An Eco-friendly, Convenient, and Practical Conversion of Arylamines to Oxazolidinones

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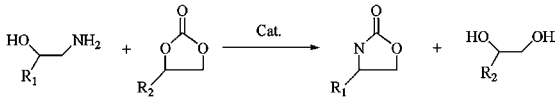
A one-step procedure for efficient synthesis of oxazolidinone only using ethylene carbonate and arylamines in the presence of 1,4-diazabicyclo[2,2,2]octane (DABCO) was developed. In most cases, moderate to high yield of products were obtained. This reaction can be considered a carbon dioxide fixation reaction since ethylene carbonate was synthesized via reaction of ethylene oxide with carbon dioxide.

Oxazolidinones, a well-known class of organic compounds, have many chemical and biological uses. They can be used as protecting groups in organic synthesis and chiral auxiliaries (Evans' chiral auxiliaries) in asymmetric synthesis and as biologically active reagents.[1] Usually oxazolidinones are synthesized by reactions of β-aminoalcohols or other β-amino compounds with reagents such as phosgene,[2] urea,[3] dialkyl carbonates,[4] or a mixture of carbon monoxide and oxygen via oxidative carbonylation.[5] The synthesis of oxazolidinones by using urea is limited due to the necessity of high temperature and the formation of large quantities of polyurea.[6] Oxazolidinones can also be produced from aziridines and carbon dioxide. However, this route also requires high temperature or has the drawback of polymer formation.[7] The synthetic route using phosgene and oxidative carbonylations are not eco-friendly owing to the risk from using poisonous phosgene or carbon monoxide in the reaction procedure.[2,5] It should be noted that synthesis of dialkyl carbonates also requires such hazardous reagents.[8] Recently, Bhanage and co-workers developed a method which carbon dioxide was used directly to produce oxazolidinones under high pressure and high temperature conditions.[9]

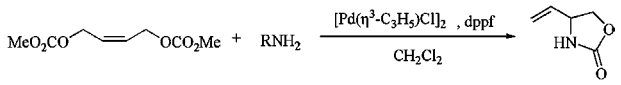
Very recently, the synthesis of oxazolidinones via ethylene carbonate (EC) and β-aminoalcohols in the presence of homogenous base catalyst[10] or heterogeneous base catalyst[11] were reported (Scheme 1). These reactions can be considered as a carbon dioxide fixation reaction since EC is synthesized via reaction of ethylene oxide with carbon dioxide.[12]

Tanimori and Kirihata have reported that the reaction of dimethyl (*Z*)-2-butenylene dicarbonate with primary amines in the presence of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and 1,1′-bis(diphenylphosphino)-ferrocene (dppf) produced vinyloxazolidone compounds in 70% yield[13] (Scheme 2). However, there are very few reports on the direct conversion of simple primary amines into oxazolidinones.

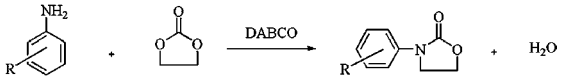
Herein, we report a convenient and practical synthesis of oxazolidinones from EC and aryl amine in the presence of 1,4-diazabicyclo[2,2,2]octane (DABCO) for the first time. This



Scheme 1. The reaction of ethylene carbonate and β-aminoalcohols in the presence of base catalyst.



Scheme 2. The reaction of dimethyl (*Z*)-2-butenylene dicarbonate with primary amines in the presence of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and dppf.



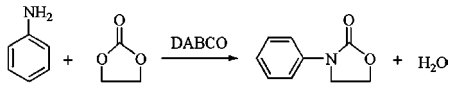
Scheme 3. Synthesis of oxazolidinones from EC and aryl amine in the presence of DABCO.

synthetic method has several advantages: (1) the reaction can be considered as a carbon dioxide fixation reaction since EC is synthesized via reaction of ethylene oxide with carbon dioxide; (2) the oxazolidinones were obtained under mild conditions that are neither dangerous nor toxic; (3) this reaction is wasteless and pollution-free; (4) readily available aryl amines are used as substrate; (5) no transition-metal catalyst is necessary. Thus, this reaction process is environmentally benign and highly atom economic (Scheme 3).

To begin our study, the commercially available and inexpensive aniline and ethylene carbonate were used as model substrates and DABCO was used as a base catalyst. We found that the temperature of reaction influences the yield significantly. No product was observed even if the temperature increased to 60 °C (Table 1, Entries 1 and 2). A moderate yield of product was obtained when the reaction was carried out at 80 °C (Table 1, Entry 3) and the yield could be improved to 96% by increasing the temperature to 100 °C in 16 h (Table 1, Entry 4). The reaction time could be reduced to 5 h which still could give the desired product in 95% yield (Table 1, Entry 9). Excess DABCO is required to get a high yield, the yield decreased to 55% when the amount of DABCO was reduced to one equiv (Table 1, Entry 10). It is worth noting that the reaction should proceeded under an inert atmosphere of argon to avoid the oxidation of aniline.

With the optimized conditions in hand, the scope of the reaction with respect to anilines and ethylene carbonate was investigated. The results are presented in Table 2. The results showed that aryl amines bearing electron-withdrawing groups or no substituent at the para- or meta position on the benzene ring give the corresponding oxazolidinones in high yields (Table 2, Entries 1 and 2, 4 and 5). Aryl amines with electron-donating substituents at the para- or meta position on the benzene ring provide the desired products in moderate to good yields. (Table 2, Entries 8–10). In particular, if there is a substituent at the ortho position of the benzene ring of the aryl amine, the reaction yields are much lower (Table 2, Entries 3, 6, 7, and 11). Perhaps the lower yield is partially caused by the steric effect of the ortho substituent.

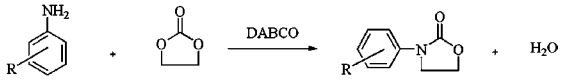
Table 1. Results for the reaction of EC with aniline[a]



Entry	Aniline: DABCO	T/°C	Time/h	Isolated yield/%
1	1:2	40	16	0
2	1:2	60	16	trace
3	1:2	80	16	42
4	1:2	100	16	96
5	1:2	100	1	63
6	1:2	100	2	66
7	1:2	100	3	81
8	1:2	100	4	92
9	1:2	100	5	95
10	1:1	100	5	55
11	1:0.5	100	5	47

[a]Reaction conditions: aniline, 1 mmol; EC, 1 g; free of solvent; under argon.

Table 2. Results for the reaction of EC with arylamines[a]



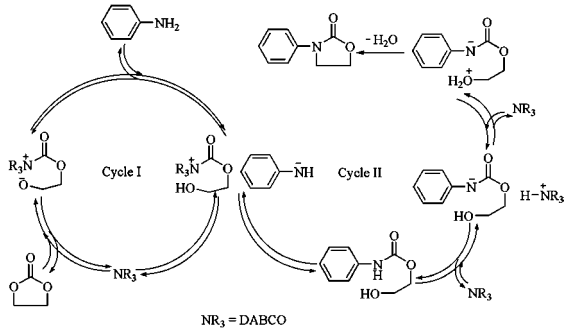
Entry	R	Product	Isolated yield/%
1	H	**1a**	95
2	*p*-NO_2	**2a**	84
3	*o*-NO_2	**3a**	49
4	*m*-NO_2	**4a**	98
5	*p*-Br	**5a**	91
6	*o*-Br	**6a**	47
7	*o*-Cl	**7a**	41
8	*p*-MeO	**8a**	57
9	*m*-MeO	**9a**	57
10	*p*-Me	**10a**	82
11	*o*-Me	**11a**	22
12	2,4,6-trichloro	**12a**	57
13	*n*-$C_4H_9NH_2$	**13a**	0

[a]Reaction conditions: amine, 1 mmol; EC, 1 g; DABCO, 224 mg (2 mmol); temperature, 100 °C; reaction time 5 h; free of solvent; under argon.

All the products were characterized by ^{1}H NMR, ^{13}C NMR, and elemental analysis (Tables 1 and 2).[14]

A proposed mechanism for the reaction of ethylene carbonate with aniline catalyzed by DABCO is shown in Scheme 4, which is similar to the DABCO-catalyzed indole benzylation.[15] The DABCO acts as nucleophilic catalyst in cycle I and as a base in cycle II.

In summary, we have demonstrated a new, convenient, transition-metal-free, and practical pathway for the synthesis of oxazolidinones. The readily available arylamines were reacted with eco-friendly reagent ethylene carbonate in the presence of



Scheme 4. Proposed mechanism for the synthesis of 2-oxazolidinones.

DABCO. Since ethylene carbonate was prepared from epoxides and carbon dioxide, the title reactions will be chemical fixation of carbon dioxide to important chemicals indirectly.

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