A New Type of Deoxygenation of Quinoxaline *N*-Oxides

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The reaction of 6-chloro-2-[2-(*p*-chlorobenzylidene)-1-methylhydrazino]quinoxaline 4-oxide **3a** or 2-[2-(*p*-bromobenzylidene)-1-methylhydrazino]-6-chloroquinoxaline 4-oxide **3b** with dimethyl acetylenedicarboxylate under reflux in *N*,*N*-dimethylformamide resulted in deoxygenation to give 6-chloro-2-[2-(*p*-chlorobenzylidene)-1-methylhydrazino]quinoxaline **4a** or 2-[2-(*p*-bromobenzilidene)-1-methylhydrazino]-6-chloroquinoxaline **4b**, respectively, while the reaction of compound **3a** or **3b** with dimethyl acetylenedicarboxylate under reflux in dioxane precipitated dimethyl 8-chloro-4-[2-(*p*-chlorobenzyli-dene)-1-methylhydrazino]-3a*H*-isoxazolo[2,3-*a*]quinoxaline-2,3-dicarboxylate **6a** or dimethyl 4-[2-(*p*-bromobenzylidene)-1-methylhydrazino]-8-chloro-3a*H*-isoxazolo[2,3-*a*]quinoxaline-2,3-dicarboxylate **6b**, respectively. Further refluxing of compound **6a** or **6b** in *N*,*N*-dimethylformamide provided compound **4a** or **4b**, respectively.

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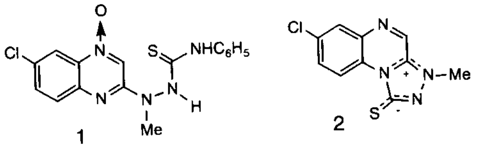
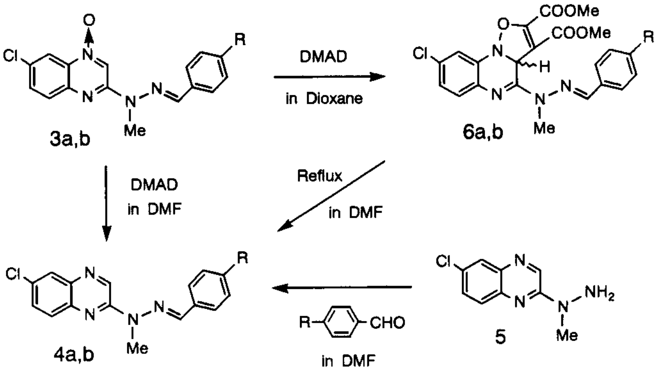
Many papers have been reported concerning the methods for the deoxygenation of heterocyclic *N*-oxides [1], which include the reduction with complex hydrides such as lithium aluminum hydride (1), catalytic hydrogenation (2), deoxygenation with phosphorus compounds, sulphur compounds, amines, hydrogen halides, carbenes, or acyl compounds (3), electrolytic or polarographic reduction (4), thermal and oxidative reduction (5) and photochemical deoxygenation (6). Recently, we have reported the deoxygenative cyclization of the quinoxaline 4-oxide **1** into the mesoionic triazolo[4,3-*a*]quinoxaline **2** (Chart 1) [2], which was involved in the above deoxygenation category (3). In the present investigation, we found an exceptional deoxygenation of quinoxaline *N*-oxides *via* the 1,3-dipolar cycloaddition reaction. Namely, the reaction of the quinoxaline 4-oxides **3a,b** [3] with dimethyl acetylenedicarboxylate under reflux in *N*,*N*-dimethylformamide afforded the deoxygenated compounds **4a,b** which were also formed from the isoxazolo[2,3-*a*]quinoxalines **6a,b** under reflux in *N*,*N*-dimethylformamide (Scheme). This paper describes a new type of deoxygenation different from the above categories (1-6).

Chart 1



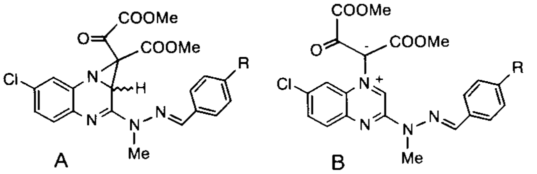
Scheme



a R = Cl, b R = Br DMAD : Dimethyl Acetylenedicarboxylate

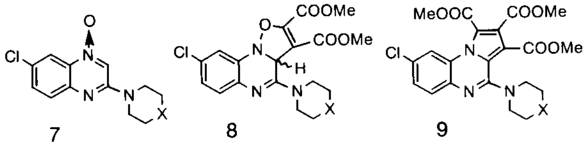
The reaction of 6-chloro-2-[2-(*p*-chlorobenzylidene)-1-methylhydrazino]quinoxaline 4-oxide **3a** or 2-[2-(*p*-bromobenzylidene)-1-methylhydrazino]-6-chloroquinoxaline 4-oxide **3b** with dimethyl acetylenedicarboxylate under reflux in *N*,*N*-dimethylformamide gave 6-chloro-2-[2-(*p*-chlorobenzylidene)-1-methylhydrazino]quinoxaline **4a** (22%) or 2-[2-(*p*-bromobenzylidene)-1-methylhydrazino]-6-chloroquinoxaline **4b** (30%), respectively, whose structure was confirmed by an alternate synthesis from the reaction of 6-chloro-2-(1-methylhydrazino)quinoxaline **5** [2] with *p*-chlorobenzaldehyde or *p*-bromobenzaldehyde, respectively. On the other hand, the reaction of compound **3a** or **3b** with an equimolar amount of dimethyl acetylenedicarboxylate under reflux in dioxane precipitated dimethyl 8-chloro-4-[2-(*p*-chlorobenzylidene)-1-methylhydrazino]-3a*H*-isoxazolo[2,3-*a*]quinoxaline-2,3-dicarboxylate **6a** (96%) or dimethyl 4-[2-(*p*-bromobenzylidene)-1-methylhydrazino]-8-chloro-3a*H*-isoxazolo[2,3-*a*]quinoxaline-2,3-dicarboxylate **6b** (99%), respectively. Further refluxing of compound **6a** or **6b** in *N,N*-dimethylformamide afforded compound **4a** (16%) or **4b** (17%), respectively. Since refluxing of compound **3a** or **3b** in *N,N*-dimethylformamide did not give compound **4a** or **4b**, but recovered the starting material, dimethyl acetylenedicarboxylate was found to be indispensable for the deoxygenation of compounds **3a,b**. Thus, the above results suggested that the deoxygenation of compounds **3a,b** proceeded *via* the isoxazolo[2,3-*a*]quinoxalines **6a,b**, aziridinoquinoxalines **A** [4] and then N$_4$-ylides **B** [4] (Chart 2).

Chart 2



Our previous paper [5] clarified that the reaction of the quinoxaline 4-oxides **7** with dimethyl acetylenedicarboxylate under reflux in dioxane effected the 1,3-dipolar cycloaddition reaction to furnish the isoxazolo[2,3-*a*]quinoxalines **8** (96-98%), whose reaction with another dimethyl acetylenedicarboxylate under reflux in dioxane resulted in the ring transformation to provide the pyrrolo[1,2-*a*]quinoxalines **9** (20-30%) (Chart 3). In contrast, the present investigation showed that the reaction of the quinoxaline 4-oxides **3a,b** with dimethyl acetylenedicarboxylate afforded the deoxygenated compounds **4a,b** presumably *via* the isoxazolo[2,3-*a*]quinoxalines **6a,b**. Moreover, this deoxygenation route was different from that of the previous work [2], which synthesized the mesoionic triazolo[4,3-*a*]quinoxalines **2** from the quinoxaline 4-oxide **1** using triphenyl phosphine or phenyl isothiocyanate as a deoxidizing agent.

Chart 3



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 ^{1}H nmr spectra of **4a,b** and **6a,b** were measured in deuteriotrifluoroacetic acid and deuteriochloroform, respectively, with 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.

6-Chloro-2-[2-(*p*-chlorobenzylidene)-1-methylhydrazino]quinoxaline **4a**.

From compound **5**.

A solution of compound **5** (2 g, 9.59 mmoles) and *p*-chlorobenzaldehyde (2.02 g, 14.4 mmoles) in *N,N*-dimethylformamide (50 ml) was refluxed in an oil bath for 2 hours to give a clear solution. The solution was allowed to stand overnight at room temperature to precipitate yellow needles **4a**, which were collected by suction filtration and then washed with ethanol to afford an analytically pure sample (2.89 g, 91%).

From compound **6a**.

A solution of **6a** (1 g, 2.04 mmoles) in *N,N*-dimethylformamide (40 ml) was refluxed in an oil bath for 2 hours to give a clear solution. Evaporation of the solvent *in vacuo* afforded an oily residue, which was dissolved in hot ethanol and then allowed to stand overnight at room temperature to furnish yellow needles **4a** (110 mg, 16%).

From compound **3a**.

A solution of compound **3a** (2 g, 5.78 mmoles) and dimethyl acetylenedicarboxylate (990 mg, 6.94 mmoles) in *N,N*-dimethylformamide (40 ml) was refluxed in an oil bath for 2 hours to give a clear solution. The solution was allowed to stand overnight at room temperature to precipitate yellow needles **4a**, which were collected by suction filtration and then washed with ethanol (420 mg, 22%).

Compound **4a** had mp 244-246°; ir: ν 1590, 1570, 1540 cm^{-1}; ms: m/z 330 (M$^+$), 332 (M$^+$+2); pmr: 9.00 (s, 1H, C$_3$-H), 8.12 (s, 1H, hydrazone CH), 7.81 (s, 1H, C$_5$-H), 7.54 (s, 2H, C$_7$-H and C$_8$-H), 7.43 (d, J = 8.0 Hz, 2H, aromatic), 7.10 (d, J = 8.0 Hz, 2H, aromatic), 3.65 (s, 3H, NCH$_3$).

Anal. Calcd. for $C_{16}H_{12}Cl_2N_4$: C, 58.02; H, 3.65; Cl, 21.41; N, 16.92. Found: C, 57.95; H, 3.63; Cl, 21.47; N, 16.88.

2-[2-(*p*-Bromobenzylidene)-1-methylhydrazino]-6-chloroquinoxaline **4b**.

From compound **5**.

A solution of compound **5** (3 g, 14.4 mmoles) and *p*-bromobenzaldehyde (4.0 g, 21.6 mmoles) in *N,N*-dimethylformamide (50 ml) was refluxed in an oil bath for 2 hours to give a clear solution. The solution was allowed to stand overnight at room temperature to precipitate yellow needles **4b**, which were collected by suction filtration and then washed with ethanol to provide an analytically pure sample (4.70 g, 87%).

From compound **6b**.

A solution of compound **6b** (5 g, 9.37 mmoles) in *N,N*-dimethylformamide (200 ml) was refluxed in an oil bath for 10 hours to give a clear solution. Evaporation of the solvent *in vacuo* afforded an oily product, which was dissolved in hot ethanol and then allowed to stand at room temperature to provide yellow needles **4b** (606 mg, 17%).

From compound **3b**.

A solution of compound **3b** (2 g, 5.11 mmoles) and dimethyl acetylenedicarboxylate (870 mg, 6.13 mmoles) in *N*,*N*-dimethylformamide (40 ml) was refluxed in an oil bath for 2 hours to precipitate yellow needles **4b**, which were collected by suction filtration and then washed with ethanol (570 mg, 30%).

Compound **4b** had mp 257-259°; ir: ν 1595, 1590, 1575, 1565, 1540 cm^{-1}; ms: m/z 375 (M^+) 377 ($M^+ + 2$); pmr: 9.06 (s, 1H, C_3-H), 8.16 (s, 1H, hydrazone CH), 7.87 (s, 1H, C_5-H), 7.59 (s, 2H, C_7-H and C_8-H), 7.41 (d, J = 8.0 Hz, 2H, aromatic), 7.32 (d, J = 8.0 Hz, 2H, aromatic), 3.70 (s, 3H, NCH_3).

Anal. Calcd. for $C_{16}H_{12}BrClN_4$: C, 51.16; H, 3.22; N, 14.91. Found: C, 51.18; H, 3.22; N, 14.99.

Dimethyl 8-Chloro-4-[2-(*p*-chlorobenzylidene)-1-methylhydrazino]-3a*H*-isoxazolo[2,3-*a*]quinoxaline-2,3-dicarboxylate **6a**.

A solution of compound **3a** (10 g, 28.8 mmoles) and dimethyl acetylenedicarboxylate (4.91 g, 34.6 mmoles) in dioxane (200 ml) was refluxed in an oil bath for 3 hours to precipitate red needles **6a**, which were collected by suction filtration and then washed with ethanol to furnish an analytically pure sample (13.58 g, 96%), mp 268-270°; ir: ν 3080, 2980, 2940, 1735, 1660 cm^{-1}; ms: m/z 488 (M^+), 490 ($M^+ + 2$); pmr: 9.28 (s, 1H, C_{3a}-H), 8.08 (d, J = 2.0 Hz, 1H, C_9-H), 7.89 (d, J = 9.0 Hz, 1H, C_6-H), 7.88 (s, 1H, hydrazone CH), 7.78 (dd, J = 2.0 Hz, J = 9.0 Hz, 1H, C_7-H), 7.64 (d, J = 8.5 Hz, 2H, aromatic), 7.39 (d, J = 8.5 Hz, 2H, aromatic), 3.99 (s, 3H, OCH_3), 3.81 (s, 3H, NCH_3), 3.69 (s, 3H, OCH_3).

Anal. Calcd. for $C_{22}H_{18}Cl_2N_4O_5$: C, 54.00; H, 3.71; Cl, 14.49; N, 11.45. Found: C, 53.84; H, 3.72; Cl, 14.51; N, 11.40.

Dimethyl 4-[2-(*p*-Bromobenzylidene)-1-methylhydrazino]-8-chloro-3a*H*-isoxazolo[2,3-*a*]quinoxaline-2,3-dicarboxylate **6b**.

A solution of compound **3b** (10 g, 25.5 mmoles) and dimethyl acetylenedicarboxylate (4.35 g, 30.6 mmoles) in dioxane (200 ml) was refluxed in an oil bath for 2 hours to precipitate red needles **6b**, which were collected by suction filtration and then washed with ethanol to provide an analytically pure sample (13.5 g, 99%), mp 271-273°; ir: ν 3070, 2970, 2930, 1730, 1600 cm^{-1}; ms: m/z 533 (M^+), 535 ($M^+ + 2$); pmr: 9.29 (s, 1H, C_{3a}-H), 8.09 (d, J = 2.0 Hz, 1H, C_9-H), 7.91 (d, J = 9.0 Hz, 1H, C_6-H), 7.87 (s, 1H, hydrazone CH), 7.79 (dd, J = 2.0 Hz, J = 9.0 Hz, 1H, C_7-H), 7.58 (s, 4H, aromatic), 3.99 (s, 3H, OCH_3), 3.82 (s, 3H, NCH_3), 3.69 (s, 3H, OCH_3).

Anal. Calcd. for $C_{22}H_{18}BrClN_4O_5$: C, 49.50; H, 3.40; N, 10.50. Found: C, 49.64; H, 3.42; N, 10.47.

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