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Transition Metal Directed Synthesis of Moracin M, a Phytoalexin of *Morus alba* Linn.

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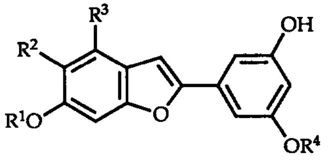
Abstract *2-(5-Resorcinyl)benzofurans have been synthesised by the palladium catalysed cross coupling of 2-trimethylstannyl- or 2-bromozinc benzofurans with the appropriately functionalised 5-iodoresorcinols These were synthesised by the tri-isopropylsilyloxy directed remote (C–5) lithiation/iodination of the O,O-di(tri-isopropylsilyl)resorcinoltricarbonylchromium(0) complex The method was applied to the synthesis of moracin M a phytoalexin of* Morus alba *Linn*

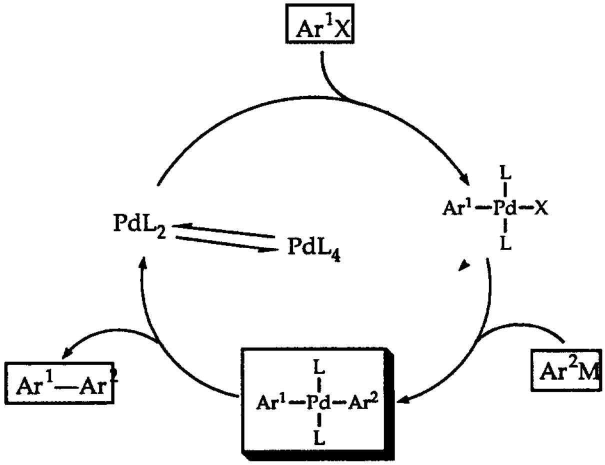
Upon infection with *Fusarium solani* f sp *mori* and other fungi, the white mulberry (*Morus alba* Linn) produces a series of phytoalexins with varying amounts of oxygenation and terpenoid functionalisation of a basic structure, moracin M (**1**)[1] In order to produce material for biological assessment, we have devised a convergent synthesis of this class of compound which allows ready modification for the synthesis of many of the structural variants[2] Previous approaches[3] to the synthesis of such molecules, as exemplified by moracins A (**2**) and B (**3**), have used a strategy involving the formation of the furan ring from an appropriate aryl–C_2–aryl or aryl–O–C–aryl precursor



1, $R^1 = R^2 = R^3 = R^4 = H$
2, $R^1 = Me, R^2 = R^4 = H, R^3 = OMe$
3, $R^1 = R^4 = Me, R^2 = OH, R^3 = H$

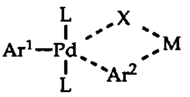
Our synthetic approach to (1) which takes the radically different, and conceptually simpler route of creating the benzofuran to resorcinol bond as the key step by the use of the palladium catalysed cross coupling reaction (Scheme 1)[4] Biaryl synthesis by this means has been widely studied by ourselves[5] and others[4,6] and the structural requirements for effective coupling are well established[5]

Scheme 1



4, $L = PPh_3$

The coupling process uses the 2-metallated (or halogenated) benzofurans and the 5-halogenated (or metallated) resorcinols A key feature of the cross coupling process is the influence of steric crowding on the formation of the congested diarylpalladium intermediate (**4**) and the precise choice of coupling partners would be guided by this phenomenon From our studies of hindered biaryl synthesis, we have proposed a transition state model for the formation of (**4**) based on an S_E2 closed mechanism and depicted at its simplest as the distorted trigonal bipyramid (**5**)[5], or the analogous S_E2 open process which would involve the same stereochemical constraints In this model the Ar^1 ring is σ-bonded to the palladium atom which is therefore on the edge of the ring and the Ar^2 ring approaches in a π-facial manner (see later) The spatial requirements of the two rings are therefore quite different



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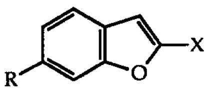

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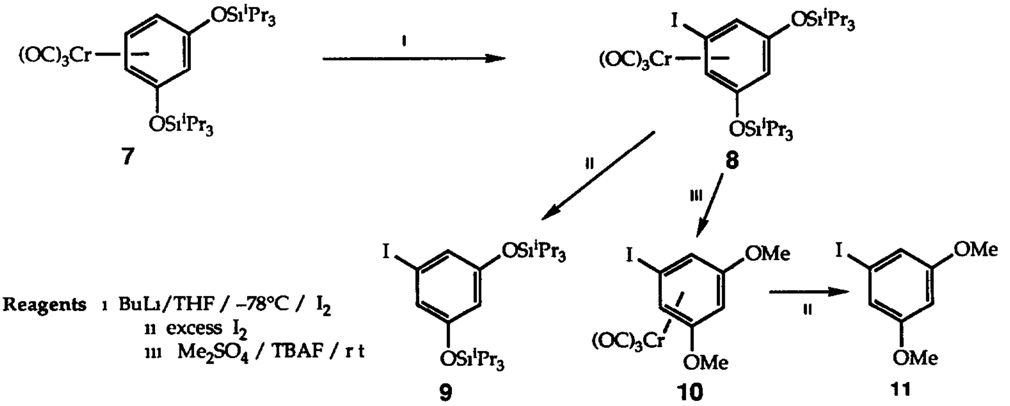
The 2-functionalised benzofurans (**6**, R = H, X = I) and (**6**, R = H, X = $SnMe_3$) were readily prepared by lithiation[7] (BuLi) of the benzofuran and quenching the lithio- species with the appropriate electrophile [I_2 (81%) or Me_3SnCl[6] (79%)] In the 6-methoxy series, lithiation at –78°C was found to give a 1 1 mixture of 2- and 7-substituted products At room temperature the ratio became 4 1 in favour of the 2-lithio- species In order to avoid this complication, the 6-

methoxybenzofuran[8] was demethylated (EtSNa/DMF[9]) and the 6-hydroxy function, protected with the bulky *t*-butyldiphenylsilyl group This silyl ether (**6**, R = *t*-BuPh$_2$SiO, X = H) lithiated cleanly at C-2 but the stannylated product (**6**, R = *t*-BuPh$_2$SiO, X = SnMe$_3$), in common with the other 2-stannylated benzofurans, proved to be very labile and was not usually isolated but used immediately in cross coupling reactions

The 5-functionalised resorcinol compounds were synthesised by use of the remote directing ability of a tri-isopropylsilyloxy group in an arenetricarbonylchromium(0) complex[10] Thus lithiation of 1,3-bis(tri-isopropylsilyloxy)benzenetricarbonylchromium(0) (**7**) with butyl lithium at −78°C, followed by an electrophilic quench gave the 5-substituted complex (**8**) directly (Scheme 2)

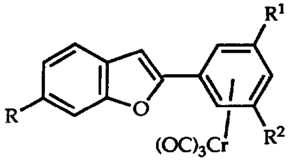
Scheme 2



Reagents i BuLi/THF / -78°C / I$_2$
ii excess I$_2$
iii Me$_2$SO$_4$ / TBAF / r t

The use of excess iodine gave the decomplexed material (**9**) Alternatively, a 'one pot' sequence of desilylation (TBAF) and methylation (Me$_2$SO$_4$) of (**8**) gave the dimethoxy-complex (**10**) Decomplexation (I$_2$) of this, usually without isolation, gave the 5-iodoresorcinol dimethyl ether (**11**) The 5-metallated resorcinols were simply prepared from the lithio- species by transmetallation with the appropriate anhydrous metal halide (ZnBr$_2$ or CuBr SMe$_2$) and used immediately, without isolation

With these materials to hand, the cross coupling process could be evaluated The coupling of η^6-(phenylbromozinc)tricarbonylchromium(0) and 2-iodobenzofuran gave the required product (**12**, $R = R^1 = R^2 = H$) in 82% yield (70% from the 2-bromobenzofuran) (Table 1, Runs 1,2) but when the fully functionalised resorcinol substrate (**8**) was used for the formation of the organometal (copper



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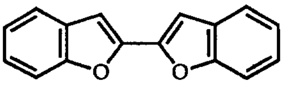

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in this case), the yield of cross coupled product dropped to zero and the homocoupled 2,2'-

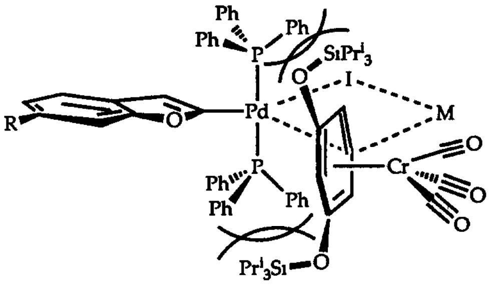
bisbenzofuran (13) (77%) was isolated (Run 3) This is indicative of resistance to formation of the congested diaryl intermediate (4)

Table 1 Cross couplings with arylzinc halides.

Run No	Benzofuran (6)	AreneCr(CO)$_3$	Yield(%)
1	R = H, X = I	$BrZnC_6H_5Cr(CO)_3$	82
2	R = H, X = Br	$BrZnC_6H_5Cr(CO)_3$	70
3	R = H, X = I	(7, 5-CuBr)	0^a
4	R = H, X = ZnBr	$IC_6H_5Cr(CO)_3$	36
5	R = t-Bu(Ph)$_2$SiO, X = ZnBr	$IC_6H_5Cr(CO)_3$	28
6	R = H, X = ZnBr	(8)	22
7	R = H, X = ZnBr	(10)	31

[a] 2,2'-Bisbenzofuran was the isolated product

Application of the model (5) to the system produced the transition state (14) This, and the inversely functionalised alternative (15), were analysed with the CLASH spatial assessment program which suggested that the latter would be less congested and of lower energy Thus whereas in (14), the 3,5-silyloxy- groups would strongly interact with the apical triphenylphosphines, in (15) they would be remote Conversely, the carbonyls of the Cr(CO)$_3$ tripod, which would be expected to destabilise (15), could cogwheel with the apical phosphine and thus avoid too much adverse spatial interaction



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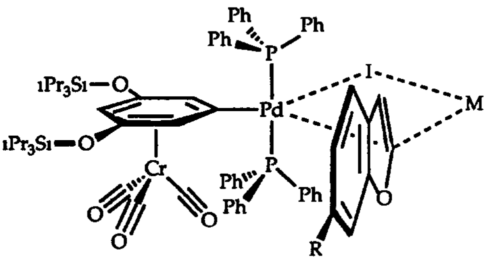

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It was gratifying therefore when, in addition to the successful simpler couplings (Runs 4 – 6), inverse coupling of the 2-metallated benzofuran (6, R = H, X = ZnBr) with η^6–1,3-bis(triisopropylsilyloxy)-5-iodobenzenetricarbonylchromium(0) (8) (Run 7) gave a 22% yield of the coupled product (12, R = H, $R^1 = R^2 = OSi^iPr_3$)

In an attempt to improve the coupling, we turned to the 2-trimethylstannylbenzofurans (6, X = SnMe$_3$) (Table 2)

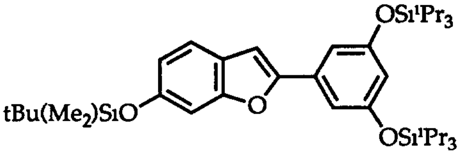
Couplings were all as good or significantly better in the stannylated analogues than in the zinc couplings As predicted by the above model for this coupling sequence, the yields decreased with increasing functionalisation in the haloarene but was largely unaffected by the presence of the 6-*t*-butyldimethylsilyloxy group.

Table 2 Cross couplings with 2-trimethylstannylbenzofurans

Run No.	Benzofuran (6) (X = $SnMe_3$)	Halo-arene	Yield[a](%)
1	R = H	$IC_6H_5Cr(CO)_3$	64
2	R = H	$ClC_6H_5Cr(CO)_3$	80
3	R = H	**8**	20
4	R = H	**9**	73
5	R = H	**10**	46
6	R = H	4-IC_6H_4OMe	30
7	R = *t*-Bu(Me_2)SiO	4-IC_6H_4OMe	40[b]
8	R = *t*-Bu(Me_2)SiO	**9**	90
9	R = *t*-Bu(Me_2)SiO	**10**	54

[a] Yields are quoted for the two (stannylation / coupling) steps

[b] Isolated as the 6-hydroxy compound after desilylation with TBAF in THF



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In particular, for the target molecule, the coupling of 6-oxygenated furan (6, R = *t*-Bu(Me_2)SiO, X = $SnMe_3$) with an excess (3,8 equiv) of the iodoresorcinol (9) gave the product (16) in 90% yield (Run 8) Desilylation of (16) (TBAF/THF, room temperature, 86%) completed the synthesis of moracin M

We thank ICI Agrochemicals and the SERC for the award of a CASE Studentship (to ISM), Dr K J Heritage of ICI Agrochemicals for running CLASH program on the transition state models and Johnson Matthey plc for the loan of palladium chloride

EXPERIMENTAL.

General materials and techniques were as previously described[5] Compounds or methods not previously reported in full are given below

2-Iodobenzofuran (6, R = H, X = I) — Butyl lithium (15 4ml, 1 3M, 20mmol) was added to a solution of benzofuran (2 36g, 2 2ml, 20mmol) in dry ether at −78°C the reaction was allowed to warm to −10°C and stirred for 2h, after which iodine (5.18g, 20mmol) was added *via* a solid addition funnel After a further 30 min, the reaction was allowed to warm to room temperature and diluted with aqueous ammonium chloride (25ml, 2 8M) The mixture was extracted with ether and the ethereal extracts washed successively with aqueous sodium metabisulphite and water, dried ($MgSO_4$) and the solvent evaporated under reduced pressure The residual oil was distilled to give the iodobenzofuran (6, R = H, X = I), (3 95g, 81%) b p 90°C / 1.05mm Hg, ν_{max} (neat) 3132, 3065, 3035, 1614, 1524 cm^{-1}, δ_H ($CDCl_3$) 6 8 (1H, d, *J* 0 8 Hz), 7 17-7 21 (2H, m), 7 44-7 51 (2H, m), *m/z* 244 (M^+, 100%)

2-Trimethylstannylbenzofuran (6, R = H, X = $SnMe_3$) — Butyl lithium (11 1ml, 1 44M, 16mmol) was added to a solution of benzofuran (1 89 g, 1 76 ml, 16 mmol) in ether (16 ml) at −78°C and the reaction stirred for 2 5 h whilst warming to −10°C Chlorotrimethylstannane (3 24 g, 16 mmol) was added and after 16 h, the reaction was quenched with water The mixture was dried ($MgSO_4$) and the solvent evaporated under reduced pressure Distillation of the residual oil gave the *stannane* (6, R = H, X = $SnMe_3$), (3 56 g, 79%), b p 80°C / 0 04 mm Hg, ν_{max} ($CHCl_3$) 3020, 2970, 1510, 1465, 1290, 1150 cm^{-1}; δ_H ($CDCl_3$) 0 4 (9H, s), 6 93 (1H, d, *J* 0 9 Hz), 7 20 (1H, dd, *J* 1 4, 7 2 Hz), 7 26 (1H, dt, *J* 1 4, 7 2 Hz), 7 48-7 58 (2H, m), *m/z* 282 (M^+), 267 (100%) Found M^+ 282 0069, $C_{11}H_{14}OSn$ requires 282 0066

6-Methoxy-2-trimethylsilylbenzofuran (6, R = OMe, X = $SiMe_3$) *and 6-Methoxy-7-trimethylsilylbenzofuran* — Butyl lithium (1 3 ml, 1 55 M, 2 mmol) was added to a solution of 6-methoxybenzofuran (0 296 g, 2 mmol) in THF (2 ml) and ether (1 ml) at room temperature. After 2 h, chlorotrimethylsilane (0 5 ml, 5 4 mmol) was added and after a further hour, the mixture worked up as usual to give the crude mixture of the silylated materials in 71% total yield (ratio 2- 7- = 4 1) These were separated by column chromatography to give firstly the *2-silylated isomer* (6, R = OMe, X = $SiMe_3$) as a gum, ν_{max} ($CHCl_3$) 3149, 3116, 2899, 2836, 1593, 1538 cm^{-1}, δ_H ($CDCl_3$) 0 30 (9H, s), 3 85 (3H, s), 6 84 (1H, dd, *J* 2 3, 8 6 Hz), 6 88 (1H, d, *J* 0 8 Hz), 7 04 (1H, d, *J* 8.6 Hz), *m/z* 220 (M^+), 205, 175 (100%) Found C, 64 32, H, 7 18 $C_{12}H_{16}O_2Si$ requires. C, 65 41, H, 7 32%

The second fraction gave the *7-silylated isomer*, isolated as an oil, ν_{max} (neat) 3150, 3120, 2854, 1619, 1592 cm^{-1}, δ_H ($CDCl_3$) 0 20 (9H, s), 3 85 (3H, s), 6 66 (1H, d, *J* 2 2 Hz), 6 85 (1H, d, *J* 8 4 Hz), 7 52 (1H, d, *J* 2 2 Hz), 7 55 (1H, d, *J* 2 2 Hz), *m/z* 220 (M^+), 205 (100%) Found C, 65 11, H, 7 57 $C_{12}H_{16}O_2Si$ requires C, 65 41, H, 7 32%

6-Hydroxybenzofuran (6, R = OH, X = H) — Ethanethiol (0 62 g, 10 mmol) was deprotonated with sodium hydride (0 842 g, 20 mmol) in DMF (30 ml) at room temperature during 10 min 6-Methoxybenzofuran[8] (1 48 g, 10 mmol) was added and and the mixture refluxed for 4 h The reaction was cooled, quenched with 2M hydrochloric acid and the mixture extracted with ether The organic extract was washed with 2M sodium hydroxide and the basic extract reacidified with 2M hydrochloric acid The resulting solution was extracted with ether and the ether phase dried ($MgSO_4$) and evaporated under reduced pressure Column chromatography gave the 6-hydroxybenzofuran (6, R = OH, X = H) (0 80 g, 60%), m p 56°C (lit[11] 56°C)

6-(t-Butyldiphenylsilyloxy)benzofuran (6, R = *t*-$BuPh_2SiO$, X = H) — 6-Hydroxybenzofuran (0 86 g, 6 42 mmol) was treated with imidazole (1 1 g, 16 mmol) and *t*-butylchlorodiphenylsilane (1 9 ml, 7 1 mmol) in DMF (5 ml) and the mixture stirred at 50°C for 16 h Saturated aqueous sodium bicarbonate was added and the mixture extracted with petrol The organic phase was dried ($MgSO_4$), the solvent evaporated under reduced pressure and the residual oil distilled, b p. 210°C / 15 mm Hg The silyl ether (6, R = *t*-$BuPh_2SiO$, X = H) (90%) solidified on standing, m p. 68°C, ν_{max} (Nujol) 3071, 2926, 1621, 1485 cm^{-1}; δ_H 0 85 (9H, s), 6 35 (1H, dd, *J* 1 1, 2 2 Hz), 6 50 (1H, dd, *J* 2 3, 8 8 Hz), 6 63 (1H, br d, *J* 2 3 Hz), 7 02 (1H, d, *J* 8 8 Hz), 7 20 (1H, d, *J* 2.2 Hz), 7 05–7 18 (6H, m), 7 45–7 50 (4H, m); *m/z* 372 (*M*$^+$), 315 (100%) Found C, 77 12, H, 6 45 $C_{24}H_{24}O_2Si$ requires C, 77 38, H, 6 49%

1,3-Bis(tri-isopropylsilyloxy)benzene — Resorcinol (2 2 g, 20 mmol) and imidazole (6 8 g, 100 mmol) in dry DMF (6 ml) were treated with chlorotri-isopropylsilane (8 47 g, 9 4 ml, 44 mmol) at room temperature during 48 h Saturated sodium hydrogen carbonate solution (20 ml) was added and the mixture extracted with petrol The extracts were washed with 2N sodium hydroxide solution followed by water, dried ($MgSO_4$) and the solvent evaporated under reduced pressure to give the silyl ether (4 9 g, 99%), b p 130°C / 7 mm Hg; ν_{max} (neat) 2950, 2865, 1590, 1480, 1380, 1260, 1070, 1000, 920, 880, 770, 680 cm^{-1}, δ_H ($CDCl_3$) 1 08 (36H, d, *J* 7 Hz), 1 2 (6H, septet, *J* 7 Hz), 6 43 (1H, t, *J* 2 1 Hz), 6 48 (2H, dd, *J* 2 1, 7 9 Hz), 7 03 (1H, t, *J* 7 9 Hz), *m/z* 250 (*M*$^+$), 208, 207, 179, 165, 152, 151 (100%) Found C, 71 77, H, 10 74 $C_{15}H_{26}OSi$ requires. C, 71 94, H, 10 46%)

η^6–*1,3-Bis(tri-isopropylsilyloxybenzene)tricarbonylchromium(0)* (7) — A mixture of 1,3-bis(tri-isopropylsilyloxy)benzene (2 5 g, 10 mmol) and hexacarbonylchromium (2 42 g, 11 mmol) in deoxygenated di-n-butyl ether–THF (10 1) (93 ml) were heated under reflux for 48 h using a simplified Strohmeier apparatus The resulting orange solution was cooled, filtered through Celite with ether, and concentrated under reduced pressure Recrystallisation of the residue (petrol) gave the complex (7) (5 02 g, 90%), m p 88-89°C, ν_{max} ($CHCl_3$) 1955, 1890, 1510, 1180, 878 cm^{-1}, δ_H ($CDCl_3$) 1 1 (36H, d, *J* 7 Hz), 1 12 (6H, septet, *J* 7 Hz), 4 7 (2H, dd, *J* 7, 2 Hz), 5 15 (1H, t, *J* 2 Hz), 5 5 (1H, t, *J* 7 Hz), *m/z* 558 (*M*$^+$), 502, 474, 442, 379 (100%), 351, 337, 323, 309 Found C, 58 26, H, 8 42 $C_{27}H_{46}CrO_5Si_2$ requires C, 58 04, H, 8 30%

η^6–*1,3-Bis(tri-isopropylsilyloxy)-5-iodobenzenetricarbonylchromium(0)* (8) — Butyl lithium (1 8 ml, 1 6 M in hexane, 1 5 eq) was added to a solution of η^6–1,3-bis(tri-isopropylsilyloxy)benzenetricarbonylchromium(0) (1 116 g, 2 mmol) in THF (70 ml) at –78°C After 1 h at that temperature, iodine (0 762 g, 3 mmol) was added *via* a solid addition funnel to the rapidly stirred solution After a further hour, the reaction was allowed to warm to room temperature and quenched with aqueous sodium metabisulphite The mixture was extracted with ether and the extracts washed with brine and water, dried ($MgSO_4$) and evaporated under reduced pressure The residue was purified by column chromatography and recrystallisation from petrol to give the yellow *complex* (8), (0 78 g, 57%), m p 66-67°C, ν_{max} ($CHCl_3$) 1985, 1900 cm^{-1}, δ_H ($CDCl_3$) 1 1 (36H, d, *J* 7 Hz), 1 2 (6H, septet, *J* 7 Hz), 5 04 (1H, t, *J* 2 2 Hz), 5 18 (2H, d, *J* 2 2 Hz), *m/z* 684 (*M*$^+$), 628, 600 (100%) Found C, 47 56, H, 6 69 $C_{27}H_{45}CrIO_5Si_2$ requires C, 47 36, H, 6 62%

η^6–*1,3-Dimethoxy-5-iodobenzenetricarbonylchromium(0)* (10) — η^6–1,3-Bis(trimethylsilyloxy)-5-iodobenzenetricarbonylchromium(0) (0 53 g, 0 775 mmol) in THF (10 ml) was treated with sodium hydride (0 36 g, 15 mmol), dimethyl sulphate (1 5 ml, 9 mmol) and TBAF (1 5 ml, 1M in THF) during 16 h Standard work-up gave, after filtration through a Celite plug and evaporation of the solvents, the complex (10) (0 217 g, 70%) which was not further purified, but used directly for the cross coupling experiments

1,3-Dimethoxy-5-iodobenzene. (**11**)— η ^{6}– [1,3-Bis(tri-isopropylsilyloxy)-5-iodobenzene]tricarbonylchromium(0) (2 18 g, 3.2 mmol) in THF (10 ml) was treated with dimethyl sulphate (7 ml, 23 eq)) followed by tetrabutylammonium fluoride in THF (7 ml, 1M, 2 2 eq) and the reaction stirred overnight The mixture was quenched with aqueous ammonia The organic phase was separated, washed with water, dried ($MgSO_4$). The ethereal solution was treated with an excess of iodine to decomplex the chromium, the resultant product worked up conventionally and purified by column chromatography to give *1,3-dimethoxy-5-iodobenzene* (**11**), (0 76 g, 90%) m p 72.5-73.5°C, ν_{max} ($CHCl_3$) 3028, 2964, 2837, 1597, 1570 cm^{-1}; δ_H ($CDCl_3$) 3.76 (6H, s), 6.40 (1H, t, *J* 2.2 Hz), 6 85 (2H, d, *J* 2 2 Hz), *m/z* 264 (*M*$^+$, 100%), 234 Found· C36.32; H, 3 35 $C_8H_9IO_2$ requires. C, 36 39; H, 3 44%

General Procedure for the Palladium Catalysed Cross Coupling of arylbromozinc compounds. — Butyl lithium (1 mmol) was added to a solution of the first arene in THF (1 ml) at –10°C (for benzofurans) or -78°C (for arenetricarbonylchromium(0) complexes) followed, after 2 h, by anhydrous zinc bromide (1 5 mmol) [generated *in situ* by refluxing a mixture of zinc dust and 1,2-dibromoethane in THF (10 ml)] and the mixture stirred at room temperature for a further hour To this was added a mixture of the iodinated (or brominated) second arene (1 mmol) and tetrakistriphenylphosphinepalladium (2-4 mol%) in THF and the reaction stirred overnight The mixture was quenched with aqueous ammonium chloride, the product extracted with ether and purified by column chromatography and/or crystallisation as appropriate

So prepared were —

η^6–(2-Benzofuranyl)benzenetricarbonylchromium(0) (**12**, R = R^1 = R^2 = H) — From η^6–benzenetricarbonylchromium(0) and 2-iodobenzofuran in 82% yield, (70% from 2-bromobenzofuran) or conversely, from benzofuran and η^6–iodobenzenetricarbonylchromium(0) in 36% yield, m p 148-149°C, ν_{max} ($CHCl_3$) 1970, 1900 cm^{-1}, δ_H ($CDCl_3$) 5 36 (1H, tt, *J* 1 7, 6 3 Hz), 5 49 (2H, t, *J* 6 3 Hz), 5 95 (2H, dd, *J* 1 7, 6 3 Hz), 6 94 (1H, d, *J* 0 97 Hz), 7 25 (1h, dt, *J* 1.2, 7 2, Hz), 7.33 (1H, dt, *J* 1 5, 8 2, Hz), 7 50 (1H, dd, *J* 1 2, 8 2 Hz), 7 58 (1H, br d, *J* 7 2 Hz); *m/z* 330 (*M*$^+$), 274, 246 (100%) Found C, 61 82, H, 2 93 $C_{17}H_{10}CrO_4$ requires C, 61 83; H, 3 05%

2,2'-Bisbenzofuran (**13**) — From at attempt to cross couple η^6–3,5-bis(tri-isopropylsilyloxy)-benzenetricarbonylchromium(0) [*via* the use of CuBr SMe_2 (1 eq) instead of zinc bromide] and 2-iodobenzofuran, a 77% yield of the homocoupled material (**13**), m p 190-192°C (lit[15] 192 5-195 5°C) was obtained as the only detectable and isolable product

η^6–5-(2-Benzofuranyl)-1,3-bis(tri-isopropylsilyloxy)benzenetricarbonylchromium(0) (**12**, R = H, R^1 = R^2 = OSi^{i}Pr$_3$) — From benzofuran and η^6–1,3-bis(trimethylsilyloxy)-5-iodobenzenetricarbonylchromium(0) in 22% yield as yellow crystals from ethanol, m p 68-69°C, ν_{max} ($CHCl_3$) 1965, 1890 cm^{-1}, δ_H ($CDCl_3$) 1 15 (36H, d, *J* 7 Hz), 1 27 (6H, septet, *J* 7 Hz), 5 13 (1H, t, *J* 1 8 Hz), 5 36 (2H, d, *J* 1 8 Hz), 6 95 (1H, d, *J* 0 75 Hz), 7 26 (1H, dd, *J* 1 4, 7 3 Hz), 7 32 (1H, dt, *J* 1 4, 7 3 Hz), 7 56 (1H, br t, *J* 7 3 Hz), 7 58 (1H, br d, *J* 7 3 Hz), *m/z* 538 [*M*$^+$– Cr(CO)$_3$], 495, 422, 379 (100%) Found C, 62 32, H, 7 70 $C_{35}H_{50}CrO_6Si_2$ requires C, 62 28; H, 7 47%

η^6–5-(2-Benzofuranyl)-1,3-dimethoxybenzenetricarbonylchromium(0) (**12**, R = H, R^1 = R^2 = OMe) — From benzofuran and η^6–1,3-dimethoxy-5-iodobenzenetricarbonylchromium(0) in 31% yield, m p 138°C, ν_{max} ($CHCl_3$) 1966, 1892 cm^{-1}; δ_H ($CDCl_3$) 3 85 (6H, s), 5 19 (1H, t, *J* 1 9 Hz), 5 45 (2H, d, *J*

1 9 Hz), 7 01 (1H, d, *J* 0 6 Hz), 7 2–7 4 (2H, m), 7 5–7 6 (2H,m); *m/z* 390 (M^+), 334, 306 (100%) Found C, 58.27, H, 3 56. $C_{19}H_{14}CrO_6$ requires C, 58 47; H, 3 62%

η^6–*(6–t-Butyldiphenylsilyloxybenzofuranyl)benzenetricarbonylchromium(0)* (**12**, R = $OSiMe_2{}^tBu$, R^1 = R^2 = H) — From 6-*t*-butyldiphenylsilyloxybenzofuran and η^6–iodobenzenetricarbonylchromium(0) in 28% yield, m p 162–164°C; ν_{max} ($CHCl_3$) 1975, 1905 cm^{-1}, δ_H ($CDCl_3$) 1 10 (9H, s), 5 30 (1H, t, *J* 6 2 Hz), 5 44 (2H, t, *J* 6 2 Hz), 5 83 (2H, d, *J* 6 2 Hz), 6 75 (1H, br d, *J* 8 4 Hz), 6 80 (1H, s), 6 87 (1H, br s,), 7 24 (1H, d, *J* 8 4 Hz), 7 40 (6H, m), 7 74 (4H, m), *m/z* 584 (M^+), 500 (100%) Found M^+, 584 1121 $C_{33}H_{28}CrO_5Si$ requires 584 1111

General Procedure for the Palladium Catalysed Cross Coupling of 2-benzofuranyltrimethylstannanes — The lithiated benzofuran (**6**, X = Li) (0 25–1 5 mmol, *vide supra*) in ether (2 ml) was treated with a solution of chlorotrimethylstannane (0 25–1 5 mmol) in ether at room temperature under an atmosphere of nitrogen during 1 h The resulting solution was transferred, by nitrogen pressure,*via* a cannula to a solution of the iodoarene (1 eq) and palladium tetrakistriphenylphosphine (4 mol%) in THF or benzene or toluene (20 ml) and the reaction refluxed for *ca* 16 h Products were isolated by conventional work-up and purification by column chromatography and / or crystallisation as appropriate

So prepared were —

η^6–*(2-Benzofuranyl)benzenetricarbonylchromium(0)* (**12**, R = R^1 = R^2 = H) — From benzofuran and η^6–iodobenzenetricarbonylchromium(0) (64%) or η^6–chlorobenzenetricarbonylchromium(0) (80%) in THF, identical with the material obtained above

η^6–*5-(2-Benzofuranyl)-1,3-bis(tri-isopropylsilyloxy)benzenetricarbonylchromium(0)* (**12**, R = H, R^1 = R^2 = OSi^iPr_3) — From benzofuran and η^6–1,3-bis(tri-isopropylsilyloxy)-5-iodobenzenetricarbonylchromium(0) (**8**) in THF in 20% yield, identical with the material obtained above

η^6–*5-(2-Benzofuranyl)-1,3-dimethoxybenzenetricarbonylchromium(0)* (**12**, R = H, R^1 = R^2 = OMe) — From benzofuran and η^6–5-iodo-1,3-dimethoxybenzenetricarbonylchromium(0) in THF in 46% yield, identical with the material obtained above

5-(2-Benzofuranyl)-1,3-bis(tri-isopropylsilyloxy)benzene (**16**, R = H, R^1 = = R^2 = Si^iPr_3) — From benzofuran and 1,3-bis(tri-isopropyltri-isopropylsilyloxy)-5-iodobenzene in THF in 73% yield as an oil, ν_{max} (neat) 2945, 2868, 1607, 1592, 1568 cm^{-1}, δ_H ($CDCl_3$) 1 13 (36H, d, *J* 7 2 Hz) 1 30 (6H, septet, *J* 7 2 Hz), 6 43 (1H, t, *J* 2 2 Hz), 6 94 (1H, d, *J* 1 6 Hz), 7 0 (2H, d, *J* 2 2 Hz), 7 22 (1H, dd, *J* 1 6, 7 6 Hz), 7 27 (1H, dt, *J* 1 6, 7 6 Hz), 7 5–7 6 (2H, m), *m/z* 538 (M^+), 495 (100%) Found C, 71 12, H, 9 63 $C_{32}H_{50}O_3Si_2$ requires C, 71 32, H, 9 35%

4-(2-Benzofuranyl)anisole — From benzofuran and 4-iodoanisole in 30% yield, m p 147-148°C, ν_{max} (Nujol) 1611, 1505, 1464 cm^{-1}, δ_H ($CDCl_3$) 3 87 (3H,s), 6 88 (1H, d, *J* 0 7 Hz), 6 98 (2H, d, *J* 9 Hz), 7 22 (1H, dd, *J* 1 8, 5 2 Hz), 7 24 (1H, dd, *J* 1 8, 5 2 Hz), 7 47–7 58 (2H, m), 7 8 (2H, d, *J* 9 Hz), *m/z* 224 (M^+, 100%) Found C, 80 46, H, 5 38 $C_{15}H_{12}O_2$ requires C, 80 34, H, 5 39%

4-(6-Hydroxy-2-benzofuranyl)anisole — From 6-*t*-butyldiphenylsilyloxybenzofuran and 4-iodoanisole, followed by desilylation with TBAF in THF (16h, room temperature), in 40% overall yield, m p 205–207°C, ν_{max} (Nujol) 3293, 3027, 3009, 1622, 1507 cm^{-1}, δ_H ($CDCl_3$) 3 86 (3H, s), 4 82 (1H, br s, 6 76 (1H, dd, *J* 2 2, 8 5 Hz), 6 80 (1H, d, *J* 0 8 Hz), 6 96 (2H, d, *J* 9 0 Hz), 7 00 (1H, br d, *J* 2 2 Hz), 7 37 (1H, d, *J* 8 5 Hz), 7 74 (2H, d, *J* 9 Hz), *m/z* 240 (M^+), 225

η^6–5-(6-t-Butyldiphenylsilyloxy-2-benzofuranyl)-1,3-dimethoxybenzenetricarbonylchromium(0) (**12**, R = *t*-Bu(Me$_2$)SiO, R^1 = R^2 = MeO). — From 6-*t*-butyldiphenylsilyloxybenzofuran and η^6–1,3-dimethoxy-5-iodobenzenetricarbonylchromium(0) in refluxing benzene in 54% yield, m.p. 163°C; ν_{max} (CHCl$_3$) 1965, 1891 cm^{-1}; δ_H (CDCl$_3$) 1.12 (9H, s), 3.82 (6H, s), 5.11 (1H, t, *J* 1.8 Hz), 5.31 (2H, d, *J* 1.8 Hz), 6.75 (1H, dd, *J* 2.0, 8.5 Hz), 6.83 (1H, d, *J* 1.0 Hz), 6.87 (1H, br.d, *J* 2.0 Hz), 7.26 (1H, d, *J* 8.5 Hz), 7.3–7.8 (10H, m); *m/z* 560 (M^+ – 3 x CO), 508. Found: C, 65.23; H, 5.00. $C_{35}H_{32}CrO_7Si$ requires: C, 65.20; H, 5.00%.

1,3-Bistri-isopropylsilyloxy-5-(6-t-butyldiphenylsilyloxy-2-benzofuranyl)benzene (**16**). — From 6-*t*-butyldiphenylsilyloxybenzofuran and 1,3-bistri-isopropylsilyloxy-5-iodobenzene (3.8 equiv.) in THF in 90% yield as a colourless oil, ν_{max} (CHCl$_3$) 3135, 3072, 3051, 3017, 1621, 1592, 1567, 1489 cm^{-1}; δ_H (CDCl$_3$)1.05–1.15 (45H, m), 1.2–1.4 (6H, m), 6.37 (1H, t, *J* 2.0 Hz), 6.72 (1H, dd, *J* 2.4, 8.1 Hz), 6.80 (1H, d, *J* 0.8 Hz), 6.88 (2H, d, *J* 2.0 Hz), 6.94 (1H, br.d, *J* 2.4 Hz), 7.23 (1H, d, *J* 8.1 Hz), 7.3–7.5 (10H, m); *m/z* 749 (M^+ – ^{i}Pr), 735 (100%). Found: C, 72.77; H, 8.65. $C_{48}H_{68}O_4Si_3$ requires: C, 72.67; H, 8.64%.

Moracin M (**1**). — 1,3-Bistri-isopropylsilyloxy-5-(6-t-butyldiphenylsilyloxy-2-benzofuranyl)benzene (0.207 g. 0.26 mmol) in THF (10 ml) was treated with tetrabutylammonium fluoride (0.8 ml, 1M in THF, 0.8 mmol) during 16 h. The solvent was evaporated, the residue diluted with aqueous acetic acid, and the mixture extracted with ethyl acetate. The organic phase was dried (MgSO$_4$) and purified by column chromatography to give moracin M, (0.043 g, 86%), m.p. 259–262°C (lit[12] m.p. 262°C); ν_{max} (Nujol) 3274, 2925, 1614, 1579, 1464 cm^{-1}; δ_H (d$_6$-acetone, 500 MHz) 3.5 (1H, br.s), 6.38 (1H, t, *J* 2.4 Hz), 6.81 (1H, dd, *J* 2.1, 8.3 Hz), 6.87 (2H, d, *J* 2.4 Hz), 6.98 (1H, br.d, *J* 2.1 Hz), 7.02 (1H, d, *J* 0.9 Hz), 7.40 (1H, d, *J* 8.3 Hz), 8.50 (2H, br.s); *m/z* 242 (M^+, 100%).

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