Tetrahedron 65 (2009) 9180–9187

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Microwave-assisted synthesis of α-ethoxycarbamates

Alexandre Lumbroso [a], Floris Chevallier [a], Isabelle Beaudet [a], Jean-Paul Quintard [a], Thierry Besson [b,*], Erwan Le Grognec [a,*]

[a] Université de Nantes, CNRS, Chimie et Interdisciplinarité: Synthèse, Analyse, Modélisation (CEISAM), UMR CNRS 6230, Faculté des Sciences et des Techniques, 2 rue de la Houssinière, BP 92208, 44322 Nantes Cedex 3, France
[b] Université de Rouen, UMR CNRS 6014—C.O.B.R.A.—I.R.C.O.F., rue Tesnière, F-76130 Mont Saint-Aignan, France

ARTICLE INFO

Article history:
Received 8 July 2009
Received in revised form 26 August 2009
Accepted 7 September 2009
Available online 11 September 2009

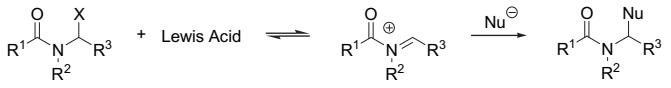
Keywords:
α-Ethoxycarbamate
N-Acyliminium ion
Imine
Microwave-assisted synthesis

ABSTRACT

An efficient and reproducible synthesis of various α-ethoxycarbamates is described via a microwave heating mode. Compared to the thermal process, the microwave dielectric heating induces a dramatic reduction of the reaction time and the improvement of the yields. The reaction is general since applicable to aromatic and aliphatic aldehydes with various primary amines. Several examples involving chiral aldehydes have also been considered.

1. Introduction

N-Acyliminium ions are versatile electrophilic species with many applications in the synthesis of nitrogen-containing compounds and have received a significant amount of interest over the past two decades.[1] These reactive species can be generated starting from alkyl chloroformate and an imine as described by Yamamoto.[2] This preparation is however limited to imines displaying no enolisable proton due to the presence of chloride. *N*-acyliminium ions can also be obtained from the corresponding more stable α-substituted *N*-acylamines by treatment with a Lewis acid or a protic acid (Scheme 1).



X = SO_2Ph, Bt, OH, OMe, OEt, OTMS

Scheme 1.

The preparation of *N*-acyliminium ions starting from the corresponding α-alkoxycarbamates in the presence of a Lewis acid appears to be one of the more convenient ones (Scheme 1, R_1=OAlkyl, X=OEt or OMe). The preparation of α-ethoxycarbamates involves reaction of an imine with a dialkyl pyrocarbonate in ethanol through an iminium ion, which is trapped by the solvent (ethanol or methanol).[3]

Among the nucleophiles considered for the addition to these in situ generated electrophiles, several studies involving organometallic reagents like allylsilane,[4] allenylsilane and propargylsilane,[5] allyltin,[6] propargyltin,[7] allenyltin,[8] alkenylalane,[9] allenylzinc,[10] organozinc,[11] organocopper,[12] have been reported. As part of our ongoing research on the synthesis of polyhydroxylated nitrogen-containing heterocycles, we have been interested in the addition of γ-alkoxyallyltins and γ-silyloxyallyltins to *N*-acyliminium ions.[6e,f] In the latter case, we have shown that the reaction affords cleanly the *syn* adduct whatever the configuration of the carbon–carbon double bond or the steric hindrance of the α-substituent on the allyltins. Using this highly selective allylstannation followed by a ring-closing metathesis, we have developed a rapid synthesis of polyhydroxypiperidines and (±)-1-deoxy-6,8a-di-*epi*-castanospermine.[6e,f]

However, in the course of the development of this program, we encountered some difficulties to prepare efficiently *N*-ethoxycarbamates in a reproducible manner and in a short time. Therefore, we decided to consider their preparation by using microwave heating. The use of microwave-assisted reactions has increased dramatically over the past decade[13] and notably by improving yields or by allowing significant rate enhancements of chemical reactions. Considering the preparation of α-ethoxycarbamates by reaction of diethyl pyrocarbonate (DEPC) with an imine in ethanol, we assumed that the strong dipolar momentum

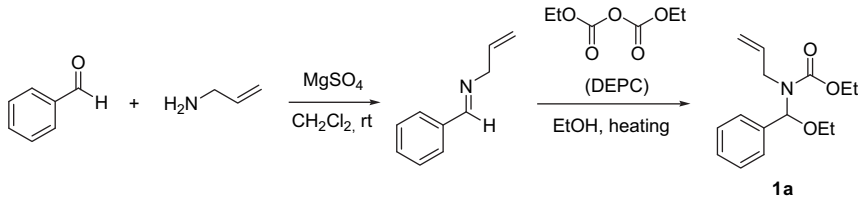
* Corresponding authors. Tel.: +33 (0)251125409; fax: +33 (0)251125402 (E.L.G.); tel.: +33 (0)235592905/148399; fax: +33 (0)235148423 (T.B.).
E-mail addresses: thierry.besson@univ-rouen.fr (T. Besson), erwan.legrognec@univ-nantes.fr (E. Le Grognec).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.09.023

of both reagents and solvent would allow the reaction to benefit from significant microwave heating.

2. Results and discussion

The generation of α-ethoxycarbamates was initially carried out using the imine prepared from reaction of benzaldehyde and allylamine in dichloromethane in the presence of $MgSO_4$ at room temperature (Scheme 2). The imine was isolated in a quantitative yield after filtration and evaporation of the solvent. We treated the imine with 1.2 equiv of diethyl pyrocarbonate (DEPC) in ethanol at 70 °C during 24 h according to Hiemstra and Speckamp.[3] In spite of numerous attempts, we encountered some difficulties to reproduce the high yields reported[3,6e] and a low conversion of 15% in **1a** was only observed by ^{1}H NMR (Table 1, entry 1). The conversion remains low by using 2 equiv of DEPC (22%, Table 1, entry 2) or moderate with 4 equiv of DEPC (59%, Table 1, entry 3).



Scheme 2.

Table 1
Experimental conditions used for the preparation of α-ethoxycarbamate **1a**

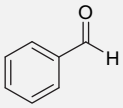
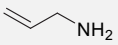
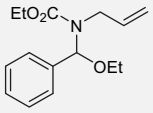
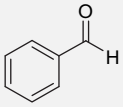
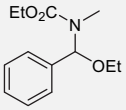
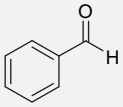
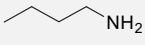
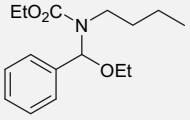
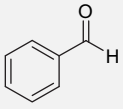
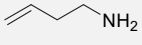
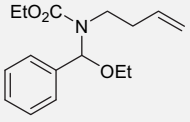
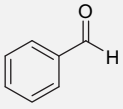
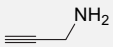
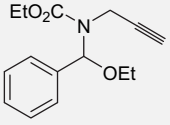
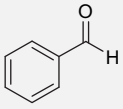
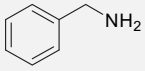
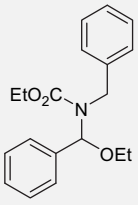
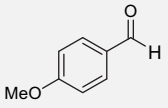
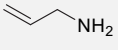
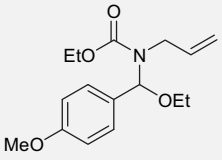
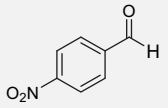
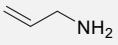
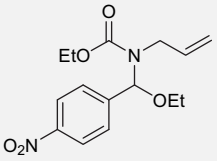
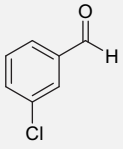
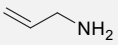
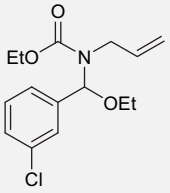
Entry	DEPC (equiv)	Conditions, temperature	Reaction time	Conversion[a] (%)
1	1.2	Δ, 70 °C	24 h	15[b]
2	2	Δ, 70 °C	24 h	22[b]
3	4	Δ, 70 °C	24 h	59[b]
4	2	MW (150 W), 110 °C	15 min	58[b]
5	4	MW (150 W), 110 °C	15 min	64[b]
6	2	MW (200 W), 120 °C	20 min	62[b]
7	2	MW (350 W), 150 °C	15 min[c]	50[b]
8	2	MW (350 W), 150 °C	15 min[c]	85[d]
9	2	MW (350 W), 130 °C	15 min[c]	77[d]
10	2	MW (350 W), 130 °C	30 min[c]	80[d]
11	2	Δ, 70 °C	24 h	25[d]

[a] Determined by ^{1}H NMR on the crude reaction mixture.
[b] Imine prepared using $MgSO_4$.
[c] 3 min ramp with a power input of 350 W.
[d] Imine prepared using molecular sieves 4 Å.

We then decided to consider the incidence of a higher temperature under pressurized conditions for the preparation of **1a**. To present a synthetic work with a facile and rapid process, which can be readily run on different scale, we decided to perform these new experiments under microwave irradiation conditions using the novel 'hybrid' microwave platform MultiSYNTH® (Milestone S.r.l, Italy).[14] Reaction conditions were optimized by varying applied power and temperature (measured by both fibre-optic contact thermometer and infrared pyrometer). By using 2 equiv of DEPC and carrying out the reaction with a fixed power input of 150 W during 15 min, a conversion of 58% was obtained (entry 4, Table 1). The use of an excess (4 equiv) of DEPC did not improve significantly the reaction conversion under these conditions (64%, entry 5, Table 1). A moderate conversion was also obtained under 200 W during 20 min (62%, entry 6, Table 1). By controlling the reaction temperature at 150 °C and allowing an available power of 350 W, a moderate conversion was also observed (50%, entry 7). At this stage, a careful examination of the ^{1}H NMR of the crude reaction mixture indicates the presence of benzaldehyde. As the imine was obtained with a complete conversion and dry ethanol was used, the presence of benzaldehyde was attributed to a partial hydrolysis of the imine due to the presence of some fine powder of $MgSO_4$. Under microwave irradiation, desorption of water from $MgSO_4$ should occur and might be responsible for the hydrolysis of the imine. Additionally, it has to be noted that DEPC rapidly decomposes in the presence of moisture. The use of molecular sieves 4 Å instead of $MgSO_4$ was then preferred for the preparation of the imine, which was easily isolated after filtration. Following this procedure, a significant enhancement of the conversion was observed (85%, entry 8, Table 1) confirming our assumption on the hydrolysis of the imine. However, due to the liberation of CO_2 during this reaction, to the nature of the solvent (2.3 ml of ethanol) and to the reaction conditions (150 °C, 350 W, 15 min with a 3 min ramp in a sealed tube of 5 ml), the pressure was estimated to be too close from the safety pressure (reported to be around 14 bar by Milestone). In order to avoid the breakage of the pressure valve, we decided to work at 130 °C instead of 150 °C and then a 77% conversion could be obtained after 15 min (entry 9, Table 1). By extending the reaction time to 30 min, the conversion was slightly improved to 80% (entry 10, Table 1) and we decided to keep conditions of entry 9 to get a reproducible and rapid preparation of **1a**. The use of a 2 equiv of DEPC, which was not justified by considering the stœchiometry of the reaction can be explained by the facile thermal decomposition of DEPC and by the scale of the experiment (5 mmol).[15] A control experiment involving a thermal activation with an imine prepared in the presence of molecular sieves was also carried out (entry 11, Table 1) and did not improved the low yield obtained previously (entry 2, Table 1).

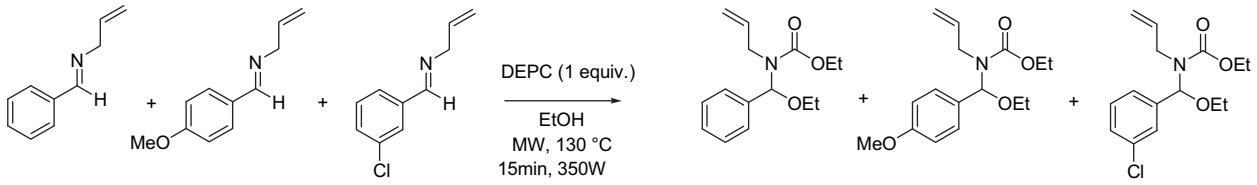
Having established the experimental conditions allowing good conversions for **1a**, we examined various imines derived from benzaldehydes in order to evaluate the scope of the method. Good to excellent conversions were obtained for the preparation of α-ethoxycarbamates derived from benzaldehyde. The use of methyl-, butyl-, butenyl- and propargylamine allowed conversions between 71 and 100% (entries 2–5, Table 2). A lower conversion was obtained with the imine derived from benzaldehyde and benzylamine (52% after 15 min, entry 6, Table 2). This result can be explained by the higher stability of this imine, which can be easily purified on silica gel. As observed previously for the preparation of **1a** (entry 10, Table 1), the extension of the reaction time to 30 min did not improved significantly the conversion (61% after 30 min, footnote c, Table 2). These last results confirm that a prolonged reaction time does not improve the conversion in α-ethoxycarbamate due to thermal decomposition of DEPC. This known phenomenon can be observed for usual thermal heating of this reactant after 1 h in refluxing benzene.[16] Recently, data were published on the possibility of microwaves to activate thermal decomposition of reactants into reactive or unreactive chemical species.[17] On behalf of the good yields obtained, we assume that the temperature and the pressure accelerate the reactivity of DEPC instead of its degradation. Our strict control of reaction parameters (temperature and reaction time) confirms the possibility of operational benefits. Its usefulness affords in our case good to high conversions compared to traditional heating conditions. In addition, the reaction time was significantly reduced from 24 h or 16 h to 15 min.

Table 2
Scope of the synthesis of α-ethoxycarbamates derived from benzaldehydes

Entry	Aldehyde	Amine	α-Ethoxycarbamates		Conversion[a] (%)	Yield[b] (%)
1				**1a**	77 (22)	70
2		Me–NH_2		**1b**	100 (84)	98
3				**1c**	71 (36)	66
4				**1d**	100 (41)	87
5				**1e**	74 (6)	68
6				**1f**	52[c] (19)	47
7				**2a**	95 (30)	89
8				**3a**	47 (15)	35
9				**4a**	89 (17)	77

[a] Conversion determined by ^{1}H NMR on the crude reaction mixture. Conversion obtained by microwave irradiation (2 equiv of DEPC, 15 min at 130 °C, with 3 min ramp and a power input of 350 W). Conversions in brackets were obtained by thermal heating at 70 °C using 2 equiv of DEPC during 16 h.
[b] Yield obtained after flash chromatography following the microwave heating procedure.
[c] The conversion was only improved to 61% by extending the reaction time to 30 min.

The electron-donating or withdrawing property of the imine was also examined and was shown to have a dramatic influence on the reaction course. As expected, the use of *p*-methoxybenzaldehyde affords a higher conversion (95%, entry 7, Table 2) and reaction with the imine derived from *p*-nitrobenzaldehyde exhibits a moderate 47% conversion (entry 8, Table 2). These results were in good agreement with the trend also observed under thermal heating and can be explained by a simple consideration of the electronic effect. However, a high conversion was obtained for the α-ethoxycarbamate **4a** derived from *m*-chlorobenzaldehyde (89%, entry 9, Table 2) in spite of the inductive effect of the halogen atom, while conversion under thermal heating was lower than for **1a** (in agreement with the electronic effect of the *m*-Cl substituent). This apparent difference observed for these two heating modes was subsequently re-examined by considering two competitive experiments under microwave irradiation mode (Scheme 3), which



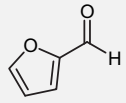
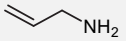
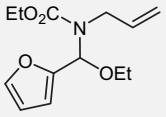
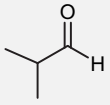
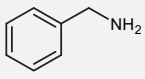
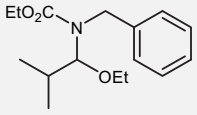
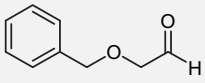
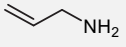
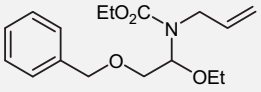
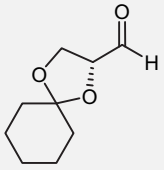
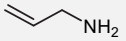
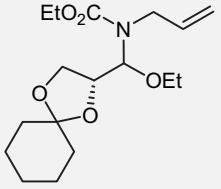
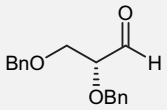
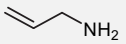
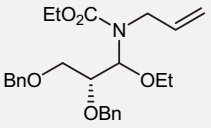
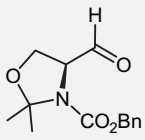
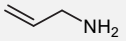
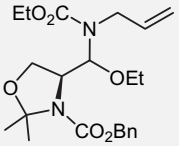
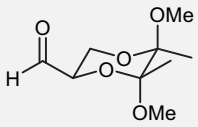
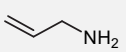
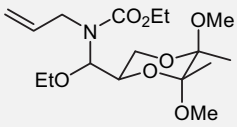
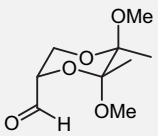
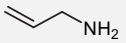
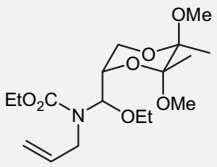
1a **2a** **4a**

Entry	Substrate stoechiometry			Product ratio[a]		
1	0.5	0	0.5	60	-	40
2	0	0.5	0.5	-	67	33

[a] Product ratio measured on the crude reaction mixture by ^{1}H NMR

Scheme 3.

Table 3
Scope of the preparation of α-ethoxycarbamates not derived from benzaldehyde

Entry	Aldehyde	Amine	Product		Yield[a] (%)	Ratio[b] (%)
1				**5a**	91 (85)	100/0
2				**6f**	84 (68)	100/0
3				**7a**	66 (71)	100/0
4				**8a**/**8a**′	71 (70)	70/30
5				**9a**/**9a**′	82 (89)	55/45
6				**10a**/**10a**′	60 (78)	46/54
7				**11a**/**11a**′	58 (57)	75/25
8				**12a**/**12a**′	60 (57)	91/9[c]

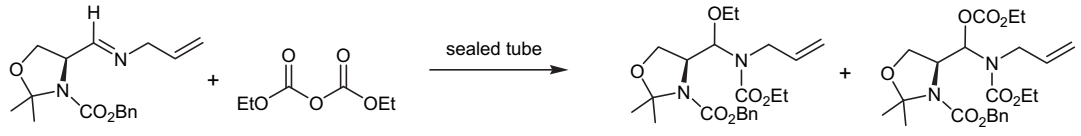
[a] Yields obtained after chromatography on silica gel (conversions were complete); reaction conditions: 2 equiv of DEPC, 3 min at 70 °C and a power input of 150 W; yields in brackets correspond to isolated yields obtained after flash chromatography following the reaction conditions: thermal heating, 70 °C, 2 equiv of DEPC, 16 h.
[b] α-Ethoxycarbamate/α-ethoxycarbonate ratio evaluated by ^{1}H NMR.
[c] The α-ethoxycarbonate has not been isolated in this case.

points out a sequence in agreement with the electronic effect and an unexplained higher yield obtained for **4a** under microwave irradiation.

The results displayed in Table 2 demonstrate that the microwave irradiation mode affords a significant enhancement of the conversion and a dramatic reduction of the reaction time compared to the thermal heating one. It has to be noted that all the α-ethoxycarbamates reported in Table 2 have been isolated by flash chromatography on silica gel in good yields and were fully characterized (see Experimental section).

We then extended our work on other imines not derived from benzaldehydes. By considering furfuraldehyde and allylamine, no trace of the desired α-ethoxycarbamate **5a** was observed using our previous optimized conditions. The ^{1}H NMR spectrum only reveals decomposition indicating that our conditions were too harsh. By reducing the reaction time to 3 min, some decomposition was also observed but with a conversion in **5a** about 85% (determined by ^{1}H NMR). Then, by decreasing the reaction temperature to 70 °C and with a power input at 150 W, we found that a high conversion (91%) could be obtained. By extending these conditions to other imines, a complete conversion in α-ethoxycarbamates was systematically observed. Aliphatic derivative **6f** or benzyloxy derivative **7a** was isolated in 84% and 66% yields, respectively, after flash chromatography (entries 2 and 3, Table 3). We also examined the preparation of chiral α-ethoxycarbamates. The cyclohexylidene- and the dibenzyloxy-glyceraldehyde derivatives were obtained in good yields (entries 4 and 5, Table 3), while the Garner type aldehyde furnished a moderate 60% yield (entry 6, Table 3). Similarly, two functionalized aldehydes developed by Ley[18] were considered and furnished two chiral α-ethoxycarbamates. Despite the complete conversions observed on the crude reaction mixture by ^{1}H NMR, the yields obtained for these compounds were about 60%. The highly functionalized structures of these compounds, which can decompose on silica gel, could explain these results. For these functionalized imines reported in Table 3, the reduction of the reaction time constitutes the major benefit of these new conditions performed under microwave irradiation mode since yields obtained by the two heating modes are similar (yields increased for **5a** and **6f**, similar yields for **8a**, **11a** and **12a**, decreased in the case of **7a**, **9a** and **10a**).

Curiously, the formation of α-carbonates derivatives was also observed in these last five examples. The formation of the latter can be explained by the reaction of an ethyl carbonate on the intermediate iminium. The presence of an electronegative atom (oxy gen) in the β-position to the iminium could reinforce the electrophilicity of the corresponding iminium and facilitate the reaction with the ethyl carbonate anion, which can occur before its decarboxylation, instead of the ethoxy one. A control experiment carried out with the imine derived from Garner aldehyde in a sealed tube and under classical thermal heating also affords a significant amount (28%) of the carbonate (Scheme 4).



Scheme 4.

This last experiment indicates that the carbonate formation is not the result of a specific microwave effect and is simply due to the pressure of the reaction. However, this unexpected by-product does not detract the synthetic appeal of the present preparation of α-ethoxycarbamates since both α-ethoxycarbonates and the α-ethoxycarbamates should lead to the similar iminium intermediates in the presence of a Lewis acid affording the same adduct in the presence of nucleophiles.

3. Conclusion

The present work describes an efficient preparation of a library of α-ethoxycarbamate derivatives or useful equivalents able to furnish *N*-acyliminium intermediates in the presence of Lewis acids. The microwave irradiation mode allows their rapid syntheses often in higher yields and always in a shorter reaction time compared to the classical thermal heating. In the case of the synthesis of chiral α-ethoxycarbamates, the formation of α-ethoxycarbonates was also observed. These reactive precursors are useful for the synthesis of nitrogen-containing compounds and work is currently in progress in our group in order to exploit their potential in highly diastereoselective reactions involving γ-substituted allyltins.

4. Experimental

4.1. General

Aldehydes and amines were purchased from commercial suppliers and used without further purification. Garner aldehyde,[19] (2*S*, 5*R*, 6*R*)-5,6-dimethoxy-5,6-dimethyl-[1,4] dioxane-2-carbaldehyde[18a] and (2*R*, 5*R*, 6*R*)-5,6-dimethoxy-5,6-dimethyl-[1,4] dioxane-2-carbaldehyde,[18b] (2*R*)-2,3-*O*-cyclohexylidene-glyceraldehyde,[20] (2*R*)-2,3-dibenzyl-glyceraldehyde[21] were prepared according to previous described procedure. Diethyl pyrocarbonate was purchased from Acros. NMR spectra were recorded on a Bruker Avance 300 spectrometer operating at 300.13 MHz for ^{1}H, 75.47 MHz for ^{13}C and on a Bruker ARX 400 spectrometer operating at 400.13 MHz for ^{1}H, 100.62 MHz for ^{13}C. Chemical shifts are given in parts per million as δ values related to tetramethylsilane (^{1}H, ^{13}C). Mass spectra were obtained in EI mode (70 eV) using a quadrupolar analyser (HP apparatus, Engine 5989A) in direct introduction mode. HRMS analyses were performed in Rennes (Centre Régional de Mesures Physiques de l'Ouest, Univ. Rennes 1) and in Lyon (Centre Commun de Spectrométrie de Masses, Univ Lyon 1). IR spectra were recorded with a Bruker IFS Vector 22 apparatus. Ethanol was distilled from CaH_2. TLC analyses were carried on silica-coated plates (Merck Kieselgel 60F_{254}). All reactions were carried out under an argon atmosphere.

The 'hybrid' microwave platform MultiSYNTH® (Milestone S.r.l.) is a novel dedicated microwave system for synthetic applications. It allows a fast reaction optimization providing high energy density in a single-mode like configuration and an efficient scale-up (maximum working volume 300 ml) through parallel synthesis in a multi-

equipped with an indirect pressure control through pre-calibrated springs at the bottom of the vessels shields and with both, contactless infrared pyrometer (IRT) and fibre-optic contact thermometer (FO) for accurate temperature measurement. It is noteworthy that the IRT can be calibrated directly on the temperature read by the FO to ensure the highest accuracy and reproducibility.

4.1.1. Procedure for the preparation of α-ethoxycarbamates by thermal heating. To a solution of imine freshly prepared (4.71 mmol) in ethanol (25 ml) in a round-bottom flask, was added diethyl pyrocarbonate (1.53 g, 9.42 mmol). The reaction mixture was stirred and heated to 70 °C for 16 h. The reaction mixture was concentrated under reduced pressure and the crude product was analysed by NMR to measure the conversion rate. Purification by flash chromatography on silica gel using Et_2O/hexanes 1/9 or AcOEt/hexanes 1/9 as eluent gave the desired α-ethoxycarbamates as a colourless oil.

4.1.2. Typical procedure for the preparation of α-ethoxycarbamates derived from benzaldehyde under microwave heating. A solution of a freshly prepared imine (1.85 mmol) and diethyl pyrocarbonate (0.60 g, 3.7 mmol) in dry ethanol (2.3 ml) was prepared in a sealed 5 ml vial. The mixture was irradiated during 15 min at a temperature maintained at 130 °C and the maximal power output at 350 W. The reaction vessel was rapidly cooled to ambient temperature and the reaction mixture was concentrated under reduced pressure. Purification by flash chromatography on silica gel using EtOAc/hexanes 1/9 as eluent gave the desired product as a colourless oil.

4.1.3. Typical procedure for the preparation of α-ethoxycarbamates not derived from benzaldehydes under microwave heating. A solution of a freshly prepared imine (1.85 mmol) and diethyl pyrocarbonate (0.60 g, 3.7 mmol) in dry ethanol (2.3 ml) was prepared in a sealed 5 ml vial. The mixture was irradiated during 3 min at a temperature maintained at 70 °C and the maximal power output at 150 W. The reaction vessel was rapidly cooled to ambient temperature and the reaction mixture was concentrated under reduced pressure. Purification by flash chromatography on silica gel using EtOAc/hexanes 1/9 as eluent gave the desired product as a colourless oil.

4.2. Characterization of the α-ethoxycarbamates

*4.2.1. Ethyl N-allyl-N-(ethoxyphenylmethyl)carbamate (**1a**).* Yield 341 mg (70%); IR (neat) cm^{-1} 2978, 2932, 1699, 1318, 1258, 1090, 915, 698; R_f (hexanes/Et_2O 9/1)=0.45; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.52, 7.00 (m, 5H), 6.66 (br s, 1H), 5.68 (m, 1H), 4.87 (br d, 1H, *J*=17.2 Hz), 4.80 (br d, 1H, *J*=10.0 Hz), 4.11 (q, 2H, *J*=7.0 Hz), 3.71–3.31 (m, 4H), 1.09 (t, 3H, *J*=7.0 Hz), 1.03 (t, 3H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 157.2, 139.8, 135.7, 130.3–126.8 (5C), 115.9, 85.7, 63.4, 61.3, 44.6, 14.5, 14.7; (FAB^+, 3-nitrobenzylalcohol matrix)-HRMS: *m*/*z* calcd for $C_{15}H_{22}NO_3$ $[M+H]^+$ 264.1600 found 264.1627.

*4.2.2. Ethyl N-(ethoxyphenylmethyl)-N-methylcarbamate (**1b**).* Yield 430 mg (98%); IR (neat) cm^{-1} 3032, 2978, 1703, 1450, 1397, 1318, 1153, 1090, 714; R_f (hexanes/Et_2O 9/1)=0.45; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.64–7.14 (m, 5H), 6.69 (br s, 1H), 4.21 (q, 2H, *J*=7.2 Hz), 3.61–3.32 (m, 2H), 2.61 (br s, 3H), 1.60 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 157.1, 139.6, 129.0–126.7 (5C), 85.4, 63.3, 61.5, 27.3, 15.0, 14.8; (FAB^+, 3-nitrobenzylalcohol matrix)-HRMS: *m*/*z* calcd for $C_{13}H_{20}NO_3$ $[M+H]^+$ 238.1443 found 238.1460.

*4.2.3. Ethyl N-butyl-N-(ethoxyphenylmethyl)carbamate (**1c**).* Yield 341 mg (66%); IR (neat) cm^{-1} 2960, 2873, 1699, 1414, 1291, 1089, 708; R_f (hexanes/Et_2O 9/1)=0.45; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.60–7.08 (m, 5H), 6.74 (m, 1H), 4.21 (q, 2H, *J*=7.2 Hz), 3.71 (m, 1H), 3.55 (m, 1H), 3.24–3.20 (m, 2H), 1.57–1.36 (m, 2H), 1.14 (m, 8H), 0.82 (t, 3H, *J*=7.3 Hz); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 157.1, 142.2, 128.4–126.9 (5C), 85.6, 63.5, 61.4, 41.9, 32.5, 20.6, 15.1, 14.8, 13.9; CI/NH_3-HRMS: *m*/*z* calcd for $C_{16}H_{29}N_2O_3$ $[M+NH_4]^+$ 297.2178 found 297.2169.

*4.2.4. Ethyl N-(but-3-enyl)-N-(ethoxyphenylmethyl)carbamate (**1d**).* Yield 446 mg (87%); IR (neat) cm^{-1} 2977, 1700, 1413, 1088, 912, 710; R_f (hexanes/Et_2O 9/1)=0.45; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.55–7.02 (m, 5H), 6.60 (br s, 1H), 5.50 (m, 1H), 4.87 (m, 2H), 4.16 (q, 2H, *J*=7.0 Hz), 3.64 (m, 1H), 3.46 (m, 1H), 3.28 (m, 1H), 3.10 (m, 1H), 2.31 (m, 1H), 2.10 (m, 1H), 1.13 (t, 3H, *J*=7.0 Hz), 1.08 (t, 3H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 157.1, 140.0, 136.3, 129.6–126.9 (5C), 115.9, 85.9, 63.6, 61.4, 42.0, 34.4, 15.0, 14.7; (FAB^+, 3-nitrobenzylalcohol matrix)-HRMS: *m*/*z* calcd for $C_{16}H_{24}NO_3$ $[M+H]^+$ 278.1756 found 278.1743.

*4.2.5. Ethyl N-(ethoxyphenylmethyl)-N-propargylcarbamate (**1e**).* Yield 329 mg (68%); IR (neat) cm^{-1} 2979, 1705, 1443, 1402, 1260, 1091, 697; R_f (hexanes/Et_2O 9/1)=0.45; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.52–7.50 (m, 2H), 7.16–7.08 (m, 3H), 6.67 (br s, 1H), 4.16 (q, 2H, *J*=7.0 Hz), 3.81 (m, 1H), 3.80 (m, 1H), 3.60 (d, 1H, *J*=16.0 Hz), 3.51 (m, 1H), 1.77 (br s, 1H), 1.18 (t, 3H, *J*=7.0 Hz), 1.09 (t, 3H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 156.5, 139.2, 128.5–126.9 (5C), 85.7, 81.2, 69.8, 63.8, 61.9, 31.3, 14.9, 14.6; (FAB^+, 3-nitrobenzylalcohol matrix)-HRMS: *m*/*z* calcd for $C_{15}H_{20}NO_3$ $[M+H]^+$ 262.1443 found 262.1420.

*4.2.6. Ethyl N-benzyl-N-(ethoxyphenylmethyl)carbamate (**1f**).* Yield 272 mg (47%); IR (neat) cm^{-1} 3064, 3032, 2978, 2932, 1699, 1451, 1412, 1212, 1089, 1030, 699; R_f (hexanes/Et_2O 9/1)=0.45; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.54–7.01 (m, 10H), 6.77 (br s, 1H), 4.68–4.05 (m, 4H), 3.45 (m, 2H), 1.01 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 157.2, 139.9, 139.7, 128.7–126.7 (10C), 86.3, 63.6, 61.7, 46.0, 14.6, 14.4; (FAB^+, 3-nitrobenzylalcohol matrix)-HRMS: *m*/*z* calcd for $C_{19}H_{24}NO_3$ $[M+H]^+$ 314.1756 found 314.1758.

*4.2.7. Ethyl N-allyl-N-[ethoxy-(4-methoxyphenyl)methyl]carbamate (**2a**).* Yield 483 mg (89%); IR (neat) cm^{-1} 2977, 2933, 2837, 1699, 1451, 1386, 1213, 1036, 916; R_f (hexanes/Et_2O 9/1)=0.48; ^1H NMR (500 MHz, C_6D_6, 340 K) δ 7.44 (d, 2H, *J*=9.0 Hz), 6.78 (d, 1H, *J*=9.0 Hz), 6.70 (m, 1H), 5.85 (m, 1H), 4.95 (d, 1H, *J*=17.0 Hz), 4.87 (d, 1H, *J*=10.5 Hz), 4.16 (q, 2H, *J*=7.0 Hz), 3.86–3.74 (m, 1H), 3.69–3.57 (m, 2H), 3.47 (m, 1H), 3.35 (s, 3H), 1.13 (t, 3H, *J*=7.0 Hz), 1.07 (t, 3H, *J*=7.0 Hz); ^{13}C NMR (125 MHz, C_6D_6, 340 K) δ 162.2, 160.2, 136.0, 132.0, 128.2 (2C), 116.1, 114.0 (2C), 85.7, 65.7, 61.4, 54.9, 44.6, 15.0, 14.7; CI/NH_3-MS: *m*/*z* 264 [(M+NH_3)−EtOH].

*4.2.8. Ethyl N-allyl-N-[ethoxy-(4-nitrophenyl)methyl]carbamate (**3a**).* Yield 199 mg (35%); IR (neat) cm^{-1} 2978, 2933, 2835, 1700, 1523, 1350, 1259, 1084; R_f (hexanes/Et_2O 9/1)=0.43; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.84 (d, 2H, *J*=8.8 Hz), 7.27 (d, 1H, *J*=8.8 Hz), 6.51 (m, 1H), 5.60 (m, 1H), 4.82 (br d, 1H, *J*=15.3 Hz), 4.78 (br d, 1H, *J*=10.1 Hz), 4.11 (q, 2H, *J*=7.1 Hz), 3.63–3.49 (m, 2H), 3.42–3.31 (m, 2H), 1.06 (t, 3H, *J*=7.0 Hz), 1.05 (t, 3H, *J*=7.1 Hz); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 156.9, 148.4, 146.2, 135.2, 127.7 (2C), 123.4 (2C), 116.6, 84.9, 63.8, 61.8, 44.7, 14.8, 14.6; CI/NH_3-MS: *m*/*z* 263 [(M+H)−EtOH].

*4.2.9. Ethyl N-allyl-N-[ethoxy-(3-chlorophenyl)methyl]carbamate (**4a**).* Yield 424 mg (77%); IR (neat) cm^{-1} 2978, 2932, 1699, 1576, 1385, 1258, 1097, 1076, 924, 741; R_f (hexanes/Et_2O 9/1)=0.45; ^1H NMR (500 MHz, C_6D_6, 340 K) δ 7.63 (br s, 1H), 7.22 (d, 1H, *J*=7.5 Hz), 7.07 (d, 1H, *J*=8.0 Hz), 6.89 (m, 1H), 6.55 (m, 1H), 4.86 (br d, 1H, *J*=17.6 Hz), 4.82 (br d, 1H, *J*=10.5 Hz), 4.11 (q, 2H, *J*=7.0 Hz), 3.80–3.30 (m, 4H), 1.08–1.02 (m, 6H); ^{13}C NMR (125 MHz, C_6D_6, 340 K)

δ 156.8, 142.1, 135.5, 134.8, 129.7, 128.3, 127.3, 125.1, 116.3, 85.0, 65.7, 61.6, 44.7, 14.8, 14.6; CI/NH_3-MS: *m/z* 252 [$(M+H)^+-EtOH$].

*4.2.10. Ethyl N-allyl-N-(ethoxy-furan-2-ylmethyl)carbamate (**5a**).* Yield 426 mg (91%); IR (neat) cm^{-1} 2980, 2934, 1823, 1763, 1704, 1409, 1260, 1156, 1092, 1003, 883, 739; R_f (hexanes/AcOEt 9/1)=0.48; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.15 (s, 1H), 6.76 (m, 1H), 6.46 (s, 1H), 6.16 (s, 1H), 5.86 (m, 1H), 5.07 (br d, 1H, *J*=17.2 Hz), 4.99 (br d, 1H, *J*=10.0 Hz), 4.19 (q, 2H, *J*=7.0 Hz), 4.01–3.82 (m, 2H), 3.67 (m, 1H), 3.55 (m, 1H), 1.18 (t, 3H, *J*=7.0 Hz), 1.13 (t, 3H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 152.5, 149.1, 142.1, 135.6, 115.8, 110.4, 108.5, 81.9, 63.7, 61.6, 44.9, 14.9, 14.6; CI/NH_3-MS: *m/z* 252 [$(M+H)^+-EtOH$].

*4.2.11. Ethyl N-benzyl-N-(1-ethoxy-2-methylpropyl)carbamate (**6f**).* Yield 434 mg (84%); IR (neat) cm^{-1} 2975, 2930, 1702, 1415, 1331, 1153, 1083, 949, 699; R_f (hexanes/AcOEt 9/1)=0.43; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.58–7.11 (m, 5H), 5.17 (m, 1H), 4.41 (m, 2H), 4.11 (m, 2H), 3.31–3.08 (m, 2H), 1.87 (m, 1H), 1.02–0.95 (m, 9H), 0.77 (m, 3H); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 157.4, 140.5, 129.0–127.1 (5C), 92.3, 63.8, 61.3, 45.2, 32.0, 19.4, 18.3, 14.8, 14.7; (FAB^+, 3-nitrobenzylalcohol matrix)-HRMS: *m/z* calcd for $C_{16}H_{26}NO_3$ $[M+H]^+$ 280.1913 found 280.1916.

*4.2.12. Ethyl N-allyl-N-(2-benzyloxy-1-ethoxyethyl)carbamate (**7a**).* Yield 375 mg (66%); IR (neat) cm^{-1} 2978, 2932, 1703, 1318, 1268, 1111, 698; R_f (hexanes/AcOEt 9/1)=0.54; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.35–7.17 (m, 5H), 6.02 (m, 1H), 5.84 (m, 1H), 5.20 (br d, 1H, *J*=17.2 Hz), 5.06 (br d, 1H, *J*=9.6 Hz), 4.50 (m, 2H), 4.18 (m, 2H), 3.94 (m, 2H), 3.63 (m, 3H), 3.49 (m, 1H), 1.16 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 156.6, 139.2, 136.7, 128.5–127.7 (5C), 115.5, 85.0, 73.5, 70.9, 63.8, 61.3, 44.2, 15.0, 14.6; (FAB^+, 3-nitrobenzylalcohol matrix)-HRMS: *m/z* calcd for $C_{17}H_{26}NO_4$ $[M+H]^+$ 308.1862 found 308.1862.

*4.2.13. Ethyl N-[(R)-1,4-dioxaspiro[4.5]dec-2-yl-ethoxymethyl]-N-(prop-2-en-1-yl)carbamate (**8a**).* Yield 294 mg (44%); IR (neat) cm^{-1} 2935, 1705, 1100, 926; ESI-HRMS: *m/z* calcd for $C_{17}H_{29}NO_5Na$ $[M+Na]^+$ 350.1943 found 350.1942. Diastereomeric ratio (43/57).

First eluted diastereomer: R_f (hexanes/AcOEt 9/1)=0.64; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 6.03 (ddt, 1H, *J*=16.0, 10.8, 6.0 Hz), 5.40 (m, 1H), 5.16 (d, 1H, *J*=16 Hz), 5.01 (d, 1H, *J*=10.8 Hz), 4.15–4.05 (m, 2H), 4.05–4.00 (m, 1H), 3.97 (m, 1H), 3.92–3.83 (m, 3H), 3.42 (dq, 1H, *J*=9.6, 7.2 Hz), 3.27 (bdq, 1H, *J*=9.6, 7.2 Hz), 1.80–1.20 (m, 10H), 1.05 (t, 3H, *J*=7.2 Hz), 0.97 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 157.4, 137.2, 116.2, 111.1, 87.6, 75.1, 67.9, 63.9, 61.9, 44.6, 37.5, 36.1, 26.2, 25.0, 24.8, 15.2, 15.4; $[\alpha]_D^{19}$ +12.4 (*c* 0.7, $CHCl_3$). *Second eluted diastereomer*: R_f (hexanes/AcOEt 9/1)=0.51; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 5.85 (m, 1H), 5.50 (m, 1H), 5.04 (d, 1H, *J*=17.2 Hz), 4.90 (d, 1H, *J*=10.4 Hz), 4.22 (br q, 1H, *J*=6.8 Hz), 4.05 (dq, 1H, *J*=13, 7.2 Hz), 4.03 (dq, 1H, *J*=13, 7.2 Hz), 3.80–3.90 (m, 4H), 3.36–3.53 (m, 2H), 1.85–1.15 (10H), 1.07 (t, 3H, *J*=7.2 Hz), 1.00 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 157.1, 136.8, 117.0, 111.5, 87.6, 78.0, 66.7, 64.7, 62.1, 45.1, 37.4, 36.5, 26.2, 25.0, 24.8, 15.5, 15.1. $[\alpha]_D^{19}$ +7.5 (*c* 1.0, $CHCl_3$).

*4.2.14. ((R)-1,4-Dioxaspiro[4.5]dec-2-yl)-[(prop-2-en-1-yl-ethoxycarbonyl)amino]methyl ethyl carbonate (**8a′**).* Yield 202 mg (27%); Attempts to separate by chromatography the two diastereomers obtained as a mixture (50/50) were unsuccessful. R_f (hexanes/AcOEt 9/1)=0.42; IR (neat) cm^{-1} 2935, 1757, 1714, 1202, 1144, 925; ESI-HRMS: *m/z* calcd for $C_{18}H_{29}NO_7Na$ $[M+Na]^+$ 394.1842 found 394.18445.

First diastereomer: ^1H NMR (400 MHz, C_6D_6, 340 K) δ 6.80 (d, 1H, *J*=7.6 Hz), 6.10 (ddt, 1H, *J*=17.2, 10.4, 5.6 Hz), 5.29 (dq, 1H, *J*=17.2, 1.6 Hz), 5.12 (dq, 1H, *J*=10.4, 1.6 Hz), 4.57 (dt, 1H, *J*=7.6, 5.9 Hz), 3.90–4.30 (m, 8H), 1.25–1.95 (m, 10H), 1.14 (m, 3H), 1.04 (t, 3H, *J*=7.2 Hz); *Second diastereomer*: ^1H NMR (400 MHz, C_6D_6, 340 K) δ 6.73 (d, 1H, *J*=8.0 Hz), 5.92 (ddt, 1H, *J*=17.2, 10.4, 6.0 Hz), 5.16 (dq, 1H, *J*=17.2, 1.2 Hz), 5.04 (dq, 1H, *J*=10.4, 1.2 Hz), 4.41 (dt, 1H, *J*=8.0, 6.0 Hz), 3.90–4.30 (m, 8H), 1.25–1.95 (m, 10H), 1.14 (m, 3H), 1.05 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 156.2, 156.0, 155.3, 154.8, 136.3, 135.9, 117.4, 116.7, 112.1, 111.6, 85.9, 85.7, 76.7, 74.7, 67.2–62.6 (6C), 47.1, 46.9, 37.3–36.2 (4C), 26.2–24.8 (6C), 15.10–14.6 (4C).

*4.2.15. Ethyl N-allyl((2R)-2,3-bis(benzyloxy)-1-ethoxypropyl)carbamate (**9a**).* Yield 397 mg, (51%); Attempts to separate by chromatography the two diastereomers obtained as a mixture (ratio 40/60) were unsuccessful. R_f (hexanes/AcOEt 9/1)=0.29; IR (neat) cm^{-1} 3064, 3030, 2977, 1699, 1097, 921, 736, 698; ESI-HRMS: *m/z* calcd for $C_{25}H_{33}NO_5Na$ $[M+Na]^+$ 450.2256 found 450.2259; ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.08–7.35 (m, 10H), 6.03 (m, 1H), 5.12 (d, 1H, *J*=6.2 Hz), 4.97 (d, 1H, *J*=10.4 Hz), 4.36–4.86 (m, 5H), 4.08 (m, 2H), 3.67–3.87 (m, 5H), 3.41 (m, 2H), 0.95–1.07 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 156.9, 139.6, 139.3, 136.7, 136.3, 128.6–127.5 (10C), 116.3, 115.8, 87.3, 85.6, 80.4, 78.9, 74.1–71.2 (3C), 64.5, 63.7, 61.8, 61.3, 45.4, 44.9, 15.0, 14.7.

*4.2.16. Ethyl N-allyl((2R)-2,3-bis(benzyloxy)-1-(ethoxycarbonyloxy)propyl)carbamate (**9a′**).* Yield 330 mg (38%); Attempts to separate by chromatography the two diastereomers obtained as a mixture (ratio 44/56) were unsuccessful. R_f (hexanes/AcOEt 9/1)=0.19; ^1H NMR (300 MHz, $CDCl_3$, 300 K) δ 7.40–7.26 (m, 10H), 6.49 (d, 1H, *J*=7.5 Hz), and 6.41 (d, 1H, *J*=8.1 Hz) for the second isomer, 5.80 (m, 1H), 5.20–5.00 (m, 2H), 4.45–4.75 (m, 4H), 4.20–4.10 (m, 2H), 4.20–3.55 (m, 7H), 1.35–1.15 (m, 6H); No ^{13}C NMR experiment could be recorded due to the unstability of the products.

*4.2.17. Benzyl 4-{[allyl(ethoxycarbonyl)amino](ethoxy)methyl}-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (**10a**).* Yield 264 mg (34%); Attempts to separate by chromatography the two diastereomers obtained as a mixture (ratio 86/14) were unsuccessful. R_f (hexanes/AcOEt 9/1)=0.72; IR (neat) cm^{-1} 3068, 3032, 2978, 1879, 1704, 1404, 1257, 1088, 699. ESI-HRMS: *m/z* calcd for $C_{22}H_{32}N_2O_6Na$ $[M+Na]^+$ 443.2158 found 443.2159.

Major diastereomer: ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.06–7.26 (m, 5H), 5.93 (m, 1H), 5.49 (m, 1H), 4.90–5.24 (m, 4H), 3.95–4.15 (m, 5H), 3.60–3.75 (m, 2H), 3.35–3.50 (m, 1H), 3.15–3.30 (m, 1H), 1.80 (s, 3H), 1.46 (s, 3H), 1.05 (t, 1H, *J*=7.2 Hz), 0.96 (t, 3H, *J*=7.2 Hz); Minor isomer (meaningful signals): ^1H NMR (C_6D_6, 400 MHz, 340 K) δ 5.85 (m, 1H), 5.55 (m, 1H), 4.20 (m, 1H), 3.80–3.90 (m, 1H), 3.55–3.60 (m, 1H); Major isomer ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ156.4, 153.3, 137.4, 136.7, 127.8–128.7 (5C), 116.0, 95.2, 86.0, 67.3, 65.7, 61.2, 61.2, 58.8, 45.9, 27.3, 24.4, 14.7, 14.6; Minor isomer (meaningful signal) ^{13}C NMR (C_6D_6, 400 MHz, 340 K) δ 94.9, 86.6, 67.1, 65.2, 64.5, 61.5, 59.2, 44.2, 27.5, 24.0.

*4.2.18. (4S)-Benzyl 4-(5-allyl-4,8-dioxo-3,7,9-trioxa-5-azaundecan-6-yl)-2,2-dimethyloxazolidine-3-carboxylate (**10a′**).* Yield 223 mg, (26%); Attempts to separate by chromatography the two diastereomers obtained as a mixture (ratio 63/37) were unsuccessful. R_f (hexanes/AcOEt 9/1)=0.47; IR (neat) cm^{-1} 3067, 2982, 2938, 1759, 1709, 1404, 1244, 1091, 699; ESI-HRMS: *m/z* calcd for $C_{23}H_{32}N_2O_7Na$ $[M+Na]^+$ 487.2056 found 487.20587.

Major diastereomer: ^1H NMR (400 MHz, C_6D_6, 340 K) δ 7.40–7.10 (m, 5H), 6.65 (d, 1H, *J*=7.2 Hz), 5.95 (m, 1H), 5.23–4.92 (m, 4H), 4.36 (m, 1H), 4.15–3.75 (m, 7H), 3.71 (m, 1H), 1.78 (s, 3H), 1.44 (s, 3H), 1.04 (m, 3H), 0.97 (m, 3H); Minor diastereomer (meaningful signals) ^1H NMR (C_6D_6, 400 MHz, 340 K) δ 6.83 (d, 1H, *J*=8.4 Hz), 5.80 (m, 1H), 4.48 (m, 1H), 3.62 (m, 1H), 1.50 (s, 3H); Major diastereomer: ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 155.5–153.1 (3C), 137.1, 135.7,

116.3, 95.50, 84.20, 67.40, 65.2–61.8 (3C), 58.4, 47.8, 27.5, 23.5, 14.6, 14.1; Minor diastereomer (meaningful signals) ^{13}C NMR (C_6D_6, 400 MHz, 340 K) δ 154.5–153.1 (3C), 137.3, 135.4, 116.6, 95.3, 84.4, 67.6, 58.6, 46.1.

*4.2.19. Ethyl N-[(2R,5R,6R)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl(ethoxy)methyl]-N-(prop-2-en-1-yl)carbamate (**11a**).* Yield 325 mg, (49%); Attempts to separate by chromatography the two diastereomers obtained as a mixture (ratio 20/80) were unsuccessful. R_f (hexanes/AcOEt 9/1)=0.49; IR (neat) cm^{-1} 2978, 1705, 1142, 1039, 879; ESI-HRMS: *m/z* calcd for $C_{17}H_{31}NO_7Na$ $[M+Na]^+$ 384.1998 found 384.1998.

Major diastereomer: ^{1}H NMR (400 MHz, C_6D_6, 340 K) δ 6.04 (m, 1H), 5.35 (m, 1H), 5.18–4.90 (m, 2H), 4.16–3.98 (m, 4H), 3.83–3.68 (m, 3H), 3.49–3.40 (m, 1H), 3.28–3.18 (m, 1H), 3.11 and 3.08 (s, 6H), 1.27–1.24 (s, 6H), 1.07–0.99 (t, 3H, *J*=6.8 Hz), 0.97 (t, 3H, *J*=6.8 Hz); Minor diastereomer (meaningful signals): ^{1}H NMR (C_6D_6, 400 MHz, 340 K) δ 5.90 (m, 1H), 5.42 (m, 1H), 3.20 (s, 3H); Major diastereomer: ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 156.8, 136.6, 116.0, 98.6, 98.5, 86.5, 67.3, 63.7, 61.5, 61.4, 48.1, 47.6, 45.3, 17.9 (2C), 14.9 (2C); Minor diastereomer (meaningful signals): ^{13}C NMR (C_6D_6, 400 MHz, 340 K) δ 136.0, 116.7, 99.7, 98.4, 86.3, 69.2, 64.5, 60.6, 60.1, 45.1, 17.8 (2C), 14.6 (2C).

*4.2.20. N-[(2R,5R,6R)-5,6-Dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl][(ethoxycarbonyl)-N-(prop-2-en-1-yl)amino]methyl ethyl carbonate (**11a′**).* Yield 69 mg (9%); Attempts to separate by chromatography the two diastereomers obtained as a mixture (ratio 42/58) were unsuccessful. R_f (hexanes/AcOEt 9/1)=0.33; IR (neat) cm^{-1} 3080, 2987, 2949, 2833, 1758, 1714, 1374, 1264, 1143, 1120, 1038, 789; ESI-HRMS: *m/z* calcd for $C_{18}H_{31}NO_9Na$ $[M+Na]^+$ 428.1897 found 428.1897.

Major diastereomer: ^{1}H NMR (400 MHz, C_6D_6, 340 K) δ 6.55 (d, 1H, *J*=6.5 Hz), 6.07 (ddt, 1H, *J*=16.2, 10.3, 6.2 Hz), 5.10 (dq, 1H, *J*=16.2, 2.8, 1.2 Hz), 4.94 (m, 1H, *J*=10.3, 2.8, 1.2 Hz), 4.5–4.4 (m, 1H), 4.30–3.70 (m, 7H), 3.59 (dd, 1H, *J*=10.8, 3.2 Hz), 3.20–3.00 (s, 6H), 1.29–1.25 (s, 6H), 0.98 (t, 3H, *J*=7.0 Hz), 0.90 (t, 3H, *J*=7.2 Hz); Minor diastereomer (meaningful signals) ^{1}H NMR (C_6D_6, 400 MHz, 340 K) δ 6.68 (d, 1H, *J*=8.5 Hz), 5.86 (ddt, 1H, *J*=16.4, 10.4, 6.0 Hz), 5.2 (dq, 1H, *J*=16.4, 3.2, 1.6 Hz), 5.02 (m, 1H, *J*=10.4, 2.8, 1.2 Hz), 3.47 (dd, 1H, *J*=12, 3.2 Hz), 1.0 (t, 3H, *J*=6.8 Hz), 0.91 (t, 3H, *J*=7.2 Hz); Major diastereomer: ^{13}C NMR (100 MHz, C_6D_6, 340 K) δ 154.8–156.3 (2C), 135.6, 117.8, 99.0–100.4 (2C), 84.7, 68.6, 60.4–64.8 (3C), 47.6–48.6 (3C), 18.3–18.5 (2C), 14.6–15.0 (2C); Minor diastereomer, meaningful signals ^{13}C NMR (C_6D_6, 400 MHz, 340 K): δ 136.4, 116.9, 84.8, 67.8, 60.4–64.8 (3C).

*4.2.21. Ethyl N-[(2S,5R,6R)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxan-2-yl(ethoxy)methyl]-N-(prop-2-en-1-yl)carbamate (**12a**).* Yield 206 mg, (60%); Attempts to separate by chromatography the two diastereomers obtained as a mixture (ratio 93/7) were unsuccessful. R_f (hexanes/AcOEt 9/1)=0.36; IR (neat) cm^{-1} 3079, 2978, 2833, 1706, 1374, 1249, 1117, 947, 877, 774. ESI-MS: *m/z* 745.4 $[2M+Na]^+$, 384.2 $[M+Na]^+$.

Major diastereomer: ^{1}H NMR (500 MHz, C_6D_6, 340 K) δ 6.40 (m, 1H), 5.73–5.54 (m, 1H), 5.16 (br d, 1H, *J*=16.5 Hz), 5.02 (br d, 1H, *J*=10.0 Hz), 4.19–3.70 (m, 7H), 3.51–3.40 (m, 1H), 3.36–3.20 (m, 4H), 3.16 (s, 3H), 1.36 (s, 3H), 1.33 (s, 3H), 1.04 (br t, 3H, *J*=7.0 Hz), 0.96 (br t, 3H, *J*=7.0 Hz); no meaningful signals for the minor diastereomer has be identified from the mixture; ^{13}C NMR (125 MHz, C_6D_6, 340 K) δ 157.0, 136.5, 115.7, 100.7, 100.2, 86.2, 68.8, 63.5, 63.0, 61.2, 48.5, 44.3, 47.9, 18.7, 18.4, 14.9, 14.7; Minor diastereomer (meaningful signals) ^{13}C NMR (C_6D_6, 125 MHz, 340 K) δ 101.9, 70.5, 61.4, 15.6, 15.4.

Acknowledgements

We thank the CNRS and the ICSN (A.L. Ph.D. fellowship), the MESR (F.C. Ph.D. fellowship) for financial support. T.B. thanks Milestone S.r.l. (Italy) for financial and technical support.

References and notes

1. (a) Hiemstra, H.; Speckamp, W. N. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, Chapter 4.5; (b) Maryanoff, B. E.; Zhang, H.-C.; Cohen, J. H.; Turchi, I. J.; Maryanoff, C. A. *Chem. Rev.* **2004**, *104*, 1431–1628; (c) Speckamp, W. N.; Moolenaar, M. J. *Tetrahedron* **2000**, *56*, 3817–3856; (d) Shimizu, M.; Hachiya, I.; Mizota, I. *Chem. Commun.* **2009**, 874–889; (e) Yazici, A.; Pyne, S. G. *Synthesis* **2009**, 339–368; (f) Yazici, A.; Pyne, S. G. *Synthesis* **2009**, 513–541.
2. Yamamoto, Y.; Nakada, T.; Nemoto, H. *J. Am. Chem. Soc.* **1992**, *114*, 121–125.
3. Esch, P. M.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron* **1992**, *48*, 3445–3462.
4. (a) Dhimane, H.; Vanucci, C.; Lhommet, G. *Tetrahedron Lett.* **1997**, *38*, 1415–1418; (b) Remuson, R. *Beilstein J. Org. Chem.* **2007**, *3*, 1–7; (c) Remuson, R.; Gelas-Mialhe, Y. *Mini-Rev. Org. Chem.* **2008**, *5*, 193–208; (d) Veerman, J. J. N.; Bon, R. S.; Hue, B. T. B.; Girones, D.; Rutjes, F. P. J. T.; van Maarseveen, J. H.; Hiemstra, H. *J. Org. Chem.* **2003**, *68*, 4486–4494.
5. (a) Hiemstra, H.; Fortgens, H. P.; Stegenga, S.; Speckamp, W. N. *Tetrahedron Lett.* **1985**, *26*, 3151–3154; (b) Speckamp, W. N.; Hiemstra, H. *Tetrahedron* **1985**, *41*, 4367–4416; (c) Lipomi, D. J.; Panek, J. S. *Org. Lett.* **2005**, *7*, 4701–4704; (d) Berkheij, M.; Dijkink, J.; David, O. R. P.; Sonke, T.; IJzendoorn, D. R.; Blaauw, R. H.; van Maarseveen, J. H.; Schoemaker, H. E.; Hiemstra, H. *Eur. J. Org. Chem.* **2008**, 914–924; (e) Mentink, G.; van Maarseveen, J. H.; Hiemstra, H. *Org. Lett.* **2002**, *4*, 3497–3500.
6. (a) Schuch, C. M.; Pilli, R. A. *Tetrahedron: Asymmetry* **2000**, *11*, 753–764; (b) Klitzke, C. F.; Pilli, R. A. *Tetrahedron Lett.* **2001**, *42*, 5605–5608; (c) Yamamoto, Y.; Schmid, M. *J. Chem. Soc., Chem. Commun.* **1989**, 1310–1312; (d) Marshall, J. A.; Gill, K.; Seletsky, B. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 953–956; (e) Chevallier, F.; Beaudet, I.; Le Grognec, E.; Toupet, L.; Quintard, J.-P. *Tetrahedron Lett.* **2004**, *45*, 761–764; (f) Chevallier, F.; Le Grognec, E.; Beaudet, I.; Fliegel, F.; Evain, M.; Quintard, J.-P. *Org. Biomol. Chem.* **2004**, *2*, 3128–3133.
7. Jacobi, P. A.; Lee, K. *J. Am. Chem. Soc.* **1997**, *119*, 3409–3410.
8. Karsten, W. F. J.; Rutjes, F. P. J. T.; Hiemstra, H. *Tetrahedron Lett.* **1997**, *35*, 6275–6278.
9. Pierce, J. G.; Waller, D. L.; Wipf, P. *J. Organomet. Chem.* **2007**, *692*, 4618–4629.
10. Roy, B.; Pérez-Luna, A.; Ferreira, F.; Botuha, C.; Chemla, F. *Tetrahedron Lett.* **2008**, *49*, 1534–1537.
11. (a) Millot, N.; Piazza, C.; Avolio, S.; Knochel, P. *Synthesis* **2000**, 941–948; (b) Fischer, C.; Carreira, E. M. *Org. Lett.* **2004**, *6*, 1497–1499.
12. Collado, I.; Ezquerra, J.; Pedregal, C. *J. Org. Chem.* **1995**, *60*, 5011–5015.
13. For a recent book see:*Microwaves in Organic Synthesis*; Loupy, A., Ed.; Wiley-VCH GmbH & KGaA: Weinheim, 2006.
14. Detailed description, pictures and applications of this novel reactor system are available at www.milestonesrl.com and were recently published in: Leadbeater, N. E.; Schmink, J. R. *Tetrahedron* **2007**, *63*, 6764–6773.
15. It has to be noted that DEPC was checked by ^{1}H NMR after receiving from ACROS and the spectrum already exhibits some decomposition.
16. In a control experiment, we have observed by ^{1}H NMR a complete decomposition of DEPC when heated during 1 h in the sealed vial and under the reaction conditions in C_6D_6. No decomposition products could be however identified.
17. (a) Nouira, I.; Kostakis, I. K.; Dubouilh, C.; Chosson, E.; Iannelli, M.; Besson, T. *Tetrahedron Lett.* **2008**, *49*, 7033–7036; (b) Mésangeau, C.; Yous, S.; Pérès, B.; Lesieur, D.; Besson, T. *Tetrahedron Lett.* **2005**, *46*, 2465–2468; (c) Wan, Y.; Alterman, M.; Larhed, M.; Hallberg, A. *J. Org. Chem.* **2002**, *67*, 6232–6235.
18. (a) Ley, S. V.; Michel, P. *Synthesis* **2004**, 147–150; (b) Michel, P.; Ley, S. V. *Synthesis* **2003**, 1598–1602.
19. Marshall, J. A.; Beaudoin, S. *J. Org. Chem.* **1996**, *61*, 581–586.
20. (a) Yin, H.; Franck, R. W.; Chen, S. L.; Quigley, G. J.; Todaro, L. *J. Org. Chem.* **1992**, *57*, 644–651; (b) Daumas, M.; Vo-Quang, Y.; Vo-Quang, L.; Le Goffic, F. *Synthesis* **1989**, 64–65.
21. (a) Xia, J.; Hui, Y.-Z. *Tetrahedron: Asymmetry* **1997**, *8*, 451–458; (b) van Boeckel, C. A. A.; Visser, G. M.; van Boom, J. H. *Tetrahedron* **1985**, *41*, 4557–4565.