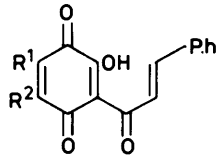
Oxidative Rearrangement of Quinochalcones. Part 2.[1] A Facile Synthesis of Linderone

Graham J. Bennett and Hiok-Huang Lee,*
Department of Chemistry, National University of Singapore, Kent Ridge, Singapore 0511.

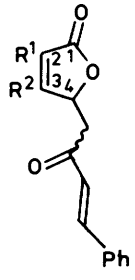
Friedel-Crafts acylation of 1,2,3,5-tetramethoxybenzene in diethyl ether afforded besides the acetophenone (**6a**), an abnormal product shown to be 3-ethoxy-2-hydroxy-4,6-dimethoxyacetophenone (**6b**). Methylpedicinin (**1b**), prepared from compound (**6a**), was found to react with acetic anhydride–DMSO, yielding linderone acetate (**3d**), linderone cinnamate (**3e**), the ester (**9**), and the ylide (**10a**). The acetate (**3d**) was readily hydrolysed to linderone (**3b**).

Reaction of quinochalcone (**1e**) with acetic anhydride–DMSO gave, on the other hand, the ylide (**10b**) as the major product besides the ester (**9**). A trace amount of a butenolide was also isolated and shown to be a mixture of the *Z*- and *E*- isomers (**2c**) and (**2d**). Electronic and steric factors are invoked to rationalize the different reaction pathways of quinochalcones (**1a**), (**1b**), and (**1e**).

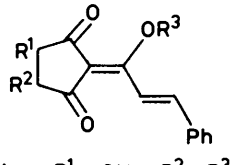
In the previous part of this series,[1] quinochalcone (**1a**) was shown to react with acetic anhydride–dimethyl sulphoxide (DMSO) to afford the butenolide (**2a**) which, in the presence of sodium methoxide, was readily converted into lucidone (**3a**). It was of interest to extend this type of oxidative rearrangement to other quinochalcones with a view to utilizing it as a convenient method for the preparation of other natural acylcyclopentenediones. This paper reports the application of the reaction to the synthesis of linderone (**3b**).



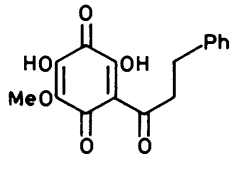
(**1**) **a**; R^1 = OMe, R^2 = H
b; R^1 = R^2 = OMe
c; R^1 = OMe, R^2 = OEt
d; R^1 = OMe, R^2 = OH
e; R^1 = H, R^2 = OMe



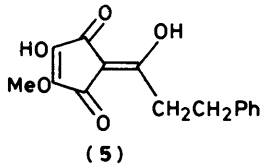
(**2**) **a**; R^1 = OMe, R^2 = H, 4-*E*
b; R^1 = R^2 = OMe
c; R^1 = H, R^2 = OMe, 4-*Z*
d; R^1 = H, R^2 = OMe, 4-*E*



(**3**) **a**; R^1 = OMe, R^2 = R^3 = H
b; R^1 = R^2 = OMe, R^3 = H
c; R^1 = R^2 = OMe, R^3 = Me
d; R^1 = R^2 = OMe, R^3 = Ac
e; R^1 = R^2 = OMe, R^3 = PhCH=CHCO



(**4**)



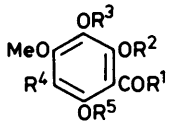
(**5**)

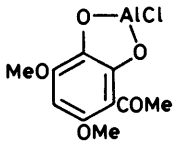
An earlier synthesis[2] of linderone (**3b**) started with the alkaline rearrangement of the 1,4-quinone (**4**) to demethyldihydrolinderone (**5**). Methylation of compound (**5**), followed by dehydrogenation gave methyl linderone (**3c**) and hence linderone (**3b**). A more direct approach, patterned after the lucidone synthesis,[1] would be the oxidative rearrangement by acetic anhydride–DMSO of methylpedicinin (**1b**)[3] to the butenolide (**2b**), which would be expected to undergo a base-catalysed conversion into linderone (**3b**).

Methylpedicinin (**1b**), isolated from the leaves of *Didymocarpus pedicellata*, has been synthesized in four steps from 2-hydroxy-3,4,6-trimethoxyacetophenone (**6a**).[4] A number of methods[5–8] have in the past been used in the preparation of (**6a**) from 1,2,3,5-tetramethoxybenzene. From the point of simplicity and yield, the Friedel-Crafts acetylation employing aluminium chloride in diethyl ether appears to be the method of choice.[6] This reaction, however, has been reported to give a product contaminated by 10% of an ethoxy-containing compound.[9] In this work, the ethoxy-containing compound has been isolated from the mother liquors (methylene dichloride–hexane) used in the recrystallizations of compound (**6a**) and shown to be 3-ethoxy-2-hydroxy-4,6-dimethoxyacetophenone (**6b**). The position of the ethoxy substituent was established by (i) conversion of compound (**6b**) through (**6c**) and (**6d**), into ethylpedicinin (**1c**)[10] [analogous to the preparation of methylpedicinin (**1b**)], followed by alkaline hydrolysis to pedicinin (**1d**),[4] and (ii) dealkylation with hydrogen bromide–acetic acid[7] to the known 2,3-dihydroxy-4,6-dimethoxyacetophenone (**6e**) and 3-ethoxy-2,6-dihydroxy-4-methoxyacetophenone (**6f**) which was identified as the triethoxymethoxy-derivative (**6g**). The yield of compound (**6b**) was observed to decrease (12 to 7%) when the reaction time was reduced (16 to 6 h). A small amount of compound (**6e**) was also found amongst the products of the Friedel-Crafts reaction.

It is well known that aluminium chloride complexes with diethyl ether and readily cleaves a phenolic ether group *ortho* or *peri* to a carbonyl function.[11] A methoxy group *ortho* to a hydroxy group has also been reported to undergo demethylation in the presence of this reagent.[12] The formation of compound (**6b**) may arise from reaction of the cyclic five-membered intermediate (**7**) with the diethyl ether–aluminium chloride complex. Selective ether exchange at position 3 has also been observed in the reaction of 2,3,4,6-tetramethoxybenzaldehyde (**6h**) with aluminium chloride in diethyl ether.[13] The 3-ethoxy compound (**6i**) in this case was present to a larger extent (38%).

The ^{1}H n.m.r. spectra of methylpedicinin (**1b**) and ethylpedicinin (**1c**) in deuteriochloroform solutions at 35 °C show

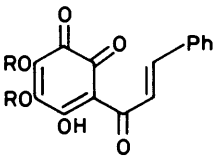




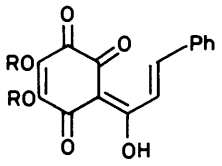
(7)

(6) **a**; $R^1 = R^3 = R^5 = Me$, $R^2 = R^4 = H$
b; $R^1 = R^5 = Me$, $R^2 = R^4 = H$, $R^3 = Et$
c; $R^1 = PhCH{=}CH$, $R^2 = R^4 = H$, $R^3 = Et$, $R^5 = Me$
d; $R^1 = PhCH{=}CH$, $R^2 = H = R^3 = Et$, $R^4 = OH$, $R^5 = Me$
e; $R^1 = R^5 = Me$, $R^2 = R^3 = R^4 = H$
f; $R^1 = Me$, $R^2 = R^4 = R^5 = H$, $R^3 = Et$
g; $R^1 = Me$, $R^2 = R^3 = R^5 = Et$, $R^4 = H$
h; $R^1 = R^4 = H$, $R^2 = R^3 = R^5 = Me$
i; $R^1 = R^2 = R^4 = H$, $R^3 = Et$, $R^5 = Me$

splitting of the alkoxy signals into two separate sets of approximately equal intensity. A small splitting is also observed in the absorptions of the vinyl protons from the cinnamoyl side chain. This is indicative of (**1b**) and (**1c**) both existing as a tautomeric mixture of their respective 1,4- and 1,2-quinones (**8a**) and/or (**8b**). However, in $(CD_3)_2SO$ solution at the same temperature, a single spectrum was obtained for both (**1b**) and (**1c**).

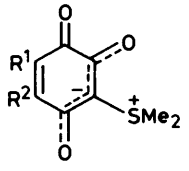


(8a)

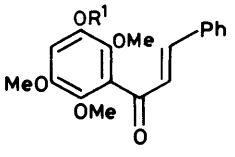


(8b)

$MeSCH_2OCOCH{=}CHPh$
(9)



(10) **a**; $R^1 = R^2 = OMe$
b; $R^1 = H$, $R^2 = OMe$



(12) **a**; $R^1 = H$
b; $R^1 = Me$

The reaction of methylpedicinin (**1b**) with acetic anhydride–DMSO at 75 °C for 1 h gave a complex mixture which was separated by p.l.c. The major product, isolated in 42% yield, was a yellow solid identified as linderone acetate (**3d**).[14] A second yellow solid, obtained in trace quantity, was shown to be linderone cinnamate (**3e**). A relatively non-polar colourless liquid and a strongly polar orange solid were also isolated, and on the basis of their molecular formulae and spectroscopic data were assigned the structures of methylthiomethyl cinnamate (**9**) and 1-dimethylsulphonio-4,5-dimethoxy-2,3,6-trioxocyclohex-4-en-1-ide (**10a**) respectively. Mild acid hydrolysis of compound (**3d**) readily afforded linderone (**3b**).

The absence of the expected butenolide (**2b**) and the formation instead of the cyclopentenedione (**3d**) was at first rather surprising as the quinone (**1a**) had yielded only the butenolide (**2a**). Also in an earlier study[15] of the reaction of hydroxyquinones with acetic anhydride–DMSO, only the desired butenolides were produced except in unsuccessful cases which gave either acetylated hydroxyquinones or substituted dimethylsulphonio-1,4-dioxocyclohexenides.

Examination with molecular models, however, suggests that cyclopentenedione formation may not be contradictory to the proposed mechanism of Wikholm and Moore[15] (see Scheme 1). Approach of the methine carbon with its appendages above the plane of the 1-carbonyl function (**11b**; $R^1 = R^2 = OMe$) appears to be relatively strain-free and a concerted fragmentation followed by nucleophilic addition would lead to an acylcyclopentenedione (**3b**). On the other hand, for butenolide formation, either the 1-carbonyl or the 4-carbonyl group must be tilted out of conjugation with the 5,6-double bond and there seems to be steric interaction between the 5-methoxy group with either the acyl chain or the anhydride moiety (**11a**; $R^1 = R^2 = OMe$) which may impose a higher energy barrier for pathway (b) relative to (c). The ring closure reaction of (**11a** and **b**) may not necessarily be concerted, but may also occur in two stages *via* an intermediate enolate (**11c**; $R^1 = R^2 = OMe$, $R^3 = Ac$) reminiscent of that postulated by Clemo, Gedge, and Pattenden[16] in their base-catalyzed rearrangement of butenolides to acylcyclopentenediones. In the case of (**11c**; $R^1 = H$, $R^2 = OMe$, $R^3 = Me$ or Bu^t), they failed to obtain compound (**3a**).

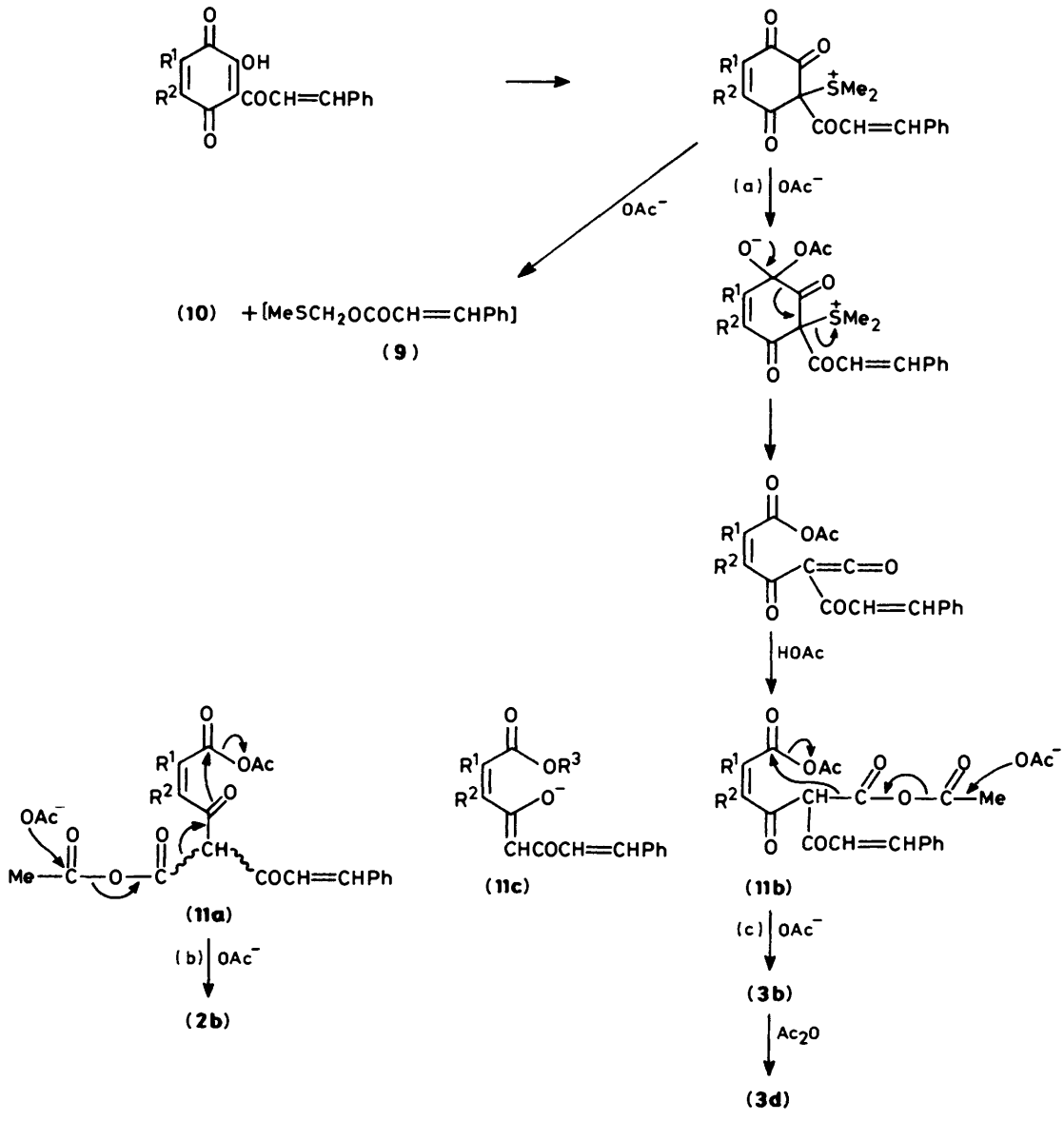
The presence of the ylide (**10a**) and the ester (**9**) reflects, to some extent, the difficulty with which step (a) occurs, probably due to the mesomeric effect of the 5-methoxy group in decreasing the electrophilicity of the 1-carbonyl carbon. Addition of the acetate anion to the cinnamoyl carbonyl carbon followed by cleavage of the acyl carbon to carbon-3 bond would lead to compound (**10a**). Reaction of the resultant mixed anhydride with DMSO and a subsequent Pummerer reaction[17] of the product would give the ester (**9**).

An alternative mechanism, which takes into account the resonance influence of the 5-methoxy group mentioned above, would be the preferential addition of the acetate anion to the 2-carbonyl group, followed by simultaneous rearrangement and displacement of dimethyl sulphide as depicted in Scheme 2. In order to ascertain the importance of the electronic factor involved, quinochalcone (**1e**), which is devoid of an adjacent methoxy group to off-set its mesomeric effect on the 1-carbonyl function, was prepared. Either oxidation of chalcone (**12a**) with thallium(III) nitrate (TTN)[18] or oxidative demethylation[19] of (**12b**) with nitric acid yielded (**1e**), which on treatment with acetic anhydride–DMSO afforded the ylide (**10b**) as the major product (69%). The ester (**9**) was also obtained together with a trace amount of a yellow solid which, based on the ^1H n.m.r. spectrum, was a mixture of the butenolides (**2c**) and (**2d**), with the former predominating. Multiple development p.l.c. enabled the isolation of the pure *Z*-butenolide (**2c**) whose physical properties were in agreement with published values.[16] The fact that cyclopentenedione formation is not observed in this case appears to discount Scheme 2.

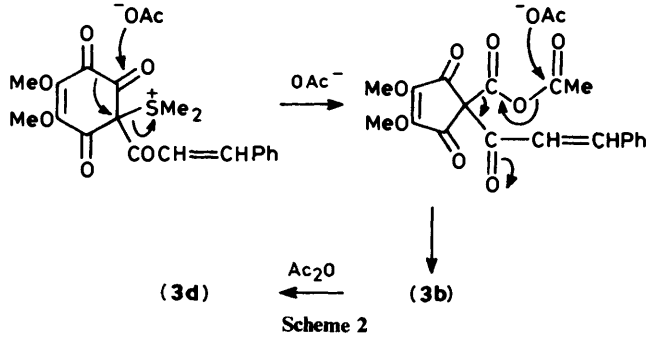
Considering the significant differences in the products from the three quinochalcones, (**1a**), (**1b**), and (**1e**), it would seem that the discrepancies may be attributed to electronic and possibly steric factors. In the case of (**1a**), the reaction proceeds in the expected manner with the more nucleophilic oxygen adding to the 1-carbonyl function to give butenolide (**2a**). At the other extreme is quinone (**1e**), and attack at the side-chain carbonyl carbon becomes the predominant course of the reaction. With the quinone (**1b**), where steric interaction is greatest, a new mode of ring closure becomes operative, leading to compounds (**3d**) and (**3e**).

Experimental

For general experimental details see the previous part.[1] Unless otherwise stated, ^1H n.m.r. spectra were determined in



Scheme 1



Scheme 2

$CDCl_3$ solutions at 90 MHz with a Perkin-Elmer R32 spectrometer using Me_4Si as internal reference.

Acetylation of 1,2,3,5-*Tetramethoxybenzene.*—1,2,3,5-Tetramethoxybenzene[6] (10 g, 50 mmol) in dry ether (70 ml) was treated with acetyl chloride (5 g, 60 mmol) in the presence of aluminium chloride (10 g, 75 mmol) in accordance with published procedure.[6] The crude product (10.4 g) was boiled with methylene dichloride, filtered to remove a small amount of insoluble solid and then hexane was added until crystallisation occurred. Five recrystallisations from this solvent mixture afforded pure 2-hydroxy-3,4,6-trimethoxyacetophenone (**6a**) (6.0 g, 53%) as yellow rods, m.p. 112—114 °C (lit.,[5] 113—114 °C); $\nu_{max.}$ 1 621, 1 599, 1 582, and 1 130 cm^{-1}; δ 2.61 (3 H, s, MeCO), 3.81, 3.90, and 3.95 (3 H each, s, 3 × OMe), 5.85 (1 H, s, 5-H), and 13.85 (1 H, s, 2-OH). The methylene dichloride-insoluble solid (300 mg) was identified as 2,3-dihydroxy-4,6-dimethoxyacetophenone, m.p. 165—167.5 °C (from EtOH) (lit.,[7] 165.2—166.5 °C) (Found: M^+, 212.0681. Calc. for $C_{10}H_{12}O_5$: *M*, 212.0684); $\nu_{max.}$(Nujol) 3 400br, 1 620, and 1 590 cm^{-1}; δ[$CDCl_3$–$(CD_3)_2SO$] 2.60 (3 H, s, MeCO), 3.90, and 3.93 (3 H each, s, 2 × OMe), 6.13 (1 H, s, 5-H), 7.5—7.9 (1 H, br s, 3-OH), and 13.55 (1 H, s, 2-OH); dibenzoyl derivative, m.p. 186—188 °C (lit.,[8] 185—188 °C) (Found: M^+, 420.1210. Calc. for $C_{24}H_{20}O_7$: *M*, 420.1209). The mother liquors from the recrystallisations were combined, concentrated to dryness, and the residue recrystallised several times from aqueous methanol

to give 3-*ethoxy*-2-*hydroxy*-4,6-*dimethoxyacetophenone* (**6b**) (1.4 g, 12%) as yellow needles, m.p. 74—75 °C (Found: C, 59.8; H, 6.7%; M^+, 240.0984; $C_{12}H_{16}O_5$ requires C, 60.0; H, 6.7%; *M*, 240.0998); $\nu_{max.}$ 1 619, 1 598, 1 270, and 1 129 cm^{-1}; δ 1.35 (3 H, t, *J* 7 Hz, *Me*CH_2), 2.61 (3 H, s, MeCO), 3.89 and 3.92 (3 H each, s, 2 × OMe), 4.03 (2 H, q, *J* 7 Hz, CH_2Me), 5.98 (1 H, s, 5-H), and 13.80 (1 H, s, 2-OH); *m/z* 240 (100%), 211 (100), 197 (53), 183 (67), 165 (43), and 43 (74).

In a subsequent experiment, when the reaction mixture was stirred for 6 h at 30 °C instead of 16 h, the yields of compounds (**6a**) and (**6b**) were 66 and 7% respectively.

2-*Cinnamoyl*-3-*hydroxy*-5,6-*dimethoxy*-1,4-*benzoquinone* (*Methylpedicinin*) (**1b**).—Methylpedicinin (**1b**) was prepared from the acetophenone (**6a**) according to the published methods.[4] The crude product was used directly for the subsequent reaction without further purification. It had m.p. 100—104 °C (lit.,[4] 110—112 °C) (Found: M^+ 314.0786. Calc. for $C_{17}H_{14}O_6$: *M*, 314.0790); $\nu_{max.}$ 1 616 and 1 596 cm^{-1}; δ 4.00, 4.07, 4.18, and 4.20 (1.5 H each, s, 2 × OMe in two tautomeric forms), 7.3—7.8 (5 H, m, Ph) 8.05 and 8.35 (1 H each, d, *J* 16 Hz, CH=CH); δ[$(CD_3)_2SO$] 3.94, and 4.02 (3 H each, s, 2 × OMe), 7.4—7.9 (5 H, m, Ph), and 7.98 (2 H, s, CH=CH).

3′-*Ethoxy*-2′-*hydroxy*-4′,6′-*dimethoxychalcone* (**6c**).—Chalcone (**6c**) was prepared according to the known procedure[4] from the 3-ethoxyacetophenone (**6b**) and benzaldehyde in ethanolic sodium hydroxide solution. The *product* crystallised from ethanol as orange-red needles, m.p. 132.5—134 °C (Found: C, 69.55; H, 6.4%; M^+, 328.1310. $C_{19}H_{20}O_5$ requires C, 69.5; H, 6.1%; *M*, 328.1311); $\nu_{max.}$ 1 630, and 1 565 cm^{-1}; δ 1.37 (3 H, t, *J* 7 Hz, *Me*CH_2), 3.94 (6 H, s, 2 × OMe), 4.04 (2 H, q, *J* 7 Hz, CH_2Me), 6.00 (1 H, s, 5′-H), 7.3—7.7 (5 H, m, Ph), 7.78 and 7.80 (1 H each, s, CH=CH), and 13.82 (1 H, s, 2′-OH); *m/z* 328 (65%), 195 (100), 167 (54), 103 (24), and 77 (17).

3′-*Ethoxy*-2′,5′-*dihydroxy*-4′,6′-*dimethoxychalcone* (**6d**).—The Elbs persulphate oxidation of the preceding chalcone (**6c**) (3.5 g, 10.7 mmol) was by essentially the same procedure as that described for the preparation of pedicinin.[4] The *product* was obtained as a dark brown oil which solidified with time and was further purified by chromatography over silica gel. Elution with hexane–ethyl acetate (3:1) gave a bright red solid (0.43 g) which crystallised from methylene dichloride–hexane as very long red needles, m.p. 111.5—113 °C (Found: C, 66.0; H, 5.9%; M^+, 344.1266. $C_{19}H_{20}O_6$ requires C, 66.25; H, 5.85%; *M*, 344.1260); $\nu_{max.}$ 3 530, 1 635, and 1 570 cm^{-1}; δ 1.40 (3 H, t, *J* 7 Hz *Me*CH_2), 3.85 and 4.13 (3 H each, s, 2 × OMe), 4.12 (2 H, q, *J* 7 Hz, CH_2Me), 5.40 (1 H, s, exchangeable, 5′-OH), 7.3—7.8 (5 H, m, Ph), 7.89 (2 H, s, CH=CH), and 13.80 (1 H, s, 2′-OH); *m/z* 344 (67%), 240 (48), 211 (100), 197 (47), 183 (20), 131 (35), 103 (50), 100 (35), and 77 (28).

2-*Cinnamoyl*-6-*ethoxy*-3-*hydroxy*-5-*methoxy*-1,4-*benzoquinone* (*Ethylpedicinin*) (**1c**).—The preceding hydroquinone (**6d**) was oxidised with silver oxide and the product hydrolysed with aqueous sodium hydrogen carbonate according to published procedures[4] to give ethyl pedicinin (**1c**), m.p. 112—114 °C (benzene–hexane) (lit.,[10] 113—114 °C) (Found: C, 65.85; H, 4.9%; M^+, 328.0944. Calc. for $C_{18}H_{16}O_6$: C, 65.8; H, 4.9%; *M*, 328.0947); $\nu_{max.}$ 1 670, 1 616, and 1 595 cm^{-1}; δ 1.46 (3 H, t, *J* 7 Hz, *Me*CH_2), 4.00 and 4.08 (1.5 H each, s, OMe in two tautomeric forms), 4.45 and 4.52 (1 H each, q, *J* 7 Hz, CH_2Me in two tautomeric forms), 7.3—7.8 (5 H, m, Ph) and 8.05 and 8.35 (1 H each d, *J* 16 Hz, CH=CH); δ[$(CD_3)_2SO$] 1.34 (3 H, t, *J* 7 Hz, *Me*CH_2), 3.94 (3 H, s, OMe), 4.32 (2 H, q, *J* 7 Hz, CH_2Me), 7.4—7.9 (5 H, m, Ph), and 7.99 (2 H, s, CH=CH); *m/z* 328 (24%), 300 (47), 168 (39), 131 (100), 103 (68), and 77 (33).

Reaction of ethylpedicinin (**1c**) with 5% aqueous sodium hydroxide followed by acidification afforded pedicinin (**1d**), m.p. and mixed m.p. 202—204 °C. The i.r. and ^1H n.m.r. spectra of the product were identical with those of an authentic sample.

Ether Cleavage of Compound (**6b**) *in Hydrogen Bromide–Acetic Acid.*[7]—To a solution of the 3-ethoxyacetophenone (**6b**) (0.26 g, 1.1 mmol) in glacial acetic acid (4 ml) was added hydrogen bromide in acetic acid (30%; 1 ml) and the red solution was allowed to stand at room temperature for 48 h. After dilution with water the products were isolated with chloroform and separated by p.l.c. developed with hexane–ethyl acetate (2:1). The major, more polar component was identified as 2,3-dihydroxy-4,6-dimethoxyacetophenone (**6e**) by mixed m.p., and i.r. and ^1H n.m.r. spectroscopy. The minor component was 3-*ethoxy*-2,6-*dihydroxy*-4-*methoxyacetophenone* (**6f**), m.p. 108.5—110 °C (Found: C, 58.2; H, 6.2%; M^+, 226.0847. $C_{11}H_{14}O_5$ requires C, 58.4; H, 6.2%; *M*, 226.0841); $\nu_{max.}$ 3 480, 1 635, and 1 605 cm^{-1}; δ 1.36 (3 H, t, *J* 7 Hz, *Me*CH_2), 2.69 (3 H, s, MeCO), 3.87 (3 H, s, OMe), 4.05 (2 H, q, *J* 7 Hz, CH_2Me), 6.03 (1 H, s, 5-H), 6.84 (1 H, s, 6-OH), and 13.34 (1 H, s, 2-OH); *m/z* 226 (55%), 197 (100), 183 (28), and 43 (22). Treatment of compound (**6f**) with diethyl sulphate in boiling acetone in the presence of anhydrous potassium carbonate gave 2,3,6-*triethoxy*-4-*methoxyacetophenone* [**6g**), whose i.r., ^1H n.m.r. and mass spectra were with those of an authentic sample prepared as described below.

2,3,6-*Triethoxy*-4-*methoxyacetophenone* (**6g**).—Following the published method,[20] 2,5-diethoxy-1,3-dimethoxybenzene [10] was treated with boron trifluoride–diethyl ether and anhydrous acetic acid at 80 °C for 5 h, to give, after hydrolysis, 3,6-diethoxy-2-hydroxy-4-methoxyacetophenone in 50% yield, m.p. 101—103 °C (lit.,[10] 104—105 °C). Reaction of the acetophenone with diethyl sulphate in boiling acetone solution in the presence of anhydrous potassium carbonate for 10 h afforded compound (**6g**), b.p. 115 °C (bath temp.) at 0.05 mmHg (Found: C, 63.8; H, 7.85. $C_{15}H_{22}O_5$ requires C, 63.8; H, 7.85%); $\nu_{max.}$(film) 1 700 and 1 605 cm^{-1}; δ 1.31, 1.36, and 1.38 (3 H each, t, *J* 7 Hz, 3 × *Me*CH_2), 2.49 (3 H, s, MeCO), 3.86 (3 H, s, OMe), 4.01, 4.03, and 4.13 (2 H each, q, *J* 7 Hz, 3 × CH_2Me), and 6.26 (1 H, s, 5-H).

Reaction of Methylpedicinin (**1b**) *with Acetic Anhydride–DMSO.*—A solution of compound (**1b**) (0.5 g, 1.6 mmol) in dimethyl sulphoxide (3.0 ml) and acetic anhydride (1.8 ml) was stirred at 75 °C for 1 h and then the excess solvent was removed under reduced pressure. The brown residue was applied to two p.l.c. plates and developed 4 times in benzene to give 3 separate bands. The major and most polar band afforded yellow shiny prisms (methylene dichloride–hexane) identified as linderone acetate (**3d**) (220 mg, 42%) by i.r. and ^1H n.m.r. spectra, m.p. and mixed m.p. 161—162 °C (lit.,[14] 160—161 °C (Found: C, 65.8; H, 4.95%; M^+, 328.0944. Calc. for $C_{18}H_{16}O_6$: C, 65.85; H, 4.9%; *M*, 328.0947); $\nu_{max.}$ 1 778, 1 673, 1 631, 1 593, and 1 340 cm^{-1}; δ 2.43 (3 H, s, $MeCO_2$), 4.21 and 4.25 (3 H each, s, 2 × OMe), and 7.2—8.2 (7 H, m, PhCH=CH); *m/z* 328 (20%), 286 (100), 241 (52), 227 (43), 131 (55), 103 (45), 77 (30), and 43 (50). The middle band gave *linderone cinnamate* (**3e**) as fine yellow matted needles (absolute ethanol) (20 mg), m.p. 225—226 °C (Found: C, 71.9; H, 4.5%; M^+, 416.1261. $C_{25}H_{20}O_6$ requires C, 72.1; H, 4.8%; *M* 416.1260); $\nu_{max.}$ 1 740, 1 674, 1 622, and 1 330 cm^{-1}; δ 4.20 and 4.26 (3 H each, s, 2 × OMe), and 7.2—8.3 (14 H, m, 2 × PHCH=CH); *m/z* 416 (10%), 286 (18), 285 (11), 241 (10), 131 (100), 103 (85), and 77 (22), identified by mixed m.p. and comparison of i.r. and ^1H n.m.r. spectra with those of an authentic sample prepared from linderone and cinnamoyl chloride in pyridine.

The least polar band yielded *methylthiomethyl cinnamate* (**9**) as an almost colourless oil, b.p. 130 °C (bath temp.) at 0.2 mmHg (Found: C, 63.1; H, 5.8%; M^+, 208.0554. $C_{11}H_{12}O_2S$ requires C, 63.4; H, 5.8%; *M*, 208.0558); $\nu_{max.}$(neat) 1 150, 1 638, and 1 715 cm^{-1}; δ 2.28 (3 H, s, MeS), 5.27 (2 H, s, OCH_2S), 6.46 (1 H, d, *J* 16 Hz, Ph–CH=C*H*), and 7.3—7.8 (6 H, m, *Ph*–C*H*=CH); *m/z* 208 (7%), 131 (100), 103 (35), 77 (23), and 61 (30).

In a separate experiment, the residue from the same reaction of methylpedicinin (130 mg) was chromatographed on p.l.c. plates using methylene dichloride containing methanol (5%). Elution of the most polar band with ethyl acetate gave 1-*dimethylsulphonio*-4,5-*dimethoxy*-2,3,6-*trioxocyclohex*-4-*en*-1-*ide* (**10a**) (29 mg, 28%) which crystallised from benzene as fine pale orange needles, m.p. 160—162 °C (Found: S, 13.4%; M^+, 244.0404. $C_{10}H_{12}O_5S$ requires S, 13.1%; *M*, 244.0405); $\nu_{max.}$ 1 581 and 1 675 cm^{-1}; δ 3.09 (6 H, s, Me_2S), and 3.88 and 4.16 (3 H each, s, 2 × OMe); *m/z* 244 (32%), 216 (28), 201 (23), 183 (73), and 62 (100).

2-*Cinnamoyl*-4,5-*dimethoxycyclopent*-4-*ene*-1,3-*dione*(*Linderone*) (**3b**).—A solution of linerone acetate (**3d**) (100 mg) in 10% methanolic hydrochloric acid (20 ml) was heated to reflux for 45 min, and then cooled and diluted with water. The orange product (70 mg, 80%) was identified as linderone by m.p., mixed m.p. and i.r. spectrum.

3′-*Hydroxy*-2′,5′,6′-*trimethoxychalcone* (**12a**).—3-Acetyl-2,5,6-trimethoxyacetophenone[21] was converted into 3-acetoxy-2,5,6-trimethoxyacetophenone according to published procedure.[22,23] The latter was then hydrolysed with 10% sodium hydroxide in methanol to 3-*hydroxy*-2,5,6-*trimethoxyacetophenone*, b.p. 150—160 °C (bath temp.) at 0.1 mmHg, which solidified with time, m.p. 71—72 °C (Found: C, 58.3; H, 6.2. $C_{11}H_{14}O_5$ requires C, 58.4; H, 6.2%); $\nu_{max.}$ 3 540, 1 700, and 1 600 cm^{-1}; δ 2.53 (3 H, s, MeCO), 3.75, 3.78, and 3.83 (9 H, each s, 3 × OMe), 5.80 (1 H, s, 3-OH), and 6.60 (1 H, s, 4-H). Condensation of the acetophenone with benzaldehyde in ethanolic sodium hydroxide solution afforded the *chalcone* (**12a**) as a viscous orange liquid, b.p. 200—210 °C (bath temp.) at 0.08 mmHg (Found: C, 68.5; H, 5.7. $C_{18}H_{18}O_5$ requires C, 68.8; H, 5.8%); $\nu_{max.}$ 3 540, 1 640, 1 625, and 1 600 cm^{-1}; δ 3.74 (6 H, s, 2 × OMe), 3.84 (3 H, s, OMe), 6.0 (1 H, s, 3-OH), 6.65 (1 H, s, 4-H), 7.0 (1 H, d, *J* 16 Hz, PhCH=C*H*), and 7.2—7.6 (6 H, m, *Ph*C*H*=CH).

3-*Cinnamoyl*-2-*hydroxy*-5-*methoxy*-1,4-*benzoquinone* (**1e**).—(*a*) To a stirred solution of the preceding chalcone (**12a**) (1.57 g, 5 mmol) in methanol (15 ml), was added a solution of TTN (1.95 g, 5 mmol) in methanol (15 ml). The mixture was heated to reflux for 1 h, poured into water (100 ml), and the product collected and dried. The crude quinone (1.2 g) after purification by passage through a column of silica gel (30 g) with methylene dichloride as the eluant, crystallised from methylene dichloride–hexane as orange-yellow rods, m.p. 204—206 °C (Found: C, 67.4; H, 4.2. $C_{16}H_{12}O_5$ requires C, 67.5; H, 4.25%); $\nu_{max.}$(Nujol) 1 655 and 1 615 cm^{-1}; δ[$(CD_3)_2SO$] 3.88 (3 H, s, OMe), 6.30 (1 H, s, 6-H), and 7.40—8.10 (7 H, m, PhCH=CH).

(*b*) Reaction of 2,3,5,6-tetramethoxyacetophenone (**12b**)[23] with benzaldehyde in ethanolic sodium hydroxide solution gave 2′,3′,5′,6′-*tetramethoxychalcone* (**12b**) which crystallised from aqueous ethanol as colourless prisms, m.p. 96—97 °C (Found: C, 69.65; H, 6.1. $C_{19}H_{20}O_5$ requires C, 69.5; H, 6.1%); $\nu_{max.}$ 1 640 and 1 600 cm^{-1}; δ 3.75 and 3.90 (6 H each, s, 4 × OMe), 6.63 (1 H, s, 4-H), 6.95 (1 H, d, *J* 16 Hz), and 7.2—7.6 (6 H, m, *Ph*C*H*=CH). To a stirred solution of the chalcone (**12b**) (1 g) in glacial acetic acid (8 ml) was added concentrated nitric acid (3 ml). After 2 min the red solution was poured into ice-cold water (100 ml). The dried product (0.6 g) was purified as described in (*a*) and had m.p. and mixed m.p. 204—206 °C.

Reaction of 3-*Cinnamoyl*-2-*hydroxy*-5-*methoxy*-1,4-*benzoquinone* (**1e**) *with Acetic Anhydride–DMSO*.—The quinone (**1e**) (1 g, 3.5 mmol) was dissolved with stirring at 70 °C in dimethyl sulphoxide (12 ml), and allowed to cool to 40 °C before acetic anhydride (4 ml) was added. The mixture was heated for a further 1 h at 75 °C, after which the excess of solvent was removed under reduced pressure. The residue was stirred with methylene dichloride (3 ml) and the insoluble yellow solid (520 mg, 69%) collected and recrystallised from chloroform–cyclohexane to give 1-*dimethylsulphonio*-5-*methoxy*-2,3,6-*trioxocyclohex*-4-*en*-1-*ide* (**10b**) as light brown prisms, m.p. 257—259 °C (Found: C, 50.5; H, 4.8; S, 15.1%; M^+, 214.0308. $C_9H_{10}O_4$ requires C, 50.45; H, 4.7; S, 15.0%; *M*, 214.0300); $\nu_{max.}$(Nujol) 1 565, 1 575, 1 605, and 1 664 cm^{-1}; δ[$(CD_3)_2SO$] 3.02 (6 H, s, Me_2S), 3.79 (3 H, s, OMe), and 5.94 (1 H, s, 6-H); *m/z* 214 (4%), 186 (39), 171 (13), 153 (52), and 62 (100). The methylene dichloride filtrate was chromatographed over silica gel (60 g) with the same solvent as the eluant. The first fractions contained methylthiomethyl cinnamate (**9**). Further elution gave a yellow solid (25 mg), which appeared by ^1H n.m.r. spectroscopy to be a mixture of the *Z*- and *E*-butenolides (**2c**) and (**2d**). The mixture was partially separated by p.l.c. [methylene dichloride–hexane (9:1), 2 developments] and the predominant *Z*-isomer (**2c**) was obtained pure as yellow needles (methanol), m.p. 149—150 °C (lit.,[16] 149—150 °C) (Found: M^+, 256.0736. $C_{15}H_{12}O_4$ requires 256.0735); $\nu_{max.}$ 1 618 and 1 796 cm^{-1}; δ 4.01 (3 H, s, OMe), 5.42 (1 H, s, 2-H), 6.00 (1 H, s, 5-H), and 7.25—7.80 (7 H, m, PhCH=CH); *m/z* 256 (41%), 255 (18), 131 (37), 128 (100), and 77 (25). The *E*-isomer isolated was estimated to be 80% pure; δ 3.88 (3 H, s, OMe), 5.40 (1 H, d, *J* 1.5 Hz, 2-H), 6.39 (1 H, d, *J* 1.5 Hz, 5-H), 6.85 (1 H, d, *J* 16 Hz, PhCH=C*H*), and 7.30—7.63 (6 H, m, *Ph*C*H*=CH). The mass spectrum of the *E*–*Z* mixture was almost identical with that of the pure *Z*-isomer.

(*b*) In a separate experiment, when a mixture of the quinone (**1e**) (242 mg, 0.85 mmol), dimethyl sulphoxide (1.6 ml) and acetic anhydride (1.0 ml) was stirred and heated at 70 °C, some starting material appeared to remain undissolved. After 50 min at 70 °C, excess solvent was removed under reduced pressure and the residue triturated with methylene dichloride (1 ml). The insoluble ylide (**10b**) (100 mg, 53%) was collected and after recrystallisation from chloroform–cyclohexane, had m.p. 258—260 °C. The filtrate was applied to two p.l.c. plates (0.5 mm thickness) which were developed in methylene dichloride. Two partially resolved yellow bands were collected. The relatively less polar band afforded a yellow solid (*ca.* 4 mg), m.p. 145—147 °C, which was shown by ^1H n.m.r. to be mainly the *Z*-butenolide (**2c**). The other band gave a yellow solid (*ca.* 3 mg) which based on its ^1H n.m.r. spectrum was identified as a mixture of the *E*- and *Z*-butenolides (**2d**) and (**2c**).

References

1 H. H. Lee, Y. T. Que, and S. Ng, *J. Chem. Soc., Perkin Trans. 1*, 1985, 453.
2 H. H. Lee and C. H. Tan, *J. Chem. Soc. C*, 1967, 1583.
3 T. R. Seshadri, *Rev. Pure Appl. Chem.*, 1951, **1**, 186.
4 K. V. Rao and T. R. Seshadri, *Proc. Indian Acad. Sci., Sect. A*, 1948, **27**, 375.
5 G. Bargellini and S. M. Zoras, *Gazz. Chim. Ital.*, 1934, **64**, 192.
6 W. Baker, *J. Chem. Soc.*, 1941, 662.
7 P. D. Gardner, W. J. Horton, and R. E. Pincock, *J. Am. Chem. Soc.*, 1956, **78**, 2541.
8 W. J. Horton and M. G. Stout, *J. Org. Chem.*, 1962, **27**, 830.
9 B. D. Cavell and J. Macmillan, *J. Chem. Soc. C*, 1967, 310.

10 G. S. K. Rao, K. V. Rao, and T. R. Seshadri, *Proc. Indian Acad. Sci., Sect. A*, 1948, **28**, 103.
11 E. Hardegger, E. Widmer, K. Steiner, and A. Pfiffner, *Helv. Chim. Acta*, 1964, **47**, 2027, 2031.
12 G. R. Pettit and D. M. Piatak, *J. Org. Chem.*, 1960, **25**, 721; R. G. Lange, *ibid.*, 1962, **27**, 2037.
13 E. G. Paul and P. S. C. Wang, *J. Org. Chem.*, 1979, **44**, 2307.
14 A. K. Kiang, H. H. Lee, and K. Y. Sim, *J. Chem. Soc.*, 1962, 4338.
15 H. W. Moore and R. J. Wikholm, *Tetrahedron Lett.*, 1968, 5049; R. J. Wikholm and H. W. Moore, *J. Am. Chem. Soc.*, 1972, **94**, 6152.
16 N. G. Clemo, D. R. Gedge, and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1448.
17 S. Oae, Y. Kitao, S. Kawamura, and Y. Kitaoka, *Tetrahedron*, 1963, **19**, 817.
18 A. McKillop, D. H. Perry, M. Edwards, S. Antus, L. Farkas, M. Nogradi, and E. C. Taylor, *J. Org. Chem.*, 1976, **41**, 282.
19 G. S. K. Rao, K. V. Rao, and T. R. Seshadri, *Proc. Indian Acad. Sci., Sect. A*, 1948, **27**, 245.
20 G. P. Schiemenz and U. Schmidt, *Liebigs Ann. Chem.*, 1982, 1509.
21 M. Healey and R. Robinson, *J. Chem. Soc.*, 1934, 1625.
22 H. H. Lee and C. H. Tan, *J. Chem. Soc.*, 1965, 2743.
23 T. Horie, M. Tsukayama, M. Masumura, M. Nakayama, and S. Hayashi, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 2950.

Received 19*th July* 1985; *Paper* 5/1228