Mixed Diglycerides Containing 4-Arsonophenylglycine[1]

By Robert L. McGeachin and Robert E. Cox

The purpose of this investigation was the preparation of fat-soluble glycerides of 4-arsonophenylglycine, previously unreported in the literature. We have prepared and isolated the calcium salts of mixed diglycerides of myristic, lauric and stearic acids with 4-arsonophenylglycine.

The diglycerides were formed by the reaction of 4-arsonophenylglycine with fatty acid monoglycerides in the presence of diacetin. The free diglycerides formed were always contaminated with fatty acid monoglycerides and we were unable to separate these mixtures by use of any of the usual solvents. However, the calcium salts of the diglycerides were separated from the monoglycerides by extraction of the mixture with chloroform which removed the monoglycerides. It was found that the mixtures of the calcium salts and the monoglycerides must be thoroughly dried prior to the chloroform extraction to prevent formation of unseparable emulsions. All attempts to obtain the free acids from these calcium salts have been unsuccessful due to some hydrolysis of the ester bonds in the presence of acid.

Attempts to form the diglycerides by the reaction of fatty acids with α-4-arsonophenylglycylmonoglyceride were unsuccessful as were condensations of sodium salts of fatty acids with 1-(4-arsonophenylglycyl)-2-hydroxy-3-chloropropane.

Experimental

Fatty acid monoglycerides were prepared by a modification of the method of Hilditch and Rigg[2] using a five molar excess of glycerol and omitting the β-naphthalenesulfonic acid catalyst.

Reaction of Fatty Acid Monoglycerides with 4-Arsonophenylglycine.—Ten grams of 4-arsonophenylglycine, 15 g. of monoglyceride (myristoyl, lauroyl or stearoyl), 5 g. of diacetin and 0.1 g. of zinc chloride were heated at 150° for 4 hours at 20 mm. pressure. The mixture was dissolved in 50 ml. of 95% alcohol, charcoaled and filtered hot. Two hundred ml. of water was added to the filtrate and the mixture placed in the ice-box overnight. The precipitated solids were filtered off, washed with cold water and redissolved in 30 ml. of hot 95% alcohol. The solution was neutralized to a *p*H of 7 with sodium hydroxide and 20 ml. of 10% calcium chloride added, precipitating a white solid. The solid was centrifuged, washed with water and recentrifuged several times. This product was dried over calcium chloride *in vacuo* and extracted three times with chloroform. The yields were 4 to 5 g. (20–25%) of a white powder.

Anal.[3] Calcd. for $C_{46}H_{74}O_{16}N_2As_2Ca$: As, 13.6. Found: As, 13.4. *Anal.* Calcd. for $C_{50}H_{82}O_{16}N_2As_2Ca$: As, 13.0. Found: As, 12.7. *Anal.* Calcd. for $C_{58}H_{98}O_{16}N_2As_2Ca$: As, 11.8. Found: As, 11.5.

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(1) Taken from the M.S. thesis of Robert E. Cox.

(2) T. P. Hilditch and J. G. Rigg, *J. Chem. Soc.*, 1774 (1935).

(3) A modification of the method of F. E. Cislak and C. S. Hamilton, This Journal, **52**, 638 (1930), was used in the arsenic analyses.

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Esterification of Polyvinyl Alcohol with Trifluoroacetic Acid or Anhydride

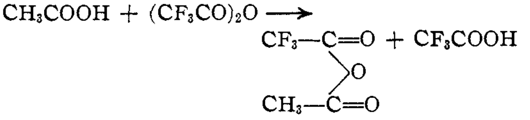
By Paul W. Morgan

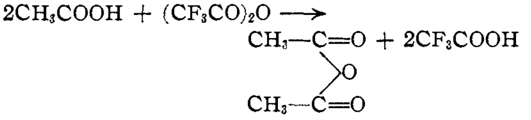
The "impelling" action of chloroacetic acids and their anhydrides on the esterification of cellulose by other organic acids was described years ago by Malm and Clarke.[1] This reaction requires an additional catalyst but no esterification by the chloracetic acid takes place when a second carboxylic acid is present. Polyvinyl alcohol, on the other hand, reacts with a mixture of a carboxylic acid and monochloroacetic acid or its anhydride to form a soluble mixed ester[2] with or without the use of a catalyst. Very little esterification of polyvinyl alcohol is obtained with glacial acetic acid alone.

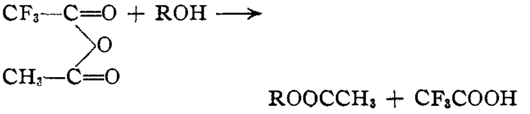
Trifluoroacetic acid or its anhydride differ from monochloroacetic acid because they promote the esterification of polyvinyl alcohol, or other alcohols, by a carboxylic acid without the introduction of trifluoroacetyl groups into the polymer and without the use of any other catalyst. Trifluoroacetic acid acts as an esterification catalyst.

Stacey and his co-workers[3] have described the esterification of various alcohols with carboxylic acids in the presence of relatively large amounts of trifluoroacetic anhydride. A mixed anhydride mechanism was suggested (see equations 1 and 3) but no evidence presented to support it. In their experiments an anhydride to alcohol ratio greater than one was required for good yields of ester. Their experiments seem to show a reaction by means of a mixed anhydride or the anhydride of the carboxylic acid and no, or at least low, catalytic activity on the part of the by-product trifluoroacetic acid.

We have obtained evidence from freezing point depressions which indicates that when trifluoroacetic anhydride is added to glacial acetic acid a molecule of mixed anhydride and a molecule of trifluoroacetic acid are formed, in accordance with equation 1, rather than a molecule of new anhydride as shown by the second equation


$$CH_3COOH + (CF_3CO)_2O \longrightarrow \begin{matrix} CF_3{-}C{=}O \\ \;\;\rangle O \\ CH_3{-}C{=}O \end{matrix} + CF_3COOH \quad (1)$$


$$2CH_3COOH + (CF_3CO)_2O \longrightarrow \begin{matrix} CH_3{-}C{=}O \\ \;\;\rangle O \\ CH_3{-}C{=}O \end{matrix} + 2CF_3COOH \quad (2)$$


$$\begin{matrix} CF_3{-}C{=}O \\ \;\;\rangle O \\ CH_3{-}C{=}O \end{matrix} + ROH \longrightarrow ROOCCH_3 + CF_3COOH \quad (3)$$

This supports the hypothesis that esterification of polyvinyl alcohol or other alcohols by a carboxylic acid in the presence of trifluoroacetic anhydride might proceed through the mixed anhydride to form the unhalogenated ester. However, high degrees of acetylation also are easily obtained by adding small amounts of trifluoroacetic acid or its anhydride to a slurry of polyvinyl alcohol in glacial acetic acid. In these cases the yield of ester must come from a direct esterification catalyzed by trifluoroacetic acid.

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(1) H. T. Clarke and C. J. Malm, U. S. Patent 1,880,808 (Oct. 4, 1932); British Patent 313,408 (Aug. 27, 1929).

(2) E. F. Izard and P. W. Morgan, *Ind. Eng. Chem.*, **41**, 619 (1949).

(3) M. Stacey, E. J. Bourne, J. C. Tatlow and T. M. Tedder, *Nature*, **164**, 705 (1949); *J. Chem. Soc.*, 2976 (1949).

In the absence of a second carboxylic acid, polyvinyl alcohol is quite readily esterified with anhydrous trifluoroacetic acid, yielding trifluoroacetyl esters soluble in many common organic solvents. These esters have been found to lack hydrolytic stability, but form tough, flexible, transparent films, which are slightly plasticized by water and which have low flammability. The hydrolytic instability probably results from the catalytic effect of traces of trifluoroacetic acid. Polyvinyl trifluoroacetate has been made previously by Howk and Jacobson by vinyl polymerization[4] and, except for the hydrolytic instability encountered here, the reported properties were quite similar.

Experimental

Esterification with Acetic Acid Plus Trifluoroacetic Acid.—High viscosity polyvinyl alcohol (Elvanol 91A–65 which was pretreated with dilute alkali to assure complete deacetylation; 5 g.) was heated at 90–100° for 2 hours in a mixture of 18 ml. of glacial acetic acid and 1 ml. of trifluoroacetic acid. At one hour a clear viscous solution was obtained. The viscosity dropped some during the second hour. The product was isolated by diluting the solution with acetone and casting a film. The plastic film was soluble in numerous organic solvents and was highly softened by water. The polymer contained no fluorine and was 74.3% substituted by acetyl groups. Trifluoroacetic anhydride, used in place of the trifluoroacetic acid, produced the same product in a somewhat shorter time.

In a similar reaction with glacial acetic acid alone polyvinyl alcohol remained as a white swollen mass and was still easily water soluble.

Esterification with Trifluoroacetic Acid or Anhydride.—Polyvinyl alcohol (5 g.) was mixed with 45 ml. of trifluoroacetic acid and heated under reflux by an oil-bath at 85° with only initial stirring. The powder dissolved in a very few minutes and esterifications were continued for the periods of time given in the table. The products were isolated by diluting the mixture with acetone, casting a film and washing the film with water. The films were freed of excess water and dried at 85°. They softened somewhat in air at 80° and were limp at 100°.

TABLE I

ANALYSIS FOR CF_3CO– GROUPS

Reacn. time, hours	Fluorine,[5] %	Substn. from F analysis, %	Substn. by sapon., %
0.5	36.6	58.3	58.3
1.5	39.9	70.0	69.5
4.0	44.1	89.7	90.2

Esterification of polyvinyl alcohol with trifluoroacetic anhydride or mixtures of anhydride and acid were more rapid than with the acid alone but the final products were similar in properties.

Tests for Interaction of Trifluoroacetic Anhydride and Acetic Acid.—Glacial acetic acid (10 g.) and trifluoroacetic anhydride (19 g., b.p. 40°) were mixed. Considerable heat was evolved but similar heats of mixing were noted for trifluoroacetic acid with acetic acid or acetic anhydride. The mixture was distilled slowly and distillation started at 73°, the boiling point of trifluoroacetic acid. The boiling point rose slowly to 115° and no definite fractions were obtained, although several cuts were made. The higher fractions had the odor characteristic of acetic anhydride. Titration of the fractions gave no indication of a definite composition. Distillation of mixtures of trifluoroacetic and acetic acids and of trifluoroacetic acid and acetic anhydride gave similar results with no indication of constant boiling fractions. Of course with the acids alone, no odor of anhydride was noted.

As a means of distinguishing between no reaction at all and those represented by equations 1 and 2, freezing point depressions in glacial acetic acid were determined, using a Beckmann thermometer and about 30 g. of additive per 1000 g. of acetic acid. A molal depression of 3.90° was used in the calculations.

TABLE II

MOLECULAR WEIGHTS DETERMINED IN GLACIAL ACETIC ACID

Additive	Molal depression	Mol. wt. Calcd.	Mol. wt. Obsd.
Acetic anhydride	3.68	102	108
Trifluoroacetic acid	3.74	114	119
	3.85		115
Trifluoroacetic anhydride	7.93	210	103
	7.34		112

Since the molal depression of trifluoroacetic anhydride is twice that expected from no reaction, equation 1 must represent the reaction. If equation 2 were correct, the freezing point depression would be three times the normal value.

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[4] B. W. Howk and R. A. Jacobson, U. S. Patent 2,436,144 (1948).

[5] Qualitative test: J. H. Simons and E. O. Ramler, THIS JOURNAL, **65**, 391 (1943). Quantitative analysis: M. L. Nichols and J. S. Olsen, *Ind. Eng. Chem., Anal. Ed.*, **15**, 342 (1943), and N. H. Furman, "Scott's Standard Methods of Chemical Analysis," 5th ed., Vol. I, D. Van Nostrand Co., Inc., New York, N. Y., 1939, p. 405.

Physical Properties of Some 1,1-Difluoro-2,2-dichloroethyl Alkyl Ethers[1,2]

BY J. D. PARK, CURTIS M. SNOW AND J. R. LACHER

We have previously reported on the base-catalyzed action of alkanols on $CF_2{=}CFCl$,[3] $\underline{CF_2{-}CF_2{-}CF{=}CF}$[4] and $\underline{CF_2{-}CF_2{-}CCl{=}CCl}$.[5]

The present study reports on some of the properties of some 1,1-difluoro-2,2-dichloroethyl alkyl ethers obtained by the reaction of $CF_2{=}CCl_2$ and some alkanols described above.[3,4,5] The

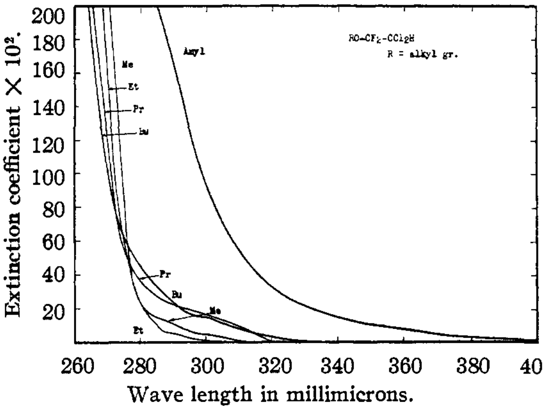

Fig. 1.—Ultraviolet absorption spectra of $ROCF_2{-}CCl_2H$, R is alkyl group.

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[1] This paper represents part of a thesis submitted by Curtis M. Snow to the Graduate School, University of Colorado, in partial fulfillment of the requirements for the degree Doctor of Philosophy, February, 1950.

[2] This work was supported in part by a grant from the Office of Naval Research, contract N6-onr-231, Task Order 6, project No. NR-056-105.

[3] J. D. Park, D. K. Vail, K. R. Lea and J. R. Lacher, THIS JOURNAL, **70**, 1550 (1948).

[4] J. D. Park, M. L. Sharrah and J. R. Lacher, *ibid.*, **71**, 2337 (1949).

[5] J. D. Park, C. M. Snow and J. R. Lacher, Abstract of Papers, 118th Meeting of the American Chemical Society, Division of Ind. and Eng. Chemistry, p. 22L.