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

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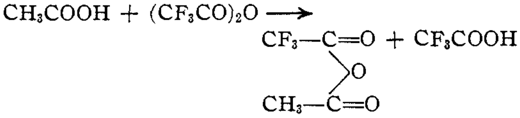
The "impelling" action of chloroacetic acids and their anhydrides on the esterification of cellulose by other organic acids was described years ago by Malm and Clarke.[1] This reaction requires an additional catalyst but no esterification by the chloracetic acid takes place when a second carboxylic acid 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.

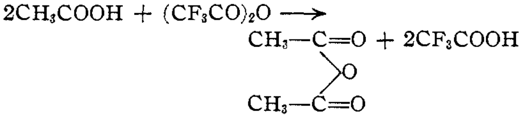
Trifluoroacetic acid or its anhydride differ from monochloroacetic acid because they promote the esterification of polyvinyl alcohol, or other alcohols, by a carboxylic acid without the introduction of trifluoroacetyl groups into the polymer and without the use of any other catalyst. Trifluoroacetic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

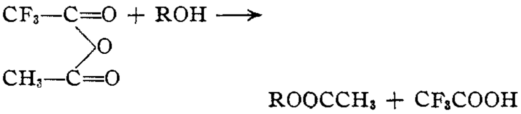
We have obtained evidence from freezing point depressions which indicates that when trifluoroacetic anhydride is added to glacial acetic acid a molecule of mixed anhydride and a molecule of trifluoroacetic acid are formed, in accordance with equation 1, rather than a molecule of new anhydride as shown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



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



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



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

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).