Preparation of Tricaprylin

By E. B. Hershberg

Pure tricaprylin was required in quantity for use as a solvent medium in animal experiments now being conducted by Dr. Shields Warren with the carcinogenic compounds produced in this Laboratory.[1] The technical 90% caprylic acid produced by Armour and Company (Neo-Fat No. 7) proved to be a suitable source of the acid component. Purification is best effected by conversion with thionyl chloride to the acid chloride, for on careful fractionation octanoyl chloride can be obtained in a state of high purity. A large supply of the technical acid chloride was kindly supplied for the present work by the Armour and Company through the courtesy of H. M. Corley.

A detailed procedure for condensing octanoyl chloride with glycerol in the presence of quinoline was kindly made available to us by Dr. H. H. Young, Swift and Company, who obtained tricaprylin, m. p. 8.6–8.8°, by this method in 82% yield based on glycerol. A disadvantage of this process, noted by Dr. Young and in this Laboratory, is that the crude glyceride is contaminated with a yellow impurity which is retained on distillation and which is rather troublesome to eliminate by adsorption from solution when working with large quantities.

On trying the Schotten–Baumann method under conditions recommended by Menalda[2] it was found that the crude reaction product is completely colorless and that very pure tricaprylin can be obtained in this way in nearly 90% yield.

The technical (90%) octanoyl chloride was first distilled from a Claisen flask at a pressure of 10–30 mm. to make a rough separation and then carefully fractionated in a 1-meter column packed with glass helices. The material used boiled at 89.3–89.6° at 20 mm. (about 80% of the total). A 5-l., three-necked flask was charged with 73.5 g. of anhydrous[3] (vacuum distilled) glycerol, which was washed in with 25–50 cc. of water, and fitted with a Chromel wire stirrer[4] working through a wide glass tube mounted in the center opening to prevent loss by splashing. One of the side openings was fitted with a cork carrying a toluene thermometer and a small glass funnel; the other was equipped with a similar funnel. Simultaneous addition was then made of 410 g. of octanoyl chloride through one funnel and of a solution of 181 g. of 85% potassium hydroxide pellets in 375 cc. of water through the other. The liquids were run from constant-rate funnels[5] under a common air pressure of about 5 lb., which facilitated regulation. Since troublesome emulsions sometimes result from the presence of excess alkali, it is well to keep the acid chloride addition 25–50 cc. ahead of the alkali. The reagents were added in the course of about one hour, controlling the temperature to -5 to 0° by ice–salt cooling. Toward the end a stable emulsion formed; 75–100 cc. of ether was added to thin the mixture and provide better temperature distribution. Vigorous stirring was continued for three hours after the addition at a temperature of -10 to $-5°$; water and ether (1–1.5 l.) were then added and the layers separated. The ether layer was washed once with water and once with saturated sodium chloride solution and then filtered through a paper covered with a little anhydrous sodium sulfate.

After evaporation of the ether the colorless residue was distilled in a modified Claisen flask[6] connected with a ground-glass joint to a receiver (water cooling not required). After separation of a small fore-run (14 g., b. p. 150–233°) of mono- and diglycerides, the main fraction was distilled rapidly with a free flame and a good vacuum to avoid cracking. There was obtained 333 g. of colorless tricaprylin; as registered in the rapid distillation the b. p. was 233–235° at 1 mm. The yield is 89% based on the glycerol and 84% calculated from the acid chloride used. Careful distillation of a small sample gave the b. p. 233–233.5° corr. at 1.0 mm. (oil manometer[7]), freezing point 9.8–10.1° (compare 8–8.3°,[8] 9.45°[9]). Further purification by partial freezing and centrifugation was repeated twice without altering the freezing point.

When stirring was continued for only two hours

---

[1] We are indebted to Drs. M. J. Shear and M. B. Shimkin of the U. S. Public Health Service for making a trial of certain possible substitutes for lard as a medium for the injection of carcinogens, including the triglycerides suggested [Fieser, *Am. J. Cancer*, **34**, 37 (1938)] and certain other more readily available esters. In the first experiments with commercial esters, purified where required by Dr. Hershberg, tricaprylin appeared particularly satisfactory and large-scale tests with this glyceride were then initiated by Dr. Shimkin using a quantity of tricaprylin kindly prepared for us by Dr. H. H. Young of the Swift and Co. Research Laboratories.—L. F. Fieser.

[2] Menalda, *Rec. trav. chim.*, **49**, 967 (1930).

[3] Wet glycerol is suitable if the water content is determined from the density.

[4] Hershberg, *Ind. Eng. Chem., Anal. Ed.*, **8**, 313 (1936).

[5] Hershberg, *Org. Syn.*, **18**, 16 (1938).

[6] Adams and Marvel, *ibid.*, Coll. Vol. I, 1932, p. 125.

[7] Chadwick and Palkin, *Ind. Eng. Chem., Anal. Ed.*, **10**, 399 (1938).

[8] Scheij, *Rec. trav. chim.*, **18**, 193 (1899).

[9] Verkade and Willigen, *ibid.*, **54**, 353 (1935).

after the addition, the yield was slightly lower (324 g. or 86%). Substitution of sodium for potassium hydroxide in equivalent amount did not alter the results.

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY
CAMBRIDGE, MASS.
RECEIVED OCTOBER 20, 1939

A Photosensitized Production of Reducing Sugars from Starch

BY LAWRENCE J. HEIDT

Substances which reduce the Shaffer–Hartmann–Somogyi reagent are produced when light is absorbed by aqueous solutions containing uranyl sulfate and *starch*. The apparatus used to illuminate the solutions is described in *Science*, **90,** 473 (1939). The experimental procedure was the same as that given in THIS JOURNAL, **61,** 3223 (1939), for *sucrose*–uranyl solutions.

The ml. of hypo entered in Table I are calculated from the differences between S.–H.–S. estimations made simultaneously on the illuminated portions of a solution and on a portion kept in the dark, at the same temperature. When 5 ml. of water was added to 5 ml. of the S.–H.–S. reagent, the titration required 46.2 ml. of hypo, but 5 ml. of the unphotolyzed portions in Expts. 1, 2, 3, 4, 5 and 6 required 43.0, 45.5, 45.7, 42.8, 44.8 and 44.8 ml. of hypo, respectively. The potato starch, kindly supplied by Professor C. B. Purves, therefore contained very little reducing sugar, and both the illuminated and unphotolyzed solutions of starch in Expt. 4 appeared water-white.

Solutions were irradiated in quartz tubes at 21° with 8.5×10^{18} photons of λ 254 mμ per minute incident on each 11 ml. sample. The starch solutions were 0.008 M in uranyl sulfate in Expts. 1, 2 and 3; 0.0004 M in quinine sulfate in Expt. 5; 0.0003 M in the sodium salt of fluorescein (Eastman Kodak Technical Grade) in Expt. 6 and contained only starch and water in Expt. 4. Each ml. of hypo entered in Table I was equivalent to 5.7×10^{-5} g. of glucose in the uranyl sulfate solutions and to 5.5×10^{-5} g. of glucose in the others.

TABLE I

Expt.	Starch in 50 ml., g.	pH in soln. before photolysis	pH in soln. after photolysis	Min. photolyzed	Ml. of hypo	ϕ
1a	0.5024	3.0	2.8	21.5	85	0.09
b			2.9	7.2	38	.12
c			2.9	5.0	29.5	.13
d			...	1.45	14.1	.22
2a	.1935	3.35	3.25	8.5	25.5	.07
b			...	4.0	18.0	.10
c			...	3.0	16.0	.12
d			...	2.0	12.1	.14
3a	.0658	3.5	3.4	24.0	26.0	.024
b			...	12.0	17.8	.033
c			...	6.0	13.2	.050
d			...	3.0	8.8	.066
4	.4894	4.35	3.55	860.0	34.5	...
5a	.1935	3.9	3.6	49.5	4.0	<.002
b			3.0	624.0	79.0	<.002
6a	.1956	6.2	6.2	94.5	2.5	
b			5.6	283.0	6.6	

The experiments with quinine and fluorescein were undertaken to discover for this reaction other photosensitizers—preferably dyes and natural products that absorb sunlight. The amount of reducing substances produced when quinine or fluorescein was present, however, was less or little more than when they were absent and very much less than when uranyl sulfate was used. The intense blue fluorescence initially present in Expt. 5b disappeared toward the end of this photolysis and a light straw solution was formed, but in Expt. 6b the yellow fluorescence was only diminished. This also occurred in parallel experiments with solutions of quinine and fluorescein without starch and the pH likewise decreased but in the quinine solution the amount of reducing substances produced was less than 10% of that formed in Expt. 5b and none was formed from the fluorescein or from the uranyl sulfate alone in water.

Quantum yields, ϕ, represent the number of oxygen bridges (linking the glucose units) broken per photon of λ 254 mμ absorbed by the system if the measured product is glucose and one bridge is broken per molecule of glucose produced. This may be too simple an hypothesis except, perhaps, for the initial reaction.

In Expts. 4 and 6, ϕ is not given because the extinction coefficients of these solutions were not known at this wave length. Nevertheless, Expt. 4 shows that the measured reaction in Expts. 1, 2 and 3 is mainly a photosensitized reaction. Also in Expts. 1, 2 and 3, ϕ is smaller and falls more rapidly than for the photosensitized decomposition of sucrose at the same concentration of oxygen bridges, if there is one bridge per sucrose molecule and one per glucose unit in starch. This decrease in ϕ probably is due to the colloidal nature of starch solutions and the chain character of the starch molecule, both of which