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Terminal oxazolinyloxiranes: synthesis, reaction with amines and regioselective β-lithiation

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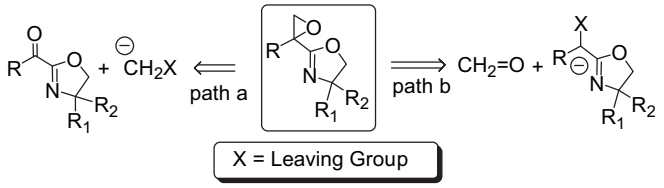
ABSTRACT

The synthesis of terminal oxazolinyloxiranes, even in enantioenriched form, has been performed by Darzens-type reaction of lithiated chloroalkyloxazolines with benzotriazolylmethanol ($BtCH_2OH$) or by chloromethylation of 2-acyl-2-oxazolines. The synthetic utility of such oxiranes based on their ability to act either as electrophiles, undergoing ring-opening reactions with nucleophiles, or as nucleophiles in form of the oxiranyl anions, generated by stereoselective β-deprotonation, has been investigated.

1. Introduction

Di-, tri- and tetrasubstituted oxazolinyloxiranes, promptly available by the Darzens reaction of 2-haloalkyloxazolines and carbonyl compounds,[1] have become very useful building blocks in synthetic organic chemistry. As α- or β-lithiated derivatives, which could be seen as masked epoxyenolates and homoenolates, oxazolinyloxiranes[2] have been successfully employed for the stereoselective synthesis of a variety of substances such as optically active cyclopropane carboxylates,[3] spirocyclic compounds,[4] oxazolinyl allylic alcohols,[5] iminooxetanes,[6] α-epoxy-β-aminoacids [7] and α,β-epoxy-γ-amino acids.[8] Terminal oxazolinyloxiranes, which seem to be even more interesting from the synthetic point of view, are very rare. To the best of our knowledge, there is just one patent on the synthesis of such compounds, which relies on the Corey reaction of 2-benzoyloxazolines.[9] We envisaged two main strategies for the preparation of terminal oxazolinyloxiranes, based either on the reaction of 2-acyl-2-oxazolines with halogenated methylene nucleophiles (path a, Scheme 1) or via the Darzens-like reaction of lithiated haloalkyloxazolines with formaldehyde or a synthetic equivalent (path b, Scheme 1).



Scheme 1.

Herein, we wish to report the synthesis of 2-acyl-2-oxazolines, their conversion into the corresponding α-substituted oxazolinyloxiranes and reactions of the latter with nucleophiles. The β-lithiation-trapping sequence (LTS) of the above epoxides has been investigated as well.

2. Results and discussion

2.1. Synthesis of 2-acyl-2-oxazolines

Our work began with the preparation of 2-acyl-2-oxazolines **2**. The existing methods for the synthesis of this type of ketones, including lithiation/electrophile trapping with oxygen[10] and the SeO_2-oxidation of 2-alkyloxazoline, suffer from low yields.[11] The adaptation of the methodology reported for the synthesis of 2-acyl-2-oxazoles,[12] based on the copper-mediated acylation of 2-oxazolylzinc, to 4,4-dimethyl-2-oxazoline **1** proved to be successful also for the synthesis of 2-acyl-2-oxazolines **2**. When 4,4-dimethyl-2-oxazoline **1** was reacted with *n*-BuLi at −78 °C and then transmetallated with $ZnCl_2$/CuI, the putative bimetallic intermediate **3** could be trapped with acylchlorides giving 2-acyl-2-oxazolines **2a–g** in moderate to good yields (Table 1, entries 1–7).

2-Acyl-2-oxazolines **2** proved to be very sensitive to acidic conditions (even to the residual HCl of the $CDCl_3$ solution) undergoing the known rearrangement to the dihydrooxazinones **4** almost quantitatively (Scheme 2).[10,13] Nevertheless, the rearrangement could be avoided working under inert conditions and in the absence of Lewis acids and proton sources.

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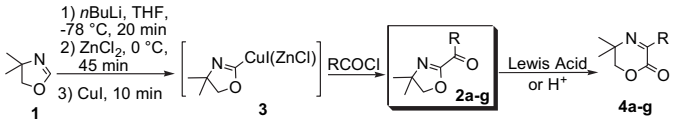
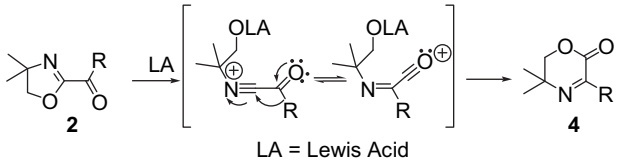
Table 1
Preparation of 2-acyl-2-oxazolines **2**



Entry	RCOCl	2-Acyl-2-oxazoline **2** (yield %)[a]	Oxazinone **4** (yield %)
1	4-Cl–C_6H_4COCl	**2a** (45)	**4a** (>98)
2	PhCOCl	**2b** (70)	**4b** (>98)
3[b]	Me_3CCOCl	**2c** (60)	**4c**[b] (0)
4	2-FurylCOCl	**2d** (45)	**4d** (>98)
5	2-Br–C_6H_4COCl	**2e** (60)	**4e** (>98)
6	PhCH=CHCOCl	**2f** (35)	**4f** (>98)
7	3-F–C_6H_4COCl	**2g** (75)	**4g** (>98)

[a] Isolated yield.
[b] A complex mixture of products was observed in the crude.



Scheme 2.

2.2. Synthesis of terminal oxazolinyloxiranes

With 2-acyl-2-oxazolines in hand, the preparation of terminal α,α-disubstituted oxazolinyloxiranes was pursued. Treatment of 2-acyl-2-oxazolines **2b**,**c** with $ClCH_2Li$, generated from $ClCH_2I$ and *n*-BuLi in THF at −78 °C, gave chlorohydrins **5a**,**b** (not isolated), which were straightforwardly converted into epoxides **6a**,**b** (50–60% yield) upon treatment with NaOH (Scheme 3). Alternatively, terminal oxazolinyloxiranes **6b**,**c** could be prepared in good yield (70–90%) by lithiation of 2-chloroalkyl-2-oxazolines **7a**,**b** followed by hydroxymethylation with benzotriazolylmethanol ($BtCH_2OH$), a synthetic equivalent of formaldehyde (Scheme 3).[14,15]

Four optically active terminal oxazolinyloxiranes (2*S*,4′*R*)-, (2*R*,4′*R*)-, (2*R*,4′*S*)- and (2*S*,4′*S*)-**10** were prepared starting from 2-benzoyloxazoline (*S*)-**8**[16] or from an equimolar mixture of diastereomeric oxazolines (1*R*,4′*R*)/(1*S*,4′*R*)-**9** (Scheme 4). In both cases ($ClCH_2Li$-mediated epoxidation or Darzens reaction), a mixture of two diastereomeric oxiranes was obtained (dr=1:1), which could be easily separated by preparative HPLC. It is worth noting that the Darzens methodology gave better overall yields.

The absolute configuration of the optically pure stereoisomer (2*R*,4′*S*)-**10** was determined by an X-ray analysis (Fig. 1).[17]

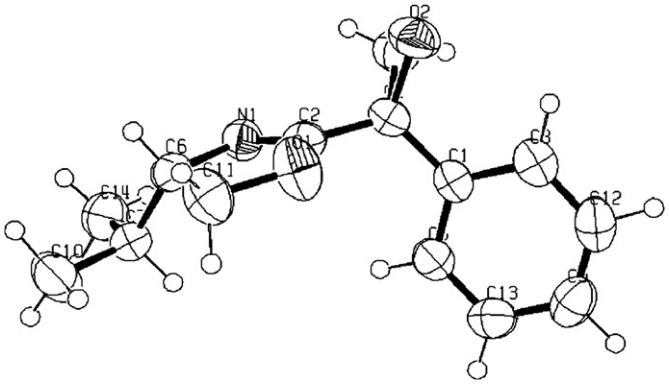
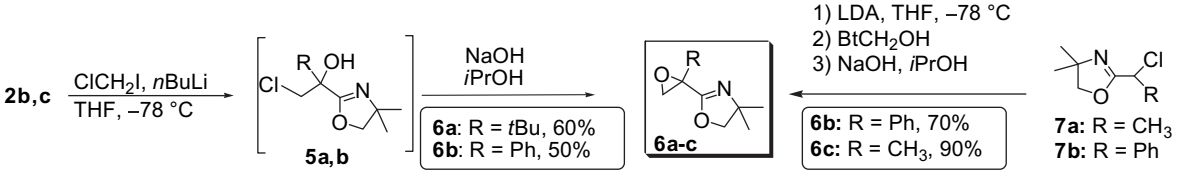


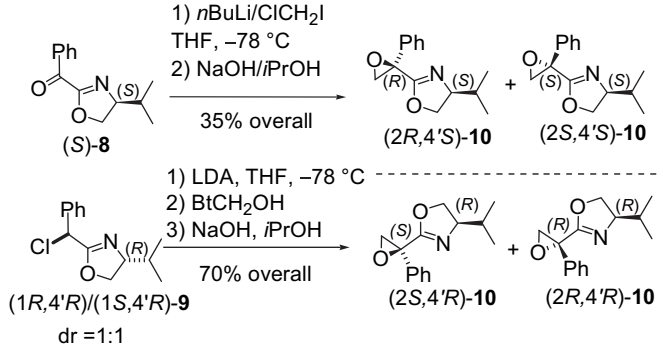
Figure 1. ORTEP diagram of compound (2*R*,4′*S*)-**10**.

2.3. Oxazolinyloxirane-ring-opening reaction with secondary amines

Next, the reactivity of oxazolinyloxiranes was investigated with reference to their capability to behave as electrophiles and nucleophiles in the form of oxiranyl anions. Oxazolinyloxiranes **6b**, (2*S*,4′*S*)- and (2*R*,4′*S*)-**10** were used as model compounds. Treatment of **6b** with secondary amines such as Et_2NH, pyrrolidine, piperidine and morpholine at 60 °C in ethanol, gave aminoalcohols **11a**–**c**,**e**, respectively, in very good yield (Table 2, entries 1–3, 5). Likely for steric reasons, no reaction was observed with *N*-benzyl-*tert*-butylamine and a lower yield of the expected aminoalcohol **11d** was obtained in the case of *N*-allylcyclohexylamine (Table 2, entry 4).



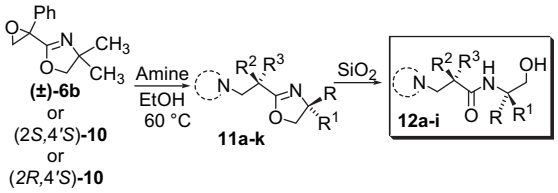
Scheme 3.



Scheme 4.

The reaction of optically active oxazolinyloxiranes (2*R*,4′*S*)- and (2*S*,4′*S*)-**10** with pyrrolidine, diethylamine and triazole afforded highly enantioenriched aminoalcohols **11f**–**h** and **11i**–**k**, respectively, in excellent yields (Table 2, entries 6–11). The triazole derivatives **11h** and **11k** are particularly appealing considering that some oxazolinyl triazolylmethylcarbinols have been reported to act as efficient antifungal agents.[18] Aminoalcohols **11** were found to be particularly prone to undergo smooth hydrolysis of the oxazolinyl ring, under acidic conditions or in the presence of silica gel, to give interesting α-hydroxy-β-aminoalkanamides **12**, which are strictly related to unnatural $\beta^{2,2}$-amino acids (according to Seebach's definition).[19] As reported in Table 2, α-hydroxy-β-aminoalkanamides **12a**–**i** could be easily obtained in racemic or enantioenriched form.

Table 2
Ring-opening reaction of oxazolinyloxirane



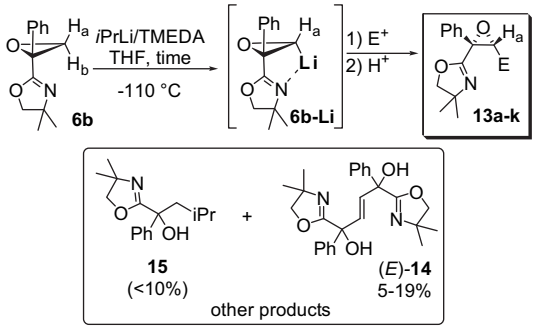
Entry	Oxazoline	Amine	R	R^1	R^2	R^3	Aminoalcohol **11** (yield %)	Amide **12** (yield %)
1	(±)-**6b**	Diethylamine	CH_3	CH_3	Ph	OH	**11a** (>98)[a]	**12a** (>98)[a]
2		Pyrrolidine					**11b** (>98)[a]	**12b** (>98)[a]
3		Piperidine					**11c** (>98)[a]	**12c** (>98)[a]
4		*N*-Allylcyclo-hexylamine					**11d** (46)[b]	**12d** (46)[b]
5		Morpholine					**11e** (90)[b]	**12e** (90)[b]
6	(2*R*,4′*S*)-**10**	Pyrrolidine	*i*-Pr	H	OH	Ph	**11f** (>98)[a,c]	**12f** (>98)[a]
7		Diethylamine					**11g** (>98)[a,c]	**12g** (>98)[a]
8		Triazole[e]					**11h** (90)[b,c]	—
9	(2*S*,4′*S*)-**10**	Pyrrolidine			Ph	OH	**11i** (>98)[a,d]	**12h** (>98)[a]
10		Diethylamine					**11j** (>98)[a,d]	**12i** (>98)[a]
11		Triazole[e]					**11k** (84)[b,d]	—

[a] Based on the crude reaction mixture; no further purification was needed.
[b] Isolated yield.
[c] In this case, enantioenriched oxazolinyloxirane (2*R*,4′*S*)-**10** (er >98:2) was employed.
[d] Enantioenriched oxazolinyloxirane (2*S*,4′*S*)-**10** (er >98:2) was employed.
[e] Reaction run in DMF at 50 °C.

2.4. Epoxide functionalization by stereospecific β-lithiation

The possibility that the above oxazolinyloxiranes, once lithiated, could be employed for the epoxide functionalization, as in the case of other oxazolinyloxiranyllithiums,[20] was evaluated. Lithiation of **6b** under optimized experimental conditions (*i*-PrLi, 3 equiv, −98/−110 °C, 20 min) produced lithiated species **6b**–Li which, upon treatment with D_2O, furnished deuterated oxirane **13a** in 50% yield and 85% D (Table 3). The formation of **13a** was accompanied by variable amount of enediol (*E*)-**14** (5–19%),[21] which likely results from an 'eliminative dimerization' of **6b**–Li (the typical carbene-like reactivity often associated to α-lithiated ethers),[22] and alcohol

Table 3
Stereoselective lithiation and nucleophilic reactivity of terminal oxazolinyloxiranyllithium **6b**–Li



Electrophile (E^+)	Time	Oxazolinyloxirane **13**	Yield %[a]
D_2O	20 min	**13a**	50 (85% D)
Me_3SiCl	0[b]	**13b**	90
$(i\text{-Pr})_3SiCl$		**13c**	77
$AllylMe_2SiCl$		**13d**	74
$PhMe_2SiCl$		**13e**	68
$Ph_2MeSiCl$		**13f**	68
Bu_3SnCl	20 min	**13g**	50
MeI		**13h**	25[c]
AllylBr		**13i**	35
PhCHO[d]	5 min	**13j**	25[c]
Cyclopentanone[d]		**13k**	24

[a] Isolated yield.
[b] In situ quenching conditions.
[c] In this case, two diastereomers formed, dr=78:22, calculated by ^1H NMR on the crude reaction mixture.
[d] The reaction was performed in Et_2O as the solvent, recovering about 50% of the starting oxirane.

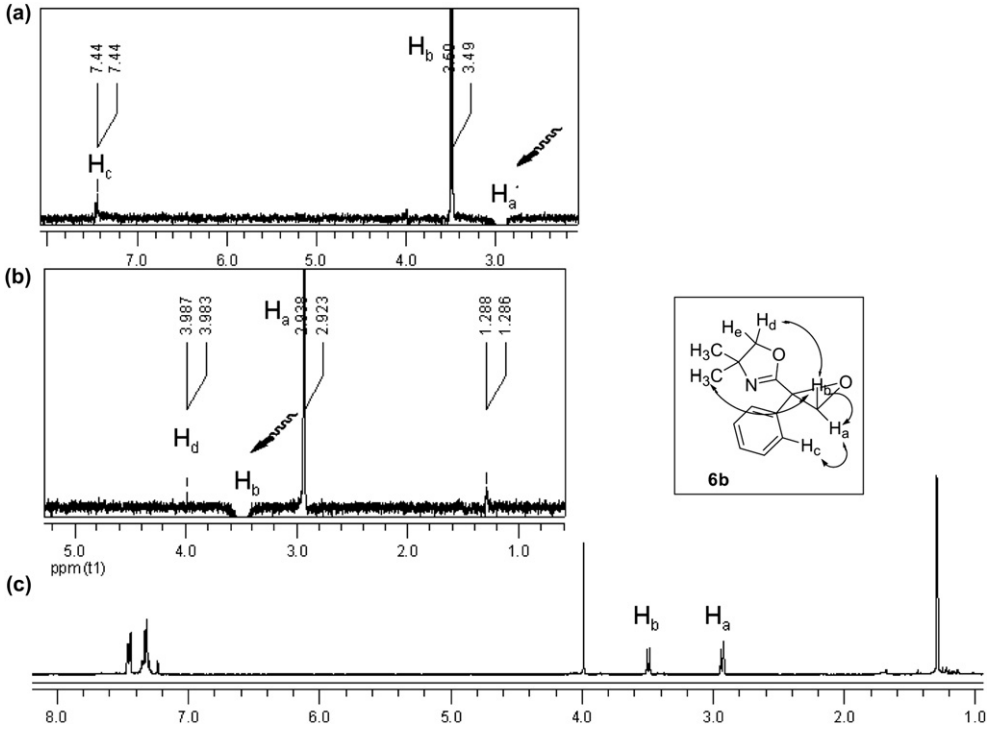
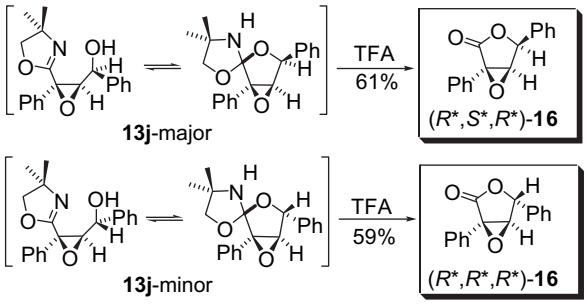


Figure 2. Panels (a) and (b) represent 1D-NOESY spectra of **6b** obtained after applying a selective pre-irradiation of protons H_a and H_b, respectively. Panel (c) represents ^1H NMR spectrum of **6b**.

15 (<10%) most probably as the result of nucleophilic attack of *i*-PrLi at the oxirane ring. Enediol (*E*)-**14** was obtained with high stereoselectivity (75%, *E*/*Z* >98:2) by carrying out the deprotonation reaction in Et_2O at −98 °C with LDA and TMEDA.[23] The capture of β-lithiated oxazolinyloxirane **6b**–Li with other electrophiles was investigated. At −110 °C, in situ trapping of **6b**–Li with various alkyl(aryl)silylchlorides furnished β-silylated oxazolinyloxiranes **13b–f** in very good yield (68–90%) (Table 3),[24] whereas external trapping with Bu_3SnCl, MeI, allylbromide, PhCHO and cyclopentanone took place with a lower yield (24–50%), furnishing oxiranes **13g–k**, due to the previously described side reactions.

In all cases, the reaction proceeded in a stereoselective way, always involving a retentive substitution cis to the oxazoline ring as ascertained by 1D-NOESY experiments (see Supplementary data), thus proving that the lithiated intermediate **6b**–Li is configurationally stable. The only diastereotopic proton removed was H_b cis to the oxazolinyl ring likely due to the coordinating and stabilizing effect of the oxazolinyl group on the lithiated intermediate.[25] By using as a model compound oxazolinyloxirane **6b**, the assignment of the two diastereotopic protons H_a and H_b was accomplished by detecting positive NOE effects, after applying selective ^1H pre-irradiations within a double pulsed field gradient spin-echo NOE (DPFGSE-NOE) sequence (Fig. 2).[26]

Pre-irradiation of H_a enhanced *ortho*-aromatic proton H_c (Fig. 2a), whereas pre-irradiation of H_b slightly enhanced resonances of both the oxazoline geminal methyl groups and the oxazoline methylenic protons (H_e and H_d, Fig. 2a and Supplementary data). The diastereomeric hydroxyalkylated oxiranes derived from benzaldehyde, **13j**-major and **13j**-minor (dr=78:22), once separated by chromatography, were found to equilibrate in solution to the corresponding spirocyclic compounds, which could be hydrolyzed to the α,β-epoxy-γ-butyrolactones[3,7] (*R**,*S**,*R**)-**16** and (*R**,*R**,*R**)-**16**, respectively (Scheme 5).[27]



Scheme 5.

3. Conclusions

In conclusion, in this paper terminal oxazolinyloxiranes were synthesized by two routes and their reactivity was investigated. New and interesting aminoalcohols **11** and **12** could be obtained by an oxazolinyloxirane-ring-opening reaction with secondary amines, whereas more functionalized oxazolinyloxiranes and epoxylactones were formed upon a preliminary stereospecific β-lithiation. Work is in progress to further expand the synthetic utility of terminal oxazolinyloxiranes and their derivatives.

4. Experimental

4.1. General

Tetrahydrofuran (THF) was freshly distilled under a nitrogen atmosphere over sodium/benzophenone ketyl. Compounds **7a**,**b**[1] and (*S*)-**8**[16] were prepared according to the reported procedures. Petroleum ether refers to the 40–60 °C boiling fraction. For the ^1H and ^{13}C NMR spectra (^1H NMR 400, 500 MHz; ^{13}C NMR 100, 125 MHz), $CDCl_3$, DMSO-d_6 and CD_3OD were used as the solvent. MS-ESI analyses were performed on LC/MSD trap system VL. Melting points were uncorrected. Analytical thin layer chromatography (TLC) was carried out on precoated 0.25 mm thick plates of Kieselgel 60 F_{254}; visualization was accomplished by UV light (254 nm) or by spraying a solution of 5% (w/v) ammonium molybdate and 0.2% (w/v) cerium(III) sulfate in 100 mL 17.6% (w/v) aq sulfuric acid and heating to 200 °C for some time until blue spots appear. All reactions involving air-sensitive reagents were performed under nitrogen in oven-dried glassware using syringe-septum cap technique.

4.2. General procedure for the preparation of 2-acyl-2-oxazolines (2a–g)

To a solution of 4,4-dimethyl-2-oxazoline (198 mg, 2 mmol) in THF (15 mL) at −78 °C, under a nitrogen atmosphere, *n*-BuLi (1.1 equiv, 0.9 mL hexanes solution, 2.5 M) was added. The resulting yellow solution was stirred for 20 min and $ZnCl_2$ (4 mmol, 4 mL of a 1 M solution in ether) was then added. The mixture was warmed to 0 °C, stirred for 45 min and anhydrous CuI (380 mg, 2 mmol) was added. After 10 min, acylchloride (2 mmol) was also added. The reaction was over within 1 h. The organic solution was diluted with AcOEt and washed sequentially with 1:1 NH_4OH/water, water and brine. Flash chromatography (silica gel, petroleum ether/AcOEt 7:3) afforded 2-acyl-2-oxazoline (**2a**–**g**).

*4.2.1. 4-Chlorophenyl(4,4-dimethyl-2-oxazolin-2-yl)ketone (**2a**).*[9] White solid, mp 95.7−97.7 °C, yield 45%. ^1H NMR (500 MHz, $CDCl_3$): δ=8.25 (d, $^3J_{H,H}$=8.7 Hz, 2H), 7.44 (d, $^3J_{H,H}$=8.7 Hz, 2H), 4.13 (s, 2H), 1.42 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ=182.5, 157.4, 140.8, 133.1, 132.1, 128.8, 78.8, 69.3, 28.1 ppm. GC–MS (70 eV) *m*/*z* 237 $[M]^+$ (9), 209 (11), 194 (9), 141 (28), 99 (24), 69 (18), 57 (83), 56 (100), 55 (16), 41 (41). FT-IR (KBr): ν=3082, 2970, 1675, 1632, 1150, 992 cm^{-1}.

*4.2.2. (4,4-Dimethyl-2-oxazolin-2-yl)phenylketone (**2b**).*[10] Yellow oil, yield 70%. ^1H NMR (500 MHz, $CDCl_3$): δ=8.27 (d, $^3J_{H,H}$=7.0 Hz, 2H), 7.62 (t, $^3J_{H,H}$=7.0 Hz, 1H), 7.48 (t, $^3J_{H,H}$=8.0 Hz, 2H), 4.15 (s, 2H), 1.45 (s, 6H) ppm. GC–MS (70 eV) *m*/*z* 203 $[M]^+$ (6), 175 (9), 119 (13), 105 (100), 91 (13), 77 (38), 51 (11). FTIR (film): ν=1670, 1630 cm^{-1}.

*4.2.3. 1-(4,4-Dimethyl-2-oxazolin-2-yl)-2,2-dimethylpropan-1-one (**2c**).* Yellow oil, yield 60%. ^1H NMR (500 MHz, $CDCl_3$): δ=4.01 (s, 2H), 1.35 (s, 6H), 1.31 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ=199.2, 156.5, 78.3, 68.5, 44.1, 27.9, 26.2 ppm. GC–MS (70 eV) *m*/*z* 183 $[M]^+$ (7), 140 (28), 99 (24), 70 (18), 57 (83), 56 (100), 55 (16), 41 (41). FT-IR (KBr): ν=2970, 1704, 1463, 1366, 1042, 1000 cm^{-1}. HRMS (ESI), calcd for $C_{10}H_{18}NO_2$, $[M+H]^+$: 184.1338. Found: 184.1336.

*4.2.4. (4,4-Dimethyl-2-oxazolin-2-yl)furan-2-yl-ketone (**2d**).* White solid, mp 86.5−88 °C, yield 45%. ^1H NMR (500 MHz, $CDCl_3$): δ=7.89 (dd, $J_{H,H}$=3.6, 0.8 Hz, 1H), 7.72 (dd, $J_{H,H}$=1.6, 0.8 Hz, 1H), 6.56 (dd, $^3J_{H,H}$=3.6, 1.6 Hz, 1H), 4.11 (s, 2H), 1.38 (s, 6H) ppm. ^{13}C NMR (125 MHz $CDCl_3$): δ=170.0, 157.1, 150.4, 149.0, 124.9, 112.7, 79.0, 68.9, 28.0 ppm. GC–MS (70 eV) *m*/*z* 193 $[M]^+$ (8), 165 (7), 109 (12), 95 (100), 70 (8). FT-IR (KBr): ν=3145, 2975, 1675, 1629, 1467, 1031, 993, 780 cm^{-1}. HRMS (ESI), calcd for $C_{10}H_{12}NO_3$, $[M+H]^+$: 194.0817. Found: 194.0810.

*4.2.5. 2-Bromophenyl-(4,4-dimethyl-2-oxazolin-2-yl)ketone (**2e**).* White solid, mp 58.2–59.2 °C, yield 60%. ^1H NMR (500 MHz, $CDCl_3$): δ 7.60 (dd, $^3J_{H,H}$=7.6, 1.2 Hz, 1H), 7.57 (dd, $J_{H,H}$=7.5, 1.8 Hz, 1H), 7.40 (dt, $J_{H,H}$=7.5, 1.2 Hz, 1H), 7.36 (dt, $J_{H,H}$=7.6, 1.8 Hz, 1H), 4.17 (s, 2H), 1.38

(s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ=186.3, 157.9, 137.9, 133.5, 132.9, 130.6, 127.3, 120.6, 79.8, 69.0, 27.7 ppm. GC–MS (70 eV) *m/z* 283 $[M]^+$ (13), 202 (100), 185 (96), 182 (99), 174 (20), 157 (27), 155 (28), 148 (23), 76 (20), 75(18). FT-IR (KBr): ν=3059, 2973, 1693, 1638, 1187, 983, 756 cm^{-1}. El. An. $C_{12}H_{12}BrNO_2$: calcd C, 51.09; H, 4.29; N, 4.96; found C, 50.91; H, 4.32; N, 4.84.

*4.2.6. (2E)-1-(4,4-Dimethyl-2-oxazolin-2-yl)-3-phenylprop-2-en-1-one (**2f**).* White solid, mp 93−95 °C, yield 35%. ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.88 (d, *J*=15.9 Hz, 1H), 7.67−7.63 (m, 2H), 7.59 (d, *J*=15.9 Hz, 1H), 7.44−7.36 (m, 3H), 4.13 (s, 2H), 1.40 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ=181.0, 159.3, 146.2, 134.2, 131.2, 129.0, 128.9, 121.5, 79.5, 68.7, 28.1 ppm. GC–MS (70 eV) *m/z* 229 $[M]^+$ (79), 200 (25), 186 (46), 145 (90), 131 (100), 103 (92), 102 (28), 77 (62). FT-IR (KBr): ν=1684, 1633, 1605, 1339, 1059 cm^{-1}. El. An. $C_{14}H_{15}NO_2$: calcd C, 73.34; H, 6.59; N, 6.11; found C, 73.52; H, 6.72; N, 5.88.

*4.2.7. 3-Fluorophenyl-(4,4-dimethyl-2-oxazolin-2-yl)ketone (**2g**).* White solid, mp 56.2–57 °C, yield 75%. ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.09–8.06 (m, 1H), 8.00–7.97 (m, 1H), 7.46–7.41 (m, 1H), 7.30–7.26 (m, 1H), 4.12 (s, 2H), 1.41 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ=182.3, 162.3 (d, $J_{F,C}$=247.0 Hz), 157.2, 136.5 (d, $J_{F,C}$=7.7 Hz), 130.1 (d, $J_{F,C}$=7.6 Hz), 126.4 (d, $J_{F,C}$=2.9 Hz), 121.1 (d, $J_{F,C}$=21.0 Hz), 117.3 (d, $J_{F,C}$=25.7 Hz), 78.8, 69.2, 28.0 ppm. GC–MS (70 eV) *m/z* 221 $[M]^+$ (11), 124 (8), 123 (100), 95 (30), 75 (9). FT-IR (KBr): ν=3084, 2968, 2928, 1682, 1628, 1585, 1240, 1126, 998 cm^{-1}. El. An. $C_{12}H_{12}FNO_2$: calcd C, 65.15; H, 5.47; N, 6.33; found C, 64.98; H, 5.47; N, 6.13.

4.3. Preparation of 5,5-dimethyl-5,6-dihydro[1,4]-oxazin-2-ones (4a–g)

By leaving the 2-acyloxazoline in $CDCl_3$ solution for few days it was possible to observe, by ^{1}H NMR, the spontaneous conversion of 2-acyloxazoline into the corresponding oxazinone. Alternatively, a solution of 2-acyloxazoline in AcOEt (15 mg/mL) added of silica gel (30–100 mg) was kept under magnetic stirring at rt until conversion was complete (TLC or GC monitoring). The solution was filtered on a Celite pad, washed with CH_2Cl_2 (10–30 mL) and the solution was concentrated under reduced pressure to leave the resulting oxazinone.

*4.3.1. 3-(4-Chlorophenyl)-5,5-dimethyl-5,6-dihydro[1,4]oxazin-2-one (**4a**).* Waxy solid, yield >98%. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.86 (d, $^3J_{H,H}$=8.7 Hz, 2H), 7.33 (d, $^3J_{H,H}$=8.7 Hz, 2H), 4.24 (s, 2H), 1.34 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ=154.8, 154.6, 137.1, 132.5, 130.0, 128.3, 74.3, 55.1, 24.5 ppm. GC–MS (70 eV) *m/z* 237 $[M]^+$ (15), 181 (15), 179 (47), 140 (33), 138 (100), 56 (72). FT-IR (KBr): ν=3078, 2970, 1728, 1632, 1150, 992 cm^{-1}. El. An. $C_{12}H_{12}ClNO_2$: calcd C, 60.64; H, 5.09; N, 5.89; found C, 60.71; H, 5.09; N, 5.65.

*4.3.2. 3-Phenyl-5,5-dimethyl-5,6-dihydro[1,4]oxazin-2-one (**4b**).* In agreement with literature (see Refs. 10 and 13).

*4.3.3. 3-(2-Furyl)-5,5-dimethyl-5,6-dihydro[1,4]oxazin-2-one (**4d**).* Waxy solid, yield >98%. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.52 (dd, $J_{H,H}$=3.6, 0.8 Hz, 1H), 7.38 (dd, $J_{H,H}$=1.6, 0.8 Hz, 1H), 6.46 (dd, $J_{H,H}$=3.6, 1.6 Hz, 1H), 4.21 (s, 2H), 1.35 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=153.8, 149.4, 147.8, 145.7, 118.5, 112.1, 74.3, 54.4, 24.7 ppm. GC–MS (70 eV) *m/z* 193 $[M]^+$ (67), 135 (99), 94 (100), 95 (100), 56 (87). FT-IR (KBr): ν=3372, 3141, 2973, 2605, 1738, 1652, 1465, 1053, 768 cm^{-1}. HRMS (ESI), calcd for $C_{10}H_{12}NO_3$, $[M+H]^+$: 194.0817. Found: 194.0810.

*4.3.4. 3-(2-Bromophenyl)-5,5-dimethyl-5,6-dihydro[1,4]oxazin-2-one (**4e**).* White solid, mp 61−63 °C, yield >98%. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.59–7.54 (m, 1H), 7.43–7.37 (m, 2H), 7.33–7.26 (m, 1H), 4.38 (s, 2H), 1.41 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ=158.7, 154.3, 136.2, 132.2, 131.0, 129.8, 127.5, 121.4, 74.3, 55.6, 24.1 ppm. GC–MS (70 eV) *m/z* 283 $[M]^+$ (6), 225 (33), 183 (98), 181 (100), 102 (41), 56 (71). FT-IR (KBr): ν=3059, 2973, 1733, 1638, 1187, 983, 756 cm^{-1}. El. An. $C_{12}H_{12}BrNO_2$: calcd C, 51.09; H, 4.29; N, 4.96; found C, 50.91; H, 4.42; N, 4.64.

*4.3.5. 5,5-Dimethyl-3-styryl-5,6-dihydro[1,4]oxazin-2-one (**4f**).* Waxy yellow solid, yield >98%. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.67 (d, $^3J_{H,H}$=16.5 Hz, 1H), 7.55–7.50 (m, 2H), 7.36–7.26 (m, 3H), 7.10 (d, $^3J_{H,H}$=16.5 Hz, 1H), 4.18 (s, 2H), 1.33 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ=155.7, 153.9, 138.8, 135.6, 129.4, 128.7, 127.7, 121.9, 74.2, 54.7, 24.8 ppm. GC–MS (70 eV) *m/z* 229 $[M]^+$ (63), 170 (40), 129 (100), 115 (35), 56 (23). FT-IR (KBr): ν=2974, 2933, 1735, 1629, 1581, 1102, 745, 690 cm^{-1}. El. An. $C_{14}H_{15}NO_2$: calcd C, 73.34; H, 6.59; N, 6.11; found C, 73.61; H, 6.72; N, 5.81.

*4.3.6. 3-(3-Fluorophenyl)-5,5-dimethyl-5,6-dihydro[1,4]oxazin-2-one (**4g**).* White solid, mp 62–63 °C, yield >98%. ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.75–7.71 (m, 1H), 7.70–7.65 (m, 1H), 7.38–7.32 (m, 1H), 7.16–7.10 (m, 1H), 4.26 (s, 2H), 1.37 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ=162.4 (d, $J_{F,C}$=245.7 Hz), 154.7, 154.5 (d, $J_{F,C}$=2.8 Hz), 136.1 (d, $J_{F,C}$=7.6 Hz), 129.7 (d, $J_{F,C}$=8.0 Hz), 124.5 (d, $J_{F,C}$=2.8 Hz), 117.7 (d, $J_{F,C}$=21.3 Hz), 115.5 (d, $J_{F,C}$=23.7 Hz), 74.2, 55.2, 24.5 ppm. GC–MS (70 eV) *m/z* 221 $[M]^+$ (13), 163 (50), 122 (100), 95 (16), 56 (75). FT-IR (KBr): ν=2972, 1725, 1649, 1580, 1445, 1276, 1180, 948, 678 cm^{-1}. El. An. $C_{12}H_{12}FNO_2$: calcd C, 65.15; H, 5.47; N, 6.33; found C, 64.91; H, 5.67; N, 6.03.

4.4. Chlorination of the (4*S*)-2-benzyl-4-isopropyl-2-oxazoline was carried out as reported in Ref. 1a to give an inseparable mixture 1:1 of diastereomers of 2-(1-chloro-1-phenylmethyl)-(4*S*)-isopropyl-2-oxazoline (9)

Colourless oil, 75%. ^{1}H NMR ($CDCl_3$, 500 MHz, selected data): δ=7.57–7.52 (m, 2H), 7.41–7.33 (m, 6H), 5.62 (s, 2H), 4.35 and 4.34 (2×d, AB system, $J_{H,H}$=8.0 Hz, 1H), 4.32 and 4.30 (2×dd, AB system, $J_{H,H}$=8.0, 1.4 Hz, 1H), 4.09 (dd, like t, $J_{H,H}$=8.2 Hz, 1H), 4.06 (dd, like t, $J_{H,H}$=8.2 Hz, 1H), 1.88–1.80 (m, 1H), 1.77 (sextet, $^3J_{H,H}$=6.5 Hz, 1H), 0.98 (d, $^3J_{H,H}$=6.5 Hz, 3H), 0.92 (d, $^3J_{H,H}$=6.5 Hz, 3H), 0.91 (d, $^3J_{H,H}$=6.6 Hz, 3H), 0.82 (d, $^3J_{H,H}$=6.6 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ=163.9 and 164.0, 136.3 and 136.4, 128.9 and 129.0, 128.6, 127.7 and 127.8, 71.9 and 72.0, 71.0 and 71.1, 55.1, 32.3 and 32.4, 18.5 and 18.6, 17.8 and 17.9 ppm. GC–MS (70 eV) *m/z* (rel int.) 237 $[M]^+$ (3), 202 (100), 125 (72). FT-IR (film): ν=2960, 1664, 1185, 1024, 968, 758, 697 cm^{-1}.

4.5. General procedures for the preparation of terminal α-substituted oxazolinyloxiranes 6a–c, (2*S*,4′*S*)-, (2*R*,4′*S*)-, (2*S*,4′*R*)- and (2*R*,4′*R*)-10

4.5.1. Method A, using 2-acyloxazolines. Preparation of **6b** is representative. To a stirred and pre-cooled (−78 °C) THF solution (5 mL) of benzoyloxazoline **2b** (204 mg, 1.0 mmol) and chloroiodomethane (211 mg, 1.2 mmol) a solution of *n*-BuLi (1.3 mmol, 2.5 M in hexane) was added dropwise. The resulting orange mixture was stirred for 1 h at this temperature, quenched with saturated aq NH_4Cl, extracted with AcOEt (3×10 mL) and concentrated in vacuo to give the crude chlorohydrin, which was converted into the epoxide **6b** upon treatment with NaOH 10% w/w in *i*-PrOH (3 mL) and purified by column chromatography (silica gel, petroleum ether/AcOEt 7:3).

4.5.2. Method B, using the Darzens-type reaction. Preparation of **6b** is representative. To a stirred and pre-cooled (−78 °C) THF solution (10 mL) of LDA (5.58 mmol), chlorobenzyloxazoline **7b** (415 mg,

1.86 mmol) and, after 2 h, benzotriazolylmethanol (3.72 mmol, 5 mL in THF) were added dropwise. The resulting orange mixture was stirred for 3 h at this temperature, quenched with saturated aq NH_4Cl, extracted with Et_2O (3×20 mL) and the solvent evaporated in vacuo to give the crude chlorohydrin, which was converted into the epoxide **6b**, upon treatment with NaOH 2% w/w in *i*-PrOH (5 mL), and purified by flash chromatography (silica gel, petroleum ether/AcOEt 9:1).

*4.5.2.1. 3-(4,4-Dimethyl-2-oxazolin-2-yl)-2,2-dimethyl-1,2-epoxybutane (**6a**).* Colourless oil, yield 60% (Method A). ^{1}H NMR ($CDCl_3$, 400 MHz): δ=3.91 and 3.87 (2×d, AB system, $^2J_{H,H}$=8.15 Hz, 2H), 2.87 and 2.82 (dd, AB system, $^2J_{H,H}$=5.1 Hz, 1H), 1.21 (s, 6H), 0.98 (s, 9H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ=162.9, 78.8, 66.8, 60.4, 49.6, 32.4, 28.0, 27.8, 25.7 ppm. GC–MS (70 eV) *m*/*z* 197 (1) $[M]^+$ 154 (70), 140 (40), 113 (87), 98 (100), 57 (92), 56 (44). FT-IR (film): ν=2971, 1659, 1367, 1124 cm^{-1}. HRMS (ESI), calcd for $C_{11}H_{19}NaNO_2$, $[M+Na]^+$: 220.1313. Found: 220.1316.

*4.5.2.2. 2-(4,4-Dimethyl-2-oxazolin-2-yl)-2-phenyloxirane (**6b**).* Colourless oil, yield 50% (Method A), yield 70% (Method B). ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.50–7.45 (m, 2H), 7.38–7.33 (m, 3H), 4.01 (s, 2H), 3.52 (d, $^2J_{H,H}$=6.1 Hz, 1H), 2.96 (d, $^2J_{H,H}$=6.1 Hz, 1H), 1.32 (s, 3H), 1.31 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=162.3, 135.2, 128.3, 128.1, 126.3, 79.4, 67.6, 55.3, 55.0, 28.0, 27.9 ppm. GC–MS (70 eV) *m*/*z* 217 $[M]^+$ (6), 216 (17), 200 (7), 186 (4), 129 (5), 105 (100), 91 (13), 77 (17), 56 (6), 41 (5). FT-IR (film): ν=3383, 2973, 1667, 1449, 1275 cm^{-1}. HRMS (ESI), calcd for $C_{13}H_{15}NaNO_2$, $[M+Na]^+$: 240.1000. Found: 240.1009.

*4.5.2.3. 2-(4,4-Dimethyl-2-oxazolin-2-yl)-1,2-epoxypropane (**6c**).* Colourless oil, yield 90% (Method B). ^{1}H NMR ($CDCl_3$, 400 MHz): δ=3.92 (s, 2H), 3.14 (d, $^2J_{H,H}$=5.9 Hz, 1H), 2.76 (d, $^2J_{H,H}$=5.9 Hz, 1H), 1.58 (s, 3H), 1.26 (s, 3H), 1.25 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=163.9, 79.5, 69.5, 66.8, 53.0, 28.2, 28.1, 18.7 ppm. GC–MS (70 eV) *m*/*z* 155 (6) $[M]^+$ 140 (17), 95 (7), 70 (4), 43 (5). FT-IR (film): ν=2971, 1659, 1367, 1124 cm^{-1}. HRMS (ESI), calcd for $C_8H_{13}NaNO_2$, $[M+Na]^+$: 178.0844. Found: 178.0839.

*4.5.2.4. (−)-(2S,4′S)-2-(4-Isopropyl-2-oxazolin-2-yl)-2-phenyloxirane [(2S,4′S)-**10**].* Colourless oil, yield 25% (Method A), yield 35% (Method B). Separation by preparative HPLC employing a Porasil column (300×19 mm), *n*-hexane/EtOAc 9:1, flow 15 mL/min. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.52–7.43 (m, 2H), 7.38–7.33 (m, 3H), 4.30 (dt, $^2J_{H,H}$=7.6 Hz, $^3J_{H,H}$=1.5 Hz, 1H), 3.52 (d, $^2J_{H,H}$=6.1 Hz, 1H), 4.06–3.99 (m, 2H), 2.92 (d, $^2J_{H,H}$=6.1 Hz, 1H), 1.90–1.70 (m, 1H), 0.94 (d, $^3J_{H,H}$=6.5 Hz, 3H), 0.87 (d, $^3J_{H,H}$=6.5 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ=163.9, 135.3, 128.3, 128.1, 126.4, 72.3, 70.5, 55.4, 54.9, 32.3, 18.5, 17.8 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 231 $[M]^+$ (13), 215 (12), 172 (45), 144 (14), 105 (100), 77 (23). FT-IR (film): ν=2960, 1664, 1185, 1024, 968, 758, 697 cm^{-1}. er >99:1 [t_R=25.4 min] by HPLC employing a Daicel Chiracel OD-H column (250×4.6 mm), *n*-hexane/*i*-PrOH 99:1, flow 0.5 mL/min, 230 nm, $[\alpha]_D^{20}$ −45.6 (*c* 1, $CHCl_3$). HRMS (ESI), calcd for $C_{14}H_{17}NaNO_2$, $[M+Na]^+$: 254.1157. Found: 254.1152.

*4.5.2.5. Compound (+)-(2R,4′R)-**10**.* $[\alpha]_D^{20}$ +44.8 (*c* 1, $CHCl_3$).

*4.5.2.6. (−)-(2R,4′S)-2-(4-Isopropyl-2-oxazolin-2-yl)-2-phenyloxirane [(1R,4′S)-**10**].* White solid, mp 65–67 °C (hexane), yield 25% (Method A), yield 35% (Method B). Separation by preparative HPLC employing a Porasil column (300×19 mm), *n*-hexane/EtOAc 9:1, flow 15 mL/min. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.51–7.47 (m, 2H), 7.36–7.31 (m, 3H), 4.29 (t, $^3J_{H,H}$=7.9 Hz, 1H), 4.05–3.99 (m, 2H), 3.51 (d, $^2J_{H,H}$=6.1 Hz, 1H), 2.98 (d, $^2J_{H,H}$=6.1 Hz, 1H), 1.82–1.75 (m, 1H), 0.95 (d, $^3J_{H,H}$=6.5 Hz, 3H), 0.88 (d, $^3J_{H,H}$=6.5 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ=163.9, 135.3, 128.4, 128.3, 126.5, 72.3, 70.5, 55.6, 55.0, 32.2, 18.7, 17.8 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 231 $[M]^+$ (13), 215 (16), 172 (67), 144 (19), 105 (100), 77 (22). FT-IR (KBr): ν=2960, 1668, 1452, 1256, 1133, 969, 767, 702 cm^{-1}. El. An. $C_{14}H_{17}NO_2$: calcd C, 72.70; H, 7.41; N, 6.06; found C, 72.64; H, 7.30; N, 6.12. er: >99:1 [t_R=31.1 min] by HPLC employing a Daicel Chiracel OD-H column (250×4.6 mm), *n*-hexane/*i*-PrOH 99:1, flow 0.5 mL/min, 230 nm, $[\alpha]_D^{20}$ −87.1 (*c* 1, $CHCl_3$).

*4.5.2.7. Compound (+)-(2S,4′R)-**10**.* $[\alpha]_D^{20}$ +87.8 (*c* 1, $CHCl_3$).

4.6. General procedure for the preparation of aminoalcohols 11a–g and 11i–j

Preparation of **11b** is representative. To a solution of oxazolinyloxirane **6b** (50 mg, 0.23 mmol) in dry EtOH (3 mL), pyrrolidine (24 mg, 0.34 mmol) was added and the mixture was stirred for 24 h at 60 °C. Then, the solvent and the excess of amine were removed in vacuo to give the aminoalcohol **11b**. The products **11d**,**e**,**h**,**k** were purified by flash chromatography (silica gel, petroleum ether/ethyl acetate 1:1).

*4.6.1. N,N-Diethyl-1-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenylethanolamine (**11a**).* Pale yellow oil, yield >98%. ^{1}H NMR ($CDCl_3$, 600 MHz): δ=7.63–7.59 (m, 2H), 7.34–7.27 (m, 3H), 3.94 and 3.89 (2×d, AB system, $^2J_{H,H}$=8.2 Hz, 2H), 3.52 (d, $^2J_{H,H}$=13.2 Hz, 1H), 2.78 (d, $^2J_{H,H}$=13.2 Hz, 1H), 2.51–2.64 (m, 4H), 1.27 (s, 3H), 1.25 (s, 3H), 0.97 (t, $^3J_{H,H}$=7.1 Hz, 6H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ=167.6, 144.7, 128.1, 127.3, 124.8, 79.4, 71.2, 67.8, 62.0, 47.5, 28.0, 11.7 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 290 $[M]^+$ (<1%), 105 (12), 86 (100), 77 (7), 58 (6). FT-IR (film): ν=3383, 2970, 1660, 1448, 1066 cm^{-1}. HRMS (ESI), calcd for $C_{17}H_{26}N_2NaO_2$, $[M+Na]^+$: 313.1892. Found: 313.1884.

*4.6.2. 1-(4,4-Dimethyl-2-oxazolin-2-yl)-1-phenyl-2-(pyrrolidin-1-yl)-ethanol (**11b**).* Pale yellow oil, yield >98%. ^{1}H NMR ($CDCl_3$, 600 MHz): δ=7.60 (d, $^3J_{H,H}$=7.6 Hz, 2H), 7.32 (t, $^3J_{H,H}$=7.6 Hz, 2H), 7.25 (t, $^3J_{H,H}$=7.3 Hz, 1H), 4.86–4.23 (br s, 1H), 3.91 and 3.89 (2×d, AB system, $^2J_{H,H}$=8.2 Hz, 2H), 3.49 (d, $^2J_{H,H}$=12.7 Hz, 1H), 2.92 (d, $^2J_{H,H}$=12.7 Hz, 1H), 2.61–2.48 (m, 4H), 1.69–1.67 (m, 4H), 1.24 (s, 3H), 1.22 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ=167.6, 142.6, 128.1, 127.4, 125.0, 79.5, 72.2, 67.1, 64.1, 54.9, 28.0, 23.9 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 288 $[M]^+$ (<1%), 105 (12), 84 (100), 85 (6), 77 (7), 55 (5). FT-IR (film): ν=3383, 2988, 1660, 1447, 1069 cm^{-1}. HRMS (ESI), calcd for $C_{17}H_{24}N_2NaO_2$, $[M+Na]^+$: 311.1735. Found: 311.1737.

*4.6.3. 1-(4,4-Dimethyl-2-oxazolin-2-yl)-1-phenyl-2-(piperidin-1-yl)-ethanol (**11c**).* White solid, mp 91–94 °C, yield >98%. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.60 (d, $^3J_{H,H}$=7.6 Hz, 2H), 7.33 (t, $^3J_{H,H}$=7.6 Hz, 2H), 7.28–7.25 (m, 1H), 5.88–4.88 (br s, 1H), 3.94 and 3.91 (2×d, AB system, $^2J_{H,H}$=8.1 Hz, 1H), 3.40 (d, $^2J_{H,H}$=13.2 Hz, 1H), 2.72 (d, $^2J_{H,H}$=13.2 Hz, 1H), 2.55 (br s, 2H), 2.43–2.40 (m, 2H), 1.54–1.50 (m, 4H), 1.40–1.38 (m, 2H), 1.28 (s, 3H), 1.26 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ=167.7, 142.9, 128.2, 127.4, 124.9, 79.6, 71.7, 67.1, 66.5, 55.6, 28.02, 28.01, 26.2, 23.8 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 302 $[M]^+$ (<1%), 105 (15), 98 (100), 77 (8). FT-IR (KBr): ν=3332, 2933, 1642, 1530, 1069 cm^{-1}. HRMS (ESI), calcd for $C_{18}H_{26}N_2NaO_2$, $[M+Na]^+$: 325.1892. Found: 325.1897.

*4.6.4. N-Allyl-N-cyclohexyl-1-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenylethanolamine (**11d**).* Pale yellow oil, yield 46%. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.60–7.57 (m, 2H), 7.33–7.26 (m, 3H), 5.78–5.68 (m, 1H), 5.62–5.12 (br s, 1H), 5.07–5.03 (m, 2H), 3.94 and 3.88 (2×d, $^2J_{H,H}$=7.9 Hz, 2H), 3.52 (d, $^2J_{H,H}$=13.4 Hz, 1H), 3.23 and 3.04 (2×dd, AB system, $^2J_{H,H}$=14.6, $^3J_{H,H}$=6.7 Hz, 2H), 2.79 (d, $^2J_{H,H}$=13.4 Hz, 1H),

2.48–2.38 (m, 1H), 1.69–1.58 (m, 5H), 1.55 (m, 1H), 1.27 (s, 3H), 1.25 (s, 3H), 1.20–0.97 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ=167.8, 143.4, 136.8, 128.2, 127.3, 124.8, 116.8, 79.5, 71.2, 67.1, 59.9, 58.6, 53.9, 30.0, 28.6, 28.1, 28.0, 26.1, 26.0 ppm. ESI-MS *m*/*z*: 379 $[M+Na]^+$. FT-IR (film): ν=2928, 2854, 1660, 1449, 1070 cm^{-1}. HRMS (ESI), calcd for $C_{22}H_{32}N_2NaO_2$, $[M+Na]^+$: 379.2361. Found: 379.2365.

*4.6.5. 1-(4,4-Dimethyl-2-oxazolin-2-yl)-2-morpholin-4-yl-1-phenylethanol (**11e**).* Pale yellow oil, yield 90%. ^{1}H NMR ($CDCl_3$, 600 MHz): δ=7.57 (d, $^2J_{H,H}$=8.2 Hz, 2H), 7.33–7.26 (m, 3H), 3.95 and 3.93 (2×d, AB system, $^2J_{H,H}$=8.2 Hz, 2H), 3.66–3.60 (m, 4H), 3.34 (d, $^2J_{H,H}$=13.2 Hz, 1H), 2.77 (d, $^2J_{H,H}$=13.2 Hz, 1H), 2.60–2.54 (m, 2H), 2.52–2.48 (m, 2H), 1.26 (s, 6H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ=167.6, 142.1, 128.3, 127.6, 124.9, 79.8, 72.8, 67.1, 66.2, 58.2, 54.7, 28.1, 27.9 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 304 $[M]^+$ (<1%), 204 (4), 105 (15), 100 (100), 77 (6), 56 (6). FT-IR (film): ν=3383, 2965, 1668, 1446, 1069 cm^{-1}. HRMS (ESI), calcd for $C_{17}H_{24}N_2NaO_3$, $[M+Na]^+$: 327.1684. Found: 327.1688.

*4.6.6. (+)-(1R,4′S)-1-(4-Isopropyl-2-oxazolin-2-yl)-1-phenyl-2-pyrrolidin-1-yl-ethanol (**11f**).* Colourless oil, yield >98%, $[\alpha]_D^{20}$ +8.2 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.67–7.60 (m, 2H), 7.38–7.23 (m, 3H), 4.27 (dd, like t, $^3J_{H,H}$=7.7 Hz, 1H), 3.99–3.85 (m, 2H), 3.52 (d, $^2J_{H,H}$=12.6 Hz, 1H), 2.95 (d, $^2J_{H,H}$=12.6 Hz, 1H), 2.57–2.47 (m, 4H), 1.82–1.69 (m, 1H), 1.69–1.62 (m, 4H), 0.94 (d, $^3J_{H,H}$=6.6 Hz, 3H), 0.82 (d, $^3J_{H,H}$=6.6 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ=169.0, 151.4, 142.6, 128.0, 127.3, 125.1, 72.7, 71.8, 70.6, 64.2, 55.0, 32.3, 23.8, 18.9, 17.9 ppm. FT-IR (film): ν=2960, 1661, 1448, 1385, 1228, 1049, 700 cm^{-1}. HRMS (ESI), calcd for $C_{18}H_{27}N_2O_2$, $[M+H]^+$: 303.2073. Found: 303.2074.

*4.6.7. (+)-(1R,4′S)-N,N-Diethyl-1-(4-isopropyl-2-oxazolin-2-yl)-1-phenylethanolamine (**11g**).* Colourless oil, yield >98%, $[\alpha]_D^{20}$ +14.4 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.60–7.56 (m, 2H), 7.33–7.26 (m, 2H), 7.24–7.18 (m, 1H), 5.6–5.02 (br s, exchanges with D_2O, 1H), 4.29–4.17 (m, 1H), 3.92–3.82 (m, 2H), 3.46 (d, $^2J_{H,H}$=13.5 Hz, 1H), 2.81 (d, $^2J_{H,H}$=13.5 Hz, 1H), 2.56–2.40 (m, 4H), 1.78–1.65 (m, 1H), 0.93 (t, $^3J_{H,H}$=6.6 Hz, 6H), 0.91 (d, $^3J_{H,H}$=6.9 Hz, 3H), 0.79 (d, $^3J_{H,H}$=6.6 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=169.0, 143.2, 128.0, 127.2, 124.9, 71.9, 71.5, 70.5, 62.1, 47.5, 32.5, 19.1, 18.0, 11.7 ppm. ESI-MS *m*/*z* 305 $[M+H]^+$. FT-IR (film): ν=2966, 1661, 1449, 1386, 1067, 700 cm^{-1}. HRMS (ESI), calcd for $C_{18}H_{29}N_2O_2$, $[M+H]^+$: 305.2230. Found: 305.2236.

*4.6.8. (−)-(1S,4′S)-1-(4-Isopropyl-2-oxazolin-2-yl)-1-phenyl-2-pyrrolidin-1-yl-ethanol (**11i**).* Colourless oil, yield >98%, $[\alpha]_D^{20}$ −73.1 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ=0.80 (d, $^3J_{H,H}$=6.6 Hz, 3H), 0.92 (d, $^3J_{H,H}$=6.6 Hz, 3H), 1.82–1.65 (m, 5H), 2.58–2.51 (m, 4H), 2.92 (d, $^2J_{H,H}$=12.6 Hz, 1H), 3.49 (d, $^2J_{H,H}$=12.6 Hz, 1H), 3.94–3.88 (m, 1H), 3.97 (dd, like t, $^3J_{H,H}$=7.7 Hz, 1H), 4.20 (dd, like t, $^3J_{H,H}$=8.2 Hz, 1H), 7.35–7.23 (m, 3H), 7.59–7.64 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=18.0, 19.0, 23.9, 32.6, 55.0, 64.1, 70.7, 72.0, 72.4, 125.1, 127.4, 128.1, 142.7, 169.0. ESI-MS *m*/*z*: 303 $[M+H]^+$. FT-IR (film): ν=3413, 2960, 1661, 1448, 1385, 1228, 1049, 700 cm^{-1}. HRMS (ESI), calcd for $C_{18}H_{27}N_2O_2$, $[M+H]^+$: 303.2073. Found: 303.2078.

*4.6.9. (−)-(1S,4′S)-N,N-Diethyl-1-(4-isopropyl-2-oxazolin-2-yl)-1-phenylethanolamine (**11j**).* Colourless oil, yield >98%, $[\alpha]_D^{20}$ −86.3 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.58–7.53 (m, 2H), 7.32–7.27 (m, 2H), 7.25–7.19 (m, 1H), 6.0–5.06 (br s, exchanges with D_2O, 1H), 4.17 and 4.14 (2×d, AB system, $^2J_{H,H}$=8.0 Hz, 1H), 3.96 (dd, like t, $^3J_{H,H}$=8.0 Hz, 1H), 3.92–3.84 (m, 1H), 3.55 (d, $^2J_{H,H}$=13.5 Hz, 1H), 2.71 (d, $^2J_{H,H}$=13.5 Hz, 1H), 2.63–2.44 (m, 4H), 1.73 (sextet, $^3J_{H,H}$=6.6 Hz, 1H), 0.93 (t, $^3J_{H,H}$=7.3 Hz, 6H), 0.91 (d, $^3J_{H,H}$=6.9 Hz, 3H), 0.80 (d, $^3J_{H,H}$=6.6 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=169.1, 143.4, 128.1, 127.2, 124.8, 71.9, 71.4, 70.5, 61.8, 47.5, 32.6, 23.8, 18.9, 17.9, 11.7 ppm. ESI-MS $[M+H]^+$ 305. FT-IR (film): ν=2964, 1663, 1385, 1067, 699 cm^{-1}. El. An. $C_{18}H_{28}N_2O_2$: calcd C, 71.02; H, 9.27; N, 9.20; found C, 71.23; H, 9.32; N, 9.07.

4.7. General procedure for the preparation of aminoalcohols 11h and 11k

To a pre-cooled (0 °C) solution of triazole (16 mg, 0.23 mmol) in 3 mL of dry DMF, NaH (0.46 mmol) and, after 15 min, the oxirane (2*R*,4′*S*)-**10** were added. The mixture was stirred for 2 h at 50 °C. Then, the reaction mixture was quenched with saturated aq NH_4Cl, extracted with AcOEt (3×5 mL), and the solvent evaporated in vacuo to give the crude aminoalcohol **11h**, which was purified by column chromatography on silica gel (EtOAc/methanol 95:5).

*4.7.1. (−)-(1R,4′S)-1-(4-Isopropyl-2-oxazolin-2-yl)-1-phenyl-2-(1H-1,2,4-triazol-1-yl)ethanol (**11h**).* Colourless oil, yield 90%, $[\alpha]_D^{20}$ −39.1 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.20 (s, 1H), 7.85 (d, $^3J_{H,H}$=1.6 Hz, 1H), 7.72–7.61 (m, 2H), 7.44–7.30 (m, 3H), 4.96 (dd, $^2J_{H,H}$=14.2, $^3J_{H,H}$ 1.1 Hz, 1H), 4.72–4.60 (br s, 1H), 4.45 (d, $^2J_{H,H}$=14.1 Hz, 1H), 4.39 (td, $^2J_{H,H}$=8.8, $^3J_{H,H}$=1.1 Hz, 1H), 4.09 (td, $^2J_{H,H}$=8.8, $^3J_{H,H}$=1.1 Hz, 1H), 3.77–3.68 (m, 1H), 1.61–1.49 (m, 1H), 0.81 (t, $^3J_{H,H}$=6.7 Hz, 3H), 0.75 (d, $^3J_{H,H}$=6.7 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ=167.0, 151.4, 144.9, 138.8, 128.6, 125.5, 74.2, 73.0, 71.5, 57.0, 32.4, 19.0, 18.0 ppm. ESI-MS *m*/*z*: 301 $[M+H]^+$. FT-IR (film): ν=3144, 2960, 1664, 1508, 1277, 1136, 1028, 948, 706 cm^{-1}. El. An. $C_{16}H_{20}N_4O_2$: calcd C, 63.98; H, 6.71; N, 18.65; found C, 64.08; H, 6.51; N, 18.68.

*4.7.2. (−)-(1S,4′S)-1-(4-Isopropyl-2-oxazolin-2-yl)-1-phenyl-2-(1H-1,2,4-triazol-1-yl)ethanol (**11k**).* Colourless oil, yield 84%, $[\alpha]_D^{20}$ −33.1 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.15 (s, 1H), 7.85 (s, 1H), 7.61 (m, 2H), 7.39–7.26 (m, 3H), 4.91 (d, $^2J_{H,H}$=14.2 Hz, 1H), 4.77 (br s, 1H), 4.42 (d, $^2J_{H,H}$=14.2 Hz, 1H), 4.35 (t, $^3J_{H,H}$=8.8 Hz, 1H), 4.04 (t, $^3J_{H,H}$=8.8 Hz, 1H), 3.82–3.75 (m, 1H), 1.55 (m, 1H), 0.81 (t, $^3J_{H,H}$=6.7 Hz, 3H), 0.75 (d, $^3J_{H,H}$=6.7 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ=167.0, 151.4, 144.8, 138.8, 128.6, 125.4, 74.3, 73.1, 71.6, 57.1, 32.4, 18.7, 18.4 ppm. ESI-MS *m*/*z*: 301 $[M+H]^+$. FT-IR (film): ν=3132, 2962, 1667, 1505, 1274, 1137, 755 cm^{-1}. El. An. $C_{16}H_{20}N_4O_2$: calcd C, 63.98; H, 6.71; N, 18.65; found C, 63.78; H, 6.59; N, 18.60.

4.8. General procedure for the preparation of amides 12a–i

Aminoalcohols **11** were spontaneously transformed into the corresponding hydroxyamides **12** simply by leaving them in a $CDCl_3$ solution and monitoring by ^{1}H NMR the course of the reaction. Usually, it could take from 1 to 4 weeks. Alternatively, a solution of **11** in $CHCl_3$ (5 mL/mmol) added of silica gel (50 mg/mmol) was stirred at rt until conversion was complete (TLC or GC monitoring). The solution was filtered on a Celite pad, washed with CH_2Cl_2 (10–30 mL) and the solution concentrated under reduced pressure to leave the hydroxyamide **12**.

*4.8.1. 2-Hydroxy-N-(1-hydroxymethyl-1-methylethyl)-2-phenyl-3-(N,N-diethylamino)propanamide (**12a**).* Colourless oil, yield >98%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.62–7.57 (m, 2H), 7.36–7.28 (br s, 1H), 7.30–7.18 (m, 3H), 6.04–4.47 (br s, 1H), 3.59 (d, $^2J_{H,H}$=13.2 Hz, 1H), 3.48 and 3.47 (2×d, AB system, $^2J_{H,H}$=11.7 Hz, 2H), 2.60–2.46 (m, 5H), 1.23 (s, 3H), 1.16 (s, 3H), 0.96 (t, $^3J_{H,H}$=7.0 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ=175.8, 142.3, 128.2, 127.3, 124.7, 74.0, 70.6, 60.6, 55.6, 47.0, 24.5, 24.4, 11.8 ppm. FT-IR (film): ν=3400, 2966, 2831, 1651, 1519, 1448, 1069 cm^{-1}. HRMS (ESI), calcd for $C_{17}H_{29}N_2O_3$, $[M+H]^+$: 309.2178. Found: 309.2177.

*4.8.2. 2-Hydroxy-N-(1-hydroxymethyl-1-methylethyl)-2-phenyl-3-(pyrrolinin-1-yl)propanamide (**12b**).* Colourless oil, yield >98%. ^{1}H

NMR ($CDCl_3$, 300 MHz): δ=7.62–7.54 (m, 2H), 7.35–7.18 (m, 4H), 5.80–4.77 (br s, 1H), 3.51 (d, $^2J_{H,H}$=12.4 Hz, 1H), 3.49 (s, 2H), 2.82 (d, $^2J_{H,H}$=12.4 Hz, 2H), 2.70–2.52 (m, 4H), 1.80–1.70 (m, 4H), 1.24 (s, 3H), 1.17 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ=175.4, 142.0, 128.4, 127.8, 125.0, 75.6, 70.7, 63.0, 55.9, 54.5, 24.9, 24.6, 24.1 ppm. FT-IR (film): ν=3400, 2966, 2831, 1651, 1519, 1448, 1069 cm^{-1}. HRMS (ESI), calcd for $C_{17}H_{27}N_2O_3$, $[M+H]^+$: 307.2022. Found: 307.2027.

*4.8.3. 2-Hydroxy-N-(1-hydroxymethyl-1-methylethyl)-2-phenyl-3-(piperidin-1-yl)propanamide (**12c**).* White solid, mp 100–102 °C, yield >98%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.60–7.54 (m, 2H), 7.35–7.18 (m, 4H), 6.04–4.66 (br s, 1H), 3.48 (s, 2H), 3.47 (d, $^2J_{H,H}$=13.2 Hz, 1H), 2.59–2.40 (m, 2H), 2.48 (d, $^2J_{H,H}$=13.2 Hz, 1H), 2.44–2.35 (m, 2H), 1.62–1.46 (m, 4H), 1.45–1.35 (m, 2H), 1.24 (s, 3H), 1.16 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ=175.8, 142.4, 128.4, 127.7, 125.0, 74.6, 70.8, 65.6, 56.0, 55.1, 26.3, 24.9, 24.8, 23.9 ppm. ESI-MS *m*/*z*: 343 $[M+Na]^+$. FT-IR (film): ν=3400, 2966, 2831, 1651, 1519, 1448, 1069 cm^{-1}. El. An. $C_{18}H_{28}N_2O_3$: calcd C, 67.47; H, 8.81; N, 8.74; found C, 67.23; H, 8.42; N, 8.77.

*4.8.4. 2-Hydroxy-N-(1-hydroxymethyl-1-methylethyl)-2-phenyl-3-(N-allyl-N-cyclohexylamino)propanamide (**12d**).* Pale yellow solid, mp 82–84 °C, yield >98%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.62–7.56 (m, 2H), 7.34–7.21 (m, 4H), 5.78–5.65 (m, 1H), 5.14–5.05 (m, 1H), 5.07–5.03 (m, 2H), 5.46–4.56 (br s, 1H), 3.57 (d, $^2J_{H,H}$=13.5 Hz, 1H), 3.48 and 3.47 (2×d, AB system, $^2J_{H,H}$=11.7 Hz, 2H), 3.19–3.02 (m, 2H), 2.58 (d, $^2J_{H,H}$=13.5 Hz, 1H), 2.49–2.39 (m, 1H), 1.85–1.51 (m, 6H), 1.23 (s, 3H), 1.16 (s, 3H), 1.20–0.97 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ=175.9, 142.4, 135.9, 128.1, 127.4, 124.8, 117.4, 73.9, 70.7, 59.4, 57.1, 55.8, 53.2, 31.1, 27.1, 26.0, 25.9, 25.7, 24.7, 24.6 ppm. ESI-MS *m*/*z*: 397 $[M+Na]^+$. FT-IR (film): ν=2928, 2854, 1660, 1449, 1070 cm^{-1}. El. An. $C_{22}H_{34}N_2O_3$: calcd C, 70.55; H, 9.15; N, 7.48; found C, 70.75; H, 9.10; N, 7.27.

*4.8.5. 2-Hydroxy-N-(1-hydroxymethyl-1-methylethyl)-2-phenyl-3-(piperidin-1-yl)propanamide (**12e**).* White solid, mp 69–72 °C, yield >98%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.60–7.54 (m, 2H), 7.35–7.18 (m, 4H), 5.44–4.66 (br s, 2H), 3.67–3.54 (m, 4H), 3.48 (d, $^2J_{H,H}$=13.2 Hz, 1H), 3.45 (s, 2H), 2.53 (d, $^2J_{H,H}$=13.2 Hz, 1H), 2.54–2.38 (m, 2H), 1.20 (s, 3H), 1.14 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ=175.0, 141.5, 128.2, 127.6, 124.6, 74.7, 70.3, 66.8, 65.2, 55.6, 53.9, 24.5, 24.4 ppm. ESI-MS *m*/*z*: 345 $[M+Na]^+$. FT-IR (film): ν=3400, 2966, 2831, 1651, 1519, 1448, 1069 cm^{-1}. El. An. $C_{17}H_{26}N_2O_4$: calcd C, 63.37; H, 8.13; N, 8.69; found C, 63.23; H, 8.22; N, 8.77.

*4.8.6. (−)-(2R,1′S)-2-Hydroxy-N-(1-hydroxymethyl-2-methylpropyl)-2-phenyl-3-pyrrolidin-1-yl-propanamide (**12f**).* Colourless oil, yield >98%, $[\alpha]_D^{20}$ −33.8 (*c* 0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.67–7.57 (m, 2H), 7.42–7.33 (br s, 1H), 7.33–7.23 (m, 3H), 4.30–3.12 (br s, 2H), 3.73–3.45 (m, 1H), 3.63–3.55 (m, 2H), 3.55 (d, $^2J_{H,H}$=12.4 Hz, 1H), 2.85 (d, $^2J_{H,H}$=12.4 Hz, 1H), 2.70–2.50 (m, 4H), 1.85–1.75 (m, 1H), 1.79–1.68 (m, 4H), 0.81 (d, $^3J_{H,H}$=6.6 Hz, 3H), 0.75 (d, $^3J_{H,H}$=6.6 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ=175.7, 142.1, 128.1, 127.4, 124.7, 75.4, 64.5, 62.9, 57.4, 54.4, 29.2, 23.9, 19.3, 18.4 ppm. FT-IR (film): ν=3350, 2943, 2831, 1655, 1523, 1449, 1028 cm^{-1}. HRMS (ESI), calcd for $C_{18}H_{29}N_2O_3$, $[M+H]^+$: 321.2172. Found: 321.2177.

*4.8.7. (−)-(2R,1′S)-2-Hydroxy-N-(1-hydroxymethyl-2-methylpropyl)-2-phenyl-3-(N,N-diethylamino)propanamide (**12g**).* Colourless oil, yield >98%, $[\alpha]_D^{20}$ −55.6 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.67–7.57 (m, 2H), 7.42–7.33 (br s, 1H), 7.33–7.18 (m, 3H), 4.25–3.12 (br s, 2H), 3.70–3.48 (m, 4H), 2.66–2.46 (m, 5H), 1.85–1.72 (m, 1H), 0.97 (t, $^3J_{H,H}$=7.0 Hz, 3H), 0.81 (d, $^3J_{H,H}$=6.6 Hz, 3H), 0.75 (d, $^3J_{H,H}$=6.6 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ=176.2, 142.7, 128.1, 127.3, 124.7, 74.2, 64.4, 60.6, 57.3, 47.0, 29.1, 19.3, 18.3, 11.7 ppm. FT-IR (film): ν=3400, 2966, 2831, 1651, 1519, 1448, 1069 cm^{-1}. HRMS (ESI), calcd for $C_{18}H_{31}N_2O_3$, $[M+H]^+$: 323.2335. Found: 323.2336.

*4.8.8. (−)-(2S,1′S)-2-Hydroxy-N-(1-hydroxymethyl-2-methylpropyl)-2-phenyl-3-pyrrolidin-1-yl-propanamide (**12h**).* White solid, mp 97–99 °C, yield >98%, $[\alpha]_D^{20}$ −65.1 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.67–7.57 (m, 2H), 7.42–7.33 (br s, 1H), 7.33–7.23 (m, 3H), 4.1–2.12 (br s, 2H), 3.62–3.46 (m, 4H), 2.90 (d, $^2J_{H,H}$=12.4 Hz, 1H), 2.72–2.54 (m, 4H), 1.85–2.02 (m, 1H), 1.82–1.76 (m, 4H), 0.93 (d, $^3J_{H,H}$=6.6 Hz, 3H), 0.87 (d, $^3J_{H,H}$=6.6 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ=175.4, 141.9, 128.2, 127.6, 124.8, 75.6, 64.1, 62.7, 58.0, 54.4, 28.7, 23.7, 19.6, 18.7 ppm. FT-IR (film): ν=3400, 2934, 2831, 1655, 1521, 1450, 1032 cm^{-1}. HRMS (ESI), calcd for $C_{18}H_{29}N_2O_3$, $[M+H]^+$: 321.2172. Found: 321.2178. El. An. $C_{18}H_{28}N_2O_3$: calcd C, 71.49; H, 8.67; N, 9.26; found C, 71.63; H, 8.92; N, 8.97.

*4.8.9. (+)-(2S,1′S)-2-Hydroxy-N-(1-hydroxymethyl-2-methylpropyl)-2-phenyl-3-(N,N-diethylamino)propanamide (**12i**).* White solid, mp 81–83 °C, yield >98%, $[\alpha]_D^{20}$ +15.2 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.67–7.57 (m, 2H), 7.40–7.33 (br s, 1H), 7.33–7.18 (m, 3H), 3.61 (d, $^2J_{H,H}$=13.5 Hz, 1H), 3.57–3.44 (m, 3H), 2.57 (d, $^2J_{H,H}$=13.5 Hz, 1H), 2.63–2.46 (m, 4H), 1.95–1.86 (m, 1H), 0.96 (t, $^3J_{H,H}$=7.0 Hz, 3H), 0.93 (d, $^3J_{H,H}$=6.6 Hz, 3H), 0.87 (d, $^3J_{H,H}$=6.6 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ=176.2, 142.8, 128.1, 127.3, 124.7, 74.2, 64.1, 60.8, 57.6, 47.0, 28.6, 19.6, 18.5, 11.8 ppm. ESI-MS $[M+H]^+$ 323. FT-IR (film): ν=3430, 2966, 1648, 1519, 1448, 1069 cm^{-1}. El. An. $C_{18}H_{30}N_2O_3$: calcd C, 67.05; H, 9.38; N, 8.69; found C, 67.18; H, 9.39; N, 8.60.

4.9. General procedure for the preparation of β-silylated-α-oxazolinyloxiranes 13b–f

To a stirred and pre-cooled (−110 °C) THF solution (10 mL) of oxazolinyloxirane **6b** (100 mg, 0.46 mmol), TMEDA (0.2 mL, 1.38 mmol) and silylchloride (1.38 mmol), a solution of *i*-PrLi (1.38 mmol, 1.9 mL, 0.7 M in pentane) was added dropwise. The resulting orange mixture was stirred for 1 h at this temperature and then allowed to warm to rt, quenched with saturated aq NH_4Cl, extracted with Et_2O (3×5 mL), and the combined organic phases were dried with Na_2SO_4. Removal of the solvent in vacuo gave a yellow oil, which was purified by column chromatography (1:9 to 2:4 EtOAc/petroleum ether) to give silyloxiranes **13b–f**.

4.9.1. (1R,2S*)-2-Trimethylsilyl-1-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenylepoxyethane (**13b**).* Colourless oil, yield 90%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.53–7.49 (m, 2H), 7.35–7.31 (m, 3H), 3.97 and 3.96 (2×d, AB system, $^2J_{H,H}$=8.2 Hz, 2H), 2.42 (s, 1H), 1.30 (s, 3H), 1.28 (s, 3H), 0.16 (s, 9H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=161.9, 138.5, 128.3, 128.1, 125.7, 79.1, 67.8, 62.5, 59.7, 28.2, 28.1, −2.47 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 289 (14) $[M]^+$, 275 (23), 274 (100), 246 (12), 202 (20), 105 (97), 73 (86). FT-IR (film): ν=2967, 2929, 1670, 1450, 1248 cm^{-1}. HRMS (ESI), calcd for $C_{18}H_{23}NNaO_2Si$, $[M+Na]^+$: 312.1396. Found: 312.1392.

4.9.2. (1R,2S*)-2-Triisopropylsilyl-1-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenylepoxyethane (**13c**).* Colourless oil, yield 77%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.52–7.57 (m, 2H), 7.34–7.26 (m, 3H), 3.92 (br s, 2H), 2.50 (s, 1H), 1.27 (s, 3H), 1.25 (s, 3H), 1.20–1.10 (m, 18H), 1.03 (s, 6H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=161.9, 139.1, 128.3, 128.0, 125.9, 79.0, 67.7, 60.3, 59.4, 28.1, 27.8, 18.9, 11.4 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 373 (10) $[M]^+$, 331 (27), 330 (100), 276 (10), 258 (20), 59 (10). FT-IR (film): ν=2943, 2866, 1669, 1463, 1095 cm^{-1}. HRMS (ESI), calcd for $C_{22}H_{36}NO_2Si$, $[M+H]^+$: 374.2515. Found: 374.2511.

4.9.3. (1R,2S*)-2-Allyldimethylsilyl-1-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenylepoxyethane (**13d**).* Colourless oil, yield 74%. ^{1}H NMR

($CDCl_3$, 500 MHz): δ=7.54–7.49 (m, 2H), 7.40–7.24 (m, 3H), 5.88–5.78 (m, 1H), 4.93 (dq, $J_{H,H}$=16.9, 1.5 Hz, 1H), 4.96–4.86 (m, 1H), 3.99 and 3.98 (2×d, AB system, $^2J_{H,H}$=8.2 Hz, 2H), 2.48 (s, 1H), 1.76–1.74 (m, 2H), 1.33 (s, 3H), 1.31 (s, 3H), 0.18 (s, 3H), 0.17 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ=161.9, 138.3, 133.7, 128.3, 128.1, 125.7, 114.0, 79.1, 67.8, 61.2, 59.6, 28.2, 28.1, 22.2, −4.6, −4.7 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 315 (7) $[M]^+$, 274 (100), 220 (29), 203 (23), 202 (95), 139 (27), 105 (29). HRMS (ESI), calcd for $C_{18}H_{26}NO_2Si$, $[M+H]^+$: 316.1733. Found: 316.1732.

4.9.4. (1R,2S*)-2-Dimethylphenylsilyl-1-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenylepoxyethane (**13e**).* Colourless oil, yield 68%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.62–7.57 (m, 3H), 7.48–7.53 (m, 2H), 7.37–7.25 (m, 5H), 3.80 and 3.78 (2×d, AB system, $^2J_{H,H}$=8.1 Hz, 2H), 2.61 (s, 1H), 0.43 (s, 3H), 1.23 (s, 3H), 1.20 (s, 3H), 0.47 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=161.9, 138.3, 136.5, 133.0, 132.9, 129.6, 129.5, 129.2, 128.2, 127.9, 127.7, 78.9, 67.7, 61.8, 59.9, 28.1, 28.0, −3.7, −3.9 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 351 (11) $[M]^+$, 336 (72), 274 (48), 207 (87), 135 (100), 105 (80), 77 (22), 44 (23). FT-IR (film): ν=2964, 2928, 1661, 1428, 1118 cm^{-1}. HRMS (ESI), calcd for $C_{21}H_{26}NO_2Si$, $[M+H]^+$: 352.1733. Found: 352.1742.

4.9.5. (1R,2S*)-2-Diphenylmethylsilyl-1-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenylepoxyethane (**13f**).* Colourless oil, yield 68%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.70–7.20 (m, 15H), 3.48 and 3.39 (2×AB system, $^2J_{H,H}$=8.0 Hz, 2H), 2.89 (s, 1H), 1.01 (s, 3H), 0.95 (s, 3H), 0.74 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=161.9, 137.0, 135.0, 134.7, 129.7, 129.6, 128.3, 128.2, 128.0, 127.9, 125.9, 78.5, 67.5, 61.0, 60.0, 27.7, 27.6, −5.1 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 413 $[M]^+$ (<1%), 214 (18), 200 (18), 199 (100), 137 (10), 77 (6). FT-IR (film): ν=3069, 2962, 1666, 1428, 1119, 792 cm^{-1}. HRMS (ESI), calcd for $C_{26}H_{28}NO_2Si$, $[M+H]^+$: 414.1889. Found: 414.1884.

4.10. General procedure for the preparation of oxazolinyloxiranes 13a,g–k

To a stirred and pre-cooled (−110 °C) THF solution (10 mL) of oxazolinyloxirane **3b** (100 mg, 0.46 mmol) and TMEDA (0.2 mL, 1.38 mmol), a solution of *i*-PrLi (1.38 mmol, 1.9 mL, 0.7 M in pentane) was added dropwise and, after 20 min, the suitable electrophile was added neat or in (0.5 M) THF solution if solid (1.38 mmol). The resulting mixture was stirred for 1 h at this temperature and then allowed to warm to rt, quenched with saturated aq NH_4Cl, extracted with Et_2O (3×5 mL), and the combined organic phases were dried with Na_2SO_4. Removal of the solvent in vacuo gave a yellow oil, which was purified by column chromatography (1:4 to 1:9 EtOAc/petroleum ether) to give the desired oxirane **13**. In the case of oxiranes **13j**,**k**, Et_2O was used as the solvent at −98 °C, and the carbonyl compound was added after 5 min.

4.10.1. (1R,2R*)-2-Deuterio-1-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenylepoxyethane (**13a**).* Colourless oil, yield 50% (85% D). ^{1}H NMR ($CDCl_3$, 500 MHz, selected data): δ=7.48 (d, $^3J_{H,H}$=7.9 Hz, 2H), 7.38–7.33 (m, 3H), 4.01 (s, 2H), 2.96 (s, 1H), 1.32 (s, 3H), 1.31 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz, selected data): δ=162.5, 135.3, 128.4, 128.3, 126.4, 79.6, 67.7, 55.5, 54.8 (t, $J_{C,D}$=27.4 Hz), 28.0, 27.9 ppm. GC–MS (70 eV) *m*/*z* 218 (6) $[M]^+$, 217 (17), 201 (7), 187 (4), 130 (5), 106 (100), 92 (13), 78 (17), 57 (6), 42 (5). FT-IR (film): ν=3383, 2973, 1739, 1667, 1449, 1275 cm^{-1}. HRMS (ESI), calcd for $C_{13}H_{14}DNNaO_2$, $[M+Na]^+$: 241.1062. Found: 241.1069.

4.10.2. (1R,2S*)-2-Tributyltin-1-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenylepoxyethane (**13g**).* Colourless oil, yield 50%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.49–7.45 (m, 2H), 7.36–7.29 (m, 3H), 3.97 and 3.96 (2×d, AB system, $^2J_{H,H}$=8.2 Hz, 2H), 2.82 (s, 1H), 1.64–1.54 (m, 12H), 1.38–1.25 (m, 12H), 1.02–0.97 (m, 9H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=163.5, 138.6, 128.2, 127.8, 126.0, 124.8, 79.4, 67.8, 65.1, 58.2, 29.0, 28.4, 28.2, 27.4, 13.7, 10.8 ppm. FT-IR (film): ν=2957, 2924, 2854, 1661, 1463, 1377 cm^{-1}. HRMS (ESI), calcd for $C_{25}H_{41}NNaO_2Sn$, $[M+Na]^+$: 530.2057. Found: 530.2059.

4.10.3. (1R,2R*)-1-(4,4-Dimethyl-2-oxazolin-2-yl)-1-phenyl-1,2-epoxypropane (**13h**).* Colourless oil, yield 40%, inseparable mixture of **13h** and **6b**. ^{1}H NMR ($CDCl_3$, 400 MHz, selected data for **13h**): δ=7.49–7.47 (m, 2H), 7.34–7.28 (m, 3H), 3.98 (s, 2H), 3.19 (q, $^3J_{H,H}$=5.5 Hz, 1H), 1.45 (d, $^3J_{H,H}$=5.5 Hz, 3H), 1.32 (s, 3H), 1.30 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, selected data): δ=160.8, 136.2, 128.4, 128.2, 125.9, 94.4, 79.2, 62.3, 59.9, 28.4, 28.1, 15.0 ppm. GC–MS (70 eV) *m*/*z* (rel int) 231 (1) $[M]^+$, 142 (5), 115 (7), 106 (9), 105 (100), 89 (6), 77 (16), 56 (6). FT-IR (film): ν=2973, 1739, 1667, 1449, 1275 cm^{-1}. HRMS (ESI), calcd for $C_{14}H_{17}NNaO_2$, $[M+H]^+$: 254.1157. Found: 254.1153.

4.10.4. (1R,2R*)-2-Allyl-1-(4,4-dimethyl-2-oxazolin-2-yl)-1-phenylepoxyethane (**13i**).* Colourless oil, yield 35%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.52–7.47 (m, 2H), 7.40–7.34 (m, 3H), 5.98–5.81 (m, 1H), 5.23 (dq, $J_{H,H}$=17.1, 1.6 Hz, 1H), 5.16 (dq, J=10.4, 1.1 Hz, 1H), 4.01 (s, 2H), 3.18 (t, $^3J_{H,H}$=5.8 Hz, 1H), 2.54–2.37 (m, 2H), 1.36 (s, 3H), 1.34 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ=160.9, 136.1, 132.6, 128.4, 126.1, 118.0, 79.4, 67.8, 65.1, 59.9, 33.9, 28.4, 28.1 ppm. GC–MS (70 eV) *m*/*z* (rel int.) 256 (1) $[M-1]^+$, 216 (23), 152 (12), 105 (100), 77 (21). FT-IR (film): ν=2967, 1668, 1520, 1450, 1190, 759, 698 cm^{-1}. HRMS (ESI), calcd for $C_{16}H_{20}NO_2$, $[M+H]^+$: 258.1494. Found: 258.1490.

4.10.5. (1R,2R*,3R*)-1,3-Diphenyl-3-(4,4-dimethyl-2-oxazolin-2-yl)-2,3-epoxypropan-1-ol and 3,3-dimethyl-7,9-diphenyl-8,9-epoxy-1,6-dioxa-4-azaspiro[4.4]nonane (**13j**-major).* Colourless oil, yield 19%, 1:1 unseparable mixture. ^{1}H NMR ($CDCl_3$, 500 MHz, selected data): δ=7.71–7.25 (m, 20H, spirocyclic and hydroxyalkylated forms), 5.06 (s, 1H, spirocyclic form), 4.86 (d, J=7.0 Hz, 1H, spirocyclic form), 4.05 and 4.04 (2×d, AB system, $^2J_{H,H}$=9.1 Hz, 2H, hydroxyalkylated form), 3.86 (s, 1H, spirocyclic form), 3.71 and 3.50 (2×d, AB system, $^2J_{H,H}$=7.7 Hz, 2H, spirocyclic form), 3.34 (d, J=6.9 Hz, 1H, hydroxyalkylated form), 1.34 and 1.32 (2×s, 6H, hydroxyalkylated form), 1.26 and 0.75 (2×s, 6H, spirocyclic form) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, selected data): δ=161.3 (*C*═*N*, hydroxyalkylated form), 139.7, 136.5, 135.4, 131.7, 128.7, −126.1 (Ar *C*–*H*), 119.1 (spiro *C*), 79.7, 76.7, 76.2, 70.8, 69.2, 67.7, 66.2, 63.8, 60.8, 55.1, 28.3, 28.2, 28.1, 28.0 ppm. FT-IR (film): ν=3178, 2925, 1673, 1452, 1364, 1164, 1048, 757, 698 cm^{-1}. ESI-MS *m*/*z*: 324 $[M+H]^+$. El. An. $C_{20}H_{21}NO_3$: calcd C, 74.28; H, 6.55; N, 4.33; found C, 74.18; H, 6.39; N, 4.60.

4.10.6. (1R,2S*,3S*)-1,3-Diphenyl-3-(4,4-dimethyl-2-oxazolin-2-yl)-2,3-epoxypropan-1-ol and 3,3-dimethyl-7,9-diphenyl-8,9-epoxy-1,6-dioxa-4-azaspiro[4.4]nonane (**13j**-minor).* Colourless oil, 1:1 unseparable mixture, yield 6%. ^{1}H NMR ($CDCl_3$, 500 MHz, selected data): δ=7.82–7.74 (m, 2H, spirocyclic form), 7.53–7.46 (m, 2H, hydroxyalkylated form), 7.41–7.24 (m, 8H, hydroxyalkylated form), 7.46–7.26 (m, 4H, spirocyclic form), 7.25–7.06 (m, 4H, spirocyclic form), 5.49 (d, J=2.6 Hz, 1H, hydroxyalkylated form), 4.66 (s, 1H, spirocyclic form), 4.52 (dd, J=8.4, 2.6 Hz, 1H, hydroxyalkylated form), 4.13 and 4.09 (2×d, AB system, $^2J_{H,H}$=8.4 Hz, 2H, hydroxyalkylated form), 4.06 and 4.01 (2×d, AB system, $^2J_{H,H}$=8.0 Hz, 2H, spirocyclic form), 3.76 (s, 1H, spirocyclic form), 3.14 (d, J=8.4 Hz, 1H, hydroxyalkylated form), 2.37 (br s, 1H, spirocyclic form), 1.41 and 1.37 (2×s, 6H, hydroxyalkylated form), 1.26 and 1.13 (2×s, 6H, spirocyclic form) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, selected data): δ=161.3 (*C*═*N*, hydroxyalkylated form), 139.6, 136.5, 135.4, 131.6, 128.7−126.1 (Ar *C*–*H*), 119.2 (spiro *C*), 79.8, 77.5, 76.2, 70.8, 69.2, 67.7, 66.2, 63.9, 60.9, 57.0, 28.3, 28.1, 27.8, 26.5 ppm. FT-IR (film): ν=3178, 2925, 1673, 1452 cm^{-1}.

HRMS (ESI), calcd for $C_{16}H_{22}NO_3$, $[M+H]^+$: 324.1600. Found: 324.1606.

4.10.7. Unseparable mixture 1:3 of 1-[3-(4,4-dimethyl-2-oxazolin-2-yl)-3-phenyloxiranyl]cyclopentanol and 3,3-dimethyl-13-phenyl-12,13-epoxy-1,6-dioxa-4-azadispiro[4.1.4.2]tridecane ***13k***. White solid, mp=81–83 °C, yield 24%. ^{1}H NMR ($CDCl_3$, 500 MHz, selected data): δ=7.64–7.53 (m, 2H, spirocyclic form), 7.48–7.41 (m, 2H, hydroxyalkylated form), 7.38–7.25 (m, 3H, hydroxyalkylated form and 3H spirocyclic form), 4.2 and 3.99 (2×d, AB system, $^2J_{H,H}$=8.0 Hz, 2H, hydroxyalkylated form), 3.61 and 3.35 (2×d, AB system, $^2J_{H,H}$=7.3 Hz, 2H, spirocyclic form), 3.53 (s, 1H, spirocyclic form), 3.09 (s, 1H, hydroxyalkylated form), 2.15–1.48 (m, 16H, spirocyclic and hydroxyalkylated forms), 1.31 (s, 6H, hydroxyalkylated form), 1.23 and 0.67 (2×s, 6H, spirocyclic form) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, selected data): δ=162.0 (*C*=*N*, hydroxyalkylated form),136.3,132.1, 128.7,128.4,128.1,127.6,125.4, 118.9 (spiro *C*), 87.3, 79.7, 79.6, 71.5, 67.1, 66.2, 56.6, 38.6, 38.2, 35.3, 33.8, 28.1, 27.6, 26.4, 24.4, 23.9, 23.8 ppm. FT-IR (film): ν=3361, 2965, 1665, 1448, 1254, 1054, 698 cm^{-1}. El. An. $C_{18}H_{23}NO_3$: calcd C, 71.73; H, 7.69; N, 4.65, 4.11; found C, 71.63; H, 7.65; N, 4.61.

4.11. General procedures and spectral data for (*E*)-enediol (14)

To a stirred and pre-cooled (−98 °C) Et_2O solution (7 mL) of oxazolinyloxirane **6b** (74 mg, 0.34 mmol) and TMEDA (1.38 mmol), a Et_2O solution of LDA (1.38 mmol, 0.3 M) was added dropwise. The resulting orange mixture was stirred for 3 h at this temperature, quenched with saturated aq NH_4Cl, extracted with EtOAc (3×5 mL) and the combined organic phases were dried with Na_2SO_4. Removal of the solvent in vacuo gave a yellow oil that was purified by column chromatography (3:2 EtOAc/petroleum ether) to give (*E*)-**14** (75%).

4.11.1. (1R,2E,4R*)-1,4-Bis-(4,4-dimethyl-4,5-dihydro-1,3-oxazol-2-yl)-1,4-diphenyl-but-2-ene-1,4-diol (**14**).* White solid, yield 85%, mp 152–153 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.53–7.47 (m, 4H), 7.36–7.24 (m, 6H), 6.60 (s, 2H), 4.21 (br s, exchanges with D_2O, 2H), 4.08 and 4.03 (2×d, AB system, $^2J_{H,H}$=8.0 Hz, 4H), 1.29 (s, 12H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ=168.3, 141.7, 131.6, 128.5, 128.3, 128.0, 126.1, 81.2, 74.5, 66.7, 28.1, 28.0 ppm. ESI-MS *m*/*z*: 435 (11) $[M+H]^+$, 457 (100) $[M+Na]^+$. FT-IR (KBr): ν=3326, 2975, 1632, 1450, 1151, 1031, 697 cm^{-1}. El. An. $C_{26}H_{30}N_2O_4$: calcd C, 71.87; H, 6.95; N, 6.44; found C, 71.97; H, 6.65; N, 6.48.

*4.11.2. 1-(4,4-Dimethyl-2-oxazolin-2-yl)-3-methyl-1-phenylbutan-1-ol (**15**).* Colourless oil, <10%. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.64–7.60 (m, 2H), 7.38–7.30 (m, 3H), 4.09 and 4.03 (2×d, AB system, $^3J_{H,H}$=8.2 Hz, 2H), 3.80 (br s, exchanges with D_2O, 1H), 2.06 (dd, $J_{H,H}$=14.2, 6.6 Hz, 1H), 1.96 (dd, $J_{H,H}$=14.2, 5.5 Hz, 1H), 1.84 (heptet, $^3J_{H,H}$=6.5 Hz, 1H), 1.32 (s, 3H), 0.9 (d, $^3J_{H,H}$=6.5 Hz, 3H), 1.21 (s, 3H), 0.97 (d, $^3J_{H,H}$=6.5 Hz, 3H) ppm. ^{13}H NMR ($CDCl_3$, 500 MHz): δ=169.4, 143.8, 128.0, 127.2, 125.3, 80.9, 74.7, 66.7, 48.0, 28.1, 28.0, 24.5, 23.6, 22.8 ppm. GC–MS (70 eV) *m*/*z* 261 (1) $[M]^+$, 204 (100), 105 (68). FT-IR (film): ν=3391, 2954, 1658, 1463, 1366, 1278, 1139, 1070, 698 cm^{-1}. HRMS (ESI), calcd for $C_{16}H_{24}NO_2$, $[M+H]^+$: 262.1807. Found: 262.1809.

4.12. General procedure and spectral data for the preparation of epoxylactones (1*R**,4*R**,5*R**)-16 and (1*R**,4*S**,5*R**)-16

To the equilibrating mixture of the spirocyclic compound and hydroxyalkyl derivative **13j** (100 mg, 0.3 mmol) in dioxane/H_2O (4:1, 5 mL) CF_3COOH (0.26 mmol, 20 μL) was added and the resulting mixture stirred for 24 h at rt. Then, the reaction mixture was poured into water, extracted with AcOEt (3×10 mL), dried on Na_2SO_4, filtered and the volatiles were removed under reduced pressure. Column chromatography (AcOEt/petroleum ether, 1:9) furnished epoxylactones **16**.

4.12.1. (1R,4R*,5R*)-1,4-Diphenyl-3,6-dioxabicyclo[3.1.0]hexan-2-one **16**.* Waxy solid, yield 59%. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.56–7.49 (m, 2H), 7.46–7.37 (m, 6H), 7.34–7.27 (m, 2H), 5.57 (s, 1H), 4.19 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.3, 134.6, 129.7, 129.5, 129.3, 128.7, 126.9, 126.0, 124.8, 79.1, 67.6, 59.2 ppm. GC–MS (70 eV) *m*/*z* 252 (<1) $[M]^+$, 207 (20), 105 (100), 77 (26), 44 (25). FT-IR (KBr): ν=3065, 2919, 2850, 1779, 1451, 1311, 1139, 1042, 942, 754, 696 cm^{-1}. HRMS (ESI), calcd for $C_{16}H_{12}NaO_3$, $[M+Na]^+$: 275.0684. Found: 275.0678.

4.12.2. (1R,4S*,5R*)-1,4-Diphenyl-3,6-dioxabicyclo[3.1.0]hexan-2-one **16**.* White solid, mp 126–128 °C, yield 61%. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.64–7.40 (m, 10H), 5.55 (d, $^3J_{H,H}$=1.6 Hz, 1H), 4.35 (d, $^3J_{H,H}$=1.6 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ=170.1, 133.2, 129.4, 129.3, 128.7, 128.6, 128.1, 126.9, 77.9, 66.2, 60.4 ppm. GC–MS (70 eV) *m*/*z* 252 (1) $[M]^+$, 207 (8), 105 (100), 90 (13), 77 (25). FT-IR (KBr): ν=3064, 1774, 1317, 1244, 1152, 1062, 963, 762, 745, 697 cm^{-1}. El. An. $C_{16}H_{12}O_3$: calcd C, 76.17; H, 4.79; found C, 75.83; H, 4.87.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.08.040.

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