the aluminum chloride-catalyzed reaction of isobutyryl chloride with toluene.[21]

p-Tolylacetone (b.p. 108–112° at 12 mm., 45% yield) was prepared by the reaction of di-*p*-xylylcadmium with acetyl chloride according to the method of Gilman and Nelson.[22]

(21) C. F. H. Allen, *Org. Syntheses*, **14**, 1 (1934).

(22) H. Gilman and J. F. Nelson, *Rec. trav. chim.*, **55**, 518 (1936).

CHICAGO 37, ILL.

[CONTRIBUTION FROM THE GRASSELLI CHEMICALS DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DE NEMOURS & CO., INC.]

The Synthesis of DL-*threo*- and DL-*erythro*-1-(5-Nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediols and Related Compounds

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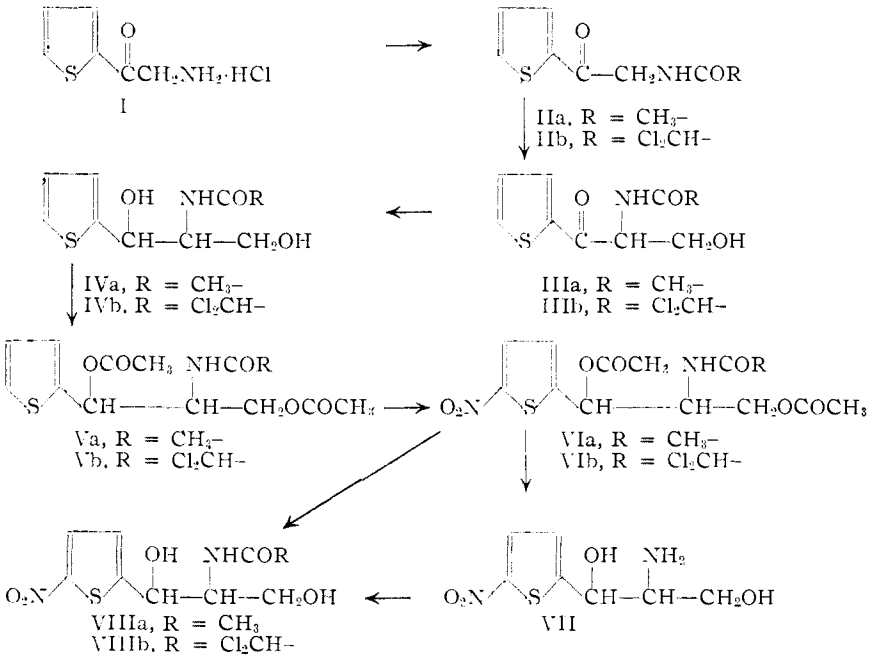
Two syntheses of both diastereoisomeric racemates of 1-(5-nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediol have been described. Both syntheses, which start with 2-acetylthiophene, include reductions of intermediate DL-N-[2-hydroxy-1-(2-thenoyl)-ethyl]-acylamides with sodium borohydride. The mixtures of isomeric racemates formed in this reduction have been separated and have led to a series of pure *threo*- and pure *erythro*-racemates.

This paper describes two syntheses of both diastereoisomeric racemates of 1-(5-nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediol (VIIIb) starting from 2-acetylthiophene.

Carrara and Weitnauer[1] have reported the preparation of DL-*threo*-1-(5-nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediol by a route similar to those described in this paper. Keskin, Mason and Nord[2] have recorded a partial synthesis of this same compound which terminated with the preparation of DL-*threo*-1-(2-thienyl)-2-acetamido-1,3-propanediol (IVa).



Some of these steps have been described for the benzene series in connection with the synthesis of Chloramphenicol.[3,4]

In the present work DL-N-[2-hydroxy-1-(2-thenoyl)-ethyl]-acetamide (IIIa) was reduced with sodium borohydride, rather than with aluminum isopropoxide as reported by the previous workers. This reduction has led to both the *threo*- and *erythro*-racemates and the previously unreported *erythro* series is described here. In addition, a second synthesis involving dichloroacetylation rather than acetylation of the intermediate N-2-thenoylmethylamine hydrochloride (I) has led to an entirely new series of compounds.

The first synthesis of the two diastereoisomeric racemates of (VIIIb) involved initially the bromination of 2-acetylthiophene and conversion of the resulting 2-bromoacetylthiophene to N-2-thenoylmethylamine hydrochloride (I) by means of a Delépine reaction through the intermediate N-2-thenoylmethylhexamethylenetetraminium bromide. The aminoketone hydrochloride (I) was next acetylated and the resulting N-2-thenoylmethylacetamide (IIa) was hydroxymethylated with aqueous formaldehyde in the presence of sodium bicarbonate to give IIIa. This synthesis to this point has been described by the previous workers[1,2] and consequently has not been described in detail in the experimental part of this paper.

Next, IIIa was reduced in 94% yield with sodium borohydride in methanol solution. This reduction was rapid and very convenient to carry out and appears to be the first case in which sodium borohydride has been used to reduce compounds of this type. The reduction product was a mixture of the *threo*- and *erythro*-racemates of IVa. The exact ratio of *threo* to *erythro* forms produced in this reaction was not determined, but it appeared to be

(1) G. Carrara and G. Weitnauer, *Gazz. chim. ital.*, **81**, 142 (1951).

(2) H. Keskin, C. D. Mason and F. F. Nord, *J. Org. Chem.*, **16**, 1333 (1951).

(3) J. Controulis, M. C. Rebstock and H. M. Crooks, Jr., THIS JOURNAL, **71**, 2463 (1949).

(4) L. M. Long and H. D. Troutman, *ibid.*, **71**, 2469 (1949); **71**, 2473 (1949).

approximately 1:1. Separation of the two racemates by fractional crystallization at this stage was not successful because they have nearly identical melting points and solubility characteristics. However both racemates of IVa have been prepared in pure form as described below.

Acetylation of the isomeric mixture IVa with acetic anhydride and pyridine gave an isomeric mixture of the corresponding triacetyl compounds (Va). By successive crystallizations of this product from absolute ethanol one may obtain a pure *erythro*-racemate, but the *threo*-racemate is not easily recoverable at this stage. A low-temperature hydrolysis of the *erythro*-racemate of Va with dilute sodium hydroxide in aqueous acetone solution[5] afforded a method of preparing the *erythro*-racemate IVa in good yield.

When the *threo* series of compounds was desired, the isomeric mixture obtained by the acetylation of IVa was dissolved in hot water and the resulting solution was concentrated by boiling at atmospheric pressure to about one-sixth the original volume. On cooling this solution a crystalline N,O-diacetyl compound belonging to the *threo* series separated, the corresponding compound of the *erythro* series remaining in solution. The position of the O-acetyl group in this diacetyl compound has not been determined. Reacetylation of this *threo*-N,O-diacetyl compound gave the corresponding *threo*-triacetyl compound (Va) in quantitative yield. On the other hand, a Kunz hydrolysis[5] of this *threo*-N,O-diacetyl compound gave the *threo*-racemate of IVa in pure form.

From this point on the synthesis was carried through separately in both the *erythro* and *threo* series of compounds. Va was nitrated with fuming nitric acid in acetic anhydride to give the corresponding 5-nitro compound (VIa).

Acid hydrolysis of VIa and subsequent liberation of the amine from its hydrochloride using sodium hydroxide gave the nitrated base VII. Both the *erythro*- and *threo*-racemates of VII appeared to be quite photosensitive and were difficult to purify. Reaction of VII with methyl dichloroacetate gave the corresponding 1-(5-nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediol (VIIIb).

The second synthesis of the diastereoisomeric racemates of VIIIb involved the conversion of I to the corresponding N-dichloroacetyl derivative (IIb) by reaction with dichloroacetyl chloride in the presence of sodium hydroxide in a mixture of ethylene dichloride and water. Monohydroxymethylation of IIb yielded IIIb which was subsequently reduced in high yield with sodium borohydride to a mixture of the *threo*- and *erythro*-racemates of IVb. The *erythro*-racemate of IVb was separated from this mixture as a crystalline solid, the *threo*-racemate being obtained as a highly viscous oil which could not be induced to crystallize.

From this point the synthesis was carried through separately in both the *threo* and *erythro* series. Both racemates of IVb yielded crystalline diacetyl derivatives (Vb). Nitration of the racemates of Vb gave the corresponding 5-nitro-compounds (VIb) which in turn were converted to the desired 1-(5-nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediols (VIIIb) by a Kunz hydrolysis.[5] The racemates of VIIIb prepared by this synthesis were compared with the samples prepared by the first synthesis by m.p. and mixed m.p determinations.

(5) A. Kunz and C. S. Hudson, THIS JOURNAL, **48**, 1982 (1926); M. L. Wolfrom, M. Konigsberg and S. Soltzberg, *ibid.*, **58**, 490 (1936).

Experimental[6]

N-(2-Thenoylmethyl)-hexamethylenetetraminium bromide was prepared by the reaction of 2-bromoacetylthiophene with hexamethylenetetramine in chloroform.[7] For analysis a sample of the crude product was dissolved in water (20°) and the resulting solution was treated with decolorizing charcoal and filtered. Dioxane (4 volumes) was added to the filtrate until a white crystalline precipitate formed. The purified material was separated by filtration and dried in a vacuum over phosphorus pentoxide at room temperature (*ca.* 25°). When purified in this manner, the salt had a m.p. of 160° (dec.) (ref. 1 gives m.p. 150° and ref. 2 gives 148–149°).

Anal. Calcd. for $C_{12}H_{17}BrN_4OS$: N, 16.23. Found: N, 16.26.

2-Thenoylmethylamine hydrochloride (I) was prepared by the hydrolysis of N-(2-thenoylmethyl)-hexamethylenetetraminium bromide with concentrated hydrochloric acid in 95% ethanol.[2] An analytical sample was recrystallized three times from 6 *N* hydrochloric acid giving colorless plates, m.p. 215–217° (dec.) (refs. 1 and 2 give no m.p. or analysis; ref. 8 gives m.p. 215–218°).

Anal. Calcd. for C_6H_8ClNOS: C, 40.56; H, 4.54; N, 7.89. Found: C, 40.82; H, 4.63; N, 7.60.

DL-*erythro*- and DL-*threo*-1-(2-Thienyl)-2-acetamido-1,3-propanediol (IVa).—A solution of 3.8 g. (0.1 mole) of 95% sodium borohydride in 75 ml. of methanol was added over a period of 20 minutes to a solution of 75 g. (0.35 mole) of IIIa[1] in 300 ml. of methanol at 20–25°. The reaction mixture was stirred for 15 minutes after the addition of the sodium borohydride solution, and the methanol was then removed by distillation under reduced pressure. The residue was mixed with 200 ml. of water and the resulting solution was heated on a steam-bath for one-half hour. The aqueous solution was then saturated with sodium chloride and extracted continuously in a liquid–liquid extractor with 1 l. of ethyl acetate for 20 hours. The ethyl acetate extract was dried over sodium sulfate. The ethyl acetate was then removed by distillation under reduced pressure and the solid residue was triturated with 50 ml. of ether, filtered and washed twice with 15 ml. of ether; yield 71 g. (94%), m.p. 111–118°.

Separation of the two isomers formed in this reaction by fractional crystallization from either ethyl acetate or dioxane was not successful because the two isomers have nearly identical solubilities in these solvents .However, the isomers can be prepared in pure form as described below.

DL-*erythro*- and DL-*threo*-1-(2-Thienyl)-2-acetamido-1,3-propanediol Diacetates (Va).—An isomeric mixture of IVa (m.p. 111–118°) was acetylated using acetic anhydride and pyridine.[3] By successive crystallizations of the product from absolute ethanol the pure *erythro*-racemate of Va (m.p. 113–114°) could be obtained. However, in practice it was more convenient and more efficient to separate this compound as described below.

DL-*threo*-1-(2-Thienyl)-2-acetamido-1,3-propanediol 1(or 3)-Acetate.—An isomeric mixture of Va (194 g., 0.65 mole) was dissolved in about 3.5 l. of boiling water. The resulting solution was concentrated by boiling at atmospheric pressure to a volume of about 700 ml. During this concentration the odor of acetic acid was detected in the vapors. The concentrate was then chilled in an ice-bath, yielding 51.5 g. of crystals, m.p. 140.5–142°. The aqueous mother liquors were concentrated to dryness under reduced pressure, giving a gummy residue. This residue was acetylated with 150 ml. of acetic anhydride and 150 ml. of pyridine. The residue obtained after concentration of the mixture was dissolved in

(6) All melting points were determined using a Fischer-Johns melting point apparatus.

(7) E. C. Hermann (to E. I. du Pont de Nemours & Co.), U. S. Patent 2,579,494 (1951).

(8) G. Barger and A. P. T. Easson, *J. Chem. Soc.*, 2100 (1938).

1300 ml. of water, decolorized, concentrated to about 300 ml., and refrigerated to yield, 29 g., m.p. 141–142.5°. The mother liquors were concentrated to dryness and reacetylated using 86 g. each of acetic anhydride and pyridine. Processing as above yielded an additional 12.5 g., m.p. 141–143°, total yield 93.0 g. (56%). An analytical sample of this N,O-diacetyl compound was recrystallized from water to a constant m.p. of 142.5–143° (ref. 1 reports the m.p. of DL-*threo*-1-(2-thienyl)-2-acetamido-1,3-propanediol 3-acetate as 138–139°).

Anal. Calcd. for $C_{11}H_{15}NO_4S$: C, 51.34; H, 5.88; N, 5.44. Found: C, 51.25; H, 5.89; N, 5.40.

A corresponding N,O-diacetyl compound of the *erythro* series has not been isolated.

DL-*erythro*-1-(2-Thienyl)-2-acetamido-1,3-propanediol Diacetate (*erythro*-Racemate of Va).—The mother liquors from the separation of the *threo*-N,O-diacetyl compound described above may be concentrated to dryness under reduced pressure and then acetylated with a mixture of acetic anhydride and pyridine. The acetylated product may be crystallized by trituration with ether, giving a crystalline solid rich in the *erythro*-racemate of Va. A typical melting point on such a product is 105.5–108°. An analytical sample was recrystallized from absolute ethanol to give a product with a constant m.p. of 113–114°.

Anal. Calcd. for $C_{13}H_{17}NO_5S$: C, 52.16; H, 5.73; N, 4.68; S, 10.71. Found: C, 52.45; H, 5.79; N, 4.74; S, 10.70.

DL-*threo*-1-(2-Thienyl)-2-acetamido-1,3-propanediol Diacetate (*threo*-Racemate of Va).—A sample of 25.0 g. (0.097 mole) of the *threo*-N,O-diacetyl compound (m.p. 140–142°) was acetylated with 50 ml. of acetic anhydride and 50 ml. of pyridine.[3] The product was crystallized from 50 ml. of ether; yield 25.5 g. (87.6%), m.p. 70–71°. An analytical sample was recrystallized once from isooctane to give a product with a m.p. of 72–73° (ref. 1 gives m.p. 74–75°).

Anal. Calcd. for $C_{13}H_{17}NO_5S$: C, 52.16; H, 5.73; N, 4.68. Found: C, 52.08; H, 5.80; N, 4.67.

DL-*erythro*-1-(2-Thienyl)-2-acetamido-1,3-propanediol (*erythro*-Racemate of IVa).—One gram of the *erythro*-racemate of Va (m.p. 110–112°) was hydrolyzed using 50 ml. of 0.2 *N* sodium hydroxide and 50 ml. of acetone.[5] The product was extracted with five 25-ml. portions of ethyl acetate and dried over magnesium sulfate. The dried combined extracts were concentrated by distillation under reduced pressure giving 0.65 g., m.p. 138–142°. This residue was recrystallized from ethyl acetate to give colorless plates, m.p. 144.5–145°. Mixtures of this product with the *threo*-N,O-diacetyl compound described above (m.p. 142.5–143°) and also with the *threo*-racemate of IVa (m.p. 142.5–143.5°, described below) gave depressed melting points.

Anal. Calcd. for $C_9H_{13}NO_3S$: C, 50.21; H, 6.09; N, 6.51. Found: C, 50.12; H, 6.29; N, 6.31.

DL-*threo*-1-(2-Thienyl)-2-acetamido-1,3-propanediol (*threo*-Racemate of IVa).—One gram of the *threo*-N,O-diacetyl compound (m.p. 140–142.5°) was hydrolyzed using 50 ml. of 0.1 *N* sodium hydroxide and 50 ml. of acetone.[5] The product was extracted with five 25-ml. portions of ethyl acetate. The dried combined extracts were concentrated by distillation under reduced pressure, giving a crystalline residue, m.p. 139–142°. The residue was recrystallized from 25 ml. of ethyl acetate, giving prisms, m.p. 142.5–143.5°. Mixtures of this product with the starting material and also with the *erythro*-racemate of IVa (m.p. 144.5–145°) both gave depressed melting points (ref. 1 reports the m.p. of this compound as 142–143°).

Anal. Calcd. for $C_9H_{13}NO_3S$: C, 50.21; H, 6.09; N, 6.51. Found: C, 50.36; H, 6.29; N, 6.51.

DL-*erythro*-1-(5-Nitro-2-thienyl)-2-acetamido-1,3-propanediol Diacetate (*erythro*-Racemate of VIa).—A mixture of 13.0 g. of the *erythro*-racemate of Va (m.p. 114–115°) and 17.3 g. of acetic anhydride was cooled to a temperature of −5°. To this mixture was added with rapid stirring, 4.3 g. of yellow fuming nitric acid (90%) over a period of 33 minutes. The temperature was maintained between 0 and −5° during this addition. Stirring was continued for about one-half hour after the addition of nitric acid. The reaction mixture was then poured into 100 ml. of ice-water and neutralized by the addition of solid sodium bicarbonate. The resulting mixture was extracted eight times with 50 ml. of ethyl acetate. The combined extracts were dried and concentrated by distillation under reduced pressure. The crystalline residue was recrystallized from a mixture of 300 ml. of water and 25 ml. of absolute ethanol, including treatment with decolorizing charcoal; yield 9.0 g. (60%), m.p. 136.5–137.5°.

For analysis, a sample was recrystallized from water to a constant m.p. of 139–141°.

Anal. Calcd. for $C_{13}H_{16}N_2O_7S$: C, 45.34; H, 4.68; N, 8.14; S, 9.31. Found: C, 45.30; H, 4.66; N, 8.06; S, 9.25.

DL-*threo*-1-(5-Nitro-2-thienyl)-2-acetamido-1,3-propanediol Diacetate (*threo*-Racemate of VIa).—A mixture of 120 g. of the *threo*-racemate of Va (m.p. 70.5–73°) and 160 g. of acetic anhydride was cooled to −5° in an ice–methanol-bath and 40.0 g. of yellow fuming nitric acid (90%) was added with rapid stirring over a period of 47 minutes. Stirring was continued for 1.25 hours. The temperature was maintained between 0 and −5° throughout the reaction. The mixture was then poured onto 650 g. of crushed ice and neutralized by the addition of solid sodium carbonate. During the neutralization the mixture was maintained at about 0°. The product was extracted with four portions of ethyl acetate (one 500-ml. and three 300-ml. portions). The combined extracts were decolorized, dried and then concentrated by distillation under reduced pressure. Ether (200 ml.) was added to the highly viscous yellow residue and the resulting mixture was cooled (0°) with stirring. The resulting solid amounted to 117 g. of yellow crystals, m.p. 100–105° with preliminary softening.

An analytical sample was recrystallized twice from isobutanol and then twice from water giving slightly yellow plates with a constant m.p. of 119–120° (ref. 1 gives a m.p. of 117–118°).

Anal. Calcd. for $C_{13}H_{16}N_2O_7S$: C, 45.34; H, 4.68; N, 8.14. Found: C, 45.45; H, 4.77; N, 7.94.

DL-*threo*-1-(5-Nitro-2-thienyl)-2-acetamido-1,3-propanediol (*threo*-Racemate of VIIIa).—A sample of 4.0 g. of the *threo*-racemate of VIa (m.p. 116–117°) was hydrolyzed using 200 ml. of acetone and 200 ml. of 0.2 *N* aqueous sodium hydroxide.[5] The crude product (3.9 g.) was recrystallized from 750 ml. of ethyl acetate to give 1.5 g., m.p. 182–183°. An analytical sample was recrystallized again from ethyl acetate to give a m.p. of 182.5–183.5° (ref. 1 gives m.p. 181–183°).

Anal. Calcd. for $C_9H_{12}N_2O_5S$: C, 41.53; H, 4.65; N, 10.76. Found: C, 41.62; H, 4.70; N, 10.54.

DL-*erythro*-1-(5-Nitro-2-thienyl)-2-amino-1,3-propanediol (*erythro*-Racemate of VII).—A sample of 10.3 g. of the *erythro*-racemate of VIa (m.p. 134–136.5) and 103 ml. of 1.5 *N* hydrochloric acid was heated on a steam-bath for one hour. The mixture was then cooled and extracted twice with 50-ml. portions of ether and the aqueous solution of the hydrochloride was concentrated to dryness by distillation under reduced pressure (bath temperature < 50°). The crude crystalline residue of the hydrochloride was dissolved in 25 ml. of ice-cold water and the *p*H of this solution was adjusted to 10 by the careful addition of concentrated aqueous sodium hydroxide. The product separated as gray colored needles; 3.7 g., m.p. 104–107°.

Attempts to recrystallize this product from water were unsuccessful. Melting points of the crude products varied somewhat from run to run. The highest melting point recorded was 110–115°.

DL-*threo*-1-(5-Nitro-2-thienyl)-2-amino-1,3-propanediol (*threo*-Racemate of VII).—A sample of 59.0 g. of the *threo*-racemate of VIa was hydrolyzed with 590 ml. of 1.5 *N* hydrochloric acid as described above for the *erythro*-racemate. However, in this case an additional amount of product was obtained by extraction with ethyl acetate.

The total crude product (30.4 g.) was recrystallized including treatment with decolorizing charcoal from 590 ml. of 1:4 isopropyl alcohol–ethylene dichloride; yield 25.3 g. slightly yellow, photosensitive needles, m.p. 130–131° (dec.). An analysis indicated that the product was not highly pure (ref. 1 gives the m.p. of the pure product as 137–138°).

Anal. Calcd. for $C_7H_{10}N_2O_4S$: C, 38.52; H, 4.62; N, 12.84. Found: C, 38.93; H, 5.03; N, 10.93.

DL-*erythro*-1-(5-Nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediol (*erythro*-Racemate of VIIIb).—A mixture of 2.9

g. of the *erythro*-racemate of VII (m.p. 110–115°) and 25 ml. of methyl dichloroacetate (b.p. 143–144°, redistilled) was heated on the steam-bath for 1.5 hours. The product partially crystallized during the reaction. The mixture was then cooled and extracted three times with 100 ml. of petroleum ether. The residue which did not dissolve in the petroleum ether was recrystallized from ethyl acetate, including treatment with decolorizing charcoal to give 1.68 g., m.p. 155–159°. This product was then recrystallized from water to a constant m.p. of 168.5–169.5°.

Anal. Calcd. for $C_9H_{10}Cl_2N_2O_5S$: C, 32.84; H, 3.06; N, 8.51. Found: C, 33.02; H, 3.32; N, 8.39.

The ultraviolet absorption spectrum of an aqueous solution of this compound contains a maximum at 330 mμ (log ε 3.967) (see Fig. 1).

DL-*threo*-1-(5-Nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediol (*threo*-Racemate of VIIIb).—A mixture of 31.3 g. of the *threo*-racemate of VII (m.p. 122–126°) and 168 g. of methyl dichloroacetate was heated with gentle stirring for 1.5 hours on the steam-bath. The resulting solution was cooled and poured into 1 l. of petroleum ether with stirring. The petroleum ether was then decanted and the residue was extracted twice with 200-ml. portions of petroleum ether. The dark oily residue was dissolved in 350 ml. of boiling ethyl acetate, decolorized and concentrated to dryness by distillation under reduced pressure. The residue was crystallized from 1 l. of water. Slow cooling was necessary in order to prevent the product from precipitating from the solution as an oil. The flat yellow needles which were obtained amounted to 17.5 g., m.p. 132.5–134°. The filtrate was concentrated by distillation under reduced pressure to a volume of about 200 ml., giving 6.0 g., m.p. 126–129°. The first crop (m.p. 132.5–134°) was recrystallized from 260 ml. of water with slow cooling, giving 13.9 g., m.p. 133–134°. The second crop (m.p. 126–129°) was recrystallized twice from water to give 2.2 g., m.p. 132.5–133.5° (ref. 1 reports m.p. 133°).

Anal. Calcd. for $C_9H_{10}Cl_2N_2O_5S$: C, 32.84; H, 3.06; N, 8.51; S, 9.74. Found: C, 32.67; H, 3.39; N, 8.45; S, 9.83.

The ultraviolet absorption spectrum of an aqueous solution of this compound contains a single maximum at 330 mμ (log ε 3.949) (see Fig. 1).

N-(2-Thenoylmethyl)-dichloroacetamide (IIb).—Dichloroacetyl chloride (29.6 g., 0.2 mole) was added in one portion with vigorous stirring to a mixture of 17.8 g. (0.1 mole) of I and 200 ml. of ethylene dichloride which had been cooled to 0°. Aqueous sodium hydroxide (35 ml., containing 16.0 g., 0.4 mole, of sodium hydroxide) was added dropwise to the resulting mixture at 0° over a period of 15 minutes. Stirring was continued for an additional 15 minutes, and then the reaction mixture was filtered. The solid amounted to 27.0 g. The aqueous layer of the filtrate was separated, and the ethylene dichloride layer was washed successively with two 100-ml. portions of water, and 100 ml. of saturated aqueous sodium bicarbonate solution and dried over sodium sulfate. The ethylene dichloride was removed by evaporation, yielding a residue of 5.5 g.

The 27.0 g. of solid obtained by filtering the reaction mixture above was extracted with 200 ml. of boiling ethylene dichloride. The ethylene dichloride extracts yielded upon evaporation 3.5 g. This material was combined with the 5.5 g. obtained above, and the combined product (9.0 g.) was recrystallized from 300 ml. of a 1:1 mixture of ethylene dichloride and petroleum ether, yielding 6.5 g. (25.7%), m.p. 135–136.5°. An analytical sample, recrystallized twice from a 1:1 mixture of ethylene dichloride and petroleum ether, had a m.p. of 136–137°.

Anal. Calcd. for $C_8H_7Cl_2NO_2S$: C, 38.11; H, 2.80; S, 12.72. Found: C, 38.03; H, 2.88; S, 12.77.

N-[2-Hydroxy-1-(2-thenoyl)-ethyl]-dichloroacetamide (IIIb).—A mixture of 24 g. (0.095 mole) of IIb, 190 ml. of methanol, 0.76 g. of sodium bicarbonate and 16.0 g. (0.19 mole) of 36% aqueous formaldehyde was stirred mechanically and heated to 35–40°. A clear solution was obtained in approximately 40 minutes. The reaction was continued for another 20 minutes and then allowed to cool to room temperature (one hour). The clear solution was poured slowly and with vigorous stirring into 300 g. of ice-water. A colorless semi-solid separated which crystallized in several minutes. The solid was washed with 100 ml. of water and dried. The product (24.4 g., m.p. 112.5–117.5°) was recrystallized from 250 ml. of benzene including treatment with decolorizing charcoal, yielding 18.2 g. (67.8%), m.p. 117.5–119.5°. An analytical sample which was recrystallized from ethyl acetate twice and then from benzene had a m.p. of 119.5–120°.

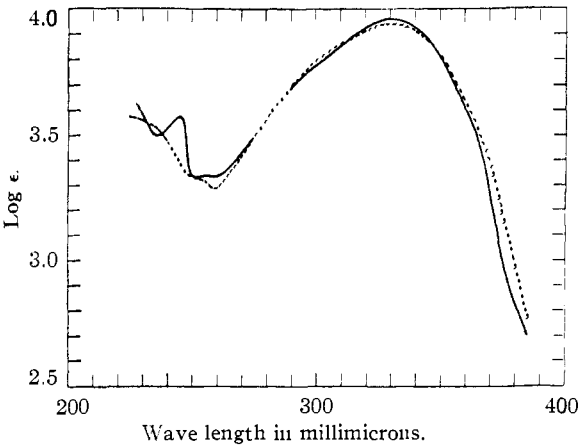


Fig. 1.—Ultraviolet absorption spectra, solvent water: —, DL-*erythro*-1-(5-nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediol; ----, DL-*threo*-1-(5-nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediol.

Anal. Calcd. for $C_9H_9Cl_2NO_5S$: C, 38.31; H, 3.21; S, 11.36. Found: C, 38.67; H, 3.33; S, 11.43.

DL-*threo*- and DL-*erythro*-1-(2-Thienyl)-2-dichloroacetamido-1,3-propanediol (IVb).—To a well-stirred mixture of 3.42 g. (0.012 mole) of IIIb and 20 ml. of methanol was added over a period of five minutes 7 ml. of a methanolic solution containing 0.13 g. (3.5 millimoles) of sodium borohydride; the temperature was maintained at 25°. Stirring was continued for one hour at 25°. The methanol was then removed by distillation under reduced pressure. The residue was dissolved in 10 ml. of water and heated on a steam-bath for 15 minutes. The resulting mixture was extracted with three 20-ml. portions of ethyl acetate, and the combined ethyl acetate extracts were dried over sodium sulfate, treated with 5 ml. of petroleum ether and refrigerated overnight. The DL-*erythro*-racemate was obtained, 0.16 g., m.p. 148–150°. The filtrate was evaporated to dryness and dissolved in 15 ml. of ethyl acetate. The hot ethyl acetate solution was decolorized, cooled, filtered and seeded. The solid amounted to 0.64 g., m.p. 142–149°. This was recrystallized from 10 ml. of ethyl acetate, yielding 0.30 g., m.p. 151–153°. This material was combined with the 0.16 g. of product obtained above and recrystallized twice more from ethyl acetate, yielding 0.26 g. (7.6%), m.p. 151.5–153° of the DL-*erythro*-racemate.

Anal. Calcd. for $C_9H_{11}Cl_2NO_5S$: C, 38.04; H, 3.90; S, 11.28. Found: C, 37.77; H, 4.24; S, 11.28.

The *threo*-racemate could not be induced to crystallize and was converted directly to the diacetyl derivative.

DL-*erythro*-1-(2-Thienyl)-2-dichloroacetamido-1,3-propanediol Diacetate (*erythro*-Racemate of Vb).—A one-gram sample (3.5 millimoles) of the *erythro*-racemate of IVb was acetylated using 3 ml. of pyridine and 3 ml. of acetic anhydride.[3] The product was crystallized from 25 ml. of ether and recrystallized from 30 ml. of petroleum ether with enough ethylene dichloride added dropwise to effect solution; yield 0.78 g. (60%), m.p. 92–93°. An analytical sample was recrystallized as indicated above to a constant m.p. of 93.5–94.5°.

Anal. Calcd. for $C_{13}H_{15}Cl_2NO_5S$: C, 42.40; H, 4.11; S, 8.71. Found: C, 42.47; H, 4.23; S, 8.66.

DL-*threo*-1-(2-Thienyl)-2-dichloroacetamido-1,3-propanediol Diacetate (*threo*-Racemate of Vb).—A sample of 2.9 g. (0.01 mole) of the *threo*-racemate of IVb was acetylated using 5 ml. of pyridine and 5 ml. of acetic anhydride.[3] The product crystallized from ether after standing one month and was recrystallized from 40 ml. of a 3:1 mixture of ethylene dichloride and petroleum ether, yielding 1.34 g. (36%), m.p. 122–123°. An analytical sample was recrystallized from 25 ml. of petroleum ether with enough ethylene dichloride added dropwise to effect solution, m.p. 123–124°.

Anal. Calcd. for $C_{13}H_{15}Cl_2NO_5S$: C, 42.40; H, 4.11. Found: C, 42.64; H, 4.16.

A Kuhn hydrolysis[5] of this product yielded a viscous oil which could not be induced to crystallize.

DL-*erythro*-1-(5-Nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediol (VIIIb).—Nitration of the *erythro*-racemate of Vb (m.p. 93.5–94.5°) gave the crystalline 5-nitro compound (VIb), m.p. 123.5–126°. An analytical sample after recrystallization from a 2:1 mixture of petroleum ether–ethylene dichloride had a m.p. of 126.5–127.5°.

Anal. Calcd. for $C_{13}H_{14}Cl_2N_2O_7S$: C, 37.78; H, 3.41; Cl, 17.16. Found: C, 37.83; H, 3.60; Cl, 17.46.

One gram (2.4 millimoles) of VIb (m.p. 127.5–128.5°) was hydrolyzed using 50 ml. of acetone and 50 ml. of 0.1 *N* aqueous sodium hydroxide.[5] The product amounted to 0.51 g., m.p. 125–135°. This was recrystallized twice from 20 ml. of ethylene dichloride yielding 0.10 g., m.p. 167–168°. It was finally recrystallized from 8 ml. of water yielding 0.06 g. of long fine slightly yellow needles, m.p. 168.5–169.5°. A mixture of this product and the *erythro*-racemate of VIIIb prepared above (m.p. 169.5–170.5°) had a m.p. of 169.5–170.5°.

DL-*threo*-1-(5-Nitro-2-thienyl)-2-dichloroacetamido-1,3-propanediol (VIIIb).—Nitration of the *threo*-racemate of Vb (m.p. 123–124°), gave a dark red oil which could not be crystallized. Hydrolysis of 0.90 g. (2.2 millimoles) of this crude nitration product with 50 ml. of acetone and 50 ml. of 0.1 *N* aqueous sodium hyroxide[5] gave 0.22 g., m.p. 121.5–126°. The material was recrystallized successively from 10 ml. of ethylene dichloride, then 10 ml. of water yielding 0.02 g., m.p. 131.5–132.5°. A mixture of this product and the *threo*-racemate of VIIIb prepared above (m.p. 131.5–133°) had a m.p. of 132–133°.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

On the Structure of Dehydroacetic Acid

BY JEROME A. BERSON

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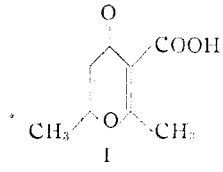
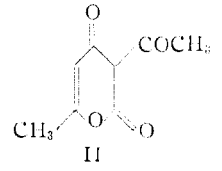
A consideration of the acidic dissociation constants and ultraviolet spectra of dehydroacetic acid, triacetic lactone and certain of their derivatives provides confirmatory evidence for the presently accepted formulations of these substances.

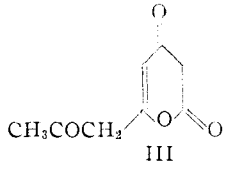
The structure of dehydroacetic acid has been unquestioned since the demonstration[1] that the observed isomerization of the substance by hot 85% sulfuric acid to 2,6-dimethylpyrone-4-carboxylic acid-3 (I) was most easily rationalizable in terms of the Feist structure[2] (II). The possibility that



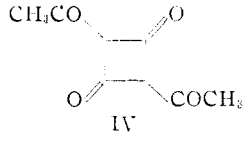
I



II



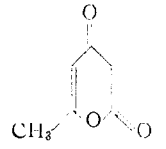
III



IV

the structure (III) proposed by Collie[3] or some other alternative (*e.g.*, IV) might also be convertible to I under the drastic conditions of the isomerization, as well as the observation (*vide infra*) of certain apparent anomalies in the ultraviolet absorption behavior of the dehydroacetate ion have led us to re-examine the structural question.

With 90% sulfuric acid, dehydroacetic acid is converted to triacetic lactone, formulated as V.[4] Alcoholysis of triacetic lactone leads to ethyl triacetate, formulated as VIa, which on careful saponification yields the unstable triacetic acid (VIb). This acid readily suffers decarboxylation to acetylacetone.[5] Triacetic lactone is regenerated when ethyl triacetate is warmed with 70% sulfuric acid.[6] These observations leave only two possible structures for triacetic acid, VIb and VIIb.

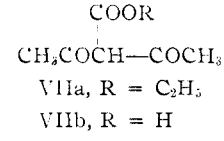


V

$CH_3COCH_2COCH_2COOR$

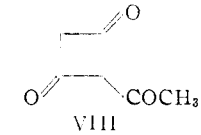
VIa, R = C_2H_5

VIb, R = H



VIIa, R = C_2H_5

VIIb, R = H



VIII

β-Lactone structures for triacetic lactone can be rejected in view of the relatively high stability of the lactone to acids and bases.[4,5] There remain, therefore, only two possible structures for triacetic lactone derivable from VIa or VIIa by the loss of alcohol, namely, V and VIII.

Triacetic lactone readily undergoes O-alkylation,[7] is a monobasic acid, gives a blood-red color with ferric chloride and is therefore to be considered

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