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32. Tanezo Taguchi, Munemitsu Tomoeda, and Toshitaka Koga : Studies in Stereochemistry. XIII. *dl*-Phenylserinols : A New Synthesis and its Stereochemical Findings. (5)[1]

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In the course of the new synthesis of N-benzoyl-*dl-threo*-phenylserinol which was reported in the previous papers, the formation of *dl-erythro*-1-phenyl-1,2-dibromoprop-3-yl benzimino ether[2] from *dl-erythro*-1-phenyl-1,2-dibromopropan-3-ol (I) and benzonitrile is involved as an intermediate. It is interesting both from the standpoints of synthetic method and stereochemistry to examine the usage of another nitrile instead of benzonitrile in the analogous process. For this purpose, acetonitrile was chosen as a nitrile and the whole process was studied.

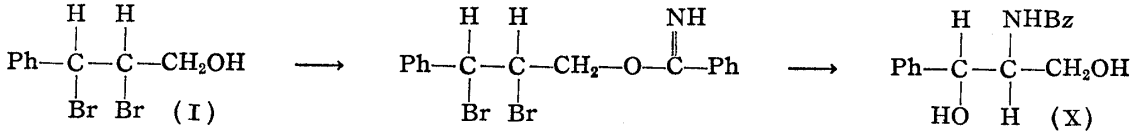

Chart 1.

A dehyd. ether solution of (I) and acetonitrile after saturation with hydrogen chloride was allowed to stand in the cold to give *dl-erythro*-1-phenyl-1,2-dibromoprop-3-yl acetimino ether (II) hydrochloride, which was converted to the free base (II) by treatment with sodium carbonate. Boiling of (II) in toluene with anhyd. sodium carbonate gave an oily product, which was thought by analogy to consist chiefly of *dl-threo*-2-methyl-4-phenyl-bromomethyl-Δ^2-oxazoline (III) by the similar finding reported previously.[2] The oil gave a picrate, though purification of the oil itself failed, which was treated with hydr. methanol to give *dl-threo*-1-phenyl-1-bromo-2-amino-3-acetoxypropane (IV) picrate as a result of ring opening of the oxazoline. Picrate of (IV) was then converted by treatment with hydrochloric acid in ethanol into the hydrochloride which was also obtained directly from the supposed oxazoline (III) by treatment with hydrochloric acid in methanol. The structure of (IV) hydrochloride was confirmed by the observation that catalytic reduction of C_1-Br followed by successive saponification and benzoylation gave a product identical with *dl*-1-phenyl-2-benzoylamino-3-benzoyloxypropane (VI) derived from *dl*-1-phenyl-2-benzoylaminopropan-3-ol (V).[3]

The pH of an aqueous solution of (IV) hydrochloride, upon boiling, rapidly decreased from 5.2 to 1.4, suggesting the liberation of hydrogen bromide by hydrolysis of the C_1-bromine atom. The solution was concentrated *in vacuo* and the remaining oily product was benzoylated with benzoyl chloride and pyridine to yield *dl-threo*-1-phenyl-2-benzoylamino-1,3-dibenzoyloxypropane (VII) and another substance in the ratio of 3 : 1. This substance was proved to be a mixture of *dl-threo*- and *-erythro*-1-phenyl-2-benzoyl-

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1) Part 4 : This Bulletin, 4, 487(1956).
2) Part 1 : J. Am. Chem. Soc., 78, 1468(1956).
3) Part 3 : This Bulletin, 4, 473(1956).

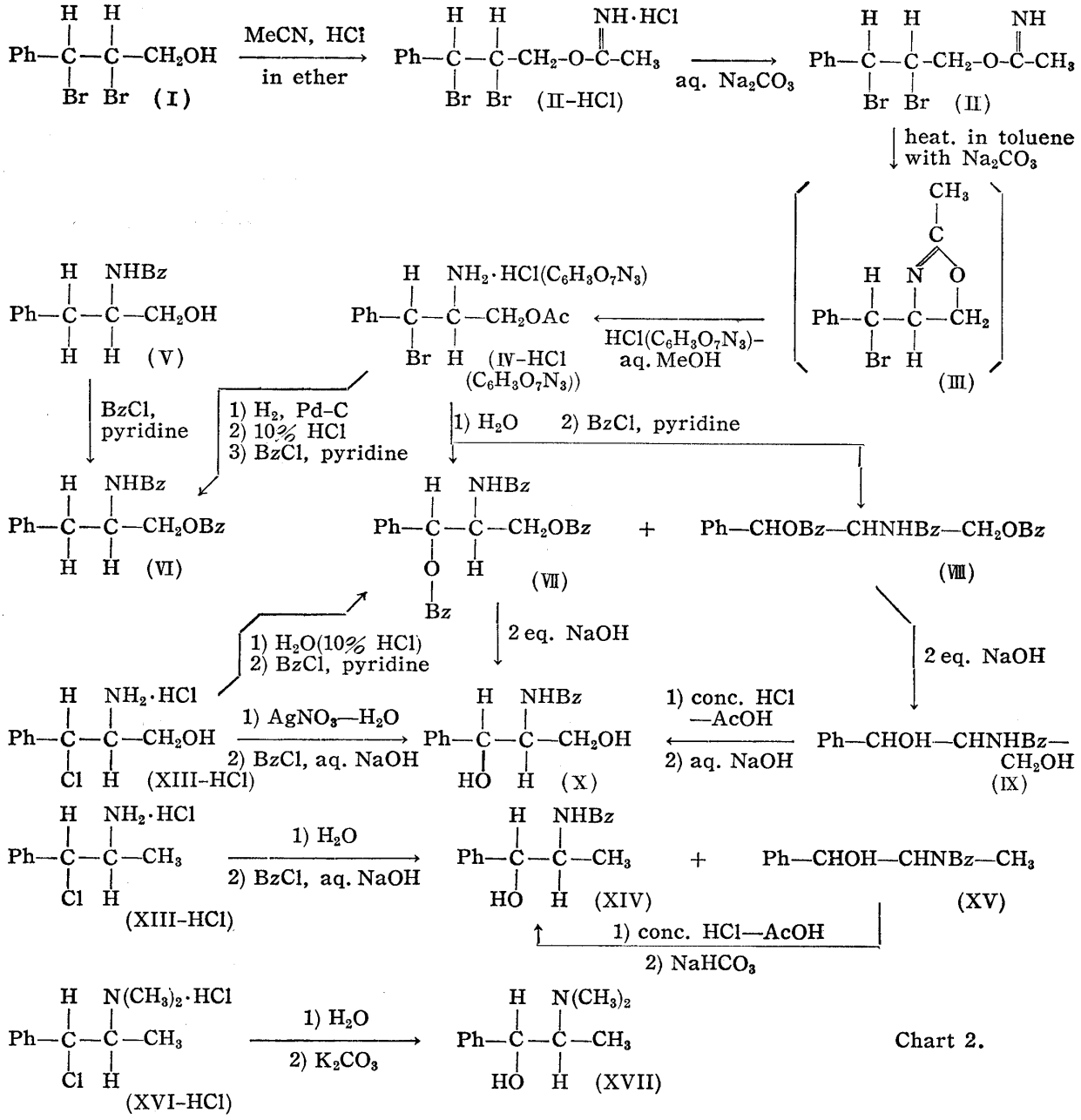


Chart 2.

amino-1,3-dibenzoyloxypropane (VIII) by the microanalytical data and by the fact that after alkaline hydrolysis of O-benzoyl it was introduced to overall *dl-threo*-1-phenyl-2-benzoylaminopropane-1,3-diol (X) by N→O and reverse acyl migration reactions which have been used for the identification of a mixture of *erythro*- and *threo*-β-aminoalcohols.[4] By the yield of the tribenzoate (VII and VIII) it was indicated that the fission of O-acetyl also occured in the course of hydrolysis. But it has been previously reported[4] that the similar hydrolysis followed by caustic soda treatment of the O-benzoyl analog (XI) of (IV)-HCl resulted in the formation of a mixture of epimeric N-benzoyl-*dl*-phenylserinols

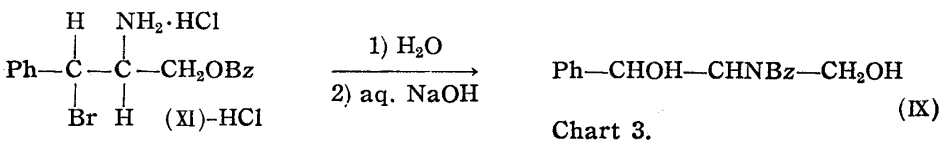


Chart 3.

4) Part 2 : *Ibid.*, 4, 80(1956).

(IX) and without fission of O-benzoyl. In the resulting mixture the predominance of the *threo*-isomer was beyond recognition, showing that the reaction may proceed through simple SN 1 without the participation of adjacent groups. In contrast with the O-benzoyl analog (XI), it is worth noting that the similar hydrolysis of the O-acetyl compound (IV) resulted clearly in the preference of *dl-threo*-phenylserinol over its *erythro*-isomer in yield, especially accompanying with the fission of O-acetyl radical. Therefore, to examine the effect of fission of O-acyl radical on the way of reaction on stereochemical results in the hydrolysis of C_1-halogen, *dl-threo*-1-phenyl-1-chloro-2-aminopropan-3-ol (XII) hydrochloride[5] was submitted to hydrolysis in water or 10% hydrochloric acid, followed by benzoylation with benzoyl chloride and pyridine, and gave rise to the *threo*-tribenzoate (VII) as a sole product. Also hydrolysis in water with silver nitrate, followed by N-benzoylation afforded *threo*-N-benzoate (X). Thus in the hydrolysis of *dl-threo*-1-phenyl-1-halo-2-aminopropan-3-ol hydrochloride the replacement of halogen by OH occurs predominantly in the *threo* manner when OH at C_3 is free or became free in the reaction course even if it has been masked by acyl. The furnishment with retention of configuration under SN 1 condition such as in the acidic hydrolysis might be due to the participation of adjacent group which is either OH or NH_2 in here-hydrolyzed compounds. The lone-pair electrons on N in these compounds seem to be lost by the salt-formation of NH_2 with hydrochloric acid, therefore the anchimeric property of NH_2 is supposed to decay. But to ascertain this point experimentally, *dl-threo*-1-phenyl-1-chloro-2-aminopropane (XIII) hydrochloride,[6] as a compound lacking OH at C_3, was hydrolyzed under the same conditions. The benzoylation of the resulted product gave rise to *dl-threo*-1-phenyl-2-benzoylaminopropan-1-ol (XIV) and a mixture of *dl-threo*- and *-erythro*-1-phenyl-2-benzoylaminopropan-1-ol (XV) in the formation ratio of 2 : 1, the latter of which was proved as itself by derivation of it to the pure *threo*-isomer (XIV) by N→O and reverse acyl migration reactions. Thus this stereochemical result showed the preferential formation of the *threo*-isomer (XIV) with retention over the *erythro*-isomer with inversion. Additionally also the acidic hydrolysis of (+)-*threo*-1-phenyl-1-chloro-2-dimethylaminopropane (XVI) hydrochloride[7] was examined and treated kinetically. Though the treatment resulted in the formation of (+)-*threo*-1-phenyl-2-dimethylaminopropan-1-ol (XVII) and no existence of its *erythro*-isomer was detected, the participation of amino group with hydrochloric acid was found to be negligible as indicated in Fig. 1; that

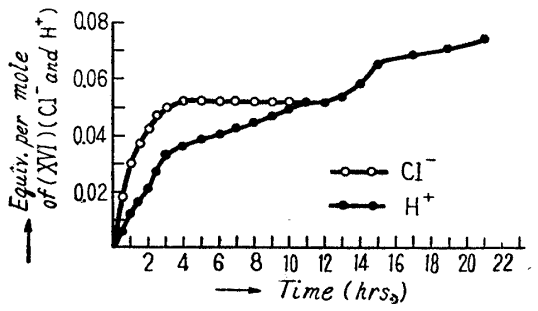


Fig. 1.

Titration Curves in Solvolysis of (+)—*threo*-1-Phenyl-1-chloro-2-dimethylaminopropane (XVI) Hydrochloride in Water (1 g. in 100 cc.) at 50°.

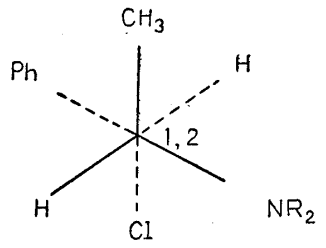
Liberated Cl^- was titrated with 0.01*N* $AgNO_3$ using K_2CrO_4 as an indicator. Liberated H^+ was titrated with 0.01*N* NaOH using methyl orange as an indicator which was adopted because the initial pH of (XVI-HCl) solution is 4.6. The titration curve with $AgNO_3$ was constructed from data which eliminated equivalence of $AgNO_3$ per 1 mole of HCl.

is, the inconsistency of titration curves by 0.01*N* sodium hydroxide and 0.01*N* silver nitrate in the range of 0 and 0.05 equivalents consumed suggests the probable participation of the amino group with hydrochloric acid narrowly in the limited range, but it is not enough for affecting the formation ratio of epimers. Therefore it is concluded that the one-sided formation of the *threo*-isomer (VII or X) in such acidic solvolysis of *dl-threo*-1-phenyl-1-halo-2-aminopropan-3-ol, as mentioned above, depends upon the par-

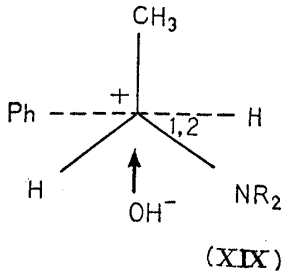
5) S. Ikuma, M. Nagawa : J. Pharm. Soc. Japan, **72**, 310(1952).
6) T. Taguchi, M. Kojima : This Bulletin, **3**, 4(1955).

ticipation of hydroxyl group at C_3, but not of amino group with hydrochloric acid, and the same conclusion is adapted to the case of the O-acetyl derivative (IV) which suffers the fission of O-acyl in the course of hydrolysis.

On the other hand, in spite of the negligible participation of amino group with hydrochloric acid, why was the preferential formation of *threo*-isomer over *erythro*-isomer observed commonly in the unimolecular displacement of C_1-halogen by OH^- in ψ-ephedrine series lacking hydroxyl group at C_3 of the present study or the other's ?[7~9] The reason is not clear, though, for example, the explanation for it is possible as follows: The carbonium cation (XIX) is transiently formed in the unimolecular displacement of 1-substituted ψ-ephedrine series, the conformation of which is more extensively believed as shown in (XVIII). The OH^- can approach C_1^+ easier from the reverse direction of the C_3-methyl group than along it. Thus the conformational requirement makes stereochemical result incline to the furnishment with retention in the *threo* manner.



(XVIII)



(XIX)

Chart 4.

The authors are indebted to the Ministry of Education for the Grant in Aid for Scientific Research. Their thanks are also due to the members of the Microanalytical Room of this Institute for the microanalyses.

Experimental

***dl-erythro*-1-Phenyl-1,2-dibromoprop-3-yl Acetimino Ether (II) Hydrochloride**—A solution of 30 g. of *dl-erythro*-1-phenyl-1,2-dibromopropan-3-ol (I)[2] and 4.5 g. of acetonitrile in 30 cc. of dehyd. ether was saturated with dry HCl at 0° and kept in the cold for several days. The deposited solid was filtered, washed with dehyd. ether, and dried, m.p. 151~152°. Recrystallization from MeOH-ether gave colorless needles, m.p. 157~159°; yield, 33 g. *Anal.* Calcd. for $C_{11}H_{14}ONBr_2Cl$ (II-HCl): N, 3.77. Found: N, 4.11.

***dl-erythro*-1-Phenyl-1,2-dibromoprop-3-yl Acetimino Ether (II)**—Thirty-three g. of (II)-HCl was ground with 170 cc. of 10% Na_2CO_3 in a mortar for 15 mins. and the remaining solid was filtered, washed with water, and dried, m.p. 107~111°. Recrystallization from acetone gave colorless prisms, m.p. 111°; yield, 29 g, *Anal.* Calcd. for $C_{11}H_{13}ONBr_2$ (II): C, 39.42; H, 3.61; N, 4.48. Found: C, 39.09; H, 3.82; N, 4.23.

Salts of *dl-threo*-1-Phenyl-1-bromo-2-amino-3-acetoxypropane (IV) Hydrochloride—a) From (II): A solution of 3 g. of (II), 6 g. of anhyd. Na_2CO_3, 0.3 cc. of H_2O[10] in 30 cc. of toluene was boiled with occasional shaking for 1 hr. The filtrate was concentrated *in vacuo* to leave an oily residue, which was dissolved in a solution of 0.9 cc. of conc. HCl in 50 cc. of MeOH, the solution was boiled for 10 mins., concentrated *in vacuo*, and with addition of ether deposited a solid. Recrystallization from MeOH-ether gave colorless needles, m.p. 154~155°(decomp.); yield, 830 mg. *Anal.* Calcd. for $C_{11}H_{15}O_2NBrCl$ (IV-HCl): C, 42.80; H, 4.91; N, 4.54. Found: C, 42.68; H, 4.63; N, 4.57.

b) From (IV)-Picrate: A solution of 350 mg. of (IV)-picrate, described below, and 0.07 cc. of conc. HCl in 50 cc. of 90% EtOH was concentrated *in vacuo* to leave a yellow residue. After extraction with benzene several times, the remaining solid was filtered and recrystallized from MeOH-ether to give colorless prisms, m.p. 155°(decomp.); yield, 180 mg.

Picrate: A solution of 1 g. of (II) and 2 g. of anhyd. Na_2CO_3 in 10 cc. of toluene was boiled with

7) K. Tanaka, T. Sugawa: J. Pharm. Soc. Japan, **72**, 1548(1952).
8) K. Tanaka: *Ibid.*, **70**, 212(1950).
9) K. Tanaka: *Ibid.*, **70**, 220(1950).
10) Addition of small volume of H_2O seemed to cause (II) to react with Na_2CO_3 smoothly.

occasional shaking for 1 hr. The filtrate was concentrated *in vacuo* to leave an oily residue, which was dissolved in a small amount of benzene and added with 3 cc. of a saturated benzene solution of picric acid to deposit a yellow solid. The soild (m.p. 115~117°) was filtered, dissolved in aq. MeOH, boiled for 1 hr., and concentrated to afford yellow crystals. Recrystallization from MeOH gave yellow prisms, m.p. 157°; yield, 620 mg. *Anal.* Calcd. for $C_{17}H_{17}O_9N_4Br$ (IV-Picrate): C, 40.72; H, 3.37: N, 11.18. Found: C, 40.67; H, 3.17; N, 11.27.

***dl*-1-Phenyl-2-benzoylamino-3-benzoyloxypropane (VI)**—a) From *dl*-1-Phenyl-2-benzoylaminopropan-3-ol (V)[3]: 200 mg. of (V) was added to a solution of 135 mg. of BzCl in 4 cc. of pyridine in the cold and the solution was kept for 6 hrs., and poured into ice water to deposit a solid. After filtration, the solid was recrystallized from 70% EtOH to give colorless needles, m.p. 149~152°; yield, 270 mg. *Anal.* Calcd. for $C_{23}H_{21}O_3N$(VI): C, 76.85; H, 5.90; N, 3.90. Found: C, 76.85; H, 5.82; N, 3.91.

b) From (IV)-HCl: One g. of (IV)-HCl was added to a pre-reduced suspension of 250 mg. of 20% Pd-C in 25 cc. of MeOH and the mixture hydrogenated at 11° under atmospheric pressure till 76.4 cc. of H_2-consumption during ca. 40 mins. The mixture was filtered and the filtrate was concentrated *in vacuo* to leave an oily residue, which then crystallized. The crystals were dissolved in 40 cc. of 10% HCl and the solution was boiled for 1 hr., concentrated to dryness *in vacuo*, and dried over NaOH to give an oily residue. To the residue was added 1.5 g. of BzCl in 15 cc. of pyridine and the solution kept over night in the cold. The reaction mixture was poured into ice water, extracted with AcOEt, and the AcOEt layer was washed with dil. H_2SO_4, sat. $NaHCO_3$, and dried over anhyd. Na_2SO_4. After concentration of the filtrate, crystals deposited, m.p. 147~149°, and were recrystallized from AcOEt to give colorless needles, m.p. 150~152°, alone and on admixture with a sample of (VI) obtained by procedure (a); yield, 1.10 g. *Anal.* Calcd. for $C_{23}H_{21}O_3N$ (VI): C, 76.85; H, 5.90; N, 3.90. Found: C, 77.12; H, 6.57; N, 4.39.

Hydrolysis of *dl-threo*-1-Phenyl-1-bromo-2-amino-3-acetoxypropane (IV) Hydrochloride: Formation of *dl-threo*-1-Phenyl-2-benzoylamino-1,3-dibenzoyloxypropane (VII) and a Mixture of *dl-threo*- and *-erythro*-1-Phenyl-2-benzoylamino-1,3-dibenzoyloxypropane (VIII)—A solution of 1 g. of (IV)-HCl in 100 cc. of H_2O was boiled for 2 hrs.; the pH of the solution changed from 5.2 to 1.4. The solution was concentrated to dryness *in vacuo* to give an oily residue. After drying over NaOH, benzoylation of the residue was effected by the usual method with 2.5 g. of BzCl in 20 cc. of pyridine. The reaction product was dissolved in AcOEt and crystals appeared, m.p. 189~193°; wt. 890 mg. Recrystallization from MeOH gave colorless needles, m.p. 194~195°, alone and on admixture with a sample of *dl-threo*-1-phenyl-2-benzoylamino-1,3-dibenzoyloxypropane (VII) described below. The needles (VII) were then converted into *dl-threo*-1-phenyl-2-benzoylaminopropane-1,3-diol (X) after the manner of the process described below.

Further concentration of the AcOEt mother-liquor afforded another crystals, m.p. 170~184°; wt. 310 mg. Several recrystallization from AcOEt or MeOH failed to obtain a further crop of (VII) and gave colorless needles of a supposed mixed substances, m.p. 173~190°. *Anal.* Calcd. for $C_{30}H_{25}O_5N$ (VIII): C, 75.13; H, 5.27: N, 2.92. Found: C, 75.05; H, 5.66; N, 2.93. The needles (VIII) were then converted into (X) via a mixture of *dl-threo-* and *-erythro*-1-phenyl-2-benzoylaminopropane-1,3-diol (IX) by the process described below.

Hydrolyses of *dl-threo*-1-Pheny-1-chloro-2-aminopropan-3-ol (XII) Hydrochloride[5]—a) In H_2O: Formation of (VII)—A solution of 110 mg. of (XII)-HCl in 10 cc. of H_2O was boiled for 2 hrs.; the pH of the solution changed from 5.2 to 1.4. The solution was concentrated to drynees *in vacuo* and dried over NaOH to leave an oily residue. Benzoylation of the residue was effected by the usual method with 360 mg. of BzCl in 3 cc. of pyridine to afford crystals, m.p. 191~192°. Recrystallization from MeOH gave colorless needles, m.p. 194~195°, alone and on admixture with a sample of (VII); yield, 170 mg.

b) In 10% HCl: Formation of (VII)—A solution of 66.5 mg. of (XII)-HCl in 10 cc. of 10% HCl was boiled for 4 hrs., concentrated to dryness *in vacuo*, and dried over NaOH to give an oily residue. Benzoylation of the residue was effected by the usual method with 150 mg. of BzCl in 2 cc. of pyridine to afford crystals, m.p. 181~191°; wt. 130 mg. Recrystallization from MeOH gave colorless needles, m.p. 195°, alone and on admixture with a sample of (VII); yield, 122 mg.

c) In aq. $AgNO_3$: Formation of *dl-threo*-1-Phenyl-2-benzoylaminopropane-1,3-diol (X)—100 mg. of (XII)-HCl was added to a solution of 210 mg. of $AgNO_3$ in 1.3 cc. of H_2O and the solution was boiled for 1 hr. After cooling, 10% HCl was added to the solution until excess of $AgNO_3$ was entirely converted into AgCl. After filtration, the filtrate was concentrated *in vacuo* to a small volume and benzoylated with 65 mg. of BzCl in 0.8 cc. of benzene and 10% NaOH after the manner of the Schotten-Baumann's method. The resulting solid product was treated with 9 mg. of NaOH in a small volume of MeOH for 1 hr. and the solution was concentrated *in vacuo* to afford crystals, m.p. 156°; wt. 60 mg. Recrystallization from AcOEt gave colorless needles, m.p. 163~164°, alone and on admixture with an authentic sample of (X)[1]; yield, 50 mg.

From the AcOEt mother-liquor of the recrystallization of the needles (X), only a trace of an oily residue was obtained.

***dl-threo*-1-Phenyl-2-benzoylamino-1,3-dibenzoyloxypropane (VII)**—200 mg. of *dl-threo*-1-phenyl-2-benzoylaminopropane-1,3-diol (X)[1] was benzoylated with 310 mg. of BzCl in 5 cc. of pyridine by means of the usual method to afford crystals. Recrystallization from MeOH gave colorless needles, m.p. 194~195°; Yield, 280 mg. *Anal.* Calcd. for $C_{30}H_{25}O_5N$ (VII): C, 75.13; H, 5.27; N, 2.92. Found: C, 74.81; H, 5.22; N, 3.34.

***dl-threo*-1-Phenyl-2-benzoylaminopropane-1,3-diol (X)**—a) From (VII): Derived from (IV)-HCl by Hydrolysis: A solution of 890 mg. of (VII) and 153 mg. of NaOH in 89 cc. of MeOH was boiled for 1 hr. and concentrated *in vacuo* to afford a solid residue. The solid was filtered, washed with satd. $NaHCO_3$ and then H_2O, and dried; m.p. 161~162°. Recrystallzation from AcOEt gave colorless needles, m.p. 163~164°, alone and on admixture with an authentic sample of (X); yield, 430 mg. *Anal.* Calcd. for $C_{16}H_{17}O_3N$ (X): C, 70.83; H, 6.32; N, 5.16. Found: C, 70.95; H, 5.99; N, 5.47.

b) From (VIII): Derived from (IV)-HCl by Hydrolysis, via a Mixture of *dl-threo*- and *-erythro*-1-Phenyl-2-benzoylaminopropane-1,3-diol (IX): A solution of 150 mg. of (VIII) and 27 mg. of NaOH in 15 cc. of MeOH was boiled for 1 hr., and concencentrated *in vacuo* to afford a solid residue. Recrystallization from AcOEt gave colorless needles, m.p. 122~123°; yield, 70 mg. *Anal.* Calcd. for $C_{16}H_{17}O_3N$ (IX): N, 5.16. Found: N, 4.88.

A solution of 70 mg. of the needles (IX) in a mixture of 280 mg. of conc. HCl and 560 mg. of AcOH was boiled for 5 mins. and concentrated *in vacuo* to leave an oily residue. The oil was dissolved in H_2O and the solution was made alkaline with 10% NaOH to leave an oil, which then crystallized, m.p. 161~163°; yield, 50 mg. Recrystallization from AcOEt gave colorless needles, m.p. 163~164°, alone and on admixture with an authentic sample of (X).

Hydrolysis of *dl-threo*-1-Phenyl-1-chloro-2-aminopropane (XIII) Hydrochloride: Formation of *dl-threo*-1-Phenyl-2-benzoylaminopropan-1-ol (XIV) and a Mixture of *dl-threo*- and *-erythro*-1-Phenyl-2-benzoylaminopropan-1-ol (XV)—A solution of 400 mg. of (XIII)-HCl in 40 cc. of H_2O was boiled for 2 hrs.; the pH of the solution changed from 5.4 to 1.2. After cooling, the solution was concentrated *in vacuo* to a small volume, and benzoylated with 300 mg. of BzCl in 3 cc. of benzene and 5 cc. of 10% NaOH by means of the Schotten-Baumann's method to afford crystals, m.p. 108~109°; wt. 520 mg. Recrystallization from 50% EtOH gave colorless needles, m.p. 127~128°, alone and on admixture with an authentic sample of (XIV)[6]; yield, 330 mg. *Anal.* Calcd. for $C_{16}H_{17}O_2N$ (XIV): C, 75.27; H, 6.71; N, 5.49. Found: C, 75.42; H, 6.60; N, 5.79.

After concentration of the 50% EtOH mother-liquor, another colorless needles (XV) were obtained and melted at 107~108°, wt. 170 mg.; further recrystallizations showed no raising of m.p. Then, a solution of 100 mg. of the needles in a mixture of 0.4 g. of conc. HCl and 0.8 g. of AcOH was boiled for 5 mins. and concentrated *in vacuo* to leave a solid residue. The solid was dissolved in H_2O and the solution was made alkaline by addition of $NaHCO_3$ to leave an oil, which then crystallized, m.p. 125~126°; wt. 80 mg. Recrystallization from 50% EtOH gave colorless needles, m.p. 127~128°, alone and on admixture with an authentic sample of (XIV).

Salts of (+)-*threo*-1-Phenyl-1-chloro-2-dimethylaminopropane (XVI) Hydrochloride—To a solution of 20 g. of $SOCl_2$ in 30 cc. of $CHCl_3$, 10 g. of (−)-N-methylephedrine hydrochloride was added, the solution was boiled for 2 hrs., and concentrated *in vacuo* to leave a red-brown oily residue. After treatment of the residue with a mixture of MeOH and ether, it crystallized and melted at 144~145° after drying over P_2O_5 *in vacuo*; yield, 5.7 g. Recrystallization from EtOH-ether gave colorless needles (hygroscopic), m.p. 146~147°. $[\alpha]_D^{20}$ +114.1° (in H_2O, c=4.79).[11]

Picrate: Recrystallization from MeOH gave yellow needles, m.p. 170~171° (decomp.). *Anal.* Calcd. for $C_{17}H_{19}O_7N_4Cl$ (XVI-Picrate): C, 47.83; H, 4.49; N, 13.13. Found: C, 47.50; H, 4.49; N, 13.09.

Hydrolysis of (+)-*threo*-1-Phenyl-1-chloro-2-dimethylaminopropane (XVI) Hydrochloride in H_2O; Formation of (+)-*threo*-1-Phenyl-2-dimethylaminopropan-1-ol (XVII)—A solution of 2 g. of (XVI)-HCl in 200 cc. of H_2O was boiled for 10 hrs.; the pH of the solution changed from 4.6 to 1.2. The solution was concentrated to one-half volume *in vacuo* and made alkaline with K_2CO_3 to leave an oily product, which was extracted with ether, washed with H_2O, and dried over K_2CO_3. After concentraion of the ethereal solution, the remaining oily product was purified by vacuum distillation to give colorless oil, b.p_2 82~92°[12]; yield, 958 mg. *Anal.* Calcd. for $C_{11}H_{17}ON$ (XVII): N, 7.81. Found: N, 7.72, $[\alpha]_D^9$: +48.1° (in MeOH, c=1.66).[12]

Picrate: To a solution of 736 mg. of the oil in 30 cc. of ether, 30 cc. of a saturated ethereal solution of picric acid was added and kept over night. The precipitated yellow needles were filtered, m.p. 148~150°; wt. 1.307 g. Recrystallization from 70% EtOH gave yellow needles, m.p. 152~153°,

11) m.p. 147°; $[\alpha]_D^{20}$ +100.5°.[7]

12) b.p_2 105~107°; $[\alpha]_D^{18}$ +48.5.[7] b.p_{24} 145~145.5°; $[\alpha]_D^{28}$ +48.0 (N. Nagai and S. Kanao: J. Pharm. Soc. Japan, **49**, 305(1929)).

alone and on admixture with a sample of (+)-*threo*-1-phenyl-2-dimethylaminopropan-1-ol (XVII) picrate[7]; yield, 1.251 g. *Anal.* Calcd. for $C_{17}H_{30}O_8N_4$(XVII-Picrate): C, 49.99; H, 4.95; N, 13.72. Found: C, 50.19; H, 4.91; N, 13.83.

Further concentration of the EtOH mother liquor afforded only a small crop of (XVII)-picrate, m.p. 150~151°.

Summary

In the new route to N-benzoyl-*dl*-*threo*-phenylserinol which has been reported in the previous papers, the formation of *dl*-*erythro*-1-phenyl-1,2-dibromoprop-3-yl benzimino ether is intermediately involved. In the present series acetonitrile was used instead of benzonitrile in the analogous process and the whole process was placed under consideration. It was found that in the acidic solvolysis of *dl*-*threo*-1-phenyl-1-bromo-2-amino-3-acetoxypropane hydrochloride, the displacement of C_1-Br by OH^- was effected with overall retention, particularly accompanying with the fission of O-acetyl group. In contrast with the same treatment of the O-benzoyl analog which as has been reported, resulted in inversion and retention without fission of the O-benzoyl group, the effect of the O-acetyl fission upon stereochemical results was examined and the mechanism was discussed.

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33. **Shin Matsuura**: The Structure of Cryptostrobin and Stropopinin, the Flavanones from the Heartwood of *Pinus strobus*.

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Erdtman[1] once isolated a flavanone, stropopinin (m.p. 225~227°), from the heartwood of *Pinus strobus* and proposed for its structure, C-methyl-5,7-dihydroxyflavanone. Lindstedt[2] also isolated stropopinin from the heartwood of *P. monticola* DOUGL. Later, Alvarez-Nóvoa and others[3] isolated another flavanone, cryptostrobin, m.p. 202~203°, from *P. strobus* and assumed it to be an isomer of stropopinin.

Lindstedt and others[4] obtained a mixture of stropopinin and cryptostrobin in a low yield by the condensation of 2-methylphloroglucinol and cinnamoyl chloride by Fujise's method,[5] and isolated *dl*-stropopinin, m.p. 231~233°, alone from this mixture. Methylation of this racemic compound with diazomethane afforded a monomethyl ether, m.p. 96~97°, and its further methylation with dimethyl sulfate and potassium carbonate in acetone yielded orange red 2′-hydroxy-3′-methyl-4′,6′-dimethoxychalcone (X). A mixture of chalcone and flavanone had been obtained by methylation of the monomethyl ether from natural cryptostrobin. Boiling of (X) with ethanolic sulfuric acid had afforded 5,7-dimethoxy-8-methylflavanone (XI). From these facts, they reported that stropopinin is probably 5,7-dihydroxy-8-methylflavanone (III) and its isomer, cryptostrobin, will then be the 6-methyl compound.

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