

## SPECTRAL UV AND IR DETERMINATIONS OF NEW XANTHINE DERIVATIVES

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### Abstract

The aim of this study is ultraviolet and infrared spectral characterization of eight new xanthine derivatives. Spectral analysis was performed using an Agilent 8453 Series spectrophotometer and a Tensor 27 Optics FT-IR spectrophotometer. The UV and IR spectra for xanthine derivatives were obtained and in addition, the wavelength maxima of absorption bands and characteristics have been established.

### Rezumat

Scopul acestei lucrări este caracterizarea spectrală în ultraviolet și infraroșu a 8 noi derivați xantini. Analiza spectrofotometrică s-a realizat folosind un spectrofotometru Agilent seria 8453 și un spectrofotometru Tensor 27 Optics FT-IR. S-au trasat curbele de absorbție în UV și IR pentru cei 8 derivați xantini, stabilind maximele lungimilor de undă și caracteristicile benzilor de absorbție.

**Keywords:** UV, IR spectra of methylxanthines

### Introduction

UV spectroscopy is useful in the structure elucidation of organic molecules, the presence or absence of unsaturation, the presence of heteroatoms. From the location of peaks and combination of peaks, it can be concluded whether the compound is saturated or unsaturated, if heteroatoms are present or not [1,6].

In the infrared spectroscopy, the vibration spectrum of a molecule is considered a unique physical property and is a characteristic of the molecule. As such, the infrared spectrum can be used as a fingerprint for identification by the comparison of the spectrum from an "unknown" with previously recorded reference spectra. This is the basis of computer-based spectral searching. In the absence of a suitable reference data, it is possible to perform an elementary interpretation of the spectrum from basic principles, leading to characterization, and possibly even identification of an unknown sample. This first principle approach is based on the fact that structural features of the molecule, whether they are the backbone of the molecule or the functional groups attached to the molecule, produce characteristic and

reproducible absorptions in the spectrum. This information can indicate the backbone of the structure and whether the backbone consists of linear or branched chains. Furthermore, it is possible to determine if there are multiple bonds and/or aromatic rings in the structure. Finally, it is possible to deduce whether specific functional groups are present. If detected, one is also able to determine the local orientation of the group and its local environment and/or location in the structure.

The qualitative aspects of infrared spectroscopy are one of the most powerful attributes of this various and versatile analytical technique. Over the years, many studies have been published in terms of the fundamental absorption frequencies (also known as group frequencies) which are the key to unlocking the structure–spectral relationships of the associated molecular vibrations [3,7].

The infrared spectrum can provide information on the existence of most of the linear, branched or cyclic hydrocarbon structures, either directly or by inference. The introduction of unsaturation in the form of a double or triple bond has a profound impact on the chemistry of the molecule, and likewise it has a significant influence on the infrared spectrum. Similarly, the same is observed when an aromatic structure is present within a molecule [1].

In this article, we present the IR spectral interpretation compared with UV-VIS molecular spectra of different xanthine compounds.

## Materials and Methods

### *Chemicals and reagents*

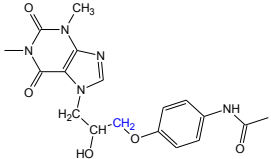
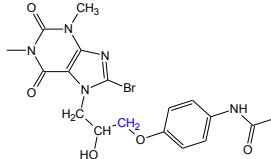
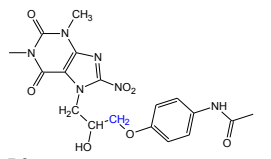
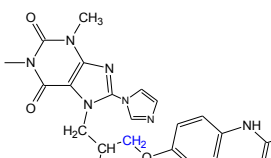
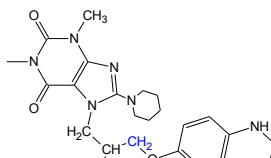
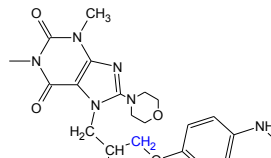
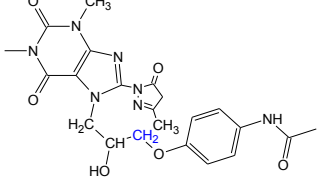
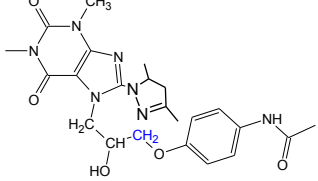
Eight new different xanthine derivatives were used (Table I), HPLC grade methanol supplied by Merck KGaA was used for sample dissolution and appropriate dilution. Potassium bromide of spectroscopic purity was supplied by Merck KGaA, Germany.

### *Instrument*

IR analyses were performed using a Tensor 27 Opitcs FT-IR spectrophotometer from Bruker, Germany, with a spectral range 7500-370 $\text{cm}^{-1}$ , using KBr beam splitter, resolution  $<1\text{cm}^{-1}$  (apodized), wavenumbers accuracy  $<0.01\text{cm}^{-1}$ , photometric accuracy  $<0.1\%$  T, signal to noise (minimum) – 5 sec  $> 6000:1$  (peak-to-peak), resolution  $4\text{cm}^{-1}$ , permanently aligned interferometer, scanning speed – 3 speed, 2.2 to 20KHz and detector – DATGS.

Specac UK provided the tablet press used for sample preparation. UV-Vis spectra were recorded on an Agilent 8453 Series spectrophotometer with a spectral range of 190-1100nm, wavelength accuracy  $\pm 0.5$ nm, wavelength reproductibility – min  $\pm 0.02$ nm and a resolution of minimum 1.6.

**Table I**  
Chemical structure of analyzed compounds

 <p>P1</p>	 <p>P2</p>	 <p>P3</p>
<p><i>N</i>-{4-[3-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)-2-hydroxypropoxy]phenyl}acetamide</p>	<p><i>N</i>-{4-[3-(8-bromo-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)-2-hydroxypropoxy]phenyl}acetamide</p>	<p><i>N</i>-{4-[3-(8-nitro-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)-2-hydroxypropoxy]phenyl}acetamide</p>
 <p>P4</p>	 <p>P5</p>	 <p>P6</p>
<p><i>N</i>-{4-[3-(8-1H-imidazole-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)-2-hydroxypropoxy]phenyl}acetamide</p>	<p><i>N</i>-{4-[3-(8-piperidin-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)-2-hydroxypropoxy]phenyl}acetamide</p>	<p><i>N</i>-{4-[3-(8-morfolin-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)-2-hydroxypropoxy]phenyl}acetamide</p>
 <p>P7</p>	 <p>P8</p>	
<p><i>N</i>-{4-[3-(8-5-methyl-2,4-dihydro-3H-pyrazol-3-one-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)-2-hydroxypropoxy]phenyl}acetamide</p>	<p><i>N</i>-{4-[3-(8-3,5-dimethyl-4,5-dihydro-1H-pyrazole-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)-2-hydroxypropoxy]phenyl}acetamide</p>	

### Samples preparation

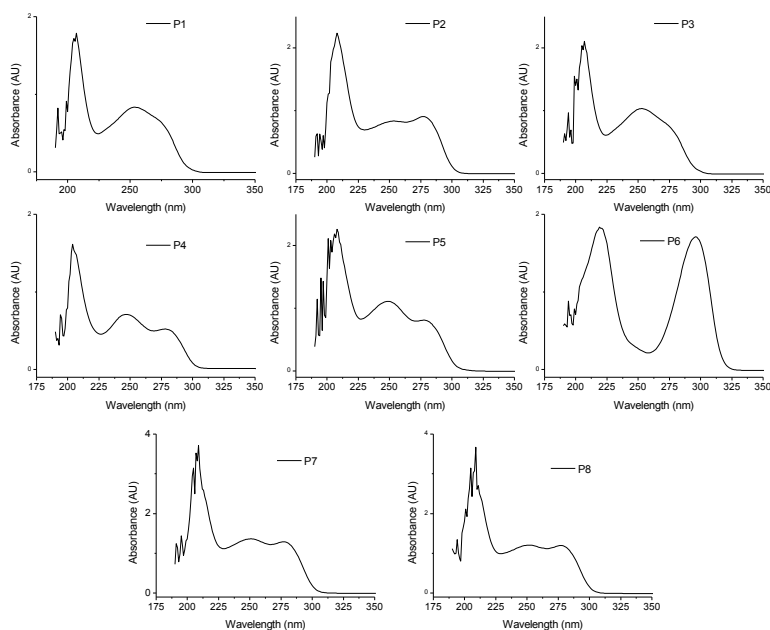
For UV-VIS determinations, about 2 mg of each component were individually dissolved in HPLC grade methanol and diluted to 10mL. Ultrasonication was used for complete dissolution. Methanol was also used as blank solution.

For the IR analysis, samples were prepared according to European Pharmacopoeia 7<sup>th</sup> edition [2]. Approximate 2mg of each component was triturated with 300-400mg potassium bromide.

The obtained tablets were subjected to Fourier Transformed Infrared (FTIR) measurements. Recorded spectra were further processed to eliminate differences between the amplitudes of the baselines and to achieve normalization with respect to differences between the minimum and maximum of absorption.

## Results and Discussion

The UV spectra of the new xanthine compounds are shown in figure 1.



**Figure 1**  
UV-VIS spectra recorded on P1-P8 samples

Sample P1 is the parent compound and displays an intense band at 209 nm and a broad adsorption band at 253 nm, followed by a weak shoulder centered at 275 nm. The absorption band at 275 nm is typical for the chromophore found in most xanthine compounds (like caffeine, pentoxifylline, diprophylline, etofylline, theobromine, theophylline). The other chromophore in this molecule has a maximum at 253 nm, and is an anilide-type chromophore [3].

Bromide compounds show absorption maximum in UV spectrum at 210 nm. Thus, no significant modifications of the UV spectrum are

observed for sample P2. Still, small differences are observed with respect to the intensity of the bands. Specifically, the absorption band at 253 nm is less intense for sample P2, while the band at 275 nm suffers a bathochromic effect to 279 nm.

The nitro chromophore group, present in the sample P3, should give an intense absorption band at 210 nm. In the case of compound P3, this overlaps with the band present at 209 nm in the parent molecule. The bathochromic shift is observed also in this sample (255 nm, 278 nm respectively), probably due to the presence of  $-\text{NO}_2$  functional group.

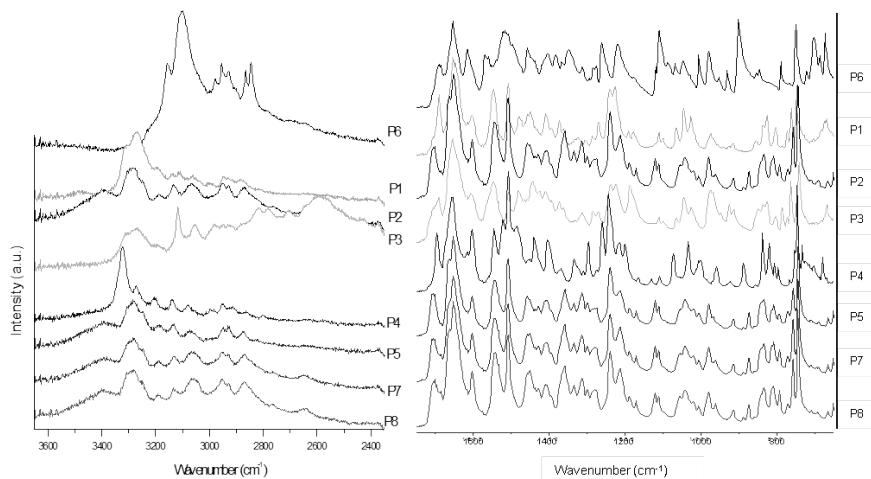
The UV spectra recorded on compound P4 resembles with the one recorded for the parent compound. However, a hypsochromic shift is observed for the first two absorption bands (shift to 206 nm, respectively to 247 nm), while the last absorption band shifts to 278 nm.

Compound P5 shows an UV spectrum resembling with the ones recorded for compounds P7 and P8. Two absorption bands are observed for these samples at 206 nm and 210 nm, one band at 250 nm and one at 278 nm characteristic to xanthine compounds.

Sample P6 shows a different UV spectrum with two distinct absorption maximums at 220 nm, respectively 296 nm. The adsorption band centered at 220 nm has been previously found in morpholine. On the other hand, the UV absorption maximum at 275 nm in the parent molecule suffers a bathochromic shift (to 296 nm) that could be determined by the presence of morpholine-like chromophore group.

#### *IR identification*

The IR spectra of the new xanthine compounds are shown in figure 2.



**Figure 2**

IR spectra recorded for the xanthine-compounds

Generally, in the fingerprint region ( $1750\text{-}650\text{cm}^{-1}$ ), each spectrum of the 8 samples show absorption bands characteristic to the parent molecule represented by compound P1. All compounds display adsorption bands at  $1470\text{-}1430\text{cm}^{-1}$  and at  $2960\text{cm}^{-1}$  characteristic to asymmetric C – H stretch of methyl groups. Weak absorption bands at  $1380\text{-}1370\text{cm}^{-1}$  and at  $2925\text{cm}^{-1}$ , respectively  $2875\text{-}2855\text{cm}^{-1}$  characteristic to symmetric C – H stretch of methylene groups are also observed for all compounds. Moreover, adsorption bands are observed for all compounds at  $1450\text{cm}^{-1}$  and  $1480\text{cm}^{-1}$ , assigned to C – H bend of the methylene groups. On the other hand, bands characteristic to the aromatic ring stretch are obvious in the region  $1615\text{-}1450\text{cm}^{-1}$  for all compounds, along with absorption bands in the region  $3130\text{-}3070\text{cm}^{-1}$  characteristic to aromatic C – H stretch.

The adsorption bands observed for all samples in the IR region  $1700\text{-}1600\text{cm}^{-1}$  are characteristic to C = O stretching present in amide compounds. All samples display this type of functional group, thus all spectra show this absorption bands.

The C – O stretch of the tertiary alcohol group is observed in all spectra by the presence of the adsorption band at  $1170\text{cm}^{-1}$ , while the adsorption bands observed in the region  $1410\text{-}1310\text{cm}^{-1}$ , prove the O – H bend of the same functional group. In addition, the etheric functional group is highlighted in all spectra by the presence of the adsorption bands in the region  $1140\text{-}1070\text{cm}^{-1}$ .

The difference of band intensities in the fingerprint region is due to the bending vibrations out-of-plane of  $\text{sp}^2$  C atoms involved in the C – H bond. The broad band observed in all compounds, with the exception of sample P6, in the region  $3200\text{-}3300\text{cm}^{-1}$  is usually assigned to polymeric O – H stretching.

The presence of the Br atom in the molecule of the compound P2 does not give rise to any new bands that could be assigned to C – Br vibration. This is because this bond vibrates generally in a region that is too crowded by other important group frequencies ( $700\text{-}600\text{cm}^{-1}$  for aliphatic C – Br stretch or  $1500\text{-}1000\text{cm}^{-1}$  for aromatic C – Br stretch).

Regarding the spectrum recorded for the sample P3, a sharp absorption band is observed at  $1181\text{cm}^{-1}$ , generally assigned to symmetric stretch of  $\text{NO}_2$  group in organic nitrates [2]. Other  $\text{NO}_2$  vibration characteristic bands are impossible to distinguish because their absorptions occur within the crowded and highly overlapping region of the spectrum, mainly between  $1300$  and  $1350\text{cm}^{-1}$ .

For sample P4, most of the characteristic bands appear in the fingerprint IR region. Specifically, sample P4 should display adsorption

bands characteristic to C = N bond stretch, which usually occur in the IR region  $1655\text{-}1640\text{cm}^{-1}$  [5]. Since this vibration occur already for all compounds due to the presence of this imide in the parent molecule, no new absorption bands are observed in the IR spectrum recorded on sample P4. Still, a medium intensity absorption band is observed at  $1256\text{cm}^{-1}$ . This band is generally assigned to C – N stretching vibration in amine compounds.

The IR spectrum recorded on sample P6 displays a new absorption band at  $1110\text{cm}^{-1}$ , typically attributed to O – C stretching present in oxygen compounds (other than carboxylic acids, esters, anhydrides, ketones), like morpholine. In addition, the IR bands observed in the region  $3200\text{-}2800\text{cm}^{-1}$  are characteristic to morpholine. Moreover this spectrum shows two weak absorption bands at  $901\text{cm}^{-1}$  and  $1220\text{cm}^{-1}$ , that have been previously attributed to epoxy or oxirane rings [4]. These bands are usually more characteristic in the Raman spectrum.

### Conclusions

The the majority of the recorded spectra (excepting sample P6) show three absorption bands at 209, 253, 275nm. The intense band at 209nm most likely comes from the presence of the aliphatic chain in the molecule of all xanthine compounds.

Taken individually, infrared spectra should display few differences, by the presence or absence of absorption bands characteristic to the functional groups. Also, in the high wave number region, a broad shoulder is observed for compounds P2, P5, P7 and P8 in the region  $3550\text{-}3340\text{cm}^{-1}$  which is attributed to monomeric O – H stretch of the hydroxyl group. This effect most likely appears due to the water adsorbed on the surface of the molecule, since no thermal treatment was applied to the samples before IR measurements subjecting.

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