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Practical Pd/C-Mediated Allylic Substitution in Water

François-Xavier Felpin* and Yannick Landais*

Université Bordeaux-I, Laboratoire de Chimie Organique et Organométallique, 351 Cours de la Libération, 33405 Talence Cedex, France

fx.felpin@lcoo.u-bordeaux1.fr; y.landais@lcoo.u-bordeaux1.fr

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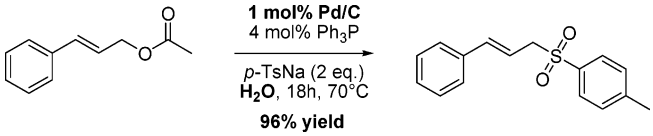
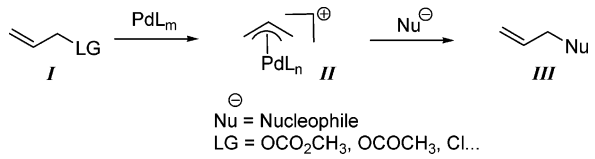


Pd/C-mediated allylic substitution in water is described as an interesting alternative to classical homogeneous conditions. The reaction applied to allylic acetates showed a wide range of compatibility with various nitrogen, sulfur, oxygen, and carbon nucleophiles. Notably, the method features inexpensive reagents and a nontoxic solvent. Moreover, measurement of the palladium content in water by ICP-MS shows low palladium contamination (4 ppm) of the solvent, rendering this method safer for the environment compared to homogeneous conditions. The first asymmetric example of Pd/C-mediated allylic substitution is also disclosed.

Introduction

Palladium-catalyzed allylic substitution constitutes one of the most important tools for carbon−carbon and carbon−heteroatom bond formation (Scheme 1).[1] Very high catalytic activities and stereo- and regioselectivities under mild conditions can be achieved using these transformations. The usual conditions, however, have several drawbacks and suffer from some limitations from an industrial point of view. Most of the studies have been carried out using expensive and air-sensitive Pd catalysts ($Pd(PPh_3)_4$, $Pd_2(dba)_3$, ...) where Pd contamination of the solvent and the product constitutes a limitation for large-scale applications. Moreover, Pd-catalyzed reactions are generally carried out in organic and often toxic solvents. The problem of contamination from the metal has been addressed by using polymer-supported catalysts[2] or heterogeneous Pd catalysts.[3] In this context, palladium on activated charcoal (Pd/C) has recently emerged as a powerful catalyst for various carbon−carbon bond formation reactions.[4] Another important feature is the compatibility of Pd/C with water as solvent or cosolvent. Water possesses many advantages over usual organic solvents.[5]

SCHEME 1. General Mechanism in Homogeneous Conditions



It is the least expensive and safest solvent available that is nonflammable, inexplosive, and nontoxic. From a practical point of view, organic transformations in water represent the "ideal" conditions for a chemist, as dry catalysts, reagents, and glassware are not required. The reaction can even sometimes be performed under air atmosphere. In an effort to develop "green" transformations during the course of a project requiring the preparation of various allyl sulfones through Pd-catalyzed allylation,[6] it was found that Pd/C could advantageously replace $Pd(Ph_3)_4$ as a catalyst and that the reaction could be carried out in water.[7,8] This interesting observation led us to explore more in depth the potential of this

(1) For comprehensive reviews, see: (a) Trost, B. M.; Van Vranken, V. L. *Chem. Rev*. **1996**, *96*, 395−422. (b) Trost, B. M.; Crawley, M. L. *Chem. Rev*. **2003**, *103*, 2921−2943. (c) *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vols. I−III.

(2) (a) Danjo, H.; Tanaka, D.; Hayashi, T.; Uozumi, Y. *Tetrahedron* **1999**, *55*, 14341−14352. (b) Uozumi, Y.; Shibatomi, K. *J. Am. Chem. Soc*. **2001**, *123*, 2919−2920, and references cited herein.

(3) Dos Santos, S.; Tong, Y.; Quignard, F.; Choplin, A.; Sinou, D.; Dutasta, J. P. *Organometallics* **1998**, *17*, 78−89.

(4) For recent reviews, see: (a) Blaser, H.-U.; Indolese, A.; Schnyder, A.; Steiner, H.; Studer, M. *J. Mol. Catal. A: Chem.* **2001**, *173*, 3−18. (b) Biffis, A.; Zecca, M.; Basato, M. *J. Mol. Catal. A: Chem.* **2001**, *173*, 249−274.

(5) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159−164.

(6) (a) James, P.; Landais, Y. *Org. Lett.* **2004**, *6*, 325−328. (b) James, P.; Felpin, F.-X.; Landais, Y.; Schenk, K. Unpublished results.

(7) For reviews on palladium reactions in water, see: (a) Genet, J.-P.; Savignac, M. *J. Organomet. Chem*. **1999**, *576*, 305−317. (b) Lindström, U. M. *Chem. Rev*. **2002**, *102*, 2751−2772. (c) Manabe, K.; Kobayashi, S. *Chem. Eur. J*. **2002**, *8*, 4094−4101. (d) Sinou, D. *Adv. Synth. Catal*. **2002**, *344*, 221−237.

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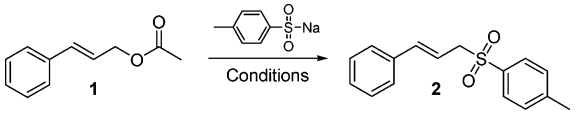
TABLE 1. Optimization of Reaction Conditions



Entry	Solvent	T(°C)	Pd/C (mol%)	Ph_3P (mol%)	t (h)	Conv.[a] (%)	Yield[b] (%)
1	H_2O	40	5	20	36	40	n.d.
2	H_2O	70	5	20	10	>95	75
3	**H_2O**	**70**	**1**	**4**	**18**	**>95**	**96**
4	H_2O/DME	70	1	4	18	>95	84
5	H_2O	70	1	0	24	>95	90
6	H_2O	70	0	20	12	0	0
7	H_2O	70	0	0	12	0	0

[a] Determined on the crude reaction mixture by ^1H NMR. [b] Yields are for isolated products. n.d.: not determined.

catalytic system, which to our knowledge remains unknown for such a reaction.[9] We report here the scope and limitations of this methodology along with some mechanistic considerations.

Results and Discussion

Optimization of Reaction Conditions. To evaluate the potential of the Pd/C-mediated allylic alkylation in water, we first selected cinnamyl acetate **1** as a model substrate with the sodium salt of *p*-toluenesulfinic acid (*p*-TsNa) as the nucleophile (Table 1). A number of parameters were evaluated. Under optimized conditions cinnamyl acetate **1** in water reacted with *p*-TsNa in the presence of 10% Pd/C[10] corresponding to 1 mol % and 4 mol % PPh_3 under air to give the corresponding allylic sulfone **2** in 96% yield (entry 3). A decrease of the temperature from 70 °C to 40 °C resulted in a lower conversion (40%) after 36 h of stirring (entry 1). Increasing the catalyst loading led somewhat to an enhanced reaction rate but with a significant diminished yield (entry 2). Alternatively, a mixture of water and DME as a solvent system could be used albeit with lower yield in this case (vide infra) (entry 4). When triphenylphosphine was omitted, allylic alkylation occurred at a slower rate but with total conversion after 24 h of stirring. However, subsequent studies showed that lower conversions were observed with branched allylic acetates under PPh_3-free Pd/C conditions. The phosphine probably acts as a stabilizing agent for Pd, generating in situ a more reactive Pd(0)−PPh_3 complex. Palladium-free allylic alkylation has recently been reported.[11] However in our case no reaction occurred in the absence of Pd/C. Starting material was recovered quantitatively (entries 6, 7). This result indicates a genuine Pd/C-catalyzed reaction. From these preliminary results, it should be highlighted that neither water-soluble phosphines nor phase-transfer catalysts or surfactants were required in order to obtain high yield.

Scope of the Reaction. To explore further the scope of this new process, we examined the reaction of three different allylic acetates with a variety of nucleophiles. The reaction showed a wide range of compatibility with various nitrogen, sulfur, oxygen, and carbon nucleophiles.

Linear allylic acetate **1** gave good to excellent yields (up to 96%) irrespective of the nature of the nucleophile. When morpholine was used as nucleophile, better conversion was found when DME was used as cosolvent (entry 5). It should be noted, however, that no improvement was observed using the same cosolvent and *p*-TsNa (entry 2). While no base was required with *p*-TsNa and morpholine, K_2CO_3 emerged as a base of choice with oxygen and carbon nucleophiles. With Meldrum's acid, only the product resulting from the double alkylation could be isolated in high yield (94%, entry 6). Another important point that deserves comment is the regioselectivity of the reaction. Similar to most homogeneous Pd-catalyzed reactions, only linear compounds were formed, except in the case of morpholine, where 4% of the branched regioisomer was also isolated (entry 5).

As expected, branched allylic acetates were found to be less reactive, and 5 mol % Pd/C associated with 20 mol % Ph_3P was required to complete the reaction in practicable yields. Reducing the amount of Pd/C−Ph_3P led to a dramatic increase of reaction time, and competitive hydrolysis side reaction of acetate into its corresponding alcohol occurred. This phenomenon was not observed with cinnamyl acetate **1**, even with prolonged reaction times. However with 5 mol % Pd/C, hydrolysis was present in less than 5% with acetates **3** and **4**. Whereas Meldrum's acid afforded a single product resulting from a dialkylation process (entries 11, 15), the use of diethylmalonate yielded exclusively the monoalkylation product (entry 14). These results were unanticipated, as monoalkylation is the major result of similar homogeneous Pd-catalyzed reaction. Although reaction of Meldrum's acid with acetate **4** is known in the literature,[12] to the best of our knowledge, compounds resulting from a double alkylation have not been described. Other nucleophiles also reacted well with branched acetates and broaden the scope of this catalytic system (entries 8, 10, 12).

Dry 10% Pd/C, although inexpensive and commercially available, is pyrophoric under air atmosphere, requiring specific attention during manipulations on a large scale. To make the reaction safer on a large scale, we envisioned the use of wet Pd/C. While $Pd(OH)_2$ did not work at all, 5% Pd/C (E 105 CA/W from Degussa AG) gave yields and reaction times similar to those of dry 10% Pd/C (entries 3, 9, 13).

On a substrate (i.e., acetate **14**) required for our radical cyclization project[6] we compared the results obtained by using $Pd(PPh_3)_4$[13] and Pd/C for the preparation of the

(8) For recent examples of palladium-catalyzed allylic substitution in water, see: (b) Blart, E.; Genet, J.-P.; Safi, M.; Savignac, M.; Sinou, D. *Tetrahedron* **1994**, *50*, 505−514. (b) Lemaire-Audoire, S.; Blart, E.; Savignac, M.; Pourcelot, G.; Genet, J.-P.; Bernard, J.-M. *Tetrahedron Lett*. **1994**, *35*, 8783−8786. (c) Rabeyrin, C.; Nguefack, C.; Sinou, D. *Tetrahedron Lett*. **2000**, *41*, 7461−7464. (d) Kobayashi, S.; Lam, W.; Manabe, K. *Tetrahedron Lett*. **2000**, *41*, 6115−6117. (e) Hashizume, T.; Yonehara, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **2000**, *65*, 5197−5201. (f) Feuerstein, M.; Laurenti, D.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2001**, *42*, 2313−2315.

(9) An isolated report described the allylation of diethylamine with allyl acetate catalyzed by Pd/C in toluene. But to have acceptable yields in their conditions authors used 2650 equiv of Ph_3P. They concluded that "...hetereogeneous palladium catalysts such as Pd/C are generally not useful for this reaction..." See: Bergbreiter, D. E.; Chen, B. *J. Chem. Soc., Chem. Commun.* **1983**, 1238−1239.

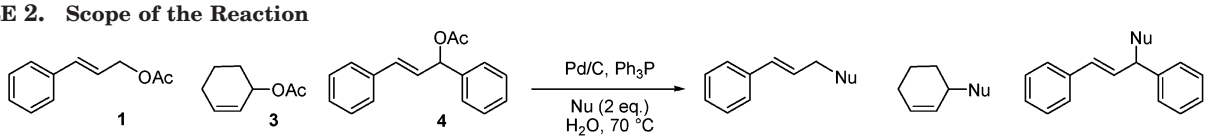
(10) 10% Pd/C was purchased from Aldrich.

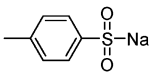
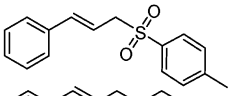
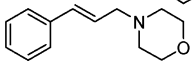
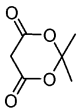
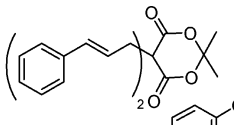
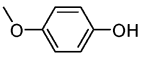
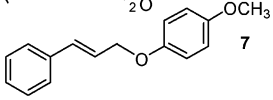
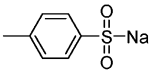
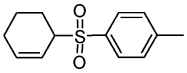
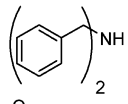
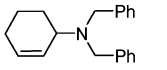
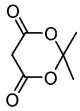
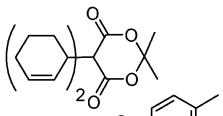
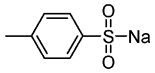
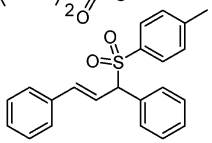
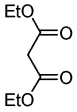
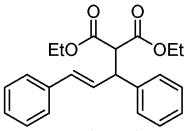
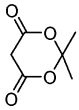
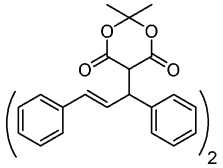
(11) Chevrin, C.; Le Bras, J.; Hénin, F.; Muzart, J. *Tetrahedron Lett*. **2003**, *44*, 8099−8102.

(12) Chen, W.; Xu, L.; Chatterton, C.; Xiao, J. *Chem. Commun*. **1999**, 1247−1248.

(13) Inomata, K.; Yamamoto, T.; Kotake, H. *Chem. Lett*. **1981**, 1357−1360.

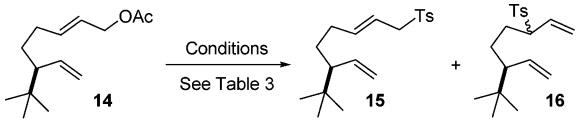
TABLE 2. Scope of the Reaction



Entry	Nucleophile	Pd/C (mol%)	PPh_3 (mol%)	Base	Solvent	t (h)	Product	Conversion [a] (%)	Yield [b] (%)
1		1	4	-	H_2O	18	 **2**	>95	96
2		1	4	-	H_2O/DME	36		>95	84
3[d]		1	4	-	H_2O	18		>95	89
4		1	4	-	H_2O	14	 **5**	89	84[c]
5		1	4	-	H_2O/DME	4		>95	93[c]
6		1	4	K_2CO_3	H_2O	5	 **6**	>95	94
7		1	4	K_2CO_3	H_2O	5	 **7**	>95	91
8		5	20	-	H_2O	12	 **8**	>95	65
9[d]		5	20	-	H_2O	12		>95	63
10		5	20	-	H_2O	12	 **9**	95	69
11		5	20	K_2CO_3	H_2O	6	 **10**	>95	71
12		5	20	-	H_2O	31	 **11**	>95	68
13[d]		5	20	-	H_2O	31		>95	69
14		5	20	K_2CO_3	H_2O	5	 **12**	95	70
15		5	20	K_2CO_3	H_2O	5	 **13**	>95	66

[a] Determined on the crude reaction mixture by ^1H NMR. [b] Yields of isolated products. [c] 4% of the branched isomer was also isolated. [d] 5% Pd/C (E 105 CA/W) from Degussa AG was used.

TABLE 3. Comparison $Pd(PPh_3)_4$–Pd/C



Entry	Conditions	15/16 [a]	Yield (%) [b]
1	Pd/C (1 mol%), PPh_3 (4 mol%), TsNa (1.1 eq.), H_2O, 70 °C, 16 h	95/5	95
2	$Pd(PPh_3)_4$ (5 mol%), TsNa (1.1 eq.), THF/MeOH (4/1), 25 °C, 12 h	80/20	86

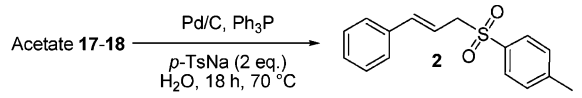
[a] Ratio determined on the crude reaction mixture by ^1H NMR. [b] Yields of isolated products. Combined yield of **15** and **16**.

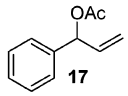
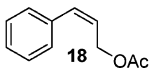
corresponding allyl sulfone **15**. The optimized procedures for each catalytic system are reported in Table 3. Although a higher temperature was required, the use of Pd/C led to the corresponding allyl sulfone **15** in higher yield (95%) and with greater regiodiscrimination favoring the desired linear isomer **15** compared to $Pd(PPh_3)_4$. These results highlight the efficiency of the heterogeneous Pd/C catalyst compared to the "classical" homogeneous $Pd(PPh_3)_4$ catalyst.

Mechanistic Studies. The mechanism of homogeneous Pd-mediated allylic alkylation has been extensively studied[1] and is summarized in Scheme 1. Oxidative addition of an allylic leaving group ***I*** to Pd(0) gives an (η^3-allyl)palladium(II) complex ***II***, which reacts with various nucleophiles to furnish allylic compounds ***III***.

To gain further insight into the Pd/C-mediated allylic alkylation mechanism, we examined the reaction of *p*-TsNa with two different acetates, **17** and **18**, which should give the same product (i.e., sulfone **2**) according to the above mechanism (Table 4). As expected, allylic sulfone **2** was the only product observed with very similar

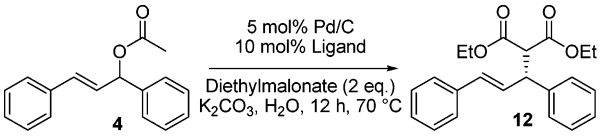
TABLE 4. Mechanistic Studies



Entry	Acetate	t (h)	Conv. (%)[a]	Product	Yield (%)[b]
1	 17	18	>95	**2**	92%
2	 18 OAc	18	>95	**2**	94%

[a] Determined on the crude reaction mixture by ^{1}H NMR. [b] Yields of isolated products.

TABLE 5. Asymmetric Attempts



Entry	Ligand	Product	ee (%)[a]	Configuration	Yield (%)[b]
1	(-)-DIOP	**12**	8	(*R*)	10
2	(*R*)-BINAP	**12**	80	(*R*)	21

[a] Determined by chiral HPLC. [b] Yields of isolated products.

yields irrespective of the nature of the acetate. Branched acetate **17** rearranges to the linear allylic sulfone **2** (entry 1), and (*Z*)-allyl acetate **18** isomerizes into (*E*)-allyl product (entry 2). From these observations we concluded that Pd/C-mediated allylic substitution in water proceeds through a mechanism close to that of homogeneous Pd catalysis.

Several recent studies have shown that Pd/C-mediated Heck[14] and Suzuki[15] reactions proceeded through homogeneous catalytic pathways via Pd species dissolved in solution. For our reaction, ICP-MS was used to evaluate the amount of Pd leaching into the solvent that did not redeposit on the charcoal. After 18 h of stirring during the transformation of **1** to **2**, the concentration of solubilized Pd was only 4 ppm (based on 0.029 mmol Pd introduced), indicating 1.3% of the metal used for the reaction had leached into the solvent.

Asymmetric Attempts. Finally, we studied an asymmetric version of this new catalytic system by using chiral diphosphine ligands (Table 5). Whereas (−)-DIOP induced negligible enantioselectivity, (*R*)-BINAP afforded **12** in 80% ee, albeit in low yield. Although these results are far from satisfactory, they show that enantioselective Pd/C-mediated allylation is possible, in principle. Moreover, to our knowledge, this result is the first example of a Pd/C-catalyzed asymmetric C−C bond formation reaction. Further optimization of these preliminary results is thus currently under investigation.

Conclusion

In conclusion, we reported the first Pd/C-mediated allylic substitution in water. This catalytic process is attractive, environment friendly, and requires an inexpensive source of Pd catalyst. This process should be appealing for industrial scale purposes. We have demonstrated, for the first time, the feasibility of an asymmetric version, although the yield remains modest. The developed methodology may find numerous applications because of its practicability. Total synthesis of natural products using this methodology will be reported shortly.

Experimental Section

***trans*-Cinnamyl-*p*-tolyl Sulfone (2).** A solution of cinnamyl acetate **1** (264 mg, 1.5 mmol) in H_2O (4 mL) was treated with *p*-TsNa (534 mg, 3 mmol), Ph_3P (15.7 mg, 4 mol %), and 10% Pd/C (15.9 mg, 1 mol %). The resulting mixture was stirred at 70 °C for 18 h. The mixture was filtered over a pad of Celite. The filtrate was washed with CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 (2×). The collected organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (20% EtOAc−pentane) gave **2** as a colorless solid (392 mg, 96%). Mp: 120 °C [lit.[16] 120−121 °C]. IR (KBr): ν 1577, 1593, 2972, 3022 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.44 (s, 3H), 3.95 (dd, 2H, J = 0.8, 7.5 Hz), 6.11 (dt, 1H, J = 7.5, 15.5 Hz), 6.41 (dd, 1H, J = 15.5 Hz), 7.29−7.34 (m, 7H), 7.77 (d, 2H, J = 8.3 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.5, 60.5, 115.3, 126.5, 128.4, 128.4, 128.6, 129.6, 135.5, 135.8, 138.9, 144.7. HRMS (ESI): calcd for $C_{16}H_{16}O_2NaS$ ($M + Na^+$) 295.0769, found 295.0757.

4-Cinnamylmorpholine (5) and 4-(1-Phenylallyl)morpholine. A solution of cinnamyl acetate **1** (264 mg, 1.5 mmol) in H_2O (2 mL) and DME (2 mL) was treated with morpholine (0.26 mL, 3 mmol), Ph_3P (15.7 mg, 4 mol %), and 10% Pd/C (15.9 mg, 1 mol %). The resulting mixture was stirred at 70 °C for 4 h. The mixture was filtered over a pad of Celite. The filtrate was washed with CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 (2×). The collected organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (20% EtOAc−pentane to 100% EtOAc) gave **5** as a colorless oil (283 mg, 93%) and its branched isomer as a colorless oil (12 mg, 4%).

4-Cinnamylmorpholine 5. IR (neat): ν 1578, 1598, 2957, 3058 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.51−2.54 (m, 4H), 3.17 (dd, 2H, J = 1.1, 6.8 Hz), 3.76 (t, 4H, J = 4.5 Hz), 6.29 (dt, 1H, J = 6.8, 13.6 Hz), 6.56 (d, 1H, J = 15.8 Hz), 7.22−7.41 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 61.4, 67.0, 126.1, 126.3, 127.5, 128.5, 133.3, 136.8. HRMS (ESI): calcd for $C_{13}H_{18}NO$ (M^+) 204.1388, found 204.1404.

4-(1-Phenylallyl)morpholine. IR (neat): ν 1602, 1640, 2956, 3027 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.30−2.37 (m, 2H), 2.48−2.53 (m, 2H), 3.63 (d, 1H, J = 5.8 Hz), 5.11 (dd, 1H, J = 1.5, 9.8 Hz), 5.24 (dd, 1H, J = 1.1, 17.3 Hz), 5.85−5.97 (m, 1H), 7.22−7.36 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 52.0, 67.1, 75.5, 116.6, 127.2, 127.9, 128.6, 139.7, 141.6. HRMS (ESI): calcd for $C_{13}H_{18}NO$ (M^+) 204.1388, found 204.1402.

5,5-Dicinnamyl-2,2-dimethyl-1,3-dioxane-4,6-dione (6). A solution of cinnamyl acetate **2** (264 mg, 1.5 mmol) in H_2O (4 mL) was treated with K_2CO_3 (414 mg, 3 mmol), Medrum's acid (432 mg, 3 mmol), Ph_3P (15.7 mg, 4 mol %), and 10% Pd/C (15.9 mg, 1 mol %). The resulting mixture was stirred at 70 °C for 5 h. The mixture was filtered over a pad of Celite. The filtrate was washed with CH_2Cl_2. The aqueous phase was

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extracted with CH_2Cl_2 (2×). The collected organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (20% EtOAc−pentane) gave **6** as a colorless solid (263 mg, 94%). Mp: 131−132 °C [lit.[17] 131 °C]. IR (KBr): ν 1576, 1596, 1741, 1773, 2996, 3056 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 1.55 (s, 6H), 2.97 (d, 4H, J = 7.9 Hz), 6.10 (dt, 2H, J = 7.9, 15.8 Hz), 6.56 (d, 2H, J = 15.8 Hz), 7.22−7.36 (m, 10H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.7, 42.1, 56.3, 106.0, 121.7, 126.3, 127.9, 128.6, 136.0, 136.2, 168.7. HRMS (ESI): calcd for $C_{24}H_{24}O_4$-Na (M + Na^+) 399.1572, found 399.1572.

1-((*E*)-3-(4-Methoxyphenoxy)prop-1-enyl)benzene (7). A solution of cinnamyl acetate **2** (264 mg, 1.5 mmol) in H_2O (4 mL) was treated with K_2CO_3 (414 mg, 3 mmol), *p*-methoxyphenol (372 mg, 3 mmol), Ph_3P (15.7 mg, 4 mol %), and 10% Pd/C (15.9 mg, 1 mol %). The resulting mixture was stirred at 70 °C for 5 h. The mixture was filtered over a pad of Celite. The filtrate was washed with CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 (2×). The collected organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (10% EtOAc−pentane) gave **7** as a colorless solid (327 mg, 91%). Mp: 106−107 °C [lit.[18] 107−109 °C]. IR (KBr): ν 1577, 1638, 2954, 3046 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.78 (s, 3H), 4.66 (dd, 2H, J = 1.5, 5.6 Hz), 6.42 (dt, 1H, J = 5.6, 15.8 Hz), 6.73 (d, 1H, J = 16.2 Hz), 6.84−6.93 (m, 4H), 7.24−7.44 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 55.7, 69.4, 114.7, 115.8, 124.8, 126.5, 127.8, 128.6, 132.8, 136.5, 152.8, 154.0. HRMS (ESI): calcd for $C_{16}H_{16}O_2Na$ (M + Na^+) 263.1048, found 263.1047.

Cyclohex-2-enyl-*p*-tolyl Sulfone (8). Prepared as described for **2**, with acetate **3** (210 mg, 1.5 mmol), *p*-TsNa (534 mg, 3 mmol), Ph_3P (78.6 mg, 20 mol %), and 10% Pd/C (79.5 mg, 5 mol %) in H_2O (4 mL) at 70 °C for 6 h. Purification by flash chromatography (20% EtOAc−pentane) gave **8** as a colorless oil (230 mg, 65%). IR (neat): ν 1597, 1649, 2936, 3034 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 1.42−1.55 (m, 1H), 1.73−1.97 (m, 5H), 2.44 (s, 3H), 3.69−3.76 (m, 1H), 5.74−5.80 (m, 1H), 6.03−6.10 (m, 1H), 7.33 (d, 1H, J = 7.9 Hz), 7.74 (d, 1H, J = 8.3 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 19.5, 21.6, 22.7, 24.3, 61.8, 118.7, 129.1, 129.6, 134.4, 135.1, 144.5. HRMS (ESI): calcd for $C_{13}H_{16}O_2NaS$ (M + Na^+) 259.0769, found 259.0776.

***N*,*N*-Dibenzylcyclohex-2-enamine (9).** A solution of acetate **3** (210 mg, 1.5 mmol) in H_2O (4 mL) was treated with dibenzylamine (0.58 mL, 3 mmol), Ph_3P (78.6 mg, 20 mol %), and 10% Pd/C (79.5 mg, 5 mol %). The resulting mixture was stirred at 70 °C for 12 h. The mixture was filtered over a pad of Celite. The filtrate was washed with CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 (2×). The collected organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (10% EtOAc−pentane) gave **9** as a colorless oil (287 mg, 69%). IR (neat): ν 1603, 1650, 2931, 3061 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 1.46−1.64 (m, 2H), 1.81−1.85 (m, 1H), 1.91−2.06 (m, 3H), 3.37−3.40 (m, 1H), 3.58 (d, 2H, J = 14.0 Hz), 3.78 (d, 2H, J = 14.0 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.8, 23.2, 25.3, 53.8, 54.5, 126.6, 128.1, 128.5, 130.0, 130.8, 140.9. HRMS (ESI): calcd for $C_{20}H_{24}N$ (M^+) 278.1909, found 278.1917.

5,5-Di(cyclohex-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (10). Prepared as described for **6**, with acetate **3** (210 mg, 1.5 mmol), Meldrum's acid (432 mg, 3 mmol), Ph_3P (78.6 mg, 20 mol %), and 10% Pd/C (79.5 mg, 5 mol %) in H_2O (4 mL) at 70 °C for 6 h. Purification by flash chromatography (10% EtOAc−pentane) gave **10** as a mixture of two inseparable diastereoisomers (1:1) (162 mg, 71%). Mp: 201 °C. IR (KBr): 1648, 1731, 1764, 2930 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 1.41−1.85 (m, 8H), 1.74 (s, 6H), 1.97 (m, 4H), 3.20 (m, 2H), 5.57−5.60 (m, 1H), 5.74−5.86 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.2, 22.2, 24.8, 25.3, 26.4, 30.1, 30.1, 40.4, 40.8, 60.7, 61.2, 105.7, 105.7, 124.8, 125.1, 130.1, 130.6, 167.2, 167.4, 167.6 (rotamers). HRMS (ESI): calcd for $C_{18}H_{24}O_4Na$ (M + Na^+) 327.1572, found 327.1570.

(*E*)-1,3-Diphenyl-2-propenyl-*p*-tolyl Sulfone (11). Prepared as described for **2**, with acetate **4** (378 mg, 1.5 mmol), *p*-TsNa (534 mg, 3 mmol), Ph_3P (78.6 mg, 20 mol %), and 10% Pd/C (79.5 mg, 5 mol %) in H_2O (4 mL) at 70 °C for 31 h. Purification by flash chromatography (20% EtOAc−pentane) gave **11** as a colorless solid (354 mg, 68%). Mp: 157−158 °C [lit.[19] 157−158 °C]. IR (KBr): ν 1596, 1639, 2920, 3060 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 2.40 (s, 3H), 4.83 (d, 1H, J = 7.2 Hz), 6.50−6.64 (m, 2H), 7.20−7.39 (m, 12H), 7.55 (d, 2H, J = 8.3 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 75.3, 120.2, 126.7, 128.4, 128.6, 128.6, 128.8, 129.3, 129.3 129.7, 132.5, 134.4, 135.9, 137.9, 144.5. HRMS (ESI): calcd for $C_{22}H_{20}NaSO_2$ (M + Na^+) 371.1082, found 371.1067.

Diethyl 2-[(*E*)-1,3-Diphenyl-2-propenyl]malonate (12). A solution of acetate **4** (378 mg, 1.5 mmol) in H_2O (4 mL) was treated with K_2CO_3 (414 mg, 3 mmol), diethyl malonate (455 μL, 3 mmol), Ph_3P (78.6 mg, 20 mol %), and 10% Pd/C (79.5 mg, 5 mol %). The resulting mixture was stirred at 70 °C for 5 h. The mixture was filtered over a pad of Celite. The filtrate was washed with CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 (2×). The collected organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (5% EtOAc−pentane) gave **12** as a colorless oil (369 mg, 70%). IR (KBr): ν 1600, 1731, 2982, 3060 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ 1.02 (t, 3H, J = 7.1 Hz), 1.21 (t, 3H, J = 7.1 Hz), 3.93 (d, 1H, J = 11.3 Hz), 3.98 (q, 2H, J = 7.1 Hz), 4.18 (q, 2H, J = 7.1 Hz), 4.27 (dd, 1H, J = 8.7, 11.3 Hz), 6.34 (dd, 1H, J = 8.3, 15.4 Hz), 6.49 (d, 1H, J = 15.8 Hz), 7.20−7.34 (m, 10H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.8, 14.1, 49.2, 57.8, 61.3, 61.5, 126.3, 127.1, 127.5, 128.0, 128.4, 128.6, 129.3, 131.7, 136.8, 140.3, 167.4, 167.8. HRMS (ESI): calcd for $C_{22}H_{24}NaO_4$ (M + Na^+) 375.1572, found 375.1563.

Diethyl 2-[(1*R*)-2*E*)-1,3-Diphenyl-2-propenyl]malonate (12). A solution of acetate **4** (378 mg, 1.5 mmol) in H_2O (4 mL) was treated with K_2CO_3 (414 mg, 3 mmol), diethyl malonate (455 μL, 3 mmol), (*R*)-BINAP (93 mg, 10 mol %), and 10% Pd/C (79.5 mg, 5 mol %). The resulting mixture was stirred at 70 °C for 5 h. The mixture was filtered over a pad of Celite. The filtrate was washed with CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 (2×). The collected organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (5% EtOAc−pentane) gave **12** as a colorless oil (111 mg, 21%), 80% ee, determined by chiral HPLC, Chiralpak AD-H (hexane/*i*-PrOH = 90/10, 11.4 min for (*S*)-**12** and 15.3 min for (*R*)-**12**).

2,2-Dimethyl-5,5-bis((*E*)-1,3-diphenylallyl)-1,3-dioxane-4,6-dione (13). Prepared as described for **6**, with acetate **4** (378 mg, 1.5 mmol), Meldrum's acid (432 mg, 3 mmol), Ph_3P (78.6 mg, 20 mol %), and 10% Pd/C (79.5 mg, 5 mol %) in H_2O (4 mL) at 70 °C for 5 h. Purification by flash chromatography (10% EtOAc−pentane) gave **11** as a mixture of two inseparable diastereoisomers (86:14) (261 mg, 66%). Mp: 106 °C. IR (KBr): ν 1599, 1650, 1728, 1760, 3060 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 0.55 (s, 6H × 0.86), 0.87 (s, 6H × 0.14), 4.36 (d, 2H × 1, J = 10.2 Hz), 6.27 (d, 2H × 0.14, J = 15.8 Hz), 6.46 (d, 2H × 0.86, J = 15.8 Hz), 6.92 (dd, 2H × 0.14, J = 10.1, 15.8 Hz), 7.17−7.45 (m, 20H × 1 + 2H × 0.86). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 28.3 (0.86), 28.7 (0.14), 54.7 (0.86), 55.4 (0.14), 63.7 (0.86), 64.0 (0.14), 106.1 (0.86), 106.2 (0.14), 124.9 (0.86), 126.5 (0.14), 126.7 (0.86), 127.2 (0.14), 127.6 (0.14), 127.7 (0.86), 127.8 (0.86), 128.4 (0.14), 128.6 (0.14), 128.6 (0.86), 129.0 (0.86), 129.2 (0.86), 130.1 (0.14), 134.3 (0.14), 135.4 (0.86), 136.7 (0.14),

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137.0 (0.86), 139.0 (0.14), 139.3 (0.86), 167.1 (0.86), 167.2 (0.14). HRMS (ESI): calcd for $C_{36}H_{32}NaO_4$ ($M + Na^+$) 551.2198, found 551.2206.

1-((*E*)-6-*tert*-Butylocta-2,7-dienylsulfonyl)-4-methylbenzene (15) and 1-(6-*tert*-Butylocta-1,7-dien-3-ylsulfonyl)-4-methylbenzene (16). With Pd/C. Prepared as described for **2**, with acetate **14** (336 mg, 1.5 mmol), *p*-TsNa (294 mg, 1.65 mmol), Ph_3P (15.7 mg, 4 mol %), and 10% Pd/C (15.9 mg, 1 mol %) in H_2O (4 mL) at 70 °C for 16 h. Purification by flash chromatography (20% EtOAc−pentane) gave **15** and **16** (**15/16**: 95/5) (456 mg, 95% combined yield).

With $Pd(PPh_3)_4$. A solution of acetate **14** (336 mg, 1.5 mmol) in THF (8 mL) and MeOH (2 mL) was treated with *p*-TsNa (294 mg, 1.65 mmol) and $Pd(PPh_3)_4$ (86.7 mg, 5 mol %). The resulting mixture was stirred for 12 h and then diluted with Et_2O and water. The organic phase was extracted three times with Et_2O. The collected organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash chromatography (15% EtOAc−pentane) gave **15** and **16** (**15/16**: 8/2) (413 mg, 86% combined yield). Some fractions from flash chromatography have been obtained pure for analysis.

1-((*E*)-6-*tert*-Butylocta-2,7-dienylsulfonyl)-4-methylbenzene (15). IR (neat): ν 1598, 1637, 1665, 2963, 3070 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ 0.81 (s, 9H), 0.95−1.10 (m, 1H), 1.35−1.57 (m, 2H), 1.67−1.85 (m, 1H), 1.95−2.09 (m, 1H), 2.43 (s, 3H), 3.72 (d, 2H, J = 6.4 Hz), 4.86 (dd, 1H, J = 2.5, 17.0 Hz), 5.01 (dd, 1H, J = 2.2, 10.1 Hz), 5.33−5.54 (m, 3H), 7.32 (d, 2H, J = 7.9 Hz), 7.72 (d, 2H, J = 8.2 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 27.6, 27.8, 31.0, 32.5, 54.5, 60.2, 116.0, 116.4, 128.5, 129.5, 135.5, 139.7, 141.7, 144.4. HRMS (LSIMS): calcd for $C_{19}H_{28}O_2S_2Na$ ($M + Na^+$) 343.1708, found 343.1710.

1-(6-*tert*-Butylocta-1,7-dien-3-ylsulfonyl)-4-methylbenzene (16). Mixture of diastereoisomers. IR (neat): ν 1597, 1638, 1738, 2963, 3071 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ 0.80 (s, 9H), 0.8−1.24 (m, 1H), 1.32−1.76 (m, 3H), 1.83−1.97 (m, 0.5H), 2.09−2.22 (m, 0.5H), 2.43 (s, 3H), 3.38−3.51 (m, 1H), 4.82−5.08 (m, 3H), 5.25−5.31 (m, 1H), 5.36−5.69 (m, 2H), 7.30 (d, 2H, J = 6.9 Hz), 7.69 (dd, 2H, J = 1.6, 6.9 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 25.3, 25.3, 26.0, 26.3, 27.6, 27.6, 32.5, 32.6, 54.3, 55.5, 69.6, 70.3, 116.8, 116.9, 123.2, 123.5, 129.2, 129.2, 129.3, 130.4, 130.8, 134.6, 139.0, 139.4, 144.4, 144.4. HRMS (LSIMS): calcd for $C_{19}H_{28}O_2S_2$ (M^+) 320.1805, found 320.1810.

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Supporting Information Available: Preparation of acetate **14** and copies of ^1H and ^{13}C NMR of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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