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A new C_2-symmetric heterobimetallic complex as a promoter for asymmetric Michael addition reactions

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Abstract: A C_2-symmetric chiral amino diol (1R,5R)-3-aza-3-benzyl-1,5-diphenyl pentan-1,5-diol [(R,R)-I] has been synthesised by a modified procedure. The heterobimetallic catalyst [I_2–Al–Li] obtained by reaction of the amino diol [(R,R)-I] with $LiAlH_4$, promotes asymmetric Michael addition of malonic esters and thiophenols to α,β-unsaturated compounds with high enantiomeric excess. © 1997 Elsevier Science Ltd

Introduction

In recent years, acceleration of asymmetric Michael addition reactions by chiral metal complexes has been recognised as an efficient method for enantioselective carbon–carbon bond formation.[1,2] There has also been sustained interest in the development and use of enantiomerically pure C_2-symmetric diols to form metal alkoxides and its derivatives as the chiral source to produce products with high enantioselectivity.[3] A recent advance in the asymmetric Michael addition reaction is the discovery of heterobimetallic multifunctional asymmetric catalyst reported by Shibasaki and co-workers.[4] In a series of reports these authors elaborated the ability of such heterobimetallic complexes of BINOL–aluminum (or lanthanide's)–alkali metals in bringing about highly enantioselective Michael addition reactions. It is interesting to note that all of these heterobimetallic complexes are derived from BINOLS having only two oxygen atoms for coordination. In this paper we report the synthesis of a new C_2-symmetric heterobimetallic complex that has a ligand with one nitrogen atom along with two oxygen atoms for coordination. This catalyst promotes asymmetric Michael addition reactions.

The synthesis of a new C_2-symmetric titanium alkoxide complex derived from amino diol (1R,5R)-3-aza-3-benzyl-1,5-diphenyl pentan-1,5-diol [(R,R)-I], which successfully promotes Diels–Alder and ene reactions, was reported by us.[5] Although this titanium alkoxide failed to promote Michael addition reactions, the aluminate of amino diol (R,R)-I obtained by its reaction with $LiAlH_4$ is able to promote and effect asymmetric induction in such reactions. We report here our findings on the asymmetric Michael addition reactions with this new chiral heterobimetallic complex.

Results and discussion

The synthesis of amino diol (R,R)-I from the reaction of 2 eqs. of (R)-(+)-styrene oxide with 1 eq. of benzylamine under neat conditions was reported by Trost.[6] We find it more convenient to prepare the diol with ethanol or methanol as a solvent, where the reaction time is decreased from 13h to 4h. Upon removing the solvent, a syrupy mass was left behind. Purification of this residue by flash column chromatography with EtOAc:hexane (20:80) as eluent, gave the isomeric diols (R,R)-I (major) and (R,S)-II (minor) [equ.1]. The structure of the two isomers were assigned based on the respective ^1H and ^{13}C NMR and mass spectral data (*vide* Experimental). The specific rotation of the major diol (R,R)-I is $[\alpha]_D^{25}=-131.9$ (c=2.45, CCl_4) and that of the minor diol is $[\alpha]_D^{25}=+42.15$ (c=2.38, CCl_4).

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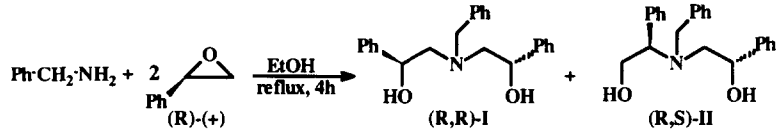


---equ. 1

The amino diol (R,R)-I (2 eqs.) reacts readily with $LiAlH_4$ (1 eq.) in THF with accompanying evolution of hydrogen. Removal of solvent yielded a semi-solid which eluded crystallisation and hence further characterisation by XRD. However, by conventional downward displacement of water we were able to measure the hydrogen evolved from the reaction as 2 moles per 1 mole of the amino diol, (R,R)-I. From the infra-red spectrum it was clear that there were no free hydroxyl groups belonging to unreacted amino-diol. Based on these observations, we suggest the formation of a heterobimetallate of formula, [I_2–Al–Li] and that is similar to the structure proposed for $LiAlH_4$–BINOL complexes.[4b]

In order to evaluate the efficiency of the heterobimetallate [I_2–Al–Li] towards promoting asymmetric Michael addition reactions, we adopted a procedure similar to the one reported by Shibasaki.[4b] Typically, the heterobimetallic complex was generated in situ by the reaction of the amino diol (R,R)-I (2 eqs.) with $LiAlH_4$ (1 eq.). To this the enones and the donors were added and the reaction was followed by TLC. After completion of the reaction, the mixture was quenched with 1 N HCl. The amino diol (R,R)-I and the Michael adducts were separated by flash column chromatography with acetone:hexane (10:90) as eluent. The recovered amino diol was recycled. Various malonic esters were reacted with cyclic and acyclic enones in the presence of [I_2–Al–Li]. The results obtained are detailed in Table 1.

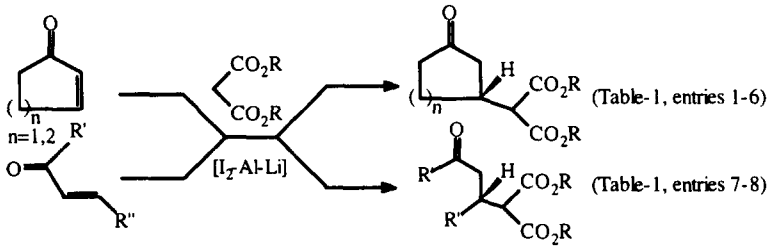
The results shown in Table 1, reveal that the reaction time for the formation of Michael adducts is less compared with those employing Na–Ga–BINOL (143 h),[4a] Li–Al–BINOL (72 h),[4b] and K–La–BINOL (12 h)[4d] complexes as promoters. The specific rotation values and the ees of the products are comparable with these catalysts. The enantiomeric excesses of the products were calculated with the maximum specific rotation values available in the literature.[8] We also performed Michael addition of malonic ester with β-nitro styrene (entry 8) to demonstrate the versatility of the method with substrates other than α,β-unsaturated carbonyl compounds.

To compare the relative efficiency of heterobimetallic complex [I_2–Al–Li], we also prepared the heterobimetallic complex of TADDOL (2 eq.) [(4R,5R)-4,5-bis(diphenyl-hydroxymethyl)-2,2-dimethyl-dioxolane][9] and $LiAlH_4$ (1 eq.) in THF. The complex so generated, also promotes Michael addition reaction of diethyl malonate to cyclohexenone. Here products of Michael additions have comparable enantiomeric excesses with those obtained in the presence of catalyst based on BINOL or (R,R)-I (*vide* Experimental). The isolated yields, however, are lower (60%) than that obtained with the heterobimetallic catalyst [I_2–Al–Li] (87%) for the same reaction time of 5 h.

We also noticed many reports in the literature on asymmetric induction in Michael addition of thiols to α,β-unsaturated ketones in the presence of cinchona alkaloids,[10] quinine and quinidine,[11] chiral crown ethers[12] and natural proteins[13] as catalysts. Surprisingly however, the use of heterobimetallic catalyst for asymmetric Michael addition reactions of thiophenol to α,β-unsaturated ketones is not known. This prompted us to study such types of asymmetric Michael addition reactions. To the heterobimetallic aluminium complex [I_2–Al–Li] prepared by the above-mentioned procedure, cyclic alkenones and thiophenols were added and stirred for 60 seconds at 0°C. The mixture was quenched with 1 N HCl and extracted with EtOAC. Purification by flash column chromatography gave the Michael adducts in excellent yield. The results are summarised in Table 2.

In most cases, the Michael addition is achieved in less than a minute. The time required for the conversion of products is less compared to the addition reaction of thiols to α,β-unsaturated ketones, which was previously described by Hodge[10a] using cinchona alkaloid and its derivatives as catalysts (24 to 240 h). The enantiomeric excesses of the products were calculated with the maximum specific rotation values available in the literature.[14]

Table 1. Michael addition of malonic esters to acyclic and cyclic enones in the presence of heterobimetallic complex [I_2–Al–Li]



Compd. No.	Enone	Donor (R)	Time (h)[a]	Yield (%)[b]	$[\alpha]_D^{25}$	%ee[c, d]
1.	n = 1	Et	5	86	+ 29.9 (c=1.71, $CHCl_3$)	86
2.	n = 1	^{t}Bu	6	83	+ 12.4 (c =1.88, $CHCl_3$)	90
3.	n = 1	CH_2Ph	8	78	+ 28.3 (c =1.73, $CHCl_3$)	83
4.	n = 2	Et	5	87	+ 2.8 (c =2.51, $CHCl_3$)	80
5.	n = 2	^{t}Bu	6	80	+ 6.4 (c =1.37, $CHCl_3$)	94
6.	n = 2	CH_2Ph	7	83	+ 1.15 (c =1.18, $CHCl_3$)	92
7.	R' = Ph R" = Me	Et	4	95	+ 12.6 (c =1.51, CCl_4)	62
8.	R' = Ph R" = NO_2	Et	4	93	+ 4.9 (c =1.73, CCl_4)	e

[a] For cyclic enones using 1. Al-BINOL = 72h[4b]; 2. La-BINOL = 12h[4d].

[b] Isolated yields. [c] %ee based on the specific rotation values. [d] Absolute configuration is R. [e] See ref.7 under reference and notes.

In conclusion, we have developed a new C_2-symmetric heterobimetallic catalyst [I_2–Al–Li] as a promoter for asymmetric Michael addition reaction of malonic esters to acyclic and cyclic enones with good yield and with high enantioselectivity. Addition of thiolphenols to α,β-unsaturated compounds are also accelerated by this heterobimetallic catalyst [I_2–Al–Li] resulting in greater yield with moderate enantioselectivity. The amino diol (R,R)-I is easily synthesised and can be recycled. The isolation and structural characterisation of the C_2-symmetric heterobimetallic catalyst [I_2–Al–Li] and the elucidation of the mechanism leading to the observed high enantioselectivity are in progress.

Experimental section

All reactions were performed under an atmosphere of dry nitrogen by employing Schlenk technique.[15] 2-Cyclopentenone,[16] 2-cyclohexenone,[16] β-nitro styrene[17] and malonic esters[18] were synthesised according to the literature procedure. (R)-(+)-styrene oxide, $LiAlH_4$, thiophenols and

Table 2. Michael addition of thiophenols to acyclic/cyclic enones in the presence of heterobimetallic complex [I$_2$–Al–Li]

Compd. No	Enone	Donor	Time (Sec.)	Yield (%)[a]	$[\alpha]_{578}^{25}$	% ee[b,c]
9.	n = 1	C_6H_5SH	60	97	+2.6 (c = 1.42, CCl_4)	32
10.	n = 1	p-Me-C_6H_4SH	60	96	+2.1 (c = 2.08, CCl_4)	26
11.	n = 2	C_6H_5SH	60	97	+32.3 (c = 1.08, C_6H_6)	45
12.	n = 2	p-Me-C_6H_4SH	60	97	+28.3 (c = 1.52, C_6H_6)	40
13.	R' = Ph R'' = NO_2	p-Me-C_6H_4SH	90	97	+ 5.1 (c = 2.00, $PhCH_3$)	d

a Isolated yields. b %ee based on optical rotation. [c] Absolute configuration is R. [d] See ref.7 under reference and notes.

benzylamine were purchased from E-Merck and used as recieved. Anhydrous THF was obtained by distillation over sodium–benzophenone ketyl.

The ^1H and ^{13}C NMR were recorded in $CDCl_3$ with JEOL 400 MHz (model GSX 400). IR spectra were recorded with Shimadzu (model 470) IR spectrophotometer. Optical rotations were measured with a JASCO DIP-370 digital Polarimeter (with 10 mm cell). Mass spectra (high resolution mass spectra and low resolution mass spectra) were obtained from Finnigan MAT (model 8230) high resolution Mass Spectrometer.

Synthesis of (1R,5R)-3-aza-3-benzyl-1,5-diphenyl pentan-1,5-diol (R,R)-I

Trost[6] has synthesised the amino diol [(R,R)-I] by heating a neat mixture of benzylamine and (R)-(+)-styrene oxide at 120°C for 13 h (Yield 78%). The modified procedure is as follows: To a cooled solution of benzylamine (1.07 g, 9.985 mmol) in 2 ml ethanol, (R)-(+)-styrene oxide (2.40 g, 19.975 mmol) in 4 ml ethanol was added at 0°C and stirred for 1 h. It was then refluxed for 4 h. After completion of the reaction, the solvent was removed under reduced pressure to give isomeric diols as syrupy mass which on flash column chromatography using EtOAc:hexane (20:80) as eluent yield the major isomer as a colourless oil (Yield 85%).

Major isomer (1R,5R)-I

^1H NMR: δ 2.69 (dd_{ABX}, 2H, 13.80 and 15.32 Hz), 2.75 (dd_{ABX}, 2H, 13.51 and 17.42 Hz), 3.10–3.35 (br s, 2H, OH), 3.62 (dd_{AB}, 1H, 14.02 Hz), 3.88 (dd_{AB}, 1H, 13.96 Hz), 4.68 (dd, 2H, 4.12 and 8.52 Hz), 7.15–7.27 (m, 15H); ^{13}C NMR: δ 59.74, 62.53, 70.77, 125.86, 127.41, 127.53, 128.33, 128.50, 129.14, 138.03, 142.10; IR (neat): 3376, 3024, 2832, 1946, 1875, 1805, 1491, 1446, 1242, 1056, 758, 701; M.S. (EI): 240 (- Ph-CH-OH), 132 (- 2(Ph-CH-OH)), 105 (- $PhCH_2N$), 91 (base peak, $PhCH_2$), 77, 65; HRMS: Calcd for $C_{23}H_{25}NO_5$-C_7H_6O: 241.14655, Found: 241.14539; $[\alpha]_D^{25}$=−131.7 (c=2.45, CCl_4), [with chloroform as solvent $[\alpha]_D^{25}$=−135.7 (c=1.11, $CHCl_3$)].

Minor isomer (1R,4S)-3-aza-3-benzyl-1,4-diphenyl pentan-1,5-diol (R,S)-II

^1H NMR: δ 2.74 (dd, 1H, 7.81 and 13.67 Hz), 2.95 (dd, 1H, 4.88 and 13.67 Hz), 2.86–3.00 (br s, 2H, OH), 3.36 (dd_{AB}, 1H, 13.67 Hz), 3.72–3.75 (m, 1H) 3.84 (dd_{AB}, 1H, 13.67 Hz), 3.95 (t, 2H, 3.00 Hz), 4.46 (dd, 1H, 5.37 and 7.82 Hz), 7.18–7.36 (m, 15H); ^{13}C NMR: δ 55.90, 59.95, 61.68, 66.70, 72.88, 126.19, 127.57, 127.91, 128.07, 128.73, 128.80, 129.24, 137.33, 139.59, 142.98; IR (neat): 3386, 3024, 2932, 1946, 1880, 1805, 1491, 1446, 1252, 1060, 758, 701; M.S. (EI): 240 (- Ph-CH-

OH), 120 (- Ph-CH-CH_2-OH)), 103, 91 (base peak $PhCH_2$), 77, 65; HRMS: Calcd for $C_{23}H_{25}NO_5$-C_7H_6O: 241.14655, Found: 241.14583; $[\alpha]_D^{25}$=+42.15 (c=2.38, CCl_4), [with chloroform as solvent $[\alpha]_D^{25}$=+47.1 (c=1.68, $CHCl_3$)].

General procedure for the Michael addition reaction of malonic ester to cyclic enones

Enantiomerically pure amino diol (R,R)-I (183 mg, 0.53 mmol) in dry THF was added to a cooled solution of $LiAlH_4$ (10 mg, 0.268 mmol) in dry THF. The mixture was stirred for 30 minutes at 0°C, then 2-cyclohexenone (91 mg, 0.95 mmol) and diethylmalonate (127 mg, 0.8 mmol) were added. The mixture was warmed to room temperature and stirred for 5 h. The reaction was then quenched with 1N HCl and the mixture extracted with ethyl acetate. The organic layer was washed successively with 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 column chromatography gave the product as a colourless oil (178 mg, 87% yield).

(R)-3-[Bis(ethoxy carbonyl)methyl]cyclopentenone 1

Yield 86%; ^{1}H NMR: δ 1.20 (t, 3H, 7.32 Hz), 1.21 (t, 3H, 7.32 Hz), 1.58–1.66 (m, 1H), 1.93–2.00 (m, 1H), 2.10–2.31 (m, 3H), 2.45 (dd, 1H, 7.82 and 18.56 Hz), 2.75–2.86 (m, 1H), 3.27 (d, 1H, 9.28 Hz), 4.12–4.19 (m, 4H); ^{13}C NMR: δ 13.93, 27.34, 36.18, 38.06, 42.77, 56.38, 61.47, 61.57, 167.95, 168.04, 217.11; IR (CCl_4): (C=O) 1744, 1734; M.S. (EI): 242 (M^+), 197 (- OCH_2CH_3), 160 (base peak), 83, 55; HRMS: Calcd for $C_{12}H_{18}O_5$: 242.11542, Found: 242.11539; $[\alpha]_D^{25}$=+29.9 (c=1.71, $CHCl_3$) 86% ee [Lit:[4d] $[\alpha]_D^{25}$=+28.35 (c=1.89, $CHCl_3$) 82% ee].

*(R)-3-[Bis(*tert*-butoxy carbonyl)methyl]cyclopentenone 2*

Yield 83%; ^{1}H NMR: δ 1.38 (s, 9H), 1.40 (s, 9H), 1.54–1.61 (m, 1H), 1.94 (dd, 1H, 7.85 and 18.07 Hz), 2.10–2.29 (m, 3H), 2.43 (dd, 1H, 7.81 and 18.06 Hz), 2.64–2.75 (m, 1H), 3.09 (d, 1H, 9.76 Hz); ^{13}C NMR: δ 27.41, 27.83, 36.22, 38.17, 42.86, 58.51, 58.61, 81.84, 81.87, 167.40, 167.48, 217.69; IR (KBr): (C=O) 1741, 1718; M.S. (EI): 298 (M^+), 186, 82, 57 (base peak); HRMS: Calcd for $C_{16}H_{26}O_5$: 298.17802, Found: 298.17531; $[\alpha]_D^{25}$=+12.4 (c=1.88, $CHCl_3$) 90% ee [Lit:[2a] $[\alpha]_D^{23}$=+13.2 (c=2.0, $CHCl_3$) 96% ee].

(R)-3-[Bis(benzyloxy carbonyl)methyl]cyclopentenone 3

Yield 78%; ^{1}H NMR: δ 1.58–1.77 (m, 1H), 1.97–2.42 (m, 5H), 2.75–2.98 (m, 2H), 5.11 (s, 2H), 5.12 (s, 2H), 7.20–7.41 (m, 10H); ^{13}C NMR: δ 24.41, 38.32, 40.53, 41.06, 55.72, 66.28, 128.13, 128.24, 128.53, 135.13, 135.24, 170.83, 170.92, 217.30; IR (CCl_4): (C=O) 1747, 1733; M.S. (EI): 381 (M^++1), 289, 107 (base peak), 91; HRMS: Calcd for $C_{22}H_{22}O_5$: 366.14672, Found: 366.14833; $[\alpha]_D^{25}$=+28.3 (c=1.73, $CHCl_3$) 83% ee [Lit:[4d] $[\alpha]_D^{25}$=+28.35 (c=1.89, $CHCl_3$) 85% ee].

(R)-3-[Bis(ethoxy carbonyl)methyl]cyclohexenone 4

Yield 87%; ^{1}H NMR: δ 1.27 (t, 3H, 7.33 Hz), 1.28 (t, 3H, 7.27 Hz), 1.52 (dddd, 1H, 3.42, 12.70, 12.70 and 12.70 Hz), 1.69 (dddd, 1H, 3.90, 12.70, 12.70 and 12.70 Hz), 1.96–2.00 (m, 1H), 2.10–2.11 (m, 1H), 2.22–2.31 (m, 2H), 2.38–2.47 (m, 2H), 2.49–2.57 (m, 1H), 3.35 (d, 1H, 7.82 Hz), 4.20 (q, 2H, 7.32 Hz), 4.21 (q, 2H, 7.32 Hz); ^{13}C NMR: δ 13.97, 24.43, 28.67, 37.91, 40.90, 44.98, 56.78, 61.42, 167.69, 167.77, 209.55; IR (CCl_4): (C=O) 1754, 1724; M.S. (EI): 256 (M^+), 211 182 (- $CO_2CH_2CH_3$), 160, 97 (base peak); HRMS: Calcd for $C_{13}H_{20}O_5$: 256.13107, Found: 256.12757; $[\alpha]_D^{25}$=+2.8 (c=2.50, $CHCl_3$) 80% ee [Lit:[4d] $[\alpha]_D^{25}$=+2.9 (c=2.56, $CHCl_3$) 81% ee].

Amino diol [R,R]-I recovered: 83%, $[\alpha]_D^{25}$=−129.1 (c=2.32, CCl_4).

Using Li–Al–(TADDOL)$_2$ catalyst: Yield: 60%; $[\alpha]_D^{25}$=+3.120 (c=1.37, $CHCl_3$) 87% ee.

*(R)-3-[Bis(*tert*-butoxy carbonyl)methyl]cyclohexenone 5*

Yield 80%; ^{1}H NMR: δ 1.39 (s, 9H), 1.40 (s, 9H), 1.41–1.47 (m, 1H), 1.55–1.65 (m, 1H), 1.89–1.92 (m, 1H), 1.96–2.02 (m, 1H), 2.14–2.21 (m, 2H), 2.30–2.40 (m, 3H), 3.01 (d, 1H, 7.81 Hz); ^{13}C NMR: δ 24.60, 27.72, 27.83, 27.94, 28.79, 37.83, 41.08, 45.17, 58.75, 81.85, 167.13, 167.23, 210.02; IR

(CCl_4): (C=O) 1740, 1724; M.S. (EI): 312 (M^+), 256(- CH_2=CMe_2) , 96, 57 (base peak); HRMS: Calcd for $C_{17}H_{28}O_5$: 312.19367, Found: 312.18732; $[\alpha]_D^{25}$=+6.4 (c=1.73, $CHCl_3$) 94% ee [Lit:[2a] $[\alpha]_D^{26}$=+4.2 (c=1.02, $CHCl_3$) 65% ee].

(R)-3-[Bis(benzyloxy carbonyl)methyl]cyclohexenone ***6***

Yield 83%; ^{1}H NMR: δ 1.40 (dddd, 1H, 3.41, 12.21, 12.21 and 12.21 Hz), 1.54 (dddd, 1H, 3.90, 12.70, 12.70 and 12.70 Hz), 1.81–1.83 (m, 1H), 1.90–1.96 (m, 1H), 2.11–2.19 (m, 2H), 2.27–2.38 (m, 2H), 2.43–2.51 (m, 1H), 3.33 (d, 1H, 7.81 Hz) 5.06 (s, 2H), 5.07 (s, 2H), 7.17–7.25 (m, 10H); ^{13}C NMR: δ 24.46, 28.59, 38.06, 40.90, 45.00, 56.63, 56.76, 67.21, 128.30, 128.47, 128.51, 135.07, 167.48, 209.34; IR (neat): (C=O) 1753, 1721; M.S. (EI): 289 (M^++1), 91 (base peak); HRMS: Calcd for $C_{23}H_{24}O_5$: 380.16237, Found: 380.16513; $[\alpha]_D^{25}$=+1.15 (c=1.18, $CHCl_3$) 92% ee [Lit:[4d] $[\alpha]_D^{24}$=+1.1 (c=2.21, $CHCl_3$) 88% ee].

(R)-3-[Bis(ethoxy carbonyl)methyl]benzylideneacetone ***7***

Yield 95%; ^{1}H NMR: δ 1.00 (t, 3H, 6.83 Hz), 1.25 (t, 3H, 6.84 Hz), 2.01 (s, 3H), 2.82–3.00 (m, 2H), 3.69 (d, 1H, 10.25 Hz), 3.94–4.00 (m, 3H) 4.18 (q, 2H, 7.33 Hz), 7.18–7.26 (m, 5H); ^{13}C NMR: δ 13.67, 13.94, 30.21, 40.41, 47.35, 57.35, 61.24, 61.56, 127.15, 128.07, 128.39, 140.35, 167.58, 168.13, 206.03; IR (CCl_4): (C=O) 1753, 1725; M.S. (EI) 306 (M^+),186, 146 (base peak), 77, 55; HRMS: Calcd for $C_{17}H_{22}O_5$: 306.14672, Found: 306.14172; $[\alpha]_D^{25}$=+12.6 (c=1.18, CCl_4) 62% ee [Lit:[2c] $[\alpha]_D^{24}$=+10.8 (c=1.04, CCl_4) 53% ee].

(R)-2-[Phenyl-1,1-bis(ethoxy carbonyl)methyl]nitroethane ***8***

Yield 93%; ^{1}H NMR: δ 1.04 (t, 3H, 6.83 Hz), 1.25 (t, 3H, 6.84 Hz), 3.82 (d, 1H, 9.27 Hz), 4.19–4.26 (m, 3H), 4.88 (q, 2H, 13.00 Hz), 4.90 (q, 2H, 12.68 Hz), 7.22–7.31 (m, 5H); ^{13}C NMR: δ 13.64, 13.67, 13.85, 13.93, 42.86, 42.95, 54.89, 61.74, 61.82, 61.89, 62.09, 127.95, 128.24, 128.83, 128.92, 136.16, 166.76, 167.40; IR (neat): (C=O) 1750, 1728; M.S. (EI): 309 (M^+),263, 189 (base peak), 77, 51; HRMS: Calcd for $C_{15}H_{19}NO_6$: 309.12124, Found: 309.11325; $[\alpha]_D^{25}$=+4.9 (c=1.73, CCl_4).

General procedure for Michael addition reaction of thio phenols to cyclic enones

To the stirred solution of the complex [I_2–Al–Li] (refer above) at 0°C, 2-cyclohexenone (100 mg, 1.04 mmol) and p-methyl-thiophenol (100 mg, 0.91 mmol) were added. It was stirred at 0°C for 60 seconds and quenched with 1 N HCl. The extraction procedure was followed as described previously. Purification by flash column chromatography gave the product as a yellow colour oil (207 mg, 97% yield).

(R)-3-(Phenylthio)cyclopentenone ***9***

Yield 97%; ^{1}H NMR: δ 1.96–2.18 (m, 1H), 2.21–2.29 (m, 2H), 2.31–2.37 (m, 1H), 2.45 (dd, 1H, 6.83 and 18.06 Hz), 2.59 (dd, 1H, 6.83 and 18.50 Hz), 3.85–3.92 (m, 1H), 7.24–7.41 (m, 5H); ^{13}C NMR: δ 29.18, 36.62, 43.22, 45.09, 127.27, 128.98, 131.81, 134.08, 216.60; IR (CCl_4): (C=O) 1748; M.S. (EI): 192 (M^+, base peak), 110, 83, 55; HRMS: Calcd for $C_{11}H_{12}SO$: 192.06081, Found: 192.05950; $[\alpha]_{578}^{25}$=+2.6 (c=1.42, CCl_4) 32% ee. [Lit:[10b] $[\alpha]_{578}^{24}$=+1.8 (c=1.54, CCl_4) 22.5% ee].

(R)-3-(4-Methyl-phenylthio)cyclopentenone ***10***

Yield 96%; ^{1}H NMR: δ 1.94–2.20 (m, 1H), 2.14–2.30 (m, 2H), 2.34 (s, 3H), 2.46 (dd, 1H, 6.82 and 18.3 Hz), 2.55 (dd, 2H, 6.80 and 18.30 Hz), 3.77–3.89 (m, 1H), 7.12 (d, 2H, 8.5 Hz), 7.3 (d, 2H, 8.5 Hz); ^{13}C NMR: δ 21.08, 29.26, 36.73, 43.80, 45.14, 129.85, 130.26, 132.77, 137.71, 216.43; IR (CCl_4): (C=O) 1747; M.S. (EI): 206 (M^+, base peak), 124, 91, 55; HRMS: Calcd for $C_{12}H_{14}SO$: 206.07646, Found: 206.07897; $[\alpha]_{578}^{25}$=+2.1 (c=2.08, CCl_4) 26% ee. [Lit:[10b] $[\alpha]_{578}^{24}$=+1.8 (c=2.00, CCl_4) 22.8% ee].

(R)-3-(Phenylthio)cyclohexenone ***11***

Yield 97%; ^{1}H NMR: δ 1.67–1.78 (m, 2H), 2.10–2.15 (m, 2H), 2.28–2.40 (m, 3H), 2.66 (dd, 1H, 4.40 and 14.16 Hz), 3.39–3.45 (m, 1H), 7.25–7.32 (m, 3H), 7.40–7.43 (m, 2H); ^{13}C NMR: δ 23.90, 31.09, 40.75, 45.98, 47.62, 127.66, 128.95, 132.92, 133.08, 208.61; IR (CCl_4): (C=O) 1715; M.S. (EI): 206 (M^+, base peak), 110, 97, 77, 55; HRMS: Calcd for $C_{12}H_{14}SO$: 206.07646, Found: 206.07186; $[\alpha]_{578}^{25}$=+32.3 (c=1.08, C_6H_6) 45% ee. [Lit:[5c] $[\alpha]_{578}^{24}$=−16.4 (c=1.00, C_6H_6) 22.5% ee for corresponding (S)-isomer].

(R)-3-(4-Methyl-phenylthio)cyclohexenone ***12***

Yield 97%; ^{1}H NMR: δ 1.65–1.72 (m, 2H), 2.09–2.15 (m, 2H), 2.32 (s, 3H), 2.27–2.37 (m, 3H), 2.62–2.67 (dd, 1H, 4.40 and 14.16 Hz), 3.31–3.37 (m, 1H), 7.11 (d, 2H, 8.3 Hz), 7.32 (d, 2H, 8.3 Hz); ^{13}C NMR: δ 21.00, 23.91, 31.12, 40.72, 46.33, 47.65, 129.70, 133.81, 137.98, 208.75; IR (CCl_4): (C=O) 1718; M.S. (EI): 220 (M^+, base peak),124, 97, 79, 55; HRMS: Calcd for $C_{13}H_{16}SO$: 220.09211, Found: 220.09346; $[\alpha]_{578}^{25}$=+28.3 (c=1.52, C_6H_6) 40% ee. [Lit:[10a] $[\alpha]_{578}^{21}$=+70.0 (c=2.00, C_6H_6) 100% ee.

(R)-2-(Phenyl-4-methyl-phenylthio)nitroethane ***13***

Yield 97%; ^{1}H NMR: δ 2.31 (s, 3H), 4.67 (dd, 1H, 10.25 and 16.6 Hz), 4.77–4.83 (m, 2H), 7.10–7.32 (m, 9H); ^{13}C NMR: δ 21.43, 50.36, 78.73, 127.88, 128.33, 128.77, 129.17, 130.37, 134.52, 136.68, 139.47; IR (CCl_4): 2976, 1372, 1174; M.S. (EI): 273 (M^+),149, 91 (base peak), 77, 65; HRMS: Calcd: 220.09211, Found for $C_{15}H_{15}SO$: 220.09346; $[\alpha]_D^{25}$=+5.1 (c=2.00, $PhCH_3$).

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