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ARTICLE

First catalyst-free CO_2 trapping of *N*-acyliminium ions at ambient conditions: Sustainable multicomponent synthesis of thia- and oxazolidinyl carbamates

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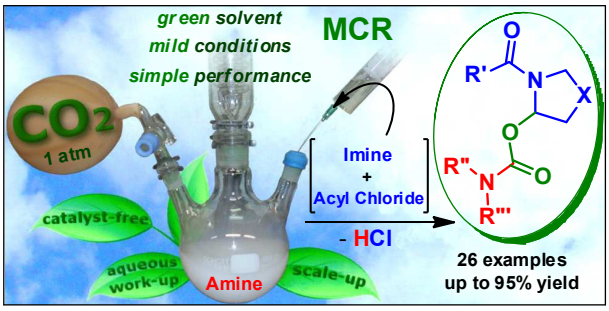
Max Franz,[a] Timo Stalling,[a] Henning Steinert[a] and Jürgen Martens[a,*]

The first trapping of *N*-acyliminium ions by in situ generated carbaminic acid (product of carbon dioxide (CO_2) and amine) is reported. This catalyst-free reaction provides a convenient and feasible approach to prepare *N*-acyl thia- and oxazolidinyl carbamates with good functional-group compatibility and high efficiency under green conditions. Furthermore, the multicomponent method features broad substrate scope, facile product diversification, smooth scale-up and notable potential for polymer applications.

keywords: Multicomponent reaction, green conditions, carbon dioxide, carbamate, *N*-acyliminium ion.



Graphical abstract.

Introduction

Carbon dioxide (CO_2) is a brilliant non-toxic, naturally available, abundant, and low-cost one-carbon (C1) source and has been utilized in a multitude of (catalytic) processes[1] resulting in the elegant synthesis of carboxylates[2], carbonates[3] and carbamates/oxazolidinones[4]. Furthermore, due to the increasing global emissions of carbon dioxide assumed as mediator of global warming the incorporation of this gas into small molecules by catalytic and base-promoted procedures has attracted a great deal of attention in many facets of modern research.[1, 5] In spite of the challenge to convert carbon dioxide because of its kinetic intertness and thermodynamic stability the conversion with amines into carbaminic acids has been highlighted to be an approved way to get various carbonyl derivatives.[6] Amongst the numerous transformations of carbamic acids to functional molecules, one of the most interesting and attractive opportunities is the carbamate formation.

Carbamates are ubiquitous in insecticides, herbicides and fungicides and are widely employed as protecting group in synthetic chemistry. In addition, the products of polymerization (= polyurethanes) bear a significant meaning in materials science. Moreover, the carbamate moiety is often the essential structural element in drug design and medicinal chemistry.[7] Some medicinally and biologically relevant compounds containing the carbamate substructure are depicted in Scheme 1. The first example is Rivastigmine (Exelon®), which was developed as acetylcholinesterase inhibitor for the treatment of Alzheimer's disease and Parkinson's.[8] The next representative is Solifenacin (Vesicare®),

[a] Institut für Chemie, Carl von Ossietzky Universität Oldenburg, P. O. Box 2503, Carl-von-Ossietzky-Str. 9–11, 26111 Oldenburg, Germany
E-mail: juergen.martens@uni-oldenburg.de; http://www.martens.chemie.uni-oldenburg.de.

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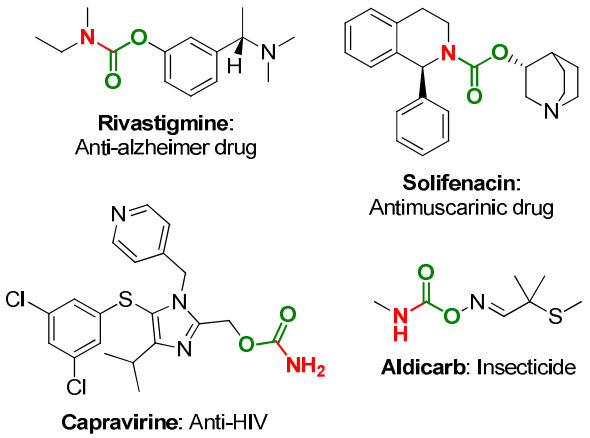
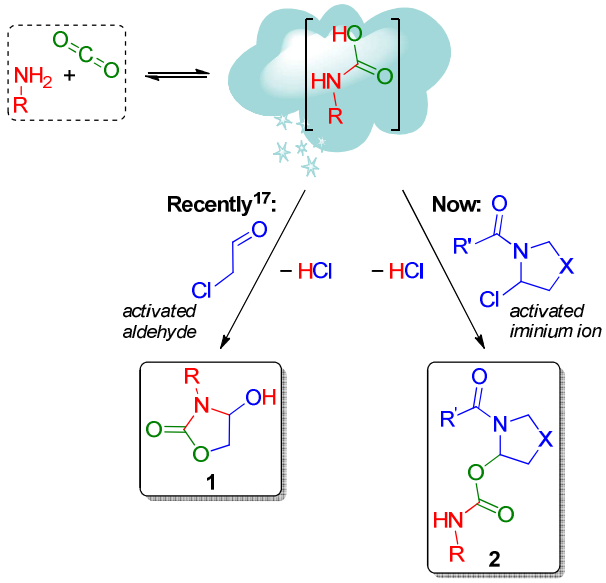
a medicine for the therapy of bladder troubles.[9] Capravirine is a transcriptase inhibitor and applicable as Anti-HIV drug[10], whereas Aldicarb (Temik®) is a cholinesterase inhibitor and therefore used as insecticide.[11]



Scheme 1 Medicinally and biologically active compounds containing carbamate substructure.

A host of synthetic approaches to the popular class of carbamates based on carbon dioxide has been reported.[12] Along these reactions, a direct and versatile route realized by a multicomponent reaction (MCR) has been recently described to productively sequester carbon dioxide as building block.[13] Multicomponent reactions offer an impressive alternative to classical organic reactions, and provide a basis to develop new reaction manifolds. They serve medicinal and organic chemists the unique method to link at least three starting materials simultaneously to a new heavy functional product in an atom economic, low cost and highly efficient fashion.[14] Accordingly, the smooth elaboration of complex and richly substituted (heterocyclic) molecules with feasible motifs often results from MCRs because of their central attribute to reduce a series of reactions into a single-step operation.[15] The design of new MCRs that take place in a green and experimentally simple way are attractive goals in diverse fields of research including carbon dioxide chemistry.[16]

With the privileges of MCRs in hand and the relevance of carbamates at the back of our mind, our group is highly interested in a catalyst-free combination of carbon dioxide, amines and activated bifunctional substrates for the smart preparation of carbamate units. In the course of these works, we have recently developed a water mediated carbon dioxide based MCR that allows an in situ generated carbaminic acid (product of carbon dioxide and amine) to react with an activated aldehyde as central building block to furnish a range of hydroxy oxazolidinones **1** (Scheme 2).[17] We extended this type of MCR to other systems and report herein about the successfull application of high value *N*-acyliminium species[18] in an analog CO_2 transformation ending in the formation of heterocyclic carbamates **2**. The properties and nature of such acyl iminium molecules regarding reactivity, stability and handling (particularly towards moisture) prompted us to find new conditions that are compatible with all components and conform with the sustainable principles of green chemistry. Accordingly, we concentrated on mild and metal-free conditions with ambient pressure of carbon dioxide, while using our experience in generation of reactive *N*-acyliminium intermediates in MCRs starting from imines by a direct acylation[19] as significant step.[20]



Scheme 2 Catalyst-free multicomponent reactions (MCRs) using carbon dioxide (CO_2) as C1 building block (simplified).

Results and discussion

To establish the new carbon dioxide based MCR for assembling heterocyclic carbamates, we started our investigations with an optimization of the two-step sequence regarding solvents, stoichiometry and reaction times (Table 1). These studies were performed by the use of tetramethyl-2,5-dihydro-1,3-thiazole, acetyl chloride, benzyl amine, carbon dioxide as easily available model substrates and triethylamine as non-nucleophilic, well-established base for capturing of hydrogen chloride. During our preliminary experiments, carbon dioxide was purged through the reaction mixture via cannula within a specified time of 30 min (Entries 1–8, Time I, Step b)). Initial attempts by utilizing DCM as classically used solvent for additions of acyl chlorides to imines led to the formation of carbamate **2a** in good yields of 53% and 69%, depending on the reaction time (Entries 1–2). When the total reaction time of 160 min (Times I–III) was transferred to various solvent combinations (DCM, MeCN, DMF, Et_3N, THF, EtOAc) (Entries 1–7), we observed that the homogenous systems THF (Entry 6) and EtOAc (Entry 7) provided the best results. However, we decided to continue our studies with EtOAc as nearly non-toxic, green and dry solvent. Due to the sensitivity of chloro amides produced by Step a) towards moisture we attached importance to totally dry EtOAc before entering in our process. This goal was reached by using molecular sieves, a simple and environmentally friendly method. Furthermore, we

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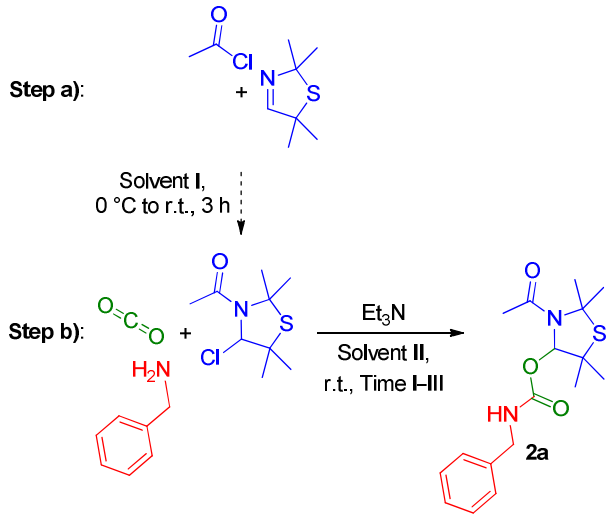
simultaneously tested an alternative method to generate an effective carbon dioxide atmosphere. We figured out that an easy-to-handle carbon dioxide balloon delivers a reliable platform to furnish carbamate **2** in moderate yield of 54% (based on the initially applied DCM system) (Entries 8–9). Focusing on this carbon dioxide source the yield was increased to 63% by the employment of EtOAc as solvent and a longer reaction time (Entry 10). Varying the equivalents of base had a slight effect on the reaction conversion and we noticed that a reduced amount of 2.5 equivalents triethylamine gave the highest yield (64%, Entries 11–13). Reducing the equivalents of benzyl amine provided less product (Entry 14). This negative influence could be compensated by a higher amount of solvents affording carbamate **2** in good yield of 65% (Entry 15). However, to improve the conditions further regarding ecological and economic aspects, we concentrated on the equivalents and times in more detail. We found that both 1.5 equivalents of benzyl amine, 2.5 equivalents of base and a total reaction time of seven hours met the intended demands forming product **2** in 64% yield (Entries 16–19). Lastly, we improved the work-up of the reaction identifying a short process of washing with water as the most efficient option (60% yield, Entry 20).

Table 1 Optimization.



Entry	Solv. I[a)]	Solv. II[b)]	Bn-NH_2[c)]	Et_3N[d)]	Time I[e)]	Time II[f)]	Time III[g)]	Yield[h)]
1	DCM / 4	DCM / 20	3	10	30	6	30	53%
2	DCM / 4	DCM / 20	3	10	30	5	120	69%
3	DCM / 4	MeCN / 20	3	10	30	5	120	54%
4	DCM / 4	DMF / 20	3	10	30	7	120	38%
5	DCM / 4	Et_3N / 20	3	Solv. II	30	7	120	40%
6	THF / 4	THF / 20	3	10	30	6	120	63%
7	EtOAc / 4	EtOAc / 20	3	10	30	5	120	62%
8[i)]	DCM / 4	DCM / 20	3	10	30	6	120	40%
9[j)]	DCM / 4	DCM / 20	3	10	30	6	120	54%
10[j)]	EtOAc / 4	EtOAc / 20	3	10	30	5	16 h	63%
11[j)]	EtOAc / 4	EtOAc / 20	3	5	30	5	16 h	51%
12[j)]	EtOAc / 4	EtOAc / 20	3	2.5	30	6	16 h	64%
13[j)]	EtOAc / 4	EtOAc / 20	3	1.5	30	7	16 h	61%
14[j)]	EtOAc / 4	EtOAc / 20	1.5	2.5	30	5	16 h	39%
15[j), k)]	EtOAc / 8	EtOAc / 40	1.5	2.5	30	10	16 h	65%
16[j), k)]	EtOAc / 8	EtOAc / 40	2.0	1.5	30	13	16 h	63%
17[j), k)]	EtOAc / 16	EtOAc / 40	1.0	1.5	30	35	16 h	51%
18[j), k)]	EtOAc / 16	EtOAc / 40	1.0	1.5	10	35	240	41%
19[j), k)]	EtOAc / 8	EtOAc / 40	1.5	2.5	10	10	240	64%
20[j), k)]	**EtOAc / 8**	**EtOAc / 40**	**1.5**	**2.5**	**10**	**10**	**240**	**60%**[l)]

Reactions were performed using the following conditions: "Step a)" 1. imine (1 eq, 1.00 mmol), 2. solvent I, 3. acetyl chloride (1.2 eq, 1.20 mmol); "Step b)" 1. CO_2 (purging via cannula), 2. solvent II, 3. Et_3N, 4. Bn-NH_2, then stirring (Time I); 5. addition of "Step a)" (Time II) (purging with CO_2 via cannula stopped after 5 min); then stirring (Time III) (for experimental details, see Experimental Section); a) mL; b) mL; c) eq; d) eq; e) min; f) min; g) min; h) Yields of isolated products; i) "Step b)" was performed at 0 °C; j) CO_2 atmosphere was generated by a balloon instead of purging via cannula; k) scale-up: imine (1 eq, 2.00 mmol) and acetyl chloride (1.2 eq, 2.40 mmol) were used; l) work-up was simplified: Slurry was washed only with water.

With the best and greenest reaction conditions in hand, we turned our attention to the scope of our newly developed MCR applying gaseous carbon dioxide as essential C1 building block. Our first target was the incorporation of a representative collection of primary amines while employing selected acyl chlorides and 2,5-dihydro-1,3-thiazole derivatives as further substrates (Scheme 3). We started our investigations with a number of (hetero-)benzylic amines and isolated carbamates **2a–f** in moderate yields (33–65%). The combination of acetyl chloride derivatives, tetramethyl-2,5-dihydro-1,3-thiazole, carbon dioxide, triethylamine, and both unsubstituted and monosubstituted (i. e. 4-OCH_3, 2-Br) benzylic amines provided rapid access to compounds **2a–c** (59–65% yield). The use of picolyl, furfuryl, and thiophenemethyl amines was also successfully applied furnishing carbamates **2d–f** in acceptable yields (33–60%). The reaction of allylic substrates proceeded smoothly affording products **2g–h** in good yields (63–83%). Subsequently, we focused on aniline derivatives and were surprised that the conversion of aniline failed. However, several attempts to include this low-priced amine starting material ended up in trace amounts of the desired carbamate structure. The inability of aniline to react with carbon dioxide is not totally understood.[21] To overcome this limitation, we tested 4-anisidine as more electron rich aniline source and were pleased to note that 4-anisidine underwent clean conversion to give corresponding carbamate **2i** in good yield (63%). These observations indicate that the nucleophilicity of the amine is a relevant property for a successful

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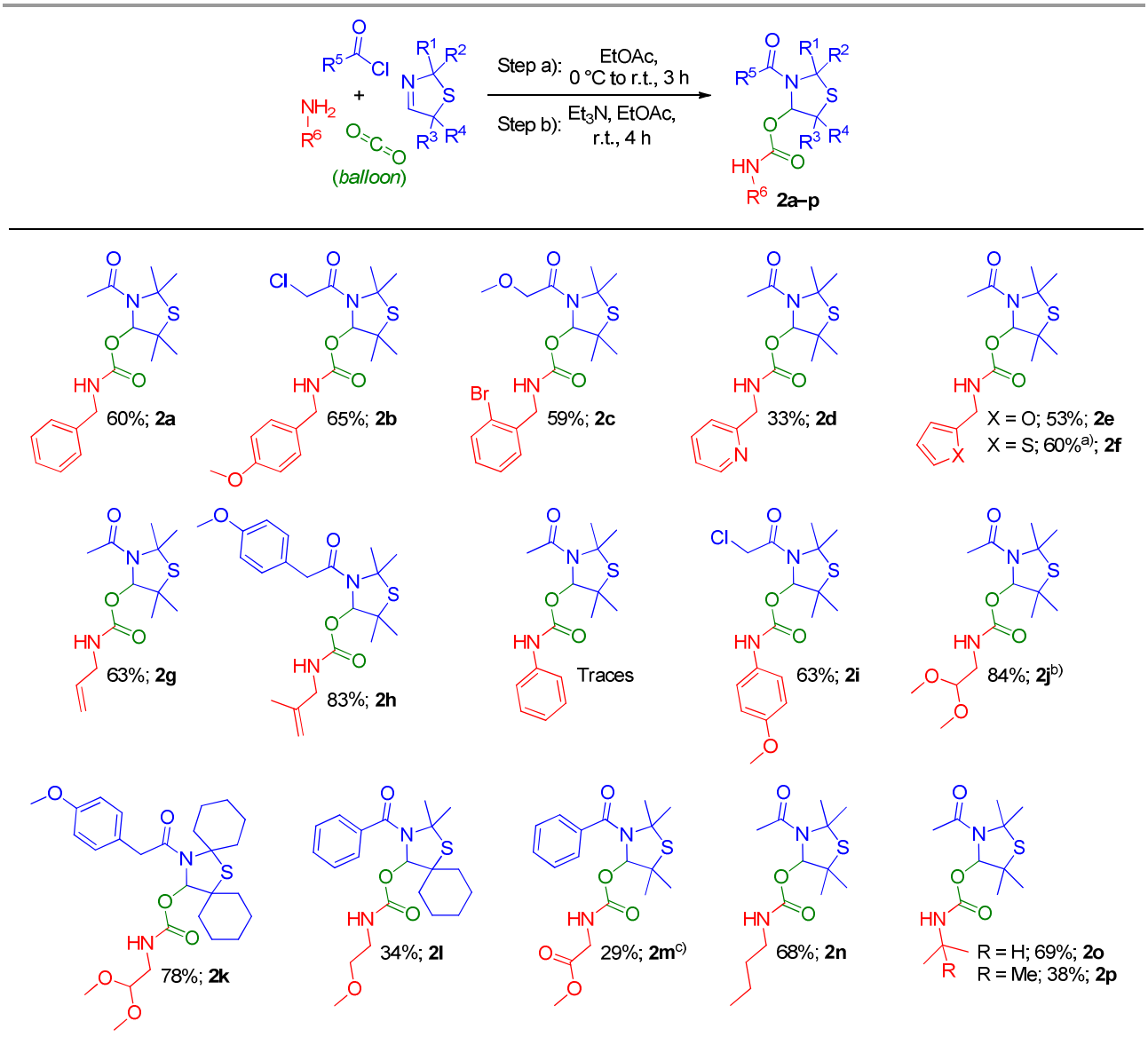
transformation with carbon dioxide. Furthermore, our established conditions offered the opportunity to obtain functionalized carbamates **2j–m** bearing powerful structural subunits for further derivatizations, such as acetal, ether, and ester motifs, in moderate to good yields (29–84%). Apart from various options to modify **2j–l**, notably, glycine derivative **2m** as a selected example for the class of amino acids represents a useful intermediate that can be elaborated to a range of cross-linked heterocyclic structures. In addition to richly functionalized amines we found that formation of sterically non-demanding (i. e. *n*-butyl, **2n**, 68%) and demanding (i. e. *i*-propyl, **2o**, 69%; *t*-butyl, **2p**, 38%) alkyl carbamates **2n–p** was also efficiently promoted.



Scheme 3 Scope of primary amines. Reactions were performed using the following conditions: "Step a)" 1. imine (1 eq, 2.00 mmol), 2. acyl chloride (1.2 eq, 2.40 mmol); "Step b)" 1. CO_2 (balloon), 2. EtOAc, 3. Et_3N (2.5 eq, 5.00 mmol), 4. amine (1.5 eq, 3.00 mmol), 5. addition of "Step a)" (for experimental details, see Experimental Section). Yields of isolated products are shown. a) scale-down: imine (1 eq, 1.00 mmol), acyl chloride (1.2 eq, 1.20 mmol), Et_3N (2.5 eq, 2.50 mmol), and amine (1.5 eq, 1.50 mmol) were used; b) scale-up: imine (1 eq, 10.00 mmol), acyl chloride (1.2 eq, 12.00 mmol), Et_3N (2.5 eq, 25.00 mmol), and amine (1.5 eq, 15.00 mmol) were used; c) The substrate methyl glycinate was introduced as hydrochloride. Additionally, 1.5 eq of Et_3N (3.00 mmol) were used.

Next, we extended our scope to the application of secondary amines as building component in our system. Simultaneously, a variation of the acyl chloride was considered. For these investigations, we concentrated on remarkable, widely used and easily available molecules. Our results are shown in Scheme 4. The first examples were implemented into the series by means of *N*-methyl benzyl amine, acetyl chloride, tetramethyl-2,5-dihydro-1,3-thia-/oxazole, triethylamine, and carbon dioxide to achieve thia- and oxazolidinyl carbamates **2q–r** in up to very good yields (63–91%). Moreover, the range

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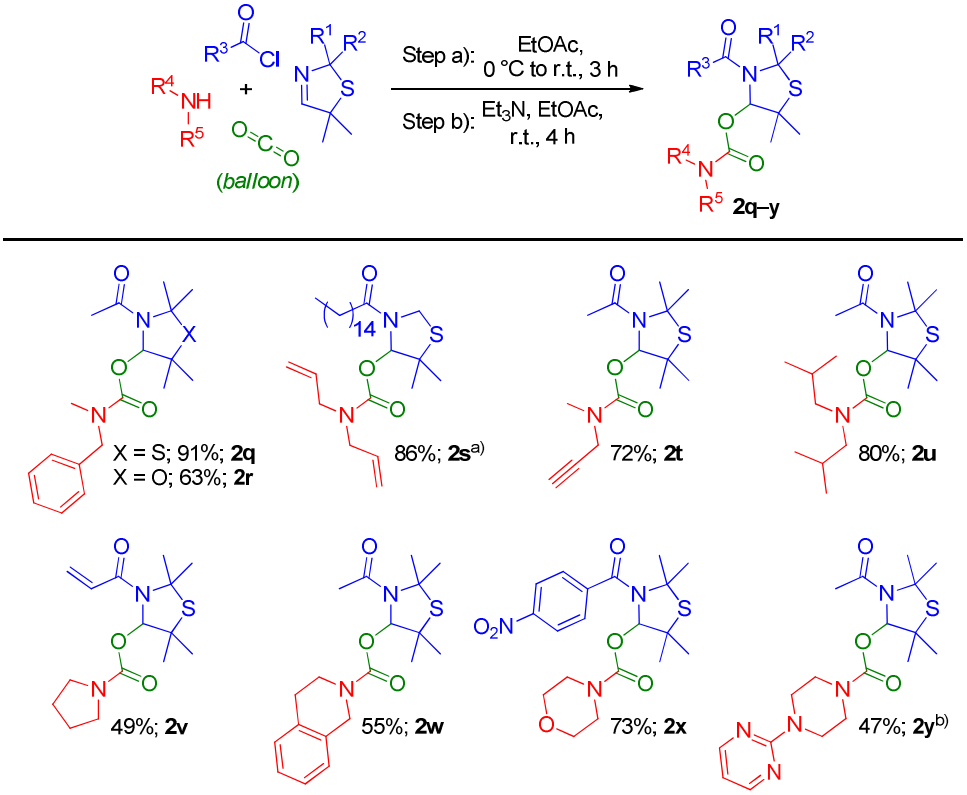
of secondary amines was expanded by the employment of allylic and propargylic starting marterials yielding products **2s–t** in good yields (72–86%). Both compounds containing readily functionalizable terminal double and triple bonds illustrate the potential for further elaboration of a diverse-orientated substance library by simple modifications. In particular, palmitic acid derivative **2s** completes the green methodology of our MCR in a good manner although the generation of **2s** required a longer reaction time. As an example for the straightforward incorporation of a sterically demanding secondary amine alkyl carbamate **2u** was produced in good yield (80%). In addition, the reaction of (hetero-)cyclic secondary amines such as pyrrolidine, tetrahydroisoquinoline, morpholine, and piperazine led to a smooth preparation of carbamates **2v–y** (47–73% yield) including various heterocyclic scaffolds. It is worth mentioning that formation of pyrimidyl piperazinyl substructure in **2y** could be realized in a single-step process demonstrating the broad substrate compatibility of the carbon dioxide based MCR.



Scheme 4 Scope of secondary amines. Reactions were performed using the following conditions: "Step a)" 1. imine (1 eq, 2.00 mmol), 2. acyl chloride (1.2 eq, 2.40 mmol); "Step b)" 1. CO_2 (balloon), 2. EtOAc, 3. Et_3N (2.5 eq, 5.00 mmol), 4. amine (1.5 eq, 3.00 mmol), 5. addition of "Step a)" (for experimental details, see Experimental Section). Yields of isolated products are shown. a) "Step a)" was stirred for 18 h; b) The substrate 1-(2-pyrimidyl)piperazine was introduced as dihydrochloride. Additionally, 3 eq of Et_3N (6.00 mmol) were used.

Finally, we figured out that our environmentally benign multicomponent protocol is also applicable for a multi-gram scale of carbamates (Scheme 5, Up-scaling). For this purpose, we selected isopropyl carbamate structure **2o** as model compound and were delighted to obtain **2o** in almost quantitative yield (95%, 5.47 g) after a facile purification by crystallization. Notably, we would like to emphasize that we had already isolated a relatively highly pure crude product after a simple aqueous work-up (for details, see SI).

Since terminal olefin groups are known to be proper precursors for polymerizations[22], we explored the possibility to create polymerizable monomers by the new carbon dioxide based MCR. In the course of these activities we succeeded in a dimerization reaction providing high-value bis-carbamate **2z** with two allyl units in a moderate yield of 56% (Scheme 5, Dimerization). From a synthetic idea, this example and analogs thereof illustrate a viable way to prepare potential monomers for polyurethane formation.

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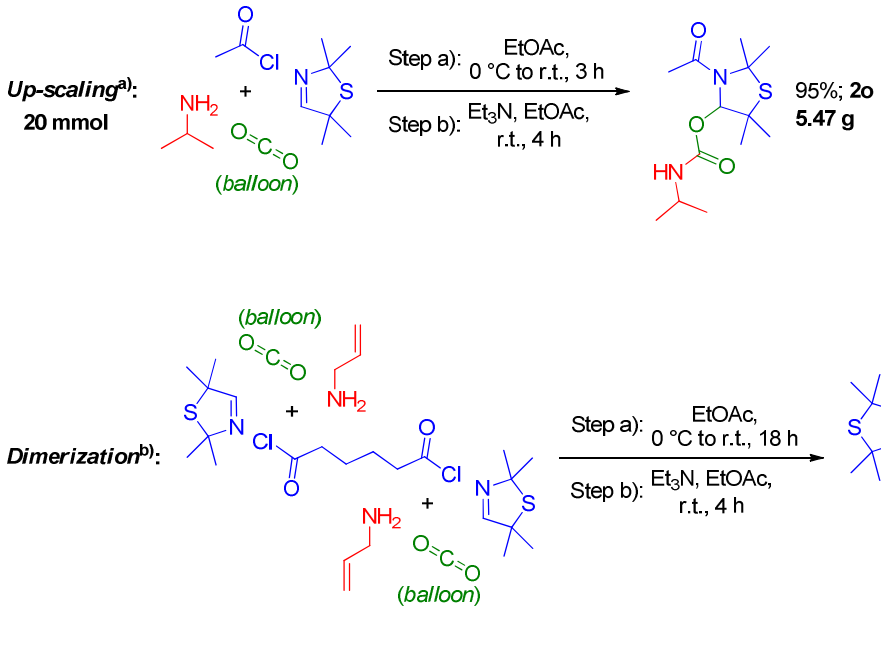
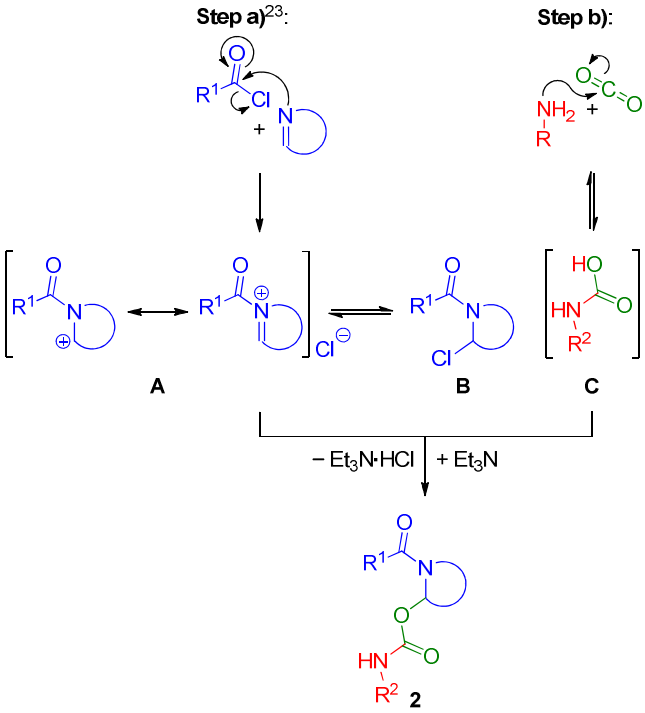


Scheme 5 Examples of up-scaling and dimerization. Reactions were performed using the following conditions: a) "Step a)" 1. imine (1 eq, 20.00 mmol), 2. acyl chloride (1.2 eq, 24.00 mmol); "Step b)" 1. CO_2 (balloon), 2. EtOAc, 3. Et_3N (2.5 eq, 50.00 mmol), 4. amine (1.5 eq, 30.00 mmol), 5. addition of "Step a)" (for experimental details, see Experimental Section). b) "Step a)" 1. imine (2 eq, 2.00 mmol), 2. acyl chloride (1 eq, 1.00 mmol); "Step b)" 1. CO_2 (balloon), 2. EtOAc, 3. Et_3N (5 eq, 5.00 mmol), 4. amine (3 eq, 3.00 mmol), 5. addition of "Step a)" (for experimental details, see Experimental Section). Yields of isolated products are shown.

Based on literature studies[23] and experimental observations, a mechanistic consideration for the generation of carbamates **2** is depicted in Scheme 6. The proposed reaction mechanism involves two steps, namely Step a) and Step b), resulting from the preparative procedure. The reaction starts (Step a) with the addition of an acyl chloride to an cyclic imine furnishing *N*-acyliminium ion **A** along with the formation of an equilibrium to chloro amide **B** as intermediate products. Meanwhile, the nucleophilic attack of an amine to carbon dioxide affords carbaminic acid **C** (Step b). This process might be the reason for a limitation of applying non-electron rich aniline derivatives in the reported MCR. Then the key addition of the carbaminic acid to the *N*-acyliminium ion occurs to give final product **2**. This step is supported by the base triethylamine to trap liberated hydrogen chloride preventing degradation and hydro chloride formation of product **2**.



Scheme 6 Proposed mechanism.[23]

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Conclusions

In conclusion, we have introduced a green multicomponent approach to form thia- and oxazolidinyl carbamates by the sustainable utilization of carbon dioxide at ambient pressure. This inexpensive, non-toxic and readily available C1 unit was incorporated by trapping of *N*-acyliminium ions under catalyst-free and mild reaction conditions. The combination of a broad substrate scope and a good functional-group tolerance enables the efficient and practical preparation of derivatizable heterocycles with valuable scaffold diversity.

Furthermore, the environmentally benign multicomponent reaction was demonstrated to be easily and productively scalable for gram-scale synthesis and to be a potentially vital tool for carbon dioxide applications in polymer chemistry.

Experimental

General considerations

Synthetic procedures, performed under argon atmosphere, were performed on a vacuum line using standard Schlenk techniques. Preparative column chromatography was carried out using Grace SiO_2 (0.035–0.070 mm, type KG 60), EtOAc and *n*-hexane. EtOAc and *n*-hexane were distilled prior to use. TLC was performed with Machery-Nagel SiO_2 F254 plates on aluminum sheets. Melting points were obtained on a melting point apparatus (Laboratory Devices) and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX R 500 (measuring frequency: ^1H NMR = 500.1 MHz, ^{13}C NMR = 125.8 MHz), a Bruker Avance III 500 (measuring frequency: ^1H NMR = 499.9 MHz, ^{13}C NMR = 125.7 MHz) or a Bruker Avance III HD 500 (measuring frequency: ^1H NMR = 500.5 MHz, ^{13}C NMR = 125.9 MHz) spectrometer in $CDCl_3$ solution. Chemical shifts are referenced to the residual peaks of the solvent [7.26 ppm (^1H NMR), 77.16 ppm (^{13}C NMR)].[24] Mass spectra were obtained with Waters Q-TOF Premier (ESI) and Thermo Scientific DFS (EI) spectrometers. IR spectra were recorded on a Bruker Tensor 27 spectrometer fitted with a "Golden Gate" diamond-ATR (attenuated total reflection) unit. Thiazolines[25], oxazolines[25] and acyl chlorides[26] were prepared according to published procedures.

General procedure for synthesis of thia- and oxazolidin-4-yl carbamates 2

Step a): The respective imine (1.0 eq), dissolved in anhydrous EtOAc (4 mL per mmol imine), was cooled to 0 °C, treated portionwise with acyl chloride (1.2 eq) and stirred for 3 h at r.t..

Step b): Meanwhile a three-necked flask, equipped with dimroth condenser, football bladder (= balloon, for rotary evaporators) and rubber septum, was purged with carbon dioxide, before anhydrous EtOAc (20 mL per mmol imine), anhydrous triethylamine (2.5 eq) and the respective amine (1.5 eq) were added. After purging with carbon dioxide via cannula (through solution), the mixture was stirred for 10 min at r.t. under carbon dioxide atmosphere at ambient pressure.

To the solution of b) the hitherto prepared solution of a) was added dropwise via syringe within 10 min and the reaction mixture was stirred for 4 h at r.t.. The resulting slurry was treated with water (10 mL per mmol imine) and the aqueous phase was extracted with EtOAc (3 x 10 mL per mmol imine). The combined organic phases were dried ($MgSO_4$) and the solvent was removed on a rotary evaporator. The crude product was purified by column chromatography on silica gel or crystallized from EtOAc/*n*-hexane.

(*RS*)-3-Acetyl-4-benzylcarbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2a): The carbamate **2a** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and benzylamine (321 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.19) to obtain 406 mg (1.21 mmol) of a colorless solid (yield: 60%).

MP: 117–118 °C (EtOAc/*n*-hexane); ^1H NMR (500.1 MHz, $CDCl_3$, 298.6 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 87:13): δ 1.34 (s, 3 H), 1.58 (s, 3 H), 1.80 (s, 3 H), 1.93 (s, 3 H), 2.21 (s, 3 H), 4.35 (dd, J = 14.8 Hz, J = 5.8 Hz, 1 H), 4.42 (dd, J = 14.8 Hz, J = 6.1 Hz, 1 H), 5.27–5.33 (m, 1 H), 6.37 (s, 1 H), 7.25–7.30 (m, 3 H), 7.31–7.36 (m, 2 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 298.5 K), major conformer: δ 23.1, 25.3, 30.65, 30.72, 32.0, 45.2, 52.6, 73.3, 93.8, 127.6, 127.8, 128.9, 138.0, 155.5, 170.2 ppm; IR (ATR): $\tilde{\nu}$ 3257, 3042, 2995, 2924, 1715, 1646, 1504, 1431, 1401, 1322, 1270, 1226, 1124, 982, 957, 888, 733, 699 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{17}H_{24}N_2NaO_3S$ $[M + Na]^+$ 359.1405, found 359.1414.

(*RS*)-3-Chloroacetyl-4-(4-methoxybenzyl)carbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2b): The carbamate **2b** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), chloroacetyl chloride (271 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and 4-methoxybenzylamine (412 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 4:1, R_f = 0.38) to obtain 518 mg (1.29 mmol) of a colorless solid (yield: 65%).

MP: 113–114 °C (EtOAc/*n*-hexane); ^1H NMR (500.1 MHz, $CDCl_3$, 299.1 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 88:12): δ 1.35 (s, 3 H), 1.59 (s, 3 H), 1.79 (s, 3 H), 1.92 (s, 3 H), 3.79 (s, 3 H), 4.03 (d, J = 12.9 Hz, 1 H), 4.27 (dd, J = 14.6 Hz, J = 5.6 Hz, 1 H), 4.35 (dd, J = 14.6 Hz, J = 6.1 Hz, 1 H), 4.45 (d, J = 12.9 Hz, 1 H), 5.24–5.30 (m, 1 H), 6.45 (s, 1 H), 6.84–6.88 (m, 2 H), 7.16–7.20 (m, 2 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 299.2 K), major conformer: δ 23.0, 30.6, 30.7, 31.3, 43.8, 44.8, 53.1, 55.4, 73.8, 92.1, 114.3, 129.0, 129.9, 155.3, 159.3, 166.1 ppm; IR (ATR): $\tilde{\nu}$ 3348, 2987, 2927, 2837, 1703, 1668, 1538, 1513, 1398, 1262, 1220, 1119, 984, 940, 892, 799, 689, 594 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{18}H_{25}ClN_2NaO_4S$ $[M + Na]^+$ 423.1121, found 423.1124.

(*RS*)-4-(2-Bromobenzyl)carbamoyloxy-3-methoxyacetyl-2,2,5,5-tetramethyl-1,3-thiazolidine (2c): The carbamate **2c** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), methoxyacetyl chloride (260 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and 2-bromobenzylamine

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(558 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.26) to obtain 524 mg (1.18 mmol) of a colorless solid (yield: 59%).

MP: 153–154 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 300.3 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 88:12): δ 1.33 (s, 3 H), 1.53 (s, 3 H), 1.82 (s, 3 H), 1.93 (s, 3 H), 3.38 (s, 3 H), 3.91 (d, *J* = 13.9 Hz, 1 H), 4.23 (d, *J* = 13.9 Hz, 1 H), 4.41–4.49 (m, 2 H), 5.36–5.39 (m, 1 H), 6.49 (s, 1 H), 7.15 (td, *J* = 7.7 Hz, *J* = 1.6 Hz, 1 H), 7.28 (td, *J* = 7.6 Hz, *J* = 1.3 Hz, 1 H), 7.34 (dd, *J* = 7.6 Hz, *J* = 1.4 Hz, 1 H), 7.53–7.56 (m, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 300.1 K), major conformer: δ 23.0, 30.6, 30.8, 31.6, 45.5, 53.3, 59.2, 73.2, 73.8, 91.4, 123.7, 127.8, 129.6, 130.0, 133.1, 137.0, 155.3, 169.0 ppm; IR (ATR): $\tilde{\nu}$ 3335, 2992, 2928, 1706, 1671, 1541, 1301, 1263, 1222, 1112, 983, 931, 887, 741 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{18}H_{25}BrN_2NaO_4S$ $[M + Na]^+$ 467.0616, found 467.0627.

(*RS*)-3-Acetyl-4-(pyridin-2-ylmethyl)carbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2d): The carbamate **2d** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and 2-picolylamine (324 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.37) to obtain 223 mg (0.66 mmol) of a colorless solid (yield: 33%).

MP: 120–121 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 300.4 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 87:13): δ 1.32 (s, 3 H), 1.55 (s, 3 H), 1.79 (s, 3 H), 1.91 (s, 3 H), 2.18 (s, 3 H), 4.47–4.50 (m, 2 H), 6.21–6.26 (m, 1 H), 6.35 (s, 1 H), 7.16–7.20 (m, 1 H), 7.21–7.25 (m, 1 H), 7.64 (td, *J* = 7.8 Hz, *J* = 1.8 Hz, 1 H), 8.51–8.54 (m, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 300.3 K), major conformer: δ 23.0, 25.3, 30.6, 30.8, 32.1, 46.0, 52.5, 73.3, 93.7, 121.7, 122.6, 136.9, 149.3, 155.6, 156.4, 170.3 ppm; IR (ATR): $\tilde{\nu}$ 3420, 2986, 2971, 2932, 1698, 1673, 1504, 1372, 1303, 1230, 1212, 1132, 938, 923, 753, 610 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{16}H_{24}N_3O_3S$ $[M + H]^+$ 338.1538, found 338.1529.

(*RS*)-3-Acetyl-4-furfurylcarbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2e): The carbamate **2e** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and furfurylamine (291 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.16) to obtain 344 mg (1.05 mmol) of a colorless solid (yield: 53%).

MP: 125–127 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 298.6 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 86:14): δ 1.30 (s, 3 H), 1.55 (s, 3 H), 1.78 (s, 3 H), 1.91 (s, 3 H), 2.18 (s, 3 H), 4.31–4.40 (m, 2 H), 5.33–5.39 (m, 1 H), 6.19–6.21 (m, 1 H), 6.28–6.31 (m, 1 H), 6.34 (s, 1 H), 7.31–7.34 (m, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 298.5 K), major conformer: δ 23.0, 25.2, 30.6, 30.7, 32.0, 38.2, 52.5, 73.3, 93.8, 107.5, 110.5, 142.5, 151.1, 155.3, 170.2 ppm; IR (ATR): $\tilde{\nu}$ 3266, 2981, 2931, 1712, 1645, 1538, 1399, 1357, 1226, 1120, 980, 927, 713, 619 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{15}H_{23}N_2O_4S$ $[M + H]^+$ 327.1379, found 327.1383.

(*RS*)-3-Acetyl-4-(thiophen-2-ylmethyl)carbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2f): The carbamate **2f** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (143 mg, 1.00 mmol), acetyl chloride (94 mg, 1.20 mmol), triethylamine (253 mg, 2.50 mmol) and 2-thiophenemethylamine (170 mg, 1.50 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.40) to obtain 206 mg (0.60 mmol) of a colorless solid (yield: 60%).

MP: 129–131 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 300.3 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 87:13): δ 1.34 (s, 3 H), 1.58 (s, 3 H), 1.79 (s, 3 H), 1.93 (s, 3 H), 2.20 (s, 3 H), 4.53 (dd, *J* = 15.4 Hz, *J* = 5.9 Hz, 1 H), 4.58 (dd, *J* = 15.4 Hz, *J* = 6.2 Hz, 1 H), 5.32–5.38 (m, 1 H), 6.37 (s, 1 H), 6.92–6.97 (m, 2 H), 7.23 (dd, *J* = 4.9 Hz, *J* = 1.4 Hz, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 300.3 K), major conformer: δ 23.1, 25.3, 30.66, 30.73, 32.0, 40.0, 52.5, 73.3, 93.9, 125.5, 126.0, 127.0, 140.9, 155.2, 170.3 ppm; IR (ATR): $\tilde{\nu}$ 3240, 2991, 2926, 1713, 1644, 1543, 1397, 1277, 1226, 1118, 978, 953, 927, 782, 703, 620 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{15}H_{22}N_2NaO_3S_2$ $[M + Na]^+$ 365.0970, found 365.0961.

(*RS*)-3-Acetyl-4-allylcarbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2g): The carbamate **2g** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and allylamine (171 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.27) to obtain 360 mg (1.26 mmol) of a colorless solid (yield: 63%).

MP: 84–85 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 298.8 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 87:13): δ 1.32 (s, 3 H), 1.56 (s, 3 H), 1.80 (s, 3 H), 1.92 (s, 3 H), 2.19 (s, 3 H), 3.77–3.85 (m, 2 H), 5.04–5.09 (m, 1 H), 5.12–5.22 (m, 2 H), 5.78–5.86 (m, 1 H), 6.33 (s, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 298.6 K), major conformer: δ 23.0, 25.3, 30.66, 30.71, 32.0, 43.5, 52.6, 73.3, 93.6, 116.5, 134.0, 155.3, 170.3 ppm; IR (ATR): $\tilde{\nu}$ 3329, 2990, 2938, 2868, 1692, 1670, 1522, 1390, 1381, 1273, 1229, 1109, 975, 937, 917, 777 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{13}H_{22}N_2NaO_3S$ $[M + Na]^+$ 309.1249, found 309.1242.

(*RS*)-3-(4-Methoxyphenyl)acetyl-4-(2-methylallyl)carbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2h): The carbamate **2h** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), 4-methoxyphenylacetyl chloride (443 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and 2-methylallylamine (213 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.33) to obtain 672 mg (1.65 mmol) of a colorless solid (yield: 83%).

MP: 87–88 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 300.3 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 87:13): δ 1.05 (s, 3 H), 1.26 (s, 3 H), 1.76 (s, 3 H), 1.85 (s, 3 H), 1.90 (s, 3 H), 3.63 (d, *J* = 15.0 Hz, 1 H), 3.71 (dd, *J* = 15.9 Hz, *J* = 5.6 Hz, 1 H), 3.78 (s, 3 H), 3.79–3.87

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(m, 2 H), 4.86–4.90 (m, 2 H), 5.11–5.15 (m, 1 H), 6.45 (s, 1 H), 6.85–6.87 (m, 2 H), 7.23–7.28 (m, 2 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 299.5 K), major conformer: δ 20.2, 22.9, 29.9, 30.8, 31.5, 43.4, 46.7, 52.6, 55.4, 73.3, 92.6, 111.1, 114.3, 126.8, 129.9, 141.8, 155.6, 158.7, 171.3 ppm; IR (ATR): $\tilde{\nu}$ 3314, 2985, 2934, 1719, 1656, 1510, 1450, 1370, 1246, 1219, 1169, 1013, 979, 821, 731 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{21}H_{30}N_2NaO_4S$ $[M + Na]^+$ 429.1824, found 429.1815.

(*RS*)-3-Chloroacetyl-4-(4-methoxyphenyl)carbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2i): The carbamate **2i** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), chloroacetyl chloride (271 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and 4-methoxyaniline (369 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 7:2, R_f = 0.50) to obtain 487 mg (1.26 mmol) of a colorless solid (yield: 63%).

MP: 118–119 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 298.0 K): δ 1.41 (s, 3 H), 1.62 (s, 3 H), 1.87 (s, 3 H), 1.96 (s, 3 H), 3.79 (s, 3 H), 4.04 (d, *J* = 12.8 Hz, 1 H), 4.49 (d, *J* = 12.8 Hz, 1 H), 6.53 (s, 1 H), 6.78 (s, 1 H), 6.85–6.89 (m, 2 H), 7.28–7.33 (m, 2 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 298.2 K): δ 23.1, 30.7, 30.8, 31.3, 43.8, 53.1, 55.7, 73.9, 92.1, 114.5, 121.2, 130.0, 152.8, 156.7, 166.1 ppm; IR (ATR): $\tilde{\nu}$ 3342, 2996, 2935, 1702, 1677, 1539, 1512, 1398, 1245, 1206, 1169, 1019, 984, 829, 739 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{17}H_{23}ClN_2NaO_4S$ $[M + Na]^+$ 409.0965, found 409.0966.

(*RS*)-3-Acetyl-4-(2,2-dimethoxyethyl)carbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2j): The carbamate **2j** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (1.432 g, 10.00 mmol), acetyl chloride (0.942 g, 12.00 mmol), triethylamine (2.530 g, 25.00 mmol) and 2,2-dimethoxyethylamine (1.577 g, 15.00 mmol). The crude product was purified by recrystallization (EtOAc/*n*-hexane) to obtain 2.793 g (8.35 mmol) of a colorless solid (yield: 84%).

MP: 81–83 °C (EtOAc/*n*-hexane); ^{1}H NMR (499.9 MHz, $CDCl_3$, 305.0 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 90:10): δ 1.31 (s, 3 H), 1.55 (s, 3 H), 1.80 (s, 3 H), 1.91 (s, 3 H), 2.17 (s, 3 H), 3.28–3.33 (m, 2 H), 3.36 (s, 6 H), 4.34–4.37 (m, 1 H), 5.08–5.14 (m, 1 H), 6.31 (s, 1 H) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$, 305.0 K), major conformer: δ 23.0, 25.2, 30.66, 30.73, 32.0, 42.6, 52.5, 54.4, 54.5, 73.3, 93.8, 102.7, 155.6, 170.2 ppm; IR (ATR): $\tilde{\nu}$ 3330, 2994, 2941, 2903, 2837, 1718, 1658, 1547, 1444, 1396, 1257, 1222, 1114, 981, 948, 828, 781, 628 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{14}H_{26}LiN_2O_5S$ $[M + Li]^+$ 341.1722, found 341.1713.

(*RS*)-15-(2,2-Dimethoxyethyl)carbamoyloxy-14-(4-methoxyphenyl)acetyl-7-thia-14-azadispiro[5.1.5^8.2^6]pentadecane (2k): The carbamate **2k** was prepared according to the general procedure using 7-thia-14-azadispiro[5.1.5^8.2^6]pentadec-14-ene (447 mg, 2.00 mmol), 4-methoxyphenylacetyl chloride (443 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and 2,2-dimethoxyethylamine (315 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.25) to obtain 814 mg (1.56 mmol) of a colorless oil (yield: 78%).

^{1}H NMR (500.1 MHz, $CDCl_3$, 299.5 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 89:11): δ 0.99–1.12 (m, 2 H), 1.14–1.20 (m, 2 H), 1.22–1.39 (m, 4 H), 1.47–1.52 (m, 2 H), 1.53–1.59 (m, 4 H), 1.66–1.70 (m, 1 H), 1.72–1.78 (m, 2 H), 1.83–1.91 (m, 1 H), 2.77–2.84 (m, 1 H), 3.07–3.13 (m, 1 H), 3.29–3.36 (m, 2 H), 3.37–3.40 (m, 6 H), 3.63 (d, *J* = 15.1 Hz, 1 H), 3.77 (s, 3 H), 3.83 (d, *J* = 15.1 Hz, 1 H), 4.36–4.40 (m, 1 H), 5.05–5.09 (m, 1 H), 6.48 (s, 1 H), 6.83–6.86 (m, 2 H), 7.21–7.24 (m, 2 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 299.0 K), major conformer: δ 21.9, 24.1, 24.5, 25.1, 25.4, 25.7, 32.6, 36.8, 37.2, 38.1, 42.6, 43.9, 54.4, 54.5, 55.4, 57.9, 80.0, 92.3, 102.6, 114.2, 127.0, 129.9, 155.8, 158.7, 171.8 ppm; IR (ATR): $\tilde{\nu}$ 3343, 2931, 1717, 1658, 1511, 1449, 1376, 1246, 1126, 1066, 906, 729 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{27}H_{40}N_2NaO_6S$ $[M + Na]^+$ 543.2505, found 543.2509.

(*RS*)-3-Benzoyl-4-(2-methoxyethyl)carbamoyloxy-2,2-dimethyl-1-thia-3-azaspiro[4.5]decane (2l): The carbamate **2l** was prepared according to the general procedure using 2,2-dimethyl-1-thia-3-azaspiro[4.5]dec-3-ene (367 mg, 2.00 mmol), benzoyl chloride (337 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and 2-methoxylethylamine (321 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.10) to obtain 277 mg (0.68 mmol) of a colorless solid (yield: 34%).

MP: 109–110 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 299.2 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 88:12): δ 1.10–1.19 (m, 2 H), 1.52–1.62 (m, 3 H), 1.64–1.75 (m, 3 H), 1.78–1.87 (m, 1 H), 1.97–2.02 (m, 7 H), 3.16–3.23 (m, 2 H), 3.34 (s, 3 H), 3.35–3.39 (m, 2 H), 5.04–5.10 (m, 1 H), 6.29 (s, 1 H), 7.32–7.35 (m, 2 H), 7.36–7.44 (m, 3 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 299.1 K), major conformer: δ 22.2, 24.2, 25.4, 31.3, 32.0, 32.7, 38.0, 40.8, 58.9, 59.3, 71.2, 72.0, 94.1, 126.2, 128.6, 130.0, 137.8, 154.4, 171.4 ppm; IR (ATR): $\tilde{\nu}$ 3255, 3061, 2979, 2932, 2860, 1721, 1646, 1528, 1449, 1390, 1368, 1332, 1250, 1219, 1128, 1013, 999, 973, 870, 735, 703 cm^{-1}; HRMS (EI, 70 eV) *m/z*: calcd for $C_{21}H_{30}N_2O_4S$ $[M]^+$ 406.1921, found 406.1929.

(*RS*)-Methyl (((3-benzoyl-2,2,5,5-tetramethylthiazolidin-4-yl)oxy)carbonyl)glycinate (2m): The carbamate **2m** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), benzoyl chloride (337 mg, 2.40 mmol), triethylamine (810 mg, 8.00 mmol) and methyl glycinate hydrochloride (377 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 7:3, R_f = 0.19) to obtain 219 mg (0.58 mmol) of a colorless oil (yield: 29%).

^{1}H NMR (500.1 MHz, $CDCl_3$, 299.0 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 87:13): δ 1.26 (s, 3 H), 1.63 (s, 3 H), 1.99 (s, 3 H), 2.06 (s, 3 H), 3.74 (s, 3 H), 3.80–3.83 (m, 2 H), 5.25–5.29 (m, 1 H), 6.18 (s, 1 H), 7.32–7.42 (m, 5 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 299.3 K), major conformer: δ 23.0, 31.0, 31.1, 31.8, 42.5, 52.5, 52.9, 73.0, 94.7, 126.0, 128.7, 129.9, 137.7, 154.4, 170.2, 171.1 ppm; IR (ATR): $\tilde{\nu}$ 3304, 3046, 2982, 2937, 2877, 1730, 1651, 1516, 1445, 1363, 1274, 1204, 1155, 1014, 995, 911, 856, 731, 700, 625 cm^{-1};

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HRMS (EI, 70 eV) *m/z*: calcd for $C_{18}H_{24}N_2O_5S$ $[M]^+$ 380.1400, found 380.1389.

(*RS*)-3-Acetyl-4-*n*-butylcarbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2n): The carbamate **2n** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and *n*-butylamine (216 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.43) to obtain 411 mg (1.36 mmol) of a colorless solid (yield: 68%).

MP: 71–72 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 298.8 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 87:13): δ 0.90–0.94 (m, 3 H), 1.33 (s, 3 H), 1.34–1.38 (m, 2 H), 1.46–1.52 (m, 2 H), 1.57 (s, 3 H), 1.81 (s, 3 H), 1.93 (s, 3 H), 2.20 (s, 3 H), 3.14–3.26 (m, 2 H), 4.84–4.90 (m, 1 H), 6.33 (s, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 298.7 K), major conformer: δ 13.8, 20.0, 23.0, 25.3, 30.69, 30.73, 32.0, 32.0, 40.9, 52.6, 73.3, 93.5, 155.4, 170.3 ppm; IR (ATR): $\tilde{\nu}$ 3319, 2961, 2931, 2873, 1706, 1650, 1534, 1441, 1397, 1357, 1378, 1219, 1127, 982, 620 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{14}H_{27}N_2O_3S$ $[M + H]^+$ 303.1742, found 303.1747.

(*RS*)-3-Acetyl-4-isopropylcarbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2o): The carbamate **2o** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and isopropylamine (177 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.24) to obtain 396 mg (1.37 mmol) of a colorless solid (yield: 69%). After scale-up (factor 10; 20 mmol) the crude product was purified by recrystallization (EtOAc/*n*-hexane) to obtain 5.47 g (18.97 mmol) of a colorless solid (yield: 95%).

MP: 125–126 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 298.5 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 86:14): δ 1.12–1.16 (m, 6 H), 1.29 (s, 3 H), 1.54 (s, 3 H), 1.78 (s, 3 H), 1.90 (s, 3 H), 2.16 (s, 3 H), 3.74–3.83 (m, 1 H), 4.81 (d, *J* = 7.7 Hz, 1 H), 6.29 (s, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 298.4 K), major conformer: δ 22.87, 22.87, 22.92, 25.3, 30.6, 30.7, 32.0, 43.3, 52.6, 73.2, 93.3, 154.5, 170.2 ppm; IR (ATR): $\tilde{\nu}$ 3279, 2973, 2933, 2874, 1712, 1651, 1539, 1399, 1362, 1220, 1059, 1040, 684, 624 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{13}H_{24}N_2NaO_3S$ $[M + Na]^+$ 311.1405, found 311.1405.

(*RS*)-3-Acetyl-4-*tert*-butylcarbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2p): The carbamate **2p** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and *tert*-butylamine (219 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.57) to obtain 229 mg (0.76 mmol) of a colorless solid (yield: 38%).

MP: 137–138 °C (EtOAc/*n*-hexane); ^{1}H NMR (499.9 MHz, $CDCl_3$, 304.7 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 91:9): δ 1.30–1.32 (m, 12 H), 1.55 (s, 3 H), 1.80 (s, 3 H), 1.91 (s, 3 H), 2.16 (s, 3 H), 4.83 (s, 1 H), 6.27 (s, 1 H) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$, 305.0 K), major conformer: δ 22.9, 25.2, 28.9, 30.6, 30.7, 32.1, 50.8, 52.6, 73.2, 92.9, 153.6, 170.2 ppm; IR (ATR): $\tilde{\nu}$ 3254, 2972, 2932, 1728, 1716, 1651, 1542, 1393, 1360, 1213, 1053, 942, 776, 688, 622 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{14}H_{27}N_2O_3S$ $[M + H]^+$ 303.1742, found 303.1740.

(*RS*)-3-Acetyl-4-benzylmethylcarbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2q): The carbamate **2q** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and *N*-benzylmethylamine (364 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.37) to obtain 635 mg (1.81 mmol) of a colorless solid (yield: 91%).

MP: 105–106 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 298.7 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 56:44): δ 1.33 (s, 3 H), 1.59 (s, 3 H), 1.82 (s, 3 H), 1.95 (s, 3 H), 2.22 (s, 3 H), 2.89 (s, 3 H), 4.41–4.46 (m, 1 H), 4.52–4.59 (m, 1 H), 6.43 (s, 1 H), 7.20–7.24 (m, 2 H), 7.25–7.29 (m, 1 H), 7.30–7.34 (m, 2 H) ppm; minor conformer: δ 1.29 (s, 3 H), 1.57 (s, 3 H), 1.72 (s, 3 H), 1.92 (s, 3 H), 2.21 (s, 3 H), 2.93 (s, 3 H), 4.41–4.46 (m, 1 H), 4.52–4.59 (m, 1 H), 6.42 (s, 1 H), 7.20–7.24 (m, 2 H), 7.25–7.29 (m, 1 H), 7.30–7.34 (m, 2 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 298.8 K), major conformer: δ 23.3, 25.4, 30.6, 30.7, 32.0, 33.7, 52.5, 52.6, 73.2, 94.3, 127.7, 127.8, 128.8, 137.1, 155.7, 170.3 ppm; minor conformer: 23.2, 25.3, 30.5, 30.7, 32.0, 34.6, 52.5, 52.6, 73.2, 94.4, 127.5, 127.7, 128.9, 136.8, 155.1, 170.1 ppm; IR (ATR): $\tilde{\nu}$ 2992, 2925, 2866, 1700, 1672, 1446, 1390, 1310, 1192, 1122, 979, 929, 757, 710 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{18}H_{26}N_2NaO_3S$ $[M + Na]^+$ 373.1562, found 373.1575.

(*RS*)-3-Acetyl-4-benzylmethylcarbamoyloxy-2,2,5,5-tetramethyl-1,3-oxazolidine (2r): The carbamate **2r** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-oxazole (254 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and *N*-benzylmethylamine (364 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.19) to obtain 420 mg (1.26 mmol) of a colorless solid (yield: 63%).

MP: 76–77 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 299.2 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 55:45): δ 1.30 (s, 3 H), 1.39 (s, 3 H), 1.58 (s, 3 H), 1.67 (s, 3 H), 2.15 (s, 3 H), 2.85 (s, 3 H), 4.45 (d, *J* = 15.1 Hz, 1 H), 4.51–4.55 (m, 1 H), 6.26 (s, 1 H), 7.19–7.22 (m, 2 H), 7.25–7.29 (m, 1 H), 7.30–7.34 (m, 2 H) ppm; minor conformer: δ 1.25 (s, 3 H), 1.37 (s, 3 H), 1.52 (s, 3 H), 1.65 (s, 3 H), 2.06 (s, 3 H), 2.96 (s, 3 H), 4.38 (d, *J* = 15.6 Hz, 1 H), 4.51–4.55 (m, 1 H), 6.22 (s, 1 H), 7.16–7.18 (m, 2 H), 7.25–7.29 (m, 1 H), 7.30–7.34 (m, 2 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 299.1 K), major conformer: δ 22.9, 23.8, 27.0, 27.7, 27.8, 33.7, 52.6, 81.8, 88.6, 96.0, 127.67, 127.74, 128.8, 137.0, 155.6, 169.2 ppm; minor conformer: 22.9, 23.7, 27.1, 27.7, 27.8, 34.9, 52.5, 81.8, 88.7, 95.9, 127.2, 127.8, 128.9, 136.9, 155.1, 169.1 ppm; IR (ATR): $\tilde{\nu}$ 2980, 2941, 1699, 1670, 1397, 1314, 1259, 1207, 1129, 1002,

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978, 939, 900, 765, 711, 623 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{18}H_{26}N_2NaO_4$ $[M + Na]^+$ 357.1790, found 357.1788.

(*RS*)-4-Diallylcarbamoyloxy-5,5-dimethyl-3-palmitoyl-1,3-thiazolidine (2s): The carbamate **2s** was prepared according to the general procedure using 5,5-dimethyl-2,5-dihydro-1,3-thiazole (230 mg, 2.00 mmol), palmitoyl chloride (660 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and diallylamine (291 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 7:1, R_f = 0.29) to obtain 847 mg (1.71 mmol) of a colorless oil (yield: 86%).

^{1}H NMR (500.5 MHz, $CDCl_3$, 300.0 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 95:5): δ 0.85–0.88 (m, 3 H), 1.23–1.30 (m, 24 H), 1.37 (s, 3 H), 1.42 (s, 3 H), 1.59–1.64 (m, 2 H), 2.38–2.48 (m, 2 H), 3.80–3.91 (m, 4 H), 4.55 (d, *J* = 9.7 Hz, 1 H), 4.72 (d, *J* = 9.7 Hz, 1 H), 5.10–5.18 (m, 4 H), 5.70–5.79 (m, 2 H), 6.33 (s, 1 H) ppm; ^{13}C NMR (125.9 MHz, $CDCl_3$, 300.0 K), major conformer: δ 14.2, 22.6, 22.8, 25.3, 28.7, 29.4, 29.5, 29.55, 29.63, 29.75, 29.78, 29.79, 29.80, 29.81, 29.82, 32.1, 34.8, 47.6, 48.8, 49.3, 55.6, 89.1, 117.49, 117.49, 133.01, 133.04, 154.8, 173.4 ppm; IR (ATR): $\tilde{\nu}$ 2922, 2853, 1702, 1671, 1460, 1411, 1286, 1244, 1143, 979, 924, 863, 764 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{28}H_{50}LiN_2O_3S$ $[M + Li]^+$ 501.3702, found 501.3712.

(*RS*)-3-Acetyl-4-methylprop-2-yn-1-ylcarbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2t): The carbamate **2t** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and *N*-methylpropargylamine (207 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.22) to obtain 427 mg (1.43 mmol) of a colorless oil (yield: 72%).

^{1}H NMR (500.1 MHz, $CDCl_3$, 300.0 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 53:47): δ 1.29 (s, 3 H), 1.57 (s, 3 H), 1.82 (s, 3 H), 1.94 (s, 3 H), 2.19 (s, 3 H), 2.24–2.26 (m, 1 H), 3.02 (s, 3 H), 4.01 (dd, *J* = 17.8 Hz, *J* = 1.7 Hz, 1 H), 4.10–4.16 (m, 1 H), 6.36 (s, 1 H) ppm; minor conformer: δ 1.31 (s, 3 H), 1.57 (s, 3 H), 1.82 (s, 3 H), 1.94 (s, 3 H), 2.19 (s, 3 H), 2.24–2.26 (m, 1 H), 3.00 (s, 3 H), 4.10–4.13 (m, 2 H), 6.36 (s, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 299.3 K), major conformer: δ 23.3, 25.4, 30.7, 30.8, 32.0, 33.5, 38.4, 52.5, 72.6, 73.3, 78.2, 94.6, 155.1, 170.3 ppm; minor conformer: 23.3, 25.4, 30.7, 30.8, 32.1, 34.3, 38.5, 52.5, 72.6, 73.3, 78.2, 94.5, 154.7, 170.3 ppm; IR (ATR): $\tilde{\nu}$ 2979, 2934, 1704, 1676, 1451, 1393, 1379, 1225, 1127, 980, 917, 849, 767 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{14}H_{22}LiN_2NaO_3S$ $[M + Li]^+$ 305.1511, found 305.1500.

(*RS*)-3-Acetyl-4-diisobutylcarbamoyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2u): The carbamate **2u** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and diisobutylamine (388 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.56) to obtain 573 mg (1.60 mmol) of a colorless solid (yield: 80%).

MP: 49–50 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 298.9 K): δ 0.82–0.89 (m, 12 H), 1.29 (s, 3 H), 1.56 (s, 3 H), 1.81 (s, 3 H), 1.93 (s, 3 H), 1.94–2.02 (m, 2 H), 2.14 (s, 3 H), 2.92–2.99 (m, 2 H), 3.16–3.25 (m, 2 H), 6.36 (s, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 298.8 K): δ 19.9, 20.0, 20.1, 20.3, 23.2, 25.2, 27.0, 27.5, 30.4, 30.7, 32.1, 52.6, 54.7, 55.2, 73.1, 94.1, 155.6, 170.2 ppm; IR (ATR): $\tilde{\nu}$ 2960, 2934, 2872, 1687, 1671, 1470, 1424, 1389, 1310, 1230, 1171, 1074, 764 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{18}H_{34}N_2NaO_3S$ $[M + Na]^+$ 381.2188, found 381.2188.

(*RS*)-3-Acryloyl-4-pyrrolidinocarbonyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2v): The carbamate **2v** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acryloyl chloride (217 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and pyrrolidine (213 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:2, R_f = 0.46) to obtain 304 mg (0.97 mmol) of a colorless oil (yield: 49%).

^{1}H NMR (500.1 MHz, $CDCl_3$, 300.3 K): δ 1.30 (s, 3 H), 1.55 (s, 3 H), 1.84 (s, 3 H), 1.84–1.88 (m, 4 H), 1.98 (s, 3 H), 3.29–3.34 (m, 1 H), 3.35–3.39 (m, 2 H), 3.40–3.45 (m, 1 H), 5.69 (dd, *J* = 1.9 Hz, *J* = 10.4 Hz, 1 H), 6.33 (dd, *J* = 1.9 Hz, *J* = 16.5 Hz, 1 H), 6.50 (s, 1 H), 6.69 (dd, *J* = 10.4 Hz, *J* = 16.5 Hz, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 300.3 K): δ 23.4, 25.0, 25.7, 30.5, 30.7, 32.2, 46.1, 46.3, 52.7, 73.5, 92.3, 129.3, 129.9, 153.5, 165.7 ppm; IR (ATR): $\tilde{\nu}$ 2975, 2936, 2882, 1700, 1668, 1408, 1360, 1284, 1225, 1168, 1074, 980, 862, 763 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{15}H_{24}LiN_2O_3S$ $[M + Li]^+$ 319.1668, found 319.1666.

(*RS*)-3-Acetyl-4-(1,2,3,4-tetrahydroisoquinolin-2-yl)carbonyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2w): The carbamate **2w** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and 1,2,3,4-tetrahydroisoquinoline (400 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:1, R_f = 0.11) to obtain 400 mg (1.10 mmol) of a colorless solid (yield: 55%).

MP: 113–114 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 298.5 K), major conformer (a double signal set is observed due to *E*/*Z*-isomers, ratio 55:45): δ 1.31 (s, 3 H), 1.58 (s, 3 H), 1.86 (s, 3 H), 1.96 (s, 3 H), 2.22 (s, 3 H), 2.86–2.90 (m, 2 H), 3.67–3.82 (m, 2 H), 4.60–4.64 (m, 1 H), 4.66–4.73 (m, 1 H), 6.44 (s, 1 H), 7.10–7.16 (m, 2 H), 7.17–7.22 (m, 1 H) ppm; minor conformer: δ 1.28 (s, 3 H), 1.58 (s, 3 H), 1.87 (s, 3 H), 1.96 (s, 3 H), 2.21 (s, 3 H), 2.86–2.90 (m, 2 H), 3.67–3.82 (m, 2 H), 4.60–4.64 (m, 1 H), 4.66–4.73 (m, 1 H), 6.44 (s, 1 H), 7.10–7.16 (m, 2 H), 7.17–7.22 (m, 1 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 298.7 K), major conformer: δ 23.4, 25.4, 29.1, 30.7, 30.8, 32.0, 42.0, 45.9, 52.7, 73.2, 94.1, 126.5, 126.6, 126.8, 128.8, 133.1, 134.3, 154.3, 170.3 ppm; minor conformer: 23.3, 25.4, 28.8, 30.7, 30.8, 32.0, 41.7, 45.9, 52.7, 73.2, 94.2, 126.4, 126.6, 126.9, 128.9, 132.6, 134.5, 154.5, 170.3 ppm; IR (ATR): $\tilde{\nu}$ 3014, 2973, 2933, 2890, 1693, 1673, 1439, 1388, 1306, 1210, 1084, 975,

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918, 740, 642 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{19}H_{26}N_2NaO_3S$ $[M + Na]^+$ 385.1562, found 385.1571.

(*RS*)-4-Morpholinocarbonyloxy-3-(4-nitrobenzoyl)-2,2,5,5-tetramethyl-1,3-thiazolidine (2x): The carbamate **2x** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), 4-nitrobenzoyl chloride (445 mg, 2.40 mmol), triethylamine (506 mg, 5.00 mmol) and morpholine (261 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 2:1, R_f = 0.42) to obtain 616 mg (1.45 mmol) of a colorless solid (yield: 73%).

MP: 180–181 °C (EtOAc/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$, 299.4 K): δ 1.24 (s, 3 H), 1.65 (s, 3 H), 1.96 (s, 3 H), 2.06 (s, 3 H), 3.25–3.37 (m, 2 H), 3.44–3.55 (m, 2 H), 3.60–3.68 (m, 4 H), 6.10 (s, 1 H), 7.48–7.52 (m, 2 H), 8.24–8.28 (m, 2 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 299.4 K): δ 23.1, 30.9, 31.0, 31.6, 44.0, 44.6, 53.2, 66.6, 66.7, 73.2, 94.4, 124.1, 127.3, 143.3, 148.5, 153.1, 168.8 ppm; IR (ATR): $\tilde{\nu}$ 2988, 2932, 2858, 1703, 1660, 1520, 1371, 1341, 1219, 1114, 1077, 979, 860, 836, 766 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{19}H_{25}N_3NaO_6S$ $[M + Na]^+$ 446.1362, found 446.1354.

(*RS*)-3-Acetyl-4-(4-pyrimidin-2-ylpiperazin-1-yl)carbonyloxy-2,2,5,5-tetramethyl-1,3-thiazolidine (2y): The carbamate **2y** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), acetyl chloride (188 mg, 2.40 mmol), triethylamine (1.113 g, 11.00 mmol) and 1-(2-pyrimidyl)piperazine dihydrochloride (711 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 3:7, R_f = 0.35) to obtain 372 mg (0.95 mmol) of a colorless oil (yield: 47%).

^{1}H NMR (500.1 MHz, $CDCl_3$, 300.2 K): δ 1.32 (s, 3 H), 1.59 (s, 3 H), 1.83 (s, 3 H), 1.95 (s, 3 H), 2.23 (s, 3 H), 3.49–3.68 (m, 4 H), 3.73–3.96 (m, 4 H), 6.42 (s, 1 H), 6.53 (t, *J* = 4.7 Hz, 1 H), 8.32 (d, *J* = 4.7 Hz, 2 H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$, 299.2 K): δ 23.3, 25.4, 30.7, 30.8, 32.0, 43.66, 43.66, 43.71, 44.1, 52.7, 73.3, 94.3, 110.7, 154.3, 157.9, 161.7, 170.3 ppm; IR (ATR): $\tilde{\nu}$ 2991, 2935, 2858, 1698, 1676, 1584, 1495, 1427, 1377, 1212, 1071, 798 cm^{-1}; HRMS (EI 70 eV) *m/z*: calcd for $C_{18}H_{27}N_5O_3S$ $[M]^+$ 393.1829, found 393.1834.

(*R*,S)- and (*R*,R**)-Adipoylbis(2,2,5,5-tetramethylthiazolidine-3,4-diyl) bis(allylcarbamate) (2z)**: The carbamate **2z** was prepared according to the general procedure using 2,2,5,5-tetramethyl-2,5-dihydro-1,3-thiazole (286 mg, 2.00 mmol), adipoyl chloride (183 mg, 1.00 mmol), triethylamine (506 mg, 5.00 mmol) and allylamine (171 mg, 3.00 mmol). The crude product was purified by column chromatography (*n*-hexane/EtOAc 7:3, R_f = 0.17) to obtain 336 mg (0.56 mmol) of a colorless oil (yield: 56%).

^{1}H NMR (500.5 MHz, $CDCl_3$, 300.0 K): δ 1.33 (s, 6 H), 1.56 (s, 6 H), 1.61–1.69 (m, 4 H), 1.80 (s, 6 H), 1.92 (s, 6 H), 2.33–2.41 (m, 2 H), 2.46–2.55 (m, 2 H), 3.73–3.89 (m, 4 H), 4.96–5.03 (m, 2 H), 5.12–5.22 (m, 4 H), 5.78–5.88 (m, 2 H), 6.39 (s, 2 H) ppm; ^{13}C NMR (125.9 MHz, $CDCl_3$, 300.0 K): δ 23.07, 23.07 24.6, 24.7, 30.75, 30.75, 30.76, 30.76, 32.11, 32.11, 36.1, 36.2, 43.54, 43.54, 52.74, 52.74, 73.39, 73.39, 92.59, 92.61, 116.62, 116.62, 134.07, 134.07, 155.26, 155.26, 172.42, 172.42 ppm; IR (ATR): $\tilde{\nu}$ 3343, 2987, 2936, 2872, 1714, 1661, 1519, 1468, 1392, 1378, 1259, 1220, 1143, 1011, 979, 944, 915, 771, 730 cm^{-1}; HRMS (ESI TOF) *m/z*: calcd for $C_{28}H_{46}N_4NaO_6S_2$ $[M + Na]^+$ 621.2756, found 621.2766.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (a) T. Sakakura, J.-C. Choi and H. Yasuda, *Chem. Rev.*, 2007, **107**, 2365; (b) D. J. Darensbourg, *Inorg. Chem.*, 2010, **49**, 10765.
2 (a) A. Correa and R. Martín, *Angew. Chem. Int. Ed.*, 2009, **48**, 6201; (b) D. Yu, S. P. Teong and Y. Zhang, *Coord. Chem. Rev.*, 2015, **293–294**, 279.
3 D. J. Darensbourg, *Chem. Rev.*, 2007, **107**, 2388.
4 (a) S. Pulla, C. M. Felton, P. Ramidi, Y. Gartia, N. Ali, U. B. Nasini and A. Ghosh, *J. CO_2 Util.*, 2013, **2**, 49; (b) Z.-Z. Yang, L.-N. He, J. Gao, A.-H. Liu and B. Yu, *Energy Environ. Sci.*, 2012, **5**, 6602.
5 (a) A. Goeppert, M. Czaun, R. B. May, G. K. Surya Prakash, G. A. Olah and S. R. Narayanan, *J. Am. Chem. Soc.*, 2011, **133**, 20164; (b) W.-J. Yoo, M. Guiteras Capdevila, X. Du and S. Kobayashi, *Org. Lett.*, 2012, **14**, 5326; (c) B. Yu, Z.-F. Diao, C.-X. Guo, C.-L. Zhong, L.-N. He, Y.-N. Zhao, Q.-W. Song, A.-H. Liu and J.-Q. Whang, *Green Chem.*, 2013, **15**, 2401; (d) A. A. Sathe, D. R. Hartline and A. T. Radosevich, *Chem. Commun.*, 2013, **49**, 5040; (e) O. Jacquet, C. Das Neves Gomes, M. Ephritikhine and T. Cantat, *ChemCatChem.*, 2013, **5**, 117; (f) Q.-W. Song, B. Yu, X.-D. Li, R. Ma, Z.-F. Diao, R.-G. Li, W. Li and L.-N. He, *Green Chem.*, 2014, **16**, 1633; (g) Z. Xin, C. Lescot, S. D. Friis, K. Daasbjerg and T. Skrydstrup, *Angew. Chem. Int. Ed.*, 2015, **23**, 6862; (h) J.-H. Ye, L. Song, W.-J. Zhou, T. Ju, Z.-B. Yin, S.-S. Yan, Z. Zhang, J. Li and D.-G. Yu, *Angew. Chem. Int. Ed.*, 2016, **55**, 10022; (i) S. Fenner and L. Ackermann, *Green Chem.*, 2016, **18**, 3804; (j) Q.-W. Song, Z.-H. Zhou and L.-N. He, *Green Chem.*, 2017, **19**, 3707; (k) S. Wang, X. Zhang, C. Cao, C. Chen and C. Xi, *Green Chem.*, 2017, **19**, 4515; (l) Q. Zhang, H.-Y. Yuan, N. Fukaya, H. Yasuda and J.-C. Choi, *ChemSusChem*, 2017, **10**, 1501; (m) Q. Zhang, H.-Y. Yuan, N. Fukaya, H. Yasuda and J.-C. Choi, *Green Chem.*, 2017, **19**, 5614; (n) Q. Zhang, H.-Y. Yuan, N. Fukaya and J.-C. Choi, *ACS Sustainable Chem. Eng.*, 2018, **6**, 6675.
6 J. Paz, C. Pérez-Balado, B. Iglesias and L. Muñoz, *J. Org. Chem.*, 2010, **75**, 3037.
7 A. K. Ghosh and M. Brindisi, *J. Med. Chem.*, 2015, **58**, 2895.
8 M. A. A. Siddiqui and A. J. Wagstaff, *CNS Drugs*, 2006, **20**, 739.
9 D. Luo, L. Liu, P. Han, Q. Wei and H. Shen, *Int. Urogynecol. J.*, 2012, **23**, 983.
10 H.-Z. Bu, W. F. Pool, E. Y. Wu, S. R. Raber, M. A. Amantea and B. V. Shetty, *Drug Metab. Dispos.*, 2004, **32**, 689.
11 R. L. Baron and T. L. Merriam, In *Reviews of Environmental Contamination and Toxicology: Toxicology of Aldicarb*; G. W. Ware, Eds.; Springer: New York, 1988, **105**, 1.
12 (a) S. L. Peterson, S. M. Stucka and C. J. Dinsmore, *Org. Lett.*, 2010, **12**, 1340; (b) D. Chaturvedi, *Tetrahedron*, 2012, **68**, 15.

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13 W. Xiong, C. Qi, H. He, L. Ouyang, M. Zhang and H. Jiang, *Angew. Chem. Int. Ed.*, 2015, **54**, 3084.
14 (a) I. Ugi, *J. Prakt. Chem.*, 1997, **339**, 499; (b) A. Dömling, I. Ugi, *Angew. Chem. Int. Ed.*, 2000, **39**, 3168.
15 E. Ruijter, R. Scheffelaar, R. V. A. Orru, *Angew. Chem. Int. Ed.*, 2011, **50**, 6234.
16 A. Sehlinger, R. Schneider and M. A. R. Meier, *Macromol. Rapid Commun.*, 2014, **35**, 1866.
17 T. Stalling, W. Saak and J. Martens, *Eur. J. Org. Chem.*, 2013, 8022.
18 For efforts on the diversity of *N*-acyliminium ions, see: P. Wu and T. E. Nielsen, *Chem. Rev.*, 2017, **117**, 7811.
19 The *N*-acylation of imines is well-known. For original efforts on this topic, see: (a) T. C. James and C. W. Judd, *Chem. Soc., Trans.*, 1914, **105**, 1427; (b) H. Leuchs, G. Wulkow and H. Gerland, *Chem. Ber.*, 1932, **62**, 1586. For efforts on this topic dealing with 2,5-dihydro-1,3-thiazoles, see: W. Schwarze, K. Drauz and J. Martens, *Chem.-Ztg.*, 1987, **111**, 149.
20 T. Schlüter, A. Ziyaei Halimehjani, D. Wachtendorf, M. Schmidtmann and J. Martens, *ACS Comb. Sci.*, 2016, **18**, 456.
21 For an example for the conversion of anline with carbon dioxide, see: M. Feroci, A. Inesi, L. Rossi, *Tetrahedron Lett.*, 2000, **41**, 963.
22 A. Sehlinger, T. Stalling, J. Martens and M. A. R. Meier, *Macromol. Chem. Phys.*, 2014, **215**, 412.
23 Step a) has been described: H. Böhme and K. Hartke, *Chem. Ber.*, 1963, **96**, 600.
24 G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw and K. I. Goldberg, *Organometallics*, 2010, **29**, 2176.
25 D. Kröger, T. Schlüter, M. Fischer, I. Geibel and J. Martens, *ACS Comb. Sci.*, 2015, **17**, 202.
26 All acyl chlorides were obtained by the conversion of the corresponding carboxylic acids with $SOCl_2$. For an example, see: M. Pittelkow, U. Boas, M. Jessing, K. J. Jensen and J. B. Christensen, *Org. Biomol. Chem.*, 2005, **3**, 508.