## Supporting Information for:

# Enantioselective direct $\alpha$-alkylation of cyclic ketones by means of photo-organocatalysis 

Elena Arceo, ${ }^{1, \hbar}$ Ana Bahamonde, ${ }^{1, \ddagger}$ Giulia Bergonzini, ${ }^{1}$ and Paolo Melchiorre* ${ }^{1,2}$<br>${ }^{l}$ ICIQ - Institute of Chemical Research of Catalonia, Avenida Països Catalans 16-43007 Tarragona, Spain<br>${ }^{2}$ ICREA - Institució Catalana de Recerca i Estudis Avançats, Passeig Lluís Companys 23-08010 Barcelona, Spain

${ }^{\ddagger} \mathrm{EA} \& \mathrm{AB}$ contributed equally to this work.
*To whom correspondence should be addressed. E-mail: pmelchiorre@iciq.es

## Supporting Information



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## A. General Information

The ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR spectra were recorded at 400 MHz or 500 MHz for ${ }^{1} \mathrm{H}$ and at 100 MHz or 125 MHz for ${ }^{13} \mathrm{C}$, respectively. The chemical shifts ( $\delta$ ) for ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ are given in ppm relative to residual signals of the solvents $\left(\mathrm{CHCl}_{3}\right.$ @ $7.26 \mathrm{ppm}{ }^{1} \mathrm{H}$ NMR, $77.0 \mathrm{ppm}{ }^{13} \mathrm{C}$ NMR). Coupling constants are given in Hz. When necessary, ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ signals were assigned by means of g-COSY 2D-NMR sequence. The following abbreviations are used to indicate the multiplicity: s , singlet; d , doublet; t , triplet; q , quartet; qn, quintet; m , multiplet; bs, broad signal.
Mass spectra (high and low resolution) were obtained from the ICIQ High Resolution Mass Spectrometry Unit on a Bruker Maxis Impact (QTOF) or Waters Micromass LCT-Premier (TOF) in Electrospray Ionization (ESI) by direct infusion.
Optical rotations were measured on a Polarimeter Jasco P-1030 and are reported as follows: $[\alpha]_{\mathrm{D}} \mathrm{rt}(c$ in g per 100 mL , solvent).

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General Procedures. All reactions were set up under an argon atmosphere in oven-dried glassware using standard Schlenk techniques, unless otherwise stated. Synthesis grade solvents were used as purchased and the reaction mixtures were deoxygenated by three cycles of freeze-pump-thaw. Chromatographic purification of products was accomplished using force-flow chromatography (FC) on silica gel (35-70 mesh). For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel $60 \mathrm{GF}_{254}, 0.25 \mathrm{~mm}$ ) were employed, using UV light as the visualizing agent and an acidic mixture of para-anisaldehyde or basic aqueous potassium permangante $\left(\mathrm{KMnO}_{4}\right)$ stain solutions, and heat as developing agents. Organic solutions were concentrated under reduced pressure on a Büchi rotatory evaporator.

Determination of Enantiomeric Purity. HPLC analysis on chiral stationary phase was performed on an Agilent 1200 -series instrumentation. Daicel Chiralpak IC and IB columns with hexane: ${ }^{i} \operatorname{PrOH}$ as the eluent were used. HPLC traces were compared to racemic samples prepared using a) a catalytic amount of benzylamine ( $20 \mathrm{~mol} \%$ ) and irradiation with a 23 W compact fluorescent bulb for the $\alpha$-benzylation of ketones (products $\mathbf{3 a}$ to $\mathbf{3 k}$ ) or $\mathbf{b}$ ) one equivalent of a preformed enamine (1-pyrrolidino-1-cyclohexene, Aldrich) and irradiation with a 15 W -black light CFL for the phenacylation of cyclic ketones (products $\mathbf{4 a}$ to $\mathbf{4 h}$ ).

Materials. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Chiral primary amine catalysts $\mathbf{A}$ and $\mathbf{E}$ were synthesized by a Mitsunobu reaction from the commercially available cinchona alkaloids, according to (1). The bifunctional catalyst $\mathbf{C}$ was synthetized following a one-step procedure from commercially available ( $1 R, 2 R$ )-1,2-diphenylethylenediamine, according to the literature procedure in (2). All the cyclic ketones used (1) are commercially available, as well as most of the alkyl halides used within the study. 2-Cyano-4-nitrobenzyl bromide $\mathbf{2 k}$ was prepared by brominating the commercially available 2-methyl-5nitrobenzonitrile, according to (3).

## B. General Procedure for the Light-driven Asymmetric Alkylation of Ketones

General procedure for the photochemical $\alpha$-asymmetric benzylation of ketones:
A 10 mL Schlenk tube was charged with the aminocatalyst $\mathbf{A}(20 \mathrm{~mol} \%)$, toluene $(0.2 \mathrm{M}$ referring to the alkyl bromide 2), trifluoroacetic acid, TFA, ( $40 \mathrm{~mol} \%$ ), the ketone $1(4 \mathrm{eq})$, sodium acetate ( 2 eq ) and the alkylating agent 2 ( 1 eq ). The reaction mixture was degassed via freeze pump thaw (x 3 cycles), and the vessel refilled with nitrogen. After the reaction mixture was thoroughly degassed, the vial was sealed and positioned approximately in the middle of a dewar flask containing an EtOH bath at $0^{\circ} \mathrm{C}, 10 \mathrm{~cm}$ away from 3 light sources. Three household full spectrum 23 W compact fluorescent light (CFL) bulbs were used for irradiating the reaction mixture. After stirring for the indicated time, the crude mixture was purified by flash column chromatography to afford the title compound $\mathbf{3}$ in the stated yield and optical purity.
(S)-2-(2,4-dinitrobenzyl)cyclohexanone (3a)


Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02$ mmol, $6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene $(0.2 \mathrm{M}, 500 \mu \mathrm{~L})$, trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%)$, sodium acetate $(0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq})$, cyclohexanone 1 a ( 0.4 mmol, $42 \mu \mathrm{~L}, 4 \mathrm{eq})$ and 2,4-dinitrobenzyl bromide $2 \mathrm{a}(0.1 \mathrm{mmol}, 26 \mathrm{mg}, 1 \mathrm{eq})$. Time of irradiation: 45 h . Purification by flash column chromatography (gradient eluent from pure pentane to $10: 1$ pentane:AcOEt mixture) afforded the title compound ( $16.5 \mathrm{mg}, 60 \%$ yield, $90 \%$ ee) as a yellow oil.
A larger scale reaction was performed according to the general procedure using the amino catalyst $\mathbf{A}$ (0.2 $\mathrm{mmol}, 65 \mathrm{mg}, 20 \mathrm{~mol} \%$ ), toluene $(0.2 \mathrm{M}, 5 \mathrm{~mL})$, trifluoroacetic acid ( $0.4 \mathrm{mmol}, 30 \mu \mathrm{~L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $2 \mathrm{mmol}, 164 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclohexanone $1 \mathbf{1 a}(4 \mathrm{mmol}, 420 \mu \mathrm{~L}, 4 \mathrm{eq})$ and 2,4-dinitrobenzyl bromide 2a ( $1 \mathrm{mmol}, 260 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 45 h . Purification by flash column chromatography (gradient eluent from pure hexane to $10: 1$ hexane:AcOEt mixture) afforded the title compound ( $206.1 \mathrm{mg}, 74 \%$ yield, $91 \% \mathrm{ee}$ ) as a yellow oil.

The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 70:30 hexane: iPrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {major }}=22.1 \mathrm{~min}, \tau_{\text {minor }}=27.5 \mathrm{~min}$.
$[\alpha]^{28}=-42.6 \pm 0.7\left(c=1.0, \mathrm{CHCl}_{3}, 90 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{13} \mathrm{H}_{14} \mathrm{~N}_{2} \mathrm{O}_{5}(\mathrm{M}+2 \mathrm{Na})$ : 301.0795 , found: 301.0802.
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathbf{M H z}\right): \delta 8.79(\mathrm{~d},=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 8.36(\mathrm{dd},=2.4 \mathrm{~Hz}, J=8.6 \mathrm{~Hz}, 1 \mathrm{H}), 7.79(\mathrm{~d}, \mathrm{~J}=8.6 \mathrm{~Hz}$, $1 \mathrm{H}), 3.53(\mathrm{dd}, J=7.6 \mathrm{~Hz}, J=13.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.88(\mathrm{dd}, J=5.1 \mathrm{~Hz}, J=13.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.70-2.69(\mathrm{~m}, 1 \mathrm{H}), 2.48-$ $2.41(\mathrm{~m}, 1 \mathrm{H}), 2.37-2.27(\mathrm{~m}, 1 \mathrm{H}), 2.24-2.01(\mathrm{~m}, 2 \mathrm{H}), 1.97-1.89(\mathrm{~m}, 1 \mathrm{H}), 1.75-1.65(\mathrm{~m}, 2 \mathrm{H}), 1.60-1.51(\mathrm{~m}$, $1 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 211.2,149.3,146.4,143.0,135.0,126.6,129.2,51.7,42.3,34.9,33.1$, 28.1, 25.4.
(S)-2-(2,4-dinitrobenzyl)-4,4-dimethylcyclohexanone (3b)


Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02$ mmol, $6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene $(0.2 \mathrm{M}, 500 \mu \mathrm{~L})$, trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), 4,4dimethylcyclohexanone 1b ( $0.4 \mathrm{mmol}, 50.5 \mathrm{mg}, 4 \mathrm{eq}$ ) and 2,4-dinitrobenzyl bromide 2a ( $0.1 \mathrm{mmol}, 26 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 60 h . Purification by flash column chromatography (eluent $2: 1 \mathrm{DCM}: h e x a n e ~ m i x t u r e) ~ a f f o r d e d ~ t h e ~ t i t l e ~ c o m p o u n d ~(~ 15.0 ~ m g, ~$ $65 \%$ yield, $82 \%$ ee) as an orange solid.
The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 70:30 hexane: iPrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {major }}=16.9 \mathrm{~min}, \tau_{\text {minor }}=19.9 \mathrm{~min}$.
$[\alpha]^{28}{ }_{\mathrm{D}}=-32 \pm 2\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 82 \%\right.$ ee $)$.

HRMS: calculated for $\mathrm{C}_{15} \mathrm{H}_{20} \mathrm{~N}_{2} \mathrm{O}_{5}(\mathrm{M}+2 \mathrm{Na})$ : 329.1108 , found: 329.1110 .
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 8.79(\mathrm{~d}, J=2.8 \mathrm{~Hz}, 1 \mathrm{H}), 8.36(\mathrm{dd}, J=2.4 \mathrm{~Hz}, J=8.5 \mathrm{~Hz}, 1 \mathrm{H}), 7.81(\mathrm{~d}, J=8.5 \mathrm{~Hz}$, $1 \mathrm{H}), 3.51(\mathrm{dd}, J=7.8 \mathrm{~Hz}, J=13.1 \mathrm{~Hz}), 2.94-2.85(\mathrm{~m}, 1 \mathrm{H}), 2.77(\mathrm{dd}, J=4.8 \mathrm{~Hz}, J=13.1 \mathrm{~Hz}, 1 \mathrm{H}), 2.53-2.46$ $(\mathrm{m}, 1 \mathrm{H}), 2.32-2.25(\mathrm{~m}, 1 \mathrm{H}), 1.83-1.74(\mathrm{~m}, 2 \mathrm{H}), 1.73-1.63(\mathrm{~m}, 1 \mathrm{H}), 1.54(\mathrm{t}, J=13.0 \mathrm{~Hz} 1 \mathrm{H}), 1.22(\mathrm{~s}, 3 \mathrm{H})$, $1.01(\mathrm{~s}, 3 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 211.7,143.0,135.0,126.6,120.2,47.5,47.4,40.2,38.4,33.0$, 31.2, 31.1, 29.7, 24.2.

## (S)-2-(2,4-dinitrobenzyl)-5,5-dimethylcyclohexanone (3c)



Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02$ $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq})$, toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( 0.04 mmol , $3 \mu \mathrm{~L}, 40 \mathrm{~mol} \%)$, sodium acetate $(0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq})$, 3,3dimethylcyclohexanone 1c ( $0.4 \mathrm{mmol}, 55.5 \mu \mathrm{~L}, 4 \mathrm{eq}$ ) and 2,4-dinitrobenzyl bromide 2a ( $0.1 \mathrm{mmol}, 26 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 60 h . Purification by flash column chromatography (eluent 2:1 DCM:hexane mixture) afforded the title compound ( 17.6 mg , $57 \%$ yield, $94 \%$ ee) as a yellow oil.
The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 70:30 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {major }}=15.6 \mathrm{~min}, \tau_{\text {minor }}=20.1 \mathrm{~min}$.
$[\alpha]^{28}{ }_{\mathrm{D}}=-28 \pm 1\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 94 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{15} \mathrm{H}_{20} \mathrm{~N}_{2} \mathrm{O}_{5}(\mathrm{M}+2 \mathrm{Na}): 329.1108$, found: 329.1110 .
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 8.79(\mathrm{~d}, J=2.3 \mathrm{~Hz}, 1 \mathrm{H}), 8.36(\mathrm{dd}, J=2.3 \mathrm{~Hz}, J=8.5 \mathrm{~Hz}, 1 \mathrm{H}), 7.80(\mathrm{~d}, J=8.5 \mathrm{~Hz}$, $1 \mathrm{H}), 3.55-3.47(\mathrm{~m}, 1 \mathrm{H}), 2.88(\mathrm{dd}, J=5.1 \mathrm{~Hz}, J=13.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.72-2.61(\mathrm{~m}, 1 \mathrm{H}), 2.25(\mathrm{~d}, J=12.7 \mathrm{~Hz}$, $1 \mathrm{H}), 2.13(\mathrm{dd}, J=2.2 \mathrm{~Hz}, J=12.7 \mathrm{~Hz}, 1 \mathrm{H}), 2.10-2.03(\mathrm{~m}, 1 \mathrm{H}), 1.73-1.59(\mathrm{~m}, 3 \mathrm{H}), 1.09(\mathrm{~s}, 3 \mathrm{H}), 0.90(\mathrm{~s}$, $3 H)$. Residual peaks of benzene and water at $\delta 7.38$ and $1.29 .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 210.7,149.3$, $146.4,143.0,135.0,126.6,102.3,55.1,50.7,38.3,37.4,32.9,31.8,30.5,29.7,25.0$.

## (2S,5R)-2-(2,4-dinitrobenzyl)-5-methylcyclohexanone (3d)



Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02$ $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq})$, toluene $(0.2 \mathrm{M}, 500 \mu \mathrm{~L})$, trifluoroacetic acid ( 0.04 $\mathrm{mmol}, 3 \mu \mathrm{~L}, 40 \mathrm{~mol} \%)$, sodium acetate $(0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq})$, (R)-3methylcyclohexanone 1d ( $0.4 \mathrm{mmol}, 49 \mu \mathrm{~g}, 4 \mathrm{eq}$ ) and 2,4-dinitrobenzyl bromide 2a ( $0.1 \mathrm{mmol}, 26 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 65 h . Purification by flash column chromatography (eluent from pure hexane to $10: 1$ hexane:EtOAc mixture) afforded the title compound ( $12.8 \mathrm{mg}, 43 \%$ yield, $10: 1 \mathrm{~d} . \mathrm{r}$ ) as a yellow oil. The diastereomeric ratio was determined by ${ }^{1} \mathrm{H}$ NMR.
$[\alpha]^{28}{ }_{\mathbf{D}}=-10 \pm 1\left(\mathrm{c}=0.5, \mathrm{CHCl}_{3}\right)$
HRMS: calculated for $\mathrm{C}_{14} \mathrm{H}_{16} \mathrm{~N}_{2} \mathrm{O}_{5}$ (M-H): 291.0986, found: 291.0992.
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 8.79(\mathrm{~d}, J=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 8.36(\mathrm{dd}, J=8.6,2.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.80(\mathrm{~d}, J=8.6 \mathrm{~Hz}$, $1 \mathrm{H}), 3.51(\mathrm{dd}, J=13.6,7.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.87(\mathrm{dd}, J=13.6,5.1 \mathrm{~Hz}, 1 \mathrm{H}), 2.74-2.61(\mathrm{~m}, 1 \mathrm{H}), 2.44-2.37(\mathrm{~m}$, $1 \mathrm{H}), 2.21-2.12(\mathrm{~m}, 1 \mathrm{H}), 2.03(\mathrm{dd}, J=12.74,12.78 \mathrm{~Hz}, 1 \mathrm{H}), 1.97-1.85(\mathrm{~m}, 2 \mathrm{H}), 1.52(\mathrm{td}, J=12.5$, $11.8,2.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.47-1.39(\mathrm{~m}, 1 \mathrm{H}), 1.05(\mathrm{~d}, J=6.2 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 210.58$, $149.30,146.39,143.03,135.02,126.60,120.25,50.80,50.39,35.88,33.94,33.69,32.89,22.29$.

## (2R,5R)-2-(2,4-dinitrobenzyl)-5-methylcyclohexanone (3e)



Prepared according to the general procedure using the amino catalyst $\mathbf{E}$ (0.02 $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq})$, toluene $(0.2 \mathrm{M}, 500 \mu \mathrm{~L})$, trifluoroacetic acid ( 0.04 $\mathrm{mmol}, 3 \mu \mathrm{~L}, 40 \mathrm{~mol} \%)$, sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), (R)-3methylcyclohexanone 1d ( $0.4 \mathrm{mmol}, 49 \mu \mathrm{~g}, 4 \mathrm{eq}$ ) and 2,4-dinitrobenzyl bromide 2a ( $0.1 \mathrm{mmol}, 26 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 65 h . Purification by flash column chromatography (eluent 3:2 hexane:DCM mixture) afforded the title compound ( $16.6 \mathrm{mg}, 57 \%$ yield, 12:1 d.r) as a yellow oil. The diastereomeric ratio was determined by ${ }^{1} \mathrm{H}$ NMR.
$[\alpha]^{27}{ }_{\mathrm{D}}=+38 \pm 1\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}\right)$

HRMS: calculated for $\mathrm{C}_{14} \mathrm{H}_{16} \mathrm{~N}_{2} \mathrm{O}_{5}$ (M-H): 291.0986, found: 291.0994.
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 8.78(\mathrm{~d}, J=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 8.36(\mathrm{dd}, J=8.5,2.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.77(\mathrm{~d}, J=8.6 \mathrm{~Hz}$, 1 H ), 3.51 (dd, $J=13.6,7.8 \mathrm{~Hz}, 1 \mathrm{H}$ ), 2.91 (dd, $J=13.6,5.2 \mathrm{~Hz}, 1 \mathrm{H}), 2.80-2.68$ (m, 1H), 2.53 (dd, $J=$ $13.0,5.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.50-2.41(\mathrm{~m}, 1 \mathrm{H}), 2.24-2.16(\mathrm{~m}, 1 \mathrm{H}), 2.09-1.91(\mathrm{~m}, 3 \mathrm{H}), 1.84-1.71(\mathrm{~m}, 1 \mathrm{H})$, $1.71-1.63(\mathrm{~m}, 1 \mathrm{H}), 0.98(\mathrm{~d}, J=7.1 \mathrm{~Hz}, 3 \mathrm{H}){ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 211.16,146.41,142.83,134.84$, 126.64, 120.27, 51.27, 48.33, 33.13, 32.30, 30.60, 29.74, 18.76.

All proton signals of compounds $\mathbf{3 d}$ and $\mathbf{3 e}$ were unambiguously assigned using traditional 1 D and 2D NMR methods. Identification of alpha proton signals was performed by selective 1D-NOESY by correlation between the substituted alpha proton and the alpha' proton in the same face $\left(\mathrm{H}^{\mathrm{a}}\right)$ [when CO$\mathbf{C H}\left(\mathrm{CH}_{2} \mathrm{Ar}\right)$ is irradiated $\mathrm{CO}-\mathrm{CH}^{\mathrm{a}} \mathrm{H}^{\mathrm{b}}-\mathrm{CH}(\mathrm{Me})$ is correlated].
To determine if proton in $\mathbf{C H}(\mathrm{Me})$ is in equatorial or axial position, coupling constants of $\mathrm{CH}(\mathrm{Me})$ and $\mathrm{CO}-\mathrm{CH}^{\mathrm{a}} \mathrm{H}^{\mathrm{b}}$ were compared between 3 d and $3 \mathrm{e} . \mathrm{CO}-\mathrm{CH}^{\mathrm{a}} \mathrm{H}^{\mathrm{b}}$ appears as a double doublet with a geminal coupling and large diaxial coupling of $12.74,12.78 \mathrm{~Hz}$ in 3d, consistent with geminal and axial-axial couplings for a six-membered ring, requiring axial orientations for $\mathrm{CO}-\mathrm{CH}^{\mathrm{a}} \mathrm{H}^{\mathrm{b}}, \mathrm{CH}(\mathrm{Me})$, and $\mathrm{CO}-$ $\mathbf{C H}\left(\mathrm{CH}_{2} \mathrm{Ar}\right)$, and enabling assignment of the relative stereochemistry shown. On the other hand, compound 3e, $\mathrm{CO}-\mathrm{CH}^{\mathrm{a}} \mathrm{H}^{\mathrm{b}}$ appears as a double doublet with a geminal coupling and smaller axialequatorial coupling of $13.0,5.4 \mathrm{~Hz}$, consistent with geminal and axial-equatorial couplings for a sixmembered ring, and enabling assignment of the relative stereochemistry shown in the drawing.
(2S,4S)-2-(2,4-dinitrobenzyl)-4-methylcyclohexanone (3f)


Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02$ mmol, $6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2$ eq), 4 -methylcyclohexanone $\mathbf{1 f}(0.4 \mathrm{mmol}, 40 \mu \mathrm{~g}, 4 \mathrm{eq})$ and 2,4-dinitrobenzyl bromide 2a $(0.1 \mathrm{mmol}, 26 \mathrm{mg}, 1$ eq). Time of irradiation: 65 h . Purification by flash column chromatography (eluent 20:1 hexane:EtOAc mixture) afforded the title compound ( $28.4 \mathrm{mg}, 94 \%$ yield, 18:1 d.r, $94 \%$ ee) as a brown. The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 85:15 hexane:iPrOH, flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {major }}=31 \mathrm{~min}, \tau_{\text {minor }}=37 \mathrm{~min}$.
$[\alpha]^{28}{ }_{\mathrm{D}}=-67 \pm 1\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 94 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{14} \mathrm{H}_{16} \mathrm{~N}_{2} \mathrm{O}_{5}(\mathrm{M}+\mathrm{Na})$ : 315.0951, found: 315.0953.
The relative stereochemistry was determined by selective 1D-NOESY correlation between the substituted alpha proton and the methyl group in position 4 [when $\mathrm{CO}-\mathrm{CH}\left(\mathrm{CH}_{2} \mathrm{Ar}\right)$ is irradiated 4-Me is correlated]
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 8.79(\mathrm{~d}, J=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 8.36(\mathrm{dd}, J=8.5,2.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.77(\mathrm{~d}, J=8.5 \mathrm{~Hz}$, $1 \mathrm{H}), 3.53-3.46(\mathrm{~m}, 1 \mathrm{H}), 2.99-2.87(\mathrm{~m}, 2 \mathrm{H}), 2.53-2.44(\mathrm{~m}, 1 \mathrm{H}), 2.35(\mathrm{dt}, J=14.3,5.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.23-$ $2.15(\mathrm{~m}, 1 \mathrm{H}), 2.00-1.90(\mathrm{~m}, 2 \mathrm{H}), 1.87-1.77(\mathrm{~m}, 2 \mathrm{H}), 1.19(\mathrm{~d}, J=7.0 \mathrm{~Hz}, 3 \mathrm{H}){ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0}\right.$ $\mathrm{MHz}): \delta 211.33,149.28,146.40,143.00,135.05,126.61,120.26,50.57,42.82,41.44,35.94,33.06$, 32.12, 21.06.
(S)-7-(2,4-dinitrobenzyl)-1,4-dioxaspiro[4.5]decan-8-one (3g)


Prepared according to the general procedure using the amino catalyst A (0.02 $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), 1,4 -cyclohexanedione monoethylene acetal $1 \mathrm{~g}(0.4 \mathrm{mmol}, 62.47 \mathrm{mg}, 4 \mathrm{eq})$ and 2,4-dinitrobenzyl bromide 2a ( $0.1 \mathrm{mmol}, 26 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 68 h . Purification by flash column chromatography (eluent 10:1 hexane: AcOEt mixture) afforded the title compound (23.5 $\mathrm{mg}, 70 \%$ yield, $95 \%$ ee) as a yellow oil.

The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 75:25 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {minor }}=38 \mathrm{~min}, \tau_{\text {major }}=41 \mathrm{~min}$.
$[\alpha]^{28}{ }_{\mathbf{D}}=-58 \pm 2\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 95 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{15} \mathrm{H}_{16} \mathrm{~N}_{2} \mathrm{O}_{7}$ (M-H): 335.0885 , found: 335.0885 .
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right) \delta 8.81(\mathrm{~d}, J=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 8.37(\mathrm{dd}, J=8.5,2.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.77(\mathrm{~d}, J=8.5 \mathrm{~Hz}, 1 \mathrm{H})$, $4.20-3.92(\mathrm{~m}, 4 \mathrm{H}), 3.56(\mathrm{dd}, J=13.7,7.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.19-3.08(\mathrm{~m}, 1 \mathrm{H}), 2.84(\mathrm{dd}, J=13.7,5.2 \mathrm{~Hz}, 1 \mathrm{H})$, $2.65(\mathrm{~m}, 1 \mathrm{H}), 2.41(\mathrm{~m}, 1 \mathrm{H}), 2.15(\mathrm{~m}, 1 \mathrm{H}), 2.12-1.95(\mathrm{~m}, 2 \mathrm{H}), 1.89(\mathrm{t}, J=13.2 \mathrm{~Hz}, 1 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0}\right.$ MHz): $\delta 209.70,149.28,146.50,142.57,134.75,126.73,120.37,106.94,64.89,64.66,47.54,41.25,38$. 11, 34.76, 32.56.
(S)-tert-butyl 3-(2,4-dinitrobenzyl)-4-oxopiperidine-1-carboxylate (3h)


Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02$ $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2$ eq), 1 -boc-4-piperidone $\mathbf{1 h}$ ( $0.4 \mathrm{mmol}, 79.7 \mathrm{mg}, 4 \mathrm{eq}$ ) and 2,4-dinitrobenzyl bromide $\mathbf{2 a}(0.1 \mathrm{mmol}, 26 \mathrm{mg}, 1$ eq). Time of irradiation: 65 h . Purification by flash column chromatography (eluent 2:1 DCM:hexane mixture) afforded the title compound ( $26.0 \mathrm{mg}, 69 \%$ yield, $94 \%$ ee) as a yellow solid.

The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 90:10 hexane: iPrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}$ : $\tau_{\text {minor }}=86 \mathrm{~min}, \tau_{\text {major }}=92 \mathrm{~min}$.
$[\alpha]^{27}{ }_{\mathrm{D}}=-22 \pm 2\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 94 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{17} \mathrm{H}_{21} \mathrm{~N}_{3} \mathrm{O}_{7}$ (M-H): 378.1307, found: 378.1309.
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, \mathbf{4 0 0} \mathbf{~ M H z}\right): \delta 8.83(\mathrm{~d}, J=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 8.39(\mathrm{dd}, J=8.5,2.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.81(\mathrm{bs}, 1 \mathrm{H}), 4.68-$ $4.01(\mathrm{~m}, 1 \mathrm{H}), 3.53(\mathrm{bs}, 1 \mathrm{H}), 3.19(\mathrm{bs}, 1 \mathrm{H}), 3.06-2.72(\mathrm{~m}, 3 \mathrm{H}), 2.67-2.34(\mathrm{~m}, 2 \mathrm{H}), 1.50(\mathrm{~s}, 10 \mathrm{H}) .{ }^{13} \mathrm{C}$ $\left.\mathbf{( C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 154.24,149.24,146.66,141.72,134.80,126.91,120.50,80.97,44.05,41.35$, 30.16, 28.28.
(S)-2-(2,4-dinitrobenzyl)cyclopentanone (3i)


Prepared according to the general procedure using the amino catalyst $\mathbf{A}$ (0.02 $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclopentanone $\mathbf{1 i}(0.4$ mmol, $35 \mu \mathrm{~g}, 4 \mathrm{eq}$ ) and 2,4-dinitrobenzyl bromide 2a ( $0.1 \mathrm{mmol}, 26 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 68 h . Purification by flash column chromatography (eluent $2: 1 \mathrm{DCM}:$ hexane mixture) afforded the title compound ( $10.8 \mathrm{mg}, 44 \%$ yield, $62 \%$ ee) as an yellow oil.

The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 70:30 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {minor }}=25 \mathrm{~min}, \tau_{\text {major }}=30 \mathrm{~min}$.
$[\alpha]^{28}{ }_{\mathrm{D}}=+31 \pm 1\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 62 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{12} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}_{5}(\mathrm{M}-\mathrm{H}): ~ 263.0673$, found: 263.0673.
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathbf{M H z}\right): \delta 8.80(\mathrm{~d}, J=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 8.39(\mathrm{dd}, J=8.5,2.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.68(\mathrm{~d}, J=8.5 \mathrm{~Hz}$, $1 \mathrm{H}), 3.50(\mathrm{dd}, J=13.8,6.1 \mathrm{~Hz}, 1 \mathrm{H}), 3.02(\mathrm{dd}, J=13.8,7.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.58-2.46(\mathrm{~m}, 1 \mathrm{H}), 2.46-2.35(\mathrm{~m}$, $1 \mathrm{H}), 2.26-2.00(\mathrm{~m}, 4 \mathrm{H}), 1.91-1.74(\mathrm{~m}, 1 \mathrm{H}), 1.70-1.52(\mathrm{~m}, 1 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 218.18$, 149.31, 146.57, 142.40, 134.14, 126.84, 120.34, 49.88, 37.45, 32.58, 29.61, 20.42.
(S)-2-(2,4-dinitrobenzyl)cycloheptanone (3j)


Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02$ $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2$ eq), cycloheptanone $\mathbf{1 i}(1$ mmol, $118 \mu \mathrm{~g}, 10 \mathrm{eq}$ ) and 2,4-dinitrobenzyl bromide 2a ( $0.1 \mathrm{mmol}, 26 \mathrm{mg}, 1 \mathrm{eq}$ ).

Time of irradiation: 96 h . Purification by flash column chromatography (eluent 10:1 hexane:EtOAc mixture) afforded the title compound ( $11.1 \mathrm{mg}, 38 \%$ yield, $74 \%$ ee) as a yellow oil.

The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 80:20 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {major }}=21 \mathrm{~min}, \tau_{\text {minor }}=29 \mathrm{~min}$. $[\alpha]^{28}{ }_{\mathrm{D}}=-80 \pm 1\left(\mathrm{c}=2.0, \mathrm{CHCl}_{3}, 74 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{14} \mathrm{H}_{16} \mathrm{~N}_{2} \mathrm{O}_{5}$ (M-H): 291.0986, found: 291.0985.
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 8.79(\mathrm{~d}, J=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 8.35(\mathrm{dd}, J=8.5,2.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.66(\mathrm{~d}, J=8.5 \mathrm{~Hz}$, $1 \mathrm{H}), 3.54-3.41(\mathrm{~m}, 1 \mathrm{H}), 3.10-2.96(\mathrm{~m}, 2 \mathrm{H}), 2.50-2.43(\mathrm{~m}, 2 \mathrm{H}), 1.99-1.79(\mathrm{~m}, 5 \mathrm{H}), 1.73-1.43(\mathrm{~m}$, 3H), $1.39-1.23(\mathrm{~m}, 3 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 213.49,149.36,146.47,142.60,134.66,126.69$, 120.34, 52.42, 43.19, 34.98, 32.03, 28.72, 23.58.
(S)-5-nitro-2-((2-oxocyclohexyl)methyl)benzonitrile (3k)


Prepared according to the general procedure using the amino catalyst $\mathbf{A}$ (0.02 mmol, $6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclohexanone $\mathbf{1 a}(0.4$ mmol, $42 \mu \mathrm{~L}, 4 \mathrm{eq}$ ) and 2-cyano-4-nitrobenzyl bromide $\mathbf{2 b}(0.1 \mathrm{mmol}, 24.1 \mathrm{mg}, 1$ eq). Time of irradiation: 65 h . Purification by flash column chromatography (gradient eluent from pure hexane to $10: 1$ hexane:AcOEt mixture) afforded the title compound ( $11.6 \mathrm{mg}, 45 \%$ yield, $86 \% \mathrm{ee}$ ) as a yellow solid.

The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IB column, 70:30 hexane: iPrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {minor }}=44.6 \mathrm{~min}, \tau_{\text {major }}=32.9 \mathrm{~min}$.
$[\alpha]^{26}{ }_{\mathbf{D}}=-19 \pm 1\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 86 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{14} \mathrm{H}_{14} \mathrm{~N}_{2} \mathrm{O}_{3}(\mathrm{M}+\mathrm{Na}): 281.0885$, found: 281.0897 .
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathbf{M H z}\right): \delta 8.49(\mathrm{~d}, J=2.4 \mathrm{~Hz}, 1 \mathrm{H}), 8.35(\mathrm{dd}, J=8.6,2.4 \mathrm{~Hz}, 1 \mathrm{H}), 7.68(\mathrm{~d}, J=8.6 \mathrm{~Hz}$, $1 \mathrm{H}), 3.47(\mathrm{dd}, J=13.8,7.2 \mathrm{~Hz}, 1 \mathrm{H}), 2.86(\mathrm{dd}, J=13.8,6.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.82-2.73(\mathrm{~m}, 1 \mathrm{H}), 2.53-2.43(\mathrm{~m}$, $1 \mathrm{H}), 2.42-2.28(\mathrm{~m}, 1 \mathrm{H}), 2.20-2.10(\mathrm{~m}, 2 \mathrm{H}), 1.98-1.87(\mathrm{~m}, 1 \mathrm{H}), 1.82-1.64(\mathrm{~m}, 2 \mathrm{H}), 1.64-1.50(\mathrm{~m}$, $2 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 210.57,152.01,146.21,132.25,127.74,127.09,116.08,114.21,51.60$, 42.16, 34.67, 34.40, 27.90, 25.22.

General procedure for the photochemical $\alpha$-asymmetric phenacylation of ketones:
A 10 mL Schlenk tube was charged with the aminocatalyst A ( $20 \mathrm{~mol} \%$ ), toluene ( 0.2 M referring to the alkyl bromide 2), trifluoroacetic acid, TFA, ( $40 \mathrm{~mol} \%$ ), cyclohexanone 1a ( 4 eq ), sodium acetate ( 2 eq ) and the alkylating agent 2 ( 1 eq). The reaction mixture was degassed via freeze pump thaw (x 3cycles), and the vessel refilled with nitrogen. After the reaction mixture was thoroughly degassed, the flask was sealed and positioned approximately 10 cm away from the light source. The mixture was irradiated with a 300 W Xe lamp (Asashi Spectra Co., Ltd.) for 14 h under magnetic stirring. The temperature of the reaction mixture was maintained at room temperature by a water bath during the reaction. After stirring for the indicated time, the crude mixture was purified by flash column chromatography to afford the title compound $\mathbf{4}$ in the stated yield and optical purity.

## (S)-2-(2-oxo-2-phenylethyl)cyclohexanone (4a)



Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02 \mathrm{mmol}$, $6.5 \mathrm{mg}, 0.2 \mathrm{eq})$, toluene $(0.2 \mathrm{M}, 500 \mu \mathrm{~L})$, trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3 \mu \mathrm{~L}, 40$ $\mathrm{mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclohexanone $1 \mathrm{a}(0.4 \mathrm{mmol}, 42$ $\mu \mathrm{L}, 4 \mathrm{eq}$ ) and 2-bromoacetophenone ( $0.1 \mathrm{mmol}, 20 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 14 h. Purification by flash column chromatography (gradient eluent from pure hexane to 10:1 hexane:AcOEt mixture) afforded the title compound ( $15.0 \mathrm{mg}, 69 \%$ yield, $90 \%$ ee) as a yellow oil.

The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 85:15 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}$ : $\tau_{\text {major }}=20 \mathrm{~min}$, $\tau_{\text {minor }}=33 \mathrm{~min}$. $[\alpha]^{28}{ }_{\mathrm{D}}=-50 \pm 2\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 90 \%\right.$ ee $)$.
Literature value for $(R)$-2-(2-oxo-2-phenylethyl)cyclohexanone $[\alpha]_{\mathbf{D}}=+57.8\left(\mathrm{c}=1, \mathrm{CHCl}_{3}\right.$, for $84 \%$ ee $)$. The ( $S$ )-absolute configuration for compound $\mathbf{4 a}$ was inferred by comparison of the optical rotation with the value reported in the literature. (4)

HRMS: calculated for $\mathrm{C}_{14} \mathrm{H}_{16} \mathrm{O}_{2}(\mathrm{M}+\mathrm{Na}):$ 239.1043, found: 239.1047.
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 8.07-7.93(\mathrm{~m}, 1 \mathrm{H}), 7.66-7.53(\mathrm{~m}, 1 \mathrm{H}), 7.53-7.42(\mathrm{~m}, 1 \mathrm{H}), 3.63(\mathrm{dd}, J=$ $17.7,6.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.28-3.12(\mathrm{~m}, 1 \mathrm{H}), 2.71(\mathrm{dd}, J=17.7,5.7 \mathrm{~Hz}, 1 \mathrm{H}), 2.54-2.41(\mathrm{~m}, 1 \mathrm{H}), 2.31-2.09$ $(\mathrm{m}, 1 \mathrm{H}), 1.98-1.62(\mathrm{~m}, 2 \mathrm{H}), 1.48(\mathrm{qd}, J=12.8,3.9 \mathrm{~Hz}, 1 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 2 5} \mathbf{~ M H z}\right): \delta 211.53,198.65$, $137.09,133.00,128.52,128.08,46.46,41.98,38.35,34.33,27.99,25.38$.

## (S)-2-(2-([1,1'-biphenyl]-4-yl)-2-oxoethyl)cyclohexanone (4b)



Prepared according to the general procedure using the amino catalyst $\mathbf{A}$ (0.02 $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq})$, toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclohexanone 1 a ( 0.4 $\mathrm{mmol}, 42 \mu \mathrm{~L}, 4 \mathrm{eq})$ and 2-bromo-4'-phenylacetophenone $(0.1 \mathrm{mmol}, 27.5 \mathrm{mg}, 1$ eq). Time of irradiation: 14 h . Purification by flash column chromatography (gradient eluent from pure hexane to $10: 1$ hexane:AcOEt mixture) afforded the title compound ( $17.3 \mathrm{mg}, 60 \%$ yield, $86 \% \mathrm{ee}$ ) as a white solid.
The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 85:15 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {minor }}=20 \mathrm{~min}, \tau_{\text {major }}=29 \mathrm{~min}$.
$[\alpha]^{27}{ }_{\mathrm{D}}=-44 \pm 2\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 86 \%\right.$ ee $)$. HRMS: calculated for $\mathrm{C}_{20} \mathrm{H}_{20} \mathrm{O}_{2}(\mathrm{M}+\mathrm{Na}): 315.1356$, found: 315.1356.
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathbf{M H z}\right): \delta{ }^{1} \mathrm{H}$ NMR $8.12-8.06(\mathrm{~m}, 2 \mathrm{H}), 7.73-7.69(\mathrm{~m}, 2 \mathrm{H}), 7.68-7.62(\mathrm{~m}, 2 \mathrm{H}), 7.55-$ $7.46(\mathrm{~m}, 2 \mathrm{H}), 7.46-7.40(\mathrm{~m}, 1 \mathrm{H}), 3.66(\mathrm{dd}, J=17.6,6.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.34-3.10(\mathrm{~m}, 1 \mathrm{H}), 2.74(\mathrm{dd}, J=$ $17.6,5.7 \mathrm{~Hz}, 1 \mathrm{H}), 2.56-2.42(\mathrm{~m}, 2 \mathrm{H}), 2.31-2.12(\mathrm{~m}, 2 \mathrm{H}), 2.00-1.90(\mathrm{~m}, 1 \mathrm{H}), 1.90-1.75(\mathrm{~m}, 1 \mathrm{H})$, $1.75-1.64(\mathrm{~m}, 1 \mathrm{H}), 1.50(\mathrm{qd}, J=12.8,3.9 \mathrm{~Hz}, 1 \mathrm{H}) .{ }^{13} \mathbf{C}_{\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 211.57,198.26,145.70,}$ 139.97, 135.80, 128.93, 128.68, 128.17, 127.28, 127.20, 46.56, 42.00, 38.38, 34.37, 28.01, 25.40.
(S)-2-(2-oxo-2-(p-tolyl)ethyl)cyclohexanone (4c)


Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02$ $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%)$, sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclohexanone 1 a ( 0.4 $\mathrm{mmol}, 42 \mu \mathrm{~L}, 4 \mathrm{eq})$ and 2-bromo-4'-methylacetophenone ( $0.1 \mathrm{mmol}, 21.3 \mathrm{mg}, 1$ eq). Time of irradiation: 14 h . Purification by flash column chromatography (gradient eluent from pure hexane to $10: 1$ hexane:AcOEt mixture) afforded the title compound ( $15.5 \mathrm{mg}, 66 \%$ yield, $92 \%$ ee) as a white solid.
The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 85:15 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}$ : $\tau_{\text {major }}=26 \mathrm{~min}, \tau_{\text {minor }}=38 \mathrm{~min}$.
$[\alpha]^{28}{ }_{\mathrm{D}}=-68 \pm 2\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 92 \%\right.$ ee $)$.
Characterization data in agreement with the literature (5).
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 7.91(\mathrm{~d}, J=8.2 \mathrm{~Hz}, 2 \mathrm{H}), 7.30-7.24(\mathrm{~d}, J=8.2 \mathrm{~Hz}, 2 \mathrm{H}), 3.60(\mathrm{dd}, J=17.6,6.4$ $\mathrm{Hz}, 1 \mathrm{H}), 3.18(\mathrm{dq}, J=12.2,6.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.69(\mathrm{dd}, J=17.6,6.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.50-2.44(\mathrm{~m}, 2 \mathrm{H}), 2.43(\mathrm{~s}$, $3 \mathrm{H}), 2.28-2.11(\mathrm{~m}, 2 \mathrm{H}), 1.95-1.87(\mathrm{~m}, 1 \mathrm{H}), 1.87-1.64(\mathrm{~m}, 2 \mathrm{H}), 1.46(\mathrm{qd}, J=12.7,3.9 \mathrm{~Hz}, 1 \mathrm{H}) .{ }^{13} \mathrm{C}$ ( $\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}$ ): $\delta 211.62,198.28,143.76,134.61,129.20,128.20,46.47,42.00,38.19,34.36,28.00$, 25.39, 21.63.

## (S)-2-(2-(4-bromophenyl)-2-oxoethyl)cyclohexanone (4d)



Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02$ $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq})$, toluene $(0.2 \mathrm{M}, 500 \mu \mathrm{~L})$, trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclohexanone $1 \mathbf{1 a}$ ( 0.4 mmol, $42 \mu \mathrm{~L}, 4 \mathrm{eq})$ and 2,2'-dibromoacetophenone ( $0.1 \mathrm{mmol}, 27.7 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 14 h . Purification by flash column chromatography (gradient eluent from pure hexane to $10: 1$ hexane:AcOEt mixture) afforded the title compound ( $15.4 \mathrm{mg}, 52 \%$ yield, $86 \%$ ee) as a yellow solid.
The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 95:5 hexane: iPrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {minor }}=36 \mathrm{~min}, \tau_{\text {major }}=41 \mathrm{~min}$.
$[\alpha]^{27}{ }_{\mathrm{D}}=-40 \pm 1\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 86 \%\right.$ ee $)$.
Characterization data in agreement with the literature (5).
${ }^{1} \mathrm{H}\left(\mathrm{CDCl}_{3}, 500 \mathrm{MHz}\right): \delta 7.87(\mathrm{~d}, J=8.7 \mathrm{~Hz}, 2 \mathrm{H}), 7.63(\mathrm{~d}, J=8.8 \mathrm{~Hz}, 2 \mathrm{H}), 3.58(\mathrm{dd}, J=17.6,6.9 \mathrm{~Hz}$, $1 \mathrm{H}), 3.26-3.11(\mathrm{~m}, 1 \mathrm{H}), 2.64(\mathrm{dd}, J=17.6,5.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.52-2.41(\mathrm{~m}, 2 \mathrm{H}), 2.33-2.11(\mathrm{~m}, 2 \mathrm{H}), 1.97$ $-1.89(\mathrm{~m}, 1 \mathrm{H}), 1.87-1.75(\mathrm{~m}, 1 \mathrm{H}), 1.75-1.65(\mathrm{~m}, 1 \mathrm{H}), 1.48(\mathrm{qd}, J=12.8,3.9 \mathrm{~Hz}, 1 \mathrm{H}) .{ }^{13} \mathrm{C}\left(\mathrm{CDCl}_{3}, 125\right.$ $\mathrm{MHz}): \delta 211.38,197.63,135.81,131.83,129.63,128.13,46.52,41.94,38.32,34.30,27.97,25.37$.

## (S)-2-(2-(4-chlorophenyl)-2-oxoethyl)cyclohexanone (4e)



Prepared according to the general procedure using the amino catalyst $\mathbf{A}$ (0.02 $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq})$, toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%)$, sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclohexanone $\mathbf{1 a}$ ( 0.4 $\mathrm{mmol}, 42 \mu \mathrm{~L}, 4 \mathrm{eq}$ ) and 2-bromo-4'-chloroacetophenone ( $0.1 \mathrm{mmol}, 23.3 \mathrm{mg}, 1$ eq). Time of irradiation: 14 h . Purification by flash column chromatography (gradient eluent from pure hexane to 10:1 hexane:AcOEt mixture) afforded the title compound ( $10 \mathrm{mg}, 40 \%$ yield, $87 \%$ ee) as a yellow solid.
The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IB column, 95:5 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}$ : $\tau_{\text {major }}=9 \mathrm{~min}, \tau_{\text {minor }}=10 \mathrm{~min}$.
$[\alpha]^{27}{ }_{\mathrm{D}}=-55 \pm 2\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 87 \% \mathrm{ee}\right)$.
Characterization data in agreement with the literature (6).
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 7.95(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 2 \mathrm{H}), 7.45(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 2 \mathrm{H}), 3.58(\mathrm{dd}, J=17.6,6.9 \mathrm{~Hz}$, 1 H ), $3.30-3.08(\mathrm{~m}, 1 \mathrm{H}), 2.64(\mathrm{dd}, J=17.6,5.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.52-2.40(\mathrm{~m}, 2 \mathrm{H}), 2.31-2.10(\mathrm{~m}, 2 \mathrm{H}), 1.98$
$-1.88(\mathrm{~m}, 1 \mathrm{H}), 1.88-1.75(\mathrm{~m}, 1 \mathrm{H}), 1.75-1.64(\mathrm{~m}, 1 \mathrm{H}), 1.48(\mathrm{qd}, J=12.8,3.8 \mathrm{~Hz}, 1 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}\right.$, $\mathbf{1 0 0} \mathbf{~ M H z}$ ): $\delta 211.41,197.44,139.42,135.40,129.51,128.83,46.52,41.94,38.34,34.31,27.97,25.37$.
(S)-4-(2-(2-oxocyclohexyl)acetyl)benzonitrile (4f)


Prepared according to the general procedure using the amino catalyst $\mathbf{A}$ (0.02 $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq})$, toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%)$, sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclohexanone 1 a ( 0.4
$\mathrm{mmol}, 42 \mu \mathrm{~L}, 4 \mathrm{eq}$ ) and 2-bromo-4'-cianoacetophenone ( $0.1 \mathrm{mmol}, 22.4 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 14 h . Purification by flash column chromatography (gradient eluent from pure hexane to 10:1 hexane:AcOEt mixture) afforded the title compound ( $10.2 \mathrm{mg}, 42 \%$ yield, $88 \%$ ee) as a yellow solid.
The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 70:30 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}$ : $\tau_{\text {major }}=34 \mathrm{~min}, \tau_{\text {minor }}=38 \mathrm{~min}$.
$[\alpha]^{28}{ }_{\mathrm{D}}=-72 \pm 2\left(\mathrm{c}=1.0, \mathrm{CHCl}_{3}, 88 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{15} \mathrm{H}_{15} \mathrm{NO}_{2}(\mathrm{M}+\mathrm{Na})$ : 264.0995, found: 264.0996 .
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 8.09(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 2 \mathrm{H}), 7.79(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 2 \mathrm{H}), 3.59(\mathrm{dd}, J=17.6,7.5 \mathrm{~Hz}$, $1 \mathrm{H}), 3.32-3.11(\mathrm{~m}, 1 \mathrm{H}), 2.64(\mathrm{dd}, J=17.6,5.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.55-2.38(\mathrm{~m}, 2 \mathrm{H}), 2.32-2.13(\mathrm{~m}, 2 \mathrm{H}), 2.06$ $-1.87(\mathrm{~m}, 1 \mathrm{H}), 1.88-1.76(\mathrm{~m}, 1 \mathrm{H}), 1.76-1.64(\mathrm{~m}, 1 \mathrm{H}), 1.51(\mathrm{qd}, J=12.9,3.8 \mathrm{~Hz}, 1 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}\right.$, 100 MHz ): $\delta 211.20,197.44,140.50,140.13,132.44,128.50,117.99,116.23,46.71,41.85,38.72,34.21$, 27.90, 25.33.

## (S)-2-(2-oxo-2-(2-(trifluoromethyl)phenyl)ethyl)cyclohexanone (4g)



Prepared according to the general procedure using the amino catalyst $\mathbf{A}(0.02 \mathrm{mmol}$, $6.5 \mathrm{mg}, 0.2 \mathrm{eq})$, toluene $(0.2 \mathrm{M}, 500 \mu \mathrm{~L})$, trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3 \mu \mathrm{~L}, 40$ $\mathrm{mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclohexanone $1 \mathrm{a}(0.4 \mathrm{mmol}, 42$ $\mu \mathrm{L}, 4 \mathrm{eq})$ and 2-bromo-2'-trifluoromethylacetophenone ( $0.1 \mathrm{mmol}, 26.7 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 14 h . Purification by flash column chromatography (gradient eluent from pure hexane to $10: 1$ hexane:AcOEt mixture) afforded the title compound ( $13.9 \mathrm{mg}, 50 \%$ yield, $76 \%$ ee) as a yellow oil.
The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 95:5 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {major }}=16 \mathrm{~min}, \tau_{\text {minor }}=20 \mathrm{~min}$.
$[\alpha]^{28}{ }_{\mathrm{D}}=-14 \pm 1\left(\mathrm{c}=0.5, \mathrm{CHCl}_{3}, 76 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{15} \mathrm{H}_{15} \mathrm{~F}_{3} \mathrm{O}_{2}(\mathrm{M}+\mathrm{Na})$ : 307.0916 , found: 307.0928 .
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta \delta 7.78-7.69(\mathrm{~m}, 2 \mathrm{H}), 7.68-7.62(\mathrm{~m}, 1 \mathrm{H}), 7.61-7.53(\mathrm{~m}, 1 \mathrm{H}), 3.42(\mathrm{dd}, J=$ $18.2,7.5 \mathrm{~Hz}, 1 \mathrm{H}), 3.26-3.16(\mathrm{~m}, 1 \mathrm{H}), 2.59(\mathrm{dd}, J=18.2,5.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.50-2.43(\mathrm{~m}, 2 \mathrm{H}), 2.29-2.22$ $(\mathrm{m}, 1 \mathrm{H}), 2.22-2.14(\mathrm{~m}, 1 \mathrm{H}), 1.98-1.91(\mathrm{~m}, 1 \mathrm{H}), 1.87-1.76(\mathrm{~m}, 1 \mathrm{H}), 1.75-1.63(\mathrm{~m}, 1 \mathrm{H}), 1.55-1.40$ $(\mathrm{m}, 1 \mathrm{H}) .{ }^{13} \mathrm{C}\left(\mathrm{CDCl}_{3}, 100 \mathrm{MHz}\right): \delta 211.29,202.80,131.84,129.87,127.65,126.4\left(\mathrm{~m}, 1 \mathrm{C}, \mathrm{CF}_{3}\right), 46.50$, 43.07, 43.06, 41.87, 33.88, 27.91, 25.32.

## (S)-2-(2-(naphthalen-2-yl)-2-oxoethyl)cyclohexanone (4h)



Prepared according to the general procedure using the amino catalyst $\mathbf{A}$ (0.02 $\mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene ( $0.2 \mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3$ $\mu \mathrm{L}, 40 \mathrm{~mol} \%)$, sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), cyclohexanone $\mathbf{1 a}(0.4$ mmol, $42 \mu \mathrm{~L}, 4 \mathrm{eq}$ ) and 2-bromoacetonaphtone ( $0.1 \mathrm{mmol}, 24.9 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 14 h . Purification by flash column chromatography (gradient eluent from pure hexane to 10:1 hexane:AcOEt mixture) afforded the title compound ( $19.4 \mathrm{mg}, 73 \%$ yield, $92 \%$ ee) as a white solid. The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak IC column, 85:15 hexane: PrOH , flow rate $1.00 \mathrm{~mL} / \mathrm{min}, \lambda=254 \mathrm{~nm}: \tau_{\text {minor }}=26 \mathrm{~min}, \tau_{\text {major }}=29 \mathrm{~min}$.
$[\alpha]^{28}{ }_{\mathrm{D}}=-19 \pm 1\left(\mathrm{c}=0.5, \mathrm{CHCl}_{3}, 92 \%\right.$ ee $)$.
HRMS: calculated for $\mathrm{C}_{18} \mathrm{H}_{18} \mathrm{O}_{2}(\mathrm{M}+\mathrm{Na})$ : 289.1199, found: 289.1199 .
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathbf{~ M H z}\right): \delta 8.55(\mathrm{~s}, 1 \mathrm{H}), 8.07(\mathrm{dd}, \boldsymbol{J}=8.6,1.8 \mathrm{~Hz}, 1 \mathrm{H}), 8.01-7.97(\mathrm{~m}, 1 \mathrm{H}), 7.94-7.87$ (m, 2H), $7.68-7.54(\mathrm{~m}, 2 \mathrm{H}), 3.78(\mathrm{dd}, J=17.5,6.5 \mathrm{~Hz}, 1 \mathrm{H}), 3.26(\mathrm{dq}, J=11.8,5.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.85(\mathrm{dd}, J$ $=17.6,5.9 \mathrm{~Hz}, 1 \mathrm{H}), 2.54-2.44(\mathrm{~m}, 2 \mathrm{H}), 2.35-2.23(\mathrm{~m}, 1 \mathrm{H}), 2.18(\mathrm{~m}, 1 \mathrm{H}), 2.00-1.90(\mathrm{~m}, 1 \mathrm{H}), 1.90-$ $1.65(\mathrm{~m}, 2 \mathrm{H}), 1.65-1.45(\mathrm{~m}, 1 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 211.66,198.60,135.60,134.42,132.54$, 129.77, 129.58, 128.37, 128.36, 127.75, 126.71, 123.89, 46.60, 42.03, 38.40, 34.41, 28.03, 25.41.
(S)-2-(2-oxo-2-phenylethyl)cyclohexanone (6)


Prepared according to the general procedure using 1 equivalent of the ketone, the amino catalyst A ( $0.02 \mathrm{mmol}, 6.5 \mathrm{mg}, 0.2 \mathrm{eq}$ ), toluene ( 0.2 $\mathrm{M}, 500 \mu \mathrm{~L}$ ), trifluoroacetic acid ( $0.04 \mathrm{mmol}, 3 \mu \mathrm{~L}, 40 \mathrm{~mol} \%$ ), sodium acetate ( $0.2 \mathrm{mmol}, 16.4 \mathrm{mg}, 2 \mathrm{eq}$ ), $5 \alpha$-cholestan- 3 -one $5(0.1 \mathrm{mmol}$, $38.7 \mathrm{mg}, 1 \mathrm{eq})$ and 2-bromoacetophenone ( $0.1 \mathrm{mmol}, 20 \mathrm{mg}, 1 \mathrm{eq}$ ). Time of irradiation: 14 h . Purification by flash column chromatography (gradient eluent from pure hexane to 20:1 hexane:AcOEt mixture) afforded the title compound ( $23 \mathrm{mg}, 47 \%$ yield, $>20: 1 \mathrm{r} . \mathrm{r},>20: 1 \mathrm{~d}$. r) as a white solid.
HRMS: calculated for $\mathrm{C}_{35} \mathrm{H}_{52} \mathrm{O}_{2}(\mathrm{M}+\mathrm{Na})$ : 527.3881 , found: 527.3860 .
The assignment of the relative stereochemistry shown in the drawing was performed by selective 1DNOESY by correlation between the substituted alpha proton and the methyl group in position 4 [when $\mathrm{CO}-\mathrm{CH}\left(\mathrm{CH}_{2} \mathrm{Ar}\right)$ is irradiated $\mathrm{CO}-\mathrm{CH}\left(\mathrm{CH}_{2} \mathrm{Ar}\right)-\mathrm{CH}_{2}-\mathrm{C}(\mathrm{Me})$ is correlated].
${ }^{1} \mathbf{H}\left(\mathbf{C D C l}_{3}, 400 \mathrm{MHz}\right): \delta 8.00(\mathrm{dd}, J=8.4,1.4 \mathrm{~Hz}, 2 \mathrm{H}), 7.68-7.53(\mathrm{~m}, 1 \mathrm{H}), 7.53-7.43(\mathrm{~m}, 2 \mathrm{H}), 3.61$ (dd, $J=17.7,6.3 \mathrm{~Hz}, 1 \mathrm{H}), 3.33-3.21(\mathrm{~m}, 1 \mathrm{H}), 2.70(\mathrm{dd}, J=17.7,5.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.54-2.40(\mathrm{~m}, 1 \mathrm{H}), 2.21$ $-2.11(\mathrm{~m}, 2 \mathrm{H}), 2.04-1.94(\mathrm{~m}, 1 \mathrm{H}), 1.84(\mathrm{ddd}, J=9.6,5.7,3.7 \mathrm{~Hz}, 1 \mathrm{H}), 1.78-1.67(\mathrm{~m}, 1 \mathrm{H}), 1.64-0.96$ $(\mathrm{m}, 28 \mathrm{H}), 0.96-0.82(\mathrm{~m}, 10 \mathrm{H}), 0.82-0.71(\mathrm{~m}, 1 \mathrm{H}), 0.70(\mathrm{~s}, 3 \mathrm{H}) .{ }^{13} \mathbf{C}\left(\mathbf{C D C l}_{3}, \mathbf{1 0 0} \mathbf{~ M H z}\right): \delta 211.33$, 198.63, 137.12, 132.96, 128.51, 128.06, 56.28, 56.26, 53.93, 48.12, 46.39, 44.66, 42.62, 42.54, 39.89, $39.51,38.43,36.67,36.15,35.77,35.24,31.77,29.71,28.81,28.23,28.01,24.22,23.82,22.82,22.56$, 21.59, 18.67, 12.42, 12.09.

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## D. NMR spectra




$\begin{array}{lllllllllllllllllllllllllll}210 & 200 & 190 & 180 & 170 & 160 & 150 & 140 & 130 & 120 & 110 & 100 & 90 & 80 & 70 & 60 & 50 & 40 & 30 & 20 & p p m\end{array}$


3b





















3j





4b










$\left|\left.\right|_{\mid} ^{+\pi}\right|^{n}$







$4 g$




4h




|||| ||






## E. HPLC Traces














DAD1 A, Sig=254,4 Ref=off (ANA_BLAB-368-K8.D)





UAD1 A, Sig=254,4 Ket=oft (ANA_BLAB-3/4-KY-KAC-y0-10.D)





DAD1 A, Sig=254,4 Ref=off (ANA_BVAB-506.D)

Totals :
2574.4105286 .14729

DAD1 A, Sig=254,4 Ret=oft (ANA_BVAB-bUb-KAC-8U-20.D)





DAD1 A, Sig=254,4 Ref=off (ANA_BICN-NO2-RAC-EAR-921-B.D)





DAD1 A, Sig=254,4 Ref=off (ANA_BVAB-516-RAC.D)



DAD1 A, Sig=254,4 Ref=off (ANA_BVAB-539.D)


| Peak \# | RetTime [min] | Type | Width <br> [min] | $\begin{gathered} \text { Area } \\ {\left[\mathrm{mAU}^{\star} \mathrm{s}\right]} \end{gathered}$ | $\begin{aligned} & \text { Height } \\ & \text { [mAU] } \end{aligned}$ | Area 응 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | 34.327 | MM | 0.7886 | 97.19407 | 2.05426 | 6.7841 |
| 2 | 38.629 | MM | 0.8852 | 1335.48450 | 25.14422 | 93.2159 |
| Totals | S : |  |  | 1432.67857 | 27.19848 |  |

1432.6785727 .19848






DAD1 A, Sig=254,4 Ref=off (ANA_BlAB-553-RAC-85-15.D)





DAD1 A, Sig=254,4 Ref=off (ANA_BIEAR-RAC-P-BR-AP-95-5.D)








DAD1 A, Sig=254,4 Ref=off (ANA_BVAB-569-2.D)



DAD1 A, Sig=254,4 Ref=off (ANA_BVAB-572-RAC-CN.D)



DAD1 A, Sig=254,4 Ref=off (ANA_BVAB-568.D)



DAD1 A, Sig=254,4 Ref=off (ANA_BVAB-588-RAC-95_5.D)



