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Synthesis of cyclic *N*-hydroxylated ureas and oxazolidinone oximes enabled by chemoselective iodine(III)-mediated radical or cationic cyclizations of unsaturated *N*-alkoxyureas

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Abstract. In this study we describe the reactivity of unsaturated *N*-alkoxyureas in the presence of different combinations of a hypervalent iodine(III) reagent and a bromide source or TEMPO. Three complementary cyclizations can be achieved depending on the reaction conditions. On the one hand, PIFA with pyridinium bromide leads to an oxybromination reaction. On the other hand, bis(*tert*-butylcarbonyloxy)iodobenzene with tetrabutylammonium bromide or TEMPO triggers aminobromination or aminooxyamination reactions, respectively. Control experiments showed that the three reactions proceed through distinct mechanisms: the first process is ionic while the other two follow a radical manifold.

Keywords: Hypervalent iodine; bromination; cyclization; radicals; TEMPO

Introduction

Cyclic *N*-hydroxylated ureas are a singular type of heterocycle that have been incorporated into various bioactive scaffolds to target anticancer[1] or herbicidal activities[2] with moderate success. This motif is also key to the activity of avibactam (**1**, Figure 1), a non β-lactam β-lactamase inhibitor[3] that was discovered and developed in the early 2000's and was approved by the FDA in 2015 in combination with Ceftazidime (a 3rd generation cephalosporin antibiotic) for the treatment of severe Gram-negative bacteria infections.[4]

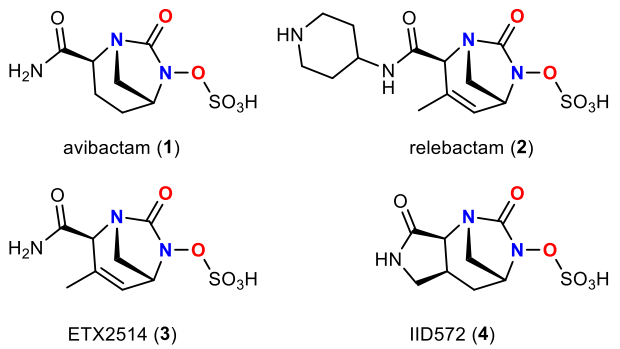


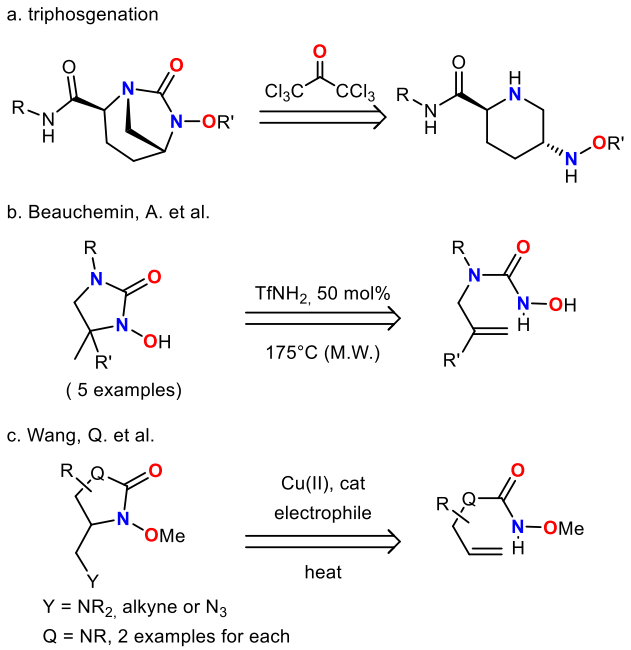
Figure 1. Examples of diazabicyclooctane β-lactamase inhibitors.

Other related diazabicyclooctane derivatives such as relebactam[5] (**2**), ETX2514[6] (**3**) or IID572[7] (**4**) are at the forefront of the development pipeline for the fight against bacterial resistance.[8] Antimicrobial resistance becomes an ever increasing threat[9] so providing modular and versatile synthetic methods to access this type of compounds is critical, especially since only few reactions can be used so far.

Initial methods employed to access cyclic *N*-hydroxylated ureas relied on the reaction of hydroxylamine with chloropropylcarbamates in an S_N2/lactamisation sequence[1] or on the double alkylation of *N*-hydroxyureas with dibromoethane[10] and were very limited in term of scope.

The synthetic route to avibactam[11] or its analogues[6,12,13] requires the formation of the urea moiety using triphosgene after the construction of the hydroxyamino-six-membered ring (Scheme 1a). This implies that variations on the carbon backbone to study structure-activity-relationships (SAR) generally require to redevise the whole synthetic route.[6] An alternative approach would be to rely on a direct cyclization protocol, but, so far, only a handful of examples have been reported. In 2017, Beauchemin reported the Cope-type hydroamination of five allyl *N*-hydroxyureas at high temperature (175°C under micro-wave irradiation) in the presence of triflimide to give *N*-hydroxy-imidazolidinones (Scheme 1b).[14] The substrates were obtained in a one-pot fashion from the corresponding allylamines and an *O*-isocyanate[15]

but the reaction only worked for *N*-hydroxy derivatives. The group of Wang developed three copper-catalyzed cyclizations of unsaturated *N*-methoxy amides, among which only featured two examples of ureas in each study.[16–18] The electrophiles can be *O*-benzoylhydroxylamines, or cyclic hypervalent iodine reagents. An amine,[16] an alkyne[17] or an azide[18] group can be introduced during the cyclization (Scheme 1c).

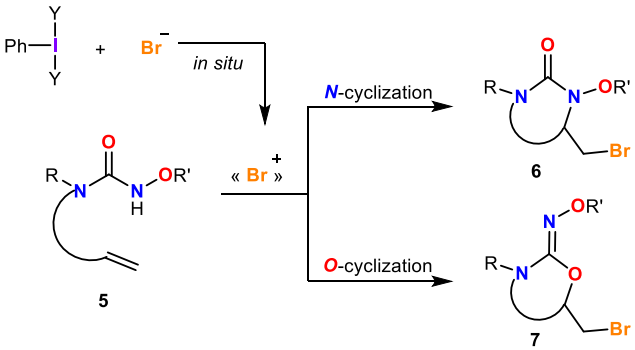


Scheme 1. Existing methods to access cyclic hydroxyureas.

This shortage of practical and efficient cyclization methods greatly limits the access to these heterocycles and precludes rapid SAR studies for the development of crucially needed β-lactamase inhibitors. Herein, we describe the direct, metal-free and chemoselective synthesis of a broad range of diversely substituted cyclic *N*-oxyureas as well as their *N*-oxycarbamimidates counterparts from unsaturated N-alkoxyureas.

Reaction Design

In order to broaden the range of substrates that could be attainable by a direct cyclization, we wished to develop a reaction following a specific blueprint: *avoiding the use of transition metals, no heating and installing a linchpin for further derivatizations*. Based on our previous studies on hypervalent iodine(III)[19–24]-mediated halogenations,[25–28] and in particular modular halocyclizations,[29,30] we chose to focus on the bromocyclization of unsaturated *N*-oxyureas (**5**, Scheme 2). These substrates are challenging in terms of regio- and chemo-selectivity. First the *N*-*O* bond is sensitive and several groups have taken advantage of this to develop cyclization processes that are concomitant with the loss of the oxygenated moiety.[31–33] Then, as for amides[34] or ureas,[35,36] either *N*- or *O*-cyclization can take place, leading to *N*-oxyurea **6** or *N*-oxycarbamimidate **7**, respectively. The former generally arises from the activation of the nitrogen, while the latter stems from the activation of the double bond, as demonstrated by the group of Liu for the Cu(II) mediated oxidative halocyclizations of *N*-alkoxyamides.[37] We assumed that careful tuning of the iodine(III)/bromide combination should allow to steer the reaction selectively towards either modes of cyclization depending on the nature of the electrophilic bromination species that would be formed in situ.[38–44] Interestingly, oxazolidinone oximes also constitute a rather underexplored class of heterocycles. Some members of this family have been studied by Narasaka for their electrophilic reactivity[45,46] and some other were patented as antidepressant compounds more than 40 years ago.[47] However, their synthesis required the use of highly toxic phosgene oxide.



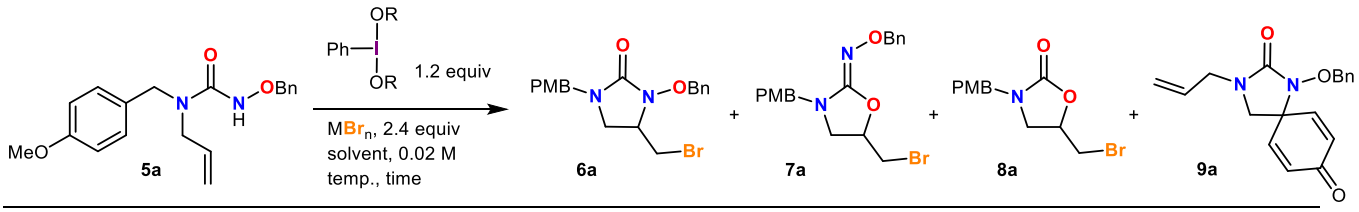
Scheme 2. Possible pathways for the bromocyclization of unsaturated *N*-oxyureas.

Results and Discussion

Optimization of the bromocyclization

We chose *N*-benzyloxyurea **5a** bearing a *p*-methoxybenzyl (PMB) group as a model substrate to explore the condition that would yield a chemoselective bromocyclization. In addition to the *N*- and *O*-cyclization onto the pending allyl chain, we expected that the electron-rich PMB could also participate in an oxidative process, which would have to be avoided. First, a combination of lithium bromide and (diacetoxyiodo)benzene in dichloromethane at -5°C was used (Table 1, entry 1). Full conversion was reached after 1h40 and a mixture of *N*-oxyimidazolidinone **6a**, oxazolidinone oxime **7a** and the corresponding oxazolidinone **8a** was obtained in a 61% overall yield. When compared to the reaction using *N*-bromosuccinimide (NBS) as the electrophilic bromination reagent (Entry 2), the combined yield is lower, yet the relative amount of **6a** arising from the *N*-cyclization process is higher.

Table 1. Optimization of the iodine(III)-mediated oxybromocyclization and aminobromocyclization of *N*-benzyloxy urea **5a**.[a)]



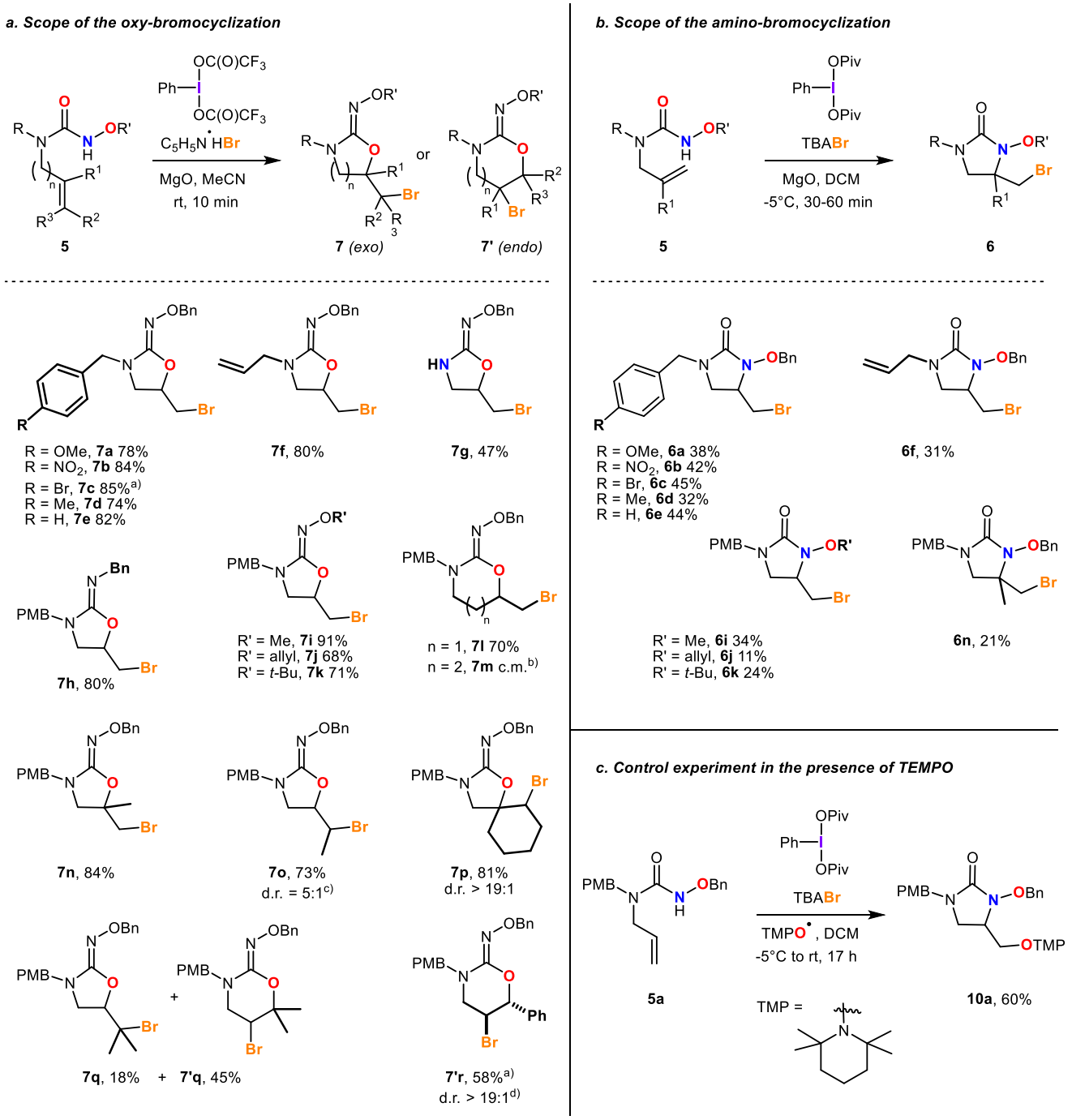
Entry	R	MBr$_n$	Solvent	additive	Temp.	Time (min)	Yield **6a** (%)	Yield **7a** (%)	Yield **8a** (%)	Yield **9a** (%)
1	Ac	LiBr	DCM	MS 3Å	-5°C	100	19	27	15	-
2	**NBS**		DCM	MgO	-5°C	15	7	65	17	-
3	Ac	LiBr	DCM	**MgO**	-5°C	90	12	51	-	-
4	**C(O)CMe$_3$**	LiBr	DCM	MgO	-5°C	60	32[b)]	31[b)]	-	-
5	**C(O)CF$_3$**	LiBr	DCM	MgO	-5°C	35	-	23	-	31
6	Ac	**none**	DCM	MgO	-5°C	90	-	-	-	32
7	Ac	**ZnBr$_2$**	DCM	MgO	-5°C	10	-	58	21	-
8	Ac	**C$_5$H$_5$N•HBr**	DCM	MgO	-5°C	15	-	77	-	-
9	Ac	**Bu$_4$NBr**	DCM	MgO	-5°C	60	32	-	-	-
10	**C(O)CMe$_3$**	**Bu$_4$NBr**	**DCM**	**MgO**	**-5°C**	**50**	**38**	**-**	**-**	**-**
11	**C(O)CF$_3$**	**C$_5$H$_5$N•HBr**	**MeCN**	**MgO**	**RT**	**10**	**-**	**78**	**-**	**-**

[a)] Reaction conditions: to a solution of **5a** in the solvent at the appropriate temperature were successively added, the additive, the bromide and the hypervalent iodine reagent; isolated yields unless stated otherwise. [b)] NMR yields.

To trap the acetic acid generated during the reaction that would be responsible for the formation of **8a**, magnesium oxide was used as the additive and only **6a** and **7a** were obtained (Entry 3). Variation of the acetoxy group of the iodine(III) reagent showed that, in combination with LiBr, bis(*tert*-butylcarbonyloxy)iodobenzene could favor the formation of *N*-oxyimidazolidinone **6a** in addition to **7a**, while bis(trifluoroacetoxy)iodobenzene (PIFA) led to **7a** along with spiro adduct **9a** (Entries 4 & 5). By analogy to what had previously been reported with PIFA for the corresponding *N*-methoxyamides[48,49] or aryl-alkoxyureas,[50] the latter would arise from the direct oxidation of the hydroxyl amine moiety into a nitrenium and subsequent nucleophilic trapping by the PMB group. Indeed, in the absence of a bromide source, **9a** was the sole product that could be isolated from the reaction (Entry 6). Keeping DIB as the oxidant, different types of bromide sources were screened and were found to have a dramatic impact on the course of the reaction. Zinc bromide favored the *O*-cyclization process as well as the hydrolysis of the oxime moiety and a mixture of **7a** and **8a** was obtained in a 79% combined yield (Entry 7). A comparable chemoselectivity was observed with pyridinium bromide, although the hydrolysis could be avoided, thus furnishing **7a** with 77% yield (Entry 8). In sharp contrast, when tetrabutylammonium bromide was employed, only the *N*-cyclization process took place and **6a** was isolated with 32% (Entry 9). Despite extensive screening of the reaction parameters (see Supporting Information), the aminobromocyclization of **5a** could only be improved to give 38% of **6a** by using a combination of Bu_4NBr and bis(*tert*-butylcarbonyloxy)iodobenzene (Entry 10). As for the oxybromocyclization of **5a**, the use of PIFA with C_5H_5N•HBr at room temperature allowed the reaction to be completed in 10 minutes, to give **7a** in 78% yield (Entry 11).

Scope of the oxy-bromocyclization

We started the exploration of the scope of the oxybromocyclization by varying the nature of the *para* substituent of the *N*-benzyl group. Both electron donating (OMe, **5a**) and withdrawing (NO_2, **5b**) groups as well as a halogen (Br, **5c**), a methyl (**5d**) or a hydrogen (**5e**) were equally tolerated and the corresponding oxazolidinone oximes **7a-e** were obtained in 74-85% yields (Scheme 3a). Having an allyl group (**5f**) or an unprotected nitrogen (**5g**) was also possible, although the unprotected product **7g** was obtained with a lower yield (47%). The reaction also proceeded with a urea (**5h**) and gave oxazolidinone imine **7h** in 80% yield. The oxygen protecting group could also be modified and the *O*-methyl, -allyl or- *t*-butyl oximes **7i-k** could be isolated with 68-91% yields. When the unsaturated chain was homologated, the *6-exo* cyclization went on smoothly (**7l**,70%). Adding another methylene (**5m**), proved detrimental and the expected 7-member ring could not be isolated. We then scrutinized the effect of the substitution of the double bond. The reaction worked well, following a *5-exo* cyclization mode with a methallyl (**5n**) a crotyl (**5o**) and a cyclohexene (**5p**), to give **7n**, **7o** and the



Scheme 3. Scope of the oxy-bromocyclization and the amino-bromocyclization, control experiment in the presence of TEMPO. – Reaction conditions: to a solution of **5** in the indicated solvent [0.02 M] at the indicated temperature, were successively added MgO (2.4 equiv.), the bromide (2.4 equiv.) and the hypervalent iodine reagent (1.2 equiv.); isolated yields; Piv = $C(O)C(CH_3)_3$. [a]) An X-ray crystal structure was obtained. [b]) c.m = complex mixture. [c]) *E:Z* ratio of **5o** was 5:1. [d]) *E:Z* ratio of **5r** was >19:1.

spiro compound **7p** with excellent yields. With a prenyl chain (**5q**), **7q** was obtained in 18% yield while the main adduct **7'q** (45%) resulted from a *6-endo* cyclization. This *endo* mode which became the sole pathway for cinnamyl derivative **5r** furnishing **7'r** as the *trans* diastereoisomer (confirmed by X-ray analysis of a monocrystal).

Scope of the amino-bromocyclization

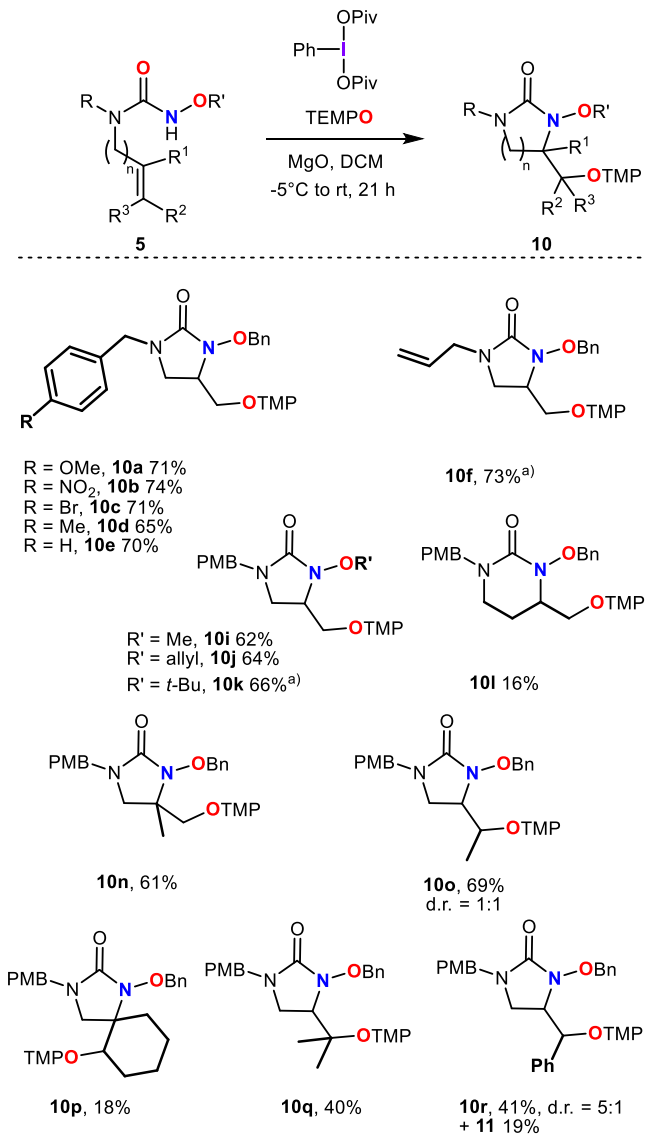
While the oxybromocyclization appeared to be fairly general, the aminobromocyclization scope proved to be more limited. *Para* substituted *N*-benzyl derivatives **5a-e** reacted similarly, giving **6a-e** with yields between 32% and 45% (Scheme 3b), significantly lower than what was observed for **7a-e**. If the allyl group of **5f** was tolerated, neither the unprotected benzyloxyurea **5g**, which decomposed, nor the *N*-benzylurea **5h** that remained intact were

suitable substrates for the reaction. Nevertheless, the reaction did proceed with other substituents on the oxygen and *O*-methyl, -allyl and -*t*-butyl oxyimidazolidinones **6i-k** were obtained with modest yields, in particular **6j** for which numerous side-products were also formed. Finally, *N*-methallyl substrate **5n** gave **6n** with 21% yield.

Discovery and scope of the amino-oxycyclization

In view of the modest yields obtained for the aminobromocyclization reaction, we suspected that highly reactive intermediates such as free radicals could be involved. To test this hypothesis we ran the reaction in the presence of the persistent radical TEMPO ((2,2,6,6-tetramethylpiperidin-1-yl)oxyl).[51] Doing so, the bromocyclization was totally shut down and, after 17 h, a cyclization with the incorporation of the TEMPO moiety occurred instead,[52] delivering oxyimidazolidinone **10a** in 60% yield (Scheme 3c). Since this process appeared far superior to the bromocyclyzation in terms of efficiency, it was rapidly optimized (see Supporting Information).

Without any bromide source, using an excess of TEMPO (2.0 equiv.) in combination with bis(*tert*-butylcarbonyloxy)iodobenzene for a longer time (21 h), **10a** was isolated with 71% yield (Scheme 4). Like for the previously explored processes, variation of the *para* substituent of the *N*-benzyl group did not alter the reaction and compounds **10b-e** were obtained with 65%-74% yields. *N*-Allylated substrate **5f** cyclized to **10f** in 73% yield but the unprotected **5g** decomposed under the reaction conditions, while *N*-benzyl urea **5h** did not react. The oxygen substituent could be changed to a methyl, an allyl or a *t*-butyl and compounds **10i-k** were obtained with good yields. Although substrate **5m** did not lead to the desired 7-membered ring, the 6-membered **10l** could be isolated in moderate yield. Various substituents could be accommodated on the double bond. With a methallyl (**5n**), a crotyl (**5o**), a cyclohexenyl (**5p**), a prenyl (**5q**) and a cinnamyl group (**5r**), the cyclization proceeded by a *5-exo* mode to give **10n-r** with moderate to excellent yields. In the case of **10r**, 19% of the corresponding ketone **11** were also isolated. The ketone presumably comes from the cleavage of the TMP to give the corresponding alcohol that would be oxidized in the presence of TEMPO and the iodine(III) reagent.[53] However submitting **10r** again to the reaction conditions for a prolonged time did not yield **11**.

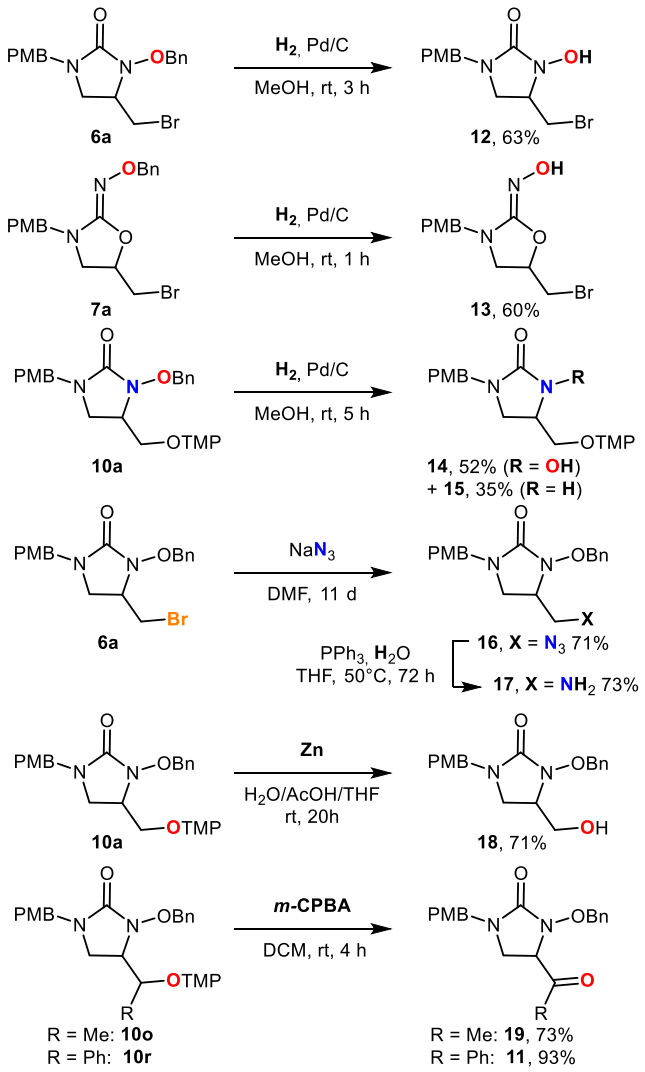


Scheme 4. Scope of the amino-oxycyclization. – Reaction conditions: to a solution of **5a** in DCM [0.02 M] at -5°C, were successively added MgO (2.0 equiv.), TEMPO (2.0 equiv.) and bis(*tert*-butylcarbonyloxy)iodobenzene (1.2 equiv.); isolated yield; Piv = $C(O)C(CH_3)_3$ [a] An X-ray crystal structure was obtained.

Synthetic applications of the cyclic adducts

Several groups have used cyclic *N*-oxyureas as platforms to access bioactive ureas after the cleavage of the N-O bond.[54,55] In a complementary approach, we wished to further functionalize the various heterocycles synthetized so as to keep the hydroxylamine moiety, which is essential for β-lactamase inhibition activities. First we explored the hydrogenolysis of the *O*-benzyl group on compounds **6a**, **7a** and **10a** (Scheme 5).Using palladium on charcoal as the catalyst, *N*-hydroxyimidazolidinone **12** could be isolated in 63% yield avoiding the potential reduction of the alkyl bromide function. The same protocol could yield **13** from **7a** with 60% yield. The main challenge in this case was to avoid the hydrolysis of the oxime to the oxazolidinone. Finally, the hydrogenolysis could be carried out in the presence of the 2,2,6,6-tetramethylpiperidin-1-yl)oxy group to give 52% of **14** from **10a**, concomitantly with 35% of urea **15**. The primary bromide of **6a** could efficiently be substituted by an azide to give **16**. Staudinger reduction of the latter using triphenylphosphine and water gave primary amine **17**. The TEMPO group could either be reduced to an alcohol such as **18** obtained from **10a** using Zn(0), or oxidized to a ketone such as **18** and **11** that were isolated with 73 and 93%

yields, respectively, after reaction of **10o** and **10r** with *m*-CPBA.



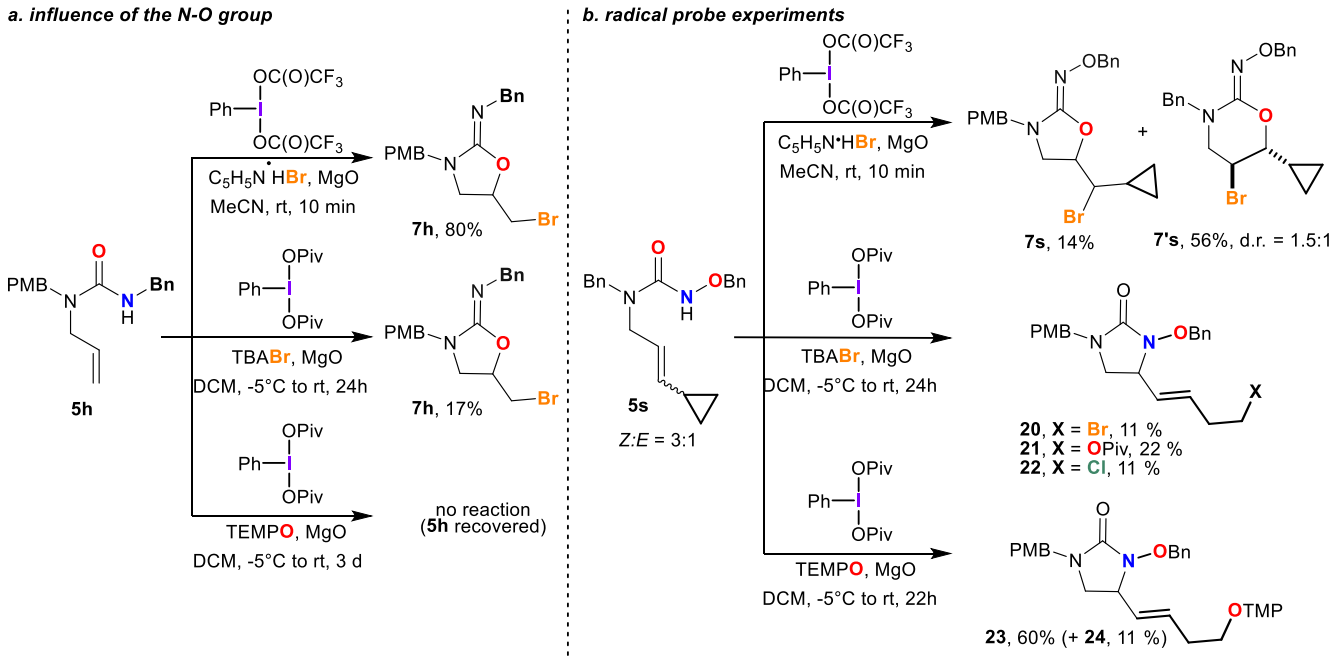
Scheme 5. Derivatization of the cyclized compounds. – Isolated yield.

Control Experiments

Although the three sets of reaction conditions that were developed could appear as almost identical, the outcome of the reaction can be drastically altered by minor modifications. The strong dichotomy resulting from the use of pyridinium bromide or tetrabutylammonium bromide (or other tetraalkyl bromides, see Supporting Information) is particularly striking. These variations indicate that the electrophilic species that are generated *in situ* must be different enough to react chemoselectively with the substrate. We first turned our attention to the role of the *N*-oxy moiety for the success of theamino-cyclization process (Scheme 6a). Indeed, under the oxy-bromocyclization conditions (PIFA with C_5H_5N•HBr), **7h** was obtained in 80% yield, while no reaction occurred in 1 h when **5h** was subjected to the amino-bromocyclization conditions (Bu_4NBr with bis(*tert*-butylcarbonyloxy)iodobenzene). Yet, if the reaction time was prolonged to 24 h, **7h** was eventually obtained. However, no reaction occurred when **5h** was reacted with TEMPO and bis(*tert*-butylcarbonyloxy)iodobenzene. To gain further insight on these transformations, substrate **5s** bearing a vinyl cyclopropyl was synthetized to detect[56] putative radical intermediates (Scheme 6b). The oxy-bromocyclization proceeded smoothly giving a mixture of 5-membered (**7s**) and 6-membered (**7s'**) rings, in line with what was observed for prenylated substrate **5q**, without any detectable opening of the cyclopropyl. The outcome was strikingly different when **5s** was reacted with TBABr and $PhI(OPiv)_2$. Only products arising from an opening of the cyclopropyl ring differing by the terminal substituent– Br (**20**), OPiv (**21**)and Cl (**22**) – were isolated in a 44 % combined yield. The latter two products presumably arise from the substitution of the un-hindered primary bromide in **20** by residual pivalate (from the hypervalent iodine reagent) and chloride (from the solvent). Finally, in the presence of TEMPO and bis(*tert*-butylcarbonyloxy)iodobenzene, **5s** was mostly converted into **23**, with concomitant opening of the cyclopropyl, along with minor amounts of diene **24** resulting from the elimination of the OTMP group (see ESI for details).

Mechanistic proposal

Based on all these observations a general mechanism proposal could be drafted. First, based on the isolation of **9a** (in which the PMB moiety reacts rather than the allylic chain) when **5a** was reacted with PIFA only (Table 1, entry 6), it appears that the initial activation of the double bond by the electrophilic iodine(III) reagent is not operative in our setting. Therefore, starting from substrate **5** and the hypervalent iodine(III) reagent **A**, three pathways leading to the three different type of products can be envisioned (Scheme 7). In the presence of an acidic source of bromide such as pyridinium hydrobromide, ligand exchanges around the iodine atom would give mixed species **B** that could undergo a reductive elimination to give iodobenzene and an acetylhypobromite **C** (***pathway a***). This highly electrophilic species[57] could react with the double bond of **5** to give bromiranium intermediate **D**. Intramolecular (in an *exo* or *endo* fashion depending on the olefin substituents) addition of the carbonyl[34] would give cyclic iminium **E** and finally compound **7**. The formation of oxazolidinone **8** (see Table 1) would probably occur from **E** in the presence of traces of water (when using the highly hydroscopic $ZnBr_2$ for instance). Because the double bond would be the one reacting with the electrophilic bromination species, this process can be equally efficient for both *N*-oxy-ureas and *N*-alkyl-ureas such as **5h**. Additionally the



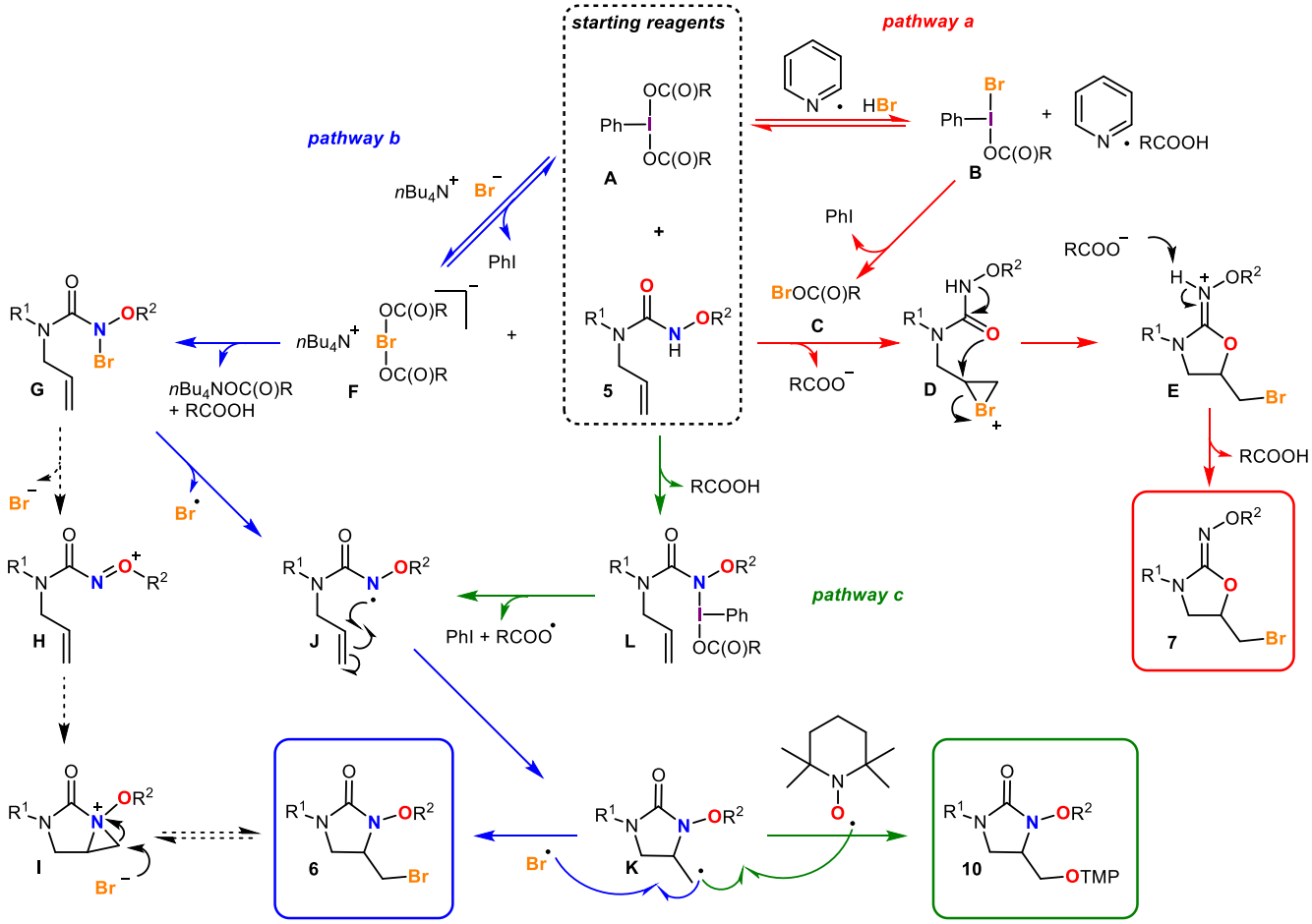
Scheme 6. Control experiments with amide **5h** and cyclopropyl **5s**. – Reaction conditions: to a solution of **5** in the solvent at the appropriate temperature were successively added, MgO, the bromide or the TEMPO and the hypervalent iodine reagent, the reaction was stirred for the indicated time; isolated yields.

formation of the bromonium is presumably stereospecific, which is in line with the conservation of the *E:Z* ratio into the d.r. ratio for **7o**, **7p** and **7'r** (see Scheme 3). The formation of **7r'** as the *trans* isomer from *E*-**5r** (that was confirmed by X-ray crystallography) is consistent with the S_N2 ring opening of a *trans* bromiranium.

When the source of bromide is a quaternary ammonium salt, such as TBABr, the formation of bis(acyloxy)bromate **F**, akin to the reagents previously reported by Kirschning[58–62] and later by Muniz for iodates,[63] would take place (***pathway b***). The modulated reactivity of this Br(I) species would favor its reaction with the *N*-oxy-urea moiety rather than the olefin, presumably through the bromination of the nitrogen atom to give **G**.[64,65] The *N*-oxy function seems essential for this pathway, as evidenced by the absence of *N*-bromocylization with urea **5h**. Nevertheless, over prolonged reaction time (see Scheme 6a), the equilibria can eventually be shifted towards the formation of **B** and **C** to give the *O*-bromocylization product **7h**. From **G**, an ionic pathway could lead to imino-oxonium **H** and after reaction with the olefin to aziridinium **I**. Opening of the latter by a bromide would give **6**. The intermediacy of an oxonium was previously proposed for the formation of the spiro adducts analogous to **9a** from methoxyamides.[48,49] Indeed, **9a** could arise from the trapping of **H** by the pending PMB group. Nevertheless, the opening of the cyclopropyl ring during the reaction of **5s** under these reaction conditions rather points towards a radical mechanism. This hypothesis is also consistent with the 1:1 diastereomeric ratio observed for the formation of **10o**, which contrasts with the 5:1 ratio observed for **7o**.Thus, from **G**, homolytic cleavage would give *N*-centered radical **J** whose reaction with the double bond would lead to **K**. Recombination with a bromo radical would then give **6**. Under the conditions described in Scheme 3c, when *n*-Bu_4NBr and TEMPO are both present, trapping with TEMPO would give **10**. Alternatively, under these specific conditions, bis(acyloxy)bromate **F** could promote the oxidation[61,66,67] of TEMPO into the corresponding oxoammonium that would act as the electrophile. However, under the optimized reaction conditions of Scheme 4, *i.e.* without any bromide, the activation of the nitrogen would occur directly with the hypervalent iodine(III) derivative[68] **A** to give **L** and then **J** (***pathway c***). This pathway is proper to *N*-alkoxy substrates and is ineffective for **5h**. From **J**, in the presence of an excess TEMPO, *exo* cyclization followed by trapping would lead to **10**.

Conclusion

By using iodine(III) reagents as the promoters, we have been able to develop the chemoselective cyclization of unsaturated *N*-hydroxylated ureas to give *N*-oxyimidazolidinones or oxazolidinone oximes. In this metal-free process, the oxy-cyclization happens through an ionic mechanism, while the amino-cyclization takes place by a radical manifold. In this case, the final trapping of the free radical can be achieved by a bromine or by TEMPO. The diverse saturated heterocycles obtained in this fashion can be further functionalized, notably by using the added function as a linchpin.



Scheme 7. General Mechanistic proposal.

Overall, we have shown that using widely available reagents and under rather similar conditions, cationic or radical manifolds can be triggered to achieve highly chemoselective transformations. In particular, this method can grant access to a broad range of diversely substituted cyclic *N*-hydroxylated ureas for which only few methods existed. The development of original non β-lactam β-lactamase inhibitor by using this methodology is currently undergoing in our group.

Experimental Section

For full experimental data, see SupportingInformation.

General procedure for the oxybromocyclization

To a solution of the urea derivative (1.0 equiv.) in anhydrous acetonitrile (0.025 M) at room temperature, were added MgO (2.4 equiv.), pyridine hydrobromide (2.4 equiv.) and PIFA (1.2 equiv.). After stirring at room temperature for 10 min, the reaction mixture was concentrated under reduced pressure before purification by flash chromatography.

General procedure for the aminobromocyclization

To a solution of the urea derivative (1.0 equiv.) in anhydrous CH_2Cl_2 (0.02 M) at -10 °C (ice-salt bath), were added MgO (2.4 equiv.), tetrabutylammonium bromide (2.4 equiv.) and $PhI(OPiv)_2$ (1.2 equiv.). After stirring at -10 °C for 1 hour, $PhI(OPiv)_2$ (0.3 equiv.) was added every 30 minutes to reach completion (2 or 3 additions). The reaction mixture was stirred until completion then concentrated under reduced pressure before purification by flash chromatography.

General procedure for the aminooxycyclization

To a solution of the urea derivative (1.0 equiv.) in anhydrous CH_2Cl_2 (0.02 M) at -10 °C (ice-salt bath), were added MgO (2.0 equiv.), Tempo (2.0 equiv.) and $PhI(OPiv)_2$ (1.2 equiv.). After stirring overnight at room temperature, $PhI(OPiv)_2$ (0.3 equiv.) was added every four hours to reach completion (1 or 2 additions). The reaction mixture was stirred at room temperature until completion then concentrated under reduced pressure before purification by flash chromatography.

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Synthesis of cyclic *N*-hydroxylated ureas and oxazolidinone oximes enabled by chemoselective iodine(III)-mediated radical or cationic cyclizations of unsaturated *N*-alkoxyureas

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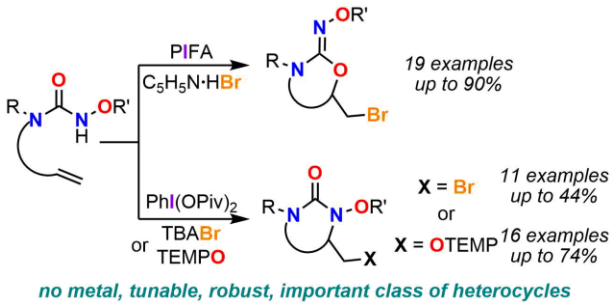
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