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SUBSTITUTION REACTIONS OF 2-PHENYLSULPHONYL-PIPERIDINES AND -PYRROLIDINES WITH CARBON NUCLEOPHILES: SYNTHESIS OF THE PYRROLIDINE ALKALOIDS NORRUSPOLINE AND RUSPOLINONE

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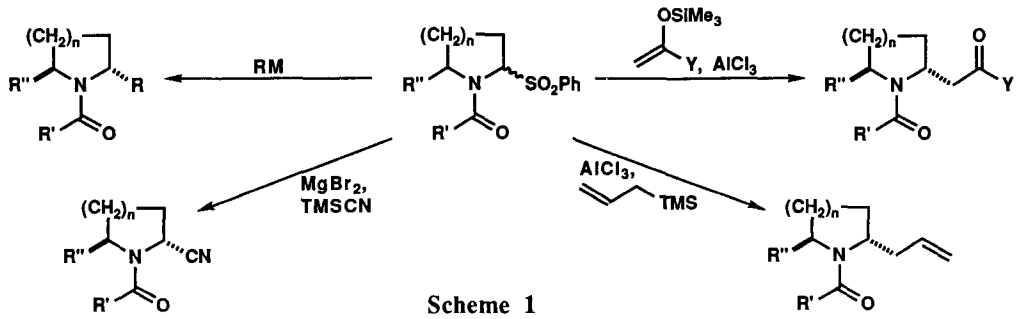
Abstract: *Several 2-phenylsulphonyl-piperidines and -pyrrolidines were prepared from the corresponding N-acyl aminals by treatment with benzenesulphinic acid. On reaction with various carbon nucleophiles these sulphones gave good yields of substitution products. Typical nucleophiles used in these studies were organometallic reagents derived from Grignard reagents and zinc halide together with silyl enol ethers, silyl ketene acetals, allylsilanes and trimethylsilyl cyanide in the presence of a Lewis acid. These methods were employed in the synthesis of two natural product alkaloids; Norruspoline (38) and Ruspolinone (40).*

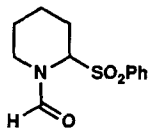
A wide variety of alkaloids and many biologically important compounds contain piperidine or pyrrolidines ring systems. Moreover, many of these products contain carbon-carbon bond substitution at the positions adjacent to the heteroatom. In order to facilitate the preparation of such systems we have been developing new chemistry based upon the direct displacement of 2-phenylsulphonyl moeity using carbon nucleophiles.[1] We have previously demonstrated the synthetic ability of anomeric sulphones during related studies on cyclic ethers.[2] Although there are now several ways for introducing carbon substituents by nucleophilic displacement at the 2-position of pyrrolidines and piperidines[3] not all of these methods show a wide selection of nucleophiles or functional group tolerance.

We have found that a number of carbon nucleophiles, including alkyl, aryl, vinyl or alkynyl organometallics and also silyl enol ethers, silyl ketene acetals, allyl silanes and trimethyl silyl cyanide in the presence of a Lewis acid, undergo reaction with 2-phenylsulphonyl cyclic-amines to give substitution products often in high yield, under mild conditions and with excellent stereoselectivity (scheme 1).

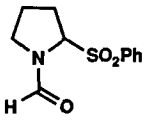


Scheme 1

For this work several piperdine and pyrrolidine sulphones (1-6) have been prepared. In the majority of cases these were synthesised from the corresponding *N*-acyl aminal ethers (7,8 and 10-12) by treatment with benzenesulphinic acid, although the *N*-acyl hemi-aminal (13) has also been used. All of these conversions proceeded in excellent yields provided a basic work-up is used to remove excess acid. While some of these starting aminal derivatives are commercially available (7 and 8) the others (10-13) are readily prepared either by electrochemical oxidation in methanol of the corresponding amide (10) using the Shono procedure[4] or by partial reduction of succinamides.[5,6] The *N*-tosyl sulphone (6) was prepared from **7** by sequential formamide hydrolysis,[7] sulphonation and treatment with benzenesulphinic acid.



(1)



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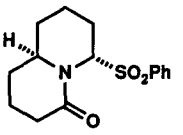
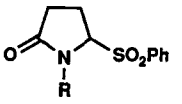
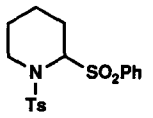


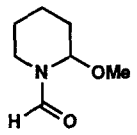
(3)



(4) R=H
(5) R=Bn



(6)



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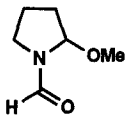

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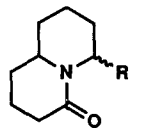
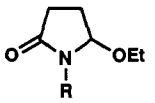
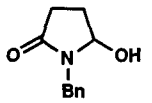


(9) R=H
(10) R=OMe



(11) R=H
(12) R=Bn



(13)

In the first series of displacement reactions we have investigated reactions of sulphones with aryl and vinyl organometallic reagents generated from Grignard reagents and zinc bromide. In some examples organolithium reagents may be employed, however, in these experiments both the addition of magnesium bromide and zinc bromide are necessary to bring about the substitution reaction. Although the reactions fail in the absence of magnesium salts, the precise role of these additives and the nature of the generated organometallic species is uncertain. From the **table 1** it should be noticed that reactions proceed with aryl, heteroaryl, alkynyl, vinyl reagents. Optimum yields were obtained from treatment of the appropriate Grignard reagent (generated from the aryl or vinyl halide or from the acetylene by deprotonation using *iso*-propyl magnesium bromide) with zinc bromide[8] in dry tetrahydrofuran and this species stirred with the sulphone for several hours at room temperature. Normal acidic work-up and extraction affords the substitution products in yields usually greater than 80%.

For substitution reactions with alkyl substituents we have found it necessary to use methylene chloride[9] as the solvent, with ethereal solutions of zinc chloride[10] and Grignard reagent. Once again the reaction procedure is simple and conveniently carried out at room temperature (table 2). The examples show that substitution with primary groups is not surprisingly higher yielding than with secondary or tertiary organometallic species. Although we have not investigated a very wide range of substituents in these reactions we have shown that alkene and acetal

TABLE 1
ARYL, VINYL AND ALKYNYL SUBSTITUTION OF SULPHONES

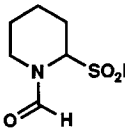
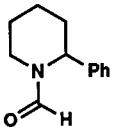
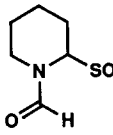
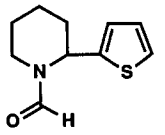
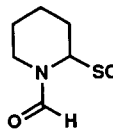
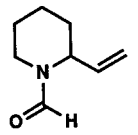
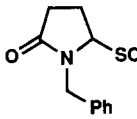
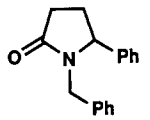
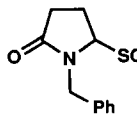
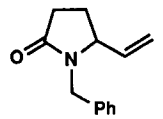
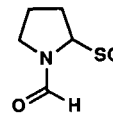
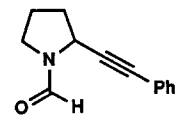
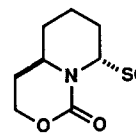
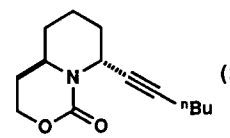
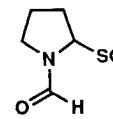
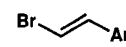
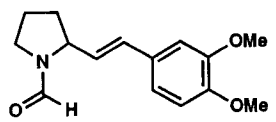
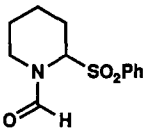
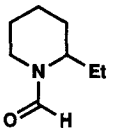
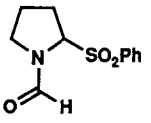
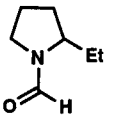
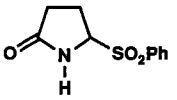
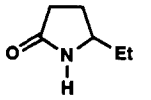
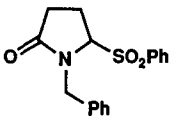
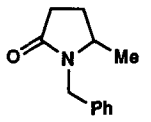
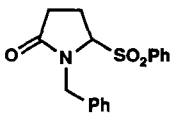
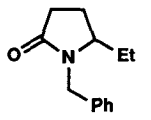
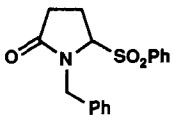
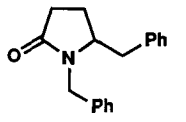
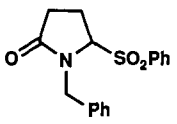
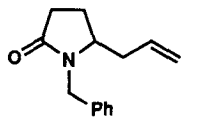
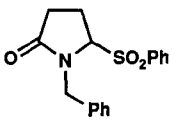
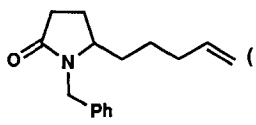
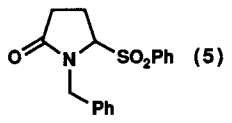
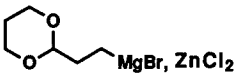
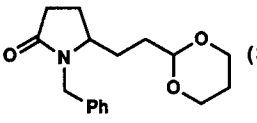
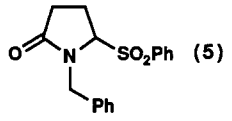
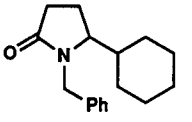
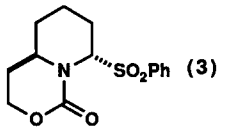
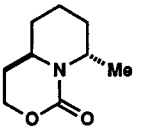
ENTRY	SULPHONE	REAGENTS	PRODUCT		YIELD
1	 (1)	$PhMgBr, ZnBr_2$		(14)	87%
2	 (1)	 $MgBr, ZnBr_2$		(15)	81%
3	 (1)	$CH_2=CHMgBr, ZnBr_2$		(16)	84%
4	 (5)	$PhMgBr, ZnBr_2$		(17)	81%
5	 (5)	$CH_2=CHMgBr, ZnBr_2$		(18)	82%
6	 (2)	$^{i}PrMgBr$, PhC≡CH, $ZnBr_2$		(19)	87%
7	 (3)	$^{i}PrMgBr$, $^{n}BuC\equiv CH$, $ZnBr_2$		(20)	87%
8	 (2)	 Ar, $^{t}BuLI$, $MgBr_2, ZnBr_2$		(21)	86%

TABLE 2
ALKYL SUBSTITUTION OF SULPHONES

ENTRY	SULPHONE	REAGENTS	PRODUCT		YIELD
1	 (1)	$EtMgBr, ZnCl_2$		(22)	16%
2	 (2)	$EtMgBr, ZnCl_2$		(23)	57%
3	 (4)	$EtMgCl, ZnCl_2$		(24)	52%
4	 (5)	$MeMgBr, ZnCl_2$		(25)	85%
5	 (5)	$EtMgCl, ZnCl_2$		(26)	75%
6	 (5)	$PhCH_2MgCl, ZnCl_2$		(27)	84%
7	 (5)	$CH_2{=}CHCH_2MgBr, ZnCl_2$		(28)	92%
8	 (5)	$CH_2{=}CH(CH_2)_3MgBr, ZnCl_2$		(29)	81%

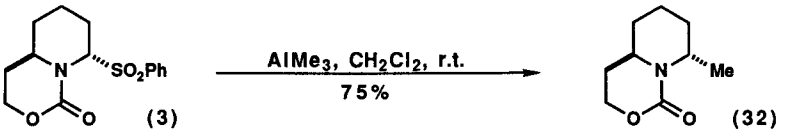
Cont.

TABLE 2 (Continued)
ALKYL SUBSTITUTION OF SULPHONES

ENTRY	SULPHONE	REAGENTS	PRODUCT	YIELD
9	 (5)		 (30)	79%
10	 (5)	c-$C_6H_{11}MgBr$, $ZnCl_2$	 (31)	30%
11	 (3)	MeMgBr, $ZnCl_2$	 (32)	71%

functional groups are tolerated. The *N*-formyl group is also stable to the conditions and can play a role as a protecting group or by later reduction with lithium aluminium hydride afford N-methyl substituent which is commonly found in many alkaloid natural products.

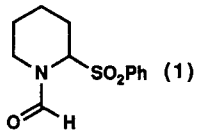
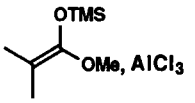
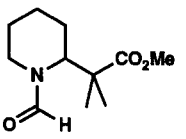
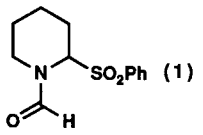
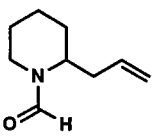
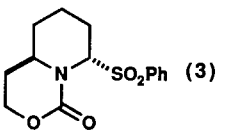
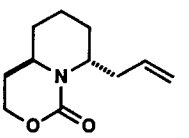
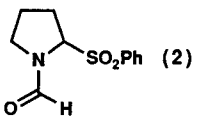
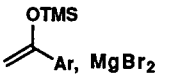
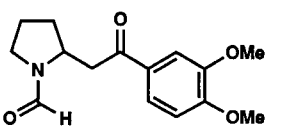
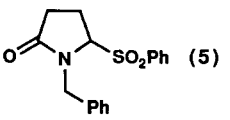
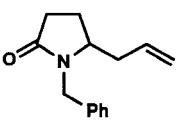
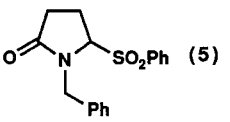
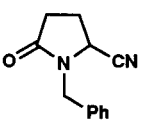
Simple alkyl substituents can be inserted using trialkylaluminiums, thus the methyl product **32** (table 2, entry 12) was also prepared using trimethylaluminium (scheme 2).



Scheme 2

We have also studied the use of silyl enol ethers, silyl ketene acetals, allyl silane and trimethyl silyl cyanide as carbon nucleophiles for displacement of the phenylsulphonyl unit (table 3). As with the cyclic ether series[2] we have found that aluminium chloride conditions give excellent yields at low temperature while with magnesium bromide as the Lewis acid the reaction takes place at 0°C or room temperature. These later conditions are probably more appropriate to larger scale operation.

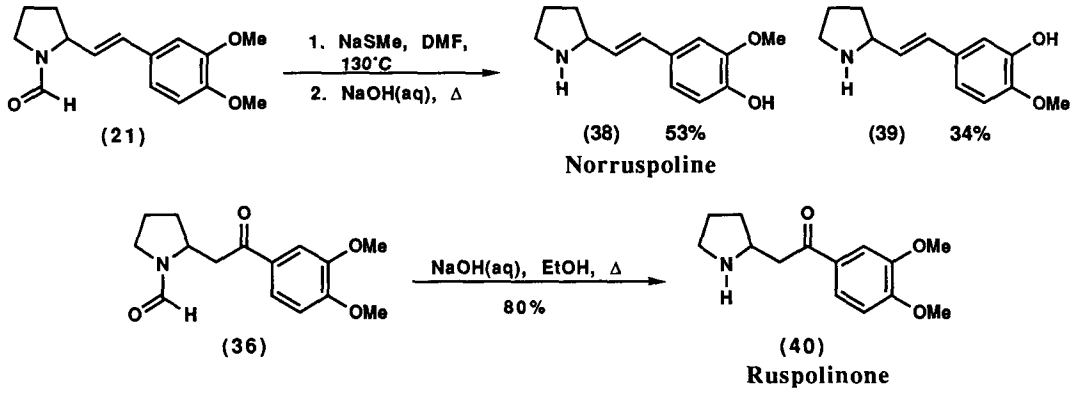
TABLE 3
SUBSTITUTION OF SULPHONES WITH SILYL DERIVATIVES

ENTRY	SULPHONE	REAGENTS	PRODUCT	YIELD
1			 (33)	89%
2			 (34)	90%
3			 (35)	93%
4			 (36)	89%
5			 (28)	69%
6		TMSCN, $MgBr_2$	 (37)	96%

The above displacement reactions of the 2-phenylsulphonyl leaving group constitutes a versatile highly stereoselective method. The method compliments existing literature procedures but we believe it also gives added flexibility with milder conditions.

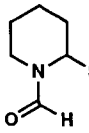
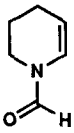
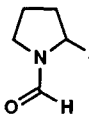
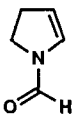
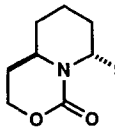
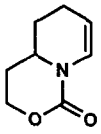
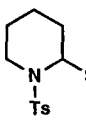
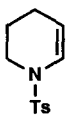
We have illustrated these methods during the synthesis of two alkaloid natural products isolated from the plant *Ruspolia hypercrateriformis*, a member of the *Acanthaceae* family.[11] The first of these compounds, Norruspoline (38), was prepared in 53% overall yield from the product (21, table 1) by deprotection[12] using sodium methanethiolate in DMF at 130°C followed by aqueous hydrolysis of the formamide with sodium hydroxide. The

other regioisomer (39), formed during the demethylation reaction, was also obtained in 34% yield. The substitution product (36, table 3) could be similarly hydrolysed to give the alkaloid Ruspolinone (40) in 80% yield.



Finally, in four examples, we have shown that the 2-phenylsulphonyl group can also be eliminated to afford enamine derivatives by using a mixture of magnesium bromide and trimethylamine under ultrasonication[13] (table 4). The products of these reactions are useful intermediates for further chemical synthesis.[14]

TABLE 4
ELIMINATION OF ANOMERIC SULPHONES

ENTRY	SULPHONE	REAGENTS	PRODUCT	YIELD
1	 (1)	$MgBr_2$, Et_3N,)))))	 (41)	96%
2	 (2)	$MgBr_2$, Et_3N,)))))	 (42)	73%
3	 (3)	$MgBr_2$, Et_3N,)))))	 (43)	85%
4	 (6)	$MgBr_2$, Et_3N,)))))	 (44)	96%

These results on the displacement of 2-phenylsulphonyl piperidines and pyrrolidines together with the work reported for the corresponding cyclic ether series provides convincing evidence of the versatility of these systems in the formation of carbon-carbon bonds at positions adjacent to the heteroatom.

Acknowledgements: *We thank the SERC (Instant Award to DSB), Rhône-Poulenc Santé (study leave grant to PC), University of Lund, Sweden (study leave to TH), Schering Agrochemicals Ltd for financial support and Drs. G. Kneen and P. Dudfield for useful discussions.*

Experimental:

Solutions were dried over anhydrous sodium sulphate or anhydrous magnesium sulphate and solvents were purified by standard methods.[15] The products were purified by column chromatography on Merck silica gel 60 (Art. 9385 230-400 mesh) under pressure unless otherwise stated. HPLC was carried out on a 21.4mm Dynamax-60A 8μm silica gel column using 4% ^{i}PrOH in 40-60 petrol as the eluent. Melting points were measured on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 983G spectrophotometer as liquid films or chloroform solutions. ^{1}H NMR spectra were recorded in $CDCl_3$ on Bruker WM-250, Jeol GSX-270 or Bruker AM-500 spectrometers. Mass spectra were recorded on a VG Micromass 7070B instrument.

Preparation of the Sulphones:

2-(Phenylsulphonyl)-1-piperidinecarboxaldehyde (1).- A mixture of 2-methoxy-1-piperidinecarboxaldehyde (7) (1.35 ml, 1.43 g, 10 mmol), benzenesulphinic acid (4.26 g, 30 mmol), and anhydrous calcium chloride (3.33 g, 30 mmol) in dry dichloromethane (40 ml) was stirred at room temperature for 20 hours under argon. The reaction mixture was quenched with water and extracted with dichloromethane. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrating *in vacuo*. Purification by chromatography (1:3 to 1:1 ethyl acetate:petrol) gave **1** (2.33 g, 92%) as a white solid, m.p. 82-82.5°C; ν_{max} ($CHCl_3$) 3012, 2953, 1676, 1446, 1396, 1319, 1235, 1144, 992, 719, and 687 cm^{-1}; δ_H (270 MHz) 1.35-1.55, 1.65-1.92, 2.12-2.35, 2.63-2.80 (6H, m, 3-H 4-H 5-H), 3.29 (0.25H, td, *J* 13.2, 3.1 Hz, 6-H_{ax}), 3.49 (0.75H, br dd, *J* 13.2, 4.3 Hz, 6-H_{eq}), 3.83 (0.75H, td, *J* 13.2, 2.8 Hz, 6-H_{ax}), 4.29 (0.25H, br dd, *J* 13.2, 4.4 Hz, 6-H_{eq}), 4.48 (0.25H, d, *J* 6.3 Hz, 2-H), 5.51 (0.75H, d, *J* 6.8 Hz, 2-H), 7.31 (0.25H, s, CHO), 7.50-7.72 (3H, m, *m*-H *p*-H), and 7.80-7.92 (2.75H, m, *o*-H CHO); m/z 253 (M^+, 0.1%) and 112; (Found: C, 56.91; H, 5.96; N, 5.38. $C_{12}H_{15}NO_3S$ requires C, 56.90; H, 5.97; N, 5.53%).

2-(Phenylsulphonyl)-1-pyrrolidinecarboxaldehyde (2).- A mixture of 2-methoxy-1-pyrrolidinecarboxaldehyde (8) (1.29 g 10 mmol), benzenesulphinic acid (4.26 g, 30 mmol), and anhydrous calcium chloride (3.33 g, 30 mmol) in dry dichloromethane (40 ml) was stirred at room temperature for 18 hours under argon. The reaction mixture was quenched with water and extracted with dichloromethane. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrating *in vacuo*. Purification by chromatography (1:1:2 to 1:1:0 then 1:2:0 dichloromethane:ethyl acetate:petrol) gave **2** (2.13 g, 89%) as a white solid, m.p. 123-124°C; ν_{max} ($CHCl_3$) 3021, 2895, 1675, 1447, 1371, 1319, 1309, 1148, 1085, 720, and 687 cm^{-1}; δ_H (270 MHz) 1.80-2.03, 2.18-2.38, 2.50-2.63, 2.68-2.78 (4H, m, 3-H 4-H), 3.36 (0.77H, dt, *J* 12.4, 6.2 Hz, 5-H), 3.55-3.78 (1.23H, m, 5-H), 4.84 (0.77H, dd, *J* 8.3, 2.0 Hz, 2-H), 5.36 (0.23H, dd, *J* 7.9, 3.0 Hz, 2-H), 7.50-7.75 (3H, m, *m*-H *p*-H), 7.80-7.92 (2.77H, m, *o*-H CHO), and 7.98 (0.23H, s, CHO); m/z 98 (M^+-$PhSO_2H$, 100%); (Found: C, 55.17; H, 5.42; N, 5.80. $C_{11}H_{13}NO_3S$ requires C, 55.21; H, 5.48; N, 5.85%).

***cis*-Hexahydro-8-(phenylsulphonyl)-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (3).-** A solution of hexahydro-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (9) (1.55 g, 10 mmol), and tetraethylammonium *p*-toluenesulphonate (0.5 g) in methanol (100 ml) was electrolysed (16 mA, 95 hours) using the procedure of T. Shono.[4] The solution was concentrating *in vacuo* and the residue dissolved in dichloromethane (40 ml). Benzenesulphinic acid (4.26 g, 30 mmol), and anhydrous calcium chloride (3.33 g, 30 mmol) were added and the mixture was stirred at room temperature for 18 hours under argon. The reaction was quenched with water and extracted with dichloromethane. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrated *in vacuo*.

Purification by chromatography (1:3 to 1:1 ethyl acetate:petrol) gave **3** (0.53 g, 18%) as a white solid, m.p. 124-124.5°C; ν_{max} ($CHCl_3$) 2952, 1695, 1422, 1310, 1273, 1147, and 687 cm^{-1}; δ_H (270 MHz) 1.20-1.37, 1.70-2.00, 2.05-2.37, 2.60-2.73 (8H, m, 4-H 5-H 6-H 7-H), 4.00-4.23 (3H, m, 3-H 4a-H), 5.69 (1H, d, *J* 5.6 Hz, 8-H_{eq}), 7.55-7.65 (2H, m, *m*-H), 7.65-7.73 (1H, m, *p*-H), and 7.93-7.98 (2H, m, *o*-H); m/z 154 (M^+-$PhSO_2$, 53%), 153, 127, and 77; (Found: C, 56.89; H, 5.77; N, 4.58. $C_{14}H_{17}NO_4S$ requires C, 56.93; H, 5.80; N, 4.74%).

5-(Phenylsulphonyl)-2-pyrrolidinone (4).- A mixture of 5-ethoxy-2-pyrrolidinone (11) (0.87 g, 6.7 mmol)[5], benzenesulphinic acid (2.90 g, 20.4 mmol), and anhydrous calcium chloride (2.26 g, 20.4 mmol) in dry dichloromethane (50 ml) was stirred at room temperature for 48 hours under argon. The reaction mixture was quenched with water and extracted with dichloromethane. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrating *in vacuo*. Purification by chromatography (1:1:1 to 1:1:0 then 2:1:0 ethyl acetate:dichloromethane:petrol) gave **4** (1.25 g, 83%) as a white solid, m.p. 124°C; ν_{max} (film) 3318, 2689, 1700, 1445, 1307, 1260, 1139, 1082, 764, 728, and 690 cm^{-1}; δ_H (500 MHz) 1.93-2.04 (2H, m, 4-H), 2.44-2.59 (2H, m, 3-H), 4.66 (1H, dt, *J* 8.56, 1.5 Hz, 5-H), 6.02 (1H, br s, NH) 7.61-7.65 (2H, m, *m*-H), 7.73-7.76 (1H, m, *p*-H), and 7.92-7.94 (2H, m, *o*-H); m/z 84 (M^+-$PhSO_2$, 42%), 83, 78, and 77; (Found: C, 53.30; H, 4.74; N, 5.93. $C_{10}H_{11}NO_3S$ requires C, 53.31; H, 4.92; N, 6.21%).

1-(Phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5).- Method a). A mixture of 5-ethoxy-1-(phenylmethyl)-2-pyrrolidinone (12) (8.35 g, 38 mmol), benzenesulphinic acid (16.24 g, 114 mmol), and anhydrous calcium chloride (12.68 g, 114 mmol) in dry dichloromethane (150 ml) was stirred at room temperature for 20 hours under argon. The reaction mixture was quenched with water and extracted with dichloromethane. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrating *in vacuo*. Purification by chromatography (20:10:70 to 40:20:40 ethyl acetate:dichloromethane:petrol) gave **5** (9.37 g, 78%) as a white solid, m.p. 100°C; ν_{max} (film) 1706, 1445, 1396, 1305, 1220, 1203, 1146, 1130, 1082, 738, 690, and 656 cm^{-1}; δ_H (270 MHz) 1.62-1.74, 2.04-2.40 (4H, m, 3-H 4-H), 4.26 (1H, dd, *J* 14.6, 1.0 Hz, CHPh), 4.55 (1H, br d, *J* 8.2 Hz, 5-H), 5.27 (1H, d, *J* 14.4 Hz, CHPh), 7.19-7.38 (5H, m, Ph), 7.60-7.67 (2H, m, *m*-H), 7.73-7.79 (1H, m, *p*-H), and 7.88-7.92 (2H, m, *o*-H); m/z 174 (M^+-$PhSO_2$, 10%), 173, 142, 110, and 91; (Found: C, 64.64; H, 5.29; N, 4.58. $C_{17}H_{17}NO_3S$ requires C, 64.74; H, 5.43; N, 4.44%).

Method b). A mixture of 5-hydroxy-1-(phenylmethyl)-2-pyrrolidinone (13) (1.13 g, 5.9 mmol), benzenesulphinic acid (2.52 g, 17.7 mmol), and anhydrous calcium chloride (1.96 g, 17.7 mmol) in dry dichloromethane (30 ml) was stirred at room temperature for 18 hours under argon. The reaction mixture was quenched with water and extracted with dichloromethane. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrating *in vacuo*. Purification by chromatography (15:10:75 to 25:10:65 then 35:15:50 ethyl acetate:dichloromethane:petrol) gave **5** (1.58 g, 85%) as a white solid, m.p. 100°C; identical with previous sample by i.r., n.m.r. and mass spectroscopy.

1-[(4-Methylphenyl)sulphonyl]-2-(phenylsulphonyl)piperidine (6) 2-Methoxy-1-piperidinecarboxaldehyde (7) (7.83 g, 55 mmol) was dissolved in a methanolic solution of hydrogen chloride (165 ml, 3.3 % in weight) and the mixture was heated at reflux for 4 hours. The solvent was evaporated *in vacuo* to give 2-methoxypiperidine hydrochloride (7.88 g)[7] as a yellow solid. This solid was dissolved in a stirring solution of triethylamine (18.2 ml, 13.21 g, 131 mmol) in dry dichloromethane (220 ml) then *p*-toluenesulphonyl chloride (11.01 g, 58 mmol) was added portionwise at room temperature. The mixture was stirred at room temperature under argon for 2 hours, quenched with 1 N HCl and extracted with dichloromethane. The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give an orange solid which was partially purified on a pad of silica gel (1:9 ethyl acetate:petrol) to give a mixture of 1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulphonyl]pyridine and 1-[(4-methylphenyl)sulphonyl]-2-(methoxy)piperidine (89:11) as a white solid. A solution of this solid and benzenesulphinic acid (7.87 g, 55 mmol) in dry dichloromethane (550 ml)was stirred at room temperature for 16 hours under argon. The reaction mixture was quenched with water and extracted with dichloromethane. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrated *in vacuo* to give a pale yellow solid. This solid was recrystallised (dichloromethane/petrol) to give **6** (15.44 g, 74 %) as a white solid, m.p. 64°C (dec.); ν_{max} (film) 2952, 1596, 1445, 1359, 1338, 1307, 1159, 1148, 1083, 930, 817, 729, 695, 658, and 624 cm^{-1}; δ_H (270 MHz) 1.48-1.63 (4H, m, 4-H 5-H), 2.01-2.22 (1H, m, 3-H), 2.41 (3H, s, *p*-CH_3), 2.56-2.68 (1H, m, 3-H), 3.63 (1H, br d, *J* 14.1 Hz, 6-H), 3.78 (1H, td, *J* 14.3, 2.7 Hz, 6-H), 5.18 (1H, d, *J* 6.8 Hz, 2-H), 7.19-7.25 (2H, m, *m*-H), 7.45-7.82 (5H, m, SO_2Ph), and 7.90-8.01 (2H, m, *o*-H); m/z 237 (M^+-$PhSO_2H$, 1%), 158, 142, 141, 125, 109, 91, 78, and 77; (Found: C, 56.88; H, 5.39; N, 3.40. $C_{18}H_{21}NO_4S$ requires C, 56.97; H, 5.58; N, 3.69%).

Hexahydro-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (9).- A mixture of 2-piperidine-ethanol (6.46 g, 50 mmol), dimethyl carbonate (25 ml), methanol (25 ml), and a solution of sodium methoxide in methanol (1 ml) was stirred at room temperature under argon for 6 days. The reaction was quenched with water (1 ml) and concentrating *in vacuo*. Then saturated aqueous NH_4Cl was added and the mixture extracted with dichloromethane. The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Distillation (kugelrohr) (b.p. *ca.* 200°C, 0.1 mmHg) gave **9** (7.62 g, 98%) as a colourless oil; ν_{max} (film) 2933, 2856, 1684, 1477, 1439, 1259, 1125, 1014, and 760 cm^{-1}; δ_H (270 MHz) 1.25-1.90 (7H, m, 4-H_{ax} 5-H 6-H 7-H), 2.12 (1H, dddd, *J* 14.2, 6.1, 5.6, 3.2 Hz, 4-H_{eq}), 2.60-2.73 (1H, m, 8-H_{ax}), 3.23-3.35 (1H, m, 4a-H_{ax}), 4.12 (1H, ddd, *J* 11.0, 9.0, 3.2 Hz, 3-H_{ax}), 4.20 (1H, ddd, *J* 11.0, 5.6, 4.0 Hz, 3-H_{eq}), and 4.37-4.47 (1H, m, 8-H_{eq}); m/z 155 (M^+, 86%) and 126; (Observed M^+, 155.0946. Calc. for $C_8H_{13}NO_2$ M, 155.0946).

5-Ethoxy-1-(phenylmethyl)-2-pyrrolidinone (12).- Approximately every 15 minutes for 4 hours, 7-8 drops of 2N hydrochloric acid was added to a stirred mixture of *N*-benzylsuccinimide (9.45 g, 50 mmol)[16] and sodiumborohydride (2.87 g, 76 mmol) in ethanol (220 ml) at 0°C.[5] Then the excess sodiumborohydride was destroyed by slowly adding 2N hydrochloric acid until pH=3 (*ca.* 15 minutes). The mixture was stirred for an additional 30 minutes at 5°C and then evaporated *in vacuo* to dryness. The residue was extracted with chloroform and the combined extracts were washed with saturated aqueous NaCl, dried ($MgSO_4$) and concentrated *in vacuo* to afforded a brown oil. Purification by chromatography (30:20:50 ethyl acetate:dichloromethane:petrol) gave **12** (9.85 g, 90 %) as a colourless oil; ν_{max} (film) 2927, 1679, 1497, 1454, 1360, 1284, 1168, 1071, 988, 950, 705, and 663 cm^{-1}; δ_H (270 MHz) 1.17 (3H, t, *J* 6.96 Hz, CH_3), 1.90-2.16 (2H, m, 4-H), 2.30-2.42 (1H, m, 3-H), 2.52-2.65 (1H, m, 3-H), 3.33-3.43 (2H, m, OCH2), 4.03 (1H, d, *J* 14.6 Hz, CHPh), 4.76 (1H, dm, *J* 6.23 Hz, 5-H), 4.94 (1H, d, *J* 14.6 Hz, CHPh), and 7.23-7.36 (5H, m, Ph); m/z 219 (M^+, 18%), 174, 146, 104, 91, and 65; (Found: C, 71.19; H, 7.68; N, 6.30. $C_{13}H_{17}NO_2$ requires C, 71.21; H, 7.81; N, 6.39%).

5-Hydroxy-1-(phenylmethyl)-2-pyrrolidinone (13).- Sodiumdiethyldihydroaluminate (3.87 ml, 2 M solution in toluene, 7.75 mmol) was added dropwise to a stirred solution of *N*-benzylsuccinimide (1.464 g, 7.75 mmol)[16] in dry THF (50 ml) at -78°C under argon.[6] The reaction was stirred for 30 minutes at -78°C, quenched by adding 10 % H_2O in THF and stirred for further 5 minutes before allowing the mixture to warm to room temperature. Saturated aqueous NH_4Cl was added and the mixture was filtered under suction to remove the aluminium salts. The filtrate was extracted with dichloromethane, the combined extracts were washed with water, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by chromatography (30:20:50 ethyl acetate:dichloromethane:petrol) gave **13** (1.30 g, 88 %) as a white solid, m.p. 108°C; ν_{max} (film) 3203, 2926, 1638, 1477, 1333, 1262, 1155, 1076, 997 and 700 cm^{-1}; δ_H (270 MHz) 1.83-1.93 (1H, m, 4-H), 2.22-2.45 (3H, m, 3-H 4-H OH), 2.58-2.70 (1H, m, 3-H), 4.23 (1H, d, *J* 14.6 Hz, CHPh), 4.84 (1H, d, *J* 14.9 Hz, CHPh), 5.06-5.12 (1H, m, 5-H), and 7.23-7.38 (5H, m, Ph); m/z 191 (M^+, 17%), 173, 146, 106, 91, and 65; (Found: C, 69.34; H, 6.85; N, 7.29. $C_{11}H_{13}NO_2$ requires C, 69.09; H, 6.85; N, 7.32%).

General Procedure for Anomeric Substitution with Aryl- or Vinyl-Grignard Reagents.- Anhydrous zinc bromide (1.2 equiv., 1M solution in THF) was added to a THF solution (4 ml/mmol) of the Grignard reagent prepared from the appropriate aryl or vinyl bromide (2.0 equiv.), and magnesium (2.1 equiv.). The mixture was stirred at room temperature under argon for 30 minutes to afford the organozinc species. A solution of the sulphone (1.0 equiv.) in dry THF (4 ml/mmol) was then added and stirring continued at room temperature for 3-24 hours. The reaction was quenched with 1N HCl and extracted with ether or dichloromethane, the combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Products were purified by chromatography.

2-Phenyl-1-piperidinecarboxaldehyde (14).- Reaction of 2-(phenylsulphonyl)-1-piperidinecarboxaldehyde (1) (253 mg, 1.0 mmol) with the organozinc prepared from bromobenzene and purification by chromatography (1:2 ethyl acetate:petrol) gave **14** (165 mg, 87%) as a colourless oil; ν_{max} (film) 3057, 2938, 2862, 1663, 1449, 1420, 1246, 1222, 1154, 995, 749, 727, and 701 cm^{-1}; δ_H (270 MHz) 1.47-1.97, 2.37-2.45 (6H, m, 3-H 4-H 5-H), 2.96 (0.45H, td, *J* 12.5, 3.8 Hz, 6-H_{ax}), 3.08 (0.55H, td, *J* 13.0, 3.5 Hz, 6-H_{ax}), 3.45 (0.45H, br d, *J* 12.5 Hz, 6-H_{eq}), 4.09 (0.55H, dt, *J* 13.0, 3.5 Hz, 6-H_{eq}), 4.76 (0.55H, t, *J* 4.3 Hz, 2-H), 5.75 (0.45H, dd, *J* 3.8, 1.3 Hz, 2-H), 7.23-7.43 (5H, m, Ar-H), 8.15 (0.55H, s, CHO), and 8.27 (0.45H, s, CHO); m/z 189 (M^+, 72%), 188, 160, 112, 104, and 91; (Found: C, 75.94; H, 8.16; N, 7.21. $C_{12}H_{15}NO$ requires C, 76.16; H, 7.99; N, 7.40%).

2-Thien-2-yl-1-piperidinecarboxaldehyde (15).- Reaction of 2-(phenylsulphonyl)-1-piperidinecarboxaldehyde (1) (253 mg, 1.0 mmol) with the organozinc prepared from 2-bromothiophene and purification by chromatography (1:2 ethyl acetate:petrol) gave

compound **15** (158 mg, 81%) as a colourless oil; ν_{max} (film) 2938, 2860, 1670, 1425, 1269, 1248, 988, and 703 cm^{-1}; δ_H (270 MHz) 1.37-2.33 (6H, m, 3-H 4-H 5-H), 2.92 (0.5H, ddd, *J* 13.4, 12.0, 3.4 Hz, 6-H_{ax}), 3.23 (0.5H, td, *J* 13.0, 3.0 Hz, 6-H_{ax}), 3.44 (0.5H, dd, *J* 13.0, 4.0 Hz, 6-H_{eq}), 4.18 (0.5H, dt, *J* 13.4, 3.7 Hz, 6-H_{eq}), 4.97 (0.5H, br s, 2-H), 5.89 (0.5H, d, *J* 4.6 Hz, 2-H), 6.85-6.90 (1H, m, 3'-H), 6.93-7.03 (1H, m, 4'-H), 7.18-7.28 (1H, m, 5'-H), 8.14 (0.5H, s, CHO), and 8.19 (0.5H, s, CHO); m/z 195 (M^+, 100%), 166, 97, and 83; (Found: C,61.65; H,6.99; N,7.02. $C_{10}H_{13}NOS$ requires C,61.51; H,6.71; N,7.17%).

2-Ethenyl-1-piperidinecarboxaldehyde (16).- Reaction of 2-(phenylsulphonyl)-1-piperidinecarboxaldehyde (1) (253 mg, 1.0 mmol) with the organozinc prepared from vinyl bromide (3.0 equiv.), and purification by chromatography (1:2 ethyl acetate:petrol) gave compound **16** (105 mg, 84%) as a colourless oil; ν_{max} (film) 2938, 2859, 1670, 1402, 1249, 1000, and 922 cm^{-1}; δ_H (270 MHz) 1.27-1.82 (6H, m, 3-H 4-H 5-H), 2.93 (0.55H, td, *J* 13.0, 2.7 Hz, 6-H_{ax}), 3.16 (0.45H, td, *J* 13.1, 2.6 Hz, 6-H_{ax}), 3.36 (0.45H, dd, *J* 13.1, 4.1 Hz, 6-H_{eq}), 3.98 (0.55H, dt, *J* 13.0, 3.7 Hz, 6-H_{eq}), 4.12 (0.55H, br s, 2-H), 5.00-5.27 (2.45H, m, 2-H 2'-H), 5.63-5.87 (1H, m, 1'-H), and 8.05 (1H, s, CHO); m/z 139 (M^+, 93%), 112, and 110; (Found: C,69.03; H,9.63; N,9.97. $C_8H_{13}NO$ requires C,69.03; H,9.41; N,10.06%).

5-Phenyl-1-(phenylmethyl)-2-pyrrolidinone (17).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5) (78.8 mg, 0.25 mmol) with the organozinc prepared from bromobenzene and purification by chromatography (1:1:8 to 2:1:7 then 3:2:5 ethyl acetate:dichloromethane:petrol) gave **17** (53.7 g, 81%) as a colourless oil; ν_{max} (film) 2919, 1683, 1491, 1451, 1410, 1362, 1253, 1153, 1079, 761, and 704 cm^{-1}; δ_H (270 MHz) 1.33-1.97 (1H, m, 4-H), 2.33-2.71 (3H, m, 3-H 4-H), 3.48 (1H, d, *J* 14.6 Hz, CHPh), 4.41 (1H, dd, *J* 7.9, 5.5 Hz, 5-H), 5.12 (1H, d, *J* 14.4 Hz, CHPh), and 7.05-7.41 (10H, m, Ph); m/z 251 (M^+, 100%), 189, 160, 146, 132, 118, 104, and 91; (Found: C, 81.06; H, 6.82; N, 5.62. $C_{17}H_{17}NO$ requires C, 81.24; H, 6.82; N, 5.57%).

5-Ethenyl-1-(phenylmethyl)-2-pyrrolidinone (18).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5) (78.8 mg, 0.25 mmol) with the organozinc prepared from vinyl bromide and purification by chromatography (10:5:85 to 20:10:70 ethyl acetate:dichloromethane:petrol) gave **18** (41.2 mg, 82%) as a colourless oil; ν_{max} (film) 3062, 2977, 1684, 1493, 1357, 1250, 1168, 1081, 993, 885, 819, and 681 cm^{-1}; δ_H (270 MHz) 1.69-1.81 (1H, m, 4-H), 2.10-2.24 (1H, m, 4-H), 2.32-2.70 (2H, m, 3-H), 3.81-3.91 (1H, m, 5-H), 3.85 (1H, d, *J* 14.6 Hz, CHPh), 4.99 (1H, *J* 14.6 Hz, CHPh), 5.14 (1H, dd, *J* 17.0, 0.7 Hz, 2'-H), 5.22 (1H, dd, *J* 10.0, 0.7 Hz, 2'-H), 5.65 (1H, ddd, *J* 17.0, 10.0, 8.4 Hz, 1'-H), and 7.18-7.35 (5H, m, Ph); m/z 201 (M^+, 78%), 174, 146, 104, and 91; (Found: C, 77.44; H, 7.73; N, 6.94. $C_{13}H_{15}NO$ requires C, 77.58; H, 7.51; N, 6.96%).

General Procedure for Anomeric Substitution with Alkynyl-Grignard Reagents- A mixture of *iso*-propyl magnesium chloride (2.0 equiv., 2M solution in THF), and the appropriate alkyne (2.0 equiv.) in dry THF (2 ml/mmol) was stirred at room temperature for 1 hour to prepare the alkynyl Grignard reagent (for 1-hexyne, the solution was heated at reflux for 1-2 hours in order to form 1-hexynyl magnesium bromide). This solution was treated with anhydrous zinc bromide (1.2 equiv., 1M solution in THF) at room temperature for 30 minutes under argon to afford the organozinc species. A solution of the sulphone (1.0 equiv.) in dry THF (4 ml/mmol) was then added and stirring continued at room temperature for 18-24 hours. The reaction was quenched with 1N HCl and extracted with ether or dichloromethane, the combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Products were purified by chromatography.

2-(2-Phenylethynyl)-1-pyrrolidinecarboxaldehyde (19).- Reaction of 2-(phenylsulphonyl)-1-pyrrolidinecarboxaldehyde (2) (120 mg, 0.5 mmol) with the organozinc prepared from phenylacetylene and purification by chromatography (1:9 to 1:4 ethyl acetate:petrol) gave **19** (86.8 mg, 87 %) as a light yellow oil; ν_{max} (film) 3058, 2977, 2879, 1664, 1487, 1380, 1299, 1247, 1175, 760, 716, and 693 cm^{-1}; δ_H (270 MHz) 1.84-2.36 (4H, m, 3-H 4-H), 3.43-3.76 (2H, m, 5-H), 4.67 (0.78H, t, *J* 6.1 Hz, 2-H), 4.77-4.95 (0.22H, m, 2-H), 7.25-7.56 (5H, m, Ph), 8.25 (0.22H, s, CHO), and 8.47 (0.78H, s, CHO); m/z 199 (M^+, 17%), 170, 122, 115, 105, 86, and 84; (Found: C, 78.28; H, 6.15; N, 7.00,. $C_{13}H_{13}NO$ requires C, 78.36; H, 6.58; N, 7.03%).

***cis*-Hexahydro-8-hex-1-ynyl-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (20).-** Reaction of hexahydro-8-(phenylsulphonyl)-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (3) (103 mg, 0.35 mmol) with the organozinc prepared from 1-hexyne and purification by chromatography (1:9 to 1:1 ethyl acetate:petrol) gave **20** (71 mg, 87%) as a colourless oil; ν_{max} (film) 2930, 1694, 1474, 1428, 1372,

1274, 1232, 1214, 1121, 1099, and 760 cm^{-1}; δ_H (270 MHz) 0.89 (3H, t, *J* 7.2 Hz, 6'-H), 1.15-1.95 (11H, m, 4-H_{ax} 5-H 6-H 7-H 4'-H 5'-H), 2.05-2.17 (1H, m, 4-H_{eq}), 2.17 (1H, t, *J* 6.8 Hz, 3'-H), 2.18 (1H, t, *J* 6.8 Hz, 3'-H), 3.65-3.75 (1H, m, 4a-H_{ax}), 4.05-4.23 (2H, m, 3-H), and 5.35 (1H, d, *J* 2.2 Hz, 8-H_{eq}); m/z 235 (M^+, 23%), 234, 207, 193, and 120; (Found: C, 71.47; H, 9.10; N, 5.76,. $C_{14}H_{21}NO_2$ requires C, 71.46; H, 8.99; N, 5.95%).

(*E*)-2-[2-(3,4-Dimethoxyphenyl)ethenyl]-1-pyrrolidinecarboxaldehyde (21).- ^{t}Butyl lithium (1.24 ml, 1.7 M in pentane, 2.1 mmol) was added dropwise to a stirred solution of (*E*)-β-bromo-3,4-dimethoxystyrene (243 mg, 1.0 mmol)[17] in dry THF (3 ml) at -78°C under argon. The mixture was stirred at -78°C for 10 minutes then anhydrous zinc bromide (0.6 ml, 1M solution in THF, 0.6 mmol), and magnesium bromide etherate (258 mg, 1.0 mmol) were added. The mixture was allowed to warm to room temperature, stirred for 30 minutes to form the organozinc species and then a solution of 2-(phenylsulphonyl)-1-pyrrolidinecarboxaldehyde (2) (120 mg, 0.5mmol) in dry THF (3 ml) was added. The reaction was stirred for 18 hours, quenched with saturated aqueous NaCl and extracted with ether, the combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by chromatography (3:1 ethyl acetate:petrol to ethyl acetate) gave **21** (113 mg, 86%) as a white solid, m.p. 72-73.5°C; ν_{max} (film) 2955, 1662, 1601, 1583, 1512, 1263, 1140, 1025, 970, 861, 805, 764, 733, and 700 cm^{-1}; δ_H (270 MHz) 1.75-2.25, (4H, m, 3-H 4-H), 3.45-3.67 (2H, m, 5-H), 3.87 (0.45H, s, OMe), 3.88 (0.45H, s, OMe), 3.89 (2.55H, s, OMe), 3.91 (2.55H, s, OMe), 4.38 (0.85H, q, *J* 6.8 Hz, 2-H), 4.70-4.77 (0.15H, m, 2-H), 5.96 (0.85H, dd, *J* 15.9, 6.8 Hz, 1'-H), 6.00 (0.15H, dd, *J* 15.9, 6.1 Hz, 1'-H), 6.43 (0.15H, d, *J* 15.9 Hz, 2'-H), 6.45 (0.85H, d, *J* 15.9 Hz, 2'-H), 6.78-7.05 (3H, m, ArH), 8.25 (0.85H, s, CHO), and 8.35 (0.15H, s, CHO); m/z 261 (M^+, 100%), 190, 151, and 70; (Found: C, 68.86; H, 7.54; N, 5.34. $C_{15}H_{19}NO_3$ requires C, 68.94; H, 7.33; N, 5.36%).

General Procedure for Anomeric Substitution with Alkyl-Grignard Reagents.- The Grignard reagent (2 equiv., 0.2-3M solution in ether) was added to a solution of anhydrous zinc chloride (1.2 equiv., 1M solution in ether) in dry dichloromethane (5 ml/mmol), and the mixture was stirred at room temperature under argon for 30 minutes to afford the organozinc species. A solution of the sulphone (1.0 equiv.) in dry dichloromethane (5 ml/mmol) was then added and stirring continued at room temperature for 8-24 hours. The reaction was quenched with saturated aqueous NH_4Cl or 1N HCl and extracted with ether or dichloromethane, the combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Products were purified by chromatography.

2-Ethyl-1-piperidinecarboxaldehyde (22).- Reaction of 2-(phenylsulphonyl)-1-piperidinecarboxaldehyde (1) (152 mg, 0.6 mmol) with the organozinc prepared from ethyl bromide and purification by chromatography (1:9 ethyl acetate:petrol) gave **22** (13.5 g, 16%) as a colourless oil; ν_{max} (film) 2934, 2866, 1655, 1411, 1354, 1283, 1220, 1130, 1046, and 722 cm^{-1}; δ_H (270 MHz) 0.81-0.88 (3H, m, CH_3), 1.16-1.76 (8H, m, 3-H 4-H 5-H 1'-H), 2.65 (0.5H, td, *J* 13.1, 2.9 Hz, 6-H), 3.11 (0.5H, td, *J* 13.0, 3.2 Hz, 6-H), 3.29-3.43 (1H, m, 6-H) 4.16-4.25 (0.5H, m, 2-H), 4.36-4.47 (0.5H, m, 2-H), 8.01 (0.5H, s, CHO), and 8.03 (0.5H, s, CHO); m/z 141(M^+, 12%), 112, 84, 82, and 68; (Found: C, 67.89; H, 10.44; N, 9.74. $C_8H_{15}NO$ requires C, 68.04; H, 10.71; N, 9.92%).

2-Ethyl-1-pyrrolidinecarboxaldehyde (23).- Reaction of 2-(phenylsulphonyl)-1-pyrrolidinecarboxaldehyde (2) (239 mg, 1 mmol) with the organozinc prepared from ethyl bromide and purification by chromatography (1:9 to 2:8 ethyl acetate:petrol) gave **23** (72.6 mg, 57%) as a colourless oil; ν_{max} (film) 2965, 2875, 1668, 1457, 1414, 1383, 1331, 1193, 1161, and 699 cm^{-1}; δ_H (270 MHz) 0.82-0.93 (3H, m, CH_3), 1.30-2.05 (6H, m, 3-H 4-H 1'-H), 3.26-3.42 (1H, m, 5-H), 3.47-3.49 (1H, m, 5-H), 3.50-3.71 (0.73H, m, 2-H) 3.87-3.96 (0.27H, m, 2-H), and 8.22 (1H, s, CHO); m/z 127 (M^+, 25%), 98, 86, 84, 70 and 68; (Found: C, 66.30; H, 10.64; N, 11.10. $C_7H_{13}NO$ requires C, 66.11; H, 10.30; N, 11.01%).

5-Ethyl-2-pyrrolidinone (24).- Reaction of 5-(phenylsulphonyl)-2-pyrrolidinone (4) (135 mg, 0.6 mmol) in dry dichloromethane (9 ml) with the organozinc prepared from ethyl bromide and purification by chromatography (1:0:9 to 7:1:2 ethyl acetate:dichloromethane:petrol) gave **24** (35.3 mg, 52%) as a colourless oil; ν_{max} (film) 2963, 2928, 2876, 1683, 1458, 1383, 1310, 1265, 1070, 743, and 648 cm^{-1}; δ_H (270 MHz) 0.92 (3H, t, *J* 7.45 Hz, CH_3), 1.45-1.75 (3H, 2 m, 4-H 1'-H), 2.15-2.38 (3H, m, 4-H 3-H), 3.54-3.61 (1H, m, 5-H), and 6.51 (1H, br s, NH); m/z 113 (M^+, 6%), 88, 86, 84, and 49; (Found: C, 63.51; H, 9.75; N, 12.31. $C_6H_{11}NO$ requires C, 63.69; H, 9.80; N, 12.38%).

5-Methyl-1-(phenylmethyl)-2-pyrrolidinone (25).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5)

(126 mg, 0.4 mmol) with the organozinc prepared from methyl bromide and purification by chromatography (10:5:85 to 20:10:70 ethyl acetate:dichloromethane:petrol) gave **25** (64.3 mg, 85%) as a colourless oil; ν_{max} (film) 3027, 2966, 1684, 1412, 1359, 1312, 1255, 1181, 1028, 818, 701, and 660 cm^{-1}; δ_H (270 MHz) 1.56 (3H, d, *J* 6.35 Hz, CH_3), 1.52-1.65 (1H, m, 4-H), 2.08-2.21 (1H, m, 4-H), 2.32-2.54 (2H, m, 3-H), 3.48-3.56 (1H, m, 5-H), 3.98 (1H, d, *J* 15.1 Hz, CHPh), 4.96 (1H, d, *J* 15.1 Hz, CHPh), and 7.20-7.36 (5H, m, Ph); m/z 189 (M^+, 59%), 174, 146, 104, 98, and 91; (Found: C, 76.27; H, 8.12; N, 7.38. $C_{12}H_{15}NO$ requires C, 76.16; H, 7.99; N, 7.40%).

5-Ethyl-1-(phenylmethyl)-2-pyrrolidinone (26).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5) (78.8 mg, 0.25 mmol) with the organozinc prepared from ethyl bromide and purification by chromatography (10:5:85 to 20:10:70 ethyl acetate:dichloromethane:petrol) gave **26** (38.1 mg, 75%) as a colourless oil; ν_{max} (film) 3027, 2964, 1687, 1493, 1417, 1363, 1322, 1256, 1175, 1082, 944, 736, 703, and 665 cm^{-1}; δ_H (270 MHz) 0.82 (3H, t, *J* 7.45 Hz, CH_3), 1.28-1.45 (1H, m, 4-H), 1.61-1.76 (2H, m, 3-H 4-H), 2.01-2.14 (1H, m, 3-H), 2.32-2.52 (2H, m, 1'-H), 3.33-3.43 (1H, m, 5-H), 3.95 (1H, d, *J* 14.9 Hz, CHPh), 4.98 (1H, d, *J* 15.1 Hz, CHPh), and 7.19-7.38 (5H, m, Ph); m/z 203 (M^+, 22%), 174, 91, and 65; (Found: C, 76.62 H, 8.14; N, 6.68. $C_{13}H_{17}NO$ requires C, 76.81; H, 8.43; N, 6.89%).

1,5-Bis(phenylmethyl)-2-pyrrolidinone (27).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5) (78.8 mg, 0.25 mmol) with the organozinc prepared from benzyl bromide and purification by chromatography (10:5:85 to 20:10:70 ethyl acetate:dichloromethane:petrol) gave **27** (55.6 mg, 84%) as a colourless oil; ν_{max} (film) 3059, 2923, 1683, 1602, 1493, 1362, 1315, 1247, 1170, 1082, 1029, 733, 702, and 665 cm^{-1}; δ_H (270 MHz) 1.68-1.97 (2H, m, 4-H), 2.24-2.31 (2H, m, 3-H), 2.57 (1H, dd, *J* 13.4, 8.5 Hz, 1'-H), 3.02 (1H, dd, *J* 13.4, 4.4 Hz, 1'-H), 3.61-3.70 (1H, m, 5-H), 4.01 (1H, d, *J* 14.9 Hz, CHPh), 5.11 (1H, d, *J* 14.9 Hz, CHPh), and 7.02-7.39 (10H, m, Ph); m/z 265 (M^+, 1%), 175, 174, and 91; (Found: C, 81.33; H, 7.09; N, 5.20. $C_{18}H_{19}NO$ requires C, 81.48; H, 7.22; N, 5.28%).

1-(Phenylmethyl)-5-prop-2-enyl-2-pyrrolidinone (28).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5) (78.8 mg, 0.25 mmol) with the organozinc prepared from allyl bromide and purification by chromatography (10:5:85 to 20:10:70 ethyl acetate:dichloromethane:petrol) gave **28** (49.5 mg, 92%) as a colourless oil; ν_{max} (film) 2922, 1684, 1493, 1417, 1251, 1172, 996, 919, and 704 cm^{-1}; δ_H (270 MHz) 1.69-1.82 (1H, m, 4-H), 1.98-2.23 (2H, m, 3-H 4-H), 2.31-2.54 (3H, m, 3-H 1'-H), 3.46-3.55 (1H, m, 5-H), 3.99 (1H, d, *J* 14.9 Hz, CHPh), 5.01 (1H, d, *J* 14.9 Hz, CHPh), 5.05-5.14 (2H, m, 3'-H), 5.56-5.71 (1H, m, 2'-H), and 7.20-7.38 (5H, m, Ph); m/z 215 (M^+, 0.1%), 174, and 91; (Found: C, 77.79; H, 8.06; N, 6.49. $C_{14}H_{17}NO$ requires C, 78.10; H, 7.96; N,6.51%).

1-(Phenylmethyl)-5-pent-4-enyl-2-pyrrolidinone (29).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5) (126 mg, 0.4 mmol) with the organozinc prepared from 5-bromo-1-pentene and purification by chromatography (10:5:85 to 20:10:70 ethyl acetate:dichloromethane:petrol) gave **29** (78.7 mg, 81%) as a colourless oil; ν_{max} (film) 3063, 3027, 2930, 1684, 1416, 1357, 1232, 1170, 1082, 994, 912, and 703 cm^{-1}; δ_H (270 MHz) 1.21-1.41 (3H, m, 4-H 1'-H), 1.61-1.79 (2H, m, 2'-H), 1.93-2.15 (3H, m, 4-H 3'-H), 2.32-2.52 (2H, m, 3-H), 3.37-3.47 (1H, m, 5-H), 3.95 (1H, d, *J* 15.1 Hz, CHPh), 4.91-5.05 (3H, m, 5'-H CHPh), 5.65-5.80 (1H, m, 4'-H), and 7.20-7.37 (5H, m, Ph); m/z 243 (M^+, 11%), 200, 187, 174, 92, and 91; (Found: C, 79.04; H, 8.90; N, 5.51. $C_{16}H_{21}NO$ requires C, 78.97; H, 8.70; N, 5.76%).

1-(Phenylmethyl)-5-[2-(ethyl)-1,3-dioxane]-2-pyrrolidinone (30).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5) (126 mg, 0.4 mmol) with the organozinc prepared from 2-(2-bromoethyl)-1,3-dioxane[18] and purification by chromatography (10:5:85 to 20:10:70 then 30:10:60 ethyl acetate:dichloromethane:petrol) gave **30** (91.32 mg, 79%) as a colourless oil; ν_{max} (film) 3027, 2958, 2850, 1684, 1493, 1419, 1246, 1145, 1082, 1005, 926, 894, and 704 cm^{-1}; δ_H (270 MHz) 1.22-1.86 (6H, m, 1'-H 2'-H 4"-H), 1.93-2.12 (2H, m, 3-H), 2.30-2.50 (2H, m, 4-H), 3.38-3.47 (1H, m, 2-H), 3.71 (2H, td, *J* 12.2, and 2.4 Hz, 3"-H_{ax} 5"-H_{ax}), 3.91 (1H, d, *J* 15.1 Hz, CHPh), 4.02-4.14 (2H, m, 3"-H_{eq} 5"-H_{eq}), 4.45 (1H, t, *J* 4.8 Hz, 1"-H), 5.02 (1H, d, *J* 14.9 Hz, CHPh), and 7.20-7.35 (5H, m, Ph); m/z 289 (M^+, 7%), 187, 174, 91, and 84; (Found: C, 70.27; H, 8.31 N, 4.65. $C_{17}H_{23}NO_3$ requires C, 70.56; H, 8.01; N, 4.84%).

5-Cyclohexyl-1-(phenylmethyl)-2-pyrrolidinone (31).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5) (126 mg, 0.4 mmol) with the organozinc prepared from cyclohexyl bromide and purification by chromatography (1:9 ethyl acetate:petrol) gave **31** (30.8 mg, 30%) as a colourless oil; ν_{max} (film) 2926, 2853, 1688, 1485, 1448, 1358, 1280, 1168, 1070, 860 and 704 cm^{-1}; δ_H (270 MHz) 1.12-1.97 (13H, m, 4-H C_6H_{11}), 2.29-2.34 (1H, m, 3-H), 2.67-2.70 (1H, m, 3-H), 3.37 (1H, ddd, *J* 6.2, 3.1 and 1.7 Hz,5-H), 3.90 (1H, d, *J* 14.9 Hz, CHPh), 5.03 (1H, d, *J* 14.9 Hz, CHPh) and 7.23-7.40 (5H, m, Ph); m/z 257 (M^+, 4%), 174, 156, 91, 86, 84 and 77; (Found: C, 79.20; H, 9.24; N, 5.39. $C_{18}H_{23}NO$ requires C, 79.33; H, 9.01; N, 5.44%).

***cis*-Hexahydro-8-methyl-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (32).- Method a).** Reaction of hexahydro-8-(phenylsulphonyl)-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (3) (59 mg, 0.2 mmol) with the organozinc prepared from methyl bromide and purification by chromatography (3:1 ethyl acetate:petrol) gave **32** (24 mg, 71%) as a colourless oil; ν_{max} (film) 3478, 2934, 1684, 1429, 1288, 1235, 1216, 1131, 1104, and 763 cm^{-1}; δ_H (270 MHz) 1.20 (3H, d, *J* 7.1 Hz, CH_3), 1.20-1.85 (7H, m, 4-H_{ax} 5-H 6-H 7-H), 2.07 (1H, dtd, *J* 14.0, 5.5, 3.0 Hz, 4-H_{eq}), 3.48 (1H, dddd, *J* 11.3, 8.5, 5.6, 2.6 Hz, 4a-H_{ax}), 4.09 (1H, ddd, *J* 10.9, 9.5, 3.0 Hz, 3-H_{ax}), 4.18 (1H, ddd, *J* 10.9, 5.1, 4.2 Hz, 3-H_{eq}), and 4.67-4.75 (1H, m, 8-H_{eq}); m/z 169 (M^+, 35%), 154, and 55; (Observed M^+, 169.1103. Calc. for $C_9H_{15}NO_2$ M, 169.1103).

Method b). A solution of *cis*-hexahydro-8-(phenylsulphonyl)-3*H*-pyrido[1,2-c][1,3] oxazin-1-one (3) (59 mg, 0.2 mmol) and trimethylaluminium (0.2 ml, 0.4 mmol, 2M solution in hexanes) in dry dichloromethane (1 ml) was stirred at 0°C under argon for 3 hours then at room temperature for 3 hours. The reaction was quenched with aqueous NaOH and extracted with ether. The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by chromatography (3:1 ethyl acetate:petrol) gave **32** (25.5 g, 75%) as a colourless oil; identical with previous sample by i.r., n.m.r. and mass spectroscopy.

General Procedure for Anomeric Substitution with Silyl Reagents and Aluminium Trichloride.- The silyl reagent (2.0 equiv.) was added to a stirred suspension of anhydrous aluminium chloride (2.0 equiv.) in dry dichloromethane (2 ml/mmol) at -78°C under argon. The mixture was stirred at -78°C for 30 minutes then a solution of the sulphone (1.0 equiv.) in dry dichloromethane (3 ml/mmol) was added. The mixture was allowed to warm to -35°C and stirred at this temperature for 1-5 hours (unless otherwise stated). The reaction was quenched with 1N HCL or saturated aqueous NaCl and extracted with ether, the combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Products were purified by chromatography.

Methyl 1-formyl-α,α-dimethyl-2-piperidineacetate (33).- 2-(Phenylsulphonyl)-1-piperidinecarboxaldehyde (1) 253 mg, 1.0 mmol) was reacted with methyl trimethylsilyl dimethylketene acetal and aluminium chloride at –35°C for 3 hours then allowed to warm to room temperature over 2 hours. Purification by chromatography (2:3 ethyl acetate:petrol) gave **33** (190 mg, 89%) as a colourless oil; ν_{max} (film) 2950, 2873, 1724, 1675, 1428, 1263, 1142, and 995 cm^{-1}; δ_H (270 MHz) 1.18 (1.5H, s, CH_3), 1.19 (1.5H, s, CH_3), 1.21 (1.5H, s, CH_3), 1.22 (1.5H, s, CH_3), 1.15-1.87 (6H, m, 3-H 4-H 5-H), 2.74 (0.5H, td, *J* 13.2, 3.9 Hz, 6-H_{ax}), 3.23-3.45 (1H, m, 6-H_{ax} 6-H_{eq}), 3.60-3.70 (0.5H, m, 2-H), 3.64 (3H, s, OMe), 4.30 (0.5H, dd, *J* 13.7, 5.4 Hz, 2-H), 4.40-4.47 (0.5H, m, 6-H_{eq}), 8.01 (0.5H, s, CHO), and 8.08 (0.5H, s, CHO); m/z 213 (M^+, 2%), 182, and 112; (Found: C, 62.12; H, 9.20; N, 6.38. $C_{11}H_{19}NO_3$ requires C, 61.95; H, 8.98; N, 6.57%).

2-Prop-2-enyl-1-piperidinecarboxaldehyde (34).- 2-(phenylsulphonyl)-1-piperidinecarboxaldehyde (1) (253 mg, 1.0 mmol) was reacted with allyltrimethylsilane and purification by chromatography (1:2 ethyl acetate:petrol) gave compound **34** (138 mg, 90%) as a colourless oil; ν_{max} (film) 2938, 2858, 1670, 1429, 1256, 1011, and 918 cm^{-1}; δ_H (270 MHz) 1.25-1.75 (6H, m, 3-H 4-H 5-H), 2.05-2.55 (2H, m, 1'-H), 2.67 (0.55H, td, *J* 13.0, 3.0 Hz, 6-H_{ax}), 3.11 (0.45H, td, *J* 13.3, 2.6 Hz, 6-H_{ax}), 3.34 (0.45H, dd, *J* 13.3, 4.4 Hz, 6-H_{eq}), 3.53-3.63 (0.55H, m, 2-H), 4.17 (0.55H, br d, *J* 13.0 Hz, 6-H_{eq}), 4.57 (0.45H, q, *J* 7.0 Hz, 2-H), 4.97-5.10 (2H, m, 3'-H), 5.53-5.77 (1H, m, 2'-H), and 7.96 (1H, s, CHO); m/z 153 (M^+, 2%), and 112; (Found: C,70.43; H,9.98; N,8.84. $C_9H_{15}NO$ requires C,70.55; H,9.87; N,9.14%).

***cis*-Hexahydro-8-prop-2-enyl-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (35).-** Hexahydro-2-(phenylsulphonyl)-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (3) (103 mg, 0.35 mmol) was reacted with allyltrimethylsilane and aluminium chloride at -20°C for 6 hours. Purification by chromatography (1:3 to 3:1 ethyl acetate:petrol) gave **35** (63 mg, 93%) as a colourless oil; ν_{max} (film) 2935, 1684, 1477, 1427, 1361, 1290, 1270, 1216, 1126, 1100, 915, and 760 cm^{-1}; δ_H (270 MHz) 1.17-1.33, 1.57-1.85 (7H, m, 4-H_{ax} 5-H

6-H 7-H), 2.04 (1H, dddd, *J* 13.9, 5.9, 4.6, 2.7 Hz, 4-H_{eq}), 2.26 (1H, dtd, *J* 13.9, 6.4, 1.0 Hz, 1'-H), 2.46 (1H, dtd, *J* 13.9, 7.8, 1.0 Hz, 1'-H), 3.40 (1H, dtd, *J* 14.6, 5.9, 2.7 Hz, 4a-H_{ax}), 4.00-4.20 (2H, m, 3-H), 4.64 (1H, br t, *J* 7.8 Hz, 8-H_{eq}), 5.03 (1H, dd, *J* 10.3, 1.0 Hz, 3'-H), 5.05 (1H, dd, *J* 16.8, 1.0 Hz, 3'-H), and 5.77 (1H, dddd, *J* 16.8, 10.3, 7.8, 6.4 Hz, 2'-H); m/z 195 (M^+, 0.5%), 154, and 55; (Observed M^+, 195.1259. Calc. for $C_{11}H_{17}NO_2$ M, 195.1259).

General Procedure for Anomeric Substitution with Silyl Reagents and Magnesium Bromide.- The silyl reagent (2.0 equiv.) was added to a stirred suspension of anhydrous magnesium bromide etherate (2.0 equiv.) in dry dichloromethane (2 ml/mmol) at -78°C under argon. The mixture was stirred at -78°C for 30 minutes then a solution of the sulphone (1.0 equiv.) in dry dichloromethane (3 ml/mmol) was added. The mixture was allowed to warm to 0°C and stirred at this temperature for 7 hours. The reaction was quenched with saturated aqueous NaCl and extracted with ether or dichloromethane, the combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Products were purified by chromatography.

1,2-Dimethoxy-4-[1-[(1,1-dimethylethyl)dimethylsilyloxy]ethenyl]benzene.- *tert*-Butyldimethylsilyl trifluoromethanesulphonate (5.05 ml, 5.82 g, 22 mmol) was added dropwise to a stirred suspension of 3',4'-dimethoxyacetophenone (3.60 g, 20 mmol), and triethylamine (3.07 ml, 2.23 g, 22 mmol) in dry ether (20 ml) at 0°C under argon. The reaction mixture was allowed to warm to room temperature and stirred for 2 hours. The lower layer was removed *via* a syringe and the remainder concentrated *in vacuo*. Distillation (kugelrohr) (b.p. 130-150°C, *ca.* 1 mmHg) gave 1,2-dimethoxy-4-[1-[(1,1-dimethylethyl)dimethylsilyloxy]ethenyl]benzene (4.68 g, 80%) as a colourless oil; δ_H (270 MHz) 0.21 (6H, s, $SiMe_2$), 1.01 (9H, s, ^tBu), 3.91 (6H, s, OMe), 4.35 (1H, d, *J* 1.7 Hz, 2'-H), 4.79 (1H, d, *J* 1.7 Hz, 2'-H), 6.82 (1H, d, *J* 8.3 Hz, 6-H), 7.16 (1H, d, *J* 2.1 Hz, 3-H), and 7.19 (1H, dd, *J* 8.3, 2.1 Hz, 5-H).

2-[2-(3,4-Dimethoxyphenyl)-2-oxoethyl]-1-pyrrolidinecarboxaldehyde (36).- Reaction of 2-(phenylsulphonyl)-1-pyrrolidinecarboxaldehyde (2) (718 mg, 3.0 mmol) with 1,2-dimethoxy-4-[1-[(1,1-dimethylethyl)dimethylsilyloxy]ethenyl]benzene, and magnesium bromide etherate at 0°C for 7 hours then purification by chromatography (3:1 ethyl acetate:petrol then ethyl acetate) gave **36** (743 mg, 89%) as a colourless oil; ν_{max} (film) 2966, 1659, 1592, 1513, 1416, 1383, 1271, 1152, 1022, 876, 811, and 767 cm^{-1}; δ_H (270 MHz) 1.73-2.25, (4H, m, 3-H 4-H), 2.76 (0.55H, dd, *J* 14.9, 10.2 Hz, 1'-H), 3.08 (0.45H, dd, *J* 16.8, 7.3 Hz, 1'-H), 3.26 (0.45H, dd, *J* 16.8, 6.1 Hz, 1'-H), 3.35-3.70 (2H, m, 2-H 5-H), 3.89 (0.55H, dd, *J* 14.9, 3.1 Hz, 1'-H), 3.94 (1.65H, s, OMe), 3.95 (1.65H, s, OMe), 3.96 (2.70H, s, OMe), 4.37-4.60 (1H, m, 2-H 5-H), 6.89 (0.45H, d, *J* 8.3 Hz, 5"-H), 6.91 (0.55H, d, *J* 8.3 Hz, 5"-H), 7.49 (0.45H, d, *J* 2.0 Hz, 2"-H), 7.53 (0.45H, dd, *J* 8.3, 2.0 Hz, 6"-H), 7.61 (0.55H, d, *J* 2.0 Hz, 2"-H), 7.74 (0.55H, dd, *J* 8.3, 2.0 Hz, 6"-H), 8.30 (0.55H, s, CHO), and 8.35 (0.45H, s, CHO); m/z 277 (M^+, 31%), 180, 165, 112, and 98; (Found: C, 65.00; H, 7.17; N, 5.06. $C_{15}H_{19}NO_4$ requires C, 64.97; H, 6.91; N, 5.05%).

1-(Phenylmethyl)-5-prop-2-enyl-2-pyrrolidinone (28).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5) (78.8 mg, 0.25 mmol) with allyl trimethylsilane and purification by chromatography (10:5:85 to 20:10:70 ethyl acetate:dichloromethane:petrol) gave **28** (36.7 mg, 69%) as a colourless oil; identical with previous sample by i.r., n.m.r. and mass spectroscopy.

5-Cyano-1-(phenylmethyl)-2-pyrrolidinone (37).- Reaction of 1-(phenylmethyl)-5-(phenylsulphonyl)-2-pyrrolidinone (5) (78.8 mg, 0.25 mmol) with trimethylsilyl cyanide and purification by chromatography (10:5:85 to 20:10:70 ethyl acetate:dichloromethane:petrol) gave **37** (48.1 mg, 96%) as a colourless oil; ν_{max} (film) 2922, 1699, 1493, 1405, 1359, 1233, 1083, and 704 cm^{-1}; δ_H (270 MHz) 2.31-2.73 (4H, m, 3-H 4-H), 3.98 (1H, d, *J* 14.89 Hz, CHPh), 4.15 (1H, t, *J* 6.23 Hz, 2-H), 5.17 (1H, d, *J* 14.89 Hz, CHPh), and 7.24-7.54 (5H, m, Ph); m/z 200 (M^+, 92%), 146, 118, 104, 91, and 77; (Found: C, 71.87; H, 5.77; N, 13.90. $C_{12}H_{12}N_2O$ requires C, 71.98; H, 6.04; N, 13.99%).

Norruspoline - (*E*)-2-Methoxy-4-[2-pyrrolidin-2-ylethenyl]phenol (38)[11] and (*E*)-2-Methoxy-5-[2-pyrrolidin-2-ylethenyl]phenol (39).- A stirred mixture of (*E*)-2-[2-(3,4-dimethoxyphenyl)ethenyl]-1-pyrrolidinecarboxaldehyde (78 mg, 0.3 mmol), and sodium thiomethoxide (105 mg, 1.5 mmol) in dry DMF (1.5 ml) was heated at 130°C for 45 minutes under argon.[12] The reaction mixture was cooled and concentrated *in vacuo*. The residual orange gum was dissolved in 3M aqueous NaOH (3 ml), and the solution was heated at 80°C for 2 hours. The reaction was cooled, acidified (pH ≈ 5) with 3N HCl then basified with saturated aqueous $NaHCO_3$ (pH > 7), and extracted with dichloromethane. The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by chromatography (100:8:1 dichloromethane:methanol:0.88 ammonia) gave Norruspoline **38** (36 mg, 53%) as a

yellow oil; ν_{max} (film) 2958, 1586, 1512, 1462, 1275, 1156, 1125, 1034, and 730 cm^{-1}; δ_H (500 MHz) 1.53-1.60, 1.75-1.93, 1.95-2.05 (4H, m, 3"-H 4"-H), 2.95 (1H, ddd, *J* 10.1, 8.3, 6.7 Hz, 5"-H), 3.11 (1H, ddd, *J* 10.1, 7.8, 5.6 Hz, 5"-H), 3.6-4.1 (1H, br s, NH), 3.69 (1H, q, *J* 7.4 Hz, 2"-H), 3.86 (3H, s, OMe), 6.03 (1H, dd, *J* 15.7, 7.4 Hz, 2'-H), 6.41 (1H, d, *J* 15.7 Hz, 1'-H), 6.81 (2H, s, ArH), and 6.87 (1H, s, ArH); δ_C (67.9 MHz) 146.9, 145.5, 130.1, 129.8, 129.6, 120.0, 114.6, 108.2, 61.0, 55.8, 46.4, 32.4, and 25.3; m/z 219 (M^+, 100%), 190, 137, 96, and 70; (Observed M^+, 219.1259. Calc. for $C_{13}H_{17}NO_2$ M, 219.1259).

Further elution gave the regio-isomer **39** (22 mg, 34%) as a pink oil; ν_{max} (film) 2955, 1579, 1504, 1439, 1257, 1223, 1131, 1028, and 730 cm^{-1}; δ_H (500 MHz) 1.50-1.57, 1.75-1.90, 1.95-2.03 (4H, m, 3"-H 4"-H), 2.94 (1H, ddd, *J* 10.1, 8.1, 6.7 Hz, 5"-H), 3.10 (1H, ddd, *J* 10.1, 7.7, 5.7 Hz, 5"-H), 3.1-3.7 (1H, br s, NH), 3.67 (1H, q, *J* 7.4 Hz, 2"-H), 3.89 (3H, s, OMe), 6.04 (1H, dd, *J* 15.7, 7.4 Hz, 2'-H), 6.39 (1H, d, *J* 15.7 Hz, 1'-H), 6.77 (1H, d, *J* 8.3 Hz, 3-H), 6.82 (1H, dd, *J* 8.3, 2.0 Hz, 4-H), and 6.96 (1H, d, *J* 2.0 Hz, 5-H); δ_C (67.9 MHz) 146.5, 146.0, 130.8, 130.5, 129.6, 118.4, 112.3, 110.7, 61.0, 55.9, 46.4, 32.5, and 25.3; m/z 219 (M^+, 100%), 204, 190, 176, 137, and 96; (Observed M^+, 219.1259. Calc. for $C_{13}H_{17}NO_2$ M, 219.1259).

Ruspolinone – 1-(3,4-Dimethoxyphenyl)-2-pyrrolidin-2-ylethanone (40).-[11] A stirred mixture of 2-[2-(3,4-dimethoxyphenyl)-2-oxoethyl]-1-pyrrolidinecarboxaldehyde (108 mg, 0.39 mmol), 3M aqueous NaOH (2 ml), and ethanol (2 ml) was heated at reflux for 75 minutes. The solution was cooled, diluted with saturated aqueous NaCl and extracted with dichloromethane. The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by chromatography (100:8:1 dichloromethane:methanol:0.88 ammonia) gave Ruspolinone **40** (78 mg, 80%) as a yellow oil; ν_{max} (film) 3337, 2958, 1670, 1594, 1511, 1459, 1414, 1267, 1152, 1023, 879, 818, and 768 cm^{-1}; δ_H (270 MHz) 1.33-1.45, 1.65-2.03 (4H, m, 3-H 4-H), 2.70 (1H, br s, NH), 2.84-3.07 (2H, m, 5'-H), 3.08 (1H, d, *J* 7.0 Hz, 2-H), 3.09 (1H, d, *J* 7.0 Hz, 2-H), 3.54 (1H, quin., *J* 7.0 Hz 2'-H), 3.89 (3H, s, OMe), 3.90 (3H, s, OMe), 6.84 (1H, d, *J* 8.4 Hz, 5"-H), 7.48 (1H, d, *J* 2.0 Hz, 2"-H), and 7.56 (1H, dd, *J* 8.4, 2.0 Hz, 6"-H); m/z 249 (M^+, 27%), 180, 165, and 70; (Observed MH^+, 250.1443. Calc. for $C_{14}H_{20}NO_3$ MH, 250.1443).

General Procedure for Elimination of Anomeric Sulphones.- A mixture of the sulphone (1.0 equiv.), triethylamine (1.5 equiv.), and magnesium bromide etherate (2.0 equiv.) in dry THF (6 ml/mmol) under argon was placed in an ultrasound bath for 18 hours. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with ether or dichloromethane, the combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Products were purified by chromatography.

3,4-Dihydro-2*H*-pyridine-1-carboxaldehyde (41).- Reaction of 2-(phenylsulphonyl)-1-piperidinecarboxaldehyde (1) (127 mg, 0.5 mmol) with triethylamine and magnesium bromide etherate and purification by chromatography (1:9 to 3:7 ethyl acetate:petrol) gave **41** (53.4 mg, 96%) as a colourless oil; ν_{max} (film) 2928, 2661, 1680, 1462, 1355, 1283, 1176, 995, 871, 743, and 622 cm^{-1}; δ_H (270 MHz) 1.70-1.95 (2H, m, 5-H), 2.09-2.20 (2H, m, 4-H), 3.48-3.53 (0.3H, m, 6-H), 3.60-3.70 (0.7H, m, 6-H), 5.02 (0.7H, dt, *J* 8.31, and 4.15 Hz, 3-H), 5.17 (0.3H, dtd, *J* 8.30, 4.4, and 1.47 Hz, 3-H), 6.44 (0.7H, dt, *J* 8.06, and 1.9 Hz, 2-H), 7.00(0.3H, dt, *J* 8.06, 1.9 Hz, 2-H) 7.96 (0.3H, s, CHO), and 8.17 (0.7H, s, CHO); m/z 111 (M^+, 100%), 86, 84, 82, and 68; (Found: C, 64.79; H, 8.01; N, 12.59. C_6H_9NO requires C, 64.84; H, 8.16; N, 12.6%).

2,3-Dihydro-1-pyrrolecarboxaldehyde (42).- Reaction of 2-(phenylsulphonyl)-1-pyrrolidinecarboxaldehyde (2) (119.6 mg, 0.5 mmol) with triethylamine and magnesium bromide etherate and purification by chromatography (1:9 to 3:7 ethyl acetate:petrol) gave **42** (35.4 mg, 73%) as a colourless oil; ν_{max} (film) 2922, 1657, 1617, 1424, 1381, 1201, 1042, 925, 802 and 719 cm^{-1}; δ_H (270 MHz) 2.62-2.73 (2H, m, 4-H), 3.76-3.89 (2H, m, 5-H), 5.23-5.26 (0.8H, m, 3-H), 5.27-5.34 (0.2H, m, 3-H), 6.43-6.46 (0.8H, m, 2-H), 8.12 (0.2H, s, CHO), and 8.35 (0.8H, s, CHO); m/z 97 (M^+, 88%), 86, 68 and 41; (Found: C, 61.96; H, 7.48; N, 14.40. C_5H_7NO requires C, 61.84; H, 7.27; N, 14.42%).

4,4a,5,6-Tetrahydro-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (43).- Reaction of hexahydro-8-(phenylsulphonyl)-3*H*-pyrido[1,2-c][1,3]oxazin-1-one (3) (59 mg, 0.2 mmol), and purification by chromatography (3:1 ethyl acetate:petrol) gave **43** (26 mg, 85%) as a white solid m.p. xx°C; ν_{max} ($CHCl_3$) cm^{-1}; δ_H (270 MHz) 1.50-2.20 (6H, m, 4-H 5-H 6-H), 3.57 (1H, tdd, *J* 11.4, 4.6, 2.4 Hz, 4a-H_{ax}), 4.25 (1H, td, *J* 11.3, 2.5 Hz, 3-H_{ax}), 4.34 (1H, ddd, *J* 11.0, 4.7, 2.4 Hz, 3-H_{eq}), 5.05-5.13 (1H, m, 7-H), and 6.95 (1H, td, *J* 8.5, 1.7 Hz, 8-H); m/z 153 (M^+, 100%), 108, 94, 80, 67, and 54; (Found: C, 62.72; H, 7.21; N, 9.00. $C_8H_{11}NO_2$ requires

C, 62.73; H, 7.24; N, 9.14%).

Tetrahydro-1-[(4-methylphenyl)sulphonyl]pyridine (44).- Reaction of 1-[(4-methylphenyl)sulphonyl]-2-(phenylsulphonyl)piperidine (6) (189 mg, 0.5 mmol) with triethylamine and magnesium bromide etherate and purification by chromatography (1:9 ethyl acetate:petrol) gave **44** (113.8 mg, 96%) as a white solid, mp 56°C; ν_{max} (film) 2928, 1645, 1594, 1394, 1337, 1163, 1109, 683, and 637 cm^{-1}; δ_H (270 MHz) 1.61-1.72 (2H, m, 5-H), 1.85-1.96 (2H, m, 4-H), 2.42 (3H, s, *p*-CH_3), 3.34-3.41 (2H, m, 6-H), 4.96 (1H, dt, *J* 8.3, 3.9 Hz, 3-H), 6.63 (1H, dt, *J* 8.5, 1.8 Hz, 2-H) 7.20-7.29 (2H, m, *m*-H), and 7.67-7.76 (2H, m, *o*-H); m/z 237 (M^+, 100%), 155, 91, 82, and 55; (Found: C, 60.67; H, 6.46; N, 5.76. $C_{12}H_{15}NO_2S$ requires C, 60.73; H, 6.37; N, 5.90%).

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