crystallizations from acetic acid raised the melting point to 259–260° dec.

Anal. Calcd. for $C_{13}H_{10}N_2O_6S$: C, 48.44; H, 3.13; N, 8.69. Found: C, 48.27, 48.33; H, 3.19, 2.95; N, 8.50, 8.41.

Ethyl N-*p'*-Nitrobenzenesulfonyl-N-(3,3-diethoxy-2-hydroxypropyl)-*p*-aminobenzoate (IV).—A mixture of 12.0 g. of I, 5.8 g. of 2,3-oxidopropionaldehyde diethyl acetal and 3 drops of pyridine was heated at 135° for 2 hours. The dark brown melt was crystallized from 60 ml. of 2-propanol to give 15.9 g. (93.1% yield) of IV, m.p. 109–112°. Several recrystallizations from 2-propanol gave material melting 115–117°.

Anal. Calcd. for $C_{22}H_{28}N_2O_9S$: C, 53.22; H, 5.68; N, 5.64. Found: C, 53.33, 53.38; H, 5.60, 5.53; N, 5.73, 5.69.

Diethyl N-[N'-*p'*-Nitrobenzenesulfonyl-*p*-aminobenzoyl]-L-glutamate (III).—Diethyl *p*-aminobenzoyl-L-glutamate (3.22 g.) was dissolved in 6.3 ml. of pyridine and 2.22 g. of *p*-nitrobenzenesulfonyl chloride added. After the initial reaction the mixture was warmed on the steam-bath for one hour and then poured into 100 ml. of ice-water. The product collected by filtration, weighed 4.5 g. and melted at 154–161°. Several recrystallizations from dilute acetone raised the melting point to 165–167°.

Anal. Calcd. for $C_{22}H_{25}N_3O_9S$: C, 52.06; H, 4.96; N, 8.28. Found: C, 58.18; H, 4.97; N, 8.11.

Diethyl N-[N'-*p'*-Nitrobenzenesulfonyl-N'-(3,3-diethoxy-2-hydroxypropyl)-*p*-aminobenzoyl]-L-glutamate (IVa).—A mixture of 5.1 g. of III and 1.75 g. of 2,3-oxidopropionaldehyde diethyl acetal, and 3 drops of pyridine was fused at 140° for 2 hours. The dark melt was crystallized from 30 ml. of 2-propanol to give 5.3 g. (81.2% yield) of IVa which melted at 130–134°. Recrystallization from ethyl acetate gave white crystals, m.p. 136–138°.

Anal. Calcd. for $C_{29}H_{39}N_3O_{12}S$: C, 53.28; H, 6.01; N, 6.43. Found: C, 53.32, 53.68; H, 5.76, 5.84; N, 6.30, 6.21.

N-(*p'*-Nitrobenzenesulfonyl)-N-(2,3-dihydroxypropyl)-*p*-aminobenzoic Acid (V).—After fusion at 135° for 2 hours a mixture of 14.00 g. of I, 5.6 g. of glycidol acetate and 5 drops of pyridine was dissolved in 100 ml. of 80% ethanol and 40 ml. of 10% sodium hydroxide. This solution was heated under reflux for 1 hour, the alcohol distilled under vacuum, and the residue diluted with 100 ml. of H_2O. The cloudy solution was extracted with ethyl acetate and the extract discarded. Acidification of the aqueous fraction followed by extraction gave an acid fraction which when crystallized from 2-propanol weighed 6.8 g. (42.9% yield). It melted at 175–185°. After recrystallization from 2-propanol an analytical sample, m.p. 205–209°, was obtained.

Anal. Calcd. for $C_{16}H_{16}N_2O_8S$: C, 48.48; H, 4.07; N, 7.07. Found: C, 48.59, 48.74; H, 3.86, 4.10; N, 7.08, 7.21.

***p*-[(2-Amino-4-hydroxy-6-pteridylmethyl)-*p'*-nitrobenzenesulfonylamino]-benzoic Acid (VII).**—A heterogeneous mixture of 4.96 g. of hydroxyacetal IV, 5.26 g. of sodium dichromate, 35 ml. of chlorobenzene, 7 ml. of sulfuric acid and 23 ml. of water was stirred at 2–5° for 3 hours. The dark reaction mixture was diluted with ethyl acetate and washed with water and sodium bicarbonate solution. Evaporation of the solvent gave 4.9 g. of non-crystalline VI. This keto-acetal was not further purified but added to a mixture of 2.14 g. of 2,4,5-triamino-6-hydroxypyrimidine hydrochloride,[3] 1.7 g. of sodium acetate and 0.25 g. of potassium iodide in 50 ml. of acetic acid. This reaction mixture was stirred at 25° for one hour and heated under reflux for 2 hours. The solvent was distilled under vacuum. The residue was triturated twice with 20 ml. of 80% ethanol and then dried. It weighed 3.5 g.

One gram of crude pteridine was triturated with 30 ml. of concentrated hydrochloric acid. The acid solution was treated with 0.25 g. of Norite A and this diluted to 180 ml. with water. The precipitate was collected at the centrifuge and dried. It weighed 0.35 g. and showed the following ultraviolet maxima: $\lambda_{max}^{0.1\ N\ NaOH}$ 258 mμ, $E_{1\ cm}^{1\%}$ 541; 364 mμ, $E_{1\ cm}^{1\%}$ 135. A slurry of 0.15 g. of the partially purified VII and 0.80 g. of calcium hydroxide in 10 ml. of 0.1 *N* sodium hydroxide and 400 ml. of water was stirred at 25° for one hour, heated to 95° and filtered. The *p*H was adjusted to 3.0 and as the solution slowly cooled yellow needles of VII (0.07 g.) precipitated, $\lambda_{max}^{0.1\ N\ NaOH}$ 258 mμ, $E_{1\ cm}^{1\%}$ 700; 285 mμ, $E_{1\ cm}^{1\%}$ 311; 364 mμ, $E_{1\ cm}^{1\%}$ 180.

Anal. Calcd. for $C_{20}H_{15}N_7O_7S$: C, 48.29; H, 3.04; N, 19.71; S, 6.44. Found: C, 48.38, 48.34; H, 3.27, 3.43; N, 20.04; S, 6.57, 6.64.

N-[*p*-[(2-Amino-4-hydroxy-6-pteridylmethyl)-*p'*-nitrobenzenesulfonylamino]-benzoyl]-L-glutamic Acid (VIIa).—Diethyl N-[N'-*p*-nitrobenzenesulfonyl-N'-(3,3-diethoxy-2-hydroxypropyl)-*p*-aminobenzoyl]-L-glutamate was oxidized as described above in the preparation of VI to give crude crystalline VIa, m.p. 145–150° (75.5% yield). This product was not purified but condensed with 2,4,5-triamino-6-hydroxypyrimidine to give 28% of a crude pteridine fraction. This material was not further investigated.

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(3) W. Traube, *Ber.*, **33**, 1371 (1900).

Chloromycetin.[1] The Conversion of L-*threo*-*p*-Nitrophenylserinol to L-*erythro*-*p*-Nitrophenylserinol

BY GEORGE W. MOERSCH AND DAVID P. HYLANDER

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The recent publication by Logemann, *et al.*,[2] describing the production of L-*erythro*-*p*-nitrophenylserinol from the L-*threo*-form has prompted us to publish some of our own work in this direction. It is particularly interesting that while very similar methods were used, the reaction courses appear to be decidedly dissimilar.

Logemann, *et al.*, prepared L-*threo*-1-*p*-nitrophenyl-1-tosyloxy-2-dichloroacetamido-3-benzoyloxypropane by tosylation of the L-*threo*-diacylated *p*-nitrophenylserinol. Treatment of this tosyl derivative with potassium acetate in ethanol led to replacement by acetate with partial inversion or racemization at the C_1 center. By acid hydrolysis, an L-*erythro*-*p*-nitrophenylserinol, m.p. 112°, and an unknown, m.p. 154°, were found. The latter was suspected of being L-*threo*-*p*-nitrophenylserinol which melts 8 to 10° higher. The zero rotation reported is inapplicable to either substance.

Our own experience in converting *threo*-*p*-nitrophenylserinol to the *erythro*-form has been through mesylation of L-*threo*-1-*p*-nitrophenyl-2-benzamido-3-benzoyloxy-1-propanol.[3] On treatment of the 1-mesylate with potassium acetate in absolute ethanol potassium mesylate separates and from the solution is obtained a thick oil identifiable as the L-*erythro*-oxazoline by its infrared and by its subsequent reactions. Dilute acid readily opens the oxazoline and O → N shift in base gives an N,O-dibenzoyl derivative which can be hydrolyzed in base to L-*erythro*-N-benzoyl-*p*-nitrophenylserinol. Acid hydrolysis removes the amide to yield L(−)-*erythro*-*p*-nitrophenylserinol.

In order to obtain a crystalline *erythro*-oxazoline, the O-benzoyl was removed from L-*threo*-1-*p*-

(1) Chloromycetin is the registered trademark which Parke, Davis and Company has adopted for the antibiotic drug, chloramphenicol.

(2) W. Logemann, F. Lauria and E. Pella, *Gazz. chim. ital.*, **83**, 407 (1953).

(3) This substance has been reported by C. G. Alberti, *et al.*, *Chim. ind.*, **33**, 5 (1951). Our preparation will be reported in another connection.

nitrophenyl-1-mesyloxy-2-benzamido-3-benzoyloxypropane by mild alkaline hydrolysis and the product cyclized with potassium acetate in ethanol to yield L-*erythro*-2-phenyl-4-hydroxymethyl-5-*p*-nitrophenyl-Δ^2-oxazoline.

We have also employed the mesylation procedure on L-*threo*-N,O-diacetyl-*p*-nitrophenylserinol to effect the *threo*- to *erythro*-conversion. The final product was isolated as L-*erythro*-chloramphenicol. In this case, the intermediates were all syrups and furnished no evidence that the conversion was through an intermediate oxazoline.

We also attempted the use of the tosylate of the N,O-dibenzoyl-*p*-nitrophenylserinol but found that tosylation gave considerably lower yields than did mesylation.

The elimination of the sulfonates with neighboring group participation has been recognized principally by Winstein, *et al.*[4] An entirely analogous inversion with participation of the benzamido group was reported[5] in the preparation of the *trans*-oxazoline from the appropriate *allo*-threonine derivative.

We are indebted to Dr. George Rieveschl, Jr., for his interest in this problem. Infrared data were obtained by R. B. Scott and Ernest Schoeb. Microanalyses are from the Parke, Davis and Co. microanalytical laboratory under the direction of Charles Childs.

Experimental

L-*threo*-1-*p*-**Nitrophenyl-1-mesyloxy-2-benzamido-3-benzoyloxypropane.**—By the usual method with methanesulfonyl chloride and pyridine, 75% yield, m.p. 112°, from ethanol.

Anal. Calcd. for $C_{24}H_{22}O_8N_2S$: C, 57.8; H, 4.44. Found: C, 57.27; H, 4.73.

In some preparations of the mesylate, a by-product (up to 30% yield), L-*erythro*-O,O'-dibenzoyl-*p*-nitrophenylserinol methanesulfonic acid salt, m.p. 191–192°, was obtained.[6]

Anal. Calcd. for $C_{24}H_{24}O_9N_2S$: C, 56.06; H, 4.70. Found: C, 56.40; H, 4.56.

On treatment with alkali this salt was converted to L-*erythro*-N,O-dibenzoyl-*p*-nitrophenylserinol, m.p. 185°.

L-*erythro*-2-**Phenyl-4-benzoyloxymethyl-5-*p*-nitrophenyl-Δ^2-oxazoline.**—The mesylate, 7 g., in 250 ml. of abs. ethanol was treated with 15 g. of freshly fused potassium acetate and heated at reflux for four hours. Precipitation occurred during the first hour. The mixture was cooled and filtered. The filtrate was evaporated to a thick sirup, taken into ethyl acetate and washed with water. The ethyl acetate solution was dried and evaporated *in vacuo* to leave a viscous sirup.

Infrared measurements showed C=N at 6.04 μ; benzoate ester at 5.79, 7.86 and 8.98 μ. No amide II band was discernible nor any other ester carbonyl.

L-*erythro*-O,O'-**Dibenzoyl-*p*-nitrophenylserinol Hydrochloride.**—The oxazoline was taken into ethyl acetate and treated with concd. HCl to precipitate the salt; 50% yield, m.p. 209°.

Anal. Calcd. for $C_{23}H_{21}O_6N_2Cl$: C, 60.6; H, 4.6. Found: C, 60.37, 60.23; H, 4.91, 4.86.

L-*erythro*-**N,O-Dibenzoyl-*p*-nitrophenylserinol.**—A sample of the oxazoline sirup was treated with acid and then with NaOH in alcohol. Concentration crystallized a white solid, m.p. 183°; recryst. from alcohol–water, m.p. 185°, 81% yield.

Anal. Calcd. for $C_{23}H_{20}O_6N_2$: C, 65.6; H, 4.79. Found: C, 65.44; H, 4.79.

L-*erythro*-**N-Benzoyl-*p*-nitrophenylserinol.**—A sample (13 g.) of the dibenzoyl derivative was warmed with sodium hydroxide in ethanol–water and separated crystals on dilution with water, m.p. 215°, 9.5 g., 97% yield; recryst. from methanol, m.p. 217°, $[\alpha]^{26}D$ +114° in dimethylformamide.

Anal. Calcd. for $C_{16}H_{16}O_5N_2$: C, 60.7; H, 5.10. Found: C, 60.95, 60.74; H, 5.01, 5.11.

L-*erythro*-*p*-**Nitrophenylserinol.**—The N-benzoyl derivative (6 g.) was heated for one hour at reflux in 200 ml. of 6 *N* HCl. The solution was cooled, filtered and evaporated *in vacuo*. The residual solid was taken into 50 ml. of water and made basic with NH_4OH. The solution was extracted with methyl ethyl ketone, the extract dried over Na_2SO_4 and evaporated. The residue was crystallized from ethylene dichloride. Crystallization was very slow. The yield was 0.8 g., m.p. 112–113°, $[\alpha]^{26.5}D$ −2.5° in ethanol.

Reaction of the residual sirup from the crystallization with methyl dichloroacetate in methanol gave 2.0 of L-*erythro*-chloramphenicol, m.p. 176°, $[\alpha]^{26}D$ +12.5° in ethanol.

L-*threo*-**1-Nitrophenyl-1-mesyloxy-2-benzamido-3-propanol.**—L-*threo*-1-*p*-Nitrophenyl-1-mesyloxy-2-benzamido-3-benzoyloxypropane (34 g.) was suspended in one liter of methanol and treated with 75 ml. of 1 *N* NaOH. After two hours, the yellow precipitate was separated, 15.4 g., m.p. 146–147°, 58% yield.

Anal. Calcd. for $C_{17}H_{18}O_7N_2S$: C, 51.77; H, 4.60. Found: C, 51.68; H, 4.64.

L-*erythro*-2-**Phenyl-4-hydroxymethyl-5-*p*-nitrophenyl-Δ^2-oxazoline.**—The mesylate amide (above), 3.93 g., in 100 ml. of abs. ethanol was treated with 2 g. of freshly fused potassium acetate, refluxed four hours and let stand overnight. The potassium mesylate was separated and the filtrate evaporated *in vacuo*. The yellow product was crystallized from ether, 1.3 g., m.p. 179°, 43% yield.

Anal. Calcd. for $C_{16}H_{14}O_4N_2$: C, 64.5; H, 4.73; N, 9.38. Found: C, 64.54; H, 5.11; N, 9.48.

Infrared spectra support this assignment by showing O–H at 2.97 μ; C=N at 6.07 μ with the absence of N–H and of amide II.

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Trichloromethyl Arenethiolsulfonates

BY CHIEN-PEN LO, HAROLD F. WILSON AND W. J. CROXALL

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Trichloromethanesulfenyl chloride reacts with a variety of compounds, the primary reaction being the replacement of a reactive hydrogen or its equivalent by a Cl_3CS– group. Such reactions with hydroxy[1] or sulfhydryl[2] compounds, amines,[3] imides[4] and others[5] have been reported in the literature. We have found that trichloromethanesulfenyl chloride reacts with sodium arenesulfinates

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