Homodienyl 1,5-Hydrogen Shifts in Vinyl Aziridines

Jens Åhman,[a] Peter Somfai*[a] and David Tanner[b]

[a] *Department of Organic Chemistry 2, Chemical Center, Lund Institute of Technology, University of Lund, P.O. Box 124, S-221 00 Lund, Sweden*

[b] *Department of Organic Chemistry, University of Uppsala, Box 531, S-751 21 Uppsala, Sweden*

The thermal 1,5-hydrogen shift of the enantiomerically pure vinyl aziridines **1** yields allylic imines **3** in quantitative yields and as single diastereomers.

Recently we described the base induced aza 2,3-Wittig rearrangement of vinyl aziridines **1** to afford tetrahydropyridines **2** in excellent yield and as single diastereomers (Scheme 1).[1] Based on the reaction outcome we proposed a possible transition-state orientation in which the vinyl and *tert*-butyl acetate groups are *cis* so as to facilitate bond formation. It was also suggested that the vinyl group should adopt an *endo* orientation, projecting over the three-membered ring, while the enolate moiety is oriented so as to minimise steric interactions with the other ring substituents (*exo*), thus accounting for the observed formation of the *cis*-2,6-disubstituted derivative **2**. During this work it occurred to us that **1** should also be able to participate in a homodienyl 1,5-hydrogen shift to form allylic imines **3**. Although the corresponding rearrangement of vinyl cyclopropanes is a well investigated process,[2] the analogous transformation of vinyl aziridines has hitherto been documented in only a few cases.[3,4] Herein we detail the results of such a study and also, based on the product stereochemistry, propose a possible transition-state orientation for the rearrangement.

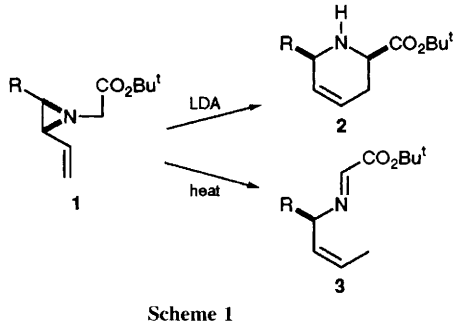
The vinyl aziridines used in the present study were prepared in good overall yield and in high enantiomeric purity from the corresponding epoxy alcohols by a series of standard transformations.[1] As evident from their ^{1}H NMR spectra aziridines **1a–c** exist as equilibrating mixtures of nitrogen invertomers at room temperature, while the spectrum of **1d** indicates the presence of a single invertomer, presumably with the *tert*-butyl acetate *trans* to the sterically most demanding ring substituent.

The results from the homodienyl 1,5-hydrogen shift of vinyl aziridines **1a–d** are summarised in Scheme 2. Thus, by simply heating a solution of **1a** in benzene at reflux for 150 min resulted in smooth formation of allylic imine **3a** in quantitative yield and as a single diastereomer.† In a similar way **1b–d** were quantitatively rearranged into **3b–d**‡ and in all cases only a single isomer of the product could be detected. The stereochemistry of the olefinic portion in **3a–d** was determined from their ^{1}H NMR spectra, showing a coupling constant for the vinylic protons (J = 9–11 Hz) characteristic for (*Z*)-alkenes. For the imine moiety, however, the double bond geometry could not be deduced from the spectral data at hand and the assigned (*E*)-stereochemistry is based solely on our proposed transition-state structure (*vide infra*).

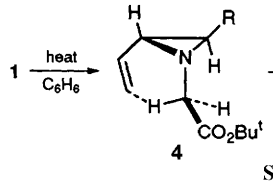
A transition-state orientation that accounts for the reaction outcome is shown in Scheme 2. As can be seen in **4** only the nitrogen invertomer in which the vinyl group, adopting an *endo* orientation, and the *tert*-butyl acetate moiety are *cis* with respect to each other can participate in the reaction, thus securing a close proximity of the rearrangement origin and terminus. Furthermore, the bulky acetate group should occupy an *exo* position so as to avoid unfavourable steric interactions with the other ring substituents. Structure **4** then accounts satisfactorily for the exclusive formation of the observed (*Z*)-olefin stereochemistry in **3** while the preferred orientation of the acetate group should transform into an (*E*)-imine. The proposed transition-state structure **4** is in agreement with that originally suggested by Daub and Berson[5] for the analogous rearrangement of vinyl cyclopropanes. For that case it was argued that the *endo* preference of the vinyl group most probably is associated with orbital overlap factors, which has later been supported by *ab initio* calculations.[6] It is thus reasonable to assume that the same stereoelectronic factors also dictate the *endo* preference in the present reaction. Concerning the stereochemistry at the rearrangement origin, it has been shown in the vinyl cyclopropane series that 1,1-diethyl-2-vinyl cyclopropane upon heating is transformed into an almost equal mixture of (2*E*,5*Z*)- and (2*Z*,5*Z*)-3-ethylhepta-2,5-diene.[7] The reaction outcome was rationalised in terms of similar steric interactions for the transition states leading to the two isomeric products. Although our results are in contrast to these findings we can at present offer no satisfactory explanation for this discrepancy.§ Finally, it should also be noted that **4** bears strong resemblance to the transition state recently suggested by us for the *aza* 2,3-Wittig rearrangement of **1**.[1]

The necessity of having both the rearrangement origin and terminus *cis* with respect to each other was demonstrated with 2,3-*cis*-aziridine **5** which exists as a single nitrogen invertomer, presumably with the *tert*-butyl acetate group *trans* to the other ring substituents. Refluxing a solution of **5** in benzene for prolonged periods gave no detectable reaction while use of higher temperatures (>100 °C) resulted in complete decomposition of the starting material.

In summary, we have shown that properly substituted vinyl aziridines are excellent substrates for the homodienyl 1,5-hydrogen shift and we are currently investigating the scope and limitations of this reaction. We also note that the allylic imines formed in these reactions should be valuable intermediates for the synthesis of biologically significant alkaloids.

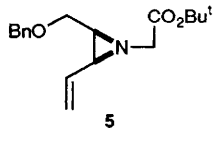


Scheme 1



	R	*t*/ min
3a	*n*-C_6H_{13}	150
b	c-C_6H_{11}	144
c	$C_6H_5CH_2OCH_2$	162
d	But	135

Scheme 2



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Footnotes

† *Data for* **3a**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.61 (1H, d, J = 0.9 Hz), 5.59 (1H, dq, J = 10.9, 6.6 Hz), 5.52 (1H, tq, J = 10.9, 1.4 Hz), 4.16 (1H, m), 1.75–1.59 (1H, m), 1.63 (3H, dd, J = 6.6, 1.4 Hz), 1.54 (9H, s), 1.47 (1H, m), 1.32–1.19 (8H, m), 0.87 (3H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.3, 153.2, 131.1, 126.1, 82.3, 67.0, 36.1, 31.7, 29.1, 28.0, 26.0, 22.6, 14.1, 13.3; $[\alpha]_D$ = −2.33 (*c* 0.84, $CHCl_3$) HRMS (CI^+). Found: *m/z* 268.2274. Calc. for $C_{16}H_{30}NO_2$ (M + H) 268.2277.

‡ All new compounds showed spectroscopic and analytical data in agreement with the assigned structures.

§ Preliminary results indicate that rearrangement of *trans*-2-*tert*-butyl-1-heptyl-3-vinylaziridine gives a single isomeric product.

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