Notes

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-D-oxazoline with AcOK-Ac₂O.

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

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, Ac₂O, 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-β-
oxazoline (I) with AcOK-Ac₂O was examined.

The oxazoline (I) was heated in 30% AcOH to yield dl-threo-1-phenyl-2-benzoyl-
aminopropane-1,3-diol (II) as a sole product, which was then converted to dl-threo-
1-phenyl-2-benzoylaminono-1,3-diacectoxypropane (III) by heating in a mixture of anhyd.
AcOK and Ac₂O with or without AcOH.

The oxazoline (I) was then heated in a mixture of anhyd, AcOK and Ac₂O with-
out AcOH to yield dl-threo-2-phenyl-4-phenylacetoxyethyl-β-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 com-
 pound (III) with ring opening by heating in a mixture of anhyd, AcOK and Ac₂O with
AcOH. When the oxazoline (I) was heated in a mixture of anhyd, AcOK and Ac₂O

* Katakasu, Fukuoka (田口晃三, 友枝宗光).
with AcOH, however, (I) was immediately converted to the dl-threo-triacetyl 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 microanalytical 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-benzoylamino-1,3-diol (VI), the composition of which was confirmed by the finding that it was derived to pure (II) by acyl migration reaction. 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, AcO, 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: In the conformation of (I), the existence of a hydrogen bond between H of Cα-ΟΗ and ring-N provides evidence of their proximity. Accordingly the backside of Cα-ΟΗ, it is supposed, is widely spread. Therefore, the substitution of OH by acetoxy group at Cα is apt to occur with Walden inversion probably through S_N2.

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Experimental

dl-threo-1-Phenyl-2-benzoylaminopropane-1,3-diol (II)—a) From dl-threo-2-Phenyl-4-phenylhydroxymethyl-4-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), yield 20 mg. Anal. Calcd. for C_{19}H_{17}O_{2}N (II): N, 5.16. Found: N, 5.27.

b) From dl-threo- and erythro-1-Phenyl-2-benzoylmino-1,3-diacetoxypropane (V) via dl-threo- and erythro-1-Phenyl-2-benzoylamino-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. NaSO_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_{19}H_{17}O_{2}N (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 oil 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 AcOH 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 C₃₉H₃₅O₅N (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 Ac₂O 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 Ac₂O 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 C₃₉H₃₅O₅N (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 C₃₉H₃₅O₅N (III): N, 3.94. Found: N, 4.01.

c) From dl-threo-2-Phenyl-4-phenylacetoxymethyl-2-oxazoline (IV): A solution of 65 mg. of (IV) and 65 mg. of anhyd. AcOK in a mixture of 0.4 cc. of Ac₂O 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. Na₂SO₄, 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-2-oxazoline (IV)—A solution of 270 mg. of (I) and 270 mg. of anhyd. AcOK in 5 cc. of Ac₂O was boiled for 1 hr. and concentrated in vacuo to leave an oily residue. The benzene extract was washed with water, dried over anhyd. Na₂SO₄ 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 C₃₉H₃₅O₅N (IV): C, 73.20; H, 5.80; N, 4.75. Found: C, 73.39; H, 5.68; N, 4.71. I.R.: λmax 5.76, 8.07 μ(–OCOCH₃); 6.05 μ(–C==N–); 6.32, 6.67 μ(–C₆H₄). (Received July 30, 1956)

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U. D. C. 547.94:582.675.1 Thalictrum

Eichi 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 these 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 (福知山市, 岩松利明).