[Chem. Pharm. Bull. 20(3) 605—606 (1972)]

UDC 547.853.7.04 : 547.791.057

The Reaction of 5-Phenylazo-6-aminopyrimidines with Lead Tetraacetate. A Convenient Synthesis of 2-Phenyl-7-amino-*v*-triazolo[4,5-*d*]-pyrimidines

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(Received July 21, 1971)

Previous papers[2,3] have demonstrated the remarkable efficacy of lead tetraacetate oxidation of 5-nitroso-4,6-diaminopyrimidines to the synthesis of 7-aminofurazano[3,4-*d*]pyrimidines which are versatile intermediates for the preparation of a variety of fused pyrimidine heterocycles.

The synthetic procedure was originally designed on the basis of the following aspects: Oxidation of aldoximes with lead tetraacetate gives the possible intermediacy of iminoxy cations (or iminoxy radicals). 5-Nitoso-6-aminopyrimidines appear to react in their imino-oxime tautomeric form under certain conditions. Accordingly, oxidation of 5-nitroso-6-aminopyrimidines with lead tetraacetate should proceed through intermediates similar to the case of oximes, and lead by intramolecular capture to derivatives of the furazano[3,4-*d*]pyrimidine ring system (*cf.* Chart 1).

The analogous principle seems to be applicable to the synthesis of 2-phenyl-*v*-triazolo-[4,5-*d*]pyrimidines from 5-phenylazo-6-aminopyrimidines: 5-phenylazo-6-aminopyrimidines might react with lead tetraacetate in the imino-hydrazone tautomeric form, corresponding to the imino-oxime form of 4-amino-5-nitrosopyrimidines, to form a conceivable intermediate $(=N-\overset{+}{N}-C_6H_5$ or $=N-\overset{\bullet}{N}-C_6H_5)$[4] which then undergoes the intramolecular cyclization affording 2-phenyl-*v*-triazolo[4,5-*d*]pyrimidines.

The present investigation was undertaken on the basis of above considerations and provides a convenient preparative method of 2-phenyl-7-amino-*v*-triazolo[4,5-*d*]pyrimidines (II: R=H, NH_2, C_6H_5).

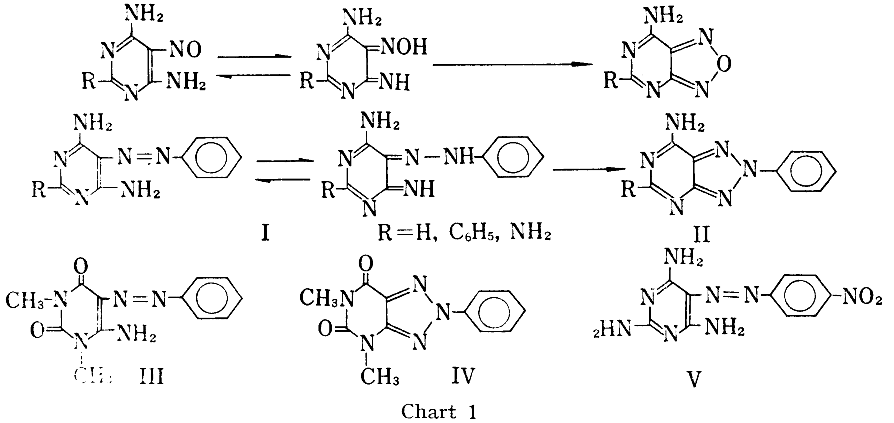

Chart 1

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[1] Locations: *a*) *Sakanoshita, Mitahora, Gifu*; *b*) *Princeton, N.J., U.S.A.*

[2] E.C. Taylor, Y. Maki and B.E. Evans, *J. Am. Chem. Soc.*, **91**, 5181 (1969).

[3] E.C. Taylor, G.P. Beardsley and Y. Maki, *J. Org. Chem.*, **34**, 3211 (1971).

[4] The reaction of aromatic ketone hydrazones with lead tetraacetate has been reported (For a review, see *Chem. Ind.* (London), **1968**, 437).

Stirring a suspension of 2-phenyl-5-phenylazo-4,5-diamino-pyrimidine (I: R=C_6H_5) in glacial acetic acid with an equimolar amount of lead tetraacetate at room temperature under nitrogen resulted in the formation of 7-amino-2,5-diphenyl-*v*-triazolo[4,5-*d*]pyrimidine, II: R=C_6H_5, in 90% yield. Structure II: R=C_6H_5 was confirmed by consonant spectra and satisfactory combustion analyses.

Similarly, (I: R=NH_2, H) underwent the oxidative cyclization to give II: R=NH_2[5] and II: R-H[6] in 75% and 86% yields respectively.

Thus, we prepare II under mild conditions in good yields. The oxidative cyclization employing copper sulphate in pyridine has been commonly used for the preparation[7] of 2-phenyl-*v*-triazolo[4,5-*d*]pyrimidines from 5-phenylazo-6-aminopyrimidines. However, this procedure often requires severe reaction conditions.

When 5-phenylazo-amino-1,3-dimethyluracil (III) was allowed to react with lead tetraacetate in a manner similar to the previous case, 2-phenyl-4,6-dimethyl-*v*-triazolo[4,5-*d*]-pyrimidine-5,7(4H, 6H)-dione (IV) was obtained only in 20% yield. The similar oxidation of 5-(*p*-nitrophenylazo)-2,4,6-triaminopyrimidine (V) did not take place.

These findings appear of interest from the mechanistic point of view.

Experimental

2-Phenyl-7-amino-*v*-triazolo[4,5-*d*]pyrimidines (II: R=C_6H_5, NH_2, H)——A total of 4.4 g (0.01 mole) of lead tetraacetate was added in portions during 5 min to 2.9 g (0.01 mole) of (I: R=C_6H_5) in 80 ml of glacial acetic acid. The reaction was run in an atmosphere of nitrogen, and stirring was continued for 24 hr, during which time the color of the reaction mixture changed from orange to yellow. The precipitated solid mass was collected by filtration, washed with water, and dried. The crude prosuct was recrystallized from ethanol to give (II: R=C_6H_5), mp 277—278° (decomp.), as colorless crystals. Yield 90%. IR ν_{max}^{Nujol} cm^{-1}: 3300 (braod), 1650. NMR (DMSO-d_6) (δ): 7.75 (6H, multiplet, aromatic protons), 8.30 (4H, multiplet, aromatic protons), 10.5 (2H, broad, NH_2). *Anal.* Calcd. for $C_{16}H_{12}N_6$: C, 66.67; H, 4.51; N, 29.17. Found: C, 66.30; H, 4.26; N, 29.48. Acetate, mp 265°. IR ν_{max}^{Nujol} cm^{-1}: 3200, 1700. *Anal.* Calcd. for $C_{18}H_{11}ON_6$: C, 65.44; H, 4.27; N, 25.44. Found: C, 65.57; H, 4.42; N, 25.50.

In the same manner as the case of (I: R=C_6H_5), (I: R=NH_2, H) were oxidized by lead tetraacetate to give (II: R=NH_2), mp 350° (decomp.) (lit.[6], mp 345° (decomp.)) and (II: R=H), mp 335° (decomp.) (lit.[5], mp 340° (decomp.)) in 75% and 86% yields respectively.

2-Phenyl-4,6-dimethyl-*v*-triazolo[4,5-*d*]pyrimidine-5,7(4H,6H)-dione (IV)——A total of 4.4 g (0.01 mole) of lead tetraacetate was added in portions during 5 min. to 2.5 g (0.01 mole) of III in 80 ml of glacial acetic acid. The reaction mixture was stirred under nitrogen for 24 hr. The resulting clear solution was concentrated to dryness under reduced pressure and diluted with water. The precipitated solid mass was collected by filteration and recrystallized repeatedly from ethanol to give IV, mp 207—208°, in 25% yield. IR ν_{max}^{Nujol} cm^{-1}: 1720, 1675. Mass Spectrum $M^+=257$. *Anal.* Calcd. for $C_{12}H_{11}O_2N_5$: C, 56.02; H, 4.31; N, 27.23. Found: C, 56.26; H, 4.34; N, 27.23. Thin-layer chromatography of the mother liquor showed the presence of III and a small amount of IV. III was recovered in 50% yield.

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[5] G.M. Timmins, D.G. Felton, H.O.T. Collier and P.C. Haskinson, *J. Pharm. Pharmacol.*, **9**, 46 (1957).

[6] E. Richter and E.C. Taylor, *J. Am. Chem. Soc.*, **78**, 5848 (1956).

[7] F.R. Benson, L.W. Hartzel and W.L. Savell, *J. Am. Chem. Soc.*, **76**, 2263 (1950).