Triazenolysis of Alkenes: Aza-version of Ozonolysis

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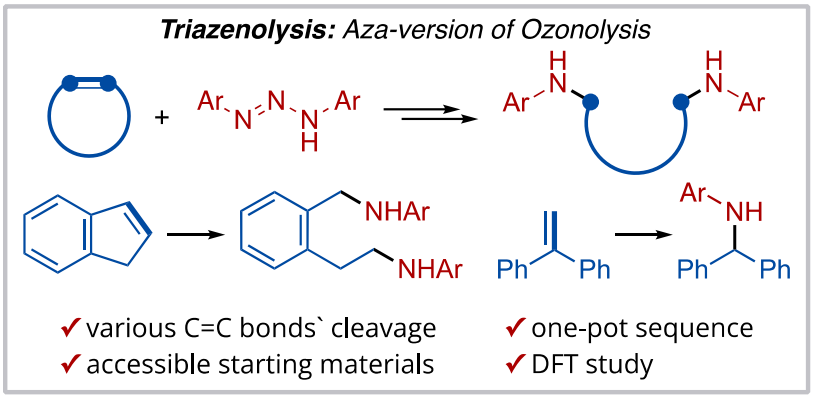
Abstract



Numerous applications of alkenes exist due to their abundance and versatility in chemical transformations. In this study, we present a unique and novel chemical transformation of alkenes, the *aza*-version of canonical ozonolysis reaction, which we termed as triazenolysis. This process offers a non-trivial and previously unfeasible synthetic disconnection, allowing the cleavage of a C=C double bond into two new C-N bonds in a reductive manner. We carefully examined the applicability of the reaction, finding that diverse cyclic alkenes are suitable for the developed process. Furthermore, we present an example of an acyclic alkene, illustrating the potential for expanding triazenolysis to other acyclic counterparts. Through DFT calculations, we explored the mechanism of the key step and demonstrated the significance of Lewis acid catalysis in achieving the desired transformation.

Introduction

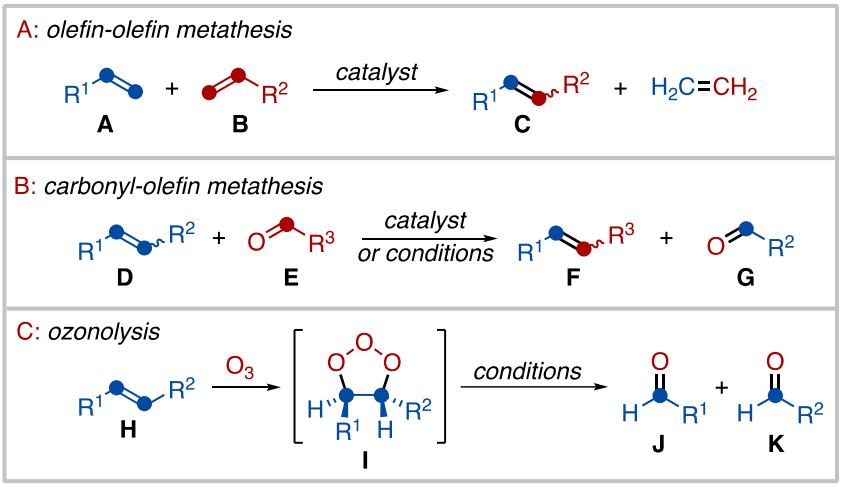
As one of the major natural and industrial feedstocks, alkenes hold a position of utmost significance in the realm of chemistry. Their role as indispensable building blocks in synthesis stems from the distinctive and versatile reactivity inherent to the carbon-carbon double bond. This reactivity empowers chemists to transform alkenes into a plethora of valuable functional groups, amplifying their utility across diverse applications.[1–5]

One class of functionalization methods involves reactions that completely cleave carbon-carbon double bonds. Those transformations have demonstrated their applicability in the synthesis of myriad of organic compounds, significantly propelling approaches for the preparation of pharmaceuticals,[6–8] materials[9–11] and agrochemicals.[12,13] The groundbreaking example of such reactivity was highlighted by the 2005 Nobel Prize for the development of olefin metathesis, which allows a construction of new C=C motif by metal-catalyzed cleavage of two starting C=C units (Fig. 1A).[14–16] Catalyst tuning allows to control the substitution pattern and the stereochemistry of the newly formed C=C bond.[17–26]

A complementary functionalization of olefins is known as carbonyl-olefin metathesis, which involves the cleavage and reconstruction of C=C and C=O bonds to prepare new olefin and carbonyl compound (Fig. 1B). This transformation can be achieved either through Paternò–Büchi reaction[27] or via Lewis acid-catalyzed C=C/C=O [2+2]-cycloaddition[28–30] followed by oxetane fragmentation. Reactions mediated by metal alkylidene were also developed.[31] Another valuable approach is the indirect hydrazine-catalyzed carbonyl-olefin metathesis, which involves the [3+2]-cycloaddition/cycloreversion of *in situ* formed azomethine imine and olefin.[32] This chemistry has had a significant impact on synthetic methods, particularly in the construction of new alkene functionalities.[33]

Ozonolysis provides another widely used method to convert C=C bond into two C=O bonds through the cleavage of the former unit (Fig. 1C). When alkene **H** is treated with ozone, it forms the primary ozonide **I**.[34–36] The molozonide intermediate can either rearrange and subsequently be decomposed to two compounds with oxygen-containing functional groups by breaking the C-C bond (e.g., carbonyls **J** and **K**), or it can be captured to yield a *syn*-diol, depending on the reaction conditions.[37] While the transformation is highly valuable in organic synthesis, ozonolysis is considered a hazardous process, especially in industrial settings.[38] Therefore, alternative approaches to convert C=C to C=O have been developed, including the cycloaddition of aromatic nitro compounds to olefins,[39] Lemieux–Johnson oxidation[40] and various modifications of these reactions.[41–43]

Figure 1. *Examples of olefin functionalization via C=C bond cleavage.*



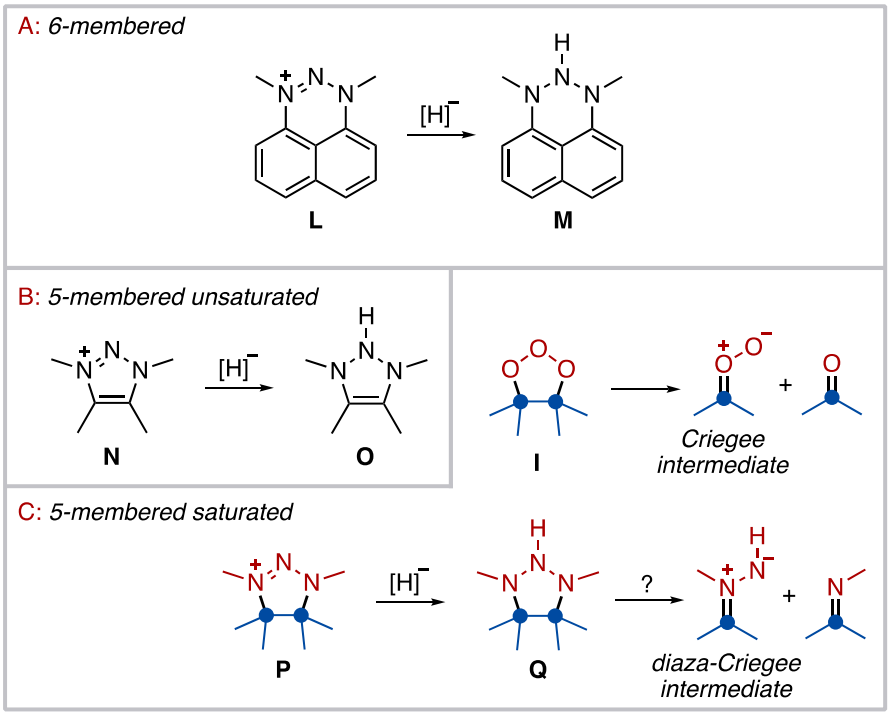
While the previously mentioned methods for converting a C=C bond to new C=C or C=O motifs are well-established, there is notable gap in the transformation of olefins into two C=N units (or corresponding amines). Several studies have focused on olefin-imine metathesis, primarily aimed at creating new C=C bonds;[44–49] however, to the best of our knowledge, the conversion of olefins to imines or amines through carbon-carbon bond cleavage remains practically unexplored.[50–55] Undoubtedly, such a transformation would offer significant benefits to the synthetic organic community.

We have initiated a research program dedicated to studying the properties and reactivity of N-heterocyclic nitrenium cations which possess a relatively low LUMO and a free *p*-orbital on the central N-atom (Fig. 2). Their unique features have enabled us and others to demonstrate that nitrenium ions can function as cationic and non-innocent ligands to transition metals,[56–60] act as acceptors in frustrated Lewis pairs,[61] serve as efficient Lewis acid catalysts for numerous reactions,[62,63,64] mediate electron-transfer processes,[65–68] and act as a platform for the preparation of persistent nitrogen-based radicals.[66,69]

Based on a cyclic 6-membered nitrenium cation **L**, we successfully synthesized and crystallized novel N-H triazanes **M** (Fig. 2A).[61,70,71] Although these unusual compounds possess three saturated nitrogen atoms in a consecutive arrangement, they demonstrated sufficient stability to enable their systematic investigations.[61,70,72] In contrast, triazanes **O** derived from unsaturated aromatic triazolium salts **N** exhibit lower stability (Fig. 2B). While not isolated, we assumed these species existed and speculated that **O** serves as the active hydride-transfer intermediate in our previously reported catalytic reduction processes.[62] However, N-H triazane **Q**, which is derivative of dihydrotriazolium cation **P**, has not, to the best of our knowledge, been previously prepared and studied (Fig. 2C). Upon evaluating this elusive compound, we reasoned that it should be isostructural and isoelectronic to trioxolane **I**, a key intermediate in olefin ozonolysis. Consequently, we wondered whether species **Q**, once formed under reductive conditions, would also rearrange similarly to trioxolane **I**? If such a reaction occurs, it would produce diaza-Criegee intermediate and imine via C-C and C-N bond cleavage. If this were confirmed, it could pave the way for an unprecedented formal *aza*-version of ozonolysis of alkenes. As C-N containing functions, including amines, have gained paramount importance throughout chemical enterprise, synthesizing

them from ubiquitous alkenes would be a valuable addition to the toolbox of synthetic chemistry.

***Figure 2**. N-heterocyclic nitrenium cations and N-H triazanes.*



In this paper, we present a novel chemical transformation for the conversion of olefins to corresponding valuable amines involving C=C bond cleavage. This formal *aza*-version of ozonolysis was achieved through a [2+3] cycloaddition of triazadienium cation to an alkene, followed by the reduction of the *in situ* formed triazolinium salt. The presumably formed triazane undergoes a spontaneous rearrangement through cycloreversion with a C-C and N-N bonds disconnection, subsequently yielding two new C-N motifs. We have termed this transformation "olefin *triazenolysis"*. In our initial investigation of this process, we found that cyclic alkenes with various degrees of ring strain are suitable to this methodology; moreover, we present one example of an acyclic olefin substrate. Both experimental observations and computational mechanistic studies indicate that triazenolysis is a Lewis acid-mediated transformation.

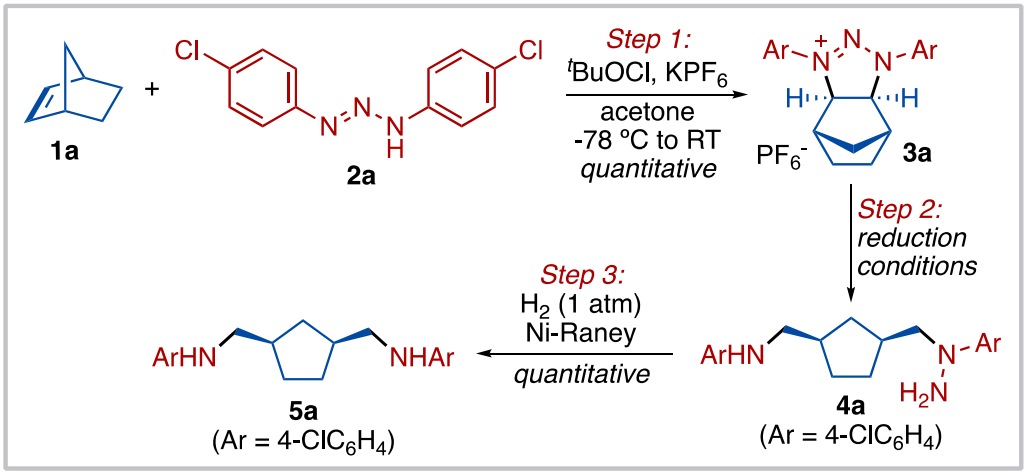
Results

Reaction Design and Optimization

To initiate our investigation, we chose norbornene **1a** as a model alkene with moderate ring strain.[73] The oxidation of triazene **2a**, accompanied by dipolar cycloaddition to norbornene, resulted in the formation of dihydrotriazolium salt **3a** in a quantitative yield (Scheme 1, *Step 1*). This nitrenium salt served as the starting point to explore the desired reduction process and possible rearrangement (*Step 2*; see also Fig. 2C). Attempting to apply our previously developed reduction method for **L** (Fig. 2A)[61,70] to nitrenium **3a** using $NaBH_4$ did not yield the expected result, and only starting material was recovered (Table 1, entry 1). Gratifyingly, when the solvent was changed to THF, the triazenolysis product **4a** was detected in a high yield (entry 2). The elusive N-H triazane (**Q**) was not observed; most likely, it underwent direct rearrangement to

form **4a**, resulting in the overall diamination of the substrate with C=C bond cleavage (mechanism is discussed below).

Scheme 1. *Optimization of the reaction conditions.*



We explored various reductants for this transformation and found that sodium and lithium borohydride salts were the most effective, providing practically the same yield of **4a** (entries 2 and 3). $LiAlH_4$ was less effective (entry 4), while the phenylsilane/CsF mixture did not yield the target product, despite its known ability to reduce azole cations (entry 5).[74] Among various solvents, only ethers proved to be suitable (entries 6-10). This observation pointed to the importance of stabilizing BH_3, formed during the reaction, by ethereal solvents (*vide infra*). Additionally, varying the temperature showed similar efficacy of reflux and 90 °C (entries 2 and 10), whereas lower temperatures led to inferior results (entries 11-12). Reducing the amount of $NaBH_4$ did not improve the outcome of the process (entry 13).

It is well-documented that borane-ether complexes are formed when BH_4^- reacts with electrophiles in ethereal solvents.[75,76] Analyzing the results of the solvent screening and considering the potential effect of BH_3 on the rearrangement process, we conducted the reaction in the presence of borane-THF complex generated *in situ* from $NaBH_4$ and iodine.[75] To our delight, the rearrangement occurred rapidly, even at room temperature, providing **4a** in a higher yield, eliminating the need to reflux the reaction mixture (entry 14). Moreover, reducing the amount of I_2 to 0.2 eq only (which decreases the amount of the borane complex; entry 15), or using an alternative method for BH_3 generation (entry 16) yielded similar performance with slightly reduced yields.

Finally, the conditions outlined in entry 14 were chosen as the standard protocol for the further evaluation of the reaction scope. In addition, we found a selective and efficient method to convert product **4a** to the more stable diamine **5a**: hydrogenation with Ni-Raney catalyst provided a quantitative yield in this transformation (Scheme 1, *Step 3*). This process did not necessitate the isolation of **4a**, allowing the entire sequence to be carried out in a one-pot manner. Notably, diamine **5a** exhibited higher stability compared to hydrazine **4a**. Since diamines have widespread applications in both laboratory[77–80] and industrial[81,82] settings across major areas of chemistry, we directed our focus towards exploring the scope of the diamine products **5** rather than the aminohydrazines **4**. However, compounds **4** can be readily isolated if necessary.

Table 1. *Optimization of the reaction conditions[a] (Step 2).*

Entry	**Reductant** (5 eq)[b]	**Solvent**	**Temperature and time**[c]	**Additives**	**Isolated yield of 4a** (%)[d]
1	$NaBH_4$	MeOH	1) RT, 1 h 2) 90 °C, 2 h	-	0
2	$NaBH_4$	THF	1) RT, 15 min 2) 90 °C, 15 min	-	81
3	$LiBH_4$	THF	1) RT, 15 min 2) reflux, 10 min	-	82
4	$LiAlH_4$	THF	1) RT, 15 min 2) 90 °C, 15 min	-	32
5	$PhSiH_3$	THF	1) RT, 15 min 2) 90 °C, 2 h	CsF (5 eq)[e]	0
6	$NaBH_4$	toluene	1) RT, 15 min 2) 90 °C, 2h	-	0
7	$NaBH_4$	DMF	1) 0 °C, 1 h 2) 90 °C, 2h	-	0
8	$NaBH_4$	dioxane	1) 0 °C, 1 h 2) 90 °C, 4h	-	12
9	$NaBH_4$	Et_2O	1) 0 °C, 1 h 2) reflux, 15h	-	61
10	$NaBH_4$	THF	1) RT, 15 min 2) reflux, 15 min	-	81
11	$NaBH_4$	THF	1) RT, 15 min 2) 40 °C, 1.5 h	-	77
12	$NaBH_4$	THF	RT, 24 h	-	75
13	$NaBH_4$ (3 eq)	THF	1) RT, 15 min 2) reflux, 15 min	-	64
14	$NaBH_4$ (6 eq)	THF	RT, 10 min	I_2 (1 eq)[f]	85
15	$NaBH_4$ (6 eq)	THF	RT, 1.5 h	I_2 (0.2 eq)[f]	81
16	$NaBH_4$ (6 eq)	THF	RT, 5 min	$BF_3 \times Et_2O$ (1 eq)[f]	72

[a] Standard reaction conditions for *Step 2*: **3a** (0.2 mmol), reductant, additive, solvent (0.1 M). [b] Unless otherwise stated. [c] The sequence and interval of reaction is indicated: 1) – nitrenium was premixed with reductant for specific period of time; 2) – the reaction mixture was heated up to indicated temperature for specific period of time. [d] Isolated yields are presented for two-step process. [e] CsF was premixed with $PhSiH_3$ for 10 minutes. [f] The additive was premixed with $NaBH_4$ at 0 °C for 5 minutes.

Reaction Scope

With the optimized conditions at hand, we assessed various substrates **1** and **2** in this transformation (Table 2). Importantly, there was no need to isolate intermediate products to proceed with triazenolysis sequence: (a) nitrenium cations did not require purification - simple filtration and wash sufficed to obtain the NMR-pure compounds for the next step; (b) there was no necessity to separate inorganic salts from the obtained nitrenium cations (see SI, optimization of step 2); (c) the reaction mixture

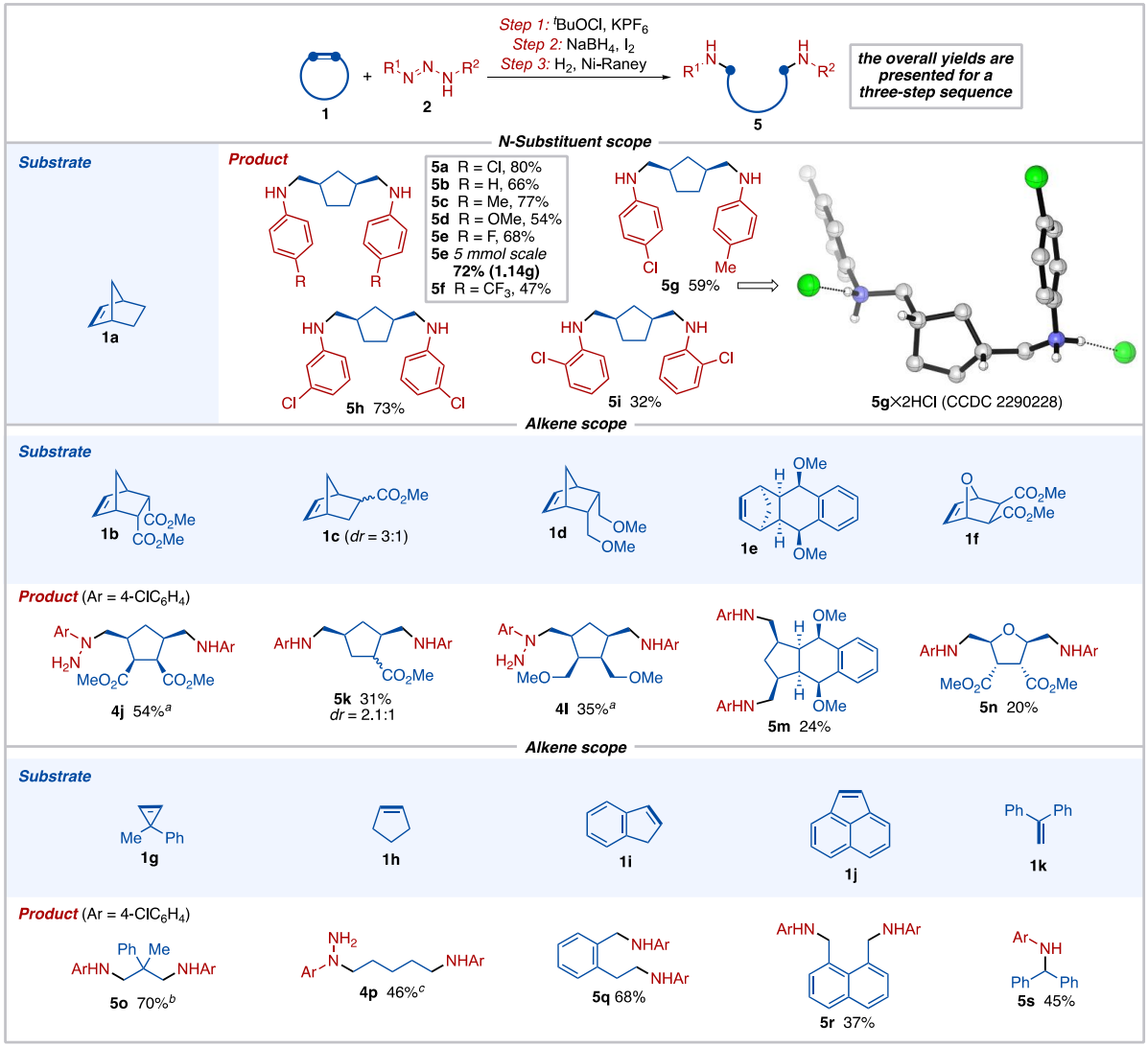
with compound **4** was evaporated and further used as is to proceed to final diamine **5**.

We found that various functional groups, both at the *N*-substituents of **2** and in the olefin skeleton, possessing diverse steric and electronic properties, are compatible with the triazenolysis protocol, providing the final amines in moderate to good yields (Table 2; the presented yields are calculated for the three-step reaction sequence). For instance, N-aryls can accommodate both electron-donating (Me (**5c**), OMe (**5d**)) and electron-withdrawing (Cl (**5a**), F (**5e**), CF_3 (**5f**)) substituents at the *para*-position, yielding final diamine products in approximately 50-80% yields. The scale-up of the reaction in the case of **5e** resulted in the desired product on a gram scale (72%, 5 mmol scale versus 68%, 0.2 mmol scale). Non-symmetrical amines can also be prepared in good yields (see product **5g**). *Meta*-substitution of *N*-Ar units does not diminish the overall yield as demonstrated in the preparation of diamine **5h**. Even *ortho*-substitution is feasible, albeit with a yield drop (32%, **5i**). Unfortunately, nitrenium ions bearing N-alkyl substituents did not undergo the desired rearrangement (see SI, unsuccessful reactions).

We also explored the scope of alkenes which mainly encompass cyclic olefins with varying degrees of ring strain. Diversely substituted norbornenes **1b**-**e**, with phenyl, alkoxy or ester groups, were found to be suitable for triazenolysis. In few particular cases (substrates **1b** and **1d**), we were unable to perform *Step 3* despite all the efforts; thus, aminohydrazines **4j**,**l** were isolated and characterized after *Step 2*. Furthermore, heterocyclic alkene **1f** successfully underwent triazenolysis, providing the corresponding substituted tetrahydrofuran **5n**, with an overall yield of 20%.

To our delight, this new rearrangement was not limited to bridged systems. Cyclopropenes, with higher ring strain energy compared to norbornene moieties,[73] were anticipated to be suitable substrates. Confirming this hypothesis, when **1g** was tested, it resulted in a good yield of the product **5o**. Additionally, cyclopentene **1h** also yielded the desired product **4p** in good three-step yield, although the removal of amino group from hydrazine **4p** posed a challenge. Other cyclic 5-membered systems, including indene **1i** and acenaphthylene **1j**, also furnished the desired diamine products (**5q**,**r**). Remarkably, we were able to employ *acyclic* 1,1-diphenylethylene **1k** which led after triazenolysis to amine **5s** in 45% yield. While this is currently a sole example, it underscores the potential to further advance this transformation for converting olefins to amines by cleaving non-strained C=C bonds.

Table 2. *Substrate scope of the reaction.*



Reaction conditions: Step 1 – **1** (2 eq), **2** (1 eq), ^{t}BuOCl (1.1 eq), KPF_6 (2 eq), acetone (0.033M), –78 °C to RT; Step 2 – **3** (1 eq), $NaBH_4$ (6 eq), I_2 (1 eq), THF (0.1M), RT; Step 3 – **4** (1 eq), Ni-Raney (40 mg per 0.1 mmol of **4**), H_2 (1 atm), MeOH (0.05M), RT; isolated yields are reported.

[a] Step 3 was not used to isolate hydrazines **4j** and **4l**.

[b] Step 3 was not needed: reaction mixture consisted only of diamine after Step 2.

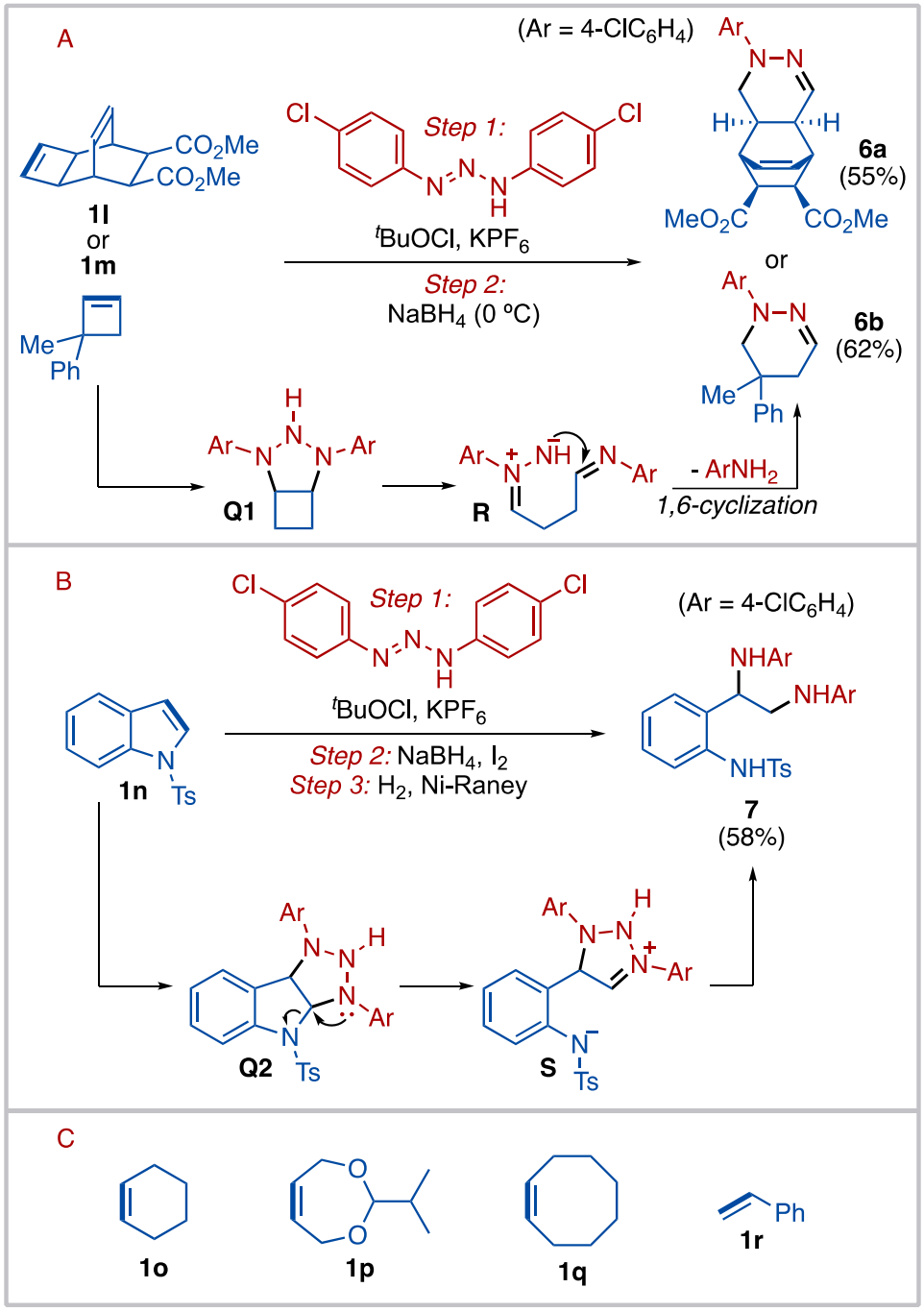
[c] Step 2 was performed with $NaBH_4$ (5 eq) at RT and reflux afterwards. Step 3 was not used to isolate hydrazine **4p**.

Furthermore, 4-memebred cyclic alkenes, specifically cyclobutenes, proved to be suitable for triazenolysis. However, the probable intermediate obtained after C-C bond disconnection undergoes an additional unexpected and interesting cyclisation due to its geometrical peculiarity. Thus, when we applied the developed protocol to cyclobutenes **1l** or **1m**, an unusual ring expansion product **6** was observed in both cases (Scheme 2A). Presumably, the obtained N-H triazane **Q1** spontaneously rearranged, involving simultaneous N-N and C-C bond cleavages under reaction conditions, resulting in the expected diaza-Criegee intermediate **R** (see the mechanism discussion and scheme 2A). Subsequently, **R** underwent 1,6-cyclization to afford the product **6**. This assumption is supported by the presence of 4-chloroaniline in the reaction mixture. Recently, the conversion of one type of (hetero)cyclic ring to another through atom insertion, so-called ring editing, has emerged as a powerful tool in synthetic and medicinal chemistry.[83–89] In this context, transformation of cyclobutenes to 6-membered cyclic compounds of type **6** represents a two-atom insertion reaction into the cyclobutene ring, making it a valuable addition to this area of chemistry.

Interestingly, when indole **1n** was employed as an alkene analog, N-C2 bond of this heterocycle was disconnected (Scheme 2B). Presumably, the sulfonamide anion played the role of a good leaving group[90,91] in intermediate triazane **Q2**, resulting in iminium cation **S** that was subsequently reduced to form **7**.

Unfortunately, the 6-,7- and 8-membered cyclic alkenes, such as cyclohexene **1o**, dihydrodioxepine **1p** and cyclooctene **1q**, did not provide the desired product of triazenolysis under standard reaction conditions (Scheme 2C). Styrene **1r** exhibited similar luck of rearrangement (see SI for more information).[92]

Scheme 2. *A,B: unregular reactivity in the reaction and plausible mechanisms of the products` formation. C: unsuccessful alkenes.*



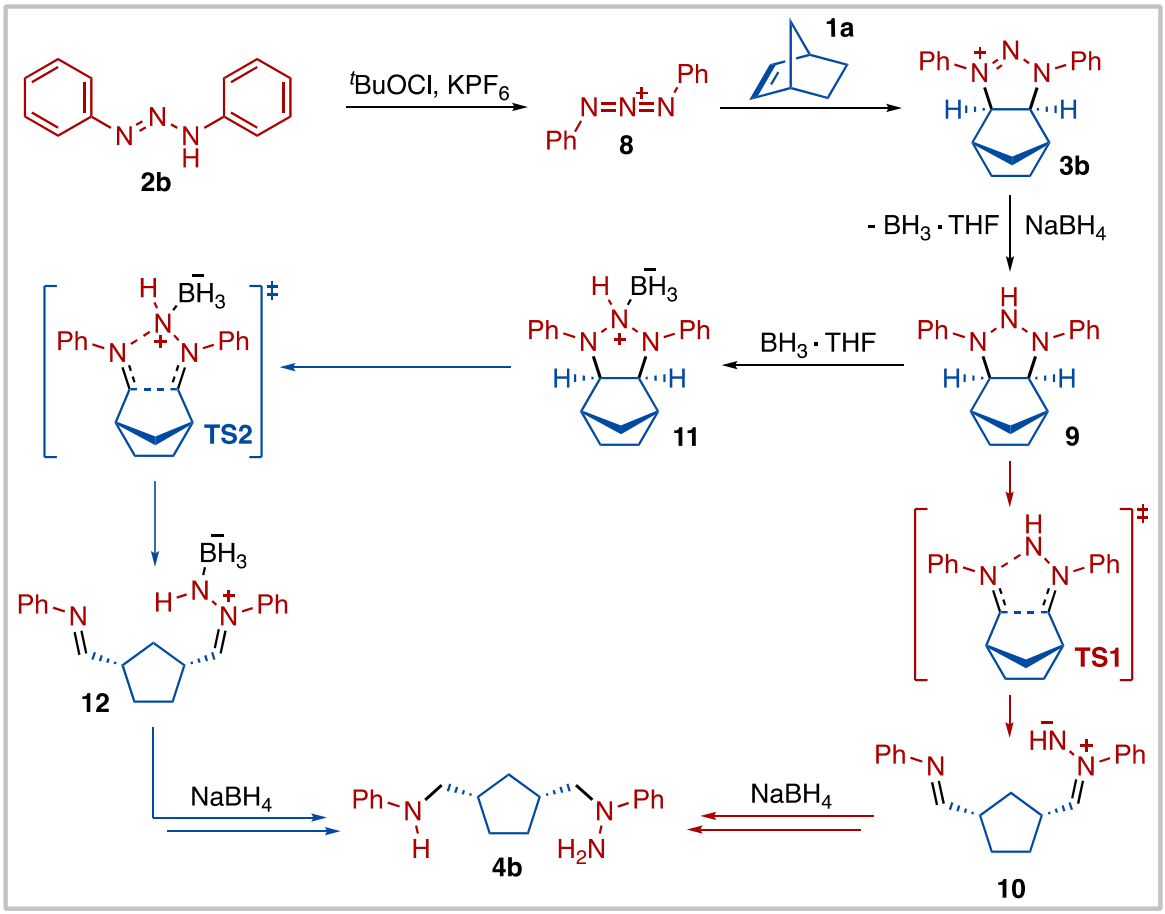
Reaction conditions for A: Step 1 – **1** (2 eq), **2** (1 eq), ^{t}BuOCl (1.5 eq), KPF_6 (2 eq), acetone (0.033M), –78 °C to RT; Step 2 – **3** (1 eq), $NaBH_4$ (5 eq), THF (0.1M), 0 °C.
Reaction conditions for B: Step 1 – **1** (2 eq), **2** (1 eq), ^{t}BuOCl (1.5 eq), KPF_6 (2 eq), acetone (0.033M), –78 °C to RT; Step 2 – **3** (1 eq), $NaBH_4$ (6 eq), I_2 (1 eq), THF (0.1M), RT; Step 3 – **4'** (1 eq), Ni-Raney (40 mg per 0.1 mmol of **4**), H_2 (1 atm), MeOH (0.05M), RT.

Mechanistic Studies

The plausible mechanism of the triazenolysis sequence for norbornene **1a** and triazene **2b** is depicted on Scheme 3. The transformation commences with the generation of triazadienium **8** from triazene **2b**. The former undergoes a [3+2] cycloaddition with the alkene, yielding nitrenium salt **3b** (step 1). The Lewis acidic **3b** is then reduced to the corresponding elusive N-H triazane **9** by hydride abstraction from $NaBH_4$. This triazane is presumably unstable and may undergo retro-cycloaddition to produce imine functionality and diaza-Criegee zwitterion in one molecule (species **10**). Further reduction with sodium borohydride, present in the solution, yields the product **4b** (step 2).

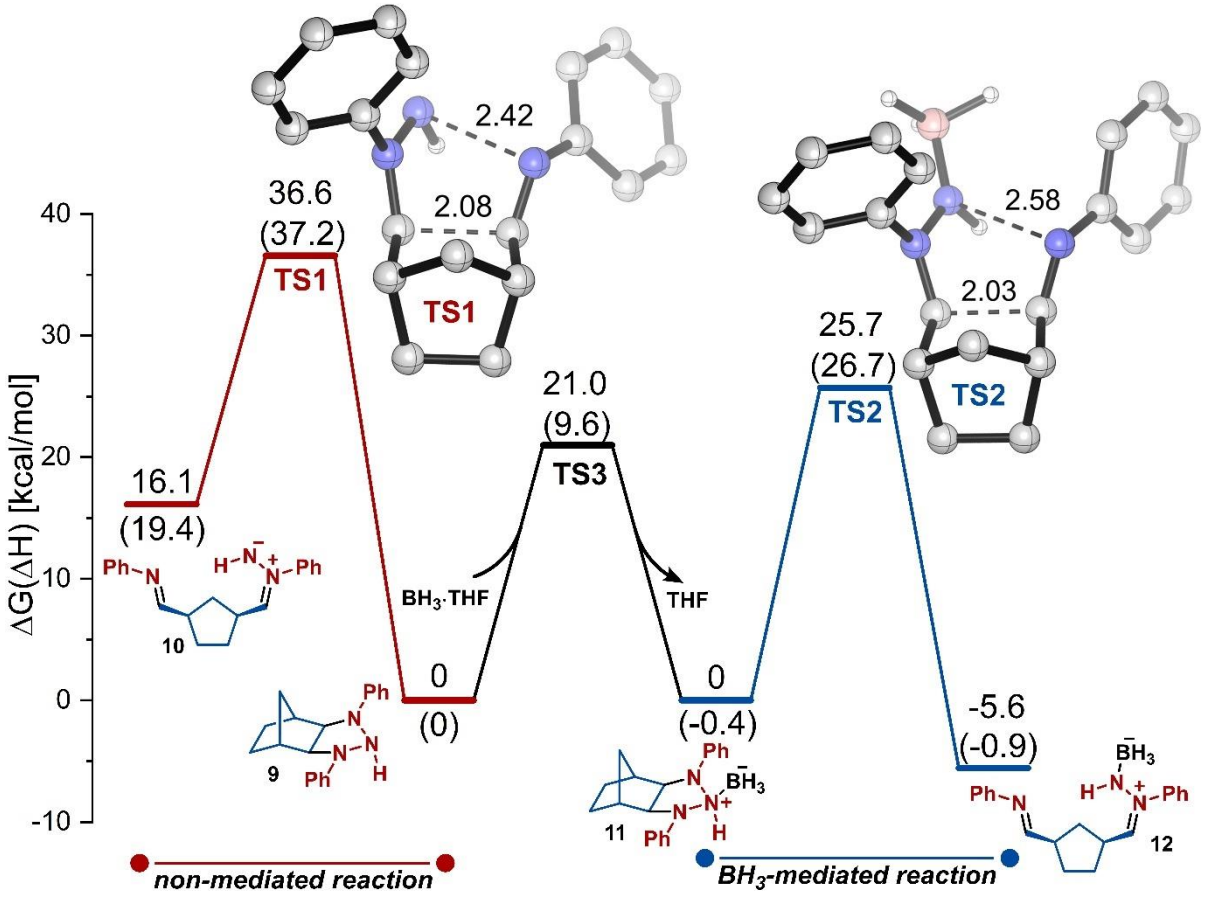
Alternatively, triazane **9** can react with the *in situ* generated borane-THF complex to produce adduct **11**. These species can undergo rearrangement via reverse cycloaddition to create BH_3-stabilized intermediate **12,** which is further reduced to yield the product **4b** while releasing BH_3 for the next turnover. Therefore, this pathway involves BH_3 as a mediator.

Scheme 3. *Plausible mechanism of the reaction.*



To evaluate the likelihood of both pathways, we conducted DFT computational studies on the ring opening steps of **9** to **10** and **11** to **12** as well as the conversion of **9** to **11**. Free energy profiles for these processes are presented in Figure 3. As shown, the non-mediated reaction proceeds with a quite high energy barrier of 36.6 kcal/mol (red trendline); moreover, this step is endergonic. Transformation of **9** to **11** is likely to occur as the energy barrier is feasible and there is sufficient amount of borane complex in the reaction mixture. In contrast to conversion of **9** to **10**, BH_3-mediated pathway requires less energy ($\Delta G^{\neq}$ = 25.7 kcal/mol, blue line) and the process is exergonic. Indeed, intermediate **10** bears an evident negative charge which is also partially present in **TS1**. Supposedly, BH_3, as a Lewis acid, stabilizes this charge and lowers the kinetic energy barrier (see compound **11** and **TS2**). Furthermore, the stabilization of the rearrangement product by BH_3 complexation is clearly observed by the energy difference between **10** and **12**. These findings align with experimental observations: the rearrangement process occurs smoothly in solvents that stabilize BH_3 formed in situ from $NaBH_4$ after hydride transfer (see Scheme 3; step from **3b** to **9**). Additionally, we found that if the transformation was carried out with a BH_3·THF and $NaBH_4$ mixture, the reaction proceeded faster and did not require heating in comparison to the reaction with sole sodium borohydride (Table 1, compare entries 10 and 14).

Figure 3. *Free energy profile for the ring opening step of the reaction; geometries were calculated at the bp86/def2SVP-D3(BJ) level of theory with energy calculation at the M062X/def2tzvp-D3 (THF) level of theory. The energy diagram is presented for one possible stereoisomer of **9**; for more information see SI.*



Conclusion

In conclusion, we have demonstrated, for the first time, the possibility to conduct the aza-version of canonical ozonolysis during which the C=C bond is cleaved and transformed into two newly formed C-N motifs. Our reaction sequence, coined triazenolysis, enables a convenient conversion of olefins to amines. Amines and diamines represent highly important classes of organic materials, and their production form abundant olefins might embody an important added value to the toolkit of organic synthetic chemistry. Our current findings indicate that this rearrangement is primarily suitable for cyclic olefins with some strain of the C-C bond. However, an example of 1,1-diphenylethylene highlights the future potential of the triazenolysis to be applicable to inactivated non-cyclic alkenes. Additionally, we revealed that cyclobutenes, upon triazenolysis, undergo an overall two-nitrogen atom ring extension, resulting in a novel type of cyclobutene ring editing. DFT calculations showed the important role of BH_3 in the triazenolysis: borane acts as Lewis acid mediating the process and making the reaction faster and more selective. Further development of triazenolysis to apply to acyclic non-strained alkenes is currently under investigation in our labs.

Methods

*General Procedure for Synthesis of Diamines **5***

The reaction sequence required three consecutive steps (*Step 1, 2 and 3*) as described below.

*General Procedure for Synthesis of Diamines **5**: Step 1*

Alkene **1** (4 mmol, 2 eq), triazene **2** (2 mmol, 1 eq), KPF_6 (736 mg, 4 mmol, 2 eq) and acetone (60 ml) were added to the Schlenk flask and nitrogen was bubbled for 10 minutes while the reaction mixture was cooled down to -78 °C with stirring (the reaction flask should be protected from light!). ^{t}BuOCl (0.3 ml, 234 mg, 1.1 eq) was added dropwise to the cooled solution and the reaction mixture was allowed to warm up to room temperature during the night in the dark. The reaction mixture was filtered through a sinter funnel (to remove KCl) and the precipitate was washed with acetone (until no triazolium was detected by TLC). The solution obtained was evaporated and diethyl ether (50 ml) was added to the solid remaining. The precipitate was triturated with spatula and then was subjected to ultrasound bath for 5 minutes. The precipitate was filtered and washed with Et_2O (3×50 ml). The resulting solid was dried in vacuo and used in the next step without further purification.

*General Procedure for Synthesis of Diamines **5**: Step 2*

The Schlenk flask was dried and flushed with nitrogen. Afterwards, it was charged with $NaBH_4$ (46 mg, 1.2 mmol, 6 eq) and THF (2 ml) and the suspension was cooled to 0 °C. Iodine (0.2 mmol, 51 mg, 1 eq) was added to the mixture and the solution was stirred for 5 minutes (until it became colorless). Then triazolium salt **3** (0.2 mmol, 1 eq) was added to the reaction media and the cooling bath was removed. The reaction mixture was stirred for 15-90 minutes (until the solution became colorless and the reaction was finished; monitored by TLC). The reaction mixture was cautiously quenched with MeOH (1 ml) and then the solvent was evaporated. The residue was dissolved in MeOH (4 ml) and the resulting mixture was used in the next step without further purification.

*General Procedure for Synthesis of Diamines **5**: Step 3*

The methanol solution of **4** was obtained from *Step 2*. Nitrogen was bubbled through the solution for 15 minutes and then Ni-Raney was added (80 mg, 40 mg per 0.1 mmol of **4**). The atmosphere in the flask was changed to hydrogen and a balloon with hydrogen gas was attached to the flask. The reaction mixture was stirred overnight at room temperature and was filtered through Celite pad upon completion (monitored by TLC). The solution was evaporated and subjected to column chromatography (Si-gel, celite dry loading) to obtain pure diamine **5**.

Data Availability

Experimental and characterization data for all new compounds prepared during these study are provided in the Supplementary Information of this manuscript. Detailed description of the DFT study may be found in the Supplementary Information as well. The X-ray crystallographic coordinates for compounds **5e**×2HCl and **5g**×2HCl have been deposited at the Cambridge Crystallographic Data Centre (CCDC) with accession codes 2290229 and 2290228.These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/.

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Author Contributions

A. Koronatov conceived the idea. A. Koronatov and P.S. performed the experiments and characterization of compounds. A. Kaushansky and A. Koronatov performed the DFT calculations. N.F. performed the X-ray crystallography characterization. A. Koronatov and M.G. co-wrote the manuscript. M.G. directed the project.

Competing Interests

All the authors declare no competing interest.

Correspondence

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