Tetrahedron 68 (2012) 3410–3416

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Regioselective reductions of β,β-disubstituted enones catalyzed by nonracemically ligated copper hydride

Karl R. Voigtritter, Nicholas A. Isley, Ralph Moser, Donald H. Aue *, Bruce H. Lipshutz *

Department of Chemistry, University of California, Santa Barbara, CA 93106, USA

ARTICLE INFO

Article history:
Received 22 July 2011
Received in revised form 7 October 2011
Accepted 14 October 2011
Available online 3 November 2011

Warmly dedicated to Professor Gerhard Bringmann on the occasion of his 60th birthday

Keywords:
Copper hydride
Asymmetric 1,2-addition
Hydrosilylation
α,β-Unsaturated ketones
Nonracemic ligands

ABSTRACT

CuH-catalyzed 1,2-additions to β,β-disubstituted α,β-unsaturated ketones have been further explored. Asymmetric reductions of enones lacking an α-substituent can be achieved with CuH complexed by DTBM-SEGPHOS in Et_2O at −25 °C leading to the generation of highly valuable nonracemic allylic alcohols. The corresponding 1,4-reductions can also be achieved using the same reaction conditions by switching the ligand to a JOSIPHOS analog affording nonracemic β,β-disubstituted ketones. DFT calculations of the enone conformations and transition-state energies for model 1,2- and 1,4-additions were carried out to clarify the factors affecting the product ratios.

1. Introduction

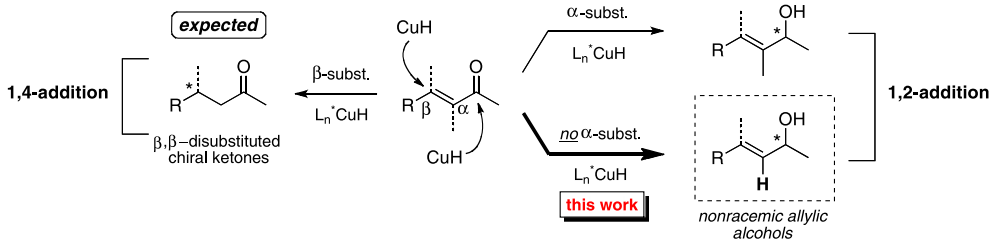
Control of regioselectivity is oftentimes a problem in transition metal catalyzed reactions. The ability to predictably change the mode of reactivity via the expediency of a change in ligand is a goal, that is, highly sought after within the synthetic community. In the case of CuH, aside from its capability to reduce aromatic ketones[1] and imines,[2] the reduction pathway toward Michael acceptors strongly favors delivery of hydride in a conjugate addition sense (Scheme 1).[3] The reduction of α,β-unsaturated ketones with nonracemically ligated CuH complexes has been extensively studied, providing facile access to valued β,β-disubstituted chiral ketones.[3a] Re-direction of CuH reactions with enones to form allylic alcohols in an enantioselective fashion, on the other hand, is quite rare. Stryker first recognized, in the achiral series, that electronic and steric changes can have a major impact on ligands so as to alter their mode of hydride delivery to Michael acceptors.[4] Our recent findings employing nonracemically ligated CuH have shown similar regioselectivities with enones leading to chiral allylic alcohols.[5a] In that prior study, the enones all possessed an α-substituent that assisted with the observed enantio- and regioselectivities realized under mild reducing conditions, as recently highlighted by Malkov.[5b] Following a recent report on the asymmetric copper-catalyzed 1,2-reduction of benzylidene acetone,[6] we questioned whether α-substitution is required for the observed shift in regioselectivity. The asymmetric 1,2-reduction of β,β-disubstituted enones, in particular, would provide nonracemic allylic alcohols that, e.g., after S_N2' displacements[7] or Claisen rearrangements,[8] would provide access to chiral quaternary centers.

2. Results and discussion

To begin a study on the effect of various ligand classes on the regioselective outcome with enone substrates lacking α-substitution, educt **1** was exposed to our previously optimized hydrosilylation conditions employing diethoxymethylsilane (DEMS) as the stoichiometric source of hydride[9] (Table 1). Within the ligands screened, both the SEGPHOS[10] and BIPHEP[11a] series favored 1,2-reductions, while selected ligands among the JOSIPHOS[12], WALPHOS, or P-PHOS[13] series (Fig. 1) favored 1,4-reduction. Notably, DTBM-SEGPHOS-complexed CuH demonstrated high regioselectivities for, and enantioselectivity in, the 1,2-reduced product **2** (Table 1, entry 3). Modified JOSIPHOS ligand **L6**, on the other hand, led to the expected conjugate reduction to provide chiral ketone **3**. Alternative hydride sources were also

* Corresponding authors. Tel.: +1 805 893 2521; fax: +1 805 893 8265; e-mail addresses: aue@chem.ucsb.edu (D.H. Aue), lipshutz@chem.ucsb.edu (B.H. Lipshutz).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.10.056



Scheme 1. Reduction pathways of CuH with α,β-unsaturated ketones.

screened; only phenylsilane (entry 4) afforded similar results in terms of reactivity, albeit with some erosion in regioselectivity. A copper source (e.g., copper nitrate) other than copper acetate led to only low conversion to the desired product (entries 5 and 9).

With optimized conditions established, substrate scope was examined so as to gauge the generality of this methodology (Table 2). Good regio- and stereoselectivities for 1,2-reductions were observed for most cases of *E*-β-aryl-substituted enones (educts **4**–**11**). Ratios of 1,2- to 1,4-addition mediated by (DTBM-SEGPHOS)CuH were found to be between 70:30 and 94:4. Enantiomeric excesses of the resulting allylic alcohols tended to be high (≥92%), although both the *ortho*-bromo example (**8**) and substituted chalcone (**9**) led to lower ees. Neither the regioselectivity nor the stereoselectivity seemed to be impacted by the nature of the substituent on the β-aryl ring. One example bearing a heteroaromatic ring in thiophene analog **7** displayed similar selectivities. Substitution of methyl for a phenyl or butyl substituent in **9** and **10** provided substrates that, likewise, exhibited good regioselectivities, although aromatic ketone **9** showed lower levels of stereo-induction for the 1,2-mode of addition. Geometrical isomers **11** and **12** showed a reversal in regioselectivity, as well as a considerable reduction in ee for the *Z*-olefin. Substrate **14** demonstrated the inherent need for an aromatic ring in the β-position to afford good regioselectivities, although the stereoselectivity for the minor product allylic alcohol was very high.

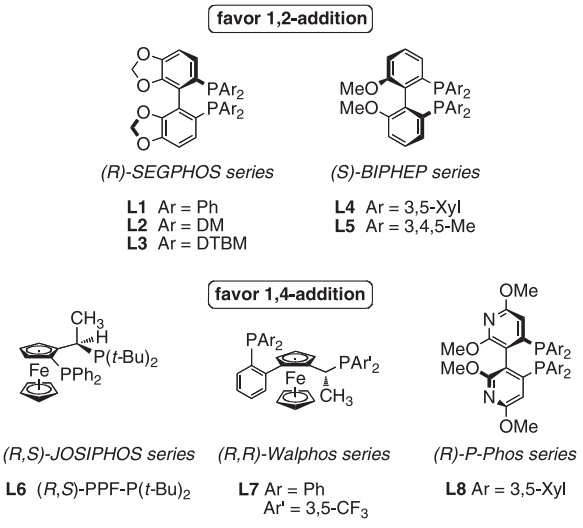
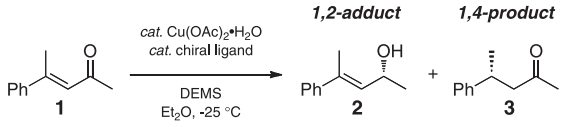


Fig. 1. Summary of the reactivity of ligands screened with CuH catalysts.

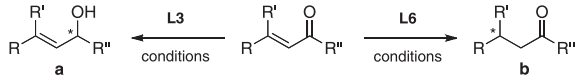
Table 1
Influence of chiral ligands on regio- and stereoselectivity[a]

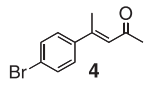
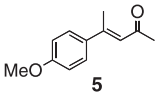
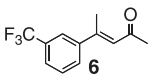
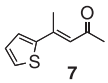
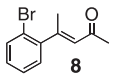


Entry	Chiral ligand	Ratio (**2**/**3**)[b]	Yield (%)[c]	ee[d] (**2**)	ee[d] (**3**)
1	L1	91/9[e]		88	76
2	L2	80/20		94	85
3	**L3**	**98/2**	**92**	**97 (R)**	**78**
4	L3	94/6[f]		97	36
5	L3	n.d.[g]		—	—
6	L4	73/27		93	87
7	L5	84:16		95	86
8	**L6**	**5/95**	**90**	**38**	**99 (R)**
9	L6	n.d.[g]		—	—
10	L7	16/84		19	92
11	L8	25/75		92	42

[a] Reaction conditions: $Cu(OAc)_2 \cdot H_2O$ (0.003 mmol), ligand (0.003 mmol), DEMS (0.3 mmol), enone (0.1 mmol), 24 h at −25 °C in Et_2O (0.33 M), NH_4F quench.
[b] Determined by GC/FID.
[c] Isolated yields of the major regioisomer for reactions run on a 0.25 mmol scale.
[d] Determined by GC or HPLC on chiral stationary phases. Absolute stereochemistry determined by comparison of optical rotation to a reported value.
[e] Low conversion.
[f] Using $PhSiH_3$ as a hydride source.
[g] Using $Cu(NO_3)_2$ as an alternative Cu source led to only low conversion.

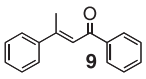
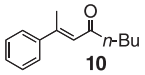
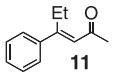
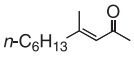
Table 2
Substrate scope



Entry	Substrate	Ligand[a]	Ratio (**a**/**b**)[b] [1,2- vs 1,4-]	ee[c] (**a**)	ee[c] (**b**)
1	 **4**	**L3**	77/23	*96*	6
2		**L6**	1/99	n.d.	99
3	 **5**	**L3**	76/24	*97*	25
4		**L6**	1/99	n.d.	98
5	 **6**	**L3**	79/21	*92*	11
6		**L6**	1/99	n.d.	86
7	 **7**	**L3**	82/18	*94*	36
8		**L6**	18/82	n.d.	96
9	 **8**	**L3**	96/4	*82*	n.d.
10		**L6**	19/81	21	92

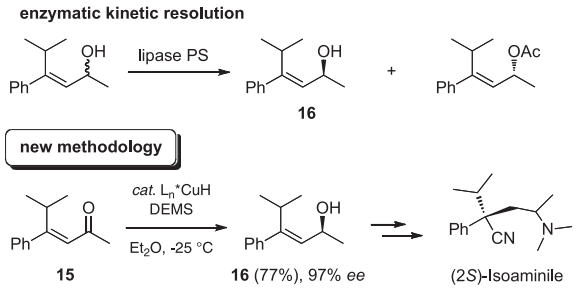
(*continued on next page*)

Table 2 (*continued*)

Entry	Substrate	Ligand[a]	Ratio (**a**/**b**)[b] [1,2- vs 1,4-]	ee[c] (**a**)	ee[c] (**b**)
11	 **9**	**L3**	81/19	*63*	30
12		**L6**	5/95	n.d.	97
13	 **10**	**L3**	88/12	*94*	62
14		**L6**	5/95	45	99
15	 **11**	**L3**	70/30	*97*	20
16		**L6**	3/97	n.d.	99
17	 **12**	**L3**	22/88	*9*	62
18		**L6**	8/92	n.d.	94
19	 **13**	**L3**	53/47	*55*	98
20		**L6**	75/25	2	3
21	 **14**	**L3**	38/62	*97*	85
22		**L6**	1/99	n.d.	99

[a] Reaction conditions: $Cu(OAc)_2 \cdot H_2O$ (0.003 mmol), ligand (0.003 mmol), DEMS (0.3 mmol), enone (0.1 mmol), 24 h at −25 °C in Et_2O (0.33 M), NH_4F quench.
[b] Determined by GC/FID.
[c] Determined by GC or HPLC on chiral stationary phases.

This methodology could be utilized in a formal, enantioselective synthesis of isoaminile (Peracon®), an antitussive agent (Scheme 2).[14] Previous routes to this target relied on a kinetic resolution to give enantiopure allylic alcohol **16**. Exposure of enone **15** to (DTBM-SEGPHOS)CuH led to the same intermediate **16** in 97% ee.



Scheme 2. Regio-, and enantioselective route to a key intermediate **16** in the synthesis of isoaminile.

Density functional theory (DFT) calculations at the B3LYP/aug-cc-pVTZ//B3LYP/6-311G(d,p) level including an SMD B3LYP/6-31+G(d,p)//B3LYP/6-311G(d,p) free-energy term for ether solvation were carried out to establish the conformations of the starting olefins with the hope that they could shed light on the reactivity differences between the substrates. Fig. 2 shows the major conformational equilibrium that exists in enone **1**. Enone **1** shows a 2.34 kcal/mol preference for the *s-cis* conformation and experimentally yields excellent regioselectivity for the 1,2 adduct **2** (Table 1, entry 3). Comparing this substrate to the cyclic analog **13**, which is locked in the *s-trans* conformation, shows no such preference for 1,2-addition. This might suggest that the desired 1,2 adduct will be favored using the DTBM-SEGPHOS ligand system when the *s-cis* conformation is favored. This generalization can be roughly applied to other cases: **8**, **11**, and **12**. For **11**, the ethyl group decreases the preference for the *s-cis* enone to 2.19 kcal/mol and results in a 70:30 preference for 1,2-addition. Geometrical isomers **11** and **12** showed a reversal in regioselectivity. In **12**, the *s-trans* conformer is preferred by 0.21 kcal/mol, while substitution of an ethyl group for the less bulky methyl in **12**, reduces this difference to 0.20 kcal/mol. Enone **8**, like **1**, shows a strong preference, 2.12 kcal/mol, for the *s-cis* conformer and affords good 1,2-selectivity. Thus, it appears that the olefin substitution pattern that affects the *s-cis*/*s-trans* equilibrium is a major factor for the observed regioselectivity with some examples using the DTBM-SEGPHOS ligand. The situation must be more complicated, however, since other ligands fail to show this trend.

To shed more light on the factors affecting the regioselectivity, we carried out DFT calculations directly on the transition states for the 1,2- and 1,4-additions to 2-butenone (**17**), and *E*-enone **1** and its *Z*-isomer, **1z**. We take these as good models for the *E* and *Z* ethyl derivatives **11** and **12** for which the reversal in regiochemistry is observed experimentally. These calculations were done for addition of monomeric CuH with a simple, non-bulky *cis*-PH_2–CH=CH–PH_2 ligand **18**. In all three enones, there was a strong preference for 1,4-addition to the C=C bond.

The transition-state calculations considered four types of transition states (see Scheme 3): (a) *TSA*: conjugate addition (1,4-) by a 4-centered addition to the C=C; (b) *TSB*: conjugate addition by a 6-centered mechanism involving copper–oxygen chelation; (c) *TSC*: 1,2-addition to the C=O of the *s-trans*-enone; and (d) *TSD*: 1,2-addition to the *s-cis*-enone. For all enones, transition state *TSA* is preferred over *TSB*, both of which were preferred over *TSC*, and then *TSD* (see Supplementary data for details). The difference in energy between the better 1,4-transition state, *TSA*, and the better 1,2-transition state, *TSC*, predict that 1,4-addition would be preferred over 1,2-addition with the simple ligand **18**, in qualitative disagreement with the experimental results with SEGPHOS. It is not expected that the theoretical energies with ligand **18**, would agree well with experiment. Rather, the theoretical energies give an

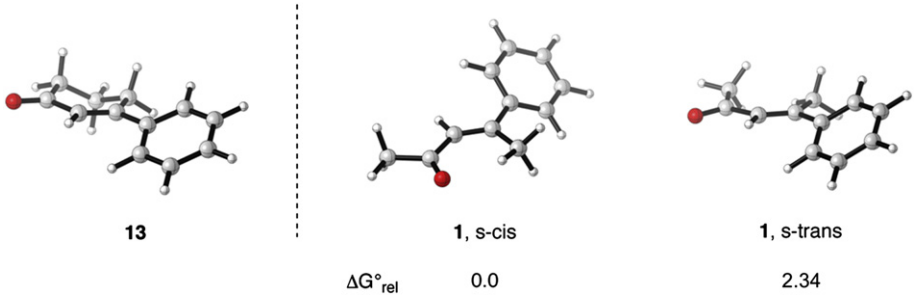
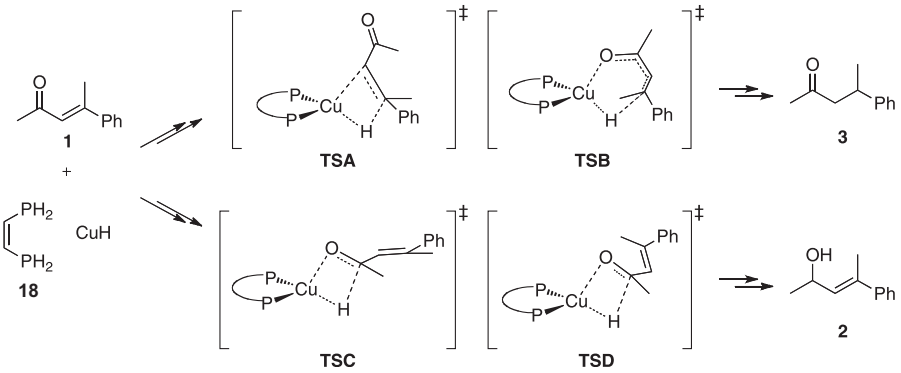


Fig. 2. Conformational analysis of enones.



Scheme 3. Transition states for copper-catalyzed reductions of **1**.

indication of what would happen in the absence of the bulky ligands used experimentally, so that one may deduce what the quantitative role of the bulky ligands is. Table 3 shows that the differences in free energies of activation (from transition-state energy differences) lead to a strong preference of 6.59 kcal/mol for 1,4-addition to the *E*-isomer of **1** with ligand **18**, while the experimental free-energy difference with SEGPHOS is in the opposite direction by 0.42 kcal/mol for the *E*-enone **11**. Thus, the bulky SEGPHOS ligand dramatically shifts the regioselectivity of the reaction toward 1,2-addition. For 2-butenone, the differences are even larger. The calculated structures of the two relevant transition states *TSA1* and *TSC1* in Fig. 3 suggest a reasonable explanation for this behavior. The 1,2-addition transition state has the copper ligand held further away from the rest of the enone substituents than in the 1,4-addition transition state, which could explain how increasing the steric bulk of the ligand could destabilize the 1,4-addition transition state to eventually make 1,2-addition the preferred path for some ligands.

The trends in product ratios for the *E*- and *Z*-isomers, however, show a reasonable correlation with one another, as one changes the nature of the ligand from **18** to SEGPHOS. The experimental free-energy differences in Table 3 show a 1.1 kcal/mol shift toward 1,4-addition for the product reversal seen in **11** and **12** as one changes from the *E*- to *Z*-enones. The predicted energies in Table 3 for **1** and **1z** show the same 1.1 kcal/mol shift in the same direction, perhaps suggesting that this experimental reversal may result from structural differences inherent in the model transition states with ligand **18**. The fact that this reversal in regiochemistry between **11** and **12** is not observed when other ligands are used experimentally and is not predicted at all of the higher theoretical levels (see Supplementary data for details), indicates, however, that the regioselectivity trends likely result from subtle and complex interactions between the substrate, solvent, and bulky ligands, and not necessarily from trends inherent simply in the substrate.

Table 3
Relative free energies of activation for 1,2-addition vs 1,4-addition for LCuH addition to enones from quantum calculations at 298 K (L=*cis*-PH_2–CH=CH–PH_2), and experiment values at 248 K with the SEGPHOS ligand (all values in kcal/mol)

	$\Delta\Delta G^{\ddagger}_{ether}$
Calculated at the M06/6-311+G(d,p) level (L=*cis*-PH_2–CH=CH–PH_2)	
From enone **15**	11.89
From *E*-enone **1**	6.59
From *Z*-enone **1z**	7.31
Experimental (L=SEGPHOS)	
From *E*-enone **1**	−1.92
From *E*-enone **11**	−0.42
From *Z*-enone **12**	0.68

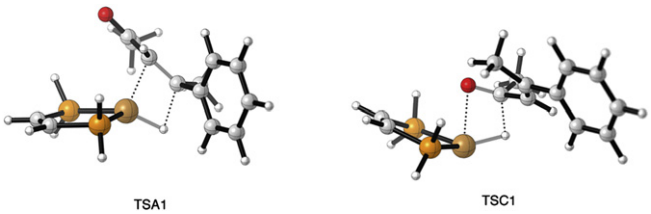


Fig. 3. Structures of the most favorable 1,4-addition and 1,2-addition transition states.

Detailed analysis of the data shows that solvation effects, modeled by a continuous dielectric mimicking diethyl ether, play some role in the energy differences, as well as inherent steric and electronic effects.

3. Conclusion

In summary, a method has been developed that shifts the inherent bias of copper(I) hydride from the conjugate reduction to a 1,2-addition manifold, which is mainly applicable to acyclic β-arylated enones. This alteration in regioselectivity is accompanied by enantioselectivities associated with the resulting nonracemic allylic alcohols. Thus, using catalytic amounts of CuH ligated by Takasago's DTBM-SEGPHOS, good yields and ees were obtained from 1,2-reductions of β,β-disubstituted enones lacking substituents at the α-site.

DFT calculations of the enone conformations and transition-state energies for model 1,2- and 1,4-additions help to gain an understanding of the factors involved in determining the regiochemistry and the reversal from 1,4-addition to 1,2-addition from *E* to *Z*-isomers (e.g., **11** and **12**) with some ligands. The calculated transition-state energies indicate what product ratios would be expected with just simple ligand **18** and predict that 1,4-addition prefers a 4-centered C=C transition state, which is about 7 kcal/mol more stable than an *s-cis* transition state for the corresponding 1,2-addition to the C=O bond. The small experimental preference for the 1,2-product from the *E*-enone **11** shows that ligands much bulkier than **18** behave very differently. The transition-state structures suggest the bulky ligands employed experimentally would disfavor the more congested 1,4-transition state, and could then make the 1,2-transition state more favorable. The trends in energy differences for 1,4- and 1,2-addition for *E*- and *Z*-enones are consistent with experimental data with the SEGPHOS ligand for **11** and **12**, but not with other bulky ligands, suggesting that these shifts in regioselectivity likely result from subtle and complex interactions between the substrate, solvent, and bulky ligands, rather than necessarily trends inherent in the substrate alone.

4. Experimental

4.1. General

Unless otherwise noted, all reactions were performed under an atmosphere of argon. Low temperature reactions were cooled in an acetone or isopropanol bath, held at the indicated temperature using a cryostat. DEMS and Et_2O were used as received. Analytical thin layer chromatography (TLC) was performed using Silica Gel 60 F254 plates (Merck, 0.25 mm thick). Flash chromatography was performed with glass columns using Silica Flash® P60 (SiliCycle, 40–63 μm). An HP-5 column (30 m×0.250 mm, 0.25 μ, Agilent Technologies) was employed for conversion analysis. General temperature program: 50 °C for 5 min; heating rate 5 °C/min; 280 °C for 10 min; split-inlet at 200 °C and 8.97 psi (H_2, constant pressure) with 40:1 split ratio, FID at 290 °C. Chiral GC analysis was performed using a Restek RT-*beta*DEXcst column (30 m×0.250 mm, 0.25 μ). Retention times (t_R) are from compound dependant temperature programs; split-inlet at 200 °C at 11.60 psi (H_2, constant pressure) with 20:1 split ratio, FID at 290 °C. ^1H and ^{13}C spectra were recorded at 22 °C on a Varian UNITY INOVA 400, 500, or 600 MHz instrument. Chemical shifts in ^1H NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, p=pentet, sep=septet, m=multiplet, br=broad), coupling constant in hertz (Hz), and integration. Chemical shifts of ^{13}C NMR spectra are reported in ppm from the central peak of $CDCl_3$ (77.23 ppm) on the δ scale. High-resolution mass analyses were obtained using a PE Sciex QStar Pulsar quadrupole/TOF instrument (API) for ESI, or a GCT Premier TOF MS (Waters Corp) for FI.

4.2. Starting materials

Starting olefins were synthesized by procedures found in the literature: **1**,[15] **4**,[15] **5**,[15] **6**,[15] **7**,[15] **8**,[16] **9**,[17] **10**,[18] **11**,[16] **12**,[16] **13**,[19] **14**,[20] and **15**.[16]

*4.2.1. (E)-4-(4-Bromophenyl)pent-3-en-2-one (**4**).* White solid, mp 49–51 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.50–7.53 (m, 2H), 7.34–7.38 (m, 2H), 6.49 (m, 1H), 2.51 (d, *J*=1.2 Hz, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.0, 152.6, 141.5, 131.9, 128.3, 124.9, 123.5, 32.5, 18.4. IR (thin film): 3013, 2957, 2921, 1914, 1680, 1600, 1558, 1487, 1421, 1400, 1356, 1264, 1179, 1108, 1080, 1008, 962, 818, 672 cm^{-1}; HRMS (FI) calcd for $C_{11}H_{11}BrO$ (M^+): 237.9993, found: 237.9986.

*4.2.2. (E)-4-(4-Methoxyphenyl)pent-3-en-2-one (**5**).* Yellow solid; mp 48–49 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45–7.49 (m, 2H), 6.88–6.92 (m, 2H), 6.50 (d, *J*=1.2 Hz, 1H), 3.84 (s, 3H), 2.53 (d, *J*=1.2 Hz, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.0, 160.7, 153.5, 134.6, 128.0, 122.9, 114.1, 35.5, 32.4, 16.2. IR (thin film): 2967, 2914, 2843, 1896, 1677, 1598, 1512, 1356, 1182, 1025, 822 cm^{-1}; HRMS (FI) calcd for $C_{12}H_{14}O_2$ (M^+): 190.0994, found: 190.0973.

*4.2.3. (E)-4-(3-(Trifluoromethyl)phenyl)pent-3-en-2-one (**6**).* Yellow oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (m, 1H), 7.63–7.67 (m, 2H), 7.52–7.54 (m, 1H), 6.53, (s, 1H), 2.55 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.9, 152.2, 143.5, 131.6, 131.2 (q, $^2J_{CF}$=31.6 Hz), 129.9, 129.3, 125.8 (q, $^3J_{CF}$=3.5 Hz), 124.1 (q, $^1J_{CF}$=271.1 Hz), 123.4 (q, $^3J_{CF}$=4.1 Hz), 32.4, 18.5. IR (neat): 3359, 3006, 2923, 1685, 1604, 1488, 1433, 1332, 1168, 1126, 1072, 801, 699 cm^{-1}; HRMS (FI) calcd for $C_{12}H_{11}F_3O$ (M^+): 228.0762; found: 228.0759.

*4.2.4. (E)-4-(Thiophen-2-yl)pent-3-en-2-one (**7**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36 (dd, *J*=3.9, 1.2 Hz, 1H), 7.34 (dd, *J*=5.2, 1.0 Hz, 1H), 7.06 (dd, *J*=5.2, 3.9 Hz, 1H), 6.63 (s, 1H), 2.57 (d, *J*=1.0 Hz, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 146.1, 145.8, 128.2, 127.5, 127.4, 121.4, 32.2, 17.6. IR (neat): 3103, 3002, 2920, 1673, 1583, 1424, 1361, 1220, 1183, 706 cm^{-1}; HRMS (EI) calcd for $C_9H_{10}OS$ (M^+): 166.0452, found: 166.0444.

4.3. General procedure for the enantioselective CuH-catalyzed 1,2-reduction of β,β-disubstituted enones

A conical 3 mL microwave vial containing a conical stir bar was charged with fine powdered $Cu(OAc)_2 \cdot H_2O$ (0.5 mg, 3 mol %, 3 μmol) and ligand (3 mol %, 3 μmol). The vial was capped with a rubber septum and placed under an Argon atmosphere, followed by the addition of 200 μL of Et_2O added via syringe. At rt, the silane (0.3 mmol) was introduced and the mixture stirred for 30 min. The vial was then placed into a pre-cooled acetone bath set to −25 °C and stirred for an additional 5 min. The enone (0.1 mmol) was subsequently introduced via syringe. The side of the reaction vial was rinsed with Et_2O (2×50 μL). The extent of conversion was monitored by TLC. All reactions were run to completion in ≤ 24h. The reaction was quenched at −25 °C after 24 h by the addition of 0.5 mL satd NH_4F/MeOH. The reaction vial was removed from the cooling bath and warmed to rt. After filtration through SiO_2, the solvent was evaporated in vacuo and the crude reaction mixture was analyzed by NMR and GC/FID. This was followed by purification by column chromatography on silica gel. The purified product was analyzed by chiral HPLC or GC for the determination of ee.

*4.3.1. (E)-4-Phenylpent-3-en-2-ol (**2**).* Pale yellow oil; $[\alpha]_D^{23}$=+26.9 (*c* 1.9, EtOH); ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.44 (m, 2H), 7.31–7.36 (m, 2H), 7.25–7.29 (m, 1H), 5.80–5.83 (m, 1H), 4.76–4.79 (m, 1H), 2.13 (d, *J*=1.35, 3H), 1.48 (s, 1H), 1.35–1.37 (m, 3H). Spectral data match previously reported data.[21] HPLC separation conditions: CHIRALCEL OB-H, 242 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=11.7 and 14.0 min.

*4.3.2. 4-Phenylpentan-2-one (**3**).* Pale yellow oil. $[\alpha]_D^{23}$=−22.8 (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.28–7.32 (m, 2H), 7.18–7.23 (m, 3H), 3.26–3.36 (m, 1H), 2.77 (dd, *J*=16.3, 6.5, 1H), 2.67 (dd, *J*=16.4, 7.7, 1H), 2.06 (s, 3H) 1.28 (d, *J*=7.0, 3H). Spectral data match previously reported data.[22] Chiral GC conditions: 110 °C for 10 min; heating 1 °C/min; 120 °C for 3 min, t_R=19.88 and 20.40 min.

*4.3.3. (E)-4-(4-Bromophenyl)pent-3-en-2-ol (**4a**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.44–7.46 (m, 2H), 7.26–7.29 (m, 2H), 5.80 (m, *J*=8.0, 1.0 Hz, 1H), 4.75 (dq, *J*=13.0, 6.0 Hz, 1H), 2.08 (d, *J*=1.0 Hz, 3H), 1.48 (br s, 1H), 1.35 (d, *J*=6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=142.0, 135.4, 132.6, 131.5, 127.6, 121.4, 65.4, 23.7, 16.2. IR (neat): ν_{max} 3348, 2966, 2925, 2855, 1483, 1449, 1400, 1074, 1008, 817, 637 cm^{-1}; $C_{11}H_{13}BrO$ (M^+): 240.0150, found: 240.0143. HPLC separation conditions: CHIRALCEL OD-H, 210 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=16.3 and 28.3 min.

*4.3.4. 4-(4-Bromophenyl)pentan-2-one (**4b**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.40–7.43 (m, 2H), 7.08–7.12 (m, 2H), 3.29 (dqd, *J*=14.0, 7.2, 6.8 Hz, 1H), 2.73 (dd, *J*=16.8, 6.8 Hz, 1H), 2.67 (dd, *J*=16.4, 7.6 Hz, 1H), 2.08 (s, 3H), 1.25 (d, *J*=6.8 Hz, 3H). Spectral data match previously reported data.[23] Chiral GC conditions: 110 °C for 10 min; heating 1 °C/min; 160 °C for 0 min, t_R=55.11 and 55.80 min.

*4.3.5. (E)-4-(4-Methoxyphenyl)pent-3-en-2-ol (**5a**).* Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35 (m, 2H), 6.88 (d, *J*=10.0 Hz, 2H), 5.75 (dd, *J*=8.0, 1.0 Hz, 1H), 4.76 (dq, *J*=12.5, 8.5, 6.5 Hz, 1H), 3.82 (s, 3H), 2.09 (d, *J*=1.5 Hz, 3H), 1.47 (br, 1H), 1.35 (d, *J*=6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.2, 135.9, 135.5, 130.5, 127.0, 113.8, 65.5, 55.5, 23.8, 16.3. IR (neat): 3389, 3060, 2967, 2914, 2843, 1896,

1677, 1598, 1182, 1025, 822 cm^{-1}; HRMS (FI) calcd for $C_{12}H_{16}O_2$ (M^+): 192.1150; found: 192.1154; HPLC separation conditions: CHIRALCEL OB-H, 242 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=33.9 and 36.4 min.

*4.3.6. 4-(4-Methoxyphenyl)pentan-2-one (**5b**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.13 (d, J=7.2 Hz, 2H), 6.84 (d, J=8.4 Hz, 2H), 3.79 (s, 3H), 3.27 (ddq, 1H), 2.73 (dd, J=12.8, 10.8 Hz, 1H), 2.63 (dd, J=12.0, 10.8 Hz, 1H), 1.56 (s, 3H), 1.25 (d, J=7.2 Hz, 3H). Spectral data match previously reported data.[24] Chiral GC conditions: 110 °C for 10 min; heating 1.00 °C/min; 160 for 0 min, t_R=46.8 and 47.4 min.

*4.3.7. (E)-4-(3-(Trifluoromethyl)phenyl)pent-3-en-2-ol (**6a**).* Yellow oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.43–7.64 (m, 4H), 5.85 (d, J=8.5 Hz, 1H), 4.78 (m, 1H), 2.13 (s, 3H), 1.52 (br, 1H), 1.37 (d, J=6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.9, 135.2, 133.6, 131.8 (q, $^2J_{CF}$=32.4 Hz), 130.0 (q, $^1J_{CF}$=235.4 Hz), 129.3, 128.9, 124.1 (q, $^3J_{CF}$=2.1 Hz), 122.8 (q, $^3J_{CF}$=4.1 Hz), 65.4, 23.7, 16.3. IR (neat): 3349, 2966, 2925, 1654, 1448, 1334, 1166, 1126, 1074, 800, 700 cm^{-1}; HRMS (FI): calcd for $C_{12}H_{13}F_3O$ (M^+): 230.0918; found: 230.0908; HPLC separation conditions: CHIRALCEL OB-H, 242 nm, 1% IPA/hexanes, 1.0 mL/min, t_R=7.0 and 8.2 min.

*4.3.8. 4-(3-(Trifluoromethyl)phenyl)pentan-2-one (**6b**).* Yellow oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.41–7.47 (m, 4H), 3.40 (ddq, J=14.0, 7.5, 5.4 Hz, 1H), 2.77 (dd, J=14.0, 7.5 Hz, 1H), 2.71 (dd, J=9.0, 7.5 Hz, 1H), 2.10 (s, 3H), 1.29 (d, J=7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 207.2, 147.4, 131.1 (q, $^2J_{CF}$=32.1 Hz), 130.6, 129.2, 124.4 (q, $^1J_{CF}$=270.5 Hz), 123.6 (q, $^3J_{CF}$=4.1 Hz), 123.4 (q, $^3J_{CF}$=3.6 Hz), 51.8, 35.2, 30.7, 22.0. IR (neat): 3361, 2957, 2926, 2855, 1723, 1685, 1604, 1433, 1357, 1331, 1254, 1168, 1127, 1073, 801 cm^{-1}; HRMS (FI): calcd for $C_{12}H_{13}F_3O$ (M^+): 230.0918; found: 230.0928. Chiral GC conditions: 110 °C for 10 min; heating 1.00 °C/min; 160 °C for 0 min, t_R=24.6 and 25.4 min.

*4.3.9. (E)-4-(Thiophen-2-yl)pent-3-en-2-ol (**7a**).* Yellow oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.16 (d, J=5.0 Hz, 1H), 7.05 (d, J=3.6 Hz, 1H), 6.98 (dd, J=5.0, 3.6, 1H), 5.95 (dd, J=8.3, 1.0 Hz, 1H), 4.46–4.80 (m, 1H), 2.12 (d, J=1 Hz, 3H), 1.67 (s, 1H), 1.33 (d, J=7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.0, 130.4, 130.3, 127.5, 124.1, 123.5, 65.1, 23.7, 16.2. IR (neat): 3342, 3104, 2971, 2925, 1637, 1435, 1369, 1241, 1057, 849, 821, 695 cm^{-1}; HRMS (FI) calcd for $C_9H_{12}OS$ (M^+): 168.0609, found: 168.0581. HPLC separation conditions: CHIRALCEL OB-H, 242 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=15.4 and 18.6 min.

*4.3.10. 4-(Thiophen-2-yl)pentan-2-one (**7b**).* Yellow oil; ^1H NMR (500 MHz, $CDCl_3$): δ 7.12 (m, 1H), 6.91 (m, 1H), 6.81 (m, 1H), 3.64 (m, 1H), 2.82 (dd, J=16.6, 7.8 Hz, 1H), 2.68 (dd, J=16.6, 7.8, 1H), 2.10 (s, 3H), 1.34 (d, J=6.8 Hz, 3H). Spectral data match previously reported data.[25] Chiral GC conditions: 110 °C for 10 min; heating rate 1 °C/min; 180 °C for 3 min, t_R=20.51 and 21.50 min.

*4.3.11. (E)-4-(2-Bromophenyl)pent-3-en-2-ol (**8a**).* Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J=8 Hz, 1H), 7.10–7.29 (m, 3H), 5.42 (dd, J=8.0, 1.2 Hz, 1H), 4.75 (dq, J=12.8, 6.4 Hz, 1H), 2.03 (s, 3H), 1.61 (br, 1H), 1.36 (d, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 137.8, 134.7, 132.9, 129.9, 128.5, 127.5, 122.2, 65.1, 23.4, 18.1. IR (neat): 3349, 3053, 2968, 2925, 2854, 1468, 1058, 1027, 754 cm^{-1}; HRMS (FI): calcd for $C_{11}H_{13}BrO$ (M^+): 240.0150; found: 240.0144; HPLC separation conditions: CHIRALCEL OD-H, 210 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=16.3 and 28.3 min.

*4.3.12. 4-(2-Bromophenyl)pentan-2-one (**8b**).* Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J=8.0 Hz, 1H), 7.20–7.30 (m, 2H), 7.06 (dt, J=2.0, 7.6, 1H), 3.78 (ddq, J=8.8, 5.4, 6.8 Hz, 1H), 2.80 (dd, J=16.4, 5.4 Hz, 1H), 2.59 (dd, J=16.4, 8.8 Hz, 1H), 2.13 (s, 3H), 1.26 (d, J=6.8 Hz, 3H). Spectral data match previously reported data.[16] HPLC separation conditions: CHIRALCEL OD-H, 210 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=8.9 and 9.7 min.

*4.3.13. (E)-1,3-Diphenylbut-2-en-1-ol (**9a**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.25–7.47 (m, 10H), 5.98–6.04 (m, 1H), 5.62–5.72 (m, 1H), 2.19 (d, J=0.5 Hz, 3H) 1.97 (s, 1H). Spectral data match previously reported data.[26] HPLC separation conditions: CHIRALCEL OD-H, 274 nm, 10% IPA/hexanes, 1.0 mL/min, t_R=9.5 and 14.1 min.

*4.3.14. 1,3-Diphenylbutan-1-one (**9b**).* Yellow oil; ^1H NMR (600 MHz, $CDCl_3$): δ 7.93–7.95 (m, 2H), 7.54–7.57 (m, 1H), 7.44–7.47 (m, 2H), 7.28–7.33 (m, 4H), 7.19–7.22 (m, 1H), 3.52 (dq, J=14.0, 7.0 Hz, 1H), 3.31 (dd, J=16.4, 5.7 Hz, 1H), 3.20 (dd, J=16.4, 8.3 Hz, 1H), 1.35 (d, J=7.0 Hz, 3H). Spectral data match previously reported data.[27] HPLC separation conditions: CHIRALCEL OD-H, 242 nm, 2% IPA/hexanes, 0.5 mL/min, t_R=13.4 and 16.0 min.

*4.3.15. (E)-2-Phenyloct-2-en-4-ol (**10a**).* Colorless oil; ^1H NMR (600 MHz, $CDCl_3$): δ 7.26–7.43 (m, 5H), 5.78 (dq, J=8.61, 1.33 Hz, 1H), 4.56 (q, J=7.41 Hz, 1H), 2.09–2.15 (m, 3H), 1.68–1.74 (m, 1H), 1.54–1.60 (m, 1H), 1.50 (s, 1H), 1.32–1.44 (m, 4H), 0.93 (t, J=6.97 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 143.2, 137.3, 131.2, 128.5, 127.5, 126.0, 69.3, 37.6, 27.8, 22.9, 16.5, 14.3. IR (neat): 3337, 2956, 2929, 2859, 1494, 1445, 1379, 1026, 757, 695 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{20}O$ (M^+): 204.1514, found: 204.1523; HPLC separation conditions: CHIRALCEL AD-H, 242 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=15.6 and 18.7 min.

*4.3.16. 2-Phenyloctan-4-one (**10b**).* Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.18–7.31 (m, 5H), 3.30–3.36 (m, 1H), 2.72 (dd, J=16.1, 6.6 Hz, 1H), 2.62 (dd, J=16.1, 7.8 Hz, 1H), 2.26–2.36 (m, 2H), 1.47–1.52 (m, 2H), 1.25 (d, J=6.8 Hz, 3H), 1.23 (tq, J=7.3, 2H), 0.86 (t, J=7.3 Hz, 3H). Spectral data match previously reported data.[28] Chiral GC conditions: 110 °C for 10 min; heating rate 1 °C/min; 180 °C for 3 min, t_R=20.51 and 21.50 min.

*4.3.17. (E)-4-Phenylhex-3-en-2-ol (**11a**).* Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.25–7.39 (m, 5H), 5.66 (d, J=8.4 Hz, 1H), 4.77 (m, 1H), 2.52–2.64 (m, 2H), 1.58 (br, 1H), 1.36 (d, J=6.4 Hz, 3H), 0.99 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 142.1, 131.8, 128.5, 127.4, 126.7, 65.1, 24.1, 23.5, 14.3. IR (neat): 3337, 3081, 3058, 3023, 2968, 2873, 1726, 1466, 1056 cm^{-1}; HRMS (FI): calcd for $C_{12}H_{16}O$ (M^+): 176.1201; found: 176.1208. HPLC separation conditions: CHIRALCEL OB-H, 242 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=9.5 and 10.7 min.

*4.3.18. 4-Phenylhexan-2-one (**11b**).* Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.25–7.32 (m, 2H), 7.14–7.24 (m, 3H), 3.03 (m, 1H), 2.74 (dd, J=16.6, 7.3 Hz, 1H), 2.70 (dd, J=16.6, 7.1 Hz, 1H), 2.01 (s, 3H), 1.67 (ddq, J=12.9, 7.6, 7.3 Hz, 1H), 1.55 (ddq, J=12.9, 7.4, 7.3 Hz, 1H), 0.77 (t, J=7.3 Hz, 3H). Spectral data match previously reported data.[16] Chiral GC conditions: 100 °C for 0 min; heating 1.00 °C/min; 130 for 0 min, t_R=42.6 and 43.3 min.

*4.3.19. (Z)-4-Phenylhex-3-en-2-ol (**12a**).* Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.06–7.29 (m, 5H), 5.40 (d, J=9.2 Hz, 1H), 4.17 (dq, J=8.8, 6.4 Hz, 1H), 2.28 (q, J=7.2 Hz, 2H), 1.47 (br, 1H), 1.16 (d, J=6.4 Hz, 3H), 0.92 (t, J=7.2 Hz, 3H). Spectral data match previously reported data.[29] HPLC separation conditions: CHIRALCEL OB-H, 242 nm, 1% IPA/hexanes, 0.5 mL/min, t_R=15.5 and 17.5 min.

*4.3.20. 3,4,5,6-Tetrahydro-[1,1′-biphenyl]-3-ol (**13a**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.46 (m, 2H), 7.31–7.36 (m, 2H), 7.25–7.30 (m, 1H), 6.14 (dt, J=3.6, 1.8 Hz, 1H), 4.41–4.45 (m, 1H),

2.44–2.54 (m, 1H), 2.33–2.42 (m, 1H), 1.87–2.02 (m, 2H), 1.65–1.83 (m, 2H), 1.53 (s, 1H). Spectral data match previously reported data.[30] HPLC separation conditions: CHIRALCEL OD-H, 242 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=17.0 and 23.8 min.

*4.3.21. 3-Phenylcyclohexanone (**13b**).* Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.29 (m, 2H), 7.28–7.17 (m, 3H), 3.00 (m, 1H), 2.66–2.32 (m, 4H), 2.24–2.00 (m, 2H), 1.95–1.70 (m, 2H). Spectral data match previously reported data.[31] HPLC separation conditions; CHIRALCEL OD-H, 210 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=12.1 and 13.4 min.

*4.3.22. (E)-4-Methyldec-3-en-2-ol (**14a**).* Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.20 (m, 1H), 4.60 (m, 1H), 1.97 (t, J=7.6 Hz, 2H), 1.67 (s, 3H), 1.23–1.43 (m, 12H), 0.88 (t, J=6.7 Hz, 3H). Spectral data match previously reported data.[32] Chiral GC conditions: 85 °C for 10 min; heating rate 0.1 °C/min; 117 °C for 0 min, t_R=56.01 and 57.47 min.

*4.3.23. 4-Methyldecan-2-one (**14b**).* Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41 (dd, J=15.6, 5.7 Hz, 1H), 2.21 (dd, J=15.6, 8.0 Hz, 1H), 2.13 (s, 3H), 1.95 (m, 1H), 1.20–1.35 (m, 10H), 0.88 (t, J=6.4 Hz, 3H), 0.82 (d, J=6.6 Hz, 3H). Spectral data match previously reported data.[33] Chiral GC conditions: 85 °C for 10 min; heating rate 0.1 °C/min; 117 °C for 0 min, t_R=39.44 and 40.19 min.

*4.3.24. 5-Methyl-4-phenylhexan-2-one (**16**).* $[\alpha]_D^{23}$=+16.5 (*c* 1.12, $CHCl_3$). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12–7.32 (m, 5H), 5.31 (d, J=8.3 Hz, 1H), 4.83 (dq, J=8.4, 6.1 Hz, 1H), 3.10 (sep, J=7.0 Hz, 1H), 1.55 (br s, 1H), 1.34 (d, J=6.1 Hz, 3H), 1.01–1.11 (m, 6H). Spectral data match previously reported data.[14] HPLC separation conditions: CHIRALCEL OD-H, 242 nm, 2% IPA/hexanes, 1.0 mL/min, t_R=13.5 and 28.6 min.

Acknowledgements

We are pleased to warmly acknowledge financial support from the NSF (CHE 0948479), and the National Center for Supercomputing Applications NSF (CHE100123) utilizing the NCSA Ember system. Ligands were generously provided by Roche (BIPHEP), Takasago (SEGPHOS) and Solvias (JOSIPHOS), for which we are most grateful.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.10.056.

References and notes

1. Lipshutz, B. H.; Noson, K.; Chrisman, W. *J. Am. Chem. Soc.* **2001**, *123*, 12917.
2. Lipshutz, B. H.; Shimizu, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 2228.
3. (a) Deutsch, C.; Krause, N.; Lipshutz, B. H. *Chem. Rev.* **2008**, *108*, 2916; (b) Yun, J.; Kim, D.; Lee, D. *Angew. Chem., Int. Ed.* **2006**, *45*, 2785; (c) Lipshutz, B. H.; Servesko, J. M.; Taft, B. R. *J. Am. Chem. Soc.* **2004**, *126*, 8352; (d) Buchwald, S. L.; Aye, Y.; Rainka, M. P. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5821; (e) Czekelius, C.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4793.
4. Chen, J.-X.; Daeuble, J. F.; Brestensky, D. M.; Stryker, J. M. *Tetrahedron* **2000**, *56*, 2153.
5. (a) Moser, R.; Boskovic, Z. V.; Crowe, C. S.; Lipshutz, B. H. *J. Am. Chem. Soc.* **2010**, *132*, 7852; (b) Malkov, A. V. *Angew. Chem., Int. Ed.* **2010**, *49*, 9814.
6. Shimizu, H.; Nagano, T.; Sayo, N.; Saito, T.; Ohshiima, T.; Mashima, K. *Synlett* **2009**, *19*, 3143.
7. (a) *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; (b) Harutyunyan, S. R.; Hartog, T. D.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824.
8. Martin Castro, A. M. *Chem. Rev.* **2004**, *104*, 2939.
9. Nishiyama, H.; Shiomi, T.; Tsuchiya, Y.; Matsuda, I. *J. Am. Chem. Soc.* **2005**, *127*, 6972.
10. Saito, T.; Yokozawa, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2001**, *343*, 264.
11. (a) Schmid, R.; Broger, E. A.; Cereghetti, M.; Crameri, Y.; Foricher, J.; Lalonde, M.; Mueller, R. K.; Scalone, M.; Schoettel, G.; Zutter, U. *Pure Appl. Chem.* **1996**, *68*, 131; (b) Schmid, R.; Foricher, J.; Cereghetti, M.; Schonholzer, P. *Helv. Chim. Acta* **1991**, *74*, 370.
12. Blaser, H.-U.; Brieden, W.; Pugin, B.; Spindler, F.; Studer, M.; Togni, A. *Top. Catal.* **2002**, *19*, 3.
13. Wu, J.; Chan, A. S. C. *Acc. Chem. Res.* **2006**, *39*, 711.
14. Antonietti, F.; Brenna, E.; Fuganti, C.; Gatti, F. G.; Giovenzana, T.; Grande, V.; Malpezzi, L. *Synthesis* **2005**, *7*, 1148.
15. Guthrie, J. P.; Wang, X. −P. *Can. J. Chem.* **1992**, *70*, 1055.
16. Tsuchiya, Y.; Hamashima, Y.; Sodeoka, M. *Org. Lett.* **2006**, *8*, 4851.
17. Kanazawa, Y.; Tsuchiya, Y.; Kobayashi, K.; Shiomi, T.; Itoh, J.-I.; Kikuchi, M.; Yamamoto, Y.; Nishiyama, H. *Chem.—Eur. J.* **2006**, *12*, 63.
18. Kojima, S.; Hidaka, T.; Yamakawa, A. *Chem. Lett.* **2005**, *34*, 470.
19. Scheaermann Tayler, C. J.; Jaekel, C. *Adv. Synth. Catal.* **2008**, *350*, 2708.
20. Lipshutz, B. H.; Butler, T.; Lower, A.; Servesko, J. H. *Org. Lett.* **2007**, *9*, 3737.
21. Abate, A.; Brenna, E.; Fronza, G.; Fuganti, C.; Gatti, F. G.; Serra, S.; Zardoni, E. *Helv. Chim. Acta* **2004**, *87*, 765.
22. Li, X.; Li, L.; Tang, Y.; Zhong, L.; Cun, L.; Zhu, J.; Liao, J.; Deng, J. *J. Org. Chem.* **2010**, *75*, 2981.
23. Biswas, S.; Maiti, S.; Jana, U. *Eur. J. Org. Chem.* **2010**, 2861.
24. Berthiol, F.; Doucet, H.; Santelli, M. *Tetrahedron* **2006**, *62*, 4372.
25. Lopez, F.; Harutyunyan, S. R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2004**, *126*, 12784.
26. Arai, N.; Azuma, K.; Nii, N.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 7457.
27. Inagaki, T.; Phong, L. T.; Furuta, A.; Ito, J. i; Nishiyama, H. *Chem.—Eur. J.* **2010**, *16*, 3090.
28. Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229.
29. Chou, S. S. P.; Kuo, H. L.; Wang, C. J.; Tsai, C. Y.; Sun, C. M. *J. Org. Chem.* **1989**, *54*, 872.
30. Uyanik, M.; Fukatsu, R.; Ishihara, K. *Org. Lett.* **2009**, *15*, 3470.
31. Hahn, B. T.; Tewes, F.; Frohlich, R.; Glorius, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 1143.
32. Kauffmann, T.; Stach, D. *Chem. Ber.* **1992**, *125*, 913.
33. Lipshutz, B. H.; Servesko, J. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4789.