REMSPEC

Correction of FTIR data for the effect of temperature variation

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Temperature Correction of FTIR Data

- Why is FTIR used ?
  - To identify the species in solution in a reaction mixture or crystallization process
  - To measure the changes in concentration of species in solution as a function of time
  - To gain process understanding from the first two items

Temperature Correction of FTIR Data

- How does an FTIR with ATR measure species concentration in solution ?
  - Beers law

$$Abs = \mathrm{Log}_{10}(I_o/I_s) = \varepsilon\, C\, d$$

- $\textit{Reference signal} = I_o$
- $\textit{Sample signal} = I_s$
- $\textit{Optical Path through sample} = d$
- $\textit{Sample concentration} = C$
- $\textit{Extinction coefficient} = \varepsilon$

Temperature correction of FTIR Data

- The important parameters are *d* and ε
  - ε is a property of the molecule and the molecular bond being measured
  - *d* is given by the ATR equation

$$d = \frac{\lambda}{2\pi n\left(\sin^2\theta - nr^2\right)^{1/2}}$$

  - While n and nr are temperature dependent the effect is negligible compared to temperature effects on ε

Temperature correction of FTIR Data

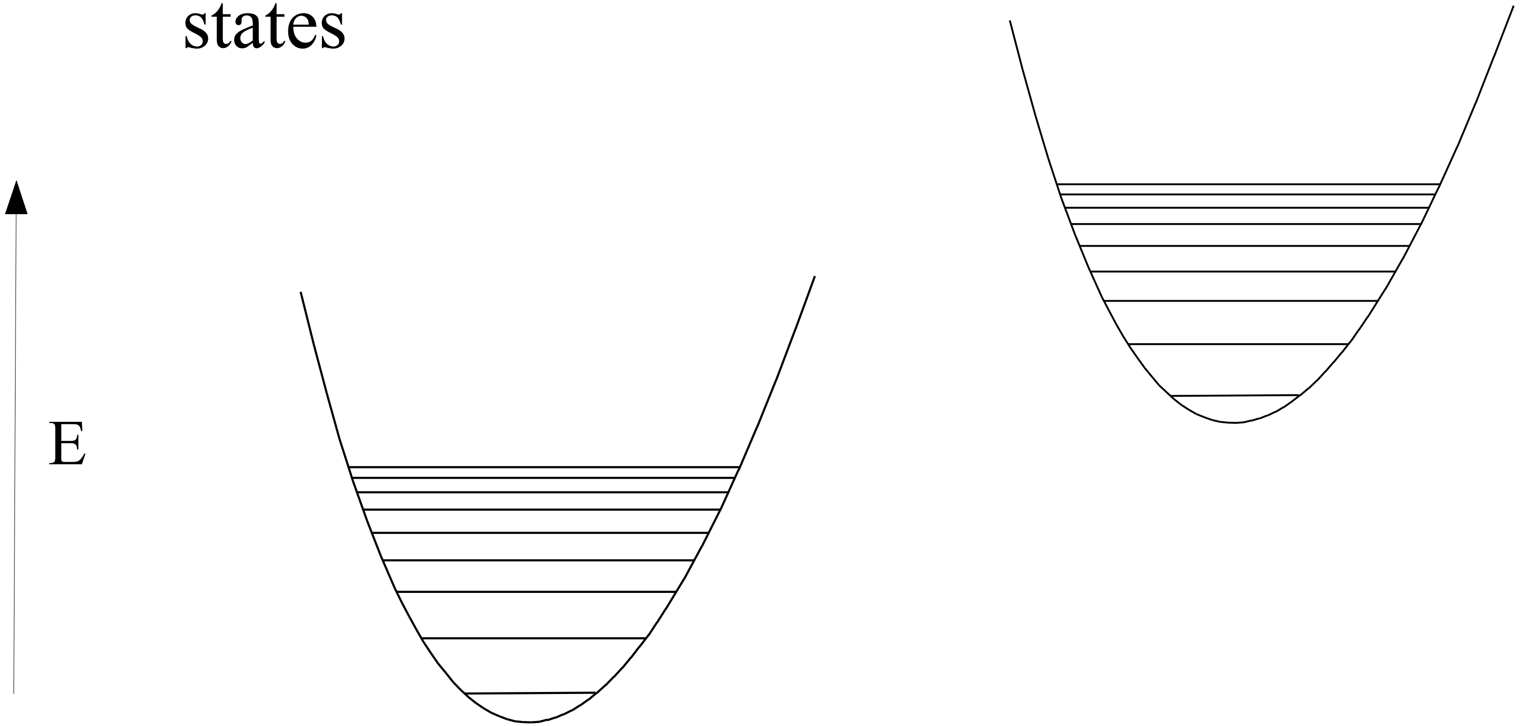
- As long as Θ is fixed and constant, the probe can be considered analytically stable. That is movement of the probe or disassembly and reassembly will not change d and so the measured absorbance will not change
  - This property of analytical stability is dependent on which vendor and which probe is used
- If the probe is analytically stable then there will be no temperature effects from thermally driven mechanical movements changing Θ

Temperature correction of FTIR Data

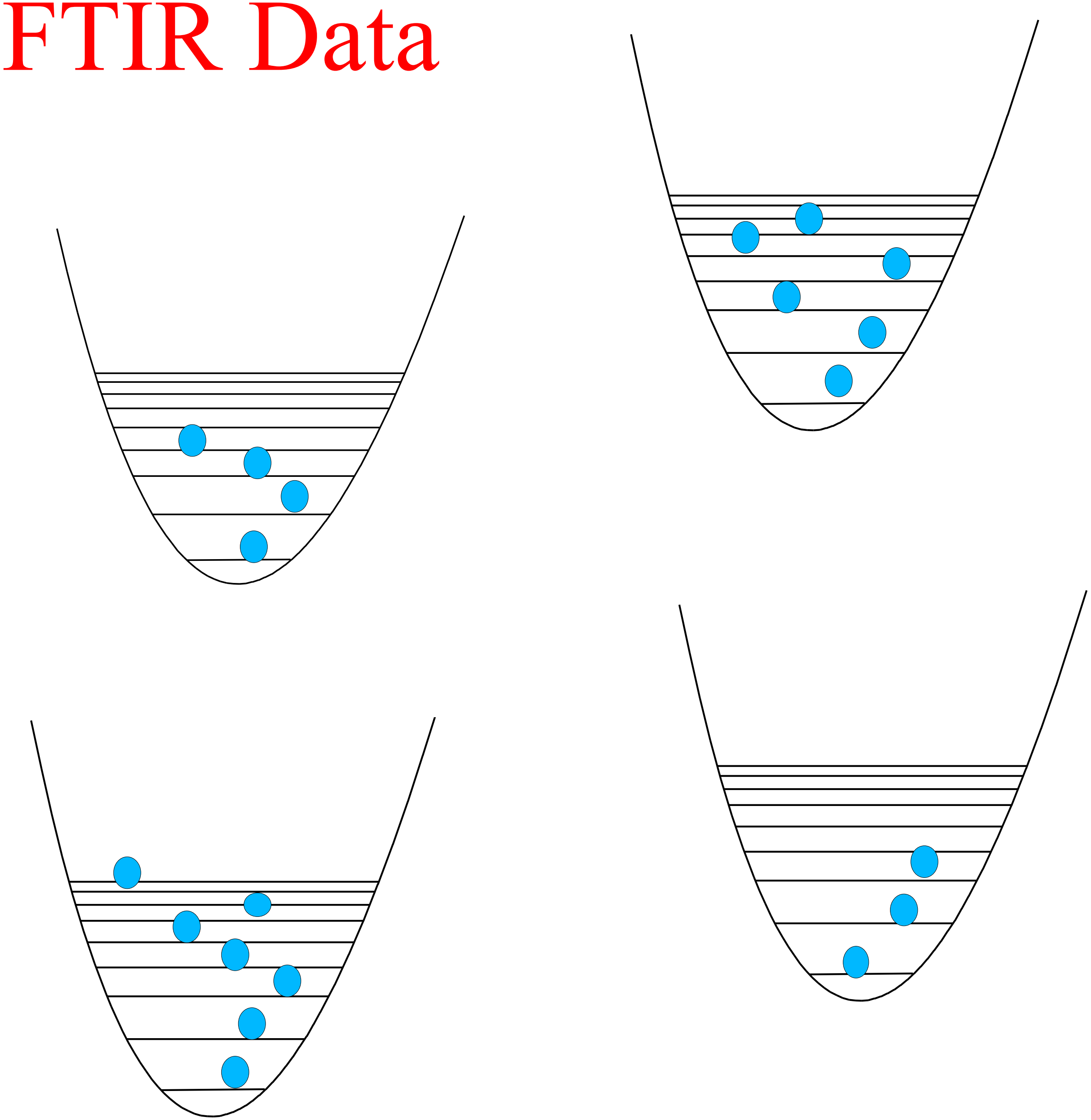
- What changes with temperature?
  - The extinction coefficient ε
    - For an IR peak ε is directly related to the transition probabilities between the vibrational states in the molecule
    - The transition probability is effectively the probability that a photon of the right energy will be absorbed when it interacts with a molecule

Temperature correction of FTIR Data

- Why can ε change with temperature?
  - Thermal energy or to put it another way thermal phonons are in the correct energy range to excite molecular transitions and so change the relative populations of the ground and excited vibrational states



Temperature correction of FTIR Data



HOT

COLD

Temperature correction of FTIR Data

- If this were the only phenomenon occurring then all IR absorptions would become less intense with increasing temperature which is generally what happens.
- However each bond is not an isolated entity in a molecule and energy can be distributed or redistributed between different bond vibrations. The result is that some vibrations can become more intense as the temperature increases

Temperature correction of FTIR Data

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- In practical terms this means that every IR (or Raman) peak intensity is temperature dependent and each peak in a molecule can and usually will have a different temperature dependence than any other peak in the same molecule
- As a result any attempt to use an internal standard or peak intensity ratio is automatically suspect and liable to give bogus answers unless the temperature conditions are tightly defined and a proper calibration made under those conditions

Collecting Data

- Fortunately collection of the necessary data to correct IR data for the effect of temperature is quite simple and straight forward
- All that is needed is a system for logging IR spectra and temperature data together on the same time scale such as:
  - An automated reactor system such as the HEL Automate™ with a direct data link to an IR system such as ReactionView®

OR

  - An IR system such as ReactionView® with direct temperature logging capability and a constant temperature bath for temperature control of the sample

Collecting Data

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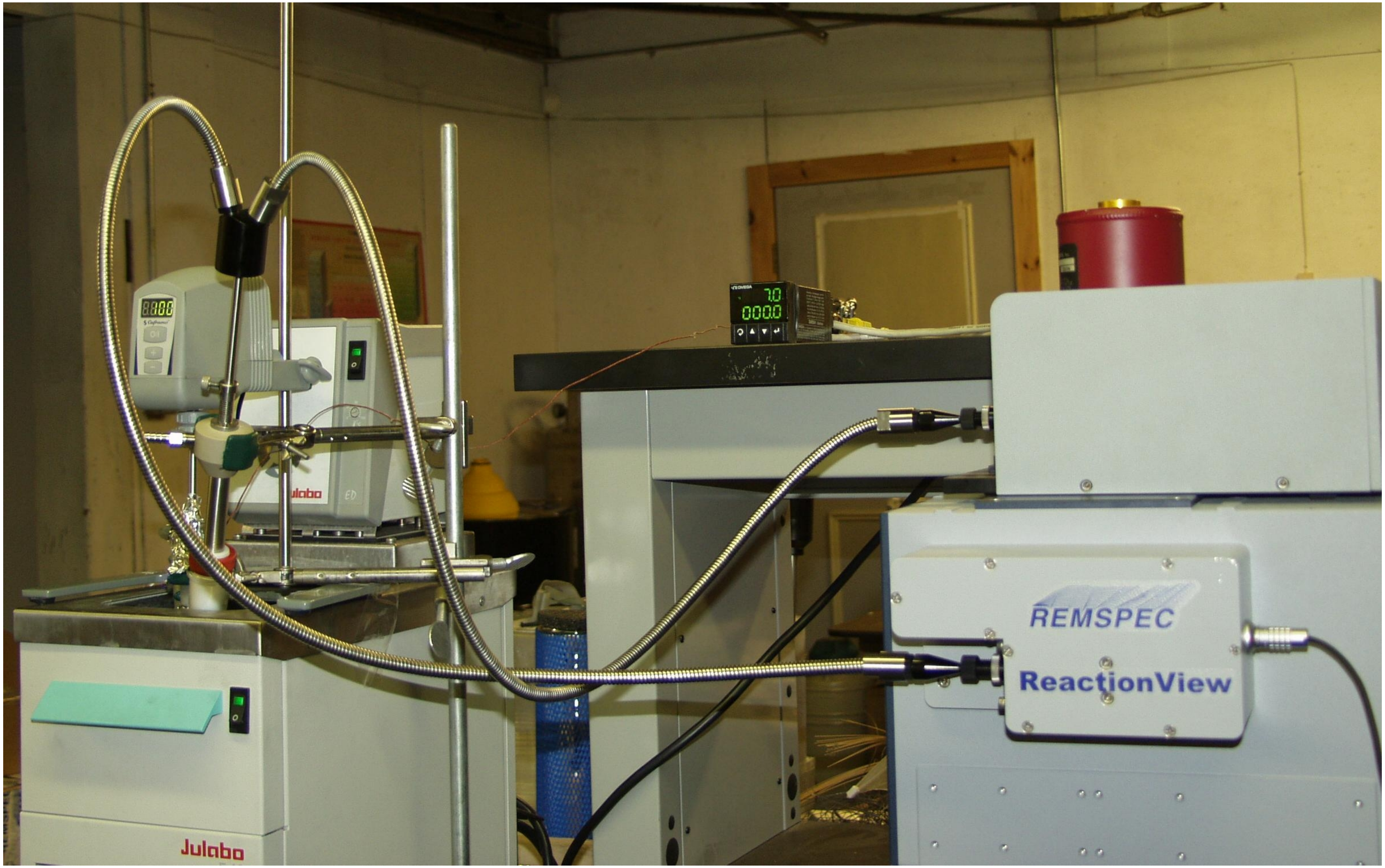

Collecting Data

- The combination of components shown on the previous slide meets the requirements for collecting good temperature calibration data.
  - Analytically stable optical probe
  - Convenient temperature measurement
  - Real time logging of temperature with each IR spectrum
  - Precision temperature control
  - Stirring to ensure thermal and chemical homogeneity of the system being analysed

Aspirin in ethanol

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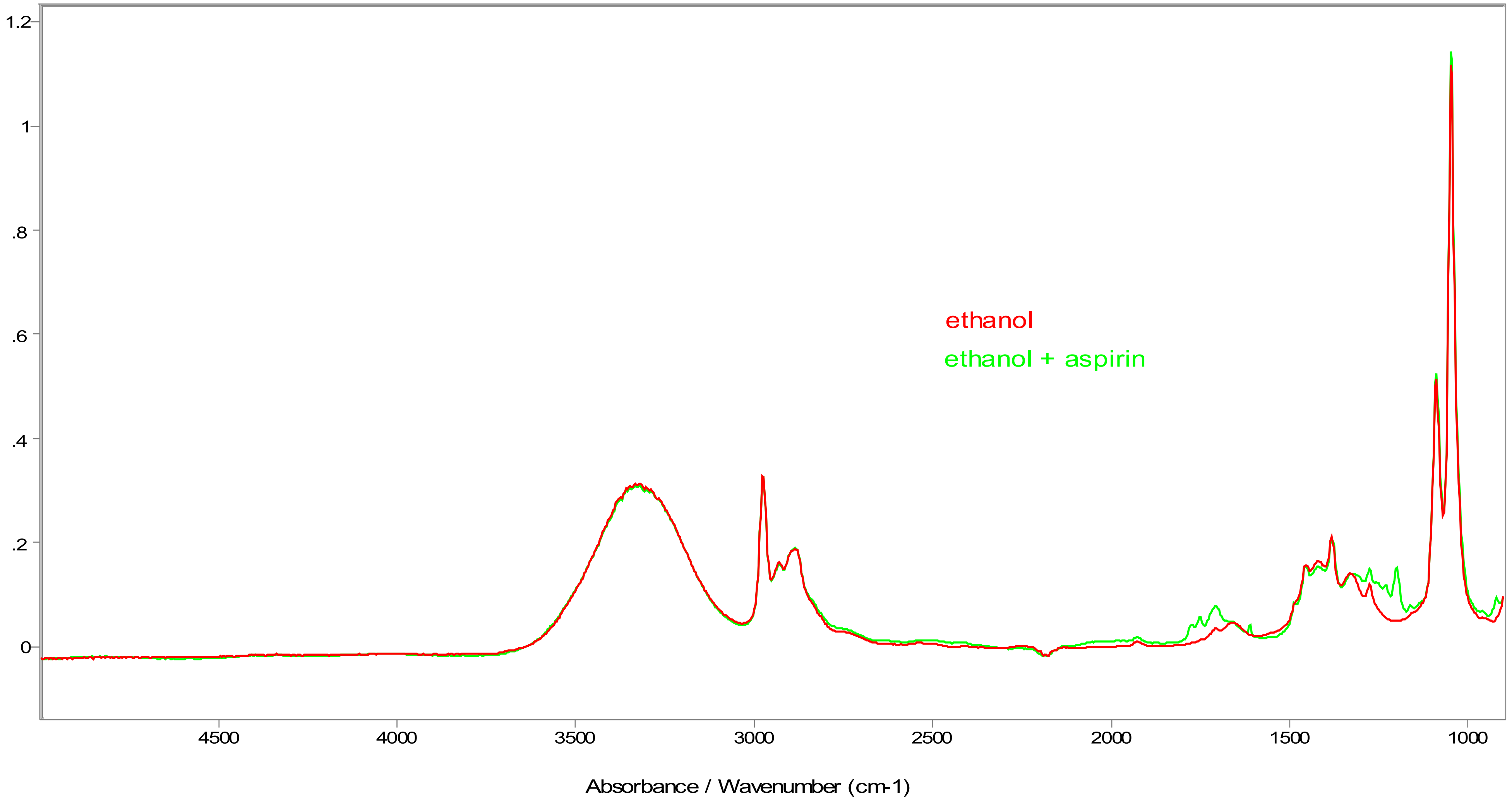
  - An automated reactor system such as the Automate with a direct link to an IR system such as ReactionView®

OR

  - An IR system such as ReactionView® with direct temperature logging capability and a chiller for temperature control of the sample

Aspirin in ethanol



Aspirin in ethanol

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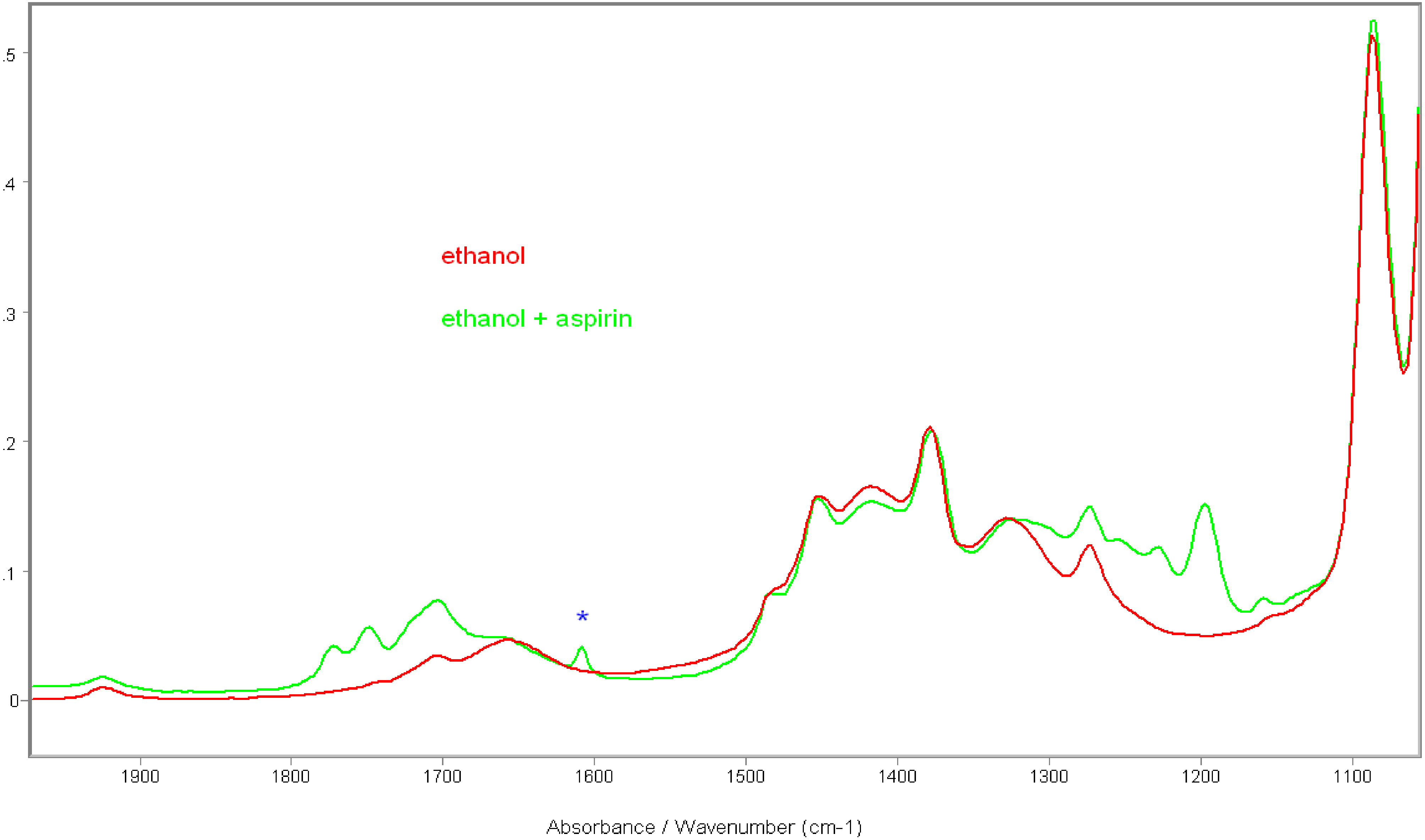
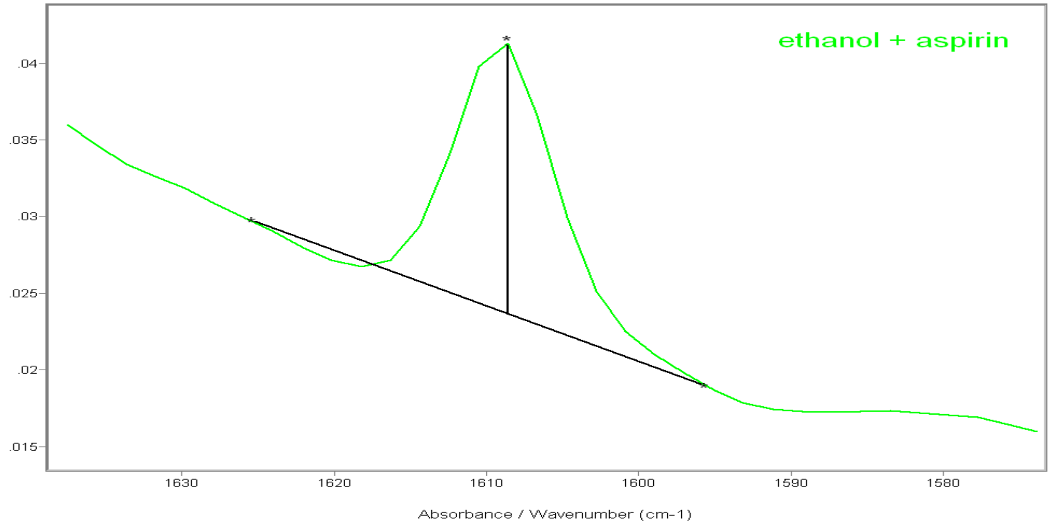
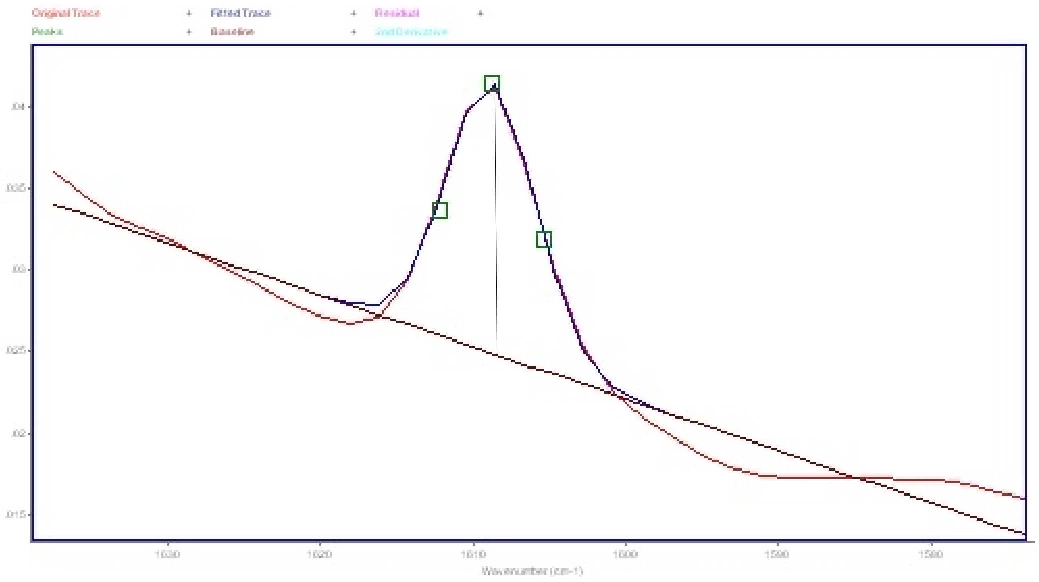


Aspirin in ethanol

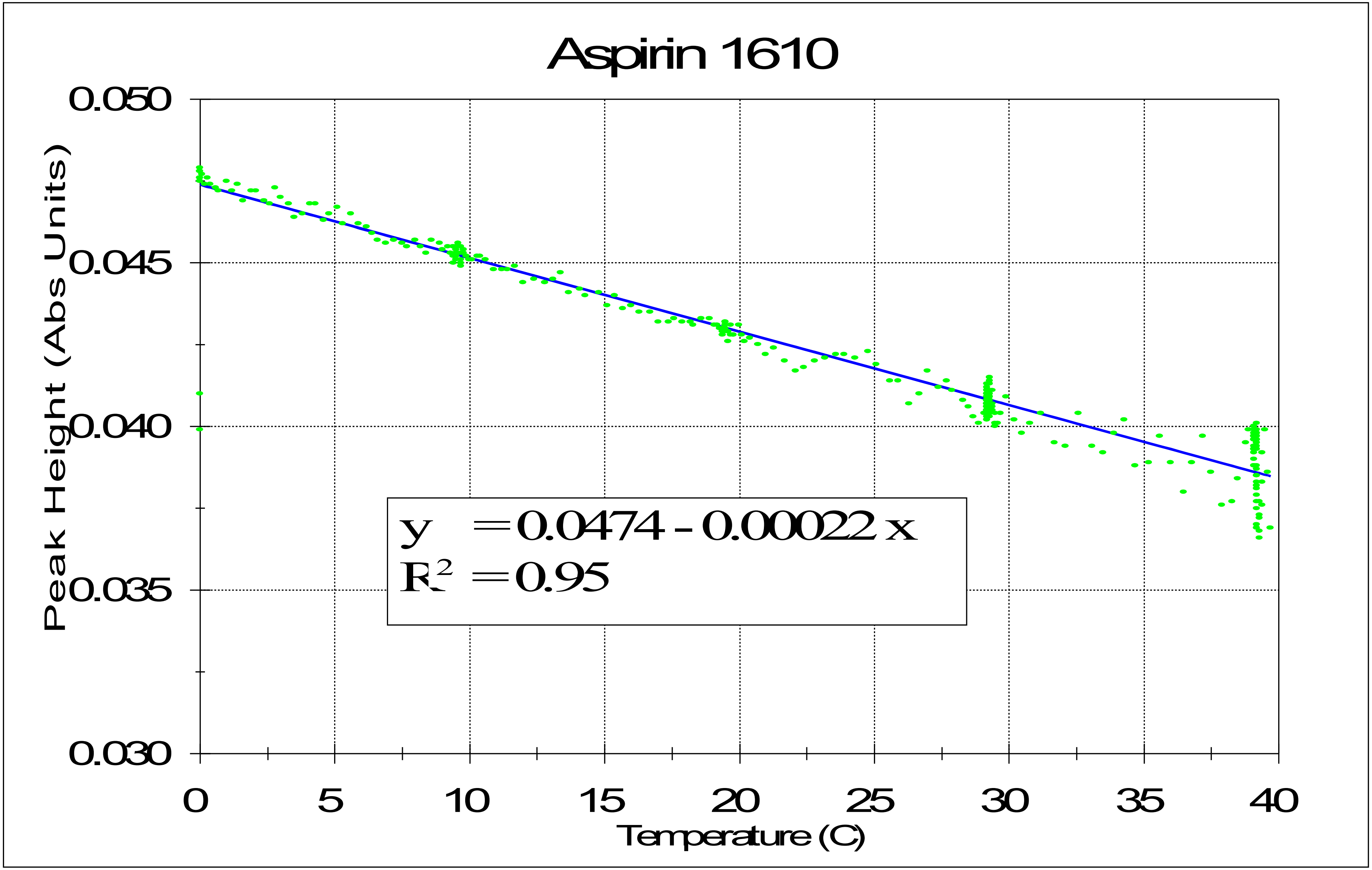
3 point trend line



Fitted peak with
linear baseline



Aspirin in ethanol



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Aspirin in ethanol

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- In this system using this peak in the examined temperature range a linear relationship has been found
- This is very encouraging because a linear temperature correction is very easy to apply to the data and it could easily be applied in real time
- With a properly configured IR and automatic reactor the data can be obtained quickly and easily

$$Ab_{corr} = Ab_{meas}(T) \times \left[\frac{Ab_{CALTref}}{Ab_{CALTexp}(T)} \right]$$

Acetaminophen in ethanol

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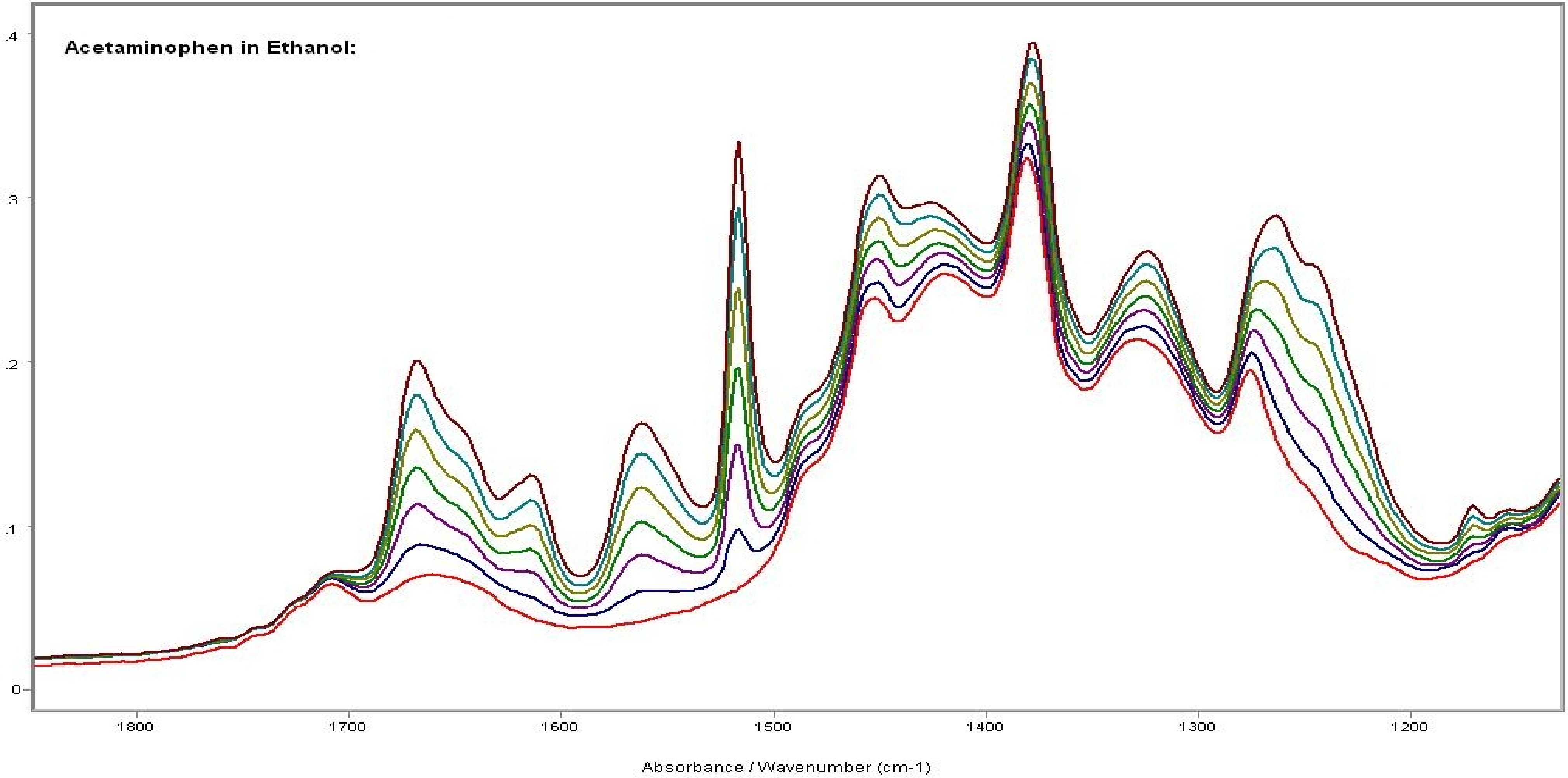
Concentration calibration data



Acetaminophen in ethanol

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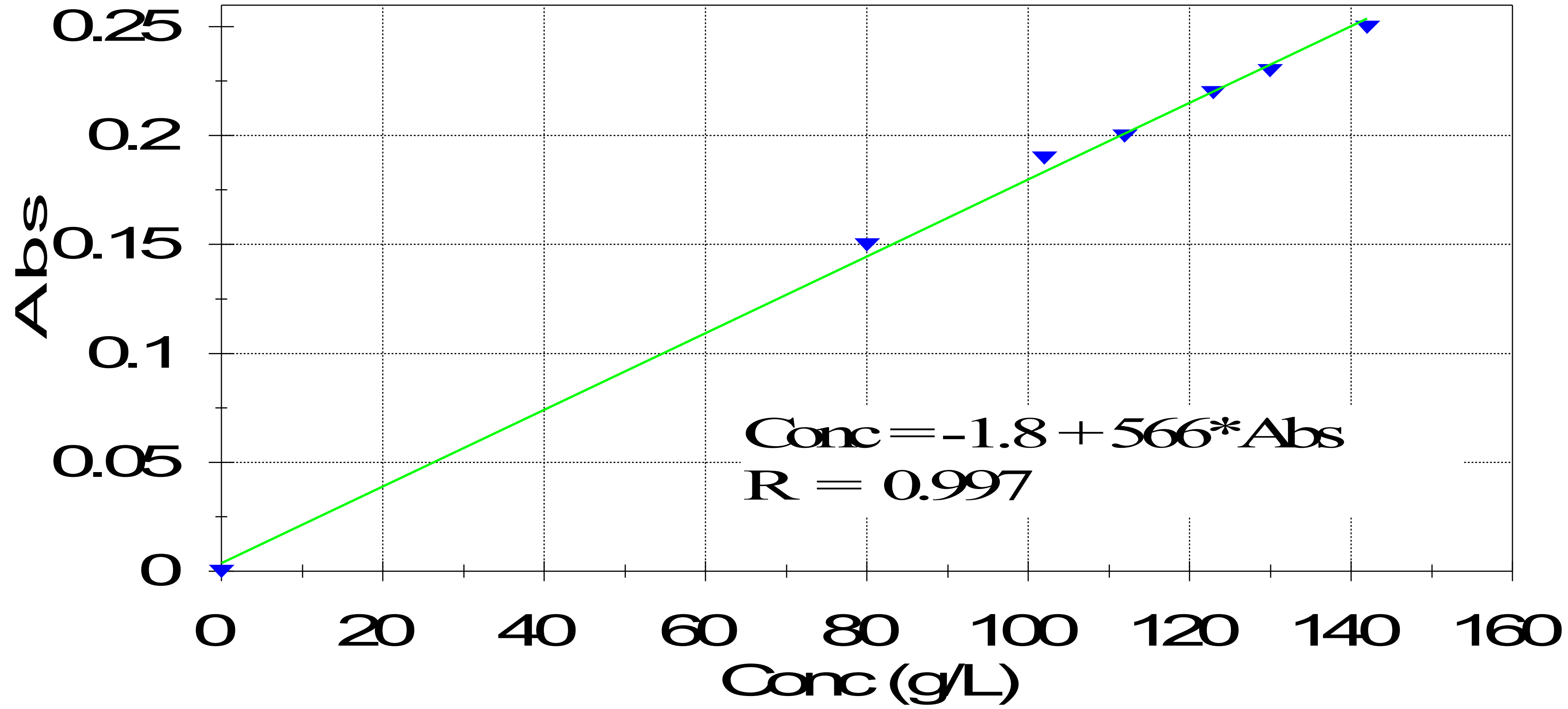
concentration calibration
at constant temperature



Acetaminophen in ethanol

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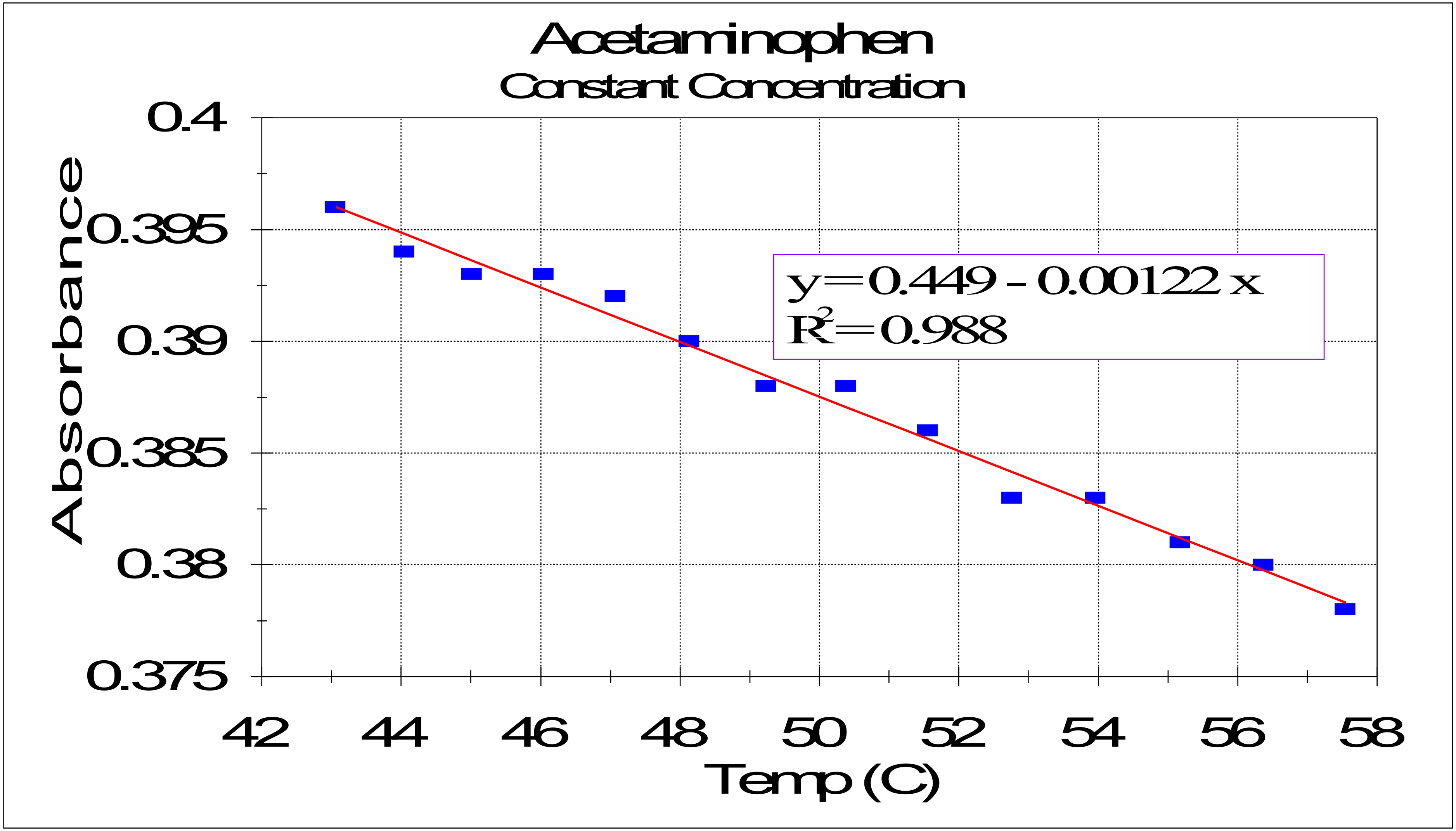
Temperature correction calibration



Acetaminophen in ethanol

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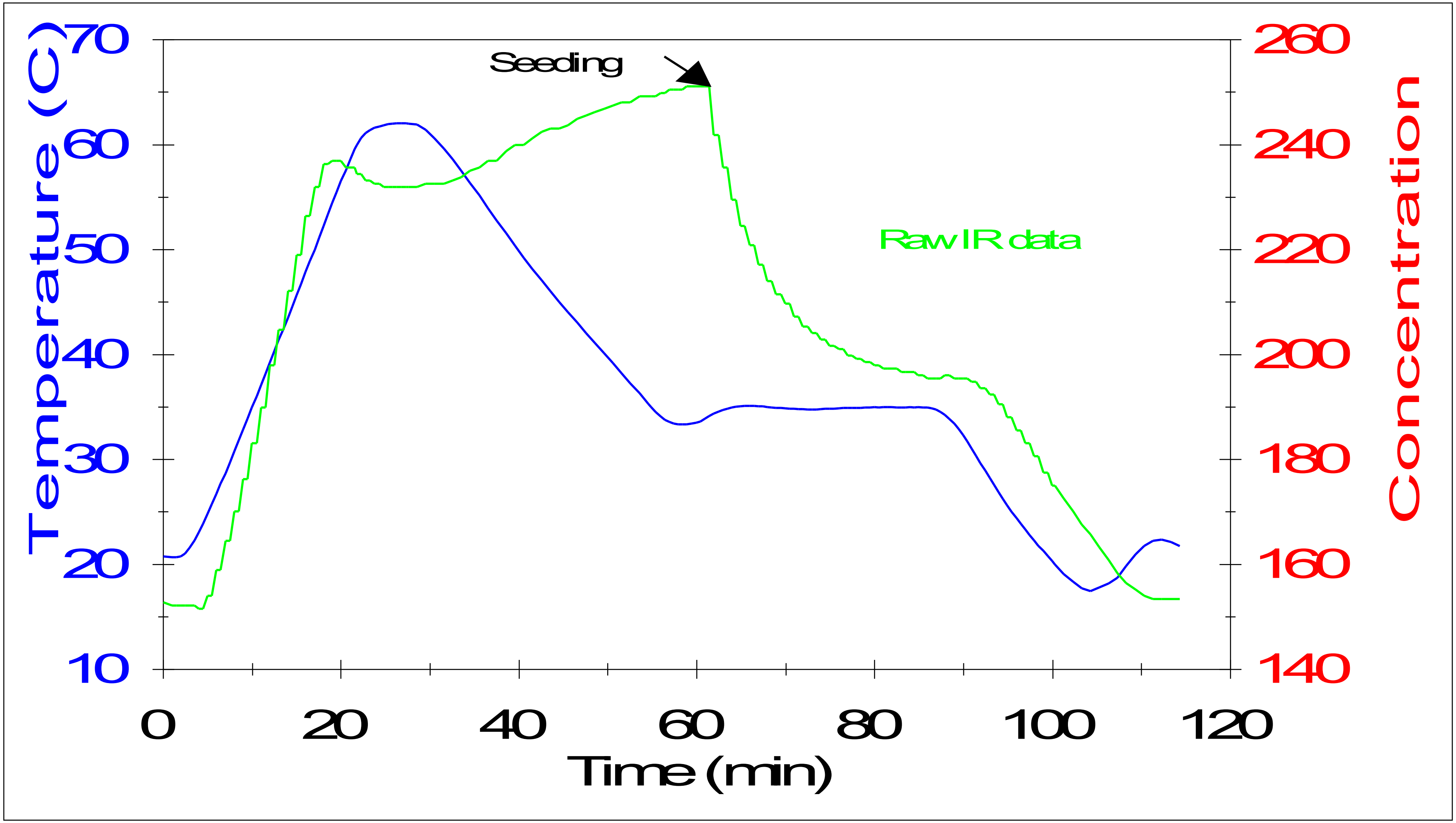
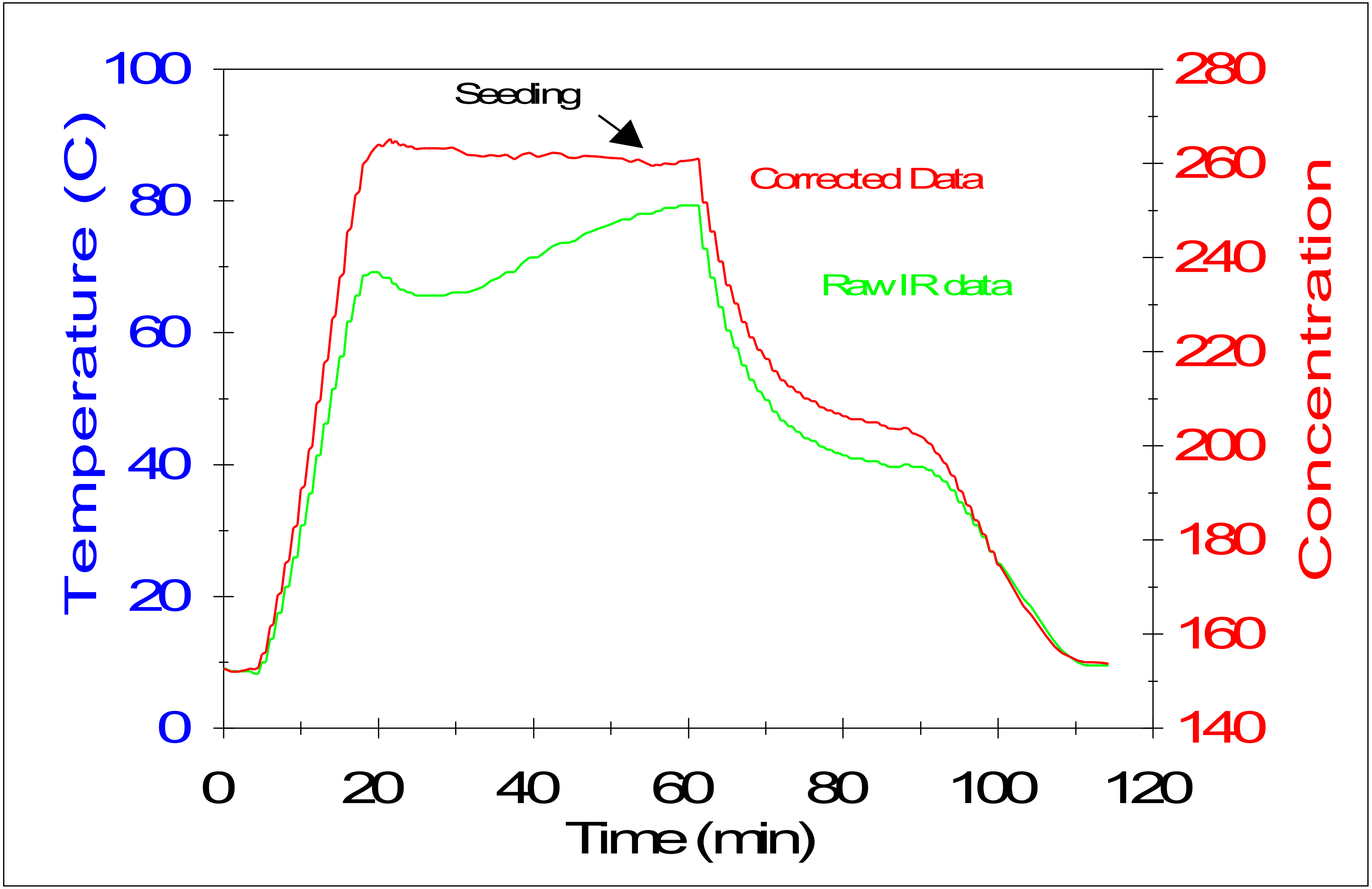
Raw Data



Acetaminophen in ethanol

Effect of temperature correction



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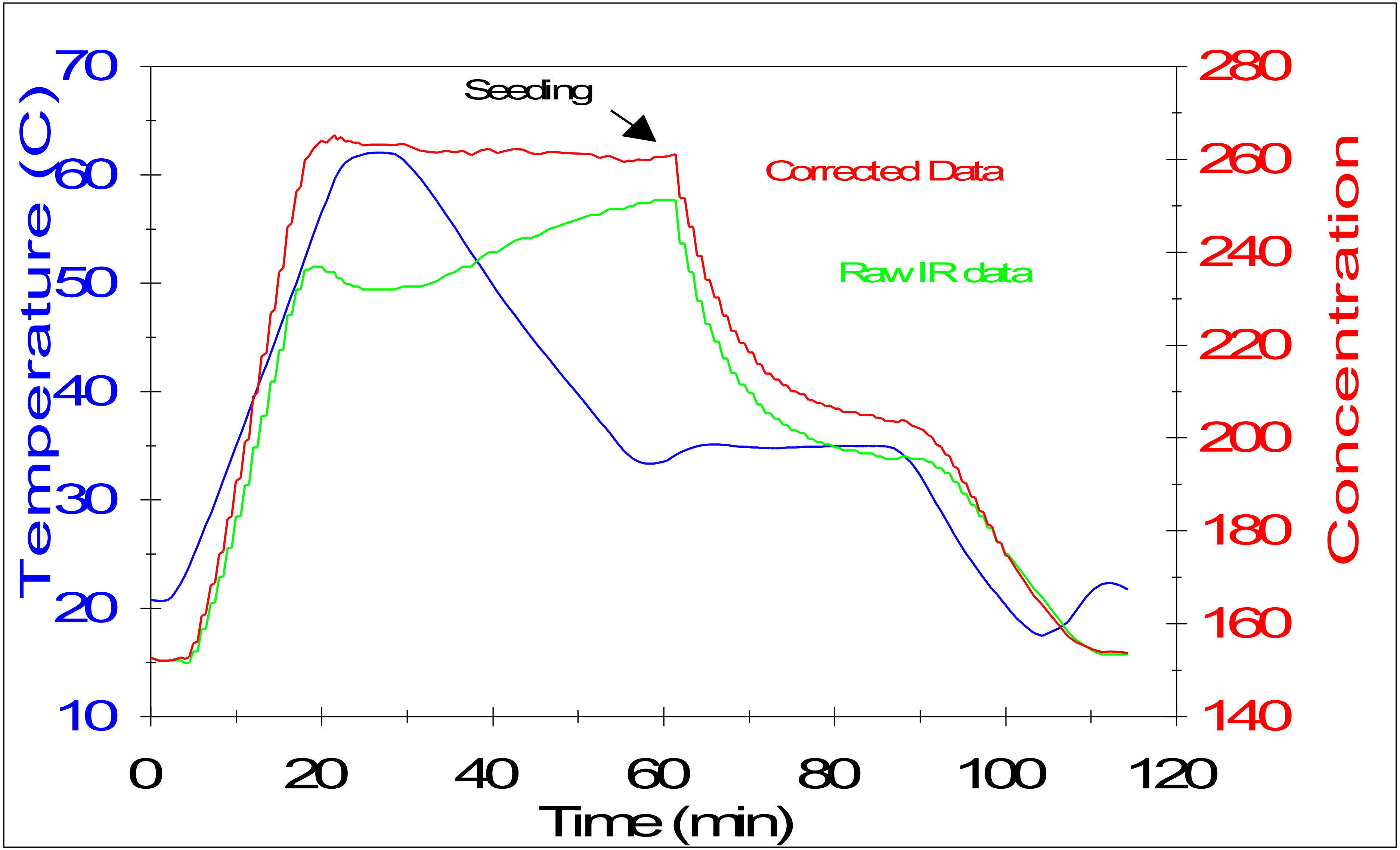
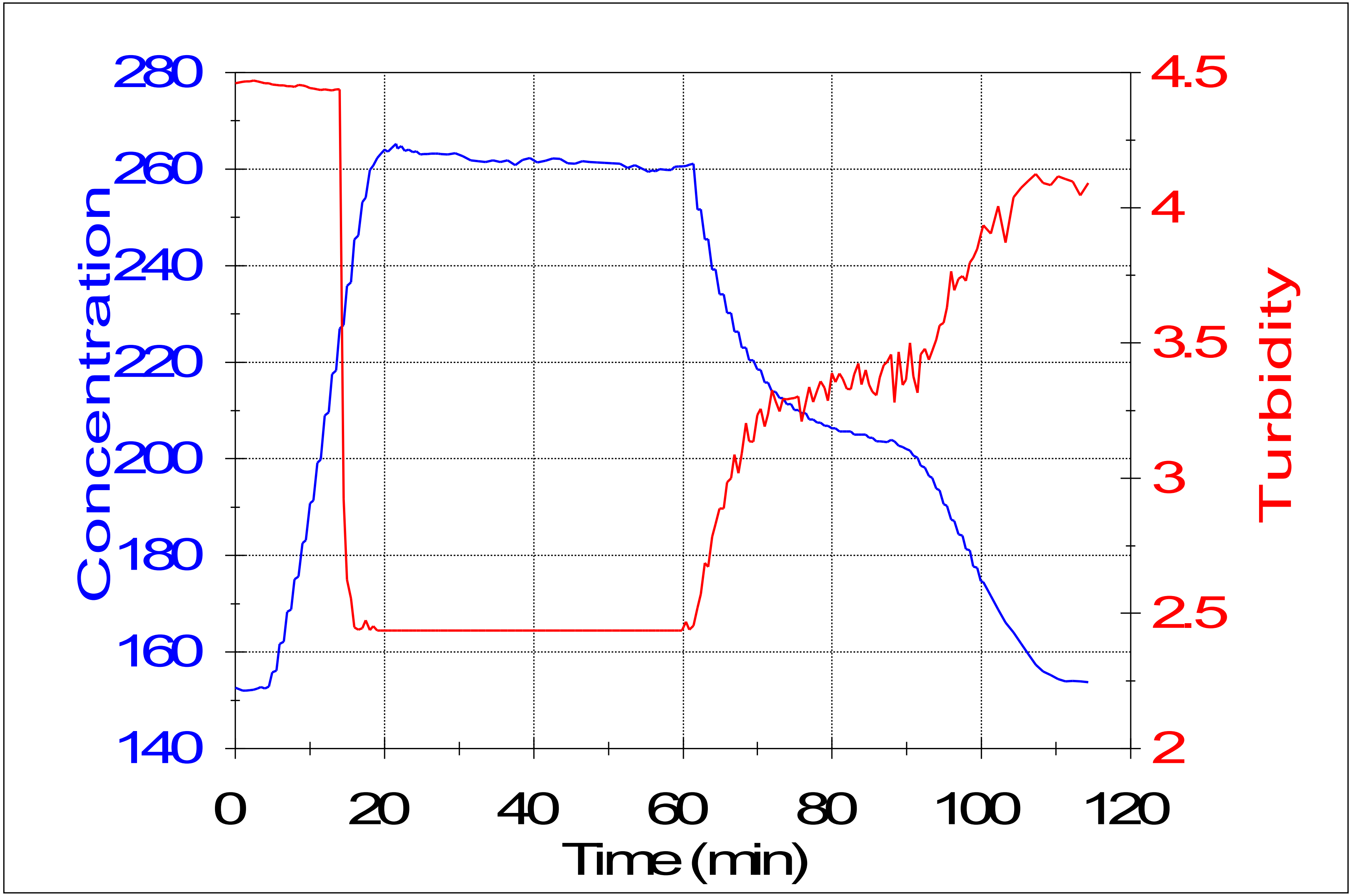
Acetaminophen in ethanol

Effect of temperature correction



Acetaminophen in ethanol

Comparison of corrected IR data with turbidity measurements



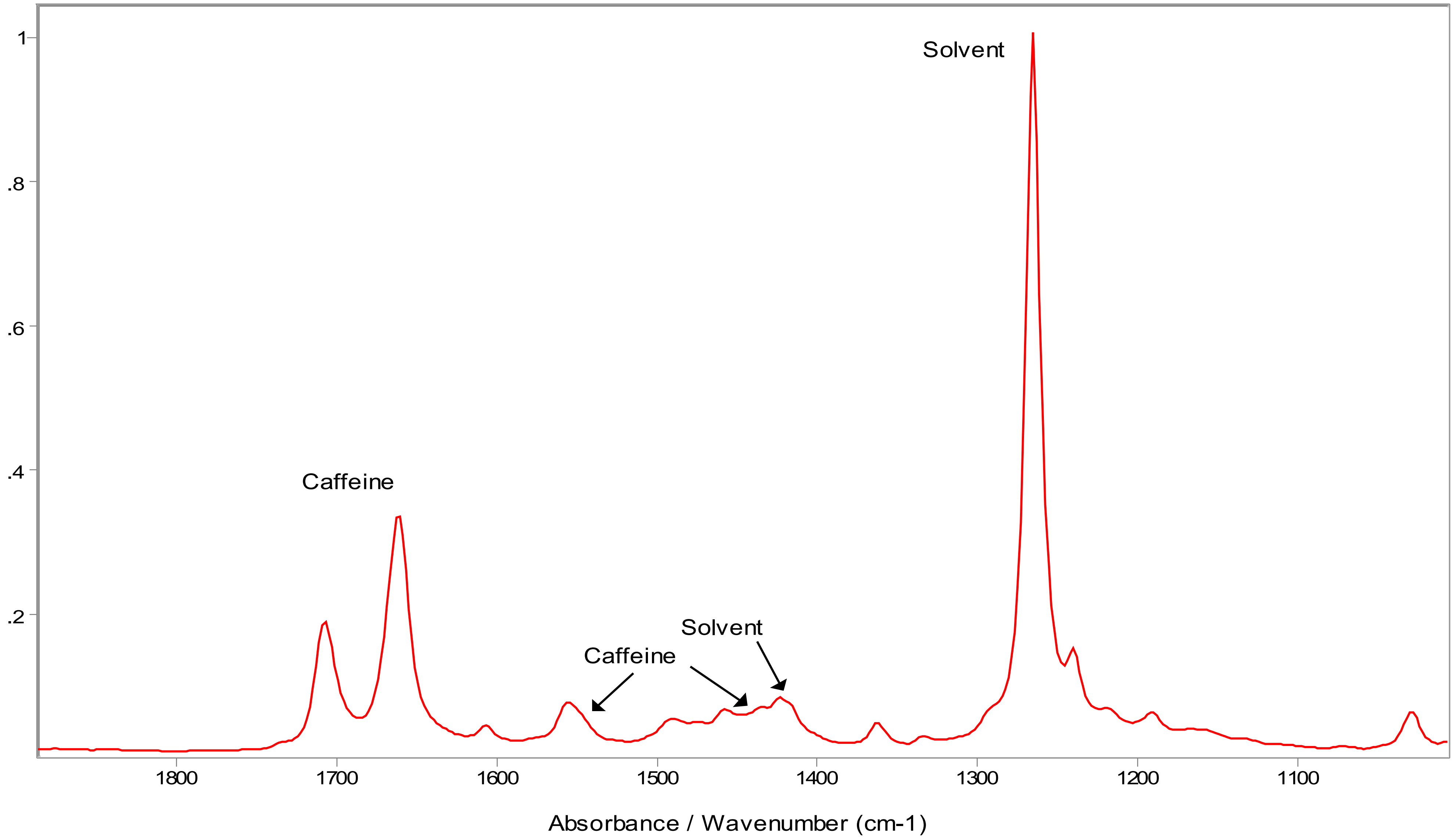
Temperature Correction

- Two examples do not make a general law however

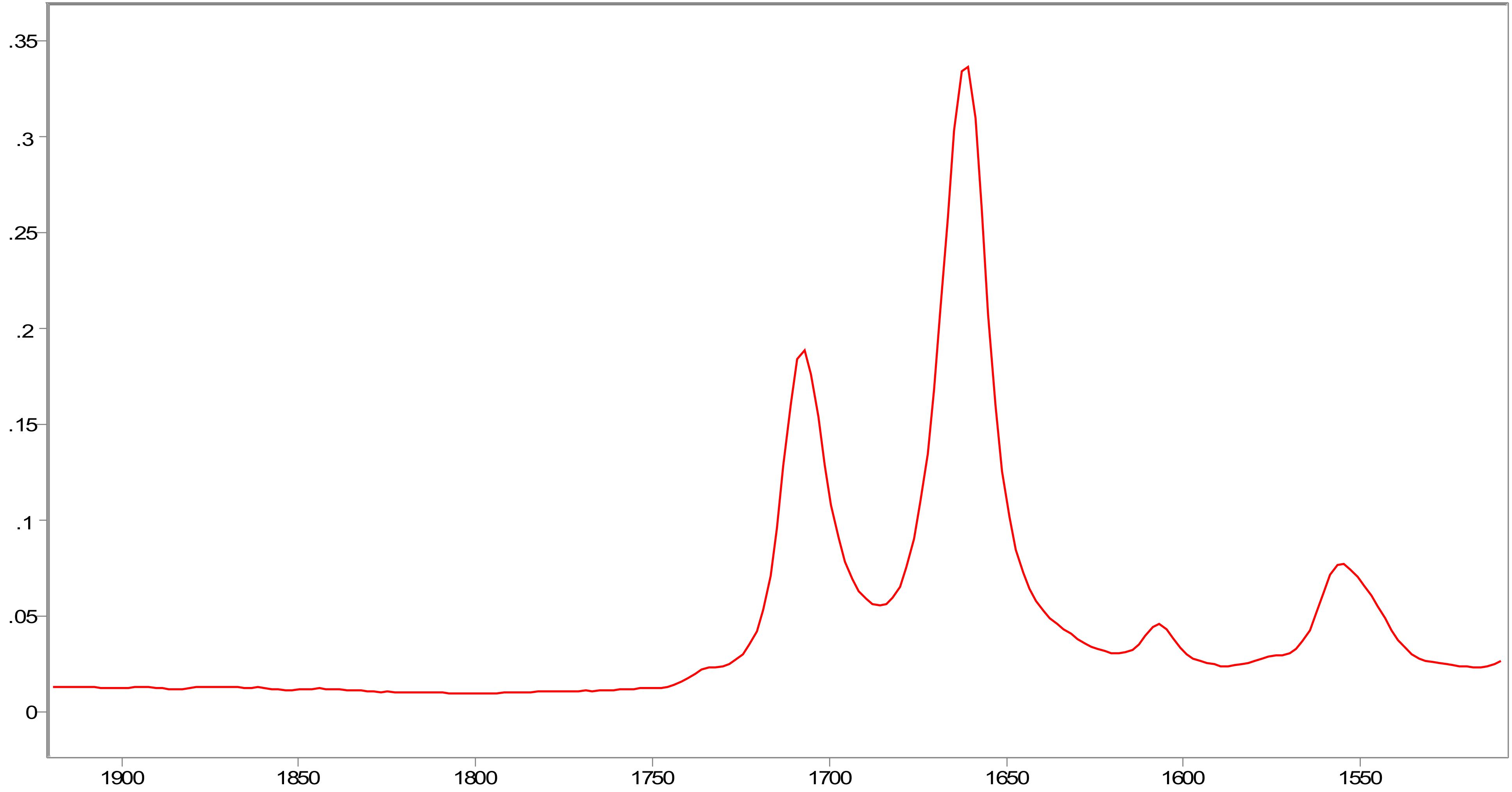
$$Ab_{corr} = Ab_{meas}(T) \times \left[\frac{Ab_{CALTref}}{Ab_{CALTexp}(T)} \right]$$

- As long as $Ab_{CALTexp}(T)$ is linear in T life is very simple and temperature correction is easy but we need to check by looking at other compounds in other solvent systems
- For this reason we have looked at caffeine and at the temperature dependence of ethanol over a wider temperature range

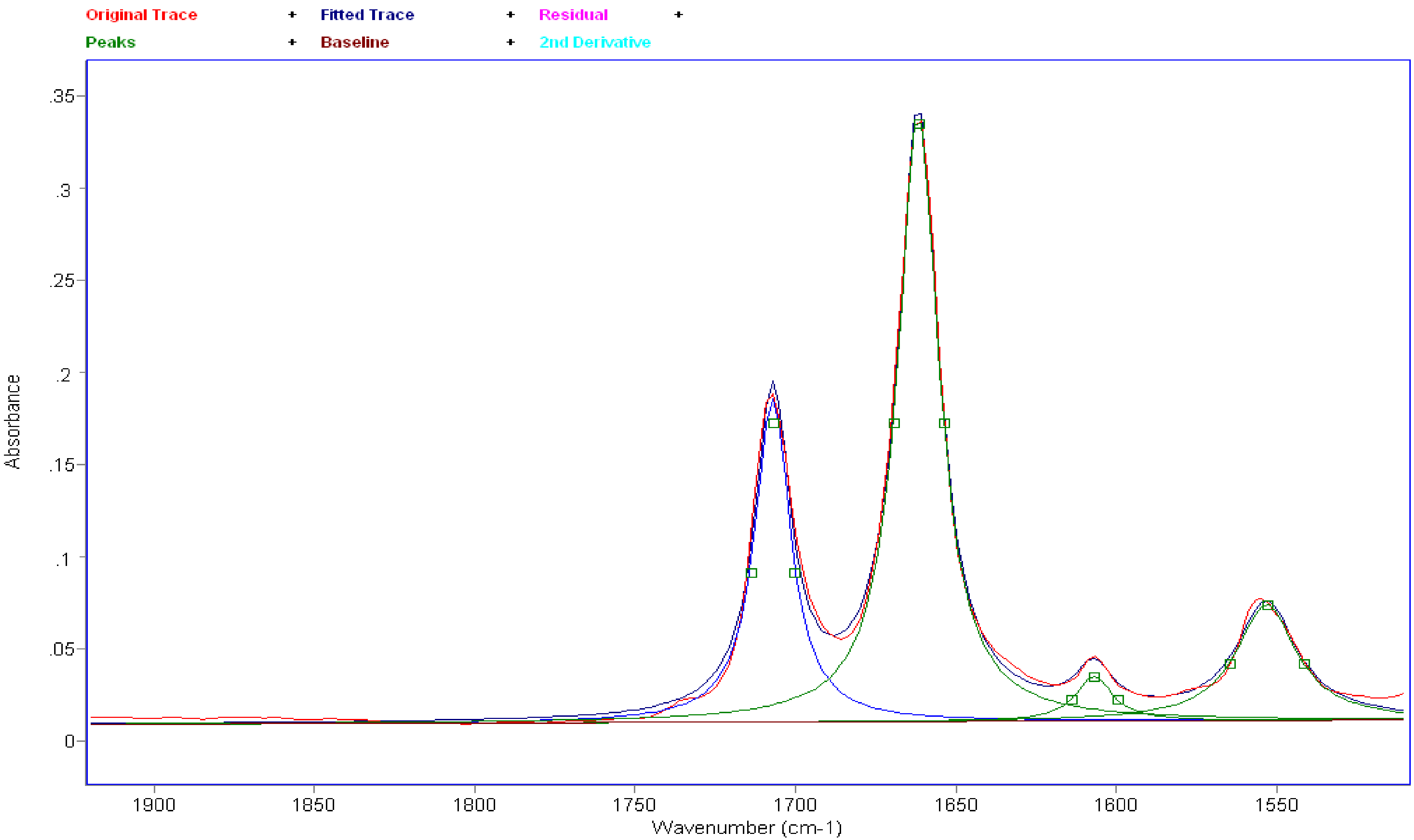
Caffeine in dichloromethane



Caffeine in dichloromethane



Caffeine in dichloromethane



Caffeine in dichloromethane

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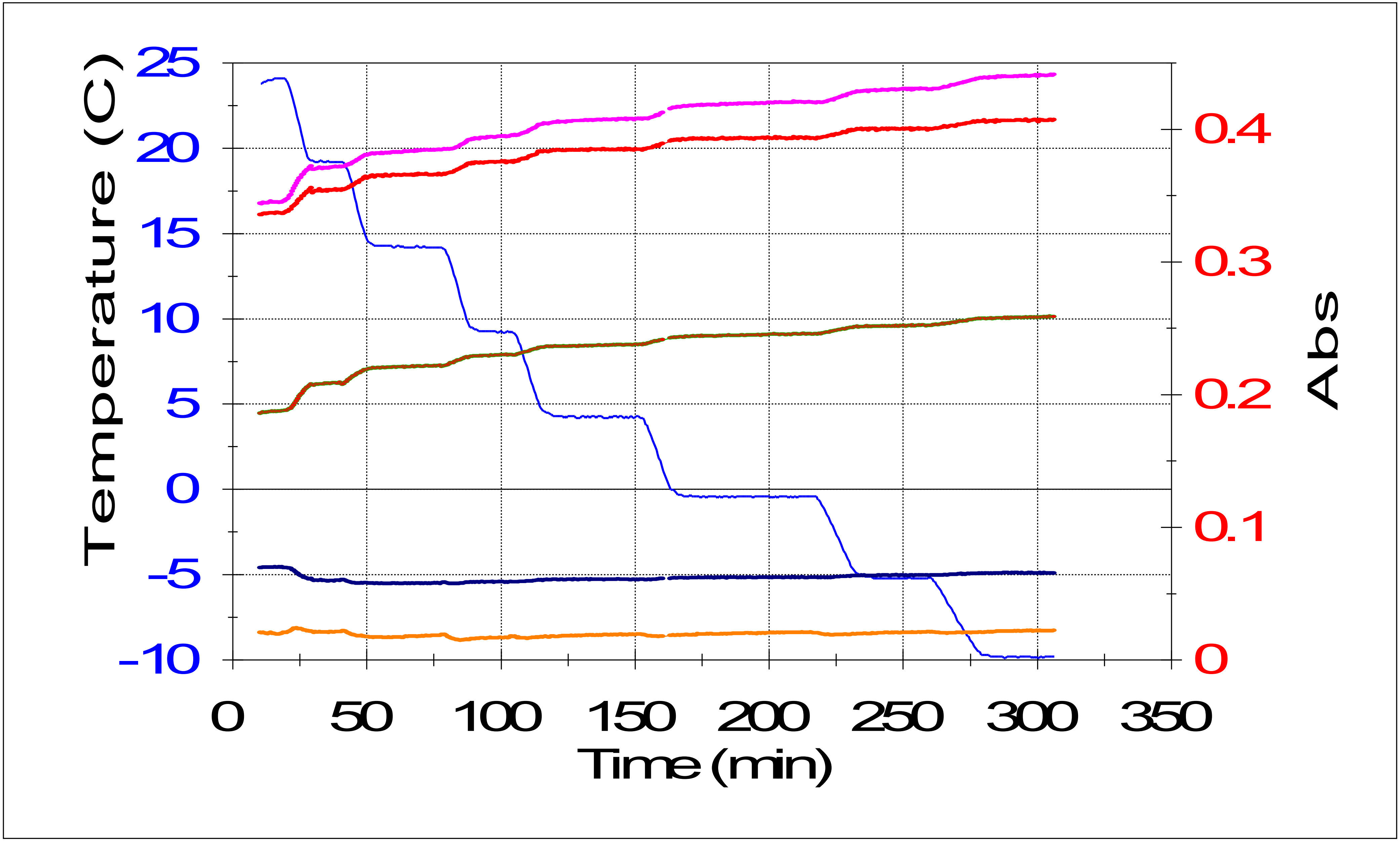

Caffeine in dichloromethane

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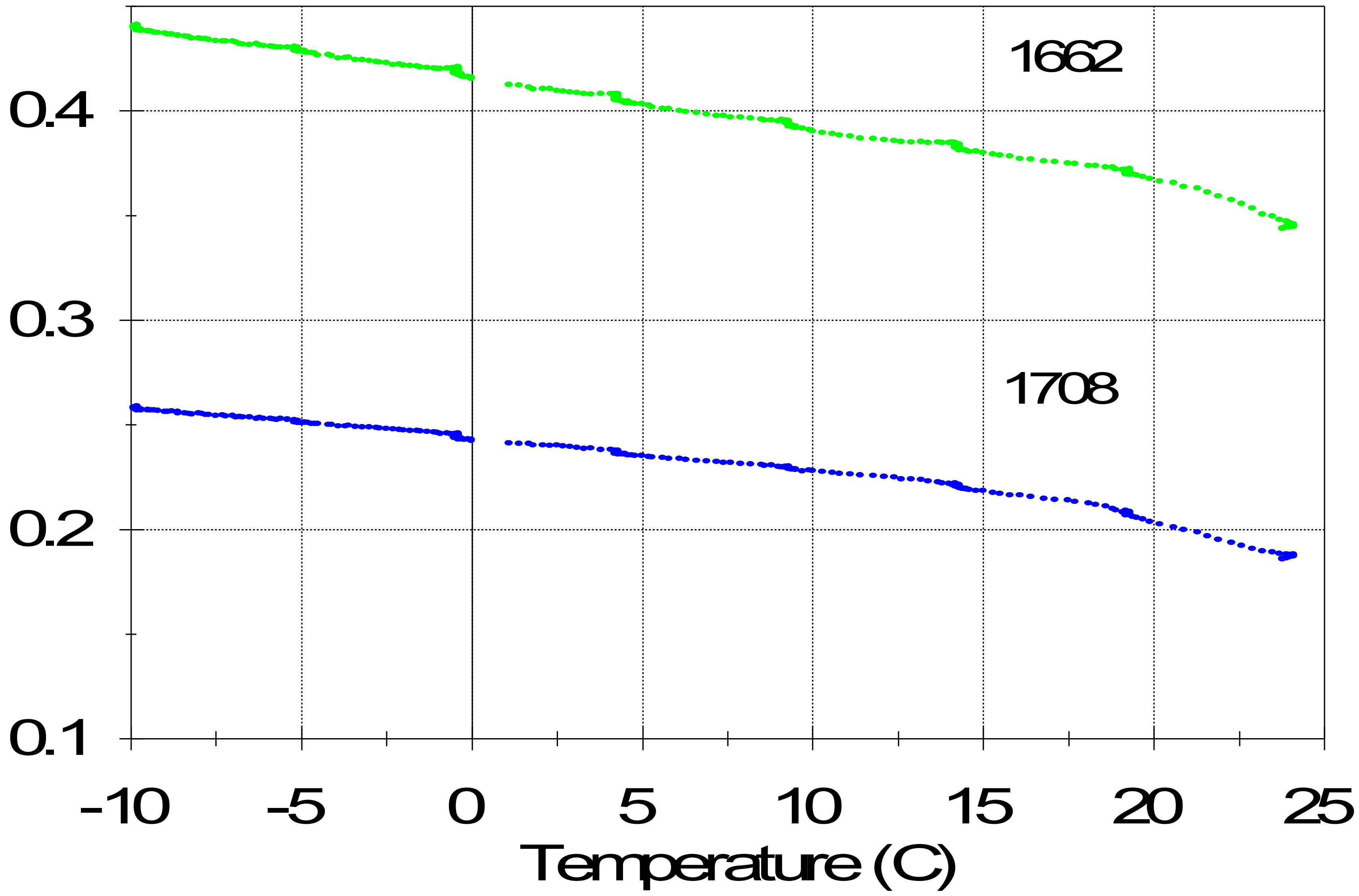
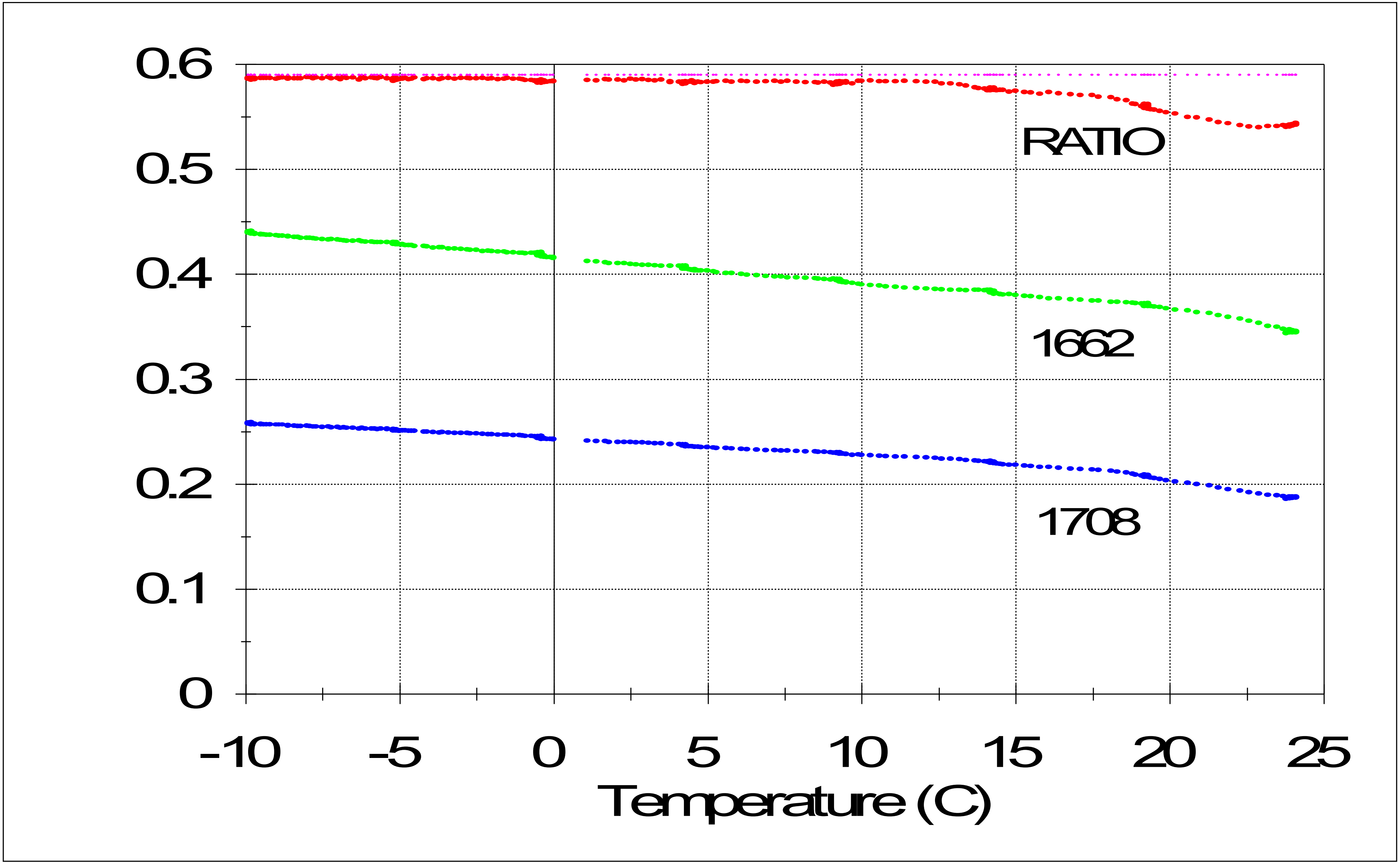
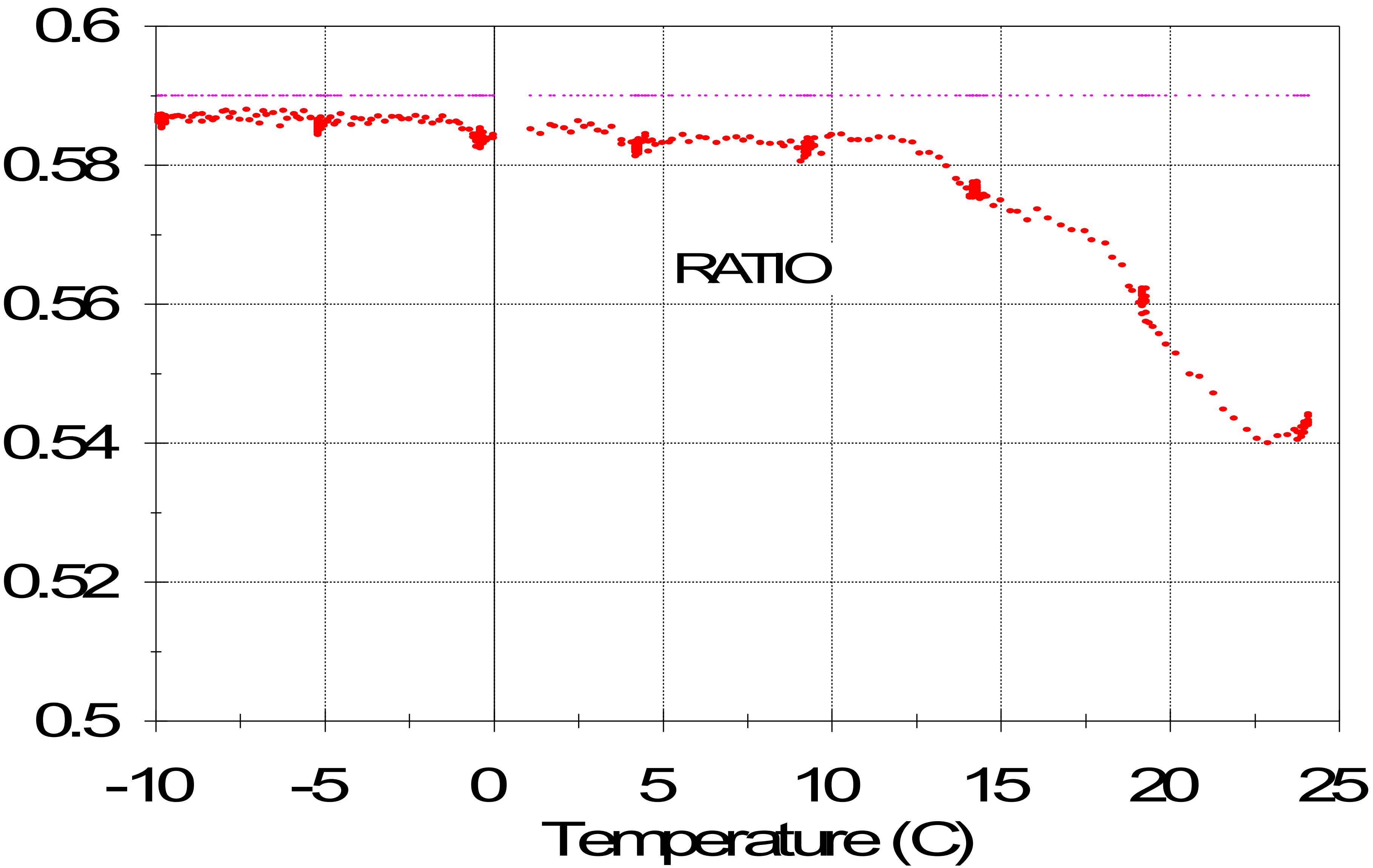


Caffeine in dichloromethane



Caffeine in dichloromethane



Caffeine in dichloromethane

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- The peaks at 1662 and 1708 are both non-linear with temperature
- The peaks at 1662 and 1708 both have decreasing absorbance with increasing temperature
- Both peaks have limited temperature ranges where a linear approximation will work well
- From the ratio plot we can see the temperature dependence of these two peaks is different and the difference is very non-linear

Caffeine in dichloromethane

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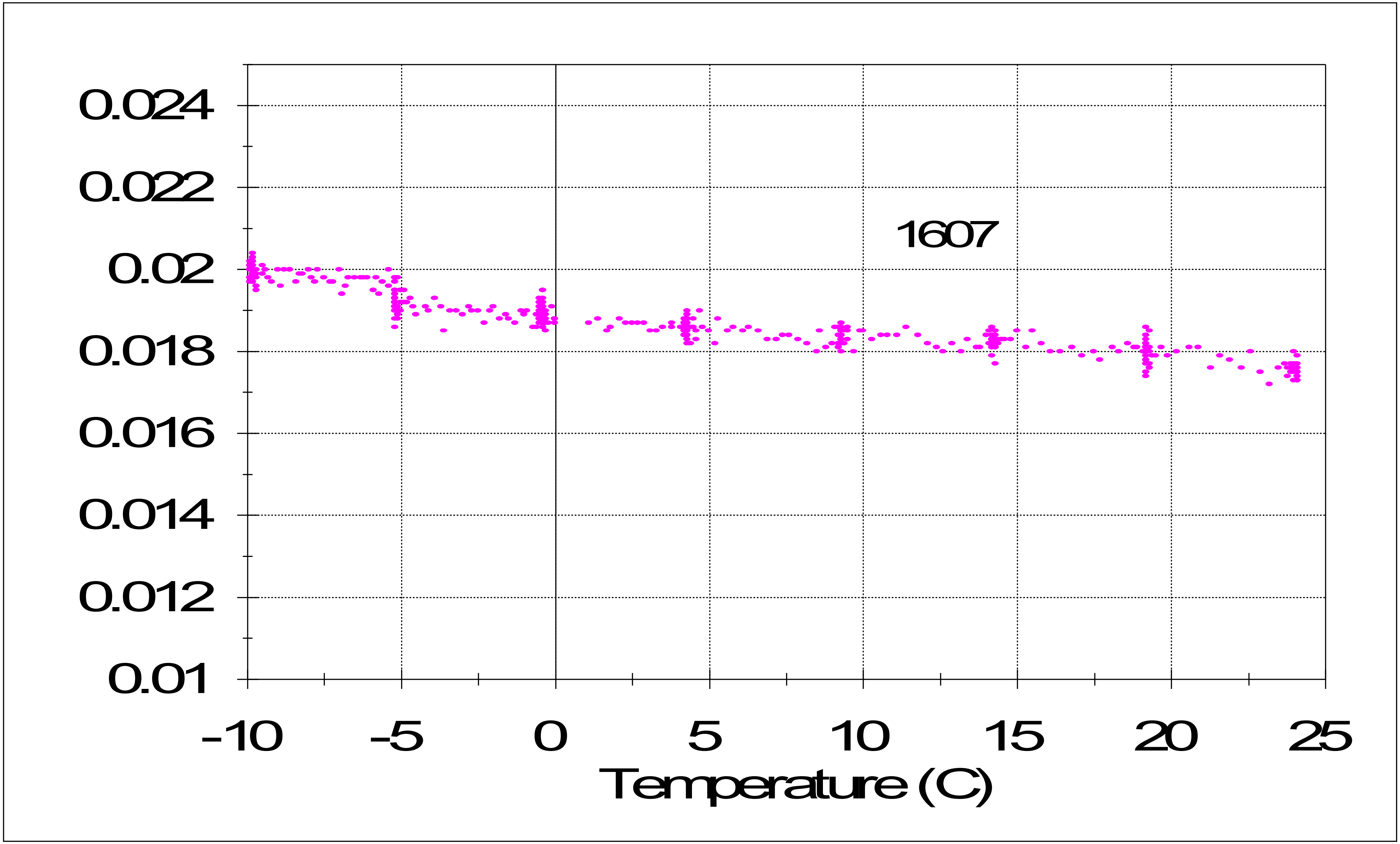
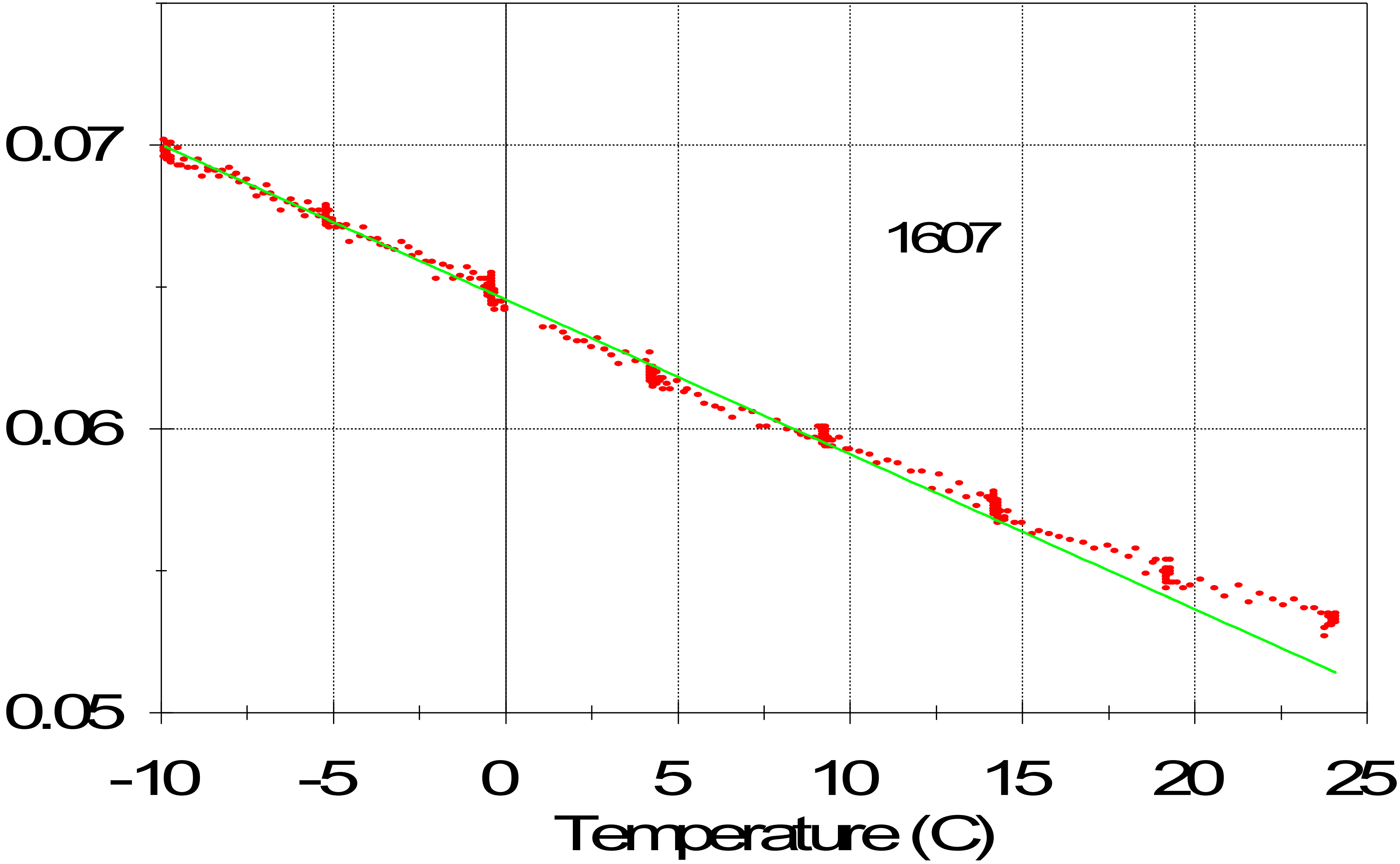


Caffeine in dichloromethane



Caffeine in dichloromethane

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- The peaks at 1662 and 1708 both have decreasing absorbance with increasing temperature
- Both peaks have temperature ranges where a linear approximation will work well
- The peak at 1607 is nonlinear in temperature and the curvature is opposite to the curvature observed in the peaks at 1662 and 1708

Solvents

- We have further investigated these effects by looking at some more typical solvents
  - Ethyl acetate
  - NMP

Ethyl acetate

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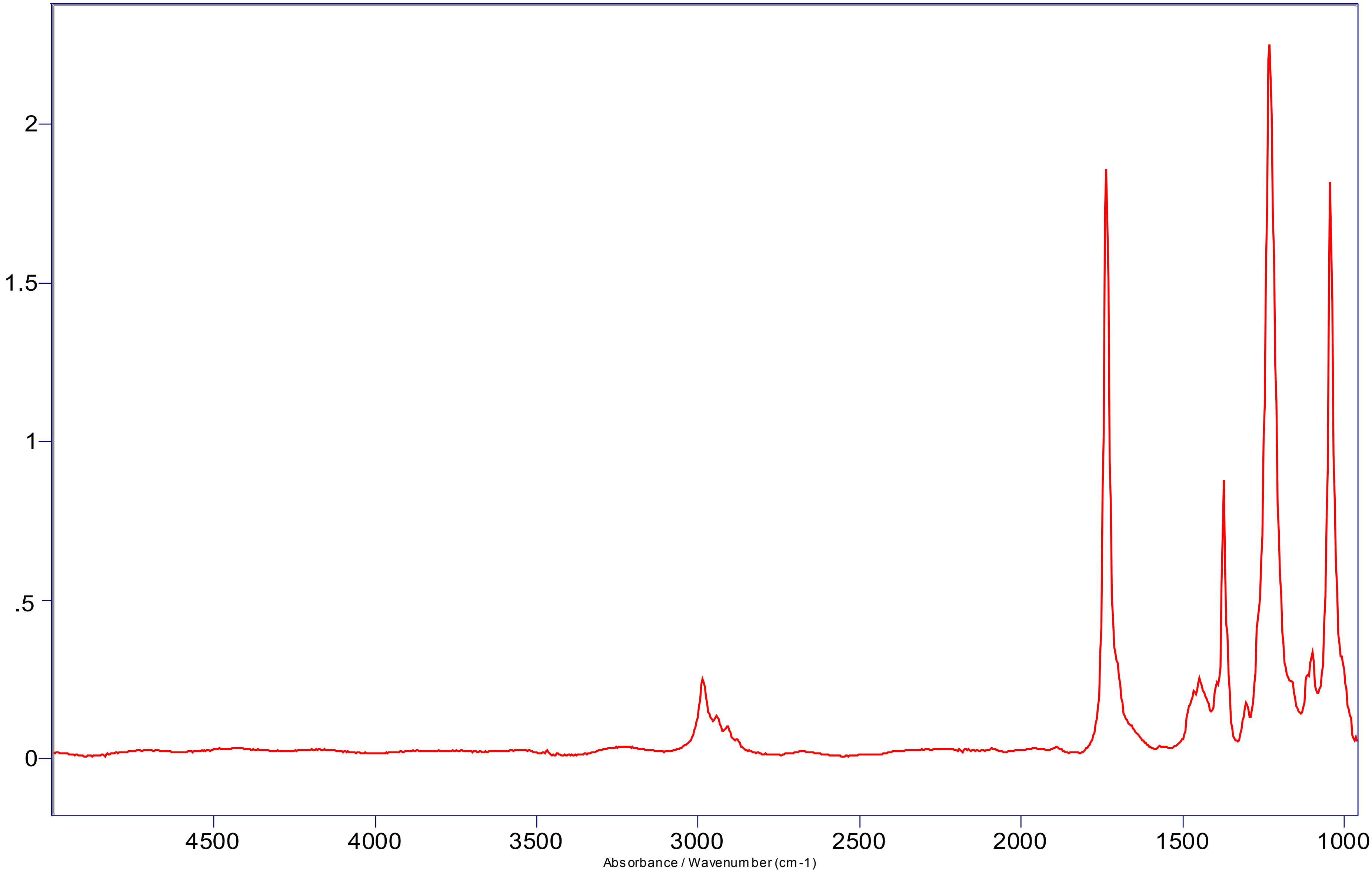

Ethyl Acetate

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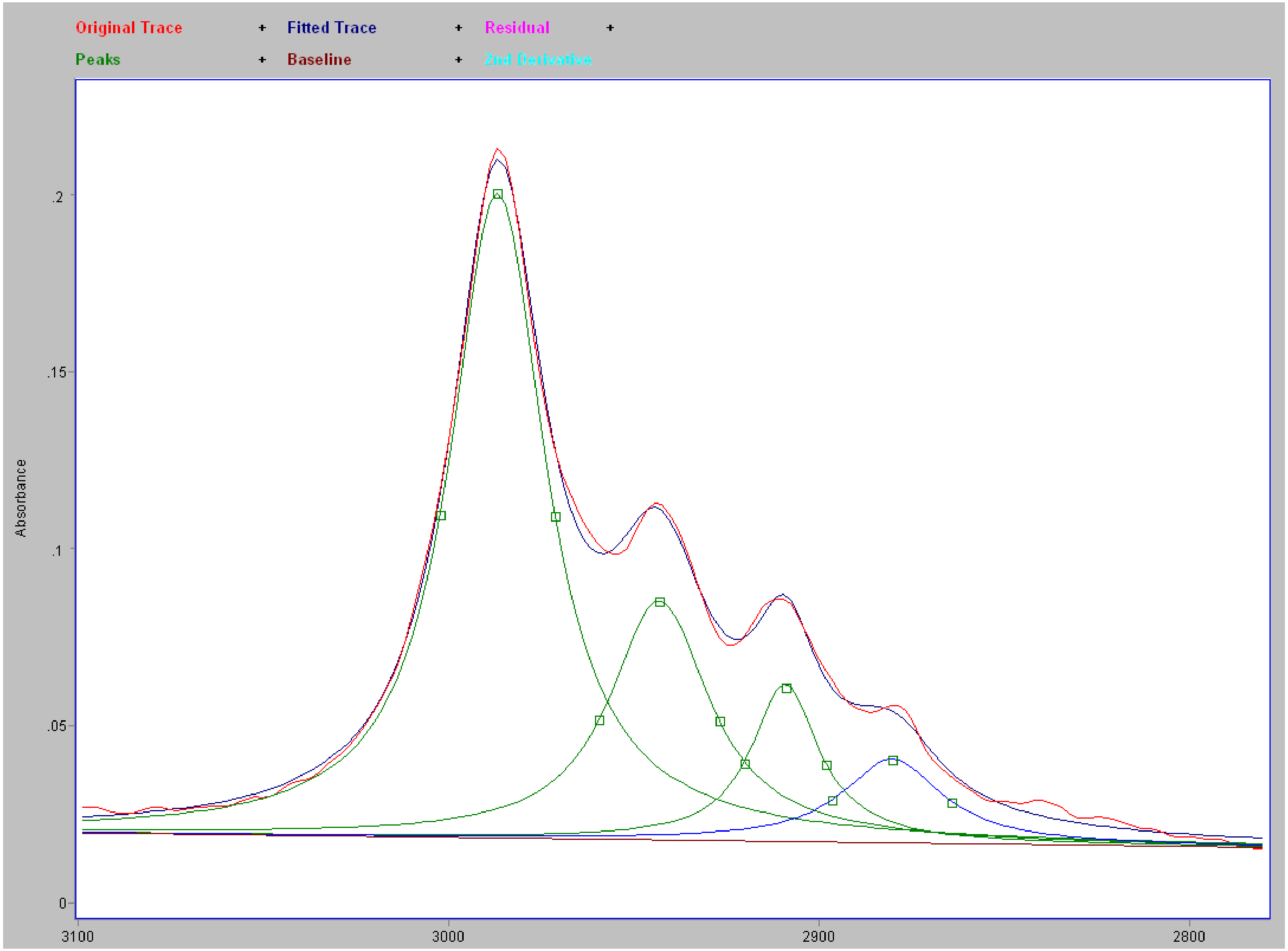

Ethyl Acetate

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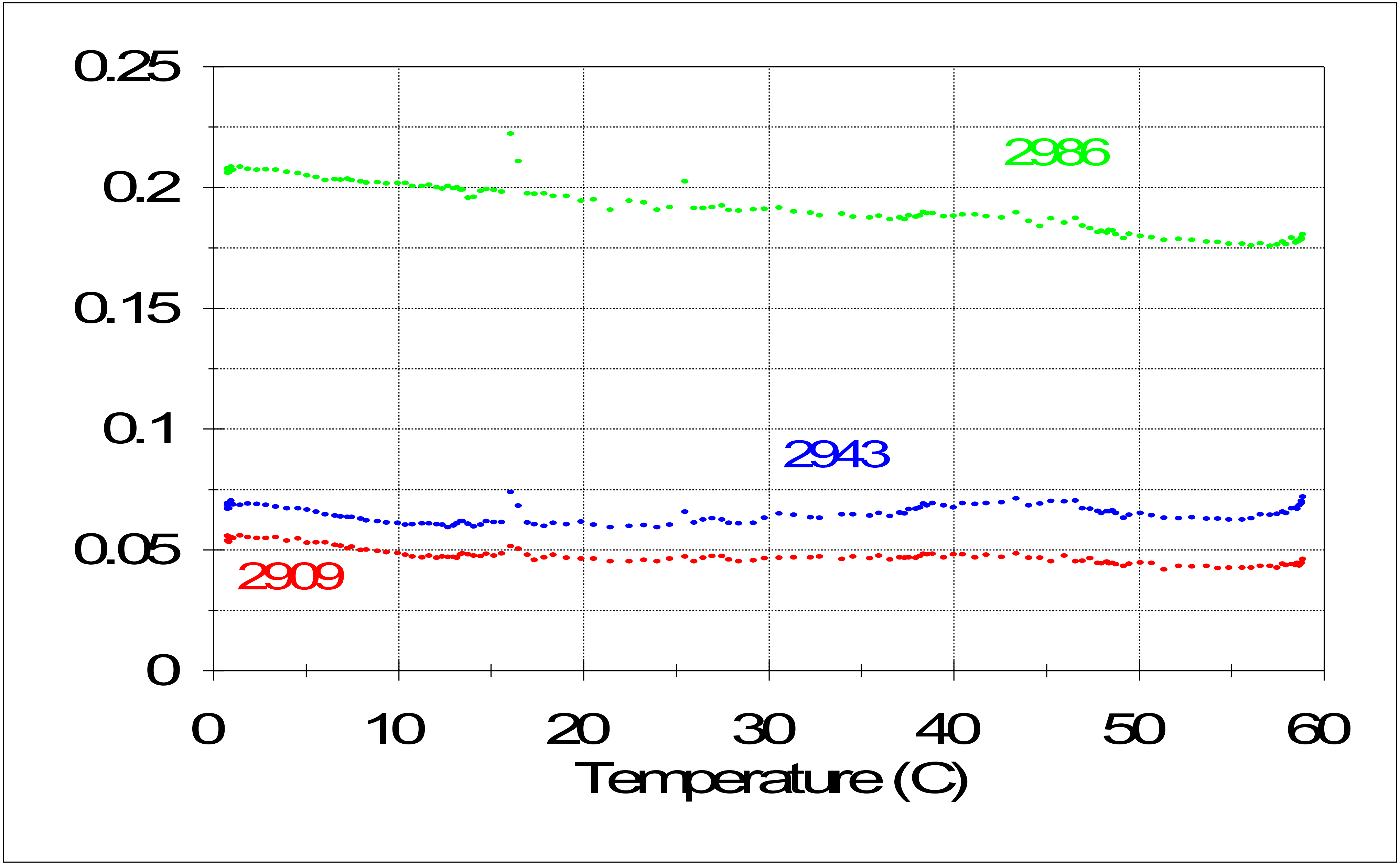
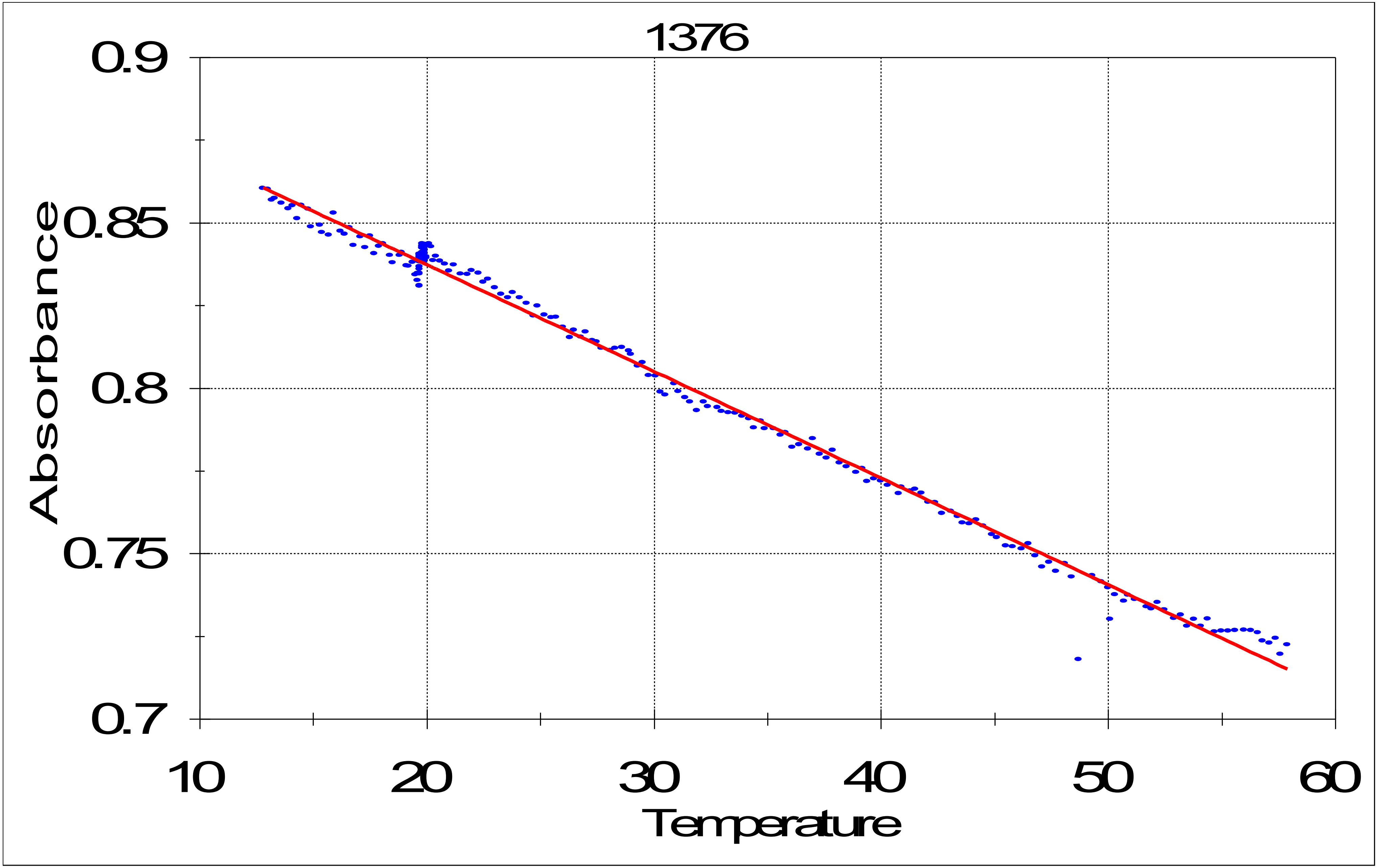
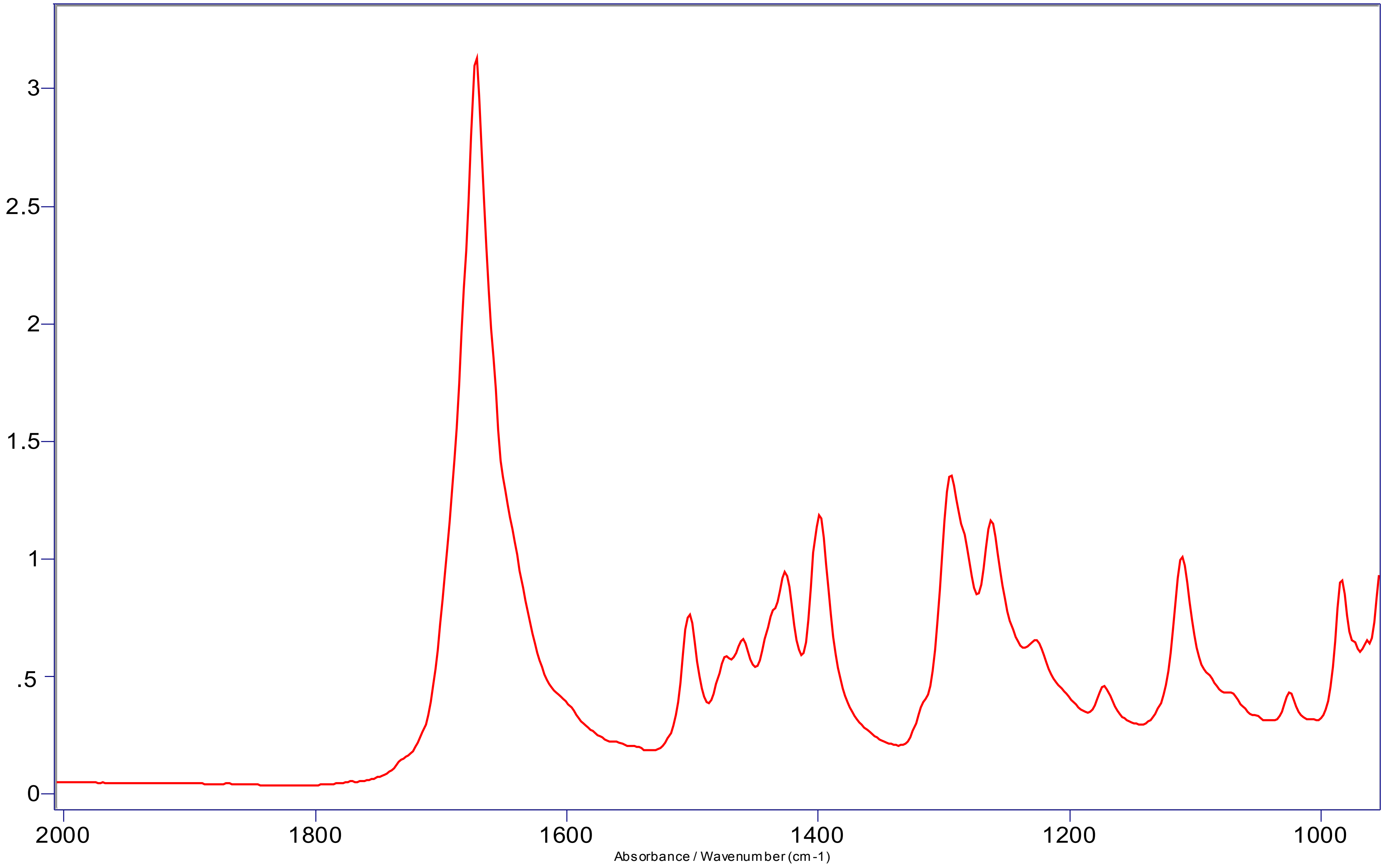


Ethyl Acetate

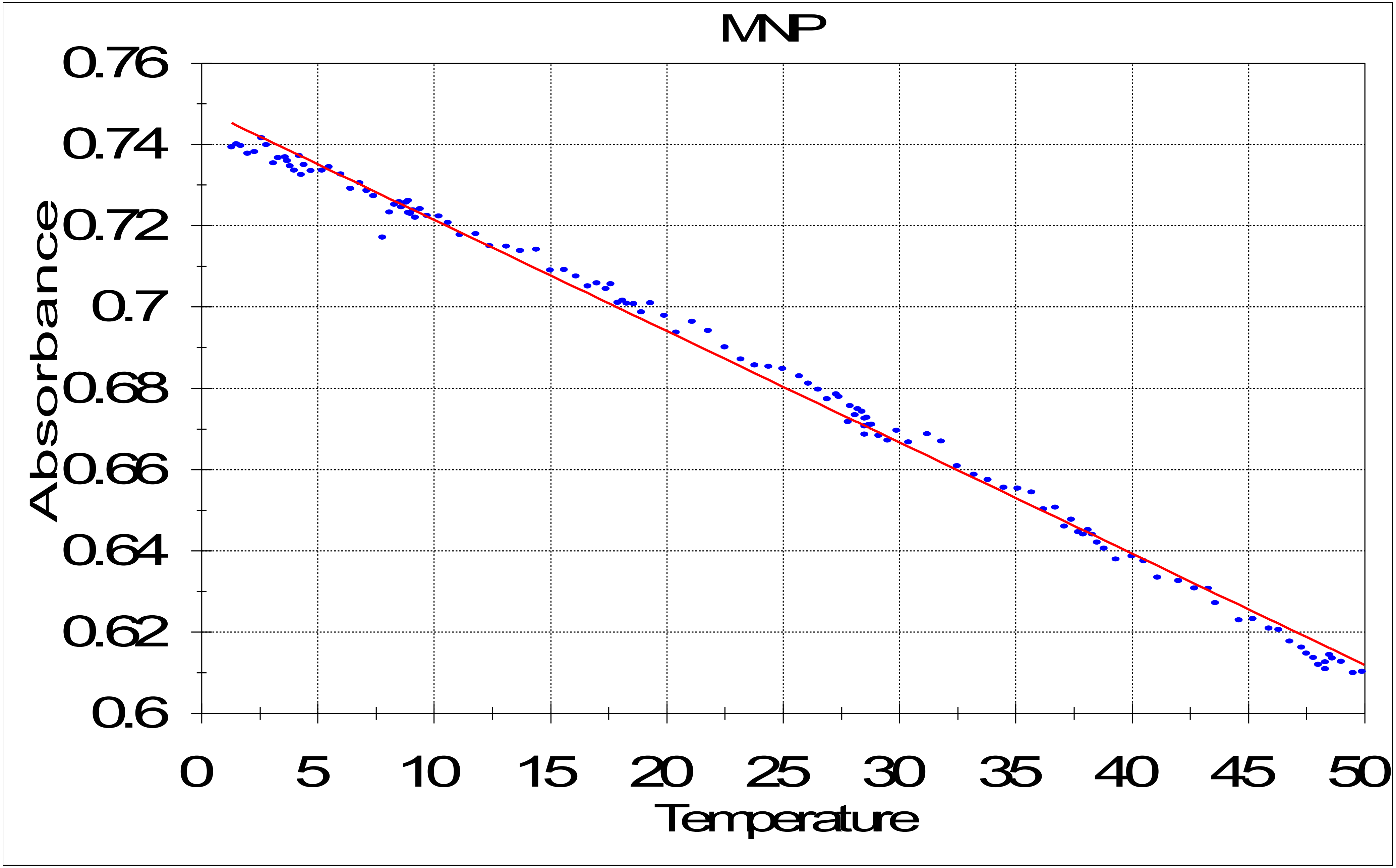


NMP


3
2.5
2
1.5
1
.5
0
2000
1800
1600
1400
1200
1000
Absorbance / Wavenumber (cm-1)

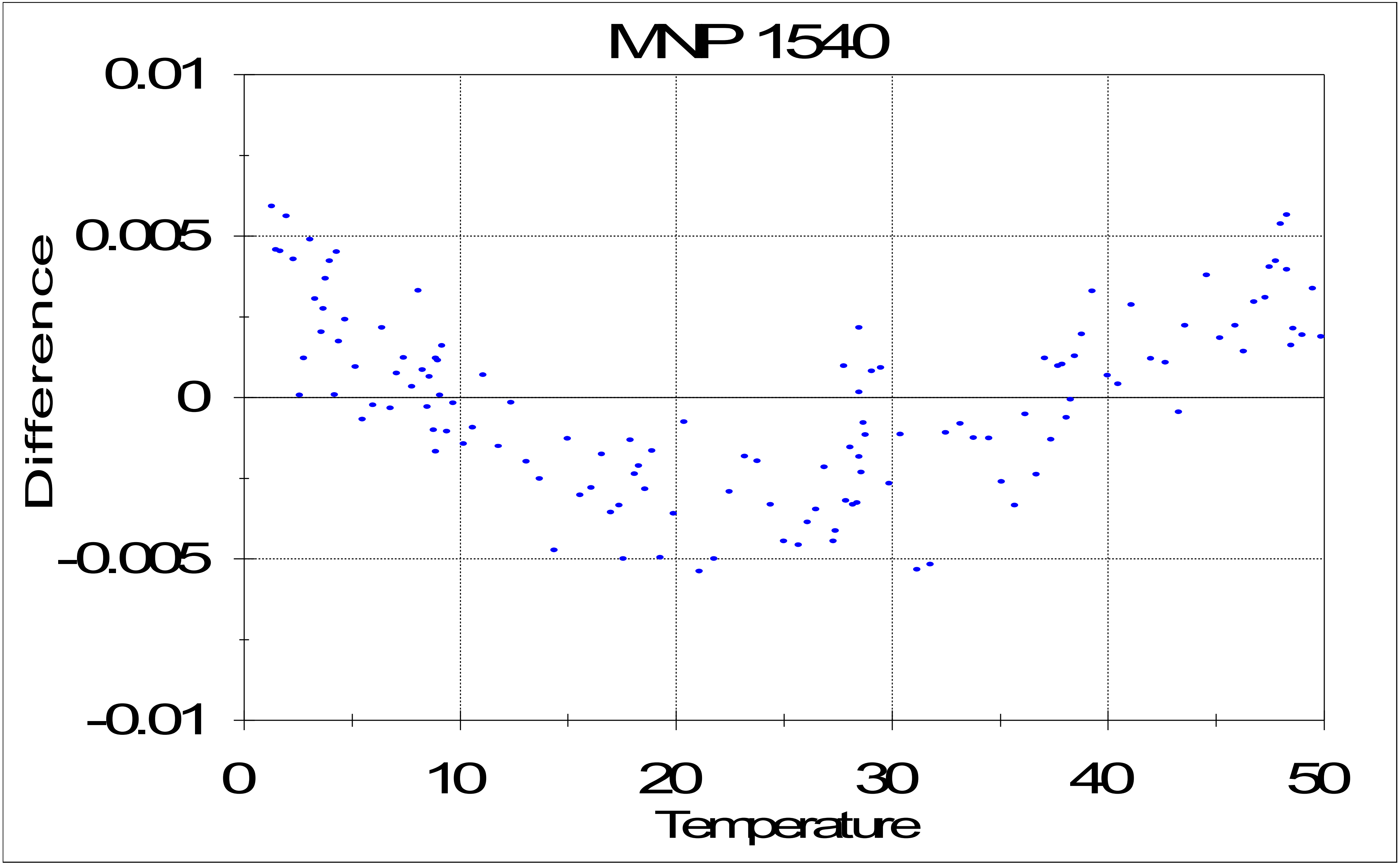
NMP

REMSPEC


MNP
Absorbance
0.76
0.74
0.72
0.7
0.68
0.66
0.64
0.62
0.6
0
5
10
15
20
25
30
35
40
45
50
Temperature

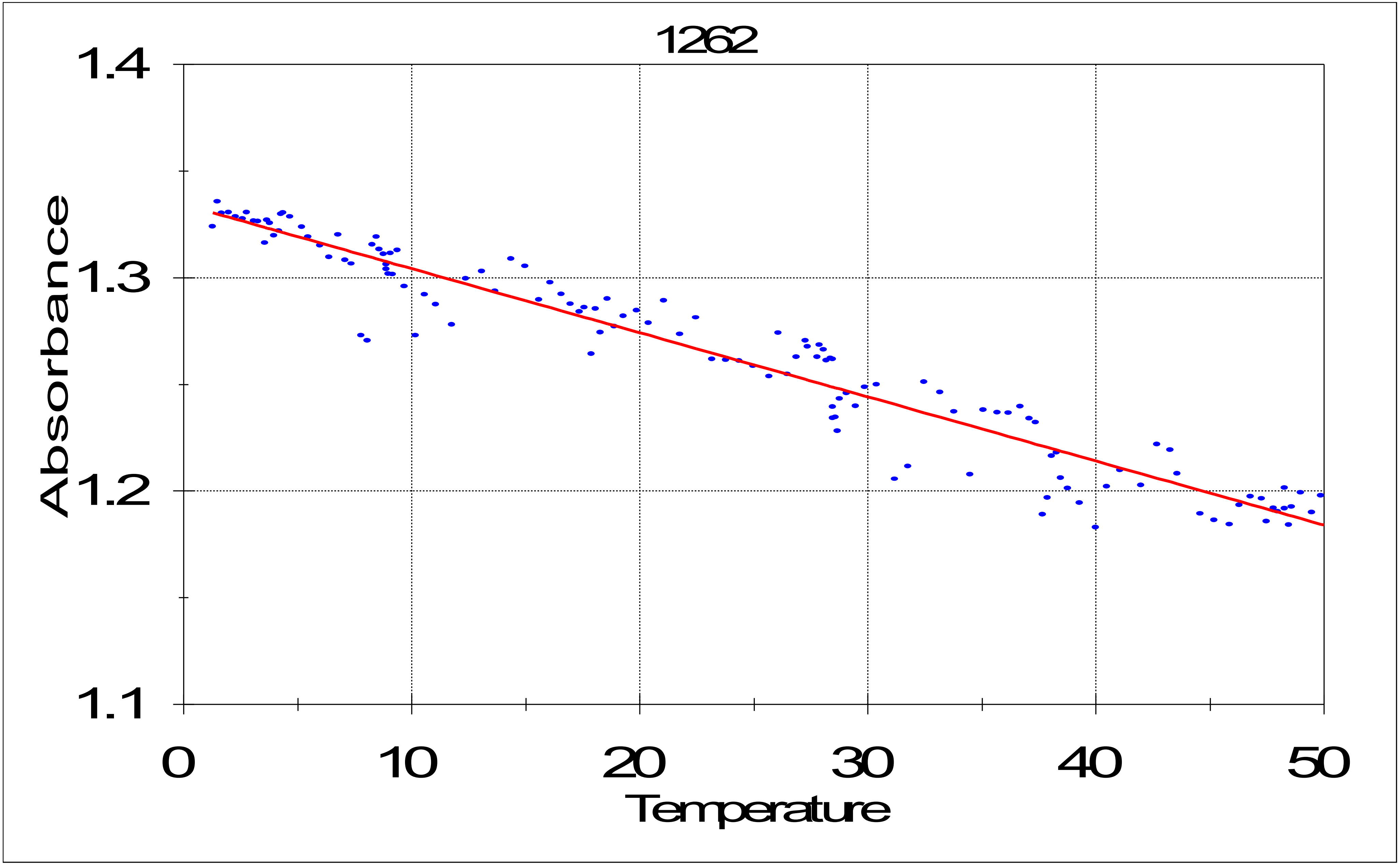
NMP

REMSPEC


MNP 1540
Difference
Temperature
0.01
0.005
0
-0.005
-0.01
0
10
20
30
40
50

NMP

REMSPEC



NMP

- In the case of the two peaks we looked at both can be modelled with a simple linear approximation.
- With the peak at 1540 while as a practical matter a linear approximation can be used the relationship is actually a curve

Conclusions

- Almost all IR peak intensities vary with temperature in a way that can cause significant errors in concentration predictions. This is a fundamental consequence of the physics of IR vibrations.
- The temperature dependence of IR peak intensities is different from peak to peak even in the same molecule
    - This means that peak height ratios are not stable or constant in variable temperature systems.
- Using modern equipment to do proper temperature correction calibrations is simple easy and quick.
- Often the temperature correction is a simple linear relationship.

Acknowledgements

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- Graham Hibbert HEL USA
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- Mary Thomson Remspec