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Stereoselective Isomerisation of N-Allyl Aziridines into Geometrically Stable *Z* Enamines by Using Rhodium Hydride Catalysis

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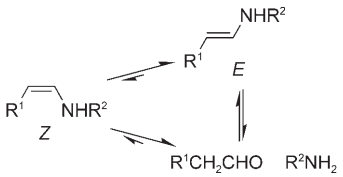
Abstract: In the presence of rhodium(I) hydride catalysts, tertiary N-allylamines are known to isomerise into *E* enamines. In contrast, we have recently found that N-allylaziridines isomerise to form *Z* enamines. On the basis of literature data, the most likely mechanism of isomerisation would involve a rhodium hydride addition/β-hydride elimination sequence. We show that the observed selectivity cannot be adequately explained by this pathway and is more consistent with initial CH-activation followed by rearrangement to form a five-membered cyclometallated rhodium intermediate. This intermediate subsequently undergoes reductive elimination to form a C–H bond. The resulting geometrically stable *Z* enamines are useful building blocks for stereoselective synthesis.

Keywords: aziridines · enamines · isomerisation · metallacycles · rhodium

Introduction

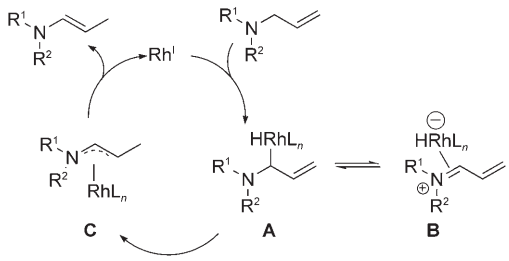
Enols, metal enolates and enamines are amongst the most important carbon nucleophiles in both biological and chemical synthesis.[1] Many useful transformations owe their efficiency to selective formation of *E* or *Z* metal enolates. In contrast, the chemistry of enamines is restricted to reactions of their *E* isomers because the classical condensation between amine and carbonyl functional groups is an equilibrium process that affords thermodynamically favoured *E* products. There are no useful, kinetically controlled reactions that result in *Z* enamine formation. Although strong base-promoted isomerisation of N-allylamines into *Z* enamines was reported,[2] attempts to isolate the *Z* products result in rapid *Z*-to-*E* isomerisation or hydrolysis (Scheme 1). Even in the metal-catalysed cross-coupling of geometrically pure (*Z*)-vinyl bromides with amine nucleophiles, formation of *E* enamines is observed due to in-situ isomerisation of the kinetic *Z* product into the *E* isomer.[3]

Cationic rhodium(I) diphosphine complexes are known to induce selective isomerisation of N-allylamines into enamines.[4] Once again, the *E* geometry is strongly favoured.



Scheme 1. *Z* enamines are difficult to prepare, often isomerising or hydrolysing during isolation.

Noyori's BINAP/rhodium(I) catalyst has been used in one of the most acclaimed asymmetric processes practiced in industry, synthesis of menthol.[5] In a generally accepted mechanistic description of the reaction depicted in Scheme 2, CH-activation at the allylic position leads to an organometallic species **A**, which is stabilised through iminium complex **B**. Subsequent hydride migration to the terminal olefinic carbon atom affords intermediate **C** which undergoes decomplexation, releasing the *E* enamine product. Interesting-



Scheme 2. Accepted mechanism of isomerisation of allyl amines with cationic rhodium(I) diphosphine complexes.

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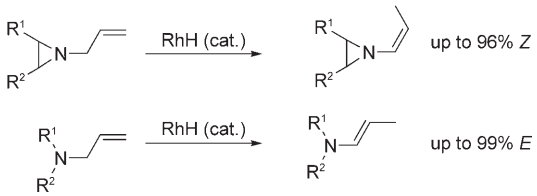
ly, failure of the cationic rhodium(I) catalysts to induce isomerisation of allyl amines derived from ethylene imine has been used as an indirect piece of evidence in favour of iminium complex formation.[6]

Rhodium(I) hydride catalysts are also known to induce isomerisation of N-allylamines.[7,8] The generally accepted mechanism of isomerisation in this case involves metal hydride addition across the carbon–carbon double bond followed by β-hydride elimination, resulting in double-bond migration. This transformation generally leads to *E* enamine geometry in both the kinetic and thermodynamic product.

Previous work by our group revealed that NH-aziridines behave differently from other secondary amines with respect to palladium-catalysed allylic amination.[9,10a] With common secondary amine nucleophiles, thermodynamically favoured linear products are formed due to in-situ palladium-catalysed isomerisation. On the other hand, with NH-aziridine nucleophiles, the kinetically favoured branched products do not undergo further isomerisation into the linear allyl amines. This mechanistic insight has allowed us to find conditions under which any primary or secondary amine can undergo palladium-catalysed allylic amination with high branched selectivity.[10b] With a reliable route to allyl aziridines in hand, we opted for examine transition-metal-promoted isomerisation of N-allylaziridines into enamines. As a result, we uncovered yet another instructive aberration in aziridine chemistry: N-allylaziridines behave differently from N-allylamines with respect to metal-catalysed isomerisation. Whereas N-allylamines form *E* isomers upon exposure to rhodium(I) hydride catalysts, it was found that isomerisation of N-allylaziridines results in unusual selectivity for the thermodynamically disfavoured (*Z*)-N-propenylaziridine (Scheme 3).[11] As aziridine rings are stepping stones to more complex amines by means of diverse ring-opening processes, this chemistry is expected to find useful synthetic applications.



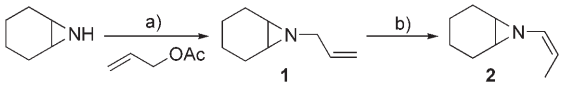
Scheme 3. Isomerisation of N-allylaziridines and N-allylamines leads to different geometries. cat. = < 5 mol %; RhH = $[Rh(CO)H(PPh_3)_3]$.

It should be noted that unexpected *Z* geometry has been observed with other substrates, including simple elimination reactions with base,[12] isomerisation of olefins varying in chain length from 1-butene to 1-heptene,[13,14,15,16] allyl vinyl ethers,[17] and N-allylamides.[18] The classical hydride mechanism is often mentioned in relation to both isomerisation[8,14,15,18] and hydrogenation[7,19] with $[Rh(CO)H(PPh_3)_3]$, but this mechanism is expected to produce *E* products. Alternate mechanisms have been suggested to explain the *Z* selectivity in transition-metal-catalysed isomerisations, although the levels of selectivity are generally quite low. These mechanisms often involve some form of coordination between the transition-metal catalyst and the substrate, forming a metallocycle, such as in the case of N-allylamides.[18] What is unique about N-allylaziridines are the high *Z* selectivities observed.

In this study, we put forth mechanistic evidence in support of a cyclometallated rhodium intermediate, which operates concurrently with a non-productive, hydride addition–elimination mechanism that has traditionally been suggested as the sole mechanism of catalytic olefin isomerisation with late transition-metal hydrides.

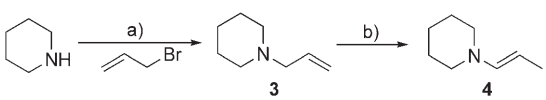
Results

With our recently disclosed approach to allyl aziridines,[9,10a] we investigated the isomerisation of N-allylcyclohexene imine **1** with 1.5 mol % of [Rh(binap)(cod)]OTf as a source of rhodium(I) prepared in situ from $[Rh(cod)_2]OTf$ and *rac*-BINAP.[11] In contrast to previous reports with allylated ethylene imine, we did obtain the N-(1-propenyl)aziridine **2**, albeit with a low 25 % conversion (Scheme 4). The rearrangement of **1** ($t_{1/2}$ = 164.0 min) was significantly slower than the rearrangement of N-allylmorpholine under similar conditions ($t_{1/2}$ = 1.3 min). Interestingly, unexpected selectivity for the *Z* isomer of **2** was observed. There was no evidence for isomerisation into the *E* isomer in the course of isolation.



Scheme 4. Initial isomerisation studies. a) $[Pd(\eta\text{-}C_3H_5)Cl]_2$ (1.5 mol %), PPh_3, K_2CO_3, THF, RT, 16 h, 76 %; b) $[Rh(cod)_2]OTf$, *rac*-BINAP, THF, reflux, 60 °C, 16 h, 25 % conv. cod = 1,5-cyclooctadiene; BINAP = (2*R*,3*S*)-2,2′-bis(diphenylphosphino)-1,1′-binapthyl.

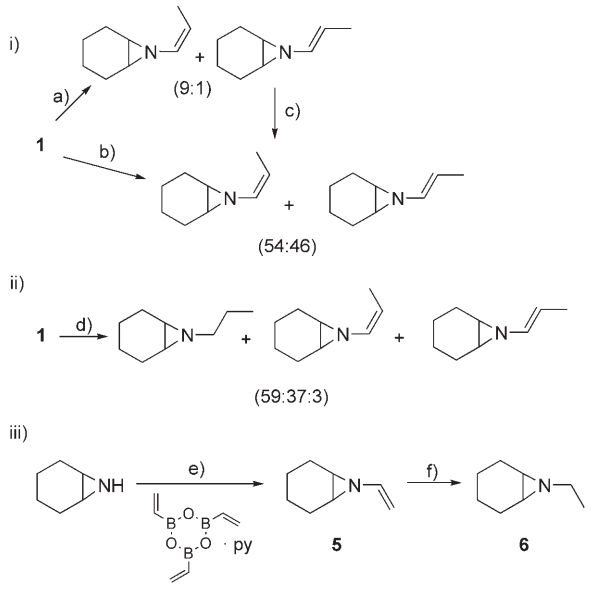
Similar to cationic rhodium(I) catalysts equipped with bidentate ligands, such as BINAP, rhodium(I) hydride catalysts are known to induce allyl amine isomerisation. Reports in the literature have previously indicated that amines such as *N*-allylpiperidine (**3**) can be isomerised with $[Rh(CO)H(PPh_3)_3]$, leading exclusively to the *E* isomer **4** (Scheme 5).[8] In our hands, treatment of N-allylmorpholine with $[Rh(CO)H(PPh_3)_3]$ also showed exclusive preference for the *E* enamine, whereas treatment of N-allylcyclohexene imine under similar conditions gave the *Z* product. Notably, the



Scheme 5. Isomerisation of 1-allylpiperidine.[8] a) NaH, THF, RT, 16 h, 54 % conv.; b) RhH (1.5 mol %), THF, RT, 16 h, 31 %.

rearrangement of N-allylmorpholine ($t_{1/2}=330.0$ min) was significantly slower than the rearrangement of N-allylaziridine under similar conditions ($t_{1/2}=29.0$ min).

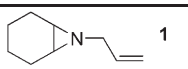
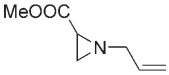
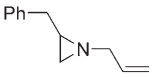
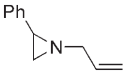
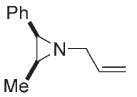
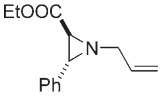
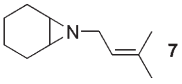
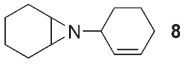
The *Z* stereoselectivity in the course of allyl aziridine isomerisation, observed with $[Rh(CO)H(PPh_3)_3]$ as the catalyst, was increased to 95:5 when the reaction was performed at −78 °C. The same selectivity was achieved in both toluene and dichloromethane. The double-bond migration consistently afforded high *Z* selectivity with full conversion at room temperature (Scheme 6a). GC analysis of N-allylcyclohexene imine (**1**) isomerisation, performed with 1.5 mol % of $[Rh(CO)H(PPh_3)_3]$ in THF at room temperature, indicated that the *E* and *Z* aziridine isomers do not interconvert under the reaction conditions or during isolation. This isomerisation protocol was extended to a number of different allyl aziridine substrates (Table 1). All of the terminal olefins were reactive, consistent with the known selectivity of $[Rh(CO)H(PPh_3)_3]$ towards unhindered terminal double bonds.[7] Moreover, all of the substrates showed high selectivity for the *Z* enamine product. A conversion to a thermodynamic mixture of geometric isomers was effected upon extended treatment of **1** with a stoichiometric amount of rhodium(I) hydride catalyst, which caused slow isomerisation to a 54:46 *Z*/*E* isomeric mixture over five days (Scheme 6b). A similar thermodynamic ratio was photochemically induced upon UV irradiation ($\lambda_{max}=254$ nm; Scheme 6c).



Scheme 6. Isomerisation and hydrogenation experiments. a) RhH (1.5 mol %), C_6H_6 or THF, RT, 1 d; b) RhH (1 equiv), THF, RT, 5 d; c) *hν* ($\lambda_{max}=254$ nm), quartz, THF, RT, 6 h; d) H_2 (1 atm), RhH (cat.), THF, RT, 16 h, 91 %; e) $Cu(OAc)_2$, pyridine, RT, 10 h, 27 %; f) H_2 (1 atm), RhH (1 mol %), C_6H_6, RT, 1 week, 32 %.

In the presence of H_2, $[Rh(CO)H(PPh_3)_3]$ acts as a mild and efficient hydrogenation catalyst, able to reduce terminal carbon–carbon double bonds under an atmospheric pressure of hydrogen.[7] The mechanism of hydrogenation passes through the same rhodium–carbon intermediates as those formed in the course of double-bond migration. To detect and trap these rhodium–carbon intermediates, isomerisations were carried out in the presence of hydrogen gas. Hydrogenation of **1** resulted in a mixture of hydrogenated and isomerised products in a *Z*/*E* ratio consistent with the ratios observed in the absence of H_2 gas (Scheme 6d). Furthermore, hydrogenation of **5** was extremely slow and resulted in low yields (Scheme 6f), demonstrating the inhibitory effect of having a nitrogen substituent proximal to the site of hydrogenation.

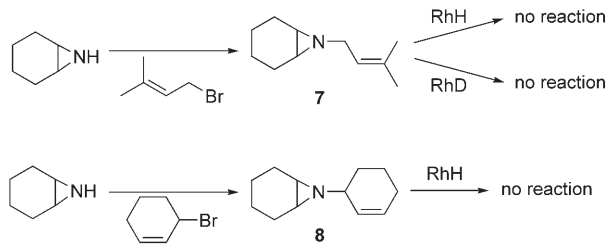
Table 1. Selected substrate scope for isomerisation of N-allylaziridines to N-vinylaziridines with $[Rh(CO)H(PPh_3)_3]$ catalyst.[a]

Entry	Substrate	Conv. [%][b]	*Z*/*E* selectivity [%][b]
1	 **1**	100	95:5
2[c]		100	82:18
3[d]		100	76:24
4[e]		100	91:9
5		100	96:4
6[c]		80	75:25
7[f]	 **7**	trace	–
8[f]	 **8**	trace	–

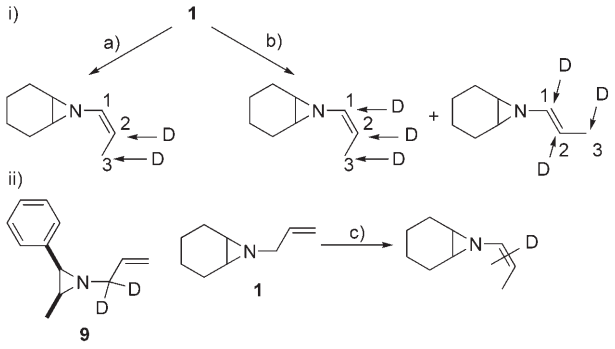
[a] [Substrate] = 0.7 M, [substrate]/[Rh] = 66 at −78 °C in THF under N_2. [b] Determined by GC analysis. [c] [Substrate]/[Rh] = 10 at 60 °C, 72 h. [d] [Substrate]/[Rh] = 20 at 60 °C, 24 h. [e] [Substrate]/[Rh] = 66 at 20 °C, 24 h. [f] Only starting material was recovered.

Substitution at the allylic position was found to impede isomerisation.[7] Furthermore, the addition of substituents to the N-allyl chain creates a tri- (**7**) or di-substituted (**8**) olefin that does not isomerise because of the thermodynamic stability of the starting material (Scheme 7).

Deuterium-labelling studies were undertaken to elucidate the mechanism of isomerisation. Scheme 8a shows a stoichiometric isomerisation of **1** with $[Rh(CO)D(PPh_3)_3]$ which resulted in deuterium incorporation at the methyl (C3) and central vinylic (C2) positions. Extended treatment with stoichiometric $[Rh(CO)D(PPh_3)_3]$ over five days resulted in scrambling of deuterium across all three positions, as well as formation of a thermodynamic mixture of *Z*/*E* isomers (Scheme 8b). Experiments to trap the rhodium–carbon intermediate **A** (Scheme 2) by using the 3,3-dimethyl substrate, which did not undergo isomerisation, showed no deu-



Scheme 7. Substituted N-allylaziridines do not isomerise under RhH catalysis.

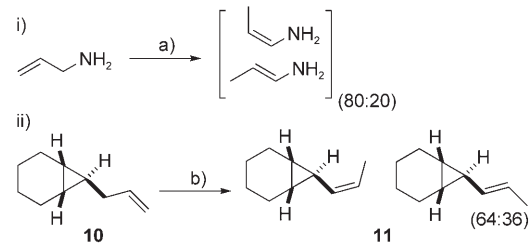


Scheme 8. Deuterium labelling and crossover experiments. a) RhD (1 equiv), THF, RT, 30 min; b) RhD (1 equiv), THF, RT, 5 d; c) RhH (3 mol%), THF, RT, 12 h. RhH = $[Rh(CO)H(PPh_3)_3]$; RhD = $[Rh(CO)D(PPh_3)_3]$.

terium incorporation at position 1 (Scheme 7). Finally, a crossover experiment allowed us to observe deuterium transfer from one aziridine substrate to another, indicating that deuterium from C1 of the 1,1-dideuterioallylaziridine is transferred to the rhodium(I) complex, which in turn transfers deuterium onto the protio-aziridine substrate (Scheme 8c).

To further probe the mechanism, the isomerisations were investigated on simple allylamine and allylcyclopropanes. The use of 1-allylamine as a substrate revealed transient formation of the unstable 1-aminopropene in a *Z*/*E* ratio of 80:20 with a half-life ($t_{1/2}$) of 142.2 min (Scheme 9a). Isomerisation of **10**, the cyclopropane equivalent of **1**, resulted in poor selectivity, with a *Z*/*E* ratio of 64:36 (Scheme 9b). This suggests that the presence of a three-membered aziridine ring played an important role in determining high *Z* selectivity.

It is evident that allylaziridines differ from other allylamine substrates, including tertiary amines, in that they show very strong selectivity for the *Z* enamine product. Why is it that the aziridine nitrogen induces such unique stereoselectivity? We propose a mechanism that explains these results.



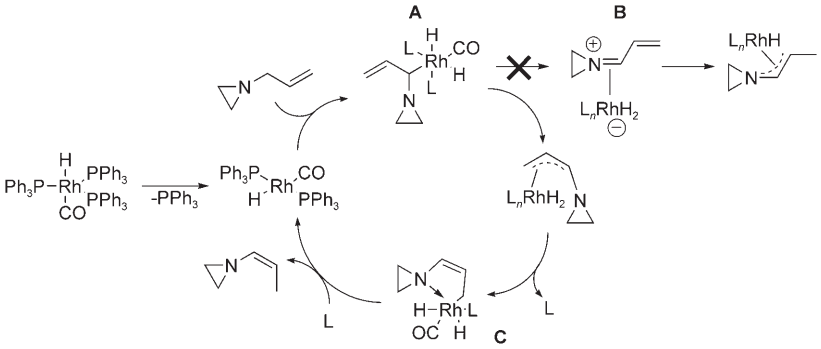
Scheme 9. Further isomerisation studies. a) RhH (15 mol%), C_6D_6, in-situ experiment (utilising NMR spectroscopy); b) RhH (cat.), THF, RT, 16 h, 94% conv.

Discussion

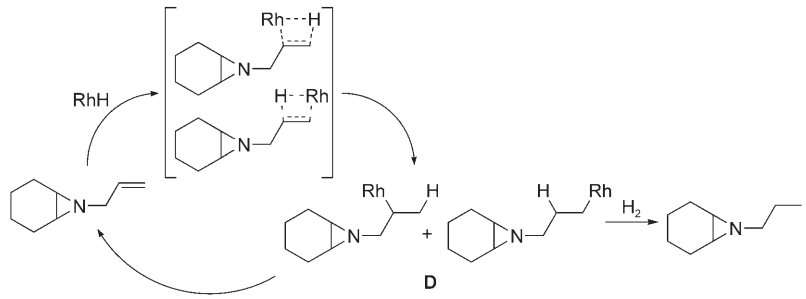
This study was designed to elucidate differences between the isomerisation of N-allylaziridines and allyl amines, as the same rhodium(I) hydride catalyst leads to two different enamine geometries from these substrates. We previously postulated a mechanism of methylene CH-activation, followed by the formation of a cyclic intermediate and reductive CH-bond elimination of the *Z* enamine (Scheme 10).[11]

However, isomerisation of **1** into the *Z* enamine product by using stoichiometric rhodium(I) deuteride resulted in deuterium incorporation at the C2- and C3-positions of isolated product, suggesting that a hydride-based mechanism may be involved. This pathway would proceed by means of hydride addition across the double bond and subsequent β-hydride elimination to re-form the C2–C3 double bond in a cycle that we have termed the "hydride loop" (Scheme 11). The intermediate rhodium–carbon species **D** was trapped when we isolated *n*-propyl cyclohexene imine under hydrogenation conditions.

If β-hydride elimination from intermediate **D** were also responsible for forming the C1–C2 double bond of the enamine product, it should result in *E* enamine geometry because the activation barrier to form the *Z* isomer is known to be significantly higher.[20] However, our experiments demonstrate the kinetic nature of the isolated *Z* product. The *Z*/*E* ratio remained constant throughout the reaction. This suggests that the enamine product is relatively unreactive to further isomerisation via hydride addition and subsequent β-hydride elimination.[7] However, isomerisation can be forced



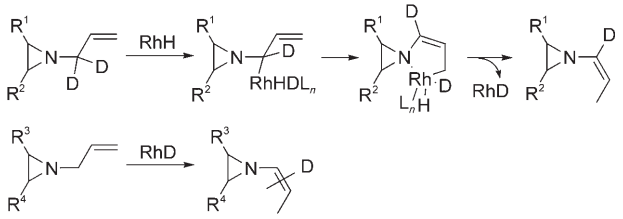
Scheme 10. Proposed mechanism of rhodium hydride catalysed CH-activation/isomerisation (L = PPh_3).



Scheme 11. Hydride addition and β-hydride elimination (the "hydride loop"). The rhodium-substrate intermediates may be trapped by hydrogenation.

by prolonged exposure to stoichiometric $[Rh(CO)H(PPh_3)_3]$, resulting in a thermodynamic mixture of *Z* and *E* enamines. Importantly, deuterium scrambling and partial isotope incorporation at the C1-position was also observed upon extended treatment with the RhD catalyst. Such extended treatment causes scrambling of deuterium throughout the three-carbon substituent by means of slow hydride addition followed by β-hydride elimination. The *E* product was formed after such prolonged exposure: accordingly, *E* enamine formation must proceed by means of β-hydride elimination. By the principle of microscopic reversibility, the reverse reaction—addition to the enamine double bond—is slow, which is reflected in the slow rate of *Z*-to-*E* conversion as well as the fact that neither *E* nor *Z* aziridine enamine, nor the unsubstituted vinyl aziridine **5**, undergo hydrogenation at a reasonable rate when using the $[Rh(CO)H(PPh_3)_3]$ catalyst (Scheme 6).

The conventional hydride mechanism alone cannot explain *Z* enamine formation in the case of allyl aziridines. We conclude that a lower-barrier *Z*-selective pathway must operate. Concurrently with the non-productive addition across the C2–C3 double bond ("hydride loop", Scheme 11), the RhH catalyst can enter into a methylene CH-bond activation manifold (Scheme 10). The resulting rhodium intermediate cannot be stabilised by the iminium ion **B** due to high strain. Thus, the formation of any *E* product by means of the tertiary allyl amine isomerisation mechanism is not expected along this pathway. On the other hand, formation of an isomeric five-membered cyclometallated rhodium complex **C** can be expected to take place, via a σ-allyl intermediate. It is important to mention that at this point we do not have experimental evidence ruling out direct hydride migration from the π-allyl intermediate which should also result in *Z* enamine formation. The rhodium complex **C** has not been directly observed by NMR spectroscopy, but several arguments speak in its favour. The ω_A/π interaction is known to stabilize the bisected geometry in stereoelectronically related vinylcyclopropanes.[21] This interaction, coupled with Rh–N coordination, is expected to contribute towards the formation of **C**. Furthermore, five-membered ring organometallic intermediates have been postulated to account for *Z* selectivity in the case of alkali base-induced rearrangements.[22] Following the formation of **C**, facile reductive elimination is expected to take place to form a new C–H bond, releasing the *Z* enamine product. Crossover of deuterium has been observed between the deuterated and protio-aziridine (Scheme 8), suggesting that $[Rh(CO)D(PPh_3)_3]$ is formed in situ following CH-activation of the deuterated substrate and reductive elimination from the ensuing cyclometallated rhodium intermediate. RhD then enters the CH-activation path with the protio-aziridine substrate to effect crossover of deuterium (Scheme 12).



Scheme 12. Mechanism of deuterium crossover. 1,1-Dideuterioallylaziridine transfers deuterium to rhodium(I), forming $[Rh(CO)D(PPh_3)_3]$ in situ.

Why is it that β-hydride elimination cannot be responsible for *Z* enamine formation? We attribute this intriguing finding to the special properties of the aziridine nitrogen, including its high degree of pyramidalisation and its high barrier to inversion. In contrast to other amines, two substituents on aziridine rings are locked in a three-membered heterocycle and thus are swept back from the nitrogen (Figure 1).

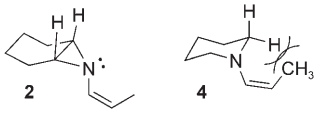
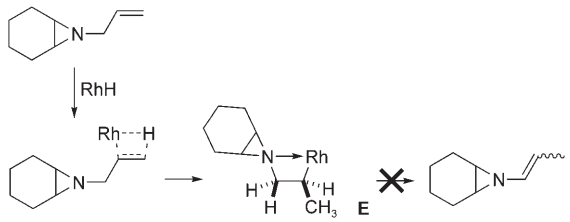


Figure 1. Representations of (*Z*)-N-vinylaziridine **2** and (*Z*)-N-vinylpiperidine **4**.

This relieves steric strain in the cyclometallated intermediate and the resulting *Z* enamines that are formed. Furthermore, coordination of rhodium(I) to the sterically unencumbered lone pair of nitrogen in intermediate **E** (Scheme 13) would prevent formation of a *syn*-periplanar rotamer, which is a prerequisite for β-hydride elimination. Interestingly, a similar coordinative arrangement between palladium(II) and hydroxyl group was reported to affect the regioselectivity of β-hydride elimination in the Heck reaction.[23] Tertiary amines, which lead to the formation of *E* enamines, do not appear to exhibit this behaviour.[8] This explains why N-allylmorpholine and *N*-allylpiperidine isomerisations occur with *E* selectivity—although they have a nitrogen lone pair that



Scheme 13. Aziridine nitrogen may coordinate to rhodium(I), forming a transient four-membered ring that precludes *syn*-periplanar arrangement and β-hydride elimination.

appears capable of forming a cyclometallated intermediate, such a ring would be subject to severe steric constraint. The only pathway open to tertiary amine isomerisation is β-hydride elimination. Further work was done with the unsubstituted parent allyl amine, which was subjected to the isomerisation protocol. This reaction produced a kinetic preference for the *Z* isomer (80:20), suggesting that unencumbered Rh–N coordination is a critical factor that contributes to retarding the rate of β-hydride elimination.

Conclusion

We have shown that the special properties of the aziridine nitrogen allow allyl aziridines to undergo isomerisation into *Z* enamines through a CH-activation manifold that is not accessible to common tertiary amines. Our mechanistic investigations are consistent with two concurrent reaction pathways operating during the isomerisation. The hydride addition and β-hydride elimination ("hydride loop") are nonproductive with respect to enamine formation, while the principal reaction pathway proceeds by means of CH-activation, rearrangement to a five-membered intermediate, and subsequent reductive elimination producing (*Z*)-vinylaziridine. The involvement of highly strained π intermediates has not been ruled out. This catalytic method provides facile access to a heretofore underutilised class of substrates—geometrically stable *Z* enamines. These molecules can be used as carbon nucleophiles in stereoselective reactions and should facilitate explorations of *Z* enamine transformations.[11] Current efforts are aimed at further understanding the relative reactivity of σ and π intermediates involved in this reaction.

Experimental Section

General procedures: THF was freshly distilled from sodium benzophenone ketyl prior to use. Anhydrous acetone was stored over 4 Å molecular sieves. All procedures involving $[Rh(CO)H(PPh_3)_3]$ were carried under Ar/N_2 in flame-dried glassware. *n*-Butyllithium was titrated with *N*-benzylbenzamide prior to use.[24] *N*-Benzylbenzamide was synthesised and purified according to literature procedures.[24] Triphenylphosphine (PPh_3) was recrystallised from hot ethanol prior to use to remove triphenylphosphine oxide (Ph_3PO). Other solvents and reagents were purchased from Aldrich and used as received. Rhodium(III) chloride trihydrate was used as purchased from Strem Chemicals without further purification. NMR spectra were referenced to TMS and run at 25 °C. $CDCl_3$ was stored over anhydrous K_2CO_3. Sodium deuteride (98 atom % D) and EtOD (99 atom % D) were purchased from Aldrich and were used as received. Isotopic purity of metal catalysts was determined by ^1H NMR spectroscopy. Deuterium-labelled products were detected by ^2H NMR spectroscopy. GC runs were carried out on a Hewlett Packard 6890 gas chromatograph with an HP-5 column (crosslinked 5 % phenyl methyl siloxane, 30 m × 0.32 mm × 0.25 mm film thickness), and were configured to start at 50 °C, run 1.0 min at 50 °C, ramp 10 °C min^{-1} to 150 °C; hold 2.0 min, then ramp 15 °C min^{-1} to 250 °C, and hold 6.0 min.

Cyclohexene imine:[9,10a] In a 100 mL round-bottomed flask equipped with stirrer bar and condenser, NaN_3 (5.08 g, 77.5 mmol) was dissolved in 1:1 H_2O/acetone (35 mL). Cyclohexene oxide was then added to this solution (3.1 mL, 30.7 mmol). The reaction was refluxed for 16 h and cooled, at which point a biphasic system was observed. Without separating the layers, the acetone was evaporated under reduced pressure and then the layers were extracted with diethyl ether (3 × 20 mL). Organic extracts were combined, washed with brine, dried with Na_2SO_4, then evaporated in vacuo. Crude *trans*-2-azidocyclohexanol (4.98 g) was recovered as an orange oil, all of which was dissolved in dry THF (26 mL). PPh_3 (9.3 g, 35.5 mmol) was added with stirring to this solution. Bubbling of N_2 gas was observed as the solution was refluxed for 16 h. The solvent was removed gently under reduced pressure. Pentanes were poured in and triphenylphosphine oxide precipitate was repeatedly filtered. Pentanes in the filtrate were removed under reduced pressure and the oil was distilled in vacuo to yield 1 g of cyclohexene imine (10.3 mol, 34 %, GC time: 4.3 min) as a clear, colourless liquid that solidified upon standing at −20 °C. ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.10$ (2H, m), 1.80 (4H, m), 1.30 ppm (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.3$, 24.8, 29.5 ppm.

7-Allyl-7-azabicyclo[4.1.0]heptane (1): In a flame-dried 50 mL Schlenk flask equipped with stirrer bar, $[Pd(\eta\text{-}C_3H_5)Cl]_2$ (28 mg, 0.08 mmol, 1.5 mol %), PPh_3 (70 mg, 0.27 mmol, 4 mol %), and K_2CO_3 (1.7 g, 17.0 mmol) were suspended in THF (11 mL). Allyl acetate (0.6 mL, 6.1 mmol) and cyclohexene imine (0.5 g, 5.2 mmol) were then added to this solution. The contents were stirred for 16 h under N_2, then poured into pentanes (25 mL) and filtered through a pad of Celite. The filtrate was concentrated in vacuo, then distilled under reduced pressure to yield 537 mg of **1** in 75 % yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.90$ (1H, m), 5.20 (1H, d, $J = 17$ Hz), 5.10 (1H, d, $J = 8.6$ Hz), 2.80 (2H, d, $J = 5.3$ Hz), 1.75 (4H, m), 1.50 (2H, m), 1.35 (2H, m), 1.18 ppm (2H, m).

Hydrogenation of 1 to a mixture of saturated and isomerised products: A 50 mL flame-dried Schlenk flask equipped with stirrer bar was charged with $[Rh(CO)H(PPh_3)_3]$ (5 mg, 0.005 mol, 5 mol %) under inert atmosphere. The flask was evacuated, then filled with H_2 at 1 atm. Dry THF (1.5 mL) was added by syringe, and the yellow solution was stirred for 5 min. The flask was equipped with a H_2-filled balloon, then **1** (15 mg, 0.11 mmol) was added by syringe. After stirring the reaction overnight, GC analysis revealed a 91 % conversion, with 54 % consisting of hydrogenated product, 34 % (*Z*)-N-vinylaziridine, 3 % (*E*)-N-vinylaziridine and 9 % 7-allyl-7-azabicyclo[4.1.0]heptane (**1**, starting material). The reaction solution was reduced to 0.2 mL in vacuo, then chromatographed on silica gel (9:1 hexanes/EtOAc, I_2 stain) to yield 6.5 mg (0.05 mmol, 43 % yield) of crude hydrogenated product 7-propyl-7-azabicyclo[4.1.0]heptane ($R_f = 0.55$). The starting material, N-vinylaziridines and product all eluted together upon column chromatography and were not separable. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.16$ (2H, t, $J = 7.3$ Hz), 1.75 (m), 1.56 (2H, q, $J = 7.4$ Hz), 0.9 ppm (m); ESI-MS: *m*/*z* (%): 140.1(100) $[M+1^+]$, 141.1 (10) $[M+2^+]$.

***N*-Allylpiperidine (3)**: In a 100 mL round-bottomed flask equipped with stirrer bar, 60 % NaH in oil (1.83 g, 45.8 mmol) was suspended in THF (25 mL). Piperidine (2.5 mL, 2.1 g, 24.7 mmol) was added followed by allyl bromide (2.3 mL, 3.3 g, 27.3 mmol). After stirring overnight, water was poured in and the solution was extracted with EtOAc, dried with anhydrous $MgSO_4$, and reduced in vacuo. The resulting oil was distilled under reduced pressure to yield 1.9 g (54 % isolated yield) of **3** (GC time: 4.4 min). ^1H NMR (200 MHz, $CDCl_3$): $\delta = 5.90$ (1H, m), 5.10 (2H, m), 2.90 (2H, d), 2.40 (4H, br s), 1.60 ppm (m, 4H), 1.45 ppm (m, 2H).

2,4,6-Trivinylcyclotriboroxane–pyridine complex:[25] THF (75 mL) with trimethylborate (10 mL, 9.32 g, 90 mmol) was cooled under N_2 to −78 °C. Vinylmagnesium bromide (60 mL, 1.0 M in THF, 60 mmol) was added dropwise by means of an addition funnel over 35 min. The reaction was stirred for 1 h, at which point HCl (1 M, 25 mL) was added. The reaction was warmed to room temperature, then brine (20 mL) was added. The slurry was extracted with ether (4×50 mL). The organic extracts were washed with water (50 mL), brine (50 mL), dried with Na_2SO_4, reduced to 25 mL in vacuo, and then pyridine (10 mL, 9.83 g, 0.12 mol) was added under N_2. This solution was stirred for 4 h. The solvent was removed under high vacuum, then the remaining oil was distilled at 200 °C under reduced pressure. The complex (2.5 g, 10 mmol, 52%), which freezes to form oily white crystals when cooled to −20 °C, was isolated.

7-Vinyl-7-azabicyclo[4.1.0]heptane (5): Copper(II) acetate (0.92 g, 4.6 mmol, >1 equiv) and 4 Å molecular sieves (0.3 g) were added to a flame-dried 50 mL Schlenk flask. 2,4,6-Trivinylcyclotriboroxane–pyridine complex (0.33 g, 2.0 mmol, 6.0 mmol vinyl equivalents), pyridine (0.9 mL, 11.2 mmol) and cyclohexene imine (0.35 mL, 3.6 mmol) were added in succession, and the system was connected to a drying tube with oxygen flow-through. The reaction was stirred for 10 h, poured into pentanes (75 mL) and then filtered through a 1 cm pad of silica gel. The filtrate was reduced to 3–4 mL in vacuo, and the resulting liquid was distilled under reduced pressure to yield 235 mg of 7-vinyl-7-azabicyclo-[4.1.0]heptane (**5**) contaminated with 70.5 mg pyridine (equivalent to 164.5 mg of product or 27%, GC time: 4.8 min). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.33 (1H, dd, J_1 = 15.2, J_2 = 7.8 Hz), 4.46 (1H, d, J = 15.2 Hz), 4.35 (1H, d, J = 7.9 Hz), 1.70–1.95 (m, 6H), 1.40 (m, 2H), 1.25 ppm (m, 2H).

7-Ethyl-7-azabicyclo[4.1.0]heptane (6): $[Rh(CO)H(PPh_3)_3]$ (6 mg, 0.0065 mmol, 1 mol%) was dissolved in THF (6 mL) in a dry 25 mL Schlenk flask with stirrer bar. The flask was flushed twice with H_2, filled with H_2 (1 atm), then 7-vinyl-7-azabicyclo[4.1.0]heptane **5** (80 μL, 0.65 mmol) was added by syringe. The reaction was followed by GC analysis and observed to have slowed after two days, thus 6 mg of additional catalyst were added every two days. After six days (and two 6 mg supplements of catalyst), 32% conversion was achieved. The solvent was evaporated in vacuo, and chromatographed on silica gel (7:3 hexanes/EtOAc, I_2 stain) to yield trace amounts of **6** (R_f = 0.15, GC time: 4.4 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.13 (q), 1.80 (m), 1.30 (m), 1.15 (t); ESI-MS: m/z (%): 126.1 (75) $[M+1^+]$, 127.1 ppm (10) $[M+2^+]$.

7-(3-Methylbut-2-enyl)-7-azabicyclo[4.1.0]heptane (7):[9] In a 50 mL Schlenk flask, K_2CO_3 (1.35 g, 13.4 mmol) was suspended in anhydrous acetone (30 mL). Cyclohexene imine (500 μL, 4.9 mmol) was added by syringe, followed by the dropwise addition of prenyl bromide (575 μL, 4.9 mmol). The reaction was stirred for 1.5 h under N_2, filtered, and acetone was removed under reduced pressure. The resulting yellow oil was chromatographed on silica gel (95:5→90:10 hexanes/EtOAc) to isolate 667 mg of pure **7** in 79% yield (R_f = 0.25 under 95:5 EtOAc/hexanes, GC time: 9.3 min). The branched product (7-(2-methylbut-3-en-2-yl)-7-azabicyclo[4.1.0]heptane) was found at R_f = 0.5 but was not isolated. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.29 (1H, t), 2.83 (2H, d, J = 6.5 Hz), 1.71 (3H, m), 1.58 (3H, s), 1.50–1.80 (8H, m), 1.15 ppm (2H, m).

7-(Cyclohex-2-enyl)-7-azabicyclo[4.1.0]heptane (8): In a 100 mL round-bottomed flask equipped with septum and stirrer bar, K_2CO_3 (945 mg, 6.8 mmol) was suspended in anhydrous acetone (30 mL). Cyclohexene imine (350 μL, 3.4 mmol) was added by syringe, followed by 3-bromocyclohexene (394 μL, 549 mg, 3.4 mmol). The reaction was left stirring for 22 h, filtered, and the acetone was removed under reduced pressure. The resulting oil was chromatographed on silica gel (95:5→90:10 hexanes/EtOAc) to yield 264 mg of a clear, colourless oil **8** in 44% isolated yield (GC time: 11.2 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.75 (1H, m), 5.65 (1H, m), 2.10 (1H, m), 1.95 (1H, m), 1.80 (m), 1.55 (m), 1.35 (2H, m), 1.16 ppm (2H, m); ESI-MS: m/z (%): 178.1 (100) $[M+1^+]$, 179.1 (13) $[M+2^+]$.

1,1-Dideuterioallyl alcohol: A 250 mL flame-dried three-necked flask fitted with magnetic stirrer bar, thermometer, addition funnel and nitrogen inlet was charged with $LiAlD_4$ (2.2 g, 47.6 mmol) and anhydrous ether (100 mL). The mixture was cooled to −10 °C and a solution of acryloyl chloride (6.68 mL, 74.7 mmol) was added dropwise while the temperature was controlled at −10 ± 2 °C. The mixture was stirred at −10 °C for 3 h, after which time, water (2.6 mL) was added slowly, followed by 15% aqueous NaOH (2.6 mL) and more water (2.6 mL). The resulting slurry was stirred for 1 h and then filtered. The filtrate was concentrated at 60 °C and the resulting crude oil was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.01 (1H, dd), 5.20 ppm (2H, m).

1,1-Dideuterioallyl tosyl ester: A 250 mL Schlenk flask was charged with 1,1-dideuterioallyl alcohol (5 g, 82.2 mmol, crude product from previous step), tosyl chloride (15.8 g, 83.2 mmol) and anhydrous ether (80 mL). The mixture was cooled to 0 °C and powdered NaOH (9.15 g, 0.228 mol) was added in portions under N_2. The reaction was then warmed to room temperature and stirred for 12 h. The precipitate was filtered and the filtrate concentrated in vacuo. The resulting oil was subjected to column chromatography (silica gel, 90:10 hexane/EtOAc) to the yield pure product (16.5 g, 95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80 (2H, d), 7.33 (2H, d), 5.81 (1H, dd), 5.28 (1H, d, ^3J = 17.4 Hz, $^2J_2$ = 1.6 Hz), 5.16 (1H, d, ^3J = 10.2 Hz, $^2J_2$ = 1.6 Hz), 2.46 ppm (3H, s).

***N*-1-(1,1-Dideuterioallyl)-2-methyl-3-phenylaziridine (9)**: A 25 mL flask was charged with 2-methyl-3-phenylaziridine[11] (220 mg, 1.66 mmol), K_2CO_3 (382 mg, 2.76 mmol) and DMF (4 mL). A solution of 1,1-dideuterioallyl tosyl ester (296 mg, 1.38 mmol) in DMF (2 mL) was added to the reaction mixture and stirred at room temperature for 12 h. When TLC showed no starting material remained, water (15 mL) was added and the solution was extracted with EtOAc (2×10 mL). The combined organic layers were washed with brine (15 mL) then dried over Na_2SO_4. The drying agent was filtered off and filtrate was concentrated in vacuo. The resulting oil was subjected to column chromatography (silica gel, 80:20 hexane/EtOAc) to yield pure **9** (240 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (4H, m), 7.22 (1H, m), 5.99 (1H, dd), 5.25 (1H, d, $^3J_1$ = 17.2, $^2J_2$ = 2 Hz), 5.11 (1H, dd, $^3J_1$ = 10.4, $^2J_2$ = 2 Hz), 2.53 (1H, d, J = 6.8 Hz), 1.80 (1H, m), 0.94 ppm (d, J = 5.6 Hz).

7,7-Dibromobicyclo[4.1.0]heptane:[26] Benzyltriethylammonium chloride (293 mg, 1.29 mmol, 2 mol%) and cyclohexane (6.08 mL, 4.93 g, 60.0 mmol) were mixed in a flask under N_2. The suspension was cooled to 0 °C, then dichloromethane (6 mL), absolute EtOH (0.25 mL), bromoform (7.9 mL, 22.8 g, 90.3 mmol) and 50% aqueous NaOH (30 mL) were added in succession. The solution turned light brown, and was stirred for 16 h as the bath slowly warmed to room temperature. Water was added and the slurry was extracted with hexanes (3×100 mL), then dried with anhydrous $MgSO_4$. Solvent was evaporated under reduced pressure, then the oil was chromatographed on silica gel (hexanes) to yield 15.8 g of a clear, colourless liquid (R_f = 0.9, GC time: 10.5 min) of crude 7,7-dibromobicyclo[4.1.0]heptane ($\rho_{25\,°C}$ = 2 g mL^{-1}) contaminated with bromoform. This compound was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.00 (2H, m), 1.83 (2H, m), 1.58 (2H, m), 1.35 (2H, m), 1.18 ppm (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 41.1, 27.3, 20.9, 20.4 ppm.

***trans*-7-Bromobicyclo[4.1.0]heptane**:[26] 7,7-Dibromobicyclo[4.1.0]heptane (1.5 mL, 3.0 g, 11.9 mmol) in THF (20 mL) was cooled to −95 °C under N_2, at which point, *n*-butyllithium (8.2 mL, 1.5 M in hexanes, 12.3 mmol) was added. The solution was stirred for 10 min, quenched with absolute EtOH (4 mL) and stirred for 1 h while allowed to warm to room temperature. Water (15 mL) was poured into the solution, and the layers were extracted with hexanes (4×30 mL). The extracts were combined, dried with $MgSO_4$, then reduced in vacuo. The oil was chromatographed on silica gel (hexanes, R_f = 0.95, GC time: 6.9 min) to yield 1.9 g crude *trans*-7-bromobicyclo[4.1.0]heptane, contaminated with hexanes. This compound was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.60 (1H, t, J = 3.5 Hz), 1.80 (2H, m), 1.70 (2H, m), 1.38 (2H, m), 1.10–1.30 ppm (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.0, 22.7, 21.5, 21.1 ppm.

7-Allylbicyclo[4.1.0]heptane (10):[27] Copper(I) iodide (0.75 g, 3.94 mmol) was suspended in THF (14 mL) under N_2 at −48 °C. To this solution, *n*-butyllithium (5.7 mL, 1.4 M in hexanes, 7.98 mmol) was added, followed by *trans*-7-bromobicyclo[4.1.0]heptane (163 mg, crude). After stirring for 30 min, allyl bromide (1 mL, 1.40 g, 11.6 mmol) was added and the reac-

tion was stirred for a further 30 min. The reaction was quenched with MeOH (4 mL), then water. The copper salts were filtered through a pad of Celite and then the filtrate was extracted with hexanes. Hexane extracts were dried with $MgSO_4$ and then chromatographed on silica gel (hexanes, $R_f = 0.95$, GC time: 6.05 min) to yield 167 mg of crude **9**, contaminated with hexanes. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.88$ (1H, m), 5.05 (1H, d, $J = 17.2$ Hz), 4.95 (1H, d, $J = 10.2$ Hz), 1.94 (2H, m), 1.85 (2H, m), 1.62 (2H, m), 1.10–1.40 (4H, m), 0.60 (2H, m), 0.43 ppm (1H, m).

General protocol for the isomerisation of N-allylaziridines to N-vinylaziridines:[11] In a flame-dried 25 mL Schlenk flask equipped with stirrer bar, $[Rh(CO)H(PPh_3)_3]$ (30 mg, 0.03 mmol, 1.5 mol%) was dissolved in THF or C_6H_6 (8 mL). N-Allylaziridine **1** (2.0 mmol) was added via syringe and the solution was stirred overnight. Progress of the reaction may be monitored by GC analysis. Reactions were worked up by one of two methods:

Method A, large scale: THF was evaporated under reduced pressure to 1 mL of solution, then the residue was distilled under reduced pressure to produce clear, colourless N-vinylaziridine **2** (1.2 mmol, 60%).

Method B, microscale: The reaction solution was poured into pentanes (20–40 mL) and filtered on a pad of Celite. The filtrate was reduced in vacuo and the residue washed with pentanes and filtered again. This can be repeated once more to isolate a clear, yellow oil of N-vinylaziridine **2**, contaminated with trace amounts of rhodium salts and triphenylphosphine oxide.

7-(Prop-1-enyl)-7-azabicyclo[4.1.0]heptane (2): Procedure as above, following workup method A. Conversion to product: 97%; isolated yield: 57% (GC time: *Z* isomer: 6.5 min, 90%; *E* isomer: 6.8 min, 10%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.95$ (d, 0.1H, $J = 13.5$ Hz), 5.78 (1H, d, $J = 7.9$ Hz), 5.02 (0.1H, m), 4.78 (1H, m), 1.67 (3H, dd), 1.56 (0.3H, dd), 1.10–2.00 ppm (m).

1-[(*E*)-Prop-1-enyl]piperidine (4):[8] Procedure as above, following workup method A. Isolated yield: 31% (GC time: 5.8 min). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.83$ (1H, d, $J = 13.9$ Hz), 4.40 (1H, m), 2.73 (4H, m), 1.50–1.70 ppm (6H, m).

7-(Prop-1-enyl)bicyclo[4.1.0]heptane (11): Procedure as above, following workup method B. 94% conversion was achieved, as determined by GC analysis (GC time: *Z* isomer: 6.8 min; *E* isomer: 7.0 min). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.43$ (0.6H, dq, $J_1 = 15$, $J_2 = 7$ Hz), 5.31 (1H, dq, $J_1 = 11.5$, $J_2 = 7$ Hz), 4.95 (0.6H, m), 4.80 (1H, m), 1.72 (3H, dd), 1.64 (1.8H, dd), 0.85–1.90 ppm (10H, m).

Deuterium crossover study: Procedure as above with 1 equiv of each aziridine and $[Rh(CO)H(PPh_3)_3]$ (3 mol%) in THF for 12 h at room temperature. The reaction was not worked up; rather, an aliquot of solution was run under ESI-MS in which the $[M+2^+]$ ($137+2=139$) peak was detected, indicating the presence of deuterated product beyond normal isotopic distributions.

Preparative photochemical synthesis of (*E*)-N-vinylaziridine 2: An aliquot of **2** (50 μL), as prepared by rhodium(I)-catalysed isomerisation of **1**, was added by syringe to dry THF (10 mL) purged with N_2 for 10 min. The sample was irradiated for 6 h through quartz ($\lambda_{max} = 254$ nm), then solvent was evaporated in vacuo to leave an oil (0.5 mL). GC analysis indicated isomerisation to an equilibrium mixture of (*Z*)- and (*E*)-N-vinylaziridine (*Z*/*E* 54:46).

Compounds listed in Table 1 without bold numerical labels were reported in reference [11], a previous communication from our group.

General protocol for NMR spectroscopic experiments: A dry NMR tube was loaded with $[Rh(CO)H(PPh_3)_3]$ (20.1 mg, 0.022 mmol, 1 equiv) and C_6D_6 (0.75 mL). The aziridine (0.022 mmol) was then dispensed into the tube by syringe. The tube was sealed with a NMR cap, shaken and then spectra were taken at ten minute intervals on a 400 MHz spectrometer at 25°C. Product ratios for kinetics, if applicable, were measured by ^{1}H NMR spectroscopic integration.

Propenyl-1-amine: Procedure as above, except 15 mol% $[Rh(CO)H(PPh_3)_3]$ was used. Freshly distilled 1-allylamine (8.1 μL, 0.11 mmol) was mixed with C_6D_6 (0.75 mL) in an NMR tube. To this solution, $[Rh(CO)H(PPh_3)_3]$ (15 mg, 0.016 mmol, 15 mol%) was added. NMR scans were taken in five minute intervals to monitor progression of the reaction ($t_{1/2} = 142.2$ min). The ratio of *Z*/*E* remained constant at 80:20 but the peaks decreased in intensity, likely due to degradation of the highly unstable enamine product. The product propenyl-1-amine was not isolated, and only one vinylic proton from the product was clearly discernible by NMR spectroscopy. ^{1}H NMR (400 MHz, C_6D_6): $\delta = 4.49$ (0.2H, dq, $^3J_{trans} = 13.3$ Hz; $CH_3CH{=}CHNH_2$), 4.31 (0.8H, dq, $^3J_{cis} = 8.4$ Hz; $CH_3CH{=}CHNH_2$).

Chlorocarbonylbis(triphenylphosphine)rhodium(I):[28] Triphenylphosphine (1.1 g, 4.2 mmol) was dissolved in absolute EtOH (43 mL) in a 250 mL three-necked flask equipped with condenser and stirrer bar under N_2. The solution was heated to reflux, then $RhCl_3{\cdot}3H_2O$ (284 mg, 1.1 mmol) suspended in hot EtOH (10 mL) was added by syringe. To the red solution, 40% aqueous formaldehyde (5 mL) was quickly added. The suspension was refluxed for 5 min, cooled, filtered, and dried in vacuo to recover 699 mg $[Rh(CO)Cl(PPh_3)_2]$ as pale-yellow crystals in 94% yield. M.p.: 195–199°C decomp., lit. 195–197°C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.70$ (12H, m), 7.40 ppm (18H, m); ^{31}P NMR (120 MHz, $CDCl_3$): $\delta = 30.0$ ppm (d, $J = 127$ Hz).

Deuteriocarbonyltris(triphenylphosphine)rhodium(I):[19,29] In a 250 mL three-necked flask equipped with condenser and stirrer bar, chlorocarbonylbis(triphenylphosphine)rhodium(I) (599 mg, 0.89 mmol) and PPh_3 (0.9 g, 3.4 mmol) were suspended in EtOD (20 mL) and heated to reflux. $NaBD_4$ (300 mg, 7.2 mmol) in EtOD (20 mL) was added over one minute. The resulting solution was refluxed for 20 min, cooled, and filtered. The collected product was washed once with EtOH and once with ether, then dried in vacuo to yield 770 mg $[Rh(CO)D(PPh_3)_3]$ in 97% yield (97 atom D%). ^{1}H NMR (400 MHz, C_6D_6): $\delta = 7.40$ (18H, m), 6.90 ppm (27H, m); ^{31}P NMR (120 MHz, C_6D_6): $\delta = 40.5$ ppm (d, $J = 155$ Hz); ^{2}H NMR (60 MHz, C_6H_6): $\delta = -9.3$ ppm (br s).

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