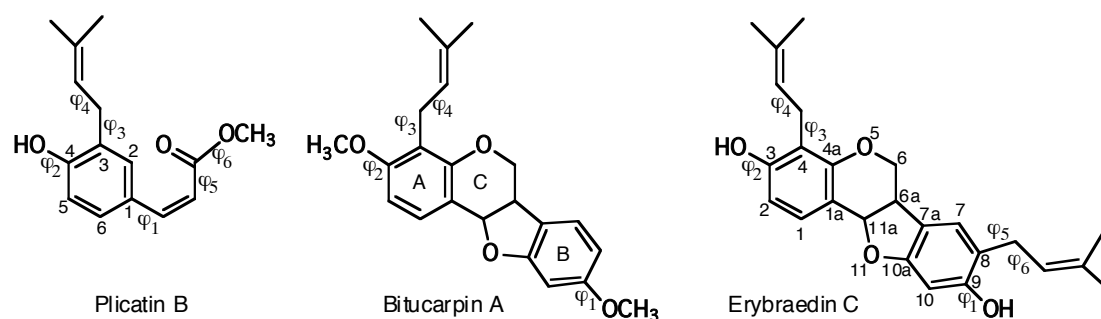


Plicatin B Conformational Landscape and Copper (I) and (II) Chelation Ability. A Comparative DFT Study

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Flavonoids constitute a large class of benzo- γ -pyrone derivatives that are ubiquitous in plants, fruits and vegetables. Most of the pharmacological effects of flavonoids seem to be associated with their potency as antioxidants. Actually, oxidation of lipoproteins, particularly of low-density lipoprotein (LDL), appears to play a primary role in initiating the atherogenic process. Attempts to inhibit or reduce the process of LDL oxidation, which may slow down the progression of atherosclerosis, appear attractive. LDL oxidation can be macrophage-mediated and can also be induced by transition metal ions like copper ions. The understanding of the structural origin of the antioxidant activity in natural products can help design more potent antioxidants to treat and prevent diseases caused by oxidative stress.



The conformational landscape of plicatin B, a substituted cinnamyl ester, was thus considered at the B3LYP/6-31G* level, for the sake of comparison to prior studies [1] on erybraedin C and bitucarpin A (two structurally related prenylated pterocarpanes), allowing a variety of low energy conformers to be identified. Their affinities to Cu(I) and Cu(II) metal ions have been explored and compared to those of bitucarpin A and erybraedyn C. Since the antioxidant activity of these natural compounds is supposed to be related to their copper chelation ability, several complexes with the Cu^+ and Cu^{2+} metal cations have been taken into account describing the metal ions with effective core potentials in the LANL2DZ valence basis set. The preferred binding sites on low-energy conformers of plicatin B as well as of erybraedin C and bitucarpin A have been determined and their affinity values have been compared. Both cations give stable complexes with plicatin B, but the stability order of the metalated species at the various coordination sites strongly depends on the cation nature. In particular, the most stable Cu^+ -plicatin B ground-state structure features the metal cation bridged between the hydroxy O lone pairs and the prenyl π density, while in the most stable Cu^{2+} complex the cation is coordinated with the inner lone pairs of the oxygens in the methyl ester moiety bearing an anti methyl group. Comparison of the Cu^+ and Cu^{2+} affinity values demonstrates that the affinity to Cu^{2+} is decidedly much higher (by a factor of 5) than that to Cu^+ .

[1] Alagona *et al.*: (a) *PCCP* 2004, **6**, 2849; (b) *JPCB* 2005, **109**, 16918; (c) *JPCA* 2006, **110**, 647.