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# Enantioselective synthesis of heteroaromatic epoxyketones under phase-transfer catalysis using D-glucose- and D-mannose-based crown ethers

Zsolt Rapi [a], Tamás Szabó [a], György Keglevich [a], Áron Szöllősy [b], László Drahos [c], Péter Bakó [a,*]

[a] *Department of Organic Chemistry and Technology, Budapest University of Technology and Economics, PO Box 91, 1521 Budapest, Hungary*
[b] *Department of Inorganic and Analytical Chemistry, H-1525 Budapest, Hungary*
[c] *Chemical Research Center, Hungarian Academy of Sciences, H-1025 Budapest, Hungary*

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ABSTRACT

Heteroaromatic epoxyketones have been synthesized in an asymmetric Darzens condensation of 2-chloroacetylfuran or 2- and 3-chloroacetylthiophene with aromatic aldehydes and in the enantioselective epoxidation of α,β-enones with an *N*-methylpyrrole unit, in both cases in the presence of D-glucose- **1** or D-mannose-based **2** crown ethers as phase transfer catalysts. The use of D-glucose-based **1** lariat ether as the catalyst gave the best results. The α,β-epoxyketones with a furan or a thiophene moiety were obtained in good enantioselectivities (up to 86% ee) as well as excellent diastereoselectivities (up to 98:2), but the epoxyketones with a pyrrole-ring were formed in the Darzens condensation in low yields and enantioselectivities. The epoxyketones with an *N*-methylpyrrole moiety isolated from the epoxidation of the corresponding α,β-enones were obtained in significant enantioselectivities (in ee values up to 81%) in the presence of catalyst **1** under mild reaction conditions.



## 1. Introduction

While epoxides are important functional groups in organic synthesis as targets in their own right, they are perhaps more important as intermediates that yield bifunctional compounds after stereoselective ring-opening with a nucleophile. Starting from an enantiopure epoxide, the absolute stereochemistry at the two adjacent stereogenic centers can be controlled, and consequently epoxides not only have a long history as targets for asymmetric catalysis, but a variety of enantioselective catalytic methods for their synthesis also exists.[1]

Two essential methods are known for the preparation of α,β-epoxy carbonyl compounds: the Darzens condensation and the epoxidation of α,β-enones. Both methods can be also performed under phase-transfer conditions.[2]

For the synthesis of α,β-epoxycarbonyls and related compounds, one of the most powerful methodologies (one-step method) is the Darzens condensation between a carbonyl compound and an α-halo-carbonyl compound (or related species).[3] Recently, progress has been made in developing asymmetric variants of this epoxide synthesis.

North et al. used a cobalt(salen) complex to catalyze the asymmetric Darzens condensation of α-haloamides and aldehydes. The *cis*-epoxides could be obtained in up to 50% enantiomeric excess, while the *trans*-epoxides could be obtained in up to 43% enantiomeric excess.[4] Aggarwal et al. have developed a highly enantioselective variation of the Darzens condensation to give *trans*-glicidic amides by replacing the halide leaving group with a chiral sulfonium salt.[5] A simple method for the preparation of chiral epoxides involves the Darzens condensation carried out under phase transfer catalytic conditions in the presence of optically active catalysts. Arai et al. have used cinchona alkaloid derivatives as chiral phase transfer catalysts for asymmetric Darzens condensations, obtaining enantioselectivities of up to 86% using cyclic α-chloroketone substrates,[6] up to 79% for reactions involving α-chloroacetophenone,[6,7] and up to 83% for reactions using chloromethyl phenyl sulfone.[7] Recently, Arai et al. reported the use of a synthetic bis-ammonium salt as an asymmetric phase transfer catalyst for the Darzens condensation of *N*,*N*-diphenyl α-haloamides, predominantly obtaining the *cis*-epoxides with up to 64% ee for the *cis*-epoxide, and up to 70% ee for the *trans*-epoxide.[8]

Chiral monoaza-15-crown-5 type macrocycles incorporating an α-D-glucopyranoside or an α-D-mannopyranoside unit **1** and **2** were synthesized in our laboratory, and proved to be efficient catalysts in a few asymmetric reactions.[9] The Darzens condensation between the benzaldehyde and α-chloroacetophenone was achieved with up to 72% ee in the presence of catalyst **1** (see Fig. 1).[10]

Herein we report the asymmetric Darzens condensation of some heteroaromatic chloromethyl ketones with various aromatic aldehydes (there was no asymmetric induction with the aliphatic aldehydes). Our preliminary results concerning the enantioselective

* Corresponding author.
*E-mail address:* pbako@mail.bme.hu (P. Bakó).

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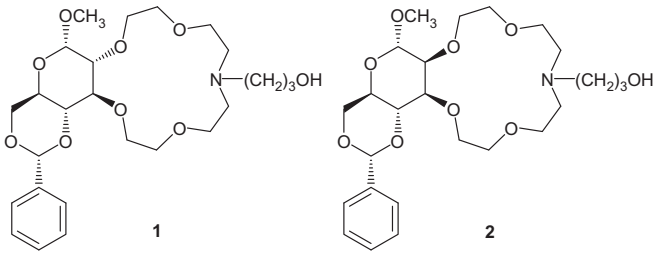



**Figure 1.** Crown ethers containing an α-D-glucopyranoside **1** or an α-D-mannopyranoside **2** unit.

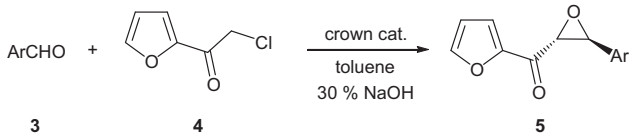
Darzens reactions using catalysts **1** and **2** have already been reported.[11]

## 2. Results and discussion

### 2.1. Darzens condensation

The starting 2-chloroacetylfuran, 2-chloroacetylthiophene and 3-chloroacetylthiophene were prepared by the selective α-chlorination of the corresponding acetyl derivatives by benzyltrimethylammonium dichloroiodate in dichloroethane/methanol,[12] or in the case of the 2-chloroacetylpyrrole and 2-chloroacetyl-*N*-methylpyrrole in a tetrahydrofuran solution.[13]

The Darzens reactions were carried out in a liquid–liquid two-phase system in toluene, employing 30% aq NaOH as the base and 7 mol % of chiral crown catalysts **1** and **2** at a temperature of −5 °C. The products were isolated by preparative TLC. The *trans*-epoxyketones were obtained in all experiments in a diastereomeric excess (de) of >98%. The asymmetric induction expressed in the terms of the enantiomeric excess (ee) was determined by $^1$H NMR analysis in the presence of Eu(hfc)$_3$ as a chiral shift reagent. First, the reaction of 2-chloroacetylfuran **4** and substituted benzaldehydes **3** was studied (Scheme 1). Experimental data are listed in Table 1.




**Scheme 1.**

The *trans*-epoxyketones **5a–f** had negative specific rotation values and were obtained in yields of 30–77%. The reaction of **4** with benzaldehyde gave the (2*R*,3*S*)-epoxyketone **5a** in an enantiomeric excess of 54%.[14] The use of substituted benzaldehydes led to higher ee values that were dependent on the nature of the substitution pattern of the phenyl ring (57–70%). The *o*-methyl product **5b** and the *p*-chloro derivative **5d** were obtained with an ee of 57% and 62%, respectively (entries 2 and 4). The maximum selectivity was detected in the reaction of 2-chlorobenzaldehyde and epoxide **5c** was formed in 70% (entry 3). The recrystallization of epoxyketones **5b** and **5c** from ethanol resulted in higher ee's of 84% and 91%, respectively. The reaction of **4** with piperonal took place with an enantioselectivity of 64% (entry 5). The lowest ee value (28%) was detected in the reaction with 2-naphthaldehyde (entry 6).

A reverse trend was observed for the phase-transfer catalyzed Darzens reaction of 2-chloroacetyl-thiophene **6** (Scheme 2, Table 2).

In the reaction of 2-chloroacetylthiophene **6** with benzaldehyde, the (2*R*,3*S*) antipode of product **7a** was formed in 71% ee.[15] The reaction of substituted benzaldehydes provided lower ee values of 51–68% (Table 2, entries 2–6). In the substituted series, 2-methylbenzaldehyde gave the best enantiomeric purity (68% ee). After recrystallization, the enantiomeric purity was increased to 85% (entry 6). The degree of asymmetric induction was affected by the position of the chloro atom in the benzaldehyde: 2-Cl-, 3-Cl- and 4-Cl derivatives **7b**, **7c**, **7d**) were formed with 51%, 60% and 65% ee, respectively. It was observed, that the further the chloro atom was situated from the reaction center, the greater the extent of asymmetric induction, that is, the best ee (65% ee) was obtained with *p*-chlorobenzaldehyde (entry 4). It is worth mentioning that the use of 1-naphthaldehyde and 2-naphthaldehyde led to products **7g** and **7h** with opposite specific rotations, but approximately the same ee value (entries 7 and 8). The reaction of 2-chloroacetylthiophene with piperonal gave the best enantioselectivity (86%). Moreover, after completion of the reaction, nearly half of the epoxyketone **7i** precipitated from the mixture as a pure enantiomer (100% ee).

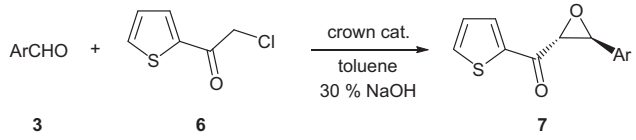
To the best of our knowledge, only Arai et al. have reported high enantioselectivities of up to 86% ee for the reaction of cyclic α-chloroketones and aldehydes in the presence of a cinchonine derivative after prolonged (80–200 h) reaction times.[6]

In the reactions shown in Schemes 2 and 3, the mannose-based crown ether **2** generated lower enantioselectivities when using

**Table 1**
Asymmetric Darzens condensation of 2-chloroacetylfuran **4** with aromatic aldehydes in the presence of catalyst **1** at −5 °C

| Entry | Ar | Time (h) | Yield[a] (%) | $[\alpha]_D^{22}$[b] | ee[c] (%) |
|---|---|---|---|---|---|
| 1 | Ph | 8 | **5a:** 55 | −117.7 | 54[d] |
| 2 | 2-$H_3C$-$C_6H_4$ | 12 | **5b:** 64 | −33.1 | 57 (84) |
| 3 | 2-Cl-$C_6H_4$ | 5 | **5c:** 77 | −14.9 | 70 (91) |
| 4 | 4-Cl-$C_6H_4$ | 3 | **5d:** 67 | −146.5 | 62 |
| 5 | Piperonyl | 3 | **5e:** 45 | −151.3 | 64 |
| 6 | 2-Naphthyl | 1 | **5f:** 30 | −73.6 | 28 |

[a] Based on preparative TLC.
[b] In $CH_2Cl_2$, *c* 1.
[c] Determined by $^1$H NMR spectroscopy, the ee given in the parentheses was obtained after one recrystallization from EtOH.
[d] Ref. 14.

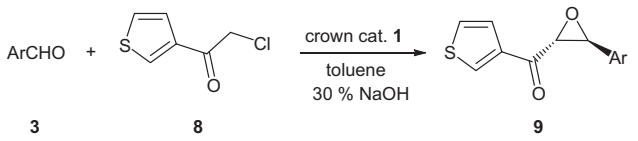



**Scheme 2.**

**Table 2**
Asymmetric Darzens condensation of 2-chloroacetylthiophene **6** with aromatic aldehydes in the presence of catalyst **1** at −5 °C

| Entry | Ar | Time (h) | Yield[a] (%) | $[\alpha]_D^{22}$[b] | ee[c] (%) |
|---|---|---|---|---|---|
| 1 | Ph | 5 | **7a**: 63 | −169.8 | 71 (84)[d] |
| 2 | 2-Cl-$C_6H_4$ | 4.5 | **7b**: 53 | −10.0 | 51 |
| 3 | 3-Cl-$C_6H_4$ | 6 | **7c**: 56 | −142.1 | 60 (75) |
| 4 | 4-Cl-$C_6H_4$ | 20 | **7d**: 54 | −139.0 | 65 (79) |
| 5 | 4-F-$C_6H_4$ | 22 | **7e**: 55 | −119.7 | 62 (73) |
| 6 | 2-$H_3C$-$C_6H_4$ | 3 | **7f**: 79 | −45.7 | 68 (85) |
| 7 | 1-Naphthyl | 5 | **7g**: 87 | +54.0 | 64 (75) |
| 8 | 2-Naphthyl | 6 | **7h**: 54 | −163.0 | 62 |
| 9 | Piperonyl | 5 | **7i**: 57 | −131.5 | 86 (100) |

[a] Based on preparative TLC.
[b] In $CH_2Cl_2$, *c* 1.
[c] Determined by $^1$H NMR spectroscopy, the ee given in parentheses was obtained after one recrystallization from EtOH.
[d] Ref. 15.

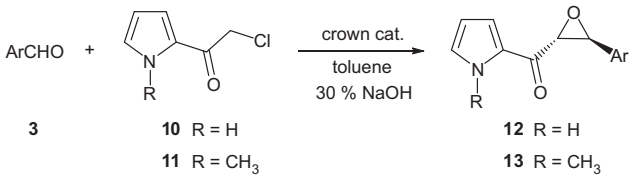



**Scheme 3.**

**Table 3**
Asymmetric Darzens condensation of 3-chloroacetylthiophene **8** with aromatic aldehydes in the presence of catalyst **1** at −5 °C

| Entry | Ar | Time (h) | Yield[a] (%) | $[\alpha]_D$[b] | ee[c] (%) |
|---|---|---|---|---|---|
| 1 | Ph | 4 | **9a**: 53 | −72.2 | 52 (66) |
| 2 | 2-$H_3C$-$C_6H_4$ | 3 | **9b**: 51 | −19.3 | 52 (85) |
| 3 | 1-Naphthyl | 4 | **9c**: 66 | +51.9 | 54 |

[a] Based on preparative TLC.
[b] In $CH_2Cl_2$, *c* 1.
[c] Determined by $^1$H NMR spectroscopy, the ee given in parentheses was obtained after one recrystallization from EtOH.




**Scheme 4.**

**Table 4**
Asymmetric Darzens condensation of 2-chloroacetylpyrrole **10** and 2-chloroacetyl-*N*-methylpyrrole **11** with aromatic aldehydes in the presence of catalyst **1** at −5 °C

| Entry | R | Ar | Time (h) | Yield[a] (%) | $[\alpha]_D$[b] | ee[c] (%) |
|---|---|---|---|---|---|---|
| 1 | H | Ph | 0.8 | **12a:** 33 | −77.3 | 36 |
| 2 | H | 2-$CH_3$-$C_6H_4$ | 0.5 | **12b:** 28 | −1.2 | 20 |
| 3 | H | 1-Naphthyl | 0.8 | **12c:** 22 | +24.9 | 51 (64) |
| 4 | H | 2-Naphthyl | 2.5 | **12d:** 29 | −40.0 | 18 |
| 5 | $CH_3$ | Ph | 5 | **13a:** 72 | −41.5 | 16 |
| 6 | $CH_3$ | 2-Cl-$C_6H_4$ | 4.5 | **13b:** 59 | −2.9 | 19 |

[a] Based on preparative TLC.
[b] In $CHCl_3$, *c* 1.
[c] Determined by $^1$H NMR spectroscopy, the ee given in parentheses was obtained after one recrystallization from EtOH.

benzaldehyde. The products **5a** and **7a** (both with positive specific rotations) were obtained in ee of 42% and 59%, respectively.

Repeated recrystallization of products **7f** and **7i** led to pure enantiomers whose absolute configurations were determined by single crystal X-ray analysis. In both cases, the configurations of the stereogenic carbon atoms were found to be (2*R*,3*S*).[11] The phase transfer catalyzed Darzens reactions of 3-chloroacetylthiophene were also investigated (Scheme 3).

It can be seen from the data in Table 3 that the substitution pattern of the thiophene ring also influenced the extent of the asymmetric induction: the reaction of 3-chloroacetylthiophene with a few aromatic aldehydes (benzaldehyde, 2-methylbenzaldehyde and 1-naphthaldehyde) took place with lower enantioselectivities (52%, 52% and 54%), in the presence of catalyst **1**, as compared to the reaction of 2-chloroacetylthiophene (71%, 68%, 64%) and the asymmetric induction was found to be not dependent on the nature of the substituents.

Analogous reactions between aromatic aldehydes and 2-chloroacetylpyrrole **10** were carried out under similar conditions (Scheme 4), but the yields were low (22–33%) and the enantioselectivities variable (16–51% ee, Table 4, entries 1–4). The best result was achieved with 1-naphthaldehyde, and product **12c** (Ar = 1-naphthyl) obtained in 51% ee could be purified by repeated recrystallization to afford suitable crystals. The absolute configuration was found to be (2*R*,3*S*) after single crystal X-ray analysis.[11]

The low yields and ee values were attributed to side reactions under basic conditions arising from the acidity of the NH moiety of the pyrrole (entries 1–4). For this, experiments were carried out with *N*-methyl-2-chloroacetylpyrrole **11** (Scheme 4), but in reactions with benzaldehyde and *o*-chlorobenzaldehyde only the yields were improved, while the ee values remained low (16% and 19% ee, Table 4, entries 5 and 6).

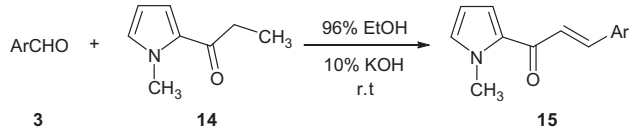
## 2.2. Synthesis of chiral epoxides with an *N*-methylpyrrole moiety by epoxidation of α,β-enones

Following the unsuccessful Darzens conditions, the epoxyketones with *N*-methylpyrrole moieties were prepared by the epoxidation of the corresponding α,β-enones. In the first step, the unsaturated ketones were synthesized, then oxidized in the presence of a chiral catalyst.

Many methodologies have been developed regarding asymmetric epoxidation.[1,2] A variety of catalytic asymmetric epoxidations of electron-deficient olefins, in particular α,β-unsaturated ketones have been published involving the use of hydrogen peroxide, alkylperoxides, *tert*-butyl hydroperoxide or sodium and potassium hypochlorites, as the oxidative agents, in the presence of various polyaminoacids, chinchona alkaloids, chiral platinium(II) complexes, lanthanoid–binaphthol complexes and chiral quaternary ammonium salts as the phase transfer catalysts, or various organocatalysts, and so on.[1,2,16]

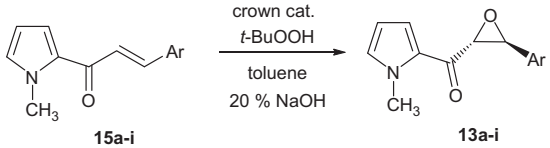
We have described the asymmetric epoxidation of a variety of chalcone derivatives with *tert*-butyl hydroperoxide under phase transfer catalytic conditions in the presence of azacrown **1** or **2**.[17] We wished to study the epoxidation of unsaturated ketones containing an *N*-methylpyrrole unit in the presence of catalysts **1** and **2**.

The starting ketones **15** were prepared by the condensation of corresponding aromatic aldehydes **3** with 2-*N*-methylacetylpyrrole **14** in ethanol, in the presence of 10% KOH/$H_2O$. Compounds **15a–i** were obtained in variable yields (37–86%, Scheme 5).




**Scheme 5.**

In our experiments, the epoxidation of ketones **15** with *tert*-butylhydroperoxide (TBHP, 2 equiv) was carried out in a liquid–liquid two-phase system employing toluene, 20% aq NaOH (3.5 equiv) and 7 mol % of a chiral crown catalyst at room temperature (Scheme 6). In most cases, the reactions were complete after 46–240 h. After the usual work-up, the product was isolated by preparative TLC. The asymmetric induction, expressed in terms of the enantiomeric excess (ee%), was determined by $^1$H NMR




**Scheme 6.**

**Table 5**
Asymmetric epoxidation of unsaturated ketones containing an *N*-methylpyrrole unit **15a–i** in the presence of catalyst **1** at 22 °C

| Entry | Ar | Time (h) | Yield[a] (%) | $[\alpha]_D^{22}$ [b] | ee[c] (%) |
|---|---|---|---|---|---|
| 1 | Ph | 46 | **13a**: 80 | −209.5 | 79 |
| 2 | 2-Cl-$C_6H_4$ | 100 | **13b**: 73 | −7.0 | 51 |
| 3 | 3-Cl-$C_6H_4$ | 122 | **13c**: 88 | −207.0 | 79 |
| 4 | 4-Cl-$C_6H_4$ | 240 | **13d**: 92 | −211.4 | 81 |
| 5 | 2-$H_3C$-$C_6H_4$ | 160 | **13e**: 83 | −49.7 | 65 |
| 6 | 3-$H_3C$-$C_6H_4$ | 68 | **13f**: 79 | −196.8 | 70 |
| 7 | 4-$H_3C$-$C_6H_4$ | 48 | **13g**: 83 | −216.3 | 79 |
| 8 | 1-Naphthyl | 168 | **13h**: 72 | +88.0 | 70 |
| 9 | 2-Naphthyl | 52 | **13i**: 69 | −219.7 | 77 |

[a] Based on preparative TLC.
[b] In $CHCl_3$, *c* 1.
[c] Determined by $^1H$ NMR spectroscopy.

spectroscopy using (+)-Eu(hfc)$_3$ as the chiral shift reagent. The *trans*-epoxyketones were obtained in all experiments in a high diastereoselectivity (de >98%). The results of the epoxidations are shown in Table 5.

The oxidation reaction of unsaturated ketones catalyzed by crown ether **1** afforded the corresponding epoxides **13a–i** in excellent diastereoselectivity (de >98%), in moderate to good yields and in an enantioselectivity that was highly dependent on the nature of the substituents and on their positions on the phenyl ring. The epoxidation of compound **15a** (Ar = Ph) took place with an ee of 79% (Table 5. entry 1). The 2-chloro-, 3-chloro- and 4-chlorophenyl epoxyketones were obtained in 51%, 79% and 81% ee values, respectively (Table 5, entries 2–4), while the 2-methyl-, 3-methyl- and 4-methyl-derivatives were obtained in 65%, 70% and 79% enantioselectivities, respectively (entries 5–7). It can be seen that the further the substituent was located from the reaction center, the more considerable the asymmetric induction. This suggests the role of steric hindrance. It is worth noting that while in the epoxidation of 2-naphthyl-derivative **15i** (Ar = 2-naphthyl) epoxyketone **13i** was obtained with a negative specific rotation (77% ee); the reaction of 1-naphthyl-derivative **15h** led to product **13h** with a positive specific rotation (70% ee).

The use of mannose-based macrocycle **2** led to a smaller extent of asymmetric induction as compared to that of the glucose-based **1**. For example, the epoxyketones **13d** and **13g** were obtained in 72% and 70% ee in the presence of catalyst **2**. The antipode with a positive specific rotation was formed in excess.

## 3. Conclusion

The glucose-based crown ether **1** induced a greater extent of asymmetric induction both in Darzens condensation and epoxidation as compared to mannose-based **2**. In the Darzens condensation of 2-chloroacetylfuran **4**, 2-chloroacetylthiophene **6** and 3-chloroacetyl-thiophene **8** 28–70%, 51–86% and 52–54% ee values were measured, respectively, in the presence of catalyst **1**. In the case of 2-substituted derivatives **4** or **6** the enantioselectivity depended strongly on the substitution pattern of the benzaldehyde reagent. In the case of 3-substituted compound **8**, there was no such dependence. The epoxyketones containing a pyrrole and an *N*-methylpyrrole moiety **12a–d** and **13a–b** were obtained in poor yields and low enantioselectivities in the Darzens condensation, but the epoxidation of the corresponding α,β-enones gave the products **13a–i** in much better yields and ee values (51–81% ee). The monosaccharide unit of the catalyst was decisive with respect to the configuration of the epoxyketone formed. The glucose-based catalyst **1** mostly promoted the formation of the (2*R*,3*S*)-enantiomer with a negative specific rotation (except the 1-naphthyl-derivatives were formed with a positive specific rotation), while the mannose-based crown **2** enhanced the predominant formation of the enantiomer with a positive specific rotation.

## 4. Experimental

### 4.1. General

Melting points were taken on using a Büchi 510 apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter at 22 °C. $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker 300 and a Bruker DRX-500 or a Varian Inova 500 instrument in $CDC1_3$ with TMS as the internal standard. Analytical and preparative thin layer chromatography was performed on silica gel plates (60 GF-254, Merck), while column chromatography was carried out using 70–230 mesh silica gel (Merck). Chemicals and the shift reagent Eu(hfc)$_3$ were purchased from Aldrich Chem. Co. The exact mass measurements were performed using Q-TOF Premier mass spectrometer (Waters Corporation, 34 Maple St, Milford, MA, USA) in positive electrospray ionization mode. The melting points of the epoxyketones were determined after crystallization from ethanol.

### 4.2. General procedure for the Darzens condensation

A toluene solution (3 mL) of aromatic α-chloro-ketone (1.87 mmol), aromatic aldehyde (2.8 mmol) and the crown ether (0.14 mmol) was cooled to −5 °C, and treated with 30% NaOH (1 mL). The mixture was stirred at this temperature, until completion of the reaction (1–22 h), after which toluene (7 mL) and water (3 mL) were added and the mixture was stirred for 10 min. The organic phase was washed with cold 10% HCl (3 × 10 mL) and water (20 mL), dried ($Na_2SO_4$ and $Na_2CO_3$) and concentrated. The crude product was purified on silica gel by preparative TLC with hexane–EtOAc (10:1) as the eluent. The enantioselectivities were determined by $^1H$ NMR spectroscopy in the presence of Eu(hfc)$_3$ as the chiral shift reagent.

The configuration of the major enantiomer of compounds **5a** and **7a** were determined by comparison with the literature data;[14,15] for epoxyketones **7f**, **7i** and **12c**, the configuration was determined by single crystal X-ray analysis.[11]

#### 4.2.1. (2*R*,3*S*)-2,3-Epoxy-1-(2-furyl)-3-phenylpropan-1-one 5a

Yield: 55%; $[\alpha]_D^{22} = -117.7$ (*c* 1, $CHCl_3$) 54% ee; mp 44–47 °C {lit.[14b] $[\alpha]_D^{26} = -190$ (*c* 1, $CHCl_3$) 87% ee}; $^1H$ NMR ($CDCl_3$, 500 MHz) δ (ppm): 7.68 (d, *J* = 1.5 Hz, 1H), 7.45 (d, *J* = 3.5 Hz, 1H), 7.39–7.36 (m, 3H), 7.35–7.33 (m, 2H), 6.59 (dd, *J* = 3.5 Hz, 1.5 Hz, 1H), 4.15 (d, *J* = 1.5 Hz, 1H), 4.14 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{13}H_{10}O_3$ 214.0630, found 214.0628.

#### 4.2.2. *trans*-(−)-2,3-Epoxy-1-(2-furyl)-3-(2-tolyl)-propan-1-one 5b

Yield: 64%; $[\alpha]_D^{22} = -33.1$ (*c* 1, $CHCl_3$) 57% ee; mp 86 °C; $^1H$ NMR ($CDCl_3$, 300 MHz) δ (ppm): 7.69 (d, *J* = 1.5 Hz, 1H), 7.49–7.46 (m, 1H), 7.32–7.28 (m, 1H), 7.27–7.22 (m, 2H), 7.20–7.16 (m, 1H), 6.61 (dd, *J* = 3.5 Hz, 1.5 Hz, 1H), 4.27 (d, *J* = 1.5 Hz, 1H), 4.04 (d, *J* = 1.5 Hz, 1H), 2.36 (s, 3H). HRMS calcd for $C_{14}H_{12}O_3$ 228.0786, found 228.0789.

#### 4.2.3. *trans*-(−)-2,3-Epoxy-1-(2-furyl)-3-(2-chlorophenyl)-propan-1-one 5c

Yield: 77%; $[\alpha]_D^{22} = -14.9$ (*c* 1, $CHCl_3$, 70% ee); mp 82–85 °C; $^1H$ NMR ($CDCl_3$, 300 MHz) δ (ppm): 7.69 (d, *J* = 1.5 Hz, 1H), 7.47 (d, *J* = 3.5 Hz, 1H), 7.40–7.28 (m, 4H), 6.61 (dd, *J* = 3.5 Hz, 1.5 Hz, 1H), 4.48 (d, *J* = 1.5 Hz, 1H), 4.03 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{13}H_9ClO_3$ 248.0240, found 248.0243.

#### 4.2.4. *trans*-(−)-2,3-Epoxy-1-(2-furyl)-3-(4-chlorophenyl)-propan-1-one 5d

Yield: 67%; $[\alpha]_D^{22} = -146.5$ (*c* 1, $CHCl_3$) 62% ee; mp 102–103 °C; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 7.68 (d, *J* = 1.5 Hz, 1H), 7.45 (d, *J* = 3.5 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 6.60 (dd, *J* = 3.5 Hz, 1.5 Hz, 1H), 4.13 (d, *J* = 1.5 Hz, 1H), 4.10 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{13}H_9ClO_3$ 248.0240, found 248.0242.

#### 4.2.5. *trans*-(−)-2,3-Epoxy-1-(2-furyl)-3-pyperonyl-propan-1-one 5e

Yield: 45%; $[\alpha]_D^{22} = -151.3$ (*c* 1, $CHCl_3$) 64% ee; mp 82–84 °C; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ (ppm): 7.67 (d, *J* = 1.5 Hz, 1H), 7.45 (d, *J* = 3.5 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.77 (s, 1H), 6.60 (dd, *J* = 3.5 Hz, 1.5 Hz, 1H), 5.99 (s, 2H), 4.09 (d, *J* = 1.5 Hz, 1H), 4.07 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{14}H_{10}O_5$ 258.0528, found 258.0525.

#### 4.2.6. *trans*-(−)-2,3-Epoxy-1-(2-furyl)-3-(2-naphthyl)-propan-1-one 5f

Yield: 30%; $[\alpha]_D^{22} = -73.6$ (*c* 1, $CHCl_3$) 28% ee; mp 114–117 °C; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 7.88–7.82 (m, 4H), 7.67 (d, *J* = 1.5 Hz, 1H), 7.53–7.50 (m, 2H), 7.47 (d, *J* = 3.5 Hz, 1H), 7.38 (dd, *J* = 8.5 Hz, 1.5 Hz, 1H), 6.59 (dd, *J* = 3.5 Hz, 1.5 Hz, 1H), 4.32 (d, *J* = 1.5 Hz, 1H), 4.24 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{17}H_{12}O_3$ 264.0786, found 264.0784.

#### 4.2.7. *trans*-(−)-2,3-Epoxy-1-(2-thienyl)-3-phenylpropan-1-one 7a

Yield: 63%; $[\alpha]_D^{22} = -169.8$ (*c* 1, $CH_2Cl_2$) 71% ee; mp 49–50 °C; $^1H$ NMR ($CDCl_3$, 500 MHz), $\delta$ (ppm): 8.00 (d, *J* = 3.5 Hz, 1H), 7.73 (d, *J* = 5 Hz, 1H), 7.39–7.37 (m, 3H), 7.35–7.33 (m, 2H), 7.17 (t, *J* = 4.5 Hz, 1H), 4.17 (d, *J* = 1.5 Hz, 1H), 4.07 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{13}H_{10}O_2S$ 230.0402, found 230.0406.

#### 4.2.8. *trans*-(−)-2,3-Epoxy-1-(2-thienyl)-3-(2-chlorophenyl)-propan-1-one 7b

Yield: 53%; $[\alpha]_D^{22} = -10$ (*c* 1, $CH_2Cl_2$) 51% ee; mp 49–50 °C; $^1H$ NMR ($CDCl_3$, 300 MHz), $\delta$ (ppm): 8.02 (d, *J* = 3 Hz, 1H), 7.76 (d, *J* = 4.8 Hz, 1H), 7.29–7.21 (m, 4H), 7.19 (t, *J* = 3.9 Hz, 1H), 4.49 (d, *J* = 1.5 Hz, 1H), 3.97 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{13}H_9ClO_2S$ 264.0012, found 264.0008.

#### 4.2.9. *trans*-(−)-2,3-Epoxy-1-(2-thienyl)-3-(3-chlorophenyl)-propan-1-one 7c

Yield: 56%; $[\alpha]_D^{22} = -142.1$ (*c* 1, $CH_2Cl_2$) 60% ee; mp 78–80 °C; $^1H$ NMR ($CDCl_3$, 500 MHz), $\delta$ (ppm): 8.00 (dd, *J* = 3.5 Hz, 1 Hz, 1H), 7.76 (dd, *J* = 5 Hz, 1 Hz, 1H), 7.34 (s, 1H), 7.34–7.30 (m, 1H), 7.31 (d, *J* = 8 Hz, 1H), 7.25–7.23 (m, 1H), 7.19 (t, *J* = 4.5 Hz, 1H), 4.15 (d, *J* = 1.5 Hz, 1H), 4.04 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{13}H_9ClO_2S$ 264.0012, found 264.0007.

#### 4.2.10. *trans*-(−)-2,3-Epoxy-1-(2-thienyl)-3-(4-chlorophenyl)-propan-1-one 7d

Yield: 54%; $[\alpha]_D^{22} = -139$ (*c* 1, $CH_2Cl_2$) 65% ee; mp 80–82 °C; $^1H$ NMR ($CDCl_3$, 500 MHz), $\delta$ (ppm): 8.00 (d, *J* = 3.5 Hz, 1H), 7.75 (d, *J* = 5 Hz, 1H), 7.37 (d, *J* = 8 Hz, 2H), 7.28 (d, *J* = 8 Hz, 2H), 7.18 (t, *J* = 4.5 Hz, 1H), 4.15 (d, *J* = 1.5 Hz, 1H), 4.02 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{13}H_9ClO_2S$ 264.0012, found 264.0014.

#### 4.2.11. *trans*-(−)-2,3-Epoxy-1-(2-thienyl)-3-(4-fluorophenyl)-propan-1-one 7e

Yield: 55%; $[\alpha]_D^{22} = -119.7$ (*c* 1, $CH_2Cl_2$) 62% ee; mp 64–66 °C; $^1H$ NMR ($CDCl_3$, 500 MHz), $\delta$ (ppm): 8.01 (d, *J* = 3.5 Hz, 1H), 7.75 (d, *J* = 4.5 Hz, 1H), 7.33 (d, *J* = 5.5 Hz, 1H), 7.31 (d, *J* = 5.5 Hz, 1H), 7.18 (t, *J* = 4.5 Hz, 1H), 7.09 (d, *J* = 3.5 Hz, 1H), 7.07 (d, *J* = 3.5 Hz, 1H), 4.16 (d, *J* = 1.5 Hz, 1H), 4.03 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{13}H_9FO_2S$ 248.0307, found 248.0311.

#### 4.2.12. (2*R*,3*S*)-2,3-Epoxy-1-(2-thienyl)-3-(2-tolyl)-propan-1-one 7f

Yield: 79%; $[\alpha]_D^{22} = -45.7$ (*c* 1, $CH_2Cl_2$) 68% ee; mp 72–74 °C; $^1H$ NMR ($CDCl_3$, 500 MHz), $\delta$ (ppm): 8.03 (dd, *J* = 4 Hz, 1 Hz, 1H), 7.75 (dd, *J* = 5 Hz, 1 Hz, 1H), 7.30 (dd, *J* = 7 Hz, 2 Hz, 1H), 7.27–7.23 (m, 2H), 7.19 (t, *J* = 4.5 Hz, 1H), 7.18–7.17 (m, 1H), 4.29 (d, *J* = 1.5 Hz, 1H), 3.98 (d, *J* = 1.5 Hz, 1H), 2.37 (s, 3H). HRMS calcd for $C_{14}H_{12}O_2S$ 244.0558, found 244.0563.

#### 4.2.13. *trans*-(+)-2,3-Epoxy-1-(2-thienyl)-3-(1-naphthyl)-propan-1-one 7g

Yield: 87%; $[\alpha]_D^{22} = +54$ (*c* 1, $CH_2Cl_2$) 64% ee; mp 108–110 °C; $^1H$ NMR ($CDCl_3$, 300 MHz), $\delta$ (ppm): 8.03 (d, *J* = 3.5 Hz, 1H), 8.01–7.99 (m, 1H), 7.92–7.89 (m, 1H), 7.86 (d, *J* = 8 Hz, 1H), 7.77 (dd, *J* = 5 Hz, 1 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.54–7.51 (m, 2H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.19 (t, *J* = 4.5 Hz, 1H), 4.80 (d, *J* = 1.5 Hz, 1H), 4.11 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{17}H_{12}O_2S$ 280.0558, found 280.0554.

#### 4.2.14. *trans*-(−)-2,3-Epoxy-1-(2-thienyl)-3-(2-naphthyl)-propan-1-one 7h

Yield: 54%; $[\alpha]_D^{22} = -163$ (*c* 1, $CH_2Cl_2$) 62% ee; Oil; $^1H$ NMR ($CDCl_3$, 500 MHz), $\delta$ (ppm): 8.02 (d, *J* = 3 Hz, 1H), 7.90–7.82 (m, 4H), 7.75 (d, *J* = 4.8 Hz, 1H), 7.54–7.79 (m, 2H), 7.38 (d, *J* = 8.7 Hz, 1H), 7.18 (t, *J* = 4.2 Hz, 1H), 4.34 (d, *J* = 1.5 Hz, 1H), 4.18 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{17}H_{12}O_2S$ 280.0558, found 280.0561.

#### 4.2.15. (2*R*,3*S*)-2,3-Epoxy-1-(2-thienyl)-3-piperonyl-propan-1-one 7i

Yield: 57%; $[\alpha]_D^{22} = -131.5$ (*c* 1, $CH_2Cl_2$) 86% ee; After crystallization: $[\alpha]_D^{22} = -268.8$ (*c* 1, $CH_2Cl_2$) 100% ee; mp 108–110 °C; $^1H$ NMR ($CDCl_3$, 500 MHz), $\delta$ (ppm): 8.00 (d, *J* = 4 Hz, 1H), 7.74 (d, *J* = 5 Hz, 1H), 7.17 (t, *J* = 4.5 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.77 (s, 1H), 5.98 (s, 2H), 4.09 (d, *J* = 1.5 Hz, 1H), 4.02 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{14}H_{10}O_4S$ 274.0300, found 274.0306.

#### 4.2.16. *trans*-(−)-2,3-Epoxy-1-(3-thienyl)-3-phenylpropan-1-one 9a

Yield: 53%; $[\alpha]_D^{22} = -72.2$ (*c* 1, $CH_2Cl_2$) 52% ee; mp 91–93 °C; $^1H$ NMR ($CDCl_3$, 500 MHz), $\delta$ (ppm): 8.37 (dd, *J* = 2.5 Hz, 1 Hz, 1H), 7.65 (dd, *J* = 5 Hz, 1 Hz, 1H), 7.40 (dd, *J* = 5 Hz, 3 Hz, 1H), 7.39–7.36 (m, 3H), 7.36–7.33 (m, 2H), 4.11 (d, *J* = 1.5 Hz, 1H), 4.06 (d, *J* = 1.5 Hz, 1H). HRMS calcd for $C_{13}H_{10}O_2S$ 230.0402, found 230.0399.

#### 4.2.17. *trans*-(−)-2,3-Epoxy-1-(3-thienyl)-3-(2-tolyl)-propan-1-one 9b

Yield: 51%; $[\alpha]_D^{22} = -19.3$ (*c* 1, $CH_2Cl_2$) 52% ee; mp 72–74 °C; $^1H$ NMR ($CDCl_3$, 500 MHz), $\delta$ (ppm): 8.39 (dd, *J* = 2.5 Hz, 1 Hz, 1H), 7.67 (dd, *J* = 5 Hz, 1 Hz, 1H), 7.37 (dd, *J* = 5 Hz, 3 Hz, 1H), 7.30 (dd, *J* = 8 Hz, 2.5 Hz, 1H), 7.23–7.26 (m, 2H), 7.16–7.19 (m, 1H), 4.24 (d, *J* = 1.5 Hz, 1H), 3.96 (d, *J* = 1.5 Hz, 1H), 2.35 (s, 3H). HRMS calcd for $C_{14}H_{12}O_2S$ 244.0558, found 244.0562.

#### 4.2.18. *trans*-(−)-2,3-Epoxy-1-(3-thienyl)-3-(1-naphthyl)-propan-1-one 9c

Yield: 66%; $[\alpha]_D^{22} = +51.9$ (*c* 1, $CH_2Cl_2$) 54% ee; Oil. $^1H$ NMR ($CDCl_3$, 500 MHz), $\delta$ (ppm): 8.40 (dd, *J* = 3 Hz, 1 Hz, 1H), 8.00–7.97 (m, 1H), 7.93–7.89 (m, 1H), 7.86 (d, *J* = 8.5 Hz, 1H), 7.72 (dd, *J* = 5 Hz, 1 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.54–7.51 (m, 2H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.38 (dd, *J* = 5 Hz, 3 Hz, 1H), 4.74 (d, *J* = 1.5 Hz,

1H), 4.09 (d, $J$ = 1.5 Hz, 1H). HRMS calcd for $C_{17}H_{12}O_2S$ 280.0558, found 280.0553.

#### 4.2.19. *trans*-(−)-2,3-Epoxy-1-(2-pyrrolyl)-3-phenylpropan-1-one 12a

Yield: 33%; $[\alpha]_D^{22} = -77.3$ ($c$ 1, $CHCl_3$) 36% ee; mp 139–140 °C; $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ (ppm): 9.69 (br s, 1H), 7.41–7.31 (m, 5H), 7.18 (m, 1H), 7.14 (m, 1H), 6.34 (m, 1H), 4.17 (d, $J$ = 1.5 Hz, 1H), 4.01 (d, $J$ = 1.5 Hz, 1H). HRMS calcd for $C_{13}H_{11}NO_2$ 213.0790, found 213.0785.

#### 4.2.20. *trans*-(−)-2,3-Epoxy-1-(2-pyrrolyl)-3-(2-tolyl)-propan-1-one 12b

Yield: 28%; $[\alpha]_D^{22} = -1.2$ ($c$ 1, $CHCl_3$) 20% ee; mp 125–127 °C; $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ (ppm): 9.88 (br s, 1H), 7.33–7.29 (m, 1H), 7.26–7.22 (m, 2H), 7.19 (m, 2H), 7.16 (m, 1H), 6.34 (m, 1H), 4.30 (d, $J$ = 1.5 Hz, 1H), 3.92 (d, $J$ = 1.5 Hz, 1H), 2.36 (s, 3H). HRMS calcd for $C_{14}H_{13}NO_2$ 227.0946, found 227.0950.

#### 4.2.21. (2*R*,3*S*)-2,3-Epoxy-1-(2-pyrrolyl)-3-(1-naphthyl)-propan-1-one 12c

Yield: 22%; $[\alpha]_D^{22} = +24.9$ ($c$ 1, $CHCl_3$) 51% ee; After repeated crystallizations: $[\alpha]_D^{22} = +56.5$ ($c$ 1, $CHCl_3$) 100% ee; mp 168 °C (decompd.); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 9.67 (br s, 1H), 8.02–7.99 (m, 1H), 7.91–7.90 (m, 1H), 7.86 (d, $J$ = 8.5 Hz, 1H), 7.58 (d, $J$ = 7 Hz, 1H), 7.54–7.50 (m, 2H), 7.49 (d, $J$ = 8.5 Hz, 1H), 7.20–7.16 (m, 2H), 6.35 (dd, $J$ = 5 Hz, 2.5 Hz, 1H), 4.79 (d, $J$ = 1.5 Hz, 1H), 4.04 (d, $J$ = 1.5 Hz, 1H). HRMS calcd for $C_{18}H_{13}NO_2$ 263.0946, found 263.0944.

#### 4.2.22. *trans*-(−)-2,3-Epoxy-1-(2-pyrrolyl)-3-(2-naphthyl)-propan-1-one 12d

Yield: 29%; $[\alpha]_D^{22} = -40$ ($c$ 1, $CHCl_3$) 18% ee; mp 138–141 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 9.65 (br s, 1H), 7.83–7.88 (m, 4H), 7.49–7.53 (m, 2H), 7.39 (dd, $J$ = 8.5 Hz, 1.5 Hz, 1H), 7.19 (m, 1H), 7.14 (m, 1H), 6.33–6.35 (m, 1H), 4.34 (d, $J$ = 1.5 Hz, 1H), 4.11 (d, $J$ = 1.5 Hz, 1H). HRMS calcd for $C_{18}H_{13}NO_2$ 263.0946, found 263.0949.

### 4.3. General procedure for the preparation of α,β-enones having an *N*-methylpyrrole unit (15)

To a stirred solution of 2-acetyl-*N*-methylpyrrole (10 mmol) and the appropriate aromatic aldehyde (10 mmol) in 96% ethanol (8 $cm^3$), 10% aqueous KOH (8 $cm^3$) was added and stirred at rt. After the reaction was completed (monitored by TLC), the precipitate was filtered, washed with 96% ethanol and water, then dried. In case there was no precipitation, the solvent was removed from the mixture and the solid phase was filtered, then washed with 96% ethanol, with water, and finally dried. The crude product was crystallized from 96% ethanol (These procedures were not optimized).

#### 4.3.1. 1-(2-*N*-Methylpyrrolyl)-3-phenylpropen-2-en-1-one 15a

Yield: 86%; mp 108–110 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 7.73 (d, $J$ = 15.5 Hz, 1H), 7.61 (d, $J$ = 7 Hz, 2H), 7.42 (m, 1H), 7.39 (m, 2H), 7.38 (d, $J$ = 15.5 Hz, 1H), 7.11 (d, $J$ = 3 Hz, 1H), 6.88 (m, 1H), 6.20 (dd, $J$ = 3.5 Hz, 2.5 Hz, 1H), 4.04 (s, 3H).

#### 4.3.2. 1-(2-*N*-Methylpyrrolyl)-3-(2-chlorophenyl)-propen-2-en-1-one 15b

Yield: 62%; mp 82–84 °C; $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ (ppm): 8.13 (d, $J$ = 15.6 Hz, 1H), 7.71 (dd, $J$ = 5.7 Hz, 3.6 Hz, 1H), 7.42 (dd, $J$ = 5.7 Hz, 3.6 Hz, 1H), 7.37 (d, $J$ = 15.6 Hz, 1H), 7.29 (dd, $J$ = 5.7 Hz, 3.6 Hz, 2H), 7.10 (dd, $J$ = 4.2 Hz, 1.5 Hz, 1H), 6.89 (m, 1H), 6.20 (dd, $J$ = 4.1 Hz, 2.4 Hz, 1H), 4.04 (s, 3H).

#### 4.3.3. 1-(2-*N*-Methylpyrrolyl)-3-(3-chlorophenyl)-propen-2-en-1-one 15c

Yield: 45%; mp 87–88 °C; $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ (ppm): 7.66 (d, $J$ = 15.6 Hz, 1H), 7.59 (s, 1H), 7.48–7.44 (m, 1H), 7.38 (d, $J$ = 15.6 Hz, 1H), 7.35–7.32 (m, 2H), 7.11 (dd, $J$ = 4.2 Hz, 1.5 Hz, 1H), 6.89 (m, 1H), 6.21 (dd, $J$ = 3.9 Hz, 2.4 Hz, 1H), 4.03 (s, 3H).

#### 4.3.4. 1-(2-*N*-Methylpyrrolyl)-3-(4-chlorophenyl)-propen-2-en-1-one 15d

Yield: 52%; mp 122–124 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm):7.67 (d, $J$ = 15.5 Hz, 1H), 7.54 (d, $J$ = 8.5 Hz, 2 H), 7.37 (d, $J$ = 8.5 Hz, 2H), 7.36 (d, $J$ = 15.5 Hz, 1 H), 7.10 (d, $J$ = 3 Hz, 1H), 6.89 (m, 1H), 6.20 (dd, $J$ = 3.5 Hz, 2.5 Hz, 1H), 4.03 (s, 3H).

#### 4.3.5. 1-(2-*N*-Methylpyrrolyl)-3-(2-tolyl)-propen-2-en-1-one 15e

Yield: 55%; mp 90–91 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 8.03 (d, $J$ = 15.5 Hz, 1H), 7.66 (d, $J$ = 7.5 Hz, 1H), 7.32 (d, $J$ = 15.5 Hz, 1H), 7.28–7.20 (m, 3H), 7.11 (dd, $J$ = 4.2 Hz, 1.5 Hz, 1H), 6.88 (m, 1H), 6.20 (dd, $J$ = 4.1 Hz, 2.4 Hz, 1H), 4.04 (s, 3H), 2.47 (s, 3H).

#### 4.3.6. 1-(2-*N*-Methylpyrrolyl)-3-(3-tolyl)-propen-2-en-1-one 15f

Yield: 37%; mp 59–60 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 7.71 (d, $J$ = 15.5 Hz, 1H), 7.42 (s, 1H), 4.41 (d, $J$ = 4.5 Hz, 1H), 7.39 (d, $J$ = 15.5 Hz, 1H), 7.29 (t, $J$ = 3 Hz, 1H), 7.19 (d, $J$ = 4.5 Hz, 1H), 7.12 (dd, $J$ = 4.2 Hz, 1.5 Hz, 1H), 6.87 (m, 1H), 6.20 (dd, $J$ = 3.5 Hz, 2.5 Hz, 1H), 4.03 (s, 3H), 2.39 (s, 3H).

#### 4.3.7. 1-(2-*N*-Methylpyrrolyl)-3-(4-tolyl)-propen-2-en-1-one 15g

Yield: 41%; mp 65–66 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 7.72 (d, $J$ = 15.5 Hz, 1H), 7.51 (d, $J$ = 7.5 Hz, 2H), 7.36 (d, $J$ = 15.5 Hz, 1H), 7.21 (d, $J$ = 7.5 Hz, 2H), 7.11 (dd, $J$ = 4.2 Hz, 1.5 Hz, 1H), 6.87 (m, 1H), 6.20 (dd, $J$ = 3.5 Hz, 2.5 Hz, 1H), 4.03 (s, 3H), 2.38 (s, 3H).

#### 4.3.8. 1-(2-*N*-Methylpyrrolyl)-3-(1-naphthyl)-propen-2-en-1-one 15h

This product was extracted with $CHCl_3$ from the mixture after removal of the solvent, then column chromatographed on silica gel (eluent hexane/ethyl-acetate 100:5).

Yield: 63%; Oil. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ (ppm): 8.58 (d, $J$ = 15.3 Hz, 1H), 8.27 (d, $J$ = 8.1 Hz, 1H), 7.90–7.86 (m, 2H), 7.85 (d, $J$ = 7.2 Hz, 1H), 7.59–7.52 (m, 2H), 7.49 (d, $J$ = 8.1 Hz, 1H) 7.47 (d, $J$ = 15.3 Hz, 1H), 7.15 (dd, $J_2$ = 4.2 Hz, 1.5 Hz, 1H), 6.90 (m, 1H), 6.21 (dd, $J$ = 4.1 Hz, 2.4 Hz, 1H), 4.07 (s, 3H).

#### 4.3.9. 1-(2-*N*-Methylpyrrolyl)-3-(2-naphthyl)-propen-2-en-1-one 15i

Yield: 42%; mp 126–128 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 8.00 (s, 1H), 7.89 (d, $J$ = 15.5 Hz, 1H), 7.89–7.82 (m, 3H), 7.77 (d, $J$ = 8.5 Hz, 1H), 7.53 (d, $J$ = 15.5 Hz, 1H), 7.52–7.49 (m, 2H), 7.17 (dd, $J$ = 4.2 Hz, 1.5 Hz, 1H), 6.89 (m, 1H), 6.22 (dd, $J$ = 3.5 Hz, 2.5 Hz, 1H), 4.05 (s, 3H).

### 4.4. General procedure for the epoxidation of α,β-enones 15a–i with a 2-*N*-methylpyrrole unit

To a solution of α,β-enone (1.44 mmol) and the appropriate catalyst (0.1 mmol) in toluene (3 mL) was added 20% aq NaOH (1 mL) and the mixture was treated with 0.5 mL 5.5 M *tert*-butyl hydroperoxide in decane (2.88 mmol). The mixture was stirred at rt for 46–240 h. A new portion of toluene (7 mL) and water (2 mL) was then added and the mixture was stirred for several minutes. The organic phase was washed with 10% aqueous hydrochloric acid

(2 × 10 mL) and then with water (10 mL). The organic phase was dried ($Na_2CO_3$). The crude product obtained after evaporating the solvent was purified by preparative TLC (silica gel, hexane–ethyl acetate, 10:1 as the eluant) to give the chiral epoxyketone in a pure form. The enantiomeric excess was determined by $^1H$ NMR spectroscopy in the presence of Eu(hfc)$_3$ as a chiral shift reagent.

#### 4.4.1. *trans*-(−)-2,3-Epoxy-1-(2-*N*-methylpyrrolyl)-3-phenylpropan-1-one 13a

Yield: 80%; Oil. $[\alpha]_D^{22} = -209.5$ (*c* 1, $CHCl_3$) 79% ee; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm):7.39–7.34 (m, 5H), 7.14 (dd, *J* = 4 Hz, 1.5 Hz, 1H), 6.91 (m, 1H), 6.17 (dd, *J* = 4 Hz, 2.5 Hz, 1H), 4.11 (d, *J* = 1.5 Hz, 1H), 4.06 (d, *J* = 1.5 Hz, 1H), 3.99 (s, 3H). HRMS calcd for $C_{14}H_{13}NO_2$ 227.0946, found 227.0941.

#### 4.4.2. *trans*-(−)-2,3-Epoxy-1-(2-*N*-methylpyrrolyl)-3-(2-chlorophenyl)-propan-1-one 13b

Yield: 73%; $[\alpha]_D^{22} = -7$ (*c* 1, $CHCl_3$) 51% ee; mp 61–64 °C; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 7.38 (t, *J* = 2.5 Hz, 1H), 7.36 (t, *J* = 2.5 Hz, 1H), 7.30–7.28 (m, 2H), 7.16 (dd, *J* = 4.5 Hz, 1.5 Hz, 1H), 6.93 (m, 1H), 6.18 (dd, *J* = 4 Hz, 2.5 Hz, 1H), 4.44 (d, *J* = 2 Hz, 1H), 4.01 (s, 3H), 3.95 (d, *J* = 2 Hz, 1H). HRMS calcd for $C_{14}H_{12}ClNO_2$ 261.0557, found 261.0560.

#### 4.4.3. *trans*-(−)-2,3-Epoxy-1-(2-*N*-methylpyrrolyl)-3-(3-chlorophenyl)-propan-1-one 13c

Yield: 88%; $[\alpha]_D^{22} = -207$ (*c* 1, $CHCl_3$) 79% ee; mp 81–83 °C; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 7.33 (s, 1H), 7.32 (m, 2H), 7.25–7.23 (m, 1H), 7.14 (dd, *J* = 3.8 Hz, 1.5 Hz, 1H), 6.93 (m, 1H), 6.18 (dd, *J* = 4 Hz, 2.5 Hz, 1H), 4.10 (d, *J* = 2 Hz, 1H), 4.02 (*J* = 2 Hz, 1H), 3.99 (s, 3H). HRMS calcd for $C_{14}H_{12}ClNO_2$ 261.0557, found 261.0563.

#### 4.4.4. *trans*-(−)-2,3-Epoxy-1-(2-*N*-methylpyrrolyl)-3-(4-chlorophenyl)-propan-1-one 13d

Yield: 92%; $[\alpha]_D^{22} = -211.4$ (*c* 1, $CHCl_3$) 81% ee; mp 89–90 °C; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 7.35 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.13 (dd, *J* = 3.8 Hz, 1.5 Hz, 1H), 6.93 (m, 1H), 4.10 (d, *J* = 2 Hz, 1H), 4.01 (*J* = 2 Hz, 1H), 3.99 (s, 3H). HRMS calcd for $C_{14}H_{12}ClNO_2$ 261.0557, found 261.0554.

#### 4.4.5. *trans*-(−)-2,3-Epoxy-1-(2-*N*-methylpyrrolyl)-3-(2-tolyl)-propan-1-one 13e

Yield: 83%; Oil. $[\alpha]_D^{22} = -49.7$ (*c* 1, $CHCl_3$) 65% ee; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ (ppm): 7.33–7.30 (m, 1H), 7.26–7.22 (m, 2H), 7.18–7.17 (m, 1H), 7.16 (dd, *J* = 3.8 Hz, 1.5 Hz, 1H), 6.93 (m, 1H), 6.18 (dd, *J* = 4 Hz, 2.5 Hz, 1H), 4.25 (d, *J* = 1.8 Hz, 1H), 4.01 (s, 3H), 3.97 (d, *J* = 1.8 Hz, 1H), 2.37 (s, 3H). HRMS calcd for $C_{15}H_{15}NO_2$ 241.1103, found 241.1106.

#### 4.4.6. *trans*-(−)-2,3-Epoxy-1-(2-*N*-methylpyrrolyl)-3-(3-tolyl)-propan-1-one 13f

Yield: 79%; Oil. $[\alpha]_D^{22} = -196.8$ (*c* 1, $CHCl_3$) 70% ee; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ (ppm): 7.27–7.24 (m, 1H), 7.17–7.13 (m, 4H), 6.91 (m, 1H), 6.16 (dd, *J* = 4 Hz, 2.5 Hz, 1H), 4.08 (d, *J* = 1.5 Hz, 1H), 4.06 (d, *J* = 1.5 Hz, 1H), 3.99 (s, 3H), 2.37 (s, 3H). HRMS calcd for $C_{15}H_{15}NO_2$ 241.1103, found 241.1098.

#### 4.4.7. *trans*-(−)-2,3-Epoxy-1-(2-*N*-methylpyrrolyl)-3-(4-tolyl)-propan-1-one 13g

Yield: 83%; Oil. $[\alpha]_D^{22} = -216.3$ (*c* 1, $CHCl_3$) 79% ee; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ (ppm): 7.24 (d, *J* = 8.1 Hz, 2H), 7.18 (*J* = 8.1 Hz, 2H), 7.13 (dd, *J* = 4.2 Hz, 1.5 Hz, 1H), 6.91 (m, 1H), 6.16 (dd, *J* = 4.5 Hz, 2.4 Hz, 1H), 4.07 (d, *J* = 1.8 Hz, 1H), 4.05 (d, *J* = 1.8 Hz, 1H), 3.99 (s, 3H), 2.36 (s, 3H). HRMS calcd for $C_{15}H_{15}NO_2$ 241.1103, found 241.1107.

#### 4.4.8. *trans*-(+)-2,3-Epoxy-1-(2-*N*-methylpyrrolyl)-3-(1-naphthyl)-propan-1-one 13h

Yield: 72%; Oil. $[\alpha]_D^{22} = +88$ (*c* 1, $CHCl_3$) 70% ee; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ (ppm): 8.04–8.01 (m, 1H), 7.92–7.89 (m, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.59 (d , *J* = 6.9 Hz, 1H), 7.55–7.50 (m, 2H), 7.48 (d, *J* = 9 Hz, 1H), 7.14 (dd, *J* = 3.9 Hz, 1.5 Hz, 1H), 6.94 (m, 1H), 6.17 (dd, *J* = 3.9 Hz, 2.4 Hz, 1H), 4.75 (d, *J* = 1.8 Hz, 1H), 4.09 (d, *J* = 1.8 Hz, 1H), 4.06 (s, 3H). HRMS calcd for $C_{18}H_{15}NO_2$ 277.1103, found 277.1106.

#### 4.4.9. *trans*-(−)-2,3-Epoxy-1-(2-*N*-methylpyrrolyl)-3-(2-naphthyl)-propan-1-one 13i

Yield: 69%; $[\alpha]_D^{22} = -219.7$ (*c* 1, $CHCl_3$) 77% ee; mp 92–96 °C; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ (ppm): 7.88–7.82 (m, 4H), 7.52–7.48 (m, 2H), 7.40 (dd, *J* = 8.7 Hz, 1.2 Hz, 1H), 7.15 (dd, *J* = 4.2 Hz, 1.2 Hz, 1H), 6.92 (m, 1H), 6.17 (dd, *J* = 3.9 Hz, 2.4 Hz, 1H), 4.28 (d, *J* = 1.5 Hz, 1H), 4.16 (d, *J* = 1.5 Hz, 1H), 4.01 (s, 3H). HRMS calcd for $C_{18}H_{15}NO_2$ 277.1103, found 277.1100.

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