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picoSpin™ 45: Regioisomers of Butanol

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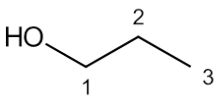
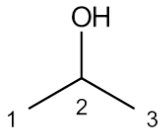
1. Introduction

Isomers are compounds that have the same molecular formula but which the connectivity of the atoms differ. There are different types of isomers: constitutional isomers, positional isomers, conformational isomers, configurational isomers (geometric and optical) and functional group isomers. In this lab we consider positional isomers (regioisomers); isomers that have the same molecular formula but differ in the substitution position of a functional group, and constitutional isomers; molecules having the same molecular formula but different carbon connectivity.

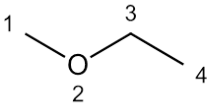
An easy example to consider is isomers of C_3H_8O. This molecular formula has three possible stable isomers, two alcohols and an ether. Placing an alcohol group on the terminal, or 1, position of propane (C_3H_8) yields the primary alcohol 1-propanol (propan-1-ol). Another isomer is 2-propanol (propan-2-ol); it is formed by placing the alcohol in the 2 position on the carbon backbone, making it a secondary alcohol. If we look at all of the isomers of the molecular formula C_3H_8O, then we also need to write down the structural formula for ethyl methyl ether (methoxyethane). Ethyl methyl ether is a constitutional isomer, while the propanol isomers are positional isomers.



1-propanol

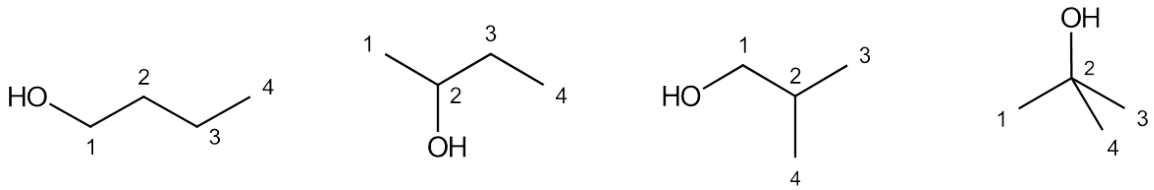


2-propanol



ethyl methyl ether

Let us now consider the isomers of $C_4H_{10}O$. There are eight possible isomers, five of them are isomers of butanol (C_4H_9OH; 2-butanol has an **R** and **S** stereoisomer due to the chiral center at C_2 and are consider together as a single isomer), the remaining three are isomers of the ether form ($C_4H_{10}O$). The ether isomers are diethyl ether ($CH_3CH_2OCH_2CH_3$), propyl methyl ether ($CH_3CH_2CH_2OCH_3$) and isopropyl methyl ether ($(CH_3)_2CHOCH_3$). The object of this laboratory exercise is isomers of butanol: 1-butanol (butan-1-ol), 2-butanol (butan-2-ol), isobutanol (2-methylpropan-1-ol) and *tert*-butanol (2-methylpropan-1-ol).



1-butanol 2-butanol isobutanol *tert*-butanol

Two of the isomers are positional isomers, 1-butanol and 2-butanol, while isobutanol and *tert*-butanol, having different carbon backbone connectivity, are constitutional isomers. The NMR spectrum of these isomers is distinct due to the changes in connectivity, which in turn affects the local molecular symmetry and splitting patterns arising from differences in the number of ^{1}H-^{1}H couplings. As the OH functional is repositioned along the carbon backbone, it influences both splitting patterns and the chemical shift position of adjacent protons, often resulting in improved spectral clarity. With NMR, these structural changes are easily observed in the ^{1}H spectrum.

2. Purpose

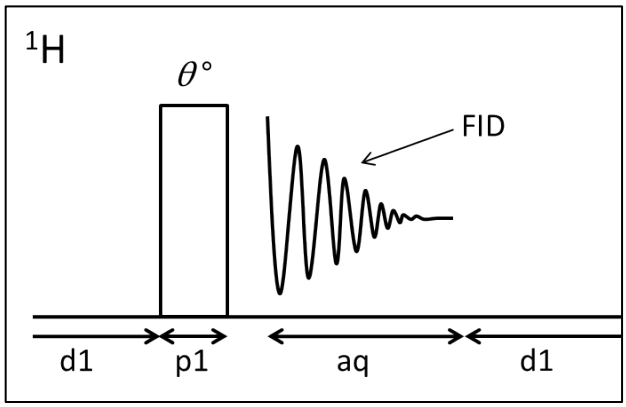
The purpose of this experiment is to gain an understanding of the utility of NMR in structure characterization by assigning the spectra of regioisomers of butanol (C_4H_9OH). Solutions of the isomers of butanol, 1-butanol, 2-butanol, isobutanol and *tert*-butanol will be prepared in protonated solvents chloroform ($CHCl_3$) and acetone. The solutions will be analyzed using the Thermo Scientific™ picoSpin™ 45 NMR spectrometer.

3. Literature

Francis A. Carey *Organic Chemistry*, 7th ed., McGraw-Hill, 2007.

4. Pulse Sequence

In this experiment, we use a standard 90° single pulse experiment. The recycle delay time (d1) is adjusted to maximize signal intensity prior to signal averaging the next FID.



Sequence: d1–[θ°–aq–d1]$_{ns}$
θ°: Pulse rotation angle (flip angle)
FID: Free induction decay
d1: Recycle delay (µs) for spin-lattice relaxation
p1: R.F. transmitter pulse length (µs)
aq: Acquisition time (ms)
ns: # of scans (individual FIDs)

5. Procedures and Analysis

Time requirements: 1-1.5 hrs

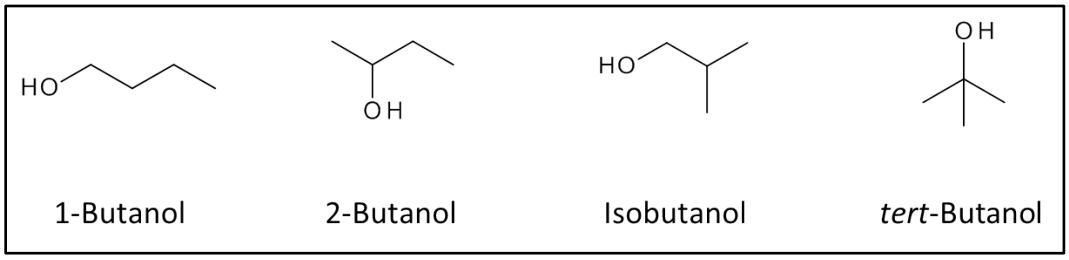
Difficulty: Easy

Sample: 1-butanol, 2-butanol, isobutanol, *tert*-butanol, chloroform, acetone

Equipment/materials:

- Thermo Scientific™ picoSpin™ 45
- 1-Butanol (C_4H_9OH)
- 2-Butanol (C_4H_9OH)
- Isobutanol (C_4H_9OH)
- *tert*-Butanol (C_4H_9OH)
- Chloroform ($CHCl_3$)
- Acetone
- NMR solvent: $CDCl_3$ w/ 1% TMS
- NMR solvent: Acetone-d_6 w/ 1% TMS
- Several 2 mL vials with PTFE cap liner
- 1 mL polypropylene syringes
- 22 gauge blunt-tip dispensing needles
- Mnova NMR Processing Suite
- picoSpin accessory kit:
  - Port plugs
  - Syringe port adapter
  - Drain tube assembly

Molecules:



Physical data:

Substance	FW (g/mol)	Quantity	MP (°C)	BP (°C)	Density (g/mL)
1-butanol	74.12	0.2 mL	-89.8	117.7	0.81
2-butanol	74.12	0.2 mL	-115	98-100	0.808
isobutanol (2-methylpropanol)	74.12	0.2 mL	-101.9	226.4	0.802
tert-butanol	74.12	0.2 mL	25	82	0.775
chloroform	119.38	0.2 mL	-82.3	61.2	1.48
acetone	58.08	0.2 mL	-95	56	0.791
chloroform-d ($CDCl_3$) w/1%TMS*	120.384		-64	61	1.50
acetone-d_6 (Ac-d_6) w/ 1%TMS*	64.12		-94	56	0.872

*Optional NMR solvents

ThermoFisher SCIENTIFIC

Safety Precautions


CAUTION Eye protection should be worn at all times while using this instrument.

CAUTION Avoid shock hazard. Each wall outlet used must be equipped with a 3-prong grounded outlet. The ground must be a noncurrent-carrying wire connected to earth ground at the main distribution box.

Experimental

Preparing Samples

Several samples will be prepared for analysis. These solutions will be prepared in chloroform ($CHCl_3$) or acetone. For $CHCl_3$ solutions, the proton NMR signal from $CHCl_3$, at 7.24 ppm, is used to shift reference the spectrum. For acetone solutions, the proton NMR signal from acetone, at 2.05 ppm, is used to shift reference the spectrum. Pay attention to label your vial and NMR data file to reflect the solvent used.

- Sample 1: To a labeled 2 mL vial, add about 0.20 mL of 1-butanol then add about 0.2 mL of $CHCl_3$. Cap, shake the vial to mix the components and save for NMR analysis.
- Sample 2: To a labeled 2 mL vial, add about 0.20 mL of 2-butanol then add about 0.2 mL of acetone. Cap, shake the vial to mix the components and save for NMR analysis.
- Sample 3: To a labeled 2 mL vial add about 0.20 mL of isobutanol then add about 0.2 mL acetone. Cap, shake the vial to mix the components and save for NMR analysis.
- Sample 4: To a labeled 2 mL vial add about 0.20 mL of warm *tert*-butanol then add about 0.2 mL of $CHCl_3$ (or acetone). Cap, shake the vial to mix the components and save for NMR analysis.

Instrumental procedure

The general procedure for sample analysis using a picoSpin NMR spectrometer is as follows:

Shim

- Ensure the NMR spectrometer is shimmed and ready to accept samples.

Pre-sample preparation

- Displace the shim fluid from the picoSpin capillary cartridge with air.
- Flush the cartridge with 0.1 mL of chloroform, and then displace the solvent with an air push.
- Set up the *onePulse* script according to parameters listed in the Pulse Script table.

Injection

- Using a 1 mL disposable polypropylene syringe fitted with a 1.5” long, 22 gauge blunt-tip needle, withdraw a 0.2 mL aliquot of sample.
- Inject about half the sample. Ensure all air bubbles have been displaced from the cartridge by examining the drain tube.
- Cap both the inlet and outlet ports with PEEK plugs.

Acquire

- Execute the onePulse script according to the values in the table of parameters provided
- Once the onePulse script has finished, prepare the cartridge for the next user by displacing the sample from the cartridge according to the following protocol: air, solvent, air.

Pulse Script: onePulse

Parameter	Value
tx frequency (tx)	proton Larmor frequency (MHz)
scans (ns)	4 or 10
pulse length (p1)	Instrument specific 90° pulse length
acquisition time (aq)	1000 ms
rx recovery delay (r1)	500 µs
T1 recycle delay (d1)	8 s
bandwidth (bw)	4 kHz

post-filter atten. (pfa)	10 (11)[a]
phase correction (ph)	0 degrees (or any value)
exp. filter (LB)	0 Hz
max plot points	400
max time to plot	250 ms
min freq. to plot	-200 Hz
max freq. to plot	+1000 Hz
zero filling (zf)	8192
align-avg. data	✓
live plot	✓
JCAMP avg.	✓
JCAMP ind.	Unchecked

[a] Choose the instrument's default pfa values

6. Processing

Download the experimental JCAMP spectra files and open them by importing into Mnova. The free induction decay (FID) will undergo automatic Fourier transformation and a spectrum will be displayed. To each spectrum, apply the following processing steps using the given settings:

Function	**Value**
Zero-filling (zf) & Linear Predict (LP)	16 k
Forward predict (FP)	From aq → 16 k
Backward predict (BP)	From -2 → 0
Phase Correction (PH)	PH0: Manually adjust
	PH1: 0
Apodization	
Exponential (LB)	0.6 Hz
First Point	0.5
Shift reference (CS)	Manually reference
Peak Picking (pp)	Manually Select Peaks
Integration (I)	Automatic Selection
Multiplet Analysis (J)	-

- Import each data file into the same workspace in Mnova. Manually apply Ph0 phase correction to each spectrum.
- Manually shift reference each spectrum using Mnova's TMS tool. Assign the $CHCl_3$ signal (7.24 ppm) or acetone signal (2.05 ppm), whichever is present.
- Identify and assign each signal in the spectra.
- Save the Mnova document, print each spectrum and paste into your lab notebook.

7. Results

Figure 1 compiles the experimental ^{1}H NMR spectra of the four regioisomer of butanol. From bottom up, the spectra are of 1-butanol in $CHCl_3$, 2-butanol in acetone, isobutanol in acetone and *tert*-butanol in $CHCl_3$. Samples are diluted to 50% by volume and the solvent proton signals are used to shift reference each spectrum.

Isobutanol and *tert*-butanol are constitutional isomers of butanol, having the same molecular formula but different carbon connectivity, whereas 1-butanol and 2-butanol are positional isomers of butanol, having the same carbon backbone structure but differ in the location of the functional group. Salient features in their NMR spectra are the changing chemical shift and multiplicity of the hydroxyl (OH) proton signal and adjacent methylene (CH_2) or methine (CH) signal with changes in carbon backbone structure or OH position change. Monitoring the hydroxyl signal, we see its multiplicity changing from a triplet (t) to doublet (d) on going from 1-butanol to 2-butanol, then back to a triplet then singlet (s) in structural isomers isobutanol and *tert*-butanol, respectively. The location of the OH group influences the coupling pattern of adjacent protons as well as their chemical shift. The inclusion the functional group OH results in changes in shielding effects on attached and adjacent protons, and the electron withdrawing effect of the O atom helps disperse signals along the *x*-axis. Branching, as in the isopropyl functional group, $-CH(CH_3)_2$, in isobutanol, also helps 'clean up' the spectrum by introducing symmetry, thus simplifying the ^{1}H spectrum.

Overlapping signals makes unambiguous assignment of splitting patterns challenging. Examining the theoretical multiplicities of the isomers of butanol, we can begin to recognize and anticipate expected patterns in ^{1}H NMR spectra. Figure 2 shows theoretical splitting patterns for proton groups in each isomer of butanol. Signal groups are dispersed along the *x*-axis to emphasize multiplicity patterns and provide clarity. We clearly see how the OH group signal splitting changes based on the number of adjacent protons, and also how the adjacent proton signal at position C_2 differs with changes in substitution (e.g., 1-butanol and 2-butanol) and symmetry (e.g., isobutanol and *tert*-butanol). At the opposite end, the terminal methyl, CH_3, signal also benefits from changes in substitution and symmetry. In isobutanol, for example, we see the classic isopropyl splitting pattern, an asymmetric doublet due to splitting of the terminal methyl's by a single methine proton and low intensity methine multiplet (m). We can recognize this pattern in the experimental spectrum. Notice how the multiplet at C_3 is similar in 1-butanol and 2-butanol. In both cases, there are four adjacent protons, though they are distributed differently in each compound. In 1-butanol, C_3 protons are coupled to two different, but symmetrically related, CH_2 groups, thus making them equivalent; in 2-butanol, C_3 protons are coupled to CH and CH_3 protons. According to the n+1 rule, first-order coupling will generate a pentet splitting pattern, with n = 4, so long as the proton-proton coupling constants are similar. The slight asymmetry in 2-butanol and the presence of the OH group at C_2 will manifest small differences in coupling constants and experimentally this will result in broadening of the signal.

Figure 3 shows the predicated ^{1}H NMR spectrum of 1-butanol and corresponding experimental spectrum of a solution of 1-butanol in $CHCl_3$. According to the simulation, five distinct proton signal groups arise from excitation of 1-butanol. The OH appears farthest downfield and its influence on the chemical shift of the CH_2 and CH_3 protons diminishes the further away the carbon center is from the OH group. The hydroxyl functional group contains an electronegative O atom, this deshields the attached proton, drawing electron density away from it and shifting its signal downfield to 4.15 ppm. It is coupled to two protons on the adjacent methylene carbon at position C_2, which, according to the n+1 rule, results in splitting of the hydroxyl signal into a triplet. The electron withdrawing effect of the O atom on the adjacent methylene protons at C_2 is demonstrated by its downfield position at 3.34 ppm. These methylene protons are coupled to both the OH proton and two protons on the adjacent C_3 carbon, giving rise to a quartet (q) structure (n = 3). The slightly broadened C_2 proton signals suggests the HO-C_2 coupling constant is not identical to the C_2-C_3 coupling constant, as mentioned above.

The electron withdrawing influence of O on the chemical shifts of methylene protons at positions C_3 and C_4 is minimal. Collectively these protons appear at an average chemical shift of 1.25 ppm. Spectral features overlap, making unambiguous assignment of individual splitting patterns difficult. Theoretically, however, C_3 protons will experience scalar coupling to C_2 and C_4 protons. If their coupling constants are nearly identical and according to the n+1 rule this will manifest (n = 4) in a pentet splitting pattern; C_4 protons couple to C_3 and C_5 (n = 5) protons to yield a sextet pattern; the terminal methyl group (C_5) couples only to two C_4 protons (n = 2) to generate a triplet pattern. The chemical shift of the terminal CH_3 group, 0.74 ppm, is not influenced by the O atom 5 bonds away.

In Figure 4 the predicted and experimental ^{1}H NMR spectrum of 2-butanol is shown. It is a positional isomer, where the OH functional group appears at the C_2 position along the linear alkane chain. The OH signal, 4.02 ppm, splits into a doublet (n = 1) due to coupling to one adjacent proton at C_2. The methine proton at C_2 shifts to 3.58 ppm due to the proximity of the electronegative O atom, and appears as a multiplet due to coupling to protons at C_1, C_3 and a hydroxyl proton. The influence of OH on the chemical shift of protons at C_1 and C_3 shifts their signals slightly downfield. This, and the change in the number of adjacent protons, brings better chemical shift resolution to the aliphatic signals centered at 1.05 ppm. The C_1 (n = 1) doublet and C_4 (n = 2) triplet signals are better resolved and easier to recognize and assign, whereas the multiplet signal from C_3 (n = 5) spans a wider range, overlaps and appears on the downfield side of the C_1 signal.

The high symmetry of the isopropyl group in isobutanol reduces the complexity of its ^{1}H spectrum (Figure 5). Protons on the terminal methyl groups at C_4 and C_5 (0.83 ppm) are split into a doublet by one adjacent proton at C_3 (n = 1), whereas the C_3 proton is coupled to seven adjacent protons ($C_{4,5}$ and C_2; n = 7) yielding a low intensity multiplet (1.53 ppm). The OH group (4.17 ppm) couples to two adjacent protons on C_2 (n = 2), splitting into a triplet.

Protons on C_2 (3.25 ppm) generate a triplet pattern as well, due to coupling to two adjacent protons (n = 2), one on C_3 and the other a hydroxyl proton.

The ^{1}H NMR spectrum of *tert*-butanol is simplest to analyze since it generates only two signals, one at 3.11 ppm due to a single uncoupled OH proton, and one at 0.95 ppm due to nine equivalent, but uncoupled *t*-butyl group protons. There are no adjacent protons to couple to, thus each group appears as a singlet in the spectrum. The electron withdrawing effect of the O atom on the terminal methyl protons is minimal, with only a slight apparent downfield shift.

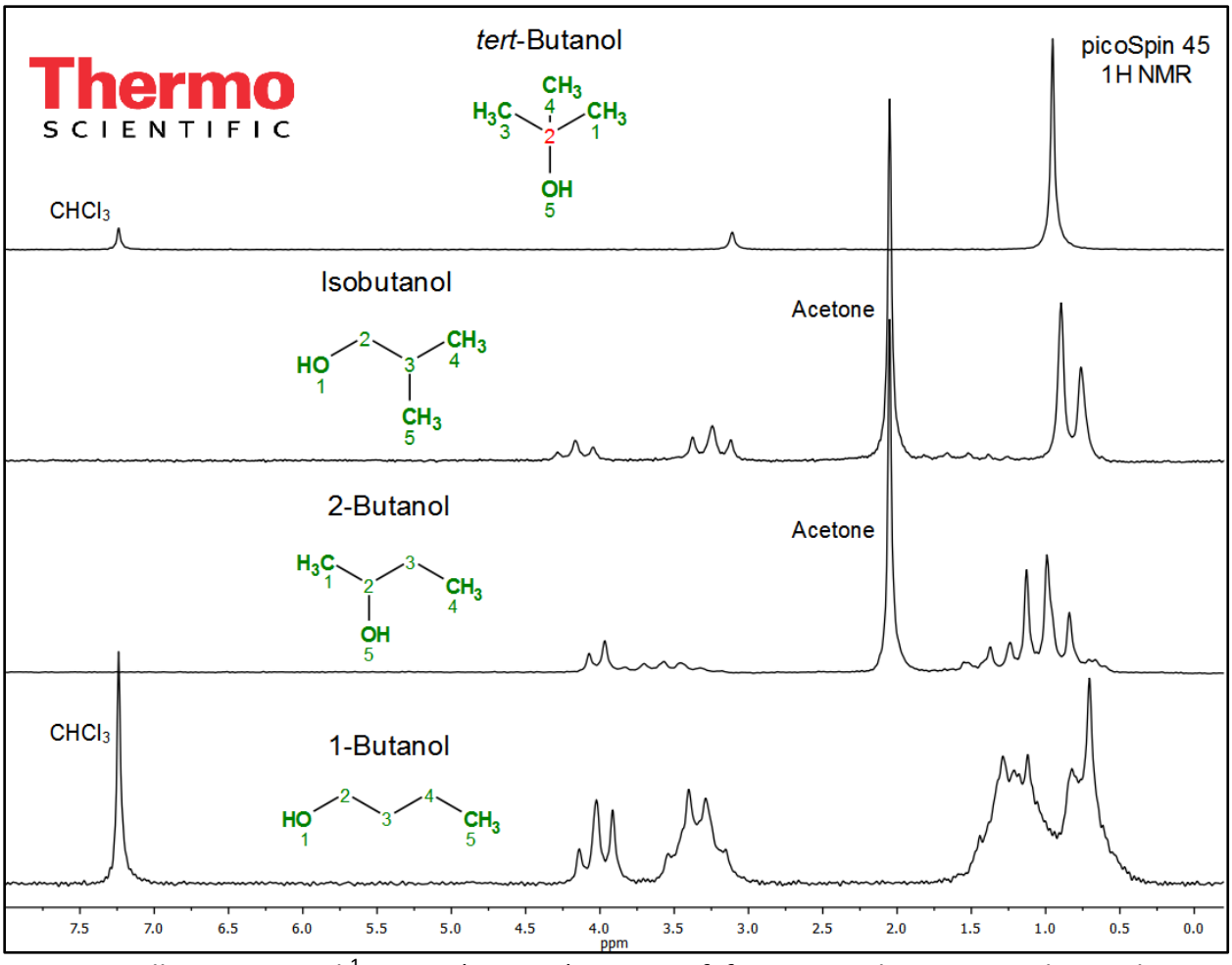


Figure 1. Full experimental ^{1}H NMR (45 MHz) spectra of, from top to bottom, *tert*-butanol, isobutanol, 2-butanol and 1-butanol.

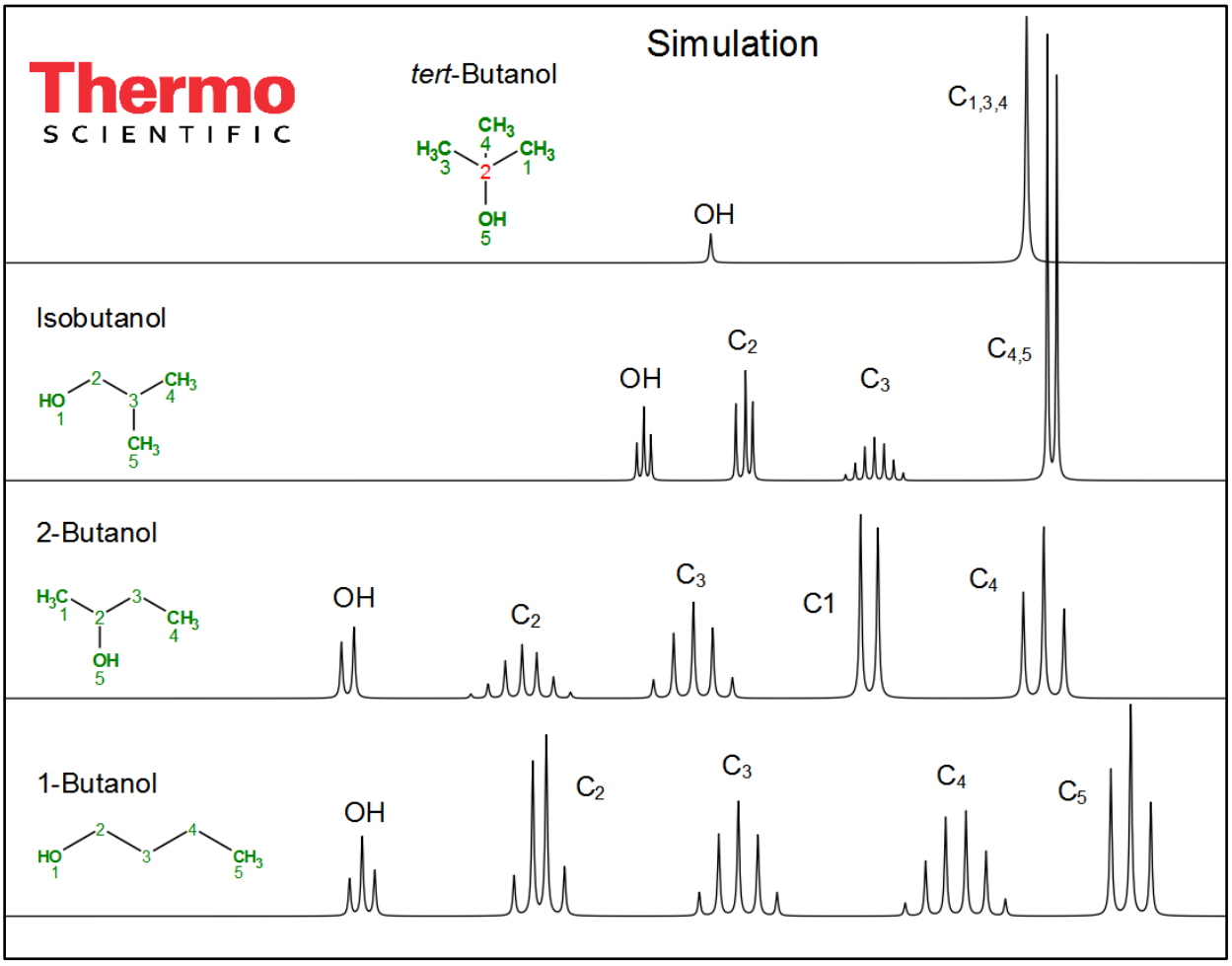


Figure 2. Simulated multiplet patterns for the regioisomers of butanol: from top to bottom, *tert*-butanol, isobutanol, 2-butanol and 1-butanol. Signals are dispersed arbitrarily along the *x*-axis for clarity but roughly retain their relative local chemical shift positions.

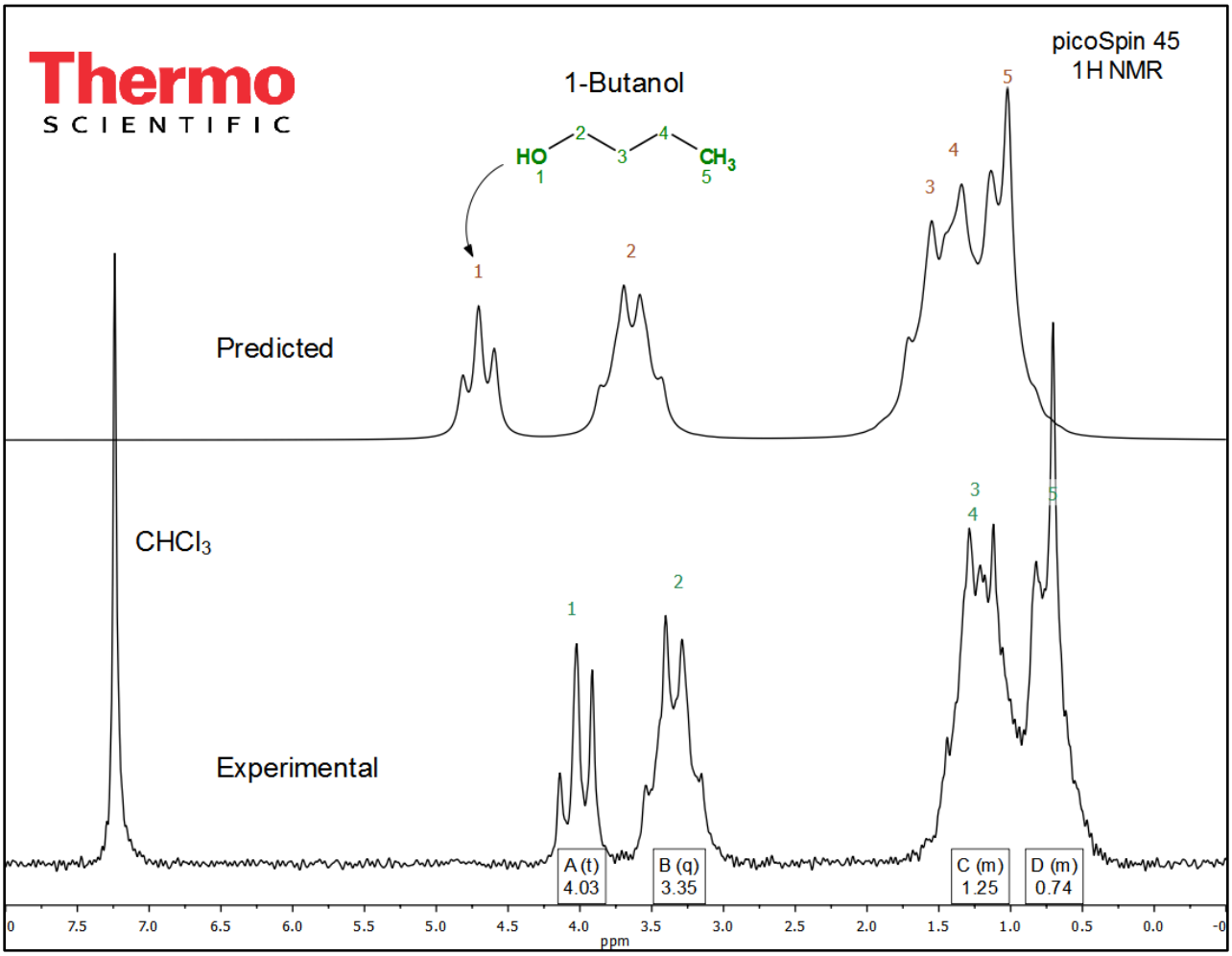


Figure 3. Full experimental (bottom) and predicted (top) ^{1}H NMR (45 MHz) spectrum of 1-butanol in CHCl3 (50:50 v/v).

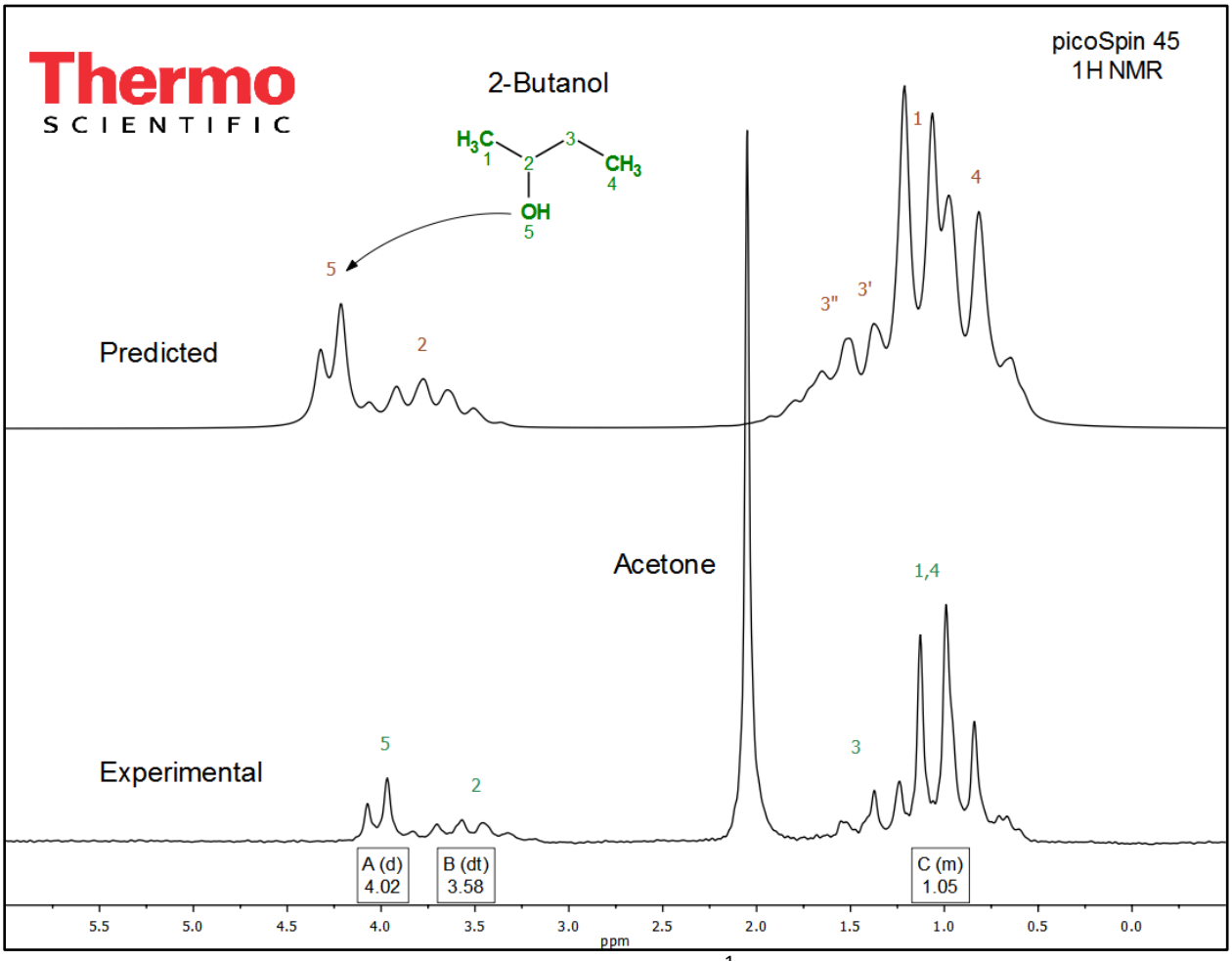


Figure 4. Full experimental (bottom) and predicted (top) ^{1}H NMR (45 MHz) spectrum of 2-butanol in acetone (50:50 v/v).

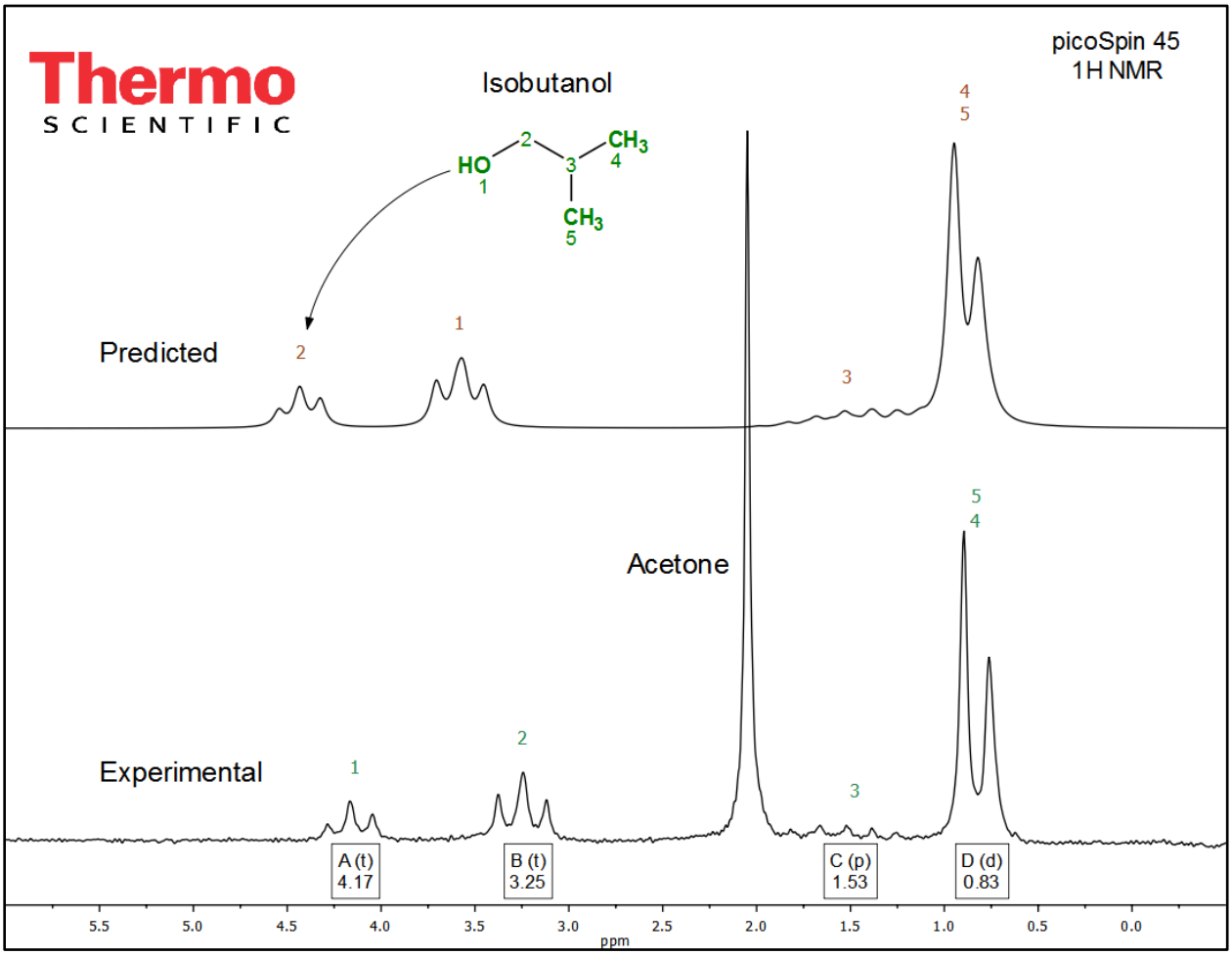


Figure 5. Full experimental (bottom) and predicted (top) ^{1}H NMR (45 MHz) spectrum of isobutanol in acetone (50:50 v/v).

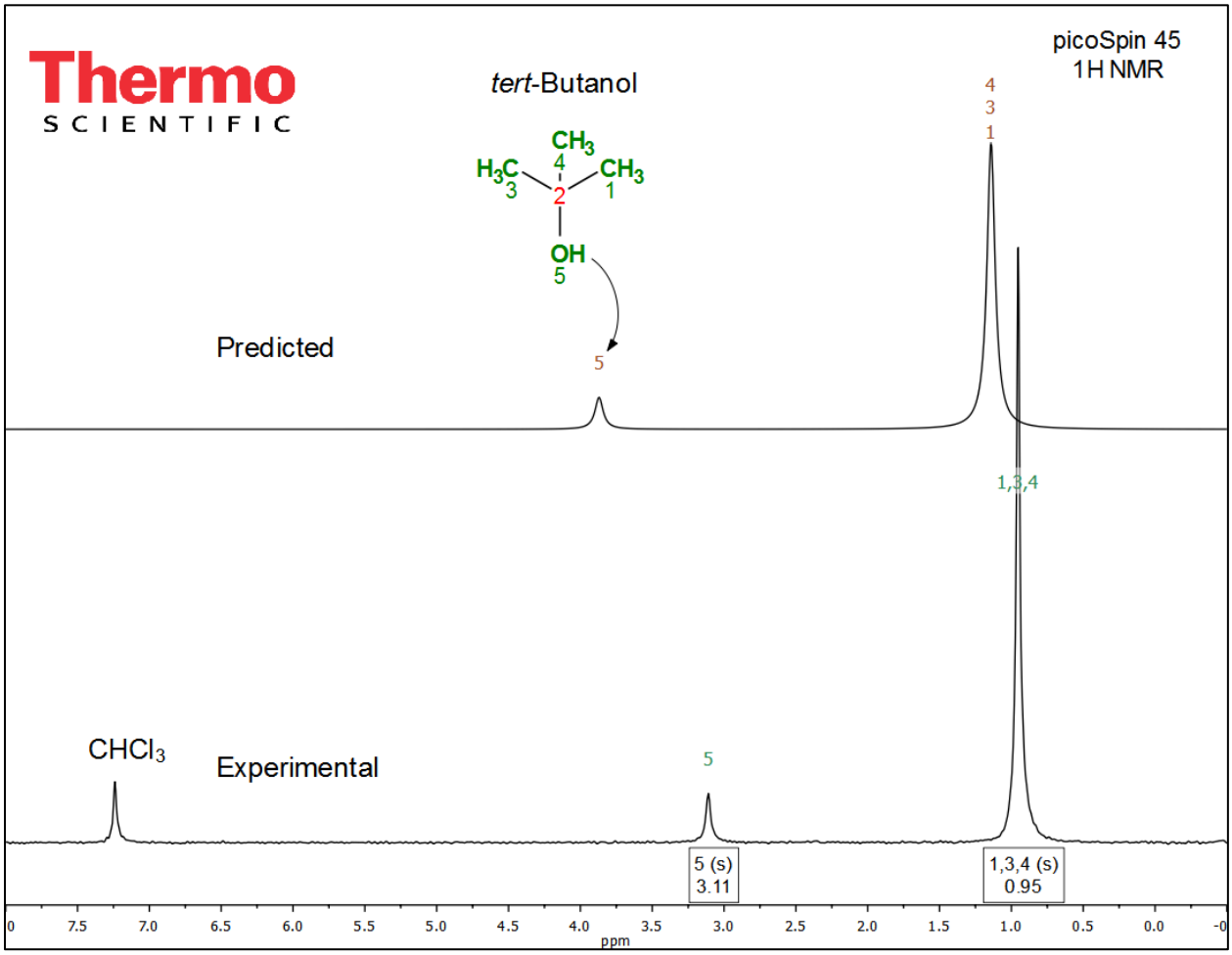


Figure 6. Full experimental (bottom) and predicted (top) ^{1}H NMR (45 MHz) spectrum of *tert*-butanol in $CHCl_3$ (50:50 v/v).

Table 1. ^{1}H NMR Spectral Data

Figure	Compound	Signal Group	Chemical Shift (ppm)	Nuclides	Multiplicity
	TMS	$Si(CH_3)_4$	0	12 H	singlet
1,2	1-butanol	$CH_3CH_2CH_2CH_2$-OH	0.76	3 H	triplet
		$CH_3CH_2CH_2CH_2$-OH	1.20	2 H	multiplet
		$CH_3CH_2CH_2CH_2$-OH	1.20	2 H	multiplet
		$CH_3CH_2CH_2CH_2$-OH	3.35	2 H	quartet
		$CH_3CH_2CH_2CH_2$-OH	4.03	1 H	triplet
1,4	2-butanol	$CH_3CH(OH)CH_2CH_3$	0.99	3 H	doublet
		$CH_3CH(OH)CH_2CH_3$	1.32	2 H	multiplet
		$CH_3CH(OH)CH_2CH_3$	0.99	3 H	quartet
		$CH_3CH(OH)CH_2CH_3$	3.58	1 H	multiplet
		$CH_3CH(OH)CH_2CH_3$	4.02	1 H	doublet
1,5	isobutanol	$(CH_3)_2CHCH_2$-OH	0.83	6 H	doublet
		$(CH_3)_2CHCH_2$-OH	1.53	1 H	multiplet
		$(CH_3)_2CHCH_2$-OH	3.25	2 H	triplet
		$(CH_3)_2CHCH_2$-OH	4.17	1 H	triplet
1,6	*tert*-butanol	C_4H_9-OH	0.95	9 H	triplet
		C_4H_9-OH	3.11	1 H	triplet
1,3,6	Chloroform	$CHCl_3$	7.24	1 H	singlet
1,4,5	Acetone	$O=C(CH_3)_2$	2.05	6 H	singlet

8. Comments

With the exception of *tert*-butanol, which is a solid at room temperature and needs to be dissolved in a solvent, the remaining isomers of butanol are liquids and can be injected directly into the picoSpin NMR capillary cartridge without dilution. However, these liquids are slightly viscous and result in broadened spectral lines; dilution to 50% improves spectral resolution and the solvent signal provides a well-defined, non-interfering signal for chemical shift referencing. The choice of solvent was twofold, to enhance spectral resolution, and to minimize solvent proton signal overlap. For 1-butanol and *tert*-butanol, acetone or $CHCl_3$ produces similar spectral results. Chloroform in preferred for *tert*-butanol since the acetone signal overlaps with ^{13}C satellite signals arising from ^{1}H-^{13}C coupling in the *t*-butyl group.

Acetone was chosen for isobutanol despite partial signal overlap with the multiplet due to the methine proton in the isopropyl group, -*CH*$(CH_3)_2$. Coupling of the hydroxyl (OH) and methylene (HO-*CH*$_2$-) protons is adversely affected in $CHCl_3$, with a distinct loss of spectral resolution for these signals; acetone solvent recovers the spectral resolution of these signals. Likewise, 2-butanol experiences better spectral resolution of the –OH and HO-*CH*- signal groups with discernible improvement of coupling in acetone.

9. Own Observations

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Belgium +32 53 73 42 41	+46 8 556 468 00	Latin America +1 561 688 8700	Switzerland +41 61 716 77 00
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