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1,3-Oxazinan-2-ones from Amines and 1,3-Diols through Dialkyl Carbonate Chemistry

Con Robert McElroy, Fabio Aricò, Pietro Tundo*

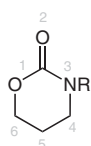
Università Ca' Foscari di Venezia, Dipartimento Scienze Ambientali, Informatica e Statistica, Dorsoduro 2137, 30123 Venice, Italy
Fax +39(041)2348620; E-mail: tundop@unive.it

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Abstract: A one-pot green synthesis of 1,3-oxazinan-2-ones from amines and 1,3-diols in the presence of a dialkyl carbonate and potassium *tert*-butoxide is described. Four dialkyl carbonates were utilised: dimethyl carbonate, diethyl carbonate, diprop-2-yl carbonate, and *tert*-butyl methyl carbonate. The more hindered the dialkyl carbonate used, the higher the yield of 1,3-oxazinan-2-one. Four 1,3-diols were reacted having primary–primary, primary–secondary, primary–tertiary, and secondary–tertiary functionalities, with the yield of oxazinanone decreasing with increasing hindrance of the diol. In the case of the diols containing primary and either secondary or tertiary functionality, the substituent(s) were selectively found in the 6-position of the so-formed oxazinanone. The optimized conditions were then employed with different nucleophiles, namely phenylhydrazine, aniline, and *n*-octylamine.

Key words: green chemistry, cyclisation, heterocycles, diols, dialkyl carbonates

1,3-Oxazinan-2-ones (Figure 1) are compounds of great interest due to their biological activity. In fact, recently, they have appeared in numerous patents as intermediates in the synthesis of pharmaceutical drugs used in the treatment of Alzheimer,¹ diseases mediated by the activation of β 3-adrenoceptor, diseases related to kinases activity,³ and for the regulation of cholesterol.⁴ They are also used as herbicides with excellent crop-weed selectivity.⁵



R = aromatic, aliphatic

Figure 1 The 1,3-oxazinan-2-one motif

There are many routes to 1,3-oxazinan-2-ones, the majority involve phosgene and isocyanate⁶ or alkyl halide⁷ chemistry, while those that are considered green routes either require not easy available starting materials⁸ or mul-

tiples steps.⁹ Recently, our group described a new route to 1,3-oxazinan-2-ones, via the two-step reaction of a primary amine or phenylhydrazine with a dicarbonate derivative of 1,3-diols synthesised by dimethyl carbonate (DMC) chemistry (Scheme 1);¹⁰ the latter being an established green reagent.¹¹ The reaction mechanism was discussed representing the first example of a carbonate reacting selectively and sequentially, firstly at the carbonyl centre to form a linear carbamate and then as a leaving group to yield a cyclic carbamate.

In this paper, the cyclisation reaction is performed in one-step by synthesising the bis(dialkyl)propane-1,3-diyl-dicarbonate in situ, through a cascade reaction (Scheme 2); the general application of this methodology and the influence on the yield of differently substituted 1,3-diols and dialkyl carbonates (DAC) were investigated. The synthesis was carried out on different nucleophiles, that is, aliphatic and aromatic amines and phenylhydrazine.

All reactions followed Scheme 3 where substituents R¹, R², and R³ are selected so to modify the functionality of the 1,3-diol. DAC selected for this study were DMC, diethyl carbonate (DEC), diprop-2-yl carbonate (Di-PrC) and *tert*-butyl methyl carbonate (Mt-BuC).

The unsymmetrical carbonate Mt-BuC was used instead of the di-*tert*-butyl carbonate as the latter is too sterically hindered for any reaction to occur.¹²

The base selected was potassium *tert*-butoxide as it gave the best results, although other alkoxides (sodium methoxide) are also efficient bases, but gave lower yields. Carbonate derivatives of the 1,3-diols having the *tert*-butoxy functionality were present in all the reaction mixtures, but only in small amounts.

For this study a primary amine, benzylamine, was selected as substrate. It is noteworthy that the reactions do not require the presence of a solvent.



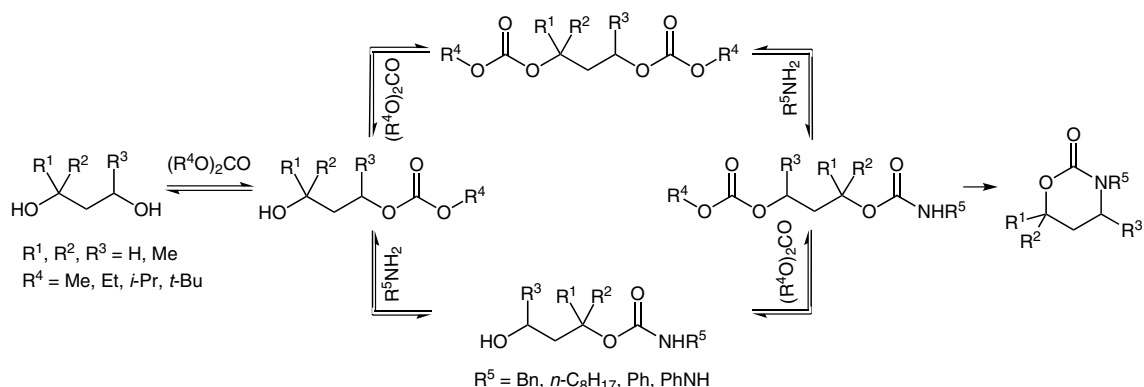
Scheme 1 Intermolecular cyclisation of an amine with dimethyl propane-1,3-diyl-dicarbonate¹⁰

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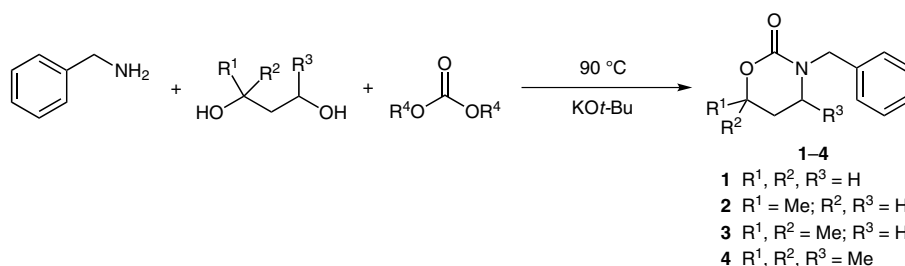
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Scheme 2 An example of in situ cascade reaction to an 1,3-oxinan-2-one described in this paper; all reactions are equilibria with exception of the final cyclisation step



Scheme 3 Synthesis of 1,3-oxazin-2-ones via DAC chemistry

Benzylamine was reacted with propane-1,3-diol in the presence of different DAC to give 3-benzyl-1,3-oxazin-2-one **1** (Scheme 3). As propane-1,3-diol contains two primary alcohols with identical reactivity, the sole variable is the DAC used. The results are reported in Table 1.

When DMC or DEC were employed, 3-benzyl-1,3-oxazin-2-one (**1**) was isolated in 21% and 36% yield, respectively (Table 1, entries 1 and 2). In our previous paper,¹⁰

the reaction of dimethyl propane-1,3-diyl-dicarbonate with benzylamine (Scheme 1) gave an isolated yield of oxazinanone **1** of 40%. However, when the reactions were carried out utilising *Di-PrC* and *Mt-BuC* (Table 1, entries 3 and 4) oxazinanone **1** was isolated in higher yields than those achieved employing the presynthesised bis(dialkylcarbonate) in a two-step reaction. It is noteworthy that in the reaction depicted in Scheme 3, only three equivalents

Table 1 Reaction of Benzylamine with 1,3-Propanediol in the Presence of a DAC and Potassium *tert*-Butoxide to Yield Oxazinone **1**^a

Entry	DAC	Conv. (%)	HPLC yield (area, %)	1 Isolated yield (%)
1		98	29	21
2		96	38	36
3		95	43	47
4		96	50	57

^a All reactions were carried out at 90 °C for 2 h, in the absence of a solvent with a 1.0:1.0:2.0:3.0 molar ratio of benzylamine/diol/base/DAC, respectively. Due to the large number of parasitic reactions and their related products, HPLC data has not been calibrated, as to isolate every byproduct would be too complex.

of DAC are required to yield oxazinanone **1**, and no solvent is used. The reduced amount of reagents/solvents represents a significant saving in terms of reaction volume, energy usage, and consumption of reagents.

Table 1 shows a significant trend in increasing yield of cyclic product from entry 1 through to entry 4. The formation of the oxazinanone **1** is the consequence of a cascade reaction (Scheme 2) that requires both alcohol and amine functionalities to react with the DAC through a B_{Ac}2 pathway. Due to the many consecutive steps involved and the different DAC utilized, it is not easy to compare the different reaction pathways and intermediates from entries 1–4 and thus to clearly justify the trend in yields observed.

It is already known, however, that, when reacting an amine with a DAC in the presence of a base, the more hindered the DAC, the easier the formation of a carbamate, as more hindered alcoxides are better leaving groups.¹³ Conversely, when an alcohol is reacted with a DAC in basic conditions the trend of the leaving group is almost the reverse of that observed with an amine.¹⁴

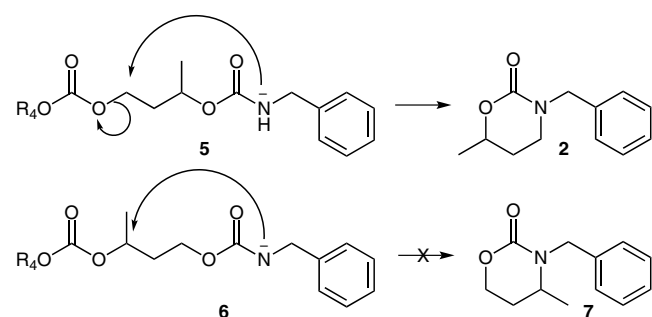
Although it is not the objective of this paper to investigate the reaction mechanism, the results shown here seem to be in good agreement with the previous observations^{13,14} even if the presence of many equilibrium reactions makes the question not easy to clarify.

The cyclisation reaction was then investigated employing butane-1,3-diol that incorporates primary and secondary functionalities. In this case the product formed is 3-benzyl-6-methyl-1,3-oxazinan-2-one (**2**). The aim is to observe the effect, if any, of the influence of steric factors of the substrate on the synthesis of the oxazinanone **2**. The results are reported in Table 2.

The trend of increasing yield of the cyclic product when utilising more hindered DAC is similar to the one seen in

Table 1. It is noteworthy that the reaction of benzylamine with the presynthesised dimethyl 3-methylpropane-1,3-diyl-dicarbonate gave the 1,3-oxazinan-2-one **2** in only 18% yield.¹⁰ On the other hand, employing the one-pot synthetic approach and more hindered DAC (Table 2, entries 2–4), oxazinanone **2** was isolated in better yields up to 45%.

Significantly, ¹H NMR analysis of the cyclic product synthesised confirmed that the methyl group is exclusively located in the 6-position of the oxazinanone ring. This suggests that intramolecular attack on the soft electrophilic centre of the carbonate functionality (B_{Al}2 pathway) preferentially occurs on a CH₂ group (Scheme 4). As a consequence, this cyclisation reaction results in high selectivity towards substituents in the 6- and not in the 4-position of the oxazinanone ring.



Scheme 4 Selectivity towards 6-methyl oxazinanones

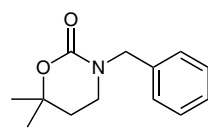
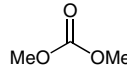
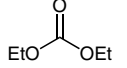
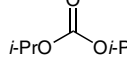
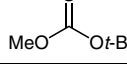
Accordingly, in the case of butane-1,3-diol only one reaction pathway selectively leads to the formation of the oxazinanone, so a much lower yield of the cyclic product would be expected. However, the yields observed in Table 2 are not dramatically lower than those in Table 1; this

Table 2 Reaction of Benzylamine with Butane-1,3-diol in the Presence of a DAC and Potassium *tert*-Butoxide to Yield Oxazinanone **2**^a

Entry	DAC	Conv. (%)	HPLC yield (area, %)	Isolated yield (%)
1		98	28	14
2		98	39	27
3		98	46	44
4		96	51	45

^a All reactions were carried out at 90 °C for 2 h, in the absence of a solvent with a 1.0:1.0:2.0:3.0 molar ratio of benzylamine/diol/base/DAC, respectively. Due to the large number of parasitic reactions and their related products, HPLC data has not been calibrated, as to isolate every byproduct would be too complex.

Table 3 Reaction of Benzylamine with 3-Methylbutane-1,3-diol in the Presence of a DAC and Potassium *tert*-Butoxide to Yield Oxazinanone **3**^a

Entry	DAC	Conv. (%)	HPLC yield (area, %)	 3 Isolated yield (%)
1		97	28	16
2		96	39	21
3		94	46	29
4		94	51	32

^a All reactions were carried out at 90 °C for 2 h, in the absence of a solvent with a 1.0:1.0:2.0:3.0 molar ratio of benzylamine/diol/base/DAC, respectively. Due to the large number of parasitic reactions and their related products, HPLC data has not been calibrated, as to isolate every byproduct would be too complex.

might be attributed to the reversible nature of the cascade reactions leading up finally to the formation of the product **2** (Scheme 2). As the compound **5** is consumed, while **6** is not, the concentration gradient might push the equilibrium of a number of reactions to give more of the intermediate which leads irreversibly to the oxazinanone **2**.

Finally, it must be mentioned that the presence of the secondary alcohol does effect, to an extent, the yields of oxazinanone **2** being lower than those of oxazinanone **1**.

Benzylamine was then reacted with 3-methylbutane-1,3-diol, containing primary and tertiary functionalities, in the presence of a DAC and the base to give 3-benzyl-6,6-dimethyl-1,3-oxazinan-2-one (**3**).

The results, reported in Table 3 confirmed once again the influence of the steric factors previously observed.

Due to the difficulty in isolating 3-benzyl-6,6-dimethyl-1,3-oxazinan-2-one (**3**), for this set of reactions only the HPLC data has been scrutinised.¹⁵

The same trend of increasing yield with increasing steric hindrance of the DAC previously observed in Tables 1 and 2, is also seen in Table 3. The yields for oxazinanone **3** are lower compared to those observed for oxazinanones **1** and **2**, most likely as a result of the low reactivity of the tertiary alcohol in transesterification reactions. Also in this case, ¹H NMR confirmed that the two methyl substituents are solely in the 6-position.

To further support the results observed the diol 2-methylpentane-2,4-diol was reacted with benzylamine and *Mt*-BuC in the presence of potassium *tert*-butoxide to give 3-benzyl-4,6,6-trimethyl-1,3-oxazinan-2-one (**4**). The *Mt*-BuC was selected as in the previous reactions. It has been shown to give the highest yield of oxazinanone.

In this case, analysis of the reaction by GC–MS indicated that the major product was methyl *N*-benzylcarbamate most likely as a result of the steric hindrance both of the diol and of the α -carbon in the intramolecular cyclisation step (Scheme 4). A very small yield of cyclic product **4** was detected (0.3%).¹⁶ Therefore nucleophilic displacement of the carbonate group upon attack of a hindered carbon is probably not energetically favored. This confirms that cyclisation occurs preferably via intramolecular nucleophilic attack on a CH₂ group (Scheme 2).

The general applicability of the one-pot synthesis to 1,3-oxazinan-2-ones was then investigated employing several nucleophiles, that is, aniline, phenylhydrazine, and *n*-octylamine. These substrates were reacted with differently substituted 1,3-diols in the presence of the preferred DAC, *Mt*-BuC, (Scheme 5).

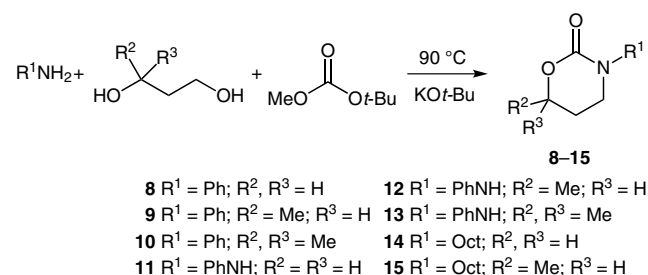
**Scheme 5** Reaction of a 1,3-diol with an amine or phenylhydrazine to give the 1,3-oxazinan-2-ones **8–15**

Table 4 shows that this cascade synthetic approach to oxazinanones can be employed efficiently to several amines and also to phenylhydrazine, giving adequate to good

Table 4 Reaction of Amines and Phenylhydrazine with a 1,3-Diol in the Presence of Methyl *tert*-Butyl Carbonate with Potassium *tert*-Butoxide^a

Entry	Nucleophile	Diol	GC–MS area (%)	Isolated yield (%)
1	aniline	propane-1,3-diol	46	8 34
2	aniline	butane-1,3-diol	62	9 41
3	aniline	3-methylbutane-1,3-diol	34	10 32
4	phenylhydrazine	propane-1,3-diol	61	11 24
5	phenylhydrazine	butane-1,3-diol	76	12 53
6	phenylhydrazine	3-methylbutane-1,3-diol	52	13 18
7	<i>n</i> -octylamine	propane-1,3-diol	51	14 25
8	<i>n</i> -octylamine	butane-1,3-diol	32	15 17

^a All reactions were carried out at 90 °C for 2 h, in the absence of a solvent with a 1.0:1.0:2.0:3.0 molar loading of amine/phenylhydrazine/diol/base/dialkyl carbonate, respectively. Due to the large number of parasitic reactions and their resultant products for each entry, the HPLC data has not been calibrated, as to isolate every byproduct would be too complex.

yields. Notably oxazinanones **9** and **12** were achieved in 62% and 76% yields, respectively (according to GC–MS).

In particular, while *n*-octylamine follows a similar trend to that of benzylamine in terms of decreasing yield as the hindrance of the diol increases, aniline and phenylhydrazine showed a different trend. This is possibly a result of steric hindrance between the rigid aromatic system of the amine/hydrazine and the methyl group(s) on the carbon α to the carbamate. In all cases, ¹H NMR analysis of the oxazinanones confirmed that methyl substituent(s) were found solely in the 6-position.

Table 4 shows a disparity between the observed and isolated yields since products **8–13** were isolated by crystallisation and not by column chromatography as in Tables 1–3, thus, it is expected that a certain amount of the compounds remain within the liquor. Also, in the case of oxazinanones **7–9** the large hydrophobic chain present in the compound made its separation from other byproducts via column chromatography somewhat difficult.

In conclusion, a one-pot synthesis of oxazinanones from amines or phenyl hydrazine, 1,3-diols and DAC through a cascade reaction in the presence of a base and without any solvent has been described. According to the results obtained we can make several observations on this novel synthetic approach to 1,3-oxazinan-2-ones:

Structure of the 1,3-Diol. A very high level of selectivity is found when reacting a 1,3-diol with both primary functionality and a substituent α to the other OH group. For cyclisation to occur through nucleophilic displacement, primary CH₂ functionality α to the carbonate must be present, as substituents on the oxazinanone ring are found in the 6-position, never in the 4-position. Comparing the results from Tables 1–4, it is evident that in the case of aliphatic amines, the more hindered the diol the lower the yield of oxazinanone.

Structure of the DAC. The role of the DAC in the cascade cyclisation reaction is multifunctional. They act as leaving

groups, entering groups and protecting groups. Comparing the results from entries 1–4 in each Table, the more hindered the DAC the greater the yield of oxazinanone observed.

One-Pot Reaction. Synthesising the 1,3-dicarbonate in situ removes a lengthy step from the production of the oxazinanone, requires far less equivalents of DAC and reduces the energy consumption for the process. This one-pot reaction has many variables: temperature, reaction time, base, 1,3-diol, DAC, and amine. The present work has established the effect of DAC and 1,3-diols on the reaction yields; it should be noted that the latter are already definitely higher than those previously reported in the literature. However, reaction conditions such as different DAC, time, temperature, and base should be investigated individually for each novel 1,3-oxazinan-2-ones in order to achieve optimised yields.

Experimental Data

All experimental procedures described were carried out under air and in oven-dried glassware. All reagents were ACS grade and were employed without further purification. Alkyl carbamates DPrC and Mt-BuC were synthesised and purified as described in our previous paper.¹⁴ ¹H NMR and ¹³C NMR spectra were obtained on a Bruker AVANCE 300 spectrometer at 25 °C and referred to deuterated CHCl₃ as internal standard. Melting point analyses carried out are uncorrected. HPLC analyses were carried out at 20 °C on a C18 5 μ m column (4.6 \times 150 mm) using an eluting system of acidified H₂O–MeCN (65:35) at 0.8 mL/min and detecting at λ = 210 nm. A typical sample size was 100 μ L of a solution comprising of 0.1 g of the reaction mixture, 5 mL of 18.8 mM solution of nitrobenzene in MeCN as standard, and 20 mL of MeCN–H₂O (50:50). GC–MS analyses were performed at 70 eV (MS) with a 30 m HP 5 capillary GC column. A typical sample size was 0.2 μ L of a solution of 1 mg of the reaction mixture in 1 mL of CH₂Cl₂.

General Synthesis of an 1,3-Oxazinan-2-one

To an oven dried 50 mL round-bottom flask equipped with a magnetic stirrer bar and condenser was added the amine/hydrazine (10 mmol), the 1,3 diol (10 mmol), and the required alkyl carbonate–DMC (2.7 g, 30 mmol), DEC (3.54 g, 30 mmol), DPrC (4.38 g, 30

mmol), or *Mt*-BuC (3.96 g, 30 mmol), which were reacted at 90 °C for 2 h in the presence of *KOt*-Bu (2.24 g, 20 mmol). The reaction was then quenched with H₂O (5 mL) and the mixture extracted with CH₂Cl₂ (2 × 10 mL), dried over Na₂SO₄ and the solvent removed under vacuum to give a yellow/orange oil, which was further purified depending upon the product.

Additional Purification for 1, 2, and 14

The oil was then purified via column chromatography on silica using Et₂O to remove the byproducts and then MeOH to give the product.

Additional Purification for 3 and 15

The oil was then purified via column chromatography on silica using Et₂O–cyclohexane (1:1) to give adequate separation of the byproducts and the product.

Purification for 8–13

The product was then precipitated out in Et₂O and recrystallised in *PrOH*.

Spectroscopic data for products 1, 8, and 11 has previously been reported.¹⁰

3-Benzyl-1,3-oxazinan-2-one (1)

The product was recrystallised in Et₂O to give a white crystalline solid (DMC: 0.402 g, 2.09 mmol, yield 21%; DEtC: 0.684 g, 3.58 mmol, yield 36%; *Di*-*PrC*: 0.892 g, 4.67 mmol, yield 47%; *MCt*-*Bu*: 1.086 g, 5.69 mmol, yield 57%).

3-Benzyl-6-methyl-1,3-oxazinan-2-one (2)

The product was recrystallised in Et₂O (at –18 °C) to give a yellow crystalline solid (DMC: 0.284 g, 1.39 mmol, yield 14%; DEtC: 0.563 g, 2.75 mmol, yield 28%; *Di*-*PrC*: 0.897 g, 4.38 mmol, yield 44%; *MCt*-*Bu*: 0.928 g, 4.53 mmol, yield 45%); mp 52.4–54.3 °C. ¹H NMR (300 MHz, CDCl₃): δ = 1.30–1.33 (d, *J* = 6.3 Hz, 3 H), 1.64–1.77 (m, 1 H), 1.87–1.95 (m, 1 H), 3.07–3.25 (m, 2 H), 4.28–4.38 (m, 1 H), 4.42–4.61 (m, 2 H), 7.22–7.32 (m, 5 H). ¹³C NMR (75 MHz, CDCl₃): δ = 20.7, 28.7, 43.5, 52.3, 73.4, 127.5, 127.9, 128.6, 136.7, 154.1. HRMS: *m/z* calcd for C₁₂H₁₅NO₂ + H⁺: 206.1182; found: 206.1202.

3-Benzyl-6,6-dimethyl-1,3-oxazinan-2-one 3

The product was then recrystallised in Et₂O (–18 °C) to give a white crystalline solid, mp 65.7–68.3 °C. ¹H NMR (300 MHz, CDCl₃): δ = 1.36 (s, 6 H), 1.81–1.86 (t, *J* = 6.5 Hz, 2 H), 3.16–3.20 (t, *J* = 6.4 Hz, 2 H), 4.57 (s, 2 H), 7.24–7.36 (m, 5 H). ¹³C NMR (75 MHz, CDCl₃): δ = 27.0, 32.4, 41.5, 52.3, 78.0, 127.5, 127.9, 128.6, 136.8, 153.7. HRMS: *m/z* calcd for C₁₃H₁₇NO₂ + H⁺: 220.1338; found: 220.1354.

3-Phenyl-1,3-oxazinan-2-one (8)

White crystalline product (0.610 g, 3.41 mmol, yield 34%).

6-Methyl-3-phenyl-1,3-oxazinan-2-one (9)

White crystalline product (0.791 g, 4.14 mmol, yield 41%); mp 78.3–78.6 °C (lit.⁶ 78–79 °C). ¹H NMR (300 MHz, CDCl₃): δ = 1.47–1.49 (d, *J* = 6.3 Hz, 3 H), 1.94–2.19 (m, 2 H), 3.62–3.82 (m, 2 H), 4.53–4.64 (m, 1 H), 7.24–7.43 (m, 5 H). ¹³C NMR (75 MHz, CDCl₃): δ = 21.4, 29.7, 48.5, 74.5.3, 126.3, 127.2, 129.6, 143.2, 153.4.

6,6-Dimethyl-3-phenyl-1,3-oxazinan-2-one (10)

White crystalline product (0.654 g, 3.19 mmol, yield 32%), mp 123.3–123.7 °C. ¹H NMR (300 MHz, CDCl₃): δ = 1.51 (s, 6 H), 2.03–2.07 (t, *J* = 6.4 Hz, 2 H), 3.69–3.73 (t, *J* = 6.4 Hz, 2 H), 7.23–7.43 (m, 5 H). ¹³C NMR (75 MHz, CDCl₃): δ = 27.7, 33.4, 46.4, 79.0.3, 126.4, 127.2, 129.7, 143.3, 153.1. HRMS: *m/z* calcd for C₁₂H₁₅NO₂ + Na⁺: 228.1964; found: 228.1935.

3-Phenylamino-1,3-oxazinan-2-one (11)

White crystalline product (0.468 g, 2.44 mmol, yield 24%).

6-Methyl-3-phenylamino-1,3-oxazinan-2-one (12)

White crystalline product (1.092 g, 5.30 mmol, yield 53%); mp 156.5–157.5 °C. ¹H NMR (300 MHz, CDCl₃): δ = 1.35–1.37 (d, *J* = 6.3 Hz, 3 H), 1.82–2.03 (m, 2 H), 3.39–3.46 (m, 1 H), 3.53–3.63 (m, 1 H), 4.37–4.44 (m, 1 H), 6.68–6.75 (m, 3 H), 6.82–6.86 (t, *J* = 7.3 Hz, 1 H), 7.15–7.20 (t, *J* = 8.2 Hz, 2 H). ¹³C NMR (75 MHz, CDCl₃): δ = 21.1, 29.8, 48.2, 74.4, 113.5, 121.2, 129.7, 145.8, 155.0. HRMS: *m/z* calcd for C₁₁H₁₄N₂O₂ + H⁺: 207.1134; found: 207.1152.

6,6-Dimethyl-3-phenylamino-1,3-oxazinan-2-one (13)

White crystalline product (0.404 g, 1.84 mmol, yield 18%); mp 184.3–185.0 °C. ¹H NMR (300 MHz, CDCl₃): δ = 1.47 (s, 6 H), 2.01–2.06 (t, *J* = 6.4 Hz, 2 H), 3.63–3.67 (t, *J* = 6.4 Hz, 2 H), 6.71–6.74 (d, *J* = 6.7 Hz, 2 H), 6.86–6.91 (t, *J* = 7.4 Hz, 1 H), 7.19–7.26 (t, *J* = 7.5 Hz, 2 H). ¹³C NMR (75 MHz, CDCl₃): δ = 27.6, 33.6, 46.4, 79.6, 113.7, 121.6, 129.8, 146.9, 154.3. HRMS: *m/z* calcd for C₁₂H₁₆N₂O₂ + H⁺: 221.1290; found: 221.1306.

3-Octyl-1,3-oxazinan-2-one (14)

Yellow oil (0.541 g, 2.54 mmol, yield 25%). ¹H NMR (300 MHz, CDCl₃): δ = 0.61–0.66 (t, *J* = 6.4 Hz, 3 H), 1.03–1.05 (m, 10 H), 1.29–1.38 (quin, *J* = 6.9 Hz, 2 H), 1.76–1.84 (quin, *J* = 6.1 Hz, 2 H), 3.04–3.11 (m, 4 H), 3.97–4.01 (t, *J* = 5.3 Hz, 2 H). ¹³C NMR (75 MHz, CDCl₃): δ = 14.2, 22.4, 22.7, 26.8, 27.1, 29.3, 29.4, 31.9, 45.2, 49.5, 66.6, 153.6.

6-Methyl-3-octyl-1,3-oxazinan-2-one (15)

Yellow oil (0.378 g, 1.67 mmol, yield 17%). ¹H NMR (300 MHz, CDCl₃): δ = 0.62–0.66 (m, 3 H), 1.05–1.15 (m, 10 H), 1.12–1.14 (d, *J* = 6.3 Hz, 3 H), 1.51–1.60 (m, 2 H), 1.76–1.80 (m, 1 H), 1.81–1.84 (m, 1 H), 2.92–3.21 (m, 4 H), 4.08–4.19 (m, 1 H). ¹³C NMR (75 MHz, CDCl₃): δ = 14.3, 21.1, 22.8, 26.9, 27.3, 29.2, 29.4, 29.5, 32.0, 44.6, 49.4, 73.5, 153.8. HRMS: *m/z* calcd for C₁₃H₂₅NO₂ + H⁺: 224.1287; found: 224.1300.

Supporting Information for this article is available online at <http://www.thieme-connect.com/ejournals/toc/synlett>.

References and Notes

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- (12) Benzylamine (0.16 g, 1.5 mmol), propane-1,3-diol (0.12 g, 1.5 mmol), di-*tert*-butyl carbonate (0.79 g, 4.5 mmol), and KO*t*-Bu (0.34 g, 3 mmol) were reacted at 90 °C for 2 h; the only product of the reaction was a small quantity of dibenzyl urea.
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- (15) 3-Benzyl-6,6-dimethyl-1,3-oxazinan-2-one (**3**) was isolated by combining the reaction products from entries 2–4 (Table 3) prior to column chromatography. Due to many byproducts having similar *R_f* values to that of **3**, only a small amount was isolated.
- (16) Product **4** was attributed to this low yield compound as HPLC retention time and GC–MS data were consistent with such an oxazinanone.