Diastereoselective Dearomative 1,3-Dipolar Cycloaddition of Bicyclobutanes with Pyridinium Ylides: A Modular Approach to Multisubstituted Azabicyclo[3.1.1]heptanes

Kushal Dhake,[†[a]] Kyla J. Woelk,[†[a]], Liam D. N. Krueckl,[a] Faith Alberts,[a] James Mutter,[a] Matthew O. Pohl,[a] Gilian T. Thomas,[a] Muskan Sharma,[a] Jaelyn Bjornerud-Brown,[a] Nahiane Pipaón Fernández,[a] Nathan D. Schley,[b] and David C. Leitch*[a]

[a] K. Dhake, K. J. Woelk, L. D. N. Krueckl, F. Alberts, J. Mutter, M. O. Pohl, Dr. G. T. Thomas, M. Sharma, J. Bjornerud-Brown, N. P. Fernández, Prof. Dr. D. C. Leitch
Department of Chemistry
University of Victoria
3800 Finnerty Rd., Victoria, BC V8P 5C2 (Canada)
E-mail: dcleitch@uvic.ca

[b] Prof. Dr. Nathan D. Schley
Department of Chemistry
Vanderbilt University
2301 Vanderbilt Place Nashville, TN, 37235, (United States)

[†] These authors contributed equally to this work. Supporting information for this article is given via a link at the end of the document.

Abstract: We describe a formal 1,3-dipolar cycloaddition between bicyclobutanes and pyridinium ylides to form azabicycloheptanes *via* diastereoselective pyridine dearomatization. Microscale high-throughput experimentation led to identification of conditions affording high yield and stereoselectivity without the need for catalysis. These reactions proceed using as-received reagents and solvents under ambient atmosphere. The resulting ring-fused azabicyclo[3.1.1]heptanes have diverse synthetic handles for further transformations, making them potentially valuable scaffolds for the design of C*sp*^{3}-rich drug candidates. We also demonstrate a diastereoselective photochemical skeletal rearrangement to give a 1,1,3,3-tetrasubstitued cyclobutane.

For over a decade, 'escaping from flatland' – increasing the fraction of *Csp*^{3} centers in target molecules – has been a rallying cry in medicinal chemistry.[1,2] One approach is to exploit the concept of bioisosterism[3] to replace aromatic units with rigid, C*sp*^{3}-rich multicyclic ring systems. This is demonstrated to improve the pharmacokinetic and physicochemical properties of existing drug candidates and marketed approved drug molecules.[4,5] Most published research to date focuses on bicyclic compounds as phenyl bioisosteres,[6] such as small-ring bicycloalkanes,[7–9] and cubanes[10,11] (Figure 1A).

In contrast, there are a dearth of approaches toward bioisosteres of aromatic *N*-heterocycles, despite the fact such heterocycles are an essential part of pharmaceuticals and drug discovery.[12] This is due to the limited number of modular approaches for synthesizing the relevant azabicyclic scaffolds (Figure 1B).[13] In 2023, Mykhailiuk and co-workers reported a novel synthesis of azabicyclo[3.1.1]heptanes from spirocyclic oxetanes.[14] Subsequent work from several groups exploited the reactivity of bicyclobutanes (BCBs) to effect formal cycloaddition reactions, including with nitrones (Deng and co-workers),[15] isocyanides (Glorius and co-workers),[16] and vinyl azides (Zheng and co-workers,[17] and Li/Wang and co-workers[18]). While finalizing this paper, we noted that Li and co-workers reported a Cu-catalyzed cycloaddition of azomethine ylides to BCBs to give azabicyclo[3.1.1]heptanes.[19]

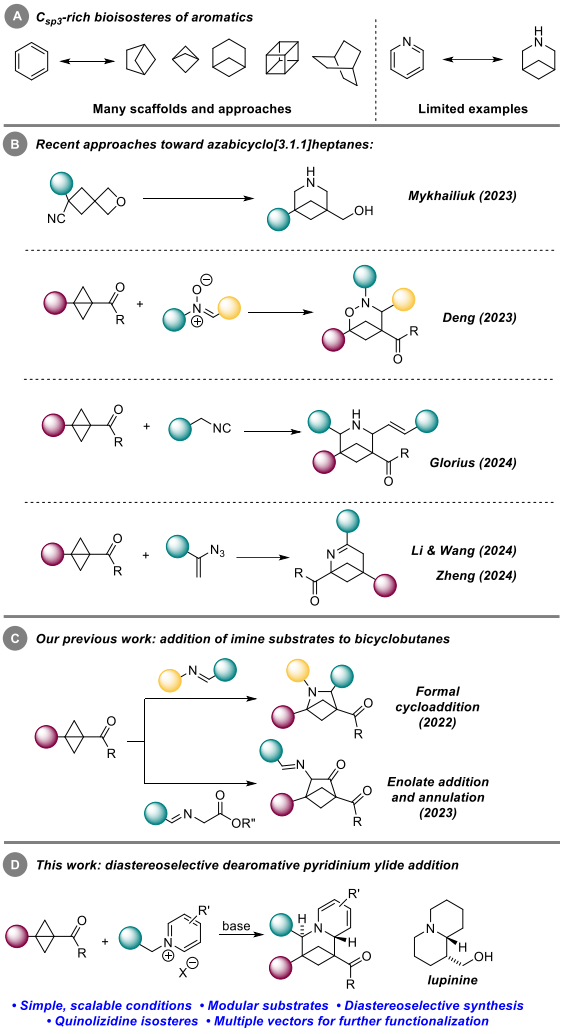
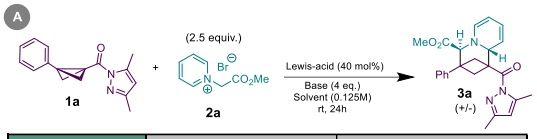


Figure 1. A) Bioisosteres for substituted phenyl and pyridine rings. **B)** Existing routes to azabicyclo[3.1.1]heptanes. **C)** Our previous work on imine and enolate addition to bicyclobutanes. **D)** Diastereoselective 1,3-dipolar cycloaddition approach to 3-azabicyclo[3.1.1]heptanes.



3a % Yield		THF			MeCN		
		Cs_2CO_3	K_3PO_4	NEt_3	Cs_2CO_3	K_3PO_4	NEt_3
		1	2	3	4	5	6
LiOTf	A	57%	46%	0%	57%	30%	0%
$Mg(OTf)_2$	B	**61%**	38%	0%	56%	**82%**	6%
$Zn(OTf)_2$	C	52%	25%	0%	**65%**	50%	0%
AgOTf	D	31%	**68%**	0%	**64%**	36%	0%
none	E	**69%**	**70%**	0%	**73%**	**86%**	0%

Diastereomeric Ratio (dr)		THF			MeCN		
		Cs_2CO_3	K_3PO_4	NEt_3	Cs_2CO_3	K_3PO_4	NEt_3
		1	2	3	4	5	6
LiOTf	A	2.4 : 1	5.6 : 1	-	>20 : 1	>20 : 1	-
$Mg(OTf)_2$	B	3.1 : 1	2.8 : 1	-	>20 : 1	>20 : 1	>20 : 1
$Zn(OTf)_2$	C	4.8 : 1	4.0 : 1	-	>20 : 1	>20 : 1	-
AgOTf	D	3.4 : 1	8.7 : 1	-	>20 : 1	>20 : 1	-
none	E	1.1 : 1	1.6 : 1	-	>20 : 1	>20 : 1	-

1a % Remaining		THF			MeCN		
		Cs_2CO_3	K_3PO_4	NEt_3	Cs_2CO_3	K_3PO_4	NEt_3
		1	2	3	4	5	6
LiOTf	A	15%	37%	90%	15%	3%	>99%
$Mg(OTf)_2$	B	17%	50%	81%	0%	0%	74%
$Zn(OTf)_2$	C	24%	60%	80%	3%	6%	58%
AgOTf	D	32%	18%	94%	5%	16%	68%
none	E	3%	3%	>99%	3%	3%	70%

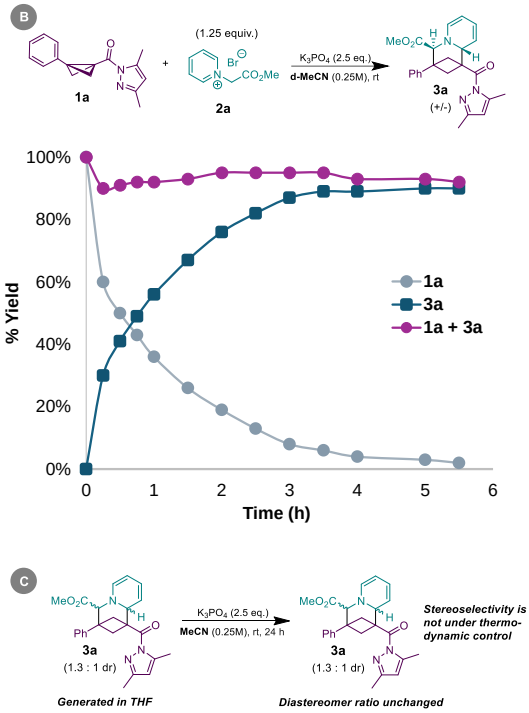


Figure 2. A) Microscale high-throughput screening results (^{1}H NMR spectroscopy solution yields and diastereoselectivities using 1,3,5-trimethoxybenzene internal standard) for pyridinium ylide **2a** addition to bicyclobutane **1a**. **B)** Reaction progress plot monitored by ^{1}H NMR spectroscopy. **C)** Test for thermodynamic control of diastereoselectivity, revealing no epimerization of **3a** under the optimized conditions (K_3PO_4, MeCN).

Our group has been focused on exploiting polar mechanisms for elaborating BCBs to more complex ring systems (Figure 1C), including the first examples of formal [2σ+2π] cycloaddition between imines and BCBs (giving azabicyclo[2.1.1]hexanes),[20] and the first examples of enolate addition to BCBs (giving 2-oxobicyclohexanes after annulation).[21] This latter work in particular provides the key precedent for carbon nucleophile addition to BCBs as a first step in stepwise polar cycloadditions, such as those from Glorius[16] and now from Li.[19] We envisioned that combining the mechanistic aspects of the imine addition and enolate addition processes would enable formal 1,3-dipolar cycloaddition. Herein we report a dearomative, diastereoselective, dipolar cycloaddition of BCBs with pyridinium ylides in the presence of a mild base to give highly substituted, ring-fused azabicyclo[3.1.1]heptanes (Figure 1D). Beyond the potential for simple pyridine bioisosterism, these multicyclic scaffolds could serve as pharmacophores in their own right, given the core quinolizidine structure is present in several alkaloid families, including the lupinine alkaloids.[22,23]

Since our initial report in 2022,[20] many groups have exploited the Lewis acid catalyzed reactivity of BCBs.[24–41] Based on this now ample precedent, we hypothesized that Lewis acids could effect a dipolar cycloaddition between BCBs and pyridinium ylides. In addition to the complex multicyclic scaffold that would result, pyridinium ylides are modular reagents that are simple to access from *N*-alkylpyridinium salts.[42] Initial reaction discovery was enabled by microscale high-throughput experimentation (Figure 2). Using Glorius's acylpyrazole BCB (**1a**)[30] and simple pyridinium **2a**, we screened a variety of solvents, bases, and Lewis acids. A 30-reaction multivariate array was conducted at room temperature, selecting four Lewis acids (LiOTf, $Mg(OTf)_2$, $Zn(OTf)_2$, and AgOTf), three bases (Cs_2CO_3, K_3PO_4, NEt_3) and two solvents (THF and MeCN). We also included a set of control experiments where no Lewis acid was used (Figure 2A).

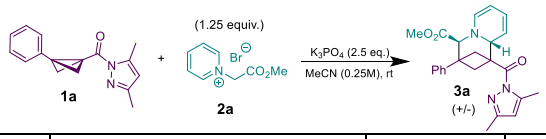
A holistic analysis of the resulting data reveals that: **1)** Lewis acids are not required, and are even detrimental in most cases; **2)** an inorganic base is required, with K_3PO_4 giving the best results; **3)** diastereoselectivity is solvent dependent, with THF giving diastereomeric ratio (dr) values between 1:1 - 9:1, whereas only a single diastereomer is observed in MeCN. The major diastereomer is assigned as the structure with the two methine hydrogens *anti* to one another (*vide infra*). Finally, screening at 60 °C revealed poor stereoselectivity across all conditions tested (Table S2, Supporting Information).

Overall, using K_3PO_4 as the base with no Lewis acid in acetonitrile gave the highest solution yield of 86%. These conditions were carried forward into a full factorial screen to optimize the reagent loadings and reaction concentration. These studies revealed the yield and stereoselectivity are relatively insensitive to changes in these factors. Best results are obtained with lower pyridinium loadings (1.25 equiv **2a**), higher base loadings (2.5 equiv), and higher reaction concentrations (0.25 M) (Table S3, Supporting Information). We then monitored reaction progress by ^{1}H NMR spectroscopy (Figure 2B). The conversion to **3a** is fairly rapid at room temperature, with a first half-life of 30 min, and subsequent half-lives of 1 h. Throughout the course of NMR monitoring, we observe no clear intermediates, and no evidence of the minor diastereomer. Tracking the mass balance further supports these observations, with the %**1a** + %**3a** averaging 93% with a standard deviation of only 2% (excluding *t* = 0). Finally, to test whether the diastereomer ratio is under thermodynamic control *via* rapid epimerization in MeCN, we subjected a nearly 1:1 mixture of **3a** diastereomers to the optimized reaction conditions (K_3PO_4 in MeCN, rt, 24 h); no change to the dr is observed, confirming stereochemistry is under kinetic control.

Finally, we studied the impact of the base, water content, and temperature on the reaction (Table 1). As expected, without

K_3PO_4 the reaction does not proceed, returning 84% of **1a** after 24 h. Slightly elevated temperature (30 °C) or addition of 10 equiv water (from Na_2SO_4•$10H_2O$) does not significantly affect the reaction yield. Adding 4 Å molecular sieves reduced the solution yield to 66%. This may be due to the aforementioned detrimental effect of Lewis acids on the reaction, or may be simply due to inefficient mixing by addition of more insoluble material. Overall, this reaction is insensitive to oxygen, water, as well as slight changes in temperature or reactant/reagent charges.

Table 1. Control reactions for the synthesis of **3a** with optimized conditions.



Entry	Deviation from standard[a]	3a[b][c]	1a[b]
1	No K_3PO_4 added	0	84
2	Run at 30 °C	81	5
3	Na_2SO_4•$10H_2O$ (1 equiv)	81	6
4	4 Å molecular sieves	66	12

[a]Reactions are performed at room temperature for 24 hours with 0.05 mmol of **1a**. [b]Amounts of **1a** and **3a** are obtained by ^{1}H NMR spectroscopy by relative integration vs. internal standard, 1,3,5-trimethoxybenzene (TMB). [c]Only one diastereomer of **3a** is observed.

With robust conditions identified, we next explored the reaction scope using a diverse set of bicyclobutanes and *N*-alkyl pyridinium salts possessing various functional groups and steric/electronic properties (Figure 3). Initial isolation attempts revealed that the dihydropyridine-containing products are not stable to silica gel chromatography; therefore, we used basic alumina as an alternative stationary phase. Isolation is achieved by reaction solvent evaporation, redissolution in dichloromethane, and passage of this solution through a pad of basic alumina followed by exhaustive elution with additional dichloromethane. The prototype compound **3a** was prepared in this manner on 0.30 mmol scale in 88% yield, and 65% yield on 2.0 mmol scale. Once isolated, the 3-azabicyclo[3.1.1]heptane compounds are stable in their respective physical states.

With respect to bicyclobutane scope, other arylbicyclobutanes possessing the acylpyrazole electron-withdrawing group are suitable, affording **3b**, **3c,** and **3d** with good to moderate yields. We also conducted single-crystal X-ray diffraction for **3c**, which confirms the relative configuration of the major diastereomer. Importantly, this cycloaddition reactivity also occurs using mono-substituted bicyclobutanes, making this chemistry a relatively rare example that can function with both mono and disubstituted BCBs, albeit with modest yields. To enable this, we prepared a monosubstituted *N*-acylpyrazole BCB, **1e**, inspired by Glorius's BCB **1a**.[20] Product **3e** is formed as a single diastereomer, whereas **3f** (derived from a ketone-based pyridinium ylide) gives a similar yield but with a diminished 6:1 diastereomer ratio. In addition to *N*-acylpyrazole BCBs, mono and disubstituted BCBs containing aryl ketones also react, giving **3g**, **3h**, and **3i**. Notably, BCBs with weaker electron-withdrawing groups (esters, amides) do not react in this chemistry (see Supporting Information).

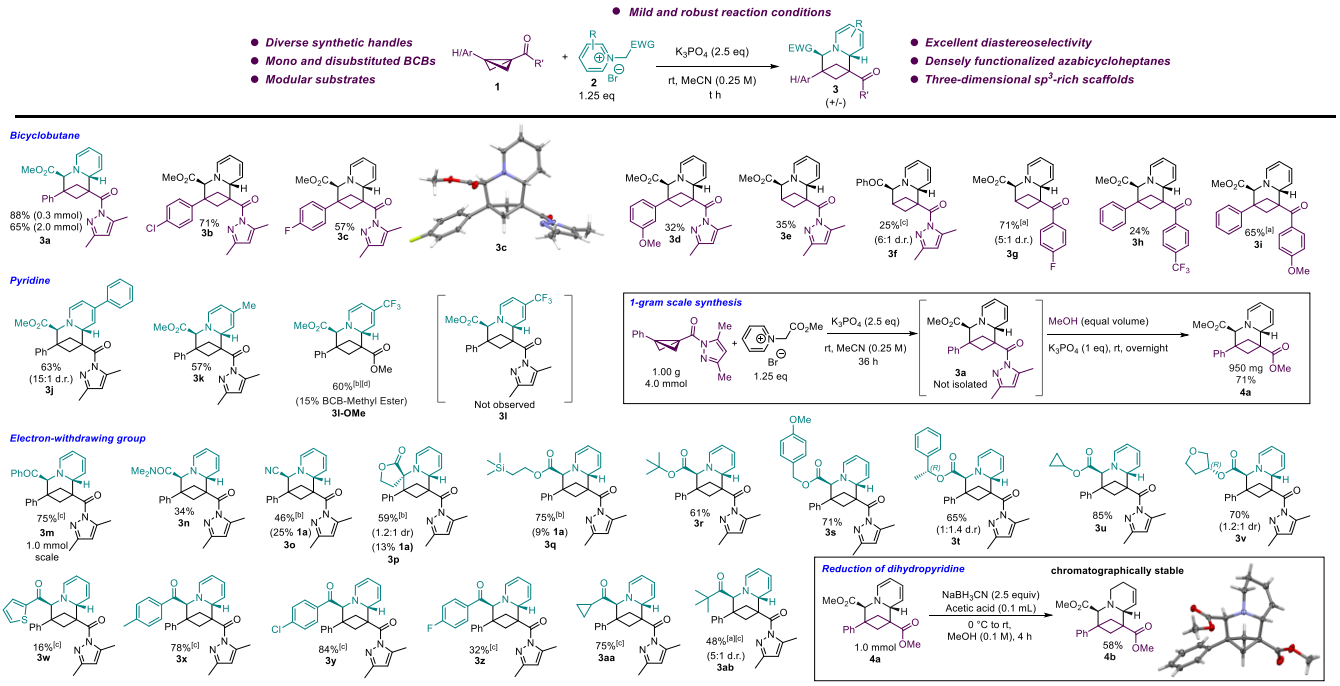


Figure 3. Scope of azabicyclo[3.1.1]heptanes **3** via pyridinium ylide addition to bicyclobutanes. Yields are for isolated compounds following a basic alumina plug purification and are obtained as a single diastereomer unless otherwise noted with dr values in parentheses (determined by ^{1}H NMR spectroscopy). Two examples of further reactivity are shown, including telescoped methanolysis to give **4a**, and monoreduction of **4a** to give silica-stable product **4b.** [a]Yield determined by ^{1}H NMR spectroscopy (with internal standard 1,3,5-trimethoxybenzene). [b]Isolated yield as part of a mixture with unreacted bicyclobutane starting material. [c]Reaction performed using $NaPF_6$ (1.3 equiv) as an additive. [d]Reaction performed in methanol. Single crystal XRD structures are deposited with the CCDC: 2374388-2374389.

We also examined the effect of pyridinium ylide substituents on reactivity. Direct substitution of the pyridine ring led to significant differences in reactivity. For instance, using 4-phenyl or 4-methyl pyridiniums, we isolated **3j** and **3k** in 63% and 57% yield, respectively, with high diastereoselectivity; however, when we tested a 4-CF_3 pyridinium, we observed only a 7% solution yield of product **3l**, with the mass balance mainly unreacted bicyclobutane. Taking inspiration from prior studies of pyridinium ylide cycloadditions and the role of bases and solvents,[43,44] we examined the use of a protic reaction solvent to increase reactivity. With MeOH as the solvent, we are able to effect cycloaddition accompanied by methanolysis of the *N*-acylpyrazole to yield **3l-OMe** in 60% yield (along with 15% of co-eluting unreacted bicyclobutane). Given that ester-substituted BCBs are unreactive toward cycloaddition, we propose that this reaction proceeds by rapid cycloaddition followed by slower methanolysis of the acylpyrazole unit.

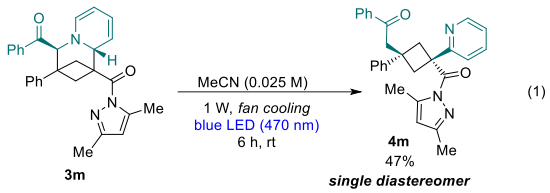
With respect to the electron-withdrawing group of the pyridinium ylide, we examined a wide range of functional groups and substituents, including ketone (**3m**), amide (**3n**), and nitrile (**3o**) EWGs. Using a ketone-based EWG to generate **3m** initially led to low yield, which we improved to 80% solution yield by the addition of catalytic $Mg(OTf)_2$ (the only reasonably successful Lewis acid in MeCN, Figure 2A). This prompted us to consider the potential role of $Mg(OTf)_2$ given its relatively poor solubility. We hypothesized that, rather than acting as a Lewis acid to activate the BCB and/or ylide, it may simply effect salt metathesis to convert the pyridinium bromide salt into a pyridinium triflate.

To test this salt metathesis possibility, we investigated $NaPF_6$ as an additive; NaBr is almost completely insoluble in MeCN, so this should be an effective method to swap the pyridinium counterion. With 1.3 equiv of $NaPF_6$, we were able to isolate **3m** in 75% yield. This method was adopted for all ketone-based pyridinium ylides (**3f** and **3w-3ab**). Both (hetero)aryl and alkyl ketones are suitable, including the cyclopropyl ketone resulting in **3aa** in 75% isolated yield. In each case, we observe a single diastereomer, except for the *t*-butyl-substituted ketone product **3ab**. This product is generated as a mixture of diastereomers and does contain additional impurities after alumina treatment; however, the fact that such a sterically-encumbered ylide can still undergo cycloaddition to some degree is remarkable.

In general, ester-based pyridinium ylides are superior substrates for this chemistry (**3p**-**3v**). Primary (**3q**, **3s**), secondary (**3t**, **3u**, **3v**), and even tertiary (**3r**) substituents at oxygen are amenable, as is the highly substituted lactone in **3p**. Notably, this derivative is formed in a nearly 1:1 mixture of diastereomers. Chiral esters in **3t** and **3v** do not induce any significant stereocontrol over the absolute stereochemistry of the resulting products, and the dr values given reflect the ratio between the two different *anti* diastereomers.

To further demonstrate synthetic utility, we carried out the preparation **3a** on gram scale, and telescoped **3a** into a methanolysis of the acylpyrazole to generate the corresponding methyl ester **4a** in 71% isolated yield. We also successfully monoreduced the dihydropyridine in **4a** on 1.0 mmol scale using sodium cyanoborohydride to afford 58% of **4b** as a single diastereomer. Importantly, this compound is stable on silica, enabling purification by flash column chromatography. We also subjected a single crystal of **4b** to X-ray diffraction, confirming the site of reduction.

As a further demonstration of synthetic versatility, we hypothesized that a light-mediated aza-Norrish II rearrangement – hydrogen atom transfer and concomitant C–N cleavage – of **3m** could lead to a highly functionalized and stereochemically-defined cyclobutane.[45,46] Irradiating an acetonitrile solution of **3m** with blue LED light (470 nm) for 6 h with fan cooling affords 47% of **4m**, which contains two quaternary centers on a cyclobutane unit with complete control over relative stereochemistry (eq. 1).



(1)

Mechanistically, this cycloaddition could proceed via several possible pathways. Our working hypothesis, based on our previous work (Figure 4A and B),[12,13] is a stepwise polar mechanism (Figure 4C). Initial nucleophilic attack by the *in situ* generated ylide proceeds to give a reactive cyclobutane enolate with a pendant electrophile. Intramolecular attack by the enolate to the pyridinium then proceeds to close the bicyclic system. A simple diastereoselectivity model (analogous to that proposed for imine addition stereoselectivity[20]) based on strain minimization in the cyclization transition state is consistent with the observed major diastereomer, and work is underway to fully elucidate the mechanistic features and aforementioned solvent dependence.

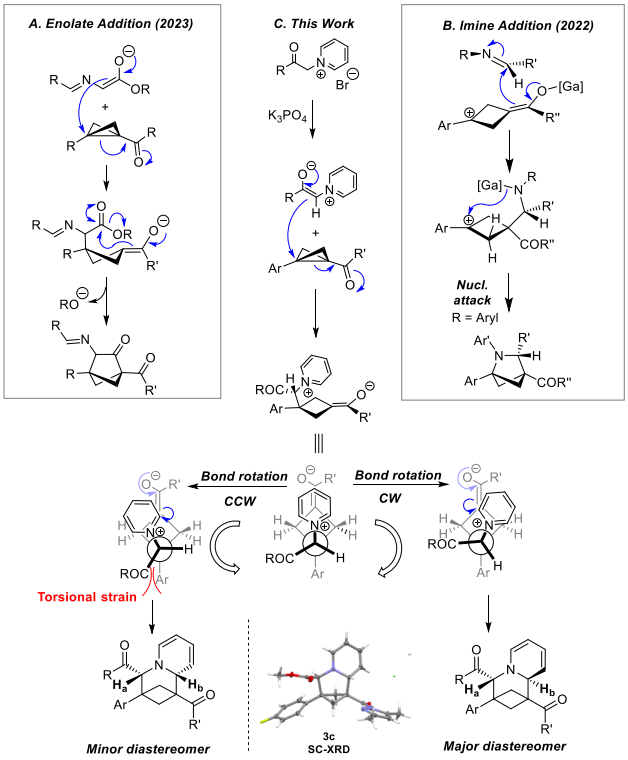


Figure 4. A) Previously reported mechanism for enolate addition to bicyclobutanes.[21] **B)** Previously reported mechanism for imine addition to bicyclobutanes.[20] **C)** Proposed mechanism for the formation of azabicycloheptanes **3**, and simple stereochemical model for the observed diastereoselectivity (CW = clockwise; CCW = counterclockwise).

In summary, we have developed a modular approach to synthesize densely functionalized azabicyclo[3.1.1]heptanes *via* a formal (3+3) dipolar cycloaddition of pyridinium ylides with bicyclo[1.1.0]butanes. The resulting azabicycloheptanes possess a multicyclic core analogous to the quinolizidine family of heterocycles, and thus offer an opportunity to explore new chemical space in the search for new drug candidates with higher three-dimensionality and rigidity. The product synthetic handles provide a platform to derivatize different vectors. Work is ongoing to explore the structure-reactivity relationships of pyridinium (and other) ylides in cycloaddition reactions with small strained rings, as well as to elucidate the mechanistic details underpinning stereoselectivity. These efforts are in line with our objective of developing techniques to access complex, Csp^3-rich scaffolds pertinent to the synthesis and development of new pharmaceuticals, ideally beyond their use as simple isosteric replacements.

Acknowledgments

We acknowledge with respect the Lekwungen peoples, on whose traditional territory the University of Victoria (UVic) stands, and the Songhees, Esquimalt, and WSÁNEĆ peoples whose historical relationships with the land continue to this day. We also thank UVic, NSERC, CFI, and BCKDF for general operating and equipment funds. This work was also funded by a New Directions Grant from the ACS Petroleum Research Fund (66652-ND1).

Keywords: dearomatization • cycloaddition • heterocycles • stereoselective • bicyclobutane • azabicycloheptane

[1] F. Lovering, J. Bikker, C. Humblet, *J. Med. Chem.* **2009**, *52*, 6752–6756.
[2] F. Lovering, *Med. Chem. Commun.* **2013**, *4*, 515-519.
[3] G. A. Patani, E. J. LaVoie, *Chem. Rev.* **1996**, *96*, 3147–3176.
[4] M. A. M. Subbaiah, N. A. Meanwell, *J. Med. Chem.* **2021**, *64*, 14046–14128.
[5] M. R. Bauer, P. Di Fruscia, S. C. C. Lucas, I. N. Michaelides, J. E. Nelson, R. I. Storer, B. C. Whitehurst, *RSC Med. Chem.* **2021**, *12*, 448–471.
[6] P. K. Mykhailiuk, *Org. Biomol. Chem.* **2019**, *17*, 2839–2849.
[7] R. Gianatassio, J. M. Lopchuk, J. Wang, C.-M. Pan, L. R. Malins, L. Prieto, T. A. Brandt, M. R. Collins, G. M. Gallego, N. W. Sach, J. E. Spangler, H. Zhu, J. Zhu, P. S. Baran, *Science* **2016**, *351*, 241–246.
[8] C. B. Kelly, J. A. Milligan, L. J. Tilley, T. M. Sodano, *Chem. Sci.* **2022**, *13*, 11721-11737.
[9] V. V. Semeno, V. O. Vasylchenko, I. M. Fesun, L. Yu. Ruzhylo, M. O. Kipriianov, K. P. Melnykov, A. Skreminskyi, R. Iminov, P. Mykhailiuk, B. V. Vashchenko, O. O. Grygorenko, *Chem. Eur. J.* **2024**, *30*, e202303859.
[10] B. A. Chalmers, H. Xing, S. Houston, C. Clark, S. Ghassabian, A. Kuo, B. Cao, A. Reitsma, C.-E. P. Murray, J. E. Stok, G. M. Boyle, C. J. Pierce, S. W. Littler, D. A. Winkler, P. V. Bernhardt, C. Pasay, J. J. De Voss, J. McCarthy, P. G. Parsons, G. H. Walter, M. T. Smith, H. M. Cooper, S. K. Nilsson, J. Tsanaktsidis, G. P. Savage, C. M. Williams, *Angew. Chem. Int. Ed.* **2016**, *55*, 3580–3585.
[11] M. P. Wiesenfeldt, J. A. Rossi-Ashton, I. B. Perry, J. Diesel, O. L. Garry, F. Bartels, S. C. Coote, X. Ma, C. S. Yeung, D. J. Bennett, D. W. C. MacMillan, *Nature* **2023**, *618*, 513–518.
[12] C. M. Marshall, J. G. Federice, C. N. Bell, P. B. Cox, J. T. Njardarson, *J. Med. Chem.* **2024**, *67*, 11622–11655.
[13] J. Tsien, C. Hu, R. R. Merchant, T. Qin, *Nat Rev Chem* **2024**, 1–23.
[14] D. Dibchak, M. Snisarenko, A. Mishuk, O. Shablykin, L. Bortnichuk, O. Klymenko-Ulianov, Y. Kheylik, I. V. Sadkova, H. S. Rzepa, P. K. Mykhailiuk, *Angew. Chem. Int. Ed.* **2023**, *62*, e202304246.
[15] J. Zhang, J.-Y. Su, H. Zheng, H. Li, W.-P. Deng, *Angew. Chem.* **2024**, *136*, e202318476.
[16] Y. Liang, R. Nematswerani, C. G. Daniliuc, F. Glorius, *Angew. Chem. Int. Ed.* **2024**, *63*, e202402730.
[17] Z. Lin, H. Ren, X. Lin, X. Yu, J. Zheng, *J. Am. Chem. Soc.* **2024**, *146*, 18565–18575.
[18] Y. Liu, S. Lin, Z. Ding, Y. Li, Y.-J. Tang, J.-H. Xue, Q. Li, P. Li, H. Wang, *ChemRxiv* **2024**, DOI: 10.26434/chemrxiv-2024-n3wlw.
[19] X. Wang, R. Gao, X. Li, *J. Am. Chem. Soc.* **2024**, DOI: 10.1021/jacs.4c06436.
[20] K. Dhake, K. J. Woelk, J. Becica, A. Un, S. E. Jenny, D. C. Leitch, *Angew. Chem. Int. Ed.* **2022**, *61*, e202204719.
[21] K. J. Woelk, K. Dhake, N. D. Schley, D. C. Leitch, *Chem. Commun.* **2023**, *59*, 13847–13850.
[22] I. A. Schepetkin, Z. S. Nurmaganbetov, S. D. Fazylov, O. A. Nurkenov, A. I. Khlebnikov, T. M. Seilkhanov, A. S. Kishkentaeva, E. E. Shults, M. T. Quinn, *Molecules* **2023**, *28*, 3357.
[23] P. H. Lam, J. K. Kerkovius, S. E. Reisman, *Org. Lett.* **2023**, *25*, 8230–8233.
[24] L. Tang, Y. Xiao, F. Wu, J.-L. Zhou, T.-T. Xu, J.-J. Feng, *Angew. Chem. Int. Ed.* **2023**, *62*, e202310066.
[25] A. Guin, S. Bhattacharjee, M. S. Hararіya, A. T. Biju, *Chem. Sci.* **2023**, *14*, 6585–6591.
[26] L. Tang, Q.-N. Huang, F. Wu, Y. Xiao, J.-L. Zhou, T.-T. Xu, W.-B. Wu, S. Qu, J.-J. Feng, *Chem. Sci.* **2023**, *14*, 9696–9703.
[27] S.-L. Lin, Y.-H. Chen, H.-H. Liu, S.-H. Xiang, B. Tan, *J. Am. Chem. Soc.* **2023**, *145*, 21152–21158.
[28] D. Ni, S. Hu, X. Tan, Y. Yu, Z. Li, L. Deng, *Angew. Chem. Int. Ed.* **2023**, *62*, e202308606.
[29] L. Tang, Y. Xiao, F. Wu, J.-L. Zhou, T.-T. Xu, J.-J. Feng, *Angew. Chem. Int. Ed.* **2023**, *62*, e202310066.
[30] Y. Liang, F. Paulus, C. G. Daniliuc, F. Glorius, *Angew. Chem. Int. Ed. Engl* **2023**, *62*, e202305043.
[31] N. Radhoff, C. G. Daniliuc, A. Studer, *Angew. Chem. Int. Ed.* **2023**, *62*, e202304771.
[32] J.-J. Wang, L. Tang, Y. Xiao, W.-B. Wu, G. Wang, J.-J. Feng, *Angew. Chem. Int. Ed.* **2024**, *63*, e202405222.
[33] L. Yang, H. Wang, M. Lang, J. Wang, S. Peng, *Org. Lett.* **2024**, *26*, 4104–4110.
[34] J.-Y. Su, J. Zhang, Z.-Y. Xin, H. Li, H. Zheng, W.-P. Deng, *Org. Chem. Front.* **2024**, DOI 10.1039/D4QO00511B.
[35] A. Guin, S. Deswal, M. S. Hararіya, A. T. Biju, *Chem. Sci.* **2024**, DOI 10.1039/D4SC02194K.
[36] S. Hu, Y. Pan, D. Ni, L. Deng, *Nat. Commun.* **2024**, *15*, 6128.
[37] S. Nicolai, J. Waser, *Chem. Sci.* **2024**, *15*, 10823–10829.
[38] S. Zhu, X. Tian, S.-W. Li, *Org. Lett.* **2024**, DOI 10.1021/acs.orglett.4c01512.
[39] Y. Xiao, F. Wu, L. Tang, X. Zhang, M. Wei, G. Wang, J.-J. Feng, *Angew. Chem. Int. Ed.* **2024**, *63*, e202408578.
[40] K. Zhang, S. Tian, W. Li, X. Yang, X.-H. Duan, L.-N. Guo, P. Li, *Org. Lett.* **2024**, *26*, 5482–5487.
[41] Q.-Q. Hu, L.-Y. Wang, X.-H. Chen, Z.-X. Geng, J. Chen, L. Zhou, *Angew. Chem. Int. Ed.* **2024**, *63*, e202405781.
[42] L. D. Funt, M. S. Novikov, A. F. Khlebnikov, *Tetrahedron* **2020**, *76*, 131415.
[43] S. Bonte, I. O. Ghinea, R. Dinica, I. Baussanne, M. Demeunynck, *Molecules* **2016**, *21*, 332.
[44] Z. Dega-Szafran, G. Schroeder, M. Szafran, A. Szwajca, B. Łęska, M. Lewandowska, *J. Mol. Struct.* **2000**, *555*, 31–42.
[45] D. Zhang, Z. Su, Q. He, Z. Wu, Y. Zhou, C. Pan, X. Liu, X. Feng, *J. Am. Chem. Soc.* **2020**, *142*, 15975–15985.
[46] R.-B. Hu, S. Sun, Y. Su, *Angew. Chem. Int. Ed.* **2017**, *56*, 10877–10880.