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COMPELLED AZEPINE RING FORMATION IN THERMAL RING EXPANSION OF 2H-AZIRINE*

Kazuaki ISOMURA, Hiroshi TAGUCHI, Tatsuyoshi TANAKA, and Hiroshi TANIGUCHI
Department of Applied Chemistry, Faculty of Engineering, Kyushu University,
Hakozaki, Higashiku, Fukuoka 812

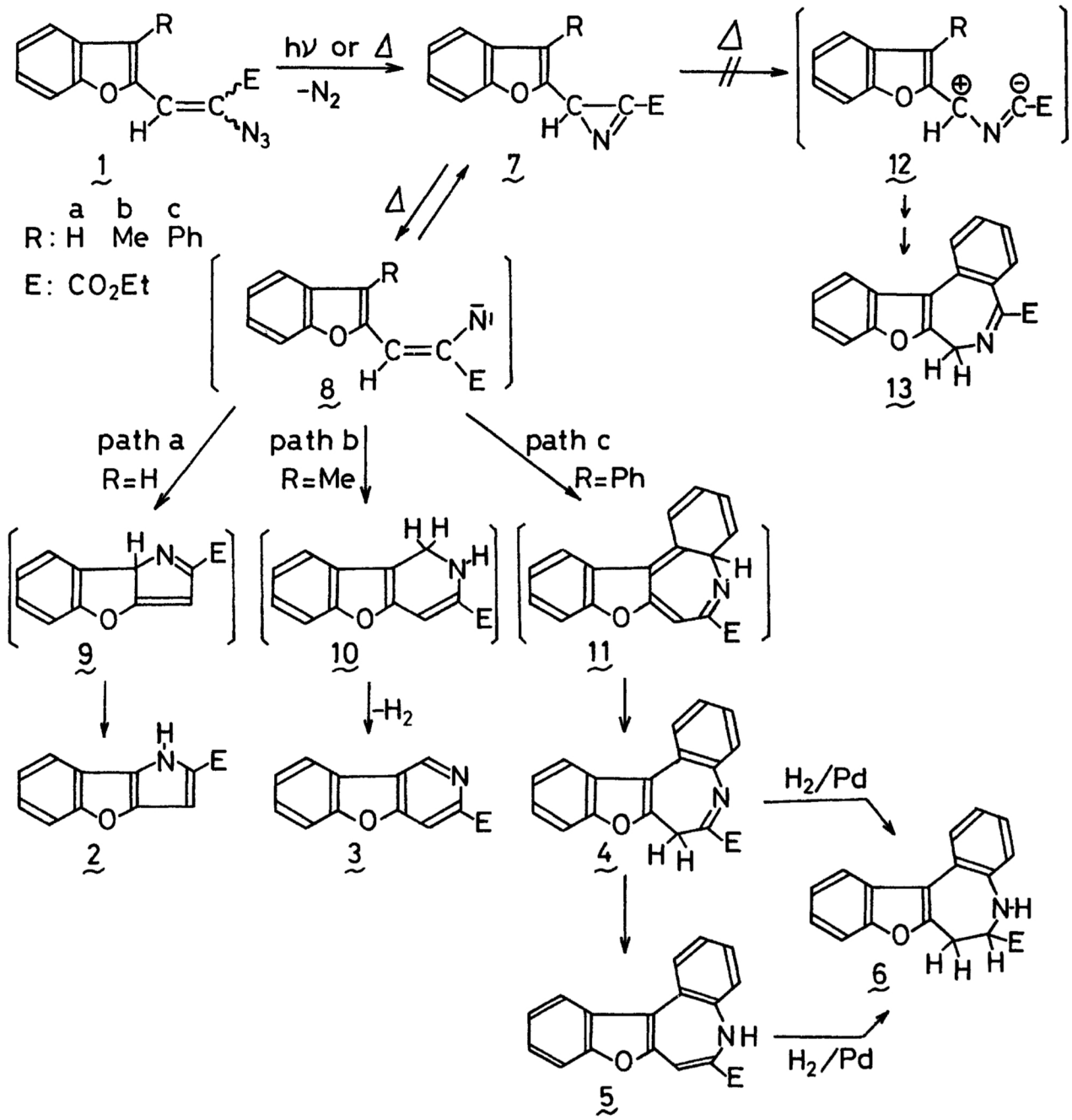
Thermolyses of three β-(benzofuran-2-yl)vinyl azides, 1a, 1b, and 1c, in which the benzofuran ring bears a hydrogen, a methyl, and a phenyl group at the 3-position, gave a benzofuropyrrole 2, a benzofuropyridine 3, and a benzofurobenzazepine 4, respectively. Photolyses of these azides gave the corresponding 2H-azirines, 7a, 7b, and 7c, which on heating afforded the same heterocyclic compounds as the products of the thermolyses of the vinyl azides.

It is well known that 2H-azirines, bearing an unsaturated group at their 2-position, undergo facile thermal rearrangement into five-membered heterocyclic compounds, i.e., indoles, pyrroles, isoxazoles, and pyrazoles.[1] Previously, we reported that 3-methyl-2-(naphth-2-yl)-2H-azirine afforded 2-methylbenz[g]indole regioselectively, and that 3-methyl-2-(1-methylnaphth-2-yl)-2H-azirine, which bears a methyl group at the selective cyclization position to form five-membered ring, gave 3-methylbenz[h]isoquinoline instead of five-membered heterocycle.[2] Other examples of six-membered ring formation were reported recently.[3] These reactions may be explained by insertion reaction of vinyl nitrene into the methyl group situated at the favorable position, followed by oxidation of the transient dihydropyridine ring. We now report the formation of seven-membered ring by thermal reaction of 2H-azirine and its precursor, i.e., vinyl azide, in which the selective cyclization position was substituted by a phenyl group.

Three ethyl α-azido-β-(benzofuran-2-yl)acrylates, 1a, 1b, and 1c, were synthesized by base catalyzed condensation of the corresponding benzofuran-2-carboxaldehyde with ethyl azidoacetate.[1e] Thermal decomposition of 1a and 1b in refluxing xylene for 2 hr gave 2-carbethoxybenzofuro[3,2-b]pyrrole 2,[4] mp 158∿159°C, and 3-carbethoxybenzofuro[3,2-c]pyridine 3,[4] mp 137.5∿138.5°C, respectively, in quantitative yield. Under the same conditions 1c gave reddish solid. Recrystallization from hexane—ethyl acetate afforded pale yellow needles 4, mp 150∿151°C, in 67% yield. In its NMR spectrum, a singlet at δ 3.82, corresponding to two protons, was observed, in addition to the signals of aromatic protons (δ 7.23∿8.23, 8H, m) and carbethoxy ethyl protons (δ 1.41, 3H, t and 4.33, 2H, q). Area ratio of the NMR spectrum indicated that one of the two protons of the singlet originated from aromatic protons. IR spectrum of 4 showed the presence of imino linkage at 1620 cm^{-1} and the absence of mono-substituted phenyl group (no absorption was observed in 685∿715 cm^{-1}). On the basis of the above

and other data,[4] the structure of 4 was assigned as 6-carbethoxy-7H-benzofuro [2,3-d][1]benzazepine. When 4 was heated in ethanol or treated with a small amount of HCl or KOH, 4 changed into red viscous oil, 5. In its NMR spectrum, the singlet of 4 was no longer observed, but two singlets, each corresponding to one proton, were observed at δ 6.03 (broad and exchangeable, N-H) and 6.70 (=CH-). Its IR spectrum showed a broad band at 3400 cm^{-1}(ν_{N-H}). From these results, 5 was assigned as 6-carbethoxy-5H-benzofuro[2,3-d][1]benzazepine, an isomer of 4.

Scheme



Catalytic hydrogenation of 4 and 5 over Pd-black afforded a same product 6, mp 106.5∿108°C, with uptake of one mole equivalent of H_2 gas. This compound was assigned as 6-carbethoxy-6,7-dihydro-5H-benzofuro[2,3-d][1]benzazepine on the basis of NMR double doublet absorptions at δ 3.35, 3.57, and 3.92 and a broad exchangeable singlet at δ 4.48 (N-H) and IR spectrum (3350 cm^{-1}, ν_{N-H}).[4)]

Photolyses of these azides 1a, 1b, and 1c, in hexane—acetone at 0°C gave labile oily products, which were assigned as the corresponding 2H-azirines, 7a, 7b, and 7c, by comparing their IR (ca. 1745 and 1720 cm^{-1}) and NMR spectra (proton at the 2-position of the azirine ring; δ 3.53, 3.56, and 3.63 for 7a, 7b, and 7c, respectively) with those of 3-carbethoxy-2-phenyl-2H-azirine.[5)] These 2H-azirines underwent smooth ring expansion into the corresponding heterocyclic compounds, 2, 3, and 4, in $CDCl_3$ at 55°C with a half life of 15, 33, and 44 min, respectively.

The course of the reactions forming three different types of the heterocyclic compounds would be depicted as shown in Scheme, where vinyl nitrenes, 8a, 8b, and 8c, are the common key intermediates. The vinyl nitrene 8a attacks the 3-position of the benzofuran ring forming pyrrolenine 9 followed by 1,5-sigmatropic hydrogen shift giving 2 (path a). When the 3-position is substituted by a methyl group, the insertion of the nitrene 8b into the C-H bond of the methyl group followed by oxidation gives 3 (path b). When the 3-position is substituted by a phenyl group, the nitrene 8c is forced to attack the ortho-position of the phenyl group followed by 1,5-sigmatropic hydrogen shift forming 4 (path c).

It was already reported that a benzazepine was formed by the photolysis of Z-3-phenyl-2-styryl-2H-azirine and its formation was interpreted by recyclization of the nitrile ylide which was formed by photochemical C-C bond fission of the azirine.[1i)] If a similar reaction path was assumed, the azepine would be 5-carbethoxy-7H-benzofuro[2,3-d][2]benzazepine 13. But our results, especially the NMR spectrum of 6, unambiguously established that 4 was formed, which can only be explained by C-N bond fission of the azirine ring. Recently, Padwa's group claimed that an azepine was formed by thermal reaction of 2-(4-carbomethoxybuta-1,3-dienyl)-3-phenyl-2H-azirine.[3a)] In the preceeding paper, we showed that the structural assignment of the Padwa's azepine was in error and that the thermal reaction of three 2-(buta-1,3-dienyl)-2H-azirines afforded 2-vinylpyrroles and evidence for azepine formation has not yet obtained. Therefore, our present result appears to provide the first example of azepine ring formation by a thermal reaction of 2H-azirine via vinyl nitrene, although the azepine formation by a photochemical path via nitrile ylide has a precedence.

References and Notes

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4 Elemental analyses (EA) and spectral data of 2, 3, 4, and 6.

2 EA Found C; 68.14, H; 4.82, N; 6.11%
Calcd. for $C_{13}H_{11}NO_3$ C; 68.11, H; 4.84, N; 6.11%
IR (nujol, cm^{-1}) 3400 vs, 1700 vs. NMR (δ in $CDCl_3$) 1.54 (3H, t J 7 Hz), 4.52 (2H, q J 7 Hz), 6.98 (1H, d J 2 Hz), 7.24∿7.94 (4H, m), 10.41 (1H, exchangeable bs). MS (m/e) 229 (M^+). UV [λ_{max} (log ε) in cyclohexane, nm] 295 (4.44), 305 (4.59), 310 (4.65), 319 (4.17).

3 EA Found C; 69.59, H; 4.65, N; 5.82%
Calcd. for $C_{14}H_{11}NO_3$ C; 69.70, H; 4.59, N; 5.80%
IR (nujol, cm^{-1}) 1700 vs. NMR (δ in $CDCl_3$) 1.50 (3H, t J 7 Hz), 4.65 (2H, q J 7 Hz), 7.21∿8.12 (4H, m), 8.21 (1H, s), 9.13 (1H, s). MS (m/e) 241 (M^+). UV [λ_{max} (log ε) in cyclohexane, nm] 219 (4.42), 257 (4.20), 277 (4.26), 283sh (4.23), 294 (4.10), 306 (4.23).

4 EA Found C; 74.70, H; 4.92, N; 4.59%
Calcd. for $C_{19}H_{15}NO_3$ C; 74.74, H; 4.95, N; 4.59%
IR (nujol, cm^{-1}) 1700 vs, 1620 m. NMR (δ in $CDCl_3$) 1.40 (3H, t J 7 Hz), 3.82 (2H, s), 4.43 (2H, q J 7 Hz), 7.23∿8.23 (8H, m). MS (m/e) 305 (M^+). UV [λ_{max} (log ε) in cyclohexane, nm] 248 (4.26), 276sh (4.00), 284 (3.92), 304 (2.63).

6 EA Found C; 74.21, H; 5.59, N; 4.65%
Calcd. for $C_{19}H_{17}NO_3$ C; 74.25, H; 5.58, N; 4.56%
IR (nujol, cm^{-1}) 3350 s, 1700 vs. NMR (δ in $CDCl_3$) 1.27 (3H, t J 7 Hz), 3.35 (1H, dd J 17 and 11 Hz), 3.57 (1H, dd J 17 and 3.5 Hz), 3.92 (1H, dd J 11 and 3.5) 4.23 (2H, q J 7 Hz), 4.88 (1H, exchangeable bs), 6.80∿8.00 (8H, m). MS (m/e) 307 (M^+).

5 Prepared by thermolysis of ethyl α-azidocinnamate[1e] in heptane under reflux for 2 hr.

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