THERMAL REACTIONS OF 2-CYCLOPROPYL-2*H*-AZIRINES

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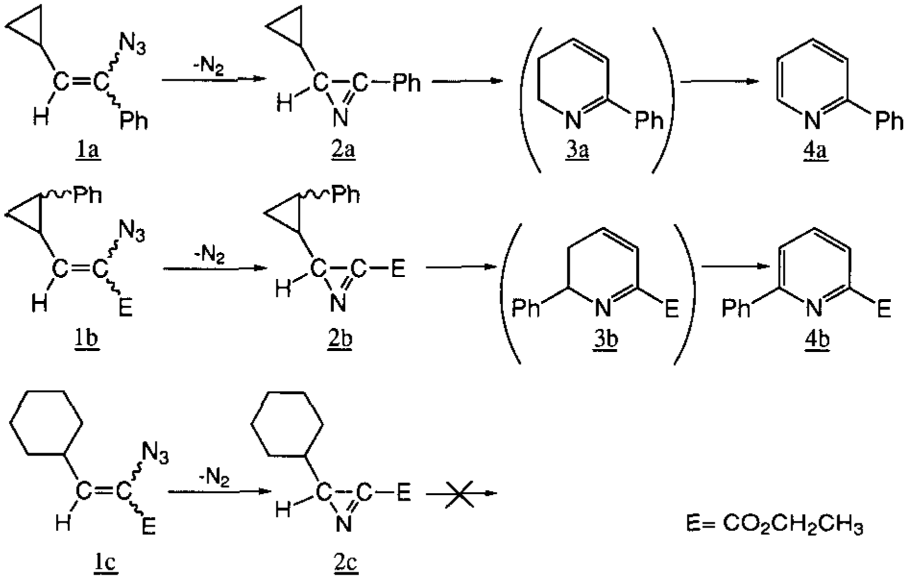
Abstract-Thermal rearrangement of 2*H*-azirines having a cyclopropane ring was revealed to give pyridines. Ene reaction involving a C=N bond to form tricyclic compound was observed in the case of 2-cyclopropyl-2*H*-azirine having an isobutenyl group *cis* to the azirine ring, whereas the *trans* isomer gave a pyridine ring exclusively.

Thermal rearrangement of 2*H*-azirines, having unsaturated group at 2-position of azirine ring,usually gave five-membered nitrogen containing heterocycles, such as pyrroles, indoles, and isoxazoles.[1] Formation of 5-membered ring compounds was shown to proceed by 2-step mechanism involving vinylnitrene intermediate by examining thermal behavior of optically active 2*H*-azirines.[2] Our study further revealed that pyridines and azepines were also formed when the unsaturated group at 2-position was suitably functionalized. These reactions could be also well explained by concerted mechanism from vinylnitrene.[3]

Here, we describe our investigation on thermal rearrangement of 2-cyclopropyl-2*H*-azirines which provided the first example of pyridine ring formation by participation of cyclopropane ring and ene reaction of azirine ring.

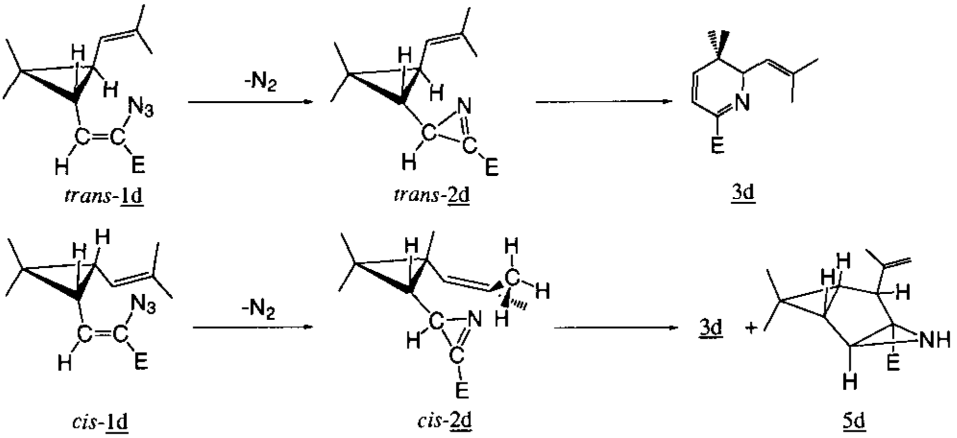
This communication is dedicated to Professor Rolf Hüisgen on the occasion of his 75th birthday.



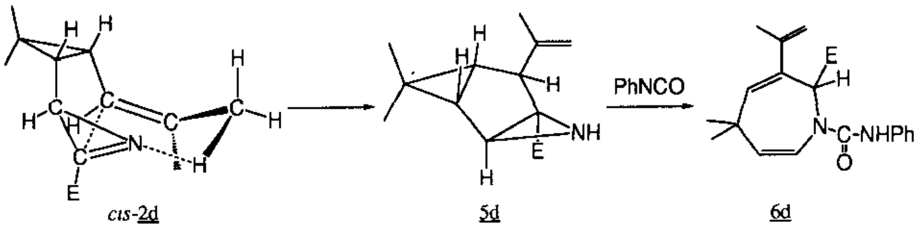
Addition of IN_3 to styrylcyclopropane followed by dehydroiodonation gave α-azido-β-cyclopropylstyrene (1a). Thermolysis of 1a in heptane under reflux for 2 h gave 2-cyclopropyl-3-phenyl-2*H*-azirine (2a), quantitatively. Thermal rearrangement of 2a was performed by heating its xylene solution at 185 °C under argon for 48 h in a sealed tube. Separation of the product by chromatography on silica gel gave 2-phenylpyridine (4a), in 46 % yield, as the sole product, presumably *via* dihydropyridine derivative (3a). In the case of ethyl α-azido-β-(2-phenylcyclopropyl)acrylate (1b) (*cis/trans*=1/2), prepared from 2-phenylcyclopropanecarbaldehyde by base catalyzed condensation with ethyl azidoacetate, thermal rearrangement of azirine was examined by direct thermolysis of 1b in refluxing xylene for 2 h, without isolating the azirine (2b), as azirines are generally formed by decomposition of vinyl azides. Separation of the product by chromatography on silica gel afforded ethyl 6-phenylpyridine-2-carboxylate (4b) as the sole identifiable product.

Thermolysis of ethyl α-azido-β-cyclohexylacrylate (1c) gave ethyl 2-cyclohexyl-2*H*-azirine-3-carboxylate (2c) under the same conditions as thermolysis of 1b, and 2c was intact on heating for a longer time. From these results, cyclopropane ring situated at 2-position of azirine ring can participate in thermal ring enlargement reaction of azirine to form 6-membered heterocycle, pyridines.

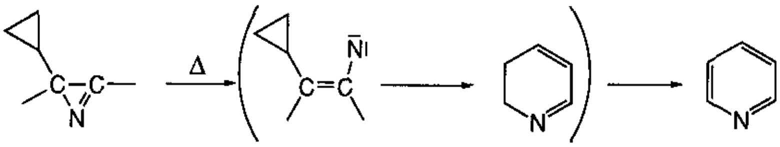
In order to examine the effect of the stereochemistry of cyclopropane ring and the possibility of the participation of unsaturated group on cyclopropane ring, we further synthesized isomeric vinyl azides *cis*- (1d)



and *trans*- (1d), from *cis*- and *trans*-2-isobutenylcyclopropanecarbardehydes by the same way as the synthesis of 1b. These azides were thermolyzed under the same conditions as 1b. In the case of thermolysis of *trans*-1d, separation of the product on silica gel afforded a single product in 79 % yield. On the basis of spectral results,[4] this compound was assigned as ethyl 5,5-dimethyl-6-isobutenyl-5,6-dihydropyridine-1-carboxylate (3d), especially by the nmr spectrum showing the presence of two olefinic protons at δ 6.17 and 6.48 and a methyne proton at δ 4.28 coupled only with the vinylic proton of the isobutenyl group. However, thermolysis of *cis*-1d gave a complex product mixture. By careful separation of the product, in addition to the same dihydropyridine 3d (16 %), another compound (5d) was obtained as oily product (34 %). This compound (5d) showed N-H stretching band at 3300 cm^{-1} in ir spectrum. The nmr spectrum[4] of 5d showed no longer presence of isobutenyl group but isopropenyl group. By further inspection of the nmr spectrum, 5d was assigned as ethyl 3,3-dimethyl-5-isopropenyl-7-azatricyclo[4.1.0.0^{2,4}]heptane-6-carboxylate. When 5d was reacted with phenyl isocyanate, crystalline adduct (6d), mp 209-211 °C was obtained. The adduct (6d) could be assigned to have dihydroazepine structure on the basis of spectral results. This would substantiate the structure of 5d, although in 6d both cyclopropene and aziridine ring were cleaved.



Formation of 5d would be explained by intramolecular ene reaction of the C=N bond of azirine ring[5] and isobutenyl group, which is impossible in the case of the *trans* isomer sterically. The azirine *cis*-2d prepared by photolysis of *cis*-1d at 3 °C with a high pressure mercury lamp equipped with a Pyrex filter, gave exclusively 5d at room temperature. This observation means that formation of 3d required higher energy than concerted ene reaction, as C-N bond of the azirine ring would be cleaved.



From the results in this paper, it was established that cyclopropane ring can participate in thermal ring expansion reaction of 2-cyclopropyl-2*H*-azirine.

Studies on ene reaction of azirine ring in progress and will be published in near future.

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2. K. Isomura, G. Ayabe, S.Hatano, and H. Taniguchi, *J. Chem. Soc., Chem.Comm.*, 1980, 1252.
3. a) K. Isomura , S. Taguchi, T. Tanaka and H. Taniguchi, *Chem. Lett.*, 1977, 401.
   b) K. Isomura, S. Noguchi, M. Saruwatari, S. Hatano, and H. Taniguchi, *Tetrahedron Lett.*, 1980, 21, 3879.
   c) K. Isomura, M. Saruwatari, and H. Taniguchi, *Heterocycles*, 1989, 30, 752.
4. Spectral data for 4d, 5d, and 6d.

   4d; ^{1}H-Nmr (δ in $CDCl_3$); 0.87 (3H, s), 1.02 (3H, s), 1.35 (3H, t, J=7 Hz), 1.70 (3H, d, J=1 Hz), 1.76 (2H, d, J=1 Hz), 4.28 (1H, d, J=10 Hz), 4.34 (2H, q, J=7 Hz), 5.29 (1H, br d, J=10 Hz), 6.17 (1H, d, J=10 Hz), 6.48 (1H, d, J=10 Hz). Ir (cm^{-1}, nujol mull); 1722.

   5d; ^{1}H-Nmr (δ in $CDCl_3$); 0.88 (1H, dd, J=6 and 2 Hz), 0.98 (3H, s), 1.03 (3H, s), 1.25 (3H, t, J=7 Hz), 1.51 (1H, d, J=6 Hz), 1.58 (1H, exchangeable br s), 1.81 (3H, br s), 2.62 (1H, d, J=2 Hz), 3.39 (1H, br s), 4.18 (2H, q, J=7 Hz), 4.88 (2H, m). Ir (cm^{-1}, nujol mull); 3300, 1717.

   6d; ^{1}H-Nmr (δ in $CDCl_3$); 1.25 (3H, t, J=7 Hz), 1.60 (3H, s), 1.79 (3H, s), 3.86 (1H, s), 4.20 (2H, q, J=7 Hz), 4.90 (2H, br s), 5.50 (1H, s), 6.15 (1H, d, J=6 Hz), 6.40 (1H, exchangeable br s), 6.61 (1H, d, J=6 Hz), 7.08-7.37 (5H, m).
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