Organic Synthesis with α-Chloro Sulphides. Preparation of Aromatic γ-Lactones from Phenols and α-Chloro Sulphide Carboxylates

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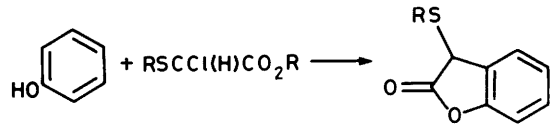
Lewis acid-catalysed alkylation of *para*-substituted phenols using α-chloro sulphides as electrophiles yields sulphenylated γ-lactones which can be desulphurised with zinc in acetic acid or Raney nickel. This synthesis has been applied to *p*-cresol, 2-naphthol, and two phenolic dihydrocinnamates. Alkylation of 1,4-dimethoxybenzene yields homogentisic acid dimethyl ether after desulphurisation and hydrolysis.

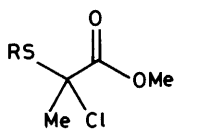
In connection with work directed towards the synthesis of perhydroazulenic lactones[1] we required a method of attaching a γ-lactone ring to phenols.[2] We chose to examine the alkylation of phenols using α-chloroacetates as electrophiles, expecting to obtain *o*-hydroxyphenylacetates which could then be condensed into γ-lactones (Scheme). However, α-halogenated



Scheme.

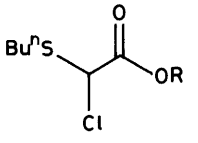
acetates, unless strongly activated, are not good electrophiles for aromatic alkylation. A convenient way of activating such systems is to attach an alkylthio or arylthio group at the position geminal to the halogen atom, and thereby benefit from the ease with which the sulphur atom promotes ionisation of the C–halogen bond. As a result, α-chloro sulphides are very efficient electrophiles in aromatic alkylation.[3] Several groups have used α-chloro sulphide carboxylates in this way with substrates such as benzene,[4] isobutylbenzene,[5] 2-methoxynaphthalene,[5] phenol,[5] and thiophene,[5] reaction requiring a mild Lewis acid catalyst. Aromatic alkylation with ketonic α-chlorosulphides has also been demonstrated[6] and Lee and his co-workers[7] have recently applied this variation to the synthesis of benzofurans from phenols. Depending on the precise structure of the chloro-sulphide, phenol forms largely or exclusively the product of alkylation at the *para*-position. In the substrates that we wished to alkylate the *para*-position was already substituted and *ortho*-substitution was therefore assured. Two general types of electrophile were employed: the tertiary system (**1**) with the sulphur atom bearing either a phenyl group (**1a**) or an n-butyl group (**1b**) and the secondary system (**2**) in which only the n-butylthio group was used in the form of the methyl (**2a**) and ethyl (**2b**) esters. All the chlorosulphides were prepared by chlorination of the appropriate sulphide using *N*-chlorosuccinimide in carbon tetrachloride and the procedure of Arai *et al.*[5] (see Experimental section).

The first lactone required was that derived from the *p*-hydroxy dihydrocinnamic acid (**3a**). Treatment of (**3a**) with methyl α-chloro-α-(phenylthio)propanoate (**1a**) in a mixture of nitromethane and dichloromethane with tin(IV) chloride catalysis afforded a separable mixture of the sought after lactone (**4**), the bis-sulphenylated ester (**5**) [a known decomposition product of chlorosulphide (**1a**)], and a dimeric product tentatively identified as (**6**). Fleming and Iqbal[8] recorded products similar to (**6**) in their investigation of phenylthioalkylation of phenols. Standard flash chromatography of the product



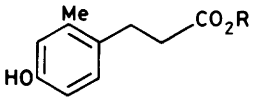
(**1**)

a; R = Ph
b; R = Bu^n



(**2**)

a; R = Me
b; R = Et

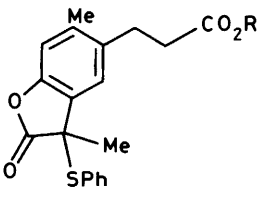


(**3**)

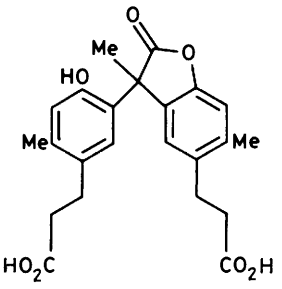
a; R = H
b; R = Me

$(PhS)_2C(Me)CO_2Me$

(**5**)



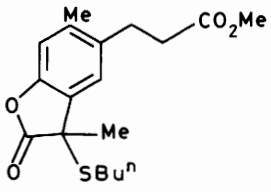
(**4**) R = H



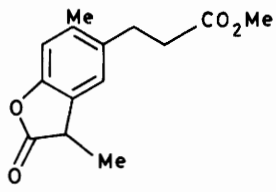
(**6**)

mixture furnished the (phenylthio)lactone (**4**) in pure form in 26% yield, m.p. 140–141 °C, readily identified from its NMR and IR spectra. The efficiency of the synthesis could be improved as follows. First, replacing the phenylthio group by the butylthio group usually imparts greater electrophilicity to a chloro sulphide, suggesting that (**1b**) might be a more appropriate choice of reactant than (**1a**). Secondly, to remove possible interference by the carboxylic acid function, substrate (**3**) was used in the form of the methyl ester (**3b**). Thirdly, anhydrous zinc chloride was found to be the catalyst of choice in the dihydrocinnamate series. Thus treatment of (**3b**) with the α-chloro-(butylthio)propionate (**1b**) afforded the sulphenylated lactone (**7**) in 70% yield. Desulphurisation of (**7**) was readily brought about with zinc in acetic acid to furnish lactone (**8**) in excellent yield. Raney nickel desulphurisation of (**4**) had been tried and abandoned when we discovered that, although the product was sulphur-free, it had retained the phenyl substituent at the α-position.

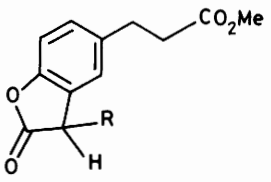
The butylthio group is sufficiently activating to permit the alkylation of phenols with sulphenylated electrophiles derived



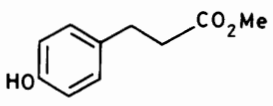
(7)



(8)

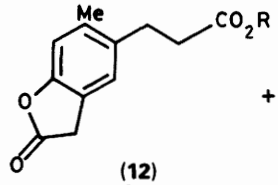


(10) R = SBu^n
(11) R = H



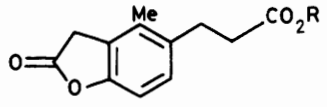
(9)

from secondary chloro sulphides such as α-chloroacetates. For example, treatment of methyl *p*-hydroxydihydrocinnamate (**9**) with methyl α-chloro-α-(butylthio)acetate (**2a**) in the presence of zinc chloride afforded lactone (**10**) which on desulphurisation afforded lactone (**11**), m.p. 67–68 °C, in 58% yield over the two stages. However, in terms of regioselectivity of alkylation of unsymmetrical phenols the secondary chloro sulphide was much less discriminating than the tertiary system (**1b**). This fact

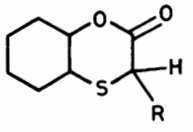


(12)
a; R = Me
b; R = H

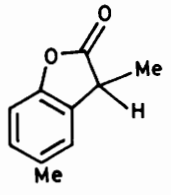
+



(13)
a; R = Me
b; R = H



(14)
a; R = H
b; R = Cl



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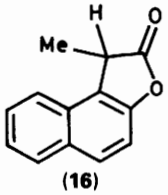
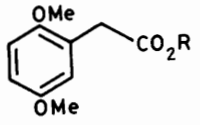


(16)



(17)
a; R = Et
b; R = H

emerged when we attempted to prepare lactone (**12**). Whereas phenolic dihydrocinnamate (**3b**) gave a single alkylated product (**7**) with chloro sulphide (**1b**), a similar reaction with chloro sulphide (**2a**) gave, after desulphurisation, a 40:60 mixture of lactones (**12a**) and (**13a**) in 35% yield. Saponification of the mixture produced lactone acids (**12b**) and (**13b**) from which the preponderant isomer (**13b**) could be isolated by fractional crystallisation. Attempts to modify the regiochemistry of alkylation of (**3b**) with secondary chloro sulphides containing different alkylthio groups, *e.g.* t-butylthio, were unsuccessful. However, when we used the bicyclic chloro sulphide lactone[9] (**14b**) as the electrophile for alkylation of (**3b**) a noticeable change in the regiochemistry was observed with a 90:10 preference (after desulphurisation) for isomer (**13b**).

Three final examples illustrate the application of this aromatic alkylation to two simple phenols and 1,4-dimethoxybenzene. *p*-Cresol and 2-naphthol underwent smooth lactonisation with chloro sulphide (**1a**) in the presence of zinc chloride producing, after desulphurisation, lactones (**15**)[10] (72%) and (**16**)[11] (65%), respectively. Alkylation of 1,4-dimethoxybenzene with the secondary chloro sulphide (**2b**) was best conducted with tin(IV) chloride catalysis to afford, after desulphurisation with Raney nickel in this instance, ester (**17a**) in 79% yield. Hydrolysis of (**17a**) furnished homogentisic acid dimethyl ether (**17b**)[12] in 99% yield.

Experimental

M.p.s were determined on a Thomas Hoover apparatus and are uncorrected. ^1H NMR spectra were recorded at 60 MHz on an Hitachi Perkin-Elmer R-20A spectrometer and ^{13}C spectra at 15 MHz on a Jeol FX60 spectrometer. Elemental analyses were performed by the Microanalysis Laboratory, University College, Cork. Merck PF_{254} silica gel was used for chromatography. Magnesium sulphate was employed as the drying agent.

Methyl 2-(*Phenylthio*)*acetate*.—Esterification of commercially available (phenylthio)acetic acid in methanol with sulphuric acid catalysis yielded the liquid *title ester*, b.p. 68 °C at 0.03 mmHg (Found: C, 59.7; H, 5.9. $C_9H_{10}O_2S$ requires C, 59.3; H, 5.5%); $\delta_H(CDCl_3)$ 3.56 (3 H, s, Me), 3.62 (2 H, s, CH_2), and 7.24 (5 H, m, ArH).

Methyl 2-(*Phenylthio*)*propanoate*.—Benzenethiol (3.6 g) was added to a solution of sodium (1.5 g) in ethanol (100 ml). After 20 min. 2-bromopropionic acid (4.0 g) was added dropwise with stirring during 20 min. After a further 2 h the solvent was removed under reduced pressure and the residue was dissolved in water. Following acidification with conc. hydrochloric acid the mixture was extracted with dichloromethane (3 × 25 ml). The combined extracts were washed with brine, dried, and concentrated. The residue was taken up in methanol (75 ml), conc. sulphuric acid (0.75 ml) was added, and the solution heated under reflux for 48 h. The solvent was removed under reduced pressure and the residue was taken up in dichloromethane. Sodium carbonate was added and the mixture was stirred for 1.5 h, after which it was filtered and concentrated to give the liquid ester (86%), which was sufficiently pure for chlorination in the next stage.

Preparation of Chloro Sulphides (**1a**), (**1b**), *and* (**2a**).—The foregoing sulphide esters in carbon tetrachloride (4 ml per gram of substrate used) at room temperature were each treated with *N*-chlorosuccinimide (1.05 mol equiv.) according to the procedure of Arai *et al.*[5] The *N*-chlorosuccinimide was added in portions with stirring under nitrogen during 3–12 h. When reaction was complete the mixture was cooled to 0 °C and filtered to remove the by-product succinimide. The solid was rinsed with a little cold carbon tetrachloride (3 ml per gram of substrate), and the resulting solution of the chlorosulphide was stored in a freezer. The solution was used on a 'by-weight' basis as the reagent in the phenol alkylations. Yields were quantitative. Bearing in mind the sensitive nature of these chloro sulphides it was found expedient to check their quality by

^{1}H NMR spectroscopy prior to their use. The following chloro sulphides were thus prepared as carbon tetrachloride solutions. Chloro sulphide (**2b**) was already available.

Methyl 2-chloro-2-(phenylthio)propanoate (**1a**). Methyl 2-(phenylthio)propanoate furnished chloro sulphide (**1a**); $\delta_H(CCl_4)$ 1.93 (3 H, s, Me), 3.60 (3 H, s, OMe), and 7.40 (5 H, m, ArH).

Methyl 2-chloro-2-(butylthio)propanoate (**1b**). Methyl 2-(butylthio)propanoate furnished chloro sulphide (**1b**); $\delta_H(CCl_4)$ 1.00 (3 H, m, Me), 1.53 (4 H, m, CH_2CH_2), 1.99 (3 H, s, Me), 2.88 (2 H, t, SCH_2), and 3.76 (3 H, s, OMe).

Methyl 2-chloro-2-(butylthio)acetate (**2a**). Methyl 2-(butylthio)acetate furnished chloro sulphide (**2a**); $\delta_H(CCl_4)$ 1.00 (3 H, m, Me), 1.57 (4 H, m, CH_2CH_2), 2.78 (2 H, t, SCH_2), 3.80 (3 H, s, OMe), and 5.30 (1 H, s, CHCl).

3-(4-*Hydroxy*-2-*methylphenyl*)*propanoic Acid* (**3a**).—2-Methyl-4-methoxycinnamic acid[13] was hydrogenated in ethanol over Adam's catalyst at 40 psi. The crude product was demethylated as follows. A sample (1.0 g) was dissolved in dichloromethane (15 ml) and cooled to 0 °C. A solution of boron tribromide (1.59 ml, 3 equiv.) in dichloromethane (4.8 ml) was added dropwise with stirring under nitrogen during 30 min. The resulting red solution was stirred for a further 45 min at 0 °C before being poured into ice–water (100 ml). The mixture was diluted with acetone (10 ml) and the dichloromethane layer and dichloromethane extracts of the aqueous layer (3 × 30 ml) were combined and dried. Removal of the solvent under reduced pressure afforded the *acid* (**3**), (0.89 g, 96%), m.p. 98.5–99.5 °C (from chloroform) (Found: C, 66.7; H, 6.8. $C_{10}H_{12}O_3$ requires C, 66.7; H, 6.7%); $\delta_H(CDCl_3$–$CD_3COCD_3)$ 2.21 (3 H, s, Me), 2.40–3.00 (4 H, m, CH_2CH_2), 6.50–7.10 (3 H, m, ArH), and 8.53br (2 H, s, OH, CO_2H).

Methyl 3-(4-*Hydroxy*-2-*methylphenyl*)*propanoate* (**3b**).—The acid (**3a**) was treated with hot methanol containing a catalytic amount of conc. sulphuric acid for 13 h to afford the liquid ester (**3b**) of sufficient purity for use directly in the aromatic alkylation reactions described below; $\delta_H(CDCl_3)$ 2.27 (3 H, s, Me), 2.40–3.10 (4 H, m, CH_2CH_2), 3.62 (3 H, s, OMe), and 6.50–7.20 (3 H, m, ArH).

Lactone (**4**) [2,3-*Dihydro*-3,6-*dimethyl*-2-*oxo*-3-(*phenylthio*)*benzofuran*-5-*propanoic Acid*].—A solution of chloro sulphide (**1a**) (0.54 g, 2.34 mmol) in carbon tetrachloride was prepared as described above and the solvent was removed immediately before use and replaced by dichloromethane (10 ml). The solution was then added dropwise with stirring under nitrogen to a mixture of the acid (**3a**) (0.20 g, 1.11 mmol), and anhydrous zinc chloride (0.32 g, 2.35 mmol) in dichloromethane (10 ml) at room temperature. After 3 h the mixture was poured into water and the dichloromethane layer and dichloromethane extracts of the aqueous layer were combined, washed with water, and dried. Removal of the solvent followed by flash chromatography of the residue using ethyl acetate as the eluant afforded the *lactone* (**4**) as a crystalline solid (99 mg, 26%), m.p. 140–141 °C (Found: C, 66.8; H, 5.55. $C_{19}H_{18}O_4S$ requires C, 66.7; H, 5.3%); ν_{max}(KBr) 1 800 and 1 703 cm^{-1}; $\delta_H(CDCl_3)$ 1.76 (3 H, s, Me), 2.28 (3 H, s, Me), 2.50–3.10 (4 H, m, CH_2CH_2), 6.69 (1 H, s, ArH), 7.14 (1 H, s, ArH), and 7.25 (5 H, s, ArH); $\delta_C(CDCl_3)$ 19.69, 22.16, 27.61, 34.44, 53.15, 112.15, 124.03, 126.96, 128.71, 129.30, 129.95, 134.56, 136.51, 138.14, 150.74, 176.92, and 178.93. Further elution of the column furnished the double addition product (**6**) (132 mg) as an amorphous solid; ν_{max}(KBr) 3 300br, 1 770, and 1 700 cm^{-1}; $\delta_H(CD_3COCD_3)$, 1.74 (3 H, s, Me), 2.20 (3 H, s, Me), 2.30 (3 H, s, Me), 2.40–3.00 (8 H, m, 2 × CH_2CH_2), 6.57 (1 H, s, ArH), 6.80 (1 H, s, ArH), 6.90 (1 H, s, ArH), 7.35 (1 H, s, ArH), and 8.50br (3 H, s, OH); $\delta_C(CD_3COCD_3)$ 18.91, 19.56, 24.50, 28.52, 29.82, 34.96, 35.28, 48.54, 112.08, 117.93, 123.84, 125.33, 128.32, 130.73, 132.68, 135.34, 137.36, 136.77, 152.69, 153.54, 174.39, 174.65, and 180.49.

Lactone (**7**) [*Methyl* 3-(*Butylthio*)-2,3-*dihydro*-3,6-*dimethyl*-2-*oxobenzofuran*-5-*propanoate*].—A solution of chloro sulphide (**1b**) (4.8 g, 0.023 mol) in carbon tetrachloride (20 ml) was added dropwise during 50 min to a stirred mixture of (**3b**) (4.0 g, 21 mmol) and zinc chloride (3.7 g, 0.027 mol) in nitromethane (7 ml) and dichloromethane (20 ml) under nitrogen. After 2 h the mixture was poured into ice–water (30 ml), and after stirring for 30 min the organic layer and dichloromethane extracts of the aqueous layer (3 × 15 ml) were combined, washed with saturated aqueous sodium hydrogen carbonate, and dried. Removal of the solvent left a viscous oil (6.71 g). Flash chromatography afforded the *lactone* (**7**) as a colourless liquid (4.85 g, 70% yield), b.p. 230 °C at 0.01 mmHg (Found: C, 64.7; H, 7.3; S, 9.5. $C_{18}H_{24}O_4S$ requires C, 64.3; H, 7.1; S, 9.5%); ν_{max}(film) 2 950, 1 805, and 1 735 cm^{-1}; $\delta_H(CDCl_3)$ 0.79 (3 H, t, Me), 1.36 (4 H, m, CH_2CH_2), 1.71 (3 H, s, Me), 2.33 (3 H, s, Me), 2.43 (2 H, m, CH_2), 2.56 (2 H, t, CH_2), 2.92 (2 H, t, CH_2), 3.66 (3 H, s, Me), 6.89 (1 H, s, ArH), and 7.07 (1 H, s, ArH).

Lactone (**8**) (*Methyl* 2,3-*Dihydro*-3,6-*dimethyl*-2-*oxobenzofuran*-5-*propanoate*).—Freshly activated zinc powder (5 g) was added to a solution of (**7**) (2.3 g, 7.0 mmol) in glacial acetic acid (50 ml), and the mixture was heated under reflux with stirring for 12 h. The cooled mixture was filtered and the solids were washed thoroughly with dichloromethane. The solvents were removed under reduced pressure and a solution of the residue in dichloromethane (50 ml) was washed with saturated aqueous sodium hydrogen carbonate (2 × 20 ml) and dried. Removal of the solvent afforded the *lactone* (**8**) as a white crystalline solid (1.67 g, 98%), m.p. 86–88 °C (from ether–hexane) (Found: C, 67.3; H, 6.1. $C_{14}H_{16}O_4$ requires C, 67.7; H, 6.45%); ν_{max}(melt) 1 805 and 1 735 cm^{-1}; $\delta_H(CDCl_3)$ 1.53 (3 H, d, Me), 2.33 (3 H, s, Me), 2.56 (2 H, t, CH_2), 2.93 (2 H, t, CH_2), 3.66 (1 H, q, CH), 3.67 (3 H, s, Me), 6.90 (1 H, s, ArH), and 7.02 (1 H, s, ArH).

Lactone (**11**) (*Methyl* 2,3-*Dihydro*-2-*oxobenzofuran*-5-*propanoate*).—A solution of (**2a**) (3.27 g, 0.017 mol) in carbon tetrachloride (20 ml) was added dropwise over 45 min to a mixture of (**9**) (3.0 g, 0.017 mol) and zinc chloride (2.27 g, 0.017 mol) in nitromethane (10 ml) and dichloromethane (10 ml) with stirring under nitrogen. After 2 h the mixture was processed as just described for the preparation of (**7**) to afford (**10**) as an oil; ν_{max}(film) 1 810 and 1 735 cm^{-1}; $\delta_H(CDCl_3)$ 0.95 (3 H, s, Me), 1.50 (4 H, m, CH_2CH_2), 2.50–3.20 (6 H, m, CH_2, CH_2CH_2), 3.67 (3 H, s, Me), 4.57 (1 H, s, CH), and 6.90–7.40 (3 H, m, ArH); $\delta_C(CDCl_3)$ 13.51 (q), 21.83 (t), 30.08 (t), 30.54 (t), 30.86 (t), 35.73 (t), 42.62 (d), 51.65 (q), 110.72 (d), 124.88 (s), 125.14 (d), 129.82 (d), 137.22 (s), 152.04 (s), 172.96 (s), and 174.84 (s). The crude product was dissolved in glacial acetic acid (50 ml), activated zinc (10 g) was added, and the mixture was heated under reflux for 12 h. The cooled mixture was worked up as described for the preparation of (**8**) to afford the *lactone* (**11**) after purification by chromatography (dichloromethane) (2.13 g, 58%), m.p. 67–68 °C (from ether) (Found: C, 65.7; H, 5.5. $C_{12}H_{12}O_4$ requires C, 65.5; H, 5.5%); ν_{max}(film) 1 810 and 1 735 cm^{-1}; $\delta_H(CDCl_3)$ 2.50–3.10 (4 H, m, CH_2CH_2), 3.65 (5 H, m, Me and CH_2), and 7.14 (3 H, m, ArH); $\delta_C(CDCl_3)$ 30.47 (t), 33.01 (t), 35.80 (t), 51.65 (q), 110.58 (d), 123.32 (s), 124.68 (d), 128.71 (d), 136.57 (s), 153.21 (s), 173.09 (s), and 175.25 (s).

Methyl 2,3-*Dihydro*-4-*methyl*-2-*oxobenzofuran*-5-*propanoate* (**13a**) *and Methyl* 2,3-*Dihydro*-6-*methyl*-2-*oxobenzofuran*-5-*propanoate* (**12a**).—A solution of (**2b**) (11.93 g, 0.056 mol) in

carbon tetrachloride (60 ml) was added dropwise over 1 h to a stirred mixture of the ester (**3b**) (10.0 g, 0.051 mol) and zinc chloride (10.53 g, 0.077 mol) in nitromethane (40 ml) and dichloromethane (40 ml) under nitrogen. After 1 h the mixture was processed as just described for the preparation of (**7**) to afford the crude product which was treated with zinc (40 g) in glacial acetic acid for 16 h under reflux. The cooled mixture was worked up as described for the preparation of (**8**) to afford a solid mixture of (**12a**) and (**13a**) (3.58 g, 30%) after purification by chromatography (dichloromethane–hexane), m.p. 55–70 °C (Found: C, 66.7; H, 5.9. Calc. $C_{13}H_{14}O_4$; C, 66.65; H, 6.0%); the NMR spectrum indicated that the ratio of (**13a**) to (**12a**) was 60:40.

Hydrolysis of Ester Mixture (**12a**) *and* (**13a**).—The lactone ester mixture (8.0 g, 0.034 mol) and sodium hydroxide (6.94 g, 0.174 mol) in water (200 ml) were heated under reflux with stirring under nitrogen for 1 min and stirring was continued at room temperature for 20 h. The aqueous solution was washed with ether (2 × 40 ml) and then cautiously acidified with conc. hydrochloric acid. The product was extracted into ether (3 × 60 ml), and the combined extracts were washed with brine, dried, and evaporated under reduced pressure to afford the crude hydroxy diacids which were re-lactonised as follows. The product was dissolved in dichloromethane (150 ml), and ether (20 ml) and toluene-*p*-sulphonic acid (0.10 g) were added. The solution was heated under reflux with stirring under nitrogen for 22 h, then was cooled, washed with water (2 × 100 ml) and brine (200 ml), and dried. Removal of the solvent under reduced pressure gave the mixture of the lactone acids (**12b**) and (**13b**) as a yellow solid (7.06 g, 96%); ν_{max}(KBr) 1 801 and 1 705 cm^{-1}. Trituration of the mixture with ether left the major *isomer* (**13b**) (3.2 g) as yellow plates, m.p. 188–191 °C (from methanol) (Found: C, 65.3; H, 5.5. $C_{12}H_{12}O_4$ requires C, 65.4; H, 5.5%); ν_{max}(KBr) 1 800 and 1 704 cm^{-1}, δ_H($CDCl_3$–CD_3SOCD_3) 2.19 (3 H, s, Me), 2.40–3.00 (4 H, m, CH_2CH_2), 3.81 (2 H, s, CH_2), and 6.80–7.30 (2 H, ABq, ArH); δ_C(CD_3SOCD_3), 15.46, 27.42, 32.22, 34.57, 107.27, 123.51, 128.26, 132.61, 134.50, 152.17, 173.67, and 174.32.

Alkylation of (**3b**) *with Chloro Sulphide* (**14b**).—Sulphide (**14a**) was prepared by the literature procedure and chlorinated using *N*-chlorosuccinimide in carbon tetrachloride as described above for chloro sulphides (**1a**), (**1b**), and (**2a**). A solution of chloro sulphide (**14b**) (0.30 g, 1.45 mmol) in dichloromethane was added dropwise with stirring under nitrogen to a solution of ester (**3b**) (0.268 g, 1.38 mmol) and zinc chloride (0.283 g, 2.08 mmol) in nitromethane (2 ml) and dichloromethane (2 ml). After 10 h the reaction was processed as described for (**12a**) and (**13a**), and the crude product was desulphurised with zinc in acetic acid to afford a mixture of (**12a**) and (**13a**) (0.126 g, 39%). By NMR integration the isomer ratio was 90:10 [(**13a**):(**12a**)].

Lactone (**15**) [3,5-*Dimethylbenzofuran*-2(3H)-*one*].—A solution of (**1a**) (2.35 g, 0.010 mol) in carbon tetrachloride (12 ml) was added dropwise over 15 min to a stirred solution of *p*-cresol (1 g, 0.009 mol) and zinc chloride (1.90 g, 0.014 mol) in nitromethane (15 ml) and dichloromethane (10 ml) under nitrogen. After 1 h the reaction mixture was poured onto ice–water (100 ml), and the product was isolated as described for lactone (**7**). The product (2.76 g) was dissolved in glacial acetic acid (70 ml), activated zinc dust (6.7 g) was added, and the mixture was heated under reflux for 8 h. The cooled mixture was worked up as described for the preparation of (**8**) to afford *lactone* (**15**) as a colourless oil (1.08 g, 72%) after purification by chromatography with ethyl acetate–hexane as eluant (Found: C, 73.8; H, 6.1. $C_{10}H_{10}O_2$ requires C, 74.05; H, 6.2%); ν_{max}(film) 1 797 cm^{-1}; δ_H($CDCl_3$) 1.52 (3 H, d, Me), 2.36 (3 H, s, Me), 3.60 (1 H, q, CH), and 6.80–7.20 (3 H, m, ArH); δ_C($CDCl_3$) 15.92 (q), 21.05 (q), 38.46 (d), 110.26 (d), 124.62 (d), 128.71 (s), 129.17 (d), 133.85 (s), 151.52 (s), and 178.35 (s).

Lactone (**16**) [1-*Methylnaphtho*[2,1-*b*]*furan*-2(1H)-*one*].—β-Naphthol (1 g, 0.007 mol) in dichloromethane (15 ml) and nitromethane (10 ml) containing zinc chloride (1.42 g, 0.010 mol) was treated with chloro sulphide (**1a**) (1.76 g, 0.007 mol) in carbon tetrachloride (9 ml) as described for the synthesis of lactone (**15**). The crude product was desulphurised with zinc in acetic acid to afford lactone (**16**) as a crystalline solid (0.89 g, 65%), m.p. 125–127 °C (lit.,[11] 121–124 °C), after purification by chromatography using ethyl acetate–hexane as eluant; ν_{max}(KBr) 1 783 cm^{-1}; δ_H($CDCl_3$), 1.69 (3 H, d, Me), 3.91 (1 H, q, CH), and 7.10–7.90 (6 H, m, ArH); δ_C($CDCl_3$): 16.70 (q), 38.53 (d), 111.50 (d), 121.50 (s), 122.47, 124.68, 127.48, 129.43, 129.82, 130.86 (s), 150.93 (s), and 178.55 (s).

Homogentisic Acid Dimethyl Ether (**17b**) [(2,5-*Dimethoxyphenyl*)*acetic Acid*].—A solution of chloro sulphide (**2b**) (2.4 mmol) in carbon tetrachloride (3 ml) and dichloromethane (4 ml) was added dropwise with stirring over 30 min to a solution of tin(IV) chloride (0.38 mol, 2.4 mmol) and 1,4-dimethoxybenzene (0.3 g, 2.2 mmol) in dichloromethane (3 ml) under nitrogen. After 1 h the mixture was washed with water and dried. Removal of the solvents left an oil which was taken up in ethanol (15 ml) to which was added a suspension of Raney nickel (*ca.* 3 g) in ethanol (15 ml). The mixture was heated under reflux for 4 h, then cooled and the supernatant removed by decantation. The residue was washed thoroughly with dichloromethane. The combined solutions were concentrated under reduced pressure and the residue was purified by chromatography using dichloromethane to afford the ester (**17a**) (0.386 g, 79%). Saponification of the ester using sodium hydroxide in aqueous dioxane afforded acid (**17b**) (0.334 g, 98%) as a crystalline solid, m.p. 124–125 °C (from hexane–dichloromethane) (lit.,[12] 124.5 °C).

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