We have reported\(^1\) the synthesis of 6,5'-bis-1,2,4-triazinyls and 6,6'-bis-1,2,4-triazinyls by the cyclization of 1-heteroaryl-2-(3-N,N-dimethylamino-1,2,4-triazin-6-yl)-ethandione derivatives with methylthiosemicarbazide hydrogen iodide (1), where we assumed that the major product was the 6,5'-bis-1,2,4-triazinyls. As extension of our previous research, we attempt to synthesize the 3-N,N-dimethylamino-1,2,4-triazin-6-yl-glyoxal (2). We believed that the carbon of aldehyde group is definitely more electrophilic than that of keto, and the reaction with methylthiosemicarbazide hydrogen iodide (1) will produce the 6,5'-bis-1,2,4-triazinyls as major product. By comparing \(^1\)H NMR of compounds 7 and 8, we could easily distinguish between 6,5'- (7) and 6,6'-bis-1,2,4-triazinyls (8). Now we would like to report the synthesis of the first 1,2,4-triazinylglyoxal derivative, which is very important intermediate for the synthesis of 1,2,4-triazines\(^2\) and imidazoles.\(^3\)

3-N,N-dimethylamino-1,2,4-triazin-6-yl-acetylene (3) was hydrated under acidic condition to 6-acetyl-3-N,N-dimethylamino-1,2,4-triazine (4).\(^4\) Since SeO\(_2\) oxidation\(^5\) of acetyl to glyoxal did not work, compound 4 was brominated with HBr/AcOH to give 6-bromoacetyl-3-N,N-dimethylamino-1,2,4-triazine (5)\(^6\) in order to convert to glyoxal by DMSO oxidation.\(^7\) But unfortunately DMSO oxidation of bromoacetyl to glyoxal did not work either. Finally, we try to convert the bromo compound 5 to nitrate ester 6 with AgNO\(_3\) and then hydrolyze to 3-N,N-dimethylamino-1,2,4-triazin-6-yl-glyoxal (2).\(^8\) This time compound 2 was successfully obtained in yield of 69%. The glyoxal derivative was readily reacted with compound 1 to give 6,5'-bis-1,2,4-triazinyl (7) exclusively as expected. The corresponding 6,6'-bis-1,2,4-triazinyl derivative 8 was not obtained at all (Scheme 1).

The proton NMR of 6,5'-bis-1,2,4-triazinyl 7 showed two protons at \(\delta\) 9.13 and \(\delta\) 9.93 respectively. The big difference in chemical shift means that the one at \(\delta\) 9.13 is 5-H and the other at \(\delta\) 9.93 is 6'-H. Usually the 6-H of 1,2,4-triazine was shown at lower field than 5-H of 1,2,4-triazine.\(^9\) Compound 7 was further reacted with excess methyl iodide to give compound 11, which has \(N,N\)-dimethylamino group on both rings. The proton NMR of compound 11 showed two different peaks at \(\delta\) 9.11 and \(\delta\) 9.52 respectively. Definitely one at \(\delta\) 9.11 is 5-H and the other at \(\delta\) 9.52 must be 6'-H of 1,2,4-triazine ring. Here again showed quite big difference in chemical shift between 5-H and 6'-H. When the glyoxal 2 was reacted with aminoguanidine, both 6,5'- (9) and 6,6'-bis-1,2,4-triazinyls (10) were produced (Scheme 2).

In this case, 6,6'-bis-1,2,4-triazinyl 10 was the major product. Similar results were observed in other literature too.\(^10\) In order to clarify the structural difference between compound 9 and 10, they were separated by column and compound 10 was further reacted with excess methyl iodide to give 6,6'-bis-1,2,4-triazinyl (12), which is symmetric and has only 5-H proton. Actually compound 12 showed only one peak at \(\delta\) 9.18 for 5-H. This proves that our structural determination of compound 11 was correct.

In summary, 1,2,4-triazine glyoxal (2) was first synthesized and used to synthesize the bis-1,2,4-triazinyls. The
synthesis of imidazole derivatives by using 1,2,4-triazine glyoxal (2) will be published later. Also 3-N,N-dimethylamino-6-(3-N,N-dimethylamino-1,2,4-triazin-5-yl)-1,2,4-triazine (11) and 3-N,N-dimethylamino-6-(3-N,N-dimethylamino-1,2,4-triazin-6-yl)-1,2,4-triazine (12) were first synthesized in good yields, and they were checked the possibility to form the “complex with many transition metals as weak ligands.” and the experiment of the complex formation is in progress.

**Experimental Section**

All chemicals were purchased from Aldrich, and used without further purification. NMR, mass spectra and elemental analysis were recorded on Varian Unit INOVA 300, Shimadzu Corporation, QP-1000A and Carlo Erba, EA 1108, respectively. Melting points were determined on a Electrothermal melting point apparatus and are uncorrected.

**6-Acetyl-3-N,N-dimethylamino-1,2,4-triazine (4).** A mixture of 3-N,N-dimethylamino-6-ethyl-1,2,4-triazine (3) (0.9 g, 6.1 mmol), mercury(II) sulfate (1.8 g, 6.1 mmol), conc-sulfuric acid (30 mmol) in 70-85% aqueous acetone (150 mL) was refluxed for 2h. After removal of acetone, the residue was made alkaline with aqueous potassium carbonate, and then, extracted with chloroform. The chloroform solution was dried over MgSO₄, filtered, and concentrated in vacuo. Purification by silical gel column chromatography with ethyl acetate/n-hexane (1/1) gave 0.61 g (60%) of title compound as a pale yellow solid: mp 80-81 °C; ¹H NMR (CDCl₃) δ 3.29 (3H, NCH₃), 3.32 (3H, NCH₃), 9.13 (s, 1H, Tri-H), 9.24 (s, 1H, Tri-H); Mass m/e (rel. intensity) 166 (M⁺, 55), 123 (10), 70 (100).

**6-Bromoacetyl-3-N,N-dimethylamino-1,2,4-triazine (5).** Bromine (0.057 g, 3.6 mmol) was very slowly added to the solution of 6-acetyl-3-N,N-dimethylamino-1,2,4-triazine (4) (0.6 g, 3.61 mmol) in 30% HBr in AcOH at room temperature. The resulting solution was stirred for 48h at room temperature, and then, poured into water and extracted with ether. The extract was dried over MgSO₄, filtered, and concentrated in vacuo. Purification by silical gel column chromatography with ethyl acetate/n-hexane (2/1) gave 0.70 g (79%) of title compound as a yellow solid: mp 118-119 °C; ¹H NMR (CDCl₃) δ 2.74 (s, 3H, CH₃), 3.29 (s, 3H, NCH₃), 3.47 (s, 3H, NCH₃), 9.75 (s, 1H, Tri-H); Mass m/e (rel. intensity) 218 (M⁺, 85), 190 (20), 148 (22), 120 (97); Anal. Calcd. for C₉H₁₀N₇S; C, 43.36; H, 4.17; N, 39.52; S, 12.51.

**3-N,N-Dimethylamino-6-(3-amino-1,2,4-triazin-5-yl)-1,2,4-triazine (9) and 3-N,N-Dimethylamino-6-(3-amino-1,2,4-triazin-6-yl)-1,2,4-triazine (10).** A solution of 3-N,N-dimethylamino-1,2,4-triazin-6-yl-glyoxal (2) (0.1 g, 0.5 mmol) in water and ethyl alcohol (2 mL : 1 mL) was added to a suspension of aminoguanidine bicarbonate (0.077 g, 0.92 mmol) in ice water and ethyl alcohol (2 mL). The mixture was stirred for 1h at room temperature, and then, extracted with chloroform. The solution was dried over MgSO₄, filtered, and concentrated in vacuo. Purification by silical gel column chromatography with benzene/ethyl acetate (4/1) followed by recrystallization from ethyl acetate gave 0.23 g (91%) of title compound as a pale yellow solid: mp 205-206 °C; ¹H NMR (CDCl₃) δ 2.73 (s, 3H, CH₃), 3.32 (s, 3H, NCH₃), 3.51 (s, 3H, NCH₃), 9.13 (s, 1H, Tri-H), 9.93 (s, 1H, Tri-H); Mass m/e (rel. intensity) 249 (M⁺, 53), 221 (5), 148 (22), 123 (14); Anal. Calcd. for C₉H₁₀N₆S; C, 43.36; H, 4.45; N, 39.33; S, 12.86. Found: C, 43.42; H, 4.17; N, 39.52; S, 12.51.

**3-N,N-Dimethylamino-6-(3-amino-1,2,4-triazin-5-yl)-1,2,4-triazine (11) and 3-N,N-Dimethylamino-6-(3-amino-1,2,4-triazin-6-yl)-1,2,4-triazine (12).** A mixture of 6-bromoacetyl-3-N,N-dimethylamino-1,2,4-triazine (10) (0.1 g, 0.51 mmol) and sodium bicarbonate (0.077 g, 0.92 mmol) in 70-85% aqueous acetone (150 mL) was refluxed for 2h. After removal of acetone, the residue was made alkaline with aqueous potassium carbonate, and then, extracted with chloroform. The chloroform solution was dried over MgSO₄, filtered, and concentrated in vacuo. Purification by silical gel column chromatography with ethyl acetate/n-hexane (1/1) gave 0.1 g (0.51 mmol) as a yellow solid: mp 110-118 °C; ¹H NMR (DMSO-d₆) δ 3.32 (s, 3H, NCH₃), 3.73 (s, 2H, NH₂), 8.74 (s, 1H, Tri-H); Mass m/e (rel. intensity) 180 (1), 152 (26), 123 (24).

**Notes**

3-N,N-Dimethylamino-6-(3-N,N-dimethylamino-1,2,4-triazin-5-y1)-1,2,4-triazine. (11). A mixture of 3-N,N-dimethylamino-6-(3-methylthio-1,2,4-triazin-5-y1)-1,2,4-triazine (7) (0.1 g, 0.40 mmol) in 40% dimethylamine (2 mL) was stirred at 60 °C for 12 h, and then extracted with chloroform. The chloroform solution was dried over MgSO₄, filtered, and concentrated in vacuo. Purification by silical gel column chromatography with ethyl acetate/n-hexane (1/1) followed by recrystallization from ethyl acetate gave 0.089 g (90%) of title compound as a yellow solid: mp 161-162 °C; ¹H NMR (CDCl₃) δ 3.33 (s, 6H, N(CH₃)₂), 3.46 (s, 6H, N(CH₃)₂), 9.11 (s, 1H, Tri-H), 9.52 (s, 1H, Tri-H); Mass m/e (rel. intensity) 246 (M⁺, 34), 218 (2), 148 (21), 120 (27); Anal. Calcd. for C₁₀H₁₄N₈: C, 48.77; H, 5.73; N, 45.50. Found: C, 48.73; H, 5.86; N, 45.46.

3-N,N-Dimethylamino-6-(3-N,N-dimethylamino-1,2,4-triazin-6-y1)-1,2,4-triazine (12). Iodomethane (0.08 g, 0.56 mmol) was added to DMF solution of 3-N,N-dimethylamino-6-(3-amino-1,2,4-triazin-6-y1)-1,2,4-triazine (10) (0.061 g, 0.28 mmol) and sodium hydride (0.017 g, 0.71 mmol). The mixture was stirred at room temperature for 30 min. The solvent was evaporated to dryness under reduced pressure. The residue was dissolved in water and extracted with chloroform. The chloroform solution was dried over MgSO₄, filtered, and concentrated in vacuo. Purification by silical gel column chromatography with ethyl acetate/n-hexane (2/1) followed by recrystallization from ethyl acetate gave 0.059 g (86%) of 12: mp 240-241 °C; ¹H NMR (CDCl₃) δ 3.34 (s, 12H, 2N(CH₃)₂), 9.18 (s, 2H, Tri-H); Mass m/e (rel. intensity) 246 (M⁺, 28), 148 (21), 120 (25); Anal. Calcd. for C₁₀H₁₄N₈: C, 48.77; H, 5.73; N, 45.50. Found: C, 48.48; H, 5.86; N, 45.56.

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References