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Application of ferrocenyl substituted aziridinylmethanols (FAM) as chiral ligands in enantioselective conjugate addition of diethylzinc to enones

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Abstract—Easily available ferrocenyl substituted aziridinylmethanol FAM-**4a** complexes with nickel and catalyzes the enantioselective diethylzinc addition to various enones with enantiomeric excesses reaching 80%. The ligand can be recovered and used without losing its activity. The sense of induction was found to be dependent on the configuration of the aziridine ring.

1. Introduction

Development of a new chiral catalyst for enantioselective C–C bond formation is one of the most studied fields in organic chemistry. Among the C–C bond forming reactions, diethylzinc addition to aldehydes has been studied extensively and considered as a test reaction for understanding the catalytic potential of new chiral catalysts.[1] Another useful C–C bond formation reaction is the diethylzinc addition to enones which has not been studied as extensively as the previous reaction.[2] Diethylzinc addition to enones requires a metal catalyst such as Cu(I)[3] or Ni(II)[4] generally. Aziridine based ligands have recently gained increasing importance and have been used as catalysts in diethylzinc addition reactions to aldehydes.[5] In a recent study by Nayak et al., *N*-tritiyl aziridinyl methanol was used as the chiral catalyst for the enantioselective diethylzinc addition reaction to chalcones to give the products in good yields and up to 90% ee's.[6] We recently synthesized novel ferrocenyl substituted aziridinyl methanols and used them as chiral catalysts for 1,3-dipolar cycloaddition reactions of azomethine ylides to obtain pyrrolidines with ee's up to 95%.[7] The use of these ligands in diethylzinc addition reactions to aldehydes gave the secondary alcohols with ee's up to 96%.[8] These results prompted us to use these ligands with $Ni(acac)_2$ as a chiral catalyst for the enantioselective diethylzinc addition reactions to enones. Herein, we report the full details of this study.

2. Results and discussion

Chiral ligands **4a**–**d** were prepared in high yields and enantiomeric excess from acryloylferrocene following the literature procedure[7] (Scheme 1). First the efficiency of the ligands in the enantioselective diethylzinc addition to chalcone was tested by adapting the literature procedure.[4a] The reaction of chalcone with diethylzinc (1.5 equiv) in the presence of 25 mol % of ligand **4a** and 1 mol % $Ni(acac)_2$ gave the expected product in 82% yield and 80% ee (Table 1, entry 1) at −35 °C. Under the same reaction conditions, the other ligands **4b**–**d** were less efficient (Table 1, entries 2–4). Previous studies carried out with aminoalcohols as ligands on the enantioselective diethylzinc addition to chalcones showed that the test solvent is acetonitrile and Co, Cu, and Zn salts are less efficient than $Ni(acac)_2$. We found similar results, when using toluene as the solvent and $Cu(OTf)_2$ instead of $Ni(acac)_2$ to give the product in low yield and ee.

After determining that ligand **4a** catalyzed the reaction with the highest yield and ee, the effect of ligand and $Ni(acac)_2$ concentrations on the yield and enantioselectivity of the reaction was explored. When the ligand concentration was lowered to 15 mol % or 5 mol %, both the yield and the ee of the product were low (Table 1, entries 5 and 6). On the other hand, increasing the ligand concentration

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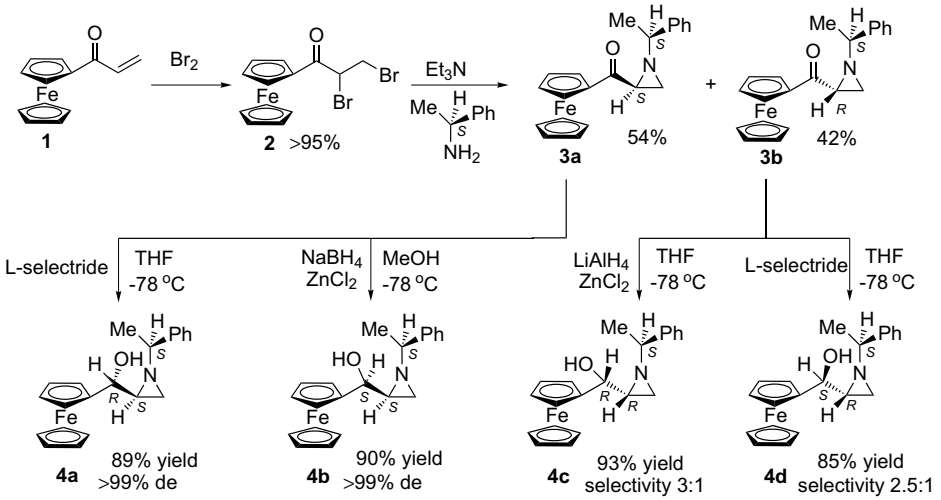
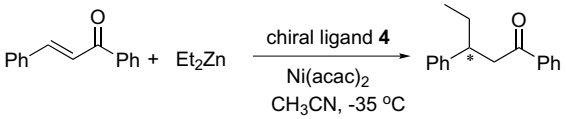


Scheme 1.

Table 1. Diethylzinc addition to chalcone under different conditions



Entry	Ligand	Ligand mol %	$Ni(acac)_2$ mol %	Yield[a] (%)	ee[b] (%)	Config.[c]
1	**4a**	25	1.0	82	80	*R*
2	**4b**	25	1.0	61	42	*R*
3	**4c**	25	1.0	72	3	*S*
4	**4d**	25	1.0	65	34	*S*
5	**4a**	15	1.0	61	69	*R*
6	**4a**	5	1.0	40	47	*R*
7	**4a**	35	1.0	78	82	*R*
8	**4a**	25	0.5	71	76	*R*
9	**4a**	15	0.5	78	70	*R*
10	**4a**	5	0.2	84	44	*R*

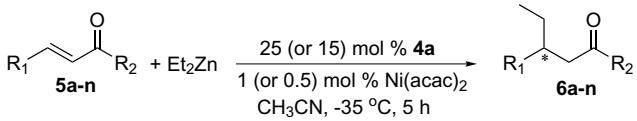
[a] Isolated yield.
[b] Determined by HPLC using a Chiracel AD column.
[c] Determined by comparing the reported specific rotation data.

from 25 mol % to 35 mol % did not show a significant effect on the yield and ee (Table 1, entry 7). By keeping the ligand concentration at 25 mol % and reducing the $Ni(acac)_2$ concentration from 1 mol % to 0.5 mol % the product was formed in a slightly lower yield and ee (Table 1, entry 8). Interestingly, at a concentration of 5 mol % ligand and 0.2 mol % Ni, the product was formed in 84% yield and 44% ee (Table 1, entry 10). These results are very similar to the findings of previous studies where Bolm et al.[4a] and Feringa et al.[4d] reported that the ligand to nickel ratio is crucial for obtaining high enantioselectivity. They also reported that the asymmetric induction depends upon the equilibrium between the chiral nickel complex and catalytically active nickel species which lead to the racemic product.

In order to show the catalytic effect of ligand **4a**, enantioselective diethylzinc addition reaction to various enones were carried out under the optimized conditions (25 mol % ligand, 1 mol % Ni-salt, acetonitrile, and −35 °C). The results of these reactions are summarized in Table 2.

As can be seen from Table 2, the enantioselective diethylzinc addition to enonones, where R_1 and R_2 are aromatic took place smoothly to give the β-ethylated ketones in good chemical yields and ee's in the range of 42–80%. Enantioselective diethylzinc addition to an enone with R_2 being methyl formed the product in acceptable yield but low ee (Table 2, entry 13). In the study of Bolm et al.,[4a] the same substrate gave the product in 76% yield as a racemic mixture. Enones with methyl or cyclohexyl groups at the β-position gave the products in reasonable yields and ee's (Table 2, entries 14 and 15). However, when a sterically hindered *tert*-butyl group is introduced at either R_1 (R_2 = Ph) or R_2 (R_1 = Ph) position of the enone, most of the starting materials were recovered, no β-ethylated ketone was observed. A similar result was also seen when

Table 2. Diethylzinc addition to various enones[a]



Entry	R_1	R_2	Substrate	Yield[b] (%)	ee[c] (%)	Config.[d,e]
1[f]	Ph	Ph	**5a**	85	80	*R*
2[g]	*p*-MeC_6H_4	Ph	**5b**	90(95)	72(62)	−
3[g]	*p*-$CF_3C_6H_4$	Ph	**5c**	80(86)	70(52)	+
4	*p*-ClC_6H_4	Ph	**5d**	77(94)	70(60)	*R*
5	*p*-$MeOC_6H_4$	Ph	**5e**	75(96)	76(60)	*R*
6	*m*-$MeOC_6H_4$	Ph	**5f**	85(71)	80(74)	−
7	*o*-$MeOC_6H_4$	Ph	**5g**	60(85)	66(54)	*R*
8	*o*-ClC_6H_4	Ph	**5h**	55(88)	50(40)	+
9	*o*-FC_6H_4	Ph	**5i**	77(94)	76(70)	+
10[f]	*o*-FC_6H_4	Ph	**5i**	82	76	+
11[g]	2-Naphthyl	Ph	**5j**	57(63)	78(72)	+
12[g,h,i]	Fc	Ph	**5k**	71(63)	42(40)	+
13[h]	Ph	Me	**5l**	49(66)	22(16)	*R*
14	Me	Ph	**5m**	57(60)	60(53)	*R*
15	*c*-C_6H_{11}	Ph	**5n**	45(55)	70(57)	*S*

[a] An amount of 1 mol % $Ni(acac)_2$ with 25 mol % of **4a** or 0.5 mol % $Ni(acac)_2$ with 15 mol % of **4a** (data in parenthesis) were used.
[b] Isolated yield.
[c] Determined by chiral HPLC.
[d] Absolute configuration was assigned by comparing the reported specific rotation data.
[e] The + or − signs refer to the optical rotation.
[f] The recovered ligand was used.
[g] Enone was dissolved in CH_2Cl_2 because of solubility problems in CH_3CN.
[h] Reaction was conducted at 0 °C.
[i] Yield was 13% and ee was 56% at −35 °C.

R_2 (R_1 = Ph) was a ferrocenyl group.[9] The numbers in parenthesis in Table 2 obtained by using 15 mol % ligand and 0.5 mol % $Ni(acac)_2$ indicate that at low ligand concentration, products are formed in high yield but low ee. Once again these results support the hypothesis that at low ligand concentration less chiral nickel-complex which leads to the enantiomerically enriched product is formed. Interms of substituent effect, stereoselectivity did not significantly change with the electronic nature of the substituents at the *para*-position of the β-phenyl group of the enones (entries 2–5), which is contrary to the findings of the literature where considerably lower stereoselectivities were reported for the *p*-CF_3 substituent.[3b,g] These results show that our catalyst is active enough to react with enones having electron donating and withdrawing *para*-substituents. For the *ortho*-substituted enones (entries 7–9), it seemed that the size of the substituent was more important than its electronic nature because electronegative fluoride on the substrate gives the product in high yield and ee as compared to the less electronegative chloride. Steric effects can also be seen by the results of the *p*-, *m*-, and *o*-methoxy substituted enones (entries 5–7), where the first two gave the product in about the same yield and ee but the last one gave the product in lower yield and ee.

Based on the assigned configurations, the configuration of ligand **4** at the aziridine center is important in determining the configuration of the product. Thus ligands with (*S*)-configuration at the aziridine center gave the product with (*R*)-configuration (Table 2, entries 1, 4, 5, 7, 13, and 14) and vice versa (Table 1, entries 3 and 4). β-Cyclohexylenone (Table 2, entry 15) is an exception to this observation.

3. Conclusion

It has been shown that the aziridine based chiral ligand FAM-**4a** can be used as a catalyst for the enantioselective diethylzinc addition reaction to enones to give β-ethylated ketones in up to 80% ee. The advantage of this ligand is that it can easily be prepared on a gram scale in enantiomerically pure form in three easy steps. It can be recovered in >90% yield and used without losing its activity. Another advantage of this ligand is that its antipode can be easily prepared starting from (*R*)-methylbenzylamine. Thus one can synthesize β-alkylated ketones with the desired configuration by choosing the appropriate ligand. The catalytic effect of these ligands for other asymmetric reactions is currently under investigation in our laboratory and will be reported in due course.

4. Experimental

The ^1H and ^{13}C NMR spectra were recorded in CCl_4/$CDCl_3$ (2/3, v/v) solvent system on a Bruker Spectrospin Avance DPX 400 spectrometer. ^1H NMR spectra were reported in parts per million using TMS as an internal standard (TMS at 0.00 ppm). ^{13}C NMR spectra were reported in parts per million using solvent as an internal standard

($CDCl_3$ at 76.9 ppm). Infrared spectra were recorded on a Perkin Elmer 16 PC FT-IR spectrometer using $CHCl_3$ as the solvent. GC–MS spectra were obtained with a ThermoQuest (TSP) TraceGC-2000 Series instrument equipped with a Phenomenex Zebron ZB-5 capillary column (5% phenylmethylsiloxane, 30 m, 250 μm), MS: Thermo Quest Finnigan multi Mass (EI, 70 eV). Optical rotations were measured in a 1 dm cell using a Rudolph Autopol III polarimeter at 25 °C. HPLC measurements were performed with Dionex System instrument. Separations were carried out on Chiralcel AD, OD-H or OD analytical columns (250 × 4.60 mm) with hexane/2-propyl alcohol as eluent. Flash column chromatography was performed on silica gel (60 mesh, Merck). Analytical thin layer chromatography (TLC) was performed on precoated silica gel (60 F_{254}, Merck). Solvents CH_3CN and CH_2Cl_2 were distilled from CaH_2 before use. All other reagents were commercially available and used without further purification. Melting points were obtained using an electrothermal digital melting point apparatus (Gallenkamp) and were uncorrected.

4.1. Synthesis of aziridino ketones 3a and 3b

Applying the literature procedure[7] aziridino ketone **3a** was obtained in 54% yield, $[\alpha]_D^{25} = -90.0$ (*c* 1.0, $CHCl_3$) and **3b** was obtained in 42% yield, $[\alpha]_D^{25} = -220.0$ (*c* 1.0, $CHCl_3$) as an orange solid from L-(−)-α-methylbenzylamine. All spectroscopic data of the ketones were identical to those synthesized from D-(+)-α-methylbenzylamine.

4.2. Synthesis of chiral ligands FAM-4a–d

Using the literature procedure[7] FAM-**4a** was obtained as a yellow oil in 89% yield as the only diastereomer, $[\alpha]_D^{25} = -45.2$ (*c* 1.00, $CHCl_3$); for FAM-**4b**: 90% yield (obtained as the only diastereomer), $[\alpha]_D^{25} = -46.3$ (*c* 1.00, $CHCl_3$); for FAM-**4c**: 70% yield, $[\alpha]_D^{25} = -3.0$ (*c* 1.0, $CHCl_3$), for FAM-**4d** 68% yield, $[\alpha]_D^{25} = -20.9$ (*c* 1.00, $CHCl_3$); all spectroscopic data are in good agreement with those previously reported for the enantiomers.

4.3. General procedure for the synthesis of enones[10]

The aldehyde (43.2 mmol) was added gradually to a solution of NaOH (2.2 g) in H_2O (20.0 mL) and ketone (43.3 mmol) in ethanol (12 mL) at 0 °C. The mixture was then allowed to warm to room temperature and stirred for 4 h. At the end of this period, sat. NH_4Cl solution was added to the flask, followed by extraction with ether. The combined organic layers were dried over Na_2SO_4 and concentrated to give a solid which was washed successively with hexane to get pure enones **5a**–**l**. Enone **5n** was obtained as an oil and purified by flash column chromatography using EtOAc–hexanes (1:30). Enone **5m** was synthesized from *trans*-crotonyl chloride and benzene according to the literature procedure.[11] All spectroscopic data of the enones were identical to those reported in the literature.[12]

4.4. General procedure for the asymmetric addition of diethylzinc to enones

Chiral ligands **4a**–**d** and $Ni(acac)_2$ were benzene azeotroped and used from a stock solution in acetonitrile. Method A: Chiral ligand (0.88 mL, 0.079 M, 25 mol %, freshly prepared) and $Ni(acac)_2$ (30 μL, 0.093 M, 1 mol %) or Method B: Chiral ligand (0.53 mL, 0.079 M, 15 mol % freshly prepared) and $Ni(acac)_2$ (60 μL, 0.023 M, 0.5 mol %) were mixed and refluxed under an argon atmosphere for 1 h. At the end of this period, the reaction mixture was cooled to room temperature and enone (0.280 mmol) in CH_3CN (0.2 mL) was added. Diethylzinc (0.42 mL, 0.42 mmol, 1 M in hexane) was then added slowly over a period of 10 min to the reaction mixture cooled to −35 °C. The color of the reaction mixture was changed from orange to dark brown. After stirring for 5 h at this temperature, the mixture was quenched with sat. NH_4Cl solution followed by extraction with ether (2 × 10 mL). The combined organic layers were dried over Na_2SO_4, concentrated, and purified by flash column chromatography (EtOAc/hexanes 1:20) to obtain the pure product.

4.4.1. 1,3-Diphenyl-1-pentanone 6a. Using method A, **6a** was obtained as a white solid (54.7 mg, 82% yield), mp: 55–56 °C; $[\alpha]_D^{25} = -4.3$ (*c* 1.35, EtOH) for 80% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (+)-**6a**: 7.3 min; for (*S*), t_R (−)-**6a**: 8.9 min for (*R*). All spectroscopic data are in good agreement with those reported in the literature.[3b,i,13a,b]

4.4.2. 1-Phenyl-3-*p*-tolylpentan-1-one 6b. Using method A, **6b** was obtained as a pale yellow oil (63.6 mg, 90% yield), $[\alpha]_D^{25} = -9.4$ (*c* 2.22, EtOH) for 72% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (+)-**6b**: 6.7 min, t_R (−)-**6b**: 9.2. All other spectroscopic data are in good agreement with those reported in the literature.[13a]

4.4.3. 3-(4-(Trifluoromethyl)phenyl)-1-phenylpentan-1-one 6c. Using method A, **6c** was obtained as a yellow waxy oil (68.6 mg, 80% yield), $[\alpha]_D^{25} = +4.2$ (*c* 1.92, EtOH) for 70% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (−)-**6c**: 6.5 min, t_R (+)-**6c**: 8.6 min. All other spectroscopic data are in good agreement with those reported in the literature.[3b]

4.4.4. 3-(4-Chlorophenyl)-1-phenylpentan-1-one 6d. Using method A, **6d** was obtained as a colorless oil (58.8 mg, 77% yield), $[\alpha]_D^{25} = -1.8$ (*c* 1.97, EtOH) for 70% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (+)-**6d**: 7.8 min for (*S*), t_R (−)-**6d**: 11.1 min for (*R*). All other spectroscopic data are in good agreement with those reported in the literature.[3i,13a]

4.4.5. 3-(4-Methoxyphenyl)-1-phenylpentan-1-one 6e. Using method A, **6e** was obtained as a pale yellow solid (56.4 mg, 75% yield), mp: 49–50 °C; $[\alpha]_D^{25} = -12.4$ (*c* 1.49, EtOH) for 76% ee; HPLC: Chiralcel AD column, UV

detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (+)-**6e**: 9.2 min for (*S*), t_R (−)-**6e**: 13.7 min for (*R*). All other spectroscopic data are in good agreement with those reported in the literature.[3i,13a]

4.4.6. 3-(3-Methoxyphenyl)-1-phenylpentan-1-one 6f. Using method A, **6f** was obtained as a pale yellow waxy oil (63.9 mg, 85% yield), $R_f = 0.35$, 1:10 EtOAc–hexanes, $[\alpha]_D^{25} = -3.4$ (*c* 2.06, EtOH) for 80% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (+)-**6f**: 8.3 min, t_R (−)-**6f**: 9.8 min; IR ($CHCl_3$): $\nu = 3039$, 3008, 2964, 2930, 2878, 2835, 1687, 1604, 1486, 1452, 1363, 1316, 1261, 1155, 1047, 1013, 976, 923 cm^{-1}; ^{1}H NMR ($CDCl_3$–CCl_4): δ 0.82 (t, $J = 7.3$ Hz, 3H), 1.57–1.67 (m, 1H), 1.72–1.82 (m, 1H), 3.17–3.27 (m, 3H), 3.77 (s, 3H), 6.68 (d, $J = 8.0$ Hz, 1H), 6.73 (s, 1H), 6.79 (d, $J = 7.6$ Hz, 1H), 7.16 (t, $J = 7.9$ Hz, 1H), 7.40 (t, $J = 7.6$ Hz, 2H), 7.50 (t, $J = 7.3$ Hz, 1H), 7.88 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR ($CDCl_3$–CCl_4): δ 12.13, 29.10, 43.04, 45.58, 54.93, 111.32, 113.67, 119.94, 128.05, 128.42, 129.29, 132.69, 137.40, 146.32, 159.68, 198.44; MS (EI) *m*/*z* (%): 268 (18) [M$^+$], 239 (25), 185 (20), 163 (75), 148 (95), 134 (8), 121 (40), 105 (83), 91 (36), 77 (100), 65 (13), 55 (17), 50 (24).

4.4.7. 3-(2-Methoxyphenyl)-1-phenylpentan-1-one 6g. Using method A, **6g** was obtained as a pale yellow oil (45.1 mg, 60% yield), $[\alpha]_D^{25} = -5.7$ (*c* 1.80, EtOH) for 66% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (+)-**6g**: 7.7 min for (*S*), t_R (−)-**6g**: 9.4 min for (*R*). All other spectroscopic data are in good agreement with those reported in the literature.[3a,6]

4.4.8. 3-(2-Chlorophenyl)-1-phenylpentan-1-one 6h. Using method A, **6h** was obtained as a pale yellow solid (42.0 mg, 55% yield), mp: 61–62 °C; $[\alpha]_D^{25} = +16.4$ (*c* 1.30, EtOH) for 50% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (−)-**6h**: 7.2 min, t_R (+)-**6h**: 8.7 min. All other spectroscopic data are in good agreement with those reported in the literature.[3a]

4.4.9. 3-(2-Fluorophenyl)-1-phenylpentan-1-one 6i. Using method A, **6i** was obtained as a pale yellow solid (55.2 mg, 77% yield), $R_f = 0.48$, 1:10 EtOAc–hexanes; mp: 38–39 °C; $[\alpha]_D^{25} = +10.0$ (*c* 2.19, EtOH) for 76% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (−)-**6i**: 7.3 min, t_R (+)-**6i**: 8.4 min; IR ($CHCl_3$): $\nu = 3072$, 3039, 2967, 2934, 2874, 1685, 1599, 1586, 1490, 1448, 1365, 1289, 1243, 1180, 1117, 1022, 985, 929 cm^{-1}; ^{1}H NMR ($CDCl_3$–CCl_4): δ 0.83 (t, $J = 7.4$ Hz, 3H), 1.65–1.85 (m, 2H), 3.23–3.36 (m, 2H), 3.46–3.54 (m, 1H), 6.95–7.05 (m, 2H), 7.11–7.16 (m, 1H), 7.21 (td, $J = 7.4$, 1.6 Hz, 1H), 7.40 (t, $J = 7.6$ Hz, 2H),7.50 (t, $J = 7.3$ Hz, 1H), 7.90 (d, $J = 7.3$ Hz, 2H); ^{13}C NMR ($CDCl_3$–CCl_4): δ 12.16, 27.82, 37.53, 43.90, 115.60 (d, $J = 22.9$ Hz), 123.94 (d, $J = 3.7$ Hz), 127.66 (d, $J = 8.9$ Hz), 128.04, 128.43, 129.55 (d, $J = 5.5$ Hz), 131.13 (d, $J = 13.6$ Hz), 132.72, 137.23, 161.22 (d, $J = 243.8$ Hz), 198.00; MS (EI) *m*/*z* (%): 256 (22) [M$^+$], 227 (94), 137 (7), 135 (39), 120 (59), 105 (100), 76 (65), 50 (41).

4.4.10. 3-(Naphthalen-2-yl)-1-phenylpentan-1-one 6j. Using method A, **6j** was obtained as a pale yellow solid (46.03 mg, 57% yield), $R_f = 0.42$, 1:10 EtOAc–hexanes; mp: 51–52 °C; $[\alpha]_D^{25} = +1.1$ (*c* 1.99, EtOH) for 78% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (−)-**6j**: 8.8 min, t_R (+)-**6j**: 11.1 min; IR ($CHCl_3$): $\nu = 3061$, 3004, 2970, 2929, 2868, 1677, 1602, 1582, 1507, 1446, 1385, 1354, 1286, 1235, 1198, 1174, 1099, 1021, 983, 925 cm^{-1}; ^{1}H NMR ($CDCl_3$–CCl_4): δ 0.83 (t, $J = 7.3$ Hz, 3H), 1.54–1.77 (m, 1H), 1.79–1.91 (m, 1H), 3.21–3.32 (m, 2H), 3.35–3.44 (m, 1H), 7.35–7.42 (m, 4H), 7.47 (t, $J = 7.3$ Hz, 1H), 7.62 (s, 1H), 7.74 (d, $J = 8.2$ Hz, 3H), 7.88 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR ($CDCl_3$–CCl_4): δ 12.23, 29.13, 43.06, 45.63, 125.22, 125.84 (2C), 126.24, 127.57, 127.63, 128.06, 128.13, 128.44, 132.42, 132.71, 133.62, 137.38, 142.03, 198.20; MS (EI) *m*/*z* (%): 288 (15) [M$^+$], 259 (15), 241 (5), 182 (21), 168 (61), 152 (22), 140 (35), 127 (14), 114 (10), 104 (91), 76 (100), 54 (10), 50 (27).

4.4.11. 3-Ferrocenyl-1-phenylpentan-1-one 6k. Using method A, **6k** was obtained as a yellow oil (12.6 mg, 13% yield), $[\alpha]_D^{25} = +42.9$ (*c* 0.84, EtOH) for 56% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 95:5 flow 1.0 mL min^{-1}, 20 °C, t_R (+)-**6k**: 9.4 min, t_R (−)-**6k**: 16.8 min. All other spectroscopic data are in good agreement with those reported in the literature.[3i]

4.4.12. 4-Phenylhexan-2-one 6l. Using method A, **6l** was obtained as a yellow oil (24.2 mg, 49% yield), $[\alpha]_D^{25} = -3.5$ (*c* 1.61, EtOH) for 22% ee; HPLC: Chiralcel OD-H column, UV detection at 220 nm, eluent: hexane/2-propanol = 99:1 flow 1.0 mL min^{-1}, 20 °C, t_R (+)-**6h**: 9.8 min for (*S*), t_R (−)-**6h**: 10.8 min for (*R*). All other spectroscopic data are in good agreement with those reported in the literature.[3i,13b,c]

4.4.13. 3-Methyl-1-phenylpentan-1-one 6m. Using method A, **6m** was obtained as a colorless oil (28.1 mg, 57% yield), $[\alpha]_D^{25} = -10.4$ (*c* 1.87, Et_2O) for 60% ee; HPLC: Chiralcel OD column, UV detection at 240 nm, eluent: hexane/2-propanol = 99.8:0.2 flow 0.5 mL min^{-1}, 20 °C, t_R (−)-**6m**: 24.3 min for (*R*), t_R (+)-**6m**: 25.8 min for (*S*). All other spectroscopic data are in good agreement with those reported in the literature.[13b,d]

4.4.14. 3-Cyclohexyl-1-phenylpentan-1-one 6n. Using method A, **6n** was obtained as a white waxy oil (30.8 mg, 45% yield), $[\alpha]_D^{25} = +0.7$ (*c* 1.54, EtOH) for 70% ee; HPLC: Chiralcel AD column, UV detection at 240 nm, eluent: hexane/2-propanol = 99.9:0.1 flow 1.0 mL min^{-1}, 20 °C, t_R (−)-**6n**: 22.4 min for (*R*), t_R (+)-**6n**: 25.4 min for (*S*). All other spectroscopic data are in good agreement with those reported in the literature.[3i]

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