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DIELS-ALDER REACTION OF 1,2,3-TRIAZINE WITH ENAMINES

Teruyo Sugita*, Junko Koyama, Kiyoshi Tagahara, and Yukio Suzuta

Kobe Women's College of Pharmacy, Kobe 658, Japan

Abstract —— 1,2,3-Triazine has been shown to react with enamines to afford products of [4+2] cycloaddition reaction. Loss of nitrogen and pyrrolidine from the initial bicycloadducts afford 2,3-disubstituted pyridines.

In a recent report, heterocyclic azadienes have been shown to participate in Diels-Alder reactions with a variety of diene systems. The review[1], however, dose not mention as concerns the reaction of 1,2,3-triazine in detail. Now we report here the results obtained by the treatment of 4-methyl-1,2,3-triazine with cycloalkanone pyrrolidine enamines.

4-Methyl-1,2,3-triazine was synthesized from 3-methylpyrazole according to the method of Igeta and co-workers[2]. Treatment of 4-methyl-1,2,3-triazine with several cycloalkanone pyrrolidine enamines by the following methods gave 2,3-disubstituted pyridines.

Method A : A solution of enamine (1.3 ∿ 1.4 equiv) in dry $CHCl_3$ was treated with 4-methyl-1,2,3-triazine in $CHCl_3$ under nitrogen, and resulting solution was warmed at 50-60°C for 20-23 h.

Method B : A mixture of 4-methyl-1,2,3-triazine and enamine (1.3 ∿ 1.4 equiv) in dry $CHCl_3$ was heated in a sealed glass tube at 60-150°C for 0.5-19 h.

The crude products were separated by preparative thin layer chromatography on silica gel.

The results are summarized in Table. In each case cycloaddition occurs across N-3/C-6 of the 1,2,3-triazine nucleus and the nucleophilic carbon of the dienophile attaches to C-6 of the 1,2,3-triazine. Product (10) is an alkaloid isolated and characterised by Edwards and Elmore from a South American plant, Fabiana imbricata[3].

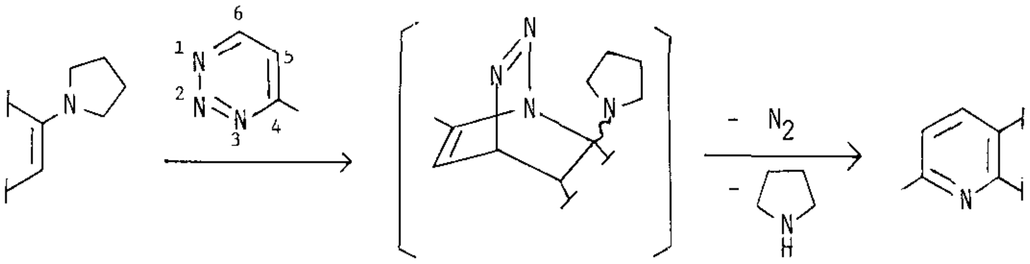
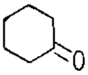
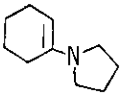
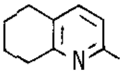
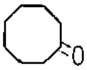
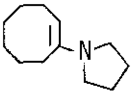
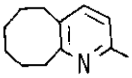
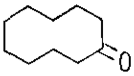
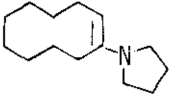
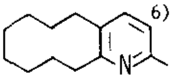
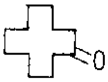
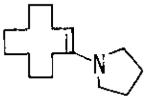
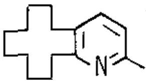
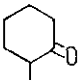
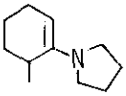
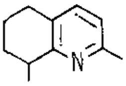
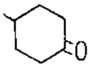
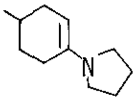
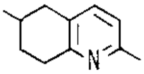
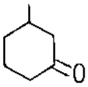
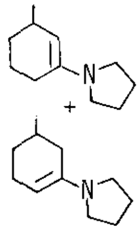
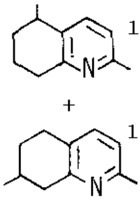


Table Reaction of enamines with 4-methyl-1,2,3-triazine

cycloalkanone	enamine	product	method	reaction conditions	yield %
		 4)	A B B B	50-60°C, 23h 60°C, 19h 100°C, 1.5h 150°C, 0.5h	17 20 45 26
		 5)	B B	50-60°C, 23h 100°C, 2h	44 69
		6) 	B B	50-60°C, 24h 100°C, 2h	10 27
		 7)	B B	50-60°C, 23h 100°C, 2h	11 34
		 8)	A	50-60°C, 20h	16
		 9)	A	50-60°C, 23h	25
		 10)* 10')	A B	50-60°C, 21h 100°C, 2h	15 (10:10' =1:6) 56 (10: 10' =1:4)

* The used enamine was a mixture of Δ^1- and Δ^6- isomers, so that the product was found from its NMR spectrum to be the corresponding mixture of 5- and 7-methyl isomers.

REFERENCES AND NOTES

1) Dale L. Boger, Tetrahedron, 1983, 39, 2869.

2) A. Ohsawa, H. Arai, H. Ohnishi, and H. Igeta, Chem. Comm., 1980, 1182.

3) D. E. Edwards and N. F. Elmore, Can. J. Chem., 1962, 40, 256.

4) picrate, mp 152-153°C ; ^{1}H-NMR($CDCl_3$) δ : 2.45(3H, s, 2-Me), 6.76(1H, d, J=8Hz, 3-H), 7.13(1H, d, J=8Hz, 4-H) ; MS m/z : 147.1050(M^+, calcd for $C_{10}H_{13}N$, 147.1047).

5) picrate, mp 161-162.5°C ; ^{1}H-NMR($CDCl_3$) δ : 2.50(3H, s, 2-Me), 2.72 and 2.94(4H, t each, J=6Hz, 5 and 10-H_2), 6.91(1H, d, J=8Hz, 3-H), 7.26(1H, d, J=8Hz, 4-H) ; MS m/z : 175.1358(M^+, calcd for $C_{12}H_{17}N$, 175.1360).

6) picrate, mp 166-168°C ; ^{1}H-NMR($CDCl_3$) δ : 2.51(3H, s, 2-Me), 2.81 and 2.95(4H, t each, J=6.5Hz, 5 and 12-H_2), 6.92(1H, d, J=8Hz, 3-H), 7.34(1H, d, J=8Hz, 4-H) ; MS m/z : 203.1664(M^+, calcd for $C_{14}H_{21}N$, 203.1672).

7) picrate, mp 143-144°C ; ^{1}H-NMR($CDCl_3$) δ : 2.49(3H, s, 2-Me), 2.62 and 2.81(4H, t each, J=7.5Hz, 5 and 14-H_2), 6.91(1H, d, J=8Hz, 3-H), 7.35(1H, d, J=8Hz, 4-H) ; MS m/z : 231.1991(M^+, calcd for $C_{16}H_{25}N$, 231.1985).

8) picrate, mp 115°C ; ^{1}H-NMR($CDCl_3$) δ : 1.35(3H, d, J=7Hz, 8-Me), 2.51(3H, s, 2-Me), 2.72(2H, t like, 5-H_2), 2.99(1H, m, 8-H), 6.88(1H, d, J=8Hz, 3-H), 7.24(1H, d, J=8Hz, 4-H) ; MS m/z : 161.1191(M^+, calcd for $C_{11}H_{15}N$, 161.1203).

9) picrate, mp 134-136°C ; ^{1}H-NMR($CDCl_3$) δ : 1.08(3H, d, J=6.5Hz, 6-Me), 2.49(3H, s, 2-Me), 6.91(1H , d, J=8Hz, 3-H), 7.26(1H, d, J=8Hz, 4-H) ; MS m/z : 161.1181(M^+, calcd for $C_{11}H_{15}N$, 161.1203).

10) + 10') MS m/z : 161.1205(M^+, calcd for $C_{11}H_{15}N$, 161.1203) ; ^{1}H-NMR($CDCl_3$) δ : 10)- 1.26(3H, d, J=7Hz, 5-Me), 2.50(3H, s, 2-Me), 6.95(1H, d, J=8Hz, 3-H), 7.41(1H, d, J=8Hz, 4-H) : 10')- 1.09(3H, d, J=6.5Hz, 7-Me), 2.50(3H, s, 2-Me), 6.91(1H, d, J=8Hz, 3-H), 7.28(1H, d, J=8Hz, 4-H).

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