

TABLE I
 3-MERCAPTOPROPIONIC ACID, ALKYL XANTHATES

Potassium Alkyl Xanthate	Yield, %	Melting Point	Refractive Index (n_D^{25})	Calcd. for	Analysis			Found:		
					C	H	S	C	H	S
Methyl	100	—	1.5511	$C_5H_8O_3S_2$	33.3	4.47	35.6	33.5	4.57	35.9
Ethyl	95	70–71°	—	$C_6H_{10}O_3S_2$	37.1	5.19	33.0	37.3	5.08	33.3
<i>n</i> -Propyl	99	50–53°	—	$C_7H_{12}O_3S_2$	40.3	5.81	30.8	40.2	5.81	30.8
Allyl	97	—	1.5505	$C_7H_{10}O_3S_2$	40.7	4.89	31.1	40.4	5.01	31.3
<i>n</i> -Butyl	100	—	1.5333	$C_8H_{14}O_3S_2$	43.2	6.35	28.8	43.3	6.46	29.2
2-Ethylhexyl	100	—	1.5177	$C_{12}H_{22}O_3S_2$	51.8	7.97	23.0	51.3	7.86	23.0

the reaction depends on a number of factors including the nature of the attacking reagent, solvent employed, and reaction conditions.

Although mercaptans and other organic sulfur compounds have been studied as nucleophiles, the reaction of xanthates with β -propiolactone has not been reported. In the present study it has been found that essentially quantitative yields of β -carboxyethyl xanthate esters are produced when β -propiolactone and potassium xanthates are allowed to react in aqueous solution at 20–30°.

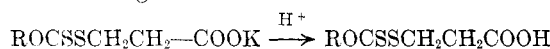
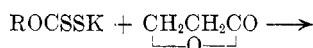


Table I summarizes the results of this investigation.

Certain of these products possess interesting fungicidal, herbicidal, and microbiological activity.

EXPERIMENTAL

The potassium alkyl xanthates employed were freshly prepared from alcoholic potassium hydroxide and carbon disulfide. Freshly distilled β -propiolactone was used in these experiments. The reaction of potassium ethyl xanthate with β -propiolactone is typical of the general procedure employed and will be discussed in detail.

To a solution of 8.0 g. (0.05 mole) of potassium ethyl xanthate in 100 ml. of water at 15–20° was added 3.7 g. (0.05 mole) of β -propiolactone over a 10-min. period. Occasional cooling was necessary to maintain the temperature below 20°. After an additional 2-hr. period at room temperature, the solution was acidified with hydrochloric acid whereupon a white crystalline solid separated. This solid was removed by filtration and was washed with water. After drying in a vacuum desiccator, there was obtained 9.4 g. of product, m.p. 69–70°. Recrystallization from Skellysolve B yielded 9.2 g. (95%) of 3-mercaptopropionic acid, ethyl xanthate, m.p. 70–71°.

In a similar manner the potassium alkyl xanthates listed in Table I were reacted with β -propiolactone. In the case of liquid products, isolation was accomplished by solvent extraction after acidification, water washing, drying, and evaporation of the solvent. Analytical data in Table I are on the products as isolated in this manner. Purification by vacuum distillation was not entirely satisfactory as there was evidence of decomposition at temperatures above 140–150°.

ST. LOUIS RESEARCH DEPARTMENT
 ORGANIC CHEMICALS DIVISION
 MONSANTO CHEMICAL CO.
 ST. LOUIS 4, MO.

Reaction of Cyclohexanone and Hydrogen Peroxide with Ferrous Sulfate and Dimethyl Maleate

G. B. PAYNE AND C. W. SMITH

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The reaction of cyclohexanone peroxide (I) (formed *in situ* from cyclohexanone and hydrogen peroxide) with ferrous ion in the presence of butadiene to give dimethyl 8,12-eicosadiene-1,20-dioate was recently reported.¹

We have now found that dimethyl maleate will also react with the intermediate radical A² to give a corresponding dimeric product, II. The latter was isolated, after esterification, as a reasonably pure distillation residue (38% yield based on unrecovered ketone, 39% based on unrecovered dimethyl maleate, 35% on hydrogen peroxide) after removal of the more volatile 1:1 products, III and IV (33% yield based on unrecovered ketone).³ Analysis of the mixture of III and IV by carbon and hydrogen values, iodine number and by quantitative hydrogenation indicated it to contain 91% of III and 9% of IV.

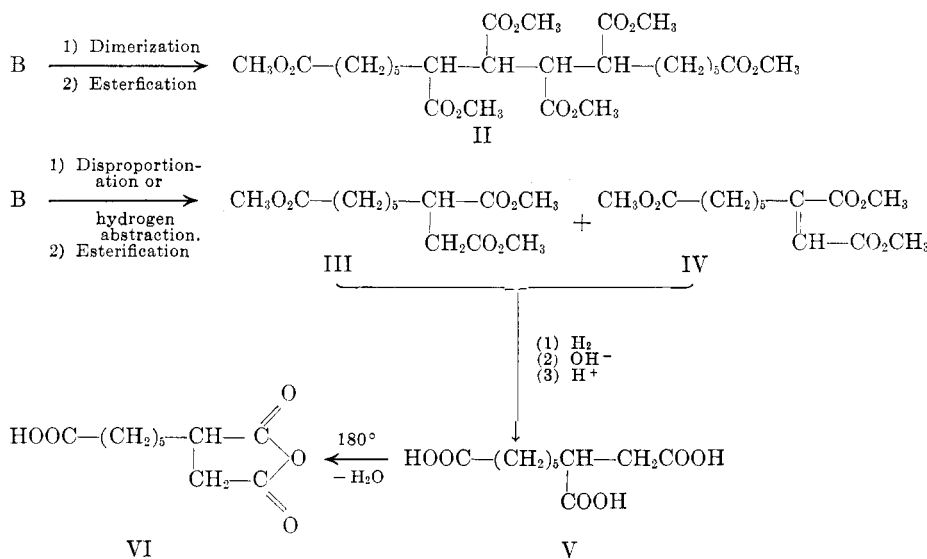
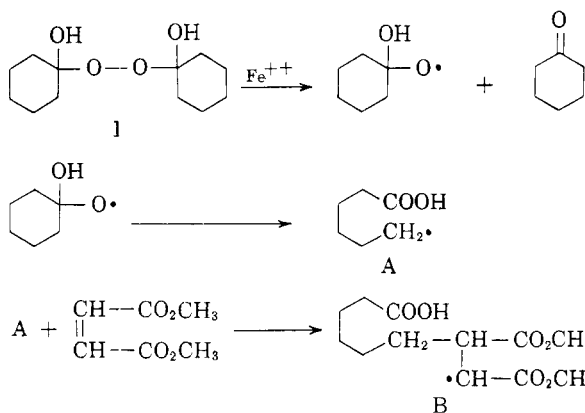
Saponification of this hydrogenated ester mixture afforded the water-soluble 3-carboxyazelaic acid (V), an apparently novel compound.

When V was heated at 180° and 1 mm. for six hours, one molecule of water was lost and a water-insoluble anhydride was formed. The infrared spectrum of the latter was compatible with that expected for the substituted succinic anhydride, VI.

(1) M. S. Kharasch and W. Nudenberg, *J. Org. Chem.*, **19**, 1921 (1954).

(2) Cf. ref. 1, footnote 4, for a brief discussion of the possible existence of A.

(3) No comparable lower molecular weight products were observed in the reaction of I with iron and butadiene (ref. 1).



EXPERIMENTAL

Reaction of cyclohexanone and hydrogen peroxide with ferrous sulfate and dimethyl maleate. To a solution of 50 g. of concentrated sulfuric acid in 750 ml. of methanol was added 196 g. (2.0 moles) of cyclohexanone, keeping the temperature below 30° by external cooling. To this solution was then added portionwise 1 mole of 30% hydrogen peroxide, again keeping the temperature below 30° by cooling.

The cyclohexanone peroxide solution thus prepared was added dropwise with stirring at 20–25° over a 2 hr. period to a mixture of 292 g. (1.05 mole) of ferrous sulfate heptahydrate, 850 ml. of water, 150 g. of concentrated sulfuric acid, 300 ml. of methanol, and 180 g. (1.25 moles) of dimethyl maleate (n_D^{20} 1.4418) contained in a 3-liter, 3-neck round-bottom flask.

After completion of the addition, stirring was continued for 15 min. before the mixture was poured into 2 l. of water and extracted with three 500 ml. portions of chloroform. The combined chloroform extract was washed with water, dried over magnesium sulfate, and concentrated on the steam bath. The concentrate, on distillation through a 1 × 50 cm. glass helices packed column, gave the following fractions after removal of the last traces of solvent.

Fraction 1: 82–84° (80 mm.), 108 g.; Fraction 2: 84–65° (80–20 mm.), 11 g.; Fraction 3: 65–98° (20 mm.), 3 g.; Fraction 4: 98–65° (20–1 mm.), 66 g., n_D^{20} 1.4420. Residue, 196 g. Fractions 1 and 2 were combined; titration with hydroxylamine hydrochloride indicated the presence of 104 g. (1.06 mole) of recovered cyclohexanone. Fraction 4 was re-

covered dimethyl maleate (0.46 mole) identified by boiling range and refractive index.

The residue was esterified by refluxing overnight in 1000 ml. of methanol containing 5 g. *p*-toluenesulfonic acid catalyst. A slight excess of potassium hydroxide in water was then added to neutralize the catalyst and the mixture was concentrated to low volume on the steam bath. The concentrate was taken up in 1000 ml. of chloroform and washed with 200 ml. of 5% potassium carbonate solution and then with water. After removal of chloroform on the steam bath, the crude ester mixture was distilled through the packed column to a maximum kettle temperature of 270°. The following fractions were obtained:

Fraction 5: 50–152° (1 mm.), 10 g.; Fraction 6: 152–158° (1 mm.), 85 g., n_D^{20} 1.4464. Residue, 98 g.

Analysis of Fraction 6 was in agreement for a mixture containing 91% by weight of dimethyl-3-carbomethoxyazelaic acid and 9% of dimethyl-3-carbomethoxy-2-nonene-1,9-dioate

(33% based on unrecovered cyclohexanone).

Anal. Calcd. for 91% $\text{C}_{13}\text{H}_{22}\text{O}_6$ and 9% $\text{C}_{13}\text{H}_{20}\text{O}_6$: C, 56.9; H, 8.1; sapon. equiv., 92; iodine no., 9. Found: C, 56.9; H, 8.1; sapon. equiv., 93; iodine no., 9.

Analysis of the residue was in fair agreement for dimethyl 7,8,9,10-tetracarboxymethoxy-1,16-hexadecanedioate (38% yield based on unrecovered ketone).

Anal. Calcd. for $\text{C}_{26}\text{H}_{42}\text{O}_{12}$: C, 57.1; H, 7.7; sapon. equiv. 91. Found: C, 57.3; H, 7.5; sapon. equiv. 98.

β-Carboxyazelaic acid. Sixty grams (0.219 mole) of Fraction 6 above was dissolved in 150 ml. of ethanol and shaken with hydrogen at room temperature and 50 pounds pressure using 10 g. of 5% palladium-on-charcoal catalyst. After 30 min., 0.018 mole of hydrogen had been absorbed and the uptake was negligible during an additional 5 hr. After removal of the catalyst by filtration, there was added a solution of 33 g. of sodium hydroxide in 150 ml. of water; the mixture was allowed to reflux overnight on the steam bath. The water-soluble product was isolated by acidification with 75 ml. of concentrated hydrochloric acid, followed by concentration to an oily residue containing sodium chloride. After trituration with warm acetone, salt was removed by filtration, and the acetone solution was adjusted to a volume of 125 ml. An equal volume of benzene was added, followed by enough petroleum ether to effect a phase separation. Long chilling produced 35 g. of a hard crystalline mass on the surface, m.p. 64–72°. Recrystallization from acetone-chloroform (1:3) afforded 27 g. of *β*-carboxyazelaic acid, m.p. 64–67°, containing one quarter of a molecule of chloroform of crystallization.

Anal. Calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_5 \cdot \frac{1}{4}\text{CHCl}_3$: C, 47.0; H, 6.3; Cl,

10.1; neut. equiv., 88. Found: C, 47.5; H, 6.4; Cl, 9.0; neut. equiv., 88.

After drying for 15 hr. at 60° and 5 mm., the neut. equiv. had fallen to 80.7; further drying at 80° and 2 mm. for 24 hr. caused the N.E. to drop to 78.1 and the material was re-analyzed.

Anal. Calcd. for $C_{10}H_{16}O_6$: C, 51.7; H, 6.9; neut. equiv., 77.4. Found: C, 51.9; H, 6.9; neut. equiv. 78.1. The melting point of the solvent-free acid was 83–84°.

A two gram sample of acid (m.p. 64–67°) lost the theoretical amount of chloroform when heated for 2 hr. at 120° and 1 mm. The same sample, when heated further at 180° and 1 mm. pressure for 6 hr. lost an additional weight corresponding to the loss of 1 molecule of water. The crude *anhydride* thus obtained melted at 81–83°; after crystallization from benzene-petroleum ether, it melted at 80–81°.

Anal. Calcd. for $C_{10}H_{14}O_5$: C, 56.1; H, 6.6; sapon. equiv., 72. Found: C, 56.3; H, 6.8; sapon. equiv., 73.

The infrared spectrum (KBr pressed plate) exhibited absorptions at 5.35 and 5.61 μ ; succinic anhydride absorption occurs at 5.36 and 5.61 μ .⁴

SHELL DEVELOPMENT COMPANY
EMERYVILLE, CALIF.

(4) H. M. Randall, R. G. Fowler, N. Fuson, and J. R. Dangle, *Infrared Determination of Organic Structures*, D. Van Nostrand Co., Inc., New York, 1949, p. 163.

***p*-Nitrophenylsemicarbazones of Trioses and Carbonyl Compounds of Biochemical Interest**

MAKEPEACE U. TSAO

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The derivatives of *p*-nitrophenylsemicarbazide with carbonyl compounds of biological origin are of interest in that they may offer a means of isolation and identification of the latter substances. It was of particular interest to us to secure a tool for the analysis of trioses. Earlier we have reported the preparation of *p*-phenylazophenylsemicarbazones of trioses and biologically related carbonyl compounds.¹ These derivatives were found unsatisfactory as analytical tools. In a search for a quantitative precipitant for glucose, Barré and Piché^{2,3} prepared 4-substituted semicarbazides and obtained *p*-nitrophenylsemicarbazones of acetone, pyruvic acid, glyoxylic acid, and glucose among others. The presence of a nitrophenyl group in the *p*-nitrophenylsemicarbazones should provide an intense coloration by its derivatives in alkaline solution. This property of possible analytical application merited exploration; consequently, *p*-nitrophenylsemicarbazones of the above mentioned trioses and several carbonyl compounds of biochemical interest were synthesized.

The one-step synthesis of *p*-nitrophenylsemicarbazide from the commercially available *p*-

nitrophenyl isocyanate and the preparation of *p*-nitrophenylsemicarbazones are described in this report. Barré and Piché have obtained *p*-nitrophenylsemicarbazide by different methods.² However, the simple conversion of isocyanate into semicarbazide with anhydrous hydrazine was not attempted. This conversion has been carried out with good yield in this laboratory. The *p*-nitrophenylsemicarbazide thus obtained was converted into its hydrochloride to increase its solubility in water. Mixing of a saturated solution of the semicarbazide hydrochloride in 0.1*N* hydrochloric acid with an aqueous solution of the carbonyl compound yields the corresponding semicarbazone at room temperature. Crude semicarbazones are purified by recrystallization from ethanol or acetic acid.

All except one of the *p*-nitrophenylsemicarbazones prepared decompose at melting temperatures; therefore, these derivatives appear to be of little value for the identification of carbonyl compounds by melting point. Paper chromatography of the *p*-nitrophenylsemicarbazones was investigated for possible analytical application and the results will be reported elsewhere. The high extinction coefficients of the solutions of these derivatives in the ultraviolet range and the intense coloration on the addition of alkali to these solutions indicate that a promising reagent for the analysis of trioses and the carbonyl compounds of biochemical interest has been found.

EXPERIMENTAL

p-Nitrophenyl isocyanate, acetaldehyde, and ethyl acetoacetate were obtained from the Distillation Products Industries; acetaldehyde was redistilled just before use. Other starting material from various sources were used without further purification. Dihydroxyacetone was obtained from Dougherty Chemical Co. Glycerinaldehyde, *alpha*-ketobutyric acid, *alpha*-ketoglutaric acid, and sodium *beta*-phenylpyruvate were from Sigma Chemical Co. Crude pyruvaldehyde (30% aqueous solution) was from Bios Laboratories, Inc. Oxalacetic acid and crude barium oxalosuccinate were from California Foundation for Biochemical Research.

Melting points are corrected. Absorption maxima, λ_{max} , and molar extinction coefficients, ϵ , were determined in ethanol unless otherwise indicated; a 0.001% solution was used for the determinations with a Beckman DU spectrophotometer.

p-Nitrophenylsemicarbazide. Commercial *p*-nitrophenyl isocyanate was partially purified by filtration in its molten state through a filter paper using a heated funnel. In 250 ml. of anhydrous toluene, 29 g. of the isocyanate was dissolved and the solution was directly filtered into a 1 l. 3-neck flask to remove the small amount of insoluble residue. A suspension of 9 ml. of anhydrous hydrazine in 350 ml. of anhydrous toluene was added dropwise into the isocyanate solution in 45 min. while vigorous stirring of the latter was maintained. Heat was generated by the reaction and immediate precipitation of an orange colored product was observed. The reaction flask was stoppered and allowed to stand overnight. The precipitate was collected on a funnel and washed with toluene, followed with petroleum ether (30–60°). The solvent was removed under vacuum in a desiccator. The crude product (33.7 g.) was recrystallized from boiling absolute ethanol yielding 22.0 g. (63%) of yellow

(1) M. U. Tsao and E. Van Dyke, *J. Am. Chem. Soc.*, **77**, 6693 (1955).

(2) R. Barré and L. Piché, *Can. J. Research*, **19B**, 158 (1941).

(3) R. Barré and L. Piché, *Can. J. Research*, **20B**, 17 (1942).