Journal of the Korean Chemical Society
1995, *Vol. 39, No. 9*
Printed in the Republic of Korea

단 신

1,2,4-Triazine(V): 3,3′-*Bis*-1,2,4-triazinyl 유도체 합성

李在謹* · 金晟年 · 李滄揆
경북대학교 자연과학대학 화학과

(1995. 5. 22 접수)

1,2,4-Triazine(V): The Synthesis of 3,3′-*Bis*-1,2,4-triazinyls

Jae-Keun Lee*, Sung-Nyun Kim, and Sang-Gyu Lee
Department of Chemistry, Kyungpook National University, Taegu 702-701, Korea

(Received May 22, 1995)

Among the possible *bis*-1,2,4-triazinyls (*Fig.* 1), only 3,3′-, and 5,5′-*bis*-1,2,4-triazinyls have been reported.[1,2]

Although the 3,3′-*bis*-1,2,4-triazinyls are reported, the method of the synthesis of 3,3′-*bis*-1,2,4-triazinyls is the reaction of 1,2-dicarbonyl compounds with *bis*-amidrazone, which is prepared by the reaction of dicyanide and hydrazine (*Scheme* 1).

According to this method, only symmetric 3,3′-*bis*-1,2,4-triazinyls can be prepared. The preparations of 3,3′-*bis*-1,2,4-triazinyls would be possible by using 3-cyano-1,2,4-triazinyls, if the 3-cyano group could be changed into amidrazone by the reaction with hydrazine.

The preparation of amidrazone has been accomplished by the reaction of hydrazine on the thioamide[3] and imidoether.[4,5] Direct preparation of amidrazone with hydrazine on the cyanide has also been reported in limited number.[6,7] 2-Cyanopyridine has been converted to the corresponding amidrazone by direct reaction of hydrazine, which is transformed to 3-(2-pyridyl)-1,2,4-triazine by the reaction with glyoxal.[1,6] As a continuation of this reaction, 4-cyanopyridine was chosen and tried to react directly with hydrazine. But formation of the corresponding amidrazone was unsuccessful. The corresponding amidrazone was formed from imidoether, which was prepared by the reaction of ethanol with HCl gas. Amidrazone was reacted with glyoxal to form 3-(4-pyridyl)-1,2,4-triazine (*Scheme* 2).

3-Cyano-5,6-diphenyl-1,2,4-triazine was prepared from 3-thiomethyl-5,6-diphenyl-1,2,4-triazine (*Scheme* 3).

The direct substitution of 3-methylthio group to cyanide could not be accomplished.

Therefore the oxidation of 3-methylthio group

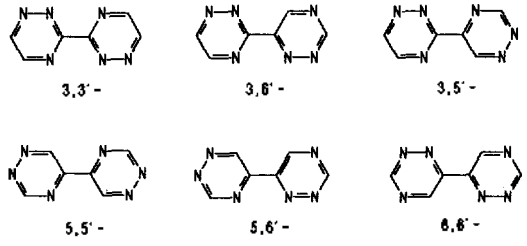
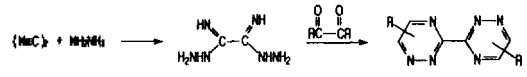
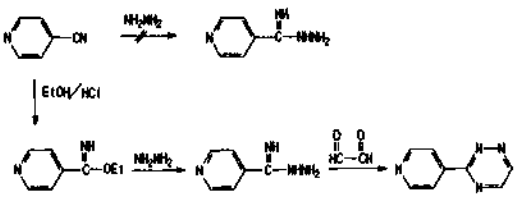


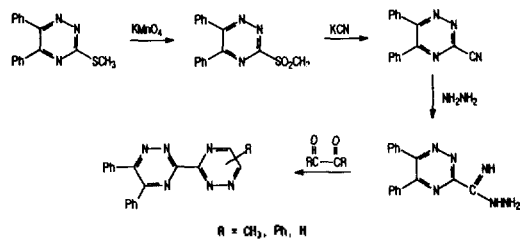
Fig. 1. Possible *bis*-1,2,4-triazinyls.



Scheme 1.



Scheme 2.



Scheme 3.

to 3-methylsulfonyl group with $KMnO_4$ in order to increase the leaving ability, was carried out, and then the substitution of 3-methylsulfonyl group to 3-cyano group was accomplished successfully.[7~9] 3-Cyano-5,6-diphenyl-1,2,4-triazine was reacted directly with hydrazine, forming the corresponding amidrazone. Amidrazone was reacted with 1,2-dicarbonyl compounds, *e.g.* benzyl, acetyl and glyoxal, forming 5,6-diphenyl-5′,6′-diphenyl-3,3′-*bis*-1,2,4-triazinyl, 5,6-diphenyl-5′,6′-dimethyl-3,3′-*bis*-1,2,4-triazinyl and 5,6-diphenyl-3,3′-*bis*-1,2,4-triazinyl respectively. The 3,3′-*bis*-1,2,4-triazinyls were identified by NMR and mass spectra.

The attempt to get 3-cyano-1,2,4-triazine from 3-methylthio-1,2,4-triazine with the same method was unsuccessful. Therefore the trial to synthesize the parent 3,3′-*bis*-1,2,4-triazinyl was abandoned. Also the attempt to get 3-cyano-5,6-dimethyl-1,2,4-triazine from 3-methylthio-5,6-dimethyl-1,2,4-triazine was not successful.

As an extension of the above method, the reaction of 6-cyano-1,2,4-triazines with hydrazine to prepare 6,3′-*bis*-1,2,4-triazinyls, another possible dimer of 1,2,4-triazines, is attempted and the result will be reported in another paper.

EXPERIMENTAL

All chemicals were purchased from Aldrich, and used without further purification. PMR spectra were recorded on Varian AM-300, and mass spectra were obtained on Shimadzu GCMS-QP 1000A.

Preparation of 3-(4-pyridyl)-1,2,4-triazine. To the ether solution of 4-cyanopyridine (2.00 g, 19.2 mmol) and absolute ethanol (1.50 g, 32.6 mmol), 1.0 mol HCl/ether solution was added dropwise until there was no more precipitation, while cooling in ice bath. After stirring at room temperature for 2 hours, the solvent was evaporated. The resulting precipitate was again dissolved in absolute ethanol, and hydrazine (0.64 g, 20.0 mmol) was added dropwise to it, while cooling in ice bath. After the yellow solution was stirred for 1 hour at room temperature, the solvent was evaporated on a rotary evaporator, yielding yellow precipitate. The yellow precipitate was dissolved in absolute methanol, and aq. glyoxal (1.90 g, 32.8 mmol) was added at one time, and then 3 mL of triethylamine was added slowly to it, while cooling at −70 ℃. After finishing addition of triethylamine, the reaction mixture was allowed to reach to room temperature slowly and was stirred for further 13 hours. The reaction mixture was extracted with chloroform and the product, 3-(4-pyridyl)-1,2,4-triazine, was separated through the silica gel column with eluent of ethyl acetate and low boiling petroleum ether (3 : 1 by volume) (0.32 g, yield 10.5%).

mp 133~135 ℃; ^{1}H NMR ($CDCl_3$) δ 8.3 (dd, J=4.4, 2.1 Hz, 2H, Py-H), 8.7 (d, J=2.4 Hz, 1H, triazine-H), 8.8(dd, J=4.4, 2.1 Hz, 2H, Py-H), 9.2 (d, J=2.4 Hz, 1H, triazine-H); MS: m/e (rel. int.) 158 (M^+, 19), 130 (55), 104 (100), 78 (5).

Preparation of 5,6-diphenyl-5′,6′-diphenyl-3,3′-*bis*-1,2,4-triazinyl. To the solution of 5,6-diphenyl-3-cyano-1,2,4-triazine (1.00 g, 3.9 mmol) in 20 mL of absolute ethanol, the solution of absolute hydrazine (0.20 g, 6.3 mmol) in 20 mL absolute ethanol was added dropwise. After the reaction mixture was stirred at room temperature for 4 hours, the solvent of the resulting yellow solution was evaporated to dryness under a rotary evaporator, yielding the amidrazone compound. The amidrazone compound without further purification was dissolved in 20 mL acetic acid with ammonium acetate, and then benzil (0.80 g, 3.8 mmol) was added to it and stirred at room temperature for 24 hours, yielding yellow precipitate. The resulting precipitate was filtered and recrystalized from acetic acid, yielding 5,6-diphenyl-5′,6′-diphenyl-3,3′-*bis*-1,2,4-triazine (0.28 g, yield 15.6%).

mp 280~282 ℃; Elemental Analysis: Cal. C, 77.56; N, 18.09; H, 4.34. Obs. C, 77.16; N, 18.06; H, 4.29; ^{1}H NMR (TFA-D) δ 7.6~8.0 (m, 20H, Ph-H); MS: m/e (rel. int.) 464 (M^+, 20), 178 (100).

Preparation of 5,6-diphenyl-5',6'-dimethyl-3,3'-*bis*-1,2,4-triazinyl. It was prepared by the same method of the above compound (yield 18.0%).

mp 290~292 ℃; ^{1}H NMR (TFA-D) δ 2.4 (s, 1H, CH_3), 2.8 (s, 3H, CH_3), 7.6~7.8 (m, 10H, Ph-H); MS: m/e (rel. int.) 340 (M^+, 15), 178 (100).

Preparation of 5,6-diphenyl-3,3'-*bis*-1,2,4-triazinyl. It was synthesized by the same method of the previous compounds. However, the product was recrystallized from DMF instead of acetic acid (yield 20.0%).

mp 284~286 ℃; ^{1}H NMR (TFA-D) δ 7.5~7.8 (m, 10H, Ph-H, 2H, triazine-H); MS: m/e (rel. int.) 312 (M^+, 9), 178 (100).

Acknowledgement. The authors appreciate the financial support from Korea Research Institute of Chemical Technology for part of this study, and the Basic Research Institute Program, Ministry of Education (BSRI-94-3402).

REFERENCES

1. Culbertson, B. M.; Parr, G. R. *J. Heterocyclic Chem.* **1967**, *4*, 422.
2. Krass, D. K.; Chen, T. K.; Paudler, W. W. *J. Heterocyclic Chem.* **1973**, *10*, 343.
3. Van der Barg, W. *Rec. Trav. Chim.* **1955**, *74*, 257.
4. Libman, D.; Slack, R. *J. Chem. Soc.* **1956**, 2253.
5. Neilsen, D. G.; Roger, R.; Heatlie, J. W. M.; Newlands, L. R. *Chem. Rew.* **1970**, *70*, 151.
6. (a) Case, F. H. *J. Org. Chem.* **1965**, *30*, 931. (b) Case, F. H. *J. Heterocyclic Chem.* **1971**, *8*, 173.
7. Neunhoeffer, H.; Hennig, H. *Chem. Ber.* **1968**, *101*, 3952.
8. Ohba, S.; Konno, S.; Yamanaka, H. *Chem. Pharm. Bull.* **1991**, *30*, 486.
9. Sagi, M.; Wada, K.; Konno, S.; Yamanaka, H. *Heterocycles* **1990**, *30*, 1009.