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Catalytic transformation of carbon dioxide into seven-membered heterocycles and their domino transformation into bicyclic oxazolidinones

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Converting carbon dioxide (CO_2) into valuable heterocycles is of great synthetic value but is usually limited to five- and six-membered ring compounds. Here, we report a catalytic approach for transforming this carbon renewable into seven-membered heterocycles using a double-stage approach, combining a silver-catalyzed alkyne/CO_2 coupling and a subsequent base-catalyzed ring-expansion. This methodology avoids the formation of thermodynamically more stable, smaller-ring by-products and has good functional group tolerance. The synthetic application of these larger-ring cyclic carbonates is further demonstrated by showing their unique ability to serve as synthons for the preparation of bicyclic oxazolidinone pharmacores through an intramolecular domino sequence that involves a transient ketimine group, and various other intermolecular transformations. The results described herein significantly expand on the use of CO_2 as a cheap and versatile carbon feedstock generating elusive heterocycles and pharmaceutically relevant compounds.

The upgrade of the greenhouse gas carbon dioxide (CO_2) into valuable products represents an attractive objective in the realm of modern sustainable, catalytic, and synthetic chemistry. Most research around the use of CO_2 in catalytic conversions focuses on two related but distinct objectives: improvement of existing processes, or the discovery of transformations that help to further valorize this carbon feedstock using a "bottom-up" approach mostly involving downstream processing[1–7]. The synthesis of heterocyclic compounds known as cyclic carbonates/carbamates has been among the more prevalent activities in this area and widely investigated over the past decade[8–17]. A series of applications for these CO_2-based heterocycles have been developed including their use as non-protic media[18–20], precursors to fine chemicals[21,22], and as polymerizable monomers[23–27]. In addition, functionalized cyclic carbonates can also serve as building blocks in transition metal-catalyzed decarboxylative stereoselective cyclizations, allylic and propargylic chemistry[21,28,29]. While efficient routes towards both five- and six-membered cyclic carbonates (Fig. 1a; 5MCCs and 6MCCs) have been described through highly efficient pathways[6–8,10,11,13,24–27], a major limitation within the area is the easy access to larger ring cyclic carbonates such as 7MCCs. As far as we are aware, there have been only sporadic reports on the preparation of elusive, thermodynamically disfavored seven-membered carbonates albeit via stoichiometric approaches in the context of polymer development[30–33].

Therefore, the development of effective strategies that allow for the straightforward preparation and isolation of such medium-sized heterocycles from CO_2 creates incentives thereby shifting the current limitations in the catalytic conversion of this carbon feedstock. Furthermore, the development of synthetic concepts coupled with the potential to transform larger-ring carbonates into pharmaceutically interesting scaffolds will open up additional avenues for CO_2 valorization. The use of CO_2 toward the preparation of various intermediates having potential as pharma-focused synthons has caught increasing attention over the years[34–43]. In this realm, the preparation of structurally simple oxazolidinones and related compounds using

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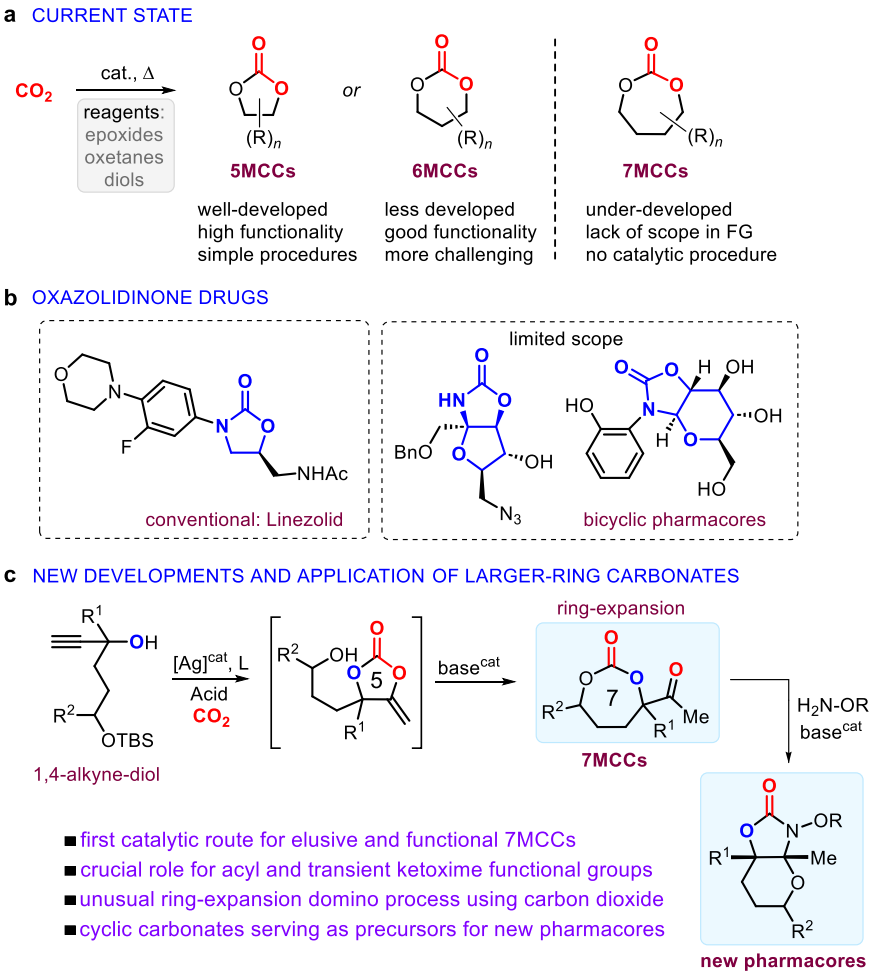

Fig. 1 | State of the art and current challenges. a Current state for the catalytic (cat.) synthesis of five- (5MCCs), six- (6MCCs) and seven-membered cyclic carbonates (7MCCs) from CO_2. **b** Selected bioactive compounds with a single (left) and bicyclic oxazolidinone core (right). **c** Catalytic strategy towards 7MCCs and their application towards bicyclic pharmacores. Cat stands for catalyst.

CO_2 has been reported by various groups, though overall with limited structural scope[12,14,15,17]. More advanced bicyclic scaffolds, as shown in Fig. 1b remain inaccessible by any known method despite their inherent potential as bioactive compounds. Here we present an approach that overcomes these current limitations and represents a catalytic process for a wider series of seven-membered cyclic carbonates from 1,4-alkyne-diols through a successive Ag/base-promoted CO_2 coupling/ring-expansion sequence (Fig. 1c).

The utilization of this stepwise strategy avoids the generation of thermodynamically more stable five- or six-membered byproducts. The seven-membered cyclic carbonates exhibit unique reactivity illustrated in a domino process that propels their structural rearrangement into bicyclic oxazolidinones (Fig. 1c). The latter compounds have biological relevance but their scope remains tremendously limited in diversity. The developed protocol will thus significantly expand the access and use of larger-ring carbonates (and related carbamates) in drug-related research programs.

Results and discussion

Screening and optimization studies

The initial hypothesis for our approach was based on the recent success attained in the preparation of acyl-functionalized five-membered cyclic carbonates prepared via an Ag-promoted cascade sequence[44]. This reported one-pot catalytic approach was only useful to extend the pool of five-membered heterocycles using 1,2-alkyne diols and CO_2 as substrates but was inadequate toward the easy preparation and isolation of six- and seven-membered analogs from 1,3- and 1,4-alkyne diols, respectively. We envisaged that the intermediacy of various reactive species with multiple functional (OH, C≡C) groups[44] would limit our options for a chemo-selective transformation of 1,4-alkyne diols and CO_2 towards seven-membered heterocycles. As an alternative strategy (Table 1), we used an O-protected 1,4-alkyne-diol (**1a**, 1.0 mmol) in the presence of catalytic AgOAc/JohnPhos (both 2 mol%) at 75 °C and 10 bar CO_2 pressure in ACN (CH_3CN) as medium. This first step (STEP 1) afforded typically, when combined with in situ *O*-deprotection under acidic conditions, the free-alcohol, five-membered α-alkylidene carbonate **2a** in > 95% yield (see Supplementary Fig. 1 in the Supporting Information, SI, for details). The conditions in Table 1, however, specifically refer to STEP 2 under base catalysis, giving rise to the target product **3a**, while previously reported **4a** was also identified in some cases as a by-product[44] underlining the intrinsic, thermodynamic challenge of this protocol.

The use of DIPEA as a base catalyst to transform intermediate carbonate **2a** into seven-membered cyclic carbonate **3a** was not very productive (12%). Other bases, such as NMM and DMAP provided somewhat better results (entries 2 and 3; **3a** up to 46%), and increasing the amount of DMAP (entry 4; 20 mol%) resulted in more productive catalysis (**3a**, 57%). The strong *N*-heterocyclic base DBU gave full substrate conversion but with low chemo-selectivity towards **3a** (entry 5, < 10%). When DABCO was used, a significant improvement was noted (entries 6–8), with the highest yield for **3a** obtained when 20 mol% of this base was present (entry 7; **3a** 75%, 73% isolated). Other

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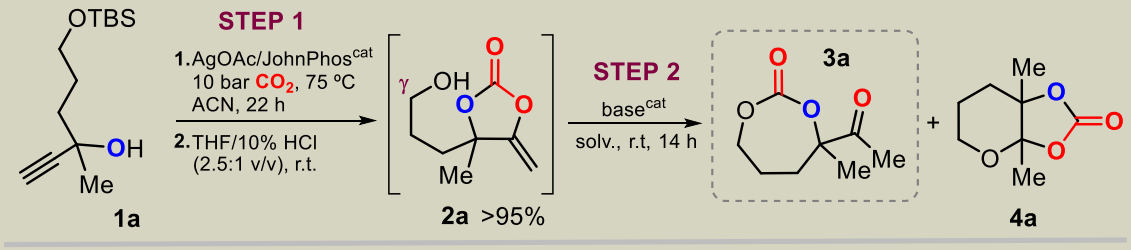
Table 1 | Screening and optimization of the reaction conditions for the conversion of semi-protected 1,4-alkyne diol 1a into targeted seven-membered acyl cyclic carbonate 3a[a]



Entry	Base (mol%)	Solv.	Conv. 1a (%)[b]	3a (%)[b]	4a (%)[b]
1	DIPEA, 10	ACN	29	12	–
2	NMM, 10	ACN	24	20	–
3	DMAP, 10	ACN	51	46	–
4	DAMP, 20	ACN	64	57	–
5	DBU, 10	ACN	> 99	< 10	24
6	DABCO, 10	ACN	65	54	–
7	DABCO, 20	ACN	90	75 (73)[c]	–
8	DABCO, 30	ACN	> 95	56	–
9	TBD, 20	ACN	> 99	[d]	[d]
10	DBN, 20	ACN	> 99	[d]	[d]
11	HQ, 20	ACN	> 95	46	–
12	QUI, 20	ACN	94	70	–
13	DABCO, 20	THF	45	30	–
14	DABCO, 20	DCM	> 95	79 (78)[c]	–
15	DABCO, 20	Tol	90	28	–
16[e]	DABCO, 20	DCM	> 95	56	trace

[a]Reaction conditions for STEP 1: 1.0 mmol 1a, AgOAc (2 mol%), JohnPhos (2 mol%), 75 °C, 10 bar CO_2, ACN; then addition of 3.5 mL of THF/10% HCl (2.5:1 v/v), then isolation of 2a. The conditions for STEP 2 are provided in the Table: catalytic base, solvent, r.t., 14 h using 0.2 mmol of 2a. [b]Determined by ^{1}H NMR ($CDCl_3$) analysis with mesitylene as internal standard. [c]Yield of the isolated product in brackets. [d]Intractable reaction mixtures were attained. [e]Run for 24 instead of 14 h. Note that TBS stands for *tert*-butyl-dimethylsilyl.

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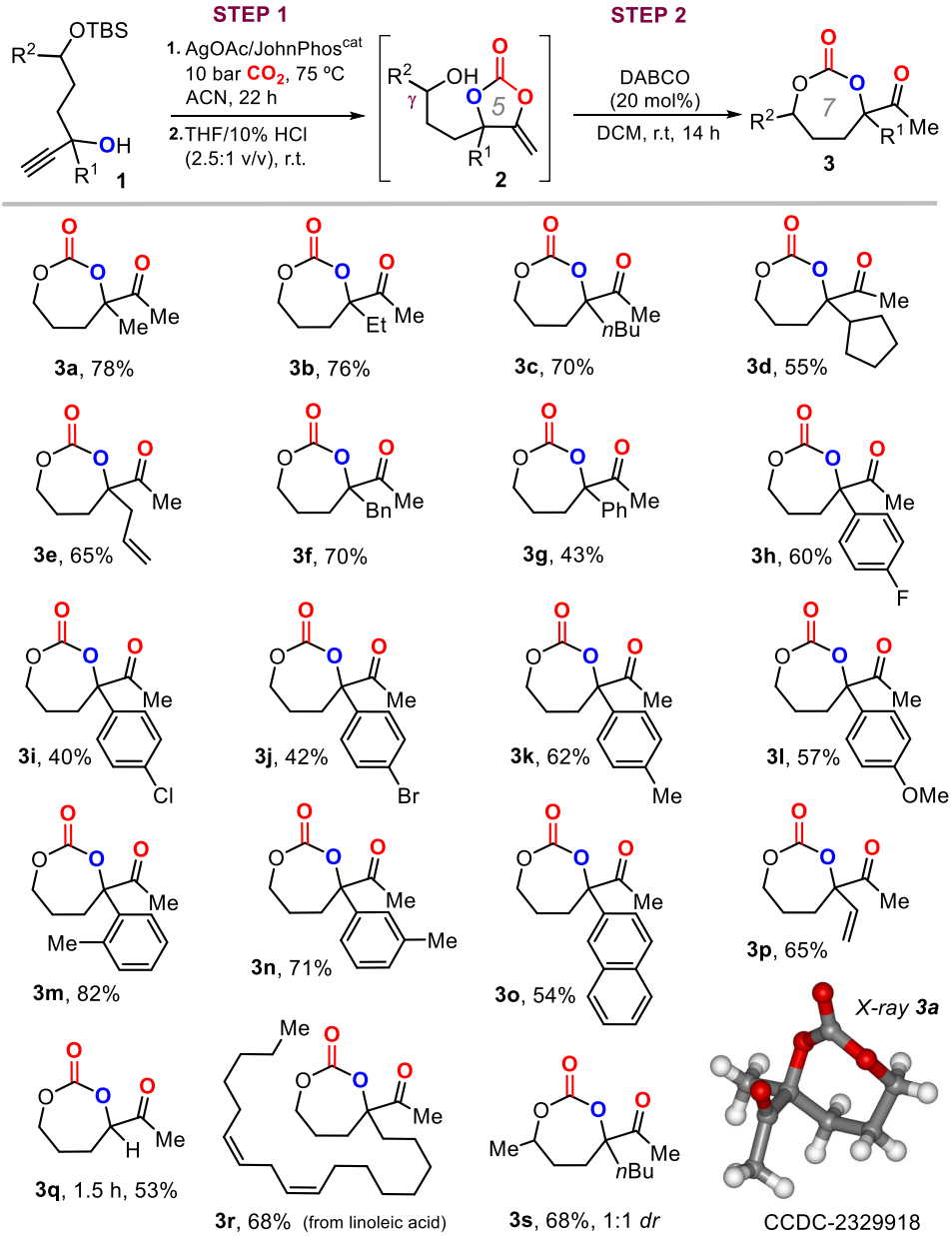

Fig. 2 | Carbonate diversity. Scope of seven-membered acyl-carbonates **3** using various 1,4-alkyne diols **1** and CO_2 as reagents. All products **3** were obtained under the conditions reported in entry 14 of Table 1 using 0.2 mmol of **2**. All reported yields are of the column-purified, isolated products. The yields and analytical data for intermediates **2** are reported in the SI. Cat stands for catalyst.

N-heterocyclic bases including DBN, TBD, hydroquinine (HQ) and quinine (QUI) were all less efficient compared to DABCO (entries 9–12). The solvent effect was then further probed (entries 13–15), showing that the use of DCM (entry 14; **3a** 79%, 78% isolated) was slightly more productive. Notably, prolonging the reaction time of the second step from 14 to 24 h decreased the yield of the desired product to 56% (entry 16), indicating some decomposition of the initially formed seven-membered cyclic carbonate **3a**. When ^{1}H NMR solutions were followed over time, we found indications for the presence of oligomeric species caused by ring-opening polymerization (ROP) of the 7MCC likely initiated by the base in line with previous reports[45,46]. These observations also emphasize the lower thermodynamic stability of **3a** compared to their highly stable, five-membered analogs (i.e., 5MCCs in Fig. 1a).

It should be emphasized that the formation of the thermodynamically more stable bicyclic derivative **4a** (Table 1) and other products could be largely suppressed under the optimized reaction conditions. This shows the value of developing a catalytic procedure towards 7MCC, with the chemoselectivity control being under kinetic (i.e., catalyst) control. As a result, parasitic substrate conversion pathways such as ROP can be minimized or even prevented. The basicity (pK_b) of the catalyst plays a crucial role as shown by previous work on the functionalization of alcohol-derived 6MCC[47]. Finally, efforts to prepare eight-membered analogs of **3a** failed probably due to both thermodynamic and kinetic reasons (see Supplementary Table 1 in the SI).

Scope and further optimization of the developed protocol

Next, we further investigated the scope of the two-step, catalytic transformation of various 1,4-alkyne-diols and CO_2 into acyl-functionalized seven-membered cyclic carbonates (Fig. 2) using the conditions in entry 14 of Table 1 as a starting point. Both the yields of

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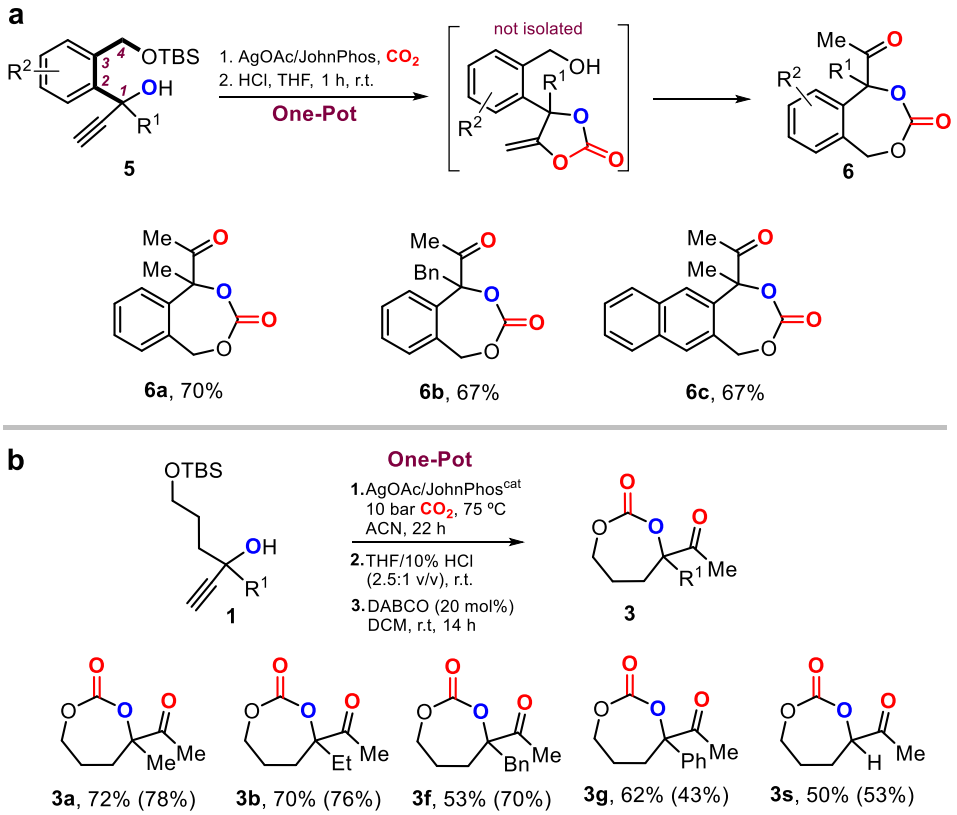

Fig. 3 | One-pot approaches to seven-membered acyl carbonates. a Use of a more rigid substrate design. **b** Using the original but further optimized approximation with the comparative yield for the two-step approach provided in parentheses. Cat stands for catalyst.

the five-membered precursors (compounds **2**; see the SI for details, note a different synthetic approach for precursor **2q**: DavePhos as ligand, 20 bar and at 40 °C) and their seven-membered acyl carbonates (compounds **3**) are provided. Variations in both R^1 and R^2 in the 1,4-alkyne diol **1** were feasible providing both compounds **2** and **3** with a structural diversity, and typically in good to excellent isolated yields. Various linear, branched, cyclic alkyls and functional alkyls (allyl, vinyl), and substituted aryl-substituents (including larger ones such as 2-naphthyl) were tolerated in this protocol. Noteworthy examples include seven-membered acyl carbonates **3p** (65%) with an additional vinyl group and **3r** (68%, derived from linoleic acid), illustrating that more complex/functional scaffolds are also accessible. Overall, appreciable yields of seven-membered acyl carbonates **3** could be attained (most of them in > 60% yield) using the two-step, catalytic approach, which significantly expands the larger-ring cyclic carbonate chemical space compared to the reported examples in the literature[30–33]. Substrates of type **2** with a substituted C=C bond proved to be unproductive towards ring expansion (see the SI for details). The atom-connectivity and identity of the 7MCCs was supported by a combination of diagnostic features, including ^{13}C NMR analysis ($\delta = 152.8$ ppm), IR spectroscopy ($\nu = 1744\ cm^{-1}$), and X-ray diffraction (Fig. 2, inset; **3a** as exemplary case). As far as we know, crystallographically characterized seven-membered cyclic carbonates are unknown.

In order to further address the efficiency of this catalytic approach towards seven-membered cyclic carbonates, we examined whether it would be feasible to design a one-pot catalytic protocol (Fig. 3). In this approximation, we first considered a different and more rigid substrate design (compounds **5**, Fig. 3a) that have both ends of the 1,4-alkyne diol tethered via an aryl fragment at the 2- and 3-position. This alternative substrate design allowed to combine the initial carboxylation of the 1,4-alkyne diol, the subsequent *O*-deprotection, and isomerization steps to take place without the need to isolate the intermediate α-alkylidene carbonate species. Bicyclic seven-membered acyl carbonates **6a**–**6c** were thus directly isolated from the reaction mixtures in good yields up to 70%. Inspired by these encouraging results, we then also attempted a one-pot approximation for selected examples (**3a**, **3b**, **3 f**, **3 g** and **3 s**; see Fig. 3b) of the scope of seven-membered acyl carbonates reported in Fig. 2, and found that also in these cases a fairly similar isolated yield of the target product could be attained. This clearly shows that one-pot catalytic approaches, if properly designed, can further increase the overall process efficiency.

Synthetic explorations and domino conversion of 7MCCs

We then set out to design synthetic applications for cyclic carbonates **3** using the intrinsic acyl functionality as a key enabling fragment (Fig. 4a; full experimental details are provided in the SI) taking **3a** (scaled up to 2.4 mmol: 79%) and **3 g** as exemplary cases. Treatment of **3 g** with $NaBH_4$ afforded five-membered cyclic carbonate **7** in 85% yield. This result may seem unexpected, but the reduction of the acyl fragment would initially result in secondary alcohol, which can then induce a Payne-type isomerization based on backbiting at the seven-membered ring and causing a thermodynamically driven isomerization[13,48].

Bicyclic (5 + 6) cyclic carbonate **8** was formed in 23% yield in the presence of catalytic DBU (see Supplementary Fig. 298 in the SI for a mechanistic proposal), but we found that under Cu-catalysis, the yield could be significantly improved to 80%. Such a bicyclic, partially strained carbonate[49,50] is potentially useful in the context of ring-opening polymerization providing polycarbonate architectures[24–27].

We further examined the use of hydroxyl-amine reagents as a means to transform the acyl into a ketimine fragment, and treatment of **3a** with either the HCl salt of H_2NO-allyl or H_2N-OBn smoothly provided the ketimine based seven-membered cyclic carbonates **9** (79%) and **10** (71%) in good yields. Contrary to what is observed in these

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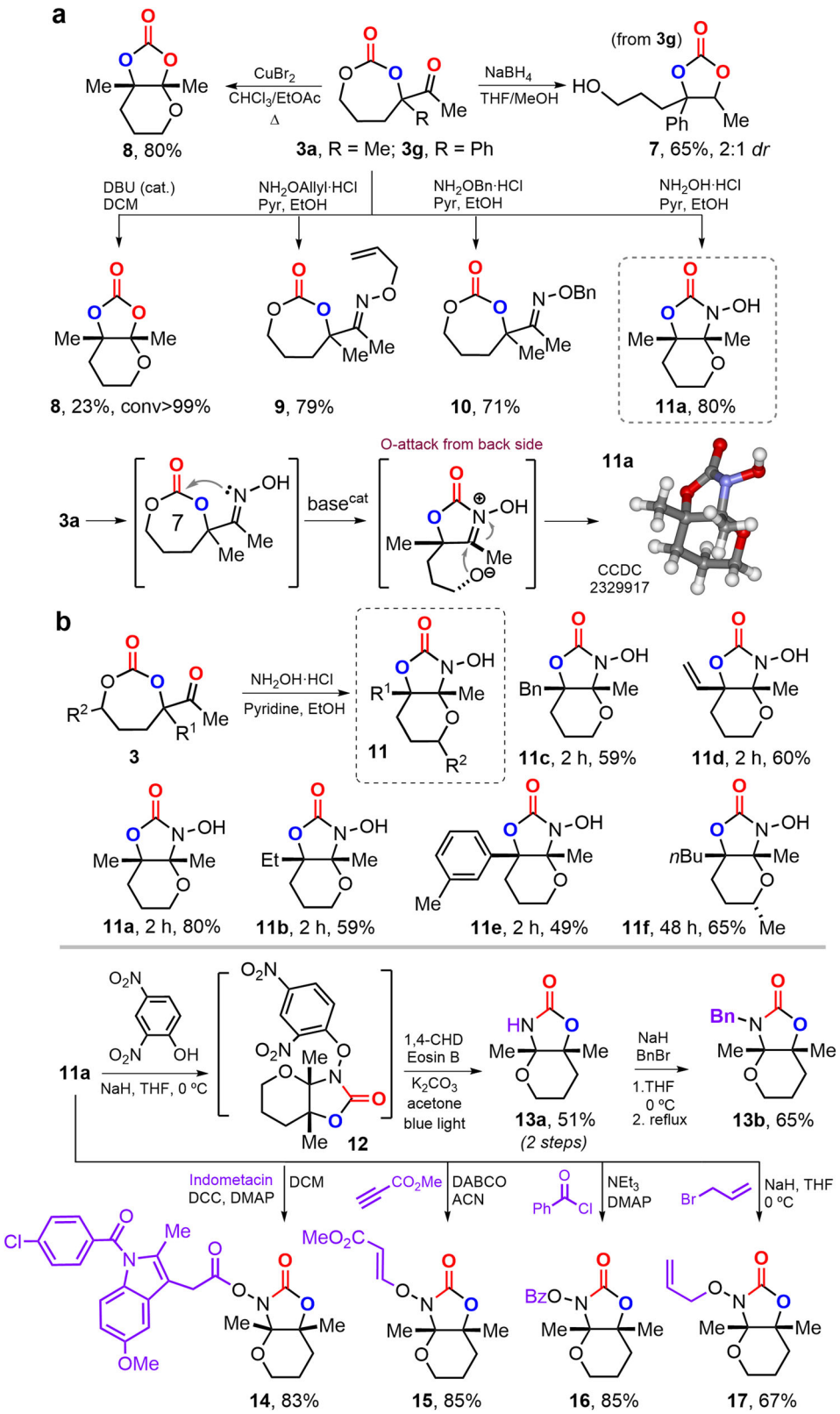

Fig. 4 | Product diversification and synthetic applications. a Transformations of seven-membered cyclic carbonate **3a** and **3 g**. **b** Various strategies to access functional bicyclic oxazolidinones. Cat stands for catalyst.

latter two cases, when **3a** is treated with the unprotected reagent NH_2-OH·HCl, bicyclic oxazolidinone **11** was produced in 80% yield. The envisioned mechanism through which **11** is generated involves the formation of the ketimine group that subsequently acts as an intramolecular nucleophile triggering a domino sequence involving carbonate ring-opening and an *oxa*-Mannich type addition to forge a bicyclic carbamate as presented in Fig. 4a.

Given the success of the formation of **11a**, we then evaluated a wider synthetic scope of such structures by variation of the starting seven-membered acyl carbonate (**3**) and assessing the potential of

transformations at other sites in the scaffold to maximize diversity (Fig. 4b). First, we expanded the hydroxylamine-initiated domino cascade using different seven-membered acyl carbonates **3** allowing to prepare **11a-f** in consistent yields of up to 80% (Fig. 4b, top). Both aryl and (functional) alkyl groups are tolerated in this domino sequence with vinyl-based **11 d** providing a synthetic handle to further structurally modify the backbone. Compound **11 f** (65%, relative stereochemistry determined by GOESY NMR, see the SI) required a longer reaction time (48 h) due to an increased steric impediment in the ring closure leading to the pyran ring. Then, we turned to a different strategy (Fig. 4b, lower part) focusing on the modification of the pendent N-OH fragment in **11a**. Protection of the latter with 3,5-dinitrophenol in the presence of NaH produced carbamate ether **12** (*not isolated*) followed by a photochemically based reduction of **12** promoted by Eosin B giving the *N*-unprotected bicyclic oxazolidinone **13a** in an overall yield of 51%, which could be subsequently alkylated using BnBr/NaH (**13b**, 65%). Conjugation of **11a** with Indometacin (a non-steroidal anti-inflammatory drug) proceeds smoothly under standard esterification conditions using DCC/DMAP and furnished **14** in 83%. Formal etherification is also feasible, and a Michael addition of the N-OH bond to a propargylic ester produced **15** in 85% yield. Compounds **16** (85%) and **17** (67%) were obtained using slightly different etherification procedures, but exemplify that *N*-functionalization/substitution in the bicyclic oxazolidinones is fairly simple.

We then sought to expand the synthetic potential of the formal domino synthesis of the seven-membered heterocycles and designed the corresponding alkyne-1,4-aminoalcohols **18** (Fig. 5a). Using a similar one-pot, catalytic approach as developed for the 7MCCs (Fig. 3b), an easy entry towards the preparation of seven-membered carbamates **20** via intermediate five-membered cyclic carbonates **19** was achieved. Compounds **20a-g** were typically isolated in > 70% yield (except for **20 d**: 47%) with various substituents on the heterocyclic ring. In addition, attempts were made to extend this protocol to the synthesis of eight-membered cyclic carbamates (**20h-j**), however, in these cases, only low product yields were attained, marking currently a limitation for the developed protocol. Nonetheless, the combined results point out that other types of products can also be attained by changing the nature of the heteroatoms in the substrates. In order to take advantage of the free –NH group in bicyclic oxazolidinone **13a** (Fig. 5b), it was treated with an acyl chloride after activating it by *n*-BuLi delivering compound **21** (61%), which is a close mimic to oxazolidinone OSL07, a known bioactive modulator[51,52]. Thus, with the present work, bicyclic analogs of OSL07 are now accessible providing potential to study their bioactivity and pharmaceutical value.

As opposed to the intramolecular chemistry that is involved in the formation of bicyclic oxazolidinones **11** (Fig. 4a), we carried out ring-opening reactions between 7MCC **9** and various nucleophiles (see Fig. 5c)[53]. We first focused on the synthesis of nonsymmetrical linear carbonate **22** (47%), which could be prepared from **9** and BnOH using TBD as a catalyst under mild reaction conditions. Replacing BnOH for its sulfur analog (BnSH) under comparable conditions provided smooth access to thiocarbonate **23** in 66% yield. Amine nucleophiles such as morpholine also are effective reagents for the ring-opening of **9** giving easy access to **24** (78%) that was isolated as a mixture of regioisomers (*rr* = 2:1)[53]. As the final endeavor, vinyl-substituted seven-membered cyclic carbonate **3p** was subjected to Pd-catalyzed decarboxylative amination[21], resulting in the formation of α-β-unsaturated ketone **25** (58%) as a single stereoisomer (*E*). The vinyl group in **3p** could also be used in a formal radical-promoted, decarboxylative difunctionalization process using a TMS-based carbazole as a radical precursor furnishing dicarbazole-substituted **26** (30%)[54].

Mechanistic considerations

Finally, we carried out some control experiments (Fig. 6) that demonstrate several features and the unique reactivity of the seven-membered acyl carbonates compared to their five/six-membered analogs. When a 1,3- instead of a 1,4-alkyne diol (Fig. 5a, **27**) was used as a substrate in a one-pot approach similar to the one presented in Fig. 3b, we observed the near quantitative formation of intermediate **29**. Raising the temperature to 50 °C induced product formation, and in this case, the target and known six-membered acyl carbonate **30**[44] could be produced. It contained about 16% of its precursor **29**, which could not be separated. Nonetheless, this outcome suggests that one-pot approaches to other types of acyl-carbonates are feasible. The thermal stability of **3a** was tested at 70 °C (Fig. 5b), showing that after 18 h most of the initial material was still intact. Next, silyl-protected **2a´** was subjected to typical desilyation conditions (Fig. 5c, TBAF) to produce the free-alcohol species and to initiate isomerization. This afforded bicyclic carbonate **8** in 47% yield and established that a completely different chemo-selectivity is attained under these conditions. When ketimine-based, seven-membered carbonate **9** was thermally activated (Fig. 5d) to see if it would isomerize at elevated temperature, we observed a low conversion but no desired bicyclic oxazolidinone **17** was formed. At this stage, the more sterically demanding character of the ketimine fragment is likely responsible for this. A larger ketimine fragment reduces the conformational potential of this heterocycle for productive isomerization akin to what is observed in the synthesis of compounds **11**. Finally, we attempted to use six-membered cyclic carbonate **30** (Fig. 5e) as a starting point for the envisioned synthesis of a (5 + 5) bicyclic oxazolidinone, but in this case, we could only observe (by ^{1}H NMR) the in situ formation of ketimine-derived **31**, which proved to be unstable under these conditions. This is an important observation and suggests that only the seven-membered acyl carbonates of type **3** possess sufficient reactivity enabling the formation of the bicyclic oxazolidinone pharmacores of type **11**.

In summary, we report here a catalytic protocol for the formation of thermodynamically disfavored acyl-functionalized seven-membered cyclic carbonates (note the exemplary formation of thermodynamically stable five-membered carbonate **7** from seven-membered **3 g** in Fig. 4a as support for this notion) that can be achieved either via a two-step or one-pot sequence using 1,4-alkyne diols and CO_2 as precursors. This work significantly expands the portfolio of larger-ring heterocycles that can be derived from CO_2 and offers a versatile entry towards under-represented bicyclic oxazolidinone pharmacores. Control experiments demonstrate the unique reactivity of the seven- versus five/six-membered cyclic carbonates in the latter context, making them thus privileged synthons for the developed domino process that involves the intermediacy of hydroxyl-ketimine functional groups. We believe that the cascade process with properly designed substrates having built-in pro nucleophilic sites[55] holds great future promise for the creation of complex synthons derived from carbon dioxide as feedstock.

Methods

Experimental procedure for the one-pot synthesis of carbonates 3 from substrates 1

In a typical experiment, 0.2 mmol of propargyl alcohol **1**, AgOAc (0.7 mg, 2 mol%), JohnPhos (1.2 mg, 2 mol%), and ACN (0.4 mL) were added in a stainless steel reactor. The reactor was purged twice with CO_2 (10 bar) and then charged with CO_2 (10 bar). The mixture was stirred at 75 °C for 22 h, then cooled with an ice/water bath and carefully depressurized. The solvent was removed in vacuo, and the residue was dissolved in 1 mL of THF/10% HCl (THF:10% HCl = 5:2 v/v). The mixture was stirred at room temperature (r.t.) for 0.5 h then diluted with water and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and dissolved in 0.4 mL of DCM, then DABCO (4.5 mg, 0.04 mmol, 0.2 equiv) was added. After stirring at r.t. for 14 h (note that for **2r**, the reaction time was 1.5 h; extending the reaction time will cause the product to decompose), the mixture was transferred to a

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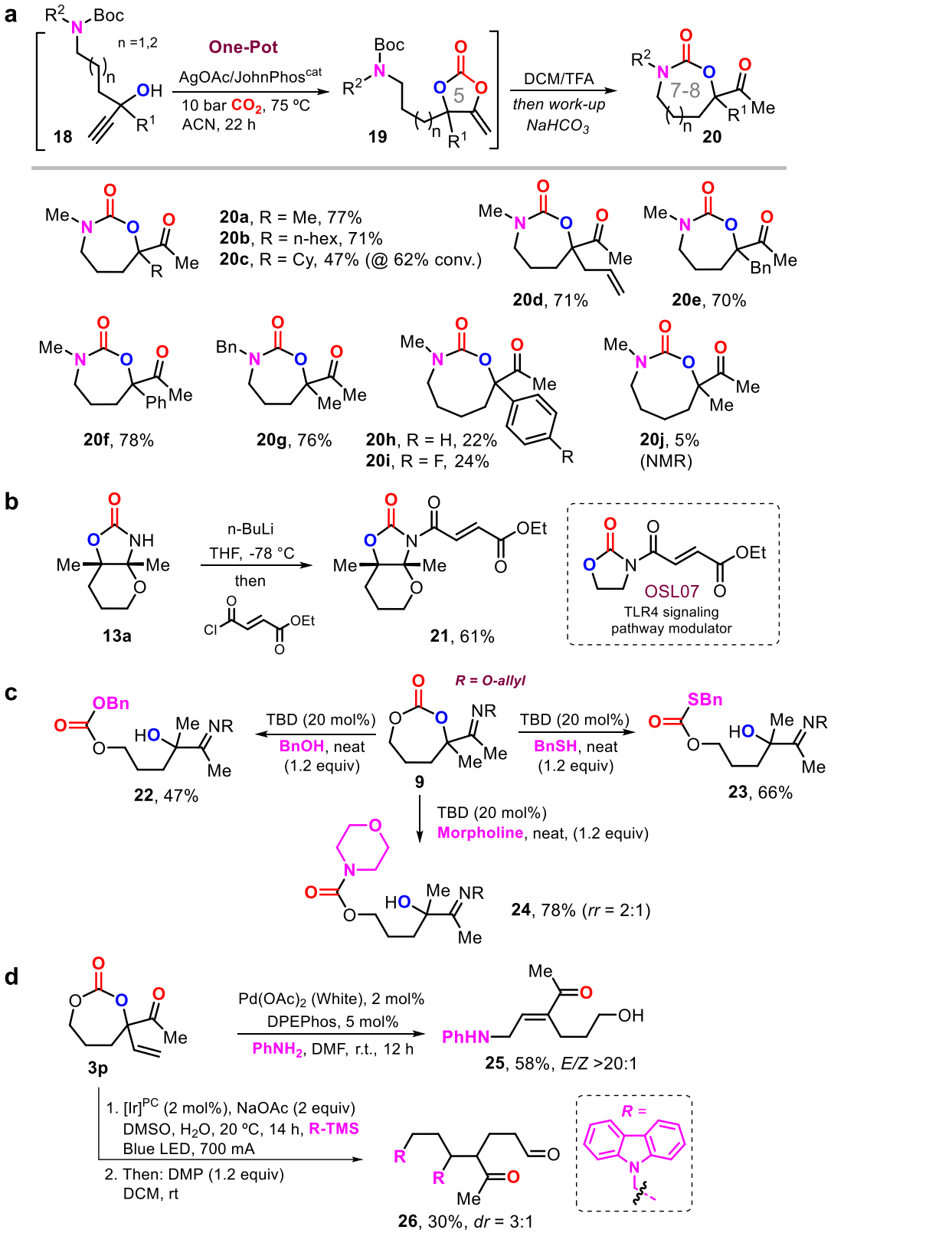

Fig. 5 | Extending the protocol to other heterocycles and further uses. a Formation of 7-membered carbamates. **b** Preparation of a structural mimic of the bioactive compound OSL07. **c** Intermolecular ring-opening of **9**. **d** Derivatization of vinyl-substituted **3p**. Cat stands for catalyst.

round-bottom flask, concentrated, and purified by flash column chromatography with ethyl acetate/hexane as eluent. Note: For **1r**, AgOAc (0.7 mg, 2 mol%) and DavePhos (1.6 mg, 2 mol%) were used under 20 bar of CO_2. The mixture was stirred at 40 °C for 24 h. Full details are provided in the SI.

Experimental procedure for the synthesis of oxazolidinones 11 from carbonates 3

To a stirred solution of hydroxylamine hydrochloride (13.9 mg, 0.2 mmol, 2 equiv), pyridine (15.8 mg, 0.2 mmol, 2 equiv) in ethanol (2 mL) at r.t. was added carbonate **3** (0.1 mmol, 1 equiv).

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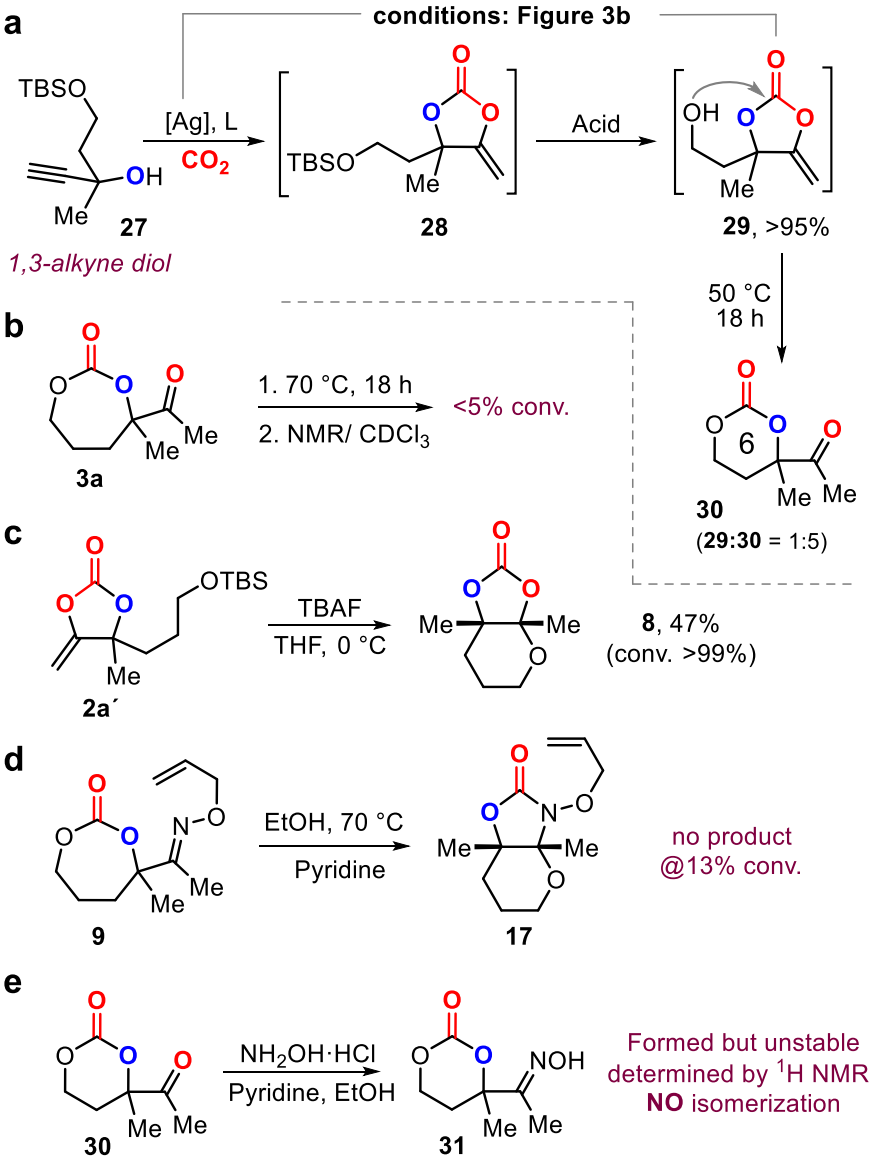

Fig. 6 | Control experiments. a Use of 1,3-alkyne diols furnishing 6 M acyl carbonate **30**. **b** Thermal stability check on seven-membered carbonate **3a**. **c** Utilization of a different O-protecting group in the 5MCC precursor. **d** Attempted thermal activation of the pendant ketimine to force the domino synthesis of **17**. **e** Attempted synthesis of a (5 + 5) bicyclic oxazolidinone from **31**.

After the substrate was completely consumed (determined by TLC), the solvent was removed under reduced pressure. To the residue was added water and the product was extracted twice with methylene chloride (20 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography employing ethyl acetate/hexane as a gradient eluent to obtain the pure product. Full details are provided in the SI.

Data availability

The authors declare that the data to support the findings of this study are available within the paper and its Supplementary Information. Data supporting the findings of this manuscript are also available from the corresponding author upon request

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Author contributions

A.W.K. managed and directed the overall project and supervised the experimental work; W.S. discovered the protocol leading to the target 7MCC and derived products, and performed all the experimental work; J.B.-B. performed the crystallographic studies with input from both A.W.K. and W.S. All authors analyzed the data together, discussed the results, and wrote and commented on the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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