

Yoshihisa Kurasawa*, Ho Sik Kim [1], Tae Kawano,

Ritsuko Katoh and Atsushi Takada

School of Pharmaceutical Sciences, Kitasato University,
Shirokane, Minato-ku, Tokyo 108, Japan

Yoshihisa Okamoto

Division of Chemistry, College of Liberal Arts and Sciences, Kitasato University,
Kitasato, Sagami-hara, Kanagawa 228, Japan

Received August 10, 1990

The reaction of the 1,2-diazepino[3,4-*b*]quinoxalines **2a,b** or **3a,b** with *N*-bromosuccinimide/water resulted in ring transformation to give the 1,4-dihydro-4-oxopyridazino[3,4-*b*]quinoxalines **4a,b**, respectively.

J. Heterocyclic Chem., **28**, 199 (1991).

In a previous paper [2], we reported that the reaction of the hydrazones **1a,b** with 2-chloroacrylonitrile resulted in the 1,3-dipolar cycloaddition reaction to give the 5-cyano-4-hydroxy-1,2-diazepino[3,4-*b*]quinoxaline hydrochlorides **2a,b**, which were converted into the 5-(2-hydroxyethoxy)-4-oxo-1,2-diazepino[3,4-*b*]quinoxalines **3a,b**, respectively. On the other hand, some 1,2-diazepines have been reported so far to undergo the interesting ring transformations into a furan [3], pyrroles [4,5], pyridines [5-7] and pyridazines [8-11]. Moreover, cyclohexane or benzene ring fused 1,2-diazepines have also been transformed into a quinoxaline [12] or isoquinolines [13-16], respectively. Thus, our quinoxaline ring condensed 1,2-diazepines **2a,b** or **3a,b** were expected to be converted into quinoxaline condensed furans, pyrroles, pyridines or pyridazines. Accordingly, we further studied the ring transformation of the 1,2-diazepino[3,4-*b*]quinoxalines **2a,b,3a,b**, and found that the oxidative ring transformation of **2a,b** or **3a,b** with *N*-bromosuccinimide/water conveniently produced the 1,4-dihydro-4-oxopyridazino[3,4-*b*]quinoxalines **4a,b**, respectively. This paper describes the above oxidative ring transformation together with the reaction mechanism.

The reaction of the 5-cyano-4-hydroxy-1,2-diazepino[3,4-*b*]quinoxaline hydrochlorides **2a,b** with *N*-bromosuc-

cinimide/water gave 7-chloro-3-(*p*-chlorophenyl)-1-methyl-4-oxo-1,4-dihydropyridazino[3,4-*b*]quinoxaline **4a** and 3-(*p*-bromophenyl)-7-chloro-1-methyl-4-oxo-1,4-dihydropyridazino[3,4-*b*]quinoxaline **4b**, respectively, both in 74% yield. A similar reaction of the 5-(2-hydroxyethoxy)-4-oxo-1,2-diazepino[3,4-*b*]quinoxalines **3a,b** also afforded compounds **4a,b** in 19% and 21% yields, respectively. The postulated reaction mechanism is shown in Scheme 2. The oxidation at the N₂- and C₃-positions and the hydrolytic elimination of the cyano and 2-hydroxyethoxyl groups [2] in **2a,b** and **3a,b** would provide an intermediate **A**, which would change into **4a,b** via intermediates **B-E**.

The ¹³C-nmr spectra of **4a,b** showed the carbonyl carbon signals at δ 164.94 and 165.02 ppm, respectively, and the ir spectra of **4a,b** exhibited the carbonyl absorption bands both at 1635 cm⁻¹. However, the carbonyl groups of **4a,b** were not reactive to an active methylene compound. Namely, the reaction of **4a,b** with malononitrile in the presence of a base recovered the starting materials presumably due to the electrostatic repulsion at the C₄-carbon influenced by the electron donating N₁-methyl moiety.

In conclusion, the present investigation provides a new type of ring transformation of condensed 1,2-diazepines into condensed pyridazines.

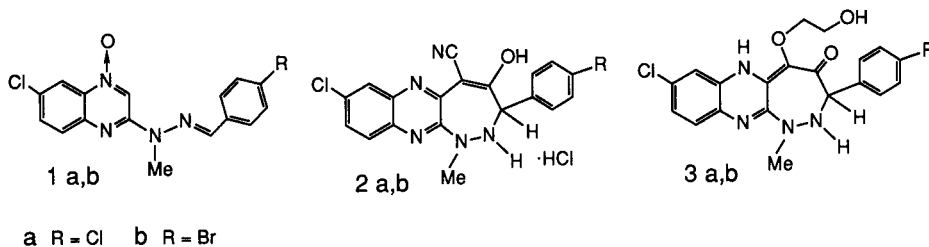
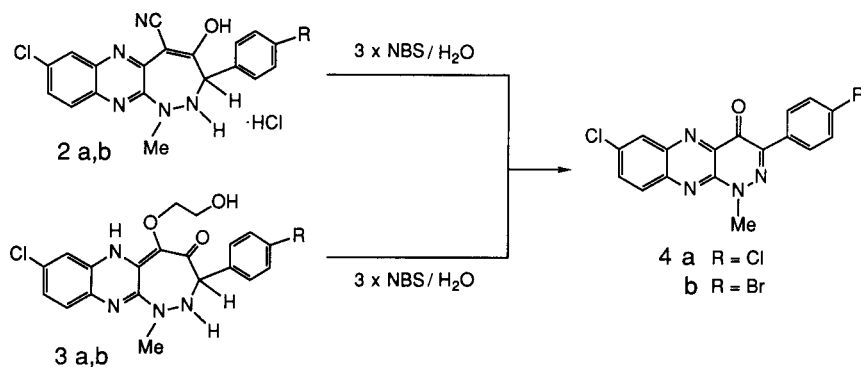
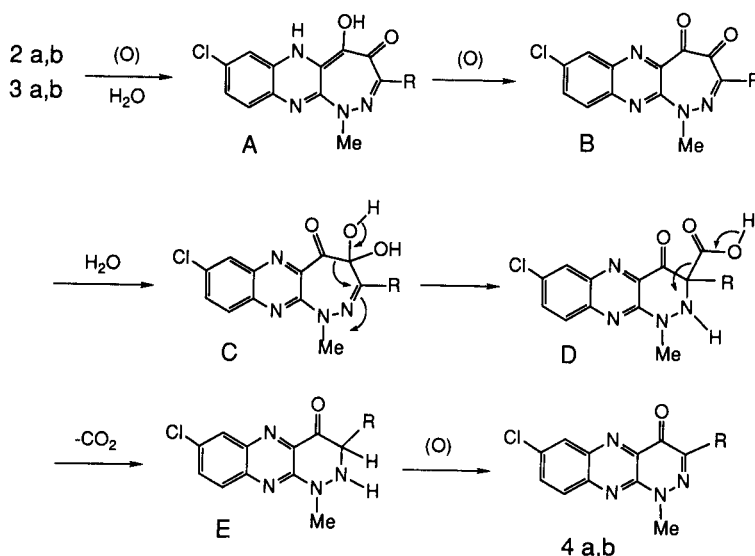


Chart 1



Scheme 1



Scheme 2

EXPERIMENTAL

All melting points were determined on a Yazawa micro melting point BY-2 apparatus and are uncorrected. The ir spectra (potassium bromide) were recorded with a JASCO IRA-1 spectrophotometer. The nmr spectra were measured in deuteriotrifluoroacetic acid with a VXR-300 spectrometer at 300 MHz. Chemical shifts are given in the δ scale. The mass spectra (ms) were determined with a JEOL JMS-01S spectrometer. Elemental analyses were performed on a Perkin-Elmer 240B instrument.

7-Chloro-3-(*p*-chlorophenyl)-1-methyl-4-oxo-1,4-dihydropyridazino[3,4-*b*]quinoxaline **4a** and 3-(*p*-Bromophenyl)-7-chloro-1-methyl-4-oxo-1,4-dihydropyridazino[3,4-*b*]quinoxaline **4b**.

From compounds **2a,b**.

A suspension of **2a** (5 g, 11.5 mmoles) and *N*-bromosuccinimide (6.15 g, 34.5 mmoles) in dioxane (200 ml)/water (100 ml) was heated on a boiling water bath for 2 hours to precipitate yellow needles **4a**, which were collected by suction filtration (3.07 g, 74%).

Compound **4b** (yellow needles, 1.23 g, 74%) was obtained by a similar manner to the above from the reaction of **2b** (2 g, 4.18 mmoles) with *N*-bromosuccinimide (2.23 g, 12.5 mmoles) in dioxane (100 ml)/water (50 ml).

From compounds **3a,b**.

A solution of **3a** (3 g, 6.92 mmoles) and *N*-bromosuccinimide (3.08 g, 17.3 mmoles) in dioxane (120 ml)/water (80 ml) was heated on a boiling water bath for 4 hours to precipitate yellow needles **4a**, which were collected by suction filtration (0.46 g, 19%).

Compound **4b** (0.52 g, 21%) was obtained by a similar manner to the above from the reaction of **3b** (3 g, 6.28 mmoles) with *N*-bromosuccinimide (2.79 g, 15.7 mmoles) in dioxane (120 ml)/water (80 ml).

Compound **4a** was recrystallized from *N,N*-dimethylformamide/ethanol to give yellow needles, mp above 310°; ir: ν cm⁻¹ 1635; ms: m/z 356 (M⁺), 358 (M⁺ + 2); pmr: 8.29 (d, J = 2.0 Hz, 1H, C₆-H), 8.22 (d, J = 9.5 Hz, 1H, C₉-H), 8.03 (dd, J = 2.0 Hz, J = 9.5 Hz, 1H, C₈-H), 7.89 (d, J = 8.5 Hz, 2H, aromatic), 7.25 (d, J = 8.5 Hz, 2H, aromatic), 4.53 (s, 3H, CH₃).

Anal. Calcd. for C₁₇H₁₀Cl₂N₄O: C, 57.16; H, 2.82; Cl, 19.85; N, 15.69. Found: C, 56.92; H, 2.79; Cl, 19.99; N, 15.67.

Compound **4b** was recrystallized from *N,N*-dimethylformamide/ethanol to give yellow needles, mp above 310°; ir: ν cm⁻¹ 1635; ms: m/z 400 (M⁺), 402 (M⁺ + 2); pmr: 8.29 (d, J = 2.0 Hz, 1H, C₆-H), 8.21 (d, J = 9.5 Hz, 1H, C₉-H), 8.02 (dd, J = 2.0 Hz, J = 9.5 Hz, 1H, C₉-H), 7.80 (d, J = 8.5 Hz, 2H, aromatic), 7.37 (d, J = 8.5 Hz, 2H, aromatic), 4.53 (s, 3H, CH₃).

Anal. Calcd. for C₁₇H₁₀BrClN₄O: C, 50.89; H, 2.51; N, 13.96. Found: C, 50.59; H, 2.46; N, 13.99.

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