The Heck Reaction of Allylic Alcohols Catalysed by an Air-Stable Phosphinito Complex of Palladium(II)

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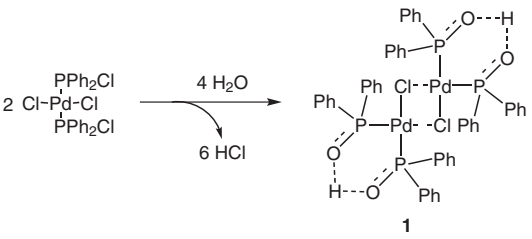
Abstract: The Heck coupling of aryl bromides with primary and secondary allylic alcohols, performed in the presence of an air-stable phosphinito complex of palladium(II), produced the corresponding carbonyl compounds. Reactions with tertiary allylic alcohols under the same conditions generated the aromatic conjugated alcohols.

Key words: allylic alcohols, Heck reaction, palladium, aldehydes, ketones

Transition-metal-mediated reactions allow transformations of organic substrates that are difficult to achieve via transition-metal-free procedures.[1] The importance of these reactions has stimulated the creativity of chemists to design new catalytic systems and ligands. Recently, as part of our research on the Heck reaction,[2] we have demonstrated the utility of the phosphinito complex **1** of palladium(II)[3] (Scheme 1) in the formation of C–C bonds.[4] This type of palladium compound has not been thoroughly explored in homogeneous catalysis despite its high air and water stability. These properties, however, have recently attracted interest in the phosphinito complexes because of their potential as catalysts in homogeneous reactions. Similar transition-metal compounds containing hydrogen-bonded P–O–H–O–P ligands have been synthesised, including complexes of palladium,[5] platinum,[6] molybdenum,[7] iridium[8] and ruthenium.[9] The stability of these ligand pairs is an interesting result of the additional hydrogen bonding. This proton can be substituted by other Lewis acids to furnish a complex with 'hard' and 'soft' centres. Additionally, the same proton is easily removed by titration with a base.[10] The term 'diphenylphosphinito' was introduced by Roundhill[11] to differentiate this type of compound from diphenylphosphinate ($Ph_2PO_2^-$). The application of these phosphinito ligands in catalysis has been limited to the platinum phosphinito complex [PtCl(PR_2OH){($PR_2O)_2H$}] (R = Me, Ph), which hydrolyses nitriles to amides[12] and catalyses the hydration of cyanohydrins to obtain a-hydroxy amides.[13] Tanaka and co-workers have demonstrated that similar complexes of platinum and palladium are useful in the hydrophosphinylation of alkynes.[14] Recently, Trzeciak and co-workers[15] reported the use of a palladium phosphinito complex in the methoxycarbonylation of iodobenzene and the Heck cross-coupling of bromobenzene with butyl acrylate. Based on this interesting background, we aimed to synthesise aldehydes and ketones by means of the Heck reaction of allylic alcohols using the phosphinito complex **1** of palladium(II).

The palladium-catalysed reaction of allylic alcohols with aryl halides is one of the most powerful methods for the formation of C–C bonds in the synthesis of saturated[16] and a,b-unsaturated[17] aldehydes and ketones, and in the synthesis of allylic alcohols,[18] which represent an attractive building block in organic synthesis.[19] One of the drawbacks of using the Heck reaction of allylic alcohols to obtain aldehydes and ketones is the formation of a reaction mixture[17] with both saturated and unsaturated carbonyl compounds as principal products, which must be controlled to exclusively obtain the saturated[16] or unsaturated product.[20] In this context, we now disclose that the phosphinito complex **1** of palladium(II) can be used in the b-arylation of allylic alcohols with highly regioselective results, without recourse to strict anhydrous reaction conditions.



Scheme 1 Phosphinito complex of palladium(II)

A simple hydrolysis reaction of a chlorodiphenylphosphine complex of palladium made it possible to obtain a binuclear chloride-bridged organopalladium(II) complex (Scheme 1). It is noteworthy that, in our hands, the complex has been stable for two years, stored at room temperature and without any special conditions. ^{31}P NMR spectroscopy showed that the complex was stable in the presence of water or methanol for 5 and 10 hours, respectively. Considering these previous observations, we initially decided to explore the reaction of 4-bromobenzophenone (**2**) with 1-phenyl-2-propen-1-ol (**3**) in *N*,*N*-dimethylformamide at different temperatures, as a simple model to find the best conditions for the reaction. When the reaction was performed at room temperature, the ketone **4** was not observed (Table 1, entry 1); howev-

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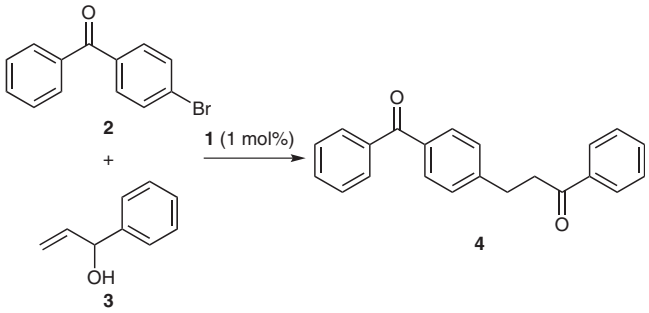
Table 1 Heck Coupling of Aryl Bromide **2** with Allylic Alcohol **3** in the Presence of Complex **1**[a]



Entry	Solvent	Temp (°C)	Time (h)	Yield[b] (%)
1	DMF	r.t.	18	0
2	DMF	50	18	74
3	DMF	90	18	91
4	DMF	90	6	92
5	DMF	90	2	53
6	toluene	90	18	31
7	DMSO	140	18	27
8	THF	reflux	18	0

[a] Reaction conditions: **2** (1 mmol), **3** (1 mmol), NaOAc (1.2 mmol), catalyst **1** (1 mol%).
[b] Yield of isolated product after chromatographic purification.

er, **4** was obtained in a 74% yield when the reaction was performed at 50 °C (Table 1, entry 2). The yield increased to 91% when the reaction mixture was heated to 90 °C for 18 hours (Table 1, entry 3). The yield remained similar after only 6 hours (92%; Table 1, entry 4); however, a shorter reaction time affected the yield of the reaction: only 53% of **4** was observed after 2 hours (Table 1, entry 5). Next, we explored the reaction with other solvents commonly used for the Heck reaction. When the reaction was performed in toluene at 90 °C, ketone **4** was obtained in a 31% yield (Table 1, entry 6). The yield decreased to 27% when dimethyl sulfoxide was used (Table 1, entry 7), and the worst result was obtained when the reaction was performed in tetrahydrofuran under reflux (Table 1, entry 8). Santelli and co-workers have demonstrated the importance of *N*,*N*-dimethylformamide in similar reactions.[16c]

To examine the scope of the reaction, we performed experiments with the aryl bromides **2** and **7** and the primary allylic alcohol **9** under the optimised reaction conditions, which produced good yields of the corresponding aldehydes **13** and **23** (Table 2, entries 1 and 10). Next, the reaction was performed with the aryl bromides **5** to **8** and the secondary allylic alcohols **3**, **11** and **12** to obtain the corresponding ketones **16** to **19**, **22**, and **24** to **26** (Table 2, entries 3–6, 9, and 11–13). In the case of fluorene **7** as starting material, the products were the corresponding fluorenones. Those reactions were carried out in the presence and absence of oxygen, and in both cases the fluorenones were obtained (Table 2, entries 9–11).

Table 2 Scope of the Palladium-Catalysed Allylic Alcohol Heck Reaction[a]

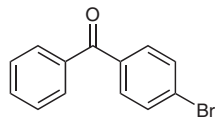
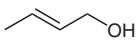
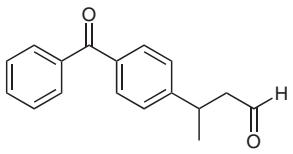
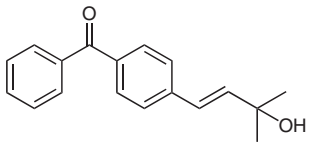
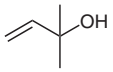
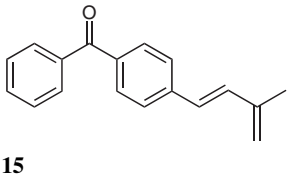
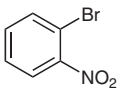
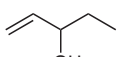
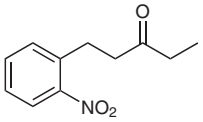
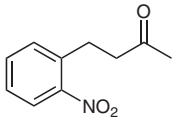
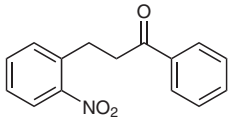
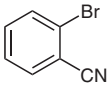
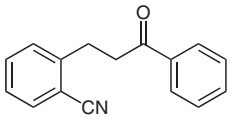
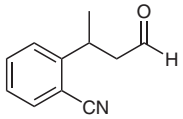
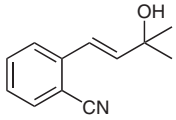
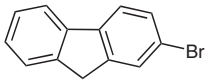
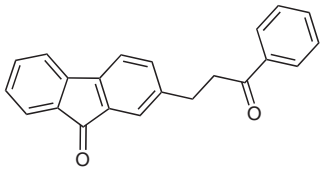
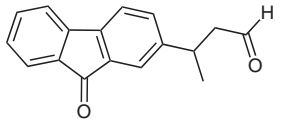
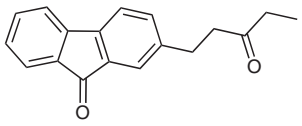
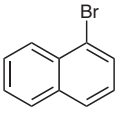
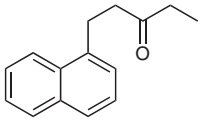
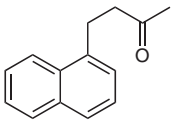
Entry	Aryl bromide	Alcohol	Product	Yield[b] (%)
1	 **2**	 **9**	 **13**	85
			 **14**	
2	**2**	 **10**	 **15**	89 94[c]
3	 **5**	 **11**	 **16**	91

Table 2 Scope of the Palladium-Catalysed Allylic Alcohol Heck Reaction[a] (continued)

Entry	Aryl bromide	Alcohol	Product	Yield[b] (%)
4	**5**	 **12**	 **17**	91
5	**5**	**3**	 **18**	79
6	 **6**	**3**	 **19**	57
7	**6**	**9**	 **20**	68
8	**6**	**10**	 **21**	80
9	 **7**	**3**	 **22**	80
10	**7**	**9**	 **23**	70
11	**7**	**11**	 **24**	85
12	 **8**	**11**	 **25**	72
13	**8**	**12**	 **26**	61

[a] Reaction conditions: aryl bromide (1 mmol), allylic alcohol (1.1 mmol), NaOAc (1.2 mmol), catalyst **1** (1 mol%), DMF, 90 °C, 6 h.
[b] Yield of isolated product after chromatographic purification.
[c] The reaction was performed under microwave conditions: aryl bromide (1 mmol), allylic alcohol (1.1 mmol), NaOAc (1.2 mmol), catalyst **1** (1 mol%), DMF, 200 °C, 20 min.

Based on these results, we tried to extend the methodology to the tertiary allylic alcohol **10**. Thus, we conducted the b-arylation reaction of alcohol **10** with aryl bromide **2**, focusing on the possible formation of elimination products. As shown in Table 2 (entry 2), the allylic alcohol **14** was exclusively obtained in excellent yield. Despite the basicity of the reaction medium, no elimination products (dienes) were observed; however, when the reaction of alcohol **10** was carried out under microwave conditions, the diene **15** was formed as the only product. This observation allowed our group to glimpse the possibility of obtaining 1-aryl-1,3-dienes, which is currently under investigation. Finally, we attempted the reaction with electron-rich aryl bromides; unfortunately, formation of the desired products was not observed.

Following these results, we tried to extend this methodology to other aromatic systems. First, this study focused on the reaction of 3-bromopyridine with allylic alcohols. The alkylation approach for the synthesis of 3-alkylpyridines can be classified into three categories: alkylation of 3-pyridyllithium,[21] alkylation via nicotinic acid[22] and palladium-catalysed alkylation.[23] In this context, and with the purpose of preparing useful building blocks for employment in the synthesis of alkaloids, 3-bromopyridine (**27**) was alkylated with the allylic alcohol **3** under the same reaction conditions used for aryl bromide **2**. Surprisingly, when the reaction was performed in *N*,*N*-dimethylformamide at 90 °C, only the starting material was recovered. To our delight, however, the carbonyl compound **32** was obtained in good yield (78%) under microwave conditions (Table 3, entry 1). The reaction performed with the tertiary allylic alcohol **10** provided compound **33** as the only product, in a similar yield and with high regioselectivity (Table 3, entry 2). Next, the reaction was performed with 3,5-dibromopyridine (**28**) and 2-methyl-3-buten-2-ol (**10**; 2.2 equiv), which produced compound **34** in 84% yield (Table 3, entry 3). Similar results were obtained when 3-bromoquinoline (**29**) and 4-bromoisoquinoline (**30**) were subjected to the alkylation conditions (Table 3, entries 4–9). To test the extension of the palladium-catalysed reaction to other heterocyclic aromatics, we also investigated the reaction of allylic alcohols **3** and **9** to **12** with 5-bromo-2-furaldehyde (**31**) which gave compounds **41** to **45** in good yields (Table 3, entries 10–14). Oxidation products of aldehydes were not observed in ^{1}H NMR analysis of the crude reaction mixtures of these examples, and it was generally possible to obtain an extremely clean reaction. Finally, we attempted the alkylation of 2-iodothiophene, which represents an interesting template for building more complex molecules. Unfortunately, when the reaction was performed under standard conditions with 1-phenyl-2-propen-1-ol (**3**) in *N*,*N*-dimethylformamide, the desired product was not formed.

Table 3 Heck Reaction of Heteroaryl Bromides with Allylic Alcohols[a]

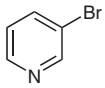
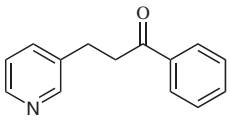
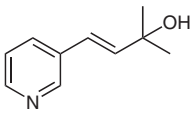
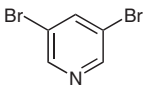
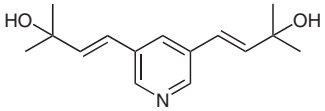
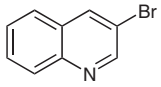
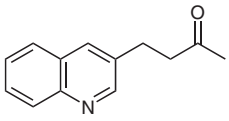
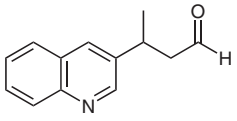
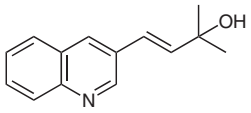
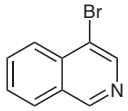
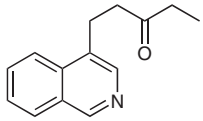
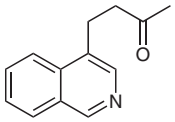
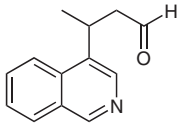
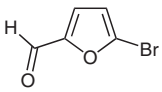
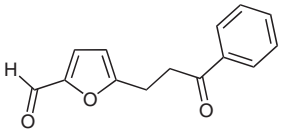
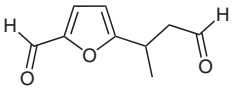
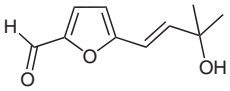
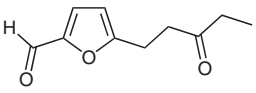
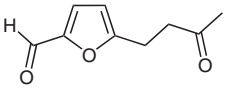
Entry	Aryl bromide	Alcohol	Product	Yield[b] (%)
1	 **27**	**3**	 **32**	78[c]
2	**27**	**10**	 **33**	88
3	 **28**	**10**	 **34**	84[d]
4	 **29**	**12**	 **35**	77
5	**29**	**9**	 **36**	88

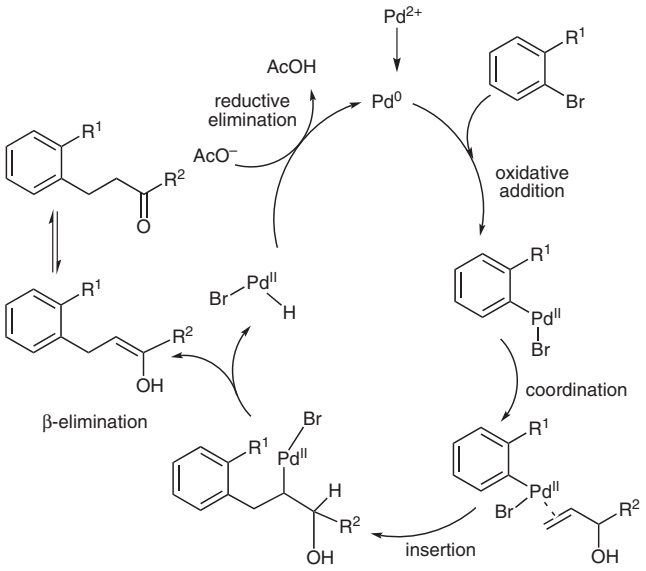
Table 3 Heck Reaction of Heteroaryl Bromides with Allylic Alcohols[a] (continued)

Entry	Aryl bromide	Alcohol	Product	Yield[b] (%)
6	**29**	**10**	 **37**	92
7	 **30**	**11**	 **38**	87
8	**30**	**12**	 **39**	84
9	**30**	**9**	 **40**	91
10	 **31**	**3**	 **41**	91
11	**31**	**9**	 **42**	89
12	**31**	**10**	 **43**	88
13	**31**	**11**	 **44**	83
14	**31**	**12**	 **45**	80

[a] Reaction conditions: aryl bromide (1 mmol), allylic alcohol (1.1 mmol), NaOAc (1.2 mmol), catalyst **1** (1 mol%), DMF, 90 °C, 6 h.
[b] Yield of isolated product after chromatographic purification.
[c] The reaction was performed under microwave conditions: aryl bromide (1 mmol), allylic alcohol (1.1 mmol), NaOAc (1.2 mmol), catalyst **1** (1 mol%), DMF, 200 °C, 20 min.
[d] The reaction was carried out with 2.2 mmol of **10**.

A plausible reaction mechanism for how the phosphinito complex **1** of palladium(II), as catalytic precursor, catalyses the alkylation of aryl halides is shown in Scheme 2. The first step involves the oxidative addition of aryl halides, followed by regioselective alkene insertion and Pd–H b-elimination involving the carbinol hydrogen, which furnishes the desired carbonyl compound. Norrby and coworkers have demonstrated, by deuterium labelling, that the carbinol hydrogen can undergo elimination.[24] The reaction conditions were modified in an attempt to obtain the thermodynamically favoured a,b-unsaturated carbonyl compounds. Thus, the reaction of aryl bromide **2** and allylic alcohol **3** was performed in the presence of oxygen with the goal of promoting a second insertion of palladi-

um;[20] however, the formation of the a,b-unsaturated ketone was not observed. Additionally, cinnamyl alcohol was treated with the phosphinito complex **1** of palladium(II) in *N*,*N*-dimethylformamide at 80 °C for 24 hours to confirm that the carbonyl compounds obtained in the present protocol were not products of a Pd–H elimination–readdition process. Thus, the reaction was performed in an NMR tube and monitored for 6 hours. The ^{1}H NMR spectrum of the reaction mixture showed only the presence of the (*E*)-cinnamyl alcohol (67%), cinnamaldehyde (24%), 3-phenyl-1-propanol (6%) and (*Z*)-cinnamyl alcohol (2%); however, 3-phenylpropanal was not observed. Based on these observations, it is reasonable to explain our results by the reaction mechanism depicted in Scheme 2. It is noteworthy that Santelli has proposed that the interaction of the alcohol function with the palladium centre plays an important role in olefin migration.[16c] In our case, there is no evidence of a similar interaction.



Scheme 2 Proposed reaction mechanism

In conclusion, we have demonstrated that it is possible to use an air-stable phosphinito complex of palladium(II) to perform the alkylation of aromatic systems. Because complex **1** does not need to be used under anhydrous conditions, this compound can be readily utilised for the synthesis of attractive building blocks. The procedure provides efficient access to functionalised aldehydes, ketones and aromatic allylic alcohols with full regioselectivity, which can provide avenues for the preparation of molecule libraries. Additionally, the proposed method has applications in the preparation of biologically valuable substances.

All the chemicals were purchased from Aldrich Chemical Co. and were used without further purification unless stated otherwise. Yields refer to the chromatographically and spectroscopically (^{1}H and ^{13}C NMR) homogeneous materials, unless otherwise stated. All glassware utilized was flame-dried before use. Reactions were monitored by TLC carried out on 0.25-mm Macherey Nagel silica gel plates. Developed TLC plates were visualized under a short-wave UV lamp and by heating plates that were dipped in $Ce(SO_4)_2$. Flash column chromatography (FCC) was performed using flash silica gel (230–400 mesh) and employed a solvent polarity correlated with TLC mobility. Microwave reactions were performed in an Anton Paar Monowave 300 in sealed reaction vessels. NMR experiments were conducted on Bruker Avance 400 MHz, Bruker Avance 300 MHz and Varian Genimi 200 MHz instruments using $CDCl_3$ (99.9% D) as the solvent, with chemical shifts (δ) referenced to internal standards $CDCl_3$ (7.26 ppm for ^{1}H, 77.0 ppm for ^{13}C) or Me_4Si as an internal reference (0.00 ppm). Chemical shifts are in parts per million (ppm). Mass spectra were recorded on a Jeol JS102 high-resolution mass spectrometer.

Palladium(II) Complex 1

A soln of Ph_2PCl (0.75 mL, 4.05 mmol) in THF (5 mL) was added dropwise whilst stirring to a soln of $[PdCl_2(C_6H_5CN)_2]$ (0.76 g, 2.0 mmol) in THF (10 mL) placed in a Schlenk flask at r.t. When the complete formation of the dichlorophosphane complex was confirmed by ^{31}P NMR spectroscopy (d = 87 ppm), H_2O (0.5 mL) was added to the reaction mixture, which was stirred at r.t. After 48 h, the ^{31}P NMR analysis of an aliquot exclusively showed the signal of complex **1** at 78.6 ppm. After this time, the solvent was removed under reduced pressure. A yellow crystalline powder was obtained; yield: 92%; mp 113–116 °C.

IR: 3441 (m, O–H–O), 1479 (w), 1435 (Ph), 1023 cm^{-1} (m, P–O).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.7–7.2 (Ph).

^{31}P NMR (121.4 MHz, $CDCl_3$): δ = 78.6.

General Procedure for the Catalytic Reactions

In all Heck reactions, a soln of aryl bromide (1 mmol), allylic alcohol (1.1 mmol), NaOAc (1.2 mmol) and catalyst **1** (1 mol%) in DMF (3 mL) was heated for 6 h, in a 90 °C silicon oil bath, using a condenser system. Then, the mixture was cooled to r.t., diluted with EtOAc (15 mL), washed with brine (3 × 10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (25 × 2.5 cm, EtOAc–hexane gradient).

3-(4-Benzoylphenyl)-1-phenyl-1-propanone (4)
[CAS Reg. No. 1093625-76]

Following the general procedure, the reaction was carried out starting from 4-bromobenzophenone (**2**; 261 mg, 1 mmol), 1-phenyl-2-propen-1-ol (**3**; 147 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **4**; yield: 287 mg (92%).

IR: 1670 (C=O), 1647 cm^{-1} (C=O).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.10–7.30 (m, 14 H), 3.36 (t, *J* = 7.0 Hz, 2 H), 3.16 (t, *J* = 7.0 Hz, 2 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 198.6, 196.3, 146.3, 137.6, 136.5, 135.4, 133.1, 132.2, 130.4, 129.8, 128.5, 128.3, 128.1, 127.9, 39.7, 29.9.

MS (EI): *m*/*z* (%) = 105 (88), 77 (37), 58 (34), 43 (100), 28 (85).

HRMS–FAB: *m*/*z* calcd for $C_{22}H_{18}O_2$: 314.1307; found: 314.1301.

3-(4-Benzoylphenyl)butanal (13)

Following the general procedure, the reaction was carried out starting from 4-bromobenzophenone (**2**; 261 mg, 1 mmol), crotyl alcohol (**9**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **13**; yield: 214 mg (85%).

IR: 1708 (C=O), 1672 cm^{-1} (C=O).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.74 (t, *J* = 1.7 Hz, 1 H), 7.80 (m, 4 H), 7.58 (t, *J* = 8.0 Hz, 1 H), 7.42 (t, *J* = 8.0 Hz, 2 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 3.43 (sextet, *J* = 7.0 Hz, 1 H), 2.82 (ddd, *J* = 1.6, 6.8, 17 Hz, 1 H), 2.73 (ddd, *J* = 1.9, 7.5, 17 Hz, 1 H), 1.35 (d, *J* = 7 Hz, 3 H).

^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 201.0, 196.3, 150.4, 137.6, 135.9, 132.3, 130.5, 129.9, 128.2, 126.7, 51.3, 34.1, 21.9.

MS (EI): *m*/*z* (%) = 252 (48), 209 (82), 191 (49), 105 (100), 77 (51).

HRMS–FAB: *m*/*z* calcd for $C_{17}H_{16}O_2$: 252.1150; found: 252.1144.

{4-[(*E*)-3-Hydroxy-3-methyl-1-butenyl]phenyl}(phenyl)methanone (14)
[CAS Reg. No. 943897-30-1]

Following the general procedure, the reaction was carried out starting from 4-bromobenzophenone (**2**; 261 mg, 1 mmol), 2-methyl-3-buten-2-ol (**10**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **14**; yield: 237 mg (89%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (m, 4 H), 7.60 (t, *J* = 8.0 Hz, 1 H), 7.50 (m, 4 H), 6.67 (d, *J* = 16.0 Hz, 1 H), 6.49 (d, *J* = 16.0 Hz, 1 H), 1.61 (s, 1 H, OH), 1.45 (s, 6 H).

^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 196.2, 141.2, 140.3, 137.8, 136.3, 132.3, 130.6, 129.9, 128.3, 126.2, 125.6, 71.1, 29.9.

HRMS–FAB: *m*/*z* calcd for $C_{18}H_{18}O_2$: 266.1307; found: 266.1298.

{4-[(*E*)-3-Methyl-1,3-butadienyl]phenyl}(phenyl)methanone (15)
A mixture of 4-bromobenzophenone (**2**; 261 mg, 1 mmol), 2-methylbut-3-en-2-ol (**10**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%) in DMF (3 mL) was reacted in an Anton Paar Monowave 300 in a sealed reaction vessel at 200 °C and 27 bar for 20 min. Then, the mixture was cooled to r.t., diluted with EtOAc (15 mL), washed with brine (3 × 10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (25 × 2.5 cm, EtOAc–hexane gradient) to give **15**; yield: 232 mg (94%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.90–7.40 (m, 9 H), 7.01 (d, *J* = 15.9 Hz, 1 H), 6.59 (d, *J* = 15.9 Hz, 1 H), 5.21 (s, 1 H), 5.18 (s, 1 H), 2.01 (s, 3 H).

HRMS–FAB: *m*/*z* calcd for $C_{18}H_{16}O$: 248.1201; found: 248.1297.

1-(2-Nitrophenyl)-3-pentanone (16)
[CAS Reg. No. 1094463-35-0]

Following the general procedure, the reaction was carried out starting from 1-bromo-2-nitrobenzene (**5**; 202 mg, 1 mmol), 1-penten-3-ol (**11**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **16**; yield: 188 mg (91%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.0 Hz, 1 H), 7.60–7.20 (m, 3 H), 3.10 (t, *J* = 7.4 Hz, 2 H), 2.78 (t, *J* = 7.4 Hz, 2 H), 2.39 (q, *J* = 7.4 Hz, 2 H), 1.00 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 209.7, 149.0, 136.3, 133.1, 132.3, 127.3, 124.7, 42.6, 35.7, 27.1, 7.6.

HRMS–FAB: *m*/*z* calcd for $C_{11}H_{13}NO_3$: 207.0895; found: 207.0887.

4-(2-Nitrophenyl)-2-butanone (17)
[CAS Reg. No. 58751-62-5]

Following the general procedure, the reaction was carried out starting from 1-bromo-2-nitrobenzene (**5**; 202 mg, 1 mmol), 3-buten-2-ol (**12**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **17**; yield: 176 mg (91%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.0 Hz, 1 H), 7.60–7.30 (m, 3 H), 3.11 (t, *J* = 7.0 Hz, 2 H), 2.83 (t, *J* = 7.0 Hz, 2 H), 2.13 (s, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 206.8, 148.9, 136.0, 133.0, 132.1, 127.2, 124.6, 43.9, 29.7, 27.0.

HRMS–FAB: *m*/*z* calcd for $C_{10}H_{11}NO_3$: 193.0739; found: 193.0734.

3-(2-Nitrophenyl)-1-phenyl-1-propanone (18)
[CAS Reg. No. 58751-63-6]

Following the general procedure, the reaction was carried out starting from 1-bromo-2-nitrobenzene (**5**; 202 mg, 1 mmol), 1-phenyl-2-propen-1-ol (**3**; 147 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **18**; yield: 201 mg (79%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.95 (m, 3H), 7.60–7.30 (m, 6 H), 3.47–3.26 (m, 4 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 198.4, 149.2, 136.5, 136.4, 133.2, 133.1, 132.5, 128.5, 128.0, 127.4, 124.8, 39.3, 27.6.

HRMS–FAB: *m*/*z* calcd for $C_{15}H_{13}NO_3$: 255.0895; found: 255.0889.

2-(3-Oxo-3-phenylpropyl)benzonitrile (19)
[CAS Reg. No. 898793-86-7]

Following the general procedure, the reaction was carried out starting from 2-bromobenzonitrile (**6**; 182 mg, 1 mmol), 1-phenyl-2-propen-1-ol (**3**; 147 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **19**; yield: 134 mg (57%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.94 (m, 2 H), 7.70–7.20 (m, 7 H), 3.45–3.20 (m, 4 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 197.8, 145.1, 136.3, 133.1, 132.8, 132.7, 129.9, 128.5, 127.9, 126.7, 117.9, 112.2, 38.9, 28.6.

HRMS–FAB: *m*/*z* calcd for $C_{16}H_{13}NO$: 235.0997; found: 235.0991.

2-(1-Methyl-3-oxopropyl)benzonitrile (20)
Following the general procedure, the reaction was carried out starting from 2-bromobenzonitrile (**6**; 182 mg, 1 mmol), crotyl alcohol (**9**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **20**; yield: 118 mg (68%).

IR: 2225 (CN), 1711 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.84 (t, *J* = 1.4 Hz, 1 H), 7.75–7.50 (m, 2 H), 7.30–7.10 (m, 2 H), 3.69 (sextet, *J* = 7.2 Hz, 1 H), 2.75 (dd, *J* = 7.2, 16 Hz, 1 H), 2.66 (dd, *J* = 7.2, 16 Hz, 1 H), 1.34 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 200.2, 148.9, 133.3, 133.1, 127.0, 126.4, 117.8, 112.0, 50.5, 32.4, 21.4.

MS (EI): *m*/*z* (%) = 143 (100), 130 (60), 103 (19), 77 (13), 28 (20).

HRMS–FAB: *m*/*z* calcd for $C_{11}H_{11}NO$: 173.0841; found: 173.0837.

2-[(*E*)-3-Hydroxy-3-methyl-1-butenyl]benzonitrile (21)
Following the general procedure, the reaction was carried out starting from 2-bromobenzonitrile (**6**; 182 mg, 1 mmol), 2-methyl-3-

buten-2-ol (**10**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **21**; yield: 150 mg (80%).

IR: 3434 (OH), 2225 cm^{-1} (CN).

^1H NMR (200 MHz, $CDCl_3$): δ = 7.60–7.30 (m, 3 H), 7.16 (dt, *J* = 2.0, 8.0 Hz, 1 H), 6.79 (d, *J* = 16.0 Hz, 1 H), 6.43 (d, *J* = 16.0 Hz, 1 H), 2.50 (s, 1 H, OH), 1.34 (s, 6 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 142.9, 140.3, 132.7, 132.6, 127.2, 125.7, 122.2, 117.8, 110.6, 71.0, 29.4.

MS (EI): *m*/*z* (%) = 172 (30), 144 (40), 130 (100), 43 (46), 28 (24).

HRMS–FAB: *m*/*z* calcd for $C_{12}H_{13}NO$: 187.0997; found: 187.0989.

2-(3-Oxo-3-phenylpropyl)-9*H*-fluoren-9-one (22)
Following the general procedure, the reaction was carried out starting from 2-bromofluorene (**7**; 245 mg, 1 mmol), 1-phenyl-2-propen-1-ol (**3**; 147 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **22**; yield: 250 mg (80%).

IR: 1713 (C=O alkyl), 1684 cm^{-1} (C=O fluorenyl).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.40–7.20 (m, 7 H), 3.48 (t, *J* = 7.4 Hz, 2 H), 2.84 (t, *J* = 7.4 Hz, 2 H), 2.47 (q, *J* = 7.2 Hz, 2 H), 1.17 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 198.7, 194.0, 144.5, 142.7, 142.5, 136.7, 134.9, 134.7, 134.6, 134.3, 133.2, 128.7, 128.6, 128.0, 124.3, 124.2, 120.4, 120.1, 39.8, 29.8.

MS (EI): *m*/*z* (%) = 312 (39), 207 (44), 193 (23), 105 (100), 77 (35).

HRMS–FAB: *m*/*z* calcd for $C_{22}H_{16}O_2$: 312.1150; found: 312.1145.

3-(9-Oxo-9*H*-fluoren-2-yl)butanal (23)
Following the general procedure, the reaction was carried out starting from 2-bromofluorene (**7**; 245 mg, 1 mmol), crotyl alcohol (**9**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **23**; yield: 176 mg (70%).

IR: 1708 (C=O), 1605 cm^{-1} (C=O).

^1H NMR (200 MHz, $CDCl_3$): δ = 9.75 (t, *J* = 1.6 Hz, 1 H), 8.00–7.20 (m, 7 H), 3.57 (sextet, *J* = 7.2 Hz, 1 H), 2.89 (ddd, *J* = 1.4, 6.8, 17.2 Hz, 1 H), 2.77 (ddd, *J* = 1.4, 7.4, 17.2 Hz, 1 H), 1.40 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 200.8, 194.4, 144.6, 142.8, 138.1, 136.9, 135.3, 134.5, 133.8, 124.8, 124.4, 124.1, 123.9, 122.6, 50.9, 26.9, 21.3.

MS (EI): *m*/*z* (%) = 250 (70), 235 (20), 221 (30), 207 (100), 178 (20).

HRMS–FAB: *m*/*z* calcd for $C_{17}H_{14}O_2$: 250.0994; found: 250.0991.

2-(3-Oxopentyl)-9*H*-fluoren-9-one (24)
Following the general procedure, the reaction was carried out starting from 2-bromofluorene (**7**; 245 mg, 1 mmol), 1-penten-3-ol (**11**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **24**; yield: 224 mg (85%).

IR: 1708 (C=O), 1605 cm^{-1} (C=O).

^1H NMR (200 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.0 Hz, 1 H), 7.50–7.20 (m, 6 H), 2.90 (t, *J* = 7.2 Hz, 2 H), 2.76 (t, *J* = 7.2 Hz, 2 H), 2.43 (q, *J* = 7.4 Hz, 2 H), 1.05 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 210.4, 194.4, 144.6, 142.8, 138.1, 136.9, 135.3, 134.5, 133.8, 124.8, 124.4, 124.1, 123.9, 122.6, 43.8, 29.8, 20.6, 7.5.

MS (EI): *m*/*z* (%) = 264 (74), 235 (31), 207 (51), 193 (100).

HRMS–FAB: *m*/*z* calcd for $C_{18}H_{16}O_2$: 264.1150; found: 264.1144.

1-(1-Naphthalenyl)-3-pentanone (25)
[CAS Reg. No. 1099621-55-2]

Following the general procedure, the reaction was carried out starting from 1-bromonaphthalene (**8**; 207 mg, 1 mmol), 1-penten-3-ol (**11**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **25**; yield: 152 mg (72%).

IR: 1712 cm^{-1} (C=O).

^1H NMR (200 MHz, $CDCl_3$): δ = 8.40–7.20 (m, 7 H), 3.48 (t, *J* = 7.4 Hz, 2 H), 2.84 (t, *J* = 7.4 Hz, 2 H), 2.47 (q, *J* = 7.2 Hz, 2 H), 1.17 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 210.4, 137.0, 133.6, 131.7, 128.7, 127.7, 127.1, 125.8, 125.4, 125.3, 123.3, 42.8, 35.8, 26.6, 7.6.

MS (EI): *m*/*z* (%) = 212 (81), 210 (41), 181 (100), 155 (61), 141 (94).

HRMS–FAB: *m*/*z* calcd for $C_{15}H_{16}O$: 212.1201; found: 212.1198.

4-(1-Naphthalenyl)-2-butanone (26)
[CAS Reg. No. 3506-84-1]

Following the general procedure, the reaction was carried out starting from 1-bromonaphthalene (**8**; 207 mg, 1 mmol), 3-buten-2-ol (**12**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **26**; yield: 121 mg (61%).

IR: 1715 cm^{-1} (C=O).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.90–7.30 (m, 7 H), 3.30 (t, *J* = 7.5 Hz, 2 H), 2.79 (t, *J* = 7.5 Hz, 2 H), 2.07 (s, 3 H).

^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 207.7, 136.9, 133.6, 131.5, 128.8, 127.8, 126.8, 125.9, 125.8, 125.4, 125.3, 44.2, 29.9, 26.6.

MS (EI): *m*/*z* (%) = 198 (100), 183 (38), 155 (90), 141 (66), 127 (70), 101 (50), 43 (33).

HRMS–FAB: *m*/*z* calcd for $C_{14}H_{14}O$: 198.1045; found: 198.1041.

1-Phenyl-3-(3-pyridinyl)-1-propanone (32)
[CAS Reg. No. 39976-56-2]

A mixture of 3-bromopyridine (**27**; 158 mg, 1 mmol), 1-phenylprop-2-en-1-ol (**3**; 147 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%) in DMF (3 mL) was reacted in an Anton Paar Monowave 300 in a sealed reaction vessel at 200 °C and 27 bar for 20 min. Then, the mixture was cooled to r.t., diluted with EtOAc (15 mL), washed with brine (3 × 10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (25 × 2.5 cm, EtOAc–hexane gradient) to give **32**; yield: 164 mg (78%).

^1H NMR (200 MHz, $CDCl_3$): δ = 8.44 (s, 1 H), 8.35 (d, *J* = 3.6 Hz, 1 H), 7.86 (d, *J* = 7.0 Hz, 2 H), 7.60–7.10 (m, 5 H), 3.19 (t, *J* = 7.2 Hz, 2 H), 2.98 (t, *J* = 7.2 Hz, 2 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 198.1, 149.3, 146.9, 136.5, 136.2, 136.1, 133.0, 128.4, 127.7, 123.2, 39.3, 26.7.

HRMS–FAB: *m*/*z* calcd for $C_{14}H_{13}NO$: 211.0997; found: 211.0991.

(*E*)-2-Methyl-4-(3-pyridinyl)-3-buten-2-ol (33)
[CAS Reg. No. 943897-36-7]

Following the general procedure, the reaction was carried out starting from 3-bromopyridine (**27**; 158 mg, 1 mmol), 2-methyl-3-buten-2-ol (**10**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **33**; yield: 143 mg (88%).

IR: 3356 cm^{-1} (OH).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.80 (s, 1 H), 8.64 (d, *J* = 5.6 Hz, 1 H), 7.72 (t, *J* = 5.6 Hz, 1 H), 7.26 (t, *J* = 5.6 Hz, 1 H), 6.59 (d, *J* = 16.0 Hz, 1 H), 6.42 (d, *J* = 16.0 Hz, 1 H), 2.47 (s, 1 H, OH), 1.43 (s, 6 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 151.2, 147.7, 142.3, 134.7, 133.3, 124.5, 122.6, 70.9, 29.8.

MS (EI): *m*/*z* (%) = 163 (27), 148 (100), 121 (25), 105 (27).

HRMS–FAB: *m*/*z* calcd for $C_{10}H_{13}NO$: 163.0997; found: 163.0989.

3,5-Bis[(*E*)-3-hydroxy-3-methyl-1-butenyl]pyridine (34)
Following the general procedure, the reaction was carried out starting from 3,5-dibromopyridine (**28**; 237 mg, 1 mmol), 2-methyl-3-buten-2-ol (**10**; 190 mg, 2.2 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **34**; yield: 207 mg (84%).

IR: 3361 cm^{-1} (OH).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.56 (d, *J* = 2.1 Hz, 2 H), 7.98 (t, *J* = 2.1 Hz, 1 H), 6.51 (d, *J* = 16.0 Hz, 2 H), 6.38 (d, *J* = 16.0 Hz, 2 H), 2.37 (s, 2 H, OH), 1.39 (s, 12 H).

^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 149.0, 141.7, 135.3, 121.4, 120.8, 70.9, 29.8.

MS (EI): *m*/*z* (%) = 247 (25), 226 (100), 201 (47), 199 (37), 184 (30).

HRMS–FAB: *m*/*z* calcd for $C_{15}H_{21}NO_2$: 247.1572; found: 247.1568.

4-(3-Quinolinyl)-2-butanone (35)
Following the general procedure, the reaction was carried out starting from 3-bromoquinoline (**29**; 208 mg, 1 mmol), 3-buten-2-ol (**12**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **35**; yield: 153 mg (77%).

IR: 1715 cm^{-1} (C=O).

^1H NMR (200 MHz, $CDCl_3$): δ = 8.70 (s, 1 H), 8.06 (s, 1 H), 7.88 (d, *J* = 8.0 Hz, 1 H), 7.57 (d, *J* = 8.0 Hz, 1 H), 7.52 (t, *J* = 8.0 Hz, 1 H), 7.38 (t, *J* = 8.0 Hz, 1 H), 2.85 (t, *J* = 7.4 Hz, 2 H), 2.63 (t, *J* = 7.4 Hz, 2 H), 1.95 (s, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 206.6, 150.9, 146.3, 136.8, 129.4, 129.1, 127.3, 127.1, 126.9, 44.0, 29.7, 26.5.

MS (EI): *m*/*z* (%) = 199 (38), 198 (92), 184 (13), 155 (76), 141 (100), 128 (33).

HRMS–FAB: *m*/*z* calcd for $C_{13}H_{13}NO$: 199.0997; found: 199.0985.

3-(3-Quinolinyl)butanal (36)
Following the general procedure, the reaction was carried out starting from 3-bromoquinoline (**29**; 208 mg, 1 mmol), crotyl alcohol (**9**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **36**; yield: 175 mg (88%).

IR: 2725 (C–H), 1722 cm^{-1} (C=O).

^1H NMR (200 MHz, $CDCl_3$): δ = 9.73 (t, *J* = 1.4 Hz, 1 H), 8.81 (d, *J* = 2.3 Hz, 1 H), 8.08 (d, *J* = 7.0 Hz, 1 H), 7.97 (d, *J* = 2.3 Hz, 1 H), 7.78 (d, *J* = 7.0 Hz, 1 H), 7.64 (t, *J* = 7.0 Hz, 1 H), 7.56 (t, *J* = 7.0 Hz, 1 H), 3.57 (sextet, *J* = 7.2 Hz, 1 H), 2.89 (ddd, *J* = 1.4, 6.8, 17.2 Hz, 1 H), 2.77 (ddd, *J* = 1.4, 7.4, 17.2 Hz, 1 H), 1.40 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 200.5, 150.5, 146.9, 137.9, 132.8, 128.9 (2C), 127.9, 127.4, 126.7, 51.2, 31.6, 21.8.

MS (EI): *m*/*z* (%) = 199 (40), 184 (18), 156 (100), 128 (21).

HRMS–FAB: *m*/*z* calcd for $C_{13}H_{13}NO$: 199.0997; found: 199.0994.

(*E*)-2-Methyl-4-(3-quinolinyl)-3-buten-2-ol (37)
Following the general procedure, the reaction was carried out starting from 3-bromoquinoline (**29**; 208 mg, 1 mmol), 2-methyl-3-buten-2-ol (**10**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **37**; yield: 196 mg (92%).

IR: 3380 cm^{-1} (OH).

^1H NMR (200 MHz, $CDCl_3$): δ = 8.64 (d, *J* = 3.2 Hz, 1 H), 8.04 (d, *J* = 3.2 Hz, 1 H), 7.90 (d, *J* = 8.0 Hz, 1 H), 7.44 (m, 1 H), 7.42 (m, 1 H), 7.36 (t, *J* = 7.2 Hz, 1 H), 6.60 (d, *J* = 16.0 Hz, 1 H), 6.44 (d, *J* = 16.0 Hz, 1 H), 3.75 (s, 1 H, OH), 1.33 (s, 6 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 150.9, 145.8, 140.3, 136.8, 129.4, 129.1, 128.6, 126.6 (2C), 122.6, 116.8, 70.3, 29.7.

MS (EI): *m*/*z* (%) = 213 (100), 128 (86), 101 (44), 75 (23), 28 (23).

HRMS–FAB: *m*/*z* calcd for $C_{14}H_{15}NO$: 213.1154; found: 213.1149.

1-(4-Isoquinolinyl)-3-pentanone (38)
Following the general procedure, the reaction was carried out starting from 4-bromoisoquinoline (**30**; 208 mg, 1 mmol), 1-penten-3-ol (**11**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **38**; yield: 185 mg (87%).

IR: 1712 cm^{-1} (C=O).

^1H NMR (200 MHz, $CDCl_3$): δ = 9.13 (s, 1 H), 8.38 (s, 1 H), 7.88 (d, *J* = 8.2 Hz, 2 H), 7.65 (ddd, *J* = 1.4, 8.2, 8.2 Hz, 1 H), 7.51 (ddd, *J* = 1.0, 8.2, 8.2 Hz, 1 H), 3.32 (t, *J* = 8.0 Hz, 2 H), 2.86 (t, *J* = 8.0 Hz, 2 H), 2.37 (q, *J* = 7.2 Hz, 2 H), 1.07 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 209.5, 151.0, 141.9, 133.9, 130.0, 129.9, 127.9, 127.8, 126.5, 122.1, 42.1, 35.6, 23.3, 7.3.

MS (EI): *m*/*z* (%) = 213 (100), 184 (22), 156 (97), 142 (84).

HRMS–FAB: *m*/*z* calcd for $C_{14}H_{15}NO$: 213.1154; found: 213.1151.

4-(4-Isoquinolinyl)-2-butanone (39)
Following the general procedure, the reaction was carried out starting from 4-bromoisoquinoline (**30**; 208 mg, 1 mmol), 3-buten-2-ol (**12**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **39**; yield: 167 mg (84%).

IR: 1713 cm^{-1} (C=O).

^1H NMR (200 MHz, $CDCl_3$): δ = 9.10 (s, 1 H), 8.60 (s, 1 H), 8.04 (d, *J* = 8.0 Hz, 1 H), 7.84 (d, *J* = 8.0 Hz, 1 H), 7.70 (t, *J* = 8.0 Hz, 1 H), 7.60 (t, *J* = 8.0 Hz, 1 H), 3.27 (t, *J* = 7.2 Hz, 2 H), 2.85 (t, *J* = 7.2 Hz, 2 H), 2.16 (s, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 206.8, 151.3, 144.2, 134.1, 129.2, 127.8, 127.3, 125.3, 119.2, 43.4, 29.6, 23.2.

MS (EI): *m*/*z* (%) = 199 (100), 156 (92), 142 (65), 129 (22), 28 (42).

HRMS–FAB: *m*/*z* calcd for $C_{13}H_{13}NO$: 199.0997; found: 199.0993.

3-(4-Isoquinolinyl)butanal (40)

Following the general procedure, the reaction was carried out starting from 4-bromoisoquinoline (**30**; 208 mg, 1 mmol), crotyl alcohol (**9**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **40**; yield: 181 mg (91%).

IR: 1721 cm^{-1} (C=O).

^1H NMR (200 MHz, $CDCl_3$): δ = 9.84 (t, *J* = 1.4 Hz, 1 H), 9.15 (s, 1 H), 8.44 (s, 1 H), 8.08 (d, *J* = 8.6 Hz, 1 H), 8.00 (dd, *J* = 8.4, 1.0 Hz, 1 H), 7.77 (ddd, *J* = 1.4, 6.8, 8.6 Hz, 1 H), 7.63 (ddd, *J* = 1.0, 7.0, 8.4 Hz, 1 H), 4.16 (sextet, *J* = 6.8 Hz, 1 H), 3.00 (ddd, *J* = 1.2, 5.6, 17.6 Hz, 1 H), 2.88 (ddd, *J* = 1.8, 8.2, 17.6 Hz, 1 H), 1.48 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 200.8, 151.6, 140.0, 134.4, 133.7, 130.6, 128.6, 128.4, 126.9, 121.9, 50.9, 26.9, 21.3.

MS (EI): *m*/*z* (%) = 199 (26), 156 (100), 128 (21), 43 (18), 28 (21).

HRMS–FAB: *m*/*z* calcd for $C_{13}H_{13}NO$: 199.0997; found: 199.0992.

5-(3-Oxo-3-phenylpropyl)-2-furaldehyde (41)

Following the general procedure, the reaction was carried out starting from 5-bromo-2-furaldehyde (**31**; 175 mg, 1 mmol), 1-phenyl-2-propen-1-ol (**3**; 147 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **41**; yield: 207 mg (91%).

^1H NMR (400 MHz, $CDCl_3$): δ = 9.41 (s, 1 H), 7.87 (d, *J* = 7.5 Hz, 2 H), 7.60–7.20 (m, 3 H), 7.11 (d, *J* = 3.6 Hz, 1 H), 6.25 (d, *J* = 3.6 Hz, 1 H), 3.32 (t, *J* = 7.2 Hz, 2 H), 3.08 (t, *J* = 7.2 Hz, 2 H).

^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 197.4, 176.7, 162.0, 151.6, 136.0, 132.9, 128.4, 127.7, 123.7, 109.1, 35.7, 22.4.

HRMS–FAB: *m*/*z* calcd for $C_{14}H_{12}O_3$: 228.0786; found: 228.0781.

5-(1-Methyl-3-oxopropyl)-2-furaldehyde (42)

[CAS Reg. No. 1001388-45-9]

Following the general procedure, the reaction was carried out starting from 5-bromo-2-furaldehyde (**31**; 175 mg, 1 mmol), crotyl alcohol (**9**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **42**; yield: 148 mg (89%).

^1H NMR (400 MHz, $CDCl_3$): δ = 9.78 (t, *J* = 1.6 Hz, 1 H), 9.54 (s, 1 H), 7.18 (d, *J* = 3.6 Hz, 1 H), 6.29 (d, *J* = 3.6 Hz, 1 H), 3.55 (sextet, *J* = 6.8 Hz, 1 H), 2.96 (ddd, *J* = 1.6, 6.4, 17.6 Hz, 1 H), 2.72 (ddd, *J* = 1.6, 7.6, 17.6 Hz, 1 H), 1.37 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 199.8, 177.1, 167.3, 151.9, 123.2, 107.9, 48.5, 27.9, 18.6.

HRMS–FAB: *m*/*z* calcd for $C_9H_{10}O_3$: 166.0630; found: 166.0629.

5-[(*E*)-3-Hydroxy-3-methyl-1-butenyl]-2-furaldehyde (43)

[CAS Reg. No. 117252-40-1]

Following the general procedure, the reaction was carried out starting from 5-bromo-2-furaldehyde (**31**; 175 mg, 1 mmol), 2-methyl-3-buten-2-ol (**10**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **43**; yield: 158 mg (88%).

^1H NMR (200 MHz, $CDCl_3$): δ = 9.45 (d, *J* = 0.6 Hz, 1 H), 7.17 (dd, *J* = 0.6, 3.6 Hz, 1 H), 6.64 (d, *J* = 16.0 Hz, 1 H), 6.45 (d, *J* = 16.0 Hz, 1 H), 6.34 (d, *J* = 3.6 Hz, 1 H), 2.84 (s, 1 H, OH), 1.34 (s, 6 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 176.9, 158.3, 151.2, 143.1, 124.1, 113.8, 109.9, 70.7, 29.5.

HRMS–FAB: *m*/*z* calcd for $C_{10}H_{12}O_3$: 180.0786; found: 180.0782.

5-(3-Oxopentyl)-2-furaldehyde (44)

[CAS Reg. No. 1262222-47-8]

Following the general procedure, the reaction was carried out starting from 5-bromo-2-furaldehyde (**31**; 175 mg, 1 mmol), 1-penten-3-ol (**11**; 95 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **44**; yield: 149 mg (83%).

IR: 1713 (C=O), 1675 cm^{-1} (C=O).

^1H NMR (200 MHz, $CDCl_3$): δ = 9.65 (s, 1 H), 7.33 (d, *J* = 3.6 Hz, 1 H), 6.43 (d, *J* = 3.6 Hz, 1 H), 3.16 (t, *J* = 6.8 Hz, 2 H), 3.02 (t, *J* = 6.8 Hz, 2 H), 2.62 (q, *J* = 7.4 Hz, 2 H), 1.21 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 208.9, 176.7, 161.9, 151.7, 123.6, 109.0, 39.2, 35.7, 22.2, 7.5.

MS (EI): *m*/*z* (%) = 180 (14), 123 (100), 109 (30), 57 (23), 28 (24).

HRMS–FAB: *m*/*z* calcd for $C_{10}H_{12}O_3$: 180.0786; found: 180.0779.

5-(3-Oxobutyl)-2-furaldehyde (45)

Following the general procedure, the reaction was carried out starting from 5-bromo-2-furaldehyde (**31**; 175 mg, 1 mmol), 3-buten-2-ol (**12**; 79 mg, 1.1 mmol), NaOAc (100 mg, 1.2 mmol) and catalyst **1** (10 mg, 1 mol%). When the reaction was finished, the reaction crude was purified by flash column chromatography on silica gel (EtOAc–hexane gradient) to give **45**; yield: 132 mg (80%).

^1H NMR (300 MHz, $CDCl_3$): δ = 9.43 (s, 1 H), 7.12 (d, *J* = 3.6 Hz, 1 H), 6.21 (d, *J* = 3.6 Hz, 1 H), 2.93 (m, 2 H), 2.82 (m, 2 H), 2.11 (s, 3 H).

^{13}C NMR (50 MHz, DEPT, $CDCl_3$): δ = 206.0, 176.7, 161.8, 151.6, 123.5, 109.0, 40.5, 29.6, 22.1.

HRMS–FAB: *m*/*z* calcd for $C_9H_{10}O_3$: 166.0630; found: 166.0628.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis. It includes the ^1H and ^{13}C NMR spectra of all compounds prepared.

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