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'*Syn-effect*' in the diastereoselective alkylation of $3-[(E)-\alpha,\beta$ -unsaturated- γ -substituted]-*N*-acyloxazolidinones



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ABSTRACT

Synthetic methods for the formation of alkenes usually produce the *E*-alkene because it is more stable. However, in isomerization reaction (double bond migration) that takes place in α , β -unsaturated carbonyl compounds, when these carbonyl compounds are exposed to strong bases, furnish *Z*-alkenes highly stereoselective depending on the γ -substituent in the α , β -unsaturated carbonyl. This stereoselectivity can be attributed to the known *Syn-effect*. The synthetic value of this methodology is the achievement of chiral alcohol bearing an electron rich *Z*-alkene, as well as substituted, which was accomplished via removal of the oxazolidinone moiety under treatment with NaBH₄, THF-H₂O.

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1. Introduction

Isomerization of conjugated α,β -unsaturated carbonyl compounds to deconjugated β , γ -unsaturated carbonyl compounds has been widely studied.¹ An important feature of this reaction is that it produces the thermodynamically less favorable and often difficult to access Z-alkene with high stereoselectivity. The reaction of dienolates derived from α,β -unsaturated carbonyl compounds with electrophiles, such as proton or alkyl halide, often affords α substituted β_{γ} -unsaturated carbonyl compounds.¹ Chiral lithium dienolates generated from chiral N-enoyl amides undergo allylation² and methylation³ at the α -position to afford α -substituted β , γ olefinic amides with high diastereo- and Z-selectivity. The cause of this unexpected stereoselectivity was rationalized by 'conforma*tional acidity*', which essentially implies *syn-effect*.⁴ In the transition state for deprotonation of the γ -H by strong base it is proposed that hyperconjugation of developing anion is more effective in the eclipsed conformations, wherein the developing anion is aligned with the $\pi^*C=C$ orbital. Furthermore, the *syn*-transition state is favored because it is stabilized by 6π -electron homoaromaticity, which involves the developing charge at the γ -position and

a pseudo p-orbital of δ -CH₂. Alternatively, there is a lone pair of electrons in a p-orbital of a hetero atom at the δ -position (Fig. 1).

The stereochemistry in the conversion of (E)- α , β -unsaturated esters to the corresponding β , γ -unsaturated esters is well ratio-



Fig. 1. a) *Syn effect* rationalized by 'conformational acidity'; $\sigma \rightarrow \pi$ in two conformations. b) *Syn effect* rationalized by 6π -electron homoaromaticity.

nalized by *syn-effect* and the relative degree of this depends on the γ -substituents, where it has seen that the fluorine atom at this γ -position favor the highest Z-selectivity, as shown in Fig. 2.

Kobayashi described an efficient method for the stereoselective construction of chiral quaternary α -carbon by regio- and stereoselective alkylation of chiral dienolate *N*-enoyl oxazolidinone.⁵

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Fig. 2. Relative isomerization's rate in terms of highest Z-selectivity to lowest Z-selectivity.

Davies described the synthesis of α -vinyl- β -hydroxyesters and α ethylidene- β -hydroxyesters via the dienolate aldol reaction of (*E*)-*N*-crotonyl oxazolidinone with high levels of *syn*-diastereoselectivity.⁶ We previously described a high *Z*-selective and diastereoselective alkylation reaction carried out on chiral *N*-enoyl oxazolidinones.⁷ This highly stereoselective isomerization reaction has been little exploited for the enantioselective production of chiral molecules. Therefore, this work presents the obtaining of chiral alcohols bearing an electron rich *Z*-alkene from the alkylation in *N*-enoyl oxazolidinone followed by removal of oxazolidinone moiety.

2. Results and discussion

The (E)- α , β -unsaturated carboxylic acids **3a**–**b** were prepared according to a methodology described by Han and Ito.⁸ The ethyl but-2-ynoate **1** was treated with the respective alcohol, triphenyl phosphine and a catalytic amount of acetic acid to give the esters **2a**–**b** in good yields. A subsequent basic hydrolysis with LiOH in THF/H₂O⁸ delivered the acids **3a**–**b** in 90% and 96% yield respectively, as shown in Scheme 1.



Scheme 1. Synthesis of (E)- α , β -unsaturated carboxylic acids.

The γ-(OTBS) substituted (*E*)- α , β -unsaturated carboxylic acid **7** was achieved via reduction reaction of the mono-ethyl fumarate **4** with BH₃-THF 1M to give the compound **5** in good yield,⁹ followed by protection of the hydroxyl group with *tert*-butyldimethylsilyl chloride.¹⁰ A subsequent basic hydrolysis of **6** with NaOH in MeOH and addition of a solution of 10% KHSO₄ delivered the acid **7** in 95% yield,11 as shown in Scheme 2.



Scheme 2. Synthesis of (E)- α , β -unsaturated carboxylic acid.

The γ -substituted α , β -unsaturated carboxylic acids **3a**–**b** and **7** were treated with triethylamine and pivaloyl chloride in THF, followed by addition of the respective oxazolidinones¹¹ (SuperQuat)¹² at 0 °C and after stirring for 18 h at room temperature afforded **8** and **9** as a white solid in 60 and 70% yield, respectively and **10** and

11 as a colorless liquid in 35 and 40% yield, respectively. Despite the fact that chemical yields are moderate, both starting materials can be easily recovered and once again subjected to the reaction, as shown in Scheme 3.



Scheme 3. *N*-acylation of oxazolidinones.

In contrast to traditional methods (LiHMDS, HMPA, $-78 \, ^{\circ}$ C),⁶ very low temperature ($-78 \, ^{\circ}$ C) did not favor the extraction of the H γ from α , β -unsaturated carbonyl derivative in the compound **8**; however, when **8** was treated with NaHMDS in the presence of LiCl at $-60 \, ^{\circ}$ C for 30 min and subsequent addition of a solution of NH₄Cl led to a migration of the double bond in 95% yield on the conjugated **8** to deconjugated **8**' in a highly stereoselective manner (*Z*/*E*>95:5). The *cis*-alkene geometry was established based on the measurement of coupling constants of vinyl protons in the ¹H NMR spectrum (³*J*_{H-H}=6.3 Hz), as shown in Scheme 4.



Taking advantage of this high stereoselectivity (*Z*/*E*), the *N*-enoyl oxazolidinones **8**–**10** were treated under the reaction conditions above described to form the corresponding enolates, followed by addition of iodomethane. The alkylation took place; when the reaction mixture reached at temperature of -45 °C, after stirring for 7 h at this temperature, the alkylated compounds **8a–10b** were achieved with high stereoselectivity (*Z*/*E*), moderate yields and moderate diastereoselectivity at the newly created α -stereogenic center. In all three cases, the like compounds **8a–10a** (*R*,*R*) were predominant. Despite the differences in bulkiness of the γ -substituents (OBn, OMe, OTBS) in the *N*-enoyl oxazolidinones **8–10**, the reaction always led to a high *Z*-selectivity in the alkylated products **8a–10b**, as shown in Table 1.

The use of other metals on the base (M'HMDS) (M'=Na, Li) did not lead to a significant change neither in yields of **8a–8b** nor in stereoselectivity of the reaction. However, the KHMDS provided the best results. It is noteworthy to mention that the absence of LiCl in the alkylation reaction led to a fast deacylation of the chiral auxiliary even at -78 °C. The presence of LiCl is necessary to achieve the alkylated products. It is probably due to the formation of a LiCl complex of the acyloxazolidinone, which produces considerable stabilization. The dienolate was successfully alkylated with allyl bromide and benzyl bromide to provide the like compounds **12a–13a** (*R*,*R*)¹³ in good yields and moderate diastereomeric ratios, as shown in Table 2.¹⁴ However, the treatment of the dienolate with ethyl iodide did not produce its respective alkylated compound, instead leading to isomerized compound **8**' (Scheme 4). T-1-1- 4



^a Yield corresponding to purified mixture of diastereomers.

80

60

OMe

OTBS

^b The ratios Z/E and diastereomeric ratios to the new stereogenic centers at C α were determined by ¹H NMR of the crude reaction mixture. *E*-isomers were not observed by ¹H NMR.

>95:5

>95.5

85/15

76/24

Table 2

2

3

Z-selective migration of the double bond and alkylation with different alkyl halides

Ph Ph Ph	OBn	1) LiCl 2) Base <u>30 min60°C</u> 3) R-X, - 60°C to -45°C 7h, -45°C 4) ag. NH ₂ Cl soln.	Ph	OBn Ph	O H R OBn Ph
	8	1/ 44/ 14/ 40/ 00/11	8a R = Me	8b R	= Me
			12a R = CH ₂ CH	=CH ₂ 12b R	= CH ₂ CH=CH ₂
			13a R = Bn	13b R	= Bn
Entry	Base	R-X	Yield ^a (%)	Z/E^{b}	d.r. ^b a/b
1	NaHMDS	CH ₃ I	74	>95:5	85/15
2	LiHMDS	CH ₃ I	50	>95:5	83/17
3	KHMDS	AllylBr	85	>95:5	72/28
4	KHMDS	BnBr	85	>95:5	76/24
5	KHMDS	EtI	0	0	0
-					

^a Yield corresponding to purified mixture of diastereomers.

^b The ratios Z/E and diastereomeric ratios to the new stereogenic center at C α were determined by ¹H NMR of the crude reaction mixture. *E*-isomers were not observed by ¹H NMR.

The dienolate of the *N*-enoyl oxazolidinone **11** was treated with alkyl halides to furnish the like compounds **14a–16a** (*S*,*S*) as the major products in moderate yields (50-60%), high diastereoselectivity (98:2) and with high *Z*-selectivity (Z/E) (>95:5). From these results, it can be argued that the chiral auxiliary bearing an isopropyl group provided higher levels of stereocontrol than chiral auxiliary with phenyl group as substituent in the respective alkylation reaction of the dienolates, as shown in Table 3.

Table 3

Z-Selective migration of double bond and highly diastereoselective alkylation

	1) LiCI OBn 2) KHM <u>30 min</u> 3) R-X, - 60°C 7h, -45 4) aq. N	LDS 60°C to -45°C Me Me Me Me Me Me 14a R = 15a R = 16a R =	$ \begin{array}{c} 0 \\ H \\ 1 \\ \hline \\ 7 \\ \hline \\ 8 \\ CH_2CH=CH_2 \\ Bn \end{array} + $	$Me \xrightarrow{0} H H H$ $Me \xrightarrow{14b} R = Me$ $15b R = CH_2CH=CH_2$ $16b R = Bn$
Entry	R-X	Yield ^a (%)	Z/E ^b	d.r. ^b a/b
1	CH₃I	60	>95:5	98/2
2	AllylBr	52	>95:5	98/2
3	BnBr	50	>95:5	98/2

^a Yield corresponding to purified diastereomer.

^b The ratios Z/E and diastereomeric ratios to the new stereogenic center at C α were determined by ¹H NMR of the crude reaction mixture. E-isomers were not observed by ¹H NMR.

Reaction of *N*-enoyl oxazolidinone **8** with KHMDS and in the presence of *tert*-butyldimethylsilyl chloride gave the respective vinylketene silyl *N*,*O*-acetyl **17** in 95% yield. Only one product was detected by ¹H NMR.¹⁵ Alkylation reaction of **17** was carried out with tetrabutyl ammonium fluoride and an excess of MeI in THF to provide the α -alkylated product **8a** in 75% yield, high *Z*-selectivity (*Z*:*E*) (>95:5) and with a diastereomeric ratio (80/20). The reaction was also regioselective, the γ -alkylated product was not detected, as shown in Scheme 5.



Scheme 5. Alkylation reaction via vinylketene silyl N,O-acetal.

The stereochemistry at the newly formed chiral center of **8a** was established as *R* by comparison to the known compounds **19–20**.¹⁶ Compounds **19–20** were prepared via a sequence of reactions as described below: hydrogenation of **8a** with Pd–C in EtOH provided the compound **18** in quantitative yield, removal of the chiral auxiliary with LiOH, H_2O_2 in THF/ H_2O^{17} delivered the carboxylic acid **19** in 80% yield. The alcohol **20** was achieved as a colorless liquid in 83% yield by reduction of **18** with NaBH₄ in THF/ $H_2O_1^{18}$ as shown in Scheme 6.



Scheme 6. Chiral auxiliary removal. Reagent and conditions i) H₂, Pd/C, EtOH, 16 h, 25 °C; ii) LiOH, H₂O₂, THF/H₂O 0–25 °C, 90 min, aq. Na₂SO₃, 1M HCl soln.; iii) NaBH₄ THF/H₂O 25 °C 3 h.

Removal of the chiral auxiliary under Evans' experimental conditions in the compound **8a** led to a diastereomeric mixture of liquid γ -lactones¹⁹ **21a–b** in 80% yield and with d.r. 70:30. The carboxylic acid **22** was achieved in 80% yield under Evans' experimental conditions if the aqueous solution 1M HCl was replaced with an aqueous solution of KHSO₄. However, the carboxylic acid can be transformed to the corresponding γ -lactones **21a–b** after storage by several days, as shown in Scheme 7.

Removal of the oxazolidinone moiety from alkylated adduct **8a** with Sm(OTf)₃ or Sn(OTf)₂ as Lewis acids in MeOH²⁰ did not afford the corresponding carboxylic ester. Apparently, under this reaction condition the double bond of **8a** was not stable in the presence of these Lewis acids. The reaction mixture led to a decomposition of the starting material. On the other hand, treatment of alkylated adducts **8a**–**13b** with sodium borohydride in a mixture of THF-H₂O gave rise to chiral alcohol **23a–25b** bearing a *cis*-alkene in 80–84%



Scheme 7. Chiral auxiliary removal. *Reagent and conditions* i) LiOH, H_2O_2 , THF/ H_2O 0–25 °C, 90 min, aq. Na₂SO₃, 1M HCl soln.; ii) LiOH, H_2O_2 , THF/ H_2O 0–25 °C, 90 min, aq. Na₂SO₃, aq. KHSO₄ soln.; iii) three day at room temperature.

yields. The enantiomeric purities of the alcohols were determined by HPLC (equipped with chiral OD and AS-H columns) analysis and comparison with racemic samples. The achieved results are shown in Fig. 3.



Fig. 3. Chiral alcohols bearing cis-alkene.

3. Conclusion

In conclusion we described a diastereomeric alkylation reaction carried out in 3-[(*E*)- α , β -unsaturated- γ -substituted]-*N*-acylox-azolidinones with strong bases to provide 3-[(*Z*)- α -substituted- β , γ -unsaturated]-*N*-acyloxazolidinones in moderate yields. The reaction was highly regioselective giving only product of alkylation at α -position. Depending on the chiral auxiliary (oxazolidinone moiety) the diastereoselectivity can be moderate to high. A high *Z*-selectivity was observed (*Z*/*E*) (>95:5) in the formation of a *cis*-alkene in the alkylated product. This *Z*-selectivity was attributed to the important *Syn-effect*. The synthetic relevance of this methodology is that chiral molecules can be achieved bearing an electron rich *cis*-alkenes as substituent, which may be useful in organic synthesis.

4. Experimental section

4.1. General information

All moisture-sensitive reactions were carried out in oven-dried glassware under argon atmosphere. Dichloromethane was distilled from CaH₂ under argon. THF was distilled from Na/benzophenone under argon. Optical rotations were measured in a polarimeter with sodium p-line (589 nm) and are reported on a concentration (c) of grams/100 mL of solvent. ¹H and ¹³C NMR spectra and ¹H-¹H COSY, DEPT and HMQC, experiments were measured with a 400 MHz FTNMR spectrometer. ¹H NMR chemical shifts (δ) are reported in parts per million (ppm) relative to Me₄Si (δ =0.0 ppm) with coupling constants (J) reported in Hertz (Hz). Multiplicities are reported as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad singlet (br s). ¹³C NMR spectra are reported using

77.0 ppm (CDCl₃) as internal reference. High resolution mass spectra were performed with QQHQ mass analyzer type. HPLC, were performed with Photodiode Array Detector using chiral columns OD and AS-H.

4.2. Procedure for the N-acylation of oxazolidinones

4.2.1. (4R.E)-3-(4'-Benzvloxy-but-2'-enovl)-4.5.5-triphenvl-oxazolidinone 8. To an oven-dried 100 mL round-bottom equipped with a magnetic stir bar, anhydrous LiCl (0.42 g, 10.0 mmol) was added followed of THF (10 mL), dry triethylamine (2.43 g, 24.0 mmol) and pivaloyl chloride (1.45 g, 12.0 mmol). To reaction mixture a solution of the corresponding carboxylic acid (2.30 g, 12.0 mmol) in THF (5 mL) under an argon atmosphere at 0 °C was added. The reaction mixture was stirred for 1 h at the same temperature and oxazolidinone (3.15 g, 10.0 mmol) in 5 mL THF was added. Then, the reaction mixture was warmed up to room temperature and continued being stirred for 18 h. Then, the reaction was quenched by the addition of a saturated solution of NH₄Cl (3 mL), and THF was removed under reduced pressure. The organic layer was extracted with CH₂Cl₂ (3×30 mL), and washed with a solution of NaHCO₃, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography eluting with hexane-ethyl acetate (90:10) to give the respective N-enoyl oxazolidinone 8 (2.94 g, 60%) as a white solid, mp 115.6 °C, [α]²⁵_D +156.6 (*c* 1.60, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.65 (2H, dt, J=8.0, 1.6 Hz, Ph), 7.55 (1H, dt, J=15.3, 2.0 Hz, CH=), 7.45-7.00 (19H, m, Ph, CH=), 6.28 (1H, s, CH), 4.56 (2H, s, CH₂Ph), 4.19 (2H, dd, *I*=4.4, 2.0 Hz, CH₂O); ¹³C NMR (100 MHz, CDCl₃) δ: 163.8, 152.6, 146.8, 141.6, 137.9, 135.6, 134.0, 129.0128.8, 128.7, 128.6, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.5, 127.4, 127.0, 126.4, 126.2, 126.0, 120.1, 89.0, 72.8, 69.0, 66.0; IRumax: 2844.1, 1786, 1688.4, 1640.2, 1587.0, 1496.0, 1450.1, 1364.0, 1022.6, 1000.1, 753.8, 693.4 cm⁻¹; EI-HRMS: calculated for (C₃₂H₂₇NO₄), 489.1940; found, 489.1942.

4.2.2. (4R,E)-3-(4'-Methoxybut-2'-enoyl)-4,5,5-triphenyl-oxazolidinone **9**. Purified by flash chromatography with hexane—ethyl acetate (95:5) to afford the desired product as a white solid, (18.3 mg, 70%), mp 143–144 °C, $[\alpha]_{25}^{D5}$ +109.7 (*c* 0.9, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 7.64 (2H, dt, *J*=7.5, 1.6 Hz, Ph), 7.48–7.34 (4H, m, Ph, CH=), 7.11–7.00 (11H, m, Ph, CH=), 6.27 (1H, s, CH), 4.10 (2H, dd, *J*=4.5, 2.0 Hz, CH₂), 3.38 (3H, s, OCH₃); ¹³C NMR (125 MHz, CDCl₃) δ : 163.8, 152.6, 146.8, 141.6, 137.9, 135.6, 134.0, 129.0128.9, 128.3, 128.2, 128.4, 127.7, 127.5, 127.4, 126.2, 126.0, 120.0, 89.1, 71.4, 66.1, 58.7; IR_{ymax}: 3061.6, 1775.4, 1691.5, 1334.1, 1208.2, 991.8, 751.9, 689.54 cm⁻¹; FAB-HRMS: calculated for (C₂₆H₂₄NO₄), 414.1705; found, 414.1888.

4.2.3. (4R,E)-3-[(4'-tert-Butyldimethylsilyloxy)but-2'-enoyl]-4,5,5triphenyloxazolidinone **10**. Purified by flash chromatography with hexane—ethyl acetate (97:3) to afford the desired product as a liquid, (1.80 g, 35%); [α]_D²⁵ +145.0 (*c* 1.3, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.65 (2H, dt, *J*=7.2, 1.2 Hz, Ph), 7.58 (1H, dt, *J*=14.8, 2.4 Hz, =CH), 7.44–7.34 (3H, m, Ph), 7.13–7.00 (11H, m, =CH, Ph), 6.28 (1H, s, CHN), 4.35 (2H, dd, *J*=3.6, 2.4 Hz, CH₂), 0.93 (9H, s, *t*-Bu-), 0.08 (3H, s, CH₃), 0.07 (3H, s, CH₃); ¹³C NMR (100 MHz, CDCl₃) 164.1, 152.5, 150.2, 141.7, 138.0, 135.7, 129.0, 128.8, 128.2, 128.0, 127.6, 127.4, 127.3, 126.12, 126.0, 118.4, 88.8, 66.0, 62.5, 25.7, 18.2, 5.5; FAB-HRMS: calculated for C₃₁H₃₆NO₄Si: 514.2414; found, 514.2379.

4.2.4. (4S,E)-3-(4'-Benzyloxy-but-2'-enoyl)-4-isopropyl-5,5dimethyl-oxazolidinone **11**. Purified by flash chromatography with hexane–ethyl acetate (95:5) to afford the desired product as a liquid, (1.33 g, 40%); $[\alpha]_D^{25}$ +23.0 (*c* 1.7, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.60 (1H, dt, *J*=15.2, 2.0 Hz, CH=), 7.40–7.30 (5H, m, Ph), 7.14 (1H, dt, *J*=15.6, 4.6 Hz, CH=), 4.60 (2H, s, CH₂Ph), 4.24 (2H, dd, *J*=4.8, 2.0 Hz, CH₂O), 4.22 (1H, d, *J*=3.2 Hz, CHN), 2.16 (1H, m, CH(CH₃)₂), 1.52 (3H, s, CH₃), 1.39 (3H, s, CH₃), 1.04 (3H, d, *J*=6.8 Hz, CH₃), 0.96 (3H, d, *J*=7.2 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 165.3, 153.4, 146.0, 137.6, 128.4, 127.7, 120.6, 82.8, 72.8, 69.0, 66.3, 26.6, 28.7, 21.4, 21.3, 17.0; IR_{umax}: 2966.8, 2912.6, 1766.2, 1685.0, 1636.8, 1453.3, 1363.0, 959.8, 740.2, 695.1 cm⁻¹; FAB-HRMS: calculated for (C₁₉H₂₆NO₄), 332.1862; found, 332.1820.

4.3. Procedure for the isomerization (double bond migration)

4.3.1. (4R,Z)-3-(4'-Benzyloxy-but-3'-enoyl)-4,5,5triphenyloxazolidinone 8'. To an oven-dried 100 mL round-bottom equipped with a magnetic stir bar was added anhydrous LiCl (15.3 mg, 0.36 mmol) under an argon atmosphere followed of Nenoyl oxazolidinone 8 (150 mg, 0.30 mmol). Both solids were dissolved in anhydrous THF (25 mL) and the reaction mixture was stirred for 15 min at -60 °C and then was added 1.0 M NaHMDS (0.54 mL, 0.54 mmol) and the resulting solution was stirred vigorously. After 30 min the temperature was increased at-45 °C and the reaction was stirred for 7 h. After the reaction was quenched by the addition of a saturated solution of NH₄Cl (3 mL), THF was removed under reduced pressure. The organic layer was extracted with CH_2Cl_2 (3×30 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The oily residue was purified by flash column chromatography eluting with hexane-ethyl acetate (95:5) to give the compound **8**' as a liquid (140 mg, 95%); $[\alpha]_{\rm D}^{25}$ +136.9 (c 2.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.63 (2H, dt, J=7.0, 1.5 Hz, Ph), 7.44-7.25 (8H, m, Ph), 7.10-6.98 (10H, m, Ph), 6.21 (1H, s, CHN), 6.12 (1H, dt, J=6.4, 1.5 Hz, CH=), 4.74 (2H, s, CH₂Ph), 4.58 (1H, dt, J=6.4, 6.8 Hz, CH=), 3.80 (1H, ddd, J=19.2, 6.8, 1.5 Hz, CH_a), 3.75 (1H, ddd, *J*=19.2, 6.8, 1.5 Hz, CH_b); ¹³C NMR (100 MHz, CDCl₃) δ: 170.6, 152.6, 146.8, 141.7, 138.0, 137.2, 135.7, 128.8, 128.7, 128.4, 128.3, 128.1, 128.0, 127.8, 127.6, 127.4, 127.3, 127.2, 126.1, 125.9, 97.5, 89.0, 73.6, 66.0, 31.5; IR_{umax}: 2923.4, 1788.7, 1712.8, 1496.1, 1450.5, 1364.2, 1347.4, 997.0, 845.0, 759.7 cm⁻¹; EI-HRMS: calculated for (C₃₂H₂₇NO₄), 489.1940; found, 489.1942.

4.4. General procedure for the alkylation reaction

4.4.1. (2'R,4R,Z)-3-(4'-Benzyloxyl-2'-methylbut-3'-enoyl)-4,5,5triphenyloxazolidinone 8a. To an oven-dried 100 mL round-bottom equipped with a magnetic stir bar was added anhydrous LiCl (0.24 mmol, 10.3 mg) under an argon atmosphere followed of Nenoyl oxazolidinone 8 (0.2 mmol, 0.10 g). Both solids were dissolved in anhydrous THF (25 mL) and the reaction mixture was stirred for 15 min at-60 °C and then was added NaHMDS (0.41 mmol, 0.41 mL) and the resulting solution was stirred vigorously during 30 min. After, was added CH₃I (1.2 mmol, 0.17 g), the temperature was increased at-45 °C and the reaction mixture was stirred for 7 h. After the reaction was guenched by the addition of a saturated solution of NH₄Cl (3 mL), THF was removed under reduced pressure. The organic layer was extracted with CH₂Cl₂ (3×30 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The oily residue was purified by flash column chromatography eluting with hexane-ethyl acetate (95:5) to give a diastereomeric mixture of the compounds 8a and 8b. Their isolation was carried out by preparative thin layer chromatography eluting twice with hexane-CH₂Cl₂ 9:1, to give the compound **8a** as a liquid (144.0 mg, 70%); $[\alpha]_D^{25}$ +82.9 (*c* 2.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.60 (2H, dd, *J*=7.0, 1.6 Hz, Ph), 7.38–7.22 (8H, m, Ph), 7.12–7.00 (10H, m, Ph), 6.20 (1H, s, CHN), 5.90 (1H, dd, J=6.0, 1.2 Hz, CH=), 4.73 (1H, dq, J=8.4, 7.0 Hz, CHCH₃), 4.60 (1H, d, J=12.8 Hz, CH_aH_bPh), 4.56 (1H, d, J=12.8 Hz, CH_bH_aPh), 4.53 (1H, dd, J=8.4, 6.0 Hz, CH=), 1.21 (3H, d, J=7.0 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 174.7, 152.2, 145.1, 141.8, 138.1, 137.3, 136.0, 128.7, 128.6, 128.3, 128.2, 128.0, 127.7, 127.6, 127.3, 127.1, 126.2, 126.0, 105.7, 88.6, 73.4, 66.2, 34.5, 17.8; IR₉max: 2922.1, 1782.0, 1703.7, 1450.7, 1329.8, 989.6, 696.7. cm⁻¹; FAB-HRMS: calculated for $(C_{33}H_{30}NO_4)$, 504.2175; found, 504.2154.

4.4.2. (2'S,4R,Z)-3-(4'-Benzyloxyl-2'-methylbut-3'-enoyl)-4,5,5triphenyloxazolidinone **8b**. Liquid, (20.5 mg, 10%); [α]_D²⁵ +138.7 (c 0.75, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.63 (2H, dt, *J*=7.2, 1.6 Hz, Ph), 7.44–7.28 (8H, m, Ph), 7.08–7.00 (10H, m, Ph), 6.21 (1H, s, CHN), 6.02 (1H, dd, *J*=6.4, 1.2 Hz, CH=), 4.77 (1H, dq, *J*=8.4, 7.0 Hz, CHCH₃), 4.75 (1H, d, *J*=12.4 Hz, CH₄H_bPh), 4.71 (1H, d, *J*=12.4 Hz, CH₄H_bPh), 4.71 (1H, d, *J*=12.4 Hz, CH₄H_bPh), 4.75 (1H, dd, *J*=8.4, 6.0 Hz, CH=), 1.11 (3H, d, *J*=7.2 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 174.7, 152.2, 145.6, 141.8, 138.0, 137.3, 135.6, 128.8, 128.4, 128.3, 128.1, 128.0, 127.8, 127.6, 127.5, 127.4, 127.3, 126.3, 126.1, 105.4, 88.7, 73.7, 66.0, 34.6, 17.9; IR_{Jmax}: 2922.1, 1782.0, 1703.7, 1450.7, 1329.8, 989.6, 696.7. cm⁻¹; EI-HRMS: calculated for (C₃₃H₂₉NO₄), 503.2097; found, 503.2085.

4.4.3. (2'R, 4R, Z)-3-(4'-Methoxy-2'-methylbut-3'-enoyl)-4,5,5triphenyloxazolidinone **9a**. Waxy, purified by flash chromatography with hexane–ethyl acetate (95:5) to afford the desired product as a liquid, (70.7 mg, 80%); $[\alpha]_{25}^{25}$ +86.7 (*c* 1.1, CHCl₃); r.d. 96:4; ¹H NMR (500 MHz, CDCl₃) 7.63 (2H, d, *J*=7.5, Hz, Ph), 7.42–7.34 (3H, m, Ph), 7.10–7.00 (10H, m, Ph), 6.20 (1H, s, CHN), 5.77 (1H, dd, *J*=6.0, 1.0 Hz, CH=), 4.63 (1H, dq, *J*=8.0, 7.0 Hz, CHCH₃), 4.47 (1H, dd, *J*=8.0, 6.0 Hz, CH=), 3.36 (3H, s, OMe), 1.20 (3H, d, *J*=7.0 Hz, CH₃); ¹³C NMR (125 MHz, CDCl₃) 174.8, 152.3, 147.0, 142.0, 138.2, 136.0, 136.0, 128.8, 128.7, 128.2, 128.1, 127.6, 127.4, 126.3, 126.2, 105.0, 88.7, 66.2, 60.0, 34.4, 17.9; IR_{Umax}: 2930.0, 1784.0, 1704.0, 1451.0, 1215.0, 1105.0, 756.0, 699.0. cm⁻¹; FAB-HRMS: calculated for (C₂₇H₂₆NO₄), 428.1862; found, 428.1884.

4.4.4. (2'R,4R,Z)-3-[(4'-tert-Butyldimethylsilyloxy)-2'-methylbut-3'enoyl]-4,5,5-triphenyloxazolidinone 10a. Purified by flash column chromatography eluting with hexane-ethyl acetate (97:3) to give a diastereomeric mixture of the compounds **10a** and **10b**. Their isolation was carried out by preparative thin layer chromatography eluting with hexane-CH₂Cl₂ 7:3, to give the compound **10a** as a white solid (120 mg, 44%); m.p. 80.2 °C. $[\alpha]_{D}^{25}$ +85.8 (*c* 1.9, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.64 (2H, dt J=7.6, 1.2 Hz, Ph), 7.44–7.34 (3H, m, Ph), 7.13-7.00 (10H, m, Ph), 6.21 (1H, s, CHN), 6.13 (dd, *J*=5.7 Hz, =CH), 4.84 (1H, dq, *J*=8.8, 7.2 Hz, CH), 4.61 (1H, dd, *J*=8.8, 5.7 Hz, =CH), 1.22 (3H, d, J=7.2 Hz, CH₃), 0.83 (9H, s, t-Bu), 0.05 (3H, s, CH₃), 0.01 (3H, s, CH3). ¹³C NMR (100 MHz, CDCl₃) δ: 175.0, 152.0, 141.8, 139.5, 138.2, 136.0, 128.8, 128.6, 128.2, 128.0, 127.6, 127.3, 126.2126.0, 108.5, 88.5, 66.1, 33.8, 25.4, 18.0, -5.6; FAB-HRMS: calculated for (C₃₂H₃₈NO₄Si): 528.2570; found: 528.2574.

4.4.5. (2'R,4R,Z)-3-(4'-Benzyloxyl-2'-allylbut-3'-enoyl)-4,5,5triphenyloxazolidinone **12a**. Purified by flash column chromatography eluting with hexane—ethyl acetate (95:5) to give a diastereomeric mixture of the compounds **12a** and **12b**. Their isolation was carried out by preparative thin layer chromatography eluting with hexane-CH₂Cl₂ 9:1, to give the compound **12a** as a liquid (160 mg, 61%); $[\alpha]_D^{25}$ +69.5 (*c* 1.34, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.60 (2H, dt, *J*=6.4, 1.6 Hz, Ph), 7.36–7.20 (8H, m, Ph), 7.10–7.00 (10H, m, Ph), 6.20 (1H, s, CHN), 5.94 (1H, dd, *J*=6.0, 0.8 Hz, CH=), 5.63 (1H, m, CH=), 4.88 (1H, m, CH), 4.84 (2H, s, CH₂=), 4.56 (1H, d, *J*=12.8 Hz, CH_aH_bPh), 4.52 (1H, d, *J*=12.8 Hz, CH_bH_aPh), 4.46 (1H, dd, *J*=8.4, 6.0 Hz, CH=), 2.49 (1H, m, CH_aH_b), 2.23 (1H, m, CH_bH_a); ¹³C NMR (100 MHz, CDCl₃) δ : 173.6, 152.2, 146.0, 142.0, 138.1, 137.2, 136.0, 134.7, 128.7, 128.6, 128.3, 128.1, 128.0, 127.7, 127.6, 127.5, 127.3, 127.0, 126.2, 126.0, 117.0, 103.7, 88.6, 73.4, 66.2, 39.1, 36.7; IR_{ymax}: 3065.9, 2917.3, 1789.4, 1704.6, 1496.0, 1450.5, 1209.0, 994.0, 916.0, 759.8, 751.9 cm⁻¹; EI-HRMS: calculated for (C₃₅H₃₁NO₄), 529.2253; found, 529.2259.

4.4.6. (2'S,4R,Z)-3-(4'-Benzyloxyl-2'-allylbut-3'-enoyl)-4,5,5triphenyloxazolidinone **12b**. Its isolation was carried out by preparative thin layer chromatography eluting with hexane-CH₂Cl₂ 9:1, to give the compound **12b** as a liquid (63 mg, 24%); $[\alpha]_{2}^{D5}$ +159.5 (c 1.71, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.63 (2H, dt, *J*=6.8, 1.6 Hz, Ph), 7.44–7.28 (8H, m, Ph), 7.00 (10H, br s, Ph), 6.20 (1H, s, CHN), 6.04 (1H, dd, *J*=6.0, 1.2 Hz, CH=), 5.55 (1H, m, CH=), 4.97 (1H, m, CH), 4.74 (1H, dd, *J*=15.6, 1.6 Hz, CH_aH_b=), 4.73 (2H, s, CH₂Ph), 4.66 (1H, dd, *J*=10.2, 1.6 Hz, CH_bH_a=), 4.43 (1H, dd, *J*=8.7, 6.0 Hz, CH=), 2.32 (1H, m, CH_aH_b), 2.21 (1H, m, CH_bH_a); ¹³C NMR (100 MHz, CDCl₃) 173.5, 152.3, 146.1, 141.8, 138.0, 137.3, 135.6, 134.6, 128.8, 128.4, 128.0, 127.9, 127.7, 127.6, 127.4, 127.3, 127.2, 126.2, 126.1, 116.7, 103.6, 88.6, 73.7, 66.1, 39.4, 37.2; IR_{Umax}: 3065.9, 2917.3, 1789.4, 1704.6, 1496.0, 1450.5, 994.0, 916.0, 759.8, 751.9 cm⁻¹; FAB-HRMS: calculated for (C₃₅H₃₂NO₄), 530.2331; found, 530.2355.

4.4.7. (2'R,4R,Z)-3-(4'-Benzyloxyl-2'-benzylbut-3'-enoyl)-4,5,5triphenyloxazolidinone 13a. Purified by flash column chromatography eluting with hexane-ethyl acetate (95:5) to give a diastereomeric mixture of the compounds 13a and 13b. Their isolation was carried out by preparative thin layer chromatography eluting with hexane-CH2Cl2 9:1, to give the compound 13a as a Liquid (190 mg, 65%); $[\alpha]_D^{25}$ +67.2 (*c* 1.43, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.61 (2H, dt, J=6.8, 1.6 Hz, Ph), 7.38-7.23 (6H, m, Ph), 7.17–6.90 (17H, m, Ph), 6.20 (1H, s, CHN), 5.86 (1H, dd, *J*=6.0, 1.0 Hz, CH=), 5.18 (1H, m, CH), 4.44 (1H, dd, J=8.4, 6.0 Hz, CH=), 4.43 (1H, d, *I*=12.8 Hz, CH_aH_bO), 4.35 (1H, d, *I*=12.8 Hz, CH_bH_aO), 3.14 (1H, dd, J=13.2, 6.8 Hz, CH_aH_bPh), 2.64 (1H, dd, J=13.2, 8.0 Hz, CH_bH_aPh); ¹³C NMR (100 MHz, CDCl₃) 173.6, 152.2, 146.1, 141.9, 138.5, 138.1, 137.2, 135.8, 134.7, 129.4, 129.1, 128.8, 128.6, 128.3, 128.2, 128.0, 127.8, 127.6, 127.3, 127.0, 126.9, 126.3, 126.1, 103.6, 88.6, 73.3, 66.2, 41.0, 38.4; IR_{umax}: 3035.7, 2920.7, 1781.9, 1701.8, 1496.1, 1450.9, 1366.6, 1330.6, 1211.5, 743.8, 696.3 cm⁻¹; EI-HRMS: calculated for (C₃₉H₃₃NO₄), 580.2410; found, 580.2395.

4.4.8. (2'S,4R,Z)-3-(4'-Benzyloxyl-2'-benzylbut-3'-enoyl)-4,5,5triphenyloxazolidinone **13b**. Its isolation was carried out by preparative thin layer chromatography eluting with hexane-CH₂Cl₂ 7:3, to give the compound **13b** as a liquid (59.1 mg, 20%); $[\alpha]_D^{25}$ +136.4 (*c* 1.03, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.54 (2H, dt, *J*=6.4, 1.6 Hz, Ph), 7.41–7.19 (6H, m, Ph), 7.11–6.98 (6H, m, Ph), 6.15 (1H, s, CHN), 6.01 (1H, d, *J*=6.0 Hz, CH=), 5.17 (1H, m, CH), 4.67 (1H, d, *J*=12.8 Hz, CH_aH_bO), 4.60 (1H, d, *J*=12.8 Hz, CH_bH_aO), 4.42 (1H, dd, *J*=8.8, 6.0 Hz, CH=), 2.94 (1H, dd, *J*=13.2, 6.8 Hz, CH_aH_bPh), 2.70 (1H, dd, *J*=13.6, 7.6 Hz, CH_bH_aPh); ¹³C NMR (100 MHz, CDCl₃) 173.2, 152.1, 146.5, 141.7, 138.5, 138.0, 137.3, 135.7, 129.1, 128.8, 128.7, 128.4, 128.0, 127.9, 127.7, 127.5, 127.4, 127.3, 127.2, 126.3, 126.1, 126.0, 103.4, 88.5, 73.6, 66.1, 41.5, 38.4; IR_{ymax}: 3035.7, 2920.7, 1781.9, 1701.8, 1496.1, 1450.9, 1366.6, 1330.6, 1211.5, 743.8, 696.3 cm⁻¹; FAB-HRMS: calculated for (C₃₉H₃₄NO₄), 580.2488; found, 580.2450.

4.4.9. (2'S, 4S, Z)-3-(4'-Benzyloxy-2'-methylbut-3'-enoyl)-4isopropyl-5,5-dimethyloxazolidinone **14a**. Purified by flash column chromatography eluting with hexane–ethyl acetate (95:5) to give the compound **14a** as a liquid (100 mg, 60%); $[\alpha]_D^{25}$ +67.7 (*c* 1.29, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.35–7.26 (5H, m, Ph), 6.06 (1H, dd, *J*=6.0, 1.0 Hz, CH=), 4.82 (1H, dqd, *J*=8.0, 7.0, 1.0 Hz, CHCH₃), 4.80 (1H, d, *J*=12.4 Hz, CH_aH_bPh), 4.76 (1H, d, *J*=12.8 Hz, CH_bH_aPh), 4.65 (1H, dd, *J*=8.0, 6.0 Hz, CH=), 4.12 (1H, d, *J*=3.2 Hz, CHN), 2.12 (1H, m, CH(CH₃)₂), 1.48 (3H, s, CH₃), 1.35 (3H, d, *J*=7.0 Hz, CH₃CH), 1.26 (3H, s, CH₃), 1.01 (3H, d, *J*=6.6 Hz, CH₃), 0.95 (3H, d, *J*=6.6 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 176.3, 153.1, 145.2, 137.3, 128.4, 127.8, 127.3, 106.3, 82.6, 73.7, 66.3, 34.2, 29.5, 28.4, 21.5, 21.3, 18.9, 16.9; IR_{umax}: 2970.8, 2929.2, 1770.2, 1701.9, 1452.3, 1369.1, 1066.0, 730.2, 697.0 cm⁻¹; EI-HRMS: calculated for (C₂₀H₂₇NO₄), 345.1940; found, 345.1932.

4.4.10. (2'S, 4S, Z)-3-(4'-Benzyloxyl-2'-allylbut-3'-enovl)-4isopropyl-5.5-dimethyloxazolidinone **15a**. Purified by flash column chromatography eluting with hexane-ethyl acetate (95:5) to give the compound **15a** as a liquid (96.6 mg, 52%); $[\alpha]_D^{25}$ +52.2 (*c* 2.71, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.36–7.26 (5H, m, Ph), 6.10 (1H, dd, J=6.0, 1.2 Hz, CH=), 5.85 (1H, ddt, J=17.2, 10.4, 6.8 Hz, CH=), 5.10 (1H, dd, *J*=17.2, 2.0 Hz, CH=), 5.03 (1H, dd, *J*=10.4, 2.0 Hz, CH=), 4.97 (1H, m, CH), 4.78 (1H, d, J=2.4 Hz, CH₂Ph), 4.57 (1H, dd, J=8.2, 6.0 Hz, CH=), 4.11 (1H, d, J=3.2 Hz, CHN), 2.62 (1H, ddd, J=14.0, 7.0, 6.8 Hz, CH_aH_b), 2.38 (1H, ddd, *J*=14.0, 7.0, 6.8 Hz, CH_bH_a), 2.11 (1H, m, CH(CH₃)₂), 1.47 (3H, s, CH₃), 1.23 (3H, s, CH₃), 1.00 (3H, d, J=7.2 Hz, CH₃), 0.94 (3H, d, J=7.2 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 175.0, 153.2, 146.0, 137.2, 135.3, 128.4, 127.8, 127.3, 117.0, 104.5, 82.5, 73.8, 66.5, 38.7, 37.5, 29.5, 28.3, 21.4, 21.3, 16.8; IR_{umax}: 2972.1, 2917.7, 1773.8, 1690.9, 1459.2, 1364.9, 913.0, 732.9, 695.0 cm⁻¹; EI-HRMS: calculated for (C₂₂H₂₉NO₄), 371.2097; found, 371.2096.

4.4.11. (2'S, 4S, Z)-3-(4'-Benzyloxyl-2'-benzylbut-3'-enoyl)-4isopropyl-5,5-dimethyloxazolidinone 16a. Purified by flash column chromatography eluting with hexane-ethyl acetate (95:5) to give the compound **16a** as a liquid (110 mg, 50%); $[\alpha]_D^{25}$ +50.6 (*c* 1.73, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.34–7.15 (10H, m, Ph), 6.02 (1H, dd, J=6.4, 1.2 Hz, CH=), 5.30 (1H, dtd, J =, 8.2, 8.0, 1.2 Hz, CHCH₂), 4.70 (1H, d, J=12.4 Hz, OCH_aH_b), 4.62 (1H, d, J=12.4 Hz, OCH_bH_a), 4.54 (1H, dd, J=8.2, 6.4 Hz, CH=), 4.08 (1H, d, J=3.2 Hz, CHN), 3.23 (1H, dd, *J*=13.2, 6.8 Hz, CH_aH_bPh), 2.81 (1H, dd, *J*=13.2, 8.4 Hz, CH_bH_aPh), 2.02 (1H, m, CH(CH₃)₂), 1.44 (3H, s, CH₃), 1.22 (3H, s, CH₃), 0.85 (3H, d, *J*=6.8 Hz, CH₃), 0.74 (3H, d, *J*=6.8 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 175.0, 153.1, 146.2, 138.8, 137.1, 129.4, 128.3, 128.0, 127.7, 127.2, 126.1, 104.4, 82.4, 73.6, 66.5, 40.6, 39.2, 29.4, 28.4, 21.3, 16.5; IR_{umax}: 2956.4, 2917.5, 1779.2, 1695.6, 1495.4, 1450.6, 1364.0, 1113.0, 1065.2, 739.6, 697.7 cm⁻¹; EI-HRMS: calculated for (C₂₆H₃₁NO₄), 421.2253; found, 421.2258.

4.4.12. (2'R,4R)-3-(4'-Benzyloxy-2'-methylbutanoyl)-4,5,5triphenyloxazolidinone 18. To an oven-dried 100 mL round-bottom equipped with a magnetic stir bar, the compound 8a (100 mg, 0.20 mmol) was added followed of EtOH (3 mL), and 10% Pd/C (20 mg). The reaction mixture was stirred for 16 h at room temperature. Then, the reaction was filtered over celite and EtOH was removed under reduced pressure. The residue was purified by flash column chromatography eluting with hexane-ethyl acetate (95:5) to give the respective product 18 (97.0 mg, 99%) as a white solid, mp 93.4 °C, [α]_D²⁵ +121.5 (*c* 1.64, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.62 (2H, dd, J=8.2, 1.2 Hz, Ph), 7.40-7.20 (7H, m, Ph), 7.11-7.00 (11H, m, Ph), 6.23 (1H, s, CHN), 4.23 (1H, d, *I*=12.0, CH_aH_bPh), 4.18 (1H, d, J=12.0, CH_bH_aPh) 3.91 (1H, m, CH), 3.38–3,26 (2H, m, CH₂O), 1.98 $(1H, m, CH_aH_b), 1.60 (1H, m, CH_bH_a), 1.07 (3H, d, J=6.9 Hz, CH_3); {}^{13}C$ NMR (100 MHz, CDCl₃) 176.0, 152.4, 141.7, 138.3, 138.0, 135.8, 128.9, 128.8, 128.2, 128.1, 127.6, 127.5, 127.4, 127.2, 126.1, 126.0, 88.7, 72.7, 67.7, 66.0, 35.0, 33.0, 17.3; IR_{vmax}: 2927.3, 2850.7, 1785.4, 1703.1, 1495.5, 1450.6, 986.1, 968.6, 846.0, 751.6, 692.1, 667.4 cm⁻¹; El-HRMS: calculated for (C₃₃H₃₁NO₄), 505.2253; found, 505.2239.

4.4.13. (*R*)-4-*Benzyloxy-2-methylbutyric acid* **19**. To 100 mL roundbottom equipped with a magnetic stir bar, the compound **18** (97 mg, 0.19 mmol) in THF (6 mL) and H₂O (2 mL) at 0 °C were added followed of 30% H₂O₂ (0.13 g, 1.14 mmol) and LiOH (15.9 mg, 0.38 mmol). The reaction mixture was stirred for 1.5 h at room temperature. Then, the reaction was quenched by the addition of an aqueous saturated solution of Na₂SO₃ (5 mL) at 0 °C. Then, the pH of solution was adjusted in a range of 9–10 by the addition of a saturated solution of NaHCO3 and the THF was removed under reduced pressure. The organic layer was extracted with CH₂Cl₂ (3×30 mL), and dried over Na₂SO₄, filtered and concentrated under reduced pressure to yield the oxazolidinone. The pH of the aqueous phase was adjusted between 1 and 2 by the addition of a aqueous solution of 1M HCl and the organic laver was extracted with AcOEt (3×30 mL), and dried over Na₂SO₄, filtered and concentrated under reduced pressure to give **19** as a liquid (31.7 mg, 80%); $[\alpha]_D^{25}$ –11.0 (*c* 1.9, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.33-7.31 (5H, m, Ph), 4.51 (1H, d, *J*=11.6 Hz, CH_aH_bPh), 4.48 (1H, d, *J*=11.6 Hz, CH_bH_aPh), 3.53 (2H, t, J=6.4 Hz, CH₂O), 2.67 (1H, m, CH), 2.04 (1H, m, CH_aH_b), 1.72 (1H, m, $CH_{b}H_{a}$), 1.20 (3H, d, J=6.8 Hz, CH_{3}); ¹³C NMR (100 MHz, CDCl₃) 182.7, 138.2, 128.3, 127.6, 127.5, 73.0, 67.8, 36.4, 33.1, 17.0; IR_{vmax}: 3450.0, 3250.0, 2919.3, 2850.5, 1704.2, 1455.6, 1110.2, 1092.7, 746.1, 696.5 cm⁻¹; EI-HRMS: calculated for (C₁₂H₁₆O₃), 208.1099; found, 208.1074.

4.4.14. (2R)-4-(Benzyloxyl)-2-methylbutan-1-ol 20. To 100 mL round-bottom equipped with a magnetic stir bar, the compound 18 (97 mg, 0.19 mmol) in THF (6 mL) and H₂O (1 mL) were added followed of a solution of NaBH₄ (28.8 mg, 0.76 mmol) in H₂O (1 mL). The reaction mixture was stirred for 3 h at room temperature. Then, the reaction was quenched by the addition of a aqueous solution of 2N HCl (3 mL), and THF was removed under reduced pressure. The organic layer was extracted with CH₂Cl₂ (3×30 mL), and washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The oily residue was purified by preparative thin layer chromatography eluting with CH₂Cl₂-hexane 9:1, to give the compound **20** as a liquid (30.6 mg, 83%); $[\alpha]_D^{25}$ +10.5 (*c* 0.35, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.37-7.28 (5H, m, Ph), 4.52 (2H, s, CH₂Ph), 3.60 (1H, m, CH_aH_bO), 3.52 (1H, m, CH_bH_aO), 3.51 (1H, dd, J=11.0, 4.8 Hz, CH_aH_bOH), 3.43 (1H, dd, J=11.0, 6.8 Hz, CH_bH_aOH), 1.82 (1H, m, CHCH₃), 1.70 (1H, m, CH_aH_b), 1.60 (1H, m, CH_bH_a), 0.92 (3H, d, J=6.8 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 137.8, 128.4, 127.8, 127.7, 73.1, 68.5, 68.1, 34.2, 34.0, 17.2; IR_{vmax}: 3422.3, 2917.3, 2844.1, 1454.5, 1269.9, 1092.2, 1022.6, 737.0, 695.2 cm⁻¹; EI-HRMS: calculated for (C₁₂H₁₈O₂), 194.1307; found, 194.1306.

(3*R*, 5*S*)-5-(benzyloxy)-3-methyldihidrofuran-2-(3*H*)-one **21a**; Purified by preparative thin layer chromatography eluting with hexane-AcOEt 8:2, to give the compound **21a** as a liquid (10 mg, 30%); $[\alpha]_D^{25}$ –42.4 (*c* 0.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.38–7.31 (5H, m, Ph), 5.55 (1H, dd, *J*=5.6, 4.3 Hz, H-4), 4.90 (1H, d, *J*=11.6 Hz, CH_aH_bPh), 4.61 (1H, d, *J*=11.6 Hz, CH_bH_aPh), 2.64 (1H, dqd, 9.5, 7.0, 6.5 Hz, H-1), 2.62 (1H, ddd, *J*=13.0, 9.5, 5.6 Hz, H-3), 1.87 (1H, ddd, *J*=13.0, 6.5, 4.3, Hz, H-2), 1.35 (3H, d, *J*=7.0 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 178.7, 136.3, 128.5, 128.2, 128.1, 101.7, 71.4, 36.3, 34.4, 16.6; IR_{vmax}: 2926.6, 1779.6, 1455.6, 1162.8, 953.9, 904.1, 738.7, 698.9 cm⁻¹; FAB-HRMS: calculated for (C₁₂H₁₅O₃), 207.1021; found, 207.1044.

4.4.15. (3*R*, 5*R*)-5-(*Benzyloxy*)-3-*methyldihidrofuran*-2-(3*H*)-one **21b**. Purified by preparative thin layer chromatography eluting with hexane-AcOEt 8:2, to give the compound **21b** as a liquid (30 mg, 69%); $[\alpha]_D^{55}$ +109.1 (*c* 0.7, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.37–7.31 (5H, m, Ph), 5.52 (1H, d, *J*=5.6 Hz, H-4), 4.82 (1H, d, *J*=11.6 Hz, CH₄H_bPh), 4.57 (1H, d, *J*=11.6 Hz, CH_bH₄Ph), 2.87 (1H, ddq, *J*=10.8, 8.6, 7.2 Hz, H-1), 2.42 (1H, dd, *J*=13.2, 8.5 Hz, H-3), 2.00 (1H, ddd, *J*=13.2, 10.8, 5.6 Hz, H-2), 1.26 (3H, d, *J*=7.2 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 179.6, 136.4, 128.5, 128.2, 100.5, 70.6, 37.2, 32.5, 15.2; IR_{vmax}: 2926.6, 1779.6, 1455.6, 1162.8, 953.9, 904.1, 738.7, 698.9 cm⁻¹; EI-HRMS: calculated for (C₁₂H₁₄O₃), 206.0943; found, 206.0923.

4.4.16. (2R, Z)-4-Benzyloxyl-2-methylbut-3-enoic acid **22**. To 100 mL round-bottom equipped with a magnetic stir bar, the

compound **8a** (100 mg, 0.0.20 mmol) in THF (6 mL) and $H_2O(2 mL)$ at 0 °C were added followed of 30% H₂O₂ (0.14 g, 1.20 mmol) and LiOH (16.8 mg, 0.40 mmol). The reaction mixture was stirred for 1.5 h at room temperature. Then, the reaction was quenched by the addition of an aqueous saturated solution of Na₂SO₃ (5 mL) at 0 °C. Then, the pH of solution was adjusted in a range of 9–10 by the addition of a saturated solution of NaHCO3 and the THF was removed under reduced pressure. The organic layer was extracted with CH₂Cl₂ (3×30 mL), and dried over Na₂SO₄, filtered and concentrated under reduced pressure to yield the oxazolidinone. The pH of the aqueous phase was adjusted between 1 and 2 by the addition of a aqueous solution of KHSO₄ and the organic layer was extracted with AcOEt (3×30 mL), and dried over Na₂SO₄, filtered and concentrated under reduced pressure to give 22 as a liquid (33.0 mg, 80%); $[\alpha]_D^{25}$ –54.3 (*c* 0.8, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.38–7.28 (5H, m, Ph), 6.12 (1H, dd, J=6.0, 1.2 Hz, CH=), 4.85 (1H, dd, J=12.6, CH_aH_b), 4.80 (1H, dd, J=12.6, CH_bH_a), 4.53 (1H, dd, J=8.8, 6.0 Hz, CH=), 3.68 (1H, m, CH), 1.26 (3H, d, J=6.8 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 181.2, 145.7, 137.1, 128.5, 128.0, 127.3, 106.0, 74.0, 35.3, 17.8; IR_{vmax}: 3457.0, 3257.2, 2924.0, 2912.3, 1782.6, 1700.4, 1451.0, 1360.0,1104.7, 1067.1, 905.2, 732.1, 696.9 cm⁻¹; EI-HRMS: calculated for (C₁₂H₁₄O₃), 206.0943; found, 206.0923.

4.4.17. (R,Z)-4-(Benzyloxy)-2-methylbut-3-en-1-ol 23a. To 100 mL round-bottom equipped with a magnetic stir bar, the compound 8a (100 mg, 0.19 mmol) in THF (6 mL) at 0 °c were added followed of a solution of NaBH₄ (30 mg, 0.79 mmol) in H₂O (2 mL). The reaction mixture was stirred for 16 h at room temperature. Then, the reaction was guenched by the addition of a saturated solution of NaCl (10 mL), and THF was removed under reduced pressure. The organic layer was extracted with AcOEt (3×20 mL), and dried over Na₂SO₄, filtered and concentrated under reduced pressure. The oily residue was purified by preparative thin layer chromatography eluting with Hexane/AcOEt 8:2, to give the oxazolidinone as a white solid (50 mg, 80%) and the compound **23a** as a liquid (32 mg, 84%); $[\alpha]_{D}^{25}$ +3.5 (c 2.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.38-7.28 (5H, m, Ph), 6.12 (1H, dd, J=6.2, 1.2 Hz, =CH), 4.80 (2H, s, CH₂Ph), 4.23 (1H, dd, *J*=8.8, 6.2 Hz, =CH), 3.51 (1H, dd, *J*=10.2, 5.4 Hz, CH_aH_bO), 3.36 (1H, dd, J=10.2, 8.2 Hz, CH_bH_aO), 2.88 (1H, m, CH), 1.80 (1H, br s, OH), 0.96 (3H, d, J=6.8 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 145.6, 137.2, 128.5, 128.0, 127.3, 110.0, 73.8, 67.0, 32.4, 17.1; IR_{vmax}: 3449.0, 2927.0, 2871.0, 2362.0, 2339.0, 1663.0, 1457.0, 1029.0, 743.0, 698.0 cm⁻¹; EI-HRMS: calculated for (C₁₂H₁₆O₂), 192.1150; found,192.1145.

4.4.18. (R, Z)-2-[(2-Bezyloxy)vinyl]pent-4-en-1-ol 24a. Purified by preparative thin layer chromatography eluting with Hexane/AcOEt 8:2, to give the oxazolidinone as a white solid (23.8 mg, 80%) and the compound 24a as a liquid (16.4 mg, 80%); [\alpha]_D^{25} +14.7 (c 1.9, CHCl₃); ¹H NMR (400 MHz,CDCl₃) 7.38–7.30 (5H, m, Ph), 6.18 (1H, dd, J=6.0, 1.2 Hz, =CH), 5.77 (1H, ddt, J=17.0, 10.0, 6.8 Hz, =CH), 5.03 (1H, ddd, J=17.0, 3.6, 1.6 Hz, =CH), 5.00 (1H, ddt, J=10.0, 1.6, 1.2 Hz, =CH), 4.80 (2H, s, CH₂Ph), 4.24 (1H, dd, J=9.2, 6.0 Hz, =CH), 3.60 (1H, dd, J=10.0, 5.2 Hz, CH_aH_bO), 3.42 (1H, dd, J=10.0, 7.6 Hz, CH_bH_aO), 2.88 (1H, m, CH), 2.18 (1H, ddd, J=14.0, 6.4, 6.4 Hz, CH_aH_b), 2.04 (1H, ddd, J=14.0, 7.2, 7.2 Hz CH_bH_a), 1.70 (1H, br s, OH); ¹³C NMR (100 MHz, CDCl₃) 146.4, 137.2, 136.6, 128.5, 128.0, 127.0, 116.0, 107.8, 73.8, 66.2, 37.5, 36.2; IR_{ymax}: 3422.0, 2925.0, 2873.0, 2368.0, 2340.0, 1663.0, 1455.0, 1103.0, 1071.0, 737.0, 694.0. cm⁻¹; FAB-HRMS: calculated for (C₁₄H₂₀O₂), 220.1463; found, 220.1435.

4.4.19. (*R*, *Z*)-2-Benzyl-4-(benzyloxy)but-3-en-1-ol **25a**. Purified by preparative thin layer chromatography eluting with Hexane/AcOEt 8:2, to give the oxazolidinone as a white solid (34.4 mg, 80%) and the compound **25a** as a liquid (29.6 mg, 80%); $[\alpha]_{25}^{25}$ +4.4

(c 2.3, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.34–7.16 (10H, m, Ph), 6.10 (1H, dd, *J*=6.2, 1.2 Hz, =CH), 4.73 (1H, d, *J*=12.8 Hz, OCH_aH_bPh), 4.67 (1H, d, *J*=12.8 Hz, OCH_bH_aPh), 4.25 (1H, dd, *J*=9.2, 6.2 Hz, =CH), 3.60 (1H, dd, J=10.4, 5.2 Hz, OCH_aH_b), 3.44 (1H, dd, J=10.4, 7.4 Hz, OCH_bH_a), 3.11 (1H, m, CH), 2.75 (1H, dd, J=13.6, 6.8 Hz, CH_aH_bPh), 2.56 (1H, dd, *J*=13.6, 8.0 Hz, CH_bH_aPh), 1.80 (1H, br s. OH): ¹³C NMR (100 MHz, CDCl₃) 146.5, 140.0, 137.2, 129.0, 128.4, 128.0, 127.8, 127.2, 125.7, 107.6, 73.6, 65.8, 39.3, 38.0; IR_{vmax}: 3447.0, 2926-0, 2862.0, 2361.0, 2343.0, 1658.0, 1496.0, 1456.0, 739.0, 700.0 cm⁻¹; EI-HRMS: calculated for (C₁₈H₂₀O₂), 268.1463; found, 268.1469.

4.4.20. (S,Z)-4-(Benzyloxy)-2-methylbut-3-en-1-ol 23b. Purified by preparative thin layer chromatography eluting with Hexane/AcOEt 8:2, to give the oxazolidinone as a white solid (25 mg, 80%) and the compound **23b** as a liquid (16 mg, 84%); $[\alpha]_D^{25}$ -3.3 (*c* 0.5, CHCl₃); ¹H NMR (400 MHz,CDCl₃) 7.38–7.31 (5H, m, Ph), 6.13 (1H, d, J=6.2 Hz, =CH), 4.80 (2H, s, CH₂Ph), 4.23 (1H, dd, J=9.2, 6.2 Hz, =CH), 3.52 (1H, dd, J=10.4, 5.2 Hz, CH_aH_bO), 3.36 (1H, dd, J=10.4, 8.0 Hz, CH_bH_aO), 2.89 (1H, m, CH), 0.96 (3H, d, J=6.8 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) 145.6, 137.2, 128.5, 128.0, 127.4, 110.0, 73.8, 68.0, 32.5, 17.1; IR_{vmax}: 3449.0, 2927.0, 2871.0, 2362.0, 2339.0, 1663.0, 1457.0, 1029.0, 743.0, 698.0 cm⁻¹; EI-HRMS: calculated for (C₁₂H₁₆O₂), 192.1150; found,192.1145.

4.4.21. (S, Z)-2-[(2-Bezyloxy)vinyl]pent-4-en-1-ol 24b. Purified by preparative thin layer chromatography eluting with Hexane/AcOEt 8:2. to give the oxazolidinone as a white solid (28.5 mg, 80%) and the compound **24b** as a liquid (19.7 mg, 80%); Liquid, Yield 80%; $[\alpha]_{D}^{25}$ –14.7 (c 1.6, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.38–7.30 (5H, m, Ph), 6.18 (1H, dd, J=6.0, 1.2 Hz, =CH), 5.77 (1H, ddt, J=17.0, 10.0, 6.8 Hz, =CH), 5.03 (1H, ddd, /=17.0, 3.6, 1.6 Hz, =CH), 5.00 (1H, ddt, J=10.0, 1.6, 1.2 Hz, =CH), 4.80 (2H, s, CH₂Ph), 4.24 (1H, dd, J=9.2, 6.0 Hz, =CH), 3.60 (1H, dd, J=10.0, 5.2 Hz, CH_aH_bO), 3.42 (1H, dd, J=10.0, 7.6 Hz, CH_bH_aO), 2.88 (1H, m, CH), 2.18 (1H, ddd, J=14.0, 6.4, 6.4 Hz, CH_aH_b), 2.04 (1H, ddd, *J*=14.0, 7.2, 7.2 Hz CH_bH_a), 1.70 (1H, br s, OH); ¹³C NMR (100 MHz, CDCl₃) 146.4, 137.2, 136.6, 128.5, 128.0, 127.0, 116.0, 107.8, 73.8, 66.2, 37.5, 36.2; IR_{vmax}: 3422.0, 2925.0, 2873.0, 2368.0, 2340.0, 1663.0, 1455.0, 1103.0, 1071.0, 737.0, 694.0. cm^{-1} ; FAB-HRMS: calculated for (C₁₄H₂₀O₂), 220.1463; found, 220.1435.

4.4.22. (S. Z)-2-Benzvl-4-(benzvloxv)but-3-en-1-ol 25b. Purified by preparative thin layer chromatography eluting with Hexane/AcOEt 8:2, to give the oxazolidinone as a white solid (26.1 mg, 80%) and the compound **25b** as a liquid (22.2 mg, 80%); $[\alpha]_D^{25}$ -4.7 (*c* 1.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃) 7.34-7.16 (10H, m, Ph), 6.10 (1H, dd, J=6.2, 1.2 Hz, =CH), 4.73 (1H, d, J=12.8 Hz, OCH_aH_bPh), 4.67 (1H, d, J=12.8 Hz, OCH_bH_aPh), 4.25 (1H, dd, J=9.2, 6.2 Hz, =CH), 3.60 (1H, dd, *J*=10.4, 5.2 Hz, OCH_aH_b), 3.44 (1H, dd, *J*=10.4, 7.4 Hz, OCH_bH_a), 3.11 (1H, m, CH), 2.75 (1H, dd, *J*=13.6, 6.8 Hz, CH_aH_bPh), 2.56 (1H, dd, *J*=13.6, 8.0 Hz, CH_bH_aPh), 1.80 (1H, br s, OH); ¹³C NMR (100 MHz, CDCl₃) 146.5, 140.0, 137.2, 129.0, 128.4, 128.0, 127.8, 127.2, 125.7, 107.6, 73.6, 65.8, 39.3, 38.0; IR_{vmax}: 3447.0, 2926.0, 2862.0, 2361.0, 2343.0, 1658.0, 1496.0, 1456.0, 739.0, 700.0 cm⁻¹; EI-HRMS: calculated for (C₁₈H₂₀O₂), 268.1463; found, 268.1469.

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Supplementary data

Supplementary data (¹H NMR and ¹³C NMR, spectra of all compounds.) related to this article can be found at http:// dx.doi.org/10.1016/i.tet.2015.05.037.

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