A Synthesis of 1,3-Dihydroxyacetone Convenient for ^{14}C-labelling

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A synthesis of $^{14}C-2$- and $^{14}C-1,3$-labelled dihydroxyacetone was previously described [1] but this method was rather tedious and did not give very high yield. In the following synthesis it was possible to obtain either ^{14}C-2- or ^{14}C-1-dihydroxyacetone by using $HOCH_2{}^{14}COOH$ or $HO{}^{14}CH_2COOH$ which had previously been prepared [2].

$$CH_3-COCl + HOCH_2-COOH \rightleftharpoons CH_3-COOCH_2-COOH \xrightarrow{SOCl_2} CH_3-COOCH_2-COCl \xrightarrow{CH_2N_2} CH_3-COOCH_2-CO-CHN_2 \xrightarrow{H_2SO_4} HOCH_2-CO-CH_2OH$$

The hydrolysis of acetoxydiazoacetone which was hard to control and easily gave rise to methylglyoxal and products of polymerisation has been followed attentively with paper chromatography.

Experimental. (1) *Acetylglycolic acid.* 5.0 g (0.066 mole) glycolic acid was refluxed with 10.0 g (0.127 mole) acetyl chloride for 45 minutes [3]. The excess of acetyl chloride was driven off on a water bath at reduced pressure. The residue was acetylglycolic acid, m. p. 66—68°

(2) *Acetylglycolic acid chloride.* The above acetylglycolic acid was immediately refluxed with 11.2 g (0.102 mole) thionyl chloride for 90 minutes. By fractional distillation of the solution at reduced pressure acetylglycolic acid chloride was obtained at 52—54°/12—14 mm Hg. Yield 8.0 g (0.059 mole) or 89 % from acetylglycolic acid.

(3) *Acetoxydiazoacetone.* 3.50 g (0.0256 mole) acetylglycolic acid chloride dissolved in 5 ml abs. ether was added drop by drop during 1 hour to 0.1 mole diazomethan dissolved in 150 ml abs. ether with mechanical stirring and cooling with ice-water. The solution was left for another hour at room temperature with continued stirring and was then evaporated on a water bath at reduced pressure. The residue was dissolved in 10 ml abs. ethanol.

(4) *Dihydroxyacetone.* From the alcoholic solution of acetoxydiazoacetone 3.0 ml were taken and diluted with 3 ml water and 3 ml of 4 *M* sulfuric acid was added dropwise. When about half the amount of sulfuric acid had been added the nitrogen evolution increased violently. The solution was cooled with ice-water until the reaction had decreased. The solution was kept at room temperature until only a very faint gas evolution remained and was then placed on a water bath (bath temp. 75 °) for 45 minutes. The colour of the solution was lemon yellow at first but grew deeper during the heating. After cooling with ice-water the solution was diluted with some water and neutralized with solid barium carbonate. The precipitated barium sulfate was removed by centrifugation and the filtrate was evaporated on a water bath (bath temp. about 35°) at reduced pressure. The concentrate was kept in a vacuum-desiccator with conc. sulfuric acid for 2 days. The solid glass-like residue was triturated with acetone and a fine white powder was formed. This substance reduced Fehling's solution in the cold and was identified as dihydroxyacetone with paper chromatography and m. p. 75—76°. The yield was 0.42 g (0.0047 mole), *i. e.* 61 % from acetylglycolic acid or 53 % from glycolic acid, respectively.

Attempts have been made to find a convenient method to synthesise ^{14}C-labelled dihydroxyacetone phosphoric acid. The following reaction series has been tested:

$$C_6H_5-CH_2OCH_2-COCl \xrightarrow{CH_2N_2} C_6H_5-CH_2OCH_2-COCHN_2 \xrightarrow{HO_2P(OCH_2-C_6H_5)_2} C_6H_5-CH_2OCH_2-COCH_2-OPO(OCH_2C_6H_5)_2 \xrightarrow{H_2} HOCH_2-CO-CH_2OPO_3H_2$$

These reactions gave a very low yield of dihydroxyacetone phosphoric acid especially owing to the difficulty of controlling the hydrogenation of the tribenzyl derivative. These experiments are still being continued.

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1. Arnstein, H. R. V. and Bentley, R. *J. Chem. Soc.* **1951** 2385.
2. Hughes, D. M. and Tolbert, B. M. *Nucleonics* **7** (1950) 57.
3. Anschütz, R. and Bertram, W. *Chem. Ber.* **36** (1903) 467.

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