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Novel Ring Contraction of 1,2-Diazocine System. Hydrolysis of 7-Substituted 4-Acetoxy- and 4-Phthalimido-3,8-diphenyl-1,2-diazocines Leading to the Formation of Pyrazoles#

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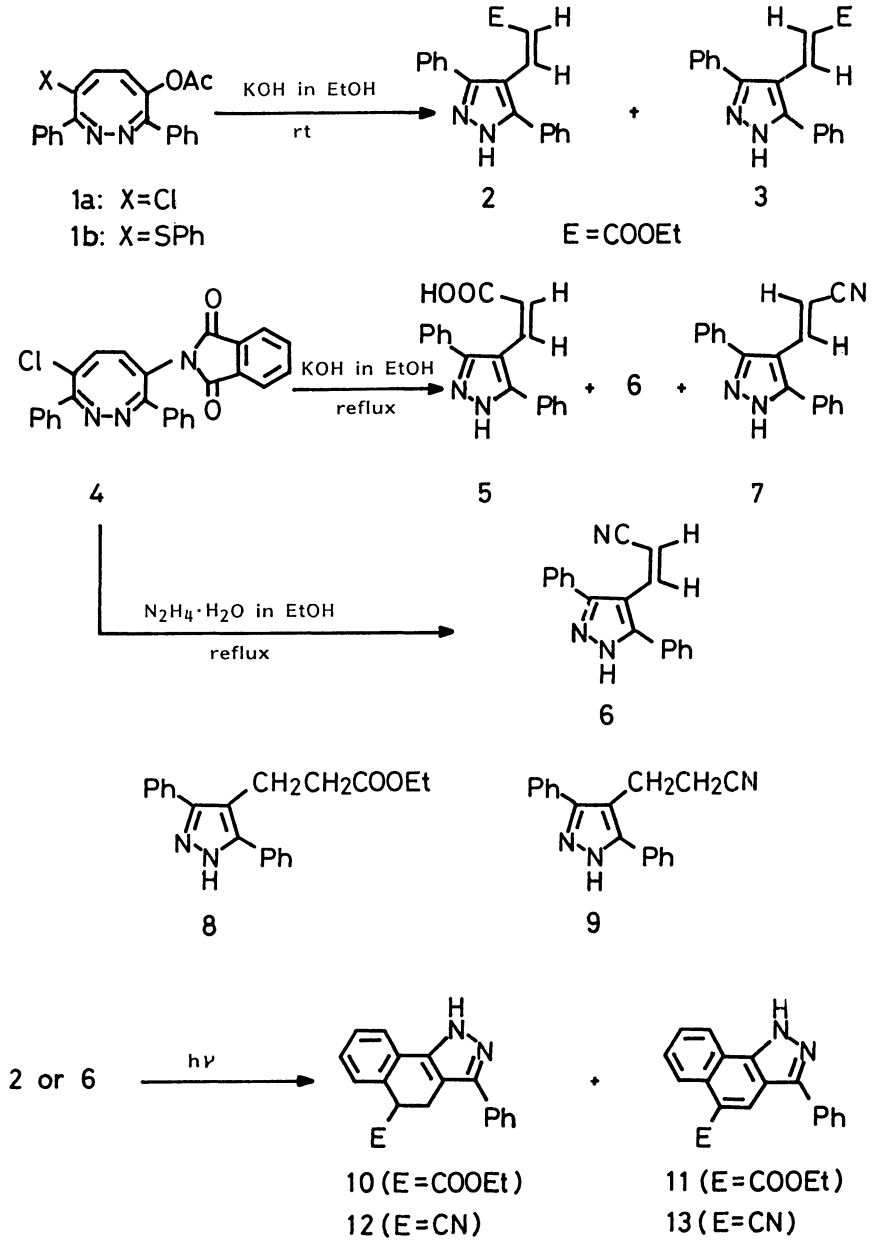
A novel ring contraction of 1,2-diazocine system to pyrazoles via [5.5]bicyclic intermediates has been demonstrated by hydrolysis of 7-substituted 4-acetoxy- and 4-phthalimido-3,8-diphenyl-1,2-diazocines.

We recently reported the synthesis of various 4,7-disubstituted 3,8-diphenyl-1,2-diazocines which are the first example for stable substituted monocyclic 1,2-diazocines.[1-4] In contrast to the parent 1,2-diazocine which decomposed slowly in solution at room temperature, and rapidly neat to benzene and pyridine with comparable rates,[5] our stable 1,2-diazocines thermally decomposed to only pyridine derivatives via their valence tautomers, diazabicyclo[4.2.0]octatrienes, providing a new route for the synthesis of various substituted pyridines which are difficult to prepare by other methods.[1-4] In this communication we describe a novel ring contraction of 7-substituted 4-acetoxy- and 4-phthalimido-3,8-diphenyl-1,2-diazocines, via [5.5]bicyclic intermediates, induced by hydrolysis of 4-substituents.

When 4-acetoxy-7-chloro-3,8-diphenyl-1,2-diazocine (1a)[1] was stirred in a 3.3% ethanolic potassium hydroxide solution at room temperature for 4 h, ethyl (Z)-β-(3,5-diphenylpyrazol-4-yl)acrylate (2) and its (E)-isomer (3) were isolated in 50 and 0.8% yields, respectively. Hydrolysis of 4-acetoxy-7-phenylthio-3,8-diphenyl-1,2-diazocine (1b)[2] under similar conditions afforded the same pyrazoles, 2 (60%) and 3 (13%), together with benzenethiol (27%). Structural elucidation of the pyrazoles, 2 and 3, was accomplished on the basis of spectral data[6] as well as of chemical conversions. The pyrazoles, 2 and 3, correspond to ring contraction products accompanied by both the hydrolysis of 4-acetoxy group and elimination of 7-substituent in 1.

7-Chloro-4-phthalimido-3,8-diphenyl-1,2-diazocine (4)[4] was less susceptible to hydrolysis under similar conditions. The 1,2-diazocine 4 was heated in an ethanolic potassium hydroxide solution under reflux for 4 h to give (Z)-β-(3,5-diphenylpyrazol-4-yl)acrylic acid (5), mp 253-254 °C, which was readily obtained by hydrolysis of 2, in 62% yield, together with small amounts of (Z)-β-(3,5-diphenylpyrazol-4-yl)-acrylonitrile (6) and its (E)-isomer (7) (each 4% yield). On treatment with hydra-

#Dedicated to Professor Teruaki Mukaiyama on the occasion of his 60th birthday.



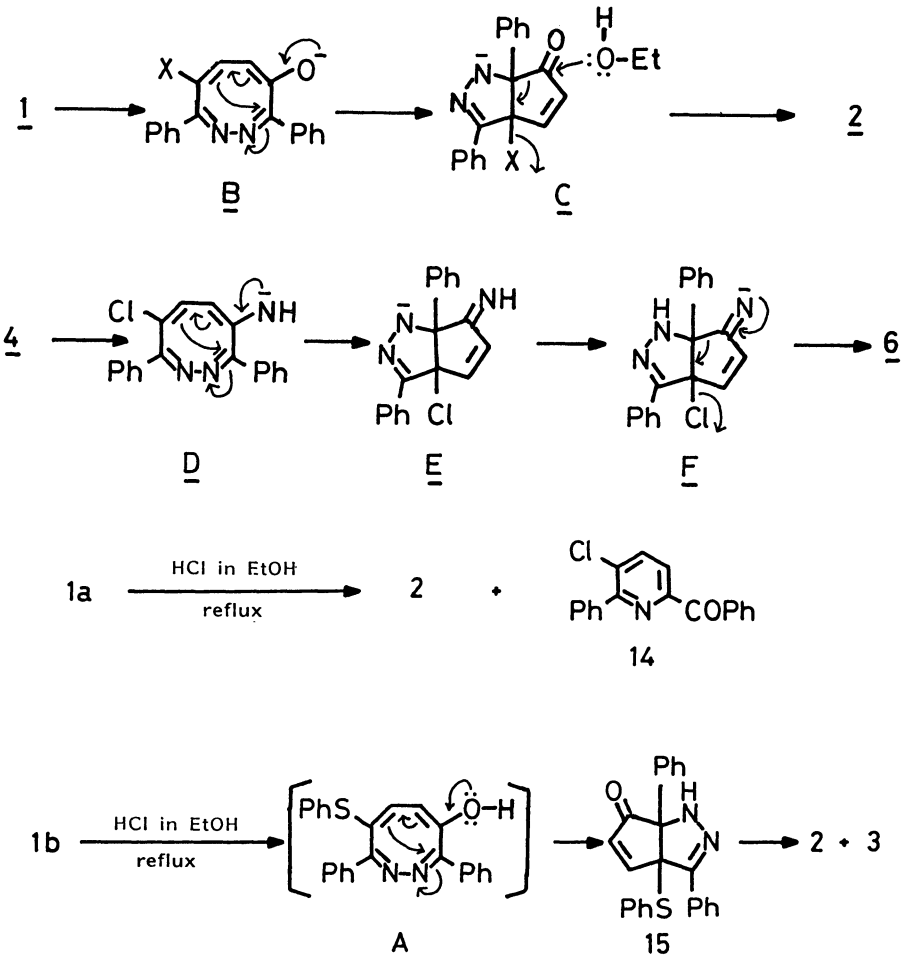
Scheme 1.

zine hydrate (3 equiv.) in refluxing ethanol for 5 h, however, 4 gave (Z)-isomer (6) in 73% yield; in this case (E)-isomer (7) was not detected. The structures of 6 (mp 226-227 °C) and 7 (mp 203-205 °C), which are similar to those of 2 and 3 respectively, were again assigned on the basis of spectral data as well as of chemical conversions.

On catalytic hydrogenations over Pd/charcoal in ethanol at room temperature, isomeric two pyrazoles, 2 and 3, or 6 and 7, gave tha same hydrogenated products, 8 or 9, in good yields, respectively.[7] Irradiation of a benzene solution of 2 with a 150W high-pressure mercury lamp afforded intramolecularly cyclized products, 5-ethoxycarbonyl-3-phenyl-4,5-dihydronaptho[1,2-c]pyrazole (10) and its aromatized compound (11), in 59 and 16% yields, respectively. Similarly, photochemical cycli-

zation of 6 gave 5-cyano analogs, 12 (73%) and 13 (4%)[8] (Scheme 1).

Next, we have investigated hydrolysis of the 1,2-diazocines (1) under acidic conditions. When 1a was treated with hydrochloric acid in ethanol under reflux for 2 h, the pyrazole 2 and 6-benzoyl-3-chloro-2-phenylpyridine (14)[1], which was derived from thermolysis of 1a, were obtained in 52 and 2% yields, respectively. On the other hand, hydrolysis of 1b under similar conditions gave a 65% yield of a new bicyclic compound, 1,4-diphenyl-5-phenylthio-2,3-diazabicyclo[3.3.0]octa-3,6-dien-6-one (15), whose structure was confirmed on the basis of spectral data.[9] On treatment with an ethanolic potassium hydroxide solution (room temp, 4 h), 15 was converted into 2 (62%) and 3 (14%). The formation of 15 can be assumed via a transannular ring contraction of intermediary hydroxydiazocine A (Scheme 2), and provides a significant information for the formation of pyrazoles in hydrolysis of diazocines 1 and 4 under basic conditions.



Scheme 2.

The pathways for the formation of pyrazoles 2 and 6 from 1 and 4 respectively are illustrated in Scheme 2. The acetoxydiazocine 1 yields a bicyclic anion C via a transannular reaction of an enolate intermediate B, and subsequent attack of ethanol on the carbonyl group in C with concurrent ring opening and elimination of X (Cl or SPh) gives 2.[10] Similarly, 4 gives 6 via a ring opening of F, which is produced

from E through D, with concurrent elimination of the chloride ion.

References

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6) All the new compounds reported herein gave satisfactory elemental analyses. 2: Mp 170-171 °C; colorless needles; IR (KBr) 3200, 2900-3100, 1720, 1700, 1630, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.89 (3H, t), 3.54 (2H, q), 5.90, 6.91 (each 1H, d, =CH, J=12.0 Hz), 7.1-7.6 (10H, m), 9.10 (1H, broad s, NH); ^{13}C NMR ($CDCl_3$) δ= 13.88 (q), 60.00 (t), 111.59 (s, ring 4-C), 122.48 (d, =CH-COOEt), 127.77, 128.36, 128.83 (each d), 131.89 (s), 134.25 (d, CH=CH-COOEt), 147.24 (s, ring 3-, 5-C), 166.06 (s, C=O); MS m/z 318 (M^+). 3: Mp 160-161 °C; colorless needles; IR (KBr) 3200, 2800-3050, 1705, 1690, 1630, 955, 860, 600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.20 (3H, t), 4.12 (2H, q), 5.85, 7.65 (each 1H, d, =CH, J=16.0 Hz), 6.74 (1H, broad s, NH), 7.30-7.57 (10H, m); ^{13}C NMR (CD_3CN) δ=14.30 (q), 60.30 (t), 111.77 (s, ring 4-C), 117.66 (d, =CH-COOEt), 129.13 (d), 131.42 (s), 135.83 (d, CH=CH-COOEt), 148.77 (s, ring 3-, 5-C), 167.71 (s, C=O); MS m/z 318 (M^+).
7) 8: Mp 153-154 °C; colorless needles; IR (KBr) 3200, 1725, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.31 (3H, t), 2.15-2.5, 2.9-3.3 (each 2H, m), 3.95 (2H, q), 7.2-7.7 (10H, m), 7.9 (1H, broad s, NH); MS m/z 320 (M^+). 9: Mp 186-187 °C; colorless needles; IR (KBr) 2208 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.1-2.5, 2.9-3.3 (each 2H, m), 7.3-7.8 (11H, m, ArH and NH); MS m/z 273 (M^+).
8) 10: Mp 172-173 °C; colorless needles; IR (KBr) 3200, 1700 cm^{-1}; ^1H NMR ($CDCl_3$-DMSO-d_6) δ=1.10 (3H, t), 4.00 (2H, q), 3.0-3.5 (2H, m), 3.9-4.1 (1H, m), 7.1-8.0 (9H, m), 9.0 (1H, broad s, NH); MS m/z 318 (M^+). 11: Mp 204-206 °C; colorless needles; IR (KBr) 3300, 1680 cm^{-1}; ^1H NMR ($CDCl_3$-DMSO-d_6) δ=1.45 (3H, t), 3.2-3.8 (1H, broad, NH), 4.45 (2H, q), 7.3-7.8 (5H, m), 7.8-8.05 (2H, m), 8.4-8.6 (1H, m), 8.68 (1H, s), 8.8-9.05 (1H, m); MS m/z 316 (M^+). 12: Mp 210-211 °C; colorless needles; IR (KBr) 2800-3300, 2240 cm^{-1}; ^1H NMR ($CDCl_3$-DMSO-d_6) δ=3.0-3.4 (2H, q), 3.7-4.2 (1H, m), 7.1-7.9 (10H, m, ArH and NH); MS m/z 271 (M^+). 13: Mp 289-291 °C; colorless needles; IR (KBr) 2800-3200, 2220 cm^{-1}; MS m/z 269 (M^+).
9) 15: Mp 174-175 °C; yellow prisms; IR (KBr) 3300, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ= 6.63, 8.14 (each 1H, d, =CH, J=6.0 Hz), 6.7-7.2 (6H, m, ArH and NH), 7.2-7.5 (8H, m), 7.9-8.2 (2H, m); ^{13}C NMR (CD_3CN-DMSO-d_6) δ=74.30 (s, 1-C), 82.12 (s, 5-C), 126.18, 128.01, 128.30, 128.54, 130.18 (each d), 131.54 (s), 133.30 (d, 7-C), 136.42 (d), 146.30 (s, 4-C), 165.79 (d, 6-C), 206.77 (s, C=O); MS m/z 273 (M^+ - PhS, 100%).
10) The (E)-isomer 3 was assumed to be formed via a reverse Michael reaction of (Z)-isomer 2 with a leaving anion.

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