SYNTHESIS OF AZEPINES BY INTRAMOLECULAR AMINO-PALLADATION

Noriyuki Okada, Sumiko Hatano, Masumi Saruwatari, Kazuaki Isomura,
and Hiroshi Taniguchi
Department of Applied Chemistry, Faculty of Engineering, Kyushu University,
Hakozaki, Higashiku, Fukuoka 812, Japan

Intramolecular amino-palladation reactions of ethyl α-amino-β-(4,6-dimethyl-3-alkenylbenzofuran)acrylates 1a-d, which were obtained in the course of our investigation on thermal rearrangement of 2H-azirines, were examined to establish a new route to azepines. Reaction of 1-propenyl derivative 1a with $PdCl_2(PhCN)_2$ in acetonitrile at room temperature for 20 hr followed by filtration of Pd-black and separation by chromatography gave ethyl 1,7,9-trimethyldibenzofuran-3-carboxylate 2a and ethyl 8,10-dimethyl-1-methylene-2,3-dihydro-1H-benzofuro[2,3-d]azepine-4-carboxylate 3a. The dibenzofuran 2a was proved to be formed by the action of HCl produced in the reaction. In the presence of Na_2CO_3, 3a was obtained as the sole product. When the enamine 1b, having a vinyl group instead of 1-propenyl group, was reacted, tarry product was obtained. Its N-acetyl derivative 1b' also gave tarry product. Finally, when the product of 1b' was hydrogenated using the precipitated Pd-black as the catalyst, the expected ethyl 3-acetyl-8,10-dimethyl-2,3-dihydro-1H-benzofuro[2,3-d]azepine-4-carboxylate 3b' was obtained. By the same way, propenyl 1c' and styryl derivative 1d' also gave 2,3-dihydro-1H-benzofuroazepines 3c' and 3d'. In order to get mechanistic insight into this reaction, E- and Z-isomers of 1c' were isolated and reacted with Pd(II). When E-1c' and Z-1c' were reacted under the same conditions, precipitation of Pd-black was faster in the reaction of Z-1c' than that in E-1c'. When carbon monoxide and methanol was introduced after the reactions were performed at 0°C for 66 hr, 50.7% of E-1c' and 63.8% of Z-1c' were recovered. The azepines obtained in this reactions had methoxycarbonyl group at 1-position and had different configurations at 1-and 2-positions, which showed that amino-palladation proceeded stereospecifically. From these results, this reaction can be rationalized by cis-addition of Pd and N forming palladium σ-complex followed by cis-elimination of Pd-H. When Pd(II) was reacted with ethyl N-benzoyl-α-amino-β-(o-vinylphenyl)acrylate 4, which was easily obtained by the reaction of o-vinylbenzaldehyde with N-benzoylglycine followed by ethanolysis, ethyl 2-benzoyl-1-methyldihydroquinoline-3-carboxylate 5 was obtained as the major product with small amount of ethyl 3-benzoyl-2,3-dihydro-1H-benz[1]azepine-4-carboxylate 6. The difference between the reactions of benzofuran and benzene systems would be explained in terms of the conformation of the alkenyl group.