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Regioselective Rh-catalyzed hydroformylation of 1,1,3-trisubstituted allenes using BisDiazaPhos ligand

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Abstract

The efficient hydroformylation of 1,1,3-trisubstituted allenes is accomplished with low loadings of a Rh catalyst supported by a BisDiazaPhos (BDP) ligand. The ligand identity is key to achieving high regioselectivity, while the mild reaction conditions minimize competing isomerization and hydrogenation to produce β,ɤ-unsaturated aldehydes and their derivatives in excellent yields.

Introduction

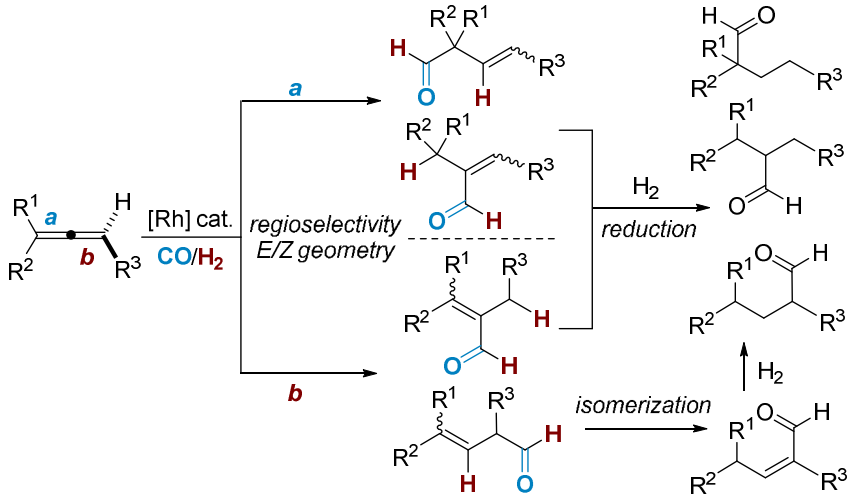
Rh-catalyzed hydroformylation is a powerful and atom-economical method to introduce valuable aldehyde functionality into a range of unsaturated substrates.[1] While hydroformylations of alkene[2,3] and 1,3-diene[4-7] substrates have been well-explored, only a handful of reports describe the analogous reactions of allenes. Over 40 years ago, Fell and Beutler reported a single example of the hydroformylation of a terminal allene catalyzed by $HRh(CO)(PPh_3)_3$ to produce complex mixtures of mono- and dialdehydes as products.[8] Nearly three decades after this initial report, Jiao et al. carried out computational studies of Co-catalyzed allene hydroformylation and surmised that addition of H to the central carbon of the allene to give an η^3–allyl complex is both

kinetically and thermodynamically preferred.[9] This prediction was borne out in 2015, when the Breit group demonstrated the hydroformylation of 1,1-disubstituted allenes using catalytic $Rh(acac)(CO)_2$ supported by a 6-DPPon ligand (Table 1) at 430 psi, producing β,γ–unsaturated aldehydes in good yields and varying *Z:E* ratios.[10]

The ability to employ trisubstituted allenes in hydroformylation reactions would yield valuable chiral β,γ-unsaturated aldehydes not accessible from typical 1,3-dienes or terminal allenes. Chiral β,γ-unsaturated aldehydes are useful building blocks that have been employed in strategies directed towards the total synthesis of diverse natural products that include premonensin, palmerolide C, matsone and the eicosanoids.[10] However, the additional substitution and chirality at the carbon in the α-position to the aldehyde makes these compounds particularly susceptible to migration of the double bond to place it into conjugation with the carbonyl group. This can render purification by standard techniques, such as flash column chromatography, untenable. Thus, mild methods that yield pure aldehydes under neutral conditions that minimize isomerization are highly desirable.

There are several challenges associated with the hydroformylation of trisubstituted allenes, due to multiple competing reaction pathways that can be envisaged (Scheme 1). For example, hydroformylation can occur at either of the two double bonds of the allene with two different regioselectivities to produce four different potential aldehyde products. In addition to issues of regioselectivity, competing alkene hydrogenation and secondary hydroformylation products must also be considered.[11] Finally, isomerization of the desired β,γ-unsaturated aldehydes to α,β-unsaturated aldehydes must be avoided. In this paper, we discuss our strategies to address these issues and achieve

high regioselectivity under mild reaction conditions, while minimizing competing isomerization and hydrogenation to produce β,ϒ-unsaturated aldehydes and their derivatives in excellent yields.



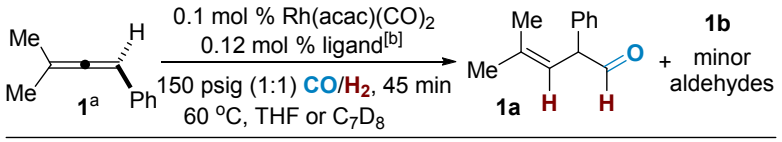
Scheme 1. Possible reaction pathways for trisubstituted allenes under hydroformylation conditions.

Results and Discussion

Initial optimization studies were carried out with the 1,1,3-trisubstituted allene **1** (Table 1), which is available in three simple steps from the corresponding aldehyde.[12,13] A selection of phosphine-based ligands previously demonstrated to promote the hydroformylation of alkenes and terminal allenes were tested.[14,15] The ligands 6-DPPon, *i*Pr-DuPhos, Ph-BPE and BINAP all failed to yield significant conversion to aldehyde products. Limited conversion to the desired **1a** was achieved using the (*R,R*)-QuinoxP* and (+)-DIOP ligands (entries 6-7), although small amounts of minor aldehydes were also observed. Unique among the tested ligands was BisDiazaPhos (BDP) (entry 8), which gave 64% conversion of **1** to **1a**. In all cases, the formyl group was installed at the less substituted terminal allene carbon; no addition of the formyl group to the central

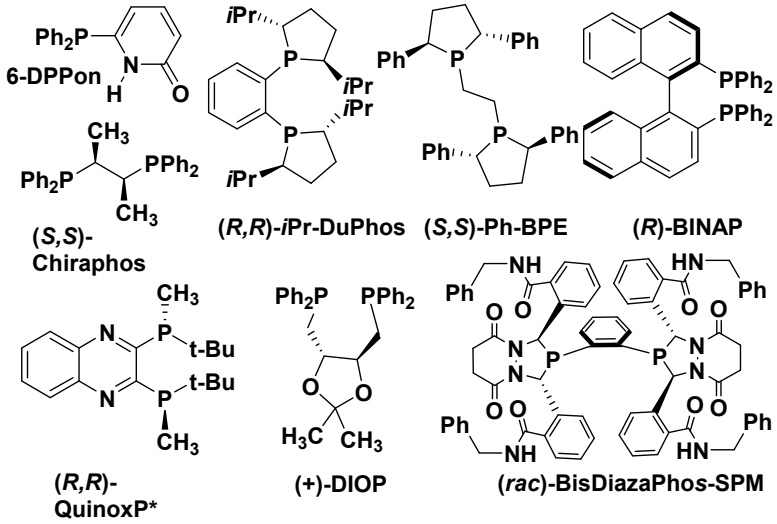
allenic carbon was detected in the reactions of **1a**. While we do not fully understand the reasons for the superior performance of BDP compared to other ligands in Table 1, we speculate that the highly sterically congested environment of BDP yields a quadrant map that places the less substituted allene carbon in an orientation that enables delivery of the H to the central allene carbon, with the formyl group installed at the

Table 1. Influence of ligand structure on the conversion and selectivity for hydroformylation of **1**.



entry	ligand	conversion[c]	selectivity **1a**:**1b**
1	6-DPPon	< 5%	1:1
2	(*R,R*)-*i*Pr-DuPhos	< 5%	1:1
3	(*S,S*)-Phen-BPE	< 5%	1:1
4	(*R*)-BINAP	< 5%	1:1
5	(*S,S*)-Chiraphos	6%	5:1
6	(*R,R*)-QuinoxP*	12%	11:1
7	(+)-DIOP	14%	13:1
8	(*rac*)-BisDiazaphos	64%	>64:1

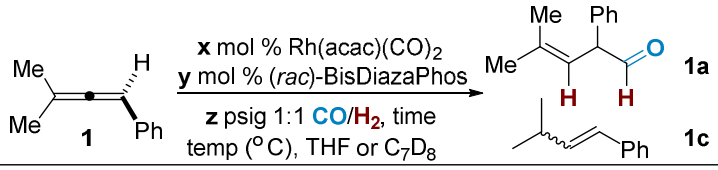
[a]Conditions: 0.588 mmol **1** was used. [b]Conditions: 1:1.2 Rh:ligand for bidentate ligands; 1:2.4 Rh:ligand for monodentate ligands. [c]Conditions: Determined by ^{1}H NMR of the crude reaction mixture using 5 μL of mesitylene as an internal standard.



carbon proximal to the least substituted terminal allene carbon.

The influence of reaction conditions on the Rh-catalyzed hydroformylation of **1** in the presence of BDP ligand is summarized in Table 2. Variation of the ligand loading from 1.0 mol % to 0.1 mol % (entries 2-5) indicates that complete conversion of **1** to primarily the β,γ-unsaturated aldehyde **1a** is achievable with only 0.1 mol % Rh loading if the reaction time was increased to 2 h. However, longer reaction times resulted in significant isomerization of **1a** to the corresponding α,β-unsaturated aldehyde. Increasing the reaction temperature to 80 °C (entry 6) resulted in competing allene hydrogenation, yielding 18% of hydrogenation product **1c** in addition to the desired **1a**. Because racemic BDP is not soluble in toluene, the ligand was switched to the more

Table 2. Hydroformylation results for **1** given as % NMR yield (% conversion) under varying reaction conditions (mol % of BDP and Rh, solvent, syngas pressure (psig), temperature (°C), and reaction time (hours).



entry	mol% Rh	mol% L	solvent	psig	temp	hr	% **1a**[a,b]	**1c**
1	0.0	0.0	THF	150	60	---	0(0)	---
2	1.0	1.2	THF	150	60	0.5	>99 (>99)	---
3	0.5	0.6	THF	150	60	1.0	>99 (>99)	---
4	0.25	0.3	THF	150	60	1.5	>99 (>99)	---
5	0.1	0.12	THF	150	60	2.0	>99 (>99)	---
6	1.0	1.2	THF	150	80	0.5	82 (>99)	18
7[c]	1.0	1.2	C_7D_8	150	60	0.5	82(82)	---
8	0.1	0.12	THF	120	60	2.0	96(>99)	4
9	0.1	0.12	THF	90	60	2.0	91(>99)	9
10	0.1	0.12	THF	60	60	2.0	73 (>99)	27

[a]Conditions: Determined by ^{1}H NMR of the crude reaction mixture, using 5 μL of mesitylene as the internal standard. 0.588 mmol of **1** was used. [b]Conditions % conversion is indicated in parenthesis. [c]Conditions: Run with (*S,S,S*)-BDP.

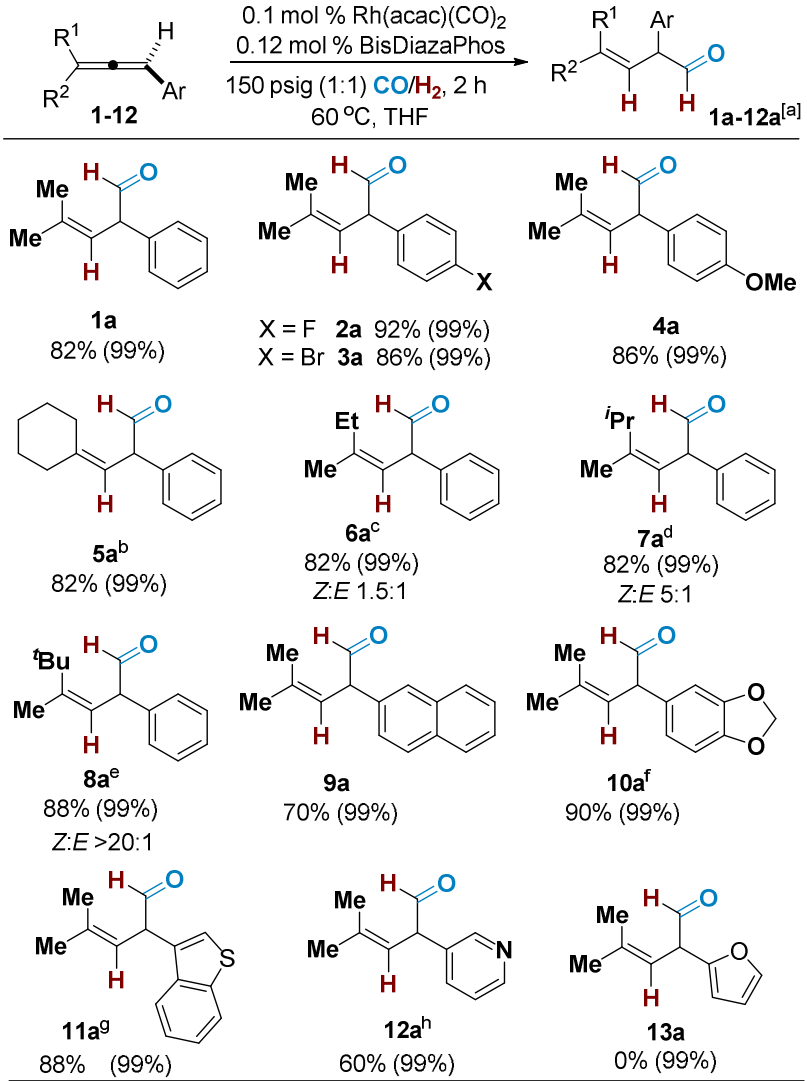
soluble (*S,S,S*)-BisDiazaPhos (entry 7) to test the influence of solvent polarity; slightly higher yields were obtained in THF solvent than toluene. Variations in the pressure of a 1:1 mixture of $CO:H_2$ (compare entry 5 to entries 8-10) showed interesting selectivity between hydroformylation **1a** and hydrogenation **1c**. At 120 psig, excellent yields of **1a** were obtained, however lower pressures yielded increasing amounts of **1c** via competing allene hydrogenation. Based on these results, optimized conditions of 0.1 mol % $Rh(acac)(CO)_2$, 0.12 mol % BisDiazaPhos and 150 psig 1:1 $CO:H_2$ in THF at 60 °C were chosen for subsequent studies.

The scope of the Rh-catalyzed allene hydroformylation was first explored with a series of 1,1-dialkyl-3-aryl-trisubstituted allenes **1-12** (Table 3). Variations in the electronics of the *para* substituents of the aryl groups in **2**-**4** did not appear to influence either the yield or selectivity, delivering the desired aldehydes **2a**-**4a** in good isolated yields. Substitution of the dimethyl substituents in **1-4** with a cyclohexyl group in **5** gave **5a** in 82% yield, although the reaction required an additional 0.5 h to ensure complete conversion was achieved. A series of racemic, chiral allenes **6-8** produced the β,ϒ-unsaturated aldehydes **6a-8a** in good yields with varying *Z:E* ratios, depending on the steric differences in the two substituents at the allene terminus. As the size of the alkyl group increased from Et to *i*Pr to *t*Bu, the *Z:E* ratio improves from 1.5 to 5 to >20, suggesting that control of the alkene stereoselectivity is kinetic in nature.[11]

Substitution of the phenyl group of the allene with other aromatic rings, including the naphthyl and heterocyclic groups in **9-13**, provided aldehydes **9a-12a** with excellent regioselectivity under the standard hydroformylation conditions, although increased catalyst loadings and reaction times were necessary for high conversion in some cases.

The aldehyde of **12a** was observed to decompose upon isolation. Therefore, *in situ* Horner-Wadsworth-Emmons (HWE) derivatization was carried out to give 60% yield of the olefinated product over two steps. The only unsuccessful substrate was the furan

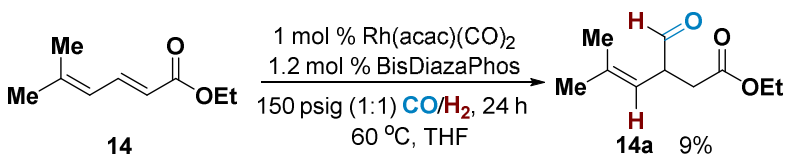
Table 3. Results for hydroformylation of aryl-substituted allenes given as % isolated yield (% conversion) for the indicated reaction conditions.



[a]Condistions: Isolated yield, conversion in parentheses. [b]Condistions: Run for 2.5 h. [c]Condistions: Run for 4 h. [d]Condistions: 1 mol % catalyst for 1 h. [e]Condistions: 1 mol % catalyst for 4 h. [f]Condistions: 7 h reaction time. [g]Condistions: 1 mol % catalyst for 6 h. [h]Condistions: Run at 40 °C for 2 h. Isolated yield over two steps after the HWE reaction.

13; while complete conversion was noted, complex product mixtures were obtained, presumably because both the substrate and the product **13a** are susceptible to Diels-Alder reactions.

The data in Table 3 establish high regioselectivity for the hydroformylation of aryl allenes. To investigate the regioselective hydroformylation of non-aryl allenes, the trialkyl substituted allenes **15-21** (Table 4) were examined. Substrates **15-18** were prepared through an *ortho*-Claisen rearrangement of the parent propargyl alcohol; these substrates introduce another useful functional group in the product aldehyde.[16] In keeping with results observed for the hydroformylation of aryl alkenes and allylic alcohols, the regiodirecting influence of the aryl substituents proved greater than those of the hydroxymethyl or carboethoxymethyl groups. As a result, the hydroformylation of **15** yields 89% of **15b**, 4% of **14** (see Scheme 2) and 7% of two minor aldehydes (one of the minor aldehydes results from formylation at the central carbon of the allene). In principle, the aldehyde product **15a** may result from isomerization of **15** to the diene **14**, which then undergoes hydroformylation (Scheme 2). The hydroformylation of **14** was performed to test the viability of this pathway. Hydroformylation of **14** under standard conditions produced only a 9% yield of **15a**, along with several other by-products (see the Supplementary Information for further details). This result supports direct hydroformylation of the allene as the primary pathway for the production of **15a**.



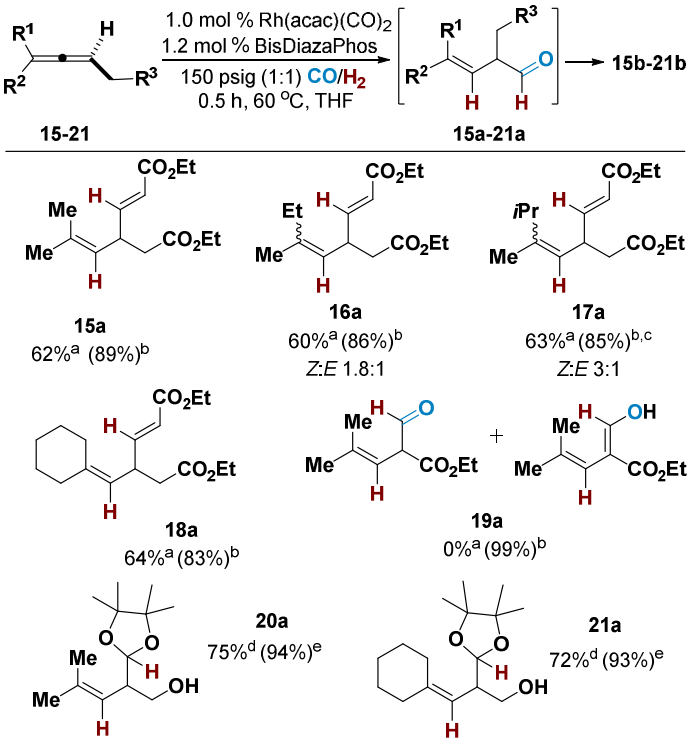
Scheme 2. Hydroformylation of 1,3-diene **14**.

The scope of the homoallenylic ester was explored (Table 4, **15-18**). Due to low yield in the isolation of **15a**, the aldehydes were converted to the corresponding unsaturated esters **15b-18b** using an *in situ* HWE reaction. In this manner, **15b** was furnished in 62% yield over the two steps and **18b** in 64% isolated yield. Hydroformylation of the chiral allenes **16-17** resulted in 60% and 63% isolated yields over the two steps, with *Z*:*E* ratios similar to those noted for the analogous Ph-substituted allenes **6**-**7** (Table 3).

The conjugated allenic ester precursor **19** was readily synthesized through a Wittig reaction of a ketene with a stabilized phosphonium ylide.[17] While **19** (Table 4) undergoes successful hydroformylation, the product **19a** rapidly tautomerizes to yield the enol. Reducing the ester of **19** to an alcohol[18,19] in **20** mitigated tautomerization of the aldehyde; however, the tendency of the β-hydroxyaldehyde product to dimerize upon concentration of the reaction mixture complicated isolation efforts.[20] Thus, the aldehyde **20a** was protected as a pinacol acetal **20b** to facilitate isolation in 75% yield over the two steps. Similarly, hydroformylation of the allene **21** delivered **21b** in 72% yield after the pinacol synthesis.

The data presented thus far indicate that hydroformylation of trisubstituted allenes is particularly fast and selective when: (1) BisDiazaphos (BDP) ligands are used and (2) the monosubstituted terminus of the allene (R^3 in Scheme 1) bears an inductively electron-withdrawing group (such as aryl, carboethoxymethyl, or hydroxymethyl). To

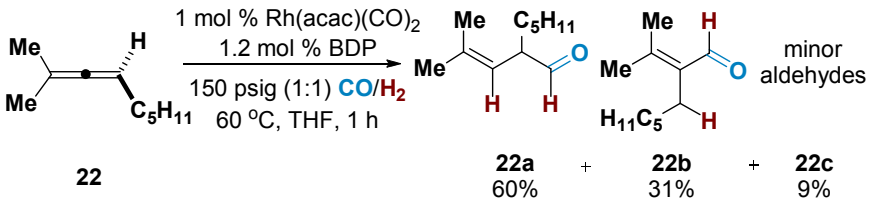
Table 4. Results for hydroformylation of allenes bearing hydroxymethyl and carboethoxymethyl substituents given as % isolated yield of the HWE derivatives (% NMR yield) for the indicated reaction conditions.



[a]Conditions: Isolated yield over two steps after HWE reaction. [b]Conditions: The NMR yield of the aldehyde is shown in parentheses. [c]Conditions: Ran for 0.45 h. [d]Conditions: Isolated yield after two steps, following protection of the aldehyde as the pinacol acetal. Run for 2 h using 4:1 $CO:H_2$ and 1 mol% of catalyst. [e]Conditions: The NMR yield of the aldehyde is shown in parenthesis.

further explore the influence of the R^3 substituent, the hydroformylation of **22** was performed (Scheme 3). In the event, only a 60% yield of **22a** was observed, resulting from formylation at the less substituted terminal allene carbon. Furthermore, a 31% yield of product **22b** was observed, a result of formylation at the central carbon of the allene **22**. The observation of large amounts of **22b** when R^3 is substituted with an

electron-donating group (C_5H_{11}) suggests that electronic effects are primarily responsible for controlling the regioselectivity of the hydrogen addition to the central

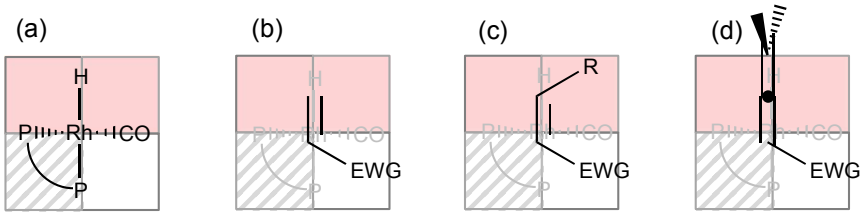


Scheme 3. Hydroformylation of trisubstituted allene **22**.

carbon of the allene in hydroformylations of trisubstituted allenes using our Rh-BDP catalyst system.

We have previously proposed a stereoelectronic mnemonic that summarizes the empirical observations regarding the asymmetric hydroformylations of 1- and 1,2-substituted alkenes with BisDiazaPhos ligands.[21] To place the reactivity and selectivity patterns for allene hydroformylation in the proper context, we have extended this mnemonic as shown in Figure 1. Note that the allene hydroformylation results are for racemic catalysts only; at this point, no experimental data regarding the enantiofacial selectivity of allene hydroformylation is implied, although studies directed towards this goal are ongoing in our labs. Placement of the EWG in the lower right-hand quadrant enables delivery of the H to the central allene carbon, with the formyl group installed at the carbon proximal to the EWG. Also shown in Figure 1 are approximate catalyst turnover frequencies (TOFs) for the different substrates at 60°C and 150 psig synthesis gas; these data highlight the high TOFs obtained with allenes and the BisDiazaPhos ligands.

Figure 1. Quadrant mnemonic diagrams showing (a) the metal coordination geometry, and approximate catalyst rates (TOFs) and preferred substrate orientations for (b) 1-alkenes (c) (*Z*)-1,2-alkenes and (d) trisubstituted allenes. (EWG=electron-withdrawing group).



In conclusion, Rh-catalyzed hydroformylation supported by a BisDiazaPhos ligand offers a practical and efficient synthetic route to useful β,ɤ-unsaturated aldehyde building blocks. A variety of trisubstituted aryl allenes, heterocyclic allenes, homoallenylic esters and allenols undergo hydroformylation with high conversions and regioselectivities using loadings as low as 0.1 mol % catalyst. For substrates containing an inductively EWG, the data indicate a kinetic preference for the addition of H to the central carbon of the allene. The results reported here suggest hydroformylation can successfully be extended to di- and tetrasubstituted allenes, including enantioselective transformations and kinetic resolutions of racemic allenes.

Experimental section

General information. All glassware was either oven-dried overnight at 130 °C or flame-dried immediately before use. Flame-dried glassware was cooled under vacuum while purging with nitrogen. Unless otherwise specified, reagents were used as obtained from

the vendor without further purification. Diethyl ether was freshly distilled from purple Na/benzophenone ketyl. Tetrahydrofuran was either distilled from purple Na/benzophenone ketyl or dried over alumni columns before use. Dichloromethane, acetonitrile and toluene were dried over CaH_2 and distilled before use. All other solvents were purified using "Purification of Laboratory Chemicals".[22] Analytical thin layer chromatography (TLC) was performed utilizing pre-coated silica gel 60 F_{254} plates containing a fluorescent indicator. Columns were conducted using a gradient method. $KMnO_4$ was used as stains reagent. Bisdiazaphospholane ligands were prepared as reported in the literature.[23] $[Rh(acac)(CO)_2]$ was received from Dow Chemical and purified by passing it through cold toluene; the purified $[Rh(acac)(CO)_2]$ was stored in a N_2-filled glovebox. The 1:1 $CO:H_2$ was obtained from Airgas. All pressures given are gauge pressures, unless otherwise noted. Carbon monoxide (CO) is very toxic and hydrogen is flammable; therefore, reactions should be conducted in a flame hood with adequate airflow. CO detectors should be present in case of a CO leak.

^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra were obtained using Bruker-300, Varian-300, Avance III 400, or Varian Inova-500, or Varian Unity-500 spectrometers. ^{13}C NMR spectra were obtained using 125 MHz or 75 MHz instruments. ^1H NMR spectra chemical shifts were reported in accordance to residual protiated solvent peaks (δ 77.2, 39.5, 128.0 and 137.9 ppm for $CDCl_3$, $(CD_3)_2SO$, C_6D_6, and $CD_3C_6D_5$, respectively).

Synthesis and characterization of allene substrates.[13,24]

Method I: General procedure for the synthesis and characterization of aryl allenes. The syntheses of the aryl allene substrates were based on a reported literature procedure. Slight modifications to this procedure were made as necessary, as indicated in the

following typical experimental set-up. An oven-dried, round bottom flask was cooled to rt under vacuum. Benzaldehyde (1.0 g, 9.4 mmol) and freshly distilled diethyl ether (8.8 mL) were added to the flask and the mixture cooled to 0 °C. A solution of 1-propynylmagnesium bromide (0.5 M in tetrahydrofuran, 28.3 mL, 14.1 mmol) was added dropwise, the reaction mixture warmed to rt and monitored by TLC. Once complete consumption of the starting material was noted, the reaction mixture was quenched with a saturated $NH_4Cl_{(aq)}$ solution. The organic layer was extracted with portions of diethyl ether, the combined organics washed with brine, then dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude material was used in the next step without any further purification.

An oven-dried round bottom flask was charged with the crude propargylic alcohol prepared above, distilled dichloromethane (7.3 mL), and triethylamine (2.6 mL, 18.8 mmol) at room temperature. To this mixture were added acetic anhydride (1.8 mL, 18.8 mmol) and 4-dimethylaminopyridine (0.58 g, 4.7 mmol). The reaction mixture was stirred at room temperature until TLC indicated complete consumption of the substrate, then quenched with water. The organic layer was extracted with portions of dichloromethane (20 mL x 3), the combined organics washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude material was purified by column chromatography (20% ethyl acetate/ hexane).

A cooled, oven-dried round bottom flask was charged with purified CuCN (3.2 g, 35.2 mmol) and dried THF (57 mL). The mixture was cooled to 0 °C and a solution of MeMgBr (3.0 M in tetrahydrofuran, 11.7 mL, 35.2 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h, a solution of the acylated propargylic alcohol

in THF was added and the reaction mixture stirred at rt for an additional 48 h. The reaction was quenched with a 1:1 volume of saturated $Na_2CO_{3(aq)}$ and hexane, extracted with three portions of ethyl acetate and the combined organic layers dried with Na_2SO_4. The crude material was purified via column chromatography (10% ethyl acetate/hexane). The yield reported is the yield of the organocuprate reaction.

(4-Methylpenta-2,3-dien-1-yl)benzene (**1**). The organocuprate reaction was run on a 12.25 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **1** as a colorless oil in 73% (1.3 g) isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 4H), 7.18 – 7.14 (m, 1H), 5.98 (hept, *J* = 2.9 Hz, 1H), 1.82 (d, *J* = 2.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.3, 136.1, 128.6, 126.8, 126.5, 99.3, 92.6, 20.4. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{11}H_{13}$ 145.1012; found 145.1010.

1-Fluoro-4-(4-methylpenta-2,3-dien-1-yl)benzene (**2**). The organocuprate reaction was run on a 0.97 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **2** as a colorless oil in 55% (0.09g) isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.18 (m, 2H), 7.02 – 6.93 (m, 2H), 5.95 (hept, *J* = 2.9 Hz, 1H), 1.82 (d, *J* = 2.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.0, 163.0, 160.5, 132.0, 132.0, 128.1, 128.0, 115.6, 115.4, 110.1, 99.6, 91.7, 20.4. ^{19}F NMR (377 MHz, $CDCl_3$) δ -116.4. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{11}H_{12}F$ 163.0918; found 163.0916.

1-Bromo-4-(4-methylpenta-2,3-dien-1-yl)benzene (**3**). The organocuprate reaction was run on a 9.89 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **3** as a colorless oil in 73% (1.61 g) isolated yield. ^{1}H

NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.38 (m, 2H), 7.15 – 7.06 (m, 2H), 5.92 (hept, *J* = 2.9 Hz, 1H), 1.81 (d, *J* = 2.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.3, 135.0, 131.5, 128.1, 119.9, 99.7, 91.7, 20.2. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{11}H_{12}Br$ 223.0117; found 223.0111.

1-Methoxy-4-(4-methylpenta-2,3-dien-1-yl)benzene (**4**). The organocuprate reaction was run on a 6.20 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **4** as a colorless oil in 77% (0.83 g) isolated yield**.** ^1H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.14 (m, 2H), 6.87 – 6.78 (m, 2H), 5.94 (hept, *J* = 2.9 Hz, 1H), 3.80 (s, 3H), 1.81 (d, *J* = 2.9 Hz, 6H).^{13}C NMR (126 MHz, $CDCl_3$) δ 201.9, 136.4, 128.6, 126.4, 126.4, 112.8, 94.2, 34.4, 29.3, 14.8. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{12}H_{15}O$ 175.1116; found 175.1146.

(2-Cyclohexylideneethenyl) benzene (**5**). The organocuprate reaction was run on a 9.96 mmol scale. The compound was made following a reported literature procedure.[25] The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield 5 as a colorless oil in 82% (1.52 g) isolated yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 4H), 7.19 – 7.12 (m, 1H), 5.99 (p, *J* = 2.2 Hz, 1H), 2.30 – 2.24 (m, 2H), 2.23 – 2.16 (m, 2H), 1.75 – 1.55 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.8, 136.3, 128.6, 126.6, 126.4, 106.6, 92.5, 31.5, 27.8, 26.3. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{14}H_{17}$ 185.1325; found 185.1325.

(4-Methylhexa-2,3-dien-1-yl)benzene (**6**). The organocuprate reaction was run on a 5.31 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **6** as a colorless oil in 92% (0.77 g) isolated yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 4H), 7.21 – 7.11 (m, 1H), 6.08 (h, *J* = 3.0 Hz, 1H),

2.09 (m, 2H), 1.82 (d, *J* = 2.8 Hz, 3H), 1.06 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.5, 136.3, 128.6, 126.6, 126.5, 105.6, 94.5, 27.3, 18.9, 12.4. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{12}H_{15}$ 159.1168; found 159.1167.

(4,5-Dimethylhexa-2,3-dien-1-yl)benzene (**7**). The organocuprate reaction was run on a 5.31 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **7** as a colorless oil in 89% (0.81 g) isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 5.5 Hz, 4H), 7.20 – 7.13 (m, 1H), 6.08 (p, *J* = 2.8 Hz, 1H), 2.25 (heptd, *J* = 6.8, 2.3 Hz, 1H), 1.81 (d, *J* = 2.9 Hz, 3H), 1.10 (dd, *J* = 8.3, 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.7, 136.1, 128.5, 126.4, 126.2, 109.8, 94.6, 32.5, 21.7, 21.5,17.1. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{13}H_{17}$ 173.1325; found 173.1313.

(3Z)-4,5,5-Trimethyl-2-phenylhex-3-enal (**8**). The organocuprate reaction was run on a 20.43 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **8** as a colorless oil in 74% (2.81 g) isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 4H), 7.20 – 7.11 (m, 1H), 6.05 (q, *J* = 2.8 Hz, 1H), 1.81 (d, *J* = 2.8 Hz, 3H), 1.13 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.9, 136.4, 128.6, 126.4, 126.4, 112.8, 94.2, 34.4, 29.3, 14.8. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{14}H_{19}$ 187.1481; found 187.1480.

1-(4-Methylpenta-2,3-dien-1-yl)naphthalene (**9**). The organocuprate reaction was run on a 10.76 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **9** as a white solid in 83% (1.73 g) isolated yield. m.p. 62-65 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.70 (m, 3H), 7.65 – 7.57 (m, 1H), 7.50 – 7.35 (m, 3H), 6.16 (hept, *J* = 2.9 Hz, 1H), 1.86 (d, *J* = 2.9 Hz, 6H). ^{13}C NMR (126 MHz,

$CDCl_3$) δ 203.9, 133.9, 133.7, 132.6, 128.2, 127.8, 127.7, 126.2, 125.5, 125.2, 125.0, 99.6, 93.0, 20.5. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{15}H_{15}$ 195.1168; found 195.1169. The characterization data match the reported data.[29]

4-(4-Methylpenta-2,3-dien-1-yl)-2H-1,3-benzodioxole (**10**). The organocuprate reaction was run on a 11.00 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **10** as a colorless oil in 86% (1.79 g) isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (d, *J* = 1.7 Hz, 1H), 6.73 (d, *J* = 7.9 Hz, 1H), 6.69 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.96 – 5.89 (m, 3H), 1.80 (d, *J* = 2.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.3, 147.9, 146.3, 130.2, 120.2, 108.2, 106.5, 100.9, 99.4, 92.3, 20.4. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{12}H_{13}O_2$ 189.0910; found 189.0911.

4-(4-Methylpenta-2,3-dien-1-yl)-2H-1,3-benzodioxole (**11**). The organocuprate reaction was run on a 5.91 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **11** as a colorless oil in 75% (0.89 g) isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.32 – 7.24 (m, 2H), 7.13 (s, 1H), 6.27 (hept, *J* = 3.1 Hz, 1H), 1.80 (d, *J* = 3.1 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.5, 140.8, 137.5, 130.6, 124.4, 124.2, 122.8, 122.6, 122.6, 98.1, 86.1, 20.8. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{13}H_{13}S$ 201.0733; found 201.0733.

3-(3-Methylbuta-1,2-dien-1-yl)pyridine (**12**). The organocuprate reaction was run on a 8.50 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **12** as a brown oil in 78% (0.96 g) isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.2 Hz, 1H), 8.39 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.55 (dt, *J* =

7.9, 2.0 Hz, 1H), 7.20 (ddd, *J* = 7.9, 4.8, 0.9 Hz, 1H), 5.96 (hept, *J* = 2.9 Hz, 1H), 1.83 (d, *J* = 2.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.8, 148.4, 147.6, 133.5, 132.0, 123.5, 100.2, 89.5, 20.3. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{10}H_{12}N$ 146.0964; found 146.0963.

2-(3-Methylbuta-1,2-dien-1-yl)furan (**13**). The organocuprate reaction was run on a 10.35 mmol scale. The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **13** as a yellow oil in 38% (0.53 g) isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 1.9, 0.8 Hz, 1H), 6.35 (dd, *J* = 3.3, 1.9 Hz, 1H), 6.14 (dd, *J* = 3.3, 0.8 Hz, 1H), 5.96 (hept, *J* = 3.0 Hz, 1H), 1.81 (d, *J* = 3.0 Hz, 6H).^{13}C NMR (126 MHz, $CDCl_3$) δ 202.2, 145.0, 141.7, 111.4, 106.5, 100.00, 83.4, 20.7. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_9H_{11}O$ 135.0804; found 135.0804.

Method II: General procedure for the synthesis and characterization of homoallenylic ester substrates.[16] All allenyl esters were prepared according to a reported literature procedure. A cooled, oven-dried round bottom flask was charged with 2-methylbut-3-yne-2-ol (4.9 mL, 50.6 mmol), triethyl orthoacetate (11.2 mL, 60.7 mmol) and propanoic acid (0.38 mL, 5.1 mmol). The reaction mixture was heated to 100-150 °C under nitrogen until TLC indicated complete consumption of the starting material. The mixture was cooled to rt, diluted with ethyl acetate, washed with 0.1 M HCl (2x), aqueous $NaHCO_3$, then brine. The combined organics were dried over Na_2SO_4, the solvent removed under reduced pressure and the crude material purified by column chromatography (10% ethyl acetate or 20% ether/hexane) to give the desired homoallenic ester.

Ethyl 5-methylhexa-3,4-dienoate (**15**). The product was purified by silica gel flash chromatography (8:2 hexane/ether) to yield **15** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.15 – 5.03 (m, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 2.97 (d, *J* = 7.1 Hz, 2H), 1.69 (d, *J* = 2.9 Hz, 6H), 1.27 (t, *J* = 7.1 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.0, 172.0, 96.4, 82.0, 60.6, 35.4, 20.5, 14.3. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_8H_{13}O_2$ 141.0910; found 141.0910.

Ethyl 5-methylhepta-3,4-dienoate (**16**). The product was purified by silica gel flash chromatography (9.5:0.5 hexane/ethyl acetate) to yield **16** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.22 – 5.15 (m, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 2.98 (d, *J* = 7.1 Hz, 2H), 1.94 (qd, *J* = 7.4, 3.2 Hz, 2H), 1.69 (d, *J* = 2.8 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.99 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.3, 172.1, 102.8, 84.1, 60.7, 35.7, 27.0, 19.0, 14.3, 12.3. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{10}H_{17}O_2$ 169.1223; found 169.1222.

Ethyl 5,6-dimethylhepta-3,4-dienoate (**17**). The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **17** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.21 – 5.14 (m, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.97 (d, *J* = 7.1 Hz, 2H), 2.10 (hept d, *J* = 6.8, 2.3 Hz, 1H), 1.69 (d, *J* = 2.8 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 6H).^{13}C NMR (126 MHz, $CDCl_3$) δ 201.6, 171.9, 107.0, 84.1, 60.5, 35.6, 31.9, 21.4, 21.3, 17.2, 14.2. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{11}H_{19}O_2$ 183.1380; found 183.1381.

Ethyl 4-cyclohexylidene-3-butenoate (**18**). The product was purified by silica gel flash chromatography (9:1 hexane/ethyl acetate) to yield **18** as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.09 (tp, *J* = 6.5, 2.1 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.98 (d, *J* = 7.1

Hz, 2H), 2.21 – 2.06 (m, 4H), 1.64 – 1.45 (m, 6H), 1.27 (t, *J* = 7.2 Hz, 3H).[13]C NMR (126 MHz, $CDCl_3$) δ 199.7, 172.1, 103.7, 81.9, 60.7, 35.8, 31.4, 27.4, 26.2, 14.3. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{12}H_{19}O_2$ 195.1380; found 195.1379.

Ethyl 4-methylpenta-2,3-dienoate (**19**). The compound was made following a reported literature procedure. The NMR data matched the published data.[26]

Method III: General procedure for the synthesis and characterization of allenols.[18,19] All allenol substrates were prepared according to a reported literature procedure. A cooled, oven-dried round bottom flask was charged with *p*-toluenesulfonate (1.78 g, 7.10 mmol, 5 mol %), CH_2Cl_2 (60 mL), 2-methylbut-3-yne-2-ol (12.0 g, 143 mmol) and 3,4-dihydropyran (50.0 g, 594 mmol). The reaction was stirred at rt until complete conversion of the substrate was observed by TLC. The solvent was removed under reduced pressure, diethyl ether was added and the organics washed with water. The organic layer was dried with $MgSO_4$ and the solvent was removed. The crude material was distilled under reduced pressure to give pure 1,1-dimethylprop-2-ynyl tetrahydropyran-2-yl-ether.

An oven-dried round bottom flask was charged with the protected propargyl alcohol prepared above (0.5 g, 2.9 mmol) and distilled diethyl ether (2.96 mL) and the mixture cooled to -78 °C. A solution of *n*-butyllithium (2.64 M, 1.7 mL, 4.4 mmol) was added dropwise to the reaction mixture and stirred at -78 °C for 45 min. A solution of paraformaldehyde (0.27 g, 8.9 mmol) in ether was added dropwise, the reaction mixture warmed to rt and vigorously stirred until TLC indicated complete consumption of the substrate. The reaction was quenched with an ice water, extracted with ether (20 mL x 3) and the combined organics dried with $MgSO_4$. The solvent was removed under

reduced pressure and the product was purified via column chromatography (40% ethyl acetate/hexane) to give 4-methyl-4-[(tetrahydro-2H-pyran-2-yl)oxy]pent-2-yn-1-ol.

An oven-dried round bottom flask was charged with lithium aluminium hydride (LAH, 0.28 g, 7.6 mmol) and distilled diethyl ether (10.1 mL) and cooled to 0 °C. A solution of the propargyl alcohol substrate (0.50 g, 2.52 mmol) in distilled ether (2.5 mL) was added dropwise to the suspension of LAH. The reaction was warmed to rt and stirred overnight. Once TLC indicated complete consumption of the propargyl alcohol, the reaction mixture was diluted with ether and cooled to 0 °C. Quenching was carried out carefully according to the method of Fieser and Fieser using sequential addition of 0.3 mL of water, 0.3 mL of 15% aqueous NaOH, and 3 x 0.3 mL of water.[27] The mixture was warmed to rt and stirred until a white precipitate was observed. A portion of $MgSO_4$ was added and stirring continued for an additional 30 min. The solids were filtered, the solvent removed under reduced pressure and the residue purified by column chromatography to give the allenic alcohol product.

4-Methylpenta-2,3-dien-1-ol (**20**). The reduction with $LiAH_4$ was run on a 10.53 mmol scale. The product was purified by silica gel flash chromatography (8:2 hexane/ethyl acetate) to afford **20** as a colorless oil in 72% (0.74 g) isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.24 – 5.16 (m, 1H), 4.07 (t, *J* = 5.7 Hz, 2H), 1.73 (d, *J* = 2.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.5, 98.6, 89.9, 61.0, 20.6. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_6H_{11}O$ 99.0810; found 99.0804.

3-Cyclohexylidene-2-propen-1-ol (**21**). The product was purified by silica gel flash chromatography (8:2 hexane/ethyl acetate) to afford **21** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.25 – 5.15 (m, 1H), 4.07 (t, *J* = 5.5 Hz, 2H), 2.14 (m, 4H), 1.65 – 1.49

(m, 6H).^{13}C NMR (126 MHz, $CDCl_3$) δ 197.3, 105.9, 89.8, 61.3, 31.6, 27.5, 26.1. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_9H_{15}O_3$ 139.1117; found 139.1117.

2-Methylnona-2,3-diene (**22**). The compound was made following a reported literature procedure.[25]

General method for hydroformylation. In a nitrogen-filled glovebox, a 15 mL Ace Glass glass pressure bottle equipped with a magnetic stir bar was charged with a THF stock solution of (0.005 M or 0.1 M) $Rh(acac)(CO)_2$ and (0.005 M or 0.05 M) bisdiazaphospholane ligand using 1000 µL and 200 µL Eppendorf® pipets. The glass bottle was attached to a pressure reactor head and the apparatus was removed from the glovebox. The apparatus was placed inside a fume hood and was charged with 5 pressurizations (150 psi)/ depressurization (0 psi) cycle with 1:1 CO:H_2. This allows for complete replacement of nitrogen with syngas. The apparatus was filled with 150 psi of syngas and placed in an oil bath at desired temperature. The solution was stirred vigorously for 30-60 min to ensure formation of the pre-activated catalyst. The reaction apparatus was removed from the oil bath and cooled for 5 min. The pressure was reduced to 0 psi syngas and a solution of allene in THF was injected with a gas-tight syringe using a 12'' needle. The reaction was charged with 3 x 150 psi pressurization/ 0 psi depressurization cycles, taken to a final pressure of 150 psi and placed in the oil bath at the desired temperature. The reaction mixture was vigorously stirred until completion. Completion was determined by taking crude NMR sample of the hydroformylation mixture. Once the reaction was complete, the reactor was removed from the oil bath for 5 minutes, cooled to rt and depressurized. A crude NMR sample

was taken in $CDCl_3$ using 5 µL of mesitylene as an internal standard. The allene peak and the aldehyde peak were used to mentor reaction progress.

4-Methyl-2-phenylpent-3-enal (**1a**)**.** The hydroformylation was run on a 0.588 mmol scale at 40 °C. After completion of the hydroformylation, the crude mixture was filtered through a plug of silica and washed with dichloromethane to give 82% (0.08 g) isolated yield of **1a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.51 (d, *J* = 2.5 Hz, 1H), 7.33 – 7.27 (m, 2H), 7.24 – 7.19 (m, 1H), 7.18 – 7.15 (m, 2H), 5.52 – 5.40 (m, 1H), 4.34 (dd, *J* = 9.0, 2.5 Hz, 1H), 1.75 (d, *J* = 1.4 Hz, 3H), 1.63 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.5, 138.1, 136.9, 129.2, 128.6, 127.5, 118.5, 58.3, 26.2, 18.7. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{12}H_{15}O$ 175.1123; found 175.1115.

2-(4-Fluorophenyl)-4-methylpent-3-enal (**2a**). The hydroformylation reaction was run on a 1.18 mmol scale at 60 ^{o}C. After completion of the hydroformylation reaction, the crude mixture was filtered through a plug of silica and washed with dichloromethane to give 82% (0.21 g) isolated yield of **2a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.56 (d, *J* = 2.4 Hz, 1H), 7.20 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.06 (t, *J* = 8.7 Hz, 2H), 5.52 – 5.45 (m, 1H), 4.40 (dd, *J* = 9.0, 2.3 Hz, 1H), 1.83 (d, *J* = 1.3 Hz, 3H), 1.69 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.0, 198.0, 163.1, 161.1, 138.4, 132.4, 132.4, 118.1, 116.0, 115.8, 57.3, 26.0, 18.6. ^{19}F NMR (377 MHz, $CDCl_3$) δ -115.2. HRMS (ESI-TOF) m/z: [M-H]- calcd for $C_{12}H_{12}FO$ 191.0872; found 191.0878.

2-(4-Bromophenyl)-4-methylpent-3-enal (**3a**). The hydroformylation was run on a 0.588 mmol scale at 60 °C. After completion of the hydroformylation, the crude mixture was filtered through a plug of silica and washed with dichloromethane to give 86% (0.13 g) isolated yield of **3a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.49 (d, *J* = 2.4 Hz,

1H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 5.40 (m, 1H), 4.30 (dd, *J* = 9.0, 2.3 Hz, 1H), 1.76 (d, *J* = 1.3 Hz, 3H), 1.62 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 138.7, 135.7, 132.1, 130.1, 121.4, 117.8, 57.5, 26.0, 18.6. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{12}H_{13}OBr$ 253.0223; found 253.0218.

2-(4-Methoxyphenyl)-4-methylpent-3-enal (**4a**). The hydroformylation was run on a 0.588 mmol scale at 60 °C. The crude hydroformylation mixture was filtered through a plug of silica and washed with dichloromethane to give **4a** in 86% (0.10 g) isolated yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (d, *J* = 2.5 Hz, 1H), 7.15 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 5.54 – 5.46 (m, 1H), 4.35 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.80 (s, 3H), 1.82 (d, *J* = 1.4 Hz, 3H), 1.69 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.5, 159.0, 137.7, 129.6, 128.7, 118.72, 114.6, 57.4, 55.3, 26.1, 18.6. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{13}H_{17}O_2$ 205.1223; found 205.1223.

3-Cyclohexylidene-2-phenylpropanal (**5a**). The hydroformylation reaction was run on a 0.588 mmol scale at 60 °C. The crude mixture was filtered through a plug of silica and washed with dichloromethane to give 80% (0.10 g) isolated yield of **5a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.52 (d, *J* = 2.6 Hz, 1H), 7.30 (s, 2H), 7.24 – 7.19 (m, 1H), 7.19 – 7.16 (m, 2H), 5.38 (m, 1H), 4.40 (dd, *J* = 8.8, 2.6 Hz, 1H), 2.21 – 2.03 (m, 5H), 1.57 – 1.34 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.6, 146.1, 137.1, 129.1, 128.6, 127.5, 115.0, 57.3, 37.4, 29.8, 28.7, 27.7, 26.7. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{15}H_{19}O$ 215.1430; found 215.1429.

(3Z)-4-Methyl-2-phenylhex-3-enal (**6a**). The hydroformylation reaction was run on a 0.588 mmol scale at 60 °C. The crude mixture was filtered through a plug of silica and washed with dichloromethane to give 82% (0.09 g, *Z*:*E* 1.5:1) isolated yield of **6a** as a

yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (d, *J* = 2.6 Hz, 1H, major), 9.58 (d, *J* = 2.7 Hz, 1H, minor), 7.41 – 7.35 (m, 4H), 7.33 – 7.25 (m, 2H), 7.25 – 7.22 (m, 4H), 5.55 – 5.51 (m, 1H, minor), 5.51 – 5.47 (m, 1H, major), 4.43 (ddd, *J* = 7.7, 4.8, 2.6 Hz, 2H), 2.16 – 2.07 (m, 4H), 1.82 (d, *J* = 1.4 Hz, 3H, major), 1.69 (d, *J* = 1.4 Hz, 3H, minor), 1.05 (t, *J* = 7.4 Hz, 3H, minor), 0.96 (t, *J* = 7.6 Hz, 3H, major). ^{13}C NMR (126 MHz, $CDCl_3$) δ Major: 198.5, 143.5, 136.9, 129.0, 128.4, 127.4, 117.9, 58.0, 25.5, 23.2, 12.5. Minor: 198.3, 143.5, 136.8, 129.0, 128.5, 127.4, 116.8, 57.8, 32.6, 16.9, 12.5. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{13}H_{17}O$ 189.1274; found 189.1273.

(3Z)-4,5-Dimethyl-2-phenylhex-3-enal (**7a**). The hydroformylation was run on a 0.588 mmol scale at 60 °C. The crude mixture was filtered through a plug of silica and washed with dichloromethane to give 82% (0.1 g, *Z*:*E* 5:1) isolated yield of **7a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.58 (d, *J* = 2.6 Hz, 1H, major), 9.56 (d, *J* = 2.8 Hz, 1H, minor), 7.39 – 7.34 (m, 4H), 7.31 – 7.27 (m, 2H), 7.26 – 7.22 (m, 4H), 5.56 (m, 1H, minor), 5.48 – 5.39 (m, 1H, major), 4.51 (dd, *J* = 9.1, 2.5 Hz, 1H, major), 4.41 (dd, *J* = 8.7, 2.8 Hz, 1H, minor), 2.82 (hept, *J* = 6.8 Hz, 1H, major), 2.41 – 2.33 (m, 1H, minor), 1.73 (d, *J* = 1.4 Hz, 3H, major), 1.65 (d, *J* = 1.4 Hz, 1H, minor), 1.05 (dd, *J* = 6.9, 4.8 Hz, 2H, minor), 1.01 (d, *J* = 6.8 Hz, 3H, major), 0.89 (d, *J* = 6.9 Hz, 3H, major).^{13}C NMR (126 MHz, $CDCl_3$) δ Major: 198.6, 147.8, 137.1, 129.2, 128.6, 127.5, 117.4, 57.4, 29.6, 20.9, 20.6, 18.5. Minor: 198.3, 147.1, 136.9, 129.1, 128.6, 127.5, 115.9, 57.9, 37.3, 21.5, 14.60. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{14}H_{19}O$ 203.1436; found 203.1429.

(3Z)-4,5,5-Trimethyl-2-phenylhex-3-enal (**8a**). The hydroformylation reaction was run on a 0.588 mmol scale at 60 °C. After hydroformylation, the crude hydroformylation

mixture was filtered through a plug of silica and washed with dichloromethane to give 88% (0.11 g, *Z*:*E* >20:1) isolated yield of **8a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.57 (d, *J* = 2.7 Hz, 2H), 7.37 (m, 4H), 7.31 – 7.27 (m, 2H), 7.24 (m, 4H), 5.63 (dd, *J* = 8.6, 1.3 Hz, 1H, minor), 5.50 (dq, *J* = 10.7, 1.5 Hz, 1H, major), 4.81 (dd, *J* = 10.6, 2.7 Hz, 1H,major), 4.40 (dd, *J* = 8.5, 2.8 Hz, 1H, minor), 1.87 (d, *J* = 1.4 Hz, 3H, major), 1.67 (d, *J* = 1.3 Hz, 3H, minor), 1.15 (s, 9H), 1.09 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ Major: 198.7, 148.8, 137.1, 129.2, 128.6, 127.5, 118.7, 58.7, 35.9, 30.8, 24.8. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{15}H_{21}O$ 217.1587; found 217.1584.

4-Methyl-2-(naphthalen-2-yl)pent-3-enal (**9a**). The hydroformylation reaction was run on a 0.588 mmol scale at 60 °C. The crude mixture was filtered through a plug of silica and washed with dichloromethane to give 70% (0.09 g) isolated yield of **9a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.67 (d, *J* = 2.4 Hz, 1H), 7.88 – 7.78 (m, 3H), 7.72 – 7.69 (m, 1H), 7.51 – 7.45 (m, 2H), 7.35 (dd, *J* = 8.5, 1.8 Hz, 1H), 5.65 (m, 1H), 4.57 (d, *J* = 2.4 Hz, 1H), 1.86 (d, *J* = 1.4 Hz, 3H), 1.73 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.5, 138.3, 134.3, 133.8, 132.7, 129.0, 127.9, 127.8, 127.4, 126.5, 126.5, 126.2, 118.4, 58.4, 26.2, 18.8. HRMS (ESI-TOF) m/z: [M+H]+ + calcd for $C_{16}H_{17}O$ 225.1274; found 225.1270.

2-(2H-1,3-Benzodioxol-5-yl)-4-methylpent-3-enal (**10a**). The hydroformylation reaction was run on a 0.588 mmol scale at 60 °C. The crude mixture was filtered through a plug of silica and washed with dichloromethane to give 90% (0.23 g) isolated yield of **10a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.53 (d, *J* = 2.5 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.73 – 6.67 (m, 2H), 5.95 (s, 2H), 5.48 (m, 1H), 4.31 (dd, *J* = 8.9, 2.4 Hz, 1H), 1.82 (d, *J* = 1.4 Hz, 3H), 1.68 (d, *J* = 1.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.3, 148.4,

147.1, 138.1, 130.5, 121.8, 118.5, 108.9, 108.9, 101.3, 57.8, 26.2, 18.7. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{13}H_{15}O_3$ 219.1016; found 190.1013.

2-(1-Benzothiophen-2-yl)-4-methylpent-3-enal (**11a**). The hydroformylation reaction was run on a 0.588 mmol scale at 60 °C. The crude mixture was filtered through a plug of silica and washed with dichloromethane to give 88% (0.12 g) isolated yield of **11a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.56 (d, *J* = 2.7 Hz, 1H), 7.95 – 7.77 (m, 1H), 7.79 – 7.69 (m, 1H), 5.59 (m,1H), 4.77 (dd, *J* = 8.8, 2.7 Hz, 1H), 1.84 (d, *J* = 1.4 Hz, 3H), 1.75 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.0, 140.5, 138.8, 138.0, 131.0, 124.7, 124.3, 124.1, 123.0, 121.8, 117.0, 52.6, 26.1, 18.7. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{14}H_{15}OS$ 231.0838; found 231.0835.

The Horner-Wadsworth-Emmons reactions were run following a reported literature procedure.[28]

Ethyl (2E)-6-methyl-4-(pyridin-3-yl)hepta-2,5-dienoate (**12b**). The hydroformylation reaction was run on a 2.94 mmol scale at 60 °C with 4:1 CO:H_2 and then a Horner-Wadsworth-Emmons reaction was carried out to facilitate isolation of **12b**. A solution of NaH (0.14 g, 3.23 mmol) in dry THF (5 mL) at 0 °C was treated with dropwise addition of triethyl phosphonoacetate (0.64 mL, 3.23 mmol). The mixture was stirred at 0 °C for 45 min. Dry THF (5 mL) was added to the crude hydroformylation mixture and this solution added slowly to the ylide solution. The mixture was warmed to rt, stirred overnight, then quenched by the addition of an aqueous saturated solution of NH_4Cl. The mixture was extracted with three portions of ethyl acetate, the combined organic layers dried over $MgSO_4$, concentrated under reduced pressure and purified by column chromatography (40% ethyl acetate /hexanes) to furnish a 60% (0.40 g) isolated yield of **12a** as a yellow

oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J* = 2.2 Hz, 1H), 8.58 – 8.44 (m, 2H), 7.68 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.25 – 7.22 (dd, 1H), 6.13 (dd, *J* = 7.1, 1.3 Hz, 1H), 5.84 – 5.81 (m, 1H), 4.20 (q, *J* = 7.1 Hz, 3H), 3.25 – 3.17 (m, 1H), 1.92 (d, *J* = 1.4 Hz, 4H), 1.54 (d, *J* = 1.2 Hz, 4H), 1.31 (t, *J* = 7.1 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.7, 148.3, 148.1, 138.9, 137.6, 136.6, 133.7, 123.0, 122.2, 120.7, 60.8, 35.3, 25.5, 19.8, 14.2. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{15}H_{20}NO_2$ 246.1489; found 246.1489.

Diethyl (2E)-4-(2-methylprop-1-en-1-yl)hex-2-enedio-ate (**15b**). The hydroformylation reaction was run on a 2.94 mmol scale at 60 °C and then a Horner-Wadsworth-Emmons reaction was carried out to facilitate isolation of **12b**. To a solution of NaH (0.14 g, 3.23 mmol) in dry THF (5 mL) at 0 °C was added triethyl phosphonoacetate (0.64 mL, 3.23 mmol) dropwise. The mixture was stirred at 0 °C for 45 min. Dry THF (5 mL) was added to the crude hydroformylation mixture and this added slowly to the solution of the ylide. The mixture was warmed to rt, stirred overnight, then quenched by the addition of an aqueous saturated solution of NH_4Cl. The mixture was extracted with ethyl acetate (3x), the combined organic layers dried over $MgSO_4$, concentrated under reduced pressure and purified by column chromatography (20% ether /hexanes) to furnish a 62% (0.46 g) isolated yield of **15b** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.84 (dd, *J* = 15.7, 6.7 Hz, 1H), 5.80 (dd, *J* = 15.6, 1.5 Hz, 1H), 4.95 (heptd, *J* = 9.3, 1.5 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 3.61 (dddd, *J* = 14.5, 9.3, 6.8, 1.5 Hz, 1H), 2.47 (dd, *J* = 15.0, 6.9 Hz, 1H), 2.37 (dd, *J* = 15.0, 7.8 Hz, 1H), 1.71 (d, *J* = 1.5 Hz, 3H), 1.65 (d, *J* = 1.4 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 166.7, 149.5, 135.2, 123.0, 120.5, 60.5, 60.3, 39.4, 37.7,

25.8, 18.1, 14.3, 14.2. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{14}H_{23}O_4$ 255.1591; found 255.1587.

Diethyl (2E)-4-[(1Z)-2-methylbut-1-en-1-yl]hex-2-ene-dioate (**16b**). The hydroformylation reaction was run on a 2.94 mmol scale at 60 °C and then a Horner-Wadsworth-Emmons reaction was carried out to facilitate isolation of **12b** as described above. Purified of the crude material by column chromatography (10% ethyl acetate /hexanes) furnished a 60% (0.47 g, *Z*:*E* 1.8:1) isolated yield of **16b** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (ddd, *J* = 15.7, 6.7, 1.6 Hz, 2H), 5.80 (ddd, *J* = 15.6, 3.1, 1.5 Hz, 2H), 4.94 (m, 1H, minor), 4.93 – 4.89 (m, 1H, major), 4.24 – 4.05 (dq, 8H), 3.68 – 3.58 (m, 2H), 2.47 (ddd, *J* = 14.7, 7.2, 6.1 Hz, 2H), 2.37 (ddd, *J* = 14.8, 7.9, 6.1 Hz, 1H), 1.71 (d, *J* = 1.4 Hz, 3H, major), 1.65 (d, *J* = 1.2 Hz, 3H, minor), 1.28 (t, *J* = 7.1, 3H, minor), 1.24 (t, *J* = 7.1 Hz, 3H, major), 0.98 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ Major: 171.4, 166.7, 149.8, 149.6, 140.7, 122.5, 120.5, 60.5, 60.3, 39.7, 37.3, 32.3, 25.1, 22.9, 14.2, 12.7. Minor: 171.5, 166.7, 149.8, 149.6, 140.7, 121.4, 120.5, 60.5, 60.3, 39.5, 37.5, 32.3, 16.4, 14.3, 12.6. HRMS (ESI-TOF) m/z: [M+H]+ calcd for $C_{15}H_{25}O_4$ 269.1747; found 269.1742.

Diethyl (2E)-4-[(1Z)-2,3-dimethylbut-1-en-1-yl]hex-2-enedioate (**17b**). The hydroformylation reaction was run on a 2.94 mmol scale at 60 °C and then a Horner-Wadsworth-Emmons reaction was carried out to facilitate isolation of **12b** as described above. The crude material was purified by column chromatography (10% ethyl acetate/hexanes) to furnish a 63% (0.52 g, *Z*:*E* 3:1) isolated yield of **17b** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) 15.7, 6.5, 1.5 Hz, 2H), 4.96 (d, *J* = 9.2 Hz, 1H, minor), 4.86 (d, *J* = 9.41 Hz, 1H, major), 4.21 – 4.14 (q, 2H), 4.14 – 4.08 (q, 2H), 3.72 (p, *J* = 7.4 Hz, 1H, major), 3.62 (p,

J = 7.5 Hz, 1H, minor), 2.81 (hept, *J* = 6.87 Hz, 1H, major), 2.52 – 2.43 (m, 1H), 2.40 – 2.30 (m, 1H), 2.24 (hept, *J* = 6.83 Hz, 1H, minor) 1.62 (d, *J* = 1.4 Hz, 3H, major), 1.61 (d, *J* = 1.3 Hz, 3H, minor), 1.28 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.8 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 6H, minor), 0.99 – 0.94 (m, 6H, major). ^{13}C NMR (126 MHz, $CDCl_3$) δ Major: 171.4, 166.7, 149.9, 149.6, 144.1, 122.1, 120.5, 60.5, 60.3, 39.8, 37.4, 36.8, 29.0, 21.3, 20.8,14.3, 13.9. Minor: 171.5, 166.7, 149.8, 144.7, 122.1, 120.5, 60.5, 60.3, 39.6, 37.3, 36.8, 36.8, 21.3, 20.5, 18.1, 14.3, 13.9, 12.8. HRMS (ESI-TOF) m/z: [M+Na]+ calcd for $C_{16}H_{26}O_4Na$ 305.1723; found 305.1718.

Diethyl (2E)-4-(cyclohexylidenemethyl)hex-2-enedioate **(18b).** The hydroformylation reaction was run on a 1.76 mmol scale at 60 °C and then a Horner-Wadsworth-Emmons reaction was carried out to facilitate isolation of **12b** as previously described. The crude material was purified by column chromatography (10% ethyl acetate/hexanes) to furnish a 64% (0.34 g) isolated yield of **18b** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 (dd, *J* = 15.7, 6.6 Hz, 1H), 5.80 (dd, *J* = 15.8, 1.2 Hz, 1H), 4.91 – 4.86 (m, 1H), 4.21 – 4.09 (dq, 4H), 3.72 – 3.61 (m, 1H), 2.48 (dd, *J* = 15.0, 6.8 Hz, 1H), 2.37 (dd, *J* = 15.0, 8.0 Hz, 1H), 2.21 – 1.98 (m, 4H), 1.64 – 1.44 (m, 6H), 1.28 (t, *J* = 7.1, 0.9 Hz, 3H), 1.24 (t, *J* = 7.1, 0.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 166.7, 150.0, 143.1, 120.5, 119.6, 60.5, 60.3, 39.7, 37.1, 36.7, 29.2, 28.6, 27.8, 26.7, 14.3, 14.2. HRMS (ESI-TOF) m/z: [M+Na]+ calcd for $C_{17}H_{26}O_4Na$ 295.1903; found 295.1898.

4-Methyl-2-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)pent-3-en-1-ol (**20b**). The hydroformylation reaction was run on a 2.94 mmol scale at 60 °C. After the hydroformylation was complete, dry benzene (7 mL), pinacol (0.3 g, 2.5 mmol) and *p*-toluenesulfonic acid (0.01 g, 0.58 mmol) were added directly to the crude mixture in the

glass pressure bottle. The bottle was sealed with a rubber septum secured with black electrical tape and placed under a nitrogen atmosphere. The pressure bottle was placed in a oil bath at 80 °C for 2 h, after which it was cooled, concentrated under reduced pressure and purified by column chromatography (20% ethyl acetate /hexanes) to furnish a 75% (0.52 g) isolated of **20a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.99 (d, *J* = 6.3 Hz, 1H), 4.97 – 4.93 (m, 1H), 3.69 (ddd, *J* = 11.6, 8.2, 3.7 Hz, 1H), 3.49 (ddd, *J* = 11.6, 8.0, 4.5 Hz, 1H), 2.93 (dd, *J* = 8.1, 3.9 Hz, 1H), 2.69 (dd, *J* = 8.5, 5.2 Hz, 1H), 1.74 (d, *J* = 1.3 Hz, 3H), 1.69 (d, *J* = 1.3 Hz, 3H), 1.23 (d, *J* = 3.0 Hz, 6H), 1.21 (d, *J* = 4.5 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.6, 119.7, 103.5, 82.4, 81.8, 63.7, 46.3, 26.3, 24.4, 24.1, 22.3, 22.1, 18.7. HRMS (ESI-TOF) m/z: [M+Na]+ calcd for $C_{13}H_{24}O_3Na$ 251.1618; found 251.1616.

3-Cyclohexylidene-2-(4,4,5,5-tetramethyl-1,3-dioxo-lan-2-yl)propan-1-ol (**21b**). The hydroformylation reaction was run on a 2.94 mmol scale at 60 °C. After the reaction was complete, dry benzene (7 mL), pinacol (0.3 g, 2.5 mmol), and *p*-toluenesulfonic acid (0.01 g, 0.58 mmol) were added directly to the crude hydroformylation mixture in the glass pressure bottle. The bottle was sealed with a rubber septum secured with black electrical tape and placed under a nitrogen atmosphere. The pressure bottle was placed in a oil bath at 80 °C for 2 h, then cooled and concentrated under reduced pressure. The residue was purified by column chromatography (20% ethyl actate /hexanes) to furnish a 72% (0.58 g) isolated yield of **21a** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.98 (d, *J* = 6.1 Hz, 1H), 4.89 (dt, *J* = 9.5, 1.2 Hz, 1H), 3.69 (ddd, *J* = 11.1, 8.2, 4.1 Hz, 1H), 3.48 (ddd, *J* = 11.1, 7.9, 4.6 Hz, 1H), 2.90 (dd, *J* = 7.9, 4.1 Hz, 1H), 2.73 (dddd, *J* = 9.5, 8.1, 6.1, 4.6 Hz, 1H), 2.26 – 2.09 (m, 4H), 1.66 – 1.44 (m, 6H), 1.21 (dd, *J* = 8.9, 6.2

Hz, 12H).^{13}C NMR (126 MHz, $CDCl_3$) δ 144.6, 116.1, 103.3, 82.3, 81.6, 63.9, 45.1, 37.4, 29.7, 28.6, 28.0, 26.8, 2.3, 24.0, 22.2, 22.0. HRMS (ESI-TOF) m/z: [M+Na]+ calcd for $C_{16}H_{28}O_3Na$ 291.1931; found 291.1928.

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Supporting Information

The supporting information contains additional experimental procedures, optimization studies and characterization data for all new compounds.

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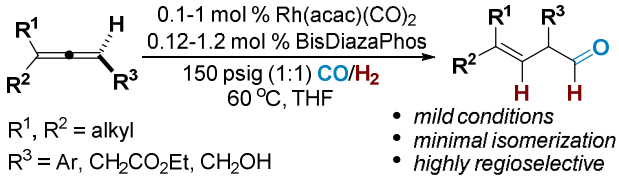

R^1, R^2 = alkyl

R^3 = Ar, CH_2CO_2Et, CH_2OH

- *mild conditions*
- *minimal isomerization*
- *highly regioselective*