SYNTHESIS OF PYRROLES, PYRIDINES, AND AZEPINES FROM 2H-AZIRINES

Masumi Saruwatari, Sumiko Hatano, Kazuaki Isomura, and Hiroshi Taniguchi

Department of Applied Chemistry, Faculty of Engineering,
Kyushu University, Hakozaki, Higashiku, Fukuoka, Japan

The controlling factor for the formation of pyrroles, pyridines, and azepines from 2H-azirines are discussed with mechanistic detail to establish new synthetic method of heterocycles.

1. Mechanism for pyridine and azepine formation: Thermal rearrangement of ethyl 2-(2-benzofuranyl)-2H-azirine carboxylate 1 having a methyl group at 3-position of the benzofuran ring gave benzofuropyridine 2. But in the cases, where the benzofuran ring had an ethyl or a 1-propyl group, thermal rearrangement gave ethyl α-amino-β-(3-alkenyl-2-benzofuranyl)acrylates 3, which gave 2 or its dihydro-derivative 4 on heating at higher temperatures. The key intermediate is elucidated to be the imine 5, which is formed by hydrogen shift from the alkyl group to the nitrogen of vinyl nitrene 6. This intermediate gives 3, if the terminal olefinic carbon has allylic hydrogen, but gives 2 by electro-cyclic reaction, if the allylic hydrogen is not present. Cyclization of 3 is also proved to proceed via 5 by deuterium-scrambling experiment. Formation of benzofurobenzazepine 7 from the azirine having a phenyl group is rationalized by electrocyclic reaction of vinyl nitrene followed by hydrogen shift.

2. Controlling factor: Thermal rearrangement of ethyl 2-(1-cyclohexenyl)- 8, and 2-(1-cyclopentenyl)-2H-azirine carboxylate 9, which had a methyl or a phenyl group at 2-position of cycloalkenyl group, were examined and compared with those of open-chain ones and 1. Both 8-Me and 9-Me gave 2H-pyrroles and pyridines. Increased yields of pyridines from these two azirines compared with open-chain one and more predominant pyridine formation from 9-Me than from 8-Me is explained by the strain energy of 2H-pyrroles imposed by their bicyclic structures. Thermal rearrangement of 8-Ph gave 2H-pyrrole as the sole product but 9-Ph gave 2H-pyrrole and azepine. These results are also explained by the same reason as above. Exclusive formation of pyridine and azepine from benzofuranyl derivatives 1 can be recognized by higher strain energy of 2H-pyrrole caused by fusing additional phenyl ring.