

A Convenient, Room-Temperature – Organic Base Protocol for Preparing Chiral 3-(Enoyl)-1,3-oxazolidin-2-ones

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Dedicated to Professor *Dieter Seebach* on the occasion of his 65th birthday. Our warmest regards and best wishes for many more years of excellent science.

In this study, we developed a new protocol for the preparation of the chiral 3-[(*E*)-enoyl]-1,3-oxazolidin-2-ones under the ultimately simple reaction conditions starting with the corresponding enoyl chlorides and 1,3-oxazolidin-2-ones with Et₃N/LiCl at room temperature. The method generally allows efficient preparation of various derivatives regardless of the steric and electronic nature of the substituents on both the enoyl or the oxazolidinone sites. Excellent yields, combined with the simplicity of the experimental procedures, render the present method immediately useful for preparing the target compounds.

Introduction. – *Michael*-addition reactions, generally defined, are among a handful of truly fundamental reactions in organic chemistry [1]. Of particular interest are the *Michael*-addition reactions between nucleophilic glycine equivalents and α,β -unsaturated carboxylic acid derivatives, which represent the most methodologically concise and generalized approach to the family of χ -constrained¹⁾ five-C-atom amino acids (*Scheme 1*). These reactions leading to the direct formation of glutamic (**1**) or pyroglutamic acids (**2**) (depending on the work-up procedure) should be a reliable source also for synthetic, tailor-made²⁾ glutamines (**3**), prolines (**4**), ornithines (**5**), and arginines (**6**) (*Scheme 1*)³⁾. The issue of stereoselectivity in these reactions has received a great deal of attention in the past [5]. Many research groups systematically studied application of various chiral glycine equivalents (*A* in *Scheme 1*) or chiral *Michael* acceptors (*B* in *Scheme 1*) to control the stereochemical outcome of such reactions.

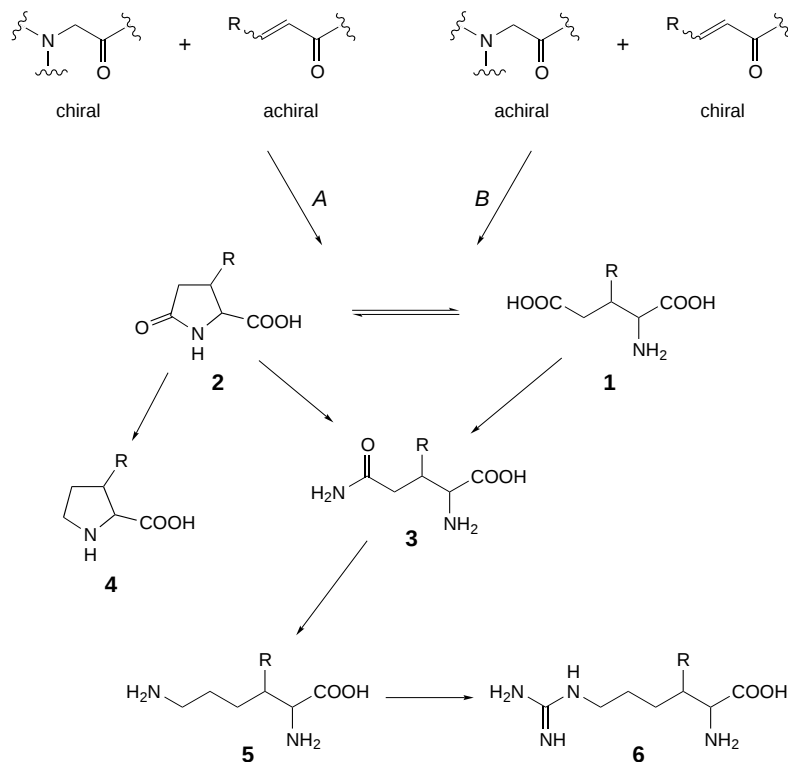
In 1992, *Seebach*'s group first reported the ultimate level of stereoselectivity (only one detectable stereoisomer) in the *Michael* addition reactions between (*S*)-imidazolidinone **7** and 2,6-di(*tert*)-butyl-4-(methoxy)phenyl esters **8** (*Scheme 2*) giving rise to the corresponding pyroglutamic acids **2** of (2*S*,3*R*) (R=Alk) and (2*S*,3*S*) (R=i-Pr, Ar) absolute configuration. To account for the virtually complete

¹⁾ For recent reviews on χ -constrained amino acids, see [2].

²⁾ The rapidly growing list of amino acids isolated from various natural sources makes the terms *unnatural*, or *nonproteinogenic* amino acids, which are most frequently used in the literature, dependent on the success of specific scientific achievements. For instance, amino acids containing the xenobiotic element fluorine have been shown to be synthesized by microorganisms [3]. Therefore, the time-independent term *tailor-made*, meaning rationally designed/synthesized amino acids, in the absence of a better definition, is more objective, and we suggested its use in the literature.

³⁾ For a recent review on various synthetic transformations of pyroglutamic acid and its derivatives, see [4].

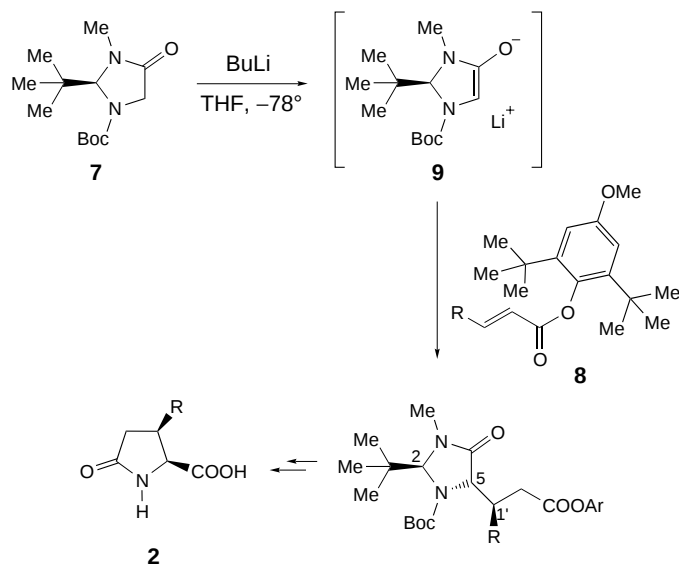
Scheme 1



stereoselectivity in these addition reactions, *Seebach* suggested (based on molecular-mechanics calculations and modeling) that only the *s-cis* conformer of **8** enters the reaction with enolate **9**, while the corresponding *s-trans* conformer of **8** does not react with **9** due to steric shielding of its C_β -atom of the enoate system by the *t*-Bu group [6].

Drawing inspiration from these results and mechanistic rational, we assumed that the geometric homogeneity of a glycine equivalent and conformational homogeneity of a *Michael* acceptor might be of critical importance in controlling the stereochemical outcome of the corresponding *Michael*-addition reactions. This idea turned out to be very fruitful, allowing us to develop highly diastereoselective addition reactions between the Ni-complex **10** and *Michael* acceptors **11** (Scheme 3) [7a]. Compounds **10** and **11** perfectly meet the requirements for geometric/conformational homogeneity. Thus, due to its cyclic structure, complex **10** can give rise to only a (*E*)-enolate, while *Michael* acceptors **11** exist in a *s-cis* configuration due to the unfavorable repulsive steric and electrostatic interactions in the corresponding *s-trans* conformer [7]. The synthetically advantageous characteristics of these reactions over other methods [5] are that they occur at *room temperature* in the presence of *nonchelating organic bases* and with *virtually complete* stereochemical outcome (>98% d.e.). Thus, we have found that, in the absence of any coordinating species, the *Michael* acceptors **11** were remarkably effective in controlling both simple and face diastereoselectivity of these addition

Scheme 2



R = Me, Et, PhCH₂, i-Pr, Ph

(2*S*,5*S*,1'*R*) R = Alk

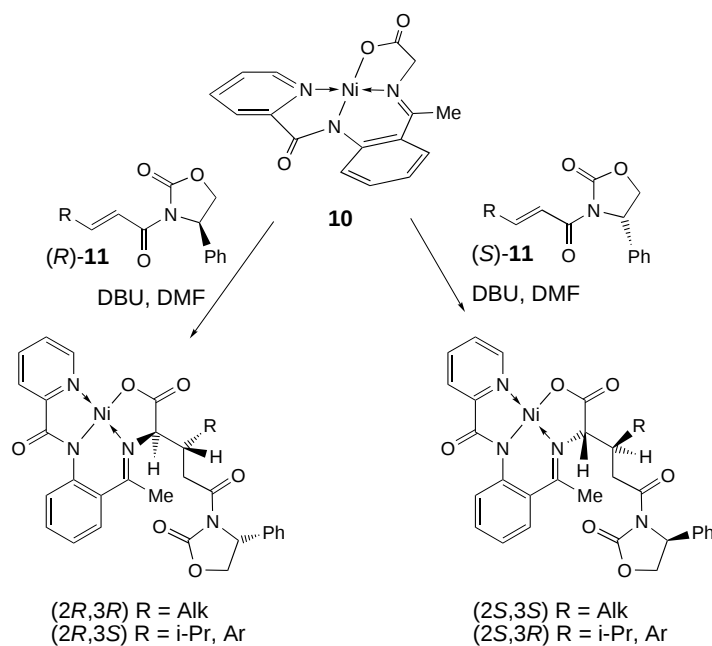
(2*S*,5*S*,1'*S*) R = i-Pr, Ar

reactions. However, while the conditions we found for the addition reactions render our method practical and convenient for large-scale preparation of β -substituted glutamic/pyroglutamic acids, the necessity of preparing starting *Michael* acceptors **11**, according to the standard *Evans* procedures [8], at -78° with BuLi, substantially compromised the synthetic efficiency of our method as a whole. Recent reports improving on the *Evans* procedures allow avoidance of the use of BuLi at -78° , but require preparation of the corresponding *N*-trimethylsilyl derivatives [9] or mixed anhydrides [10] to react with acyl chlorides at high temperatures ($>115^\circ$, long reaction times), or with 4-substituted-1,3-oxazolidin-2-ones, at still low temperatures (-20°), respectively. Therefore, we wanted to find simple and synthetically efficient *room-temperature* conditions for large-scale preparations of the starting 2-[(*E*)-enoyl]-4-phenyl-1,3-oxazolidin-2-ones **11**.

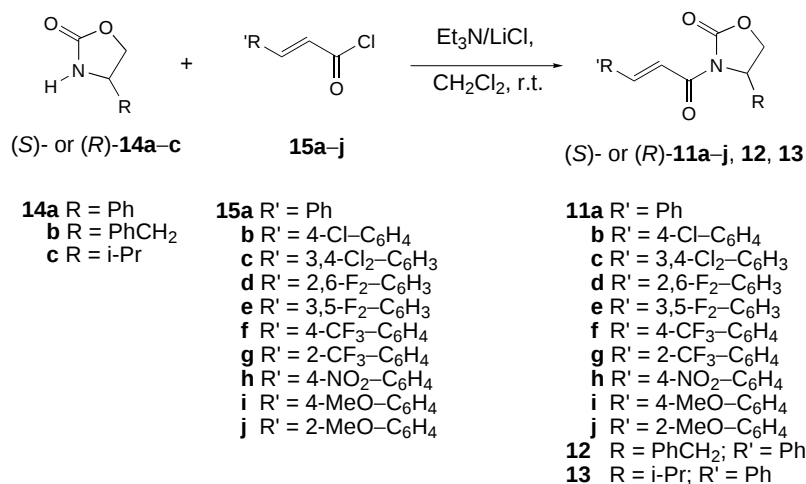
Results. – We now report a very simple method for the preparation of *Michael* acceptors **11** and related compounds (R=PhCH₂, i-Pr) **12** and **13** in high yields at room temperature by direct reaction of 4-substituted 1,3-oxazolidin-2-ones **14** with the corresponding acyl chlorides **15a–e** with Et₃N as a base (*Scheme 4*).

For the reaction medium, we decided to use commercial-grade CHCl₃ or CH₂Cl₂, as these solvents could be used without prior drying. Our first attempt to conduct the direct reaction between oxazolidin-2-one **14a** with enoyl chloride **15a** in a solution of CHCl₃ or CH₂Cl₂ at room temperature in the presence of Et₃N was quite promising.

Scheme 3



Scheme 4



Though the reaction occurred relatively slowly, the target product **11a** was isolated in good yield (90%) (Table 1, Entries 1 and 2). In the case of the reaction conducted in CHCl₃ containing about 1% of EtOH as a preservative, we observed formation (2–5%) of ethyl cinnamate, which substantially complicated the purification of the product

Table 1. Reactions between 1,3-Oxazolidin-2-one **14a** and Enoyl Chloride **15a**^{a)}

Entry	Base	<i>t</i> [h]	Ratio ^{b)} 14a/11a
1	Et ₃ N	1	19/81
2	Et ₃ N	24	4/96 ^{c)}
3	DABCO ^{d)}	1	47/53
4	DBU ^{d)}	1	41/59
5	Et(i-Pr) ₂ N	1	12/88
6	Et ₃ N	1	< 1/ > 99 ^{c)}

^{a)} All reactions were run in CH₂Cl₂ in the presence of 5 mol of the indicated base at r.t. Ratio (mol) **14a/15a** 1.0 : 1.12. ^{b)} Determined by ¹H-NMR on crude reaction mixtures. ^{c)} The product **11a** was isolated in 90% yield. ^{d)} For abbreviations, see text. ^{e)} The reaction was conducted with 5 mol of Et₃N/LiCl.

11a. Therefore, we used CH₂Cl₂ as a solvent for the rest of the study. The results suggested that the direct reaction between the corresponding enoyl chloride **15a** and the oxazolidinone **14a** is synthetically feasible.

What we sought next were the proper reaction conditions to make this reaction preparatively useful. To accelerate the reaction we decided to use a stronger base such as Et(i-Pr)₂N, 1,4-diazabicyclo[2.2.2]octane (DABCO), or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). In contrast to our expectations, the reactions conducted in the presence of DABCO and DBU occurred at lower rates than the reaction with Et₃N (*Entries* 3 and 4 vs. 1). On the other hand, the reaction with Et(i-Pr)₂N proceeded at a somewhat higher rate (*Entry* 5 vs. 1). Since Et(i-Pr)₂N is much more expensive than Et₃N, a small increase in the reaction rate did not justify the application of this base. Once again in this study drawing inspiration from Seebach's results [11], we decided to use LiCl as an additive. Thus, application of Et₃N/LiCl resulted in a surprisingly dramatic increase of the reaction rate and, therefore, in a complete conversion of the starting compounds in less than 1 h (*Entry* 6). After a simple work-up procedure, the target compound **11a** was obtained in >98% yield. This 1-h reaction was successfully reproduced on up to a 4-g scale, indicating its synthetic efficiency and practicability.

With these results in hand, we decided to check the generality of the method. The results are summarized in *Table 2*. The reactions of Cl/F mono- and disubstituted cinnamoyl chlorides **15b–e** with oxazolidinone **14a** conducted under the optimized standard conditions were complete in 1 h, giving rise to the target products **11b–e** in quantitative yields (*Entries* 2–5, *Table 2*). Introduction of electron-withdrawing substituents on the phenyl ring of the starting enoyl chloride **15** was expected to facilitate the reaction. Indeed, the reactions of 4-CF₃- and 4-NO₂-substituted derivatives occurred at relatively higher rates than the reaction of unsubstituted cinnamoyl chloride **15a** (*Entries* 6 and 9). However, the reaction of the 2-CF₃-substituted derivative proceeded noticeably slower. Thus a 1-h reaction resulted in about 90% conversion of the starting materials (*Entry* 7). Nevertheless, a prolonged reaction time (overnight) allowed us to obtain the product **11g** in quantitative yield (*Entry* 8, *Table 2*). The same steric effect of *ortho*-substitution was observed in a series of MeO-containing derivatives **15i,j**. While the reaction of the *para*-substituted **15i** was complete in 1 h (*Entry* 10) the reaction of the 2-MeO-substituted **15j** required a longer

Table 2. Reactions between 1,3-Oxazolidin-2-ones **14a–c** and Enoyl Chlorides **15a–j**^{a)}

Entry	(S)-4-R-1,3-Oxazolidin-2-one	R	(E)-3-R'-2-Enoyl chloride	R'	Product	Yield ^{b)} [%]
1	14a	Ph	15a	Ph	11a	> 98
2	14a	Ph	15b	4-Cl–C ₆ H ₄	11a	> 98
3	14a	Ph	15c	3,4-Cl ₂ –C ₆ H ₃	11c	> 98
4	14a	Ph	15d	2,6-F ₂ –C ₆ H ₃	11d	> 98
5	14a	Ph	15e	3,5-F ₂ –C ₆ H ₃	11e	> 98
6	14a	Ph	15f	4-CF ₃ –C ₆ H ₄	11f	> 98
7	14a	Ph	15g	2-CF ₃ –C ₆ H ₄	11g	^{c)}
8	14a	Ph	15g	2-CF ₃ –C ₆ H ₄	11g	> 98 ^{d)}
9	14a	Ph	15h	4-NO ₂ –C ₆ H ₄	11h	> 98
10	14a	Ph	15i	4-MeO–C ₆ H ₄	11i	> 98
11	14a	Ph	15j	2-MeO–C ₆ H ₄	11j	92 ^{c)}
12	14a	Ph	15j	2-MeO–C ₆ H ₄	11j	> 97 ^{d)}
13	14b	PhCH ₂	15a	Ph	12	> 98
14	14c	i-Pr	15a	Ph	13	> 98

^{a)} All reactions were run in CH₂Cl₂ for 1 h in the presence of 5 mol of Et₃N/LiCl at room temperature. Ratio (mol) **14/15** 1.0 : 1.12. ^{b)} Isolated yield of pure (> 99% by ¹H-NMR) product. ^{c)} About 90% conversion of the starting compounds. ^{d)} The reaction was run overnight.

time for completion. Next, we conducted the reactions between cinnamoyl chloride **15a** and the most frequently used chiral oxazolidin-2-ones **14b,c** containing PhCH₂ and i-Pr groups, respectively. Similar to the reaction with **14a**, these acylations occurred at high reaction rates, furnishing the target products **12** and **13** in excellent isolated yields (Entries 13 and 14).

Conclusions. – We have demonstrated that the preparation of chiral 3-[(E)-enoyl]-1,3-oxazolidin-2-ones can be efficiently conducted at room temperature in a commercial-grade solvent. The method generally allows practical large-scale preparation of various derivatives regardless of the steric and electronic nature of the substituents on both the enoyl and the oxazolidinone sites. Simple reaction conditions and excellent yields render the method immediately useful for preparing the target compounds.

Experimental Part

General. All reagents and solvents, unless otherwise stated, are commercially available and were used as received. The known compounds were confirmed by ¹H-NMR, and the new compounds were characterized by ¹H-, ¹⁹F-, ¹³C-NMR, optical rotation, and HR-MS. M.ps.: uncorrected; obtained in open capillaries. Optical rotation: *Jasco P-1010* polarimeter; measured at r.t. in commercial-grade CHCl₃ containing 1% EtOH as preservative. ¹H-, ¹³C-, and ¹⁹F-NMR: *Varian 300*; measured at 299.94, 75.4, and 282 MHz, resp. in CDCl₃; Me₄Si, CDCl₃, and CCl₃F as internal standards; δ in ppm and *J* in Hz. HR-MS: *Jeol HX110A*.

General Procedure for the Reactions of 4-Substituted 1,3-Oxazolidin-2-ones 14a–c with 3-Substituted (E)-Prop-2-enoyl Chlorides 15a–j. *Synthesis of 3-[(E)-Enoyl]-1,3-oxazolidin-2-ones 11a–j, 12, and 13.* A suspension of the corresponding α,β -unsaturated acid (1.05 equiv.) in SOCl₂ (8 equiv.) was refluxed until a homogeneous soln. was formed (ca. 5 h). The resulting soln. was cooled to r.t. and evaporated several times with CH₂Cl₂ to give a residue free of SOCl₂ and HCl. To a soln. of the acyl chloride **15a–j** (1.12 equiv.) thus prepared

in CH_2Cl_2 , the corresponding oxazolidinone **14a–c** (1.0 equiv.), LiCl (5 equiv.), and Et_3N (5 equiv.) were added at r.t. The mixture was stirred for 1 h (or longer, see Table 2) and quenched by adding 1N HCl soln. The org. phase was washed with sat. NaHCO_3 soln. and brine, and dried (MgSO_4). Filtration and evaporation of the org. phase gave the crude product, which can be purified by column chromatography (SiO_2 , AcOEt/hexanes) or recrystallized from AcOEt/hexanes. Yields of the products **11a–j**, **12**, and **13** are given in Table 2, the physico-chemical, chiroptical, and spectral data are listed below.

(*R*)-4-Phenyl-3-[(*E*)-3-phenylprop-2-enoyl]-1,3-oxazolidin-2-one ((*R*)-**11a**) [12]. $^1\text{H-NMR}$: 4.33 (part of *ABX*, $J = 9.0, 3.9, 1 \text{ H}$); 4.75 (*t*, $J = 8.8, 1 \text{ H}$); 5.57 (part of *ABX*, $J = 8.8, 3.9, 1 \text{ H}$); 7.38–7.40 (*m*, 7 H); 7.58–7.61 (*m*, 3 H); 7.79, 7.94 (*AB*, $J = 15.9, 2 \text{ H}$).

(*R*)-3-[(*E*)-3-(4-Chlorophenyl)prop-2-enoyl]-4-phenyl-1,3-oxazolidin-2-one ((*R*)-**11b**). M.p. 135.0–135.5°. $[\alpha]_{\text{D}}^{25} = +21.2$ ($c = 1.4$). $^1\text{H-NMR}$: 4.33 (*dd*, $J = 9.0, 3.9, 1 \text{ H}$); 4.75 (*t*, $J = 8.8, 1 \text{ H}$); 5.56 (*dd*, $J = 8.8, 3.9, 1 \text{ H}$); 7.34–7.40 (*m*, 7 H); 7.52 (*d*, $J = 8.5, 1 \text{ H}$); 7.72 (*d*, $J = 15.9, 1 \text{ H}$); 7.91 (*d*, $J = 15.9, 1 \text{ H}$). $^{13}\text{C-NMR}$: 57.8; 70.0; 117.3; 126.0; 128.7; 129.1; 129.2; 129.7; 132.9; 136.6; 138.9; 145.1; 153.8; 164.5. FAB-HR-MS: 328.0740 (calc. for $\text{C}_{18}\text{H}_{15}\text{ClNO}_3$, $[M + \text{H}]^+$; found 328.0739).

(*S*)-3-[(*E*)-3-(3,4-Dichlorophenyl)prop-2-enoyl]-4-phenyl-1,3-oxazolidin-2-one ((*S*)-**11c**). M.p. 148.0–148.5°. $[\alpha]_{\text{D}}^{25} = 25.9$ ($c = 1.0$). $^1\text{H-NMR}$: 4.33 (*dd*, $J = 9.0, 3.9, 1 \text{ H}$); 4.75 (*t*, $J = 8.8, 1 \text{ H}$); 5.56 (*dd*, $J = 8.8, 3.9, 1 \text{ H}$); 7.34–7.40 (*m*, 7 H); 7.52 (*d*, $J = 8.5, 2 \text{ H}$); 7.72 (*d*, $J = 15.9, 1 \text{ H}$); 7.91 (*d*, $J = 15.9, 1 \text{ H}$). $^{13}\text{C-NMR}$: 57.8; 70.0; 117.3; 126.0; 128.7; 129.1; 129.2; 129.7; 132.9; 136.6; 138.9; 145.1; 153.8; 164.5.

(*S*)-3-[(*E*)-3-(2,6-Difluorophenyl)prop-2-enoyl]-4-phenyl-1,3-oxazolidin-2-one ((*S*)-**11d**). M.p. 168.0–168.5°. $[\alpha]_{\text{D}}^{25} = +34.4$ ($c = 1.1$). $^1\text{H-NMR}$: 4.33 (*dd*, $J = 8.8, 4.0, 1 \text{ H}$); 4.75 (*t*, $J = 8.8, 1 \text{ H}$); 5.55 (*dd*, $J = 8.8, 3.9, 1 \text{ H}$); 6.93 (*m*, 2 H); 7.26–7.44 (*m*, 6 H); 7.86, 8.15 (*AB*, $J = 16.1, 2 \text{ H}$). $^{19}\text{F-NMR}$: –108.8 (*t*, $J = 7.6$).

(*S*)-3-[(*E*)-3-(3,5-Difluorophenyl)prop-2-enoyl]-4-phenyl-1,3-oxazolidin-2-one ((*S*)-**11e**). M.p. 121.0–121.5°. $[\alpha]_{\text{D}}^{25} = +12.5$ ($c = 1.3$). $^1\text{H-NMR}$: 4.34 (*dd*, $J = 8.8, 3.9, 1 \text{ H}$); 4.58 (*t*, $J = 8.8, 1 \text{ H}$); 5.54 (*dd*, $J = 8.8, 3.9, 1 \text{ H}$); 6.83 (*m*, 1 H); 7.08 (*m*, 2 H); 7.30–7.44 (*m*, 5 H); 7.63, 7.90 (*AB*, $J = 15.6, 2 \text{ H}$). $^{19}\text{F-NMR}$: –108.4 (*t*, $J = 7.6$).

(*S*)-4-Phenyl-3-[(*E*)-3-[4-(trifluoromethyl)phenyl]prop-2-enoyl]-1,3-oxazolidin-2-one ((*S*)-**11f**). M.p. 112.0–113.0°. $[\alpha]_{\text{D}}^{25} = +20.2$ ($c = 1.4$). $^1\text{H-NMR}$: 4.35 (part of *ABX*, $J = 9.0, 3.9, 1 \text{ H}$); 4.77 (*t*, $J = 8.7, 1 \text{ H}$); 5.56 (part of *ABX*, $J = 8.7, 3.9, 1 \text{ H}$); 7.32–7.44 (*m*, 5 H); 7.63, 7.69 (*AB*, $J = 8.4, 4 \text{ H}$); 7.77, 8.00 (*AB*, $J = 15.6, 2 \text{ H}$). $^{13}\text{C-NMR}$: 57.9; 70.1; 119.3; 125.8 (q , $J = 3.0$); 126.0; 128.7; 128.8; 129.2; 137.8; 138.8; 144.6; 153.8; 164.3; the resonance of CF_3 was not observed due to its low intensity. $^{19}\text{F-NMR}$: –64.0 (*s*). FAB-HR-MS: 362.1004 (calc. $\text{C}_{19}\text{H}_{15}\text{F}_3\text{NO}_3$ $[M + \text{H}]^+$; found 362.1004).

(*S*)-4-Phenyl-3-[(*E*)-3-[2-(trifluoromethyl)phenyl]prop-2-enoyl]-1,3-oxazolidin-2-one ((*S*)-**11g**). M.p. 80.0–80.5°. $[\alpha]_{\text{D}}^{25} = -7.1$ ($c = 1.0$). $^1\text{H-NMR}$: 4.34 (part of *ABX*, $J = 8.8, 3.9, 1 \text{ H}$); 4.76 (*t*, $J = 8.8, 1 \text{ H}$); 5.55 (part of *ABX*, $J = 8.8, 3.9, 1 \text{ H}$); 7.26–7.45 (*m*, 5 H); 7.48 (*t*, $J = 7.45, 1 \text{ H}$); 7.58 (*t*, $J = 6.8, 1 \text{ H}$); 7.68 (*dd*, $J = 8.3, 0.7, 1 \text{ H}$); 7.85 (*d*, $J = 7.82, 1 \text{ H}$); 7.90 (*d*, $J = 15.5, 1 \text{ H}$); 8.15 (*dq*, $J = 15.5, 2.08, 1 \text{ H}$). $^{19}\text{F-NMR}$: –58.0 (*s*). FAB-HR-MS: 362.1004 (calc. for $\text{C}_{19}\text{H}_{15}\text{F}_3\text{NO}_3$, $[M + \text{H}]^+$; found 362.1004).

(*S*)-3-[(*E*)-3-(4-Nitrophenyl)prop-2-enoyl]-4-phenyl-1,3-oxazolidin-2-one ((*S*)-**11h**). M.p. 191.0–191.5°. $[\alpha]_{\text{D}}^{25} = -24.1$ ($c = 1.5$). $^1\text{H-NMR}$: 4.36 (part of *ABX*, $J = 9.0, 3.9, 1 \text{ H}$); 4.78 (*t*, $J = 8.8, 1 \text{ H}$); 5.56 (part of *ABX*, $J = 8.8, 3.9, 1 \text{ H}$); 7.31–7.45 (*m*, 5 H); 7.68–7.80 (*m*, 3 H); 8.04 (*d*, $J = 15.8, 1 \text{ H}$); 8.20–8.27 (*m*, 2 H). $^{13}\text{C-NMR}$: 57.8; 70.0; 120.8; 123.9; 125.8; 128.7; 128.9; 129.0; 138.4; 140.2; 143.0; 148.4; 153.5; 163.6.

(*S*)-3-[(*E*)-3-(4-Methoxyphenyl)prop-2-enoyl]-4-phenyl-1,3-oxazolidin-2-one ((*S*)-**11i**). M.p. 145.0–146.0°. $[\alpha]_{\text{D}}^{25} = -46.1$ ($c = 1.0$). $^1\text{H-NMR}$: 3.84 (*s*, 3 H); 4.31 (part of *ABX*, $J = 3.8, 8.9, 1 \text{ H}$); 4.74 (*t*, $J = 9.0, 1 \text{ H}$); 5.56 (part of *ABX*, $J = 9.0, 3.9, 1 \text{ H}$); 6.90 (part of *AB*, $J = 8.8, 2 \text{ H}$); 7.33–7.42 (*m*, 5 H); 7.55 (part of *AB*, $J = 9.0, 2 \text{ H}$); 7.75, 7.82 (*AB*, $J = 15.9, 2 \text{ H}$). $^{13}\text{C-NMR}$: 55.4; 57.9; 69.9; 114.2; 114.3; 126.0; 127.3; 128.6; 129.2; 130.5; 139.2; 146.6; 153.9; 161.8; 165.0. FAB-HR-MS: 324.1236 (calc. for $\text{C}_{19}\text{H}_{18}\text{NO}_4$, $[M + \text{H}]^+$; found 324.1224).

(*S*)-3-[(*E*)-3-(2-Methoxyphenyl)prop-2-enoyl]-4-phenyl-1,3-oxazolidin-2-one ((*S*)-**11j**). M.p. 144.0–145.0°. $[\alpha]_{\text{D}}^{25} = +47.8$ ($c = 1.2$). $^1\text{H-NMR}$: 3.87 (*s*, 3 H); 4.31 (part of *ABX*, $J = 8.8, 3.9, 1 \text{ H}$); 4.73 (*t*, $J = 8.8, 1 \text{ H}$); 5.56 (part of *ABX*, $J = 3.9, 8.8, 1 \text{ H}$); 6.89 (part of *AB*, $J = 8.2, 1.1, 2 \text{ H}$); 6.95 (*dd*, $J = 7.8, 1.1, 0.5, 1 \text{ H}$); 7.26–7.45 (*m*, 6 H); 7.61 (*ddt*, $J = 7.7, 1.8, 0.5, 1 \text{ H}$); 7.99 (*d*, $J = 15.9, 1 \text{ H}$); 8.13 (*d*, $J = 15.9, 1 \text{ H}$). $^{13}\text{C-NMR}$: 55.4; 55.8; 69.8; 110.1; 116.9; 120.5; 123.3; 125.8; 128.4; 128.9; 129.2; 131.8; 139.0; 141.8; 153.6; 158.4; 164.9. FAB-HR-MS: 324.1236 (calc. for $\text{C}_{19}\text{H}_{18}\text{NO}_4$, $[M + \text{H}]^+$; found 324.1227).

(*S*)-4-Benzyl-3-[(*E*)-3-(phenylprop-2-enoyl)-1,3-oxazolidin-2-one ((*S*)-**12**) [13]. $^1\text{H-NMR}$: 2.86, 3.38 (*ABX*, $J = 13.4, 9.5, 3.2, 2 \text{ H}$); 4.19–4.29 (*m*, 2 H); 4.77–4.85 (*m*, 1 H); 7.24–7.44 (*m*, 8 H); 7.63–7.67 (*m*, 2 H); 7.93 (*s*, 2 H).

(*S*)-4-Isopropyl-3-[(*E*)-3-phenylprop-2-enoyl]-1,3-oxazolidin-2-one ((*S*)-**13**) [8]. ¹H-NMR: 0.92 (*d*, *J* = 7.1, 3 H); 0.96 (*d*, *J* = 6.8, 3 H); 2.41–2.50 (*m*, 1 H); 4.25, 4.32 (part of *ABX*, *J* = 9.0, 8.3, 3.2, 2 H); 4.54–4.59 (*m*, 1 H); 7.39–7.41 (*m*, 3 H); 7.60–7.65 (*m*, 2 H); 7.85, 7.96 (*AB*, *J* = 15.6, 2 H).

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REFERENCES

- [1] D. A. Oare, C. H. Heathcock, in 'Topics in Stereochemistry', Vol. 19, Eds. E. L. Eliel, S. H. Wilen, N. L. Allinger, Wiley, New York, 1990, pp. 227–407; D. A. Oare, M. A. Henderson, M. A. Sanner, C. H. Heathcock, *J. Org. Chem.* **1990**, *55*, 132.
- [2] S. E. Gibson, N. Guillo, M. J. Tozer, *Tetrahedron* **1999**, *55*, 585; V. J. Hruby, G. Li, C. Haskell-Luevano, M. D. Shenderovich, *Biopolymers* **1997**, *43*, 219.
- [3] 'Fluorine-Containing Amino Acids: Synthesis and Properties', Eds. V. P. Kukhar and V. A. Soloshonok, Wiley, Chichester, 1994; 'Enantiocontrolled Synthesis of Fluoro-Organic Compounds: Stereochemical Challenges and Biomedical Targets', Ed. V. A. Soloshonok, Wiley, Chichester, 1999.
- [4] C. Najera, M. Yus, *Tetrahedron: Asymmetry* **1999**, *10*, 2245.
- [5] V. A. Soloshonok, *Current Org. Chem.* **2002**, *6*, 1.
- [6] K. Suzuki, D. Seebach, *Liebigs Ann. Chem.* **1992**, 51.
- [7] a) V. A. Soloshonok, C. Cai, V. J. Hruby, *Org. Lett.* **2000**, *2*, 747; b) V. A. Soloshonok, C. Cai, V. J. Hruby, *Angew. Chem., Int. Ed.* **2000**, *39*, 2172; c) V. A. Soloshonok, C. Cai, V. J. Hruby, *Tetrahedron Lett.* **2000**, *41*, 9645; d) V. A. Soloshonok, C. Cai, V. J. Hruby, L. V. Meervelt, T. Yamazaki, *J. Org. Chem.* **2000**, *65*, 6688.
- [8] D. A. Evans, K. T. Chapman, J. Bisaha, *J. Am. Chem. Soc.* **1988**, *110*, 1238.
- [9] C. Thom, P. Kocienski, *Synthesis* **1992**, 582.
- [10] G. J. Ho, D. J. Mathre, *J. Org. Chem.* **1995**, *60*, 2271.
- [11] D. Seebach, A. K. Beck, A. Studer, 'Some Effects of Lithium Salts, Strong Bases, and of the Cosolvent DMPU in Peptide Chemistry, and Elsewhere', in 'Modern Synthetic Methods 1995; Vol. 7, Eds. B. Ernst and C. Leumann, Verlag Helvetica Chimica Acta, Basel, VCH, Weinheim, 1995, 1–178.
- [12] E. Nicolás, K. C. Russell, V. J. Hruby, *J. Org. Chem.* **1993**, *58*, 766.
- [13] N. Kise, S. Mashiba, N. Ueda, *J. Org. Chem.* **1998**, *63*, 7931.

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