

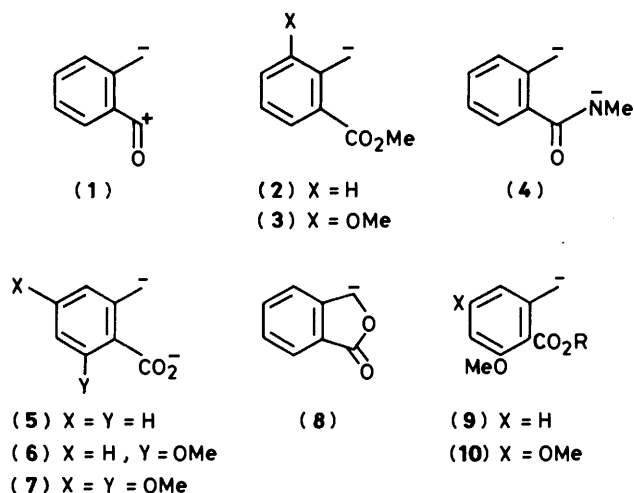
# Reactions of the Carbanion from an Orsellinate Derivative with Electrophiles<sup>1</sup>

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Esters of orsellinic acid dimethyl ether (**11**) are attacked by alkyl-lithium reagents to give ketones and in some cases smaller amounts of alkenes as a result of a second nucleophilic attack. However at  $-78^{\circ}\text{C}$  attack on (**11**) by its own anion (**10**) is sufficiently slow that the anion can be generated almost quantitatively by lithium di-isopropylamide. Reactions of the anion (**10**) with various simple electrophiles ( $\text{D}_2\text{O}$ ,  $\text{CO}_2$ ,  $\text{MeI}$ ,  $\text{Me}_3\text{SiCl}$ , and  $\text{Me}_3\text{SnCl}$ ) give the expected products of nucleophilic addition. With aldehydes ( $\text{PhCHO}$  and  $\text{MeCHO}$ ) the initially formed alcohol lactonizes to give a dihydroisocoumarin. The anion was acylated with acetyl chloride to give the ketone (**18**). The reactions of the trimethylsilyl derivative (**14**) are in most cases very similar to the parent compound (**11**) but the trimethylstannyl derivative (**15**) regenerates the anion (**10**) on treatment with  $\text{MeLi}$  or  $\text{Bu}^n\text{Li}$ . Finally, reaction of the anion (**10**) with  $\alpha$ -pyrone (**42**) unexpectedly gave the naphthopyrone (**43**).

Recently much interest has been shown in the synthesis of linear polycyclic aromatic systems such as are found in the anthracycline antibiotics, the olivomycins, and many other important polyketide-derived natural products. An attractive starting point for building up this type of skeleton would be a compound with reactivity as shown in (**1**). This synthon is effectively present in toluate anions such as (**2**) or (**3**). However Hauser and Rhee<sup>2</sup> have reported that the anion (**2**) dimerizes very rapidly and cannot be used synthetically. The same has been observed for the substituted *o*-toluate (**3**).<sup>3</sup> As a result many modifications have been adopted. The dianions (**4**)<sup>4</sup> and (**5**)<sup>5</sup> are reasonably stable and the substituted dianions (**6**)<sup>6</sup> and (**7**)<sup>7</sup> have been used synthetically.



Another method that has been used to stabilize *o*-toluate anions employs an electron-withdrawing substituent on the methyl group. Thus sulphides,<sup>8</sup> sulphoxides,<sup>2</sup> and sulphones<sup>9</sup> have all been used as well as methoxycarbonyl<sup>10</sup> and cyano<sup>9</sup> groups. The unsubstituted phthalide anion (**8**) appears to be more stable and has been used on several occasions.<sup>11,12</sup> However the use of electron-withdrawing groups to stabilize the anion and act as a leaving group is again common.<sup>2,12,13</sup>

We have found that *o*-toluate anions (**9**) and (**10**) which have a methoxy substituent in the other position *ortho* to the carbonyl are sufficiently stable at low temperatures to be synthetically useful without stabilising groups.<sup>1</sup> We assume that the extra stability of these anions over that of (**2**) and (**3**) is due to the second *ortho* substituent which hinders the carbonyl from

nucleophilic attack. We would like to present here reactions of the anion (**10**)<sup>†</sup> with simple electrophiles and in the following paper reactions with pyrones and pyrylium salts as electrophiles.

## Results

There are many reported routes to the esters of orsellinic acid dimethyl ether (**11**)<sup>14</sup> and we have employed two methods for large scale syntheses.<sup>15</sup> It was found that treatment of (**11**) with  $\text{MeLi}$  in THF at  $-78^{\circ}\text{C}$  had no effect but on warming to  $-10^{\circ}\text{C}$  nucleophilic attack occurred to give the methyl ketone (**21**) and smaller amounts of alkene (**29**), the product of a second attack. With  $\text{Bu}^n\text{Li}$  nucleophilic attack occurred even at  $-78^{\circ}\text{C}$  to give the corresponding products (**22**) and (**30**) and quenching with  $\text{D}_2\text{O}$  or  $\text{Me}_3\text{SiCl}$  showed that no deprotonation of the aromatic methyl group had occurred. Reaction of (**11**) with  $\text{Bu}^n\text{Li}$  at  $-78^{\circ}\text{C}$  gave the ketone (**23**) and recovered starting material. If quenched with  $\text{D}_2\text{O}$ , this reaction gave some incorporation of deuterium into the recovered (**11**) indicating that some deprotonation had occurred.  $\text{Bu}^n\text{Li}$  on the other hand gave only the ketone (**24**) in good yield. Trityllithium at room temperature most unexpectedly demethylated (**11**) to give (**36**). The mechanism for this reaction is not certain.

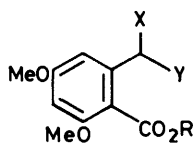
With the less nucleophilic base, lithium di-isopropylamide, rapid deprotonation of (**11**) occurred at  $-78^{\circ}\text{C}$  in THF to give (**10**).<sup>‡</sup> Quenching the anion with  $\text{D}_2\text{O}$  gave levels of deuteration approaching 100% by n.m.r. and mass spectrometry. The anion (**10**) is stable for a few hours if kept at  $-78^{\circ}\text{C}$  but after longer periods or at higher temperature decomposition is observed. The decomposition products (**33**) and (**34**), produced by self-condensation, and the dimer (**35**) can also be isolated as by-products of some of the reactions of anion (**10**).

The anion (**10**) reacts with a variety of electrophiles to give the expected products in good yield.§ Thus with  $\text{CO}_2$ ,  $\text{MeI}$ ,  $\text{Me}_3\text{SiCl}$ , and  $\text{Me}_3\text{SnCl}$  the products (**12**)–(**15**) are formed. With  $\text{Me}_3\text{SnCl}$  it was found that the distannylated product (**16**)

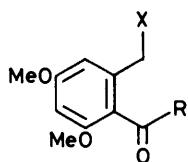
<sup>†</sup> In all reactions where both the methyl and ethyl esters of (**10**) have been used, their behaviour was identical and so they have not been distinguished in the main text—see Experimental section for details.

<sup>‡</sup> Structure (**10**) is not intended to suggest that the lithium atom is attached to carbon. In fact preliminary n.m.r. work suggests an extended enolate structure with the lithium attached to oxygen.

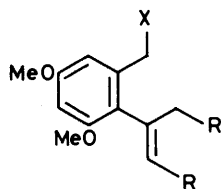
§ A report has recently appeared describing the sulphenation and selenation of the anion (**10**) with  $\text{PhSSPh}$  and  $\text{PhSeSePh}$  respectively.<sup>3</sup>



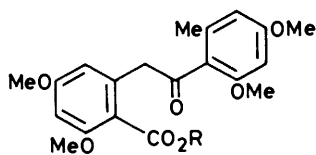
- (11) X = Y = H  
 (12) X = CO<sub>2</sub>H, Y = H  
 (13) X = Me, Y = H  
 (14) X = SiMe<sub>3</sub>, Y = H  
 (15) X = SnMe<sub>3</sub>, Y = H  
 (16) X = Y = SnMe<sub>3</sub>  
 (17) X = Y = SiMe<sub>3</sub>  
 (18) X = COCH<sub>3</sub>, Y = H  
 (19) X = SiMe<sub>3</sub>, Y = Li  
 (20) X = SiMe<sub>3</sub>, Y = Me



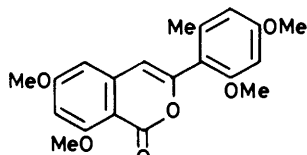
- (21) R = Me, X = H  
 (22) R = Bu<sup>n</sup>, X = H  
 (23) R = Bu<sup>s</sup>, X = H  
 (24) R = Bu<sup>t</sup>, X = H  
 (25) R = Me, X = SiMe<sub>3</sub>  
 (26) R = Bu<sup>n</sup>, X = SiMe<sub>3</sub>  
 (27) R = Bu<sup>s</sup>, X = SiMe<sub>3</sub>  
 (28) R = Bu<sup>t</sup>, X = SiMe<sub>3</sub>



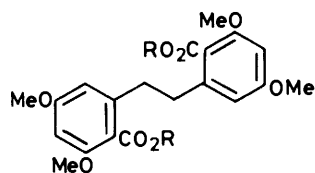
- (29) R = X = H  
 (30) R = Pr, X = H  
 (31) R = H, X = SiMe<sub>3</sub>  
 (32) R = Pr, X = SiMe<sub>3</sub>



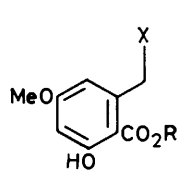
(33)



(34)



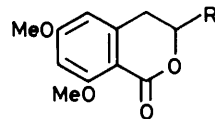
(35)



- (36) X = H  
 (37) X = SiMe<sub>3</sub>

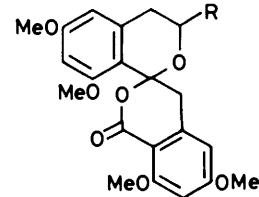
was a by-product and this proved difficult to separate from the monostannylated product. The disilylated product (17) was also sometimes observed as a minor by-product in the reaction with Me<sub>3</sub>SiCl and was produced in greater amounts if excess of base was present.

Controlled acetylation of the anion (10) proved more difficult. Under normal conditions reaction with acetyl chloride gave very low yields of the expected product and other acylating agents were no more successful. Moderate yields of the ketone (18) could however be obtained by inverse addition of anion (10) to a dilute solution of acetyl chloride cooled to -78 °C. (Hauser and Rhee<sup>6</sup> have reported that they were unable to acetylate a similar anion directly and used a sequence of four reactions to achieve the same end.)



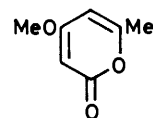
(38) R = Ph

(39) R = Me

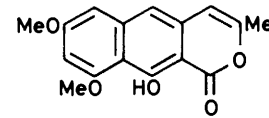


(40) R = Ph

(41) R = Me



(42)



(43)

Reaction of the anion (10) with aldehydes is accompanied by lactonisation of the intermediate. Thus benzaldehyde and acetaldehyde gave the dihydroisocoumarins (38) and (39). However major by-products of these reactions were (40) and (41) respectively (stereochemistry unknown) arising from further attack of (10) on the product. The increase in reactivity of the carbonyl of the dihydroisocoumarins (38) and (39) compared with the starting ester (11) is because the C=O bond in the former can lie in the plane of the aromatic ring and so is not hindered towards attack perpendicular to the plane, whereas in (11) the carbonyl is forced out of the plane by the bulky *ortho* substituents and so these substituents are then hindering attack at both faces. For the reaction with acetaldehyde the side-reaction was eliminated by inverse addition of anion (10) to an excess of the aldehyde at -78 °C.

It was found that the silyl derivative (14) could, to a small extent, be deprotonated by Bu<sup>n</sup>Li to give (19) (as shown by deuterium incorporation on quenching with D<sub>2</sub>O) but nucleophilic attack by this base was the major reaction giving (26) and, in smaller amounts, (32). MeLi, Bu<sup>n</sup>Li and Bu<sup>t</sup>Li were each also tried as bases to deprotonate (14) but the results were analogous to those obtained with (11). Thus the ketones (25), (27), and (28) were obtained and, with MeLi, smaller amounts of the alkene (31). The yield of (28) was excellent (96%) which is very surprising for the reaction of two such hindered molecules. Again trityl-lithium at room temperature caused demethylation, this time giving (37). A more convenient base therefore was LDA which caused relatively slow deprotonation at -78 °C but at -15 °C deprotonation was more rapid. This anion also gave good yields of the expected products with MeI and Me<sub>3</sub>SiCl (20) and (17) respectively. Reaction of the silyl anion with aldehydes (Peterson reaction), however, did not give good yields of any one product. The trimethylsilyl group of (14) could be removed by treatment with Bu<sub>4</sub>N<sup>+</sup>F<sup>-</sup> in THF. Although the anion (10) must be formed in this reaction it was of no synthetic use since it was protonated by residual moisture in the reagent; thus, 22% was the highest incorporation that could be obtained on quenching with D<sub>2</sub>O. Treatment of the stannyl derivative (15) with Bu<sup>n</sup>Li or MeLi did not cause deprotonation or addition to the carbonyl group, but instead S<sub>N</sub>2 attack at the tin atom produced the anion (10) again. The anion thus produced is free from di-isopropylamine which may modify its reactivity—indeed in deuteration and reaction with acetaldehyde the yields obtained by this method were superior to those obtained with the anion (10) generated using LDA.

With the aim of synthesizing higher polyketides, the anion (10) was treated with triacetic lactone methyl ether (42). The expected attack of the anion at the carbonyl (C-2) was not observed, instead attack was at C-4 and on warming to room temperature cyclization occurred to give as almost the sole

product the naphthopyrone (43)\* which was identified as a methyl ether of naturally occurring toralactone.<sup>16</sup> Again an improved yield of the naphthopyrone could be obtained using the anion (10) obtained from the trimethylstannyl derivative (15). Thus, in a single step from our title anion we have built up the tricyclic skeleton and oxygenation pattern of a typical heptaketide. Further details of this and other reactions of the anion (10) leading to polyketide metabolites will be given in the following paper and will serve to emphasize the synthetic usefulness of anion (10) which this paper has illustrated.

### Experimental

Melting points were determined using a Kofler hot-stage apparatus and are uncorrected. U.v. spectra were recorded on a Unicam SP 1800 or SP 8000 spectrophotometer on solutions in 95% EtOH unless otherwise stated. I.r. spectra were recorded on a Perkin-Elmer 297 spectrometer; unless otherwise stated all samples were dissolved in CCl<sub>4</sub> and all reported peaks were strong. <sup>1</sup>H N.m.r. spectra were recorded using a Varian EM 360 A, EM 390, CFT 20 or XL 100, or a Bruker WH 400 spectrometer; all samples were dissolved in CDCl<sub>3</sub> and  $\delta$  values are quoted relative to tetramethylsilane. Deuterium n.m.r. spectroscopy was performed on the Bruker instrument. Mass spectra were obtained on an AEI MS 30 spectrometer. Qualitative thin layer chromatography (t.l.c.) was carried out on commercially prepared plates coated with Merck Kieselgel GF<sub>254</sub>. Preparative layer chromatography (p.l.c.) was performed on plates (20 × 20 × 0.1 cm) coated with the same material. Tetrahydrofuran (THF) was dried by distillation from LiAlH<sub>4</sub>, stored over Na wire, and then redistilled from LiAlH<sub>4</sub> immediately before use.

For work-up A the reaction mixture was poured into an excess of dilute H<sub>2</sub>SO<sub>4</sub> and extracted twice with diethyl ether and twice with ethyl acetate. The organic layers were washed with saturated aqueous sodium hydrogen carbonate, and then saturated brine, dried over Na<sub>2</sub>SO<sub>4</sub> (or MgSO<sub>4</sub>) and evaporated to dryness under reduced pressure. Work-up B was the same except that only one extraction with ethyl acetate and no washes with aqueous sodium hydrogen carbonate or brine were used.

1-(2,4-Dimethoxy-6-methylphenyl)ethanone (21) and 1,5-Dimethoxy-3-methyl-2-(1-methylethenyl)benzene (29).—Methyl-lithium-lithium bromide (1.4M in diethyl ether) was added dropwise to stirred, dry THF (3 ml) containing one small crystal of triphenylmethane under nitrogen at -78 °C until after a few drops a persistent pink colour indicated complete dryness. A solution of ethyl 2,4-dimethoxy-6-methylbenzoate (11; R = Et) (56 mg, 0.25 mmol) in THF (1.5 ml) was added dropwise at -78 °C followed by methyl-lithium-lithium bromide (1.4M; 0.27 ml, 0.38 mmol). When this mixture was stirred for 1.5 h at -78 °C, quenched with D<sub>2</sub>O (1 ml) in THF (1 ml), and stirred while warming to room temperature, work-up A gave only the starting material (11; R = Et), which showed no deuteration by n.m.r. or mass spectroscopy. Alternatively when the mixture was stirred for 1.5 h while warming to -40 °C and then further methyl-lithium-lithium bromide (1.4M in ether; 0.1 ml, 0.14 mmol) was added and the mixture stirred for 1 h while warming to -10 °C, work-up with D<sub>2</sub>O as before yielded a colourless oil which was purified by p.l.c. [diethyl ether-light petroleum (b.p. 60–80 °C), 1 : 1] giving no starting material and two products. The first product, R<sub>F</sub> 0.4, gave the ketone (21) (23 mg, 47%) as an oil which crystallised to give prisms, m.p. 40–42 °C (from ethyl acetate-hexane) (lit.,<sup>18</sup> m.p. 41–42 °C). N.m.r. and mass

spectroscopy data indicated an average of 1.5 deuterium atoms per molecule present in the methyl group next to the ketone but negligible deuteration on the aromatic methyl group. The second product, R<sub>F</sub> 0.6, gave the alkene (29) (2 mg, 4%) as an oil pure by n.m.r. and t.l.c. (Found: M<sup>+</sup>, 192.1163. C<sub>12</sub>H<sub>16</sub>O<sub>2</sub> requires M, 192.1150);  $\nu_{\max}$ , 2860m, 1645w, 1610, and 1590sh cm<sup>-1</sup>;  $\lambda_{\max}$ , 226sh and 278 nm;  $\delta_{\text{H}}$  1.96 (3 H, br s), 2.23 (3 H, s), 3.78 (6 H, s), 4.77 (1 H, m), 5.26 (1 H, m), and 6.34 (2 H, m); m/z 192 (M<sup>+</sup>, 95%), 177 (100), and 162 (40).

1-(2,4-Dimethoxy-6-methylphenyl)pentan-1-one (22) and 2-(1-Butylpent-1-enyl)-1,5-dimethoxy-3-methylbenzene (30).—Ethyl 2,4-dimethoxy-6-methylbenzoate (11; R = Et) (56 mg, 0.25 mmol) was dissolved in dry THF (5 ml) under nitrogen and cooled to -78 °C with stirring. n-Butyl-lithium (1.7M in hexane; 0.32 ml, 0.54 mmol) was injected dropwise and the solution stirred for 1 h at -78 °C. D<sub>2</sub>O (1 ml) in dry THF (1 ml) was added dropwise and the orange colour was instantly discharged. The mixture was allowed to warm to room temperature and after work-up B a pale yellow semi-solid was obtained which was purified by p.l.c. [diethyl ether-light petroleum (b.p. 60–80 °C), 1 : 1] giving three major bands. The first band, R<sub>F</sub> 0.4, gave starting material (11; R = Et) (4 mg, 7%) containing no deuterium. The second band, R<sub>F</sub> 0.5, gave the ketone (22) (42 mg, 71%) as an oil, b.p. 100 °C/0.01 mmHg, which was found to be deuteriated on the methylene next to the ketone to the extent of nearly one deuterium per molecule on average (Found: M<sup>+</sup>, 238.1569, 237.1523, and 236.1424. C<sub>14</sub>H<sub>18</sub>D<sub>2</sub>O<sub>3</sub>, C<sub>14</sub>H<sub>19</sub>DO<sub>3</sub>, and C<sub>14</sub>H<sub>20</sub>O<sub>3</sub> requires M, 238.1569, 237.1491, and 236.1412);  $\nu_{\max}$ , 2830w, 1695, 1605, 1590, and 1465 cm<sup>-1</sup>;  $\lambda_{\max}$  (MeOH) 228 and 268 nm;  $\delta_{\text{H}}$  0.8–1.8 (7 H, m), 2.19 (3 H, s), 2.73 (1 H, t, J 7 Hz, COCHDCH<sub>2</sub>), 3.76 (3 H, s), 3.78 (3 H, s), and 6.29 (2 H, s); m/z 238 (M<sup>+</sup> + 2, 5%), 237 (M<sup>+</sup> + 1, 10), 236 (M<sup>+</sup>, 5), and 179 (100). The third band, R<sub>F</sub> 0.65, gave the alkene (30) (12 mg, 17%) as an oil, b.p. 110 °C/0.01 mmHg (Found: M<sup>+</sup>, 276.2081. C<sub>18</sub>H<sub>28</sub>O<sub>2</sub> requires M, 276.2089);  $\nu_{\max}$ , 2860, 1605, 1580, 1490, and 1465 cm<sup>-1</sup>;  $\lambda_{\max}$  (MeOH) 230 and 280 nm;  $\delta_{\text{H}}$  0.8–1.7 (12 H, m), 2.0–2.4 (7 H, m), 3.72 (3 H, s), 3.77 (3 H, s), 5.14 (1 H, t, J 7 Hz), and 6.31 (2 H, m); m/z 276 (M<sup>+</sup>, 25%), 219 (60), and 179 (43).

1-(2,4-Dimethoxy-6-methylphenyl)-2-methylbutan-1-one (23).—s-Butyl-lithium (1.4M in cyclohexane) was added dropwise to stirred dry THF (2 ml) containing one small crystal of triphenylmethane under argon at -78 °C until a persistent pink colour indicated complete dryness. A solution of ethyl 2,4-dimethoxy-6-methylbenzoate (11; R = Et) (56 mg, 0.25 mmol) in THF (1.5 ml) was added dropwise, followed by s-butyl-lithium (1.4M in cyclohexane; 0.72 ml, 1.0 mmol) which produced an orange colour after stirring for 30 min at -78 °C. Water (1 ml) in THF (1 ml) was then added and stirring was continued while warming to room temperature over 1 h. Work-up A yielded an oil which gave two main bands after p.l.c. [diethyl ether-light petroleum (b.p. 60–80 °C), 1 : 1]. The first band, R<sub>F</sub> 0.4, gave starting material (11; R = Et) (20 mg, 36%). The second band, R<sub>F</sub> 0.5, gave the ketone (23) (34 mg, 58%) as an oil which was pure by t.l.c. (Found: M<sup>+</sup>, 236.1417. C<sub>14</sub>H<sub>20</sub>O<sub>3</sub> requires M, 236.1412);  $\nu_{\max}$ , 2880m, 2840m, 1695, 1605, and 1590 cm<sup>-1</sup>;  $\lambda_{\max}$ , 219, 265, and 282sh nm;  $\delta_{\text{H}}$  0.90 (3 H, t, J 7 Hz), 1.09 (3 H, d, J 7 Hz), 1.2–2.0 (2 H, m), 2.20 (3 H, s), 2.97 (1 H, m, J 7 Hz), 3.76 (3 H, s), 3.79 (3 H, s), and 6.30 (2 H, s); m/z 236 (M<sup>+</sup>, 5%) and 179 (100).

In another experiment the same procedure was followed except that s-butyl-lithium (1.4M in cyclohexane; 0.36 ml, 0.50 mmol) was used and D<sub>2</sub>O (1 ml) in THF (1 ml) used to quench the reaction. This gave starting material (11; R = Et) (30 mg, 54%) which was shown to be 55% monodeuteriated in the aromatic methyl group by n.m.r. and mass spectroscopy, and

\* Similar Michael addition of the anion (10) to a  $\beta$ -methoxy enone has recently been reported in a synthesis of the olivin skeleton.<sup>17</sup>

the ketone (23) (26 mg, 48%) which was shown to be over 80% monodeuterated by mass spectroscopy; n.m.r. showed that the deuterium was approximately half in the aromatic methyl group and half next to the ketone.

**1-(2,4-Dimethoxy-6-methylphenyl)-2,2-dimethylpropan-1-one (24).**—The previous procedure was followed but both additions of *s*-butyl-lithium were replaced by *t*-butyl-lithium (1.5M in *n*-pentane). After the second addition of *t*-butyl-lithium (1.5M; 0.34 ml, 0.51 mmol) and stirring for 0.5 h at  $-78^\circ\text{C}$ , a yellow-orange colour had formed which was quickly discharged on quenching with  $\text{D}_2\text{O}$  (1 ml) in THF (1 ml). Work-up A followed by p.l.c. [diethyl ether–light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ ), 1 : 2] gave one main band,  $R_F$  0.5, which gave the ketone (24) (50 mg, 85%) as prisms, m.p.  $82\text{--}84^\circ\text{C}$  (from *n*-hexane–acetone) which showed 5% monodeuteriation (presumably in the aromatic methyl group) by mass spectroscopy (Found: C, 70.9; H, 8.8.  $\text{C}_{14}\text{H}_{20}\text{O}_3$  requires C, 71.16; H, 8.53%;  $\nu_{\text{max}}$ , 2 870m, 2 840m, 1 695, 1 610, and 1 590  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ , 220, 270, and 276sh nm;  $\delta_{\text{H}}$ , 1.15 (9 H, s), 2.10 (3 H, s), 3.70 (3 H, s), 3.75 (3 H, s), and 6.25 (2 H, br s);  $m/z$  236 ( $M^+$ , 30%), 180 (15), and 179 (100).

**Ethyl 2-Hydroxy-4-methoxy-6-methylbenzoate (36; R = Et).**—To a solution of triphenylmethane (244 mg, 1.0 mmol) in dry THF (3 ml) under nitrogen at room temperature was added *n*-butyl-lithium (1.7M in *n*-hexane; 0.56 ml, 0.95 mmol), giving a deep red colour. After the mixture had been stirred for 1 h, a solution of ethyl 2,4-dimethoxy-6-methylbenzoate (11; R = Et) (56 mg, 0.25 mmol) in THF (1.5 ml) was added dropwise and stirring was continued for 20 h at room temperature. Water (1 ml) was then added and after work-up A, a yellow oil was obtained, which was purified by p.l.c. [diethyl ether–light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ ), 1 : 3, 2 elutions] to give two main bands. The first band,  $R_F$  0.75, gave the phenol (36) (45 mg, 86%) as needles, m.p.  $76\text{--}77^\circ\text{C}$  (lit.,<sup>19</sup>  $74\text{--}76^\circ\text{C}$ ) (Found:  $M^+$ , 210.0904. Calc. for  $\text{C}_{11}\text{H}_{14}\text{O}_4$ :  $M$ , 210.0892;  $\nu_{\text{max}}$ , 3 400–2 800w, 2 850w, 1 650, 1 620, and 1 580  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ , 262 and 300 nm;  $\delta_{\text{H}}$ , 1.39 (3 H, t,  $J$  7 Hz), 2.50 (3 H, s), 3.78 (3 H, s), 4.38 (2 H, q,  $J$  7 Hz), 6.29 (2 H, ABq,  $J$  2 Hz), and 11.38 (1 H, s);  $m/z$  210 ( $M^+$ , 30%), 165 (25), 164 (100), and 136 (25). The second band,  $R_F$  0.9, gave colourless crystals (232 mg) having the same  $R_F$  value as triphenylmethane but showing an extra n.m.r. peak at  $\delta$  2.2, which can be accounted for if a quarter of the material had been methylated giving 1,1,1-triphenylethane.

**2-Ethoxycarbonyl-3,5-dimethoxybenzyl-lithium (10; R = Et) (0.5 mmol).**—To dry THF (3 ml) containing a small crystal of triphenylmethane under nitrogen was added dropwise *n*-butyl-lithium (1.7M in hexane) until after a few drops a persistent pink colour indicated complete dryness. Di-isopropylamine (0.1 ml, 0.7 mmol) and *n*-butyl-lithium (1.7M in hexane; 0.33 ml, 0.56 mmol) were added and the mixture stirred for 15 min at room temperature. After cooling to  $-78^\circ\text{C}$ , ethyl 2,4-dimethoxy-6-methylbenzoate (11; R = Et) (112 mg, 0.5 mmol) in dry THF (1.5 ml) was added dropwise to give an orange-red colour which indicated anion formation. The solution was stirred for 30 min at  $-78^\circ\text{C}$  before use. Later experiments showed that anion formation was, in fact, complete after as little as 2 min. In an alternative procedure, useful for larger-scale reactions, the solution of the orsellinate (11; R = Et) was present in a side-arm to the main flask and was introduced by tipping the whole flask. This allowed rapid mixing of the two solutions without raising the temperature.

**2-Methoxycarbonyl-3,5-dimethoxybenzyl-lithium (10; R = Me) (0.5 mmol).** This was made in the same way from the methyl ester (11; R = Me) (105 mg, 0.5 mmol).

**Deuterium Incorporation.**—To a solution of the anion (10; R = Et) (0.17 mmol) at  $-78^\circ\text{C}$  was added dropwise  $\text{D}_2\text{O}$  (1 ml) in THF (1 ml); the colour was discharged immediately. The mixture was stirred for 2 h while warming to room temperature. After work-up B a yellow oil was obtained which was purified by p.l.c. [diethyl ether–light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ ), 2 : 1] giving in the only major band, starting material (11; R = Et) (28 mg, 74%) as an oil, which was not purified further. N.m.r. and mass spectroscopy indicated ca. 95% deuteration.

**Ethyl 2,4-Dimethoxy-6-[2-(2,4-dimethoxy-6-methylphenyl)-2-oxoethyl]benzoate (33; R = Et) and 3-(2,4-Dimethoxy-6-methylphenyl)-6,8-dimethoxy-1H-2-benzopyran-1-one (34).**—When the anion (10; R = Et) (0.25 mmol) was generated as before but at  $0^\circ\text{C}$  the orange-red colour of the anion was produced but after 20 min of stirring the colour had faded to yellow.  $\text{D}_2\text{O}$  (1 ml) in THF (1 ml) was added and the mixture was allowed to warm to room temperature and stirred for 1 h. After work-up A, the yellow oil obtained was purified by p.l.c. (ethyl acetate–toluene, 1 : 2; 2 elutions). Eight main bands were visible but only three identifiable compounds were isolated. The band at  $R_F$  0.9 gave unchanged starting material (11; R = Et) (4 mg, 7%) showing negligible deuteration by n.m.r. and mass spectroscopy. The band at  $R_F$  0.8 gave the keto ester (33; R = Et) (3 mg, 6%) as an oil (Found:  $M^+$ , 402.1684.  $\text{C}_{22}\text{H}_{26}\text{O}_7$  requires  $M$ , 402.1679;  $\nu_{\text{max}}$ , 2 840m, 1 725, 1 715, 1 605, 1 590, and 1 465  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ , 257 and 282sh nm;  $\delta_{\text{H}}$ , 1.26 (3 H, t,  $J$  7 Hz), 2.14 (3 H, s), 3.78 (9 H, br s), 3.81 (3 H, s), 4.15 (2 H, s), 4.22 (2 H, q,  $J$  7 Hz), 6.29 (2 H, s), and 6.37 (2 H, s);  $m/z$  402 ( $M^+$ , 20%) and 357 (100). In the product from  $\text{D}_2\text{O}$  work-up the signal at  $\delta$  4.15 was reduced to about half its normal size indicating the incorporation of one deuterium atom at the benzylic position. The third band,  $R_F$  0.4, showed a blue fluorescence under u.v. light. It yielded the benzopyrone (34) (6 mg, 13%) as an oil which was crystallised to give plates, m.p.  $176\text{--}178^\circ\text{C}$  [from ethyl acetate–light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ )] (lit.,<sup>20</sup>  $168^\circ\text{C}$  unrecrystallised) (Found:  $M^+$ , 356.1262.  $\text{C}_{20}\text{H}_{20}\text{O}_6$  requires 356.1260;  $\nu_{\text{max}}$ , (CHCl<sub>3</sub>) 2 925, 2 855, 1 715, 1 660, 1 600, 1 590, 1 570, 1 485, and 1 460  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ , 245 and 328 nm;  $\delta_{\text{H}}$ , 2.27 (3 H, s), 3.73, 3.80, 3.89, 3.96 (4  $\times$  3 H, s), 6.30 (1 H, s), 6.34 (2 H, br s), 6.39 (1 H, d,  $J$  2 Hz), and 6.47 (1 H, d,  $J$  2 Hz);  $m/z$  356 ( $M^+$ , 100%) and 313 (45).

**(2-Ethoxycarbonyl-3,5-dimethoxyphenyl)acetic Acid (12; R = Et).**—Dry  $\text{CO}_2$  gas was passed through a solution of the anion (10; R = Et) (0.5 mmol) and the colour was discharged almost instantaneously. The solution was warmed to room temperature and water (25 ml) was added. This mixture was extracted with diethyl ether (2  $\times$  50 ml) and the aqueous layer acidified to pH 2 with dilute HCl and extracted with chloroform (2  $\times$  75 ml). The ether extract afforded the starting material (11; R = Et) (28 mg, 25%) and the chloroform gave the arylacetic acid (81 mg, 60%), m.p.  $103\text{--}104^\circ\text{C}$  (from diethyl ether–pentane) (lit.,<sup>18,21</sup>  $103\text{--}104^\circ\text{C}$ ) (Found:  $M^+$ , 268.0943. Calc. for  $\text{C}_{13}\text{H}_{16}\text{O}_6$ : 268.0947;  $\nu_{\text{max}}$ , (CHCl<sub>3</sub>) 2 950br, 1 740, 1 715, and 1 600  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ , 316 and 346 nm;  $\delta_{\text{H}}$ , 1.38 (3 H, t,  $J$  7 Hz), 3.64 (2 H, s), 3.81 (6 H, s), 4.41 (2 H, q,  $J$  7 Hz), 6.41 (1 H, d,  $J$  2 Hz), and 6.45 (1 H, d,  $J$  2 Hz);  $m/z$  268 ( $M^+$ ), 224, 222, 195, 194, and 179 (100%).

**Ethyl 2-Ethyl-4,6-dimethoxybenzoate (13; R = Et).**—To a solution of the anion (10; R = Et) (10 mmol) at  $-78^\circ\text{C}$  was added dropwise methyl iodide (0.80 ml, 1.82 g, 12.8 mmol). The mixture was stirred for 1 h at  $-78^\circ\text{C}$ , allowed to warm to room temperature over 4 h, and then diluted with EtOH (95%, 30 ml); it was then stirred overnight. After work-up A a yellow oil was obtained, which was purified by chromatography on UG1 alumina with diethyl ether as eluant to give the major product

as an oil. Distillation gave the *benzoate* (**13**; R = Et) as an oil (2.19 g, 92%), b.p. 105–110 °C/0.1 mmHg (Found:  $M^+$ , 238.1217.  $C_{13}H_{18}O_4$  requires  $M$ , 238.1205);  $\nu_{\max}$ . 2 840w, 1 730, 1 610, and 1 590  $cm^{-1}$ ;  $\lambda_{\max}$ . 241sh and 280 nm;  $\delta_H$  1.19 (3 H, t,  $J$  7 Hz), 1.34 (3 H, t,  $J$  7 Hz), 2.58 (2 H, q,  $J$  7 Hz), 3.77 (3 H, s), 3.78 (3 H, s), 4.34 (2 H, q,  $J$  7 Hz), and 6.32 (2 H, ABq,  $J$  2 Hz);  $m/z$  238 ( $M^+$ , 65%), 193 (100), 192 (60), and 191 (32). The distillation also yielded a slightly higher boiling fraction identified as *diethyl 4,4',6,6'-tetramethoxy-2,2'-dimethylenedibenzoate* (**35**; R = Et) (20 mg, 1%) which was identical with the by-product obtained in several other reactions of the anion (**10**; R = Et), as needles, m.p. 107–109 °C (from ethanol) (Found: C, 64.4; H, 6.8.  $C_{24}H_{30}O_8$  requires C, 64.56; H, 6.77%);  $\nu_{\max}$ . 2 840m, 1 730, 1 605, and 1 590  $cm^{-1}$ ;  $\lambda_{\max}$ . 250 and 282 nm;  $\delta_H$  1.35 (6 H, t,  $J$  7 Hz), 2.84 (4 H, s), 3.74 (6 H, s), 3.78 (6 H, s), 4.38 (4 H, q,  $J$  7 Hz), 6.25 (2 H, d,  $J$  7 Hz), and 6.31 (2 H, d,  $J$  2 Hz);  $m/z$  446 ( $M^+$ , 5%), 401 (15), 400 (15), 355 (35), and 354 (100).

*Methyl and Ethyl 2,4-Dimethoxy-6-trimethylsilylmethylbenzoate* (**14**; R = Me and Et).—To a solution of the anion (**10**; R = Me) (0.48 mmol) at  $-78$  °C was added dropwise trimethylchlorosilane (0.3 ml) in THF (2 ml). After being stirred for 30 min at  $-78$  °C, the mixture was allowed to warm to room temperature over 2 h. The solvent was evaporated under reduced pressure and the residue was shaken with water and diethyl ether (30 ml). The aqueous layer was further extracted with diethyl ether (30 ml) and ethyl acetate (30 ml) and the combined organic layers were washed with 10% aqueous NaOH (20 ml) and saturated brine (20 ml), dried over  $Na_2SO_4$ , and evaporated to dryness under reduced pressure. Purification of the yellow oil by p.l.c. ( $CH_2Cl_2$ , 2 elutions) gave two main bands. The first band,  $R_F$  0.75, gave the *monosilylated benzoate* (**14**; R = Me) (74 mg, 55%) as needles, m.p. 48–50 °C (from pentane) (Found:  $M^+$ , 282.1280.  $C_{14}H_{22}O_4Si$  requires  $M$ , 282.1287);  $\nu_{\max}$ . ( $CHCl_3$ ) 2 840m, 1 720, 1 605, and 1 585  $cm^{-1}$ ;  $\lambda_{\max}$ . (MeOH) 254 and 283 nm;  $\delta_H$  0.0 (9 H, s), 2.15 (2 H, s), 3.75 (6 H, s), 3.80 (3 H, s), and 6.15 (2 H, ABq,  $J$  2 Hz);  $m/z$  282 ( $M^+$ , 25%), 267 (80), 251 (55), 178 (100), and 73 (40). The second band,  $R_F$  0.8, gave *methyl 2-bis(trimethylsilyl)methyl-4,6-dimethoxybenzoate* (**17**; R = Me) (40 mg, 23%) as needles, m.p. 71–73 °C (from pentane) (see later).

In a similar fashion the anion (**10**; R = Et) (7.01 mmol) in THF at  $-78$  °C was treated with trimethylchlorosilane (5.5 ml) which had been kept at  $-78$  °C in a side-arm of the same flask. After the same work-up a yellow oil was obtained which was crystallised from hexane without the need for chromatography to give the corresponding *ethyl ester* (**14**; R = Et) (1.40 g). More of the same product was obtained from the mother liquors by p.l.c. [diethyl ether–light petroleum (b.p. 60–80 °C), 1:2, 2 elutions] (total yield, 1.80 g, 87%), m.p. 44–45 °C (from hexane) (Found: C, 61.0; H, 8.4.  $C_{15}H_{24}O_4Si$  requires C, 60.78; H, 8.16%);  $\nu_{\max}$ . 2 840w, 1 725, 1 605, and 1 590  $cm^{-1}$ ;  $\lambda_{\max}$ . 252 and 281 nm;  $\delta_H$  0.00 (9 H, s), 1.34 (3 H, t,  $J$  7 Hz), 2.14 (2 H, s), 3.76 (6 H, s), 4.32 (2 H, q,  $J$  7 Hz), 6.13 (1 H, d,  $J$  2 Hz), and 6.20 (1 H, d,  $J$  2 Hz);  $m/z$  296 ( $M^+$ , 15%), 281 (38), 265 (15), 251 (35), 178 (60), and 73 (100).

*Ethyl 2,4-Dimethoxy-6-trimethylstannylmethylbenzoate* (**15**; R = Et).—To a solution of the anion (**10**; R = Et) (0.5 mmol) at  $-78$  °C was added dropwise trimethylstannyl chloride (120 mg, 0.6 mmol) in THF (2 ml). After being stirred for 1 h the solution was allowed to warm to room temperature during 1.5 h and then evaporated to dryness under reduced pressure to give an oil, which was purified by p.l.c. [diethyl ether–light petroleum (b.p. 60–80 °C), 1:1,  $R_F$  0.5] to give the *trimethylstannyl compound* (**15**; R = Et) (139 mg, 72%) as an oil which crystallised as prisms, m.p. 35–36 °C (from aqueous EtOH) (Found: C, 46.4; H, 6.15.  $C_{15}H_{24}O_4Sn$  requires C, 46.55; H, 6.25%);  $\nu_{\max}$ .

2 840m, 1 720, 1 600, and 1 585  $cm^{-1}$ ;  $\lambda_{\max}$ . (MeOH) 255 and 285 nm;  $\delta_H$  0.06 (9 H, s), 1.34 (3 H, t,  $J$  7 Hz), 2.29 (2 H, s), 3.76 (6 H, s), 4.34 (2 H, q,  $J$  7 Hz), and 6.11 (2 H, ABq,  $J$  2 Hz);  $m/z$  388, 386, 384 ( $M^+$ , 5, 4, 2%), 373, 371, 369 (100, 90, 50), and 343, 341, and 339 (30, 20, 10). On a larger scale reaction however, significant quantities of the bis(trimethylstannyl) compound were produced and this proved extremely difficult to separate. Eventually small amounts were obtained pure by p.l.c. ( $CH_2Cl_2$ –toluene, 1:1, 4 elutions) to give *ethyl 2-bis(trimethylstannyl)methyl-4,6-dimethoxybenzoate* (**16**; R = Et) (48 mg, 4%) as an oil, b.p. 115–120 °C/0.1 mmHg (Found: C, 39.5; H, 6.15.  $C_{18}H_{32}O_4Sn_2$  requires C, 39.32; H, 5.87%);  $\nu_{\max}$ . 2 840w, 1 730, 1 600, and 1 580  $cm^{-1}$ ;  $\lambda_{\max}$ . (MeOH) 255sh and 286 nm;  $\delta_H$  0.10 (18 H, s), 1.32 (3 H, t,  $J$  7 Hz), 1.97 (1 H, s), 3.73 (6 H, s), 4.31 (2 H, q,  $J$  7 Hz), and 6.02 (2 H, ABq,  $J$  2 Hz);  $m/z$  (no  $M^+$ ), 537, 535, 533 ( $M$ –Me, 70, 100, 100%), and 507, 505, and 503 (7, 10, 10).

*1-(2-Ethoxycarbonyl-3,5-dimethoxyphenyl)propan-2-one* (**18**; R = Et).—A solution of the anion (**10**; R = Et) (0.25 mmol) at  $-78$  °C was transferred *via* a double-ended needle to a flask containing freshly distilled acetyl chloride (0.5 ml) at  $-78$  °C under argon. The resulting solution was warmed to room temperature, water (10 ml) was added, and the mixture extracted with diethyl ether (3 × 50 ml). The extracts were dried over  $MgSO_4$  and evaporated to dryness under reduced pressure to give a yellow oil, which was purified by p.l.c. (diethyl ether–hexane, 2:1,  $R_F$  0.3) to give the ketone **18** (33 mg, 50%) as a colourless oil, pure by t.l.c. and n.m.r. (Found:  $M^+$ , 266.1176. Calc. for  $C_{14}H_{18}O_5$ :  $M$ , 266.1154);  $\nu_{\max}$ . ( $CHCl_3$ ) 1 705br, 1 600, and 1 580  $cm^{-1}$ ;  $\lambda_{\max}$ . 318 and 346 nm;  $\delta_H$  1.33 (2 H, t,  $J$  7 Hz), 2.14 (3 H, s), 3.68 (2 H, s), 3.80 (3 H, s), 3.81 (3 H, s), 4.32 (2 H, q,  $J$  7 Hz), 6.30 (1 H, d,  $J$  2 Hz), and 6.40 (1 H, d,  $J$  2 Hz);  $m/z$  266 ( $M^+$ , 21%), 224 (32), 221 (34), 179 (100), and 178 (28).

*3,4-Dihydro-6,8-dimethoxy-3-phenyl-1H-2-benzopyran-1-one* (**38**).—To a solution of the anion (**10**; R = Et) (0.5 mmol) at  $-78$  °C was added dropwise freshly distilled benzaldehyde (0.12 ml, 1.2 mmol) in THF (1 ml) and the orange-red colour was discharged within 1 min. The mixture was stirred for a further 4 h at  $-78$  °C and then diluted with ethanol (2 ml) and allowed to warm rapidly to room temperature. After work-up A, a yellow oil was obtained which was purified by p.l.c. [diethyl ether–ethyl acetate–light petroleum (b.p. 60–80 °C), 1:1:4, 2 elutions]. The major band,  $R_F$  0.1, gave a solid 88 mg which was further purified by p.l.c. (diethyl ether–ethyl acetate–toluene, 1:1:3, 4 elutions) to give two main products. The first band,  $R_F$  0.5, gave *3,4-dihydro-6,6',8,8'-tetramethoxy-3-phenylspiro[1H-2-benzopyran-1,3'-(3H-2-benzopyran)]-1'(4'H)-one* (**40**) (24 mg, 21%) as prisms, m.p. 219–221 °C (from acetone– $CH_2Cl_2$ ) (Found: C, 69.9; H, 5.6.  $C_{27}H_{26}O_7$  requires C, 70.12; H, 5.67%);  $\nu_{\max}$ . ( $CHCl_3$ ) 2 840m, 1 710, 1 610, and 1 590  $cm^{-1}$ ;  $\lambda_{\max}$ . 264 and 296 nm;  $\delta_H$  2.90 (1 H, dd,  $J$  3.9 and 15.6 Hz,  $ArCH_AH_BCH$ ), 2.92 (1 H, d,  $J$  16.6 Hz,  $Ar'CH_AH_B$ ), 2.97 (1 H, dd,  $J$  10.7 and 15.6,  $ArCH_AH_BCH$ ), 3.80 (3 H, s), 3.81 (3 H, s), 3.85 (3 H, s), 3.89 (3 H, s), 4.53 (1 H, d,  $J$  16.6 Hz,  $Ar'CH_AH_B$ ), 5.18 (1 H, dd,  $J$  3.9 and 10.7 Hz,  $ArCH_2CH$ ), 6.30 (1 H, d,  $J$  2 Hz), 6.32 (1 H, d,  $J$  2 Hz), 6.37 (1 H, d,  $J$  2 Hz), 6.40 (1 H, d,  $J$  2 Hz), and 7.23 (5 H, m), these assignments were confirmed by decoupling experiments;  $m/z$  462 ( $M^+$ , 5%), 418 (5), 417 (5), and 387 (100). The second product,  $R_F$  0.6, was the expected *dihydrobenzopyrone* (**38**) (26 mg, 18%) as prisms, m.p. 52–54 °C (from ethyl acetate–hexane) (Found:  $M^+$ , 284.1040.  $C_{17}H_{16}O_4$  requires  $M^+$ , 284.1048);  $\nu_{\max}$ . 2 845m, 1 735, 1 605, and 1 585  $cm^{-1}$ ;  $\lambda_{\max}$ . 263 and 297 nm;  $\delta_H$  3.00 (1 H, dd,  $J$  16 and 4 Hz), 3.25

\* Compound (**18**; R = Et) has been characterized as its semi-carbazone.<sup>22</sup>

(1 H, dd,  $J$  16 and 11 Hz), 3.86 (3 H, s), 3.94 (3 H, s), 5.40 (1 H, dd,  $J$  11 and 4 Hz), 6.33 (1 H, d,  $J$  2 Hz), 6.45 (1 H, d,  $J$  2 Hz), and 7.3–7.5 (5 H, m);  $m/z$  284 ( $M^+$ , 15%) and 178 (100).

**3,4-Dihydro-6,8-dimethoxy-3-methyl-1H-2-benzopyran-2-one (39).**—A solution of the anion (**10**; R = Et) (0.5 mmol) was prepared as before but in the side-arm of a flask. It was then added gradually to a solution of acetaldehyde (0.13 ml, 101 mg, 2.3 mmol) in THF (0.5 ml) also at  $-78^\circ\text{C}$  in the main body of the flask. The colour of each portion of the anion solution was discharged rapidly. After addition was complete (10 min) the solution was stirred while warming to room temperature over 2 h, and then ethanol (2 ml) was added. After work-up A a yellow oil was obtained which was purified by p.l.c. (ethyl acetate–toluene, 1 : 1, 2 elutions,  $R_F$  0.4) to give the benzopyrone (**39**) (78 mg, 70%) as prisms, m.p.  $105\text{--}107^\circ\text{C}$  [from ethyl acetate–light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ )] (lit.,<sup>23</sup>  $102\text{--}103.5$  from benzene–light petroleum) (Found:  $M^+$ , 222.0905. Calc. for  $\text{C}_{12}\text{H}_{14}\text{O}_4$ :  $M$ , 222.0892;  $\nu_{\text{max}}$ . 2 840m, 1 735, 1 605, and 1 585  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ . 262 and 295 nm;  $\delta_{\text{H}}$  1.45 (3 H, d,  $J$  6.8 Hz), 2.78 (1 H, dd,  $J$  15.6 and 2.9 Hz), 2.87 (1 H, dd,  $J$  15.6 and 10.7 Hz), 3.85 (3 H, s), 3.91 (3 H, s), 4.50 (1 H, m), 6.29 (1 H, d,  $J$  2 Hz), and 6.39 (1 H, d,  $J$  2 Hz);  $m/z$  222 ( $M^+$ , 95%) and 178 (100).

In another experiment the anion (**10**; R = Et) (0.5 mmol) was prepared in the usual manner and acetaldehyde (0.05 ml, 39 mg, 0.89 mmol) in THF (1 ml) was added dropwise to the solution at  $-78^\circ\text{C}$  (rather than the inverse addition described above) and the mixture became colourless. After the mixture had been stirred for 4 h at  $-78^\circ\text{C}$ , ethanol (2 ml) was added and the mixture was allowed to warm rapidly to room temperature. Work-up and p.l.c. as before afforded two main products. The first,  $R_F$  0.4, was the above benzopyrone (**39**) (35 mg, 32%). The second,  $R_F$  0.5, was obtained as an impure oil which was crystallised to give **3,4-dihydro-6,6',8,8'-tetramethoxy-3-methylspiro(1H-2-benzopyran-1,3'-(3H-2-benzopyran))-1'(4'H)-one (41)** (35 mg, 35%) as prisms, m.p.  $190\text{--}192^\circ\text{C}$  (from acetone) (Found: C, 65.9; H, 5.9.  $\text{C}_{22}\text{H}_{24}\text{O}_7$  requires C, 65.99; H, 6.04%);  $\nu_{\text{max}}$ . ( $\text{CHCl}_3$ ) 2 840m, 1 710, 1 610, and 1 590  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ . 262 and 295 nm;  $\delta_{\text{H}}$  1.15 (3 H, d,  $J$  5.9 Hz), 2.57 (1 H, dd,  $J$  15.6 and 2.9 Hz), 2.64 (1 H, dd,  $J$  15.6 and 10.7 Hz), 2.79 (1 H, d,  $J$  16.6 Hz), 3.76 (3 H, s), 3.79 (3 H, s), 3.85 (3 H, s), 3.94 (3 H, s), 4.24 (1 H, m), 4.48 (1 H, d,  $J$  16.6 Hz), 6.23 (1 H, d,  $J$  2 Hz), 6.30 (1 H, d,  $J$  2 Hz), 6.35 (1 H, d,  $J$  2 Hz), and 6.40 (1 H, d,  $J$  2 Hz);  $m/z$  400 ( $M^+$ , 5%), 356 (10), 355 (10), and 325 (100).

**1-(2,4-Dimethoxy-6-trimethylsilylmethylphenyl)pentan-1-one (26)** and **2-(1-Butylpent-1-enyl)-1,5-dimethoxy-3-trimethylsilylmethylbenzene (32).**—Ethyl 2,4-dimethoxy-6-trimethylsilylmethylbenzoate (**14**; R = Et) (60 mg, 0.2 mmol) was dissolved in dry THF (5 ml) under an atmosphere of argon and cooled to  $-78^\circ\text{C}$ . *n*-Butyl-lithium (0.17M in hexane; 0.26 ml, 0.44 mmol) was injected dropwise and the mixture stirred for 1 h at  $-78^\circ\text{C}$ .  $\text{D}_2\text{O}$  (1 ml) in THF (1 ml) was injected and the stirring continued while the mixture warmed to room temperature. After work-up B, a yellow oil was obtained which was purified by p.l.c. [diethyl ether–light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ ), 1 : 1, 2 elutions] to give three compounds. The first band,  $R_F$  0.6, gave starting material (**11**; R = Et) (4 mg, 7%) containing a negligible amount of deuterium (by n.m.r.). The second band,  $R_F$  0.7, gave the *pentanone* (**26**) (36 mg, 58%) as an oil; n.m.r. data indicated an average of one deuterium per molecule on the methylene next to the ketone, there was little di- or un-deuterated material (Found  $M^+$ , 309.1856.  $\text{C}_{17}\text{H}_{27}\text{DO}_3\text{Si}$  requires  $M$ , 309.1869);  $\nu_{\text{max}}$ . ( $\text{CHCl}_3$ ) 1 685, 1 600, and 1 580  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ . (MeOH) 230 and 274 nm;  $\delta_{\text{H}}$  0.02 (9 H, s), 0.8–1.8 (7 H, m), 2.02 (2 H, s), 2.72 (2 H, t,  $J$  7 Hz), 3.77 (3 H, s), 3.78 (3 H, s), 6.15 (1 H, d,  $J$  2 Hz), and 6.21 (1 H, d,  $J$  2 Hz);  $m/z$  309 ( $M^+$ , 10%), 294 (30), 280 (50), 251 (25), and 73 (100). The third product,  $R_F$  0.8, was the *alkene*

(**32**) (8 mg, 11%) as an oil (Found:  $M^+$ , 348.2488.  $\text{C}_{21}\text{H}_{36}\text{O}_2\text{Si}$  requires  $M$ , 348.2484);  $\nu_{\text{max}}$ . 2 875m, 2 860m, 1 600, and 1 580  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ . (MeOH) 230sh and 275 nm;  $\delta$  0.02 (9 H, s), 0.7–1.7 (12 H, m), 2.02 (2 H, s), 2.0–2.3 (4 H, m), 3.72 (3 H, s), 3.78 (3 H, s), 5.10 (1 H, t,  $J$  7 Hz), and 6.22 (2 H, s);  $m/z$  348 ( $M^+$ , 100%), 333 (85), 319 (5), and 291 (50). The same products were also formed in reactions of the methyl ester (**14**; R = Me) with  $\text{Bu}^n\text{Li}$ .

**1-(2,4-Dimethoxy-6-trimethylsilylmethylphenyl)ethanone (25)** and **1,5-Dimethoxy-2-(1-methylethenyl)-3-trimethylsilylmethylbenzene (31).**—Methyl lithium–lithium bromide (1.4M in diethyl ether) was added dropwise to stirred, dry THF (3 ml) containing one small crystal of triphenylmethane under nitrogen at  $-78^\circ\text{C}$ , until the persistent pink colour indicated complete dryness. A solution of ethyl 2,4-dimethoxy-6-trimethylsilylmethylbenzoate (**14**; R = Et) (60 mg, 0.20 mmol) in THF (1.5 ml) was added dropwise at  $-78^\circ\text{C}$  followed by methyl lithium–lithium bromide (1.4M in diethyl ether; 0.22 ml, 0.31 mmol). The mixture was allowed to warm to  $-40^\circ\text{C}$  over 1.5 h and then more methyl lithium–lithium bromide (1.4M; 0.1 ml, 0.14 mmol) was added; it was then allowed to warm to  $-20^\circ\text{C}$  over a further 30 min when  $\text{D}_2\text{O}$  (1 ml) in THF (1 ml) was added. After work-up A, an oil was obtained, which was purified by p.l.c. [diethyl ether–light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ ), 1 : 1] to give two bands. The first band,  $R_F$  0.5, gave an oil which was further purified by p.l.c. [diethyl ether–light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ ), 1 : 5, 2 elutions] to give:  $R_F$  0.4, starting material (**14**; R = Et) (3 mg, 5%) showing 93% monodeuteration in the aromatic methylene group by n.m.r. and mass spectroscopy; and  $R_F$  0.5, the *ketone* (**25**) (23 mg, 43%) as an oil, pure by t.l.c., containing an average of one deuterium atom per molecule in the methyl group next to the ketone by n.m.r. (Found:  $M^+$ , 268.1487, 267.1409, and 266.1324.  $\text{C}_{14}\text{H}_{22}\text{-D}_n\text{O}_3\text{Si}$  ( $n = 2, 1$ , and 0) requires  $M$ , 268.1495, 267.1416, and 266.1338);  $\nu_{\text{max}}$ . 2 840m, 1 680, 1 600, and 1 580  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ . 228 and 273 nm;  $\delta_{\text{H}}$  0.00 (9 H, s), 2.16 (2 H, s), 2.41 (2 H, t,  $J$  2 Hz,  $\text{CH}_2\text{D}$ ), 3.78 (6 H, s), 6.14 (1 H, d,  $J$  2 Hz), and 6.20 (1 H, d,  $J$  2 Hz);  $m/z$  268 ( $M^+$  + 2, 5%), 267 ( $M^+$  + 1, 15), 266 ( $M^+$ , 5), 254 (10), 253 (30), 252 (100), and 251 (30). The second band,  $R_F$  0.7, from the original p.l.c. yielded the *alkene* (**31**) (3 mg, 6%) as an oil pure by t.l.c. and n.m.r. (Found:  $M^+$ , 264.1559.  $\text{C}_{13}\text{H}_{24}\text{O}_2\text{Si}$  requires  $M$ , 264.1546);  $\nu_{\text{max}}$ . 2 840m, 1 645m, 1 600, and 1 580  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$ . 278 nm;  $\delta_{\text{H}}$  0.02 (9 H, s), 1.96 (3 H, br s), 2.13 (2 H, s), 3.77 (6 H, s), 4.75 (1 H, m), 5.26 (1 H, m), and 6.23 (2 H, s);  $m/z$  264 ( $M^+$ , 20%), 249 (40), 234 (5), 73 (100).

In another experiment the reagents were all mixed at room temperature and stirred for 1 h before work-up and p.l.c. as before to give the *ketone* (**25**) (33 mg, 61%) and *alkene* (**31**) (6 mg, 11%).

**1-(2,4-Dimethoxy-6-trimethylsilylmethylphenyl)-2-methylbutan-1-one (27).**—*s*-Butyl-lithium (1.4M in cyclohexane) was added dropwise to stirred, dry THF (2 ml) containing one small crystal of triphenylmethane under argon at  $-78^\circ\text{C}$ , until after a few drops a persistent pink colour indicated complete dryness. A solution of ethyl 2,4-dimethoxy-6-trimethylsilylmethylbenzoate (**14**; R = Et) (60 mg, 0.20 mmol) in THF (1.5 ml) was added dropwise, followed by *s*-butyl-lithium (1.4M in cyclohexane; 0.57 ml, 0.80 mmol). The mixture was stirred for 0.5 h at  $-78^\circ\text{C}$ , after which water (1 ml) in THF (1 ml) was added, discharging the deep red colour. Stirring was continued while the mixture warmed to room temperature over 1 h. After work-up A the resulting yellow oil was purified by p.l.c. [diethyl ether–light petroleum (b.p.  $60\text{--}80^\circ\text{C}$ ), 1 : 1] to give two bands. The first band,  $R_F$  0.6, gave starting material (**14**; R = Et) (7 mg, 12%) and the second band,  $R_F$  0.7, gave the *ketone* (**27**) (51 mg, 82%) as an oil which was pure by t.l.c. (Found:  $M^+$ , 308.1803.

$C_{17}H_{28}O_3Si$  requires  $M$ , 308.1807;  $\nu_{max}$ . 2 880m, 2 840m, 1 690, 1 600, and 1 580  $cm^{-1}$ ;  $\lambda_{max}$ . 228 and 270 nm;  $\delta_H$  0.03 (9 H, s), 0.89 (3 H, t,  $J$  7 Hz), 1.07 (3 H, d,  $J$  7 Hz), 1.4–1.8 (2 H, m), 1.93 (2 H, s), 2.93 (1 H, m,  $J$  7 Hz), 3.76 (3 H, s), 3.77 (3 H, s), and 6.18 (2 H, ABq,  $J$  2 Hz);  $m/z$  308 ( $M^+$ , 25%), 293 (35), 251 (60), and 73 (100).

In another experiment *s*-butyl-lithium (1.4M in cyclohexane; 0.29 ml, 0.41 mmol) was used and the reaction quenched with  $D_2O$  (1 ml) in THF (1 ml). This produced starting material (14; R = Et) (25 mg, 42%) which, as judged by mass spectroscopy, was 17% monodeuterated and the ketone (27) (35 mg, 56%) in which approximately 50% of the molecules were deuterated. N.m.r. suggested that the deuterium was almost equally distributed in the aromatic methylene and the methine next to the ketone.

1-(2,4-Dimethoxy-6-trimethylsilylmethylphenyl)-2,2-dimethylpropan-1-one (28).—The previous procedure was followed but both additions of *s*-butyl-lithium were replaced by *t*-butyl-lithium (1.5M in *n*-pentane). After the second addition of *t*-butyl-lithium (1.5M; 0.27 ml, 0.41 mmol), the solution was stirred for 0.5 h at  $-78^\circ C$  and then quenched with  $D_2O$  as usual. After work-up A and p.l.c. [diethyl ether–light petroleum (b.p. 60–80  $^\circ C$ ), 1:2], a single band,  $R_F$  0.7, was obtained, which yielded the ketone (28) (60 mg, 96%) as an oil which was pure by t.l.c. and showed 9% monodeuteriation by mass spectroscopy (Found:  $M^+$ , 308.1815.  $C_{17}H_{28}O_3Si$  requires  $M$ , 308.1807;  $\nu_{max}$ . 2 880m, 2 840m, 1 690, 1 605, and 1 585  $cm^{-1}$ ;  $\lambda_{max}$ . 224, 273, and 280sh nm;  $\delta_H$  0.0 (9 H, s), 1.15 (9 H, s), 1.80 (2 H, s), 3.70 (3 H, s), 3.75 (3 H, s), and 6.15 (2 H, br s);  $m/z$  308 ( $M^+$ , 10%), 293 (15) and, 251 (100).

Ethyl 2-Hydroxy-4-methoxy-6-trimethylsilylmethylbenzoate (37).—To a solution of triphenylmethane (197 mg, 0.81 mmol) in dry THF (3 ml) under nitrogen at room temperature was added *n*-butyl-lithium (1.7M in *n*-hexane; 0.46 ml, 0.78 mmol) giving a deep red colour. The mixture was stirred for 1 h, after which ethyl 2,4-dimethoxy-6-trimethylsilylmethylbenzoate (14; R = Et) (60 mg, 0.20 mmol) in dry THF (1.5 ml) was added dropwise; stirring was then continued for 21 h at room temperature. The mixture was diluted with water (1 ml) and after work-up A and p.l.c. [diethyl ether–light petroleum (b.p. 60–80  $^\circ C$ ), 1:4, 2 elutions], two bands were obtained. The first band,  $R_F$  0.65, gave the phenol (37; R = Et) (47 mg, 82%) as an oil, pure by t.l.c. (Found:  $M^+$ , 282.1300.  $C_{14}H_{22}O_4Si$  requires  $M$ , 282.1287;  $\nu_{max}$ . 3 500–2 800, 2 855w, 1 650, 1 615, and 1 570  $cm^{-1}$ ;  $\lambda_{max}$ . 224, 266, and 305 nm;  $\delta_H$   $-0.03$  (9 H, s), 1.42 (3 H, t,  $J$  7 Hz), 2.60 (2 H, s), 3.77 (3 H, s), 4.38 (2 H, q,  $J$  7 Hz), 6.09 (1 H, d,  $J$  2 Hz), 6.24 (1 H, d,  $J$  2 Hz), and 11.37 (1 H, br s);  $m/z$  282 ( $M^+$ , 30%), 267 (75), 239 (100), and 238 (30). The second band,  $R_F$  0.8, gave colourless crystals (183 mg) which appeared by t.l.c. and n.m.r. to be triphenylmethane containing 25% 1,1,1-triphenylethane as before.

Deuteration of the Trimethylsilyl Derivative (14; R = Et or Me).—Lithium di-isopropylamide (0.30 mmol) was prepared as before from di-isopropylamine (0.07 ml, 0.5 mmol) in dry THF (1 ml) under nitrogen and *n*-butyl-lithium (1.7M in hexane; 0.18 ml, 0.30 mmol). The mixture was stirred for 15 min at room temperature after which the solution was cooled to  $-15^\circ C$  and a solution of ethyl 2,4-dimethoxy-6-trimethylsilylmethylbenzoate (14; R = Et) (60 mg, 0.2 mmol) in dry THF (1.5 ml) added dropwise to it giving a deep orange-red colour. After 5 min the solution was cooled to  $-78^\circ C$  and after a further 10 min  $D_2O$  (1 ml) in THF (1 ml) was added dropwise, discharging the colour immediately. After warming to room temperature over 2 h and work-up A, the reaction mixture gave a yellow oil which was purified by p.l.c. [diethyl ether–light petroleum (b.p. 60–80  $^\circ C$ ), 2:1] to give the deuterated starting material (60

mg, 100%). Deuterium incorporation was shown to be 93% by n.m.r. and mass spectroscopy.

Generation of the anion of (14; R = Me) and (14; R = Et) with lithium di-isopropylamide (1.1 equiv.) at  $-78^\circ C$  for 30 min gave starting material with only 55% incorporation of deuterium. Using lithium di-isopropylamide (2.1 equiv.) at  $-78^\circ C$ , the incorporations were 70 and 63%. Thus the higher temperature appears necessary for complete anion formation.

Ethyl 2,4-Dimethoxy-6-(1-trimethylsilylethyl)benzoate (20; R = Et).—Lithium di-isopropylamide (0.44 mmol) was prepared as before under nitrogen in dry THF (1 ml) and cooled to  $-78^\circ C$ . Ethyl 2,4-dimethoxy-6-trimethylsilylmethylbenzoate (14; R = Et) (119 mg, 0.40 mmol) in THF (1.5 ml) was added dropwise and after the mixture had been stirred for 30 min, methyl iodide (0.1 ml, 1.6 mmol) was added discharging the colour immediately. After the mixture had been stirred for 1 h at  $-78^\circ C$  and for 4 h while warming to room temperature, methanol (3 ml) was added to it; it was then stirred overnight at room temperature. After work-up A, a brown oil was obtained which was purified by p.l.c. ( $CH_2Cl_2$ –toluene, 1:1, 6 elutions) giving two bands which were just separated. The first band,  $R_F$  0.7, gave starting material (14; R = Et) (52 mg, 44%). The second band,  $R_F$  0.8, gave the 6-(1-trimethylsilylethyl)benzoate (20; R = Et) (42 mg, 34%) as an oil (Found:  $M^+$ , 310.1608.  $C_{16}H_{26}O_4Si$  requires  $M$ , 310.1601;  $\nu_{max}$ . 2 880w, 2 840w, 1 730, 1 605, and 1 585  $cm^{-1}$ ;  $\lambda_{max}$ . 220sh and 281 nm;  $\delta_H$   $-0.02$  (9 H, s), 1.31 (3 H, d,  $J$  7 Hz), 1.33 (3 H, t,  $J$  7 Hz), 2.20 (1 H, q,  $J$  7 Hz), 3.72 (6 H, s), 4.33 (2 H, q,  $J$  7 Hz), and 6.23 (2 H, s);  $m/z$  310 ( $M^+$ , 20%), 295 (10), 281 (20), 279 (10), 265 (50), and 192 (100).

The conditions for anion formation in this experiment were later found to be not optimal since quenching with  $D_2O$  gave only 56% incorporation of deuterium (see previous experiment).

Methyl and Ethyl 2-Bis(trimethylsilyl)methyl-4,6-dimethoxybenzoate (17; R = Me or Et).—Lithium di-isopropylamide (0.19 mmol) was prepared as before in THF (1 ml) under nitrogen and cooled to  $-78^\circ C$ . Methyl 2,4-dimethoxy-6-trimethylsilylmethylbenzoate (14; R = Me) (50 mg, 0.18 mmol) was added dropwise and the mixture stirred for 30 min before addition of trimethylchlorosilane (0.3 ml) in dry THF (1 ml). After a further hour at  $-78^\circ C$ , the mixture was allowed to warm slowly to room temperature and then stirred overnight. Extraction as for previous silylation experiments yielded a yellow oil, which was purified by p.l.c. (ethyl acetate–toluene, 1:5) to give two major bands. The first band,  $R_F$  0.6, gave starting material (14; R = Me) (13 mg, 26%). The second band,  $R_F$  0.7, gave the bis(trimethylsilyl) compound (17; R = Me) (44 mg, 70%) as colourless needles, m.p. 71–73  $^\circ C$  (from pentane) (Found: C, 57.4; H, 8.4.  $C_{17}H_{30}O_4Si_2$  requires C, 57.58; H, 8.53%);  $\nu_{max}$ . 2 830m, 1 725, 1 605, and 1 585  $cm^{-1}$ ;  $\lambda_{max}$ . 252sh and 283 nm;  $\delta$  0.04 (18 H, s), 1.57 (1 H, s), 3.76 (6 H, s), 3.83 (3 H, s), and 6.15 (2 H, ABq,  $J$  2 Hz);  $m/z$  354 ( $M^+$ , 58%), 339 (60), and 323 (95).

For the ethyl ester the same procedure was followed using lithium di-isopropylamide (0.43 mmol) and ethyl 2,4-dimethoxy-6-trimethylsilylmethylbenzoate (14; R = Et) (60 mg, 0.20 mmol). The oil obtained was purified by p.l.c. [diethyl ether–light petroleum (b.p. 60–80  $^\circ C$ ), 1:1] to give one major band,  $R_F$  0.5, which yielded the ethyl ester (17; R = Et) (69 mg, 93%) as plates, m.p. 53–55  $^\circ C$  (from aqueous EtOH) (Found: C, 58.6; H, 8.85.  $C_{18}H_{32}O_4Si_2$  requires C, 58.65; H, 8.75%);  $\nu_{max}$ . 2 840m, 1 730, 1 600, and 1 580  $cm^{-1}$ ;  $\lambda_{max}$ . 252sh and 281 nm;  $\delta_H$  0.04 (18 H, s), 1.34 (3 H, t,  $J$  7 Hz), 1.61 (1 H, s), 3.76 (3 H, s), 3.77 (3 H, s), 4.33 (2 H, q,  $J$  7 Hz), 6.13 (1 H, d,  $J$  2 Hz), and 6.18 (1 H, d,  $J$  2 Hz);  $m/z$  368 ( $M^+$ , 95%), 353 (90), 338 (30), 337 (100), and 323 (70).

**Desilylation of (14; R = Et).**—Tetra-*n*-butylammonium fluoride trihydrate (73 mg, 0.23 mmol) was dried *in vacuo* at room temperature over P<sub>2</sub>O<sub>5</sub> for 3 days and then dissolved in dry THF (2 ml) and stirred over 4A molecular sieves (0.2 g) under argon for 3 days at room temperature. Ethyl 2,4-dimethoxy-6-trimethylsilylmethylbenzoate (14; R = Et) (60 mg, 0.20 mmol) in dry THF (1.5 ml) was added dropwise to the solution cooled to  $-78^{\circ}\text{C}$ . The orange-red colour appeared immediately and after the mixture had been stirred for 1 min D<sub>2</sub>O (1 ml) in dry THF (1 ml) was added, discharging the colour immediately. The mixture was stirred while warming to room temperature over 30 min and after work-up A, a yellow oil was obtained which was purified by p.l.c. [diethyl ether–light petroleum (b.p. 60–80 °C), 1:1] to give two bands. The first band,  $R_F$  0.6, gave starting material (14; R = Et) (17 mg, 28%). The second band,  $R_F$  0.5, gave ethyl 2,4-dimethoxy-6-methylbenzoate (11; R = Et) (18 mg, 40%) as an oil which was not purified further. Mass spectroscopy indicated 22% deuterium incorporation and n.m.r. showed that the deuterium was in the aromatic methyl group. The above conditions gave the highest deuterium incorporation into (11; R = Et). Other conditions tried gave greater yields of product (70–75%) but the deuterium incorporation was, as judged by mass spectroscopy, 5% or less.

**Destannylation of (15; R = Et).**—To dry THF (3 ml) under argon containing triphenylmethane (one crystal) was added methyl-lithium–lithium bromide (1.4M in diethyl ether) until a persistent pink colour indicating complete dryness appeared. The solution was cooled to  $-78^{\circ}\text{C}$ , ethyl 2,4-dimethoxy-6-trimethylstannylmethylbenzoate (15; R = Et) (98 mg, 0.25 mmol) in dry THF (1 ml) was added followed by further methyl-lithium–lithium bromide (1.4M in diethyl ether; 0.24 ml, 0.34 mmol), giving the orange-red colour of the anion (10; R = Et). After the mixture had been stirred for 10 min D<sub>2</sub>O (1 ml) in THF (1 ml) was added and the whole allowed to warm rapidly to room temperature. After work-up A, an oil was obtained which was purified by p.l.c. [diethyl ether–light petroleum (b.p. 60–80 °C), 1:1] to give ethyl 2,4-dimethoxy-6-methylbenzoate (48 mg, 84%) as an oil which was not purified further. N.m.r. and mass spectroscopy indicated 98% monodeuteriation on the aromatic methyl group. A similar experiment using *n*-butyl-lithium (1.7M in hexane; 0.19 ml, 0.32 mmol) instead of the methyl-lithium, with the trimethylstannyl compound (15; R = Et) (82 mg, 0.21 mmol) gave the same product (11; R = Et) (35 mg, 73%), which was 97% monodeuteriated.

**3,4-Dihydro-6,8-dimethoxy-3-methyl-1H-2-benzopyran-1-one (39) from the Trimethylstannyl Derivative (15; R = Et).**—The anion (10; R = Et) was prepared as described above from ethyl 2,4-dimethoxy-6-trimethylstannylmethylbenzoate (15; R = Et) (88 mg, 0.23 mmol) and *n*-butyl-lithium (1.7M in hexane; 0.21 ml, 0.36 mmol) in the side-arm of a flask, at  $-78^{\circ}\text{C}$  under argon. After 10 min the anion solution was added gradually over a further 10 min to a solution of acetaldehyde (0.07 ml, 54 mg, 1.2 mmol) in THF (0.5 ml) contained in the main body of the flask. The mixture was then stirred while warming to room temperature over 2 h and ethanol (2 ml) was added. After work-up A, an oil was obtained, which was purified by p.l.c. (ethyl acetate–toluene, 1:1, 2 elutions,  $R_F$  0.4) to give the benzopyrone (39) (40 mg, 79%) as prisms.

**10-Hydroxy-7,9-dimethoxy-3-methyl-1H-naphtho[2,3-*c*]pyran-1-one (43).**—Into a solution of 2-methoxycarbonyl-3,5-dimethoxybenzyl-lithium (1 mmol) and an excess of lithium diisopropylamide (1 mmol) in THF at  $-78^{\circ}\text{C}$  was injected dropwise a solution of 4-methoxy-6-methyl-2H-pyran-2-one

(152 mg, 1.05 mmol) in THF (1 ml). The colour faded to an orange-yellow as the last drops were added. The solution was stirred for a further 30 min at  $-78^{\circ}\text{C}$  and then allowed to warm to room temperature when it was stirred for 15 min. Concentrated HCl (1 ml) was added and after a further 15 min water was added and the mixture extracted with CH<sub>2</sub>Cl<sub>2</sub>. The extracts were dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated to dryness under reduced pressure. The residue was dissolved as far as possible in hot MeOH (4 ml) and left at 0–5 °C overnight. The naphthopyrone was filtered off and further product could be obtained, by chromatography of the mother liquors, as pale yellow needles (60 mg, 21%), m.p. 209 °C (from MeOH) (Found: C, 67.25; H, 5.1 C<sub>16</sub>H<sub>14</sub>O<sub>5</sub> requires C, 67.13; H, 4.93%);  $\nu_{\text{max}}$  (CHCl<sub>3</sub>) 1 680, 1 625, and 1 580 cm<sup>-1</sup>;  $\lambda_{\text{max}}$  (EtOH) 245 ( $\epsilon$  26 000), 257 (36 000), 266 (56 000), 275 (60 000), 290 (29 000), and 365 (7 300);  $m/z$  286 ( $M^+$ );  $\delta_{\text{H}}$  2.27 (3 H, s), 3.94 (3 H, s), 4.02 (3 H, s), 6.20 (1 H, br s), 6.45 (1 H, d,  $J$  2 Hz), 6.61 (1 H, d,  $J$  2 Hz), 6.91 (1 H, s), and 12.9 (1 H, s);  $\delta_{\text{C}}$  (CDCl<sub>3</sub>) 167.9 (C-7), 163.8 (C-9), 161.9 (C-1), 160.7 (C-10), 152.6 (C-3), 142.5 (C-4a), 132.8 (C-5a), 111.6 (C-6), 110.2 (C-10a), 104.5 (C-4), 99.1 (C-9a), 98.8 and 98.2 (C-5 and C-8), 56.3 (OMe), 55.6 (OMe), and 19.4 (CH<sub>3</sub>). This compound gave a positive Gibb's test.<sup>24</sup>

**Naphthopyrone (43) from the Trimethylstannyl Compound (15).**—The anion (10; R = Et) was prepared as described previously from ethyl 2,4-dimethoxy-6-trimethylstannylmethylbenzoate (15; R = Et) (194 mg, 0.5 mmol) using Bu<sup>n</sup>Li (1.7M in hexane; 0.44 ml, 0.75 mmol). After 15 min at  $-78^{\circ}\text{C}$ , 4-methoxy-6-methyl-2H-pyran-2-one (42) (70 mg, 0.5 mmol) in dry THF (1.5 ml) was added dropwise. After 3 h at  $-78^{\circ}\text{C}$ , the mixture was allowed to warm to room temperature over 2 h, stirred overnight, and then poured into water (15 ml) and adjusted to pH 3 with concentrated HCl. The mixture was extracted with ethyl acetate (4 × 10 ml) and the organic layers washed with brine (10 ml), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated to dryness under reduced pressure to give a red oil, which was purified by p.l.c. [ethyl acetate–light petroleum (b.p. 60–80 °C) 1:2, 2 elutions and 1:1, 1 elution]. A broad blue fluorescent band,  $R_F$  0.3–0.4, gave the naphthopyrone (43) (54 mg, 38%) as yellow needles, m.p. 208–210 °C (from aqueous MeOH).

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