Amoxicillin: Melting or Degradation? DSC and TGA-FT-IR Provide Answers!

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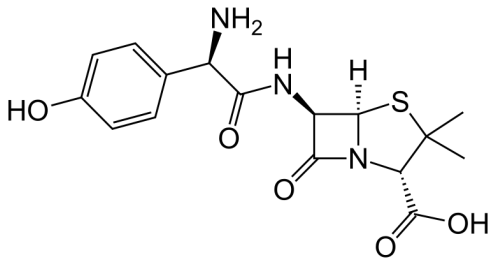


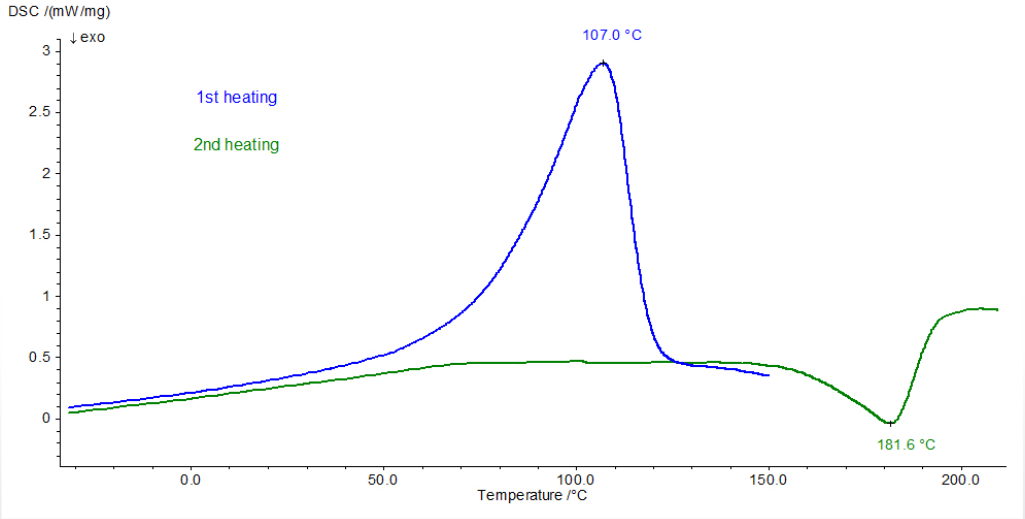
1 Formula of amoxicillin [1]

Introduction

Amoxicillin (figure 1) is an antibiotic from the aminopenicillin group. It is used for the treatment of bacterial infections such as middle ear infections, pneumonia, and skin infections [2]. Here, it was measured by means of DSC and TG-FT-IR in order to obtain information about some of its thermal properties such as melting point and degradation temperature along with degradation products.

Test Results

The DSC measurement was carried out on an amoxicillin trihydrate sample (1.622 mg) with the DSC 204 ***F1*** *Phoenix®*. An aluminum crucible with a manually pierced lid (3 holes) was used. The sample was heated twice from -80°C at a heating rate of 10 K/min; the first time to 150°C, the second time to 210°C. Between the two heating runs, the sample was cooled at a controlled rate of 10 K/min. The DSC measurement of the heating runs is depicted in figure 2.



2 1st and 2nd heating of the DSC measurement on amoxicillin trihydrate

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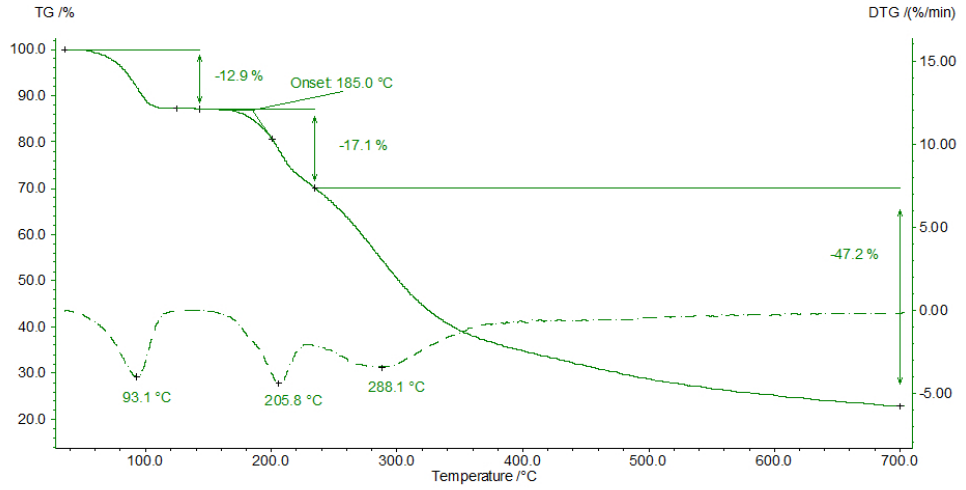
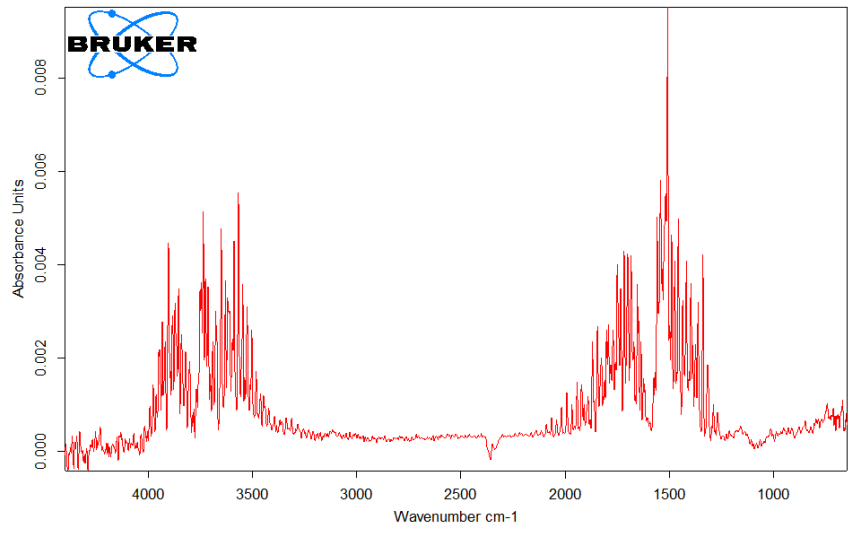
For the TGA measurement, a sample (4.79 mg) was prepared in an aluminum oxide crucible and heated to 700°C in a dynamic nitrogen atmosphere at 10 K/min. The TGA curve is depicted in figure 3.

The endothermal peak detected at 107°C (DSC curve, 1st heating, figure 2) is associated with a mass loss of 12.9%. This process – which can be related to the release of volatiles – is recorded at a higher temperature in the DSC measurement than the corresponding mass loss in the TGA curve. The temperature at which the evaporation occurs is dependent on the presence of a lid on the crucible and on the size of the holes in the crucible lid. Since no lid was used for the TGA measurement, volatilization occurs at a lower temperature than for the DSC measurement, where a pierced lid is employed.

The FT-IR spectrum of the products released at 93°C (figure 4) is characteristic for water.



3 Results of the TGA measurement on amoxicillin trihydrate. Solid line: TGA signal; dotted line: DTG signal.



4 FT-IR-spectrum of the products released at 92.9°C, characteristic absorption bands for water.

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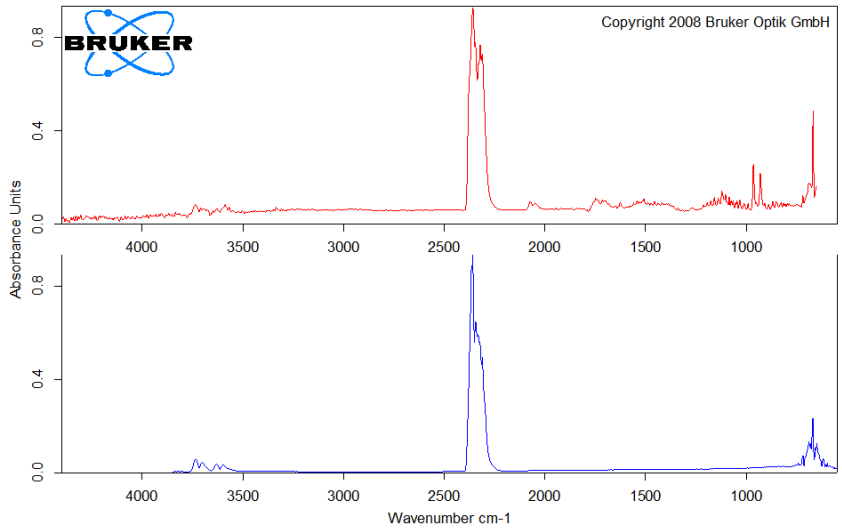
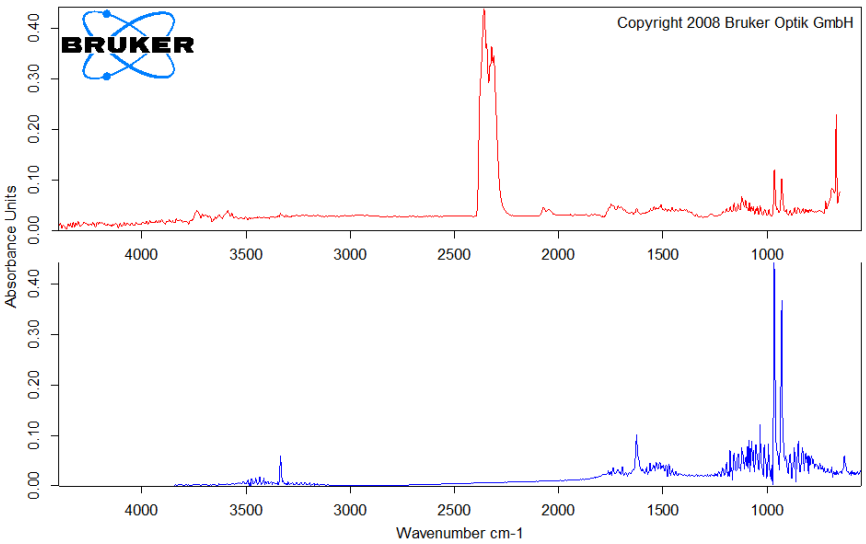
Amoxicillin has a molar mass of 365.4 g/mol [2]. This results in a molar mass of amoxicillin trihydrate of 419.4 g/mol. Consequently, the release of all of the water from amoxicillin trihydrate would theoretically yield a mass change of about 12.9%. Here (figure 3), the measurement results are in excellent accordance with the theoretical values.

A 2nd mass-loss step occurs at 185°C (onset value of the TGA curve). The corresponding FT-IR spectra reveal that degradation of amoxicillin begins with the release of carbon dioxide (figure 5) and ammonia (figure 6). It is associated with an exothermal effect in the DSC curve.

Degradation continues such that amoxicillin loses more than 77% of its initial mass during heating to 700°C.



5 FT-IR spectra of the released products at 202.2°C (red curve) and of carbon dioxide (blue curve)



6 FT-IR spectra of the released products of 202.2°C (red curve) and of ammonia (blue curve)

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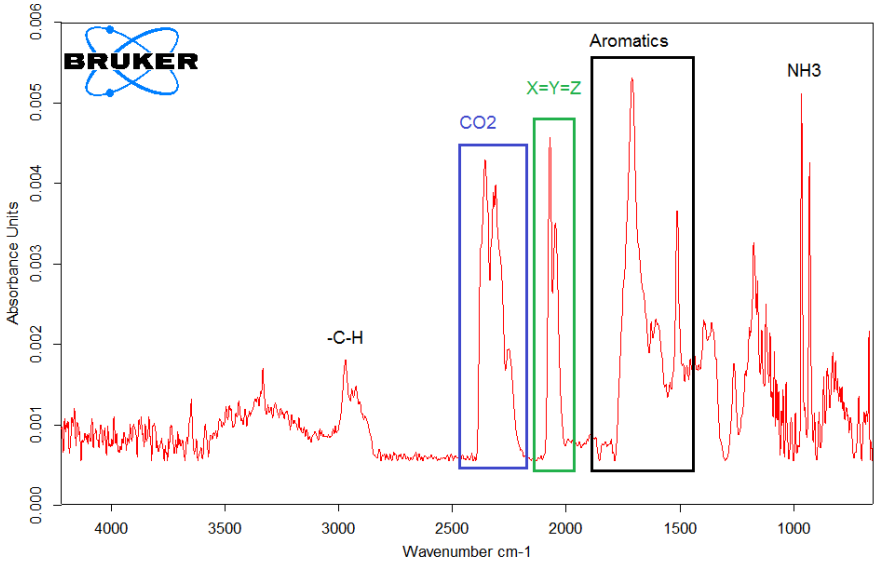
The FT-IR spectrum for the substances released at 294°C is given in figure 7. The characteristic bands for CO_2 and NH_3, which were already discussed, were found as well. However, there are additional absorbance bands visible: The bands between 3000 and 2800 cm^{-1} indicate the presence of –C-H bonds, whereas the bands found between 1500 and 1800 cm^{-1} can result from aromatics. The domain between 1900 and 2300 cm^{-1} is typical for triple bonds or double bonds X_Y_Z. [3, 4] .



7 FT-IR spectrum of the released products of 294°C

Summary

The effects detected by means of DSC measurements during the thermal treatment of amoxicillin cannot solely be explained by interpretation of the DSC results. Only by additional measurement with the TGA-FT-IR method combination can be confirmed that the DSC effect at 107°C ist due to the evaporation of water and not to melting, causing an endothermal DSC peak, but no mass loss. The mass loss continuing after the evaporation of water is a result of the decomposition. The decomposition products, carbon dioxide and ammonia among others, can clearly be identified with the help of the FT-IR.

References

[1] www.pharmawiki.ch
[2] https://en.wikipedia.org/wiki/Amoxicillin
[3] www.uni-stuttgart.de/ochem/lehre/praktika/2011/2011wise/2011wise-umwa/Handout_IR_6.pdf
[4] www.analytik.ethz/Vorlesungen/Spektroskopie_Schmidt/06_IRSpektreninterpretation.pdf

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