



Research Article

THERMAL ANALYSIS OF EMBELIN SUBSTITUTED BENZOYL HALIDE DERIVATIVES

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ABSTRACT

This paper describes the extraction of embeline from its plant source. The embelin is highly handy in the medical management viz., cytotoxic, antibacterial, wound healing, chemo preventive, lipid lowering agent and many other medical usages. The substituted benzoyl ester derivative of the embelin molecule will also have the medical properties more or less than the parent embelin molecule. They substituted derivatives were synthesized by reacting embelin with different substituted benzoyl halides in the presence of pyridine as base and dichloromethane as solvent. Amongst them, Fluoro, bromo and Iodo (halides) substituted benzoate esters exhibited different thermal activities than its parent embeline molecule. These substituted benzoyl halides showed different thermal activities. These properties are varying with respect to the position of halide in the phenyl substituted ring. The thermal prosperities played vital role in altering lipid lowering activity of the molecule.

Keywords: Embelin, substituted benzoyl halides, Thermal analysis, Differential Scanning Calorimeter.

INTRODUCTION

The traditional molecule Embelin (2, 5-dihydroxy-3-undecyl-1, 4-benzoquinone) is a naturally occurring alkyl substituted hydroxy benzoquinone; it is extracted from *Embelia ribes* burm. (Family: Myrsinaceae). This Embelin molecule is widely used in the medical applications; like urinary tract infections, scorpion-sting, tooth ache and snake-bite¹. It has been reported that the molecule also possess antioxidant properties, diabetic and anti-inflammatory to relive fever². Embelin showed that has antifertility³, anti implantation⁴, lipid lowering activity⁵ and anticonvulsant activities. Hence; it is highly significant to study the substituted derivative of this drug molecule also important because of its medical properties. This paper describes the technical challenges confronting the Thermal characterization of embelin substituted benzoyl halides derivatives using standard DSC (Differential Scanning Calorimeter)⁶⁻⁸. The molecule structure is confirmed with the help of various spectroscopic techniques viz., NMR (Nuclear Magnetic Resonance) for its proton position confirmations and (MS) Mass Spectra for its molecular weight confirmations; analysis followed by the embelin isolations. The positions of the halide in the benzoate esters are Ortho, Meta and Para respectively.

MATERIALS AND METHOD

Isolation of Embelin (RLS-01)

The fine powdered berries of *Embelia ribes* around (250 g) were sequentially extracted with petroleum ether, chloroform, ethyl acetate, methanol and water and by cold extraction method, collected organic extracts were separately concentrated under reduced pressure. The chloroform extract was first chromatographed on silica gel and then triturated with petroleum ether, the crude embelin separates out. The petroleum ether layer was decanted, the residue was filtered through Buchner funnel and suck dried to yield around 25 g of crude embelin. The crude embelin is crystallized using Petroleum ether, the pure crystallized embelin is obtained in orange color flakes.

General method for the preparation of compounds (RLS-34, 36, 37, 38 and 41)

To a stirred solution of 2, 5-dihydroxy-3-undecyl-1,4-benzoquinone (1.0 g, 3.4 mille moles) in dichloromethane (20 ml) was added pyridine (1.1 ml, 13.6 mille moles). Clear solution of reaction mixture was obtained. into this 2-bromo benzoylchloride (1.35 g, 8.5 mille moles) was added in 15–20°C and stirred, allowed to attain 30°C (RT) and stirring was continued for next 24 h (TLC monitoring). The reaction was decomposed by adding water (200 ml). The aqueous layer was extracted with dichloromethane (3 x 50 ml), washed with water, brine and dried over anhydrous Na₂SO₄. The organic layer was concentrated to minimum, pre-adsorbed on silica gel and purified by silica gel (100 – 200 mesh) column chromatography with increase in concentration of ethyl acetate in petroleum ether obtained the pure mass (0.96 g, 52.45 %). Using these reaction conditions, the compounds RLS 34, RLS 36, RLS 37, RLS 38 and RLS 41 were synthesized with appropriate benzoyl halide substituted derivatives.

The derivatives chemical names are as follows:-

- 2,5-Di-O-(2-bromophenylcarbonyl)-3-undecyl-1,4-benzoquinone (RLS 34)
- 2,5-Di-O-(4-bromophenylcarbonyl)-3-undecyl-1,4-benzoquinone (RLS 36)
- 2,5-Di-O-(2-iodophenylcarbonyl)-3-undecyl-1,4-benzoquinone (RLS 37)
- 2,5-Di-O-(3-fluorophenylcarbonyl)-3-undecyl-1,4-benzoquinone (RLS 38)
- 2,5-Di-O-(2-fluorophenylcarbonyl)-3-undecyl-1,4-benzoquinone (RLS 41)

Tools and Aids

Aluminum cup and seal / cover used for crimping the solid sample.

Instrument

The DSC analysis was performed on a Shimadzu DSC (TA-60)

Preparation of sample

Weigh accurately about 5.0 mg of each of the five samples in to an aluminum cup and crimped with aluminum cover separately.

Differential Scanning Calorimetry (DSC) method

The temperature program is followed as From 25°C to 600°C @ 10°C/ Min.

Analysis by DSC

Thermal analysis has been extremely important analytical tool within the pharmaceutical industry. The instrument DSC has been generated renewed enthusiasm in thermal analysis for all the molecules. In the pharmaceutical industry the drug composition (formulation) is achieved based on the dissolution factor of the drug. The drug dissolution properties based up on the crystalline and amorphous solid state of drug product. The rate of drug dissolution is the only base factor for bio availability and this is one of the prime requirements of pharmaceutical scientists. In general the crystalline solid state of the molecules are arranged more regular manner than the amorphous solid state. Due to this solid state property, the crystalline state of the molecule, more stable and less soluble than amorphous state of molecules. Literature describes the solubility increase from crystalline to amorphous material has been reported to be between 10 and 1600 fold. In the DSC thermal analysis provides various solid state information's, among this analysis two of the information's will be consider

in this study. The Melting points and Heat capacity of the five derivative molecules were given in the Table 1 and the Histogram of DSC is given in the Figure 1 to 6. It is very important to determine the presence of amorphous compound in the molecule, this amorphous compound quantity in the solid substance determine the rate of dissolution, storage stability and hygroscopic nature. The most common DSC measurement of amorphous structure is that of the glass transition (T_g). It is important to know the size of the transition in heat flow or heat capacity units and the temperature (T_g) at which it occurs. The size provides quantitative information on the amount of amorphous structure in the sample, while the temperature identifies the point where a large change in physical properties occurs. Crystalline materials often exist in multiple crystal forms (polymorphs) that have different physical, chemical and biological properties. The molecular structures were given in the Figure 7 to 12.

Molecular structure confirmations

The RLS 34, 36, 37, 38 and 41 molecules used for this study is confirmed further for its structure by analysis and interpreting NMR, Mass and IR spectra.

These molecules has almost same range of exothermic temperature, where as different ranges of endothermic peak as per its crystallinity nature along with it moisture or its solvent combinations. These thermal property, heat capacity could vary based up on the solvent combinations used during the parent and derivative molecule synthesis. Because the internal / residual solvent amount trapped during the crystal formation of compound could changes the thermal properties.

Table 1: Comparison Table

Sample	M. P (°C)	Heat (mJ)	Substituted Halide	Halide Substituted position
RLS-34	80.81	-894.10	Br	Ortho
RLS-36	125.97	-125.77	Br	Para
RLS-37	67.07	-115.51	I	Ortho
RLS-38	76.32	-311.10	F	Meta
RLS-41	125.25	-309.35	F	Ortho
RLS-01	144.7	-292.8	-	Parent

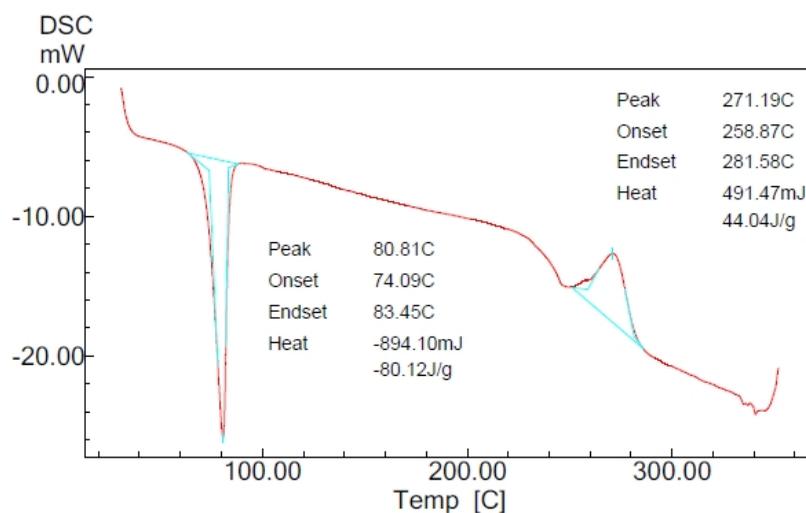


Figure 1: DSC of RLS-34

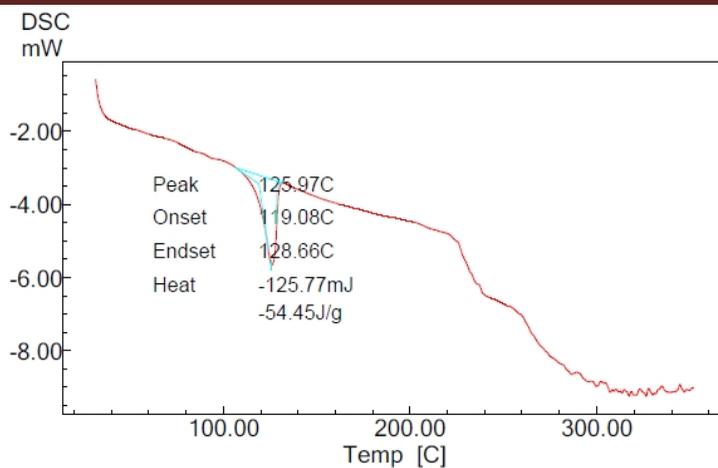


Figure 2: DSC of RLS-36

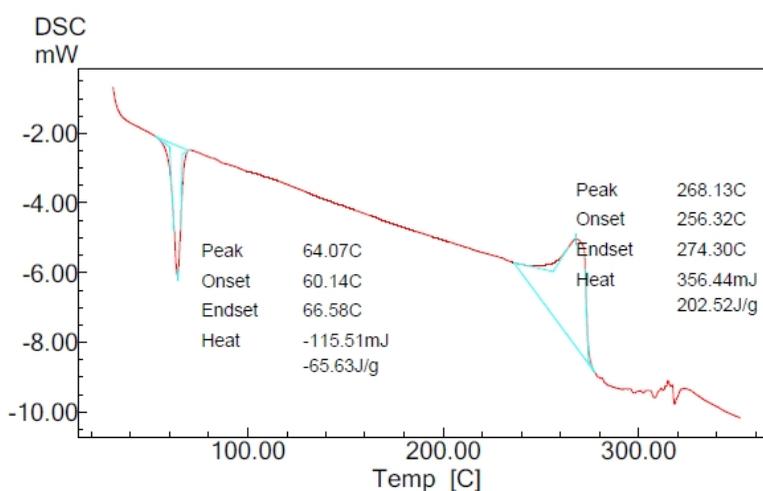


Figure 3: DSC of RLS-37

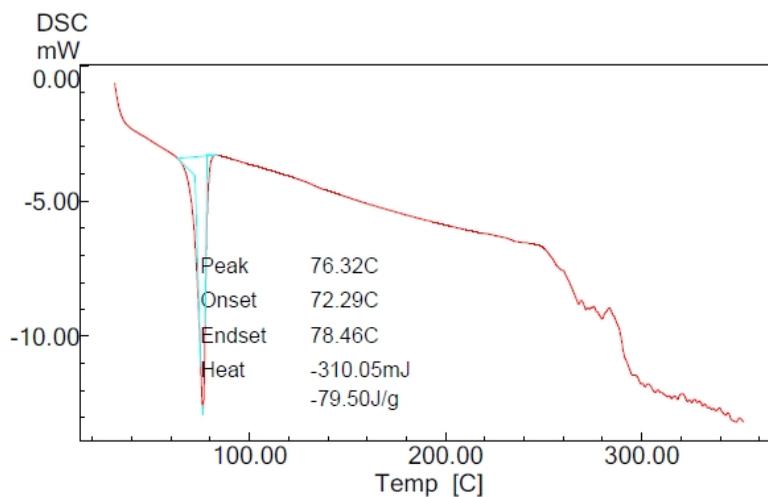


Figure 4: DSC of RLS-38

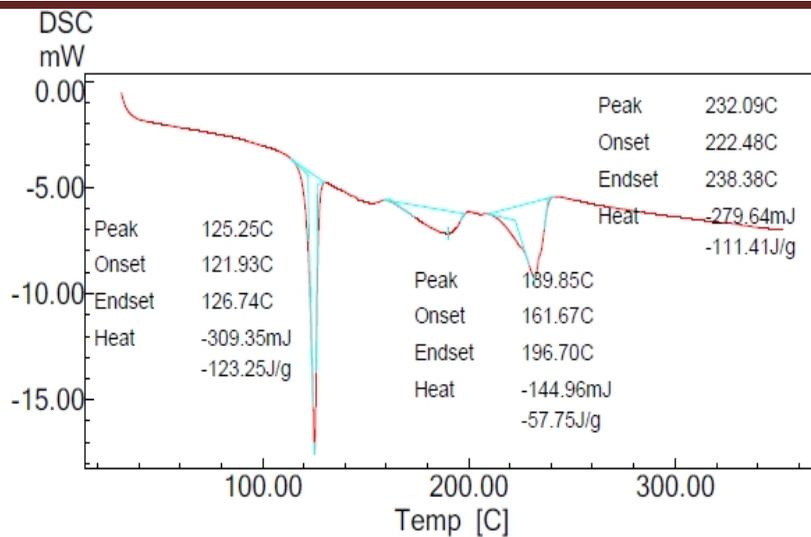


Figure 5: DSC of RLS-41

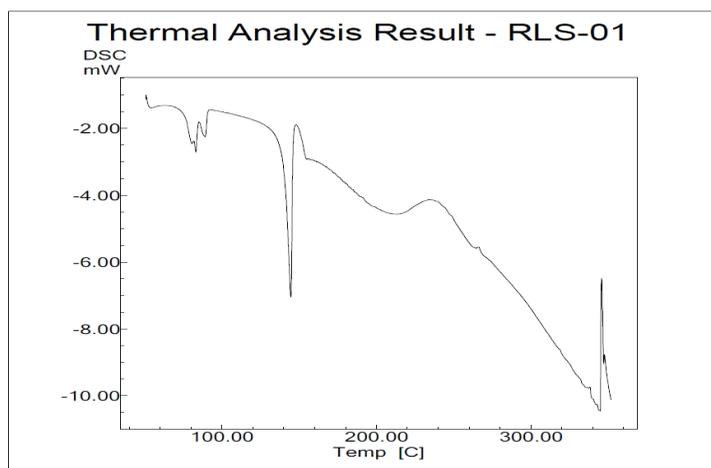


Figure 6: DSC of RLS-01

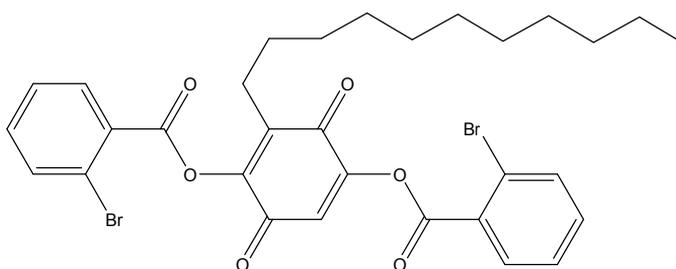


Figure 7: RLS-34 Molecule Structure

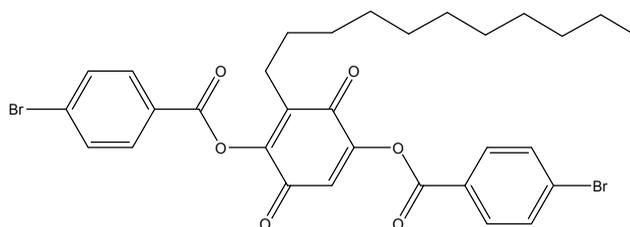


Figure 8: RLS-36 Molecule Structure

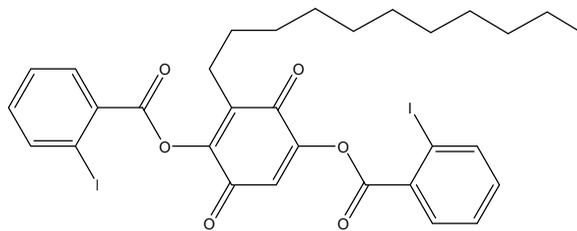


Figure 9: RLS-37 Molecule Structure

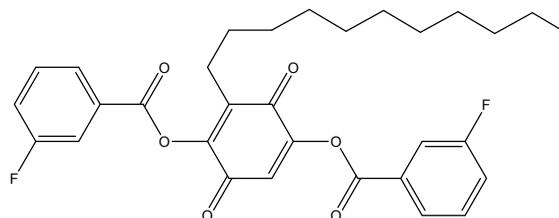


Figure 10: RLS-38 Molecule Structure

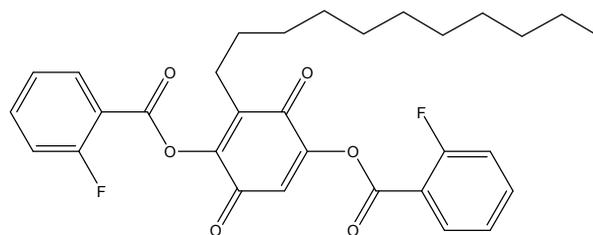


Figure 11: RLS-41 Molecule Structure

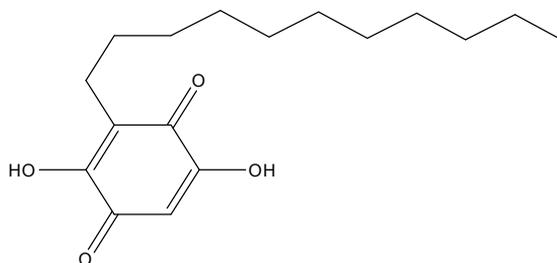


Figure 12: RLS-01 Molecule Structure

CONCLUSION

The ortho substituted iodo derivative (RLS-37) and para bromo substituted derivative (RLS-36) has less Heat capacity than the parent molecule Embelin (RLS-01). The Meta and ortho fluoro substituted derivatives (RLS-38 and RLS-41) are more or less equal heat capacity than the parent molecule Embelin. The only molecule ortho bromo derivative (RLS-34) has very high heat capacity than the parent molecule. This data interoperating that the bio availability of this derivative could be more than its parent molecule.

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