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Asymmetric Michael addition reactions using a chiral La–Na aminodiolate catalyst

N. Prabagaran and G. Sundararajan*

Department of Chemistry, Indian Institute of Technology Madras, Chennai 600036, India

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Abstract—(*R*,*R*)-(+)-2-[Benzyl-(2-hydroxy-2-phenylethyl)amino]-1-phenylethanol **1** is used as a chiral ligand in the synthesis of an optically active lanthanum–sodium amino diol complex **LS-1**. This heterobimetallic catalyst is quite effective as an asymmetric catalyst for various Michael addition reactions, ^{1}H NMR study indicates the co-ordination of enone to the central lanthanum atom in **LS-1**. The reaction conditions were optimized and the adducts were obtained in high yield with moderate to high enantiomeric excess under extremely mild conditions.

1. Introduction

Preparation of synthetic enzymes (chemzymes)[1] remains an interesting and challenging goal in the field of supramolecular chemistry. Considerable new work concerning reactions mediated by heterobimetallic complexes has been reported.[2] The use of chiral heterobimetallic complexes is now common in Michael addition,[3] nitroaldol,[4] hydrophosphorylation,[5] epoxide ring opening,[6] epoxidation of α,β-unsaturated ketones,[7] Diels–Alder,[8] and nitro-Mannich[9] reactions. The heterobimetallic complex, which contains an early and a late transition metal showed some interesting properties such as multifunctionality,[10] that is to have both acidic and basic centers in the same complex. In the complex, the metal centers possibly 'communicate' with one another, show some cooperative effects[11] in the positioning of the reactants, enhance the reactivity of both reactants and ultimately increase the stereoselectivity in product formation.

The asymmetric Michael reaction which is an important technique for carbon–carbon and carbon–heteroatom bond formation has been studied using chiral auxiliaries,[12] chiral monometallic,[13] chiral heterobimetallic[14] and chiral crown ether complexes.[15] The C_2-symmetric amino diol (*R*,*R*)-(+)-2-[benzyl-(2-hydroxy-2-phenylethyl)amino]-1-phenylethanol **1** has been used previously by our group for generating a heterobimetallic lithium–aluminum complex. Herein, we discuss the synthesis and catalytic applications of the lanthanum–sodium aminodiol–heterobimetallic complex for asymmetric Michael addition reactions.

2. Results and discussion

The heterobimetallic complex was synthesised from lanthanum chloride,[16] sodiated amino diol **Na_2-1** and sodium *tert*-butoxide.[17] The combined analysis of the product by inductively coupled plasma spectroscopy (icp) analysis of lanthanum, sodium and the recovered amount of amino diol showed that the **LS-1** complex consisted of lanthanum, sodium and amino diol in a ratio of 1:3:3. The single crystal XRD of the ligand **1** was reported earlier[18] by our group and a single crystal XRD study of the catalyst is currently in progress. The MMX energy-minimized structure of the lanthanum–sodium amino diol complex **LS-1** show the vacant site at lower axis for substrate coordination. The central lanthanum ion in the heterobimetallic catalyst is the origin of Lewis acidity, while the dioxo-sodium moiety was incorporated as a Bronsted base.[19] The basicity of the catalyst can be estimated by the abstraction of protons from different substrates (Scheme 1).

To investigate the chiral induction properties of the complex, the changes in the chemical shift of the C(1) proton of the amino diol **1** in **LS-1** was observed over time. It was found that the complex was stable for 24 h, but with longer times, the complex decomposed.[20]

* Corresponding author. Tel.: +0-091-257-8254; fax: +0-091-257-8241; e-mail: gsundar@iitm.ac.in

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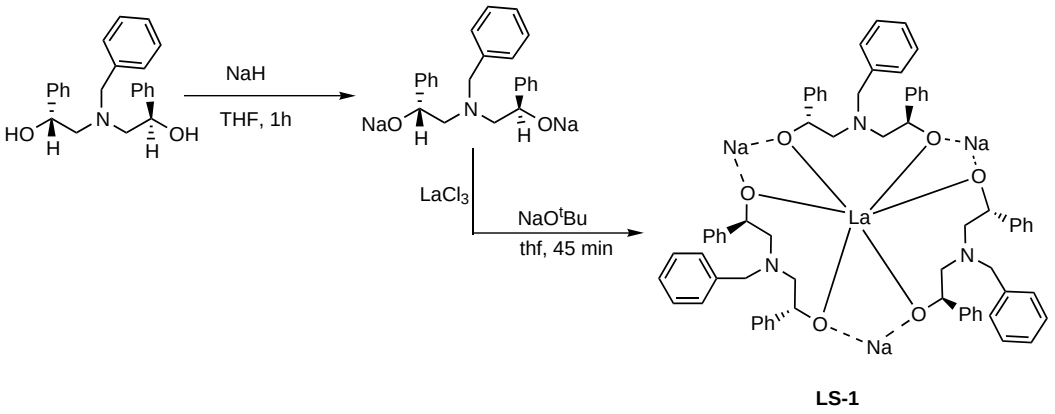
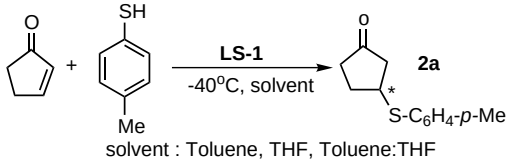


Scheme 1. Synthesis of **LS-1**.

In the presence of 10 mol% of the catalyst **LS-1**, the reaction of *p*-methyl thiophenol with cyclopentenone was complete in 20 min in dry THF at –40°C but the ee was poor. We next investigated the reaction in two different solvents and found that the use of toluene:THF (1:1) gave the best result (48% ee) in a short reaction time (Table 1).

Table 1. Change of solvents and its effect in asymmetric Michael addition reaction



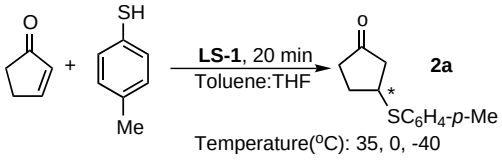
Solvent	Time (min)	ee (%)	Yield (%)
Toluene:THF	20	48	92
Toluene	35	48	90
THF	10	16	90

We assume here that in high polarity solvents the complex dissociates and gives poor enantiomeric excess.[21] In low polar solvents the Michael acceptor and donor possibly remain part of the ensemble to afford the product with high enantiomeric excess.

When the temperature was lowered to –40°C, a higher enantiomeric excess was observed in the product. Possibly, at lower temperatures, the catalyst and the transition state are more immobilized, leading to enhanced ee[22] (Table 2).

The Michael additions of dialkyl malonates to cycloalkenones were also performed with the **LS-1** complex (Table 3) showing moderate to high enantiomeric excess. However, the ee values are lower when compared with the chiral induction seen when reactions are carried out using the lithium–aluminum aminodiolate **Li-Al-1**.

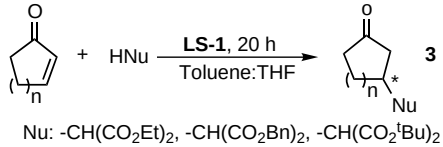
Table 2. Effect of temperature variation in asymmetric Michael addition reaction



Temperature (°C)	Time (min)	ee (%)	Yield (%)
35	10	28	90
0	15	42	90
−40	20	48	92

The results shown in Table 3 indicate that the yield and enantiomeric excess of the Michael adduct depends not only on the nature of the catalyst but also on the Michael acceptors and donors.

Table 3. Asymmetric Michael addition reaction of dialkyl malonates to cycloalkenones



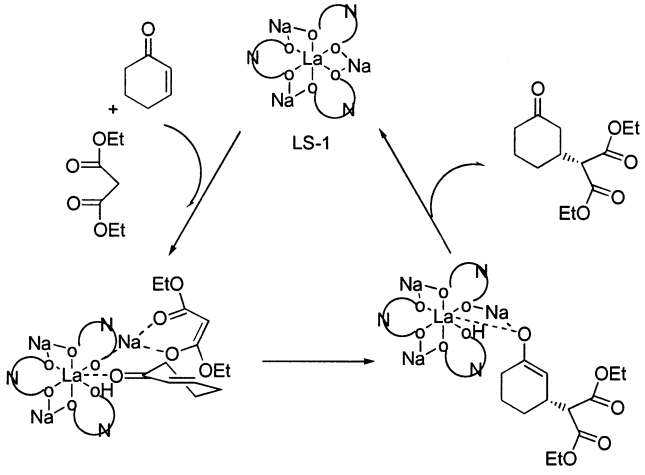
Product	Nu	*n*	Time (h)	Yield (%)	ee (%)	ee[a] (%)
3a	$CH_2(CO_2Et)_2$	1	20	82	78	86
3b	$CH_2(CO_2Et)_2$	2	20	85	77	80
3b	$CH_2(CO_2Et)_2$	2	20	83	67[b]	–
3c	$CH_2(CO_2Bn)_2$	1	20	84	93	83
3d	$CH_2(CO_2Bn)_2$	2	20	86	95	92
3e	$CH_2(CO_2{}^tBu)_2$	1	20	86	77	90
3f	$CH_2(CO_2{}^tBu)_2$	2	20	80	80	94

[a] Addition using **Li-Al-1**.
[b] Cyclohexenone reacted with **LS-1** prepared from lanthanum isopropoxide

To examine the activity of the **LS-1** complex, cyclohexenone was added at different times to the catalyst

and the changes in the chemical shifts of the α-proton of cyclohexenone were also followed and it was observed that the **LS-1** complex is active for 24 h and after that, it decomposed slowly. The changes in the chemical shifts of the α-proton of cyclohexenone show that the carbonyl group of the enone is coordinated to the lanthanum atom in the **LS-1** molecule indicating the Lewis acidity of the complex.

Based on these observations, a mechanism, almost matching Shibasaki's work on the formation of Michael adducts, can be proposed where the enone coordinates with the central metal ion and the donor is deprotonated by the basic heterobimetallic complex. The sodium enolate attacks the Michael acceptor and holds it in a specific position leading to stereoinduction. After the 1,4-addition, the cyclohexenone is released from the lanthanum center, abstracting a proton from the hydroxyl group in the complex to afford the 1,4-adduct (Scheme 2).



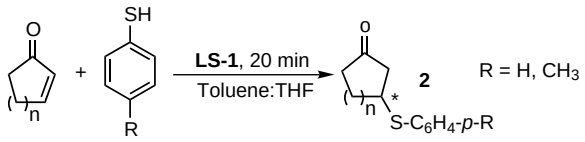
Scheme 2. Proposed mechanism for asymmetric Michael addition reaction using **LS-1**.

Asymmetric Michael additions of thiols to cycloalkenones were also carried out leading to moderate enantiomeric excess but comparatively higher than the induction caused by the **Li-Al-1** complex (Table 4).

We also performed some Michael addition reactions of diethyl malonates and thiophenol using **LS-1** prepared from lanthanum isopropoxide and observed nearly equivalent enantiomeric excess to that of **LS-1** prepared from lanthanum chloride.

Asymmetric catalytic Michael addition of thiophenols and diethyl malonates with 2-methyl cyclopentenone, where two stereogenic centers[23] were created by simple Michael addition reaction, gave an ee of 47% for the thiophenol adduct and the diastereoselectivity was 45%. Whereas on using diethylmalonate as Michael donor, we obtained 60% de and 25% ee (Table 5, Fig. 1).

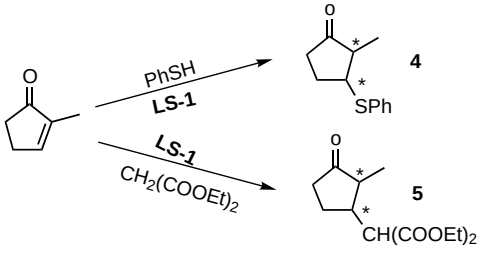
Table 4. Asymmetric Michael addition of thiophenols to cycloalkenones



Product	R	*n*	Time (min)	Yield (%)	ee (%)	ee[a] (%)
2a	CH_3	1	20	92	48	26
2b	H	2	20	95	39	40
2b	H	2	20	90	34[b]	–
2c	CH_3	2	20	90	43	40
2d	H	1	20	91	54	32

[a] Addition using **Li-Al-1**.
[b] Cyclohexenone reacted with **LS-1** prepared from lanthanum isopropoxide.

Table 5. Asymmetric Michael addition reactions of 2-methyl cyclopentenone



Product	Donor	Time	Yield (%)	de (%)	ee (%)
4	PhSH	20 min	90	45	47
5	$CH_2(CO_2Et)_2$	20 h	86	60	25

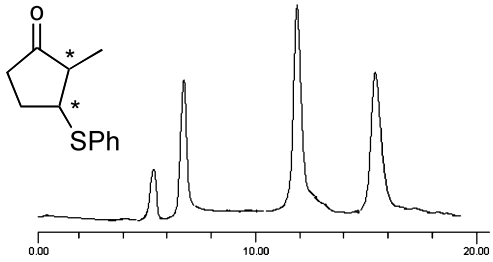


Figure 1. HPLC spectra of compound **4**, using isopropanol:hexane (2:98) solvent mixture and 0.5 mL/min flow rate.

3. Conclusion

The lanthanum sodium aminodiol complex **LS-1** is a good chiral catalyst for Michael addition reactions of dialkyl malonates and thiols giving high enantiomeric excess. Our ^1H NMR study indicates that the catalysts are stable for 24 h and suggests prior coordination of enone to the central metal atom. 2-Methyl cyclopen-

tenone also underwent asymmetric Michael addition giving moderate enantiomeric excesses and diastereoselectivity.

4. Experimental

All reactions were performed under an inert atmosphere of dry nitrogen. (*R*)-(+)-Styrene oxide, 2-cyclopentenone, 2-cyclohexenone, $LaCl_3$, $La(O^iPr)_3$, thiophenols, and *p*-methyl thiophenols were purchased from E. Merck and used as such. Anhydrous THF was obtained by distillation over sodium-benzophenone ketyl. All other reagents were purified by literature procedures.

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ with JEOL 400 MHz (model GSX 400). ^1H and ^{13}C NMR data are reported in parts per million (δ) downfield from tetramethylsilane. The following abbreviations are used for the observed resonance patterns: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. IR spectra were recorded with a Shimadzu (model 470) IR spectrophotometer. Optical rotations were measured with a JASCO DIP-370 digital polarimeter (with 50 and 10 mm cells). Mass spectra (high and low resolution mass spectra) were obtained from Finnigan MAT (model 8230) high resolution mass spectrometer. Waters HPLC with Waters 486 Tunable absorbance detector (λ) containing chiralcel OD column for studying enantiomeric excess. ICP–AES analysis was carried out by ARC 3410 ICP-AES with mini torch.

4.1. Synthesis of LS-1

To a suspension of sodium hydride (41 mg, 1.71 mmol) in THF was added amino diol **1** (290 mg, 0.836 mmol). The mixture was allowed to stir for 1 h to obtain sodiated amino diol.

To $LaCl_3$ (68 mg) the above sodiated amino diol (327 mg, 0.836 mmol) was added with sodium *tert*-butoxide (0.4 mmol). The mixture was allowed to stir for 45 min and the solution was filtered. Half of the filtrate could be used 'as is' or alternatively the dried complex could be used as catalyst for the Michael addition reactions.

4.2. ICP analysis of the LS-1 complex

A suspension of $LaCl_3$ (68 mg, 0.278 mmol) in dry THF was treated with a solution of sodiated amino diol (327 mg, 0.836 mmol) in dry THF and the mixture stirred for 45 min at 0°C with sodium *tert*-butoxide (0.4 mmol). After separating and drying the supernatant solution, a portion of the complex (26 mg) was taken and made up to a volume of 10 mL using a 1:1 mixture of water and conc. nitric acid. The aqueous solution was filtered and this solution was used for ICP analysis. The metal contents were found to be La: 286.57 mg/L (calculated 290.58 mg/L) and Na: 140.21 mg/L (calculated 144.28 mg/L).

4.3. Michael addition reaction of donors to cycloalkenones

To 10 mol% of **LS-1** complex, the cycloalkenone (1 equiv.) and the Michael donor (1 equiv.) were added sequentially using THF solvent. After 30 min the reaction mixture was quenched with 1N HCl, and the product was extracted with ethyl acetate. The organic layer was washed successively with a saturated $NaHCO_3$ solution, brine and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave a syrupy mass, which on flash chromatography using acetone:hexane (4:96) as eluent gave the products.

4.3.1. 3-(*p*-Methyl-phenylthio)cyclopentanone, 2a. Yield: 90%; MS (EI, *m*/*z*): 206 (M^+), 124, 91, 55; IR (CCl_4, cm^{-1}): 3024, 2944, 1747, 1149. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.94–2.24 (m, 2H, C-4), 2.25–2.30 (m, 2H, C-5), 2.34 (s, 3H), 2.46 (dd, 1H, 6.8 and 18.3 Hz, C-2), 2.55 (dd, 1H, 6.8 and 18.3 Hz, C-2) 3.77–3.89 (m, 1H, C-3), 7.12 (d, 2H, 8.5 Hz), 7.3 (d, 2H, 8.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.08 (C-4), 29.26, 36.73 (C-5), 43.80 (C-2), 45.14 (C-3), 129.85, 130.26, 132.77, 137.71, 216.43; $[\alpha]_D = 3.5$ ($c = 1.20$, CCl_4) ee = 43% (lit: $[\alpha]_D = +1.8$ ($c = 2.00$, CCl_4) ee = 22.8%).

4.3.2. 3-(Phenylthio)cyclohexanone, 2b. Yield: 91%; MS (EI, *m*/*z*): 206 (M^+), 110, 97, 77, 55. IR (CCl_4, cm^{-1}): 3072, 2928, 1715 (C=O), 1433, 1302, 1213. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.67–1.78 (m, 2H, C-5), 2.10–2.15 (m, 2H, C-4), 2.28–2.66 (m, 4H, C-2, C-6), 3.39–3.45 (m, 1H, C-3), 7.25–7.32 (m, 3H), 7.4–7.43 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 23.9 (C-5), 31.09 (C-4), 40.75 (C-6), 45.98 (C-2), 47.62 (C-3), 127.66, 128.95, 132.92, 133.08, 208.61. $[\alpha]_D = 38.45$ ($c = 1.6$, benzene) ee = 54% (lit: $[\alpha]_D = 16.4$ ($c = 1.0$, benzene) ee = 22.5%).

4.3.3. 3-(*p*-Methylphenylthio)cyclohexanone, 2c. Yield: 90%. MS (EI, *m*/*z*) 220 (M^+), 124, 97, 79, 55. IR (CCl_4, cm^{-1}): 2928, 1718, 1485, 1443, 1305, 1273. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.65–1.72 (m, 2H, C-5), 2.09–2.15 (m, 2H, C-4), 2.32 (s, 3H), 2.27–2.67 (m, 4H, C-2, C-6), 3.31–3.37 (m, 1H, C-3), 7.11 (d, 2H, 8.3 Hz), 7.32 (d, 2H, 8.3 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.00 (C-5), 23.91 (C-4), 31.12, 40.72 (C-6), 46.33 (C-2), 47.65 (C-3), 129.70, 133.81, 137.98, 208.75. $[\alpha]_D = +32.1$ ($c = 1.2$, benzene) ee = 45% (lit: $[\alpha]_D = +70$ ($c = 2.0$, benzene) ee = 100%).

4.3.4. 3-(Phenylthio)cyclopentanone, 2d. Yield: 95%; MS (EI, *m*/*z*): 192 (M^+) 110, 83, 55; IR (CCl_4, cm^{-1}): 3024, 2945, 1748 (C=O), 1150; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.96–2.23 (m, 2H, C-4), 2.26–2.37 (m, 2H, C-5) 2.45 (dd, 1H, 6.8 and 18.0 Hz, C-2), 2.59 (dd, 1H, 6.8 and 18.5 Hz, C-2), 3.85–3.92 (m, 1H, C-3), 7.24–7.41 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 29.18 (C-4), 36.62 (C-5), 43.22 (C-2), 45.09 (C-3), 127.27, 128.98, 131.81, 134.08, 216.6; $[\alpha]_D = +3.2$ ($c = 1.0$, CCl_4) ee = 39% (lit: $[\alpha]_D = 1.8$ ($c = 1.54$, CCl_4) for ee = 22.5%).

4.3.5. 3-[Bis(ethoxycarbonyl)methyl]cyclopentanone, 3a. Yield: 82%; MS (EI, m/z): 242 (M^+), 197, 160, 83. IR (CCl_4, cm^{-1}): 2976, 2928, 1744, 1734, 1148; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.20 (t, 3H, 7.3 Hz), 1.21 (t, 3H, 7.32 Hz), 1.58–1.66 (m, 1H, C-4), 1.93–2.0 (m, 1H, C-4), 2.1–2.31 (m, 1H, C-3), 2.45–2.86 (m, 4H, C-2, C-5), 3.27 (d, 1H, 9.28 Hz, C-6), 4.12–4.19 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.93, 27.34 (C-4), 36.18 (C-3), 38.06 (C-5), 42.77 (C-2), 56.38 (C-6), 61.47, 61.57, 167.95, 168.04, 217.11; $[\alpha]_D = +27.1$ ($c = 1.05$, $CHCl_3$) ee = 28% (lit: $[\alpha]_D = +28.35$ ($c = 1.89$, $CHCl_3$) ee = 82%).

4.3.6. 3-[Bis(ethoxycarbonyl)methyl]cyclohexanone, 3b. Yield: 85%; MS (EI, m/z): 256 (M^+), 211, 182, 160, 97; IR (CCl_4, cm^{-1}): 2968, 2930, 1754, 1724, 1443, 1359, 1134; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.27 (t, 3H, 7.33 Hz), 1.28 (t, 3H, 7.27 Hz), 1.52–1.69 (m, 2H, C-5), 1.96–2.11 (m, 2H, C-4), 2.22–2.31 (m, 1H, C-3), 2.38–2.47 (m, 2H, C-6), 2.49–2.57 (m, 2H, C-2), 3.35 (d, 1H, 7.82 Hz, C-7), 4.20 (q, 2H, 7.32 Hz), 4.21 (q, 2H, 7.32 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.07, 14.10, 27.50 (C-5), 29.35 (C-4), 36.32 (C-3), 38.20 (C-6), 42.91 (C-2), 56.52 (C-7), 61.62, 61.45, 168.09, 168.18, 217.27; $[\alpha]_D = +2.9$ ($c = 2.13$, $CHCl_3$) ee = 84% (lit: $[\alpha]_D = +2.9$ ($c = 2.56$, $CHCl_3$) ee 81%).

4.3.7. 3-[Bis(benzyloxycarbonyl)methyl]cyclopentanone, 3c. Yield: 84%; MS (EI, m/z): 366 (M^+), 289, 107, 91; IR (CCl_4, cm^{-1}): 2978, 2928, 1747, 1733, 1452, 1398; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.58–1.77 (m, 2H, C-4), 1.97–2.98 (m, 5H, C-2, C-3, C-5), 3.33 (d, 1H, 7.81 Hz, C-6), 5.11 (s, 2H), 5.12 (s, 2H), 7.20–7.41 (m, 10H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 24.41 (C-4), 38.32 (C-3), 40.53 (C-5), 41.06 (C-2), 55.72 (C-6), 66.28, 66.30, 128.13, 128.24, 128.53, 135.13, 135.24, 170.83, 170.92, 217.30. $[\alpha]_D = +31.9$ ($c = 1.27$, $CHCl_3$) ee = 93% (lit: $[\alpha]_D = +28.35$ ($c = 1.89$, $CHCl_3$) ee = 85%).

4.3.8. 3-[Bis(benzyloxycarbonyl)methyl]cyclohexanone, 3d. Yield: 86%; MS (EI, m/z): 380 (M^+), 289, 91. IR (CCl_4, cm^{-1}): 3040, 2944, 1753, 1721; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.40–1.60 (m, 2H, C-5), 1.81–1.96 (m, 2H, C-4), 2.11–2.19 (m, 1H, C-3), 2.27–2.38 (m, 2H, C-6), 2.43–2.51 (m, 2H, C-2), 3.33 (d, 1H, 7.81 Hz, C-7), 5.06 (s, 2H), 5.07 (s, 2H), 7.17–7.25 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 24.46 (C-5), 28.59 (C-4), 38.06 (C-3), 40.90 (C-6), 45.00 (C-2), 56.63 (C-7), 66.76, 67.21, 128.30, 128.47, 128.51, 135.07, 135.17, 167.48, 167.58, 209.34; $[\alpha]_D = +1.2$ ($c = 1.68$, $CHCl_3$) ee = 95% (lit: $[\alpha]_D = +1.1$ ($c = 2.21$, $CHCl_3$) ee = 88%.

4.3.9. 3-[Bis(*tert*-butoxycarbonyl)methyl]cyclopentanone, 3e. Yield: 86%; MS (EI, m/z): 298 (M^+), 186, 82, 57; IR (KBr, cm^{-1}): 2976, 1741, 1718, 1401, 1129; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.38 (s, 9H), 1.4 (s, 9H), 1.54–1.94 (m, 2H, C-4), 2.10–2.29 (m, 3H, C-3, C-5), 2.43–2.75 (m, 2H, C-2), 3.09 (d, 1H, 9.76 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.41, 27.83 (C-4), 36.22 (C-3), 38.17 (C-5), 42.86 (C-2), 58.51 (C-6), 81.84, 81.87, 167.4, 167.48, 217. 69; $[\alpha]_D = +12.7$ ($c = 1.54$, $CHCl_3$) ee = 92% (lit: $[\alpha]_D = +13.2$ ($c = 2.0$, $CHCl_3$) ee = 96%.

4.3.10. 3-[Bis(*tert*-butoxycarbonyl)methyl]cyclohexanone, 3f. Yield: 80%; MS (EI, m/z): 312 (M^+), 256, 200, 96, 57. IR (CCl_4, cm^{-1}): 2976, 2928, 1740, 1724, 1366, 1158; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.39 (s, 9H), 1.40 (s, 9H), 1.41–1.65 (m, 2H, C-5), 1.89–2.02 (m, 2H, C-4), 2.14–2.21 (m, 1H, C-3), 2.30–2.40 (m, 4H, C-2, C-6), 3.01 (d, 1H, 7.81 Hz, C-7); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.56, 27.94 (C-5), 28.79 (C-4), 37.88 (C-3), 41.1 (C-6), 45.2 (C-2), 58.75 (C-7), 81.85, 81.83, 167.18, 167.28, 210.09; $[\alpha]_D = +6.5$ ($c = 2.0$, $CHCl_3$) ee = 96% (lit: $[\alpha]_D = 4.2$ ($c = 1.02$, $CHCl_3$) ee = 65%.

4.3.11. 3-(Phenylthio)-2-methylcyclopentanone, 4. Yield: 90%; MS (EI, m/z): 206 (M^+); IR (CCl_4, cm^{-1}): 1744; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.11 (d, 3H, 6.9 Hz, C-6), 1.77–1.80 (m, 2H, C-4), 2.08–2.18 (m, 3H, C-2, C-5), 2.25–2.37 (m, 1H, C-3), 7.27–8.1 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 10.2 (C-6), 28.43 (C-4), 36.77 (C-5), 44.29 (C-2), 45.53 (C-3), 128.43, 129.58, 130.03, 133.59, 219.82.

4.3.12. 3-[Bis(ethoxycarbonyl)methyl]-2-methylcyclopentanone, 5. Yield: 86%; MS (EI, m/z): 256 (M^+). IR (CCl_4, cm^{-1}): 1731, 1651; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.1 (d, 3H, 6.9 Hz, C-6), 1.27 (m, 6H), 1.68–1.76 (m, 2H, C-4), 2.03–2.20 (m, 1H, C-3), 2.33–2.54 (m, 2H, C-5), 2.95 (m, 1H, C-2), 3.27 (d, 1H, 6.8 Hz, C-7), 4.20 (q, 4H, 3.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.19, 14.05 (C-6), 24.68 (C-4), 36.73 (C-3), 43.62 (C-5), 47.83 (C-2), 54.7 (C-7), 61.50, 61.55, 167.95, 168.37, 216.82.

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