β-Lithiation of oxazolinyloxiranes: synthetic utility

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Dedicated to Professor Branko Stanovnik

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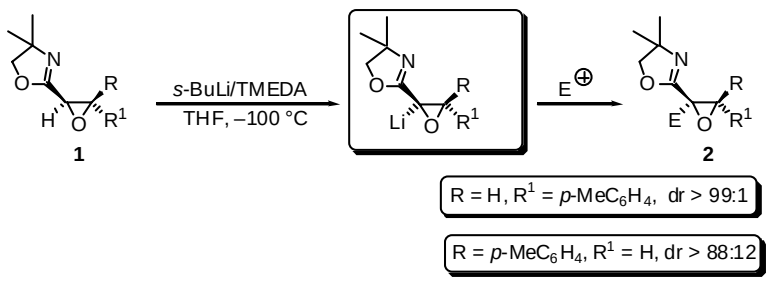
Abstract

β–Lithiated oxazolinyloxirane **13a**, generated by deprotonation of (*R**, *R**) trisubstituted oxazolinyloxirane **12a** with *s*-BuLi/TMEDA in Et_2O at –100 °C, was found to be chemically and configurationally stable for at least 1 h at this temperature and reacted stereospecifically with electrophiles to give the corresponding tetrasubstituted derivatives **14a–j** with complete retention of configuration at the β–carbon.

Keywords: Lithiation, oxazolinyloxiranes, oxiranyllithiums

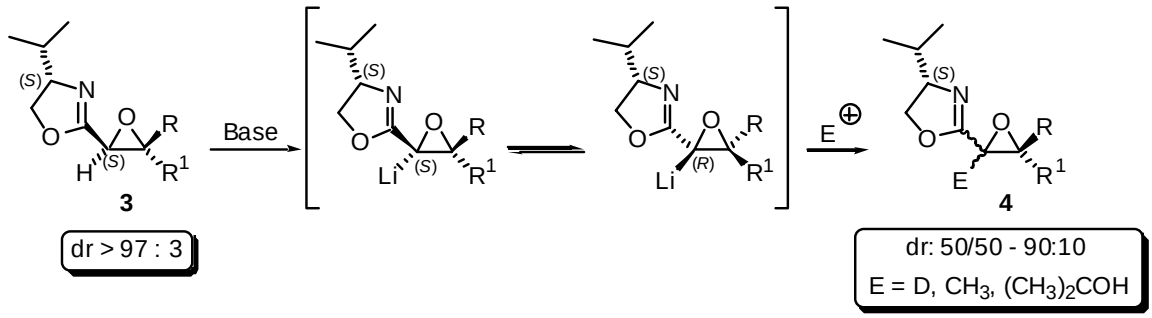
Introduction

Over the past fifteen years the oxiranyl anion-based methodology, a useful synthetic route to functionalized epoxides,[1] has been addressed a considerable interest due to the contribution of numerous research groups,[2] our research group included. In previous papers we demonstrated that α-lithiated oxazolinyloxiranes are sufficiently stable to be trapped with electrophiles.[3] In particular, we could prove that lithiation of *cis* and *trans* oxazolinyloxiranes of the kind of **1** followed by the reaction with electrophiles proceeded stereospecifically with retention of configuration under proper conditions to give α-substituted oxazolinyloxiranes **2** (Scheme 1).[4]



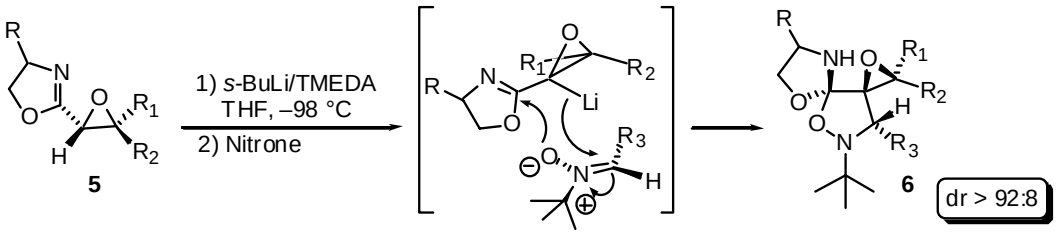
Scheme 1

However, oxiranyllithiums generated by lithiation of optically enriched oxazolinyloxiranes **3** underwent deuteration, alkylation and hydroxyalkylation (addition to carbonyl compounds) to give the corresponding α-substituted derivatives **4** in a poor diastereoselective manner (Scheme 2).[4,5]



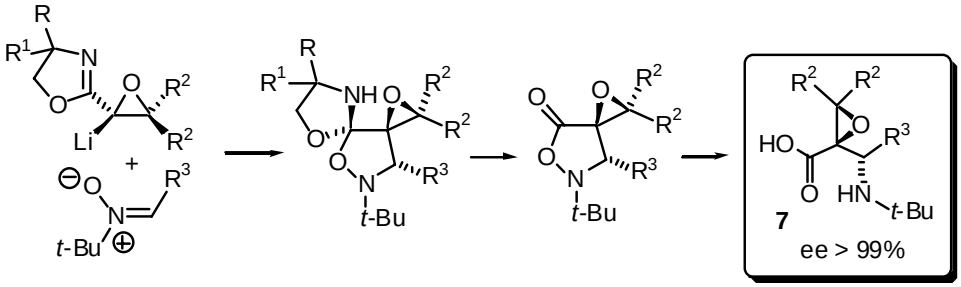
Scheme 2

In contrast, the addition of oxazolinyloxiranyllithiums derived from oxazolinyloxiranes **5** to nitrones occurred highly stereoselectively to give 1,5,9-trioxa-8,10-diazadispiro[2.0.4.3] undecanes **6** (Scheme 3).[6]



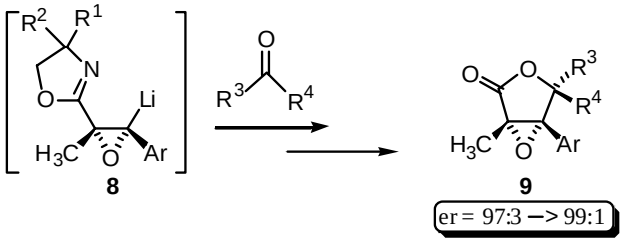
Scheme 3

This observation led us to develop a strategy for the synthesis of α-epoxy-β-amino acids **7** (Scheme 4).[7]



Scheme 4

Counting on the configurational stability of aryl-substituted lithiated oxiranes which allowed us to synthesize styrene oxide derivatives and an optically active oral antifungal agent of industrial interest,[8] we have also reported[9] that oxazolinyl α-β–aryltrisubstituted oxiranes can be β-lithiated and trapped with electrophiles. In particular, the reaction of (*R**, *S**) configured lithiated isomers **8** with carbonyl compounds allowed the development of a synthetic procedure to α,β-epoxy-γ-butyrolactones **9**, which are a recurrent structural motif in many natural products of interest in medicinal chemistry (Scheme 5).

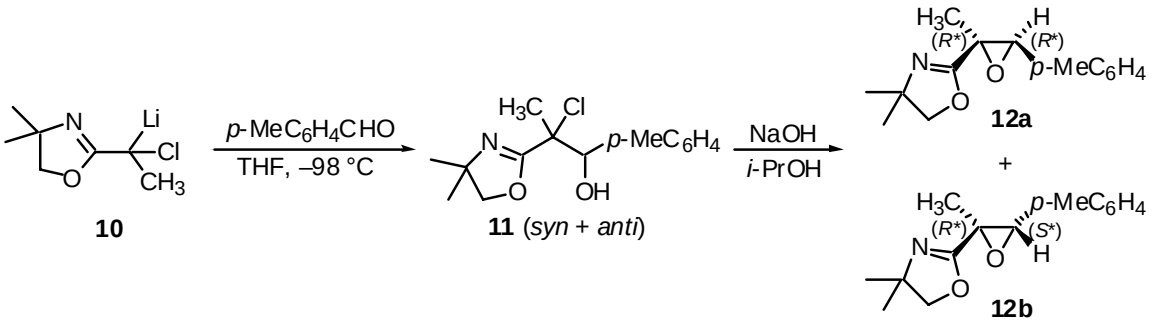


Scheme 5

In connection with a research project mainly based on the use of this oxiranyl anion-based methodology for synthetic purposes we report herein on the β-lithiation of (*R**, *R**) configured α,β–disubstituted oxazolinyloxiranes. One example of β-lithiation in substituted oxiranes has been recently reported.[10]

Results and Discussion

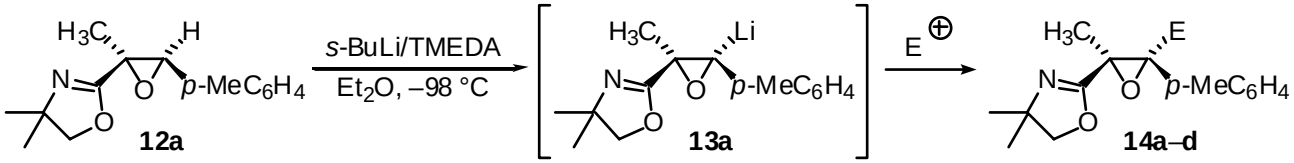
(1*R**, 2*R**)- and (1*R**, 2*S**)-1,2-Epoxy-2-(4,4-dimethyl-2-oxazolin-2-yl)-1-*p*-tolylpropanes **12a,b** were synthesized by the Darzens reaction[11] of lithiated 2-(1-chloroethyl)-4,4-dimethyl-2-oxazoline **10** with 4-methylbenzaldehyde according to a reported general procedure.[12] The addition of 4-methylbenzaldehyde to a precooled THF solution of 10 at –98 °C furnished a diastereomeric mixture (*syn* + *anti*) of the chlorohydrins **11**, which, without separation, were cyclized to the epoxides **12** upon treatment with NaOH/*i*-PrOH.[12] Column chromatography separation (petroleum ether/AcOEt 7/3) gave pure 1,2-epoxy-2-(4,4-dimethyl-2-oxazolin-2-yl)-1-*p*-tolylpropanes **12a** and **12b** (overall yield 71 %, 1*R**, 2*S**/1*R**, 2*R** ratio = 1.3/1) whose configuration was established by ^{13}C NMR, as reported (Scheme 6).[9,13]



Scheme 6

Then, pure (1*R**, 2*R**)–**12a** was subjected to lithiation. Treatment of **12a** with *s*-BuLi (1.2 equiv) in the presence of TMEDA (1.2 equiv) in Et_2O at –100 °C produced a red solution of **13a**, which proved to be chemically and configurationally stable at this temperature for at least 1 h. Indeed, the deuterium quenching of the warmed up solution of **13a** gave the corresponding β-deuterated starting epoxide **14a** (> 98 % D) in excellent yield (> 98 %). Such a configurational stability is not unexpected if we just consider that lithiated styrene oxides (and **13a** is a lithiated substituted styrene oxide) are configurationally stable.[8,9] The stabilizing assistance in this case should be likely provided only by the aryl group. The configurational stability of **13a** was also confirmed by its reactions with other electrophiles: methylation, trimethylsilylation and allylation took place stereospecifically with complete retention of configuration at the β-carbon to give trisubstituted epoxides **14b-d** (Table 1).

Table 1. Reaction of **13a** with electrophiles



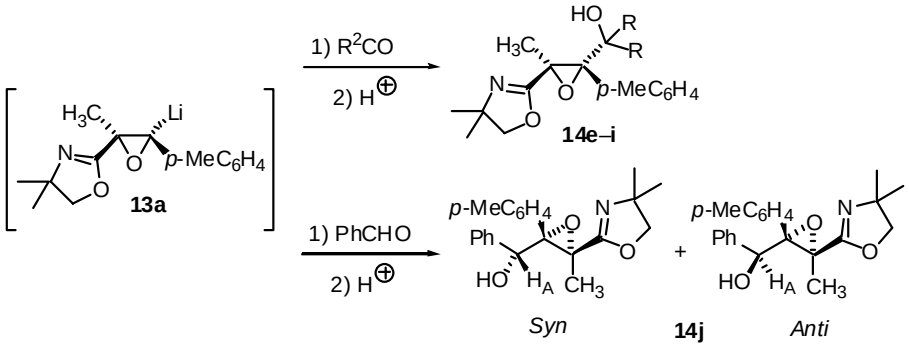
Electrophile	Product (% yield)[a]	dr[b]
D_2O	**14a** (>98)	> 98:2
MeI	**14b** (85)	"
TMSCl	**14c** (41)	"
CH_2=$CHCH_2Br$	**14d** (65)	"

[a] Isolated yield by column chromatography. [b] Diastereomeric ratio determined by ^{1}H NMR spectroscopy; only one diastereomer in the ^{1}H NMR spectrum of the crude product.

Oxiranes **14b–d** were assigned the same *R**, *R** configuration of the starting epoxide **12a** on the basis of the opposite stereochemistry found in the reaction of lithiated **12b** with the same

electrophiles.[9] The reaction of **13a** with symmetrical aliphatic, aromatic and alicyclic ketones similarly occurred with retention of configuration providing in good yields the corresponding oxazolinyl-β-epoxy alcohols **14e–i** (Table 2).

Table 2. Reaction of **13a** with carbonyl compounds



Electrophile	Product (% yield)[a]	dr[b]
$(CH_3)_2CO$	**14e** (46)	> 98:2
$(CH_3CH_2)_2CO$	**14f** (42)	"
Ph_2CO	**14g** (70)	"
Cyclopentanone	**14h** (63)	"
Cyclohexanone	**14i** (89)	"
Benzaldehyde	**14j** (44)[c]	"

[a] Isolated yield by column chromatography. [b] Diastereomeric ratio determined by ^{1}H NMR spectroscopy; only one diastereomer in the ^{1}H NMR spectrum of the crude product.[c] Overall isolated yield in both *syn* and *anti* stereoisomers (*syn*/*anti* = 1.2/1) separable by column chromatography (silica gel, AcOEt/petroleum ether 8/2).

The reaction of **13a** with benzaldehyde furnished a mixture of *syn* and *anti* oxazolinyl epoxy alcohols **14j**[14] with no stereoselectivity with reference to the newly created stereogenic center. These stereoisomers could be easily separated by column chromatography even if in a low overall yield as, in consequence of a prolonged contact on silica gel, they tended to revert to the starting epoxide and the corresponding carbonyl compound (retroaldol reaction) (Table 2). The assignment of *syn* (or *anti*) stereochemistry was made on the basis of the characteristic resonance of the carbinol hydrogen (H_A) that in the case of the *anti* isomer was shifted downfield compared to that of the *syn* isomer, as reported for similar oxazolinyl epoxy alcohols.[4]

Conclusions

In conclusion, we have applied the oxiranyl anion-based methodology for the β-functionalization of trisubstituted β-aryloxazolinyloxiranes (*R**, *R**) configured obtaining the corresponding stereodefined tetrasubstituted derivatives that seem to be promising in synthetic organic chemistry for the possible elaboration of one or both the oxazolinyl and the oxiranyl ring. The β-deprotonation occurred with complete retention of configuration at the β-carbon. It is worth noting that there is no influence of steric effects on the configurational stability of such lithiated styrene oxide derivatives. The chiral version of the above-described deprotonation-trapping sequence of oxazolinyl aryl oxiranes is under way in our lab and results will be reported in due course.

Experimental Section

General Procedures. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were freshly distilled under a nitrogen atmosphere over sodium/benzophenone ketyl. *N*, *N*, *N*', *N*'-Tetramethylethylenediamine (TMEDA) was distilled over finely powdered calcium hydride. All other chemicals were of commercial grade and used without further purification. Petroleum ether refers to the 40-60 °C boiling fraction. Commercial solutions of *n*-BuLi (2.5 M solution in hexanes) and *s*-BuLi (1.3 M solution in cyclohexane) were titrated by using *N*-pivaloyl-*o*-toluidine prior to use.[15] For the ^1H and ^{13}C NMR spectra (^1H NMR 300, 500 MHz; ^{13}C NMR 75.4, 125 MHz), $CDCl_3$ was used as the solvent. GC-MS spectrometry analyses were performed on a gas chromatograph HP 5890 II (dimethylsilicon capillary column, 30 m, 0.25 mm i.d.) equipped with a mass selective detector operating at 70 eV (EI). Melting points were uncorrected. TLC was performed on Merck silica gel plates with F-254 indicator; visualization was accomplished by UV light (254 nm) or by exposing to I_2 vapour. All reactions involving air-sensitive reagents were performed under nitrogen in oven-dried glassware using syringe-septum cap technique.

General procedure for preparation of β-substituted oxazolinyl *p*-tolyloxiranes 14a-j
A solution of **12a** (100 mg, 0.41 mmol) and TMEDA (0.074 mL, 0.50 mmol) in 5 mL of dry Et_2O at –98 °C (methanol/liquid nitrogen bath) and under N_2 was treated with *s*-BuLi (0.42 mL, 0.50 mmol, 1.2 M), and the resulting orange mixture was stirred for 1 h at –98 °C. Then, the electrophile (1.2 mmol) was added at once at this temperature, as pure liquid or as a solution in 1 mL of Et_2O if solid. The resulting reaction mixture was allowed to warm up to room temperature, and quenched with sat. aq. NH_4Cl. Then it was poured into saturated brine (20 mL), extracted with Et_2O (3 × 10 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The crude mixture was flash-chromatographed (silica gel; petroleum ether/AcOEt 8-7/2-3) to give the corresponding β-substituted epoxides, which showed the following data:

(*R, *R**)-1-Deutero-1,2-epoxy-2-(4,4-dimethyl-2-oxazolin-2-yl)-*p*-tolylpropane (14a).** >98 %, >98 % D, dr > 98:2, oil. ^{1}H NMR (500 MHz) δ: 0.94 (s, 3 H), 1.01 (s, 3 H), 1.64 (s, 3 H), 2.25 (s, 3 H), 3.62 (s, 2 H), 7.07–7.20 (m, 4 H). GC-MS (70 eV) *m/z* (%): 246 (1, M^+), 231 (5), 203 (4), 147 (100), 119 (8), 91 (7), 43 (7).

(*R, *R**)-2,3-Epoxy-2-(4,4-dimethyl-2-oxazolin-2-yl)-3-*p*-tolylbutane (14b).** 85 %, dr > 98:2, oil. ^{1}H NMR (500 MHz) δ: 0.77 (s, 3 H), 0.91 (s, 3 H), 1.64 (s, 3 H), 1.66 (s, 3 H), 2.26 (s, 3 H), 3.47 (d, *J* = 8.0 Hz, 1 H), 3.54 (d, *J* = 8.0 Hz, 1 H), 7.02–7.22 (m, 4 H). ^{13}C NMR (125 MHz) δ: 16.9, 20.3, 27.5, 27.7, 61.7, 66.0, 66.9, 78.9, 126.1, 128.1, 136.7, 163.1. GC-MS (70 eV) *m/z* (%): 228 (10, M^+–31), 202 (5), 146 (100), 119 (11), 91 (13), 43 (93). FT-IR (film, cm^{-1}): 2967, 2929, 1657 (C=N), 1516, 1461, 1382, 1185, 1091, 975, 821. Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.47; H, 8.39; N, 5.55.

(*R,*R**)-1,2-Epoxy-1-trimethylsilyl-2-(4,4-dimethyl-2-oxazolin-2-yl)-1-*p*-tolylpropane (14c).** 41 %, dr > 98:2, oil. ^{1}H NMR (500 MHz) δ: 0.07 (s, 9 H), 0.77 (s, 3 H), 0.94 (s, 3 H), 1.71 (s, 3 H), 2.26 (s, 3 H), 3.31 (d, *J* = 8.0 Hz, 1 H), 3.54 (d, *J* = 8.0 Hz, 1 H), 6.92–7.14 (m, 4 H). ^{13}C NMR (125 MHz) δ: –1.11, 19.2, 21.3, 27.9, 61.6, 65.8, 67.1, 79.0, 125.7, 127.9, 129.4, 135.9, 137.0, 164.2. GC-MS (70 eV) *m/z* (%): 317 (15, M^+), 316 (53), 260 (12), 244 (35), 218 (100), 176 (27), 161 (35), 119 (30), 100 (74), 73 (98). FT-IR (film, cm^{-1}): 2965, 2928, 1654 (C=N), 1510, 1461, 1364, 1250, 1108, 972, 842, 757. Anal. Calcd for $C_{18}H_{27}NO_2Si$: C, 68.09; H, 8.57; N, 4.41. Found: C, 68.43; H, 8.80; N, 4.45.

(*R, *R**)-4,5-Epoxy-5-(4,4-dimethyl-2-oxazolin-2-yl)-4-*p*-tolylhex-1-ene (14d).** 65 %, dr > 98:2, oil. ^{1}H NMR (500 MHz) δ: 0.76 (s, 3 H), 0.94 (s, 3 H), 1.71 (s, 3 H), 2.26 (s, 3 H), 2.54–2.80 (m, 2 H), 3.44 (d, *J* = 8.0 Hz, 1 H), 3.55 (d, *J* = 8.0 Hz, 1 H), 4.91–5.02 (m, 2 H), 5.48–5.74 (m, 1 H), 7.02–7.20 (m, 4 H). ^{13}C NMR (125 MHz) δ: 16.8, 27.7, 38.5, 46.8, 61.6, 67.0, 68.2, 78.9, 118.3, 127.0, 128.0, 132.2, 134.8, 136.7, 163.2. GC-MS (70 eV) *m/z* (%): 270 (2, M^+-15), 186 (38), 143 (23), 128 (30), 119 (19), 115 (11), 91 (15), 69 (100), 41 (66). FT-IR (film, cm^{-1}): 2965, 2928, 1655 (C=N), 1461, 1365, 1184, 1076, 990, 818. Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91. Found: C, 75.89; H, 8.50; N, 4.94.

(*R, *S**)-3,4-Epoxy-4-(4,4-dimethyl-2-oxazolin-2-yl)-2-methyl-3-*p*-tolylpentan-2-ol (14e).** 46 %, dr > 98:2, mp 102–104 °C (Et_2O). ^{1}H NMR (500 MHz) δ: 0.64 (s, 3 H), 0.98 (s, 3 H), 1.03 (s, 3 H), 1.50 (s, 3 H), 1.97 (s, 3 H), 2.28 (s, 3 H), 2.41 (br. s, exchanges with D_2O), 3.43 (d, *J* = 8.0 Hz, 1 H), 3.52 (d, *J* = 8.0 Hz, 1 H), 6.99–7.32 (m, 4 H). ^{13}C NMR (125 MHz) δ: 16.1, 21.1, 24.9, 27.4, 27.7, 30.4, 62.8, 66.9, 71.0, 79.1, 108.2, 111.4, 126.9, 127.3, 128.4, 128.6, 133.7, 137.2, 163.4. GC-MS (70 eV) *m/z* (%): 244 (100, M^+-CH_3COHCH_3), 204 (16), 161 (44), 142 (34), 119 (44), 91 (24). FT-IR (film, cm^{-1}): 3372 (br. OH), 2965, 1648 (C=N), 1461, 1364, 1316, 1191, 1111, 1076, 813. Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62. Found: C, 71.59; H, 8.70; N, 4.56.

(*R, *S**)-4,5-Epoxy-5-(4,4-dimethyl-2-oxazolin-2-yl)-3-ethyl-4-*p*-tolylhexan-3-ol (14f).** 42 %, dr > 98:2, mp 83–84 °C (hexane). ^{1}H NMR (500 MHz) δ: 0.57 (s, 3 H), 0.85–0.88 (m, 3 H), 0.97 (s, 3 H), 1.13–1.16 (m, 3 H), 1.29–1.37 (m, 2 H), 1.79–1.86 (m, 2 H), 1.97 (s, 3 H), 2.20 (br. s, exchanges with D_2O, 1 H), 2.28 (s, 3 H), 3.44 (d, *J* = 8.0 Hz, 1 H), 3.47 (d, *J* = 8.0 Hz, 1 H),

6.98–7.40 (m, 4 H). ^{13}C NMR (125 MHz) δ: 11.3, 18.0, 26.8, 27.8, 28.1, 28.3, 36.5, 37.5, 56.9, 66.8, 73.9, 78.3, 80.8, 127.6, 128.2, 128.4, 129.1, 135.6, 137.3, 172.0. GC-MS (70 eV) *m/z* (%): 302 (3, M^+-29), 284 (1), 244 (100), 189 (18), 142 (32), 119 (30), 105 (11), 91 (13), 43 (7). FT-IR (film, cm^{-1}): 3418 (br. OH), 2968, 2885, 1652 (C=N), 1514, 1462, 1366, 1297, 1174, 1086, 973, 812. Anal. Calcd for $C_{20}H_{29}NO_3$: C, 72.47; H, 8.82; N, 4.23. Found: C, 72.55; H, 8.93; N, 4.25.

(*R, *S**)-2,3-Epoxy-3-(4,4-dimethyl-2-oxazolin-2-yl)-1,1-diphenyl-2-*p*-tolylbutan-1-ol (14g).** 70 %, dr > 98:2, mp 139–141 °C (hexane). ^{1}H NMR (500 MHz) δ:0.63 (s, 3 H), 1.03 (s, 3 H), 1.50–1.65 (br. s, exchanges with D_2O, 1 H), 1.70 (s, 3 H), 2.14 (s, 3 H), 3.53 (d, *J* = 8.0 Hz, 1 H), 3.56 (d, *J* = 8.0 Hz, 1 H), 6.73–7.64 (5 m, 14 H). ^{13}C NMR (125 MHz) δ: 17.3, 21.2, 27.6, 28.0, 63.8, 67.2, 72.6, 79.5, 80.9, 127.1, 127.4, 127.7, 128.1, 129.5, 130.2, 133.2, 137.1, 142.6, 163.8. GC-MS (70 eV) *m/z* (%): 410 (1, M^+-17), 286 (21), 244 (100), 183 (14), 142 (20), 119 (37), 105 (46), 77 (32), 43 (48). FT-IR (film, cm^{-1}): 3475 (br. OH), 3060, 2926, 1656 (C=N), 1448, 1365, 1305, 1185, 1112, 1046, 974, 732, 703. Anal. Calcd for $C_{28}H_{29}NO_3$: C, 78.66; H, 6.84; N, 3.28. Found: C, 78.71; H, 6.93; N, 3.21.

(*R,*S**)-1,2-Epoxy-2-(4,4-dimethyl-2-oxazolin-2-yl)-1-(1-hydroxycyclopentyl)-1-*p*-tolylpropane (14h).** 63 %, dr > 98:2, mp 68–69 °C (hexane). ^{1}H NMR (500 MHz) δ: 0.97 (s, 3 H), 0.99 (s, 3 H), 1.33–1.55 (m, 4 H), 1.92 (s, 3 H), 1.64–2.08 (m, 4 H), 2.29 (s, 3 H), 2.34 (br. s, exchanges with D_2O, 1 H), 3.43 (d, *J* = 8.0 Hz, 1 H), 3.54 (d, *J* = 8.0 Hz, 1 H), 6.98–7.32 (m, 4 H). ^{13}C NMR (125 MHz) δ: 16.4, 23.4, 23.8, 27.4, 27.2, 36.4, 40.1, 67.0, 79.2, 106.2, 108.2, 112.0, 114.0, 127.0, 127.4, 128.6$_0$, 128.6$_4$, 134.1, 137.1, 163.6. GC-MS (70 eV) *m/z* (%): 329 (1, M^+), 286 (5), 244 (100), 230 (20), 187 (81), 159 (42), 142 (48), 119 (46), 105 (32), 91 (24), 43 (12). FT-IR (KBr, cm^{-1}): 3406 (br. OH), 2967, 2871, 1673 (C=N), 1516, 1461, 1365, 1262, 1118, 1080, 969, 808. Anal. Calcd for $C_{20}H_{27}NO_3$: C, 72.92; H, 8.26; N, 4.25. Found: C, 73.04; H, 8.44; N, 4.25.

(*R,*S**)-1,2-Epoxy-2-(4,4-dimethyl-2-oxazolin-2-yl)-1-(1-hydroxycyclohexyl)-1-*p*-tolylpropane (14i).** 89 %, dr > 98:2, mp 158–159 °C (hexane). ^{1}H NMR (500 MHz) δ: 0.62 (s, 3 H), 0.88–0.96 (m, 2 H), 0.97 (s, 3 H), 1.52–1.79 (m, 6 H), 1.88–1.92 (m, 2 H), 1.96 (s, 3 H), 2.11 (br. s, exchanges with D_2O, 1 H), 2.28 (s, 3 H), 3.41 (d, *J* = 8.0 Hz, 1 H), 3.51 (d, *J* = 8.0 Hz, 1 H), 6.99–7.28 (m, 4 H). ^{13}C NMR (125 MHz) δ: 16.2, 21.1, 21.4, 25.3, 27.4, 27.7, 32.1, 37.2, 62.3, 64.0, 66.8, 67.3, 71.9, 73.2, 79.0, 79.1, 126.4, 127.2, 128.3, 128.8, 133.6, 137.0, 163.4. GC-MS (70 eV) *m/z* (%): 244 (100, M^+-$C_6H_{10}OH^•$), 201 (13), 142 (16), 119 (25), 55 (6). FT-IR (KBr, cm^{-1}): 3395 (br. OH), 2925, 1651 (C=N), 1445, 1385, 1315, 1264, 1115, 992, 882, 815. Anal. Calcd for $C_{21}H_{29}NO_3$: C, 73.44; H, 8.51; N, 4.08. Found: C, 73.59; H, 8.90; N, 4.14.

(*R,*S**)-2,3-Epoxy-3-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenyl-2-*p*-tolylbutan-1-ol (14j).** Overall yield in both diastereomers 44 %, dr *syn*/*anti* 1.2/1, separable by column chromatography (silica gel, AcOEt/petroleum ether 8/2). **(*syn*).** mp 169–170 °C (hexane). ^{1}H NMR (500 MHz) δ: 0.73 (s, 3 H), 0.98 (s, 3 H), 2.00 (s, 3 H), 2.22 (s, 3 H), 2.98 (br. s, exchanges with D_2O, 1 H), 3.40 (d, *J* = 8.0 Hz, 1 H), 3.59 (d, *J* = 8.0 Hz, 1 H), 4.98 (s, 1 H), 6.86–7.22 (4 m, 9 H). ^{13}C NMR (125 MHz) δ: 16.4, 21.1, 27.5, 27.7, 62.1, 67.0, 70.3, 74.6, 79.2, 126.5, 127.5, 127.6, 127.7, 128.4, 130.9, 137.1, 139.6, 163.5. GC-MS (70 eV) *m/z* (%): 244 (100, M^+-$C_6H_5CHOH^•$), 209 (13), 181

(16), 142 (16), 119 (32), 91 (16), 77 (13). FT-IR (KBr, cm^{-1}): 3167 (br. OH), 2965, 1646 (C=N), 1450, 1367, 1305, 1184, 1118, 967, 700, 573. Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 74.75; H, 7.54; N, 3.85. **(*anti*).** mp 93–95 °C (hexane). ^{1}H NMR (500 MHz) δ: 0.70 (s, 3 H), 1.00 (s, 3 H), 2.22 (br. s, 4 H, 3 H after exchanges with D_2O), 3.42 (d, *J* = 8.0 Hz, 1 H), 3.54 (d, *J* = 8.0 Hz, 1 H), 5.07 (s, 1 H), 6.79–7.28 (4 m, 9 H). ^{13}C NMR (125 MHz) δ: 17.5, 21.1, 27.4, 27.7, 67.0, 71.8, 74.4, 79.2, 126.2, 127.4, 127.7, 128.1, 128.9, 130.0, 137.2, 139.2, 162.8. GC-MS (70 eV) *m/z* (%): 244 (100, M^+-$C_6H_5CHOH^{\bullet}$), 209 (12), 181 (15), 142 (14), 119 (42), 91 (20), 77 (17). FT-IR (KBr, cm^{-1}): 3406 (br. OH), 3030, 2964, 2925, 1672 (C=N), 1451, 1367, 1319, 1188, 1113, 969, 722, 699, 665, 573. Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 74.87; H, 7.42; N, 3.89.

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