Synthesis of Isoaspertetronin, Isogregatin and Related *O*-Methyltetronic Acids. Reassignment of 5-Methoxyfuran-3(2*H*)-one Structures to the Aspertetronin Group of Natural Products

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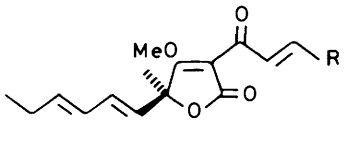
Reaction between (3*E*,5*E*)-octa-3,5-dien-2-one and the vinylic anion (**10**) derived from (**9**) leads, in one step, to the *O*-methyltetronic acid (**12**). The tetronate (**12**) was also obtained by treatment of the lithium anion derived from ethyl propiolate with the octadienone (**11**), followed by reaction of the resulting hydroxyester (**17**) with methanolic sodium methoxide.

Metallation of the *O*-methyltetronic acid (**12**), followed by treatment of the resulting C-2(α-)-vinylic anion (**19**) with methyl acetate and methyl (*E*)-butenoate then gave the acylated *O*-methyltetronic acids (**20**) and (**22**) respectively. The *O*-methyltetronic acids (**20**) and (**22**) are shown, by comparison of physical and spectroscopic data, to be enol ether isomers of the natural products gregatin B and aspertetronin A found in *Aspergillus* sp. and *Cephalosporium gregatum*.

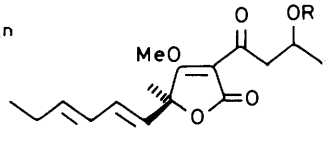
The aspertetronin (also known as gregatin and graminin) group of natural products are all shown to have the 5-methoxyfuran-3(2*H*)-one structure (**25**) rather than the previously assigned *O*-methyl tetronic acid structure *e.g.* (**1**). We propose the names isoaspertetronin and isogregatin B for the synthetic *O*-methyltetronic acids (**22**) and (**20**) respectively.

The aspertetronins are a family of oxygen heterocycles found in *Aspergillus* and *Cephalosporium* sp. The names 'gregatin' and 'graminin' have also been used to describe some members of the group. The first two members of this family of natural products were isolated in 1969 from *Aspergillus rugulosus*,[1] and structural investigations suggested that the metabolites had the novel *O*-methyltetronic acid structures (**1a**) and (**2a**). Optical antipodes of (**1a**) and (**2a**), accompanied by the acyl analogues (**3a**) and (**3b**) and the methyl ether (**2b**) were later isolated from *Cephalosporium gregatum*[2] and *A. panamensis*,[3] and the homologue (**1b**) of (**1a**) has been found in *C. gramineum*.[4] The aspertetronins all show significant antibacterial and antifungal activity. 'Gregatin A' [the enantiomer of the aspertetronin (**1a**)] and 'graminin A' (**1b**) have also been implicated as the causal



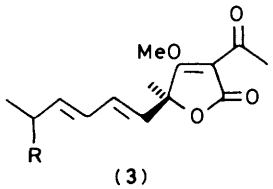
(1)

a; R = Me; **b**; R = Pr^n



(2)

a; R = H; **b**; R = Me

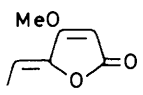


(3)

a; R = H; **b**; R = OH

agents of brown stem rot of adzuki beans[5] and stripe disease of wheat.[6]

In the preceding paper[7] we showed that lithium di-isopropylamide removes the α-protons from the *O*-methyltetronic acids (**4**) and (**6**) in a totally regiospecific manner, giving the novel vinylic carbanions (**5**) and (**7**) respectively. These anions were then found to react readily with a range of electrophiles at −78 °C in tetrahydrofuran to provide a preparatively useful procedure for the synthesis of the corresponding α-(C-2)-substituted *O*-methyltetronic acids. In this paper we describe the extension of this chemistry to provide an exceptionally short synthesis of the acylated *O*-methyltetronic acid structures (**1a**) and (**3a**) assigned for natural aspertetronin A and gregatin B.[8]



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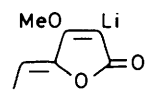

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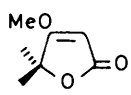
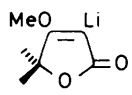


(6)



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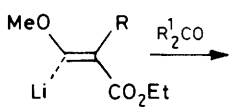
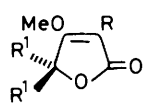
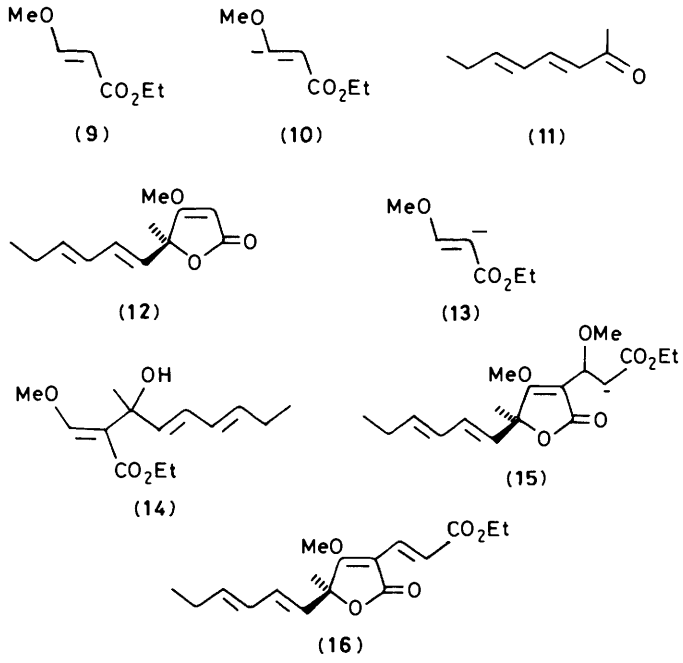




(8)

Studies by Uda *et al*[9] have shown that metallated (*E*)-3-methoxypropenoates react with carbonyl compounds in one step to provide the substituted tetronic acid ring system (**8**). Accordingly we first examined the one-step synthesis of the tetronic acid derivative (**12**) using the vinyl anion (**10**) derived from ethyl (*E*)-3-methoxypropenoate (**9**) and the (3*E*,5*E*)-octadienone (**11**). Thus, metallation of ethyl (*E*)-3-methoxypropenoate at −78 °C, using lithium di-isopropylamide in tetrahydrofuran, and treatment of the resulting vinyl carbanion (**10**)[10] within 1 min, with the octadienone (**11**), gave on work-up a 45% yield of the *O*-methyltetronic acid (**12**) in one step. In some experiments, using an excess of lithium di-isopropylamide and longer periods for the metallation of (**9**), the yield of (**12**) was greatly reduced and significant amounts of the by-products (**14**) and (**16**) were separated by chromatography. Carbinol (**14**)

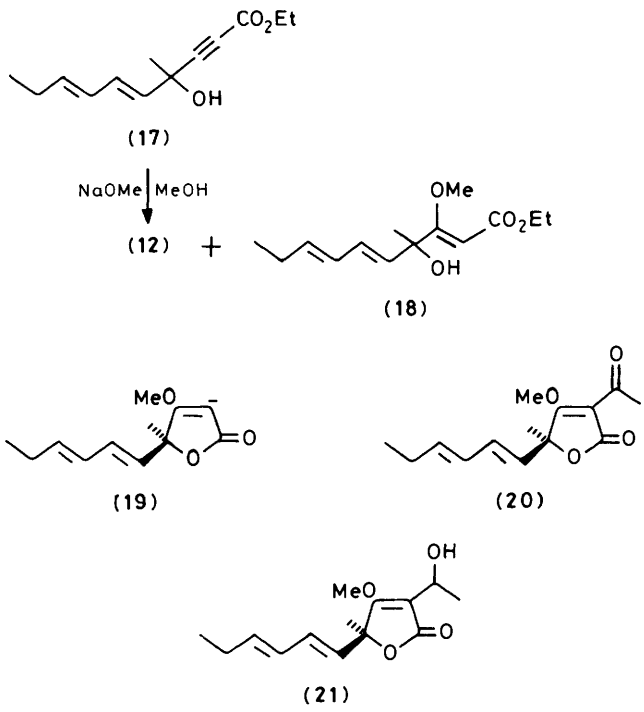
is produced as a result of addition of the alternative (thermodynamic) vinyl anion (**13**)[11] produced from (**9**) to the octadienone (**11**), and the substituted tetronic acid (**16**) results from *in situ* Michael reaction from the first-formed tetronic acid (**12**) with ethyl (*E*)-3-methoxypropenoate [to (**15**)], followed by elimination of methoxide ion.



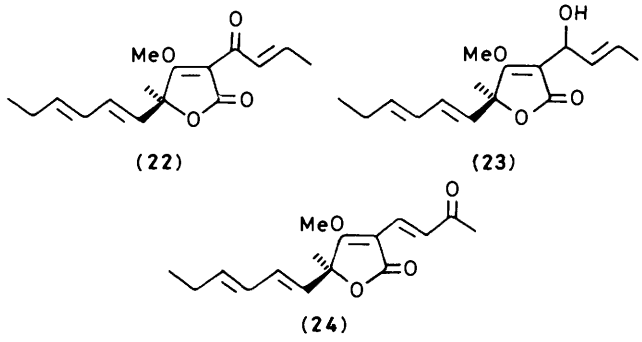
Although the synthesis of (**12**) *via* the vinyl anion (**10**) can be commended for its simplicity, its capricious nature and modest yield led us to investigate an alternative method. Treatment of the lithium anion derived from ethyl propiolate with the octadienone (**11**) led to the hydroxy ester (**17**), which was isolated as a pale yellow oil in 52% yield. When this hydroxy ester was treated with methanolic sodium methoxide,[11] a mixture of the required *O*-methyltetronic acid (**12**) (43%) and the (*Z*)-α,β-unsaturated ester (**18**) (34%) was produced, which could be separated by chromatography. Although this alternative route to (**12**) lacked stereospecificity, it has the preparative advantage over that involving the vinyl anion (**10**) in that it can be carried out on significantly larger scale.

With the 5,5-disubstituted *O*-methyltetronate (**12**) in hand, it only remained to acylate the α-(C-2) anion derived from (**12**) with appropriate acylating agents in order to produce the natural aspertetronins (**1**)—(**3**). Metallation of (**12**) using lithium di-isopropylamide at −78 °C, followed by acylation of the resulting vinyl anion (**19**) with methyl acetate, as expected from our previous investigations,[7] led exclusively to the 2-substituted product (**20**). The yield of (**20**) from direct acylation of (**12**) was only modest (max. 20%), and we found that it was preparatively more convenient to synthesize (**20**) from (**12**) in two stages following reaction of the desired anion (**19**) with acetaldehyde (84%), and oxidation of the resulting carbinol (**21**) with either pyridinium dichromate in dimethylformamide or better with manganese dioxide in dichloromethane.

In a parallel series of reactions the vinyl anion (**19**) was treated with methyl crotonate and with crotonaldehyde leading to the *O*-methyl tetronic acids (**22**); (20%) and (**23**); (64%) respectively. Subsequent oxidation of the carbinol (**23**) using manganese dioxide then led to the same acyl tetronate (**22**) produced from direct acylation of (**19**), but oxidation with



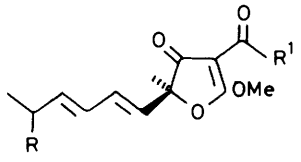
pyridinium chlorochromate instead led to the isomeric enone (**24**) resulting from oxidation of the transposed allylic alcohol corresponding to (**23**).



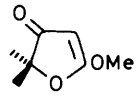
The *O*-methyltetronic acids (**20**) and (**22**) are the structures proposed for two members, *i.e.* aspertetronin A and gregatin B respectively, of the aspertetronin group of natural products. It came as somewhat of a surprise however, to find that neither the physical or spectroscopic data recorded for (**20**) and (**22**) correlated with those data reported for the corresponding natural products. Thus, both the synthetic *O*-methyltetronic acids (**20**) and (**22**) were obtained as viscous oils, and each showed a single maximum in the electronic absorption spectrum centred at about 225 nm. By contrast, naturally derived aspertetronin A and gregatin B are crystalline solids (m.p. 72 and 83 °C respectively), and each shows strong absorption above 230 nm in its u.v. spectrum, *i.e.* 230, 240sh and 300 nm for aspertetronin A and 235 and 266 nm for gregatin B. Moreover, whereas (**20**) and (**22**) show two very strong carbonyl absorption maxima, near 1 760 and 1 750 cm^{-1}, in their i.r. spectra, the corresponding natural products instead show a single carbonyl absorption at 1 705 cm^{-1}, with a small shoulder at 1 740 cm^{-1}. Although significant differences were also noted between the mass spectra of (**22**) and natural aspertetronin A,

apart from a difference in chemical shift between the methoxy resonances (δ 3.72 natural, δ 4.05 synthetic) their ^{1}H n.m.r. spectra were closely similar.

The above data, and particularly the i.r. data led us to suggest that our synthetic *O*-methyltetronic acids and the natural aspertetronins were enol ether isomers of one another, with the natural products having the 5-methoxyfuran-3(2*H*)-one structure (**25**).[12] To substantiate this idea we examined the spectral data of the authentic 5-methoxyfuran-3(2*H*)-one (**26**) obtained as a minor product from methylation of 5,5-dimethyltetronic acid[13] with diazomethane. The u.v. and i.r. spectral data recorded for the isomeric furanones (**26**) and (**27**)[14] are summarised on the formulae.



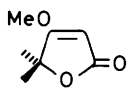
(25)



(26)

$\lambda_{max.}$ 249 nm (ε 14 000)

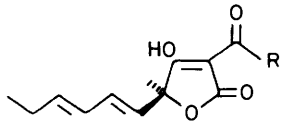
ν_{max} 1700 cm^{-1}



(27)

$\lambda_{max.}$ 218 nm (ε 13 000)

ν_{max} 1745 cm^{-1}



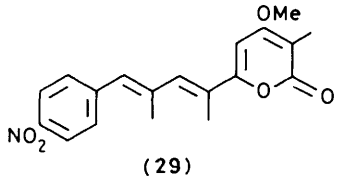
(28)

a; R = Me; b; R = HC=CHMe

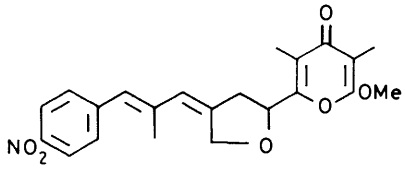
Comparison of the above set of spectral data with those recorded for synthetic (**20**) and (**22**) and for natural aspertetronin A and gregatin B establish firmly that the latter have 5-methoxyfuran-3(2*H*)-one structures [*viz.* (**25**)]. Since the structures of the related metabolites from *Aspergillus* and *Cephalosporium* sp. have all been deduced by comparison of spectral data with those of aspertetronin A, it follows that all known aspertetronins ('gregatins' and 'graminins') have the 5-methoxyfuran-3(2*H*)-one ring system rather than the *O*-methyltetronic acid structure previously proposed for them. We therefore suggest the names isoaspertetronin A and isogregatin B for the synthetic *O*-methyltetronic acids (**22**) and (**20**) respectively.

After publication of our work in preliminary form,[8,12] two other groups of researchers published their studies of the synthesis of isoaspertetronin A and isogregatin B.[15,16] In addition, Takaiwa and Yamashita[17] subsequently effected a synthesis of (±)-gregatin B (**25**; R = H, R^1 = Me) *via* methylation of the free tetronic acid (**28a**) using diazomethane, followed by extensive chromatography. Our own attempts to synthesize (±)-gregatin B and (±)-aspertetronin A (**25**; R = H, R^1 = HC=CHMe) *via* methylation of the corresponding free tetronic acids (**28a**) and (**28b**) respectively, using diazomethane were less successful; instead we isolated only the *O*-methyltetronic acids (**20**) and (**22**).

To our knowledge 5-methoxyfuran-3(2*H*)-ones have not previously been reported in Nature, whereas natural tetronic acids are widely distributed. It is interesting, that in the corresponding pyrone series of natural products, both α- and γ-pyrones, *e.g.* luteoreticulin[18] (**29**) and aureothin (**30**),[19] have been found in *Streptomyces* sp.



(29)



(30)

Experimental

For general experimental details see ref. 20.

(3E,5E)-*Octa*-3,5-*dien*-2-*one* (**11**).—A solution of diethyl acetylmethylphosphonate (2.6 g) in dry dimethoxyethane (5 cm^3) was added over 5 min to a stirred suspension of sodium hydride (0.35 g) in dry dimethoxyethane (30 cm^3) at 0 °C under an atmosphere of nitrogen. The mixture was stirred at 0 °C for 0.25 h, and was then added dropwise to a stirred solution of (*E*)-pent-2-enal (1.13 g) in dry dimethoxyethane (5 cm^3) maintained at 0 °C under nitrogen. The mixture was stirred at 0 °C for 0.5 h and then at 23 °C for 24 h when it was acidified with 2M-hydrochloric acid. The organic layer was separated, and the aqueous layer was then extracted with ether (2 × 20 cm^3). The combined organic extracts were washed with water and brine, then dried and evaporated to leave an orange oil. Chromatography on silica using 9:1 n-pentane–ether as the eluant gave the *dienone* (0.52 g, 34%)[21] as an almost colourless oil, b.p. 93—96 °C at 17 mmHg, $\lambda_{max.}$(EtOH) 273 nm; $\nu_{max.}$(film) 1 688, 1 665, 1 640, and 1 598 cm^{-1}; δ 0.99 (t, *J* 7.5, CH_2*Me*), 2.2 (COMe), 2.4—2.05 (m, 2H), 6.34—5.96 (m, 3 × =C*H*), and 7.07 (ddd, *J* 15.5, 6, and 3.5, C*H*=CHCO). The same dienone was also produced, but in lower yield, from an aldol condensation between (*E*)-pent-2-enal and acetone in the presence of pulverised barium hydroxide.

Ethyl (5E,7E)-4-*Hydroxy*-4-*methyldeca*-5,7-*dien*-2-*ynoate* (**17**).—Ethyl propiolate (0.85 g) was added to a stirred solution of lithium di-isopropylamine (1.1 equiv.) in dry tetrahydrofuran (20 cm^3) at −78 °C under an atmosphere of nitrogen. The solution was stirred at −78 °C for 5 min and then a solution of (3*E*,5*E*)-octa-3,5-dien-2-one (0.98 g) in dry tetrahydrofuran (2 cm^3) was introduced during 0.25 h. The resulting mixture was kept at −78 °C for 6 h and then allowed to warm to 23 °C, where it was diluted with pH 7 phosphate buffer and extracted with ether (3 × 20 cm^3). The combined ether extracts were washed with water and brine, then dried and evaporated under reduced pressure to leave an orange oil. Chromatography on flash silica using 3:7 ether–n-pentane as the eluant gave the *decadienoate* (0.91 g, 52%) as a pale yellow oil, $\nu_{max.}$(film) 3 400, 2 250, and 1 720 cm^{-1}; δ 1.02 (t, *J* 7.5, CH_2*Me*), 1.3 (t, *J* 8, *Me*CH_2O), 1.61 (Me), 2.38—1.94 (m, =CHCH_2Me), 3.46 (br, OH), and 4.25 (q, *J* 8, OCH_2Me), and 6.65—5.58 (m, 4 H).

5-[(1E,3E)-*Hexa*-1,3-*dienyl*]-4-*methoxy*-5-*methylfuran*-2(5H)-*one* (**12**).—(*i*) A solution of ethyl 3-methoxypropenoate

(**9**) (0.65 g) in dry tetrahydrofuran (0.5 cm^3) was added to a stirred solution of lithium di-isopropylamide (5 mmol) in dry tetrahydrofuran (40 cm^3) maintained at −72 °C under an atmosphere of nitrogen. The mixture was stirred at −72 °C for 0.5 min, and then a solution of (3*E*,5*E*)-octa-3,5-dien-2-one (0.62 g) in dry tetrahydrofuran (0.5 cm^3) was added all at once. The resulting yellow-green solution was stirred at −72 °C for 1.25 h and then allowed to warm to −40 °C when it was quenched with saturated aqueous ammonium chloride (25 cm^3). The mixture was extracted with ether, and the combined ether extracts were then dried and evaporated to leave an orange oil (1.15 g). Chromatography on flash silica using ether–light petroleum (b.p. 60—80 °C) (9:1) as the eluant gave the *furanone* (0.46 g, 44%)[22] as a colourless oil, b.p. 110 °C (oven) at 0.05 mmHg, $\lambda_{max.}$(EtOH) 224 nm; $\nu_{max.}$(film) 1 758 and 1 638 cm^{-1}; δ 0.95 (t, *J* 5, CH_2*Me*), 1.51 (Me), 2.05 (m, 2 H), 3.84 (OMe), 4.92 (=CHCO), 5.51 (d, *J* 17, =C*H*CMe), and 6.44—5.7 (m, 3 H); (Found: M^+, 208.1060. $C_{12}H_{16}O_3$ requires *M*, 208.1099).

In some experiments with an excess of lithium di-isopropylamide and longer periods for the metallation of (**9**), the yield of the furanone was greatly reduced and the by-products (**14**) [δ 1.29 (t, *J* 7, CO_2CH_2*Me*), 3.8 (OMe), 4.26 (q, *J* 7, CO_2CH_2Me), and 6.72 (MeOC*H*=)] and (**16**) [$\lambda_{max.}$(EtOH) 220infl. and 275 nm; $\nu_{max.}$ 1 745, 1 708, 1 640, and 1 610 cm^{-1}; δ 1.05 (t, *J* 7, =CH, CH_2*Me*), 1.34 (t, *J* 7, CO_2CH_2*Me*), 1.62 (Me), 2.17 (m, =CHCH_2Me), 4.23 (q, *J* 7, CO_2CH_2Me), 4.3 (OMe), 6.5—5.5 (m, 4 H), 7.0 (d, *J* 15, =C*H*CO_2Et), and 7.62 (d, *J* 15, C*H*:CH) (Found M^+, 306.1469. $C_{17}H_{22}O_5$ requires *M*, 306.1467)] were separated by chromatography.

(*ii*) A solution of ethyl (5*E*,7*E*)-4-hydroxy-4-methyldeca-5,7-dien-2-ynoate (0.91 g) in dry methanol (5 cm^3) was added dropwise to a stirred solution of sodium methoxide [prepared from Na, (30 mg)] in methanol (20 cm^3) at 23 °C under an atmosphere of nitrogen. The mixture was stirred at 23 °C for 2 days and then poured into water (20 cm^3) and extracted with ether (3 × 15 cm^3). The combined ether extracts were washed with water and brine and then dried and evaporated under reduced pressure to leave a brown oil. Chromatography on silica using 4:1 n-pentane–ether as the eluant gave (*a*) the *furanone* (**12**) (0.37 g, 43%) showing spectral data identical with those described above, and (*b*) methyl (2*Z*,5*E*,7*E*)-4-*hydroxy*-3-*methoxy*-4-*methyldeca*-2,5,7-*trienoate* (**18**) (0.33 g, 34%) as a colourless oil, $\nu_{max.}$(film) 1 715 and 1 630 cm^{-1}; δ 1.46 (Me), 3.01 (br, OH), 3.7 (CO_2Me), 3.98 (OMe), 5.67 (=CH), and 6.47—5.76 (m, 4 H) (Found M^+, 240.1330. $C_{13}H_{20}O_4$ requires *M*, 240.1362).

Metallation and Alkylation of 5-[(1E,3E)-*Hexa*-1,3-*dienyl*]-4-*methoxy*-5-*methylfuran*-2(5H)-*one* (**12**).—*General procedure.* A solution of the furan-2(5*H*)-one (**12**), (0.37 g) in dry tetrahydrofuran (4 cm^3) was added dropwise over 10 min to a stirred solution of lithium di-isopropylamide (1.1 equiv.) in dry tetrahydrofuran (5 cm^3) and hexamethylphosphoric triamide (0.7 cm^3) at −78 °C under an atmosphere of nitrogen. The solution was stirred at −78 °C for 10 min and then the aldehyde (3.0 equiv.) was added at −78 °C during 0.25 h. The resulting mixture was kept at −78 °C for 1 h and then poured into pH 7 phosphate buffer. The aqueous layer was separated and then extracted with ether. The combined organic extracts were washed with water and brine and then dried and evaporated under reduced pressure. Chromatography of the residue on flash silica which had been deactivated with triethylamine, using 2:3 n-pentane–ether as the eluant, gave the alkylated product.

[(1E,3E)-*Hexa*-1,3-*dienyl*]-3-(1-*hydroxyethyl*)-4-*methoxy*-5-*methylfuran*-2(5H)-*one* (**21**).—By the general procedure, alkylation of the anion derived from (**12**), with acetaldehyde, followed by chromatography gave the substituted *furanone* (84%) as a pale yellow oil, $\nu_{max.}$(film) 1 749 and 1 650 cm^{-1}; δ 0.95 (t, *J* 7.5, CH_2*Me*), 1.47 [d, *J* 6, CH(OH)*Me*], 1.49 (Me), 2.07 (m, =CHCH_2Me), 3.65 (br d, *J* 11, OH), 4.06 (OMe), 4.93, 4.72 [q, *J* 5.5, C*H*(OH)Me, diastereoisomers], and 6.41—5.38 (m, 4 H) (Found: M^+, 252.1352. $C_{14}H_{20}O_4$ requires *M*, 252.1362).

3-*Acetyl*-5-[(1E,3E)-*hexa*-1,3-*dienyl*]-4-*methoxy*-5-*methylfuran*-2(5H)-*one. Isogregatin B* (**20**).—(*i*) By the procedure described for the preparation of isoaspertetronin A (below), oxidation of the carbinol (**21**) with manganese dioxide (or with pyridinium dichromate gave the *furanone* (62%) as a pale yellow oil, $\nu_{max.}$(film) 1 755, 1 685, 1 660, and 1 612 cm^{-1}; δ 0.95 (t, *J* 7.5, CH_2*Me*), 2.53 (Me), 4.12 (OMe), and 5.49 [d, *J* 17, HC=C*H*C(Me)], and 6.5—5.7 (m, 3 H); δ_C 195.1, 183.9, 169.5, 139.9 (d), 132.3 (d), 127.6 (d), 126.3 (d), 103, 82.4, 63.7 (q), 30.6 (q), 25.7 (t), 23.4 (q), and 13.2 (q) (Found: M^+, 250.1232. $C_{14}H_{18}O_4$ requires *M*, 250.1205).

(*ii*) The same furanone was also obtained (19%) by direct acylation of the anion derived from (**12**) with methyl acetate.

5-[(1E,3E)-*Hexa*-1,3-*dienyl*]-3-[1-*hydroxy*-(E)-*but*-2-*enyl*]-4-*methoxy*-5-*methylfuran*-2(5H)-*one* (**23**).—By the general procedure, alkylation of the anion derived from (**12**), with crotonaldehyde, followed by chromatography, gave the substituted *furanone* (64%) as a pale yellow oil, $\nu_{max.}$(film) 3 400, 1 740, and 1 640 cm^{-1}; δ 0.94 (t, *J* 7.5, CH_2*Me*), 1.52 (Me), 1.7 (d, *J* 7, =CH*Me*), 1.92—2.29 (m, =CHCH_2Me), 4.19 (OMe plus C*H*OH), and 6.45—5.08 (m, 6 H) (Found: M^+, 278.1530. $C_{16}H_{22}O_4$ requires *M*, 278.1518).

3-*Crotonoyl*-5-[(1E,3E)-*hexa*-1,3-*dienyl*]-4-*methoxy*-5-*methylfuran*-2(5H)-*one. Isoaspertetronin A* (**22**).—A solution of the allylic alcohol (**23**), (0.37 g) in dry dichloromethane (20 cm^3) was stirred at 23 °C in the presence of manganese dioxide (3.5 g) for 18 h. The mixture was filtered and then evaporated to dryness under reduced pressure to leave a pale yellow oil. Chromatography on silica using 7:3 n-pentane–ether as the eluant gave the *furanone* (0.2 g, 55%) as a colourless oil, $\lambda_{max.}$226 (24 800), 230 (24 100) and 258 nm (9 200); $\nu_{max.}$(film) 1 760, 1 750, 1 670, 1 650, and 1 620 cm^{-1}; δ 1.02 (t, *J* 7.5, CH_2*Me*), 1.61 (Me), 1.99 (d, *J* 7, =CH*Me*) 2.31—1.97 (m, =CHCH_2Me), 4.08 (OMe), and 7.13—5.58 (m, 6 H); δ_C 186.9, 183.1, 169.2, 145.8 (d), 139.5 (d), 132.2 (d), 131.4 (d), 127.7 (d), 126.6 (d), 102.3, 82.7, 62.8 (q), 25.6 (t), 23.3 (q), 18.4 (q), and 13.2 (q) (Found: M^+, 276.1367. $C_{16}H_{20}O_4$ requires *M*, 276.1362).

The same furanone was also obtained (20%) by direct acylation of the anion derived from (**12**) with methyl crotonate. The product from this reaction, however, was contaminated with *ca.* 10% of the adduct [δ 3.77 (OMe) and 3.8 (CO_2Me) M^+, 308.1617] resulting from 1,4-addition to the methyl crotonate.

5-[(1E,3E)-*Hexa*-1,3-*dienyl*]-4-*methoxy*-5-*methyl*-3-[(E)-3-*oxobut*-1-*enyl*]*furan*-2(5H)-*one* (**24**).—A solution of the allylic alcohol (**24**) (25 mg) in dry dichloromethane (2 cm^3) was added to a suspension of pyridinium chlorochromate (0.1 g) in dry dichloromethane (3 cm^3), and the mixture was stirred at 25 °C for 4 h, then diluted with ether and filtered through Celite. The ether extract was evaporated to dryness, and the residue was chromatographed on silica using ether as the eluant to give the furanone (5 mg), $\lambda_{max.}$(EtOH) 282 nm; δ 2.27 (*Me*COCH=), 7.34 (d, *J* 15.5, MeCOC*H*=) and, 7.54 (d, *J* 15.5, MeCOCH=C*H*).

5-*Methoxy*-2,2-*dimethylfuran*-3(2H)-*one* (**26**).—A solution of diazomethane in ether was added dropwise to a cooled (5 °C) solution of 4,4-dimethyltetronic acid (0.2 g)[13] in methanol (10 cm^3), until the solution remained pale yellow. The solution was

kept at 23 °C for 1 h and then evaporated to dryness under reduced pressure to leave a solid residue. Chromatography on flash silica using ether as the eluant gave (*i*) 4-methoxy-5,5-dimethylfuran-2(5*H*)-one (**27**) (0.15 g, 66%) which showed spectral data identical with those of an authentic sample,[14] and (*ii*) the *furanone* (**26**) (0.09 g, 37%), m.p. 49—50 °C (light petroleum, b.p. 40—60 °C), $\lambda_{max.}$(EtOH) 250 nm (14.000); $\nu_{max.}$(film) 3 100, 1 700, and 1 600 cm^{-1}; δ 1.45 (2 × Me), 4.0 (OMe), and 4.72 (:CH) (Found M^+, 142.0636. $C_7H_{10}O_3$ requires *M*, 142.0630).

3-*Acetyl*-5-[(1E,3E)-*hexa*-1,3-*dienyl*]-4-*hydroxy*-5-*methylfuran*-2(5H)-*one* (**28a**).—Sodium hydroxide solution (0.4M, 2.3 cm^3) was added to a solution of the *O*-methyl ether (**20**) (87 mg) in methanol (1 cm^3), and the resulting bright orange mixture was kept at 23 °C for 10 min before it was acidified (conc. HCl) and evaporated to dryness. The residue was diluted with water, and then extracted with dichloromethane. Evaporation of the dichloromethane extracts left the furanone (69 mg, 85%) as a yellow oil, $\lambda_{max.}$($CHCl_3$) 2 960, 2 930, 1 760, 1 685, 1 660, and 1 605 cm^{-1}; δ 1.0 (t, *J* 7.5, CH_2Me), 1.58 (CMe), 2.1 (m, =CHCH_2Me), 2.53 (COMe), and 6.5—5.5 (m, 4 H), 9.0 (OH); *m/z* 236 ($C_{13}H_{16}O_4$). Treatment of this hydroxyfuranone with diazomethane in ether at 5 °C for 0.5 h led to only the corresponding 4-methoxyfuranone (**20**).

3-*Crotonoyl*-5-[(1E,3E)-*hexa*-1,3-*dienyl*]-4-*hydroxy*-5-*methylfuran*-2(5H)-*one* (**28b**).—Concentrated sulphuric acid (1 drop) was added to a solution of the *O*-methyl ether (**22**) (0.1 g) in tetrahydrofuran (5 cm^3), and the resulting solution was stirred at 23 °C for 16 h before it was treated with anhydrous potassium carbonate (0.1 g) and evaporated to dryness. The residue was dissolved in ether, and the ether extracts were washed with aqueous sodium hydrogen carbonate. The separated aqueous extracts were acidified with hydrochloric acid, and then extracted with ethyl acetate. Evaporation of the dried organic extracts left the *furanone* (32 mg, 33%) as an orange oil, $\lambda_{max.}$(EtOH) 226 and 312.5 nm, $\nu_{max.}$($CHCl_3$) 3 670, 3 000, 2 870, 1 755, 1 680, 1 640, and 158 cm^{-1}; δ 1.0 (t, *J* 7.5, CH_2Me), 1.58, 1.56 (CMe, enolic forms), 2.08 (d, *J* 6.5, =CMe), 2.1 (m, =CHCH_2Me), 6.5—5.5 (m, 4 H), and 7.5—7.0 (m, 2 H), 9.7 (OH) (Found: M^+, 262.1205. $C_{15}H_{18}O_4$ requires *M*, 262.1205).

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