

Catalytic Asymmetric Alkylation in Water in the Presence of Surfactants

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Abstract: Asymmetric palladium-catalyzed alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate occurs in water in the presence of surfactants and a base. The efficiency as well as the enantioselectivity of the coupling reaction depend strongly on the nature and the concentration of the surfactant. The highest yield and enantioselectivity (up to 91%) was obtained using Binap as the ligand in the presence of a cationic surfactant, while neutral or zwitterionic surfactants gave poorer results; anionic surfactants gave no reaction at all. The best results

were obtained using Na_2CO_3 , NaHCO_3 , or K_2CO_3 , among the bases used. The highest enantioselectivities were obtained when the reaction was performed in the presence of chiral atropoisomeric diphosphines such as Binap, Biphemp, or MeOBiphep. A supported cationic surfactant was also used successfully in this reaction, allowing an easier separation of the product.

Keywords: allylic substitution; asymmetric catalysis; palladium; surfactants; water

Introduction

Organometallic homogeneous catalysis is now a widely-used methodology in organic synthesis, and the number of applications for the mild and highly selective production of various chemicals is increasing.^[1,2] However, most chemical transformations of organic substrates are performed in organic solvents, in the laboratory as well as in industry. The substitution of organic solvents by water in both industrial and academic research seems advantageous;^[3] indeed, water is safe, benign, non-toxic, environmentally friendly, and cheap compared to organic solvents. However, most organic products as well as organometallic catalysts are insoluble in water. In order to circumvent these problems, one possibility is the use of a two-phase organic solvent-water system, the catalyst being localized in the water by the use of water-soluble ligands. The main drawback of such a system is the phase-transfer limitation leading to very low reaction rates.

The use of water-soluble ligands also offers the possibility to perform organometallic catalysis in water alone. Many water-soluble ligands have been used in association with organometallic complexes; however, these ligands are generally difficult to prepare, particularly in the case of chiral ligands. Moreover, the organic substrates have to show some significant water solubility. Another elegant approach is the use of surfactants, which solubilize both the organic reactants and products and the organometallic catalyst. This

approach has been successfully applied in asymmetric hydrogenation,^[4–15] hydroformylation,^[16] Suzuki coupling,^[12,17–20] and aldol reactions.^[21] In asymmetric hydrogenation, higher enantioselectivities than those observed in organic solvents have been obtained under these conditions in the reduction of α -amino acid precursors using rhodium complexes, and this concept has been extended to the asymmetric hydrogenation in a membrane reactor equipped with an ultrafiltration membrane.

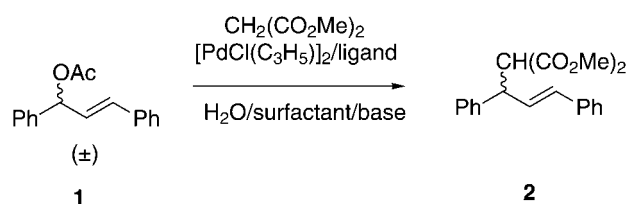
Carbon-carbon bond formation is a general aim in transition metal-catalyzed organic synthetic chemistry, in particular in an asymmetric fashion. One of the most widely used methodologies for this purpose is the palladium-catalyzed reaction of allylic acetates with carbon nucleophiles, the so-called Tsuji–Trost reaction.^[22] Very high enantioselectivities have been obtained using diphosphines, aminophosphines, or bisoxazolines as the chiral ligands.^[23] Uozumi et al. showed that an amphiphilic resin-supported palladium complex was active in this alkylation reaction, the catalyst being recycled without loss of activity.^[24] Asymmetric allylic alkylation was also performed using an immobilized palladium complex of a chiral ligand on an amphiphilic resin, with an enantioselectivity of up to 98%.^[25,26]

We^[27] and Kobayashi and coworkers^[28] recently showed that the palladium-catalyzed alkylation of hydrophobic substrates can be performed with high rates in water in the presence of various surfactants, including in an asymmetric fashion. Here we report a

more detailed study on this palladium-catalyzed alkylation reaction in water in the presence of surfactants, and the influence of various parameters (nucleophile, surfactant, base, ligand, etc.) on both the efficiency and the enantioselectivity of the reaction.

Results and Discussion

We chose the asymmetric palladium-catalyzed alkylation of 1,3-diphenyl-2-propenyl acetate **1** with dimethyl malonate as the standard reaction for our study (Scheme 1).



Scheme 1.

Influence of the Nature of the Surfactant

The effect of the nature of the surfactant on both the enantioselectivity and the catalytic activity was first investigated, using $[\text{Pd}(\eta^3\text{-C}_3\text{H}_5)\text{Cl}]_2$ associated with (*R*)-Binap as the catalyst, and K_2CO_3 as the base. The results obtained are summarized in Table 1.

The highest catalytic activity and enantioselectivity were obtained using the cationic surfactant *n*- $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{HSO}_4$: the alkylation product **2** was obtained quantitatively after only 1 h reaction with 91% ee (Table 1, entry 2). The use of *n*- $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{Br}$ gave only 47% conversion to **2** with 29% enantioselectivity (Table 1, entry 3). When *n*- $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{OH}$ was used both as the surfactant and as the base, no alkylation product was detected, 1,3-diphenyl-2-propen-1-ol being formed quantitatively instead (Table 1, entry 4).

No reaction occurred at all when anionic surfactants such as $\text{C}_{12}\text{H}_{25}\text{OSO}_3\text{Na}$ or $\text{C}_{12}\text{H}_{25}\text{SO}_3\text{Na}$ were used (Table 1, entries 5 and 6), although these surfactants were among the most effective in the asymmetric hydrogenation of amino acid precursors in water.^[5,9]

The use of neutral surfactants such as Brij 35, Tween 40, or Triton X-100, allowed the complete conversion of the allylic acetate, although the observed enantioselectivities are lower: 81, 67, and 86% ee, respectively (Table 1, entries 7–9). Finally, zwitterionic surfactants such as DeDAPS, DDAPS, or HDAPS, gave lower conversions; however, enantioselectivities up to 74%, 82%, and 81% ee were obtained, respectively (Table 1, entries 10–12).

It is well known that the nature of the surfactant plays a very important role in micellar catalysis.^[29] If we

Table 1. Influence of the nature of the surfactant on the yield and enantioselectivity.^[a]

Entry	Surfactant	Yield in 2 [%] ^[b]	ee [%] ^[b] (<i>S</i>)
1	none	45 (62) ^[c]	85 (89) ^[c]
2	$\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{HSO}_4$	100	91
3	$\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{Br}$	47	29
4	$\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{OH}$ ^[d]	0 ^[e]	–
5	$\text{C}_{12}\text{H}_{25}\text{OSO}_3\text{Na}$	0	–
6	$\text{C}_{12}\text{H}_{25}\text{SO}_3\text{Na}$	3	–
7	Brij 35	98	81
8	Tween 40	100	67
9	Triton X-100	98	86
10	DeDAPS	89	74
11	DDAPS	78	82
12	HDAPS	76	81

^[a] **[1]** = 75 mmol L^{−1}; **[1]**/**[Pd]**/**[(*R*)-Binap]**/**[surfactant]**/**[CH₂(CO₂CH₃)₂] / **[base]** = 20/1/2/13.3/60/60; H₂O = 8 mL; 25 °C; 1 h. $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{HSO}_4$ or cetyltrimethylammonium hydrogen sulfate; $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{Br}$ or cetyltrimethylammonium bromide; $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{OH}$ or cetyltrimethylammonium hydroxide; $\text{C}_{12}\text{H}_{25}\text{OSO}_3\text{Na}$ or sodium dodecyl sulfate; $\text{C}_{12}\text{H}_{25}\text{SO}_3\text{Na}$ or sodium dodecyl sulfonate; Brij 35 or polyoxyethylene[23] lauryl ether; Tween 40 or polyoxyethylene sorbitan monopalmitate; Triton X-100 or polyethyleneglycol mono[4-(1,1,3,3-tetramethylbutylphenyl)]-ether; DeDAPS or *N*-decyl-*N,N*-dimethyl-3-ammonio-1-propanesulfonate; DDAPS or *N*-dodecyl-*N,N*-dimethyl-3-ammonio-1-propanesulfonate; HDAPS or *N*-hexadecyl-*N,N*-dimethyl-3-ammonio-1-propanesulfonate.**

^[b] Determined by GC and HPLC.

^[c] After 4 h reaction.

^[d] Without K_2CO_3 , 3 equiv. $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{OH}$.

^[e] 99% alcohol was formed.

consider that the alkylation reaction is roughly a bimolecular reaction between a neutral substrate, namely the π -allyl system, and an anion, in this case the malonate anion, then the rate of the reaction will increase in the presence of cationic surfactants. Moreover, Trost et al.^[30] noticed a very important influence of the nature of the ion pair of the attacking nucleophile on the enantioselectivity of the reaction. In the case of $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{HSO}_4$, probably some ammonium salt of dimethyl malonate exists in equilibrium with the corresponding potassium salt. The enhancement in activity could be due to the formation of this ammonium salt, with a structure quite close to the surfactant. The different behavior observed for *n*- $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{HSO}_4$, *n*- $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{Br}$, and *n*- $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{OH}$ are due to the different counterions and, perhaps, to the degree of dissociation of these ion pairs.

Conversely, no reaction was observed at all using anionic surfactants. These surfactants probably inhibited the alkylation reaction by repelling the reactive anionic nucleophile and keeping it away from the micellar solubilized π -allyl intermediate. Another possibility is an exchange between $\text{C}_{12}\text{H}_{25}\text{OSO}_3^-$ or

$C_{12}H_{25}OSO_3^-$ and Cl^- , leading to a new palladium catalyst bound to the cationic micelle which stays outside on the surface of the micelle; since the hydrophobic allylic acetate is expected to be inside the micelle, the π -allyl complex cannot be formed and the alkylation reaction cannot occur. Finally it is well known that neutral or zwitterionic surfactants generally do not have a large effect on such reaction.

Influence of the Nature of the Base

The effect of inorganic bases on both the enantioselectivity and the catalytic activity was then investigated, using $[Pd(\eta^3-C_3H_5)Cl]_2$ associated with (*R*)-Binap as the catalyst, and $n-C_{16}H_{33}NMe_3 HSO_4$ as the surfactant. All the experiments were performed in water with and without surfactant. The results summarized in Table 2 show that the best results were obtained using potassium carbonate, sodium carbonate, or sodium hydrogen carbonate as the base. Enantioselectivities as high as 94% were obtained in the presence of $NaHCO_3$ or Na_2CO_3 (Table 2, entries 1 and 2 and 4–7); it is to be noted that the observed enantioselectivity in water without surfactant was lower. Comparison of the experi-

ments conducted in water in the absence and the presence of surfactant showed the beneficial effect of this surfactant on the catalytic activity, the alkylation being almost quantitative in the presence of this surfactant; alkylation consistently occurred in water without surfactant but with lower conversion except in the case of $NaHCO_3$. The use of silver, calcium, barium, or caesium carbonate gave lower conversions in the presence of this surfactant, although the observed enantioselectivities are also high (Table 2, entries 8–13 and 15 and 16); the formation of a large amount of 1,3-diphenyl-2-propenol arising from the saponification of the acetate was also observed in these cases. The same trends were noticed using the neutral surfactant Brij. High activity and enantioselectivity were observed using K_2CO_3 as the base (Table 2, entry 3), and very low activities were found in the presence of $BaCO_3$ or Cs_2CO_3 (Table 2, entries 14 and 17).

While the nature of the base seemed to have little influence on the enantioselectivity, except for $CaCO_3$, the highest conversions were obtained in the presence of the more water-soluble bases K_2CO_3 , Na_2CO_3 , and $NaHCO_3$. While the solubility of $CsCO_3$ in water is very high, the lower activity observed in this case could be due to the larger radius of caesium compared to potassium and sodium.

Table 2. Influence of the base on the yield and enantioselectivity.^[a]

Entry	Base	Surfactant	Yield in 2 [%] ^[b]	ee [%] ^[b] (<i>S</i>)
1	K_2CO_3	none	45	85
2	K_2CO_3	CTAHSO ₄	100	91 ^[c]
3	K_2CO_3	Brij	98	81
4	Na_2CO_3	none	7	87
5	Na_2CO_3	CTAHSO ₄	86	94
6	$NaHCO_3$	none	62	91
7	$NaHCO_3$	CTAHSO ₄	95	94
8	Ag_2CO_3	none	2	–
9	Ag_2CO_3	CTAHSO ₄	4 ^[d]	91
10	$CaCO_3$	none	13 ^[e]	64
11	$CaCO_3$	CTAHSO ₄	33 ^[f]	54
12	$BaCO_3$	none	8	90
13	$BaCO_3$	CTAHSO ₄	35 ^[e, g]	82
14	$BaCO_3$	Brij	2 ^[h]	–
15	Cs_2CO_3	none	4	87
16	Cs_2CO_3	CTAHSO ₄	64 ^[i]	90
17	Cs_2CO_3	Brij	15 ^[j]	66

^[a] **[1]** = 75 mmol L^{−1}; **[1]/[Pd]/[(*R*)-Binap]/[surfactant]/[CH₂(CO₂CH₃)₂]/[base] = 20/1/2/13.3/60/60; H₂O = 8 mL; 25 °C; 1 h.**

^[b] Determined by GC and HPLC.

^[c] $[\alpha]_D^{20}$: −12.5 (*c* 2, CHCl₃).

^[d] 40% alcohol was formed.

^[e] 8% alcohol was formed.

^[f] 24% alcohol was formed.

^[g] 11% alcohol was formed.

^[h] 35% alcohol was formed.

^[i] 18% alcohol was formed.

Influence of the Surfactant Concentration

We thought that the increase in activity was due to micellar effects. In order to prove this assumption, we performed the alkylation reaction using K_2CO_3 as the base under different concentrations of $n-C_{16}H_{33}NMe_3 HSO_4$ (Table 3). Indeed, the conversion was low when the reaction was performed using a concentration of the surfactant lower than its cmc (0.4 mmol L^{−1});^[31] below

Table 3. Influence of the surfactant concentration on the yield and enantioselectivity.^[a]

Entry	[Surfactant] mmol L ^{−1}	Yield in 2 [%] ^[b]	ee [%] ^[b] (<i>S</i>)
1	0	45	85
2	0.18	56	86
3	0.51	61	87
4	0.88	95	89
5	14.50	92	88
6	24.60	89	94
7	33.75	94	90
8	50.00	100	91
9	59.50	44	85
10	75.75	27	79

^[a] **[1]** = 75 mmol L^{−1}; **[1]/[Pd]/[(*R*)-Binap]/[CH₂(CO₂CH₃)₂]/[base] = 20/1/2/60/60; H₂O = 8 mL; 25 °C; 1 h.**

^[b] Determined by GC and HPLC.

0.51 mmol L⁻¹ (Table 3, entries 1–3), conversions not higher than 61% were obtained, with enantioselectivities of up to 87% ee. When the concentration of *n*-C₁₆H₃₃NMe₃ HSO₄ was higher than the cmc, the conversion of the allylic acetate **1** was almost quantitative (Table 3, entries 4–8), with enantioselectivities reaching 94% ee. It is to be noted that increasing amount of *n*-C₁₆H₃₃NMe₃ HSO₄ could also afford a higher concentration of the ammonium salt of dimethyl malonate in the medium, leading to higher activity and enantioselectivity. However, when the concentration of the surfactant was higher than 50 mmol L⁻¹ (Table 3, entries 9 and 10), the conversion as well as the enantioselectivity decreased; the lower activity could be due to the stickiness of the solution, or eventually to a change in aggregation-morphology of the amphiphile.

Influence of the Temperature

The influence of the temperature on both the catalytic activity and the enantioselectivity was also studied (Table 4). Increasing the temperature of the reaction in the presence of *n*-C₁₆H₃₃NMe₃ HSO₄ gave lower conversion to the alkylation product: 88%, 55%, and 65%, at 35, 55, and 75 °C, respectively, while performing the reaction at 0 °C gave practically no conversion. Increasing the reaction temperature disfavored the micelle formation, and consequently gave lower conversion. We noticed also that the enantioselectivity of the alkylation reaction decreased with increasing temperature, as usually expected in such a process.

Influence of the Nucleophile Concentration

The results relating to the influence of the concentration of the nucleophile, the ratio [CH₂(CO₂CH₃)₂]/[K₂CO₃] being held constant, on both the catalytic activity and the enantioselectivity are summarized in Table 5. In water without surfactant, we observed only a slight increase in conversion after 1 h with increasing amount

Table 5. Influence of the nucleophile concentration on the yield and enantioselectivity.^[a]

Entry	[Nucleophile]/[1]	Surfactant	Yield in 2 [%] ^[b]	ee [%] ^[b] (<i>S</i>)
1	0.6	yes	0 ^[c]	–
2	1.5	no	0	–
3	1.5	no	70 ^[d]	90
4	1.5	yes	4 ^[e]	90
5	1.5	yes	90 ^[d]	70
6	2.0	yes	6 ^[f]	91
7	2.5	no	17	89
8	2.5	yes	93 ^[g]	95
9	3	no	45	85
10	3	yes	100	91
11	4	no	21	84
12	4 ^[h]	yes	100	91

^[a] [**1**] = 75 mmol L⁻¹; [**1**]/[Pd]/[(*R*)-Binap]/[CTAHSO₄] = 20/1/2/13.3; [CH₂(CO₂CH₃)₂]/[K₂CO₃] = 1/1; H₂O = 8 mL; 25 °C; 1 h.

^[b] Determined by GC and HPLC.

^[c] 62% alcohol was formed.

^[d] After 4 h.

^[e] 20% alcohol was formed.

^[f] 21% alcohol was formed.

^[g] 7% alcohol was formed.

^[h] 16 mL water was used.

of nucleophile, the enantioselectivity varying from 70 to 89%. When 1.5 equivalents of nucleophile were used, 70% transformation of the acetate **1** was observed after 4 h reaction. In the presence of the surfactant, the activity increased drastically with increasing amount of nucleophile, the observed enantioselectivity being quite high and varying from 90 to 95% ee; as for the experiment conducted in water alone, using 1.5 equivalents of nucleophile reduced the catalytic activity, complete conversion being obtained only after 4 h. One reason for this increase in activity could be the higher concentration of potassium malonate as well as ammonium malonate. Indeed, while the formation of the alcohol was observed in the case of a small number of equivalents of dimethyl malonate, this hydrolysis decreased with increasing amount of dimethyl malonate; we expected a competition between the attack of a hydroxide anion and the carbon nucleophile on the π -allyl intermediate, although the former attack is not well documented in the literature. Increasing the amount of the potassium or ammonium salt of dimethyl malonate favored the attack of the carbon nucleophile over the attack of the hydroxide.

Influence of the Ligand

Finally we investigated the influence of the chiral ligand on both the activity and the enantioselectivity of the

Table 4. Influence of the temperature on the yield and enantioselectivity.^[a]

Entry	T [°C]	Yield in 2 [%] ^[b]	ee [%] ^[b] (<i>S</i>)
1	0	9	83
2	20	100	91
3	35	88	90
4	55	55	87
5	75	65	84

^[a] [**1**] = 75 mmol L⁻¹; [**1**]/[Pd]/[(*R*)-Binap]/[CTAHSO₄]/[CH₂(CO₂CH₃)₂]/[base] = 20/1/2/13.3/60/60; H₂O = 8 mL; 1 h.

^[b] Determined by GC and HPLC.

Table 6. Influence of the ligand on the yield and enantioselectivity.^[a]

Entry	Ligand	Surfactant	Yield in 2 [%] ^[b]	ee [%] ^[b]
1	(<i>S,S</i>)-Chiraphos	CTAHSO ₄	0	–
2	(<i>R</i>)-Binap	CTAHSO ₄	100	91 (<i>S</i>)
3	(<i>R</i>)-Binap	none	62	89 (<i>S</i>)
4	(<i>S</i>)-Biphemp	CTAHSO ₄	100	88 (<i>R</i>)
5	(<i>S</i>)-Biphemp	none	62	88 (<i>R</i>)
6	(<i>R</i>)-MeOBiphep	CTAHSO ₄	100	92 (<i>S</i>)
7	(<i>R</i>)-MeOBiphep	none	56	90 (<i>S</i>)
8	(<i>R</i>)-Quinap	CTAHSO ₄	50	65 (<i>R</i>)
9	(<i>R</i>)-Quinap	Tween 40	2	–
10	(<i>R,R</i>)-Trost ligand	CTAHSO ₄	56	52 (<i>R</i>)
11	(<i>R,S</i>)-Josiphos	CTAHSO ₄	10	66 (<i>S</i>)
12	(<i>R</i>)-Ph-Box	CTAHSO ₄	0	–
13	(<i>R</i>)-Ph-Box	Tween 40	0	–

^[a] **[1]** = 75 mmol L^{−1}; **[1]**/**[Pd]**/**[ligand]**/**[surfactant]**/**[CH₂(CO₂CH₃)₂]/**[base]** = 20/1/2/13.3/60/60; H₂O = 8 mL; 25 °C; 1 h. (*S,S*)-Chiraphos or (*2S,3S*)-2,3-bis(diphenylphosphanyl)butane, (*R*)-Binap or (*R*)-2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl, (*S*)-Biphemp or (*S*)-6,6'-dimethyl-2,2'-bis(diphenylphosphanyl)-1,1'-biphenyl, (*R*)-MeOBiphep or (*R*)-6,6'-dimethoxy-2,2'-bis(diphenylphosphanyl)-1,1'-biphenyl, (*R*)-Quinap or (*R*)-(2-diphenylphosphanyl-1-naphthyl)isoquinoline, (*R,R*)-Trost ligand or (*1R,2R*)-1,2-bis[2'-(diphenylphosphanyl)benzoyl]aminocyclohexane, (*R,S*)-Josiphos or (*R*)-1-[(*S*)-2-(diphenylphosphanyl)ferrocenyl]ethylidicyclohexylphosphine, (*R*)-Ph-Box or (*R*)-2,2'-isopropylidenebis(4-phenyl-2-oxazoline).**

^[b] Determined by GC and HPLC.

^[c] 40% alcohol was formed.

alkylation reaction, CTAHSO₄ being used as the surfactant. Chiraphos gave no reaction at all (Table 6, entry 1). Among the other ligands used, the atropoisomeric ligands gave the more active and enantioselective catalysts. Binap, Biphemp, and MeOBiphep, gave a complete conversion in the alkylation product with enantioselectivities of 91%, 88%, and 92%, respectively (Table 6, entries 2, 4, and 6). Performing the reaction without surfactant gave nearly the same enantioselectivities, although the observed activities are lower (Table 6, entries 3, 5, and 7). It is to be noted that these enantioselectivities are quite close to those observed when the reaction was performed in THF.^[32] Quinap or Trost's ligand gave moderate enantioselectivities (65% and 52% ee, respectively), and conversions (Table 6, entries 8 and 10), lower than those obtained in an organic solvent^[32]. Josiphos gave also moderate enantioselectivity (66% ee), but with very low conversion (10%) (Table 6, entry 11). Practically no conversion was observed using Quinap as the ligand in the presence of a neutral surfactant such as Tween 40 (Table 6, entry 9). Finally, the bisoxazoline ligand Ph-Box gave no reaction at all in the presence of CTAHSO₄ or Tween 40 (Table 6, entries 12 and 13). The very low activities observed in the case of ligands bearing an imine function (Josiphos, Ph-Box) could be due to the hydrolysis of this double bond in water; as the reaction did not occur in the presence of a neutral surfactant, the possible quaternization of the nitrogen by the cationic surfactant can be excluded.

Supported Surfactant

One difficulty in performing organic reactions in water in the presence of surfactants is the extraction of the products. Indeed, the phase separation after reaction becomes difficult due to the amphiphilization of the interface. One way to solve this problem and eventually to recycle the surfactant and the catalyst is the use of immobilized surfactant. Such an approach has already been demonstrated by different groups using amphiphilic resin-supported organometallic catalysts^[14,24–26,33–39] or by anchoring the surfactant on a mesoporous material.^[40,41]

We used the supported cationic surfactant **3** (Scheme 2), having a loading value in ammonium salt of *ca.* 0.67 mmol g^{−1} in this asymmetric alkylation reaction. The results obtained using different amounts of this immobilized surfactant are summarized in Table 7. The highest conversion (74%) was obtained

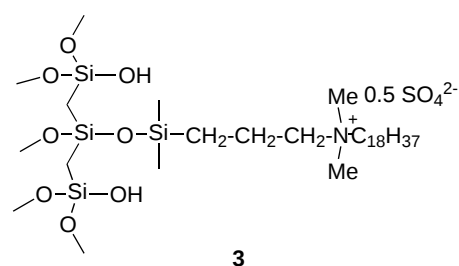
**Scheme 2.**

Table 7. Yield and enantioselectivity obtained using the immobilized surfactant **3**.^[a]

Entry	[Cation]	Yield in 2 [%] ^[b]	ee [%] ^[b] (<i>S</i>)
1	5.3	21	92
2	6.2	41	86
3	10.4	74	91
4	13.7	67	80
5	18.7	48	92

^[a] **[1]** = 75 mmol L⁻¹; **[1]**/**[Pd]**/**[(R)-Binap]**/**[CH₂(CO₂CH₃)₂]/**[K₂CO₃]** = 20/1/2/60/60; H₂O = 8 mL; 1 h.**

^[b] Determined by GC and HPLC.

using a concentration of the surfactant around 10 mmol L⁻¹; however this value is lower than that obtained using CTAHSO₄ itself. The same enantioselectivity, up to 92%, was obtained however. Unfortunately although the separation of the products was easier, all attempts to recycle the catalyst and the surfactant were unsuccessful.

Conclusion

In conclusion, we have shown that palladium-catalyzed alkylation of allylic acetates occurred in water in the presence of suitable surfactants with both very high activity and enantioselectivity. The activity was lower when the reaction was performed in the absence of surfactants. The highest activities were obtained in the presence of cationic surfactants, and also neutral or zwitterionic surfactants, while no reaction occurred in the presence of anionic surfactants. A suitable choice of the surfactant (*n*-C₁₆H₃₃NMe₃HSO₄), the base (Na₂CO₃, NaHCO₃, or K₂CO₃), the surfactant concentration (higher than the cmc), the nucleophile concentration ([dimethyl malonate]/[allylic acetate] = 3), the temperature (25 °C), and the nature of the chiral ligand (Binap, Biphep, or MeOBiphep) allowed the quantitative preparation of the alkylated product with an enantioselectivity up to 92%. A supported cationic surfactant gave the same enantioselectivity under these optimized conditions, although the activity of the catalyst was lower.

Experimental Section

General Remarks

All reactions were conducted in Schlenk tubes under nitrogen. NMR spectra were recorded on a Bruker 300 MHz instrument and referenced to Me₄Si as internal standard. Conversion was determined by GC using a Quadrex OV1 column (30 m × 0.25 mm), enantiomeric excess was determined by HPLC with

Chiralpak^{AD} column (25 cm × 4.6 mm) using hexane-propanol (6/4) as the eluent.

All detergents and most of the ligands were purchased from commercial sources and used as obtained. CTAHSO₄, CTABr, CTAOH, SDS, Brij 35, Tween 40, Triton X-100, DeDAPS, DDAPS, HDAPS, Chiraphos, Josiphos, Ph-Box, were obtained from Aldrich, [PdCl(C₃H₅)₂], Binap, Quinap, Trost's ligand, from Strem, SDS from Acros. Biphep and MeOBiphep were a gift from Hoffmann la Roche Ltd. The supported cationic surfactant was a gift from Professor G. Oehme (Rostock). 1,3-Diphenylprop-2-enyl acetate was prepared in accordance with the literature.^[42]

Typical Procedure

A mixture of [PdCl(C₃H₅)₂] (5.5 mg, 15 μmol), the appropriate ligand (60 μmol), and eventually the surfactant (0.2 mmol) in water (4 mL) was stirred in a Schlenk tube for 15 min. This solution was added to a Schlenk tube containing the allylic 1,3-diphenyl-2-propenyl acetate (151.4 mg, 0.6 mmol) and diphenyl ether (102.1 mg, 0.6 mmol), as the internal standard. After 10 min, this solution was transferred to another Schlenk tube containing K₂CO₃ (249 mg, 1.8 mmol), dimethyl malonate (237.8 mg, 1.8 mmol), and eventually the surfactant (0.2 mmol) in water (4 mL). After being stirred for the indicated time, THF (2 mL) was added to the mixture and the solution was filtered. Evaporation of the solvents gave a residue which was purified by chromatography. The conversion was determined by GC and the enantioselectivity by HPLC.

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