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Carbon Dioxide as a Carbonylating Agent in the Synthesis of 2-Oxazolidinones, 2-Oxazinones, and Cyclic Ureas: Scope and Limitations

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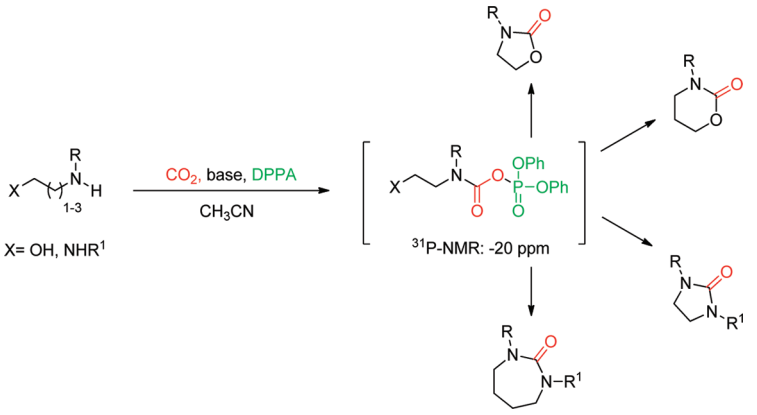

Carbon dioxide can be used as a convenient carbonylating agent in the synthesis of 2-oxazolidinones, 2-oxazinones, and cyclic ureas. The transient carbamate anion generated by treating a primary or secondary amine group in basic media can be activated with phosphorylating agents such as Diphenylphosphoryl azide (DPPA) and Diphenyl chlorophosphate (DPPCl) but also with other types of electrophiles such as $SOCl_2$, TsCl, or AcCl. The intramolecular trapping of the activated carbamate by a hydroxyl group leads to the formation of 2-oxazolidinones or 2-oxazinones in good to excellent yields. This methodology was successfully applied to the synthesis of cyclic ureas up to 7-membered rings from the corresponding diamines.

Introduction

The continuing search for safe, environmentally friendly, and inexpensive reagents is one of the driving forces in organic chemistry and has contributed a great deal to the development of efficient synthetic routes that are feasible on an industrial scale. As a result of its unique properties and ready availability, CO_2 has emerged as an attractive source of carbon that has found numerous applications.[1] Among these, the successful use of CO_2 as a carbonylating agent in the synthesis of dialkyl carbonates and ester carbamates has shown that carbon dioxide is a convenient alternative to the highly toxic phosgene derivatives.[2] Despite the advantages of CO_2 as a carbonyl source, only a few reports on the synthesis of 2-oxazolidinones from amino alcohols and CO_2 have been published to date. To the best of our knowledge, Kodaka and co-workers reported the first synthesis of 2-oxazolidinones

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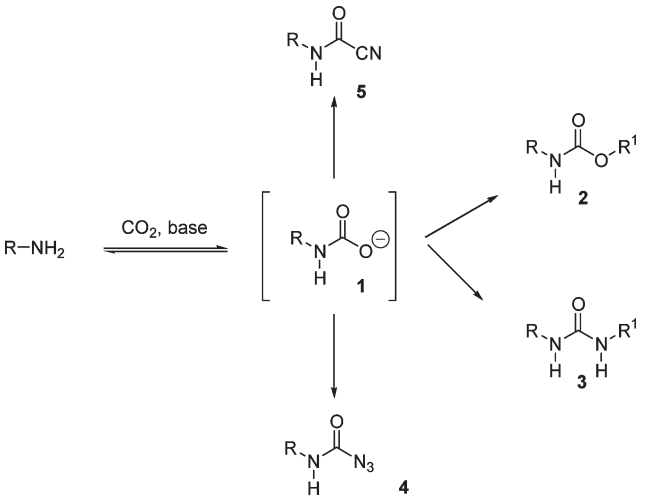
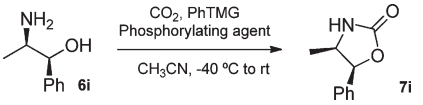
SCHEME 1



from 1,2-amino alcohols and carbon dioxide under Mitsunobu conditions in 1993.[3] Almost at the same time, Kubota et al. published a slightly modified procedure that involved the use of a combination of triphenylphosphine and CCl_4.[4] In 2000, Feroci's group described the carbonylation of 1,2-amino alcohols in the presence of an electrogenerated base, CO_2, and tosyl chloride to give 2-oxazolidinones in good to moderate yields.[5] In 2004, Dinsmore and Mercer established the scope of the CO_2-carbonylation under Mitsunobu conditions and explored the stereochemical issues associated with this transformation, in which the inversion of configuration of the carbon bearing the oxygen was observed.[6] Very recently, our group has reported the preparation of 2-oxazolidinones under mild conditions from 1,2-amino alcohols in the presence of CO_2 and diverse phosphorus electrophiles.[7] We wish to report here a full account of our research into the synthesis of 2-oxazolidinones with carbon dioxide and several types of electrophiles. The stereochemical outcome of the reaction has been studied, and our synthetic strategy has been further expanded to include the preparation of 2-oxazinones and cyclic ureas.

It is well-known that primary and secondary amines are in equilibrium with carbamate anions **1** in the presence of carbon dioxide under basic conditions. The generation of these anionic species is responsible for the trapping of CO_2 by these amines, which usually requires the presence of an additional base. Nonprotic amines such as DBU (1,8-diazabicyclo[5.4.0]-undec-7-ene), DBN (1,5-diazabicyclo[4.3.0]non-5-ene), pentaalkyl guanidines, or Et_3N have been utilized for this purpose. These carbamate anions are versatile species that can be used in the synthesis of a variety of carbonylated products such as alkyl carbamates **2**,[8] dialkyl ureas **3**,[9] carbamoyl azides **4**,[10] and carbamoyl cyanides **5**[11] (Scheme 1). The results of our investigations into the synthesis of carbamoyl azides **4**[10] suggested that in the presence of a phosphorus electrophile, a carbamate anion can be eventually transformed into an activated carbonyl species, which in turn could behave as an acylating agent in the presence of an appropriate nucleophile. According to this proposal, 2-oxazolidinones could be easily obtained from 1,2-amino alcohols, CO_2, and a phosphorylating agent under basic conditions.

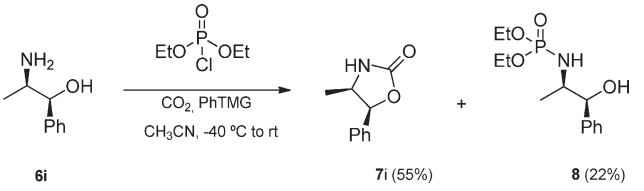
TABLE 1. Screening of Phosphorylating Agents



entry	phosphorylating agent	yield (%)
1	diphenylphosphoryl azide (150 mol %), NaN_3 (300 mol %)	78[a]
2	diphenylphosphoryl azide (100 mol %)	75[a]
3	diphenyl chlorophosphate (100 mol %)	82[a]
4	diethyl chlorophosphate (100 mol %)	55[a]
5	diphenyl cyanophosphonate (150 mol %)	87[a]
6	diethyl cyanophosphonate (100 mol %)	86[b]

[a]Isolated yield. [b]Determined by ^1H NMR spectroscopy.

SCHEME 2



Results and Discussion

The conditions developed by our group for the preparation of carbamoyl azides were initially assayed with norephedrine **6i** as a readily available 1,2-amino alcohol (Table 1). Thus, diphenylphosphoryl azide (DPPA) was added dropwise to a CO_2-saturated solution of norephedrine **6i** in acetonitrile at −40 °C containing 1,1,3,3-tetramethyl-2-phenylguanidine (PhTMG) as a base and NaN_3. The expected 4-methyl-5-phenyloxazolidin-2-one **7i** was isolated in 78% yield (Table 1, entry 1). Encouraged by this preliminary result, we directed our attention toward the key role of the phosphorylating agent and the nature of the intermediates involved in the reaction. Although the addition of NaN_3 was necessary for the synthesis of carbamoyl azides in good yields, we found that the 2-oxazolidinone **7i** was obtained in nearly the same yield when the reaction was performed with DPPA in the absence of NaN_3 (Table 1, entry 2). The use of related phosphates as carbonyl activating agents also proved effective in the formation of the 2-oxazolidinone. Diphenyl chlorophosphate (DPPCl), the most inexpensive reagent in the series, afforded **7i** in 82% yield (Table 1, entry 3), whereas diethyl chlorophosphate (DEPCl) gave **7i** in only moderate yield (Table 1, entry 4). In this case,

(3) Kodaka, M.; Tomohiro, T.; Okuno, H. *J. Chem. Soc., Chem. Commun.* **1993**, 81.
(4) Kubota, Y.; Kodaka, M.; Tomohiro, T.; Okuno, H. *J. Chem. Soc., Perkin Trans. 1* **1993**, 5.
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(6) Dinsmore, C. J.; Mercer, S. P. *Org. Lett.* **2004**, *6*, 2885.
(7) Paz, J.; Pérez-Balado, C.; Iglesias, B.; Muñoz, L. *Synlett* **2009**, 395.
(8) (a) McGhee, W.; Riley, D.; Christ, K.; Pan, Y.; Parnas, B. *J. Org. Chem.* **1995**, *60*, 2820. (b) Ion, A.; Van Doorslaer, C.; Parvulescu, V.; Jacobs, P.; De Vos, D. *Green Chem.* **2008**, *10*, 111.
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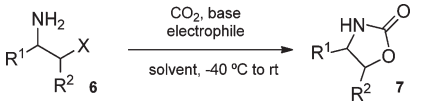
(10) García-Egido, E.; Fernández-Suárez, M.; Muñoz, L. *J. Org. Chem.* **2008**, *73*, 2909.
(11) García-Egido, E.; Paz, J.; Iglesias, B; Muñoz, L. *Org. Biomol. Chem.* **2009**, *7*, 3991.

TABLE 2. Synthesis of 2-Oxazolidinones



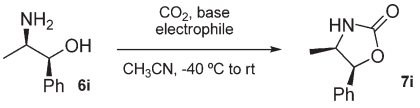
						yield (%)		
entry	R^1	R^2	X	**6**	**7**	DPPA	DPPCl	AcCl
1	Ph	H	OH	**a** (2*R*)	**a** (4*R*)	80[a]	95[b]	94[b]
2	Bn	H	OH	**b** (2*R*)	**b** (4*R*)	75[a]	97[b]	89[b]
3	*i*-Pr	H	OH	**c** (2*S*)	**c** (4*S*)	75[a]	97[b]	86[a] 97[b]
4	*t*-Bu	H	OH	**d** (2*S*)	**d** (4*S*)	74[a]	85[a]	
5	*s*-Bu	H	OH	**e** (2*S*,3*S*)	**e** (4*S*,1'*S*)		94[b]	
6	1*H*-indol-3-ylmethyl	H	OH	**f** (2*S*)	**f** (4*S*)		92[b]	
7	CO_2Et	H	OH	**g** (2*S*)	**g** (4*S*)	73[a] 94[b]	76[a]	82[b]
8	CO_2Et	Me	OH	**h** (2*S*,3*R*)	**h** (4*S*,5*R*)	73[a]	78[a]	94[a] 96[b]
9	Me	Ph	OH	**i** (1*S*,2*R*)	**i** (4*R*,5*S*)	75[a] 97[b]	96[b]	96[a] 97[b]
10	CO_2Me	H	SH	**j** (2*R*)	**j** (4*R*)	95[a]		
11	CO_2Et	H	SH	**k** (2*R*)	**k** (4*R*)	73[a]		

[a]PhTMG as a base (100−200 mol %). [b]Et_3N as a base (200−250 mol %).

besides the 2-oxazolidinone, the phosphoramide **8** was isolated (Scheme 2). Apparently, the ethoxy substituents render DEPCl more reactive than DPPCl and the formation of the phosphoramide **8** competes with the generation of the carbamate anion **1** under the reaction conditions. Although diphenyl cyanophosphonate is quite effective in the synthesis of **7i** (87% yield, Table 1, entry 5), it is not commercially available. Finally, diethyl cyanophosphonate also led to the 2-oxazolidinone **7i** in good yield (Table 1, entry 6). However, the cost and the commercial technical grade[12] make this phosphonate of little interest for synthetic purposes.

Having discovered that diphenylphosphoryl azide (DPPA) or diphenyl chlorophosphate (DPPCl) enabled the efficient carbonylation of norephedrine with CO_2 to give the corresponding 2-oxazolidinone, we continued our study by assaying other 1,2-amino alcohols in order to study the scope of this methodology.[13] As shown in Table 2, the 2-oxazolidinones derived from primary amines were obtained in good yields regardless of the nature of the substituents. Even in the presence of the secondary amino group of the tryptophan derivative **6f**, the 2-oxazolidinone **7f** was obtained in 92% yield (Table 2, entry 6). 1,2-Amino thiols derived from cysteine (**6j** and **6k**) also underwent carbonylation to afford the corresponding 2-thioxazolidinones **7j** and **7k** in yields similar to those of the 2-oxazolidinones (entries 10 and 11). The initial conditions for the formation of the 2-oxazolidinones involved the use of DPPA (120 mol %) and PhTMG (100−120 mol %) as a base and acetonitrile at −40 °C. In an attempt to develop a more versatile system, we explored different reaction conditions. In our experience, the use of PhTMG as a base is crucial for the reactivity of some carbamate anions.[10,11] However, we found that in the synthesis of 2-oxazolidinones PhTMG can be advantageously replaced by DBN or by the readily available Et_3N (200 mol %). This change even led to improved yields in some cases (see Table 2, entries 1−3 and 7−9). In some other cases, we encountered problems regarding the solubility of certain 1,2-amino alcohols in acetonitrile at low temperature. In these cases, CH_2Cl_2 was used as a solvent to obtain a homogeneous reaction medium.[14] This switch of solvent apparently did not affect the course of the reaction and gave the corresponding 2-oxazolidinones in the same range of yields (75−95%). To complete our survey, we tried other types of electrophiles that could play the role of DPPA or DPPCl as carbonyl activating agents. We were delighted to find that the carbonylation of norephedrine **6i** can be successfully performed with a variety of sulfur and carbon electrophiles (Table 3). Among these carbonyl activating agents, acetyl chloride (AcCl) was especially suitable for our purposes.

TABLE 3. Screening of Electrophiles



entry	electrophile	conditions	yield (%)
1	$SOCl_2$	PhTMG (100 mol %)	88
2	MsCl	PhTMG (200 mol %)	68
3	TsCl	Et_3N (200 mol %)	81
4	4-nitrobenzenesulfonyl chloride (*p*NsCl)	Et_3N (200 mol %)	92
5	Tf_2O	Et_3N (200 mol %)	88
6	AcCl	Et_3N (200 mol %)	97
7	AcBr	PhTMG (200 mol %)	94
8	$ClCO_2Et$	PhTMG (200 mol %)	86

It can be seen from Table 2 that the use of AcCl gave the 2-oxazolidinones **7** in comparable or even better yields than with the phosphorus electrophiles. The simplicity and efficiency of the new conditions were exemplified by the preparation of the 2-oxazolidinone derived from norephedrine **6i** on a 2 g scale using CO_2, Et_3N as a base, and acetyl chloride in CH_2Cl_2 (91% yield).

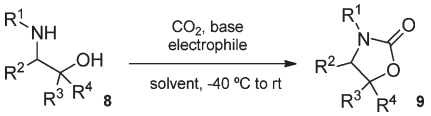
The carbonylation of *N*-alkyl 1,2-amino alcohols **8** gave the corresponding *N*-alkyl-2-oxazolidinones **9** in good yields

(12) Diethyl cyanophosphonate was purchased from Sigma-Aldrich as a technical grade reagent with 90% purity.

(13) DPPA can be quantitatively prepared from DPPCl by treatment with an excess of NaN_3; see the Supporting Information.

(14) See the Supporting Information for details.

TABLE 4. Synthesis of *N*-Alkyl-2-oxazolidinones

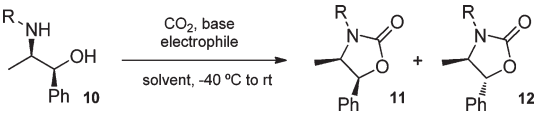


							yield (%)	
entry	R^1	R^2	R^3	R^4	**8**	**9**	DPPA	DPPCl
1	Bn	*i*-Pr	H	H	**a** (2*S*)	**a** (4*S*)	84[a]	
2	Bn	*s*-Bu	H	H	**b** (2*S*,3*S*)	**b** (4*S*,1'*S*)	97[b]	
3	3-phenylpropyl	Me	H	H	**c** (2*S*)	**c** (4*S*)		83[b]
4	1,3-diphenylprop-2-yl	H	H	H	**d**	**d**	94[b]	95[b]
5	*i*-Bu	1*H*-indol-3-ylmethyl	H	H	**e** (2*S*)	**e** (4*S*)	96[b]	
6	-$(CH_2)_3$-		Ph	Ph	**f** (2*S*)	**f** (4*S*)	49[a]	98[a] 94[b]
7	Et	CO_2Et	Me	H	**g** (2*S*,3*R*)	**g** (4*S*,5*R*)	77 [b]	
8	*i*-Bu	CO_2Et	Me	H	**h** (2*S*,3*R*)	**h** (4*S*,5*R*)	70 [b]	
9	Me	Me	Ph	H	**i** (1*S*,2*S*)	**i** (4*S*,5*S*)	72[a] 78[b]	79[a]

[a]PhTMG as a base (120 mol %). [b]Et_3N as a base (200 mol %).

when DPPA or DPPCl were used as carbonyl activating agents (Table 4). However, the yields were only moderate when the reaction was performed with AcCl. This drop in yield is explained by the formation of undesired byproducts, which seems to indicate that acetyl chloride is too reactive for this type of substrate and other reaction pathways must compete with the formation of the 2-oxazolidinone. The noncommercial *N*-alkyl derivatives were prepared in a straightforward manner from the unsubstituted 1,2-amino alcohols by condensation of the primary amine group with the corresponding aldehyde or ketone and subsequent reduction of the intermediate imine.[14,15] The bulkiness of the *N*-alkyl chain had little effect on the carbonylation of unsubstituted or C2-substituted 1,2-amino alcohols (entries 1−5, Table 4). Conversely, steric hindrance does seem to have a detrimental effect on C1,C2-disubstituted 1,2-amino alcohols, as evidenced by the lower yields of 2-oxazolidinones **9g**−**i** (entries 6−9, Table 4). Although in these cases the anticipated 2-oxazolidinones were isolated as a single isomer, in the case of *N*-alkyl 1,2-amino alcohols derived from norephedrine (i.e., **10a**−**f**) a mixture of *syn* and *anti* diastereoisomers was surprisingly obtained (Table 5). The expected *syn*-2-oxazolidinones **11** were still the major products, with ratios from 4/1 to >98/2, but the *anti* 2-oxazolidinones **12** also appear as a result of the inversion of configuration at the oxygen-bearing center. The relative and absolute configurations were established by comparison of the spectroscopic data of **11a** and **12a** with data reported in the literature.[16] Such an inversion of configuration was also observed by Dinsmore and Mercer in the carbonylation of *N*-alkyl 1,2-amino alcohols with CO_2 under Mitsunobu conditions.[6] The use of ^{18}O isotopically marked carbon dioxide enabled the authors to show that the inversion takes place through nucleophilic substitution of the oxygen (presumably transformed into a good leaving group) of the 1,2-amino alcohol by the oxygen of the carbamate anion. According to this rationale, the ring closure of the oxazolidinone ring could follow two different pathways.

TABLE 5. *N*-Alkyl-2-oxazolidinones Derived from Norephedrine



entry	R	**10**	2-oxazolidinones	yield (%) DPPA	*syn*/*anti* ratio[c]
1	Me	**a**	**11a** + **12a**	88[b]	4:1
2	Et	**b**	**11b** + **12b**	86[b]	6:1
3	*i*-Pr	**c**	**11c** + **12c**	69[a]	5:1
4	*i*-Bu	**d**	**11d** + **12d**	83[b]	4:1
5	neopentyl	**e**	**11e** + **12e**	70[a]	>98:2
6	Bn	**f**	**11f** + **12f**	67[a]	4:1

[a]PhTMG as a base (120 mol %). [b]Et_3N as a base (200 mol %). [c]Determined by ^1H NMR spectroscopy.

In the case of retention of configuration, the activated carbamate group undergoes nucleophilic attack of the hydroxyl oxygen, and in the case of inversion, the oxygen of the amino alcohol undergoes nucleophilic substitution (Scheme 3). Two factors seem to favor the inversion pathway for the (1*R*,2*S*)-norephedrine derivatives: (i) the oxygen-bearing center (C1) is an activated benzylic position and (ii) the steric interactions between the methyl and the phenyl groups (**13**) during the ring-closure step should penalize the retention pathway. This would explain why in the case of pseudoephedrine **8i** (1*S*,2*S*) only the 2-oxazolidinone **9i** with retention of configuration is found (Table 4). Interestingly, the *syn*/*anti* ratio was found to be dependent on the nature of the alkyl group bound to the amino nitrogen as can be seen from the results in Table 5. For groups such as methyl, ethyl, isopropyl, isobutyl, and benzyl (entries, 1, 2, 3, 4, and 6) the *syn*/*anti* ratio determined by ^1H NMR spectroscopy varies between 6/1 and 4/1. However, for the neopentyl group (entry 5), the *syn* 2-oxazolidinone **11e** is the major product (*syn*/*anti* >98/2). This result is difficult to explain

(15) (a) Chen, L.; Wiemer, D. F. *Tetrahedron Lett.* **2002**, *43*, 2705. (b) Parrott, R. W., II; Hitchcock, S. R. *Tetrahedron: Asymmetry* **2008**, *19*, 19. (c) Hitchcock, S. R.; Davis, R. A.; Richmond, D. M.; Dore, D. D.; Kuschel, S. L.; Vaughn, J. F.; Wolfe, J. A.; Hamaker, C. G.; Casper, D. M.; Dingle, J. *J. Heterocycl. Chem.* **2008**, *45*, 1265. (d) Parrott, R. W., II; Hamaker, C. G.; Hitchcock, S. R. *J. Heterocycl. Chem.* **2008**, *45*, 873. (e) Effenberger, F.; Gutterer, B.; Jäger, J. *Tetrahedron: Asymmetry* **1997**, *8*, 459. (f) Borch, R. F.; Bernstein, M. D.; Durst, H. D. *J. Am. Chem. Soc.* **1971**, *93*, 2897.

(16) The relative and absolute configurations were established by comparison of the spectroscopic data of samples of **11a** and **12a** described in the literature. Claridge, T. D. W.; Davies, S. G.; Polywka, M. E. C.; Roberts, P. M.; Russell, A. J.; Savory, E. D.; Smith, A. D. *Org. Lett.* **2008**, *23*, 5433.

SCHEME 3

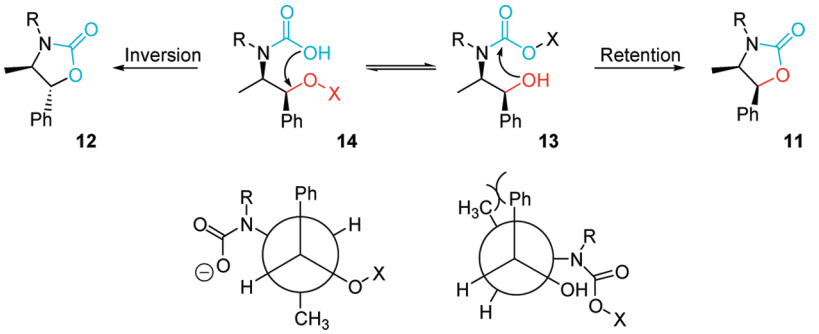
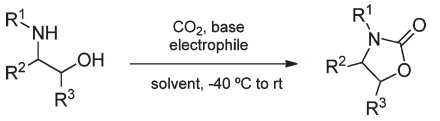


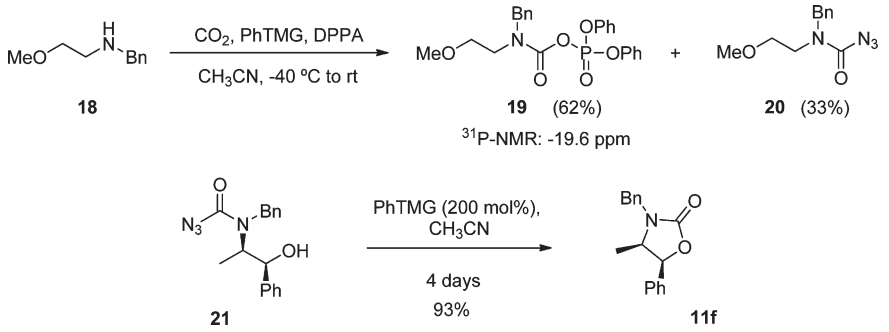
TABLE 6. Carbonylation Using SO_2Cl_2 as the Activating Agent



entry	R^1	R^2	R^3	1,2-amino alcohol	2-oxazolidinones	yield (%)	*Ret*/*Inv* ratio[c]
1	H	Me	Ph	**6i** (1*S*,2*R*)	**7i** (4*R*,5*S*) + **15** (4*R*,5*R*)	68[b]	1:10
2	Me	Me	Ph	**8i** (1*S*,2*S*)	**9i** (4*S*,5*S*) + **16** (4*S*,5*R*)	34[b]	1:4
3	H	CO_2Et	Me	**6h** (2*S*,3*R*)	**7h** (4*S*,5*R*) + **17** (4*S*,5*S*)	44[a]	1:3.6

[a]PhTMG as a base (120 mol %). [b]Et_3N as a base (200 mol %). [c]Determined by ^1H NMR spectroscopy.

SCHEME 4



only in terms of steric hindrance, taking into account the bulkiness of the aforementioned *N*-alkyl groups.

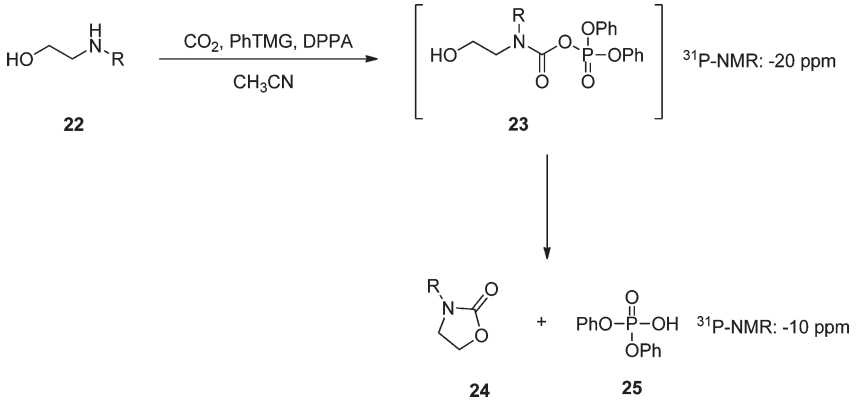
A more striking case of the inversion of configuration was observed during the carbonylation of norephedrine **6i** in the presence of different electrophiles. When SO_2Cl_2 was utilized as an electrophile, a mixture of diastereomeric 2-oxazolidinones was found (Table 6) in which the product due to inversion of configuration (**15**) was the major one with a **7i**:**15** ratio of 1:10. When other 1,2-disubstituted amino alcohols were assayed (**8i** and **6h**), we again found a mixture enriched in the product arising from inversion of configuration. Although the yields and the diastereomeric ratios are modest, the reactivity of SO_2Cl_2 does not appear to be affected by the substitution of the amino group or the nature of the substituent at C1, which means that the stereochemical outcome of the reaction can be potentially tuned as a function of the electrophile used. It has been reported that 1,2-amino alcohols afford aziridines in excellent yields in the presence of SO_2Cl_2.[17] A more efficient activation of the hydroxyl group, instead of the carbamate anion, must account for the bias for the inversion pathway in this case.

In order to assess the mechanistic aspects of the carbonyl activation mediated by DPPA, the carbonylation of several *N*-alkyl-1,2-amino alcohols was monitored by TLC, and the presence of a reaction intermediate was found. This intermediate disappeared completely during the workup and purification. Despite its short life, the intermediate was separated by flash chromatography and the ^{31}P NMR spectrum was recorded. A transient signal was observed at around −20 ppm, and this disappeared rapidly, while a signal at around −10 ppm increased in intensity; this latter value is typical for diphenyl hydrogen phosphate **25**.[18] The ^1H NMR spectrum of this fraction showed the presence of the expected 2-oxazolidinone and a phosphorus derivative. With the aim of verifying whether a mixed anhydride could be the intermediate, the secondary amine **18**, bearing a

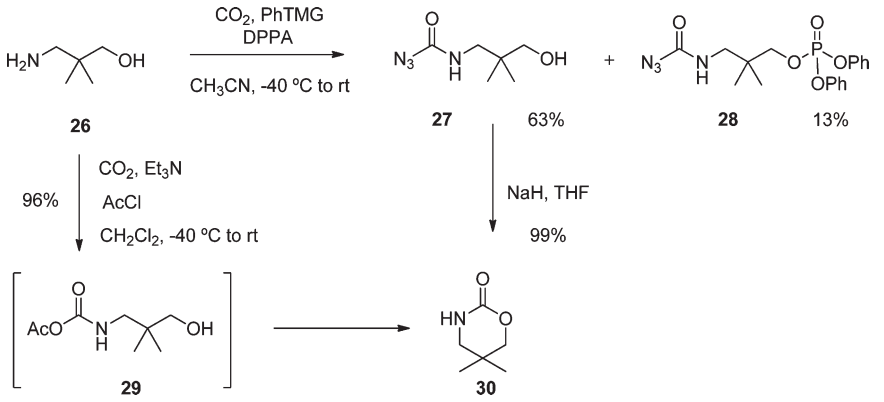
(17) (a) Kuyl-Yeheskiely, E.; Lodder, M.; Van der Marel, G. A.; Van Boom, J. H. *Tetrahedron Lett.* **1992**, *33*, 3013. (b) Pilkington, M.; Wallis, J. D. *J. Chem. Soc., Chem. Commun.* **1993**, 1857.

(18) Nilsson, J.; Kraszewski, A.; Stawinski, J. *J. Chem. Soc., Perkin Trans. 2* **2001**, 2263.

SCHEME 5. Mechanistic Proposal



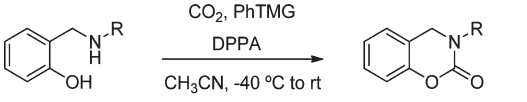
SCHEME 6



methoxy group instead of a hydroxyl function, was submitted to the carbonylation conditions with DPPA (Scheme 4). In this case, a mixture of the mixed anhydride **19** (62%) and the carbamoyl azide **20** (33%) was obtained. The ^{31}P NMR spectrum of **19** showed a characteristic peak at −19.6 ppm, which is very close to the value displayed by the transitory intermediate observed previously. A further experiment with the *N*-benzylated carbamoyl azide **21**[19] showed that the participation of a carbamoyl azide as an intermediate is unlikely, since the ring closure of **21** in the presence of 200 mol % of PhTMG is a slow reaction that takes 4 days to reach completion (Scheme 4). These observations taken together seem to support the involvement of a transient mixed anhydride in the carbonylation with DPPA. This anhydride should serve to activate the carbonyl group and would undergo the ring closure to give the 2-oxazolidinone (Scheme 5).

In order to explore the synthetic scope of our methodology, we next turned our attention to the carbonylation of other types of substrates. We first tried the carbonylation of 1,3-amino alcohols to give the corresponding 2-oxazinones. When 3-amino-2,2-dimethylpropanol **26** was treated with CO_2, PhTMG, and DPPA in acetonitrile, a mixture of the carbamoyl azide **27** (63% yield) and the phosphorylated carbamoyl azide **28** (13% yield) was obtained (Scheme 6). Although under these conditions the expected 2-oxazinone was not found, the carbamoyl azide **27** easily underwent the ring closure in the presence of NaH as base to afford quantitatively the 2-oxazinone **30**. Assuming that a more reactive system was required to proceed to the formation of the 2-oxazinone in a single step, we performed the reaction with acetyl chloride as the activating agent. Fortunately, under these conditions the 2-oxazinone **30** was isolated in 96% yield (Scheme 6). Presumably, the transient mixed anhydride **29** is reactive enough to undergo the ring-closure, whereas the postulated carbamoyl phosphate formed with DPPA is less reactive and evolves toward the formation of the carbamoyl azides **27** and **28**. Nevertheless, in substrates such as the 2-aminomethylphenol derivatives **31** and **32**,[20] the carbonylation took place on using DPPA as the electrophile (Scheme 7), which indicates that the conformational rigidity as well as the higher acidity of the phenol moiety must contribute to the successful carbonylation with DPPA.

SCHEME 7

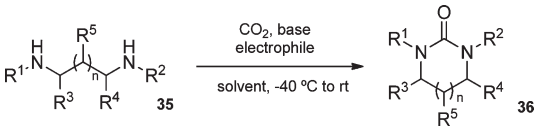


R= *n*Bu **31** R= *n*Bu **33** 77%
R= *i*Pr **32** R= *i*Pr **34** 28%

(19) The carbamoyl azide **21** was isolated in 25% yield from the carbonylation reaction of the *N*-benzylated norephedrine **10f** with DPPA.

(20) The amino alcohols **31** and **32** were prepared by condensation of 2-hydroxybenzaldehyde with *n*-butylamine and isopropylamine, respectively, and subsequent reduction of the corresponding imines with $NaBH_4$.

TABLE 7. Carbonylation of Diamines

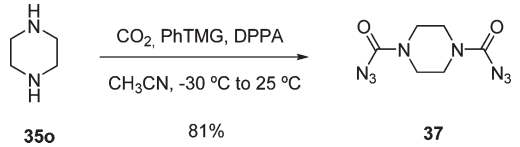


entry	*n*	R^1	R^2	R^3	R^4	R^5	**35**	**36**	yield (%)
1	0	H	H	Me	H		**a**	**a**	86
2	0	H	H	$-(CH_2)_4-$			**b** (1*S*,2*S*)	**b**	73
3	0	H	Bn	$-(CH_2)_4-$			**c** (1*S*,2*S*)	**c**	96
4	0	H	*i*-Pr	$-(CH_2)_4-$			**d** (1*S*,2*S*)	**d**	91
5	0	Bn	Bn	H	H		**e**	**e**	85
6	0	cyclohexyl	cyclohexyl	H	H		**f**	**f**	93
7	0	H	1,3-diphenylprop-2-yl	H	H		**g**	**g**	86
8	0	*i*-Pr	1,3-diphenylprop-2-yl	H	H		**h**	**h**	91
9	1	Bn	Bn	H	H	H	**i**	**i**	94
10	1	H	H	H	$-Ph-^a$		**j**	**j**	92
11	1	3-pentyl	H	H	$-Ph-^b$		**k**	**k**	87
12	2	Bn	Bn	H	H	H	**l**	**l**	73
13	3	Bn	Bn	H	H	H	**m**		
14	3	Bn	Bn	CO_2Et	H	H	**n** (2*S*)		
15	0	$-(CH_2)_2-$		H	H		**o**		

[a] **35j** is 2-(aminomethyl)aniline. [b] **35k** is a derivative of 2-(aminomethyl)aniline.

Finally, we studied the carbonylation of diamines to afford the corresponding cyclic ureas. Although this transformation has been classically carried out with phosgene or phosgene derivatives, these reactions lead to considerable amounts of bis-carbamoyl derivatives, which explains the modest yields of the cyclic ureas.[21] Since our methodology involves the initial formation of an ionic carbamate with CO_2, we thought that the unlikely formation of a bis-ionic carbamate should favor the formation of ureas over other byproducts. Much to our delight, our assumption was confirmed when the carbonylation of diamines was performed with PhTMG as base and DPPA as the carbamate activating agent in either acetonitrile or dichloromethane. The results in Table 7 show that 1,2-diamines gave the corresponding 5-membered cyclic ureas in good yields regardless of the substitution of one or both amino groups (Table 7, entries 1−8). 6-Membered cyclic ureas were obtained in good yields when 1,3-diamines were used as substrates (entries 9−11), and even the 7-membered cyclic urea **36l** was also synthesized (entry 12). However, these conditions failed to afford 8-membered ureas (entries 13−14) and the bicyclic urea derived from 1,4-piperazine (entry 15). In the latter case, the bis-carbamoyl azide **37** was obtained. The use of 200 mol % of PhTMG and DPPA led to the isolation of **37** in 81% yield (Scheme 8).

SCHEME 8



Conclusions

In summary, we have shown that carbon dioxide can be used as a convenient carbonylating agent in the synthesis of 2-oxazolidinones, 2-oxazinones, and cyclic ureas. Activation of the transient carbamate anion generated by treating a primary or secondary amine group in basic media can be effected with phosphorylating agents such as DPPA and DPPCl, as well as with other types of electrophiles such as $SOCl_2$, TsCl, or AcCl. The intramolecular trapping of the activated carbamate by a hydroxyl group leads to the formation of 2-oxazolidinones or 2-oxazinones in good to excellent yields. Although the formation of the 2-oxazolidinones takes place with full retention of configuration for a variety of *N*-alkyl 1,2-amino alcohols, we found that the *N*-alkyl derivatives of norephedrine undergo partial inversion of configuration at C1 and that this is dependent on the nature of the alkyl group at the amino function. Interestingly, the compounds arising from inversion of configuration at C1 become the major products when SO_2Cl_2 is utilized as an electrophile. This methodology was also successfully applied to the synthesis of cyclic ureas with up to 7-membered rings.

Experimental Section

General Experimental Procedure A for the Reductive Alkylation of Amines. (2*S*,3*S*)-2-(Benzylamino)-3-methylpentan-1-ol (8b). A solution of L-isoleucinol (500 mg, 4.27 mmol, 100 mol %) and benzaldehyde (680 mg, 6.41 mmol, 150 mol %) in EtOH (20 mL) was stirred for 12 h at 25 °C. The reaction mixture was cooled to 0 °C, and $NaBH_4$ (323 mg, 8.54 mmol, 200 mol %) was added portionwise with stirring at 0 °C for 1.5 h. The solvents were removed under reduced pressure, the residue was dissolved in 1 M aq NaOH (50 mL) and then extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4, and the solvents were removed under reduced pressure. The crude material was purified by flash chromatography (silica gel, AcOEt/CH_2Cl_2 1:3→AcOEt) to give the title compound **8b** (823 mg, 93% yield) as a yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.4−7.2 (m, 5H), 3.84 (d, J = 12.8 Hz, 1H), 3.73 (d, J = 12.8 Hz, 1H), 3.63 (dd, J = 10.6, 4.1 Hz, 1H), 3.36 (dd, J = 10.6, 7.6 Hz, 1H), 2.61 (ddd, J = 7.6, 5.8, 4.1 Hz, 1H), 2.29 (br s, 1.65H), 1.68 (m, 1H), 1.47 (dqd, J = 13.4, 3 × 7.4, 4.6 Hz, 1H), 1.21 (m, 1H), 0.93 (t, J = 2 × 7.4 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 128.4, 128.1, 127.0, 62.0, 60.1, 51.2, 35.1, 26.2, 14.3, 11.7 ppm. FT-IR (NaCl):

(21) Thomas, E. W.; Nishizawa, E. E.; Zimmermann, D. C.; Williams, D. J. *J. Med. Chem.* **1989**, *32*, 228.

ν 3328, 3061, 3028, 2960, 2926, 2875, 1598, 1457, 1378 cm^{-1}. $[\alpha]^{26}_D$: +18 (*c* 1.00, $CHCl_3$). MS (ESI^+): *m*/*z* 208 ($[M + H]^+$, 100), 139 (12), 117 (20). HRMS (ESI^+): calcd for $C_{13}H_{22}NO$ 208.1696, found 208.1701.

2-(1,3-Diphenylpropan-2-ylamino)ethanol (8d). ^1H NMR (400 MHz, $CDCl_3$): δ 7.4−7.3 (m, 4H), 7.3−7.2 (m, 6H), 3.53 (m, 2H), 3.12 (p, $J = 4 \times 6.6$ Hz, 1H), 2.92 (br s, 2H), 2.9−2.6 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.8, 128.9, 128.1, 125.9, 60.4 (2C), 48.4, 40.3 ppm. MS (EI^+): *m*/*z* 255 ($[M]^+$, 1), 165 (99), 164 (100), 146 (99), 132 (20), 131 (16), 130 (28), 129 (31), 120 (82), 119 (41), 118 (38), 117 (86), 115 (23), 105 (70), 104 (20), 103 (76), 92 (18), 91 (99), 78 (15), 77 (54), 65 (80). HRMS (EI^+): calcd for $C_{17}H_{21}NO$ 255.1623, found 255.1622.

General Experimental Procedures for the Synthesis of 2-Oxazolidinones. Procedure A (phosphorus electrophiles): A solution of the 1,2-amino alcohol (100 mol %) and the base (100−150 mol %) in CH_3CN or CH_2Cl_2 was cooled to the indicated initial temperature using H_2O/ice, ice/NaCl, or acetone/CO_2 cooling baths and was saturated with CO_2 by bubbling CO_2 gas through the solution for 5−10 min. The phosphorus electrophile (100−200 mol %) was added dropwise over 5−20 min. The solution was stirred at the same temperature for an additional 15−20 min and was allowed to reach room temperature slowly and stirred overnight under a CO_2 atmosphere. The reaction mixture was concentrated to dryness, and the residue was dissolved in $CHCl_3$ (20 mL) and washed with a 10% aqueous Na_2CO_3 saturated with NaCl (1×). The aqueous solution was further extracted with $CHCl_3$ (1×), and the combined organic layers were washed with 10% aqueous HCl saturated with NaCl (1×). The final aqueous layer was extracted with $CHCl_3$ (1×), the combined organic layers were dried over Na_2SO_4, and the solvents were removed under reduced pressure. The crude reaction mixture was purified by flash chromatography on silica gel to give the corresponding oxazolidinone. **Procedure B** (carbon and sulfur electrophiles): A solution of the 1,2-amino alcohol (100 mol %) and the base (200−250 mol %) in CH_3CN or CH_2Cl_2 cooled to the indicated initial temperature using H_2O/ice, ice/NaCl, or acetone/CO_2 cooling baths was saturated with CO_2 by bubbling CO_2 gas through the solution for 5−10 min. The electrophile (100 mol %) was added dropwise, and the solution was stirred at the same temperature for an additional 5 min. The cooling bath was then removed, and the mixture was stirred for 30−40 min under a CO_2 atmosphere. The reaction mixture was concentrated to dryness, and the crude product was purified by flash chromatography on silica gel to give the corresponding oxazolidinone.

(*R*)-4-Phenyloxazolidin-2-one (7a). Procedure A (DPPA): Following the general procedure, (*R*)-phenylglycinol **6a** (150 mg, 1.09 mmol, 100 mol %), PhTMG (250 mg, 1.31 mmol, 120 mol %), and DPPA (0.23 mL, 1.09 mmol, 100 mol %) in CH_3CN (10 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:4 to 1:2), the title compound **7a** (143 mg, 80% yield) as a colorless solid. **Procedure A** (DPPCl): Following the general procedure, (*R*)-phenylglycinol **6a** (110 mg, 0.80 mmol, 100 mol %), Et_3N (0.22 mL, 1.60 mmol, 200 mol %), and DPPCl (0.20 mL, 0.96 mmol, 120 mol %) in CH_3CN (12 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:5 to 1:2), the title compound **7a** (124 mg, 95% yield) as a colorless solid. **Procedure B** (AcCl): Following the general procedure (*R*)-phenylglycinol **6a** (120 mg, 0.87 mmol, 100 mol %), Et_3N (0.30 mL, 2.18 mmol, 250 mol %), and AcCl (0.06 mL, 0.87 mmol, 100 mol %) in CH_3CN (12 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1.5:1), the title compound **7a** (133 mg, 94% yield) as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$): δ 7.4−7.3 (m, 5H), 6.67 (br s, 1H), 4.94 (m, 1H), 4.69 (t, $J = 2 \times 8.7$ Hz, 1H), 4.13 (dd, $J = 8.6$, 7.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 139.5, 129.0, 128.6, 125.9, 72.4, 56.2 ppm. FT-IR (NaCl): ν 3246, 3152, 3026, 1736, 1711 cm^{-1}. $[\alpha]^{24}_D$: −50 (*c* 1.76, $CHCl_3$). MS (EI^+): *m*/*z* 163 ($[M]^+$, 27), 162 (11), 133 (58), 105 (51), 104 (100), 69 (31). HRMS (EI^+): calcd for $C_9H_9NO_2$ 163.0633, found 163.0639.

(*S*)-4-*tert*-Butyloxazolidin-2-one (7d). Procedure A (DPPA): Following the general procedure, (*S*)-2-amino-3,3-dimethylbutan-1-ol **6d** (210 mg, 1.79 mmol, 100 mol %), PhTMG (370 mg, 1.93 mmol, 108 mol %), and DPPA (0.38 mL, 1.79 mmol, 100 mol %) in CH_3CN (10 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:3 to 1:2), the title compound **7d** (190 mg, 74% yield) as a colorless solid. **Procedure A** (DPPCl): Following the general procedure, (*S*)-2-amino-3,3-dimethylbutan-1-ol **6d** (170 mg, 1.45 mmol, 100 mol %), PhTMG (555 mg, 2.90 mmol, 200 mol %), and DPPCl (0.45 mL, 2.17 mmol, 150 mol %) in CH_3CN (10 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:1.5), the title compound **7d** (176 mg, 85% yield) as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$): δ 7.43 (br s, 1H), 4.29 (t, $J = 2 \times 9.0$ Hz, 1H), 4.11 (dd, $J = 9.0$, 5.8 Hz, 1H), 3.53 (ddd, $J = 9.0$, 5.8, 0.8 Hz, 1H), 0.83 (br s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 66.3, 61.4, 33.1, 24.5 ppm. FT-IR (NaCl): ν 3238, 3136, 2963, 2874, 1736 cm^{-1}. $[\alpha]^{25}_D$: +12 (*c* 1.80, $CHCl_3$). MS (EI^+): *m*/*z* 143 ($[M]^+$, 1), 88 (5), 87 (100), 86 (21), 85 (14). HRMS (EI^+): calcd for $C_7H_{13}NO_2$ 143.0946, found 143.0947.

(*S*)-4-[(1*H*-Indol-3-yl)methyl]oxazolidin-2-one (7f). Procedure A (DPPCl): Following the general procedure, (*S*)-tryptophanol **6f** (211 mg, 1.11 mmol, 100 mol %) was treated with Et_3N (0.31 mL, 2.22 mmol, 200 mol %) and DPPCl (0.28 mL, 1.33 mmol, 120 mol %) in CH_3CN (15 mL) cooled initially to −40 °C. Instead of the aqueous workup, the reaction mixture was concentrated to dryness and the residue was purified by flash chromatography (silica gel, AcOEt/hexane 2:1) to give the title compound **7f** (221 mg, 92% yield) as a colorless solid. ^1H NMR (400 MHz, DMSO-d_6): δ 10.94 (br s, 1H), 7.80 (br s, 1H), 7.55 (m, 1H), 7.36 (dt, $J = 8.1$, 2×0.9 Hz, 1H), 7.23 (d, $J = 2.4$ Hz, 1H), 7.08 (ddd, $J = 8.1$, 7.0, 1.1 Hz, 1H), 7.00 (ddd, $J = 8.0$, 7.0, 1.1 Hz, 1H), 4.29 (t, $J = 2 \times 8.3$ Hz, 1H), 4.10 (m, 1H), 3.99 (dd, $J = 8.3$, 5.4 Hz, 1H), 2.95 (dd, $J = 14.4$, 4.9 Hz, 1H), 2.84 (dd, $J = 14.4$, 7.5 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.7, 136.1, 127.4, 123.7, 121.0, 118.4, 118.1, 111.4, 108.8, 68.6, 51.9, 30.3 ppm. FT-IR (NaCl): ν 3402, 3292, 3055, 3008, 2973, 2912, 1740 cm^{-1}. $[\alpha]^{28}_D$: +4 (*c* 2.60, MeOH). MS (ESI^+): *m*/*z* 239 ($[M + Na]^+$, 100), 217 ($[M + H]^+$, 60). HRMS (ESI^+): calcd for $C_{12}H_{13}N_2O_2$ 217.0971, found 217.0970.

(4*R*,5*S*)-4-Methyl-5-phenyloxazolidin-2-one (7i). Procedure A (DPPA): Following the general procedure, (1*S*,2*R*)-norephedrine **6i** (210 mg, 1.39 mmol, 100 mol %), PhTMG (290 mg, 1.52 mmol, 109 mol %), and DPPA (0.30 mL, 1.39 mmol, 100 mol %) in CH_3CN (10 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:4 to 1:2), the title compound **7i** (185 mg, 75% yield) as a colorless solid. **Procedure A** (DPPCl): Following the general procedure, (1*S*,2*R*)-norephedrine **6i** (200 mg, 1.32 mmol, 100 mol %), PhTMG (300 mg, 1.57 mmol, 119 mol %), and DPPCl (0.27 mL, 1.32 mmol, 100 mol %) in CH_3CN (10 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:2 to 1:1), the title compound **7i** (192 mg, 82% yield) as a colorless solid. **Procedure A** (DPPCl): Following the general procedure, (1*S*,2*R*)-norephedrine **6i** (150 mg, 0.99 mmol, 100 mol %), Et_3N (0.28 mL, 1.98 mmol, 200 mol %), and DPPCl (0.25 mL, 1.19 mmol, 120 mol %) in CH_3CN (15 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1.5:1), the title compound **7i** (168 mg, 96% yield) as a colorless solid. **Procedure B** (AcCl): Following the general procedure, (1*S*,2*R*)-norephedrine **6i** (110 mg, 0.73 mmol, 100 mol %), PhTMG (280 mg, 1.46 mmol, 200 mol %), and AcCl (0.05 mL, 0.73 mmol, 100 mol %) in CH_3CN

(10 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1.5:1), the title compound **7i** (124 mg, 96% yield) as a colorless solid. **Procedure B** (AcCl): Following the general procedure, (1*S*,2*R*)-norephedrine **6i** (110 mg, 0.73 mmol, 100 mol %), Et_3N (0.21 mL, 1.46 mmol, 200 mol %), and AcCl (0.05 mL, 0.73 mmol, 100 mol %) in CH_3CN (15 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1.5:1), the title compound **7i** (126 mg, 97% yield) as a colorless solid. **Procedure B** (AcCl): Following the general procedure, (1*S*,2*R*)-norephedrine **6i** (110 mg, 0.73 mmol, 100 mol %), Et_3N (0.21 mL, 1.46 mmol, 200 mol %), and AcCl (0.05 mL, 0.73 mmol, 100 mol %) in CH_3CN (15 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1.5:1), the title compound **7i** (126 mg, 97% yield) as a colorless solid. **Procedure B** (AcBr): Following the general procedure, (1*S*,2*R*)-norephedrine **6i** (100 mg, 0.66 mmol, 100 mol %), Et_3N (0.18 mL, 1.32 mmol, 200 mol %), and AcBr (0.05 mL, 0.66 mmol, 100 mol %) in CH_3CN (10 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:1.5), the title compound **7i** (110 mg, 94% yield) as a colorless solid. **Procedure B** ($SOCl_2$): Following the general procedure, (1*S*,2*R*)-norephedrine **6i** (100 mg, 0.66 mmol, 100 mol %), PhTMG (250 mg, 1.32 mmol, 200 mol %), and $SOCl_2$ (0.05 mL, 0.66 mmol, 100 mol %) in CH_3CN (10 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:1.5 to 1:1), the title compound **7i** (103 mg, 88% yield) as a colorless solid. **Procedure B** (*p*NsCl): Following the general procedure, (1*S*,2*R*)-norephedrine **6i** (100 mg, 0.66 mmol, 100 mol %), PhTMG (250 mg, 1.32 mmol, 200 mol %), and a solution of *p*-NsCl (210 mg, 0.66 mmol, 100 mol %) in CH_3CN (2 mL) in CH_3CN (10 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:1), the title compound **7i** (153 mg, 92% yield) as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.5−7.2 (m, 5H), 7.05 (br s, 1H), 5.72 (d, J = 8.1 Hz, 1H), 4.25 (m, 1H), 0.83 (d, J = 6.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 134.8, 128.2, 128.1, 125.7, 80.8, 52.2, 17.2 ppm. FT-IR (NaCl): ν 3240, 2980, 1756 cm^{-1}. $[\alpha]^{24}_D$: +176 (*c* 0.82, $CHCl_3$). MS (EI$^+$): *m*/*z* 178 (33), 177 ([M]$^+$, 8), 107 (100), 79 (41). HRMS (EI$^+$): calcd for $C_{10}H_{11}NO_2$ 177.0790, found 177.0792.

(*S*)-3-Benzyl-4-isopropyloxazolidin-2-one (9a). Procedure A (DPPA): Following the general procedure, (*S*)-2-(benzylamino)-3-methylbutan-1-ol **8a** (160 mg, 0.83 mmol, 100 mol %), PhTMG (200 mg, 1.05 mmol, 126 mol %), and DPPA (0.20 mL, 0.91 mmol, 110 mol %) in CH_3CN (20 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:8 to 1:4), the title compound **9a** (154 mg, 84% yield) as a yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.4−7.2 (m, 5H), 4.88 (d, J = 15.2 Hz, 1H), 4.18 (t, J = 2 × 9.0 Hz, 1H), 4.08 (dd, J = 8.9, 5.9 Hz, 1H), 4.01 (d, J = 15.2 Hz, 1H), 3.57 (m,1H), 2.08 (m, 1H), 0.88 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 135.7, 128.6, 127.9, 127.7, 62.6, 58.0, 45.7, 26.9, 17.4, 13.9 ppm. FT-IR (NaCl): ν 3062, 3031, 2963, 2929, 2877, 1748 cm^{-1}. $[\alpha]^{24}_D$: −25 (*c* 1.68, $CHCl_3$). MS (EI$^+$): *m*/*z* 219 ([M]$^+$, 7), 176 (31), 92 (6), 91 (100), 65 (6). HRMS (EI$^+$): calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1267. MS (ESI$^+$): *m*/*z* 242 ([M + Na]$^+$, 97), 220 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{13}H_{17}NO_2Na$ 242.1152, found 242.1159.

3-(1,3-Diphenylpropan-2-yl)oxazolidin-2-one (9d). Procedure A (DPPA): Following the general procedure, 2-(1,3-diphenylpropan-2-ylamino)ethanol **8d** (204 mg, 0.80 mmol, 100 mol %), Et_3N (0.22 mL, 1.60 mmol, 200 mol %), and DPPA (0.21 mL, 0.96 mmol, 120 mol %) in CH_3CN (12 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:3), the title compound **9d** (211 mg, 94% yield) as a colorless oil. **Procedure A** (DPPCl): Following the general procedure, 2-(1,3-diphenylpropan-2-ylamino)ethanol **8d** (204 mg, 0.80 mmol, 100 mol %), Et_3N (0.22 mL, 1.60 mmol, 200 mol %), and DPPCl (0.20 mL, 0.96 mmol, 120 mol %) in CH_3CN (12 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:3 to 1:2), the title compound **9d** (214 mg, 95% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.4−7.1 (m, 10H), 4.23 (tt, J = 2 × 9.1, 2 × 6.2 Hz, 1H), 4.1−3.9 (m, 2H), 3.3−3.1 (m, 2H), 3.01 (dd, J = 14.1, 9.1 Hz, 2H), 2.94 (dd, J = 14.1, 6.2 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 137.8, 128.7, 128.4, 126.5, 61.7, 56.5, 42.3, 38.1 ppm. FT-IR (NaCl): ν 3086, 3061, 3027, 3002, 2951, 2919, 2858, 1746, 1602 cm^{-1}. MS (ESI$^+$): *m*/*z* 304 ([M + Na]$^+$, 37), 282 ([M + H]$^+$, 100). HRMS (ESI$^+$): calcd for $C_{18}H_{20}NO_2$ 282.1489, found 282.1496.

(*S*)-1,1-Diphenyltetrahydropyrrolo[1,2-*c*]oxazol-3(1*H*)-one (9f). Procedure A (DPPA): Following the general procedure, (*S*)-diphenyl(pyrrolidin-2-yl) methanol **8f** (170 mg, 0.67 mmol, 100 mol %), PhTMG (180 mg, 0.94 mmol, 140 mol %), and DPPA (0.17 mL, 0.80 mmol, 120 mol %) in CH_2Cl_2 (15 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:8 to 1:4), the title compound (92 mg, 49% yield) as a colorless solid. **Procedure A** (DPPCl): Following the general procedure, (*S*)-diphenyl(pyrrolidin-2-yl) methanol **8f** (139 mg, 0.55 mmol, 100 mol %), PhTMG (210 mg, 1.10 mmol, 200 mol %), and DPPCl (0.17 mL, 0.82 mmol, 150 mol %) in CH_2Cl_2 (12 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:5), the title compound (151 mg, 98% yield) as a colorless solid. **Procedure A** (DPPCl): Following the general procedure, (*S*)-diphenyl(pyrrolidin-2-yl)methanol **8f** (157 mg, 0.62 mmol, 100 mol %), Et_3N (0.17 mL, 1.24 mmol, 200 mol %), and DPPCl (0.15 mL, 0.74 mmol, 120 mol %) in CH_2Cl_2 (15 mL) cooled initially to −40 °C afforded, after flash chromatography (silica gel, AcOEt/hexane 1:5), the title compound (163 mg, 94% yield) as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.6−7.5 (m, 2H), 7.4−7.2 (m, 8H), 4.56 (dd, J = 10.5, 5.5 Hz, 1H), 3.73 (dt, J = 11.2, 2 × 8.1 Hz, 1H), 3.24 (ddd, J = 11.2, 9.7, 3.7 Hz, 1H), 2.05−1.79 (m, 2H), 1.73 (m, 1H), 1.12 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.3, 143.2, 140.1, 128.4, 128.2 (2×), 127.6, 125.8, 125.3, 85.7, 69.1, 45.9, 28.8, 24.7 ppm. FT-IR (NaCl): ν 3060, 3030, 2974, 2903, 1754 cm^{-1}. $[\alpha]^{26}_D$: −211 (*c* 1.44, $CHCl_3$). MS (EI$^+$): *m*/*z* 279 ([M]$^+$, 12), 165 (55), 146 (35), 105 (65), 81 (45), 69 (100). HRMS (EI$^+$): calcd for $C_{18}H_{17}NO_2$ 279.1259, found 279.1266.

(4*R*,5*S*)-3-Isopropyl-4-methyl-5-phenyloxazolidin-2-one (11c) and (4*R*,5*R*)-3-Isopropyl-4-methyl-5-phenyloxazolidin-2-one (12c). Procedure A (DPPA): Following the general procedure, a mixture of (1*S*,2*R*)-2-(isopropylamino)-1-phenylpropan-1-ol **10c** (130 mg, 0.67 mmol, 100 mol %), PhTMG (170 mg, 0.89 mmol, 133 mol %), and DPPA (0.29 mL, 1.34 mmol, 200 mol %) in CH_2Cl_2 (20 mL) was cooled to −30 °C for 20 h. CO_2 was bubbled through the solution for 20 min, and the mixture was stirred and allowed to warm to room temperature slowly over 14 h. Flash chromatography (silica gel, AcOEt/hexane 1:10 to 1:5) gave a fraction containing diastereoisomers **11c** and **12c** in a 5:1 ratio (101 mg, 69% yield). These compounds were finally separated by HPLC (AcOEt/hexane 1:4). **(4*R*,5*S*)-3-Isopropyl-4-methyl-5-phenyloxazolidin-2-one (11c):** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.4−7.2 (m, 5H), 5.53 (d, J = 7.9 Hz, 1H), 4.11 (m, 1H), 3.95 (sept, J = 6 × 6.9 Hz, 1H), 1.35 (d, J = 6.9 Hz, 3H), 1.31 (d, J = 6.8 Hz, 3H), 0.81 (d, J = 6.5 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8, 135.1, 128.4, 128.2, 126.0, 78.8, 54.4, 45.9, 21.6, 19.9, 16.9 ppm. FT-IR (NaCl): ν 3033, 2980, 2938, 2880, 1733 cm^{-1}. $[\alpha]^{24}_D$: +109 (*c* 0.72, $CHCl_3$). MS (EI$^+$): *m*/*z* 219 ([M]$^+$, 14), 204 (92), 160 (91), 132 (11), 118.06 (44), 117 (53), 105 (38), 85 (73), 91 (55), 77 (34), 70 (100). HRMS (EI$^+$): calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1268. **(4*R*,5*R*)-3-Isopropyl-4-methyl-5-phenyloxazolidin-2-one (12c):** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.4−7.3 (m, 5H), 4.87 (d, J = 6.5 Hz, 1H), 3.97 (sept, J = 6 × 6.9 Hz, 1H), 3.69 (p, J = 4 × 6.2 Hz, 1H), 1.42 (d, J = 6.2 Hz, 3H), 1.30 (d, J = 6.9 Hz, 3H), 1.27 (d, J = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 138.5, 128.8, 128.8,

125.6, 82.0, 58.6, 45.8, 21.4, 20.4, 19.5 ppm. FT-IR (NaCl) ν 3064, 3034, 2974, 2934, 2878, 1747 cm^{-1}. $[\alpha]^{24}_D$: −10 (*c* 0.26, $CHCl_3$). MS (EI^+): *m*/*z* 219 ($[M]^+$, 8), 204 (68), 160 (100), 132 (9), 118 (42), 117 (32), 105 (23), 91 (30), 85 (21), 70 (53). HRMS (EI^+): calcd for $C_{13}H_{17}NO_2$ 219.1259; found 219.1257.

Synthesis of 2-Oxazinones. 5,5-Dimethyl-1,3-oxazinan-2-one (30). Procedure B (with AcCl): Following the general procedure for the synthesis of 2-oxazolidinones, the 1,3-amino alcohol **26** (130 mg, 1.26 mmol, 100 mol %) was treated with Et_3N (0.44 mL, 3.15 mmol, 250 mol %), AcCl (0.09 mL, 1.26 mmol, 100 mol %), and CO_2 in CH_3CN (15 mL). The reaction mixture was concentrated to dryness, and the resulting crude material was purified by flash chromatography (silica gel, AcOEt), to give the title compound **30** (156 mg, 96% yield) as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$): δ 6.85 (br s, 1H), 3.86 (br s, 2H), 3.00 (br s, 2H), 1.03 (s, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3, 76.0, 51.4, 27.7, 22.5 ppm. IR (NaCl): ν 3295, 2973, 2938, 2878, 1705, 1665 cm^{-1}. MS (EI^+): *m*/*z* 129 ($[M]^+$, 100), 84 (12), 82 (4), 73 (6), 71 (4), 70 (18), 68 (7). HRMS (EI^+): calcd for $C_6H_{11}N_1O_2$ 129.0790, found 129.0789.

General Procedure for the Synthesis of Cyclic Ureas. A solution of the diamine (100 mol %) and the base (100−200 mol %) in CH_3CN or CH_2Cl_2 cooled to the indicated initial temperature using H_2O/ice, ice/NaCl, or acetone/CO_2 cooling baths was saturated with CO_2 by bubbling CO_2 gas through the solution for 5−10 min. DPPA (100−120 mol %) was added dropwise over 5−20 min, and the solution was stirred at the same temperature for an additional 15−20 min. The reaction mixture was allowed to warm to room temperature slowly and stirred overnight under a CO_2 atmosphere. The reaction mixture was concentrated to dryness, and the residue was purified by flash chromatography to give the corresponding cyclic urea. **(±)-4-Methylimidazolidin-2-one (36a):** Following the general procedure, propane-1,2-diamine **35a** (120 mg, 1.62 mmol, 100 mol %) was treated with PhTMG (340 mg, 1.78 mmol, 110 mol %) and DPPA (0.38 mL, 1.78 mmol, 110 mol %) in CH_3CN (30 mL) cooled initially to −40 °C to afford, after flash chromatography (silica gel, MeOH/CH_2Cl_2 1:20), the title compound **36a** (139 mg, 86% yield) as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$): δ 5.93 (d, J = 8.5 Hz, 1H), 5.82 (d, J = 7.5 Hz, 1H), 3.84 (m, 1H), 3.53 (t, $J = 2 \times 8.5$ Hz, 1H), 3.00 (t, $J = 2 \times 7.6$ Hz, 1H), 1.18 (d, J = 6.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.7, 48.3, 48.0, 21.1 ppm. IR (NaCl): ν 3208, 3105, 3080, 2967, 2929, 2862, 1698 cm^{-1}. MS (EI^+): *m*/*z* 100 ($[M]^+$, 21), 85 ($[M(-NH_2)]^+$, 100). HRMS (EI^+): calcd for $C_4H_8N_2O$ 100.0637, found 100.0636.

1,3-Dibenzyl-1,3-diazepan-2-one (36l). Following the general procedure, *N*,*N*′-dibenzylbutane-1,4-diamine **35l** (99 mg, 0.37 mmol, 100 mol %) was treated with PhTMG (121 mg, 0.63 mmol, 170 mol %) and DPPA (0.08 mL, 0.37 mmol, 100 mol %) in CH_2Cl_2 (20 mL) cooled initially to −35 °C to afford, after flash chromatography (silica gel, AcOEt/hexanes 1:4), the title compound **36l** (80 mg, 73%) as a pale yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.5−7.2 (m, 10H), 4.55 (s, 4H), 3.20 (m, 4H), 1.54 (m, 4H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.7, 138.8, 128.3, 128.2, 126.9, 53.5, 48.7, 26.3 ppm. IR (NaCl): ν 3060, 3028, 2932, 2856, 1635 cm^{-1}. MS (ESI^+): *m*/*z* 317 ($[M + Na]^+$, 100), 295 ($[M + H]^+$, 15), 227 (4). HRMS (ESI^+): calcd for $C_{19}H_{23}N_2O$ 295.1805, found 295.1805.

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Supporting Information Available: Experimental procedures and characterization data for those compounds not included in the Experimental Section and copies of ^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.