HETEROCYCLES, Vol 19, No 2, 1982

THERMAL RING-EXPANSION OF 6-ETHYNYL-1,2,5,6-TETRAHYDROPYRIDINE N-IMIDES INTO DIAZONINE DERIVATIVES

Haruki Sashida and Takashi Tsuchiya*

School of Pharmacy, Hokuriku University,
Kanagawa-machi, Kanazawa, 920-11, Japan

Abstract —— The thermolysis of the 6-ethynyl-1,2,5,6-tetrahydropyridine N-imides (5 and 6) resulted in the [2,3]-sigmatropic rearrangement with the ethynyl group to give the novel dihydrodiazonines (9) *via* the allene intermediates (8).

Much attention has been given recently to the utilization of thermal sigmatropic rearrangements of various kinds of ylides in organic synthesis.[1] As regards to aminimides, open-chain allylamine N-imides are known to undergo competing [1,2]- and [2,3]-sigmatropic rearrangements, but the latter rearrangement usually predominates over the former, whereas pentadienylamine N-imides undergo [1,2]- and [2,5]-rearrangements predominantly over the [2,3]-rearrangement.[2] As for cyclic amines, saturated piperidine and pyrrolidine N-imides have been shown to undergo the [1,2]-rearrangement to give the corresponding ring-expansion products.[3] These results and those of the thermolysis of cyclic S-ylides[4] prompted us to examine the thermal behavior of unsaturated cyclic amine ylides and we have already reported that the

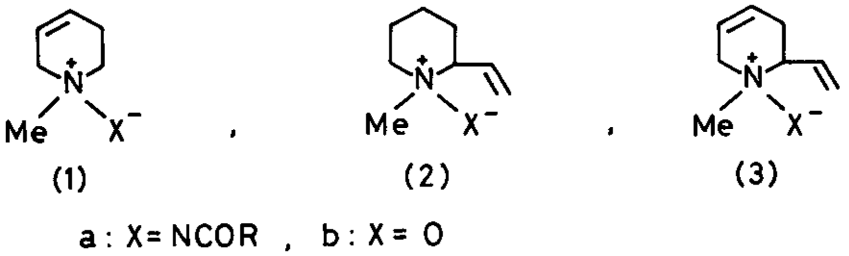


Chart 1

N-imides (1a-3a) undergo only [2,3]-rearrangement and no [1,2]-rearrangement.[5] In contrast, the thermolysis of the N-oxides (1b-3b) results in the [1,2]-rearrangement to give the corresponding 1,2-oxazepine derivatives.[6]

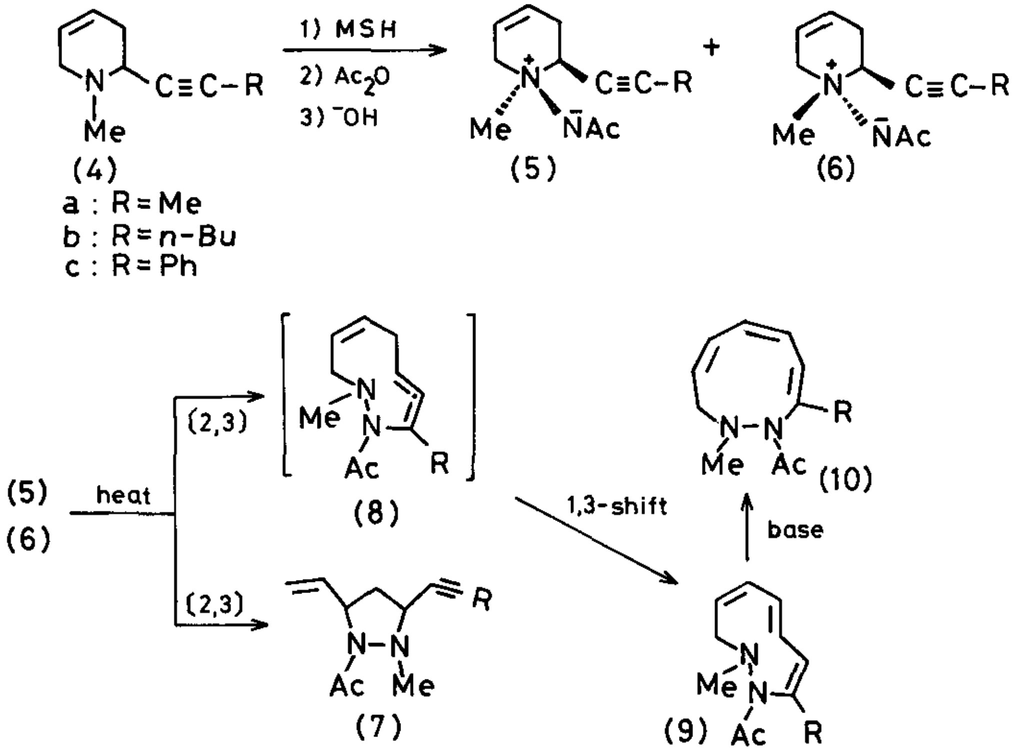
In connection with these results and the thermal behavior of prop-2-ynylamine ylides,[7] we studied the thermolysis of the title N-imides with an ethynyl group and report here the formation of novel nine-membered heterocycles, diazonines, by the [2,3]-rearrangement with the triple bond *via* allene intermediates.

The 6-ethynyl-1,2,5,6-tetrahydropyridines (4a-c)[8] were aminated with O-mesitylenesulfonylhydroxylamine (MSH)[9] and the resulting N-aminopyridinium salts were acetylated with acetic anhydride followed by base treatment to give ca. 4:1 mixtures of N-acylimides (5) and (6) in 50-75% yields, which were separated by alumina chromatography. Structures including stereochemistry of these N-imide diastereomers were elucidated by ^{1}H-NMR spectral analyses.[10] By analogy to the piperidine alkylation,[10] axial approach of the amination reagent on the diequatorial conformer of the amine (4) may predominates to give the diastereomer (5) as the major product.

Thermolysis of both N-imides (5) and (6) in refluxing xylene for 1-2 h gave the tetrahydropyrazoles (7) and the 5,6-*trans*-dihydrodiazonines (9) in the yields shown in Chart 2, respectively.[11] The pyrazoles (7) may be formed directly from the imides by the [2,3]-rearrangement with the double bond in the ring analogous to that observed for the N-imides (1).[5] On the other hand, the formation of the ring-expansion products (9) may involve initial formation of the allene intermediates (8) by another [2,3]-rearrangement with the triple bond by analogy with the cases of open-chain prop-2-ynylamine ylides.[7] The allene intermediates (8) then undergo a 1,3-hydrogen shift to give the products (9).

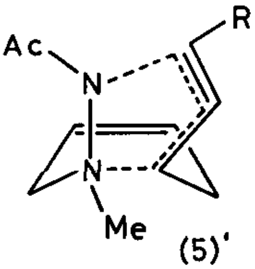
The results collected in Chart 2 show that the yields of 9 from the imides (6), in which the imide group and the ethynyl group are *trans*, are 3-4 times higher than those from 5. In addition, the thermolysis of 5 required somewhat longer times than those for 6. This lower or reduced susceptibility of the *cis*-imides (5) toward the reaction is probably due to the transition state of the concerted rearrangement requiring the unfavored boat form of the tetrahydropyridine ring, in contrast, the *trans*-diastereomers (6) may be able to form the favored chair form transition state, as indicated in the structures (5') and (6').

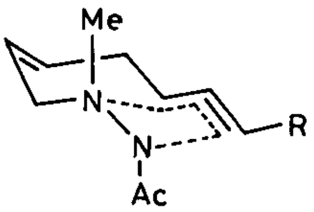
Treatment of the *trans*-dihydrodiazonines (9) with sodium ethoxide in toluene



5a	7%	15%
5b	8%	18%
5c	—	16%
6a	6%	55%
6b	7%	48%
6c	—	70%

Chart 2


(5)'


(6)'

resulted in the isomerization to give the *cis*-isomers (10) in high yields.[12] Studies on the detailed stereochemistry of the present reaction and on synthetic application of the results are further in progress.

References and Notes

1) For reviews, see W.J. Mckillip, E.A. Sedor, B.M. Culbertson, and S. Wawzonek, *Chem. Rev.*, 1973, **73**, 255; T.L. Gilchrist and C.J. Moody, *ibid.*, 1977, **77**, 409; E.C. Taylor and I.J. Turchi, *ibid.*, 1979, **79**, 181; H. Hayashi, *J. Syn. Org. Chem. Japan*, 1976, **34**, 396; T. Nakai and K. Mikami, *ibid.*, 1980, **38**, 381.
2) K. Chantrapromma, W.D. Ollis, and I.O. Sutherland, *J. Chem. Soc. Chem. Commun.*, 1977, 97.
3) S. Wawzonek and R.C. Gueldner, *J. Org. Chem.*, 1965, **30**, 3031; S. Wawzonek and J.G. Stephanie, *ibid.*, 1971, **36**, 2467.
4) For examples, E. Vedejs, J.P. Hagen, B.L. Roach, and K.L. Spear, *J. Org. Chem.*, 1978, **43**, 1185; E. Vedejs, M.J. Arco, D.W. Powell, J.M. Renga, and S.P. Singer, *ibid.*, 1978, **43**, 4831; V. Cere, C. Paolucci, S. Pollicino, E. Sandri, and A. Fava, *ibid.*, 1979, **44**, 4128.
5) T. Tsuchiya, H. Sashida, and H. Sawanishi, *Chem. Pharm. Bull.*, 1978, **26**, 2880; T. Tsuchiya and H. Sashida, *ibid.*, 1981, **29**, 1887.
6) T. Tsuchiya and H. Sashida, *Heterocycles*, 1980, **14**, 1925.
7) J.C. Greig, N.N. Ekwuribe, and L.D. Gruenke, *Tetrahedron Lett.*, 1979, 4025; G. Hallstrom, B. Lindke, A.H. Khuthier, and A.M. Al-Iraqi, *ibid.*, 1980, 667; S. Mageswaran, W.D. Ollis, D.A. Southam, I.O. Sutherland, and Y. Thebtranonth, *J. Chem. Soc. Perkin I*, 1981, 1969.
8) These compounds were prepared from 2-bromopyridine by successive ethynylation, methylation, and $NaBH_4$ reduction.
9) Y. Tamura J. Minamikawa, and M. Ikeda, *Synthesis*, 1977, 1.
10) T.M. Bare, N.D. Hershey, H.O. House, and C.G. Swain, *J. Org. Chem.*, 1972, **37**, 997.
11) Satisfactory elemental analyses and spectral data were obtained for all new compounds reported.
12) The ^{1}H-NMR spectra of the *trans*-diazonines (9) showed a temperature dependence consistent with the predictable temperature-dependent inversion of the ring, in contrast, those of the *cis*-isomers (10) showed no such dependence.

Received, 11th November, 1981