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# Synthesis of purpurasol, a highly oxygenated coumarin from *Pterocaulon purpurascens*

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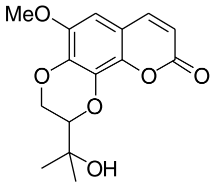
**Abstract**—Purpurasol **1**, a 6,7,8-trioxygenated coumarin, isolated from *Pterocaulon purpurascens* (Asteraceae) and *Haplophyllum obtusifolium* (Rutaceae), was synthesized for the first time by a three-step synthesis starting from the natural coumarin fraxetin. This synthesis confirmed unambiguously the structure of purpurasol **1** and obtusifol.

## 1. Introduction

The genus *Pterocaulon* is widely distributed in north eastern Argentina, southern Brazil and Paraguay. Plants of this genus are traditionally used in folk medicine for various purposes. The aerial parts of *Pterocaulon purpurascens* are used against snakebites and as an insecticide.[1,2] A number of strongly related tri- and tetraoxygenated coumarins were isolated from *P. purpurascens*, more precisely purpurenol **2**,[1] purpurasol **1**[2] and purpurasolol **3**.[3] Isopurpurasol **4**, a regioisomer of purpurasol, was isolated from another *Pterocaulon* species, namely *Pterocaulon virgatum*.[4] All these coumarins show a characteristic benzodioxine moiety, which is very rare in natural coumarins.[5] The present report deals with the synthesis of purpurasol **1** in order to secure unambiguously its structure and those of analogous coumarins **2** and **3**. The structure of purpurasol **1** was revealed based on spectroscopic data and by comparison with the earlier described purpurenol, of which the structure was unequivocally established based on X-ray spectroscopic analysis.[1] Later it was discovered that the spectroscopic, as well as the physical data obtained for purpurasol **1**, matched completely with those from an earlier described coumarin from *Haplophyllum obtusifolium*.[6,7] The structure of this coumarin, which was given the trivial name obtusifol, was first proposed as **5**,[6] but was later revised to **6**.[7,8] Based on spectroscopic evidence it was shown that the coumarin from *H. obtusifolium* was identical to purpurasol **1**.[9] In order to confirm this hypothesis, a synthesis of purpurasol was developed.



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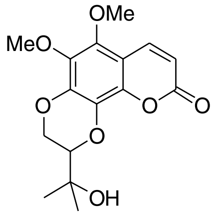

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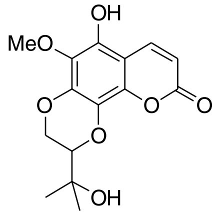

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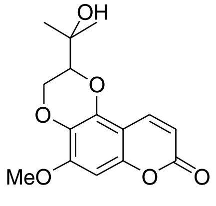

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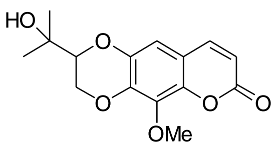
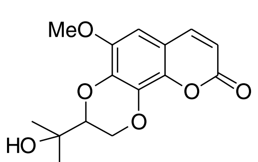


**5**



**6**

## 2. Results and discussion

Purpurasol **1** was synthesized starting from 7,8-dihydroxy-6-methoxy-2*H*-1-benzopyran-2-one, known as fraxetin **7**. Fraxetin **7** is a natural coumarin that occurs in many plant

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*Keywords*: Coumarin; Purpurasol; Pterocaulon purpurascens.

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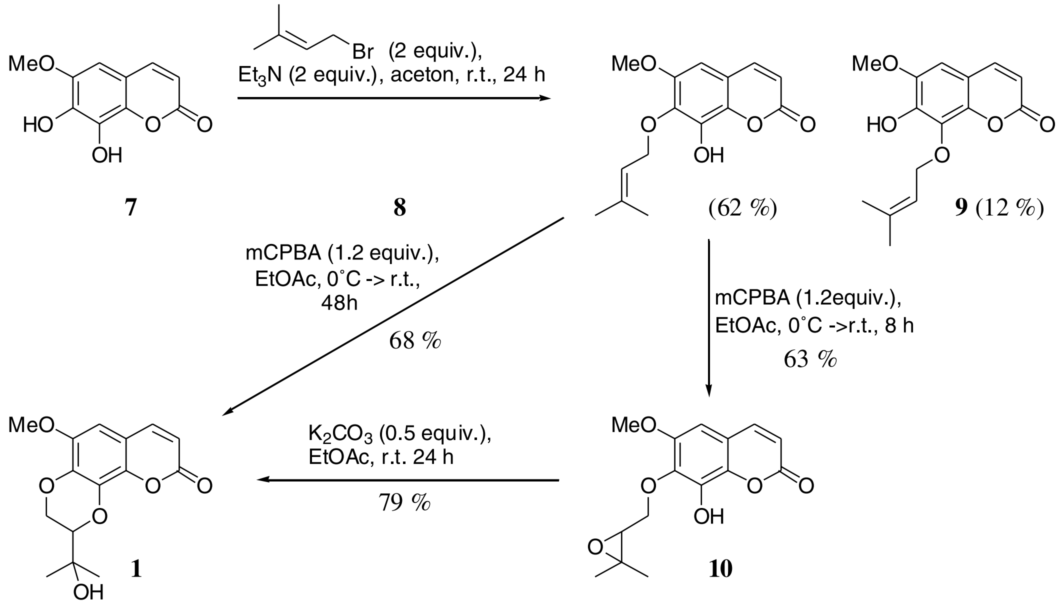
species, including *Aesculus turbinate* (Hippocastanacea)[10] and several *Fraxinus* spp. (Oleaceae).[11,12] Fraxetin **7** was also isolated from *P. purpurascens*,[3] which indicates that fraxetin **7** might be a natural precursor in the biosynthesis of purpurasol. The first synthetic step involved regioselective prenylation of fraxetin. Because of delocalization towards the electron withdrawing carbonyl group, the 7-OH group is more acidic than the OH group at the 8-position. Although selective prenylation of fraxetin **7** was described before in 70% yield using sodium bicarbonate and 4-bromo-2-methyl-2-butene,[13] in our hands only, and after numerous experiments under these and other reaction conditions, very low yields of the desired capensin **8** [8-hydroxy-6-methoxy-7-(3′-methyl-2′-butenyloxy)coumarin] were obtained. This problem of reproducibility is probably due to hydrolysis during aqueous workup. However, when the workup only consisted of the filtration of the reaction mixture, followed by rinsing the filter with dry acetone, the obtained yields were also very low. These low yields demanded for further evaluation of the reaction conditions. Much better results were obtained when the reaction was performed with triethylamine as a base. When fraxetin **7** was reacted with 2 equiv of prenylbromide and 2 equiv of triethylamine at room temperature for 24 h, the desired product, capensin **8** [8-hydroxy-6-methoxy-7-(3′-methyl-2′-butenyloxy)coumarin] was isolated in 62% yield. The regioisomeric 7-hydroxy-6-methoxy-8-(3′-methyl-2′-butenyloxy)coumarin **9** was isolated in 12% yield. In this reaction, purification was achieved by evaporating acetone from the reaction mixture and purifying the residual crude mixture by column chromatography. Capensin **8** is a naturally occurring coumarin and was isolated from several plant species, including *Phyllosma capensis*[14] and *Bupleurum fruticosum*.[15] To our knowledge 7-hydroxy-6-methoxy-8-(3′-methyl-2′-butenyloxy)coumarin **9** has never been reported from natural sources. The next step in the synthesis involved the epoxidation of the double bond of the prenyl group of capensin **8**. When capensin **8** was treated with 3-chloroperbenzoic acid in ethyl acetate, after 8 h 63% of 7-(2,3-epoxy-3-methylbutoxy)-8-hydroxy-6-methoxy-coumarin **10** was obtained. Cyclisation of epoxide **10** to purpurasol **1** was accomplished by treating it with potassium carbonate in ethyl acetate, affording purpurasol **1** in 79% yield. Purpurasol **1** could also be obtained in one step from capensin **8** by reaction with 3-chloroperbenzoic acid in ethyl acetate for 48 h, affording purpurasol **1** in 68% yield.



## 3. Experimental

### 3.1. General

$^1$H NMR spectra (300 MHz) and $^{13}$C NMR spectra (75 MHz) were recorded with a Joel Eclipse FT 300 NMR spectrometer. IR spectra were recorded on a Perkin Elmer Spectrum One spectrophotometer. Mass spectra were recorded on an Agilent 1100 Series VL mass spectrometer (ES 70 eV) or on a Varian MAT 112 mass spectrometer (EI 70 eV). Melting points were measured with a Büchi B-450 apparatus. Elemental analyses were measured with a Perkin-Elmer 2400 Elemental Analyzer. Flash chromatography was performed with ACROS silica gel (particle size 0.035–0.070 mm, pore diameter ca. 6 nm) using a glass column. 7,8-Dihydroxy-6-methoxycoumarin was obtained from Aldrich Chemical Company. All other reagents were obtained from Acros Organics and were used as such, except for 3-chloroperbenzoic acid. 3-Chloroperbenzoic acid ($\leq$77%, remainder 3-chlorobenzoic acid and water) was obtained from Acros Organics and was kept under reduced pressure (5 mmHg) at room temperature for 3 h in order to remove most of the water.

### 3.2. Synthetic procedures

**3.2.1. 8-Hydroxy-6-methoxy-7-(3′-methyl-2′-butenyloxy)-coumarin (capensin) 8 and 7-hydroxy-6-methoxy-8-(3′-methyl-2′-butenyloxy)coumarin 9.** 7,8-Dihydroxy-6-methoxycoumarin **7** (208 mg, 1 mmol) was dissolved in 10 ml acetone, and 202 mg (2 mmol) of triethylamine and 298 mg (2 mmol) of 4-bromo-2-methyl-2-butene were added.