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Nickel-Catalyzed Reductive Allylation of Aldehydes with Allyl Acetates

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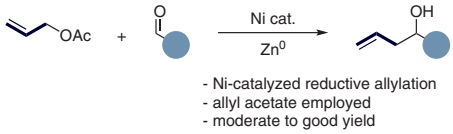

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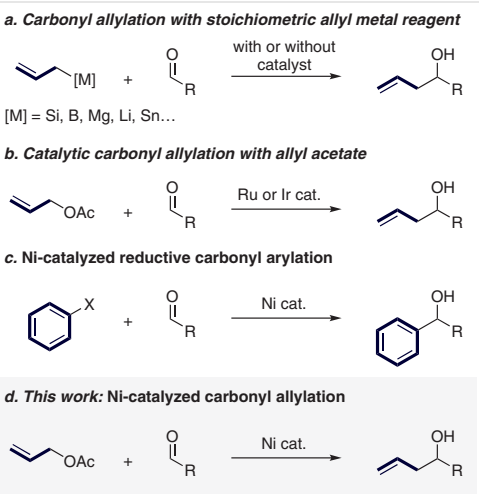
Abstract Carbonyl allylation reactions constitute an important step in the formation of carbon–carbon reactions, and involve various related reactions that chiefly use allylmetal reagents. This report presents a nickel-catalyzed carbonyl allylation reaction using allyl acetate, which produces homoallyl alcohols in moderate to good yields, as an efficient methodology under reductive coupling conditions.

Key words reductive allylation, nickel complex, allyl acetate, carbonyl addition, transition-metal catalysis

The formation of carbon–carbon bonds by the addition of carbon nucleophiles on carbonyl is important for organic synthesis.[1,2] In particular, the allylation of carbonyls using allylmetal reagents is now universally used and accepted as one of the most reliable methods for the formation of C–C bonds.[3] This system allows the further possible conversion of the introduced allylic moiety, due to readily transformable double bonds. Consequently, a remarkable method for carbonyl allylation reactions using allylic metal reagents has been developed (Scheme 1a).[4–6] Generally, the preparation of allylmetal reagents involves the multistep combination of an allylic precursor (allyl halide, carbonate, or acetate) with a stoichiometric amount of the organometallic reagent.[7] Although the catalytic allylation of carbonyls with the in situ transformation of the allylic precursor into an allylmetal reagent has also been developed to avoid the preparation of a discrete organometallic reagent, unstable organometallic reagents are required.[8] Therefore, there has been a demand for green and sustainable chemistry with simple methodology without the use of a preformed organometallic reagent.



Scheme 1 Carbonyl allylation chemistry

In 1989, Tsuji et al. reported ruthenium-catalyzed carbonyl allylation using allyl acetate.[9] Their pioneering work inspired the development of transition-metal-catalyzed carbonyl allylation reactions without the use of stoichiometric amounts of organometallic reagents. Over the past few decades, the topic of catalytic reactions has been extensively studied, and many methodologies have been proposed (Scheme 1b). Accordingly, Krische et al. developed iridium-catalyzed carbonyl allylation protocols in which allyl acetate serves as a precursor to allylmetal nucleophiles.[10,11] Moreover, Denmark et al. independently developed a methodology for Ru-catalyzed carbonyl allylation using allyl acetate.[12] These procedures provide simple and efficient methodologies for the allylation of aliphatic and aromatic aldehydes.

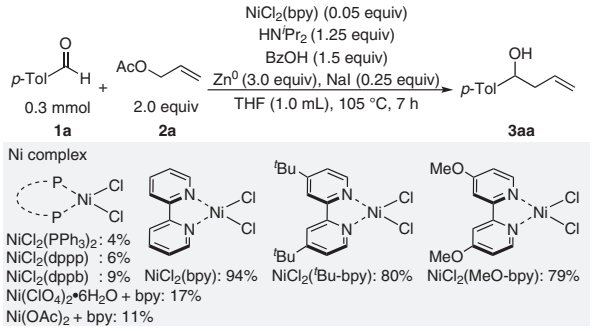
Conversely, we have previously developed a reductive carbonyl addition reaction of aldehydes with aryl halides catalyzed by a nickel complex (Scheme 1c).[13] In the original report, the aryl halide transforms into a transient nucleophile under Ni catalysis. Driven by the authors' interest in carbonyl addition chemistry, the research focused on the synthesis of homoallyl alcohols by the reaction of carbonyl with allyl acetate via Ni catalysis. The reported Ni-catalyzed reductive coupling reactions are now one of the fundamental approaches toward coupling reactions between two electrophiles.[14] However, the proposal of a methodology for reductive carbonyl allylation using allyl acetate catalyzed by Ni complexes is unprecedented. Therefore, this study reports the first example of a Ni-catalyzed reductive carbonyl allylation reaction of aldehydes with allyl acetate (Scheme 1d).

First, this study examined the reaction of *p*-tolualdehyde (**1a**) with allyl acetate (**2a**) (Table 1).[15] Various Ni complexes bearing phosphine ligands, such as $NiCl_2(PPh_3)_2$, $NiCl_2(dppp)_2$, and $NiCl_2(dppb)_2$, $Ni(ClO_4)_2{\cdot}6H_2O$ or $NiCl_2(dme)_2$ with bipyridyl, and Ni complexes bearing nitrogen ligands, such as $NiCl_2(bpy)$, $NiCl_2(^tBu\text{-}bpy)$, and $NiCl_2(MeO\text{-}bpy)$, were screened. The expected allylation reaction was confirmed to occur at 105 °C in a pressure tube when aldehyde **1a** was treated with allyl acetate (**2a**) in the presence of diisopropylamine, benzoic acid, Zn dust, and sodium iodide in tetrahydrofuran as solvent. The best catalyst for this allylation was the Ni complex bearing bipyridyl, namely $[NiCl_2(bpy)_2]$, which provided the desired product **3aa** in an isolated yield of 88% (entry 1). Inferior results were obtained with other metal reductants, which included Mn, Cr, and Mg (entries 2–4). These metal reductants were inefficient in supplying the required allylation product. The use of other amines, such as EtN^iPr_2 and pyridine, reduced the reaction efficiency, providing product **3aa** in 18% and 31% yield, respectively (entries 5 and 6). The suitable selection of the acid was critical for this reaction, as no product formation occurred, with the recovery of the starting materials, when *p*-toluenesulfonic acid or trifluoroacetic acid was used (entries 7 and 8). Solvent screening showed that the allylation reaction tends to be accelerated by an ethereal solvent (entries 9 and 10). Further screening suggested that both the Ni complex and the Zn reductant are critical in this reaction (entries 11 and 12).

Next, the investigation assessed the scope of the reaction. A combination of various substituted benzaldehydes **1** with allyl acetate (**2a**) provided the desired allylation products **3** (Scheme 2). Alkyl (**1a–c**), unsubstituted (**1d**), and alkoxy-substituted (**1e**) benzaldehydes transformed into the corresponding homoallyl alcohols **3** under optimal conditions in yields of 66–88%. This method was also successful with benzaldehydes bearing *m*- (**1b**) and *o*-methyl (**1c**) substituents. Although synthetically modifiable halo-substituted benzaldehydes **1f–h** were used under the optimal conditions to produce both fluoro- and chloro-containing products **3fa** and **3ga** in moderate yields, the bromo-substituted benzaldehyde did not function as a good substrate under the same conditions.[16] Unfortunately, the reactions employing aldehydes bearing electron-withdrawing groups, such as the cyano (**3i**) and nitro groups (**3j**), resulted in a significant reduction in yield. The protocol was successful with 1-naphthaldehyde (**1k**), 2-naphthaldehyde (**1l**), and 2-furaldehyde (**1m**), affording **3ka**, **3la**, and **3ma** in yields of 60%, 65%, and 62%, respectively.

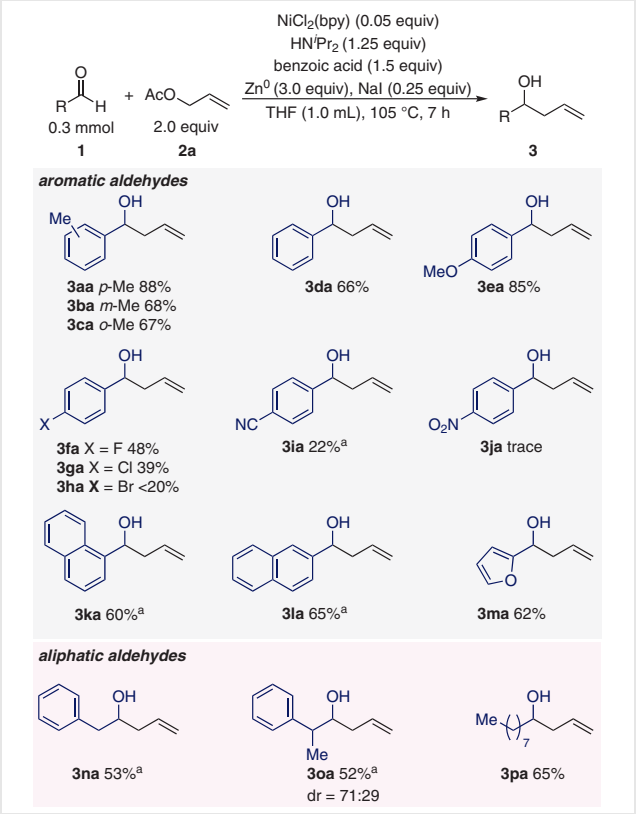
Then, to further assess the scope of the substrates, the same approach was applied to aliphatic aldehydes (Scheme 2). Under optimal conditions, phenylacetaldehyde (**1n**) provided a good yield of the corresponding allylation product **3na**. When the reaction was performed using 2-phenylpropanal (**1o**) with allyl acetate, the corresponding homoallyl alcohol was obtained in 52% yield with 71:29 *syn* diastereoselectivity. This finding confirmed that the carbonyl addition step proceeded through a Felkin–Anh-type addition model.[17] The linear aliphatic-chain aldehyde nonanal (**1p**)

Table 1 Optimization of Reaction Conditions



Entry	Deviation from standard conditions	Yield of **3aa** (%)[a]
1	standard conditions	94 (88)
2	Mn instead of Zn	0
3	Cr instead of Zn	0
4	Mg instead of Zn	0
5	EtN^iPr_2 instead of HN^iPr_2	18
6	pyridine instead of HN^iPr_2	31
7	PTSA instead of BzOH	0
8	TFA instead of BzOH	0
9	CPME[b] instead of THF	63
10	toluene instead of THF	58
11	without $NiCl_2(bpy)$	0
12	without Zn dust	0

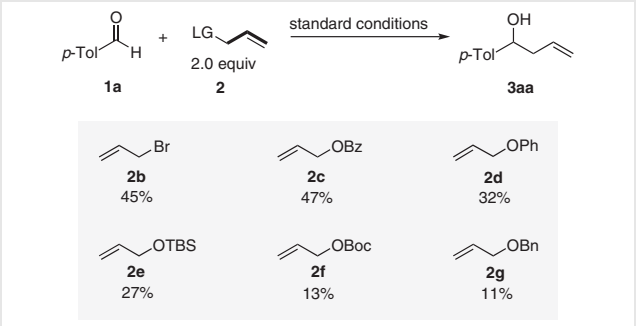
[a] Yields were determined by ^1H NMR analysis of the crude reaction mixture using 1,1,2,2-tetrachloroethane as an internal standard. The number in parentheses is the isolated yield.
[b] CPME = cyclopentyl methyl ether.



Scheme 2 Evaluation of aldehydes **1**. [a] Reaction performed at 115 °C.

also acted as a good substrate for this allylation reaction, providing the corresponding product **3pa** in 65% yield, without the formation of any byproducts.[18]

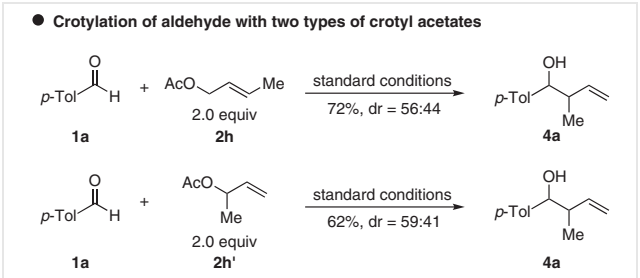
Following the investigation into the substrate scope of aldehydes, the study then examined the variation in allyl sources **2** (Scheme 3).[19] The use of allyl bromide (**2b**) instead of allyl acetate provided the corresponding product **3aa**, although the yield was significantly reduced to 45%. Additionally, other allyl alcohol-bearing protecting groups were also investigated. When allyl benzoate (**2c**) was used as an allyl reagent for the reaction, 47% yield of homoallyl alcohol **3aa** was produced. With allyl phenyl ether (**2d**) and *tert*-butyldimethylsilyl- and *tert*-butoxycarbonyl-protected



Scheme 3 Evaluation of allyl sources

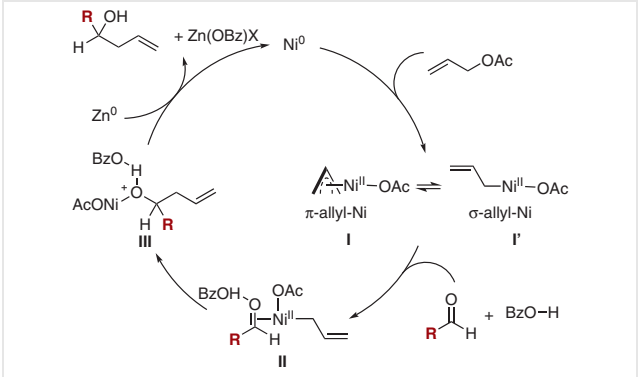
allyl alcohols **2e** and **2f**, the reaction efficiency was significantly reduced. Surprisingly, a benzyl allyl ether (**2g**) also acted as an allyl source under the same reaction conditions.

When the evaluation of substrates for the allylation reaction was completed, the use of crotyl acetate as allylation reagent was then investigated. Control experiments were conducted to identify an intermediate for the reaction. When the crotylation reactions of aldehyde **1a** using the two possible crotyl donors (*E*)-but-2-enyl acetate (**2h**) and but-3-en-2-yl acetate (**2h'**) were investigated, good yields of the same product **4a** were obtained with similar diastereoselectivities under the optimal conditions (Scheme 4). The results indicate that the developed reaction is initiated by the formation of a π-allyl Ni complex from the in situ generated Ni^0 species with allyl acetate; the resulting Ni complex is in equilibrium with the π-allyl and the σ-allyl complexes.[20] Moreover, the observed diastereoselectivity of the reaction indicated that possible intermediates such as η^1-(*E*)-crotyl–Ni and (*Z*)-crotyl–Ni were in equilibrium under the catalytic cycle (Scheme 4a vs 4b).[14g]



Scheme 4 Control experiments

Based on these experiments and the previously proposed reaction mechanism, a plausible reaction mechanism (Scheme 5) is presented. The reduction of Ni^{II} with Zn^0 forms Ni^0, and the oxidative addition of allyl acetate forms π-allyl–Ni^{II} intermediate **I** and σ-allyl–Ni^{II} intermediate **I'**. The generated **I** interacts with aldehyde and acid H–X to form a reactive intermediate **II**. The 1,2-migratory insertion of the allyl group into the aldehyde could form an alkoxy–Ni^{II}



Scheme 5 Plausible reaction mechanism

intermediate **III**. Although there was evidence of trace formation of the corresponding ketone side product, which is generated by β-elimination of the alkoxy–Ni^{II} intermediate, a route for the direct release of the product from **II** cannot be excluded. Finally, the catalytic cycle is completed by the alkoxy exchange reaction of **III** and the reduction of Ni^{II}.[21]

In summary, this research developed an efficient methodology for the allylation of carbonyl using allyl acetate under conditions of reductive coupling. Further laboratory-based investigations into the mechanism and the development of an asymmetric version of the methodology are currently underway.

All dry solvents were obtained from Kanto Kagaku Co., Ltd. and Wako Pure Chemical Industries, Ltd. Other chemicals used were of reagent grade and were obtained from Tokyo Kasei Kogyo Co., Ltd., Wako Pure Chemical Industries, Ltd., Nacalai Tesque, and Sigma Aldrich Co., Ltd. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were obtained on a JEOL AL 400 instrument at room temperature of samples in $CDCl_3$ as a solvent (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR). Chemical shifts (δ) are expressed in parts per million and are internally referenced [δ = 0.00 (TMS) for ^{1}H NMR and δ = 77.0 ($CDCl_3$) for ^{13}C NMR]. TLC was carried out on precoated plates of silica gel (Merck, silica gel F-254, 0.5 mm). Subsequent to elution, plates were visualized using UV radiation (254 nm) of Handy UV lamp SLUV-4 254 nm (AS ONE Co.) Preparative TLC (PTLC) was carried out on precoated plates of silica gel (Merck, silica gel F-254, 0.5 mm). Flash column chromatography was performed on Kanto silica gel 60N (Spherical, Neutral, 40–50 mm) and on a Biotage Isolera® automated chromatography system using normal phase cartridges with YMC*GEL SIL (YMC Co., Ltd., 25 μm).

1-*p*-Tolylbut-3-en-1-ol (3aa); Typical Procedure[22]

A screw-capped test tube (16.5 cm × 1.5 cm) containing a mixture of *p*-tolualdehyde (**1a**; 35.4 μL, 0.3 mmol), allyl acetate (**2a**; 64.5 μL, 0.6 mmol, 2.0 equiv), $NiCl_2$(bpy) (4.3 mg, 0.015 mmol, 0.05 equiv), BzOH (54.9 mg, 0.45 mmol, 1.5 equiv), NaI (11.2 mg, 0.075 mmol, 0.25 equiv), Zn^0 (58.8 mg, 0.9 mmol, 3.0 equiv), and HN^iPr_2 (52.7 μL, 0.375 mmol, 1.25 equiv) in anhydrous THF (1.0 mL) was degassed by freeze–pump–thaw cycles (3×) and backfilled with argon. The resulting solution was stirred at 105 °C for 7 h. The solution was filtrated through a Celite pad, which was washed with chloroform several times, and concentrated *in vacuo*. The resulting mixture was purified by flash column chromatography (silica gel, *n*-hexane/EtOAc, 10:1) to give **3aa**.

Yield: 42.8 mg (0.26 mmol, 88%); colorless oil.

TLC (silica gel): R_f = 0.33 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 7.3 Hz, 2 H), 7.16 (d, *J* = 7.8 Hz, 2 H), 5.87–5.76 (m, 1 H), 5.19–5.12 (m, 2 H), 4.71 (t, *J* = 6.4 Hz, 3 H), 2.52–2.49 (m, 2 H), 2.35 (s, 3 H), 1.97 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.9, 137.2, 134.6, 129.1, 125.8, 118.3, 73.2, 43.8, 21.1.

1-*m*-Tolylbut-3-en-1-ol (3ba)[23]

Yield: 33.1 mg (0.20 mmol, 68%); colorless oil.

TLC (silica gel): R_f = 0.33 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.08 (m, 4 H), 5.86–5.76 (m, 1 H), 5.19–5.13 (m, 2 H), 4.71–4.68 (m, 1 H), 2.52–2.46 (m, 2 H), 2.36 (s, 3 H), 2.03 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.9, 138.2, 134.7, 128.4, 128.4, 126.6, 123.0, 118.5, 73.4, 44.0, 21.6.

1-*o*-Tolylbut-3-en-1-ol (3ca)[24]

Yield: 32.6 mg (0.20 mmol, 67%); colorless oil.

TLC (silica gel): R_f = 0.33 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 7.8 Hz, 1 H), 7.25–7.12 (m, 3 H), 5.91–5.81 (m, 1 H), 5.21–5.14 (m, 2 H), 4.98 (m, 1 H), 2.54–2.39 (m, 2 H) 2.34 (s, 3 H), 1.96 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.9, 134.7, 134.3, 130.3, 127.2, 126.2, 125.1, 118.3, 69.6, 42.6, 19.0.

1-Phenylbut-3-en-1ol (3da)[24]

Yield: 29.3 mg (0.20 mmol, 66%); colorless oil.

TLC (silica gel): R_f = 0.33 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.27 (m, 5 H), 5.86–5.78 (m, 1 H), 5.20–5.14 (m, 2 H), 4.75 (ddd, J = 8.0, 4.6, 2.9 Hz, 1 H), 2.47–2.57 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.8, 134.4, 128.4, 127.6, 125.8, 118.5, 73.3, 43.9.

1-(4-Methoxyphenyl)but-3-en-1-ol (3ea)[24]

Yield: 45.4 mg (0.26 mmol, 85%); colorless oil.

TLC (silica gel): R_f = 0.17 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 8.7 Hz, 2 H), 6.89 (d, *J* = 8.7 Hz, 2 H), 5.85–5.75 (m, 1 H), 5.18–5.12 (m, 2 H), 4.69 (t, *J* = 6.4 Hz, 1 H), 3.81 (s, 3 H), 2.50 (t, *J* = 6.4 Hz, 2 H), 1.97 (s 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 136.0, 134.6 127.1, 118.3, 113.8, 72.9, 55.3, 43.8.

1-(4-Fluorophenyl)but-3-en-1-ol (3fa)[22]

Yield: 23.9 mg (0.14 mmol, 48%); colorless oil.

TLC (silica gel): R_f = 0.17 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.31 (m, 2 H), 7.05–7.02 (m, 2 H), 5.83–5.75 (m, 1 H), 5.18–5.15 (m 2 H), 4.74–4.71 (m, 1 H), 2.54–2.43 (m, 2 H), 2.05 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.1 (d, *J* = 245.9 Hz), 139.5 (d, *J* = 2.4 Hz), 134.1, 127.4 (d *J* = 8.4 Hz), 118.7, 115.2 (d, *J* = 21. 4 Hz), 72.6, 44.0.

1-(4-Chlorophenyl)but-3-en-1-ol (3ga)[22]

Yield: 21.3 mg (0.12 mmol, 39%); colorless oil.

TLC (silica gel): R_f = 0.17 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.29 (m, 4 H), 5.84–5.73 (m, 1 H), 5.19–5.15 (m, 2 H), 4.75–4.71 (m, 2 H), 2.55–2.42 (m, 2 H), 2.05 (d, *J* = 3.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.3, 134.0, 133.2, 128.5, 127.2, 118.9, 72.5, 43.9.

4-(1-Hydroxybut-3-enyl)benzonitrile (3ia)[22]

Yield: 11.4 mg (0.07 mmol, 22%); colorless oil.

TLC (silica gel): R_f = 0.10 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.0 Hz, 2 H), 7.48 (d, *J* = 8.0 Hz, 2 H), 5.82–5.74 (m, 1 H), 5.21–5.17 (m, 2 H), 4.83–4.80 (m, 1 H), 2.57–2.41 (m, 2 H), 2.15 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.0, 133.3, 132.3, 126.5, 119.6, 118.8, 111.2, 72.3, 43.9.

1-(1-Naphthyl)but-3-en-1-ol (3ka)[25]

Yield: 49.7 mg (0.18 mmol, 66%); colorless oil.

TLC (silica gel): R_f = 0.33 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 8.0 Hz, 1 H), 7.88 (d *J* = 7.8 Hz, 1 H), 7.79 (d, *J* = 8.2 Hz, 1 H), 7.68 (d, *J* = 7.3 Hz, 1 H), 7.55–7.47 (m, 3 H), 5.99–5.89 (m, 1 H), 5.56–5.54 (m, 1 H), 5.26–5.18 (m, 2 H), 2.80–2.57 (m, 2 H), 2.16 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.4, 134.8, 133.8, 130.2, 129.0, 128.0, 126.1, 125.5, 125.4, 123.0, 122.8, 118.4, 69.9, 42.8.

1-(2-Naphthyl)but-3-en-1-ol (3la)[25]

Yield: 53.8 mg (0.20 mmol, 65%); colorless oil.

TLC (silica gel): R_f = 0.20 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.71 (m, 4 H), 7.50–7.45 (m, 3 H), 5.88–5.80 (m, 1 H), 5.21–5.15 (m 2 H), 4.93–4.90 (m, 1 H), 2.60–2.58 (m, 2 H), 2.14 (s 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.2, 134.3, 133.2, 133.0, 128.2, 127.9, 127.8, 126.1, 125.8, 124.5, 123.9, 118.6, 73.3, 43.7.

1-(2-Furyl)but-3-en-1-ol (3ma)[22]

Yield: 25.7 mg (0.19 mmol, 62%); colorless oil.

TLC (silica gel): R_f = 0.20 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (m, 1 H), 6.35–6.33 (m, 1 H), 6.27–6.26 (m, 1 H), 5.87–5.77 (m, 1 H), 5.21–5.14 (m, 2 H), 4.78–4.74 (m, 1 H), 2.65–2.61 (m, 2 H), 2.02 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155,9 142.0, 133.7, 118.7, 110.1, 106.1, 66.9, 40.1.

1-Phenylpent-4-en-2-ol (3na)[26]

Yield: 25.8 mg (0.17 mmol, 53%); colorless oil.

TLC (silica gel): R_f = 0.33 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.22 (m, 5 H), 5.95–5.83 (m, 1 H), 5.18–5.15 (m, 2 H), 3.89 (m, 1 H), 2.85–2.71 (m, 2 H), 2.36–2.20 (m, 2 H), 1.68 (d, *J* = 2.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4, 134.7, 129.4, 128.5, 126.5, 118.2, 71.7, 43.3, 41.2.

2-Phenylhex-5-en-3-ol (3oa)[26]

52 % yield, 27.5 mg, 0.16 mmol, colorless oil.

TLC (silica gel): R_f = 0.40 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.20 (m, 5 H), 5.95–5.75 (m, 1 H), 5.16–5.08 (m, 2 H), 3.77–3.71 (m 2 H), 2.84–2.75 (m, 1 H), 2.23–1.99 (m, 2 H), 1.68 (m, 1 H) (mixture of diastereomers).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.5, 143.4, 135.2, 135.1, 128.6, 128.6, 128.5, 127.9, 126.8, 126.6, 118.3, 117.9, 75.1, 75.0, 45.7, 45.5, 39.6, 39.1, 17.8, 16.5 (mixture of diastereomers).

Dodec-1-en-4-ol (3pa)[27]

Yield: 35.9 mg (0.20 mmol, 65%); colorless oil.

TLC (silica gel): R_f = 0.50 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.87–5.80 (m, 1 H), 5.16–5.11 (m, 2 H), 3.67–3.61 (m, 1 H), 2.34–2.12 (m, 2 H), 1.63 (s, 1 H), 1.50–1.27 (m, 14 H), 0.88 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.9, 118.0, 70.7, 41.9, 36.8, 31.9, 29.64, 29.55, 29.2, 25.6, 22.7, 14.1.

2-Methyl-1-*p*-tolylbut-3-en-1-ol (4a)[28]

Yield: 38.0 mg (0.22 mmol, 72%); colorless oil.

TLC (silica gel): R_f = 0.50 (*n*-hexane/EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.14 (m, 4 H, *syn* and *anti*), 5.86–5.71 (m, 1 H, *syn* and *anti*), 5.23–5.17 (m, 2 H, *syn*), 5.08–5.03 (m, 1.6 H, *anti*), 4.58 (m, 1 H, *syn*), 4.32 (m, 0.8 H, *anti*), 2.62–2.54 (m, 1 H, *syn*), 2.52–2.44 (m, 0.8 H, *anti*), 2.35 (s, 3 H), 2.09 (d, *J* = 2.7 Hz, 0.8 H, *anti*), 1.86 (d, *J* = 3.6 Hz, 1 H, *syn*), 1.01 (d, *J* = 6.8 Hz, 3 H, *syn*), 0.86 (d, *J* = 6.4 Hz, 2.4 H, *anti*).

^{13}C NMR (100 MHz, $CDCl_3$): δ (*anti*) = 140.8, 139.6, 137.3, 128.9, 126.8, 116.7, 77.7, 46.3, 21.1, 14.1; δ (*syn*) = 140.4, 139.4, 137.0, 128.8, 126.4, 115.4, 77.2, 44.6, 21.1, 16.6.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1705961.

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