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Acrolein Diethyl Acetal: A Three-Carbon Homologating Reagent for the Synthesis of β-Arylpropanoates and Cinnamaldehydes by Heck Reaction Catalyzed by a Kaiser Oxime Resin Derived Palladacycle

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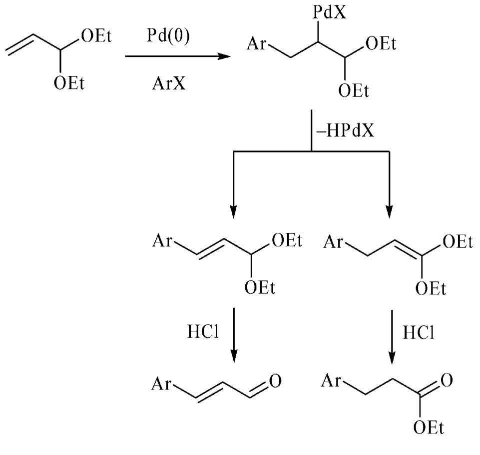
Keywords: Heck reaction / Palladacycles / Aldehydes / Esters / Polymers

A polymer palladacycle derived from Kaiser oxime resin was used as a source of palladium(0) in the chemoselective Heck reaction of acrolein diethyl acetal with aryl halides under ligand-free conditions. The use of typical Heck conditions afforded 3-arylpropionic esters, and the process can be directed to the synthesis of cinnamaldehydes under Cacchi conditions. These processes take place with rather low loading of the catalyst, which can be recovered by simple filtration and reused for at least five runs without competitive dehalogenation. This is the first time that a supported palladium complex has been reused under Cacchi conditions. ICP-OES analyses of the Pd content of the crude products in both transformations indicated lower leaching for the esters than for the aldehydes in the range up to 0.08 ppm for the esters and 0.8 ppm for the aldehydes.

Introduction

The direct Heck reaction of aryl halides and acrolein is not a general method for the synthesis of cinnamaldehyde derivatives because of the problems associated with competing polymerization reactions[1] and the formation of β,β-diarylated products.[2] However, the arylation of acrolein acetals was found to be a much better alternative for the synthesis of cinnamaldehydes and conjugate dienals.[1a,3] In addition, Cacchi and coworkers described appropriate reaction conditions to direct this arylation either to the synthesis of cinnamaldehydes[4] or 3-arylpropionic esters[5] by Heck reaction of acrolein diethyl acetal. Depending on the reaction conditions it is possible to promote the regioselective elimination of one of the two β-hydrogens from the carbopalladated intermediate (Scheme 1). Several soluble catalysts, such as $Pd(OAc)_2$,[4,5] the Herrmann's palladacycle,[2b] and $[PdCl(C_3H_5)]_2$ with the tetraphosphane Tedicyp,[6] have been used for the chemoselective synthesis of cinnamaldehydes or 3-arylpropionic esters. These methods require high palladium loadings (2–5 mol-%) under ligand-free conditions and only recently tetrakis(amine)palladium–NaY zeolite $\{[Pd(NH_3)_4/NaY]\}$ has been evaluated as a heterogeneous catalyst in order to recover the palladium.[7] Under classical Heck conditions (*N*-methyl-2-pyrrolidone, base, 140 °C), 3-arylpropionic esters were obtained, and the catalyst was stable only over the two first runs. However, for the preparation of cinnamaldehydes under Cacchi conditions [DMF, KCl, tetra-*n*-butylammonium acetate (TBAA), base, 110 °C], the catalyst could not be reused and high dehalogenation rates were observed.



Scheme 1. Heck arylation of acrolein diethyl acetal.

We recently described the use of commercially available oxime-derived palladacycles **1** and **2** (Figure 1) as catalysts for C–C bond forming reactions,[8] such as the Heck,[9] Suzuki,[10] Hiyama,[11] Ullmann,[10b] Sonogashira,[12] and Glaser[12b] reactions, and for the acylation of alkynes.[13] By using these catalysts in the arylation of acrolein diethyl acetal[9g] with aryl bromides for the synthesis of 3-arylpropionic esters under Heck conditions [*N*,*N*-dimethylacetamide (DMAc)/H_2O, Cy_2NMe, 120 °C], the loading of Pd could be reduced down to 0.1 mol-%. When Cacchi condi-

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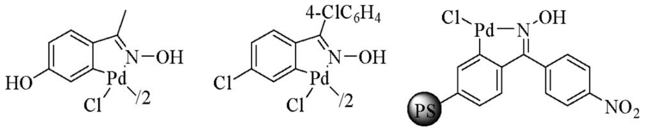
tions [DMAc, KCl, TBAA, K_2CO_3, 120 °C] were employed for the synthesis of cinnamaldehydes, aryl iodides, bromides, and chlorides were employed as arylating reagents with the use of 1 mol-% of Pd. Recently, we showed that the palladacycle derived from Kaiser oxime resin **3**,[9h,9i,9j] can be used as reusable catalyst in Heck reactions, both in organic and aqueous solvents. In this contribution, we report for the first time the use of polymeric catalyst **3** as a reusable immobilized complex for the chemoselective Heck reaction of acrolein diethyl acetal with aryl halides under ligand-free conditions.

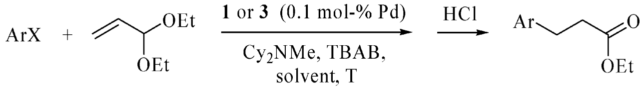


1 **2** **3**

Figure 1. Oxime-derived palladacycles.

Results and Discussion

Following our previous work[9g] on the arylation of acrolein diethyl acetal, the typical Heck conditions using palladacycles **1** and **3** followed by acid hydrolysis were applied to the synthesis of ethyl 3-arylpropanoates **4** (Scheme 2 and Table 1). The reaction of aryl halides with 1.5 equiv. of acrolein diethyl acetal was performed with a Pd loading of 0.1 mol-% by using (dicyclohexyl)methylamine as the base. The reaction of an activated aryl halide such as 4-chloroiodobenzene could be performed by using polymer **3** as a catalyst at 90 °C in aqueous DMAc with good chemoselectivity, and product **4a** was isolated in higher yield than that obtained when palladacycle **1** was used[9g] (Table 1, Entries 1 and 2). The reaction could be performed in DMF with similar results to those obtained in aqueous DMAc (Table 1, compare Entries 1 and 3).

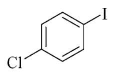
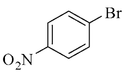
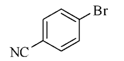
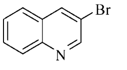
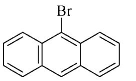


4

Scheme 2. Synthesis of ethyl 3-arylpropanoates **4**.

The Heck reaction with aryl bromides needed the presence of 1 equiv. of tetra-*n*-butylammonium bromide (TBAB) as an additive for the stabilization of the palladacycle-generated Pd nanoparticles.[9h,9j] When an activated bromide such as 4-nitrobromobenzene was allowed to react with acrolein diethyl acetal in aqueous DMAc at 120 °C the corresponding ester **4b** was obtained with high chemoselectivity and good yield (Table 1, Entry 4). Concerning the catalyst, a similar yield was observed with polymer **3** and dimeric palladacycle **1**[9g] (Table 1, Entries 4 and 5). However, this arylation needed longer reaction times in DMF than in aqueous DMAc (Table 1, compare Entries 4 and 6). The coupling with 4-bromobenzonitrile took place with high chemoselectivity in both aqueous DMAc and DMF in 3 and 4 h, respectively (Table 1, Entries 7 and 9). Palladacycles **3** and **1** both afforded compound **4c** with the same yields (Table 1, compare Entries 7 and 8). In the case of 3-bromoquinoline, both catalysts gave the same selectivity, which was also observed with the use of {[$Pd(NH_3)_4$/NaY]} as the catalyst.[7] Product **4d** was obtained in good yield with a lower loading of Pd (Table 1, Entries 10 and 11), whereas deactivated 9-bromoanthracene required a longer reaction time to give mainly product **4e** in good yield (Table 1, Entries 12 and 13). It can be concluded that both catalytic systems provided similar yields and selectivities and that aqueous DMAc was a better solvent that DMF for aryl bromides.

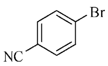
Table 1. Synthesis of ethyl 3-arylpropanoates by arylation of acrolein diethyl acetal.[a]

Entry	ArX	Cat.	Solvent	*T* [°C]	*t* [h]	Isomer ratio (**4**/**5**)[b]	No.	Yield [%][c]
1		**3**	DMAc/H_2O[d]	90[e]	5	94/6	**4a**	91 (84)
2		**1**	DMAc/H_2O[d]	90[e]	4	95/5	**4a**	88
3		**3**	DMF	90[e]	4	–	**4a**	(79)[f]
4		**3**	DMAc/H_2O[d]	120	3	91/9	**4b**	91 (85)
5		**1**	DMAc/H_2O[d]	120	2	–	**4b**	(86)[f]
6		**3**	DMF	120	6	92/8	**4b**	92
7		**3**	DMAc/H_2O[d]	120	3	96/4	**4c**	92 (81)
8		**1**	DMAc/H_2O[d]	120	3	–	**4c**	(86)[f]
9		**3**	DMF	120	4	97/3	**4c**	95
10		**3**	DMAc/H_2O[d]	120	10	75/25	**4d**	61
11		**1**	DMAc/H_2O[d]	120	8	80/20	**4d**	70 (67)
12		**3**	DMAc/H_2O[d]	120	24	89/11	**4e**	71
13		**1**	DMAc/H_2O[d]	120	24	91/9	**4e**	74 (69)

[a] Reaction conditions: aryl halide (1 mmol), acrolein diethyl acetal (1.5 mmol), catalyst (0.1 mol-% Pd), Cy_2NMe (1.5 mmol), TBAB (1 mmol), solvent (5 mL) heated (see column) in a pressure tube. [b] Determined by GC of the crude product. [c] Determined by ^1H NMR spectroscopy by using diphenylmethane as an internal standard for product **4**. Yield of product **4** after flash chromatography is in parentheses. [d] Ratio 4:1. [e] Without TBAB. [f] Ref.[9g]

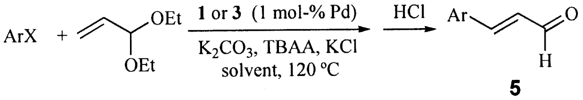
For studying the reuse of polymeric catalyst **3** and the Pd leaching, the Heck reaction of 4-bromobenzonitrile and acrolein diethyl acetal was chosen (Table 2). Thus, under the optimized reaction conditions and by using 0.1 mol-% of Pd, the reaction was heated at 120 °C for 5 h, and when the reaction was finished, the polymer was filtered off, washed, and dried under vacuum. The recycled polymer was then used in the next run. The reaction time was between 5 and 14 h and the yield was maintained between 92 and 86% after four runs. In the fifth cycle, the yield decreased to 65% and the reaction time increased to 24 h, probably not only due to Pd^0 leaching but also to partial loss of the polymer during the successive manipulations. The selectivity of the reaction over the five runs was maintained between 92 and 86%. Inductively coupled plasmaoptical emission spectrometry (ICP-OES) of the crude product during the first cycles gave a Pd content of ca. 0.18 mg/g of product. These results are better than those described with the use of {[Pd(NH_3)$_4$/NaY]} as the catalyst,[7] which gave 65% conversion in the third run and <5% in the fifth run by using a larger loading of Pd (2 mol-%).

Table 2. Recycling experiments of the Heck reaction of acrolein diethyl acetal and 4-bromobenzonitrile: Synthesis of ethyl 4-cyanopropanoate **4c**.[a]

Run	ArX	t [h]	Isomer ratio (**4c**/**5c**)[b]	Yield [%][c]	Pd leaching [ppm] (mg Pd/g product)[d]
1		5	96/4	92	0.081 (0.187)
2		8	96/4	88	0.084 (0.179)
3		13	95/5	91	0.063 (0.185)
4		14	96/4	86	–
5		24	93/7	65	–

[a] Reaction conditions: 4-bromobenzonitrile (1 mmol), acrolein diethyl acetal (1.5 mmol), **3** (0.1 mol-% Pd), Cy_2NMe (1.5 mmol), TBAB (1 mmol), DMAc/H_2O (4:1) (5 mL), heated at 120 °C in a pressure tube. [b] Determined by GC of the crude product. [c] Determined by ^1H NMR spectroscopy by using diphenylmethane as an internal standard for product **4c**. [d] Determined by ICP-OES of the crude product.

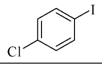
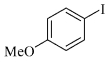
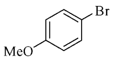
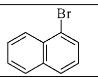
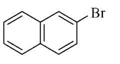
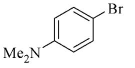
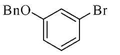
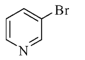
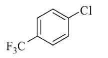
The Cacchi conditions (K_2CO_3 as base and TBAA and KCl as additives at 120 °C), previously described with the use of palladacycle **1**[9g] were used for the synthesis of cinnamaldehydes **5** (Scheme 3 and Table 3). Initial studies of 4-chloroiodobenzene with catalyst **3** (1 mol-% Pd) in aqueous DMAc afforded a 3:1 mixture of products **5a** and **4a** (Table 3, Entry 1). However, total selectivity was observed with polymer **3** and dimer **1**[9g] in DMAc (Table 3, Entries 2 and 3). Again, the same influence of the solvent in the selectivity was obtained with 4-iodoanisole, which provided 4-methoxycinnamaldehyde (**5f**) (Table 3, Entries 4–6).



Scheme 3. Synthesis of cinnamaldehydes **5**.

The arylation with aryl bromides were performed in DMAc to afford cinnamaldehydes **5** with very good selectivity (Table 3, Entries 7–18). In the case of 4-bromoanisole and 1-bromonaphthalene, only the formation of 4-methoxycinnamaldehyde (**5f**) and **5g**, respectively, was observed with both catalysts (Table 3, Entries 7–10). However, 2-bromonaphthalene provided product **5h** in lower selectivity (Table 3, Entries 11 and 12). Deactivated 4-(dimethylamino)phenyl bromide and 3-benzyloxybromobenzene gave exclusively the corresponding products **5i** and **5j**, respectively, in high yields either by using polymer **3** or dimer **1** (Table 3, Entries 13–16). 4-(Dimethylamino)cinnamaldehyde (**5i**) is an important unit for nonlinear optics[4] and 3-(benzyloxy)cinnamaldehyde (**5j**) possess a potent inhibitory activity against cyclin-dependent kinases, especially D1-CDK4.[14]

Table 3. Synthesis of cinnamaldehydes by arylation of acrolein diethyl acetal.[a]

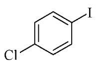
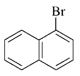
Entry	ArX	Cat.	Solvent	t [h]	Isomer ratio (**5**/**4**)[b]	No.	Yield [%][c]
1		**3**	DMAc/H_2O[d]	2	71/29	**5a**	(65)
2		**3**	DMAc	3	100/0	**5a**	93 (85)
3		**1**	DMAc	2	100/0	**5a**	99 (82)[e]
4		**3**	DMAc/H_2O[d]	9	80/20	**5f**	96 (79)
5		**3**	DMAc	3	91/9	**5f**	91
6		**1**	DMAc	3	–	**5f**	(79)[e]
7		**3**	DMAc	3	100/0	**5f**	99 (92)
8		**1**	DMAc	3	–	**5f**	(75)[e]
9		**3**	DMAc	3	100/0	**5g**	94 (87)
10		**1**	DMAc	2	–	**5g**	(80)[e]
11		**3**	DMAc	4	85/15	**5h**	80 (72)
12		**1**	DMAc	3.5	88/12	**5h**	88 (80)
13		**3**	DMAc	2.5	100/0	**5i**	81 (77)
14		**1**	DMAc	3	–	**5i**	(67)[e]
15		**3**	DMAc	3	100/0	**5j**	81 (77)
16		**1**	DMAc	3	–	**5j**	(67)[e]
17		**3**	DMAc	24	75/25	**5k**	46
18		**1**	DMAc	14	80/20	**5k**	54 (48)
19		**3**	DMAc	20	100/0	**5l**	78 (72)
20		**1**	DMAc		–	**5l**	(71)[e]

[a] Reaction conditions: aryl halide (1 mmol), acrolein diethyl acetal (1.5 mmol), catalyst (1 mol-% Pd), K_2CO_3 (1.5 mmol), TBAA (2 mmol), KCl (1 mmol), DMAc/H_2O (5 mL) or DMAc(4 mL) heated at 120 °C in a pressure tube. [b] Determined by GC of the crude product. [c] Determined by ^1H NMR spectroscopy by using diphenylmethane as an internal standard for product **5**. Yield of product **5** after flash chromatography is in parentheses. [d] Ratio 4:1. [e] Ref.[9g]

In the case of 3-bromopyridine, the reaction needed longer reaction times and afforded product **5k** with lower selectivity and moderate yields (Table 3, Entries 17 and 18). The activated aryl chloride 4-chloro-1-(trifluoromethyl)benzene gave exclusively 4-(trifluoromethyl)cinnamaldehyde (**5l**) in good yield (Table 3, Entries 19 and 20).

Two representative examples for the synthesis of cinnamaldehydes were selected for recycling studies (Table 4). In the arylation of acrolein diethyl acetal with 4-chloroiodobenzene, the reaction time was increased from 2.5 h in the first run to 24 h in the sixth, and the yield of product **5a** was maintained between 96 and 86% over five runs and started to decrease in the sixth run to 62%. Similar results were observed in the case of 1-bromonaphthalene, which afforded product **5g** in 92 to 74% yield over five runs. The selectivity remained high and was 96:4 in all cycles for both examples. The Pd leaching in product **5g** was rather low (0.154–0.257 mg Pd/g of product). The role of polymer **3** as a precatalyst and source of Pd^0 nanoparticles is supported by the following experiments: After XPS analyses of the recycled polymer, only Pd^{II} was detected.[9h] Furthermore, 6–8-nm sized Pd nanoparticles were found in solution by TEM analyses (Figure 2). In addition, when Hg^0 (300 equiv. with respect to Pd) was added to the reaction mixture, the Heck reaction stopped.

Table 4. Recycling experiments of the Heck reaction of acrolein diethyl acetal for the synthesis of cinnamaldehydes **5a** and **5g**.[a]

Run	ArX	t [h]	Isomer ratio (**5**/**4**)[b]	No.	Yield [%][c]	Pd leaching [ppm] (mg Pd/g product)[d]
1		2.5	100/0	**5a**	96	0.51 (0.160)
2		3.5	100/0	**5a**	90	0.56 (0.187)
3		5.5	100/0	**5a**	92	0.63 (0.20)
4		9	97/3	**5a**	90	–
5		14	96/4	**5a**	84	–
6		24	96/4	**5a**	62	–
1		3	100/0	**5g**	91	0.681 (0.205)
2		6	100/0	**5g**	92	0.742 (0.221)
3		7.5	98/2	**5g**	87	0.814 (0.257)
4		14	98/2	**5g**	85	0.476 (0.154)
5		24	96/4	**5g**	74	0.520 (0.193)

[a] Reaction conditions: aryl halide (1 mmol), acrolein diethyl acetal (1.5 mmol), **3** (1 mol-% Pd), K_2CO_3 (1.5 mmol), TBAA (2 mmol), KCl (1 mmol), DMAc (4 mL), heated at 120 °C in a pressure tube. [b] Determined by GC of the crude product. [c] Determined by ^1H NMR spectroscopy by using diphenylmethane as an internal standard for product **5**. [d] Determined by ICP-OES of the crude product.

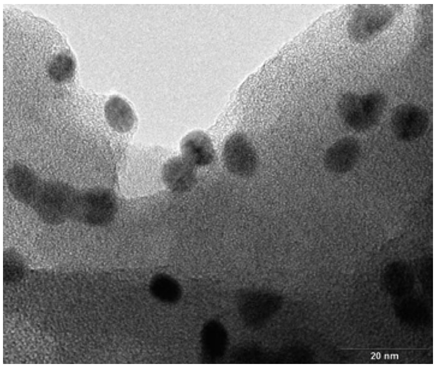


Figure 2. TEM images of the reaction solution after Heck reaction of acrolein diethyl acetal with 4-chloroiodobenzene.

Conclusions

The polymer-anchored palladacycle derived from Kaiser oxime resin has shown similar catalytic efficiency in the chemoselective Heck reaction of acrolein diethyl acetal with aryl halides than the unsupported dimeric 4-hydroxyacetophenone oxime palladacycle. The arylation with aryl iodides and bromides took place in short reaction times under Heck conditions (Cy_2NMe, TBAB, DMAc/H_2O, 120 °C) to afford ethyl 3-arylpropanoates with very low catalyst loading (0.1 mol-% Pd). This polymeric complex can be reused for at least five cycles; it also acts as a palladium reservoir and leaches a very low amount of palladium nanoparticles (0.06–0.08 ppm) into the solution. When Cacchi reaction conditions (K_2CO_3, TBAA, KCl, DMAc, 120 °C) were used, aryl iodides, bromides, and chlorides can be coupled with acrolein diethyl acetal to provide cinnamaldehydes in short reaction times with 1 mol-% loading of Pd. The stability of this polymeric complex under these reaction conditions was remarkable, and it could be reused over five cycles with the use of aryl iodides and bromides. In this case, very low amounts of palladium were found in the product (0.47–0.81 ppm) without competitive dehalogenation. These are the first examples in which the catalyst has been recycled, because when {[Pd(NH_3)$_4$/NaY]} was used as the catalyst,[7] mainly dehalogenation was observed.

Experimental Section

General Remarks: The reagents and solvents were obtained from commercial sources and were generally used without further purification. Melting points were determined with a Reichert Thermovar hot plate apparatus and are uncorrected. Only the structurally most important peaks of the IR spectra (recorded with a Nicolet 510 P-FT) are listed. ^1H (300 MHz) and ^{13}C NMR (75 MHz) spectra were obtained with a Bruker AC-300 by using $CDCl_3$ as the solvent and TMS as an internal standard, unless otherwise stated. Low-resolution electron impact (EI) mass spectra were obtained at 70 eV with a Shimadzu QP-5000. Analytical TLC was performed on Schleicher & Schuell F1400/LS silica-gel plates, and the spots were visualized under UV light (λ = 254 nm). For flash chromatography we employed Merck silica gel 60 (0.040–0.063 mm). The catalysts were weighed in an electronic microscale (Sartorius, XM1000P) with precision of 1 µg. ICP-OES analyses were performed with a Perkin–Elmer Optima 4300 spectrometer (1% aqueous HNO_3 solution). Palladacycle **1** and Kaiser oxime resin are commercially available. Palladacycle **3** was prepared as described in ref.[9i]

General Method for the Synthesis of Ethyl 3-Arylpropanoates 4: A solution of aryl halide (1 mmol), acrolein diethyl acetal (1.5 mmol, 0.229 mL), (dicyclohexyl)methylamine (1.5 mmol, 0.321 mL), tetra-*n*-butylammonium bromide (1 mmol, 322 mg, only for aryl bromides), palladium catalyst (0.1 mol-% Pd) in *N*,*N*-dimethylacetamide (4 mL) and water (1 mL) was stirred at 90 °C (aryl iodides) or at 120 °C (aryl bromides) (bath temperature) in a pressure tube. Upon completion of the reaction (GC), the resulting solution was cooled to room temperature, poured into ethyl acetate (20 mL), and washed successively with HCl (2 M, 2 × 20 mL) and H_2O (20 mL). The organic layer was dried with $MgSO_4$, and the solvent was evaporated (15 Torr); the residue was purified by flash chromatography to afford product **4**.

General Method for the Synthesis of Cinnamaldehydes 5: A suspension of aryl halide (1 mmol), acrolein diethyl acetal (1.5 mmol, 0.229 mL), potassium carbonate (1.5 mmol, 207 mg), tetra-*n*-butylammonium acetate (2 mmol, 602 mg), potassium chloride (1 mmol, 75 mg), palladium catalyst (1 mol-% Pd), and *N*,*N*-dimethylacetamide (4 mL) was stirred at 120 °C (bath temperature) in a pressure tube. Upon completion of the reaction (GC), the solution was cooled and an aqueous solution of HCl (2 M, 10 mL) was added slowly. The mixture was stirred at room temperature for 10 min. Then, the reaction crude was poured into ethyl acetate (20 mL) and washed successively with HCl (2 M, 20 mL) and H_2O (2 × 20 mL). The organic layer was dried with $MgSO_4$, and the solvent was evaporated (15 Torr); the resulting residue was purified by flash chromatography to provide compounds **5**.

General Method for Recycling Experiments: The reaction was performed under any previous described conditions: aromatic halide (1 mmol), acrolein diethyl acetal (0.229 mL, 1.5 mmol), base (1.5 mmol), **1** (0.1–1 mol-%, 8.2–82 mg), solvent (5 mL DMA/H_2O, 4:1 or 4 mL DMA) and TBAB (322 mg, 1 mmol) for aryl bromides, heating at corresponding temperature. Upon completion of the reaction, the catalyst was filtered off in a porous plate 4 (1 cm diameter and 8 cm height), washed with ethyl acetate, and dried under vacuum for 20 min. Workup of the crude product was performed as was previously described.

Ethyl 3-(4-chlorophenyl)propanoate (**4a**),[15] ethyl 3-(4-nitrophenyl)propanoate (**4b**),[9g] ethyl 3-(4-cyanophenyl)propanoate (**4c**),[16] 4-chlorocinnamaldehyde (**5a**),[4] 4-methoxycinnamaldehyde (**5f**),[4] (*E*)-3-(1-naphthyl)propenal (**5g**),[9g] (*E*)-3-(naphthalen-2-yl)propenal (**5h**),[17] 4-(dimethylamino)cinnamaldehyde (**5i**),[4] 3-(benzyloxy)cinnamaldehyde (**5j**),[14] (*E*)-3-(pyridin-3-yl)propenal (**5k**),[18] and 4-(trifluoromethyl)cinnamaldehyde (**5l**)[19] are known compounds.

Ethyl 3-(Quinolin-3-yl)propanoate (4d): Yellow oil, 153 mg (67%). R_f = 0.36 (*n*-hexane/ethyl acetate, 3:2). IR (film): $\tilde{\nu}$ = 1194, 1161, 1375, 1502, 1575, 1729, 2860, 2924, 2978, 3051 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.21 (t, J = 7.2 Hz, 3 H, CH$_3$), 2.72 (t, J = 7.6 Hz, 2 H, CH_2CH$_2$O), 3.13 (t, J = 7.6 Hz, 2 H, CH_2O), 4.12 (q, J = 7.2 Hz, 2 H, OCH_2), 7.51 (dt, J = 7.9 and 1.1 Hz, 1 H, ArH), 7.65 (dt, J = 8.4 and 1.4 Hz, 1 H, ArH), 7.75 (d, J = 8.1 Hz, 1 H, ArH), 7.94 (d, J = 1.2 Hz, 1 H, ArH), 8.08 (d, J = 8.4 Hz, 1 H, ArH), 8.80 (d, J = 2.2 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 14.1 (CH$_3$), 28.2, 35.3, 60.6 (CH$_2$), 126.7 127.4 (ArCH), 127.9 (ArC), 128.8, 129.1 (ArCH), 133.2 (ArC), 134.4 (ArCH), 146.9 (ArC), 151.6 (ArCH), 172.3 (COO) ppm. MS (EI): *m/z* (%) = 230 (14) [M + 1]$^+$, 229 (80) [M]$^+$, 185 (48), 184 (24), 158 (70), 157 (11), 156 (44), 155 (100), 154 (31), 142 (77), 128 (23), 127 (13), 115 (24). HRMS: calcd. for C$_{14}$H$_{15}$NO$_2$ 229.1103; found 229.1113.

Ethyl 3-(Anthracen-9-yl)propanoate (4e): Yellow oil, 192 mg (69%). R_f = 0.49 (*n*-hexane/ethyl acetate, 5:1). IR (film): $\tilde{\nu}$ = 1175, 1362, 1441, 1616, 1730, 2978, 3044 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.24 (t, J = 7.1 Hz, 3 H, CH$_3$), 2.75 (t, J = 8.5 Hz, 2 H, CH_2CH$_2$O), 3.94 (t, J = 8.5 Hz, 2 H, CH_2O), 4.17 (q, J = 7.1 Hz, 2 H, OCH_2), 7.43 (t, J = 7.0 Hz, 2 H, ArH), 7.50 (dt, J = 7.6 and 1.3 Hz, 2 H, ArH), 7.96 (d, J = 8.2 Hz, 2 H, ArH), 8.24 (d, J = 8.8 Hz, 2 H, ArH), 8.31 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 14.3 (CH$_3$), 23.4 (CH$_2$), 35.4 (CH$_2$), 60.7 (OCH_2), 124.0 (2 × ArCH), 125.0 (2 × ArCH), 126.0 (2 × ArCH), 126.4 (ArCH), 129.4 (2 × ArCH), 129.6 (2 × ArC), 131.6 (2 × ArC), 132.5 (ArC), 173.2 (COO) ppm. MS (EI): *m/z* (%) = 279 (10) [M + 1]$^+$, 278 (51) [M]$^+$, 204 (12), 203 (15), 192 (16), 191 (100). HRMS: calcd. for C$_{19}$H$_{18}$O$_2$ 278.1307; found 278.1301.

(*E*)-3-(Quinolin-3-yl)propenal (5h): Yellow solid, m.p. 81–83 °C. R_f = 0.24 (*n*-hexane/ethyl acetate, 3:2). IR (KBr): $\tilde{\nu}$ = 1129, 1335, 1376, 1491, 1560, 1618, 1681, 2820, 2912, 2963, 3050 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.95 (dd, J = 16.1 and 7.5 Hz, 1 H, CH) = 7.62 (dt, J = 8.0 and 1.1 Hz, 1 H, ArH), 7.64 (d, J = 16.1 Hz, 1 H, CH), 7.80 (dt, J = 8.4 and 1.4 Hz, 1 H, ArH), 7.89 (d, J = 8.1 Hz, 1 H, ArH), 8.14 (d, J = 8.4 Hz, 1 H, ArH), 8.31 (d, J = 2.0 Hz, 1 H, ArH), 9.10 (d, J = 2.2 Hz, 1 H, ArH), 9.79 = (d, J = 7.5 Hz, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 126.9, 127.5 (ArC) = 127.7, 128.6, 129.5, 129.9, 131.3 (ArCH), 136.0 (CH), 148.8 (ArCH), 149.0 (ArC), 149.2 (CH), 193.1 (CHO) ppm. MS (EI): *m/z* (%) = 184 (12) [M + 1]$^+$, 183 (100) [M]$^+$, 155 (24), 154 (94), 129 (27), 128 (13), 127 (25). HRMS: calcd. for C$_{12}$H$_9$NO 183.0684; found 183.0672.

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[1] a) T. C. Zebovitz, R. F. Heck, *J. Org. Chem.* **1977**, *42*, 3907–3909; b) T. Jefferey, *J. Chem. Soc., Chem. Commun.* **1984**, 1287–1289; c) M. R. Unroe, B. A. Reinhardt, *Synthesis* **1987**, 981–986.

[2] a) A. Nejjar, C. Pinel, L. Djakovitch, *Adv. Synth. Catal.* **2003**, *345*, 612–619; b) S. Nöel, L. Djakovitch, C. Pinel, *Tetrahedron Lett.* **2006**, *47*, 3839–3842.

[3] a) B. A. Patel, J. I. Kim, D. D. Bender, L.-C. Kao, R. F. Heck, *J. Org. Chem.* **1981**, *46*, 1061–1067; b) F. Berthiol, H. Doucet, M. Santelli, *Catal. Lett.* **2005**, *102*, 281–284.

[4] G. Battistuzzi, S. Cacchi, G. Fabrizi, *Org. Lett.* **2003**, *5*, 777–780.

[5] G. Battistuzzi, S. Cacchi, G. Fabrizi, R. Bernini, *Synlett* **2003**, 1133–1136.

[6] M. Lemhadri, H. Doucet, M. Santelli, *Tetrahedron* **2004**, *60*, 11533–11540.

[7] S. Nöel, C. Luo, C. Pinel, L. Djakovitch, *Adv. Synth. Catal.* **2007**, *349*, 1128–1140.

[8] For accounts, see: a) E. Alacid, D. A. Alonso, L. Botella, C. Nájera, M. C. Pacheco, *Chem. Recueil* **2006**, *6*, 117–132; b) D. A. Alonso, L. Botella, C. Nájera, M. C. Pacheco, *Synthesis* **2004**, 1713–1718.

[9] a) D. A. Alonso, C. Nájera, M. C. Pacheco, *Org. Lett.* **2000**, *2*, 1823–1826; b) D. A. Alonso, C. Nájera, M. C. Pacheco, *Adv. Synth. Catal.* **2002**, *344*, 172–183; c) L. Botella, C. Nájera, *Tetrahedron Lett.* **2004**, *45*, 1833–1836; d) L. Botella, C. Nájera, *Tetrahedron* **2004**, *60*, 5563–5570; e) L. Botella, C. Nájera, *Tetrahedron Lett.* **2004**, *45*, 1833–1836; f) L. Botella, C. Nájera, *J. Org. Chem.* **2005**, *70*, 4360–4369; g) L. Botella, C. Nájera, *Tetrahedron* **2005**, *61*, 9688–9695; h) E. Alacid, C. Nájera, *Synlett* **2006**, 2959–2964; i) E. Alacid, C. Nájera, *Adv. Synth. Catal.* **2007**, *349*, 2572–2584; j) E. Alacid, C. Nájera, *ARKIVOC.* **2008**, *viii*, 50–67.

[10] a) L. Botella, C. Nájera, *Angew. Chem. Int. Ed.* **2002**, *41*, 179–181; b) D. A. Alonso, C. Nájera, M. C. Pacheco, *J. Org. Chem.* **2002**, *67*, 5588–5594; c) L. Botella, C. Nájera, *J. Organomet. Chem.* **2002**, *663*, 46–57; d) A. Costa, C. Nájera, J. M. Sansano, *J. Org. Chem.* **2002**, *67*, 5216–5225.

[11] a) E. Alacid, C. Nájera, *Adv. Synth. Catal.* **2006**, *348*, 945–952; b) E. Alacid, C. Nájera, *Adv. Synth. Catal.* **2006**, *348*, 2085–2091; c) E. Alacid, C. Nájera, *J. Org. Chem.* **2008**, *73*, 2315–2322.

[12] a) D. A. Alonso, C. Nájera, M. C. Pacheco, *Tetrahedron Lett.* **2002**, *43*, 9365–9368; b) D. A. Alonso, C. Nájera, M. C. Pacheco, *Adv. Synth. Catal.* **2003**, *345*, 1146–1158.

[13] D. A. Alonso, C. Nájera, M. C. Pacheco, *J. Org. Chem.* **2004**, *69*, 1615–1619.

[14] H.-W. Jeong, M.-R. Kim, K.-H. Son, M. Y. Han, J.-H. Ha, M. Garnier, L. Meijer, B.-M. Kwon, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1819–1822.

[15] S. Condon, D. Dupré, G. Falgayrac, J.-Y. Nédélec, *Eur. J. Org. Chem.* **2002**, 105–111.

[16] S. Condon-Gueugnot, E. Léonel, J.-Y. Nédélec, J. Périchon, *J. Org. Chem.* **1995**, *60*, 7684–7686.

[17] T. D. Avery, D. Caiazza, J. A. Culbert, D. A. Taylor, E. R. Tiekink, *J. Org. Chem.* **2005**, *70*, 8344–8351.

[18] G. B. Ellam, C. D. Jonson, *J. Org. Chem.* **1971**, *36*, 2284–2288.

[19] J. E. Baldwin, S. C. MacKenzie Turner, M. G. Moloney, *Tetrahedron* **1994**, *50*, 9411–9424.

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