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Enantioselective desymmetrization of prochiral ketones via an organocatalytic deprotonation process

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ABSTRACT

The first desymmetrization of 4-substituted cyclohexanones by organocatalytic asymmetric deprotonation at low catalyst loading is reported. The combination of *N,O-bis*(trimethylsilyl)acetamide (BSA) and chiral quaternary ammonium aryloxide salts has been used as an efficient organocatalytic system to provide silyl enolates in high yields and with modest ee.

1. Introduction

Due to their importance in the pharmaceutical and agrochemical fields, impressive efforts have been directed towards the development of efficient routes to gain access to enantiopure compounds. These strategies can be grouped into two mains categories: asymmetric synthesis or kinetic resolution (or kinetic dynamic resolution), the desymmetrization pathway belongs to the first class of transformations. Historically speaking, desymmetrization reactions mediated by enzymes are preferred over chemical catalysts because of their high levels of chemo-, regio- and stereoselectivities.[1] Nevertheless, asymmetric catalysis by means of metallo- or organocatalysts has benefited from huge contributions from the chemistry community allowing asymmetric desymmetrizations to be achieved with high levels of enantioinduction.[2] Among all of the substrates assessed in desymmetrization processes, much attention has been devoted to prochiral ketones as underlined by the large number of reactions in which they are involved, namely enamine catalysis,[3–8] Baeyer–Villiger oxidations,[9] olefination reactions,[10] ring expansions,[11] enantioselective desymmetrization–fragmentation reactions[12] or enantioselective deprotonations providing transiently chiral enolates.[13–18] This last class of transformation mainly involves the use of stoichiometric amounts of chiral lithium[13,14] or magnesium amides[15] to obtain the corresponding enantioenriched silyl enol ether (upon silylation of the transient enolate by Me_3SiCl) or β-hydroxyketones[16] (by trapping the enolate with aldehydes). To the best of our knowledge, only one example of a catalytic process has been reported to date by Koga et al.[17] for the desymmetrization of prochiral 4-substituted cyclohexanones via the formation of silyl enol ethers. The authors made use of a catalytic amount of a chiral bidentate amine (30 mol %) in the presence of an achiral tridentate lithium amide (2.4 equiv), HMPA (2.4 equiv) and DABCO (1.5 equiv) in THF at −78 °C. By implementing these rather complex conditions, the corresponding silyl enol ether was obtained with up to 76% ee after quenching with TMSCl (external quench). More recently, Simpkins et al.[18] reported a study implementing competition reactions between chiral and achiral lithium amides during the deprotonation of prochiral ketones and imides with the aim of developing new catalytic processes. Although the results of this study demonstrated that the presence of an achiral base, such as LDA, does not erode the level of stereoinduction induced by the

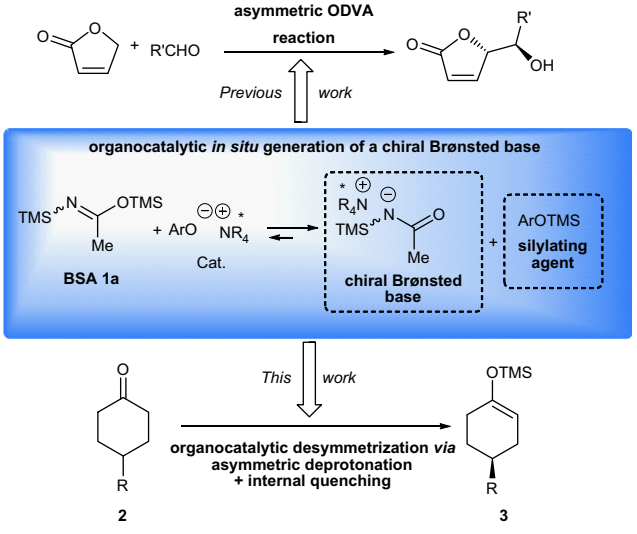

Figure 1. Organocatalytic in situ generation of chiral quaternary ammonium amide salts.

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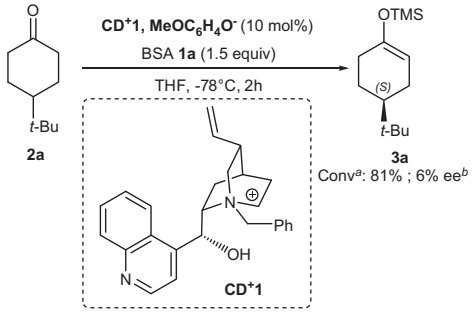


Scheme 1. Preliminary result. [a]Determined by GC-FID analysis of the crude mixture. [b]Measured by GC-FID analysis using a chiral column (see Section 4).

chiral amide, no catalytic version has been reported so far. Recently, we reported the catalytic in situ generation of chiral quaternary ammonium amide salts from *N,O-bis*(trimethylsilyl)acetamide (BSA) **1a** and quaternary ammonium aryloxides (Fig. 1, middle part). This system was successfully applied to an *anti*-selective organocatalytic direct vinylogous aldol (ODVA) reaction of (*5H*)-furan-2-one derivatives with both aliphatic or (hetero)aromatic aldehydes to afford several 5-(1′-hydroxy)-γ-butenolides in good diastereomeric ratios (up to 95/5) and with excellent enantioselectivities (up to 94%) (Fig. 1, upper part).[19]

We postulated that this catalytic system could be extrapolated to the desymmetrization of prochiral cycloalkanones **2** (Fig. 1, bottom part). After deprotonation of the ketone by the chiral quaternary ammonium amide salt, the resulting enolate could be silylated by ArOTMS generated during the catalytic cycle, thus avoiding the use of an external silylating agent.

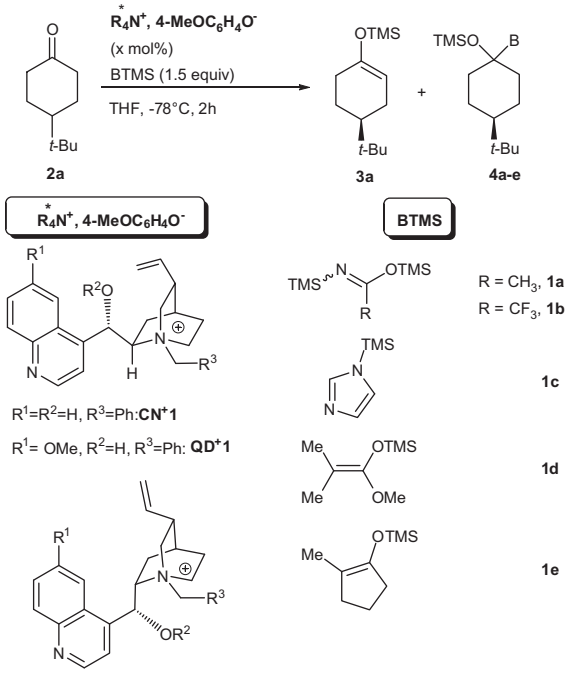
2. Results and discussion

With this basic idea in mind, several quaternary ammonium aryloxide salts derived from *Cinchona* alkaloids were synthesized according to known procedures[19,20] and, among them, the readily accessible **CD$^+$1**, **ArO**$^-$ was evaluated in the desymmetrization of 4-*tert*-butylcyclohexanone, used as a model substrate in the presence of BSA (Scheme 1).

By performing the reaction in THF at −78 °C for 2 h, we observed the formation of the corresponding silyl enol ether **3a** of 4-*tert*-butylcyclohexanone with good conversion, as a slightly enantioenriched mixture.[21] This result prompted us to perform a survey of other catalysts and silylated bases using THF at −78 °C as the optimized solvent and temperature. The results are reported in Table 1.

First, all of the *N*-benzyl ammonium backbones derived from *Cinchona* alkaloids (i.e. quininium QN$^+$, quinidinium QD$^+$, cinchoninium CN$^+$ and cinchonidinium CD$^+$) were evaluated (Table 1, entries 1–4) revealing that catalysts in the quininium series provided a higher enantioselection (34% ee, Table 1, entry 4).[22] We thus paid attention to the catalyst charge and found that no erosion of the enantiomeric excess occurred with a catalyst loading as low as 2 mol %, thus indicating the efficiency of the catalytic process (Table 1, entries 4–6). Next, we decided to explore the influence of modification of the quininium pattern on the enantioselectivity of the reaction (Table 1, entries 7–11). All of the modifications made resulted in a decrease in the enantiomeric excesses. Moreover, it is noteworthy that substitution of the nitrogen by an anthracenyl group led to an inversion of the enantioselectivity (Table 1, entry 11). We then studied other N- or O-silylated bases (Table 1, entries 12–15).[23] All other N-silylated bases **1b–c** (Table 1, entries 12 and 13) gave lower conversions than BSA **1a** (Table 1, entry 4). Lastly, attempts to use O-silylated

Table 1
Screening of catalysts ($\mathbf{R_4^*N^+}$, **4-MeOC$_6$H$_4$O$^-$**) and silylated bases (BTMS)



Entry	BTMS	$R_4^*N^+$	*x* (mol %)	Conversion[a] (%)	**3a**/**4**	ee[b] (%)
1	**1a**	**CD$^+$1**	10	81	100/0	6
2		**CN$^+$1**	10	85	100/0	−4
3		**QD$^+$1**	10	92	100/0	−12
4		**QN$^+$1**	10	90	100/0	34[c]
5			5	91	100/0	34
6			2	80	100/0	32
7		**QN$^+$2**	10	41	100/0	20
8		**QN$^+$3**	10	75	100/0	25
9		**QN$^+$4**	10	95	100/0	0
10		**QN$^+$5**	10	84	100/0	24
11		**QN$^+$6**	10	94	100/0	−6
12	**1b**	**QN$^+$1**	10	0	100/0	nd
13	**1c**		10	36	100/0	0
14	**1d**		10	91	70/30	−35
15	**1e**		10	93	85/15	−6

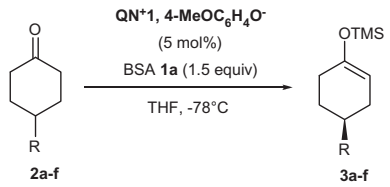
nd: not determined.
[a] Measured by GC-FID analysis.
[b] Measured by GC-FID analysis using a chiral column (see Section 4).
[c] No variation of the ee was observed over the course of the reaction.

bases such as **1d**, which were revealed to be more nucleophilic, led to the formation of a 70/30 mixture of **3a**/**4d**, with **3a** being obtained with the same level of enantioselectivity as previously obtained from BSA **1a**, but with the opposite configuration. The chemoselectivity could be slightly enhanced by using **1e** instead of **1d** but at the expense of the enantioselectivity (Table 1, entry 14 vs 15).

With the optimized conditions in hand, we next examined the scope of the reaction (Table 2).

Several 4-substituted cyclohexanone derivatives **2a–f** were tested (Table 2, entries 1–6). All substrates led to high levels of conversion providing silyl enolates **3a–f** with fair to good isolated

Table 2
Desymmetrization of the prochiral 4-substituted cyclohexanone derivatives **2a–f**



Entry	R	2	3	Yield[a] (Conv.) (%)	ee (%)[b]
1	*t*-Bu	**2a**	**3a**	79 (91)	34
2	Me	**2b**	**3b**	75 (88)	24
3	*n*-Pr	**2c**	**3c**	84 (96)	22
4	*i*-Pr	**2d**	**3d**	73 (85)	26
5	Ph	**2e**	**3e**	68 (78)	25
6	OTBS	**2f**	**3f**	70 (81)	25[c]

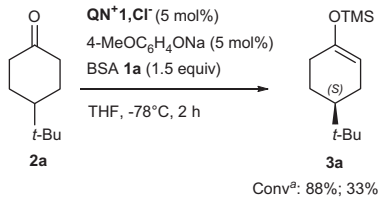
[a] Measured by GC-FID analysis.
[b] Measured by GC-FID analysis using a chiral column unless otherwise indicated (see Section 4).
[c] Determined by the specific rotation (see Section 4).

yields after careful work-up. Modest enantioselectivities of approximately about 25% were obtained whatever the substituents at the C-4 position (alkyl, aryl or OTBS). It should be noted that despite those rather modest levels of stereoinduction, the reaction is very clean and reaches completion within 2 h with only 5 mol % of catalyst, which represents so far the first example of a low-loading catalytic system for this reaction (with respect to the 30 mol % required in Koga's procedure).

In order to facilitate the implementation of the procedure, we looked at the possibility of generating in situ the quaternary ammonium aryloxide salt by means of an ionic metathesis reaction between the corresponding quaternary ammonium halide and sodium aryloxide salts (Scheme 2).

Starting the reaction from the corresponding **QN$^+$1**, **Cl$^-$** and 4-$MeOC_6H_4ONa$ (1 M solution in THF), the same level of enantioselectivity to that obtained with the preformed catalyst (Table 1, entry 4) could be achieved, thus avoiding the preparation of the quaternary ammonium aryloxide salt, which can be sometimes difficult to isolate.

In order to gain insight into the mechanism of this organocatalytic desymmetrization process, several control experiments were conducted. First, we sought to determine which species was responsible for the silylation of the transient enolate. In order to do so, we generated the tetramethylammonium enolate derived from ketone **2a** by desilylation of the corresponding silyl enolate **3a** with Me_4NF. Next, we attempted to trap this enolate by adding 3 equiv of either BSA **1a** or 4-$MeOC_6H_4OTMS$ (presumed to be formed during the activation step of BSA). When BSA was used as the silylating agent, GC–MS analysis showed no detectable traces of compound **3a** after 5 min. When using 4-$MeOC_6H_4OTMS$ as the silylating agent, a low but significant (28%) conversion into compound **3a** was observed after 5 min. Although this last experiment strongly argues in favour of 4-$MeOC_6H_4OTMS$ as the silylating agent, a single step concerted mechanism involving all partners of the reaction, namely the chiral ammonium aryloxide, BSA and the prochiral ketone cannot be ruled out. Regarding these results, the following catalytic cycle was proposed (Fig. 2).



Scheme 2. The in situ generation of chiral quaternary ammonium aryloxide: simplification of the procedure. [a]Determined by GC-FID analysis of the crude mixture. [b]Measured by GC-FID analysis using a chiral column (see Section 4).

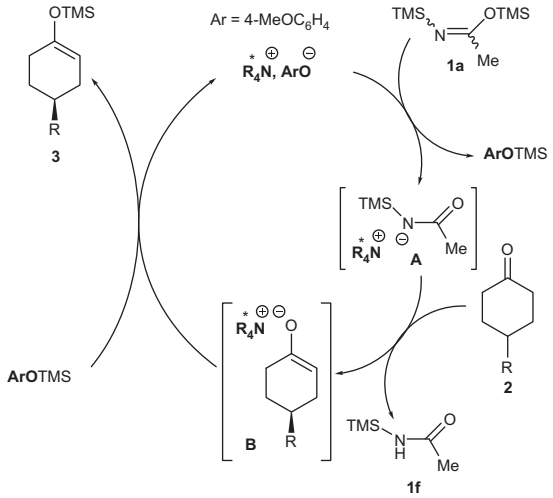
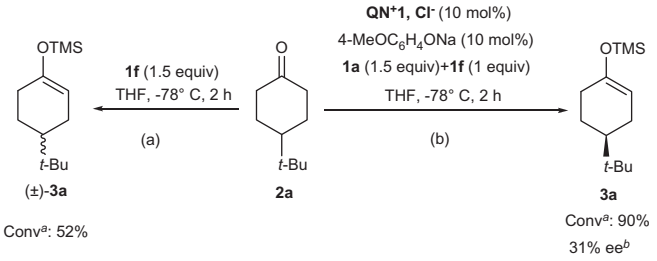


Figure 2. Proposed catalytic cycle.



Scheme 3. Control experiments. [a]Determined by GC-FID analysis of the crude mixture. [b]Measured by GC-FID analysis using a chiral column.

First, desilylation of BSA **1a** triggered by the ammonium phenoxide catalyst would give the active chiral Brønsted base intermediate **A** along with ArOTMS. Then, deprotonation of ketone **2** by the chiral base **A** would occur to provide the protonated BTMS **1f** and the enantioenriched ammonium enolate **B** which upon silylation, likely by ArOTMS, would furnish the corresponding silyl enol ether **3** with concomitant regeneration of the catalyst. Given that **1f** generated during the reaction was also found to be effective in the formation of the silyl enol ether **3** as a racemic mixture (Scheme 3a), we ascertained that the presence of **1f** from the start of the reaction did not lead to an erosion of the enantioselectivity (Scheme 3b). This control experiment showed that **1f** does not compete with the putative reactive catalyst **A** in the deprotonation step and consequently is not responsible for the modest enantioselectivities observed.

3. Conclusion

In conclusion, we have developed the first organocatalytic asymmetric desymmetrization reaction of 4-substituted prochiral

ketones **2** by an asymmetric deprotonation–silylation sequence providing the corresponding silyl enol ethers **3** in good yields and with modest ee values. However, the modest ee values are counterbalanced by the low charge of catalyst required and by the ease of implementation in comparison with the only previous catalytic example reported in the literature.[17] The use of a silylated base (that acts both as a base and a silylating agent) in association with a chiral ammonium phenoxide catalyst could be advantageous to the combination of an achiral lithium amide, chiral amine and TMSCl previously reported by Koga et al.[17] in terms of atom economy. Further developments of this catalytic in situ generation of chiral quaternary ammonium amides to other reactions are currently under investigation.

4. Experimental

4.1. General

MeOH was distilled from CaH_2. THF was distilled from Na/benzophenone. All reagents were used as received unless otherwise indicated. The NMR spectra were recorded on a Bruker AVANCE 300 at 300 MHz (^{1}H) and 75 MHz (^{13}C) using $CDCl_3$ (δ 7.26, ^{1}H; δ 77.16, ^{13}C) or MeOD (δ 3.31, ^{1}H; δ 49.00, ^{13}C) as solvent. Chemical shifts are reported in ppm and calibrated using residual solvent peaks: $CHCl_3$ (δ 7.26, ^{1}H; δ 77.16, ^{13}C), MeOH (δ 3.31, ^{1}H; δ 49.00, ^{13}C). Melting points are uncorrected. Flash chromatography was performed with silica gel (70–230 μm) unless otherwise indicated. Gas chromatographies with an achiral column were performed on a Varian 3900 using a DB-5 column (30 m × 0.25 mm × 0.25 μm) equipped with FID detector (carrier gas: He (1 mL min^{-1}), starting temperature: 50 °C [hold 2 min], rate of temperature increase: 25 °C min^{-1} up to 250 °C [hold 15 min]). Enantiomeric excesses were determined by gas chromatographies using a chiral column Supelco-Beta-Dex 120® column (30 m × 0.25 mm × 0.25 μm) on a Varian 3900 equipped with FID detector unless otherwise indicated. All experiments were conducted under a nitrogen atmosphere in oven-dried glassware with magnetic stirring using standard Schlenk techniques. $[\alpha]_D^{20}$ are reported in mL dm^{-1} g^{-1} as follows: (*c*, solvent) with *c* = concentration in g/100 mL.

4.2. Preparation of the catalysts

4.2.1. General procedure I

Ammonium phenoxides were prepared according to the following general procedure I previously reported.[19,20] Ion-exchange resin Amberlyst A-26 (OH^-) (1.0 g) was added to a stirred solution of ammonium halide (1 mmol) in dry methanol (10 mL) at room temperature. The mixture was stirred for 10 h at the same temperature, filtered and washed with methanol. 4-Methoxyphenol (1 mmol, 124 mg) was added to the filtrate, and the resulting mixture was co-evaporated three times with toluene. Crystallization of the residue with diethyl ether and filtration afforded the ammonium phenoxide which can be used without further purification. Spectroscopic data of ammonium phenoxides **CN$^+$1**, **4-MeOC$_6$H$_4$O$^-$**, **CD$^+$1**, **4-MeOC$_6$H$_4$O$^-$**, **QD$^+$1**, **4-MeOC$_6$H$_4$O$^-$**, **QN$^+$1-5**, **4-MeOC$_6$H$_4$O$^-$** were in agreement with those previously reported.[19]

4.2.2. *N*-(9′-Anthracenylmethyl)quininium 4-methoxyphenoxide (QN$^+$6, 4-MeOC$_6$H$_4$O$^-$)

Compound **QN$^+$6**, **4-MeOC$_6$H$_4$O$^-$** (535 mg, 99% yield) was prepared according to the general procedure I from the corresponding ammonium chloride (451 mg, 1 mmol) and was obtained as a yellow solid (mp: 151–151 °C). $[\alpha]_D^{20} = -145.0$ (*c* 0.50, $CHCl_3$). ^{1}H NMR (300 MHz, CD_3OD, δ): 1.54–1.57 (m, 3H), 1.90–1.91 (m, 1H), 2.04–2.35 (m, 3H), 2.82–3.01 (m, 1H), 3.02–3.12 (m, 1H), 3.60 (s, 3H), 3.60–3.69 (m, 2H), 4.09 (s, 3H), 4.32–4.48 (s, 1H), 4.18–4.39 (m, 1H), 4.69–4.84 (m, 1H), 4.92–5.02 (m, 1H), 5.68–5.76 (m, 2H), 6.55–6.60 (m, 6H), 7.03 (s, 1H), 7.54–7.66 (m, 4H), 7.77–7.81 (m, 2H), 8.01–8.09 (m, 2H), 8.21–8.25 (m, 2H), 8.54–8.65 (m, 2H), 8.80–8.86 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD, δ): 22.6, 26.2, 27.3, 39.7, 54.0, 56.3, 56.4, 57.4, 63.0, 66.8, 71.0, 102.8, 115.8, 117.6, 118.6, 119.0, 121.9, 123.1, 124.7, 125.2, 126.6, 126.7, 127.5, 129.4, 129.5, 131.1, 131.4, 131.9, 133.0, 133.1, 133.8, 134.6, 138.6, 144.7, 146.8, 148.4, 152.1, 158.2, 160.0. IR (ATR, cm^{-1}): 832, 1028, 1227, 1465, 1513, 1618. HRMS (ESI$^+$) calcd for $[C_{35}H_{34}N_2O_2]^+$ *m*/*z* 514.2605, found: 514.2608. HRMS (ESI$^-$) calcd for $[C_7H_7O_2]^-$ *m*/*z* 123.0446, found: 123.0445.

4.3. Organocatalytic enantioselective deprotonation of prochiral cyclohexanones

4.3.1. General procedure II

To a solution of cyclohexanone **2a**–**f** (0.25 mmol) and **QN$^+$1**, **4-MeOC$_6$H$_4$O$^-$** (0.0125 mmol, 7 mg) in THF (0.25 mL) at −78 °C was added BSA (0.375 mmol, 92 μL) as a solution in THF (0.25 mL). The reaction mixture was stirred at the same temperature for 2 h. The conversion was measured by GC-FID. Next, 100 μL of a saturated solution of $NaHCO_3$ was added at −78 °C. The reaction mixture was dried over Na_2SO_4, filtered and concentrated. The crude product **3a**–**f** was purified on silica gel by using petroleum ether/Et_2O (95:5) as eluent and then subjected to GC-FID analysis using chiral column in order to determine the enantiomeric excess.

4.3.2. (4-*tert*-Butylcyclohex-1-enyloxy)trimethylsilane 3a

The title compound was obtained in 91% conversion according to general procedure II (GC analysis using a DB-5 column: t_R = 7.7 min (**2a**), t_R = 8.4 min (**3a**)) and isolated as a colourless oil (79% yield). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.17 (s, 9H), 0.86 (s, 9H), 1.18–1.28 (m, 2H), 1.77–1.84 (m, 2H), 1.96–2.08 (m, 3H), 4.82–4.86 (m, 1H). ee = 35% (GC analysis using a Supelco-Beta-Dex 120® column: conditions, carrier gas: He (20 psi), isotherm 105 °C, t_R = 32.97 min (major, *S*), t_R = 33.64 min (minor, *R*)).

4.3.3. (4-Methylcyclohex-1-enyloxy)trimethylsilane 3b

The title compound was obtained in 88% conversion according to general procedure II (GC analysis using a DB-5 column: t_R = 5.8 min (**2b**), t_R = 6.8 min (**3b**)) and isolated as a colourless oil (75% yield). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.17 (s, 9H), 0.95 (d, *J* = 6.3 Hz, 3H), 0.95–1.37 (m, 1H), 1.56–1.72 (m, 3H), 1.91–2.09 (m, 3H), 4.81–4.82 (m, 1H). ee = 24% (GC analysis using a Supelco-Beta-Dex 120® column: conditions, carrier gas: He (20 psi), 50 °C [hold 0 min], rate of temperature increase: 2 °C min^{-1} up to 130 °C [hold 0 min], t_R = 21.89 min (major, *S*), t_R = 22.11 min (minor, *R*)).

4.3.4. (4-*n*-Propylcyclohex-1-enyloxy)trimethylsilane 3c

The title compound was obtained in 96% conversion according to general procedure II (GC analysis using a DB-5 column: t_R = 7.3 min (**2c**), t_R = 8.0 min (**3c**)) and isolated as a colourless oil (84% yield). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.17 (s, 9H), 0.88 (t, *J* = 7.0 Hz, 3H), 1.19–1.42 (m, 6H), 1.60–1.73 (m, 2H), 1.96–2.10 (m, 3H), 4.94–4.96 (m, 1H). ee = 22% (GC analysis using a Supelco-Beta-Dex 120® column: conditions, carrier gas: He (20 psi), isotherm 95 °C, t_R = 30.96 min (major, *S*), t_R = 31.53 min (minor, *R*)).

4.3.5. (4-*iso*-Propylcyclohex-1-enyloxy)trimethylsilane 3d

The title compound was obtained in 85% conversion to general procedure II (GC analysis using a DB-5 column: t_R = 7.3 min (**2d**), t_R = 8.0 min (**3d**)) and isolated as a colourless oil (73% yield). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.17 (s, 9H), 0.88 (dd, *J* = 6.6, 3.0 Hz,

6H), 1.20–1.35 (m, 2H), 1.42–1.54 (m, 1H), 1.71–1.81 (m, 2H), 1.93–2.08 (m, 3H), 4.83–4.84 (m, 1H). ee = 26% (GC analysis using a Supelco-Beta-Dex 120® column: conditions, carrier gas: He (20 psi), isotherm 105 °C, t_R = 32.59 min (major, *S*), t_R = 33.40 min (minor, *S*)).

4.3.6. (4-Phenylcyclohex-1-enyloxy)trimethylsilane 3e

The title compound was obtained in 78% conversion according to general procedure II (GC analysis using a DB-5 column: t_R = 9.5 min (**2e**), t_R = 10.1 min (**3e**)) and isolated as a colourless oil (68% yield). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.21 (s, 9H), 1.82–2.29 (m, 6H), 2.73–2.75 (m, 1H), 4.94–4.96 (m, 1H), 7.20–7.31 (m, 5H). ee = 25% (GC analysis using a Supelco-Beta-Dex 120® column: conditions, carrier gas: He (20 psi), 50 °C [hold 0 min], rate of temperature increase: 2 °C min^{-1} up to 130 °C [hold 30 min], t_R = 110.58 min (major, *S*), t_R = 112.18 min (minor, *R*)).

4.3.7. (4-*tert*-Butyldimethylsilyloxy-1-enyloxy)trimethylsilane 3f

The title compound was obtained in 81% conversion according to general procedure II (GC analysis using a DB-5 column: t_R = 8.5 min (**2f**), t_R = 9.4 min (**3f**)) and isolated as a colourless oil (70% yield). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.05 (s, 6H), 0.17 (s, 9H), 0.88 (s, 9H), 1.25–1.77 (m, 2H), 1.97–2.11 (m, 3H), 2.16–2.23 (m, 1H), 3.84–3.89 (m, 1H), 4.69–4.71 (m, 1H). ee = 25% {$[\alpha]_D^{20} = -9.0$ (*c* 0.2, $CHCl_3$) corresponding to ee = 25% (*S*). Lit.[24] $[\alpha]_D^{20}$ (*S*) = −28.8 (*c* 0.3, $CHCl_3$, 80% ee)}.

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References

1. For a review, see: García-Urdiales, E.; Alfonso, I.; Gotor, V. *Chem. Rev.* **2011**, *111*, PR110–PR180.
2. For recent reviews, see: (a) Willis, M. C. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1765–1784; (b) Diaz de Villegas, M. D.; Galvez, J. A.; Etayo, P.; Badorrey, R.; Lopez-Ram-de-Viu, P. *Chem. Soc. Rev.* **2011**, *40*, 5564–5587; (c) Enriquez-Garcia, A.; Kuendig, E. P. *Chem. Soc. Rev.* **2012**, *41*, 7803–7831; (d) Rodriguez-Docampo, Z.; Connon, S. J. *ChemCatChem* **2012**, *4*, 151–168.
3. For examples of aldolisation reactions, see: (a) Itagaki, N.; Kimura, M.; Sugahara, T.; Iwabuchi, Y. *Org. Lett.* **2005**, *7*, 4185–4188; (b) Majewski, M.; Niewczas, I.; Palyam, N. *Synlett* **2006**, 2387–2390; (c) Pihko, P. M.; Laurikainen, K. M.; Usano, A.; Nyberg, A. I.; Kaavi, J. A. *Tetrahedron* **2006**, *62*, 317–328; (d) Jiang, J.; He, L.; Luo, S.-W.; Cun, L.-F.; Gong, L.-Z. *Chem. Commun.* **2007**, 736–738; (e) Luo, S.; Xu, H.; Li, J.; Zhang, L.; Mi, X.; Zheng, X.; Cheng, J.-P. *Tetrahedron* **2007**, *63*, 11307–11314; (f) Rodríguez, B.; Bruckmann, A.; Bolm, C. *Chem. Eur. J.* **2007**, *13*, 4710–4722; (g) Companyó, X.; Valero, G.; Crovetto, L.; Moyano, A.; Rios, R. *Chem. Eur. J.* **2009**, *15*, 6564–6568; (h) Diaba, F.; Bonjoch, J. *Org. Biomol. Chem.* **2009**, *7*, 2517–2519; (i) Aitken, D. J.; Bernard, A. M.; Capitta, F.; Frongia, A.; Guillot, R.; Ollivier, J.; Piras, P. P.; Secci, F.; Spiga, M. *Org. Biomol. Chem.* **2012**, *10*, 5045–5048.
4. For examples of Michael-type additions, see: (a) Luo, S.; Zhang, L.; Mi, X.; Qiao, Y.; Cheng, J.-P. *J. Org. Chem.* **2007**, *72*, 9350–9352; (b) Chen, J.-R.; Lai, Y.-Y.; Lu, H.-H.; Wang, X.-F.; Xiao, W.-J. *Tetrahedron* **2009**, *65*, 9238–9243.
5. For example of hydroxylation reactions, see: Ramachary, D. B.; Barbas, C. F. *Org. Lett.* **2005**, *7*, 1577–1580.
6. For examples of alkylation reactions, see: (a) Zhang, L.; Cui, L.; Li, X.; Li, J.; Luo, S.; Cheng, J.-P. *Chem. Eur. J.* **2010**, *16*, 2045–2049; (b) Zhang, L.; Cui, L.; Li, X.; Li, J.; Luo, S.; Cheng, J.-P. *Eur. J. Org. Chem.* **2010**, 4876–4885; (c) Weng, Z.-T.; Li, Y.; Tian, S.-K. *J. Org. Chem.* **2011**, *76*, 8095–8099.
7. For an example of a ring expansion reaction, see: Capitta, F.; Frongia, A.; Ollivier, J.; Piras, P. P.; Secci, F. *Synlett* **2011**, 89–93.
8. For examples of Friedländer condensations, see: (a) Li, L.; Seidel, D. *Org. Lett.* **2010**, *12*, 5064–5067; (b) Li, L.; Seidel, D. *Synthesis* **2011**, 1853–1858.
9. (a) Murahashi, S.-I.; Ono, S.; Imada, Y. *Angew. Chem., Int. Ed.* **2002**, *41*, 2366–2368; (b) Watanabe, A.; Uchida, T.; Ito, K.; Katsuki, T. *Tetrahedron Lett.* **2002**, *43*, 4481–4485; (c) Bolm, C.; Frison, J.-C.; Zhang, Y.; Wulff, W. D. *Synlett* **2004**, 1619–1621; (d) Malkov, A. V.; Friscourt, F.; Bell, M.; Swarbrick, M. E.; Kocovský, P. *J. Org. Chem.* **2008**, *73*, 3996–4003; (e) Xu, S.; Wang, Z.; Zhang, X.; Zhang, X.; Ding, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 2840–2843; (f) Xu, S.; Wang, Z.; Li, Y.; Zhang, X.; Wang, H.; Ding, K. *Chem. Eur. J.* **2010**, *16*, 3021–3035; (g) Zhou, L.; Liu, X.; Ji, J.; Zhang, Y.; Hu, X.; Lin, L.; Feng, X. *J. Am. Chem. Soc.* **2012**, *134*, 17023–17026.
10. (a) Hanessian, S.; Delorme, D.; Beaudoin, S.; Leblanc, Y. *J. Am. Chem. Soc.* **1984**, *106*, 5754–5756; (b) Arai, S.; Hamaguchi, S.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 2997–3000; (c) Gramigna, L.; Duce, S.; Filippini, G.; Fochi, M.; Franchini, M. C.; Bernardi, L. *Synlett* **2011**, 2745–2749.
11. Hashimoto, T.; Naganawa, Y.; Maruoka, K. *Chem. Commun.* **2010**, *46*, 6810–6812.
12. Dickmeiss, G.; De Sio, V.; Udmark, J.; Poulsen, T. B.; Marcos, V.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 6650–6653.
13. Simpkins, N. S.; Weller, M. D. *Top. Stereochem.* **2010**, *26*, 1–52.
14. (a) Whitesell, J. K.; Felman, S. W. *J. Org. Chem.* **1980**, *45*, 755–756; (b) Shirai, R.; Tanaka, M.; Koga, K. *J. Am. Chem. Soc.* **1986**, *108*, 543–545; (c) Simpkins, N. S. *J. Chem. Soc., Chem. Commun.* **1986**, 88–90; (d) Sugasawa, K.; Shindo, M.; Noguchi, H.; Koga, K. *Tetrahedron Lett.* **1996**, *37*, 7377–7380; (e) Ma, L.; Williard, P. G. *Tetrahedron: Asymmetry* **2006**, *17*, 3021–3029; (f) Matsubara, H.; Maeda, L.; Sugiyama, H.; Ryu, I. *Synthesis* **2007**, 2901–2912; (g) Bunn, B. J.; Simpkins, N. S.; Spavold, Z.; Crimmin, M. J. *J. Chem. Soc., Perkin Trans. 1* **1993**, *0*, 3113–3116; (h) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, *25*, 495–498.
15. (a) Henderson, K. W.; Kerr, W. J.; Moir, J. H. *Tetrahedron* **2002**, *58*, 4573–4587; (b) Carswell, E. L.; Hayes, D.; Henderson, K. W.; Kerr, W. J.; Russell, C. J. *Synlett* **2003**, 1017–1021; (c) Bennie, L. S.; Kerr, W. J.; Middleditch, M.; Watson, A. J. B. *Chem. Commun.* **2011**, *47*, 2264–2266; (d) Kerr, W. J.; Middleditch, M.; Watson, A. J. B. *Synlett* **2011**, 177–180.
16. Majewski, M.; Gleave, D. M. *J. Org. Chem.* **1992**, *57*, 3599–3605.
17. Yamashita, T.; Sato, D.; Kiyoto, T.; Kumar, A.; Koga, K. *Tetrahedron* **1997**, *53*, 16987–16998.
18. Prestly, M. R.; Simpkins, N. S. *Angew. Chem., Int. Ed.* **2012**, *51*, 12068–12071.
19. Claraz, A.; Oudeyer, S.; Levacher, V. *Adv. Synth. Catal.* **2013**, *355*, 841–846.
20. Tozawa, T.; Nagao, H.; Yamane, Y.; Mukaiyama, T. *Chem. Asian J.* **2007**, *2*, 123–134.
21. The absolute configuration was determined by comparison with Ref. 18.
22. Other aryloxides [PhO^-, mono or di-(*R*)-binaphtolate] gave similar or lower enantiomeric excesses.
23. No conversion was observed when using other type of silyl groups such as TES (TES-**1d**) or TBDMS (TBDMS-**1a**).
24. Parker, K. A.; Dermatakis, A. *J. Org. Chem.* **1997**, *62*, 6692–6696.