Anal. Calcd. for $C_6H_{10}O_2Cl_2$: C, 38.94; H, 5.45; Cl, 38.32; neut. equiv., 185. Found: C, 39.01; H, 5.18; Cl, 37.99; neut. equiv., 186.

This acid is presumed to be α,β-dichloro-α-ethylbutyric acid (V), since heating a dioxane solution under reflux with zinc dust gave the solid form of II, m.p. 38.5–41°.

A similar experiment in which chlorination was effected at −3° gave 7.6 g. of oil, which after four distillations from a modified Claisen flask gave 1.45 g. (19%) of II; b.p. 91.5–94° (3 mm.); $n^{25}D$ 1.4451 (*cf.* above); b.p. reported[7] 107–108° (10 mm.); rapid decolorization of aqueous potassium permanganate and bromine in carbon tetrachloride (with hydrogen bromide evolution). The identity of the presumed II was confirmed by conversion as described above to the stable form, m.p. 38–40.5°, and by formation of the β-naphthylamide, m.p. 92–95° (reported[7] 96°).

Concentration of the benzene-extracted aqueous layer from another chlorination gave a hygroscopic viscous liquid which was strongly acidic (neut. equiv. 98) and gave a heavy precipitate with barium chloride but none with silver nitrate; it apparently consisted in large part of sulfuric acid. Neutralization with sodium hydroxide followed by evaporation and recrystallization of the resulting solid gave sodium sulfate; Na, 31.6 (calcd. 32.4).

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N,N′-(Oxoethylene)-bis-(DL-β-phenylalanine)

BY WILLIAM S. FONES

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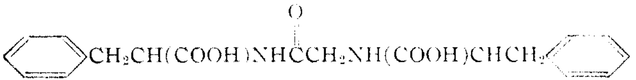
In the course of the preparation of N-bromoacetyl-DL-β-phenylalanine by the conventional Schotten–Baumann reaction between DL-β-phenylalanine and bromoacetyl bromide there was isolated in addition to the desired product a substance insoluble in dilute mineral acid, ethyl acetate or acetone. The same material could be obtained in somewhat larger yield if only one-half molar amounts of bromoacetyl bromide were used. This fact, together with the analyses for carbon, hydrogen and nitrogen, indicated that the substance was N N′-(oxoethylene)-bis-(DL-β-phenylalanine) (I).



$C_6H_5CH_2CH(COOH)NH\overset{O}{\overset{\|}{C}}CH_2NH(COOH)CHCH_2C_6H_5$

(I)

That this was the correct formulation was shown in two ways. First, the compound was also prepared by the condensation of N-bromoacetyl-DL-β-phenylalanine methyl ester with DL-β-phenylalanine ethyl ester, followed by basic hydrolysis and acidification. Second, (I) was hydrolyzed with concentrated hydrochloric acid to DL-β-phenylalanine and DL-β-phenylalanine-N-acetic acid.[1] The latter compound was isolated from the hydrolysate and identified by its analysis and by conversion to the known hydrochloride.[2] The presence of β-phenylalanine in the hydrolysate was shown by paper chromatography utilizing an alcohol–water solvent (77% alcohol). No ninhydrin reacting materials other than the two substances mentioned were observed in the developed chromatogram.

The author is indebted to Dr. H. A. Sober of this Laboratory for the chromatographic analysis.

Experimental[3]

N-Bromoacetyl-DL-β-phenylalanine Methyl Ester.—To a 10% excess of diazomethane[4] in 200 ml. of ether there was added in small portions 21.5 g. of N-bromoacetyl-DL-β-phenylalanine.[5] After one-half hour the excess diazomethane was destroyed with dilute hydrochloric acid following which the ethereal solution was washed with sodium bicarbonate solution and saturated sodium chloride. After drying over sodium sulfate the ether was concentrated and petroleum ether (b.p. 35–70°) was added. There was thus obtained 18.0 g. (80%) of ester, m.p. 80–82°. The melting point was not changed by recrystallization from the same solvents.

Anal.[6] Calcd. for $C_{12}H_{14}O_3NBr$: C, 48.0; H, 4.7; N, 4.7; Br, 26.6. Found: C, 48.0; H, 4.9; N, 4.8; Br, 26.6.

N,N′-(Oxoethylene)-bis-(DL-β-phenylalanine) (I). Method (A).—In a 500-ml. three neck round-bottomed flask, cooled by an ice-bath and equipped with a stirrer and two addition funnels there was placed 33 g. of DL-β-phenylalanine and 100 ml. of 2 *N* sodium hydroxide. To the stirred solution, kept below 5° there was added dropwise from one funnel 20 g. of bromoacetyl bromide and from the other funnel 2 *N* sodium hydroxide was added at such a rate as to just keep the solution alkaline. After the addition was complete the ice-bath was removed and the reaction mixture stirred for three hours.

At the end of this period acetic acid (50 ml.) was added and the resulting precipitate collected by filtration. This was taken up in sodium bicarbonate solution and again precipitated with acetic acid to give 15 g. of material m.p. 210–215° dec. After two more precipitations from bicarbonate by the addition of acetic acid followed by washing of the precipitate with ethanol and ether, there was obtained 9.5 g. (26%) of N,N′-(oxoethylene)-bis-(DL-β-phenylalanine), m.p. 224–227° dec.

Anal.[6] Calcd. for $C_{20}H_{22}O_5N_2$: C, 64.8; H, 5.9; N, 7.6. Found: C, 64.8; H, 6.2; N, 7.6.

Method B.—Eleven and one-half grams of DL-β-phenylalanine ethyl ester hydrochloride was treated with a slight excess of alkali and the free ester was extracted into 150 ml. of ether. To this ethereal solution there was added a solution of 7.5 g. of N-bromoacetyl-DL-β-phenylalanine methyl ester in 150 ml. of ether. Seventy-five ml. of ethyl acetate was then added and most of the ether was removed by boiling, following which the mixture was allowed to stand overnight.

The solvent was removed in a stream of air and the residue triturated with ether. The solid amine hydrobromide was collected by filtration and the ether removed from the filtrate *in vacuo* following which the oily residue was dissolved in 50 ml. of ethanol and treated overnight at room temperature with 2.5 g. of sodium hydroxide in 50 ml. of water. The acid was precipitated by the addition of acetic acid to give 5.9 g. of material, m.p. 200–220° dec. After one precipitation by dilute hydrochloric acid and one by acetic acid from sodium bicarbonate solution, 4.2 g. (45%) of N,N′-(oxoethylene)-bis-(DL-β-phenylalanine), m.p. 224–227° was obtained. A mixed melting point with I from A showed no depression.

Hydrolysis of N,N′-(Oxoethylene)-bis-(DL-β-phenylalanine).—One and eight-tenths grams of I (from A) was refluxed for 6 hr. in 50 ml. of concentrated hydrochloric acid following which the solution was taken to dryness *in vacuo*. Most of the hydrochloric acid was removed by taking the residue up in 50-ml. portions of water and evaporating to dryness *in vacuo* three times. After the third evaporation the residue was taken up in 10 ml. of water and treated with excess aniline to remove bound hydrogen chloride. An equal volume of alcohol was added and the solution placed in the refrigerator overnight. Filtration gave 1.5 g. of crystals, m.p. 195° (dec.). Two recrystallizations from water gave 0.1 g. of DL-β-phenylalanine-N-acetic acid, m.p. 233–236° dec. (lit.[2] 225–226°).

Anal. Calcd. for $C_{11}H_{13}O_4N$: C, 59.2; H, 5.8; N, 6.3. Found: C, 59.2, 58.9; H, 5.9, 5.8; N, 6.0, 6.0.

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(1) D. A. Hahn and A. Litzinger, THIS JOURNAL, **54**, 4665 (1932).

(2) D. A. Hahn and M. M. Endicott, *ibid.*, **60**, 1040 (1938).

(3) All melting points are corrected.

(4) "Organic Syntheses," Coll. Vol. II, J. Wiley and Sons, Inc., New York, N. Y., 1943, p. 165.

(5) E. Abderhalden and F. Schweitzer, *Fermentforschung*, **11**, 224 (1930).

(6) Analyses by R. J. Koegel and staff of this Laboratory.

The filtrate from the first precipitation was chromatographed on filter paper using 77% ethanol as solvent to show the presence of DL-β-phenylalanine in the hydrolysate.

DL-β-Phenylalanine-N-acetic Acid Hydrochloride.—Sixty mg. of the DL-β-phenylalanine-N-acetic acid was converted to the hydrochloride[2] to give 50 mg. of material, m.p. 203–206° dec. (lit.[2] 200–201°).

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[7] Federal Security Agency, Public Health Service.

A Note on the Occurrence of Panstroside[1]

BY ROBERT FOPPIANO AND M. R. SALMON

RECEIVED MARCH 19, 1952

v. Euw and Reichstein[2] have reported on the glycoside content of the seeds of *Strophanthus petersianus*, Klotzsch, from which they isolated sarmentocymarin, sarmentogenin and three new substances identified as No. 792, 793 and 794. We find that in addition the seeds of this species contain panstroside which we isolated in a crude yield of 0.035%.

The seeds were received from Mr. P. Topham, Nyasaland, Africa, through the courtesy of the New York Botanical Garden. A flowering specimen and a mericarp sent as botanical vouchers for the seeds were identified as *S. petersianus* at the New York Botanical Gardens. We wish to thank Mr. Topham for the collection and Mr. Joseph Monachino for the botanical examination of this sample.

Panstroside frequently crystallizes slowly or not at all[3] and may be easily overlooked. When the presence of this glycoside is suspected we regularly crystallize the chloroform extract from acetone from which panstroside crystallizes more readily than from methanol and ether.

Experimental

The seeds (1111 g.) were extracted as previously described.[4] The chloroform extract on concentration gave 2.58 g. (0.23%) of crude total glycoside. This was dissolved in about 10 cc. of acetone, and allowed to crystallize in the refrigerator. We obtained 366 mg. of crude panstroside, $[\alpha]_D$ +25°; m.p. 210–219°. An additional 19 mg. was isolated by chromatography of the mother liquors.

Recrystallization of this panstroside gave preparations that agreed in rotation and melting point with our former preparations but the absorption spectrum showed that a small amount of impurity was retained tenaciously. It was accordingly chromatographed on alumina, and from the eighth and ninth fractions eluted with chloroform and chloroform–methanol (99:1), 193 mg. of panstroside was obtained after crystallization from methanol; $[\alpha]_D$ +27°. Panstroside was recrystallized three times and yielded 154 mg.; $[\alpha]_D$ +31.0°; m.p. 222–228°; Keller–Kiliani test negative; legal test positive. Color test with 84% sulfuric acid pink becoming red in 2 min., developing a blue edge in 3 min., and becoming blue in 20 min. The mixed melting point with panstroside from *S. intermedius* showed no depression. Ultraviolet absorption spectrum maximum at 218 mμ, log ε 4.23; plateau at 265–280 mμ, log ε 1.93.

Anal. Calcd. for $C_{30}H_{44}O_{11}$: C, 62.06; H, 7.64. Found: C, 61.84, 61.63; H, 7.43, 7.61.

We wish to thank Dr. W. G. Bywater for advice and suggestions and the Upjohn Company for encouragement and support.

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[1] J. v. Euw, H. Hess, P. Speiser and T. Reichstein, *Helv. Chim. Acta*, **34**, 1821 (1951).

[2] J. v. Euw and T. Reichstein, *ibid.*, **33**, 1551 (1950).

[3] See for example J. v. Euw and T. Reichstein, *ibid.*, **33**, 2153 (1950).

[4] M. R. Salmon, Eric Smith and W. G. Bywater, THIS JOURNAL, **73**, 3824 (1951).

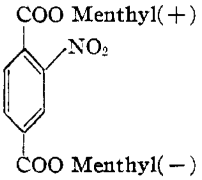
Active (+) Menthyl (−) Menthyl Nitroterephthalates

BY P. J. HEARST AND C. R. NOLLER

RECEIVED APRIL 25, 1952

Compounds containing two like asymmetric groups of opposite configuration, A(+) and A(−), and no other asymmetric groups, but which nevertheless have molecular asymmetry, are of interest in that they have some bearing on the entrenched idea of internal compensation. It might be argued that the rotation of A(+) should cancel that of A(−) or that, if it did not, the rotation of the compound would be small. An example of such compounds would be those of the type (+)A-Z-X-Y-Z-A(−) and (−)A-Z-X-Y-Z-A(+), where X, Y and Z are not asymmetric. It is difficult to be certain that this type of compound has not been discussed or prepared previously, but an examination of several available books on stereochemistry and a search of the literature for likely specific compounds have not revealed a reference to this aspect of the problem.

We have prepared one pair of enantiomorphs of this type, namely, the 1-(+)menthyl 4-(−)menthyl 2-nitroterephthalate (I) and the 1-(−)menthyl 4-(+)menthyl 2-nitroterephthalate (II). These compounds have specific rotations in benzene solution of +59.1 and −59.7°, respectively. Thus the molecular asymmetry not only confers activity on these compounds, but the rotation is appreciable.



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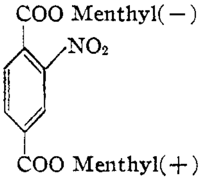

II

Experimental

Nitroterephthalic acid was prepared from terephthalic acid in 78% yield by a procedure essentially the same as that of Wegscheider[1] except that 70% nitric acid and 30% fuming sulfuric acid were used instead of fuming nitric acid and pyrosulfuric acid. It was converted to the (−)**menthyl ester** by the procedure of Cohen and de Pennington[2] except that, in the preparation of the acyl chloride, twice the calculated amount of phosphorus pentachloride was used and a small amount of phosphorus oxychloride was added to start the reaction. The purified ester, obtained in over-all yield of 59%, melted at 86–88°; $[\alpha]^{25}_D$ −159° (*c* 1.996 in benzene).

1-(−)**Menthyl 2-nitroterephthalate** was obtained in 42% yield by the partial saponification of the (−)menthyl ester.[2] After crystallization from aqueous ethyl alcohol, it melted at 73.5–75°, compared to the 75° previously reported. Recrystallization from hexane, however, raised the melting point to 128.5–129.5°. A determination of neutralization equivalents showed that the product melting at 75° contains one molecule of water of crystallization, whereas that melt-

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[1] R. Wegscheider, *Monatsh.*, **21**, 621 (1900).

[2] J. B. Cohen and H. S. de Pennington, *J. Chem. Soc.*, **113**, 57 (1918).