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SYNTHESIS OF ^{13}C=O-LABELLED TERTIARY ALKANOIC ACIDS BY THE KOCH-HAAF-REACTION*

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Summary: Good yields of tertiary alkanoic acids are obtained from the Koch-Haaf-synthesis even when only stoichiometric amounts of carbinol and HCOOH are used. This offers a new approach to ^{13}CO-labelled tertiary alkanoic acids. -

An excess of HCOOH is generally used in the Koch-Haaf-synthesis[1] of carboxylic acids from carbinols and HCOOH in conc. H_2SO_4.

$$ROH + HCOOH \xrightarrow{H_2SO_4} R\text{-}COOH + H_2O$$

For this reason this reaction has not been previously used for the synthesis of ^{13}CO-labelled acids. Because ^{13}CO-labelled 1-adamantane carboxylic acid was required for related work[2] we have developed a variation of the Koch-Haaf-reaction using only a stoichiometric amount of HCOOH:

2.0 g (13.2 mmol) 1-hydroxyadamantane are mixed with 0.61 g (13.2 mmol) HCOOH (99%) and added with stirring to 23.2 g conc. H_2SO_4 at 10°C. Stirring is continued for 2h and the mixture is then kept at 10°C for an additional 27h without stirring, before it is added to 150 g crushed ice. The precipitated acid is purified in the usual way[3]. Yield: 2.0 g (84.4%). The lit. procedure[3] using ROH:HCOOH in the molar ratio 1:12 yields 96%. Even when 1 mol hydroxyadamantane is reacted with only 0.7 mol HCOOH a 51% yield is obtained. The ^{13}CO-labelled acid was also successfully prepared by this procedure using $H^{13}COOH$[2].

The success of the reaction is somewhat dependent on the rate of stirring[4] and is illustrated with the examples listed in Table 1.

Table 1 Koch-Haaf Synthesis of Tertiary Alkanoic Acids.

ROH	stirring rate[a)]	T °C	reagent ratio[b)]	yield %	RCOOH[c)]
2-methyl-cyclohexanol	slow	25-30	1:1:24	66	1-methylcyclo-hexanecarboxylic acid[5)]
	fast	15-20	1:1:24	44	
1-pentanol	medium	20-25	1:1:10	46	2,2-dimethyl-butyric acid[1a)]
1-hydroxy-adamantane	fast	10	1:1:24	84	1-adamantane-carboxylic acid[3)]
	fast	10	1:1:12	80	
	fast	10	1:0.7:18	51	
1-adamantyl-methanol	fast	-15	1:1:24	28	3-homoadamantane-carboxylic acid[6)]

a) slow: 200, medium: 500, fast: 1200 revs. per minute.

b) molal ratio ROH:HCOOH:H_2SO_4

c) Lit. refers to publications, where these acids have been prepared using excess HCOOH.

*) Dedicated to Prof.Dr.Siegfried Hünig on the occasion of his 60th birthday

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