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Heck arylations of pent-4-enoates or allylmalonate using a palladium/tetraphosphine catalyst

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Abstract

The Heck reaction of aryl halides with functionalised alk-1-enes should be a powerful method for the synthesis of functionalised (*E*)-1-arylalk-1-ene derivatives. The major problem of this reaction is the palladium-catalysed migration of the carbon–carbon double bond along the alkyl chain when there are no substituents on the C3 carbon of the alk-1-enes. We observed that for the arylation of ethyl pent-4-enoate, ethyl 2-methylpent-4-enoate or dimethyl allylmalonate this migration could be partially or completely controlled using appropriate reaction conditions. The ramification on the alkyl chain and the substituents on the aryl halide have also an important influence on this migration. Moreover, the *cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane/1/2$[PdCl(C_3H_5)]_2$ system catalyses this reaction with a wide range of aryl bromides using very high ratio substrate/catalyst in good yields.

Keywords: Tetraphosphine; Palladium; Heck-vinylation; Alkenes; Aryl bromides

1. Introduction

The palladium-catalysed Heck vinylation is one of the most powerful methods for the formation of C–C bonds. The reactivity of alkenes such as acrylates with aryl halides has been studied in detail [1]. On the other hand, despite the rich chemistry of the other ester-containing alk-1-enes, these palladium-catalysed Heck vinylations have attracted much less attention. Substrates such as pent-4-enoates have long been known to give mixtures of regio- and stereoisomers due to the palladium-catalysed migration of the carbon–carbon double bond of the alkene, which often rendered these catalytic reactions quite ineffective. A few examples of vinylations using pen-4-enoates have been described [2–6]. In most cases, $Pd(OAc)_2/PPh_3$ was used as catalyst. For example, the reaction of 4-bromobenzonitrile with pent-4-enoic acid using 3 mol% of $Pd(OAc)_2/PPh_3$ with a substoichiometric amount of tetrabutylammonium chloride gave quite selectively (*E*)-5-(4-cyanophenyl)-pent-4-enoic acid in 54% yield [2]. The vinylation of 4-fluoroiodobenzene with pent-4-enoic acid and tetrabutylammonium chloride as additive affords a 1/1 mixture of 4-(*E*)-pent-1-enoic acid and 3-(*E*)-pent-1-enoic acid. This mixture could be partially purified by recrystallisation, but was preferably used directly for the next step of the synthesis [3]. The reaction of an iodoanisole with methyl pen-4-enoate using the expensive base Ag_2CO_3 gave an inseparable mixture of (*Z*)- and (*E*)-5-arylpent-4-enoates and several other isomers [4]. Using ethyl pent-4-enote and aryl bromide with $Pd(OAc)_2/P(o\text{-tol})_3$ as catalyst a mixture of 51% of (*E*)-5-arylpent-4-enoate, 14% of (*E*)-5-arylpent-3-enoate, 9% of (*E*)-5-aryl-pent-2-enoate and

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24% of (*E*)-4-aryl-pent-4-enoate was obtained [5]. Iodophthalonitrile and benzyl pent-4-enoate were reacted using 5 mol% of $Pd(OAc)_2$ and tetrabutylammonium bromide to give a mixture of isomers which was directly hydrogenated on Pd/C [6]. A few examples of arylations using hex-5-enoate, oct-7-enoate or undec-10-enoate have also been reported [7–9]. The reactivity of allylmalonate has also been described. Balme et al. reported the reaction of allylmalonate with iodobenzene using $Pd(dba)_2$ and dppe as catalyst to give (*Z*)- and (*E*)-3-phenylallylmalonates and the branched isomer as a mixture in a 1/1/1 ratio and in 65% yield [10]. The use of 2-(hex-5-enyl)malonate gave (*E*)-2-(6-phenylhex-5-enyl)malonic acid dimethyl ester with an higher selectivity and a yield of 60% [8]. Finally, the reaction also proceeds with $Pd(OAc)_2$ without added ligand. Iodobenzene reacted with allylmalonate using $N(n\text{-}Bu)_3$ as base and 2 mol% $Pd(OAc)_2$ gave 90% of 3-phenylprop-2-en-1-yl propanedioate [11]. If monophosphine ligands have been successfully used for the reaction with pent-4-enoate or allylmalonate derivatives, to the best of our knowledge, the efficiency of polydentate ligands has not been demonstrated. Moreover, an effective and more regio- and stereoselective method for the arylation of these alkenes employing lower amounts of catalyst especially in the presence of aryl bromides is still subject to very significant improvements.

The nature of the phosphine ligand on complexes has an important influence on the stability of the catalysts, on the reaction rates, and also on the regio- and stereoselectivities of the reactions. In order to find more stable and more efficient palladium catalysts, we have prepared the tetrapodal phosphine ligand, *cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl) cyclopentane or Tedicyp (Fig. 1) [12] in which the four diphenylphosphinoalkyl groups are stereospecifically bound to the same face of the cyclopentane ring. We have reported that the complex formed by association of Tedicyp with $[PdCl(C_3H_5)]_2$ is an extremely efficient catalyst for allylic substitution [12], for the Suzuki cross-coupling, for the Sonogashira alkynylation [13], for Negishi reaction [14], and also for Heck vinylation [15]. Here, we wish to describe the results obtained with the functionalised alkenes: ethyl pent-4-enoate, ethyl 2-methylpentenoate or dimethylallylmalonate with a variety of aryl halides using Tedicyp as ligand.

Fig. 1. Tedicyp ligand.

2. Experimental

2.1. General

All reactions under argon were run using vacuum lines in Schlenk tubes in oven-dried glassware. DMAc (99%) and DMF (99%) were not distilled before use. Some of the aryl halides were distilled before use. The reactions were followed by GC and NMR. ^1H (300 MHz) and ^{13}C (75 MHz) spectra were recorded in $CDCl_3$ solutions. Chemical shift (δ) are reported in ppm relative to $CDCl_3$. Flash chromatography were performed on silica gel (230-400 mesh) eluting with ether/pentane mixtures.

2.2. Preparation of the Pd–Tedicyp catalyst [12]

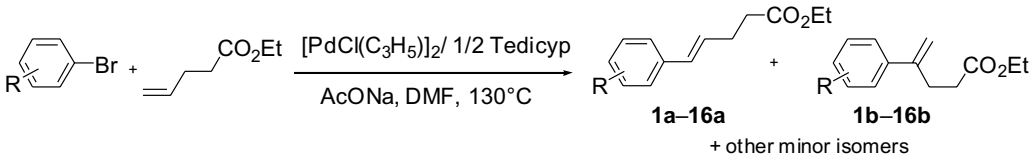
An over-dried 40-mL Schlenk tube equipped with a magnetic stirring bar, under argon atmosphere, was charged with $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (4.2 mg, 11.6 μmol) and Tedicyp (20 mg, 23.2 μmol). 2.5 mL of anhydrous DMF were added, then the solution was stirred at room temperature for 10 min.

2.3. Catalytic procedure for Heck reactions

As a typical experiment, the reaction of aryl halide (1 mmol), alkene (2 mmol) and AcONa, $NaHCO_3$ or KF (2 mmol, see tables) at 130 °C during 20 h in DMF or DMAc (3 mL, see tables) in the presence of *cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane/1/2$[PdCl(C_3H_5)]_2$ complex under argon affords the products after addition of water, extraction with ether or dichloromethane, separation, drying ($MgSO_4$), evaporation and chromatography on silica gel.

2.4. Vinylation products with ethyl pent-4-enoate (Table 1)

*5-(4-Acetylphenyl)-pent-4-enoic acid ethyl ester (**1a**)* (Table 1, entry 1), 4-bromoacetophenone (0.199 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **1a** in 84% (0.207 g) isolated yield. ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.86$ (d, $J = 8.5$ Hz, 2H), 7.37 (d, $J = 8.5$ Hz, 2H), 6.44 (d, $J = 15.8$ Hz, 1H), 6.32 (dt, $J = 15.8$, 6.2 Hz, 1H), 4.12 (q, $J = 6.9$ Hz, 2H), 2.55 (s, 3H), 2.49 (m, 4H), 1.23 (t, $J = 6.9$ Hz, 3H). ^{13}C NMR



Scheme 1.

Table 1
Palladium-catalysed Heck reactions with ethyl pent-4-enoate (Scheme 1)

Entry	Aryl bromide	Ratio of substrate/catalyst	Products	Ratio of **a**/**b**/other isomers[a]	Yield (%)
1	4-Bromoacetophenone	1000	**1a**, **1b**	87/7/6	100 (84)
2	4-Bromoacetophenone	10000	**1a**, **1b**	85/6/9	62
3	4-Bromobenzaldehyde	1000	**2a**, **2b**	88/9/3	100 (83)
4	4-Bromobenzaldehyde	10000	**2a**, **2b**	86/7/7	82
5	Methyl 4-bromobenzoate	1000	**3a**, **3b**	88/7/5	100 (81)
6	Methyl 4-bromobenzoate	10000	**3a**, **3b**	85/7/8	32
7	4-Trifluoromethylbromobenzene	1000	**4a**, **4b**	87/8/5	100 (80)
8	4-Trifluoromethylbromobenzene	10000	**4a**, **4b**	87/7/6	76
9	4-Bromobenzonitrile	1000	**5a**, **5b**	89/8/3	100 (84)
10	4-Bromobenzonitrile	10000	**5a**, **5b**	88/9/3	43
11	3,5-Bis(trifluoromethyl)bromobenzene	1000	**6a**, **6b**	85/9/6	100 (80)
12	3,5-Bis(trifluoromethyl)bromobenzene	10000	**6a**, **6b**	85/6/9	92
13	4-Fluorobromobenzene	1000	**7a**, **7b**	87/8/5	100 (81)
14	4-Fluorobromobenzene	10000	**7a**, **7b**	86/7/7	79
15	Bromobenzene	1000	**8a**, **8b**	89/10/1	100 (84)
16	Bromobenzene	10000	**8a**, **8b**	88/9/3	66
17	Iodobenzene	1000	**8a**, **8b**	80/8/12	100 (77)
18	Iodobenzene	10000	**8a**, **8b**	82/7/11	87
19	4-*t*-Butylbromobenzene	250	**9a**, **9b**	88/8/4	100 (81)
20	4-*t*-Butylbromobenzene	1000	**9a**, **9b**	84/14/2	52
21	4-Bromoanisole	250	**10a**, **10b**	85/14/1	94 (77)
22	4-Bromoanisole	1000	**10a**, **10b**	84/13/3	54
23	4-*N*,*N*-Dimethylaminobromobenzene	100	**11a**, **11b**	88/7/5	46 (35)
24	3-Bromobenzaldehyde	1000	**12a**, **12b**	86/9/5	100 (82)
25	3-Bromobenzaldehyde	10000	**12a**, **12b**	86/9/5	52
26	2-Bromo-6-methoxynaphthalene	1000	**13a**, **13b**	85/12/3	100 (81)
27	2-Bromo-6-methoxynaphthalene	10000	**13a**, **13b**	86/11/3	22
28	2-Bromotoluene	100	**14a**, **14b**	90/4/6	100 (85)
29	2-Bromotoluene	250	**14a**, **14b**	92/5/3	62
30	3-Bromopyridine	250	**15a**, **15b**	86/10/4	100 (81)
31	3-Bromopyridine	1000	**15a**, **15b**	85/10/5	88
32	3-Bromoquinoline	1000	**16a**, **16b**	88/10/2	100 (80)
33	3-Bromoquinoline	10000	**16a**, **16b**	87/9/4	37

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/Tedicyp 1/2, aryl halide (1 eq.), ethyl pent-4-enoate (2 eq.), AcONa (2 eq.), DMF, 130 °C, 20 h, GC yields of the mixture of isomers, yields in parenthesis are isolated yields of isomer **1a**–**16a**.

[a] See Scheme 1.

(75 MHz, $CDCl_3$): $\delta = 197.4$, 172.6, 141.9, 135.6, 131.6, 130.0, 128.6, 125.9, 60.3, 33.6, 28.2, 26.4, 14.1. Anal. Calc. for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.31; H, 7.54%. Before purification isomer **1b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.37$ (s, 1H), 5.17 (s, 1H).

*5-(4-Formylphenyl)-pent-4-enoic acid ethyl ester (**2a**)* (Table 1, entry 3), 4-bromobenzaldehyde (0.187 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **2a** in 83% (0.193 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 9.94$ (s, 1H), 7.78 (d, $J = 8.3$ Hz, 2H), 7.46 (d, $J = 8.3$ Hz, 2H), 6.47 (d, $J = 16.1$ Hz, 1H), 6.37 (dt, $J = 16.1$, 5.7 Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.50 (m, 4H), 1.24 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 191.6$, 172.7, 143.4, 135.1, 132.5, 130.1, 129.9, 126.5, 60.5, 33.6, 28.3, 14.2. Anal. Calc. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.10; H, 7.07%. Before purification isomer **2b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.45$ (s, 1H), 5.25 (s, 1H).

*4-(4-Ethoxycarbonylbut-1-enyl)-benzoic acid methyl ester (**3a**)* (Table 1, entry 5), methyl 4-bromobenzoate (0.215 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **3a** in 81% (0.212 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.93$ (d, $J = 8.3$ Hz, 2H), 7.35 (d, $J = 8.3$ Hz, 2H), 6.43 (d, $J = 15.8$ Hz, 1H), 6.30 (dt, $J = 15.8$, 6.4 Hz, 1H), 4.12 (q, $J = 7.2$ Hz, 2H), 3.87 (s, 3H), 2.50 (m, 4H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.7$, 166.8, 141.8, 131.4, 130.1, 129.8, 128.5, 125.8, 60.4, 51.9, 33.7, 28.3, 14.2. Anal. Calc. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.98; H, 6.79%. Before purification isomer **3b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.77$ (s, 1H), 5.36 (s, 1H).

*5-(4-Trifluoromethylphenyl)-pent-4-enoic acid ethyl ester (**4a**)* (Table 1, entry 7), 4-trifluoromethylbromobenzene (0.225 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **4a** in 80% (0.218 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.52$ (d, $J = 8.3$ Hz, 2H), 7.36 (d, $J = 8.3$ Hz, 2H), 6.44 (d, $J = 16.0$ Hz, 1H), 6.30 (dt, $J = 16.0$, 6.4 Hz, 1H), 4.14 (q, $J = 7.2$ Hz, 2H), 2.50 (m, 4H), 1.24 (t, $J = 7.2$ Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.4$, 140.8, 131.3, 129.7, 128.6 (q, $J = 27.5$ Hz), 126.1, 125.3 (q, $J = 3.8$ Hz), 124.2 (q, $J = 272$ Hz), 60.4, 33.7, 28.2, 14.2. Anal. Calc. for $C_{14}H_{15}F_3O_2$: C, 61.76; H, 5.55. Found: C, 61.59; H, 5.56%. Before purification isomer **4b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.35$ (s, 1H), 5.18 (s, 1H).

*5-(4-Cyanophenyl)-pent-4-enoic acid ethyl ester (**5a**)* (Table 1, entry 9), 4-bromobenzonitrile (0.182 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **5a** in 84% (0.193 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.51$ (d, $J = 8.3$ Hz, 2H), 7.40 (d, $J = 8.3$ Hz, 2H), 6.40 (d, $J = 15.8$ Hz, 1H), 6.32 (dt, $J = 15.8$, 6.2 Hz, 1H), 4.10 (q, $J = 7.2$ Hz, 2H), 2.47 (m, 4H), 1.24 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.6$, 141. 8, 132.7, 129.5, 126.5, 118.9, 110.2, 60.4, 33.5, 28.2, 14.2. Anal. Calc. for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59. Found: C, 73.57; H, 6.41%. Before purification isomer **5b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.38$ (s, 1H), 5.22 (s, 1H).

*5-(3,5-Bis(trifluoromethyl)phenyl)-pent-4-enoic acid ethyl ester (**6a**)* (Table 1, entry 11), 3,5-bis(trifluoromethyl)bromobenzene (0.293 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **6a** in 80% (0.272 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.72$ (s, 2H), 7.68 (s, 1H), 6.49 (d, $J = 16.1$ Hz, 1H), 6.38 (dt, $J = 16.1$, 5.8 Hz, 1H), 4.15 (q, $J = 7.2$ Hz, 2H), 2.52 (m, 4H), 1.25 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.6$, 139.4, 132.9, 131.8 (q, $J = 32.7$ Hz), 128.5, 125.9, 123.2 (q, $J = 273.5$ Hz), 120.5 (q, $J = 4.0$ Hz), 60.5, 33.5, 28.1, 14.2. Anal. Calc. for $C_{15}H_{14}F_6O_2$: C, 52.95; H, 4.15. Found: C, 52.87; H, 4.40%. Before purification isomer **6b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.41$ (s, 1H), 5.27 (s, 1H).

*5-(4-Fluorophenyl)-pent-4-enoic acid ethyl ester (**7a**)* (Table 1, entry 13), 4-fluorobromobenzene (0.175 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **7a** in 81% (0.180 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.28$ (dd, $J = 8.6$, 5.5 Hz, 2H), 6.96 (t, $J = 8.6$ Hz, 2H), 6.37 (d, $J = 15.8$ Hz, 1H), 6.10 (dt, $J = 15.8$, 6.4 Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.46 (m, 4H), 1.25 (t, $J = 7.2$ Hz, 3H). Before purification isomer **7b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.23$ (s, 1H), 5.12 (s, 1H).

*5-Phenylpent-4-enoic acid ethyl ester (**8a**)* (Table 1, entry 17), iodobenzene (0.204 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **8a** in 77% (0.157 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.28$ (m, 5H), 6.42 (d, $J = 15.8$ Hz, 1H), 6.17 (dt, $J = 15.8$, 6.4 Hz, 1H), 4.14 (q, $J = 7.0$ Hz, 2H), 2.49 (m, 4H), 1.25 (t, $J = 7.0$ Hz, 3H). Before purification isomer **8b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.29$ (s, 1H), 5.08 (s, 1H).

*5-(4-tert-Butylphenyl)-pent-4-enoic acid ethyl ester (**9a**)* (Table 1, entry 19), 4-*t*-butylbromobenzene (0.213 g, 1 mmol), Pd complex (4 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **9a** in 81% (0.211 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.33$ (d, $J = 8.3$ Hz, 2H), 7.27 (d, $J = 8.3$ Hz, 2H), 6.42 (d, $J = 15.8$ Hz, 1H), 6.16 (dt, $J = 15.8$, 6.4 Hz, 1H), 4.14 (q, $J = 7.1$ Hz, 2H), 2.48 (m, 4H), 1.31 (s, 9H), 1.26 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 173.0$, 150.1, 134.6, 130.6, 127.7, 125.7, 125.4, 60.3, 34.5, 34.1, 31.3, 28.3, 14.2. Anal. Calc. for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.34; H, 9.29%. Before purification isomer **9b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.32$ (s, 1H), 5.05 (s, 1H).

*5-(4-Methoxyphenyl)-pent-4-enoic acid ethyl ester (**10a**)* (Table 1, entry 21), 4-bromoanisole (0.187 g, 1 mmol), Pd complex (4 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **10a** in 77% (0.180 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.26$ (d, $J = 8.7$ Hz, 2H), 6.82 (d, $J = 8.7$ Hz, 2H), 6.36 (d, $J = 16.2$ Hz, 1H), 6.04 (dt, $J = 16.2$, 6.5 Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 3.78 (s, 3H), 2.46 (m, 4H), 1.24 (t, $J = 7.2$ Hz, 3H). Before purification isomer **10b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.22$ (s, 1H), 4.99 (s, 1H).

*5-(4-Dimethylaminophenyl)-pent-4-enoic acid ethyl ester (**11a**)* (Table 1, entry 23), 4-*N*,*N*-dimethylaminobromobenzene (0.200 g, 1 mmol), Pd complex (10 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **11a** in 35% (0.087 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.22$ (d, $J = 8.7$ Hz, 2H), 6.66 (d, $J = 8.7$ Hz, 2H), 6.33 (d, $J = 15.9$ Hz, 1H), 5.98 (dt, $J = 15.9$, 6.6 Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.93 (s, 6H), 2.46 (m, 4H), 1.25 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 173.2$, 149.8, 130. 7, 126. 9, 126.1, 124.2, 112.5, 60.3, 40.6, 34. 5, 28.4, 14.2. Anal. Calc. for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56. Found: C, 73.00; H, 8.61%. Before purification isomer **11b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.42$ (s, 1H), 4.94 (s, 1H).

*5-(3-Formylphenyl)-pent-4-enoic acid ethyl ester (**12a**)* (Table 1, entry 24), 3-bromobenzaldehyde (0.187 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **12a** in 82% (0.190 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 9.98$ (s, 1H), 7.81 (s, 1H), 7.68 (d, $J = 7.4$ Hz, 1H), 7.55 (d, $J = 7.9$ Hz, 1H), 7.19 (t, $J = 7.4$ Hz, 1H), 6.47 (d, $J = 15.8$ Hz, 1H), 6.80 (dt, $J = 15.8$, 6.1 Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.49 (m, 4H), 1.23 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 191.9$, 172.3, 137.9, 136.2, 131.5, 130.1, 129.2, 128.7, 127.7, 126. 5, 60.0, 33.3, 27.7, 13.8. Anal. Calc. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.17; H, 7.09%. Before purification isomer **12b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.40$ (s, 1H), 5.22 (s, 1H).

*5-(6-Methoxynaphthalen-2-yl)-pent-4-enoic acid ethyl ester (**13a**)* (Table 1, entry 26), 2-bromo-6-methoxynaph-

thalene (0.237 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **13a** in 81% (0.230 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.68$ (d, $J = 7.8$ Hz, 1H), 7.65 (d, $J = 7.8$ Hz, 1H), 7.60 (s, 1H), 7.52 (dd, $J = 8.5$, 1.7 Hz, 1H), 7.13 (m, 2H), 6.55 (d, $J = 15.8$ Hz, 1H), 6.26 (dt, $J = 15.8$, 6.4 Hz, 1H), 4.16 (q, $J = 7.2$ Hz, 2H), 3.90 (s, 3H), 2.54 (m, 4H), 1.27 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 173.0$, 157.5, 133.8, 132.7, 131.0, 129.3, 129.0, 127.8, 126.9, 125.4, 124.0, 118.8, 105.8, 60.3, 55.2, 34.1, 28.4, 14.2. Anal. Calc. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.19; H, 7.21%. Before purification isomer **13b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.41$ (s, 1H), 5.14 (s, 1H).

*5-o-Tolylpent-4-enoic acid ethyl ester (**14a**)* (Table 1, entry 28), 2-bromotoluene (0.171 g, 1 mmol), Pd complex (10 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **14a** in 85% (0.185 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.37$ (d, $J = 8.3$ Hz, 1H), 7.20–7.05 (m, 3H), 6.62 (d, $J = 15.8$ Hz, 1H), 6.05 (dt, $J = 15.8$, 5.9 Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.50 (m, 4H), 2.31 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.9$, 136.5, 135.0, 130.1, 129.8, 128.8, 127.0, 126.0, 125.5, 60.3, 34.2, 28.6, 19.7, 14.2. Anal. Calc. for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.20; H, 8.19%. Before purification isomer **14b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.20$ (s, 1H), 4.89 (s, 1H).

*5-(Pyridin-3-yl)pent-4-enoic acid ethyl ester (**15a**)* (Table 1, entry 30), 3-bromopyridine (0.158 g, 1 mmol), Pd complex (4 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **15a** in 81% (0.166 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.51$ (s, 1H), 8.40 (d, $J = 4.7$ Hz, 1H), 7.60 (dt, $J = 7.9$, 1.9 Hz, 1H), 7.19 (dd, $J = 7.9$, 4.7 Hz, 1H), 6.40 (d, $J = 15.8$ Hz, 1H), 6.25 (dt, $J = 15.8$, 5.9 Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.50 (m, 4H), 1.24 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.7$, 148.1, 147.9, 132.8, 132.4, 130.9, 127.4, 123.3, 60.4, 33.7, 28.2, 14.2. Anal. Calc. for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37. Found: C, 70.04; H, 7.17%. Before purification isomer **15b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.33$ (s, 1H), 5.17 (s, 1H).

*5-(Quinolin-3-yl)pent-4-enoic acid ethyl ester (**16a**)* (Table 1, entry 32), 3-bromoquinoline (0.208 g, 1 mmol), Pd complex (1 μmol) and ethyl pent-4-enoate (0.256 g, 2 mmol). The residue was purified by column chromatography to give **16a** in 80% (0.204 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.93$ (s, 1H), 8.04 (d, $J = 8.5$ Hz, 1H), 7.97 (s, 1H), 7.75 (d, $J = 8.5$ Hz, 1H), 7.63 (t, $J = 8.3$ Hz, 1H), 7.49 (t, $J = 7.2$ Hz, 1H), 6.57 (d, $J = 16.1$ Hz, 1H), 6.42 (dt, $J = 16.1$, 6.1 Hz, 1H), 4.14 (q, $J = 7.2$ Hz, 2H), 1.25 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.7$, 149.1, 147.2, 131.9, 131.2, 130.2, 129.1, 128.9, 128.0, 127.8, 127.7, 126.8, 60.4, 33.7, 28.4, 14.2. Anal. Calc. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71. Found: C, 75.41; H, 6.47%. Before purification isomer **16b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.53$ (s, 1H), 5.30 (s, 1H).

2.5. Vinylation products with ethyl 2-methylpent-4-enoate (Table 3)

*5-(4-Acetylphenyl)-2-methylpent-4-enoic acid ethyl ester (**17**)* (Table 3, entry 1), 4-bromoacetophenone (0.199 g, 1 mmol), Pd complex (0.1 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **17** in 94% (0.244 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.85$ (d, $J = 8.4$ Hz, 2H), 7.36 (d, $J = 8.4$ Hz, 2H), 6.42 (d, $J = 15.8$ Hz, 1H), 6.26 (dt, $J = 15.8$, 6.8 Hz, 1H), 4.10 (q, $J = 7.0$ Hz, 2H), 2.54 (s, 3H), 2.51 (m, 2H), 2.34 (m, 1H), 1.20 (t, $J = 7.0$ Hz, 3H), 1.17 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 197.4$, 175.7, 141.9, 135.6, 131.1, 130.5, 128.6, 126.0, 60.3, 39.4, 37.0, 26.4, 16.7, 14.2. Anal. Calc. for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 74.01; H, 7.80%.

*5-(4-Formylphenyl)-2-methylpent-4-enoic acid ethyl ester (**18**)* (Table 3, entry 4), 4-bromobenzaldehyde (0.187 g, 1 mmol), Pd complex (0.01 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **18** in 91% (0.224 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 9.94$ (s, 1H), 7.79 (d, $J = 8.3$ Hz, 2H), 7.45 (d, $J = 8.3$ Hz, 2H), 6.47 (d, $J = 15.8$ Hz, 1H), 6.33 (dt, $J = 15.8$, 6.8 Hz, 1H), 4.11 (q, $J = 7.2$ Hz, 2H), 2.59 (m, 2H), 2.36 (m, 1H), 1.24 (t, $J = 7.2$ Hz, 3H), 1.20 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 191.6$, 175.7, 143.4, 135.1, 131.4, 131.1, 130.1, 126.5, 60.3, 39.4, 37.1, 16.8, 14.2. Anal. Calc. for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.31; H, 7.48%.

*5-(4-Benzoylphenyl)-2-methylpent-4-enoic acid ethyl ester (**19**)* (Table 3, entry 5), 4-bromobenzophenone (0.261 g, 1 mmol), Pd complex (0.1 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **19** in 88% (0.283 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.78$–7.73 (m, 4H), 7.56 (t, $J = 7.0$ Hz, 1H), 7.48–7.40 (m, 4H), 6.47 (d, $J = 15.9$ Hz, 1H), 6.31 (dt, $J = 15.9$, 6.8 Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.60 (m, 2H), 2.40 (m, 1H), 1.23 (t, $J = 7.2$ Hz, 3H), 1.21 (d, $J = 6.3$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 196.1$, 175.8, 141.5, 137.8, 135.9, 132.2, 131.2, 130.5, 130.4, 129.8, 128.2, 125.8, 60.3, 39.5, 37.1, 16.7, 14.2. Anal. Calc. for $C_{21}H_{22}O_3$: C, 78.23; H, 6.88. Found: C, 78.40; H, 6.59%.

*5-(4-Cyanophenyl)-2-methylpent-4-enoic acid ethyl ester (**20**)* (Table 3, entry 6), 4-bromobenzonitrile (0.182 g, 1 mmol), Pd complex (0.1 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **20** in 91% (0.221 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.55$ (d, $J = 8.1$ Hz, 2H), 7.38 (d, $J = 8.1$ Hz, 2H), 6.39 (d, $J = 15.8$ Hz, 1H), 6.28 (dt, $J = 15.8$, 6.8 Hz, 1H), 4.12 (q, $J = 7.2$ Hz, 2H), 2.57 (m, 2H), 2.36 (m, 1H), 1.23 (t,

$J = 7.2$ Hz, 3H), 1.19 (d, $J = 6.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 175.6$, 141.8, 132.3, 131.6, 129.1, 126.5, 119.0, 110.3, 60.4, 39.3, 37.0, 16.8, 14.2. Anal. Calc. for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04. Found: C, 74.24; H, 7.01%.

*2-Methyl-5-(4-nitrophenyl)-pent-4-enoic acid ethyl ester (**21**)* (Table 3, entry 8), 4-bromonitrobenzene (0.202 g, 1 mmol), Pd complex (0.1 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **21** in 87% (0.229 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.13$ (d, $J = 8.7$ Hz, 2H), 7.43 (d, $J = 8.7$ Hz, 2H), 6.48 (d, $J = 15.8$ Hz, 1H), 6.33 (dt, $J = 15.8$, 6.0 Hz, 1H), 4.13 (q, $J = 7.1$ Hz, 2H), 2.60 (m, 2H), 2.39 (m, 1H), 1.23 (t, $J = 7.1$ Hz, 3H), 1.19 (d, $J = 6.5$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 175.6$, 146.6, 143.8, 132.7, 130.2, 126.5, 123.9, 60.4, 39.3, 37.0, 16.8, 14.2. Anal. Calc. for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51. Found: C, 63.90; H, 6.40%.

*5-(4-Fluorophenyl)-2-methylpent-4-enoic acid ethyl ester (**22**)* (Table 3, entry 9), 4-fluorobromobenzene (0.175 g, 1 mmol), Pd complex (0.1 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **22** in 93% (0.220 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.27$ (dd, $J = 5.5$, 8.7 Hz, 2H), 6.96 (t, $J = 8.7$ Hz, 2H), 6.37 (d, $J = 15.7$ Hz, 1H), 6.05 (dt, $J = 15.7$, 6.9 Hz, 1H), 4.12 (q, $J = 7.2$ Hz, 2H), 2.55 (m, 2H), 2.32 (m, 1H), 1.23 (t, $J = 7.2$ Hz, 3H), 1.20 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 176.0$, 163.7 (d,$J = 246.2$ Hz), 133.6, 130.8, 127.5 (d,$J = 7.5$ Hz), 127.0 (d, $J = 2.3$ Hz), 115.5 (d, $J = 21.2$ Hz), 60.3, 39.6, 37.0, 16.7, 14.3. Anal. Calc. for $C_{14}H_{17}FO_2$: C, 71.16; H, 7.25. Found: C, 71.41; H, 7.34%.

*2-Methyl-5-p-tolylpent-4-enoic acid ethyl ester (**23**)* (Table 3, entry 11), 4-bromotoluene (0.171 g, 1 mmol), Pd complex (4 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **23** in 95% (0.221 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.21$ (d, $J = 8.1$ Hz, 2H), 7.08 (d, $J = 8.1$ Hz, 2H), 6.38 (d, $J = 15.6$ Hz, 1H), 6.08 (dt, $J = 15.6$, 7.0 Hz, 1H), 4.12 (q, $J = 7.2$ Hz, 2H), 2.56 (m, 2H), 2.33 (m, 1H), 2.31 (s, 3H), 1.23 (t, $J = 7.2$ Hz, 3H), 1.18 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 176.1$, 136.8, 134.6, 131.8, 129.1, 126.2, 125.9, 60.2, 39.7, 37.1, 21.1, 16.7, 14.3. Anal. Calc. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.38; H, 8.49%.

*5-(4-Methoxyphenyl)-2-methylpent-4-enoic acid ethyl ester (**24**)* (Table 3, entry 13), 4-bromoanisole (0.187 g, 1 mmol), Pd complex (4 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **24** in 90% (0.223 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.26$ (d, $J = 8.7$ Hz, 2H), 6.82 (d, $J = 8.7$ Hz, 2H), 6.35 (d, $J = 15.7$ Hz, 1H), 5.99 (dt, $J = 15.7$, 6.7 Hz, 1H), 4.12 (q, $J = 7.0$ Hz, 2H), 3.79 (s, 3H), 2.55 (m, 2H), 2.31 (m, 1H), 1.23 (t, $J = 7.0$ Hz, 3H), 1.18 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 176.1$, 158.9, 130.3, 127.7, 127.2, 125.1, 114.2, 60.2, 55.3, 39.8, 37.1, 16.7, 14.3. Anal. Calc. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.74; H, 8.24%.

*5-(2-Cyanophenyl)-2-methylpent-4-enoic acid ethyl ester (**25**)* (Table 3, entry 15), 2-bromobenzonitrile (0.182 g, 1 mmol), Pd complex (10 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **25** in 89% (0.216 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.58$ (d, $J = 8.7$ Hz, 2H), 7.49 (t, $J = 7.2$ Hz, 1H), 7.29 (t, $J = 7.2$ Hz, 1H), 6.77 (d, $J = 15.4$ Hz, 1H), 6.36 (dt, $J = 15.4$, 7.2 Hz, 1H), 4.14 (q, $J = 7.2$ Hz, 2H), 2.60 (m, 2H), 2.42 (m, 1H), 1.25 (t, $J = 7.2$ Hz, 3H), 1.22 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 175.6$, 140.6, 132.9, 132.8, 132.6, 128.0, 127.2, 125.5, 117.9, 110.6, 60.4, 39.4, 36.9, 16.7, 14.2. Anal. Calc. for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04. Found: C, 74.21; H, 7.17%.

*2-Methyl-5-o-tolylpent-4-enoic acid ethyl ester (**26**)* (Table 3, entry 17), 2-bromotoluene (0.171 g, 1 mmol), Pd complex (10 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **26** in 94% (0.218 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.37$ (d, $J = 8.3$ Hz, 1H), 7.14 (m, 2H), 7.12 (m, 1H), 6.62 (d, $J = 15.5$ Hz, 1H), 6.01 (dt, $J = 15.5$, 7.0 Hz, 1H), 4.14 (q, $J = 7.1$ Hz, 2H), 2.58 (m, 2H), 2.37 (m, 1H), 2.36 (s, 3H), 1.25 (t, $J = 7.1$ Hz, 3H), 1.21 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 176.0$, 136.6, 135.0, 130.1, 130.0, 128.6, 127.0, 126.0, 125.6, 60.2, 39.7, 37.3, 19.7, 16.6, 14.2. Anal. Calc. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.40; H, 8.79%.

*2-Methyl-5-(naphthalen-1-yl)pent-4-enoic acid ethyl ester (**27**)* (Table 3, entry 19), 1-bromonaphthalene (0.207 g, 1 mmol), Pd complex (1 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **27** in 94% (0.252 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.10$ (d, $J = 8.8$ Hz, 1H), 7.83 (d, $J = 8.8$ Hz, 1H), 7.75 (d, $J = 7.9$ Hz, 1H), 7.53 (t, $J = 7.5$ Hz, 1H), 7.49 (m, 2H), 7.41 (t, $J = 7.5$ Hz, 1H), 7.16 (d, $J = 15.5$ Hz, 1H), 6.17 (dt, $J = 15.5$, 6.9 Hz, 1H), 4.17 (q, $J = 7.1$ Hz, 2H), 2.68 (m, 2H), 2.48 (m, 1H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.23 (d, $J = 6.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 176.0$, 135.3, 133.5, 131.1, 130.6, 129.3, 128.4, 127.5, 125.9, 125.6, 125.6, 123.8, 123.7, 60.3, 39.7, 37. 5, 16.7, 14.3. Anal. Calc. for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.39; H, 7.59%.

*5-(2-Methoxyphenyl)-2-methylpent-4-enoic acid ethyl ester (**28**)* (Table 3, entry 21), 2-bromoanisole (0.187 g, 1 mmol), Pd complex (10 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **28** in 93% (0.231 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.38$ (d, $J = 7.7$ Hz, 1H), 7.18 (t, $J = 7.4$ Hz, 1H), 6.89 (t, $J = 8.1$ Hz, 1H), 6.84 (d, $J = 8.1$ Hz, 1H), 6.74 (d, $J = 15.7$ Hz, 1H), 6.12 (dt, $J = 15.7$, 6.8 Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 3.82 (s, 3H), 2.57 (m, 2H), 2.37 (m, 1H), 1.24 (t, $J = 7.2$ Hz, 3H), 1.19 (d, $J = 6.6$ Hz, 3H). ^{13}C

NMR (75 MHz, $CDCl_3$): $\delta = 176.1$, 132.5, 128.1, 127.9, 126.7, 126.5, 120.6, 116.4, 110.8, 60.2, 55.4, 39.8, 37.5, 16.6, 14.2. Anal. Calc. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.47; H, 8.21%.

*2-Methyl-5-(pyridin-3-yl)pent-4-enoic acid ethyl ester (**29**)* (Table 3, entry 23), 3-bromopyridine (0.158 g, 1 mmol), Pd complex (0.1 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **29** in 90% (0.197 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.54$ (s, 1H), 8.42 (d, $J = 5.6$ Hz, 1H), 7.63 (d, $J = 8.0$ Hz, 1H), 7.20 (t, $J = 5.6$ Hz, 1H), 6.40 (d, $J = 15.6$ Hz, 1H), 6.20 (dt, $J = 15.6$, 6.8 Hz, 1H), 4.12 (q, $J = 7.2$ Hz, 2H), 2.59 (m, 2H), 2.36 (m, 1H), 1.24 (t, $J = 7.2$ Hz, 3H), 1.20 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 175.8$, 148.1, 147.9, 133.0, 132.6, 129.9, 128.5, 123.4, 60.4, 39.5, 37.1, 16.8, 14.3. Anal. Calc. for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81. Found: C, 71.34; H, 7.70%.

*2-Methyl-5-(pyridin-4-yl)pent-4-enoic acid ethyl ester (**30**)* (Table 3, entry 25), 4-bromopyridine (0.158 g, 1 mmol), Pd complex (1 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **30** in 90% (0.197 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.49$ (d, $J = 6.1$ Hz, 2H), 7.43 (d, $J = 6.1$ Hz, 2H), 6.42 (d, $J = 15.2$ Hz, 1H), 6.33 (dt, $J = 15.2$, 5.7 Hz, 1H), 4.12 (q, $J = 7.2$ Hz, 2H), 2.59 (m, 2H), 2.36 (m, 1H), 1.24 (t, $J = 7.2$ Hz, 3H), 1.21 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 175.6$, 150.0, 144.6, 132. 6, 129.8, 120.6, 60.4, 39.3, 36.9, 16.8, 14.2. Anal. Calc. for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81. Found: C, 71.50; H, 7.97%.

*2-Methyl-5-(quinolin-3-yl)pent-4-enoic acid ethyl ester (**31**)* (Table 3, entry 27), 3-bromoquinoline (0.208 g, 1 mmol), Pd complex (0.1 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **31** in 94% (0.253 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.93$ (s, 1H), 8.03 (d, $J = 8.3$ Hz, 1H), 8.97 (s, 1H), 7.75 (d, $J = 8.1$ Hz, 1H), 7.63 (t, $J = 8.3$ Hz, 1H), 7.49 (t, $J = 8.1$ Hz, 1H), 6.55 (d, $J = 15.8$ Hz, 1H), 6.37 (dt, $J = 15.5$, 6.7 Hz, 1H), 4.14 (q, $J = 7.1$ Hz, 2H), 2.63 (m, 2H), 2.41 (m, 1H), 1.24 (t, $J = 7.1$ Hz, 3H), 1.21 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 175.8$, 149.2, 147.2, 131.8, 130.2, 130.0, 129.1, 128.9, 128.8, 128.0, 127.7, 126.8, 60.3, 39.5, 37.2, 16.8, 14.3. Anal. Calc. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11. Found: C, 75.87; H, 7.25%.

*5-(Isoquinolin-4-yl)-2-methylpent-4-enoic acid ethyl ester (**32**)* (Table 3, entry 29), 4-bromoisoquinoline (0.208 g, 1 mmol), Pd complex (1 μmol) and ethyl 2-methylpent-4-enoate (0.284 g, 2 mmol). The residue was purified by column chromatography to give **32** in 92% (0.248 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 9.09$ (s, 1H), 8.51 (s, 1H), 7.99 (d, $J = 8.5$ Hz, 1H), 7.90 (d, $J = 8.5$ Hz, 1H), 7.67 (t, $J = 7.1$ Hz, 1H), 7.55 (t, $J = 7.1$ Hz, 1H), 6.97 (d, $J = 15.7$ Hz, 1H), 6.20 (dt, $J = 15.7$, 7.0 Hz, 1H), 4.12 (q, $J = 7.2$ Hz, 2H), 2.59 (m, 2H), 2.42 (m, 1H), 1.24 (t, $J = 7.2$ Hz, 3H), 1.20 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 175.8$, 151.5, 140.4, 133.5, 132.3, 130.2, 128.6, 127.9, 126.3, 126.0, 122.9, 60.3, 39.5, 37.4, 16.7, 14.19. Anal. Calc. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11. Found: C, 75.67; H, 7.07%.

2.6. Vinylation products with dimethyl allylmalonate (Table 5)

*2-[3-(4-Acetylphenyl)-allyl]-malonic acid dimethyl ester (**33a**)* (Table 5, entry 2), 4-bromoacetophenone (0.199 g, 1 mmol), Pd complex (1 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **33a** in 76% (0.220 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.84$ (d, $J = 8.0$ Hz, 2H), 7.36 (d, $J = 8.0$ Hz, 2H), 6.47 (d, $J = 15.8$ Hz, 1H), 6.25 (dt, $J = 15.8$, 7.2 Hz, 1H), 3.71 (s, 6H), 3.52 (t, $J = 7.3$ Hz, 1H), 2.80 (t, $J = 7.3$ Hz, 2H), 2.54 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 197.3$, 169.0, 141.5, 135.8, 131. 9, 128.6, 128.5, 126.1, 52.5, 51.3, 32.1, 26.4. Anal. Calc. for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.27; H, 6.10%. Before purification product **33b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.44$ (d, $J = 15.9$ Hz, 1H), 2.50 (m, 4H).

*2-[3-(4-Formylphenyl)-allyl]-malonic acid dimethyl ester (**34a**)* (Table 5, entry 4), 4-bromobenzaldehyde (0.187 g, 1 mmol), Pd complex (1 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **34a** in 72% (0.199 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 9.95$ (s, 1H), 7.79 (d, $J = 8.3$ Hz, 2H), 7.45 (d, $J = 8.3$ Hz, 2H), 6.51 (d, $J = 15.9$ Hz, 1H), 6.32 (dt, $J = 15.9$, 7.2 Hz, 1H), 3.74 (s, 6H), 3.54 (t, $J = 7.3$ Hz, 1H), 2.83 (t,$J = 7.3$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 191.6$, 169.0, 142.9, 135.3, 131.9, 130.1, 129.4, 126.7, 52.6, 51.3, 32.3. Anal. Calc. for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84. Found: C, 65.30; H, 5.89%. Before purification product **34b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.47$ (d, $J = 15.9$ Hz, 1H), 2.50 (m, 4H).

*2-[3-(4-Benzoylphenyl)-allyl]-malonic acid dimethyl ester (**35a**)* (Table 5, entry 6), 4-bromobenzophenone (0.261 g, 1 mmol), Pd complex (1 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **35a** in 81% (0.285 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.77$ (d, $J = 7.6$ Hz, 2H), 7.75 (d, $J = 7.6$ Hz, 2H), 7.57 (t, $J = 7.0$ Hz, 1H), 7.49–7.40 (m, 4H), 6.53 (d, $J = 15.9$ Hz, 1H), 6.29 (dt, $J = 15.9$, 7.2 Hz, 1H), 3.75 (s, 6H), 3.55 (t, $J = 7.3$ Hz, 1H), 2.84 (t,$J = 7.3$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 196.1$, 169.1, 141.0, 137.7, 136.3, 132.2, 132.0, 130.5, 129.9, 128.4, 128.2, 126.0, 52.6, 51.4, 32.3. Anal. Calc. for $C_{21}H_{20}O_5$: C, 71.58; H, 5.72. Found: C, 71.37; H, 5.80%. Before purification product **35b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.48$ (d, $J = 15.9$ Hz, 1H), 2.54 (m, 4H).

*2-[3-(4-Trifluoromethylphenyl)-allyl]-malonic acid dimethyl ester (**36a**)* (Table 5, entry 8), 4-trifluoromethylb-

romobenzene (0.225 g, 1 mmol), Pd complex (1 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **36a** in 80% (0.253 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.52$ (d, $J = 8.3$ Hz, 2H), 7.40 (d, $J = 8.3$ Hz, 2H), 6.50 (d, $J = 15.7$ Hz, 1H), 6.23 (dt, $J = 15.9$, 7.2 Hz, 1H), 3.74 (s, 6H), 3.54 (t, $J = 7.2$ Hz, 1H), 2.82 (t, $J = 7.2$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 169.1$, 140.4, 131.6, 129.2 (q, $J = 27.5$ Hz), 128.2, 126.3, 125.4 (q, $J = 3.8$ Hz), 124.0 (q, $J = 272$ Hz), 52.6, 51.4, 32.2. Anal. Calc. for $C_{15}H_{15}F_3O_4$: C, 56.96; H, 4.78. Found: C, 56.89; H, 4.88%. Before purification product **36b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.43$ (d, $J = 15.9$ Hz, 1H), 2.49 (m, 4H).

*2-[3-(4-Cyanophenyl)-allyl]-malonic acid dimethyl ester (**37a**)* (Table 5, entry 10), 4-bromobenzonitrile (0.182 g, 1 mmol), Pd complex (1 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **37a** in 85% (0.232 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.56$ (d, $J = 7.9$ Hz, 2H), 7.45 (d, $J = 7.9$ Hz, 2H), 6.51 (d, $J = 15.7$ Hz, 1H), 6.32 (dt, $J = 15.9$, 7.2 Hz, 1H), 3.74 (s, 6H), 3.53 (t, $J = 7.2$ Hz, 1H), 2.82 (t, $J = 7.2$ Hz, 2H). Before purification product **37b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.40$ (d, $J = 15.9$ Hz, 1H), 2.49 (m, 4H).

*2-[3-(4-Methoxycarbonylphenyl)-allyl]-malonic acid dimethyl ester (**38a**)* (Table 5, entry 12), methyl 4-bromobenzoate (0.215 g, 1 mmol), Pd complex (1 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **38a** in 87% (0.266 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.95$ (d, $J = 8.1$ Hz, 2H), 7.36 (d, $J = 8.1$ Hz, 2H), 6.49 (d, $J = 15.8$ Hz, 1H), 6.26 (dt, $J = 15.8$, 7.2 Hz, 1H), 3.89 (s, 3H), 3.74 (s, 6H), 3.53 (t, $J = 7.6$ Hz, 1H), 2.82 (t, $J = 7.6$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 169.1$, 166.8, 141.4, 132.1 129.9, 128. 9, 128.3, 126.1, 52.6, 52.0, 51.4, 32.2. Anal. Calc. for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.55; H, 5.81%. Before purification product **38b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.43$ (d, $J = 15.9$ Hz, 1H), 2.51 (m, 4H).

*2-(3-p-Tolylallyl)-malonic acid dimethyl ester (**39a**)* (Table 5, entry 14), 4-bromotoluene (0.171 g, 1 mmol), Pd complex (10 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **39a** in 91% (0.239 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.21$ (d, $J = 7.7$ Hz, 2H), 7.09 (d, $J = 7.7$ Hz, 2H), 6.44 (d, $J = 15.7$ Hz, 1H), 6.07 (dt, $J = 15.7$, 7.1 Hz, 1H), 3.73 (s, 6H), 3.51 (t, $J = 7.6$ Hz, 1H), 2.78 (t, $J = 7.6$ Hz, 2H), 2.31 (s, 3H). Before purification product **39b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.50$ (m, 4H).

*2-[3-(4-Methoxyphenyl)-allyl]-malonic acid dimethyl ester (**40a**)* (Table 5, entry 16), 4-bromoanisole (0.187 g, 1 mmol), Pd complex (10 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **40a** in 92% (0.256 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.24$ (d, $J = 8.3$ Hz, 2H), 6.82 (d, $J = 8.3$ Hz, 2H), 6.40 (d, $J = 15.7$ Hz, 1H), 5.98 (dt, $J = 15.7$, 7.1 Hz, 1H), 3.79 (s, 3H), 3.73 (s, 6H), 3.50 (t, $J = 7.7$ Hz, 1H), 2.77 (t, $J = 7.7$ Hz, 2H). Before purification product **40b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.37$ (d, $J = 15.9$ Hz, 1H), 2.48 (m, 4H).

*2-[3-(2-Cyanophenyl)-allyl]-malonic acid dimethyl ester (**41b**)* (Table 5, entry 18), 2-bromobenzonitrile (0.182 g, 1 mmol), Pd complex (10 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **41b** in 85% (0.183 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.58$ (m, 2H), 7.50 (t, $J = 7.6$ Hz, 1H), 7.30 (t, $J = 7.6$ Hz, 1H), 6.77 (d, $J = 15.7$ Hz, 1H), 6.40 (dt, $J = 15.7$, 7.1 Hz, 1H), 3.70 (s, 6H), 3.58 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 173.1$, 140.6, 134.0, 132.9, 132.6, 127.3, 127.0, 125.5, 117.9, 110.6, 51.7, 33.3, 28.2. Anal. Calc. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.41; H, 5.99%.

*2-(3-o-Tolylallyl)-malonic acid dimethyl ester (**42b**)* (Table 3, entry 20), 2-bromotoluene (0.171 g, 1 mmol), Pd complex (10 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **42b** in 87% (0.178 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.36$ (d, $J = 8.3$ Hz, 1H), 7.20–7.05 (m, 3H), 6.62 (d, $J = 15.8$ Hz, 1H), 6.05 (dt, $J = 15.8$, 5.9 Hz, 1H), 3.68 (s, 3H), 2.50 (m, 4H), 2.31 (s, 3H).

*2-[(3-Naphthalen-1-yl)allyl]-malonic acid dimethyl ester (**43a**)* (Table 5, entry 22), 1-bromonaphthalene (0.207 g, 1 mmol), Pd complex (10 μmol) and dimethyl allylmalonate (0.344 g, 2 mmol). The residue was purified by column chromatography to give **43a** in 62% (0.185 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.05$ (d, $J = 7.9$ Hz, 1H), 7.83 (d, $J = 7.9$ Hz, 1H), 7.75 (d, $J = 7.9$ Hz, 1H), 7.47 (m, 4H), 7.22 (d, $J = 15.8$ Hz, 1H), 6.15 (dt, $J = 15.8$, 7.2 Hz, 1H), 3.77 (s, 6H), 3.62 (t, $J = 7.3$ Hz, 1H), 2.80 (t, $J = 7.3$ Hz, 2H). Before purification product **42b** was also observed. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.50$ (m, 4H).

2.7. CAS registry numbers

Compound **7a**, 463934-03-4; **8a**, 22768-07-6; **10a**, 89861-42-7; **37a**, 212777-67-8; **39a**, 164527-49-5; **40a**, 212777-65-6; **42b**, 445477-05-4; and **43a**, 212777-61-2.

3. Results and discussion

3.1. Heck vinylation with ethyl pent-4-enoate

First, we examined the reactivity of ethyl pent-4-enoate in the presence of the system $[PdCl(C_3H_5)]_2$/2Tedicyp in DMF using AcONa as base at 130 °C (Scheme 1). The results presented in Table 1 disclose a low influence of the substituents on the aryl bromide on the selectivity of the reaction. Using these conditions, the major isomer was (*E*)-5-arylpent-4-enoates **1a**–**16a**, but the formation of the branched isomers 4-arylpent-4-enoates **1b**–**16b** and of other isomers was also observed as minor products.

The reaction with electron-deficient aryl bromides such as 4-bromoacetophenone, 4-bromobenzaldehyde or 4-bromobenzonitrile can be performed with as little as 0.01 mol% catalyst. In all cases, the (*E*)-5-arylpent-4-enoates **1a**–**7a** were obtained in 85–89% selectivity (Table 1, entries 1–14). As expected, lower turnover numbers (TONs) of 46–540 were obtained with electron-excessive aryl bromides such as 4-bromoanisole or 4-*N*,*N*-dimethylaminobromobenzene. However, the products **9a**–**11a** were obtained in high selectivities of 84–88% (Table 1, entries 19–23). We also compared the selectivity and reactivity of this reaction using bromobenzene and iodobenzene. With both substrates the isomer **8a** was obtained using 0.1–0.01 mol% catalyst, but the selectivity was slightly higher using bromobenzene: 89 instead of 80% (Table 1, entries 15–18). The *ortho*-substituted aryl bromide 2-bromotoluene also gave isomer **a** in high selectivity (90–92%). With this sterically congested aryl bromide, a lower amount of the branched isomer **b** was formed, probably for steric reasons (Table 1, entries 28 and 29). Then, we studied the reactivity of a few heteroaryl bromides with ethyl pent-4-enoate. Pyridines and quinolines are π-electron-excessive heterocycles. Using 3-bromopyridine or 3-bromoquinoline, isomers **15a** and **16a** were obtained in 85–88% selectivity and in 880 and 3700 TONs, respectively (Table 1, entries 30–33).

3.2. Heck vinylation with ethyl 2-methylpent-4-enoate

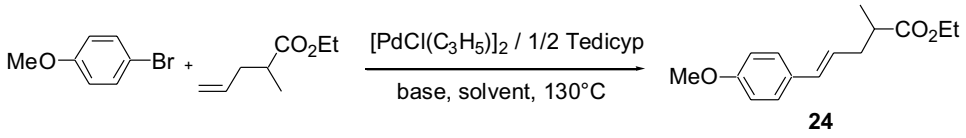
Then, we examined the reactivity of ethyl 2-methylpentenoate (Schemes 2 and 3, Tables 2 and 3). This branched ester is slightly more congested than ethyl pent-4-enoate. Surprisingly, we observed that using similar reaction conditions for the coupling with 4-bromoanisole than with ethyl pent-4-enoate: DMF associated with AcONa, a low conversion was obtained. After screening of several bases and solvents we found that using DMAc as solvent and $NaHCO_3$ as base, in the presence of 1 mol% catalyst, the expected (*E*)-5-(4-methoxyphenyl)-2-methyl-pent-4-enoate **24** was obtained in 100% conversion (Table 2, entry 9). It should be noted that with this relatively hindered alkene, the formation of the branched isomer and the migration of the carbon–carbon double bond of the alkene was not observed. In the presence of bases such as NEt_3, KF or in xylene or NMP, no formation of product **24** was detected.

Table 2
Palladium-catalysed Heck reactions with ethyl 2-methylpent-4-enoate and 4-bromoanisole (Scheme 2)

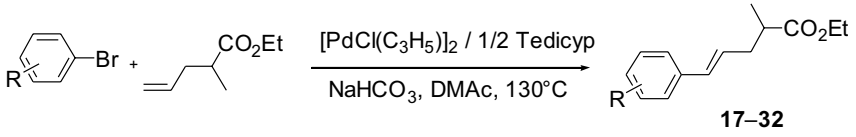
Entry	Base	Solvent	Yield of **24** (%)
1	K_2CO_3	DMF	0
2	$NaHCO_3$	DMF	42
3	AcONa	DMF	25
4	NEt_3	DMF	0
5	KF	DMF	0
6	$NaHCO_3$	Xylene	0
7	$NaHCO_3$	NMP	0
8	K_2CO_3	DMAc	73
9	$NaHCO_3$	DMAc	100
10	AcONa	DMAc	80
11	NEt_3	DMAc	0
12	KF	DMAc	0

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/Tedicyp 1/2 (0.01 eq.), 4-bromoanisole (1 eq.), ethyl 2-methylpent-4-enoate (2 eq.), base (2 eq.), 130 °C, 20 h, GC yields.

Then, we explored the scope and limitations of the vinylation with ethyl 2-methylpentenoate using a variety of aryl bromides under these reaction conditions (Scheme 3, Table 3). The electron-poor aryl bromides, such as 4-bromoacetophenone, 4-bromobenzonitrile or 4-bromonitrobenzene were selectively converted to the corresponding (*E*)-5-aryl-2-methylpent-4-enoates **17**–**22** in very high TONs of 10 000–95 000 (Table 3, entries 1–10). Again, the electron-rich 4-bromotoluene and 4-bromoanisole were found to be less reactive, but the products were still obtained in good yields using 0.4–0.1 mol% catalyst (Table 3, entries 11–14). These results seem to indicate that with this catalyst, the oxidative addition of the aryl bromide to the palladium centre is probably the rate-limiting step of the catalytic cycle. Using *ortho*-substituted aryl bromides, we could expect to observe some migration of the alkene carbon–carbon double bond for steric reasons. However, using 2-bromobenzonitrile, 2-bromotoluene, 1-bromonaphthalene or 2-bromoanisole, products **25**–**28** were also obtained selectively. Finally, the reactivity of four electron-poor heteroaryl bromides was examined. 3-Bromopyridine and 3-



Scheme 2.



Scheme 3.

Table 3
Palladium-catalysed Heck reactions with ethyl 2-methylpent-4-enoate (Scheme 3)

Entry	Aryl bromide	Ratio of substrate/catalyst	Products	Yield (%)
1	4-Bromoacetophenone	10000	**17**	100 (94)
2	4-Bromoacetophenone	100000	**17**	62
3	4-Bromobenzaldehyde	10000	**18**	100
4	4-Bromobenzaldehyde	100000	**18**	95 (91)
5	4-Bromobenzophenone	10000	**19**	92 (88)
6	4-Bromobenzonitrile	10000	**20**	100 (91)
7	4-Bromobenzonitrile	100000	**20**	65
8	4-Bromonitrobenzene	10000	**21**	100 (87)
9	4-Fluorobromobenzene	10000	**22**	100 (93)
10	4-Fluorobromobenzene	100000	**22**	32
11	4-Bromotoluene	250	**23**	100 (95)
12	4-Bromotoluene	1000	**23**	91
13	4-Bromoanisole	250	**24**	100 (90)
14	4-Bromoanisole	1000	**24**	79
15	2-Bromobenzonitrile	100	**25**	100 (89)
16	2-Bromobenzonitrile	250	**25**	23
17	2-Bromotoluene	100	**26**	100 (94)
18	2-Bromotoluene	250	**26**	64
19	1-Bromonaphthalene	1000	**27**	100 (94)
20	1-Bromonaphthalene	10000	**27**	82
21	2-Bromoanisole	100	**28**	100 (93)
22	2-Bromoanisole	250	**28**	52
23	3-Bromopyridine	10000	**29**	100 (90)
24	3-Bromopyridine	100000	**29**	32
25	4-Bromopyridine	1000	**30**	100 (90)
26	4-Bromopyridine	10000	**30**	82
27	3-Bromoquinoline	10000	**31**	100 (94)
28	3-Bromoquinoline	100000	**31**	81
29	4-Bromoisoquinoline	1000	**32**	100 (92)
30	4-Bromoisoquinoline	10000	**32**	52

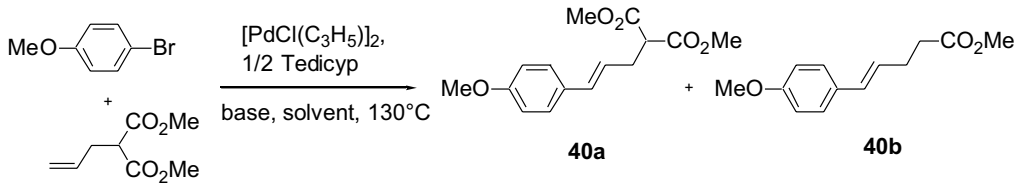
Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/Tedicyp 1/2, aryl bromide (1 eq.), ethyl 2-methylpent-4-enoate (2 eq.), $NaHCO_3$ (2 eq.), DMAc, 130 °C, 20 h, GC yields, yields in parenthesis are isolated.

bromoquinoline gave **29** and **31** in good yields using as low as 0.01–0.001 mol% catalyst (Table 3, entries 23, 24, 27 and 28). Slightly slower reactions were observed using 4-bromopyridine or 4-bromoquinoline and 0.1–0.01 mol% catalyst had to be used in order to obtain high yields of products **30** and **32** (Table 3, entries 25, 26, 29 and 30).

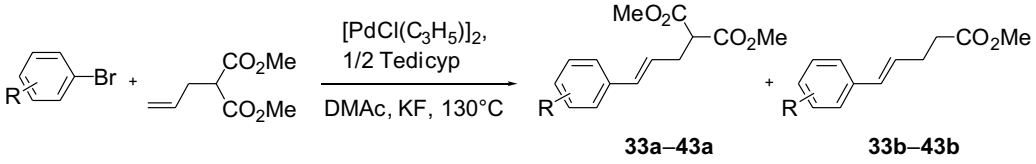
3.3. Heck vinylation with dimethyl allylmalonate

We also examined the reaction between dimethyl allylmalonate and aryl bromides (Schemes 4 and 5, Tables 4 and 5). 2-(3-Arylallyl)-malonates are quite unstable compounds under basic conditions. They can decarboxylate to give the 5-aryl-pent-4-enoates [16]. First, we explored several reaction conditions for the vinylation of 4-bromoanisole with allylmalonate. As expected the base has a large influence on the decarboxylation side-reaction. Relatively strong bases such as AcONa or K_2CO_3 gave large amounts of decarboxylated product **40b** (Table 4, entries 1, 3, 8 and 10). On the other hand, $NaHCO_3$ and especially KF, which are less basic, led to 70–100% of (*E*)-2-[3-(4-methoxyphenyl)-allyl]-malonic acid dimethyl ester**40a** (Table 4, entries 2, 5, 9 and 12). The solvent has also an influence on the yield and selectivity. Solvents such as xylene or NMP gave no product, and DMAc was found to give a higher selectivity in **40a** than DMF. Therefore, for the coupling of dimethyl allylmalonate with aryl bromides, DMAc was chosen as the solvent and potassium fluoride as the base.

Then, we tried to determine the scope and limitations of the reaction of aryl bromides with dimethylallylmalonate (Scheme 5, Table 5). Quite similar TONs of 2000–8200 were observed for the reaction of electron-deficient aryl bromides such as 4-bromobenzophenone, 4-trifluorobromobenzene, 4-bromobenzonitrile or methyl 4-bromobenzoate with allylmalonate (Table 5, entries 1–13). The (*E*)-2-(3-arylallyl)-malonates **33a**–**38a** were obtained in 78–95% selectivity. However, in all cases, the formation of the decarboxylated (*E*)-5-aryl-pent-4-enoates was also observed as minor products. Lower TONs, but higher



Scheme 4.



Scheme 5.

selectivities in favour of the formation of products **39a** and **40a** were obtained with electron-rich aryl bromides such as 4-bromotoluene or 4-bromoanisole, indicating that for this reaction also, the oxidative addition of the aryl bromide to palladium is probably the rate-limiting step of the reaction (Table 5, entries 14–17). Finally, we examined this reaction using the sterically congested aryl bromides: 2-bromobenzonitrile, 2-bromotoluene and 1-bromonaphthalene (Table 5, entries 18–23). Surprisingly, with these three substrates a very important decarboxylation was observed. Using 2-bromobenzonitrile or 2-bromotoluene, only 5–9% of **41a** and **42a** were obtained, and **41b** and **42b** were the major products of these reactions.

We have also investigated the Heck vinylation of aryl bromides with *n*-butyl but-3-enoate (Scheme 6). For this reaction disappointing results were obtained due to the fast migration of the carbon–carbon double bond of the alkene during the catalytic reaction to form *n*-butyl crotonate [17]. Therefore, this Heck reaction gave the corresponding 3-aryl-but-2-enoic acid *n*-butyl esters as the major product (Scheme 6). Several reaction conditions have been employed in order to reduce this isomerisation. However, in DMF, DMAc or NMP using AcONa or $NaHCO_3$ as bases, the formation of 87–91% of *n*-butyl crotonate was observed after 2 h. A few aryl bromides such as 4-bromoanisole, 4-bromobenzonitrile or 4-bromoacetophenone

Table 4
Palladium-catalysed Heck reactions with dimethylallylmalonate and 4-bromoanisole (Scheme 4)

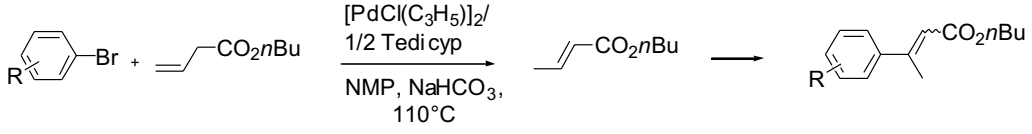
Entry	Base	Solvent	Ratio of **40a/40b**	Yield (%)
1	K_2CO_3	DMF	42/58	100
2	$NaHCO_3$	DMF	70/30	100
3	AcONa	DMF	25/75	100
4	NEt_3	DMF	–	0
5	KF	DMF	92/8	100
6	$NaHCO_3$	Xylene	–	0
7	$NaHCO_3$	NMP	–	0
8	K_2CO_3	DMAc	52/48	100
9	$NaHCO_3$	DMAc	75/25	100
10	AcONa	DMAc	32/68	100
11	NEt_3	DMAc	–	0
12	KF	DMAc	100/0	100

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/Tedicyp 1/2 (0.01 eq.), 4-bromoanisole (1 eq.), dimethyl allylmalonate (2 eq.), base (2 eq.), 130 °C, 20 h. Ratio of **40a/40b** determined by GC and NMR, GC yields of the mixture of isomers **40a/40b**.

Table 5
Palladium-catalysed Heck reactions with dimethylallylmalonate using various aryl bromides (Scheme 5)

Entry	Aryl bromide	Ratio of substrate/catalyst	Products	Ratio of **a/b**	Yield (%)
1	4-Bromoacetophenone	100	**33a**, **33b**	95/5	100
2	4-Bromoacetophenone	1000	**33a**, **33b**	82/18	100 (76)
3	4-Bromoacetophenone	10000	**33a**, **33b**	78/22	65
4	4-Bromobenzaldehyde	1000	**34a**, **34b**	78/22	100 (72)
5	4-Bromobenzaldehyde	10000	**34a**, **34b**	81/19	44
6	4-Bromobenzophenone	1000	**35a**, **35b**	87/13	100 (81)
7	4-Bromobenzophenone	10000	**35a**, **35b**	85/15	20
8	4-Trifluoromethylbromobenzene	1000	**36a**, **36b**	87/13	100 (80)
9	4-Trifluoromethylbromobenzene	10000	**36a**, **36b**	86/14	72
10	4-Bromobenzonitrile	1000	**37a**, **37b**	93/7	100 (85)
11	4-Bromobenzonitrile	10000	**37a**, **37b**	86/14	82
12	Methyl 4-bromobenzoate	1000	**38a**, **38b**	93/7	100 (87)
13	Methyl 4-bromobenzoate	10000	**38a**, **38b**	91/9	32
14	4-Bromotoluene	100	**39a**, **39b**	97/3	100 (91)
15	4-Bromotoluene	250	**39a**, **39b**	91/9	48
16	4-Bromoanisole	100	**40a**, **40b**	100/0	100 (92)
17	4-Bromoanisole	250	**40a**, **40b**	100/0	56
18	2-Bromobenzonitrile	100	**41a**, **41b**	7/93	100 (85)
19	2-Bromobenzonitrile	250	**41a**, **41b**	5/95	42
20	2-Bromotoluene	100	**42a**, **42b**	5/95	100 (87)
21	2-Bromotoluene	250	**42a**, **42b**	9/91	22
22	1-Bromonaphthalene	100	**43a**, **43b**	79/21	100 (62)
23	1-Bromonaphthalene	250	**43a**, **43b**	54/46	70

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/Tedicyp 1/2, aryl bromide (1 eq.), dimethyl allylmalonate (2 eq.), KF (2 eq.), DMAc, 130 °C, 20 h, GC yields of the mixture of isomers, yields in parenthesis are isolated yields of products **33a**–**40a**, **41b**, **42b** or **43a**.



Scheme 6.

have been tested using 1 mol% catalyst at 100 °C in NMP using $NaHCO_3$ as base, but in all cases, mixtures of isomers were obtained and the major products was the 3-aryl-but-2-enoates. Due to the high price of *n*-butyl but-3-enoate compare to *n*-butyl crotonate this reaction is not really useful. Therefore, we did not explored this coupling with other aryl bromides.

4. Conclusion

The Heck reaction using but-3-enoate, pen-4-entoates or allylmalonate is less straightforward than in the presence of alkenes such as acrylate or styrene. With these substrates, the migration of the carbon–carbon double bond might occur and the formation of side-products from decarboxylation can be observed. Using *n*-butyl but-3-enoate the fast isomerisation into butyl crotonate led to 3-arylbut-2-enoate instead of 4-arylbut-3-enoate, therefore this reaction is economically not attractive. With ethyl pent-4-enoate, more satisfactory results were obtained, and the (*E*)-5-aryl-pent-4-enoates were obtained in 80–92% selectivity together with the branched isomer and a few side products arising from the migration of the carbon–carbon double bond. With the sterically more hindered ethyl 2-methyl-pent-4-enoate, even more selective reactions were obtained. Using this substrate the (*E*)-5-aryl-2-methylpent-4-enoates were obtained selectivity in all cases. For steric reasons, the formation of the branched isomer was not observed. Finally, dimethyl allylmalonate was reacted successfully with several aryl bromides to give the (*E*)-2-(3-arylallyl)-malonates in 78–95% selectivity. The formation of (*E*)-5-aryl-pent-4-enoates due to decarboxylation was also observed as side-products, especially when using sterically congested aryl bromides or relatively strong bases. It should be noted that with the Pd/Tedicyp system, most of these reactions could be performed using low catalyst loadings. With the most reactive aryl bromides and pent-4-enoates, substrates/catalyst ratios up to 100 000 have been used; and in general 0.1 mol% of catalyst led to high yield of product. A wide range of functions such as methyl, methoxy, fluoro, trifluoromethyl, acetyl, formyl, benzoyl, carboxylate, nitro, nitrile or dimethylamino on the aryl bromide are tolerated. To date, no other ligands have achieved this objective with such substrates. Moreover, most of the other ligands were used with the more reactive, but more expensive aryl iodides and at high catalyst loadings. These results represent economically attractive procedures and due to the high price of palladium, the practical advantage of such low catalyst loading reactions can become increasingly important for industrial processes.

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