How to cite: *Angew. Chem. Int. Ed.* **2023,** *62,* e202215856
International Edition: doi.org/10.1002/anie.202215856
German Edition: doi.org/10.1002/ange.202215856

Cycloaddition

Photochemical Decarbonylation of Oxetanone and Azetidinone: Spectroscopy, Computational Models, and Synthetic Applications**

*Manvendra Singh, Pawan Dhote, Daniel R. Johnson, Samuel Figueroa-Lazú, Christopher G. Elles, and Zarko Boskovic**

Abstract: Photoexcitation of cyclic ketones leads to the expulsion of carbon monoxide and a mixture of products derived from diradical intermediates. Here we show that synthetic utility of this process is improved if strained heterocyclic ketones are used. Photochemistry of 3-oxetanone and *N*-Boc-3-azetidinone has not been previously described. Decarbonylation of these 4-membered rings proceeds through a step-wise Norrish type I cleavage of the C–C bond from the singlet excited state. Ylides derived from both compounds are high-energy species that are kinetically stable long enough to undergo [3+2] cycloaddition with a variety of alkenes and produce substituted tetrahydrofurans and pyrrolidines. The reaction has a sufficiently wide scope to produce scaffolds that were either previously inaccessible or difficult to synthesize, thereby providing experimental access to new chemical space.

Introduction

Rich chemistry of 1,3-dipoles such as carbonyl ylides (CY) and azomethine ylides (AMY) rests on reliable methods by which these reactive intermediates can be obtained (Figure 1). In 1976 the Griffin and Joullié groups demonstrated that tetraphenyl-substituted CY can be formed under photochemical conditions from tetraphenyl 3-oxetanone [Figure 1, Eq. (1)]; this method has apparently not been applied synthetically.[1,2] The most versatile method for CY generation—the Padwa approach—is based on the transition metal-catalyzed (often rhodium) decomposition of diazo compounds in the presence of ketones; the reaction of an electrophilic carbene and a basic carbonyl reliably gives rise to CY in a variety of structural contexts [Figure 1, Eq. (2)].[3] Beeler in 2017 designed a pyrylium-based photo-catalyst that promoted formation of CY from certain epoxides (mostly stilbene oxides) with visible light [Figure 1, Eq. (3)].[4] Pioneer of [3+2] cycloadditions, Rolf Huisgen, was the first to achieve thermal and photochemical, heterolytic cleavage of aziridine C–C bond to form AMYs [Figure 1, Eq. (4)].[5,6] They are now most commonly prepared through a condensation reaction between aldehydes

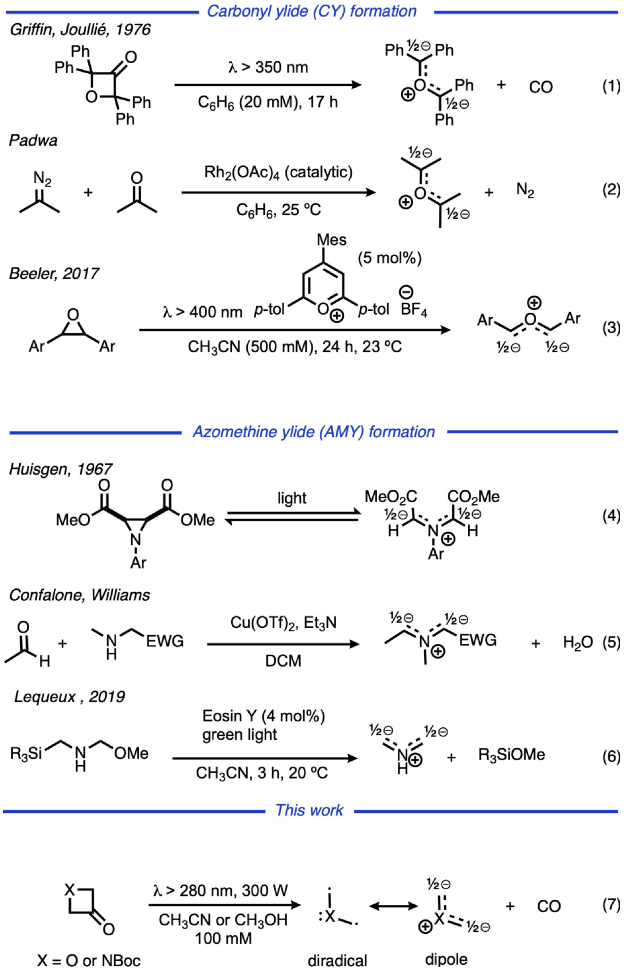

Figure 1. Main strategies to access carbonyl ylides [Eq. (1)–(3)] and azomethine ylides [Eq. (4)–(6)]. We describe a synthetically useful new way of making these valuable intermediates through a photochemical decarbonylation of strained 4-membered rings [Eq. (7)].

[*] M. Singh, P. Dhote, Z. Boskovic
Department of Medicinal Chemistry,
University of Kansas
Lawrence, 66045 KS (USA)
E-mail: zarko@ku.edu
D. R. Johnson, C. G. Elles
Department of Chemistry,
University of Kansas
Lawrence, 66045 KS (USA)
S. Figueroa-Lazú
Independent researcher
Lawrence, 66044 KS (USA)

[**] A previous version of this manuscript has been deposited on a preprint server (https://doi.org/10.26434/chemrxiv-2022-06c0l).

and secondary amines that contain acidic protons on the α-carbon [Figure 1, Eq. (5)].[7–9] Non-stabilized AMY has recently been made from N,O-acetals containing α-silyl groups by using sub-stoichiometric amounts of a Eosin Y dye and green light-emitting diodes [Figure 1, Eq. (6)].[10]

3-Oxetanone[11] and other 4-membered heterocycles have been promoted by Carreira and others from early 2000s as building blocks that may impart desirable properties to potentially biologically active compounds.[12] They have since become readily commercially available and relatively inexpensive. Surprisingly, chemists have neither attempted to form CY from 3-oxetanone, or AMY from 3-azetidinone photochemically, nor to investigate their synthetic potential to form substituted tetrahydrofurans and pyrrolidines through a [3+2] cycloaddition with olefins.

Our goal has been to combine opening of small, strained ketones with the photochemical electronic excitation and to access simplest, non-stabilized 1,3-dipoles in a straightforward manner, without the need to use additional metal catalysts, ligands, photosensitizers, or auxiliary additives. In the following material, we will discuss 1) the physical organic chemistry aspects of generating CY and AMY from such strained cyclic ketones, and 2) the broad scope of reactions in which they can be used efficiently to generate novel or previously difficult-to-access products.

Results and Discussion

The strategy we describe here is based on structural insights obtained from electronic and vibrational spectra, and computational simulations. Like other ketones, UV-vis absorption spectra of 3-oxetanone (3-OX), *N*-Boc-3-azetidinone (3-AZ), and cyclobutanone (CB) show a weak absorption centered around 280 nm (Figure 2A) with extinction coefficients between 10 and 20 $M^{-1}cm^{-1}$. This band corresponds to the symmetry-forbidden transition of non-bonding carbonyl oxygen p_x electron to the antibonding π* orbital of the carbonyl (Figure 3). Stronger bands ($\varepsilon = 300$ to 400 $M^{-1}cm^{-1}$) at $\lambda_{max} = 222$ nm (3-AZ), and $\lambda_{max} = 210$ nm (3-OX), are due to n-π* allowed charge transfer from the suitably positioned p_y orbital of the ring heteroatom into the π* orbital of the carbonyl, reminiscent of π-π* transfer in, β,γ-unsaturated ketones.[13] That this band may indeed be due to this allowed n-π* transition is further supported by the absorption spectrum of 3-thietanone. Its λ_{max} (250 nm) is at a significantly longer wavelength compared to 3-oxetanone ($\lambda_{max} = 210$ nm), indicating a higher energy HOMO (cf. ionization potential of sulfur at 10.4 eV versus that of oxygen at 13.6 eV) and thus smaller energy gap between non-bonding and π* orbitals.[14] We also detected a small blue shift of these bands on switching from non-hydrogen bonding solvents to methanol, in accordance with the ground state stabilization in hydrogen bonding solvents.

We anticipated that the excitation of the 220 nm-band would lead to chemistry other than decarbonylation, or that it would slow down the desired reaction, so we prevented this excitation by using a filter. Exposing solutions of 3-OX, 3-AZ, and CB in acetonitrile to ultraviolet light filtered to block wavelengths shorter than 280 nm led to a steady release of carbon monoxide that could be detected within

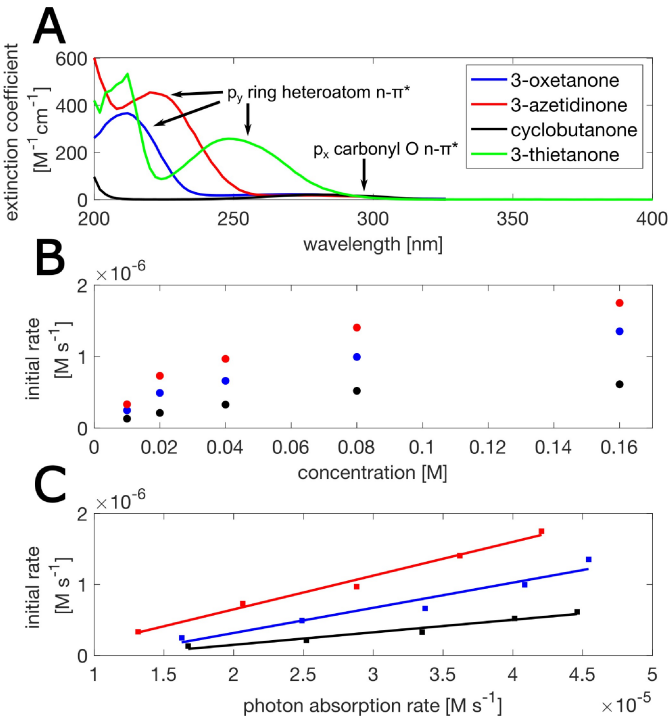

Figure 2. Taking synthetic advantage of n-π* absorption of strained rings. A) UV-vis absorption spectra of 3-OX (blue), 3-AZ (red), CB (black), and 3-thietanone (green). The bands corresponding to symmetry-forbidden and symmetry-allowed n-π* absorptions are indicated with arrows. B) Irradiating solutions of these strained heterocyclic ketones with $\lambda > 280$ nm light leads to CO formation. Initial rate of the reaction is shown as a function of the concentration of the reactants. C) Calculating the rate of absorption of photons from substrate extinction coefficients, lamp irradiance, filter properties, and reactor irradiated area leads to a linear dependence of initial rate of the reaction and the rate of photon absorption. The slopes of straight lines give quantum yields: 0.47 for 3-AZ, 0.35 for 3-OX, and 0.18 for CB.

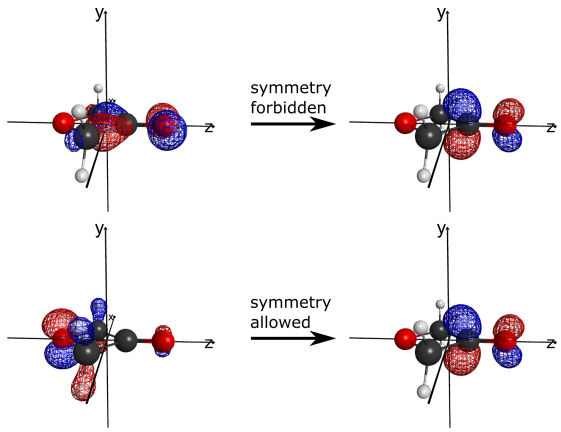

Figure 3. Symmetry-forbidden excitation of an electron from the non-bonding p_x orbital into the antibonding π* is reflected in a weak ε in the absorption spectrum, whereas symmetry-allowed excitation of the p_y orbital corresponds to a stronger band in UV-vis absorption spectra.

minutes (depending on substrate concentration) in the headspace of the reactor with a commercial electrochemical CO-specific monitor (Supporting Information, section 3.4). Knowing the volume of the headspace, we computed the initial rates of this cheletropic CO extrusion process at five different concentrations of strained rings (Figure 2B). We observed the fastest rate of CO release with 3-AZ, followed by 3-OX, and CB. Saturation kinetics (slowing of the initial rates with increasing substrate concentration) can be expected for photochemical processes when absorption of light by the substrate starts to compete with the photochemical reaction, i.e. the photons become limiting "reagent." By estimating the rate of photon absorption, we were able to arrive at linear dependence of photon absorption rate and the initial rates of three substrates (Figure 2C). The quantum yields derived from the dependence of initial rate of the reaction on the rate of photon absorption are 0.47 for 3-AZ, 0.35 for 3-OX, and 0.18 for CB. Irradiating solution of 3-thietanone leads to a very slow CO formation (10 mM solution takes about 50 min to reach 1000 ppm of CO in reactor headspace, whereas 3-AZ at the same concentration takes about 10 min) and ultimately different photochemical products entirely (see Figure 7B below).

Ring strain of these 4-atom cyclic ketones is reflected in the vibration frequencies of their carbonyls.[15] The carbonyl stretching frequency of CB is 1774 cm^{-1} (compared to 1747 cm^{-1} for cyclopentanone, and 1717 cm^{-1} for cyclohexanone), whereas for 3-OX and 3-AZ carbonyls the values are 1816 cm^{-1} and 1818 cm^{-1}. These values track with the observed rates of decarbonylation (Figure 2B).

The importance of the ring heteroatom for the CO release is also evidenced by a slower CO formation in the case of CB. The propyl diradical formed through the Norrish type I mechanism (Figure 4C) would not benefit from the dipole stabilization that the heteroatom provides.[16] Highlighting the unique ability of photons to enable access to high-energy states through electronic activation, no CO was detected when 3-OX or 3-AZ were "vibrationally activated" by heating them up to 110 °C in refluxing toluene (Supporting Information, section 3.2) as predicted through computational analysis (Figure 4).

Sophisticated computational models of relatively simple structures such as 3-OX, 3-AZ and CB can, at the present level of computational development, be remarkably accurate. These models provide quantitative insights into the reactivity of these molecules. We modeled the relevant geometries of 3-OX, 3-AZ, and CB by using B3LYP/6-311+G(2d,p) DFT for the ground states and B3LYP/6-311+G(2d,p) TD-DFT for the excited states of these molecules (Figure 4). We found that in each case the preferred pathway involves the absorption of the photon to populate the excited state around 100 kcal mol^{-1} higher than the ground state. This is in good agreement with the energy of the photon of light with a 280 nm wavelength (102.1 kcal mol^{-1}). This Franck–Condon state relaxes to a minimum on the excited state potential energy surface. This is the singlet excited state. Its geometry is typical of ketones undergoing π*←n transition, the result of which is a bending

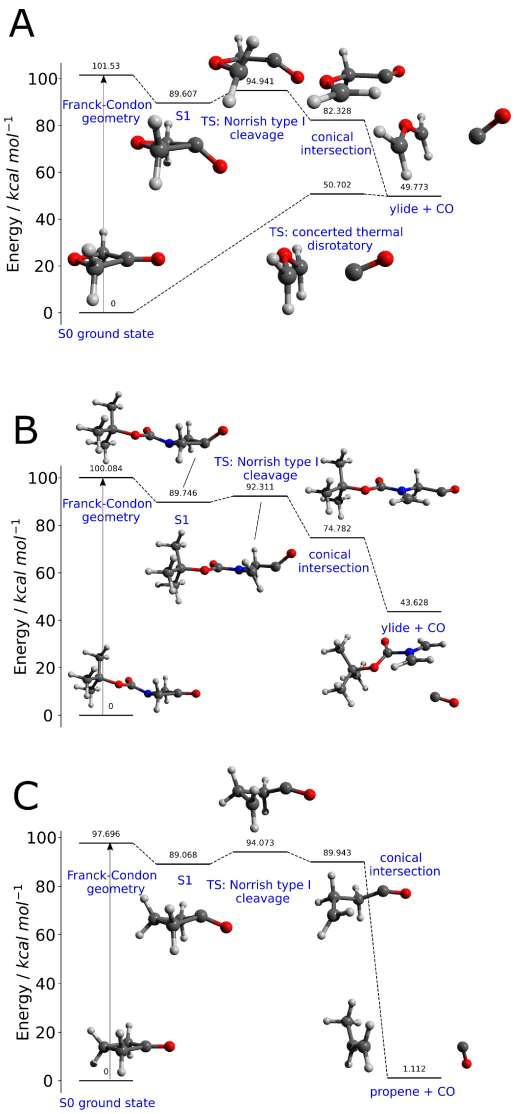

Figure 4. Norrish type I, step-wise mechanism is favored for the decarbonylation of these 4-membered rings in computational models. Computed energies of relevant geometries in Ha were converted to kcal mol^{-1}. B3LYP/6-311+G(2d,p) DFT calculations were used to determine energies and geometries of key points in the ground or excited state. A) 3-OX reaction. B) 3-AZ reaction. C) CB reaction.

of the planar carbonyl to a carbanion-like structure (π* orbital being primarily localized on C) and a slight lengthening of the C–O bond. The transition state geometry of the asymmetric cleavage of the C–CO bond is located around 5 kcal mol^{-1} higher than the singlet excited state for both 3-OX and CB, whereas for 3-AZ this is only 3 kcal mol^{-1}, suggestive of a faster process. These transition structures evolve to a conical intersection geometry which connects the excited and ground state potential energy surfaces. The conical intersection geometry proceeds to products through cleavage of the second C–CO bond in the vibrationally excited ground state without an energy barrier.

CY and AMY are high-energy, metastable species that can rapidly form cycloadducts with olefins. Unlike CY and AMY, the trimethylene $(CH_2)_3$ diradical, formed from

decarbonylation of CB, rapidly undergoes H-atom transfer to produce stable propene and CO.[17,18] It is instructive to note that the ground-state reactions to form the ylides through a concerted disrotatory reaction are prohibitively uphill by around 50 kcal mol^{-1} for 3-OX and 3-AZ, and as much as 79 kcal mol^{-1} for CB. Activation energy for the thermal decomposition of CB into ketene and ethylene has been experimentally determined to be 52 kcal mol^{-1}.[19] Resisting extensive efforts, no transition state or conical intersection could be located that would indicate that conrotatory concerted process is operative in the excited state.[20,21]

Consistent with the calculated energy levels (Figure 4) and the proposed photo-decomposition mechanisms for 3-OX and 3-AZ, ultrafast transient absorption measurements reveal the formation of CY and AMY on a picosecond timescale following excitation at 280 nm (Figure 5A). The formation of the ylide products is evident from the appearance of new electronic absorption features near 350 and 390 nm, respectively, in agreement with the calculated transitions for CY and AMY using TD-DFT at the B3LYP/6-311+G(2d,p) (Figure 5B). In the case of 3-OX, the transient absorption spectra also reveal a short-lived excited-state absorption feature near 500 nm due to excited-state population that does not immediately overcome the barrier on the S_1 potential energy surface. This transient population decays on a timescale of around 200 ps due to the required barrier crossing before accessing the conical intersection. The approximate 50% branching between direct C–CO cleavage and relaxation to the S_1 local minimum of 3-OX is similar to the observed behavior for CB that was reported previously.[22] In the case of 3-AZ, there is only a weak excited-state absorption feature in the 450–500 nm range that decays in circa 5 ps. The weaker feature and shorter lifetime for the S_1 species in 3-AZ is consistent with the lower barrier for this compound, which results in both a smaller fraction of the population being trapped and a faster reaction (Figure 4B).

With the insights about the release of CO, we speculated that CY and AMY are formed from the 3-OX, and 3-AZ as the second product of the degradation of these strained ketones. Confirming our expectations, we were able to intercept these intermediates with *N*-propargyl acrylamide dipolarophile, and we obtained products **8a** and **8b** in 68 % and 71 % yield, respectively. These dipolar cycloadditions proceed through a concerted asynchronous mechanism, which is often characterized by a flat plateau at the potential energy surface near the transition state.[23] This observation was also confirmed by modeling the transition state of the CY cyclization with acrylonitrile.

Having found a way to access the reactive CY and AMY 1,3-dipoles in an economical and efficient way with CO as the only by-product, we turned our attention to assessing the scope of suitable dipolarophiles that would yield substituted tetrahydrofurans or pyrrolidines. Such saturated heterocyclic moieties are common structural units in various natural products, pharmaceuticals, pesticides, and catalyst scaffolds.[24] Increased interest in complex and rigid structures, in the face of difficulty of their synthesis using existing

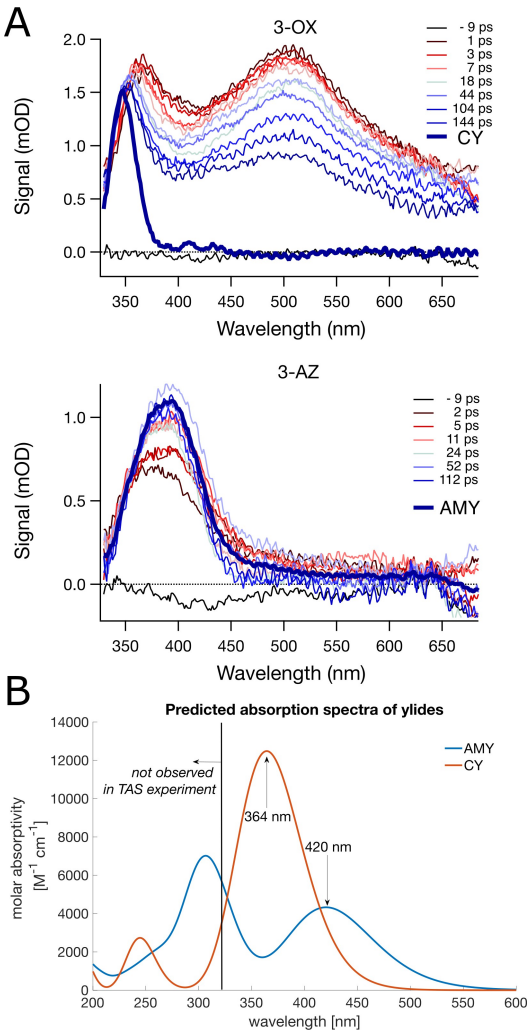

Figure 5. A) Transient absorption spectra of 3-OX and 3-AZ following excitation at 280 nm in acetonitrile. The thick blue lines are the product spectra obtained from fits to the data using a sum of exponentials. The strong absorption band centered near 500 nm for 3-OX decays with a time constant of 200 ps. B) The ground state absorption spectra of CY and AMY were calculated with TD-DFT at the B3LYP/6-311+G(2d,p) level of theory.

methods, accentuates the need to develop new and efficient methods for their synthesis in the context of complex molecules. As we will show by cogent examples below, the breadth of the substrates that engage in cyclization reactions with CY and AMY appears to be quite wide.

Saturated 5-membered heterocycles such as tetrahydrofurans and pyrrolidines are commonly found in valuable compounds important for human health, crop control, or fundamental biology. Facility with which these fully saturated rings can be made through [3+2] cycloadditions of two π systems by simultaneous formation of two carbon-carbon bonds makes this an effective synthetic strategy. We have accessed over 60 compounds through this method (Figure 6A). As expected, conjugated double bonds react preferentially with the 1,3-dipoles. Esters, amides, ketones, and nitriles can all be suitable electron-withdrawing,

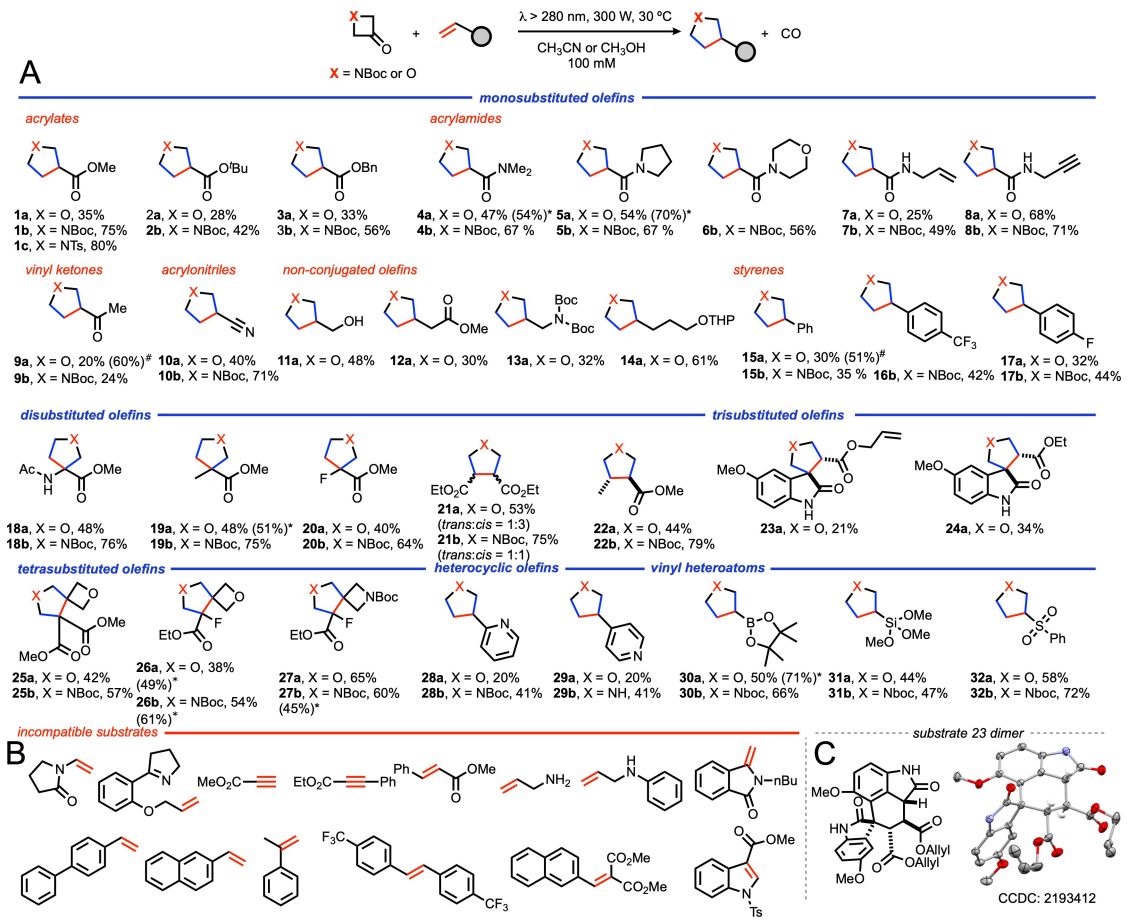

Figure 6. The breadth of the substrates that engage in cyclization reactions with CY and AMY appears to be quite wide. A) Products obtained in cycloaddition of CY (marked "**a**") and AMY (marked "**b**") with competent dipolarophiles. Yields obtained through GC-MS analysis are denoted with "#" and those obtained from NMR analysis are denoted with a "*". B) Incompetent dipolarophiles fail to give product for various reasons. C) Dimer leading to a diminished yield of **23 a**. Crystal structure deposited to CCDC 2193412;[26] Carbon, gray; Nitrogen, blue; Oxygen, red.

LUMO-lowering groups (products **1**–**10**). Methyl ester **1b** was easily hydrolyzed to an *N*-Boc-β-proline **1d** (Supporting Information, section 4.2, page S45). Acrylamides are prone to polymerization under reaction conditions, but running these reactions in the presence of molecular oxygen efficiently stalled the chain-growing process and favored cyclization with dipoles (Supporting Information, section 3.2). Terminal, non-conjugated double bonds lead to the formation of tetrahydrofurans, but not pyrrolidines (products **11 a**–**14 a**). Sluggish reaction with a dipolarophile allows a competing homo-coupling between two molecules of 3-AZ to occur preferentially (Figure 7A). Styrenes with electron-withdrawing substituents on the aromatic ring, or vinyl-substituted electron-poor heteroaromatics such as pyridine can also be used (products **15**–**17** and **28**–**29**). If a substrate contains both conjugated and non-conjugated double bonds (products **7** and **23**), the conjugated double bond reacts first, allowing chemoselective functionalization. Such chemoselectivity represents a significant advantage over other methods of ylide generation. Lower yield en route to products **23 a** is chiefly due to a dearomative [4+2] homodimerization of the isatine-derived enedioates, which is followed by a rearomatizing 1,3-hydride shift (Figure 6C, CCDC 2193412).[25,26] Vinyl boronates, vinyl silanes, or vinyl sulfones give saturated heterocycles substituted with these useful functional handles (products **30**–**32**).[27] Pyrrolidines with boron at the 3-position have recently been prepared by initially *bis*-borylating an olefin containing a tethered amine, followed by intramolecular amination of one of the boronate esters—a multistep sequence requiring high temperatures.[28]

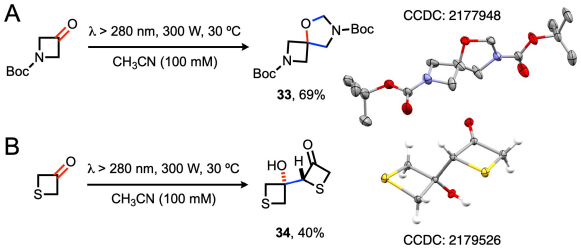

Figure 7. Substrate photochemistry that competes with dipole-dipolarophile cycloadditions. A) Reluctant dipolarophiles permit 3-AZ to engage in homocoupling. B) 3-Thietanone does not produce sulfur-stabilized dipole readily and primarily yields aldol product. Crystal structures of **33** and **34** have been deposited to CCDC;[26] Carbon, gray; Nitrogen, blue; Oxygen, red; Sulfur, yellow; Hydrogen, white.

Alternatively, 3-bromopyrrolidine can be converted to a 3-boron derivative under Cu-catalytic reaction conditions.[29,30] Mono-, di-, and tri-substituted double bonds give the expected products. Tri- or tetra-substituted double bonds, where one side of the double bond is exocyclic, give spiro-cyclized adducts (products **23**–**27**).

Cyclization is stereospecific, but evidence for this can be confounded by the light-promoted isomerization of the double bond in the dipolarophile. For example, pure *trans* fumarate ester photoisomerizes under UV light, so the cyclic products are formed as mixtures of separable *cis* and *trans* pyrrolidines and THFs (products **21a** and **21b**). Substrates for **23** and **24** do not undergo such *E*/*Z* isomerization before cyclization; hence the products obtained have lactam and ester in *trans* configuration. It is conceivable that such 3,4-disubstituted tetrahydrofurans could be derived from a non-conjugated polyene substrate and provide entry to novel ionophoric polyether scaffolds with potential antibiotic activity. Dehydroalanine-derived **18a** and **18b** may find use in applications aiming to rigidify polypeptide chains. To fully investigate the potential of this technology in polypeptide rigidifying it would be necessary to establish whether tryptophan or tyrosine interfere with photochemistry of dipole generation, and whether the reaction can be run in aqueous, or partly aqueous, conditions. The main consideration in using the above method should be the photochemical reactivity of dipolarophiles themselves under the reaction conditions ([2+2] dimerization of dipolarophiles, radical polymerization, etc.). These can often be addressed with suitable modification of reaction conditions that do not affect dipole formation (e.g., running the reaction under oxygen to prevent chain-propagating polymerization).

Substrates that did not give the expected products are shown in Figure 6B. Importantly, alkynes do not give the dihydrofurans and pyrrolines. Styrenes with neutral substituents, or the ones where polymerization competes with the cyclization are also unsuitable. Presence of basic amines or even N–H bond seems to inhibit the reaction.

To gain further insights into the molecular details of the process, the reaction was carried out in the presence of 2 equivalents of radical traps like tetramethylpiperidine-*N*-oxide or *p*-methoxyphenol. Interestingly, we did not observe any deviation from the yield under standard conditions, which may be the evidence against diradical formation (Supporting Information, section 3.2). To rule out the possibility that the decarbonylation leads to the transient formation of an epoxide, we exposed styrene oxide to the reaction conditions, but no cycloadduct was observed. Weaker light sources, such as a hand-held ultraviolet lamp (6 W), or a 365 nm LED (14 W) were not synthetically useful. Blocking the 280 nm absorption with a 305 nm long pass filter, while irradiating at 300 W was also not productive. When we included sensitizers such as thioxanthone, xanthone, benzophenone, or acetophenone under these conditions, we detected a very slow release of CO, but no product formation (Supporting Information, section 3.3).

If the dipolarophile is very unreactive, or if it is omitted altogether, *N*-Boc-3-azetidinone undergoes homo-dimerization through a hetero-[3+2] cycloaddition between a dipole formed from CO extrusion and a carbonyl of still unreacted material (**33**, Figure 7A, CCDC 2177948).[26] Attempts to extend this method to 3-thietanone as a substrate, which would yield tetrahydrothiophenes as products, only produced an aldol homo-adduct (**34**, Figure 7B, CCDC 2179526).[26]

Next, we assessed whether this method could furnish products on gram-scale [Figure 8, Eq. (1)]. We were able to successfully prepare 1.6 g (9.6 mmol) of **1b**. This molecule is a common intermediate in the synthesis of related spirocyclic natural products horsfiline and coerulescine.[31] We were also able to access the allylic alcohol-derived 3-hydroxymethyl THF in a straightforward manner [Figure 8,

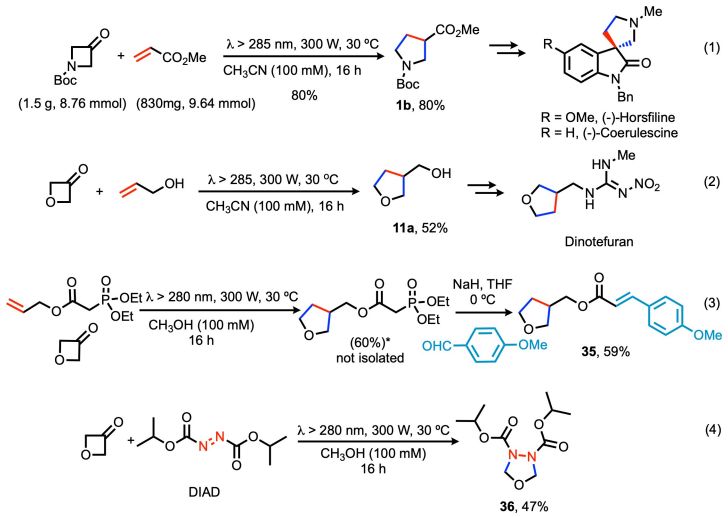

Figure 8. The method is applicable to reactions at a larger scale and provides access to useful building blocks en route to naturally occurring compounds [Eq. (1)], or pesticides [Eq. (2)]. Phosphonoacetates can be "telescoped" from [3+2] cycloaddition to Horner–Wadsworth–Emmons coupling with an aldehyde [Eq. (3); "*" indicates NMR yield]. Activated azo compounds (as in diisopropyl azodicarboxylate, DIAD) yield 1,3,4-oxadiazolidines [Eq. (4)].

Eq. (2)]. Previous preparation of this intermediate en route to herbicidal dinotefuran involved a 4-step process: Rh-catalyzed hydroformylation of ketalized but-2-en-1,4-diol, $NaBH_4$ reduction of the aldehyde, diol deprotection, and thermal 5-exo-tet cyclization to form THF.[32] Phosphonate ester can be prepared in situ and without purification used further in Horner–Wadsworth–Emmons coupling with aromatic aldehydes leading to **35** [Figure 8, Eq. (3)]. Extending the described method to 5-membered rings other than THF and pyrrolidines also seems feasible. Azo double bonds (as in DIAD) cyclize with CY to give **36** with 3 heteroatoms in a 5-membered ring [Figure 8, Eq. (4)].

Conclusion

The ease with which dipoles can be obtained from strained ketones upon light-induced decarbonylation enabled syntheses of simple but difficult-to-access products which were previously either entirely unknown or took several synthetic steps to prepare. With this study, we are filling an unexpected gap in synthetic methods that rely on the formation of 1,3-dipoles and provide, computational model, and quantitative description of the kinetics of the process.

Acknowledgments

Part of this research was financially supported through an NIH COBRE Chemical Biology of Infectious Disease (P20GM113117) Pilot Project. NSF MRI grant CHE-0923449 was used to purchase the X-ray diffractometer and software used in this study. LCT premier was purchased with support from NIH SIG S10 RR019398. The ultrafast spectroscopy measurements were supported by NSF award CHE-1956387 (PI: CGE). Computational resources were provided through the NSF Access project CHE200120 and used on Bridges-2 nodes operated at the Pittsburgh Supercomputer Center. We thank Dr. Scott Lovell (University of Kansas) for collecting the X-ray diffraction data for the compounds in this publication and Professor Emeritus Robert Hanzlik for critical comments, suggestions, and edits during the preparation of this manuscript. We also wish to thank Dr. Todd Williams and Mr. Larry Seib of the KU mass spectrometry laboratory for their efforts in acquiring the ESI spectra.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

A Supporting Information document contains thorough descriptions of experiments pertaining to this manuscript. In addition, a repository associated with this manuscript which contains .sdf formatted assigned NMR data, MatLab script for recreating Figure 2, and Gamess input files and log files for geometry optimization, saddle points search, conical intersections search, and trajectories can be found at https://github.com/boskovicgroup/cy_amy.

Keywords: Computational Models · Cycloaddition · Decarbonylation · Kinetics · Photochemistry

[1] J. P. Wasacz, M. M. Joullie, U. Mende, I. Fuss, G. W. Griffin, *J. Org. Chem.* **1976**, *41*, 572–574.
[2] G. W. Griffin, K. Ishikawa, I. J. Lev, *J. Am. Chem. Soc.* **1976**, *98*, 5697–5699.
[3] A. Padwa, *Acc. Chem. Res.* **1991**, *24*, 22–28.
[4] E. Alfonzo, F. S. Alfonso, A. B. Beeler, *Org. Lett.* **2017**, *19*, 2989–2992.
[5] R. Huisgen, W. Scheer, H. Huber, *J. Am. Chem. Soc.* **1967**, *89*, 1753–1755.
[6] U. C. Yoon, S. J. Cho, Y.-J. Lee, M. J. Mancheno, P. S. Mariano, *J. Org. Chem.* **1995**, *60*, 2353–2360.
[7] P. N. Confalone, E. M. Huie, *J. Org. Chem.* **1983**, *48*, 2994–2997.
[8] P. N. Confalone, E. M. Huie, *J. Am. Chem. Soc.* **1984**, *106*, 7175–7178.
[9] R. M. Williams, W. Zhai, D. J. Aldous, S. C. Aldous, *J. Org. Chem.* **1992**, *57*, 6527–6532.
[10] T. Thierry, C. Lebargy, E. Pfund, T. Lequeux, *J. Org. Chem.* **2019**, *84*, 5877–5885.
[11] J. A. Wojtowicz, R. J. Polak, *J. Org. Chem.* **1973**, *38*, 2061–2066.
[12] E. M. Carreira, T. C. Fessard, *Chem. Rev.* **2014**, *114*, 8257–8322.
[13] R. Cookson, N. Wariyar, *J. Chem. Soc.* **1956**, 2302–2311.
[14] J. N. Murrell, *The theory of the electronic spectra of organic molecules*, Chapman and Hall, London, **1971**.
[15] J. S. Gibson, D. O. Harris, *J. Chem. Phys.* **1972**, *57*, 2318–2328.
[16] S. Pedersen, J. Herek, A. Zewail, *Science* **1994**, *266*, 1359–1364.
[17] F. E. Blacet, A. Miller, *J. Am. Chem. Soc.* **1957**, *79*, 4327–4329.
[18] S. W. Benson, G. B. Kistiakowsky, *J. Am. Chem. Soc.* **1942**, *64*, 80–86.
[19] M. N. Das, F. Kern, T. D. Coyle, W. D. Walters, *J. Am. Chem. Soc.* **1954**, *76*, 6271–6274.
[20] H. Longuet-Higgins, E. Abrahamson, *J. Am. Chem. Soc.* **1965**, *87*, 2045–2046.
[21] R. B. Woodward, R. Hoffmann, *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 781–853; *Angew. Chem.* **1969**, *81*, 797–869.
[22] M.-H. Kao, R. K. Venkatraman, M. N. R. Ashfold, A. J. Orr-Ewing, *Chem. Sci.* **2020**, *11*, 1991–2000.
[23] K. N. Houk, J. Gonzalez, Y. Li, *Acc. Chem. Res.* **1995**, *28*, 81–90.
[24] G. Li Petri, M. V. Raimondi, V. Spanó, R. Holl, P. Barraja, A. Montalbano, *Top. Curr. Chem.* **2021**, *379*, 34.
[25] A. Itai, Y. Iitaka, A. Kubo, *Acta Crystallogr. Sect. B* **1978**, *34*, 3775–3777.
[26] Deposition Numbers 2193412, 2177948, and 2179526 contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.
[27] O. S. Liashuk, I. A. Ryzhov, O. V. Hryshchuk, B. V. Vashchenko, P. V. Melnychuk, Y. M. Volovenko, O. O. Grygorenko, *Chem. Eur. J.* **2022**, e202202117.
[28] P. Xu, M. Zhang, B. Ingoglia, C. Allais, A.-M. R. Dechert-Schmitt, R. A. Singer, J. P. Morken, *Org. Lett.* **2021**, *23*, 3379–3383.

[29] C.-T. Yang, Z.-Q. Zhang, H. Tajuddin, C.-C. Wu, J. Liang, J.-H. Liu, Y. Fu, M. Czyzewska, P. G. Steel, T. B. Marder, L. Liu, *Angew. Chem. Int. Ed.* **2012**, *51*, 528–532; *Angew. Chem.* **2012**, *124*, 543–547.
[30] M. Presset, N. Fleury-Brégeot, D. Oehlrich, F. Rombouts, G. A. Molander, *J. Org. Chem.* **2013**, *78*, 4615–4619.
[31] J. A. Murphy, R. Tripoli, T. A. Khan, U. W. Mali, *Org. Lett.* **2005**, *7*, 3287–3289.
[32] S. K. Potluri, A. R. Ramulu, M. Pardhasaradhi, *Synth. Commun.* **2005**, *35*, 971–978.

Manuscript received: October 31, 2022
Accepted manuscript online: November 18, 2022
Version of record online: December 13, 2022