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Enantioselective radical allylation reactions using chiral lanthanide Lewis acids

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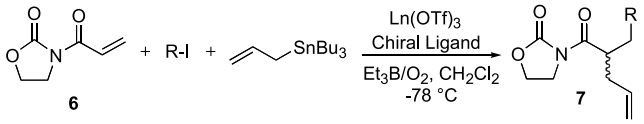
Abstract—Radical additions to oxazolidinone acrylate followed by allyl trapping were studied with chiral Lewis acids derived from lanthanide salts. Chiral ligands were evaluated to establish the α-stereocenter. Ligands with a prolinol framework along with achiral additives proved to be effective. The observed trends are compared with those in the literature.

1. Introduction

Lanthanide salts have been established as useful catalysts and reagents in a variety of asymmetric transformations.[1,2] The lanthanide triflates, as a family of Lewis acids, possess attractive properties for application in catalysis.[3] They are generally air and moisture stable and have a longer shelf life compared to certain main group and transition metal Lewis acids. Their Lewis acidity is strong enough for activation of substrates towards many reactions. The variation of ionic radii among the lanthanides provides a convenient handle for modification of the chiral environment for a particular transformation. Chiral Lewis acids are known to catalyze enantioselective radical reactions, especially, carbon–carbon bond forming reactions.[4] The majority of these reactions have employed main group Lewis acids. The use of lanthanide triflates as Lewis acids in radical reactions has been limited so far.[5]

Radical additions to enoates followed by trapping of the resultant α-acyl radicals with allylstannane have been studied. Allylstannanes are a good trap for electrophilic radicals and a ready source for the introduction of allyl moiety.[6] Upon addition of the radical, fragmentation of the trialkyltin group readily generates a chain carrying tin radical. Porter et al. have utilized chiral Lewis acids derived from zinc triflate and bisoxazoline ligands in stoichiometric amounts to perform addition to acrylimide **6** (cf. Scheme 1) followed by trapping with allylstannane.[7] Moderate to good yields and good ee's were obtained. The generation of α-acyl radicals from α-bromo compounds were also studied



6 **7**

Scheme 1.

using the same chiral Lewis acid and trapping with either allylstannane or allyl silanes.[8] The two approaches were also compared in terms of the steric effect of the β-substituent.[9] Toru and co-workers have investigated radical addition to sulfones followed by allyl trapping under similar conditions as reported by Porter.[10] We recently reported the first examples of vicinal stereocontrol proceeding with high diastereo- and enantioselectivity using radical chemistry. In these reactions magnesium or copper Lewis acids along with aminoindanol-derived bisoxazoline ligands were used.[11]

Our interest in lanthanide triflates as activators for conjugate addition of nucleophilic radicals to enoates has met with considerable success. Both diastereoselective and enantioselective radical conjugate additions have been documented (Eqs. (1) and (2)). These efforts have focused on establishing the stereochemistry in either the initial addition of the radicals to the prochiral faces of the substrate or the trapping of α-acyl radical with allylstannanes. In one example, the lanthanide triflate organizes the substrate **1** in a conformation where the diphenylmethyl group shields the pro-*R* face of the radical (Eq. (1)).[12] Excellent yields and diastereoselectivities were obtained for the product **2**. In the second case, samarium triflate with the chiral ligand **5** derived from proline in conjunction with benzoyl oxazolidinone (achiral additive) provided moderate yields and high selectivity for establishing the β-stereocenter (Eq. (2)).[13]

Keywords: lanthanide triflates; radical; allylation; additives.
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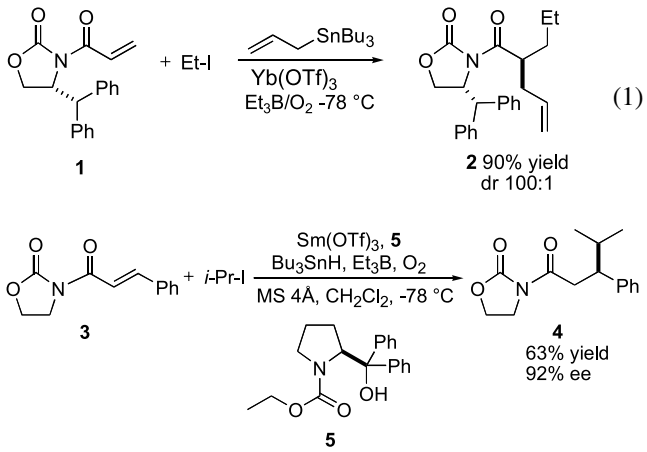
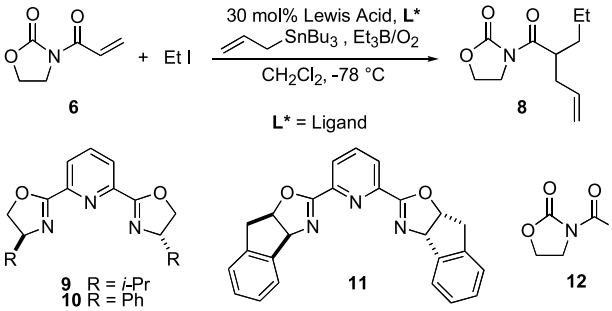


In an effort to evaluate the efficacy of the chiral lanthanide Lewis acids in establishing α-stereochemistry, we have now explored the addition-trapping reactions of acrylimide **6** as outlined in Scheme 1. This addition-trapping reaction provides products that could be further transformed to complex systems. For example, our laboratory has shown that products obtained from the addition of olefin containing alkyl halides followed by trapping with allylstannane can be useful substrates for RCM reactions.[14] Furthermore, a product derived from acrylimide containing a *t*-butoxycarbonyl substituent at the β-position has been converted to BB-1101, a potent MMP inhibitor.[15]

2. Results and discussion

Different family of chiral ligands have been shown to be successful with lanthanide Lewis acids in enantioselective transformations. These include chiral BINOLs, bisoxazolines, Py-BOX etc. Initially Py-BOX ligands were chosen for evaluation in radical allylation due to their ready availability and success in a variety of asymmetric transformations.[16] The allylation reactions were performed with 30 mol% of chiral Lewis acids obtained from yttrium, ytterbium and samarium triflates and Py-BOX ligands **9**, **10** and **11** (Table 1). The chiral Lewis acids were formed by mixing the lanthanide triflates and the chiral ligands in dichloromethane followed by cooling to −78°C and addition of substrate **6**. The reactions were performed with 5–10 equiv. of alkyl iodide, 5 equiv. of allyltributyl stannane and 3 equiv. of triethylborane as the radical initiator in the presence of oxygen. For the initial screening, we chose the addition of ethyl radical followed by allyl trapping and these results are shown in Table 1. In general, the reactions with all the different Lewis acids gave low enantioselectivities for **8** (entries 1–12). Of the Lewis acids examined, reactions with yttrium triflate were the most successful with respect to chemical yield as well as enantioselectivity (entries 1, 7 and 10). Based on the results in the literature regarding the possibility of dimeric complexes of lanthanides with PyBOX ligands, we surmised that the low ee's could arise from catalyst dimerization.[17] To suppress this, addition of an achiral additive was evaluated to aid in the availability of the monomeric chiral Lewis acid for catalysis.[18] Accordingly, benzoyl oxazolidinone **12** was used as an additive in both 1

Table 1. Evaluation of Py-Box ligands



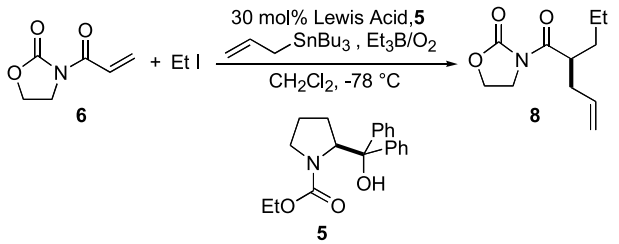
Entry	Lewis acid	Ligand	Yield (%)[a]	ee (%)[b]
1	$Y(OTf)_3$	**9**	72	18
2[c]	$Y(OTf)_3$	**9**	48	9
3[d]	$Y(OTf)_3$	**9**	46	0
4	$Yb(OTf)_3$	**9**	48	9
5	$Y(NTf_2)_3$	**9**	30	3
6	$Sm(OTf)_3$	**9**	60	20
7	$Y(OTf)_3$	**10**	41	6
8	$Yb(OTf)_3$	**10**	14	4
9	$Sm(OTf)_3$	**10**	34	4
10	$Y(OTf)_3$	**11**	78	22
11	$Yb(OTf)_3$	**11**	62	4
12	$Sm(OTf)_3$	**11**	73	22

[a] Isolated yields.
[b] Chiral HPLC analysis.
[c] 2 equiv. of **12** was used as an additive.
[d] 300 mg MS 4 Å was used.

and 2 equiv. (entry 2) compared to the chiral Lewis acid. Surprisingly in both of these reactions, the selectivity dropped further to provide racemic products (compare entry 1 with 2). Similar effect was also observed on addition of 4 Å molecular sieves (entry 3). At the present time we do not have a good explanation for the results obtained with additives.

Due to the low ee's provided by the Py-BOX ligands, we then evaluated alternate systems that had shown promise with lanthanide Lewis acids. Recently Kobayashi et al. have reported that prolinol based ligands are efficient in the conjugate addition of thiols to enoates.[19] During our work on conjugate radical additions, we had also developed a family of proline-derived ligands which proved to be efficient with lanthanide Lewis acids.[13] Although in the example shown in Eq. (2), we had found that the optimal Lewis acid was samarium triflate, it was not apparent why the same Lewis acid should prove to be optimal in establishing the α-stereocenter. Hence a survey of various lanthanide Lewis acids was undertaken (Table 2). The lanthanides with larger ionic radii, lanthanum and cerium gave racemic products when used in combination with ligand **5** (entries 1 and 2). Additionally, a regular trend in selectivity with the ionic radii of the lanthanide metal ions was not discerned (entries 1–9). However, we were pleased to find that yttrium and ytterbium triflates provided the product in moderate yield and selectivity (entries 5 and 7). Other lanthanides in general led to lower yields and selectivities. As observed in Table 1, the use of 4 Å molecular sieves decreased the ee's drastically in this case too (compare entry 5 with 6). The solubility and the Lewis acidity of the Lewis acids can be modified by varying the counterion. Triflimide salts have been used as Lewis acids in

Table 2. Screening of Lewis acids with **5**



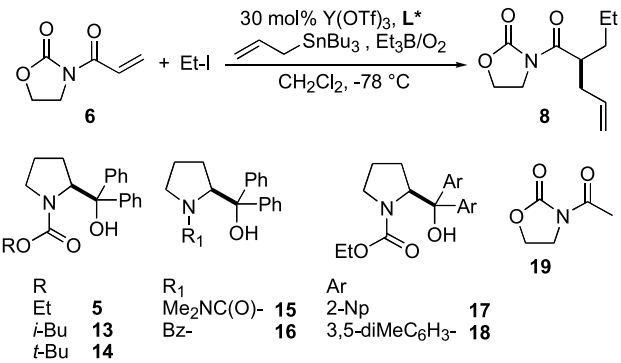
Entry	Lewis acid	Yield (%)[a]	ee (%)[b]
1	$La(OTf)_3$	56	0
2	$Ce(OTf)_4$	53	0
3	$Sm(OTf)_3$	35	52
4	$Er(OTf)_3$	35	37
5	$Y(OTf)_3$	61	70
6[c]	$Y(OTf)_3$	50	20
7	$Yb(OTf)_3$	45	50
8	$Yb(NTf_2)_3$	22	7
9	$Sc(OTf)_3$	10	10

[a] Isolated yields.
[b] Chiral HPLC analysis.
[c] 300 mg MS 4 Å was used.

a few cases and we have shown that they are effective in radical conjugate addition.[20] As shown in entry 8, ytterbium triflimide led to decreased reactivity and selectivity in the presence of ligand **5** in contrast to the use the corresponding triflate (compare entry 7 with 8).

After determining yttrium triflate to be the optimal Lewis acid, the effect of ligand structure was evaluated using ethyl radical addition followed by allyl trapping as the standard reaction. The ligands were prepared using literature procedures.[21] The results from these experiments are presented in Table 3. As described earlier, addition/trapping with ligand **5** gave the product in good enantioselectivity (entry 1). The effect of additives in combination with **5** was also explored. The use of *N*-acetyl (entry 2) or *N*-benzoyl oxazolidinone (entry 3) as achiral additives led to improvements in enantioselectivity. Similar enhancements in ee were also observed by the use of additives in our previous work on conjugate radical addition.[13] The effect of ligand structure on selectivity was explored by varying the carbamate substituent, the size of the proline substituent, and the nature of the acyl group. Of the three carbamate substituents investigated (**5**, **13** and **14**), the smallest R group, ethyl, gave the highest selectivity (compare entry 1 with 4 and 5). Replacement of the carbamate group by a urea type substituent (**15**) or an amide group (**16**), led to lower enantioselectivities (compare entry 1 with 6 and 7). The size of the aryl group is the primary determinant of face selectivity in these proline-based ligands. Only marginal improvements in selectivity were observed by varying the aryl substituents from phenyl (**5**) to naphthyl (**17**) to a 3,5-dimethylphenyl group (**18**) (entries 1, 8, and 9). The absolute stereochemistry for the allyl product was established by hydrolysis and comparison of the sign of optical rotation with that reported in the literature.[22]

Table 3. Effect of ligand structure on selectivity

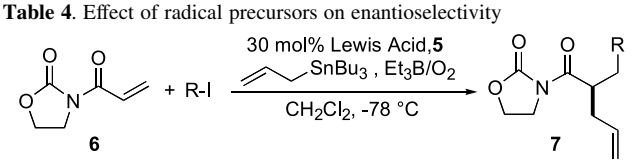


Entry	Ligand	Yield (%)[a]	ee (%)[b]
1	**5**	61	70 (*S*)
2[c]	**5**	69	79 (*S*)
3[d]	**5**	71	80 (*S*)
4	**13**	59	67 (*S*)
5	**14**	73	53 (*S*)
6	**15**	63	29 (*S*)
7	**16**	59	5 (*S*)
8	**17**	52	73 (*S*)
9	**18**	60	73 (*S*)

[a] Isolated yields.
[b] Chiral HPLC analysis.
[c] 2 equiv. of **19** was used as an additive.
[d] 2 equiv. of **12** was used as an additive.

Porter and co-workers in their studies on radical allylations using main group Lewis acids have shown that the size of the radical has a large impact on selectivity: the larger the radical, the higher the selectivity.[9] In an effort to understand if this trend is also the case with lanthanide Lewis acids, we carried out addition/trapping experiments by varying the size of the radical and the results from these experiments are tabulated in Table 4. For these experiments 30 mol% of yttrium triflate and ligand **5** was used as the chiral Lewis acid. Addition of chloromethyl radical followed by trapping gave the allylated product in moderate yield and selectivity (entry 1). As illustrated earlier, addition of ethyl radical and allyl trapping proceeds with good selectivity (70% ee, entry 2) and the ee could be enhanced to 80% by using **12** as an

Table 4. Effect of radical precursors on enantioselectivity



Entry	R	Product	Yield (%)[a]	ee (%)[b]
1	$ClCH_2$–	**7a**	56	42
2	Et	**8**	61	70
3[c]	Et	**8**	46	66
4	*n*-Pr	**7b**	57	60
5	*n*-Bu	**7c**	41	38
6	*i*-Pr	**7d**	50	56
7[d]	*i*-Pr	**7d**	67	68
8	*t*-Bu	**7e**	40	24
9[c]	*t*-Bu	**7e**	48	24
10[d]	*t*-Bu	**7e**	46	42
11	*c*-Hex	**7f**	53	31

[a] Isolated yields.
[b] Chiral HPLC analysis.
[c] 100 mol% of the chiral Lewis acid was used.
[d] 2 equiv. of **12** was used as an additive.

additive (see Table 3). To determine if the non-catalyzed addition was responsible for the observed modest selectivity, a reaction with stoichiometric amount of the chiral Lewis acid was carried out (entry 3). This change led to a small decrease in selectivity (compare entry 3 with 2). Increasing the chain length of the radical from ethyl to *n*-propyl to *n*-butyl led to a systematic lowering of selectivity (compare entries 2, 4, and 5). Addition of isopropyl radical was moderately effective, however, the enantioselectivity was lower than that for ethyl addition (compare entry 2 with 6). This result is in stark contrast to Porter's observation.[9] A small enhancement in selectivity for isopropyl radical addition could be realized by using **12** as an additive (compare entry 7 with 6). Addition of the bulky *t*-butyl radical addition was neither chemically efficient nor the enantioselectivity was high (entry 8). Reaction with stoichiometric amount of the Lewis acid was similar to that with 30 mol% of the catalyst (compare entry 9 with 8). As observed earlier with ethyl and isopropyl radicals, a modest increase in ee was achieved using **12** as an additive (entry 10). Reaction with cyclohexyl radical gave the allylated product in modest yield and low selectivity (entry 11).

In general, addition/trapping reactions with chiral lanthanide Lewis acids described in this work are less selective as compared to reactions with chiral main group Lewis acids reported by Porter et. al.[7–9] Furthermore, in our work, increasing the size of the radical led to a systematic decrease in selectivity. This trend is opposite to what was observed by Porter.[9] A simple plot of log(*S*/*R*) vs. the Taft steric parameter for ethyl, isopropyl, and *t*-butyl radicals showed a linear relationship (R^2=0.99).[23] In Porter's work, the ligand and the alkyl substituent (derived from the radical precursor) act in concert to provide higher selectivity with bulky radicals. The lack of geometry information for the reactive complex in our work precludes us from arriving at a reasonable explanation for the observed trend.

3. Conclusions

In conclusion we have demonstrated that chiral lanthanide Lewis acids are marginally effective in controlling stereochemistry α- to a carbonyl. Additionally, as observed in our work on conjugate additions using lanthanide Lewis acids, achiral additives enhanced the face shielding provided by the ligand. This concept proves to be of general value in improving enantioselectivities obtained in a transformation. Experiments are underway to better understand the geometry of the reactive complex, to improve face selection in addition/trapping, and extension to other enantioselective transformations.

4. Experimental

4.1. General

Dichloromethane and THF were dried using Solv-tek solvent purification system employing activated alumina prior to use. Flash chromatography was performed using EM Science silica gel 60 (230–400 mesh). Melting points were determined using the Fisher–Johns melting point apparatus. All glassware was oven dried, assembled hot, and cooled under a stream of dry nitrogen before use. Reactions with air sensitive materials were carried out by standard syringe techniques.

^{1}H NMR spectra were recorded on a Varian Unity/Inova-500 NB (500 MHz), or a Varian Unity/Inova-400 NB (400 MHz). Chemical shifts are reported in parts per million (ppm) down field from TMS, using residual $CDCl_3$ (7.27 ppm) as an internal standard. Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, dd=doublets of doublets, m=multiplet, b=broad), coupling constant(s) and integration. ^{13}C NMR spectra were recorded on a Varian Unity/Inova-500 NB (125 MHz) or a Varian Unity/Inova-400 (100 MHz) spectrometers using broad band proton decoupling. Chemical shifts are reported in parts per million (ppm) down field from TMS, using the middle resonance of $CDCl_3$ (77.0 ppm) as an internal standard. HPLC analyses were carried out on a Waters 515 HPLC pump and a 2487 dual λ absorbance detector connected to a PC with Millennium^{32} workstation. Optical rotations were recorded on a JASCO-DIP-370 instrument. High-resolution mass spectra (HRMS) [EI+] were obtained at the Mass spectrometry Laboratory, Ohio State University, Columbus, OH. Allyltributyl stannane was obtained from Aldrich and distilled prior to use. Lanthanide triflates, (*S*)-proline and acetyl oxazolidinone were purchased from Aldrich Chemical Company.

4.1.1. 3-(2-Propenoyl)-2-oxazolidinone (6). The title compound was prepared using literature procedure.[24] mp 80–81°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (t, J=8.0 Hz, 2H), 4.43 (t, J=8.0 Hz, 2H), 5.89 (dd, J=10.5, 1.6 Hz, 1H), 6.54 (dd, J=17.2, 1.6 Hz, 1H), 7.46 (dd, J=17.2, 10.6 Hz, 1H).

4.2. Representative experimental procedure for chiral Lewis acid catalyzed conjugate addition of radicals to enoate 6

Under N_2, a mixture of Lewis acid (0.06 mmol) and ligand (0.06 mmol) [and 0.06 mmol of additive, for experiments with additives] in CH_2Cl_2 (1 mL) was stirred at rt for 45 min and cooled to −78°C. *N*-Acryloyl oxazolidinone **6** (0.2 mmol in 1 mL CH_2Cl_2) was added and the mixture was allowed to stir for an additional 30 min at this temperature. The reaction was initiated by sequential addition of iodo alkane (2 mmol), allyltributyl stannane (1.0 mmol), Et_3B (0.6 mmol, 1 M solution in hexanes) and oxygen (introduced via syringe). The reaction was monitored by TLC (30% EtOAc in hexane) and when judged complete was quenched with silica gel, concentrated, washed with 10 mL hexanes to remove the excess allylstannane and product was eluted with 40 mL ethyl ether. The ether extract was concentrated over silica gel and purified by silica gel chromatography (CH_2Cl_2) to give pure product as colorless liquid. The enantiomeric purity was determined by HPLC.

4.2.1. 3-(*S*)-[2-(2-Chloroethyl)-pent-4-enoyl)-oxazolidin-2-one (7a). Colorless oil; HPLC t_R 14 min; t_R 18 min [Chiralcel AD (0.46 cm×25 cm) (from Daicel Chemical

Ind., Ltd.) hexane/*i*-PrOH, 95/5, 1.0 mL/min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91–2.46 (m, 4H), 3.46–3.59 (m, 2H), 3.94–4.11 (m, 3H), 4.37–4.39 (m, 2H), 5.02–5.08 (m, 2H), 5.74 (dddd, J=17.0, 10.0, 7.3, 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.0, 36.9, 40.4, 42.8, 62.1, 118.0, 134.7, 153.4, 175.2. HRMS Exact mass calcd for $C_{10}H_{14}ClNO_3Na$ $[M+Na]^+$: 254.0554. Found: 254.0533.

4.2.2. 3-(*S*)-(2-Butyl-pent-4-enoyl)-oxazolidin-2-one (7b). Colorless oil; HPLC t_R 45 min; t_R 50 min [Chiralcel AD+AD (0.46 cm×25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 99/1, 0.5 mL/min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, J=7.0 Hz, 3H), 1.19–1.32 (m, 4H), 1.43–1.72 (m, 2H), 2.2–2.4 (m, 2H), 3.98 (dddd, J=8.1, 8.0, 5.9, 5.8 Hz, 1H), 3.96–4.04 (m, 2H), 4.32–4.41 (m, 2H), 4.95–5.04 (m, 2H), 5.74 (dddd, J=17.3, 10.0, 7.1, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.9, 29.5, 31.7, 36.7, 42.5, 42.9, 62.0, 117.0, 135.7, 153.5, 176.5. HRMS Exact mass calcd for $C_{12}H_{19}NO_3Na$ $[M+Na]^+$: 248.1257. Found: 248.1262.

4.2.3. 3-(*S*)-(2-Pentyl-pent-4-enoyl)-oxazolidin-2-one (7c). Colorless oil; HPLC t_R 30 min; t_R 36 min [Chiralcel AD+AD (0.46 cm×25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 99/1, 1.0 mL/min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, J=6.7 Hz, 3H), 1.19–1.32 (m, 6H), 1.42–1.72 (m, 2H), 2.20–2.40 (m, 2H), 3.84–4.04 (m, 3H), 4.36 (t, J=8.1 Hz, 2H), 4.96–5.04 (m, 2H), 5.69–5.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 22.7, 27.0, 31.9, 32.0, 36.7, 42.5, 42.9, 62.0, 117.0, 135.7, 153.5, 176.5. HRMS Exact mass calcd for $C_{13}H_{21}NO_3Na$ $[M+Na]^+$: 262.1414. Found: 262.1412.

4.2.4. 3-(*S*)-(2-(2-Methyl-propyl)-pent-4-enoyl)-oxazolidin-2-one (7d).[7] Colorless oil; HPLC t_R 72 min; t_R 78 min [Chiralcel OD+OD−H (0.46 cm×25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 98/2, 0.5 mL/min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (dd, J=6.7, 2.1 Hz, 6H), 1.23–1.70 (m, 3H), 2.19–2.37 (m, 2H), 3.96–4.02 (m, 2H), 4.36 (t, J=8.2 Hz, 2H), 4.97–5.04 (m, 2H), 5.70–5.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8, 23.0, 26.3, 37.4, 40.5, 40.9, 42.9, 61.9, 117.1, 135.9, 153.4, 176.8.

4.2.5. 3-(*S*)-(2-(2,2-Dimethyl-propyl)-pent-4-enoyl)-oxazolidin-2-one (7e).[7] Colorless oil; HPLC t_R 37 min; t_R 43 min [Chiralcel AS+AS (0.46 cm×25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 99/1, 0.5 mL/min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (s, 9H), 1.26 (dd, J=14.1, 6.1 Hz, 1H), 1.98 (dd, J=14.0, 10.0 Hz, 1H), 3.96 (m, 2H), 4.02–4.09 (m, 1H), 4.33–4.37 (m, 2H), 4.97–5.02 (m, 2H), 5.66–5.79 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.7, 30.9, 38.4, 39.9, 43.1, 45.0, 61.9, 117.4, 135.3, 153.5, 177.4.

4.2.6. 3-(*S*)-(2-Cyclohexylmethyl-pent-4-enoyl)-oxazolidin-2-one (7f).[7] Colorless oil; HPLC t_R 24 min; t_R 30 min [Chiralcel AD (0.46 cm×25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 99/1, 0.5 mL/min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.77–0.87 (m, 2H), 1.02–1.28 (m, 5H), 1.54–1.66 (m, 6H), 2.14–2.32 (m, 2H), 3.89–4.01 (m, 3H), 4.32 (t, J=8.3 Hz, 3H), 4.91–4.99 (m, 2H), 5.65–5.76 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4, 26.5, 26.7, 33.5, 33.6, 35.7, 37.4, 39.4, 39.9, 42.9, 62.0, 117.1, 135.6, 153.4, 176.

4.2.7. 3-(*S*)-(2-Propyl-pent-4-enoyl)-oxazolidin-2-one (8).[7] Colorless oil; HPLC t_R 16.6 min (*R* enantiomer); t_R 19.2 min (*S* enantiomer) [Chiralcel AD (0.46 cm×25 cm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 99/1, 1.0 mL/min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, J=7.3 Hz, 3H), 1.28 (m, 2H), 1.40–1.70 (m, 2H), 2.19–2.40 (m, 2H), 3.86–4.00 (m, 3H), 4.35 (t, J=8.2 Hz, 2H), 4.95–5.03 (m, 2H), 5.68–5.79 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 20.5, 34.1, 36.7, 42.3, 42.9, 62.0, 117.0, 135.7, 153.5, 176.5.

4.2.8. Hydrolysis of 3-(*S*)-(2-propyl-pent-4-enoyl)-oxazolidin-2-one to (*S*)-2-propyl-pent-4-enoic acid. To a solution of 3-(*S*)-(2-propyl-pent-4-enoyl)-oxazolidin-2-one (**8**, 80% ee, 85 mg, 0.4 mmol) in 6 mL THF–H_2O (3/1) was added $LiOH{\cdot}H_2O$ (34 mg, 0.8 mmol) followed by H_2O_2 (0.2 mL, 0.2 mmol) at 0°C. The mixture was stirred at 0°C for 3 h, then most of the THF was evaporated. The aqueous solution after dilution with water (pH=12) was extracted with CH_2Cl_2 (3×10 mL). The aqueous phase was acidified with HCl (1 M) until pH 2 and extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were dried over Na_2SO_4, concentrated in vacuo to provide 40 mg (72%) of (*S*)-2-propyl-pent-4-enoic acid as a colorless liquid. $[\alpha]_D^{25}$=−3.7 (*c* 0.97, $CHCl_3$) {lit.[22] $[\alpha]_D^{25}$=−5.5 (*c* 0.97, $CHCl_3$) for (*S*)-enantiomer}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, J=7.1 Hz, 3H), 1.27–1.66 (m, 4H), 2.19–2.48 (m, 3H), 5.0–5.09 (m, 2H), 5.75 (dddd, J=17.0, 10.3, 6.9, 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 20.6, 33.8, 36.3, 45.2, 117.1, 135.4, 182.4.

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