Tetrahedron Vol 47, No 37, pp 7991-8000, 1991
Printed in Great Britain

0040-4020/91 $3 00+ 00

Transition Metal Mediated Synthesis of Some Prenylated Phytoalexins of *Morus alba* Linn.

Inderjit S Mann and David A. Widdowson*
Department of Chemistry, Imperial College, London SW7 2AY, U K

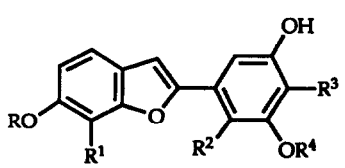
John M. Clough
ICI Agrochemicals, Jealott's Hill Research Station, Bracknell, Berks RG12 6EY, U K.

(*Received in UK* 3 *July* 1991)

Key Words Phytoalexin synthesis, arenetricarbonylchromium(0) complexes, directed lithiation, palladium catalysed cross coupling

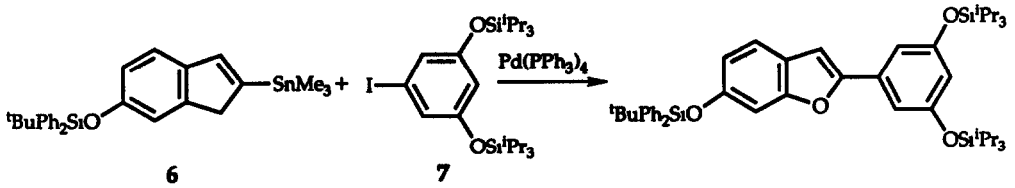
Abstract· *Directed functionalisation of resorcinol and benzofuran rings was achieved by activation with a coordinated tricarbonylchromium(0) unit and vicinal or remote lithiation directed by methoxy or t-butyldiphenylsilyloxy groups respectively The process was applied either before [to the geranylbenzofuran (16) for mulberrofuran B (5)] or after [for moracin C (2)] palladium catalysed coupling of the 2-stannylated benzofuran and the 5-iodinated resorcinol moieties In addition moracin I (4) was synthesised by a Stille coupling of the stannylated benzofuran (6) with the phloroglucinol triflate (14) Application to the synthesis of albafuran A (3) gave, unexpectedly, the 3-geranylbenzofuran (11)*

We have recently described a new approach (Scheme 1) to the synthesis of the resorcinylbenzofuran nucleus of the phytoalexins of mulberry (*Morus alba* Linn)[1] and in particular to the parent phytoalexin moracin M (1) This route used palladium catalysed cross coupling of a 5-iodoresorcinol derivative with a 2-trimethylstannyl- or 2-bromozincbenzofuran to form the key benzofuran–resorcinol bond. The 5-iodination of the resorcinol ring was effected *via* a chromium mediated *meta* lithiation process[2].



1, Moracin M. R = R^1 = R^2 = R^3 = R^4 = H
2, Moracin C· R = R^1 = R^2 = H, R^3 = prenyl, R^4 = Me
3, Albafuran A: R = R^1 = R^3 = R^4 = H, R^2 = geranyl
4, Moracin I : R = R^1 = R^3 = H, R^2 = prenyl, R^4 = Me
5, Mulberrofuran B: R = Me, R^1 = geranyl, R^2 = R^3 = R^4 = H

Scheme 1

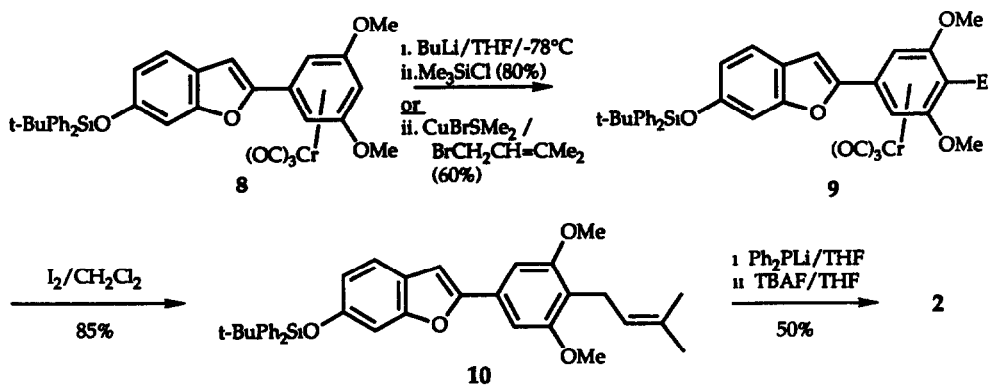


6 **7**

It was a key facet of the strategy that the coupling process would be effective in the presence of a tricarbonylchromium unit on the resorcinol ring and thus would allow further chromium mediated functionalisation of that ring after as well as before the coupling process. This paper reports the realisation of that strategy in the synthesis of three terpene substituted resorcinylbenzofurans, moracin C (**2**)[3], moracin I (**4**)[4] and mulberrofuran B (**5**)[5]

Moracin C (**2**) was synthesised by manipulation of the resorcinol ring *post* coupling (Scheme 2) The site of directed lithiation[6] of the coupled complex (**8**) was first checked by quenching the anion with chlorotrimethylsilane. The product (**9**, E = $SiMe_3$) (80%) was readily identified as the 4-substituted compound from the nmr spectrum (see Experimental) Repeat of the process with a copper bromide dimethyl sulphide complex/prenyl bromide (3-methylbut-2-enyl bromide) quench gave the 4-prenyl (3-methylbut-2-enyl) analogue (**9**, E = $CH_2CH{=}CMe_2$) in 60% yield

Scheme 2



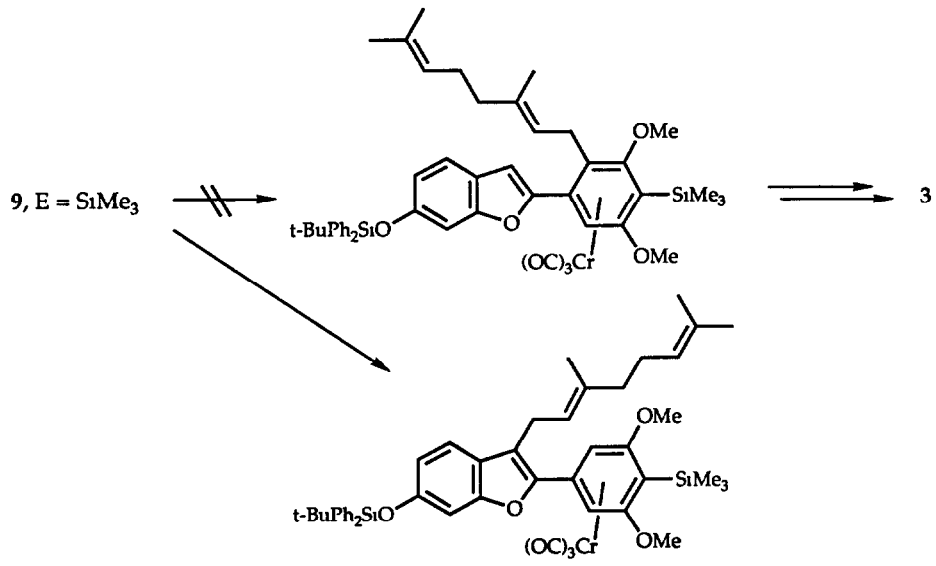
8 **9** **10**

Sequential decomplexation (I_2/ CH_2Cl_2/r t.) to give (**10**), monodemethylation (1 equiv Ph_2PLi/THF/reflux) and desilylation (TBAF/THF/r t.) gave moracin C (**2**) in 42% overall yield.

Although the complexed resorcinol ring in (**9**) is relatively congested, it was expected that further lithiation of (**9**, E = $SiMe_3$) would occur in the resorcinol ring[7] and lead to the synthesis of albafuran A (**3**)[8]. In the event (Scheme 3) lithiation, transmetallation with copper bromide dimethyl

sulphide complex and reaction with geranyl bromide gave a product in 67% yield, which did not contain the expected geranylresorcinol unit Instead, the nmr spectrum showed that the resorcinol ring still had *two* protons and that the 3-proton of the benzofuran ring was missing The product is therefore formulated as the 3-geranylbenzofuran (**11**). This requires that a normally unactivated proton, H-3 of benzofuran[9], is removed in preference to the ostensibly more acidic protons on the complexed resorcinol ring The deprotonation is presumably the result of (i) remote labilisation by the tricarbonylchromium unit, a process we have observed previously in the activation of H-2 in 1-methylindoletricarbonylchromium(0)[10] and (ii) the blocking of the vacant sites on the complexed ring by the $SiMe_3$ group forcing the MeO-groups into a conformation overlying the aryl hydrogens

Scheme 3



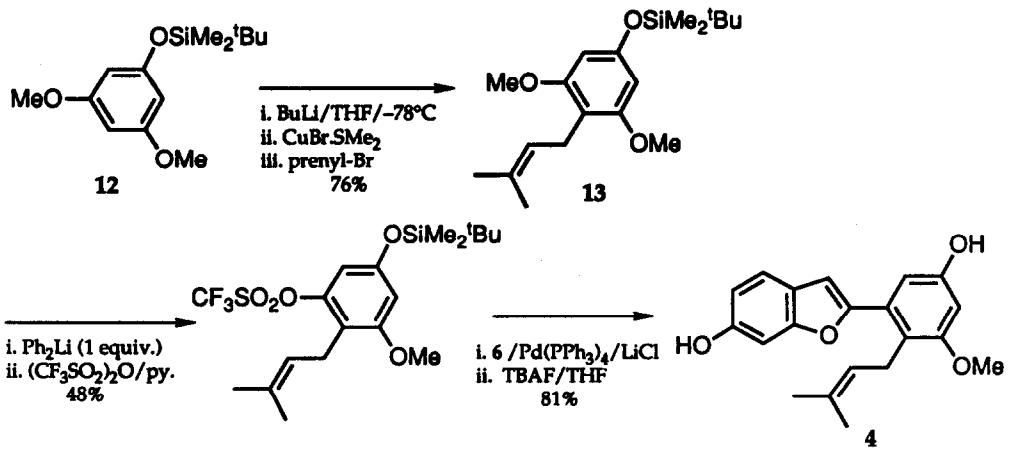
11

The approach to this functional array was therefore switched to *pre*-coupling manipulation of the resorcinol ring and the target was switched to the similar prenyl substituted moracin I (**3**) Appropriate chromium mediated functionalisation *via* a sequence of directed lithiations of 3-tri-isopropylsilyloxyanisoletricarbonylchromium(0) gave unexpected results and was ultimately abortive for moracin synthesis These studies have been reported elsewhere[11]

In consequence, we adopted a strategy based upon Stille coupling[12] for the formation of the key aryl – aryl bond (Scheme 4) Thus phloroglucinol dimethyl (*t*-butyldimethylsilyl) ether (**12**) was lithiated, trans-metallated with copper bromide dimethyl sulphide complex and the cuprate coupled with prenyl bromide to give the 2-prenylated derivative (**13**) (76%) Monodemethylation was best carried out with lithium diphenylphosphide[13] (50%) and conventional triflation[14]

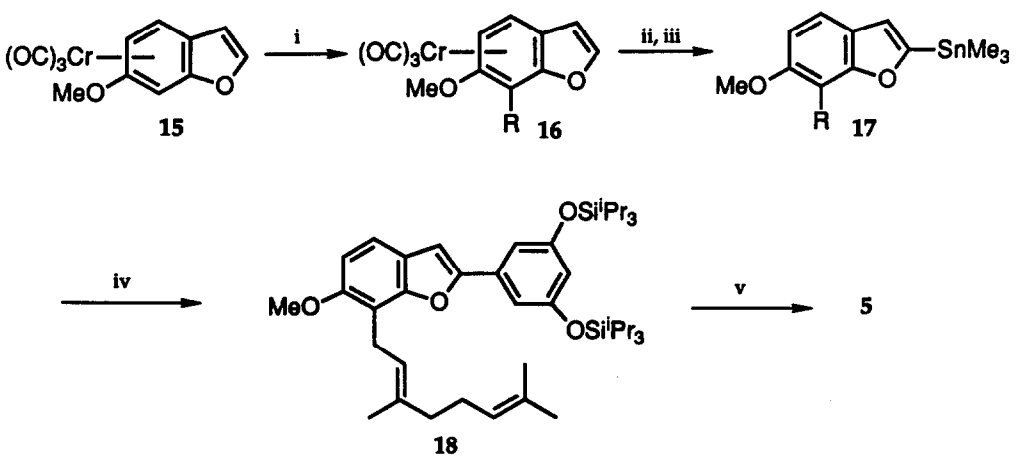
(Tf_2O/py, 96%) produced the required partner (14) for the Stille coupling. Coupling of (14) with 2-stannylated benzofurans proved to be very effective for both benzofuran itself (91%) and the 6-oxygenated analogue (6) (84%). Deprotection (TBAF, 96%) completed the synthesis of moracin I (4).

Scheme 4



As a final exemplification of chromium mediated functionalisation, we chose to control substitution of the benzofuran system in the synthesis of mulberrofuran B (5) (Scheme 5).

Scheme 5



Reagents: i. BuLi/THF/-78°C, Me_3SiCl or $CuBr.SMe_2$/geranyl bromide; ii. hv/air; iii. BuLi/THF/-78°C, Me_3SnCl; iv. 7, $Pd(PPh_3)_4$, THF; v. TBAF/THF/r.t.

Since lithiation of 6-methoxybenzofuran gave a 1:1 mixture of 2- and 7-substitution, the ring was complexed with a tricarbonylchromium unit (20%, unoptimised). Lithiation of this product (15) (BuLi/THF/–78°C, 2h) and chlorosilane quench gave exclusively the 7-silylated product (16, R = $SiMe_3$) (67%) The lithiation was repeated with a copper bromide dimethyl sulphide complex/geranyl bromide quench and oxidative work up to give the 7-geranylbenzofuran (16, R = geranyl, decomplexed) (60%). Lithiation, now exclusively at C-2, stannylation [to give (17)] and cross coupling as before gave the protected mulberrofuran (17). Desilylation (TBAF/THF/r t) completed the synthesis of mulberrofuran B (5) in 40% overall yield from (16, R = geranyl, decomplexed).

We thank ICI Agrochemicals and the SERC for the award of a CASE Studentship (to ISM) and Johnson Matthey plc for the loan of palladium chloride.

EXPERIMENTAL

General procedures: chromium complexation[15], lithiation/electrophilic quench[15] and palladium catalysed cross couplings[16] and their associated work up techniques were as previously described Compounds and methods not fully reported previously are given below

2-[η⁶–3,5-Dimethoxy-4-trimethylsilylphenyltricarbonylchromium(0)]-6-(t-butyldiphenylsilyloxy)-benzofuran (9, E = $SiMe_3$) — A solution of 2-[η⁶–3,5-dimethoxyphenyltricarbonylchromium(0)]-6-(t-butyldiphenylsilyloxy)benzofuran (8)[1] (0.644g, 1mmol) in THF (35ml) at –78°C was treated with butyl lithium in hexane (0.6ml, 1mmol) during 1h. Chlorotrimethylsilane (0.5ml) was added and the reaction stirred for a further hour before being allowed to warm to room temperature Standard work up and flash chromatography gave the *silylated complex* (9, E = $SiMe_3$) (573mg, 80%), m.p 184-5°C, ν_{max} ($CHCl_3$) 1960, 1887 cm^{-1}; δ_H ($CDCl_3$) 0 35 (9H, s), 1 10 (9H, s), 3 75 (6H, s), 5 20 (2H, s), 6 76 (1h, dd, *J* 2.3, 8 5Hz), 6 86 (1H, br.s,), 6 89 (1H, br d, *J* 2 3Hz), 7.26 (1H, d, *J* 8 5Hz), 7 3-7 8 (10H, m), *m/z* 716 (M^+), 632 (100%) Found: C, 63 45; H, 5 63, $C_{38}H_{40}CrO_7Si_2$ requires C, 63 67, H, 5 62%.

2-[η⁶–3,5-Dimethoxy-4-(3-methylbut-2-enyl)phenyltricarbonylchromium(0)]-6-(t-butyldiphenyl-silyloxy)benzofuran (9, E = $CH_2CH{=}CMe_2$) — A solution of 2-[η⁶–3,5-dimethoxyphenyltricarbonyl-chromium(0)]-6-(t-butyldiphenylsilyloxy)benzofuran[1] (8) (0.322g, 0.5mmol) in THF (20ml) at –78°C was treated with butyl lithium in hexane (0.3ml, 0.5mmol) during 1h. Copper bromide dimethyl sulphide complex (0 103g, 0.5mmol) was added at –20°C during 1h followed by 3-methylbut-2-enyl bromide (0 1ml) and the reaction stirred for a further 2h. at –20°C and allowed to warm to room temperature overnight. Standard work up followed by flash chromatography gave the *prenylated complex* (9, E = $CH_2CH{=}CMe_2$) (214mg, 60%), m p 166-7°C, ν_{max} ($CHCl_3$) 1959, 1886 cm^{-1}, δ_H ($CDCl_3$) 1.12 (9H, s), 1.70 (3H, s), 1.75 (3H, s), 3.25 (2H, d, *J* 8Hz), 3.91 (6H, s), 5.15 (1H, t, *J* 8Hz), 5 29 (2H, s), 6 78 (1H, dd, *J* 2.2, 8 4Hz), 6.86 (1H, br.s), 6.90 (1H, br d, *J* 2 2Hz), 7 28 (1H, d, *J* 8 4Hz), 7 35-7 76 (10H, m); *m/z* 712 (M^+), 628, 576 (100%). Found· C, 67 43; H, 5 76, $C_{40}H_{40}CrO_7Si$

requires C, 67.40; H, 5.66%.

2-[3,5-dimethoxy-4-(3-methylbut-2-enyl)phenyl-6-(t-butyldiphenylsilyloxy)benzofuran (10). — A solution of 2-[η^6–3,5-dimethoxy-4-(3-methylbut-2-enyl)phenyltricarbonylchromium(0)]-6-(t-butyldiphenylsilyloxy)benzofuran (9, E = $CH_2CH{=}CMe_2$) (0.190g, 0,27mmol) in dichloromethane was shaken with an excess of iodine for a few minutes. The excess iodine was removed with aqueous sodium hydrogen sulphite and the organic layer separated, dried (Na_2SO_4) and evaporated under reduced pressure. The residual oil crystallised upon addition of petroleum ether to give the *resorcinyl benzofuran* (10), (0.130g, 85%), m.p 135-7°C; ν_{max} ($CHCl_3$) 3071, 1622, 1596 cm^{-1}; δ_H ($CHCl_3$) 1.10 (9H, s), 1.64 (3H, s), 1.75 (3H, s),3.33 (2H, d, *J* 7.7Hz), 3.86 (6H, s), 5.15 (1H, t, *J* 7 7Hz), 6 74 (1H, dd, *J* 2.25, 8.5Hz), 6.83 (1H, d, *J* 1Hz), 6 90 (3H, br.s), 7.24 (1H, d, *J* 8 5Hz), 7 3-7.8 (10H, m); *m/z* 576 (M^+). Found: C, 76.92; H, 7.08; $C_{37}H_{40}O_4Si$ requires C, 77.05; H, 6.99%.

Moracin C (2). — Butyl lithium (1 mmol) was added to a solution of diphenylphosphine (0.186g, 0.17ml, 1mmol) in THF (3ml) at 0°C during 1h. The compound (10) (0.1g, 0.17mmol) was added to the resulting red solution and the mixture refluxed for 16 h. The reaction was quenched with 2.5M sodium hydroxide solution and the mixture washed with ether, adjusted to pH 4 with 2M hydrochloric acid and extracted with ethyl acetate. The organic extract was dried (Na_2SO_4), evaporated under reduced pressure and the residue dissolved in THF. Thus solution was treated with TBAF (1ml, 1M solution in THF) at room temperature for 16h then the reaction was quenched with aqueous acetic acid. The mixture was extracted with ethyl acetate and the extract dried (Na_2SO_4) and evaporated under reduced pressure to give *moracin C* (2) (27mg, 50%), m p 197-9°C (lit[3] m p 199°C); ν_{max} (Nujol) 3235, 2927, 2727, 1621, 1602, 1580, 1550, 1514, 1502, 1301, 1288, 1226, 1201, 1162, 1145, 1117 cm^{-1}; δ_H (d^6-acetone, 500MHz) 1 63 (3H,s), 1.76 (3H, s), 3.37 (2H, d, *J* 7Hz), 5 30 (1H, t, *J* 7Hz), 6 78 (1H, dd, *J* 2.0, 8 5Hz), 7 73 (1H, d, *J* 8 5Hz), 8 3 (2H, s), 8.5 (1H, s); *m/z* 310 (M^+, 100%), 295, 255.

Attempted synthesis of albafuran A (3): *2-(3,5-dimethoxyphenyl)-3-geranyl-6-hydroxybenzofuran* (11) — Butyl lithium (0.35ml, 1 1eq) was added to a solution of 2-[η^6–3,5-dimethoxy-4-trimethylsilylphenyltricarbonylchromium(0)]-6-(t-butyldiphenylsilyloxy)benzofuran (9, E = $SiMe_3$) (0.385g, 0.5mmol) in THF (20ml) at -78°C and the mixture stirred for 1h. Copper bromide dimethyl sulphide complex (0.103g, 0 5mmol) was added and the reaction stirred for a further 2h at –20°C before being allowed to warm to room temperature overnight. Standard work up gave an oil which was taken up in THF (5ml) and further treated with TBAF (1ml, 1mmol) overnight at room temperature. the solvent was evaporated, the residue extracted with dichloromethane and the extract left in contact with air until decomplexation was complete (t.l.c.). The solution was filtered through a Celite pad, the solvent evaporated and the residue purified by p.l.c. to give the *geranylbenzofuran* (11), (136mg, 67%), as a gum, ν_{max} ($CHCl_3$) 3029, 3008, 2937, 2844, 1601,1491 1459, 1423, 1376, 1304, 1265, 1229, 1212, 1201 cm^{-1}, δ_H ($CDCl_3$) 1 54 (3H,s), 1.63 (3H, s), 1 71 (2H, m), 1.8 (3H, s), 2.0 (2H, m), 3.57 (2H, d, *J* 7.7Hz), 5.06 (1H, br t, *J* 7Hz), 5 29 (1H, br.t, *J* 7 7Hz), 6.46 (1H, t, *J* 2.25Hz), 6 77 (1H, dd, *J* 2 0, 8 0Hz), 6.88 (2H, d, *J* 2 25Hz), 6.97 (1H, d, *J* 2 0Hz), 7.35 (1H, d, *J* 8.0Hz); *m/z* 406 (M^+) found.

M^+ 406.2153; $C_{26}H_{30}O_4$ requires 406.2144.

1-t-Butyldimethylsilyloxy-3,5-dimethoxy-4-(3-methylbut-2-enyl)benzene (13). — Butyl lithium (2.5ml, 4mmol) was added to a solution of 1,3-dimethoxy-5-*t*-butyldimethylsilyloxybenzene (12)[17] (1 072g, 4mmol) in THF (4ml) and ether (2ml) at 0°C and the mixture stirred at room temperature for 3h. The reaction was cooled to 0°C and treated with copper bromide dimethyl sulphide complex (0 824g, 4mmol) After 1h. at 0°C, 3-methylbut-2-enyl bromide (0.5ml, 4mmol) was added and the mixture stirred for a further 2h at 0°C and allowed to warm to room temperature overnight Standard work up and flash chromatography gave the *prenylated phloroglucinol ether* (13), (1 02g, 76%), m.p. 64-6°C; ν_{max} ($CHCl_3$) 2926, 2855, 1587, 1492 cm^{-1}; δ_H ($CDCl_3$) 0.20 (6H, s), 0 98 (9H, s), 1.65 (3H, s), 1.75 (3H, s), 3.25 (2H br.d, *J* 6.8Hz), 3 74 (6H, s), 5.15 (1H, br.t, *J* 6 8Hz), 6 05 (2H, s), *m/z* 336 (M^+), 321, (100%), 279, 268. Found: C, 67.83; H, 9.63; $C_{19}H_{32}O_3Si$ requires C, 67 81; H, 9 58%.

1-t-Butyldimethylsilyloxy-3-hydroxy-5-methoxy-4-(3-methylbut-2-enyl)benzene. — Butyl lithium (1.25ml, 2mmol) was added to a solution of diphenylphosphine (0 36ml, 2mmol) in THF (10ml) at 0°C and the solution allowed to warm to room temperature during 1h 1-*t*-Butyldimethylsilyloxy-3,5-dimethoxy-4-(3-methylbut-2-enyl)benzene (13) (0.672g, 2mmol) in THF was added and the reaction refluxed overnight. Standard work up and flash chromatography gave the *title phenol*, (320mg, 50%), m p. 53-4°C; ν_{max} ($CHCl_3$) 3408, 3007, 2959, 2859, 1618, 1588, 14991465, 1452 cm^{-1}, δ_H ($CDCl_3$) 0 20 (6H, s), 0.98 (9H, s), 1 73 (3H, br s), 1 79 (3H, br.s), 3 32 (2H, br.d, *J* 7 1Hz), 3 75 (3H, s), 5 22 (1H, br t, *J* 7 1Hz), 6.00 (2H, s); *m/z* 322 (M^+, 100%), 307, 265, 254 Found· C, 67 18; H, 9 39, $C_{18}H_{30}O_3Si$ requires C, 67 03; H, 9 38%

1-t-Butyldimethylsilyloxy-3-methoxy-4-(3-methylbut-2-enyl)-5-trifluoromethanesulphonyloxybenzene (14). — The phenol (0 281g, 0 87mmol) in pyridine (3ml) was treated at 0°C with trifluoromethanesulphonic anhydride (0.16ml, 0 96mmol) and the mixture stirred at room temperature for 16 h. Saturated aqueous sodium bicarbonate was added and the mixture extracted with ether. The organic extract was dried (Na_2SO_4), evaporated and the residue chromatographed to give the *phenyl triflate* (14), (380mg, 96%) as an oil, ν_{max} (film) 2959, 2933, 2861, 1620, 1597, 1495, 1420 cm^{-1}; δ_H ($CDCl_3$) 0 21 (6H, s), 0 97 (9H, s), 1 67 (3H, br.s), 1.73 (3H, br.s), 3 30 (2H, d, *J* 7 1Hz), 3 80 (3H,s), 5.09 (1H, br.t, *J* 7 1Hz), 6 35 (1H, d, *J* 2 2Hz), 6 37 (1H, d, *J* 2.2Hz); *m/z* 454 (M^+, 100%), 439, 397, 383. Found: C, 50.40; H, 6.46; $C_{19}H_{29}F_3O_5SSi$ requires C, 50.20; H, 6.43%

2-[3-t-Butyldimethylsilyloxy-5-methoxy-2-(3-methylbut-2-enyl)phenyl]benzofuran. — The phenyl triflate (14) (0.109g, 0 24ml), lithium chloride (0.03g, 0.72mmol), and tetrakistriphenylphosphine-palladium(0) (11mg, 4mol%) in dioxan (3ml) were treated with a solution of 2-trimethylstannylbenzofuran (73mg, 0.36mmol) in dioxan and the mixture refluxed overnight Saturated aqueous sodium bicarbonate was added and the mixture extracted with ether The ethereal extract was dried (Na_2SO_4) and evaporated and the residue purified by flash chromatography to give the *title resorcinylbenzofuran* (92mg, 91%), as a gum, ν_{max} ($CHCl_3$) 3056, 2957, 2932, 1603, 1577, 1456, 1408 cm^{-1}; δ_H ($CDCl_3$) 0 15 (6H, s), 0 93 (9H, s), 1.60 (6H, br.s), 3.42 (2H, br d, *J* 7.1Hz), 3 75 (3H, s), 5 12 (1H, br t, *J* 7.1Hz), 6 38 (1H, d, *J* 2.2Hz), 6 74 (1H, d, *J* 0 9Hz), 6 75

(1H, d, *J* 2.2Hz), 7.15-7.27 (2H, m), 7.41-7.53 (2H, m); *m/z* 422 (M^+, 100%) 407, 379, 365. Found: M^+ 422.2283; $C_{26}H_{34}O_3Si$ requires 422.2277.

2-[3-t-Butyldimethylsilyloxy-5-methoxy-2-(3-methylbut-2-enyl)phenyl]-6-t-butyldiphenylsilyloxybenzofuran. — A solution of 6-*t*-butyldiphenylsilyloxybenzofuran[1] (0.58g, 1.56mmol) in ether (2ml) at –10°C was treated with butyl lithium (0.95ml, 1.6mmol). After 2h. at –10°C trimethyltin chloride (0.32g, 1.6mmol) in ether was added and the reaction stirred at room temperature for a further 1h. This solution was then added to a mixture of the aryl triflate (**14**) (0.354g, 0.78mmol), lithium chloride (0.066g, 1.56mmol) and tetrakistriphenylphosphinepalladium(0) (30mg, 4mol%). The ether was evaporated with a stream of nitrogen and dioxan (10ml) added and the solution refluxed overnight. Standard work up and flash chromatography gave the *title resorcinylbenzofuran*, (0.890g 84%), m.p. 109-10°C; ν_{max} (Nujol) 2955, 2926, 2855, 1622, 1607, 1580, 1488, 1462, 1428 cm^{-1}; δ_H ($CDCl_3$) 0.20 (6H, s), 0.98 (9H, s), 1.12 (9H, s), 1.60 (3H, s), 1.68 (3H, s), 3.43 (2H, br.d, *J* 5.4Hz), 3.78 (3H, s), 5.14 (1H, br.t, *J* 5.4Hz), 6.39 (1H, d, *J* 2.4Hz), 6.66 (1H, d, *J* 0.8Hz), 6.73 (1H, d, *J* 2.4Hz), 6.74 (1H, dd, *J* 2.1, 8.3Hz), 6.90 (1H, br.d, *J* 2.1Hz), 7.26 (1H, d, *J* 8.3Hz), 7.35-7.45 (6H, m), 7.73-7.77 (4H, m); *m/z* 676 (M^+, 100%), 661, 619, 563. Found: C, 74.60; H, 7.87; $C_{42}H_{52}O_4Si_2$ requires C, 74.51; H, 7.74%.

Moracin I (**4**). — 2-[3-*t*-Butyldimethylsilyloxy-5-methoxy-2-(3-methylbut-2-enyl)phenyl]-6-*t*-butyldiphenylsilyloxybenzofuran (0.39g, 0.58mmol) in THF (10ml), was treated with TBAF (1.5ml, 1,5mmol) and the solution left at room temperature overnight. Saturated aqueous ammonium chloride was added and the mixture extracted with ethyl acetate. The extract was dried (Na_2SO_4) and evaporated and the residue triturated with toluene to give crystalline *moracin I* (**4**), (180mg, 96%), m.p. 139-40°C; ν_{max} (Nujol) 3304, 2925, 2854, 1620, 1590, 1487, 1462, 1378, 1283, 1206, 1181, 1154, 1117, 1041, 984 cm^{-1}; δ_H (d^6-acetone, 500MHz), 1.64 (3H, s),1.68 (3H, s), 3.47 (2H, d, *J* 6.5Hz), 3.84 (3H, s), 5.14 (1H, br.t, *J* 6.5Hz), 6.54 (1H, d, *J* 2.2Hz), 6.80 (1H, s), 6.81 (1H, d, *J* 2.2Hz), 6.83 (1H, dd, *J* 2.0, 8.0Hz), 6.98 (1H, br.d, *J* 2.0Hz), 7.44 (1H, d, *J* 8.0Hz); *m/z* 324 (M^+), 309, 281, 202, 92, 91 (100%).

η^6-6-Methoxybenzofurantricarbonylchromium(0) (**16**). — 6-Methoxybenzofuran[18] (1.48g, 0.01mol) was refluxed with hexacarbonylchromium (2.20g, 0.01mol) in THF-dibutyl ether 10:1 (50ml) in a Ströhmeier apparatus for 16h. The resulting solution was evaporated and the residue purified by flash chromatography to give yellow crystals of the *benzofuran complex* (**16**) (570mg, 20%), m.p. 143-5°C; ν_{max} ($CHCl_3$) 1967, 1891 cm^{-1}; δ_H $CDCl_3$) 3.75 (3H, s), 4.95 (1H, dd, *J* 2, 7Hz), 6.04 (1H, br.d, *J* 2Hz), 6.23 (1H, d, *J* 7Hz), 6.55 (1H, br.d, *J* 3Hz), 7.45 (1H, d, *J* 3Hz); *m/z* 284 (M^+), 228, 200 (100%). Found: C, 50.98; H, 2.68; $C_{12}H_8CrO_5$ requires C, 50.72; H, 2.84%.

η^6-6-Methoxy-7-trimethylsilylbenzofurantricarbonylchromium(0) (**16**, R = $SiMe_3$). — η^6-6-Methoxybenzofurantricarbonylchromium(0) (**15**) (0.142g, 0.5mmol) in THF (20ml) at –78°C was treated with butyl lithium (0.3ml, 0.5 mmol). After 1h., trimethylsilyl chloride (0.3 ml) was added, the mixture stirred for a further 30min. and then allowed to warm to room temperature. Standard work up and flash chromatography gave the *silylated benzofuran* (**16**, R = $SiMe_3$) (120mg, 67%), m.p.

128-9°C, ν_{max} ($CHCl_3$) 1962, 1888 cm^{-1}; δ_H ($CDCl_3$) 0.5 (9H, s), 3 67 (3H, s), 4.75 (1H, d, *J* 7Hz), 6.30 (1H, d, *J* 7Hz), 6.45 (1H, d, *J* 3Hz), 7.40 (1H, d, *J* 3Hz); *m/z* 356 (M^+), 300, 272 (100%). Found. C, 50 58, H, 4.59; $C_{15}H_{16}CrO_5Si$ requires C, 50.56; H, 4.53%.

7-Geranyl-6-methoxybenzofuran (16, R = geranyl, decomplexed). — η^6-6-Methoxybenzofuran-tricarbonylchromium(0) (15) (0 426g, 1.5mmol) in THF (50ml) at –78°C was treated with butyl lithium (0.9ml, 1.5ml) during 1h. Copper bromide dimethyl sulphide complex (0 309g, 1 5mmol) was added and the mixture allowed to warm to –20°C, maintained at this temperature for a further 2h and stirred at room temperature overnight Standard work up gave an oil which was diluted with dichloromethane and allowed to contact with air during 16h. The resulting mixture was filtered through a silica pad, evaporated and the residue purified by flash chromatography to give *7-geranyl-6-methoxybenzofuran* (16, R = geranyl, decomplexed) (256mg, 60%) as a colourless oil, ν_{max} (film) 3147, 3113, 2911 , 2728, 1625, 1601, 1541, 1490, 1462, 1422 cm^{-1}; δ_H ($CDCl_3$) 1 52 (3H, s), 1 60 (3H, s), 1 67-1 70 (4H, m), 1 80 (3H, s), 3.60 (2H, d, *J* 6 5Hz), 3 88 (3H, s), 5 07 (1H, br t, *J* 5 4Hz), 5 34 (1H, br t, *J* 6 5Hz), 6 68 (1H, d, *J* 2 5Hz), 6 88 (1H, d, *J* 9Hz), 7 35 (1H, d, *J* 9Hz), 7 52 (1H, d, *J* 2.5Hz), *m/z* 284 (M^+), 215, 201, 161 (100%) Found· C, 80.21; H, 8.66; $C_{19}H_{24}O_2$ requires C, 80 24; H, 8 51%

Mulberrofuran B (5) —7-Geranyl-6-methoxybenzofuran (16, R = geranyl, decomplexed) (0 140g, 0 5mmol) in ether (2 ml) was lithiated as above and treated with a solution of chlorotrimethylstannane (0 1g, 0.5 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 1,3-bis(tri-isopropylsilyloxy)-5-iodobenzene (7) (1 28g, 3 8 eq) and palladium tetrakistriphenylphosphine (4 mol%) in THF (20 ml) and the reaction refluxed for 16 h Standard work-up and purification by column chromatography gave 1,3-bistri-isopropylsilyloxy-5-(7-geranyl-6-methoxy-2-benzofuranyl)benzene (18) which was treated in THF (10 ml) 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 mulberrofuran B (5) (79mg, 40%), m.p 59-61°C (lit[5] m p 68-70°C); ν_{max} ($CHCl_3$) 3295, 3007, 2928, 2956, 1621, 1579, 1494, 1465, 1446, 1421, 1366, 1306, 1271, 1235, 1220, 1212, 1199, 1159, 1093, 1039, 1002 cm^{-1}; δ_H (d^6-acetone, 500MHz) 1.48 (3H, s), 1.54 (3H, s), 1.88 (3H, s), 1.9-2.0 (4H, m), 3 63 (2H, d, *J* 7 5Hz), 3.89 (3H, s), 5 03 (1H, br t, *J* 7.0Hz), 5.38 (1H, br.t, *J* 7.5Hz), 6 37 (1H, t, *J* 2 0Hz), 6.90 (2H, d, *J* 2.0Hz), 6.96 (1H, d, *J* 8 0Hz), 7 05 (1H, s), 7 37 (1H, d, *J* 8.0Hz); *m/z* 392 (M^+, 100%), 323, 269

REFERENCES

1 I S Mann, D A Widdowson and J M Clough, *Tetrahedron*, **1991**, *47*, 7981.

2 M Fukui, T Ikeda and T Oishi, *Tetrahedron Lett.*, **1982**, *23*, 1605, N F Masters and D A Widdowson, *J Chem Soc., Chem Commun*, **1983**, 955

3 M. Takasugi, S. Nagao, S Ueno, T. Masamune, A. Shirata and K Takahashi, *Chem Lett.*, **1978**, 1239.

4 M. Takasugi, S Nagao, L Munoz, S Ishikawa, T Masamune, A. Shirata and K Takahashi, *Koen Yoshishu — Tennen Yuki Kagobutsu Toronkai, 22nd*, **1979**, 275. (C A *92*, 160540d)

5 T. Nomura and T Fukai, *Planta Med*, **1981**, *42*, 197; T. Nomura, T Fukai, T Fujimoto and Y Hano, *Heterocycles*, **1984**, *22*, 2805.

6 For comprehensive accounts see. B J. Wakefield, *Organolithium Methods*; Academic Press, London, 1988;; H W Gschwend and H.R Rodriguez, *Org. React*, **1979**, *26*, 1

7 J P Gilday and D A Widdowson, *Tetrahedron Lett*, **1986**, *27*, 5525

8. M. Takasugi, S Ishikawa and T Masamune, *Chem. Lett*, **1982**, 1221

9 M Cugnon de Sevricourt and M Robba, *Bull. Soc Chim Fr*, **1977**, 142

10 G Nechvatal and D A Widdowson, *J Chem Soc, Chem Commun*, **1982**, 467

11 J M Clough, I S. Mann and D.A Widdowson, *Synlett*, **1990**, 469

12 J K Stille and A M. Echavarren, *J Am Chem. Soc*, **1987**, *109*, 5478

13 R.E Ireland and D M Walba, *Org Synth*, **1988**, *Coll. Vol. 6*, 567

14 P J Stang, M Hanack and L R. Subramanian, *Synthesis*, **1982**, 85

15 C A L Mahaffy and P L Pauson, *Inorg. Synth*, **1979**, *19*, 154

16. D A Widdowson and Y Z. Zhang, *Tetrahedron*, **1986**, *42*, 2111

17. B M Trost and M G. Saulmer, *Tetrahedron Lett.*, **1985**, *26*, 123

18. L Rene and R. Royer, *Bull Soc Chim Fr*, **1973**, 2355