

Application of the Rosenmund reaction to the synthesis of saturated fatty aldehydes

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SUMMARY A method is described for the simple and rapid formation of saturated fatty aldehydes from the corresponding acid chlorides. It is not suitable for the preparation of unsaturated aldehydes because of the partial reduction and positional and geometrical isomerization of the double bond in the chain.

KEY WORDS decanaldehyde · palmitaldehyde
stearaldehyde · arachidaldehyde · fatty acid chloride
· Rosenmund reduction

LONG-CHAIN ALDEHYDES are not readily available commercially. Difficulties encountered during their preparation by the Rosenmund reduction (1) and by the Sakurai and Tanabe modification of the Rosenmund reduction (2) led us to study these reactions and to make further modifications which allow the synthesis of pure fatty aldehydes with 10–20 carbon atoms in high yield. The product was examined by TLC and GLC.

Materials and Methods. To 10 ml of acetone [distilled over Drierite (W. A. Hammond Drierite Co., Xenia, Ohio)] in a 50 ml flask equipped with a sidearm and containing a magnetic stirring bar was added 125 mg of 5% palladium-on-barium sulfate catalyst (Engelhard Industries, Inc., Newark, N. J.). The flask was attached to an assembly connected with a hydrogen supply and to a combination gas burette and manometer with leveling bulb. Air was swept out of the system with H₂, the sidearm was sealed with a rubber septum, and the contents of the flask were stirred under H₂ at about 5 cm Hg pressure for 20 min. During this period the catalyst suspension turned black. Additions of the *N,N*-dimethylaniline or the *N,N*-dimethylacetamide (0.5 ml) as HCl neutralizer and later of the acid chloride (300 mg) obtained from The Hormel Institute (Austin, Minn.) were made by means of a syringe through the sidearm. The reaction, was run at room temperature, constantly stirred, and kept under slight pressure (2–4 mm Hg) by periodically raising the leveling bulb. It was terminated after 30 min by the addition of water (5 ml). The catalyst

Abbreviations: TLC, thin-layer chromatography; GLC, gas-liquid chromatography.

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was removed by filtration of the mixture into a separatory funnel, and purified pentane (15 ml) was added. After the hydrocarbon layer had been washed with water, 5% HCl, water, 10% K₂CO₃, and water, in that order, the solution was dried over anhydrous sodium sulfate and the solvent was removed on a rotary evaporator. The product was sealed either under vacuum in a glass ampule or under nitrogen in a test tube.

Gas chromatographic analyses were done on an instrument equipped with a hydrogen flame ionization detector. The column was a 120 cm × 3 mm I.D. glass tube packed with 5% diethyleneglycol succinate polyester on 80–100 mesh Diatoport S, (Hewlett-Packard, F & M Scientific Div., Avondale, Pa.) with a flow rate (helium) of 75 ml/min and temperature programming from 100° to 210°C at 3°/min.

Choice of HCl Neutralizer. Although the Sakurai and Tanabe procedure, which used *N,N*-dimethylaniline to neutralize the HCl, gave good yields of pure longer-chain fatty aldehydes, e.g. arachidaldehyde and stearaldehyde, shorter-chain fatty aldehydes so prepared contained considerable amounts of volatile impurities: more than 10% for palmitaldehyde and more than 50% for decanaldehyde. Under the above GLC conditions, the palmitaldehyde emerged after 10 min, the first impurity after 20 min, and the third impurity after 31 min.

The impurities were found to result from reaction between the shorter-chain acid chlorides and *N,N*-dimethylaniline; they can be removed on a silicic acid column. The reaction mixture in anhydrous ethyl ether was added to the silicic acid column (100 mesh) and the column was eluted with hexane–ethyl ether 9:1. The impurities probably were the result of contaminants in the *N,N*-dimethylaniline (“Mono-free,” Eastman Organic Chemicals, Rochester, N. Y.), although it had been washed with 10% potassium carbonate and thrice distilled.

Under the anhydrous conditions of the reaction, *N,N*-dimethylacetamide was found to neutralize the HCl effectively and to give rise to no impurities when used with short- or long-chain acid chlorides.

Rate of Reaction. Aldehyde formation as a function of time was determined by GLC analysis of aliquots withdrawn from the reaction mixture at various intervals by means of a syringe and squirted into methanol. Peak height analysis of the aldehyde and methyl ester components on isothermal chromatograms revealed 52, 79, and 96% conversion of the acid chloride to aldehyde in 3, 10, and 30 min, respectively. Uptake of H₂ in the initial period was so fast that it was continually necessary to move the mercury leveling reservoir upwards to maintain a slight positive H₂ pressure on the system.

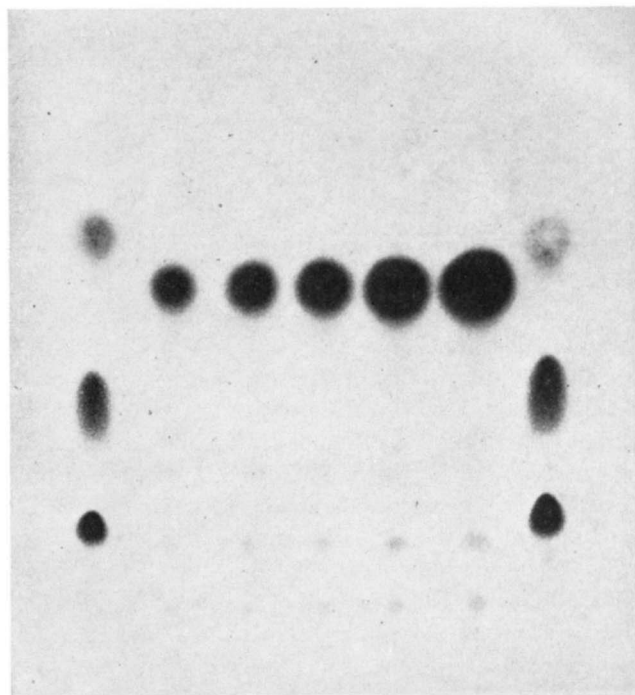


Fig. 1. Thin-layer chromatogram of different quantities of palmitaldehyde product, along with a standard mixture, showing separation of different lipid classes (11). Solvent: *n*-hexane–ethyl ether–acetic acid 70:30:1. Development time: 30 min. Detection: methanol–sulfuric acid 1:1 and charring. Amounts: 50, 100, 150, 300, 500 μg (in progressive order) of aldehyde; 150 μg of standard mixture (extreme left and right) containing equal proportions of methyl stearate (top), oleic acid, and octadec-9-enol. Lowest spots: just above origin.

The rate of reaction under our experimental conditions was not directly proportional to the amount of catalyst added. Catalyst in amounts of 120, 60, and 12 mg led to hydrogen uptakes in the first 2 min in the ratio 3.5:2.7:1. When 1/20 of the usual weight of catalyst was added, the reaction apparently ceased after 3 hr, with only 48% of the theoretical amount of gas consumed.

Analysis of Product. With palmitoyl chloride (300 mg, 1.09 mmoles) as reactant, the yield of palmitaldehyde as a white solid was 252 mg (1.05 mmoles) or 96.3%. GLC of the product gave only one peak. In the thin-layer chromatogram of the product only traces of nonaldehyde components were seen (Fig. 1). The 2,4-dinitrophenylhydrazone had mp 107.5–108°C (corr); reported 108°C (3).

The IR spectrum of palmitaldehyde in chloroform showed, as expected (4), strong absorption bands for carbon–hydrogen bonds (3.4 and 3.5 μ; aldehyde C–H at about 3.7 μ) and for the carbonyl group (5.7 μ).

Similar results were found with decanaldehyde (yield, 96.3%), stearaldehyde (yield, 96.0%), and arachidaldehyde (yield, 71.5%).

Stability of Aldehyde Product. Since aliphatic aldehydes

TABLE 1 STABILITY OF PALMITALDEHYDE
Expressed as % aldehyde remaining

Storage Conditions	Days		
	2	7	14
Under vacuum (23 °C)	100	100	100
Under nitrogen (0 °C)	100	100	98
In corked containers (23 °C)	100	43	7

are known to be unstable, the stability of palmitaldehyde was studied by GLC (Table 1) and TLC.

Table 1 shows that palmitaldehyde stored under vacuum at room temperature showed no decomposition in 2 wk. The sample stored under nitrogen with refrigeration also showed very little alteration, but of the sample stored in air at room temperature less than 10% remained after 2 wk. GLC data indicated that one of the principal products during storage was the corresponding carboxylic acid. This was true of all the fatty aldehydes prepared by the above procedure; the rate of acid formation decreased with increasing chain length of the aldehyde (50% oxidation of decanaldehyde after 2 days, none detectable for the C₂₀ aldehyde in the same period). The percentage of aldehyde remaining was estimated by comparison of the areas under GLC peaks for the aldehydes and for other volatile components.

A simultaneous study carried out on the same samples by means of TLC confirmed the observations made by GLC. The major difference was for the sample stored in air: the spot corresponding to palmitic acid increased

in size. There were also traces of a component running near the solvent front, which could be the aldehyde trimer (5). These TLC data were confirmed by use of another solvent system, xylene-ethyl ether 97:3.

Reaction with Oleoyl Chloride. Although unsaturated aldehydes can be synthesized by other methods (6-8), their preparation by the procedure described would be a desirable additional method. It was found, however, that with oleoyl chloride several reactions other than the formation of unsaturated aldehyde took place. GLC showed that 1.7 and 10% of stearaldehyde were produced by hydrogenation after 2 min and 20 min, respectively. Moreover, in a sample run 5 min, IR spectrophotometry revealed the presence of 26.6% *trans* bonds (9). Finally, extensive migration of the double bond in the chain was shown by exposure of the 30 min reduction product to periodate-permanganate (10), purification of the resulting dicarboxylic acids by TLC, and GLC of the methyl esters (Fig. 2). The double bond was found scattered from the 6- through the 14-positions and less than half remained in the original 9-position.

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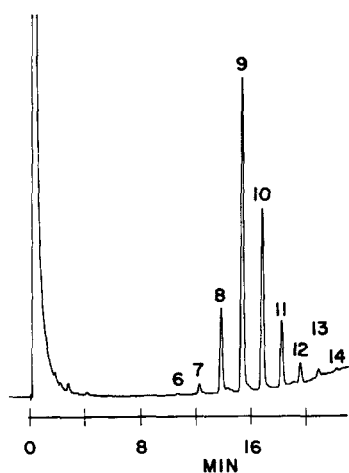


FIG. 2. Gas-liquid chromatographic analysis of dicarboxylic acids, as their methyl esters, from oxidative cleavage of oleoyl chloride reduction product. Designation above peaks shows number of carbon atoms in fragments.