<http://www.diva-portal.org>

Postprint

This is the accepted version of a paper published in *Journal of Organic Chemistry*. This paper has been peer-reviewed but does not include the final publisher proof-corrections or journal pagination.

Citation for the original published paper (version of record):

Massaro, L., Yang, J., Krajangsri, S., Silvi, E., Singh, T. et al. (2019)
Stereodivergent Synthesis of Trisubstituted Enamides: Direct Access to Both Pure Geometrical Isomers
Journal of Organic Chemistry, 84(21): 13540-13548
<https://doi.org/10.1021/acs.joc.9b01803>

Access to the published version may require subscription.

N.B. When citing this work, cite the original published paper.

Permanent link to this version:

<http://urn.kb.se/resolve?urn=urn:nbn:se:su:diva-176596>

Stereodivergent Synthesis of Trisubstituted Enamides: Direct Access to Both Pure Geometrical Isomers.

Luca Massaro^{†[a]}, Jianping Yang^{†[a]}, Suppachai Krajangsri^[a], Emanuele Silvi^[a], Thishana Singh^[b], Pher G. Andersson^{[a][b]*}

^[a]Department of Organic Chemistry, Stockholm University, Arrhenius-laboratory, 10691, Stockholm, Sweden

^[b]School of Chemistry and Physics, University of Kwazulu-Natal, Private Bag X54001, Durban, 4000, South Africa.

ABSTRACT: A stereodivergent strategy has been developed to access either (*E*)- or (*Z*)- isomers of trisubstituted enamides. Starting from an extensive range of ketones, it was possible to synthesize and isolate the desired pure isomer by switching the reaction conditions. Lewis Acid activation enables the formation of the (*E*)-isomers in high stereoselectivity (>90:10) and good yields. On the other hand, the use of a Brønsted acid allows the preparation of the (*Z*)-isomers, again in high selectivity (up to 99:1), with moderate yields.

Introduction

Enamides are a very versatile class of compounds in organic synthesis.¹ Their motif can be found in many bioactive and natural products² due to their high stability compared to the more unstable enamines.³ The polarization of the double bond and the presence of the nitrogen atom confer them a reactivity that spans over a wide range; such as asymmetric hydrogenation via transition metal catalysis, cycloadditions, cyclopropanations and even nucleophilic additions.⁴ The most widely applicable methodologies to synthesize enamides involve couplings with Cu and Pd in catalytic amount,⁵ but other valuable methods have been recently developed using ynamides as substrates.⁶ Coupling methodologies and other recent strategies for the synthesis of disubstituted enamides show in most of the cases good stereoselectivity.⁷ For trisubstituted enamides instead, the access to pure isolated (*Z*)- or (*E*)-isomers becomes more challenging, especially for α,β substitutions. In the last few years, the Zhu group achieved remarkable results via a Pd-catalyzed arylation and alkynylation of ynamides.⁸ Successively, a similar alkynylation and the carboxylation of ynamides were also successfully developed.⁹ One of the latest methodology, reported by Maulide and

co-workers, showed good results in the stereoselective synthesis of α,β -disubstituted enamides via formation of a keteniminium ion intermediate.¹⁰

However, in spite of the availability of different preparative methodologies, a general and simple method to obtain diastomerically pure enamides is yet to be achieved. In contrast to the state of the art, an ideal approach would couple a carbonyl compound with an amide or a carbamate (the simplest retrosynthetic disconnection) avoiding the need for tailored substrates and elaborate synthetic pathways.

Since the 1980s, condensation reactions to synthesize enamides and derivatives have been extensively investigated, for example using Brønsted acids.¹¹ Among the most recent methodologies, the results obtained using titanium-based Lewis acids were notable.¹² The Touré group developed a synthesis of sterically hindered enamides obtaining high regio- and stereoselectivity.¹³ Despite the promising results, this work was mainly limited to the condensation of the more reactive aldehydes and to access exclusively the geometrical (*E*)-isomers.

In this context, we wanted to extend the usefulness of condensation reactions to the less reactive ketones, tar-

getting a rapid access to the synthesis of both (*E*)- and (*Z*)-enamide isomers.

We herein demonstrate two simple strategies that allow the diastereoselective synthesis of either of the diastereomeric trisubstituted enamide by switching the reaction conditions starting from a common, readily available substrate. (Figure 1)

Figure 1. Condensation of ketones to the desired enamide isomer.

Results and Discussion

Preliminary screenings using oxazolidinone **1** and substrate **2a** were performed according to the existing literature procedures available for the condensation of aldehydes.¹³⁻¹⁴ Carbonyl activation via Brønsted acid catalysis was used to synthesize the (*Z*)-isomer (Figure 1, pathway **a**). This reaction is likely to follow the thermodynamic pathway and can be considered as an equilibrium process between a carbonyl compound and the corresponding enamide, which leads to the more stable (*Z*)-isomer of the product (for computational details see SI). On the other hand, a combination of TiCl_4 and Et_3N was employed to access to the (*E*)-isomer of the product (Figure 1, pathway **b**). The Ti-NEt_3 adduct is assumed to first coordinate to the carbonyl oxygen activating the carbonyl group for reaction with oxazolidinone **1** to yield a Ti-coordinated carbinol amide. This intermediate then follows the E_2 -elimination mechanism in the more sterically favored conformation affording the *E*-isomer of the enamide. For the first transformation, different solvents and Brønsted acids were screened under refluxing conditions (Table 1). Benzene and 10 mol% of *p*-TSA gave the best results in terms of selectivity (11:89 *E/Z*) (entry 5), though toluene showed higher conversion (50%)(entry 6).

Table 1. Screening of Brønsted acid conditions for synthesis of (*Z*)-enamides.

Entry	catalyst (mol%)	Oxazolidinone (equiv)	solvent	d.r. [<i>E</i> : <i>Z</i>]	conv. [%]
1	H_2SO_4 (10)	2	toluene	22:78	4
2	CSA ^[a] (10)	2	toluene	25:75	16
3	<i>p</i> -TSA ^[b] (10)	2	toluene	15:85	40
4	<i>p</i> -TSA(10)	2	PhCF_3	21:79	35
5	<i>p</i> -TSA(10)	2	Benzene	11:89	30
6 ^[c]	<i>p</i> -TSA(10)	3	toluene	15:85	50
7 ^[d]	<i>p</i> -TSA(10)	3	toluene	-	nr

(a) CSA= Camphorsulfonic acid. (b) *p*-TSA = *para*-toluenesulfonic acid. (c) Reaction refluxed for 36 h. (d) Addition of molecular sieves $3\text{\AA}$.

We could observe significant amounts of unreacted starting material **2a** and oxazolidinone **1**, indicating the possibility of an equilibrium reaction. However, the addition of molecular sieves and other dehydrating agents was detrimental (entry 7 and SI). Meanwhile, the second method was also optimized (Table 2). A screening of Lewis acid revealed that the combination of TiCl_4 and Et_3N was the more efficient catalytic couple (entry 3).¹³ The initial conditions involved the use of the oxazolidinone **1** as the limiting reagent, giving 38% of conversion. Increasing the oxazolidinone amount to 2 equivalents, the conversion increased to 44% and with 3 equivalents it reached up to 55% (entries 4 and 5).

Also in this case the reaction resulted to be extremely selective (97:3 *E/Z*) and in the crude ^1H NMR only the signals of the starting ketone **2** and corresponding product **3** could be detected (see SI). A kinetic study revealed that the reaction rate was high at the beginning, reaching 40% of conversion in the first 10 minutes, and then drastically slowing down, reaching the final 55% of ketone consumption in the following hours. For this reason, different strategies of addition of the reagents were explored (see SI), but the results could not be significantly

Table 2. Screening of Lewis acid conditions for the synthesis of (*E*)-enamides.

Entry	Oxazolidinone (equiv)	L.A. (equiv)	Base (equiv)	d.r. [<i>E</i> : <i>Z</i>]	conv. [%]
1	0.9	AlCl ₃ (1.2)	-	-	nr
2	0.9	TiCl ₄ (1.2)	-	-	nr
3	0.9	TiCl ₄ (1.2)	Et ₃ N(5)	98:2	38
4	2	TiCl ₄ (1.2)	Et ₃ N(5)	97:3	44
5	3	TiCl ₄ (1.2)	Et ₃ N(5)	97:3	55
6	3	TiCl ₄ (2.4)	Et ₃ N(10)	96:4	50
7 ^[a]	3	TiCl ₄ (1.2)	Et ₃ N(5)	96:4	38

(a) Addition of molecular sieves 3Å.

improved. With the best conditions in hands, we started to explore the scope of these two stereoselective transformations. Firstly, ketones bearing an aryl group and an alkyl chain respectively in the α and β positions were investigated. Different substituents on the aryl were tested (Table 3, entries 2-5), showing comparable results for electron donating and electron withdrawing groups (for more examples see SI). The thiophene substituent was well tolerated (entry 6) and the naphthalene group gave impressive selectivity (entry 7, see SI). The alkyl chain on the β carbon was also varied, showing an increment of the diastereomeric ratio for the bulkier *i*-propyl substituent and a decrement for smaller groups (entries 8, 9 and more examples with d.r. in SI). Although the yields obtained in these reactions are not particularly high, the reactions are very clean and the unreacted starting material can easily be recovered. In most of the cases the untouched ketone can be recovered and corrected yields based on the real amount of reacted ketones are also reported (column 5, Table 3). The same substrates were also tested under Lewis acid conditions (Table 4). Noteworthy, this second pathway showed a perfect

Table 3. Substrate scope for (*Z*)-enamides.

Entry	Enamide	Yield ^[a] [%]	Recovered s.m. ^[b] [%]	Corrected Yield ^[c] [%]
1		33	49	65
2		21	70	70
3		18	64	50
4		24	70	80
5		20	70	67
6		14	72	50
7		20	61	51
8		30	67	91
9		30	44	54

(a) Isolated (*Z*)-enamide (>99:1). (b) Isolated amount of ketones after purification. (c) Yield based on recovered starting material.

Table 4. Substrate scope for (*E*)-enamides.

Entry	Enamide	Yield ^[a] [%]	Recovered s.m. ^[b] [%]	Corrected Yield ^[c] [%]
1		48	44	86
2		20	67	60
3		31	64	86
4		33	43	58
5		20	61	51
6		24	34	37
7		33	59	80
8		30	69	97
9		40	55	89

(a) Isolated (*E*)-enamide (>99:1). (b) Isolated amount of ketone after purification. (c) Yield based on recovered starting material.

Table 5. Substrate scope for α,β -diaryl (*Z*)-enamides.

Entry	Enamide	Yield ^[a] [%]	Recovered s.m. ^[b] [%]	Corrected Yield ^[c] [%]
1		10	85	67
2		15	80	75
3		18	74	69
4		17	77	74
5		16	80	80
6		15	76	63
7		14	84	88
8		20	77	87
9		16	68	50
10		12	70	40

Table 6. Substrate scope for α,β -diaryl (*E*)-enamides.

Entry	Enamide	Yield ^[a] [%]	Recovered s.m. ^[b] [%]	Corrected Yield ^[c] [%]
1		30	68	94
2		40	55	89
3		45	49	88
4		38	56	86
5		37	56	66
6		34	52	71
7		32	78	73
8		39	58	93
9		30	50	60
10		20	62	52

stereocontrol for most of the ketones with a benzene ring in the α position (entry 2-5 and 8-9, see SI). A somewhat lower selectivity was found both for the thiophene substituent and, conversely to the *p*-TSA methodology, the naphthalene moiety. In the same way as for the first pathway, it was possible to recover the starting material and both isolated and corrected yields are reported.

To further expand the scope of the reaction, other classes of unsymmetrical ketones were also included. Ketones with two aryl substituents were screened in both conditions, without any further optimization. The simplest biphenyl ketone (Table 5, entry 1) gave a lower conversion and isolated yield compared to the previous class (Table 2), but a similar selectivity in favor of the stable (*Z*)-isomer (see SI). Substituents on the α ring produced a slightly increment in terms of reactivity, with the same selectivity (entries 2-4). The same trend of reactivity was detected for ketones with a *para*-substituted β ring (entries 5-7). The naphthyl ring gave the best result (entry 8) and heteroaromatic compounds were again well tolerated.

The results obtained for the synthesis of the corresponding (*E*)-isomers were more successful, giving ex-

Table 7. Substrate scope for β,β -disubstituted (*Z*)-enamides.

Entry	Enamide	Method	d.r. [<i>E</i> : <i>Z</i>]	Yield ^[a] [%]
1		TiCl ₄	8:92	50
2		<i>p</i> -TSA	29:71	28
3		TiCl ₄	2:98	40
4		<i>p</i> -TSA	30:70	38
5		TiCl ₄	1:99	50
6		<i>p</i> -TSA	10:90	60
7		TiCl ₄	1:99	51
8		<i>p</i> -TSA	5:95	61

(a) Isolated yield of the pure major isomer (ratio >99:1).

cellent selectivity and even higher reactivity of the α aryl alkyl ketones, with an average yield of 35% (Table 6, SI). In this case as well, all the starting materials **2** were recovered from the respective reactions, and the corrected yields (up to 94%) show the efficiency of these reactions, which minimize the waste of compounds.

Finally we tested the disubstituted aldehydes **4**, since previous results aiming to the (*E*)-isomers had shown bad selectivity.¹³ However, for this class of substrates the two methodologies converged to give the (*Z*)-isomers (Table 7, NOE experiments to verify the enamide geometry are reported in the SI). Increasing the bulkiness of the R group, TiCl₄ catalyzed reactions reached perfect level of selectivity, improving the previous results obtained with Brønsted acid catalysis.¹⁴ In the cases of *n*-propyl and *n*-butyl groups the reactions also resulted in a higher isolated yield (entries 1 and 2, SI), but for *i*-propyl and cyclohexyl substituents the method with *p*-TSA was more effective (entries 3 and 4).

Experimental section

All reagents were used as supplied commercially without further purification. Chromatographic separations were performed on Kiesel gel 60 H silica gel (particle size: 0.063-0.100 mm) or Brockmann I, activated. Thin layer chromatography (TLC) was performed on aluminum plates coated with Kieselgel 60 (0.20 mm, UV254) and visualized under ultraviolet light ($\nu = 254$ nm). ¹H NMR spectra were recorded on a Bruker 400 or 500 at 400/500 MHz in CDCl₃ and referenced internally to the residual CHCl₃ peak (7.26 ppm). ¹³C NMR spectra were recorded at 75/125 MHz in CDCl₃ and referenced to the central peak of CDCl₃ (77.0 ppm). Chemical shifts are reported in ppm (δ scale). HRMS data were obtained using a Bruker MicroTOF-Q II instrument operation at ambient temperature.

General procedure for preparation of α -Aryl-alkyl Ketones 2b-h

Grignard reagent (15 mmol, 1.5 equiv.) was slowly added to a solution of cyano (-CN) (10 mmol, 1.0 equiv.) aromatic compounds in dry THF (30 mL) at 0°C. The reaction was allowed to stir at room temperature for 16 h. The reaction was quenched by addition of a saturated aqueous NH₄Cl solution, and 1M HCl was added and the mixture was stirred for 1 h. The mixture was extracted with Et₂O (3x100 mL). The combined organic phases were combined and washed with brine and dried over Na₂SO₄. The solvent was evaporated under reduced pressure to afford the crude products which then were purified by column chromatography on silica gel [pentane/ ethyl acetate (90:10)].

The chemical shifts of the compounds reflected the literature values.¹⁵

General procedure for preparation of α , β -DiAryl Ketones 2j-s

To a solution of aromatic acetic acid (15 mmol, 1.0 equiv.) and aromatic methyl ester (15 mmol, 1.0 equiv.) in DMF (45 mL) was added NaHMDS (2.0 M in THF) (30 mL, 60 mmol, 4.0 equiv.) at -10°C over 1 min. The resulting mixture was stirred at -10°C for 3.5 hours. To the resulting solution was then added saturated aqueous NH₄Cl solution. The resulting mixture was extracted with EtOAc (2x100 mL). The combined organic phase was washed with brine, dried over sodium sulfate and concentrated in vacuo. The residue was purified by silica gel column chromatography to give the desired product.

The chemical shifts of the compounds are in agreement with the literature values.¹⁶

Aldehydes **4a-d** were prepared from ethyl phenyl acetate and the corresponding bromide according to the literature.¹⁷

General procedure for the preparation of the α,β -enecarbamates 3a-s(*Z*-isomer)

A solution of the ketone (10 mmol, 1.0 equiv.), 2-oxazolidinone (30 mmol, 2.610g, 3 equiv.), and 10 mol% of *p*-toluenesulfonic acid (1 mmol, 190mg) in toluene (30 mL: 10 mmol ketone) was heated to reflux and the formed water was removed by azeotropic distillation over 36hrs. After cooling the solution to room temperature, it was washed with a saturated, aqueous solution of NH₄Cl (10 mL) and water (10 mL), and the combined organic layers were dried over Na₂SO₄. After evaporation of the organic solvent and purification by silica-gel flash chromatography (pentane/ ethyl acetate 80:20 to 70:30), the pure *E*- or *Z*-isomers of the enecarbamates were obtained.

(*Z*)-enecarbamates **3k**, **3l**, **3n**, **3o**, **3q**, **3r** are in agreement with the reported datas.^{8b}

(*Z*)-3-(1-phenylpent-1-en-1-yl)oxazolidin-2-one (**3a**)

Colorless oil, 0.726g (33% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.30 (m, 5H), 6.04 (t, *J* = 7.2 Hz, 1H), 4.55 – 4.42 (m, 2H), 3.73 – 3.65 (m, 2H), 2.24 (q, *J* = 7.3 Hz, 2H), 1.65 – 1.54 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.5, 135.8, 133.9, 130.6, 128.7, 128.2, 125.9, 62.3, 45.7, 30.3, 22.1, 14.1. HRMS (ESI-TOF) calcd for C₁₄H₁₇NO₂Na [M+Na]⁺: 254.1151, found: 254.1151.

A large scale for the synthesis of compound **3a** was carried out according to the general procedure for the preparation of the α,β -enecarbamates (*Z*-isomer). Ketone **2a**

(10g, 61.7mmol), oxazolidinone **1** (16g, 185.1mmol) and PTSA (1.18g, 6.17mmol) were refluxed in 100 ml toluene to afford product **3a** (4.53g, 32% yield).

(Z)-3-(1-(3-methoxyphenyl)pent-1-en-1-yl)oxazolidin-2-one (**3b**)

Colorless oil, 0.548g (21% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.26 (d, *J* = 15.9 Hz, 1H), 6.93 (ddd, *J* = 7.7, 1.7, 1.0 Hz, 1H), 6.88 – 6.86 (m, 1H), 6.84 (ddd, *J* = 8.1, 2.6, 0.9 Hz, 1H), 6.01 (t, *J* = 7.2 Hz, 1H), 4.52 – 4.39 (m, 2H), 3.81 (s, 3H), 3.71 – 3.58 (m, 2H), 2.20 (q, *J* = 7.3 Hz, 2H), 1.54 (q, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 160.1, 156.5, 137.6, 133.8, 130.9, 129.9, 118.6, 113.5, 112.0, 62.4, 55.5, 45.9, 30.5, 22.2, 14.2. HRMS (ESI-TOF) calcd for C₁₅H₁₉NO₃Na [M+Na]⁺: 284.1257, found: 284.1256.

(Z)-3-(1-(4-bromophenyl)pent-1-en-1-yl)oxazolidin-2-one (**3c**)

Colorless oil, 0.556g (18% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.53 – 7.43 (m, 2H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.01 (t, *J* = 7.2 Hz, 1H), 4.54 – 4.41 (m, 2H), 3.69 – 3.46 (m, 2H), 2.19 (q, *J* = 7.3 Hz, 2H), 1.54 (q, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.5, 135.1, 133.2, 132.0, 131.5, 127.6, 122.3, 62.4, 45.8, 30.5, 22.2, 14.2. HRMS (ESI-TOF) calcd for C₁₄H₁₆BrNO₂Na [M+Na]⁺: 332.0257, found: 332.0262.

(Z)-3-(1-(4-fluorophenyl)pent-1-en-1-yl)oxazolidin-2-one (**3d**)

Colorless oil, 0.598g (24% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.30 (m, 2H), 7.13 – 6.98 (m, 2H), 5.96 (t, *J* = 7.2 Hz, 1H), 4.56 – 4.43 (m, 2H), 3.71 – 3.58 (m, 2H), 2.21 (q, *J* = 7.3 Hz, 2H), 1.65 – 1.48 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 162.6 (d, *J* = 270.4 Hz) 156.43, 133.00, 132.07 (d, *J* = 3.3 Hz), 130.49 (d, *J* = 1.4Hz), 127.65, 127.57, 115.74, 115.52, 62.27, 45.67, 30.28, 22.08, 14.02. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -113.7. HRMS (ESI-TOF) calcd for C₁₄H₁₆FNO₂Na [M+Na]⁺: 272.1057, found: 272.1059.

(Z)-3-(1-(4-(trifluoromethyl)phenyl)pent-1-en-1-yl)oxazolidin-2-one (**3e**)

Colorless oil, 0.598g (20% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.61 (dt, *J* = 7.9, 0.8 Hz, 2H), 7.45 (dt, *J* = 7.9, 0.8 Hz, 2H), 6.12 (t, *J* = 7.2 Hz, 1H), 4.56 – 4.42 (m, 2H), 3.73 – 3.58 (m, 2H), 2.24 (q, *J* = 7.4 Hz, 2H), 1.62 – 1.49 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.5, 139.7, 133.3, 133.1, 130.3 (q, *J* = 32.5, 31.7 Hz), 126.2, 128.3 – 125.8 (m), 123.4 (q, *J* = 271.9 Hz), 62.4, 45.8, 30.6, 22.1, 14.2.

¹⁹F NMR (377 MHz, Chloroform-*d*) δ -62.7. HRMS (ESI-TOF) calcd for C₁₅H₁₆F₃NO₂Na [M+Na]⁺: 322.1035, found: 322.1025.

(Z)-3-(1-(thiophen-2-yl)pent-1-en-1-yl)oxazolidin-2-one (**3f**)

Brown oil, 0.332g (14% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.20 – 7.17 (m, 1H), 6.99 – 6.95 (m, 2H), 6.07 (t, *J* = 7.3 Hz, 1H), 4.53 – 4.47 (m, 2H), 3.82 – 3.76 (m, 2H), 2.17 (q, *J* = 7.4 Hz, 2H), 1.56 – 1.48 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 156.2, 140.4, 130.3, 128.8, 127.6, 124.8, 123.7, 62.4, 46.0, 30.0, 22.0, 14.0. HRMS (ESI-TOF) calcd for C₁₂H₁₅NO₂SNa [M+Na]⁺: 260.0716, found: 260.0738.

(Z)-3-(1-(naphthalen-2-yl)pent-1-en-1-yl)oxazolidin-2-one (**3g**)

Colorless oil, 0.562g (20% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.82 (dd, *J* = 8.9, 4.4 Hz, 3H), 7.75 (s, 1H), 7.55 – 7.42 (m, 3H), 6.15 (t, *J* = 7.2 Hz, 1H), 4.58 – 4.45 (m, 2H), 3.77 – 3.65 (m, 2H), 2.27 (q, *J* = 7.3 Hz, 2H), 1.59 (h, *J* = 7.3 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 156.53, 133.91, 133.31, 133.24, 133.06, 131.14, 128.45, 128.10, 127.58, 126.43, 126.23, 124.78, 123.82, 62.27, 45.78, 30.40, 22.13, 14.06. HRMS (ESI-TOF) calcd for C₁₈H₁₉NO₂Na [M+Na]⁺: 304.1308, found: 304.1307.

(Z)-3-(3-methyl-1-phenylbut-1-en-1-yl)oxazolidin-2-one (**3h**)

Colorless oil, 0.693g (30% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.30 (m, 5H), 6.04 (t, *J* = 7.2 Hz, 1H), 4.55 – 4.42 (m, 2H), 3.73 – 3.65 (m, 2H), 2.24 (q, *J* = 7.3 Hz, 2H), 1.65 – 1.54 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.5, 135.8, 133.9, 130.6, 128.7, 128.2, 125.9, 62.3, 45.7, 30.3, 22.1, 14.1. HRMS (ESI-TOF) calcd for C₁₄H₁₇NO₂Na [M+Na]⁺: 254.1151, found: 254.1151.

(Z)-3-(1-phenylbut-1-en-1-yl)oxazolidin-2-one (**3i**)

Colorless oil, 0.651g (30% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.30 (m, 4H), 7.31 – 7.28 (m, 1H), 5.98 (t, *J* = 7.2 Hz, 1H), 4.52 – 4.38 (m, 2H), 3.72 – 3.59 (m, 2H), 2.24 (p, *J* = 7.5 Hz, 2H), 1.12 (t, *J* = 7.5 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.7, 135.9, 133.4, 132.3, 128.8, 128.3, 126.0, 62.4, 45.8, 21.8, 13.6. HRMS (ESI-TOF) calcd for C₁₃H₁₅NO₂Na [M+Na]⁺: 240.0995, found: 240.0987.

(Z)-3-(1,2-diphenylvinyl)oxazolidin-2-one (**3j**)^{8b}

White solid, mp 102.7–104.6 °C, 0.265g (10% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.56 – 7.26 (m, 10H), 6.90 (s, 1H), 4.53 – 4.40 (m, 2H), 3.77 – 3.63 (m, 2H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.4, 136.4, 135.3, 134.6, 128.9, 128.8, 128.3, 128.2, 127.0, 125.9, 62.6, 45.4. HRMS (ESI-TOF) calcd for C₁₇H₁₅NO₂Na [M+Na]⁺: 288.0995, found: 288.0990.

(Z)-3-(2-phenyl-1-(*p*-tolyl)vinyl)oxazolidin-2-one (**3K**)
0.418g (15% yield). The compound is in agreement with the reported datas.^{8b}

(Z)-3-(1-(4-methoxyphenyl)-2-phenylvinyl)oxazolidin-2-one (**3I**)

0.531g (18% yield). The compound is in agreement with the reported datas.^{8b}

(Z)-3-(2-phenyl-1-(4-(trifluoromethyl) phenyl) vinyl) oxazolidin-2-one (**3m**)

White solid, mp 80.8–81.2 °C, 0.566g (17% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.62 – 7.55 (m, 2H), 7.45 – 7.37 (m, 2H), 7.16 – 7.09 (m, 3H), 6.99 – 6.91 (m, 2H), 6.81 (s, 1H), 4.44 – 4.37 (m, 2H), 3.75 – 3.66 (m, 2H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.4, 140.3, 134.8, 133.6, 130.8 (q, *J* = 32.5 Hz), 129.0, 128.9, 128.8, 128.6, 126.3, 126.0 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 272.6 Hz), 62.8, 45.3. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -62.7. HRMS (ESI-TOF) calcd for C₁₈H₁₄F₃NO₂Na [M+Na]⁺: 356.0874, found: 356.0884.

(Z)-3-(1-phenyl-2-(*p*-tolyl)vinyl)oxazolidin-2-one (**3n**)

0.446g (16% yield). The compound is in agreement with the reported datas.^{8b}

(Z)-3-(2-(4-methoxyphenyl)-1-phenylvinyl)oxazolidin-2-one (**3o**)

0.443g (15% yield). The compound is in agreement with the reported datas.^{8b}

(Z)-3-(1-phenyl-2-(4-(trifluoromethyl)phenyl)vinyl) oxazolidin-2-one (**3p**)

White solid, mp 127.1–129.7 °C, 0.466g (14% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.31 (m, 5H), 7.30 – 7.24 (m, 2H), 7.01 (d, *J* = 8.2 Hz, 2H), 6.88 (s, 1H), 4.40 – 4.33 (m, 2H), 3.65 – 3.59 (m, 2H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.1, 139.1, 136.7, 135.9, 129.9 (q, *J* = 32.7, 32.2 Hz), 129.6, 129.1, 128.6, 126.4, 125.9 (q, *J* = 3.8 Hz), 125.6, 122.8 (q, *J* = 273.1 Hz), 62.7, 45.7. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -62.6. HRMS (ESI-TOF) calcd for C₁₈H₁₄F₃NO₂Na [M+Na]⁺: 356.0874, found: 356.0882.

(Z)-3-(1-(naphthalen-2-yl)-2-phenylvinyl)oxazolidin-2-one (**3q**)

0.630g (20% yield). The compound is in agreement with the reported datas.^{8b}

(Z)-3-(1-(furan-2-yl)-2-phenylvinyl)oxazolidin-2-one (**3r**)

0.408g (16% yield). The compound is in agreement with the reported datas.^{8b}

(Z)-3-(2-phenyl-1-(thiophen-3-yl)vinyl)oxazolidin-2-one (**3s**)

Brown foams, 0.325g (12% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.39 (m, 3H), 7.39 – 7.34 (m, 2H), 7.34 – 7.27 (m, 2H), 7.27 – 7.23 (m, 1H), 6.93 (s, 1H), 4.48 – 4.39 (m, 2H), 3.73 – 3.64 (m, 2H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.7, 138.7, 134.9, 130.4, 128.9, 128.4, 128.3, 127.0, 126.7, 125.3, 122.2, 62.7, 45.4. HRMS (ESI-TOF) calcd for C₁₅H₁₃NO₂SNa [M+Na]⁺: 294.0565, found: 294.0545.

General procedure for the preparation of the α,β-enecarbamates (*E*-isomer)

A nitrogen-flooded sealed vial containing corresponding ketones (10 mmol, 1.0 equiv.) in dry dichloromethane was cooled down to 0 °C before titanium tetrachloride (1.2 equiv.) was added dropwise. The resulting light yellow/orange solution was stirred at this temperature for 5 min. 2-oxazolidone (3.0 equiv.) pre-dissolved in dichloromethane (5 mL) was added slowly followed by dropwise addition of triethylamine (5 equiv.). The color of the reaction mixture turned black upon addition of the base, a color change that did not occur when using most other bases. The reaction mixture was allowed to warm up to r.t. and was stirred over 3 h with regular monitoring using thin layer chromatography plates. The crude mixture was cooled to 0 °C, quenched by water (4 equiv.) and diluted with dichloromethane followed by portionwise addition of silica. The mixture was filtered by celite and the filtrate was washed with water. The layers were separated and the organic phase was extracted with dichloromethane (3 × 50 mL). The combined organic layers were dried over magnesium sulfate and concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel (ethyl ace-

tate/pentane, gradient from 1:4 to 1:2) to provide clean *E*-enamides.

(E)-3-(1-phenylpent-1-en-1-yl)oxazolidin-2-one (**3a'**)

White solid, mp 52.2-53.2 °C, 1.109g (48% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.28 (m, 3H), 7.27 – 7.22 (m, 2H), 5.83 (t, *J* = 7.7 Hz, 1H), 4.32 – 4.24 (m, 2H), 3.57 – 3.49 (m, 2H), 2.07 (td, *J* = 7.7, 6.5 Hz, 2H), 1.43 (h, *J* = 7.3 Hz, 2H), 0.88 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.5, 134.7, 134.6, 128.9, 128.4, 128.2, 125.5, 61.5, 46.2, 30.0, 23.1, 13.8. HRMS (ESI-TOF) calcd for C₁₄H₁₇NO₂Na [M+Na]⁺: 254.1151, found: 254.1151.

A large scale for the synthesis of compound **3a'** was carried out according to the general procedure for the preparation of the α,β-enecarbamates (*E*-isomer). Ketone **2a** (8.0g, 49.4mmol), oxazolidinone **1** (12.9g, 148.1mmol) were treated with TiCl₄ (9.4g, 49.4mmol) and NEt₃ in 200ml DCM to afford product **3a'** (5.40g, 47% yield).

(E)-3-(1-(3-methoxyphenyl)pent-1-en-1-yl)oxazolidin-2-one (**3b'**)

Brown solid, mp 50.5-53.8 °C, 0.522mg (20% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.27 (m, 1H), 6.89 – 6.84 (m, 2H), 6.80 (dd, *J* = 2.6, 1.6 Hz, 1H), 5.87 (t, *J* = 7.8 Hz, 1H), 4.34 – 4.28 (m, 2H), 3.57 – 3.52 (m, 2H), 2.14 – 2.05 (m, 2H), 1.50 – 1.39 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 159.6, 156.5, 136.1, 134.3, 129.4, 125.7, 121.3, 114.5, 113.6, 61.5, 55.3, 46.1, 30.1, 23.1, 13.7. HRMS (ESI-TOF) calcd for C₁₅H₁₉NO₃Na [M+Na]⁺: 284.1257, found: 284.1275.

(E)-3-(1-(4-bromophenyl)pent-1-en-1-yl)oxazolidin-2-one (**3c'**)

Brown solid, mp 49.5-51.1 °C, 0.958g (31% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.53 – 7.48 (m, 2H), 7.18 – 7.12 (m, 2H), 5.80 (t, *J* = 7.8 Hz, 1H), 4.36 – 4.30 (m, 2H), 3.60 – 3.55 (m, 2H), 2.09 – 2.01 (m, 2H), 1.47 – 1.39 (m, 2H), 0.93 – 0.85 (m, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 156.3, 133.7, 133.6, 131.6, 130.5, 125.8, 122.3, 61.5, 46.1, 30.0, 23.0, 13.7. HRMS (ESI-TOF) calcd for C₁₄H₁₆BrNO₂Na [M+Na]⁺: 332.0257, found: 332.0265.

(E)-3-(1-(4-fluorophenyl)pent-1-en-1-yl)oxazolidin-2-one (**3d'**)

Colorless oil, 0.821g (33% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.25 (m, 2H), 7.13 – 7.06 (m, 2H), 5.83 (t, *J* = 7.7 Hz, 1H), 4.38 – 4.32 (m, 2H), 3.62 –

3.56 (m, 2H), 2.08 (q, *J* = 7.6 Hz, 2H), 1.46 (h, *J* = 7.3 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 162.4 (d, *J* = 247.9 Hz), 156.2, 133.7, 130.7, 130.6 (d, 8.1 Hz), 125.4, 115.4 (d, 21.6 Hz), 61.4, 46.1, 29.9, 23.0, 13.7. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -113.1. HRMS (ESI-TOF) calcd for C₁₄H₁₆FNO₂Na [M+Na]⁺: 272.1057, found: 272.1054.

(E)-3-(1-(4-(trifluoromethyl)phenyl)pent-1-en-1-yl)oxazolidin-2-one (**3e'**)

Brown oil, 0.598g (20% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 8.1 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 5.84 (t, *J* = 7.8 Hz, 1H), 4.38 – 4.32 (m, 2H), 3.65 – 3.57 (m, 2H), 2.06 (q, *J* = 7.5 Hz, 2H), 1.45 (h, *J* = 7.4 Hz, 2H), 0.89 (t, *J* = 7.3 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.3, 138.6, 133.8, 130.4 (q, *J* = 32.6 Hz), 129.4, 126.5, 125.5 (q, *J* = 3.8 Hz), 122.8 (q, *J* = 272.8, 272.1, 271.2 Hz), 61.7, 46.3, 30.1, 23.1, 13.8. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -62.7. HRMS (ESI-TOF) calcd for C₁₅H₁₆F₃NO₂Na [M+Na]⁺: 322.1035, found: 322.1025.

(E)-3-(1-(thiophen-2-yl)pent-1-en-1-yl)oxazolidin-2-one (**3f'**)

Colorless oil, 0.569g (24% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.30 (m, 1H), 7.04 (d, *J* = 3.3 Hz, 2H), 5.92 (t, *J* = 7.6 Hz, 1H), 4.43 – 4.28 (m, 2H), 3.76 – 3.62 (m, 2H), 2.27 (q, *J* = 7.5 Hz, 2H), 1.56 – 1.44 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.6, 137.0, 129.7, 128.4, 127.7, 127.2, 126.3, 61.8, 46.7, 30.7, 23.0, 13.9. HRMS (ESI-TOF) calcd for C₁₂H₁₅NO₂SNa [M+Na]⁺: 260.0716, found: 260.0723.

(E)-3-(1-(naphthalen-2-yl)pent-1-en-1-yl)oxazolidin-2-one (**3g'**)

Colorless oil, 0.927g (33% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.90 – 7.81 (m, 3H), 7.80 – 7.72 (m, 1H), 7.55 – 7.47 (m, 2H), 7.38 (dd, *J* = 8.4, 1.7 Hz, 1H), 5.95 (t, *J* = 7.8 Hz, 1H), 4.37 – 4.27 (m, 2H), 3.61 – 3.51 (m, 2H), 2.15 (q, *J* = 7.6 Hz, 2H), 1.48 (h, *J* = 7.3 Hz, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.6, 134.5, 133.1, 133.0, 132.2, 128.3, 128.2, 128.1, 127.7, 126.5, 126.4, 126.4, 126.2, 61.5, 46.2, 30.1, 23.1, 13.8. HRMS (ESI-TOF) calcd for C₁₈H₁₉NO₂Na [M+Na]⁺: 304.1308, found: 304.1291.

(E)-3-(3-methyl-1-phenylbut-1-en-1-yl)oxazolidin-2-one (**3h'**)

White solid, mp 98.2–102.1 °C, 0.693g (30% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.33 (m, 3H), 7.31 – 7.28 (m, 2H), 5.68 (d, *J* = 10.5 Hz, 1H), 4.35 – 4.29 (m, 2H), 3.59 – 3.54 (m, 2H), 2.46 (dp, *J* = 10.5, 6.6 Hz, 1H), 1.04 (d, *J* = 6.6 Hz, 6H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 156.2, 135.0, 132.7, 132.11, 128.8, 128.4, 128.2, 61.4, 46.1, 27.4, 23.3. HRMS (ESI-TOF) calcd for C₁₄H₁₇NO₂Na [M+Na]⁺: 254.1151, found: 254.1151.

(E)-3-(1-phenylbut-1-en-1-yl)oxazolidin-2-one (**3i'**)

White solid, mp 62.5–64.3 °C, 0.868g (40% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.32 (m, 3H), 7.29 – 7.26 (m, 2H), 5.85 (t, *J* = 7.8 Hz, 1H), 4.38 – 4.24 (m, 2H), 3.63 – 3.46 (m, 2H), 2.12 (p, *J* = 7.5 Hz, 2H), 1.03 (t, *J* = 7.5 Hz, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.6, 134.8, 134.2, 128.9, 128.6, 128.4, 127.3, 61.6, 46.2, 21.6, 14.6. HRMS (ESI-TOF) calcd for C₁₃H₁₅NO₂Na [M+Na]⁺: 240.0995, found: 240.1003.

(E)-3-(1,2-diphenylvinyl)oxazolidin-2-one (**3j'**)

White solid, mp 98.5–100.2 °C, 0.795g (30% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.34 (ddd, *J* = 3.7, 3.2, 2.5 Hz, 3H), 7.31 – 7.27 (m, 2H), 7.14 – 7.06 (m, 3H), 6.99 – 6.94 (m, 2H), 6.83 (s, 1H), 4.39 – 4.33 (m, 2H), 3.65 – 3.59 (m, 2H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.2, 135.6, 135.5, 134.5, 129.6, 129.3, 129.0, 128.9, 128.1, 126.9, 122.9, 61.7, 46.1. HRMS (ESI-TOF) calcd for C₁₇H₁₅NO₂Na [M+Na]⁺: 288.0995, found: 288.1007.

(E)-3-(2-phenyl-1-(*p*-tolyl)vinyl)oxazolidin-2-one (**3k'**)

White foams, 1.116g (40% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.07 (m, 7H), 7.01 – 6.96 (m, 2H), 6.78 (s, 1H), 4.39 – 4.31 (m, 2H), 3.65 – 3.58 (m, 2H), 2.36 (s, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.3, 138.9, 135.7, 135.6, 131.4, 129.7, 129.5, 129.3, 128.1, 126.8, 122.6, 61.7, 46.1, 21.5. HRMS (ESI-TOF) calcd for C₁₈H₁₇NO₂Na [M+Na]⁺: 302.1157, found: 302.1150.

(E)-3-(1-(4-methoxyphenyl)-2-phenylvinyl)oxazolidin-2-one (**3l'**)

Colorless oil, 1.328g (45% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.24 – 7.18 (m, 2H), 7.14 – 7.05 (m, 3H), 7.01 – 6.96 (m, 2H), 6.88 – 6.82 (m, 2H), 6.74 (s,

1H), 4.40 – 4.31 (m, 2H), 3.82 (s, 3H), 3.67 – 3.58 (m, 2H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 160.0, 156.2, 135.8, 135.3, 130.9, 129.3, 128.1, 126.7, 126.6, 122.3, 114.4, 61.7, 55.4, 46.1. HRMS (ESI-TOF) calcd for C₁₈H₁₇NO₃Na [M+Na]⁺: 318.1106, found: 318.1102.

(E)-3-(2-phenyl-1-(4-(trifluoromethyl)phenyl)vinyl)oxazolidin-2-one (**3m'**)

White foams, 1.265g (38% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.61 – 7.55 (m, 2H), 7.42 (dt, *J* = 7.8, 0.9 Hz, 2H), 7.17 – 7.10 (m, 3H), 6.98 – 6.91 (m, 2H), 6.81 (s, 1H), 4.45 – 4.35 (m, 2H), 3.75 – 3.65 (m, 2H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.0, 138.2, 134.9, 134.5, 130.8 (q, *J* = 33.1, 32.7 Hz), 130.1, 129.3, 128.4, 127.4, 125.9 (q, *J* = 3.6 Hz), 123.9, 123.3 (q, *J* = 272.4 Hz), 61.8, 46.2. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -62.7. HRMS (ESI-TOF) calcd for C₁₈H₁₄F₃NO₂Na [M+Na]⁺: 356.0874, found: 356.0868.

(E)-3-(1-phenyl-2-(*p*-tolyl)vinyl)oxazolidin-2-one (**3n'**)

White solid, mp 105.6–107.4 °C, 1.032g (37% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.27 (m, 5H), 6.91 (d, *J* = 7.8 Hz, 2H), 6.85 (d, *J* = 8.2 Hz, 2H), 6.78 (s, 1H), 4.42 – 4.24 (m, 2H), 3.71 – 3.54 (m, 2H), 2.24 (s, 3H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 156.3, 136.7, 134.8, 134.7, 132.5, 129.6, 129.2, 129.0, 128.8, 128.8, 123.2, 61.7, 46.1, 21.3. HRMS (ESI-TOF) calcd for C₁₈H₁₇NO₂Na [M+Na]⁺: 302.1157, found: 302.1154.

(E)-3-(2-(4-methoxyphenyl)-1-phenylvinyl)oxazolidin-2-one (**3o'**)

White solid, mp 111.8–113.1 °C, 0.443g (34% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.28 (m, 5H), 6.93 – 6.88 (m, 2H), 6.76 (s, 1H), 6.67 – 6.62 (m, 2H), 4.37 – 4.31 (m, 2H), 3.73 (s, 3H), 3.63 – 3.56 (m, 2H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 158.6, 156.5, 134.8, 133.7, 130.6, 129.6, 129.0, 128.8, 127.9, 123.3, 113.6, 61.7, 55.3, 46.0. HRMS (ESI-TOF) calcd for C₁₈H₁₇NO₃Na [M+Na]⁺: 318.1106, found: 318.1103.

(E)-3-(1-phenyl-2-(3-(trifluoromethyl)phenyl)vinyl)oxazolidin-2-one (**3p'**)

White solid, mp 85.8–87.5 °C, 1.066g (32% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.50 – 7.39 (m, 5H), 6.85 (s, 1H), 4.51 – 4.44 (m, 2H), 3.74 – 3.66 (m, 2H). ¹³C{¹H} NMR (101 MHz, Chloroform-*d*) δ 155.9, 139.5, 137.9, 133.9, 129.5, 129.4, 129.4, 129.2, 128.5 (q, *J* = 32.6, 32.2 Hz), 125.0 (q, *J* = 3.8 Hz), 122.9 (q, *J* = 273.6, 273.1 Hz), 120.2, 61.7, 46.0. ¹⁹F NMR (377 MHz, Chloroform-

d) δ -62.6 . HRMS (ESI-TOF) calcd for $C_{18}H_{14}F_3NO_2Na$ $[M+Na]^+$: 356.0874, found: 356.0858.

(E)-3-(1-(naphthalen-2-yl)-2-phenylvinyl)oxazolidin-2-one (**3q'**)

White solid, mp 106.5–107.9 °C, 1.228g (39% yield). 1H NMR (400 MHz, Chloroform-*d*) δ 7.81 (td, J = 14.1, 13.3, 7.8 Hz, 4H), 7.50 (pd, J = 6.8, 1.5 Hz, 2H), 7.38 (dd, J = 8.4, 1.7 Hz, 1H), 7.12 – 7.06 (m, 3H), 7.04 – 6.99 (m, 2H), 6.91 (s, 1H), 4.43 – 4.32 (m, 2H), 3.72 – 3.51 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 156.4 , 135.4 , 133.4 , 133.4 , 131.9 , 129.4 , 128.9 , 128.7 , 128.3 , 128.1 , 127.9 , 127.1 , 127.0 , 126.8 , 126.5 , 123.6 , 61.7 , 46.1 . HRMS (ESI-TOF) calcd for $C_{21}H_{17}NO_2Na$ $[M+Na]^+$: 338.1151, found: 338.1158.

(E)-3-(1-(furan-2-yl)-2-phenylvinyl)oxazolidin-2-one (**3r'**)

Brown oil, 0.765g (30% yield). 1H NMR (400 MHz, Chloroform-*d*) δ 7.41 (dd, J = 1.8, 0.8 Hz, 1H), 7.26 – 7.18 (m, 3H), 7.13 – 7.08 (m, 2H), 6.79 (s, 1H), 6.38 (dd, J = 3.4, 1.8 Hz, 1H), 6.31 (dd, J = 3.4, 0.8 Hz, 1H), 4.45 – 4.39 (m, 2H), 3.83 – 3.76 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 156.3 , 147.4 , 142.8 , 135.3 , 128.9 , 128.3 , 127.6 , 126.0 , 125.5 , 112.0 , 111.5 , 61.9 , 46.4 . HRMS (ESI-TOF) calcd for $C_{15}H_{13}NO_3$ $[M+Na]^+$: 278.0793, found: 278.0798.

(E)-3-(2-phenyl-1-(thiophen-3-yl)vinyl)oxazolidin-2-one (**3s'**)

Brown solid, mp 87.9–91.6 °C, 0.542g (20% yield). 1H NMR (400 MHz, Chloroform-*d*) δ 7.30 (dd, J = 5.0, 3.0 Hz, 1H), 7.22 (dd, J = 3.0, 1.3 Hz, 1H), 7.19 – 7.11 (m, 3H), 7.05 – 7.00 (m, 2H), 6.94 (dd, J = 5.0, 1.3 Hz, 1H), 6.81 (s, 1H), 4.40 – 4.34 (m, 2H), 3.71 – 3.64 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 156.2 , 135.6 , 135.1 , 130.6 , 129.1 , 128.2 , 128.2 , 127.1 , 126.4 , 125.9 , 123.8 , 61.7 , 46.2 . HRMS (ESI-TOF) calcd for $C_{15}H_{13}NO_2SNa$ $[M+Na]^+$: 294.0565, found: 294.0539.

General procedure for the preparation of the β,β -enecarbamates 5a-d

The procedures follow the general methods for α,β -enecarbamates mentioned above.

(Z)-3-(2-phenylpent-1-en-1-yl)oxazolidin-2-one (**5a**)

Colorless oil, with $TiCl_4$: 1.155g (50% yield); with p-TSA: 0.647g (28% yield). 1H NMR (500 MHz, Chloroform-*d*) δ 7.36 – 7.26 (m, 3H), 7.22 – 7.18 (m, 2H), 6.56 (s, 1H), 4.15 – 4.09 (m, 2H), 3.07 – 3.02 (m, 2H), 2.36 – 2.30 (m, 2H), 1.34 (h, J = 7.4 Hz, 2H), 0.89 (t, J = 7.3

Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, Chloroform-*d*) δ 157.3, 139.0, 129.1, 128.0, 127.3, 126.4, 120.5, 62.5, 45.1, 39.8, 21.2, 13.5. HRMS (ESI-TOF) calcd for $C_{14}H_{17}NO_2Na$ $[M+Na]^+$: 254.11551, found: 254.1149.

(Z)-3-(2-phenylhex-1-en-1-yl)oxazolidin-2-one (**5b**)

With $TiCl_4$: 0.980g (40% yield); with p-TSA: 0.931g (38% yield). The compound is in agreement with literature data.⁶

(Z)-3-(3-methyl-2-phenylbut-1-en-1-yl)oxazolidin-2-one (**5c**)

White solid, mp 77.2–79.2 °C, with $TiCl_4$: 1.155g (50% yield); with p-TSA: 1.386g (60% yield). 1H NMR (400 MHz, Chloroform-*d*) δ 7.3 – 7.3 (m, 3H), 7.2 – 7.1 (m, 2H), 6.6 (d, J = 1.1 Hz, 1H), 4.1 – 4.0 (m, 2H), 3.0 – 2.9 (m, 2H), 2.6 (sd, J = 6.9, 1.1 Hz, 1H), 1.0 (d, J = 6.9 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.3, 138.3, 132.0, 130.1, 127.8, 127.4, 119.7, 62.5, 45.2, 35.5, 22.0. HRMS (ESI-TOF) calcd for $C_{14}H_{17}NO_2Na$ $[M+Na]^+$: 254.11551, found: 254.1148.

(Z)-3-(2-Phenyl-2-cyclohexyl)oxazolidin-2-one (**5d**)

With $TiCl_4$: 1.382g (51% yield); with p-TSA: 1.409g (61% yield). The compound is in agreement with literature data.¹⁸

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Additional conditions screening, additional analytical data and NMR spectra for the products (PDF)

AUTHOR INFORMATION

Corresponding Author

*Pher.Andersson@su.se

Author Contributions

‡ L.M. and J.Y. contributed equally.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

The Swedish Research Council (VR), Stiftelsen Olle Engkvist Byggmästare, Knut and Alice Wallenberg Foundation (KAW 2016.0072 and KAW 2018:0066) supported this work. We thank the University of Camerino, School of Science and Technology, Chemistry Division, for the collaboration through the Erasmus+ program. We are also thankful to Dr. Cristiana Margarita for proof reading the manuscript.

REFERENCES

- (a) Matsubara, R.; Kobayashi, S., Enamides and Enecarbamates as Nucleophiles in Stereoselective C–C and C–N Bond-Forming Reactions. *Acc. Chem. Res.* **2008**, *41* (2), 292-301; (b) Gopalaiah, K.; Kagan, H. B., Use of Nonfunctionalized Enamides and Enecarbamates in Asymmetric Synthesis. *Chem. Rev.* **2011**, *111* (8), 4599-4657.
- (a) Yet, L., Chemistry and Biology of Salicylilalamide A and Related Compounds. *Chem. Rev.* **2003**, *103* (11), 4283-4306; (b) Kuranaga, T.; Sesoko, Y.; Inoue, M., Cu-mediated enamide formation in the total synthesis of complex peptide natural products. *Nat. Prod. Rep.* **2014**, *31* (4), 514-532.
- Courant, T.; Dagousset, G.; Masson, G., Enamide Derivatives: Versatile Building Blocks for Total Synthesis. *Synthesis* **2015**, *47* (13), 1799-1856.
- (a) Hughes, R. A.; Thompson, S. P.; Alcaraz, L.; Moody, C. J., Total Synthesis of the Thiopetide Antibiotic Amythiamicin D. *J. Am. Chem. Soc.* **2005**, *127* (44), 15644-15651; (b) Lu, T.; Song, Z.; Hsung, R. P., A Mutually π -Facial Selective Cyclopropanation of Chiral Enamides Using Dirhodium(II) Carbenoids. *Org. Lett.* **2008**, *10* (4), 541-544; (c) Zhao, F.; Li, N.; Zhang, T.; Han, Z.-Y.; Luo, S.-W.; Gong, L.-Z., Enantioselective Aza-Ene-type Reactions of Enamides with Gold Carbenes Generated from α -Diazoesters. *Angew. Chem.* **2017**, *129* (12), 3295-3299; (d) Bernasconi, M.; Müller, M.-A.; Pfaltz, A., Asymmetric Hydrogenation of Maleic Acid Diesters and Anhydrides. *Angew. Chem. Int. Ed.* **2014**, *53* (21), 5385-5388.
- (a) Shen, R.; Porco, J. A., Synthesis of Enamides Related to the Salicylate Antitumor Macrolides Using Copper-Mediated Vinylic Substitution. *Org. Lett.* **2000**, *2* (9), 1333-1336; (b) Jiang, L.; Job, G. E.; Klapars, A.; Buchwald, S. L., Copper-Catalyzed Coupling of Amides and Carbamates with Vinyl Halides. *Org. Lett.* **2003**, *5* (20), 3667-3669.
- Gourdet, B.; Lam, H. W., Stereoselective Synthesis of Multisubstituted Enamides via Rhodium-Catalyzed Carbozincation of Ynamides. *J. Am. Chem. Soc.* **2009**, *131* (11), 3802-3803.
- (a) Evano, G.; Blanchard, N.; Toumi, M., Copper-Mediated Coupling Reactions and Their Applications in Natural Products and Designed Biomolecules Synthesis. *Chem. Rev.* **2008**, *108* (8), 3054-3131; (b) Bolshan, Y.; Batey, R. A., Enamide Synthesis by Copper-Catalyzed Cross-Coupling of Amides and Potassium Alkenyltrifluoroborate Salts. *Angew. Chem. Int. Ed.* **2008**, *47* (11), 2109-2112; (c) Bolshan, Y.; Batey, R. A., Copper-catalyzed cross-coupling of amides and potassium alkenyltrifluoroborate salts: a general approach to the synthesis of enamides. *Tetrahedron* **2010**, *66* (27), 5283-5294; (d) Cartwright, K. C.; Tunge, J. A., Decarboxylative Elimination of N-Acyl Amino Acids via Photoredox/Cobalt Dual Catalysis. *ACS Catal.* **2018**, *8* (12), 11801-11806; (e) Cartwright, K. C.; Lang, S. B.; Tunge, J. A., Photoinduced Kochi Decarboxylative Elimination for the Synthesis of Enamides and Enecarbamates from N-Acyl Amino Acids. *J. Org. Chem.* **2019**, *84* (5), 2933-2940.
- (a) Yang, Y.; Wang, L.; Zhang, J.; Jin, Y.; Zhu, G., An unprecedented Pd-catalyzed trans-addition of boronic acids to ynamides. *Chem. Commun.* **2014**, *50* (18), 2347-2349; (b) Yang, Y.; Wang, L.; Zhang, F.; Zhu, G., Preparation of (Z)- α,β -Disubstituted Enamides via Palladium-Catalyzed Addition of Boronic Acids to Ynamides. *J. Org. Chem.* **2014**, *79* (19), 9319-9324.
- (a) Dwivedi, V.; Hari Babu, M.; Kant, R.; Sridhar Reddy, M., N-Substitution dependent stereoselectivity switch in palladium catalyzed hydroalkynylation of ynamides: a regio and stereoselective synthesis of ynenamides. *Chem. Commun.* **2015**, *51* (81), 14996-14999; (b) Takimoto, M.; Gholap, S. S.; Hou, Z., Cu-Catalyzed Alkylative Carboxylation of Ynamides with Dialkylzinc Reagents and Carbon Dioxide. *Chem. Eur. J.* **2015**, *21* (43), 15218-15223.
- Baldassari, L. L.; de la Torre, A.; Li, J.; Lüdtkke, D. S.; Maulide, N., Ynamide Preactivation Allows a Regio- and Stereoselective Synthesis of α,β -Disubstituted Enamides. *Angew. Chem. Int. Ed.* **2017**, *56* (49), 15723-15727.
- Zeza, C. A.; Smith, M. B., Stereoselective Synthesis of N-Augenyl Lactams. *Synth. Commun.* **1987**, *17* (6), 729-740.
- Reeves, J. T.; Tan, Z.; Han, Z. S.; Li, G.; Zhang, Y.; Xu, Y.; Reeves, D. C.; Gonnella, N. C.; Ma, S.; Lee, H.; Lu, B. Z.; Senanayake, C. H., Direct Titanium-Mediated Conversion of Ketones into Enamides with Ammonia and Acetic Anhydride. *Angew. Chem. Int. Ed.* **2012**, *51* (6), 1400-1404.
- Genovino, J.; Lagu, B.; Wang, Y.; Touré, B. B., Synthesis of sterically hindered enamides via a Ti-mediated condensation of amides with aldehydes and ketones. *Chem. Commun.* **2012**, *48* (53), 6735-6737.
- Adam, W.; Bosio, S. G.; Turro, N. J.; Wolff, B. T., Enecarbamates as Selective Substrates in Oxidations: Chiral-Auxiliary-Controlled Mode Selectivity and Diastereoselectivity in the [2+2] Cycloaddition and Ene Reaction of Singlet Oxygen and in the Epoxidation by DMD and mCPBA. *J. Org. Chem.* **2004**, *69* (5), 1704-1715.
- Meltzer, P. C.; Butler, D.; Deschamps, J. R.; Madras, B. K., 1-(4-Methylphenyl)-2-pyrrolidin-1-yl-pentan-1-one (Pyrovalerone) Analogues: A Promising Class of Monoamine Uptake Inhibitors. *J. Med. Chem.* **2006**, *49* (4), 1420-1432.
- (a) Talero, A. G.; Martins, B. S.; Burtoloso, A. C. B., Coupling of Sulfoxonium Ylides with Arynes: A Direct Synthesis of Pro-Chiral Aryl Ketosulfoxonium

Ylides and Its Application in the Preparation of α -Aryl Ketones. *Org. Lett.* **2018**, *20* (22), 7206-7211; (b) Buzzetti, L.; Prieto, A.; Roy, S. R.; Melchiorre, P., Radical-Based C–C Bond-Forming Processes Enabled by the Photoexcitation of 4-Alkyl-1,4-dihydropyridines. *Angew. Chem.* **2017**, *129* (47), 15235-15239; (c) Sävmarker, J.; Lindh, J.; Nilsson, P., Deoxybenzoins from Stille carbonylative cross-couplings using molybdenum hexacarbonyl. *Tetrahedron Lett.* **2010**, *51* (52), 6886-6889; (d) Wommack, A. J.; Moebius, D. C.; Travis, A. L.; Kingsbury, J. S., Diverse Alkanones by Catalytic Carbon Insertion into the Formyl C–H Bond. Concise Access to the Natural Precursor of Achyrofuran.

Org. Lett. **2009**, *11* (15), 3202-3205; (e) Fu, W. C.; So, C. M.; Yuen, O. Y.; Lee, I. T. C.; Kwong, F. Y., Exploiting Aryl Mesylates and Tosylates in Catalytic Mono- α -arylation of Aryl- and Heteroarylketones. *Org. Lett.* **2016**, *18* (8), 1872-1875.

17. Joosten, A.; Lambert, É.; Vasse, J.-L.; Szymoniak, J., Diastereoselective Access to trans-2-Substituted Cyclopentylamines. *Org. Lett.* **2010**, *12* (22), 5128-5131.

18. Gourdet, B.; Lam, H. W., Catalytic Asymmetric Dihydroxylation of Enamides and Application to the Total Synthesis of (+)-Tanikolide. *Angew. Chem. Int. Ed.* **2010**, *49* (46), 8733-8737.