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# An Improved Synthesis of 1,1,1-Trichloro-2-methyl-2-propanol (Chlorobutanol)

**Short Communication**

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Varying reaction time, temperature, and the amount of catalyst and reactants the synthesis of chlorobutanol from chloroform and acetone with KOH as catalyst is optimized to 71% yield.

*(Keywords: Anesthetic; Antibacterial; Chlorobutanol; Germicidal)*

*Eine verbesserte Synthese von 1,1,1-Trichlor-2-methyl-2-propanol (Chlorbutanol) (Kurze Mitteilung)*

Es wird die Synthese von Chlorbutanol aus Chloroform und Aceton mit KOH als Katalysator bezüglich Reaktionszeit, Reaktionstemperatur, Katalysatormenge und Verhältnis der eingesetzten Reaktanten auf 71% Ausbeute optimiert.

## Introduction

Chlorobutanol (**1**) is prepared by addition of chloroform to acetone under the catalytic influence of powdered potassium hydroxide[1]. It has a local anesthetic potency to a mild degree and is used as an anesthetic dusting powder. Chlorobutanol has antibacterial and germicidal properties and also has been mainly used as a preservative for pharmaceutical preparations[2].

Chlorobutanol was first prepared by the condensation of $CHCl_3$ and acetone in the presence of a complex catalyst formed from potassium hydroxide and methylal at $-4°$[3,4] and later with aqueous NaOH as catalyst at 0—10°[5,6]. Using carbon tetrachloride and acetone in the



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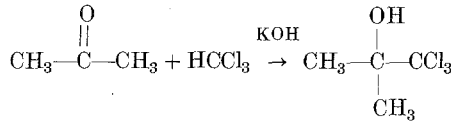
Table 1. *Experimental conditions*

| Experiment No. | Acetone (ml) | Chloroform (ml) | Acetone/Chloroform (mol) |
|---|---|---|---|
| 1 | 24.0 | 26.0 | 1:1 |
| 2 | 24.0 | 26.0 | 1:1 |
| 3 | 16.0 | 34.0 | 1:2 |
| 4 | 32.5 | 17.5 | 2:1 |
| 5 | 36.5 | 13.5 | 3:1 |
| 6 | 39.0 | 11.0 | 4:1 |
| 7 | 42.3 | 7.7 | 6:1 |
| 8 | 44.0 | 6.0 | 8:1 |
| 9 | 45.0 | 5.0 | 10:1 |
| 10 | 45.0 | 5.0 | 10:1 |
| 11 | 45.0 | 5.0 | 10:1 |
| 12 | 45.0 | 5.0 | 10:1 |
| 13 | 45.0 | 5.0 | 10:1 |

presence of powdered KOH at −5° gave also **1**[7]. In the latest method the yield of the desired product **1** has been increased from 23.3% (preparation for the first time) to 41.2%[8,9]. In this study, an attempt was made to find the best experimental conditions in order to increase the yield of the reaction of acetone and chloroform with KOH as catalyst by varying parameters of time, temperature, amount of catalyst and reactants.

## Experimental

*General Procedure*: Acetone (0.33 mol), chloroform (0.33 mol) and anhydrous powdered potassium hydroxide (2 g) were mixed in a 250 ml two-necked flask and the reaction mixture stirred at −5 °C for 2 h. The resulting suspension was then filtered, the filtrate distilled off and the remaining acetone and chloroform was recovered as an azeotropic mixture at 62—65 °C and collected in a container immersed in crashed ice. The residue (a yellowish oily material) was mixed with cold water, chlorobutanol **1** was precipitated, as a white crystalline compound, filtered off and dried in a desiccator; yield 14%, mp. 78.4°.




**1**

*UV-Analysis*: To identify the amount of recovered acetone and chloroform, the maximum ultraviolet absorption ($\lambda_{max}$) of acetone in *n*-hexane was

*for the synthesis of chlorobutanol*

| KOH (g) | Time (h) | Temp. (°C) | Reacted Acetone (ml) | Reacted Chloroform (ml) | Yield (%) |
|---|---|---|---|---|---|
| 2 | 2 | −5 | 11.4 | 13.1 | 14.1 |
| 4 | 2 | −5 | 14.4 | 14.6 | 13.3 |
| 2 | 2 | −5 | 9.5 | 16.5 | 5.9 |
| 2 | 2 | −5 | 11.7 | 9.3 | 16.3 |
| 2 | 2 | −5 | 15.0 | 11.0 | 26.9 |
| 2 | 2 | −5 | 13.5 | 6.0 | 32.7 |
| 2 | 2 | −5 | 20.0 | 4.0 | 52.2 |
| 2 | 2 | −5 | 17.8 | 4.5 | 64.2 |
| 2 | 2 | −5 | 14.9 | 4.4 | 69.3 |
| 1 | 2 | −5 | 11.1 | 5.0 | 71.0 |
| 0.5 | 2 | −5 | 8.1 | 4.5 | 51.9 |
| 1 | 1 | −5 | 11.9 | 5.0 | 68.4 |
| 1 | 2 | 0 | 11.8 | 5.0 | 63.2 |

determined separately and in the presence of various amounts of chloroform and in both cases was found to be 275 nm, which revealed $CHCl_3$ has no effect on the maximum absorption of acetone. This clarified that UV spectroscopic analysis can be applied to determine the reacted amounts of acetone and chloroform used in the reaction. The concentration of unreacted acetone in the recovered solution after measurement of standard and unknown absorbances at 275 nm can be directly determined from the standard curve or calculated as follows: $C_s = C_r A_s/A_r$.

Experiments number 1 to 13 were conducted as outlined in the general procedure. The yield and the molar ratio of acetone-chloroform for a volume of 50 ml varied in a range as given in Table 1. To calculate the volume of acetone (ml) in one ml of recovered solution, $C_s$ (mol/l) was multiplied by $73 \cdot 10^{-3} \cdot 625$ in which 625 was the dilution coefficient.

## Results and Discussion

Table 1 summarizes the results of the synthesis of **1** at different conditions. The best yield (71%) was obtained when the proportion of acetone to chloroform was 10 : 1 (experiment 10). On the other hand, the data obtained by UV analysis showed that at the end of this experiment no chloroform remains in the reaction mixture and the only recovered subtance is unreacted acetone. The remaining acetone can be readily used in further experiments. It is interesting that increasing the ratio of chloroform to acetone results in a decrease of the yield of the product (experiment 3). The results are in accordance with the aim of

this investigation, namely to find a simple procedure with low cost as well as the highest yield ever reported for this drug.

It can be seen from Table 1 that if the proportion of acetone to chloroform was (1:1)—experiment 1—the yield would be 14%. By changing the molar ratio of the starting materials, time, temperature and KOH within 13 experiments, the condition for the experiment number 10 was found to be the best. The same results were obtained when the conditions of experiment 10 were maintained for higher molar ratios of $CHCl_3$ and acetone.

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