Chinese Chemical Letters 37 (2026) 111498

Contents lists available at ScienceDirect

Chinese Chemical Letters

journal homepage: www.elsevier.com/locate/cclet

Retro aza-[2+2] cycloaddition as stereochemical editing logic for multi-substituted azacyclobutanes

Fujie Liu[a], Yuzhu Yan[a], Xi Wang[a], Lingfei Hu[b], Gang Lu[b], Tao Xu[a,*]

[a] Molecular Synthesis Center & Key Laboratory of Marine Drugs, MOE, School of Medicine and Pharmacy & Qingdao Marine Science and Technology Center, Ocean University of China, Qingdao 266003, China
[b] School of Chemistry and Chemical Engineering, Key Laboratory of Colloid and Interface Chemistry, Ministry of Education, Shandong University, Ji'nan 250100, China

ARTICLE INFO

Article history:
Received 23 February 2025
Revised 13 June 2025
Accepted 23 June 2025
Available online 24 June 2025

Keywords:
Dearomatization
Retro aza-[2+2] cycloaddition
Azacyclobutane
Visible light catalysis

ABSTRACT

Multi-substituted azetidines have been an under-utilized bioisosteres in modern drug entities, due to the scarcity of mild and stereo-controllable synthetic methods. The state-of-art aza-[2+2] cycloaddition suffers from two drawbacks, namely limited C=N scope and the dearth of stereochemical control. Herein, we extend a photocatalytic direct *N*-heteroarene dearomative aza-[2+2] cycloaddition under white light *via* energy transfer mechanism. A key protonic solvent triggered retro aza-[2+2] cycloaddition process was discovered and utilized as a stereochemical editing logic to address the challenge of diastereomeric control (controlling three contiguous stereocenters).

© 2025 Published by Elsevier B.V. on behalf of Chinese Chemical Society and Institute of Materia Medica, Chinese Academy of Medical Sciences.

Nitrogen-containing heterocycles (*N*-heterocycles) have been identified as the most commonly employed subunits in the approved molecular entities, as evidenced by the statistical analyses that 88% of all the approved small molecule drugs contain *N*-heterocycles during 2015 to 2020 [1–6]. Among them, the four membered azacyclobutanes also known as azetidines display unique pharmacokinetic properties as well as enhanced bioavailability that draw attentions from medicinal chemists [7–10]. In addition, complex natural products that feature multi-substituted azacyclobutanes as core motifs pose grand challenge in azetidine formation and stereochemical control for synthetic chemists (Fig. 1a) [11–18]. In fact, synthesis of azetidines proved to be more difficult than its 3- to 6-membered counterparts following traditional cyclization mode, due to unfavorable confirmation and the ring strain (25.4 kcal/mol) [19–25]. The transition metal catalyzed C—N coupling [26], aza [1.1.0] ring fragmentation [27] and azaridine expansion [28] require directing group and/or complicated substrate prepration [29,30]. There is a drastic lack of powerful strategies and methodologies in constructing stereo-controllable multi-substituted azacyclobutanes, not to mention stereochemical editing of the azetidines [31–34]. The traditional ultraviolet mediated aza Paterno-Buchi reaction, reported by Tsuge in 1968, offered a straightforward pathway to assemble azacyclobutanes from imines and alkenes (Fig. 1b) [35,36]. Although many efforts had been devoted to improving efficiency and expanding C=N scope, huge room still remains to be improved especially under the context of visible photocatalysis and key problems untackled, *e.g.,* stereochemical control.

Visible light mediated aza-[2+2] cycloaddition reaction was first disclosed by Schindler group [37,38], using methyl oximes as C=N motif. This pioneering work was continued by You [39], Bach [40], Brown [41], Luo [42] and Zhong groups [43]. However, the C=N motif was largely limited to cyclic "imines" with push (electron-donating groups, EDG)-pull (electron-withdrawing group, EWG) activating handles or using quinoxalinone (Fig. 1c) [36,44]. Simultaneously, *N*-heteroarenes represent a large group of compounds that contain C=N bonds, which are completely neglected in visible light mediated aza-[2+2] cycloaddition. The benefits of using *N*-heteroarenes are quite obvious because they feature: (i) feedstock availability; (ii) inexpensive; (iii) "C=N" motifs come with various substitution, as well as in versatile ring systems; (iv) easy to derivatize with further transformations. These merits showed that *N*-heteroarene are very attractive substrate to be used in aza-[2+2] reaction. Once realized, aza-cyclobutane bearing three contiguous stereocenters can be obtained in one step, which would also offer the opportunity to "edit" current drugs entities with suitable C=N handles for de-planarity [45–47].

Keenly attractive as it can be, grand challenges and major limitations must be confronted and addressed. Ultraviolet irradiation is a prerequisition for traditional aza-[2+2] cycloaddition implied that most C=N bonds need high transferring energy (E_T)

* Corresponding author.
E-mail address: xutao@ouc.edu.cn (T. Xu).

https://doi.org/10.1016/j.cclet.2025.111498
1001-8417/© 2025 Published by Elsevier B.V. on behalf of Chinese Chemical Society and Institute of Materia Medica, Chinese Academy of Medical Sciences.

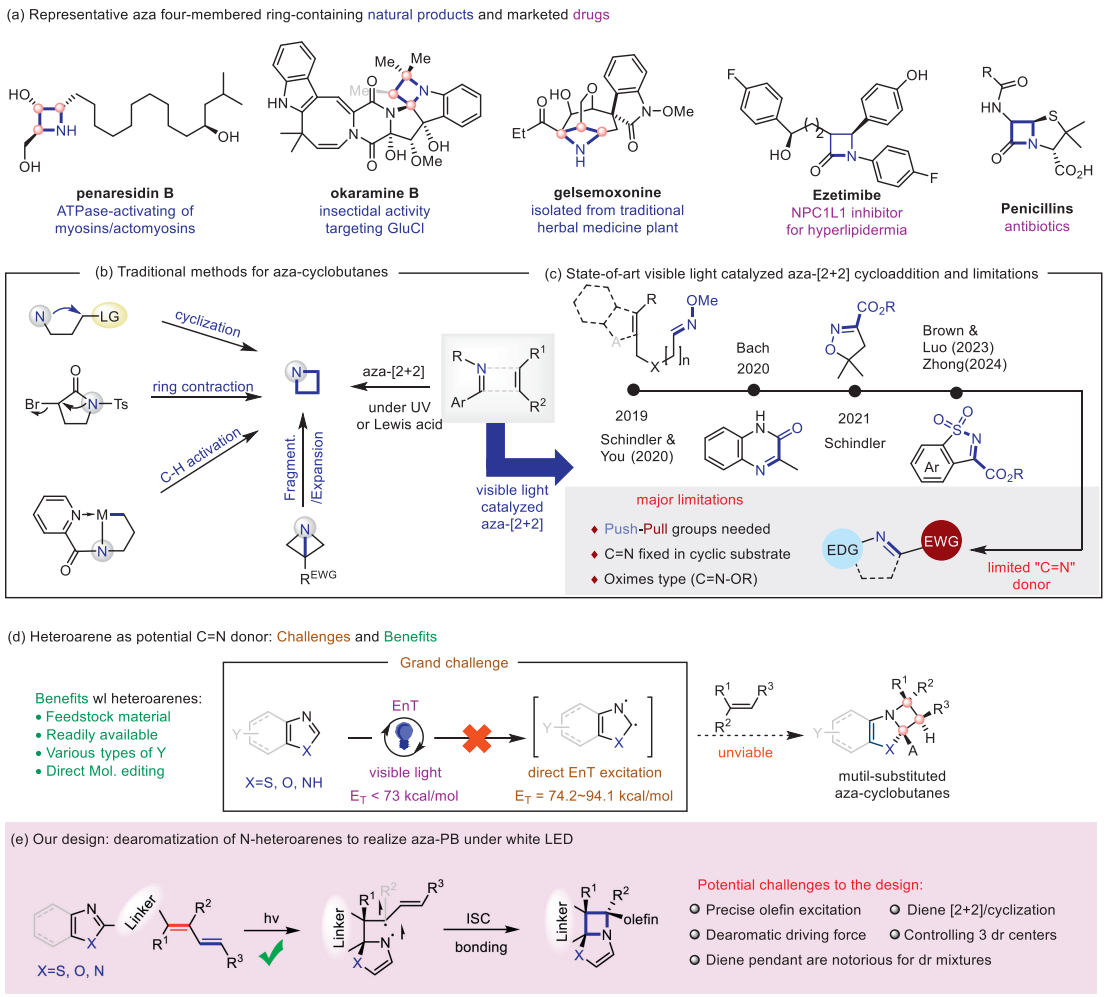


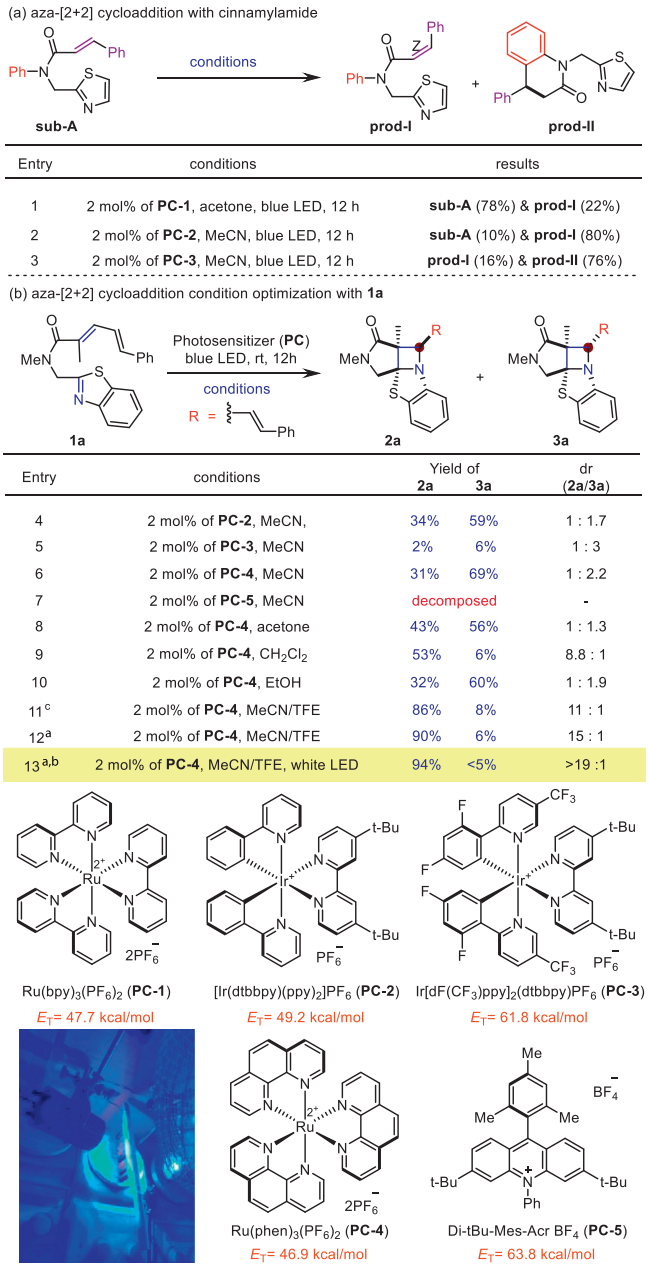
Fig. 1. Representative azetidine-containing natural products and drugs and our design of a dearomative aza-[2 + 2] cycloaddition reaction.

to be excited to their triplet states from photosensitizers or UV light source. For example, the common *N*-heteroarene such as benzothiozole, benzoxazole and benzoimidazole requires $E_T = 74.2$, 81.2 and 94.1 kcal/mol, respectively to be excited to their corresponding triplet state [48]. Contrastingly, the currently known visible light mediated photosensitizers' triplet energies are all below 73 kcal/mol, which rendered direct triplet excitation of the *N*-heteroarenes unfeasible (Fig. 1d) [49,50].

Our strategy is taking advantage of the relatively easy to excite diene moiety and speculate that the resulting diradicals would trigger a dearomative aza-[2 + 2] cycloaddition to achieve the goal (Fig. 1e). It is not without challenge to realize the design, *e.g.*, (a) how to control chemoselectivity of diene excitation; (b) the competitive 4π cyclization of diene and/or dearomative [4 + 2] cycloaddition could be interfering side reactions; (c) whether the triplet energy of diene sufficient to dearomatize the *N*-heteroarene. Last and the most challenging task is how to control the stereoselectivity of the multi-substituted azetidine, provided that dienes are notorious for their difficulty to control diastereoselectivity in aza-[2 + 2] reaction [51]. Herein, we disclose the discovery of a protonic solvent accelerated reversible dearomative aza-[2 + 2] cycloaddition between dienes and *N*-heteroarenes under white light, allowing stereochemical-selectively synthesis of multisubstituted aza-cyclubtanes.

We started with **sub-A** (Scheme 1a), which can be prepared through amide coupling between the *N*-(thiazol-2-ylmethyl)aniline and cinnamic acid (see Supporting information for details). When irradiating **sub-A** with blue LED in the presence of 2 mol% of photosensitizer (PC), no desired product can be detected except for starting material recycling (**sub-A**: 78% and 10% yield, respectively) and olefin isomerization (**prod-I**: 22% and 80% yield, respectively in entries 1 and 2). The predicted oxidative 6π cyclization **prod-II** could be detected in 76% yield, along with 16% of **prod-I** (entry 3). The olefin isomerization implied that the energy transfer took place, but the triplet diradicals' life time is too short. And thioazole dearomatization was difficult compared to the 6π cyclization as the high E_T photosensitizer, **PC-3** only triggered the latter reaction.

With the above information in hand, we designed dienamide **1a** (Scheme 1b) [52–56]. Delightedly, **1a** proved to be a suitable substrate with MeCN under blue LED irradiation with 2 mol% of **PC-2** as photosensitizer (entry 4). The desired aza-[2 + 2] products were obtained in 93% overall yield, albeit with less *dr* control (**2a**/**3a** = 1/1.7). Several photosensitizers (**PC-2~5**) and solvents were tested (entries 5~10) and the $Ru(phen)_3(PF_6)_2$ (**PC-4**) in acetonitrile proved to be the optimal choice, yielding combined aza-[2 + 2] product **2a** (31%) and **3a** (69%) with very high level of mass balance (entry 6). Surprisingly, we observed that the diastereoselectivity of aza-[2 + 2] reaction could be altered and reached to 8.8:1, when performed in CH_2Cl_2 (entry 9). The reason is not very clear and was largely attributed to solvent effect on the triplet state life time. Following this logic, it was found that when adding trifluoroethanol (TFE) as co-solvent, the diastereoselectivity of the dearomative aza-[2 + 2] could be increased to 11:1 (entry 11). Fur-



Entry	conditions	results
1	2 mol% of **PC-1**, acetone, blue LED, 12 h	**sub-A** (78%) & **prod-I** (22%)
2	2 mol% of **PC-2**, MeCN, blue LED, 12 h	**sub-A** (10%) & **prod-I** (80%)
3	2 mol% of **PC-3**, MeCN, blue LED, 12 h	**prod-I** (16%) & **prod-II** (76%)

Entry	conditions	Yield of 2a	Yield of 3a	dr (2a/3a)
4	2 mol% of **PC-2**, MeCN,	34%	59%	1 : 1.7
5	2 mol% of **PC-3**, MeCN	2%	6%	1 : 3
6	2 mol% of **PC-4**, MeCN	31%	69%	1 : 2.2
7	2 mol% of **PC-5**, MeCN	decomposed		-
8	2 mol% of **PC-4**, acetone	43%	56%	1 : 1.3
9	2 mol% of **PC-4**, CH_2Cl_2	53%	6%	8.8 : 1
10	2 mol% of **PC-4**, EtOH	32%	60%	1 : 1.9
11[c]	2 mol% of **PC-4**, MeCN/TFE	86%	8%	11 : 1
12[a]	2 mol% of **PC-4**, MeCN/TFE	90%	6%	15 : 1
13[a,b]	2 mol% of **PC-4**, MeCN/TFE, white LED	94%	<5%	>19 :1

Scheme 1. Selected condition optimization. The vial (4 mL) was irradiated by two blue LED lights with 2 mol% of PC and substrate (20mg) in MeCN (2 mL) at room temperature under N, gas for 12 h unless otherwise noted. Isolated yield. [a]Reaction time is 60 h. [b] White LED lights are used. [c]Reaction time is 24 h. PC: photosensitizer.

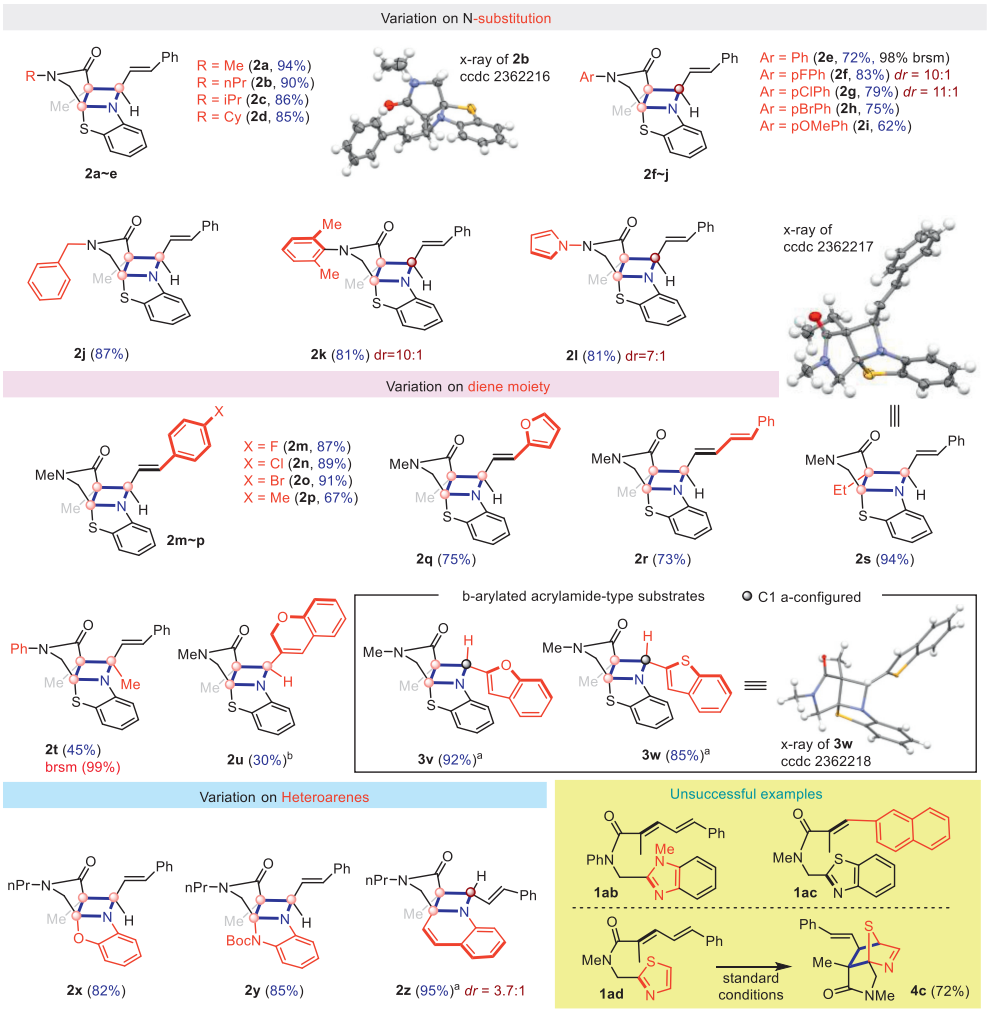
ther elongating reaction time to 60 h, the dr ratio can be reached to 15:1 without affect reaction efficiency (**2a** in 90% and **3a** in 6% yield, entry 12). Delightedly, the major C1 β-configured isomer **2a** could be isolated in 94% yield even under irradiation of white light (entry 13).

Towards this end, the optimal conditions were successfully established for the dearomative aza-[2+2] cycloaddition. The reaction scope was explored. A broad series of dienamide coupled *N*-heteroarene substrates with different steric and electronic properties have been examined (Scheme 2). Delightedly, good to high yields of diazabicyclo[3.2.0]heptanones were obtained, with good diastereomeric control. It was found that changing the steric of N substituents of dienamides (**1a-1d**) does not affect the efficacy, and 85%∼94% yields and single diastereomers (**2a-2d**) were obtained. Gratifyingly, X-ray crystallographic analysis was conducted with **2b** and the stereochemistry was verified. When *N*-substituents were switched to aryl groups (**2e-2i**), the aza-[2+2] reaction's efficiency were decreased (62%–83% yield), while maintaining good dr control (*dr* >10:1). Considering that the *N*-benzyl substituted product **2j** could be isolated in 87% yield as a single diastereomer. We speculated that π-conjugation with *N*-aryl moieties might be blamed for decreased efficiency of this reaction. Two substrates were designed **1k** and **1l** to test our hypothesis, since the sterically hindered 2,6-dimehtylphenyl and pyrrolyl groups will not form π-conjugation with the dienamide part thanks to the atropisomeric strain. As expected, the desired products **2k** and **2l** were isolated in 81% yields for both with decent *dr* control (10:1 and 7:1 *dr*, respectively).

An investigation on the substituents effects on diene motif was further conducted. When changing diene terminal substitutions, no obvious *para*-substitution effect could be observed. Only single diastereoisomers were found and the isolated yields ranged from 67% to 91% yield (**2m-2p**). It was noted that furyl group was well tolerated under such redox-neutral conditions and desired product **2q** was obtained in 75% yield as a single isomer. It is worthy to point out that even trienamide substrate **1r** could be successfully converted to the desired aza-[2+2] cycloadduct **2r** in very high chemo- and diastereo-selectivity (73% yield, single isomer). The alkyl substituent at α-position of dienamide was also investigated (**1s**). It was gratifyingly to find the ethyl-substituted products **2s** in good yield (94%), whose relative configurations were confirmed by X-ray crystallography. Moreover, vicinal quaternary carbon centers could be established (**2t** in 45% yield) with tetra-substituted olefin **1t** and **2u** was obtained in 30% yield due to unexpected decomposition. Interestingly, the diastereoisomers (**3v** and **3w**) could be isolated as the only products (92% and 85% yield, respectively), if TFE was not used as cosolvent. The relative configuration of **3w** was confirmed by X-ray crystallography.

Furthermore, the scope of *N*-heteroarenes was investigated. It was found that benzoxazole (**1x**), benzoimidazole (**1y**) even quinoline (**1z**) could be successfully dearomatization and afforded the desired aza-[2+2] cycloadducts **2x-2z** in 82%–95% yield. Notably, the isolation of **3z** and its epimer **2z** (95% yield combined in 3.7:1 *dr*) represented the first example of photocatalytic dearomtization of quinoline in a [2+2] mode instead the previously reported [4+2] cycloaddition type [57–64]. Certainly, a few substrates are reluctant to undergo the intended aza-[2+2] reaction like **1ab** and **1ac** (only starting materials were recycled). The thioazole substrate (**1ad**) was found to undergo a hetero Diels-Alder cycloaddition affording **4c** as the only product.

Our next mission is to elucidate the reason why adding TFE as co-solvent is able to control the diastereoselectivity. To probe this, we first conducted two kinetic monitoring experiments using **1a**. It was found that within the presence of TFE, the kinetic product **3a** was formed as the major isomer (72% yield, see Supporting information for details) in 2 h. And then the amount of **3a** was decreased with time until <7% yield after 36 h of irradiation). Meanwhile, the yield of thermodynamic product **2a** was correspondingly increased to 92%. In addition, their yields of **2a** and **3a** remained unchanged even after 60 h irradiation under blue LED light (Scheme 3a). On the other hand, **1a** was also subjected to TFE-free standard conditions and the ratio between product **3a** and **2a** was slowly eroded from 2.4:1 to 1.2:1, featuring kinetic isomer **3a** as the major product. These indicated that an inter-conversion from **3a** to **2a** could be existing or a reverse aza-[2+2] cycloaddition could be operating within the presence of TFE. We observed that only trace amount of kinetic product **3a** could be detected by subjecting **2a** under standard conditions. Contrastingly, 90% yield of **2a** was isolated if exposing **3a** under standard conditions. This revealed a thermodynamic control and implied why **2a** could be



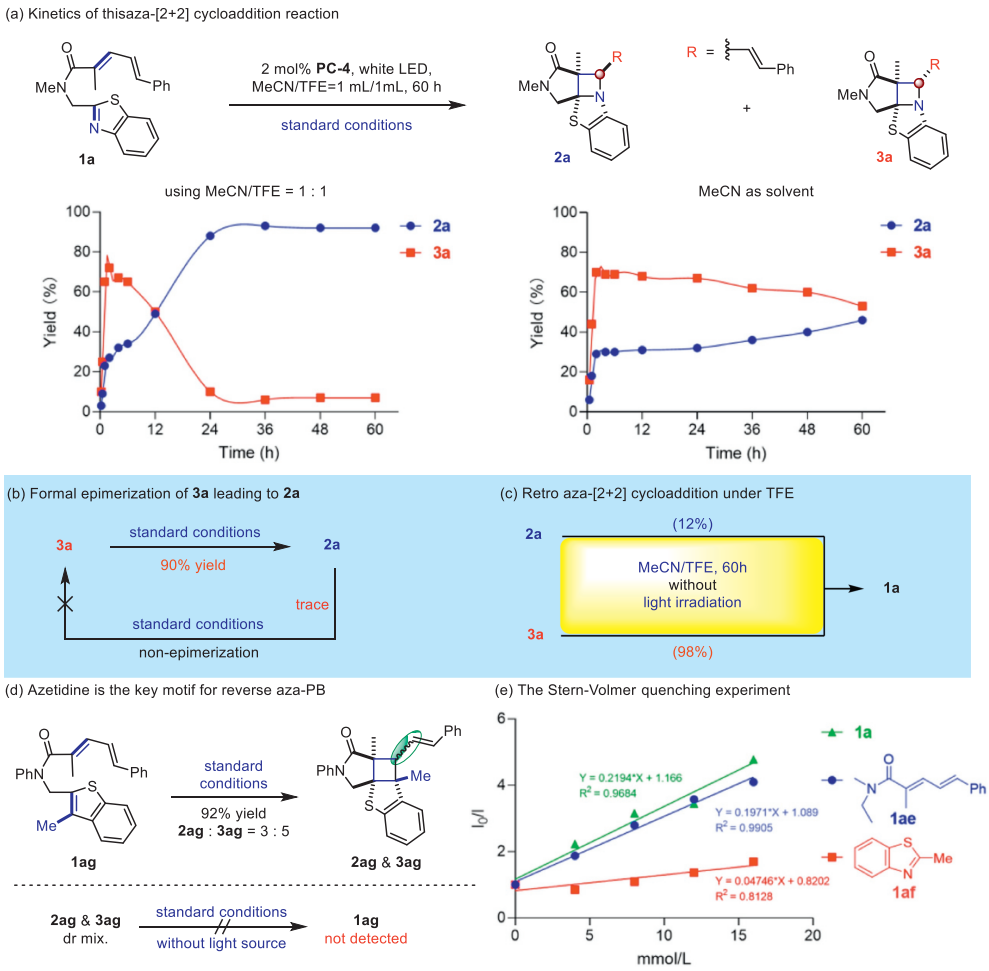
Scheme 2. Scope of the aza-[2 + 2] cycloaddition.

observed as a single diastereomer (Scheme 3b). Then we treated **2a** and **3a** with standard conditions but without light irradiation. **1a** could be isolated in 12% and 98% yield, respectively (Scheme 3c). These data revealed that a reverse aza-[2 + 2] cycloaddition was triggered under acidic additive (TFE forming H-bonding with the tertiary amine in **2a/3a**). Contrastingly, a cyclobutane analogue (**2ag/3ag**) would not undergo such a process, even within the presence of TFE (Scheme 3d). Toward this end, we have elucidated the mechanism for diastereoselective control of our aza-[2 + 2] reaction. To validate that the dienamide was key for photosensitizer triplet energy transfer, we conducted a Stern-Volmer quenching experiment with substrate **1a**, its subunits dienamide **1ae** and 2-methyl benzothiazole **1af**. The slope values indicated that dienamide moiety (**1a** and **1ae**) is key for energy transfer from the excited triplet state of photosensitizer, while the benzothiazole moiety (**1af**) should not be responsible (Scheme 3e).

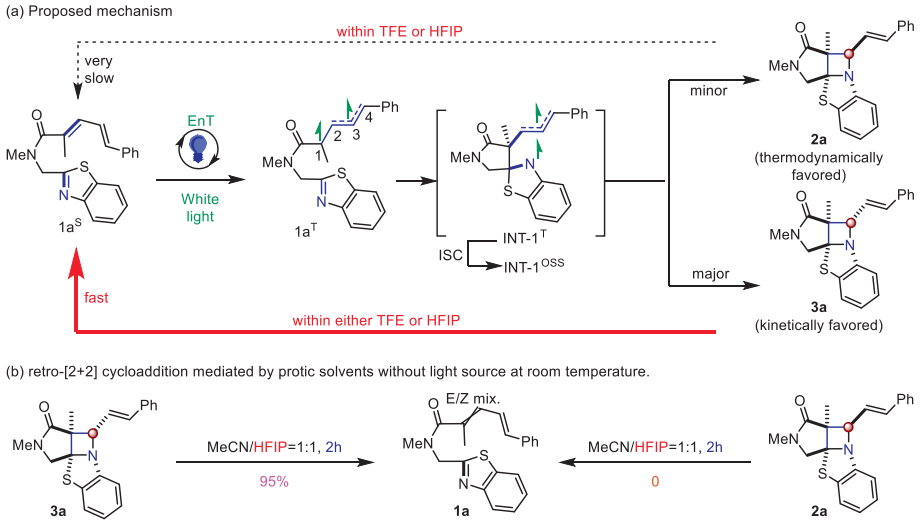
A rate-differential protonic solvent-mediated plausible mechanism were proposed (Scheme 4a). **1a** was excited to the triplet state $\mathbf{1a}^{\mathbf{T}}$ from its ground singlet state $\mathbf{1a}^{\mathbf{S}}$ *via* EnT process within the presence of photosensitizer under irradiation. $\mathbf{1a}^{\mathbf{T}}$ underwent a dearomative addition leading to diradical $\mathbf{INT\text{-}1}^{\mathbf{T}}$, which upon intersystem crossing (forming its open shell singlet state $\mathbf{INT\text{-}1}^{\mathbf{OSS}}$), led to major kinetically favored aza-[2 + 2] product **3a** and thermodynamical **2a** as minor products. However, **3a** could be quickly (**fast** in Scheme 4a) converted back to **1a** under acidic solvents such as TFE, probably due to hydrogen bond activation of azetidine that weakens C–N bond. On the contrary, **2a** displayed relative stability (very slow in Scheme 4a) under acidic solvent conditions (Scheme 4b). Such a rate-differential retro [2 + 2] reaction combined with the fast forward dearomative aza-[2 + 2] cycloaddition led to net accumulation of thermodynamic **2a**, and realized diastereoselectivity.

The robustness of the current aza-[2 + 2] reaction were tested by subjecting complex ingredients in the reaction solvents. These "liquids" were used directly after commercial purchase (Fig. 2). We found adding commercially available American bourbon or rum did not affect the efficiency of this reaction yielding **2a/3a** in 98% and 97% combined yield, respectively. The different dr ratio might imply that there are certain acidic ingredients in American bourbon that play a similar role as TFE. Surprisingly, the reaction yielded quantitative yield of **2a/3a** combined, even if the coffee concentrate were used as co-solvent, which are known to contain complex alkaloids, organic acids and lipids.

With the confidence gained from the above test, we set off to explore the aza-[2 + 2]'s synthetic applicability. Since we are able to access the densely decorated azetidines bearing contiguously stereocenters, it would be ideal to do ring expansions, which allow us to access the more commonly encountered aza five- and six-membered rings (Scheme 5). We attempted a Meisenheimer rearrangement starting from azetidine **2a**, the desired isoxazol product **7** could be obtained in 91% yield. Then a scaffold hopping from vinyl azetidine **5** to piperidine **8** (70% yield) was realized



Scheme 3. Reaction kinetics and control experiments.



Scheme 4. Proposed mechanism and proofs of retro [2 + 2] cycloaddition mediated by acidic solvents.

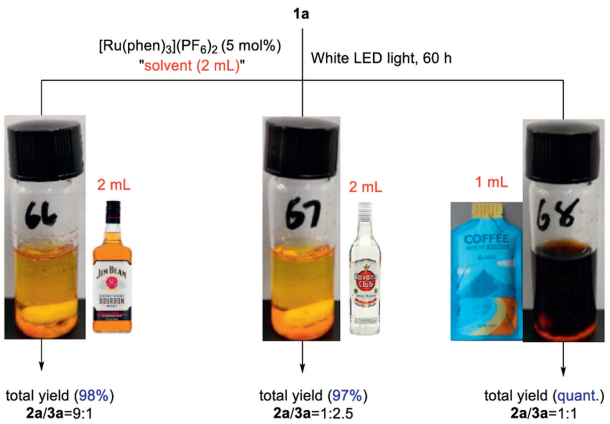


Fig. 2. The robustness of this reaction in complex solvents.

through photoredox mediated reductive quenching of **PC-4** with compound **5**. The net [4 + 2] cycloadduct proved practicality in forging piperidines from dienamide. Additionally, the C–N bond could be formally disconnected and inserted by "C=N" bond or "C=O" bond of TsC=N=O, leading to the formation of **9** (33 % yield) and **9′** (56 % yield). The structure of **9** was unambiguously verified by crystallography. The sulfur atom could be removed by treating compound **2a** with catalytic amount $Co_2(CO)_8$ under CO atmosphere. A dihydro carbazole skeleton can be formed in 55 % yield. Last but not least, a selective oxidation was performed with **2a** using hydroperoxide, obtaining benzothiazole dioxide **6**. It allowed sequential oxidation of azetidine **2a** possible.

In summary, we have disclosed the first example of a proton coupled reversible aza-[2 + 2] reaction, leading to highly diastereoselective azetidines. Feedstock *N*-heteroarenes (containing C=N bonds) were dearomatized through the aza-[2 + 2] under white light *via* energy transfer, which provide an important solution to the limited scope of aza Paterno-Buchi reaction. The rate differential retro [2 + 2] process was observed and harnessed to address the long standing stereochemical problems (controlling all three contiguous stereocenters *dr* >19:1) of aza-[2 + 2] cycloadditions with diene substrates. Over 26 examples were demonstrated with good efficiency (up to 94 % yield). The mechanism investigation and synthetic applications were carried out, providing new perspective in elevating the power of aza-[2 + 2] cycloaddition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

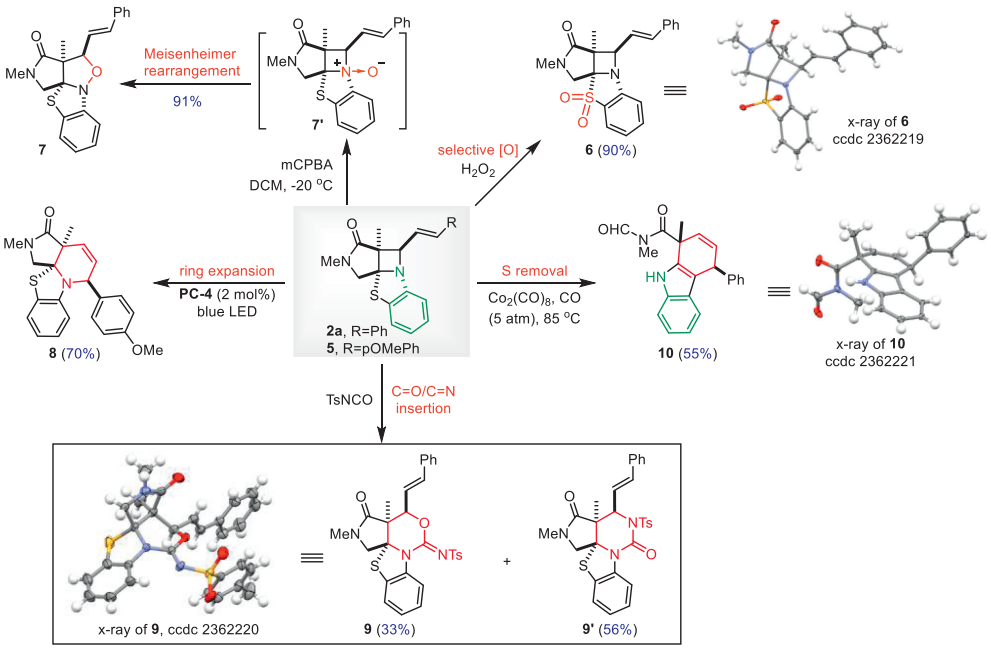
Fujie Liu: Investigation, Methodology. **Yuzhu Yan:** Methodology, Data curation, Investigation. **Xi Wang:** Data curation, Formal analysis. **Lingfei Hu:** Formal analysis. **Gang Lu:** Formal analysis. **Tao Xu:** Writing – review & editing, Writing – original draft, Funding acquisition, Project administration, Conceptualization.

Acknowledgments

The project was supported by Qingdao Marine Science and Technology Center (No. 2022QNLM030003–2) and the National Natural Science Foundation of China (Nos. 82122063 and 81991522).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cclet.2025.111498.



Scheme 5. Synthetic applications of aza-cyclobutanes.

References

[1] P. Bhutani, G. Joshi, N. Raja, et al., J. Med. Chem. 64 (2021) 2339–2381.
[2] M.S. Kinch, J. Merkel, S. Umlauf, Drug Discov. Today 19 (2014) 1682–1685.
[3] E. Vitaku, D.T. Smith, J.T. Njardarson, J. Med. Chem. 57 (2014) 10257–10274.
[4] W. Wei, S. Cherukupalli, L. Jing, X. Liu, P. Zhan, Drug Discov. Today 25 (2020) 1839–1845.
[5] E.S. Toriki, J.W. Papatzimas, K. Nishikawa, et al., ACS Cent. Sci. 9 (2023) 915–926.
[6] C. Mayor-Ruiz, S. Bauer, M. Brand, et al., Nat. Chem. Biol. 16 (2020) 1199–1207.
[7] D.R. Parmar, J.Y. Soni, R. Guduru, et al., Arch. Pharm. 354 (2021) e2100062.
[8] D.J. St. Jean Jr., C. Fotsch, J. Med. Chem. 55 (2012) 6002–6020.
[9] E. Lioudaki, S.G. Emmanuel, P.M. Dimitri, Curr. Vasc. Pharmacol. 9 (2011) 62–86.
[10] G.S. Singh, Mini-Rev. Med. Chem. 4 (2004) 93–109.
[11] J.i. Kobayashi, J.F. Cheng, M. Ishibashi, et al., J. Chem. Soc., Perkin Trans. 5 (1991) 1135–1137.
[12] J.i. Kobayashi, M. Tsuda, J.F. Cheng, et al., Tetrahedron Lett. 37 (1996) 6775–6776.
[13] K. Ohshita, H. Ishiyama, Y. Takahashi, et al., Bioorg. Med. Chem. 15 (2007) 4910–4916.
[14] H. Hayashi, K. Takiuchi, S. Murao, M. Arai, Agric. Biol. Chem. 52 (1988) 2131–2133.
[15] S. Furutani, M. Ihara, K. Lees, et al., Int. J. Parasitol.: Drugs Drug Resist. 8 (2018) 350–360.
[16] L.Z. Lin, G.A. Cordell, C.Z. Ni, J. Clardy, Phytochemistry 30 (1991) 1311–1315.
[17] M. Kitajima, N. Kogure, K. Yamaguchi, H. Takayama, N. Aimi, Org. Lett. 5 (2003) 2075–2078.
[18] L. Pang, D. Yao, F. Gao, et al., Org. Biomol. Chem. 21 (2023) 7242–7254.
[19] N.H. Cromwell, B. Phillips, Chem. Rev. 79 (1979) 331–358.
[20] A. Brandi, S. Cicchi, F.M. Cordero, Chem. Rev. 108 (2008) 3988–4035.
[21] K.C. Majumdar, S.K. Chattopadhyay, Heterocycles in Natural Product Synthesis, John Wiley & Sons, 2011, pp. 40–62.
[22] G.S. Singh, Adv. Heterocycl. Chem. 130 (2020) 1–74.
[23] V. Mehra, I. Lumb, A. Anand, V. Kumar, RSC Adv. 7 (2017) 45763–45783.
[24] B. Alcaide, P. Almendros, C. Aragoncillo, Chem. Rev. 107 (2007) 4437–4492.
[25] K.P. Malarney, S. Kc, V.A. Schmidt, Org. Biomol. Chem. 19 (2021) 8425–8441.
[26] G. He, Y. Zhao, S. Zhang, C. Lu, G. Chen, J. Am. Chem. Soc. 134 (2012) 3–6.
[27] C.M. Hsu, H.B. Lin, X.Z. Hou, et al., J. Am. Chem. Soc. 145 (2023) 19049–19059.
[28] D.C. Miller, R.G. Lal, L.A. Marchetti, F.H. Arnold, J. Am. Chem. Soc. 144 (2022) 4739–4745.
[29] U.K. Nadir, R.L. Sharma, V.K. Koul, J. Chem. Soc., Perkin Trans. 1 (1991) 2015–2019.
[30] H. Mughal, M. Szostak, Org. Biomol. Chem. 19 (2021) 3274–3286.
[31] G. Tan, F. Glorius, Angew. Chem. Int. Ed. 62 (2023) e202217840.
[32] P. Wang, W. Xiao, J. Chen, Nat. Rev. Chem. 7 (2023) 35–50.
[33] J. Zhang, Z. Zheng, C. Zhu, Chin. Chem. Lett. 35 (2024) 109160.
[34] Y. Zhang, V. Palani, A.E. Seim, et al., Science 378 (2022) 383–390.
[35] O. Tsuge, M. Tashiro, K. Oe, Tetrahedron Lett. 9 (1968) 3971–3974.
[36] A.D. Richardson, M.R. Becker, C.S. Schindler, Chem. Sci. 11 (2020) 7553–7561.
[37] M.R. Becker, A.D. Richardson, C.S. Schindler, Nat. Commun. 10 (2019) 5095.
[38] M.R. Becker, E.R. Wearing, C.S. Schindler, Nat. Chem. 12 (2020) 898–905.
[39] M. Zhu, X. Zhang, C. Zheng, S.L. You, ACS Catal. 10 (2020) 12618–12626.
[40] X. Li, J. Großkopf, C. Jandl, T. Bach, Angew. Chem. Int. Ed. 60 (2021) 2684–2688.
[41] W. Wang, M.K. Brown, Angew. Chem. Int. Ed. 62 (2023) e202305622.
[42] Y.L. Wang, P.X. Liu, H.H. Zhang, P.F. Xu, Y.C. Luo, Chem. Commun. 59 (2023) 12467–12470.
[43] J. Huang, T.P. Zhou, N. Sun, et al., Nat. Commun. 15 (2024) 1431.
[44] S.K. Kandappa, L.K. Valloli, S. Ahuja, J. Parthiban, J. Sivaguru, Chem. Soc. Rev. 50 (2021) 1617–1641.
[45] N.A. Meanwell, Chem. Res. Toxicol. 29 (2016) 564–616.
[46] M. Aldeghi, S. Malhotra, D.L. Selwood, A.W.E. Chan, Chem. Biol. Drug Des. 83 (2014) 450–461.
[47] F. Lovering, MedChemComm 4 (2013) 515–519.
[48] The triplet excited-states energies were calculated by Gaussian 09.
[49] L. Schmid, F. Glaser, R. Schaer, O.S. Wenger, J. Am. Chem. Soc. 144 (2022) 963–976.
[50] Z.D. Chen, X. Zhou, J.T. Yi, et al., Org. Lett. 24 (2022) 2474–2478.
[51] K. Teegardin, J.I. Day, J. Chan, J. Weaver, Org. Process Res. Dev. 20 (2016) 1156–1163.
[52] X. Wang, F. Liu, T. Xu, Chin. Chem. Lett. 34 (2023) 107624.
[53] J. Zhang, X. Wang, T. Xu, Nat. Commun. 12 (2021) 3022.
[54] C. Jiang, L. Hu, S. Shen, et al., Angew. Chem. Int. Ed. 63 (2024) e202405838.
[55] Y. Wang, B. Qiu, L. Hu, G. Lu, T. Xu, ACS Catal. 11 (2021) 9136–9142.
[56] X. Li, L. Hu, S. Ma, et al., ACS Catal. 13 (2023) 4873–4881.
[57] J. Ma, S. Chen, P. Bellotti, et al., Science 371 (2021) 1338–1345.
[58] M. Zhu, H. Xu, X. Zhang, C. Zheng, S.L. You, Angew. Chem. Int. Ed. 60 (2021) 7036–7040.
[59] J. Ma, F. Strieth-Kalthoff, T. Dalton, et al., Chem 5 (2019) 2854–2864.
[60] R. Guo, S. Adak, P. Bellotti, et al., J. Am. Chem. Soc. 144 (2022) 17680–17691.
[61] M. Chiminelli, A. Serafino, D. Ruggeri, et al., Angew. Chem. Int. Ed. 62 (2023) e202216817.
[62] A.E. Hurtley, Z. Lu, T.P. Yoon, Angew. Chem. Int. Ed. 53 (2014) 8991–8994.
[63] D.H. Liu, J. Ma, Angew. Chem. Int. Ed. 63 (2024) e202402819.
[64] M. Rao, W. Wu, C. Yang, Green Synth. Catal. 2 (2021) 131–144.