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단 신

N, *N'*-디히드로디아진디온의 *N*-아미노화

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N-Amination of *N*, *N'*-Dihydrodiazinediones

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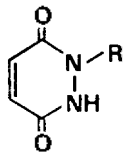
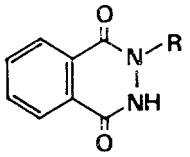
Hydroxylamine-*O*-sulfonic acid (HSA) has proved to be a reagent of great synthetic versatility because of the ability of the nitrogen center to act as either a nucleophile or electrophile. Probably so far the most well known reaction of HSA is amination on nitrogen although a significant number of aminations on both carbon and sulfur have been reported. Hydrazines can be prepared by treatment of amines with HSA under basic conditions.[1-4] Many nitrogen heterocycles can be aminated on nitrogen using HSA.[3-14] However, amination on hydrazo group has not been reported.

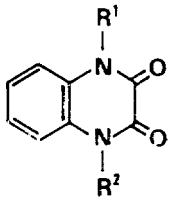
In connection with the syntheses of nitrogen heterocycles, we needed *N*-amino-*N*, *N'*-dihydrodiazinediones as the key compounds. This paper describes *N*-amination of *N*, *N'*-dihydrodiazinediones. We have previously reported[15] that the reaction of 1, 2-dihydro-3, 6-pyridazinedione(**1**) with HSA in aqueous solution containing potassium carbonate gave 1-amino-1, 2-dihydro-3, 6-pyridazinedione(**2**) in 23% yield, The yield of **2** could be improved in 60% by replacing potassium carbonate with sodium hydroxide as a base. Compound **1** was reacted with HSA in aqueous solution in the presence of a large excess of sodium hydroxide. The reaction mixture was adjusted to pH 3~4 with acetic acid to give a 37% yield of **2**. The filtrate was treated with benzaldehyde to give 1-benzylidenamino-1, 2-dihydro-3, 6-pyridazine-





1. R=H
2. R=NH_2
3. R=N=CHC_6H_5

4. R=H
5. R=NH_2
6. R=N=CHC_6H_5



7. R^1=R^2=H
8. R^1=R^2=NH_2
9. R^1=H, R^2=NH_2

dione(**3**), followed by hydrolysis with acetic acid to yield 23% of **2**.

2, 3-Dihydro-1, 4-phthalazinedione(**4**) was aminated following the same procedure except that sodium hydroxide was replaced by potassium hydroxide to increase its solubility in the reaction media. Although treating the filtrate with benzaldehyde gave 2-benzylidenamino-2, 3-dihydro-1, 4-phthalazinedione(**6**), hydrolyzing it to recover more 2, 3-dihydro-1, 4-phthalazinedione(**5**) was failed. 1, 4-Dihydro-2, 3-quinoxalinedione(**7**) was aminated as in the case of **4** to give a mixture of 1, 4-diamino-1, 4-dihydro-2, 3-quinoxalinedione(**8**) and 1-amino-1, 4-dihydro-2, 3-quinoxalinedione(**9**), which were separated by column chromatography on basic alumina using methanol as an eluent.

EXPERIMENTAL

1, 2-Dihydro-3, 6-pyridazinedione,[16] 2, 3-dihydro-1, 4-phthalazinedione,[17] 1, 4-dihydro-2, 3-quinoxalinedione[18] and HSA[19] were prepared by the literature methods. Water was redistilled from potassium permanganate.

Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian EM-360 spectrometer, and the data were given in δ units downfield from TMS. IR spectra were obtained with Perkin Elmer Model 283 infrared spectrophotometer. Elemental analyses were performed by the Lucky Central Research Institute.

***N*-Amination of 1, 2-Dihydro-3, 6-pyridazinedione(1).** To 150 m*l* of 1.5*M* sodium hydro xide solution was added 5g (44.6mmol) of 1, 2-dihydro-3, 6-pyridazinedione, and the mixture was heated to 60°C with stirring. A solution of 10g(223 mmol) of HSA in 50m*l* of water was added slowly at 60-70°C. It was cooled to room temperature and stirred for 30 min. Acetic acid was added to pH 3-4, and the solution was allowed to sit at room temperature overnight. The solid formed was filtered and recrystallized from water to give 2.1g of **2**. To the filtrate was added 2 m*l* of benzaldehyde with stirring to give 1-benzylidenamino-1, 2-dihydro-3, 6-pyridazinedione. It was filtered, washed with water and then with ether, and dissolved in a solution of 200m*l* of water and 10 m*l* of methanol by heating. Five to six drops of acetic acid was added, and the solution was refluxed for 30 min. After distilling off benzaldehyde the soulution was cooled to room temperature. The precipitated solid was filtered and recrystallized from water to give 1.3g of **2**. The total yield was 3.9g(59.6%).

***N*-Amination of 2, 3-Dihydro-1, 4-phthalazinedione(4).** To 20 m*l* of 13.4*M* potassium hydroxide solution heated nearly to boiling was dissolved 5.2g (32mmol) of 2, 3-dihydro-1, 4-phthalazinedione with stirring. A solution of 7.2g(54 mmol) of HSA in 20 m*l* of water was added slowly, and the mixture was refluxed for 2 hrs. It was cooled to room temperature and adjusted to pH 5 with acetic acid. The precipitated solid was filtered, washed with small amount of water, and recrystallized from methanol to give 2.6g (45.7%) of **5**; mp 195° C(dec); NMR(DMSO-d_6) δ 4.0 (s, 0.9H, CONH), 6.2(s, 2H, NH_2), 7.9 and 8.2 (m, 4H, C_6H_4), 11.3(s, 0.1H, enolic OH); IR 3280, 3140, 3000, 1640, 1570, 1550, 1500, 1420, 740cm^{-1}. *Anal.* Calcd for $C_8H_7O_2N_3$: C, 54.23; H, 3.99; *N*, 23.72. Found: C, 53.91; H, 4.23; N, 23.29.

***N*-Amination of 1, 4-Dihydro-2, 3-quinoxalinedione(7).** To 30m*l* of 3*M* potassium hydroxide solution heated to 60°C was dissolved 3g (18mmol) of 1, 4-dihydro-2, 3-quinoxalinedione with stirring. A solution of 4.0g (36mmol) of HSA in 10m*l* of water was added slowly, and

the mixture was stirred for 1 hr. at 60°C. It was cooled to room temperature and adjusted to pH 5 with acetic acid. The precipitated solid was filtered, washed with water, and chromatographed on basic alumina (2×11cm). Elution with methanol(400 m*l*) gave an brilliant brown powder, which was recrystallized from methanol to give 0.7g(20%) of 8. Continuous elution with methanol (1.5l) gave colorless power, which was recrystallized from methanol to give 2.4g(73%) of **9**.

1, 4-Diamino-1, 4-dihydro-2, 3-quinoxalinedione(8). mp 215°C (dec); NMR(DMOS-d_6) δ 5.9(s, 4H, NH_2), 7.3 and 7.8(m, 4H, C_6H_4); IR 3300, 3180, 1660, 1600, 1500, 1430, 760 cm^{-1}. *Anal.* Calcd for $C_8H_8O_2N_4$: C, 49.99; H, 4.20; N, 29.16; Found: C, 49.66; H, 4.37; N, 29.79.

1-Amino-1, 4-dihydro-2, 3-quinoxalinedione (9). mp 228°C(sub); NMR(DMSO-d_6) δ 6.0 (s, 2H, NH_2), 7.4 and 7.6(m, 4H, C_6H_4), 12.1 (s, 1H, enolic OH); IR 3300, 3150, 1660, 1600, 1500, 760cm^{-1}. *Anal.* Calcd for $C_8H_7O_2N_3$: C, 54.23; H, 3.99; N, 23.72. Found: C, 54.50; H, 3.89; N, 23.80.

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