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Note

NMR study of the synthesis of ^{17}O-enriched acetic acid by hydrolysis of acetic anhydride with ^{17}O-enriched water

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^{17}O-enriched acetic acid (2.5% in ^{17}O) was synthesized by hydrolysis of acetic anhydride with ^{17}O-enriched water. The reaction was monitored by ^{17}O and ^{1}H NMR spectroscopy. Acetic anhydride, ^{17}O-enriched in both the ether and the carbonyl oxygens, was observed as an intermediate. This can be ascribed to competition between acetic acid and water for nucleophilic attack on acetic anhydride. Copyright © 2003 John Wiley & Sons, Ltd.

KEYWORDS: NMR; ^{17}O NMR; ^{1}H NMR; labelling; hydrolysis; acetic acid; acetic anhydride; water

INTRODUCTION

The natural abundance of ^{17}O is only 0.037%. A large quadrupole interaction (spin number $I = 5/2, Q = -2.6 \times 10^{-30}\,m^2$)[1] causes efficient relaxation and, consequently, broadening of ^{17}O NMR resonances, particularly of compounds with high molecular weights.[2] Therefore, ^{17}O enrichment is often desirable to obtain ^{17}O NMR spectra within a reasonable time.

A variety of methods are known for the preparation of ^{17}O-enriched compounds. Starting compounds include ^{17}O-enriched oxygen, water and carbon monoxide. For example, the oxygens of carboxylic acids may be isotopically labelled via saponification of the corresponding esters with labelled NaOH in methanol or by acid-catalysed O-exchange of the free acid in labelled water.[3]

Acetic anhydride can be readily converted into acetic acid by hydrolysis.[4] This reaction is very clean; no side products are formed. Therefore, it is ideal for the preparation of ^{17}O-enriched acetic acid. In our recent ligand-exchange studies on dirhodium catalysts,[5] we employed ^{17}O-enriched acetic acid. During the preparation of this compound by the hydrolysis of acetic anhydride with a stoichiometric amount of $H_2{}^{17}O$ in $CDCl_3$, we observed some unexpected results. In the reaction where the ^{17}O-enriched acetic acid was needed, $CDCl_3$ was the solvent. Therefore, $CDCl_3$ was also used as a solvent during the preparation of the ^{17}O-enriched acetic acid. Because of the unexpected results that were observed in the initial experiments, the hydrolysis reaction was studied further by ^{17}O and ^{1}H NMR spectroscopy using acetonitrile as the solvent. This solvent was selected because of its miscibility with water.

EXPERIMENTAL

Materials

Acetic anhydride and pyridine were obtained from Aldrich, deuterated acetonitrile from Cambridge Isotope Laboratories and ^{17}O-enriched water (10% ^{17}O) from Cortec (Paris, France).

Hydrolysis of acetic anhydride

Acetic anhydride (0.0261 g, 0.256 mmol) was weighed into an NMR tube. Deuterated acetonitrile (0.7457 g) and ^{17}O-enriched water (46 μl, 2.56 mmol, 10% ^{17}O) were added and, after shaking the mixture, the tube was placed immediately in the NMR machine, which was maintained at 50 °C. The reaction was followed in time during 5 days by measuring ^{17}O and ^{1}H NMR spectra.

Hydrolysis of acetic anhydride in the presence of pyridine

Acetic anhydride (0.0221 g, 0.217 mmol) and pyridine (0.0183 g, 0.0231 mmol) were weighed into an NMR tube. Deuterated acetonitrile (0.7007 g) and ^{17}O-enriched water (39 μl, 2.17 mmol, 10% ^{17}O) were added and, after shaking the mixture, the tube was placed immediately in the NMR machine, which was maintained at 50 °C. The reaction was followed in time during 3 days by measuring ^{17}O and ^{1}H NMR spectra.

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NMR spectroscopy

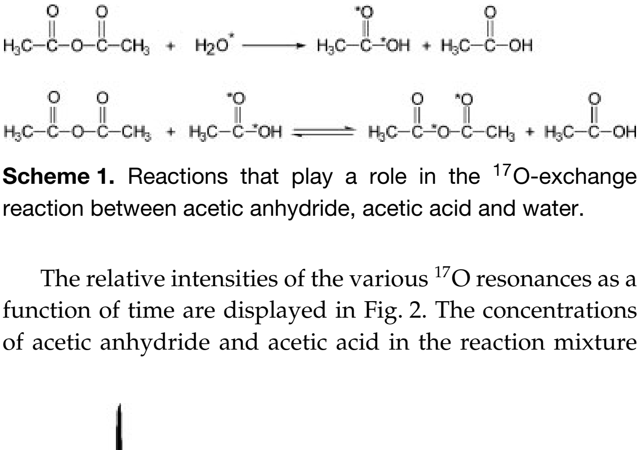
^1H (300 MHz) and ^{17}O (40 MHz) NMR spectra were recorded on a Varian Inova-300 spectrometer at 50 °C using 5 mm sample tubes. Chemical shifts are reported as δ values.

^{17}O NMR experiments were performed using water as an external reference. Typically, 3000 scans were collected using a sweep width of 29 996 Hz and an acquisition delay of 0 s. The peak positions and intensities of the ^{17}O resonances were determined by fitting the observed signals with Lorentzian line functions.

RESULTS AND DISCUSSION

Upon addition of a small amount of 10% ^{17}O-enriched water to a sample of acetic anhydride in acetonitrile, with pyridine as a catalyst,[6,7] initially only the water resonance was observable in the ^{17}O NMR spectrum. After about 5 min, three new signals (at 270, 274 and 415 ppm) became observable (Fig. 1). The resonance at 274 ppm can be assigned to the ^{17}O nuclei in acetic acid, whereas the resonances at 270 and 415 ppm are due to ^{17}O labelling of the acetic anhydride.

The ^{17}O labelling of the oxygen nuclei in acetic anhydride can be rationalized by nucleophilic attack of the initially formed ^{17}O-enriched acetic acid on the residual starting compound acetic anhydride (see Scheme 1). This reaction is similar to the well known synthesis of mixed anhydrides by reaction of a carboxylic acid with acetic anhydride.[8]



Scheme 1. Reactions that play a role in the ^{17}O-exchange reaction between acetic anhydride, acetic acid and water.

The relative intensities of the various ^{17}O resonances as a function of time are displayed in Fig. 2. The concentrations of acetic anhydride and acetic acid in the reaction mixture were determined by integration of the observed resonances in the corresponding ^1H NMR spectra (see Fig. 3).

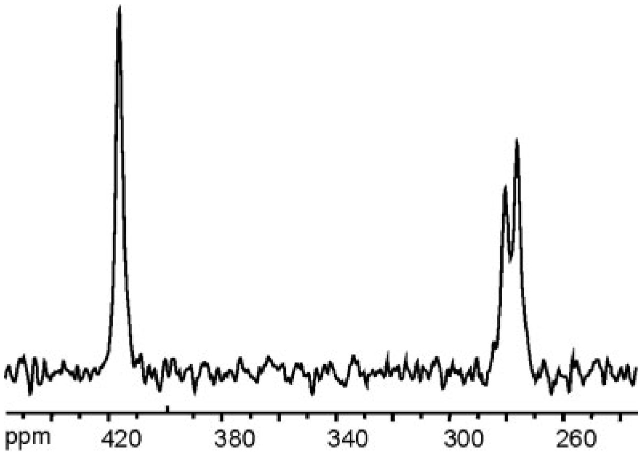


Figure 1. ^{17}O NMR spectrum of the reaction mixture of the pyridine-catalysed hydrolysis of acetic anhydride with 10% ^{17}O-enriched water in acetonitrile after 160 min of reaction. For conditions, see Experimental.

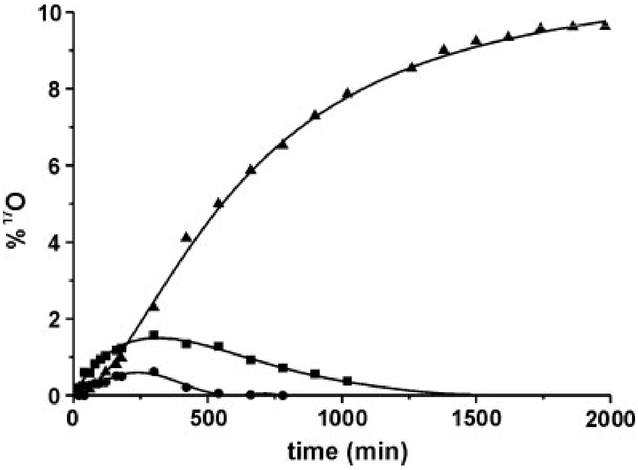


Figure 2. Relative intensities of the ^{17}O NMR signals of acetic acid (▲) and acetic anhydride (C=O, ■; C–O–C, ●) in the reaction mixture of the pyridine-catalysed hydrolysis of acetic anhydride with 10% ^{17}O-enriched water in acetonitrile.

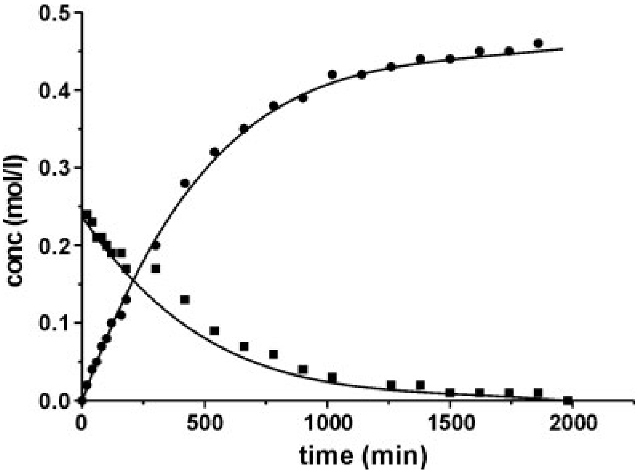


Figure 3. Concentrations of acetic acid (●) and acetic anhydride (■) in the reaction mixture of the pyridine-catalysed hydrolysis of acetic anhydride with 10% ^{17}O-enriched water in acetonitrile as determined by ^1H NMR.

From the concentrations of the species as obtained from ^1H NMR and from the relative ^{17}O intensities (see Fig. 2), the percentages of ^{17}O in acetic acid and acetic anhydride as a function of time were calculated. These data are depicted in Fig. 4, which shows that at each time, the extents of ^{17}O labelling in acetic acid and acetic anhydride are the same. Apparently, the rate of reaction between acetic acid and acetic anhydride is much faster than that between water and acetic anhydride, which can be explained by the higher nucleophilicity of acetic acid compared with water.

The reaction was also carried out without pyridine, giving similar results. However, the hydrolysis was significantly slower in this case. With pyridine the reaction was finished within 2 days, whereas it took 5 days in its absence.

It can be concluded that ^{17}O NMR reveals a side reaction that escapes observation by other techniques.[9]

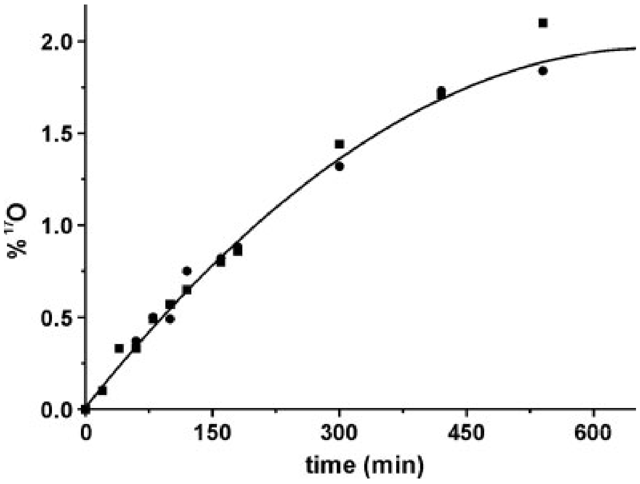


Figure 4. Percentage of ^{17}O in acetic acid (●) and acetic anhydride (■) in the reaction mixture of the pyridine-catalysed hydrolysis of acetic anhydride with 10% ^{17}O-enriched water in acetonitrile (determined by ^{17}O and ^{1}H NMR).

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