Conference paper

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1,3-Oxazinan-2-ones via carbonate chemistry: a facile, high yielding synthetic approach

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Abstract: A high yielding synthesis of 1,3-oxazinan-2-ones starting from 3-amino-1-propanols and ethylene carbonate (EC) in the presence of catalytic amount of triazabicyclodecene (TBD) is herein reported. The formation of six-membered cyclic carbonates was achieved by intermolecular cyclization reaction via double $B_{Ac}2$ mechanism. Cyclization reactions have been carried out in neat as EC acted both as solvent and reagent. Pure 1,3-oxazinan-2-ones were isolated in high yield by simple liquid-liquid extraction. Further purification can be achieved by recrystallization. The reaction resulted of general application on different substrates including an aryl bis(3-amino-proan-1-ol) compound.

Keywords: Carbonate chemistry; cyclic carbamates; cyclizations; Green Chemistry V; oxazin-2-ones.

Introduction

Since the 1980s, when it was first synthesized by a green process [1], dimethyl carbonate (DMC) has found ever-growing applications both in industrial [2–5] and laboratory scale process [6–8]. Its success as solvent and reagent can be ascribed to several highly appealing features, i.e. easy and clean synthesis [1, 9, 10], low toxicity, high selectivity and flexible reactivity [11, 12].

DMC is a well known environmentally benign substitute for dimethyl sulfate and methyl halides in methylation reactions, and for phosgene in carboxymethylation reactions. In fact, in the presence of a nucleophile and a catalyst or a base, DMC can act either as methylating agent [13, 14] ($B_{Al}2$ mechanism) or carboxymethylating agent [15, 16] ($B_{Ac}2$ mechanism) giving as by-products only methanol and eventually CO_2. Similarly, commercially available short chain dialkyl carbonates (DACs) have found numerous applications in innovative synthetic pathways and industrial processes [17–19].

It is noteworthy that DACs have also been employed as sacrificial molecules in the chlorine-free, high yielding synthesis of numerous heterocycles [20–24].

It has been reported, for instance, a convenient one-pot procedure for O-and N-based 5- and 6-membered heterocycles (Fig. 1, eqs. 1–3) [25] including industrially appealing compounds such as ambroxan and isosorbide (Fig. 1, eqs. 5–6) [17–19].

Furthermore, preliminary results on novel nitrogen mustard carbonate analogs, synthesized by DMC chemistry, have shown that they can be used for the preparation of piperidine derivatives in good yield (Fig. 1, eq. 4) [26].

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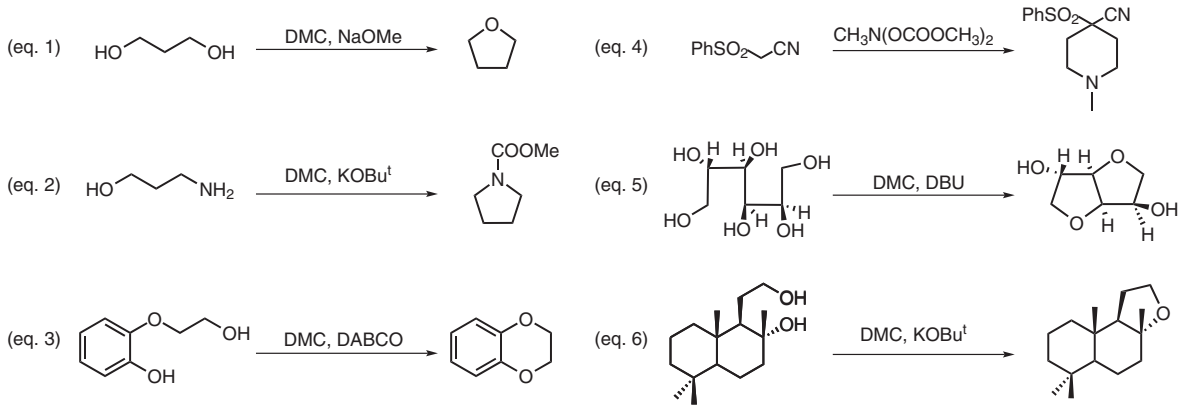


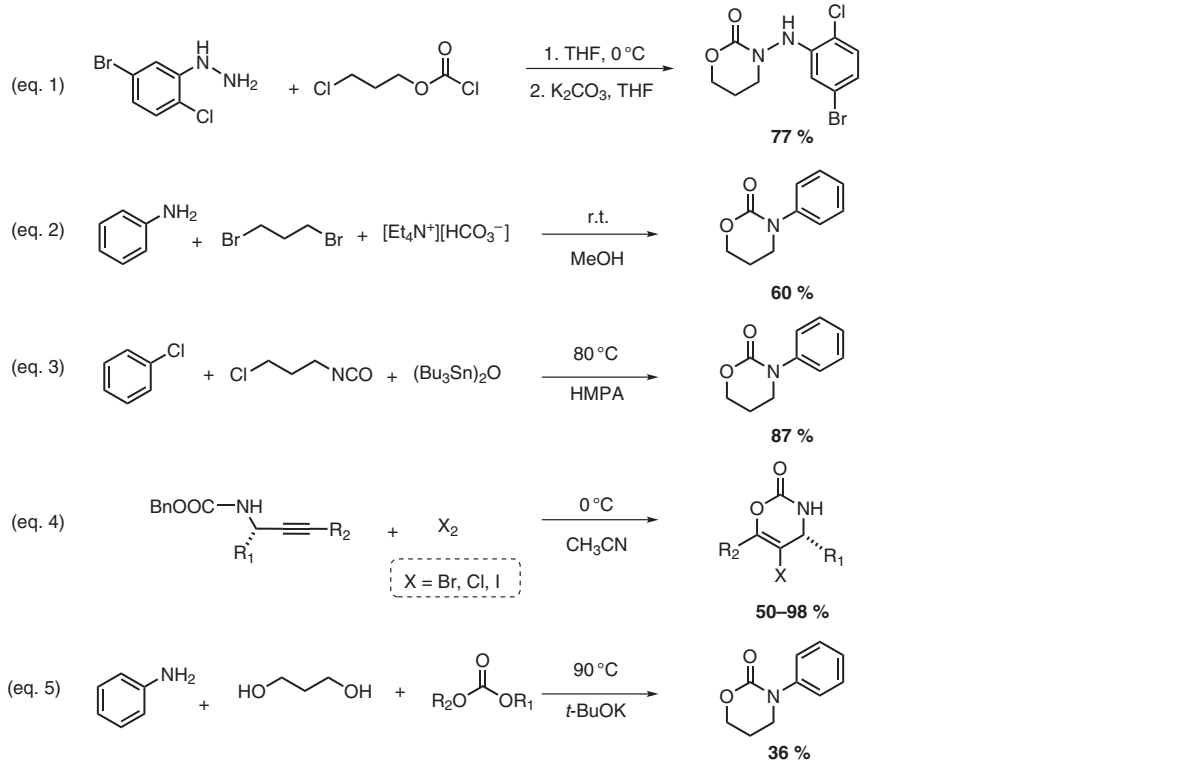
Fig. 1: Some examples of cyclization by DACs chemistry [17–28].

Recently, a one-pot convenient route to six-membered cyclic carbamates 1,3-oxazinan-2-ones has also been reported by DACs chemistry [27, 28].

Six-membered cyclic carbamates are of great interest due to their biological activity. In fact, they have been used in the treatment of Alzheimer's disease [29], diseases related to kinases activity [30] and to the activation of β3-adrenoceptor [31], as well as in the regulation of cholesterol [32]. Furthermore they have found application as herbicides with excellent crop–weed selectivity [33].

1,3-Oxazinan-2-ones have also been employed as monomers for the preparation of hyperbranched polyamines [34–36] or polyurethane by cationic ring-opening polymerisation (ROP) [37]. The major drawback of this approach is that cyclic urethanes are not easy to synthesize and give only moderate to low yields.

There are many synthetic routes to 1,3-oxazinan-2-ones. However, most of them involve phosgene or its derivatives [38, 39] (eq. 1, Scheme 1), alkyl halide chemistry [40–42] (eq. 2, Scheme 1) and isocyanate



Scheme 1: Synthetic approaches to 1,3-oxazinan-2-ones [38–50].

compounds [43, 44] (eq. 3, Scheme 1). Other procedures require complex starting materials [45–48] (eq. 4, Scheme 1) or multiple steps to give the final product [49, 50].

Recently our research group has reported a new synthetic approach to these heterocycles by DACs chemistry (eq. 5, Scheme 1). Six-membered cyclic carbamates were prepared in modest to good yield (44–68 %) by reaction of an amine with a dicarbonate derivative of 1,3-diols in the presence of a strong base [27]. Attempt to achieve 1,3-oxazinan-2-ones by a one-pot reaction of an amine with a 1,3-diol and a dialkyl carbonate (DAC) in the presence of a strong base was also attempted resulting in the formation of the cyclic carbamates in moderate yields (17–56 %) [28].

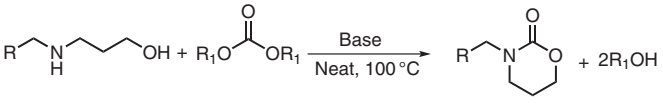
Although the synthesis of 1,3-oxazinan-2-ones via DACs were identified by EATOS software and Andraos spreadsheets analysis as very promising on the basis of their low environmental impact [51], these reactions are complicated by the formation of numerous by-products that affect the yield of the desired products. In fact, in addition to the intramolecular cyclization leading to the 1,3-oxazinan-2-one, several concurrent reactions take place resulting in the formation of aromatic carbamates, aromatic ureas and aliphatic and aromatic carbonates. As a result, although cyclic carbamates are achieved as major products, they have to be recovered by time-consuming column chromatography.

In this paper we report a high yielding and convenient approach to 1,3-oxazinan-2-ones via DACs chemistry.

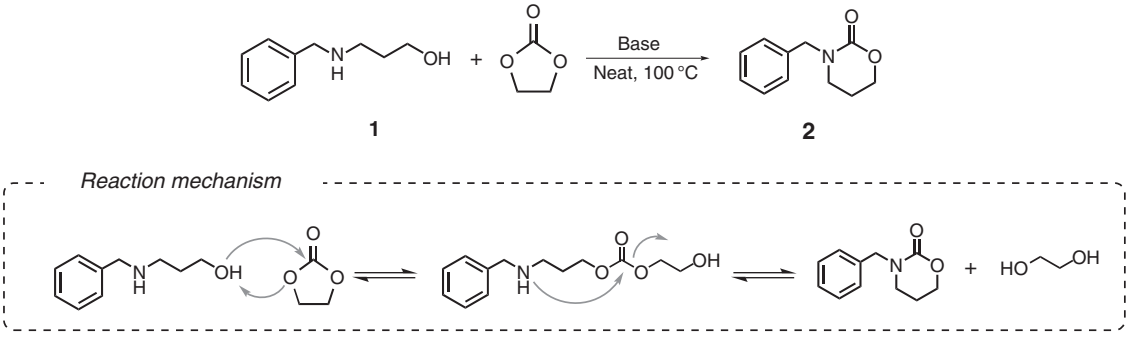
Substituted 3-amino-1-propanols, easily prepared by reductive amination, are shown to undergo efficient intermolecular cyclization in the presence of several DACs and in particular of ethylene carbonate (EC), in the presence of catalytic amount of a bicyclic nitrogen base (Scheme 2). This new synthetic procedure requires only a minimal work-up and result of general application on several substrates.

Results and discussion

In a first set of experiments the synthesis of 3-benzyl-1,3-oxazinan-2-one **2** was investigated [27, 28]. 3-(Benzylamino)propan-1-ol **1** was easily synthesized in 80 % yield by via reductive amination. The so-formed amino-alcohol **1** was then subject to intermolecular cyclization with EC (1.0:1.0 molar ratio) in the presence of a base (1.0 mol eq.) and acetonitrile as reaction medium (Scheme 3, Table 1). The yield of the cyclic carbamate **2** was calculated by a GC-MS calibration curve. In selected experiments 3-benzyl-1,3-oxazinan-2-one **2** was isolated as pure by a water/organic solvent extraction.



Scheme 2: Synthesis of 1,3-oxazin-2-one by intermolecular cyclization aided by DACs.



Scheme 3: Synthesis of 3-benzyl-1,3-oxazinan-2-one **2**.

Table 1: Synthesis of 3-benzyl-1,3-oxazinan-2-one **2** by reaction of 3-(benzylamino)-1-propanol with EC in the presence of different catalysts in CH_3CN at reflux.[a]

#	Base (mol eq.)	Time (h)	Conv. (%)	GC-MS yield 2 (%)[b]
1	K_2CO_3 (1.0)	24	0	0
2	NaOMe (1.0)	24	76	72 (58)[c]
3	*t*-BuOK (1.0)	24	72	70 (60)[c]
4	KW2000 (1:1 w)	24	0	0
5	Et_3N (1.0)	24	0	0
6	DMAP (1.0)	24	0	0
7	DBU (1.0)	24	91	85 (50)[c]
8	DABCO (1.0)	24	0	0
9	TBD (1.0)	6	100	100 (88)[c]

[a]Reaction conditions: 3-(benzylamino)-1-propanol (0.25 g, 1.00 mol eq.), EC (0.13 g, 1.00 mol eq.), base (1.00 mol eq.), CH_3CN (20 mL), T = 100 °C; [b]Yield calculated via calibrated GC-MS analysis with *p*-xylene as external standard; [c]Isolated yield.

Strong bases such as sodium methoxide (entry 2, Table 1) and potassium *t*-butoxide (entry 3, Table 1) resulted more effective in the intermolecular cyclization than the weak base K_2CO_3 (entry 1, Table 1). Hydrotalcite KW2000, an amphoter catalyst, showed no efficiency in the cyclization reaction (entry 4, Table 1). A series of aliphatic, aromatic and bicyclic nitrogen bases were also investigated, i.e. triethylamine, 4-dimethylaminopyridine (DMAP), 1,4-diazabicyclo[2.2.2]octane (DABCO), 1,5-diazabiciclo(5.4.0)undec-5-ene (DBU) and triazabicyclodecene (TBD). It should be pointed out that among the bicyclic bases selected for this study DABCO is a simple amine, meanwhile DBU has an amidine structure and TBD a guanidine one and it is therefore the strongest base. In particular, the basicity scale of biciclyc nitrogen compounds follow the trend, i.e. TBD > DBU >> DABCO [52].

As reported in Table 1 only DBU (entry 7) and TBD (entry 9) were capable of promoting the formation of the cyclic carbamate in good yield. In particular, the reaction performed with TBD, showed a quantitative conversion and selectivity toward the cyclic carbamate after only 6 h. It is also noteworthy that the pure 3-benzyl-1,3-oxazinan-2-one **2** was easily isolated by a liquid-liquid extraction in 88 % yield.

The reactivity of DMC and in general of DACs in the presence of the nitrogen bicyclic base has been extensively investigated although studies mainly focused on DBU [53–57]. Organic carbonates seem to be activated by DBU via the formation of *N*-alkoxycarbonyl DBU derivatives which are better electrophiles than DMC. In our case study, DBU, as well as TBD, might be involved in a similar reaction mechanism that favors two subsequent alkoxycarbonyl reactions via $B_{Ac}2$ mechanism. In this case study, the enhanced efficiency of TBD in the intermolecular cyclization of **1** (reaction time 6 h) might be ascribed to its higher strength as a base compared to DBU (reaction time 24 h).

Several reaction parameters were then investigated (Table 2). Interestingly, the reaction outcome was not affected by reducing the amount of solvent (entry 2, Table 2). Surprisingly, when the reaction was conducted

Table 2: Synthesis of 3-benzyl-1,3-oxazinan-2-one by reaction of 3-(benzylamino)-1-propanol with EC in neat and in the presence of different amount of TBD.[a]

#	TBD (mol eq.)	CH_3CN (mL)	Time (h)	Conv. (%)	GC-MS yield 2 (%)
1[b]	1.0	20	6	100	100 (88)[c]
2	1.0	5	6	100	100 (70)[c]
3	1.0	–	2	100	100 (66)[c]
4	0.5	–	2	100	100 (72)[c]
5	0.2	–	2	100	100 (86)[c,d]
6	0.1	–	9	100	100 (86)[c]
7	0.05	–	30	100	100 (99)[c]

[a]Reaction conditions: 3-(benzylamino)-1-propanol (0.25 g, 1.00 mol eq.), EC (0.13 g, 1.00 mol eq.), T = 100 °C; [b]This results is reported from entry 9, Table 1; [c]Isolated yield; [d]This reaction was conducted on 2 g of 3-(benzylamino)-1-propanol.

Table 3: Synthesis of 3-benzyl-1,3-oxazinan-2-one by reaction of 3-(benzylamino)-1-propanol with different DACs in the presence of catalytic amount of TBD.[a]

#	DAC (mol eq.)	Time (h)	Conv. (%)	GC-MS yield 2 (%)
1	DMC	4	100	100 (70)[b]
2	DEC	4	100	100 (80)[b]
3	DPC	4	100	100 (57)[b]
4[c]	EC	2	100	100 (99)[b]

[a]Reaction conditions: 3-(benzylamino)-1-propanol (0.25 g, 1.00 mol eq.), DACs (1.00 mol eq.), TBD (42.00 mg, 0.20 mol eq.), T = 100 °C; [b]Isolated yield; [c]This reaction is from Table 2 entry 5 and it is reported here from clarity.

in neat by directly mixing 3-amino-1-propanol **1**, EC and TBD (1:1:1 molar ration), cyclic carbamate **2** not only formed in quantitative yield, but the reaction rate was faster than in the presence of a solvent (entry 3, Table 2).

Further experiments showed that the amount of TBD can be decreased up to 5 % mol without affecting the reaction yield. (entries 4–7, Table 2).

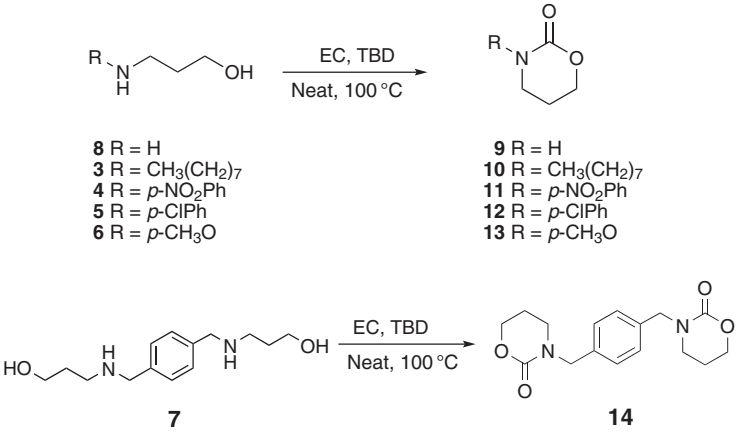
Despite the intermolecular cyclization being effective in all cases, the reaction time required for the quantitative conversion of the substrate increased proportionally when smaller amounts of TBD were employed. In fact, when the reaction was carried in the presence of 0.05 mol of TBD it required 30 h to go to completion (entry 7, Table 2).

The synthesis of cyclic carbamate **2** was then investigated in the presence of different DACs; the results are reported in Table 3. In this set of experiments 3-(benzylamino)propan-1-ol **1** was reacted in the presence of 0.2 mol of TBD with the selected DAC, i.e. DMC, diethyl carbonate (DEC) and diphenyl carbonate (DPC). Results were compared with those achieved using EC (entries 1–4, Table 3).

All of the commercially available DACs investigated showed a similar reactivity, however, the reaction conducted in the presence of EC resulted in a faster reaction rate (entry 4, Table 3). This could be possibly ascribed to the formation of ethylene glycol as by-product that might aid the cyclization functioning as reaction medium. When DPC was used as DAC, the formation of a large excess of phenol rendered the work-up of the reaction a bit more tedious. This finding might also explain the lower isolated yield of the cyclic carbamate **2** (entry 3, Table 3).

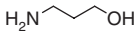
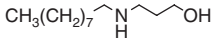
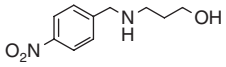
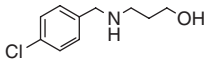
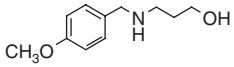
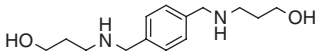
The general applicability of this improved synthetic approach was then tested on several substituted 3-amino-1-propanol. Octanal, *p*-nitro, *p*-chloro and *p*-methoxybenzaldehyde were reacted with commercially available 3-amino-1-propanol to achieve compounds **3–6** in high yield (91–97 %) via reductive amination. The modest yield (30 %) achieved for the synthesis of the bis-amino-alcohol **7** is due to its high polarity that render it quite soluble in the aqueous phase in the purification procedure.

The so-prepared substituted 3-amino-1-propanols **3–7** were tested in the intermolecular cyclization with EC catalyzed by TBD in neat as reported in Scheme 4. Cyclization of simple 3-amino-1-propanol **8** was also investigated for the synthesis of 1,3-oxazinan-2-one **9**. The results are reported in Table 4.



Scheme 4: Synthesis of 1,3-oxazinan-2-one structures by reaction of 3-amino-1-propanols **3–8** with EC in the presence of TBD.

Table 4: Synthesis of 1,3-oxazinan-2-one by reaction of several 3-amino-1-propanol with EC in the presence of catalytic amount of TBD.[a]

#	Substrate	Time (h)	Yield[b] (%)
1		5	**9** 43
2		2	**10** 93
3		6	**11** 97
4		7	**12** 95
5		19	**13** 97
6		97	**14** 78

[a]Reaction conditions: 3-amino-1-propanol (2.00 g, 1.00 mol eq.), EC (0.90 g, 1.00 mol eq.), TBD (0.28 g, 0.20 mol eq.), T = 100 °C, conversion of the substrate was always quantitative. [b]Isolated yield.

In a typical experiment the selected substituted 3-amino-propanol **4–8** was reacted with EC in neat with a catalytic amount of TBD (0.2 eq. mol) at 100 °C. The reaction was followed by GC-MS until disappearance of the starting material. Thus, the mixture was cooled down and extracted in an organic/water mixture. The organic phase was evaporated under vacuum to recover the pure cyclic carbamates **10–14**. Isolated yield of aliphatic and aromatic 1,3-oxazinan-2-ones varies from 93 to 97 % yield (entries 2–5, Table 4). In most cases it was also possible to further purify the products by crystallization in warm diethyl ether. The only exception to this procedure is related to the synthesis of the unsubstituted 1,3-oxazinan-2-one **9**, which is partially soluble in water. Therefore, its purification was carried out by column chromatography.

Noteworthy, this synthetic approach proved to be effective also in the synthesis of the aryl bis(1,3-oxazinan-2-one) **14**. This compounds was isolated as pure in 78 % yield by double intermolecular cyclization. Further purification of the compound **14** by crystallization in hot diethyl ether and dichloromethane resulted in the formation of transparent laminar crystals, suitable for an X-ray diffraction analysis as reported in Fig. 2 [58].

In the crystals of **14**, the two halves of the molecule are symmetry-related through an inversion center. The values of the torsion angles N3–C7–C8–C10 and C4–N3–C7–C8 are 23.1(3)° and 72.9(2)°, respectively (the corresponding torsion angles in the second half of the molecule have opposite signs). As a result, the molecule is significantly bent at the level of the methylene junctions, and the 1,3-oxazinan-2-ones rings are nearly perpendicular to the central phenyl ring. The conformation of the 1,3-oxazinan-2-one ring is close to the $^5H_6$

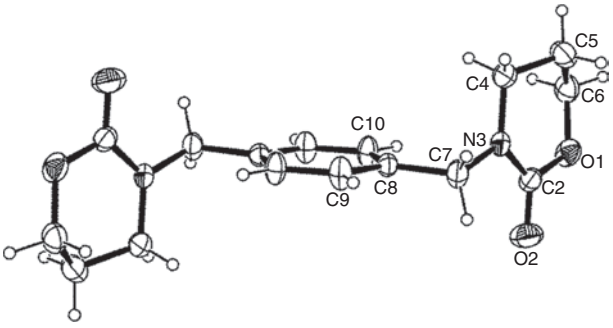


Fig. 2: X-ray diffraction structure of 3,3′-(1,4-phenylenebis(methylene))bis(1,3-oxazinan-2-one) **14** with atom labelling of the asymmetric unit. Anisotropic displacement parameters for the non-hydrogen atoms are drawn at the 30 % probability level.

(half-chair) disposition, with the following puckering parameters [59] relative to the atom sequence O1–C2–N3–C4–C5–C6: $Q_T = 0.463(2)$ Å, $\theta_2 = 48.9(2)°$, and $\phi_2 = 259.2(3)°$.

Conclusion

In this work an improved synthesis of 1,3-oxazinan-2-ones is reported. Substituted 3-amino-1-propanols, prepared by simple reductive amination, are shown to undergo efficient intermolecular cyclization with EC in the presence of catalytic amount of TBD. The procedure resulted of general application for the synthesis of aliphatic and aromatic 1,3-oxazin-2-ones via a double $B_{Ac}2$ reaction mechanism. Advantages of this reaction procedure include: easy set up and work-up of the reactions, high isolated yield, more sustainable reaction conditions, fast reaction rate and absence of any by-products. In addition, EC works perfectly both as solvent and reagent in the cyclization reaction that is carried out in neat. Other DACs could be used for the reaction although EC resulted the most efficient one.

Compared to previously reported synthetic procedures of 1,3-oxazin-2-ones, this approach avoids the use of toxic reagents such as phosgene [38, 39], alkyl halides [40–42], and isocyanate compounds [43, 44], and it does not require complex starting materials [45–48] or multiple steps to give the final product [49, 50]. Furthermore, it results in a higher yield than the previously published DACs-based procedure. As a result this synthetic approach might open the way to further exploitation of these compounds as monomers of new polymers.

Experimental section

Experimental details

In general, all reagents were purchased by Sigma Aldrich and used without any further purification. Mass spectra were run on GC-MS Agilent Technologies (GC System 6890N Network, Agilent Technologies Mass Selective Detector 5973, capillary column of silice HP-5). ^{1}H NMR spectra were recorded on a Varian Unity (400 MHz) instrument and ^{13}C NMR spectra were recorded on a Bruker AC 200 (200 MHz) instrument at 25 °C and in $CDCl_3$. Melting point analyses were obtained on an Büchi 335.

General procedure for the synthesis of 3-amino-1-propanols 1 and 3–7

To a stirring solution of 3-amino-1-propanol (3.00 g, 28.26 mmol, 1.00 mol eq.) in methanol (20 mL), was added aldehyde (28.26 mmol, 1.00 mol eq.). The reaction was cooled to 0 °C in a ice bath, and sodium borohydride (1.07 g, 28.26 mmol, 1.00 mol eq.) was added portion-wise over a period of 15 min. The mixture was stirred at 0 °C for an additional 1 h. Water (50 mL) was added to the reaction and most of the methanol was removed by evaporation under vacuum. The resulting aqueous solution was extracted with dichloromethane (3 × 50 mL). The organic phase was dried over sodium sulfate, filtered, and concentrated in vacuum to yield the secondary amine product.

3-phenylmethylamino-propan-1-ol 1 [60]

Oil product (3.65 g, 22.10 mmol, yield 80 %) had *m/z* Calc. for $C_{10}H_{15}NO$ 165.12 found: 165.1. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.71 (m, 2H), 2.86 (t, J = 4.3 Hz, 2H), 3.52 (s, 2H), 3.77 (s, 4H), 7.34–7.23 (m, 5H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 30.54, 48.65, 53.56, 63.44, 126.95, 127.95, 128.23, 138.96.

3-(4-octylbenzylamino)propan-1-ol 3 [61]

For this compound after the addition of $NaBH_4$ the reaction was left stirring for additional 5 h. The final product (4.34 g, 23.18 mmol, yield 99 %) had *m*/*z* Calc. for $C_{11}H_{25}NO$ 187.19 found: 187.2. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.83 (m, 3H), 1.22 (s, 10H), 1.42 (s, 2H), 1.66 (m, 2H), 2.55 (m, 2H), 2.81 (m, 2H), 3.61 (s, 2H), 3.73 (m, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 13.78, 22.34, 26.89, 28.91, 29.03, 29.12, 29.86, 31.50, 49.25, 63.47.

3-(4-nitrobenzylamino)propan-1-ol 4 [62]

Oil product (3.80 g 18.07 mmol, yield 91 %) had *m*/*z* Calc. for $C_{10}H_{14}N_2O_3$ 210.10 found: 210.1. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.75–1.70 (m, 2H), 2.85 (t, J = 5.9 Hz, 2H), 3.02 (s, 2H), 3.76 (t, J = 5.9 Hz, 2H), 3.88 (s, 2H), 7.80 (dd, J = 271.7 Hz, 8.7 Hz, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 30.79, 48.69, 52.85, 63.28, 123.46, 126.65, 128.54, 146.59.

3-(4-chlorobenzylamino)propan-1-ol 5 [63]

Oil product (3.92 g 19.63 mmol, yield 92 %) had *m*/*z* Calc. for $C_{10}H_{14}ClNO$ 199.08 found: 199.1. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.75–1.66 (m, 2H), 2.86 (t, J = 5.8 Hz, 2H), 3.25 (s, 2H), 3.79–3.74 (m, 4H), 7.33–7.16 (m, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 30.50, 48.62, 52.81, 63.49, 128.35, 129.29, 132.69, 137.39.

3-(4-methoxybenzylamino)propan-1-ol 6 [64]

Oil product (4.16 g, 21.30 mmol, yield 97 %) had *m*/*z* Calc. for $C_{11}H_{17}NO_2$ 195.13 found: 195.2. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.75–1.70 (m, 2H), 2.16 (s, 2H), 2.89 (t, J = 5.7 Hz, 2H), 3.78–3.75 (m, 7H), 7.04 (dd, J = 152.3 Hz, 7.5 Hz, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 30.31, 48.74, 52.92, 55.00, 63.80, 113.64, 129.20, 130.91, 154.14.

3,3′-(1,4-phenylenebis(methylene))bis(azanediyl)di propan-1-ol 7

For this compound the starting aldehyde (terephthalaldehyde) was used in 0.5 mol eq. (1.89 g, 14.13 mmol). Oil product (1.07 g, 4.24 mmol, yield 30 %) had GC-MS: calc. for $C_{14}H_{24}N_2O_2$ 252.18 found: 252.1. HRMS (CI): calc. for $[C_{14}H_{24}N_2O_2 + H]$+: 253.1916; found 253.1909. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.67–1.73 (m, 4H), 2.87 (t, J = 6 Hz, 4H), 3.75 (s, 4H), 3.77–3.80 (m, 4H), 7.23 (s, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 30.58, 48.88, 53.34, 63.75, 128.01, 138.22.

General procedure for the synthesis of 3-benzyl-1,3-oxazinan-2-ones

3-Phenylmethylamino-propan-1-ol (2.00 g, 10.47 mmol, 1.00 mol eq.), EC (0.92 g, 10.47 mmol, 1.00 mol eq.) and TBD (0.184 g, 2.09 mmol, 0.20 mol eq.) were placed in a round bottom flask equipped with magnetic stirred and with a reflux condenser. The reaction mixture was then heated at 100 °C while stirring. The progress of the reaction was monitored by TLC. After 2 h the reaction was stopped, cooled at room temperature. Water was added to the reaction (50 mL) and the resulting aqueous solution was extracted with diethyl ether (3 × 50 mL). The organic phase was dried over sodium sulfate, filtered and concentrated in vacuum to recover the product.

3-Benzyl-1,3-oxazinan-2-one 2 [27]

McElroy et al. was obtained as pure in 86 % (1.72 g, 9.00 mmol). The oil was recrystallized in diethyl ether to give a white crystalline solid. The product had m.p. 38–40 °C, *m/z* calc. for $C_{11}H_{13}NO_2$ 191.09 found: 191.1. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.96–1.84 (m, 2H), 3.14 (t, J = 6.2 Hz, 2H), 4.16 (t, J = 8Hz, 2H), 4.47 (s, 2H), 7.23 (s, 5h). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 21.96, 44.10, 52.37, 66.24, 127.38, 127.81, 128.40, 136.45, 153.68.

Tetrahydro-1,3-oxazin-2-one 9 [65]

After extraction the pure compound was isolated by silica gel chromatography using CH_2Cl_2/MeOH as elution solvent in 95/5 ratio to afford the product as white solid in 43 % (1.16 g, 11.45 mmol). The product had m.p. 78–82 °C, *m/z* calc. for $C_4H_7NO_2$ 101.05 found: 101.1. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.91–1.80 (m, 2H), 3.24 (t, J = 6.0 Hz, 2H), 4.17 (t, J = 8.2 Hz), 6.99 (s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 20.75, 39.22, 66.49, 154.67.

3-Octyl-1,3-oxazinan-2-one 10

The product was obtained as pure in 93 % (2.07 g, 9.74 mmol). GC-MS: calc. for $C_{12}H_{23}NO_2$ 213.17 found: 213.2. HRMS (EI): calc. for $C_{12}H_{23}NO_2$ 213.1729; found 213.1725. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.82–0.79 (m, 3H), 1.23 (m, 10H), 1.51 (m, 2H), 2.00–1.94 (m, 2H), 3.26–3.22 (m, 4H), 4.18–4.15 (m, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 13.70, 21.97, 22.25, 26.35, 26.70, 28.84, 28.99, 31.40, 44.73, 49.19, 66.03, 153.13.

3-(4-Nitrobenzyl)-1,3-oxazinan-2-one 11

The product was obtained as pure in 97 % (1.45 g, 6.15 mmol). The oil was recrystallized in diethyl ether to give a orange crystalline solid. The product had m.p. 138–140 °C. GC-MS: calc. for $C_{11}H_{12}N_2O_4$ 236.08 found: 236.1. HRMS (EI): calc. for $C_{11}H_{12}N_2O_4$ 236.0797; found 236.0799. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.17–1.96 (m, 2H), 3.28 (t, J = 6.2 Hz, 2H), 4.32 (t, J = 5.4 Hz, 2H), 4.65 (s; 2H), 7.80 (dd, J = 291.4 Hz, 8.8 Hz, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 21.97, 44.81, 51.98, 66.41, 123.71, 128.36, 144.01, 153.60.

3-(4-chlorobenzyl)1,3-oxazinan-2-one 12

The product was obtained as pure in 95 % (2.14 g, 9.51 mmol). The product was recrystallized in diethylether to give a white crystalline solid. The product had m.p. 52–54 °C, GC-MS: calc. for $C_{11}H_{12}ClNO_2$ 225.06 found: 225.1. HRMS (EI): calc. for $C_{11}H_{12}ClNO_2$ 225.0556; found 225.0557. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.03–1.96 (m, 2H), 3.21 (t, J = 6.2 Hz, 2H), 4.26 (t, J = 4Hz, 2H), 4.51 (s, 2H), 7.29–7.25 (m, 5H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 21.92, 44.19, 51.75, 66.29, 128.57, 129.20, 133.23, 135.00, 153.66.

3-(4-Methoxy-benzyl)-tetrahydro-[1,3]oxazin-2-one 13 [66]

The product was obtained as pure in 97 % (2.19 g, 9.93 mmol). The oil can be recrystallized in hot diethyl ether to give a white crystalline solid. The cyclic carbamate had m.p. 57–59 °C. GC-MS calc. for $C_{12}H_{15}NO_3$ 221.11 found: 221.2. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.01–1.95 (m, 2H), 3.19 (t, J = 6.2 Hz, 2H), 3.80 (s, 3H), 4.24 (t, J = 5.2 Hz, 2H), 4.49 (s, 2H), 7.05 (dd, J = 149.8 Hz, 8.6 Hz, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 21.95, 43.83, 51.77, 54.99, 66.17, 113.75, 128.54, 129.27, 153.63, 158.90.

3,3′-(1,4-phenylenebis(methylene))bis(1,3-oxazinan-2-one) 14

For this compound the amount of EC was 2.00 mol eq. (1.40 g, 15.85 mmol) and the amount of TBD was 0.40 mol eq. (0.44 g, 3.17 mmol). The product was obtained as pure in 78 % (1.88 g, 6.17 mmol). The oil can be recrystallized in hot diethyl ether and dichloromethane to give a white crystalline solid (see supporting information). The cyclic carbamate had m.p. 168–170 °C. HRMS (EI): calc. for $C_{16}H_{20}N_2O_4$ 304.1423 found: 304.1418. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.18–1.86 (m, 4H), 3.23 (t, J = 6.2 Hz, 4H), 4.28 (t, J = 4 Hz, 4H), 4.55 (s, 4H), 7.27 (s, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 21.97, 44.26, 52.07, 66.26, 128.06, 135.93, 153.66.

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