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Electrocyclic ring-opening reactions may cause failure of enolate alkylation of 1,4-oxazin-2-one based chiral glycine equivalents

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Dedicated to Professor H. Nöth with best wishes on the occasion of his 80th birthday

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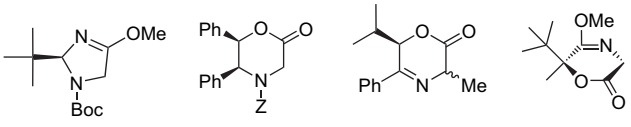
ABSTRACT

Attempted monoalkylation of 6-methyl-5,6-diphenyl-1,4-oxazin-2-one that had been designed as a chiral glycine equivalent gave even under optimized conditions only minute amounts of the desired monoalkylation product whereas an acyclic ketone was obtained repeatedly as the major product. This result indicates that the enolate of the chiral glycine equivalent is prone to an electrocyclic ring-opening reaction. This hypothesis could be further supported by additional experiments. Based on these results, it is reasonable to assume that electrocyclic ring-opening reactions are also the cause for the failure of alkylation reactions of structurally related glycine equivalents reported in the literature.

1. Introduction

Asymmetric syntheses of α-amino acids are a broad and well established field in organic chemistry. As non-natural α-amino acids often exhibit remarkable pharmacological and conformational properties—whether as free amino acids or as part of bioactive peptides—the area of research still grows at a rapid and constant pace.[1] In contrast to the numerous methods available for the asymmetric synthesis of α-monosubstituted α-amino acids, only a limited number exist for the synthesis of their α,α-disubstituted counterparts.[2]

The diastereoselective alkylation of a chiral glycine equivalent in the form of an enolate is certainly one of the most popular synthetic concepts applied to the preparation of α-monosubstituted α-amino acids.[1] High versatility and efficiency of the overall process are characteristics of many chiral glycine equivalents developed on the basis of this concept. Accordingly, a related strategy can also be expected to be a highly effective method for the synthesis of α,α-disubstituted α-amino acids. The chiral *tert*-butyl imidazole-1-carboxylate **1**[3] and the chiral oxazinone **2**[4] are well established examples developed in this field, i.e., the synthesis of α-quaternary α-amino acids. A further case is the oxazinone **3** in which one substituent of the final amino acid is already present in the scaffold as a result of its synthesis from alanine (Scheme 1). This method is therefore less flexible with respect to the substitution pattern of the final compound, i.e., the α-quaternary α-amino acid.[5]



1 2 3 4

Scheme 1.

2. Results and discussion

In a previous article, we introduced the 1,4-oxazinone **4** as a new chiral glycine equivalent for the preparation of α-monoalkylated as well as α,α-dialkylated α-amino acids. Alkylation reactions of **4** proceeded smoothly and with high diastereoselectivities for a wide variety of electrophiles and a final hydrolysis gave the target compounds in good yields.[6]

We now planned to extend our studies to the 1,4-oxazinone (*rac*)-**7**, which we expected to be of special value as a chiral glycine equivalent. As for related structures, alkylation reactions of the anion of (*rac*)-**7** can be expected to proceed with high diastereoselectivities. Just as important is the fact that the final amino acids should be easy to liberate as well. Mild acidic conditions

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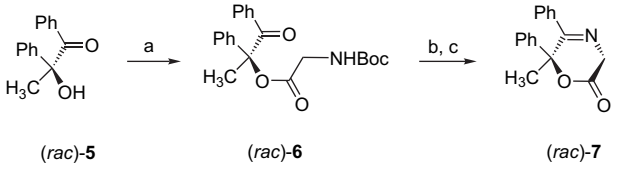
should suffice to remove the chiral auxiliary. Where appropriate, a hydrogenolytic procedure could be applied instead of a hydrolytic. The feasibility of the latter is the result of the benzylic positions of the two heteroatoms in the 1,4-oxazinone ring in (*rac*)-**7**, which was actually also an important facet in the design of (*rac*)-**7** as a chiral glycine equivalent (Scheme 2).



(*rac*)-**5** (*rac*)-**6** (*rac*)-**7**

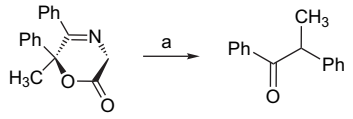
Scheme 2. (a) Boc-glycine, DCC, 4-DMAP, CH_2Cl_2, rt, 24 h, 37%; (b) TFA, CH_2Cl_2, rt,14 h; (c) acetate buffer pH 5, CH_2Cl_2, rt, 8 h, 79%.

The synthesis of the chiral glycine equivalent (*rac*)-**7** was performed according to the synthetic sequence outlined in Scheme 2 starting from 2-hydroxy-1,2-diphenylpropan-1-one [(*rac*-**5**]). For the sake of simplicity, we decided to synthesize **7** in its racemic form [(*rac*)-**7**] as neither of the two enantiomers of the chiral auxiliary present in (*rac*)-**7**, the α-hydroxyketone (*R*)-**5** or (*S*)-**5**, were available commercially. In the early phase of this study, there was yet no need to work with the chiral glycine equivalent in enantiopure form. Important characteristics, e.g., like its efficiency with respect to the asymmetric induction, could, of course, also be obtained from the racemic compound (*rac*)-**7**.

As the first step of the synthesis of (*rac*)-**7**, the racemic α-hydroxyketone (*rac*)-**5** was reacted in the presence of catalytic amounts of DMAP with Boc protected glycine activated with DCC to give the glycine ester (*rac*)-**6** in a 37% yield. In order to initiate the cyclization, (*rac*)-**6** was deprotected by treatment with trifluoroacetic acid and the reaction mixture brought to a pH of 5 whereupon the desired chiral glycine equivalent (*rac*)-**7** was formed in a 79% yield (Scheme 2).

As alkylation reactions of (*rac*)-**7** could be expected to proceed quite smoothly, our interest was largely focused on the asymmetric induction this process would proceed with. However, when (*rac*)-**7** was treated under standard conditions with 1.1 equiv of *s*-BuLi at −78 °C in THF followed by benzyl bromide as a model electrophile no alkylation product could be detected. Only the starting material and some decomposition product were present. Consequently, we varied the reaction conditions, i.e., the base (*s*-BuLi, NaHMDS, P_4-*t*-Bu, BTPP, BEMP, phase transfer reaction with KOH and Bu_4NBr in CH_2Cl_2, H_2O), the reaction temperature (−78 °C to 0 °C) and the solvent (THF, DME, CH_2Cl_2). The results, however, remained disappointing as either no alkylation product or only the double alkylated derivative (*rac*)-**9** was found (Scheme 3). In very few cases, in addition to the dibenzyl derivative (*rac*)-**9** and the starting material some of the desired monobenzylated compound (*rac*)-**8** (stereochemistry not assigned) was present in the crude reaction product (e.g., with BTPP) (Scheme 3). However, interestingly, for most of the performed alkylation reactions, no matter how the reaction conditions were adjusted, the same side product was observed, which was finally identified as the diphenylpropanone derivative (*rac*)-**10**.[7]

Searching for an explanation of this puzzling result, we wondered whether the side product (*rac*)-**10** possibly formed independently from the alkylation process simply as a consequence of treating (*rac*)-**7** with a base. To support our theory, (*rac*)-**7** was only reacted with *s*-BuLi and with NaHMDS. After aqueous workup, this led indeed to (*rac*)-**10** in each case though in varying amounts and with some starting material, (*rac*)-**7**, still present. When optimized (NaHMDS 1.1 equiv, THF, −78 °C, 4 days), the reaction went to completion providing (*rac*)-**10** after purification on silica gel in a 79% yield (Scheme 4).

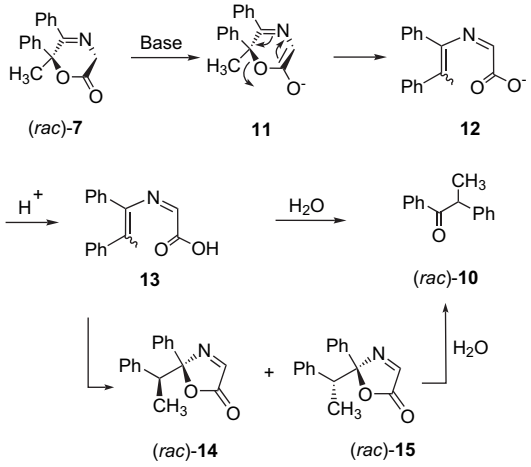


(*rac*)-**7** (*rac*)-**10**

Scheme 4. (a) NaHMDS, THF, −78 °C, 4 days, 79%.

An explanation for the formation of (*rac*)-**10** could be an electrocyclic ring-opening reaction. This seemed probable as, according to literature reports, double unsaturated six membered heterocyclic ring systems can undergo spontaneous ring-opening reactions depending on their substitution pattern.[8]

When the enolate **11**, which is the result of treating (*rac*)-**7** with a base, undergoes an electrocyclic ring-opening reaction the salt of the carboxylic acid **12** will form (Scheme 5). The higher thermodynamic stability of the carboxylic acid salt **12** compared to the enolate **11** can be considered as the driving force for the ring-opening reaction.



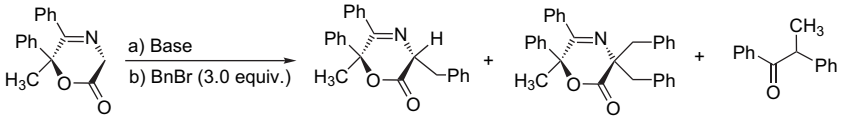
(*rac*)-**7** **11** **12**

13 (*rac*)-**10**

(*rac*)-**14** (*rac*)-**15**

Scheme 5.

In the presence of water, **12**, as a 2-azadiene, can be expected to undergo a hydrolytic cleavage, which is likely to first effect the imino subunit and subsequently the remaining enamine moiety. In any case, in addition to ammonia and glyoxalic acid, the ketone (*rac*)-**10** should form, the compound frequently found during the reactions above mentioned.



(*rac*)-**7** (*rac*)-**8** (*rac*)-**9** (*rac*)-**10**

Scheme 3.

A number of additional experiments were performed to gain more evidence whether the reaction mechanism proceeds as proposed above. Our aim was to prove the formation of the primary product of the ring-opening reaction: the carboxylic acid salt **12**. For the first experiment, the deprotonation was carried out in analogy to the set up described above, which had yielded (*rac*)-**10** in high amounts (NaHMDS 1.1 equiv, THF, −78 °C, 4 days). But the mixture was then liberated from solvent (at −40 °C) and the residue treated with trifluoroacetic acid (TFA, 1.1 equiv in CH_2Cl_2). These conditions were chosen to rule out any hydrolysis of **12** and to transform it in the free acid **13**. However, in the resulting reaction mixture significant amounts of the hydrolysis product (*rac*)-**10** (∼25%) were again present in addition to a mixture of two new stereoisomeric compounds. Under modified conditions (*s*-BuLi 1.1 equiv, THF, −78 °C, 6 days, removal of the solvent at −50 °C, TFA 1.0 equiv in MeOH at rt), the formation of (*rac*)-**10** could at last be significantly reduced (∼2%). This was a significant improvement as the two newly formed diastereomeric compounds underwent decomposition when subjected to column chromatography at silica gel or aluminium oxide for purification and therefore had to be characterized as a mixture of diastereomers out of the crude reaction mixture (^{1}H NMR, ^{13}C NMR, IR, HRMS). These compounds were found to be the oxazolinones (*rac*)-**14** and (*rac*)-**15**. Upon generation by protonation of **12**, the free acid **13** had apparently undergone a ring closure reaction by addition of the carboxylate function to the enamine moiety. In contrast to their precursors, the diastereomers (*rac*)-**14** and (*rac*)-**15** were sufficiently stable for isolation even though they underwent hydrolysis during chromatography and could also be completely converted to the ketone (*rac*)-**10** when treated with TFA (in H_2O).

Although the expected carboxylic acid **13** could not be detected, the results of these experiments, the formation of the diastereomers (*rac*)-**14** and (*rac*)-**15** as reaction products, clearly support our hypothesis on the nature of the reaction mechanism as proposed above.

Monosubstituted 1,4-oxazinone derivatives like **3** and pyrazinone analogues have been used quite extensively and with great success for enolate alkylation and the preparation of α-quaternary amino acids.[5,9] In contrast, for the parent compounds, the chiral glycine equivalents **16** and **17** (Fig. 1), only casual remarks have been reported about attempts of enolate alkylation reactions. According to these they end up with the dialkylation instead of the monoalkylation products only.[10,11] These results are similar to our observations for (*rac*)-**7** (see above), in which as far as alkylation reactions took place at all, the disubstituted derivative (*rac*)-**9** was found as the major product but still in low yields. As also outlined above, all attempts to optimize the reaction conditions for the formation of the monosubstituted derivative of (*rac*)-**7**, (*rac*)-**8**, remained fruitless. According to our results, the reason for this is the electrocyclic ring-opening reaction of the enolate **11**, which efficiently competes with the alkylation reaction. The same is likely to be true for the alkylation reactions of the oxazinone **16** and the pyrazinone **17**, too.

Interestingly, in the cases of 1,4-oxazinones and pyridazinones, as, for example, **16** and **17**, the ring-opening reaction of the individual enolates must be so fast that it does not allow an efficient subsequent trapping reaction by an electrophile, e.g., alkyl halide. But this changes when an α-substituent, as in **3**, is present. Then the ring-opening reaction of the enolate is slowed down in comparison to the alkylation reaction, which allows the latter to proceed. This is probably the reason why literature almost exclusively describes alkylation reactions of this type of chiral amino acid equivalents in which the first substituent in the α-positions of the carbonyl group is already present and a second is introduced.

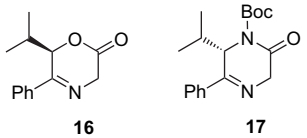


Figure 1.

3. Conclusion

In summary, the 1,4-oxazinone (*rac*)-**7** has been synthesized and evaluated for its suitability as a chiral glycine equivalent for the synthesis of α-substituted α-amino acids. But attempted monoalkylation reactions provided only minute amounts of the desired monoalkylation products if at all. Instead of significant amounts of a decomposition product, the ketone (*rac*)-**10** was found indicating that the enolate of the oxazinone (*rac*)-**7** had undergone an electrocyclic ring-opening reaction. This assumption was further supported by additional experiments in which a mixture of the diastereomeric oxazolidinones (*rac*)-**14** and (*rac*)-**15** was isolated. Obviously, under the workup conditions chosen, the initial product of the ring-opening reaction, the carboxylic acid salt **12**, undergoes a subsequent ring closure providing these compounds. The electrocyclic ring-opening reactions is likely to also be responsible for the failure of monoalkylation reactions of related chiral glycine equivalents, i.e., **16** and **17**, reported in the literature.

4. Experimental

4.1. General remarks

All experiments were carried out in oven-dried glassware under a dry N_2 atmosphere. Standard vacuum techniques were used for handling air-sensitive materials. Solvents were dried, kept under N_2 and freshly distilled before use. Reagents were used as commercially available. Mp (uncorrected values): melting point apparatus according to Dr. Tottoli (Büchi no. 510). NMR spectra: Jeol Eclipse +400 and Jeol Eclipse +500, chemical shifts (δ) are reported in parts per million. IR: FT-IR spectrometer Paragon 1000 (Perkin–Elmer), KBr pellets. MS: 5989 mass spectrometer with 59980 B Particle Beam LC/MS Interface (Hewlett–Packard). Combustion analysis: CHN Rapid (Fa. Heraeus). Column chromatography: on silica gel ((Merck 60) 0.040–0.063 mm). TLC plates 60 F-254, detection with UV (λ=254 nm) or with ammonium cerium(IV) heptamolybdate.

*4.1.1. (rac)-(1-Methyl-2-oxo-1,2-diphenylethyl) 2-[N-(1,1-dimethylethyloxycarbonyl)amino]ethanoate (rac)-**6***

N-tert-Butyloxycarbonylglycine (1.769 g, 10.10 mmol, 2.0 equiv), 2-hydroxy-1,2-diphenylpropan-1-one (1.142 g, 5.049 mmol) and DMAP (61.7 mg, 0.505 mmol, 0.1 equiv) were added to a solution of DCC (2.084 g, 10.10 mmol, 2.0 equiv) in CH_2Cl_2 (70 mL). The mixture was stirred for 72 h at rt. The solid material was filtered off and washed with CH_2Cl_2. The organic layer was washed with H_2O, dried over Na_2SO_4, filtrated and concentrated in vacuo. CC (heptane/EtOAc=8:2). Yield: 708.6 mg (37%), colourless crystals, mp 128–129 °C. TLC R_f=0.23 (heptane/EtOAc=8:2). ^{1}H NMR (400 MHz, CD_2Cl_2) δ=1.41 (s, 9H, $(CH_3)_3C$), 1.92 (s, 3H, CH_3), 3.71 (dd, J=18.3, 5.1 Hz, 1H, CH_2), 3.98 (dd, J=18.3, 6.2 Hz, 1H, CH_2), 4.77–4.86 (br s, 1H, NH), 7.26–7.80 (m, 10H, H_{aromat}) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2) δ=27.0 (CH_3), 28.6 ($(CH_3)_3C$), 43.5 (CH_2), 80.4 ($(CH_3)_3C$), 88.4 (CH_3CO), 124.7 (CH_{aromat}), 128.7 (CH_{aromat}), 128.8 (CH_{aromat}), 129.6 (CH_{aromat}), 129.6 (CH_{aromat}), 133.0 (CH_{aromat}), 135.1 (C_{aromat}), 140.6 (C_{aromat}), 156.0 (NHC=O), 169.7 (CH_2C=O), 196.6 (PhC=O) ppm. MS (CI, CH_5^+), m/z (%): 384 (16) $[M+H]^+$, 209 (100). IR (KBr): $\tilde{\nu}$=3326, 1734, 1678, 1527, 1310 cm^{-1}. $C_{22}H_{25}NO_5$ (383.45) calcd: C 68.91, H 6.57, N 3.65; found: C 68.80, H 6.65, N 3.58.

*4.1.2. (rac)-6-Methyl-5,6-diphenyl-3,6-dihydro-2H-1,4-oxazin-2-one (rac)-**7***

TFA (664 mg, 448 μL, 5.82 mmol, 10.0 equiv) was added to a solution of (*rac*)-**6** (223.0 mg, 0.5822 mmol) in CH_2Cl_2 (5.8 mL). The mixture was stirred for 14 h at rt. The solvent was evaporated in vacuo. The residue was dissolved in CH_2Cl_2 (2.4 mL), acetate buffer pH 5 (4.8 mL) was added and the mixture was stirred at rt for 14 h. The organic layer was separated and the aqueous solution was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtrated and concentrated in vacuo. CC (heptane/EtOAc=7:3). Yield: 121.1 mg (79%), colourless oil. TLC: R_f=0.28 (*iso*-hexane/EtOAc=7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ=1.92 (s, 3H, CH_3), 4.07 (d, J=21.0 Hz, 1H, CH_2), 4.75 (d, J=21.0 Hz, 1H, CH_2), 7.33–7.49 (m, 10H, H_{aromat}) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2) 27.5 (CH_3), 52.3 (CH_2), 86.2 (C), 126.8 (CH_{aromat}), 128.7 (CH_{aromat}), 129.8 (CH_{aromat}), 130.0 (CH_{aromat}), 130.4 (CH_{aromat}), 138.0 (C_{aromat}), 139.6 (C_{aromat}), 168.3 (C=O), 171.1 (C=O) ppm. MS (CI, CH_5^+), m/z (%): 266 (7) $[M+H]^+$, 211 (87), 209 (100). IR (KBr): $\tilde{\nu}$=3060, 1752, 1445, 1265 cm^{-1}. HRMS (EI$^+$, 70 eV) calcd for $C_{17}H_{15}NO_2$: 265.1103; found: 265.1111. $C_{17}H_{15}NO_2$ (265.31) calcd: C 76.96, H 6.70, N 5.28; found: C 76.45, H 5.76, N 5.17.

*4.1.3. (rac)-3,3-Dibenzyl-6-methyl-5,6-diphenyl-3,6-dihydro-2H-1,4-oxazin-2-one (rac)-**9***

KOH (8.4 mg, 0.15 mmol, 4.0 equiv), Bu_4NBr (1.2 mg, 0.004 mmol, 0.1 equiv) and benzyl bromide (19.2 mg, 13 μL, 0.112 mmol, 3.0 equiv) were added to a solution of (*rac*)-**7** (9.9 mg, 0.037 mmol) in CH_2Cl_2 (0.6 mL) at 0 °C. The mixture was stirred for 5 h at 0 °C. Phosphate buffer (pH 7) was added, the organic layer was separated and the liquid phase extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. CC (heptane/EtOAc=7:3). Yield: 5.1 mg (31%), colourless crystals, mp: 188–190 °C. TLC: R_f=0.44 (*iso*-hexane/EtOAc=7:3). ^{1}H NMR (500 MHz, CD_2Cl_2) δ=0.67 (s, 3H, CH_3), 3.31 (d, J=12.8 Hz, 1H, CH_2), 3.36 (d, J=12.8 Hz, 1H, CH_2), 3.70 (d, J=12.8 Hz, 1H, CH_2), 3.76 (d, J=12.8 Hz, 1H, CH_2), 5.93–5.97 (m, 2H, H_{aromat}), 6.85–6.88 (m, 2H, H_{aromat}), 6.89–6.94 (m, 2H, H_{aromat}), 7.10 (t, J=7.4 Hz, 1H, H_{aromat}), 7.12–7.17 (m, 2H, H_{aromat}), 7.23–7.40 (m, 11H, H_{aromat}) ppm. ^{13}C NMR (125 MHz, CD_2Cl_2) δ=24.0 (CH_3), 47.8 (CH_2), 47.9 (CH_2), 68.2 (*C*CH_2Ph), 87.5 (CH_3*C*), 128.1 (CH_{aromat}), 129.1 (CH_{aromat}), 129.3 (CH_{aromat}), 129.4 (CH_{aromat}), 129.9 (CH_{aromat}), 129.9 (CH_{aromat}), 130.0 (CH_{aromat}), 130.2 (CH_{aromat}), 130.3 (CH_{aromat}), 130.6 (CH_{aromat}), 132.8 (CH_{aromat}), 133.1 (CH_{aromat}), 138.0 (C_{aromat}), 138.1 (C_{aromat}), 138.7 (C_{aromat}), 140.5 (C_{aromat}), 166.2 (C=N), 168.7 (C=O) ppm. MS (CI, CH_5^+), m/z (%): 446 (27) $[M+H]^+$, 266 (100). IR (KBr): $\tilde{\nu}$=2921, 1721, 646, 1350, 1091, 702, 695 cm^{-1}. HRMS (EI$^+$, 70 eV) calcd for $C_{31}H_{27}NO_2$: 445.2042, found: 445.2054.

*4.1.4. (rac)-1,2-Diphenylpropan-2-one (rac)-**10***

NaHMDS (33 μL, 0.066 mmol, 2.0 M solution in THF, 1.1 equiv) was added to a solution of (*rac*)-**7** (15.9 mg, 0.060 mmol) in THF (0.7 mL) at −78 °C. The mixture was stirred for 96 h at −78 °C. Phosphate buffer was added, the organic layer was separated and the liquid phase extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. CC (heptane/EtOAc=7:3). Yield: 10 mg (79%),[7] colourless oil. TLC: R_f=0.5 (heptane/EtOAc=7:3). ^{1}H NMR (500 MHz, $CDCl_3$) δ=1.54 (d, J=6.9 Hz, 3H, CH_3), 4.70 (q, J=6.9 Hz, 1H, CH), 7.17–7.22 (m, 1H, H_{aromat}), 7.27–7.30 (m, 4H, H_{aromat}), 7.37–7.40 (m, 2H, H_{aromat}), 7.45–7.49 (m, 1H, H_{aromat}), 7.93–7.96 (m, 2H, H_{aromat}) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.5 (CH_3), 47.9 (CH), 126.9 (CH_{aromat}), 127.8 (CH_{aromat}), 128.0 (CH_{aromat}), 128.8 (CH_{aromat}), 129.0 (CH_{aromat}), 132.8 (CH_{aromat}), 136.5 (C_{aromat}), 141.5 (C_{aromat}), 200.3 (C=O) ppm. MS (CI, CH_5^+), m/z (%): 211 (100) $[M+H]^+$. IR (KBr): $\tilde{\nu}$=2973, 2927, 1677, 1447, 1224 cm^{-1}. HRMS (EI$^+$, 70 eV) $[M+H]^+$ calcd for $C_{15}H_{14}O$: 210.1045; found: 210.1057.

*4.1.5. (2RS)-2-Phenyl-2-((1RS)-1-phenylethyl)oxazol-5(2H)-one (rac)-**14** and (2RS)-2-phenyl-2-((1SR)-1-phenylethyl)-oxazol-5(2H)-one (rac)-**15***

(A) NaHMDS (53 μL, 0.11 mmol, 2.0 M solution in THF, 1.1 equiv) was added to a solution of (*rac*)-**7** (25.3 mg, 0.0954 mmol) in THF (1.0 mL) at −78 °C. The mixture was stirred for 4 days at −78 °C. The solvent was evaporated in vacuo. TFA (1.05 mL, 1.05 mmol, 0.1 M in CH_2Cl_2, 1.1 equiv) was added and the mixture was concentrated in vacuo. The oily residue was measured by ^{1}H NMR spectroscopy in $CDCl_3$. The ratio of [(*rac*)-**14**+(*rac*)-**15**]/(*rac*)-**7** was 75:25.

(B) *s*-BuLi (45 μL, 0.0634 mmol, 1.4 M solution, in cyclohexane 1.1 equiv) was added to a solution of (*rac*)-**7** (15.3 mg, 0.0577 mmol) in THF (0.6 mL) at −78 °C and stirred for 6 days at −78 °C. Then the solvent was removed at −50 °C in vacuo. TFA (577 μL, 0.0577 mmol, 0.1 M in MeOH 1.0 equiv) was added at rt, the solvent was evaporated in vacuo and the residue was measured by ^{1}H NMR spectroscopy in $CDCl_3$. The ratio of [(*rac*)-**14**+(*rac*)-**15**]/(*rac*)-**7** was 98:2.

(*rac*)-**14**+(*rac*)-**15**, colourless oil. TLC: R_f=0.26 (heptane/EtOAc=8:2). ^{1}H NMR (400 MHz, CD_2Cl_2)[12] δ=1.27 (d, J=7.2 Hz, 3H, CH_3), 1.28 (d, J=7.2 Hz, 3H, CH_3), 3.67 (q, J=7.2 Hz, 1H, CH), 3.69 (q, J=7.2 Hz, 1H, CH), 7.06–7.62 (m, 20H, H_{aromat}), 7.38 (s, 1H, CH=N), 7.67 (s, 1H, CH=N) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2)[12] δ 15.1(CH_3), 15.3 (CH_3), 49.2 (CH), 49.4 (CH), 111.8 (C(O)N), 112.1 (C(O)N), 126.3 (CH_{aromat}), 126.6 (CH_{aromat}), 127.3 (CH_{aromat}), 127.5 (CH_{aromat}), 127.8 (CH_{aromat}), 128.0 (CH_{aromat}), 128.2 (CH_{aromat}), 128.4 (CH_{aromat}), 128.6 (CH_{aromat}), 128.8 (CH_{aromat}), 129.5 (CH_{aromat}), 129.8 (CH_{aromat}), 137.4 (C_{aromat}), 137.6 (C_{aromat}), 138.26 (C_{aromat}), 138.31 (C_{aromat}), 151.0 (C=N), 152.8 (C=N), 163.9 (C=O), 164.5 (C=O) ppm. MS (CI, CH_5^+), m/z (%): 266 (100) $[M+H]^+$. IR (KBr): $\tilde{\nu}$=3442, 3062, 2979, 1785, 1683, 1450, 1214 cm^{-1}. HRMS (EI$^+$, 70 eV) calcd for $C_{17}H_{15}NO_2$: 265.1103, found: 265.1104.

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