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Cooperative Catalysis Approach to Intramolecular Hydroacylation

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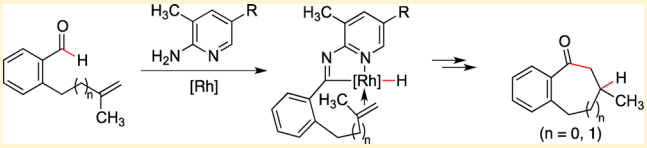
Supporting Information

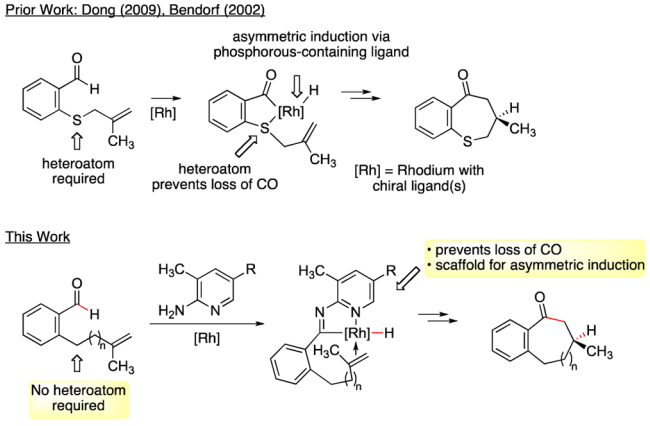
ABSTRACT: Prior examples of hydroacylation to form six- and seven-membered ring ketones require either embedded chelating groups or other substrate design strategies to circumvent competitive aldehyde decarbonylation. A cooperative catalysis strategy enabled intramolecular hydroacylation of disubstituted alkenes to form seven- and six-membered rings without requiring substrate-embedded chelating groups.



INTRODUCTION

Medium rings are traditionally challenging to prepare in synthetic organic chemistry. Although numerous strategies have been described for their preparation, metal-catalyzed hydroacylation is a potentially efficient method for the construction of medium ring ketones from simple alkenes and aldehydes.[1] Existing metal-mediated intramolecular alkene hydroacylation methods are typically limited to reactions in which cyclopentanones are generated.[2] Larger rings can only be directly accessed in cases where judiciously placed heteroatoms[3] are embedded into the starting materials (Scheme 1).[4,5] Alternatively, other strategies have employed more complex substrates that provide a proximal alkene.[6] Embedding a proximal chelating group into the substrate has been successfully applied in intermolecular hydroacylation, as well.[7] The requirement for proximal heteroatoms or alkenes to the aldehyde is often attributed to competitive aldehyde decarbonylation,[8] a process that is slowed by stabilizing the acyl metal intermediate via chelate formation. These substrate limitations are severely limiting to the broad applicability of hydroacylation.

Scheme 1. Medium Rings via Hydroacylation



An alternative to substrate-embedded chelating groups is cooperative catalysis. Over 30 years ago, Suggs suppressed decarbonylation by forming 3-methyl-2-aminopyridyl aldimines, which functioned as surrogates for aldehydes in intermolecular hydroacylation.[9] Jun expanded upon this work, describing that 2-aminopicoline-based aldimines can form in catalytic amounts under intermolecular hydroacylation conditions, again suppressing decarbonylation via transiently formed chelating groups in a process termed cooperative catalysis.[10,11] Suggs and Jun's work is largely limited to monosubstituted alkenes. Recently, Breit and co-workers described a bifunctional cocatalyst, 6-((diphenylphosphino)-methyl)-2-aminopicoline, which improved cocatalyst efficiency relative to 2-aminopicoline in intermolecular hydroacylation reactions of monosubstituted alkenes.[10b] Briet also described increased efficiency in intramolecular hydroacylation reactions of 2-vinylbenzaldehydes to form the five-membered ring of 1-indanones. Briet's cocatalyst is prepared via a five-step sequence (27% overall yield) from the pivalamide of 6-methyl-2-aminopyridine. A general metal-catalyzed intramolecular hydroacylation approach for the synthesis of six- and larger-membered rings remains elusive. Moreover, hydroacylation of 1,1-disubstituted alkenes to form ketones bearing stereocenters has only been reported for the limited substrate classes discussed above.

We were inspired by the above work to develop a general strategy that would allow traditionally challenging, direct intramolecular hydroacylation of disubstituted alkenes (Scheme 1). The aminopyridine cocatalyst is a potential platform for asymmetric catalysis. This work could greatly expand the types of intramolecular hydroacylation reactions beyond those currently possible. A potential challenge in this strategy is that aldimine formation and hydroacylation must be faster than aldehyde decarbonylation. Therefore, one of our goals was to enhance aldimine formation. Moreover, we were aware that competitive isomerization of the alkene to a more substituted

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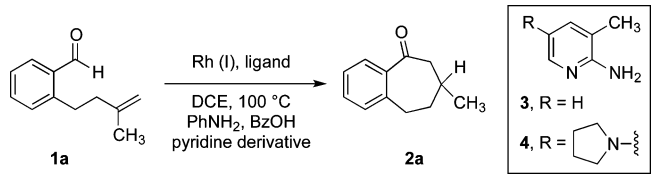
Table 1. Initial Optimization of Hydroacylation[a]



entry	Rh(I) cat.	cat. (mol %)	ligand	ligand (mol %)	2-aminopyridine (mol %)	yield **2a**[b] (%)
1	$Rh(BF_4)(cod)_2$	5	none		**3** (120)	ND
2	$Rh(BF_4)(cod)_2$	5	PPh_3	10	**3** (120)	42
3[c]	$Rh(BF_4)(cod)_2$	5	PPh_3	15	**3** (120)	72
4	$[RhCl(coe)_2]_2$	2.5	none		**3** (120)	ND
5	$[RhCl(coe)_2]_2$	2.5	PPh_3	5	**3** (120)	77
6	$RhCl(PPh_3)_3$	5	none		**3** (120)	60
7	$[RhCl(coe)_2]_2$	2.5	PPh_3	5	**3** (25)	45
8	$[RhCl(coe)_2]_2$	2.5	PPh_3	5	**4** (25)	76
9[c]	$[RhCl(coe)_2]_2$	2.5	PPh_3	5	**3** (10)	81
10	$[RhCl(coe)_2]_2$	2.5	$P(o\text{-Tol})_3$	5	**3** (25)	ND
11	$[RhCl(coe)_2]_2$	2.5	PPh_2Me	5	**3** (25)	68
12	$[RhCl(coe)_2]_2$	2.5	$PPhMe_2$	5	**3** (25)	37
13	$[RhCl(coe)_2]_2$	2.5	$PPhCy_2$	5	**3** (25)	29
14	$[RhCl(coe)_2]_2$	2.5	$P(t\text{-Bu})_3$	5	**3** (25)	ND
15	$[RhCl(coe)_2]_2$	2.5	$P(C_6F_5)_3$	5	**3** (25)	ND

[a]Conditions: Rh(I) cat, ligand, $PhNH_2$ (1.2 equiv), BzOH (10 mol %), DCE, 100 °C. [b]Yields by ^1H NMR spectroscopy of the crude reaction mixture with 4-methoxyacetophenone as an internal standard; ND = **2a** not detected. [c]Entries 3 and 9−15 used $PhCF_3$ as solvent. DCE = 1,2-dichloroethane, cod = 1,5-cyclooctadiene, coe = cyclooctene.

olefin must be avoided. Our results to these ends are reported herein.

RESULTS AND DISCUSSION

We envisioned several strategies to accelerate hydroacylation and avoid the decomposition pathways outlined above. We chose to utilize one of Jun's strategies that was successful in intermolecular hydroacylation reactions: adding $PhNH_2$ and BzOH to presumably convert free aldehyde to the aniline-derived aldimine, providing in situ protection of the aldehyde from decarbonylation.[10d] Our initial attempts to convert aldehyde **1a** to cycloheptanone **2a** using the temporary chelating imine strategy with 2-amino-3-picoline **3** (Table 1, entries 1−7)[12] required an excess of **3** (120 mol %) to achieve acceptable yield of **2a**. In attempts with BF_4 as the rhodium counterion, acceptable yields could be obtained once the ratio of Rh/PPh_3 was 1:3 (Table 1, entries 1−3). Without phosphine in the reaction mixture (Table 1, entry 1), no **2a** was detected. As phosphine was added, the hydroacylation became more efficient at 1:2 (42%, entry 2) and plateaued at 1:3 (72%, entry 3). The amount of phosphine present also impacted reactions in which Cl was the rhodium counterion. Without phosphine, $[RhCl(coe)_2]_2$ did not provide a detectable amount of ketone **2a** (entry 4). Addition of 5 mol % of PPh_3 to give a Rh/PPh_3 mole ratio of 1:1 led to an acceptable 77% yield of **2a** (entry 5). Increasing the Rh/PPh_3 ratio to 1:3 with Wilkinson's catalyst decreased the yield of **2a** to 60% (entry 6). The optimal phosphine to rhodium ratio may have changed with the counterion due to coordination of Cl, but not BF_4, to rhodium under the reaction conditions.

Taking our best conditions that used a stoichiometric amount of **3** (entry 5) and attempting to use amine **3** as a cocatalyst at 25 mol % (entry 7) led to incomplete conversion and a decrease in the yield of **2a** from 77 to 45%. We hypothesized that aldimine formation of 2-amino-3-picoline **3** with **1a** or **1a**'s *N*-phenyl imine congener was sluggish due to the poor nucleophilicity of the amino group in **3** due to the amine's conjugation with an electron-deficient aromatic system.

To reduce the loading of the 2-aminothiazole derivative to catalytic levels, we turned to exploring more reactive cocatalysts in the reaction. Commercially available 2-aminopyridine, 2-aminothiazole, 1-aminobenzotriazole, and 2-aminobenzimidazole gave only traces of product **2a** as replacements for **3** in attempted hydroacylation reactions. However, amine **4** proved to be significantly more efficient as a cocatalyst (Table 1, entry 8 vs 7). We attribute this observation to the higher nucleophilicity of the amine in **4** compared to **3** and thus higher rate of imine equilibration. Cocatalyst **4** can be prepared from **3** in two steps (46% yield overall) via a straightforward iodination/amination sequence. See the Experimental Details for information.

We examined the influence of solvent on reaction by measuring the yield of **2a** at lower temperatures to accentuate solvent effects in the conversion range of 0−20% (not shown). We found that reaction rate qualitatively increases in the order of DCE < THF < PhMe < $PhCF_3$. We could not explain these observations because they do not track well with trends in solvent polarity or Lewis basicity. It is well-known, however, that $PhCF_3$ can be a useful alternative in organic reactions that are typically conducted in chlorinated solvents.[13] In our hydroacylation reactions, it is superior to DCE as well as toluene. Changing solvent from DCE to $PhCF_3$ allowed for the reduction of the cocatalyst loading to 10 mol % while improving the yield of **2a** to 81% (entry 9).

We examined different phosphine ligands to examine the impact of phosphine basicity and sterics on the hydroacylation reaction (Table 1, entries 9−15). Coincidentally, the ligand we initially chose, triphenylphosphine, appeared to be the best ligand of those examined (entry 9). Increasing the steric bulk of the ligand (tri-*ortho*-tolyl phosphine, Table 1, entry 10)

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suppressed the formation of **2a** to below our detection limit. Mixed alkyl/aryl phosphine ligands (methyldiphenylphosphine and dimethylphenylphosphine; entries 11 and 12) decreased the efficiency of the catalytic system, providing **2a** in 68 and 37% yield, respectively when 25 mol % of **3** was employed. Bulky alkyl phosphine ligands (cyclohexyldiphenyl phosphine and tri-*tert*-butylphosphine; entries 13 and 14) proved to be largely ineffective, providing only a 29% yield of **2a** (entry 13). The steric effect might be attributed to the requirement of an extra coordination site for the catalytic directing group in these hydroacylation reactions. This is in contrast to typical cyclopentanone-forming hydroacylation reactions without 2-aminopyridine cocatalysts where the alkene serves the dual purpose of forming a metal chelate to prevent carbon monoxide loss while still undergoing migratory insertion. Therefore, the reaction exhibits high sensitivity to the steric bulk of the ligand compared to the side reactions. A less basic, wide cone angle phosphine, tris(pentafluorophenyl)phosphine, was also completely ineffective in hydroacylation (entry 15).

With the identification of several acceptable conditions (Table 1, entries 8 and 9), we turned to examine the substrate scope (Table 2). Variation of the substituent on the aryl ring (entries 1–4) did not require changes in reaction conditions from those used to obtain acceptable yields of **2a** (Table 1, entry 9). Substrates containing both electron-donating (R^1 = CH_3 or OCH_3, entries 1 and 3) and electron-withdrawing groups (R^1 = CF_3 or F, entries 2 and 4) para to the aldehyde underwent hydroacylation in acceptable yields (76–85%) using 10 mol % of cocatalyst **3**. We examined substitution of the alkene portion of the substrate. Replacing the alkene methyl group with an ethyl substituent (**1f**, R^2 = Et, entry 5), the corresponding hydroacylation product **2f** was obtained in 86% yield using 10 mol % of cocatalyst **3**. Changing R^2 from an alkyl to an aryl group, however, made the hydroacylation more challenging. Phenyl-substituted alkene **1g** required a higher loading (25 mol %) of the more nucleophilic cocatalyst **4** to provide an acceptable 77% yield of cycloheptanone **2g**.[14−16]

Allylic oxygenation on the alkene also rendered the alkene less reactive (**1h**, entry 7), requiring cocatalyst **4** (10 mol %) to provide **2h** in 78% yield (entry 6). Since **1h** was not completely consumed when **3** was the cocatalyst, the more reactive cocatalyst **4** was used. These results show the impact of alkene substitution beyond simple alkyl groups. A more reactive catalyst system is required when additional functional groups are proximal to the alkene.

We also examined substrates in which the alkene and aldehyde are linked via heterocycles rather than a benzene ring. Note that in pyrrole **1i** and indole **1j** (entries 8 and 9), the nitrogen is not a suitable donor for chelation stabilization of the rhodium hydride intermediate. These substrates reacted sluggishly under hydroacylation conditions and required 25 mol % of cocatalyst **4**, 5 mol % of $[RhCl(coe)_2]_2$, and 10 mol % PPh_3 to provide 63 and 66% yield of dihydropyrroloazepineone **2i** and dihydroazepinoindolone **2j**, respectively. We attribute the lower reactivity of these substrates to increased conjugation to the carbonyl, which may lower its electrophilicity and slow imine formation and/or subsequent hydroacylation steps.

We note that the high preference for 7-endo cyclization is completely reversed from the 6-exo selectivity recently reported for *N*-heterocyclic carbene (NHC)-catalyzed intramolecular hydroacylation with **1g** reported by Grimme, Glorius, and coworkers, which proceeds by a completely different mechanism.[17] The regioselectivity in NHC- compared to Rh-catalyzed reactions provides chemists with a powerful means of complementary regiochemical control in hydroacylation reactions.

Table 2. Scope of Intramolecular Hydroacylation

entry[a]	substrate **1**	R^1	R^2	**3** or **4** (mol %)	product **2**	yield[b]
1	**1b**	Me	Me	**3** (10%)	**2b**	84%[c]
2	**1c**	CF_3	Me	**3** (10%)	**2c**	76%
3	**1d**	OMe	Me	**3** (10%)	**2d**	85%
4	**1e**	F	Me	**3** (10%)	**2e**	80%[c]
5	**1f**	H	Et	**3** (10%)	**2f**	86%
6	**1g**	H	Ph	**4** (25%)	**2g**	77%
7	**1h**	H	CH_2OTBS	**4** (10%)	**2h**	78%
8[d]	**1i**			**4** (25%)	**2i**	63%
9[d]	**1j**			**4** (25%)	**2j**	66%
10	**1k**			**4** (90%)	**2k**	65%[e]
11	**1l**			**4** (25%) **4** (100%)	**2l**	48% 58%
12[d]	**1m**			**4** (25%)	**2m**	67%
13[d]	**1n**			**4** (100%)	**2n**	69%

[a]Conditions: $[RhCl(coe)_2]_2$ (2.5 mol %), PPh_3 (5 mol %), $PhNH_2$ (1.2 equiv), BzOH (10 mol %), $PhCF_3$, 100 °C. [b]Isolated yield after silica gel chromatography. Except where noted, regioisomeric hydroacylation products were not observed, indicating regioselectivity was >10:1. [c]Contaminated with a minor <5% of the corresponding indanone; pure sample could be obtained by preparative TLC. [d]Conditions: $[RhCl(coe)_2]_2$ (5 mol %), PPh_3 (10 mol %), $PhNH_2$ (1.2 equiv), BzOH (10 mol %). [e]Yield by ^1H NMR spectroscopy of the crude reaction mixture with 4-methoxyacetophenone as an internal standard. An attempt with 25% **4** gave 30% yield of **2k** after a challenging purification by chromatography.

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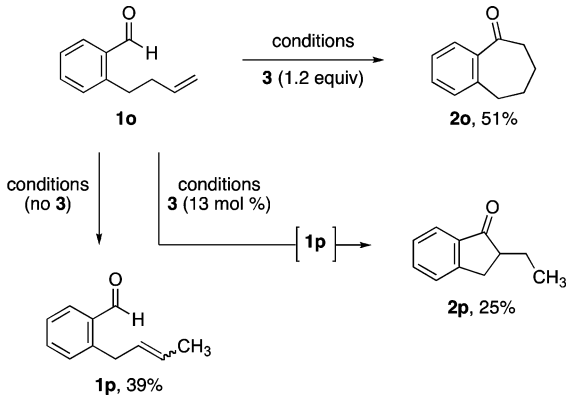
Six-membered rings are also traditionally challenging to form via metal-catalyzed intramolecular hydroacylation. As we expanded our study to target six-membered ring products, we were somewhat surprised that these substrates (**1k**−**1n**, Table 2, entries 10−13) reacted much more slowly than their longer-tether counterparts. Typically, six-membered ring formation is more facile than seven-membered ring construction.[18] In our case, however, higher loadings of aminopyridine **4** were required to achieve yields ranging from 48 to 69%, and in some cases, a full equivalent of **4** was required (entries 11 and 13). The poorer behavior of **1k**−**1n** compared to congeners targeting seven-membered rings might be explained by slower migratory insertion in these substrates compared their higher homologues. We speculate that the more proximal alkene might lead to a stable alkene complex after C−H activation, perhaps raising the barrier to migratory insertion. Alternatively, reductive elimination may be slower from the presumptive seven-membered metallacycle in the formation of **2k**−**2n** compared to their congeners that should proceed via an eight-membered metallacycle. Typically, reductive elimination is rate-limiting in intramolecular hydroacylation reactions.[19]

Interestingly, substrate **1o**, containing a monosubstituted alkene, also required higher loadings of cocatalyst for successful hydroacylation to form 1-benzosuberone (**2o**, Scheme 2). We found that, without cocatalyst **3**, isomerization from the terminal to the internal alkene (**1o** → **1p**) occurred to form a mixture of *trans*/*cis*-**1p**. Thus higher loadings of cocatalyst are required to suppress this side reaction. With low loadings of cocatalyst **3**, the isomerization is prevailing and no **2o** is observed. Instead, indanone **2p** is formed as the major product under these reaction conditions, presumably by cyclization of **1p**. A small amount of 2-methyl dihydronaphthalenone was also observed in this attempt. We also note that, under many of our optimization reactions in Table 1, a minor amount of 2-isopropyl-2,3-dihydroindenone (tentatively assigned) was observed in the crude product mixtures.

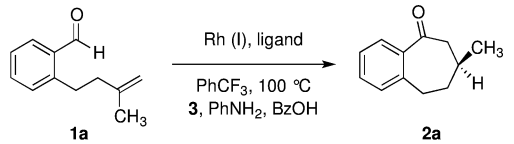
Given recent advances in asymmetric hydroacylation, we performed a preliminary investigation on asymmetric hydroacylation, using the conversion **1a** to **2a** as our test reaction. No reaction was observed when bidentate ligands (BINAP, DUPHOS, dppe, or dppp) were used as additives to various rhodium species (results not shown). Product **2a** was observed when chiral monodentate ligands (entries 2−4, Table 3) were used as additives, although yields were low in all cases examined. Given the high sensitivity of the efficiency of hydroacylation to the structure of the phosphorus-containing ligand (Table 3 and Table 2, entries 9−15), we curtailed our investigation of these types of ligands and sought new ways to induce asymmetry in the reaction.

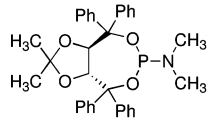
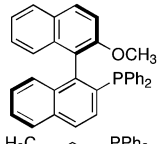
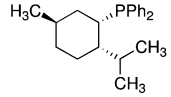
Scheme 2. Monosubstituted Alkene Hydroacylation[a]



[a]Conditions: $[RhCl(coe)_2]_2$ (2.5 mol %), PPh_3 (5 mol %), BzOH (10 mol %), $PhNH_2$ (1.2 equiv), $PhCF_3$, 100 °C.

Table 3. Effects of Chiral Ligands[a]



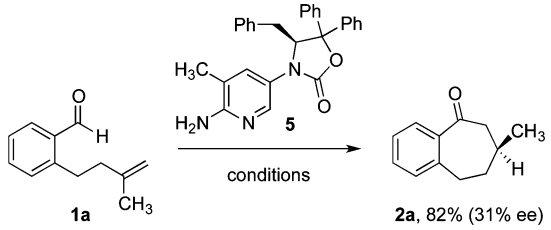
Entry	Ligand	yield[b]	ee[c]
1	(+)-MONOPHOS	ND	--
2[d]		30%	23%
3		10%	24%
4		3%	18%

[a]Conditions: $[RhCl(coe)_2]_2$ (2.5 mol %), ligand (5 mol %), $PhNH_2$ (1.2 equiv), BzOH (10 mol %), $PhCF_3$, 100 °C. [b]Yield after silica gel chromatography; ND = **2a** not detected. [c]Determined by HPLC (Chiralcel OD-H, *n*-hexane/IPA (9:1), λ = 220 nm). [d]**1a**, $PhNH_2$, and BzOH in $PhCF_3$ were premixed before adding $[RhCl(coe)_2]_2$, ligand, and **3**.

Since our optimization studies had conclusively shown that cocatalysts **3** and **4** were also necessary for hydroacylation, we hypothesized that incorporating chirality into the 2-amino-3-picoline structure would provide an entry to asymmetric hydroacylation. We decided to use analogues of **4** with a chiral 5-amino group, due to ease of preparation of these compounds and expected high reactivity from the electron-donating group.[20]

Our initial studies with **5** (Scheme 3), which was derived from a chiral oxazolidinone, showed that it is less reactive than **4** and even **3**. However, the reaction could still be successfully accomplished with 25 mol % loading of cocatalyst **5**. Promising enantioselectivity was observed in this case (**2a**, 82% yield, 31% ee). Although not yet synthetically useful, this showcases a new strategy for inducing asymmetry in hydroacylation reactions.

Scheme 3. Enantioselective Hydroacylation[a]



[a]Conditions: $[RhCl(coe)_2]_2$ (2.5 mol %), PPh_3 (5 mol %), $PhNH_2$ (1.2 equiv), BzOH (10 mol %), **5** (25 mol %), $PhCF_3$, 80 °C

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Our approach is a significant departure from prior work based on chiral phosphorus-containing ligands in hydroacylation chemistry. Given the high degree of recent interest in asymmetric hydroacylation, these results should inspire additional work, which we envision will achieve high levels of enantioinduction in the fullness of time.

CONCLUSION

In conclusion, we have reported the first effective method for metal-catalyzed synthesis of six- and seven-membered ring ketones via hydroacylation that is free of the requirement of chelating groups embedded into the substrate. The development of electron-rich 2-amino-3-picolines **4** and **5** enables the incorporation of a temporary chelate scaffold on the aldehyde that avoids decomposition via aldehyde decarbonylation and alkene isomerization pathways. For challenging substrates, **4** may also be used in stoichiometric amounts. The regiochemistry of the hydroacylation is complementary to NHC-catalyzed hydroacylation reactions,[17] which should prove useful in synthesis planning. Chiral 2-aminopyridines such as **5** represent a new strategy for asymmetric catalysis in hydroacylation. Future work will be directed at improvement of the asymmetric induction in hydroacylation and applications in target-directed synthesis.

EXPERIMENTAL DETAILS

Trifluorotoluene ($PhCF_3$) was distilled over phosphorus pentoxide, degassed by four freeze−pump−thaw cycles in a Straus flask and then stored in a nitrogen-filled glovebox. All rhodium complexes were purchased and used as received, except $[RhCl(coe)_2]_2$ which was prepared by a known procedure.[21] The preparations of aldehydes **1a**,[22] **1k**,[23] **1g**,[21] and **1o**[21] have been previously reported, and new procedures for the preparations of **1k** and **1g** are reported below. Aldehyde **1o** was prepared in analogy to **1b**. All rhodium-catalyzed processes were carried out in a N_2-filled glovebox in 1 dram vials with polytetrafluoroethylene-lined caps, and heating was applied by aluminum block heaters. HRMS measurements using electrospray ionization (ESI) were performed with a time-of-flight (TOF) mass analyzer, and HRMS measurements using chemical ionization (CI) were performed with a magnetic sector mass analyzer.

General Procedure for the Synthesis of Aldehydes 1b−1e.[24] *N,N,N*-Trimethylethyldiamine (0.41 mL, 3.2 mmol) in THF (8 mL) was added to a flame-dried flask under nitrogen, the solution was cooled to −78 °C, and *n*-BuLi (2.5 M in hexanes, 1.35 mL, 3.10 mmol) was added dropwise. The reaction was allowed to stir for 30 min at −78 °C, followed by slow addition of 2-methylbenzaldehyde derivative (3.0 mmol). The solution was warmed to −15 °C for 20 min and recooled to −55 °C for the dropwise addition of *t*-BuLi (1.7 M in pentane, 5.3 mL, 9.0 mmol). The resulting deep red solution was stirred at −55 °C for 2.5 h and recooled to −78 °C. Isobutenyl chloride (1.75 mL, 18 mmol) was added rapidly, and the pale yellow solution was allowed to warm to room temperature and stirred for 30 min. The solution was poured onto cold 1.0 M HCl (15 mL), stirred for 10 min, and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 15 mL), and the combined organics were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Silica gel chromatography (EtOAc/Hex) afforded compounds **1b−1e** in reported yields.

*4-Methyl-2-(3-methylbut-3-en-1-yl)benzaldehyde (**1b**).* See general procedure for the synthesis of aldehydes **1b−1e**. Reaction was carried out with 308 mg (2.3 mmol) of 2,4-dimethylbenzaldehyde. The crude product mixture was purified by silica gel column chromatography (1:6 EtOAc/Hex) to afford 360 mg (83% yield) of **1b** as a colorless oil: R_f 0.60 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.20 (s, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.17 (d, J = 7.8 Hz, 1H), 7.09 (s, 1H), 4.77−4.72 (m, 2H), 3.15−3.10 (m, 2H), 2.39 (s, 3H), 2.31−2.26 (m, 2H), 1.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.9, 144.96, 144.92, 144.7, 132.3, 131.6, 131.3, 127.3, 110.5, 40.1, 31.1, 22.5, 21.7; IR (film) 3047, 2973, 2919, 1691, 1607, 1451, 1300 cm^{-1}; HRMS (CI) calcd for $[C_{13}H_{16}O + NH_4]^+$ m/z 206.1539, found 206.1544.

*2-(3-Methylbut-3-en-1-yl)-4-(trifluoromethyl)benzaldehyde (**1c**).* See general procedure for the synthesis of aldehydes **1b−1e**. Reaction was carried out with 2-methyl-4-trifluoromethylbenzaldehyde (188 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography (1:6 EtOAc/Hex) to afford 203 mg (84% yield) of **1c** as a colorless oil: R_f 0.50 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.34 (s, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.55 (s, 1H), 4.79−4.71 (m, 2H), 3.26−3.20 (m, 2H), 2.33 (t, J = 8.1 Hz, 2H), 1.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.1, 145.6, 144.1, 136.0, 134.8 (q, J = 32.3 Hz), 131.9, 127.8 (q, J = 3.2 Hz), 123.5 (q, J = 272.9 Hz), 123.4 (q, J = 3.7 Hz), 111.2, 39.9, 30.9, 22.4; IR (film) 3056, 2983, 2939, 1706, 1498, 1422, 1330, 1266, 1173,1132 cm^{-1}; HRMS (CI) calcd for $[C_{13}H_{13}F_3O + H]^+$ m/z 243.0991, found 243.1015.

*4-Methoxy-2-(3-methylbut-3-en-1-yl)benzaldehyde (**1d**).* See general procedure for the synthesis of aldehydes **1b−1e**. Reaction was carried out with 4-methoxy-2-methylbenzaldehyde (345 mg, 2.3 mmol). The crude mixture was purified by silica gel column chromatography (1:4 EtOAc/Hex) to afford 388 mg (83% yield) of **1d** as a colorless oil: R_f 0.40 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.10 (s, 1H), 7.78 (d, J = 8.7 Hz, 1H), 6.85 (dd, J = 2.7, 8.7 Hz, 1H), 6.76 (d, J = 2.4 Hz, 1H), 4.74 (d, J = 11.4 Hz, 2H), 3.87 (s, 3H), 3.17−3.11 (m, 2H), 2.32−2.27 (m, 2H), 1.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.7, 163.7, 147.6, 144.9, 134.8, 127.3, 116.1, 111.6, 110.6, 55.4, 39.8, 31.3, 22.5; IR (film) 3056, 2934, 2841, 1687, 1601, 1567, 1496, 1461 cm^{-1}; HRMS (CI) calcd for $[C_{13}H_{16}O_2 + H]^+$ m/z 205.1223, found 205.1235.

*4-Fluoro-2-(3-methylbut-3-en-1-yl)benzaldehyde (**1e**).* See general procedure for the synthesis of aldehydes **1b−1e**. Reaction was carried out with 2-methoxy-4-methylbenzaldehyde (303 mg, 2.2 mmol). The crude mixture was purified by silica gel column chromatography (1:6 EtOAc/Hex) to afford 340 mg (80% yield) of **1e** as a colorless oil: R_f 0.60 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.18 (s, 1H), 7.87−7.81 (m, 1H), 7.07−6.94 (m, 2H), 4.77−4.69 (m, 2H), 3.19−3.14 (m, 2H), 2.32−2.27 (m, 2H), 1.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.5, 165.7 (d, J = 256.6 Hz), 148.4 (d, J = 9.1 Hz), 144.3, 134.7 (d, J = 10.0 Hz), 130.3 (d, J = 2.6 Hz), 117.6 (d, J = 21.7 Hz), 113.8 (d, J = 21.7 Hz), 111.0, 39.5, 30.8, 22.4; IR (film) 3054, 2984, 2937, 1695, 1606, 1583, 1491, 1266 cm^{-1}; HRMS (CI) calcd for $[C_{12}H_{13}FO + NH_4]^+$ m/z 210.1289, found 210.1292.

*2-(3-Methylenepentyl)benzaldehyde (**1f**).* *N,N,N*-Trimethylethyldiamine (0.40 mL, 3.15 mmol) in THF (8 mL) was added to a flame-dried flask under nitrogen, the solution was cooled to −78 °C, and *n*-BuLi (2.5 M in hexanes, 1.24 mL, 3.10 mmol) was added dropwise. The reaction was allowed to stir for 30 min at −78 °C, followed by slow addition of 2-methylbenzaldehyde (0.35 mL, 3.0 mmol). The solution was warmed to −15 °C for 20 min and recooled to −55 °C for the dropwise addition of *t*-BuLi (1.7 M in pentane, 3.5 mL, 6.0 mmol). The resulting deep red solution was stirred at −55 °C for 4 h. 2-Methylenebutyl-4-methylbenzenesulfonate[20] (2.16 g, 9 mmol) in THF (2 mL) was added rapidly, and the pale yellow solution was allowed to warm to room temperature and stirred for 30 min. The solution was poured onto cold 1.0 M HCl (15 mL) and stirred for 10 min. PhMe (50 mL) was added, the layers were separated, and the organic extracts were concentrated in vacuo. Silica gel chromatography (1:30 EtOAc/Hex) afforded compound **1f** (322 mg, 1.71 mmol, 57%) as a colorless oil: R_f 0.60 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.27 (s, 1H), 7.83 (dd, J = 1.5, 8.9 Hz, 1H), 7.53 (dt, J = 1.5, 7.5 Hz, 1H), 7.37 (dt, J = 0.9, 7.5 Hz, 1H), 7.28 (dd, J = 0.6, 7.5 Hz, 1H), 4.78−4.76 (m, 2H), 3.20−3.14 (m, 2H), 2.32−2.29 (m, 2H), 2.10 (dq, J = 0.3, 7.2 Hz, 2H), 1.05 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.3, 150.5, 145.1, 133.8, 131.8, 131.0, 126.5, 110.1, 108.5, 38.7, 31.3, 28.8, 12.3; IR (film) 2964, 2728, 1693, 1599 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{16}O + Na]^+$ m/z 211.1093, found 211.1098.

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*2-(3-Phenylbut-3-en-1-yl)benzaldehyde (**1g**).* *N,N,N*-Trimethylethyldiamine (0.40 mL, 3.15 mmol) in THF (8 mL) was added to a flame-dried flask under nitrogen, the solution was cooled to −78 °C, and *n*-BuLi (2.5 M in hexanes, 1.24 mL, 3.10 mmol) was added dropwise. The reaction was allowed to stir for 30 min at −78 °C, followed by slow addition of 2-methylbenzaldehyde (0.35 mL, 3.0 mmol). The solution was warmed to −15 °C for 20 min and recooled to −55 °C for the dropwise addition of *t*-BuLi (1.7 M in pentane, 3.5 mL, 6.0 mmol). The resulting deep red solution was stirred at −55 °C for 3 h and cooled to −78 °C. 3-Bromo-2-phenylpropene[25] (1.76 g, 9 mmol) in THF (2 mL) was added rapidly, and the pale yellow solution was allowed to warm to room temperature and stirred for 30 min. The solution was poured onto cold 1.0 M HCl (15 mL) and stirred for 10 min. PhMe (50 mL) was added, the layers were separated, and the organic layer was concentrated in vacuo. Silica gel chromatography (1:30 EtOAc/Hex) afforded compound **1g** (306 mg, 1.30 mmol, 43%) as a colorless oil: R_f 0.55 (1:4 EtOAc/Hex). The characterization data are consistent with those previously reported.[21]

*2-(3-(((tert-Butyldimethylsilyl)oxy)methyl)but-3-en-1-yl)-benzaldehyde (**1h**).* *N,N,N*-Trimethylethyldiamine (0.14 mL, 1.1 mmol) in THF (5 mL) was added to a flame-dried flask under nitrogen, the solution was cooled to −78 °C, and *n*-BuLi (2.5 M in hexanes, 0.44 mL, 1.10 mmol) was added dropwise. The reaction was allowed to stir for 30 min at −78 °C, followed by slow addition of 2-methylbenzaldehyde (0.12 mL, 1.0 mmol). The solution was warmed to −15 °C for 20 min and recooled to −55 °C for the dropwise addition of *t*-BuLi (1.7 M in pentane, 0.88 mL, 1.5 mmol). The resulting deep red solution was stirred at −55 °C for 3 h and cooled to −78 °C. ((2-(Bromomethyl)allyl)oxy)(*tert*-butyl)dimethylsilane[26] (619 mg, 2.34 mmol) in THF (1 mL) was added rapidly, and the pale yellow solution was stirred for 5 min and quenched with 1.0 M HCl (3 mL). The reaction mixture was allowed to warm to room temperature, PhMe (10 mL) was added, the layers were separated, and the organic extracts were concentrated in vacuo. Silica gel chromatography (1:50 EtOAc/Hex) afforded compound **1h** (74 mg, 0.24 mmol, 24%) as a colorless oil: R_f 0.50 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.20 (s, 1H), 7.76 (dd, J = 1.3, 7.5 Hz, 1H), 7.43 (dt, J = 1.5, 7.5 Hz, 1H), 7.32 (dt, J = 1.5, 7.5 Hz, 1H), 7.21 (dd, J = 1.5, 7.5 Hz, 1H), 5.01 (d, J = 1.8 Hz, 1H), 4.80 (dd, J = 1.2, 2.7 Hz, 1H), 4.04 (s, 2H), 3.11 (m, 2H), 2.24 (t, J = 8.1 Hz, 2H), 0.83 (s, 9H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.3, 147.6, 144.8, 133.8, 133.7, 131.9, 131.0, 126.6, 109.5, 65.9, 35.0, 31.3, 25.9, 18.4, −5.4; IR (film) 2953, 2928, 2855, 2730, 1697, 1600, 1249, 1114, 1086 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{28}O_2Si + Na]^+$ m/z 327.1756, found 327.1754.

*2-(2-Methyallyl)benzaldehyde (**1k**).* In a round-bottom flask equipped with a reflux condenser and magnetic stir bar under nitrogen, Mg (150 mg, 6.25 mmol) and a small crystal of I_2 were placed. The flask was flame-dried under high vacuum. THF (3 mL) and 2-(2-bromophenyl)-1,3-dioxolane[27] (1.15 g, 5 mmol) were added, and the mixture was maintained at reflux for 2 h. The resulting solution was allowed to cool to room temperature then added dropwise to a stirred solution of isobutenyl chloride (0.74 mL, 7.5 mmol) and suspension of CuI (95 mg, 0.5 mmol) in THF (5 mL) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and then allowed to warm to room temperature overnight. CH_2Cl_2 (10 mL) was added, and the mixture was washed with a saturated aqueous NH_4Cl solution. The organic phase was separated and concentrated in vacuo. TsOH (20 mg, 0.1 mmol), water (10 mL), and acetone (10 mL) were added, and the resulting solution was heated at reflux for 2 h. The reaction mixture was extracted with CH_2Cl_2 (40 mL). The organic phase was separated, dried over Na_2SO_4, and concentrated in vacuo. Silica gel chromatography (1:20 EtOAc/Hex) afforded compound **1k** (345 mg, 2.16 mmol, 43%) as a colorless oil: R_f 0.65 (1:4 EtOAc/Hex). The characterization data are consistent with those previously reported.[21]

*2-(2-Phenylallyl)benzaldehyde (**1l**).* In a round-bottom flask equipped with a reflux condenser and magnetic stir bar under nitrogen, Mg (150 mg, 6.25 mmol) and a small crystal of I_2 were placed. The flask was flame-dried under high vacuum. THF (3 mL) and 2-(2-bromophenyl)-1,3-dioxolane[25] (1.15 g, 5 mmol) were added, and the mixture was maintained at reflux for 2 h. The resulting solution was added dropwise to a stirred solution of 3-bromo-2-phenylpropene (1.48 g, 7.5 mmol) and suspension of CuI (95 mg, 0.5 mmol) in THF (5 mL) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and then allowed to warm to room temperature overnight. CH_2Cl_2 (10 mL) was added, and the mixture was washed with a saturated aqueous NH_4Cl solution. The organic phase was separated and concentrated in vacuo. TsOH (20 mg, 0.1 mmol), water (10 mL), and acetone (10 mL) were added, and the resulting solution was heated at reflux for 2 h. The reaction mixture was extracted with CH_2Cl_2 (40 mL). The organic phase was separated, dried over Na_2SO_4, and concentrated in vacuo. Silica gel chromatography (1:20 EtOAc/Hex) afforded compound **1l** (445 mg, 2.00 mmol, 40%) as a colorless oil: R_f 0.60 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.22 (s, 1H), 7.86 (dd, J = 1.5, 7.5 Hz, 1H), 7.51−7.22 (m, 8H), 5.45 (t, J = 0.9 Hz, 1H), 4.71 (dd, J = 1.5, 2.4 Hz, 1H), 4.23 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.2, 147.4, 141.7, 140.8, 134.1, 133.8, 131.5, 131.4, 128.3, 127.7, 127.0, 125.9, 114.8, 37.6; IR (film) 3055, 3029, 2855, 2753, 1696, 1599, 1210 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{14}O + Na]^+$ 245.0942, found 245.0951.

General Procedure for the Synthesis of Pyrrole- and Indole-Containing Aldehydes (1i, 1j, 1m, 1n). Aldehyde (5 mmol), 18-crown-6 (5 mmol), and powdered KOH (10 mmol) were refluxed in benzene (5 mL) for 2 h. 4-Iodo-2-methyl-1-butene or isobutenyl chloride (15.0 mmol) was added as a solution in benzene (2.5 mL), and reflux was maintained for an additional 6 h. The solution was washed with water, and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 15 mL), and the combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Silica gel chromatography (EtOAc/Hex) afforded **1i**, **1j**, **1m**, or **1n** as yellow oils in the reported yields.

*1-(3-Methylbut-3-en-1-yl)-1H-pyrrole-2-carbaldehyde (**1i**).* See general procedure for the synthesis of pyrroles and indoles **1i**, **1j**, **1m**, and **1n**. Reaction was carried out with 1*H*-pyrrole-2-carbaldehyde (475 mg, 5.0 mmol). The crude product mixture was purified by silica gel column chromatography (1:3 EtOAc/Hex) to afford 407 mg (50% yield) of **1i** as a yellow oil: R_f 0.35 (1:3 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.53 (s, 1H), 6.92 (d, J = 3.6 Hz, 2H), 6.19 (t, J = 3.6 Hz, 1H), 4.77−4.76 (m, 1H), 4.64−4.63 (m, 1H), 4.41 (t, J = 7.2 Hz, 1H), 2.44 (t, J = 7.3 Hz, 1H), 1.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.0, 141.7, 131.2, 131.0, 124.7, 112.4, 109.3, 47.5, 39.2, 22.2; IR (film) 3052, 2983, 2810, 1671, 1613, 1466, 1264 cm^{-1}; HRMS (CI) calcd for $[C_{10}H_{13}NO + H]^+$ m/z 164.1070, found 164.1086.

*1-(3-Methylbut-3-en-1-yl)-1H-indole-2-carbaldehyde (**1j**).* See the general procedure for the synthesis of pyrroles and indoles **1i**, **1j**, **1m**, and **1n**. Reaction was carried out with 1*H*-indole-2-carbaldehyde (290 mg, 2.0 mmol). The crude product mixture was purified by silica gel column chromatography (1:3 EtOAc/Hex) to afford 225 mg (53% yield) of **1j** as a yellow oil: R_f 0.50 (1:3 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.89 (s, 1H), 7.74 (dt, J = 8.1, 0.9 Hz, 1H), 7.44−7.42 (m, 3H), 7.23−7.16 (m, 1H), 4.79 (q, J = 1.5 Hz, 1H), 4.71−4.70 (m, 1H), 4.67 (t, J = 2.1 Hz, 1H), 4.64 (s, 1H), 2.46 (t, J = 7.8 Hz), 1.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.5, 142.4, 140.1, 135.2, 126.8, 126.4, 123.4, 120.9, 117.9, 112.3, 110.5, 43.6, 38.3, 22.6; IR (film) 3075, 2968, 2806, 1664, 1526, 1322, 1266, 1216 cm^{-1}; HRMS (CI) calcd for $[C_{14}H_{15}NO + H]^+$ m/z 214.1226, found 214.1236.

*1-(2-Methylallyl)-1H-pyrrole-2-carbaldehyde (**1m**).* See general procedure for the synthesis of pyrroles and indoles **1i**, **1j**, **1m**, and **1n**. This was started with 380 mg (4.0 mmol) of 1*H*-pyrrole-2-carboxaldehyde. The crude mixture was purified by silica gel column chromatography (1:3 EtOAc/Hex) to afford 423 mg (71% yield) of **1m** as yellow oil: R_f 0.35 (1:3 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.54 (s, 1H), 6.95−6.93 (m, 2H), 6.26 (t, J = 3.2 Hz, 1H), 4.90 (s, 2H), 4.84 (s, 1H), 4.48 (s, 1H), 1.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.4, 142.0, 131.5, 124.4, 111.6, 109.8, 53.8, 19.9; IR (film) 3056, 2983, 2924, 1665, 1529, 1479, 1371, 1267 cm^{-1}; HRMS (CI) calcd for $[C_9H_{11}NO + H]^+$ m/z 150.0913, found 150.0926.

*1-(2-Methylallyl)-1H-indole-2-carbaldehyde (**1n**).* See general procedure for the synthesis of pyrroles and indoles **1i**, **1j**, **1m**, and

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1n. This was started with 290 mg (2.0 mmol) of 1*H*-indole-2-carbaldehyde. The crude mixture was purified by silica gel column chromatography (1:3 EtOAc/Hex) to afford 258 mg (65% yield) of **1n** as yellow oil: R_f 0.50 (1:3 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.89 (s, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.44−7.41 (m, 1H), 7.39 (s, 1H), 7.29 (s, 1H), 7.22−7.17 (m, 1H), 5.17 (s, 2H), 4.82 (s, 1H), 4.41 (s, 1H), 1.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.5, 141.2, 140.6, 135.3, 126.9, 126.3, 123.3, 121.0, 117.9, 111.0, 110.8, 49.9, 19.9; IR (film) 3054, 2984, 2818, 1671, 1614, 1464, 1266 cm^{-1}; HRMS (CI) calcd for $[C_{13}H_{13}NO + H]^+$ m/z 200.1070, found 200.1089.

*2-(But-2-en-1-yl)benzaldehyde (mixture of E and Z) (**1p**).* 2-(But-3-en-1-yl)benzaldehyde **1o** (38.6 mg, 0.24 mmol), aniline (32 mg, 0.34 mmol), benzoic acid (2.9 mg, 0.024 mmol), and triphenylphosphine (3.1 mg, 0.012 mmol) were added to a 1 dram vial with a magnetic stir bar in the nitrogen atmosphere of the glovebox. $PhCF_3$ (0.50 mL) and chlorobis(cyclooctene)rhodium(I) dimer (4.3 mg, 0.006 mmol) were added. The resulting solution was stirred for 16 h at 100 °C, and the reaction vial was removed from the glovebox. Aqueous HCl (1.0 mL, 1M) was added, and the mixture was vigorously stirred for 10 min. The organic phase was separated and concentrated in vacuo. Column chromatography on silica gel (30:1 Hex/EtOAc) afforded **1p** as a colorless oil, which could not be separated from minor impurities (15 mg, 0.09 mmol, 39%): R_f 0.58 (4:1 Hex/EtOAc). Peaks corresponding to (*E*)-**1p**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.28 (s, 1H), 7.86−7.82 (m, 1H), 7.55−7.49 (m, 1H), 7.40−7.34 (m, 1H), 7.30−7.28 (m, 1H), 5.67−5.59, 5.49−5.39, 3.74 (d, J = 6.3 Hz, 2H), 1.74−1.65 (m, 3H).[28]

*7-Methyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (**2a**).* Aldehyde **1a** (51.3 mg, 0.29 mmol), amine **3** (3.5 mg, 0.030 mmol, 10 mol %), aniline (33 mg, 0.36 mmol), benzoic acid (4.4 mg, 0.036 mmol), and triphenylphosphine (3.9 mg, 0.015 mmol) were added to a 1 dram vial with a magnetic stir bar and brought into a nitrogen atmosphere glovebox. $PhCF_3$ (0.60 mL) and chlorobis(cyclooctene)-rhodium(I) dimer (5.4 mg, 0.0075 mmol) were added. The resulting solution was stirred for 15 h at 100 °C, and the reaction vial was removed from the glovebox. CH_2Cl_2 (1 mL) and 1 M aqueous HCl (0.6 mL) were added, and the mixture was vigorously stirred for 10 min. The organic layer was concentrated with silica gel in vacuo. Silica gel chromatography with CH_2Cl_2/Hex (2:1) provided **2a** as a colorless oil (41.7 mg, 0.24 mmol, 81%): R_f 0.43 (2:1 CH_2Cl_2/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.41−7.38 (m, 1H), 7.30−7.26 (m, 1H), 7.20 (d, J = 7.5 Hz, 1H), 3.04−2.99 (m, 1H), 2.90−2.75 (m, 1H), 2.77 (dd, J = 15 Hz, 4.5 Hz, 1H), 2.60 (dd, J = 15 Hz, 9.0 Hz, 1H), 2.10−2.00 (m, 2H), 1.55−1.51 (m, 1H), 1.06 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.5, 142.4, 138.8, 131.9, 129.7, 128.4, 126.5, 49.0, 34.3, 32.1, 28.6, 21.7; IR (neat film NaCl) 2954, 2926, 2870, 1679, 1599, 1299, 1292, 1279 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{14}O + Na]^+$ m/z 197.0942, found 197.0934. The structure was also confirmed by COSY, HMQC, and HMBC.

*(−)-7-Methyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one, (−)-**2a**.* Aldehyde (34.0 mg, 0.20 mmol), amine **5** (22 mg, 0.05 mmol, 25 mol %), aniline (22 mg, 0.24 mmol), benzoic acid (2.4 mg, 0.02 mmol), and triphenylphosphine (5.2 mg, 0.02 mmol) were added to a 1 dram vial with a magnetic stir bar in the nitrogen atmosphere of the glovebox. $PhCF_3$ (0.2 mL) and chlorobis(cyclooctene)rhodium(I) dimer (7.2 mg, 0.01 mmol) were added. The resulting solution was stirred for 15 h at 80 °C, and reaction vial was removed from the glovebox. Aqueous HCl (1.0 mL, 1M) and CH_2Cl_2 (1 mL) were added, and the mixture was vigorously stirred for 10 min. The organic phase was separated and concentrated in vacuo. Column chromatography on silica gel (1:2 Hex/CH_2Cl_2) afforded (−)-**2a** as a colorless oil (27.9 mg, 0.16 mmol, 82%): R_f, ^{1}H NMR, ^{13}C NMR, IR, and HRMS data as reported above for (±)-**2a**. HPLC analysis: ee 31% (Chiracel OD, 1:19 isopropyl alcohol/hexanes, 1.0 mL/min, 254 nm, t_{R1} = 5.5 min, t_{R2} = 5.9 min); $[\alpha]^{25}_D$ = −15 (c = 0.80, $CHCl_3$).

General Procedure for Preparation of Ketones 2b−2e. Aldehyde (0.30 mmol), amine **3** (3.5 mg, 0.030 mmol, 10 mol %), aniline (33 mg, 0.36 mmol), benzoic acid (4.4 mg, 0.036 mmol), and triphenylphosphine (3.9 mg, 0.015 mmol) were added to a 1 dram vial with a magnetic stir bar and brought into a nitrogen atmosphere glovebox. $PhCF_3$ (0.30 mL) and chlorobis(cyclooctene)rhodium(I) dimer (5.4 mg, 0.0075 mmol) were added. The resulting solution was stirred for 15 h at 100 °C, and the reaction vial was removed from the glovebox. Et_2O (1 mL) and 1 M aqueous HCl (0.5 mL) were added, and the mixture was vigorously stirred for 10 min. To the mixture was added H_2O (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL). Combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. Silica gel chromatography (EtOAc/Hex) gave the ketones **2** in the reported yields.

*2,7-Dimethyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (**2b**).* See general procedure for the hydroacylation of aldehydes **1b**−**1e**. Reaction was carried out with 56 mg (0.3 mmol) of aldehyde **1b**. The crude mixture was purified by silica gel flash column chromatography (1:9 EtOAc/Hex) to afford 47 mg (84% yield) of inseparable mixture of ketone **2b** and a very minor amount of the corresponding indanone derivative as colorless oil. Pure compound for NMR was obtained by preparative thin layer chromatography (Hex/C_6H_6/$CHCl_3$ 11:2:2, 6 elutions): R_f 0.50 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, J = 8.1 Hz, 1H), 7.09 (d, J = 7.8 Hz, 1H), 7.01 (s, 1H), 2.98−2.93 (m, 1H), 2.85 (dd, J = 6.1, 3.5 Hz, 1H), 2.78 (d, J = 3.9 Hz), 2.73 (d, J = 3.9 Hz, 1H), 2.58 (dd, J = 14.5, 9.2 Hz, 1H), 2.35 (s, 3H), 2.14−1.94 (m, 1H), 1.57−1.45 (m, 1H), 1.05 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.1, 142.7, 142.5, 136.1, 130.5, 128.7, 127.2, 49.0, 34.4, 32.1, 28.4, 21.8, 21.4; IR (neat film NaCl) 2956, 2927, 1702, 1671, 1608, 1459, 1234 cm^{-1}; HRMS (CI) calcd for $[C_{13}H_{16}O + NH_4]^+$ m/z 206.1539, found 206.1538.

*7-Methyl-2-(trifluoromethyl)-6,7,8,9-tetrahydro-5H-benzo[7]-annulen-5-one (**2c**).* See general procedure for the hydroacylation of aldehydes **1b**−**1e**. Reaction was carried out with 63 mg (0.26 mmol) of aldehyde **1c**. The crude mixture was purified by silica gel flash column chromatography (1:9 EtOAc/Hex) to afford 48 mg (76% yield) of ketone **2c** as a colorless oil: R_f 0.40 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.47 (s, 1H), 3.11−2.90 (m, 2H), 2.80 (dd, J = 14.8, 4.5 Hz, 1H), 2.60 (dd, J = 14.7, 9.3 Hz, 1H), 2.16−1.99 (m, 2H), 1.64−1.50 (m, 1H), 1.08 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.6, 142.7, 141.7, 133.1 (q, J = 32.2 Hz), 128.9, 126.6 (q, J = 3.4 Hz), 123.7 (q, J = 272.6 Hz), 123.3 (q, J = 3.4 Hz), 48.8, 34.1, 32.1, 28.7, 21.6; IR (neat film NaCl) 3032, 2957, 2929, 2872, 1686, 1577, 1330, 1168 cm^{-1}; HRMS (CI) calcd for $[C_{13}H_{13}F_3O + H]^+$ m/z 243.0991, found 243.1008.

*2-Methoxy-7-methyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (**2d**).* See general procedure for the hydroacylation of aldehydes **1b**−**1e**. Reaction was carried out with 67 mg (0.33 mmol) of aldehyde **1d**. The crude mixture was purified by silica gel flash column chromatography (1:5 EtOAc/Hex) to afford 57 mg (85% yield) of ketone **2d** as colorless oil: R_f 0.30 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J = 8.7 Hz, 1H), 6.79 (dd, J = 8.7, 2.4 Hz, 1H), 6.69 (d, J = 2.4 Hz, 1H), 3.83 (s, 3H), 3.05−2.95 (m, 1H), 2.88−2.81 (m, 1H), 2.71 (d, J = 3.9 Hz, 1H), 2.58 (dd, J = 14.7, 8.9 Hz, 1H), 2.13−1.95 (m, 2H), 1.56−1.44 (m, 1H), 1.04 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.6, 162.4, 145.3, 131.5, 131.1, 114.9, 111.6, 55.3, 48.9, 34.2, 32.5, 28.2, 21.8; IR (neat film NaCl) 3055, 2961, 1712, 1600, 1362, 1266, 1221 cm^{-1}; HRMS (CI) calcd for $[C_{13}H_{16}O_2 + H]^+$ m/z 205.1223, found 205.1219.

*2-Fluoro-7-methyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (**2e**).* See general procedure for the hydroacylation of aldehydes **1b**−**1e**. Reaction was carried out with 67 mg (0.35 mmol) of aldehyde **1e**. The crude mixture was purified by silica gel flash column chromatography (1:9 EtOAc/Hex) to afford 54 mg (80% yield) of inseparable mixture of ketone **2e** and a minor amount of the corresponding indanone derivative as colorless oil. Pure compound for NMR was obtained by preparative thin layer chromatography (Hex/C_6H_6/$CHCl_3$ 11:2:2, 6 elutions): R_f 0.50 (1:4 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (dd, J = 8.7, 6.0 Hz, 1H), 7.0−6.88 (m, 2H), 3.06−3.0 (m, 1H), 2.90−2.79 (m, 2H), 2.75 (d, J = 4.2 Hz, 1H), 2.58 (dd, J = 14.7, 9.0 Hz, 1H), 2.13−1.97 (m, 1H), 1.58−1.47 (m, 1H), 1.06 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.7,

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164.6 (d, J = 252.8 Hz), 145.7 (d, J = 8.1 Hz), 135.0, 131.3 (d, J = 9.7 Hz), 116.4 (d, J = 21.3 Hz), 113.5 (d, J = 21.3 Hz), 48.8, 34.1, 32.1, 28.3, 21.7; IR (neat film NaCl) 3061, 2957, 2928, 2870, 1708, 1677, 1606, 1582, 1459, 1247 cm^{-1}; HRMS (CI) calcd for $[C_{12}H_{13}FO + NH_4]^+$ m/z 210.1289, found 210.1280.

*7-Ethyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (**2f**).* Aldehyde **1f** (39.4 mg, 0.21 mmol), amine **3** (0.021 mmol, 10 mol %), aniline (0.45 mmol), benzoic acid (2.4 mg, 0.02 mmol), and triphenylphosphine (2.6 mg, 0.01 mmol) were added to a 1 dram vial with a magnetic stir bar and brought into a nitrogen atmosphere glovebox. $PhCF_3$ (0.18 mL) and chlorobis(cyclooctene)rhodium(I) dimer (3.6 mg, 0.005 mmol) were added. The resulting solution was stirred for 15 h at 100 °C, and the reaction vial was removed from the glovebox. CH_2Cl_2 (1 mL) and 1 M aqueous HCl (0.6 mL) were added, and the mixture was vigorously stirred for 10 min. The organic layer was concentrated with silica gel in vacuo. Silica gel chromatography with CH_2Cl_2/Hex (2:1) provided **2f** as a colorless oil (33.7 mg, 0.18 mmol, 86%): R_f 0.39 (2:1 CH_2Cl_2/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 7.8 Hz, 1H), 7.42−7.25 (m, 2H), 7.20 (d, J = 7.5 Hz, 1H), 3.06−2.76 (m, 3H), 2.63−2.55 (m, 1H), 2.07−1.97 (m, 1H), 1.85−1.76 (m, 1H), 1.60−1.49 (m, 1H), 1.45−1.35 (m, 2H), 0.92 (t, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.5, 142.4, 138.6, 131.9, 129.7, 128.4, 126.4, 46.8, 34.9, 32.0, 31.9, 28.7, 11.6; IR (neat film NaCl) 2960, 2929, 1677, 1599, 1460, 1449, 1290, 1254, 1245 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{16}O + Na]^+$ m/z 211.1093, found 211.1100.

*7-Phenyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (**2g**).* Aldehyde **1g** (31.9 mg, 0.135 mmol), amine **4** (6 mg, 0.015 mmol, 25 mol %), aniline (0.15 mmol), benzoic acid (1.7 mg, 0.014 mmol), and triphenylphosphine (1.8 mg, 0.0068 mmol) were added to a 1 dram vial with a magnetic stir bar and brought into a nitrogen atmosphere glovebox. $PhCF_3$ (0.15 mL) and chlorobis(cyclooctene)rhodium(I) dimer (2.4 mg, 0.0034 mmol) were added. The resulting solution was stirred for 15 h at 100 °C, and the reaction vial was removed from the glovebox. CH_2Cl_2 (1 mL) and 1 M aqueous HCl (0.6 mL) were added, and the mixture was vigorously stirred for 10 min. The organic layer was concentrated with silica gel in vacuo. Silica gel chromatography with CH_2Cl_2/Hex (2:1) provided **2g** as a colorless oil (24.7 mg, 0.10 mmol, 77%): R_f 0.29 (2:1 CH_2Cl_2/Hex). The characterization data are not consistent with those previously reported:[14] ^{1}H NMR (500 MHz, acetone-d_6) δ 7.68 (d, J = 7.0 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.39−7.29 (m, 6H), 7.23−7.19 (m, 1H), 3.29−3.22 (m, 2H), 3.15−3.08 (m, 1H), 3.00 (dt, J = 15 Hz, 4.5 Hz, 1H), 2.85 (dd, J = 16 Hz, 2.5 Hz, 1H), 2.23−2.16 (m, 1H), 2.06−1.99 (m, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 203.7, 147.0, 142.2, 139.6, 133.2, 130.8, 129.5, 129.3, 128.0, 127.6, 127.3, 48.6, 40.3, 35.8, 32.8; IR (neat film, NaCl) 2935, 1667, 1599, 1449, 1289. HRMS (ESI) calcd for $[C_{17}H_{16}O + Na]^+$ m/z 259.1099, found 259.1101. The structure was also confirmed by COSY, ^{1}H NMR decoupling experiments, HMQC, and HMBC.[29]

*7-(((tert-Butyldimethylsilyl)oxy)methyl)-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (**2h**).* Aldehyde (25.9 mg, 0.085 mmol), amine **4** (1.5 mg, 0.0085 mmol, 10 mol %), aniline (0.11 mmol), benzoic acid (1.0 mg, 0.009 mmol), and triphenylphosphine (1.1 mg, 0.0043 mmol) were added to a 1 dram vial with a magnetic stir bar and brought into a nitrogen atmosphere glovebox. $PhCF_3$ (0.17 mL) and chlorobis(cyclooctene)rhodium(I) dimer (1.5 mg, 0.0021 mmol) were added. The resulting solution was stirred for 15 h at 100 °C, and the reaction vial was removed from the glovebox. CH_2Cl_2 (1 mL) and 1 M aqueous HCl (0.4 mL) were added, and the mixture was vigorously stirred for 10 min. The organic layer concentrated with silica gel in vacuo. Silica gel chromatography with CH_2Cl_2/Hex (2:1) provided **2h** as a colorless oil (16.7 mg, 0.055 mmol, 78%): R_f 0.24 (2:1 CH_2Cl_2/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J = 7.8 Hz, 1H), 7.37−7.34 (m, 1H), 7.25 (t, J = 7.5 Hz, 1H), 7.16 (d, J = 7.5 Hz, 1H), 3.52−3.44 (m, 2H), 3.05−2.95 (m, 1H), 2.89−2.75 (m, 2H), 2.66−2.58 (m, 1H), 2.06−1.86 (m, 2H), 0.84 (s, 9H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.5, 142.1, 138.6, 132.1, 129.7, 128.5, 126.6, 66.6, 44.0, 35.9, 31.8, 28.7, 25.9, 18.3, −5.4; IR (neat film NaCl) 2952, 2927, 2855, 1679, 1253, 1111 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{28}O_2Si + Na]^+$ m/z 327.1756, found 327.1755.

General Procedure for the Hydroacylation of Aldehydes 1i, 1j, 1m, and 1n. Aldehyde (0.30 mmol), amine **4** (13 mg, 0.075 mmol, 25 mol %), aniline (33 mg, 0.36 mmol), benzoic acid (4.4 mg, 0.036 mmol), triphenylphosphine (8.0 mg, 0.03 mmol) and $PhCF_3$ (0.30 mL) were added to a 1 dram vial with a magnetic stir bar and brought into a nitrogen atmosphere glovebox. Chlorobis(cyclooctene)rhodium(I) dimer (11.0 mg, 0.015 mmol) was added. The resulting solution was stirred for 36 h at 100 °C, and the reaction vial was removed from the glovebox. Et_2O (1 mL) and 1 M aqueous HCl (0.5 mL) were added, and the mixture was vigorously stirred for 10 min. To the mixture was added H_2O (5 mL). The aqueous layer was thoroughly extracted with Et_2O (4 × 15 mL). Combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. Silica gel chromatography (EtOAc/Hex) gave the ketones **2** in the reported yields.

*7-Methyl-7,8-dihydro-5H-pyrrolo[1,2-a]azepin-9(6H)-one (**2i**).* See general procedure for the hydroacylation of aldehydes **1i**, **1j**, **1m**, and **1n**. Reaction was carried out with 48 mg (0.29 mmol) of aldehyde **1i**. The crude mixture was purified by silica gel flash column chromatography (1:1 EtOAc/Hex) to afford 30 mg (63% yield) of ketone **2i** as light yellow oil: R_f 0.25 (1:3 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (dd, J = 3.9, 1.8 Hz, 1H), 6.78 (t, J = 2.1 1H), 6.13 (dd, J = 4.1, 2.4 Hz, 1H), 4.28−4.09 (m, 2H), 2.78−2.61 (m, 2H), 2.31−2.12 (m, 2H), 1.68−1.58 (m, 1H), 1.07 (d, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.5, 134.2, 128.1, 117.0, 108.7, 47.9, 47.4, 35.2, 27.6, 22.2; IR (neat film NaCl) 3053, 2985, 1646, 1526, 1421, 1265 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_{13}NO + Na]^+$ m/z 186.0895, found 186.0898.

*8-Methyl-8,9-dihydro-6H-azepino[1,2-a]indol-10(7H)-one (**2j**).* See general procedure for the hydroacylation of aldehydes **1i**, **1j**, **1m**, and **1n**. Reaction was carried out with 42 mg (0.20 mmol) of aldehyde **1j**. The crude mixture was purified by silica gel flash column chromatography (1:3 EtOAc/Hex) to afford 28 mg (66% yield) of ketone **2j** as colorless oil: R_f 0.35 (1:3 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J = 7.8 Hz, 1H), 7.37 (d, J = 3.9 Hz, 2H), 7.25 (s, 1H), 7.19−7.10 (m, 1H), 4.40−4.35 (m, 2H), 2.91 (dd, J = 14.5, 4.1 Hz, 1H), 2.76 (dd, J = 14.2, 8.9 Hz, 1H), 2.39−2.21 (m, 2H), 1.82−1.72 (m, 1H), 1.14 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.7, 139.0, 126.2, 125.3, 123.2, 120.6, 110.2, 108.5, 48.6, 42.6, 35.5, 28.1, 22.1; peak at 139.0 ppm corresponds to two carbons; this was confirmed by recording ^{13}C NMR in CD_3OD, see spectra; ^{13}C NMR (75 MHz, CD_3OD) δ 196.4, 140.8, 140.0, 127.6, 126.8, 124.1, 121.9, 111.8, 109.4, 43.7, 36.7, 29.6, 22.5; one of the NMR signals for aliphatic carbons is obscured by solvent peaks; IR (neat film NaCl) 3053, 2986, 1663, 1518, 1421, 1266 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{15}NO + Na]^+$ m/z 236.1046, found 236.1051.

*3-Methyl-3,4-dihydronaphthalen-1(2H)-one (**2k**).* Aldehyde **1k** (49.5 mg, 0.30 mmol), amine **4** (13.2 mg, 0.075 mmol, 25 mol %), aniline (0.36 mmol), benzoic acid (3.6 mg, 0.03 mmol), and triphenylphosphine (3.9 mg, 0.015 mmol) were added to a 1 dram vial with a magnetic stir bar and brought into a nitrogen atmosphere glovebox. $PhCF_3$ (0.60 mL) and chlorobis(cyclooctene)rhodium(I) dimer (5.4 mg, 0.0075 mmol) were added. The resulting solution was stirred for 15 h at 100 °C, and the reaction vial was removed from the glovebox. CH_2Cl_2 (2 mL) and 1 M aqueous HCl (1.0 mL) were added, and the mixture was vigorously stirred for 10 min. The organic layer was concentrated with silica gel in vacuo. Silica gel chromatography with Hex/MeOH (98:2) provided **2k** as a colorless oil (15.0 mg, 0.094 mmol, 30%). This separation of **2k** from side products in the crude reaction mixture was challenging, and we attribute the low yield to this factor: R_f 0.39 (2:1 CH_2Cl_2/Hex). The characterization data are consistent with those previously reported.[30]

The reaction was repeated with aldehyde (34.8 mg, 0.22 mmol), amine **4** (35.4 mg, 0.20 mmol, 0.9 equiv), and accordingly scaled amounts of other reagents. ^{1}H NMR analysis of reaction mixture after HCl workup with 4′-methoxyacetophenone as an internal standard showed 65% yield of **2k**.

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*3-Phenyl-3,4-dihydronaphthalen-1(2H)-one (**2l**).* Aldehyde **1l** (66.8 mg, 0.30 mmol), amine **4** (53.1 mg, 0.30 mmol, 100 mol %), aniline (0.36 mmol), benzoic acid (3.6 mg, 0.03 mmol), and triphenylphosphine (3.9 mg, 0.015 mmol) were added to a 1 dram vial with a magnetic stir bar and brought into a nitrogen atmosphere glovebox. $PhCF_3$ (0.60 mL) and chlorobis(cyclooctene)rhodium(I) dimer (5.4 mg, 0.0075 mmol) were added. The resulting solution was stirred for 15 h at 100 °C, and the reaction vial was removed from the glovebox. CH_2Cl_2 (1 mL) and 1 M aqueous HCl (0.6 mL) were added, and the mixture was vigorously stirred for 10 min. The organic layer was concentrated with silica gel in vacuo. Silica gel chromatography with CH_2Cl_2/Hex (2:1) provided **2l** as a colorless oil (38.9 mg, 0.18 mmol, 58%): R_f 0.33 (2:1 CH_2Cl_2/Hex). The characterization data are consistent with those previously reported.[14]

*6-Methyl-6,7-dihydroindolizin-8(5H)-one (**2m**).* See general procedure for the hydroacylation of aldehydes **1i**, **1j**, **1m**, and **1n**. Reaction was carried out with 60 mg (0.4 mmol) of aldehyde **1m**. The crude mixture was purified by silica gel flash column chromatography (1:1 EtOAc/Hex) to afford 40 mg (67% yield) of ketone **2m** as light yellow oil: R_f 0.25 (1:3 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (dd, J = 4.2, 1.5 Hz, 1H), 6.84 (t, J = 2.1 Hz, 1H), 6.25 (dd, J = 4.2, 2.4 Hz, 1H), 4.15 (ddd, J = 12.3, 4.2, 1.2 Hz, 1H), 3.72 (dd, J = 12.3, 9.9 Hz, 1H), 2.65 (ddd, J = 16.7, 4.0, 1.5 Hz, 1H), 2.59−2.46 (m, 1H), 2.29 (dd, J = 16.6, 10.8 Hz, 1H), 1.14 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.1, 130.1, 125.8, 113.8, 110.4, 51.6, 44.4, 30.4, 18.3; IR (neat film NaCl) 3053, 2985, 1662, 1558, 1420, 1265 cm^{-1}; HRMS (CI) calcd for $[C_9H_{11}NO + H]^+$ m/z 150.0913, found 150.0926.

*7-Methyl-7,8-dihydropyrido[1,2-a]indol-9(6H)-one (**2n**).* See general procedure for the hydroacylation of aldehydes **1i**, **1j**, **1m**, and **1n**. Reaction was carried out with 60 mg (0.30 mmol) of aldehyde **1n**. The crude mixture was purified by silica gel flash column chromatography (1:3 EtOAc/Hex) to afford 41 mg (69% yield) of ketone **2n** as a colorless solid: mp 116 °C; R_f 0.35 (1:3 EtOAc/Hex); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75−7.72 (m, 1H), 7.39−7.37 (m, 2H), 7.27 (s, 1H), 7.20−7.14 (m, 1H), 4.41−4.36 (m, 1H), 3.81−3.73 (m, 1H), 2.84−2.77 (m, 1H), 2.70−2.59 (m, 1H), 2.46 (ddd, J = 16.5, 11.1, 0.9 Hz, 1H), 1.25 (dd, J = 6.6, 0.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.2, 137.2, 133.2, 126.8, 125.6, 123.4, 121.1, 110.3, 105.5, 48.0, 45.2, 30.1, 18.6; IR (neat film NaCl) 3053, 2986, 1675, 1527, 1421, 1265 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{13}NO + Na]^+$ m/z 222.0889, found 222.0887.

*1-Benzosuberone (**2o**).* Aldehyde **1o** (81.7 mg, 0.51 mmol), amine **3** (58.6 mg, 0.54 mmol, 100 mol %), aniline (56 mg, 0.60 mmol), benzoic acid (6.1 mg, 0.05 mmol), and triphenylphosphine (6.6 mg, 0.025 mmol) were added to a 1 dram vial with a magnetic stir bar and brought into a nitrogen atmosphere glovebox. $PhCF_3$ (2.50 mL) and chlorobis(cyclooctene)rhodium(I) dimer (9.0 mg, 0.0125 mmol) were added. The resulting solution was stirred for 20 h at 100 °C, and the reaction vial was removed from the glovebox. Aqueous HCl (3.0 mL, 1M) was added, and the mixture was vigorously stirred for 10 min. The organic layer was separated and concentrated in vacuo. Silica gel chromatography on silica gel (20:1 Hex/EtOAc) afforded **2o** as a colorless oil (41.5 mg, 0.26 mmol, 51%): R_f 0.22 (30:1 Hex/EtOAc). The characterization data are consistent with those previously reported.[31]

*2-Ethyl-2,3-dihydro-1H-inden-1-one (**2p**).* Aldehyde (161.1 mg, 1.00 mmol), amine **3** (15.9 mg, 0.13 mmol, 13 mol %), aniline (112 mg, 1.2 mmol), benzoic acid (12 mg, 0.1 mmol), and triphenylphosphine (13.1 mg, 0.05 mmol) were added to a 1 dram vial with a magnetic stir bar in the nitrogen atmosphere of the glovebox. $PhCF_3$ (3.0 mL) and chlorobis(cyclooctene)rhodium(I) dimer (18.0 mg, 0.025 mmol) were added. The resulting solution was stirred for 16 h at 100 °C, and the reaction vial was removed from the glovebox. Aqueous HCl (3.0 mL, 1M) was added, and the mixture was vigorously stirred for 10 min. The organic phase was separated and concentrated in vacuo. Column chromatography on silica gel (30:1 Hex/EtOAc) afforded **2p** as a colorless oil (39.9 mg, 0.25 mmol, 25%): R_f 0.22 (30:1 Hex/EtOAc). The characterization data are consistent with those previously reported.[32]

*3-Methyl-5-(pyrrolidin-1-yl)pyridin-2-amine (**4**).* A mixture of 2-amino-5-iodopicoline[33] (1.17 g, 5 mmol), pyrrolidine (1.07 g, 15 mmol), K_2CO_3 (1. 38 g, 10 mmol), CuI (95 mg, 0.5 mmol), and L-proline (115 mg, 1 mmol) in 5 mL of DMSO was heated in a vial at 75 °C.[34] The reaction was monitored by TLC. Upon completion, the cooled mixture was diluted with 30 mL of ethyl acetate and was filtered through a pad of Celite. The Celite pad was washed with ethyl acetate (50 mL). The filtrates were combined and washed with water (3 × 20 mL), brine (15 mL), dried over Na_2SO_4, and concentrated in vacuo. The residual paste was purified by silica gel flash chromatography (97.8:2:0.2 EtOAc/MeOH/Et_3N) to afford 580 mg (65%) of picoline **4**: R_f 0.10 (20:1 EtOAc/MeOH), pale yellow solid; mp 129−130 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, J = 2.7 Hz, 1H), 6.7 (d, J = 2.7 Hz, 1H), 3.88 (s, 2H), 3.17 (t, J = 6.6 Hz, 4H), 2.12 (s, 3H), 1.98−1.94 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.2, 139.2, 128.7, 123.4, 117.6, 48.1, 25.1, 17.5; IR (neat film NaCl) 3377, 3175, 2906, 2829, 1646, 1476, 1437, 1335, 1255, 1172,1140 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_{15}N_3 + Na]^+$ m/z 200.1158, found 200.1155.

*(S)-3-(6-Amino-5-methylpyridin-3-yl)-4-benzyl-5,5-diphenyloxazolidin-2-one (**5**).* 2-Amino-5-iodo-3-picoline[31] (234 mg, 1 mmol), (*S*)-(−)-5-benzyl-4,4-diphenyl-1,3-oxazolidinone (329 mg, 1 mmol), copper(I) iodide (19 mg, 0.1 mmol), potassium phosphate (636 mg, 3 mmol), *N*,*N*′-dimethylethylenediamine (22 μL, 0.2 mmol), toluene (2 mL), and a magnetic stir bar were placed in 1 dram vial. The vial was flushed with nitrogen and capped. The reaction mixture was stirred at 100 °C for 24 h, diluted with CH_2Cl_2 (10 mL), and washed with saturated aqueous NH_4Cl (10 mL). The organic phase was separated, dried over Na_2SO_4, and concentrated in vacuo. Purification by column chromatography on silica gel (EtOAc) followed by recrystallization from $PhCF_3$ afforded **5** as light yellow crystals (154 mg, 0.35 mmol, 35%): R_f 0.25 (EtOAc); mp 239−240 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 2.4 Hz, 1H), 7.58−7.55 (m, 2H), 7.43−7.18 (m, 9H), 7.04−7.02 (m, 2H), 6.64 (dd, J = 1.8 Hz, 5.4 Hz, 2H), 5.21 (t, J = 6.6 Hz, 1H), 4.39 (br s, 2H), 2.74 (d, J = 6.6 Hz, 2H), 1.99 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 155.6, 143.2, 142.0, 139.2, 137.1, 135.0, 129.5, 129.3, 128.9, 128.8, 127.5, 126.9, 126.6, 125.8, 117.4, 88.0, 68.2, 37.8, 17.8 (two signals in the aromatic region are not resolved); HRMS (ESI) calcd for $[C_{28}H_{25}N_3O_2 + H]^+$ m/z 436.2020, found 436.2015; $[\alpha]^{25}_D$ −234 (c = 0.68, $CHCl_3$).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR spectra for new compounds and new preparations of known compounds, assignment diagram for **2g**, and HPLC chromatograms for (±)-**2a** and (−)-**2a** are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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