Synthesis of N–H Aziridines from Unactivated Olefins Using Hydroxylamine-*O*-Sulfonic Acids as Aminating Agent

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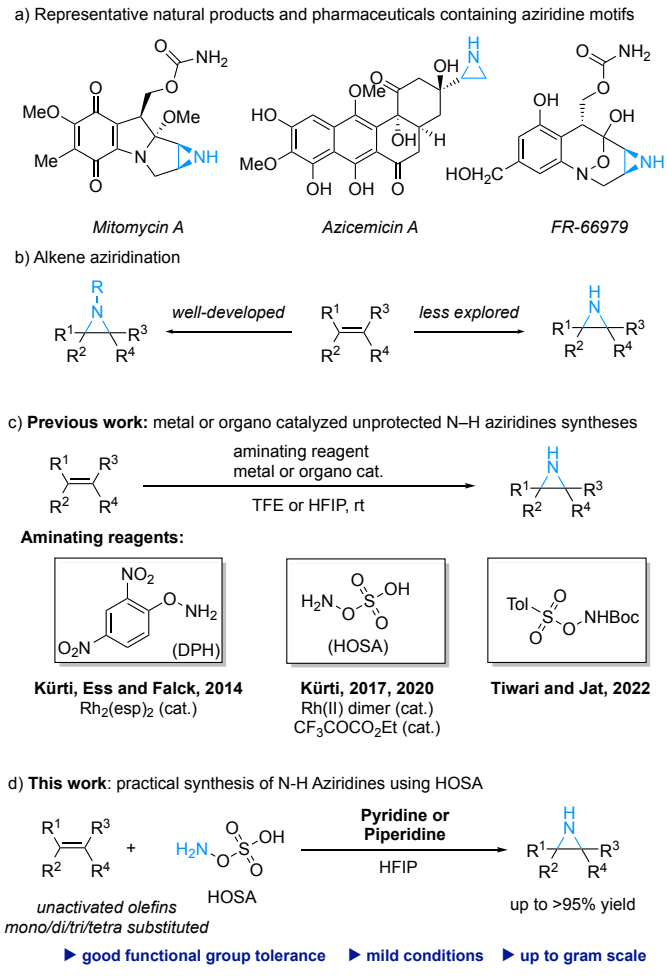
Abstract: Herein, we presented a practical methodology for the intermolecular aziridination of alkenes, using HOSA as the aminating agent, alongside pyridine or piperidine as the base, within HFIP solvent system. Notably, this approach showcases excellent reactivity, especially with non-activated alkenes, and facilitates the transformation of various alkenes substrates, including mono-, di-, tri, and tetra-substituted alkenes, into aziridines with moderate to excellent yield. This method presents a promising avenue for synthesizing aziridines from a wide range of alkenes, featuring the benefits of straightforward operation, mild reaction conditions, extensive substrate compatibility, and scalability.

Introduction

Aziridines, recognized as the smallest nitrogen-containing heterocyclic compounds, are a "privileged scaffold" extensively found in natural products and pharmaceuticals, such as Mitomycin A (antitumor agents), Azicemicin A (antimicrobial antibiotic) and FR-66979 (antitumor antibiotic) (Scheme 1a).[1–6] Notably, as a crucial building block, various methods for synthesizing aziridines have emerged.[5-10] These primarily include 1) intramolecular cyclization of amino or azido alcohols. 2) addition of carbene equivalent to imine.[8] 3) addition of nitrene equivalent to olefin.[9] Transforming simple olefins into high-value-added aziridines, given that the significance of olefins as a chemical feedstock, represents a challenging and significant task. However, most of the research studies on alkene aziridination have predominantly focused on the syntheses of activated aziridination compounds, where R is an electron-withdrawing group (Scheme 1b, R = EWG).[7,9-10] Typically, these reactions generally require transition metal catalysis. Conversely, the synthesis of free N–H aziridines has garnered relatively less attention, probably due to the scarcity of suitable nitrene precursors and approaches.[11-16] In a seminal study in 2014, the Kürti, Falck, and Ess group reported a rhodium-catalyzed N–H aziridination of alkenes utilizing *O*-(2,4-dinitrophenyl)hydroxylamines (DPHs) as the aminating reagent (Scheme 1c, left).[13] They later extended this approach to include both N–H- and N–alkyl aziridination of olefins, using hydroxylamine-*O*-sulfonic acids (HOSA) as nitrene precursors alongside Rhodium(II) dimer catalyst and pyridine as base.[14a] Subsequently, Kürti's group has advanced the field by demonstrating enantioselective aziridination using commercially available (+)-3-(trifluoroacetyl)camphor as a chiral catalyst, producing aziridines from simple alkenes through transient oxaziridines formed in situ from HOSA and electron-deficient ketones aziridination of alkenes, (Scheme 1c, middle).[15] Most recently, the Jat and Tiwari groups also reported a metal-free intermolecular N–H using

Scheme 1. Overview of aziridines.



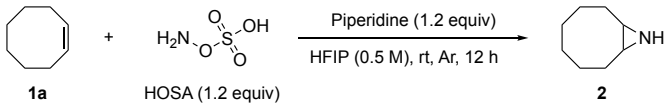
https://doi.org/10.26434/chemrxiv-2024-7v2mk-v2 **ORCID:** https://orcid.org/0000-0002-3831-2988

TsONHBoc as the aminating agent (Scheme 1c, right).[16a] However, TsONHBoc needs to be prepared through 2-steps with a lower atomic economy. Despite these advances, there is still room for developing new practical reaction systems for the synthesis of free N–H aziridines, especially from simple alkenes and commercially available inexpensive aminating agents, which remains challenging. Herein, we presented a practical methodology for intermolecular alkene aziridination using HOSA as the aminating agent, pyridine or piperidine as the base, and HFIP as the solvent (Scheme 1d). This method highlights the advantages of straightforward operation, mild reaction conditions, and excellent compatibility with various functional groups. Furthermore, it can be scaled up to gram-scale for the synthesis of aziridines.

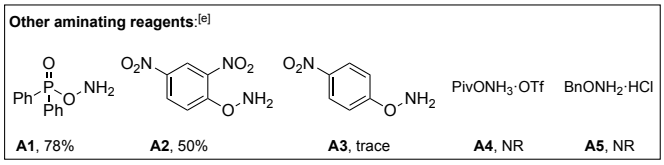
Results and Discussion

In previous reports, many nitrogen-containing heterocycles can be aminated on nitrogen using HOSA as an aminating agent.[17] In 1957, Meuwsen and Gösl discovered that tertiary amines and heterocyclic amines, such as trimethylamine (Me_3N), pyridine, and quinoline, could react with HOSA to yield *N*-aminated products through a proposed nitrene intermediate.[18] As part of an ongoing program aimed at exploring nitrene chemistry,[19] we envisioned whether olefin aziridination could be achieved in this reaction system. Drawing inspiration from Kürti's seminal work, we used (*Z*)-cyclooctene **1a** as the model substrate and HOSA as the aminating agent. Table 1 summarizes the results of the optimization study. Employing piperidine as the base in 1,1,1,3,3,3-Hexafluoroisopropanol (HFIP, 0.5 M) for 12 hours, giving the desired product **2** in 86% isolated yield (entry 1). Intriguingly, the introduction of metal catalysts such as $Rh_2(esp)_2$ and $FeCl_3$ unexpectedly hindered the reaction (entries 2-3). Similarly, the addition of an electron-deficient ketone catalyst (ethyl trifluoropyruvate) produced comparable results (entry 4). Performing the reaction in the dark did not improve the yield, showing the insensitivity of the reaction to light (entry 5). Various bases such as pyridine, DMAP, Et_3N, and DBU, cesium carbonate yielded the target product in moderate yields (55-70% yield, entries 6-10). Notably, the reaction did not proceed in the absence of base (entry 11). Replacing the solvent with trifluoroethanol (TFE) resulted in a reduced yield of 31% (entry 12), and other solvents, including methanol, toluene, dichloromethane, MeCN, THF, and water, failed to give the desired product (entry 13, see SI for more details). Additionally, the reaction displayed sensitivity to water, evidenced by a decrease in yield to 53% upon the addition of 10 equivalents of water (entry 14). [17] Lowering the reaction concentration had no discernible impact, while an increase in reaction concentration may be attributed to solubility issues with HOSA, leading to a reduced yield of 57% (entries 15-16). However, to our delight, increasing the equivalents of both HOSA and piperidine to 2.0 further enhanced the reaction yield to 97%. Furthermore, we also tried other types of aminating reagents, (aminooxy)diphenylphosphine oxide **A1**, and *O*-(2,4-dinitrophenyl)hydroxylamine **A2** yielded the desired product in 78% and 50% yield, respectively. While the other aminating reagents **A3–A5** failed to afford the desired aziridine compound.

Table 1: Conditions optimization for N–H aziridination of Cyclooctene **1a** with HOSA. [a]

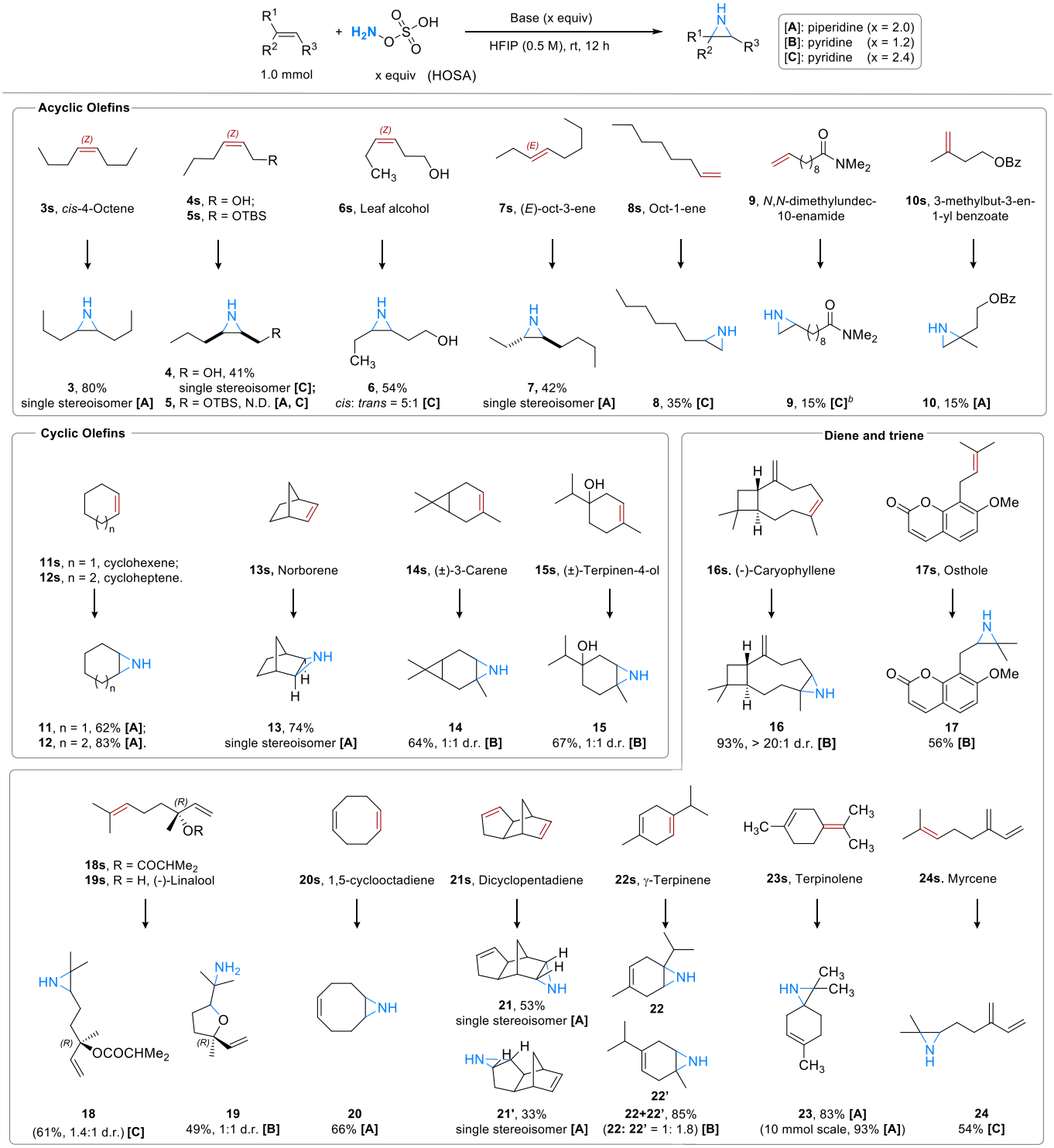


Entry	Change from the standard conditions	Yield of **2** (%)[b]
1	None	86
2	$Rh_2(esp)_2$ (2.5 mol%) as catalyst	72
3	$FeCl_3$ (5 mol%) as catalyst	38
4	$CF_3COCOOEt$ (5 mol%) as catalyst	84
5	In dark	86
6	Piperidine → Pyridine	70 [**B**]
7	Piperidine → DMAP	68
8	Piperidine → NEt_3	68
9	Piperidine → DBU	69
10	Piperidine → Cs_2CO_3	55
11	w/o Piperidine	NR
12	HFIP → TFE	31
13[c]	HFIP → other solvents	NR
14	H_2O (10.0 equiv) added	53
15	0.5 M → 0.2 M	85
16	0.5 M → 1.0 M	57
17	HOSA (2.0 equiv), Piperidine (2.0 equiv)	97 (95)[d] [**A**]



[a] In an 8 ml glass screw neck vial, **1a** (1.0 mmol), HOSA (1.2 mmol, 1.2 equiv), Base (1.2 mmol, 1.2 equiv) and HFIP (2.0 mL) for 12 hs. [b] Isolated yields are based on 1.0 mmol scale. [c] Other solvents = MeOH, toluene, CH_2Cl_2, MeCN, THF, H_2O. [d] 10 mmol scale. [e] Isolated yields of **2** using **A1**-**A5** on 1.0 mmol scale. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, DMAP = 4-dimethylamino-pyridine, TFE = trifluoroethanol. NR = no reaction (See more details in SI).

Scheme 2. Substrate scope for N–H aziridination of unactivated olefins. [a]

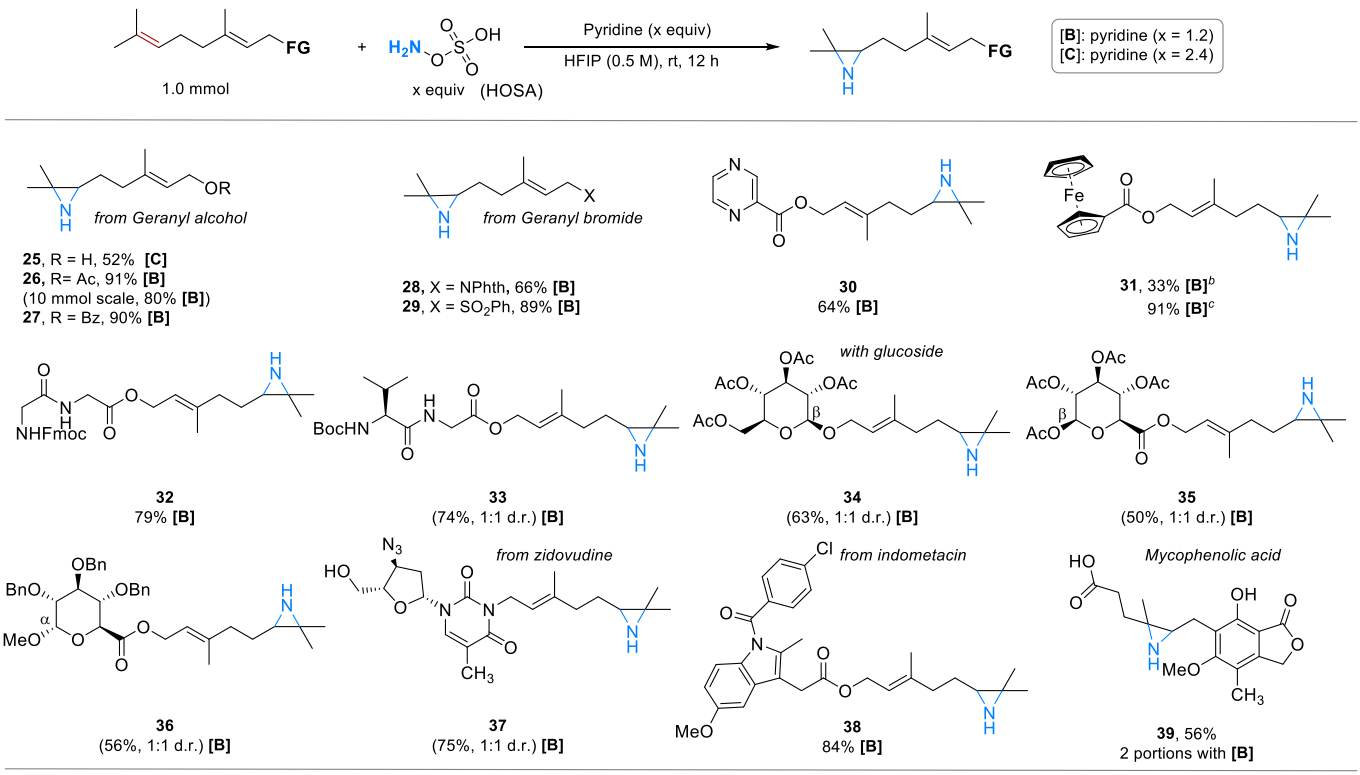


[a]All these reactions were conducted on 1.0 mmol scale. [b] conducted at 50 °C.

Next, with the optimized conditions in hand, the substrate scope of olefins was investigated. Generally, as shown in Scheme 2, mono- and di-substituted cyclic and linear olefins yielded aziridines in moderate to good yields, with electron-rich alkenes bearing more enhanced reactivity. For instance, aziridine **3** is produced in an 80% yield using *cis*-4-octene and piperidine as a base ([**A**]). However, olefins featuring the hydroxyl group (-OH) (**4s, 6s**) were incompatible under

condition [**A**]. Switching the base from piperidine to pyridine as the base affords the target products **4** and **6**, in 41% and 54% yield, respectively. Additionally, protecting the hydroxyl group of **4s** to *tert*-butyldimethylsilyl ether (-OTBS) (**5s**) did not lead to the desired product under either condition [**A**] or [**C**]. Trans linear internal olefin **7s** also gave product **7** in 42% yield. Terminal olefins, however, are less reactive and produce the target aziridines in relatively low yields (**8-10**). Subsequent investigations into cyclic olefins revealed that a majority of substrates efficiently gave the desired products. Notably, bridged cycloalkenes, such as norborene **13s**, gave **13** in 74% yield with high stereoselectivity. Terpinen-4-ol (**15s**) under condition [**B**] gaves the target product in 67% yield. However, further investigations into dienes and trienes reveal that they exhibit excellent regioselectivity regardless of the reactivity differences among the double bonds, leading exclusively to mono-aziridination products. For substrates containing multiple carbon-carbon double bonds, the reaction tends to occur specifically at the more electron-rich ones. For instance, diene **16s** containing both terminal and internal olefins, the aziridination selectively occurred on the internal olefin in 93% yield under condition [**B**]. Using Osthole **17s** as a substrate specifically yielded product at the electron-rich tri-substituted olefin site in moderate yield, while the conjugated internal olefin remained unreacted. Using (-)-Linalool as a parent substrate, when the hydroxyl group was masked by isobutyryl group (-$COCHMe_2$), the expected aziridine **18** was achieved in 61% yield with 1.4:1 d.r. under condition [**C**], however, when using free (-)-Linalool **19s** as substrate, the cascade product of aziridination followed by intramolecular nucleophilic ring-opening was obtained in 49% yield with 1:1 d.r. using pyridine as a base under condition [**B**].

Scheme 3. The investigation of functional group compatibility.[a]



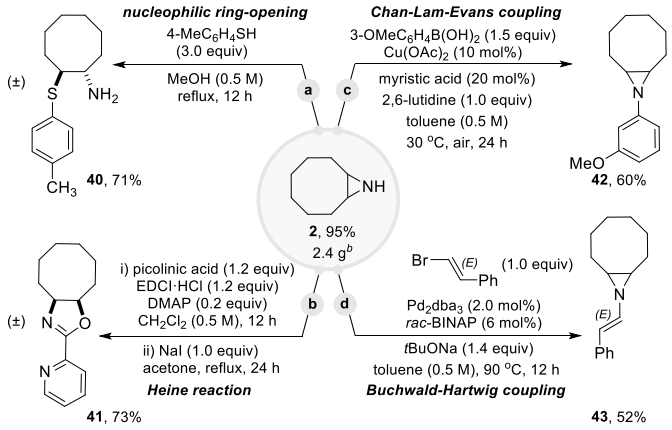
[a] All reactions were conducted on 1.0 mmol scale under atmosphere. [b] using **A1** as an aminating agent. [c] using **A1** as aminating agent with NFTB (0.5 M) as solvent, NFTB = Nonafluoro-*tert*-butyl alcohol.

Further investigations reveal that the dienes and trienes typically only react at one olefin site to yield mono-aziridination products even though increasing the amount of HOSA and the base does not lead to *bis*-aziridination. For instance, using piperidine as base under condition [**A**], 1,5-cyclooctadiene (COD, **20s**) gave the desired aziridines in 66% yield and dicyclopentadiene **21s** provided the two separable products (**21**, **21'**) in a total 86% yield (53% and 33%, respectively). Under condition [**B**], the γ-Terpinene yielded inseparable products **22+22'** in a total 85% yield (**22:22'** = 1:1.8, detected by ^{1}H NMR). Tetra-substituted olefin terpinolene **23s** as a substrate under conditions [**A**] yielded product **23** in 83%, with the reaction scalable to 10

mmol in 93% yield. Trienes, such as myrcene **24s** was also well accommodated in this system, with the reaction specifically occurring at the electron-rich internal olefin, leaving the two terminal olefins unreacted.

To elucidate the functional group compatibility of this method, we employed geranyl alcohol as the model substrate to probe its tolerance equipped with diverse functional groups (Scheme 3). Remarkably, unprotected geranyl alcohol gave the desired aziridine **25** in 52% yield under condition [**C**]. When the hydroxyl group was protected by acetyl (Ac, **26s**) and benzoyl (Bz, **27s**), the target products were achieved with excellent yields under condition [**B**]. Interestingly, substrates featuring functional groups such as NPhth (**28s**), SO_2Ph (**29s**), pyrazinoic acid ester (**30s**), and ferrocenyl carboxylic acid ester (**31s**) were efficiently converted to the desired aziridines in

Scheme 4. Synthetic applications.[a]

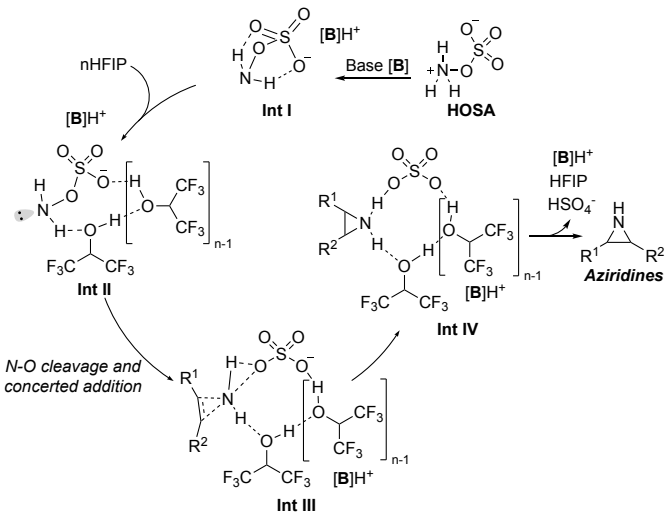


[a] All reactions were carried out on 1.0 mmol scale under atmospheric conditions, except for the synthesis of **43** under Ar. [b] 20 mmol scale under condition [**A**].

good to excellent yields (**28-31**). Notably, this reaction displayed good compatibility with complex biomolecules, including peptides and glycosyl moieties. Specifically, substrates containing a di-glycine unit (**32s**) and a Boc-Val-Gly segment (**33s**) were adeptly transformed into desired products in 79% and 74% yield, respectively. Additionally, compounds derived from L-glucopyranose (**34**), β-D-glucuronic ester (**35**), α-D-glucuronic ester (**36**) and zidovudine (**37**) were synthesized in moderate yields and diastereoselectivities. Particularly noteworthy is the transformation of the olefin substrate containing the pharmaceutical molecule indometacin (**38**) and mycophenolic acid (**39**), which were achieved in 84% and 56% yield, respectively. These examples highlight the reaction's broad substrate scopes and robust tolerance towards a wide array of functional groups.

To explore the practicability of this method and the applicability of the aziridines, the model aziridine **2** could be prepared on a 20 mmol scale in 95% yield. As shown in Scheme 4, aziridine **2** can undergo nucleophilic ring-opening reactions with nucleophilic reagents like *p*-toluenethiol to yield cyclooctamine **40** in 71% yield (Scheme 4a). [20] Additionally, **2** can also undergo condensation with picolinic acid, followed by cyclization under the NaI/acetone conditions (Heine reaction) to form oxazole compound **41** in 73% total yield (Scheme 4b). [21] Furthermore, **2** can not only engage in Chan-Lam-Evans coupling with arylboronic acid compounds under copper catalysis but also react with vinyl bromides under palladium catalysis *via* Buchwald-Hartwig coupling (Scheme 4c, d) to produce **42** and **43** in 60% and 52% yield, respectively. [22,23]

Scheme 5. Proposed mechanism



We tentatively propose a plausible mechanism for this transformation (Scheme 5). Initially, hydroxylamine-*O*-sulfonic acid undergoes neutralization with base, resulting in the formation of the hydroxylamine-*O*-sulfonic acid anion (**Int I**), which easily forms a cluster with HFIP, leading to **Int II**, stabilized by multiple hydrogen bonds.[25] Subsequently, the N–O bond cleavage assisted by hydrogen bonding to form the electrophilically active **Int III,**[26] then undergoes a concerted addition with an alkene to form the intermediate **Int IV**. Finally, the aziridine product is released.

Conclusion

In summary, we have reported a practical methodology for the synthesis of N–H aziridines from unactivated alkenes

using HOSA as an aminating agent with pyridine or piperidine as the base under mild conditions. The combination of HFIP and pyridine or piperidine is critical to achieve high yield. Notably, this approach showcases broad scope for non-activated alkenes, offering a straightforward method for the syntheses of free N–H aziridines from alkenes. Furthermore, it can be scaled up to gram-scale for the synthesis of aziridines. We hope this practical method will supply a more convenient route for the synthesis of aziridines.

Experimental section

General Information. All commercial materials were used as received unless otherwise noted. DCM were dried by distillation over CaH_2. Other solvents were purchased from J&K Chemical and used without further purification. To rule out the influence of trace metal ion completely, the base, HFIP and HOSA were purified by standard procedure. [24] TLC were performed on silica gel Huanghai HSGF254 plates and visualization of the developed chromatogram was performed by fluorescence quenching (λmax = 254 nm). Flash chromatography was performed using Silica gel (200-300 mesh) purchased from Qingdao Haiyang Chemical Co., China. Hydroxylamine-*O*-Sulfonic acid (HOSA) was washed by ether with standard procedures (mixing the HOSA with ether at room temperature and stirring at this temperature for 2 h, and then filtrated, dried *in vacuo*. Finally, stored at -20°C in dried circumstances); 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) was distilled with 3Å molecular sieves. NMR spectra were recorded on Bruker AVANCE AV 400 instruments and all NMR experiments were reported in units, parts per million (ppm), using residual solvent peaks (chloroform-*d* (δ = 7.26 ppm), or TMS (δ = 0.00 ppm) for ^{1}H NMR, chloroform (δ = 77.16 ppm) as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet. High resolution ESI mass experiments were operated on a Waters Xevo G2-XS QTof Quadrupole Time-of-Flight Mass Spectrometry.

General procedure for aziridination of alkenes: To an 8 mL glass vial equipped with magnetic bar was added alkene (1.0 mmol, 1.0 equiv), piperidine (condition [**A**]: 2.0 mmol, 2.0 equiv) or pyridine (condition [**B**]: 1.2 mmol, 1.2 equiv; condition [**C**]: 2.4 mmol, 2.4 equiv) at room temperature. HFIP (2.0 mL) was added for dissolving the reaction mixture to make the concentration 0.5 M. Hydroxylamine-*O*-sulfonic acid (HOSA) (condition [**A**]: 2.0 mmol, 2.0 equiv; condition [**B**]: 1.2 mmol, 1.2 equiv; condition [**C**]: 2.4 mmol, 2.4 equiv) was added subsequently and then sealed with PTFE cap. The reaction mixture was stirred at rt for 12 h. After that, the reaction mixture was neutralized with saturated $NaHCO_3$ (aq) and extracted with CH_2Cl_2 for four times. Finally, the concentrated resulting residue was purified by flash column chromatography to afford the desired product with CH_2Cl_2/MeOH as eluent.

9-azabicyclo[6.1.0]nonane (***2***). The title compound has been previously documented[14a] and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 97% yield as a yellow oil (121.4 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.00 (d, *J* = 14.0 Hz, 2H), 1.83 (d, *J* = 7.8 Hz, 2H), 1.64 – 1.43 (m, 4H), 1.42 – 1.25 (m, 4H), 1.08 – 0.88 (m, 2H), 0.54 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 34.0, 27.4, 27.4, 26.6.

(±)-(2R,3S)-2,3-dipropylaziridine (***3***). The title compound has been previously documented[14a] and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 80% yield as a yellow oil (101.8 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.96 – 1.90 (m, 2H), 1.53 – 1.23 (m, 8H), 1.19 – 1.10 (m, 1H), 0.92 (t, *J* = 7.2 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 34.8, 31.0, 21.3, 14.2.

(±)-((2R,3R)-3-propylaziridin-2-yl)methanol (***4***). The title compound has been previously unknown and was synthesized following general procedure condition [**C**] on 1.0 mmol scale in 41% yield as a yellow oil (47.2 mg, R_f = 0.4, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (dd, *J* = 11.8, 4.2 Hz, 1H), 3.41 (dd, *J* = 11.8, 8.1 Hz, 1H), 2.75 (brs, 2H), 2.32 – 2.21 (m, 1H), 2.10 (q, *J* = 6.3 Hz, 1H), 1.52 – 1.27 (m, 4H), 0.90 (t, *J* = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 61.0, 36.2, 35.1, 30.8, 21.3, 14.0; HRMS (ESI) *m/z*: Calculated for $C_6H_{14}NO^+$ $[M+H]^+$: 116.1070; Found: 116.1073.

2-(3-ethylaziridin-2-yl)ethan-1-ol (***6***). The title compound has been previously documented[14a] and was synthesized following general procedure condition [**C**] on 1.0 mmol scale in 54% yield as a yellow oil (62.2 mg, *trans* and *cis* mixture, 5:1 d.r., R_f = 0.4, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 – 3.56 (m, 2H), 2.95 (s, 2H), 2.13 – 2.08 (m, 1H), 1.91 (q, *J* = 6.6 Hz, 1H), 1.73 – 1.67 (m, 1H), 1.45 – 1.31 (m, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 61.1, 60.4, 38.4, 35.9, 35.5, 35.2, 32.6, 30.7, 27.0, 21.9, 11.9, 11.6.

(±)-(2R,3R)-2-butyl-3-ethylaziridine (***7***). The title compound has been previously unknown and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 42% yield as a yellow oil (53.4 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57 (d, *J* = 4.8 Hz, 2H), 1.49 – 1.10 (m, 9H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 6.9 Hz, 3H), 0.48 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 39.3, 37.6, 34.1, 29.9, 27.3, 22.5, 14.1, 11.7; HRMS (ESI) *m/z*: Calculated for $C_8H_{18}N^+$ $[M+H]^+$: 128.1434; Found: 128.1437.

2-hexylaziridine (***8***). The title compound has been previously unknown and was synthesized following general procedure condition [**C**] on 1.0 mmol scale in 35% yield as a yellow oil (44.5 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 – 1.79 (m, 1H),

1.70 (d, J = 5.7 Hz, 1H), 1.44 – 1.17 (m, 11H), 0.85 (t, J = 6.3 Hz, 3H), 0.63 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 34.6, 31.9, 30.4, 29.2, 27.6, 25.2, 22.7, 14.1; HRMS (ESI) *m/z*: Calculated for $C_8H_{18}N^+$ $[M+H]^+$: 128.1434; Found: 128.1437.

*9-(aziridin-2-yl)-N,N-dimethylnonanamide (**9**)*. The title compound has been previously documented[14a] and was synthesized following modified general procedure condition [**C**] (at 50 °C) on 1.0 mmol scale in 15% yield as a yellow oil (34.0 mg, R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 2.97 (s, 3H), 2.90 (s, 3H), 2.82 (s, 2H), 2.26 (t, J = 7.6 Hz, 2H), 1.58 (s, 3H), 1.43 – 1.05 (m, 16H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.4, 37.4, 35.4, 34.4, 33.5, 30.5, 29.5, 29.4, 27.6, 25.2, 25.2.

*2-(2-methylaziridin-2-yl)ethyl benzoate (**10**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 15% yield as a yellow oil (31.1 mg, R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.5 Hz, 2H), 7.49 – 7.42 (m, 1H), 7.38 (t, J = 7.5 Hz, 2H), 3.90 (d, J = 14.6 Hz, 1H), 3.87 – 3.76 (m, 2H), 3.73 (d, J = 14.5 Hz, 1H), 2.56 (s, 1H), 2.01 (t, J = 6.6 Hz, 2H), 1.46 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 163.3, 131.4, 128.4, 128.1, 128.0, 85.6, 66.0, 58.6, 42.5, 25.9; HRMS (ESI) *m/z*: Calculated for $C_{12}H_{16}NO_2^+$ $[M+H]^+$: 206.1176; Found: 206.1175.

*7-azabicyclo[4.1.0]heptane (**11**)*. The title compound has been previously documented[13] and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 62% yield as a yellow oil (60.3 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 2.10 (s, 2H), 1.83 – 1.64 (m, 4H), 1.30 – 1.22 (m, 2H), 1.19 – 1.12 (m, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 29.4, 24.5, 20.0.

*8-azabicyclo[5.1.0]octane (**12**)*. The title compound has been previously documented[14a] and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 83% yield as a yellow oil (92.3 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 2.02 (s, 4H), 1.64 – 1.46 (m, 3H), 1.37 – 1.18 (m, 6H), 0.93 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 34.3, 32.0, 30.6, 26.5.

*(1R,2S,4R,5S)-3-azatricyclo[3.2.1.$0^{2,4}$]octane (**13**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 74% yield as a yellow oil (80.8 mg, >20:1 d.r., R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 2H), 1.91 (s, 2H), 1.43 (d, J = 8.3 Hz, 2H), 1.25 – 1.14 (m, 2H), 1.08 (d, J = 10.7 Hz, 1H), 0.65 (d, J = 10.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 36.1, 31.3, 27.2, 25.5; HRMS (ESI) *m/z*: Calculated for $C_7H_{12}N^+$ $[M+H]^+$: 110.0964; Found: 110.0970.

*3,8,8-trimethyl-4-azatricyclo[5.1.0.$0^{3,5}$]octane (**14**)*. The title compound has been previously documented[15] and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 64% yield as a yellow oil (96.8 mg, 1:1 d.r., R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 2.11 (dd, J = 15.7, 9.5 Hz, 1H), 1.97 (dd, J = 15.5, 9.5 Hz, 1H), 1.69 (s, 1H), 1.50 (d, J = 15.7 Hz, 1H), 1.29 (dd, J = 15.5, 3.3 Hz, 1H), 1.08 (s, 3H), 0.96 (s, 3H), 0.69 (s, 4H), 0.40 (td, J = 9.2, 3.4 Hz, 1H), 0.29 (td, J = 9.2, 3.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 36.7, 32.7, 27.9, 24.9, 23.1, 18.1, 16.4, 15.6, 14.8, 13.0.

*3-isopropyl-6-methyl-7-azabicyclo[4.1.0]heptan-3-ol (**15**)*. The title compound has been previously documented[15] and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 67% yield as a yellow oil (113.4 mg, 1:1 d.r., R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 2.23 (s, 1H), 2.08 – 2.00 (m, 1H), 1.80 (d, J = 14.2 Hz, 1H), 1.73 (dd, J = 14.7, 7.3 Hz, 1H), 1.60 (dd, J = 14.2, 2.6 Hz, 1H), 1.51 (dt, J = 13.8, 7.0 Hz, 1H), 1.43 (dd, J = 13.3, 7.0 Hz, 1H), 1.31 (d, J = 7.9 Hz, 1H), 1.27 (s, 3H), 1.25 – 1.18 (m, 1H), 0.90 – 0.87 (m, 1H), 0.87 – 0.78 (m, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 72.5, 39.8, 37.7, 34.8, 31.1, 30.1, 27.2, 26.8, 17.1, 16.8.

*(1R,10S)-4,12,12-trimethyl-9-methylene-5-azatricyclo [8.2.0.$0^{4,6}$]dodecane (**16**)*. The title compound has been previously documented[15] and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 93% yield as a yellow oil (204.0 mg, >20:1 d.r., R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 4.93 (s, 1H), 4.80 (s, 1H), 2.56 (q, J = 9.3 Hz, 1H), 2.34 – 2.28 (m, 1H), 2.20 – 2.07 (m, 2H), 2.01 – 1.95 (m, 1H), 1.90 (dd, J = 11.0, 4.2 Hz, 1H), 1.70 (t, J = 9.3 Hz, 1H), 1.63 (dd, J = 9.4, 4.7 Hz, 2H), 1.59 – 1.37 (m, 3H), 1.23 – 1.09 (m, 2H), 1.07 (s, 3H), 0.96 (s, 3H), 0.94 (s, 3H), 0.63 (td, J = 12.9, 4.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 152.6, 111.9, 51.9, 48.8, 42.7, 42.1, 39.4, 37.5, 33.9, 32.1, 31.2, 30.0, 27.7, 21.8, 17.8.

*8-((3,3-dimethylaziridin-2-yl)methyl)-7-methoxy-2H-chromen-2-one (**17**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 56% yield as a yellow oil (145.2 mg, R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 9.5 Hz, 1H), 7.31 (d, J = 8.6 Hz, 1H), 6.83 (d, J = 8.6 Hz, 1H), 6.21 (dt, J = 9.5, 1.3 Hz, 1H), 3.89 (s, 3H), 3.05 (dd, J = 14.0, 6.0 Hz, 1H), 2.90 (dd, J = 13.9, 6.8 Hz, 1H), 2.05 (t, J = 6.5 Hz, 1H), 1.34 (s, 3H), 1.17 (s, 3H), 0.52 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 161.2, 160.6, 153.3, 143.9, 126.9, 116.3, 113.1, 107.5, 56.2, 42.9, 36.4, 27.2, 23.2, 20.4; HRMS (ESI) *m/z*: Calculated for $C_{15}H_{18}NO_3^+$ $[M+H]^+$: 260.1281; Found: 260.1283.

*(3R)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-1-en-3-yl isobutyrate (**18**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**C**] on 1.0 mmol scale in 61% yield as a yellow oil (146.0 mg, 1.4:1 d.r., R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 5.96 – 5.85 (m, 1H),

5.18 – 5.01 (m, 2H), 2.52 – 2.40 (m, 1H), 2.01 – 1.93 (m, 1H), 1.84 – 1.82 (m, 2H), 1.50 (d, J = 6.4 Hz, 3H), 1.42 – 1.30 (m, 1H), 1.26 (s, 3H), 1.16 (s, 2H), 1.11 (d, J = 7.1 Hz, 6H).$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 175.9, 141.9, 141.7, 113.2, 113.1, 82.1, 82.0, 43.2, 37.9, 35.7, 34.8, 34.8, 27.5, 24.2, 23.8, 23.6, 19.5, 19.0; HRMS (ESI) *m/z*: Calculated for $C_{14}H_{26}NO_2^+$ $[M+H]^+$: 240.1958; Found: 240.1959.

*2-((5R)-5-methyl-5-vinyltetrahydrofuran-2-yl)propan-2-amine (**19**).* The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 49% yield as a yellow oil (83.0 mg, 1:1 d.r., R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 5.89 (dd, J = 17.4, 10.8 Hz, 1H), 5.79 (dd, J = 17.3, 10.6 Hz, 1H), 5.12 (d, J = 17.3 Hz, 2H), 4.91 (d, J = 10.7 Hz, 2H), 3.77 – 3.68 (m, 2H), 2.35 (s, 5H), 1.84 – 1.75 (m, 4H), 1.74 – 1.54 (m, 5H), 1.23 (d, J = 3.8 Hz, 6H), 1.06 (s, 6H), 1.02 – 0.94 (m, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.4, 143.8, 111.3, 111.3, 86.4, 86.3, 82.8, 82.6, 51.8, 37.9, 37.5, 27.7, 27.5, 26.8, 26.7, 26.5, 25.8, 25.4, 25.1; HRMS (ESI) *m/z*: Calculated for $C_{10}H_{20}NO^+$ $[M+H]^+$: 170.1539; Found: 170.1539.

*(Z)-9-azabicyclo[6.1.0]non-4-ene (**20**).* The title compound has been previously documented[14a] and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 66% yield as a yellow oil (81.3 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 5.57 – 5.42 (m, 2H), 2.30 – 2.25 (m, 2H), 2.15 – 1.89 (m, 6H), 1.63 (d, J = 7.8 Hz, 2H), 0.93 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 129.2, 34.5, 29.1, 25.0.

*(1aR,2S,2aS,5aR,6R,6aS)-1,1a,2,2a,3,5a,6,6a-octahydro-2,6-methanoindeno[5,6-b]azirine (**21**).* The title compound has been previously unknown and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 53% yield as a yellow oil (78.0 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 5.61 (s, 1H), 5.56 – 5.43 (m, 1H), 3.18 – 2.98 (m, 1H), 2.59 – 2.54 (m, 1H), 2.37 (s, 1H), 2.29 (s, 1H), 2.23 – 2.15 (m, 2H), 2.09 – 1.98 (m, 1H), 1.80 – 1.69 (m, 1H), 1.20 (d, J = 10.2 Hz, 1H), 0.81 (d, J = 10.5 Hz, 1H), 0.32 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 132.3, 130.1, 53.9, 42.4, 39.3, 38.1, 31.3, 29.8, 28.5, 27.3; HRMS (ESI) *m/z*: Calculated for $C_{10}H_{14}N^+$ $[M+H]^+$: 148.1121; Found: 148.1122.

*(1bS,2S,5R,5aR)-1,1a,1b,2,5,5a,6,6a-octahydro-2,5-methanoindeno[1,2-b]azirine (**21'**).* The title compound has been previously unknown and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 33% yield as a yellow oil (48.6 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 6.12 – 6.00 (m, 2H), 2.87 (s, 1H), 2.73 (s, 1H), 2.71 – 2.68 (m, 1H), 2.47 – 2.42 (m, 1H), 2.26 (s, 2H), 2.09 (s, 1H), 1.73 (dd, J = 14.2, 9.1 Hz, 1H), 1.43 (d, J = 8.2 Hz, 1H), 1.41 – 1.32 (m, 1H), 1.28 (d, J = 8.1 Hz, 1H), 0.14 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 135.5, 134.8, 53.2, 52.0, 46.8, 46.0, 44.4, 32.1, 22.9, 22.5. ; HRMS (ESI) *m/z*: Calculated for $C_{10}H_{14}N^+$ $[M+H]^+$: 148.1121; Found: 148.1122.

*1-isopropyl-4-methyl-7-azabicyclo[4.1.0]hept-3-ene (**22**) and 4-isopropyl-1-methyl-7-azabicyclo[4.1.0]hept-3-ene (**22'**) mixture (**22:22'** = 1:1.8).* The title compound has been previously documented[15] and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in total 85% yield as a yellow oil (128.6 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 5.19 – 5.09 (m, 1H), 2.46 – 2.17 (m, 5H), 2.12 – 2.05 (m, 1H), 1.98 (s, 1H), 1.57 (s, 1H), 1.19 (s, 3H), 0.92 (dt, J = 6.8, 2.6 Hz, 7H), 0.38 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 138.6, 128.9, 117.1, 114.6, 41.1, 38.3, 37.2, 34.8, 34.2, 31.0, 30.6, 26.8, 24.9, 24.5, 23.5, 21.5, 21.1, 19.1, 17.7.

*2,2,6-trimethyl-1-azaspiro[2.5]oct-5-ene (**23**).* The title compound has been previously unknown and was synthesized following general procedure condition [**A**] on 1.0 mmol scale in 83% yield as a yellow oil (125.6 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 5.32 (s, 1H), 2.23 (d, J = 17.7 Hz, 1H), 2.16 – 2.04 (m, 1H), 2.04 – 1.85 (m, 2H), 1.64 (d, J = 8.8 Hz, 4H), 1.40 (s, 1H), 1.24 (s, 3H), 1.22 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 134.5, 119.8, 43.4, 40.2, 32.2, 29.5, 28.3, 23.5, 22.1, 21.6. ; HRMS (ESI) *m/z*: Calculated for $C_{10}H_{18}N^+$ $[M+H]^+$: 152.1434; Found: 152.1435.

*2,2-dimethyl-3-(3-methylenepent-4-en-1-yl)aziridine (**24**).* The title compound has been previously documented[15] and was synthesized following general procedure condition [**C**] on 1.0 mmol scale in 54% yield as a yellow oil (81.7 mg, R_f = 0.6, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 6.36 (dd, J = 17.6, 10.8 Hz, 1H), 5.29 – 5.17 (m, 1H), 5.05 (d, J = 10.9 Hz, 1H), 5.00 (d, J = 4.3 Hz, 2H), 2.41 – 2.24 (m, 2H), 1.77 (t, J = 6.6 Hz, 1H), 1.64 – 1.55 (m, 2H), 1.23 (s, 3H), 1.13 (s, 3H), 0.34 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.9, 138.9, 116.1, 113.4, 43.3, 35.8, 29.7, 28.7, 27.7, 19.9.

*(E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-ol (**25**).* The title compound has been previously documented[15] and was synthesized following general procedure condition [**C**] on 1.0 mmol scale in 52% yield as a yellow oil (88.0 mg, R_f = 0.4, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 5.36 (s, 1H), 4.04 (d, J = 6.4 Hz, 2H), 2.13 – 2.00 (m, 4H), 1.71 (t, J = 6.5 Hz, 1H), 1.60 (s, 3H), 1.54 – 1.41 (m, 2H), 1.18 (s, 3H), 1.10 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 137.6, 124.6, 58.6, 43.2, 37.7, 35.9, 27.9, 27.3, 19.5, 16.3.

*(E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl acetate (**26**).* The title compound has been previously documented[14a] and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 91% yield as a yellow oil (192.3 mg, R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^1H NMR (400 MHz, $CDCl_3$) δ 5.38 – 5.23 (m, 1H), 4.52 (d, J = 7.1 Hz, 2H), 2.17 – 2.03 (m, 2H), 1.98 (s, 3H), 1.66 (d, J = 4.6 Hz, 4H), 1.53 – 1.42 (m, 2H), 1.19 (s, 3H), 1.09 (s, 3H), 0.32 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz,

$CDCl_3$) δ 171.0, 141.8, 118.6, 61.3, 43.0, 37.8, 35.6, 28.1, 27.5, 21.0, 19.7, 16.5.

*(E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl benzoate (**27**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 90% yield as a yellow oil (246.1 mg, R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.5 Hz, 2H), 7.51 (t, *J* = 7.3 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 5.48 (t, *J* = 6.8 Hz, 1H), 4.82 (d, *J* = 7.0 Hz, 2H), 2.24 – 2.09 (m, 2H), 1.75 (s, 3H), 1.72 (d, *J* = 6.6 Hz, 1H), 1.59 – 1.51 (m, 2H), 1.21 (s, 4H), 1.13 (s, 3H), 0.82 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.7, 141.9, 132.9, 130.5, 129.6, 128.3, 118.8, 61.8, 43.1, 37.8, 35.8, 28.1, 27.5, 19.7, 16.6; HRMS (ESI) *m/z*: Calculated for $C_{17}H_{24}NO_2^+$ [M+H]$^+$: 274.1802; Found: 274.1809.

*(E)-2-(5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl)isoindoline-1,3-dione (**28**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 66% yield as a white solid (197.0 mg, R_f = 0.4, CH_2Cl_2: MeOH = 10:1 (v/v), m. p. 78–80 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.73 (m, 2H), 7.72 – 7.60 (m, 2H), 5.26 (s, 1H), 4.24 (d, *J* = 6.6 Hz, 2H), 2.22 – 1.94 (m, 2H), 1.78 (s, 3H), 1.64 (t, *J* = 6.6 Hz, 1H), 1.55 – 1.36 (m, 2H), 1.14 (s, 7H), 0.22 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.1, 140.3, 133.9, 132.3, 123.2, 118.4, 43.0, 37.8, 35.8, 35.6, 28.2, 27.5, 19.8, 16.4; HRMS (ESI) *m/z*: Calculated for $C_{18}H_{23}N_2O_2^+$ [M+H]$^+$: 299.1754; Found: 299.1760.

*(E)-2,2-dimethyl-3-(3-methyl-5-(phenylsulfonyl)pent-3-en-1-yl)aziridine (**29**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 89% yield as a yellow oil (260.0 mg, R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.75 (m, 2H), 7.59 – 7.55 (m, 1H), 7.49 – 7.44 (m, 2H), 5.27 – 5.06 (m, 1H), 3.75 (dd, *J* = 8.0, 1.8 Hz, 2H), 2.12 – 1.96 (m, 2H), 1.66 – 1.59 (m, 1H), 1.46 – 1.30 (m, 2H), 1.27 (s, 3H), 1.18 (s, 3H), 1.07 (s, 3H), 0.24 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.9, 138.5, 133.4, 128.8, 128.2, 110.3, 55.8, 42.5, 37.7, 35.3, 27.9, 27.3, 19.5, 16.0; HRMS (ESI) *m/z*: Calculated for $C_{16}H_{24}NO_2S^+$ [M+H]$^+$: 294.1522; Found: 294.1519.

*(E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl pyrazine-2-carboxylate (**30**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 64% yield as a yellow oil (176.3 mg, R_f = 0.4, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.70 (s, 1H), 8.66 (s, 1H), 5.47 (t, *J* = 7.3 Hz, 1H), 4.90 (d, *J* = 7.2 Hz, 2H), 2.20 – 2.05 (m, 2H), 1.74 (s, 3H), 1.67 (t, *J* = 6.6 Hz, 1H), 1.49 (q, *J* = 7.4 Hz, 2H), 1.17 (s, 3H), 1.08 (s, 3H), 0.37 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.9, 147.6, 146.3, 144.4, 143.6, 143.2, 117.8, 63.1, 42.9, 37.8, 35.6, 28.1, 27.5, 19.7, 16.6; HRMS (ESI) *m/z*: Calculated for $C_{15}H_{22}N_3O_2^+$ [M+H]$^+$: 276.1707; Found: 276.1703.

*(E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl ferrocenyl-2-carboxylate (**31**)*. The title compound has been previously unknown and was synthesized following modified general procedure condition [**B**] ((aminooxy)diphenylphosphine oxide **A1** as aminating agent, HFIP as solvent) on 1.0 mmol scale in 33% yield as a brown oil (124.0 mg, R_f = 0.3, CH_2Cl_2: MeOH = 10:1 (v/v)); modified general procedure condition [**B′**] ((aminooxy)diphenylphosphine oxide **A1** as aminating agent, NFTP as solvent) on 1.0 mmol scale in 91% yield as a brown oil (346.8 mg, R_f = 0.3, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 (t, *J* = 7.1 Hz, 1H), 4.77 (t, *J* = 2.0 Hz, 2H), 4.70 (d, *J* = 7.0 Hz, 2H), 4.35 (s, 2H), 4.16 (s, 5H), 2.24 – 2.08 (m, 2H), 1.76 (s, 3H), 1.71 (d, *J* = 6.8 Hz, 1H), 1.54 (q, *J* = 7.4 Hz, 2H), 1.22 (s, 3H), 1.13 (s, 3H), 0.36 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.7, 141.6, 119.3, 71.4, 71.3, 70.2, 69.8, 61.0, 43.0, 37.8, 35.7, 28.2, 27.6, 19.8, 16.7; HRMS (ESI) *m/z*: Calculated for $C_{21}H_{28}FeNO_2^+$ [M+H]$^+$: 382.1464; Found: 382.1471.

*(E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl (((9H-fluoren-9-yl)methoxy)carbonyl)glycylglycine-ate (**32**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 79% yield as a yellow oil (401.0 mg, R_f = 0.3, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (t, *J* = 7.2 Hz, 2H), 7.67 (d, *J* = 7.5 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), , 7.36 (q, *J* = 6.9 Hz, 2H), 7.32 – 7.23 (m, 3H), 6.06 (s, 1H), 5.33 (t, *J* = 7.2 Hz, 1H), 4.64 (t, *J* = 7.9 Hz, 2H), 4.40 (d, *J* = 6.8 Hz, 1H), 4.20 (t, *J* = 7.0 Hz, 1H), 4.07 – 3.76 (m, 3H), 2.19 – 2.04 (m, 2H), 1.78 – 1.61 (m, 4H), 1.55 – 1.48 (m, 2H), 1.46 – 1.33 (m, 1H), 1.22 (s, 3H), 1.13 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.7, 169.5, 143.8, 141.3, 128.8, 127.8, 127.1, 125.1, 120.0, 118.1, 67.1, 62.3, 62.2, 47.2, 44.6, 43.1, 43.1, 41.3, 40.9, 37.7, 36.0, 27.8, 27.3, 19.6, 16.5. ; HRMS (ESI) *m/z*: Calculated for $C_{29}H_{36}N_3O_5^+$ [M+H]$^+$: 506.2649; Found: 506.2654.

*(E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl (tert-butoxycarbonyl)-L-valylglycinate (**33**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 74% yield as a yellow oil (317.0 mg, 1:1 d.r., R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (s, 1H), 5.31 (t, *J* = 7.3 Hz, 1H), 5.22 (dt, *J* = 9.5, 4.6 Hz, 1H), 4.60 (dd, *J* = 7.1, 2.3 Hz, 2H), 3.97 (m, 3H), 2.18 – 2.03 (m, 3H), 1.67 (d, *J* = 10.2 Hz, 4H), 1.52 – 1.46 (m, 2H), 1.38 (d, *J* = 2.4 Hz, 9H), 1.20 (d, *J* = 2.0 Hz, 3H), 1.10 (d, *J* = 2.1 Hz, 3H), 0.97 – 0.91 (m, 3H), 0.88 (dd, *J* = 6.8, 1.8 Hz, 3H), 0.56 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.0, 169.7, 155.9, 142.6, 118.0, 79.8, 62.2, 59.7, 43.0, 41.2, 37.8, 35.7, 31.1, 28.3, 28.0, 27.5, 19.7,

19.3, 17.7, 16.5; HRMS (ESI) *m/z*: Calculated for $C_{22}H_{40}N_3O_5^+$ $[M+H]^+$: 426.2962; Found: 426.2962.

*(2S,3S,4R,5S,6S)-2-(acetoxymethyl)-6-(((E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl)oxy)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**34**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 63% yield as a yellow viscous oil (315.0 mg, 1:1 d.r., R_f = 0.3, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.30 – 5.20 (m, 1H), 5.14 (t, *J* = 9.4 Hz, 1H), 5.02 (t, *J* = 9.6 Hz, 1H), 4.93 (t, *J* = 8.8 Hz, 1H), 4.48 (dd, *J* = 7.9, 3.1 Hz, 1H), 4.26 – 4.02 (m, 4H), 3.68 – 3.56 (m, 1H), 2.19 – 2.09 (m, 2H), 2.03 (s, 3H), 1.97 (d, *J* = 4.2 Hz, 6H), 1.94 (s, 3H), 1.68 (dd, *J* = 8.1, 4.5 Hz, 1H), 1.62 (s, 3H), 1.51 (dd, *J* = 18.4, 11.4 Hz, 3H), 1.21 (s, 4H), 1.10 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.7, 170.3, 169.4, 169.3, 141.8, 119.5, 119.5, 98.9, 98.8, 72.9, 71.8, 71.3, 68.5, 65.3, 65.2, 62.1, 42.9, 37.8, 37.8, 35.6, 28.2, 28.1, 27.6, 20.7, 20.6, 19.7, 16.4, 16.4; HRMS (ESI) *m/z*: Calculated for $C_{24}H_{38}NO_{10}^+$ $[M+H]^+$: 500.2490; Found: 500.2494.

*(2S,3R,4S,5S,6S)-6-((((E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl)oxy)carbonyl)tetrahydro-2H-pyran-2,3,4,5-tetrayl tetraacetate (**35**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 50% yield as a yellow viscous oil (255.0 mg, 1:1 d.r., R_f = 0.3, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (dd, *J* = 7.6, 3.8 Hz, 1H), 5.30 – 5.20 (m, 2H), 5.20 – 5.13 (m, 1H), 5.12 – 5.02 (m, 1H), 4.64 – 4.49 (m, 2H), 4.10 (dd, *J* = 9.7, 3.3 Hz, 1H), 2.18 – 1.88 (m, 15H), 1.65 (s, 3H), 1.53 – 1.41 (m, 2H), 1.19 (s, 3H), 1.09 (s, 3H), 0.81 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.9, 169.2, 169.2, 168.8, 166.4, 143.2, 117.4, 91.3, 73.0, 71.9, 70.1, 68.9, 62.9, 42.9, 42.8, 37.7, 35.7, 28.0, 27.5, 20.8, 20.6, 20.5, 20.5, 19.7, 16.5; HRMS (ESI) *m/z*: Calculated for $C_{24}H_{36}NO_{11}^+$ $[M+H]^+$: 514.2283; Found: 514.2286.

*(E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl (2S,3S,4S,5R,6S)-3,4,5-tris(benzyloxy)-6-methoxyte-trahydro-2H-pyran-2-carboxylate (**36**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 56% yield as a yellow viscous oil (331.0 mg, 1:1 d.r., R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.19 (m, 15H), 5.36 – 5.32 (m, 1H), 4.95 (d, *J* = 10.9 Hz, 1H), 4.85 – 4.75 (m, 3H), 4.73 – 4.54 (m, 5H), 4.19 (d, *J* = 10.0 Hz, 1H), 3.99 (t, *J* = 9.3 Hz, 1H), 3.73 (dd, *J* = 10.0, 9.0 Hz, 1H), 3.58 (dd, *J* = 9.6, 3.5 Hz, 1H), 3.40 (s, 3H), 2.20 – 1.98 (m, 2H), 1.67 (d, *J* = 5.0 Hz, 4H), 1.52 – 1.42 (m, 2H), 1.22 (s, 3H), 1.11 (s, 3H), 0.31 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.7, 142.6, 142.6, 138.5, 138.0, 137.9, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.7, 127.6, 117.9, 117.9, 98.7, 81.3, 79.7, 79.2, 75.9, 75.0, 73.6, 70.3, 62.4, 55.6, 42.9, 37.7, 35.5, 28.0, 27.5, 19.7, 16.5; HRMS (ESI) *m/z*: Calculated for $C_{38}H_{48}NO_7^+$ $[M+H]^+$: 630.3425; Found: 630.3435.

*1-((2R,4S,5S)-4-azido-5-(hydroxymethyl)tetrahydrofuran-2-yl)-3-((E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl)-5-methylpyrimidine-2,4(1H,3H)-dione (**37**)*. The title compound has been previously unknown was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 75% yield as a colorless viscous oil (315.3 mg, 1:1 d.r., R_f = 0.2, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 4.6 Hz, 1H), 6.14 (dt, *J* = 8.3, 6.3 Hz, 1H), 5.17 (d, *J* = 7.1 Hz, 1H), 4.49 (d, *J* = 6.8 Hz, 2H), 4.38 – 4.24 (m, 1H), 3.98 – 3.76 (m, 2H), 3.70 (dd, *J* = 11.9, 2.5 Hz, 1H), 2.40 – 2.32 (m, 2H), 2.16 – 1.96 (m, 2H), 1.85 (s, 3H), 1.76 (d, *J* = 17.9 Hz, 4H), 1.49 (q, *J* = 7.5 Hz, 2H), 1.19 (s, 3H), 1.11 (s, 3H), 0.83 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.3, 150.8, 150.7, 139.5, 134.6, 134.5, 118.8, 110.2, 110.1, 86.2, 86.1, 84.8, 84.8, 61.1, 60.0, 43.4, 39.4, 37.8, 37.6, 36.5, 27.7, 27.7, 27.2, 27.1, 19.4, 16.5, 13.3; HRMS (ESI) *m/z*: Calculated for $C_{20}H_{31}N_6O_4^+$ $[M+H]^+$: 419.2401; Found: 419.2405.

*(E)-5-(3,3-dimethylaziridin-2-yl)-3-methylpent-2-en-1-yl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate (**38**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 84% yield as a yellow viscous oil (428.3 mg, R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.56 (m, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 6.94 (d, *J* = 2.6 Hz, 1H), 6.85 (d, *J* = 9.0 Hz, 1H), 6.64 (dd, *J* = 9.0, 2.6 Hz, 1H), 5.43 – 5.26 (m, 1H), 4.61 (d, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.64 (s, 2H), 2.35 (s, 3H), 2.20 – 2.15 (m, 2H), 1.67 (s, 4H), 1.50 (q, *J* = 7.5 Hz, 2H), 1.21 (s, 3H), 1.12 (s, 3H), 0.51 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.9, 168.3, 156.1, 142.2, 139.3, 136.0, 134.0, 131.2, 130.8, 130.7, 129.2, 118.5, 115.0, 112.7, 111.6, 101.4, 61.9, 55.7, 43.0, 37.8, 35.6, 30.4, 28.1, 27.6, 19.8, 16.6, 13.4; HRMS (ESI) *m/z*: Calculated for $C_{29}H_{34}ClN_2O_4^+$ $[M+H]^+$: 509.2202; Found: 509.2209.

*3-(3-((4-hydroxy-6-methoxy-7-methyl-3-oxo-1,3-dihydroisobenzofuran-5-yl)methyl)-2-methylaziridin-2-yl)propanoic acid (**39**)*. The title compound has been previously unknown and was synthesized following general procedure condition [**B**] on 1.0 mmol scale in 56% yield as a white solid (2 portions addition of pyridine and HOSA every 12 h, 188.1 mg, 1:1 d.r., R_f = 0.2, CH_2Cl_2: MeOH = 10:1 (v/v), m. p. 92–94 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (brs, 3H), 5.15 – 5.01 (m, 2H), 3.75 (s, 3H), 3.15 (dd, *J* = 10.3, 1.6 Hz, 1H), 3.05 (dd, *J* = 14.1, 1.6 Hz, 1H), 2.62 (td, *J* = 10.4, 3.3 Hz, 2H), 2.48 (dt, *J* = 17.5, 9.9 Hz, 2H), 2.10 (s, 3H), 2.00 – 1.87 (m, 1H), 1.48 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 176.4, 163.5, 146.3, 120.4, 107.8, 88.0, 69.1, 61.1, 59.2, 29.1, 29.0, 26.5, 22.5, 11.6; HRMS (ESI) *m/z*: Calculated for $C_{17}H_{22}NO_6^+$ $[M+H]^+$: 336.1442; Found: 336.1440.

*(±)-(1S,2S)-2-(p-tolylthio)cyclooctan-1-amine (**40**)*. To an 8 mL glass vial equipped with magnetic bar was added **2** (1.0 mmol, 125.2 mg, 1.0 equiv), 4-MeC_6H_4SH (3.0 mmol, 372.6 mg, 3.0 equiv) at room temperature. Methanol was added for dissolving the reaction mixture to make the concentration 0.5 M. And then the vial was placed on 70 °C heating block and stirred for overnight. After cooling down to room temperature, the solvent was removed *in vacuo* and the residue was purified by silica gel column chromatography directly to provide **40** in 71% yield as a yellow oil (176.7 mg R_f = 0.5, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.8 Hz, 2H), 7.07 (d, *J* = 7.8 Hz, 2H), 3.06 – 2.98 (m, 1H), 2.93 (dd, *J* = 10.3, 6.3 Hz, 1H), 2.29 (s, 3H), 2.14 (s, 2H), 1.87 – 1.54 (m, 7H), 1.49 – 1.27 (m, 5H).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.0, 132.7, 131.5, 129.7, 58.7, 54.7, 32.7, 30.5, 26.4, 26.1, 25.6, 25.2, 21.1; HRMS (ESI) *m/z*: Calculated for $C_{15}H_{24}NS^+$ [M+H]$^+$: 250.1624; Found: 250.1631.

*(3aS,9aR)-2-(pyridin-2-yl)-3a,4,5,6,7,8,9,9a-octahydrocycloocta[d]oxazole (**41**)*. Step 1: To an 8 mL glass vial equipped with magnetic bar was added **2** (1.0 mmol, 125.2 mg, 1.0 equiv), EDCI•HCl (1.2 mmol, 230.0 mg, 1.2 equiv), DMAP (0.2 mmol, 24.4 mg, 0.2 equiv) and picolinic acid (1.2 mmol, 147.6 mg, 1.2 equiv) at room temperature. CH_2Cl_2 was added for dissolving the reaction mixture to make the concentration 0.5 M. And then the vial was placed on 30 °C heating block and stirred for overnight. Water was added and the reaction mixture was washed with brine, extracted with CH_2Cl_2. The combined organic extracts were concentrated *in vacuo* and the residue was purified by silica gel column chromatography to provide the intermediate product as white solid in 97% yield (223.2 mg); Step 2: To an 8 mL glass vial equipped with magnetic bar was added the intermediate product (223.2 mg, 1.0 equiv) and sodium iodide (149.9 mg, 1.0 equiv). Acetone was added for dissolving the reaction mixture to make the concentration 0.5 M. And then the reaction mixture was heated to reflux on heating block and stirred for 24 h. After cooling down to room temperature, the solvent was removed *in vacuo* and the residue was purified by silica gel column chromatography directly to provide **41** as a colorless oil in 73% total yield over 2 steps. (168.1 mg, R_f = 0.4, CH_2Cl_2: MeOH = 10:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 4.7 Hz, 1H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.37 – 7.28 (m, 1H), 4.79 – 4.65 (m, 1H), 4.19 (t, *J* = 10.2 Hz, 1H), 2.11 – 1.90 (m, 3H), 1.86 – 1.72 (m, 1H), 1.70 – 1.57 (m, 2H), 1.52 – 1.25 (m, 7H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.1, 149.7, 147.1, 136.6, 125.4, 123.7, 85.1, 69.9, 28.6, 28.5, 27.5, 26.7, 25.8, 25.5; HRMS (ESI) *m/z*: Calculated for $C_{14}H_{19}N_2O^+$ [M+H]$^+$: 231.1492; Found: 231.1497.

*9-(3-methoxyphenyl)-9-azabicyclo[6.1.0]nonane (**42**)*. To an 8 mL glass vial equipped with magnetic bar was added **2** (1.0 mmol, 125.2 mg, 1.0 equiv), 3-$OMeC_6H_4B(OH)_2$ (1.5 mmol, 228.2 mg, 1.5 equiv), $Cu(OAc)_2$ (0.1 mmol, 20 mg, 0.1 equiv), myristic acid (0.2 mmol, 46 mg, 0.2 equiv) and 2,6-lutidine (1.0 mmol, 107 mg, 1.0 equiv) at room temperature. Toluene was added for dissolving the reaction mixture to make the concentration 0.5 M. And then the vial was placed on 30 °C heating block and stirred for 24 h. The solvent was removed *in vacuo* and the residue was purified by silica gel column chromatography directly to provide the **42** as a yellow oil in 60% yield (139.0 mg, R_f = 0.8, Hexane: Ethyl Acetate = 5:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (t, *J* = 8.0 Hz, 1H), 6.57 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.52 (t, *J* = 2.3 Hz, 1H), 6.48 (dd, *J* = 8.1, 2.5 Hz, 1H), 3.77 (s, 3H), 2.29 (dt, *J* = 13.6, 3.3 Hz, 2H), 2.15 – 2.03 (m, 2H), 1.72 – 1.54 (m, 4H), 1.44 (m, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.2, 156.9, 129.7, 112.9, 107.5, 106.3, 55.3, 43.7, 27.3, 27.1, 26.6; HRMS (ESI) *m/z*: Calculated for $C_{15}H_{22}NO^+$ [M+H]$^+$: 232.1696; Found: 232.1701.

*(E)-9-styryl-9-azabicyclo[6.1.0]nonane (**43**)*. To an 8 mL glass vial equipped with magnetic bar was added Pd_2dba_3 (0.02 mmol, 18.3 mg, 2 mol%), (rac)-BINAP (0.06 mmol, 37.4 mg, 6 mol%) and NaO^{t}Bu (1.4 mmol, 134.5 mg, 1.4 equiv) at room temperature. Toluene was added for dissolving the reaction mixture, and then the vial was placed on 30 °C heating block and stirred for 10 min. Afterwards, **2** and (*E*)-(2-bromovinyl)benzene (1.0 mmol, 183.0 mg, 1.0 equiv) were added successively. The vial was heated to 90 °C for 12 h. After cooling down to room temperature, the solvent was removed in vacuo and the residue was purified by silica gel column chromatography directly to provide **43** as a yellow oil in 52% yield (118.2 mg, R_f = 0.5, Hexane: Ethyl Acetate = 20:1 (v/v)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 2.3 Hz, 4H), 7.13 (td, *J* = 6.0, 2.7 Hz, 1H), 6.86 (d, *J* = 13.9 Hz, 1H), 6.00 (d, *J* = 13.9 Hz, 1H), 2.25 –2.19 (m, 2H), 1.94 – 1.88 (m, 2H), 1.69 – 1.57 (m, 4H), 1.52 – 1.38 (m, 4H), 1.36 – 1.26 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.7, 137.2, 128.6, 126.0, 125.3, 116.0, 43.9, 27.1, 26.8, 26.6; HRMS (ESI) *m/z*: Calculated for $C_{16}H_{22}N^+$ [M+H]$^+$: 228.1747; Found: 228.1752.

Associated content

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information Statement

The Supporting Information is available free of charge at XXXXXXXXXXXX

Details for mechanistic investigation, preparation of substrates, copies of the ^{1}H and ^{13}C NMR spectra

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All authors have approved the final version of this manuscript.

Notes

The authors declare no competing financial interests.

Acknowledgements

This work was supported by the National Key R&D Program of China (2022YFA1504303, 2023YFA1508800), the National Natural Science Foundation of China (22371144), Fundamental Research Funds for the Central Universities (NKU63231195).

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TOC