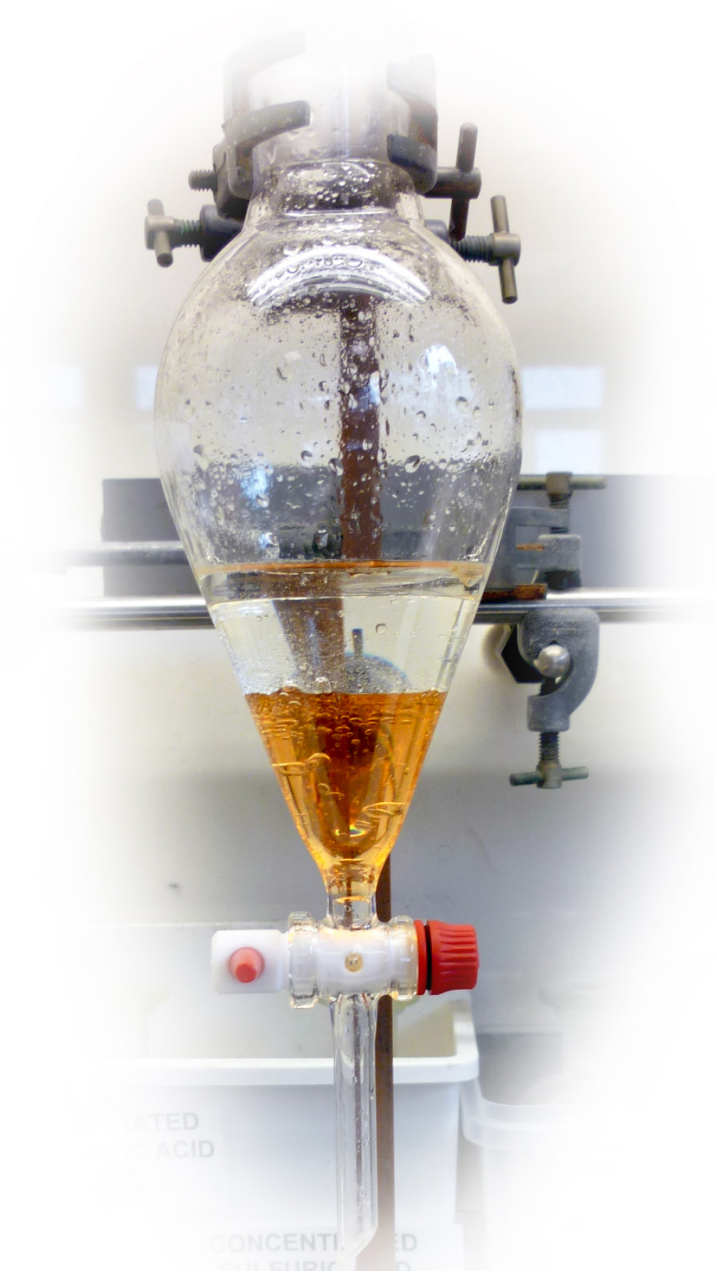
Spinsolve®

magritek
www.magritek.com

Separation of Acidic, Basic and Neutral Compounds



Spinsolve

magritek
www.magritek.com

Contents

Manuscript prepared by Dr. Almas I. Zayya, Dr. A. Jonathan Singh and Dr. Hemi Cumming.
School of Chemical and Physical Sciences, Victoria University of Wellington, New Zealand.

Objectives

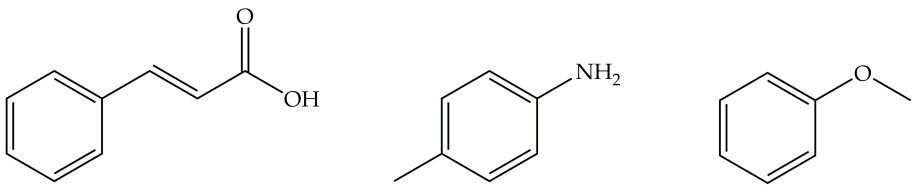
The principal aims of this experiment are to provide experience in the separation and purification of simple organic compounds using liquid/liquid extraction and acid/base extraction techniques. The various separation steps will be followed by ^{1}H NMR spectroscopy using the benchtop Spinsolve NMR spectrometer to determine and characterise the compounds present.

Introduction

Separation and purification of products from synthetic reaction mixtures is very important. Extraction methods are often employed to separate the desired product from unreacted starting materials or from undesired side products in the reaction mixture. In this experiment, a mixture containing an acidic, a basic and a neutral compound is to be separated using acid/base extraction.[1] The three organic compounds to be separated are cinnamic acid, *p*-toluidine and anisole using dichloromethane as the extraction solvent (Figure 1). You will also purify and determine the percent recovery of each compound from the mixture.

Background

The acid/base extraction method involves carrying out simple acid/base reactions in order to separate the acidic, basic and neutral compounds present in the mixture. Acidic organic compounds form salts with a Brønsted base, such as sodium hydroxide, and organic bases form salts with a Brønsted acid, such as hydrochloric acid. The ionic salts are soluble in water but are insoluble in many less polar solvents, such as dichloromethane. Neutral compounds do not react with either Brønsted acids or bases. To achieve separation, this strategy is coupled with the liquid/liquid extraction method, in which a solute is transferred from one solvent into another.[1] The two solvents must be immiscible, such as water and dichloromethane, to form two distinct layers which can be physically separated using a separatory funnel.



cinnamic acid | *p*-toluidine | anisole

Figure 1. Three organic compounds to be separated.

Experimental section

Safety

Hydrochloric acid (HCl) and sodium hydroxide (NaOH) are highly corrosive, use with caution and perform the experiment in a fume hood with the protective glass door pulled down. Dichloromethane (CH_2Cl_2) and *p*-toluidine are toxic, avoid contact with skin, eyes and clothing. Cinnamic acid is an irritant, handle with care. Anisole is a flammable liquid and may cause skin and eye irritation, handle with caution.

Separation procedure

Obtain and weigh a sample containing cinnamic acid (**1**) (1 g), *p*-toluidine (**2**) (1 g) and anisole (**3**) (6 mL). Dissolve the sample in dichloromethane (35 mL) and transfer the mixture into a separatory funnel. Take an aliquot (1 mL) for ^{1}H NMR. Extract the mixture with hydrochloric acid (2 x 15 mL, 2 M). Only the basic compound *p*-toluidine (**2**) will react to form the ionic compound, *p*-toluidinium chloride (**4**), which will dissolve in the aqueous layer and is removed.* Take an aliquot (1 mL) of the aqueous layer for ^{1}H NMR. The remaining dichloromethane layer now contains cinnamic acid (**1**) and anisole (**3**). Take an aliquot (1 mL) of this layer for ^{1}H NMR. Basify the dichloromethane layer with sodium hydroxide solution (2 x 15 mL, 2 M). This will react with **1** to form the ionic compound, sodium cinnamate (**5**), which will dissolve in the aqueous layer and is removed. Take an aliquot (1 mL) of the aqueous layer for ^{1}H NMR. The remaining dichloromethane layer now only contains the neutral compound anisole (**3**). Take an aliquot (1 mL) of this layer for ^{1}H NMR. These operations are conveniently represented in a flow diagram (Figure 2).

*** The aqueous layer will be on top since dichloromethane has a density greater (ρ = 1.33 g/mL) than that of water.**

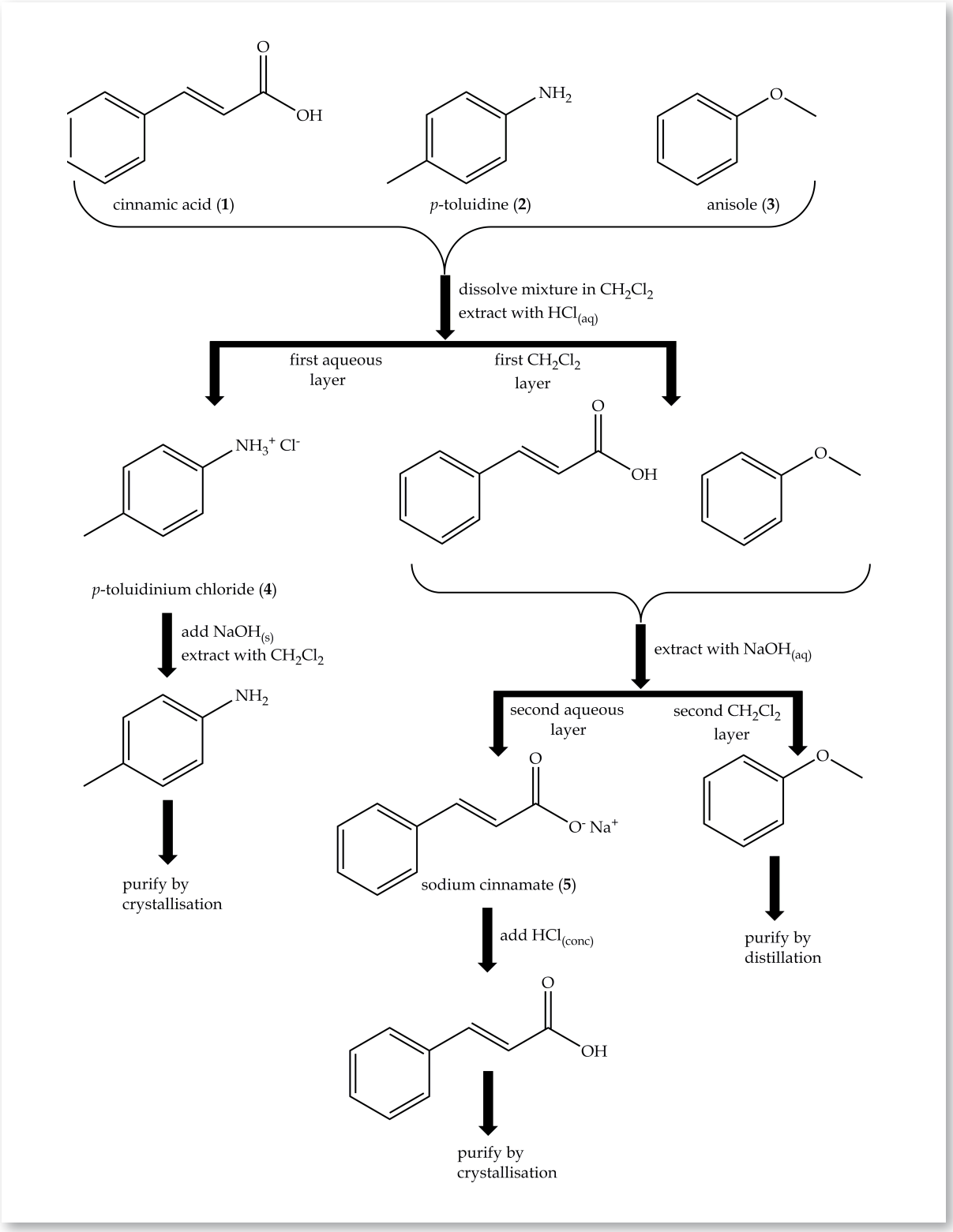


Figure 2. Flow diagram for the separation of an acid, a base and a neutral compound: cinammic acid (**1**), *p*-toluidine (**2**) and anisole (**3**).

Purification procedures

(a) Isolation and purification of cinnamic acid (**1**)

To regenerate cinnamic acid (**1**), acidify the aqueous layer containing the ionic compound **5** with concentrated hydrochloric acid. Test the solution with litmus paper to confirm its acidity. Collect the precipitate by filtration, then recrystallise from hot water. Filter the pure cinnamic acid, dry in the air and record your yield.

(b) Isolation and purification of *p*-toluidine (**2**)

To regenerate *p*-toluidine (**2**), basify the aqueous layer containing the ionic compound **4** with sodium hydroxide pellets. Test the solution with litmus paper to confirm its basicity. Transfer the basic solution into a separatory funnel and extract with dichloromethane (2 x 20 mL). Discard the top aqueous layer. Dry the dichloromethane layer with anhydrous sodium sulfate (Na_2SO_4), then take an aliquot (1 mL) for ^{1}H NMR. Remove the dichloromethane on a rotatory evaporator and recrystallise the solid from petroleum ether. Collect pure *p*-toluidine by filtration, dry in the air and record your yield.

(c) Isolation and purification of anisole (**3**)

To purify crude anisole (**3**), remove the dichloromethane on a rotary evaporator. Record the ^{1}H NMR spectrum of crude anisole as a neat liquid. Purify crude anisole by distillation, collect and record your yield.

Tasks

- Record the ^{1}H NMR spectra of all aliquots taken during the separation and purification procedures using the Spinsolve NMR spectrometer.
- Record the ^{1}H NMR spectra of purified cinnamic acid, *p*-toluidine and anisole using the Spinsolve NMR spectrometer. Prepare the NMR samples using 30 mg of cinnamic acid and *p*-toluidine in 0.6 mL of dichloromethane. For anisole, prepare the NMR sample using 0.5 mL of purified anisole.
- Assign the ^{1}H NMR spectra of cinnamic acid, *p*-toluidine and anisole.
- Compare the ^{1}H NMR spectra of cinnamic acid, *p*-toluidine and anisole with the spectra obtained during the separation procedure. Comment on the effectiveness of the extraction methods used in this experiment.
- Calculate the percentage yield recovered for each compound after the separation procedure.

^{1}H NMR Spectra

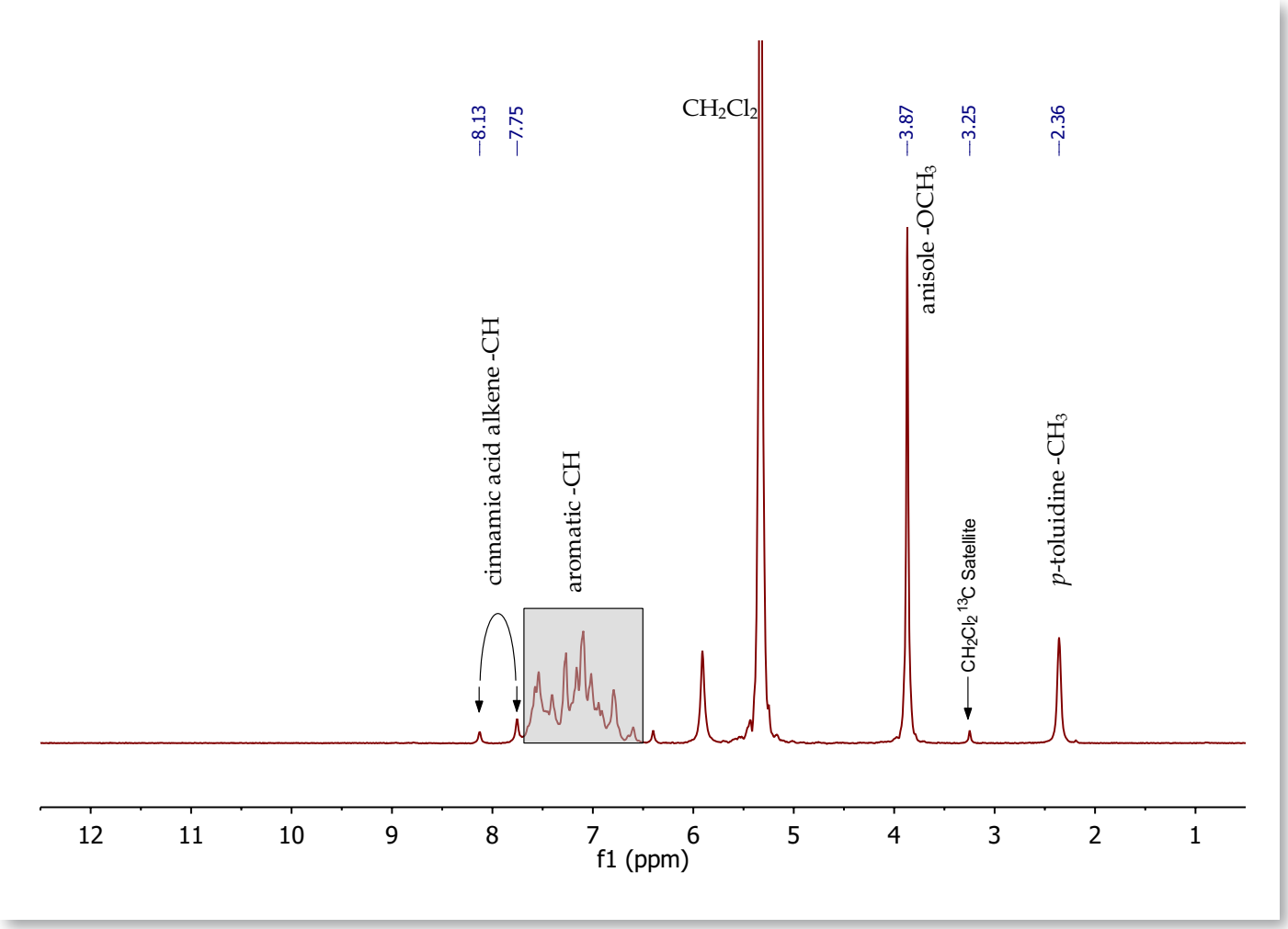


Figure 3. ^{1}H NMR spectrum of initial separation mixture containing cinnamic acid (**1**), *p*-toluidine (**2**) and anisole (**3**) in dichloromethane.

The ^{1}H NMR spectrum (Figure 3) of the initial separation mixture in dichloromethane shows the presence of all the three compounds (**1-3**) to be separated. A singlet is observed at 2.36 ppm corresponding to the methyl group of *p*-toluidine (**2**). Further downfield (higher ppm), another singlet is observed at 3.87 ppm corresponding to the OCH_3 group of anisole (**3**). The two peaks at 8.13 and 7.75 ppm make a doublet that corresponds to one of the alkene protons of cinnamic acid (**1**). A complex multiplet is observed between 6.5-7.6 ppm for the aromatic protons of all three compounds. There are also ^{13}C satellites from the methylene chloride solvent. The coupling constant is 180 Hz putting one at 3.25 ppm and the other within the aromatic region.

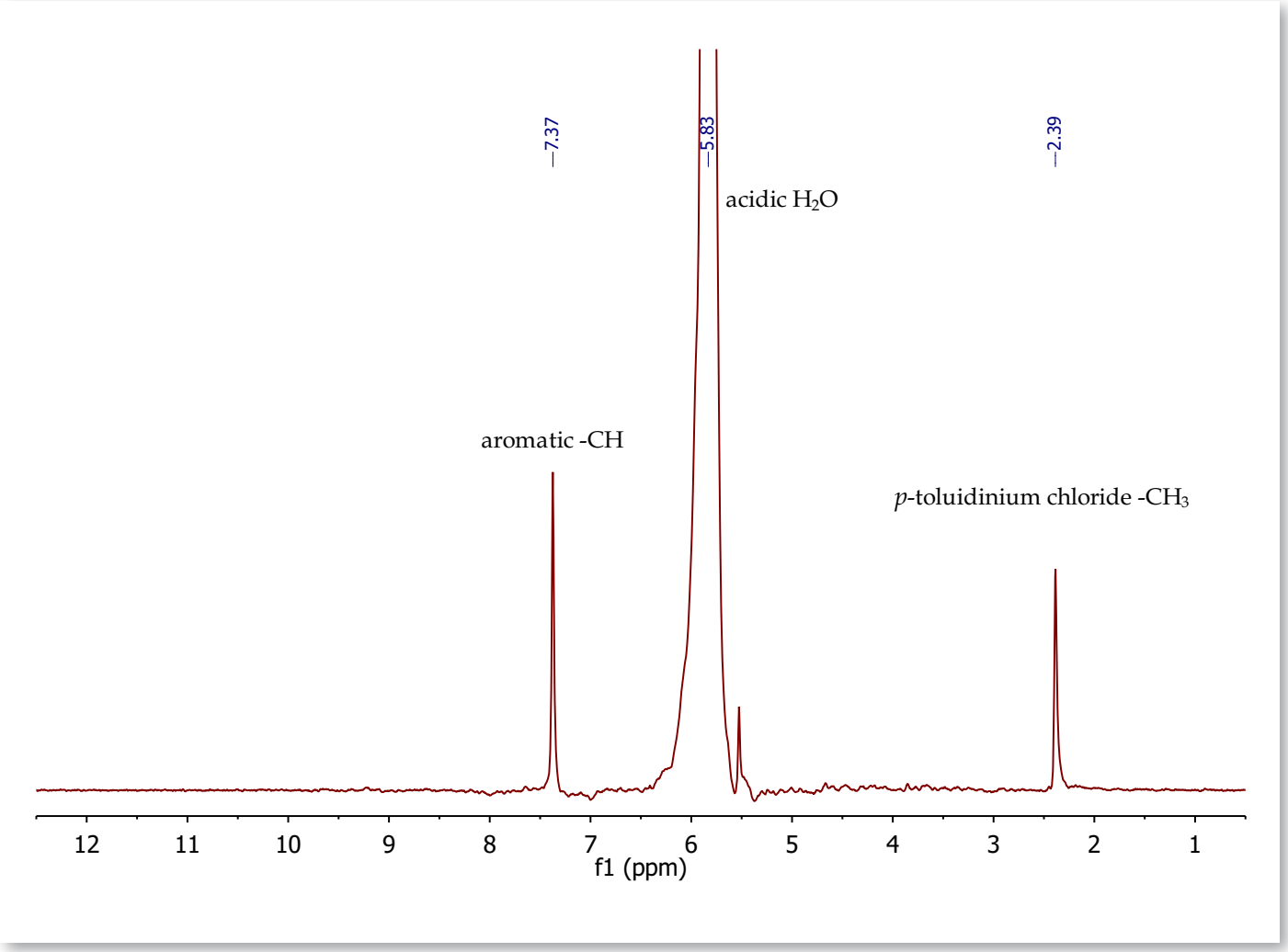


Figure 4. ^{1}H NMR spectrum of the first aqueous layer containing *p*-toluidinium chloride (**4**).

The ^{1}H NMR spectrum (Figure 4) of the first aqueous layer shows the presence of only *p*-toluidinium chloride (**4**). Two singlets are observed at 2.39 and 7.37 ppm, corresponding to the *p*-toluidinium chloride methyl group and the aromatic protons, respectively.

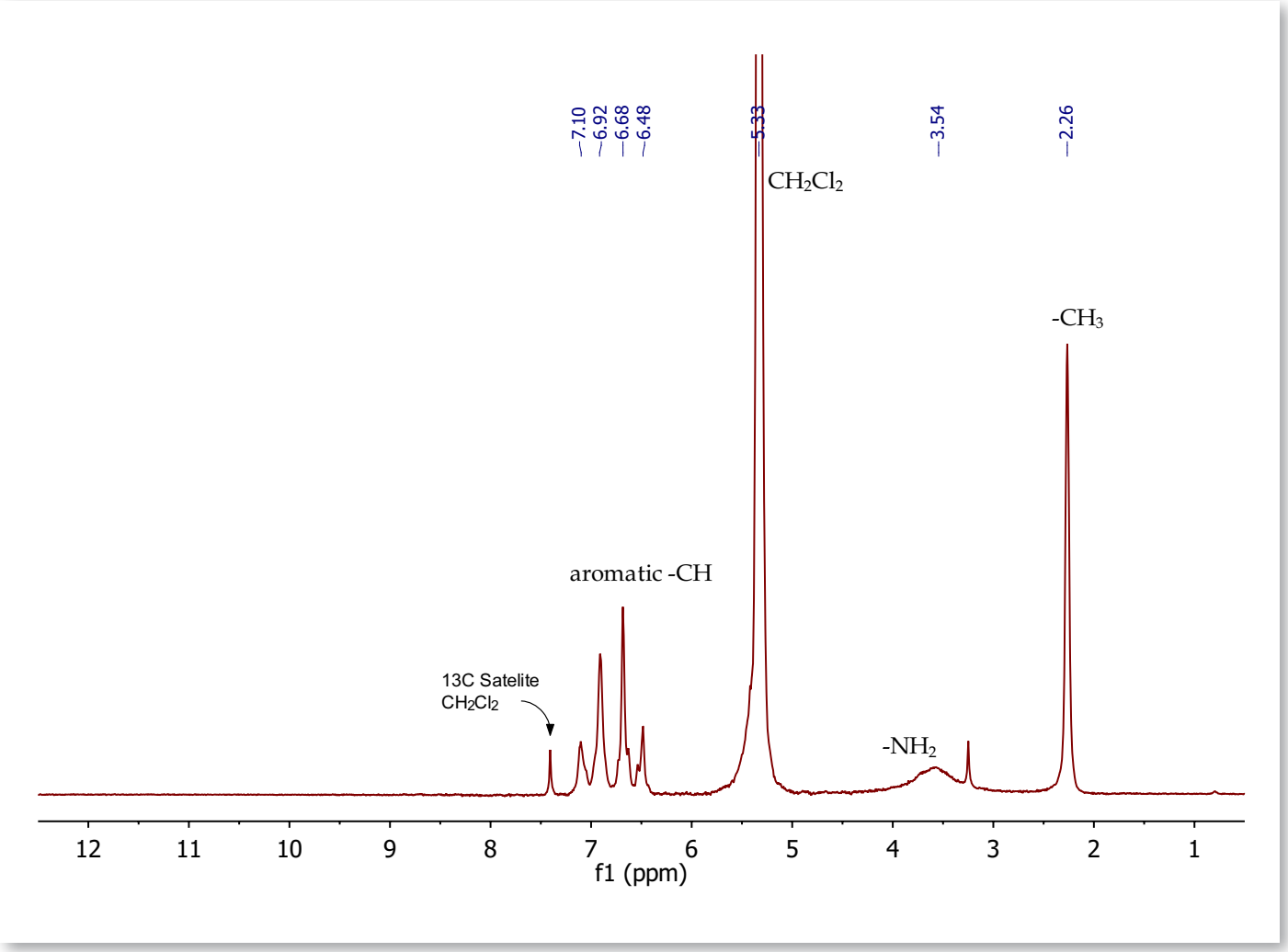


Figure 5. ^{1}H NMR spectrum of regenerated *p*-toluidine (**2**) in dichloromethane.

Figure 5 shows the ^{1}H NMR spectrum of the dichloromethane layer obtained from the addition of sodium hydroxide to the first aqueous layer containing *p*-toluidinium chloride (**4**). The ^{1}H NMR spectrum shows that *p*-toluidine (**2**) has been regenerated. A singlet is observed at 2.26 ppm corresponding to the *p*-toluidine methyl group, a very broad singlet is observed for the NH_2 protons at 3.54 ppm and a multiplet is observed between 6.48-7.10 ppm for the aromatic protons. This sample of *p*-toluidine has a high degree of purity as this spectrum is identical to the spectrum of pure *p*-toluidine after crystallisation.

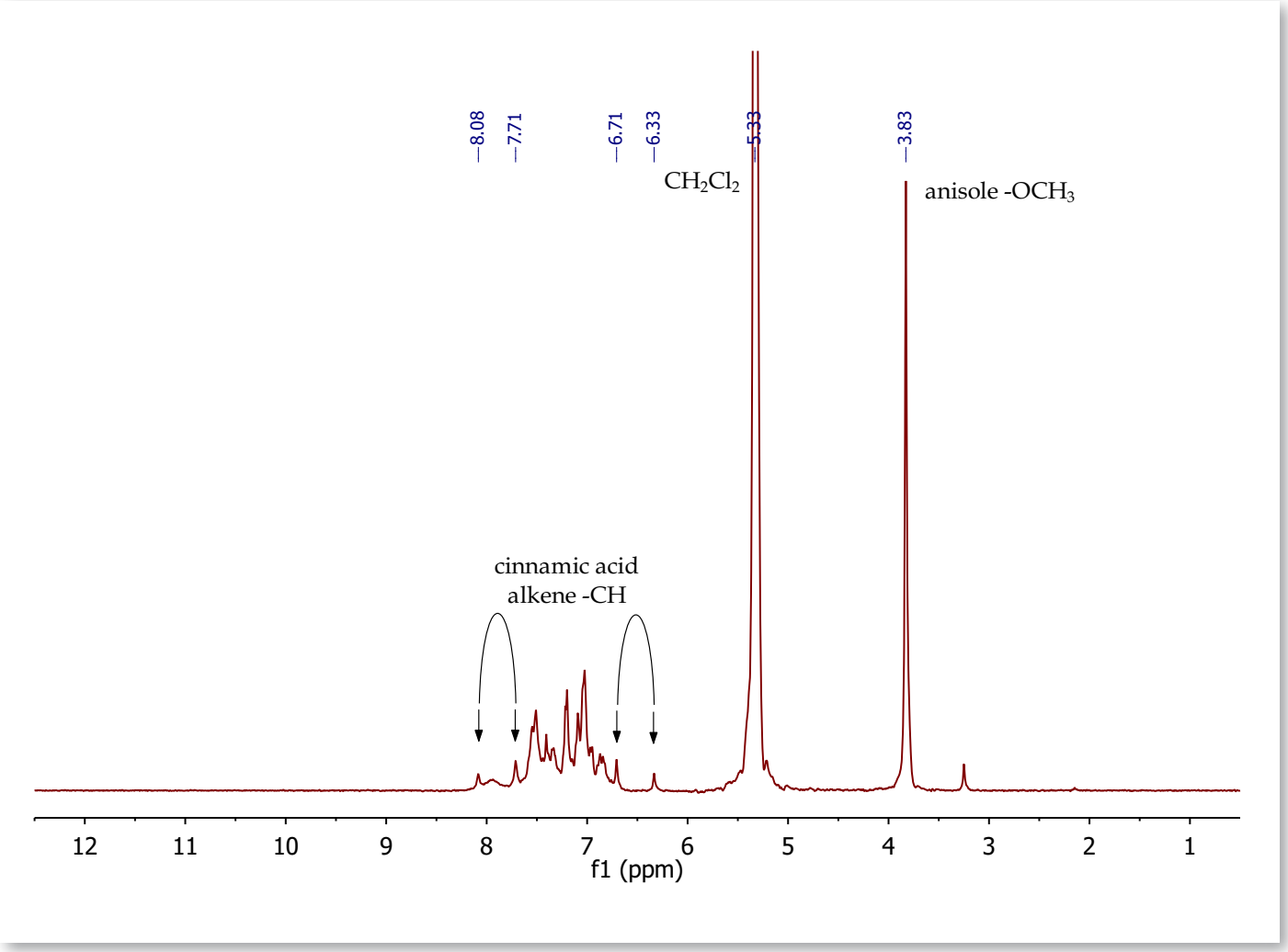


Figure 6. ^{1}H NMR spectrum of the first dichloromethane layer containing cinnamic acid (**1**) and anisole (**3**) in dichloromethane.

The ^{1}H NMR spectrum (Figure 6) of the first dichloromethane layer shows the presence of only cinnamic acid (**1**) and anisole (**3**), as *p*-toluidine (**2**) has been removed after extraction with aqueous HCl. Only one singlet is observed at 3.83 ppm corresponding to the OCH_3 group of anisole.

A complex multiplet is observed between 7.8-7.6 ppm for the aromatic protons of both compounds. Both alkene CH proton doublets of cinnamic acid are now resolved at 7.7/8.1 and 6.3/6.7 ppm. These two protons are coupled with a J-coupling constant of about 16 Hz.

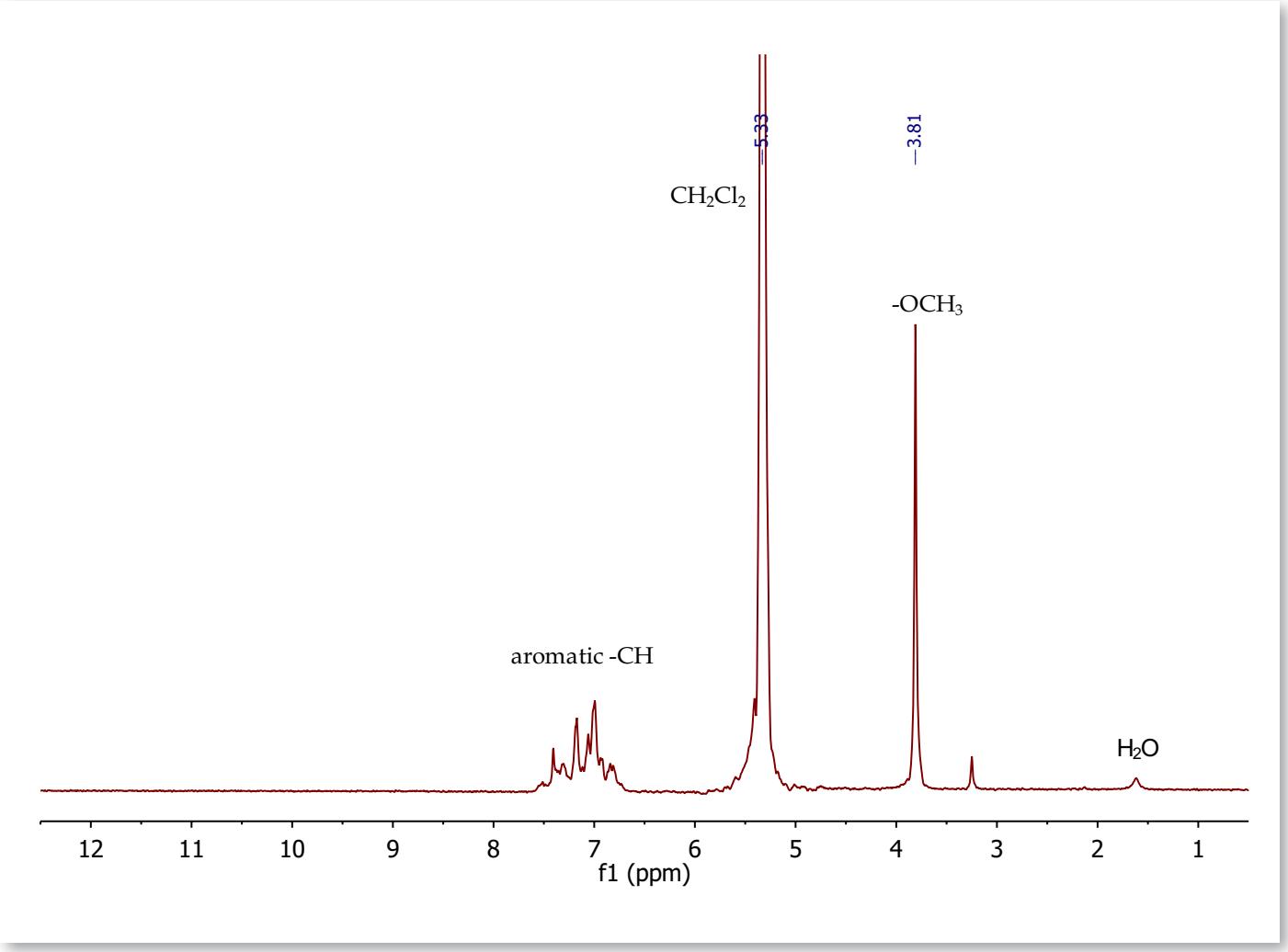


Figure 7. ^{1}H NMR spectrum of the second dichloromethane layer containing anisole (**3**).

The ^{1}H NMR spectrum (Figure 7) of the second dichloromethane layer shows the presence of only anisole (**3**), as cinnamic acid (**1**) has been removed after extraction with aqueous NaOH. A singlet is observed at 3.81 ppm corresponding to the OCH_3 group of anisole, and a complex multiplet is observed between 6.81-7.51 ppm for the aromatic protons. Notice there are no longer any doublets corresponding the alkene protons of cinnamic acid, nor is there a singlet from *p*-toluidine methyl.

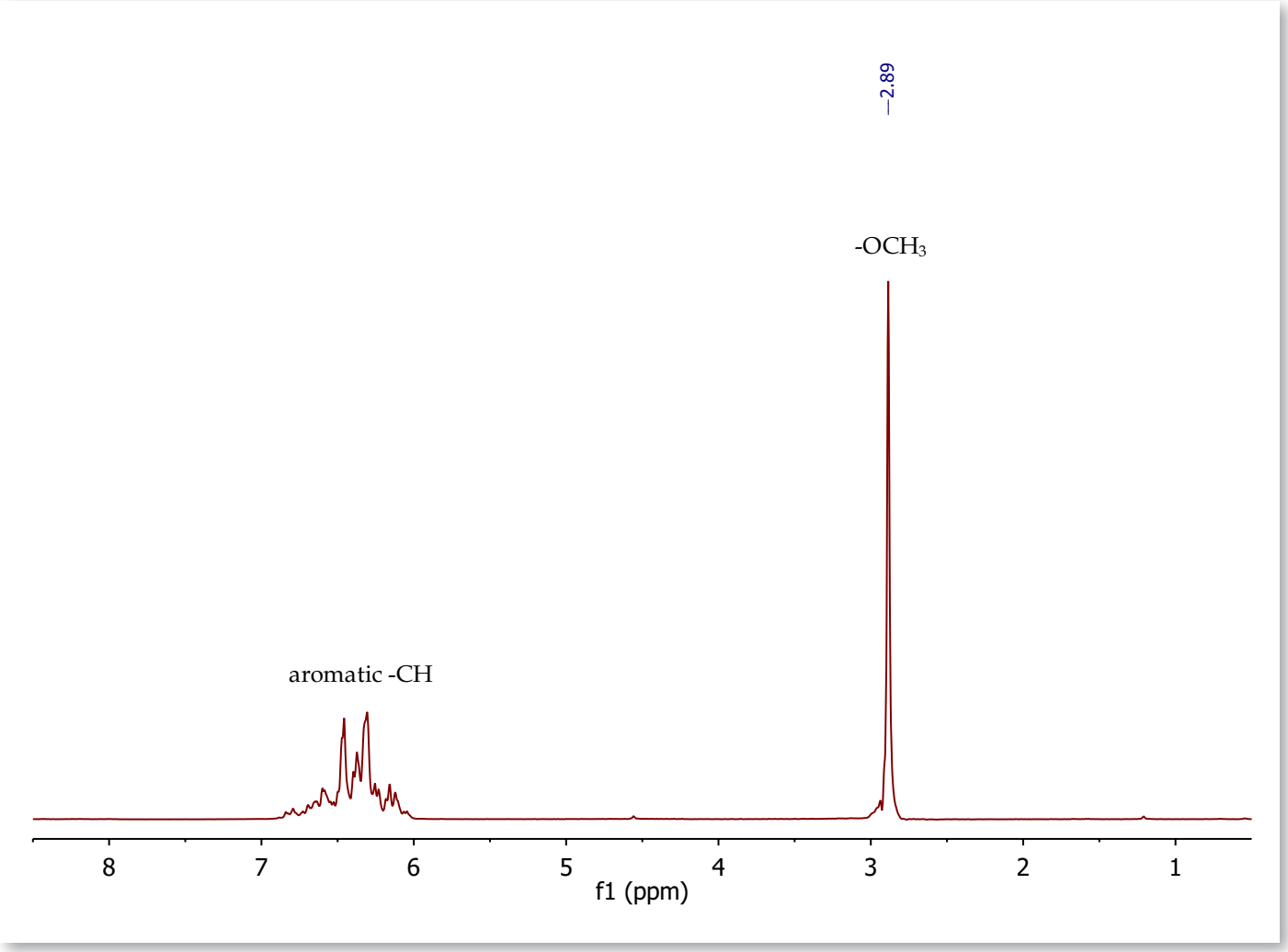


Figure 8. ^{1}H NMR spectrum of crude anisole (**3**).

The ^{1}H NMR spectrum (Figure 8) of crude anisole (**3**) after the removal of dichloromethane clearly shows that the separation procedure was very effective at separating the neutral compound from the mixture. The spectrum shows a singlet at 2.89 ppm corresponding to the OCH_3 group of anisole, and a complex multiplet between 6.12-6.69 ppm for the aromatic protons. This anisole sample has a high degree of purity as this spectrum is identical to the spectrum of pure anisole after distillation.

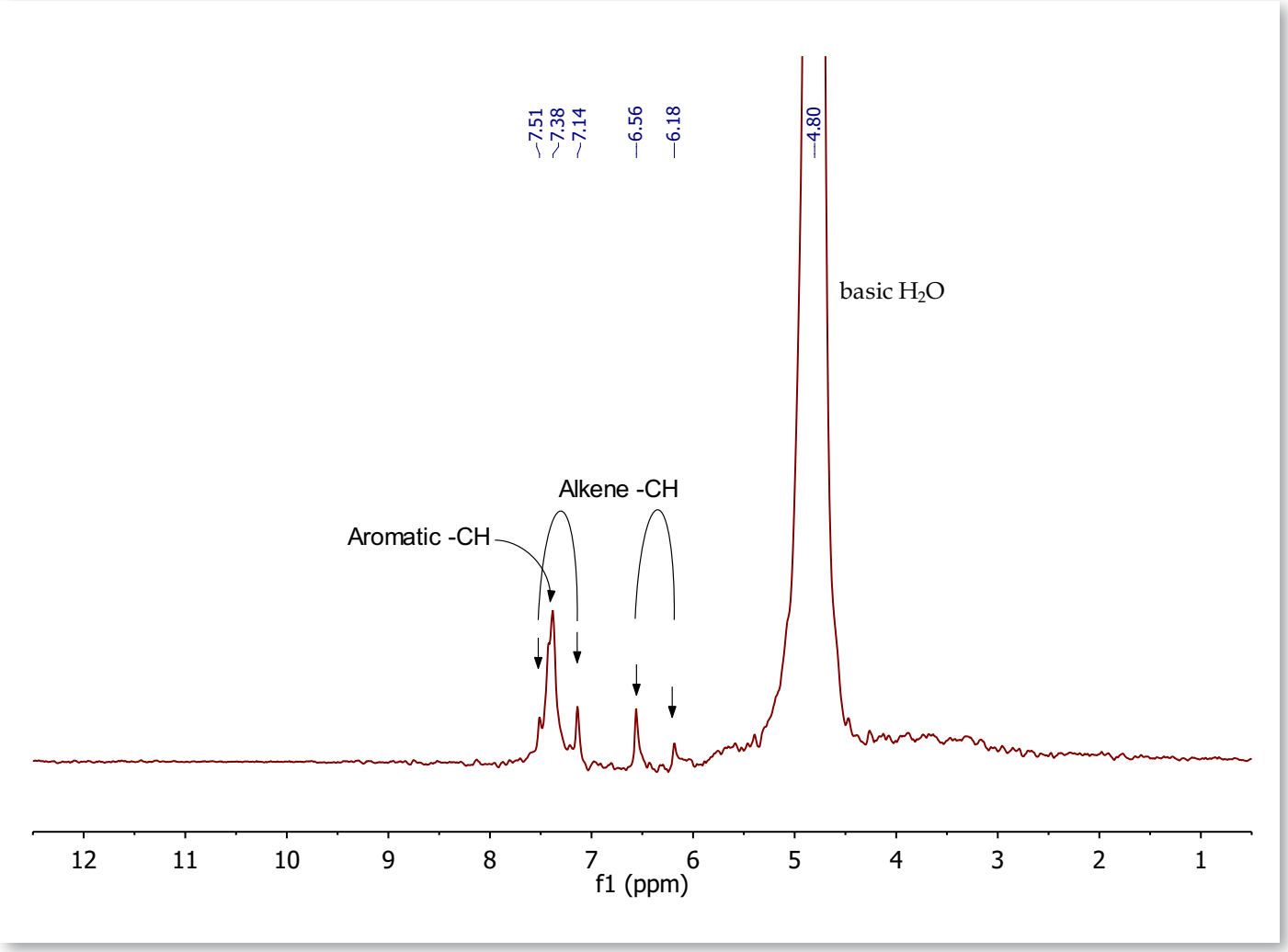


Figure 9. ^{1}H NMR spectrum of the second aqueous layer containing sodium cinnamate (**5**).

The ^{1}H NMR spectrum (Figure 9) of the second aqueous layer shows the presence of the ionic compound sodium cinnamate (**5**) after extraction with aqueous NaOH. The aromatic protons and the alkene CH protons of sodium cinnamate are observed between 6.2 and 7.5 ppm. The down field CH proton peak, corresponding to the protons closer to the carboxylate, has now shifted into the aromatic multiplet.

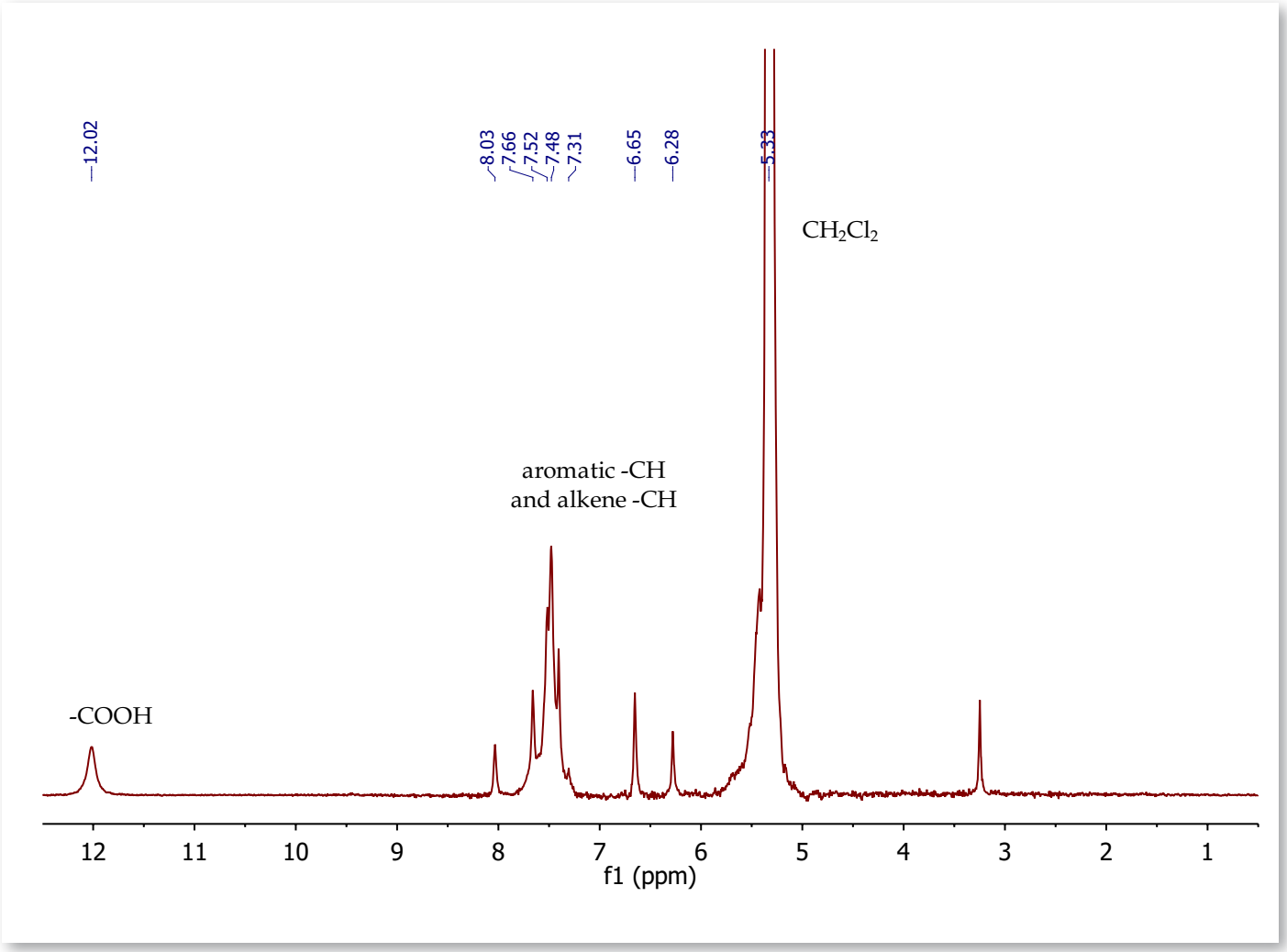


Figure 10. ^{1}H NMR spectrum of cinnamic acid (**1**) in dichloromethane.

The ^{1}H NMR spectrum (Figure 10) of purified cinnamic acid (**1**) in dichloromethane shows a multiplet between 7.41-7.52 ppm for the aromatic protons. The alkene CH protons are observed as doublets ($^{3}J_{HH}$ = 16.1 Hz) at 6.47 and 7.85 ppm. The OH proton is also observed at 12.02 ppm as a broad singlet.

magritek
www.magritek.com

Spinsolve®

References

1) Pavia, D., L.; Lampman, G., M.; Kriz, G., S.; Engel, R., G. *Introduction to Organic Laboratory Techniques: A Small Scale Approach;* Thomson Brooks/Coles, 2005.

CONTACT INFORMATION
For further information, please contact: sales@magritek.com

GERMANY

Philipsstraße 8
52068 Aachen, Germany
Tel: +49 (241) 70525-6000
Fax: +49 (241) 963 1429

NEW ZEALAND

6 Hurring Place, Unit 3
Newlands, Wellington 6037, NZ
Tel: +64 4 477 7096
Fax: +64 4 471 4665

UNITED STATES

6440 Lusk Blvd (D108)
San Diego, CA 92121, USA
Tel: +1 (855) 667-6835
+1 (866) NMR-MTEK

Or visit our website www.magritek.com