Tetrahedron Letters 50 (2009) 3933–3935

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

A novel synthetic pathway to vitisin B compounds

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ARTICLE INFO

Article history:
Received 25 March 2009
Revised 15 April 2009
Accepted 20 April 2009
Available online 23 April 2009

Keywords:
Malvidin-3-glucoside
Malvidin-3-*O*-coumaroylglucoside
Vinyloxy-trimethylsilane
Vitisin B

ABSTRACT

The hemi-synthesis of vitisin B compounds is described herein for the first time through a new, simple and suitable reaction of malvidin-3-glucoside and malvidin-3-*O*-coumaroylglucoside with vinyloxy-trimethylsilane. The obtained compounds were identified by LC/DAD-MS and fully characterized by NMR analysis for the first time.

Anthocyanins are a group of polyphenolic compounds relatively unstable and may undergo several chemical reactions in anthocyanin-rich foodstuffs like red wine. Over the years, several studies showed that a number of reactions can occur between anthocyanins and other small molecules in red wine, namely acetaldehyde (vitisin B),[1] acetoacetic acid,[2] pyruvic acid (vitisin A),[3–5] vinylphenol,[6–9] vinylguaiacol,[10] vinylcatechol (pinotin A),[8,11] and more recently, vinylcatechin[12] giving rise to new families of wine pigments. Altogether, these new compounds contribute to the orange hues observed during wine ageing.

Among these newly formed pigments vitisin B compounds appear to be interesting which are thought to contribute to the orange hues observed during wine ageing. Indeed, these compounds display unusual colour hues that are appealing to the food industry foreseeing their putative use as food colourants. Although their chemical structure has already been reported in the literature, their mechanism of formation in wine has not been totally clarified. It has been suggested that their presence in red wines arises from the reaction between anthocyanins and acetaldehyde.[1] However, vitisin B pigments are difficult to isolate directly from wine and the syntheses of these compounds have never been performed for further isolation in significant amounts. Therefore, the aim of this work was to develop a fast and simple synthetic pathway to vitisin B compounds.

The syntheses of vitisin B and the respective coumaroyl derivative (Scheme 1) are reported herein from the reaction of malvidin-3-glucoside **1** and malvidin-3-*O*-coumaroylglucoside **2** with vinyloxytrimethylsilane **3**. The obtained compounds **4** and **5** were characterized by LC/DAD-MS and all protons and carbons were fully assigned by 1D and 2D NMR techniques for the first time.

Malvidin-3-glucoside (37 mg) **1** and malvidin-3-*O*-coumaroylglucoside (47 mg) **2** were dissolved in 50 mL of a 12% (v/v) aqueous ethanol solution. The pH of the solutions was adjusted to 3.2 with a NaOH (0.01 M) solution. Then, 2.3 mL of vinyloxy-trimethylsilane **3** was added to each solution. The mixtures were left to react at room temperature with continuous agitation and were monitored by HPLC-DAD on a 250 × 4.6 mm i.d. reverse-phase C18 column as previously reported.[13] Under these conditions, the maximum amount of both compounds was reached after only 2 h. It was then possible to observe in the HPLC chromatogram two new peaks **4** and **5** (Fig. 1) with absorption maximum wavelengths quite hypsochromically shifted (490 and 492 nm, respectively) from those of malvidin-3-glucoside or malvidin-3-*O*-coumaroylglucoside (528 and 532 nm, respectively), thereby displaying more red-orange hues. No other products (by-products) were detected at other wavelengths in the UV–vis region. After this, pigments **4** and **5** were purified similarly to that described in the literature.[13]

Pigments **4** and **5** may result from the cyclic addition of vinyloxy-trimethylsilane onto carbon 4 and a hydroxyl group at the carbon 5 position of the anthocyanin (Scheme 1), yielding a fourth ring. The mechanism also involves the loss of a hydroxytrimethylsilane molecule by elimination and an oxidation leading to a re-aromatization of the chromophore moiety.

The yield obtained for the reactions was around 30%. Smaller molar ratios were also tested but the reaction yields obtained were always below 20%. The high molar ratio of vinyloxy-trimethylsilane needed for the reactions can be explained by the acid-catalyzed dimerization of the vinyl group at pH 3.2. Lower and higher pH did not improve the synthesis: at lower pH dimerization of the vinyl

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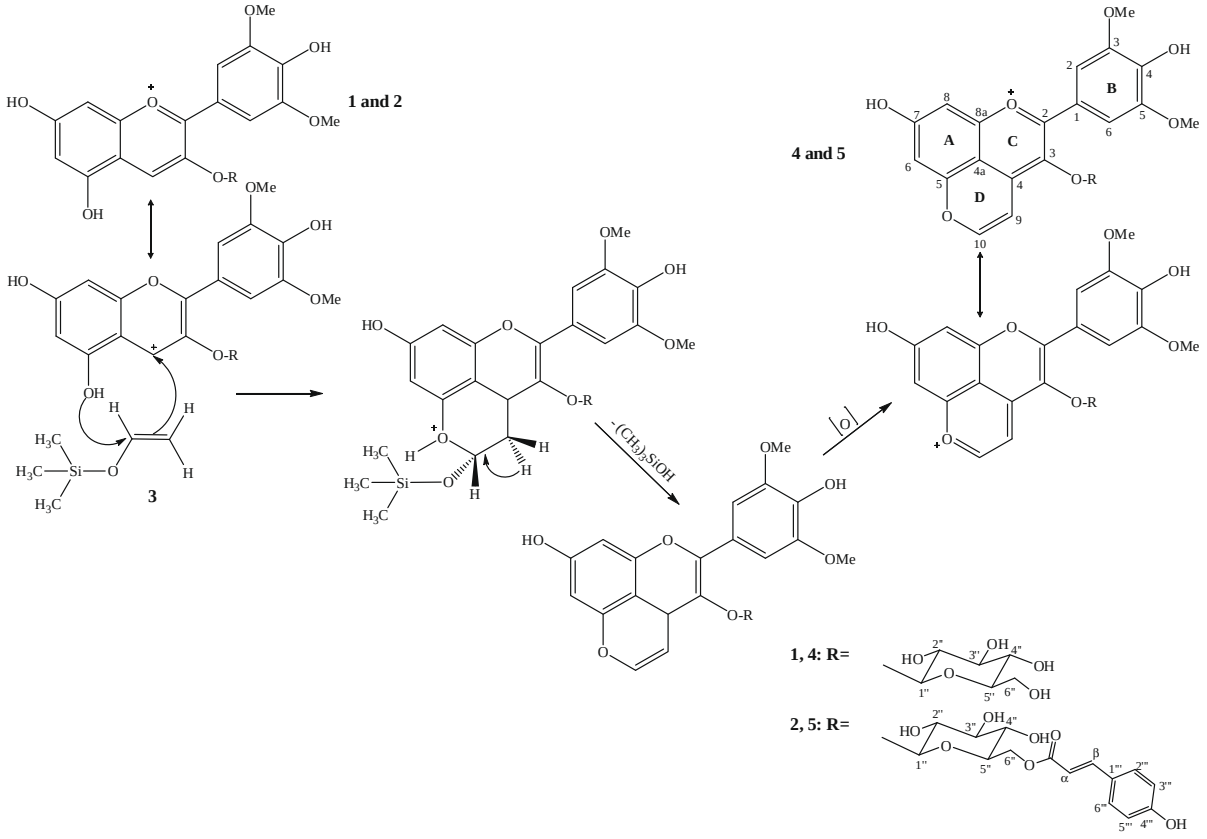
0040-4039/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2009.04.072



Scheme 1. Proposed formation mechanism of vitisins B **4** and **5** from the reaction of malvidin-3-glucoside **1** and malvidin-3-*O*-coumaroylglucoside **2** with vinyloxy-trimethylsilane **3**.

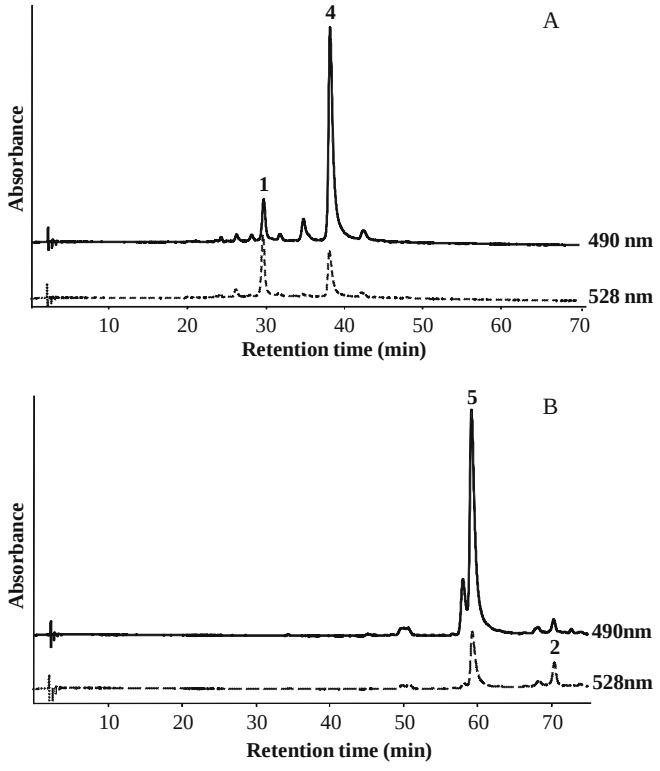


Figure 1. Chromatograms recorded from the HPLC-DAD at 490 nm and 528 nm of the reaction of malvidin-3-glucoside **1** and malvidin-3-*O*-coumaroylglucoside **2** with vinyloxy-trimethylsilane **3** to form the vitisin B of malvidin-3-glucoside **4** and the respective coumaroyl derivative **5** after 2 h at room temperature.

Table 1
^{1}H and ^{13}C chemical shifts of pigments **4** and **5**, determined in DMSO/TFA (9:1)[a]

Pigment	**4**		**5**	
Position	δ ^{1}H (ppm); *J* (Hz)	δ ^{13}C	δ ^{1}H (ppm); *J* (Hz)	δ ^{13}C
Pyranomalvidin moiety				
2	–	162.9	–	162.2
3	–	134.1	–	133.9
4	–	153.6	–	149.1
4a	–	109.7	–	109.1
5	–	153.3	–	153.4
6	7.17; d, 1.9	100.4	7.00; d, 1.9	100.8
7	–	167.7	–	167.5
8	7.39; d, 1.9	100.8	7.18; d, 1.9	100.6
8a	–	152.9	–	152.6
9	7.38; d, 5.5	103.7	7.29; d, 5.5	104.0
10	8.56; d, 5.5	160.1	8.48; d, 5.5	160.3
1′	–	118.9	–	118.7
2′, 6′	7.78; s	108.9	7.68; s	109.1
3′, 5′	–	148.8	–	148.6
4′	–	143.3	–	143.6
3′, 5′-OMe	3.91; s	56.3	3.86; s	56.5
Glucose moiety				
1″	4.70; d, 7.7	104.2	4.67; d, 7.8	104.4
2″	3.44; dd, 9.0/7.9	74.6	3.50; t, 8.4	74.1
3″	3.21; t, 8.8	76.1	3.25; t, 8.8	75.8
4″	3.11; t, 9.1	70.0	3.14; br d	70.5
5″	3.04;	77.7	3.34; dd, 9.1/1.9	74.3
6a″	3.48; dd, 11.6/1.5	61.0	4.04; dd, 11.5/1.3	63.2
6b″	3.27; dd, 11.6/5.7	61.0	4.19; dd, 11.5/7.2	63.2
Coumaroyl group				
R1CO_2R2	–	–	–	166.6
CH_{α}=$CH_{\beta}CO_2$R	–	–	5.89; d, 15.9	113.4
CH_{β}=$CHCO_2$R	–	–	7.22; d, 15.9	145.0
1‴	–	–	–	125.4
2‴,6‴	–	–	7.34; d, 8.6	130.4
3‴,5‴	–	–	6.81; d, 8.6	116.2
4‴	–	–	–	160.7

[a] Key: *, unresolved; s, singlet; d, doublet; br d, broad doublet; dd, double doublet; t, triplet.

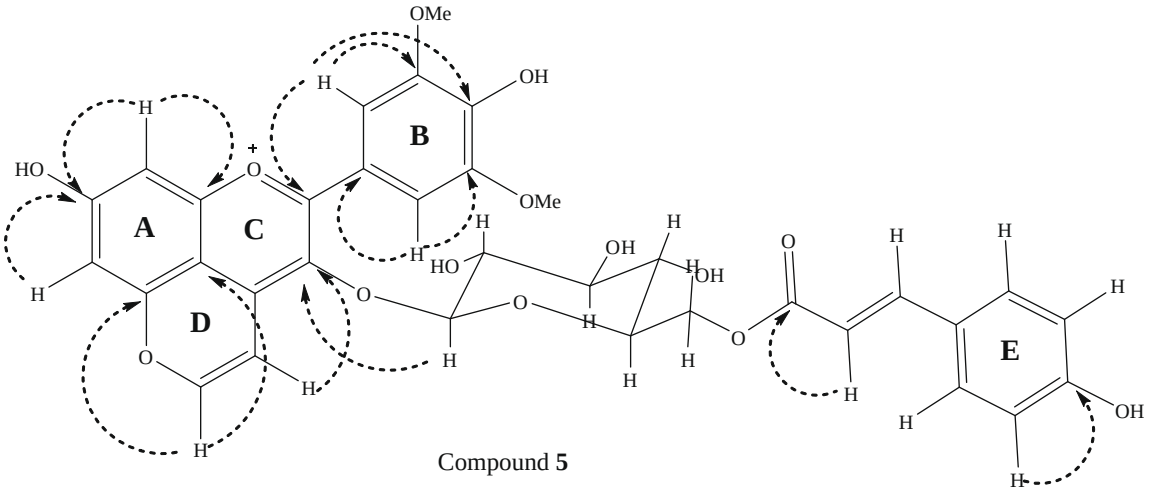


Figure 2. $^{1}H–^{13}C$ HMBC correlations of compound **5**.

group is favoured whilst at higher pH the anthocyanin form is displaced towards its neutral and thus less reactive hemiacetal form.

Compound **4** was found to correspond to vitisin B derived from malvidin-3-glucoside. In fact, the mass spectrum of the pigment obtained by LC/DAD-MS in the positive ion mode showed a molecular ion $[M]^+$ ion at *m/z* 517 and a fragment ion $[M-162]^+$ at *m/z* 355 corresponding to the loss of the glucose moiety. The structure of compound **5** was identified as the coumaroyl derivative of compound **4**. The MS data of the pigment detected yielded a $[M]^+$ ion at *m/z* 663 and a fragment ion $[M-308]^+$ at *m/z* 669 corresponding to the loss of a coumaroylglucoside residue.

The structure of these pigments was further confirmed by ^{1}H and ^{13}C NMR using 1D and 2D techniques (*g*COSY, NOESY, *g*HMBC and *g*HSQC)[14,15] (Table 1 and Fig. 2). Only the ^{1}H NMR data of the chromophore moiety of compound **4** have been described in the literature and are similar to those obtained and indicated in Table 1.[1] In this work, a complete assignment of the protons and carbons of compounds **4** and **5** was achieved. The major difference concerned the sugar moiety that in compound **5** is esterified with coumaric acid.

Acknowledgements

The authors thank Dr. Zélia Azevedo for the LC/DAD-MS analysis and Dr. Mariana Andrade for the NMR analysis. This research was supported by a PhD grant from FCT (Fundação para a Ciência e a Tecnologia—Praxis BD/22622/2005) and a grant from FCT (Fundação para a Ciência e a Tecnologia—PTDC/AGR-ALI/65503/2006, both from Portugal and by FEDER funding.

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