Spirodienones. Part 5.[1] The Synthesis and Reactions of *N*-Sulphonylcyclohexadienimines

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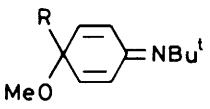
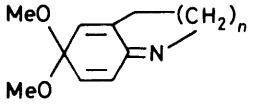
The anodic or chemical oxidation of *para*-substituted sulphonanilides gives 4,4-disubstituted *N*-sulphonylcyclohexadienimines, which, from appropriately substituted anilines, may be spirocyclic. The scope and limitations of the synthesis are described, and a mechanism proposed. The selective hydrolysis of the dienimines to the corresponding dienones provides a convenient route to the latter compounds. The reaction of some of the dienimines with dienes is discussed.

The monoimines of *para*-quinones have been little studied, because of their ease of hydrolysis and tendency to polymerise. However, if the imine nitrogen is substituted by an acyl, aryl, or especially by a sulphonyl function, the resulting imides are much more stable. The preparation and chemistry of these compounds has been investigated extensively by Adams and his co-workers,[2] who established that reactions of quinone monosulphonimides in general resemble those of the related quinones. They have been the subject of limited subsequent research,[3,4] while the synthesis and reactions of *ortho*-benzoquinone sulphonimides has recently been reported.[5] A significant new development[6] in quinone chemistry has been the use of derived monoacetals as synthetic intermediates, and it seemed of interest to investigate the preparation and reactions of analogous imide acetals.



(1) R = Me
(2) R = Ph



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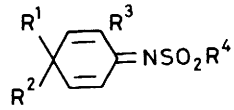
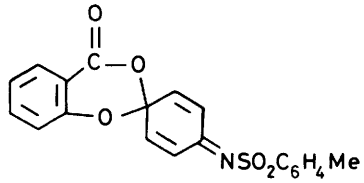
Although related structures had been postulated[7] as reaction intermediates, the compounds (**1**) and (**2**) formed on treatment of the corresponding *N*-t-butyl-*N*-chloroamines with silver cation in methanol appeared to be the only 4-alkoxycyclohexa-2,5-dienimines isolated[8] at the beginning of this work [a recent review[6] cites compounds of the type (**3**) without experimental details]. In our experience the preparation of *N*-t-butylanilines is not straightforward, but it seemed that the readily accessible *N*-arylsulphonamides, which undergo *N*-chlorination, should be equally suitable. Reaction of *N*-*p*-tolylsulphonyl-*p*-anisidine (**22**) with t-butyl hypochlorite and then with silver trifluoroacetate in methanol gave a monochloro derivative of the sulphonimide (**4**), while similar treatment of compounds (**32**) and (**24**) yielded dichlorinated derivatives of (**5**) and of the quinol (**17**) respectively. Although these results were promising, the incorporation of chlorine into the products made another synthetic approach desirable.

Electrochemical methods are among the most useful for preparing quinone acetals, and when the *p*-anisidine sulphonamides (**22**) and (**23**) were subjected to oxidation in methanol at a carbon-felt anode the dimethyl acetals (**4**) and (**7**) were obtained in 70—80% crude yield. *N*-Acyl derivatives of *p*-anisidine did not undergo anodic oxidation, while *N*-sulphonyl-*o*-anisidines gave intractable tars.



(4) $R^1 = R^2 = OMe$, $R^3 = H$, $R^4 = MeC_6H_4$-*p*
(5) $R^1 = Me$, $R^2 = OMe$, $R^3 = H$, $R^4 = MeC_6H_4$-*p*
(6) $R^1 = R^2 = OMe$, $R^3 = H$, $R^4 = Me$
(7) $R^1 = R^2 = OMe$, $R^3 = H$, $R^4 = O_2NC_6H_4$-*o*
(8) $R^2, R^2 = O(CH_2)_2O$, $R^3 = H$, $R^4 = MeC_6H_4$-*p*
(9) $R^1, R^2 = O(CH_2)_3O$, $R^3 = H$, $R^4 = MeC_6H_4$-*p*
(10) $R^1, R^2 = O(CH_2)_2O$, $R^3 = Me$, $R^4 = MeC_6H_4$-*p*
(11) $R^1, R^2 = OCH_2CO_2$, $R^3 = H$, $R^4 = MeC_6H_4$-*p*
(12) $R^1, R^2 = OCH_2CO_2$, $R^3 = H$, $R^4 = Me$
(13) $R^1, R^2 = OCH_2CO_2$, $R^3 = H$, $R^4 = O_2NC_6H_4$-*o*
(14) $R^1, R^2 = OCH_2CO_2$, $R^3 = H$, $R^4 = BrC_6H_4$-*p*
(15) $R^1, R^2 = (CH_2)_2CO_2$, $R^3 = H$, $R^4 = MeC_6H_4$
(16) $R^1, R^2 = (CH_2)_2CO_2$, $R^3 = H$, $R^4 = Me$
(17) $R^1 = OMe$, $R^2 = OH$, $R^3 = H$, $R^4 = Me$



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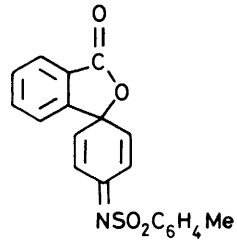

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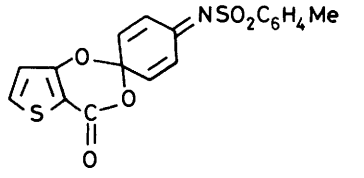

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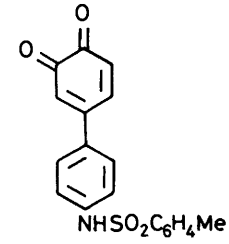

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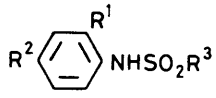
Attention was next directed to sulphonanilides *para*-substituted with side chains bearing terminal nucleophilic groups capable of forming spirocycles by intramolecular reaction. (The preparation of these oxidation substrates by standard methods is detailed in the Experimental section.) The results of the anodic oxidation in acetonitrile of a series of such

Table 1. Conversion of *N*-sulphonanilides into *N*-sulphonylcyclohexadienimines and to cyclohexadienones

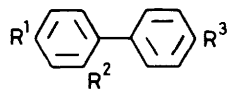
N-Sulphonanilide	Dienimine	Yield (%) of imine from anodic oxidation	Yield (%) from $Pb(OAc)_4$ oxidation	Yield[a] (%) of dienone from hydrolysis of dienimines
(22)	(4)	66—77[b]		95
(23)	(7)	73[b]		
(24)	(6)	100[b,c]		98
(25)	(8)	16[b,d]	60—80	50—70
(26)	(9)	32		
(27)	(10)		40	
(28)	(11)	68	98	
(29)	(12)	60		
(30)	(13)	38		
(31)	(14)	46		
(33)	(15)	19[d]	40	
(34)	(16)	69[e]		
(35)		*		
(36)		*		
(37)		0		
(42)	(20)	70—80		70
(47)	(20)		25	
(48)		0		
(49)	(18)	75		55
(50)	(19)	80		46

[a] Based on dienimine. [b] Oxidations in methanol. [c] Crude yield. [d] 60—70% Before recrystallisation. [e] Variable.

compounds is summarised in Table 1. Yields of spirocyclic acetals quoted are of products purified by crystallisation which often caused considerable loss of material already chromatographically homogeneous; in the experiments designated by an asterisk spectral evidence (*e.g.* the typical CN i.r. absorption at 1 550 cm^{-1}) for cyclohexadienimine formation was obtained, but no homogeneous product was isolated. Best results were obtained with the phenoxyalkanols (**25**) and (**26**), the phenoxyacetic acids (**28**)—(**31**), and the aryloxy acids (**49**) and (**50**) in all of which there is an oxygen *para* to the sulphonamide function. Less successful were the alkyl substituted substrates (**32**)—(**36**).

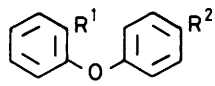


(**22**) R^1 = H, R^2 = MeO, R^3 = MeC_6H_4-*p*
(**23**) R^1 = H, R^2 = MeO, R^3 = $O_2NC_6H_4$-*o*
(**24**) R^1 = H, R^2 = MeO, R^3 = Me
(**25**) R^1 = H, R^2 = $HO(CH_2)_2O$, R^3 = MeC_6H_4-*p*
(**26**) R^1 = H, R^2 = $HO(CH_2)_3O$, R^3 = MeC_6H_4-*p*
(**27**) R^1 = Me, R^2 = $HO(CH_2)_2O$, R^3 = MeC_6H_4-*p*
(**28**) R^1 = H, R^2 = HO_2CCH_2O, R^3 = MeC_6H_4-*p*
(**29**) R^1 = H, R^2 = HO_2CCH_2O, R^3 = Me
(**30**) R^1 = H, R^2 = HO_2CCH_2O, R^3 = $O_2NC_6H_4$-*o*
(**31**) R^1 = H, R^2 = HO_2CCH_2O, R^3 = BrC_6H_4-*p*
(**32**) R^1 = H, R^2 = Me, R^3 = MeC_6H_4-*p*
(**33**) R^1 = H, R^2 = $HO_2C(CH_2)_2$, R^3 = MeC_6H_4-*p*
(**34**) R^1 = H, R^2 = $HO_2C(CH_2)_2$, R^3 = Me
(**35**) R^1 = H, R^2 = $HO_2C(CH_2)_3$, R^3 = MeC_6H_4-*p*
(**36**) R^1 = H, R^2 = $HO(CH_2)_3$, R^3 = MeC_6H_4-*p*
(**37**) R^1 = H, R^2 = $HO_2CCH{=}CH$, R^3 = MeC_6H_4-*p*
(**38**) R^1 = H, R^2 = EtO_2CCH_2O, R^3 = Me
(**39**) R^1 = H, R^2 = EtO_2CCH_2O, R^3 = $O_2NC_6H_4$-*o*
(**40**) R^1 = H, R^2 = EtO_2CCH_2O, R^3 = BrC_6H_4-*p*
(**41**) R^1 = H, R^2 = EtO_2CCH_2O, R^3 = MeC_6H_4-*p*



(**42**) R^1 = H, R^2 = CO_2H, R^3 = $NHSO_2C_6H_4Me$-*p*
(**43**) R^1 = HO_2CCH_2O, R^2 = H, R^3 = $NHSO_2C_6H_4Me$-*p*
(**44**) R^1 = EtO_2CCH_2O, R^2 = H, R^3 = NO_2
(**45**) R^1 = EtO_2CCH_2O, R^2 = H, R^3 = NH_2
(**46**) R^1 = EtO_2CCH_2O, R^2 = H, R^3 = $NHSO_2C_6H_4Me$-*p*
(**47**) R^1 = H, R^2 = MeO_2C, R^3 = $NHSO_2C_6H_4Me$-*p*

The biphenyl compound (**42**) gave a good yield of spirolactone, but the analogous cinnamic acid derivative (**37**) was recovered unchanged from the oxidation, as was the phenol (**48**). As expected for Ar_1n processes, spiro rings containing five atoms formed more readily than those containing six atoms.



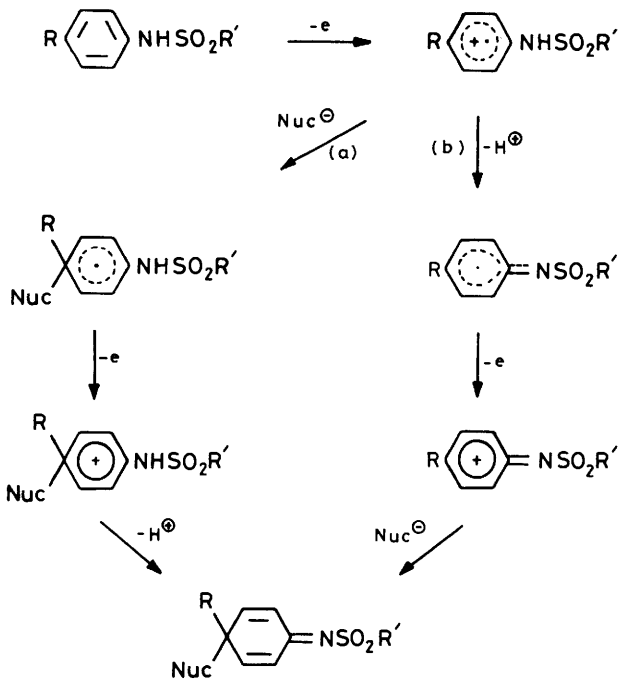
(**48**) R^1 = OH, R^2 = $NHSO_2C_6H_4Me$-*p*
(**49**) R^1 = CO_2H, R^2 = $NHSO_2C_6H_4Me$-*p*

Cyclic voltammetry has not been applied to the substrates, but results of the anodic oxidation of the alkoxybiphenylsulphonamide (**43**) cast light on the preceding results and allow a mechanism to be postulated for the oxidation of aromatic sulphonamides. In an attempt to prepare a spirolactone derivative of a diphenoquinone,* compound (**43**) was oxidised in acetonitrile at a carbon-felt anode. From the complex reaction mixture the major component was isolated as a relatively stable solid acid and was assigned the *o*-quinonoid structure (**21**) on spectral evidence. This was presumably formed by attack of water on an oxidised phenolic ring, the sulphonanilide being unaffected at the anode potential used (the acid side chain may be lost during the oxidation, or by hydrolysis of an intermediate spirolactone).

These results imply that the benzene ring of a sulphonanilide is usually susceptible to anodic oxidation only if aided by an oxygen or (less efficiently) by an alkyl substituent. Thus oxidation of the diphenyl ether (**48**) occurs in the phenolic ring with no subsequent intramolecular coupling, while the cinnamic acid (**37**), in which the sulphonamide is conjugatively substituted by an electron-withdrawing carboxy group, is resistant to oxidation; this effect is minimised in the biphenyl (**42**) where the aromatic rings are not coplanar. From these results it seems reasonable to suppose that the oxidation of *N*-arylsulphonamides parallels that of phenols[9] and phenol ethers[10] and proceeds *via* radical cation intermediates as shown in the Scheme. These intermediates can be converted into a free radical either by nucleophilic attack (path a) or by loss of an acidic sulphonamide proton (path b); by analogy with phenol oxidation[9] the latter alternative is more likely for oxidations performed in methanol, but no clear choice is possible for those carried out in acetonitrile.

The possibility of forming cyclohexadienimines by chemical oxidation was briefly explored. The phenoxyethanol (**25**) was recovered unchanged from treatment with a range of phenol oxidants such as potassium ferricyanide, dichlorodicyanobenzoquinone,[11] active manganese dioxide,[12] iron-dimethylformamide complex[13] or tris(pentane-2,4-dionato)manganese(III)[14] but reacted with lead tetra-acetate in acetic acid to

* Diphenoquinone = 4-(4-oxocyclohexa-2,5-dien-1-ylidene)-cyclohexa-2,5-diene-1-one.



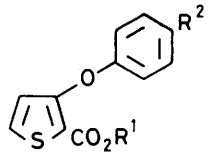
Scheme.

give a high yield of (**8**); this last reagent was also effective in the production of the acetal (**10**) from (**27**) and of the lactone (**11**) from the phenoxy acid (**28**) (see Table 1). [The acetal (**8**) was also obtained in 30% yield by the *N*-chlorination–silver cation treatment of (**25**).]

Although offering the possibility of large-scale synthesis of sulphonimides, the lead tetra-acetate oxidation gives variable yields and is strongly dependent on the purity of the oxidant; there is also some evidence of contamination of the products with materials arising from Wessely acetoxylation and anodic oxidation is probably the better route to small quantities of pure dienimines.

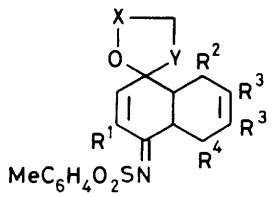
Since the dimethoxy acetals and spiro compounds with 5-membered heterocyclic rings are unchanged after storage for several months, it seemed that they should be convenient precursors of the much less stable quinone mono-acetals, provided selective hydrolysis of the imine double bond could be achieved. After conventional acid hydrolysis had failed, it was accidentally discovered that the desired bond cleavage could be effected by passage of the imides down a neutral alumina column, of Brockmann activity II. This hydrolytic procedure does not harm acetal or lactone functionality [apart from the phenoxyacetic imide (**11**) the derived dienone of which is prone[15] to easy cleavage to *p*-benzoquinone], and can give reasonable overall yields of cyclohexadienones (see Table 1), especially if no attempt is made to purify the crude imine obtained from oxidation before the hydrolysis. Contamination of the dienones with sulphonamide formed during the hydrolysis may be a problem, resolvable in most cases by careful chromatography or by judicious choice of sulphonyl substituent in the oxidation substrate.

In general, the yields of cyclohexadienones obtained from the oxidation of sulphonanilides compares well with those obtained by oxidation of phenolic precursors, and in some cases the anilines are easier to prepare. The thiophene compound (**50**) is readily obtained by reaction of methyl 3-hydroxythiophene-2-carboxylate with 4-fluoronitrobenzene to give (**51**), followed by reduction to (**52**), tosylation, and saponification; to obtain the corresponding phenol would be difficult.



(**50**) R^1 = H, R^2 = $NHSO_2C_6H_4Me$-*p*
(**51**) R^1 = Me, R^2 = NO_2
(**52**) R^1 = Me, R^2 = NH_2
(**53**) R^1 = Me, R^2 = $NHSO_2C_6H_4Me$-*p*

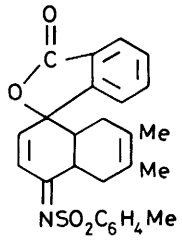
With a variety of spirocyclic cyclohexadienimines readily available, a limited investigation of their chemistry was carried out. It is well documented[2] that quinone sulphonimides readily form Diels–Alder adducts with a variety of dienes, while recently attention[16] has turned to the use of quinone monoacetals as regioselective dienophiles. Since the monoacetals often show reduced reactivity, it was of interest to establish if sulphonimide acetals would take part in Diels–Alder cyclisation. Reaction of the ethylene acetal (**8**) with 2,3-dimethylbutadiene in refluxing benzene for 2 days gave a mixture from which the adduct (**54**)



(**54**) X = CH_2, Y = O, R^1 = R^2 = R^4 = H, R^3 = Me
(**55**) X = CH_2, Y = O, R^2 = R^4 = H, R^1 = R^3 = Me
(**56**) X = CO, Y = CH_2, R^1 = R^2 = R^4 = H, R^3 = Me
(**57**) X = CH_2, Y = O, R^1 = Me, R^2 = R^3 = H, R^4 = OAc
(**58**) X = CH_2, Y = O, R^1 = Me, R^3 = R^4 = H, R^2 = OAc

was isolated in 50% yield; with the substituted acetal (**10**) (in which the reactivity of one double bond is reduced) the yield of adduct (**55**) from a cleaner reaction increased to 80%. Under similar conditions, the spirolactones (**15**) and (**20**) also reacted with dimethylbutadiene to afford (**56**) and (**59**) respectively in about 50% yield. The prolonged heating required for adduct formation caused thermal degradation of the starting imines, and the use of Lewis-acid catalysis[17] is presently being investigated.

It has been established that 1-methoxybutadiene reacts



(**59**)

regioselectively with quinone sulphonimides[3] or with quinone monoacetals[16a] to give adducts in which the methoxy substituent is adjacent to the sulphonimide or carbonyl function respectively. The more readily available 1-acetoxybuta-1,3-

diene reacted slowly (100 h in refluxing toluene) with the ethylene acetal (**10**) to give an adduct in 30% yield. Although structure (**57**) in which the acetoxy group is adjacent to the sulphonimide accords with the previously reported findings, the n.m.r. spectrum of the product in which the methylene protons of the acetal appear as two triplets makes (**58**) equally likely. The significance of the n.m.r. data is not clear, however, as the acetal methylene protons of the symmetrical adduct (**55**) also appear as a multiplet.

In all the adducts there is the possibility of two isomeric structures in which the sulphonimide substituent is *syn* or *anti* to the diene-derived ring. The n.m.r. spectrum of (**55**) contains one vinyl proton peak and one peak for the methyl group adjacent to the imine, indicating that a single isomer is formed, and since it has been shown with quinone sulphonimides that the double bond *syn* to the imide is the more activated dienophile, it seems reasonable to suggest that the adduct is as depicted. In support of this, the n.m.r. resonance for the vinyl proton *ortho* to the sulphonimide in adduct (**54**) occurs at δ 6.2; by analogy with the chemical shifts reported by Moore and co-workers,[3] this suggests that this proton is *anti* to the sulphonimide.

When attempts were made to reduce the carbon–nitrogen double bond of acetal (**8**) with zinc in acetic acid, sodium dithionite or sodium borohydride, the aromatic ethanol (**25**) was recovered in good yield. In general, reaction of the Diels–Alder adducts with sodium borohydride gave complex mixtures, but from compound (**59**) was obtained the corresponding spirocyclic sulphonamide in 75% yield.

Experimental

I.r. spectra were recorded using a Perkin-Elmer 137 grating spectrophotometer; ^{1}H n.m.r. spectra were recorded on JEOL JMN C-60 or Hitachi Perkin-Elmer R24B spectrometers with tetramethylsilene as the internal standard in the solvent indicated. Mass spectra were determined by The Boots Company, Nottingham or by Leicester Polytechnic. Microanalyses were performed by I.C.I. Pharmaceuticals Division, Alderley Edge. Melting points are corrected. Light petroleum or LP refers to b.p. 60—80 °C and ether to diethyl ether.

Preparation of Sulphonanilides as Oxidation Precursors: General Procedure.—Equimolar quantities of aromatic amine, sulphonyl chloride, and triethylamine dissolved in dry dichloromethane were mixed at 0 °C, and the temperature allowed to rise to ambient over 1 h. If t.l.c. examination showed incomplete reaction, the mixture was heated under reflux for a further hour. By this method it was usually possible to form exclusively *N*-sulphonyl derivatives even with compounds containing alcohol or phenol functions, but from the reaction of 4-aminophenoxyethanol with methanesulphonyl chloride the only product isolated was 2-(4-*methanesulphonamidophenoxy*)-*ethylmethanesulphonate*, m.p. 132—134 °C (from toluene) (Found: C, 39.1; H, 4.9; N, 4.3. $C_{10}H_{15}NO_6S_2$ requires C, 38.8; H, 4.8; N, 4.5%); $\nu_{max.}$(KBr) 3 250 (NH), 1 315, and 1 140 cm^{-1} (SO_2N). The *phenoxyacetic acids* (**28**)—(**31**) were prepared by saponification of the corresponding *esters* (**38**)—(**41**) obtained by reaction of ethyl 4-aminophenoxyacetate with the appropriate sulphonyl chloride.

3-(4-*Methanesulphonamidophenyl*)*propanoic acid* (**34**). To a solution of 3(4-nitrophenyl)propanoic acid (20 g), in dry pyridine (200 ml) was added t-butyl alcohol (9.7 ml) and toluene-*p*-sulphonyl chloride (19.4 g). The mixture was heated on a steam-bath for 17 h after which the cooled solution was poured into ice–water and extracted with dichloromethane (2 × 300 ml). The combined organic phase was washed with acid and base, dried, and evaporated to give *t-butyl* 3-(4-*nitrophenyl*)*propanoate*, (21.4 g, 83%), m.p. 53—54 °C (from methanol) (Found: C, 62.2; H, 6.7; N, 5.5%; M^+, 251. $C_{13}H_{17}NO_4$ requires C, 62.2; H, 6.7; N, 5.5%; *M*, 251); $\nu_{max.}$(KBr) 1 735 (CO), 1 515, and 1 355 cm^{-1} (NO_2). Hydrogenation of this nitro ester in dioxane with palladium catalyst (10% on carbon) gave *t-butyl* 3-(4-*aminophenyl*)*propanoate* (90%), m.p. 59—60 °C (from light petroleum) (Found: C, 70.9; H, 8.5; N, 6.3. $C_{13}H_{19}NO_2$ requires C, 70.6; H, 8.6; N, 6.3%); $\nu_{max.}$(KBr) 3 450, 3 000 (NH), and 1 730 cm^{-1} (CO). Reaction of the amino ester with toluene-*p*-sulphonyl chloride gave a gummy solid which when heated at 100 °C for 1 h yielded the *title acid* (**34**), (95%).

3-[4-(p-*Toluenesulphonamido*)*phenyl*]*propan*-1-ol (**36**). To a stirred solution of acid (**33**) (1.0 g) in dry tetrahyrofuran (20 ml) under nitrogen was added by syringe borane–dimethyl sulphide (0.8 ml). After 1 h the solution was poured into cold methanol and the solvents were evaporated under reduced pressure to give the *alcohol* (**36**) as a colourless oil, homogeneous by t.l.c., $\nu_{max.}$(film) 3 500 (OH), 3 240 (NH), and 1 325 and 1 155 cm^{-1} (SO_2N); δ_H($CDCl_3$) 1.6—1.8 (2 H, m, $CH_2CH_2CH_2$), 2.25 (3 H, s, Me), 2.4—2.7 (2 H, m, $ArCH_2$), 3.4—3.7 (2 H, m, CH_2O), 7.00 (4 H, s, ArH *ortho* to N and CH_2), 7.10 (2 H, d, *J* 9 Hz, ArH *ortho* to Me), 7.65 (2 H, d, *J* 9 Hz, ArH *ortho* to S), and 2.8 and 8.0 (2 × 1 H, 2 × s, OH, NH). The alcohol was characterised by reaction in chloroform with an excess of methanesulphonyl chloride to give (**36**) O,N-*dimethanesulphonate*.

4′-(p-*Toluenesulphonamido*)*biphenyl*-4-*yloxyacetic acid* (**43**). A stirred mixture of 4-hydroxy-4′-nitrobiphenyl[18] (2.15 g), acetone (25 ml), anhydrous potassium carbonate (5 g), sodium iodide (0.1 g), and ethyl chloroacetate (2.5 ml) was heated under reflux for 2 h, then filtered and the filtrate evaporated to give a residue which was recrystallised from ethanol to give *ethyl* 4′-*nitrobiphenyl*-4-*yloxyacetate* (**44**) (1.3 g, 44%), m.p. 97—98 °C (Found: C, 64.0; H, 5.0; N, 4.6. $C_{16}H_{15}NO_5$ requires C, 64.0; H, 5.0; N, 4.6%); $\nu_{max.}$(KBr) 1 750 cm^{-1} (ester). The nitro ester (0.5 g) in ethyl acetate (75 ml) was hydrogenated with palladium (5% on charcoal, 0.1 g) to give *ethyl* 4′-*aminobiphenyl*-4-*yloxyacetate* (**45**) (0.36 g, 80%), m.p. 72—73.5 °C (from ethanol) (Found: C, 70.3; H, 6.3; N, 5.0. $C_{16}H_{17}NO_3$ requires C, 70.8; H, 6.3; N, 5.2%); $\nu_{max.}$(KBr) 3 420, 3 320 (amine), and 1 740 cm^{-1} (ester). Reaction of the aminoester with toluene-*p*-sulphonyl chloride gave the sulphonamide (**46**), which on saponification yielded the *title acid* (**43**), $\nu_{max.}$(KBr) 3 280 (NH), 1 760, and 1 710 cm^{-1} (ester); δ_H[$CDCl_3$–$(CD_3)_2SO$] 2.35 (3 H, s, ArMe), 4.6 (2 H, s, OCH_2CO_2), 6.7—7.7 (12 H, m, ArH), and 9.7 (1 H, s, CO_2H).

2-[3-*Methyl*-4-(p-*toluenesulphonamido*)*phenoxy*]*ethanol*. To a stirred solution of 3-methyl-4-nitrophenol (30.6 g) in dry DMF (100 ml), cooled to 0 °C, was added sodium hydride (4.8 g) over 0.5 h; 2-chloroethanol was added and the mixture was heated under reflux for 5 h, cooled, and poured into water (1 l). The precipitated solid recrystallised from toluene to give 2-(3-*methyl*-4-*nitrophenoxy*)*ethanol* (21 g, 53%), m.p. 86—88 °C (Found: C, 54.4; H, 5.6; N, 7.1. $C_9H_{11}NO_4$ requires C, 54.8; H, 5.6; N, 7.1%). Hydrogenation of the nitro alcohol in ethyl acetate with palladium (5% on carbon) as catalyst gave 2-(3-*methyl*-4-*aminophenoxy*)*ethanol* (91%), m.p. 64—66 °C (from chloroform–light petroleum) (Found: C, 64.7; H, 7.8; N, 8.4. $C_9H_{13}NO_2$ requires C, 64.7; H, 7.8; N, 8.4%); $\nu_{max.}$(KBr) 3 190, 3 300, and 3 460 cm^{-1} (NH_2 and OH). Treatment of the amino alcohol with toluene-*p*-sulphonyl chloride afforded the *title sulphonamido alcohol* (**27**).

3-[4-(p-*Toluenesulphonamido*)*phenoxy*]*thiophene*-2-*carboxylic acid* (**50**). To a solution of methyl 3-hydroxythiophene-2-carboxylate[19] (3.16 g, 20 mmol) in dry methanol (25 ml) was added potassium t-butoxide (2.48 g, 22 mmol); the mixture was warmed briefly on a water-bath and the solvent removed. To the residual potassium salt was added a solution of 4-fluoronitrobenzene (3.15 g, 22 mmol) in dimethylformamide (50 ml), and the mixture was heated under reflux for 3 h. After this, it was

Table 2. Analytical data for novel sulphonamides

Compound (Formula)	Solvent*	M.p. (°C)	Found (%) (Required) C	H	N
(23) ($C_{13}H_{12}N_2O_5S$)	PhMe–LP	102—103	50.6 (50.6)	3.8 (3.9)	9.0 (9.1)
(25) ($C_{15}H_{17}NO_4S$)	PhMe–LP	126—128	58.5 (58.5)	5.5 (5.5)	4.4 (4.6)
(26) ($C_{16}H_{19}NO_4S$)	PhMe	138—139	59.8 (59.8)	5.8 (5.9)	4.3 (4.4)
(27) ($C_{16}H_{19}NO_4S$)	$CHCl_3$–LP	96—98	59.9 (59.8)	5.8 (5.9)	3.9 (4.3)
(29) ($C_9H_{11}NO_5S$)	Aq. EtOH	205—207	43.8 (44.1)	4.5 (4.5)	5.6 (5.7)
(30) ($C_{14}H_{12}N_2O_7S$)	Aq. EtOH	157—159	47.8 (47.7)	3.4 (3.4)	7.9 (7.9)
(31) ($C_{14}H_{12}BrNO_5S$)	Aq. EtOH	221—223	43.3 (43.5)	3.1 (3.1)	3.5 (3.6)
(33) ($C_{16}H_{17}NO_4S$)	Aq. EtOH	161—162	60.1 (60.2)	5.4 (5.3)	4.2 (4.4)
(34) ($C_{10}H_{13}NO_4S$)	MeOH	151—152	49.6 (49.4)	5.5 (5.3)	5.5 (5.8)
(35) ($C_{17}H_{19}NO_4S{\cdot}H_2O$)	Aq. MeOH	125—126	57.5 (58.1)	5.6 (6.0)	3.9 (4.0)
(36) *O,N*-dimethanesulphonate ($C_{18}H_{23}NO_7S_3$)	Aq. EtOH	94—95	47.1 (46.8)	5.1 (5.0)	2.7 (3.0)
(37) ($C_{16}H_{15}NO_4S$)	Aq. MeOH	223—225	60.3 (60.5)	4.6 (4.7)	4.5 (4.4)
(38) ($C_{11}H_{15}NO_5S$)	PhMe–LP	78—80	48.3 (48.3)	5.6 (5.5)	5.2 (5.1)
(39) ($C_{16}H_{16}N_2O_7S$)	PhMe	92—94	50.4 (50.3)	4.2 (4.2)	7.3 (7.4)
(40) ($C_{16}H_{16}BrNO_5S$)	PhMe–LP	110—112	46.3 (46.4)	3.8 (3.9)	3.2 (3.4)
(41) ($C_{17}H_{19}NO_5S$)	PhMe–LP	90—92	58.4 (58.1)	5.4 (5.6)	4.0 (3.9)
(42) ($C_{20}H_{17}NO_4S$)	Et_2O	185—187	65.2 (65.4)	4.7 (4.6)	3.4 (3.8)
(43) ($C_{21}H_{19}NO_5S$)	Aq. EtOH	191—192	64.7 (64.9)	5.6 (5.5)	2.9 (3.3)
(46) ($C_{23}H_{23}NO_5S$)	PhMe–LP	112—113.5	63.1 (63.4)	4.7 (4.8)	3.3 (3.5)
(47) ($C_{21}H_{19}NO_4S$)	$CHCl_3$–LP	113.5—115	66.3 (66.1)	5.1 (5.0)	3.7 (3.7)
(48) ($C_{19}H_{17}NO_4S$)	Aq. EtOH	159—160	63.7 (64.2)	4.8 (4.8)	3.8 (3.9)
(49) ($C_{20}H_{17}NO_5S$)	LP	184—186	62.4 (62.7)	4.4 (4.4)	3.8 (3.7)
(50) ($C_{18}H_{15}NO_5S_2$)	Me_2CO–Et_2O	203—205	55.8 (55.5)	4.0 (3.9)	3.5 (3.6)
(53) ($C_{19}H_{17}NO_5S_2$)	LP	138—139	56.7 (56.6)	4.3 (4.2)	3.3 (3.5)

* LP = light petroleum.

poured into 10% aqueous sodium chloride to give a yellow precipitate of *methyl* 3-(4-*nitrophenoxy*)*thiophene*-2-*carboxylate* (**51**) (4.8 g, 84%), m.p. 105—106 °C (from light petroleum) (Found: C, 52.6; H, 3.3; N, 5.0; S, 11.6. $C_{12}H_9NO_5S$ requires C, 51.6; H, 3.3; N, 5.0; S, 11.5%); $\nu_{max.}$(KBr) 1 712 cm^{-1} (ester). To a solution of the nitro ester (1.4 g, 50 mmol) in methanol (15 ml) and glacial acetic acid (1.8 g) was added iron powder (0.85 g) and the mixture was heated under reflux (nitrogen atmosphere) for 1.25 h; it was then poured into water and the solution made alkaline with sodium hydrogen carbonate. Extraction with ether provided *methyl* 3-(4-*aminophenoxy*)*thiophene*-2-*carboxylate* (**52**), (1.1 g, 90%), m.p. 102—103 °C (from light petroleum) (Found: C, 57.9; H, 4.4; N, 5.5; S, 13.0. $C_{12}H_{11}NO_3S$ requires C, 57.8; H, 4.4; N, 5.6; S, 12.8%); $\nu_{max.}$(KBr) 3 440, 3 360 (NH_2), and 1 700 cm^{-1} (ester). Reaction of the amino ester with toluene-*p*-sulphonyl chloride gave *sulphonamido ester* (**53**), which on saponification yielded the *title acid* (**50**).

Reaction of Sulphonamides with t-Butyl Hypochlorite. Methanolic Silver Trifluoroacetate.—To a solution of the sulphonamide (20 mmol) in dichloromethane (10 ml) cooled in an ice-bath, was added t-butyl hypochlorite (1 ml), followed 1 h later by a solution of silver trifluoroacetate (2 g) in methanol (50 ml). The reaction mixture was stirred and allowed to warm to room temperature over a period of 1 h, filtered, and the filtrate stirred with lithium chloride (3 g) for 15 min. The precipitate was filtered off and the filtrate evaporated to yield a gum. This was partitioned between ether (150 ml) and water

(150 ml), after which the organic layer was separated, dried ($MgSO_4$), and evaporated.

From *N*-(*p*-tolylsulphonyl)-*p*-anisidine (**22**) was obtained a gum which solidified on trituration with ether. This solid was separated by column chromatography (silica gel, chloroform–ether 1:1), to afford two crystalline products. The higher R_F fraction, colourless needles m.p. 170—172 °C (from toluene–light petroleum) was identified as *2-chloro-4,4-dimethoxy*-N-(*p-tolylsulphonyl)cyclohexa-2,5-dien-4-imine* (Found: C, 53.1; H, 4.7; Cl, 10.2; N, 4.0%; M^+, 341. $C_{15}H_{16}ClNO_4S$ requires C, 52.8; H, 4.7; Cl, 10.4; N, 4.0%; *M*, 341); $\nu_{max.}$(KBr) 1 650 (C=C), 1 550 (CN), and 1 310 and 1 145 cm^{-1} (SO_2N); δ_H(DMSO) 2.45 (3 H, s, ArMe), 3.40 [6 H, s, $(OMe)_2$], and 6.8—8.1 (7 H, m, vinyl and ArH). The lowest R_F material gave conflicting analytical and spectral data, and was assumed to be an inseparable mixture of products.

The product from *N*-methylsulphonyl-*p*-anisidine (**24**) was shown to be homogeneous by t.l.c. and crystallised on trituration with ether to yield *x,y*-dichloro-4-hydroxy-4-methoxy-*N*-methylsulphonylcyclohexa-2,5-diene-4-imine as colourless needles (140 mg), m.p. 158 °C (from toluene–light petroleum) (Found: C, 33.5; H, 2.9; N, 4.7%; M^+, 285. Calc. for $C_8H_9Cl_2NO_4S$: C, 33.7; H, 3.2; N, 4.9%; *M*, 285); $\nu_{max.}$(KBr) 3 200br (OH), 1 655, 1 630, 1 600, 1 330, and 1 165 cm^{-1} (SO_2N); $\delta_H(CDCl_3)$ 3.05 (3 H, s, SMe), 3.30 (3 H, s, OMe), 5.40 (1 H, br s, OH), and 6.60 (2 H, s, vinylic H). An examination of this substance after several days indicated that it had decomposed to a mixture of compounds, the structures of which could not be elucidated.

Trituration with ether of the oily product obtained from *N*-(*p*-tolylsulphonyl)-4-toluidine (**32**) yielded *x,y*-dichloro-4-methoxy-4-methyl-*N*-(*p*-tolylsulphonyl)cyclohexa-2,5-dien-imine, as yellow crystals (21%), homogeneous by t.l.c., m.p. 168 °C (from toluene–light petroleum) (Found: C, 51.0; H, 4.1; N, 4.1. Calc. for $C_{15}H_{15}Cl_2NO_3S$: C, 50.0; H, 4.2; N, 4.1%); $\nu_{max.}$(KBr) 1 640, 1 590, 1 545, and 1 320 and 1 150 cm^{-1} (SO_2N); $\delta_H(CDCl_3)$ 2.50 [6 H, s, $(ArMe)_2$], 3.25 (3 H, s, OMe), and 6.5—8.3 (6 H, m, vinylic and ArH). T.l.c. examination of the product after several days showed considerable decomposition had occurred.

For reaction with 2-[4-(*p*-tolylsulphonamido)phenoxy]-ethanol (**24**), the silver trifluoroacetate was added in toluene solution. The gummy product on trituration with ether, gave a colourless crystalline compound, homogeneous by t.l.c., identified as the *ethylene acetal* of 4-(p-*toluenesulphonimido)cyclohexa-2,5-dien-1-one* (**8**) (30%), $\delta_H(CDCl_3)$ 2.40 (3 H, s, Me), 4.15 (4 H, s, CH_2CH_2), and 6.4—3.2 (8 H, m, vinylic and ArH).

Electrochemical Oxidation of Substituted N-*Aryl Sulphonamides: General Anodic Oxidation Procedure.*—All anodic oxidations were carried out using a Wenking potentiostat model 70 TS 1 and standard calomel reference electrode, with a graphite felt anode (5 × 3 cm) and a platinum cathode (3 × 2 cm). The one compartment cell contained a stirred solution of tetraethylammonium perchlorate (2.5 g) in either methanol or acetonitrile (150 ml). The oxidations were carried out in air at room temperature. Substrates were added in solution of the cell solvent to an equilibrated, pre-electrolysed anodic cell, at a predetermined anodic potential, and the current monitored with time until either the current dropped to the background level or until all starting material was shown by t.l.c. examination to have reacted. The cell solution was decanted, the shredded anode washed with further solvent, and the combined organic solvents filtered, then evaporated to dryness on a rotary evaporator at room temperature. The residues were partitioned between dichloromethane or ether and water, and the organic layer separated. When the starting materials were acidic an additional wash with saturated sodium hydrogencarbonate solution was employed. The organic layers were dried ($MgSO_4$), filtered, and then rotary evaporated to dryness at room temperature.

Oxidations with Lead Tetra-acetate: General Procedure.—A suspension of lead tetra-acetate (6.5 g, 0.15 mol) in glacial acetic acid (30 ml) was added to a stirred solution of the substrate (0.07 mol) in glacial acetic acid (50 ml). The reaction mixture was stirred at room temperature for 17 h, poured into water (300 ml) and extracted into ether (3 × 100 ml). The combined ethereal extractions were washed with water (2 × 150 ml), saturated aqueous sodium hydrogencarbonate (2 × 150 ml—or until effervescence ceased), and water (150 ml), dried, ($MgSO_4$), and evaporated.

Anodic Oxidation of 4′-(p-*Toluenesulphonamido)biphenyl-4-yloxyacetic Acid* (**43**).—The acid was oxidised in acetonitrile at an anode potential of 1.4 V (s.c.e.) until the current fell to zero. The i.r. spectrum of the crude product showed absorption at 3 250 (NH), 1 820 (γ-lactone), 1 650 (CO), and 1 150 cm^{-1} (SO_2N). Preparative layer chromatography (silica gel, methanol–chloroform 1:4) yielded six fractions, of which the component of R_F 0.7—0.8, a red solid, was the most abundant. The *o*-quinone structure (**21**) is assigned to this solid on the following evidence [Found: 355.0975 (M^+ + 2, 9%) and 353.0784 (M^+, 23). $C_{19}H_{15}NO_4S$ requires (*M* + 2) 355.0948 and *M*, 353.0764]; $\nu_{max.}$(KBr) 3 200 (NH), 1 675m, 1 650s, 1 610w (*ortho*-quinone), and 1 160s cm^{-1} (SO_2N); $\delta_H(CDCl_3)$ 2.41 (3 H, s, ArMe), 6.75 (1 H, s, exchangeable with D_2O, NH), 6.8—7.5 (9 H, m, Ar and vinylic H), 7.8 (2 H, d, ArH *ortho* to SO_2).

Hydrolysis of N-*Sulphonylcyclohexadienimines to Cyclohexadienones.*—In a typical experiment, the imine (**20**) (0.3 g) in ethyl acetate (1 ml) was loaded on a neutral alumina column (Brockmann Activity II, 15 g). Elution with ethyl acetate gave cyclohexa-2,5-diene-1-spiro-1′-isobenzofuran-3′,4-dione (0.87 g, 75%), m.p. 182—183 °C (lit.,[20] 189 °C) (from ethanol); $\nu_{max.}$(KBr) 1 770 (γ-lactone), 1 670, 1 630 cm^{-1} (dienone); $\delta_H(CDCl_3$–DMSO) 6.40, 6.78 (4 H, 2d, *J* 9 Hz, vinylic H), and 7.26—7.98 (4 H, m, ArH).

Hydrolysis of the thiophene imine (**19**) gave the corresponding novel *dienone*, m.p. 123—125 °C (from ether) (Found: C, 55.8; H, 2.6; S, 13.4. $C_{11}H_6SO_4$ requires C, 56.4; H, 2.6; S, 13.7%); $\nu_{max.}$(KBr) 1 745 (δ-lactone) and 1 690 and 1 648 cm^{-1} (2,5-dienone).

Diels–Alder Reactions of Spirocyclohexadienimines.—To a solution of the imino acetal or lactone (5 mmol) in dry benzene (50 ml) was added 2,3-dimethylbuta-1,3-diene (0.82 g, 10 mmol), or (*E*)-1-acetoxybuta-1,3-diene (1.12 g, 10 mmol), and the mixture was heated under reflux for 50 h. The solvent was evaporated, and the residue purified by flash chromatography [Kieselgel 60, 230—400 mesh, ethyl acetate–light petroleum (1:4)] and by crystallisation. From the acetal (**8**) and 2,3-dimethylbutadiene was obtained the *adduct* (**54**) (46%), m.p. 105—107 °C (from light petroleum) (Found: C, 65.2; H, 6.5; N, 3.6%; M^+, 387. $C_{21}H_{25}NO_4S$ requires C, 65.1; H, 6.5; N, 3.6%; *M*, 387); $\nu_{max.}$(KBr) 1 620 (C=C) and 1 580 cm^{-1} (CN); $\delta_H(CDCl_3)$ 1.5 (6 H, s, 2 × Me), 2.0—2.2 (6 H, m, aliph.), 2.4 (3 H, s, ArMe), 4.0 (4 H, s, OCH_2CH_2O), 6.2 (1 H, d, *J* 9 Hz, vinylic H), 7.2 (3 H, d, *J* 9 Hz, 2 × ArH + 1 vinylic H), and 7.7 (2 H, d, *J* 9 Hz, ArH).

From the acetal (**10**) and 2,3-dimethylbutadiene was obtained without chromatography the *adduct* (**55**) (80%), m.p. 145—147 °C (from ether–light petroleum) (Found: C, 66.2; H, 6.5; N, 3.6%; M^+, 401. $C_{22}H_{27}NO_4S$ requires C, 65.8; H, 6.7; N, 3.5%; *M*, 401); $\nu_{max.}$(KBr) 1 570 (CN); $\delta_H(CDCl_3)$ 1.6 (6 H, s, 2 × Me),

Table 3. Analytical data for *N*-sulphonylcyclohexadienimines

Compound (Formula)	Solvent*	M.p. (°C)	Found (%) (Required) C	H	N
(4) ($C_{15}H_{17}NO_4S$)	PhMe–LP	149	58.2 (58.6)	5.5 (5.5)	4.4 (4.6)
(6) ($C_9H_{13}NO_4S$)		79—80	Unstable		
(7) ($C_{14}H_{14}N_2O_6S$)	PhMe–LP	116—118	49.7 (49.7)	3.8 (4.1)	8.0 (8.3)
(8) ($C_{15}H_{15}NO_4S$)	PhMe–LP	129—130	58.5 (59.0)	4.9 (4.9)	4.6 (4.6)
(9) ($C_{16}H_{17}NO_4S$)	Chromatography	114—116	Unstable		
(10) ($C_{16}H_{17}NO_4S$)	PhMe–LP	167—169	59.9 (60.1)	5.3 (5.3)	4.0 (4.4)
(11) ($C_{15}H_{13}NO_5S$)	PhMe–LP	144—145	55.9 (56.4)	4.2 (4.1)	4.3 (4.4)
(12) ($C_9H_9NO_5S$)	$CHCl_3$–LP	156—157	44.5 (44.4)	3.7 (3.7)	5.8 (5.8)
(13) ($C_{14}H_{10}N_2O_7S$)	$CHCl_3$–LP	167—168	47.4 (48.0)	2.8 (2.9)	7.6 (8.0)
(14) ($C_{14}H_{10}BrNO_5S$)	$CHCl_3$–LP	141—143	44.0 (43.7)	2.5 (2.6)	3.6 (3.6)
(15) ($C_{16}H_{15}NO_4S$)	EtOH	146—148	61.2 (60.6)	5.0 (4.7)	4.1 (4.4)
(16) ($C_{10}H_{11}NO_4S$)	AcOEt–Et_2O	186—188	49.7 (49.8)	4.6 (4.6)	5.7 (5.8)
(18) ($C_{20}H_{15}NO_5S$)	MeOH	159—160	63.1 (63.0)	4.1 (3.9)	3.5 (3.7)
(19) ($C_{18}H_{13}NO_5S_2$)	Et_2O	108—109	56.2 (55.8)	3.9 (3.4)	3.2 (3.6)
(20) ($C_{20}H_{15}NO_4S$)	MeOH	158—161	65.6 (65.8)	4.2 (4.1)	3.9 (3.8)

* LP = light petroleum. All compounds had $\nu_{max.}$(KBr) 1 655—1 660 (C=C), 1 540—1 560 (C=C), 1 540—1 560 (CN), and 1 310—1 330 and 1 140—1 160 cm^{-1} (SO_2N). The spirolactones (**11**)—(**14**), had ν(CO) at 1 820 and 1 800 cm^{-1}, the lactones (**15**), (**16**), and (**20**) at 1 770—1 775 cm^{-1}, and the δ-lactones (**18**) and (**19**) had bands at 1 745 cm^{-1}.

1.8 (3 H, s, Me), 2.0—2.6 (6 H, m, aliph.), 2.4 (3 H, s, ArMe), 4.0 (4 H, m, OCH_2CH_2O), 6.2 (1 H, s, vinylic H), and 7.3 and 7.8 (4 H, 2 × d, *J* 9 Hz, ArH).

From the imine lactone (**15**) and 2,3-dimethylbutadiene was obtained the *adduct* (**56**) (50%) as a yellow crystalline solid, m.p. 154—155 °C (from ether–light petroleum) (Found: C, 65.8; H, 6.1; N, 3.5%; M^+, 399. $C_{22}H_{25}NO_4S$ requires C, 66.1; H, 6.2; N, 3.5%; *M*, 399); $\nu_{max.}$(KBr) 1 770 (γ-lactone), 1 625 (C=C), and 1 570 cm^{-1} (CN); δ_H($CDCl_3$–DMSO) 1.4 (6 H, s, 2 × Me), 2.4 (3 H, s, ArMe), 1.5—3.0 (10 H, m, aliph.), 6.8—7.7 (6 H, m, Ar and vinylic H).

From the lactone imine (**20**) and 2,3-dimethylbuta-1,3-diene was formed the *adduct* (**59**) (47%), m.p. 152—154 °C (from ether–light petroleum) (Found: C, 69.6; H, 5.7; N, 3.0%; M^+, 447. $C_{26}H_{25}NO_4S$ requires C, 69.8; H, 5.6; N, 3.1%; *M*, 447); $\nu_{max.}$(KBr) 1 780 (γ-lactone), 1 620 (C=C), and 1 580 cm^{-1} (CN); δ_H($CDCl_3$) 1.5 (6 H, s, 2 × Me), 2.4 (3 H, s, ArH), 2.0—2.3 (6 H, m, aliph.), 6.2 and 6.5 (2 H, 2 × d, *J* 9 Hz, vinylic H), and 7.3—8.0 (8 H, m, ArH).

Reaction of acetal (**10**) with (*E*)-1-acetoxybuta-1,3-diene in refluxing toluene for 100 h yielded the *adduct* (**57**) or (**58**) (28%), m.p. 136—137 °C (from ethyl acetate–light petroleum) (Found: C, 61.6; H, 5.7; N, 3.1%; M^+, 431. $C_{22}H_{25}NO_6S$ requires C, 61.3; H, 5.8; N, 3.2%; *M*, 431); $\nu_{max.}$(KBr) 1 740 (ester) and 1 600 cm^{-1} (CN); δ_H($CDCl_3$) 2.1, 2.2 (6 H, 2 × s, 2 × Me), 2.4 (3 H, s, ArMe), 2.0—2.4 (5 H, m, aliph.), 4.4 (4 H, 2 × t, OCH_2CH_2O), 6.5 (1 H, s, vinylic H), and 7.0—7.6 (6 H, m, Ar and vinylic H).

Reduction of Adduct (**55**).—The adduct (**55**) (0.4 g) was added to a suspension of sodium borohydride (0.5 g) in ethanol (20 ml) and the mixture was stirred for 16 h at room temperature, diluted with water, and extracted with dichloromethane. The extract was washed, dried, and evaporated to give the corresponding *sulphonamide adduct* (75%), m.p. 151—153 °C (from ether–light petroleum) (Found: C, 65.5; H, 7.3; N, 3.6. $C_{22}H_{29}NO_4S$ requires C, 65.5; H, 7.2; N, 3.5%); $\nu_{max.}$(KBr) 3 300 (NH), 1 600 (C=C) 1 330, and 1 150 cm^{-1} (NSO_2).

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