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# Unexpected rearrangement of pyranoanthocyanidins to furoanthocyanidins

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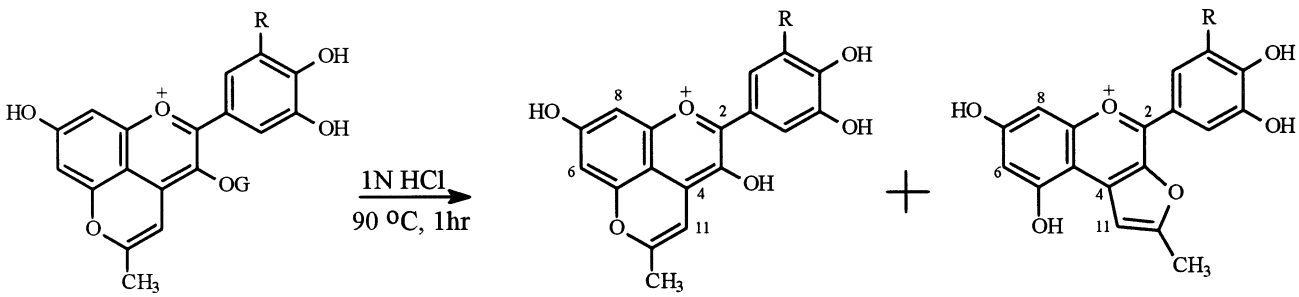
**Abstract**—Pyranoanthocyanidins generated from the respective glycosides on hydrolysis were found to undergo rearrangement to form a new type of furoanthocyanidins with a core structure of furo[2,3-*c*]-1-benzopyrylium. 

Pyranoanthocyanins with a core structure of pyrano-[4,3,2-*de*]-1-benzopyrylium are a new type of pigment. Their occurrence was first reported in red wines from which the malvidin derived wine pigments were isolated and characterised.[1] These new wine pyranoanthocyanins, understandably formed by the reaction between grape anthocyanins and pyruvic acid or vinyl phenol, are believed to be involved in the development of the final red wine colour in the course of wine maturation.[2] Compared to the common anthocyanin pigments present in flowers and fruits,[3] pyranoanthocyanins are more stable at elevated temperatures due to the extended conjugation that incorporates the benzopyrylium chromophore. Pyranoanthocyanins have subsequently been patented for potential use as stable colouring agents in the food industry.[4]

Recently, we reported the isolation and identification of pyranocyanins and pyranodelphinins from blackcurrant (*Ribes nigrum*)[5] and showed that these new blackcurrant pigments were the oxidative cycloaddition products[6] between acetone (used as the extraction solvent) and the natural blackcurrant anthocyanins, the rutinosides and glucosides of cyanidin and delphinidin.[7] Hydrolysis of these pyranoanthocyanins **1** and **2** has led to the formation of the aglycone pyranoanthocyanidins **3** and **4**, which were found in the acidic medium to undergo further rearrangement to yield the corresponding furoanthocyanidins **5** and **6** with a core structure of furo[2,3-*c*]-1-benzopyrylium. This report deals with the structural elucidation of both the newly prepared pyranoanthocyanidins and their rearranged isomers, furoanthocyanidins (**3**–**6**), by means of 2D NMR.




**1** R = H, G = rutinose
**2** R = OH, G = rutinose

**3** R = H
**4** R = OH

**5** R = H
**6** R = OH

**Scheme 1.** Acid hydrolysis of pyranoanthocyanidins.

*Keywords*: pyranoanthocyanidins; furoanthocyanidins; rearrangement; 2D NMR.
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Pyranoanthocyanins were hydrolysed in 1N HCl aqueous medium at 90°C for an hour (Scheme 1) and the products were first separated by chromatography on a Polyamide column and purified by semi-preparative HPLC. The hydrolysis product obtained from pyranocyanin A (**1**) in 41% yield gave a single broad HPLC peak and showed a peak at $m/z$ 325.0715 in its electron spray mass spectrum (ESMS), operated in the positive mode that was consistent with the molecular formula of $C_{18}H_{13}O_6$ (calcd 325.0707) for the expected aglycone. The $^1H$ and $^{13}C$ NMR spectra of the product, however, showed chemical shifts that were consistent with a mixture of two compounds. The major compound was identified as the aglycone 12-methylpyranocyanidin (**3**) based on the almost identical NMR data (Tables 1 and 2) to those of the starting pyranocyanin A (**1**)[5] minus the sugar moiety. The $^1H$ NMR spectrum of the minor compound was also similar, showing an aliphatic three-proton-singlet indicative of a methyl group and two *meta*-coupled protons for a phloroglucinol ring, a singlet for an olefinic proton and an ABX system for a catechol ring. The two *meta*-coupled protons at $\delta$ 6.69 and 6.87 of the phloroglucinol ring were markedly different from those of the corresponding protons in 12-methylpyranocyanidin ($\delta$ 7.00 and 7.08), but were in good agreement with the protons found in cyanidin-3-rutinoside ($\delta$ 6.68 and 6.87)[8] therefore suggesting that there were free hydroxyl groups at both C-5 and C-7. This deduction was further corroborated by similar comparisons of the chemical shifts of C-6 and C-8 ($\delta$ 103.54 and 96.55) with those of 12-methylpyranocyanidin ($\delta$ 101.49 and 100.81) and cyanidin-3-rutinoside ($\delta$ 103.91 and 95.73). Since the minor compound must also have the same molecular composition as the major compound as revealed by ESMS, a likely chemical structure for the minor compound was 12-methylfurocyanidin as a result of involvement of the C-3 hydroxyl to give rise to a furan ring (see below). This deduction was strongly supported by the observation of the high field chemical shift of the methyl group ($\delta_C$ 15.8) consistent with that of 2-methylfuran ($\delta$ 12.3)[9] as compared to the corresponding methyl carbon shift of 12-methylpyranocyanidin ($\delta$ 21.8). In addition, the olefinic proton ($\delta$ 7.50) and the corresponding carbon ($\delta$ 109.70) were also consistent with the H-3 and C-3 chemical shifts of furans, thus confirming the minor compound was indeed 12-methylfurocyanidin (**5**). The assignment of the chemical structures of both 12-methylpyranocyanidin (**3**) and 12-methylfurocyanidin (**5**) were fully confirmed by 2D NMR including long range coupling experiments (HMBC).

**Table 1.** $^1H$ NMR (300 MHz, $CD_3OD$/TFA 9:1) data of pyrano- and furoanthocyanidins **3**–**6**[a]

| H | 3 | 4 | 5 | 6 |
|---|---|---|---|---|
| 6 | 7.00 *d* (1.9) | 7.00 *d* (1.9) | 6.69 *d* (2.1) | 6.69 *d* (2.1)0 |
| 8 | 7.08 *d* (1.9) | 7.07 *d* (1.9) | 6.87 *d* (2.1) | 6.86 *br s* |
| 11 | 6.97 *s* | 6.97 *s* | 7.50 *d* (0.7) | 7.42 *s* |
| 2′ | 7.86 *d* (2.3) | 7.52 *s* | 7.99 *d* (2.3) | 7.60 *s* |
| 5′ | 6.94 *d* (8.8) | – | 7.09 *d* (7.7) | – |
| 6′ | 7.88 *dd* (8.8, 2.3) | 7.52 *s* | 8.08 *dd* (8.6, 2.3) | 7.60 *s* |
| $CH_3$ | 2.61 *s* | 2.63 *s* | 2.84 *s* | 2.81 *s* |

[a] Coupling constants ($J$) in parentheses.

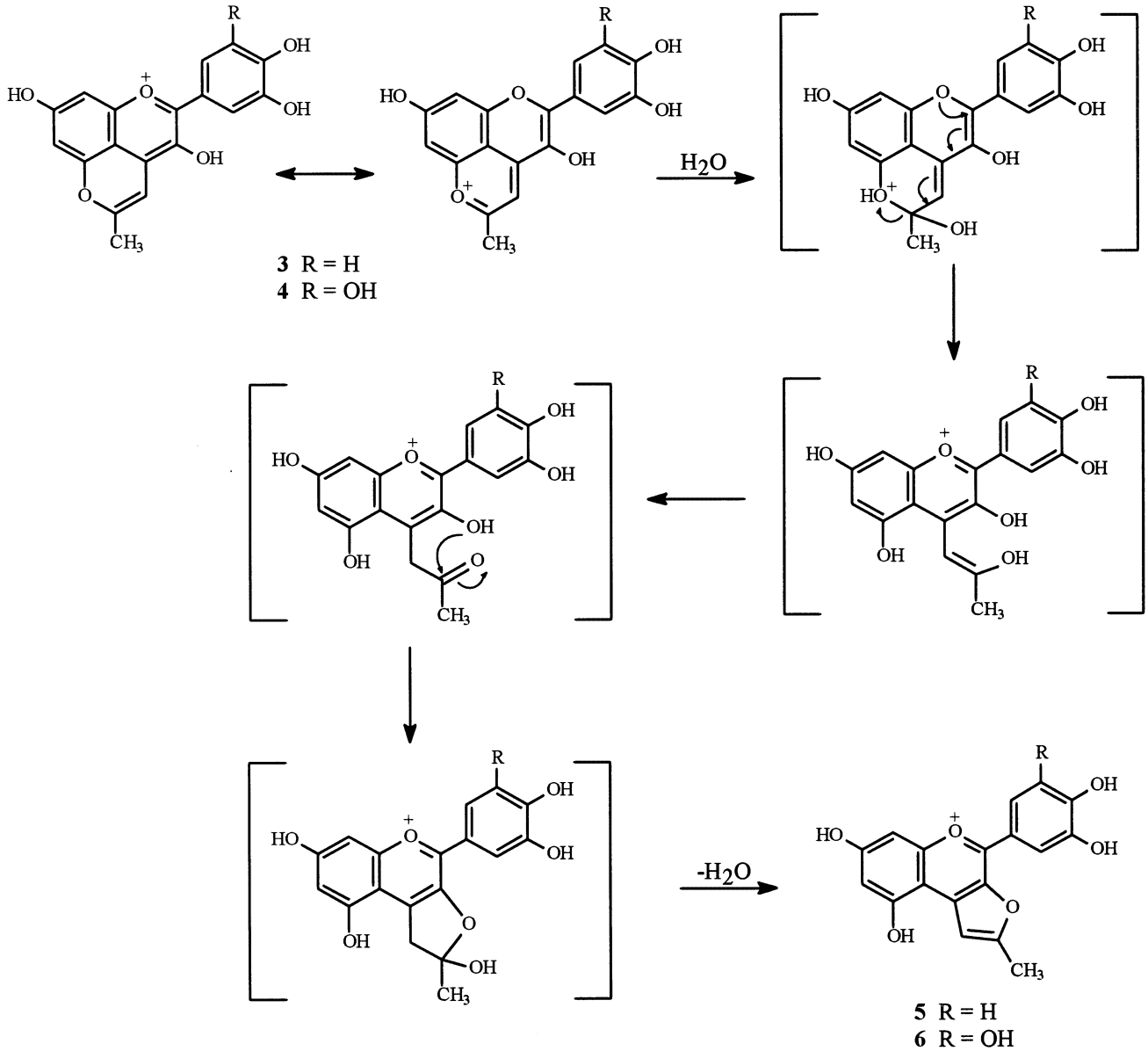
**Table 2.** $^{13}C$ NMR (75 MHz, $CD_3OD$/TFA 9:1) data of pyrano- and furoanthocyanidins **3**–**6**

| C | 3 | 4 | 5 | 6 |
|---|---|---|---|---|
| 2 | 160.41 | 159.12 | 155.87 | 155.21 |
| 3 | 135.60 | 135.05 | 142.26 | –[a] |
| 4 | 147.08 | 149.12 | 147.85 | – |
| 5 | 155.05 | 154.40 | 159.86 | 159.59 |
| 6 | 101.49 | 101.14 | 103.54 | 103.71 |
| 7 | 167.98 | 166.97 | 167.51 | 166.82 |
| 8 | 100.81 | 100.53 | 96.33 | 96.48 |
| 9 | 154.00 | 153.20 | 157.08 | 156.58 |
| 10 | 109.28 | 108.74 | 104.55 | – |
| 11 | 101.64 | 101.43 | 109.70 | 109.70 |
| 12 | 173.52 | 173.60 | 177.67 | 177.96 |
| 1′ | 122.80 | 121.38 | 119.79 | – |
| 2′ | 117.83 | 110.82 | 117.70 | 110.72 |
| 3′ | 147.32 | 146.67 | 148.55 | 148.19 |
| 4′ | 153.19 | 140.52 | 156.18 | – |
| 5′ | 117.19 | 146.67 | 118.28 | 148.19 |
| 6′ | 125.38 | 110.82 | 126.81 | 110.72 |
| $CH_3$ | 21.84 | 21.86 | 15.82 | 16.16 |

[a] Quaternary carbon signals were too weak to recognise or were obscured by TFA and/or other signals.

Hydrolysis of pyranodelphinin A (**2**) gave rise to a similar mixture of products **4** and **6** in a combined yield of about 20%. The chemical structures of both compounds, 12-methylpyranodelphinidin (**4**) and 12-methylfurodelphinidin (**6**), were deduced by NMR (Tables 1 and 2) chemical shift comparisons with the corresponding pyrano- and furocyanidin pair discussed earlier. The $^1H$ NMR spectrum of **4** showed a characteristic two-proton singlet ($\delta$ 7.52) for the pyrogalloyl ring, another singlet ($\delta$ 6.97) accounting for the pyrano ring and two *meta*-coupled doublets ($\delta$ 7.00 and 7.09) for the phloroglucinol ring in addition to a three-proton-singlet ($\delta$ 2.63) for the methyl group. The minor product **6** was distinguished from **4** by the characteristic position of the *meta*-coupled proton signals at $\delta$ 6.69 and 6.87 of the phloroglucinol ring and the singlet at $\delta$ 7.42 for the furan ring proton. The corresponding carbon signals of **6** observed at $\delta$ 103.7 (C-6), 96.5 (C-8), 109.7 (C-11) and 16.2 ($CH_3$) in the $^{13}C$ NMR spectrum were also consistent with the structure. The ESMS spectrum of the mixture only showed one peak at $m/z$ 341.0614 which was consistent with the molecular formula of $C_{18}H_{13}O_7$ (calcd 341.0656) for both compounds.

The formation of furoanthocyanidins **5** and **6** during the acid-catalysed hydrolysis of the corresponding pyranoanthocyanins suggests the unexpected relative reactivity of the pyran ring. The rearrangement can be envisaged as proceeding by an initial addition of water to the mesomeric form of the starting compounds **3** and **4** followed by delocalisation of the electron pair of the upper oxygen with concomitant ring opening to give




**Scheme 2.** Rearrangement of pyranoanthocyanidins to furoanthocyanidins.

rise to the anthocyanidin–acetone adduct intermediates (Scheme 2). Subsequent cyclization involving the C-3 hydroxyl results in the formation of the furan ring. It is conceivable that this type of rearrangement could also occur during red wine development and thereby attributing to the final matured wine colour.

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8. NMR data of cyanidin-3-rutinoside for comparison: $^{1}$H NMR (300 MHz, $CD_3OD$/TFA 9:1) $\delta$ 1.18 (d, *J* 6.3 Hz, H-6‴), 3.38–3.92 (sugar-H), 4.08 (d, *J* 9.9 Hz, H-6″a), 4.68 (d, *J* 1.2 Hz, H-1‴), 5.29 (d, *J* 7.6 Hz, H-1″), 6.68 (d, *J* 1.9 Hz, H-6), 6.87 (d *J* 1.9 Hz, H-8), 6.99 (d, *J* 8.8 Hz, H-5′), 7.98 (d, *J* 2.2 Hz, H-2′), 8.22 (dd, *J* 8.7, 2.2 Hz, H-6′), 8.89 (s, H-4); $^{13}$C NMR (75 MHz, $CD_3OD$/TFA) $\delta$ 18.30 (C-6‴), 68.21 (C-6″), 70.16 (C-5‴), 71.64 (C-4″), 72.26 (C-2‴), 72.85 (C-3‴), 74.33 (C-4‴), 75.09 (C-2″), 77.85 (C-3″), 78.42 (C-5″), 95.73 (C-8), 102.55 (C-1‴), 103.91 (C-6, 1″), 113.59 (C-10), 117.87 (C-5′), 118.77 (C-2′), 121.52 (C-1′), 128.83 (C-6′), 136.47 (C-4), 145.96 (C-3), 147.76 (C-3′), 156.23 (C-4′), 157.91 (C-5), 159.39 (C-9), 164.30 (C-2), 170.82 (C-7).
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