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Alkylation and Acylation of 5-Phenylsulphonyl- and 5-Cyanobutyrolactones†

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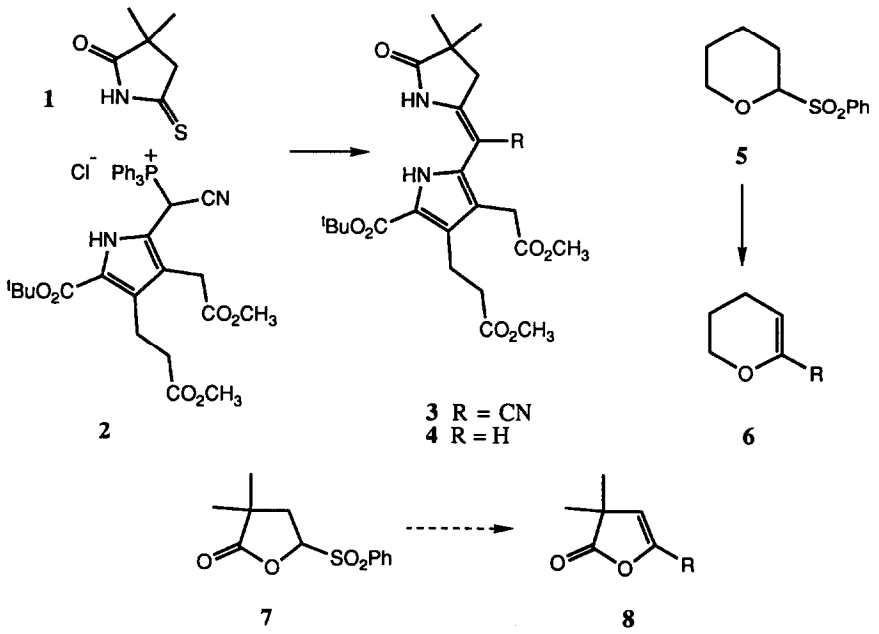
Abstract: Conditions are reported for the alkylation and acylation *alpha* to the sulphone of a butyrolactone carrying a 5-phenylsulphonyl group. Yields are good if the alkyl or acyl halide is sufficiently reactive. The phenylsulphonyl group is initially retained and studies of its elimination are described. The corresponding system with nitrile in place of phenylsulphonyl appears to be a less satisfactory synthon for the desired chemistry.

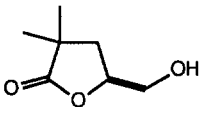
There has been a long-standing interest in Cambridge in developing methods for the synthesis of various isobacteriochlorins needed for researches on the biosynthesis of vitamin B_{12}. A key step in the successful strategy[1,2] was the coupling of a thioamide **1** with a Wittig salt **2** to generate a product **3** representing half of the isobacteriochlorin macrocycle. We wished to explore alternative ways to form the C-C bond between the pyrrolic and non-pyrrolic components if possible to reach **4**, *i.e.* lacking the nitrile residue of **3**, and were



† Dedicated to Charles Rees with all good wishes for fun in pastures new.

attracted by the possibility of using an appropriate phenylsulphonyl anion.[3] It was known from the studies of Ley's group that cyclic ethers carrying a 2-phenylsulphonyl group (*e.g.* **5**) gave anions which reacted smoothly with aldehydes, ketones or alkyl halides.[4] The products spontaneously eliminated benzenesulphinic acid to yield *e.g.* **6**. Alternatively, the phenylsulphonyl group in systems such as **5** can be displaced by carbon nucleophiles.[5] More recently, this substitution approach has been extended to *N*-acyl-2-phenylsulphonyl piperidines and pyrrolidines.[6] The present paper reports our studies on the alkylation of phenylsulphonyl derivatives of lactones. Clearly if analogous alkylation of **7** can be achieved followed by elimination of benzenesulphinic acid to afford **8** then an alternative route is open for constructing the required building block **4**.

The lactone **9**, prepared by Koga's method,[7] was opened with aqueous potassium hydroxide and the resultant diol was cleaved with periodate to give the lactol **10**. Though cyclic hemiacetals react with



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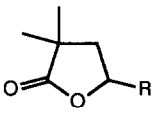
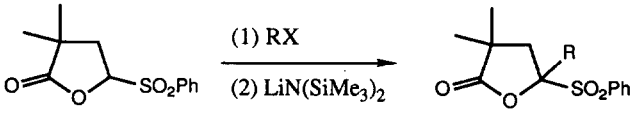
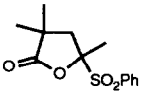
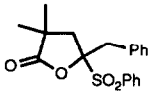
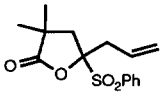
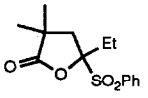
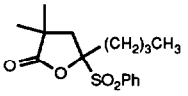
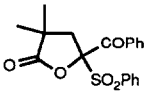


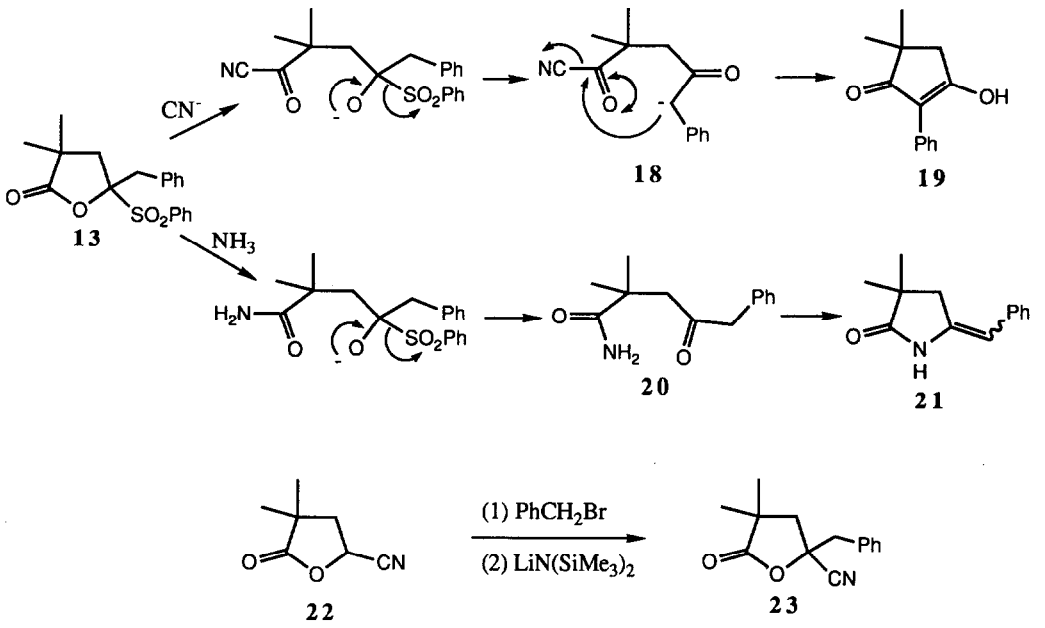
10 R = OH
11 R = SPh
7 R = SO_2Ph



ELECTROPHILE (RX)	PRODUCT		YIELD (%)
CH_3I		**12**	64
$PhCH_2Br$		**13**	66
$CH_2{=}CHCH_2Br$		**14**	85
CH_3CH_2I		**15**	14
$CH_3(CH_2)_3I$		**16**	6
PhCOCl		**17**	86

benzenesulphinic acid to yield sulphones[4] (*e.g.* **5**), the lactol **10** could not be converted into the desired sulphone **7** by this approach. However, the sulphide **11** could be prepared by treatment of the lactol **10** with benzenethiol and *p*-toluenesulphonic acid. The sulphone **7** was then obtained by oxidation of the sulphide **11** with potassium hydrogen persulphate[8] (oxone).

Treatment of the sulphone **7** as a solution in tetrahydrofuran (THF) at low temperature with various bases (lithium diisopropylamide, butyl lithium or lithium bistrimethylsilylamide) followed by addition of the alkyl halide not only failed to yield any alkylated product but resulted in complete destruction of the sulphone **7**. It was reasoned that the sulphone anion was probably forming but was unstable and if so might be trapped by having the alkylating agent present at the outset. This strategy was successful and optimum yields were obtained by using a dilute solution (20 mmolar) of the sulphone **7** with a large excess of the alkylating agent. The yields are collected in the Table which shows that good to high yields of products **12**, **13** and **14** are obtained when the more reactive halides are used. With less reactive halides, the yields of **15** and **16** are poor, no doubt because decomposition of the anion predominates. Similarly, a reactive acid chloride carrying no hydrogen *alpha* to the carbonyl group gave a good yield of ketone **17** but acetyl chloride did not react and the starting sulphone was recovered; presumably the base deprotonated part of the large excess of acid chloride.



It is interesting that all the products retained the sulphonyl group. Two studies of its elimination were carried out using the product **13**. When this was heated with potassium cyanide in dimethylformamide, ring-opening and elimination occurred to yield the enolised cyclopentandione **19** (for which **18** is a probable intermediate). The second approach involved heating the sulphone **13** with saturated methanolic ammonia; again ring-opening and elimination occurred to afford, after treatment with acid, a mixture of the *E*-, and *Z*-lactams **21** presumably by way of the keto-amide **20**.

Finally a brief study was made of the effectiveness of a nitrile residue for anion stabilisation in the lactone **22**. This was prepared essentially quantitatively from the sulphone **7** by treatment with tetrabutylammonium cyanide. When the nitrile **22** and benzyl bromide were treated with lithium bistrimethylsilylamide under

conditions identical to those used successfully with the sulphone **7**, the product **23** was formed in only 15% yield. This suggests that the anion derived from **22** has even lower stability than that from the sulphone **7**.

Though the approach *via* sulphones did not lead to a new way to carry out the desired chemistry for synthesis of isobacteriochlorins, the present work and especially the sequence **13** → **20** → **21** encouraged other studies from which a highly successful synthesis has been developed. This will be reported in a separate paper.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Infra-red spectra were recorded on a Perkin-Elmer 1310 instrument in solution ($CHCl_3$) using 0.5mm path length sodium chloride cells. Positions of absorption maxima are given relative to the polystyrene peak 1603 cm^{-1}. U.v./visible spectra were recorded on a Kontron Instruments Uvikon 860 spectrophotometer in 10mm silica cells. Proton and carbon-13 (broad band decoupled) n.m.r. spectra were recorded on a Bruker AM400 spectrometer. The deuterated solvent signal was used as the standard and chemical shifts are quoted on the δ- scale relative to tetramethylsilane. High resolution electron impact mass spectra were recorded on a Kratos MS30 machine and field desorption (f.d) mass spectra were recorded on a Kratos MS50 machine. Flash chromatography was carried out on Merck Kieselgel 60 (230-400mesh) silica, and preparative layer chromatography was carried out on plates coated to thickness of 1mm with Merck Kieselgel 60 F_{254}.

Dihydro-5-hydroxy-3,3-dimethyl-2(3H)-furanone (10).- Aqueous sodium hydroxide solution (7.3ml, 2M, 14.6mmol) was added to (5*S*)-dihydro-5-(hydroxymethyl)-3,3-dimethyl-2-furanone **9** (1.76g, 12.2mmol) in water (50ml) and stirred for 20 hours at room temperature. The mixture was cooled to 0°C while a suspension of sodium periodate (3g, 14.0mmol) in water (20ml) was added. The solution was then stirred for 3.5 hours at room temperature. Concentrated sulphuric acid was added dropwise at 0°C until pH1, and the mixture was extracted with dichloromethane (2 x 50ml). The aqueous phase was then saturated with NaCl and reextracted with dichloromethane (3 x 50ml). The combined extracts were dried (Na_2SO_4), filtered and evaporated. Purification by chromatography with hexane / ethyl acetate as eluant gave **10** (1.47g, 92%) as a white solid, m.p. 54-55°C (from hexane / ethyl acetate); $\nu_{max.}$ ($CHCl_3$) 3330, and 1765 cm^{-1}; δ_H (400MHz, $CDCl_3$) 1.20, 1.31 (each 3H, s, CH_3), 1.98 (1H, dd, *J* 3.7, 13.5 Hz, CHHCHOH), 2.26 (1H, dd, *J* 5.9, 13.5Hz, CHHCHOH), 5.49 (1H, brs, OH), and 5.84 (1H, dd, *J* 5.9, 3.7 Hz, CHOH); δC (100MHz, $CDCl_3$) 25.57, 25.76 (each CH_3), 40.16, 44.02 ($C(CH_3)_2$ and CH_2CHOH), 96.92 (CHOH), and 182.95 (CO); (Found $M^+(-H_2O)$, 112.0529. $C_6H_8O_2$ requires M, 112.0524); (Found C, 55.58; H, 7.62. $C_6H_{10}O_3$ requires C, 55.37; H, 7.74 %).

Dihydro-3,3-dimethyl-5-phenylsulphide-2(3H)-furanone (11).- A mixture of dihydro-5-hydroxy-3,3-dimethyl-2-furanone **10** (1.46g, 11.2mmol), benzenethiol (1.50ml, 14.6mmol) and toluene-*p*-sulphonic acid (80mg, 0.465mmol) in benzene (150ml) was heated under reflux under a Dean-Stark head for 30 minutes. The mixture was then cooled, washed with saturated aqueous $NaHCO_3$ solution (50ml), water (20ml), dried (Na_2SO_4), filtered and evaporated. Chromatography, with hexane / ethyl acetate as eluant gave a colourless oil **11** (1.85g, 74%). $\nu_{max.}$ ($CHCl_3$) 1770 cm^{-1}; δ_H (400MHz, $CDCl_3$) 1.25, 1.27 (each 3H, s, CH_3), 2.04 (1H, dd, *J* 8.2, 13.5 Hz, CHHCHSPh), 2.47 (1H, dd, *J* 7.0, 13.5Hz, CHHCHSPh), 5.70 (1H, dd, *J* 8.2, 7.0Hz, CHSPh), 7.25-7.34 (3H, m, Ph), and 7.50-7.53 (2H, m, Ph); δC (100MHz, $CDCl_3$) 24.75 and 24.90 (each CH_3), 40.08, 42.99 ($C(CH_3)_2$ and CH_2CHSPh), 83.66 (CHSPh), 128.32, 129.16, 132.36, 132.67 (Ph), and 180.77 (CO); m/z (f.d) 222 (M^+); (Found M^+, 222.0736. $C_{12}H_{14}O_2S$ requires M, 222.0715).

Dihydro-3,3-dimethyl-5-phenylsulphonyl-2(3H)-furanone (7).-
A suspension of oxone[8] (5.4g, 17.6 mmol) in water (25ml) was added to dihydro-3,3-dimethyl-5-phenylsulphide-2-furanone **11** (1.3g, 5.86mmol) in methanol (25ml) at 0°C, and left stirring for 18 hours at room temperature. Water (30ml) was then added, and the mixture extracted with chloroform (3 x 50ml). The combined extracts were washed with brine (20ml), water (20ml), dried (Na_2SO_4), filtered and evaporated. Chromatography eluting with hexane / ethyl acetate (7:1 to 5:1) gave a white solid **7** (1.30g, 87%), m.p. 105°C (from hexane / ethyl acetate); $\nu_{max.}$ ($CHCl_3$) 1790, 1330, and 1150 cm^{-1}; δ_H (400MHz, $CDCl_3$) 1.29, 1.36 (each 3H, s, CH_3), 2.44 (1H, dd, *J* 8.5, 14.3Hz, $CHHCHSO_2Ph$), 2.70 (1H, dd, *J* 6.5, 14.3Hz, $CHHCHSO_2Ph$), 5.14 (1H, dd, *J* 8.5, 6.5Hz, $CHSO_2Ph$), 7.57-7.59 (2H, m, Ph), 7.69-7.73 (1H, m, Ph), and 7.93-7.96 (2H, m, Ph); δC (100MHz, $CDCl_3$) 24.90, 26.56 (each CH_3), 35.09, 38.96 ($C(CH_3)_2$ and CH_2CHSO_2Ph), 86.86 ($CHSO_2Ph$), 129.40, 129.51, 134.68, 135.63 (Ph), and 179.29 (CO); m/z (f.d) 254 (M^+); (Found $M^+(-SO_2Ph)$, 113.0596. $C_6H_9O_2$ requires M, 113.0603); (Found C, 56.74; H, 5.57. $C_{12}H_{14}O_4S$ requires C, 56.68; H, 5.55 %).

General procedure for alkylation and acylation of sulphone **7**.- Lithium bistrimethylsilylamide (1.1 to 1.2 equiv., 1M solution in THF) was added over 10 minutes to a solution of the sulphone **7** and the electrophile (large excess) in dry THF at -78°C under argon. After 20 minutes stirring at -78°C, the reaction was quenched with water, and allowed to warm to room temperature. Dichloromethane was added and the solution was washed with dilute hydrochloric acid (0.1M), dried (Na_2SO_4), filtered and evaporated. Purification was achieved by chromatography eluting with hexane / ethyl acetate. The crystalline products were recrystallised from hexane / ethyl acetate.

Dihydro-3,3,5-trimethyl-5-phenylsulphonyl-2(3H)-furanone (12).- The reaction of sulphone **7** (50mg, 0.197mmol) and methyl iodide (250µl) in THF (5ml) with lithium bistrimethylsilylamide (240µl, 0.24mmol) gave a white solid **12** (34mg, 64%), m.p. 81°C; $\nu_{max.}$ ($CHCl_3$) 1785, 1315, and 1145 cm^{-1}; δ_H (400MHz, $CDCl_3$) 1.33, 1.34 (each 3H, s, CH_3), 1.60 (3H, s, $C(CH_3)SO_2Ph$), 2.12 (1H, d, *J* 14.8Hz, $C(CH_3)_2CHH$), 3.00 (1H, d, *J* 14.8Hz, $C(CH_3)_2CHH$), 7.56-7.60 (2H, m, Ph), 7.68-7.71 (1H, m, Ph), and 7.93-7.95 (2H, m, Ph); δ_C (100MHz, $CDCl_3$) 23.24, 25.28, 28.89 (each CH_3), 40.30, 41.69 ($C(CH_3)_2$ and $C(CH_3)_2CH_2$), 94.40 ($C(CH_3)SO_2Ph$), 129.15, 130.70, 133.06, 134.62 (Ph), and 179.98 (CO); (Found $M^+(-SO_2Ph)$, 127.0764. $C_7H_{11}O_2$ requires M, 127.0759).

5-Benzyldihydro-3,3-dimethyl-5-phenylsulphonyl-2(3H)-furanone (13).- The reaction of sulphone **7** (200mg, 0.787mmol) and benzyl bromide (468µl, 3.94mmol) in THF (20ml) with lithium bistrimethylsilylamide (950µl, 0.950mmol) gave a white solid **13** (178mg, 66%), m.p. 129-129.5°C; $\nu_{max.}$ ($CHCl_3$) 1790, 1310, and 1145 cm^{-1}; δ_H (400MHz, $CDCl_3$) 0.30, 1.67 (each 3H, s, CH_3), 2.16 (1H, d, *J* 15.0Hz, $C(CH_3)_2CHH$), 2.77 (1H, d, *J* 15.0Hz, $C(CH_3)_2CHH$), 3.02 (1H, d, *J* 13.8Hz, $CHHPh$), 3.13 (1H, d, *J* 13.8Hz, $CHHPh$), 7.11-7.13 (2H, m, CH_2Ph), 7.25-7.29 (3H, m, CH_2Ph) 7.62-7.66 (2H, m, SO_2Ph), 7.72-7.75 (1H, m, SO_2Ph), and 8.02-8.04 (2H, m, SO_2Ph); δ_C (100MHz, $CDCl_3$) 25.82, 25.98 (each CH_3), 36.93, 38.67, 39.94 ($C(CH_3)_2$, CH_2Ph and $C(CH_3)_2CH_2$), 96.77 ($OCSO_2Ph$), 128.09, 128.88, 129.39, 130.92, 131.17, 132.11, 133.34, 134.84 (Ph), and 180.31 (CO); m/z (f.d.) 344 (M^+); (Found $M^+(-SO_2Ph)$, 203.1071. $C_{13}H_{15}O_2$ requires M, 203.1072); (Found C, 66.40; H, 5.83. $C_{19}H_{20}O_4S$ requires C, 66.26; H, 5.85 %).

Dihydro-3,3-dimethyl-5-phenylsulphonyl-5-(2-propenyl)-2(3H)-furanone (14).- The reaction of sulphone **7** (250mg, 0.984mmol) and allyl bromide (7ml) in THF (50ml) with lithium bistrimethylsilylamide (1.08ml, 1.08mmol) gave a white solid **14** (250mg, 85%), m.p. 91.5-92.5°C; $\nu_{max.}$ ($CHCl_3$) 1795, 1310, and 1145 cm^{-1}; δ_H (400MHz, $CDCl_3$) 1.25, 1.33 (each 3H, s, CH_3), 2.25 (1H, d, *J* 15.2Hz, $(CH_3)_2CCHH$), 2.43 (1H, dd, *J* 14.1, 5.5Hz, $CHHCH=CH_2$), 2.59 (1H, dd, *J* 14.1, 8.9Hz, $CHHCH=CH_2$), 2.80 (1H, d, *J* 15.2Hz, $(CH_3)_2CCHH$), 5.16-5.28 (2H, m, $CH=CH_2$), 5.50-5.60 (1H, m, $CH=CH_2$), 7.55-7.59 (2H, m,

Ph), 7.67-7.71 (1H, m, Ph), and 7.91-7.93 (2H, m, Ph); δ_C (100MHz, $CDCl_3$) 25.68, 27.70 (each CH_3), 37.59, 37.97, 39.93 ($C(CH_3)_2$, $CH_2CH=CH_2$, and $(CH_3)_2CCH_2$), 96.25 ($OCSO_2Ph$), 122.84 ($CH_2CH=CH_2$), 128.73, 129.25, 130.75, 133.26 (PhC), 134.71 ($CH=CH_2$), and 180.33 (CO); (Found M^+(-SO_2Ph), 153.0912. $C_9H_{13}O_2$ requires M, 153.0906); (Found C, 61.19; H, 6.15. $C_{15}H_{18}O_4S$ requires C, 61.20; H, 6.16 %).

Dihydro-5-ethyl-3,3-dimethyl-5-phenylsulphonyl-2(3H)-furanone (15).- The reaction of sulphone **7** (51mg, 0.20mmol) and ethyl iodide (2ml) in THF (10ml) with lithium bistrimethylsilylamide (240ml, 0.24mmol) gave a white solid **15** (8mg, 14%), m.p. 111-112°C; $\nu_{max.}$ ($CHCl_3$) 1790, 1310, and 1130 cm^{-1}; δ_H (400MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.3Hz, CH_2CH_3), 1.33, 1.41 (each 3H, s, CH_3), 1.72 (1H, dt, *J* 7.3,14.6 $CHHCH_3$), 1.96 (1H, dt, *J* 7.3,14.6 $CHHCH_3$), 2.20 (1H, d, *J* 15.3Hz, $(CH_3)_2CCHH$), 2.87 (1H, d, *J* 15.3Hz, $(CH_3)_2CCHH$), 7.56-7.60 (2H, m, Ph), 7.67-7.71 (1H, m, Ph), and 7.91-7.95 (2H, m, Ph); δ_C (100MHz, $CDCl_3$) 6.98 (CH_2CH_3) 25.66, 28.03 ($C(CH_3)_2$), 26.61 (CH_2CH_3), 37.54, 40.08 ($C(CH_3)_2$ and $(CH_3)_2CCH_2$), 97.61 ($OCSO_2Ph$), 129.15, 130.72, 133.50, 134.54 (Ph), and 180.44 (CO); (Found M^+(-SO_2Ph), 141.0926. $C_8H_{13}O_2$ requires M, 141.0916); (Found C, 59.67; H, 6.43. $C_{14}H_{18}O_4S$ requires C, 59.55; H, 6.43 %).

5-n-Butyldihydro-3,3-dimethyl-5-phenylsulphonyl-2(3H)-furanone (16).- The reaction of sulphone **7** (51mg, 0.20mmol) and n-butyl iodide (3ml) in THF (10ml) with lithium bistrimethylsilylamide (240ml, 0.24mmol) gave a colourless oil **16** (4mg, 6%); $\nu_{max.}$ ($CHCl_3$) 1790, 1305, and 1145 cm^{-1}; δ_H (400MHz, $CDCl_3$) 0.84 (3H, t, *J* 7.0Hz, CH_2CH_3), 1.20-1.39 (10H, m, $C(CH_3)_2$ and $CH_2(CH_2)_2CH_3$), 1.60-1.67 (1H, m, $CHH(CH_2)_2CH_3$), 1.90-1.97 (1H, m, $CHH(CH_3)_2CH_3$), 2.22 (1H, d, *J* 15.3Hz, $(CH_3)_2CCHH$), 2.68 (1H, d, *J* 15.3Hz, $(CH_3)_2CCHH$), 7.54-7.60 (2H, m, Ph), 7.68-7.73 (1H, m, Ph), and 7.93-7.95 (2H, m, Ph); δ_C (100MHz, $CDCl_3$) 13.72 (CH_2CH_3) 22.46, 24.67, 33.15 ($(CH_2)_3CH_3$) 25.63, 28.10 ($C(CH_3)_2$), 38.15, 40.07 ($C(CH_3)_2$ and $(CH_3)_2CCH_2$), 97.36 ($OCSO_2Ph$), 129.14, 130.74, 133.47, 134.52 (Ph), and 180.36 (CO); m/z (f.d.) 310 (M^+); (Found M^+(-SO_2Ph), 169.1228. $C_{10}H_{17}O_2$ requires M, 169.1229).

Dihydro-3,3-dimethyl-5-phenylcarbonyl-5-phenylsulphonyl-2(3H)-furanone (17).- The reaction of sulphone **7** (250mg, 0.984mmol) and benzoyl chloride (500µl) in THF (50ml) with lithium bistrimethylsilylamide (240ml, 0.24mmol) gave a white solid **17** (304mg, 86%), m.p. 100-101°C; $\nu_{max.}$ ($CHCl_3$) 1810, 1675, 1310 and 1150 cm^{-1}; δ_H (400MHz, $CDCl_3$) 1.11, 1.34 (each 3H, s, CH_3), 2.95 (1H, d, *J* 14.8Hz, $(CH_3)_2CCHH$), 3.03 (1H, d, *J* 14.8Hz, $(CH_3)_2CCHH$), 7.23-7.27 (2H, m, Ph), 7.42-7.48 (3H, m, Ph), 7.59-7.61 (1H, m, Ph), and 7.74-7.82 (4H, m, Ph). δ_C (100MHz, $CDCl_3$) 24.59, 26.99 (each CH_3), 39.07, 41.80 ($C(CH_3)_2$ and $(CH_3)_2CCH_2$), 100.11 ($OCSO_2Ph$), 128.27, 129.14, 130.35, 130.86, 133.87, 133.99, 135.08 (Ph), 178.56 (CO_2), and 192.17 (COPh); m/z (f.d.) 358 (M^+); (Found M^+(-SO_2Ph), 217.0846. $C_{13}H_{13}O_3$ requires M, 217.0865); (Found C, 63.64; H, 4.94. $C_{19}H_{18}O_5S$ requires C, 63.67; H, 5.06 %).

3-Hydroxy-5,5-dimethyl-2-phenyl-2-cyclopentenone (19).-
A mixture of 5-benzyldihydro-3,3-dimethyl-5-phenylsulphonyl-2-furanone **13** (50mg, 0.145mmol) and potassium cyanide (28.3mg, 0.436mmol) in DMF (5ml) was heated at 120°C for 2 hours. The DMF was removed by evaporation under high vacuum. Dilute hydrochloric acid (1M, 3ml) was added and the mixture was extracted with dichloromethane (3 x 4ml). The combined extracts were dried (Na_2SO_4), filtered, and evaporated. Chromatography eluting with hexane / ethyl acetate gave **19** (25mg, 85%), m.p. 193-195°C; $\nu_{max.}$ ($CHCl_3$) 1680, 1630 and 1600 cm^{-1}; $\lambda_{max.}$ (MeOH) 205 and 249 nm; δ_H (400MHz, $CDCl_3$) 1.29 (6H, s, $C(CH_3)_2$), 2.54 (2H, s, CH_2), 7.29-7.34 (1H, m, Ph), and 7.43-7.48 (4H, m, Ph). δ_C (100MHz, DMSO d_6) 25.88 ($(CH_3)_2$), 41.43, 45.47 (CH_2 and $C(CH_3)_2$) 108.99 (CPh), 124,87, 126.59, 127.47, 133.80 (Ph),

188.15 and 205.51 ($(CH_3)_2CO$ and CH_2CO); m/z (f.d.) 202 (M^+); (Found M^+, 202.0995. $C_{13}H_{14}O_2$ requires M, 202.0994).

(E) and (Z) 5-Benzylidene-3,3-dimethylpyrrolidin-2-one (21).-
A mixture of 5-benzyldihydro-3,3-dimethyl-5-phenylsulphonyl-2-furanone **13** (64mg, 0.186mmol) in saturated methanolic ammonia solution (4ml) was heated at 60°C in a sealed tube for 40 hours. The mixture was evaporated, water (4ml) was then added and the mixture extracted with dichloromethane (3 x 5ml). The combined extracts were dried (Na_2SO_4), filtered, and evaporated. Benzene (4ml) and toluene-*p*-sulphonic acid (ca. 0.5mg) was added to the resulting mixture. This solution was then heated under reflux for 45 minutes, cooled, washed with saturated aqueous $NaHCO_3$ solution (4ml), dried Na_2SO_4, filtered, and evaporated. Chromatography eluting with hexane / ethyl acetate gave both E and Z isomers **21**.
Low R_f isomer (18mg, 48%) m.p.141-150°C (sublim.); $\nu_{max.}$ ($CHCl_3$) 3420, 1720, 1665 and 1595 cm^{-1}; $\lambda_{max.}$ (MeOH) 275 nm; δ_H (400MHz, CD_3COCD_3) 1.20 (6H, s, $C(CH_3)_2$), 2.94 (2H, d, *J* 2.2Hz, CH_2), 5.94 (1H, m, **CH**Ph), 7.08-7.12 (1H, m, Ph), 7.23-7.31 (4H, m, Ph), and 9.02 (1H, s, NH); δ_C (100MHz, CD_3OD) 25.69 ($(CH_3)_2$), 42.09, 42.16 (CH_2 and $C(CH_3)_2$) 105.54 (CHPh), 126.39, 128.45, 129.45 (Ph), 138.34, 139.44 (Ph and C=CH), and 184.59 (CO); m/z (f.d.) 201 (M^+); (Found M^+, 201.1167. $C_{13}H_{15}NO$ requires M, 201.1154); (Found C, 77.38; H, 7.46; N, 7.13. $C_{13}H_{15}NO$ requires C, 77.58; H, 7.51; N, 6.96 %).
High R_f isomer (7mg, 19%) m.p.105-117°C (sublim.); $\nu_{max.}$ ($CHCl_3$) 3420, 1720, 1680 and 1595 cm^{-1}; $\lambda_{max.}$ (MeOH) 271 nm; δ_H (400MHz, CD_3COCD_3) 1.18 (6H, s, $C(CH_3)_2$), 2.73 (2H, d, *J* 1.7Hz, CH_2), 5.47 (1H, s, **CH**Ph), 7.10-7.15 (1H, m, Ph), 7.24-7.35 (4H, m, Ph), and 8.91 (1H, s, NH). δ_C (100MHz, CD_3OD) 25.27 ($(CH_3)_2$), 41.10, 44.00 (CH_2 and $C(CH_3)_2$) 103.73 (CHPh), 126.83, 128.55, 129.65 (Ph), 136.63, 137.64 (Ph and C=CH), and 186.26 (CO); m/z (f.d.) 201 (M^+); (Found M^+, 201.1141. $C_{13}H_{15}NO$ requires M, 201.1154); (Found C, 77.34; H, 7.40; N, 6.70. $C_{13}H_{15}NO$ requires C, 77.58; H, 7.51; N, 6.96 %).

Dihydro-3,3-dimethyl-5-cyano-2(3H)-furanone (22).- A solution of sulphone **7** (423mg, 1.67mmol) and tetrabutylammonium cyanide (683mg, 2.51mmol) in dichloromethane (10ml) was stirred for 30 minutes at room temperature. The solvent was evaporated and the residue purified by column chromatography eluting with 1:1 hexane / ethyl acetate to give a colourless oil **22** (229mg, 99%); $\nu_{max.}$ ($CHCl_3$) 1795, cm^{-1}; δ_H (400MHz, $CDCl_3$) 1.27, 1.39 (each 3H, s, CH_3), 2.41 (1H, dd, *J* 8.3Hz, 13.3Hz, **CH**HCHCN), 2.51 (1H, dd, *J* 6.0, 13.3Hz, CH**H**CHCN), 5.05 (1H, dd, *J* 6.0, 8.3Hz, **CH**CN); δC (100Mhz, $CDCl_3$) 24.47 and 24.67 (each CH_3), 38.46, 41.00 (**C**$(CH_3)_2$ and CH_2CHCN), 61.67 (CHCN), 116.80 (CN), and 179.06 (CO); (Found C, 60.24; H, 6.49; N,9.89. $C_7H_9O_2N$ requires C, 60.42; H, 6.52; N, 10.07 %).

5-Benzyldihydro-3,3-dimethyl-5-cyano-2(3H)-furanone (23).- The reaction of dihydro-3,3-dimethyl-5-nitrile-2-furanone **22** (70mg, 0.504mmol) and benzyl bromide (270μl) in THF (5ml) with lithium bistrimethylsilylamide (540μl, 0.540mmol) according to the general procedure described above gave a white solid **23** (17mg, 15%), m.p. 89-91°C; $\nu_{max.}$ ($CHCl_3$) 1795 cm^{-1}; δ_H (400MHz, $CDCl_3$) 1.15, 1.44 (each 3H, s, CH_3), 2.24 (1H, d, *J* 13.7Hz, $C(CH_3)_2$CHH), 2.46 (1H, d, *J* 13.7Hz, $C(CH_3)_2$CH**H**), 3.26 (2H, s, CH_2Ph), and 7.29-7.37 (5H, m, Ph); δ_C (100Mhz, $CDCl_3$) 25.49, 25.54 (each CH_3), 39.98, 45.36, 46.02 (**C**$(CH_3)_2$, CH_2Ph and $C(CH_3)_2CH_2$), 74.72 (CCN), 118.97 (CN), 128.33, 128.85, 130.57, 131.66, (Ph), and 179.07 (CO); m/z (f.d.) 229 (M^+); (Found M^+, 229.1111. $C_{14}H_{15}O_2N$ requires M, 229.1103); (Found C, 73.30; H, 6.61; N, 6.25. $C_{14}H_{15}O_2N$ requires C, 73.34; H, 6.59; N, 6.11 %).

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