Notes

U. D. C. 547.787'532

Tanezo Taguchi and Munemitsu Tomoeda: Studies in Stereochemistry. XI. *dl*-Phenylserinols: A New Synthesis and its Stereochemical Findings. (4)[1]. The Effect of Acetic Acid Upon Treatment of *dl-threo*-2-Phenyl-4-phenylhydroxymethyl-Δ^2-oxazoline with AcOK-Ac_2O.

(*Pharmaceutical Institute, Medical Faculty, University of Kyushu**)

In general the oxazoline ring is comparatively stable to bases and unstable to acids, resulting in ring-fission. It is also known that a mixture of AcOK, Ac_2O, and AcOH reacts with the oxazoline to form β-acylaminoethylacetate derivative with ring opening. Theoretically the acetic acid among the three components plays a main role in the opening of the ring. To verify this theory experimentally the effect of acetic acid upon treatment of *dl-threo*-2-phenyl-4-phenylhydroxymethyl-Δ^2-oxazoline (I)[2] with AcOK-Ac_2O was examined.

The oxazoline (I) was heated in 30% AcOH to yield *dl-threo*-1-phenyl-2-benzoylaminopropane-1,3-diol (II) as a sole product, which was then converted to *dl-threo*-1-phenyl-2-benzoylamino-1,3-diacetoxypropane (III) by heating in a mixture of anhyd. AcOK and Ac_2O with or without AcOH.

The oxazoline (I) was then heated in a mixture of anhyd. AcOK and Ac_2O without AcOH to yield *dl-threo*-2-phenyl-4-phenylacetoxymethyl-Δ^2-oxazoline (IV) without ring opening, the structure of which was supported by microanalysis and infrared spectral determination. Subsequently, (IV) was converted to the *dl-threo*-triacyl compound (III) with ring opening by heating in a mixture of anhyd. AcOK and Ac_2O with AcOH. When the oxazoline (I) was heated in a mixture of anhyd. AcOK and Ac_2O

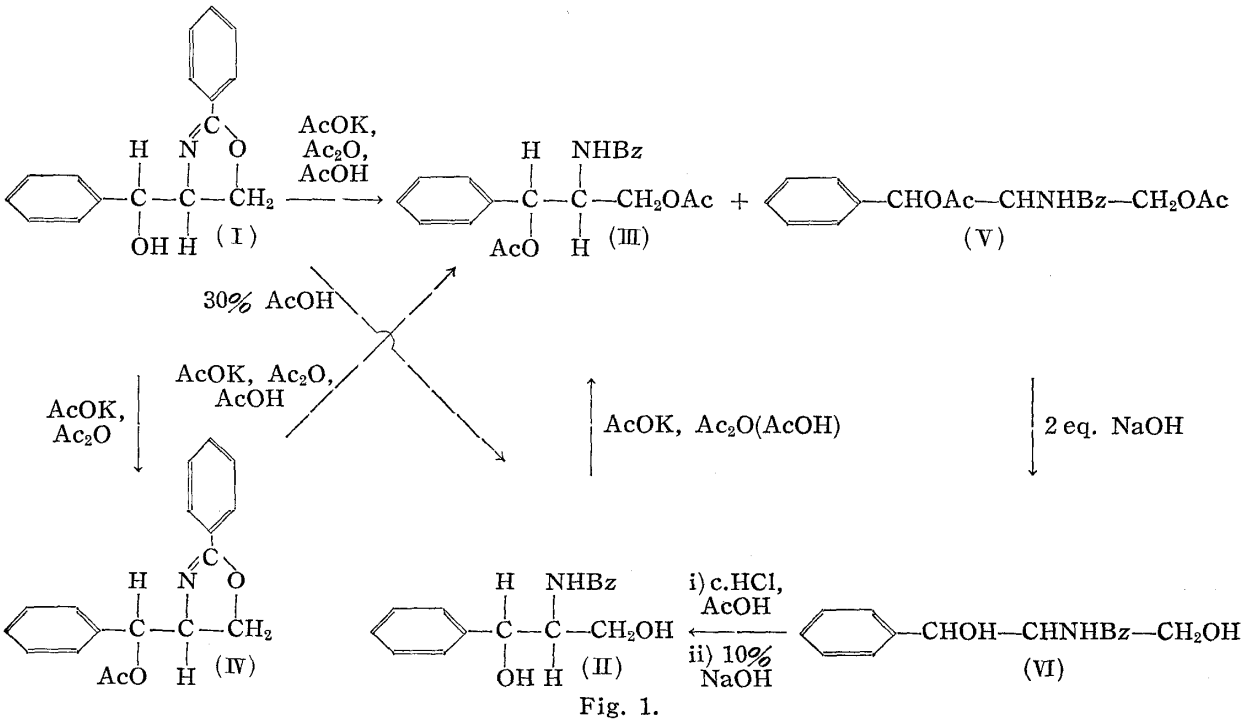

Fig. 1.

* Katakasu, Fukuoka (田口胤三, 友枝宗光).

1) Part (3). T. Taguchi, M. Tomoeda: This Bulletin, **4**, 473(1956).

2) Part (2). T. Taguchi, M. Tomoeda, H. Fukuyama: *Ibid.*, **4**, 80(1956).

with AcOH, however, (I) was immediately converted to the *dl-threo*-triacyl compound (III) with ring opening in accompanyment with unknown colorless needles in yield ratio of 1.0 : 5.2. These observations indicate that acetic acid is needed to cause ring opening of oxazoline.

The structure of the unknown colorless needles was deduced to be a mixture of *dl-threo-* and *-erythro*-1-phenyl-2-benzoylamino-1,3-diacetoxypropane (V) by micro-analytical data. It provided further evidence for the deduction that the product was hydrolyzed in aqueous solution containing 2 moles of NaOH to give a mixture of *dl-threo-* and *-erythro*-1-phenyl-2-benzoylaminopropane-1, 3-diol (VI), the composition of which was confirmed by the finding that it was derived to pure (II) by acyl migration reaction.[2] The formation of the epimeric mixture shows that the reaction involves Walden inversion at asymmetric carbon with hydroxyl group of (I). However, as stated above, the reactions from (I) to (III) via (II) or from (I) to (III) via (IV) did not involve a Walden inversion and also the prolonged treatment of (III) or (V) in a mixture of AcOK, Ac_2O, and AcOH at its b.p. did not result in any epimerization. Hence the Walden inversion in question seems to be unique for the structure of (I). Although it may be rash to postulate its mechanism from a few experiments, the following mechanism was speculatively derived from the conformation of (I) proposed in the previous paper[1]: In the conformation of (I), the existence of a hydrogen bond between H of C_{4a}-OH and ring-N provides evidence of their proximity. Accordingly the back-side of C_{4a}-OH, it is supposed, is widely spread. Therefore, the substitution of OH by acetoxyl group at C_{4a} is apt to occur with Walden inversion probably through S_N2.

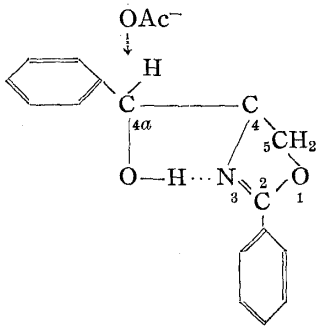

Fig. 2.

The authors are indebted to the Ministry of Education for the Grant in Aid for Scientific Research. Their thanks are also due to the Microanalytical Section of this Institute and the Service Center of Microanalyses of this University for the microanalyses and to the Sankyo Co. for the infrared spectral determination.

Experimental

***dl-threo*-1-Phenyl-2-benzoylaminopropane-1,3-diol (II)**—a) From *dl-threo*-2-Phenyl-4-phenylhydroxymethyl-Δ^2-oxazoline (I): A solution of 50 mg. of (I) in 5 cc. of 30% AcOH was boiled for 2 hrs. and concentrated *in vacuo* to leave an oily residue. The AcOEt extract of the residue was concentrated and colorless needles precipitated, m.p. 155~162°, and weighed 35 mg. After recrystallization from AcOEt, it melted at 163~165°, alone and on admixture with an authentic sample of (II)[1], yield 20 mg. *Anal.* Calcd. for $C_{16}H_{17}O_3N$ (II): N, 5.16. Found: N, 5.27.

b) From *dl-threo-* and *-erythro*-1-Phenyl-2-benzoylamino-1,3-diacetoxypropane (V) via *dl-threo-* and *-erythro*-1-Phenyl-2-benzoylaminopropane-1,3-diol (VI): A solution of 50 mg. of (V) and 25 mg. of NaOH in 5 cc. of 90% EtOH was boiled for 1 hr. and concentrated *in vacuo* to leave an oily residue. The AcOEt extract was washed with water, dried over anhyd. Na_2SO_4, and concentrated to give a solid residue. Recrystallization from AcOEt gave colorless needles, m.p. 128~133°; yield, 30 mg. *Anal.* Calcd. for $C_{16}H_{17}O_3N$ (VI): N, 5.16. Found: N, 5.27.

A solution of 30 mg. of the needles (VI) in a mixture of 0.1 cc. of conc. HCl and 0.2 cc. of AcOH was boiled for 5 mins., cooled, and diluted with water. The solution was made alkaline with 10% NaOH to give an oily product which then crystallized. Recrystallization from AcOEt gave colorless needles, m.p. 163~165°, alone and on admixture with an authentic sample of (II); yield, 15 mg.

dl-threo-**1-Phenyl-2-benzoylamino-1, 3-diacetoxypropane (III)**—a) From (II) : 1) A solution of 250 mg. of (II) and 250 mg. of anhyd. AcOK in 2.5 cc. of Ac_2O was boiled for 1 hr., cooled, and poured into ice-water to deposit a solid. Recrystallization from ether-petr. ether gave colorless prisms, m.p. 140~142°; yield, 330 mg. *Anal.* Calcd. for $C_{20}H_{21}O_5N$ (III) : C, 67.59; H, 5.96; N, 3.94. Found: C, 67.75; H, 5.80; N, 3.84.

2) A solution of 200 mg. of (II) and 200 mg. of anhyd. AcOK in a mixture of 1 cc. of Ac_2O and 3 cc. of AcOH was boiled for 10 hrs., cooled, and poured into ice water to deposit a solid precipitate. Recrystallization from AcOEt gave colorless needles, m.p. 141~143°; yield, 120 mg.

b) From (I) ; Simultaneous Formation of a Mixture of *dl-threo*- and *-erythro*-1-Phenyl-2-benzoylamino-1, 3-diacetoxypropane (V) : A solution of 1 g. of (I) and 1 g. of anhyd. AcOK in a mixture of 5 cc. of Ac_2O and 15 cc. of AcOH was boiled for 14 hrs. and concentrated *in vacuo* to leave a solid, m.p. 120~150°. Recrystallization from AcOEt deposited colorless short needles, 166~167.5°; yield 520 mg. *Anal.* Calcd. for $C_{20}H_{21}O_5N$ (V) : C, 67.59; H, 5.96; N, 3.94. Found : C, 67.37; H, 6.14; N, 3.97.

The AcOEt mother liquor was concentrated to give colorless long needles. After recrystallization from benzene it melted at 141~143°, alone and on admixture with a sample of (III) obtained by procedure (a); yield 110 mg. *Anal.* Calcd. for $C_{20}H_{21}O_5N$ (III) : N, 3.94. Found : N, 4.01.

c) From *dl-threo*-2-Phenyl-4-phenylacetoxymethyl-Δ^2-oxazoline (IV). A solution of 65 mg. of (IV) and 65 mg. of anhyd. AcOK in a mixture of 0.4 cc. of Ac_2O and 1.2 cc. of AcOH was boiled for 10 hrs. and concentrated *in vacuo* to give an oily residue. The AcOEt extract of the residue was washed with water, dried over anhyd. Na_2SO_4, and concentrated to leave a solid residue. Recrystallization from benzene gave colorless needles, m.p. 137~139°, alone and on admixture with a sample of (III), yield 30 mg.

dl-threo-**2-Phenyl-4-phenylacetoxymethyl-Δ^2-oxazoline(IV)**—A solution of 270 mg. of (I) and 270 mg. of anhyd. AcOK in 5 cc. of Ac_2O was boiled for 1 hr. and concentrated *in vacuo* to leave an oily residue. The benzene extract was washed with water, dried over anhyd. Na_2SO_4 and concentrated *in vacuo* to leave an oily residue which crystallized upon addition of a small volume of ether. After recrystallization from MeOH, it melted at 143~145°, yield 240 mg. *Anal.* Calcd. for $C_{18}H_{17}O_3N$ (IV) : C, 73.20; H, 5.80; N, 4.75. Found : C, 73.39; H, 5.65; N, 4.71. I.R. : λ_{max}^{Nujol} 5.76, 8.07 μ(-OCOCH$_3$); 6.05 μ(-C=N-); 6.32, 6.67 μ(-C_6H_5).

(Received July 30, 1956)

U. D. C. 547. 94 : 582. 675. 1 Thalictrum

Eiichi Fujita and Toshiaki Tomimatsu : Studies on the Alkaloids of *Thalictrum Thunbergii* DC. I. A Quaternary Base in the Root.

(*Faculty of Pharmacy, Tokushima University**)

Doassans,[1] Vashistha, *et al.*,[2] Nakajima,[3] Norkina, *et al.*,[4] and Yunusov, *et al.*[5] reported on the alkaloids of Thalictrum genus plants. They named 10 alkaloids and suggested three structural formulae among them. All of those alkaloids are tertiary bases and their studies are still incomplete. The present authors began systematic study of the alkaloids of *Thalictrum Thunbergii* DC. (Japanese name "Aki-karamatsu"), found a quaternary base from the root, and clarified its structure.

Thalictrum Thunbergii is a perennial herb belonging to Ranunculaceae family, and grows wild in fields or hilly districts. Studies on the components of this plant were

* Sho-machi, Tokushima (藤田栄一, 富松利明).

1) Doassans : Bull. soc. chim. France, **36**, 85(1880).
2) S. K. Vashistha, S. S. Siddiqui : J. Indian Chem. Soc., **18**, 641(1941).
3) T. Nakajima : J. Pharm. Soc. Japan, **65**, 422(1945).
4) S. S. Norkina, N. A. Pakhareva : J. Gen. Chem. U. S. S. R., **20**, 1720(1950) (C. A., **45**, 1306(1951)).
5) S. Yunusov, V. N. Progressov : J. Gen. Chem. U. S. S. R., **20**, 1197(1950); *Ibid.*, **22**, 1095(1952) (C. A., **45**, 1608(1951); **47**, 8084(1953)).