Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 6763–6765

TETRAHEDRON LETTERS

A simple green procedure for the synthesis of 2H-azirines

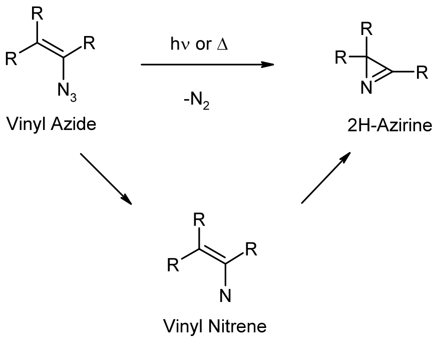
Pradeep N. D. Singh, Carrie L. Carter and Anna D. Gudmundsdóttir*

Department of Chemistry, University of Cincinnati, OH 45221-0172, USA

Received 2 June 2003; revised 19 June 2003; accepted 23 June 2003

Abstract—An efficient and environmentally friendly method preparing 2H-azirines in good yield has been achieved by microwave irradiation of vinyl azides in solvent free conditions.

2H-azirines are valuable precursors for preparing a wide range of polyfunctional acyclic and cyclic nitrogen containing compounds.[1] A number of synthetic methods are available for forming 2H-azirines such as intramolecular rearrangements of N-functionalized imines, vinyl azides, isoxaoles and oxazaphospholes. 2H-azirines have also been made by bimolecular reactions between nitriles and carbenes or nitrenes and acetylenes. The most common methods for preparing 2H-azirines are photolysis or thermal activation of vinyl azides.[2] This rearrangement can take place in a concerted manner or via vinyl nitrene intermediates (see Scheme 1).[3] Pyrolysis of vinyl azides is complicated by the fact that the products, 2H-azirines, are themselves thermally active and thus react further, decreasing the yields of the 2H-azirines and causing difficulty in their isolation. Similarly, photolysis of vinyl azides yields 2H-azirines and secondary photoproducts from the 2H-azirines, which are photolabile. To circumvent this problem, vinyl azides are generally photolyzed at low temperature and low conversion.



Scheme 1.

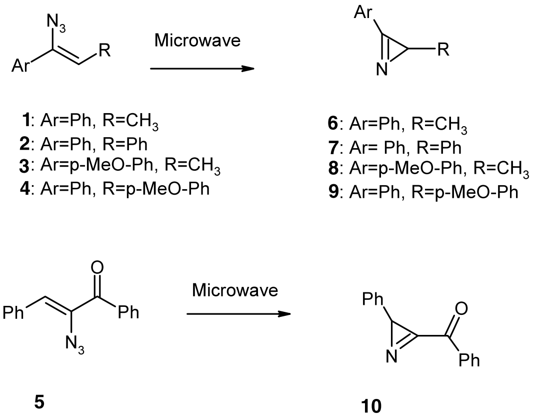
In recent years, the use of microwave irradiation in organic reactions has become popular due to short reaction times, high yields, increased selectivity and operational simplicity.[4] Microwave irradiations have been used to catalyze cycloaddition of azides.[5,6] For example microwave irradiations of alkyl azides yield triazoles through 1,3 dipolar addition to alkenes in excellent yields.[5] Similarly, tetrazoles, have been made efficiently in good yields in microwave assisted additions of azides to aryl and vinyl nitrilies.[6] Herein we report a new and efficient procedure for synthesizing 2H-azirines from rearrangements of vinyl azides by simply applying microwave irradiation for a few minutes in solvent free conditions.

We prepared vinyl azides **1**, **2**, **3**, **4** and **5** as described by Hassner et al. (see Scheme 2).[7] The ^{1}H NMR and the IR spectra of vinyl azides **1**, **2** and **5** are identical to those in the literature, whereas vinyl azides **3** and **4** have not been made previously.[8–10] Azides **1**–**5** are representative of nonterminal, alkyl, aryl and acetyl vinyl azides that generally form azirines upon pyrolysis.[3] In a typical case, neat vinyl azide (~150 mg) was placed on a watch glass and irradiated using microwaves.[11] The progress of the reaction was monitored by thin layer chromatography and the microwave irradiation was continued until all the starting material was fully depleted. Interestingly, the reaction goes to completion in only a few minutes. Vinyl azides **1**–**3** are liquids and after microwave irradiation they become reddish-brown. Vinyl azides **4** and **5**, however, are solids that liquefy and turn reddish-brown upon microwave irradiation. Afterwards, the reaction mixture was passed through a short silica column eluted

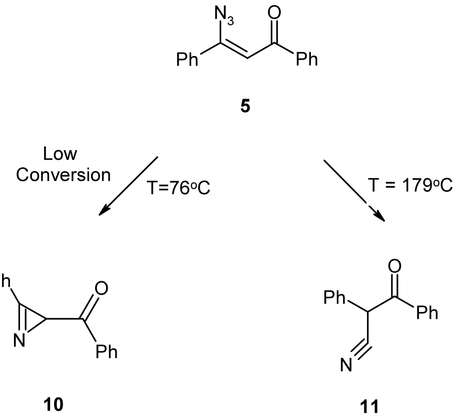
---

* Corresponding author. Tel.: 513-556-3380; fax: 513-556-9239; e-mail: anna.gudmundsdottir@uc.edu

0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0040-4039(03)01558-2



Scheme 2.



Scheme 3.

with 80:20 hexane:ethyl acetate. Vinyl azides **1**, **2**, **3** and **4** gave 2H-azirines **6**, **7**, **8** and **9**, respectively, in 80% or better isolated yields (see Table 1), whereas vinyl azide **5** yielded 2H-azirine **10** in 60% isolated yield along with some minor heterocyclic compounds that were not characterized. 2H-azirines **6**–**10** were characterized by infrared and ^{1}H NMR spectroscopy. The spectra of **6**, **7** and **10** are identical to those in the literature.[8,12,13] 2H-azirine **6** is obtained in similar yields as in conventional thermolysis whereas 2H-azirines **7** and **8** were isolated in significantly higher yields. Hassner et al. has showed that traditional thermolysis of vinyl azide **5** at high temperature ($T = 179°C$) yielded nitrile **11** as the major compound (Scheme 3),[14] whereas thermolysis at lower temperature (76°C) and low conversion gives 2H-azirine **10**.

In conclusion we have shown that microwave irradiation of vinyl azides is a simple way of preparing 2H-azirine derivatives in an environmentally friendly way. This methodology reduces the reaction times and allows the reaction to be taken to high conversion. The 2H-azirine products are formed in similar to much better yields than photolysis or conventional thermal activation of the corresponding vinyl azides.

Acknowledgements

We thank the National Science Foundation (CAREER Award #0093622) for supporting this work. Financial support from the Petroleum Research Foundation (ACS-PRF #35809-G4) is also gratefully acknowledged.

References

1. For some recent reviews, see: (a) Paliacios, F.; Ochoa de Retana, A. M.; Martines de Marigorta, E.; Manuel de los Santor, J. *J. Eur. Org. Chem.* **2001**, 2401–2414; (b) Murphee, S. S.; Padwa, A. *Three-Membered Ring Systems in Prog. Heterecycl. Chem.*; Scriven, E. F. V.; Suschitzky, H., Eds.; Pergamon Press: Oxford, 1997; Vol 9; (c) Pearson, W. H.; Lian B. W.; Bergmeier, S. C. *Comp. Heterocycl. Chem. II.*; Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol 1A, Chapter 1; (d) Heimgartner, H. *Angew. Chem., Int. Ed.* **1991**, *30*, 238–264.
2. (a) Banert, K. *Methoden Org.Chem.* Houben-Weyl, **1993**, Vol E15, part 1; (b) Backes, J. *Methoden Org. Chem.* Houben-Weyl, **1992**, Vol. E16c.
3. (a) Hassner, A. *Azides and Nitrenes. Reactivity and Utility*; Academic Press: Orlando, 1984; (b) *Nitrenes*; Lwowski, W., Ed.; Wiley & Sons: New York, 1970.
4. For some recent reviews, see: (a) Pillai, U. R.; Sahle-Demessie, E.; Varma, R. S. *J. Mat. Chem.* **2002**, *12*, 3199–3207; (b) Perreux, L.; Loupy, A. *Tetrahedron* **2001**, *57*, 9199–9223; (c) Varma, R. S. *Pure and Applied Chemistry* **2001**, *73*, 193–198; (d) Lidstrom, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225–9283; (e) Diaz-Ortiz, A.; de la Hoz, A.; Langa, F. *Green Chem.* **2000**, *2*, 165–172; (f) Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025–1074; (g) Deshayes, S.; Liagre, M.; Loupy, A.; Luche, J.-L.; Petit, A. *Tetrahedron* **1999**, *55*,

Table 1. Isolated yields of 2H-azirine from thermal and microwave activation of vinyl azide

Vinyl azide	Reaction time (min)	2H-azirine	Microwave yields (%)[a]	Thermal yield (%)[b]
1	3	**6**	85	90[6]
2	3.5	**7**	80	33[6]
3	3	**8**	90	
4	3	**9**	80	
5	5	**10**	65	16[7]

[a] The isolated yields of 2H-azirines from microwave irradiations of the corresponding vinyl azides.

[b] Literature values for isolated yields of 2H-azirines obtained from conventional thermolysis of the corresponding vinyl azides.

10851–10870; (h) Varma, R. S. *Green Chemistry* **1999**, *1*, 43–55; (i) Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacquault, P.; Mather, D. *Synthesis* **1998**, 1213–1234; (j) Caddick, S. *Tetrahedron* **1995**, *51*, 10403–10432.

5. Katritzky, A. R.; Singh, S. K. *J. Org. Chem.* **2002**, *67*, 9077–9079.
6. Alterman, M.; Hallberg, A. *J. Org. Chem.* **2000**, *65*, 7984–7989.
7. (a) Hassner, A.; Fowler, F. W. *J. Org. Chem.* **1968**, *33*, 2686–2691; (b) Fowler, F. W.; Hassner, A.; Levy, A. L. *J. Am. Chem. Soc.* **1967**, *89*, 2077–2082.
8. Bader, H.; Hansen, H.-J. *Helv. Chim. Acta* **1978**, 286–304.
9. (a) Hassner, A.; L'Abbe, G.; Miller, M. J. *J. Am. Chem. Soc.* **1971**, *93*, 981–985; (b) L'Abbe, G.; Mathys, G. *J. Hetero. Chem.* **1974**, *11*, 613–614.
10. The ^{1}H NMR and IR of the vinyl azides are as follows; **1**: ^{1}H NMR (250 Mz, $CDCl_3$) δ 7.4 (m, 10H), 5.47 (q, 7 Hz, 1H), 1.72 (d, 7 Hz, 3H) ppm. IR (neat) 2103, 1451, 1251 cm^{-1}. **2**: ^{1}H NMR (250 Mz, $CDCl_3$) δ 7.70 (d, 2H), 7.5–7.3 (m, 8H), 6.0 (s, 1H) ppm. IR (neat) 3056, 3024, 2110, 1600, 1493, 1447 cm^{-1}. **3**: ^{1}H NMR (250 Mz, $CDCl_3$) δ 7.26 (d, 7 Hz, 2H), 6.92 (d, 7 Hz, 2H), 5.42 (q, 7 Hz, 1H), 3.82 (s, 3H), 1.69 (s, 7 Hz, 1H) ppm. IR (neat) 2105, 1605, 1250 cm^{-1}. **4**: Mp: 123–125°C. ^{1}H NMR (250 Mz, $CDCl_3$) δ 7.5–6.9 (m, 10H), 3.8 (s, 3H) ppm. IR (KBr) 2096, 1604, 1513, 1252, 1030 cm^{-1}. **5**: ^{1}H NMR (250 Mz, $CDCl_3$) δ 7.78 (d, 7 Hz, 4H), 7.6–7.4 (m, 6H), 6.46 (s, 1H) ppm. IR (neat) 2115, 1649, 1262 cm^{-1}.
11. We used a conventional microwave owen, 2450 MHz, 1100 Watt.
12. Hassner, A.; Wiegand, N. H.; Gottlieb, H. E. *J. Org. Chem.* **1986**, *51*, 3176–3180.
13. The ^{1}H NMR and IR spectra of the 2H-azirine are as follows; **6**: ^{1}H NMR (250 Mz, $CDCl_3$) δ 7.86 (m, 2H), 7.58 (m, 3H), 2.30 (q, 5 Hz, 1H), 1.36 (d, 5 Hz, 3H) ppm. IR (neat) 2981, 2922, 1737, 1453 cm^{-1}. **7**: ^{1}H NMR (250 Mz, $CDCl_3$) δ 7.6 (m, 4H), 4.28 (m, 6H), 3.48 (s, 1H) ppm. IR (neat) 2985, 1742, 1374, 1243, 1048 cm^{-1}. **8**: ^{1}H NMR (250 Mz, $CDCl_3$) δ 7.80 (d, 7 Hz, 2H), 7.04 (d, 7 Hz, 2H), 3.90 (s, 3H), 2.26 (t, 4 Hz, 1H), 1.34 (d, 5 Hz, 3H) ppm. IR (neat) 2976, 1731, 1604, 1508, 1258 cm^{-1}. **9**: ^{1}H NMR (250 Mz, $CDCl_3$) δ 7.85 (d, 7 Hz, 2H), 7.3–7.0 (m, 7H), 3.88 (s, 3H), 3.3 (s, 1H) ppm. IR (KBr), 1739, 1604, 1305, 1171, 1028 cm^{-1}. **10**: ^{1}H NMR (250 Mz, $CDCl_3$) δ 8.30 (d, 2H), (m, 8H), 3.50 (s, 1H) ppm. IR (neat) 1723, 1658, 1451, 1182 cm^{-1}.
14. Belinka, B. A.; Hassner, A.; Hendler, J. M. *J. Org. Chem.* **1981**, *46*, 631–632.