A New Route to 5-Substituted Resorcinols and Related Systems

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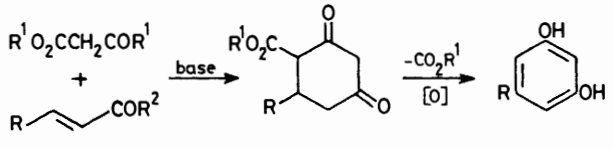
Michael-type additions of phenylsulphinylacetate esters to αβ-unsaturated ketones produce cyclohexane-1,3-dione derivatives, which, after thermal elimination of benzenesulphenic acid, give the corresponding 5-substituted resorcinols, such as olivetol. The scope of this entry into other aromatic systems, such as 3,5-disubstituted and 2,3,5-trisubstituted phenols and orsellinic acid has been explored.

5-SUBSTITUTED resorcinols have recently gained importance as starting materials for the production of benzochroman derivatives, which possess a wide range of physiological properties.[1,2] Most previous routes to 5-substituted resorcinols commence with naturally occurring aromatic precursors such as 3,5-dihydroxy-(or -dimethoxy)-benzoic acid and pyrogallol.[3,4] The classical, total synthesis involves a Michael addition of



R = alkyl, H
R^1 = Me, R^2 = OMe
R^1 = OMe, R^2 = Me

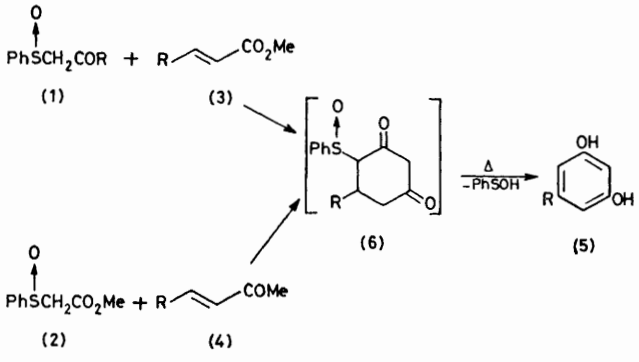
SCHEME 1

acetoacetic ester or malonate to αβ-unsaturated esters or ketones. The resulting cyclohexane-1,3-dione has to be hydrolysed, decarboxylated, and oxidised to the corresponding resorcinol (Scheme 1).[5] The oxidation is usually affected by reagents such as bromine,[5a,d] copper(II) bromide,[5b] or mercury(II) acetate.[5c] Whilst these reactions occasionally proceed in high yield, the conditions could affect sensitive substituents in the 5-position, thus limiting the generality of the method. This handicap and the general scarcity of 5-substituted resorcinols prompted us to develop a new route to these systems.[6] This paper details our results and attempts to define the scope of our route (Scheme 2).

The choice of the phenylsulphinyl substituent was made with regard to the known ease with which it can be thermally eliminated, introducing an olefinic bond into substrates.[7]

Initial attempts with phenylsulphinylacetone (1; R = Me) and methyl cinnamate (3; R = Ph) under a variety of base-catalysed conditions were unsuccessful. Examination of the reaction products revealed unchanged ester, indicating failure of the Michael-addition step. When the more reactive methyl crotonate (3; R = Me) was used in place of cinnamate, traces of orcinol (5; R = Me) were detected in the reaction mixture after prolonged periods of refluxing using an excess of magnesium methoxide as base. These results are in agreement with the few reported instances of Michael addition of β-keto-sulphoxides to αβ-unsaturated esters, where only reaction with acrylic esters was observed;[8-10] in these cases no resorcinol formation was noted. The results also indicated that either a more nucleophilic carbanion was required, or that a more electrophilic substrate was needed to enhance the Michael-type reaction. It was assumed that the carbanion of phenylsulphinylacetate was of relatively low reactivity compared with the ethyl acetoacetate anion used in the classical synthesis. The latter is known to add to αβ-unsaturated esters, including methyl cinnamate.[5a,b]

In order to enhance both the nucleophilicity of the carbanion and the electrophilicity of the substrate the activating groups were reversed. Thus, methyl phenylsulphinylacetate (2) was allowed to react with benzylideneacetone (4; R = Ph), when condensation proceeded smoothly, under the influence of magnesium methoxide, to give the cyclohexanedione intermediate (6; R = Ph)



SCHEME 2

as a mixture of configurational and tautomeric isomers. Magnesium appeared to be the best cation to use since changing to lithium or sodium tended to give lower yields of the intermediates. The thermally unstable cyclohexanediones could be separated from unchanged starting materials and minor side products by taking advantage of their acidity. Thus, extraction into sodium hydrogencarbonate solution, followed by re-acidification and extraction into organic solvents, such as ethyl acetate, gave the purified intermediates. Subsequent thermolysis of the cyclohexanediones in solution at

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temperatures up to 100 °C caused elimination of benzenesulphenic acid and formation of the resorcinol (5; R = Ph) in high yield. The thermolyses were generally carried out in the presence of powdered calcium carbonate to help trap the liberated sulphenic acid. Use of trimethyl phosphite proved less successful and caused complications in the purification of the product.

TABLE 1

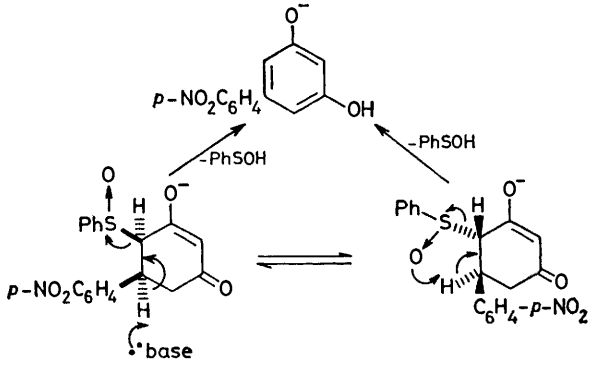
Reaction of methyl phenylsulphinylacetate with αβ-unsaturated ketones (1 mmol scale)

Ketone (4)	Method [e]	Yield (%) [d] (6)	Yield (%) [d] (5)
R = C_6H_5	A	63	43 [a]
R = C_6H_4OMe-*p*	A	70	60 [a]
R = $C_6H_4NO_2$-*p*	A		26 [a]
	B		37 [a]
R = 2-furyl	A	44	*b*
	B		30 [a]
R = n-C_5H_{11}	A	58	48 [a]
R = Pr^i	A	41	30 [c]

[a] Yields of isolated crystalline compounds; reaction yields were not optimised. [b] $P(OMe)_3$ was used in the thermolysis step. [c] Oil. [d] Yields calculated from ^1H n.m.r. data. [e] Method A, $Mg(OMe)_2$–anhydrous MeOH; method B, NaH–THF.

Benzenesulphenic acid was isolated mainly as diphenyl disulphide and phenyl benzenethiosulphinate.

The above reaction sequence was applied to a variety of different substrates (Table 1). The intermediate cyclohexanediones (6) could be detected in all cases except when *p*-nitrobenzylideneacetone was used (entry 3, Table 1). In this case the intermediates are presumably too unstable and elimination of the sulphenic acid occurred during the condensation step. This instability is attributed to the extra lability imparted to the benzylic proton in the 5-position by the *p*-nitro group. The thermal *syn*-elimination of benzenesulphenic acid should become easier because the benzylic carbon would support the negative charge in the developing transition state. Also, under the alkaline conditions

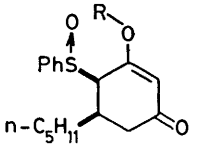


SCHEME 3

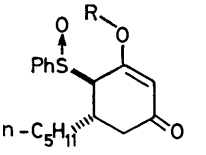
of the condensation step, the base-catalysed *anti*-elimination of benzenesulphinate anion could become important and even the dominant mode (Scheme 3). A related, base-catalysed elimination of methanesulphinate has been reported by Bartlett in a butenolide synthesis.[11]

Of the 5-arylresorcinols prepared the 5-(2-furyl)-resorcinol (5; R = 2-furyl) proved to be particularly labile and rapidly turned brown on exposure to air at room temperature. Also, in this case, use of sodium hydride in tetrahydrofuran gave a higher yield of product than use of magnesium methoxide.

The reaction sequence was also applied to the synthesis of 5-alkyl-substituted resorcinols. Preparation of olivetol (5; R = pentyl) was achieved in overall 48% yield. The required conjugated ketone (4; R = pentyl) was prepared by an efficient phase-transfer catalysed Emmons–Wittig condensation (see Experimental section). In this case the intermediate cyclohexanediones could be separated into two fractions by trituration with ether. The solid residue was shown, by ^1H n.m.r. analysis, to consist mainly of the 4,5-*cis*-isomers whilst the solution afforded a pale yellow oil, mainly comprised of the 4,5-*trans*-isomers, both fractions being predominantly in the enolic form, *i.e.* (7; R = H) and (8; R = H), re-



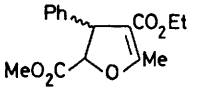
(7)



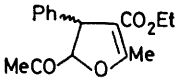
(8)

$CH_3CH{=}C(CO_2Me)_2$

(11)



(14)



(13)

$PhSO_2CH_2CO_2Me$

(15)

spectively. The methylene protons of the side-chain adjacent to the ring in (7; R = H) appeared at δ 1.9, 0.5 p.p.m. downfield from the alkyl envelope. In the *trans*-isomers (8; R = H) the corresponding protons appeared as a shoulder of the main envelope at δ 1.4. This difference is attributed to the deshielding effect of the sulphinyl group.

The observation that (7) was relatively stable at room temperature whilst (8) decomposed to olivetol with a half-life of one week confirms the above assignment. The *trans*-isomers can readily attain the configuration required for the thermal elimination of benzenesulphenic acid. Such a configuration is not possible for the *cis*-isomers. Nevertheless the *cis*-isomers were also converted into olivetol when melted or heated in solution. Since the cyclohexanedione system is itself fairly acidic (the vinyl proton is readily exchanged) it is assumed that the epimerisation to the *trans*-isomer occurs by an acid-catalysed process.

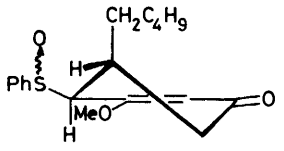
Reaction of the original mixture with diazomethane gave four separable, DL-pairs of diastereoisomeric ethers, suggesting that the enolisation was occurring to only one of the carbonyl groups. The ^1H n.m.r. data for all the

compounds is summarised in Table 2. Appropriate decoupling experiments confirmed the relevance of the assignments. The conformations depicted were postulated on the basis of the observed chemical shifts and coupling constants. Particularly noteworthy is the unusually low chemical shift of H_D in the two *anti*-diastereoisomers and in *syn*-B, readily explained by the 1,3-diaxial relationship of the proton and the phenylsulphinyl group. In *syn*-A the corresponding proton occurs 0.4—0.5 p.p.m. upfield, suggesting that the phenylsulphinyl group is equatorial. This conformation is also corroborated by the slightly lower chemical shift of H_B (characteristic feature of axial protons [12]) and the unusually high position of the methoxy signal (attributable to the shielding effect of the phenylsulphinyl group, now held in the same plane).

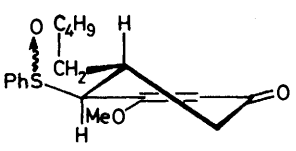
TABLE 2

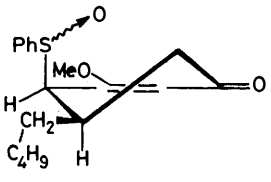
^{1}H N.m.r. chemical shifts (δ) for the methylation products of the cyclohexanediones (6; R = n-C_5H_{11}) [a]

cis-isomers (7) *trans*-isomers (8)

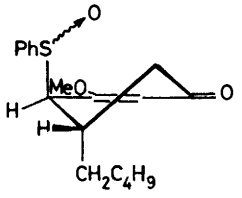


syn-A

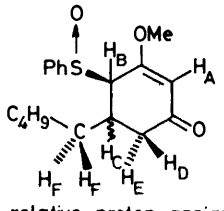




syn-B



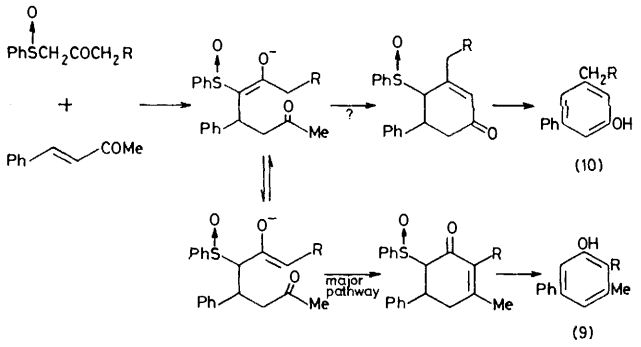
anti-A and B



relative proton assignments

	syn-A	*syn*-B	*anti*-A	*anti*-B
O*Me*	3.22 (s)	3.76 (s)	3.47 (s)	3.77 (s)
H_A	5.60 (s)	5.50 (s)	5.45 (s)	5.45 (s)
H_B	3.48 (bd, *J* 4 Hz)	3.29 (d, *J* 4 Hz)	3.28br (s)	3.24br (s)
H_C	2.68 (m)	2.6—3.2 (complex)	2.74 (m)	2.75 (m)
H_D	2.78 (bd, *J* 13 Hz)		3.13 (dd, *J* 17, 6 Hz)	3.26 (dd, *J* 18,7 Hz)
H_E	2.41 (dd, *J* 13, 2 Hz)	2.42 (bd, *J* 14 Hz)	2.34br (d, *J* 17 Hz)	2.28br (d, *J* 18 Hz)
$2H_F$	1.30— 2.08 (m)	1.80— 2.06 (m)	1.4 (shoulder)	1.4 (shoulder)
Ph	7.5 (s)	7.5 (s)	7.5— 7.7 (m)	7.5— 7.7 (m)

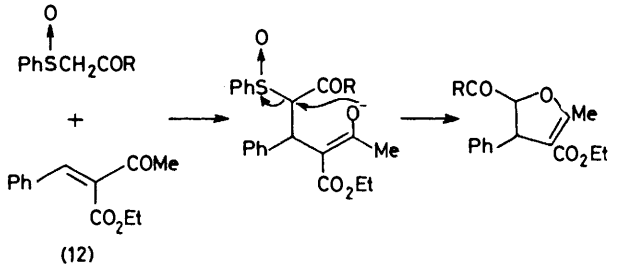
[a] The *syn*-A isomer could be obtained as a single compound; the *syn*-B isomer was always contaminated by small amounts of *anti*-B isomer; methylation of the solid *cis*-cyclohexanediones (7) afforded mainly *syn*-A, and small amounts of *syn*-B contaminated with *anti*-B.



SCHEME 4

Although phenylsulphinylacetone (1) did not react with methyl cinnamate, it did react with benzylideneacetone to give 3-phenyl-5-methylphenol (9; R = H). In this process the intermediate cyclohexanone (Scheme 4) could not be isolated and the direction in which cyclisation occurred could not be directly determined, since symmetry only allows one product [(9; R = H) or (10; R = H)]. The reaction between 1-phenylsulphinylpentan-2-one (1; R = C_3H_7) and benzylideneacetone was therefore studied. The ketone (1; R = n-C_3H_7) was conveniently prepared by alkylation of the dianion of phenylsulphinylacetone [13,14] with ethyl bromide. Only one phenol was detected in the reaction mixture, shown to be 2-ethyl-3-methyl-5-phenylphenol (9; R = Et) (50%); none of the isomer (10; R = Et) could be found. It appears, therefore, that the sulphoxide group helps to direct the cyclisation in a regioselective manner, as indicated in Scheme 4.

Changing the Michael acceptor to the more reactive dimethyl ethylidenemalonate (11) was not wholly successful and only low yields of methyl orsellinate were obtained from complex mixtures of products. The inefficiency of this reaction can be accounted for by a less favourable cyclisation step and competing αβ–βγ isomerisation of the conjugated ester. In order to avoid the latter problem reactions between ethyl benzylideneacetoacetate and both phenylsulphinylacetone and methyl phenylsulphinylacetate were attempted. In neither case were phenols isolated but, in both cases similar, unstable products could be isolated as oils. These were assigned as the dihydrofurans (13) and (14), respectively, formed as indicated in Scheme 5. The



SCHEME 5

ketone (13) showed all the expected signals in its ^1H n.m.r. spectrum including the AB double doublet at δ 4.36 and 4.68 (*J* 5 Hz), assigned to the protons at positions 4 and 5 of the dihydrofuran ring. Presumably the substituents at these positions are *trans*-oriented to one another. The ester (14) showed similar properties except that in place of the methyl singlet at δ 2.18, assigned to the methyl ketone group, it showed a signal at δ 3.87, attributed to the corresponding methoxy group. These products were unstable to prolonged storage. The compound (14) was also formed when the sulphone (15) was used in place of phenylsulphinylacetate, although the yield was lower, the major products being a mixture of the straightforward Michael adducts (16). Thus the reactivity of the carbanion formed as a consequence of the Michael addition step appears to be of importance in determining the ultimate reaction pathway.

EXPERIMENTAL

M.p.s were determined on a Kofler block and are uncorrected. ^1H N.m.r. spectra were determined on a JEOL MH 100 instrument using deuteriochloroform as solvent, except where stated otherwise and tetramethylsilane as internal reference. I.r. spectra were recorded on a P.E. 257 G instrument, for the liquid phase or solutions in chloroform. Mass spectra were determined on an A.E.I. Kratos MS 30 spectrometer and accurate mass measurements were obtained from the Physico-chemical Measurements Unit, Harwell. All solvents were purified and dried before use. Merck prepared t.l.c. plates were used for both analytical and preparative work using SiO_2 G_{254} and appropriate solvent mixtures.

Reactions were routinely carried out under a blanket of dry nitrogen or argon.

General Method for Preparation of 5-Substituted Resorcinols.—*Method A*. Methyl phenylsulphinylacetate (1 mmol) was added in methanol (4 ml) to a solution of freshly prepared magnesium methoxide (8 mmol) in methanol (4 ml). After 1 h the arylideneacetone (1 mmol) was added in methanol (4 ml) and the solution stirred at room temperature for 2 days. The solution was diluted with ether (30 ml) and washed with water (25 ml) and then saturated sodium hydrogencarbonate solution (25 ml). The aqueous phase was acidified with dilute HCl and extracted into ethyl acetate, dried (Na_2SO_4), filtered, and concentrated *in vacuo* to afford an oily foam. [The neutral ether layer generally contained unchanged starting materials (10—30%).] The acidic fraction was dissolved in benzene (20 ml), to which a little calcium carbonate powder had been added, and heated to reflux for 5 h. The cooled solution was washed with dilute HCl and finally water (10 ml portions) before drying, filtering, and evaporating to give a pale yellow solid, which could be crystallised from either chloroform or aqueous ethanol.

The method could be adapted to a one-pot procedure, either by heating the methanolic solution for 7 h at reflux prior to extraction of the resorcinol or by evaporating off the methanol, adding benzene and continuing the thermolysis as described above. Yields from the one-pot procedure were either similar to, or slightly lower than, those obtained by the two-step reaction sequence.

Method B. This was similar to method A except that sodium hydride (1 equiv.) was used in place of magnesium methoxide and tetrahydrofuran in place of methanol.

In the above manner there was obtained: 5-phenylresorcinol (5; R = Ph) (method A; 43%), m.p. 155—157° (lit.,[15] 157°); 5-(4-methoxyphenyl)resorcinol (5; R = *p*-$MeOC_6H_4$) (method A; 60%), m.p. 152—153° (lit.,[16] 158—159°); 5-(4-nitrophenyl)resorcinol (5; R = *p*-$NO_2C_6H_4$) (method A; 26%), m.p. 245—249° (decomp.); $\nu_{max.}$ 3 390, 1 600, 1 490, and 1 330 cm^{-1}; δ ([$^2H_6$]acetone) 6.47 (1 H, t, *J* 2 Hz), 6.70 (2 H, d, *J* 2 Hz), 7.81 (2 H, d, *J* 10 Hz), 8.27 (2 H, d, *J* 10 Hz), and 8.63br (2 H, s, exchanges) (Found: C, 62.6; H, 3.9; N, 6.0. $C_{12}H_9NO_4$ requires C, 62.35; H, 3.9; N, 6.1%); a better yield of this compound was obtained by using method B (37%); 5-(2-furyl)resorcinol (5; R = 2-furyl) (method B; 30%), m.p. 143—144°, δ ([$^2H_6$]acetone) 6.36 (1 H, t, *J* 2 Hz), 6.50 (1 H, m), 6.75 (1 H, d, *J* 1 Hz), 6.76 (2 H, d, *J* 2 Hz), 7.56 (1 H, d, *J* 1 Hz), and 8.40br (2 H, s, exchanges), $\nu_{max.}$ 3 200, 1 618, 1 440, 1 130, 990, 840, and 726 cm^{-1} (Found: C, 68.0; H, 4.55. $C_{10}H_8O_3$ requires C, 68.2; H, 4.6%); 5-pentylresorcinol (olivetol) (5; R = pentyl) (method A; 48%), m.p. 44—45° (lit.,[5a] 49°), δ ([$^2H_6$]acetone) 0.82—0.96 (3 H, t, *J* 7 Hz), 1.20—1.44 (6 H, m), 1.44—1.72 (2 H, m), 2.44br (2 H, t, *J* 7 Hz), 6.18 (3 H, s), and 8.0br (2 H, s, exchanges); 5-isopropylresorcinol (5; R = isopropyl) (method A; 30%), oil,[5b,17] δ 1.14 (6 H, d, *J* 7 Hz), 2.72 (1 H, m, *J* 7 Hz), 6.15br (1 H, s), 6.24br (2 H, s), and 6.0br (2 H, s, exchanges).

Isolation and Examination of Intermediate Cyclohexanediones (6).—These were generally prepared according to method A in the above procedures but keeping the reaction mixtures at room temperature throughout the procedure. For example, to a solution of magnesium methoxide (8 mmol) in methanol (10 ml) was added methyl phenylsulphinylacetate (200 mg, 1 mmol) in methanol (4 ml) and, after 1 h, benzylideneacetone (147 mg, 1 mmol) in methanol (5 ml). The solution was stirred at room temperature for 4 days and the solvent removed *in vacuo*. The resulting orange syrup was partitioned between ether and dilute HCl, the ether layer extracted with saturated aqueous sodium hydrogencarbonate solution, and then a little water. The aqueous solution was re-acidified and extracted into ethyl acetate. Work-up afforded, as a yellow oil, a crude mixture of the isomeric 4-phenylsulphinyl-5-phenylcyclohexane-1,3-diones (6; R = Ph) contaminated with some (*ca.* 20%) of the corresponding resorcinol (5; R = Ph). The resorcinol could not be completely separated from the cyclohexanedione owing to the continuous slow decomposition of the latter to the resorcinol. In the case of olivetol, the intermediate cyclohexanediones (6; R = n-pentyl) could be isolated (58% yield) relatively free from the resorcinol (<5%). Trituration of the orange foam with ether gave a solid (*ca.* 20%) and an ether-soluble oil (*ca.* 80%). The solid had m.p. 124—130° (decomp.); δ 1.0 (3 H, m), 1.3—1.6 (6 H, m), 2.0 (2 H, m), 2.3—3.2 (3 H, m), 3.4 (1 H, m), 5.7 (1 H, s), 7.55br (5 H, s), and 7.4—7.6 (1 H, exchanges) (Found: C, 66.5; H, 7.2. $C_{17}H_{22}O_3S$ requires C, 66.6; H, 7.2%). The yellow oil had δ 0.9 (3 H, m), 1.0—1.5 (8 H, m), 2.6 (1 H, m), 2.3br (1 H, d, *J* 17 Hz) and 3.15 (1 H, dd, *J* 17 Hz) (ABq), 3.3br (1 H, s), 5.62 (1 H, s), 7.5—7.7 (5 H, m), and 9.5br (1 H, s, exchanges).

The two fractions were assigned structures (7; R = H) and (8; R = H), respectively (see text). The oil (which contained *ca.* 10% of the *cis*-isomers) was unstable at room temperature decomposing to olivetol with a half-life of one

week. During this time the amount of *cis*-isomers in the ^{1}H n.m.r. sample remained approximately constant thus showing that relative instability of the *trans*-isomers.

Preparative t.l.c. of the oil failed to remove the *cis*-isomers. Methylation of the mixture with diazomethane gave four diastereoisomeric enol ethers. The isomer, designated *syn*-A, was recrystallised from ether, m.p. 129°, the *syn*-B and the two *anti*-isomers were separated by preparative t.l.c. (multiple elution, 1 : 4 EtOAc–light petroleum); *syn*-B was obtained as a solid (ether) melting with decomposition over a wide range (95—115°). *anti*-A and -B were oils which were unstable at room temperature. All isomers had virtually identical i.r. spectra, $\nu_{max.}$ 1 645, 1 610, 1 040, 750, and 690 cm^{-1} (see Table 2 for ^{1}H n.m.r.) (Found: for *syn*-A: C, 67.4; H, 7.5. Calc. for $C_{18}H_{24}O_3S$: C, 67.5; H, 7.5%).

3-*Phenyl*-5-*methylphenol* (9; R = H).—Phenylsulphinylacetone (182 mg, 1 mmol) was added to magnesium methoxide (6 mmol) in methanol (10 ml). After 15 min benzylideneacetone (146 mg, 1 mmol) in methanol (5 ml) was added and the pale yellow solution was stirred at room temperature for 16 h before heating it to reflux for 24 h. The solvent was removed *in vacuo* and the residual orange oil was partitioned between ether and dilute HCl. After further extraction of the aqueous phase the combined ethereal layer was washed with saturated aqueous sodium hydrogencarbonate solution and water, then dried (Na_2SO_4), filtered, and evaporated to give a yellow oil (254 mg). A portion (160 mg) was purified by preparative t.l.c. [1 : 1 chloroform–light petroleum (b.p. 60—80°)] to give the volatile phenol (76 mg, 62%), m.p. (hexane) 53—55° (lit.,[18] 51°), $\nu_{max.}$ 3 350, 1 600, 850, 760, and 700 cm^{-1}; δ 2.36 (3 H, s), 6.65br (1 H, s), 6.88br (1 H, s), 7.00br (1 H, s), 7.30—7.65 (5 H, m), and 5.00br (1 H, s, exchanges) (Found: C, 84.45; H, 5.7. $C_{13}H_{12}O$ requires C, 84.75; H, 5.6%).

2-*Ethyl*-3-*methyl*-5-*phenylphenol* (9; R = Et).—To a cold, stirred suspension of sodium hydride (1.2 mmol) in tetrahydrofuran (3 ml) was added 1-phenylsulphinylpentan-2-one (210 mg, 1 mmol) in tetrahydrofuran (4 ml). After liberation of hydrogen had ceased (30 min) a solution of benzylideneacetone (146 mg, 1 mmol) in tetrahydrofuran (3 ml) was added. After stirring the mixture at room temperature overnight the mixture was worked up by adding brine and ether and extracting the aqueous layer with further portions of ether. The ether extract afforded a yellow oil. Preparative t.l.c. afforded the title *phenol* (100 mg, 47%) as an oil, which crystallised at 0° to give m.p. 35—40°, $\nu_{max.}$ 3 250, 1 580, 850, 760, and 690 cm^{-1}; δ 1.16 (3 H, t, *J* 7.5 Hz), 1.35 (3 H, s), 2.72 (2 H, q, *J* 7.5 Hz), 6.89br (1 H, s), 7.06br (1 H, s), and 7.30—7.68 (5 H, m) (Found: C, 84.6; H, 7.7. $C_{15}H_{16}O$ requires C, 84.9; H, 7.6%). No sign of the expected isomeric phenol (10; R = Et) could be detected amongst the products.

Use of the reaction conditions of method A (see above) gave a similar result and the same phenol (9; R = Et) in 44% yield.

Preparation of Non-3-*en*-2-*one*.—Caproaldehyde (0.5 g, 5 mmol) and dimethyl acetylmethylphosphonate (0.83 g, 5 mmol) were added, dropwise, in dichloromethane (10 ml) to a vigorously stirred solution of sodium hydroxide (0.2 g, 5 mmol) in water (10 ml) containing tetrabutylammonium bromide (25 mg). After 12 h the two layers were separated and the aqueous layer extracted with more dichloromethane (2 × 10 ml). The organic extract was washed with water, dried, and evaporated to give the enone (0.57 g, 82%). ^{1}H N.m.r. analysis showed that the material was essentially pure, δ 0.90 (3 H, m), 1.20—1.60 (6 H, m), 2.16—2.40 (2 H, m), 2.24 (3 H, s), 6.04br (1 H, d, *J* 16 Hz), and 6.80 (1 H, dt, *J* 6, 16 Hz), $\nu_{max.}$ 1 670 and 1 625 cm^{-1}.

Preparation of 5-*Methylhex*-3-*en*-2-*one*.—In a similar manner to that described above, isobutyraldehyde (0.36 g, 5 mmol) and dimethyl acetylmethylphosphonate (0.83 g, 5 mmol) reacted together to give the title compound (414 mg, 74%) as an oil, which was used without further purification. The material showed $\nu_{max.}$ 1 673 and 1 625 cm^{-1}; δ 1.08 (6 H, d, *J* 7.5 Hz), 2.14 (3 H, s), 2.48 (1 H, m), 5.90br (1 H, d, *J* 16 Hz), 6.60 (1 H, dd, *J* 6, 16 Hz).

1-*Phenylsulphinylpentan*-2-*one* (1; R = Et).—Phenylsulphinylacetone (1.82 g, 10 mmol) in tetrahydrofuran (25 ml) was added slowly to a stirred solution of lithium diisopropylamide [from di-isopropylamine (2.2 g)] in tetrahydrofuran (15 ml) at −5 °C. After a further 30 min, ethyl bromide (1.2 g, 11 mmol) was added in tetrahydrofuran (5 ml) and the mixture stirred at room temperature for 16 h. Ether and dilute HCl were added to the mixture and the organic extract worked up in the normal manner to give the title ketone (1.72 g, 81%), m.p. (ether) 61—63°, $\nu_{max.}$ 1 700, 1 030, 730, and 690 cm^{-1}, δ 0.88 (3 H, t, *J* 7 Hz), 1.56 (2 H, m), 2.56 (2 H, t, *J* 7 Hz), 3.34 (2 H, ABq, *J* 13 Hz), and 7.56—7.74 (5 H, m) (Found: C, 63.0; H, 6.8. $C_{11}H_{14}O_2S$ requires C, 62.8; H, 6.7%).

Attempted Preparation of Methyl Orsellinate.—Dimethyl ethylidenemalonate (11) (158 mg, 1mmol) was added slowly in tetrahydrofuran (4 ml) to a 0.2M solution of the sodium enolate of phenylsulphinylacetone (182 mg, 1mmol) at −60 °C. The resultant yellow solution was allowed to warm to room temperature and stirred for a further 6 h. Ether and water were added. The aqueous alkaline layer was made acid (concentrated HCl) and extracted into ethyl acetate. The acidic fraction (brown oil, 176 mg) was taken up in ether and washed with saturated sodium hydrogencarbonate in the usual way. The new, neutral fraction (94 mg) contained some methyl orsellinate (by n.m.r. analysis). The spectrum of the new acidic portion (66 mg) was very complex. Pyrolysis of the latter in refluxing anhydrous benzene (5 h) simplified the spectrum and resulted in appearance of peaks assigned to the orsellinic ester. Chromatography of the combined neutral fraction and the thermolysis mixture gave impure methyl orsellinate (55 mg) as an orange oil, δ 2.46 (3 H, s), 3.92 (3 H, s), 6.26br (s) and 6.35br (s) (total 2 H), 8.0 (1 H, s, exchanges), and 11.64 (1 H, s, exchanges).

Reactions with Benzylideneacetoacetate.—The sodium enolate of methyl phenylsulphinylacetate (198 mg, 1mmol) was prepared in the usual way [1mmol-NaH; THF (6 ml)]. Ethyl benzylideneacetoacetate (12) (218 mg, 1mmol) was added in THF (2 ml) and the resultant yellow solution was stirred overnight at 60°. The solvent was removed, *in vacuo*, and the residual orange oil partitioned between ether and dilute HCl. The organic phase yielded an orange oil (240 mg) which was chromatographed (chloroform) to give 3-*ethoxycarbonyl*-5-*methoxycarbonyl*-2-*methyl*-4-*phenyl*-4,5-*dihydrofuran* (13), oil (55 mg, 19%); δ 1.08 (3 H, t, *J* 7 Hz), 2.40br (3 H, s), 3.87 (3 H, s), 4.07 (2 H, q, *J* 7 Hz), 4.48 (1 H, d, *J* 5 Hz), 4.90 (1 H, d, *J* 5 Hz), and 7.35br (5 H, s); $\nu_{max.}$ 1 755, 1 700, 1 650, 1 210, 1 085, 1 030, 760, and 700 cm^{-1} (Found: M^+, 290.1137. $C_{16}H_{18}O_5$ requires *M*, 290.1154). Phenylsulphinylacetone (182 mg, 1mmol) was allowed to react in an analogous manner with (12) (218

mg, 1mmol) to give an orange-brown oil (201 mg), δ 1.02 (3 H, t, *J* 7 Hz), 2.18 (3 H, s), 2.36br (3 H, s), 3.96 (2 H, q, *J* 7 Hz), 4.36br (1 H, d, *J* 5 Hz), 4.68 (1 H, d, *J* 5 Hz), 7.2br (5 H, s). The 5-acetyl-3-ethoxycarbonyl-2-methyl-4-phenyl-4,5-dihydrofuran structure (**14**) was therefore assigned to the major product.

Reaction of the sodium enolate of methyl phenylsulphonlyacetate (15) with (12) under identical conditions gave an orange oil (240 mg) which contained a small amount of (13) by n.m.r. and t.l.c. analysis.

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