New Syntheses of Pulvinic Acids *via* Reformatsky-type Reactions with Aryl-methoxymaleic Anhydrides

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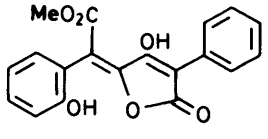
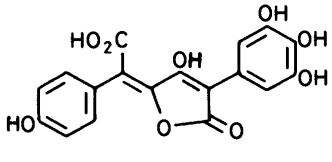
The reaction of zinc enolates, *viz* (**13**), derived from arylacetates with 2-aryl-3-methoxymaleic anhydrides gives β-hydroxy ester intermediates *viz* (**17**) which can be dehydrated to *Z*- and *E*-isomers of permethylated pulvinic acids. Thus, the intermediate (**17**) derived from (**15**) and (**16**) produces the *Z*- and *E*-isomers (**23**) and (**24**) respectively, of permethylated gomphidic acid. In a similar manner, the geometrical isomers of permethylated isogomphidic acid [(**27**) and (**28**)] and methyl leprapinate [(**29**) and (**30**)] are synthesised from appropriate arylacetate and aryl methoxymaleic anhydride precursors.

Treatment of permethylated pulvinic acids with trimethylsilyl iodide provides a facile method of producing the corresponding pulvinic acids. By this method gomphidic acid (**2**), isogomphidic acid (**31**) and atromentic acid (**32b**) have been prepared. Both (**2**) and (**32b**) were identical with the natural metabolites isolated from *Gomphidius glutinosus* and *Xerocomus chrysenteron* respectively.

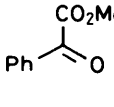
The pulvinic acids *e.g.* leprapinic acid (**1**) and gomphidic acid (**2**) are a group of natural 4-ylidenetetronic acids isolated from several lichens and higher fungi.[1] Their presence in lichens, as bright yellow and orange pigments has been known for over a century. Early structural investigations amongst this class of compound were severely hindered by the absence of a synthetic method to those members having differing substituents in the aryl ring portions of their structures. This synthetic problem was addressed recently by ourselves,[2] resulting in the development of an unambiguous synthesis of permethylated pulvinic acids, based on aldol-type condensation between methyl benzoyl formates and methyl 2-aryltetronates, *e.g.* *O*-methyl pinastric acid (**5a**) was synthesized from (**3**) and (**4a**). More recently Ramage *et al.*,[3] have described an alternative approach to the synthesis of the pulvinic acids leprapinic acid (**1**) and xerocomic acid (**6**), which has close similarities to the biosynthetic origins of the metabolites. In this paper we summarize another new approach to the permethylated pulvinic acids which involves a Reformatsky-type condensation reaction between arylacetates and aryl methoxymaleic anhydrides [*viz.* (**7**)]. We also show that the 'free' pulvinic acids can be smoothly prepared from the permethylated compounds, by treatment of the latter with trimethylsilyl iodide.



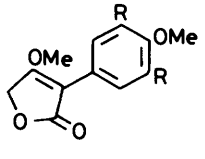
(**1**)



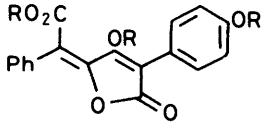
(**2**)



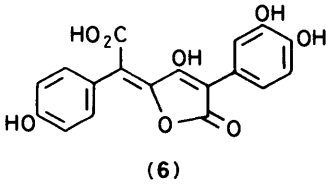
(**3**)



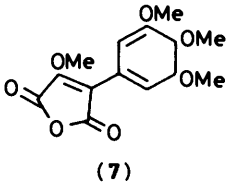
(**4**)
a; R = H
b; R = OMe



(**5**)
a; R = Me
b; R = H

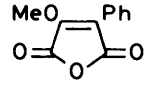


(**6**)

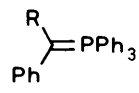


(**7**)

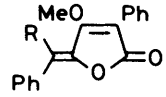
We began our investigations of the use of aryl methoxymaleic anhydrides in the synthesis of pulvinic acids by first examining the Wittig reaction between 2-methoxy-3-phenylmaleic anhydride (**8**) and the stabilized phosphorane (**9b**).[4] Our earlier work had established that the corresponding reaction, with the less substituted phosphorane (**9a**), proceeded by regioselective attack at C-1 in the anhydride (**8**), producing largely the *Z*-olefination product (**10a**).[5] Even under forcing conditions however (*e.g.* refluxing xylene, several days), we were unable to detect any sign of reaction between (**8**) and (**9b**). Instead, only starting materials, accompanied by products of decomposition, were recovered. This lack of reactivity is most likely associated with severe steric congestion in the transition state leading from the betaine intermediate to the tetrasubstituted double bond in the reaction. Our attempts to employ the more nucleophilic phosphonate ester carbanion (**11**) in condensation with the anhydride (**8**) were also frustrated, and conventional organomagnesium reactions with (**8**) were shown to lead to substantial amounts of the corresponding 2:1 adducts, *viz.* (**12**) from (**8**) and ethylmagnesium bromide.[5]



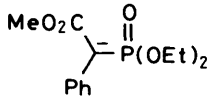
(**8**)



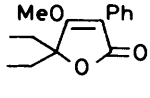
(**9**)



(**10**)
a; R = H
b; R = CO_2Me



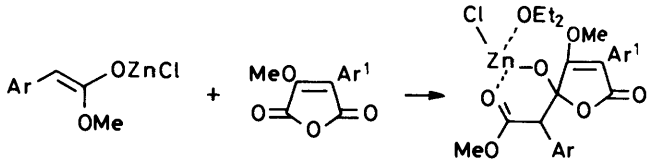
(**11**)



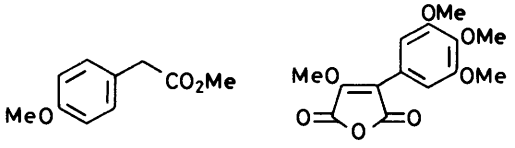
(**12**)

We reasoned that use of zinc enolates *viz.* (**13**) derived from arylphenylacetates in Reformatsky-type reactions with aryl methoxymaleic anhydrides would promote formation of zinc chelates of the corresponding β-oxy ester intermediates *viz.* (**14**)

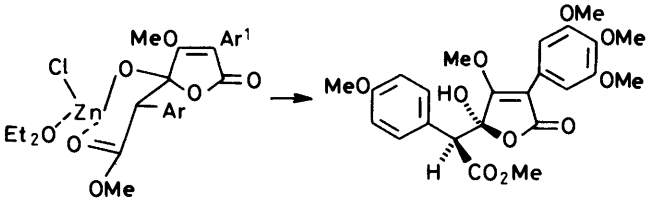
thereby: (*a*) driving the condensations to completion, and (*b*) preventing further reaction between the reagents leading to the accumulation of 2:1 adducts similar to those found from reactions using organomagnesium reagents. This was found to be the case, and the plausibility of the proposal was first examined using the arylacetate (**15**) and the maleic anhydride (**16**). The preparation of the anhydride (**16**) has already been reported.[2]



(13) (14)



(15) (16)

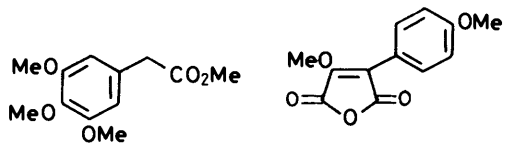


(17)

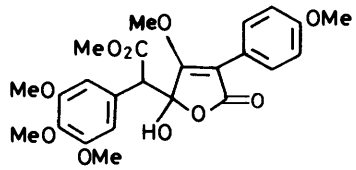
Deprotonation of the phenylacetate (**15**) with lithium di-isopropylamide at −78 °C, followed by addition of an ether solution of anhydrous zinc chloride[6] gave a clear yellow-green solution of the corresponding zinc enolate. Addition of the anhydride (**16**), followed by work-up and chromatography, then gave a low (40% based on recovered starting materials) but acceptable yield of the intermediate tertiary alcohol, produced as a single diastereoisomer. We assume from the chair-like conformation of the zinc chelate intermediate, with the bulkiest groups adopting equatorial orientations, that this diastereoisomer most likely has the *anti*-geometry shown (**17**).

In a similar manner, the Reformatsky-type condensation between the trimethoxyphenyl acetate (**18**) and the anhydride (**19**) led to a single diastereoisomer of the β-hydroxy ester (**20**). By contrast, the reaction between 2-methoxy-3-phenylmaleic anhydride and the phenylacetate (**21**) produced a 3:1 mixture of diastereoisomers of (**22**). The somewhat capricious nature of these condensations between phenylacetates and maleic anhydrides was demonstrated when it was found that in tetrahydrofuran as solvent, only starting materials were recovered. In part, we associate this feature with the greater oxygen electron pair donating capacity of tetrahydrofuran over ether, competing with the β-oxy ester intermediate for co-ordination sites on the zinc centre, thereby breaking down the zinc chelate and reversing the condensation.

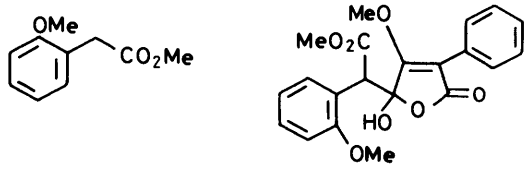
The elimination of the elements of water from the β-hydroxy esters (**17**), (**20**), and (**22**) leading to the corresponding permethylated pulvinic acids, although not completely straightforward, was achieved by treatment with methanesulphonyl chloride followed by diazabicyclononene. Thus,



(18) (19)



(20)

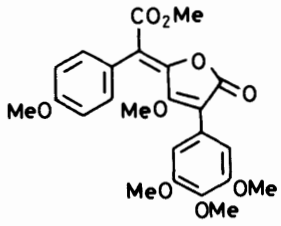


(21) (22)

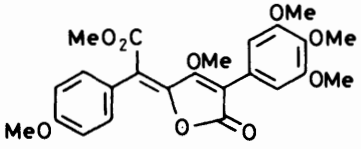
treatment of the hydroxy ester (**17**) by this procedure, produced a 5:1 mixture of *Z*- and *E*-isomers (**23**) and (**24**) respectively, of permethylated gomphidic acid, which could be separated by chromatography and crystallization as yellow solid materials m.p. 94.5—95.5 and 150—151 °C respectively. The configurations of the isomers followed unambiguously from inspection and comparison of their spectral data (see the Experimental section). In particular, the *E*-isomer (**24**) displays a distinct and characteristic low field methoxy methyl resonance at δ 3.83 in its ^{1}H n.m.r. spectrum, which is associated with the methyl tetronate methyl group deshielded by the neighbouring (*cis* to it) methoxycarbonyl group; the corresponding resonance in the *Z*-isomer is found at δ 3.4. Furthermore, when solutions of the *Z*-isomer (**23**) are left in laboratory daylight for periods of days, they rapidly undergo stereomutation leading to the corresponding *E*-geometrical isomer (**24**).[3]

The permethylated *E*-gomphidic acid (**24**) was found to be both chromatographically and spectroscopically identical with a sample obtained *via* the now classical Volhard procedure,[7] involving saponification followed by methylation and fractional crystallization of the bis-lactone (**26**) produced from condensation between the phenylacetonitriles (**25a**) and (**25b**) and diethyl oxalate. In addition, comparison by t.l.c. of both (**23**) and (**24**) with the permethylated gomphidic acid obtained earlier by us *via* condensation between the tetronate (**4b**) and 4-methoxybenzoyl formate, followed by dehydration supported the fact, noted earlier, that this isomer was largely the *Z*-isomer of permethylated gomphidic acid.[2] We now realized that even with detailed ^{1}H n.m.r. data on the two geometrical isomers of *permethylated* gomphidic acid (**23**) and (**24**), it was not possible to unambiguously confirm the structure and stereochemistry of natural gomphidic acid itself. This had to await comparison of data with the gomphidic acid produced after demethylation of (**24**) using trimethylsilyl iodide (see below), and in the light of this our earlier pronouncement on the establishment of the structure of natural gomphidic acid was hasty and indeed incorrect.[2]

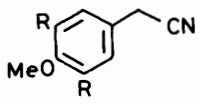
In a similar manner to that described for the dehydration of (**17**), the isomeric β-hydroxy ester (**20**) produced a mixture of geometrical isomers of permethylated isogomphidic acid [*viz.* (**27**) and (**28**)], and the β-hydroxy-ester (**22**) gave rise to the *Z*-



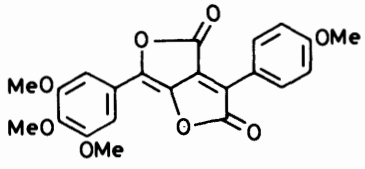
(23)



(24)

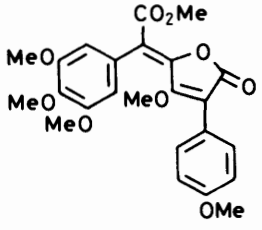


(25)
a; R = OMe
b; R = H

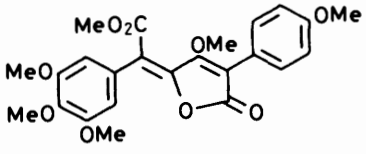


(26)

(24)
(28)



(27)



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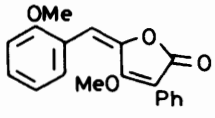
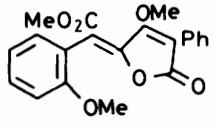


(29)



(30)

and *E*-pulvinates (**29**) and (**30**). The *E*-pulvinate (**30**) showed identical spectral features to those described by Seshadri *et al.*[8] for the methyl ether of leprapinic acid (**1**) found in *Lepraria chlorina*.

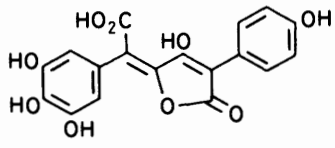
With the development of a new unambiguous route to geometrical isomers of unsymmetrically substituted permethylated pulvinic acids, finally we investigated the demethylation of these molecules to the corresponding 'free' pulvinic acids. Although some success has been achieved with hydriodic acid,[9] we were immediately attracted to trimethylsilyl iodide for carrying out these sensitive demethylations.[10] In the event, trimethylsilyl iodide proved to be an excellent demethylation agent for all the permethylated pulvinic acids examined leading to the free acids in good yield. The reactions were most conveniently carried out in deuteriochloroform solutions in ^{1}H n.m.r. tubes sealed under nitrogen and warmed to 55 °C. After approximately three days (n.m.r. monitoring) the resulting persilylated pulvinic acids were hydrolysed with methanol to give the free pulvinic acids.

Table. ^{1}H N.m.r. data (p.p.m.) for isomeric gomphidic acids.

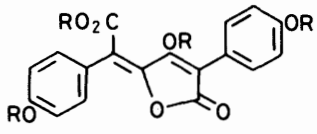
		Aryl AB system (*J* 8.3—8.5 Hz)	
Structure	Singlet	Upfield	Downfield
(**2**)	7.35	6.86	7.17
(**31**)	8.05	6.41	6.9
Natural*	7.33	6.85	7.22

* Ref. 11.

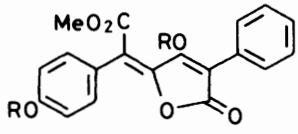
Both the geometrical isomers of permethylated gomphidic acid *viz.* (**23**) and (**24**) produced the same (*E*)-gomphidic acid (**2**) which was identical (m.p., ^{1}H n.m.r.) with a sample isolated by Steglich from *Gomphidius glutinosus*.[11] By contrast, the permethylated isogomphidic acid isomers (**27**) and (**28**) both produced isogomphidic acid (**31**) which showed ^{1}H n.m.r. data distinct from those of the natural product (Table). These data thus fully confirm the structure (**2**) for natural gomphidic acid.[11]



(31)



(32)



(33)

a; R = Me
b; R = H

As a corollary we also examined the demethylation of permethyl atromentic acid (**32a**), and of a 1:1 mixture of methyl pinastrate (**5a**) and methyl *iso*-pinastrate (**33a**) with trimethylsilyl iodide. Permethyl atromentic acid (**32a**) led to a 70% yield of atromentic acid (**32b**), which was identical (m.p. spectral data) with a sample from *Xerocomus chrysenteron*,[12] and the mixture of (**5a**) and (**33a**) produced a 1:1 mixture of 4-hydroxypulvinic acid (**5b**) and 4′-hydroxypulvinic acid (**33b**) (66%).

Experimental

For general experimental details, see ref. 13.

Methyl α-(2-Hydroxy-3-methoxy-5-oxo-4-aryl-2,5-dihydrofuran-2-yl)phenylacetates: General Procedure.—A solution of methyl arylacetate (2 mmol) in dry ether (2 cm^3) was added over 10 min to a stirred solution of lithium di-isopropylamide (2 mmol) [prepared from di-isopropylamine (0.23 g) and butyllithium (1.5M) in hexane (1.3 cm^3)] in dry ether (30 cm^3) at −78 °C under nitrogen. The solution was stirred at −78 °C for

0.5 h and then a solution of anhydrous zinc chloride (0.57M) in dry ether (3.5 cm^3), followed by more ether (200 cm^3) was added. Finely powdered 3-aryl-4-methoxyfuran-2,5-dione (2 mmol) was added, and the resulting suspension was stirred at −60 °C for 6 h, then diluted with aqueous ammonium chloride solution (50 cm^3) and chloroform (10 cm^3) and allowed to warm to 25 °C. The aqueous layer was separated and then extracted with ether (2 × 50 cm^3). Evaporation of the dried ether extracts left a residue which was purified by chromatography on silica gel to give the title compounds.

Methyl α-[2-*hydroxy*-3-*methoxy*-5-*oxo*-4-(3,4,5-*trimethoxyphenyl*)-2,5-*dihydrofuran*-2-*yl*]-4-*methoxyphenylacetate* (**17**). By the general procedure, condensation between methyl 4-methoxyphenylacetate[14] and 3-methoxy-4-(3,4,5-trimethoxyphenyl)furan-2,5-dione[2] followed by chromatography in diethyl ether, gave recovered starting materials (36% and 29% respectively) and the *carbinol* (0.27 g, 27%) as a single diastereoisomer which crystallized from methanol as needles m.p. 146.5—148 °C, $\lambda_{max.}(CHCl_3)$ 269infl. and 280 nm; $\nu_{max.}$(KBr) 3 340, 1 745, and 1 730 cm^{-1}; δ 3.62 (OMe), 3.73 (2 × OMe), 3.76 (OMe), 3.78 (OMe), 3.82 (OMe), 4.26 (C*H*CO_2Me), 5.92 (2 × =CH), 6.59 (OH), 7.11 (d, *J* 10, 2 × =CH), and 7.28 (d, (*J* 10, 2 × =CH) (Found: C, 60.8; H, 5.7%; *m/z* 442.1260. $C_{24}H_{26}O_{10}$ requires C, 60.8; H, 5.5%. M^+ − MeOH 442.1264).

Methyl α-[2-*hydroxy*-3-*methoxy*-4-(4-*methoxyphenyl*)-5-*oxo*-2,5-*dihydrofuran*-2-*yl*]-3,4,5-*trimethoxyphenylacetate* (**20**). By the general procedure, condensation between methyl 3,4,5-trimethoxyphenyl acetate[15] and 3-methoxy-4-(4-methoxyphenyl)furan-2,5-dione,[5] followed by chromatography in diethyl ether, gave recovered starting materials (37 and 14% respectively) and the *carbinol* (0.2 g, 21%) as a single diastereoisomer which crystallized from methanol as colourless needles, m.p. 118.5—119.5 °C, $\lambda_{max.}(CHCl_3)$ 270 nm; $\nu_{max.}$(KBr) 3 430, and 1 750 cm^{-1}; δ 3.6 (OMe), 3.77 (OMe), 3.86 (2 × OMe), 3.88 (2 × OMe), 4.23 (C*H*CO_2Me), 6.5 (OH), 6.59 (2 × =CH), and 6.81 (4 × =CH) (Found: C, 60.4; H, 5.8. $C_{24}H_{26}O_{10}$ requires C, 60.8, H, 5.5%).

Methyl α-[2-*hydroxy*-3-*methoxy*-5-*oxo*-4-*phenyl*-2,5-*dihydrofuran*-2-*yl*]-2-*methoxyphenylacetate* (**22**). By the general procedure, condensation between methyl 2-methoxyphenylacetate[16] and 3-methoxy-4-phenylfuran-2,5-dione[5] followed by chromatography in diethyl ether–light petroleum (b.p. 40—60 °C) (1:1), gave recovered starting materials (15 and 14% respectively) and the *carbinol* (0.22 g, 29%) as a 3:1 mixture of diastereoisomers, m.p. 63—68 °C, $\lambda_{max.}(CHCl_3)$ 272infl. and 282 nm; $\nu_{max.}$(KBr) 3 350 and 1 760 cm^{-1}, δ 3.67 (OMe), 3.81 (OMe), 3.88 (OMe), 4.95 (C*H*CO_2Me), 6.9 (OH), 6.9—7.1 (4 × =CH), and 7.2—7.5 (5 × =CH) (one diastereoisomer); δ 3.47 (OMe), 3.76 (OMe), 3.89 (OMe), 4.84 (=C*H*CO_2Me), 6.9 (OH), 6.9—7.1 (4 × =CH), and 7.2—7.5 (5 × =CH) (second diastereoisomer) (Found: *m/z* 352.0959. $C_{20}H_{16}O_6$ − MeOH requires 352.0947).

Permethylated Pulvinic Acids: General Procedure.—A solution of methanesulphonyl chloride (1.1 mol equiv.) in dry dichloromethane was added slowly to a stirred solution of the hydroxyphenylacetate (1.0 mol equiv.) in dry dichloromethane (200 cm^3) per mmol) maintained at −10 °C. The solution was stirred at room temperature for 2 h, and then washed successively with 0.2M-hydrochloric acid and water. Evaporation of the dried organic extract left a mixture of diastereoisomeric methanesulphonate) (>90%) which was used without further purification.

Diazabicyclononene (1.5 mol equiv.) was added to a solution of the diastereoisomeric methanesulphonates in dry tetrahydrofuran (200 cm^3 per mmol) at 0 °C, under nitrogen. The resulting suspension was stirred at room temperature for 2 h, then diluted to twice its volume with diethyl ether, after which the solution was washed with 0.2M-hydrochloric acid and water.

Evaporation of the dried ether extracts left a mixture of *E*- and *Z*-isomers of the permethylated pulvinic acids which were then separated by ordinary chromatography on silica or by high pressure liquid chromatography.

Methyl 4-*methoxy*-α-[3-*methoxy*-5-*oxo*-4-(3,4,5-*trimethoxyphenyl*)-2,5-*dihydrofuran*-2-*ylidene*]*phenylacetate* (*permethylated gomphidic acid*) (**24**). By the general procedure, dehydration of the hydroxyphenylacetate (**17**), followed by high pressure liquid chromatography in hexane–diethyl ether (2:3) gave: (*a*) the *Z*-isomer (**23**) of the title compound (0.32 g, 57%) (eluted first) which crystallized from diethyl ether–cyclohexane as yellow microcrystals, m.p. 94.5—95.5 °C, $\lambda_{max.}(CHCl_3)$ 356 nm, $\nu_{max.}$ 1 773 and 1 724 cm^{-1}; δ 3.4 (OMe), 3.84—3.89 (5 × OMe), 6.8 (2 × =CH), 6.9 (d, *J* 9, 2 × =CH), 7.35 (d, *J* 9, 2 × =C*H*) (Found: C, 63.0; H, 5.5%; M^+, 456.1420. $C_{24}H_{24}O_9$ requires C, 63.2; H, 5.3%; *M*, 456.1420), and (*b*) *E*-permethylated gomphidic acid (0.10 g, 18%) (eluted second) which crystallized from methanol as yellow needles m.p. 150—151 °C, $\lambda_{max.}(CHCl_3)$ 363 nm (21 800); $\nu_{max.}$(KBr) 1 767 and 1 733 cm^{-1}; δ 3.83 (OMe), 3.85 (OMe), 3.89 (OMe), 3.92 (OMe), 6.8 (2 × =CH), 6.95 (d, *J* 9, 2 × =CH), 7.66 (d, *J* 9, and 2 × =CH) (Found: C, 63.0; H, 5.5%; M^+, 456.1401). The *E*-permethylated gomphidic acid was identical in all respects (m.p., mixed m.p., chromatographic behaviour, i.r., u.v., ^{1}H n.m.r.) with a sample obtained from fractional crystallization of the mixture of pulvinates produced from the 3,4,4′,5-tetramethoxypulvinic dilactone (**26**) following saponification and methylation with diazomethane.

Methyl α-[3-*Methoxy*-4-(4-*methoxyphenyl*)-5-*oxo*-2,5-*dihydrofuran*-2-*ylidene*]-3,4,5-*trimethoxyphenylacetate* (*Permethylated Isogomphidic Acid*) (**28**).—A solution of 3,4,4′,5-tetramethoxypulvinic dilactone (**26**) (0.27 g) in 2% methanolic potassium hydroxide (25 cm^3) was kept at 25 °C for 2 h and then diluted with 2M-hydrochloric acid and extracted with chloroform. The chloroform extracts were treated with methanol whereupon a mixture of the corresponding isomeric hydroxy carboxylic acids separated as a yellow solid (0.25 g). The mixture was dissolved in ether at 0 °C and treated with a solution of diazomethane in dry ether, until no more reaction occurred. The solution was kept at 0 °C for 1 h, then at 25 °C for 2 h, and evaporated to dryness. The residue was boiled in methanol and the insoluble material was removed by filtration.

Recrystallization from benzene gave *E*-permethylated isogomphidic acid (0.056 g) as yellow needles, m.p. 205—206 °C, $\lambda_{max.}(CHCl_3)$ 364 (19 900) nm, $\nu_{max.}$(KBr) 1 760, 1 710 cm^{-1}; δ 7.52 (d, *J* 9, 2 × =CH), 6.97 (d, *J* 9, 2 × =CH), 6.94 (2 × =CH), and 3.8—3.9 (6 × OMe) (Found: C, 63.0; H, 5.7%; M^+, 456.1414. $C_{24}H_{24}O_9$ requires C, 63.2; H, 5.3%; *M*, 456.1414). The methanol filtrate, from above, was evaporated to dryness to leave a yellow powder which recrystallized from benzene to give permethylated gomphidic acid (0.08 g) showing identical spectral data to those described earlier.

By the general procedure, dehydration of the hydroxyphenylacetate (**20**) followed by chromatography in diethyl ether gave a 5:1 mixture of *Z*- and *E*-isomers of the title compound (46%) as a yellow semi-solid, δ (*Z*-isomer) 3.39 (OMe), 3.83 (OMe), 3.88 (2 × OMe), 3.9 (2 × OMe), 6.69 (2 × =CH), 6.96 (d, *J* 9, 2 × =CH), and 7.6 (d, *J* 9, 2 × =CH) (Found: M^+, 456.1414).

3,4,4′,5-*Tetramethoxypulvinic Dilactone* (**26**).—A solution of 2-(4-methoxyphenyl)-5-(3,4,5-trimethoxyphenyl)-3,4-dioxoadiponitrile (3.5 g)[11] [prepared from 3,4,5-trimethoxyphenylacetonitrile and ethyl 3-cyano-3-(4-methoxyphenyl)pyruvate] in acetic acid (33 cm^3), water (20 cm^3), and concentrated sulphuric acid (14 cm^3) was heated under reflux for 0.25 h. The

mixture was cooled and a gelatinous grey precipitate separated which was filtered off. The residue was heated under reflux in acetic anhydride (40 cm^3) for 0.25 h, then cooled and filtered. Recrystallization of the residue from acetic acid gave the dilactone (0.5 g) as orange needles, m.p. 179.5—180.5 °C, $\lambda_{max.}(CHCl_3)$ 426 nm; $\nu_{max.}$(KBr) 1 805, 1 710, and 1 680 cm^{-1}; δ 3.92 (OMe), 3.97 (OMe), 4.0 (2 × OMe), 7.04 (d, *J* 9, 2 × =CH), 7.29 (2 × =CH), and 8.04 (d, *J* 9, 2 × =CH) (Found: M^+, 410.0973. $C_{22}H_{18}O_8$ requires *M*, 410.1002).

Methyl 2-Methoxy-α-(3-methoxy-5-oxo-4-phenyl-2,5-dihydrofuran-2-ylidene)phenylacetate (*O-Methyl-leprapinic Acid*) (**30**).—By the general procedure, dehydration of the hydroxy phenylacetate (**22**), followed by chromatography in diethyl ether gave: (*a*) the *Z*-isomer (**29**) of the title compound (10%) (eluted first) as colourless crystals, m.p. 96—97 °C, $\lambda_{max.}$(MeOH) 319 and 271 nm; $\nu_{max.}(CHCl_3)$ 1 778 and 1 732 nm; δ 3.33 (OMe), 3.82 (OMe), 3.83 (OMe), 6.89—7.01 (m, 2 × =CH), 7.29—7.43 (5 × =CH), and 7.52—7.56 (m, 2 × =CH) (Found: M^+, 366.1114. $C_{21}H_{18}O_6$ requires *M* 366.1104), and (*b*) (*E*)-*O*-methyl-leprapinic acid (15%) (eluted second) as colourless crystals, m.p. 148—149 °C (Seshadri *et al.*[8] give m.p. 150—152 °C for naturally derived material), $\lambda_{max.}$(MeOH) 333, 264, and 255 nm; $\nu_{max.}(CHCl_3)$ 1 770 and 1 730 cm^{-1}; δ 3.79 (OMe), 3.8 (OMe), 3.84 (OMe), 6.8—7.05 (m, 2 × =CH), 7.3—7.5 (m, 5 × =CH), 7.52—7.56 (m, 2 × =CH).

Further amounts of (*E*)-*O*-methyl-leprapinic acid could be obtained by photoisomerisation (laboratory daylight, 2 weeks) of the corresponding *Z*-isomer in chloroform.

Pulvinic Acids: General Procedure.—A solution of permethylated pulvinic acid and trimethylsilyl iodide (10 mol equiv.) in deuteriochloroform (1 cm^3), sealed under nitrogen in an n.m.r. tube, was kept at 55 °C until the ^{1}H n.m.r. spectrum showed no absorption in the region δ 3.0—4.0 (*ca.* 72 h). The solution was evaporated to dryness under reduced pressure and the residue of persilylated pulvinic acid was dissolved in methanol (5 cm^3). The solution was kept at 25 °C for 0.25 h and then evaporated to dryness under a nitrogen atmosphere. Chromatography of the residue on silica, using benzene–ethyl formate–formic acid (13:5:4) as the eluant, followed by crystallization then gave the pulvinic acid. Combustion analyses of the pulvinic acids proved to be erratic, and meaningful data could not be recorded.

(E)-4-*Hydroxy*-α-[3-*hydroxy*-5-*oxo*-4-(3,4,5-*trihydroxyphenyl*)-2,5-*dihydrofuran*-2-*ylidene*]*phenylacetic acid* [(E)-4-(4-*hydroxy*-α-*carboxybenzylidene*)-2-(3,4,5-*trihydroxyphenyl*)-*tetronic acid: gomphidic acid*] (**2**). By the general procedure, deprotection of (*E*)-permethylgomphidic acid (65 mg) gave gomphidic acid (20 mg, 65%) which crystallized from water as a red solid, m.p. 205—215 °C (decomp.), $\lambda_{max.}$(EtOH) 260 (13 800) and 398 nm (6 500) (lit.,[11] $\lambda_{max.}$ 400 nm); $\lambda_{max.}$(EtOH–NaOH) 304 (10 000) and 402 nm (13 500); $\nu_{max.}$(Nujol) 3 360, 1 741, and 1 603 cm^{-1}; δ[$(CD_3)_2CO$] 6.86 (d, *J* 8.3, 2 × =CH), 7.17 (d, *J* 8.3, 2 × =CH), 7.35 (2 × =*H*). The synthetic sample was identical in its ^{1}H n.m.r. spectrum [lit.,[11] 6.85 (d, *J* 8.5, 2 H), 7.22 (d, *J* 8.5, 2 H), and 7.33 (2 H)] with an authentic sample from *Gomphidius glutinosus*[11]

(E)-3,4,5-*Trihydroxy*-α-[3-*hydroxy*-4-(4-*hydroxyphenyl*)-5-*oxo*-2,5-*dihydrofuran*-2-*ylidene*]*phenylacetic acid* [(*E*)-2-(4-*hydroxyphenyl*)-4-(3,4,5-*trihydroxy*-α-*carboxybenzylidene*)-*tetronic acid: isogomphidic acid*] (**31**). By the general procedure, deprotection of (*E*)-permethylisogomphidic acid (35 mg) gave isogomphidic acid (18 mg) which crystallized from water as orange-red needles, m.p. 220—228 °C (decomp.), $\lambda_{max.}$(EtOH) 263 (20 100) and 397 nm (7 800); $\lambda_{max.}$(EtOH–NaOH) 269 (17 500), and 403 (4 200) nm; $\nu_{max.}$(KBr) 3 340, 1 735, and 1 580 cm^{-1}; δ[$(CD_3)_2CO$] 6.41 (2 × =CH), 6.9 (d, *J* 8.5, 2 × =CH), 8.05 (d, *J* 8.5, 2 × =CH); *m/z* (FAB) 373(5%), 279(22), 239(18) 221(18), 178(13), 149(17), 131(100), 115(22), 61(40), and 55(11).

(E)-4-*Hydroxy*-α-[3-*hydroxy*-4-(4-*hydroxyphenyl*)-5-*oxo*-2,5-*dihydrofuran*-2-*ylidene*]*phenylacetic acid* [(E)-2-(4-*Hydroxyphenyl*)-4-(4-*hydroxy*-α-*carboxybenzylidene*)*tetronic acid: atromentic acid*] (**32b**). By the general procedure, deprotection of *E*-permethylatromentic acid (80 mg) gave atromentic acid (48 mg, 70%) which crystallized from water as red-orange needles, m.p. 287—289 °C (lit.,[12] 300 °C) $\lambda_{max.}$(EtOH) 403 nm; $\lambda_{max.}(H_2O)$ 370 nm; $\nu_{max.}$ 3 350, 1 743, and 1 595 cm^{-1}; δ[$(CD_3)_2CO$] 6.85 (d, *J* 8.2, 2 × =CH), 6.9 (d, *J* 8.2, 2 × =CH), 7.25 (d, *J* 8.2, 2 × =CH), and 8.02 (d, *J* 8.2, 2 × CH). The synthetic sample was identical in its ^{1}H n.m.r. spectrum (lit.,[17] δ 6.85, 6.87, 7.22, and 8.02) with an authentic sample from *Xerocomus chrysenteron*.[17]

(E)-α-[3-*Hydroxy*-4-(4-*hydroxyphenyl*)-5-*oxo*-2,5-*dihydrofuran*-2-*ylidene*]*phenylacetic acid:* 4-*hydroxypulvinic acid* (**5b**) *and* (E)-4-*hydroxy*-α-(3-*hydroxy*-5-*oxo*-4-*phenyl*-2,5-*dihydrofuran*-2-*ylidene*)*phenylacetic acid:* 4′-*hydroxypulvinic acid* (**33b**). By the general procedure, deprotection of a 1:1 mixture of methyl pinastrate (**5a**) and its isomer (**33a**) (130 mg) gave 4-hydroxypulvinic acid (**5b**) (32 mg, 23%) which crystallized from water as yellow needles, m.p. 174—175 °C, $\lambda_{max.}$(EtOH) 256 (13 600) and 397 nm (6 900); $\nu_{max.}$ 3 360, 1 740, and 1 600 cm^{-1}; δ[$(CD_3)_2CO$] 6.92 (d, *J* 8, 2 × =CH), 7.41 (5 × =CH), 8.02 (d, *J* 8, 2 × =CH), and 4′-hydroxypulvinic acid (**33b**) (30 mg, 21%) m.p. 160—163 °C (H_2O), $\lambda_{max.}$(EtOH) 263 (14 500) and 367 nm (9 500); $\nu_{max.}$ 3 380 and 1 733, and 1 600 cm^{-1}; δ[$(CD_3)_2CO$] 6.87 (d, *J* 8, 2 H), 7.36 (d, *J* 9, 2 H) 7.3—7.5 (m, 3 H), 8.08 (dd, *J* 7 and 2, 2 H); *m/z* 324(15%), 307(29), 306(100), 281(10), 280(37), 250(17), 194(22), 162(36), 161(26), 145(48), 134(31), 133(40), 117(16), 113(22), 105(29), 89(44), 83(13), 77(11), 70(15), 55(14), 51(18), and 43(11).

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