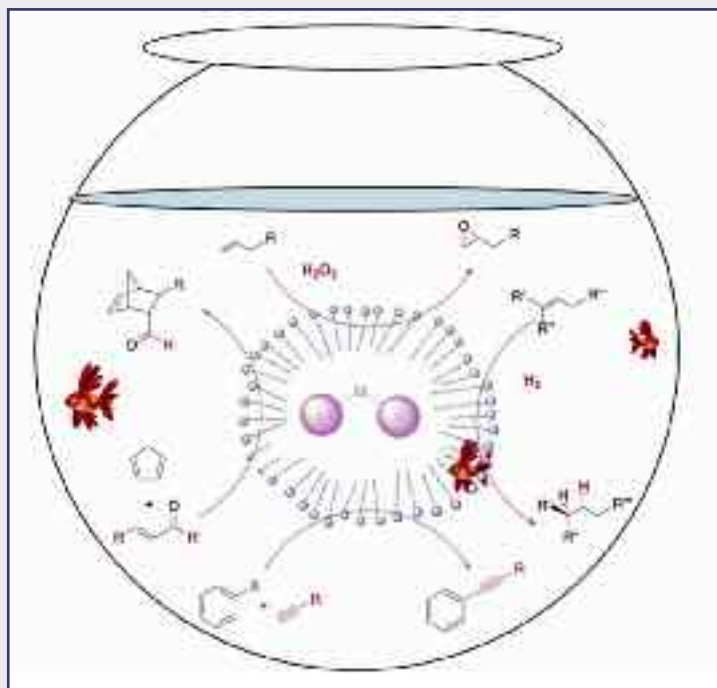**Dipartimento di Chimica**
Università di Venezia "Ca' Foscari"
alesca@unive.it

CATALYTIC REACTIONS IN MICELLAR MEDIA

Catalysis in micellar media is a new and still largely unexplored area of catalysis in environmentally friendly media. The hydrophobic effect favors dissolution and confinement of organic substrates and common organometallic catalysts avoiding the presence of solubilizing tags, leading to improved reactivity and selectivity and enabling recycling.

While chemists have been using for about two centuries a plethora of organic solvents spanning from alcohols, ethers, esters, amides to chlorinated alkanes and recently neoteric solvents like fluorinated media, supercritical CO_2 and ionic liquids to fulfill the requirements of tailored chemical transformations, Nature, on the contrary, continued to use the most abundant solvent available on earth: water. The task achieved by nature is to develop a universe of chemical transformations in water most of them characterized by being catalyzed processes that run in a narrow range of temperatures exploiting at the best the unique properties that are offered by water as solvent, most of them related to the hydrophobic effect [1]. The latter is the attitude of water as a reaction medium to pack and force hydrophobic solutes to stick together instead of being singularly solvated by water molecules, the phenomenon being basically driven by entropic effects.

Replacement of organic and especially chlorinated solvents with other characterized by a better eco-compatibility, in one word switching from old solvents to more "green" ones [2] is a common target for all chemical transformations both at the industrial and at the academic level. Water as an alternative reaction medium [3] is a not a new topic, the subject has been studied for several years and the first industrial application of water as the solvent was in the 24 years old Rhône-Poulenc and Ruhrchemie AG biphasic hydroformylation process developed in 1984. Since then, the academic community has constantly pursued the search for new processes in water and the topic has been investigated under several aspects, in particular in C-C coupling catalytic reactions [4], disclosing important concepts like "in water" catalysis when the system is homogeneous to "on water" catalysis when the reaction is catalyzed by simple mixing the reactants with water under heterogeneous conditions [5]. This large amount of data

has underlined the unique features of water that are worth of mention: it is a non flammable, abundant, economic solvent, with a large heat capacity and heat of evaporation which allows easy control of exothermic reactions, a high polarity, the coexistence of hydrogen bonds donor and acceptor which often provide a good source of catalysis, a tunable acidity and finally an E factor value equal to zero [6], which means it is not considered a waste in chemical transformations. Last but not least, the expansion of catalysis in water represents a viable way to try to mimic and better understand enzymatic catalysis, which is the ultimate goal of catalysis in terms of selectivity. Besides these properties, compared to common organic media water proved to enhance productivity as well as selectivity at regio, diastereo and enantioselective level in several catalytic reactions.

The above mentioned advantages offered by water are some of the motivations that prompt scientists to explore the use of water as solvent, with the additional advantage of possible catalyst recycling when products are extracted with a water immiscible organic phase leaving the catalyst dissolved in the aqueous one. The major drawbacks of water as solvent are basically two: firstly the impossibility to employ hard Lewis acid catalysts because of their deactivation in water with the consequent need of developing new soft Lewis acid species as catalysts, secondly the general low solubility of substrates as well as catalysts (both organic and organometallic ones) in such a solvent.

With respect to solubility in water catalysts can be classified into three general types (Fig. 1):

a) intrinsically soluble catalysts;

b) catalysts developed for organic media and covalently modified with water soluble pony tails [7] that often turns out in tedious and time consuming synthetic steps and that in some cases alter profoundly the electronic and steric properties of the catalysts;
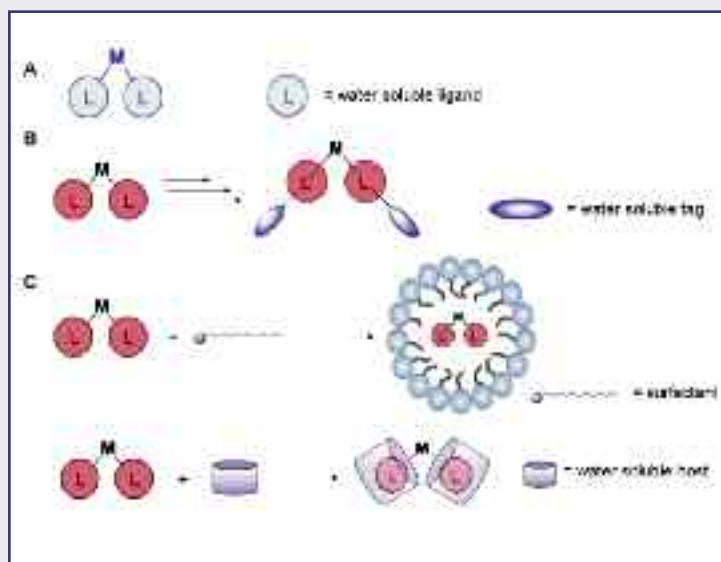

Fig. 1 - Approaches to organometallic catalysis in water: A) intrinsically water soluble catalyst; B) covalent modification of ligands with water solubilizing tags; C) solubilization of catalysts in micelles or in hosts by means of supramolecular hydrophobic effect

c) the employment of supramolecular aggregates to dissolve the catalyst thus maintaining the integrity of the original organic soluble catalyst, even though a good understanding of the aggregate formed is required to attain good catalytic performance.

Micellar catalysis is not a "*new solution to old problems*" since early review papers on the subject date back on late Seventies describing catalysis directly performed by the supramolecular aggregates [8], rather it is still the simplest and at the same time one of the most promising strategies to overcome solubilization problems that still deserve developments in terms of new surfactants and a better understanding of the unique medium effects provided by this approach but that at the same time is witnessing a sort of renaissance due to its compatibility with organometallic as well as organic catalysis [9]. Surfactants in fact, act as mediators between water and sparingly soluble substrates and catalysts and the hydrophobic effect drives the formation of micelles in solution when the surfactant is added to water above a certain minimum concentration (c.m.c., critical micellar concentration). Depending on the surfactant employed, micelles can be either charged or neutral with size and polar properties that encompass a wide range of properties. Basically they behave like cells, isolating species from the bulk solvent, playing several roles at a time, firstly they improve 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 [10]. The comparison with reactions occurring in the living systems is pertaining also in terms of concentration and amounts of substrates that can be loaded into the micelles; values are usually lower than common catalysis in organic solvents but the higher selectivities that usually are observed with micelles can partially compensate the disadvantage of working in diluted media. Micellar systems can act as nanoreactors for several organic reactions by virtue of their concentration effect and particular pH values observed on the surface of the micelle that is markedly different from that of the bulk solvent. All these features favor solubilization of organometallic catalyst providing a viable apolar nano-environment dispersed into water.

The present contribution aims at bringing the attention of the readers to the great potentials of micellar catalysis in providing a viable alternative reaction medium for catalytic reactions compared to organic solvents, with emphasis on the enhancement of selectivity and ease of catalyst recycling. Examples concerning catalysts that are dissolved or stabilized by micelles are discussed to underline features that only the micellar aggregates make possible. Rather than displaying an exhaustive overview on the most recent catalytic systems acting in micellar media, selected examples will be presented spanning from C-C, C-X (X heteroatom) formation to reduction as well as oxidation reactions. Micellar catalysis offers the great advantage of using catalysts already developed for use in organic media, while allowing a deep investigation of subtle electronic and steric effects when using the numerous commercially available ligands.
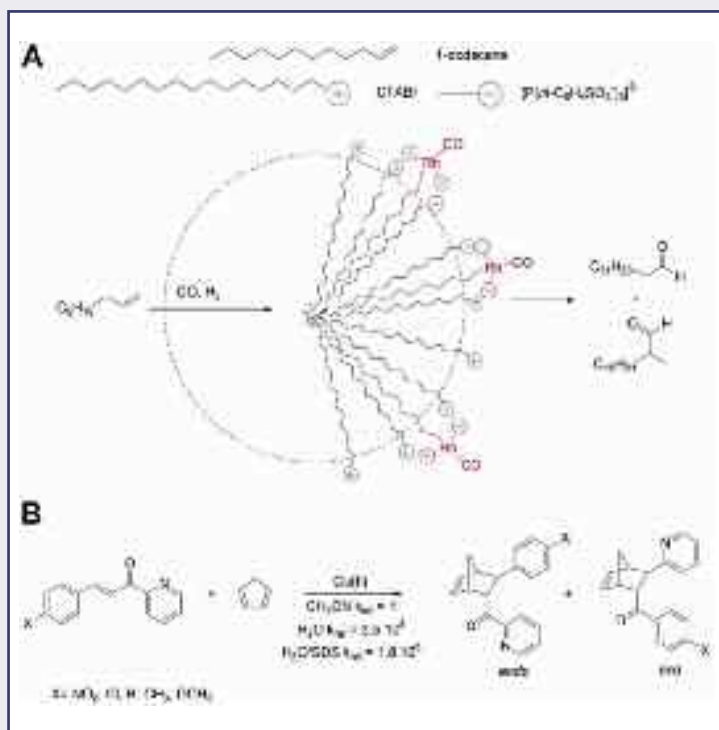
Fig. 2 - A) Catalytic hydroformylation of hydrophobic alkenes with polyanionic Rh(I) catalysts mediated by cationic micelles; B) Diels-Alder reaction catalyzed by Cu(II) in anionic micelles is about one order of magnitude faster than in pure water and several orders of magnitude compared to acetonitrile as organic solvent

C-C bond forming reactions

As a leading reaction in industrial organic chemistry, hydroformylation has been the first chemical transformation that succeeded in being extended to water media, but still effort is required for the catalysis of longer olefins which are characterized by negligible solubility in water. Besides the use of co-solvents, modified cyclodextrines have been tested as hydrophobic water soluble supramolecular carriers, but they have been largely taken over by the use of surfactants which provide better results in terms of activity and selectivity favoring H_2 and CO solubilization as well. In Fig. 2A is reported the reaction of the water soluble catalyst $(RhCl(CO)(TPPTS)_2)$ bearing 3,3',3''-phosphinidynetris(benzenesulfonic acid) trisodium salt (TPPTS) as water-soluble ligand in the presence of cationic micelles derived from cetyltrimethylammonium bromide (CTABr) as surfactant, leading to the corresponding aldehydes with good selectivity [11]. Detailed kinetic investigation underlined the crucial role played by the supramolecular attractive interaction between the positively charged micelles and the negative catalyst that places the latter in close proximity of the substrate which is dissolved into the hydrophobic core of the micelle. The overall effect was a good catalytic performance as result of solubilization of reagents and compartimentalization of the latter with the catalyst, together with a good regioselectivity between the two possible aldehydes in favor of the more valuable normal derivative that is consequence of the alignment of the substrate with the alkyl chains of the surfactant and its oriented approach to the catalyst. These features

are common observations of several other micellar catalytic systems and will be discussed in the coming examples.

Diels-Alder reaction represents the most useful sigmatropic reaction that allows the concerted formation of several C-C bonds between the diene and dienophile molecular partners. Such reaction has been extended to water media with great benefits on the catalytic activity both arising from hydrogen bonding to water and hydrophobic effect. The presence of a Lewis acid catalyst like Cu(II) cations in water accelerates the reaction up to 250,000 times compared to the reaction run in acetonitrile, but further enhancement was observed implementing micellar media in such reaction (Fig. 2B) [12]. In fact the reaction of bidentate dienophiles and cyclopentadiene resulted to be greatly accelerated (up to 1.8×10^6 times faster compared to acetonitrile) by using Cu(II) with SDS (sodium dodecylsulfate) as surfactant. The overall positive effect on the catalytic activity arises from the concentration of Cu(II) cations that binds and activates the bidentate dienophile on the surface of the negatively charged micelle which contains the lipophilic diene. It is remarkable that in the absence of Cu(II) the presence of the surfactant inhibits the reaction because the dienophile prefers to stay in bulk water rather than getting close to the diene sequestered into the hydrophobic core of the micelles.
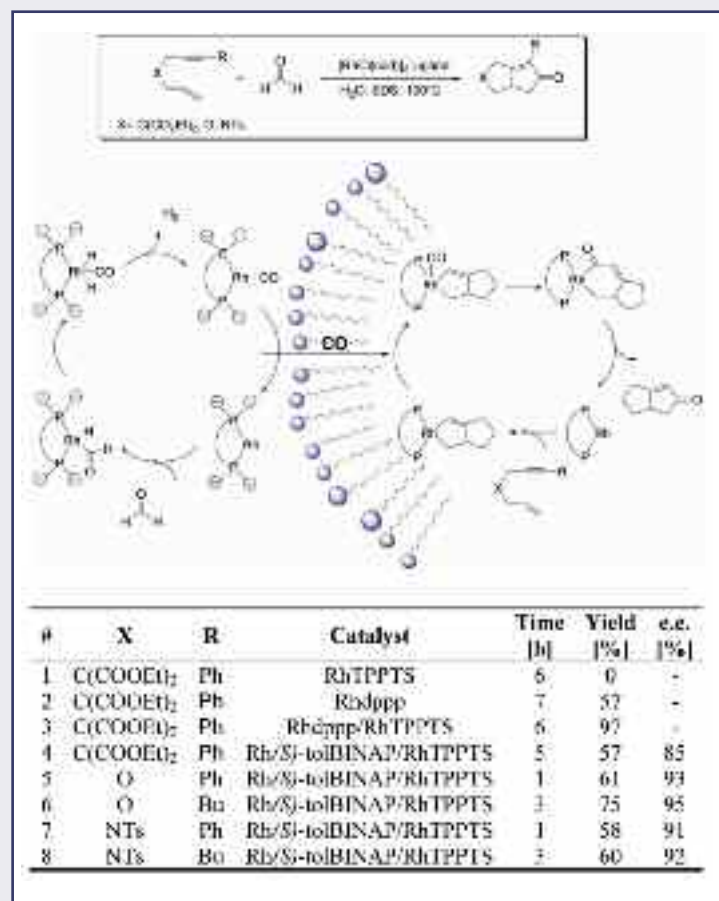

#	X	R	Catalyst	Time [h]	Yield [%]	e.e. [%]
1	C(COOEt)₂	Ph	RhTPPTS	5	0	-
2	C(COOEt)₂	Ph	Rhdppp	7	57	-
3	C(COOEt)₂	Ph	Rhdppp/RhTPPTS	6	97	-
4	C(COOEt)₂	Ph	Rh/Si-tolBINAP/RhTPPTS	5	57	85
5	O	Ph	Rh/Si-tolBINAP/RhTPPTS	1	61	93
6	O	Bu	Rh/Si-tolBINAP/RhTPPTS	3	75	95
7	NTs	Ph	Rh/Si-tolBINAP/RhTPPTS	1	58	91
8	NTs	Bu	Rh/Si-tolBINAP/RhTPPTS	3	60	92

Fig. 3 - Pauson-Khand-type reaction between enynes and carbon monoxide leading to bicyclic enones is positively affected by micellar media both for catalytic activity as well as for enantioselectivity
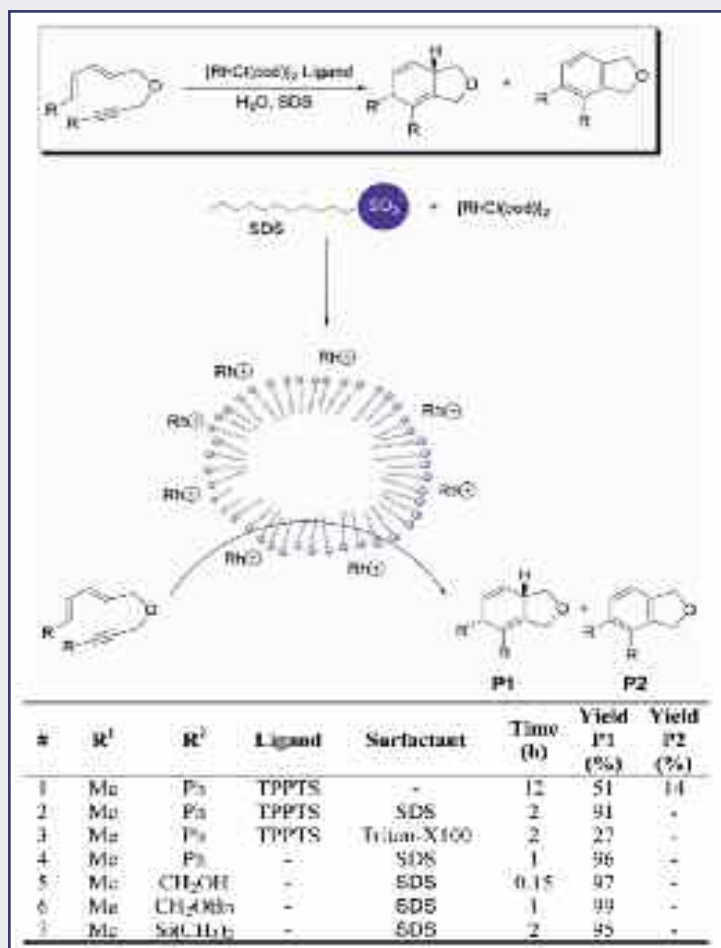
Fig. 4 - Anionic micellar media favor Rh(I) catalysts solubilization and activation promoting intramolecular [4+2] annulation of 1,3-dien-8-ynes under mild experimental conditions
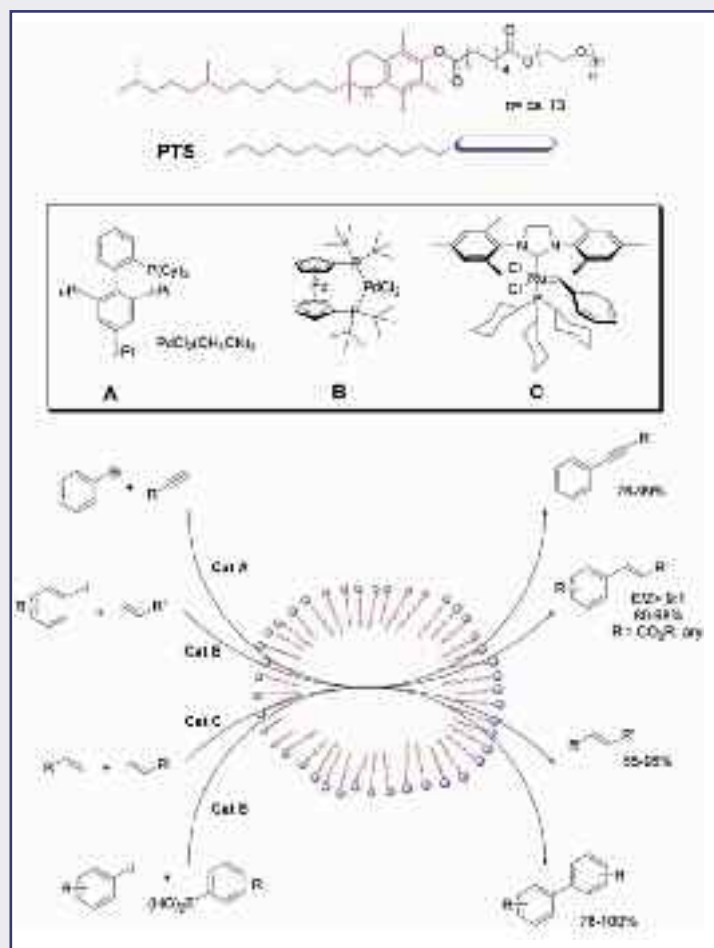

Fig. 5 - New generation neutral surfactants like PTS provide suitable micellar media for C-C coupling reactions. A) Sonogashira, B) Heck, Suzuki and C) alkene cross-metathesis catalysts are efficiently solubilized in water with PTS and the corresponding reactions run smoothly

The Pauson-Khand-type reaction between enynes and carbon monoxide is strictly related to hydroformylation, and such carbonylation turned out to be greatly influenced by the presence of anionic micelles in water (Fig. 3) [13]. In particular, the reaction with formaldehyde as a substitute of CO was favored by the coexistence of an anionic achiral and a neutral chiral Rh(I) species, the first operating in solution and involved in the decarbonylation of formaldehyde with CO liberation, and the second more apolar species embedded into the anionic micelles formed by SDS aggregation. The presence of micelles accelerated the reaction leading to the desired product in 96% yield in 6 hours at 100 °C, while the reaction performed in p-xylene at 130 °C for 24 h led to 53% yield. Also the asymmetric version of the reaction took advantage of micellar catalysis: with RhTPPTS dissolved in water and Rh-*(S)*-tol-BINAP into the micelles the reaction led to the desired product with good enantioselectivities (Fig. 3) [14]. This example is particularly interesting since it shows that micellar catalysis can be used in association with homogeneous catalysis in water, where the micelle represents a nanoscopic environment continuously exchanging with bulk water, but still separated and characterized by unique polarity and reactivity.

Rh cationic complexes are catalysts for a wide variety of organic transformations of double bonds but many of such species are insoluble in water. [RhCl(COD)]$_2$ (COD 1,5-cyclooctadiene) is a good catalyst for the intramolecular [4+2] annulation of 1,3-dien-8-ynes but it is not soluble in water. Addition of SDS as surfactant provides anionic micelles that makes ion pairs with the cationic catalyst providing a clear yellow solution and allowing the reaction to occur with good yields under mild experimental conditions (Fig. 4) [15]. Micelles cope with the low solubility of substrates and catalyst providing for the latter suitable counteranions and liberating in solution chloride anions as detected by ion-electrode analysis. Sodium methyl sulfate instead of SDS did not provide the expected products confirming the importance of the hydrophobic core of the micelle to solubilize the substrate and provide the nanometric hydrophobic phase where the reaction took place. The scope of the reaction was largely investigated, observing good to excellent yields but decreasing as the size of the substrate increases. This catalytic reaction represents a typical example of the potentialities of micellar media as a valid alternative to organic solvents, allowing catalytic systems developed for the organic phase to run smoothly in the aqueous phase.

In the kingdom of transition metal catalysis, Pd complexes lead the way thanks to their versatility and facile switch between oxidation states and are becoming common synthetic tools in the industrial and pharmaceutical synthesis. C-C coupling reactions are the most widely studied. Sonogashira coupling between aryl halides and terminal alkynes is another classic coupling reaction, highly ranked because of the high potential functionalization of the acetylenic moiety. Very recently this reaction was accomplished in water by the employment of neutral micelles derived from the PTS (PTS = *P*EG600-yl-α-tocopheryl sebacate) surfactant, with no need of adding copper to re-oxidize the Pd catalyst (Fig. 5) [16]. Aryl bromides are good partners in the present catalytic system and reaction in the presence of surfactant yielded 83% of the desired product, while in the absence only 34% conversion was attained. A wide variety of lipophilic aryl halides and alkynes were investigated with yields from good to excellent, while increasing the lipophilicity of the base led to the opposite effect decreasing product formation. Such surfactant enabled positive results in other Pd catalyzed C-C coupling reactions in water like Heck [17] and Suzuki [18] and olefin cross-metathesis [19, 20] thus representing a promising candidate for further screening of different metal catalyzed reactions.

C-heteroatom forming reactions

Carbon heteroatom bond formation is intrinsically more difficult to form in water since heteroatomic nucleophiles suffer from competition with water for metal binding and this is the main cause of the paucity of C-X bond forming catalytic reactions in water. When water itself is the nucleophile, as in the water addition to π systems, the reaction is obviously positively influenced by the employment of micellar aqueous media. Regioselective addition of water to terminal alkynes provides ketones as well as aldehydes depending on Markovnikov or anti-Markovnikov addition, respectively. Ru species that are common catalysts for such chemical transformation, were found much more selective catalyst in micellar media that positively increased the a/k (aldehyde/ketone) selectivity towards the more valuable aldehyde (Fig. 6A)
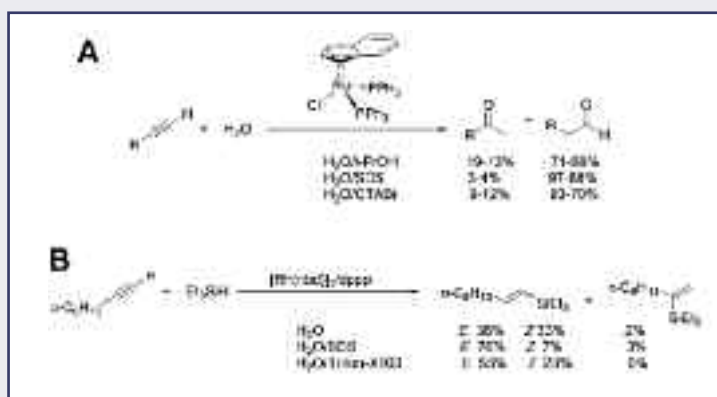

Fig. 6 - A) Alkyne hydration is efficiently performed in water with either cationic or anionic micelles leading to preferential formation of aldehydes, B) Triethylsilane addition to alkynes mediated by Rh(I) positively beneficiates of micellar conditions especially in terms of stereoselectivity

[21]. The hydration of phenylacetylene in water/*i*-propanol occurs only above 90 °C with formation of the carbonyl products with a 81/19 a/k distribution and 12% by-products. The same reaction in water with SDS led to complete conversion and 93/7 ratio between the two possible regioisomers. Moreover in the micellar medium ten times less catalyst is required to perform the reaction compared to organic media. Cationic micelles worked slight less efficiently in terms of selectivity, and the best results in terms of reactivity were observed with more hydrophobic substrates because of their lower intrinsic water solubility and hence their preference to reside within the micelles. Spectroscopic evidences showed that the anionic micelles favored chloride ligand dissociation and formation of a cationic Ru species remaining on the surface of the micelle and intercepting the alkyne buried into the hydrophobic core of the supramolecular aggregate, putting it contact with water as the second reagent.

The same dissociative effect on chloride ligands was observed in the hydrosilylation of alkynes mediated by Rh precursors that become soluble in water leading to a clear yellow solution (Fig. 6B) [22]. The reaction between 1-octyne and triethylsilane was positively catalyzed by the Rh precursor in anionic micelles upon addition of a diphosphine ligand stereoselectively favoring the *E* isomer of the alkenylsilane with traces of the terminal isomer. Water soluble sulfonated anionic diphosphines turned out to inhibit the reaction that occurred on the micellar anionic surface. A neutral surfactant like Triton-X100 was active but led to a poorly stereoselective addition, while cationic surfactants were completely inactive. The reaction was extended to a wide range of alkynes showing good activity and selectivity, while intrinsically soluble alkynes displayed generally lower yields. SDS concentration as well as SDS/catalyst ratio were both important parameters, in fact the higher the SDS amount in solution the better the selectivity and the rate of the reaction.

Hydrogenation reactions

Enantioselective hydrogenation has been one of the first reactions to be extended in water and several successful examples of surfactant use in the reduction of C=C double bonds have been reported. Worth of mention are two processes dated back to the late 90's, both based on the employment of chiral Rh(I) diphosphine catalysts in the hydrogenation of unsaturated α-aminophosphonic [23] acid derivatives and (*Z*)-acetamidocinnamate [24]. In the first case the catalytic activity in water/SDS improved compared to the reaction in methanol, and more interestingly enantioselectivity took advantage of the micellar medium with ee up to 98% and reaction completion in a few minutes. The second asymmetric hydrogenation process disclosed an impressive increase of the ee to 75% upon employment of SDS as surfactant compared to the process carried out in pure water and, with dimethyl itaconate as substrate, the same micellar systems displayed an inversion of stereoselectivity from *R* to *S* enantiomer moving from water to water/SDS media (Fig. 7). The above results have been more recently investigated in detail with the aid of new NMR techniques like
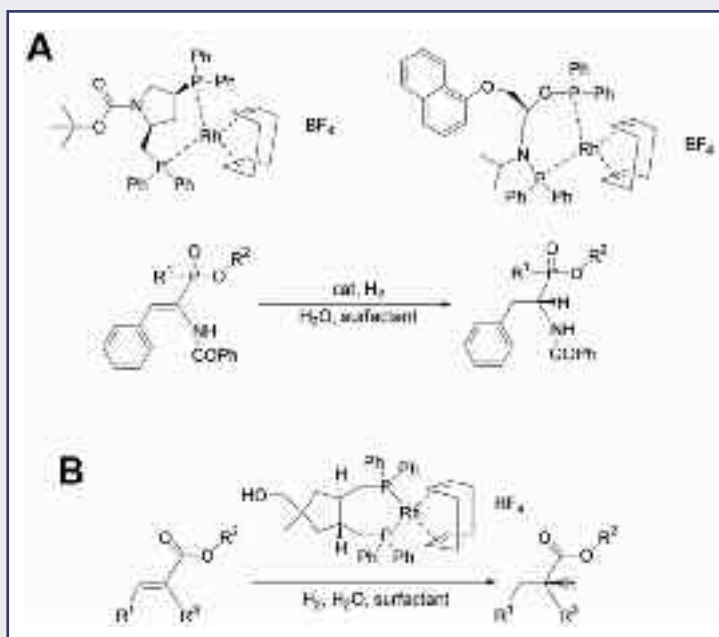
Fig. 7 - Asymmetric hydrogenation in micellar media: A) reduction of α-aminophosphonic and B) (Z)-acetamidocinnamate substrates in water/SDS compared to homogeneous media

Fig. 8 - [((R)-BINAP)PtμOH]$_2$(BF$_4$)$_2$ catalyzes asymmetric sulfoxidation of thioethers with hydrogen peroxide in water with SDS as surfactant; [((S,S)Chiraphos)Pt(C$_6$F$_5$)(H$_2$O)](OTf) catalyzed asymmetric epoxidation of terminal alkenes with hydrogen peroxide in water with neutral surfactants

PGSE [25] disclosing that every combination of substrate/catalyst/surfactant can give rise to different catalytic systems due to the intrinsic solubility, polarity and supramolecular weak interactions arising case by case [26]. In fact, distribution of catalyst and substrate between water and micelles or in the interphase between the two is crucial for the activity as well as for the enantioselectivity of the process. The latter is a general observation that applies to several reaction carried out in micellar media.

Oxidation reactions

Oxidation reactions are leading chemical transformation that are currently experiencing a profound transformation moving from the use of stoichiometric oxidants such as peracids and metals in high oxidation states to molecular oxygen and hydrogen peroxide as green oxidants associated to suitable catalysts. The employment of water as reaction medium for the development of even more environmentally friendly catalytic oxidation processes seems an obvious extension. However, oxidation reactions with hydrogen peroxide are most of the time promoted by high valent Lewis acidic transition metal ions characterized by an electrophilic character and therefore totally unfit for use in water. More recently, some Pt(II) complexes, also in their chiral version, were found extremely good catalysts for hydrogen epoxide activation in classical electrophilic oxidation of thioethers but also in the unusual nucleophilic oxidation of electron poor terminal alkenes. After sound results in organic media, such complexes (Fig. 8) that are unaffected by water have been tested in the asymmetric sulfoxidation [27] and epoxidation [28] in micellar media.

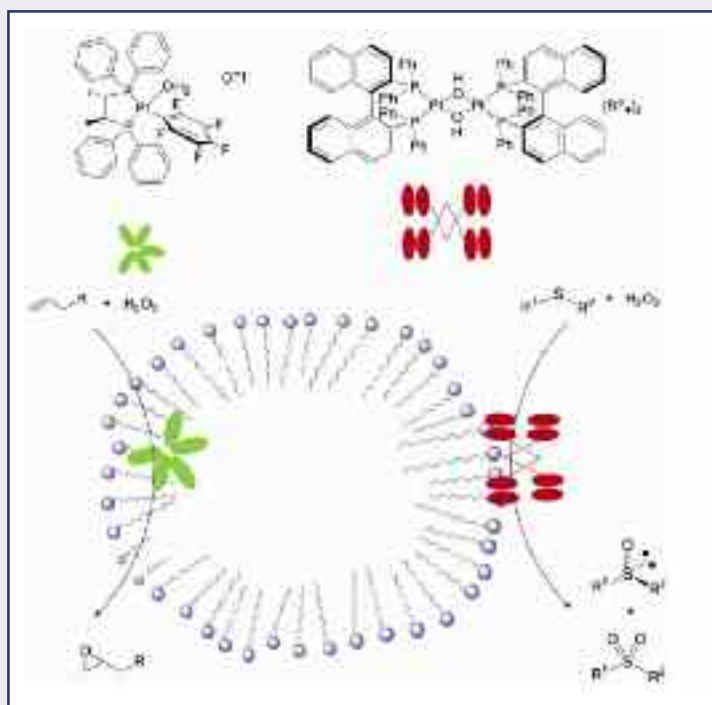It is worth noting that none of the chiral Pt(II) complexes are soluble in water, but they provide clear solutions in the presence of anionic and neutral micelles, respectively as confirmed by ^{31}P and ^{1}H spectroscopy as well as 2D NOESY experiments that showed contacts between surfactant and catalysts and allowed insight into their positioning into the micelles (Fig. 8). As long as the enantioselective sulfoxidation is concerned, enantioenriched sulfoxides with good chemoselectivity and moderate enantioselectivity were obtained with anionic surfactants, in particular SDS, with a considerable enhancement of chemo and enantioselectivity compared to the organic chlorinated solvent (Tab. 1). On the contrary, cationic and neutral surfactants led to low selectivities as well as low yields in sulfoxides.

Surfactant concentration was an important parameter, leading to an initial increase of activity due to a better catalyst and substrate solubilization, followed by a decrease down to a minimum corresponding to the highest enantioselectivity. This may be no coincidence as it is known that, in general, lower activities allow a better discrimination between the two diastereoisomeric transition states, mediated, in this case, by the average size of micelles and catalyst positioning. The system resulted of general applicability and a wide range of substrates were oxidized with good selectivities and isolated by means of simple biphasic extraction. The Lewis acid character of the complex favors the racemization of sulfoxides as extensively observed in organic media. This detrimental side-effect was minimized in micellar medium, thus emphasizing the compartmentalization effect played by micelles in keeping substrates and products dissolved into the apolar core with the catalyst residing on the surface, thus limiting the direct contact between catalyst and product. It has to be stressed once again that

Tab. 1 - Catalytic enantioselective oxidation of aryl methyl sulfides with hydrogen peroxide mediated by 1

#	R^1	R^2	Time (h)		Yield (%)	SO /SO$_2$	ee (%) Abs. Conf.	Solvent
1	C$_6$H$_5$	CH$_3$	8.5	99	80	16	R-(+)	CH$_2$Cl$_2$
2	p-NO$_2$-C$_6$H$_5$	CH$_3$	24	41	25	26	R-(+)	CH$_2$Cl$_2$
3	C$_6$H$_5$	CH$_3$	24	16	31	5	S-(-)	H$_2$O-CTABr
4	C$_6$H$_5$	CH$_3$	24	20	56	0	-	H$_2$O-Triton-X100
5	C$_6$H$_5$	CH$_3$	24	85	>200	29	R-(+)	H$_2$O-C$_{12}$H$_{25}$(C$_6$H$_5$)SO$_3$Na
6	C$_6$H$_5$	CH$_3$	24	82	180	30	R-(+)	H$_2$O-C$_{12}$H$_{25}$SO$_3$Na
7	C$_6$H$_5$	CH$_3$	24	98	>200	40	R-(+)	H$_2$O-SDS
8	2-naphthyl	CH$_3$	24	99	32	34	R-(+)	H$_2$O-SDS
9	p-CH$_3$-C$_6$H$_5$	CH$_3$	24	99	>200	31	R-(+)	H$_2$O-SDS
10	p-Cl-C$_6$H$_5$	CH$_3$	24	87	>200	48	R-(+)	H$_2$O-SDS
11	p-CN-C$_6$H$_5$	CH$_3$	48	68	21	63	R-(+)	H$_2$O-SDS
12	p-NO$_2$-C$_6$H$_5$	CH$_3$	48	63	90	88	R-(+)	H$_2$O-SDS

the higher initial stereoselectivity observed in aqueous media compared to dichloromethane is probably a consequence of the unique properties of water as solvent, in particular its *"hydrophobic effect"*.
More electron poor catalysts showed a higher affinity for H$_2$O$_2$ and, upon coordination, the activation of the latter as a good nucleophile [29]. Such catalysts were successfully employed in the asymmetric epoxidation of poorly reactive terminal alkenes in neutral micellar media [28].
Epoxidation of 4-methyl-pentene as a model substrate performed in DCE (1,2-dichloroethane) showed 56% yield with 58% ee (Tab. 2). Conversely, in pure water no catalyst solubilization occurred and no reaction was observed (entry 2). Anionic as well as cationic micelles were not suitable for such reaction, at variance with what observed in sulfoxidation in the presence of a *bis*-cationic dimeric complex, while neutral surfactants turned out to be good mediators for the reaction in water with an influence of the chemical structure and length of the surfactant itself. TritonX-100 was the best surfactant ensuring good activity and selectivity leading to the terminal epoxide with an increase of enantiomeric excess observed between chlorinated solvent (58%) and water-non ionic surfactant (84%) implying an almost doubling of the ΔΔG≠ (from -3.23 KJ/mol to -5.95 KJ/mol) by simply switching the reaction from DCE to water-TritonX-100.

The synthetic scope of the enantioselective epoxidation reaction was investigated employing other terminal alkene substrates. Terminal alkenes like linear and aromatic olefins were successfully oxidized in moderate to good yields and with good enantioselectivities that, thus far, are among the highest reported if considering the general lack of suitable enantioselective catalysts for this poorly reactive category of alkenes. The robustness of the catalyst employed allowed recycling for at least three consecutive runs with almost constant yield and ee, re-using the aqueous phase to which fresh substrate and oxidant were added. Similar results with the use of micellar media can be observed in other synthetically useful catalytic processes such as the Baeyer-Villiger oxidation of ketones.

Conclusions

Organometallic catalysis is an extremely important discipline that is quickly moving from organic to aqueous media with the aim of finding suitable answers to the quest for greener processes. The implementation of surfactants in water represent the most straightforward solution to the problem allowing to cope with the generally low solubility of both substrates and catalysts and at the same time taking advantage of the unique features offered by water as reaction medium, in particular the hydrophobic effect. The use of water as solvent intrinsically opens to biphasic extraction of products and recycle of the catalyst that resides in the micellar phase but the later often pose the problem related to emulsion formation and this still limits the number of positive examples in the area. Recycling is therefore subject to catalyst robustness as well as proper solvent choice for

Tab. 2 - Catalytic enantioselective epoxidation of terminal 4-methyl-pentene with H2O2 mediated by 1 in micellar media

#	Time (h)		Yield (%)	e.e. (%) Abs. Conf.	Solvent/Additive
1	4	56	58	R-(+)	DCE
2	24	0	-	-	H$_2$O
3	24	0	-	-	H$_2$O/SDS
4	6	28	84	R-(+)	H$_2$O/Zwitterionic
5	6	41	84	R-(+)	H$_2$O/POA
6	6	61	82	R-(+)	H$_2$O/Triton-X114
7	6	51	82	R-(+)	H$_2$O/Triton-X100

phase separation and the problem is more evident with neutral surfactants that are characterized by similar affinity for water as well as for organic solvents, while charged anionic or cationic surfactants usually are compatible with extraction with apolar solvents like alkanes or diethyl ether remaining in the aqueous phase. Micelles are real self-assembled nanoreactors and because of this they are prime actors in the catalytic process in water. It seems conceivable that the chemical nature of the surfactant, its concentration and molar ratio are all parameters with a profound influence on the outcome of the catalytic reaction and they deserve careful optimization. Yield, selectivity and recyclability are all features that result from a critical balance between catalyst, substrate and surfactant properties and these relationships must be analyzed in detail. Fortunately, this can be rather quickly performed considering that no synthetic steps are required to modify catalysts already developed for use in organic media with hydrophilic functional groups. The availability of surfactants and their generally low cost clearly speaks for their straightforward development into practical synthetic methods and also in the scale up of suitable industrial chemical productions. Thus far few examples are already known and more are on the way to come.

Alessandro Scarso earned his degree in Chemistry in 1998 and the PhD in 2002 at Università di Padova with Prof. P.M. Scrimin. In 2002 he joined the group of Prof. J. Rebek Jr. at Scripps (San Diego, CA) working on supramolecular self-assembled capsule. In 2004 he moved to Università "Ca' Foscari" di Venezia to Prof. Strukul's group were he gained the position of assistant professor in November 2005. His interest spans from organometallic catalysis to supramolecular catalysis.

References

[1] a) U.M. Lindström, *Angew. Chem. Int. Ed.,* 2006, **45,** 548.

[2] 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 *et al., Angew. Chem. Int. Ed*., 1999, **37,** 1198.

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

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

[5] a) M.C. Pirrung, *Chem. Eur. J.,* 2006, **12,** 1312; b) S. Narayan *et al., Angew. Chem. Int. Ed.,* 2005, **44,** 3275.

[6] R.A. Sheldon, *Green Chem.*, 2005, **7,** 267.

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

[8] a) E.J. Fendler, J.H. Fendler, *Adv. Phys. Org. Chem.,* 1970, **8,** 271; b) J.H. Fendler, E.J. Fendler, Catalysis in Micellar and Macromolecular Systems Academic Press, New York, 1975, 1-545.

[9] a) T. Dwars *et al., Angew. Chem. Int. Ed.,* 2005, **44,** 7174; b) S. Tascioğlu, *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.

[10] 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.

[11] Y. Zhang *et al., Catal. Today,* 2002, **74,** 23.

[12] S. Otto *et al., J. Am. Chem. Soc.,* 1998, **120,** 9517.

[13] K. Fuji *et al., Angew. Chem. Int. Ed.,* 2003, **42,** 2409.

[14] K. Fuji *et al.,Tetrahedron Lett.,* 2004, **45,** 9163.

[15] D. Motoda *et al., Angew. Chem. Int. Ed.,* 2004, **43,** 1860.

[16] B.H. Lipshutz *et al., Org. Lett.,* 2008, **10,** 3793.

[17] B.H. Lipshutz, B.R. Taft, *Org. Lett.,* 2008, **10,** 1329.

[18] B.H. Lipshutz *et al., Org. Lett.,* 2008, **10,** 1333.

[19] B.H. Lipshutz *et al., Org. Lett.,* 2008, **10,** 1325.

[20] B.H. Lipshutz *et al., Adv. Synth. Catal.,* 2008, **350,** 953.

[21] P. Alvarez *et al., Tetrahedron Lett.,* 2001, **42,** 8467.

[22] A. Sato *et al., Org. Lett.,* 2004, **6,** 2217.

[23] T. Dwars *et al., Angew. Chem. Int. Ed.,* 1998, **37,** 2851.

[24] R. Selke *et al., Chem. Eur. J.* 1998, **4,** 769.

[25] PGSE: Pulse Gradient Spin Echo, for a leading reference see: P.S. Pregosin *et al., Chem. Rev.,* 2005, **105,** 2977.

[26] M. Ludwig *et al., Chem. Eur. J.,* 2001, **7,** 3298.

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

[28] M. Colladon *et al., Adv. Synth. Catal.,* 2007, **349,** 797.

[29] a) M. Colladon *et al., J. Am. Chem. Soc.,* 2006, **128**, 14006; b) M. Colladon *et al., J. Am. Chem. Soc.,* 2007, **129,** 7680.

RIASSUNTO

Reazioni catalitiche in mezzo micellare

La catalisi in acqua, quale nuova frontiera nello sviluppo di processi eco-compatibili, risulta fortemente facilitata dall'impiego di sistemi micellari. L'effetto idrofobico che governa la formazione delle micelle è responsabile della solubilizzazione e compartimentalizzazione dei reagenti e catalizzatori che non richiedono la presenza di gruppi idrofili, del miglioramento dell'attività e selettività delle reazioni e favorisce il riciclo del catalizzatore mediante estrazione bifasica.