Comparative crystallographic x-ray analysis of three photoactive furanocoumarins

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Abstract

The molecular and crystal structure of imperatorin, phellopterin and rutaretin have been determined by using crystallographic and computational techniques. The compound of imperatorin crystallizes in triclinic space group $P\overline{1}$ with unit cell parameters $a=11.1150(10)\,\text{Å}$, $b=11.8240(10)\,\text{Å}$, $c=11.9290(10)\,\text{Å}$, $\alpha=64.90(1)^\circ$, $\beta=83.53(1)^\circ$, $\gamma=89.25(1)^\circ$. The compound of phellopterin crystallizes in triclinic space group $P\overline{1}$ with unit cell parameters $a=8.431(3)\,\text{Å}$, $b=8.947(3)\,\text{Å}$, $c=11.125(4)\,\text{Å}$, $\alpha=64.11(5)^\circ$, $\beta=71.13(5)^\circ$, $\gamma=78.04(5)^\circ$. The compound of rutaretin crystallizes in monoclinic space group $C2$ with unit cell parameters $a=24.616(8)\,\text{Å}$, $b=8.186(3)\,\text{Å}$, $c=6.632(2)\,\text{Å}$, $\beta=103.99(2)^\circ$. The number of molecules per unit cell is 4 for imperatorin and rutaretin and 2 for phellopterin. The crystal structure of imperatorin has two asymmetric molecule whereas phellopterin and rutaretin have one asymmetric molecule. The final R-factor for (imperatorin) is 0.0431, (phellopterin) 0.0592 and (rutaretin) 0.0356. All the three molecules exhibit intra and inter C-H...O hydrogen bonding. A comparative crystallographic analysis of these three photoactive furanocoumarins is reported in this paper.

Keywords: Furanocoumarins, photoactive, x-ray diffraction, pyrone ring, hydrogen bonding

1. Introduction

The photochemical behaviour in furanocoumarins is generally attributed to the carbonyl stretching (C=O) in the pyrone moiety of coumarin nucleus [1]. The derivatives of coumarins usually occur as secondary metabolites present in seeds, roots and leaves of many plant species. Their function is far from clear, though suggestions include waste products, plant growth regulators, fungistats and bacteriostats [2]. It is, therefore, of utmost importance that the synthesis of coumarin and its derivatives should be achieved by a simple and effective method. A wide spectrum of biological activity of coumarin compounds is known, e.g., antithrombotic effect, vasodilating effect on vessel, reduction on blood pressure, antispastic and photosensitising effect [3].

The compound of imperoterin was isolated by column chromatography using silica gel and n-hexane. Several fractions were collected. The fractions eluted with n-hexane: EtoAc (9:1) mixture gave a fluorescent compound homogeneous on TLC plate, further purified by preparative TLC. Recrystallized from MeOH yielded plate yellow crystals (50mg) identified as imperoterin on the basis of UV, IR, NMR ans Mass [4-5]. In present study phellopterin has been isolated from the roots of *Heracleum thomsoni* from Leh and Ladakh Region of Jammu and Kashmir State of India [6]. Dried and powdered roots (2kg) of *Heracleum thomsoni* were extracted with petroleum ether in a soxhlet extraction apparatus for 24 hour. The extract was concentrated and residue (60g) was chromatographed over deactivated alumina (1kg) containing 10% water. Elution was started with petroleum ether followed by mixture of petroleum ether and ethyl acetate.

Phellopterin was obtained from petroleum ether: ethyl acetate (9:1) eluate on repeated crystallization. In the present study third molecule rutaretin has been isolated from the seeds of *Apium graveolens*, a weed cultivated in several parts of India [7]. The seeds of this plant are valuable flavouring agents and are widely used in the Ayurvedic and Unani system of medicines for the treatment of bronchitis, asthma and also as household remedy for rheumatism and gout [7].
Dried and powdered seed of Apium graveolens were extracted with petroleum ether which was chromatographed over a column of silica gel. Elution with ethyl acetone yielded a compound having yellow fluorescence in UV light. The structure identified as rutaretin on the basis of UV, IR and NMR [8]. The chemical structures of all the three molecules are present in Figure 1.

Fig 1: Chemical structures of the molecules

2. Experimental Section

The single crystals of compounds were obtained by slow evaporation technique using n-hexane, mixture of acetone and petroleum ether and acetone as solvents. A transparent needle shaped single crystal of all three compounds with dimensions (0.3×0.1×0.1)mm was mounted on the Enraf-Nonius CAD-4 diffractometer for automatic intensity data collection by using MoKα radiation (λ = 0.71.73 Å). ω/2θ scan mode was employed for the data collection with θ-range (4.01 to 69.94°) for imperoterin, (2.04 to 28.23°) for phellopterin and (2.14 to 24.96°) for rutaretin. The compound crystallizes in the triclinic space group P1 with unit cell parameters: a=8.431(3) Å, b=8.947(3) Å, c=11.125(4) Å, α = 69.11(5)°, β=71.13(5)° and γ=78.04(5)°, Z=2, V=737.9(4) Å³. A total of 5926 reflections were recorded in case of imperoterin and out of which 5350 were found to be unique (0≤h≤13, -14≤k≤14, -14≤l≤14), 2549 were considered to be observed [Fo>4σ(Fo)]. In case of rutaretin 4258 reflections were recorded and out of which 2379 were found to be unique (-35≤h≤36, -11≤k≤12, -9≤l≤9), 2216 were considered to be observed [Fo>4σ(Fo)]. The reflection data of all three compounds was collected for Lorentz and polarization effects and no absorption correction was applied. The structures of all three compounds were determined by SHELXS97 Software [9]. Full matrix least square refinement of all non-hydrogen atoms including their corresponding thermal parameters was carried out using SHELXL97 software [10]. The final cycle of refinement with anisotropic thermal parameters for non-hydrogen atoms converged R-factor at 0.0431 for imperoterin, 0.059 for phellopterin and 0.0356 in case of rutaretin. Atomic scattering factor were taken from International Tables for Crystallography (1992, Vol. C Tables 4.2.6.8 and 6.1.1.4). The crystallographic data are listed in Table 1.

3. Results and Discussion

The bond distances for non-hydrogen atoms in the pyrone moiety of all molecules are presented in Table 2. ORTEP view of all three molecules with atomic numbering scheme [11] is in Figure 2. The geometrical calculations were performed by using PARST [12] and PLATON [13]. The bond
distances and angles are in good agreement with the values reported for some analogous structures\textsuperscript{[14-18]}. The magnitude of torsion angle C9-O17-C18-C19 present in the prenyloxy side chain located at atom C9 is 176.9(2)° (molecule-I) and 62.2(2)° (molecule-II) in case of imperoterin, 174.3(2)° in case of phellopterin and 178.4(12)° for rutaretin. However this value is in good agreement with the corresponding values reported for related furanocoumarins\textsuperscript{[14-16]} except for molecule-II of imperatorin.

The pyrone ring of all the molecules is perfectly planner with maximum deviation of 0.009(2) Å. In case of imperotrin, the bifurcated acceptor O2 is involved with two intermolecular interactions in molecule-I whereas in molecule-II, it makes one intermolecular and one intramolecular interaction. Atoms C4 and C12 act as donor atoms in all the above mentioned weak interactions. The molecules of phellopterin are linked by paired C-H...O hydrogen bonds into C(6) graph set, where C refers to chain\textsuperscript{[19]}. The molecules are linked to one another through C-H...O hydrogen bonds and hydrogen-bonding network is shown in Figure 3. The C2-H2...O14 and C5-H5...O1 intermolecular hydrogen interactions result into a linear chain like configuration. In intermolecular C2-H2...O14 interaction, C2 at (x, y, z) acts as hydrogen donor to O14 at (-1+x, 1+y, z) where as in case of C5-H5...O1 intermolecular interactions, O1 at (1+x, y, z) acts as hydrogen acceptor. The C-H...O linear chains packed along bc-plane over different layers of molecule depicts the supramolecular structure of phellopterin. The hydroxylmethyl-ethyl chain located at C2 of rutaretin is inclined more towards O1(108.4 °) than C3 (114.9 °) which might be the reason for the formation of C18-H18...O1 intermolecular interaction. Both the hydroxyl groups of the molecule located at C9 and C16 are linked through a linear intermolecular hydrogen bond O15-H15...O19 at (-x, y, 2-z) in which O19 acts as proton acceptor. All hydrogen interactions fall in the range of weak interactions as suggested by Desiraju and Steiner\textsuperscript{[20]}. The geometry of C-H...O hydrogen bonds is presented in Table 3.

4. Conclusion
The photoactivity of furanocoumarins is due to the carbonyl stretching (C=O) in the pyrone moiety of coumarin nucleus. The average value of bond distances C2=O2 and C3=C4 in the pyrone ring of coumarin moiety for all the three coumarin structure taken in this work are 1.211 and 1.34 Å, respectively, and these bond distances are responsible in the photoactivity of these coumarins. The geometry of hydrogen bonds of all the three structures fall in the range of weak interactions.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Imerotorin} & \textbf{O1-C2} & 1.381(2) & O1'-C2' & 1.386(2) \\
\textbf{C2-O2} & 1.209(2) & C2'-O2' & 1.208(2) \\
\textbf{C2-C3} & 1.438(3) & C2'-C3' & 1.433(3) \\
\textbf{C3-C4} & 1.337(3) & C3'-C4' & 1.336(3) \\
\textbf{C4-C10} & 1.444(2) & C4'-C10' & 1.443(2) \\
\textbf{C9-C10} & 1.403(2) & C9'-C10' & 1.402(2) \\
\textbf{O1-C9} & 1.386(2) & O1'-C9' & 1.380(2) \\
\hline
\textbf{Phellopterin} & \textbf{O8-C13} & 1.373(2) & O8-C13 & 1.387(15) \\
\textbf{C12-C13} & 1.401(2) & C12-C13 & 1.406(19) \\
\textbf{C5-C6} & 1.329(3) & C5-C6 & 1.358(2) \\
\textbf{C5-C12} & 1.433(2) & C5-C12 & 1.429(2) \\
\textbf{C6-C7} & 1.435(3) & C6-C7 & 1.229(16) \\
\textbf{C7-O14} & 1.198(3) & C7-O14 & 1.368(18) \\
\textbf{C7-O8} & 1.385(2) & C7-O8 & 1.358(2) \\
\hline
\end{tabular}
\end{table}
Table 3: Geometry of C-H...O hydrogen bonds.

<table>
<thead>
<tr>
<th>C-H...O</th>
<th>H...O(Å)</th>
<th>C...O(Å)</th>
<th>C-H...O(°)</th>
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<tr>
<td><strong>Imeratorin</strong></td>
<td></td>
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<tr>
<td>C4-H4...O2'</td>
<td>2.54</td>
<td>3.34</td>
<td>137.8</td>
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<tr>
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<td>3.27</td>
<td>172.4</td>
</tr>
<tr>
<td>C12'-H12...O2'</td>
<td>2.34</td>
<td>3.32</td>
<td>178.8</td>
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<td><strong>Phellopterin</strong></td>
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<tr>
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<td>137.5</td>
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<td>C5-H5...O1</td>
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<td>C18-H18...O1</td>
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<td>3.31</td>
<td>171.3</td>
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</table>

Fig 3: C-H...O hydrogen-bonding network.

5. References