

Methane Functionalization in Water with Micellar Catalysis

Riccardo Gava, Pilar Ballestín, Auxiliadora Prieto, Ana Caballero,* and Pedro J. Pérez*

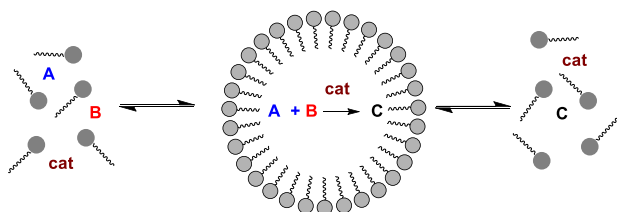
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The functionalization of methane in water as the reaction medium (where it is nearly insoluble) at room temperature, using micellar catalysis is described. Aggregates are formed from surfactant molecules and act as methane concentrator, also trapping the catalyst (a silver-based complex) and the diazo reagent (ethyl diazoacetate, EDA), providing yields into ethyl propionate up to 14 % (referred to EDA), in the first example of methane being functionalized in water at room temperature.

Micellar catalysis is growing in the last decade as a potential green alternative to homogeneous catalysis in conventional organic solvents.¹ When surfactant molecules are dissolved in water, supramolecular aggregates are formed which can accommodate apolar molecules in their inner volume, (Scheme 1) thus favoring their interactions and increasing reaction rates by order of magnitude compared with the corresponding experiments in organic solvents. This behavior has been explained as a consequence of very high local concentrations of catalyst and reactants inside the micelle, which acts as a supramolecular nanoreactor.² The rapid equilibrium between the surfactant monomers and the aggregates ($0.01\text{-}0.001\text{ s}^{-1}$)³ facilitates the trapping of reactants and release of products in the catalytic reaction.



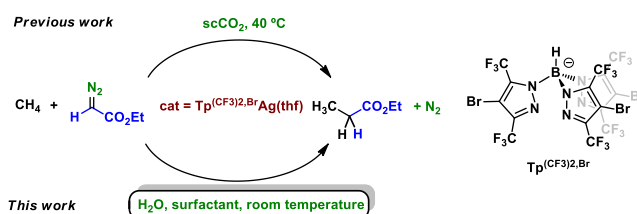
Scheme 1 General picture of micellar catalysis.

Laboratorio de Catálisis Homogénea, Unidad Asociada al CSIC CIQSO-Centro de Investigación en Química Sostenible and Departamento de Química Universidad de Huelva, 21007-Huelva (Spain)

E-mail: perez@dqcm.uhu.es; ana.caballero@dqcm.uhu.es

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A number of catalytic systems using surfactants in water have already been described, operating under milder conditions than when carried out in organic solvents. For example, Lipshutz and co-workers have developed several systems which can be commonly employed by no experts to promote transformations such as cross-coupling reactions.⁴ However, to the best of our knowledge there is no report on the use of methane as the target substrate in the context of micellar catalysis. This is not surprising since the few methodologies described for the catalytic functionalization of methane employ organometallic complexes that require organic solvents and/or inert atmosphere. Only the so-called electrophilic activation of methane operates in protic media.⁵ Our group is involved in the development of strategies for the



Scheme 2 Methane functionalization by silver-catalyzed carbene insertion: from supercritical carbon dioxide to micellar chemistry in water.

functionalization of unreactive C-H bonds,⁶ with methane being the ultimate goal. Using coinage metal complexes for the transfer from carbene unit from diazo compounds, we have been able to promote such transformation with methane, using supercritical carbon dioxide as the reaction medium (Scheme 2).⁷ We herein report the use of a silver-based catalyst capable of inducing the formation of ethyl propionate from methane and ethyl diazoacetate, at room temperature, using water as solvent and with the aid of a surfactant generating micelles. This is the first report of methane being catalytically modified using micellar catalysis.

We first investigated the trapping of methane in water solutions of several surfactants was evaluated, upon charging a pressure vessel with 160 atm of methane and observing the decrease of pressure, which was correlated with the amount of methane available in the liquid phase (see ESI). Albeit methane solubility in neat water is very low (2.8×10^{-5} ; molar

methane in neat water, thus providing a substantial concentration of methane in the supramolecular entities originated by the surfactant at those concentrations.

Once demonstrated that methane could be retained inside micellar aggregates, we run a series of experiments to evaluate whether or not the reaction of ethyl diazoacetate and methane, previously developed in scCO_2 as the reaction medium, would take place in this water-surfactant environment, using the same catalyst, the silver complex $\text{Tp}^{(\text{CF}_3)_2, \text{Br}}\text{Ag}(\text{thf})$. Thus, the catalyst (0.016 mmol) and ethyl diazoacetate (0.5 mmol) were added to water solutions of the five surfactants shown in Figure 1, within the 200-300 mM concentration, in a pressure vessel, which were pressurized with 160 atm of methane. The mixture was stirred for 14 h at room temperature before analysis (see ESI). In the blank experiment (Table 1, entry 1), carried out with the same loadings of catalyst, EDA and methane pressure, but lacking of any surfactant, neither product formation nor ethyl diazoacetate consumption were observed. Fortunately, the presence of the surfactants led, in some cases, to minor but detectable amounts of ethyl propionate, the product derived from the metal-catalyzed transfer of the CHCO_2Et unit from $\text{N}_2=\text{CHCO}_2\text{Et}$. Thus, no reaction was observed (EDA remaining unaltered) with Triton X-100 or DTAC as additives (entries 2-3). The use of TPGS-750-M allowed the formation of some ethyl propionate (2%), but it was the presence of SDS that led to a 10% yield (EDA-based) of the ester. In spite of being the latter the less efficient in terms of methane trapping (Figure 1), the aggregates are by far more appropriate to accommodate reactants and catalyst in the concentrations and time required for the catalytic reaction.

The initially added ethyl diazoacetate that is not incorporated to the product is consumed in the functionalization of the hydrocarbon chains of the surfactant,[†] as well as in the formation of ethyl glycolate ($\text{HOCH}_2\text{CO}_2\text{Et}$) derived from H_2O functionalization. Also, the olefins derived from the coupling of two carbene groups, which are frequently detected in these transformations,⁹ are formed in very low yield (< 2%).

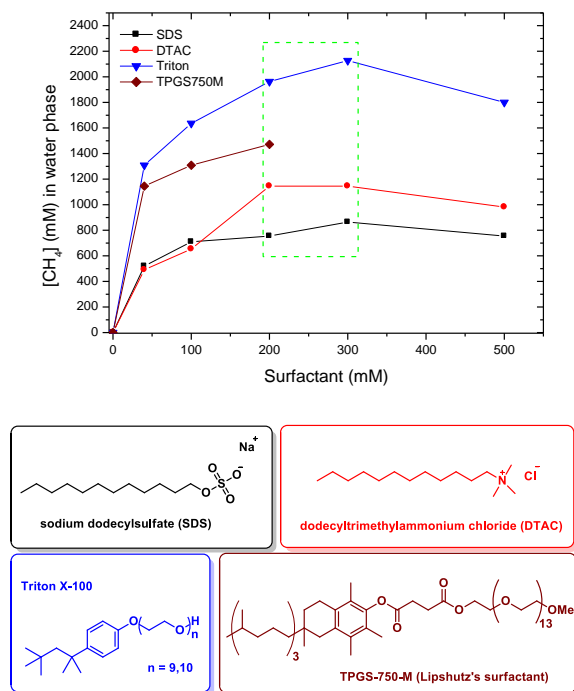


Fig. 1. Variation of the methane uptake into water solutions of surfactants, at variable concentration and at room temperature. The green box highlights the region of maximum uptake.

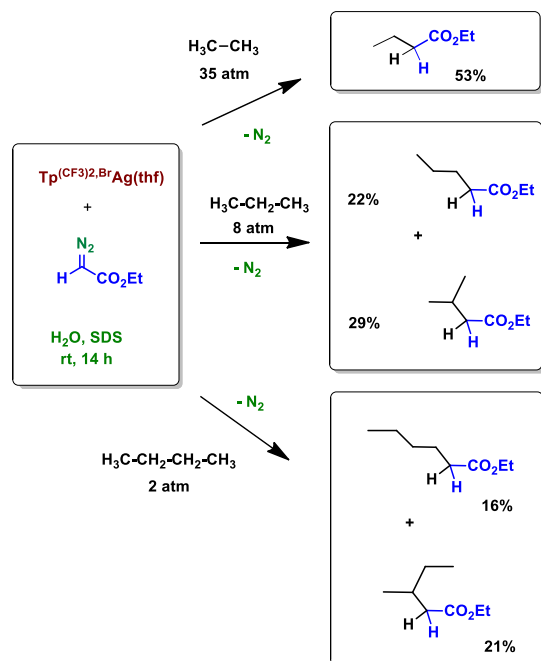
fraction),⁸ the addition of surfactant originates a remarkable increase in solubility, which can only be explained as derived from trapping by the micelles formed from surfactant molecules. We prefer the use of *methane trapped* instead of *dissolved*, since it is the micelle that concentrates the gas: in its absence, the concentration of methane in water is neglectable. Figure 1 shows the variation of methane solubility with respect to the concentration of surfactant in water, with four representative examples of the latter: sodium dodecyl sulfate (SDS), Triton X-100, dodecyltrimethylammonium chloride (DTAC) and TPGS-750-M, the most popular one due to Lipshutz's studies.⁴ As shown in Figure 1, a similar behavior was observed with the array of surfactants: methane uptake increases with the concentration of surfactant reaching a maximum in the ca. 200-300mM interval to smoothly decrease from that range. The degree of trapping of methane into the surfactant solution fall within the 700-2100 mM for that region (the green box in Figure 1). It is noteworthy that these values are several orders of magnitude higher than the solubility of

Table 1. The catalytic functionalization of methane in water-surfactant mixtures.^a

Entry	Surfactant	Yield (%)
1	none	0
2	Triton X-100	0
3	DTAC	0
4	TPGS-750-M	2
5	SDS	10

^a [Ag]:[EDA] ratio of 1:50, 0.01 mmol of catalyst employed. $P_{\text{CH}_4} = 160$ atm in 20 mL of water and 200-300 mM of surfactant. See ESI for details.

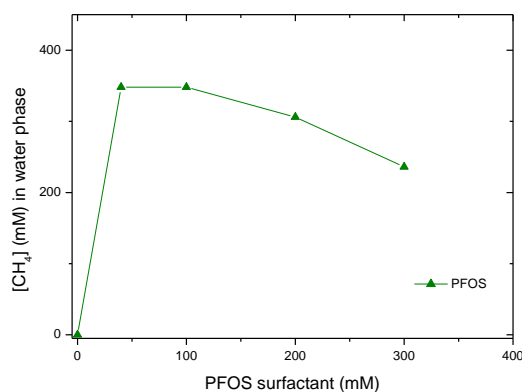
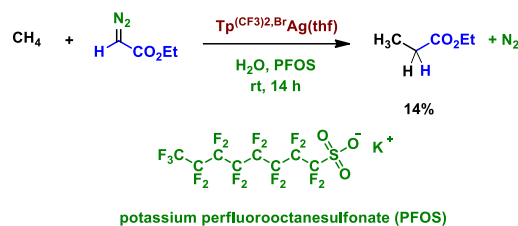
Other gaseous alkanes as ethane, propane and butane have also been tested as substrates (Scheme 3). EDA-based yields within the range of 37-53% were observed. For these alkanes the pressure employed was substantially lower than that used with methane, ranging from 35 atm for ethane to just 2 atm for butane. With propane and butane, two products are obtained, derived from the functionalization of primary and secondary sites. The regioselectivity observed, similar for both substrates (43:57, primary to secondary), was also quite



Scheme 3. Catalytic functionalization of C2-C4 gaseous alkanes in water at room temperature. Percentages correspond to yields, the ratio of products derived from primary:secondary functionalization is 43:57 in both cases.

similar to that previously found¹⁰ in *scCO*₂ (44:56), indicating that the catalytic reaction *per se* is not affected neither by the micelle nor by the reaction medium. We interpret this as a proof of the role of the micelle as the reactor vessel at the molecular scale, meaning that bringing in reactions from other media to this water-surfactant mixture should not have influence in the reaction outcome (catalyst activity and selectivity). Again, formation of ethyl glycolate and incorporation into the SDS alkyl chain were also observed.

After those studies with SDS as the surfactant, and in order to avoid the aforementioned functionalization of the alkyl chains, we decided to employ the fluorinated potassium perfluorooctanesulfonate (PFOS). As shown in Scheme 4, the study of methane uptake by water-PFOS mixtures showed a similar pattern to that of the other surfactants depicted in Figure 1. When the reaction of methane and ethyl diazoacetate in the presence of the silver catalyst was run in a 40 mM solution of PFOS, ethyl propionate was formed in 14%, based on initial EDA, the remaining diazo compound being converted into ethyl glycolate. It is worth mentioning that at a surfactant concentration of 200 mM, SDS retains ca. three

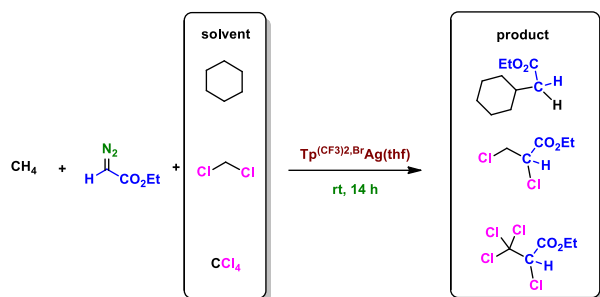


Scheme 4. Top: Methane functionalization in water-PFOS. Bottom: The variation of methane uptake in water-PFOS mixtures.

times more methane than PFOS. Thus, the yield is not only dependent of the amount of methane trapped in the aggregates but also of the relative amounts of catalyst and EDA. A theoretical model of this system is currently under development.

After the experimental results previously presented, a general comment of the benefit of this strategy must be provided. In our previous work,⁷ the formation of ethyl propionate from the silver-catalyzed reaction of methane and ethyl diazoacetate takes place at a ca. 30 % yield (EDA-based) when using supercritical carbon dioxide at 40 °C. When other solvents were employed instead the water/surfactant mixtures, under the same experimental conditions (same catalyst loading, catalyst to EDA ratio, methane pressure, room temperature, as in Table 1), the major /unique products were those resulting from C-H or C-Cl bond functionalization (Scheme 5). This is the result of two factors: on one hand, the higher nucleophilicity (and thus higher reactivity toward the silver-carbene intermediate) of those bonds compared with that of methane. A recent work¹¹ from our laboratory has provided a quantitative scale of reactivity for a number of C-H bonds of alkanes, with that of methane as the reference. For instance, the C-H bonds of hexane are 49 (C1-H), 95 (C2-H) and 40 (C3-H) times more reactive than the C-H bond of methane. On the other hand, solubility of methane in those solvents is low,¹² compared with the concentrating effect of the surfactants.

Thus, the use of water-surfactant mixtures provides an alternative reaction medium for this transformation, where



Scheme 5. Use of other solvents instead water/surfactant mixtures. Main product obtained corresponds to C-H or C-Cl solvent functionalization.

the surfactant aggregates offer an appropriate environment for the catalyst and reactants to verify the targeted transformation. The observation of similar regioselectivities for propane and butane both in scCO₂ and micellar medium indicate that catalyst-reactant interactions are similar and independent of the reaction media. The functionalization of water as a side reaction is yet a drawback that must be overcome with a better design of the micelles. However, we believe that the use of water instead of carbon dioxide or organic solvents make of this example a greener approach in the field of alkane functionalization.

Conclusions

The results described constitute the first example of the catalytic functionalization of methane in water at room temperature, using micellar catalysis. Studies with propane and butane have shown that the selectivity of the catalyst is identical to that observed in scCO₂. The mechanism of the reaction is not affected but the local high concentration inside the micelles provides milder reaction conditions. Given that metal-carbene transfer reactions constitute a model for metal-oxo transfer processes, and in view of the importance of the latter in biological reactions, we believe that this strategy

constitutes a starting point in a different biomimetic approach in the field of catalysis.

Conflicts of interest

There are no conflicts to declare.

Acknowledgments

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