Phenolic Constituents of *Glycyrrhiza* Species. Part 10.[1] Glyasperin E, a New 3-Phenoxychromen-4-one Derivative from the Roots of *Glycyrrhiza aspera*

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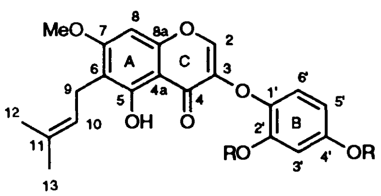
Glyasperin E **1**, a new 3-phenoxychromen-4-one derivative, has been isolated from the roots of *Glycyrrhiza aspera*. The structure of glyasperin E **1** was established first on the basis of spectroscopic evidence and then confirmed by synthesis. Glyasperin E dimethyl ether **1a** was synthesized by way of the ring closure of compound **5b** with ethoxalyl chloride in pyridine, and then decarboxylation, methylation and prenylation.

From the roots of *Glycyrrhiza aspera*, a component of Chinese Xinjiang licorice,[2] we have already reported the isolation and structure determinations of 17 known compounds,[3,4] 10 new compounds, isoglycycoumarin,[3] glyasperin A–D[4] and glyasperin F-I.[1] As a continuation of our investigations into the phenolic compounds of this plant, we now describe a further new compound, glyasperin E **1**, a 3-phenoxychromen-4-one derivative.

Glyasperin E was isolated as pale yellow prisms, m.p. 166–167 °C, $C_{21}H_{20}O_7$. Treatment of compound **1** with dimethyl



1 R = H
1a R = Me

sulfate gave a dimethyl ether **1a**, the UV spectrum of which (Table 1) resembled the spectrum of synthetic 5,7-dimethoxy-3-phenoxychromen-4-one.[5] In the ^1H NMR spectrum of **1**, the following signals were observed: protons in a 3,3-dimethylallyl (prenyl) group, protons in a methoxy group, protons in a hydrogen-bonded hydroxy group and two hydroxy groups, a singlet olefinic proton, ABC type aromatic protons and a singlet aromatic proton (Table 2). The mass fragmentation patterns of **1** were analysed with the measurements of metastable ions (m^*) and high resolution data as shown in Scheme 1. The presence of a 6-prenyl group was deduced from the following: (1) the resistance to give an aluminium-induced shift in the UV spectrum of **1**,[6] (2) the observation of an $(M-43)^+$ ion (73%) in the mass spectrum of **1** (Scheme 1),[7] (3) the coupling pattern of the unsubstituted carbon signals of A ring (C-8) of **1** and **1a** (Table 2).[7,8] All these observations suggested that compound **1** was 3-dihydroxyphenoxy-5-hydroxy-7-methoxy-6-prenylchromen-4-one. Three possible partial structures for the B ring (dihydroxyphenoxy moiety) were possible as shown in Fig. 1, *i.e.*, (a) a 2,4-substituted phenoxy moiety, (b) a 3,4-substituted phenoxy moiety and (c) a 2,5-substituted phenoxy moiety. In order to prove which one was correct, we designed the following NOE experiment. The NOE measurement was carried out on a solution of compound **1** in [$^2H_6$]acetone to which one drop of water had been added; when the signal of water at δ 2.80 was irradiated, there was saturation transfer to the hydroxy groups,[9] and enhancements were observed at the double doublet signal at δ 6.29 (J 2 and 8 Hz) for 5′-H and the doublet signal at δ 6.46 (J 2 Hz) for 3′-H (Fig. 1). From this

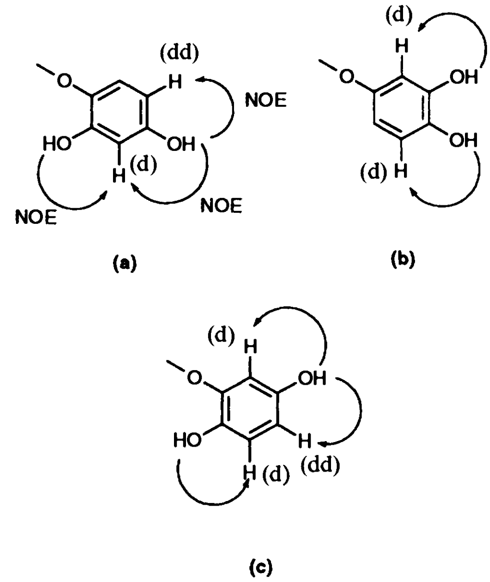


Fig. 1 Three possible substituted patterns in the B ring of compound **1**, and the result of difference NOE experiment showed that only (a) was correct. (Since the intensity of water could not be determined, an accurate percentage of NOE enhancement could not be decided.)

experiment, the structure of the B ring was established as being a 2,4-dihydroxyphenoxy moiety. The partial structure was further confirmed with an NOE experiment on **1a** with irradiation of the methoxy signals of the B ring. Consequently, the structure of glyasperin E **1** was established as 3-(2′,4′-dihydroxyphenoxy)-5-hydroxy-7-methoxy-6-(3-methylbut-2-enyl)chromen-4-one.

Since this was the first time that the 3-phenoxychromen-4-one derivative had been isolated from natural resources it was synthesized as shown in Scheme 2. Three 3-phenoxychromen-4-one derivatives, 3-phenoxychromen-4-one, 7-methoxy-3-phenoxychromen-4-one and 5,7-dimethoxy-3-phenoxychromen-4-one have been synthesized by Vince and Anikó through the reactions of 2′-hydroxy-2-phenoxyacetophenone derivatives with methyl formate and sodium *tert*-butoxide followed by dehydroxylations.[5] We chose the ring closure of 2′-hydroxy-2-phenoxyacetophenone derivatives with ethoxalyl chloride in pyridine because the reaction takes place smoothly when there is a free hydroxy group in the molecule; Baker and co-workers synthesized isoflavones in comparative high yield by this method.[10] By the reactions illustrated in Scheme 2, we synthesized several compounds of this type together with

Table 1 UV absorptions of glyasperin E **1**, glyasperin E dimethyl ether **1a**, compounds **8a,b**, **9a,b**, **10a** and **11a,b** in methanol.

Compound	λ_{max}/nm (log ε)				
1	234 (4.54)	254 (4.64)	262sh (4.62)	296 (4.29)	335sh (3.82)
1a	233 (4.13)	256 (4.41)	260sh (4.39)	293 (3.96)	335sh (3.39)
8a	230 (4.18)	252 (4.36)	259 (4.37)	295 (3.89)	330sh (3.50)
8b	230sh (4.36)	251 (4.49)	257sh (4.26)	288 (4.00)	330sh (3.80)
9a	239sh (4.16)	253sh (4.31)	259 (4.35)	299 (3.84)	333sh (3.60)
9b	231 (4.24)	251 (4.40)	258sh (4.33)	287 (3.93)	326 (3.63)
10a	230sh (4.01)	258sh (4.32)	264 (4.34)	301 (3.59)	339 (3.42)
11a	230sh (4.27)	257sh (4.51)	263 (4.53)	300 (3.84)	340 (3.70)
11b	230sh (4.23)	255 (4.38)	263sh (4.35)	300sh (3.68)	342 (3.44)

Table 2 ^1H NMR and ^{13}C NMR data for glyasperin E **1**[a] and glyasperin E dimethyl ether **1a** in [$^2H_6$]acetone

	1			**1a**		
Carbon	δ_H	δ_C	J(CH)/Hz	δ_H	δ_C	J(CH)/Hz
2	8.39 s	149.16 D[b]	198.8	8.05 s	147.19 D	198.1
3		142.89 Sd	2.2		142.11 Sd	2.2
4		178.54 Sd	6.6		177.69 Sd	5.8
4a		106.85 St	4.4		107.00 St	5.1
5(OH)	12.35 s	158.77 Sdt	4.4, 4.4	12.69 s	159.10 Sdd	5.1, 5.1
6		113.43 Sm			113.04 Sm	
7		164.77 Sm			164.34 Sm	
8	6.68 s	91.15 D	165.1	6.63 s	90.87 D	165.1
8a		157.31 Sdd	4.8, 8.1		157.09 Sdd	5.8, 8.5
9	3.33 br d	21.92 Td		3.32 br d	21.90 Td	
10	5.18 br t	122.68 Dm		5.19 br t	122.85 Dm	
11		132.08 Sm			131.94 Sm	
12	1.76 br s	17.85 Qm		1.76 br s	17.85 Qm	
13	1.63 br d	25.85 Qm		1.64 br d	25.86 Qm	
1′		139.01 Sm			140.29 Sm	
2′(OH)	8.32 br s[c]	150.70 Sm			151.95 Sm	
3′	6.46 d	105.17 Dd	157.4, 4.4	6.67 d	101.51 Dd	157.7, 5.8
4′(OH)	8.67 br s[c]	156.29 Sm			158.02 Sm	
5′	6.29 dd	107.35 Dd	161.7, 5.5	6.45 dd	104.93 Dd	162.1, 5.7
6′	7.02 d	121.43 D	158.5	7.03 d	119.85 D	159.9
MeO	3.98 s	56.79 Q		3.78 s	55.89 Q	
				3.85 s	56.28 Q	
				3.97 s	56.70 Q	

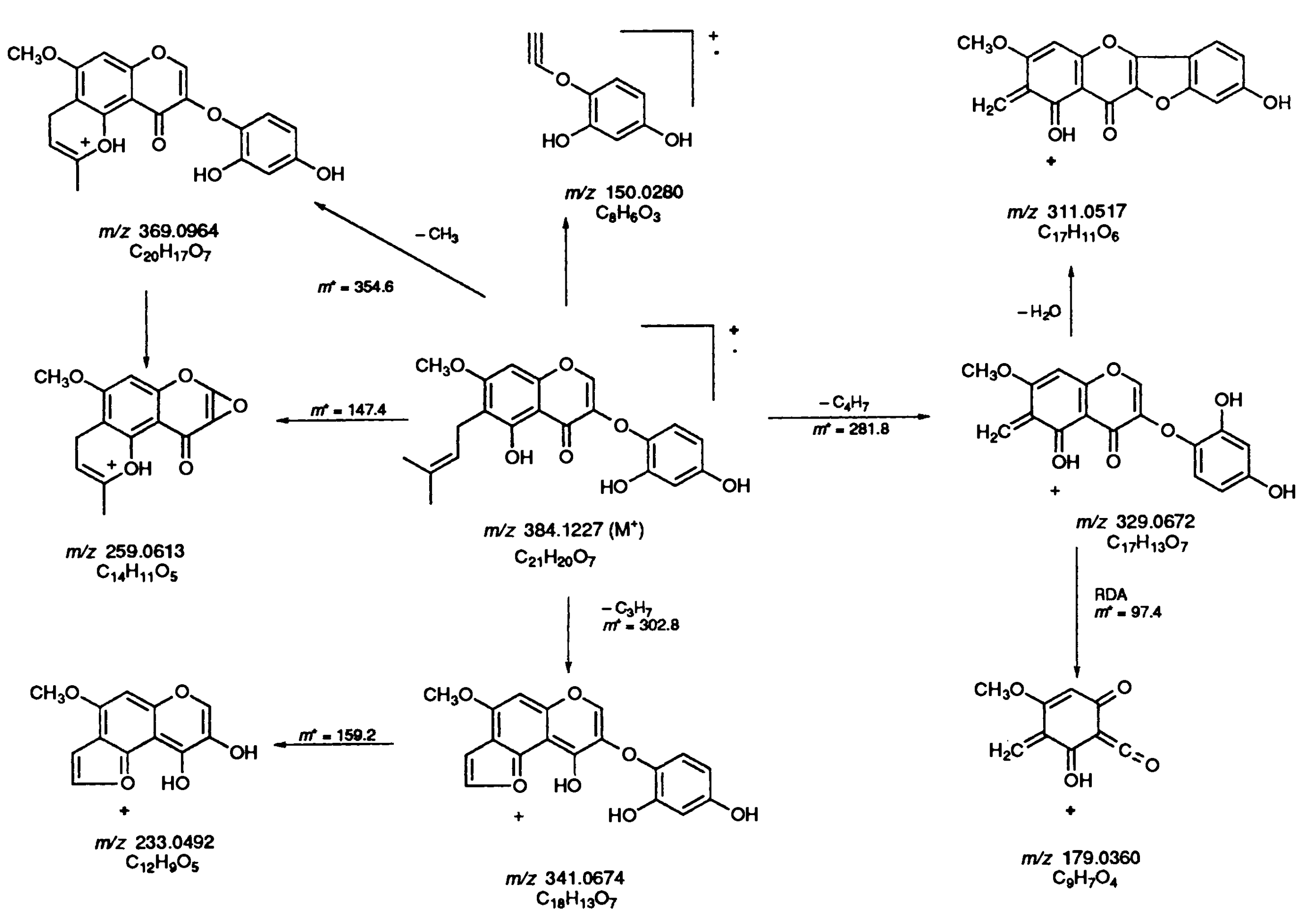
[a] The signals were assigned with ^1H-^{13}C correlation spectrum. [b] Capital letters refer to the pattern resulting from directly bonded proton(s) and lower case to long-range ^{13}C-^1H coupling. [c] The assignments may be interchangeable.

glyasperin E dimethyl ether **1a**, the spectroscopic results for which (UV, ^1H NMR and mass) were identical with those of compound **1a** derived from the glyasperin E **1**; this supported the structure deduced from spectroscopic evidence. All the 3-phenoxychromen-4-one-type compounds obtained here showed similar UV absorption in methanol (see Table 1). Further, the ^{13}C NMR data for this type of compound (Table 3) also showed similar chemical shifts for C-2 and C-3 in the ranges δ 147.24–151.35 and 138.68–142.01, respectively. All this evidence may be considered as characteristic for 3-phenoxychromen-4-one derivatives. Attempts to synthesize compounds with a free hydroxy group in the B ring starting from 2,4-dibenzyloxyphenoxyacetonitrile **4c** were unsuccessful, decarboxylation of compound **7c** giving a range of by-products.

Experimental

M.p.s were determined with Yazawa hot-stage microscope apparatus, and are uncorrected. UV spectra were measured on a Shimadzu UV-265 spectrophotometer, log ε values follow those of λ_{max}. IR spectra (KBr) were recorded on a Hitachi 260-30 spectrophotometer. Mass spectra were measured on a JEOL JMS-D-300 or a JOEL JMS-DX-303 spectrometer. ^1H NMR spectra were recorded at a Hitachi R-900 spectrometer (90 MHz), or a JEOL JNM-EX-400 spectrometer (400 MHz). ^{13}C NMR spectra were recorded on a JOEL JNM-EX-400 spectrometer (100 MHz) for solutions in [$^2H_6$]acetone unless noted otherwise. Chemical shifts are given in δ values from tetramethylsilane, observed splittings (J/Hz) are quoted. Hydroxy protons were identified by deuterium exchange. TLC used Wakogel B-5FM in 0.2 mm layers; preparative TLC employed Wakogel B-5F 20 × 20 cm plates at 0.75 mm thickness. Plates were visualised by UV (254 or 365 nm). Wakogel C-200 used for column chromatography. All reagents were commercial samples which were used as received unless otherwise indicated.

Isolation and Purification of Glyasperin E **1**.—The extraction was described in a previous paper.[1,4] The benzene eluate (33.6 g) from the Amberlite XAD-2 resin (500 g), which absorbed the ethanol extract (300 g) of the roots of *Glycyrrhiza aspera*, was subjected to column chromatography on silica gel (260 g) (column A), and eluted with hexane (fraction 1–2), hexane–benzene (5:1 to 1:7) (fr. 3–9), benzene (fr. 10–12), benzene–diethyl ether (20:1 to 1:5) (fr. 13–27), benzene–acetone (8:1 to 1:2) (fr. 28–33). The fractions (500 cm^3 each) were monitored by TLC. Fraction 15 (1.96 g) was subjected to column chromatography again on silica gel (100 g), and eluted with hexane–acetone (100:1 to 2:1) (fr. 1–19). Fraction 8 (0.5 g) was subsequently purified by preparative TLC using hexane–ethyl

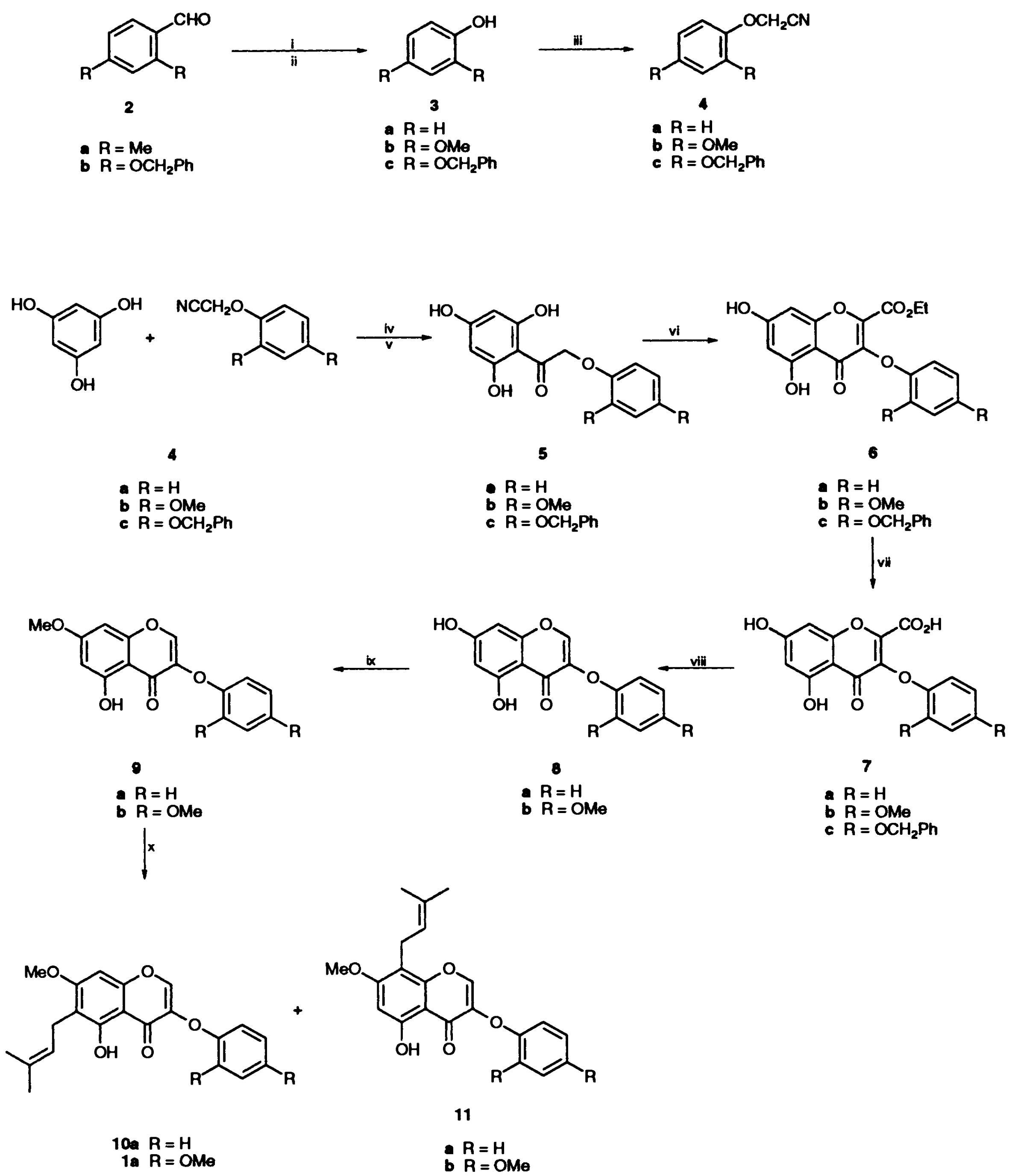


Scheme 1

Table 3 ^{13}C NNR data for compounds **6a**, **7a**, **7b**, **8a**, **8b**, **9a**, **9b**, **10a**, **11a** and **11b** in [$^2H_6$] acetone if not otherwise specified.

Carbon	6b	7a[a]	7c[b]	8a	8b	9a	9b	10a	11a	11b
2	147.40 S	147.40 Sd	147.10	151.06 D[c]	147.24 D[d]	151.24 D[e]	147.44 D[d]	151.03 D[d]	151.35 D[d]	147.62 D[f]
3	140.24 S	137.15 S	140.69	138.96 S br	141.57 S br	139.01 S br	142.01 S br	139.11 Sd	138.68 Sd	141.41 Sd
4	178.64 S	177.06 S	178.66	177.96 S br	177.54 Sd	177.99 S br	177.71 Sd	177.99 Sd	178.41 Sd	178.05 Sd
4a	106.86 Sdd	105.38 Sdd	106.88	106.76 Sdd	106.44 Sdd	107.39 Sdd	107.26 Sdd	107.03 St	106.85 St	106.60 St
5	163.28 Sd	161.15 Sdd	163.23	163.48 Sm	163.48 Sd	163.10 St	163.29 Sd	159.03 Std	161.74 St	161.79 St
6	101.55 Dd	99.19 Dddd	100.02	99.93 Ddd	99.73 Dd	98.93 Ddd	98.77 Ddd	113.35 Sm	96.03 Dd	95.97 Dd
7	166.14 St	165.29 St	166.96	165.32 Sm	165.25 St	166.84 Sm	166.79 Sm	164.46 Sm	164.05 Sm	163.85 Sm
8	94.97 Dd	94.15 Dd	94.99	95.03 Dd	94.75 Dd	93.04 Dd	93.16 Dd	91.10 D	108.91 Sm	108.63 Sm
8a	157.80 Sd	160.12 Sm	157.86	159.03[g] Sm	158.76 Sdd	158.85 Sdd	158.73 Sdd	157.29 Sdd	155.24[h] Sm	155.03 Sm
1′	141.85 Sm	157.10 Sm	142.48	158.91[g] Sm	140.12 Sm	158.78 Sm	140.26 Sm	158.88 Sm	158.90[h] Sm	140.19 Sm
2′	150.90 Sm	115.17 Ddd	149.73	116.37 Ddd	151.98 Sm	116.38 Dddd	152.20 Sm	116.32 Dddd	116.41 Dddd	152.05 Sm
3′	100.12 Dd	129.34 Ddd	104.39	130.38 Ddd	101.48 Dd	130.37 Dddd	101.74 Dd	130.35 Ddd	130.37 Ddd	101.51 Dd
4′	156.93 Sm	122.16 Dtd	155.86	123.43 Dtd	158.05 Sm	123.46 Dt	158.27 Sm	123.39 Dt	123.41 Dt	158.01 Sm
5′	104.44 Dd	129.34 Ddd	106.60	130.38 Ddd	104.92 Dd	130.37 Dddd	105.28 Dd	130.35 Ddd	130.37 Ddd	104.93 Dd
6′	116.81 D	115.07 Ddd	117.36	116.37 Ddd	120.02 D	116.37 Dddd	120.37 D	116.32 Dddd	116.41 Dddd	119.87 D
9								21.91 Td	22.01 Td	21.90 Td
10								122.73 Dm	122.74 Dm	122.85 Dm
11								132.01 Sm	132.32 Sm	131.91 Sm
12								17.85 Qm	17.84 Qm	17.85 Qm
13								25.85 Qm	25.83 Qm	25.86 Qm
CO	160.32 St	156.45 Sd	160.84							
CH_2O	63.13 Tq									
Me	14.14 Qt									
MeO	55.83 Q				55.89 Q	56.53 Q	55.96 Q	56.75 Q	56.85 Q	55.89 Q
	56.40 Q				56.28 Q		56.41 Q			56.28 Q
							56.50 Q			56.70 Q

[a] Spectrum in [$^2H_6$]Me_2SO. [b] Chemical shifts for benzyloxy groups, δ_C 71.31, 71.78, 128.17, 128.42 × 2, 128.50 × 2, 128.55 × 2, 128.61, 129.17, 129.27, 138.15 and 138.48 ppm. [c] *J* 198.6 Hz. [d] *J* 198.1 Hz. [e] *J* 198.8 Hz. [f] *J* 197.3 Hz. [g,h] The assignments may be interchangeable.



Scheme 2 *Reagents:* i, H_2O_2, SeO_2, CH_2Cl_2; ii, NaOH; iii, $ClCH_2CN$, K_2CO_3, dry acetone; iv, HCl (g), $ZnCl_2$, THF; v, H_2O; vi, $ClCOCO_2Et$, pyridine; vii, K_2CO_3, H_2O, acetone; viii, heating, 220–240 °C; ix, Me_2SO_4, K_2CO_3, dry acetone; x, $Me_2C{=}CHCH_2Br$, KOH, MeOH

acetate (3 : 1 in multiple developments, × 3), then $CHCl_3$–ethyl acetate (5 : 1, × 3), benzene–ethyl ether (6 : 1, × 3), to give glyasperin E **1** (2 mg) as pale yellow prisms.

Glyasperin E **1**.—M.p. 166–167 °C (from hexane–acetone) (Found: M^+, 384.1227. $C_{21}H_{20}O_7$ requires *M*, 384.1230); λ_{max}(MeOH)/nm, see Table 1; The spectrum did not shift immediately after addition of $AlCl_3$, but the spectrum shifted after 10 min as follows; 273 (log ε 4.69), 318 (4.31), 381 (3.89); (MeOH + AcONa) 257 (4.68), 296 (4.34), 338sh (3.82); (MeOH + MeONa) 374 (4.96) and 382 (3.89); δ_H(400 MHz) see Table 2; δ_C(100 MHz) see Table 2; *m/z* 385 (26%), 384 (M^+, 100), 369 (11), 341 (76), 330 (15), 329 (73), 328 (13), 311 (18), 297 (6), 275 (7), 260 (14), 259 (61), 245 (11), 233 (12), 232 (15), 217 (11), 203 (10), 179 (20), 150 (10), 110 (16), 97 (10) and 69 (12); *m** see Scheme 1.

Glyasperin E Dimethyl Ether **1a**.—Glyasperin E **1** (2 mg) was methylated by refluxing it with dimethyl sulphate (0.32 mg), potassium carbonate (0.2 g) and acetone (10 cm^3) to give the *title compound* **1a** (1.5 mg, 69%) as colourless prisms, m.p. 110–111 °C (from hexane–acetone) (Found: M^+, 412.1523. $C_{23}H_{24}O_7$ requires *M*, 412.1515); λ_{max}(MeOH)/nm see Table 1; (MeOH + $AlCl_3$, no shift immediately and after 15 min) 272 (log ε 4.53), 318 (4.14) and 371 (3.76); δ_H(400 MHz) and δ_H(100 MHz) see Table 2; NOE experiments; when the signal of 2'-OMe (δ 3.85) was irradiated, the 3'-H showed 11% of enhancement; when the signal of 4'-OMe (δ 3.78) was irradiated, the 3'-H (4%) and 5'-H (7%) showed enhancement; m/z 413 (6%), 412 (M^+, 25), 397 (2), 369 (27), 358 (10), 357 (50), 260 (15), 259 (100), 203 (8), 177 (7), 138 (20), 125 (6) and 69 (5).

2,4-Dimethoxyphenol **3b**.—2,4-Dimethoxybenzaldehyde **2a** (5g), selenium dioxide (0.85 g), hydrogen peroxide (100 cm^3, 30%) and CH_2Cl_2 (100 cm^3) were stirred at room temperature for 12 h. The organic layer was separated and washed with aqueous sodium hydrogen sulphite and water and evaporated to dryness. The residue was hydrolysed with aqueous sodium hydroxide and the products were purified by column chromatography on silica gel with hexane–acetone (3:1) to afford the title compound as colourless liquid (4.5 g, 97%) (lit.,[11] m.p. 34 °C); δ_H(90 MHz) 3.76, 3.82 (each 3 H, s, OMe), 6.34 (1 H, dd, J 2, 8, 5-H), 6.52 (1 H, d, J 2, 3-H) and 6.78 (1 H, d, J 8, 6-H); m/z 154 (M^+, 100).

2,4-Dibenzyloxyphenol **3c**.—2,4-Dibenzyloxybenzaldehyde **2b** (5 g) was oxidized with hydrogen peroxide and selenium dioxide in CH_2Cl_2 for 1 week and then worked up as in the preceding experiment, to yield the title compound (4.1 g, 83%) as colourless plates, m.p. 97–98 °C (from hexane–acetone) (lit.,[12] m.p. 93–94 °C) (Found: C, 78.5; H, 5.9%; M^+, 306. $C_{20}H_{18}O_3$ requires C, 78.40; H, 5.93%; M, 306); λ_{max}(MeOH)/nm 290 (log ε 3.74); δ_H(90 MHz, $CDCl_3$) 4.97 and 5.04 (each 2 H, s, OCH_2Ar), 5.31 (1 H, s, OH), 6.49 (1 H, dd, J 2, 8, 5-H), 6.64 (1 H, d, J 2, 3-H), 6.85 (1 H, d, J 8, 6-H) and 7.40 (10 H, br s, ArH); m/z 306 (M^+, 3%) and 91 (100).

2',4'-Dimethoxyphenoxyacetonitrile **4b**.—A mixture of the phenol **3b** (4.5 g), chloroacetonitrile (2.3 g), 18-crown-6-ether (5 g), potassium carbonate (10 g) and acetonitrile (100 cm^3) was refluxed for 1 h after which it was diluted with water and extracted with diethyl ether. The extract was washed with water, dried and evaporated to dryness. The residue was chromatographed on silica gel column with hexane–acetone (3:1) to give the *title compound* (4.5 g, 80%) as colourless prisms, m.p. 56–57 °C (from acetone) (Found: C, 62.1; H, 5.8; N, 7.3%; M^+, 193. $C_{10}H_{11}NO_3$ requires C, 62.15; H, 5.74; N, 7.25%; M, 193); λ_{max}(MeOH)/nm 224 (log ε 3.84) and 281 (3.46); ν_{max}(KBr)/cm^{-1} 2920, 2000 (CN), 1605 and 1590; δ_H(90 MHz) 3.75, 3.82 (each 3 H, s, OMe), 4.88 (2 H, s, OCH_2), 6.45 (1 H, dd, J 2, 8, 5'-H), 6.62 (1 H, d, J 2, 3'-H) and 7.05 (1 H, d, J 8, 6'-H); m/z 193 (M^+, 29%) and 153 (100).

2',4'-Dibenzyloxyphenoxyacetonitrile **4c**.—A mixture of the phenol **3c** (4.1 g), chloroacetonitrile (1.4 g), 18-crown-6-ether (3.5 g), potassium carbonate (10 g) and acetonitrile (100 cm^3) were refluxed for 30 min, and worked up as in the preceding experiment, to yield the *title compound* (3.5 g, 78%) as colourless prisms, m.p. 61–62 °C (from acetone) (Found: C, 76.3; H, 5.6; N, 4.3%; M^+, 345. $C_{22}H_{19}NO_3$ requires C, 76.49; H, 5.55; N, 4.06%; M, 345); λ_{max}(MeOH)/nm 281 (log ε 3.60); ν_{max}(KBr)/cm^{-1} 3000, 2850, 2005 (CN), 1600 and 1500; δ_H(90 MHz) 4.72 (2H, s, OCH_2CH), 4.95, 5.01 (each 2 H, s, OCH_2Ar), 6.50 (1 H, dd, J 2, 8, 5'-H), 6.77 (1 H, d, J 2, 3'-H), 7.02 (1 H, d, J 8, 6'-H) and 7.20–7.50 (10 H, m, ArH); m/z 345 (M^+, 4%) and 91 (100).

2',4',6'-Trihydroxy-2-phenoxyacetophenone **5a**.—Dry hydrogen chloride was passed through a solution of phenoxyacetonitrile (2.5 g), benzene-1,3,5-triol (1.3 g), zinc chloride (2 g) and tetrahydrofuran (40 cm^3), cooled in an ice-bath for 4 h after which the solution was stored overnight. It was then diluted with water and the tetrahydrofuran was evaporated. The aqueous solution was boiled for 30 min during which time a white solid was formed. This was collected, washed with water and dried. When subjected to chromatography on silica gel with hexane–acetone (4:1) it afforded the title compound (1.2 g, 48%) as colourless prisms, m.p. 275 °C (decomp.) (from methanol) (lit.,[5] m.p. 244–245 °C) (Found: C, 64.4; H, 4.8%; M^+, 260. $C_{14}H_{12}O_5$ requires C, 46.60; H, 4.65%; M, 260).

2-(2″,4″-Dimethoxyphenoxy)-2',4',6'-trihydroxyacetophenone **5b**.—Dry hydrogen chloride was passed through a solution of the nitrile **4b** (2.5 g), benzene-1,3,5-triol (1.8 g), zinc chloride (3 g) and tetrahydrofuran (100 cm^3), cooled in an ice-bath, for 4 h after which the mixture was worked up as in the preceding experiment to yield the *title compound* (2.7 g, 53%) as colourless prisms, m.p. 105–107 °C (from aqueous methanol) (Found: C, 56.8; H, 5.3%; M^+, 320. $C_{16}H_{16}O_7 \cdot H_2O$ requires C, 56.79; H, 5.37%); λ_{max}(MeOH)/nm 223 (log ε 3.88) and 281 (3.69); ν_{max}(KBr)/cm^{-1} 3500 (OH), 3280 (OH), 1635 (CO) and 1600; δ_H(400 MHz) 3.71, 3.82 (each 3 H, s, OMe), 5.27 (2 H, s, OCH_2), 5.97 (2 H, s, 3',5'-H_2), 6.38 (1 H, dd, J 2, 8, 5″-H), 6.57 (1 H, d, J 2, 3″-H) and 6.83 (1 H, d, J 8, 6″-H); δ_C(100 MHz) 55.77, 56.21 (OMex2), 75.56 (C-2), 95.83 × 2 (C-3', 5'), 101.97 (C-3″), 103.71 (C-1'), 104.44 (C-5″), 117.03 (C-6″), 143.52 (C-1″), 151.73 (C-2″), 155.95 (C-4″), 165.26 × 2 (C-2',6'), 165.90 (C-4') and 200.61 (C-1); m/z 328 (M^+, 38%) and 153 (100).

2-(2″,4″-Dibenzyloxyphenoxy)-2',4',6'-trihydroxyacetophenone **5c**.—Dry hydrogen chloride was passed through a solution of the nitrile **4c** (2 g), benzene-1,3,5-triol (4.4 g), zinc chloride (4 g) and tetrahydrofuran (100 cm^3), cooled in an ice-bath for 4 h after which the solution was stored overnight. It was then diluted with water and the tetrahydrofuran was evaporated. The aqueous solution was heated at 80–90 °C for 8 h, cooled and extracted with diethyl ether. The extract was washed, dried and evaporated to dryness. The residue was chromatographed on silica gel column with hexane–acetone (3:1) and then preparative TLC with hexane–ethyl acetate (3:1) to give the *title compound* (3.5 g, 57%) as colourless prisms, m.p. 91–92 °C (from hexane–benzene) (Found: C, 68.2; H, 5.3. $C_{28}H_{24}O_7 \cdot H_2O$ requires C, 68.54; H, 5.34%); λ_{max}(MeOH)/nm 288 (log ε 4.38); ν_{max}(KBr)/cm^{-1} 3540 (OH), 3300 (OH), 1650 (CO) and 1600; δ_H(400 MHz) 5.02, 5.17 (each 2 H, s, OCH_2Ar), 5.34 (2 H, s, OCH_2), 5.99 (2 H, s, 3',5'-H), 6.51 (1 H, dd, J 2, 8, 5″-H), 6.76 (1 H, d, J 2, 3″-H), 6.89 (1 H, d, J 8, 6″-H) and 7.27–7.53 (10 H, m, ArH); δ_C(100 MHz) 75.88 (C-2), 96.04 × 2 (C-3',5'), 103.99 (C-1'), 106.87 (C-5″), 117.73 (C-6″), 144.49 (C-1″), 150.82 (C-2″), 165.59 × 2 (C-2',6'), 166.22 (C-4') and 200.78 (C-1); next signals for benzyloxy groups, 71.10, 71.76 (OCH_2), 128.63 × 3, 128.72, 128.73, 129.41 × 3, 129.43 × 2, 138.71 and 138.78 (Ar); m/z 473 (FAB-MS), M^+ + 1).

Ethyl 5,7-Dihydroxy-4-oxo-3-phenoxychromene-2-carboxylate **6a**.—The acetophenone **5a** (0.76 g), ethoxalyl chloride (1.65 g) and pyridine (100 cm^3) were heated at 60 °C for 72 h after which the solution was poured into ice–water and extracted with ethyl acetate. The extract was washed with dilute hydrogen chloride and water, dried and evaporated to dryness. The residue was chromatographed on a silica gel column with hexane–acetone (5:1), to yield the *title compound* (0.51 g, 40%) as yellow needles, m.p. 260–261 °C (from hexane–acetone) (Found: C, 63.2; H, 4.15%; M^+, 342.0745. $C_{18}H_{14}O_7$ requires C, 63.14; H, 4.13%; M, 342.0735); λ_{max}(MeOH)/nm 267 (log ε 4.24), 318 (3.78); (MeOH + $AlCl_3$) 279 (4.27), 332 (3.82) and 405sh (3.45); ν_{max}(KBr)/cm^{-1} 3220 (OH), 1725 (CO_2R), 1640 (CO), 1580 and 1220; δ_H(90 MHz) 1.16 (3 H, t, J 7, Me), 4.32 (2 H, q, J 7, OCH_2), 6.33 (1 H, d, J 2, 6-H), 6.63 (1 H, d, J 2, 8-H), 7.00–7.38 (5 H, m, ArH) and 12.05 (1 H, s, 5-OH); m/z 340 (M^+, 90%) and 269 (100).

Ethyl 3-(2',4'-Dimethoxyphenoxy)-5,7-dihydroxy-4-oxochromene-2-carboxylate **6b**.—A mixture of the acetophenone **5b**

(1 g), ethoxalyl chloride (1.6 g) and pyridine (30 cm^3) were stored at room temperature for 1 day after which a solution of ethoxalyl chloride (0.6 g) in pyridine (5 cm^3) was added to it. After 2 days the reaction mixture was worked up as in the preceding experiment, to yield the *title compound* (0.9 g, 75%) as yellow needles, m.p. 203–204 °C (from hexane–acetone) (Found: C, 59.4; H, 4.5%; M^+, 402.0912. $C_{20}H_{18}O_9$ requires C, 59.69; H, 4.51%; *M*, 402.0945); λ_{max}(MeOH)/nm 266 (log ε 4.22), 316 (3.16); (MeOH + $AlCl_3$) 280 (4.32), 329 (3.86) and 410sh (3.46); ν_{max}(KBr)/cm^{-1} 3320 (OH), 1700 (CO_2R), 1650 (CO), 1580 and 1210; δ_H(400 MHz) 1.23 (3 H, t, *J* 7, Me), 3.75, 3.85 (each 3 H, s, OMe), 4.34 (2 H, q, *J* 7, OCH_2), 6.30 (1 H, d, *J* 2, 6-H), 6.36 (1 H, dd, *J* 2, 8, 5'-H), 6.50 (1 H, d, *J* 2, 8-H), 6.64 (1 H, d, *J* 2, 3'-H), 6.90 (1 H, d, *J* 8, 6'-H) and 12.10 (1 H, s, OH); *m/z* 402 (M^+, 100%).

Ethyl 3-(2',4'-*Dibenzyloxyphenoxy*)-5,7-*dihydroxy*-4-*oxo-chromene*-2-*carboxylate* **6c**.—A mixture of the acetophenone **5c** (1 g), ethoxalyl chloride (1.15 g) and pyridine (30 cm^3) was stored at room temperature for 2 days, after which a solution of ethoxalyl chloride (0.6 g) in pyridine (5 cm^3) was added to it. After 2 days the reaction mixture was worked up as in the preceding experiment, to yield the *title compound* (0.49 g, 44%) as yellow needles, m.p. 187–188 °C (from hexane–acetone) (Found: C, 69.3; H, 4.7. $C_{32}H_{26}O_9$ requires C, 69.29; H, 4.73%); λ_{max}(MeOH)/nm 267 (log ε 4.33) and 315 (3.88); (MeOH + $AlCl_3$) 281 (4.41), 311 (3.90) and 403 (3.58); ν_{max}(KBr)/cm^{-1} 3310 (OH), 1700 (CO_2R), 1650 (CO), 1580 and 1200; δ_H(400 MHz) 1.21 (3 H, t, *J* 7, Me), 4.13 (1 H, q, *J* 7, OCH_2), 5.03, 5.16 (each 2 H, s, OCH_2Ar), 6.29 (1 H, d, *J* 2, 6-H), 6.46 (1 H, d, *J* 2, 8-H), 6.50 (1 H, dd, *J* 2, 8, 5'-H), 6.80 (1 H, d, *J* 2, 3'-H), 6.94 (1 H, d, *J* 8, 6'-H), 7.25–7.48 (10 H, m, ArH) and 12.09 (1 H, s, 5-OH); *m/z* 555 (FAB-MS, *M* + 1).

5,7-*Dihydroxy*-4-*oxo*-3-*phenoxychromene*-2-*carboxylic Acid* **7a**.—The ester **6a** (0.51 g) was hydrolysed by potassium carbonate (0.5 g) in acetone (5 cm^3) and water (5 cm^3) at 60 °C for 4 h to give the *title compound* (0.44 g, 93%) as yellow prisms, m.p. 289–290 °C (from methanol) (Found: C, 58.5; H, 3.9%; M^+, 314.0424. $C_{16}H_{10}O_7$·MeOH requires C, 58.95; H, 4.08% *M*, 314.0427); λ_{max}(MeOH)/nm 257 (log ε 4.46) and 300 (4.40); (MeOH + $AlCl_3$) 269 (4.55) and 334 (4.10); ν_{max}(KBr)/cm^{-1} 3400 (OH), 3100 (OH), 1705 (CO_2H), 1630 (CO), 1575 and 1210; δ_H(400 MHz, [$^2H_6$]Me_2SO) 6.27 (1 H, d, *J* 2, 6-H), 6.47 (1 H, d, *J* 2, 8-H), 6.95–7.05 (3 H, m, ArH), 7.26–7.36 (2 H, m, ArH), 11.20 (1 H, br s, 7–OH) and 11.92 (1 H, s, 5-OH); δ_C(100 MHz, [$^2H_6$]Me_2SO) see Table 3; *m/z* 314 (M^+, 10%) and 270 (100).

3-(2',4'-*Dimethoxyphenoxy*)-5,7-*dihydroxy*-4-*oxochromene*-2-*carboxylic Acid* **7b**.—The ester **6b** (0.8 g) was hydrolysed by potassium carbonate (0.5 g), acetone (5 cm^3) and water (5 cm^3) at 60 °C for 30 min to give the *title compound* (0.68 g, 91%) as yellow prisms, m.p. 262–264 °C (from methanol) (Found: C, 57.7; H, 3.7%; M^+, 374.0606. $C_{18}H_{14}O_9$ requires C, 57.74; H, 3.77%; *M*, 374.0633); λ_{max}(MeOH)/nm 230sh (log ε 4.18), 258 (4.13), 290sh (3.80) and 310sh (3.84); (MeOH + $AlCl_3$) 283 (4.33), 334 (3.84) and 410sh (3.48); ν_{max}(KBr)/cm^{-1} 3460 (OH), 3100 (OH), 1705 (CO_2H), 1645 (CO), 1580 and 1205; δ_H(90 MHz) 3.75, 3.84 (each 3 H, s, OMe), 6.32 (1 H, d, *J* 2, 6-H), 6.38 (1 H, dd, *J* 2, 8, 5'-H), 6.51 (1 H, d, *J* 2, 8-H), 6.63 (1 H, d, *J* 2, 3'-H), 6.94 (1 H, d, *J* 8, 6'-H) and 12.09 (1 H, s, 5-OH); *m/z* 374 (M^+, 4%) and 330 (100).

3-(2',4'-*Dibenzyloxyphenoxy*)-5,7-*dihydroxy*-4-*oxochromene*-2-*carboxylic Acid* **7c**.—The acid **6c** (0.4 g) was hydrolysed by potassium carbonate (0.5 g) in acetone (5 cm^3) and water (5 cm^3) at 60 °C for 20 min to give the *title compound* (0.32 g, 87%) as yellow prisms, m.p. 192–193 °C (from methanol) (Found: C, 66.0; H, 4.5%. $C_{30}H_{22}O_9$·H_2O requires C, 66.15; H, 4.46%); λ_{max}(MeOH)/nm 259 (log ε 4.33) and 310sh (3.80); (MeOH + $AlCl_3$) 282 (4.39) and 330 (3.89); ν_{max}(KBr)/cm^{-1} 3480 (OH), 3180 (OH), 1700 (CO_2H), 1650 (CO) and 1580; δ_H(400 MHz) 5.03, 5.18 (each 2 H, s, OCH_2), 6.29 (1 H, d, *J* 2, 6-H), 6.48 (1 H, d, *J* 2, 8-H), 6.49 (1 H, dd, *J* 2, 8, 5'-H), 6.79 (1 H, d, *J* 2, 3'-H), 6.98 (1 H, d, *J* 8, 6'-H) and 12.11 (1 H, s, 5-OH); δ_C(100 MHz) see Table 3; *m/z* 527 (FAB-MS, *M* + 1).

5,7-*Dihydroxy*-3-*phenoxychromen*-4-*one* **8a**.—The acid **7a** (0.44 g), sealed *in vacuo* in portions (*ca.* 50 mg each) was heated at 220–240 °C on an oil-bath until evolution of carbon dioxide ceased (*ca.* 10 min). The crude products were purified by preparative TLC using hexane–acetone (3:1) to give the *title compound* (0.32 g, 86%) as pale yellow plates, m.p. 225–226 °C (from hexane–acetone) (Found: C, 66.6; H, 3.7%; M^+, 270. $C_{15}H_{10}O_5$ requires C, 66.65; H, 3.73%; *M*, 270); λ_{max}(MeOH)/nm see Table 1; (MeOH + $AlCl_3$) 268 (log ε 4.19), 314 (3.69) and 373 (4.41); ν_{max}(KBr)/cm^{-1} 3380 (OH), 1635 (CO) and 1575; δ_H(400 MHz) 6.30 (1 H, d, *J* 2, 6-H), 6.48 (1 H, d, *J* 2, 8-H), 7.02–7.08 (3 H, m, ArH), 7.27–7.35 (2 H, m, ArH), 8.36 (1 H, s, 2-H), 9.80 (1 H, br s, 7-OH) and 12.31 (1 H, s, 5-OH); δ_C(100 MHz) see Table 3; *m/z* 270 (M^+, 100%).

3-(2',4'-*Dimethoxyphenoxy*)-5,7-*dihydroxychromen*-4-*one* **8b**.—The acid **7b** (0.12 g) was decarboxylated as in the preceding experiment, to yield the *title compound* (0.04 g, 38%) as pale yellow prisms, m.p. 183–185 °C (from hexane–acetone) (Found: C, 61.9; H, 4.4; M^+, 330. $C_{17}H_{14}O_7$ requires C, 61.80; H, 4.28%; *M*, 330); λ_{max}(MeOH)/nm see Table 1; (MeOH + $AlCl_3$) 266 (log ε 4.58), 313 (4.05) and 382 (3.78); ν_{max}(KBr)/cm^{-1} 3400 (OH), 1620 (CO), 1605 and 1580; δ_H(400 MHz) 3.75, 3.78 (each 3H, s, OMe), 6.28 (1 H, d, *J* 2, 6-H), 6.40 (1 H, d, *J* 2, 8-H), 6.45 (1 H, dd, *J* 2, 8, 5'-H), 6.66 (1 H, d, *J* 2, 3'-H), 7.03 (1 H, d, *J* 8, 6'-H), 7.96 (1 H, s, 2-H) and 12.51 (1 H, s, 5-OH); δ_C(100 MHz) see Table 3; *m/z* 330 (M^+, 100%).

5-*Hydroxy*-7-*methoxy*-3-*phenoxychromen*-4-*one* **9a**.—The ketone **8a** (0.22 g), dimethyl sulphate (0.04 g) and potassium carbonate (0.5 g) were refluxed in dry acetone (20 cm^3) for 30 min after which the mixture was diluted with water and extracted by diethyl ether. The extract was washed, dried and evaporated to give a residue which was purified by preparative TLC using hexane–acetone (2:1) to yield the *title compound* (0.27 g, 79%) as colourless needles, m.p. 139–140 °C (from methanol) (Found: C, 67.3; H, 4.3%; M^+, 284.0695. $C_{16}H_{16}O_5$ requires C, 67.59; H, 4.26%, *M*, 284.0681); λ_{max}(MeOH)/nm see Table 1; (MeOH + $AlCl_3$) 269 (log ε 4.34), 312 (3.93) and 379 (3.59); ν_{max}(KBr)/cm^{-1} 3400 (OH), 1635 (CO) and 1600; δ_H(400 MHz) 3.92 (3 H, s, OMe), 6.36 (1 H, d, *J* 2, 6-H), 6.59 (1 H, d, *J* 2, 8-H), 7.00–7.10 (3 H, m, ArH), 7.29–7.35 (2 H, m, ArH), 8.39 (1 H, s, 2-H) and 12.28 (1 H, s, 5-OH); δ_C(100 MHz) see Table 3; *m/z* 284 (M^+, 100%).

3-(2',4'-*Dimethoxyphenoxy*)-5-*hydroxy*-7-*methoxychromen*-4-*one* **9b**.—The ketone **8b** (0.12 g) and dimethyl sulphate (0.02 g) were refluxed with acetone (20 cm^3) over anhydrous potassium carbonate (1 g) for 30 min, as in the preceding experiment, to yield the *title compound* (0.12 g, 96%) as pale yellow needles, m.p. 156–157 °C (from hexane–acetone) (Found: C, 62.5; H, 4.6%; M^+, 344. $C_{18}H_{16}O_7$ requires C, 62.77; H, 4.69%; *M*, 344); λ_{max}(MeOH)/nm see Table 1; (MeOH + $AlCl_3$) 267 (log ε 4.46), 311 (3.92) and 384 (3.64); ν_{max}(KBr)/cm^{-1} 3400 (OH), 1640 (CO), 1605 and 1570; δ_H(400 MHz) 3.78, 3.85, 3.91 (each 3 H, s, OMe), 6.33 (1 H, d, *J* 2, 6-H), 6.45 (1 H, dd, *J* 2, 8, 5'-H), 6.52 (1 H, d, *J* 2, 8-H), 6.66 (1 H, d, *J* 2, 3'-H), 7.04 (1 H, d, *J* 8, 6'-H), 7.99 (1 H, s, 2-H) and 12.47 (1 H, s, 5-OH); δ_C(100 MHz) see Table 3; *m/z* 344 (M^+, 100).

5-Hydroxy-7-methoxy-6-(3-methylbut-2-enyl)-3-phenoxychromen-4-one **10a** and *5-Hydroxy-7-methoxy-8-(3-methylbut-2-enyl)-3-phenoxychromen-4-one* **11a**.—A solution of the ketone **9a** (0.17 g), 1-bromo-3-methylbut-2-ene (0.36 g) and methanol (25 cm^3) and a solution of potassium hydroxide (0.17 g) in methanol (25 cm^3) were mixed together at room temperature. After 30 min the mixture was diluted with water and extracted with diethyl ether. The extract was washed with water, dried and evaporated to dryness. The residue was separated by preparative TLC using hexane–ethyl acetate (4:1, ×3) to give *compound* **11a**, R_F 0.7 (0.04 g, 19%) as pale yellow prisms, and *compound* **10a**, R_F 0.6 (0.025 g, 12%) as pale yellow prisms.

Compound **10a**. M.p. 144–145 °C (from hexane–acetone) (Found: C, 71.7; H, 5.7%, M^+, 352.1320. $C_{21}H_{20}O_5$ requires C, 71.56; H, 5.72; *M*, 352.1305); λ_{max}(MeOH)/nm see Table 1; (MeOH + $AlCl_3$) 248sh (log ε 4.35), 273 (4.42), 316 (3.87) and 400 (3.46); ν_{max}(KBr)/cm^{-1} 3400 (OH), 1635 (CO) and 1600; δ_H(400 MHz) 1.64 (3 H, br d, *J* 0.7, 11-Me), 1.75 (3 H, br s, 11-Me), 3.32 (2 H, br d, *J* 7, 9-H_2), 3.98 (3 H, s, OMe), 5.20 (1 H, br t, *J* 7, 10-H), 6.68 (1 H, s, 8-H), 7.0–7.12 (3 H, m, ArH), 7.25–7.35 (2 H, m, ArH), 8.40 (1 H, s, 2-H) and 12.49 (1 H, s, 5-OH); δ_C(100 MHz) see Table 3; *m/z* 353 (15%), 352 (M^+, 62), 338 (22), 337 (100), 297 (12), 284 (29), 283 (8), 166 (17) and 77 (11).

Compound **11a**. M.p. 121–122 °C (from hexane–ethyl acetate) (Found: C, 71.6; H, 5.6%; M^+, 352.1239. $C_{21}H_{20}O_5$ requires C, 71.56; H, 5.72%; *M*, 352.1305); λ_{max}(MeOH)/nm see Table 1; (MeOH + $AlCl_3$) 247sh (log ε 4.32), 273 (4.59), 317 (3.92) and 403 (3.73); ν_{max}(KBr)/cm^{-1} 3400 (OH), 1620 (CO) and 1600; δ_H(400 MHz) 1.65 (3 H, br d, *J* 1, 11-Me), 1.79 (3 H, br s, 11-Me), 3.43 (2 H, br d, *J* 7, 9-H_2), 3.98 (3 H, s, OMe), 5.15 (1 H, br t, *J* 7, 10-H), 6.52 (1 H, s, 6-H), 7.02–7.08 (3 H, m, ArH), 7.28–7.33 (2 H, m, ArH), 8.46 (1 H, s, 2-H) and 12.38 (1 H, s, 5-OH); δ_C(100 MHz) see Table 3; *m/z* 353 (9%), 352 (M^+, 39), 338 (5), 337 (23), 323 (5), 316 (9), 310 (20), 309 (100), 298 (15), 297 (81), 284 (14), 267 (11), 166 (4), 150 (25) and 77 (15).

3-(2',4'-Dimethoxyphenoxy)-5-hydroxy-7-methoxy-6-(3-methylbut-2-enyl)chromen-4-one **1a** and *3-(2',4'-Dimethoxyphenoxy)-5-hydroxy-7-methoxy-6-(3-methylbut-2-enyl)chromen-4-one* **11b**.—A solution of the ketone **9b** (0.1 g), 1-bromo-3-methylbut-2-ene (0.17 g) and methanol (25 cm^3), and a solution of potassium hydroxide (0.08 g) in methanol (25 cm^3) were mixed at room temperature. After 30 min the mixture was diluted with water and extracted with diethyl ether. The extract was washed with water, dried and evaporated to dryness. The residue was separated by preparative TLC using hexane–acetone (7:1, ×2) to yield *compound* **11b**, R_F 0.61 (0.012 g, 10%) as colourless prisms, and *compound* **1a**, R_F 0.54 (0.004 g, 3%) as colourless prisms.

Compound **1a**. M.p. 111–112 °C (from hexane–acetone) (Found: C, 66.8; H, 6.0%; M^+, 412.1536. $C_{23}H_{24}O_7$ requires C, 66.97; H, 5.87%; M^+, 412.1515); ν_{max}(KBr)/cm^{-1} 3400 (OH), 1640 (CO) and 1600; all other data were the same as those of glyasperin E dimethyl ether **1a**.

Compound **11b**. M.p. 128–129 °C (from acetone) (Found: C, 66.7; H, 5.9%; M^+, 412.1523. $C_{23}H_{24}O_7$ requires C, 66.97; H, 5.87%; *M*, 412.1515); λ_{max}(MeOH)/nm see Table 1; (MeOH + $AlCl_3$) 272 (log ε 4.50), 315 (3.88) and 375 (3.68); ν_{max}(KBr)/cm^{-1} 3400 (OH), 1635 (CO) and 1595; δ_H(400 MHz) 1.63 (3 H, br d, *J* 1, 11-Me), 1.76 (3 H, br s, 11-Me), 3.40 (2 H, br d, *J* 7, 9-H_2), 3.78, 3.86, 3.97 (each 3 H, s, OMe), 5.15 (1 H, br t, *J* 7, 10-H), 6.45 (1 H, dd, *J* 2, 8, 5'-H), 6.49 (1 H, s, 6-H), 6.68 (1 H, d, *J* 2, 3'-H), 7.04 (1 H, d, *J* 8, 6'-H), 8.09 (1 H, s, 2-H) and 12.58 (1 H, s, 5-OH); δ_C(100 MHz) see Table 3; *m/z* 413 (26%), 412 (M^+, 100), 398 (22), 397 (94), 381 (13), 357 (8), 344 (11), 229 (10), 179 (40), 178 (21), 177 (30), 167 (14), 153 (22), 138 (32), 125 (23), 107 (9), 91 (12), 79 (16), 77 (18) and 69 (24).

Acknowledgements

We thank the Foundation of the 60th Anniversary of Toho University for the award of a research fellowship to L. Z. We also acknowledge helpful discussions with Professor H. Akita, Toho University.

References

1 Part 9, L. Zeng, T. Fukai, T. Nomura, R.-Y. Zhang and Z.-C. Lou, *Heterocycles*, 1992, **34**, 1813.
2 L. Zeng, S.-H. Li and Z.-C. Lou, *Yaoxue Xuebao* (*Acta Pharmaceutica Sinica, Peking*), 1988, **23**, 200.
3 L. Zeng, R.-Y. Zhang, D. Wang, C.-Y. Gao and Z.-C. Lou, *Zhiwu Xuebao* (*Acta Botanica Sinica, Peking*), 1991, **33**, 124.
4 L. Zeng, T. Fukai, T. Nomura, R.-Y. Zhang and Z.-C. Lou, *Heteracycles*, 1992, **34**, 575.
5 S. Vince and K. Anikó, *Magy. Kem. Foly.*, 1978, **85**, 353.
6 T. Fukai, Q.-H. Wang and T. Nomura, *Heterocycles*, 1989, **29**, 1369.
7 T. Fukai, Q.-H. Wang, M. Takayama and T. Nomura, *Heterocycles*, 1990, **31**, 373.
8 T. Fukai and T. Nomura, *Heterocycles*, 1992, **34**, 1213.
9 J. Feeney and A. Heinrich, *J. Chem. Soc., Chem. Commun.*, 1966, 295.
10 W. Baker, J. Chadderton, J. B. Harborne and W. D. Ollis, *J. Chem. Soc.*, 1953, 1852.
11 L. Syper, *Synthesis*, 1989, 167.
12 S. J. Angyal and M. E. Tate, *J. Chem. Soc.*, 1965, 6949.

Paper 2/06618A
Received 14*th December* 1992
Accepted 23*rd February* 1993