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Ionic liquids as solvent for regioselective arylation of α-substituted allylic alcohols by aryl bromides

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Abstract

Regioselective Heck arylation of α-substituted allylic alcohols by aryl bromides was achieved by Pd-DPPP catalysis in ionic liquids, affording a β/γ ratio of up to 78/22 in the case of the coupling of 1-bromonaphthalene with but-1-en-3-ol. In addition to the effects of both ligands and reaction media, the regiocontrol toward the formation of branched products was significantly affected by the steric properties of allylic alcohols; with the increasing bulkiness of the substituent on allylic alcohol, the β/γ regioselectivity decreased. For comparison, arylation by aryl triflates in a molecular solvent was also demonstrated, which showed the same trend in regioselectivity.

Keywords: Ionic liquids; Heck reaction; Allylic alcohols; Regioselectivity; Palladium catalysis

1. Introduction

The Heck reaction has been well known as one of the most important methods for the formation of C–C bonds in synthetic chemistry [1]. In particular, the Pd-catalyzed Heck arylation of allylic alcohols has been an attractive topic of research for a long time [2], as its products, the substituted allylic alcohols, provide useful intermediates for pharmaceutical synthesis [3–5]. Under the normal Heck reaction conditions, however, the arylation is not totally regioselective, as a mixture of linear and branched products is usually obtained [6], which hampers its wider application in synthetic chemistry (Scheme 1). Therefore, there is incentive to improve the regioselectivity of the reaction.

The regiocontrol to yield the γ-substituted allylic alcohols or carbonyl products has been investigated by several research groups [7]; a review has recently been presented by Muzart [8]. It is suggested that monophosphines [4g,7e,g,h] or no ligand [4b,g,i] and neutral reaction media are generally the choice for a high regioselectivity. In some cases, a weak base such as sodium bicarbonate or triethyl amine is also favored for the regiocontrol leading to the γ product [4g,7h]. In addition, Jeffery reported that in the presence of a stoichiometric amount of silver acetate, the reaction could be altered to produce only cinnamyl alcohols in synthetically useful yields without 'isomerisation' of the double bonds [4g]. This procedure has been applied by Tietze et al. [4c] to the synthesis of Vitamin E. Kang et al. [7h] reported that hypervalent iodonium salts could facilitate the reaction to give a completely linearly arylated alcohol. Among those abovementioned, arylation of α-substituted allylic alcohols has also been demonstrated, the corresponding ketones being the major products in most cases, however [4b,7c,d,9]. The branched, β arylated alcohols or the carbonyl derivatives were usually obtained in a minor yield in these studies, the maximum proportion being 9% [2a,9e]. The utility of the methods has been seen in the synthesis of pharmaceutically active compounds [3a,b,4a].

Contrary to the γ regiocontrol, the arylation of allylic alcohol to produce a branched, β-substituted product has received much less attention. Cabri initially demonstrated the possibility by using aryl triflates [10]. Following that, the arylation of allylic alcohol by phenyltriflate was reported by Hallberg and co-workers [11]. Very recently, we reported on the internal arylation of non-substituted (homo)allylic alcohol by aryl bromides [12]. Given the deficiency in research in this direction

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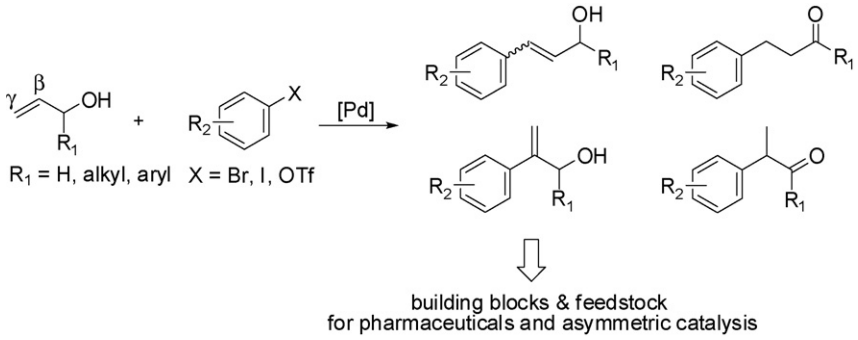


Scheme 1. Heck arylation of allylic alcohols leading to isomeric products.

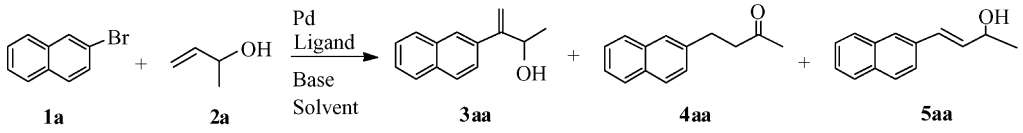
and the potential of the product in synthetic chemistry, we were interested in extending our initial finding into substituted allylic alcohols.

Both theoretical [13] and experimental [12,14] studies now suggest that the outcome of the Heck arylation of electron-rich olefins is governed by a number of parameters, such as the electronic properties of olefins, the electronic and steric properties of ligands and the solvents. Arylation of α-substituted allylic alcohols is no exception. According to the generally accepted two-pathway mechanism for the Heck reaction [13,15], the arylation of a α-substituted allylic alcohol by an aryl bromide is expected to proceed via either a neutral pathway **A** or an ionic pathway **B** to give a linear or a branched olefinic product, respectively, as outlined in Scheme 2.

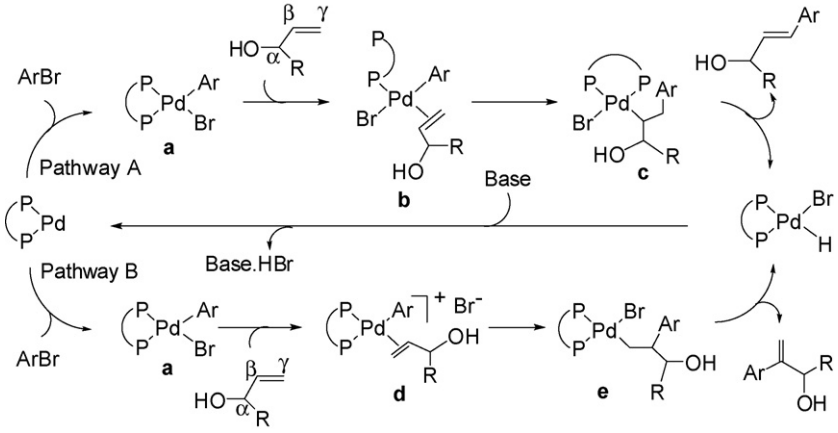
Clearly, in pathway B the dissociation of bromide anion from the Pd-aryl intermediate **a** to generate a coordinating site for the incoming olefin and subsequently form the ionic Pd-olefin species **d** plays a vital role in the formation of the branched, β-arylated product. This would be greatly impacted by both the solvent and the ligand. Therefore, we initially decided to investigate the influences of the solvent and ligand on the regiocontrol. In our recent work on the arylation of electron rich olefins, we have demonstrated that the ionic pathway could be promoted by ionic liquid solvents, which may facilitate the formation of the ionic intermediate **d** and therefore the formation of branched olefins without calling for a halide scavenger [16]. In this work, the commonly used ionic liquids based on the 1-butyl-3-methylimidazolium cation ([bmim]) were chosen as solvents and bidentate P^P, N^N, N^P compounds were screened as possible ligands.

2. Results and discussion

In our initial investigation, the coupling of 2-bromonaphthalene **1a** with but-1-en-3-ol **2a** was chosen as a model reaction (Eq. (1)). Firstly, solvent effect was examined by using both common and ionic liquid solvents. The ionic liquids [bmim]PF_6, [bmim]BF_4 and [bmim]NTf_2 (NTf: trifluoromethanesulfonylimide) were chosen as the representative ionic media. In a typical reaction, a mixture of **1a** (1.0 mmol), **2a** (1.2 mmol), $Pd(OAc)_2$ (4.0 mol%), DPPP [1,3-bis(diphenylphosphino)propane] (8.0 mol%) and Et_3N (1.5 mmol) in 1.0 mL solvent was heated at 115 °C under N_2



(1)



Scheme 2. Suggested pathways for the arylation of substituted allylic alcohols, where possible oxygen coordination to Pd(II) is not shown.

Table 1
The effect of solvent on the arylation of **2a**[a]

Entry	Solvent	Conv. (%)[b]	Proportion of the isomers[b]		
			3aa	**4aa**	**5aa**
1	DMSO	>99	16	77	7
2	CH_3CN	59	60	37	3
3	PC[c]	98	55	44	1
4	NMP[c]	>99	6	77	17
5	DMF	>99	8	66	26
6	DMA[c]	>99	8	62	30
7	[bmim]BF_4	83	70	28	2
8	[bmim]NTf_2	88	68	29	3
9	[bmim]PF_6	>99(91[d])	70	30	–
10	[bmim]PF_6[e]	85	72	26	2
11	[bmim]PF_6[f]	80	71	26	3
12	[bmim]PF_6-DMSO (v/v, 8/2)	95	71	29	–
13	[bmim]BF_4-DMSO (v/v, 8/2)	87	68	29	3
14	[bmim]NTf_2-DMSO (v/v, 8/2)	93	69	28	3
15	[bmim]BF_4-DMSO (v/v, 1/9)	79	70	27	3

[a] Reaction conditions: **1a** (1.0 mmol), **2a** (1.2 mmol), Et_3N (1.5 mmol), $Pd(OAc)_2$ (4 mol%), DPPP (8 mol%), solvent (1.0 mL), 115 °C, N_2, 12 h.
[b] Determined by ^1H NMR.
[c] DMA, *N,N'*-dimethylacetamide; PC, propylene carbonate; NMP, *N*-methylpyrorolidinone.
[d] 6 h.
[e] $^iPr_2NH$ (1.5 mmol) instead of Et_3N, 6 h.
[f] $^iPr_2NEt$ (1.5 mmol) instead of Et_3N, 6 h.

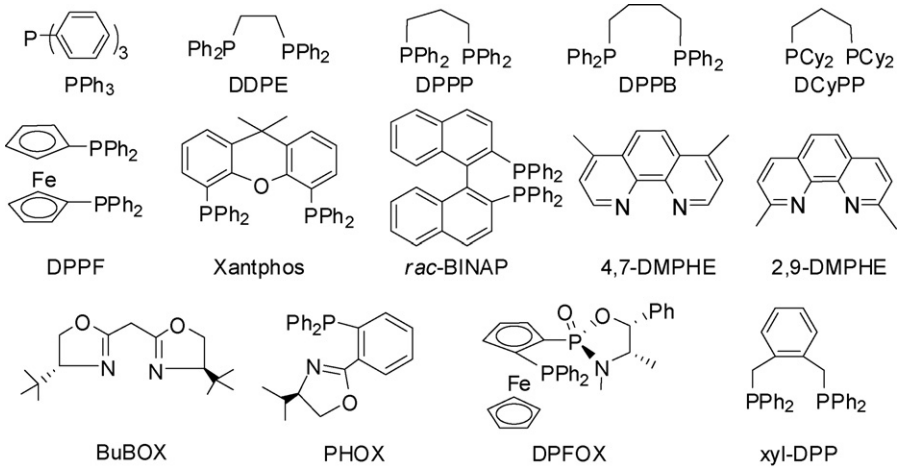
Table 2
The effect of ligands on the arylation of **2a**[a]

Entry	Ligand	Reaction time (h)	Conv. (%)	Proportion of the isomers[b]		
				3aa	**4aa**	**5aa**
1	PPh_3	4	>99	5	69	26
2	DPPE	12	70	24	50	26
3	DPPP	4	95	70	28	2
4	DPPB	12	93	9	65	26
5	DCyPP	4	0	–	–	–
6	DPPF	4	>99	10	77	13
7	Xantphos	4	81	7	73	20
8	*rac*-BINAP	4	80	15	66	19
9	4,7-DMPHE	4	60	27	65	8
10	2,9-DMPHE	8	86	8	35	57
11	BuBOX	8	78	4	66	30
12	PHOX[c]	8	4	–	–	–
13	DPFOX[c]	8	25	9	56	35
14	xyl-DPP[c]	8	0	–	–	–

[a] Reaction conditions: **1a** (1.0 mmol), **2a** (1.2 mmol), Et_3N (1.5 mmol), $Pd(OAc)_2$ (4 mol%), ligand (8 mol%), [bmim]PF_6, 115 °C, N_2.
[b] Determined by ^1H NMR.
[c] 2 mol% $Pd(OAc)_2$ and 4 mol% ligand were used.

for 12 h. In the case of using a molecular solvent, the product was obtained by evaporating the solvent to a minimum amount under reduced pressure, followed by passing the remaining product/catalyst mixture through a short pad of silica gel. In the case of an ionic liquid, the product was extracted with diethyl ether with the catalyst remaining in the ionic liquid phase. The crude product was subjected to NMR for analysis. Table 1 summarizes the results observed.

It was found that the reaction could proceed smoothly in both molecular and ionic media, although it was sluggish in CH_3CN, in which only 59% conversion was obtained after 12 h reaction time (entry 2). As might be expected, the common molecular solvents generally preferred to give the γ-arylated ketone **4aa** as the major product (entries 1–6), which resulted from the initially formed, γ-arylated allylic alcohol **5aa**, whereas the ionic liquid (entries 7–9), even when mixed with a molecular solvent (entries 12–15), provided the β-arylated allylic alcohol **3aa** as the predominate product, the ratio of β/γ being ca. 70/30 in all cases. The ionic liquid [bmim]PF_6 is the best in terms of catalyst activity. The results indicate that the cationic pathway **B** is promoted when the reaction is run in an ionic medium. This might partly be ascribed to stabilization by the ionic liquid of the ionic intermediate **d** and Br^- in Scheme 2. Electrostatic interactions and hydrogen bonding involving the C2 hydrogen on the imidazolium ring may contribute to this stabilization [17]. When replacing Et_3N with $^iPr_2NH$ (entry 10) or $^iPr_2NEt$ (entry 11), no significant difference on the regioselectivity was observed, although the proportion of the product **3aa** was slightly enhanced by using $^iPr_2NH$.



Scheme 3. Ligands screened for the reaction of **1a** and **2a**.

Table 3
Arylation of substituted allylic alcohols[a]

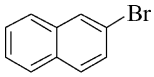
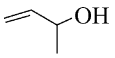
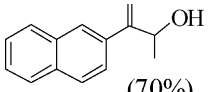
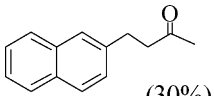
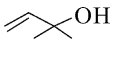
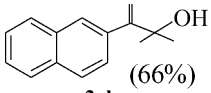
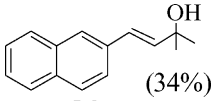
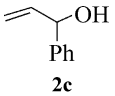
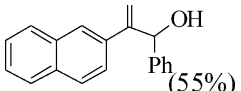
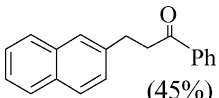
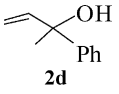
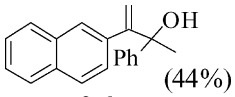
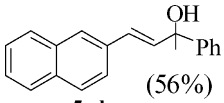
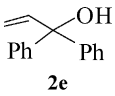
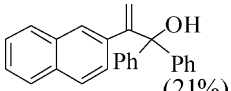
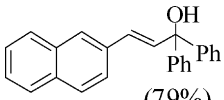
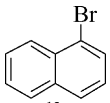
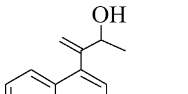
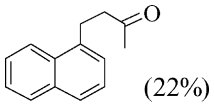
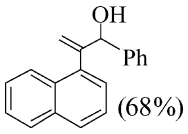
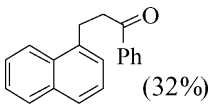
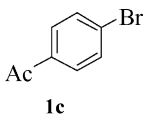
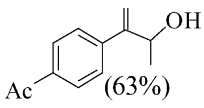
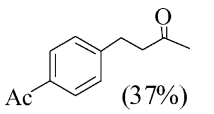
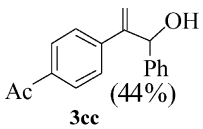
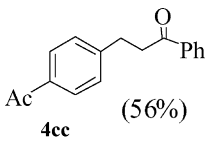
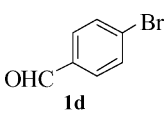
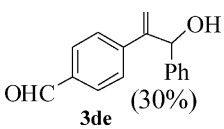
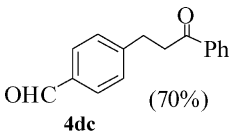
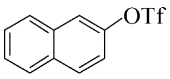
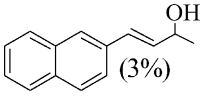
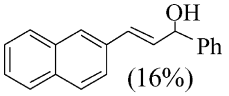
Entry	ArX	Allylic alcohol	Reaction time (h)	Conv. (%)[b]	Proportion of the Isomers (%)[b]	
					β	γ
1	 **1a**	 **2a**	12	>99	 **3aa** (70%)	 **4aa** (30%)
2	**1a**	 **2b**	24	75	 **3ab** (66%)	 **5ab** (34%)
3	**1a**	 **2c**	36	82	 **3ac** (55%)	 **4ac** (45%)
4	**1a**	 **2d**	36	73	 **3ad** (44%)	 **5ad** (56%)
5	**1a**	 **2e**	36	61	 **3ae** (21%)	 **5ae** (79%)
6	 **1b**	**2a**	6	70	 **3ba** (78%)	 **4ba** (22%)
7	**1b**	**2c**	6	37	 **3bc** (68%)	 **4bc** (32%)
8	 **1c**	**2a**	6	76	 **3ca** (63%)	 **4ca** (37%)
9	**1c**	**2c**	24	>99	 **3cc** (44%)	 **4cc** (56%)
10	 **1d**	**2c**	24	>99	 **3de** (30%)	 **4dc** (70%)

Table 3 (*Continued*)

Entry	ArX	Allylic alcohol	Reaction time (h)	Conv. (%)[b]	Proportion of the Isomers (%)[b]	
					β	γ
11[c]	 **1e**	**2a**	4	69	**3aa** (65%) **4aa** (32%)	 (3%) **5ea**
12[c]	**1e**	**2c**	6	81	**3ac** (47%) **4ac** (37%)	 (16%) **5ec**
13[c]	**1e**	**2d**	6	67	**3ad** (12%) **5ad** (88%)	

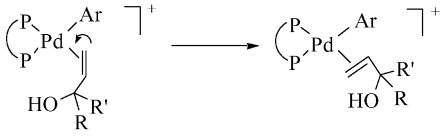
[a] Reaction conditions: **1a–e** (1.0 mmol), **2a–e** (1.2 mmol), Et_3N (1.5 mmol), $Pd(OAc)_2$ (4.0 mol%), DPPP (8.0 mol%), [bmim]PF_6 (1.0 mL), 115 °C, N_2.
[b] Determined by ^1H NMR.
[c] In DMSO (1.0 mL).

Next, the effect of ligand on the reaction was investigated. Previously, ligands had been shown to impact significantly on the regioselectivity of the arylation of other electron-rich olefins [14a]. A set of 14 ligands shown in Scheme 3 were screened, again using the arylation in Eq. (1) as the model reaction. The results are summarized in Table 2.

As can be seen in Table 2, among these ligands DPPP led to the best regioselectivity for the branched product, affording a β/γ ratio of 70/30 (entry 3). In contrast, in the presence of the other ligands, including PPh_3 (entry 1), DPPE (entry 2), DPPB (entry 4), DPPF (entry 6), Xantphos (entry 7), *rac*-BINAP (entry 8), 4,7-DMPHE (entry 9), 2,9-DMPHE (entry 10) and BuBOX (entry 11), the reaction yielded the γ-substituted ketone **4aa** as the predominate product with reasonable conversions. With DPFOX (entry13), however, the reaction was slower, furnishing a 25% conversion with a β/γ ratio of 9/91 after 8 h reaction time. With DCyPP (entry 5), PHOX (entry12) or xyl-DPP (entry 14), the reaction was too slow to be examined under the given reaction conditions.

By the above screening of both solvents and ligands, it was shown that Pd-DPPP catalysis in [bmim]PF_6 is a good choice for the formation of the branched product in the arylation of **2a** by **1a**. We then decided to extend this chemistry to other aryl bromides and allylic alcohols. With this in mind, the substituted allylic alcohols 2-methylbut-3-en-2-ol (**2b**), 3-phenylprop-1-en-3-ol (**2c**), 3-phenylbut-1-en-3-ol (**2d**) and 3,3′-diphenylprop-1-en-3-ol (**2e**) were introduced. The results are presented in Table 3. For comparison, the results from the coupling of **2a** with **1a** are also included in the table.

As can be seen, arylation of **2a–e** by **1a** in [bmim]PF_6 resulted in the expected coupling products, i.e. mixtures of β- and γ-arylated isomers. However, with the increase of the bulkiness of the substituent on allylic alcohol, in the order of $-CH_3 < -(CH_3)_2 < -Ph < -(CH_3)(Ph) < -(Ph)_2$ (entries 1–5), both the reactivity and regioselectivity decreased, indicating that the steric property of the allylic alcohol has a decisive effect. This may not be surprising, as the bulky substituent would inhibit the rotation of olefin from the initial out-of-plane position to the in-plane position and the subsequent migratory insertion of the olefin into the Pd–Ar bond that gives rise to β arylation (Eq. (2)). Changing to other aryl bromides, from **1b** to **1d**, the same trend in selectivity was observed (entries 6–10).



(2)

The reduced regioselectivity might result from the cationic pathway becoming unfavorable. For this reason, we carried out the coupling reaction of **2a**, **2c** and **2d** in DMSO with the aryl triflate **1e**; triflates are known to favor the pathway **B**. A mixture of isomeric products was again obtained (entries 11–13), indicating the erosion of regioselectivity is steric in origin rather than difficulties in bromide dissociation from Pd(II). Surprisingly somehow, when comparing the results in entries 1, 3 and 4 with those in entries 11, 12 and 13, it is found that the regioselectivity of the arylation by aryl bromides in [bmim]PF_6 is actually better than those by aryl triflates in DMSO, although the reaction was always slower in the former. Thus, for example, the arylation of **1a** by **2a** in [bmim]PF_6 provided a β/γ ratio of 70/30 (entry 1) with >99% conversion after 12 h reaction time, whilst the corresponding triflate **1e** gave a β/γ ratio of 65/35 (including 3% of the linear alcohol) in 69% conversion after 4 h (entry 11); the difference is more significant in the case of the arylation of **2d** by **1e** (entry 4 versus entry 13). Furthermore, alcohols were observed in the case of the triflate, possibly due to uncompleted isomerization to the ketones under the conditions employed. It is noted that aryl triflates are generally base sensitive, thermally labile, and rarely commercially available.

3. Conclusions

It could be concluded that the regioselectivity of the Heck arylation of α-substituted allylic alcohols is significantly affected by both solvents and the properties of ligands. Pd-DPPP

catalysis in ionic liquids is a best choice for the formation of branched arylated products, and the results obtained in this work represents the best β/γ ratios reported to date in the literature. The steric properties of allylic alcohols also have important impacts on the regiocontrol; increasing the bulkiness of the allylic alcohol resulted in a decreased β/γ ratio either in ionic liquids with aryl bromides or in DMSO with an aryl triflate.

4. Experimental

4.1. Materials and apparatus

All chemicals used were purchased from Aldrich or Lancaster and used as received. Ionic liquids were prepared according to the literature method [18], and dried *in vacuo* at 70 °C for 5 h before use. All reactions were carried out under a nitrogen atmosphere. Chromatographic purifications were performed on silica gel (mesh 230–400) by the flash technique. ^{1}H and ^{13}C NMR spectra were recorded on a Gemini 400 spectrometer at 400 MHz (^{1}H) and 100 MHz (^{13}C) in ppm with reference to TMS internal standard in $CDCl_3$ or acetone-d_6. Mass spectra were obtained by chemical ionization (CI).

4.2. General procedure for the Heck arylation

A procedure for the arylation of but-1-ene-3-ol (**2a**) with 2-bromonaphthalene (**1a**) in [bmim]PF_6 is described as an example. The other reactions followed the same procedure. An oven-dried, screw-capped reaction tube containing a stir bar was charged with **1a** (1.0 mmol), $Pd(OAc)_2$ (4 mol%), DPPP (8 mol%), [bmim]PF_6 (1 mL) under nitrogen at room temperature. Following degassing three times, **2a** (1.2 mmol) and NEt_3 (1.5 mmol) were injected sequentially under nitrogen. The mixture was heated at 115 °C and stirred at this temperature for 12 h. The reaction mixture was then cooled to room temperature. The product was extracted with diethyl ether (5 × 10 mL). The combined organic layer was washed with water to remove the byproduct salt, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. After ^{1}H NMR analysis for measuring the conversion, which was >99%, the crude product was purified by flash chromatography on silica gel using a mixture of ethyl acetate and hexane (1:3–1:0) as eluant to give **3aa** (110 mg, 0.55 mmol) as a light yellow solid in 55% yield, and **4aa** (44 mg, 0.22 mmol) as a light yellow solid in 22% yield.

4.3. Characterization of products

4.3.1. 3-(2-Naphthyl)-but-3-en-2-ol (*3aa*)

^{1}H NMR ($CDCl_3$): 7.80 (m, 4H), 7.52 (dd, J = 8.54, 1.84 Hz, 1H), 7.40 (m, 2H), 5.45 (s, 1H), 5.40 (s, 1H), 4.93 (quartet, J = 6.44 Hz, 1H), 1.35 (d, J = 6.44 Hz, 3H). ^{13}C NMR ($CDCl_3$): 153.43, 137.69, 133.78, 133.32, 128.79, 128.57, 128.37, 126.64, 125.92, 125.71, 112.52, 69.97, 23.14. MS: CI, *m/z* 216 $[M+NH_4]^+$ (1 0 0), 199 $[M+H]^+$ (20), 198 M^+ (32); HRMS, calcd. for $C_{14}H_{18}ON$ ($[M+NH_4]^+$): 216.1388; found 216.1390.

4.3.2. 4-(2-Naphthyl)-butan-2-one (*4aa*)

^{1}H NMR ($CDCl_3$): 7.75 (m, 4H), 7.42 (m, 1H), 7.31 (dd, J = 8.46, 1.76 Hz, 1H), 7.70 (dd, J = 8.58, 1.76 Hz, 1H), 3.50 (t, J = 4.03 Hz, 2H), 2.83 (t, J = 4.03 Hz, 2H), 2.13 (s, 3H). ^{13}C NMR ($CDCl_3$): 208.16, 138.92, 134.04, 132.52, 128.51, 128.02, 127.86, 127.43, 127.28, 126.80, 126.42, 45.45, 30.48, 30.18. MS: CI, *m/z* 216 $[M+NH_4]^+$ (1 0 0), 199 $[M+H]^+$ (6), 198 M^+ (9); HRMS, calcd. for $C_{14}H_{18}ON$ ($[M+H]^+$): 216.1388; found 216.1388.

4.3.3. 2-Methyl-3-(2-naphthyl)-but-3-en-2-ol (*3ab*)

^{1}H NMR ($CDCl_3$): 7.74 (m, 2H), 7.67 (s, 2H), 7.38 (m, 3H), 5.43 (d, J = 1.5 Hz, 1H), 4.49 (d, J = 1.5 Hz, 1H), 1.46 (s, 6H). ^{13}C NMR ($CDCl_3$): 156.06, 138.08, 132.02, 131.43, 126.97, 126.54, 126.38, 126.15, 125.07, 124.79, 111.98, 72.17, 28.82. MS: CI, *m/z* 230 $[M+NH_4]^+$ (1 0 0), 213 $[M+H]^+$, 212 M^+; HRMS, calcd. for $C_{15}H_{20}ON$ ($[M+NH_4]^+$): 230.1545; found 230.1539.

4.3.4. (E)-2-Methyl-4-(2-naphthyl)-but-3-en-2-ol (*5ab*)

^{1}H NMR ($CDCl_3$): 7.71 (m, 3H), 7.66 (s, 1H), 7.51 (dd, J = 8.57, 1.75 Hz, 1H), 7.36 (m, 2H), 6.67 (d, J = 16.06 Hz, 1H), 6.40 (d, J = 16.06 Hz, 1H), 1.38 (s, 6H). ^{13}C NMR ($CDCl_3$): 136.94, 133.42, 132.66, 131.94, 127.16, 126.90, 126.62, 125.56, 125.25, 125.21, 124.74, 122.67, 70.06, 28.90. MS: CI, *m/z* 230 $[M+NH_4]^+$ (1 0 0), 213 $[M+H]^+$, 212 M^+; HRMS, calcd. for $C_{15}H_{20}NO$ ($[M+NH_4]^+$): 230.1545; found 230.1544.

4.3.5. 2-(2-Naphthyl)-1-phenylprop-2-en-1-ol (*3ac*)

^{1}H NMR ($CDCl_3$): 7.69 (m, 4H), 7.43 (dd, J = 8.6, 2.0 Hz, 2H), 7.39 (m, 2H), 7.20 (m, 4H), 5.75 (s, 1H), 5.59 (s, 1H), 5.53 (s, 1H). ^{13}C NMR ($CDCl_3$): 150.82, 142.40, 133.67, 133.28, 128.91, 128.65, 128.26, 128.20, 127.96, 126.41, 125.76, 124.17, 115.00, 76.40.

4.3.6. 3-(2-Naphthyl)-1-phenylpropan-1-one (*4ac*)

^{1}H NMR ($CDCl_3$): 7.96 (m, 2H), 7.80-7.76 (m, 3H), 7.68 (s, 1H), 7.55 (m, 1H), 7.46–7.37 (m, 5H), 3.38 (t, J = 7.79 Hz, 2H), 3.23 (t, J = 7.63 Hz, 2H). ^{13}C NMR ($CDCl_3$): 199.52, 139.19, 137.33, 134.06, 133.44, 132.53, 129.00, 128.52, 128.45, 128.01, 127.85, 127.55, 126.89, 126.40, 125.70, 40.73, 30.69.

4.3.7. 3-(2-Naphthyl)-2-phenylbut-3-en-2-ol (*3ad*)

^{1}H NMR ($CDCl_3$): 7.74–7.54 (m, 5H), 7.41–7.21 (m, 6H), 7.09 (dd, J = 8.0, 1.7 Hz, 1H), 5.63 (d, J = 1.1 Hz, 1H), 5.38 (d, J = 1.1 Hz, 1H), 1.77 (s, 3H). ^{13}C NMR ($CDCl_3$): 154.97, 137.81, 132.93, 132.57, 127.89, 128.25, 128.09, 127.31, 126.99, 126.85, 126.00, 125.90, 125.65, 125.17, 114.91, 30.11.

4.3.8. (E)-4-(2-Naphthyl)-2-phenylbut-3-en-2-ol (*5ad*)

^{1}H NMR ($CDCl_3$): 7.65 (m, 4H), 7.47 (m, 3H), 7.33 (m, 2H), 7.3–7.1 (m, 3H), 6.70 (d, J = 16.0 Hz, 1H), 6.53 (d, J = 16.0 Hz, 1H), 1.78 (s, 3H). ^{13}C NMR ($CDCl_3$): 145.66, 135.80, 133.20, 132.60, 132.00, 127.31, 126.91, 126.62, 126.07, 125.94, 125.52, 125.22, 124.82, 124.28, 122.69, 29.06.

*4.3.9. 3-(1-Naphthyl)but-3-en-2-ol (**3ba**)*

^{1}H NMR ($CDCl_3$): 8.01 (m, 1H), 7.82 (m, 1H), 7.76 (d, J = 6.6 Hz, 1H), 7.44 (m, 1H), 7.42 (d, J = 3.5 Hz, 1H), 7.29 (d, J = 6.6 Hz, 2H), 5.69 (d, J = 1.0 Hz, 1H), 5.15 (d, J = 1.0 Hz, 1H), 4.67 (m, 1H), 1.24 (d, J = 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$): 152.62, 138.97, 134.21, 132.34, 128.09, 127.45, 126.35, 126.21, 125.73, 114.70, 71.70, 22.80. MS: CI, *m/z* 216 $[M+NH_4]^+$, 199 $[M+H]^+$, 198 $[M]^+$; HRMS, calcd. for $C_{14}H_{18}NO$ ($[M+NH_4]^+$): 216.1388; found 216.1391.

*4.3.10. 4-(1-Naphthyl)-butan-2-one (**4ba**)*

^{1}H NMR $CDCl_3$): 8.00 (d, J = 8.2 Hz, 1H), 7.85 (dd, J = 8.0, 1.6 Hz, 1H), 7.71 (d, J = 8.1 Hz, 1H), 7.50 (m, 2H), 7.39 (t, J = 8.1 Hz, 1H), 7.33 (m, 1H), 3.36 (t, J = 7.5 Hz, 2H), 2.88 (t, J = 7.5 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$): 208.20, 137.43, 134.33, 132.01, 129.29, 127.35, 126.41, 126.36, 125.97, 125.96, 123.80, 44.85, 30.43, 27.15. MS: CI, *m/z* 216 $[M+NH_4]^+$, 199 $[M+H]^+$, 198 $[M]^+$; HRMS, calcd. for $C_{14}H_{18}NO$ ($[M+NH_4]^+$): 216.1388; found 216.1388.

*4.3.11. 2-(1-Naphthyl)-1-phenylprop-2-en-1-ol (**3bc**)*

^{1}H NMR ($CDCl_3$): 7.79 (m, 4H), 7.63–7.60 (m, 2H), 7.33 (m, 4H), 7.24 (m, 2H), 5.75 (s, 1H), 5.29 (s, 1H), 5.23 (s, 1H). ^{13}C NMR ($CDCl_3$): 150.64, 137.06, 133.00, 131.58, 128.99, 128.88, 128.11, 126.86, 126.79, 125.43, 125.01, 112.39, 64.17. MS: CI, *m/z* 278 $[M+NH_4]^+$, 261 $[M+H]^+$, 260 M^+; HRMS, calcd. for $C_{19}H_{20}NO$ ($[M+NH_4]^+$) 278.1545; found 278.1546.

*4.3.12. 3-(1-Naphthyl)-1-phenylpropan-1-one (**4bc**)*

^{1}H NMR ($CDCl_3$): 8.05 (d, J = 8.00 Hz, 1H), 7.95 (m, 4H), 7.86 (d, J = 9.36 Hz, 1 H), 7.45 (m, 1H), 7.40–7.56 (m, 5H), 3.53 (t, J = 8.3 Hz, 2H), 3.42 (t, J = 8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$): 202.5 (d, J = 155.3 Hz), 139.83, 139.40, 139.28, 136.41, 135.57, 135.33, 134.16, 131.40, 131.05, 130.46, 129.47, 128.59, 128.10, 125.98, 42.20, 34.24. MS: CI, *m/z* 278 $[M+NH_4]^+$, 261 $[M+H]^+$, 260 M^+, 243 $[M–OH]^+$; HRMS, calcd. for $C_{19}H_{17}O$ ($[M+H]^+$): 261.1073; found 261.1072.

*4.3.13. 1-(4-(3-Hydroxybut-1-en-2-yl)phenyl)ethanone (**3ca**)*

^{1}H NMR ($CDCl_3$): 7.40 (d, J = 8.50 Hz, 2H), 7.30 (m, 2H), 5.40 (s, 1H), 5.30 (s, 1H), 4.80 (m, 1H), 2.17 (s, 3H), 1.35 (d, J = 6.36 Hz, 3H). ^{13}C NMR ($CDCl_3$, δ_{ppm}): 198.18, 148.13, 143.0, 136.0, 129.10, 111.8, 75.8, 29.07, 20.87.

*4.3.14. 4-(4-Acetylphenyl)butan-2-one (**4ca**)*

^{1}H NMR ($CDCl_3$): 7.88 (d, J = 8.43 Hz, 2H), 7.28 (d, J = 8.42 Hz, 2H), 2.95 (t, J = 7.46 Hz, 2H), 2.80 (t, J = 7.46 Hz, 2H), 2.57 (s, 3H), 2.14 (s, 3H). ^{13}C NMR ($CDCl_3$): 208.48, 198.03, 147.18, 135.75, 129.10, 44.84, 30.39, 29.97, 26.87.

*4.3.15. 1-(4-(1-Hydroxy-1-phenylprop-2-en-2-yl)phenyl) ethanone (**3cc**)*

^{1}H NMR ($CDCl_3$): 7.81 (d, J = 8.59 Hz, 2H), 7.40 (d, J = 8.60 Hz, 2H), 7.34 (m, 2H), 7.29 (m, 3H), 5.70 (s, 1H), 5.60 (s, 1H), 5.58 (s, 1H), 2.55 (s, 3H). ^{13}C NMR ($CDCl_3$): 197.76, 149.50, 144.15, 141.47, 136.08, 129.78, 128.12, 115.3, 78.60, 26.53. MS: CI, *m/z* 270 $[M+NH_4]^+$, 253 $[M+H]^+$, 252 M^+; HRMS, calcd. for $C_{17}H_{17}O_2$ ($[M+H]^+$): 253.1229, found 253.1229.

*4.3.16. 3-(4-Acetylphenyl)-1-phenylpropan-1-one (**4cc**)*

^{1}H NMR ($CDCl_3$): 7.95 (d, J = 8.18 Hz, 2H), 7.90 (d, J = 8.27 Hz, 2H), 7.57 (t, J = 1.19 Hz, 1H), 7.46 (t, J = 7.79 Hz, 2H), 7.35 (d, J = 8.58 Hz, 2H), 3.33 (t, J = 7.30 Hz, 2H), 3.14 (t, J = 7.30 Hz, 2H), 2.90 (s, 3H). ^{13}C NMR ($CDCl_3$): 198.62, 197.75, 147.09, 135.70, 135.34, 133.23, 128.68, 128.02, 39.73, 29.98, 26.57. MS: CI, *m/z* 270 $[M+NH_4]^+$, 253 $[M+H]^+$, 252 M^+; HRMS, calcd. for $C_{17}H_{17}O_2$ ($[M+H]^+$): 253.1228, found 253.1227.

*4.3.17. 4-(1-Hydroxy-1-phenylprop-2-en-2-yl)benzaldehyde (**3dc**)*

^{1}H NMR ($CDCl_3$): 9.96 (s, 1H), 7.76 (d, J = 8.27 Hz, 2H), 7.47 (d, J = 8.43 Hz, 2H), 7.40–7.26 (m, 5H), 5.73 (m, 1H), 5.65 (d, J = 7.79 Hz, 2H). ^{13}C NMR ($CDCl_3$): 191.81, 149.46, 145.56, 141.33, 135.45, 129.69, 128.65, 128.09, 127.68, 126.91, 116.30. MS: CI, *m/z* 256 $[M+NH_4]^+$, 239 $[M+H]^+$, 238 M^+; HRMS, calcd. for $C_{16}H_{18}O_2N$ ($[M+NH_4]^+$): 256.1337; found 256.1334.

*4.3.18. 4-(3-Oxo-3-phenylpropyl)benzaldehyde (**4dc**)*

^{1}H NMR ($CDCl_3$): 9.98 (s, 1H), 7.95 (d, J = 7.95 Hz, 2H), 7.82 (d, J = 7.95 Hz, 2H), 7.55 (t, J = 7.85 Hz, 1H), 7.46 (q, J = 7.79 Hz, 4H), 3.35 (t, J = 7.50 Hz, 2H), 3.17 (t, J = 7.47 Hz). ^{13}C NMR ($CDCl_3$): 197.27, 190.70, 147.55, 135.46, 133.57, 132.08, 128.88, 127.99, 127.49, 126.82, 38.44, 28.97. MS: CI, *m/z* 256 $[M+NH_4]^+$, 239 $[M+H]^+$, 238 M^+; HRMS, calcd. for $C_{16}H_{15}O_2$ ($[M+H]^+$): 239.1072; found 239.1074.

*4.3.19. (E)-4-(2-Naphthyl)-but-3-en-2-ol (**5ea**)*

^{1}H NMR ($CDCl_3$): 7.75 (m, 4H), 7.58 (dd, J = 1.83, 8.54 Hz, 1H), 7.42 (m, 2H), 6.73 (d, J = 15.90 Hz, 1H), 6.38 (dd, J = 15.90, 6.40 Hz, 1H), 4.55 (quint, J = 5.56 Hz, 1H), 1.41 (d, J = 5.56 Hz, 3H). ^{13}C NMR ($CDCl_3$): 134.39, 133.44, 129.94, 128.61, 128.34, 128.05, 126.79, 126.66, 126.27, 124.01, 69.40, 23.88. MS: CI, *m/z* 216 $[M+NH_4]^+$, 198 M^+, 181 $[M–OH]^-$ (1 0 0).

The compounds **3ae** and **5ae** could not be isolated from the reaction mixture and were characterized only by ^{1}H NMR.

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