

Table 1.

Alkylhalide	Yield %	B. p.
C ₂ H ₅ Br	73	76—80°/10 mm Hg
n-C ₃ H ₇ Br	56	86—92°/10 " "
n-C ₄ H ₉ Br	45	100—105°/10 " "
CH ₂ =CH—CH ₂ Br	74	90—95°/10 " "
C ₆ H ₅ CH ₂ Cl	59	145—150°/10 " "

In a kinetic investigation of the methylation of ethyl acetoacetate Brändström² has recently shown that the hydrolysis of ethyl acetoacetate is slow if the amount of water present in the sodium ethoxide solution is small. This suggests that it is not so important to dry the alcohol which is to be used as a solvent in alkylation of ethyl acetoacetate. In order to test this, some alkylations of ethyl acetoacetate have been undertaken where sodium hydroxide dissolved in 99.5 % alcohol was used as a base. With alkyl halides of an intermediate reactivity such as ethyl bromide the yields obtained were only slightly lower than those obtainable with "superdry" alcohol and sodium.

The use of sodium hydroxide in alcohol is thus strongly recommended as a base in alkylations of ethyl acetoacetate with alkyl halides of an intermediate or high reactivity.

It should be noted that the same base cannot be used in the alkylations of diethyl malonate or other esters which have a much lower acidity than ethyl acetoacetate.

Experimental. 40 g (1 mole) of sodium hydroxide is dissolved in 500 ml of technical absolute alcohol (containing about 0.5 % of water) in a 1 litre three-necked flask, fitted with a stirrer, a reflux condenser and a dropping funnel. 130 g (1 mole) of ethyl acetoacetate is added followed by 1.2 moles of an alkyl halide. The mixture is refluxed for several hours until it has a neutral reaction.

About 300 ml of alcohol is then distilled off. The residue is cooled and 500 ml of water is added. The layers are separated and the aqueous layer is extracted with benzene. The combined organic layers are dried with anhydrous magnesium sulphate, and then fractionated under reduced pressure. The yields and boiling points obtained are given in Table 1.

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2. Brändström, A. *Arkiv Kemi* 13 (1958) 51.

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A Method for the Preparation of *tert*-Alkylacetic Acids

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tert-Alkylacetic acids are very seldom referred to in chemical literature. The reason for this is that they are not readily available by the standard methods for the preparation of aliphatic acids. For instance, the malonic ester method has been used¹ but it gives a very low yield. The halides R-CH₂X where R is a *tert*-alkyl group are not readily available, and they do not react with cyanide ion to the corresponding nitrile. The only general method which has been used is that starting with the corresponding *tert*-alkylcyanoacetic ester which in turn can be prepared from an unsaturated cyanosubstituted ester and a Grignard reagent²⁻⁴. This method is, however, not very convenient for a large scale synthesis of *tert*-alkylacetic acids.

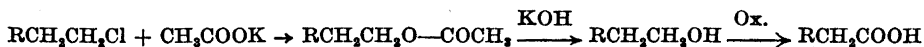
The following method is however, very useful (see p. 609).

The starting materials RCH₂CH₂Cl where R represents a tertiary alkyl group are readily available from the reaction of a tertiary chloride RCl with ethylene or by other methods⁵. All chlorides used in the following preparations are, e.g., obtained from the reaction of *tert*-butyl chloride with ethylene⁶.

The conversion of the chloride into the alcohol is conveniently carried out without isolating the intermediate ester by using polyethylene glycol as a solvent. The overall yield for the preparations of alcohols from the chlorides are 70—80 %.

The oxidation of the alcohols to the corresponding acids are the standard procedures using potassium permanganate or chromic acid.

Experimental. Preparation of 3,3-dimethylbutanol-1. 132 g (2 moles) of potassium hydroxide are dissolved in 600 ml of polyethylene glycole-300 in a 2 litres three-necked flask fitted with a strong stirrer, a reflux condenser, a thermometer and a dropping funnel. 120 g (2 moles) of conc. acetic acid are added with stirring. The water formed in the neutralisation is removed by distillation under reduced pressure. When the mixture starts foaming the distillation is discontinued. 241 g (2 moles)



of 1-chloro-3,3-dimethylbutane are added, and the mixture is refluxed for 17 h. The temperature is 118° at the beginning and 132° at the end of the reaction.

197 g (3 moles) of potassium hydroxide are dissolved in 150 ml of water and the solution is cautiously added to the reaction mixture, which is then refluxed for 2 h.

The alcohol is distilled with steam. The steam distillate is separated, and the water layer extracted with benzene. The combined organic layers are dried with anhydrous magnesium sulphate and distilled. The yield is 165 g (81 %) of 3,3-dimethylbutanol-1, boiling at 136–142°. 3,5-Dinitrobenzoate, m. p. 80.2–80.8°.

Preparation of 3,3-dimethylpentanol-1. The procedure given above is followed with the following modification: When the mixture has been refluxed for 17 h, the temperature is 140°. A water separator⁷ is now connected to the flask, and the mixture refluxed for 3 h during which time about 35 ml of water is collected in the separator. The temperature in the flask is then 195°. The solution of potassium hydroxide in water is now added, and the procedure given above is followed.

The yield of 3,3-dimethylpentanol-1 boiling at 76–66°/10 mm is 170 g or 77 %. 3,5-Dinitrobenzoate, m. p. 51.2–51.8°.

Preparation of 3,3,4-trimethylpentanol-1. The procedure given for 3,3-dimethylpentanol-1 is followed. The end temperature is 205°. The yield of 3,3,4-trimethylpentanol-1 is 182 g or 69 %. The boiling point is 78–82°/10 mm Hg. The melting point of the 3,4-dinitrobenzoate is 46.6–47.2°.

Preparation of 3,3,6,6-tetramethylheptanol-1. The method given for 3,3-dimethylpentanol-1 is followed with the modification that the water separator is connected to the flask from the beginning. The total time of reflux is 4 h during which time the temperature rises from 150° to 252°. The mixture was then allowed to cool, and the potassium hydroxide solution added. The general procedure was then followed.

The yield of 3,3,6,6-tetramethylheptanol-1 boiling at 103–108°/8 mm Hg is 294 g or 85 %.

Preparation of 3,3-dimethylbutanoic acid. A 3 litres three-necked flask is fitted with a stirrer, a reflux condenser, and a device for intermittent addition of a solid⁸. 210 g of

potassium permanganate are added in portions to a refluxing mixture of 102 g (1 mole) of 3,3-dimethylbutanol, 1.5 litres of water, and 20 g of potassium carbonate. The mixture is refluxed for 15 min after the addition, and then filtered still hot. The cake of manganese dioxide is washed with hot water. The alkaline filtrate is acidified with concentrated hydrochloric acid. The layers are separated and the aqueous layer extracted with benzene. The combined organic layers are dried with anhydrous magnesium sulphate and fractionated under reduced pressure. The yield of 3,3-dimethylbutanoic acid boiling at 76–80°/8 mm is 94 g or 81 %.

Preparation of 3,3-dimethylpentanoic acid The procedure given above is followed using one mole of 3,3-dimethylpentanol. The yield of 3,3-dimethylpentanoic acid is 80.5 g or 62 %. The boiling point is 93–97°/8 mm Hg.

Preparation of 3,3,4-trimethylpentanoic acid:
a) *Oxidation with potassium permanganate.* If the procedure given for 3,3-dimethylbutanoic acid is followed, much alcohol remains after the decolourisation of the permanganate solution. The alcohol is therefore removed by distillation with steam before the manganese dioxide is filtered off. 67 g of 3,3,4-trimethylpentanol, b. p. 78–82°/10 mm Hg, are thus recovered. From the alkaline solution obtained after the filtration of the manganese dioxide 39 g of 3,3,4-trimethylpentanoic acid are obtained. This is 53 % calculated on the alcohol not recovered. The boiling point is 105–108°/10 mm.

b) *Oxidation with chromic acid.* 118 g of 3,3,4-trimethylpentanol-1 is added to a refluxing solution of 200 g of sodium dichromate, 485 ml of water, and 140 ml of conc. sulphuric acid. The mixture is stirred and refluxed for 2 h. The reaction mixture is then distilled with steam. The distillate is separated, and the water layer is extracted with benzene. The combined organic layers are extracted with a 20 % sodium hydroxide solution. The alkaline extract is acidified with hydrochloric acid, and the acid extracted with benzene. The combined organic layers are dried with anhydrous magnesium sulphate, and fractionated under reduced pressure. The yield of 3,3,4-trimethylpentanoic acid is 55 g or 38 %.

Preparation of 3,3,6,6-tetramethylheptanoic acid. If 3,3,6,6-tetramethylheptanol-1 is oxidized with chromic acid by the method described above, 3,3,6,6-tetramethylheptanoic acid boil-

ing at 130—133°/10 mm Hg is obtained in a yield of 40 %. The acid is solid at room temperature. The melting point is 44—46°.

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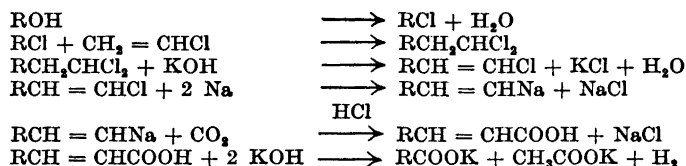
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A New Method to Prepare Trialkylacetic Acids

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There are many methods given for the preparation of trialkylacetic acids^{1,2} but no one is entirely convenient for a large scale preparation of these acids. They can, however, be prepared by the following satisfactory reactions, where R is a *tert*-alkyl group:



The yields in all these steps are excellent and the procedure very simple and rapid. Thus, great quantities of the acids are easily obtainable. As there are practically

no side reactions the acids obtained are easily purified.

The procedure is demonstrated by the synthesis of pivalic acid. Other acids can be prepared by exactly the same method.

*Experimental. tert-Butyl chloride*³. 1 kg of *tert*-butanol is shaken with 3.4 litres of conc. hydrochloric acid for 20 min in a 5-litre separatory funnel. The organic layer is separated, washed with 1 litre of water and dried with anhydrous magnesium sulphate at —20° for 10 min. The liquid is then transferred by filtration to a 5-litre three-necked flask. The yield is 1 160 g (93 %) of pure *tert*-butyl chloride.

*1,1-Dichloro-3,3-dimethylbutane*⁴. The 5-litre three-necked flask containing the *tert*-butyl chloride is chilled to —25° by means of a solid carbon dioxide-acetone bath and fitted with a stirrer, a gas inlet tube ending under the liquid, a thermometer, and a gas escape tube. 25 g of powdered anhydrous aluminium chloride is added, and the gas inlet tube connected to a 1-litre flask containing 860 ml of vinyl chloride. The vinyl chloride is distilled into the reaction mixture at such a rate that the reaction temperature can be kept at —25° to —30°. — *It is very important that the reaction starts before much vinyl chloride has been added.* This can be seen as a rapid rise in temperature if the cooling bath is temporarily removed. — After the reaction has started the vinyl chloride can usually be introduced in one hour. The reaction mixture is then kept at —25° to —30° for 15 min, and is then decanted into 500 ml of water. The mixture is thoroughly shaken, separated and dried with solid potassium hydroxide for 2 h. The yield is 1 870 g (96 %) of a nearly pure 1,1-dichloro-3,3-dimethylbutane.

1-chloro-3,3-dimethylbutene-1. 780 g of potassium hydroxide are dissolved in 3.6 litres of diethylene glycol in a 10-litre three-necked flask fitted with a dropping funnel, a reflux condenser, a thermometer, and a strong stirrer. The solution is heated to 140° and the dichlor

ide added. The mixture is refluxed with good stirring for 6 h, whereupon the product is distilled from the flask until the temperature in the liquid is 190°. The product is separated