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Mono- and β,β-Double-Heck Reactions of α,β-Unsaturated Carbonyl Compounds in Aqueous Media†

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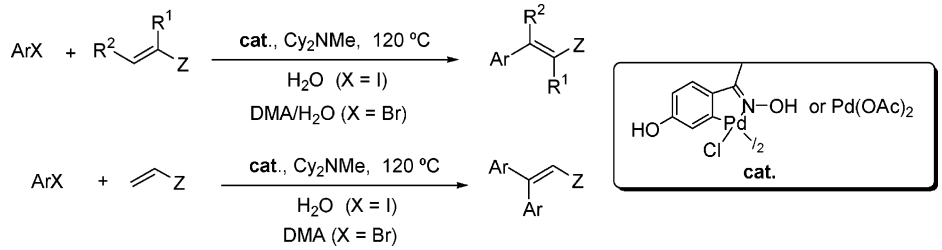

Optimized reaction conditions for the mono- and β,β-diarylation of electron-deficient alkenes in aqueous media catalyzed either by a *p*-hydroxyacetophenone oxime-derived palladacycle or by palladium(II) acetate under phosphine-free conditions and in the presence of (dicyclohexyl)-methylamine as base are described. Regioselective monoarylation of unsubstituted and substituted α,β-unsaturated carbonyl compounds takes place with aryl iodides at 120 °C in water. Aqueous *N,N*-dimethylacetamide (DMA), tetra-*n*-butylammonium bromide (TBAB) as additive, and the palladacycle as catalyst are the most efficient conditions for the coupling with aryl bromides, good stereoselectivities being also obtained in the arylation of crotonates and itaconates, whereas cinnamic derivatives afford lower steroselectivity, with the exception of cinnamic acid and nitrile. β,β-Diarylation of unsubstituted α,β-unsaturated carbonyl compounds can be controlled by using higher loading of the palladacycle and can be performed in refluxing water for aryl iodides, whereas DMA must be used for aryl bromides. Microwave irradiation can be used in the monoarylation of *tert*-butyl acrylate with aryl iodides in water or the coupling between ethyl cinnamate and aryl bromides in aqueous DMA.

Introduction

Aqueous Heck chemistry is a main field of interest because the use of water-based procedures has important environmental and technological consequences, being considered one of the most convenient tools in chemistry, not only in laboratory,[1] but also in industrial[2] scale applications. Therefore, the development of efficient catalysts and reaction conditions to perform Mirozoki–Heck couplings in aqueous media and in the presence of air is highly useful, especially for industrial applications. There are three main strategies to perform this vinylation reaction in neat water or in a mixture of organic solvent and water: using hydrophilic ligands, such as anionic or cationic phosphines,[3] in the presence of quaternary ammonium salts,[4] and with hydrophilic materials.[5] For the monoarylation of styrenes and acrylic acid derivatives in neat water, two types of palladium complexes have been recently used, the (di-2-pyridyl)methylamine-derived palladium(II) chloride **1**[6] and a cyclopalladated ferrocenylimine **2** (Figure 1).[7] These are active catalysts for coupling with aryl iodides and aryl bromides, in the latter case in the presence of ammonium salts. However, the intermolecular monoarylation of β-substituted α,β-unsaturated carbonyl compounds to give trisubstituted

† Dedicated to Prof. Rafael Suau on occasion of his 60th birthday.

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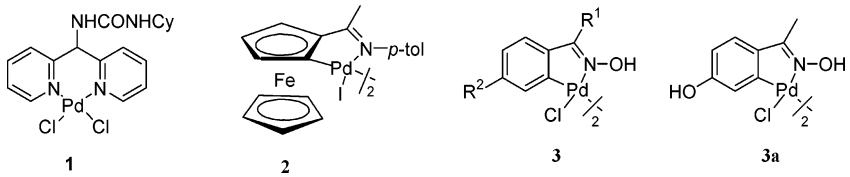

FIGURE 1. Catalysts for Heck reactions in aqueous media.

systems have only been performed in organic solvents[8−10] and in ionic liquids.[11] The coupling between a solid-supported aryl iodide and cinnamamide using $Pd(OAc)_2$ and triphenylphosphine as catalysts in the presence of ammonium salts is the only example carried out in aqueous DMF.[12] For the synthesis of symmetrical β,β-disubstituted α,β-unsaturated carbonyl compounds, the β,β-diarylation of acrylic systems is the most straightforward methodology. However, the double-Heck arylation has been scarcely investigated.[13] Thus, alkyl acrylates have been diarylated in organic solvents by Heck et al.,[9b] under high-pressure conditions[14] and in ionic liquids.[11a,15] In addition, acrylonitrile undergoes easily β-diarylation under solvent-free conditions.[16]

We have recently described that oxime-derived palladacycles **3** are very active and robust precatalysts for the slow generation of palladium nanoparticles, being used in several carbon−carbon bond-forming reactions in organic solvents, such as Heck,[17,18] Suzuki, Stille, and Ullmann couplings,[17,19] Sonogashira-type and sila-Sonogashira processes,[17,20] Glaser-type reactions,[20b] and acylation of alkynes.[21] These types of complexes are also effective catalysts in neat water or aqueous solvents for Suzuki couplings of alkyl and arylboronic acids with aryl bromides and chlorides and with allylic and benzylic chlorides.[22] We have described for the synthesis of methoxylated stilbenoids by Heck reaction of styrenes with aryl iodides that the reaction can be performed in water or in aqueous DMA by using the oxime-derived carbapalladacycle **3a** or $Pd(OAc)_2$ as catalyst and (dicyclohexyl)methylamine as base.[23] Herein, we describe the optimum reaction conditions for the monoarylation of unsubstituted and β-substituted α,β-unsaturated carbonyl compounds as well as for the β,β-diarylation of acrylic systems in aqueous media by using either the oxime-derived palladacycle **3a** or $Pd(OAc)_2$ as catalysts under phosphine-free conditions.[24]

Results and Discussion

Monoarylation of Unsubstituted α,β-Unsaturated Carbonyl Compounds. Secondary and tertiary amines were checked as bases for the Mizoroki−Heck coupling of aryl iodides with unsubstituted acrylic systems in water at 120 °C. These conditions have proved efficient in the arylation of acrylic acid esters with complex **1** in water.[6] However, inorganic bases can cause the hydrolysis of the ester function in aqueous media, especially at high temperatures and with long reaction times. *tert*-Butyl acrylate was chosen as acrylic ester in order to

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SCHEME 1. Monoarylation of Unsubstituted α,β-Unsaturated Carbonyl Compounds

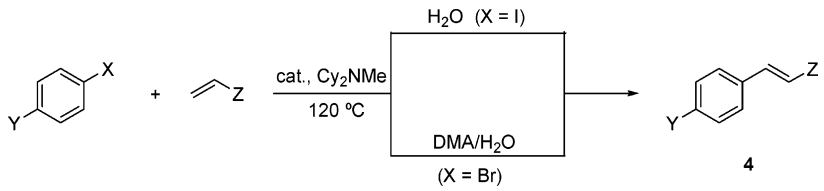
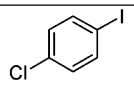
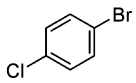


TABLE 1. Optimization of the Reaction Conditions for the Monoarylation of *tert*-Butyl Acrylate[a]

entry	ArX	cat. (mol% Pd)	solvent	base	additive	t	yield (%)[b]
1		**3a** (1.1×10^{-2})	H_2O	*i*-Pr_2NH	-	24 h	63
2		**3a** (10^{-2})	H_2O	Et_3N	-	14 h	89 (83)
3		**3a** (10^{-2})	H_2O	Cy_2NH	-	6 h	94
4		**3a** (1.1×10^{-2})	H_2O	Cy_2NMe	-	3 h	96 (94)
5		$Pd(OAc)_2$ (1.1×10^{-2})	H_2O	Cy_2NMe	-	3 h	83
6		**3a** (10^{-3})[c]	H_2O	Cy_2NMe	-	24 h	59
7		**3a** (1.3×10^{-2})	H_2O	Cy_2NMe	-	10 min[d]	91 (87)
8		$Pd(OAc)_2$ (1.2×10^{-2})	H_2O	Cy_2NMe	-	10 min[d]	98 (88)
9		**3a** (10^{-1})	H_2O	Cy_2NMe	-	14 h	5
10		**3a** (10^{-1})	H_2O	Cy_2NMe	TBAB[f]	14 h	4
11		**3a** (0.5)	DMA/H_2O[e]	Cy_2NMe	-	14 h	65 (65)
12		**3a** (0.1)	DMA/H_2O[e]	Cy_2NMe	TBAB[f]	14 h	97
13		**3a** (10^{-2})	DMA/H_2O[e]	Cy_2NMe	TBAB[f]	14 h	91 (85)
14		$Pd(OAc)_2$ (10^{-2})	DMA/H_2O[e]	Cy_2NMe	TBAB[f]	14 h	47
15		**3a** (10^{-2})	DMA/H_2O[e]	Cy_2NMe	TBAB[f]	10 min[d]	-
16		$Pd(OAc)_2$ (10^{-2})	DMA/H_2O[e]	Cy_2NMe	TBAB[f]	10 min[d]	-

[a] Reaction conditions: aryl halide (2 mmol), *tert*-butyl acrylate (3 mmol), amine (3 mmol), Pd catalyst, solvent (3 mL), 120 °C (bath temperature), pressure tube. [b] Yield for compound **4c**, determined by GC based on aryl halide using decane as internal standard. Isolated yield of compound **4c** after flash chromatography is shown in parentheses. Only the *E*-isomer was isolated in all cases. [c] An aliquot of a 2×10^{-5} M solution of palladacycle in DMA was added. [d] The reaction was performed under microwave irradiation conditions (120 W, 120 °C). [e] 4/1 (volume) mixture. [f] 1 equiv was used.

avoid possible hydrolysis of the ester function. In addition, amines, especially the tertiary di(cyclohexyl)methylamine, favor the reductive elimination of HCl from the L_2PdHCl adduct.[25] The monoarylation of *tert*-butyl acrylate with 4-chloroiodobenzene to give compound **4c** was chosen as a model reaction to find out the best reaction conditions (Scheme 1 and Table 1). The coupling was performed with palladacycle **3a** and different amines under refluxing water in a pressure tube (Table 1, entries 1−5). (Dicyclohexyl)methylamine, also used by Buchwald's group in the monoarylation of substituted acrylates,[9e] gave the best results. Under the same reaction conditions, $Pd(OAc)_2$ (10^{-2} mol %) afforded similar results (Table 1, entry 5), but only the palladacycle was active as precatalyst at lower catalyst loadings (10^{-3} mol %), with a turnover number (TON) of 59 000 (Table 1, entry 6). Under these reaction conditions, we observed that the 4-chloroiodobenzene had melted and two liquid phases were formed. When this process was carried out with both catalysts under microwave irradiation[26] at 120 W and 120 °C similar results were obtained (Table 1, entries 7 and 8).

When the monoarylation of *tert*-butyl acrylate was carried out with 4-chlorophenyl bromide in refluxing water and in the presence of (dicyclohexyl)methylamine with higher loading of palladacycle **3a** (0.1 mol % Pd), very low conversions were observed even after addition

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TABLE 2. Monoarylation of Unsubstituted α,β-unsaturated Carbonyl Compounds

						product[b]		
entry	ArX	Z	cat. (mol % Pd)	reaction conditions[a]	*t* (h)	**no.**		yield[c] (%)
1	C_6H_5I	CO_2-*t*-Bu	**3a** (10^{-2})	method A	3	**4a**	ArCH=CHCO$_2$-*t*-Bu	87
2	4-FC_6H_4I	CO_2-*t*-Bu	**3a** (10^{-2})	method A	22	**4b**	ArCH=CHCO$_2$-*t*-Bu	85
3	4-ClC_6H_4I	CO_2-*t*-Bu	**3a** (1.1×10^{-2})	method A	3	**4c**	ArCH=CHCO$_2$-*t*-Bu	94
4	4-ClC_6H_4I	CO_2-*t*-Bu	$Pd(OAc)_2$ (1.1×10^{-2})	method A	3	**4c**	ArCH=CHCO$_2$-*t*-Bu	83
5	4-$MeOC_6H_4I$	CO_2-*t*-Bu	**3a** (1.2×10^{-2})	method A	14	**4d**	ArCH=CHCO$_2$-*t*-Bu	87
6	4-$MeOC_6H_4I$	CO_2-*t*-Bu	$Pd(OAc)_2$ (2×10^{-2})	method A	14	**4d**	ArCH=CHCO$_2$-*t*-Bu	84
7	4-$MeOC_6H_4I$	$CO_2CH_2CHMeBu$	**3a** (10^{-2})	method A	14	**4e**	ArCH=CHCO$_2$ $CH_2CHMeBu$	91
8	4-FC_6H_4I	CO_2H	**3a** (10^{-1})	method A	14	**4f**	PhCH=CHCO$_2$H	66
9	C_6H_5I	$CONMe_2$	**3a** (10^{-1})	method A	14	**4g**	PhCH=CHCONMe$_2$	96
10	C_6H_5I	CN	**3a** (1)	method A	9	**4h**	PhCH=CHCN	94[d]
11	C_6H_5I	COMe	**3a** (9×10^{-3})	method A	23	**4i**	PhCH=CHCOMe	69[e]
12	4-ClC_6H_4Br	CO_2-*t*-Bu	**3a** (10^{-2})	method B	14	**4c**	ArCH=CHCO$_2$-*t*-Bu	85
13	4-$MeOC_6H_4Br$	CO_2-*t*-Bu	**3a** (10^{-1})	method B	14	**4d**	ArCH=CHCO$_2$-*t*-Bu	40
14	4-$MeOC_6H_4Br$	$CO_2CH_2CHMeBu$	**3a** (1)	method B	14	**4e**	ArCH=CHCO$_2$ $CH_2CHMeBu$	49
15	4-FC_6H_4Br	CO_2H	**3a** (1)	method B	14	**4f**	ArCH=CHCO$_2$H	56
16	C_6H_5Br	$CONMe_2$	**3a** (1)	method B	38	**4g**	ArCH=CHCONMe$_2$	46

[a] Method A: ArI (2 mmol), alkene (3 mmol), Cy_2NMe (3 mmol), and H_2O (3 mL), 120 °C (bath temperature), pressure tube. Method B: ArBr (1 mmol), alkene (1.5 mmol), Cy_2NMe (1.5 mmol), TBAB (1 mmol), DMA/H_2O (4/1, 5 mL), 120 °C (bath temperature), pressure tube. [b] *E*-Configuration. [c] Yield after flash chromatography (hexane/EtOAc). Only the *E*-isomer was isolated in all cases except for entry 10.[d] A *Z*/*E* 1/4 mixture was obtained. [e] 5% of 4,4-diphenylbut-3-en-2-one and 5% of 4,4-diphenylbutan-2-one were isolated.

of tetra-*n*-butylammonium bromide (TBAB), which favors the stabilization of palladium(0) nanoparticles[27] generated from the palladacycle (Table 1, entries 9 and 10). The use of aqueous *N,N*-dimethylacetamide (4/1:DMA/H_2O) gave a good yield (65%), probably because the reaction took place under homogeneous conditions (Table 1, entry 11). The addition of TBAB gave better results even with rather low catalyst loading (10^{-2} mol % Pd) in 14 h (Table 1, compare entries 12 and 13), whereas $Pd(OAc)_2$ yielded lower conversion under the mentioned reaction conditions (Table 1, entry 14). This coupling did not take place using complex **3a** or $Pd(OAc)_2$ under microwave irradiation[26] (Table 1, entries 15 and 16). In addition, attempts to perform the arylation of *tert*-butyl acrylate with 4-chloroacetophenone under the above-mentioned reaction conditions failed.

The application of these aqueous palladium-catalyzed protocols to the monoarylation of an array of unsubstituted α,β-unsaturated carbonyl compounds and aryl iodides and bromides to give compounds **4** is summarized in Scheme 1 and Table 2. Heck couplings of alkyl acrylates with activated and deactivated aryl iodides in refluxing water and Cy_2NMe as base (method A) proceeded under low catalyst loadings (Table 2, entries 1−7). Slightly better results were obtained using the palladacycle **3a** than using $Pd(OAc)_2$ (Table 2, compare entries 3 with 4 and 5 with 6). The arylation of acrylic acid, *N,N*-dimethylacrylamide, and acrylonitrile with iodobenzene required higher catalyst loadings than the arylation of esters, giving the (*E*)-cinnamic acid (**4f**) and the amide derivative **4g** with good diastereoselectivities, whereas the nitrile **4h** was obtained as a mixture 1/4 of *Z*/*E* diastereomers (Table 2, entries 8−10). Monoarylation was the main process observed in the arylation of methyl vinyl ketone, giving 69% of benzylidenacetone (**4i**) and about 10% of a 1/1 mixture of diarylated compounds **5h** and 4,4-diphenylbutan-2-one (Table 2, entry 11).[28]

When the coupling between the above-mentioned unsubstituted acrylic acid derivatives and activated and deactivated aryl bromides was performed, aqueous DMA was used as solvent, TBAB as additive, Cy_2NMe as base and palladacycle **3a** as precatalyst (Method B) (Scheme 1 and Table 2, entries 12−16). Compounds **4** were obtained in moderate to good yields and excellent *E*-diastereoselectivity, with only the arylation of acrylonitrile with bromobenzene being unsuccessful. With this procedure, the organic sunscreen 2-ethylhexyl *p*-methoxycinnamate (OMC) (**4e**) could be prepared either from the aryl iodide in neat water (TON 9100) or from the aryl bromide in aqueous DMA (TON 49).

From these results, it can be summarized that the monoarylation of unsubstituted acrylic acid derivatives can be performed efficiently in neat water with either palladacycle **3a** or $Pd(OAc)_2$ under thermal or microwave irradiation. However, in the case of aryl bromides, palladacycle **3a** is a better palladium source than $Pd(OAc)_2$ and the coupling must be carried out in aqueous DMA in the presence of TBAB and only under thermal conditions.

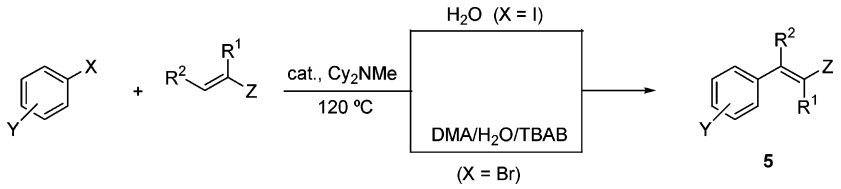
Monoarylation of Substituted α,β-Unsaturated Carbonyl Compounds. The reaction conditions described for aryl iodides (method A) and for aryl bromides (method B) were employed for the preparation of trisubstituted olefins (Scheme 2 and Table 3). When different electron-poor (activated) and electron-rich (deactivated) aryl iodides were coupled in refluxing water with ethyl cinnamate, products **5a**−**c** were obtained as a ca. 3/1 mixture of *E*/*Z* diastereomers (Table 3, entries 1−3). When $Pd(OAc)_2$ (0.1 mol %) was used as catalyst in the coupling of 4-fluoroiodobenzene and ethyl cinnamate, only a 23% (GC) of compound **5b** was formed after 1 d

(26) Microwave reactions were performed with a CEM Discover Synthesis Unit (CEM Corp., Matthews, NC) with a continuous focused microwave power delivery system in glass vessels (10 mL) sealed with a septum under magnetic stirring. The temperature of the reaction mixture inside the vessel was monitored using a calibrated infrared temperature control under the reaction vessel.

(27) TBAB has been used for the stabilization of palladium nanoparticles: Reetz, M. T.; Westermann, E. *Angew. Chem., Int. Ed.* **2000**, *39*, 165−168.

(28) Similar results have been described in organic solvents with $Pd(OAc)_2(PPh_3)_2$ as catalyst.[8a]

SCHEME 2. Monoarylation of Substituted α,β-Unsaturated Carbonyl Compounds



reaction time, this coupling also failing under microwave irradiation either with $Pd(OAc)_2$ or with complex **3a**. Products **5a** and **5c** were also prepared in lower yields and diastereoselectivities from the corresponding aryl bromides with the palladacycle **3a** as precatalyst in aqueous DMA than when using aryl iodides (Table 3, compare entries 1 with 12 and 3 with 16). Alternatively, the coupling of 4-bromoacetophenone and ethyl cinnamate was carried out with both palladium sources under microwave irradiation[26] (Table 3, entries 14 and 15).

In the arylation of ethyl crotonate with an activated and a deactivated aryl iodide using method A, products **5d** and **5e** were obtained with rather high diastereoselectivity (Table 3, entries 4 and 5). In the case of aryl bromides, the couplings with ethyl crotonate were performed in aqueous DMA in the presence of TBAB at 120 °C (method B) but also in neat DMA (method C) (Table 3, entries 17−23). In general, better yields and diastereoselectivities were obtained when the reaction was performed in aqueous DMA (method B). The diastereoselectivity in this type of coupling has been found to be due to a base-catalyzed equilibration.[9e,11a] In all of these couplings with ethyl crotonate, variable amounts of ethyl 3- and 4-arylbut-3-enoates were also obtained as secondary products (Table 3, footnotes f, h, k−p), pure ethyl (*E*)-3-arylbut-2-enoates being isolated in all cases after flash chromatography. Methyl itaconate was regio- and stereoselectively arylated with iodobenzene under method A conditions and with bromobenzene (method B) to give product **5f** in similar yields (Table 3, entries 6 and 24).

The arylation of cinnamic and crotonic acid was carried out with 4-fluoroiodobenzene (method A) to afford products **5g** and **5h** with high diastereoselectivities (Table 3, entries 7 and 8), whereas the reaction failed when using 4-chlorophenyl bromide and method B. In the case of cinnamamide and cinnamonitrile, the coupling with 4-fluoroiodobenzene using method A provided compounds **5i** and **5j** in good yields and diastereoselectivities (Table 3, entries 9 and 10). When 4-chlorobromobenzene was used as arylating agent under method B, related amide **5n** and nitrile **5o** were obtained with lower diastereoselectivities (Table 3, entries 25 and 26). In general, cinnamic acid, amide, and nitrile gave a higher diastereoselectivity than the corresponding ester. When activated 4-chloroacetophenone was coupled with ethyl cinnamate and crotonate using method B conditions, but upon heating at 140 °C, products **5a** and **5p** were obtained in moderate yields (Table 3, entries 27 and 28).

Lower TONs and TOFs were observed in general with deactivated aryl halides, which suggests that the rate-limiting step is the oxidative addition. However, the coupling between the deactivated 4-methoxyiodobenzene and cinnamonitrile to give product **5k** was, in this particular case, as fast as with the activated 4-fluoroiodobenzene (Table 3, compare entries 10 and 11).

Diarylation of Unsubstituted α,β-Unsaturated Carbonyl Compounds. In the diarylation of *tert*-butyl acrylate with iodobenzene (2 equiv) using complex **3a** as precatalyst, the amount of Pd had to be increased to 1 mol %, with different amines (3 equiv), such as diisopropylamine (DIA), triethylamine, dicyclohexylamine, and (dicyclohexyl)methylamine, being essayed at 120 °C in water during 14 h in a pressure tube (Scheme 3 and Table 4, entries 1−4). The best yields were obtained with (dicyclohexyl)methylamine (method A), whereas DIA and Et_3N failed. On the other hand, product **6a** was obtained in only 31% yield when $Pd(OAc)_2$ was used as catalyst (Table 4, entry 5). When microwave conditions (120 °C, 120 W)[26] were used only a 31% yield was observed after 10 min when using complex **3a**, whereas $Pd(OAc)_2$ failed (Table 4, entries 6 and 7). When *tert*-butyl acrylate was diarylated with 4-chlorobromobenzene in water (method A), the reaction failed and only a 14% yield of the final product **6c** was detected (method B) (Table 4, entry 8). However, when neat DMA was used as solvent (method C), a mixture of diarylated product **6c** and monoarylated **4c** was obtained in 93 and 6% yield, respectively (Table 4, entry 9), whereas $Pd(OAc)_2$ failed under these reaction conditions (Table 4, entry 10). In the presence of tetra-*n*-butylammonium chloride (TBAC) as additive, a 76% of compound **6c** was obtained (Table 4, entry 11).

The β,β-diarylation of *tert*-butyl acrylate was carried out with different aryl iodides under method A conditions to give compounds **6a**−**d** in good yields (Scheme 3, Table 5, entries 1−7). The palladacycle **3a** and $Pd(OAc)_2$ were used as catalysts for comparison, the former giving much better results (Table 5, compare entries 2 and 3, 4 and 5, 6 and 7). When 4-chloroiodobenzene was used, diisopropylamine was employed as base because mainly the homocoupling product 4,4′-dichlorobiphenyl was obtained in the presence of (dicyclohexyl)methylamine (Table 5, entry 4). *N,N*-Dimethylacrylamide and acrylonitrile were also diarylated with iodobenzene in water at 120 °C in good yields to afford products **6e** and **6f**, respectively (Table 5 entries 8 and 9). Surprisingly, in the case of acrylonitrile the diarylation is a more favored process than the monoarylation, lower loading of catalyst being necessary (compare Table 2, entry 10 and Table 5, entry 9). When methyl vinyl ketone was diarylated with iodobenzene compound **6g** and saturated 4,4-diphenylbutan-2-one were obtained due to the conjugate addition of iodobenzene to the initially formed monoarylated ketone **4i**.[29] For the double cross-coupling of aryl bromides with *tert*-butyl acrylate, *N,N*-dimethylacrylamide, and methyl vinyl ketone, the conditions of method C were used to provide products **6a**, **6h**, and **6g** in similar yields as with aryl iodides (Scheme 3, Table 5, entries 11−13). However,

(29) Saturated compounds have been obtained mainly in the diarylation of α,β-unsaturated ketones with palladium(II) acetate and triphenylphosphine in acetonitrile and in the presence of formic acid and triethylamine.[8b]

TABLE 3. Monoarylation of Substituted α,β-Unsaturated Carbonyl Compounds

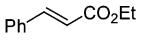
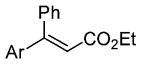
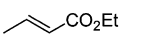
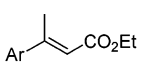
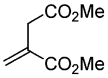
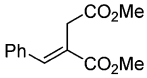
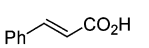
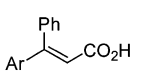
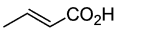
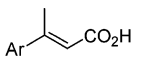
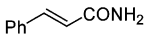
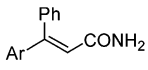
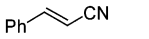
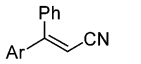
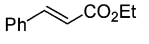
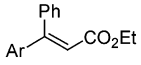
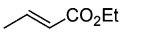
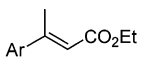
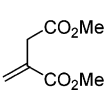
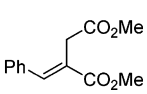
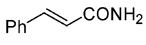
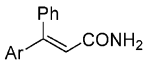
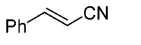
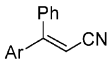
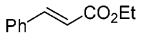
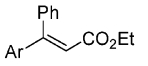
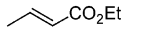
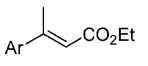
entry	ArX	alkene	cat. (mol% Pd)	reaction conditions[a]	t	product			
						no.[b]		*E/Z* ratio[c]	yield (%)[d]
1	4-MeCOC$_6$H$_4$I		**3a** (0.1)	Method A	20 h	**5a**		72/28	54[e]
2	4-FC$_6$H$_4$I		**3a** (0.1)	Method A	24 h	**5b**		70/30	73
3	4-MeOC$_6$H$_4$I		**3a** (1)	Method A	38 h	**5c**		74/26	77
4	4-FC$_6$H$_4$I		**3a** (0.5)	Method A	14 h	**5d**		93/7[f]	46[g]
5	4-MeOC$_6$H$_4$I		**3a** (0.5)	Method A	22 h	**5e**		100/0[h]	43[g]
6	C$_6$H$_5$I		**3a** (0.1)	Method A	14 h	**5f**		100/0	87[g]
7	4-FC$_6$H$_4$I		**3a** (1)	Method A	14 h	**5g**		93/7	42
8	4-FC$_6$H$_4$I		**3a** (1)	Method A	14 h	**5h**		96/4[i]	44
9	4-FC$_6$H$_4$I		**3a** (1)	Method A	14 h	**5i**		80/20	91
10	4-FC$_6$H$_4$I		**3a** (1)	Method A	7 h	**5j**		95/5	84
11	4-MeOC$_6$H$_4$I		**3a** (1)	Method A	7 h	**5k**		89/11	83[g]
12	4-MeCOC$_6$H$_4$Br		**3a** (0.1)	Method B	14 h	**5a**		66/34	48
13	4-MeCOC$_6$H$_4$Br		Pd(OAc)$_2$ (0.1)	Method B	16 h	**5a**		63/37	57
14	4-MeCOC$_6$H$_4$Br		**3a** (0.1)	Method B	10 min[j]	**5a**		63/37	33
15	4-MeCOC$_6$H$_4$Br		Pd(OAc)$_2$ (0.1)	Method B	10 min[j]	**5a**		65/35	55
16	4-MeOC$_6$H$_4$Br		**3a** (0.5)	Method B	14 h	**5c**		58/42	51
17	4-ClC$_6$H$_4$Br		**3a** (0.5)	Method B	14 h	**5l**		96/4[k]	66[g]
18	4-ClC$_6$H$_4$Br		Pd(OAc)$_2$ (0.5)	Method B	16 h	**5l**		94/6	56[g]
19	4-ClC$_6$H$_4$Br		**3a** (0.1)	Method C	13 h	**5l**		87/13[l]	69[g]
20	4-MeOC$_6$H$_4$Br		**3a** (1)	Method B	14 h	**5e**		97/3[m]	54[g]
21	4-MeOC$_6$H$_4$Br		**3a** (1)	Method C	14 h	**5e**		95/5[n]	42[g]
22	2-MeC$_6$H$_4$Br		**3a** (1)	Method B	14 h	**5m**		81/19[o]	35[g]
23	2-MeC$_6$H$_4$Br		**3a** (1)	Method C	14 h	**5m**		82/18[p]	20[g]
24	C$_6$H$_5$Br		**3a** (0.5)	Method B	14 h	**5f**		100/0	88[g]

Table 3. (Continued)

entry	ArX	alkene	cat. (mol% Pd)	reaction conditions[a]	t	product no.[b]		E/Z ratio[c]	yield (%)[d]
25	4-ClC_6H_4Br		**3a** (1)	Method B	14 h	**5n**		72/25	78
26	4-ClC_6H_4Br		**3a** (1)	Method B	14 h	**5o**		85/15	70
27	4-$MeCOC_6H_4Cl$		**3a** (1)	Method B[q]	24 h	**5a**		61/39	38
28	4-$MeCOC_6H_4Cl$		**3a** (1)	Method B[q]	24 h	**5p**		90/10	18[g]

[a] Method A: ArI (1 mmol), alkene (1.5 mmol), Cy_2NMe (1.5 mmol), H_2O (2 mL), 120 °C (bath temperature), pressure tube. Method B: ArBr (1 mmol), alkene (1.5 mmol), Cy_2NMe (1.5 mmol), TBAB (1 mmol), DMA/H_2O (4/1, 5 mL), 120 °C (bath temperature), pressure tube. Method C: ArBr (1 mmol), alkene (1.5 mmol), Cy_2NMe (1.5 mmol), DMA (2 mL), 120 °C (bath temperature), pressure tube. [b] Only the *E*-configuration has been represented. [c] Determined by ^1H NMR (300 MHz). [d] Yield of the mixture of diastereomers after flash chromatography (hexane/EtOAc). [e] 45% of 4,4′-bisacetylbiphenyl was also obtained. [f] 2% of ethyl 3-(4-iodophenyl)but-3-enoate and 4% of ethyl 4-(4-iodophenyl)but-3-enoate were also obtained. [g] Isolated yield for the (*E*)-diastereomer. [h] 3% of ethyl 3-(4-methoxyphenyl)but-3-enoate was also obtained. [i] 8% of 3-(4-fluorophenyl)but-3-enoic acid and 3% of 4-(4-fluorophenyl)but-3-enoic acid were also obtained. [j] The reaction was performed under microwave irradiation (80 W, 120 °C). [k] 4% of ethyl 3-(4-chlorophenyl)but-3-enoate was also obtained. [l] 5% of ethyl 3-(4-chlorophenyl)but-3-enoate and 6% of ethyl 4-(4-chlorophenyl)but-3-enoate were also obtained. [m] 1% of ethyl 3-(4-methoxyphenyl)but-3-enoate was also obtained. [n] 2% of ethyl 3-(4-methoxyphenyl)but-3-enoate and 4% of ethyl 4-(4-methoxyphenyl)but-3-enoate were also obtained. [o] 2% of ethyl 3-(2-methylphenyl)but-3-enoate and 10% of ethyl 4-(2-methylphenyl)but-3-enoate were also obtained. [p] 2% of ethyl 3-(2-methylphenyl)but-3-enoate and 2% of ethyl 4-(2-methylphenyl)but-3-enoate were also obtained. [q] At 140 °C.

SCHEME 3. Diarylation of Substituted α,β-Unsaturated Carbonyl Compounds

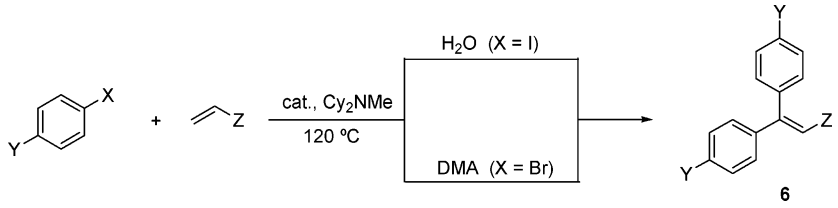


TABLE 4. Optimization of the Reaction Conditions for the Diarylation of *tert*-Butyl Acrylate[a]

entry	ArX	cat. (mol % Pd)	solvent	base	additive	t	yield[b] (%)
1	C_6H_5I	**3a** (1)	H_2O	*i*-Pr_2NH		14 h	0
2		**3a** (1)	H_2O	Et_3N		14 h	0
3		**3a** (1)	H_2O	Cy_2NH		14 h	58
4		**3a** (1)	H_2O	Cy_2NMe		14 h	65 (66)
5		$Pd(OAc)_2$ (1)	H_2O	Cy_2NMe		14 h	13
6		**3a** (1)	H_2O	Cy_2NMe		10 min[c]	31
7		$Pd(OAc)_2$ (1)	H_2O	Cy_2NMe		10 min[c]	0
8	4-ClC_6H_4Br	**3a** (1)	DMA/H_2O[d]	Cy_2NMe	TBAB[e]	14 h	14
9		**3a** (1)	DMA	Cy_2NMe		14 h	93 (83)
10		$Pd(OAc)_2$ (1)	DMA	Cy_2NMe		14 h	
11		**3a** (1)	DMA	Cy_2NMe	TABC[e]	14 h	76

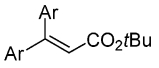
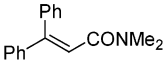
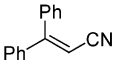
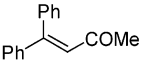
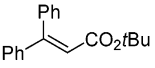
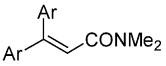
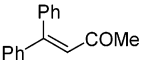
[a] Reaction conditions: aryl halide (1 mmol), *tert*-butyl acrylate (0.5 mmol), amine (1.5 mmol), Pd catalyst, solvent (2 mL), 120 °C (bath temperature), pressure tube. [b] Yield for the diarylated product **6,** determined by GC based on aryl halide using decane as internal standard. The yield of compound **6** after flash chromatography is shown in parentheses. [c] The reaction was performed under microwave irradiation conditions (120 W, 120 °C). [d] 4/1 (volume) mixture. [e] 1 mmol.

the diarylation of acrylic acid and acrylonitrile failed when aryl bromides were used.

Conclusions

We can conclude that the oxime-derived palladacycle **3a** and $Pd(OAc)_2$ are efficient precatalysts for the phosphine-free monoarylation of unsubstituted and substituted α,β-unsaturated carbonyl compounds using (dicyclohexyl)methylamine as base under thermal conditions or microwave irradiation. This Heck reaction can be performed in refluxing water for aryl iodides and in aqueous DMA in the presence of TBAB as additive for aryl bromides. For the β,β-diarylation reaction of unsubstituted α,β-unsaturated carbonyl compounds, thermal conditions and higher catalyst loading of palladacycle **3a** must be used, either in water at 120 °C for aryl iodides

TABLE 5. Diarylation of Unsubstituted α,β-Unsaturated Carbonyl Compounds

entry	ArX	Z	cat. (mol% Pd)	reaction conditions[a]	t (h)	product		
						no.		yield (%)[b]
1	C_6H_5I	CO_2-*t*-Bu	**3a** (1)	Method A	13	**6a**		66
2	4-FC_6H_4I		**3a** (0.1)	Method A	14	**6b**		92
3	4-FC_6H_4I		$Pd(OAc)_2$ (0.1)	Method A	23	**6b**		0
4	4-ClC_6H_4I		**3a** (0.1)	Method A[c]	22	**6c**		89
5	4-ClC_6H_4I		$Pd(OAc)_2$ (0.1)	Method A	14	**6c**		13
6	4-$MeOC_6H_4I$		**3a** (1)	Method A	14	**6d**		75
7	4-$MeOC_6H_4I$		$Pd(OAc)_2$ (1)	Method A	14	**6d**		34
8	C_6H_5I	$CONMe_2$	**3a** (1)	Method A	14	**6e**		77
9	C_6H_5I	CN	**3a** (0.1)	Method A	23	**6f**		86
10	C_6H_5I	COMe	**3a** (0.5)	Method A	8	**6g**		41[d]
11	C_6H_5Br	CO_2-*t*-Bu	**3a** (1)	Method C	14	**6a**		67
12	4-ClC_6H_4Br	$CONMe_2$	**3a** (1)	Method C	14	**6h**		94
13	C_6H_5Br	COMe	**3a** (1)	Method C	38	**6g**		42[e]

[a] Method A: ArI (1 mmol), alkene (0.5 mmol), Cy_2NMe (1.5 mmol), H_2O (2 mL), 120 °C (bath temperature), pressure tube. Method C: ArBr (1 mmol), alkene (0.5 mmol), Cy_2NMe (1.5 mmol), DMA (2 mL), 120 °C (bath temperature), pressure tube. [b] Yield after flash chromatography (hexane/EtOAc). [c] Diisopropylamine was used as base. [d] 53% of 4,4-diphenylbutan-2-one was also isolated. [e] 9% of 4,4-diphenylbutan-2-one was also isolated.

or in DMA for aryl bromides. The phosphine-free reaction conditions used for the Mizoroki−Heck of disubstituted alkenes using Cy_2NMe as base in aqueous media improved the already described results described by Gürtler and Buchwald[9e] in DMA because shorter reaction times and lower loadings of palladium are employed. The use of neat water as solvent for aryl iodides and the applicability of the arylation not only to esters but also to acids, amides, and nitriles as substrates are additional interesting results.

Experimental Section

Typical Procedure for the Palladium-Catalyzed Mono- and Diarylation of α,β-Unsaturated Carbonyl Compounds. Method A. A 15 mL pressure tube was charged with the aryl iodide (2 mmol), the alkene (3 mmol), (dicyclohexyl)-methylamine (0.642 mL, 3 mmol), the catalyst (0.01−1 mol % Pd, see the tables), and water (3 mL) for the monoarylation reactions. For the diarylation the following amounts were used: aryl iodide (1 mmol), alkene (0.5 mmol), (diciclohexyl)-methylamine (0.321 mL, 1.5 mmol), catalyst (0.1−1 mol % Pd), and water (2 mL). The mixture was heated at 120 °C, and the reaction was followed by GLC. After completion, the reaction was cooled and poured into EtOAc (40 mL). The organic phase was washed with 2 M HCl (2 × 30 mL) and water (2 × 30 mL) and dried (Na_2SO_4), and the solvent was evaporated to afford the corresponding crude product, which was purified by flash chromatography (hexane/EtOAc) to afford pure compounds.

Method B. A 15 mL pressure tube was charged with the aryl bromide (2 mmol), alkene (3 mmol), (dicyclohexyl)-methylamine (0.642 mL, 3 mmol), TBAB (644 mg, 2 mmol), catalyst (0.01−1 mol % Pd see the tables), DMA (4 mL), and water (1 mL) for the monoarylation reactions. The mixture was heated at 120 °C, and the reaction was controlled by GLC. The same workup as before was performed.

Method C. A 15 mL pressure tube was charged with the aryl bromide (1 mmol), alkene (1.5 mmol), (dicyclohexyl)-methylamine (0.321 mL, 1.5 mmol), catalyst (0.1−1 mol % Pd, see the tables), and DMA (2 mL) for monoarylation reactions. For diarylation 0.5 mmol of alkene was used. The mixture was heated at 120 °C, and the reaction was monitored by GLC. The same workup as before was performed.

Compounds **4e**,**f**,**h**,**i** are commercially available, and compounds **4a**,[30] **4b**,[31] **4c**,**d**,[32] **4g**,[33] **5a**,[11a] **5c**,[11a] **5d**,[34] **5e**,[35] **5f**,[36] **5h**,[37] **5k**,[38] **5m**,[39] **5o**,[10b] **6f**,[40] **6g**,[8b] and **6h**[41] have been previously reported and were characterized by comparison with their reported data. The configuration of new compounds **5** was determined by NMR NOESY experiments. Physical, analytical, and spectroscopic data of new synthesized compounds follow.

Ethyl (*E*)-3-(4-fluorophenyl)-3-phenylpropenoate (5b): oil; R_f 0.40 (hexane/EtOAc 9/1); IR (film) ν (cm^{-1}) = 1723 (C=O), 1600 (C=C), 1227, 1161 (CO), 1265 (ArCF); ^{1}H NMR δ = 1.11 (t, 3H, J = 7.1 Hz), 4.05 (q, 2H, J = 7.1 Hz), 6.31 (s, 1H), 7.00−7.04 (m, 2H), 7.17−7.37 (m, 7H); ^{13}C NMR δ = 14.0, 60.2, 115.5 (d, $^2J_{CF}$ = 22.0 Hz), 117.3, 128.0, 128.3, 129.1, 130.2 (d, $^3J_{CF}$ = 8.9 Hz), 137.0 (d, $^4J_{CF}$ = 3.3 Hz), 138.8, 155.4, 163.5 (d, $^1J_{CF}$ = 250.3 Hz), 166.0; MS *m/z* (rel int) 270 (M$^+$, 52), 242 (16), 241 (17), 179 (100), 198 (84), 197 (64), 196 (96), 183 (39), 177 (24), 176 (35), 170 (14), 123 (26), 105 (27), 98 (25), 77 (20), 51 (23); HRMS calcd for $C_{17}H_{15}FO_2$ 270.1056, found 270.1066.

(*E*)-3-(4-Fluorophenyl)-3-phenylpropenoic acid (5g): mp 164−166 °C; R_f 0.48 (hexane/EtOAc 1/1); IR (KBr) ν (cm^{-1}) = 2916 (OH), 1696 (C=O), 1213 (ArCF); ^{1}H NMR δ = 6.27 (s, 1H), 6.98−7.04 (m, 2H), 7.17−28 (s, 4H), 7.36−7.38 (m, 3H); ^{13}C NMR δ = 115.5 (d, $^2J_{CF}$ = 22.0 Hz), 116.2, 128.0, 128.6, 129.2, 130.4 (d, $^3J_{CF}$ = 8.8 Hz), 136.9 (d, $^4J_{CF}$ = 3.3 Hz), 138.2, 157.9, 163.7 (d, $^1J_{CF}$ = 250.3 Hz), 170.7; MS *m/z* (rel int) 242 (M$^+$, 100), 241 (69), 225 (20), 224 (12), 223 (44), 222 (22), 198 (11), 197 (47), 196 (66), 195 (12), 194 (18), 183 (30), 177 (12), 176 (15), 170 (13), 165 (11), 98 (11); HRMS calcd for $C_{15}H_{11}FO_2$ 242.0743, found 242.0744.

(*E*)-3-(4-Fluorophenyl)-3-phenylpropenamide (5i): mp 114−116 °C; R_f 0.13 (hexane/EtOAc 1/1); IR (KBr) ν (cm^{-1}) = 3322, 3176 (NH_2), 1651 (C=O); ^{1}H NMR δ = 5.08 (brs, 1H,), 5.55 (brs, 1H), 6.33 (s, 1H), 6.98−7.03 (m, 2H), 7.21−7.29 (m, 4H), 7.42−7.46 (m, 3H); ^{13}C NMR δ = 115.5 (d, $^2J_{CF}$ = 22.0 Hz), 121.6, 129.0, 129.1, 129.3, 129.9 (d, $^3J_{CF}$ = 8.8 Hz), 136.7 (d, $^4J_{CF}$ = 3.3 Hz), 138.0, 150.0, 163.4 (d, $^1J_{CF}$ = 250.3 Hz), 168.4; MS *m/z* (rel int) 241 (M$^+$, 51), 240 (100), 225 (17), 197 (27), 196 (63), 176 (22), 146 (13), 123 (11), 120 (10), 105 (13), 98 (20), 97 (12), 85 (13), 77 (14), 75 (16), 51 (27); HRMS cald for $C_{15}H_{12}FNO$ 241.0903, found 241.0878.

(*E*)-3-(4-Fluorophenyl)-3-phenylpropenonitrile (5j): oil; R_f 0.32 (hexane/EtOAc 9/1); IR (film) ν (cm^{-1}) = 2216 (CN); ^{1}H NMR δ = 5.69 (s, 1H), 7.03−7.09 (m, 2H), 7.25−7.31 (m, 2H), 7.40−7.48 (m, 5H); ^{13}C NMR: δ = 94.7, 115.6 (d, $^2J_{CF}$ = 22 Hz), 117.7, 128.6, 129.4, 130.1, 130.4 (d, $^3J_{CF}$ = 8.8 Hz), 135.0 (d, $^4J_{CF}$ = 2.2 Hz), 136.8, 161.9, 164.0 (d, $^1J_{CF}$ = 251 Hz); MS *m/z* (rel int) 223 (M$^+$, 100), 222 (54), 208 (19), 202 (14), 196 (23), 183 (44), 175 (10), 111, (12), 98 (27), 88 (27), 85 (20), 75 (12); HRMS calcd for $C_{15}H_{10}FN$ 223.0797, found 223.0794.

Ethyl (*E*)-3-(4-chlorophenyl)but-2-enoate (5l): oil; R_f 0.45 (hexane/EtOAc 9/1); IR (film) ν (cm^{-1}) = 1716 (C=O), 1629 (C=C), 1274, 1173 (C−O); ^{1}H NMR δ = 1.31 (t, 3H, J = 7.1 Hz), 2.55 (d, 3H, J = 0.9 Hz), 4.21 (q, 2H, J = 7.1 Hz), 6.11 (q, 1H, J = 0.9 Hz), 7.33 (d, 2H, J = 8.6 Hz), 7.40 (d, 2H, J = 8.6 Hz); ^{13}C NMR δ = 14.3, 17.8, 59.9, 117.6, 127.6, 128.7, 135.0, 140.6, 154.0, 166.6; MS *m/z* (rel int) 226 (M$^+$ + 2, 12), 224 (M$^+$, 34), 195 (35), 179 (77), 152 (22), 115 (100); HRMS calcd for $C_{12}H_{13}ClO_2$ 224.0604, found 224.0614.

(*E*)-3-(4-Chlorophenyl)-3-phenylpropenamide (5n): mp 116−118 °C; R_f 0.19 (hexane/EtOAc 1/1); IR (KBr) ν (cm^{-1}) = 3471, 3322, 3176 (NH_2), 1658 (C=O); ^{1}H NMR δ = 5.32 (brs, 1H), 6.03 (brs, 1H), 6.33 (s, 1H), 7.16−7.42 (m, 9H); ^{13}C NMR δ = 122.0, 128.7, 128.9, 129.0, 129.2, 130.8, 135.2, 137.7, 139.1, 149.9, 168.5; MS *m/z* (rel int) 259 (M$^+$ + 2, 18), 258 (M$^+$ + 1, 41), 257 (M$^+$, 50), 256 (M$^+$-1, 100), 241 (24), 213 (17), 212 (11), 205 (17), 179 (15), 178 (70), 177 (24), 176 (33), 152 (14), 151 (14), 139 (13), 110 (23), 105 (12), 89 (19), 88 (27), 77 (15), 76 (19), 75 (20), 51 (28). Anal. Calcd for $C_{15}H_{12}ClNO$: C, 69.91; H, 4.69; N, 5.43. Found: C, 69.74; H, 4.69; N, 5.99.

Ethyl (*E*)-3-(4-acetylphenyl)but-2-enoate (5p): oil; R_f 0.34 (hexane/EtOAc 9/1); IR (KBr) ν (cm^{-1}) = 1713 (CO_2), 1684 (C=O), 1628 (C=C), 1264, 1174 (CO); ^{1}H NMR δ = 1.25 (t, 3H, J = 7.1 Hz), 2.51 (d, 3H, J = 1.1 Hz), 2.55 (s, 3H), 6.11 (q, 2H, J = 1.1 Hz), 7.48 (d, 2H, J = 8.3 Hz), 7.89 (d, 2H, J = 8.3 Hz); ^{13}C NMR δ =14.3, 17.9, 26.7, 60.1, 118.9, 126.6, 128.6, 137.1, 146.7, 154.0, 166.5, 197.5; MS *m/z* (rel int) 232 (M$^+$, 100), 218 (13), 217 (97), 203 (43), 189 (75), 187 (35), 161 (22), 152 (31), 146 (13), 145 (36), 144 (12), 138 (10), 131 (25), 115 (44); HRMS calcd for $C_{14}H_{16}O_3$ 232.1099, found 232.1091.

***tert*-Butyl 3,3-diphenylpropenoate (6a):** mp 75−78 °C; R_f 0.46 (hexane/EtOAc 9/1); IR (KBr) ν (cm^{-1}) = 1717 (C=O), 1624 (C=C), 1264, 1144 (CO); ^{1}H NMR δ = 1.28 (s, 9H), 6.28 (s, 1H), 7.18−7.38 (m, 10H); ^{13}C NMR δ = 27.8, 80.3, 119.9, 127.86, 127.89, 128.2, 128.3, 129.1, 129.2, 139.4, 141.0, 154.3, 165.8; MS *m/z* (rel int) 280 (M$^+$, 4), 224 (100), 223 (91), 207 (27), 179 (69), 178 (60), 165 (10), 152 (9), 105 (9), 102 (8), 77 (11), 57 (44). Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.41; H, 7.24.

***tert*-Butyl 3,3-di(4-fluorophenyl)propenoate (6b):** mp 98−99 °C; R_f 0.63 (hexane/EtOAc 5/1); IR (KBr) ν (cm^{-1}) = 1682 (C=O), 1598 (C=C), 1299, 1148 (CO), 1220 (ArCF); ^{1}H NMR δ = 1.32 (s, 9H), 6.22 (s, 1H), 6.97−7.26 (m, 8H, ArH); ^{13}C NMR δ = 27.8, 80.6, 115.0 (d, $^2J_{CF}$ = 22 Hz), 115.4 (d, $^2J_{CF}$ = 22 Hz), 130.0 (d, $^3J_{CF}$ = 8.8 Hz), 131.0 (d, $^3J_{CF}$ = 7.7 Hz), 135.0 (d, $^4J_{CF}$ = 3.3 Hz), 137.0 (d, $^4J_{CF}$ = 3.3 Hz), 152.4, 162.6 (d, $^1J_{CF}$ = 248 Hz), 163.4 (d, $^1J_{CF}$ = 249 Hz), 165.4; MS *m/z* (rel int) 316 (M$^+$, 3), 260 (100), 259 (42), 243 (30), 215 (33), 214 (37), 201 (17), 165 (10), 123 (14), 57 (62). Anal. Calcd for $C_{19}H_{18}F_2O_2$: C, 72.14; H, 5.74. Found: C, 71.93; H, 5.55.

***tert*-Butyl 3,3-di(4-chlorophenyl)propenoate (6c):** mp 121 °C; R_f 0.68 (hexane/EtOAc 5/1); IR (KBr) ν (cm^{-1}) = 1689 (C=O), 1588 (C=C), 1314, 1164 (C−O); ^{1}H NMR δ = 1.31 (s, 9H), 6.25 (s, 1H), 7.11−7.19 (m, 4H), 7.29 (d, 2H, J = 8.6 Hz), 7.36 (d, 2H, J = 8.6 Hz); ^{13}C NMR δ = 27.9, 80.8, 120.5, 128.3, 128.7, 129.4, 130.6, 134.2, 135.5, 137.3, 139.1, 152.0, 165.2; MS *m/z* (rel int) 348 (M$^+$, 4), 292 (100), 275 (28), 212 (56), 176 (56), 139 (17), 75 (14), 57 (61).Anal. Calcd for $C_{19}H_{18}Cl_2O_2$: C, 65.34; H, 5.19. Found: C, 65.22; H, 5.15.

***tert*-Butyl 3,3-di(4-methoxyphenyl)propenoate (6d):** oil; R_f 0.46 (hexane/EtOAc 5/1); IR (film) ν (cm^{-1}) = 2837 (OMe), 1711 (CO), 1604 (C=C); ^{1}H NMR δ = 1.33 (s, 9H), 3.80 (s, 3H), 3.84 (s, 3H), 6.14 (s, 1H), 6.82 (dd, 2H, J = 6.9, 2.1 Hz), 6.89 (dd, 2H, J = 6.9, 2.1 Hz), 7.13 (dd, 2H, J = 6.9, 2.1 Hz), 7.21 (dd, 2H, J = 6.9, 2.1 Hz); ^{13}C NMR δ = 27.9, 55.2, 55.3, 79.9, 113.2, 113.6, 117.4, 129.9, 130.9, 131.8, 134.0, 154.3, 159.5, 160.5, 166.1; MS *m/z* (rel int) 340 (M$^+$, 27), 284 (100), 267 (30),

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240 (13), 225 (64), 207 (91), 191 (12), 181 (11), 177 (11), 165 (20), 153 (22), 152 (21), 151 (11), 135 (26), 134 (15), 133 (21), 119 (13), 96 (17), 73 (12), 56 (70); HRMS calcd for $C_{21}H_{24}O_4$, $[M^+ - C_4H_8]$ 284.1049, found 284.1040.

***N,N*-Dimethyl-3,3-diphenylpropenamide (6e):** mp 66−69 °C; R_f 0.20 (hexane/EtOAc 1/1); IR (KBr) ν (cm^{-1}) = 1629 (C=N), 1604 (C=C); ^1H NMR δ = 2.75 (s, 3H), 2.83 (s, 3H), 6.35 (s, 1H), 7.24−7.34 (m, 10H, ArH); ^{13}C NMR δ = 34.3, 37.6, 121.3, 128.1, 128.2, 128.3, 128.4, 129.2, 138.9, 141.0, 147.3, 168.4; MS *m/z* (rel int) 251 (M^+, 23), 207 (100), 179 (34), 178 (61), 105 (28), 77 (16). Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.37; H, 6.87; N, 5.40.

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Supporting Information Available: General experimental methods and ^1H NMR spectra for compounds **5b**,**g**,**i**,**j**,**l**,**p** and **6d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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