Isomerization of Aziridines to Allyl Amines via Titanium and Chromium Cooperative Catalysis

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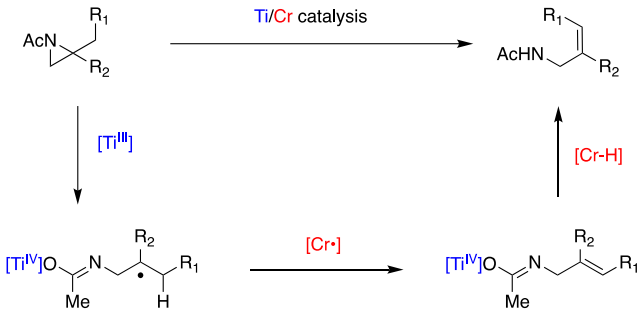
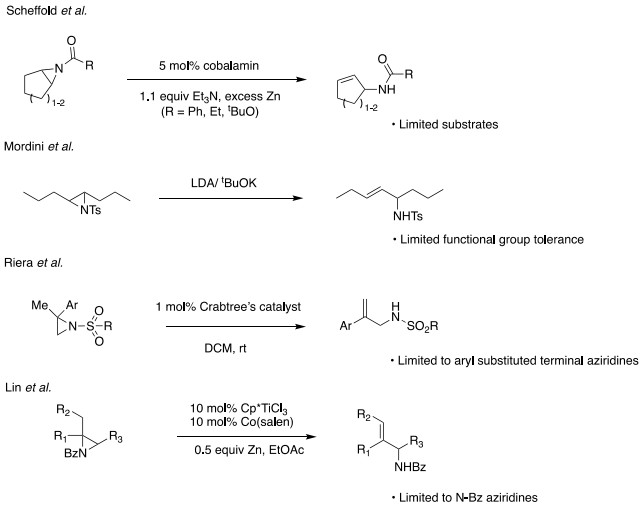
ABSTRACT: A Ti/Cr cooperative catalyst isomerizes aziridines to allyl amines under mild conditions. The reaction tolerates a broad range of aziridines with various nitrogen substituents. The titanium catalyst is most successful in opening 1,2-disubstituted aziridines, forming radical intermediates in a highly regioselective manner. The chromium catalyst appears to abstract an H• from these radical intermediates, and then to return the H• to the titanium system in the form of an H^+ and an electron. The reaction is complementary to previous reports on the isomerization of aziridines to allyl amines.



Isomerization processes are of great synthetic interest because of their perfect atom economy. While the isomerization of epoxides to aldehydes or ketones can be mediated by a wide range of reagents,[1] the use of Brønsted acids and Lewis acids,[2] most often BF_3•Et_2O[3] or $MgBr_2$,[4] is particularly common. Transition-metal complexes can also act as efficient catalysts for the same reaction (isomerization of epoxides to aldehydes or ketones), although a Lewis acid mechanism is generally not involved.[1, 5] The isomerization of epoxides to allylic alcohols — generally base catalyzed — has also been widely studied.[6-7]

The isomerization of aziridines, however, has not received as much attention. In 2002, Nakayama et al. reported the acid-catalyzed rearrangement of *N*-tosyl aziridines to the corresponding *N*-tosyl imines.[8] In 2003, Wolfe and coworkers realized the same transformation with a palladium catalyst.[9] The isomerization of aziridines to allyl amines is of synthetic interest, as allyl amines are essential intermediates in organic synthesis as well as components of biologically active compounds.[10-12] Recent developments in the synthesis of unprotected N-H aziridines from olefins, via transition-metal catalysis,[13-16] organocatalysis,[17] and electrocatalysis,[18-20] encourage the synthesis of allyl amines by this method (the isomerization of aziridines). The Scheffold group (Scheme 1) has reported a seminal contribution, using a cobalamin to catalyze the enantioselective synthesis of allyl amines;[21] however, the only successful substrates were the aziridines derived from cyclopentene or cyclohexene. (Substrates derived from cycloheptene and cyclooctene failed to undergo isomerization.) In 2002, the Mordini group described the base-promoted isomerization of aziridines with various substituents on nitrogen to the corresponding allyl amines,[22] but the requirement for a strong base limited the substrate scope. In 2018, Riera and coworkers demonstrated that Crabtree's catalyst could catalyze the same transformation,[23] although the substrate scope was limited to aryl-substituted aziridines.

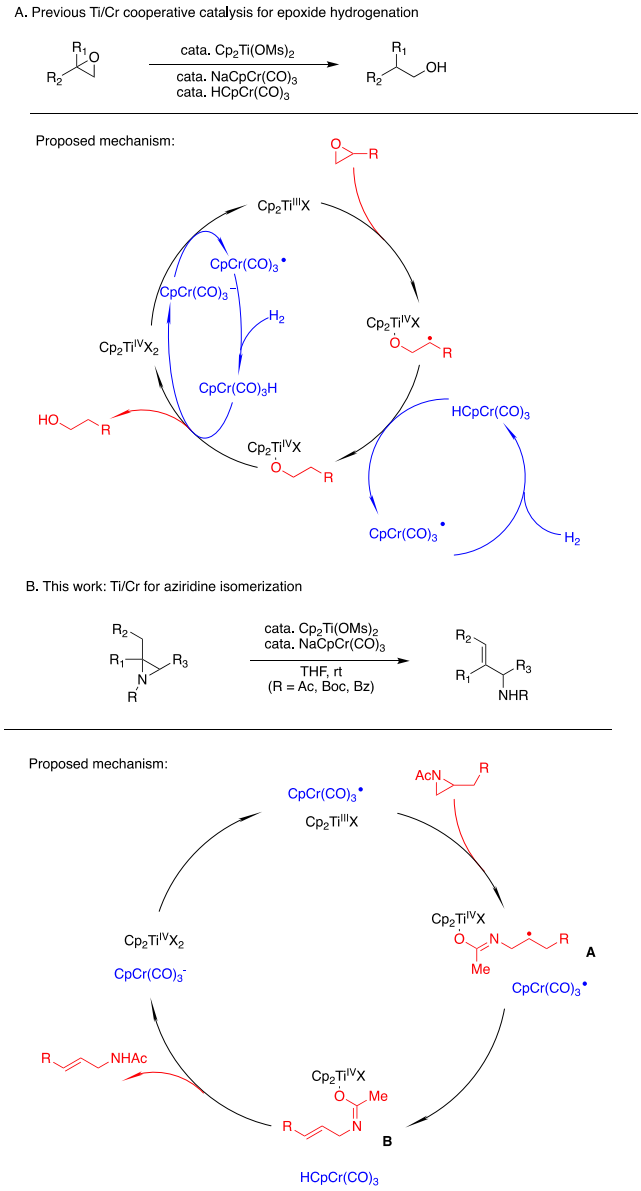
While we were preparing this manuscript, the Lin group reported a bimetallic (titanium and cobalt) radical relay system that catalyzed the same isomerization reaction.[24] However, the reaction was limited to *N*-Bz aziridines, and did not work with other common nitrogen-protecting groups, including Boc and Ac. Here, we describe a Ti/Cr cooperative catalyst for the isomerization of aziridines to allyl amines. This method is applicable to a broad range of aziridines with different nitrogen substituents.



Scheme 1. Previous reports on aziridine isomerization to allyl amines

Previously we developed a Ti/Cr cooperative catalyst for the anti-Markovnikov hydrogenation of epoxides.[25] The initial step appears to be an inner sphere electron transfer from a titanium(III) to the epoxide (a reaction discovered by Rajanbabu,[26] and later made catalytic by the Gansaüer group[27]). The chromium catalyst is responsible for the activation of H_2, and provides the titanium system with H•, H^+, and e^-. In 2017, the Lin group and the Gansaüer group independently reported Ti(III)-mediated aziridine ring openings, and applied this reaction to [3+2] cycloadditions and Giese reactions, respectively.[28-29]

We felt that our Ti/Cr system (in Scheme 2A) could be used, *if the hydrogen were omitted,* to catalyze aziridine isomerization under mild and base-free conditions. The Ti(III) should open an aziridine as it opens an epoxide, to **A**, but in the form of $CpCr(CO)_3$• the chromium should abstract an H• from **A** instead of donating one, giving **B**. The chromium should then return the H• as an H^+ (again cleaving the ligand as product) and an e^- (again reducing the titanium back to Ti(III)) — resulting in the allyl amine in Scheme 2B.



Scheme 2. Previous work and reaction design

We tested this hypothesis by treating substrate **1a** with the $NaCpCr(CO)_3$ and $Cp_2Ti(OMs)_2$ used in our epoxide hydrogenation reaction (Table 1, entry 1). The regioisomeric allyl amines **2a** and **3a** were obtained, in a combined yield of 76%; the enamine **4a** was obtained as a byproduct. (The **4a** is presumably generated by the abstraction of H•, as in eq 1, from the carbon next to the nitrogen in the initial radical **A**.) Optimization (entries 2 and 3) showed THF to be the best solvent.

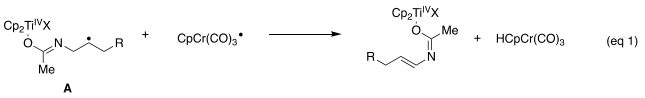
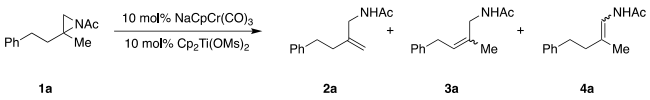


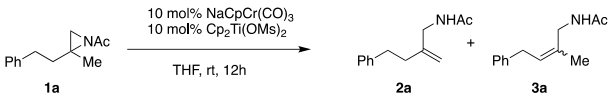
Table 1. Reaction Condition Optimization



Entry	Reaction condition	**2a**	**3a**	**4a**	**2a+3a**
1	benzene, 70 °C, 3 days	48%	28%	8%	76%
2	benzene, rt, 3 days	47%	25%	7%	72%
3	THF, rt, 3 days	55%	28%	9%	83%

With **1a** as the substrate, both the titanium and the chromium catalysts are helpful to the success of the reaction (Table 2, entries 2 and 3). If we generate Ti(III) *in situ* from zinc (entry 4), we obtain only a 30% yield, which indicates that the chromium cocatalyst does not simply act as a one-electron reductant. With 10 mol% catalyst (entry 5), the reaction is complete after an hour at room temperature, and reducing the catalyst loading to 2 mol% does not affect the yield (entry 6). However, a combination of 2 mol% catalyst loading and a one-hour reaction time gives only a 32% yield (entry 7).

Table 2. Control Experiments



Entry	Deviation from the standard condition	**2a** + **3a**
1	None	86%
2	No Ti catalyst	< 5%
3	No Cr catalyst	27%
4	No Cr catalyst, with 10 mol% Zn	30%
5	1h	85%
6	2 mol% catalysts	85%
7	2 mol% catalysts, 1h	32%
8	10 mol% Cp_2TiCl_2, $Cp^*_2TiCl_2$, $CpTiCl_3$, (salen)$TiCl_2$ instead of $Cp_2Ti(OMs)_2$	Similar yields
9	10 mol% $Co(dmgBF_2)_2(THF)_2$ instead of $NaCpCr(CO)_3$	50%
10	10 mol% $AlCl_3$, $FeCl_3$, $SnCl_4$, $TiCl_4$, or BF_3•Et_2O	< 10%

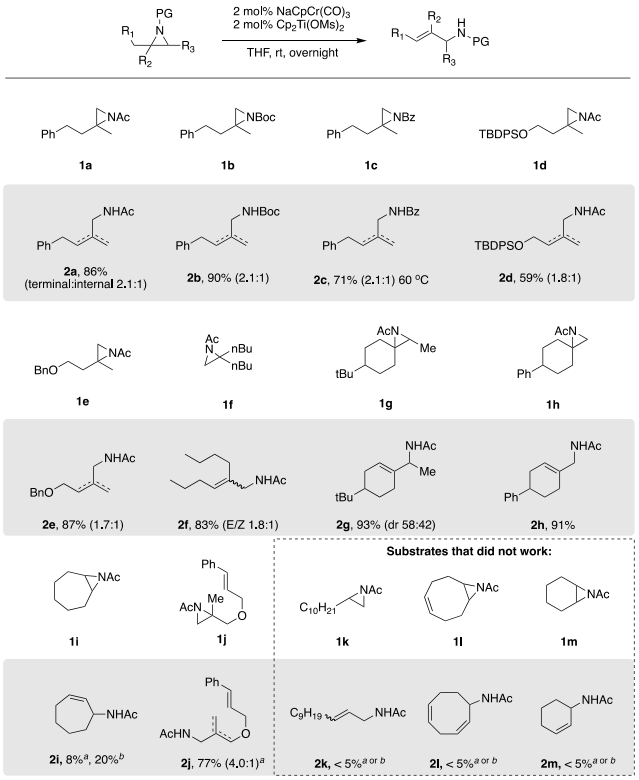
The reaction shows no sensitivity to the identity of the titanium catalyst: replacing the $Cp_2Ti(OMs)_2$ with Cp_2TiCl_2, $Cp^*_2TiCl_2$, $CpTiCl_3$, or (salen)$TiCl_2$ gives similar results (entry 8). Replacing our Cr catalyst with a cobaloxime one leads to a decrease in yield (entry 9). (We have used $Co(dmgBF_2)_2(THF)_2$ to catalyze H• transfer from H_2 in various isomerization and cycloisomerization reactions.[30-32]) Lewis acids such as $AlCl_3$, $FeCl_3$, $SnCl_4$, $TiCl_4$, or BF_3•Et_2O (entry 10) give yields under 10%, which indicates that our Ti catalyst is not just serving as a Lewis acid. In all cases the ratio between **2a** and **3a** is around 2:1, favoring **2a**.

With the optimal conditions in hand, we explored the scope of our aziridine isomerization (Scheme 3). Common protecting groups on nitrogen such as acetyl (**1a**), Boc (**1b**), and benzoyl (**1c**) provided the isomerization products in high yields. In cases **1a-1e**, a mixture of two regioisomers is obtained, with the formation of the terminal C=C double bond favored. Benzoyl-substituted aziridines are relatively unreactive and require high temperature to achieve conversion. Our method thus complements the catalytic system developed by the Lin group, which isomerized *only N*-Bz aziridines at room temperature. A tosyl-substituted aziridine (which is more difficult to reduce) gives no conversion. Various other aziridines, synthesized from cyclic or acyclic olefins, were also successfully converted to the corresponding ring-opening isomerization products (**1d-1h**). All aziridines open to form the more substituted radicals **A**, and then predominantly, after H• abstraction, give an exo methylene product from the methyl substituents (in **1a-1e**).

The reaction does not work well with a 1,2-disubsituted aziridine like **1i**. Even with an increased temperature and increased catalyst loading, the product **2i** was obtained in only 8% yield. An extensive screening on the solvent identified acetone as the optimal one. However, the yield was still as low as 20%. Structurally similar substrates **2l** and **2m** gave no conversion, even under the optimized conditions. A mono-substituted aziridine **2k** also gave no conversion. This result can be easily explained by the proposed mechanism in Scheme 2; Ti(III) will open a 1,2-disubstituted aziridine or a mono-substituted aziridine to a less stable secondary radical, and thus the electron-transfer step may be sluggish and lead to a lower yield. The substrate **1j** was synthesized to test the possibility of a radical cyclization reaction. However, the isomerized allyl amine **2j** was obtained instead of the expected cycloisomerization product, probably because H• abstraction by Cr• is faster than radical cyclization.

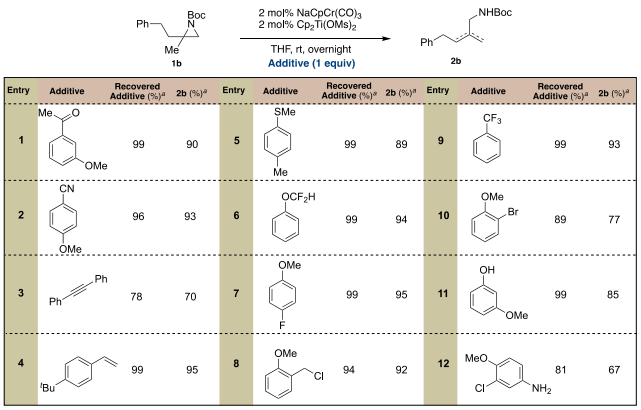
This reaction was shown to have a good functional group tolerance via an additive approach (Table 3). Common functional group tested were all well-tolerated: additives were recovered with the yield not being affected much. Reducible function groups, such as ketone and nitrile (entries 1 and 2) were well tolerated. Unsaturated bonds, as in alkene and alkyne (entries 3 and 4) and thioether (entry 5) remained intact after the reaction. Carbon-halide bonds (entries 6-10) and acidic protons (entries 11 and 12) didn't interfere with the reaction.

The reaction was easily scaled up (Scheme 4A). With 1.0 gram of the aziridine **1a**, the allyl amine **2a** was obtained in 74% yield. To support the presence of a radical intermediate in this catalytic reaction, a TEMPO trapping experiment was conducted (Scheme 4B). With 3 equivalents of TEMPO added, the reaction gave no conversion at all, which prevented us from observing any TEMPO adduct of potential radical intermediates.



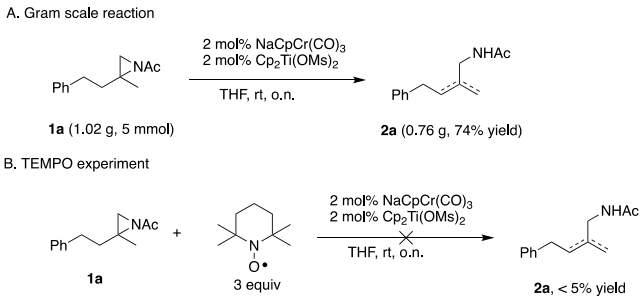
Scheme 3. Substrate scope. [a]10 mol% catalysts, 55 °C, [b]10 mol% catalysts, acetone, 50 °C

Table 3. Functional Group Tolerance



Entry	Additive	Recovered Additive (%)[a]	2b (%)[a]	Entry	Additive	Recovered Additive (%)[a]	2b (%)[a]	Entry	Additive	Recovered Additive (%)[a]	2b (%)[a]
1		99	90	5		99	89	9		99	93
2		96	93	6		99	94	10		89	77
3		78	70	7		99	95	11		99	85
4		99	95	8		94	92	12		81	67

Reaction condition: **1b** (0.1 mmol), additive (1 equiv, 0.1 mmol), $Cp_2Ti(OMs)_2$ (0.02 equiv, 0.002 mmol), $NaCrCp(CO)_3$ (0.02 equiv, 0.002 mmol), THF (1 mL). Yields are determined by GC-MS using decane as the internal standard.



Scheme 4. Gram scale reaction and TEMPO trapping experiment

Conclusions

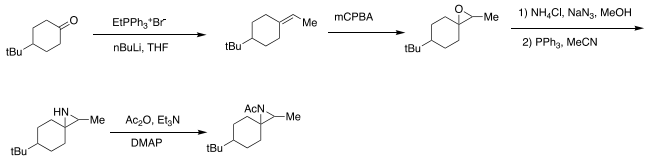
In this study, we have developed a Ti/Cr cooperative catalyst that isomerizes *N*-substituted aziridines to allyl amines. The methodology can be applied to a range of aziridines with different substitution patterns and various nitrogen substituents. The reaction relies on interactions between the titanium catalyst and the chromium catalyst; the Cr removes an H• from the opened aziridine **A**, giving the titanium(IV) intermediate **B**, and returns an H^+ and an e^- to that intermediate.

Experimental Section

General Considerations. All the reactions involving air- or moisture sensitive compounds were carried out in an inert atmosphere box (O_2 < 1 ppm) or by standard Schlenk techniques under Ar. Glassware was oven-dried or flame-dried prior to use. All commercial reagents were used as received without further purification unless specified. Benzene (C_6H_6) was distilled from sodium-benzophenone ketyl. Tetrahydrofuran was distilled from potassium-benzophenone ketyl. Acetonitrile was distilled from CaH_2 and P_2O_5. ^1H NMR and ^{13}C NMR spectra were recorded using a Bruker 500 Ascend, DRX 500, DRX 400, or DRX 300 spectrometer. Peaks are referenced relative to the solvent residual peak in $CDCl_3$. High resolution mass spectra (HRMS) were obtained from the Columbia University Chemistry Department Mass Spectrometry Facility on a Waters XEVO G2XS QToF mass spectrometer equipped with a UPC2 SFC inlet and a LockSpray source with one of the following three probes: electrospray ionization (ESI) probe, atmospheric pressure chemical ionization (APCI) probe, or atmospheric pressure solids analysis probe (ASAP). Substrates **1a**, **1b**, **1d-1f, 1i** and **1k-1m** were synthesized according to literature.[29] Substrate **1c** was prepared based on literature methods.[24]

Synthesis of the Catalysts. Cp_2TiCl_2, Cp^*TiCl_3, $(C_5H_4Me)_2TiCl_2$ and $Cp^*_2TiCl_2$ were obtained as gifts from Boulder Scientific Co. and used as received. $Cp_2Ti(OMs)_2$ was prepared according to literature, and stored in glovebox.[33] $NaCpCr(CO)_3$ was prepared according to literature, and also stored in glovebox.[25]

Substrate Synthesis. The synthetic route to substrate **1g** is as followed:



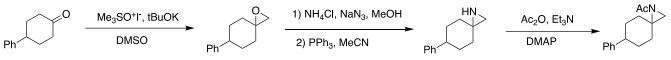
(1) In a suspension of ethyltriphenylphosphonium bromide (11.87 g, 32 mmol, 1.6 equiv) in degassed THF (60 ml) at 0 °C, was added nBuLi (1.6 M in hexane, 18.8 ml, 30 mmol, 1.5 equiv). The reaction was stirred at 0 °C for 1h. 4-tertbutyl cyclohexanone (3.08 g, 20 mmol, 1 equiv) in 10 ml THF was added. The reaction was stirred for 30 minutes before being quenched with water and concentrated. The mixture was extracted with DCM twice. And the combined organic layer was washed with brine and concentrated. Flash chromatography with 2% ethyl acetate in hexanes gave the pure product. The product was obtainend in a 90% yield (2.99 g).

(2) To a solution of 4-tert-butyl-1-ethylidene-cyclohexane (2.99 g, 18 mmol, 1 equiv) in DCM (100 ml), was added mCPBA (4.88 g, 70% wt, 19.8 mmol, 1.1 equiv) and then stirred overnight. The mixture was washed with sodium bicarbonate solution and brine. The mixture was concentrated and subjected to the next step without further purification.

(3) The epoxide (2.73 g, 15 mmol, 1 equiv), NH_4Cl (2.41 g, 45 mmol, 3 equiv), and NaN_3 (2.93 g, 45 mmol, 3 equiv) were mixed in MeOH (60 ml), and then stirred at 70 °C overnight. The reaction mixture was concentrated via rotary evaporation, then dissolved in ether, and washed with water. After the removal of ether, PPh_3 (3.93 g, 15 mmol, 1.0 equiv), and MeCN (60 ml) were added, and the mixture was then stirred at 70 °C for 12 hours. The reaction mixture was concentrated via rotary evaporator. The N-H aziridine was purified using flash column chromatography (5% methanol in dichloromethane). The product was obtained in a combined yield of 69% (2.27 g, steps 2 and 3).

(4) To a solution of the N-H aziridine (1.81 g, 10 mmol, 1 equiv), 4-dimethylaminopyridine (1.34 g, 11 mmol, 1.1 equiv), and triethylamine (2.12 g, 21 mmol, 2.1 equiv) in DCM (60 ml) at -78 °C, was added a solution of acetic anhydride (1.12 g, 11 mmol, 1.1 equiv) in 6 ml DCM dropwise. The reaction mixture was stirred at -78 °C for 3 hours. The reaction was quenched by water, and then extracted with diethyl ether twice. The combined organic layer was then washed with sodium bicarbonate solution and brine. The mixture was concentrated and purified with flash column chromatography (20% ethyl acetate in hexanes). The product was obtained in a 84% yield (1.87 g). ^1H NMR (500 MHz, $CDCl_3$) δ 2.34 (q, *J* = 5.8 Hz, 1H), 2.06 (s, 3H), 1.95 – 1.82 (m, 2H), 1.82 – 1.74 (m, 1H), 1.60 (dq, *J* = 13.4, 3.1 Hz, 1H), 1.29 (d, *J* = 5.8 Hz, 3H), 1.21 – 0.97 (m, 4H), 0.88 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 181.6, 49.3, 47.4, 41.9, 34.8, 32.4, 29.9, 27.6, 27.1, 26.1, 24.6, 13.3. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{25}NOH$ 224.2014; Found: 224.2029.

The synthetic route to substrate **1h** is as followed:

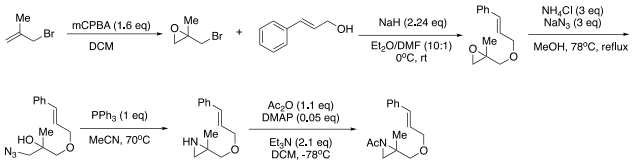


(1) To a suspension of tBuOK (2.24 g, 20 mmol, 1 equiv) in 40 ml DMSO, was added trimethylsulfoxonium iodide (4.4 g, 20 mmol, 1 equiv) at room temperature under argon. After stirring for 30 minutes, a solution of 4-phenylcyclohexanone (3.48 g, 20 mmol, 1 equiv) in 6 ml DMSO was added. The reaction mixture was stirred overnight, before being diluted with ethyl acetate and water. The two layers were then separated. The aqueous layer was extracted again with ethyl acetate. The combined organic layer was washed with brine, and then dried over Na_2SO_4. After the removal of the organic solvent via rotary evaporation, the crude mixture was directly applied to the next step without further purification.

(2) The epoxide (2.82 g, 15 mmol, 1 equiv), NH_4Cl (2.41 g, 45 mmol, 3 equiv), and NaN_3 (2.93 g, 45 mmol, 3 equiv) were mixed in MeOH (60 ml), and then stirred at 70 °C overnight. The reaction mixture was concentrated via rotary evaporation, then dissolved in diethyl ether and washed with water. After the removal of ether, PPh_3 (3.93 g, 15 mmol, 1.0 equiv), and MeCN (60 ml) were added, and the mixture was then stirred at 70 °C for 12 hours. The reaction mixture was concentrated via rotary evaporator. The N-H aziridine was purified using flash column chromatography (5% methanol in dichloromethane). The product was obtained in a combined yield of 72% (2.69 g).

(3) To a solution of the N-H aziridine (1.87 g, 10 mmol, 1 equiv), 4-dimethylaminopyridine (1.34 g, 11 mmol, 1.1 equiv), and triethylamine (2.12 g, 21 mmol, 2.1 equiv) in DCM (60 ml) at -78 °C, was added a solution of acetic anhydride (1.12 g, 11 mmol, 1.1 equiv) in 6 ml DCM dropwise. The reaction mixture was stirred at -78 °C for 3 hours. The reaction was quenched by water, and then extracted with diethyl ether twice. The combined organic layer was then washed with sodium bicarbonate solution and brine. The mixture was concentrated and purified with flash column chromatography (20% ethyl acetate in hexanes). The product was obtained in a 93% yield (2.13 g). ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 2H), 7.28 – 7.17 (m, 3H), 2.65 (tt, *J* = 12.2, 3.3 Hz, 1H), 2.26 – 2.17 (m, 4H), 2.16 (s, 3H), 2.10 – 2.03 (m, 2H), 1.75 – 1.65 (m, 2H), 1.34 (ddt, *J* = 13.4, 4.6, 2.2 Hz, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 181.5, 146.0, 128.5, 126.8, 126.3, 46.1, 43.4, 36.6, 33.7, 33.2, 24.6. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{19}NOH$ 230.1545; Found: 230.1560.

The synthetic route to substrate **1j** is as followed:



(1) In a solution of 3-bromo-2methylpropene (4.05 g, 30 mmol,1 equiv) in dichloromethane (50 ml), mCPBA (10.76 g, 48 mmol, 1.6 equiv) was added. The mixture was stirred at room temperature overnight. The reaction mixture was washed with sodium hydroxide solution three times and brine. The mixture was concentrated via rotary evaporation and subjected to the next step without further purification (3.21g, 71% yield).

(2) In a suspension of sodium hydride (0.83 g, 24.5 mmol, 60% wt, 2.24 equiv) in diethyl ether/dimethylformamide (10:1) (55ml) at 0 ℃, cinnamyl alcohol (1.47 g, 10.9 mmol, 1 equiv) was added dropwise. The reaction mixture was warmed to room temperature for 30 minutes. The reaction mixture was cooled again to 0℃ and 2-(bromomethyl)-2-methyloxirane (1.42 g, 9.4 mmol, 0.86 equiv) in diethyl ether (2 ml) was added to the reaction mixture. The mixture was left to stir at room temperature overnight. After being quenched with brine at 0℃, the aqueous layer was extracted three times with diethyl ether. All of the organic layers were combined and washed with water six times. The mixture was dried, concentrated via rotary evaporation, and purified by flash column chromatography (10% ethyl acetate in hexane, Rf = 0.2). The product was obtained in 50% yield (0.96 g).

(3) In a solution of 2-((cinnamyloxy)methyl)-2-methyloxirane (0.34 g, 1.7 mmol, 1 equiv) in methanol (50 ml), ammonium chloride (0.27 g, 5.0 mmol, 3 equiv) and sodium azide (0.32 g, 5.0 mmol, 3 equiv) were added. The reaction mixture was stirred under reflux at 70 ℃ overnight. The reaction was concentrated via rotary evaporator and was extracted with diethyl ether three times. The organic layers were concentrated and the product was subjected to the next step without further purification.

(4) In a solution of 1-azido-3-(cinnamyloxy)-2-methylpropan-2-ol (0.40 g, 1.63 mmol, 1 equiv) in acetonitrile (50 ml), triphenylphosphine (0.43 g, 1.63 mmol, 1 equiv) was added. The reaction mixture was stirred under reflux at 70 ℃ overnight. The reaction mixture was concentrated via rotary evaporator. The N-H aziridine was purified using flash column chromatography (300 ml of ethyl acetate then 15% methanol in dichloromethane, R_f = 0.1-0.2). The product was obtained in a combined yield of 69% (steps 3 and 4).

(5) To a solution of the N-H aziridine (1.52 g, 7.5 mmol, 1 equiv) in dichloromethane (50 ml), DMAP (46 mg, 0.37 mmol, 0.05 equiv) and triethylamine (1.59 g, 15.7 mmol, 2.1 equiv) were added at -78 ℃. Acetic anhydride (0.84 g, 8.2 mmol, 1.1 equiv) was added to the reaction mixture dropwise. The reaction mixture was stirred at -78 ℃ for 3 hours. The reaction mixture was quenched with water, extracted with diethyl ether three times, washed with sodium bicarbonate solution and brine. The mixture was concentrated and purified with flash column chromatography. The product was obtained in a 89% yield (1.79 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.39 (m, 2H), 7.37-7.32 (m, 2H), 7.29-7.24 (m, 1H), 6.61 (dt, *J* = 15.9, 1.6 Hz, 1H), 6.26 (dt, *J* = 15.9, 6.0 Hz, 1H), 4.18 (dd, *J* = 6.1, 1.5 Hz, 2H), 3.62 (d, *J* = 10.4 Hz, 1H), 3.54 (d, *J* = 10.4 Hz, 1H), 2.36 (s, 1H), 2.15 (d, *J* = 3.1 Hz, 4H), 1.41 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 181.4, 136.5, 132.7, 128.6, 127.8, 126.5, 125.5, 72.1, 71.7, 42.8, 33.7, 24.4, 18.5. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{19}NO_2Na$ 268.1313; Found: 268.1333.

General Procedure for Ti/Cr-Catalyzed Isomerization of N-Substituted Aziridines to Allyl Amines. In an inert atmosphere glovebox, N-substituted aziridine 1 (0.1 mmol), $Cp_2Ti(OMs)_2$ (1 mg, 0.02 equiv, 0.002 mmol), and $NaCrCp(CO)_3$ (0.5 mg, 0.02 equiv, 0.002 mmol) were weighed in a 4 ml glass vial. Degassed THF (1 ml) was then added, and the mixture was stirred at room temperature for overnight unless otherwise noted. The crude reaction mixture was directly subjected to flash column chromatography for purification.

(*Z*)-*N*-(2-methyl-4-phenylbut-2-en-1-yl)acetamide (internal) / *N*-(2-methylene-4-phenylbutyl)acetamide (external) (2a). Synthesized according to general procedure and isolated after column chromatography (50% EtOAc:Hex), where 17 mg (86% yield, external:internal = 2.1:1, colorless oil) was obtained. **For the major isomer:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H), 7.25 – 7.17 (m, 3H), 5.57 (br, s, 1H), 4.95 (q, *J* = 1.2 Hz, 1H), 4.93 (q, *J* = 1.2 Hz, 1H), 3.88 (d, *J* = 6.0 Hz, 2H), 2.88 – 2.77 (m, 2H), 2.40 – 2.33 (m, 2H), 2.02 (s, 3H). **For the minor isomer:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H), 7.24 – 7.14 (m, 3H), 5.57 (brs, 1H), 5.52 (tq, *J* = 7.4, 1.4 Hz, 1H), 3.85 (dd, *J* = 6.0, 1.3 Hz, 2H), 3.40 (d, *J* = 7.4 Hz, 2H), 2.02 (s, 3H), 1.76 (d, *J* = 1.4 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 170.0, 145.4, 141.7, 128.5, 128.4, 128.4, 126.0, 126.0, 125.2, 110.9, 46.8, 44.2, 35.7, 34.2, 34.1, 23.4, 23.3, 14.7. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{17}NONa$ 226.1208; Found: 226.1216.

***tert*-butyl (*Z*)-(2-methyl-4-phenylbut-2-en-1-yl)carbamate (internal)/*tert*-butyl (2-methylene-4-phenylbutyl)carbamate (external) (2b).** Synthesized according to general procedure and isolated after column chromatography (50% EtOAc:Hex), where 23 mg (90% yield, external:internal = 2.1:1, white solid) was obtained. **For the major isomer:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 2H), 7.25 – 7.15 (m, 3H), 4.95 (d, *J* = 1.8 Hz, 1H), 4.90 (p, *J* = 1.2 Hz, 1H), 4.64 (br, s, 1H), 3.84 – 3.73 (m, 2H), 2.88 – 2.73 (m, 2H), 2.51 – 2.29 (m, 2H), 1.55 (s, 9H). **For the minor isomer:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 2H), 7.25 – 7.15 (m, 3H), 5.52 (tq, *J* = 7.4, 1.4 Hz, 1H), 4.59 (br, s, 1H), 3.72 (d, *J* = 6.2 Hz, 2H), 3.40 (d, *J* = 7.4 Hz, 2H), 1.78 – 1.72 (m, 3H), 1.55 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 155.9, 146.8, 146.0, 141.8, 128.5, 128.4, 128.3, 125.9, 110.2, 85.2, 45.3, 35.7, 34.2, 34.0, 28.4, 27.4. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{23}NO_2Na$ 284.1627; Found: 284.1641.

(Z)-N-(2-methyl-4-phenylbut-2-en-1-yl)benzamide (internal)/N-(2-methylene-4-phenylbutyl)benzamide (external) (2c). Synthesized according to general procedure and isolated after column chromatography (30% EtOAc:Hex), where 19 mg (71% yield, external:internal = 3.0:1, white solid) was obtained. **For the major isomer:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.71 (m, 2H), 7.60 – 7.43 (m, 3H), 7.36 – 7.26 (m, 2H), 7.24 – 7.15 (m, 3H), 6.26 (s, 1H), 5.03 (d, *J* = 1.5 Hz, 1H), 4.98 (q, *J* = 1.2 Hz, 1H), 4.10 (d, *J* = 6.4 Hz, 2H), 2.89 – 2.83 (m, 2H), 2.44 (dd, *J* = 9.3, 6.8 Hz, 2H). **For the minor isomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.71 (m, 2H), 7.60 – 7.43 (m, 3H), 7.36 – 7.26 (m, 2H), 7.24 – 7.15 (m, 3H), 6.26 (s, 1H), 5.62 (ddt, *J* = 7.3, 5.9, 1.4 Hz, 1H), 4.09 (d, *J* = 7.4 Hz, 2H), 3.43 (d, *J* = 7.4 Hz, 2H), 1.83 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.4, 145.5, 141.7, 131.5, 131.5, 128.8, 128.6, 128.6, 128.6, 128.5, 128.4, 128.4, 127.0, 126.9, 126.0, 111.1, 47.2, 44.5, 35.8, 34.2, 34.1, 14.7. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{19}NONa$ 288.1364; Found: 288.1384.

(*Z*)-*N*-(4-((*tert*-butyldiphenylsilyl)oxy)-2-methylbut-2-en-1-yl)acetamide (internal)/*N*-(4-((*tert*-butyldiphenylsilyl)oxy)-2-methylenebutyl)acetamide (external) (2d). Synthesized according to general procedure and isolated after column chromatography (50% EtOAc:Hex), where 23 mg (59% yield, external:internal = 1.8:1, white solid) was obtained. **For the major isomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.66 (m, 4H), 7.50 – 7.37 (m, 6H), 5.61 (br, s, 1H), 4.98 (q, *J* = 1.5 Hz, 1H), 4.92 (q, *J* = 1.2 Hz, 1H), 3.93 – 3.78 (m, 4H), 2.40 – 2.26 (m, 2H), 1.94 (s, 3H), 1.08 (s, 9H). **For the minor isomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.67 (m, 4H), 7.51 – 7.36 (m, 6H), 5.48 (td, *J* = 6.3, 1.4 Hz, 1H), 5.30 (s, 1H), 4.36 – 4.20 (m, 2H), 3.75 (d, *J* = 6.1 Hz, 2H), 2.01 (s, 3H), 1.46 (d, *J* = 1.3 Hz, 3H), 1.07 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 135.6, 135.6, 133.7, 129.7, 129.6, 127.7, 127.6, 112.8, 63.0, 60.8, 44.5, 37.2, 26.9, 26.8, 23.2, 19.2. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{31}NO_2SiNa$ 404.2022; Found: 404.2023.

(*Z*)-*N*-(4-(benzyloxy)-2-methylbut-2-en-1-yl)acetamide (internal)/*N*-(4-(benzyloxy)-2-methylenebutyl)acetamide (external) (2e). Synthesized according to general procedure and isolated after column chromatography (50% EtOAc:Hex), where 20 mg (87% yield, external:internal = 1.7:1, colorless oil) was obtained. **For the major isomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.29 (m, 5H), 5.04 (q, *J* = 1.4 Hz, 1H), 4.97 (q, *J* = 1.1 Hz, 1H), 4.54 (s, 2H), 3.89 – 3.80 (m, 2H), 3.66 (t, *J* = 6.2 Hz, 2H), 2.39 (td, *J* = 6.3, 1.1 Hz, 2H), 1.86 (s, 3H). **For the**

minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.24 (m, 5H), 5.54 (ddt, *J* = 6.7, 5.2, 1.4 Hz, 1H), 4.54 (s, 2H), 4.14 – 4.05 (m, 2H), 3.85 (t, *J* = 6.3 Hz, 2H), 2.03 (s, 3H), 1.67 (d, *J* = 1.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.9, 143.5, 138.0, 128.5, 128.4, 127.9, 127.9, 127.9, 127.8, 127.7, 122.3, 113.2, 73.3, 72.6, 69.8, 66.3, 46.3, 23.3, 23.0, 14.9. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{19}NO_2Na$ 256.1313; Found: 256.1333.

***N*-(2-butylhex-2-en-1-yl)acetamide (2f).** Synthesized according to general procedure and isolated after column chromatography (50% EtOAc:Hex), where 16 mg (83% yield, ZE isomers 1.8:1, colorless oil) was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.41 – 5.16 (m, 2H), 3.87 (d, *J* = 5.2 Hz, 0.7H, 2H for the minor isomer), 3.82 (d, *J* = 5.4 Hz, 1.3H, 2H for the major isomer), 2.02 (s, 1.8H, 3H for the major isomer), 2.00 (s, 1.2H, 3H for the minor isomer), 2.08 – 1.99 (m, 4H), 1.42 – 1.27 (m, 6H), 0.96 – 0.89 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.8, 136.1, 129.4, 127.6, 45.1, 38.7, 35.5, 30.7, 30.4, 29.7, 29.7, 28.5, 23.4, 23.3, 23.1, 22.9, 22.8, 22.4, 14.0, 13.9, 13.9, 13.7. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{23}NONa$ 220.1677; Found: 220.1700.

***N*-(1-(4-(*tert*-butyl)cyclohex-1-en-1-yl)ethyl)acetamide (2g).** Synthesized according to general procedure and isolated after column chromatography (50% EtOAc:Hex), where 21 mg (93% yield, dr 58:42, white solid) was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72 – 5.52 (m, 1H), 5.36 (br, s, 1H), 4.45 (p, *J* = 7.1 Hz, 1H), 2.15 – 2.01 (m, 3H), 2.00 (s, 1.2H, 3H for the minor diastereomer), 1.98 (s, 1.8H, 3H for the major diastereomer), 1.90 – 1.74 (m, 2H), 1.24 (d, *J* = 6.8 Hz, 1.2H, 3H for the minor diastereomer), 1.23 (d, *J* = 6.8 Hz, 1.8H, 3H for the major diastereomer), 1.32 – 1.10 (m, 2H), 0.88 (s, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.0, 138.3, 122.4, 121.3, 49.8, 49.3, 44.1, 44.1, 32.2, 27.3, 27.2, 26.6, 26.6, 24.1, 24.0, 23.6, 23.5, 19.7, 19.5. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{25}NONa$ 246.1834; Found: 246.1850.

***N*-((1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)methyl)acetamide (2h).** Synthesized according to general procedure and isolated after column chromatography (50% EtOAc:Hex), where 21 mg (91% yield, white solid) was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 2H), 7.26 – 7.17 (m, 3H), 5.76 – 5.62 (m, 1H), 5.52 (br, s, 1H), 3.96 – 3.75 (m, 2H), 2.84 – 2.67 (m, 1H), 2.42 – 2.29 (m, 1H), 2.27 – 1.95 (m, 4H), 2.05 (s, 3H), 1.86 – 1.72 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.0, 146.7, 134.4, 128.4, 126.8, 126.1, 122.8, 45.2, 40.0, 33.2, 29.7, 27.2, 23.3. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{19}NONa$ 252.1364; Found: 252.1387.

N-(cyclohept-2-en-1-yl)acetamide (2i). Synthesized according to general procedure with the following modifications: 10 mol% of both catalysts, acetone as the solvent, and reaction at 50 °C. The product was isolated after column chromatography (50% EtOAc:Hex), where 7 mg (20% yield, white solid) was obtained. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (dddd, J = 12.3, 7.5, 5.3, 2.4 Hz, 1H), 5.60 (s, 1H), 5.53 (dddt, J = 11.5, 3.7, 1.8, 0.8 Hz, 1H), 4.66 – 4.55 (m, 1H), 2.29 – 2.09 (m, 2H), 2.00 (d, J = 0.9 Hz, 3H), 1.96 – 1.80 (m, 2H), 1.78 – 1.65 (m, 2H), 1.60 – 1.51 (m, 1H), 1.45 – 1.34 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.9, 134.7, 132.4, 50.5, 34.0, 28.6, 27.6, 26.8, 23.5. HRMS (ES+) m/z: $[M+H]^+$ Calcd for $C_9H_{15}NOH$ 154.1232; Found: 154.1253.

N-(2-((cinnamyloxy)methyl)allyl)acetamide (external) / N-((E)-3-(cinnamyloxy)-2-methylallyl)acetamide (internal) (2j). Synthesized according to general procedure and isolated after column chromatography (50% EtOAc:Hex), where 19 mg (77% yield, external:internal = 4.0:1, yellow oil) was obtained. **For the major isomer:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.38 (m, 2H), 7.38 – 7.32 (m, 2H), 7.31 – 7.24 (m, 1H), 6.64 (dt, *J* = 16.0, 1.7 Hz, 1H), 6.41 – 6.24 (m, 1H), 5.87 (s, 1H), 5.19 (d, *J* = 1.2 Hz, 1H), 5.15 (d, *J* = 1.6 Hz, 1H), 4.17 (dd, *J* = 6.0, 1.5 Hz, 2H), 4.06 (s, 2H), 3.96 (d, *J* = 5.8 Hz, 2H), 2.01 (s, 3H). **For the minor isomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.38 (m, 2H), 7.38 – 7.32 (m, 2H), 7.31 – 7.24 (m, 1H), 6.64 (dt, *J* = 16.0, 1.7 Hz, 1H), 6.41 – 6.24 (m, 1H), 6.13 (q, *J* = 1.3 Hz, 1H), 5.37 (s, 1H), 4.44 (dd, *J* = 6.0, 1.5 Hz, 2H), 3.74 (d, *J* = 5.6 Hz, 2H), 1.99 (s, 3H), 1.68 (d, *J* = 1.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 169.9, 142.2, 136.5, 133.0, 132.7, 128.6, 128.6, 128.0, 127.8, 126.6, 126.5, 125.7, 125.0, 114.4, 72.5, 72.2, 70.8, 43.2, 42.6, 23.3. HRMS (ASAP+) m/z: $[M+H]^+$ Calcd for $C_{15}H_{19}NO_2H$ 246.1494; Found: 246.1484.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Copies of NMR spectra of substrates and products

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Notes

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REFERENCES

1. Huang, C.-Y.; Doyle, A. G., The Chemistry of Transition Metals with Three-Membered Ring Heterocycles. *Chem. Rev.* **2014,** *114*, 8153-8198.
2. Meinwald, J.; Labana, S. S.; Chadha, M. S., Peracid Reactions. III. The Oxidation of Bicyclo [2.2.1]heptadiene. *J. Am. Chem. Soc.* **1963,** *85*, 582-585.
3. Kita, Y.; Kitagaki, S.; Yoshida, Y.; Mihara, S.; Fang, D.-F.; Kondo, M.; Okamoto, S.; Imai, R.; Akai, S.; Fujioka, H., Acid-Promoted Rearrangement of Cyclic α,β-Epoxy Acylates: Stereoselective Synthesis of Spirocyclanes and Quaternary Carbon Centers. *J. Org. Chem.* **1997,** *62*, 4991-4997.
4. Li, W.-D. Z.; Yang, Y.-R., Unusual Cyclopropanation of 9-Bromocamphor Derivatives: A Novel Formal C(1)−C(7) Bond Cleavage of Camphor. *Org. Lett.* **2005,** *7*, 3107-3110.
5. Vyas, D. J.; Larionov, E.; Besnard, C.; Guénée, L.; Mazet, C., Isomerization of Terminal Epoxides by a [Pd–H] Catalyst: A Combined Experimental and Theoretical Mechanistic Study. *J. Am. Chem. Soc.* **2013,** *135*, 6177-6183.
6. Ye, K.-Y.; McCallum, T.; Lin, S., Bimetallic Radical Redox-Relay Catalysis for the Isomerization of Epoxides to Allylic Alcohols. *J. Am. Chem. Soc.* **2019,** *141*, 9548-9554.
7. Magnus, A.; Bertilsson, S. K.; Andersson, P. G., Asymmetric base-mediated epoxide isomerisation. *Chem. Soc. Rev.* **2002,** *31*, 223-229.
8. Sugihara, Y.; Iimura, S.; Nakayama, J., Aza-pinacol rearrangement: acid-catalyzed rearrangement of aziridines to imines. *Chem. Commun.* **2002**, 134-135.

9. Wolfe, J. P.; Ney, J. E., A New, Mild Synthesis of N-Sulfonyl Ketimines via the Palladium-Catalyzed Isomerization of Aziridines. *Org. Lett.* **2003,** *5*, 4607-4610.
10. Rando, R. R.; Bangerter, F. W., The irreversible inhibition of mouse brain *J. Am. Chem. Soc.* **1976,** *98*, 6762-6764.
11. Petranyi, G.; Ryder Neil, S.; Stütz, A., Allylamine Derivatives: New Class of Synthetic Antifungal Agents Inhibiting Fungal Squalene Epoxidase. *Science* **1984,** *224*, 1239-1241.
12. Huleatt, P. B.; Khoo, M. L.; Chua, Y. Y.; Tan, T. W.; Liew, R. S.; Balogh, B.; Deme, R.; Gölöncsér, F.; Magyar, K.; Sheela, D. P.; Ho, H. K.; Sperlágh, B.; Mátyus, P.; Chai, C. L. L., Novel Arylalkenylpropargylamines as Neuroprotective, Potent, and Selective Monoamine Oxidase B Inhibitors for the Treatment of Parkinson's Disease. *J. Med. Chem.* **2015,** *58*, 1400-1419.
13. Jat Jawahar, L.; Paudyal Mahesh, P.; Gao, H.; Xu, Q.-L.; Yousufuddin, M.; Devarajan, D.; Ess Daniel, H.; Kürti, L.; Falck John, R., Direct Stereospecific Synthesis of Unprotected N-H and N-Me Aziridines from Olefins. *Science* **2014,** *343*, 61-65.
14. Munnuri, S.; Anugu, R. R.; Falck, J. R., Cu(II)-Mediated N–H and N-Alkyl Aryl Amination and Olefin Aziridination. *Org. Lett.* **2019,** *21*, 1926-1929.
15. Ma, Z.; Zhou, Z.; Kürti, L., Direct and Stereospecific Synthesis of N-H and N-Alkyl Aziridines from Unactivated Olefins Using Hydroxylamine-O-Sulfonic Acids. *Angew. Chem. Int. Ed.* **2017,** *56*, 9886-9890.
16. Legnani, L.; Prina-Cerai, G.; Delcaillau, T.; Willems, S.; Morandi, B., Efficient access to unprotected primary amines by iron-catalyzed aminochlorination of alkenes. *Science* **2018,** *362*, 434-439.
17. Cheng, Q.-Q.; Zhou, Z.; Jiang, H.; Siitonen, J. H.; Ess, D. H.; Zhang, X.; Kürti, L., Organocatalytic nitrogen transfer to unactivated olefins via transient oxaziridines. *Nat. Catal.* **2020,** *3*, 386-392.
18. Holst, D. E.; Wang, D. J.; Kim, M. J.; Guzei, I. A.; Wickens, Z. K., Aziridine synthesis by coupling amines and alkenes via an electrogenerated dication. *Nature* **2021,** *596*, 74-79.
19. Liu, S.; Zhao, W.; Li, J.; Wu, N.; Liu, C.; Wang, X.; Li, S.; Zhu, Y.; Liang, Y.; Cheng, X., Electrochemical Aziridination of Tetrasubstituted Alkenes with Ammonia. *CCS Chem.* **2021**, 872-882.
20. Ošeka, M.; Laudadio, G.; van Leest, N. P.; Dyga, M.; Bartolomeu, A. d. A.; Gooßen, L. J.; de Bruin, B.; de Oliveira, K. T.; Noël, T., Electrochemical Aziridination of Internal Alkenes with Primary Amines. *Chem* **2021,** *7*, 255-266.
21. Zhang, Z. D.; Scheffold, R., Asymmetric Catalysis by Vitamin B12: The Isomerization of Achiral Aziridines to Optically Active Allylic Amines. *Helv. Chim. Acta* **1993,** *76*, 2602-2615.
22. Mordini, A.; Russo, F.; Valacchi, M.; Zani, L.; Degl'Innocenti, A.; Reginato, G., Base-promoted elaboration of aziridines. *Tetrahedron* **2002,** *58*, 7153-7163.
23. Cabré, A.; Sciortino, G.; Ujaque, G.; Verdaguer, X.; Lledós, A.; Riera, A., Iridium-Catalyzed Isomerization of N-Sulfonyl Aziridines to Allyl Amines. *Org. Lett.* **2018,** *20*, 5747-5751.
24. Wood, D. P.; Guan, W.; Lin, S., Titanium and Cobalt Bimetallic Radical Redox Relay for the Isomerization of N-Bz Aziridines to Allylic Amides. *Synthesis* **2021,** *53*, 4213-4220.
25. Yao, C.; Dahmen, T.; Gansäuer, A.; Norton, J., Anti-Markovnikov alcohols via epoxide hydrogenation through cooperative catalysis. *Science* **2019,** *364*, 764-767.
26. RajanBabu, T. V.; Nugent, W. A., Selective Generation of Free Radicals from Epoxides Using a Transition-Metal Radical. A Powerful New Tool for Organic Synthesis. *J. Am. Chem. Soc.* **1994,** *116*, 986-997.
27. Gansäuer, A.; Bluhm, H.; Pierobon, M., Emergence of a Novel Catalytic Radical Reaction: Titanocene-Catalyzed Reductive Opening of Epoxides. *J. Am. Chem. Soc.* **1998,** *120*, 12849-12859.
28. Hao, W.; Wu, X.; Sun, J. Z.; Siu, J. C.; MacMillan, S. N.; Lin, S., Radical Redox-Relay Catalysis: Formal [3+2] Cycloaddition of N-Acylaziridines and Alkenes. *J. Am. Chem. Soc.* **2017,** *139*, 12141-12144.
29. Zhang, Y.-Q.; Vogelsang, E.; Qu, Z.-W.; Grimme, S.; Gansäuer, A., Titanocene-Catalyzed Radical Opening of N-Acylated Aziridines. *Angew. Chem. Int. Ed.* **2017,** *56*, 12654-12657.
30. Li, G.; Kuo, J. L.; Han, A.; Abuyuan, J. M.; Young, L. C.; Norton, J. R.; Palmer, J. H., Radical Isomerization and Cycloisomerization Initiated by H• Transfer. *J. Am. Chem. Soc.* **2016,** *138*, 7698-7704.
31. Shi, S.; Salahi, F.; Vibbert, H. B.; Rahman, M.; Snyder, S. A.; Norton, J. R., Generation of α-Boryl Radicals by H• Transfer and their Use in Cycloisomerizations. *Angew. Chem. Int. Ed.* **2021,** *60*, 22678-22682.
32. Lorenc, C.; Vibbert, H. B.; Yao, C.; Norton, J. R.; Rauch, M., H· Transfer-Initiated Synthesis of γ-Lactams: Interpretation of Cycloisomerization and Hydrogenation Ratios. *ACS Catal.* **2019,** *9*, 10294-10298.
33. Richrath, R. B.; Olyschläger, T.; Hildebrandt, S.; Enny, D. G.; Fianu, G. D.; Flowers Ii, R. A.; Gansäuer, A., Cp_2TiX Complexes for Sustainable Catalysis in Single-Electron Steps. *Chem. Eur. J.* **2018,** *24*, 6371-6379.