JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

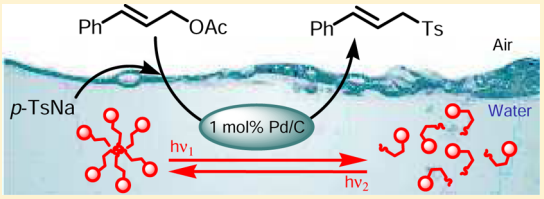
Micellar Catalysis Using a Photochromic Surfactant: Application to the Pd-Catalyzed Tsuji–Trost Reaction in Water

Muriel Billamboz, Floriane Mangin, Nicolas Drillaud, Carole Chevrin-Villette, Estelle Banaszak-Léonard, and Christophe Len*

Université de Technologie de Compiègne, Transformation Intégrée de la Matière Renouvelable, EA 4297 UTC/ESCOM, Centre de recherche de Royallieu, BP 20529, F-60205 Compiègne Cedex, France

Supporting Information

ABSTRACT: The first example of a Pd-catalyzed Tsuji–Trost reaction, applied in a photochromic micellar media under conventional heating and microwave irradiation, is reported. The surfactant activity and recycling ability were investigated and compared with those of a few commercially available surfactants. The synthetic photochromic surfactant proved to be efficient, recyclable, and versatile for Pd-catalyzed coupling reactions.



INTRODUCTION

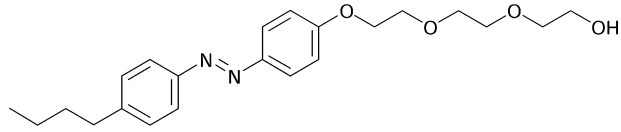
With the notion of green chemistry, organic chemists are strongly encouraged to develop safer protocols. Among the 12 principles that govern green chemistry,[1] organic reactions conducted in safer solvents have received considerable attention.[2] In this context, substantial efforts have been devoted to the development of efficient Pd-catalyzed cross-coupling reactions in aqueous media.[3]

Water as a solvent has many advantages over usual organic solvents: it is the least expensive and safest solvent that is nonflammable, inexplosive, and nontoxic. Water has unique properties in solvating organic molecules, leading to positive effects on reactivities and selectivities.[4] However, the potential scope of aqueous organometallic catalysis is drastically reduced when highly hydrophobic substrates are involved in the chemical transformations. To overcome this problem, different strategies have been studied: the use of organic cosolvents[5] or ionic liquids[6] as well as additives, such as phase transfer agents,[7] cyclodextrins,[8] polymers,[9] or surfactants.[10]

Recently, we have reported the synthesis and use of a novel photochromic azobenzene-based surfactant in acetylation reactions in water.[11] This surfactant was designed to (i) photo-organize and disorganize in aqueous solution, (ii) allow a better extraction of the products formed due to its photochromism property, (iii) facilitate the reactions taking place in an aqueous phase, and (iv) enable the recycling of the aqueous phase. On the basis of these factors, the concept of photochromic surfactant for Pd-catalyzed cross-coupling reactions in water was investigated in one of the most important reactions for carbon–carbon bond formation, the Tsuji–Trost reaction. Pd-catalyzed allylic substitution reactions are widely employed for constructing C–C, C–N, C–S, and C–O bonds with high chemo-, regio-, and stereoselectivities.[12] Surprisingly, the development of the Tsuji–Trost reaction in aqueous photoresponsive micellar media was not described. Herein, we report the scope and limitations of this methodology using conventional and microwave heating under low loading conditions (1 mol % Pd).

RESULTS AND DISCUSSION

Several photoresponsive surfactants have been reported with different photoresponsive groups used to provide structural change.[13] The nonionic surfactant C4-Azo-PEG **1** was selected for this study since ionic surfactants can inhibit the reaction due to electrostatic repulsions at the micelle–water interface.[14] It possesses an azobenzene moiety as the photochromic core, a C4 alkyl chain as a hydrophobic tail, and a polyethyleneglycol (PEG) as a nonionic hydrophilic headgroup (Figure 1).



C4-Azo-PEG **1**

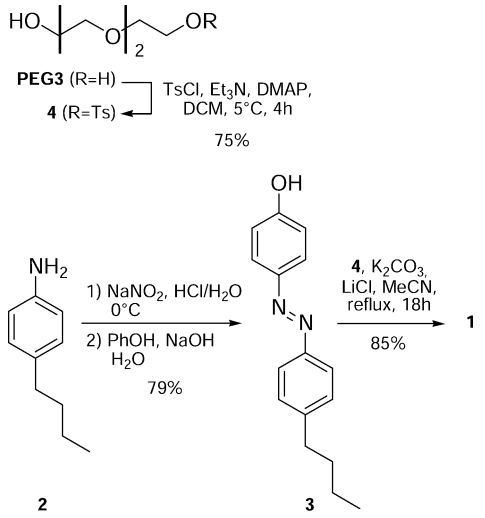
Figure 1. Structure of C4-Azo-PEG **1**.

The synthesis of **1** was first described by Shang et al. in 2003,[15] but the proposed three-step protocol suffers from a very poor overall yield of 3%. For the present work, a modified three-step protocol was followed.[16] Azobenzene **3** was synthesized by oxidative coupling of 4-butylaniline **2** and phenol via the corresponding diazonium salt. Then, a classical Williamson etherification of phenol derivative **3** with the tosylate **4** obtained by selective sulfonatation of the glycol derivative PEG3 furnished the desired C4-Azo-PEG **1** in 50% overall yield (Scheme 1).

Received: August 24, 2013
Published: December 2, 2013

   dx.doi.org/10.1021/jo401737t | J. Org. Chem. 2014, 79, 493–500

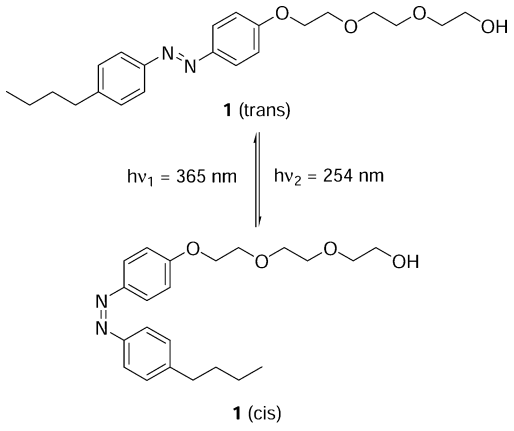
Scheme 1. Synthetic Pathways to C4-Azo-PEG 1



The surface tension measurements of **1** have been previously reported, before and after UV irradiation. It has been clearly demonstrated that **1** forms micelles, and the CMC (critical micellar concentration) of the *trans* and the *cis* forms are 4.1 and 8 μM, respectively.[15]

The *cis*/*trans* equilibrium of **1** was also previously studied with a 200 W mercury lamp.[15] To confirm the ability of the diazo function to isomerize under UV exposure (Scheme 2), **1**

Scheme 2. Isomerization Equilibrium between 1 (*trans*) and 1 (*cis*)



was analyzed by UV/vis absorption spectroscopy. In our hands, using a 500 W mercury lamp, irradiation at 365 nm of **1** (*trans*) in deionized water at room temperature resulted in a substantial change in the UV/vis spectrum of **1**, due to its switching from its *trans* to *cis* isomers. The absorption band at around 320 nm was found to decrease gradually with continued irradiation. At the same time, the bands at around 250 and 420 nm slightly increase. The absorption bands at 320, 250, and 420 nm are ascribed to $\pi-\pi^*$ and $n-\pi^*$ of the *trans* and the *cis* forms of the azo moiety, respectively,[17] which is in accordance with the *trans* photoisomer **1** (*trans*) being converted into its *cis* form. The maximum isomerization yield was obtained after 14 min of irradiation at 365 nm (Figure 2).

When irradiated at 254 nm (Figure 3), the *cis* isomer of **1** returned gradually to its *trans* form, and the maximum isomerization yield was obtained after 6 min of irradiation.

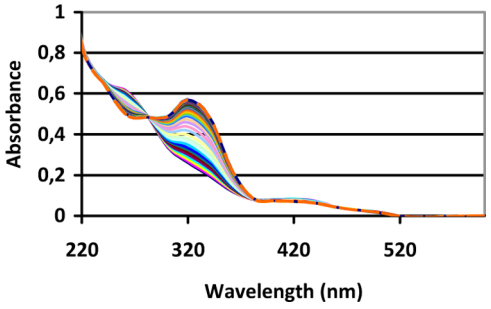


Figure 2. Overlaid UV spectra (1 scan per 15 s, from 0 to 18 min) during the isomerization of **1** at 365 nm (500 W lamp). Sample concentration: 10^{-4} mol/L.

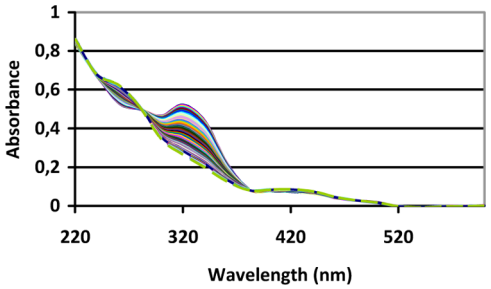


Figure 3. Overlaid UV spectra (1 scan per 15 s, from 0 to 6 min) during the isomerization of **1** at 254 nm (500 W lamp). Sample concentration: 10^{-4} mol/L.

Finally, as already shown for numerous azo derivatives, it must be pointed out that the *cis* isomer could not be isolated in pure form.[18]

Repeating the irradiation of **1** in solution, to switch between isomers did not reveal any degradation of **1**, as the maximum UV spectrum obtained after each irradiation was consistent to the previous one (Figure 4).

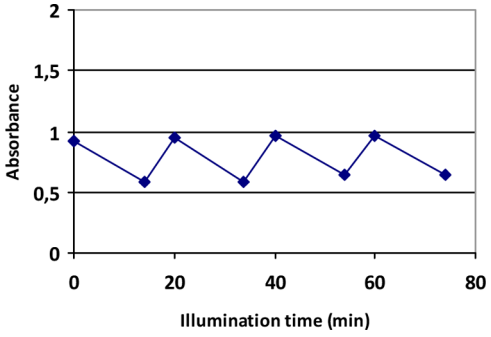


Figure 4. Reversibility of photoisomerization in **1** solution at 2×10^{-4} mol/L for the *trans*-to-*cis* and *cis*-to-*trans* processes. The solution was irradiated alternately with 365 and 254 nm for 14 and 6 min, respectively. The absorbance at the *trans* band was recorded after each illumination.

Results obtained are in accordance with the previously described ability of **1** to photoisomerize without degradation regardless of the power of the mercury lamp (500 W vs 200 W), which only allowed decreasing the time necessary to achieve equilibrium.

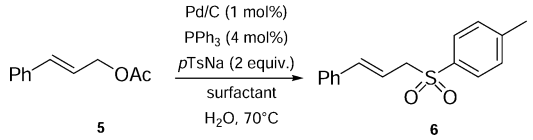
To evaluate the potential of the C4-Azo-PEG **1** in micellar catalysis, the protocol developed in 2005 by Felpin et al. for the 10%Pd/C-mediated allylic substitution in pure water was taken

dx.doi.org/10.1021/jo401737t | J. Org. Chem. 2014, 79, 493−500

as reference.[19] This heterogeneous process uses an inexpensive and environmentally friendly source of Pd since it is immobilized on a support and can be easily removed by simple filtration. Nevertheless, the optimized reaction required a prolonged heating over 18 h. Also, the authors did not evaluate the recyclability of the catalytic system. In the present study, environmental aspects have been respected by minimizing the reaction time and reusing the catalyst.

Cinnamyl acetate **5** was selected as a model substrate with the *p*-toluenesulfinic acid sodium salt (*p*-TsNa) as nucleophile (Scheme 3). Catalyst loading and temperature have been optimized previously (1 mol % of Pd and 70 °C) and will not be extended upon here.

Scheme 3. Tsuji–Trost Coupling Model Reaction in Water



Without any surfactant, a total conversion was observed after 18 h and the desired sulfone **6** was isolated in 86% yield. As the concept of this work is based on the capability of the surfactant to photo-organize and disorganize when submitted to irradiation, the concentration of **1** needs to be comprised between the CMC of the *trans* form (4.1 μM) and the CMC of the *cis* form (8 μM). In this regard, the first trial was conducted with 6 μM of **1**, but at this concentration, no enhancement of the reaction was observed. One potent explanation was the charcoal capacity in adsorbing **1**, leading to a decrease of free C4-Azo-PEG **1** in water. Indeed, UV analysis experiment showed that **1** (CMC *trans* < 6 μM < CMC *cis*) in water in the presence of 20 mg of 10%Pd/C (consistent with the tested Tsuji–Trost experiment) conducted to a concentration of free C4-Azo-PEG **1** of 0.4 μM, 10 times lower than the CMC of the *trans* form (heating this solution did not allow the desorption of the surfactant). To determine the concentration of free C4-Azo-PEG **1** comprised between CMC *trans* and CMC *cis*, a UV analysis experiment was performed. A concentration of **1** (12.3 μM, 3 CMC *trans*) in the presence of 20 mg of 10% Pd/C in water showed the decrease of **1** in solution down to 5.4 μM, between the *trans* form and the *cis* form CMCs (heating this solution desorbed the surfactant to 6.9 μM, still below the *cis* form CMC). Application of the Tsuji–Trost model reaction using **1** (12.3 μM) afforded the target compound **6** in 83% yield after 3 h when 18 h was necessary in the absence of surfactant (Figure 5). Our catalytic system in such conditions was 6 times more efficient with a TOF (turn over frequency) increasing from 1.33×10^{-3} to 7.96×10^{-3} s^{-1}. A rise in concentration of the surfactant **1** to 10 CMC was tested. UV analysis of **1** (41 μM, 10 CMC *trans*) in solution with 10%Pd/C (20 mg) showed a residual concentration of free C4-Azo-PEG **1** in solution down to 18.8 μM, largely above the *cis* form CMC. Using the concentration of surfactant **1** (41 μM), the Tsuji–Trost model reaction permitted furnishing the sulfone **6** in 58% yield after 3 h. To conclude, it seemed that the concentration of free C4-Azo-PEG **1** should be between CMC *trans* and CMC *cis*. Because of the surfactant adsorption capability of the charcoal supporting palladium, the amount of surfactant **1** in the catalyzed Tsuji–Trost reaction has to reach 3 CMC of the *trans* form (12.3 μM).

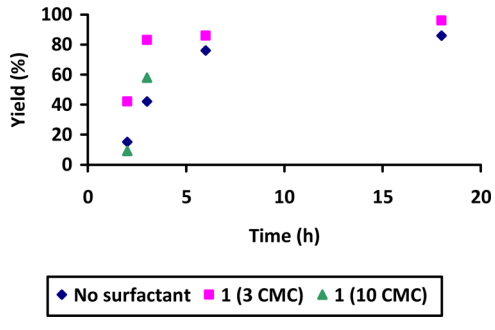


Figure 5. Evolution of yields of reaction versus time.

To test the efficiency of C4-Azo-PEG **1**, three commercially available surfactants: the anionic surfactant SDS (sodium dodecyl sulfate), the cationic surfactant CTAB (cetyl trimethylammonium bromide), and the nonionic PEG-based surfactant Tween 20 (Figure 6) were evaluated for a comparative study in the optimized conditions (*p*TsNa (2 equiv), 10%Pd/C (1 mol %), PPh_3 (4 mol %), surfactant (3 CMC), 70 °C, 3 h).

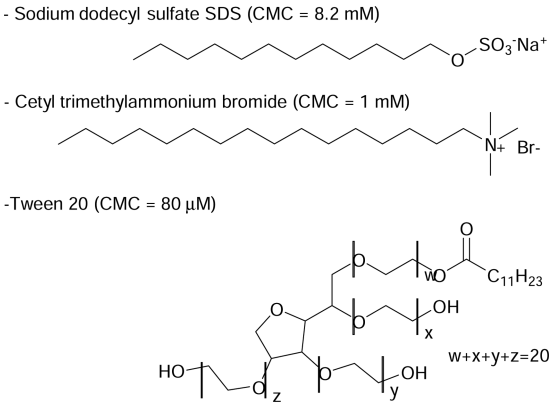


Figure 6. Structure of commercially available surfactants.

When the anionic surfactant SDS was employed, only 26% yield of **6** was isolated (Table 1, entry 2), which was significantly less than the 42% yield obtained in the absence of surfactant (Table 1, entry 1).

This inhibiting effect can be interpreted by electrostatic repulsions between the surfactant and the anionic nucleophile *p*-TsNa at the micelle–water interface.[14] The use of cationic and nonionic surfactants avoided this problem as it can be seen by comparing results for CTAB, Tween 20, and C4-Azo-PEG **1**

Table 1. Surfactant Activities in the First Run under Conventional Heating

entry	surfactant	yield of **6** (%)[b]
1	none	42
2	SDS	26
3	CTAB	80
4	Tween 20	71
5	C4-Azo-PEG	83
6	C4-Azo-PEG[a]	96

[a]Irradiation at 365 nm during 30 min just before extraction. [b]**5** (1 equiv), *p*-TsNa (2 equiv), 10%Pd/C (1 mol %), PPh_3 (4 mol %), surfactant (3 CMC), 70 °C, 3 h.

dx.doi.org/10.1021/jo401737t | J. Org. Chem. 2014, 79, 493–500

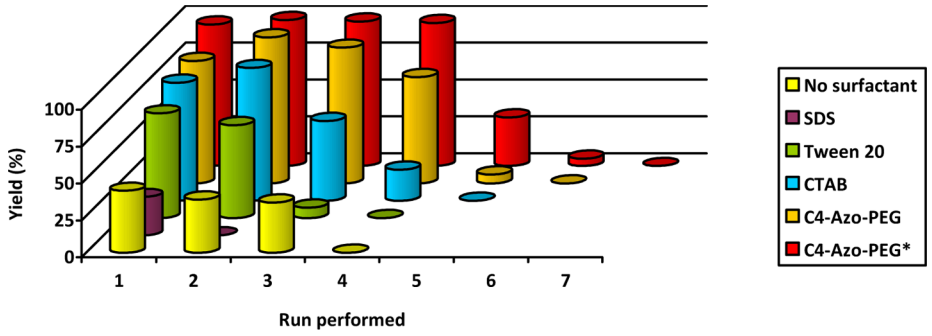


Figure 7. Comparison of recycling abilities under conventional heating.

(80, 71, and 83% yields, respectively). The good result obtained with CTAB was not surprising since it has been previously reported that the CTAB adsorption on the catalyst surface can enhance the reactivity.[20] For all experiments, samples were submitted to the same direct ethyl acetate extraction except for entry 6. It is noteworthy that irradiation coupled with extraction increased the yield to 96% yield (Table 1, entry 6). This difference in yield (13%) could be directly correlated to the photochromic properties of **1**. The photoirradiation directly acts on the surfactant to enable a better extraction of **6** from the media, due to an efficient breakdown of the emulsion, visually seen experimentally (Table 1, entries 5 and 6).

To explore further the scope of C4-Azo-PEG **1** and to develop an efficient green system, recycling experiments were performed for the reaction using 10%Pd/C (1 mol %) and the surfactants at 3 CMC concentration (Figure 7).

After completing each cycle, organic products were extracted three times with ethyl acetate, and cinnamyl acetate **5** (1 equiv), *p*-TsNa (1 equiv), and triphenyl phosphine (4 mol %) were added again to the aqueous phase. The irradiation effect was also evaluated when the reaction was conducted with C4-Azo-PEG **1** (30 min at 365 nm just before extraction). As expected, the 10%Pd/C-SDS system was not recyclable. Even if SDS is known to be a Pd stabilizer,[21] electrostatic repulsions with the anionic nucleophile are predominant and no conversion was observed for the second run. Only two runs with moderate yields (71% and 67% yield, respectively) could be performed with Tween 20 before a dramatic decrease. After five runs were performed with CTAB, a slow decrease at each run was observed until 0% yield was obtained after the fifth run. When the direct extraction treatment was applied, using C4-Azo-PEG **1**, four cycles were achievable in good yields of, respectively, 83, 99, 92, and 72%, after which no further catalytic effect was observed. However, when we pretreated for 30 min with 365 nm irradiation, an increase of yield was observed for each cycle and the catalytic system could be reused for four consecutive runs without any loss of activity. From these results, it should be highlighted that the use of the photochromic C4-Azo-PEG surfactant **1** enhanced the reactivity and recyclability of the catalytic system.

With its high dielectric constant, water is potentially a very useful solvent for microwave-mediated synthesis.[22] Indeed, microwave heating has been widely recognized as an efficient tool, and its benefits have been well-documented.[23] Since many reactions are known to result in higher yield and/or shorter reaction times, this alternative technology was developed in our group for Suzuki–Miyaura cross-coupling of various uridines in pure water.[24] Nevertheless, to the best of our knowledge, there are only a few reports on using microwave heating coupled with cross-coupling micellar catalysis, such focus on Suzuki or Sonogashira couplings.[25] As in thermal activation, different reaction times were tested to develop optimized conditions under microwave irradiation. To have a good energy saving, we decided to run the experiment no longer than 30 min.

As described in Figure 8, the best compromise between efficiency and energy saving was to react for 15 min at 70 °C.

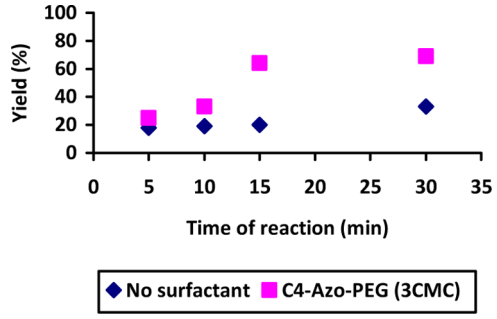


Figure 8. Evolution of yield vs time of reaction under microwave irradiation.

It was noted that increasing the time to 30 min allowed only a modest 5% yield gain. Table 2 shows the results obtained under the following conditions: *p*-TsNa (2 equiv), 10%Pd/C (1 mol %), PPh_3 (4 mol %), surfactant (3 CMC), 70 °C, microwave irradiation, 15 min. As in conventional heating, particular attention was paid to the recycling ability of the system and the role of the photochromic surfactant **1**. In the first instance, we observed that the first run under these conditions gave comparable results between thermal heating and microwave activation for all commercially available

Table 2. Surfactant Activities and Recycling Abilities under Microwave Irradiation

		yield of **6** (%)[b]					
entry	surfactant	run 1	run 2	run 3	run 4	run 5	run 6
1	none	20	22	16	0		
2	SDS	26	0				
3	Tween 20	73	0				
4	CTAB	80	100	26	0		
5	C4-Azo-PEG	64	97	28	0		
6	C4-Azo-PEG[a]	65	94	26	24	12	0

[a]Irradiation at 365 nm during 30 min just before extraction. [b]**5** (1 equiv), *p*-TsNa (2 equiv), 10%Pd/C (1 mol %), PPh_3 (4 mol %), surfactant (3 CMC), 70 °C, 3 h.

dx.doi.org/10.1021/jo401737t | J. Org. Chem. 2014, 79, 493–500

surfactants (Figure 7; Table 2, entries 2−4). When no surfactant was used, the media was recyclable twice with low yield (Table 2, entry 1).

Therefore, we can assume that the palladium source kept its activity to the same extent as with microwave irradiation. SDS is the less active surfactant under these conditions (Table 2, entry 2) and is not recyclable. More surprisingly, Tween 20, which was recyclable in conventional heating, performed a good first run (73% yield) before showing a dramatic loss of activity (Table 2, entry 3). These last commercially available surfactants SDS and Tween 20 seemed to lead to a marked deactivation of palladium in only one run. CTAB, as in conventional heating (Figure 7), is a serious concurrent to C4-Azo-PEG **1** in terms of activity and recyclability. The two surfactants CTAB and C4-Azo-PEG **1** indicated a useful potential (Table 2, entries 4 and 5). The second run was quantitative, but yields dramatically decreased for the third run. Their behavior was the same when no irradiation step of the C4-Azo-PEG **1** was included in the sample treatment (Table 2, entry 5). C4-Azo-PEG **1**, as in conventional heating, proved to be the most interesting surfactant tested, when submitted to the irradiation−extraction treatment (i.e., irradiation at 365 nm for 30 min just before extraction) (Table 2, entry 6).

According to the results presented herein, the increase of the catalytic activity observed when the reaction medium is subjected to microwave irradiation (i.e., 15 min vs 3 h under conventional heating) is due presumably to electric discharge or hot spots created within the heterogeneous catalyst. This phenomenon has been previously observed and studied in C−C and P−C couplings.[26] In both conditions, recycling of the 10%Pd/C-C4-Azo-PEG **1** system was conducted (Figure 9).

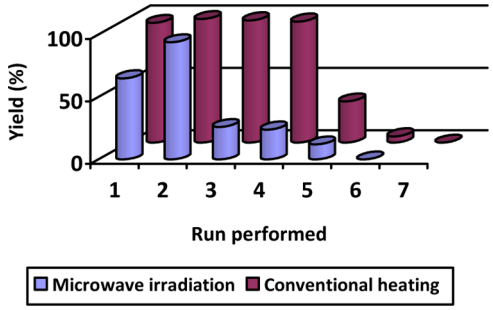


Figure 9. Comparison of recycling abilities between conventional heating and microwave irradiation in the presence of C4-Azo-PEG **1** after irradiation at 365 nm during 30 min just before extraction.

The first and the second cycles gave similar results. Nevertheless, the activity of the catalyst decreased drastically during the third cycle for the microwave heated system. This tendency was confirmed during the fourth run. In these conditions, the metal suffered the fastest deactivation under microwave irradiation than conventional heating. The decrease in catalytic activity could result from the aggregation of palladium nanoparticles or blockage of the active sites.[21] One potent explanation was that microwave heating creates small and locally superheated, highly active sites, leading to an acceleration of the deactivation when the temperature increased.[27]

To explore further the scope of this new process, the reaction of three different allylic acetates **5**, **7**, and **8** with some different nucleophiles was examined (Table 3).

Under our optimized method using C4-Azo-PEG **1** in thermal activation, all desired compounds were obtained in moderate to excellent yields (36−97%). Linear cinnamyl acetate **5** having an *E* configuration reacted smoothly with *p*-toluenesulfinic acid sodium salt to give the desired sulfone **6** in 96% yield, without any loss of configuration (Table 3, entry 1). Starting from acetate **5** with morpholine and dibenzylamine as *N*-nucleophiles led to the target compounds **11** and **14** in good yields (75% and 62%, respectively) (Table 3, entries 4 and 7). Under these conditions, with no additional base in the reaction medium, no side reaction of saponification was observed. When C-nucleophiles are tested, a base is necessary in the reaction medium but led to some competitive saponification of the starting acetate **5** (10−15% of cinnamyl alcohol isolated). In these conditions, lower yields can be achieved. However, dimer **17** was obtained with 2,4-pentanedione in a good yield of 80% (Table 3, entry 10).The use of a hardier O-nucleophile, phenol, surprisingly led to the target compound **18** in excellent yield (97%, Table 3, entry 11). The much hindered allylic acetate **7** was found to be a good substrate under the optimized conditions. As such, compounds **9**, **12**, and **15** were obtained in good to excellent yields (Table 3, entries 2, 5, and 8). Despite its high steric hindrance, compound **15** was obtained in 77% yield. Finally, the branched allylic acetate **8**, as expected, was found to be less reactive, and the sulfone **10** was obtained in 52% yield. Morpholine as *N*-nucleophile was found to react better with the acetate **8**, leading to the desired compound **13** in 60% yield. The much more hindered, dibenzylamine, gave compound **16** but in a modest 36% yield. In this case, the unreacted acetate **8** was recovered without modification. An important point that deserves comment is the regioselectivity of the reaction. Similar to most homogeneous Pd-catalyzed reactions, only substitution at the least hindered allylic position is observed. In this respect, this reaction applied to allylic acetates showed a good range of compatibility with various nitrogen or sulfur nucleophiles.

CONCLUSION

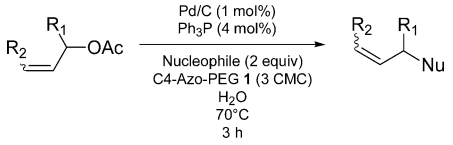
In accordance with the objective of green chemistry, the Tsuji−Trost reaction in aqueous photoresponsive micellar media proved to be efficient under conventional heating and microwave irradiation. As C4-Azo-PEG **1** can organize and disorganize in aqueous solution under UV irradiation, it allows a better extraction of the products formed due to its photochromism property and an enhancement of reactivity and recyclability of the catalytic system. For this study, conventional heating seemed to be more favorable than microwave irradiation. This attractive technique allowed a decrease in reaction time and a savings in energy, but the downside was a faster deactivation of catalyst. Our optimized method under conventional heating was extended to much hindered and branched allylic acetates, and the system showed a good range of compatibility with various nucleophiles. As photochromic surfactants based on azobenzene moieties and, in particular, C4-Azo-PEG **1** are really interesting and versatile compounds, their potential in catalysis should be more extensively explored.

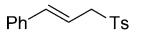
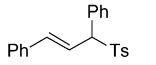
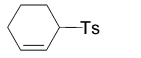
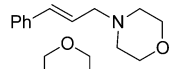
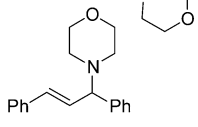
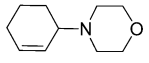
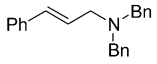
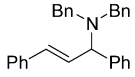
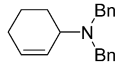
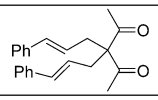
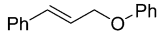
EXPERIMENTAL SECTION

Materials. All commercially available products and solvents were used without further purification. Reactions were monitored by TLC (Kieselgel 60F254 aluminum sheet) with detection by UV light or potassium permanganate acidic solution. Column chromatography was

dx.doi.org/10.1021/jo401737t | J. Org. Chem. 2014, 79, 493−500

Table 3. Scope of the Tsuji–Trost Reaction



Entry	R_1	R_2	Isomer	Acetate	Nucleophile	Product		Yield (%)*
1	H	Ph	E	**5**			**6**	96
2	Ph	Ph	E	**7**	*p*-TsNa		**9**	52
3	$(CH_2)_3$		Z	**8**			**10**	52
4	H	Ph	E	**5**			**11**	75
5	Ph	Ph	E	**7**			**12**	90
6	$(CH_2)_3$		Z	**8**			**13**	60
7	H	Ph	E	**5**			**14**	62
8	Ph	Ph	E	**7**	Bn_2NH		**15**	77
9	$(CH_2)_3$		Z	**8**			**16**	36
10**	H	Ph	E	**5**			**17**	80
11**	H	Ph	E	**5**	Ph-OH		**18**	97

* irradiation at 365 nm during 30 min just before extraction
** addition of 4 mmol of K_2CO_3 in the medium

performed on silica gel 40–60 μm. Flash column chromatography was performed on an automatic apparatus, using silica gel cartridges. UV analyses were performed on a UV/vis spectrophotometer coupled with an optic fiber. A 500 W mercuric lamp was used for the irradiation of the C4-Azo-PEG solutions. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz/54 mm ultralong hold. Chemical shifts (δ) are quoted in parts per million (ppm) and are referenced to TMS as an internal standard. Coupling constants (J) are quoted in hertz. Microwave experiments were conducted in a commercial microwave reactor especially designed for synthetic chemistry. Monowave300 (Anton Paar, Austria) is a monomode cavity with a microwave power delivery system ranging from 0 to 850 W. The temperatures of the reactions were monitored via a contactless infrared pyrometer, which was calibrated in control experiments with a fiber-optic contact thermometer. Sealed vessels and a magnetic stir bar inside the vessel were used. Temperature and power profiles were monitored in both cases through the software provided by the manufacturer.

Synthesis of C4-Azo-PEG 1. *4-Butyl-4′-hydroxyazobenzene (**3**).* To a solution of 4-butylaniline (**2**) (30 g, 0.20 mol) in 37% HCl (50 mL) and water (25 mL) was added $NaNO_2$ (16.6 g, 0.24 mol) in water (25 mL) dropwise in 30 min. The reaction was conducted in an ice bath. The crude solution was added dropwise to a solution of phenol (20.7 g, 0.22 mol) in soda (100 mL, 6 M). Finally, the solution was quenched with HCl. The product **3** was obtained after filtration and recrystallization from pentane as a red solid (40.1 g, 79%). Analyses are consistent with the literature.[15]

mp = 80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J = 8.8 Hz, 2H), 7.79 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.3 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 2.68 (t, J = 7.7 Hz, 2H), 1.75 (bs, 1H), 1.64 (quin, J = 7.6 Hz, 2H), 1.37 (sex, J = 7.5 Hz, 2H), 0.94 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 150.8, 147.1, 145.9, 129.0 (2×), 124.7 (2×), 122.5 (2×), 115.7 (2×), 35.5, 33.4, 22.3, 13.9.

*Triethyleneglycol Monotosylate (**4**).* To a solution of triethylene glycol **PEG3** (11 g, 73.3 mmol), triethylamine (2.6 mL, 19.1 mmol), and DMAP (45 mg, 0.37 mmol) in 95 mL of DCM was added tosyl chloride (3.5 g, 18.1 mmol) at 5 °C, and the mixture was stirred for 4 h. The resulting mixture was washed with 1 N HCL, H_2O, and brine. The organic layer was dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by silica gel chromatography (EtOAc/cyclohexane 7:3) to obtain the title compound **4** as yellow oil (4.2 g, 75%).[28]

dx.doi.org/10.1021/jo401737t | J. Org. Chem. 2014, 79, 493–500

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 4.16 (t, J = 4.7 Hz, 2H), 3.70 (q, J = 4.7 Hz, 4H), 3.61 (s, 4H), 3.57 (t, J = 4.5 Hz, 2H), 2.45 (s, 3H), 2.32 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.8, 132.8, 129.7 (2×), 127.9 (2×), 72.4, 70.7, 70.2, 69.1, 68.6, 61.6, 21.6.

*Triethylene Glycol Mono(4-butylazobenzene) Ether (C4-Azo-PEG **1**).* In a round-bottom flask under N_2, triethyleneglycol monotosylate (**4**) (4.4 g, 14.5 mmol), K_2CO_3 (9.9 g, 72.3 mmol), and LiCl (20 mg, 3 mol %) were dissolved in MeCN (150 mL). A solution of 4-butyl-4′-hydroxyazobenzene (**3**) (3.9 g, 15.43 mmol) in MeCN (50 mL) was added dropwise. The mixture was refluxed under N_2 for 18 h. The solvent was then evaporated under vacuum. The residue was dissolved in DCM and then washed with brine (3 × 100 mL). The organic layer was dried over $MgSO_4$ and concentrated under vacuum. The product **1** was purified by silica gel chromatography (EtOAC/cyclohexane 7:3) to obtain the desired compound as a yellow solid after recrystallization from pentane (2.6 g, 85%). Analyses are consistent with the literature.[15]

mp = 60 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 8.8 Hz, 2H), 7.82 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.2 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 4.24 (t, J = 4.6 Hz, 2H), 3.92 (t, J = 4.6 Hz, 2H), 3.72−3.78 (m, 6H), 3.65 (t, J = 4.4 Hz, 2H), 2.70 (t, J = 7.7 Hz, 2H), 2.34 (s, 1H), 1.66 (quin, J = 7.6 Hz, 2H), 1.39 (sex, J = 7.4 Hz, 2H), 0.96 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 150.9, 147.2, 145.8, 129.0 (2×), 124.5 (2×), 122.5 (2×), 114.7 (2×), 72.4, 70.8, 70.3, 69.6, 67.6, 61.7, 35.5, 33.4, 22.3, 13.9.

General Procedure for the Tsuji−Trost Reaction. A 30 mL MW vessel was charged with 10%Pd/C (20 mg, 1 mol %), PPh_3 (20 mg, 4 mol %), the desired allylic acetate (2 mmol), and nucleophile (4 mmol). When necessary, potassium carbonate (4 mmol) was added in the medium. The solution of the surfactant in water (10 mL) was then added. The mixture was heated at 70 °C for 3 h (conventional heating) or 15 min (MW irradiation. The final product was extracted with EtOAc (3 × 5 mL) before purification. When necessary, the extraction can be prefaced by a 30 min irradiation under a 365 nm lamp. For recycling tests, only allylic acetate (2 mmol), PPh_3 (4 mol %), and nucleophile (2 mmol) were introduced.

*trans-Cinnamyl-p-tolyl Sulfone (**6**).*[19] Flash chromatography (0% EtOAc−cyclohexane to 50% EtOAc−cyclohexane) gave the desired product **6** as a white powder (522 mg, 96%).

mp = 120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 8.3 Hz, 2H), 7.20−7.27 (m, 7H), 6.32 (d, J = 15.5 Hz, 1H), 6.04 (quin, J = 7.5 Hz, 1H), 3.86 (dd, J = 0.8, 7.5, 2H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.7, 138.9, 135.8, 135.5, 129.6 (2×), 128.6 (2×), 128.5 (2×), 128.4, 126.5 (2×), 115.3, 60.5, 21.5.

*1,3-Diphenyl-2-propenyl-p-tolyl Sulfone (**9**).*[19] Flash chromatography (0% EtOAc−cyclohexane to 100% EtOAc−cyclohexane) gave the desired product **9** as a colorless solid (362 mg, 52%). Analyses are consistent with the literature.

mp = 158−159 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, J = 8.4 Hz, 2H), 7.29−7.36 (m, 10H), 7,20 (d, J = 8.0 Hz, 2H), 6.55−6.58 (m, 2H), 4.81 (d, J = 7.6 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 137.9, 135.9, 134.4, 132.5 (2×), 129.7 (2×), 129.3 (5×), 128.8, 128.6 (2×), 128.4 (2×), 126.7, 120.2, 75.3, 21.6.

*Cyclohex-2-enyl-p-tolyl Sulfone (**10**).*[19] Flash chromatography (0% EtOAc−cyclohexane to 100% EtOAc−cyclohexane) gave the desired product **10** as a colorless oil (245 mg, 52%). Analyses are consistent with the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 8.3 Hz, 1H), 7.33 (d, J = 7.9 Hz, 1H), 6.02−6.09 (m, 1H), 5.73−5.78 (m, 1H), 3.69−3.72 (m, 1H), 2.44 (s, 3H), 1.80−1.85 (m, 5H), 1.46−1.49 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 135.1, 134.4 (2×), 129.6 (2×), 129.1 (2×), 61.8, 24.3, 22.7, 21.6, 19.5.

*4-Cinnamylmorpholine (**11**).*[19] Flash chromatography (0% EtOAc−cyclohexane to 100% EtOAc−cyclohexane) gave the desired product **11** as a colorless oil (304 mg, 75%). Analyses are consistent with the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20−7.38 (m, 5H), 6.52 (d, J = 16,0 Hz, 1H), 6.25 (dt, J = 6.8, 13.6 Hz, 1H), 3.73 (t, J = 4.4 Hz, 4H), 3.14 (d, J = 6,8, 2H), 2,50 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 133.3, 128.5, 127.5 (2×), 126.3, 126.1 (2×), 67.0 (2×), 61.4, 53.6 (2×).

*4-(1,3-Diphenylallyl)morpholine (**12**).*[28] Flash chromatography (0% EtOAc−cyclohexane to 50% EtOAc−cyclohexane) gave the desired product **12** as a colorless solid (502 mg, 90%). Analyses are consistent with the literature.

mp = 65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21−7.44 (m, 10H), 6.60 (d, J = 15.8 Hz, 1H), 6.32 (dd, J=16,0, J=8,8 Hz, 1H), 3,80 (d, J = 8,8 Hz, 1H), 3.74 (t, J = 4,8 Hz, 4H), 2,56 (m, 2H), 2.42 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 167.8, 140.3, 137.0 (2×), 132.0 (2×), 129.3 (2×), 128.9, 128.7, 128.0 (2×), 127.8, 127.3 (2×), 67.2, 61.4 (2×).

*4-(Cyclohex-2-enyl)morpholine (**13**).*[29] Flash chromatography (0% EtOAc−cyclohexane to 100% EtOAc−cyclohexane) gave the desired product **13** as a colorless oil (200 mg, 60%). Analyses are consistent with the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.89 (d, J = 10.4 Hz, 1H), 5.60 (d, J = 10.4 Hz, 1H), 3.66−3.69 (m, 4H), 3.11−3.12 (m, 1H), 2.50−2.52 (m, 4H), 1.94−1.95 (m, 2H), 1.76−1.78 (m, 2H), 1.50−1.53 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 130.4 (2×), 128.9 (2×), 67.6, 60.4, 49.3, 25.3, 23.1, 21.5.

*N,N-Dibenzyl-3-phenylprop-2-enamine (**14**).*[30] Flash chromatography (0% EtOAc−cyclohexane to 50% EtOAc−cyclohexane) gave the desired product **14** as a yellowish oil (388 mg, 62%). Analyses are consistent with the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18−7.26 (m, 15H), 6.52 (d, J = 15.9 Hz, 1H), 6.28 (dt, J = 6.6, 13.4 Hz, 1H), 3.61 (s, 4H), 3.20 (d, J = 6.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.6 (2×), 137.2, 132.4, 128.8, 128.5 (4×), 128.2 (2×), 127.7 (4×), 127.3, 126.8 (2×), 126.2 (2×), 57.9 (2×), 55.7.

*Dibenzyl-(1,3-diphenylallyl)amine (**15**).*[31] Flash chromatography (0% EtOAc−cyclohexane to 100% EtOAc−cyclohexane) gave the desired product **15** as a white solid (600 mg, 77%). Analyses are consistent with the literature.

mp = 112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12−7.48 (m, 20H), 6.44 (m, 2H), 4.36 (d, J = 6.9 Hz, 1H), 3.65 (d, J = 13.8 Hz, 2H), 3.52 (d, J = 13.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.0 (2×), 65.1, 126.5 (2×), 126.8 (2×), 127.1, 127.6, 127.7, 128.2 (2×), 128.3 (2×), 128.4 (4×), 126.6 (2×), 126.7 (4×), 134.1, 137.0, 140.0 (2×), 141.9.

*N,N-Dibenzylcyclohex-2-enamine (**16**).*[19] Flash chromatography (0% EtOAc−cyclohexane to 100% EtOAc−cyclohexane) gave the desired product **16** as a colorless oil (199 mg, 36%). Analyses are consistent with the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13−7.33 (m, 10H), 5.65−5.76 (m, 2H), 3.68 (d, J = 14.1 Hz, 2H), 3.46 (d, J = 14.1 Hz, 2H), 3.45 (m, 1H), 1.80−1,92 (m, 3H), 1.72 (m, 1H), 1.53 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.1 (2×), 131.0, 130.2 (4×), 128.6 (4×), 128.3 (2×), 126.8, 54.7 (2×), 54.0, 25.5 (2×), 22.0.

*3,3-Dicinnamylpentane-2,4-dione (**17**).*[32] Flash chromatography (0% EtOAc−cyclohexane to 100% EtOAc−cyclohexane) gave the desired product **17** as colorless crystals (265 mg, 80%). Analyses are consistent with the literature.

mp = 60−61 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 7.15−7.23 (m, 10H), 6.40 (d, J = 16.0 Hz, 2H), 5.86 (m, 2H), 2.78 (dd, J = 7.6 Hz, J = 1.2 Hz, 2H), 2.10 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.8 (2×), 136.8 (2×), 134.3 (2×), 128.6 (4×), 127.6 (2×), 126.2 (4×), 123.3 (2×), 70.8, 34.6 (2×), 27.4 (2×).

*Cinnamylphenylether (**18**).*[33] Flash chromatography (0% EtOAc−cyclohexane to 100% EtOAc−cyclohexane) gave the desired product **18** as a white powder (408 mg, 97%). Analyses are consistent with the literature.

mp = 64−65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 7.14−7.33 (m, 7H), 6.86−6.90 (m, 3H), 6.64 (d, J = 15.8 Hz, 1H), 6;33 (m, 1H), 4.61 (dd, J = 5.6 Hz, J = 1.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.7, 136.5, 133.0, 129.5 (2×), 128.6 (2×), 127.9, 126.6 (2×), 124.6, 120.9, 114.8 (2×), 68.6.

dx.doi.org/10.1021/jo401737t | J. Org. Chem. 2014, 79, 493−500

■ ASSOCIATED CONTENT

Supporting Information

^{1}H experiments spectra are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: christophe.len@utc.fr. Fax: (+33)(0)3 44 97 15 91.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The Région Picardie is gratefully acknowledged for its financial support. F.M. thanks ESCOM (Ecole Supérieure de Chimie Organique et Minérale) for her research fellowship. We are also grateful to some fourth year students for their implication during preliminary works on catalysis.

■ REFERENCES

(1) Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: New York, 1998; p 30.

(2) (a) Li, C. J.; Chan, T. H. *Organic Reactions in Aqueous Media*; Wiley: New York, 1997. (b) Grieco, P. A. *Organic Synthesis in Water*; Blakie Acad.: London, 1998.

(3) (a) Lamblin, M.; Nassar-Hardy, L.; Hierso, J.-C.; Fouquet, E.; Felpin, F.-X. *Adv. Synth. Catal.* **2010**, *352*, 33. (b) Lipshutz, B. H.; Abela, A. R.; Boskovic, Z. V.; Nishikata, T.; Duplais, C.; Krasovskiy, A. *Top. Catal.* **2010**, *53*, 985. (c) Le Bras, J.; Muzart, J. *Curr. Org. Synth.* **2011**, *8*, 330. (d) Polshettiwar, V.; Len, C.; Fihri, A. *Coord. Chem. Rev.* **2009**, *253*, 2599. (e) Polshettiwar, V.; Decottignies, A.; Len, C.; Fihri, A. *ChemSusChem* **2010**, *5*, 502. (f) Fihri, A.; Luart, D.; Len, C.; Solhi, A.; Chevrin, C.; Polshettiwar, V. *Dalton Trans.* **2011**, *40*, 3116. (g) Sartori, G.; Enderlin, G.; Herve, G.; Len, C. *Synthesis* **2012**, *44*, 767. (h) Hassine, A.; Sebti, S.; Solhy, A.; Zahouily, M.; Len, C.; Hedhili, M. N.; Fihri, A. *Appl. Catal., A* **2013**, *450*, 13. (i) Enderlin, G.; Sartori, G.; Herve, G.; Len, C. *Tetrahedron Lett.* **2013**, *54*, 3374.

(4) (a) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159. (b) Reichardt, C. *Solvents and Solvents Effects in Organic Chemistry*, 2nd ed.; VCH: Weinheim, 1988. (c) Shaughnessy, K. H. *Chem. Rev.* **2009**, *109*, 643. (d) Li, C. J.; Chen, L. *Chem. Soc. Rev.* **2006**, *35*, 68.

(5) Chevrin, C.; Le Bras, J.; Henin, F.; Muzart, J.; Pla-Quintana, A.; Roglans, A.; Pleixats, R. *Organometallics* **2004**, *23*, 4796.

(6) Liao, M.-C.; Duan, X.-H.; Liang, Y.-M. *Tetrahedron Lett.* **2005**, *46*, 3469.

(7) Civicos, J. F.; Gholinejad, M.; Alonso, D. A.; Najera, C. *Chem. Lett.* **2011**, *40*, 907.

(8) (a) Bricout, H.; Léonard, E.; Len, C.; Landy, D.; Hapiot, F.; Monflier, E. *Beilstein J. Org. Chem.* **2012**, *8*, 1479. (b) Torque, C.; Bricout, H.; Hapiot, F.; Monflier, E. *Tetrahedron* **2004**, *60*, 6487. (c) Decottignies, A.; Fihri, A.; Azemar, G.; Djedaini-Pilard, F.; Len, C. *Catal. Commun.* **2013**, *32*, 101. (d) Lacroix, T.; Bricout, H.; Tilloy, S.; Monflier, E. *Eur. J. Org. Chem.* **1999**, 3127.

(9) Suzuka, T.; Kimura, K.; Nagamine, T. *Polymer* **2011**, *3*, 621.

(10) Ferreira, M.; Bricout, H.; Azaroual, N.; Gaillard, C.; Landy, D.; Tilloy, S.; Monflier, E. *Adv. Synth. Catal.* **2010**, *352*, 1193.

(11) Drillaud, N.; Banaszak-Léonard, E.; Pezron, I.; Len, C. *J. Org. Chem.* **2012**, *77*, 9553.

(12) For comprehensive reviews, see: (a) Trost, B. M.; Van Vranken, V. L. *Chem. Rev.* **1996**, *96*, 395. (b) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921. (c) Poli, G.; Prestat, G.; Liron, F.; Kammerer-Pentier, C. *Top. Organomet. Chem.* **2012**, *38*, 1.

(13) (a) Hayashita, T.; Kurosawa, T.; Miyata, T.; Tanaka, K.; Igawa, M. *Colloid Polym. Sci.* **1994**, *272*, 1611. (b) Yang, L.; Takisawa, N.; Hayashita, T.; Shirahama, K. *J. Phys. Chem.* **1995**, *99*, 8799.

(14) (a) Monflier, E.; Bourdauducq, P.; Couturier, J. L.; Kervennal, J.; Suisse, I.; Mortreux, A. *Catal. Lett.* **1995**, *34*, 201. (b) Monflier, E.; Bourdauducq, P.; Couturier, J. L.; Kervennal, J.; Mortreux, A. *Appl. Catal., A* **1995**, *131*, 167.

(15) Shang, T.; Smith, K. A.; Hatton, T. A. *Langmuir* **2003**, *19*, 10764.

(16) Nalluri, S. K. M.; Voskuhl, J.; Bultema, J. B.; Boekema, E. J.; Ravoo, B. J. *Angew. Chem., Int. Ed.* **2011**, *50*, 9747.

(17) Hamon, F.; Djedaini-Pilard, F.; Barbot, F.; Len, C. *Tetrahedron* **2009**, *65*, 10105.

(18) Basheer, M. C.; Oka, Y.; Mathews, M.; Tamaoki, N. *Chem.—Eur. J.* **2010**, *16*, 3489.

(19) Felpin, F.-X.; Landais, Y. *J. Org. Chem.* **2005**, *70*, 6441.

(20) (a) Shinde, M. M.; Bhagwat, S. S. *Colloids Surf., A* **2011**, *380*, 201. (b) Arcadi, A.; Cerichelli, G.; Chiarini, M.; Correa, M.; Zorzan, D. *Eur. J. Org. Chem.* **2003**, *20*, 4080.

(21) Saha, D.; Dey, R.; Ranu, B. C. *Eur. J. Org. Chem.* **2010**, *31*, 6067.

(22) Alonso, F.; Beletskaya, I. P.; Yus, M. *Tetrahedron* **2008**, *64*, 3047.

(23) For a recent book chapter, see: Fihri, A.; Len, C. Microwave-assisted Coupling Reactions in Aqueous. In *Aqueous Microwave Assisted Chemistry*; Polshettiwar, V., Varma, R. S., Eds.; Royal Society of Chemistry: Cambridge, U.K., 2010; Chapter 3, p 55.

(24) Gallagher-Duval, S.; Hervé, G.; Sartori, G.; Enderlin, G.; Len, C. *New J. Chem.* **2013**, *37*, 1989.

(25) (a) Civicos, J. F.; Alonso, D. A.; Najera, C. *Adv. Synth. Catal.* **2012**, *354*, 2771. (b) Civicos, J. F.; Alonso, D. A.; Najera, C. *Adv. Synth. Catal.* **2013**, *355*, 203.

(26) (a) Rummelt, S. M.; Ranocchiari, M.; Van Bokhoven, J. A. *Org. Lett.* **2012**, *14*, 2188. (b) Horikoshi, S.; Osawa, A.; Abe, M.; Serpone, N. *J. Phys. Chem. C* **2011**, *115*, 23030.

(27) (a) Lasri, J.; Mac Leod, T. C. O.; Pombeiro, A. J. L. *Appl. Catal., A* **2011**, *397*, 94. (b) Sin, E.; Yi, S.; Li, Y. *J. Mol. Catal. A: Chem.* **2010**, *315*, 99.

(28) Azagarsamy, M. A.; Alge, D. L.; Radhakrishnan, S. J.; Tibbitt, M. W.; Anseth, K. S. *Biomacromolecules* **2012**, *13*, 2219.

(29) Pawlas, J.; Nakao, Y.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 3669.

(30) Krishnan, D.; Wu, M.; Chiang, M.; Li, Y.; Leung, P.-H.; Pullarkat, S. A. *Organometallics* **2013**, *32*, 2389.

(31) Chen, J.; Lang, F.; Li, D.; Cun, L.; Zhu, J.; Deng, J.; Liao, J. *Tetrahedron: Asymmetry* **2009**, *20*, 1953.

(32) Moreno-Mañas, M.; Ortuno, R. M.; Prat, M.; Galan, M. A. *Synth. Commun.* **1986**, *16*, 1003.

(33) Hajra, S.; Sinha, D. *J. Org. Chem.* **2011**, *76*, 7334.