*Chemistry of Natural Compounds, Vol. 39, No. 1, 2003*

# IR- AND UV-SPECTRAL STUDY OF LEUCOMISIN AND ITS MODIFICATIONS

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UDC 547.944/945

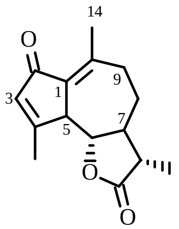
*IR and UV spectra of leucomisin and 3,4-dihydroleucomisin were investigated and compared with those of 1,10-dihydroleucomisin and tetrahydroleucomisin. It was found that the repulsive forces between the ketone carbonyl and methyl are greater in the first two. Steric factors were responsible for decreasing the mesomeric interaction between the carbonyl and double bond of the leucomisin cyclopentenone ring.*

**Key words:** IR and UV spectra, integrated intensity, frequency, leucomisin, leucomisin derivatives.

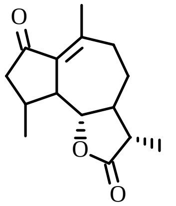
Guaianolides with the cyclopentendienone system possess high angioprotective, hypolipidemic, and anti-inflammatory activities [1, 2]. In particular, the preparation oligvon, which is based on the leucomisin sesquiterpene lactone 2-keto-1,10,3,4-dien-5,7*α*,6,11*β*(H)-guai-6,12-olide, is approved for broad medical application as an antiatherosclerotic agent.

IR- and UV-spectral methods were used successfully to study the electronic structure of organic compounds [3-9], which is the principal factor for estimating the chemical and biological properties.

It seemed interesting to investigate the frequencies (ν) and integrated intensities (A) of the bands due to stretching of the ketone carbonyl, C1=C10 and C3=C4 double bonds, and the π—π* electronic transitions corresponding to them in leucomisin (**1**) and its modifications **2-4** (Tables 1 and 2).



**1**



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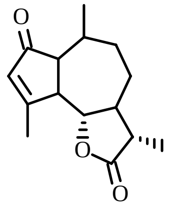
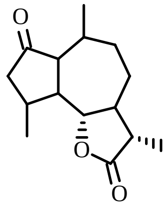


**3**



**4**

Analysis of the frequencies and integrated intensities of the stretching bands of the ketone carbonyl ($\nu_{C=O}$, $A\nu_{C=O}$) shows that they are markedly decreased in **1** ($\nu_{C=O}$ = 1696 cm$^{-1}$, $A\nu_{C=O}$ = 2.48 int. units) and **2** ($\nu_{C=O}$ = 1702 cm$^{-1}$, $A\nu_{C=O}$ = 2.95 int. units) compared with **4** ($\nu_{C=O}$ = 1729 cm$^{-1}$, $A\nu_{C=O}$ = 3.60 int. units). The lower values of these spectral parameters for **1** and **2** compared with **4** can be explained by the increased repulsion force between nonbonded atoms of the ketone carbonyl and the C10 methyl group based on investigations of $\nu_{C=O}$ and $A\nu_{C=O}$ of 2-isopropylidenecyclopentanone and natural guaianolides [10, 11].

This conclusion is consistent with the interatomic O...C14 distances and the barriers to internal rotation of the methyl around the C10—C14 bond in guaianolides **1-4** that are calculated by molecular mechanics. It should be noted that the interatomic O...C14 distances (R) are shorter than the equilibrium value 3.75 Å ($R_0$) [12] for all studied guaianolides **1-4** but much shorter for **1** and **2** (Table 2). The *β*-configuration of the C10 methyl was established previously in **1** and its derivatives **2-4** [13].

The barrier to internal rotation of the $CH_3$ is decreased significantly as the repulsive force between the nonbonded atoms of the carbonyl and methyl increases with the *β*-configuration for the $CH_3$ [12, 16-18].

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TABLE 1. Integrated Intensities of Absorption Bands and Vibrational Frequencies of Ketone Carbonyl $\nu_{C=O}$ and $\nu_{C=C}$ of Leucomisin and Its Derivatives

| Compound | $\nu_{C=O}$, cm$^{-1}$ | $A\cdot10^4\cdot L\cdot mol^{-1}\cdot cm^{-2}$ | $\nu_{C3=C4}$, cm$^{-1}$ | $A\cdot10^4\cdot L\cdot mol^{-1}\cdot cm^{-2}$ | $\nu_{C1=C10}$, cm$^{-1}$ | $A\cdot10^4\cdot L\cdot mol^{-1}\cdot cm^{-2}$ |
|---|---|---|---|---|---|---|
| **1** | 1696 | 2.48 | 1637 | 1.20 | 1620 | 2.30 |
| **2** | 1702 | 2.95 | - | - | 1608 | 1.85 |
| **3** | 1686 | 4.50 | 1620 | 2.75 | - | - |
| **4** | 1729 | 3.60 | - | - | - | - |

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$L\cdot mol^{-1}\cdot cm^{-2}$ is an intensity unit for measuring integrated intensities of bands [25].

TABLE 2. UV Spectra, Interatomic O...C14 Distances, Barrier of $CH_3$ Rotation Around the C10–C14 Bond of Leucomisin (**1**), 3,4-Dihydroleucomisin (**2**), 1,10-Dihydroleucomisin (**3**), and Tetrahydroleucomisin (**4**)

| Compound | $\lambda_{max}$, nm (lg e) | $\lambda_{max}$, nm (lg e) | R, O...C14, Å | Barrier to rotation,* kcal/mol |
|---|---|---|---|---|
| **1** | 195 (2.00) | 257 (4.38) | 2.925 | 0.740 |
| **2** | 200 (2.07) | 250 (4.17) | 2.849 | 0.555 |
| **3** | 230 (3.70) | - | 3.432 | 2.083 |
| **4** | 195 (2.20) | - | 3.208 | 4.886 |

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*$CH_3$; C10–C14 bond.

Therefore, the decreased interatomic O...C14 distance and the barrier to internal rotation of the methyl around the C10—C14 bond (more than twice) in **1** and **2** confirm that the repulsive force between the ketone carbonyl and C10 methyl are increased compared with **3** and **4**.

The increased $A\nu_{C=O}$ ($A_{C=O}$ = 4.50 int. units) and decreased $\nu_{C=O}$ ($\nu_{C=O}$ = 1686 cm$^{-1}$) of **3** relative to **4** (Table 1) and the presence in the UV spectrum of **3** of a band at 230 nm, which is due to absorption of the cyclopentenone conjugated carbonyl (Table 2) [19], are indicative of a mesomeric interaction of the ketone carbonyl with the C3=C4 bond that exhibits donor properties [20, 21].

As a result, the lower value of the integrated intensity of the band and the increased stretching frequency of the leucomisin ketone carbonyl compared with **3** (Table 1) leads to the conclusion that the overlap of the $\pi$-orbitals of the C=O and C3=C4 double bonds is weakened.

The lack in the UV spectrum of **1** of a maximum at 230 nm, which is due to absorption of a conjugated $\alpha,\beta$-unsaturated ketone, and the presence of a band at 195 nm, which is characteristic of absorption of the carbonyl of a cyclopentane ring, confirm that the polarized nature of the C=O bond is decreased [22].

The increased frequency and decreased strength of the stretching band for the C3=C4 bond of leucomisin ($\nu_{C3=C4}$ = 1637 cm$^{-1}$, $A\nu_{C3=C4}$ = 120 int. units) compared with 1,10-dihydroleucomisin ($\nu_{C3=C4}$ = 1620 cm$^{-1}$, $A\nu_{C3=C4}$ = 2.75 int. units) indicates that the C3=C4 bond is less polarized and confirms that the ketone carbonyl is more weakly conjugated [23].

The localized nature of the C3=C4 bond is also evident if $\nu_{C3=C4}$ and $A\nu_{C3=C4}$ are compared with the corresponding parameters of the leucomisin C1=C10 bond (Table 1). The changes in the frequencies and integrated intensities of the absorption bands for C1=C10, C3=C4, and C=O correspond with the appearance of a lower reactivity toward reduction of the C3=C4 and C=O bonds compared with C1=C10 [24].

Thus, the IR and UV spectra establish that the repulsive force between the carbonyl ketone and methyl is increased in **1** and **2** compared with **3** and **4**. It is found that steric factors decrease the mesomeric interaction between the carbonyl and the leucomisin cyclopentenone double bond.

## EXPERIMENTAL

IR spectra were recorded on a UR-20 double-beam IR spectrophotometer using NaCl prisms (1600-1850 $cm^{-1}$). The spectral slit width in the range 1600-1850 $cm^{-1}$ was 8 $cm^{-1}$. The scan rate was 25 $cm^{-1}$/min. Spectra were recorded in $CHCl_3$ solution with the concentration varying from 0.01 to 0.005 M. Sealed standard cuvettes with NaCl windows and path lengths 0.038, 0.060, 0.055, and 0.500 cm were used. The $CHCl_3$ used as the solvent was carefully purified and dried. The integrated intensities were measured using the Bourgin method [25]. The uncertainty of the intensity measurements was ±5%.

UV spectra were recorded on a Perkin—Elmer Lambda-16 UV spectrometer using quartz cuvettes with a path length of 1 cm.

Barriers to rotation of the $CH_3$ group around the C10–C14 bond were calculated by molecular mechanics using mm plus ($mm^+$) in the HyperChem 6.0 program set [26].

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