The Syntheses from Levulinic Acid. A Possible Use of Some 2-Methyl-5-oxopyrrolidine-2-carboxylic Esters as Plasticizers[1]

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The object of the present investigation is to search for possible uses as chemical intermediates of levulinic acid, which is often obtained in quantities as a by-product from carbohydrate materials in food industries. The application of the Strecker synthesis[2] to levulinic acid gave 2-amino-2-methylglutaric acid, from which several derivatives were prepared including 2-methyl-5-oxopyrrolidine-2-carboxylic acid. Since esters as a class are of general interest as plasticizers, some 2-methyl-5-oxopyrrolidine-2-carboxylic esters were prepared and those of higher alcohols were tested for plasticizer performance. They are compatible and efficient for

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[1] Part of the material of this report was presented at a meeting of the Chemical Society of Japan held on Oct. 2, 1952, at Niigata.

[2] A. Strecker, ***Ann.***, **75**, 27 (1850).

plasticizing vinyl chloride resin; with regard to heat stability, they are unsatisfactory only in one respect in that the plasticized sheets of polyvinyl chloride, heated at 110° for six hours, became colored light brownish violet. The results are recorded in the accompanying table.[3]

PROPERTIES OF POLYVINYL CHLORIDE SHEETS PLASTICIZED WITH 2-METHYL-5-OXOPYRROLIDINE-2-CARBOXYLIC ESTERS

	n-Octyl Ester		2-Ethylhexyl Ester		Dodecyl Ester	
Plasticizer (parts for 100 parts polyvinyl chloride with 2 parts lead stearate)	30	50	30	50	30	50
Modulus at 100% Elongation, kg./cm².	157	64	183	65	200	82
Elongation, %	268	305	263	335	275	315
Tensile Strength, kg./cm².	282	192	300	208	322	205
Tear Resistance, kg./cm.	118	74	140	82	136	78
Oil Extraction (*a*)	—	10.78	—	5.32	—	15.05
Water Extraction(*b*)	—	5.83	—	3.91	—	0.20
Low Temperature Flexibility(*c*)	—	9.30	—	13.27	—	7.65

(*a*) % gasoline-soluble substances, at 18∼23°, for 24 hrs.

(*b*) % water-soluble substances, at 50°, for 24 hrs.

(*c*) Elongation at 25∼26° / Elongation at −4 to −5°.

Experimental

2-Amino-2-methylglutaric Acid A solution of 102 g. (1.9 moles) of ammonium chloride in 240 cc. of lukewarm water was added, followed by 120 cc. (1.7 moles) of 28% ammonium hydroxide, to a solution of 86 g. (1.7 moles) of sodium cyanide in 170 cc. of water placed in a round-bottomed flask fitted with a ground-glass stopper. The mixture was stirred while 200 g. (1.7 moles) of ammonium levulinate in aqueous solution was added. The flask was then stoppered, the stopper secured firmly by means of adhesive tape, and the flask kept half immersed for six hours in a water bath at 65∼70°. The reaction mixture was then cooled, poured into 2 l. of concentrated hydrochloric acid contained in a round-bottomed flask cooled by a stream of water, and the mixture saturated with hydrogen chloride. After standing overnight, it was refluxed for three hours to hydrolyze the acid amide produced. After cooling, the precipitated inorganic salts were filtered off on a Büchner funnel. The filtrate was concentrated under reduced pressure on a water bath, and the deposited inorganic salts were filtered. When the filtrate was neutralized to a pH 3.2 with aqueous sodium hydroxide and the inner wall of the vessel scratched vigorously, 2-amino-2-methylglutaric acid separated in fine crystals, which were collected on a Büchner funnel. The yield of the product was 210 g. (70% of the theoretical amount). This crude amino acid was dissolved in hot water, charcoaled and filtered, giving fine crystalline product, m.p. 170° (Found: C, 44.73; H, 6.88; N, 8.69. Calcd. for $C_6H_{11}O_4N$: C, 44.10; H, 7.20; N, 8.23%).

2-Benzamido-2-methylglutaric Acid Benzoyl chloride (6.2 g.) was added to 2-amino-2-methylglutaric acid (8 g.) dissolved in a solution of 6.5 g. of sodium hydroxide in water, the mixture shaken for 30 minutes, acidified with hydrochloric acid, the precipitated benzoic acid filtered off, the filtrate concentrated to half the original volume, extracted with ether and ethyl acetate, the combined extracts dried over anhydrous sodium sulfate, and the solvent removed on a water bath. Recrystallization of the residue from aqueous alcohol gave the benzoyl derivative, m.p. 196∼7° (Found: N, 5.45; neutralization equiv., 132.5. Calcd. for $C_{13}H_{15}O_5N$; N, 5.28%; neutralization equiv., 132.5.).

2-Acetamido-2-methylglutaric Anhydride 2-Amino-2-methylglutaric acid (8 g.) was refluxed with 20 cc. of acetic anhydride and 15 cc. of acetic acid for 4 hours. After the excess of acetic anhydride was decomposed with water, the mixture was concentrated in vacuo and the remaining oil was induced to crystallize by rubbing with ethyl acetate, giving 2-acetamido-2-methylglutaric anhydride, m.p. 141∼2° (from ethyl acetate) (Found: N, 7.71. Calcd. for $C_8H_{11}O_4N$; N, 7.58%,).

2-Acetamido-2-methylglutaric Acid To 8 g. of 2-amino-2-methylglutaric acid and 25 cc. of acetic anhydride, aqueous sodium hydroxide was added drop by drop with vigorous shaking until the mixture was alkaline. After shaking for thirty minutes, the mixture was neutralized with hydrochloric acid, concentrated in vacuo, the precipitated inorganic salts filtered off, the

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[3] The authors are indebted to Mr. S. Takazawa of Yamato Rubber Works, Tokyo, for the performance data.

filtrate concentrated to dryness in vacuo, and the residue triturated with ethyl acetate and filtered off, giving crude crystals melting at 126~135°. An analytically pure sample was prepared by repeated crystallization from water, m.p. 182~3° (Found: N, 6.76; neutralization equiv., 110.5. Calcd. for $C_8H_{13}O_5N$: N, 6.89%; neutralization equiv., 101.5).

Diethyl 2-Amino-2-methylglutarate The diethyl ester was prepared by Fischer's method[4]. 2-Amino-2-methylglutaric acid (20 g.) was heated on a water bath with 120 cc. of absolute ethanol which had previously been saturated with dry hydrogen chloride until all the amino acid dissolved, and the heating was continued for a further five hours. The mixture was then concentrated under diminished pressure, added with 100 cc. of ethanol saturated with dry hydrogen chloride, heated and concentrated as above, the whole cycle of procedures being repeated three times. The oily product thus obtained was dissolved in a small amount of water, the solution neutralized and the ester extracted several times with ether. The combined ether extracts were dried over sodium sulfate, evaporated, and the residue distilled in vacuo, giving 7 g. of diethyl ester, b.p. 102~4° at 0.5 mm. Hg, d_4^{20} 1.0550, n_D^{20} 1.4428 (Found: N, 6.45; MR_D, 54.56. Calcd. for $C_{10}H_{19}O_4N$: N, 6.45%; MR_D, 55.11.).

2-Methyl-5-oxopyrrolidine-2-carboxylic Acid 2-Amino-2-methylglutaric acid was dehydrated to 2-methyl-5-oxopyrrolidine-2-carboxylic acid by heating at 180~200° in a practically quantitative yield, m.p. 144~5° (from hot water) (Found: N, 9.78; neutralization equiv., 143. Calcd. for $C_6H_9O_3N$: N, 9.86%; neutralization equiv., 143.).

Ethyl 2-Methyl-5-oxopyrrolidine-2-carboxylate 2-Methyl-5-oxopyrrolidine-2-carboxylic acid (15 g.), 150 cc. of ethanol, 200 cc. of benzene and 1 cc. of concentrated sulfuric acid were heated in a round-bottomed 1 l. flask fitted with a refluxing condenser and separator so arranged that the upper layer of the condensing liquid containing benzene and ethanol was returned to the reaction flask and the lower water layer withdrawn from time to time. The flask was heated until no further separation of water occurred. The solvent was removed from the reaction mixture in vacuo, the residue dissolved in ether, the ether solution washed with aqueous solution of sodium bicarbonate, the ether removed, the residue subjected to fractional distillation under reduced pressure, giving 10 g. of ethyl ester, colorless liquid, b.p. 126~130° at 0.5 mm. Hg, d_4^{20} 1.1283, n_D^{20} 1.4690 (Found: N, 8.39; MR_D, 43.24, Calcd. for $C_8H_{13}O_3N$: N, 8.18%; MR_D, 42.21.).

Butyl 2-Methyl-5-oxopyrrolidine-2-carboxylate This ester was prepared from 2-methyl-5-oxopyrrolidine-2-carboxylic acid similarly to the ethyl ester in 95% yield, b.p. 141~2° at 0.5 mm. Hg (Found: N, 7.05. Calcd. for $C_{10}H_{17}O_3N$: N, 7.03%.). It was also synthesized from 2-amino-2-methylglutaric acid by the same procedure in 80% yield, b.p. 141~2° at 0.5 mm. Hg, d_4^{20} 1.0698, n_D^{20} 1.4676 (Found: N, 7.13; MR_D, 51.68. Calcd. for $C_{10}H_{17}O_3N$; N, 7.03%; MR_D, 51.45.).

Octyl, 2-ethylhexyl, dodecyl and benzyl esters were prepared from 2-methyl-5-oxopyrrolidine-2-carboxylic acid by the same procedure as above.

Occtyl 2-Methyl-5-oxopyrrolidine-2-carboxylate (yield 75%), b.p. 173~4° at 1.0 mm. Hg, d_4^{20} 1.0062, n_D^{20} 1.4652 (Found: N, 5.63; MR_D, 70.29, Calcd. for $C_{14}H_{25}O_3N$: N, 5.48%; MR_D, 69.80.).

2-Ethylhexyl 2-Methyl-5-oxopyrrolidine-2-carboxylate (yield 85%), b.p. 179~181° at 3.0 mm. Hg, d_4^{20} 1.0106, n_D^{20} 1.4668 (Found: N, 5.48; MR_D, 70.29. Calcd. for $C_{14}H_{25}O_3N$: N, 5.48%; MR_D, 69.80.).

Dodecyl 2-Methyl-5-oxopyrrolidine-2-carboxylate (yield 50%), b.p. 198~199° at 0.5 mm. Hg, m.p. 37~9° (from ethanol) (Found: N, 4.47. Calcd. for $C_{18}H_{33}O_3N$: N, 4.49%.).

Benzyl 2-Methyl-5-oxopyrrolidine-2-carboxylate (yield 70%), b.p. 237~240° at 1 mm. Hg, m.p. 94~95° (from carbon tetrachloride) (Found: N, 6.01. Calcd. for $C_{13}H_{15}O_3N$; N, 6.00%.).

Summary

The synthesis of 2-amino-2-methylglutaric acid from levulinic acid by Strecker's method is reported. This acid gives 2-methyl-5-oxopyrrolidine-2-carboxylic acid on dehydration, and some of its esters were prepared and tested for plasticizer performance.

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[4] E. Fischer, *Ber.*, **34**, 433 (1901).