M.J. Mphahlele and M.A. Fernandes, *S. Afr. J. Chem.*, 2002, **55**, 97-110,
<http://journals.sabinet.co.za/sajchem/>,
<http://ejour.sabinet.co.za/images/ejour/chem/chem_v55_a9.pdf>.

RESEARCH ARTICLE

Isolation and Crystal Structure of 3-Aryl-1-(2-hydroxyphenyl)-3-hydroxy-1-propanones Derived from Claisen–Schmidt Condensation of 2-Hydroxyacetophenone with Benzaldehyde Derivatives

Malose J. Mphahlele*[,a] and Manuel A. Fernandes[b]

[a] Department of Chemistry and Biochemistry, Medical University of Southern Africa, P.O. Box 235, Medunsa 0204, Republic of South Africa; e-mail address: mphahlele@medunsa.ac.za.

[b] Molecular Sciences Institute, School of Chemistry, University of the Witwatersrand, P.O. Wits, 2050, Republic of South Africa.

* To whom correspondence should be addressed.

Received 3 October 2001; Revised 2 May 2002; Accepted 25 May 2002

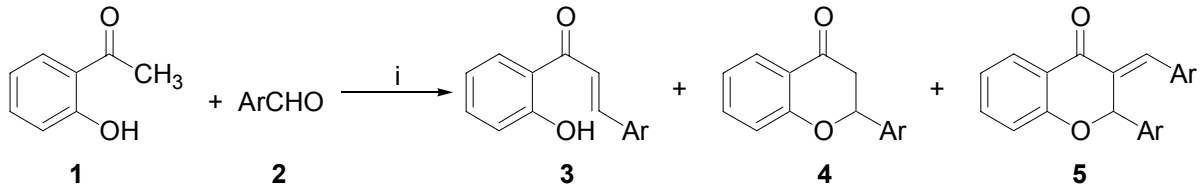
Abstract

2-Hydroxyacetophenone reacted with benzaldehyde derivatives under alkalinic conditions followed by addition of dilute hydrochloric acid solution to afford mixtures of the known 2-hydroxychalcone derivatives and the corresponding previously undescribed 3-aryl-1-(2-hydroxyphenyl)-3-hydroxy-1-propanones. The isolation of the β-hydroxyketone derivatives depends on the work-up conditions. Their structures were established using a combination of NMR, IR and mass spectroscopic techniques. The conformation of the β-hydroxyketones was probed using ^{1}H NMR spectroscopy and X-ray crystallography.

Keywords Claisen–Schmidt condensation; aldol reaction; chalcones; β-hydroxy-ketones; X-ray crystallography.

1. Introduction

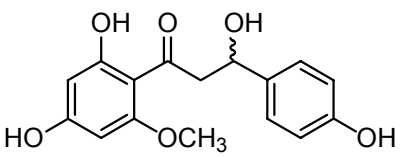
The laboratory synthesis of 2'-hydroxychalcones continues to attract considerable attention because of their isolation from plants, their striking pharmacological activities[1] and their application as synthetic intermediates for flavanones and related systems.[2] Typical laboratory synthesis of 2'-hydroxychalcones involves Claisen–Schmidt aldol condensation of 2-hydroxyacetophenones **1** with benzaldehyde derivatives **2** (Scheme 1).[3–5] Depending on the pH of the solution, this reaction is reported to give either the chalcone **3**, flavanone **4**, 3-arylmethyleneflavanone **5**, or a mixture of these (Scheme 1).[4] Weaker alkali (0.4–10%) or buffers with pH of 7.6–12 may give the flavanone, the chalcone, or a mixture of the two,[4] while polyhydroxy derivatives are reported to condense best in aqueous alcoholic potassium hydroxide (50–70%) to afford chalcones.[3a,4,5] Recently, the 4,2',4'-β-tetrahydroxy-6'-methoxy-α,β-dihydrochalcone **6** was isolated along with its chalcone derivative from the aerial parts of *Vitex leptobotrys*.[6] Claisen–Schmidt condensation products of this type are implicated in the mechanism of chalcone formation, and are known to dehydrate spontaneously *in situ* to the corresponding conjugated carbonyl compounds **3**.[7] They do not feature at all in *The Chemistry of Chalcones and Related Compounds*[2] or *Topics in Flavanoid Chemistry and Biochemistry*.[8]



1 **2** **3** **4** **5**

Scheme 1 *Reagents:* i, KOH (aq.), EtOH.

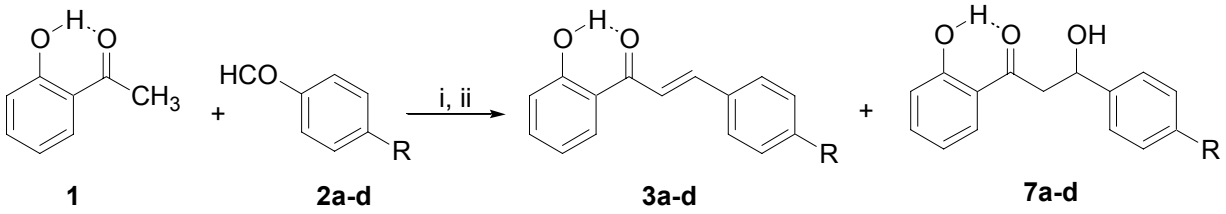
The recent isolation of compound **6** from plant material[6] coupled with our interest in flavanoid chemistry prompted us to investigate suitable work-up conditions that could lead to the trapping and isolation of the β-hydroxyketone intermediates from the Claisen–Schmidt condensation of 2-hydroxyacetophenones with 4-substituted benzaldehyde derivatives.



6

2. Results and Discussion

We repeated the literature procedure[3a,5] and quenched the cold alkalinic reaction mixture with ice-cold water followed by slow addition of ice-cold 10% HCl solution at 0–5 °C (Scheme 2). The precipitated products were subjected to column chromatography using toluene as eluent to afford two major fractions as bright yellow and colourless crystals, respectively. The melting points and the spectral data of the chalcone products (bright yellow crystals) were found to be consistent with those reported before.[5] The structures of the colourless products were unambiguously determined to be the 3-aryl-1-(2-hydroxyphenyl)-3-hydroxy-1-propanone derivatives **7** by means of a combination of ^{1}H NMR, ^{13}C NMR, IR and high-resolution mass spectroscopic techniques and elemental analysis.



1 **2a-d** **3a-d** **7a-d**

Scheme 2 (**a**) R = H; (**b**) R = F; (**c**) R = Cl; (**d**) R = Br.
Reagents: i, KOH (aq.), EtOH; ii, 10% HCl (aq.).

In addition to the aromatic signals (at δ *ca*. 6.8–7.8 ppm), the 300 MHz ^{1}H NMR spectra of systems **7** obtained in $CDCl_3$ show the presence of the following signals: (i) three pairs of well-resolved double doublets at δ *ca*. 2.50 (J_{vic} 2.8 and J_{gem} 17.7 Hz, H_a), 2.77 ppm (J_{vic} 9.2 and J_{gem} 17.6 Hz, H_b) and 4.91 (J_{vic} 2.8 and J_{vic} 9.1Hz, H_c) the first two signals corresponding to the diastereotopic methylene protons and the other to the methine proton; (ii) a relatively broad intense singlet corresponding to the secondary OH group and overlapping with the aromatic signals; and (iii) a sharp singlet at δ *ca.* 12.0 ppm corresponding to the phenolic proton, which resonates significantly downfield because of strong intramolecular hydrogen bonding with the carbonyl oxygen. The presence of the secondary OH and phenolic proton signals is further confirmed by the hydroxyl absorption band(s) at ν_{max} *ca*. 3100 and 3550cm^{-1} in their IR spectra. The presence of the double doublets corresponding to the methylene proton and the hydroxyl proton signals ruled out the possibility of the flavanones **4** and the 3-arylideneflavanones **5**.

In their pure crystalline state, the β-hydroxyketones **7** are highly stable towards strong acidic medium, for example, they resist dehydration in refluxing glacial acetic acid containing catalytic amount of sulfuric acid or in ethanol–phosphoric acid mixture under reflux. However, when subjected to 5–10% NaOH (aq.) at room temperature overnight, a stirred ethanolic suspension of system **7** affords the chalcone derivative **3** upon quenching with concentrated hydrochloric acid. The observed stability of these β-hydroxyketones in their crystalline state towards acidic media can be attributed to strong intramolecular hydrogen bonding between the carbonyl and the phenolic hydroxyl (2'-OH) groups and intermolecular hydrogen bonding between the secondary hydroxyl (2-OH) groups, which would inhibit acid-catalyzed dehydration. The first step under basic conditions would then imply base-catalyzed breakdown of the strong intramolecular and intermolecular hydrogen bonds between the carbonyl group and the hydroxyl groups.

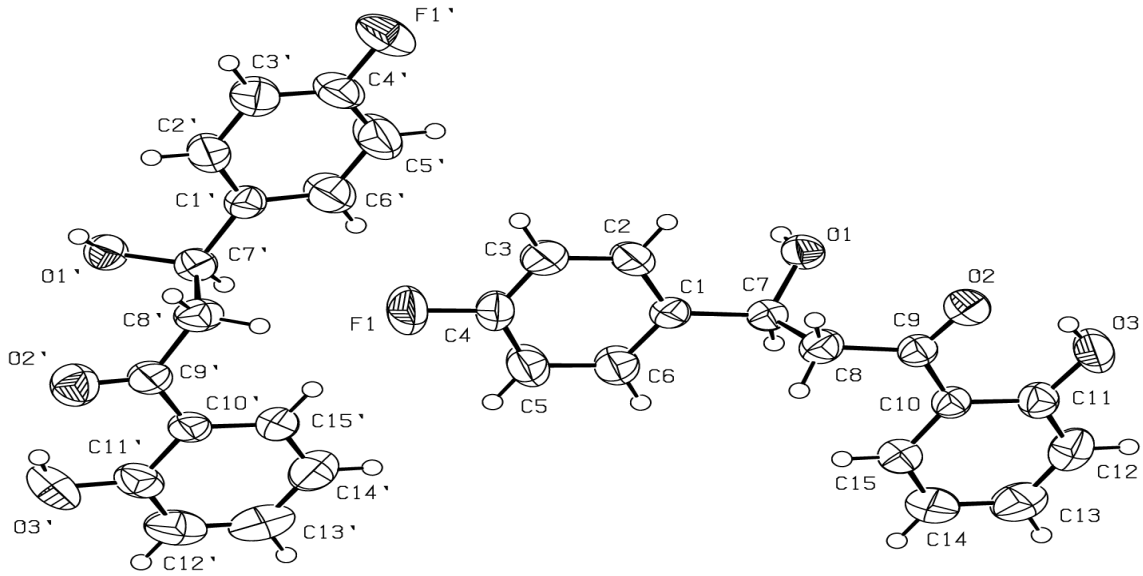
The smaller J_{vic} values (2.8 Hz) requires the methine (3-H_c) to be *gauche* to the other methylene proton (2-H_a), and the larger J_{vic} values (9.1 Hz) indicate *anti* coupling between 2-H_b and 3-H_c. A single crystal X-ray structure determination (Table 1; see Experimental) was carried out on **7b**. The molecule crystallizes in *P*1 with two independent molecules in the asymmetric unit (Fig. 1a). Moving molecule 2 through the inversion centre, *i.e*., inverting molecule 2, creates an alternative asymmetric unit in which the two molecules appear to be related by a 2-fold axis. On closer examination this is really a pseudo 2-fold axis (Fig. 1b), and no higher symmetry is detected when using the built-in symmetry checking tools in PLATON.[9d] Molecules in this structure are held together by strong intra- and intermolecular hydrogen bonds (Fig. 2; Table 2). The intramolecular hydrogen bonds, O3–H31···O2 and O3'–H31'···O2', reinforce and presumably contribute significantly to the observed co-planarity around the carbonyl and phenolic groups. Molecules 1 and 2 are kept together by hydrogen bonds between O1 and O1' (Table 2). In addition, O1 (and O1' in molecule 2) is hydrogen bonded to another O1 atom (or O1' in molecule 2) of a molecule generated by the inversion centre (Table 2; Fig. 2). The combination of the two hydrogen bonds results in a hydrogen-bonded chain (or catemer motif) of molecules extending down the *a*-axis (Fig. 2 and Fig. 3). It also provides a reason for the disorder of the hydrogen atoms on O1 (H1A and H1B) and O1' (H1A' and H1B'); since these two atoms are chemically equivalent, there is no significant energetic advantage in the hydrogen atom being directed in either direction, resulting in the

observed 50:50 disorder of H1 and H1' over the two positions (see Experimental). These hydrogen-bonded chains are then linked together through weak C–H···O and C–H···F interactions (Table 2).

Table 1 Crystal data and details of the X-ray data collection and refinements for **7b**.

Empirical formula	$C_{15}H_{13}FO_3$
CCDC-code number	186352
Formula weight	260.25
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	*P*1
Unit cell dimensions	*a* = 8.6675(12) Å; *b* = 11.7690(17) Å; *c* = 12.8421(18) Å α = 94.991(3)°; β = 104.890(3)°; γ = 93.477(3)°
Volume	1256.5(3) Å^3
Z	4
Density (calculated)	1.376 g cm^{-3}
Absorption coefficient μ	0.105 mm^{-1}
F(000)	544
Crystal size (mm)	0.36 × 0.14 × 0.11
Theta range for data collection	1.65 to 26.00°
Index ranges	$-10 \le h \le 10$; $-14 \le k \le 14$; $-15 \le l \le 10$
Reflections collected	7459
Independent reflections	4894 [R_{int} = 0.0239]
Completeness to θ	98.8% (to θ = 26.00°)
Absorption correction	Multi-scan
Max. and min. transmission	0.9886 and 0.9632
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4894 / 4 / 362
Goodness-of-fit on F^2	0.940
Final R indices [$I > 2\sigma(I)$]	*R1* = 0.0515, *wR2* = 0.1191
R indices (all data)	*R1* = 0.1177, *wR2* = 0.1420
Extinction coefficient	0.0068(15)
Largest diff. peak and hole	0.185 and –0.151 e Å^{-3}

a)



b)

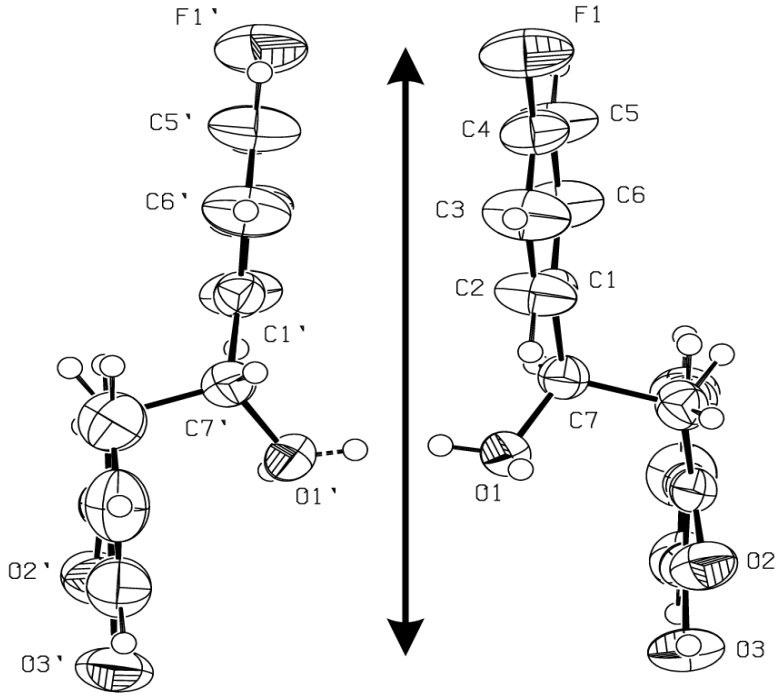


Figure 1 ORTEP diagrams (50% ellipsoids) for **7b**, showing **a)** crystallographic labelling (note the relative stereochemistry of C7 and C7') and **b)** the pseudo 2-fold axis.

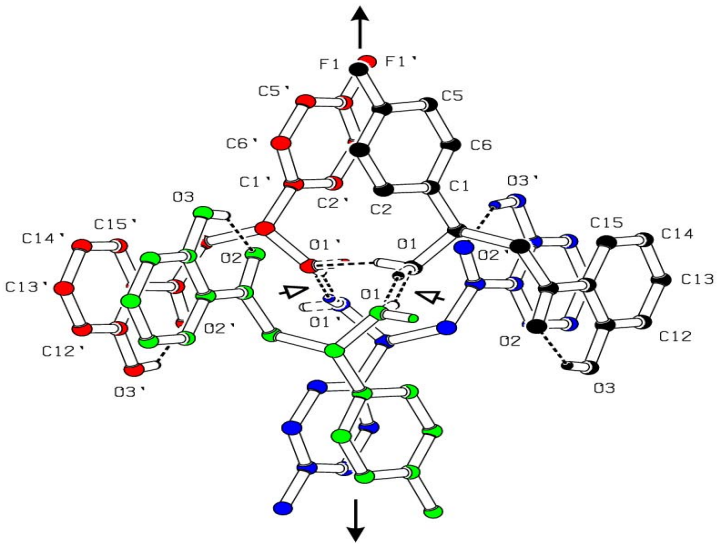


Figure 2 Platon diagram showing the hydrogen bonding pattern in the structure of **7b**. Hollow arrows indicate centres of inversion, while the solid arrows indicate the pseudo 2-fold axis.

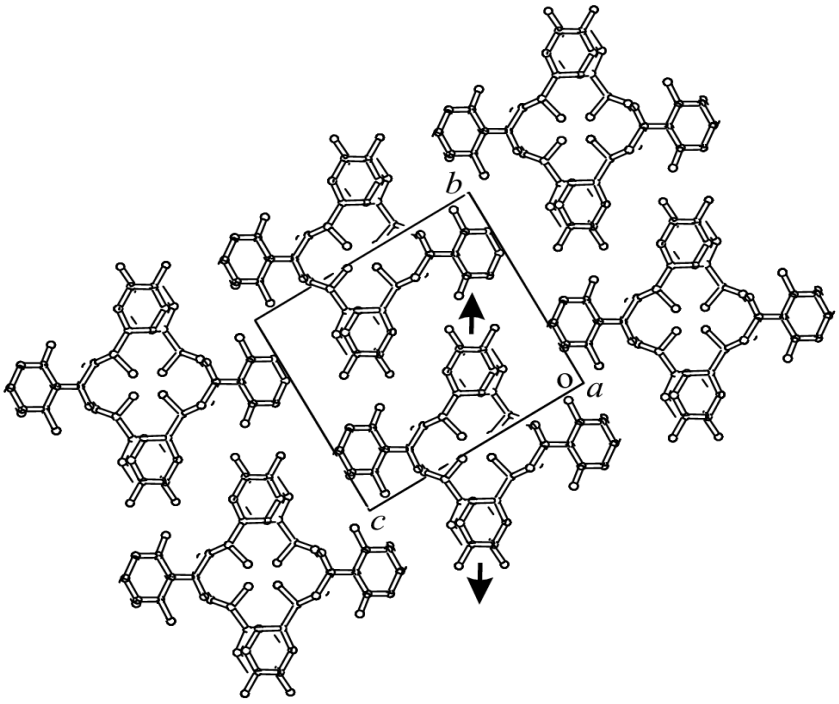
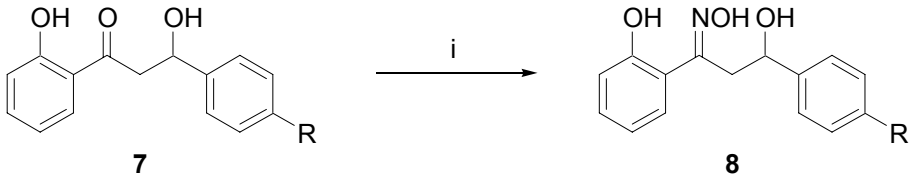


Figure 3 Molecular packing diagram as a projection down the *a*-axis. Arrows indicate the position of the pseudo 2-fold axis. Note that this axis appears to relate to one hydrogen-bonded chain but not to the rest of the structure.

Table 2 Hydrogen-bond and weak interaction distances (Å) and angles (°) in **7b**.

D–H···A	D–H	H···A	D···A	D–H···A	Symmetry code
O1–H1A···O1'	0.82(3)	1.89(3)	2.690(3)	164(3)	1–x, 1–y, 1–z
O1–H1B···O1	0.82(4)	1.97(4)	2.766(2)	162(5)	–x, 2–y, 1–z
O1'–H1A'···O1	0.82(3)	1.90(3)	2.691(3)	163(3)	1–x, 1–y, 1–z
O1'–H1B'···O1'	0.82(4)	1.97(4)	2.767(2)	164(5)	1–x, –y, 1–z
O3–H31···O2	0.82	1.84	2.559(2)	145.6	Intramolecular
O3'–H31'···O2'	0.82	1.82	2.546(3)	146.4	Intramolecular
C2–H2···O2	0.93	2.55	3.242(3)	131.2	–x, 2–y, 1–z
C6'–H6'···F1	0.93	2.54	3.468(3)	175.8	1+x, y, z
C7–H7···O2'	0.98	2.59	3.458(3)	147.1	x, 1+y, z

Systems **7** are suitable candidates for further studies of chemical transformations and biological activity. Selected systems **7** were converted into the corresponding oxime derivatives **8** with hydroxylamine hydrochloride and sodium acetate trihydrate in ethanol under reflux without any traces of dehydration product(s) (Scheme 3). The ^{1}H NMR spectra of the oxime derivatives obtained as solutions in $CDCl_3$ are characterized by the aliphatic proton signals (three sets of double doublets at δ *ca*. 3.20, 3.40 and 5.15 ppm) and the aromatic proton signals (at δ *ca*. 6.70–7.50 ppm), and did not show signals corresponding to the OH proton(s).



7 **8**

Scheme 3 (**a**) R = F; (**b**) R = Cl.
Reagents: i, $NaOAC{\cdot}3H_2O$, $NH_2OH{\cdot}HCl$, EtOH, reflux.

Nevertheless, their oxime nature was confirmed by the absence of ^{13}C=O signals and the presence of ^{13}C=N resonance at δ *ca*. 157.5 ppm, and the presence of the C=N and OH IR absorption bands at ν_{max} *ca*. 1605 cm^{-1} and in the region ν_{max} 3000–3410 cm^{-1}, respectively. The molecular formulae of systems **8** ($C_{15}H_{14}NO_3X$) represent, in each case, the closest fit (consistent with available atoms) to the experimentally determined accurate *m/z* values.

3. Experimental

Melting points were recorded on a Thermocouple digital melting point apparatus and are uncorrected. IR Spectra were recorded as KBr pellets or $CHCl_3$ solutions on a Hitachi 270–30 infrared spectrophotometer. For column chromatography, Merck Kieselgel 60 (0.063–0.200 mm) was used as a stationary phase. NMR spectra were obtained on a Varian Mercury 300 MHz spectrometer and they were calibrated using solvent signals (^{1}H 7.25 ppm and ^{13}C 77.0 ppm). High-resolution mass spectra were recorded at Cape Technikon Mass Spectrometry Unit using VG–70 SEQ MASPEC II[32] (scanning at RP 10 000). Combustion analyses (C, H, N) were carried out at the University of Cape Town.

Reaction of **1** *with* **2***. Typical procedure.*

A cold mixture of 2-hydroxyacetophenone **1** (1 equiv.) and benzaldehyde derivative **2** (1 equiv.) in EtOH (2.8 ml per mmol of **1**) was treated with a cold solution of KOH (1.3 equiv. per mmol of **1**) in H_2O (1.2 ml per mmol of **1**). The mixture was kept at 0–5 °C for 5 d with occasional shaking and then diluted with ice cold H_2O (2.8 ml per mmol of **1**). The cold (0–5 °C) aqueous solution was quenched slowly with cold 10% HCl solution until the product precipitated out of solution. The precipitate was filtered and the crude product was purified by column chromatography (elution with toluene) to afford two fractions: *3-aryl-1-(2-hydroxyphenyl)prop-2-en-1-one* **3** and *3-aryl-3-hydroxy-1-(2-hydroxyphenyl)propan-1-one* **7**, respectively. The following products were isolated and characterized:

1-(2-Hydroxyphenyl)-3-phenylprop-2-en-1-one **3a** (R = H). Solid (20%), mp 90–92 °C (EtOH) (lit.,[5] 87–88 °C).

3-Hydroxy-1-(2-hydroxyphenyl)-3-phenylpropan-1-one **7a** (R = H). Solid (45%), mp 108–110 °C (EtOH); δ_H (300 MHz, $CDCl_3$) 3.35 (1H, dd, *J* 3.3 and 17.7 Hz, 2-H), 3.45 (1H, dd, *J* 8.7 and 17.7 Hz, 2-H), 5.36 (1H, dd, *J* 3.3 and 8.9 Hz, 3-H), 6.88 (1H, dt, *J* 1.0 and 7.8 Hz, 5'-H), 6.99 (1H, dd, *J* 0.6 and 8.4 Hz, 3'-H), 7.27–7.53 (6H, m, 4'-H and C_6H_5), 7.69 (1H, dd, *J* 1.2 and 8.0 Hz, 6'-H) and 12.1 (1H, s, 2'-OH); δ_C (75 MHz, $CDCl_3$) 47.1 (C-2), 69.8 (C-3), 118.6 (C-3'), 119.1 (C-5'), 119.3 (C-1'), 125.7 (C-2" and C-6"), 127.9 (C-4"), 128.6 (C-3" and C-5"), 130.0 (C-4'), 136.9 (C-6'), 142.6 (C-1"), 162.5 (C-2') and 205.4 (C=O); ν_{max}/cm^{-1} 1630 (CO) and 3200 (OH); *m/z* 242 (M^+, 4.3),

224 (64.2), 223 (30.1), 147 (28.2), 136 (43.8), 121 (100), 120 (36.9), 105 (34.3) and 77 (40.1) (Found: M^+, 242.0945. $C_{15}H_{14}O_3$ requires *M* 242.0943).

3-(4-Fluorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one **3b** (R = F). Solid (10%), mp 118 °C (EtOH) (lit.,[5] 118–119 °C).

3-(4-Fluorophenyl)-3-hydroxy-1-(2-hydroxyphenyl)propan-1-one **7b** (R = F). Solid (60%), mp 120 °C (EtOH); δ_H (300 MHz, $CDCl_3$) 3.29 (1H, dd, *J* 3.8 and 17.6 Hz, 2-H), 3.42 (1H, dd, *J* 8.4 and 17.6 Hz, 2-H), 5.33 (1H, dd, *J* 3.8 and 8.4 Hz, 3-H), 6.88 (1H, dt, *J* 0.9 and 7.6 Hz, 5'-H), 6.99 (1H, dd, *J* 0.9 and 8.4 Hz, 3'-H), 7.40 (2H, t, *J* 8.4 Hz, 3"-H and 5"-H), 7.40 (2H, t, *J* 8.6 Hz, 2"-H and 6"-H), 7.48 (1H, dt, *J* 1.6 and 8.4 Hz, 4'-H), 7.68 (1H, dd, *J* 1.4 and 8.0 Hz, 6'-H) and 12.05 (1H, s, 2'-OH); δ_C (75.0 MHz, $CDCl_3$) 47.1 (C-2), 69.2 (C-3), 115.4 (d, $^2J_{CF}$ 21.3 Hz, C-3" and C-5"), 118.6 (C-3'), 119.1 (C-5'), 119.2 (C-1'), 127.4 (d, $^3J_{CF}$ 8.4 Hz, C-2" and C-6"), 130.0 (C-6'), 136.9 (C-4'), 138.5 (d, $^4J_{CF}$ 3.1 Hz, C-1"), 162.2 (d, $^1J_{CF}$ 244.7 Hz, C-4"), 162.5 (C-2') and 205.2 (C=O); ν_{max}/cm^{-1} 1630 (CO) and 3200 (OH); *m/z* 260 (M^+, 3.8), 242 (40.3), 136.1 (21.1), 121.0 (100), 97 (15.4) and 95 (16.9) (Found: M^+, 260.0855. $C_{15}H_{13}O_3F$ requires *M* 260.08489); Anal. calc. for $C_{15}H_{13}O_3F$ (260.35): C, 69.2; H, 5.03%. Found: C, 68.95; H, 4.85%.

3-(4-Chlorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one **3c** (R = Cl). Solid (35%), mp 148–150 °C (EtOH) (lit.,[5] 150 °C).

3-(4-Chlorophenyl)-3-hydroxy-1-(2-hydroxyphenyl)propan-1-one **7c** (R = Cl). Solid (50%), mp 122 °C (EtOH); δ_H (300 MHz, $CDCl_3$) 3.33 (1H, dd, *J* 4.2 and 17.7 Hz, 2-H), 3.431(1H, dd, *J* 8.0 and 17.7 Hz, 2-H), 5.34 (1H, dd, *J* 4.1 and 7.9 Hz, 3-H), 6.89 (1H, dt, *J* 1.2 and 7.7 Hz, 5'-H), 7.00 (1H, dd, *J* 1.0 and 8.5 Hz, 3'-H), 7.36 (4H, s, 2"-H, 3"-H, 5"-H and 6"-H), 7.50 (1H, dt, *J* 1.6 and 7.8 Hz, 4'-H), 7.68 (1H, dd, *J* 1.6 and 8.0 Hz, 6'-H), 7.87 (1H, br s, 2-OH) and 12.02 (1H, s, 2'-OH); δ_C (75.0 MHz, $CDCl_3$) 47.0 (C-2), 69.2 (C-3), 118.7 (C-3'), 119.2 (C-5'), 119.3 (C-1'), 127.4 (C-3" and C-5") 128.8 (C-2" and C-6"), 130.0 (C-4'), 133.5 (C-4"), 137.0 (C-6'), 141.1 (C-1"), 162.6 (C-2') and 205.2 (CO); ν_{max}/cm^{-1} 1640 (CO), 3100 (br, OH) and 3550 (sharp; OH); *m/z* 276 (M^+, 5.0), 258 (25.5), 147 (12.4), 139 (29.4), 136 (29.9), 121 (100), 111 (13.2) and 93 (12.5) (Found: M^+, 276.0544. $C_{15}H_{13}O_3{}^{35}Cl$ requires *M* 276.0553); Anal. calc. for $C_{15}H_{13}O_3Cl$ (276.81): C, 65.09; H, 4.73%. Found: C, 65.53; H, 4.77%.

3-(4-Bromophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one **3d** (R = Br). Solid (25%), mp 148–149 °C (EtOH) (lit.,[5] 150 °C).

3-(4-Bromophenyl)-3-hydroxy-1-(2-hydroxyphenyl)propan-1-one **7d** (R = Br). Solid (50%), mp 145 °C (EtOH); δ_H (300 MHz, $CDCl_3$) 3.33 (1H, dd, *J* 3.0 and 18.0 Hz, 2-H), 3.40 (1H, dd, *J* 8.1 and 17.9 Hz, 2-H), 5.32 (1H, dd, *J* 3.0 and 7.9 Hz, 3-H), 6.88 (1H, dt, *J* 1.0 and 7.4 Hz, 5'-H), 6.99 (1H, d, *J* 8.4 Hz, 3'-H), 7.31 (2H, d, *J* 8.4 Hz, 2"-H and 6"–H), 7.49 (1H, dt, *J* 1.5 and 7.4 Hz, 4'-H), 7.50 (2H, d, *J* 8.4 Hz, 3"-H and 5"-H), 7.67 (1H, dd, *J* 1.2 and 8.1 Hz, 6'-H) and 12.0 (1H, s, 2'-OH); δ_C (75 MHz, $CDCl_3$) 46.9 (C-2), 69.2 (C-3), 118.7 (C-3'), 119.2 (C-5'), 121.6 (C-1'), 127.5 (C-3" and C-5"), 129.9 (C-4'), 131.7 (C-2" and C-6"), 137.0 (C-6'), 141.6 (C-1"), 162.5 (C-2') and 205.1 (C=O); ν_{max}/cm^{-1} 1630 (CO) and 3200 (OH); *m/z* 320 (M^+, 15.7), 302 (10.1), 185 (35.9), 184 (25.3), 183 (34.3), 136 (48.8) and 121 (100) (Found: M^+, 320.0044. $C_{15}H_{13}O_3{}^{79}Br$ requires *M* 320.0048).

Conversion of **7** *into* **3***. General procedure.*

A stirred suspension of **7** (1 g) in ethanol (20 ml) was treated with 10% aq. NaOH (10 ml), and the mixture was left stirring overnight at room temperature. The solution was diluted with ice cold H_2O (50 ml) and then acidified with conc. HCl. The resulting precipitate was filtered and recrystallised from EtOH to afford **3**.

Reaction of **7** *with hydroxylamine hydrochloride. General procedure.*

A stirred mixture of **7** (1 equiv.), hydroxylamine hydrochloride (1.5 equiv.) and sodium acetate trihydrate (1.5 equiv.) in EtOH (5.0 ml per mmol of **7**) was refluxed for 5 h. The mixture was allowed to cool, filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography [$CHCl_3$–EtOAc (4:1 v/v)] to afford the oxime derivatives *3-aryl-3-hydroxy-1-(2-hydroxyphenyl)propan-1-one oxime* **8**. The following products were isolated and characterized:

3-(4-Fluorophenyl)-3-hydroxy-1-(2-hydroxyphenyl)propan-1-one oxime **8a** (R = F). Solid (60%), mp 144–146 °C (EtOH); δ_H (300 MHz, $CDCl_3$) 3.20 (1H, dd, 4.2 and 13.8 Hz, 2-H), 3.41 (1H, dd, *J* 9.0 and 13.5 Hz, 2-H), 5.16 (1H, dd, *J* 4.2 and 9.0 Hz, 3-H), 6.88 (1H, dt, *J* 1.4 and 7.6 Hz, 5'-H), 6.96 (1H, dd, *J* 1.2 and 8.2 Hz, 3'-H), 7.05 (2H, d, *J* 8.6 Hz, 3"-H and 5"-H), 7.26 (1H, dt, *J* 1.8 and 7.8 Hz, 4'-H), 7.35–7.45 (3H, m, 2"-H, 6'-H and 6"-H); δ_C (75.0 MHz, $CDCl_3$) 35.1 (C-2), 71.8 (C-3), 115.4 (d, $^2J_{CF}$ 21.3 Hz,

C-3" and C-5"), 117.6 (C-3'), 119.2 (C-5'), 127.2 (d, $^3J_{CF}$ 8.4 Hz, C-2" and C-6"), 128.1 (C-4'), 128.8 (C-1'), 131.2 (C-6'), 138.5 (d, $^4J_{CF}$ 3.1 Hz, C-1"), 157.6 (C-1), 160.4 (C-2') and 162.3 (d, $^1J_{CF}$ 244.7 Hz, C-4"); ν_{max}/cm^{-1} 1600 (C=N), 3000 (OH) and 3400 (OH); *m/z* 275 (M^+, 19.5), 256 (100), 213 (14.5), 162 (36.8), 133 (97.1), 97 (62.4) and 57 (96) (Found: M^+, 275.0942. $C_{15}H_{14}NO_3F$ requires *M* 275.0958).

3-(4-Chlorophenyl)-3-hydroxy-1-(2-hydroxyphenyl)propan-1-one oxime **8b** (R = Cl). Solid (70%), mp 142–144 °C (EtOH); δ_H (300 MHz, $CDCl_3$) 3.19 (1H, dd, *J* 4.2 and 13.6 Hz, 2-H), 3.39 (1H, dd, *J* 9.2 and 13.6 Hz, 2-H), 5.14 (1H, dd, *J* 4.2 and 9.1 Hz, 3-H), 6.89 (1H, dt, *J* 1.4 and 7.6 Hz, 5'-H), 6.95 (1H, dd, *J* 1.0 and 8.4 Hz, 3'-H), 7.26 (1H, dt, *J* 1.4 and 8.4 Hz, 4'-H), 7.33 (2H, s, 2"-H and 6"-H), 7.35 (1H, s, 3"-H and 5"-H) and 7.43 (1H, dd, *J* 1.6 and 8.8 Hz, 6'-H); δ_C (75.0 MHz, $CDCl_3$) 34.9 (C-2), 71.8 (C-3), 117.5 (C-3'), 119.4 (C-1'), 126.7 (C-5', C-3" and C-5"), 128.0 (C-4'), 128.7 (C-2" and C-6"), 131.2 (C-6'), 133.6 (C-4"), 142.0 (C-1"), 157.6 (C-1) and 160.2 (C-2'); ν_{max}/cm^{-1} 1605 (C=N), 2900 (OH) and 3410 (OH); *m/z* 291 (M^+, 22.3), 273 (72.0), 272 (75.5), 256 (23.4), 221 (13.4), 162 (37.4), 151 (41.0), 139 (41.7), 133 (62.9), 105 (46.2), 91 (27.4) and 77 (100) (Found: M^+, 291.0662. $C_{15}H_{14}NO_3{}^{35}Cl$ requires *M* 291.0644).

X-Ray crystallographic data collection and processing

XRD data collection and solution were carried out at the Jan Boeyens Structural Chemistry Laboratory (University of the Witwatersrand). Intensity data were collected on a Bruker SMART 1K CCD area detector diffractometer with graphite monochromated Mo K_α radiation (50 kV, 30 mA). The collection method involved ω-scans of width 0.3°. Data reduction was carried out using the program *SAINT+*[9a] and further processed using the program *SADABS.*[9b]

Structure analysis and refinement

The crystal structure was solved by direct methods using *SHELXTL.*[9c] Non-hydrogen atoms were first refined isotropically followed by anisotropic refinement by full matrix least-squares calculation based on F^2 using *SHELXTL*.[9c] With the exception of H1 and H1' all hydrogen atoms were positioned geometrically and allowed to ride on their respective parent atoms. H1 and H1' were found to be disordered and were refined over two positions as H1A and H1B [with site occupancies of 0.52(4) and 0.48(4)] and

H1A' and H1B' [with site occupancies of 0.47(4) and 0.53(4)], respectively. Diagrams and publication material were generated using *SHELXTL*[9c] and *PLATON*.[9d]

Acknowledgement

We are sincerely grateful to the Wellcome Trust (UK) for an equipment grant [060968/Z/00/Z/JC/SRD] in the form of a Varian Mercury 300 MHz NMR spectrometer, and the National Research Foundation (SA) for financial assistance. We also thank Dr P. Boshoff (Cape Technikon Mass Spectrometry Unit) and Mr. P. Benincasa (University of Cape Town) for high-resolution MS data and combustion analysis, respectively.

Supplementary Material

Tables of atomic coordinates and equivalent isotropic displacement parameters, bond lengths and angles, anisotropic displacement parameters, and hydrogen atomic coordinates and their isotropic displacement parameters as well as torsion angles for compound **7b** may be found by following the hyperlink or from Sabinet Online on request.

References

1 J.J.P. Furlong and N.S. Nudelman, *J. Chem. Soc., Perkin Trans*. *2*, 1988, 1213, and references cited therein.

2 J.J.P. Furlong and N.S. Nudelman, *J. Chem. Soc., Perkin Trans*. *2*, 1985, 633; 1988, 1213.

3 (a) F.C. Chen and C.T. Chang, *J. Chem. Soc*., 1958, 146; (b) D.N. Durga in *The Chemistry of Chalcones and Related Compounds*, John Wiley and Sons, New York, 1981.

4 S. Wawzonek in *Heterocyclic Compounds* (R.C. Elderfield, eds.), **vol. 2**, John Wiley and Sons, Inc., New York, 1951, pp. 343 - 347.

5 M.J. Mphahlele, *Ph.D. Thesis*, Rhodes University, 1994 and references cited therein.

6 T.T. Thuy, A. Porzel, H. Ripperger, T. van Sung and G. Adam, *Phytochem.*, 1998, **49**, 2603.

7 *Vogel's Textbook of Practical Organic Chemistry* (S. Furness, A.J. Hannaford, P.W.G. Smith and A.R. Tatchell, eds.), 5th edn., Longman Scientific and Technical, England, 1989, pp. 1032.

8 *Topics in Flavanoid Chemistry and Biochemistry* (L. Farkas, M. Gabor and F. Kallay, eds.), Akademiai Kiado, Budapest, 1975.

9 (a) SAINT+: Version 6.02 (includes XPREP and SADABS), Bruker AXS Inc., Madison, Wisconsin, USA. 1999; (b) G.M. Sheldrick, SADABS, 1996, University of Göttingen, Germany; (c) SHELXTL, Version 5.1. (includes XS, XL, XP, XSHELL), 1999, Bruker AXS Inc., Madison, Wisconsin, USA; (d) A.L. Spek, PLATON, *Acta Cryst.*, 1990, **A46**, C34.