EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Squaramide/Quaternary Ammonium Salt as an Effective Binary Organocatalytic System for Oxazolidinone Synthesis from Isocyanates and Epoxides

Authors: Ali Rostami, Amirhossein Ebrahimi, John Husband, Muhammad Usman Anwar, Rene Csuk, and Ahmed Al-Harrasi

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.202000153

Link to VoR: http://dx.doi.org/10.1002/ejoc.202000153

Supported by
ACES Asian Chemical Editorial Society

WILEY-VCH

10.1002/ejoc.202000153

Squaramide/Quaternary Ammonium Salt as an Effective Binary Organocatalytic System for Oxazolidinone Synthesis from Isocyanates and Epoxides

Ali Rostami,*[a] Amirhossein Ebrahimi,[a] John Husband,[b] Muhammad Usman Anwar,[a] Rene Csuk,[c] Ahmed Al-Harrasi[a]

[a] Dr. A. Rostami, A. Ebrahimi, Dr. M. U. Anwar, Prof. Dr. A. Al-Harrasi
Natural and Medical Sciences Research Center (NMSRC), University of Nizwa, 616, Nizwa, Sultanate of Oman
Email:
arostami@unizwa.edu.om, aharrasi@unizwa.edu.om
http://www.unizwa.edu.om/COMPMNP/
Tweeter: @NMSRC_UNizwa

[b] Dr. J. Husband
Department of Chemistry, College of Science, Sultan Qaboos University, PO Box 36, Al-Khod 123, Muscat, Sultanate of Oman

[c] Prof. Dr. R. Csuk
Martin-Luther-University Halle-Wittenberg, Organic Chemistry, Kurt-Mothes-str. 2, D-06120 Halle (Saale) Germany

This work is dedicated to Professor Hans‐Ulrich Reißig on the occasion of his 70th birthday.

Abstract

Squaramide/ quaternary ammonium salt is illustrated as a simple, tunable, and competent metal-free binary catalytic platform for the atom-economic conversion of epoxides and isocyanates into oxazolidinones. Although, various metal catalysts have been employed for the title reaction, application of organocatalysis is scarce. At first, a rational survey of catalytic activity of a number of air-stable and architecturally distinct squaramides was undertaken. Thereafter, the impact on catalytic capability of different parameters, such as temperature, catalyst loading, and nature of nucleophiles, was examined. This binary organocatalytic system for the oxazolidinone synthesis, composed of a squaramide entity along with a suitable halide anion, was applied to the challenging conversion of a plethora of alkyl- and aryl-substituted epoxides– including disubstituted and enantioenriched ones– and isocyanates into the corresponding oxazolidinones in high-to-excellent yields. The time-dependent formation of oxazolidinone from epoxide and isocyanate was monitored by FTIR-ATR and ^{1}H NMR spectroscopy and the scalability of this process was also described. In light of ^{1}H NMR experiment, a hydrogen-bonding/anion-binding mechanism was proposed wherein the nucleophilic ring-opening operation, and oxo- and carbamate-anions stabilization occur cooperatively towards isocyanate fixation.

KEYWORDS: oxazolidinone, organocatalysis, hydrogen-bond donor, squaramide

Introduction

Oxazolidinones constitute a valuable class of nitrogen- and oxygen-containing five-membered heterocycles with broad applications.[1] They find applications in numerous contexts: they have often been used as chiral auxiliaries[1a, 2] in asymmetric synthesis, as synthetic intermediates and precursors of β-aminoalcohols,[3] as building blocks in polymers,[4] and as emerging pharmacophores in medicinal chemistry.[5] *N*-Aryl oxazolidinones have attracted particular interest recently as precursors to antibacterial medicines that are potent against vancomycin-resistant *enterococci* (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA).[6] They have also exhibited medicinal action as remedies for depression and psychosis.[7] Therefore, exploiting atom-efficient strategies towards diversity-oriented-synthesis of libraries based on the oxazolidinone scaffold has been on the forefront of research.

In essence, the oxazolidinone core could be attained by a variety of different protocols including cyclization reaction of α-amino acids or 1,2-amino alcohols with carbonyl derivative,[8] cyclocarbamations,[9] Au- and Ag-catalyzed cyclization of *N*-Boc-propargylic amines and propargylic alcohols,[10] and [3 + 2] coupling between heterocumulenes and epoxides or aziridines.[11] Among these strategies, the [3 + 2] coupling reaction of isocyanates and epoxides is a straightforward and 100 % atom-economical method that provides a modular approach with the ability to change substrate. Since the prominent report by Speranza and Peppel in 1958 using onium salts,[12] a range of catalytic platforms have been reported to catalyze this process including lanthanide salts,[13] lithium halides,[14] magnesium halides,[15] tetraphenylantimony iodide,[16] and trialkyltin halides.[17] In addition, a great deal of effort has recently been devoted into Lewis acidic metal complexes,[18] including those based on aluminum and chromium, all of

which exhibited promising catalytic activities, yet the substrate scope was mainly limited to aryl isocyanates.

These catalytic systems (see above) require reaction conditions involving toxic metals, laborious catalyst synthesis, toxic solvents, high temperatures, and high catalyst loadings that eventually limit their catalytic utilities. In addition, slow addition of isocyanates or excessive amount of epoxides was essential to defeat the isocyanates trimerization side reaction, whereas substrate scopes were mainly limited to terminal epoxides and aryl isocyanates. In this regard, evaluating alternative catalytic platforms with a broad substrate scope, that fulfill growingly rigid environmental requirements is greatly appealing.

Hydrogen-bond donor (HBD) catalytic systems– binary or bifunctional– have appeared as exceptional organocatalytic platforms for the activation of small organic molecules through non-covalent interactions.[19] The necessary lack of metal leftovers, and successful catalyst elimination from the final product favor the use of such green processes over metal-catalyzed ones. These systems represent the current state-of-the-art organocatalytic platforms for carbon dioxide fixations,[20] yet its application in controlling cycloaddition reactions of other heterocumulenes such as isocyanates with epoxides that requires relatively harsh reaction conditions is still in its infancy.[21a] A pioneering work was accomplished by Toda and co-workers in which a bifunctional tetraarylphosphonium salt catalyzes the title reaction (Scheme 1a).[21b] An alternative process is a binary catalytic system –composed of a HBD molecule and quaternary ammonium salt as co-catalyst– that have recently become highly favored in catalyzing reactions of carbon dioxide.[22] They establish (a network of) hydrogen-bonds ideally tailored for the catalytic opening of epoxides in addition to stabilization of the essential transition states *via*

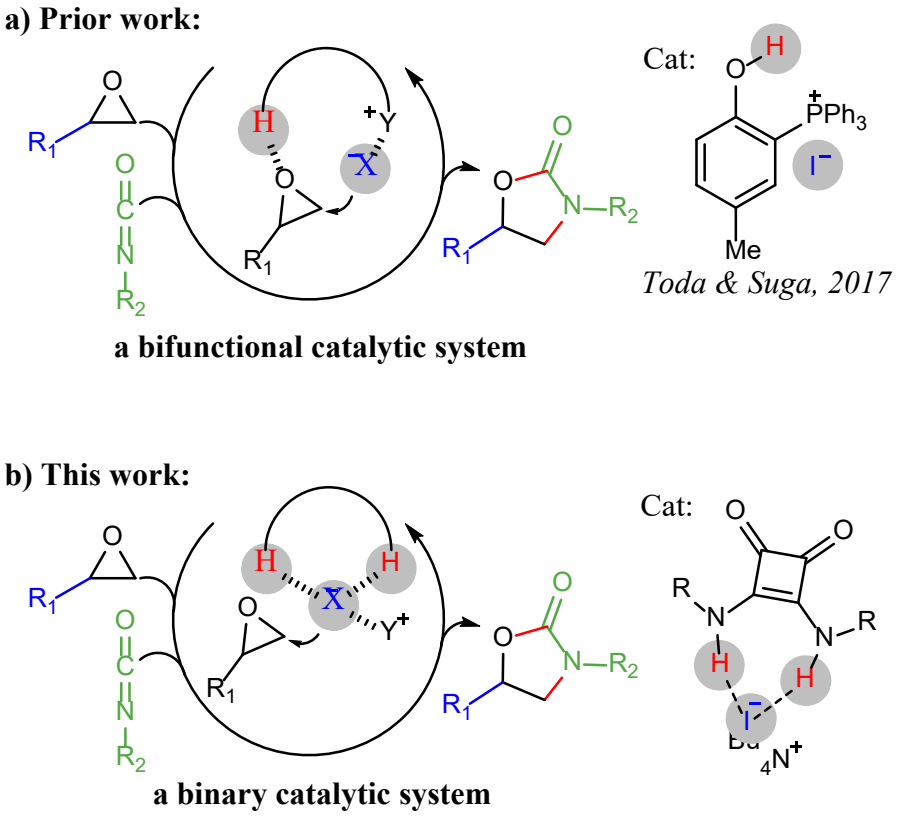
distinct hydrogen-bonding interactions. Employing such binary catalytic platforms to stabilize the adduct of epoxide and isocyanates, while effectively guiding it towards carbon-nitrogen bond formation is unprecedented (Scheme 1b).

Squaramide-an excellent anion-binding receptor,[23] has gained substantial consideration in bioconjugation,[24] medicinal chemistry,[25] as an anion transporter in trans-membrane ion channels,[23c] and lately, as a HBD in asymmetric catalysis.[19d, 26] Rivaling its analogue, thiourea, this ditopic receptor–capable of both anion and cation binding –enjoys a modular synthesis and a special skeleton, which is due to its rigidity, duality, double hydrogen-bond donation, extended canted hydrogen-bond angle and acidity, provides faster reaction rates and higher stereocontrol.[27]

After the pioneering work of Rawal's group in 2008,[26] and with the remarkable highlight of Kleij's current account on squaramide-catalyzed CO_2 fixation,[20k] squaramide catalysis has not been employed in controlling reactions of other heterocumulenes such as isocyanates.

Notably, it has been previously shown that the tetraalkylammonium halides are capable of hydrogen-bond to the squaramide carbonyl moiety, thereby restricting the conformational mobility of the receptor while providing more translational freedom for the halide anion.[28] Also, in comparison to halides, oxo-anions normally have a stronger interaction and a better stabilization with this entity, which provides a new opportunity to pre-organize both nucleophile and substrates towards isocyanate fixation. The distinct features of this molecule (e.g. hydrogen-bond donor-accepting abilities) motivated us to explore interactions between the squaramide, tetraalkylammonium halide, isocyanate and epoxide (Scheme 1b).

Scheme 1. Organocatalyzed [3 + 2] coupling reaction of isocyanates and epoxides



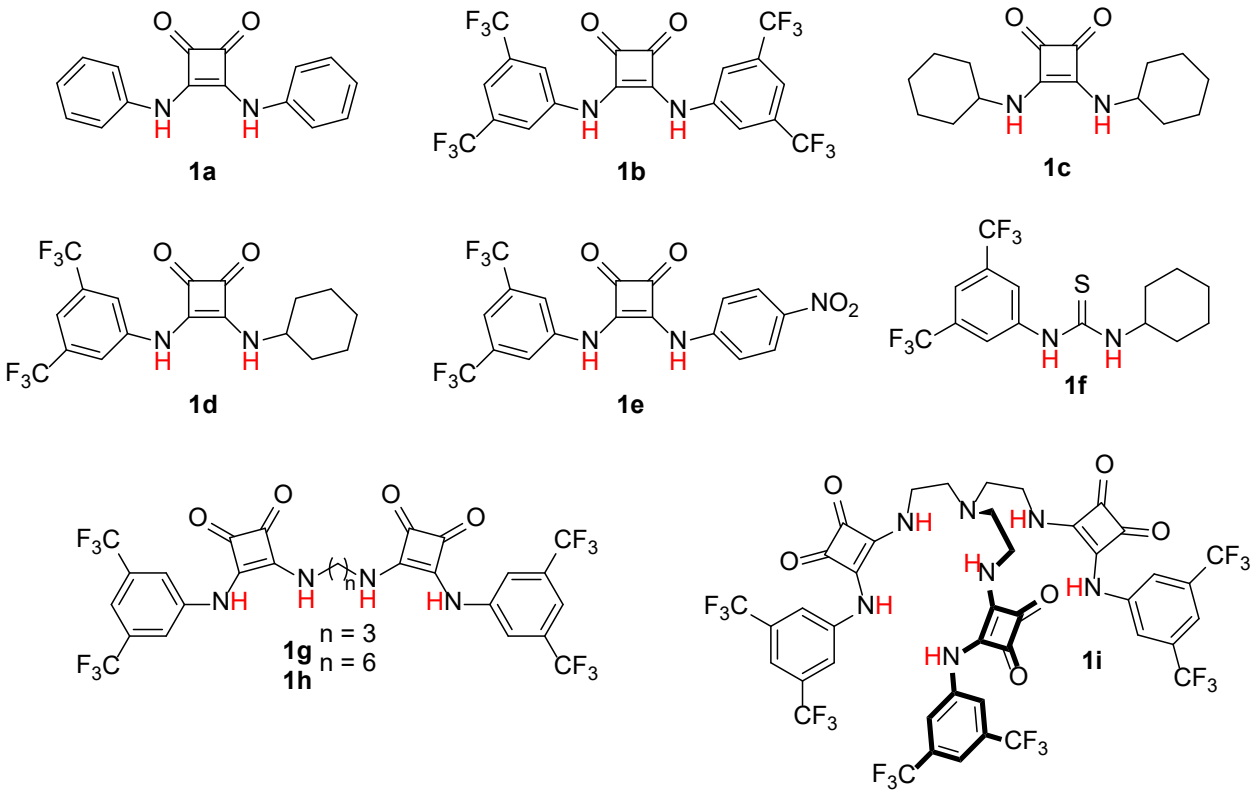
Continuing our curiosity in expanding new organocatalytic platforms for ring-opening processes,[29] we sought to investigate whether squaramide –a superb anion-binding receptor with a great double hydrogen-bond donor ability– could simultaneously participate in multiple modes of activation and stabilization, overcoming barriers to reactivity and unsuitable equilibria. These could be achieved *via* the squaramide entity by: (i) interacting reversibly with the halide anion *via* bifurcated hydrogen bonds, modulating the reactivity of the anion by attenuating the electrostatic interaction. (ii) stabilizing the oxirane-isocyanate adduct as a prelude to its use as a nitrogen nucleophile in a subsequent carbon-nitrogen bond-forming step.

In this contribution, we report, squaramide **1d** and tetrabutylammonium iodide, as a simple, metal-free, and binary catalytic system, which can mediate the [3 + 2] cycloaddition reaction of a variety of epoxides and isocyanates under neat conditions.

Results and Discussion

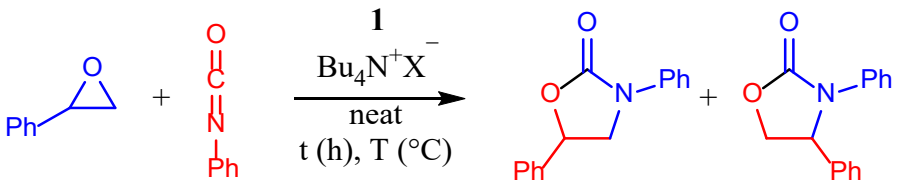
Squaramides **1a-i** (Figure 1) were readily prepared by condensation of a variety of aromatic and aliphatic amines, with squarate esters in a modular and straightforward fashion, providing access to an array of air-stable and structurally distinct catalysts.[23e, f] These catalysts vary in the type of the substituents, the number of squaramides, and/or the level of hydrogen-bond donor ability and acidity, thus providing the possibility to assess structure-activity relationships in these systems.

Figure 1. Squaramide catalysts (**1a–i**) employed for oxazolidinone synthesis



To evaluate the catalytic performance of these hydrogen-bond donors, we started to explore 100% atom-economic conversion of styrene oxide **2a** and phenyl isocyanate **3a**, as standard substrates, into oxazolidinone **4/5a,** in a process free from any generation of side products (Table 1).

Table 1. Optimization of reaction conditions[a]



2a **3a** **4a** **5a**

entry	**1** (mol %)	$Bu_4N^+X^-$ (mol %)	*t* (h)	*T* (°C)	Conv.[b] (%)	**4a**:**5a**[b]
effect of catalyst						
1	**1a** (5)	I (5)	12	50	45	81:19
2	**1a** (5)	Br (5)	12	50	32	77:23
3	**1a** (5)	Cl (5)	12	50	8	65:35
4	**1a** (5)	I (0)	12	50	0	0
5	none	I (5)	12	50	12	85:15
6	none	I (5)	12	70	20	76:24
7	**1b** (5)	I (5)	12	50	39	68:32
8	**1c** (5)	I (5)	12	50	41	72:28
9	**1d** (5)	I (5)	12	50	55	78:12
10	**1e** (5)	I (5)	12	50	14	72:28
11	**1f** (5)	I (5)	12	50	8	77:23
12	**1g** (5)	I (5)	12	50	19	70:30
13	**1h** (5)	I (5)	12	50	26	72:28
14	**1i** (5)	I (5)	12	50	15	72:28
effect of time and temperature						
15	**1d** (5)	5	20	40	62	80:20
16	**1d** (5)	5	20	50	78	75:25
17	**1d** (5)	5	20	60	88	78:22
18	**1d** (5)	5	20	70	95	76:24
19	**1d** (5)	5	24	70	>99%	76:24
effect of catalyst loading						
20	**1d** (3)	6	20	50	50	78:22
21	**1d** (6)	3	20	50	22	78:22

22	**1d** (3)	3	20	50	57	72:28
23	**1d** (4)	4	20	50	69	72:28
24	**1d** (6)	6	20	50	81	72:28

[a] Conditions: styrene oxide **2a** (0.5 mmol), phenyl isocyanates **3a** (0.5 mmol), reaction carried out as neat. [b] Conversion of styrene oxide **2a** into **4/5a** and the ratio of **4a:5a** was evaluated by ^{1}H NMR spectroscopy ($CDCl_3$) of the crude reaction mixture.

Screening surveys were undertaken employing equimolar amounts of styrene oxide **2a** and phenyl isocayante **3a** that were subjected to different conditions as depicted in Table 1. From the outset, we were delighted to observe that the employed hydrogen-bond donor motif was indeed compatible with this process: with the use of 5 mol% of *N,N′*-diphenylsquaramide **1a** and *n*-tetrabutylammonium iodide (*n*-TBAI) as a nucleophilic co-catalyst and under neat conditions, 45% conversion (measured by ^{1}H NMR spectroscopy) of styrene oxide **2a** into the corresponding oxazolidinones **4/5a** was observed; while no reaction was noticed without nucleophile (Table 1, entries 1 and 4). Presumably, ammonium halide holds an essential role in initiating the process by ring-opening the epoxide that is followed by cycloaddition reaction with the isocyanate. The kind of the nucleophile has a striking outcome on reaction conversions: proceeding from iodide to bromide and chloride significantly diminished the reaction conversion to 8% and that could be justified by stronger hydrogen-bond accepting properties of the chloride compared to bromide and iodide (Table 1. entries 1–3).[30] Without the hydrogen-bond donor catalyst **1a**, and at 50 °C only 12% background conversion of the oxazolidinone products **4/5a** was achieved, while at 70 °C the background conversion was increased to 20% with the 3,5-diphenyloxazolidinone **4a** as the major product in each case (Table 1, entries 5 and 6), thus confirming the primary role of the hydrogen-bond functionality in modulating the reactivity of the iodide and subsequent stabilization of the anionic intermediates.[20k, 31] Generally, epoxide ring-opening happens at the

less hindered carbon atom (β-cleavage), yet with respect to styrene oxide **2a**, this steric bias is outweighed by the electronic advantage at the benzylic position (α-cleavage).[32]

To determine the influence of squaramide substitution pattern and its quantity on catalytic activity, a range of symmetrically, non-symmetrically, di- and tri-substituted molecules (**1a**–**i**) with sterically and/or electronically tunable structures were prepared (Figure 1). The introduction of electron-withdrawing CF_3 and nitro groups into the squaramide structure (**1b** and **1e**) diminished the reaction conversion to 39% and 14%, respectively (Table 1, entries 7 and 10). The low observed conversion could presumably be due to the weakened nucleophilicity of the iodide anion as a result of a strong hydrogen-bond interaction between this entity and the iodide anion.[20k] Moreover, substitution with cyclohexyl groups (**1c**) slightly increased the reaction conversion to 41% (Table 1, entry 8). The reaction conversion was further increased to 50% by incorporating strong electron-withdrawing (yet poor hydrogen-bond accepting) CF_3 moieties into the phenyl group while retaining the bulky cyclohexyl substituent (**1d**) (Table 1, entry 9). Electron-withdrawing groups likely enhance the acidity of the hydrogen-bond donor motif and improves its ability to hydrogen-bonding to iodide anion while the bulky cyclohexyl substituent diminishes such hydrogen-bonding interactions. The above cases clearly reveal that the catalytic activity is highly responsive to the squaramide substitution patterns, and depends on the synergy between the type of the substituents, and its acidity in controlling the reactivity of the iodide in the ring-opening step while stabilizing the reaction intermediates. In an effort to assess the catalytic activity of this double hydrogen-bond donor entity with thiourea, a thiourea catalyst with a similar substitution pattern **1f** was made and then employed in the title reaction. A reduced activity of the thiourea catalyst **1f** in the [3 + 2] coupling reaction of styrene epoxide **2a** and

phenyl isocyanate **3a** with only 8 % conversion (Table 1, entry 11) highlights the "unique" structural motif of the squaramide.

Furthermore, increasing the number of hydrogen-bond donor groups to bis- and tris-squaramide had an unfavorable impact on the catalytic activity and reduced the reaction conversion to 15% (Table 1, entries 12–14). The observed decrease in catalytic activity is believed to be the consequence of weakened iodide nucleophilicity as the number of hydrogen-bonding interaction between the hydrogen-bond donor moiety and the halide anion increases.[23f] These results highlight the imperative role of this double hydrogen-bond donor group in modulating the halide nucleophilicity through hydrogen-bonding interactions.

The impact of three solvents with different polarities (acetonitrile, dimethylformamide, and dimethyl sulfoxide) at 50 °C was also examined; however, none of the employed solvents induced conversion enhancement, probably owning to their hydrogen-bond accepting character and possible catalyst poisoning.[33] In addition, chlorinated solvent such as chlorobenzene, which has intermediate polarity resulted in no enhancement in reaction conversion. The reaction temperature had a significant impact on reaction kinetics. Increasing the temperature to 70 °C in the case of aromatic epoxide **2a**, and 100 °C, in the case of alkyl epoxides (**2b-d)**, turned out to be optimal, providing quantitative conversion of epoxides into the corresponding oxazolidinones **4/5a-d** after 24h (Table 1, entries 15–19). Notably, in the absence of catalyst **1d**, and in the presence of just *n*-TBAI co-catalyst at 100 °C, and after 24h, only 42% background conversion of alkyl epoxide **2c** was achieved.

Comparing entries 20, 21 and 22 in Table 1, showed that a 1:1 ratio of **1a** and *n*-TBAI is crucial to achieve the optimum catalytic activity while any deviation from this ratio resulted in

conversion loss. These results suggest a cooperative effect between the two catalytic species in ring-opening of the epoxide and/or better stabilization of the reaction intermediates. In addition, lowering catalyst and co-catalyst loadings to 3 mol%, led to a remarkable decline in reaction conversion while increasing their loadings by two-fold (6 mol %), provided only a slight increase in reaction conversion (Table 1, entries 23 and 24).

The time-dependent conversion of styrene oxide **2a** was examined by a set of eight similar tirals in which the reactions were stopped after a specific time period and then investigated by ^{1}H NMR spectroscopy: in the presence of **1d**, and after 24 h, almost quantitative conversion of styrene oxide **2a** into oxazolidinone **4/5a** was noticed (see the Supporting Information, Figure S1a).

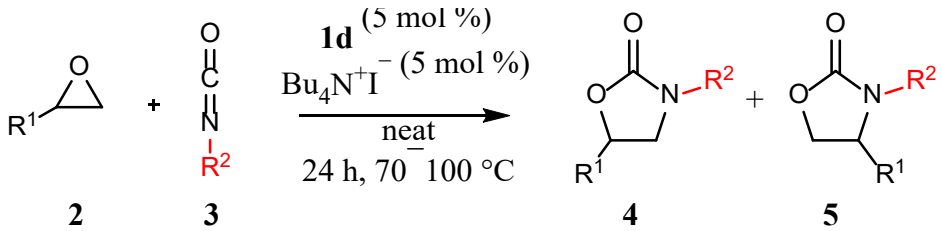
Offline attenuated total reflectance (ATR)-FTIR spectroscopy was also exploited to validate specific bands of styrene oxide **2a,** phenyl isocyanate **3a** and oxazolidinone adduct **4/5a** (see the Supporting Information, Figure S1b).[16b, 17a] In line with these assessments, we monitored the time-dependent course of the reaction by referring to the intensity of the oxazolidinone carbonyl vibration band at 1745 cm^{-1}. Throughout the reaction, the intensity of oxazolidinone carbonyl band increased considerably and reached it‘s maximum after 24 h, while the intensity of isocyanate asymmetric stretching vibration at 2261 cm^{-1} and the epoxide ring-deformation bands at 985 and 878 cm^{-1}, decreased constantly, and effectively dissapeared after 24 h.

Motivated by these results and with a wish to evaluate the generality of the squaramide-catalyzed coupling reaction, we examined different terminal alkyl- and aryl-substituted epoxides with varoius isocayantes under the optimized reaction conditions (see above) providing oxazolidinones (**4/5a–p**) in high-to-excellent yields.

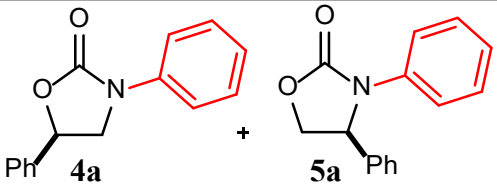
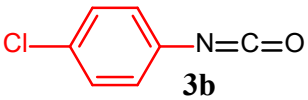
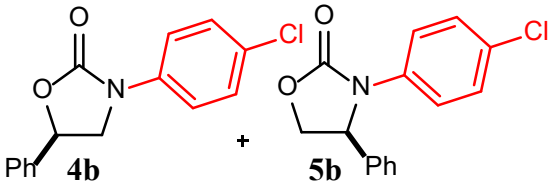
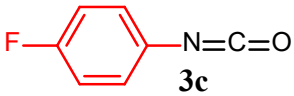
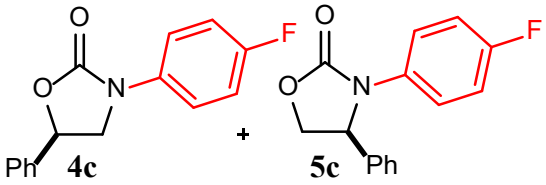
As depicted in Table 2, the compatibility of the synthesis with diverse isocyanates was explored. Styrene oxide **2a**, glycidyl methacrylate **2b,** and phenyl glycidyl ether **2c** were chosen as typical cases of aromatic and aliphatic epoxides, and they were screened with different aromatic isocyanates to furnish the corresponding oxazolidinones **4/5a–p**. For reactions that include styrene oxide **2a**, the thermodynamically favoured 3,5-oxazolidinones (**4a–g**) were consistently the major products generated in about 2:1 to 3:1 ratios with respect to 3,4-oxazolidinones (**5a–g**) (Table 2, entries 1–6). Normally, epoxide ring-opening happens at the least substituted carbon, yet for styrene oxide **2a**, such sterically constrain bias is in competition with the more electronically favoured ring-opening at the benzylic position.[18a-c, 32] As previously reported, in cases of aryl-substituted epoxides, aryl groups favour S_N1 type reaction pathway that is in competition with S_N2 type mechanism.[18] On the other hand, reactions involving glycidyl methacrylate produced only 3,5-oxazolidinone (**4h–n**) from all isocyanates, thus revealing the excellent regioselectivity via S_N2 type mechanism offered by this strategy (Table 2, entries 8–14). The yield of oxazolidinones **4/5a–n** was influenced by the electronic nature of the isocyanates employed: the highest yields observed when using electron-rich isocyanates (Table 2, entry 6); while electron-deficient isocyanates provided lower yields as epitomized by 3 5-bis(trifluoromethyl)phenyl and 4-nitrophenyl isocyanates with styrene oxide (Table 2, entries 4 and 5). The lower yields by electron-deficient isocyanates strongly suggests that the rate of the whole process is determined by the ring-closing step, which corroborates the previously reported studies.[21b, 41] To broaden the scope of this binary catalytic system, a variety of more challenging isocyanates[18a-c] including alkyl isocyanates **3g-h** and tosyl isocyanate **3i** were tested under the optimized reaction conditions. As shown in Table 2, entries 7, and 14–16, the reaction was not

limited to only aromatic isocyanates whereas tosyl and aliphatic isocyanates were also tolerated. All of the reactions proceeded without kinetic resolution of the racemic epoxides.

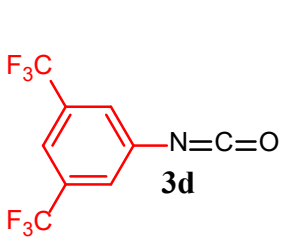
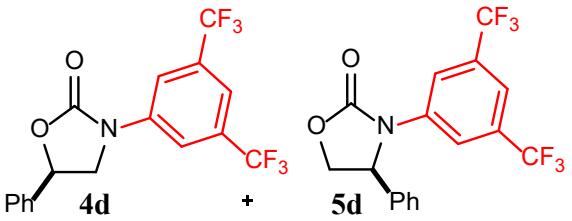
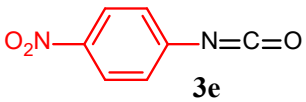
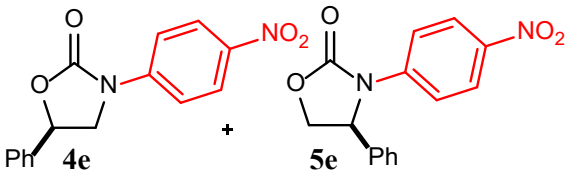
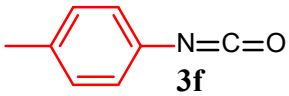
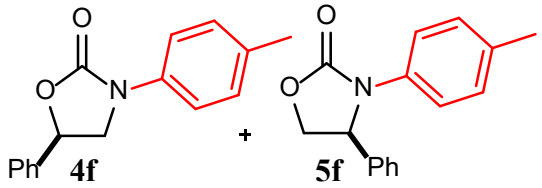
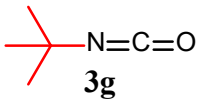
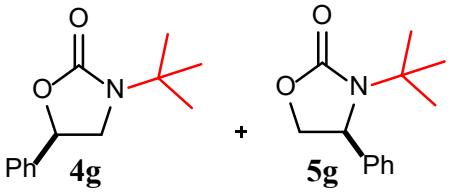
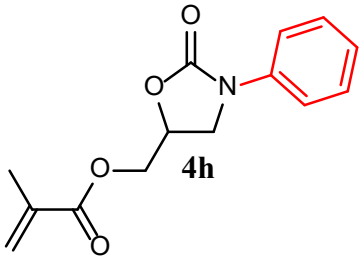
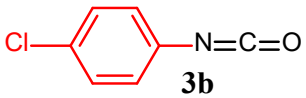
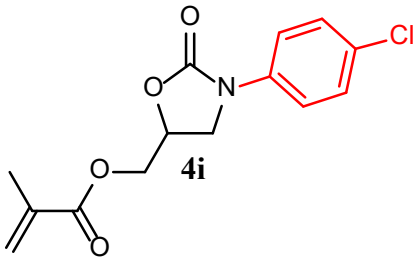
Table 2. Cycloaddition of epoxide **2a**, **2b** and **2c** with various isocyanates[a]



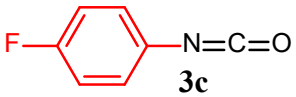
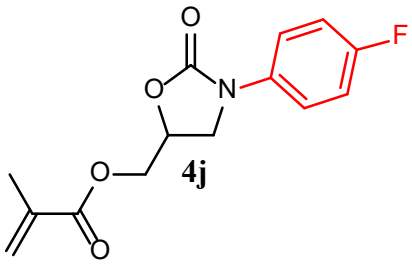
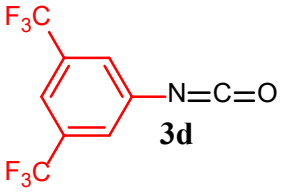
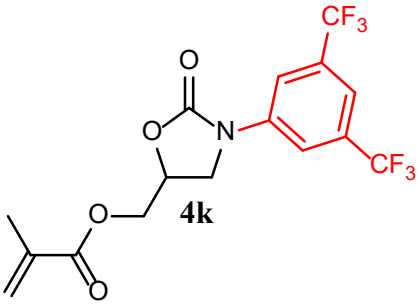
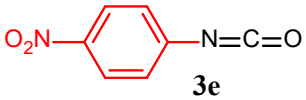
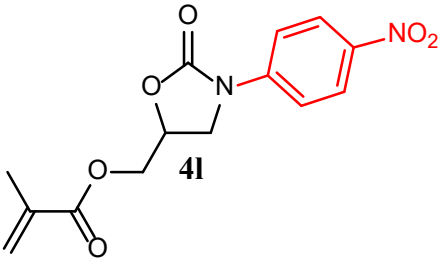
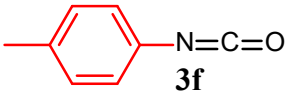
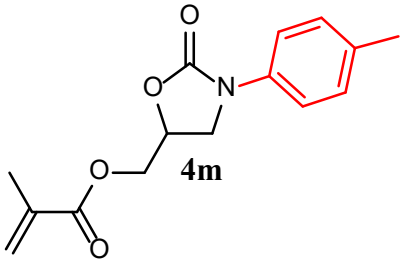
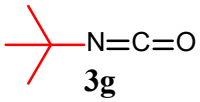
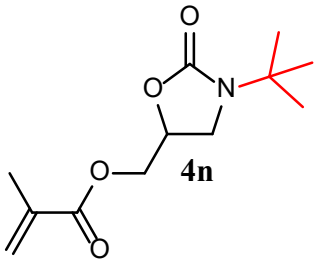
2 (R_1 =), a: Ph, b: $CH_2OCOC(CH_3)=CH_2$, c: CH_2OPh

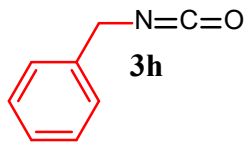
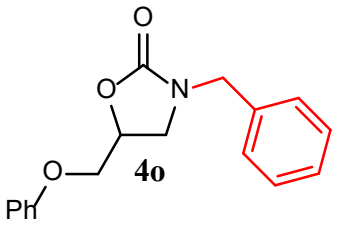
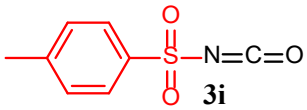
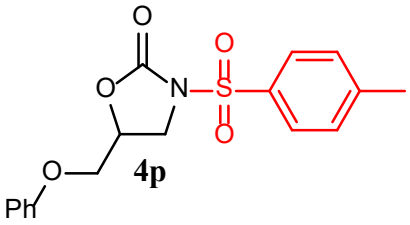
Entry	Isocyanate	Product	Yield[b] %	4:5[c]
1	 **3a**	 **4a** + **5a**	88	74:26
2	 **3b**	 **4b** + **5b**	86	78:22
3	 **3c**	 **4c** + **5c**	82	71:29

10.1002/ejoc.202000153

4	 **3d**	 **4d** + **5d**	78	70:30
5	 **3e**	 **4e** + **5e**	76	65:35
6	 **3f**	 **4f** + **5f**	90	82:18
7	 **3g**	 **4g** + **5g**	44	68:32
8	 **3a**	 **4h**	95	100:0
9	 **3b**	 **4i**	89	100:0

10.1002/ejoc.202000153

10	 **3c**	 **4j**	86	100:0
11	 **3d**	 **4k**	81	100:0
12	 **3e**	 **4l**	85	100:0
13	 **3f**	 **4m**	92	100:0
14	 **3g**	 **4n**	49	100:0

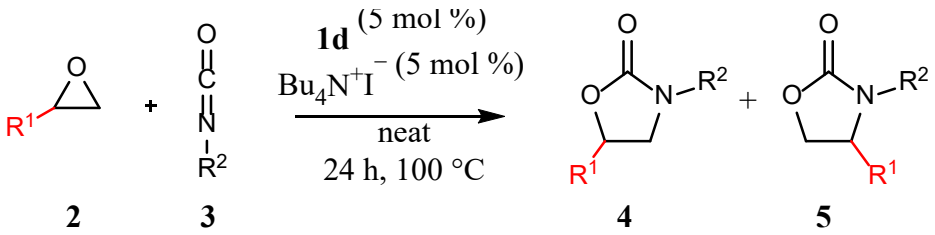
15	 **3h**	 **4o**	82	100:0
16	 **3i**	 **4p**	94	100:0

[a] Conditions: epoxide **2** (0.2 mmol), isocyanate **3** (0.2 mmol), reaction carried out as neat. **1d** (5 mol %), *n*-TBAI (5 mol %), 100 °C, 24 h. In case of epoxide **2a**, the reaction was heated to 70 °C. [b] Yields refer to product isolated by column purification. [c] The ratio of **4a:5a** was evaluated by ^{1}H NMR spectroscopy ($CDCl_3$) of the crude reaction mixture.

Next, a series of different terminal epoxides **2** were assessed in reaction with the aryl- and alkyl-substituted isocyanates **3a** and **3b**, respectively. Epoxides **2b–d** bearing alkoxy and halo groups underwent epoxide ring-opening exclusively at the less-substituted carbon atom to furnish the corresponding 3,5-oxazolidinones in high yields and regioselectivity (Table 3, entries 1–3). The observed regioselectivity could be justified by favourbale steric constrain observed in the case of alkyl-substituted epoxides (**2b-d**): nucleophilic attack occures at the less hindered carbon atom of an aliphatic epoxide by an S_N2 type mechanism (preferred attack on the methylene carbon). Surprisingly, *tert*-butyl isocyanate **3b**, a challenging case due to both the unfavorable steric and stereo electronic factors, was also well-tolerated under this catalytic system (Table 3, entries 4–6).

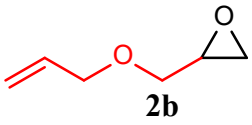
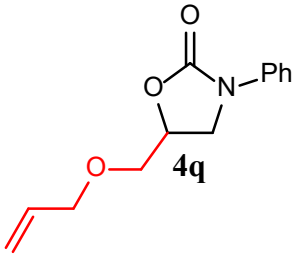
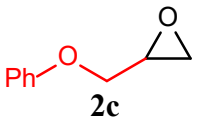
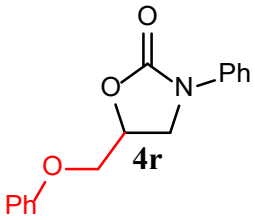
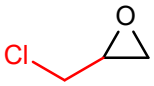
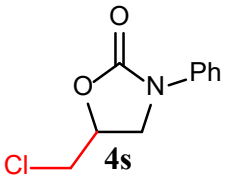
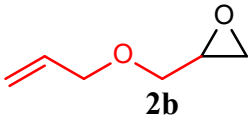
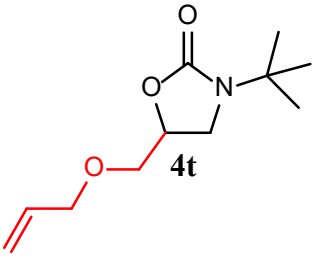
10.1002/ejoc.202000153

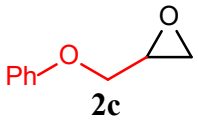
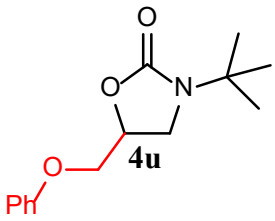
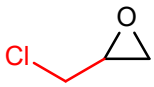
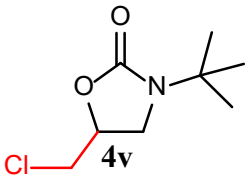
Table 3. Cycloaddition of isocyanate **3a** and **3b** with various epoxides[a]



2 **3** **4** **5**

3 (R_2 =), **a**: Ph, **b**: *t*-Bu

Entry	Epoxide	Product	Yield[b] %	4:5[c]
1	 **2b**	 **4q**	94	100:0
2	 **2c**	 **4r**	93	100:0
3	 **2d**	 **4s**	91	100:0
4	 **2b**	 **4t**	45	100:0

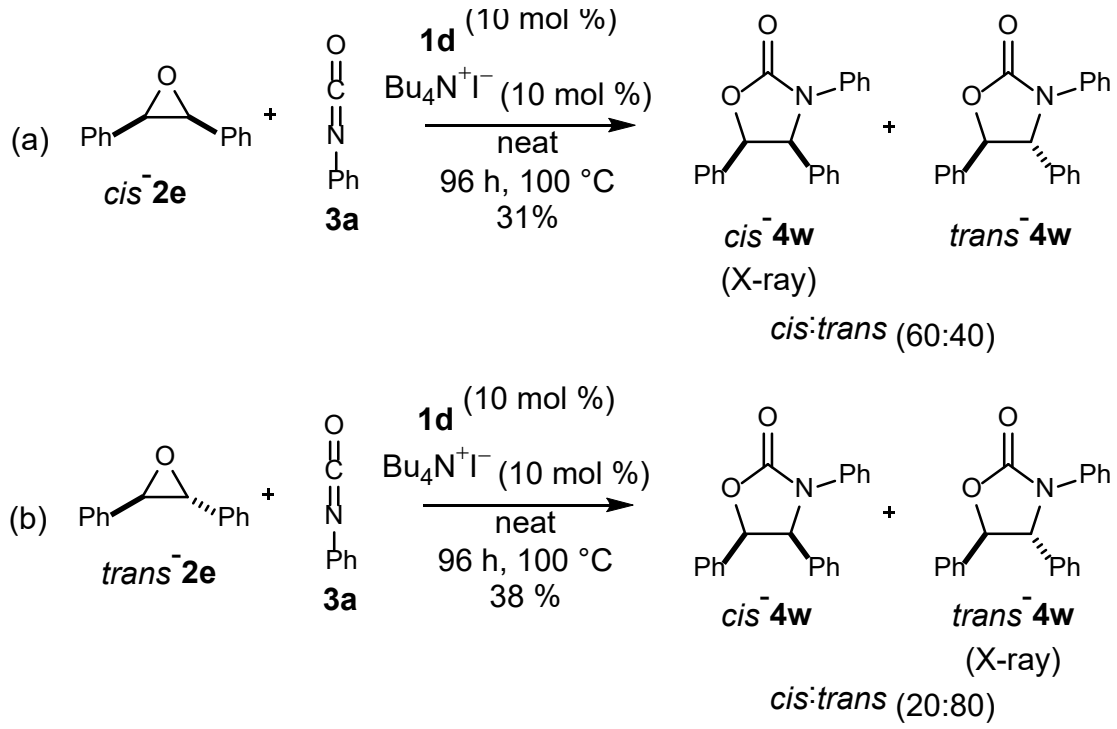
5	 **2c**	 **4u**	48	100:0
6	 **2d**	 **4v**	48	100:0

[a] Conditions: epoxide **2** (0.2 mmol), isocyanate **3** (0.2 mmol), **1d** (5 mol %), *n*-TBAI (5 mol %), 100 °C, 24 h, reaction carried out as neat.[b] Yields refer to product isolated by column purification. [c] The ratio of **4a:5a** was evaluated by ^{1}H NMR spectroscopy ($CDCl_3$) of the crude reaction mixture.

The reaction with challenging 1,2-disubstituted epoxides –a case that is problematic–[18, 21b] was examined and to our delight, the reactions proceeded smoothly to provide the corresponding oxazolidinones in moderate yields, albeit at much slower reaction rates (Scheme 2). The reaction of *cis*-stilbene oxide **2e**, proceeded to give a mixure of *cis*- and *trans*-oxazolidinone **4w** in 31% yield, with the major isomer holding the *cis* configuration (*trans/cis* isomeric ratio: 40:60, observable by ^{1}H NMR). Adding to this, the reaction of *trans*-stilbene oxide provided a mixture of *cis*- and *trans*-oxazolidinones in 65 % yield, yet with the major isomer holding the *trans* configuration (*trans/cis* isomeric ratio: 80:20, observable by ^{1}H NMR). Crystals of compounds appropriate for X-ray analysis were grown from slow evaporation of ethyl acetate solution. The following crystal structures unambiguously revealed the *cis* and *trans* configurations (see The Experimental Section and Crystallographic Information File). In addition, the ^{1}H and ^{13}C NMR data corroborate the previously reported analysis for *cis*- and *trans*-isomers of oxazolidinone.[17b, 34] The fact that these reactions were partially stereospecific implies the conversion of stilbene

oxides into the corresponding oxazolidinones could occur *via* competing pathways, including double inversion and/or S_N1 type manifolds. A similar stereochemical result has been reported earlier for the reaction of 1,2-disubstituted epoxides and heterocumulenes.[18a-c, 35]

Scheme 2. Reactions with 1,2-disubstituted epoxides.[a]

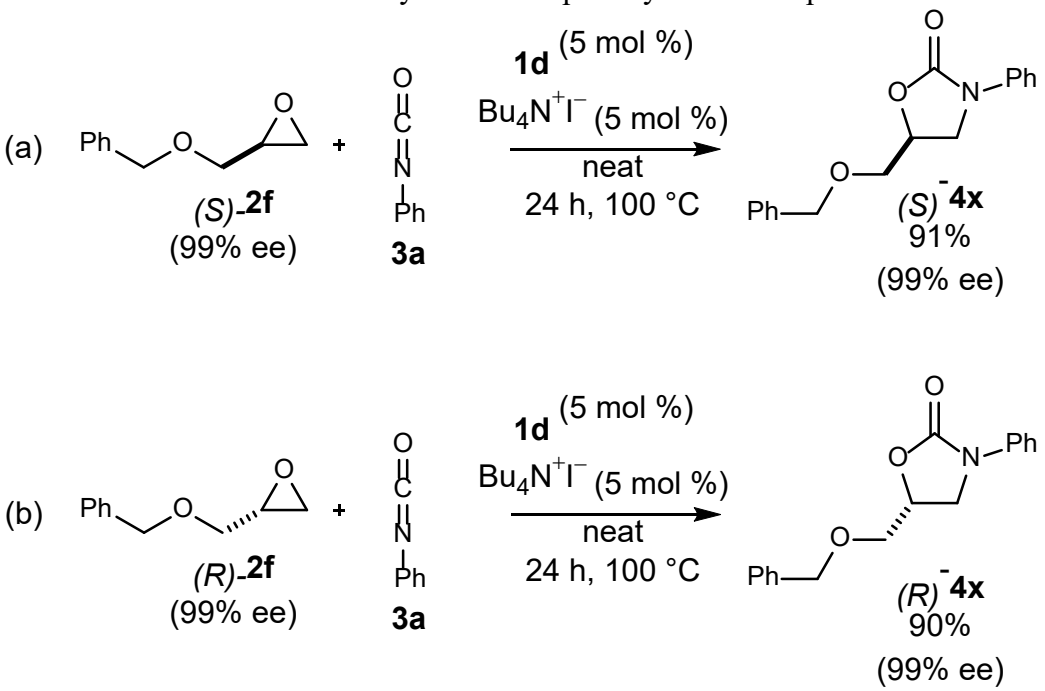


[a] Conditions: epoxide **2e** (1 mmol), isocyanate **3a** (1 mmol), reaction carried out as neat. Yields refer to product isolated by column purification. The ratio of *cis*:*trans* was evaluated by ^{1}H NMR spectroscopy ($CDCl_3$) of the crude reaction mixture.

To better understand the reaction pathway, optically pure *(R)*- and *(S)*-(+)-glycidyl benzyl ether was examined under the optimized reaction conditions to evaluate the chirality transfer from the epoxides (Scheme 3). We isolated the oxazolidinone adduct **4x** in 99% enantiomeric excess (ee) in each case, with retention of configuration starrting from epoxides with a similar ee values,

providing evidence for iodide-mediated-ring-opening of the epoxide from the less-hindered position via S_N2 pathway (preferred attack on the methylene carbon).[36] This binary catalytic platform provides an entry to enantioenriched oxazolidinones without stereochemical erosion.

Scheme 3. Synthesis of optically active compounds[a]

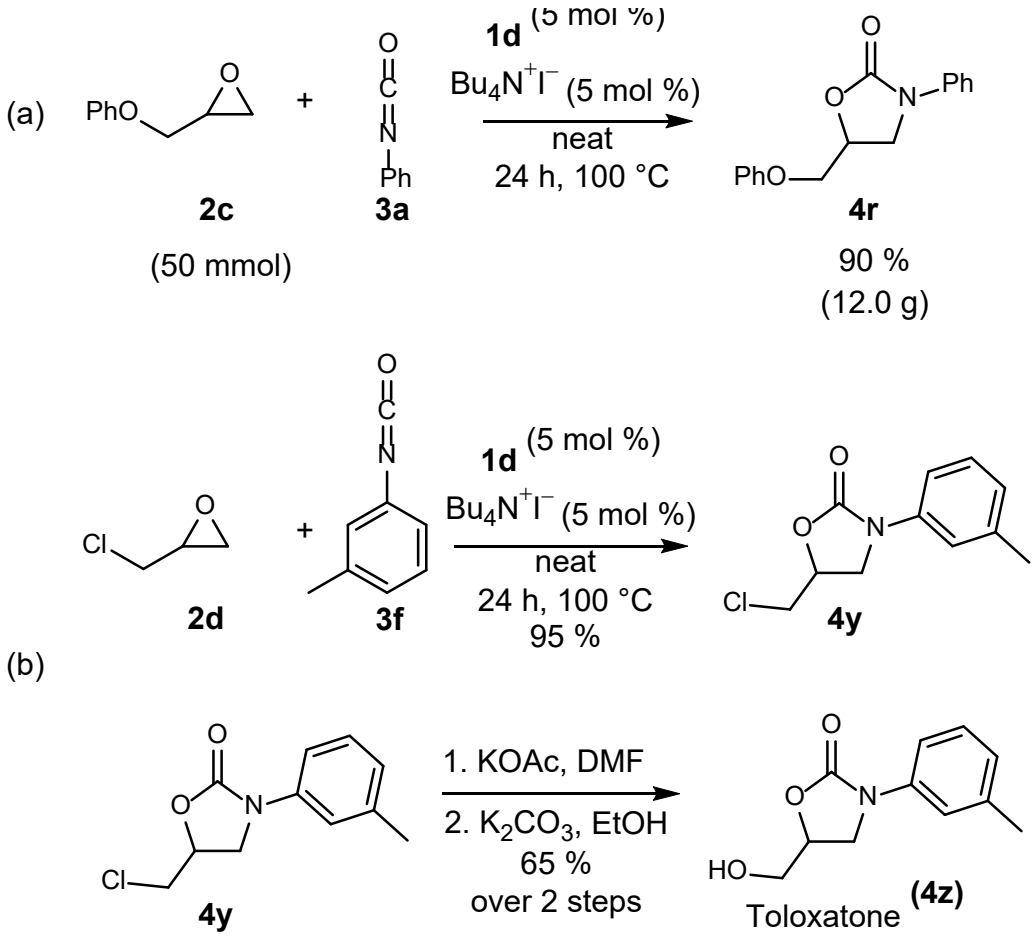


[a] Conditions: epoxide **2f** (0.2 mmol), isocyanate **3a** (0.2 mmol), **1d** (5 mol %), *n*-TBAI (5 mol %), 100 °C, 24 h, reaction carried out as neat. Yields refer to product isolated by column purification. Enantiomeric excess (ee) was analyzed using chiral HPLC (see the Supporting Information for further details).

A scale up experiment was carried out to highlight the practicality of this catalytic system (Scheme 4a). In this experiment, under the optimized reaction conditions, a mixture of phenyl glycidyl ether epoxide (**2c**) (50 mmol) and phenyl isocyanate **3a** (50 mmol) were converted to the corresponding oxazolidinone **4r** in 90 % isolated yield after column chromatography on silica gel. As shown in scheme 4b, the applicability of this process was further expanded to the synthesis of

Toloxatone (**4z**), an antidepressant agent that acts as a selective and reversible inhibitor of monoamine oxidase-A (MOA) [37] using previously reported strategy.[21b]

Scheme 4. (a) A scale up reaction with substrates **2c** and **3a**.[a] (b) Synthesis of Toloxatone **4z**[b]



[a] Conditions: (a) epoxide **2c** (50 mmol), isocyanate **3a** (50 mmol), **1d** (5 mol %), *n*-TBAI (5 mol %), 100 °C, 24 h, reaction carried out as neat. Yields refer to product isolated by column purification. [b]Conditions: (b) first step: epoxide **2d** (2 mmol), isocyanate **3a** (2 mmol), **1d** (5 mol %), *n*-TBAI (5 mol %), 100 °C, 24 h, reaction carried out as neat; Second step: KOAc (10.0 mmol), DMF (10 mL); K_2CO_3 (10.0 mmol), EtOH (10 mL).

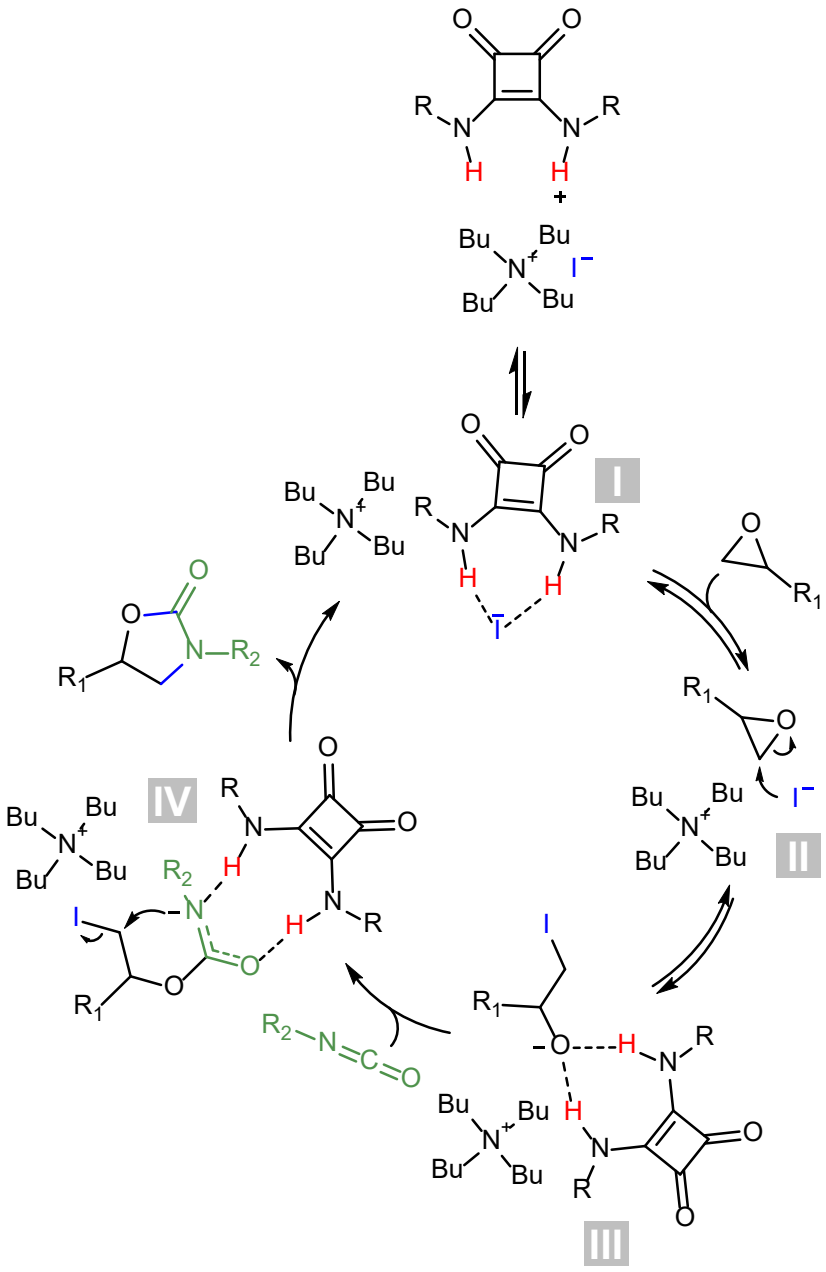
Further studies for the hydrogen-bonding interaction of epoxide and the squaramide entity as well as it's hydrogen-bonding interaction with the iodide nucleophile was demonstrated in a series of

^{1}H NMR experiments (see the Supporting Information, Figure S3). These experiments were achieved employing solutions of styrene oxide **2a** and *n*-TBAI added to a 0.2 M solution of **1d** in DMSO-d_6 at room temperature. Negligible downfield shifts (from δ = 10.02 ppm to 10.11 ppm) and (from δ = 7.72 ppm to 7.77 ppm) of the two distinctive **1d** N-H proton signals were observed as excess amount of epoxide **2a** (ten equivalents) was added to a solution of **1d** in DMSO-d_6. It seems that the interaction between squaramide **1d** and epoxide **2a** is typically weak, a phenomenon that was previously observed by Kleij and co-workers.[20k] On the other hand, when an equivalent of tetrabutylammonium iodide (*n*-TBAI) was added to a solution of **1d** in DMSO-d_6, clear downfield shifts of the two characteristic N-H protons (from δ = 10.02 ppm to 10.96 ppm) and (from δ = 7.72 ppm to 8.50 ppm) were observed which pinpoints the anion-binding properties of this double hydrogen-bond donor entity. In addition, similar downfield shifts of the two *ortho*-protons of the 3,5-bis(trifluoromethyl)-phenyl moiety (δ = 7.98 ppm to 8.25 ppm) were also observed. These downfield shifts bodes well with the squaramide N-H acidities[38], catalytic activities,[27] and anion-binding properties.[23, 39] These data suggest that the styrene oxide **2a** is unable to compete with the iodide anion to form a hydrogen-bonded complex **2a:1d**,[40] indicating squaramide's catalytic activity is mostly related to its control on the reactivity of the ion-pair through anion binding as well as its hydrogen-bonding stabilization of oxoanionic intermediates that form after iodide-mediated ring-opening of the epoxide.

We have inferred a mechanism similar to the previously proposed ones in which a hydrogen-bond donor entity could participate in anion-binding processes during the course of the reaction;[20k, 41] modulating the reactivity of the anion while stabilizing the reaction intermediates (Scheme 5). First, the squaramide **1** binds reversibly to the iodide anion of the *n*-TBAI which is

present in an equimolar ratio with respect to the host (Scheme 5, **I**) while epoxide, that is present in excess, is unlikely to compete for binding to **1** in the presence of iodide. Second, an iodide-mediated ring-opening reaction of epoxide furnishes a hydrogen-bond-stabilized iodoohydrin intermediate (Scheme 5, **II**). The *in situ* formed oxo-anions via epoxide ring-opening could easily displace the iodide nucleophile in the **1a**:I^- complex[20j-k, 41], providing **1a**-stabilized oxo-anion complex. Subsequent inclusion of isocyanate into the iodoohydrin entity results in a squaramide—stabilized carbamate intermediate (Scheme 5, **IV**). Lastly, the catalytic cycle is completed with an intramolecular ring closure of the carbamate intermediate producing the oxazolidinone **4/5** and regenerating the host **1**. Since iodide binding to **1** is significant, the host-guest assembly **1**:*n*-TBAI^- can be assumed as the resting state of this catalytic system: the host **1** captures the iodide anion that is liberated in the ring-closing step while furnishing the oxazolidinone adduct.

10.1002/ejoc.202000153



Scheme 5. Proposed catalytic cycle for squaramide/*n*-TBAI-catalyzed [3 + 2] cycloaddition of isocyanates and epoxides.

Conclusions

Organocatalysis is an emerging and promising catalytic platform that effectively catalyzes reactions of heterocumulenes for the preparation of heterocycles. The binary organocatalytic system –composed of a squaramide entity along with a suitable halide anion– developed here successfully catalyzes the [3 + 2] cycloaddition of isocyanates and epoxides towards the preparation of oxazolidinones.

This simple and tunable catalytic system is highly efficient for the synthesis of aryl- and alkyl *N*-substituted oxazolidinones in addition to the disubstituted and enantioenriched ones from a broad range of epoxides and isocyanates in high-to-excellent yields. This metal- and solvent-free platform causes halide nucleophilic ring-opening operation, and isocyanate insertion to occur in a cooperative manner producing oxazolidinones without resort to slow addition of isocyanates or excess amount of epoxides. A hydrogen bonding-anion binding mechanism was proposed in which the double hydrogen-bond donor catalyst could simultaneously participate in multiple modes of activation and stabilization. Efforts in development of other organocatalytic systems for the mild fixation of isocyanate are underway in our laboratory.

Experimental Section

Materials and general methods. Squaramide **1a-i** were prepared under argon atmosphere using Schlenk techniques and [3 + 2] cycloaddition reactions were carried out in drum vials. Stainless steel syringes were used to transfer air and moisture-sensitive liquids. Flash chromatography was performed using silica gel 60 (230-400 mesh) from Merck. Thin layer chromatography was performed on glass plates precoated with 0.25 mm Kieselgel 60 F254 (Merck). Epoxides **2a-f**, isocyanates **3a-i**, aniline, 3,5-bis(trifluoromethyl)aniline, 4-nitroaniline, 3,4-diethoxy-3-

cyclobutene-1,2-dione, cyclohexyl amine, 3,5 bis(trifluoromethyl) phenyl isothiocyanate, 1,6 diaminohexane, tris(2-aminoethyl)amine, was purchased from Sigma Aldrich. Tetrabutyl ammonium iodide, tetrabutyl ammonium bromide, tetrabutyl ammonium chloride, 1,3 diaminopropane, was purchased from Merck. Zinc trifluoromethanesulfonate was purchased from Alfa Aesar. All other reagents were purchased from commercial sources, unless otherwise noted. Solvents were purchased from Merck. Distilled water was obtained from an in-house supply. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker DRX-300 (300 MHz), Varian Mercury-500 (500 MHz) and Bruker DRX-600 (600 MHz) spectrometers. Chemical shifts for protons (δ scale) are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent (DMSO: δ 2.50, $CDCl_3$: δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent (DMSO: δ 39.51, $CDCl_3$: δ 77.23). Data represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (*J* value) in Hertz (Hz), and number of protons. Conversion was measured by the ratio of epoxide compared to those of corresponding oxazolidinones. Infrared (IR) spectra were obtained on a Thermo/Nicolet NEXUS 470 instrument equipped with a single-bounce diamond / ZnSe ATR accessory, either in the solid state or as neat liquids, as indicated. Spectral features are tabulated as follows: wavenumber (cm^{-1}); intensity (s-strong, m-medium, w-weak, br-broad). High-resolution mass spectra (HRMS) and HPLC were obtained on an Agilent technologies 6530 Q-TOF-LC-MS. All optical rotations $[\alpha]_D^{20}$ analyses were performed on a KRUSS P300 polarimeter instrument. Optical rotations are measured at the wavelength of the

sodium D-line (589.3 nm) at a temperature of 20 °C, with reference to a layer 1 dm thick of a solution containing 0.01 g of the substance per 1 milliliter.

Preparation of symmetrically substituted squaramides. Squaramides **1a-c** were prepared according to the previously reported procedures.[23e, 42]

*3,4-Bis(phenylamino)cyclobut-3-ene-1,2-dione (**1a**).* Synthesized according to the previously reported procedure:[23e] to a stirred solution of 3,4-diethoxycyclobut-3-ene-1,2-dione (397 µl, 2 mmol, 1 equiv) and zinc trifluoromethanesulfonate (146 mg, 0.4 mmol, 20 mol %) in toluene / DMF 19:1 (2 mL) was added aniline (201 µl, 2.2 mmol, 1.1 equiv). The solution was heated to 100 °C and stirred for 12 h. When the solution was cooled to room temperature, a white precipitate was observed and isolated by decanting the solvent. The solid was further washed with methanol (3 x 5 mL), and each time it was shaken vigorously and centrifuged to remove the methanol. The resulting solid was further refluxed with isopropanol to eliminate any traces of DMF and further dried *in vacuo* yielding **1a** as a white solid (470 mg, 1.78 mmol, 89% yield). *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[23e] ^{1}H NMR (600 MHz, DMSO-d_6) δ_H 9.87 (br, 2H), 7.48 (d, J = 7.8 Hz, 4H), 7.37 (t, J = 7.8 Hz, 4H), 7.08 (t, J = 7.8 Hz, 2H); ^{13}C NMR (151 MHz, DMSO) δ_C 181.6, 165.6, 138.5, 129.4, 123.4, 118.5.

*3,4-Bis(3,5-bis(trifluoromethyl)-phenylamino)cyclobut-3-ene-1,2-dione (**1b**).* Squaramide **1b** was prepared in (922 mg, 1.72 mmol, 86% yield) as a white solid by following the procedure for the preparation of **1a**. *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum:* [23e] ^{1}H NMR (600 MHz, DMSO-d_6) δ_H 10.43 (br, 2H), 7.90 (s, 4H), 7.68 (s, 2H); ^{13}C

NMR (151 MHz, DMSO-d_6) δ_C 181.7, 166.2, 141.2, 131.5 (q, J = 33 Hz), 123.4 (q, J = 273. Hz), 118.1, 115.4.

*3,4-Bis(cyclohexlamino)cyclobut-3-ene-1,2-dione (**1c**).* to a stirred solution of 3,4-diethoxycyclobut-3-ene-1,2-dione (397 µl, 2 mmol, 1 equiv) in methanol (2 mL) was added cyclohexylamine (252 µl, 2.2 mmol, 1.1 equiv) at room temperature. The solution was stirred for 12 h at room temperature. The precipitated solid was filtered and washed with di ethyl ether (2 × 2 ml) and dried *in vacuo* yielding **1c** as a white solid (498 mg, 1.80 mmol, 90% yield). *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum:* [42] ^{1}H NMR (600 MHz, DMSO-d_6) δ_H 7.31 (s, 2H), 3.74 (s, 2H), 1.86 (d, J = 8.9 Hz, 4H), 1.72 – 1.62 (m, 4H), 1.53 (d, J = 12.4 Hz, 2H), 1.27 (m, 8H), 1.20 – 1.11 (m, 2H); ^{13}C NMR (151 MHz, DMSO-d_6) δ_C 181.8, 167.0, 52.0, 33.7, 24.8, 24.0.

Preparation of unsymmetrically substituted squaramides. [23e, 43]

*3-(3,5-bis(trifluoromethyl)-phenylamino)-4-ethoxycyclobut-3-ene-1,2-dione (**II**).* To a stirred solution of 3,4-diethoxycyclobut-3-ene-1,2- dione (**I**) (0.814 ml, 5.5 mmol 1.1 equiv) and zinc trifluoromethanesulfonate (400 mg, 1.1 mmol, 20 mol %) in ethanol (10 mL) at room temperature was added 3,5-bis(trifluoromethyl)aniline (0.781 ml, 5 mmol, 1 equiv). The solution was stirred overnight at room temperature, then the mixture was concentrated under reduced pressure and purified by flash column chromatography (silica gel, 1 : 0 → 7 : 3 *n*-hexanes/ethylacetate) and dried *in vacuo* to afford 3-(3,5-bis(trifluoromethyl)-phenylamino)-4-ethoxycyclobut-3-ene-1,2-dione (**II**) as white solid (2.2 g, 4.6 mmol, 92% yield). *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum:* [43] ^{1}H NMR (600

MHz, DMSO-d_6) δ_H 11.19 (s, 1H), 8.00 (s, 2H), 7.72 (s, 1H), 4.77 (q, J = 7.1 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, DMSO-d_6) δ_C 187.7, 184.5, 179.2, 169.2, 140.1, 131.1 (q, J = 33 Hz), 123.0 (q, J = 273 Hz), 119.4, 116.3, 70.2, 15.3.

*3-(3,5-Bis(trifluoromethyl)phenylamino)-4-(cyclohexylamino) cyclobut -3-ene-1,2-dione (**1d**).* To a stirred solution of 3-(3,5-bis(trifluoromethyl)-phenylamino)-4-ethoxycyclobut-3-ene-1,2-dione (II) (777 mg, 2.2 mmol, 1.1 equiv) in methanol (4 mL) was added cyclohexylamine (229 µl, 2 mmol, 1 equiv). The solution was stirred for 12 h at room temperature. The precipitated solid was filtered and washed with diethyl ether (2 × 4 ml) and dried *in vacuo* yielding **1d** as a white solid (772 mg, 1.90 mmol, 95 % yield). *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum:* [29b] ^{1}H NMR (600 MHz, DMSO-d_6) δ_H 10.05 (br s, 1H), 8.01 (s, 2H), 7.77 (br s, 1H), 7.61 (s, 1H), 3.48−3.32 (m, 1H), 2.08−1.84 (m, 2H), 1.80−1.65 (m, 2H), 1.62 –1.50 (m, 1H), 1.38 –1.21 (m, 5H); ^{13}C NMR (151 MHz, DMSO-d_6) δ_C 184.4, 180.2, 169.0, 162.4, 141.1, 131.4 (q, J = 33 Hz), 123.1 (q, J = 273 Hz), 117.9, 114.7, 52.9, 33.4, 24.7, 24.0.

*3-(3,5-Bis(trifluoromethyl)phenylamino)-4-(4-nitrophenyla-mino) cyclobut-3-ene-1,2-dione (**1e**).* To a stirred solution of **II** (777 mg, 2.2 mmol, 1.1 equiv) and zinc trifluoromethanesulfonate (146 mg, 0.4 mmol, 20 mol %) in toluene/DMF 19:1 (4 mL) was added 4-nitroaniline (276 mg, 2 mmol, 1 equiv). The solution was heated to 100 °C and stirred for 12 h. Upon cooling to room temperature, a yellow precipitate was observed and was isolated by decanting the solvent. The solid was further washed with methanol (3 x 4 mL), and each time it was shaken vigorously and centrifuged to remove the methanol. The resulting solid was further refluxed with isopropanol to eliminate any traces of DMF and further dried in *vacuo* yielding **1e** as a yellow solid (740 mg,

1.66 mmol, 83% yield). *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum:*[23e] ^{1}H NMR (600 MHz, DMSO-d_6) δ_H 10.60 (br, 2H), 8.03 (s, 2H), 7.75 (s, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 7.6 Hz, 2H); ^{13}C NMR (151 MHz, DMSO-d_6) δ_C 183.6, 182.8, 166.6, 165.7, 142.4, 142.3, 131.3 (q, J = 33 Hz), 125.5, 123.1 (q, J = 273 Hz), 118.64, 118.57, 116.7, 116.1.

*1-(3,5-Bis(trifluoromethyl)phenyl)-3-phenylthiourea (**1f**).* At room temperature, cyclohexanamine (229 µl, 2 mmol, 1 equiv) was added drop wise to a stirred solution of 3,5-bis(trifluoromethyl)phenyl isothiocyanate (402 µl, 2.2 mmol, 1.1 equiv) in Toluene (5 mL). After stirring for 24 h at room temperature, the solvent was evaporated. The white residue was recrystallized from chloroform to give 1-(3,5- bis(trifluoromethyl)phenyl)-3-cyclohexylthiourea **1f** as a white solid (735 mg, 1.98 mmol, 99% yield). *^{1}H NMR and ^{13}CNMR spectra were in agreement with the previously reported spectrum:*[44] ^{1}H NMR (600 MHz, DMSO-d_6): δ_H 7.42 (s, 1H), 7.29 (s, 2H), 6.82 (s, 1H), 5.19 (s, 1H), 4.40 (m, 1H), 1.91-0.86 (m, 10H); ^{13}C NMR (151 MHz, DMSO-d_6): δ_C 179.2, 142.0, 130.1 (q, J = 33 Hz), 123.3 (q, J = 273 Hz), 121.8, 115.9, 52.3, 31.6, 25.1, 24.4.

1g. To a stirred solution of 3-(3,5-bis(trifluoromethyl)-phenylamino)-4-ethoxycyclobut-3-ene-1,2-dione **II** (777 mg, 2.2 mmol, 1.1 equiv) was added 1,3 diaminopropane (83 µl, 1 mmol, 1 equiv) in ethanol (4 ml). After stirring 24 h at room temperature, a white precipitate was formed and further filtered and washed with diethyl ether (2 × 4 ml) and dried *in vacuo* to get compound **1g** as white solid (379 mg, 0.55 mmol, 55% yield). IR (neat) 3251, 1799, 1697, 1583, 1452, 1375, 1275, 1123, 928, 883; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H 11.91 (s, 1H), 9.14 (s, 1H), 8.19 (s, 2H), 7.53 (s, 1H), 3.72 (m, 2H), 1.91 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C 184.6,

180.3, 170.5, 163.2, 142.2, 131.7 (q, J = 33 Hz), 125.4 (q, J = 273 Hz), 121.8, 117.7, 114.5, 41.9, 32.0; HRMS (ESI) calcd. for $C_{27}H_{16}F_{12}N_4O_4$ $[M+H]^+$: 689.1013, found: *m/z* 689.1045

1h. Squaramide **1h** was prepared in (460 mg, 0.63 mmol, 63% yield) as a white solid by following the procedure for the preparation of **1g.** IR (neat) 3248, 1795, 1701, 1586, 1497, 1374, 1271, 1128, 931, 883; ^{1}H NMR (600 MHz, DMSO-d_6) δ_H 10.17 (br, 2H), 8.00 (s, 4H), 7.80 (br, 2H), 7.61 (s, 2H), 3.61 (t, J = 7.8 Hz, 4H), 1.59 (m, 4H), 1.37 (m, 4H); ^{13}C NMR (151 MHz, DMSO-d_6) δ_C 184.8, 180.40, 169.9, 162.5, 141.2, 131.3 (q, J = 33 Hz), 123.2 (q, J = 273 Hz), 118.1, 114.6, 43.7, 30.2, 25.3; HRMS (ESI) calcd. for $C_{30}H_{22}F_{12}N_4O_4$ $[M+H]^+$: 731.1483, found: *m/z* 731.1497.

***1i**:* Squaramide **1i** was prepared in (716 mg, 0.67 mmol, 67% yield) as a white solid by following the procedure for the preparation of **1g**. *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum:*[44] IR (neat) 3232, 1788, 1675, 1602, 1429, 1371, 1278, 1123, 935, 880; ^{1}H NMR (600 MHz, DMSO-d_6) δ_H 10.15 (br, 3H), 7.85 (s, 6H), 7.51 (br, 3H), 7.39 (s, 3H), 3.73 (m, 6H), 2.82 (m, 6H); ^{13}C NMR (151 MHz, DMSO-d_6) δ_C 185.1, 179.9, 169.5, 162.3, 140.9, 131.1 (q, J = 33 Hz), 123.0 (q, J = 273 Hz), 117.5, 114.4, 53.2, 41.8; HRMS (ESI) calcd. for $C_{40}H_{27}F_{18}N_7O_6$ $[M+H]^+$: 1068.1769, found: *m/z* 1068.1801.

General procedure for the synthesis of oxazolidinones. In an oven-dried vial equipped with a stir bar was added epoxide **2** (2 mmol), isocyanate **3** (2 mmol), squaramide **1d** (41mg, 0.1 mmol, 5 mol %) and *n*-TBAI (37 mg, 0.1 mmol, 5 mol %). The reaction mixture was stirred at 70 or 100 °C for 24h, cooled to room temperature, and then purified by flash column chromatography (silica gel) to yield the corresponding **4a-x**, **5a-g.**

*3,5-diphenyloxazolidin-2-one (**4a**) and 3,4-diphenyloxazolidin-2-one (**5a**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 70 °C for 24 h. The crude product was purified by flash chromatography (silica gel, *n*-hexanes: ethyl acetate 100:0 → 80:20, R_f 0.3 (80:20)) to yield **4a** (306 mg, 1.28 mmol) and **5a** (115 mg, 0.48 mmol) as white solids for a combined 88 % yield. **4a**: *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] mp 77–79 °C; IR (neat) 3066, 2977, 1735 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.54 – 7.30 (m, 8H), 7.03 (dd, *J* = 9.0, 6.0 Hz, 1H), 5.54 (app t, *J* = 8.4 Hz, 1H), 4.27 (app t, *J* = 8.4 Hz, 1H), 3.86 (app t, *J* = 8.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 154.7, 138.5, 138.4, 129.1, 129.0, 125.7, 124.2, 118.6, 74.1, 52.8; Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.35; H, 5.52; N, 5.81. **5a:** *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] mp 128–130 °C; IR (neat) 3066, 2978, 1745 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.65 – 7.32 (m, 8H), 7.30 – 7.28 (m, 1H), 7.12 – 6.87 (m, 1H), 5.57 – 5.14 (m, 1H), 4.65 (dd, *J* = 8.2, 6.9 Hz, 1H), 4.11 (dd, *J* = 8.2, 6.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 155.9, 138.6, 137.4, 129.4, 128.9, 128.8, 126.3, 124.8, 121.2, 69.8, 60.9; Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.25; H, 5.49; N, 5.88.

*3-(4-chlorophenyl)-5-phenyloxazolidin-2-one (**4b**) and 3-(4-chlorophenyl)-4-phenyloxazolidin-2-one (**5b**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 70 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 80:20, R_f 0.3 (80:20)) to yield **4b** (365 mg, 1.34 mmol) and **5b** (104 mg, 0.38 mmol) as white solids for a combined 86 % yield. **4b**: *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] mp 114–116 °C; IR (neat)

2926, 1751 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.44 (d, *J* = 8.6 Hz, 2H), 7.35 (m, 2H), 7.26 (m, 5H), 5.51 (app t, *J* = 8.1 Hz, 1H), 4.27 (dd, *J* = 8.7, 8.1 Hz, 1H), 3.92 – 3.77 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 148.6, 137.8, 136.8, 129.7, 129.3, 129.2, 129.1, 125.8, 119.6, 74.2, 52.5; Anal. Calcd for $C_{15}H_{12}ClNO_2$: C, 65.82; H, 4.42; N, 5.12. Found: C, 65.86; H, 4.36; N, 5.28. **5b**: *^1H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] mp 127–129 °C; IR (neat) 3032, 2969, 2901, 1738 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.28 – 7.26 (m, 1H), 7.25-7.16 (m, 5H), 7.15-7.07 (m, 3H), 5.30 (app t, *J* = 7.4 Hz, 1H), 4.68 (dd, *J* = 8.1, 7.4 Hz, 1H), 4.10 (dd, *J* = 8.1, 7.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0, 136.8, 135.7, 129.5, 129.4, 129.1, 128.9, 126.2, 122.1, 69.9, 60.5; Anal. Calcd for $C_{15}H_{12}ClNO_2$: C, 65.82; H, 4.42; N, 5.12. Found: C, 65.70; H, 4.35; N, 5.24.

*3-(4-fluorophenyl)-5-phenyloxazolidin-2-one (**4c**) and 3-(4-fluorophenyl)-4-phenyloxazolidin-2-one (**5c**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 70 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 80:20, R_f 0.3(80:20)) yield **4c** (298 mg, 1.16 mmol) and **5c** (123 mg, 0.48 mmol) as white solids for a combined 82 % yield. **4c**: *^1H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] mp 79–82 °C; IR (neat) 3028, 2979, 1728 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.49 (dd, *J* = 9.0, 4.6 Hz, 2H), 7.44 – 7.29 (m, 5H), 7.05 (dd, *J* = 9.3, 8.2 Hz, 2H), 5.68 – 5.41 (m, 1H), 4.29 (dd, *J* = 8.8, 7.5 Hz, 1H), 3.87 (dd, *J* = 8.8, 7.5, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 159.6 (d, *J* = 243 Hz), 155.0, 137.9, 134.2, 129.22, 129.21, 125.7, 120.2 (d, *J* = 7 Hz), 115.7 (d, *J* = 23 Hz), 74.2, 52.9; Anal. Calcd for $C_{15}H_{12}FNO_2$: C, 70.03; H, 4.70; N, 5.44. Found: C, 70.29; H, 4.92; N, 5.80. **5c:** *^1H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] mp 95–98 °C; IR

(neat) 2980, 1739 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.45 – 7.28 (m, 7H), 6.87 (dd, *J* = 8.9, 8.1 Hz, 2H), 5.35 (app t, *J* = 8.5 Hz, 1H), 4.70 (app t, *J* = 8.5 Hz, 1H), 4.29 (app t, *J* = 8.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.2 (d, *J* = 243 Hz), 156.2, 137.8, 130.4, 129.4, 126.4, 123.1 (d, *J* = 8 Hz), 115.8 (d, *J* = 22 Hz), 69.8, 61.3; Anal. Calcd for $C_{15}H_{12}FNO_2$: C, 70.03; H, 4.70; N, 5.44. Found: C, 70.16; H, 4.83; N, 5.67.

3-(3,5-bis(trifluoromethyl)phenyl)-5-phenyloxazolidin-2-one ***(4d)*** *and 3-(3,5-bis(trifluoromethyl)phenyl)-4-phenyloxazolidin-2-one* ***(5d)****.* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 70 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 80:20, R_f 0.3 (80:20)) to yield **4d** (412 mg, 1.10 mmol) and **5d** (172 mg, 0.46 mmol) as colorless oil for a combined 78 % yield. **4d:** IR (neat) 3027, 2934, 1711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 8.09 (s, 2H), 7.64 (s, 1H), 7.36 (m, 5H), 5.73 (app t, *J* = 8.0 Hz, 1H), 4.30 (dd, *J* = 8.0, 6.7 Hz, 1H), 4.06 dd, *J* = 8.0, 6.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 155.5, 139.7, 138.7, 132.2 (q, *J* = 34 Hz), 129.14, 129.11, 121.0 (q, *J* = 273 Hz), 117.6, 117.2, 74.6, 52.2; Anal. Calcd for $C_{17}H_{11}F_6NO_2$: C, 54.41; H, 2.95; N, 3.73. Found: C, 54.52; H, 2.86; N, 3.80; HRMS (ESI) calcd. for $C_{17}H_{11}F_6NO_2$ $[M+H]^+$: 376.0728, found: *m/z* 376.0741. **5d:** IR (neat) 3031, 2945, 1718 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.95 (s, 2H), 7.54 (s, 1H), 7.51 (s, 1H), 7.44 – 7.29 (m, 4H), 5.52 (app t, *J* = 6.3 Hz, 1H), 4.87 (dd, *J* = 8.8, 5.7 Hz, 1H), 4.52 (dd, *J* = 8.8, 5.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 154.5, 137.2, 136.8, 132.5 (q, *J* = 33 Hz), 129.7, 129.4, 126.2, 120.8 (q, *J* = 273 Hz), 118.6, 118.2; Anal. Calcd for $C_{17}H_{11}F_6NO_2$: C, 54.41; H, 2.95; N, 3.73. Found: C, 54.14; H, 2.89; N, 3.98; HRMS (ESI) calcd. for $C_{17}H_{11}F_6NO_2$ $[M+H]^+$: 376.0728, found: *m/z* 376.0745.

*3-(4-nitrophenyl)-5-phenyloxazolidin-2-one (**4e**) and 3-(4-nitrophenyl)-4-phenyloxazolidin-2-one (**5e**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 70 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 75:25, R_f 0.4 (75:25)) to yield **4e** (278 mg, 0.98 mmol) and **5e** (153 mg, 0.54 mmol) as yellow oils for a combined 76 % yield. **4e**: *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.* [18a] IR (neat) 3053, 2920, 1745 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.12 (d, *J* = 8.8 Hz, 2H), 7.68 (d, *J* = 8.7 Hz, 2H), 7.39 – 7.28 (m, 5H), 5.65 (dd, *J* = 9.2, 7.5 Hz, 1H), 4.46 (app t, *J* = 8.8 Hz, 1H), 3.99 (dd, *J* = 8.8, 7.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 155.2, 143.8, 137.3, 129.8, 129.7, 126.0, 125.9, 124.9, 117.6, 74.5, 52.3; Anal. Calcd for $C_{15}H_{12}N_2O_4$: C, 63.38; H, 4.26; N, 9.85. Found: C, 63.26; H, 4.15; N, 10.11. **5e**: *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] IR (neat) 3036, 2886, 1775 cm^{-1}; 1H NMR (300 MHz, $CDCl_3$) δ_H 8.01 (d, *J* = 9.0 Hz, 2H), 7.52 (d, *J* = 9.1 Hz, 2H), 7.4−7.2 (m, 5H), 5.37 (dd, *J* = 8.8, 5.5 Hz, 1H), 4.71 (app t, *J* = 8.8 Hz, 1H), 4.18 (dd, *J* = 8.8, 5.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 154.2, 142.9, 137.3, 129.7, 129.2, 125.9, 125.8, 124.6, 119.5, 70.0, 60.1; Anal. Calcd for $C_{15}H_{12}N_2O_4$: C, 63.38; H, 4.26; N, 9.85. Found: C, 63.43; H, 4.19; N, 9.96.

*5-phenyl-3-(p-tolyl)oxazolidin-2-one (**4f**) and 4-phenyl-3-(p-tolyl)oxazolidin-2-one (**5f**):* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 70 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 80:20 R_f 0.3 (80:20)) to yield **4f** (374 mg, 1.48 mmol) and **5f** (81 mg, 0.32 mmol) as white solids for a combined 90 % yield. **4f:** *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] mp 96–99 °C; IR (neat) 2964, 1735

cm^{-1};1H NMR (300 MHz, $CDCl_3$) δ_H 7.53−7.35 (m, 7H), 7.20 (d, *J* = 8.3 Hz, 2H), 5.59 (app t, *J* = 8.3 Hz, 1H), 4.32 (app t, *J* = 9.0 Hz, 1H), 3.90 (app t, *J* = 8.3 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 154.8, 138.2, 135.6, 133.9, 129.6, 129.03, 128.97, 125.6, 118.4, 74.0, 52.8, 20.7; Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.72; H, 6.01; N, 5.60. **5f:** *^1H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] mp 106−108 °C, IR (ATR) 3037, 2973, 1742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.48 – 7.22 (m, 7H), 7.07 (d, *J* = 8.2 Hz, 2H), 5.37 (dd, *J* = 8.8, 6.3 Hz, 1H), 4.73 (app t, *J* = 8.8 Hz, 1H), 4.17 (dd, *J* = 8.8, 6.3 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 155.0, 138.6, 134.52, 134.5, 129.4, 129.2, 128.6, 126.3, 121.2, 69.5, 61.0, 19.7; Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.79; H, 5.99; N, 5.61.

*3-(tert-butyl)-5-phenyloxazolidin-2-one (**4g**) and 3-(tert-butyl)-4-phenyloxazolidin-2-one (**5g**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 70 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 →85:15, R_f 0.35 (85:15)) to yield **4g** (131 mg, 0.60 mmol) and **5g** (61 mg, 0.28 mmol) as colorless oil for a combined 44 % yield. **4g:** *^1H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[11c] IR (neat) 3007, 2932, 1713 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.33 (d, *J* = 8.1 Hz, 2H), 7.24 (m, 3H), 5.60 (app t, *J* = 8.2 Hz, 1H), 4.22 (app t, *J* = 8.2 Hz, 1H), 3.94 – 3.83 (m, 1H), 1.23 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 156.6, 138.9, 128.7, 128.6, 125.4, 73.4, 54.5, 50.9, 27.3; Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.38; H, 7.76; N, 6.48; HRMS (ESI) calcd. for $C_{13}H_{17}NO_2$ $[M+H]^+$: 220.1293, found: *m/z* 220.1301. **5g:** IR (neat) 3040, 2974, 1712 cm^{-1}; *^1H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[11c] ^1H NMR (300 MHz,

$CDCl_3$) δ_H 7.40 – 7.29 (m, 5H), 5.30 (app t, J = 8.4 Hz, 1H), 4.71 (app t, J = 8.4 Hz, 1H), 4.22 (app t, J = 8.4 Hz, 1H), 1.25 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 158.9, 137.7, 129.5, 129.2, 127.0, 69.1, 61.4, 49.8, 27.5; Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.14; H, 7.79; N, 6.45; HRMS (ESI) calcd. for $C_{13}H_{17}NO_2$ $[M+H]^+$: 220.1293, found: *m/z* 220.1299.

*(2-oxo-3-phenyloxazolidin-5-yl)methyl methacrylate (**4h**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 →75 : 25, R_f 0.35 (75:25)) to yield **4h** (496 mg, 1.90 mmol, 95 % yield) as white solid. mp 68−70 °C; IR (neat) 2953, 2923, 1739 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.53 (d, J = 8.4 Hz, 2H), 7.37 (t, J = 8.2 Hz, 2H), 7.15 (t, J = 8.2 Hz, 1H), 6.11 (s, 1H), 5.59 (s, 1H), 4.88 (dddd, J = 9.0, 7.1, 5.8, 4.9 Hz, 1H), 4.43 (dd, J = 12.5, 4.9 Hz, 1H), 4.34 (dd, J = 12.5, 5.8 Hz, 1H), 4.14 (app t, J = 9.0, Hz, 1H), 3.84 (dd, J = 9.0, 7.1 Hz, 1H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 166.8, 154.3, 138.0, 135.4, 129.2, 129.1, 128.5, 126.7, 124.2, 118.2, 70.1, 64.6, 47.1, 18.1; Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.65; H, 5.91; N, 5.55; HRMS (ESI) calcd. for $C_{14}H_{15}NO_4$ $[M+H]^+$: 262.1035, found: *m/z* 262.1048.

*(3-(4-chlorophenyl)-2-oxooxazolidin-5-yl)methyl methacrylate (**4i**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 60:40, R_f 0.35 (75:25)) to yield **4i** (525 mg, 1.78 mmol, 89% yield) as pale yellow oil. IR (neat) 2981, 2944, 1747 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.39 – 7.34 (m, 2H), 7.29 – 7.24 (m, 2H), 6.01 (s, 1H), 5.51 (s, 1H), 4.82 (app dq, J = 9.4, 4.7 Hz, 1H), 4.36 (dd, J = 12.5, 4.3 Hz, 1H), 4.26 (dd,

J = 12.5, 4.7 Hz, 1H), 4.04 (app t, *J* =9.2, Hz, 1H), 3.75 (dd, *J* = 9.1, 4.7 Hz, 1H), 1.89 (s, 3H); ^{13}C NMR (126 MHz $CDCl_3$) δ_C 166.6, 154.3, 136.7, 135.2, 129.1, 128.4, 127.0, 119.9, 70.1, 64.5, 47.2, 18.0; Anal. Calcd for $C_{14}H_{14}ClNO_4$: C, 56.86; H, 4.77; N, 4.74. Found: C 57.10; H, 4.63; N, 5.05; HRMS (ESI) calcd. for $C_{14}H_{14}ClNO_4$ $[M+H]^+$: 296.0611, found: *m/z* 296.0625.

*(3-(4-fluorophenyl)-2-oxooxazolidin-5-yl)methyl methacrylate (**4j**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 →50:50, R_f 0.30 (75:25)) to yield **4j** (480 mg, 1.72 mmol, 86% yield) as a white solid. mp 70–71 °C; IR (neat) 2930, 1734 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 – 7.39 (m, 2H), 7.07 – 6.96 (m, 2H), 6.07 (s, 1H), 5.55 (s, 1H), 4.88 (dq, *J* = 9.0, 4.5 Hz, 1H), 4.41 (dd, *J* = 12.3, 4.5 Hz, 1H), 4.32 (dd, *J* = 12.3, 4.5 Hz, 1H), 4.13 (app t, *J* = 9.0 Hz, 1H), 3.82 (dd, *J* = 9.0, 4.5 Hz, 1H), 1.87 (s, 3H); ^{13}C NMR (75 MHz $CDCl_3$) δ 166.7, 154.4, 135.3, 134.1 (d, *J* = 2.4 Hz), 126.7, 120.0 (d, *J* = 7.9 Hz), 115.8, 115.5, 70.1, 64.5, 47.2, 18.0; Anal. Calcd for $C_{14}H_{14}FNO_4$: C, 60.21; H, 5.05; N, 5.02. Found: C, 59.98; H, 4.79; N, 5.47; HRMS (ESI) calcd. for $C_{14}H_{14}FNO_4$ $[M+H]^+$: 280.0940, found: *m/z* 280.0954.

*(3-(3,5-bis(trifluoromethyl)phenyl)-2-oxooxazolidin-5-yl)methyl methacrylate (**4k**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 →50:50, R_f 0.25 (75:25)) to yield **4k** (643 mg, 1.62 mmol, 81% yield) as a white solid. mp 74–76 °C; IR (neat) 3029, 2942, 1721 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.03 (s, 2H), 7.62 (s, 1H), 6.07 (s, 1H), 5.58 (s, 1H), 5.02 (dq, *J* = 9.1, 4.3 Hz, 1H), 4.49 (dd, *J* = 12.4, 4.3 Hz, 1H), 4.40 (dd, *J* = 12.4, 4.3 Hz, 1H), 4.29 (app t, *J* = 9.1 Hz, 1H), 3.98 (dd, *J* = 9.0, 4.3 Hz, 1H),

1.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 166.7, 153.9, 139.5, 135.2, 132.5 (q, J = 33 Hz), 126.9, 123.0 (q, J = 273 Hz), 117.5 (q, J = 3 Hz), 117.2, 70.6, 64.2, 46.8, 18.0; Anal. Calcd for $C_{16}H_{13}F_6NO_4$: C, 48.37; H, 3.30; N, 3.53. Found: C, 48.14; H, 3.02; N, 3.91; HRMS (ESI) calcd. for $C_{16}H_{13}F_6NO_4$ $[M+H]^+$: 398.0780, found: *m/z* 398.0794.

*(3-(4-nitrophenyl)-2-oxooxazolidin-5-yl)methyl methacrylate (**4l**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 →45:55, R_f 0.10 (75:25)) to yield **4l** (520 mg, 1.70 mmol, 85% yield) as a yellow solid. mp 96–98 °C; IR (neat) 3055, 2951, 1739 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.14 (d, J = 9.0 Hz, 2H), 7.68 (d, J = 9.0 Hz, 2H), 6.01 (s, 1H), 5.52 (s, 1H), 5.05 (dq, 9.1, 4.8, 1H), 4.45 (dd, 12.3, 4.8 1H), 4.36 (dd, J = 12.3, 4.8 Hz, 1H), 4.27 (app t, J = 9.1 Hz, 1H), 3.96 (dd, J = 9.1, 4.8 Hz, 1H), 1.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 166.6, 153.8, 143.6, 143.2, 126.9, 124.9, 117.4, 70.6, 64.4, 46.8, 18.1; Anal. Calcd for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.61; N, 9.15. Found: C, 54.66; H, 4.45; N, 9.77; HRMS (ESI) calcd. for $C_{14}H_{14}N_2O_6$ $[M+H]^+$: 307.0885, found: *m/z* 307.0900.

*(2-oxo-3-(p-tolyl)oxazolidin-5-yl)methyl methacrylate (**4m**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 →65:35, R_f 0.20 (80:20)) to yield **4m** (506 mg, 1.84 mmol, 92% yield) as a colorless oil. IR (neat) 2954, 2921, 1747 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.29 (d, J = 8.3 Hz, 2H), 7.03 (d, J = 8.2 Hz, 2H), 5.97 (s, 1H), 5.44 (s, 1H), 4.71 (dq, J = 9.6, 4.8 Hz, 1H), 4.27 (dd, J = 12.3, 4.8 Hz, 1H), 4.17 (dd, J = 12.3, 4.8 Hz, 1H), 3.97 (app t, J = 9.6 Hz, 1H), 3.66 (dd, J = 9.6, 4.8 Hz, 1H), 2.20 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 166.5, 154.3, 135.5, 135.4, 133.4, 129.4,

126.4, 118.1, 70.1, 64.6, 46.9, 20.4, 17.9; Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 64.70; H, 5.87; N, 5.21; HRMS (ESI) calcd. for $C_{15}H_{17}NO_4$ $[M+H]^+$: 276.1191, found: *m/z* 276.1202.

*(3-(tert-butyl)-2-oxooxazolidin-5-yl)methyl methacrylate (**4n**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 75:25, R_f 0.55 (75:25)) to yield **4n** (237 mg, 0.98 mmol, 49% yield) as a yellow oil. IR (neat) 2967, 2932, 1742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 6.13 (s, 1H), 5.64 (s, 1H), 5.03 (dq, *J* = 8.8, 4.2 Hz, 1H), 4.52 (dd, *J* = 12.5, 4.2 Hz, 1H), 4.44 (dd, *J* = 12.5, 4.2 Hz, 1H), 4.28 (app t, *J* = 8.8 Hz, 1H), 3.97 (dd, *J* = 8.8, 4.2 Hz, 1H), 1.33 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 166.7, 154.2, 135.2, 126.9, 70.2, 64.5, 53.0, 46.9, 27.4, 18.1; Anal. Calcd for $C_{12}H_{19}NO_4$: C, 59.73; H, 7.94; N, 5.81. Found: C, 60.01; H, 8.13; N, 5.67; HRMS (ESI) calcd. for $C_{12}H_{19}NO_4$ $[M+H]^+$: 242.1348, found: *m/z* 242.1356.

*3-benzyl-5-(phenoxymethyl)oxazolidin-2-one (**4o**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 70:30, R_f 0.15 (85:15)) to yield **4o** (465 mg, 1.64 mmol, 82% yield) as a white solid. *^1H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[45] mp 63–64 °C;IR (neat) 3060, 2925, 1734 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ_H 7.41 – 7.38 (m, 2H), 7.36 – 7.31 (m, 5H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 2H), 4.84 (dq, *J* = 8.9, 5.0, 1H), 4.49 (ABq, *J* = 14.9 Hz, $\Delta\upsilon_{AB}$ = 17.1 Hz, 2H), 4.12 (m, 2H), 3.60 (t, *J* = 8.9 Hz, 2H), 3.46 (dd, *J* = 8.9, 5.0 Hz, 1H); ^{13}C NMR

(151 MHz, $CDCl_3$) δ_C 158.1, 157.6, 135.6, 129.7, 128.9, 128.1, 128.0, 121.6, 114.5, 70.9, 68.0, 48.3, 46.1; HRMS (ESI) calcd. for $C_{17}H_{17}NO_3$ $[M+H]^+$: 283.1208, found: *m/z* 316.1220.

*5-(phenoxymethyl)-3-tosyloxazolidin-2-one (**4p**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 50:50, R_f 0.10 (70:30)) to yield **4p** (653 mg, 1.88 mmol, 94% yield) as a white solid. *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[46] mp 155–158 °C; IR (neat) 2981, 1762; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 7.95 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.24 (t, *J* = 7.8 Hz, 2H), 6.97 (t, *J* = 7.3 Hz, 1H), 6.69 (d, *J* = 8.1 Hz, 2H), 4.83 (dq, *J* = 9.2, 4.4 Hz, 1H), 4.19 (t, *J* = 9.0 Hz, 1H), 4.08 (dq, *J* = 9.2, 4.4 Hz, 3H), 2.45 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ_C 157.7, 151.3, 145.7, 134.2, 129.9, 129.6, 128.3, 71.5, 67.4, 46.3, 21.7; HRMS (ESI) calcd. for $C_{17}H_{17}NO_5S$ $[M+H]^+$: 348.0861, found: *m/z* 348.0875.

*5-((allyloxy)methyl)-3-phenyloxazolidin-2-one (**4q**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 700:30, R_f 0.10 (80:20)) to yield **4q** (439 mg, 1.88 mmol, 94% yield) as a colorless oil. *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[21b] IR (neat) 3067, 2980, 1749 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.51 (d, *J* = 8.1 Hz, 2H), 7.33 (t, *J* = 7.9 Hz, 2H), 7.09 (t, *J* = 7.4 Hz, 1H), 5.84 (ddt, *J* = 17.2, 10.9, 5.6 Hz, 1H), 5.28 – 5.22 (dd, 17.2, 1.3 Hz, 1H), 5.17 (dd, *J* = 10.9, 1.3 Hz, 1H), 4.72 (dq, *J* = 10.9, 4.7 Hz, 1H), 4.05 – 3.98 (m, 3H), 3.88 (dd, *J* = 8.6, 6.4 Hz, 1H), 3.65 (d, *J* = 4.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 154.7, 138.4, 134.0, 129.1, 124.0, 118.2, 117.8, 72.7, 71.4, 70.1, 47.2; Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00.

Found: C, 67.33; H, 6.24; N, 6.25; HRMS (ESI) calcd. for $C_{13}H_{15}NO_3$ $[M+H]^+$: 234.1085, found: *m/z* 234.1093.

*5-(phenoxymethyl)-3-phenyloxazolidin-2-one (**4r**):* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 60:40, R_f 0.15 (80:20)) to yield **4r** (501 mg, 1.86 mmol, 93% yield) as a white solid. *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] mp 139–140 °C; IR (neat) 3059, 2961, 1735 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.60 (d, *J* = 8.2 Hz, 2H), 7.42 (t, *J* = 7.9 Hz, 2H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 2H), 5.00 (ddt, *J* = 9.1, 6.0, 4.5 Hz, 1H), 4.26 (dd, *J* = 10.0, 4.5 Hz, 1H), 4.23 (dd, 10.0, 6.0 Hz, 1H), 4.21 (t, *J* = 9.1 Hz, 1H), 4.09 (dd, *J* = 9.1, 6.0 Hz, 1H); ^{13}C NMR (75 MHz, CDCl3) δ_C 158.0, 154.4, 138.3, 129.6, 129.1, 124.2, 121.8, 118.3, 114.6, 70.4, 69.0, 47.4; Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.40; H, 5.51; N, 5.20; HRMS (ESI) calcd. for $C_{16}H_{15}NO_3$ $[M+H]^+$: 270.1085, found: *m/z* 270.1097.

*4-chloromethyl-3-phenyl oxazolidinone (**4s**):* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 →700:30, R_f 0.10 (80:20)) to yield **4s** (384 mg, 1.81 mmol, 91% yield) as a white solid. *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[18a] mp 97–100 °C; IR (neat) 3066, 2965, 1739 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 7.53 (d, *J* = 7.9 Hz, 2H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 4.85 (dddd, *J* = 9.1, 6.8, 5.7, 4.0 Hz, 1H), 4.16 (t, *J* = 9.1 Hz, 1H), 3.95 (dd, *J* = 9.1, 5.7 Hz, 1H), 3.78 (dd, *J* = 11.6, 4.0 Hz, 1H), 3.73 (dd, *J* = 11.6, 6.8 Hz, 1H); ^{13}C

NMR (151 MHz, $CDCL_3$) δ_C 153.9, 137.8, 129.2, 124.4, 118.4, 70.8, 48.2, 44.5; Anal. Calcd for $C_{10}H_{10}ClNO_2$: C, 56.75; H, 4.76; N, 6.62. Found: C, 56.52; H, 5.00; N, 6.99; HRMS (ESI) calcd. for $C_{10}H_{10}ClNO_2$ $[M+H]^+$: 213.0371, found: *m/z* 213.0377.

*5-((allyloxy)methyl)-3-(tert-butyl)oxazolidin-2-one (**4t**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 70:30, R_f 0.20 (90:10)) to yield **4t** (192 mg, 0.90 mmol, 45% yield) as a pale yellow oil. IR (neat) 3065, 2979, 1735 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.88 (ddt, *J* = 17.3, 10.3, 5.7 Hz, 1H), 5.29 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.21 (dq, *J* = 10.3, 1.5 Hz, 1H), 4.51 (dddd, *J* = 8.7, 5.2, 4.9, 4.5 Hz, 1H), 4.05 (d, *J* = 5.7 Hz, 2H), 3.65 (t, *J* = 8.7 Hz, 1H), 3.60 (dd, *J* = 10.5, 4.9 Hz, 1H), 3.57 (dd, *J* = 10.5, 5.2 Hz, 2H), 3.47 (dd, 10.5, 4.5 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.5, 134.1, 117.5, 72.6, 70.6, 70.4, 53.4, 45.5, 27.4; Anal. Calcd for $C_{11}H_{19}NO_3$: C, 61.95; H, 8.98; N, 6.57. Found: C, 62.07; H, 9.07; N, 6.78; HRMS (ESI) calcd. for $C_{11}H_{19}NO_3$ $[M+H]^+$: 214.1398, found: *m/z* 214.1406.

*3-(tert-butyl)-5-(phenoxymethyl)oxazolidin-2-one (**4u**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 100:0 →60:40, R_f 0.15 (80:20)) to yield **4u** (225 mg, 0.90 mmol, 45% yield) as a yellow oil. IR (neat) 3063, 2955, 1747 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.31 –7.24 (m, 2H), 6.98 (t, *J* = 7.8 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 2H), 4.65 (ddt, *J* = 10.0, 7.4, 4.8 Hz, 1H), 4.07 (dd, 10.2, 10.0 Hz,1H), 4.05 (dd, *J* = 10.2, 7.4 Hz, 1H), 4.01 (d, *J* = 10.0 Hz, 1H), 3.72 (dd, *J* = 10.0, 4.8 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 158.3, 154.8, 129.6, 121.5, 114.6, 74.3, 69.8, 66.2, 53.5, 45.4, 27.4; Anal.

Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.41; H, 7.70; N, 5.72; HRMS (ESI) calcd. for $C_{14}H_{19}NO_3$ $[M+H]^+$: 250.1398, found: *m/z* 250.1408.

*3-(tert-butyl)-5-(chloromethyl)oxazolidin-2-one (**4v**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 70:30, R_f 0.20 (90:10)) to yield **4v** (184 mg, 0.96 mmol, 48% yield) as a colorless oil. IR (neat) 3061, 2959, 1729 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H 4.51 (dddd, 9.1, 6.8, 5.7, 4.0 Hz, 1H), 3.65 (t, *J* = 9.1 Hz, 1H), 3.55 (dd, *J* = 9.1, 5.7 Hz, 1H), 3.42 (dd, *J* = 11.6, 4.0 Hz, 1H), 3.37 (dd, *J* = 11.6, 6.8 Hz, 1H), 1.25 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 155.8, 70.3, 53.6, 46.1, 44.9, 27.3; Anal. Calcd for $C_8H_{14}ClNO_2$: C, 50.14; H, 7.36; N, 7.31. Found: C, 50.18; H, 7.38; N, 7.47 HRMS (ESI) calcd. for $C_8H_{14}ClNO_2$ $[M+H]^+$: 193.0684, found: *m/z* 193.0692.

*cis-3,4,5-triphenyloxazolidin-2-one (cis-**4w**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale using **1d** (10 mol %) and *n*-TBAI (10 mol %) at 100 °C for 96 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 70:30, R_f 0.10 (90:10)) to yield *cis*-**4w** (194 mg, 0.62 mmol, 31 % yield) as a white solid. *^1H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[34a] mp 223–224 °C; IR (neat) 3055, 2971, 1752; ^1H NMR (600 MHz, $CDCl_3$) δ_H 7.47 (d, *J* = 8.3 Hz, 2H), 7.24 (dd, *J* = 9.7, 6.1 Hz, 2H), 7.11 – 7.08 (m, 3H), 7.65 – 7.25 (m, 4H), 7.01 – 6.97 (m, 2H), 6.90 – 6.85 (m, 2H), 5.97 (d, *J* = 7.9 Hz, 1H), 5.52 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ_C 155.5, 137.5, 134.2, 133.8, 128.9, 128.5, 128.4, 128.2, 128.0, 127.1, 126.3, 124.3, 119.9, 79.8, 65.9, HRMS (ESI) calcd. for $C_{21}H_{17}NO_2$ $[M+H]^+$: 316.1293, found: *m/z* 316.1302; CCDC No. 1958537 for *cis*-**4w** (ox_stilbene_rpt2_0m_5).

*trans-3,4,5-triphenyloxazolidin-2-one (trans-**4w**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale using **1d** (10 mol %) and *n*-TBAI (10 mol %) at 100 °C for 96 h . The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 70:30, R_f 0.15 (90:10)) to yield *trans*-**4w** (242 mg, 0.76 mmol, 38% yield) as a white solid. *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[34a] mp 111−112 °C; IR (neat) 3061, 2951, 1755; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 7.48 – 7.42 (m, 4H), 7.41 – 7.36 (m, 6H), 7.31 – 7.25 (m, 4H), 7.09 (t, *J* = 7.4 Hz, 1H), 5.35 (d, *J* = 6.5 Hz, 1H), 5.22 (d, *J* = 6.5 Hz, 1H), ^{13}C NMR (151 MHz, $CDCl_3$) δ_C 155.5, 137.6, 137.4, 137.0, 129.4, 129.2, 129.1, 128.9, 126.6, 126.1, 125.7, 124.8, 121.1, 82.9, 68.9; HRMS (ESI) calcd. for $C_{21}H_{17}NO_2$ $[M+H]^+$: 316.1293, found: *m/z* 316.1305; CCDC No. 1958536 for *trans*-**4w** (AE_131_RPT_3_0m_a).

*5-((benzyloxy)methyl)-3-phenyloxazolidin-2-one (**4x**).* The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 100:0 →60:40, R_f 0.10 (80:20)) to yield **4x** (516 mg, 1.82 mmol, 91% yield) as a white solid. mp 65−66 °C; IR (neat) 3051, 2919, 1730 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 7.52 (d, *J* = 8.2 Hz, 2H), 7.37 – 7.26 (m, 7H), 7.12 (t, *J* = 7.4 Hz, 1H), 4.76 (dq, *J* = 9.1, 6.4, 4.9 Hz, 1H), 4.59 (ABq, *J* = 12 Hz, $\Delta\upsilon_{AB}$ = 14.2 Hz, 2H, 2H), 4.04 (t, *J* = 9.1 Hz, 1H), 3.91 (dd, *J* = 8.6, 6.4 Hz, 1H), 3.70 (d, *J* = 4.9 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ_C 154.6, 138.3, 137.4, 129.1, 128.6, 128.0, 127.8, 124.0, 118.2, 73.8, 71.3, 70.1, 47.3; HRMS (ESI) calcd. for $C_{17}H_{17}NO_3$ $[M+H]^+$: 284.1242, found: *m/z* 284.1255.

*(S)-5-((benzyloxy)methyl)-3-phenyloxazolidin-2-one (S)-**4x***. The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 100:0 →60:40, R_f 0.10 (80:20)) to yield *(S)*-**4x** (516 mg, 1.82 mmol, 91% yield) as a white solid. The product was determined to be 99% ee by chiral HPLC analysis (Chiralpak IC, 8% EtOH/*n*-hexanes, 0.5 mL/min, t_r (*major*) = 47.0 min, t_r (*minor*) = 50.0 min, 260 nm, 35 °C), $[\alpha]_D^{20}$ +40° (*c* 0.01, CH_2Cl_2).

*(R)-5-((benzyloxy)methyl)-3-phenyloxazolidin-2-one (R)-**4x***. The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 100:0 →60:40, R_f 0.10 (80:20)) to yield *(R)*-**4x** (514 mg, 1.80 mmol, 90% yield) as a white solid. The product was determined to be 99% ee by chiral HPLC analysis (Chiralpak IC, 8% EtOH/*n*-hexanes, 0.5 mL/min, t_r (*minor*) = 47.3 min, t_r (*major*) = 50.5 min, 260 nm, 35 °C, $[\alpha]_D^{20}$ -40° (*c* 0.01, CH_2Cl_2).

*5-(chloromethyl)-3-(m-tolyl)oxazolidin-2-one (**4y**)*. The reaction was carried out according to the general procedure mentioned above on a 2 mmol scale, at 100 °C for 24 h. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 50:50, R_f 0.35 (90:10)) to yield **4y** (429 mg, 1.90 mmol, 95% yield) as a white solid. *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[21b] mp 65-67 °C; IR (neat) 1741, 1610, 1489 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 7.36 (s, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.25 (t, *J* = 7.8 Hz, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 4.81 (dq, *J* = 9.1, 5.8 Hz, 1H), 4.07 (t, *J* = 9.1 Hz, 1H), 3.87 (dd, *J* = 9.1, 5.8 Hz, 1H), 3.76 – 3.69 (m, 2H), 2.36 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ_C 154.1,

139.1, 137.8, 128.9, 125.2, 119.1, 115.6, 71.0, 48.1, 45.0, 21.6; HRMS (ESI) calcd. for $C_{11}H_{12}ClNO_2$ $[M+H]^+$: 227.0527, found: *m/z* 227.0535.

*5-(Hydroxymethyl)-3-(3-methylphenyl)oxazolidin-2-one (**4z**).* The oxazolidinone **4y** was dissolved in DMF (10 mL), and KOAc (981 mg, 10.0 mmol, 5 equiv.) was added to the solution. After stirring the mixture at 90 °C for 24 h, H_2O (5 mL) and Et_2O (10 mL) were added, and then the aqueous layer was extracted with Et_2O (x 2). The organic layers were combined, washed with H_2O and brine, dried over Na_2SO_4 and concentrated. The material was employed for the next step without further purification. The material was dissolved in EtOH (10 mL), and K_2CO_3 (1.381 g, 10.0 mmol) was added to the solution at 0 °C. After stirring the mixture at 0 °C for 4 h, H_2O (60 mL) and EtOAc (10 mL) were added, and then the aqueous layer was extracted with EtOAc (x 2). The organic layers were combined, washed with H_2O and brine, dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (*n*-hexanes : ethyl acetate 100:0 → 50:50, R_f 0.15 (65:35)) to yield **4z** (270 mg, 1.30 mmol, 65% yield) as a white solid. *^{1}H NMR and ^{13}C NMR spectra were in agreement with the previously reported spectrum.*[21] mp 77-79 °C; IR (neat) 3477, 2915, 1730, 1422, 1231 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 7.42 (s, 1H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.30 – 7.25 (m, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 4.78 – 4.72 (ddt, J = 8.8, 4.1, 3.4 Hz, 1H), 4.05 (t, *J* = 8.8 Hz, 1H), 4.01 (dd, *J* = 8.8, 4.1 Hz, 1H), 3.97 (dd, *J* = 12.5, 3.4 Hz, 1H), 3.78 (dd, *J* = 12.5, 4.1 Hz, 1H), 2.80 (br, 1H), 2.38 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ_C 154.7, 139.0, 138.1, 128.9, 125.0, 119.1, 115.4, 72.7, 62.9, 46.6, 21.6.

Supporting Information. Copies of analytical data/spectra for the squaramide **1a-i**, oxazolidinone products **4a-z**, **5a-g**, chiral HPLC traces of racemic and enantiomerically pure oxazolidinones **4x** and original spectra, and crystallographic experimental data for *cis*-**4w** and *trans*-**4w** (CSD deposition numbers: CCDC No. 1958536 for *trans*-**4w** (AE_131_RPT_3_0m_a), CCDC No. 1958537 for *cis*-**4w** (ox_stilbene_rpt2_0m_5). This material is available free of charge via the Internet at

AUTHOR INFORMATION

Corresponding Author

*Email for A. R.: arostami@unizwa.edu.om. Email for A.A. aharrasi@unizwa.edu.om

ORCID

Ali Rostami: 0000-0003-3250-6869

Author Contributions

Manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Funding Sources

Support was provided by Sultanate of Oman Research Council (TRC) (Grant # BFP/RGP/EI/18/021) and the University of Nizwa.

Notes

The authors declare no competing financial interest.

Acknowledgments

Financial support from Sultanate of Oman Research Council (TRC) (Grant # BFP/RGP/EI/18/021) and the University of Nizwa is gratefully acknowledged.

References:

[1] a) D. J. Ager, I. Prakash, D. R. Schaad, *Chem. Rev.* **1996**, *96*, 835–876; b) L. Aurelio, R. T. C. Brownlee, A. B. Hughes, *Chem. Rev.* **2004**, *104*, 5823–5846; c) T. A. Mukhtar, G. D. Wright, *Chem. Rev.* **2005**, *105*, 529–542; d) M. M. Heravi, V. Zadsirjan, B. Farajpour, *RSC Adv.* **2016**, *6*, 30498–30551; e) S. Pulla, C. M. Felton, P. Ramidi, Y. Garita, N. Ali, U. B. Nasini, A. Ghosh, *J. CO_2 Util.* **2013**, *2*, 49–57.

[2] a) M. E. Dyen, D. Swern, *Chem. Rev.* **1967**, *67*, 197–246; b) D. A. Evans, J. Bartroli, T. L. Shih, *J. Am. Chem. Soc.* **1981**, *103*, 2127–2129; c) D. A. Evans, *Aldrichimica Acta* **1982**, *15*, 23–32; d) D. J. Ager, I. Prakash, D. R. Schaad, *Aldrichimica Acta* **1997**, *30*, 3–12.

[3] a) W. R. Roush, R. A. James, *Aust. J. Chem.* **2002**, *55*, 141–146; b) J. A. Birrell, E. N. Jacobsen, *Org. Lett*. **2013**, *15*, 2895–2897; c) V. Laserna, W. Guo, A. W. Kleij, *Adv. Synth. Catal.* **2015**, *357*, 2849–2854; d) P. Bhaket, K. Morris, C. S. Stauffer, A. Datta, *Org. Lett.* **2005**, *7*, 875–876; e) T. Ayad, V. Faugeroux, Y. Génisson, C. André, M. Baltas, L. Gorrichon, *J. Org. Chem.* **2004**, *69*, 8775–8779.

[4] a) S. R. Sandler, F. Berg, G. Kitazawa, *J. Appl. Polym. Sci.* **1965**, *9*, 1944–1996; b) Y. Iwakura, S. Izawa, F. Hayano, *J. Polym. Sci. Part A: Polym. Chem.* **1966**, *4*, 751–760; c) R. R. Dileone, *J. Polym. Sci. Part A: Polym. Chem.* **1970**, *8*, 609–615; d) J. E. Herweh, W. Y. Whitmore, *J. Polym. Sci. Part A: Polym. Chem.* **1970**, *8*, 2759–2773; e) N. Kinjo, S. Numata, T. Koyama, T. Narahara, *J. Appl. Polym. Sci.* **1983**, *28*, 1729–1741; f) M. Azechi, T. Endo, *J. Polym. Sci. Part A: Polym. Chem.* **2014**, *52*, 1755–1760.

[5] a) M. R. Barbachyn, C. W. Ford, *Angew. Chem. Int. Ed.* **2003**, *42*, 2010–2023; b) G. Zappia, P. Menendez, G. Delle Monache, D. Misiti, L. Nevola, B. Botta, *Mini-Rev. Med. Chem.* **2007**, *7*, 389–409; c) N. Pandit, R. K. Singla, B. Shrivastava, *Int. J. Med. Chem.* **2012**, *2012*, 1–24; d) B. Guo, H. Fan, Q. Xin, W. Chu, H. Wang, Y. Huang, X. Chen, Y. Yang, *J. Med. Chem.* **2013**, *56*,

2642–2650; e) U. Trstenjak, J. Ilaš, D. Kikelj, *Eur. J. Med. Chem.* **2013**, *64*, 302–313; f) T. Xue, S. Ding, B. Guo, Y. Zhou, P. Sun, H. Wang, W. Chu, G. Gong, Y. Wang, X. Chen, Y. Yang, *J. Med. Chem.* **2014**, *57*, 7770–7791.

[6] a) W. A. Gregory, D. R. Brittelli, C. L. J. Wang, M. A. Wuonola, R. J. McRipley, D. C. Eustice, V. S. Eberly, A. M. Slee, M. Forbes, P. T. Bartholomew, *J. Med. Chem.* **1989**, *32*, 1673−1681; b) C. H. Park, D. R. Brittelli, C. L. J. Wang, F. D. Marsh, W. A. Gregory, M. A. Wuonola, R. J. McRipley, V. S. Eberly, A. M. Slee, M. Forbes, *J. Med. Chem.* **1992**, *35*, 1156−1165; c) S. C. Mueller, J. Majcher-Peszynska, H. Hickstein, A. Francke, A. Pertschy, M. Schulz, R. Mundkowski, B. Drewelow, *Antimicrob. Agents Chemother.* **2002**, *46*, 1557–1560; d) J. A. Demaray, J. E. Thuener, M. N. Dawson, S. J. Sucheck, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 4868–4871; e) E. J. Brnardic, M. E. Fraley, R. M. Garbaccio, M. E. Layton, J. M. Sanders, C. Culberson, M. A. Jacobson, B. C. Magliaro, P. H. Hutson, J. A. O'Brien, S. L. Huszar, J. M. Uslaner, K. L. Fillgrove, C. Tang, Y. Kuo, S. M. Sur, G. D. Hartman *Bioorg. Med. Chem. Lett.* **2010**, *20*, 3129–3133.

[7] a) F. Moureau, J. Wouters, D. P. Vercauteren, S. Collin, G. Evrard, F. Durant, F. Ducrey, J.-J. Koenig, F.-X. Jarreau, *Eur. J. Med. Chem.* **1994**, *29*, 269−277; b) A. Mai, M. Artico, M. Esposito, G. Sbardella, S. Massa, O. Befani, P. Turini, V. Giovannini, B. Mondovì, *J. Med. Chem.* **2002**, *45*, 1180−1183; c) C. T. Lum, S. M. Stahl, *CNS Spectrums* **2012**, *17*, 107−120.

[8] a) G. Zappia, E. Gacs-Baitz, G. Delle Monache, D. Misiti, L. Nevola, B. Botta, *Curr. Org. Synth.* **2007**, *4*, 81–135; b) G. Bratulescu, *Synthesis* **2007**, 3111–3112; c) N. Alouane, A. Boutier, C. Baron, E. Vrancken, P. Mangeney, *Synthesis* **2006**, 860–864; d) B. B. Lohray, S. Baskaran, B. S. Rao, B. Y. Reddy, I. N. Rao, *Tetrahedron Lett.* **1999**, *40*, 4855–4856; e) B. Gabriele, R. Mancuso, G. Salerno, M. Costa, *J. Org. Chem.* **2003**, *68*, 601–604; f) M. A. Casadei, F. M. Moracci, G. Zappia, A. Inesi, L. Rossi, *J. Org. Chem.* **1997**, *62*, 6754–6759; g) C. J. Dinsmore, S. P. Mercer, *Org. Lett.* **2004**, *6*, 2885–2888.

[9] a) H. W. Pauls, B. Fraser-Reid, *J. Am. Chem. Soc.* **1980**, *102*, 3956–3957; b T. Hayashi, A. Yamamoto, Y. Ito, *Tetrahedron Lett*. **1987**, *28*, 4837–4840; c) M. Hirama, T. Shigemoto, Y. Yamazaki, S. Ito, *J. Am. Chem. Soc.* **1985**, *107*, 1797–1798; d) H. M. L. Davies, M. S. Long, *Angew. Chem. Int. Ed.* **2005**, *44*, 3518–3520; e) D. N. Barman, K. M. Nicholas, *Eur. J. Org. Chem.* **2011**, 908–911; f) T. J. Donohoe, P. D. Johnson, M. Helliwell, M. Keenan, *Chem. Commun.* **2001**, 2078–2079; g) K. C. Nicolaou, Y. Zhong, P. S. Baran, *Angew. Chem. Int. Ed.* **2000**, *39*, 625–628; h) S. K. Alamsetti, A. K. Å. Persson, J.-E. Bäckvall, *Org. Lett.* **2014**, *16*, 1434–1437; i) H. Zhu, P. Chen, G. Liu, *J. Am. Chem. Soc.* **2014**, *136*, 1766–1769.

[10] a) R. Robles-Machín, J. Adrio, J. C. Carretero, *J. Org. Chem.* **2006**, *71*, 5023−5026; b) E. Lee, H. Yeom, J. Hwang, S. Shin, *Eur. J. Org. Chem.* **2007**, 3503−3507; c) K. Sekine, T. Mawatari, T. Yamada, *Synlett* **2015**, *26*, 2447−2450.

[11] a) O. Ihata, Y. Kayaki, T. Ikariya, *Angew. Chem. Int. Ed.* **2004**, *43*, 717−719; b) B. M. Trost, A. R. Sudhakar, *J. Am. Chem. Soc.* **1988**, *110*, 7933−7935; c) Z.-Z. Yang, L.-N. He, S.-Y. Peng, A.-H. Liu, *Green Chem.* **2010**, *12*, 1850−1854; d) G. Bartoli, M. Bosco, A. Carlone, M. Locatelli, P. Melchiorre, L. Sambri, *Org. Lett.* **2005**, *7*, 1983−1985; e) T. Munegumi, I. Azumaya, T. Kato, H. Masu, S. Saito, *Org. Lett.* **2006**, *8*, 379−382.

[12] G. P. Speranza, W. J. Peppel, *J. Org. Chem.* **1958**, *23*, 1922−1924.

[13] a) C. Qian, D. Zhu, *Synlett* **1994**, 129−130; b) H.-Y. Wu, J.-C. Ding, Y.-K. Liu, *J. Indian Chem. Soc.* **2003**, *80*, 36−37; c) M. T. Barros, A. M. F. Phillips, *Tetrahedron: Asymmetry* **2010**, *21*, 2746−2752.

[14] a) L. Aroua, A. Baklouti, *Synth. Commun.* **2007**, *37*, 1935−1942; b) J. E. Herweh, W. J. Kauffman, *Tetrahedron Lett.* **1971**, *12*, 809− 812; c) J. K. Herweh, *J. Heterocycl. Chem.* **1968**, *5*, 687−690; e) J. E. Herweh, T. A. Foglia, D. Swern, *J. Org. Chem.* **1968**, *33*, 4029−4033; f) H. Siegel, H. Wittmann, *Monatsh. Chem.* **1982**, *113*, 1005− 1017.

[15] X. Zhang, W. Chen, C. Zhao, C. Li, X. Wu, W. Z. Chen, *Synth. Commun.* **2010**, *40*, 3654−3659.

[16] a) A. Baba, M. Fujiwara, H. Matsuda *Tetrahedron Lett.* **1986**, *27*, 77−80; b) M. Fujiwara, A. Baba, H. Matsuda, *J. Heterocycl. Chem.* **1988**, *25*, 1351−1357; c) M. Fujiwara, A. Baba, H. Matsuda, *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1069−1073.

[17] a) I. Shibata, A. Baba, H. Iwasaki, H. Matsuda, *J. Org. Chem.* **1986**, *51*, 2177−2184; b) M. Fujiwara, A. Baba, Y. Tomohisa, H. Matsuda, *Chem. Lett.* **1986**, *15*, 1963−1966; c) A. Baba, K. Seki, H. Matsuda, *J. Heterocycl. Chem.* **1990**, *27*, 1925−1930; d) K. Yano, N. Amishiro, A. Baba, H. Matsuda, *Bull. Chem. Soc. Jpn*. **1991**, *64*, 2661−2667.

[18] a) T. Baronsky, C. Beattie, R. W. Harrington, R. Irfan, M. North, J. G. Osende, C. Young, *ACS Catal.* **2013**, *3*, 790−797; b) R. L. Paddock, D. Adhikari, R. L. Lord, M.-H. Baik, S. T. Nguyen, *Chem. Commun.* **2014**, *50*, 15187−15190; c) P. Wang, J. Qin, D. Yuan, Y. Wang, Y. Yao, *ChemCatChem* **2015**, *7*, 1145−1151; d) M. North, J. Mason, X. Wu, *Chem. Eur. J.* **2017**, *23,* 12937−12943; e) B. M. Trost, A. R. Sudhakar, *J. Am. Chem. Soc.* **1987**, *109*, 3792−3794; f) C. Larksarp, H. Alper, *J. Am. Chem. Soc.* **1997**, *119*, 3709−3715; g) C. Beattie, M. North, *RSC Adv.* **2014**, *4*, 31345−31352; h) C. Beattie, M. North, *Chem. Eur. J.* **2014**, *20*, 8182−8188.

[19] a) A. Berkessel, H. Groger, *Asymmetric Organocatalysis From Biomimetic Concepts to Applications in Asymmetric Synthesis 1st ed.,* Wiley-VCH, **2005**; b) P. M. Pihko, *Hydrogen Bonding in Organic Synthesis,* Wiley-VCH, Weinheim, **2000**; c) S. Mukherjee, J. W. Yang, S. Hoffmann, B. List, *Chem. Rev.* **2007**, *107*, 5471–5569; d) J. Alemán, A. Parra, H. Jiang, K. A. Jørgensen, *Chem. Eur. J.* **2011**, *17*, 6890–6899.

[20] a) F. Della Monica, A. Buonerba, A. Grassi, C. Capacchione, S. Milione, *ChemSusChem* **2016**, *9*, 3457–3464; b) S. Gennen, M. Alves, R. Méreau, T. Tassaing, B. Gilbert, C. Detrembleur, C. Jerome, B. Grignard, *ChemSusChem* **2015**, *8*, 1845–1849; c) M. H. Anthofer, M. E. Wilhelm, M. Cokoja, M. Drees, W. A. Herrmann, F. E. Kühn, *ChemCatChem* **2015**, *7*, 94–98; d) L. Wang, G. Zhang, K. Kodama, T. Hirose, *Green Chem.* **2016**, *18*, 1229–1233; e) M. E. Wilhelm, M. H. Anthofer, M. Cokoja, I. I. E. Markovits, W. A. Herrmann, F. E. Kühn, *ChemSusChem* **2014**, *7*, 1357–1360; f) S. Kaneko, S. Shirakawa, *ACS Sustainable Chem. Eng.* **2017**, *5*, 2836–2840; g) J. Sun, W. Cheng, Z. Yang, J. Wang, T. Xu, J. Xin, S. Zhang, *Green Chem.* **2014**, *16*, 3071–3078; h) V. B. Saptal, B. M. Bhanage, *ChemSusChem* **2017**, *10*, 1145–1151; i) H. Buettner, J. Steinbauer, T. Werner, *ChemSusChem* **2015**, *8*, 2655–2669; j) A. M. Hardman-Baldwin, A. E. Mattson, *ChemSusChem* **2014**, *7*, 3275 –3278; k) S. Sopeña, E. Martin, E. C. Escudero-Adán, A. W. Kleij, *ACS Catal.* **2017**, *7*, 3532–3539; l) J. Wang, Y. Zhang, *ACS Catal.* **2016**, *6*, 4871–4876; m) Y. Toda, Y. Komiyama, A. Kikuchi, H. Suga, *ACS Catal.* **2016**, *6*, 6906–6910

[21] a) In general, isocyanates are much more reactive than CO_2, yet their reaction with epoxides generally requires high temperature (80−120 °C), and long reaction time (24h), which could suggest that the ring-closing step controls the rate of the whole process, in which the less acidic N–H proton must be released after the rapid halohydrin formation, see: the Supporting Information and references 20m, 21b, 18a, and 32b ; b) Y. Toda, S. Gomyou, S. Tanaka, Y. Komiyama, A. Kikuchi, H. Suga, *Org. Lett.* **2017**, *19*, 5786−5789.

[22] a) C. J. Whiteoak, A. Nova, F. Maseras, A. W. Kleij, *ChemSusChem*. **2012**, *5*, 2032−2038; b) L. Martínez-Rodríguez, J. O. Garmilla, A. W. Kleij, *ChemSusChem* **2016**, *9*, 749−755.

[23] a) R. I. Storer, C. Aciro, L. H. Jones, *Chem. Soc. Rev.* **2011**, *40*, 2330–2346; b) V. Amendola, G. Bergamaschi, M. Boiocchi, L. Fabbrizzi, M. Milani, *Chem. Eur. J.* **2010**, *16*, 4368–4380; c) N. Busschaert, I. L. Kirby, S. Young, S. J. Coles, P. N. Horton, M. E. Light, P. A. Gale, *Angew. Chemie Int. Ed.* **2012**, *51*, 4426–4430; d) A. Rostami, C. J. Wei, G. Guérin, M. S. Taylor, *Angew. Chemie Int. Ed.* **2011**, *50*, 2059–2062; e) A. Rostami, A. Colin, X. Y. Li, M. G. Chudzinski, A. J. Lough, M. S. Taylor, *J. Org. Chem.* **2010**, *75*, 3983–3992; f) C. Jin, M. Zhang, L. Wu, Y. Guan, Y. Pan, J. Jiang, C. Lin, L. Wang, *Chem. Commun.* **2013**, *49*, 2025–2027.

[24] R. M. Owen, C. B. Carlson, J. Xu, P. Mowery, E. Fasella, L. L. Kiessling, *ChemBioChem* **2007**, *8*, 68–82.

[25] a) A. M. Gilbert, M. M. Antane, T. M. Argentieri, J. A. Butera, G. D. Francisco, C. Freeden,E. G. Gundersen, R. F. Graceffa, D. Herbst, B. H. Hirth, J. R. Lennox, G. McFarlane, N. W. Norton, D. Quagliato, J. H. Sheldon, D. Warga, A. Wojdan, M. Woods, *J. Med. Chem.* **2000**, *43*, 1203–1214; b) J. Valgeirsson, E. Ø. Nielsen, D. Peters, C. Mathiesen, A. S. Kristensen, U. Madsen, *J. Med. Chem.* **2004**, *47*, 6948–6957.

[26] a) J. P. Malerich, K. Hagihara, V. H. Rawal, J. Am. Chem. Soc. 2008, 130, 14416–14417; b) Y. Zhu, J. P. Malerich, V. H. Rawal, Angew. Chemie Int. Ed. 2010, 49, 153–156.

[27] P. Chauhan, S. Mahajan, U. Kaya, D. Hack, D. Enders, *Adv. Synth. Catal*. **2015**, *357*, 253−281.

[28] a) S. Tomàs, M. C. Rotger, J. González, P. M. Deyà, P. Ballester, A. Costa, *Tetrahedron Lett.* **1995**, *36*, 2523–2526; b) D. Quiñonero, A. Frontera, S. Tomàs, G. A. Suñer, J. Morey, A. Costa, P. Ballester, P. M. Deyà, *Theor. Chem. Acc.* **2000**, *104*, 50–66; c) D. Quiñonero, A. Frontera, G. A. Suñer, J. Morey, A. Costa, P. Ballester, P. M. Deyà, *Chem. Phys. Lett.* **2000**, *326*, 247–254; d) D. Quiñonero, R. Prohens, C. Garau, A. Frontera, P. Ballester, A. Costa, P. M. Deyà, *Chem. Phys. Lett.* **2002**, *351*, 115–120; e) S. Tomàs, R. Prohens, M. Vega, C. Rotger, P. M. Deyà, P. Ballester, A. Costa, *J. Org. Chem.* **1996,** *61,* 9394–9401.

[29] a) A. Rostami, M. Mahmoodabadi, A. Hossein Ebrahimi, H. Khosravi, A. Al-Harrasi, *ChemSusChem* **2018**, *11*, 4262–4268; b) A. Rostami, E. Sadeh, S. Ahmadi, *J. Polym. Sci. Part A Polym. Chem.* **2017**, *55*, 2483–2493.

[30] a) H. Büttner, K. Lau, A. Spannenberg, T. Werner, *ChemCatChem* **2015**, *7*, 459–467; b) M. O. Sonnati, S. Amigoni, E. P. T. de Givenchy, T. Darmanin, O. Choulet, F. Guittard, *Green Chem.* **2013**, *15*, 283–306.

[31] a) J. Hine, S. M. Linden, V. M. Kanagasabapathy, *J. Am. Chem. Soc.* **1985**, *107*, 1082–1083; b) C. M. Kleiner, P. R. Schreiner, *Chem. Commun.* **2006**, 4315–4317; c) T. Weil, M. Kotke, C. M. Kleiner, P. R. Schreiner, *Org. Lett.* **2008**, *10*, 1513–1516; d) E. M. Fleming, C. Quigley, I. Rozas, S. J. Connon, *J. Org. Chem.* **2008**, *73*, 948–956.

[32] (a) G.-P. Wu, S.-H. Wei, X.-B. Lu, W.-M. Ren, D. J. Darensbourg, *Macromolecules* **2010**, *43*, 9202–9204; (b) D. Tian, B. Liu, Q. Gan, H. Li, D. J. Darensbourg, *ACS Catal.* **2012**, *2*, 2029−2035

[33] P. J. Dyson, P. G. Jessop, *Catal. Sci. Technol.* **2016**, *6*, 3302–3316.

[34] a) O. Tsuge, K. Oe, T. Ohnishi, *Heterocycles* **1982**, *19,* 1609−1614; b) K. S. K. Murthy, D.

N. Dhar, *J. Heterocycl. Chem.* **1984**, *21*, 1699–1704.

[35] a) C. Beattie, M. North, P. Villuendas, C. Young, *J. Org. Chem.* **2013**, *78*, 419–426; b) J. Qin, P. Wang, Q. Li, Y. Zhang, D. Yuan, Y. Yao, *Chem. Commun.* **2014**, *50*, 10952–10955.

[36] a) Y. Shen, W. Duan, M. Shi, *Eur. J. Org. Chem.* **2004**, *2004*, 3080–3089; b) Y. Shen, W. Duan, M. Shi, *Adv. Synth. Catal.* **2003**, *345*, 337–340; c) J. Huang, M. Shi, *J. Org. Chem.* **2003**, *68*, 6705–6709.

[37] I. Berlin, R. Zimmer, H.-M. Thiede, C. Payan, T. Hergueta, L. Robin, A. J. Puech, *Br. J. Clin. Pharmacol.* **1990**, *30*, 805.

[38] Squaramides display higher acidities than the thiourea counterparts pKa (diarylsquaramide) 58.37 and pKa (diarylthuiourea) 58.50 in DMSO, see: a) X. Ni, X. Li, Z. Wang, J.-P. Cheng, *Org. Lett.* **2014**, *16*, 1786–1789; b) G. Jakab, C. Tancon, Z. Zhang, K. M. Lippert, P. R. Schreiner, *Org. Lett.* **2012**, *14*, 1724–1727.

[39] T. Lu, S. E. Wheeler, *Chem. Eur. J.* **2013**, *19*, 15141–15147.

[40] Due to the weak interaction between epoxide **2a** and squaramide **1d** in DMSO-d_6 (as probed by ^{1}H NMR), we were unable to determine a binding constant for **2a:1d** complex.

[41] X. Hu, P. Wang, W. Liu, Y. Wang, *ChemistrySelect* **2018**, *3*, 6531–6535.

[42] V. Ramalingam, N. Bhagirath, R. S. Muthyala, *J. Org. Chem.* **2007**, *72*, 3976–3979.

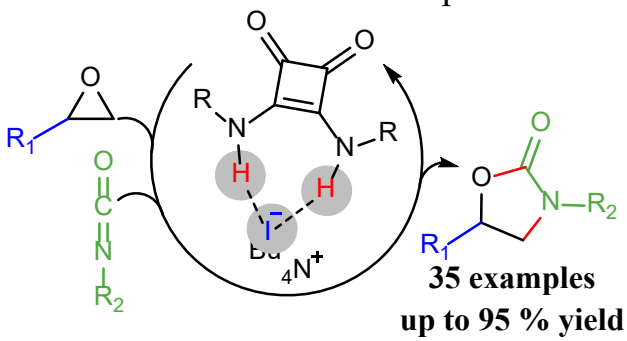
[43] M. Blain, L. Jean-Gerard, R. Auvergne, D. Benazet, S. Caillol, B. Andrioletti, B. *Green Chem.* **2014**, *16*, 4286–4291.

[44] N. Busschaert, S.-H. Park, K.-H. Baek, Y. P. Choi, J. Park, E. N. W. Howe, J. R. Hiscock, L. E. Karagiannidis, I. Marques, V. A. Félix, W. Namkung J. L. Sessler, P. A. Gale, I. Shin *Nat. Chem.* **2017**, 9, 667.

[45] C. G. McPherson, A. K. Cooper, A. Bubliauskas, P. Mulrainey, C. Jamieson, A. J. B. Watson, *Org. Lett.* **2017**, *19*, 6736–6739.

[46] W. J. Kauffman, J. Herweh, *E. J. Org. Chem.* **1972**, *37*, 1842–1845.

Table of Content Graphic



35 examples
up to 95 % yield

a binary organocatalytic system

- atom-economic oxazolidinone synthesis
- simple, cheap and air-stable catalyst
- modular synthesis of squaramide
- strong oxo-anion stabilization
- solvent-free • metal-free
- wide substrate scope
- scalable

It takes two to tango: Squaramide/quaternary ammonium salt as an efficient binary organocatalyst for the atom-economic conversion of a plethora of alkyl- and aryl-substituted epoxides and isocyanates into oxazolidinones is described. A mechanism was proposed wherein the nucleophilic ring-opening operation, and oxo- and carbamate-anions stabilization occur cooperatively towards isocyanate fixation.