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Transition metal catalyzed ring opening reactions of 2-phenyl-3-vinyl substituted 2*H*-azirines

Albert Padwa* and Thomas Stengel

Department of Chemistry, Emory University, Atlanta, GA 30322, USA

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Abstract—Treatment of 2-phenyl-3-vinyl-substituted 2*H*-azirines with Grubbs' catalyst induces a clean rearrangement and affords products derived from carbon–nitrogen bond cleavage of the 2*H*-azirine ring. However, when the reaction was carried out using Wilkinson's catalyst in an alcoholic solvent, the only product obtained in high yield corresponded to an α,β-unsaturated oxime.
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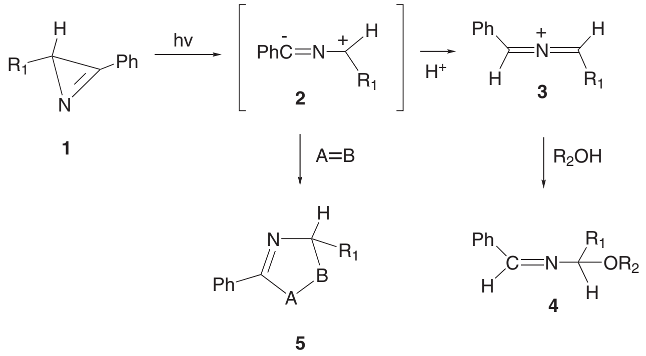
2*H*-Azirines are highly reactive three-membered unsaturated nitrogen-containing heterocycles that have been used for the preparation of a wide range of polyfunctional acyclic and cyclic nitrogen-containing compounds.[1] This small membered ring can take part in various chemical transformations since it can act as a dienophile or as a dipolarophile and can also function as an electrophile or nucleophile.[2] The ring strain undoubtedly contributes to the high reactivity of the 2*H*-azirine moiety and makes it an attractive intermediate for the preparation of complex heterocyclic ring systems. The most common method for preparing 2*H*-azirines involves the photolysis or thermolysis of vinyl azides.[3] This reaction can take place in a concerted manner or via a vinyl nitrene intermediate.[4]

Earlier work from our laboratory demonstrated that 2*H*-azirines are photochemically active substrates.[5] Upon irradiation into their n–π* absorption bands, the strained three-membered 2*H*-azirine ring opens selectively at the C–C bond in a heterolytic fashion resulting in the formation of a nitrile ylide dipole (**2**).[6] The nitrile ylide can be trapped by π-bonds to give cycloadducts of type **5**. Due to the pronounced reactivity of nitrile ylides with various dipolarophiles, 2*H*-azirines have been extensively utilized in [3 + 2]-cycloaddition reactions (Scheme 1).[5–7] In the presence of alcohols, the photochemically generated nitrile ylide **2** reacts to form alkoxyimines **4** and this reaction presumably proceeds by a pathway involving the intermediate production of an azaallenium cation (**3**).[8]



Scheme 1.

In recent years there has been considerable interest in the use of both organometallic reagents and catalysts for effecting ring cleavage of small ring systems.[9] By comparison with the extensive studies carried out on the photochemistry of the 2*H*-azirine ring system,[5–7] its behavior toward organometallic reagents has been relatively unexplored. In some earlier work, Alper and Wollowitz[10] demonstrated that group VI metal carbonyls [$M(CO)_6$, M=Cr, Mo, W] are useful reagents for converting 2-aryl 2*H*-azirines into pyrazines **7**. Interestingly, pyrroles such as **8** were obtained in modest yields when diiron enneacarbonyl was employed as the organometallic reagent.[11] Mechanistic studies indicate

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* Corresponding author. Tel.: +1-404-727-0283; fax: +1-404-727-6629; e-mail: chemap@emory.edu

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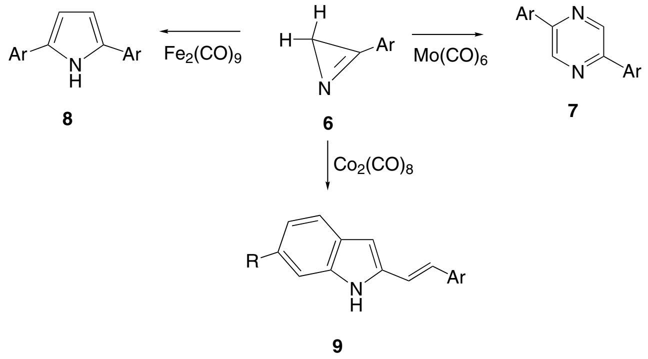
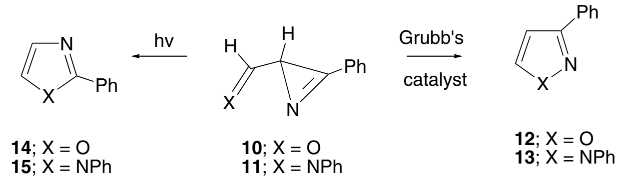


Scheme 2.

that the formation of the pyrrole proceeds via carbon–nitrogen bond cleavage of the 2*H*-azirine ring. More surprisingly, treatment of the aryl substituted 2*H*-azirine **6** with dicobalt octacarbonyl [$Co_2(CO)_8$] afforded 2-styrylindoles such as **9** in good–excellent yields (Scheme 2).[12] No mechanistic studies were carried out and the unusual chemoselectivity encountered as a function of the organometallic reagent used was not explained by the authors.[10–12]

In a continuation of our own studies dealing with the chemical reactivity of 2*H*-azirines,[5] we thought it would be of interest to further investigate the transition metal catalyzed reactions of several 2-phenyl-3-vinyl substituted 2*H*-azirines. In this letter we report that the commonly employed Grubbs' catalyst (first generation) induces a clean rearrangement, which proceeds via carbon–nitrogen bond cleavage of the 2*H*-azirine ring. However, when the reaction was carried out using the popular Wilkinson's catalyst [$Rh(PPh_3)_3Cl$] in an alcoholic solvent, the only product obtained in high yield corresponded to an α,β-unsaturated oxime (vide infra). These results provide further insight into the chemical behavior of this reactive three-membered heterocyclic ring with various transition metal catalysts.

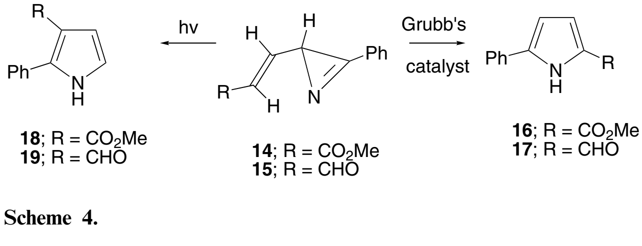
Our first transition metal catalyzed experiments centered around the use of the ruthenium 4,5-dihydroimidazo-2-ylidene complex developed by Grubbs and widely known for its application in organic and polymer synthesis.[13] To date, this catalyst is routinely used for ring closing metathesis (RCM), cross metathesis (CM), and other metathesis-type reactions. The commercial availability and effectiveness of the Grubbs' catalyst now allow olefin metathesis strategies to be viewed as practical methods for the synthesis of medium size ring,[14] spiro and polycyclic systems[15] and natural products.[16] A growing number of newly discovered catalytic processes mediated by Grubbs' carbene complex also broaden its synthetic utility beyond olefin metathesis.[17] An investigation of its chemistry with 2*H*-azirine **10** led to the discovery that it rapidly induced a rearrangement at 25 °C producing 3-phenylisoxazole (**12**) in 90% yield. Reaction of the corresponding *N*-phenylimine **11** proceeded similarly and gave 1,3-diphenylpyrazole (**13**) as the exclusive product (Scheme 3). These results stand in marked contrast to the photochemical behavior of **10** and **11**, which afforded 2-phenyloxazole (**14**) and 1,2-diphenylimidazole (**15**) as the exclusive products. The photoproducts are formed by C–C bond fragmentation and subsequent cyclization of the resulting nitrile ylide. The isolation of isoxazole **12** and pyrazole **13** by use of the Grubbs' catalyst clearly indicate that these transition metal catalyzed transformations occur by C–N bond fragmentation.



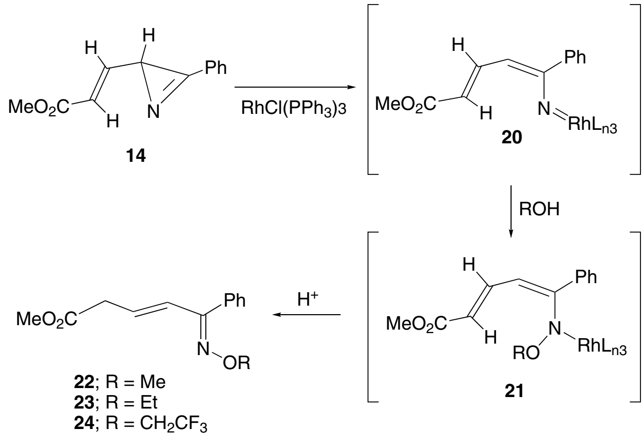
Scheme 3.

Attention was next turned to the Grubbs' catalyzed reaction of methyl (*E*)-3-phenyl-2*H*-azirine-2-acrylate (**14**). Treatment of **14** in the presence of 5 mol% $Cl_2(Cy_3P)_2Ru{=}CHPh$ in CH_2Cl_2 at 25 °C gave 2-phenyl-5-carbomethoxypyrrole (**16**) as the exclusive product in 75% isolated yield. Photolysis of **14**, on the other hand, afforded the isomeric 2-phenyl-3-carbomethoxypyrrole (**18**) in 85% yield (Scheme 4). In an analogous manner, the reaction of the aldehydic substituted 2*H*-azirine **15** with Grubbs' catalyst furnished the 2,5-disubstituted pyrrole **17** while photolysis gave the 2,3-disubstituted pyrrole **19** in high yield. The structures of the disubstituted pyrroles were readily established by examination of their characteristic NMR spectra.

Our attempts to carry out a related rearrangement using Wilkinson's catalyst [$RhCl(PPh_3)_3$] proved to be more problematic. Exposure of the 2*H*-azirinyl acrylate **14** to $RhCl(PPh_3)_3$ in CH_2Cl_2 resulted only in recovered starting material. When heated at reflux, the reaction afforded a complex mixture of products, which resisted separation and purification. However, when **14** was treated with 5 mol% of Wilkinson's catalyst in methanol, a clean reaction ensued and the major product isolated in 65% yield was identified as 5-methoxyimino-5-phenyl-pent-3-enoic acid methyl ester (**22**). Similar results were obtained using ethanol and trifluoroethanol, which furnished the α,β-unsaturated oximes **23** (40%) and **24** (53%). A possible mechanism for the 2*H*-azirine-$RhCl(PPh_3)_3$ reaction involves initial π-



Scheme 4.



Scheme 5.

complexation of the organometallic catalyst with the imino bond (Scheme 5). Ring opening by C–N bond cleavage would give **20**, which can then react with the alcohol to afford **21**. Loss of the rhodium complex occurs upon protonation to furnish the observed product.

An investigation of the reaction of variously substituted 2*H*-azirines with other commonly used transition metal catalysts is currently in progress and will be reported at a later date.

Acknowledgements

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References and notes

1. (a) Gilchrist, T. L. *Aldrichim. Acta* **2001**, *34*, 51; (b) Hassner, A. *Adv. Strained Interesting Org. Mol.* **2000**, *8*, 187–257.
2. Padwa, A.; Woolhouse, A. D. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 7, pp 47–93.
3. (a) Banert, K. *Methoden Org. Chem.* Houben-Weyl **1993**, *E15*(Part 1); (b) Blackes, J. *Methoden Org. Chem.* Houben-Weyl **1992**, *E16C*.
4. Hassner, A. *Azides and Nitrenes. Reactivity and Utility*; Academic: Orlando, 1984.
5. (a) Padwa, A.; Dharan, M.; Smolanoff, J.; Wetmore, S. I. *J. Am. Chem. Soc.* **1973**, *95*, 1954; (b) Padwa, A.; Smolanoff, J.; Tremper, A. *J. Am. Chem. Soc.* **1975**, *97*, 4682; (c) Padwa, A.; Rasmussen, J. K.; Tremper, A. *J. Am. Chem. Soc.* **1976**, *98*, 2605.
6. Hansen, H.; Heimgarten, H. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 1, pp 177–290.
7. Orahovats, A.; Heimgarten, H.; Schmid, H.; Heinzelmann, W. *Helv. Chem. Acta* **1975**, *58*, 2662.
8. Albrecht, E.; Mattay, J.; Steenken, S. *J. Am. Chem. Soc.* **1997**, *119*, 11605.
9. Ting, P. C.; Lin, Y. C.; Lee, G. H.; Cheng, M. C.; Wang, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6433.
10. Alper, H.; Wollowitz, S. *J. Am. Chem. Soc.* **1975**, *97*, 3541.
11. Alper, H.; Prickett, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 191.
12. Alper, H.; Prickett, J. E. *Tetrahedron Lett.* **1976**, 2589.
13. (a) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413; (b) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2039.
14. Yet, L. *Chem. Rev.* **2000**, *100*, 2963.
15. Lautens, M.; Hughes, G. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 129.
16. Nicolaou, K. C.; Rodriguez, R. M.; Mitchell, H. J.; Suzuki, H.; Fylaktakidou, K. C.; Baudoin, O.; Van Delft, F. L. *Chem. Eur. J.* **2000**, *6*, 3095.
17. Alcaide, B.; Almendros, P. *Chem. Eur. J.* **2003**, *9*, 1258.