

dioxide according to the method indicated, but not described by Claisen.⁴ To 125 g. of potassium hydroxide in 400 cc. of absolute alcohol was added 198 g. of α -bromo- β -ethoxypropionaldehydediethylacetal and the mixture refluxed in an atmosphere of nitrogen for two hours. Insoluble solids were filtered off and the filtrate distilled under vacuum. The residue from the distillation was extracted with ether and the extract concentrated and combined with the first distillate. Redistillation yielded 110 g. (80%) of the desired product, b. p. 94–96° (20 mm.).

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 62.1; H, 10.35. Found: C, 61.68; H, 10.51.

2-Aminopyrimidine.—A solution of 3.80 g. (0.04 mole) guanidine hydrochloride in 100 cc. of absolute alcohol was saturated with anhydrous hydrogen chloride at 0°. To this was added dropwise 3.48 g. (0.02 mole) of the acetal in 25 cc. of absolute alcohol over a period of one hour with stirring and continued cooling. The resulting orange colored solution was again saturated with hydrogen chloride, stirred at room temperature for one and one-half hours and finally warmed to 70–80° under reflux for an hour. The solvent and excess acid were removed under vacuum and the residue made strongly alkaline with 10 cc. of 50% aqueous sodium hydroxide. The liberated 2-aminopyrimidine was extracted with hot benzene, the extract dried ($MgSO_4$) and the pyrimidine hydrochloride precipitated

by bubbling in hydrogen chloride; yield, 1.37 g. (53%); m. p. hydrochloride, 194–196° (recorded 197–198°); m. p. free base, 122–126° (recorded 126°); m. p. picrate, 239–241° (recorded 237°).

Anal. Calcd. for free base, $C_4H_6N_2$: C, 50.51; H, 5.30; N, 44.2. Found: C, 51.31; H, 5.46; N, 43.97.

Anal. Calcd. for hydrochloride, $C_4H_6ClN_2$: Cl, 26.95. Found: Cl, 27.47.

The results of a number of experiments designed to determine optimum conditions for accomplishing the condensation reveal that a medium of saturated alcoholic hydrogen chloride was the most favorable tried. Dilute aqueous mineral acids gave poor yields of about 10–12%; while concentrated acids resulted in intermediate yields of about 36%. Little or no condensation apparently occurred in alkaline solutions. Yields were considerably better when double the theoretical requirement of guanidine salt was used.

Summary

A new method is described for synthesizing 2-aminopyrimidine by condensing guanidine with β -ethoxyacroleindiethylacetal in acid medium.

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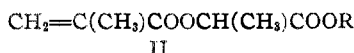
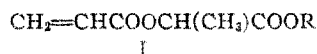
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[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY¹]

Polymerizable Esters of Lactic Acid. α -Carbalkoxyethyl Acrylates and Methacrylates

BY C. E. REHBERG, MARION B. DIXON AND C. H. FISHER

The acrylates and methacrylates of the lower aliphatic alcohols have been studied and used extensively as resin intermediates,^{2,3} but the corresponding esters prepared from alcohols substituted with carbalkoxy groups have received little attention. This paper describes the conversion of alkyl lactates⁴ into carbalkoxyethyl acrylates (I) and methacrylates (II) and the properties and polymerization of these unsaturated esters.



The carbomethoxymethyl and α -carbomethoxypropyl esters of methacrylic acid have been prepared by heating potassium methacrylate with methyl chloroacetate and methyl α -bromobutyrate.⁵ α -Carbomethoxypropyl acrylate has been made from potassium acrylate and methyl α -bromobutyrate.⁵ The reaction between glycol dilactate and methacrylic anhydride has been used to prepare glycol α -methacryloxypropionate.⁵

In the present work unsaturated esters of lactic

acid were prepared⁶ by acylating various lactic esters with acrylyl chloride, methacrylyl chloride, or methacrylic anhydride. The resulting acrylates and methacrylates (Table I) were colorless liquids that exhibited the expected tendency to polymerize.

The acrylates and methacrylates of Table I were polymerized, and the resulting resins were examined briefly. The esters having only one olefinic linkage yielded thermoplastic polymers. The acrylates prepared from alkyl lactates yielded polymers that were roughly similar in hardness and general appearance to the corresponding polyalkyl acrylates.² Comparison of polyethyl acrylate with polymerized carbomethoxyethyl acrylate indicates that substituting the carbomethoxy group for hydrogen in ethyl acrylate hardens the polymer and raises its brittle point.

The hardest and softest thermoplastic polymers of the present work were made from the methacrylate of methyl lactate and the acrylate of *n*-butyl lactate, respectively. Since alkyl glycolates, lactates, and α -hydroxyisobutyrate may be regarded as primary, secondary, and tertiary alcohols, polymerized glycolate acrylates and hydroxyisobutyrate acrylates would be expected to be softer and harder, respectively, than the corresponding polymeric acrylates prepared from alkyl lactates.^{2,7} The methacrylate of methyl α -

(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

(2) H. T. Neher, *Ind. Eng. Chem.*, **28**, 267 (1936).

(3) (a) D. E. Strain, R. G. Kennelly and H. R. Dittmar, *ibid.*, **31**, 382 (1939); (b) D. E. Strain, *ibid.*, **32**, 540 (1940).

(4) Lee T. Smith and H. V. Claborn, *ibid.*, **32**, 692 (1940).

(5) D. E. Strain, U. S. Patent 2,141,546, December 27, 1938.

(6) E. M. Filachione of this Laboratory has made carbomethoxy-methyl acrylate by treating methyl glycolate with α -acetoxypropionyl chloride and pyrolyzing the ester thus obtained.

(7) C. E. Rehberg, W. A. Faucette and C. H. Fisher, *THIS JOURNAL*, **66**, 1723 (1944).

TABLE I
 ACRYLATES AND METHACRYLATES OF LACTIC ESTERS

Lactate	Acylating agent	Yield, %	Con- version, %	B. p.		n_D^{20}	d_4^{20}	Mol. refraction		Sap. equiv.,		Brittle point of polymer °C.
				°C.	Mm.			Calcd.	Found	Calcd.	Found	
Methyl	Acrylyl chloride	38	38	58	2.8	1.4320	1.0920	37.38	37.59	79.1	78.3	15
Ethyl	Acrylyl chloride	100	51	51	0.6	1.4290	1.0496	41.98	42.29	86.1	85.7	0
<i>i</i> -Propyl	Acrylyl chloride	89	55	58	1.5	1.4255	1.0135	46.60	47.02	93.1	92.6	3
<i>n</i> -Butyl	Acrylyl chloride	82	50	60	0.8	1.4330	1.0097	51.22	51.53	100.1	99.8	-29
<i>i</i> -Butyl	Acrylyl chloride	60	48	80	2.4	1.4310	1.0057	51.22	51.54	100.1	99.0	-12
Allyl	Acrylyl chloride	40	40	62.5	1.2	1.4450	1.0540	46.14	46.51	92.1	93.4	..
Cyclohexyl	Acrylyl chloride	73	41	103.5	1.0	1.4578	1.0543	58.26	58.55	113.2	112.7	20
Methylvinyl- carbinyl	Acrylyl chloride	76	38	62	0.8	1.4418	1.0296	50.75	50.91	99.1	98.2	..
<i>n</i> -Butyl	Methacrylyl chloride	77	77	83	2.1	1.4349	0.9968	55.84	56.06	107.1	106.2	18
<i>i</i> -Butyl	Methacrylyl chloride	66	22	77	0.9	1.4330	0.9916	55.84	56.13	107.1	106.7	22
Methyl	Methacrylyl chloride	46	38	65	2	1.4338	1.0615	41.99	42.22	86.1	86.1	58
Ethyl	Methacrylic anhydride	40	40	82	5	1.4341	1.0271	46.60	47.23	93.1	93.2	44
<i>i</i> -Propyl	Methacrylic anhydride	45	45	62	1.5	1.4273	0.9962	51.22	51.63	100.1	99.4	36
<i>n</i> -Butyl	Methacrylic anhydride	41	41	75	1.0	1.4349	0.9953	55.84	56.14	107.1	106.2	18
Methallyl	Methacrylic anhydride	60	60	76	0.7	1.4480	1.0168	55.37	55.87	106.1	108.1	..

^a Based on unrecovered alkyl lactate. ^b Based on alkyl lactate placed in reaction flask.

hydroxyisobutyrate should yield the hardest polymer.

The brittle points of the polymers (Table I) roughly paralleled the hardness. Polymers made from the carbalkoxyethyl acrylates had brittle points (Table I) that were 3 to 25° higher than those of the corresponding polyalkyl acrylates.^{7,8,9} The opposite was true, however, for the polymerized carbalkoxy methacrylates, which had brittle points considerably lower than those of the polyalkyl methacrylates.¹⁰

When polymerized, the acrylates and methacrylates prepared from allyl, methallyl, and methylvinylcarbinyl lactates yielded insoluble and infusible resins (presumably cross-linked). The tendencies of these three bifunctional monomers to form cross-linked resins were compared by copolymerizing various percentages of the ester with methyl acrylate in ethyl acetate solution and comparing the minimum concentration of carbalkenoxyethyl acrylate or methacrylate required to produce gelation of the copolymer solution. Only a small proportion (0.1 to 0.2% of the monomer mixture) of the bifunctional monomers was needed to cause gelation. Earlier work^{11,12} showed that even smaller proportions of some monomers (methallyl or β -chloroallyl acrylate) are effective in producing gels, whereas larger quantities of furfuryl, citronellyl, and crotyl acrylate are required.

Experimental

Preparation of Acrylyl and Methacrylyl Chlorides.—Acrylic acid was prepared by the pyrolysis of ethyl acrylate.¹³ Methacrylic acid was obtained from the manu-

facturer, by the hydrolysis of methacrylic anhydride, and by pyrolysis of certain alkyl methacrylates.¹³

Conversion of the acids to the acyl chlorides by the reaction of phosphorus oxychloride with sodium salts of the acids¹⁴ was unsatisfactory. The reaction of phosphorus trichloride with the acids gave moderate yields, the procedure being as follows.

One mole of acrylic acid and one-third mole of phosphorus trichloride were mixed at room temperature in a flask fitted with a reflux condenser. The flask was then gently warmed until boiling or effervescence began. The reaction was exothermic, and some cooling was required. The flask was kept at 60–70° for fifteen minutes and then at room temperature for two hours. The mixture had then separated into two layers, the upper being the desired product. This was removed and, after the addition of 1 g. of cuprous chloride, was distilled at 30 to 40° (140 mm.). Upon redistillation it boiled at 30 to 32° at 140 mm. or at 74 to 76° at atmospheric pressure. Its properties were n_D^{20} 1.4343, d_4^{20} 1.1136, M^{200} calcd. 20.47, found 21.20. The yield was 66% of the theoretical. Similarly, methacrylyl chloride was obtained in 75 to 80% yield and had the properties: n_D^{20} 1.4435, d_4^{20} 1.0871, M^{200} calcd. 25.08, found 25.52, b. p. 95–96° or 50–52° (135 mm.).

Reaction of the Acid Chloride with Lactic Esters.—A 10% excess of the chloride was generally used. In a few experiments no reagent was used to combine with the hydrogen chloride evolved in the reaction; low yields of the desired products resulted and, in some cases, addition of hydrogen chloride to the olefinic double bond occurred. As hydrogen chloride absorbents, anhydrous sodium carbonate, calcium carbonate, pyridine and formamide were tested. Sodium carbonate was preferable. A 10% excess over the theoretical amount of powdered anhydrous sodium carbonate was used in most of the experiments, a fine suspension of the carbonate being maintained in the reaction mixture by an efficient mercury-sealed stirrer. The tendency of hydrogen chloride to add to the double bond was much less with the methacrylates than with the acrylates, and no hydrogen chloride absorbent was required when methacrylyl chloride was used. The acrylic and, to a less degree, the methacrylic derivatives readily polymerized when heated; so it was necessary to add a polymerization inhibitor to the reaction mixtures and to the products before redistillation. Cuprous chloride, alone or mixed with copper powder, was used for this purpose.

The usual procedure was as follows: One-half mole of the alkyl lactate, 0.28 mole of powdered, anhydrous sodium carbonate, and 5 g. of powdered cuprous chloride were placed in a 3-neck, round-bottom flask fitted with a mercury-seal stirrer, a reflux condenser, and a dropping

(8) E. Jenckel, *Kolloid-Z.*, **100**, 163 (1942).

(9) C. E. Rehberg and C. H. Fisher, *THIS JOURNAL*, **66**, 1203 (1944).

(10) P. O. Powers, "Synthetic Resins and Rubbers," John Wiley and Sons, Inc., New York, N. Y., 1943, 296 pp.

(11) C. E. Rehberg, C. H. Fisher and Lee T. Smith, *THIS JOURNAL*, **66**, 763, 1003 (1943).

(12) C. E. Rehberg and C. H. Fisher, "Preparation and Polymerization of Acrylyl Esters of Olefinic Alcohols," submitted to *THIS JOURNAL*.

(13) W. P. Ratchford, C. E. Rehberg and C. H. Fisher, *THIS JOURNAL*, **66**, 1864 (1944).

(14) (a) C. Moureu, *Ann. chim. phys.*, [7] **2**, 198 (1894); (b) E. P. Kohler, *Am. Chem. J.*, **42**, 380 (1909); (c) D. T. Mowry, *THIS JOURNAL*, **66**, 371 (1944).

funnel. The flask was kept at or below room temperature while 0.55 mole of the acid chloride was added slowly with stirring. When the addition was complete, the mixture was allowed to come to room temperature. After standing for two to eighteen hours, it was heated to 80–100° for one-half to three hours. After cooling, the reaction mixture was washed repeatedly with water to remove any acid chloride, acid, inorganic salts, and, in the case of the lower alkyl lactates, any unreacted lactic ester. The product was then dried and distilled. Fresh cuprous chloride or, preferably, diamylhydroquinone was added before distillation, and carbon dioxide rather than air was supplied through an ebullition tube to prevent bumping during distillation. Yields and other data are recorded in Table I.

Reaction of Methacrylic Anhydride with Lactic Esters.—Commercial methacrylic anhydride was used. Redistillation before use was unnecessary.

The procedure was essentially the same as that in which the acid chlorides were used, except that the hydrogen chloride absorber was omitted and a few drops of sulfuric acid were added to catalyze the reaction. The reaction proceeded sluggishly and was incomplete, even when the mixtures were heated for five hours at 130–140°. Since methacrylic anhydride is not readily soluble in water and hydrolyzes slowly, it was not easily removed from the reaction mixture before distillation. When the lower alkyl lactates, especially methyl lactate, were used, the desired product and methacrylic anhydride had boiling points so close together that complete separation by distillation was difficult. Since methacrylic anhydride is a bifunctional polymerant, even traces of it in a monofunctional monomer profoundly alter the properties of the resin obtained by polymerization, a cross-linked polymer being obtained.

Polymerization Experiments.—The acrylates and methacrylates were polymerized in aqueous emulsion.

Fifty grams of monomer, 2 g. of Tergitol no. 4, 1 g. of Triton 720, and 100 g. of water were placed in a flask fitted with a paddle-type stirrer. The flask was placed in a bath kept at 100°, and ammonium persulfate was added, 10 mg. at a time, at intervals of thirty minutes, until polymerization began. Usually only one or two

portions of catalyst were required. Heating and stirring were continued for three hours after polymerization began, although one hour appeared to be sufficient. The emulsions were steam-distilled to remove monomer or volatile impurities. Brine was added to break the emulsions, and the polymers were then washed on a small washing mill. Yields were virtually quantitative.

Since some of the polymers were too soft and tacky to be molded and handled in sheet form, and hence could not be readily tested on the standard brittle-point apparatus, the brittle points of all the polymers were determined by the rather crude procedure of immersing a strip in a cooled ethanol bath, grasping it with tongs, and flexing. A water-bath was used for determinations above room temperature. Results could be duplicated within about $\pm 3^\circ$ by this method. The brittle points of the polymers are included in Table I.

Some of the monomers of Table I were polymerized in mass and in ethyl acetate solution. The products obtained by mass polymerization were transparent and colorless; the solutions of the polymers were colorless and clear.

Determination of Cross-Linking Tendency.—The method¹² described previously was used.

Summary

α -Carbalkoxyethyl acrylates and methacrylates were prepared by acylating methyl, ethyl, isopropyl, *n*-butyl, isobutyl, cyclohexyl, allyl, methallyl, and methylvinylcarbinyl lactates with acrylyl chloride, methacrylyl chloride or methacrylic anhydride. Polymerization of these unsaturated esters yielded colorless and transparent resins. The esters having two olefinic linkages yielded insoluble and infusible polymers. The cross-linking tendency of the bifunctional monomers was less than that of methallyl acrylate but greater than that of citronellyl, furfuryl, or crotyl acrylate.

PHILADELPHIA, PA.

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[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY OF CORNELL UNIVERSITY MEDICAL COLLEGE]

The Synthesis of Optically Inactive Desthiobiotin

BY JOHN L. WOOD AND VINCENT DU VIGNEAUD¹

Desthiobiotin, ϵ -(4-methyl-5-imidazolidone-2)-caproic acid, has been found to be as effective as an equal weight of biotin in supporting the growth of yeast. It also has been shown to exhibit anti-biotin activity toward some microorganisms.^{2,3} The optically active compound ($[\alpha]^{25}_D +10.7^\circ$) has been obtained by degradation of biotin by the action of Raney nickel on the methyl ester⁴ or the sodium salt.⁵ It has furthermore been resynthesized from its further degradation product,

ζ,η -diaminopelargonic acid, by the action of phosgene in alkaline solution.⁶

A method of total synthesis of *dl*-desthiobiotin which promises to be a practical means of obtaining the compound in quantity has been devised.

(1) The authors wish to express their appreciation to Mr. Roscoe Funk of this Laboratory for carrying out the microanalyses and to Dr. Karl Dittmer, Mrs. Glenn Ellis and Miss Kate Redmond for the microbiological assays.

(2) Dittmer, Melville and du Vigneaud, *Science*, **99**, 203 (1944).

(3) Lilly and Leonian, *ibid.*, **99**, 205 (1944).

(4) du Vigneaud, Melville, Folkers, Wolf, Mozingo, Keresztesy and Harris, *J. Biol. Chem.*, **146**, 475 (1942).

(5) Melville, Dittmer, Brown and du Vigneaud, *Science*, **98**, 497 (1943).

α -Aminosuberic acid, III, was prepared by the malonic ester method from ethyl ϵ -bromocaproate, I. The amino acid was treated with acetic anhydride and pyridine according to the method of Dakin and West.⁷ The resulting ζ -keto, η -acetoaminopelargonic acid, IV, was hydrolyzed to the amino ketone derivative, V, and this was treated with potassium cyanate to produce ϵ -(4-methyl-5-imidazolone-2)-caproic acid, VI. The sodium salt of the imidazolone was reduced with hydrogen and Raney nickel catalyst at 150 atmospheres

(6) Melville, *THIS JOURNAL*, **66**, 1422 (1944).

(7) Dakin and West, *J. Biol. Chem.*, **78**, 91, 745, 757 (1928).