# *Studies on Antibiotics and Related Substances. III. Oxazolidines Derived from Some α-Hydroxy Schiff Bases and a Synthesis of* DL-*threo-1-p-Nitrophenyl-2-amino-1, 3-propanediol*[*]

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The present authors[1] previously reported that the reduction of *threo*-β-phenylserine[2] ethyl ester[3–6] by Raney nickel catalyst resulted in the formation of a new compound $C_{16}H_{17}NO_2$ (I), m. p. 138–139°C, which gave an N-acetyl oxazolidine derivative (II), m. p. 148–148.5°C, on acetylation with acetic anhydride at room temperature. II was led to DL-*threo*-1-*p*-nitrophenyl-2-amino-1, 3-propanediol by a synthetic route.

The present paper describes further investigations on the constitutions of I and II and also the synthesis of DL-chloramphenicol[7] from II in details.

The failure of II to hydrolyze under Kunz's conditions[8] demonstrated that II was an N-acetyl derivative. Consequently, the authors had assumed I to be an oxazolidine derivative. To establish the differentiation between oxazolidines and isomeric Schiff bases, the infrared and ultraviolet spectra of I and II

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[1] S. Umezawa and T. Suami, This Bulletin, 27, 477 (1954).

[2] E. Erlenmeyer, Jr., *Ber.*, **25**, 3445 (1892).

[3] G. Carrara and G. Weitnauer, *Gazz. chim. ital.*, **79**, 856 (1949).

[4] E. D. Bergmann, H. Bendas and W. Taub, *J. Chem. Soc.*, **1951**, 2673.

[5] G. W. Moersch, U. S., 2,538,792 (1951).

[6] K. N. F. Shaw and S. W. Fox, *J. Am. Chem. Soc.*, **75**, 3420 (1953).

[7] J. Controulis, M. C. Rebstock and H. M. Crooks, Jr., *J. Am. Chem. Soc.*, **71**, 2463 (1949).

[8] A. Kunz aud C. S. Hudson, *J. Am. Chem. Soc.*, **48**, 1982 (1926).

were measured. Infrared spectrum of I (Fig. 1) showed the presence of C=N bond in 1642 cm$^{-1}$, while II (acetylated product) showed no band in the absorption region of the C=N double bond and showed the triplet at 1089, 1168 and 1212 cm$^{-1}$, very likely because of the O—C—N system in the expected oxazolidine system[4], was found.

For the corresponding *p*-nitro derivatives (III and IV) of I and II, the infrared spectra were studied (Fig. 1). As was expected, DL-*threo*-1-*p*-nitrophenyl-2-benzylideneamino-1, 3-propanediol (III) prepared by the condensation of DL-*threo*-1-*p*-nitrophenyl-2-amino-1, 3-propanediol with benzaldehyde showed the presence of C=N bond in 1631 cm$^{-1}$, while the acetylated product (IV) of III showed no band in the absorption region of the C=N bond and showed the triplet at 1099, 1172 and 1217 cm$^{-1}$ [4].

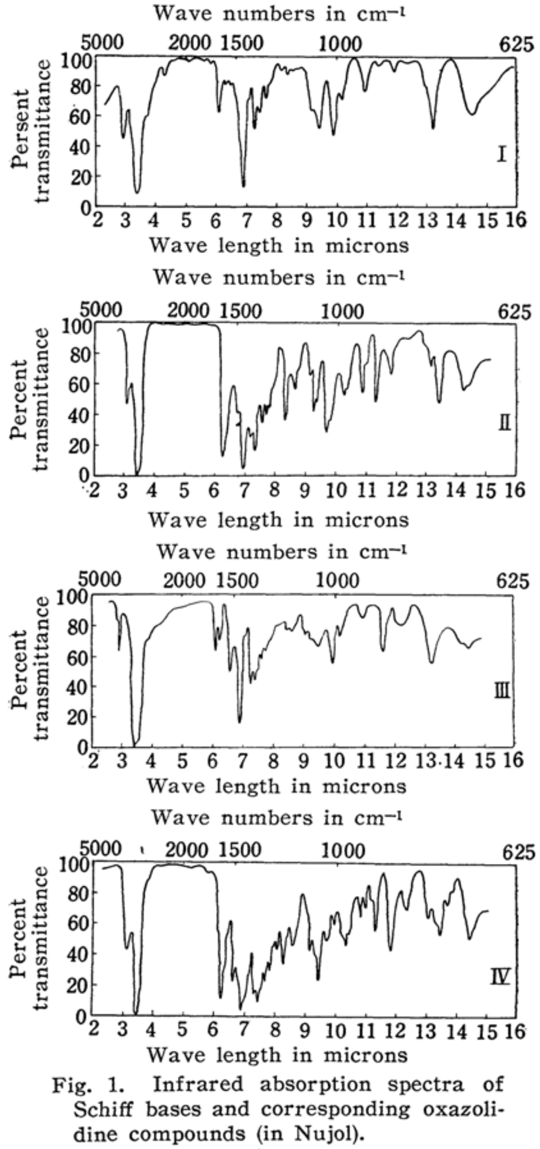

Fig. 1. Infrared absorption spectra of Schiff bases and corresponding oxazolidine compounds (in Nujol).

I) DL-*threo*-1-Phenyl-2-benzylideneamino-1, 3-propanediol.

II) DL-*threo*-N-Acetyl-2-phenyl-4-($\alpha$-hydroxybenzyl)oxazolidine.

III) DL-*threo*-1-*p*-Nitrophenyl-2-benzylideneamino-1, 3-propanediol.

IV) DL-*threo*-N-Acetyl-2-phenyl-4-($\alpha$-hydroxy-*p*-nitrobenzyl)oxazolidine.

In addition, the ultraviolet absorption spectra of I, II, III and IV were measured. As the ultraviolet absorption spectra of the Schiff base of ethyl *p*-nitrophenylserinate and its acetylated product had been reported by Bergmann et al.[9], DL-*threo*-1-phenyl-2-amino-1, 3-propanediol and DL-*threo*-1-*p*-nitrophenyl-2-amino-1, 3-propanediol were condensed with *p*-nitrobenzaldehyde to give the Schiff bases (I′, III′) respectively which were further acetylated with acetic anhydride to give N-acetyl oxazolidine derivatives (II′, IV′).

Absorption maxima of these derivatives are recorded in Table I. The melting points, analyses and yields are given in Tables II and III.

DL-*threo*-1-*p*-Nitrophenyl-2-(*p*-nitrobenzylidene)amino-1, 3-propanediol (III′) possessed an absorption maximum ($\lambda$ 2680 Å, log $\varepsilon$ 4.29) similar to that reported for the Schiff base of ethyl *p*-nitrophenylserinate ($\lambda$ 2700 Å, log $\varepsilon$ 4.39)[9]. Correspondingly, the acetylated product (IV′) of III′ possessed a maximum ($\lambda$ 2670 Å, log $\varepsilon$ 4.34) similar to that of the acetylated product of the Schiff base of ethyl *p*-nitrophenylserinate ($\lambda$ 2655 Å, log $\varepsilon$ 4.35)[9].

Acetylated product of the Schiff base obtained from DL-*threo*-1-phenyl-2-amino-1, 3-propanediol and benzaldehyde showed three maxima (2520, 2580 and 2640 Å).

The condensation products of DL-*threo*-1-phenyl-2-amino-1, 3-propanediol and DL-*threo*-1-*p*-nitrophenyl-2-amino-1, 3-propanediol with *o*-nitro and *m*-nitrobenzaldehyde were further prepared and then acetylated to give oxazolidine derivatives, which failed to hydrolyze under Kunz's conditions[8]. The melting points, analyses and yields of these products are given in Table II and III.

Two isomeric structures—one with the oxazolidine ring containing the oxygen of the primary alcohol and the other with the oxazolidine ring containing the oxygen of the secondary alcohol—were expected for the acetylated product II which was prepared from the Schiff base I.

Considering the fact that II was not further acetylated on standing with acetic anhydride for three hours at room tempera-

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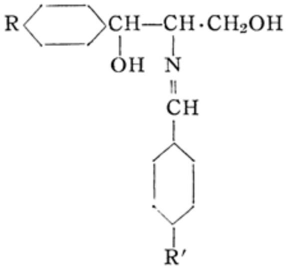
[9] E. D. Bergmann, H. Bendas and Ch. Resnick, *J. Chem. Soc.*, **1953**, 2564.

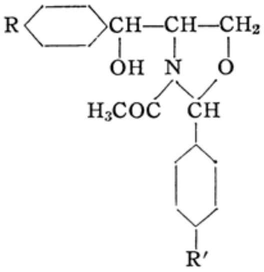
TABLE I

ULTRAVIOLET ABSORPTION MAXIMA OF SCHIFF BASES AND N-ACETYL OXAZOLIDINE DERIVATIVES

| Derivatives | Wave Lengths and Intensities of Maxima (in Chloroform) | |
|---|---|---|
| | $\lambda_{max.}$ (Å) | log $\varepsilon_{max.}$ |
| I | 2510 | 3.59 |
| II | 2580 | 2.68 |
| III*** | 2760 | 4.14 |
| IV | 2680 | 4.30 |
| I'** | 2660 | 4.16 |
| II'* | — | — |
| III' | 2680 | 4.29 |
| IV' | 2670 | 4.34 |



I R=H, R'=H
III $R=NO_2$, R'=H
I' R=H, $R'=NO_2$
III' $R=NO_2$, $R'=NO_2$



II R=H, R'=H
IV $R=NO_2$, R'=H
II' R=H, $R'=NO_2$
IV' $R=NO_2$, $R'=NO_2$

* This derivative did not crystallize.

** This derivative was reported recently by S. Umezawa et al.10)

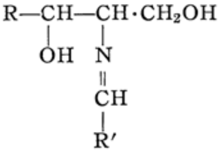
*** This derivative was reported by Iliceto et al.11)

ture, while DL-*threo*-1-phenyl-2-amino-1, 3-propanediol was acetylated by acetic anhydride in half an hour at room temperature to yield DL-*threo*-1-phenyl-2-acetamido-3-acetoxy-1-propanol12), II was considered to be of the former structure combined with the oxygen of the primary alcohol.

Recently, two analogous cases were reported. McCasland et al.13) demonstrated that the condensation product of 2-amino-cyclohexanol and benzaldehyde had the structure

TABLE II

CONDENSATION PRODUCTS OF AMINOALCOHOLS AND ALDEHYDES (SCHIFF BASES)



$$R{-}\underset{\displaystyle OH}{\underset{|}{C}H}{-}\underset{\displaystyle \overset{\|}{\underset{\displaystyle \underset{\displaystyle R'}{\underset{|}{}}}{CH}}}{\underset{|}{N}}\overset{}{CH}\cdot CH_2OH$$

| R | R' | Formula | M. p., °C | Yield, % | Carbon, % | | Hydrogen, % | | Nitrogen, % | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Calcd. | Found | Calcd. | Found | Calcd. | Found |
| Phenyl | Phenyl | $C_{16}H_{17}NO_2$ | 138–139 | 78.6 | — | — | — | — | — | — |
| Phenyl | *o*-Nitrophenyl | $C_{16}H_{16}N_2O_4$ | 122–123 | 50.1 | — | — | — | — | 9.33 | 9.17 |
| Phenyl | *m*-Nitrophenyl | $C_{16}H_{16}N_2O_4$ | 98–99 | 11.1 | — | — | — | — | 9.33 | 9.45 |
| *p*-Nitrophenyl | Phenyl | $C_{16}H_{16}N_2O_4$ | 158–159* | 77.5 | 63.99 | 64.24 | 5.37 | 5.33 | — | — |
| *p*-Nitrophenyl | *o*-Nitrophenyl | $C_{16}H_{15}N_3O_6$ | 140–141** | 55.3 | — | — | — | — | 12.17 | 11.97 |
| *p*-Nitrophenyl | *m*-Nitrophenyl | $C_{16}H_{15}N_3O_6$ | 135–136.5 | 49.2 | — | — | — | — | 12.17 | 12.52 |
| *p*-Nitrophenyl | *p*-Nitrophenyl | $C_{16}H_{15}N_3O_6$ | 173–174 | 55.3 | — | — | — | — | 12.17 | 12.32 |

* M. p. reported by Iliceto et al.11) was 155–156°C.

** M. p. reported by Iliceto et al.11) was 144–146°C.

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10) T. Suami, I. Uchida and S. Umezawa, This Bulletin, **29**, 417 (195 ).

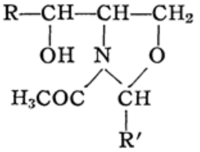
11) A. Iliceto and E. Scoffone, *Gazz. chim. ital.*, **81**, 133 (1951).

12) L. M. Long and H. D. Troutman, *J. Am. Chem. Soc.*, **71**, 2469 (1949).

13) G. E. McCasland and E. C. Horswill, *J. Am. Chem. Soc.*, **73**, 3923 (1951).

TABLE III

ACETYLATION PRODUCTS OF SCHIFF BASES (OXAZOLIDINE DERIVATIVES)



| R | R′ | Formula | M. p., °C | Yield, % | Carbon, % |  | Hydrogen, % |  | Nitrogen, % |  |
|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | Calcd. | Found | Calcd. | Found | Calcd. | Found |
| Phenyl | Phenyl | $C_{18}H_{19}NO_3$ | 148–148.5 | 42.9 | 72.70 | 72.97 | 6.44 | 6.49 | 4.71 | 4.64 |
| *p*-Nitrophenyl | Phenyl | $C_{18}H_{18}N_2O_5$ | 178–180 | 35.1 | 63.15 | 63.25 | 5.30 | 5.31 | — | — |
| *p*-Nitrophenyl | *o*-Nitrophenyl | $C_{18}H_{17}N_3O_7$ | 242–244 | 53.5 | — | — | — | — | 10.85 | 10.98 |
| *p*-Nitrophenyl | *m*-Nitrophenyl | $C_{18}H_{17}N_3O_7$ | 202–203.5 | 53.5 | — | — | — | — | 10.85 | 10.40 |
| *p*-Nitrophenyl | *p*-Nitrophenyl | $C_{18}H_{17}N_3O_7$ | 170–171 | 62.4 | — | — | — | — | 10.85 | 11.12 |

of a Schiff base, while its N-benzoyl derivative had that of oxazolidine. As mentioned above, Bergmann et al.[9] also described that the condensation products of the *threo* and *erythro*-forms of *p*-nitrophenylserine ethyl ester with *p*-nitrobenzaldehyde had the structures of Schiff bases and acetylation converted them into diastereoisomeric oxazolidines.

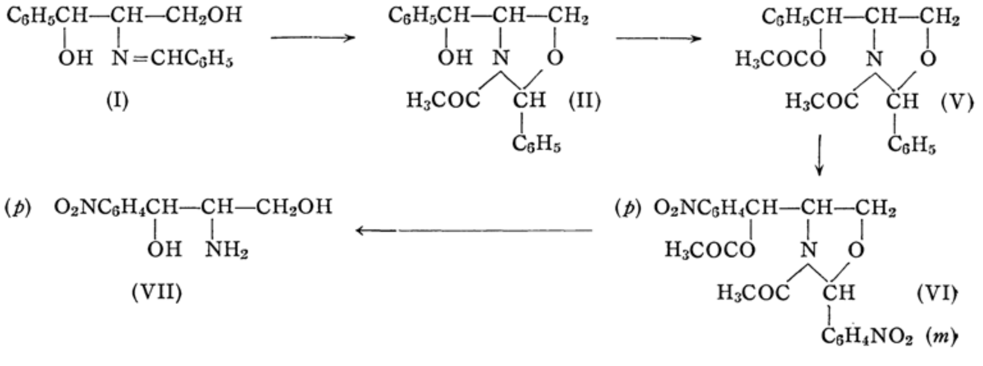
It is of interest to extend the observation that the acetylation of the Schiff bases of *β*-phenylserinol and its derivatives converted them into oxazolidine compounds.

Schiff base I was easily hydrolyzed on warming with 0.95N hydrochloric acid at 60°C for one hour, to give DL-*threo*-1-phenyl-2-amino-1, 3-propanediol and benzaldehyde.

It is interesting that the rate of catalytic reduction of the C=N bond in Schiff base I was very slow and practically stopped after the reduction of the ester group. In this regard, Goldberg and Nace[14] reported recently on the selected reduction of the unsaturated Schiff base system C=C—C=N.

Starting from the above described DL-*threo*-N-acetyl-2-phenyl-4-(*α*-hydroxybenzyl) oxazolidine II, DL-chloramphenicol[7], an important antibiotic found by scientists of Parke, Davis and Company, was synthesized through the route described below. Further acetylation of II with acetic anhydride in pyridine gave a viscous product (V), which, on nitration with mixed acid under dry ice-cooling for thirty minutes and then ice-cooling for thirty minutes, and finally at 15°C for thirty minutes, gave a viscous product containing a small amount of crystals. The latter, after recrystallization, appeared to be the diacetyl derivative of 2-(*m*-nitrophenyl)-4-(*α*-hydroxy-*p*-nitrobenzyl)oxazolidine (VI), m. p. 192–193°C. The diacetyl derivative gave one mole of acetic acid on hydrolysis under Kunz's conditions[8], demonstrating that VI is an N, O-diacetyl oxazolidine compound. VI gave *m*-nitrobenzaldehyde on refluxing with 4.5 N hydrochloric acid.

The crude, viscous-oily, nitration product containing VI mainly, was refluxed with 3 N hydrochloric acid for three hours and the reaction solution was concentrated by evaporation under reduced pressure, followed by pH adjustment with 5 N sodium hydroxide



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[14] E. P. Goldberg and H. R. Nace, *J. Am. Chem. Soc.*, 77, 359 (1955).

to 10, to give DL-*threo*-1-*p*-nitrophenyl-2-amino-1, 3-propanediol (VII) melting at 143.5–145°C, which did not depress the melting point of an authentic sample obtained by the synthetic route from *p*-nitroacetophenone[15].

VII was acylated with dichloroacetamide to yield DL-chloramphenicol.

## Experimental

**Reduction of DL-*threo*-Phenylserine Ethyl Ester with Raney Nickel Catalyst.—DL-*threo*-1-Phenyl-2-benzylideneamino-1, 3-propanediol (I).**—Ten grams of DL-*threo*-phenylserine ethyl ester[3–6] was dissolved in 50 cc. of absolute ethanol and reduced in an autoclave for six hours, at 50–60°C under 110 atms. $H_2$ with 17 g. of Raney nickel W-4[16]. After standing overnight, the catalyst was filtered off and the solvent was removed under reduced pressure to yield a pale yellow oily residue. After it was settled in a desiccator overnight, colorless crystals appeared in it. The crystals were collected and washed with ether to yield 2.5 g. (41.0%) of colorless crystals. They were recrystallized twice from ethanol. Colorless plates, m. p. 138–139°C.

*Anal.* Found: C, 75.26; H, 6.74; N, 5.53. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49%.

Infrared (Fig. 1) and ultraviolet absorption spectra (Table I) were measured.

2.0 g. of I was hydrolyzed for one hour with 10 cc. of 0.95 N hydrochloric acid at 60°C. Benzaldehyde which separated on the solution was extracted with ether, and the aqueous layer was concentrated at 40°C under reduced pressure. The residue was redissolved in 5 cc. of cold water. After an excess of potassium carbonate was added to the solution, it was extracted five times with ethyl acetate. The combined ethyl acetate solution was dried over anhydrous sodium sulfate and concentrated under reduced pressure to yield 1.0 g. (76.4%) of a pale yellow oil. This oil crystallized on standing at room temperature with two drops of ethyl acetate. The crystals were recrystallized twice from ethyl acetate. Yield, 0.59 g. (45.1%). Colorless crystals, m. p. 87–88°C. They did not depress the melting point of an authentic sample of DL-*threo*-1-phenyl-2-amino-1, 3-propanediol obtained by the method of Controulis et al.[7].

**Acetylation of DL-*threo*-1-Phenyl-2-benzylideneamino-1, 3-propanediol.—DL-*threo*-N-Acetyl-2-phenyl-4-(α-hydroxybenzyl) oxazolidine (II).**—2.0g. of DL-*threo*-1-phenyl-2-benzylideneamino-1, 3-propanediol (I) was added to 4.0 cc. of acetic anhydride with agitation at room temperature. The colorless crystals which appeared immediately were collected and washed with ether to yield 1.9 g. of the crude product melting at 145–146°C (81.5%). This was recrystallized twice from methanol to yield 1.0 g. (42.9%) of colorless crystals melting at 148–148.5°C. This product was not further acetylated on standing with ten volumes of acetic anhydride for three hours at room temperature. This failed to hydrolyze under Kunz's conditions[8].

*Anal.* Found: C, 72.97; H, 6.49; N, 4.64. Calcd. for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.44; N, 4.71%.

Infrared (Fig. 1) and ultraviolet absorption spectra (Table I) were measured.

**Condensation of DL-*threo*-1-Phenyl-2-amino-1, 3-propanediol and DL-*threo*-1-*p*-Nitrophenyl-2-amino-1, 3-propanediol with Benzaldehyde, *o*-, *m*- and *p*-Nitrobenzaldehyde.**—DL-*threo*-1-Phenyl-2-benzylideneamino-1, 3-propanediol (I) and other Schiff bases were all prepared by essentially the same procedure.

**DL-*threo*-1-Phenyl-2-benzylideneamino-1, 3-propanediol** (I). — 1.0 g. of DL-*threo*-1-phenyl-2-amino-1, 3-propanediol was added to a mixture of 0.7 g. of freshly distilled benzaldehyde and a small quantity of ethyl acetate. After the mixture was stirred at room temperature for fifteen minutes, ethyl acetate was removed in vacuo. The residual solid was washed with ether to obtain 1.5 g. (98.2%) of a colorless powder melting at 133–135°C.

It was recrystallized twice from ethanol. Yield, 1.2 g. (78.6%). Colorless crystals, m. p. 138–139°. They did not depress the melting point of the sample of I obtained by the reduction of DL-*threo*-phenylserine ethy ester with Raney nickel catalyst.

DL-*threo*-1-Phenyl-2-(*o*-nitrobenzylidene) amino-1, 3-propanediol was purified by recrystallization from acetone, DL-*threo*-1-*p*-nitrophenyl-2-(*m*-nitrobenzylidene) amino-1, 3-propanediol and DL-*threo*-1-*p*-nitrophenyl-2-(*p*-nitrobenzylidene)amino-1, 3-propanediol were purified by recrystallization from methanol, whereas, DL-*threo*-1-phenyl-2-(*m*-nitrobenzylidene)amino-1, 3-propanediol was not purified. The melting points, analyses and yields are given in Table II.

**Acetylation of the Above Described Schiff Bases.**—Acetylation products of DL-*threo*-1-phenyl-2-(*o*-nitrobenzylidene)amino-1, 3-propanediol and DL-*threo*-1-phenyl-2-(*p*-nitrobenzylidene)amino-1, 3-propanediol[10] failed to crystallize. The following four products were obtained as crystals.

Acetylated products (oxazolidine derivatives) were all prepared by essentially the same procedure as that of DL-*threo*-N-acetyl-2-phenyl-4-(α-hydroxybenzyl)oxazolidine (II), but DL-*threo*-N-acetyl-2-phenyl-4-(α-hydroxy-*p*-nitrobenzyl) oxazolidine was prepared by the following procedure.

**DL-*threo*-N-Acetyl-2-phenyl-4-(α-hydroxy-*p*-nitrobenzyl)oxazolidine** (IV).—0.5 g. of III was added to 2.0 cc. of acetic anhydride. After standing at room temperature for two hours, the reaction solution was diluted with water, neutralized with sodium bicarbonate, and extracted with ethyl acetate. The ethyl acetate solution was dried over anhydrous sodium sulfate, and evaporated under reduced pressure to yield 0.5 g. of a pale yellow oily residue. It was dissolved in a small quantity of ether and added to an equal volume of petroleum ether. After standing overnight in a refrigerator, 0.3 g. (52.6%) of colorless crystals were obtained and recrystallized from acetone. Yield, 0.2 g. (35.1%). Colorless crystals, m. p. 178–180°C.

*Anal.* Found: C, 63.25; H, 5.31. Calcd. for $C_{18}H_{18}N_2O_5$: C, 63.15; H, 5.30%.

This failed to hydrolyze under Kunz's condi-

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[15] L. M. Long and H. D. Troutman, *J. Am. Chem. Soc.*, **71**, 2473 (1949).

[16] A. A. Pavlic and H. Adkins, *J. Am. Chem. Soc.*, **68**, 1471 (1946).

tions[8]. Infrared (Fig. 1) and ultraviolet absorption spectra (Table I) were measured.

DL-*threo*-N-Acetyl-2-(*o*-nitrophenyl)-4-($\alpha$-hydroxy-*p*-nitrobenzyl)oxazolidine and DL-*threo*-N-acetyl-2-(*m*-nitrophenyl)-4-($\alpha$-hydroxy-*p*-nitrobenzyl)oxazolidine were purified by recrystallization from acetone. DL-*threo*-N-Acetyl-2-(*p*-nitrophenyl)-4-($\alpha$-hydroxy-*p*-nitrobenzyl)oxazolidine (IV′) was purified by recrystallization from acetone-petroleum ether. The melting points, analyses and yields are given in Table III.

**Synthesis of DL-Chloramphenicol from II.—DL-*threo*-N, O-Diacetyl-2-phenyl-4-($\alpha$-hydroxybenzyl) oxazolidine (V).**—5.5 g. of II was dissolved in 14.0 cc. of dry pyridine and 8.0 cc. of acetic anhydride. After standing at room temperature for forty-eight hours, the solution was poured into ice water. The mixture was extracted with ethyl acetate and the ethyl acetate solution was washed with 0.5N hydrochloric acid, 1% sodium carbonate solution, and water. Then the ethyl acetate solution was concentrated in vacuo and 6.4 g. of a yellow viscous oil was obtained.

**DL-*threo*-N, O-Diacetyl-2-(*m*-nitrophenyl)-4-($\alpha$-hydroxy-*p*-nitrobenzyl)oxazolidine (VI).**—6.4 g. of V was added to 30 cc. of a 1 : 1 mixture of nitric acid (d. 1.38) and sulfuric acid (d. 1.84) with dry ice cooling and vigorous shaking. After thirty minutes, the reaction flask was transferred to an ice bath for thirty minutes, and then kept at room temperature for thirty minutes. The solution was quenched on 200 g. of ice and immediately neutralized with sodium bicarbonate. The product was extracted five times with ethyl acetate and the combined ethyl acetate solution was washed with cold water, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to yield 8.0 g. (98.8%) of a pale yellow viscous product. The crude product was added to absolute acetone to yield 0.97 g. (12.0%) of colorless crystals melting at 192–193°C.

*Anal.* Found: C, 55.45; H, 4.24; N, 9.44; O-acetyl, 11.0. Calcd. for $C_{20}H_{19}N_3O_8$: C, 55.94; H, 4.46; N, 9.79; O-acetyl 10.0%.

This product gave one mole of acetic acid on hydrolysis under Kunz's conditions[8].

0.5 g. of these crystals were refluxed for four hours with 18 cc. of 4.5 N hydrochloric acid and then settled at room temperature overnight. Pale yellow needles melting at 56–57°C appeared in the solution and they did not depress the melting point of an authentic sample of *m*-nitrobenzaldehyde.

The solution remaining after the Kunz's determination for O-acetyl was evaporated under reduced pressure to remove acetone. The colorless crystals which precipitated in the solution were collected and washed with water. The crystals melted at 201–203°C and did not depress the melting point of DL-*threo*-N-acetyl-2-(*m*-nitrophenyl)-4-($\alpha$-hydroxy-*p*-nitrobenzyl)oxazolidine.

**DL-*threo*-1-*p*-Nitrophenyl-2-amino-1, 3-propanediol (VII).**—7.2 g. of crude VI was refluxed for three hours with 80 cc. of 3 N hydrochloric acid. The solution was washed with ether to remove an oily precipitate of nitrobenzaldehyde and concentrated under reduced pressure. The residue was dissolved in 5 cc. of cold water and the pH of the solution was adjusted to 10 with 5 N sodium hydroxide with ice cooling. After standing overnight in a refrigerator, 1.75 g. (49.2%) of the crude base melting at 129–133°C was obtained. The base was repeatedly recrystallized from hot water to yield pale yellow crystals melting at 143.5–145°C which did not depress the melting point of an authentic sample obtained by the method of Long et al.[15]

**DL-*threo*-1-*p*-Nitrophenyl-2-dichloroacetamido-1, 3-propanediol.**—2.0 g. of VII was finely mixed with 1.2 g. of dichloroacetamide, and the mixture was heated on a boiling water bath for three hours, and dissolved in ethyl acetate. The solution was filtered, washed with 0.5 N hydrochloric acid to remove the unreacted free base and then with water, dried over anhydrous sodium sulfate, passed through a short chromatographic column of 10 g. alumina to remove the coloring matter and then evaporated under reduced pressure to yield 2.3 g. of a crystalline residue melting at 128–137°C. It was recrystallized from ethylene dichloride and washed with ether. Pale yellow crystals, m. p. 147–149°C. Yield, 1.2 g. (39.1%). The product was further recrystallized from ethyl acetate-petroleum ether to yield colorless crystals melting at 149–150°C, which did not depress the melting point of an authentic sample obtained by the method of Long et al.[15]

One mg. of these crystals was equivalent to 512 γ of natural chloramphenicol[17] by the cup assay method (test organism E.coli).

## Summary

1) When Erlenmeyer's $\beta$-phenylserine ethyl ester was reduced with Raney nickel catalyst, DL-*threo*-1-phenyl-2-benzylideneamino-1, 3-propanediol (a Schiff base) was obtained as a main product. The structure was demonstrated by means of its infrared and ultraviolet absorption spectra.

2) It was found that DL-*threo*-1-phenyl-2-benzylideneamino-1, 3-propanediol gave DL-*threo*-N-acetyl-2-phenyl-4-($\alpha$-hydroxybenzyl) oxazolidine on acetylation with acetic anhydride.

3) The condensation products of DL-*threo*-1-phenyl-2-amino-1, 3-propanediol and DL-*threo*-1-*p*-nitrophenyl-2-amino-1, 3-propanediol with benzaldehyde, *o*-, *m*- and *p*-nitrobenzaldehyde were prepared and acetylated to give corresponding oxazolidine derivatives, which failed to hydrolyze under Kunz's conditions. Infrared and ultraviolet absorption spectra of some of these compounds were observed. Acetylated derivatives failed to show the characteristic absorption of $>C=N-$ bond in the 1660–1610 cm$^{-1}$ region.

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[17] J. Ehrlich, Q. R. Bartz, R. M. Smith and D. A. Joslyn, *Science*, 106, 417 (1947).

4) DL-Chloramphenicol was synthesized from DL-*threo*-N-acetyl-2-phenyl-4-($\alpha$-hydroxybenzyl)oxazolidine.

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