

**THE SYNTHESIS OF BENZOFURAN RESORCINYL
PHYTOALEXINS**

**a thesis presented by
INDERJIT SINGH MANN**

**in partial fulfilment of the requirements for
the degree of**

**DOCTOR OF PHILOSOPHY
OF THE
UNIVERSITY OF LONDON**

**DEPARTMENT OF CHEMISTRY
IMPERIAL COLLEGE
LONDON SW7 2AY**

SEPTEMBER 1988

To my family

CONTENTS

	Page
Acknowledgements	5
Abbreviations	6
Abstract	7
Review The synthesis of 2-aryl benzofurans	8
1.0 Introduction	9
1.1 Formation of the C₂-C₃ bond	10
1.1.1 Intramolecular Wittig heterocycle formation	10
1.1.2 Ring closure of (2-carbonylphenyl)benzyl ethers	12
1.1.3 Intramolecular ketene cycloadditions	13
1.2 Formation of the O-Ar bond	15
1.2.1 The displacement of the Ar-Hal bond with O nucleophiles	15
1.2.2 Photochemically induced ring closure of benzoin derivatives	17
1.2.3 Reactions of benzoin and deoxybenzoins	19
1.3 Formation of the C-Ar benzofuran bond	21
1.3.1 Ring closure of α -aryloxyketones	21
1.3.2 Reactions of vinyl sulphonates	23
1.3.3 Photochemical ring closure of α -aryloxyketones	24
1.3.4 From O-aryloximes	24
1.4 Benzofurans from other ring systems	25
1.4.1 Oxidation of flavylum salts	25
1.4.2 From dihydroxyflavanols	26
1.4.3 From <i>isoflavanone</i> epoxides	27
1.4.4 Reactions of vinyl cyclopropanes	29
1.5 Ring closure of 2-hydroxyphenyl derivatives	30
1.5.1 Ring closure and formation of 2-alkynyl phenols	30
1.5.2 Palladium mediated catalysis	31
1.5.3 Bromination of stilbenes	32
1.5.4 Flash vacuum pyrolysis of phosphoranes	33
1.5.5 Addition to quinones	34
1.5.6 Oxidation of stilbene derivatives	36
1.5.7 Oxidative rearrangement of chalcones	38

1.5.8	Reaction of α,α,β -triarylvinyl halides	39
1.5.9	Reactions of β,β -diarylvinyl halides	40
1.5.10	Reactions of α -(2-methoxyphenyl)- β,β -diarylvinyl bromides	41
1.5.11	From 1,4-benzoquinones and quinone monoimides	42
1.5.12	Reactions of benzoin	44
1.5.13	Decomposition of diazoketones	45
1.5.14	Alkaline degradation of 3-aryl benzofurans	45
1.5.15	Rearrangement of O-acylbenzyl bromides	46
1.5.16	Formation of benzoin and deoxybenzoin from phosphonates	47
1.5.17	Deoxybenzoin from sultams	48
1.6	Heck reactions of benzofurans	49
	Results and Discussion	52
2.0	Introduction	53
2.1	Routes to moracin M	54
2.1.1	Synthesis of 2-iodobenzofuran	55
2.1.2	5-Lithiation of resorcinol	55
2.1.3	Cross coupling reactions of 2-iodobenzofuran	56
2.1.4	Cross coupling reactions of 2-metallo benzofuran	60
2.1.5	Synthesis and reactions of 6- <i>t</i> -butyldiphenylsiloxybenzofuran	65
2.2	Substitution on the resorcinylyl ring	68
2.2.1	Substitution <i>ortho</i> to the benzofuran substituent	70
2.2.2	Substitution prior to cross coupling	72
2.2.3	Palladium cross couplings using aryl triflates	76
2.3	Substitution on the benzofuran ring	78
2.4	Routes to dimoracin	80
2.4.1	Routes towards the C ₁₀ moiety and (55)	81
2.4.2	Displacement and cross coupling reactions of acetates	85
2.4.3	Nucleophilic addition reactions of the enone (61)	87
2.4.4	Diels Alder approaches to compound (55)	89
2.5	Further developments	96
2.6	Conclusion	97
	Experimental	98
	Appendix:- X-ray data	139
	References	140

Acknowledgements

I would like to thank the many people who have helped me during the course of the 3 years of my PhD.

My supervisor Dr. D. A. Widdowson, and industrial supervisor, Dr. J. M. Clough for their ideas and encouragement.

My colleagues on the 7th floor and the Frankland Lab.

All the technical staff, but especially Chris Sausmann, and Pete Sulsh.

Dick Shepherd, and Ken Jones, for the n.m.r. and micro-analytical services.

Payman Ostovar, Pamela Dickens, and Michael Dickens, for doing an excellent job of proof reading this thesis.

Paul, Payman, Tim, Pam, Andy and Chris, for their friendship, during my years at Imperial College.

Finally, my family, who support me fully in everything I do.

Abbreviations

DMA	Dimethylacetamide
DMF	Dimethylformamide
DMSO	Dimethylsulphoxide
DDQ	2,3-Dichloro-5,6-dicyanoquinone
DIBAL	Di <i>isobutyl</i> aluminiumhydride
f. v. p.	Flash vacuum pyrolysis
LDA	Lithiumdi <i>isopropyl</i> amide
PPA	Polyphosphoric acid
Py. HCl	Pyridinium hydrochloride
TBAF	Tetrabutylammonium fluoride
THF	Tetrahydrofuran
TMS	Trimethylsilyl
DCE	Dichloroethane

ABSTRACT

This thesis will be divided into three sections; review, results and discussion, and experimental.

The review will be concerned with the syntheses of 2-aryl benzofurans, and will discuss six basic methods for their construction. Most of the methods have the construction of the benzofuran ring as the key step, and the review will be divided into sections on the basis of the key disconnection in forming the benzofuran ring.

The results and discussion will detail the work carried out in synthesising various resorcinyll benzofuran phytoalexins. This work has utilised chromium tricarbonyl chemistry in enabling regioselective functionalisation of the benzofuran and resorcinol rings, under mild conditions, and the two ring systems have been coupled using palladium catalysis. Using this methodology, moracin M, moracin C, and mulberrofuran B have been synthesised. Furthermore, the utilisation of aryl triflates has enabled the synthesis of moracin I. Also discussed will be the routes towards the synthesis of dimoracin, which is a dimeric adduct consisting of two resorcinyll benzofuran units, substituted on to a chromene unit in a stereoselective manner. The work will show three different routes attempted towards synthesising this chromene unit in a stereoselective manner, involving the palladium cross coupling reaction, nucleophilic attack of organometals on carbonyl groups, and finally, a Diels Alder approach towards its synthesis, which proved to be the most successful.

The final section contains the experimental details, relating to the results and discussion.

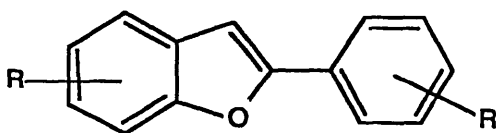
Review

The synthesis of 2-aryl benzofurans

1.0 Introduction

2-Aryl benzofurans represent a class of antifungal compounds that are widely distributed in nature. Their biosynthetic origins are not confined to a single pathway, and they are believed to arise from a variety of routes, which generally involve oxidative rearrangements of chalcones and stilbenes. This is reflected in the many syntheses of these compounds that have been developed, some utilising chalcones and stilbenes as starting materials or intermediates in a synthetic sequence.

An analysis of the structure of 2-aryl benzofurans (1) suggests that many disconnections of the furan ring are possible, and most approaches are concerned with the formation of this ring as the key step in a synthetic route. Although some reviews^{1,2} do exist for benzofuran synthesis in general, this particular review will be confined to syntheses leading to 2-aryl benzofurans.



(1)

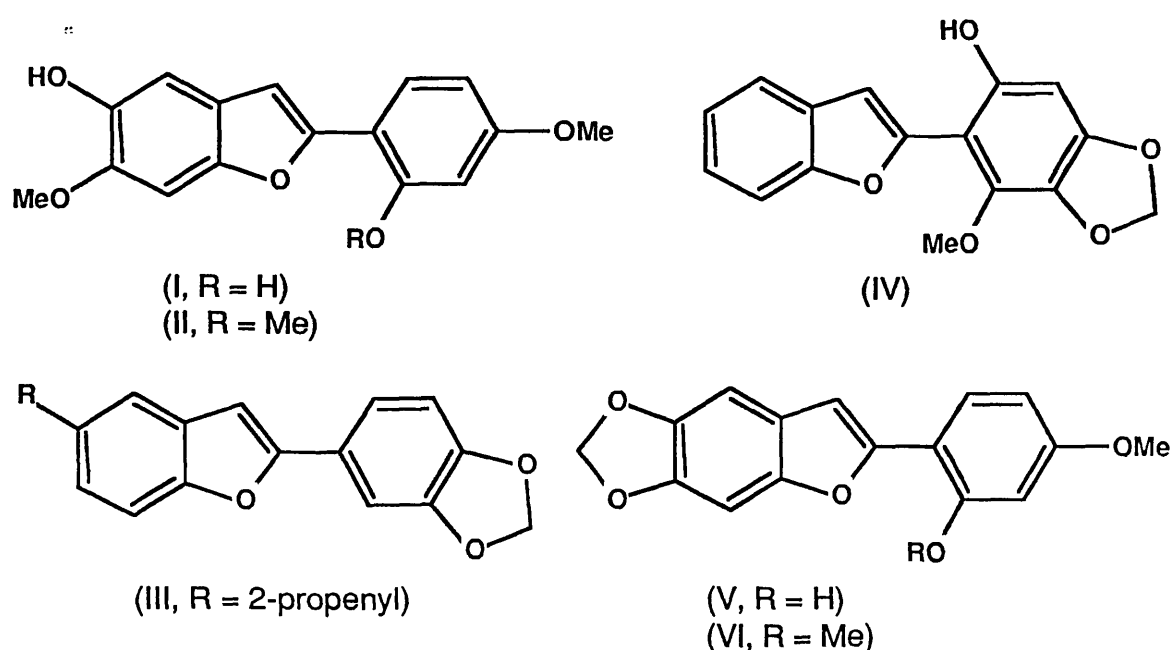
1.1 Formation of the C₂-C₃ benzofuran bond

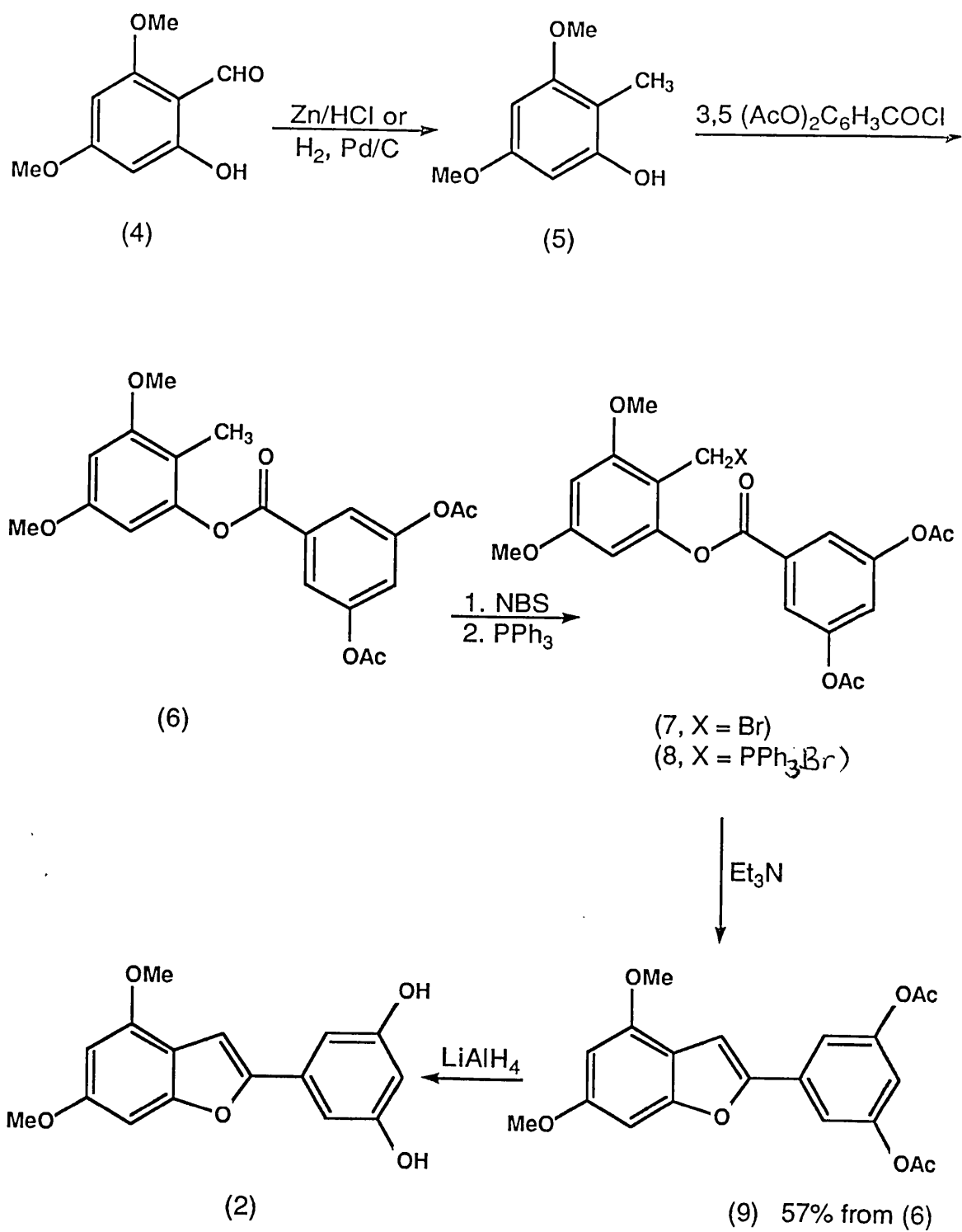
1.1.1 Intramolecular Wittig heterocycle formation

This method utilises as the key step, an intramolecular Wittig reaction to form the C₂-C₃ bond of the benzofuran ring system^{3,4}. It has been widely used by Stevenson *et al.* in the synthesis of many natural products, such as the *anti* fungal metabolites isolated from mulberry, moracins A (2) and B⁵ (Scheme1).

For this synthesis, the benzofuran ring precursor, 4,6-dimethoxysalicylaldehyde (4), is converted using standard procedures to the aryl ester (6). Benzylic bromination using N-bromosuccinimide, followed by Wittig formation and subsequent ring closure, gives moracin A diacetate (9), which is easily converted to moracin A.

Other naturally occurring 2-aryl benzofurans have been similarly synthesised, namely sainfuran (I) and methylsainfuran⁶ (II), the eupomatenoids⁷ (III), yeast *antioxidants*⁸ (IV), and the constituents of *Sophora tomentosa*⁹, sophora 1 (V) and sophora 2 (VI).

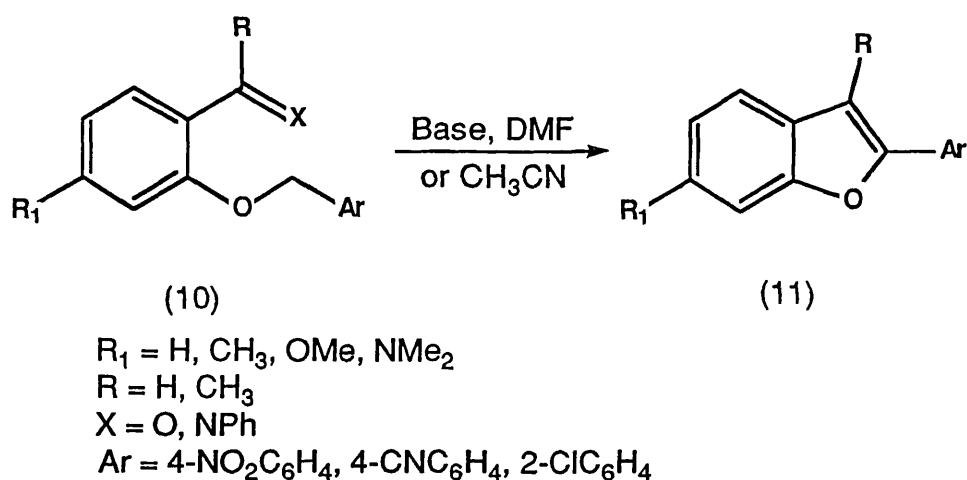




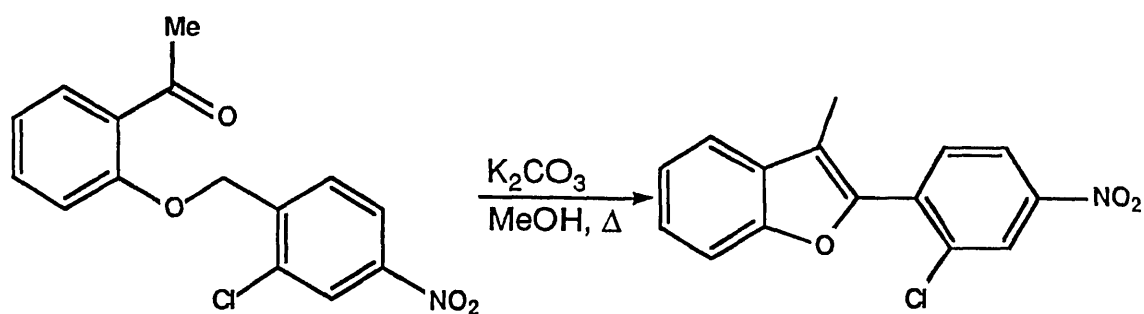
Scheme 1

1.1.2 Ring closure of (2-carbonylphenyl) benzyl ethers

Benzyl phenyl ethers (10), containing an *ortho* formyl, acetyl, or phenyliminomethyl group, can be cyclised to afford 2-aryl benzofurans (11)¹⁰⁻¹² (Scheme 2). These intramolecular condensation reactions, use strongly basic alkali metal compounds (NaOH, KOH, NaOEt, KO^tBu) in dipolar aprotic solvents, and under these conditions the cyclisation only works for compounds containing highly electron withdrawing substituents on the aryl ring of the benzyl moiety, which can stabilise the intermediate benzylic anion. For example, the 4-bromo derivative (10, Ar = 4-BrC₆H₄), does not cyclise under these conditions¹¹. However, when two electron withdrawing groups are present, the cyclisation proceeds in refluxing methanol containing potassium carbonate¹³ (Scheme 3).



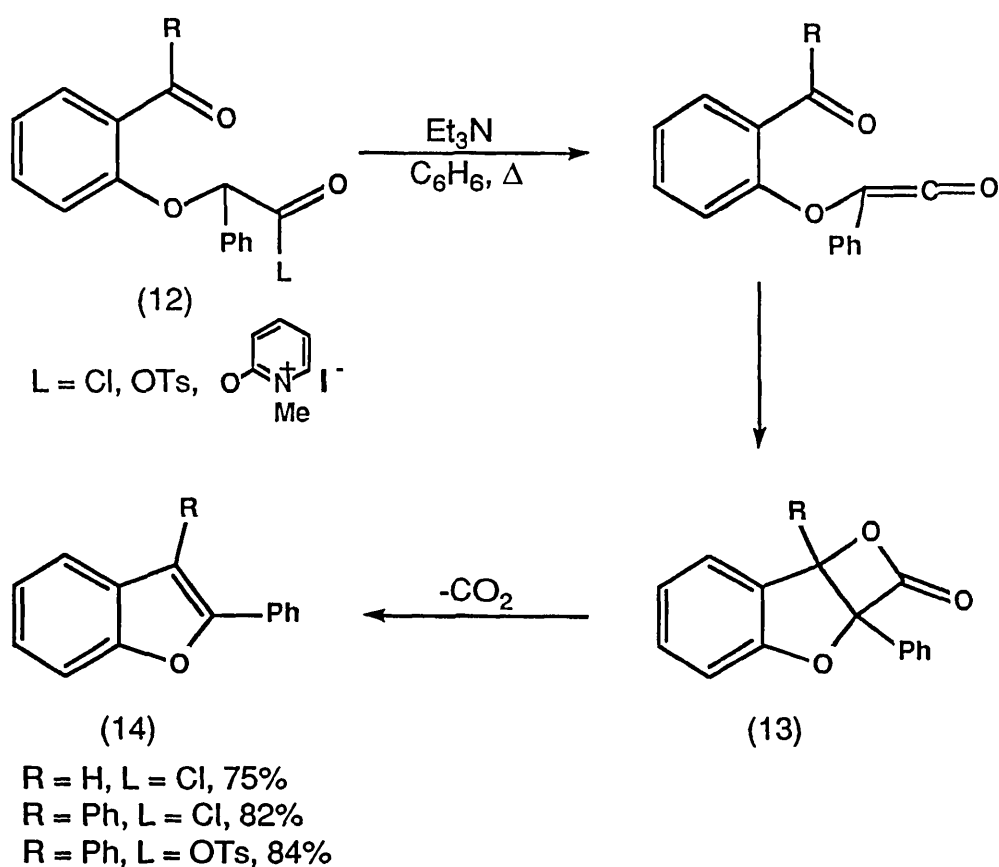
Scheme 2



Scheme 3

1.1.3 Intramolecular ketene cycloadditions

Ketenes generated from (2-carbonylphenoxy)acetic acid derivatives (12), are found to undergo intramolecular [2 + 2] cycloadditions with the carbonyl moiety, under relatively mild conditions, to yield the tricyclic β -lactones (13), which spontaneously decarboxylate to give the corresponding benzofurans (14) in good yields¹⁴ (Scheme 4).



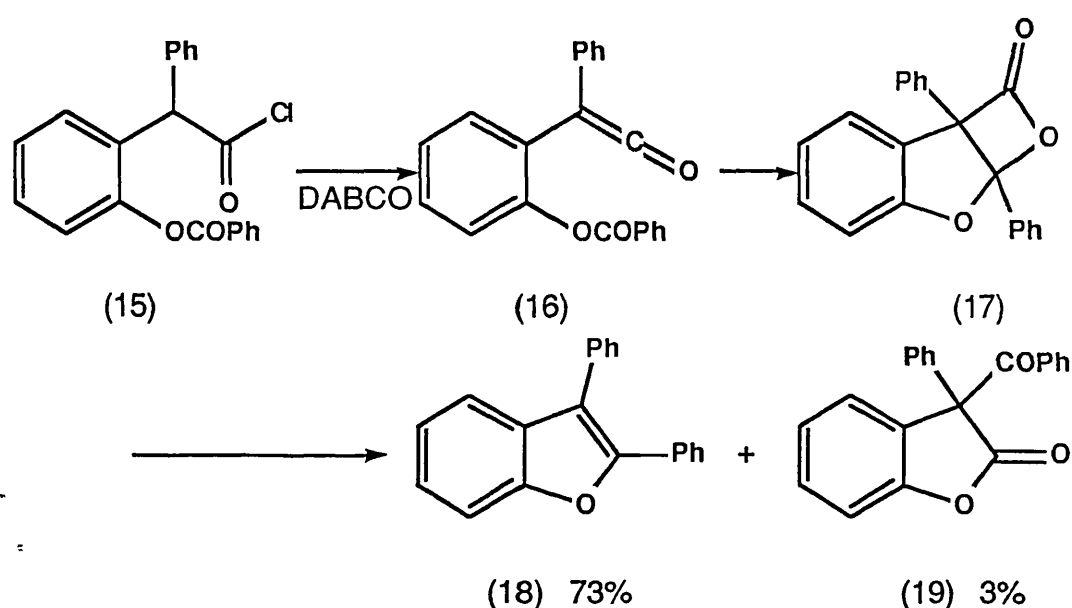
Scheme 4

The standard procedure for generating ketenes is the base induced elimination of HCl from acid chlorides. These are made by reacting the acid (12, L = OH) with oxalyl chloride, and the crude acid chlorides added to a refluxing solution of triethylamine in benzene, resulting in concomitant formation of the ketene leading to the 2-phenyl benzofuran.

Other precursors to these ketenes are the tosyl derivatives (12, L = OTs), which have the advantage that the reaction conditions employed to form this

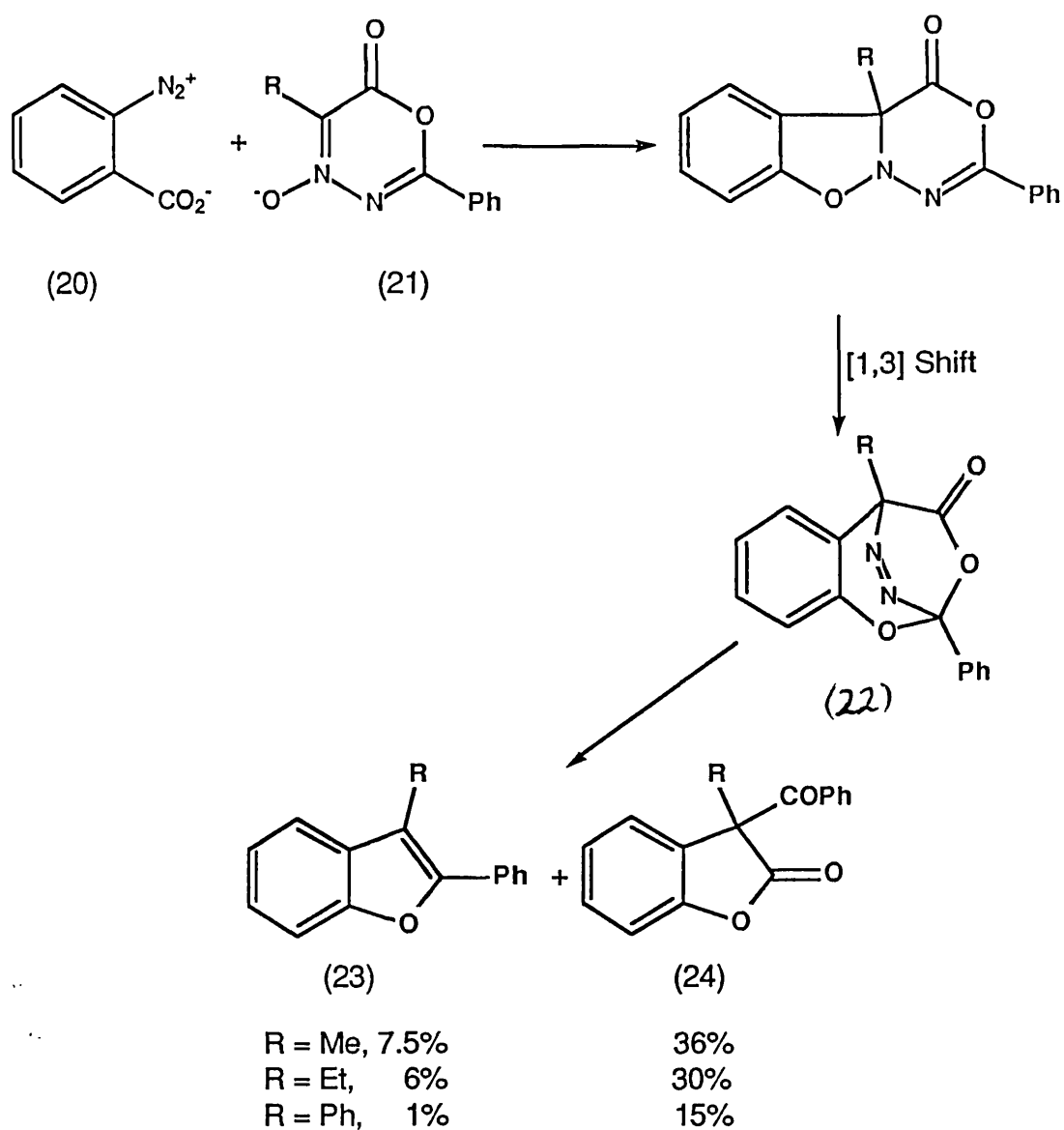
compound, leads directly to generation of the ketene, and hence the benzofuran¹⁵. The 2-pyridyl ester derivative (12, L = OPyr.), from reaction of the acid (12, L = OH) and 2-chloro-1-methylpyridinium iodide (Mukaiyama's reagent¹⁶), also generates the ketene¹⁷ when treated in an analogous manner to the aforementioned chloride and tosyl derivatives.

The ketene generated from 2-benzoyloxydiphenylacetyl chloride (15) also undergoes intramolecular cycloaddition¹⁸ to afford the the benzofuran (18) along with a trace of the benzofuranone (19), via the β -lactone (17) (Scheme 5).



Scheme 5

The same products were obtained in much lower yields, but with the benzofuranone predominating, in the reaction of benzyne with 1,3,4-oxadiazin-6-one-4-oxides¹⁸ (21). Although it was suggested that the benzofuranone (24) is derived from a ketene precursor, this would appear unlikely in view of the reaction where the benzofuran is the major product. Mechanistically, the reaction involves a 1,3-dipolar cycloaddition followed by a 1,3 shift to give the cycloadduct (22), which subsequently rearranges to the product (Scheme 6).

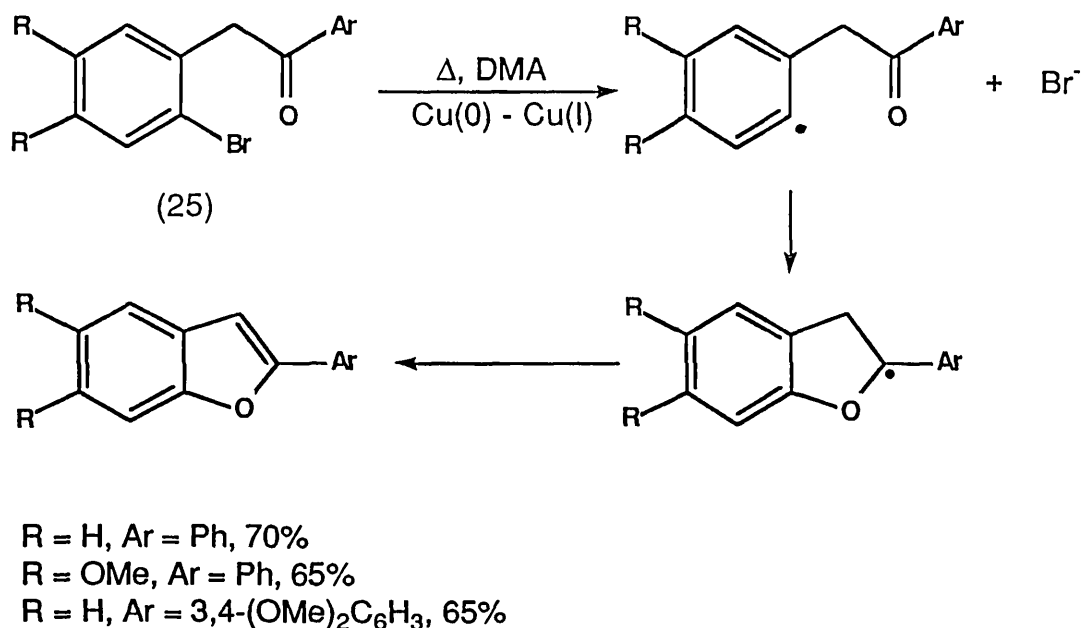


Scheme 6

1.2 Formation of the O-Ar bond

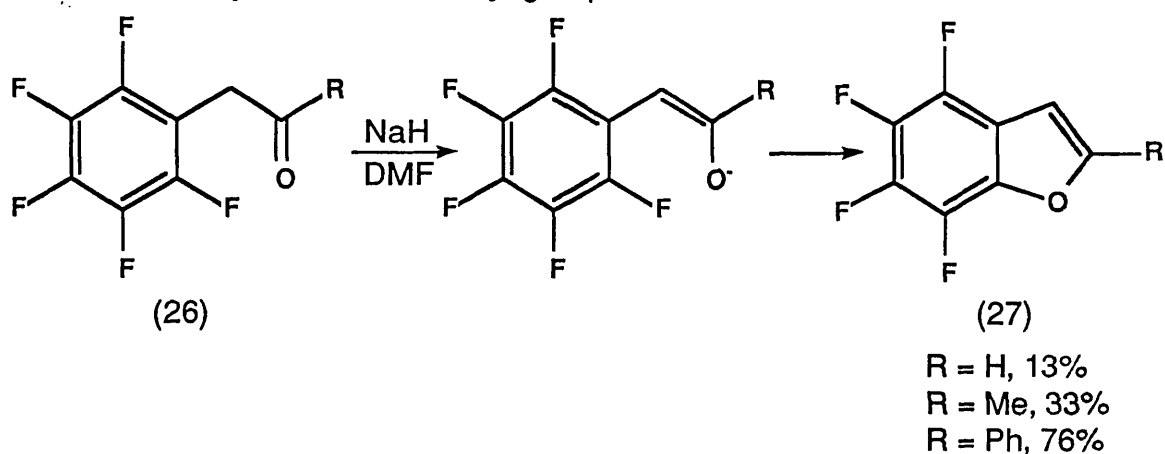
1.2.1 The displacement of the Ar-Hal bond with O nucleophiles

The reaction of 2-bromodeoxybenzoins (25) with copper powder in refluxing dimethylacetamide¹⁹, gives the corresponding 2-aryl benzofurans in good yields (Scheme 7). This is an intramolecular $S_{RN}1$ reaction proceeding via an electron transfer mechanism.



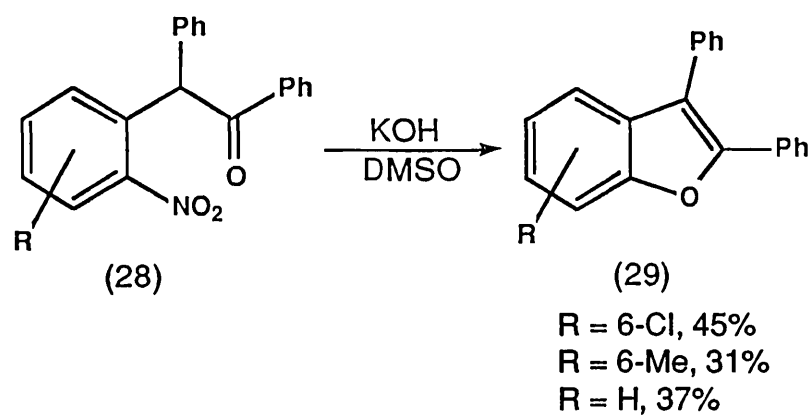
Scheme 7

Intramolecular displacements of aryl fluorine bonds by enolate anions²⁰ occur in highly electron deficient aromatic systems, such as the polyfluorinated deoxybenzoin (26) (Scheme 8). The reaction works best for ketones (26, $\text{R} = \text{Ph}$), since the intermediate enolate adopts the required *cis* configuration between the oxyanion and the aryl group.



Scheme 8

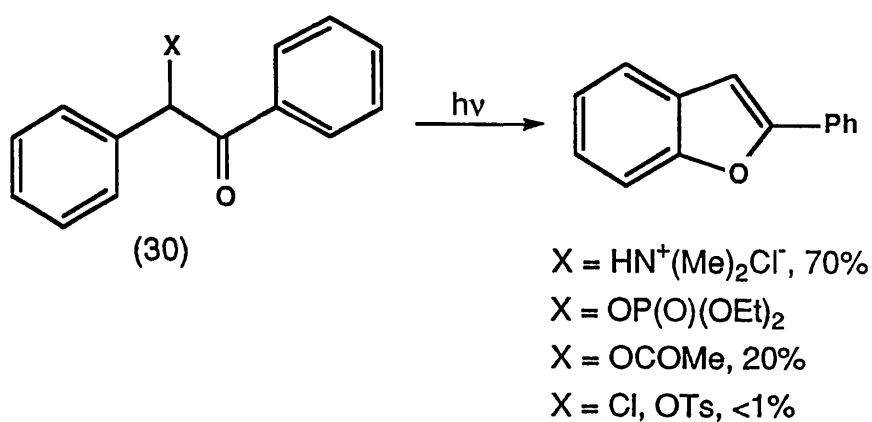
This type of reaction also occurs with α -(2-nitrophenyl)deoxybenzoins²⁰ (28), which undergo displacement of the nitro group, when the deoxybenzoin is treated with KOH in dimethylsulphoxide (Scheme 9).



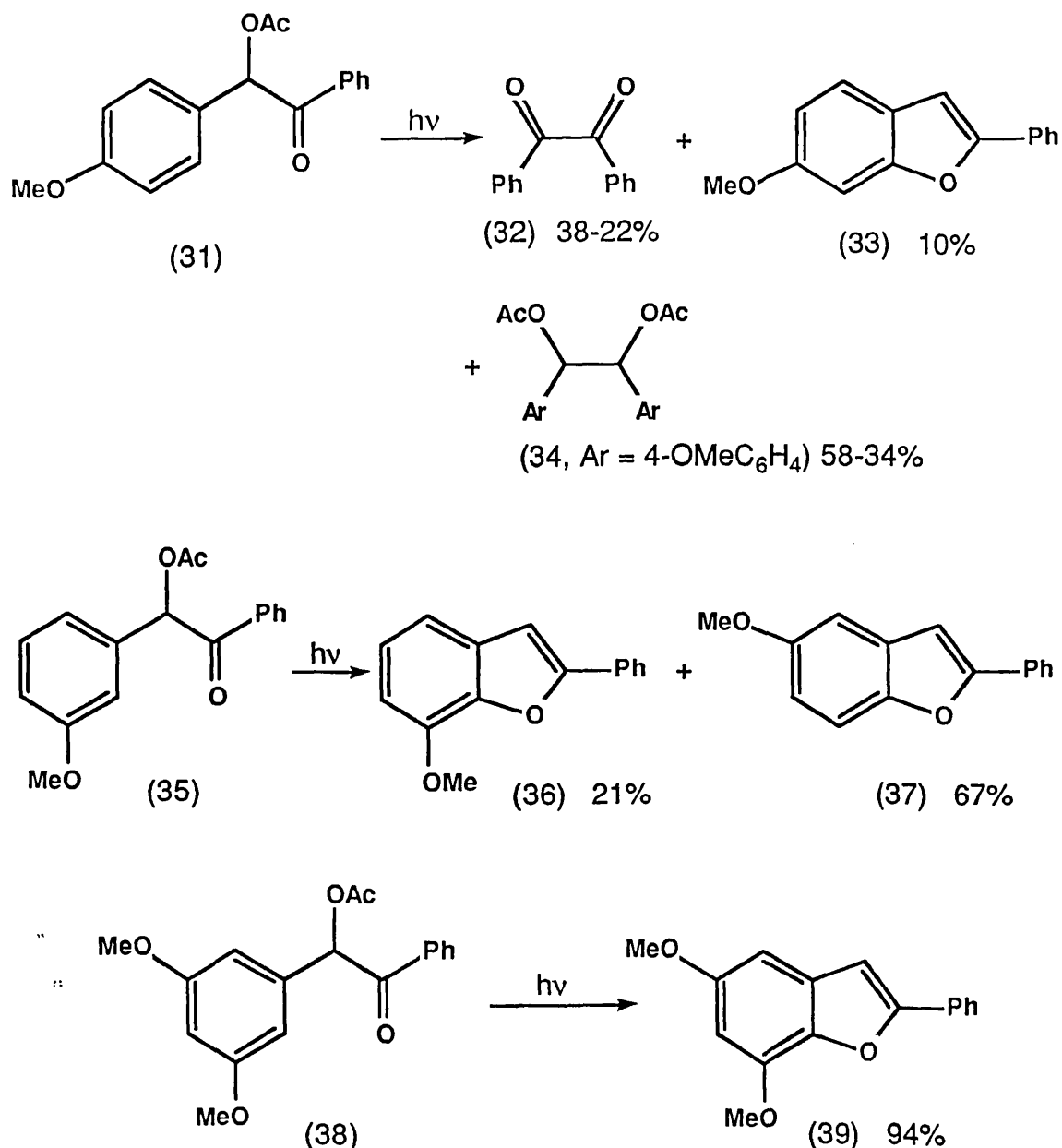
Scheme 9

1.2.2 Photochemically induced ring closure of benzoin derivatives

Benzoin derivatives (30), upon irradiation with ultra violet light, can undergo ring closure to yield the corresponding benzofurans^{22, 23} (Scheme 10). The cyclisation is critically dependent on the nature of the leaving group X, and is also affected by substitution on the phenyl rings especially on the benzyl acetate moiety (30, X = OAc) (Scheme 11).



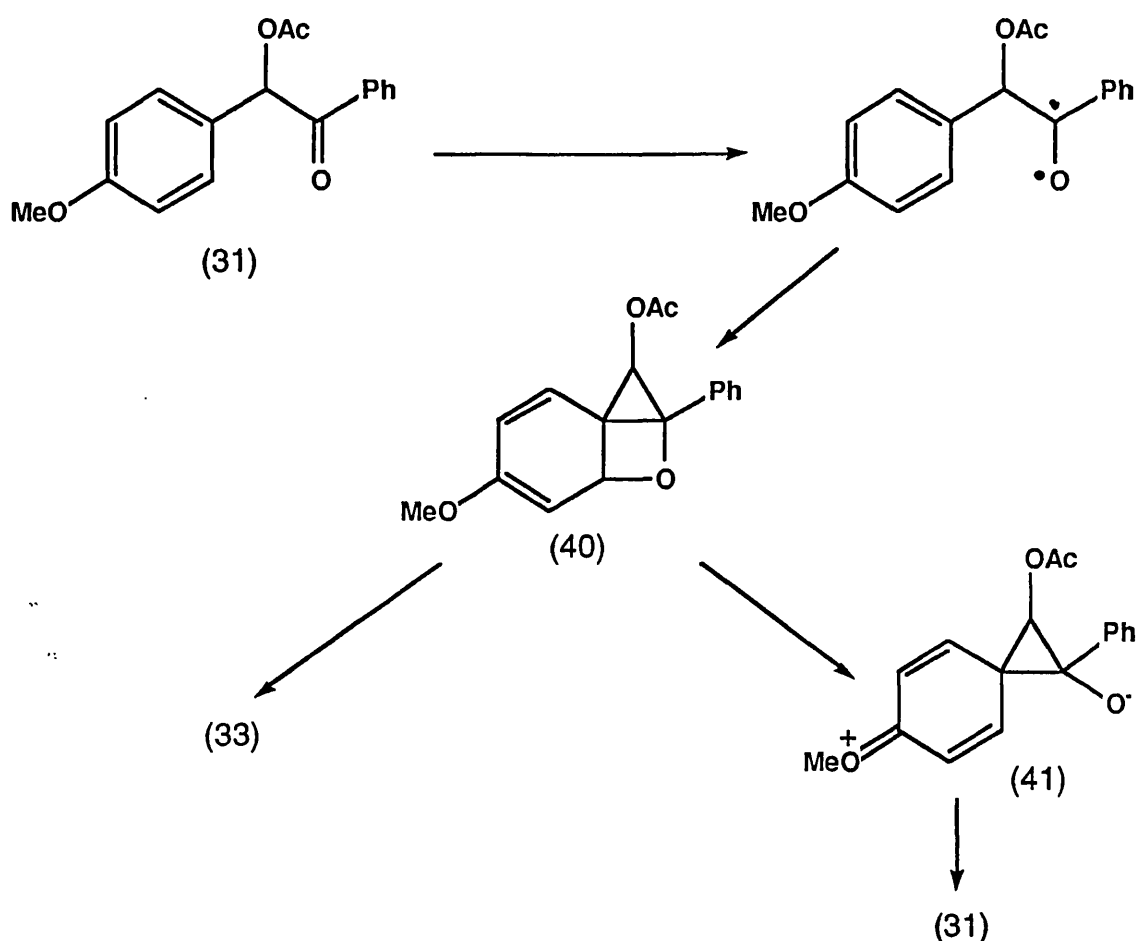
Scheme 10



Scheme 11

The 4-methoxy substituted benzoin (31) yields only 10% of the 2-phenyl benzofuran (33), with the major products (32) and (34) derived from coupling of the benzoyl and 4-methoxyphenylacetoxymethyl radicals. In contrast, the 3-methoxy substituted benzoin acetates (35) and (38) proceed to give only the 2-phenyl benzofuran derivatives in high yield.

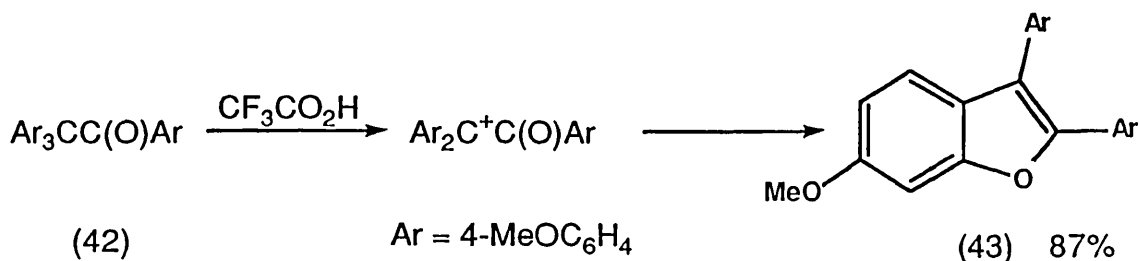
The mechanism in all cases involves an initial $n\text{-}\pi^*$ transition in the carbonyl group. This excited state is then believed to undergo formation to the oxetane intermediate (40), which either subsequently rearranges to the benzofuran or collapses back to the starting material, as occurs with the 4-methoxy substituted benzoin (31) (Scheme 12). Such a reaction is not however favoured by the 3-methoxy benzoin (35) and (38).



Scheme 12

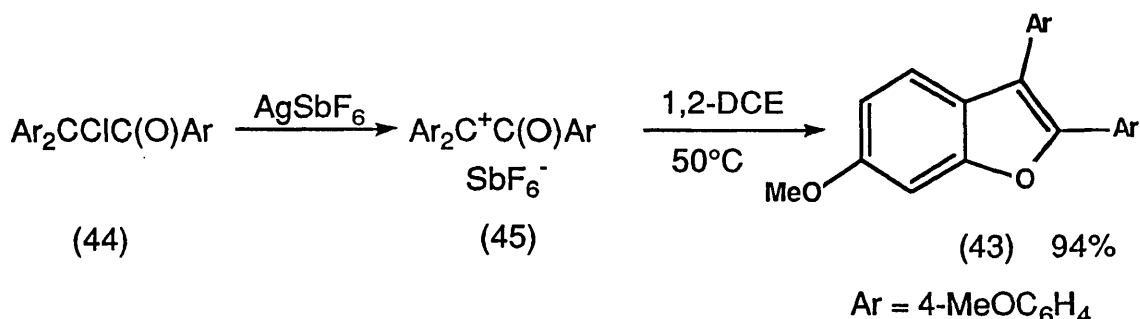
1.2.3 Reactions of benzoin and deoxybenzoin

Benzylic carbocations α to a carbonyl moiety undergo ring closure to form the 2,3-diarylbenzofuran²⁴ (43) (Scheme 13). For example the anisyl deoxybenzoin (42) rearranges under acidic conditions to form the corresponding benzofuran.



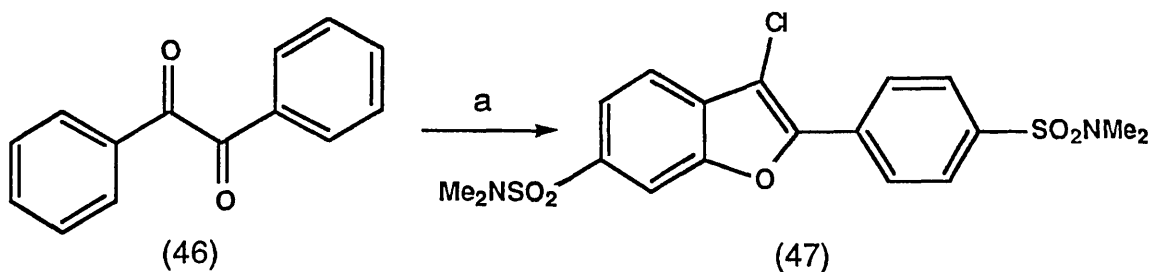
Scheme 13

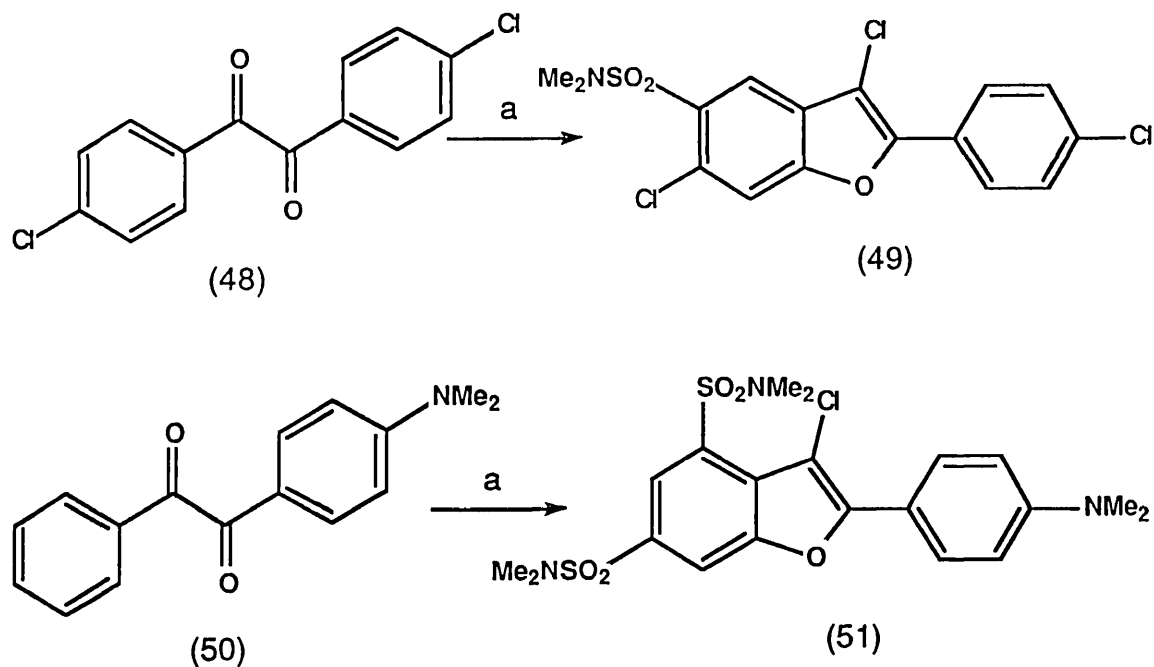
The presence of a transient carbonium ion has been established by isolating it as the hexafluoroantimonate salt²⁵ (45), by reaction of the corresponding chloride (44) with AgSbF_6 (Scheme 14). The salt (45) when heated in dichloroethane affords the expected diaryl benzofuran (43) in high yield.



Scheme 14

The cyclisation of benzils has been accomplished by their treatment with chlorosulphonic acid^{26, 27}, although the disadvantage of this method as a route towards substituted benzofurans, is the incorporation of sulphonyl groups in the product. Hence benzil (46) reacts to give 3-chloro-2-phenyl benzofuran-6,4'-disulphonyldichloride (47). With substituted benzils, similar results are obtained, with the degree and direction of sulphonylation being dependent on the substituents²⁷, as shown in Scheme 15 for 4,4'-dichlorobenzil (48), and 4-dimethylaminobenzil (50) (Scheme 15).





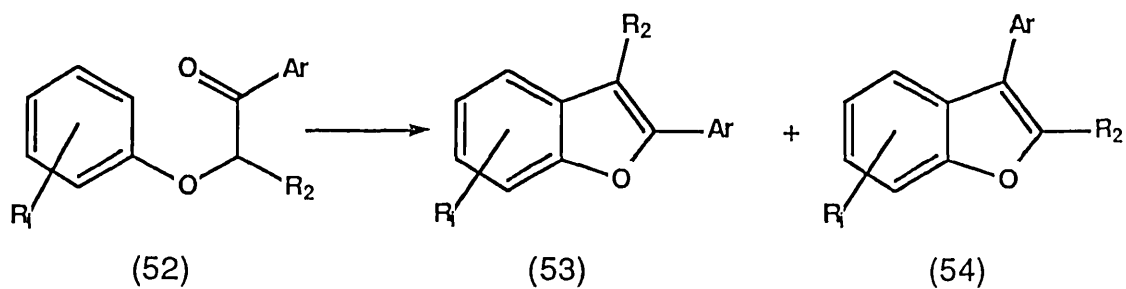
a) 1. ClSO_3H , 2. HNMe_2

Scheme 15

1.3 Formation of the C-Ar benzofuran bond

1.3.1 Ring closure of α -aryloxyketones

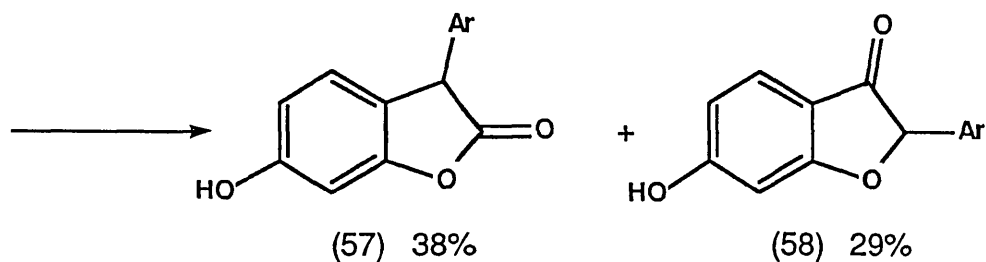
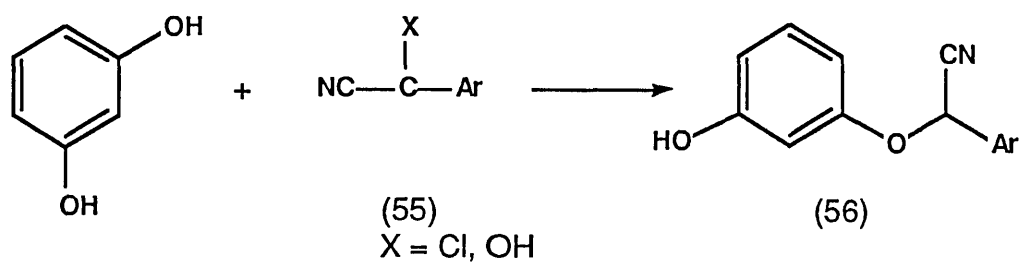
This involves the cyclodehydration reaction of α -aryloxyketones (52), usually carried out in the presence of various acids¹ (polyphosphoric acid (PPA), P_2O_5 , pyridinium hydrochloride). The presence of an inert co-solvent²⁸, generally affords higher yields (Scheme 16). The disadvantage inherent in the method is that rearrangement can occur to give mixtures of 2- and 3-substituted benzofurans, although this is dependent on the conditions and substitution pattern of the aromatic rings. See Table 1. A similar reaction^{29, 30} between polyphenols and α -hydroxy or α -haloarylacetonitriles (55) affords the corresponding benzofuranones (57, 58) which can be elaborated to their benzofuran derivatives (Scheme 17). Best yields are obtained with the α -halonitriles (55, $\text{X} = \text{Cl}$), and where the aryl group contains a 4-hydroxy group to facilitate the departure of the chloride (55, $\text{Ar} = 4\text{-HOC}_6\text{H}_4$).

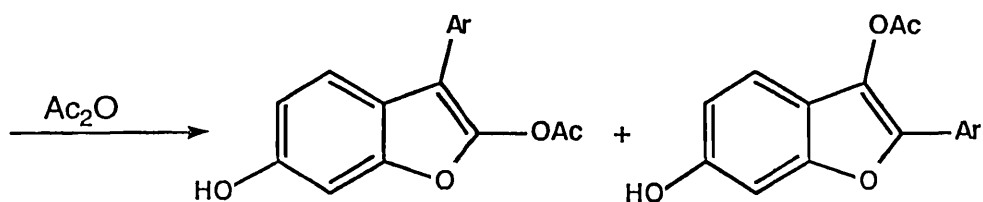


Scheme 16

Table 1

Starting compound	Benzofuran	Reagent/Temp°C
$R_1 = 2\text{-Me}, R_2 = \text{H}, Ar = \text{Ph}$	2-Ph-7-Me	PPA/140
$R_1 = 2\text{-OMe}, R_2 = \text{H}, Ar = \text{Ph}$	2-Ph-7-OMe	PPA/140
$R_1 = 4\text{-OMe}, R_2 = \text{H}, Ar = \text{Ph}$	2-Ph-5-OMe	PPA, Xylene/ Δ
$R_1 = \text{H}, R_2 = \text{H}, Ar = \text{Ph}$	3-Ph	P_2O_5 , Benzene/ Δ
$R_1 = 3\text{-Me}, R_2 = \text{H}, Ar = \text{Ph}$	3-Ph-6-OMe	Py.HCl
$R_1 = 2\text{-Me}, R_2 = \text{H}, Ar = 3\text{-xylyl}$	2-(3-xylyl)-7-Me	PPA/130
$R_1 = \text{H}, R_2 = \text{H}, Ar = 4\text{-anisyl}$	2-(4-anisyl)	PPA/80
$R_1 = 5\text{-Ac}, R_2 = \text{Me}, Ar = 4\text{-anisyl}$	2-Me-3-(4-anisyl)	PPA/130

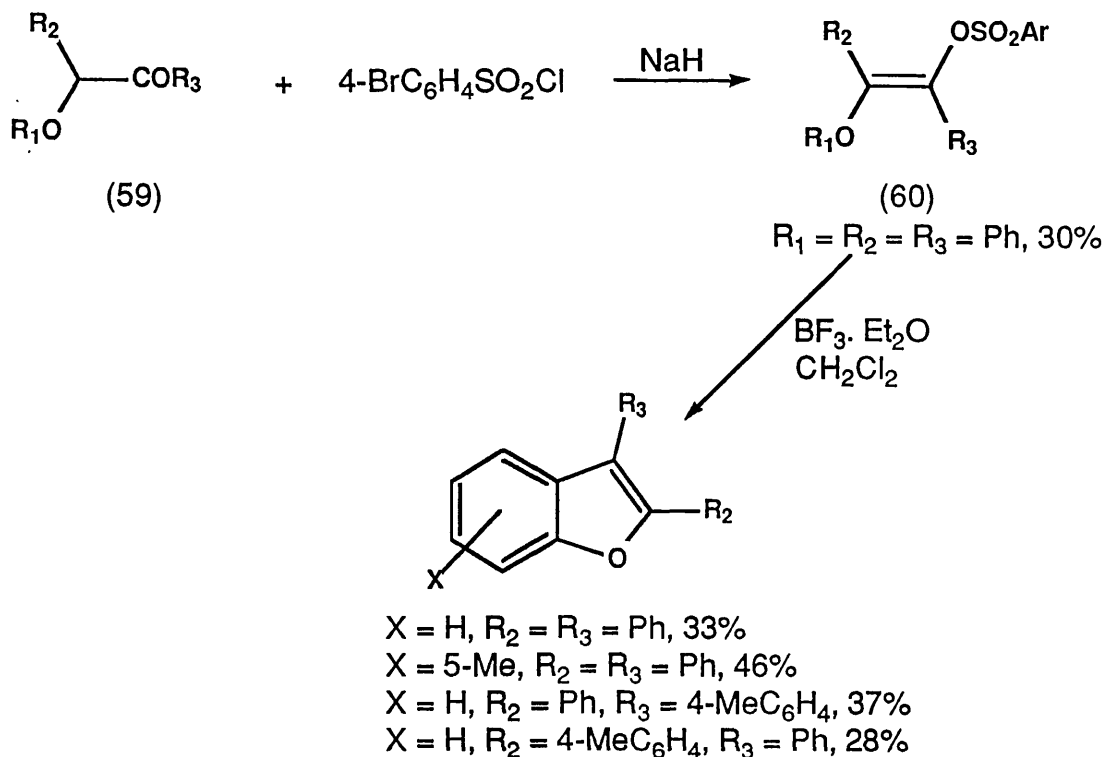




Scheme 17

1.3.2 Reactions of vinyl sulphonates

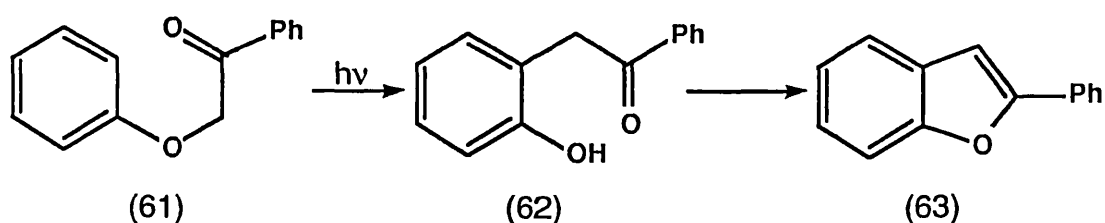
The mixtures that are usually obtained in the reactions of α -aryloxyketones may be avoided if their vinyl sulphonic ester derivatives (60) are formed³¹. Thus reaction of the α -aryloxyketones (59) with 4-bromobenzene sulphonyl chloride leads to the vinyl sulphonates (60) in low to moderate yields (Scheme 18). These are treated with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in dichloromethane to yield the corresponding benzofurans (Scheme 18). However, the reaction is limited to the formation of 2,3-diaryl benzofurans.



Scheme 18

1.3.3 Photochemical ring closure of α -aryloxyketones

Another method that overcomes the lack of selectivity and relatively harsh conditions employed in the reactions of α -aryloxyketones (61), is the photolysis of these compounds³². This leads to the formation of the 2-aryl benzofuran (63) via the 2-hydroxybenzoin (62), although the yields are extremely low (Scheme 19).

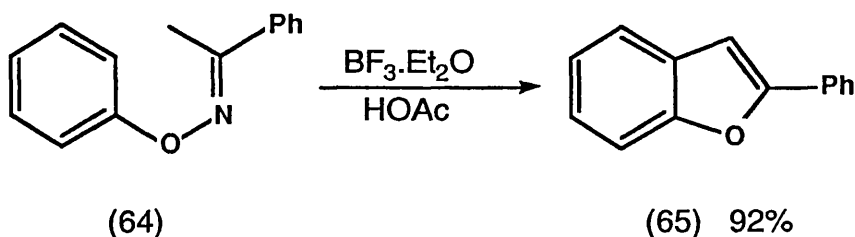


Scheme 19

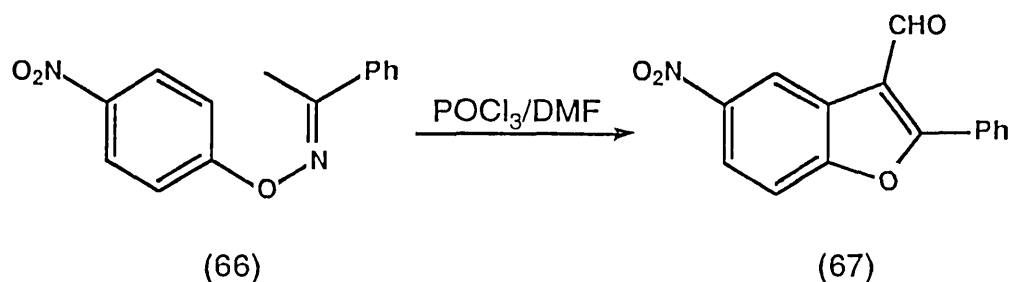
1.3.4 From O-aryloximes

This method is analogous to the Fischer indole synthesis, and has been extended to the synthesis of benzofurans^{33, 34}.

The appropriate O-aryloximes (64) are heated in acetic acid with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ to afford the corresponding benzofurans (65) in good yields (Scheme 20). Alternatively reacting the oxime (66) with POCl_3/DMF , gives the 2-aryl-3-formylbenzofuran³⁵ (67) (Scheme 21).



Scheme 20



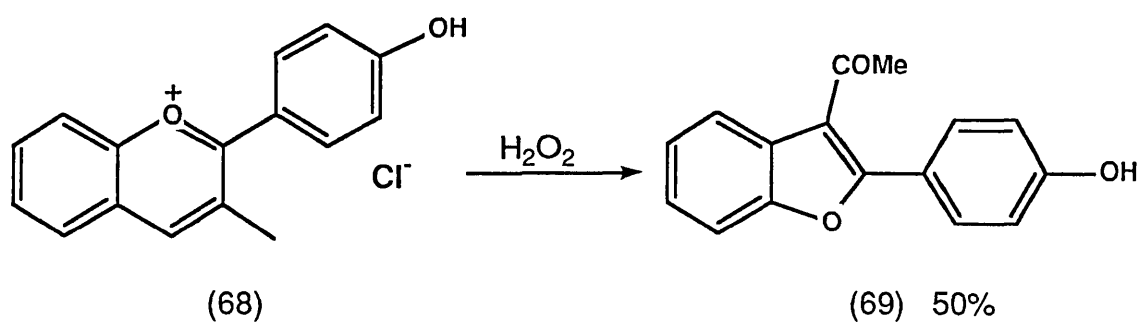
Scheme 21

1.4 Benzofurans from other ring systems

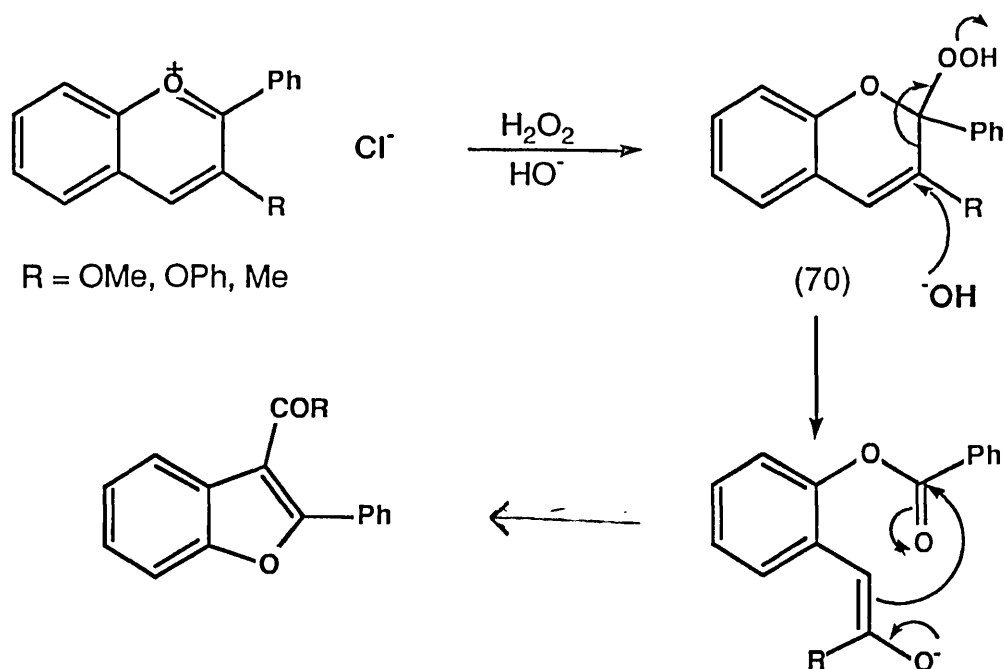
1.4.1 Oxidation of flavylum salts

Work carried out by Jurd^{36, 37} had shown that flavylum salts such as 3-methyl-4'-hydroxyflavylium chloride (68), underwent oxidative rearrangement when treated with alkaline hydrogen peroxide, to give 2-aryl benzofurans (69) (Scheme 22).

The mechanism is believed to involve initial formation of a hydroperoxide (70), and its subsequent rearrangement (Scheme 23).

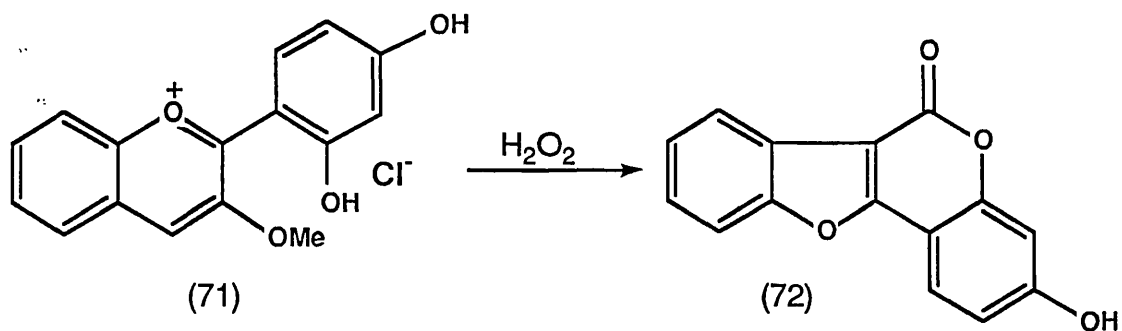


Scheme 22



Scheme 23

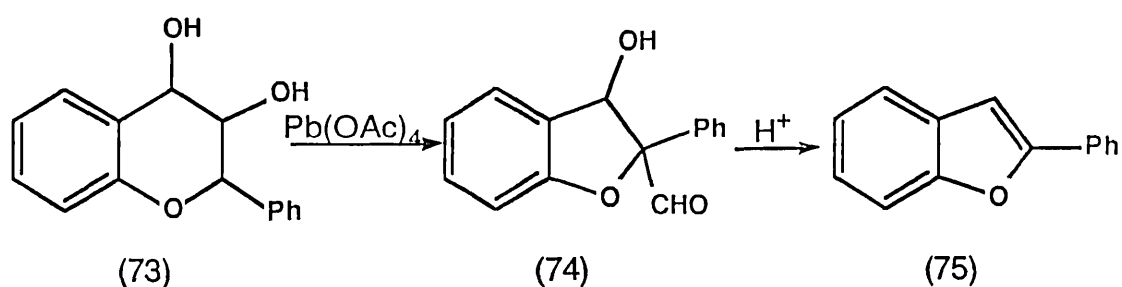
It has been applied to the synthesis of some natural products, such as coumestrol^{38, 39} (72) and trifoliol⁴⁰ (Scheme 24).



Scheme 24

1.4.2 From dihydroxyflavanols

3,4-Dihydroxyflavanols (73) are oxidised by lead tetra-acetate¹ to 2-formyl-2-phenyl-3-hydroxy-2,3-dihydrobenzofurans (74), which eliminates formic acid to give the benzofuran (75) (Scheme 25).

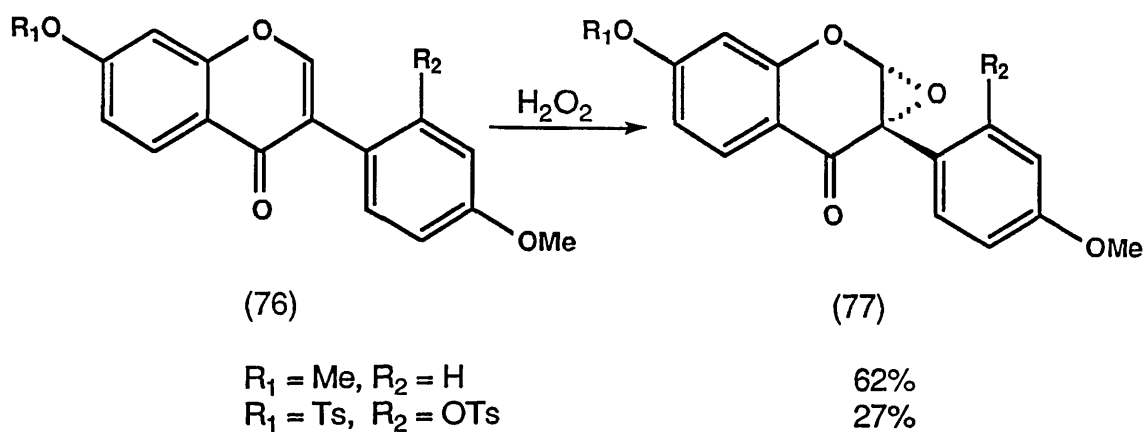


Scheme 25

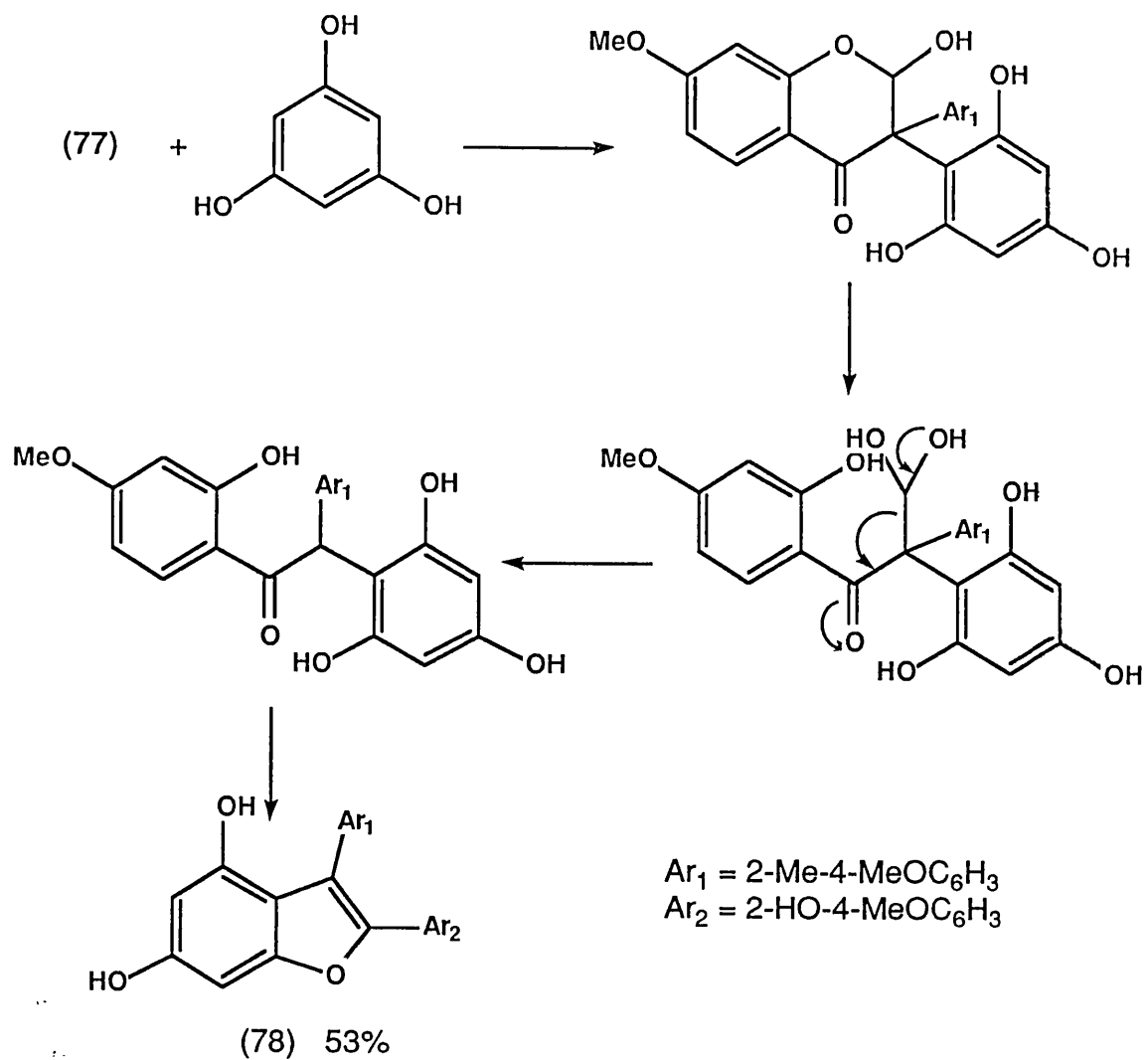
1.4.3 From isoflavanone epoxides

Isoflavanones (76) when reacted with alkaline hydrogen peroxide afford the corresponding epoxide derivatives⁴¹(77) (Scheme 26).

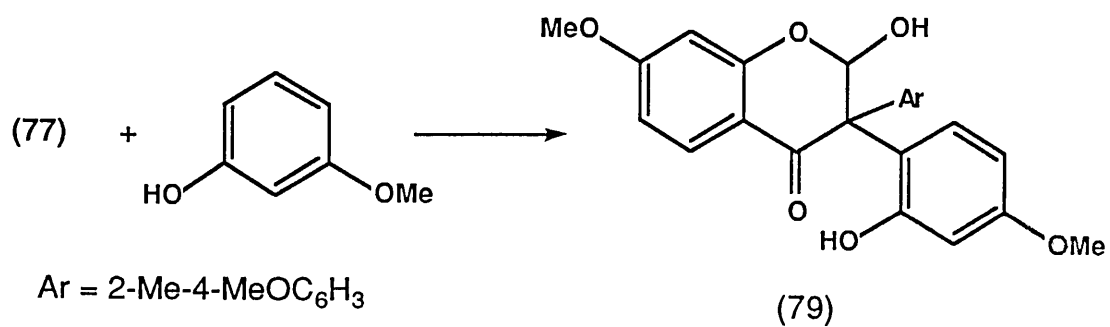
These isoflavanone epoxides (77) react with phloroglucinol to yield the 2,3-diaryl benzofurans (78) as shown in Scheme 27. A drawback with this reaction is that only phloroglucinol reacts to give the benzofuran derivative, whereas the reaction with 3-methoxy phenol gives only the 3-aryl isoflavonol (79) (Scheme 28).



Scheme 26



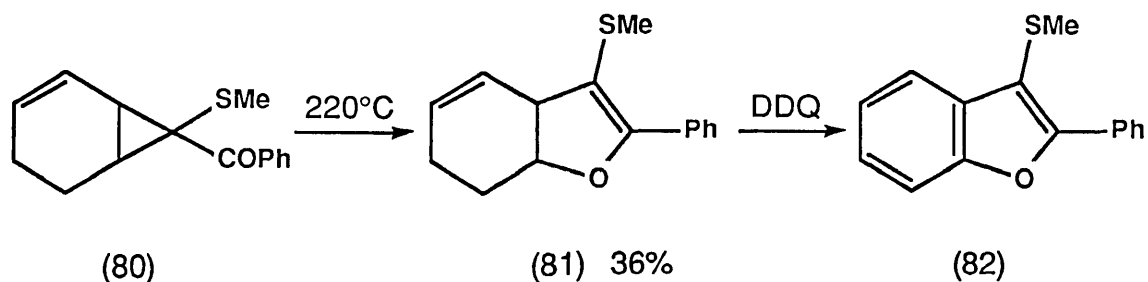
Scheme 27



Scheme 28

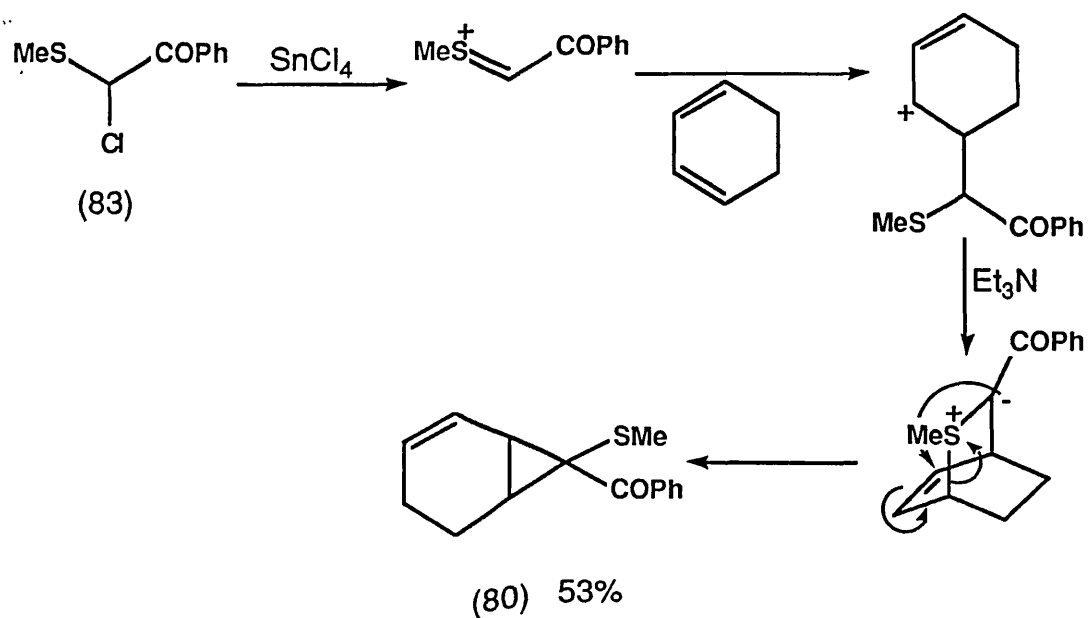
1.4.4 Reactions of vinyl cyclopropanes

An unusual method which leads to 2-aryl benzofurans is the thermolysis of vinyl cyclopropanes⁴² (80) at 220-240°C, which affords the tetrahydro derivative (81), and is subsequently oxidised to the benzofuran (82) using DDQ (Scheme 29).



Scheme 29

The vinylcyclopropanes are formed from the reaction of α -thio carbocations, derived from the α -chloromethylketone (83), with 1,3-dienes, in the presence of SnCl_4 and triethylamine (Scheme 30).

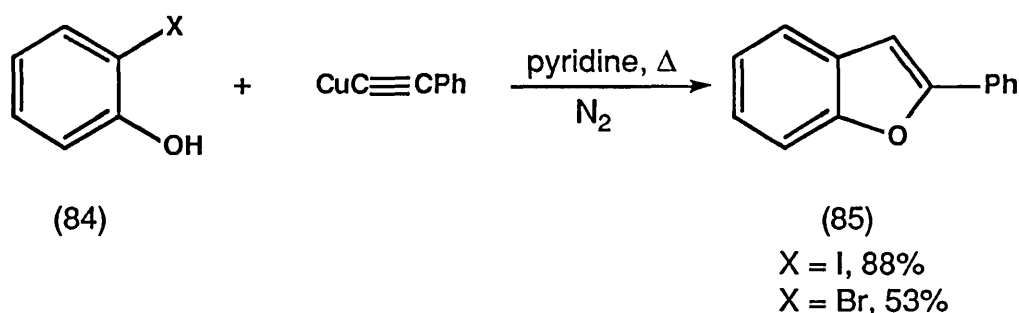


Scheme 30

1.5 Ring closure of 2-hydroxyphenyl derivatives

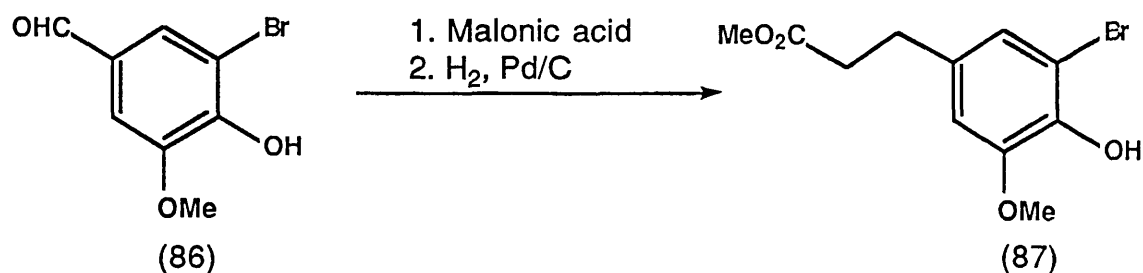
1.5.1 Ring closure and formation of 2-alkynyl phenols

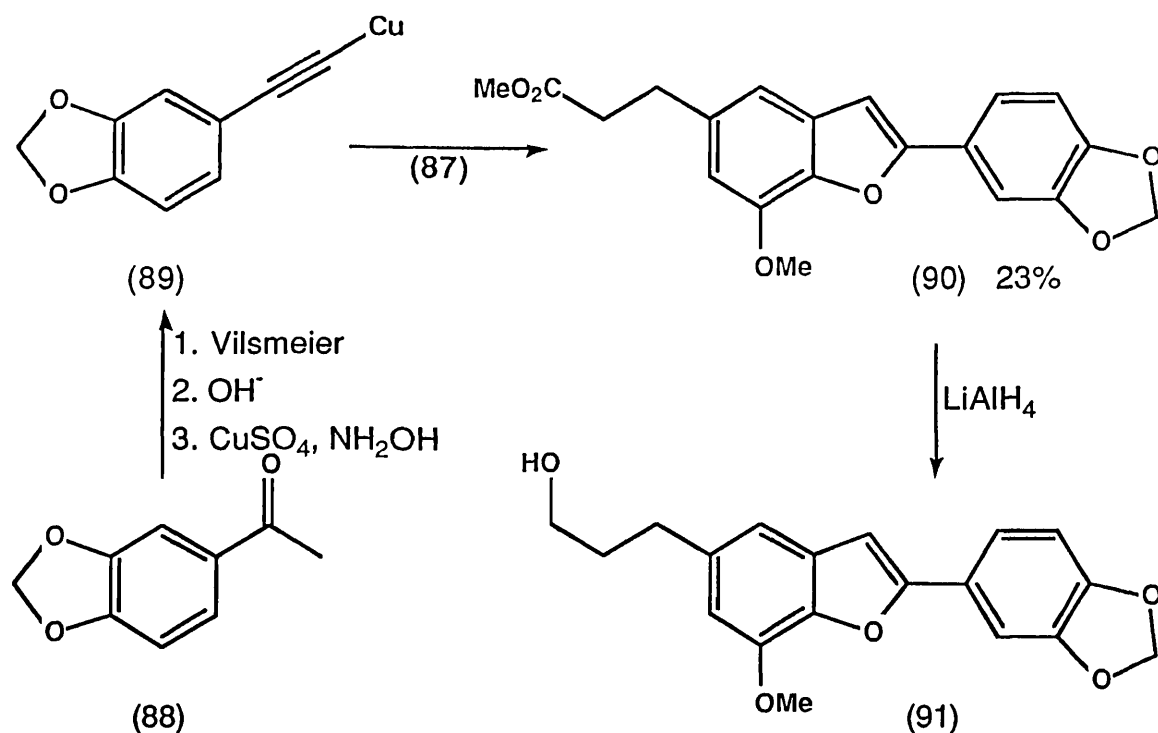
Castro^{43,44} discovered that the reaction of 2-halophenols (84) with copper acetylides in refluxing pyridine, gave rise to 2-substituted benzofurans⁴⁵ (85) via the intermediate 2-alkynyl phenols (Scheme 31).



Scheme 31

The reaction works best for iodophenols, and has been used in the synthesis of many natural products⁴⁶⁻⁵⁰, such as egonol^{51,52} (91), a benzofuran styrax derivative from the seed oil of *Styrax japonicum* (Scheme 32). The synthesis utilises 5-bromovanillin (86), which is converted using standard procedures to the requisite precursor (87). The copper acetylide (89) is also readily formed from methylenedioxyacetophenone (88).



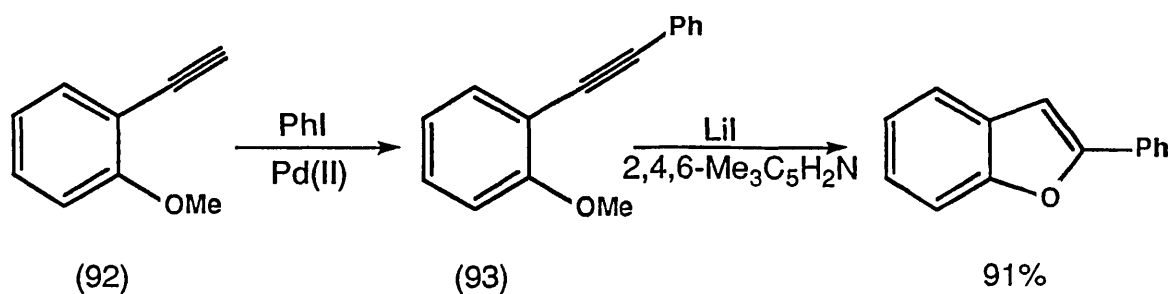


Scheme 32

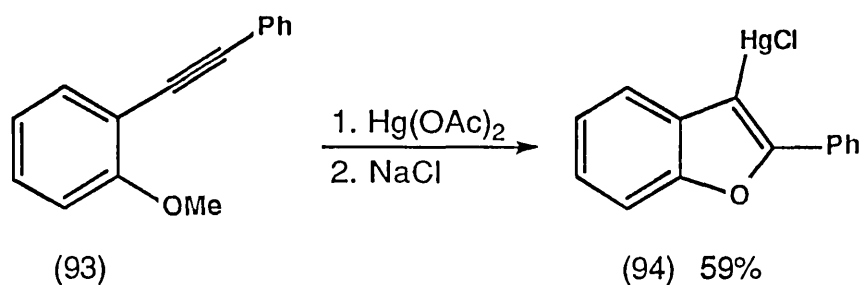
1.5.2 Palladium mediated reactions

Terminal acetylenes (92) derived from (2-methoxyphenyl)acetophenones can be coupled with aryl iodides using the palladium mediated Heck reaction. The aryl acetylene (93) thus formed is demethylated and cyclised by reaction with LiI in 2,4,6-trimethylpyridine⁵³ (Scheme 33).

A milder method for inducing cyclisation of the aryl acetylene, uses mercuric acetate⁵⁴, which affords 2-phenyl-3-mercurylchloride benzofuran (94) (Scheme 34).

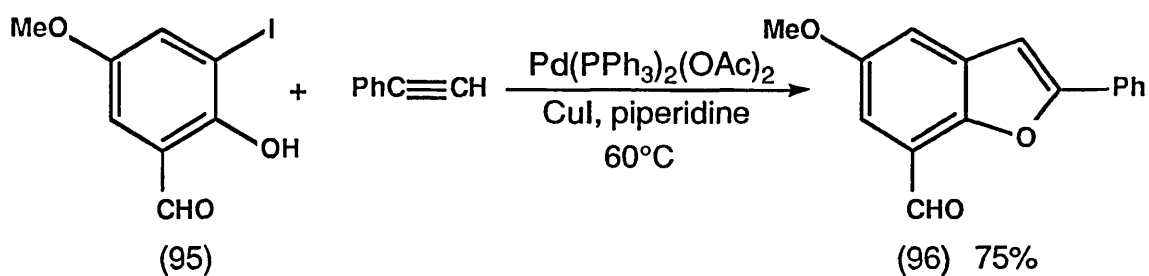


Scheme 33



Scheme 34

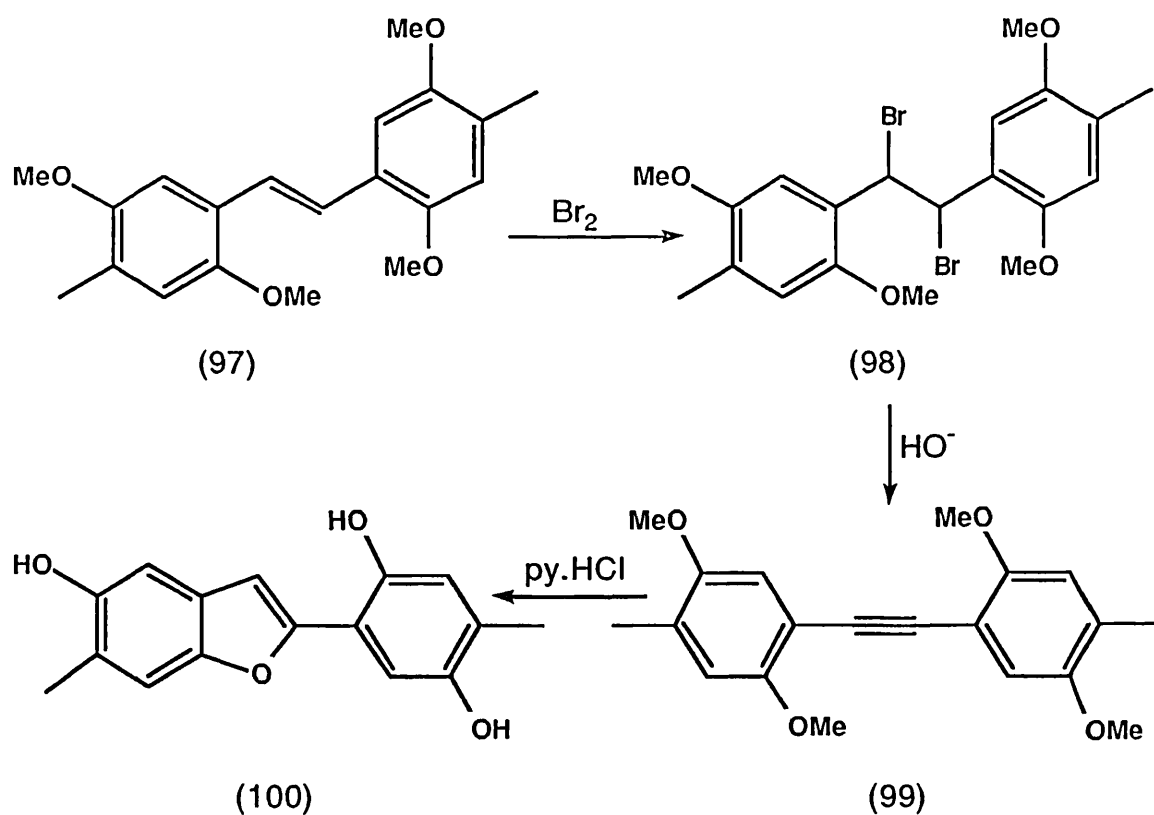
Another mild and efficient route directly to 2-aryl benzofurans⁵⁵ is the palladium cross coupling reaction of 2-iodophenols (95) with phenyl acetylenes in piperidine at 60°C (Scheme 35).



Scheme 35

1.5.3 Bromination of stilbenes

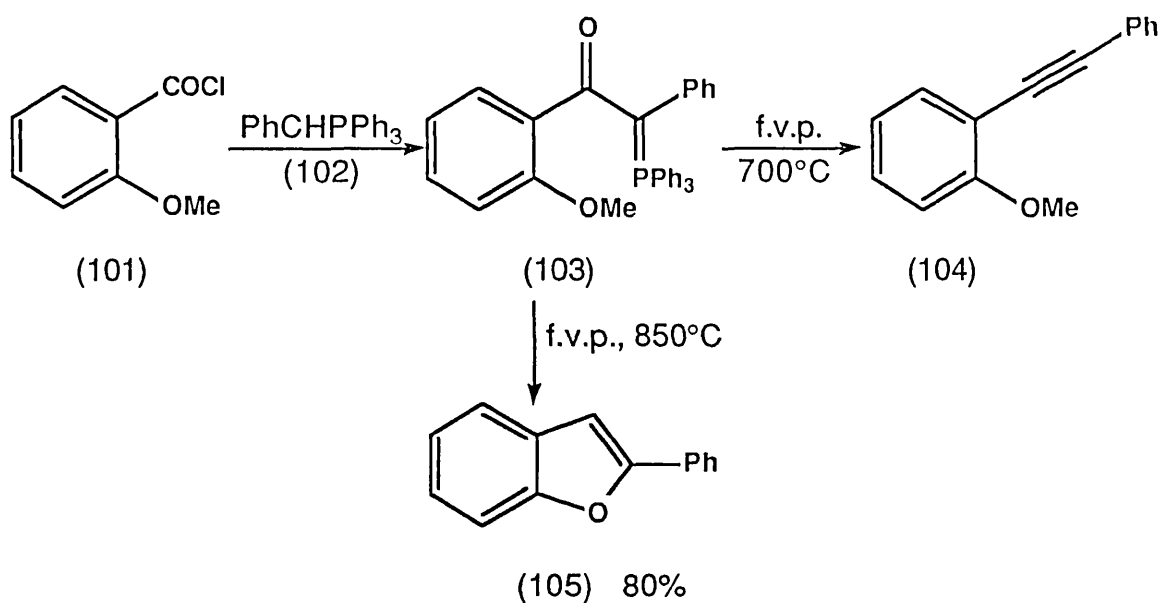
The bromination of stilbenes⁵⁶ (97) affords the corresponding dibromo derivatives (98), which undergo base induced elimination of HBr to give the disubstituted acetylenes (99), leading to benzofurans (100) (Scheme 36). However the only reference to this procedure utilises symmetrical stilbenes, although extension to unsymmetrical systems should also be possible.



Scheme 36

1.5.4 Flash vacuum pyrolysis of phosphoranes

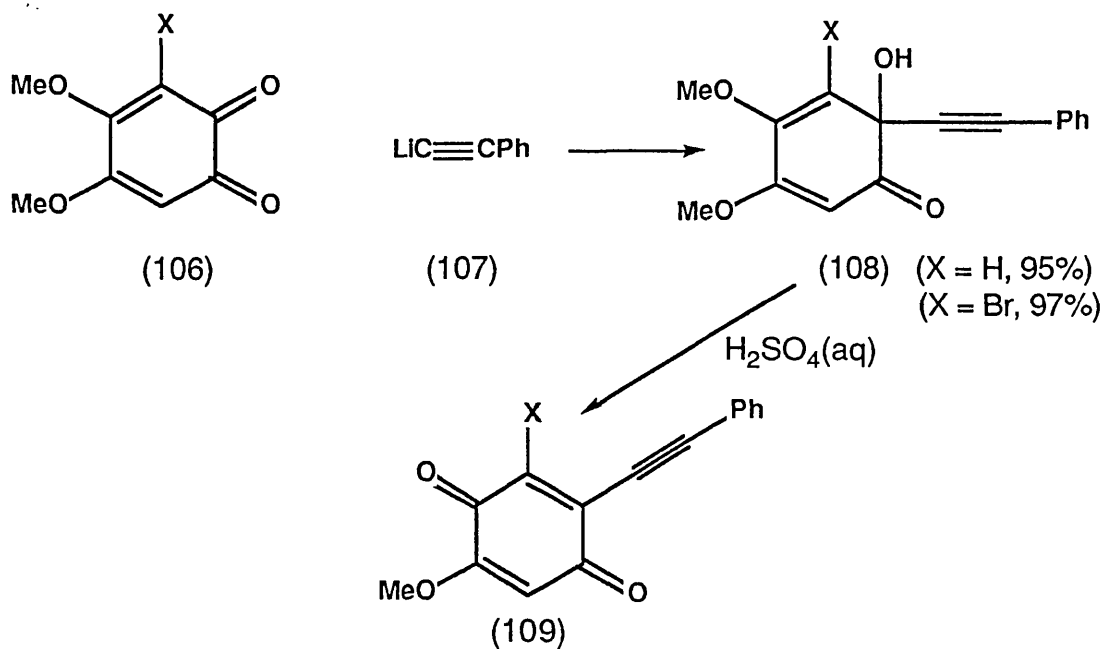
The reaction of 2-methoxybenzoyl chloride (101) with two equivalents of the Wittig reagent (102) gives the β -oxoalkylidene triphenylphosphorane⁵⁷ (103). This is subjected to flash vacuum pyrolysis (f. v. p.) at 700°C to afford the alkyne (104). At 850°C f. v. p. induces formation of the benzofuran ring (105) directly (Scheme 37).



Scheme 37

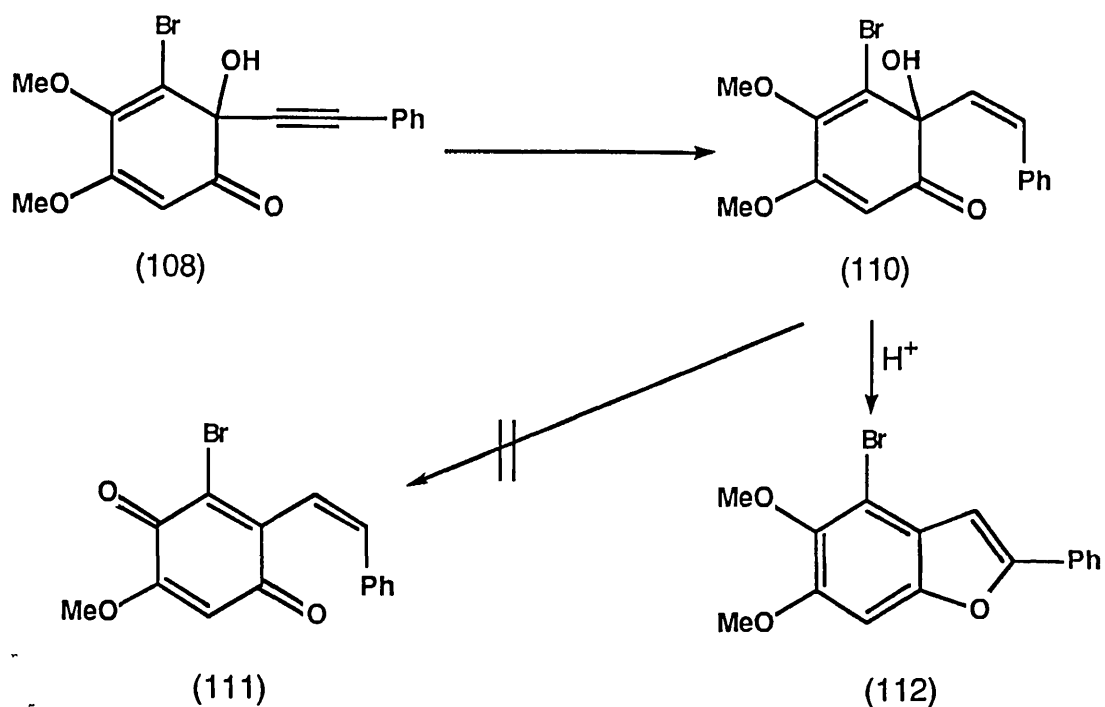
1.5.5 Addition to quinones⁵⁸

This method represents a very efficient and high yielding synthesis of aryl acetylenes. 1,2 Quinones (106) are reacted with lithium acetylides (107), to give the 1,2 addition products (108), which can be hydrolysed to the 1,4 quinones (109) (Scheme 38).

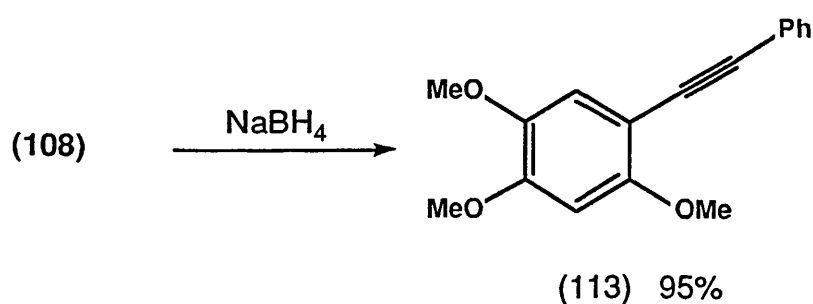


Scheme 38

Acid treatment of the vinylic compound (110), obtained by reduction of the acetylene (108, X = Br), leads not to the corresponding 1,4 quinone (111), but the 2-aryl benzofuran (112) in good yield (Scheme 39). Also sodium borohydride reduction of the acetylene (108, X = H), affords the (2-methoxyphenyl)acetylene (113) in very good yield (Scheme 40).



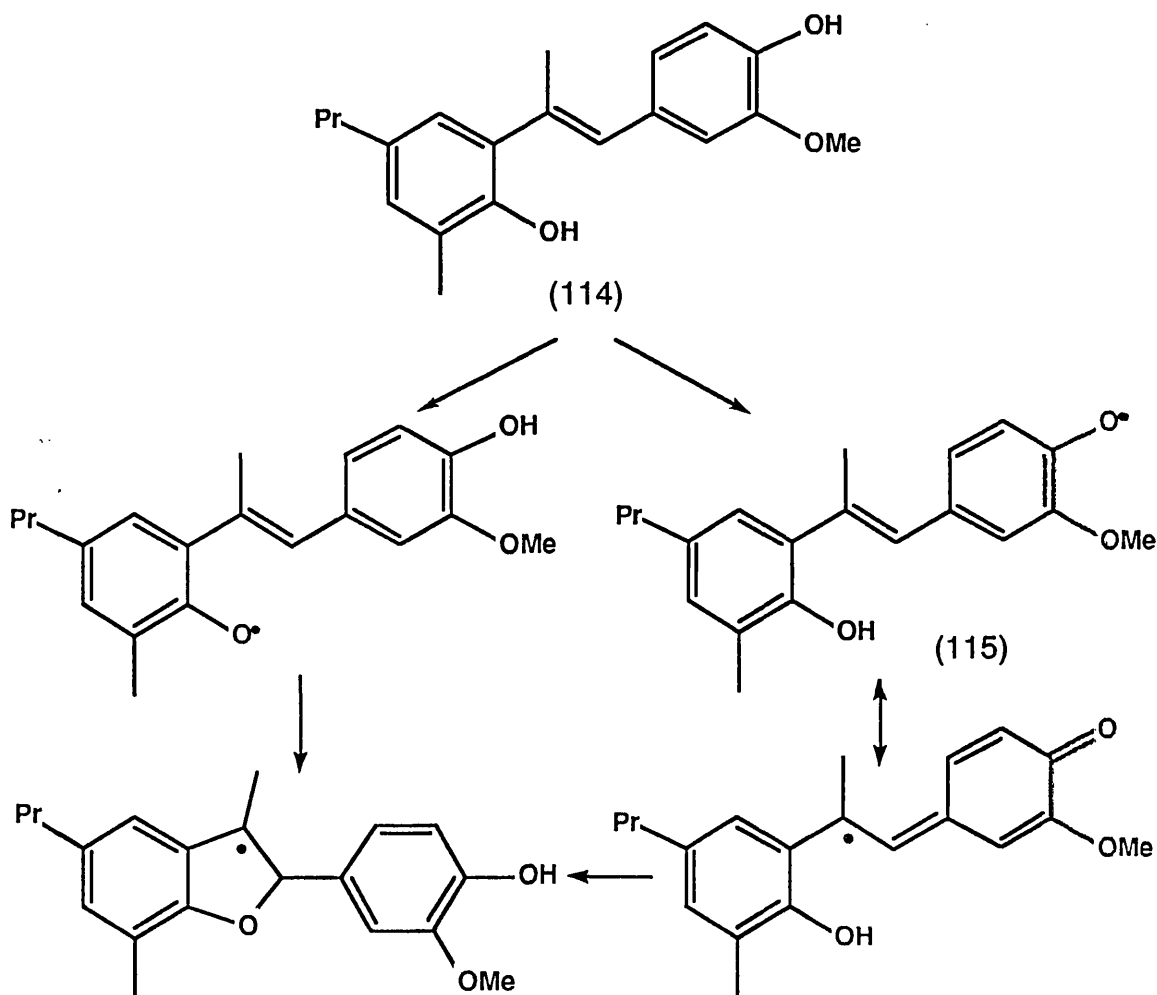
Scheme 39

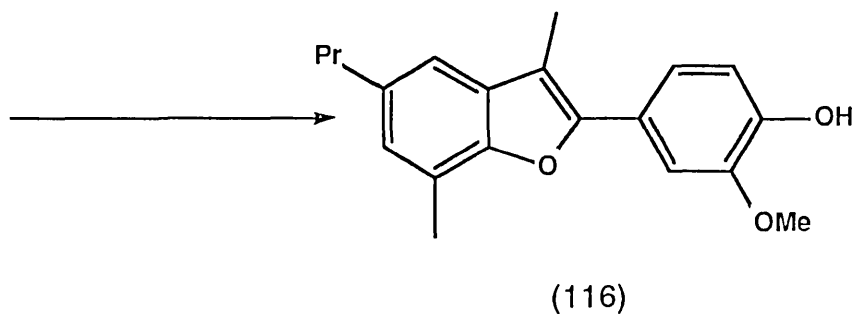


Scheme 40

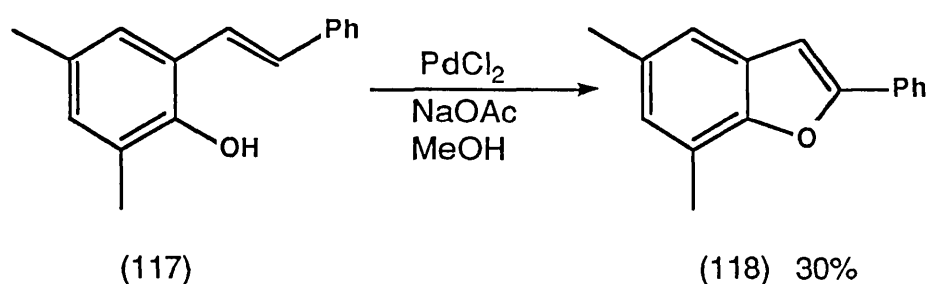
1.5.6 Oxidation of stilbene derivatives

2,2' and 2,4'-dihydroxy stilbenes (114) are oxidised to 2-aryl benzofurans by a variety of oxidising agents, such as $\text{Pb}(\text{OAc})_4$ ⁵⁹, N-iodosuccinimide⁶⁰, DDQ⁶¹, Ag_2O ⁶¹, and PdCl_2 ⁶¹. Most of these reactions are perceived as proceeding via a one electron oxidation to phenoxy radicals (115), which subsequently react with the internal double bond leading to the 2-aryl benzofuran (116) (Scheme 41). The reaction with PdCl_2 (Heck reaction) also works with 2-hydroxystilbenes (117) to afford the benzofuran (118) in low yield (Scheme 42).



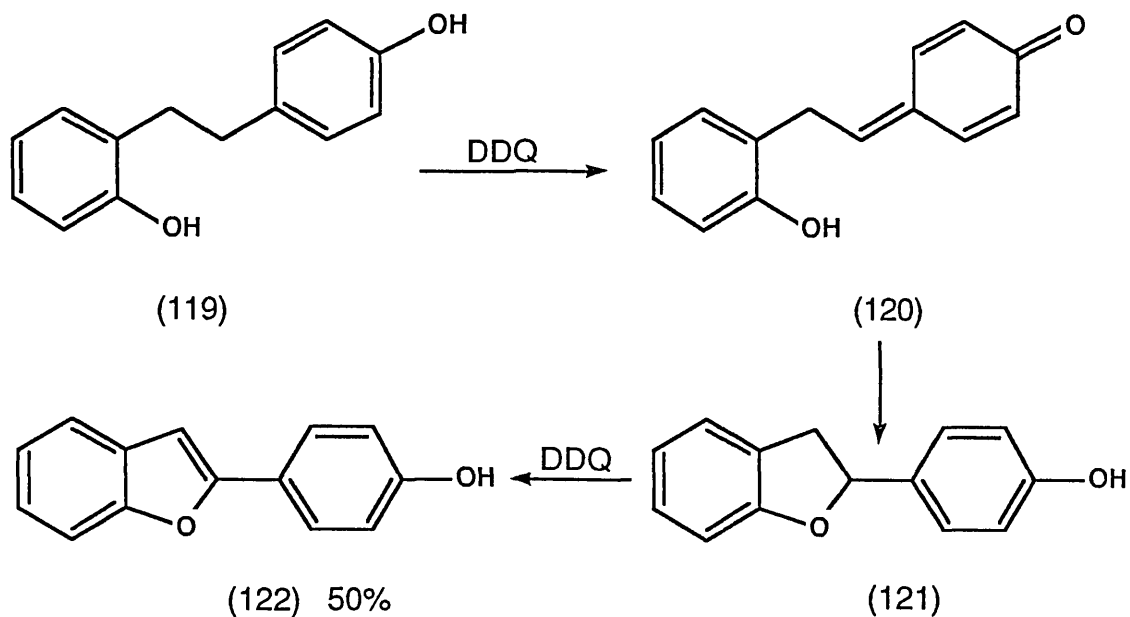


Scheme 41



Scheme 42

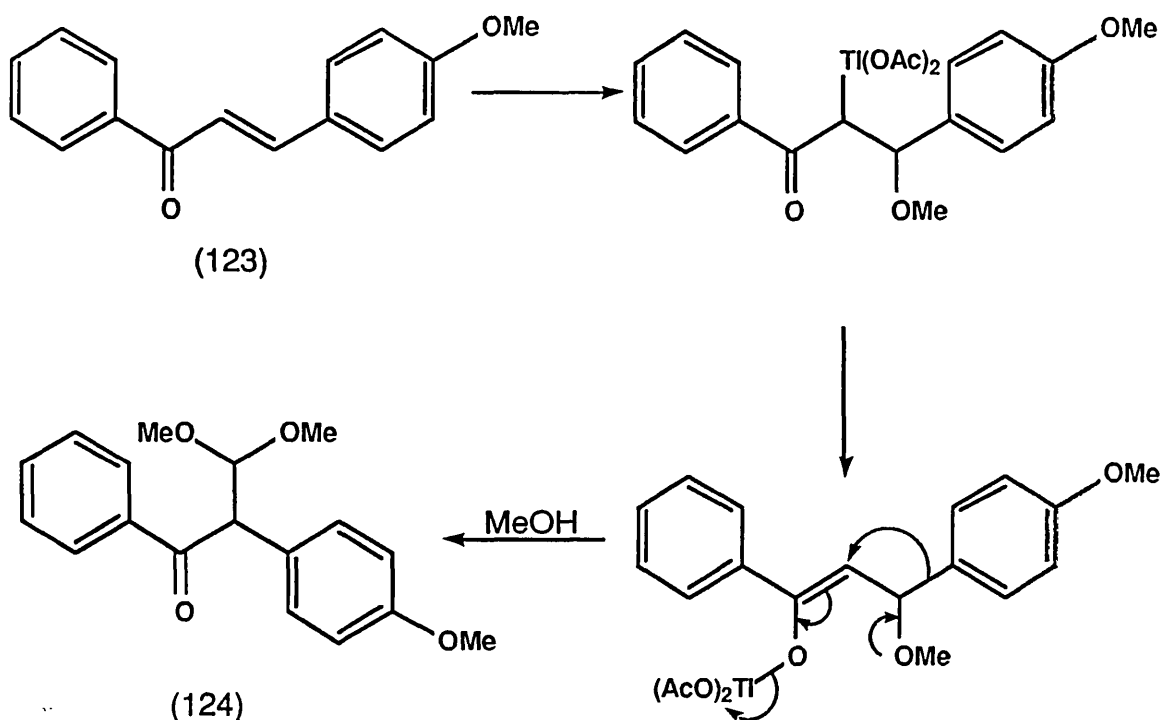
The dihydrostilbene derivative (119) also leads to the benzofuran derivative (122) when oxidised by DDQ⁶², via the dihydrobenzofuran (121). The oxidation proceeds through the quinone methide species (120) (Scheme 43).



Scheme 43

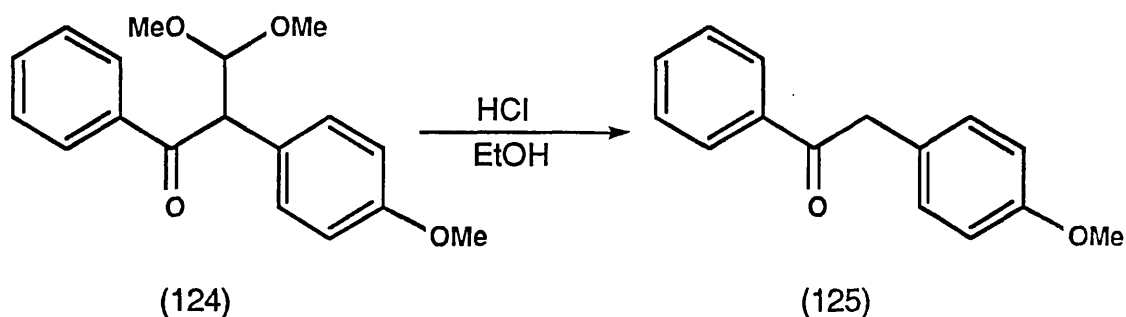
1.5.7 Oxidative rearrangement of chalcones

Thallium (III) induced oxidation of chalcones⁶³ (123) in methanol affords the rearrangement product (124). The mechanism involves an initial oxythallation reaction, followed by 1,2-aryl migration to give the acetal (124) (Scheme 44).

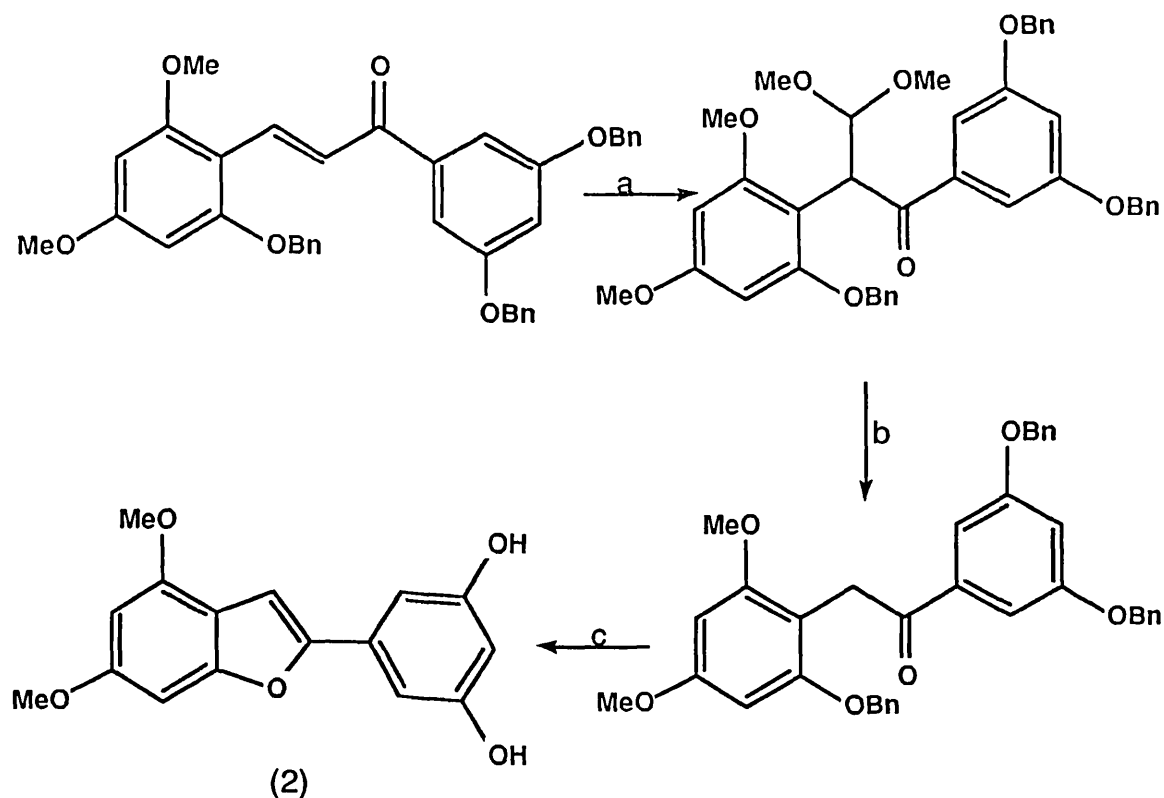


Scheme 44

Acid⁶³ or base⁶⁴ hydrolysis of the acetal (124) gives the deacetalated deoxybenzoin (125) (Scheme 45). The reaction sequence has been applied to the synthesis of 6-demethylvignafuran⁶⁵ and moracins A (2) and B⁶⁶ (Scheme 46).



Scheme 45

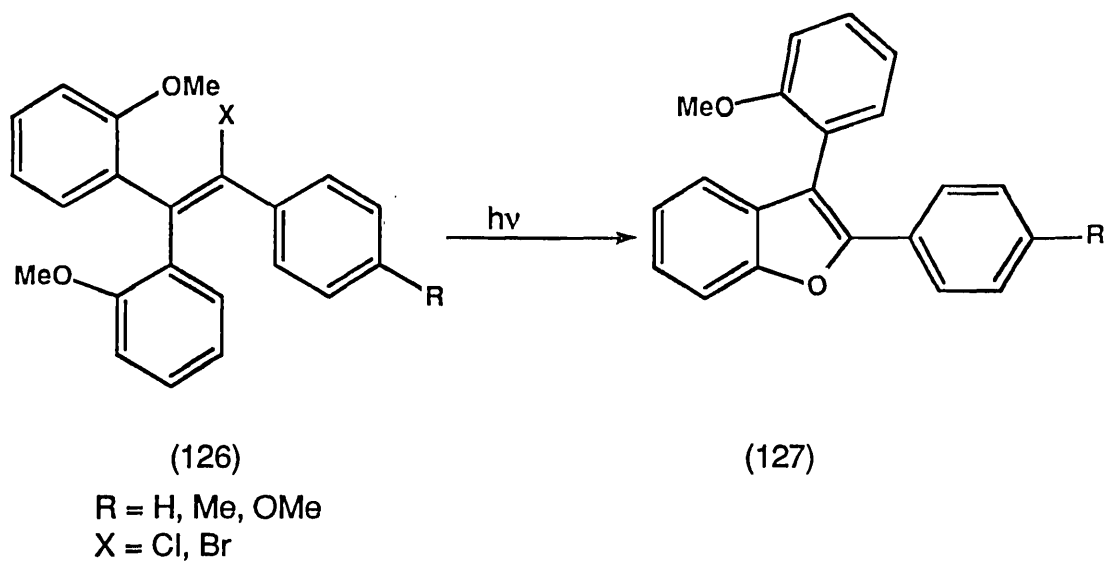


a. $\text{Ti}(\text{NO}_3)_3$; b. KOH/EtOH ; c. $\text{H}_2, \text{Pd}/\text{C}$; EtOH/HCl

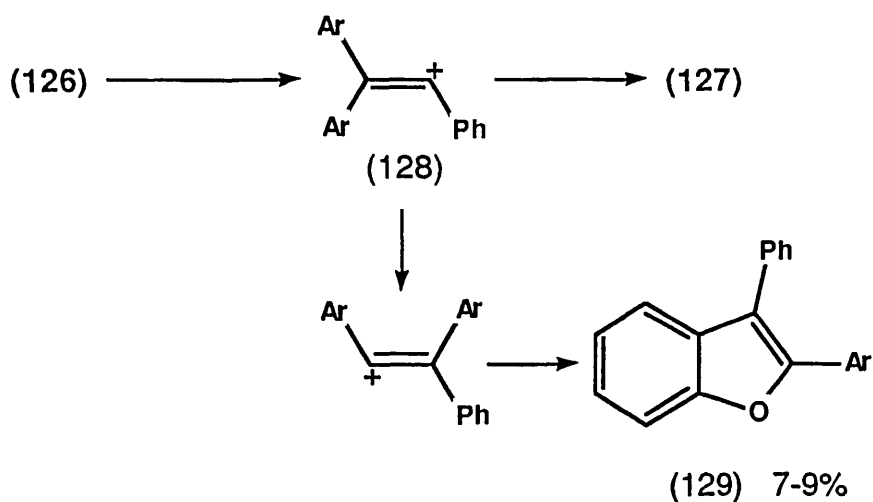
Scheme 46

1.5.8 Reactions of α, α, β -triarylvinyl halides

Vinyl halides of this type containing a β -(2-hydroxyaryl) substituent undergo photolytic^{67,68} and solvolytic^{69, 70} intramolecular benzofuran ring formation in essentially quantitative yields (Scheme 47). For the vinyl bromide (126, $\text{R} = \text{H}$), the solvolytic reaction gives a small amount (7-9%) of the rearranged benzofuran (129) due to rearrangement of the intermediate vinyl cation (128) (Scheme 48).



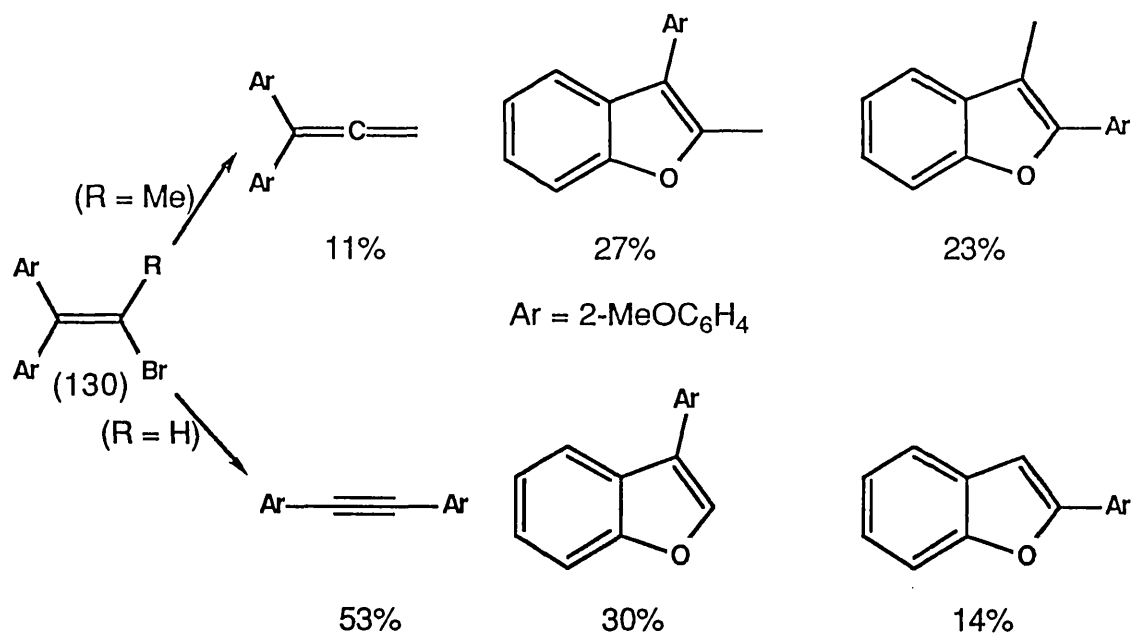
Scheme 47



Scheme 48

1.5.9 Reactions of β,β -diarylvinyl halides

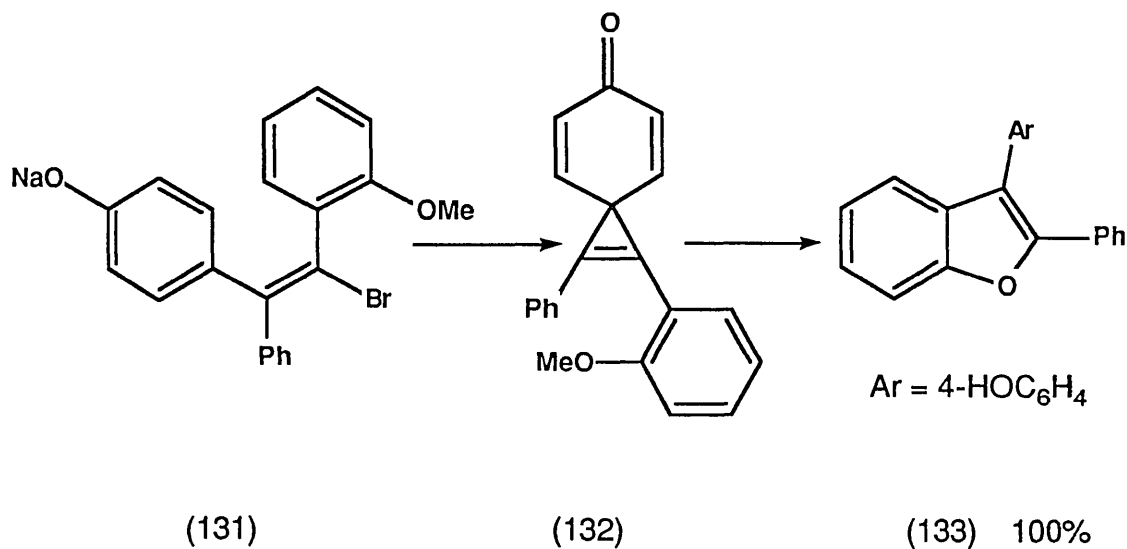
The photochemical reactions of these vinyl bromides^{67, 68} (130) proceed to yield the benzofuran derivatives. The greater instability of the intermediate carbonium ion is reflected in the larger amounts of rearranged and side products obtained (Scheme 49).

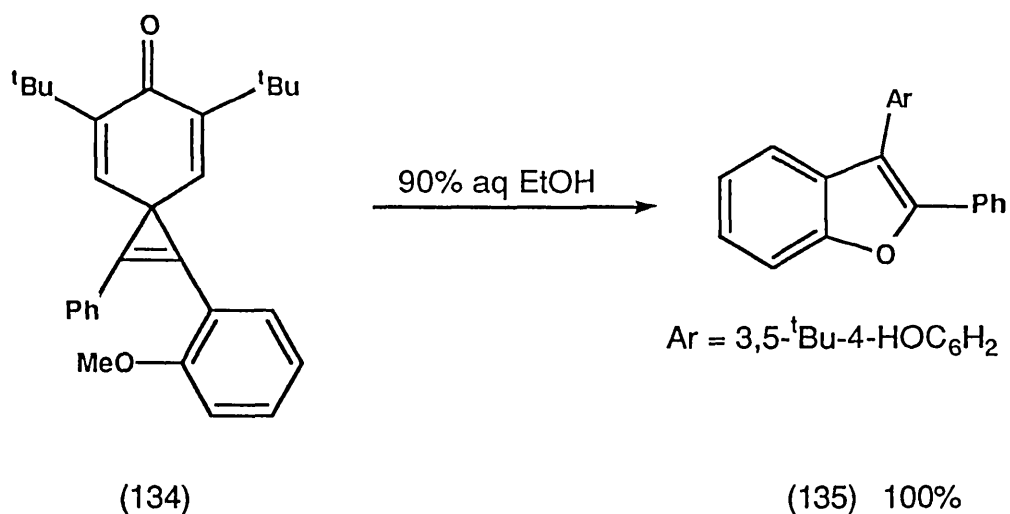


Scheme 49

1.5.10 Reactions of α -(2-methoxyphenyl) β,β -diarylvinyl bromides

The solvolysis of the vinyl bromide (131) gives rise to the benzofuran (133) via the intermediate spiro[2,5]octa-1,4,7-trien-6-one⁷¹ (132) (Scheme 50). Confirmation of this as an intermediate is found in the reaction of (134)^{72, 73} in aqueous ethanol which leads exclusively to the benzofuran derivative (135) (Scheme 50).

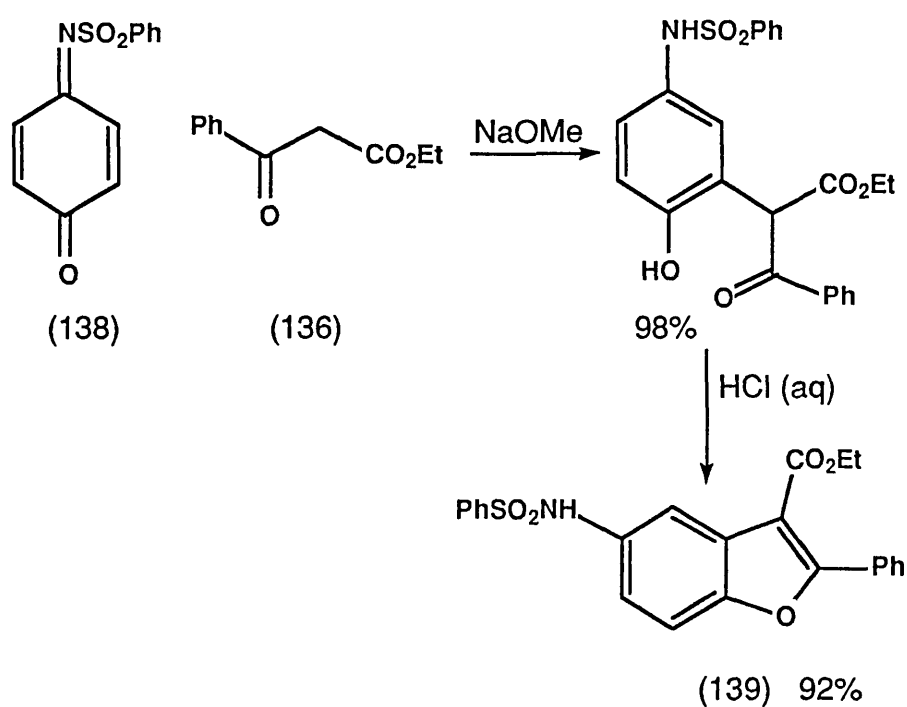




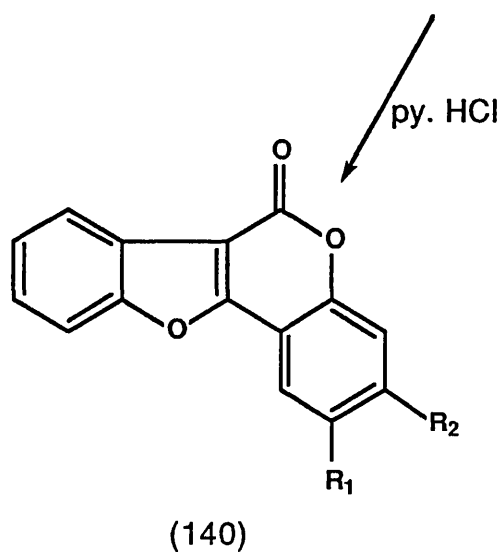
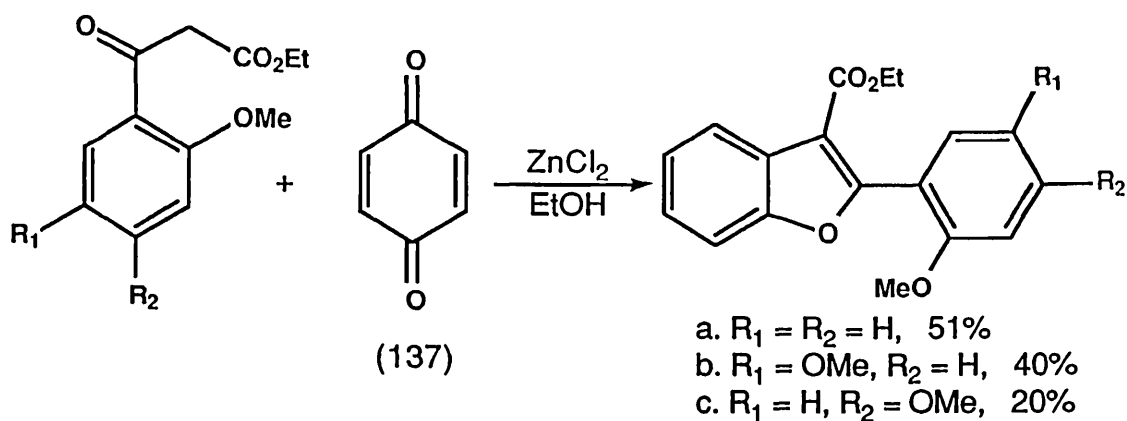
Scheme 50

1.5.11 From 1,4-benzoquinones and quinone monoimides

The Michael addition of benzoyl acetates (136) to benzoquinone⁷⁴ (137) and quinone monoimides⁷⁵ (138) affords the benzofuran derivatives (139) in moderate yields (Scheme 51). An application of this method has been found in the synthesis of various coumestan derivatives (140) (Scheme 52).



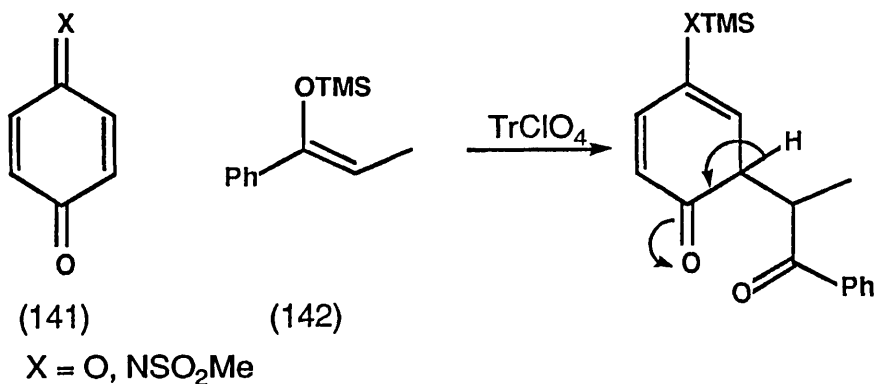
Scheme 51

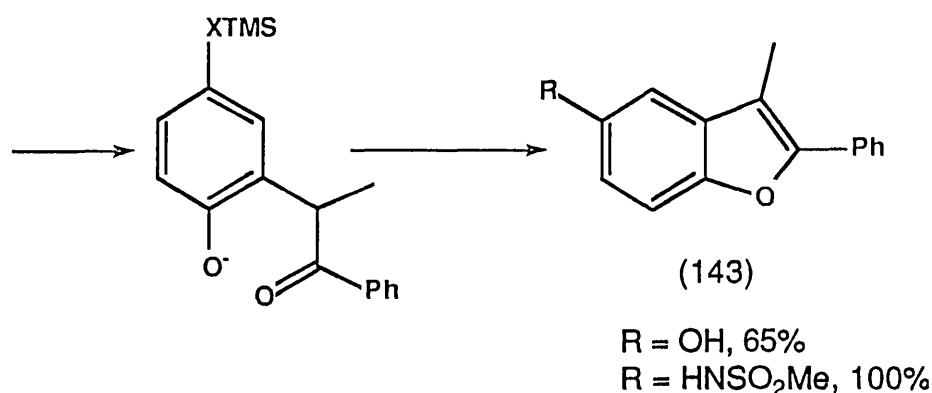


a. 84%; b. 59%; c. 55%

Scheme 52

The procedure has been extended to include silyl enol ethers⁷⁶ (142). Hence the reactions of quinones and quinone monoimides (141) with TMS-enol ethers (142) in the presence of catalytic trityl perchlorate (TrClO_4) affords the benzofuran derivatives (143) in good yields (Scheme 53).

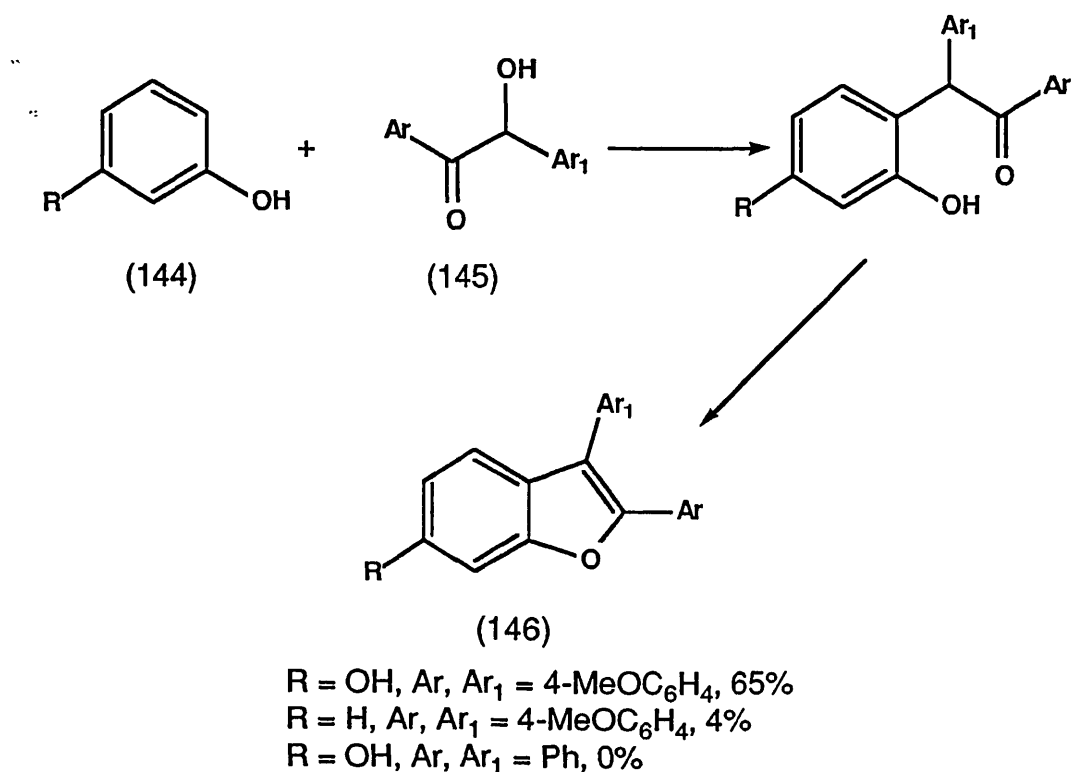




Scheme 53

1.5.12 Reactions of benzoin

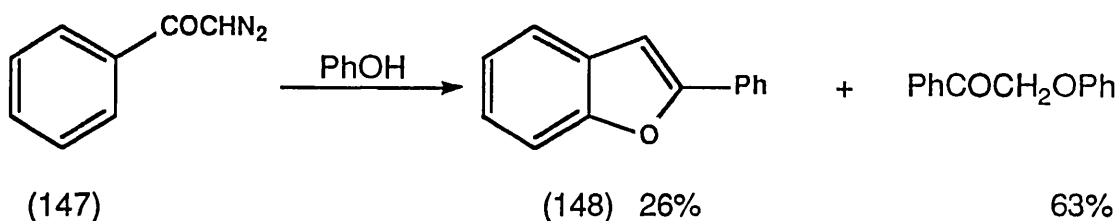
The condensation of benzoin (145) with phenols (144) leads to 2,3-diaryl benzofurans⁷⁷ (146) in poor to good yields. The reaction is however limited to the synthesis of 2,3 diaryl benzofurans and works best for benzoin having *ortho* or *para* anisyl groups on the benzyl alcohol moiety, reacting with resorcinol derivatives (Scheme 54).



Scheme 54

1.5.13 Decomposition of diazoketones

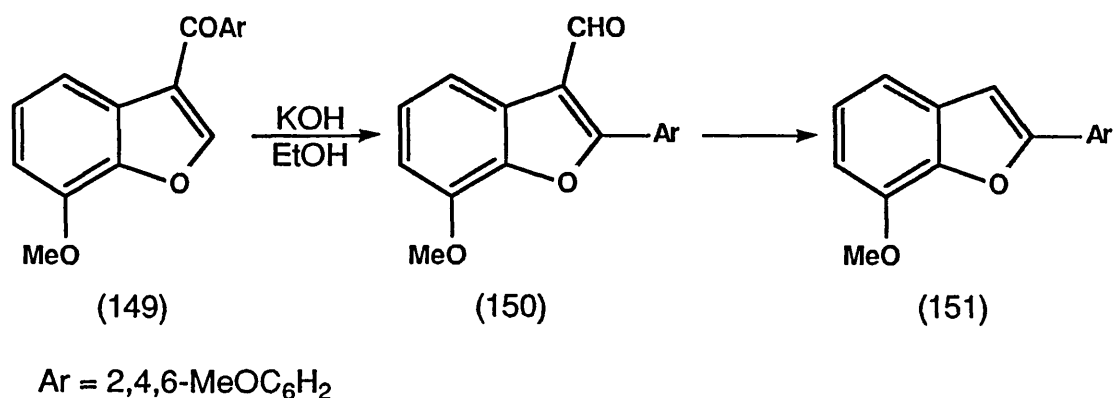
The rearrangement of diazoacetophenones (147) with a copper catalyst in the presence of phenol leads to the formation of benzofurans⁷⁸ (148) via the deoxybenzoin, in low yield, and phenoxyacetophenone as the major product (Scheme 55).



Scheme 55

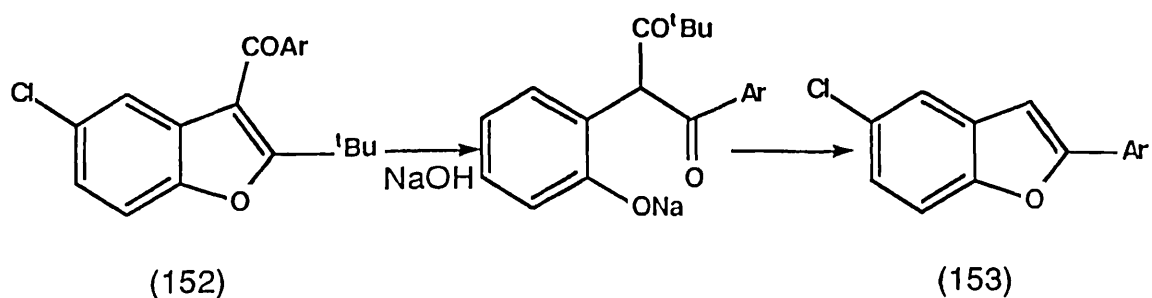
1.5.14 Alkaline degradation of 3-aryl benzofurans

The alkaline degradation of 3-aryl benzofurans leads to the corresponding 2-aryl-3-formyl benzofuran¹ (150), which can be deformylated under vigorous conditions. Thus (149) gives the 2-aryl benzofuran (151), when the alkaline medium is made acidic (Scheme 56).



Scheme 56

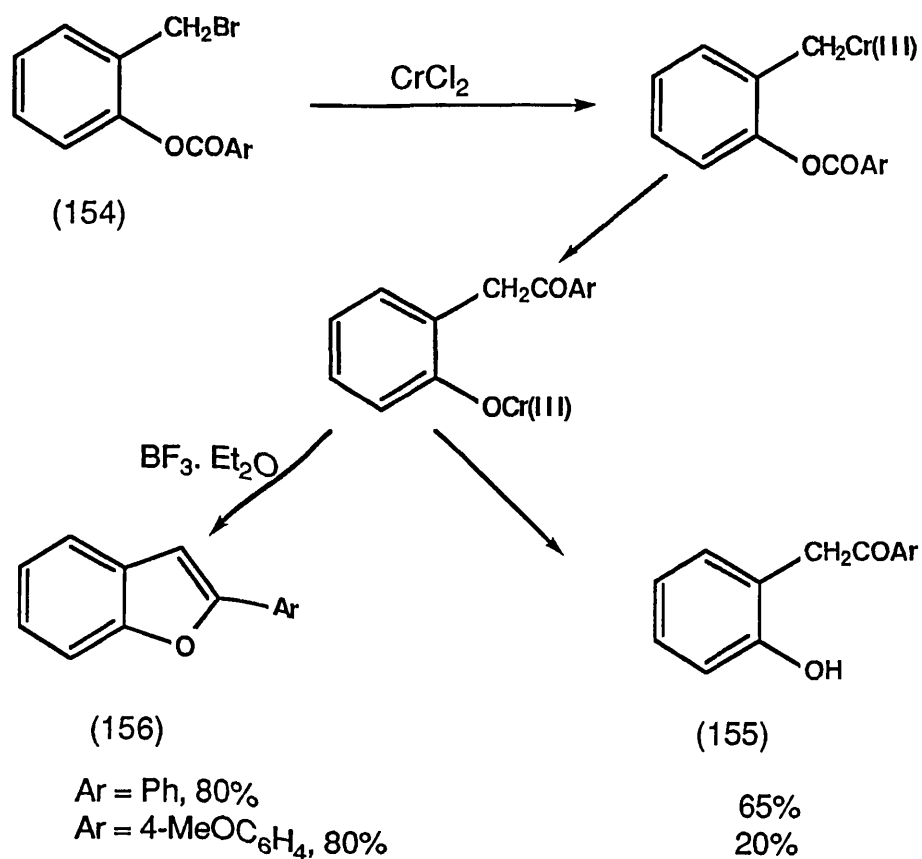
Similar results are obtained with 2-alkyl-3-aryl benzofurans⁷⁹, for example degradation of 5-chloro-3-(4-methoxybenzoyl)-2-*t*-butyl benzofuran (152) forms only the 5-chloro-2-(4-methoxyphenyl)benzofuran (153) (Scheme 57).



Scheme 57

1.5.15 Rearrangement of O-acylbenzyl bromides

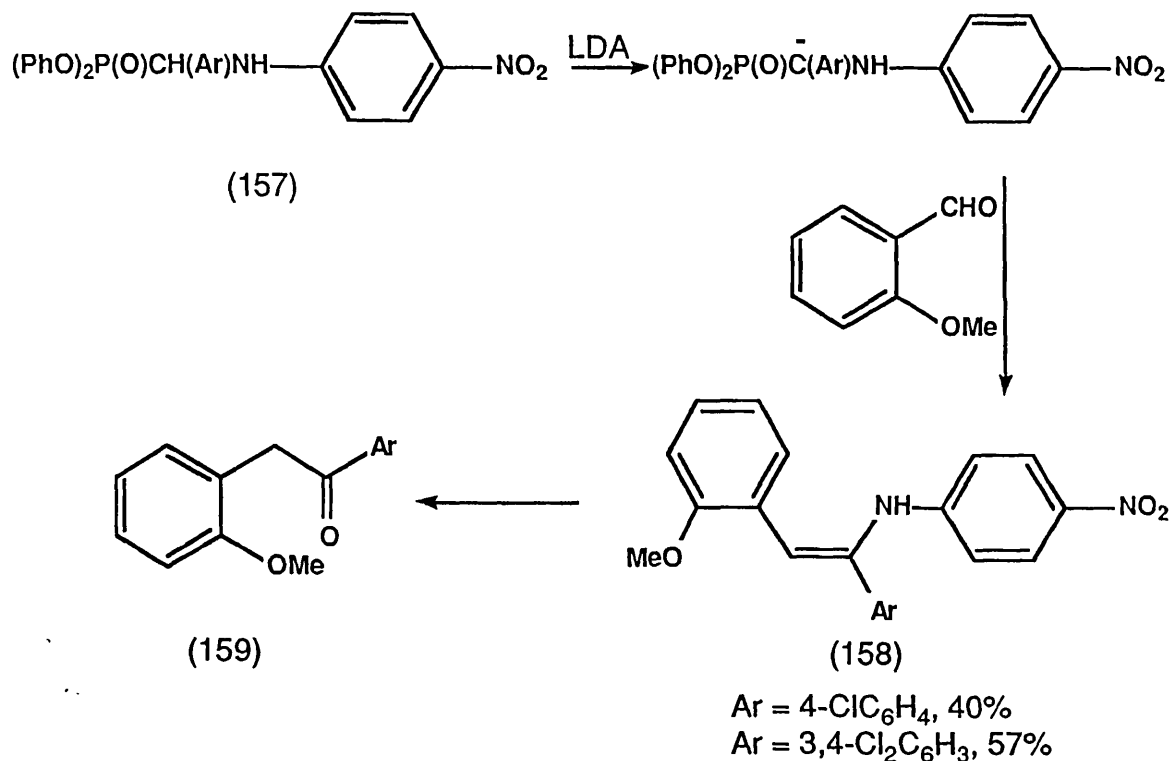
Ortho-O-acylbenzyl bromides (154) can be reductively rearranged using chromium (II) chloride to the (2-hydroxyphenyl)deoxybenzoins (155), or, are directly transformed into 2-aryl benzofurans (156) if the reaction is carried out in the presence of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (Scheme 58).



Scheme 58

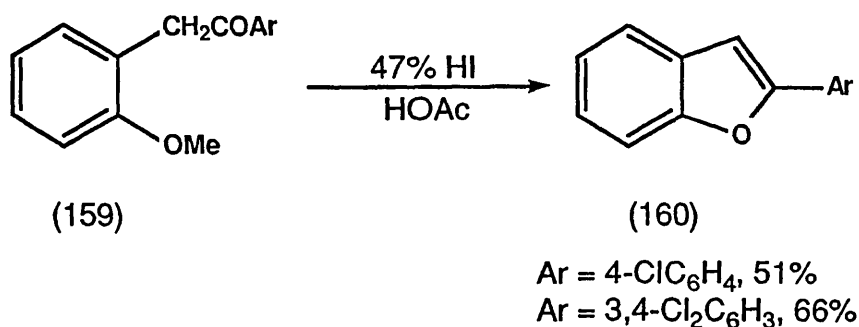
1.5.16 Formation of benzoin and deoxybenzoin from phosphonates

Deoxybenzoin (159) are formed when α -carbanions derived from the reaction of LDA with diphenyl phosphonates⁸¹ (157), undergo Wittig type reactions with various anisaldehyde derivatives. The enamine derivatives (158) thus formed can be hydrolysed to the corresponding deoxybenzoin (159) (Scheme 59).



Scheme 59

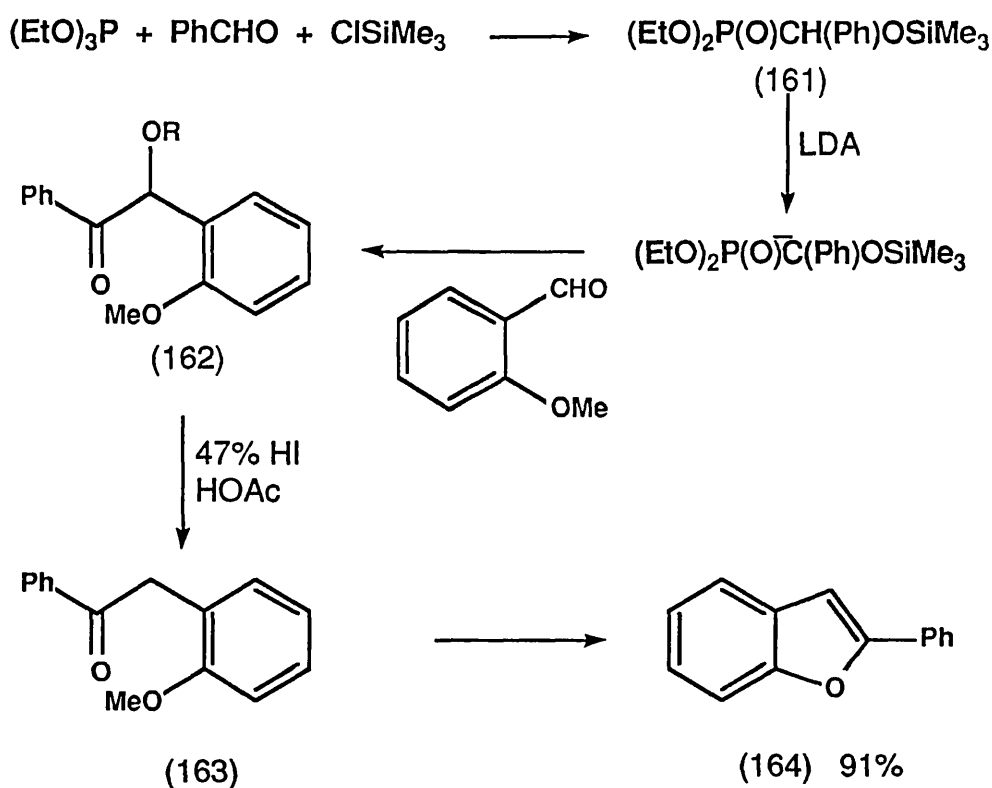
The 2-methoxydeoxybenzoin (159) when treated with 47% HI in HOAc gives the benzofuran (160) (Scheme 60).



Scheme 60

Phosphonate carbanions derived from diethyl-1-(trimethylsiloxy)-1-phenylmethane phosphonate⁸² (161) act as acyl anion equivalents. Thus their reactions with benzaldehydes and phenylketones lead to benzoin (162) and not the Wittig products (Scheme 61).

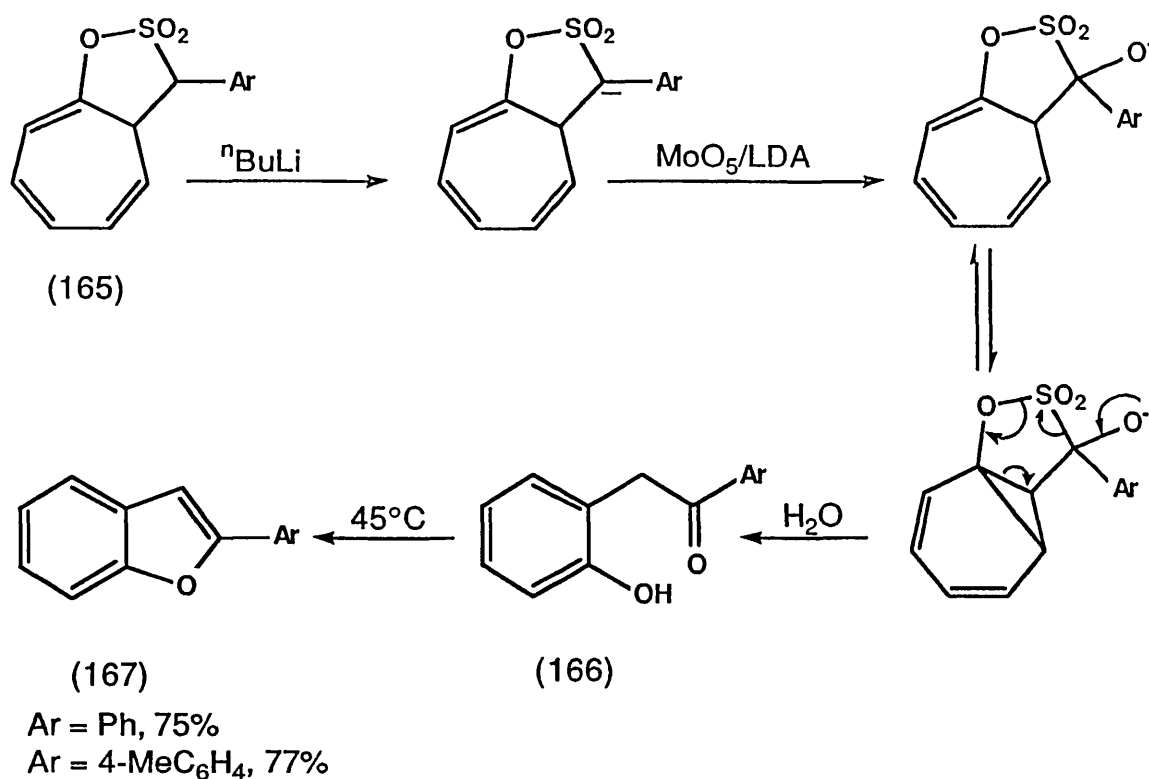
The benzoin (162, R = H) affords the benzofuran (164) upon treatment with 47% HI in HOAc, via the deoxybenzoin (163).



Scheme 61

1.5.17 Deoxybenzoin from sultams

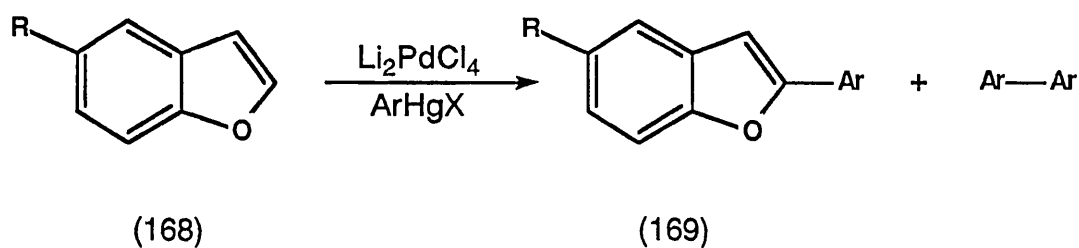
Sultams (165), derived as cycloadducts from reactions of tropones and aryl sulphenes, undergo metallation α to the sulphonyl unit⁸³. Oxidation of this anion with MoO_5/LDA leads to rearrangement to the 2-aryl benzofurans (167) via the deoxybenzoin (166) (Scheme 62).



Scheme 62

1.6 Heck reactions of benzofurans

The Heck reaction of benzofurans⁸⁴ (168) with aryl mercuric compounds in the presence of PdCl₂, leads to the formation of the 2-aryl benzofurans (169) in good yields (Scheme 63). See also Table 2.



Scheme 63

Table 2

Benzofuran (168)	ArHgX	Product (169)	Yield%
R = H	PhHgOAc	R = H, Ar = Ph	77
	4-MeC ₆ H ₄ HgCl	R = H, Ar = 4-MeC ₆ H ₄	79
	4-MeOC ₆ H ₄ HgCl	R = H, Ar = 4-MeOC ₆ H ₄	71
	3-NO ₂ C ₆ H ₄ HgCl	R = H, Ar = 3-NO ₂ C ₆ H ₄	70
R = Me	PhHgOAc	R = Me, Ar = Ph	75
	4-MeC ₆ H ₄ HgCl	R = Me, Ar = 4-MeC ₆ H ₄	72
	4-MeOC ₆ H ₄ HgCl	R = Me, Ar = 4-MeOC ₆ H ₄	66
	3-NO ₂ C ₆ H ₄ HgCl	R = Me, Ar = 3-NO ₂ C ₆ H ₄	60

1.7 Conclusion

This review has detailed most of the methods available for the synthesis of 2-aryl benzofurans. In assessing the relative merits of the various methods, consideration has to be made of their general applicability, especially in the field of natural product synthesis. With respect to this, the methods most widely used, such as the intramolecular Wittig reaction, displacement of aryl halides by copper acetylides, and the oxidation of flavylum salts, have been those allowing ready accessibility to the relevant starting materials, and this means that the natural products that have been synthesised, have tended to be relatively simple with regard to the functionality on the rings. Most of the other methods suffer from the disadvantages of being restricted in the type functionality allowed on the rings, especially those which require strongly electron withdrawing groups. Many of the syntheses are also limited to the formation of 2,3 diaryl benzofurans, such as the reactions of vinyl bromides and vinyl sulphonates, and others are limited because of the relatively harsh conditions employed in carrying out the transformations, namely the cyclodehydration reactions of α -aryloxy ketones, which also tend to give mixtures of products. Some of the best methods however employ deoxybenzoins as starting materials or intermediates, because of the relative

ease of ring closure, and the most relevant example of this is the oxidative rearrangement of chalcones, used in the synthesis of moracins A and B.

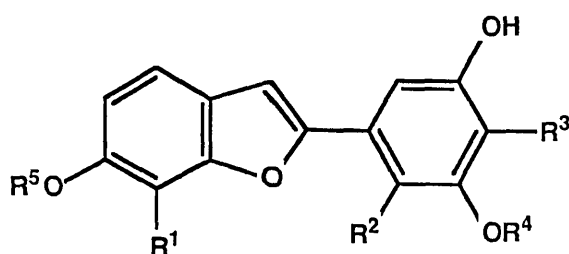
Results and Discussion

2.0 Introduction

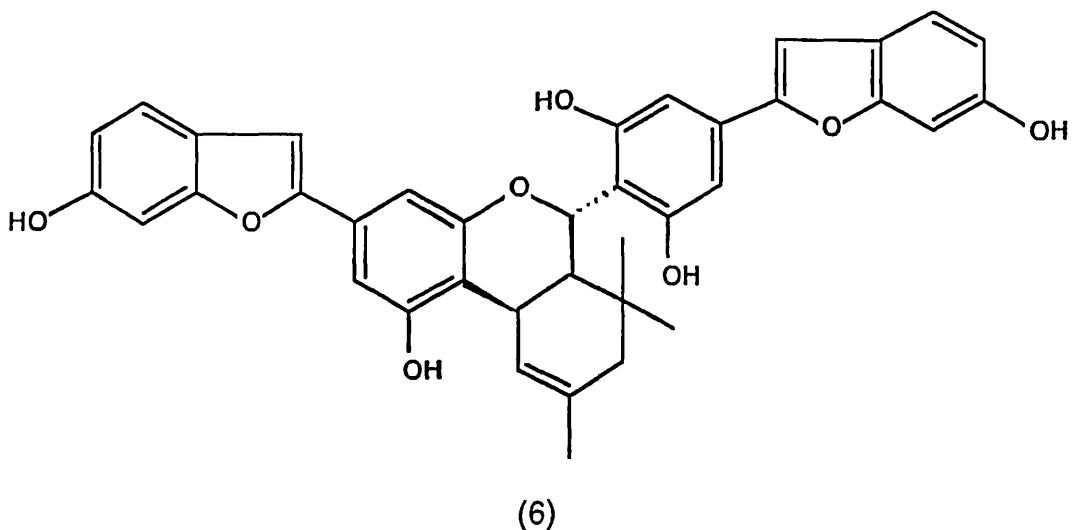
The resorcinyll benzofuran phytoalexins are examples of 2-aryl benzofurans, which have been isolated from fungally infected mulberry. (*Morus Alba* Linn). They have as their basic structural feature a benzofuran ring substituted on to a resorcinyll ring at the 2- and 5- positions respectively. This is represented at its simplest level by moracin M (1)⁸⁵, followed by inter alia the more highly functionalised analogues moracin C (2)⁸⁶, moracin I (3)⁸⁷, mulberrofuran B (4)⁸⁸; albafrican A (5)⁸⁹ which may have prenyl or geranyl substituents on either ring. At a higher level still is dimoracin (6)⁹⁰, a dimeric species which consists of two resorcinyll benzofuran units linked together via a terpenoid moiety.

With regard to their potential use as fungicides, a desirable objective is a synthetic route to the central skeleton of these compounds, the 2-(5-resorcinyll) benzofuran system, which allows for elaboration to the synthesis of the more highly substituted compounds.

To date two of the moracins, moracin A and moracin B have been synthesised by multistep processes in which the final step has been the formation of the furan ring^{5, 66}, as already described in the review section. However, the synthetic sequence would be simpler and more elegant if the benzofuran ring could be used as the initial building block, and such synthetic routes are the subject of the following discussion.

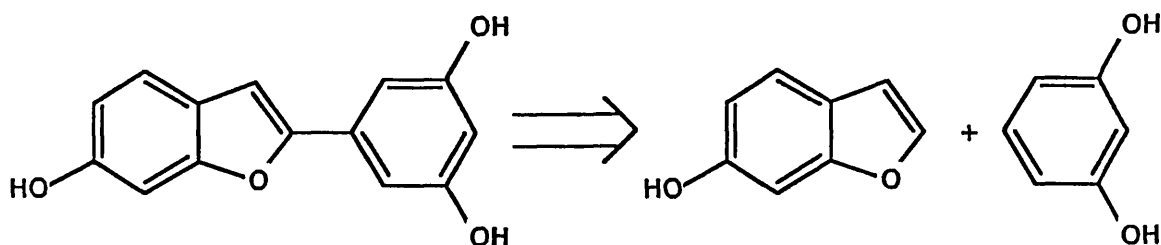


1. $R^1 = R^2 = R^3 = R^4 = R^5 = H$
2. $R^1 = R^2 = R^4 = R^5 = H$, $R^3 = \text{prenyl}$
3. $R^1 = R^3 = R^5 = H$, $R^2 = \text{prenyl}$, $R^4 = \text{Me}$
4. $R^2 = R^3 = R^4 = H$, $R^1 = \text{geranyl}$, $R^5 = \text{Me}$
5. $R^1 = R^3 = R^4 = R^5 = H$, $R^2 = \text{geranyl}$

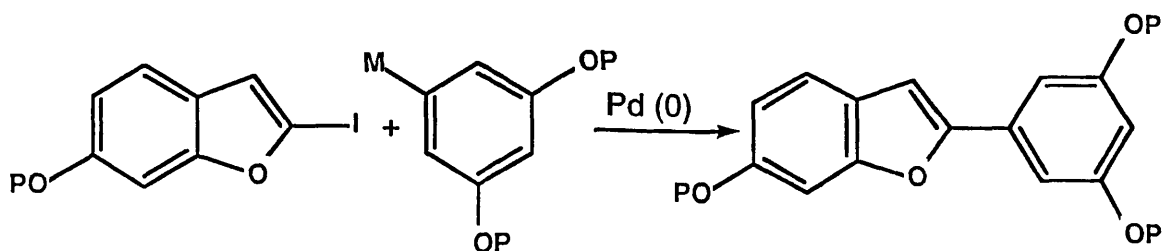


2.1 Routes to moracin M

For moracin M, a simple retrosynthetic analysis of the problem leads to benzofuran and resorcinol fragments.



A procedure which could allow coupling of the benzofuran and resorcinyl units at the 2- and 5-positions respectively is the well documented palladium cross coupling reaction⁹¹ (Scheme 1).



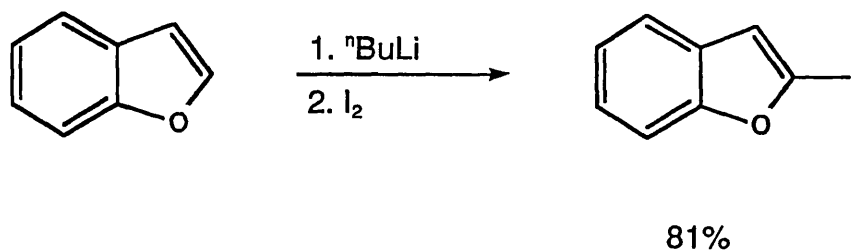
M= metal, Cu, ZnBr, SnMe₃, etc
P= protecting group

Scheme 1

Although a palladium mediated reaction to 2-aryl benzofurans, from benzofuran already existed⁸⁴ (see review); the method had the disadvantage of requiring stoichiometric amounts of the palladium reagent, and was prone to give homocoupled side products. As Scheme 1 suggests, in order to carry out the reaction using catalytic amounts of the palladium reagent, we needed to synthesise a 2-iodobenzofuran, and have access to a 5-metallated resorcinol species.

2.1.1 Synthesis of 2-iodobenzofuran

It is known that benzofuran can be readily functionalised at the 2-position⁹², by virtue of that proton being easily removed by strong base. Hence the reaction of benzofuran with *n*-butyl lithium, gave, after quenching with iodine, 2-iodobenzofuran in high yield (Scheme 2).

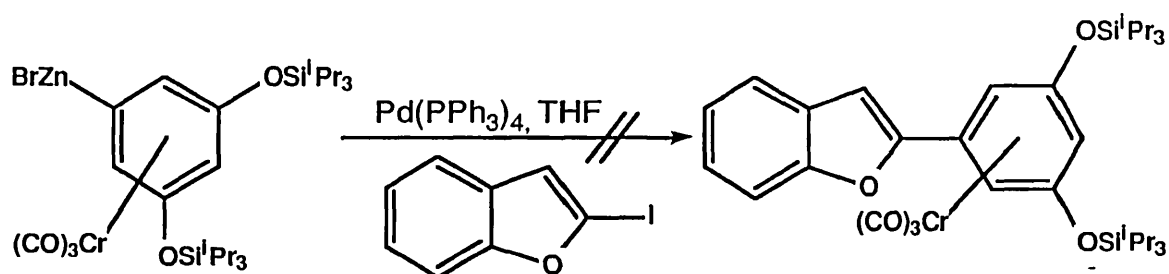


Scheme 2

2.1.2 5-Lithiation of resorcinol

Work previously carried out in our laboratories⁹³ had shown that when resorcinol was protected as its triisopropylsilyl ether, the resulting 1,3-bis(triisopropylsiloxy)benzene (7) could be complexed using chromium hexacarbonyl. This arene complex (8) could now be lithiated at the 5-position under very mild conditions, by virtue of the chromium unit enhancing the acidity of the ring protons; and the triisopropylsiloxy groups preventing any *ortho* lithiation (Scheme 3).

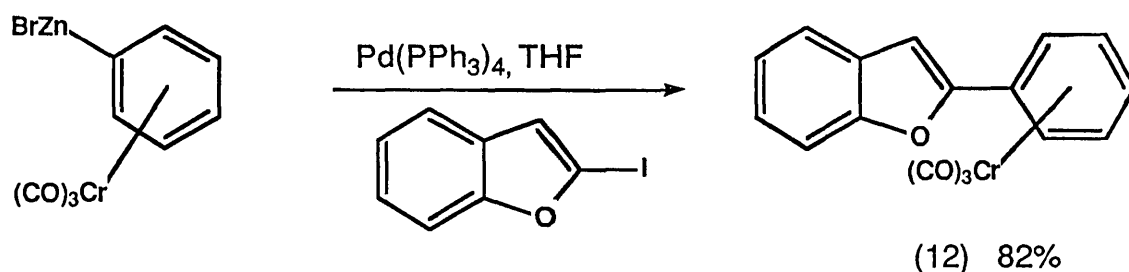
To circumvent this side reaction, the organozinc⁹⁵ derivative was formed instead; again simply by addition of zinc bromide to the organolithium complex, and the coupling reaction attempted (Scheme 5).



Scheme 5

Although no homocoupled products were obtained, unexpectedly neither was there any coupled product formed.

To investigate the reaction in more detail, the coupling reaction was repeated using benzene complex in place of the resorcinyll system (Scheme 6), and the reaction was found to proceed in high yield.



Scheme 6

This result was rationalised by considering a transition state model of the reaction, after oxidative addition has taken place. It has been suggested⁹⁶ that the following metathesis or transmetallation step involves a distorted trigonal bipyramidal species, and would therefore be susceptible to inhibition by steric crowding. In implementing this rationale to the example using benzene complex (Fig.1), there is no steric interaction which should prevent the transmetallation

step from proceeding. However, in the reaction involving the resorcinyll complex, the model (Fig. 2), shows a large steric interaction between the *triisopropylsiloxy* groups and the triphenylphosphine ligands, which would inhibit transmetallation.

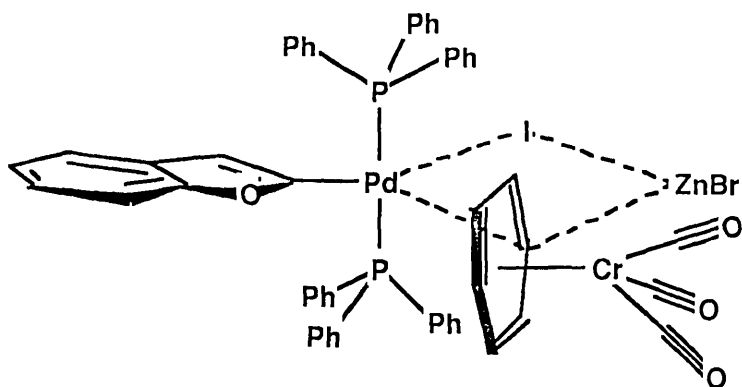


Fig. 1

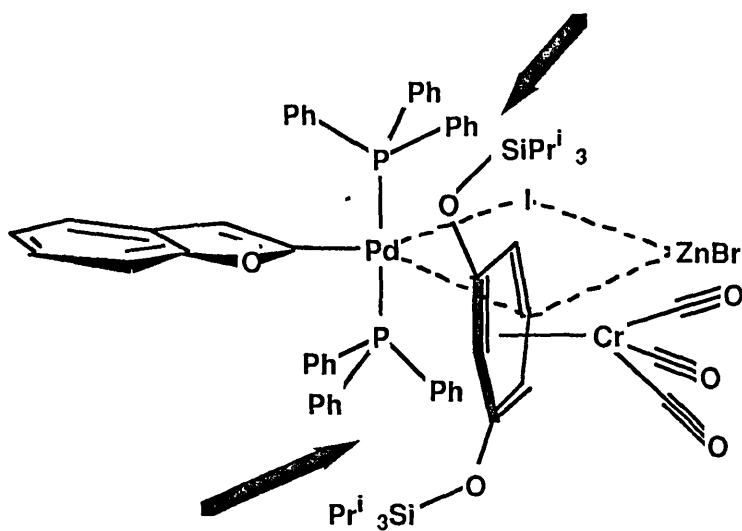
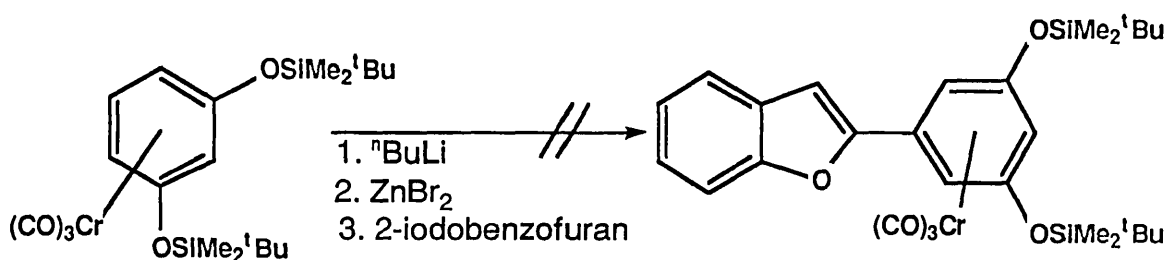


Fig. 2

There appeared to be three possible solutions to alleviate or totally remove these interactions:-

a. Reduce the size of the protecting groups on the resorcinyll ring:

This proved to be totally ineffective, since in order to maintain 5-lithiation on the ring, the protecting group size could not be significantly altered. Hence, *t*-butyldimethylsilyl was used as the protecting group which, although it gave exclusively *meta* lithiation, did not couple in the palladium mediated reaction (Scheme 7).



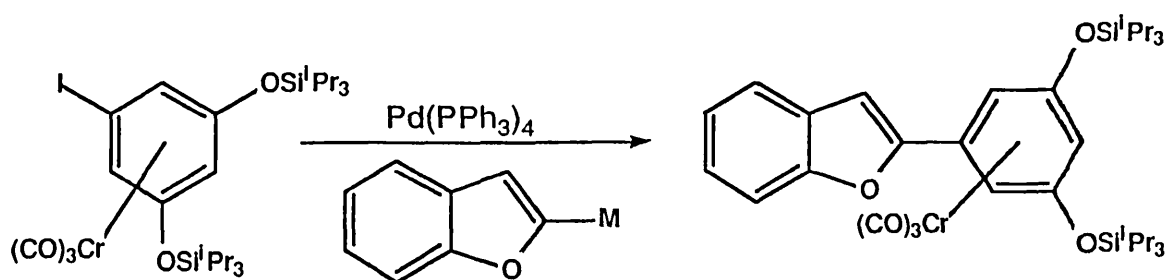
Scheme 7

b. Reduce the size of the phosphine ligands:

Replacing the triphenylphosphine ligands with their trimethyl analogues by using $\text{Pd}(\text{PMe}_3)_4$ ⁹⁷ as the catalyst, also proved unsuccessful. Presumably this was because the steric interactions, although minimised, still exist. Also, trimethylphosphine being a stronger electron donating ligand, enhances the rate of oxidative addition, but conversely would be expected to slow down the metathesis and reductive elimination steps.

c. Reverse the mode of the cross coupling reaction:

The third alternative was considered to be a means of totally removing the aforementioned interactions. To effect this, a 5-iodoresorcinyll species was reacted with a 2-metallated benzofuran (Scheme 8). Again, assessing the transition state model (Fig. 3) for this reaction, shows that since the oxidative addition step now involved the resorcinyll unit, the siloxy groups would be remote from the phosphine ligands, thus improving the chances of the reaction succeeding.



$\text{M} = \text{metal, ZnBr, Cu, SnMe}_3, \text{ etc}$

Scheme 8

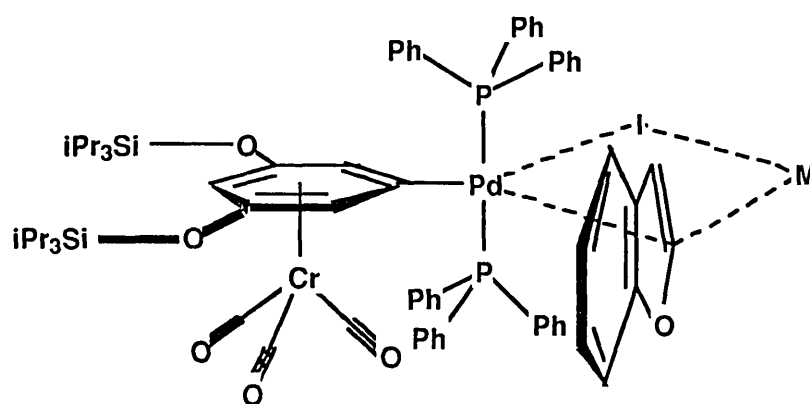
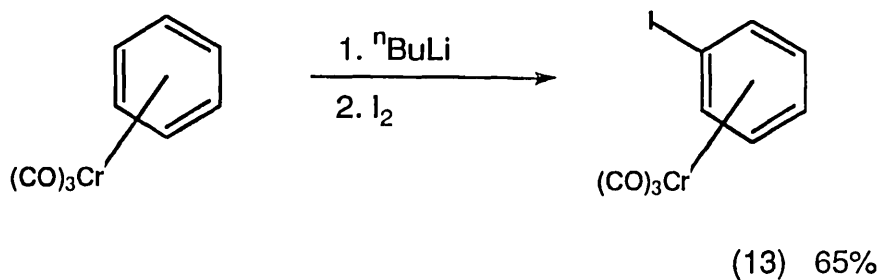


Fig. 3

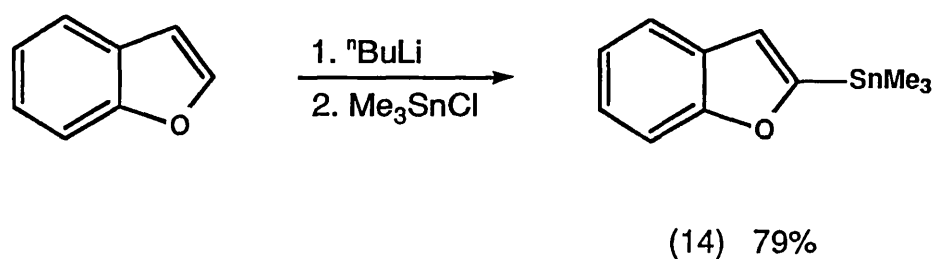
2.1.4 Cross coupling reactions of 2-metallobenzofuran

To test the feasibility of the type of reaction referred to in Scheme 8, with the tricarbonyl chromium unit attached to the iodoarene, the reactions were initially attempted using iodobenzene complex (13), which was readily made by quenching the phenyl lithium complex with iodine (Scheme 9).

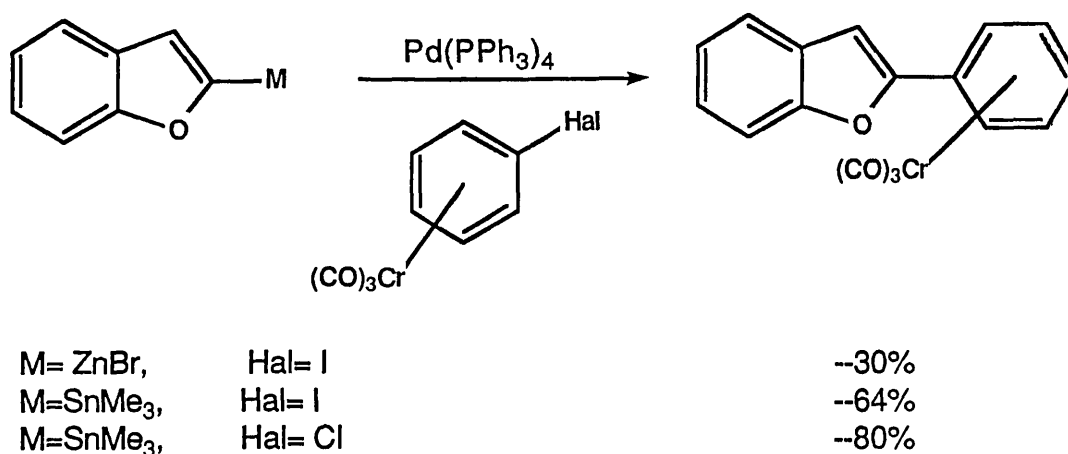


Scheme 9

Of the 2-metallobenzofurans used in the cross coupling reaction the 2-trimethylstannylbenzofuran (14), made by quenching the lithio species with trimethyltinchloride⁹⁸ (Scheme 10), proved to be the most successful. The subsequent cross coupling reactions gave best yields when reacting the organotin nucleophile with chlorobenzene complex (Scheme 11).

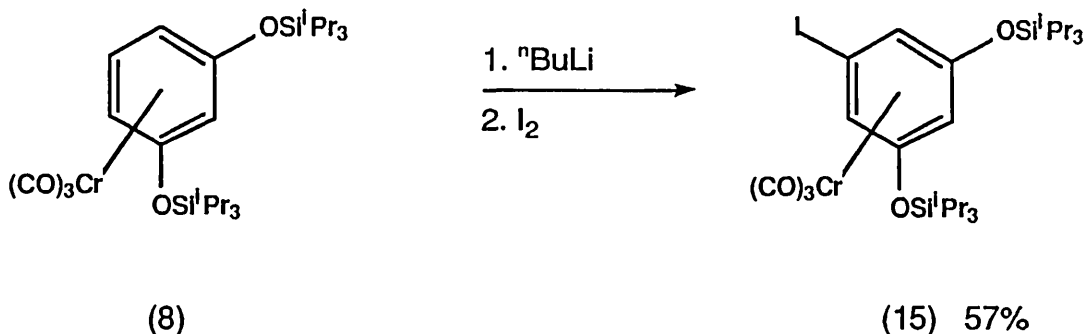


Scheme 10



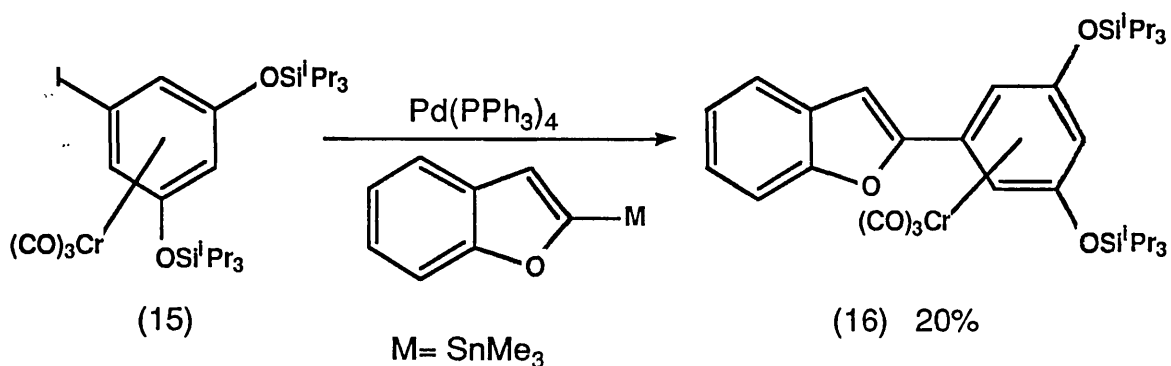
Scheme 11

Extension of this reaction to the resorcinylyl system required the synthesis of the 5-iodoresorcinylyl complex (15). This was achieved in moderate yield, by quenching the corresponding organolithium with iodine (Scheme 12).



Scheme 12

The cross coupling reaction between the 2-trimethylstannylbenzofuran (14) and the iodoarene (15) was subsequently carried out to give the coupled product (16) in a disappointingly low yield (Scheme 13).



Scheme 13

This result required a more thorough examination of the transition state model previously described. A molecular model⁹⁹ of the transition state gave a more realistic picture by taking into account all the possible steric interactions and adopting a conformation to minimise them. The diagram (Fig. 4) shows that the *triisopropylsiloxy* groups are oriented in such a way that interaction between the siloxy groups and the phosphine ligand still exists. In addition there is an interaction between the chromium unit and the other phosphine ligand. This

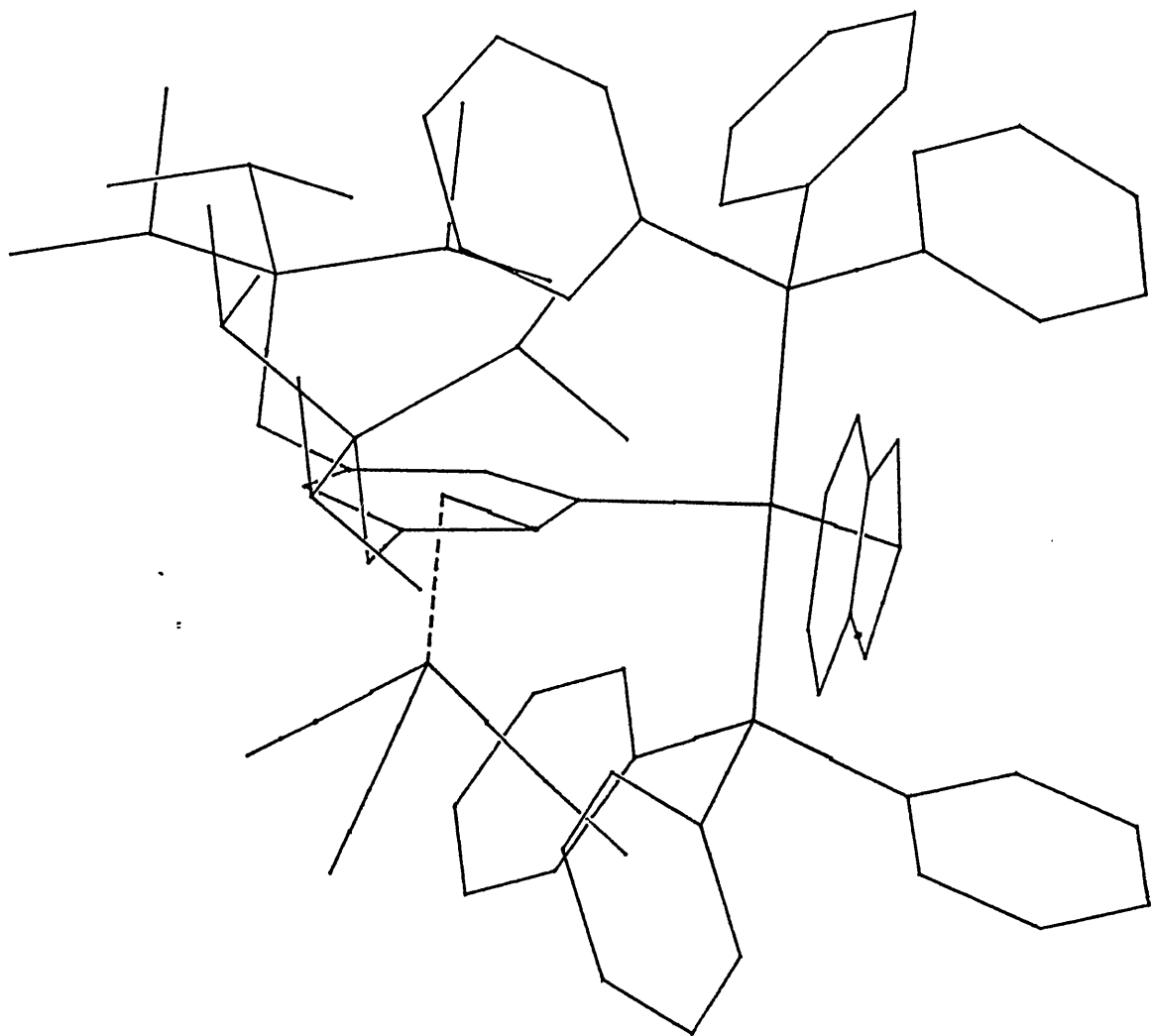
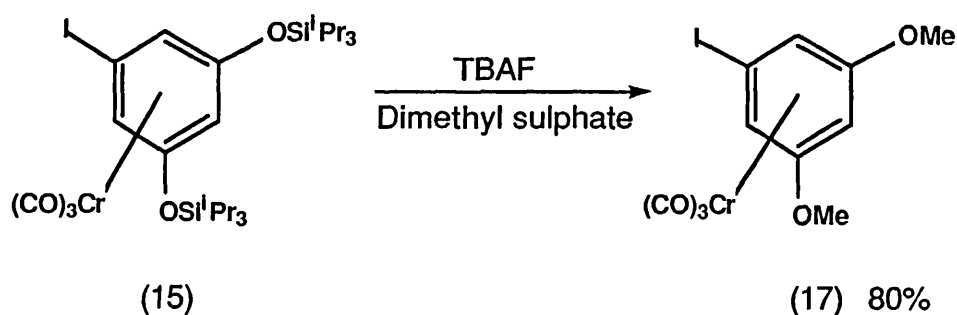


Fig. 4

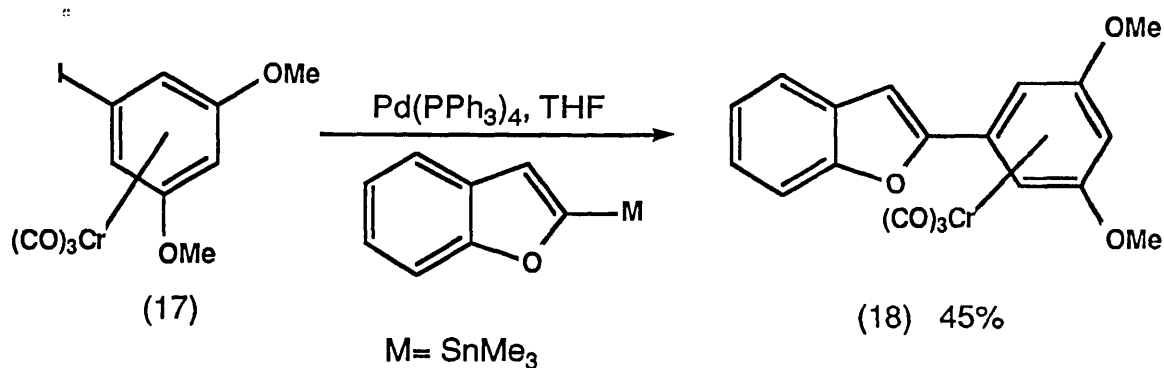
suggested that removal of the silyl groups, or the chromium unit, or both, would enhance the yield of the reaction.

The reaction was subsequently carried out taking these factors into consideration. Replacing the complex (15) with its methylated analogue (17), was readily achieved by treating the complex (15) with TBAF/dimethylsulphate (Scheme 14).



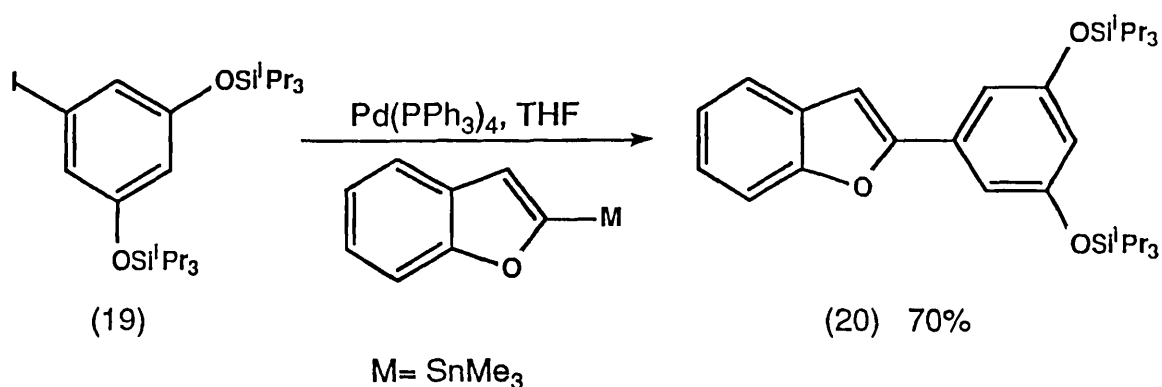
Scheme 14

Using this new iodoarene complex (17), the cross coupling reaction gave the product (18) in an improved yield of 45% (Scheme 15).



Scheme 15

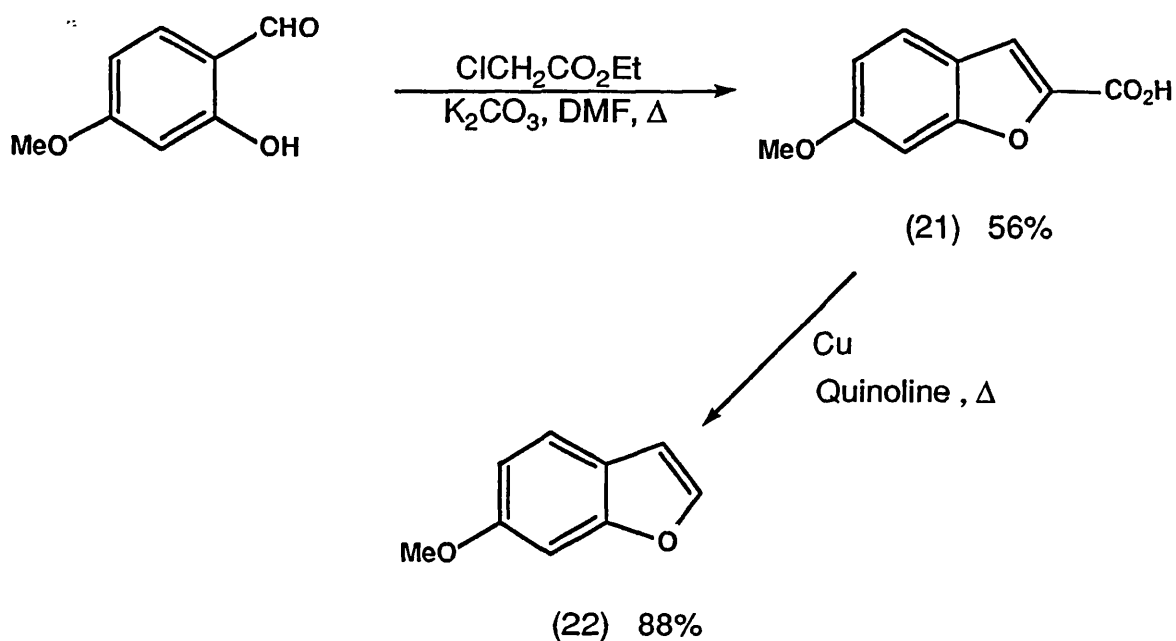
However, a more dramatic improvement in yield was realised when the chromium unit was removed. This resulted in a yield of 70% of the coupled product (20) (Scheme 16).



Scheme 16

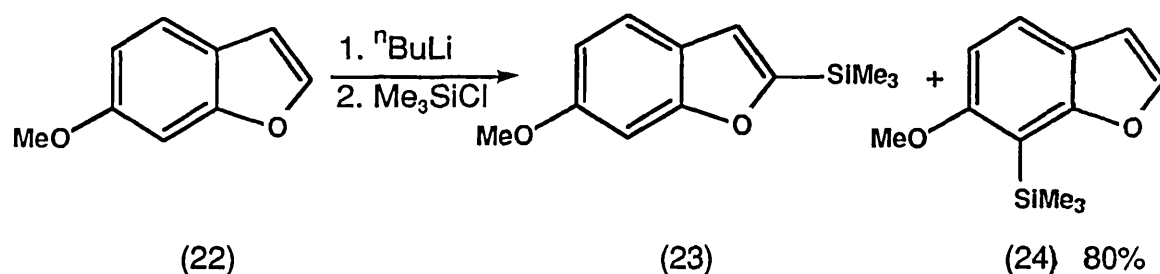
2.1.5 Synthesis and reactions of 6-*t*-Butyldiphenylsiloxybenzofuran

The application of the developed route towards the synthesis of moracin M required the initial synthesis of 6-methoxybenzofuran via a known procedure¹⁰⁰. *Para*-methoxysalicylaldehyde was condensed with ethylchloroacetate to give 2-carboxy-6-methoxybenzofuran (21) in reasonable yield. This was then decarboxylated in high yield by refluxing with copper in quinoline to give 6-methoxybenzofuran (22) (Scheme 17).



Scheme 17

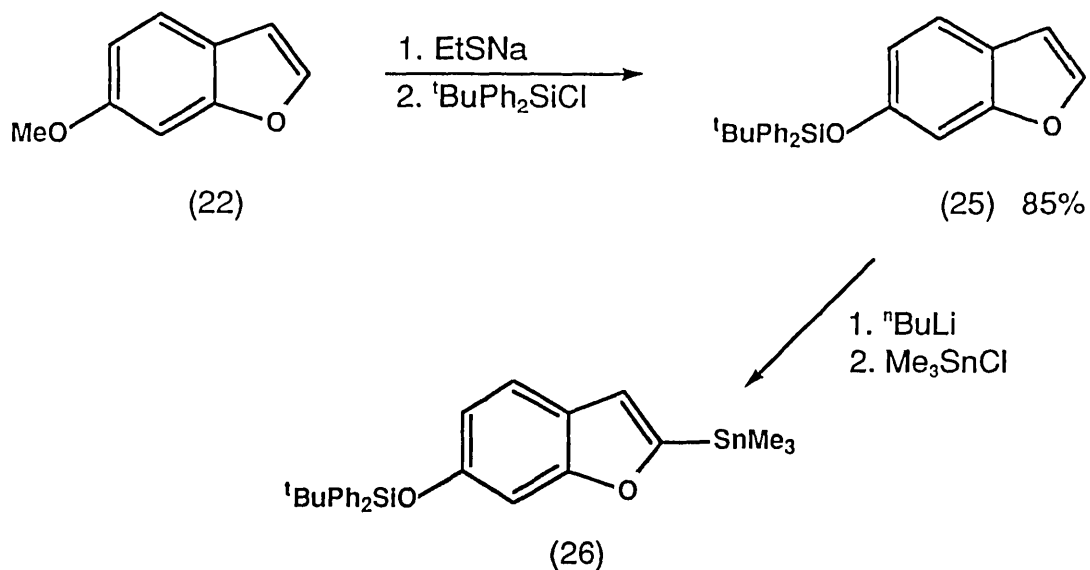
6-Methoxybenzofuran, when lithiated under conditions analogous to benzofuran lithiation, was found to give a 1:1 mixture of 2- and 7- substituted compounds when quenched with trimethylsilylchloride (Scheme 18). When the reaction was carried out at room temperature, a 4:1 ratio in favour of the 2-substituted compound (23) was obtained. This implies that the 7-lithio species (24) is the kinetic product.



Scheme 18

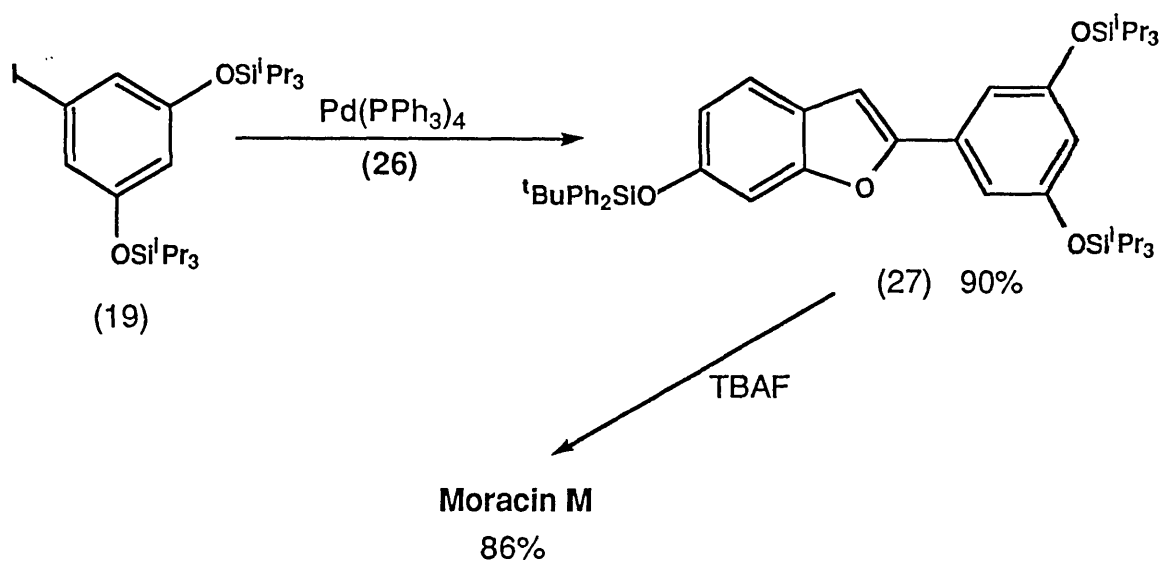
However, exclusive C-2 lithiation was achieved by protecting the oxygen with a bulky silicon group to prevent competing 7-lithiation. De-methylation of the methoxy compound (22) was effected using sodium ethanethiolate¹⁰¹, and the resulting hydroxy derivative protected as its *t*-butyldiphenylsilyl ether¹⁰² (Scheme 19).

Lithiation of the 6-siloxybenzofuran (25) under the standard conditions, followed by quenching with trimethyltin chloride gave the corresponding 2-stannyl derivative (26) (Scheme 19), which due to its instability on work up, was henceforth used *in situ* in all subsequent cross coupling reactions.



Scheme 19

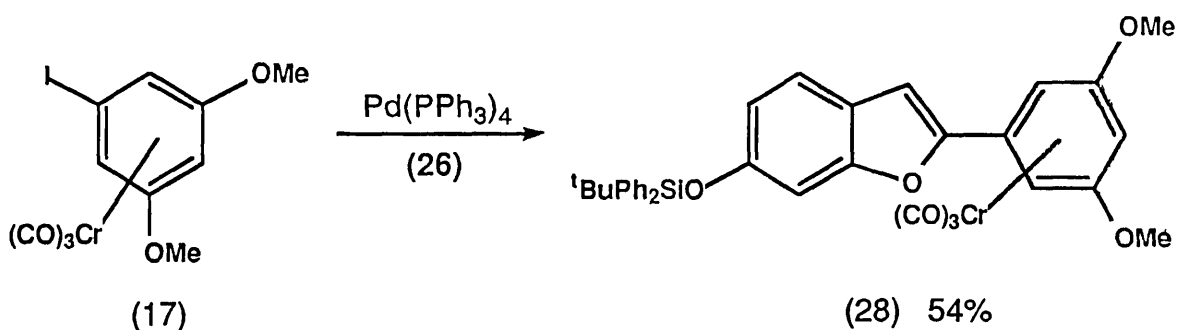
The cross coupling reaction of the stannylated benzofuran (26) with 1,3-bis(triisopropylsiloxy)benzene (19), gave the precursor to moracin M (27) in excellent yield. Desilylation with TBAF yielded moracin M (Scheme 20).



Scheme 20

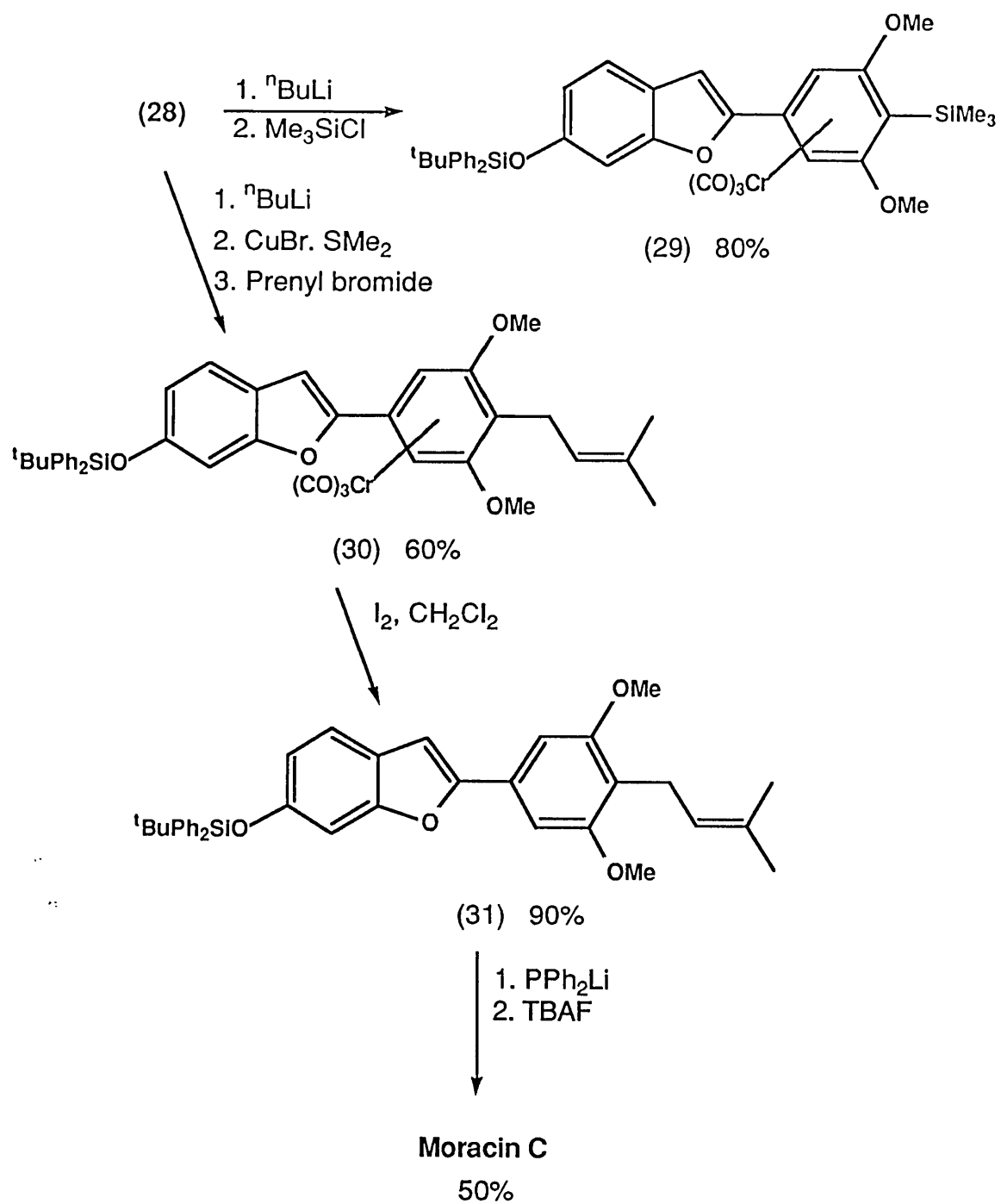
2.2 Substitution on the resorcinyll ring

It was thought that the achievement of substitution on the resorcinyll ring under mild conditions, required the chromium unit to be retained on this ring during the course of the cross coupling reaction. This was possible if the methoxy analogue (17) were used, and its coupling with the 2-stannylbenzofuran (26) gave the product (28) in reasonable yield (Scheme 21).



Scheme 21

The complex (28) when lithiated under standard conditions and quenched with trimethylsilylchloride gave substitution *ortho* to both methoxy substituents, leading to compound (29) (Scheme 22). Similarly a prenyl group was incorporated¹⁰³ by formation of the organolithium complex, transmetalation with CuBr. SMe₂, and reaction with prenyl bromide (Scheme 22), giving the prenylated complex (30). Decomplexation with iodine gave the precursor (31) to moracin C, which was demethylated using lithium diphenylphosphide¹⁰⁴, followed by desilylation with TBAF to give moracin C (Scheme 22).



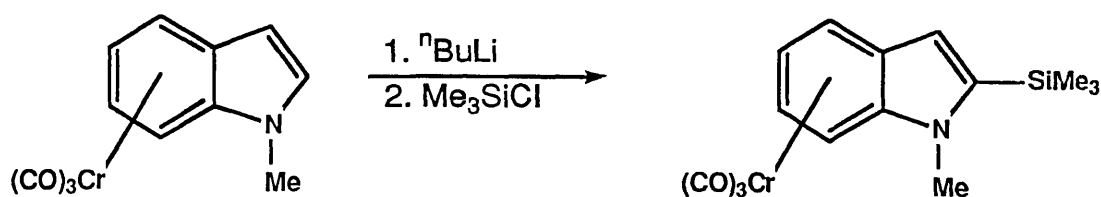
Scheme 22

2.2.1 Substitution on the resorcinyll ring *ortho* to the benzofuran substituent

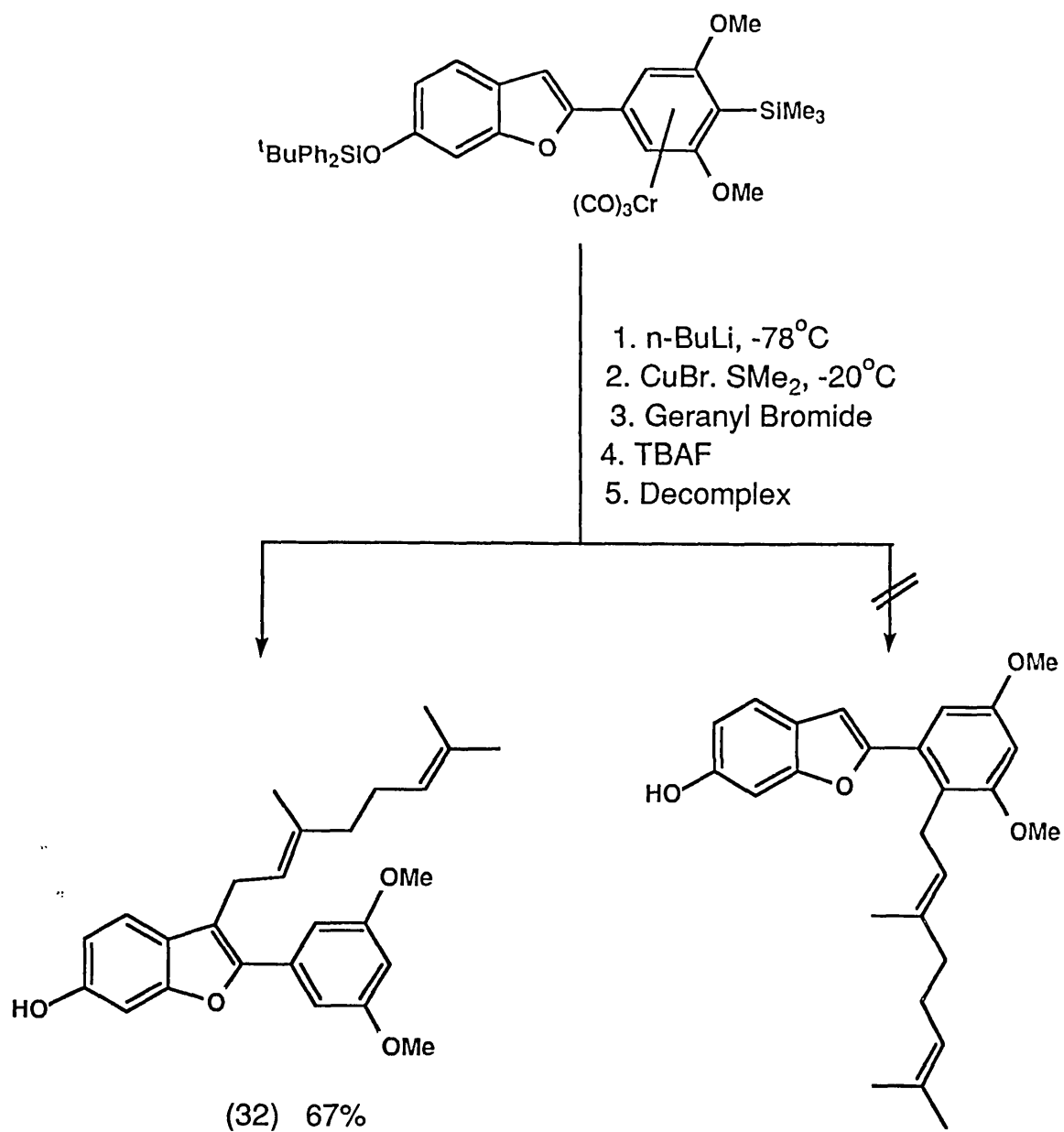
Method 1

The incorporation of substituents on the resorcinyll ring *ortho* to the benzofuran unit, was thought possible if the *para* position was blocked with a trimethylsilyl group as represented by the complex already synthesised (29).

A suitable target with substitution at this position was albafrican A, which contains a geranyl substituent in the relevant position. Reaction of the chromium complex (29) with *n*-butyl lithium, followed by transmetalation with CuBr. SMe₂ and reaction with geranyl bromide, did not give the expected product with geranyl incorporation in the resorcinyll ring. Instead it was substituted in the 3-position of the benzofuran ring (Scheme 23). This result would suggest that the 3-position of the benzofuran is also activated by the chromium unit on the resorcinyll ring, and is more accessible to lithiation than the highly substituted resorcinyll ring. This activation could be explained by analogy with benzofuran and 1-methylindole complexes, which as well as having enhanced acidity of the ring protons, has a similar affect on the 2-position. Hence 1-methylindole complex can be lithiated at -78°C in the 2-position¹⁰⁵ (Scheme 24).



Scheme 24

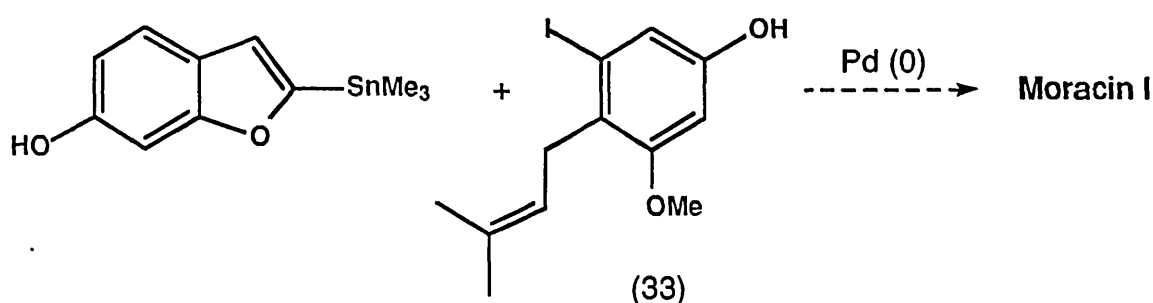


Scheme 23

2.2.2 Substitution prior to cross coupling

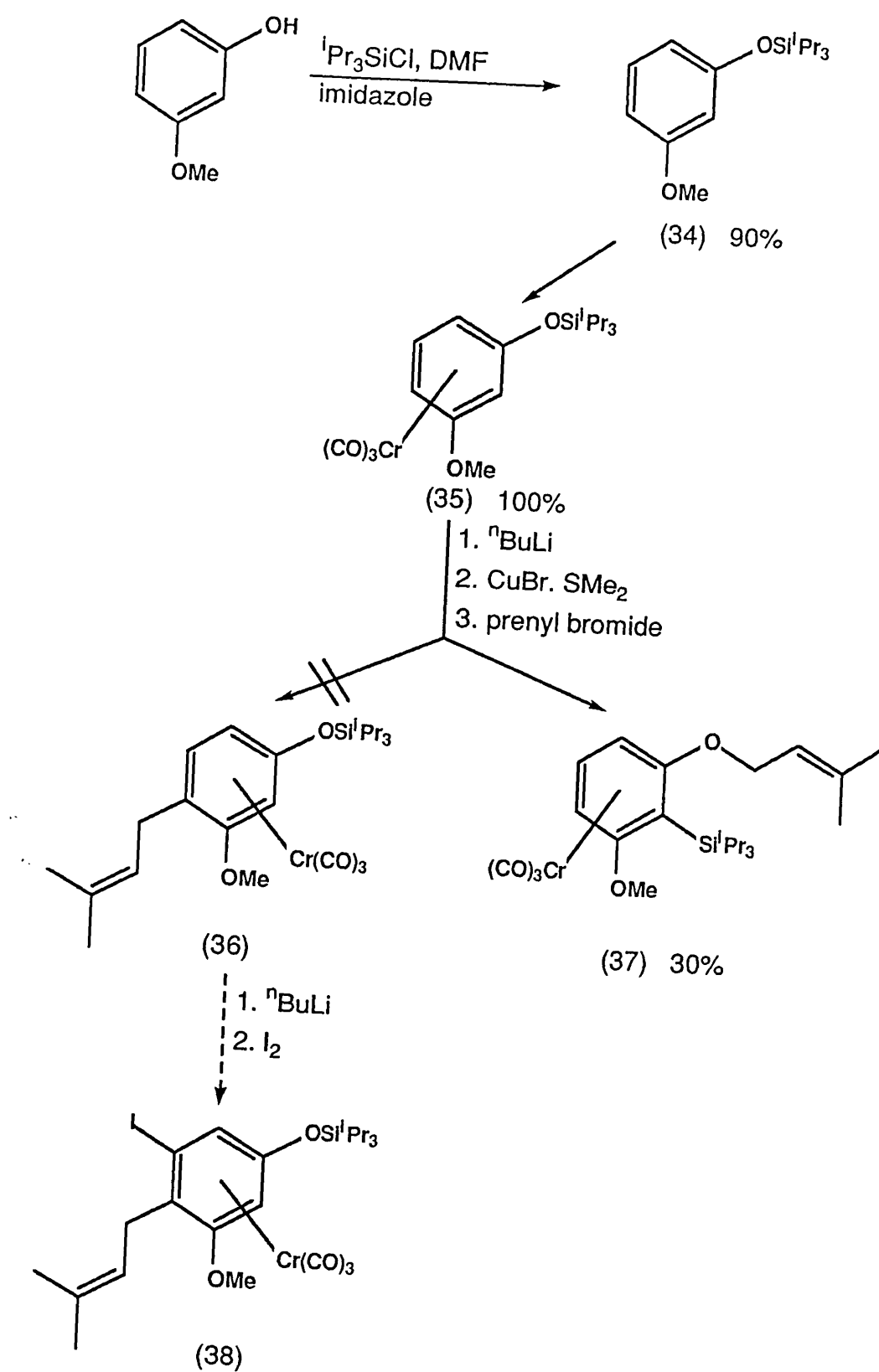
Method 2

An alternative route to substitution in this position, would be to incorporate the prenyl or geranyl groups prior to the cross coupling reaction. This required the synthesis of the prenylated resorcinol adduct (33), as shown in Scheme 25, and its synthesis was attempted as shown in Scheme 26.



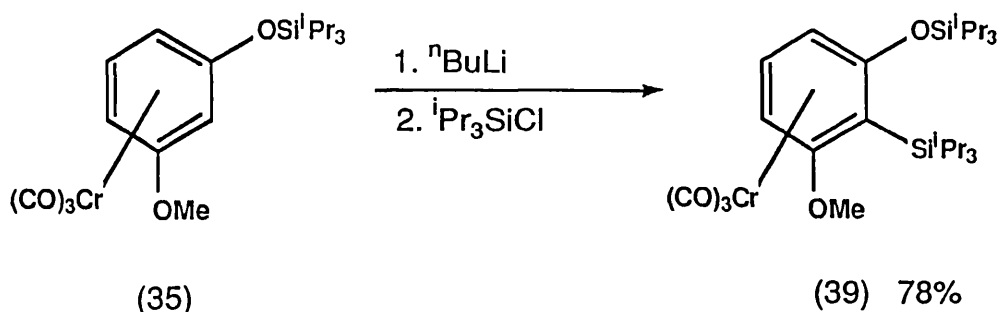
Scheme 25

The 3-triisopropylsiloxyanisole complex (35) was readily prepared from monomethylresorcinol using standard procedures. It was anticipated that subsequent lithiation and prenylation of this complex should have led to substitution of the prenyl group, *ortho* to the methoxy substituent, at the least hindered site to give the corresponding complex (36). Iodination of this complex could then be carried out to give the required substitution pattern. However lithiation of the resorcinyl complex (35) occurred exclusively between the methoxy and siloxy substituents, and the resulting organolithium complex underwent a 1,2 silyl group transfer, to give the more stable oxy-anion which subsequently reacted with prenyl bromide to give the prenyloxy complex (37). Even the use of bulkier bases such as *t*-butyl lithium and LDA led to similar results. This unexpected regioselectivity can be attributed to the extra activation of this position by the *ortho* methoxy group.



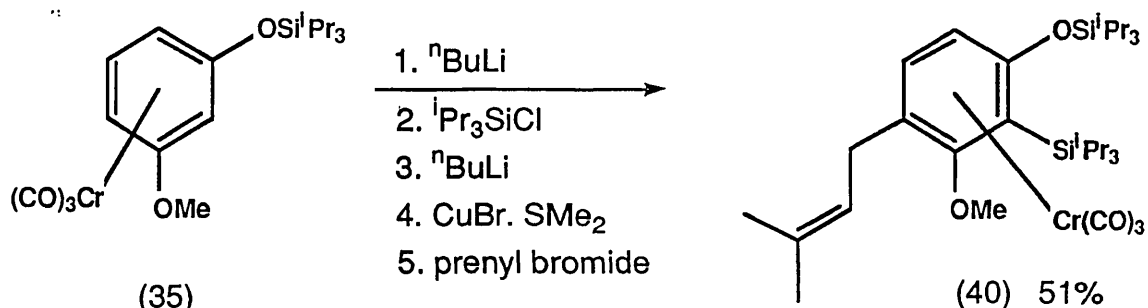
Scheme 26

To counteract this problem of regioselectivity, the lithiation of 3-triisopropylsiloxyanisole complex (35) was repeated, and quenched with triisopropylsilylchloride, to give the silylated complex (39) (Scheme 27).



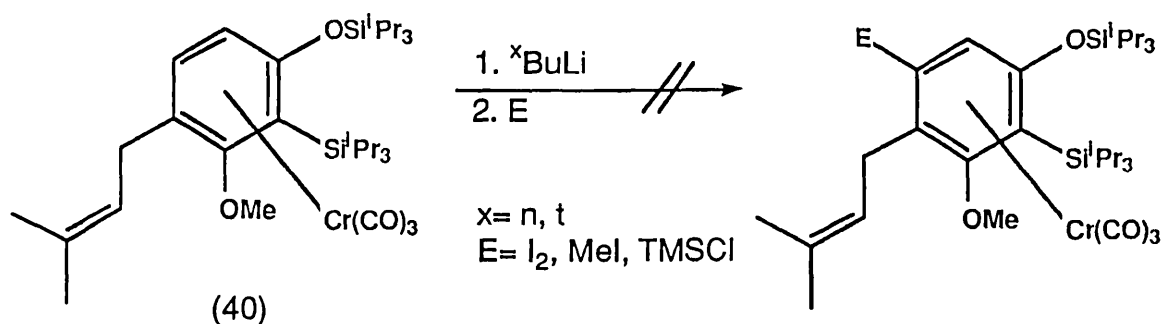
Scheme 27

Since the triisopropylsilyl group could be removed at a later stage with TBAF, it acted as an effective blocking group. Thus it should now have been possible to incorporate the prenyl group in the desired position. The complex (39) was formed as before, and without isolating, was relithiated, transmetalated with $CuBr \cdot SMe_2$, and reacted with prenyl bromide to give the complex (40) (Scheme 28).



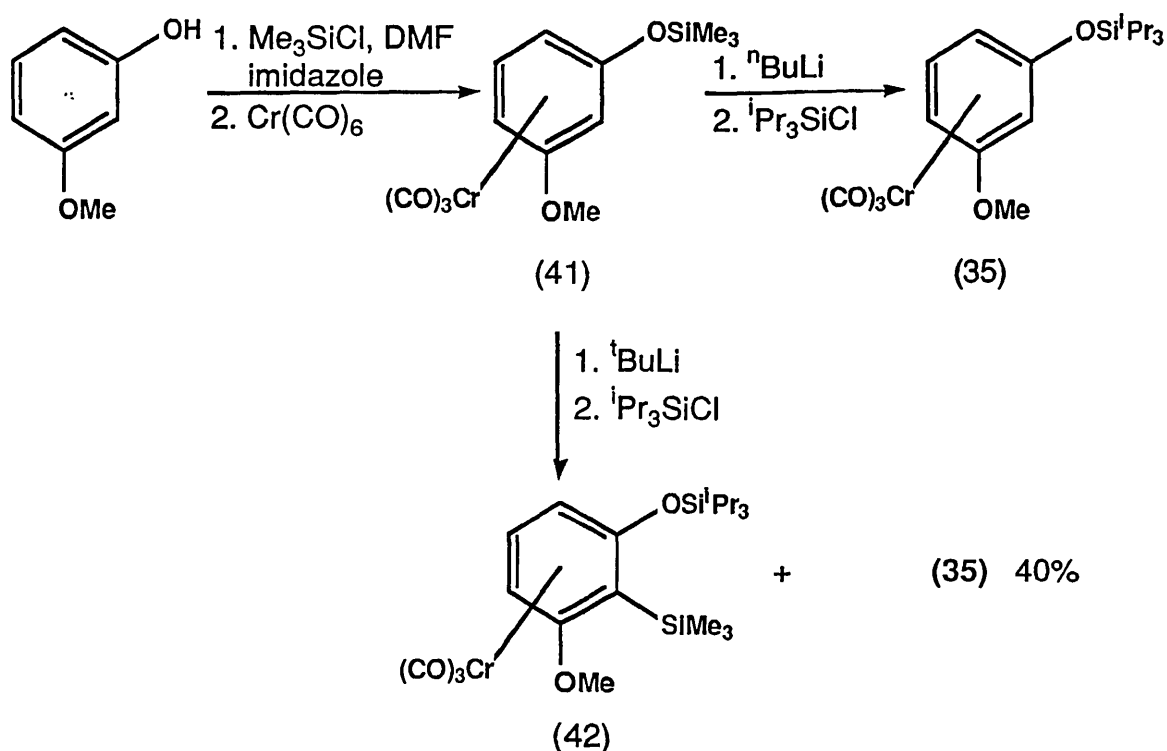
Scheme 28

The prenylated complex (40) was lithiated again and quenched with iodine (Scheme 29). Despite many attempts, only starting material was recovered from this reaction, and similar results were obtained when *t*-butyl lithium was used, and quenched with various electrophiles (MeI , $TMS-Cl$, I_2).



Scheme 29

This failure can probably be attributed to the highly substituted nature of the complex which was therefore too congested to allow ring lithiation. In an attempt to relieve some of this congestion, replacement of the *triisopropylsilyl* substituent on the ring with its trimethylsilyl counterpart was considered. The 3-trimethylsiloxyanisole complex (41), was prepared analogously to the *triisopropylsiloxy* complex (35) (Scheme 30). Reaction of this complex (41) with *n*-butyl lithium resulted simply in removal of the silyl group to yield the product (35) (Scheme 30). Using *t*-butyl lithium led to an inseparable 1:1 mixture of the required complex (42), and the complex (35) in moderate yield (Scheme 30).



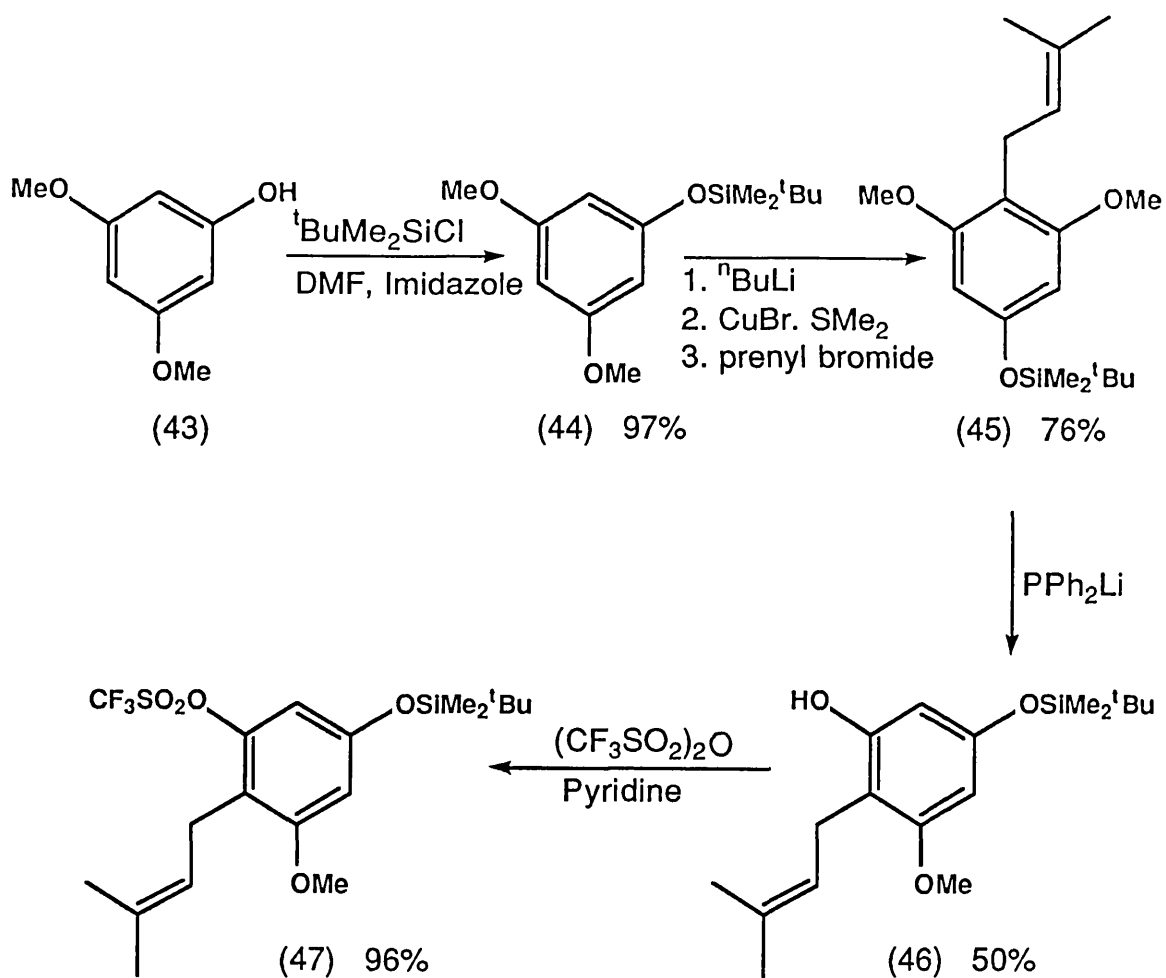
Scheme 30

2.2.3 Palladium cross couplings using aryl triflates

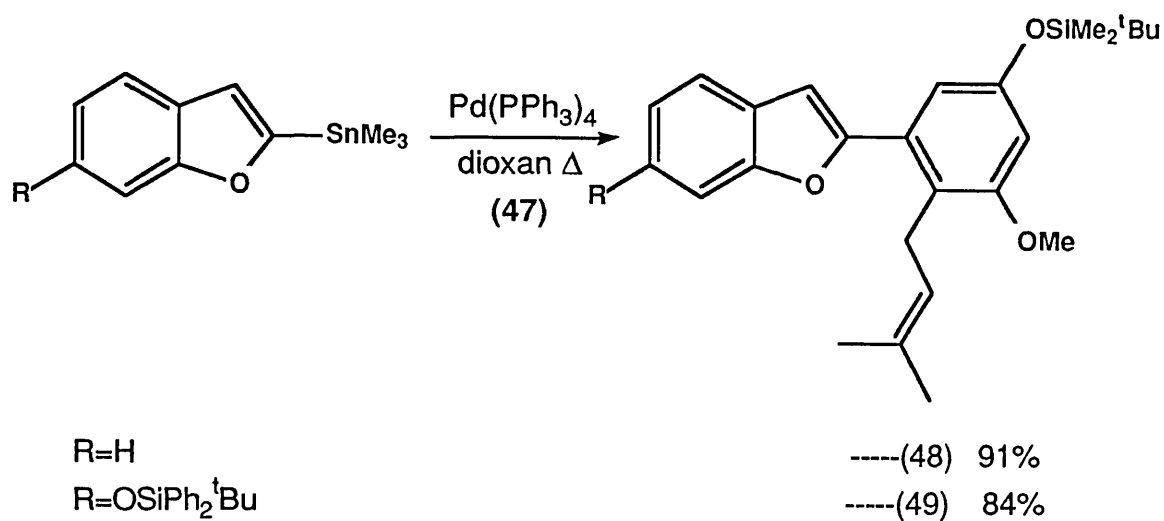
Recently it has been shown that organotin compounds react under palladium catalysis with aryl triflates¹⁰⁶, in a manner analogous to their reaction with aryl iodides and bromides. In view of this, the target prenylated adduct (33) could be modified by replacing the iodine with a triflate group. This leads to 1,3,5-trioxygenated system, as represented by phloroglucinol, and it was anticipated that this material would lead to the modified adduct (47) (Scheme 31).

Dimethylphloroglucinol (43) was protected as its *t*-butyldimethylsilyl ether. This compound¹⁰⁷ (44) was lithiated at room temperature, transmetallated with CuBr.SMe₂, and reacted with prenyl bromide to give the prenylated compound (45) in good yield. De-methylation was carried out using one equivalent of lithium diphenylphosphide, to give the corresponding phenol derivative (46), which upon reaction with triflic anhydride in pyridine yielded the desired aryl triflate (47) in good yield (Scheme 31).

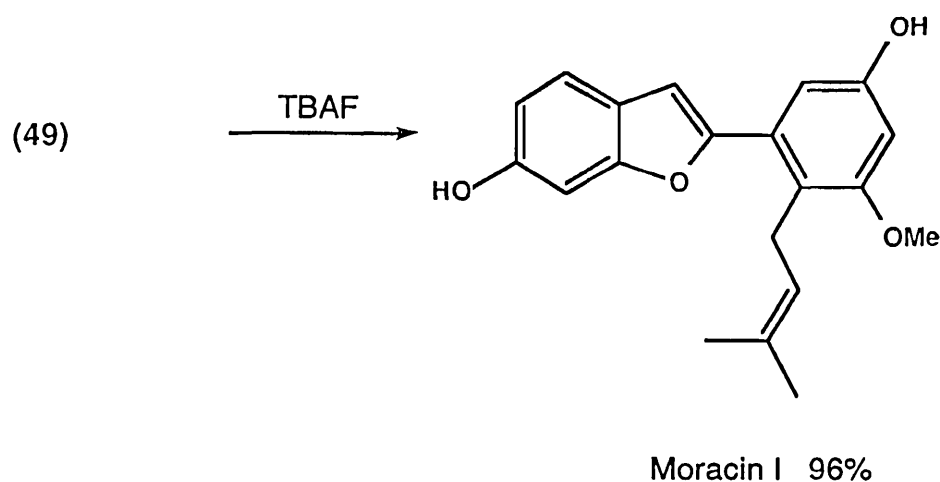
The palladium cross couplings of this triflate (47) with the 2-trimethylstannylbenzofurans proceeded in high yield (Scheme 32). The coupled product (49) (R= OSiPh₂^tBu) was desilylated with TBAF to give moracin I in good yield (Scheme 33).



Scheme 31



Scheme 32



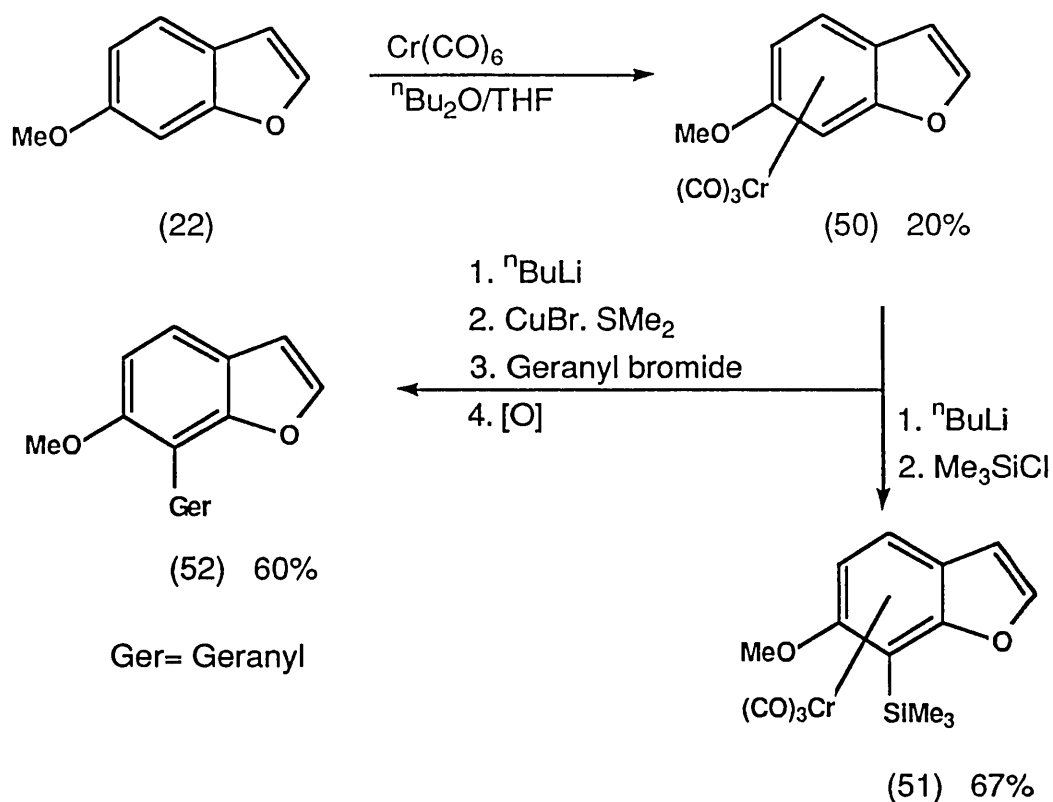
Scheme 33

2.3 Substitution on the benzofuran ring

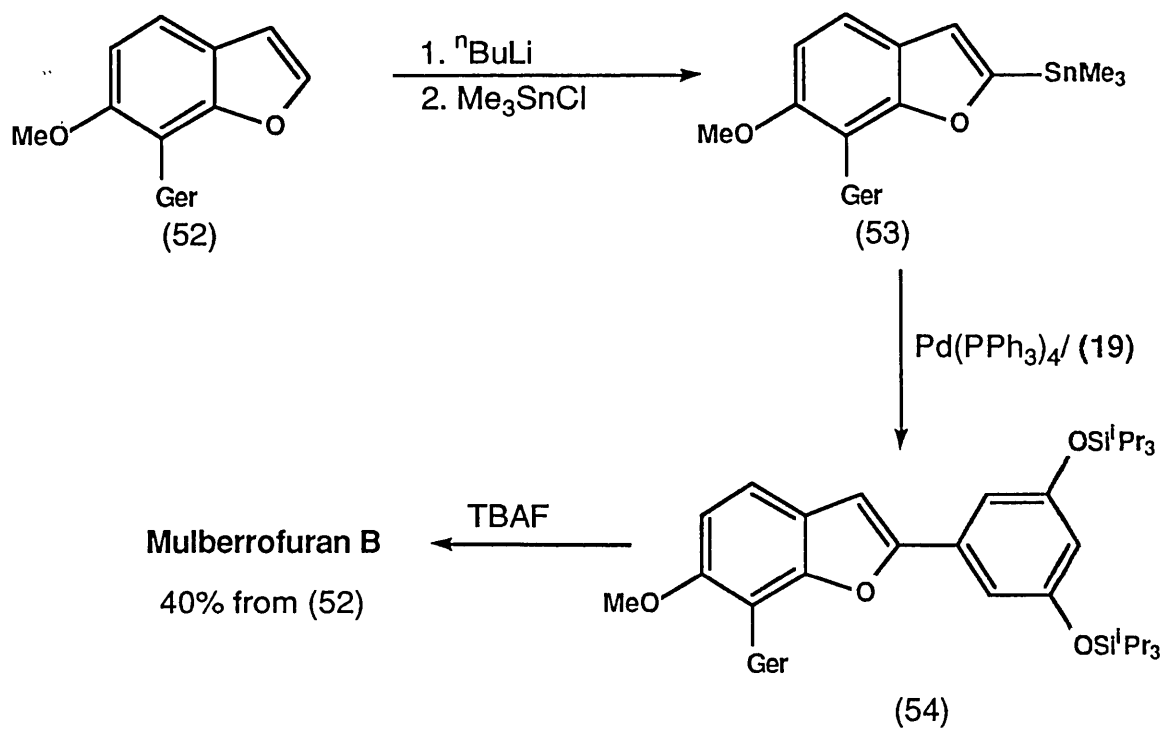
Mulberrofuran B (4), is a 7-geranyl substituted resorcinyl benzofuran phytoalexin. The approach to the synthesis of this compound required the initial formation of 6-methoxy-7-geranylbenzofuran.

As already stated, lithiation of 6-methoxybenzofuran gave a mixture of 2- and 7-lithio derivatives. In order to effect exclusive 7-lithiation, the chromium tricarbonyl complex was formed, albeit in low yield. The lithiation of this complex (50) resulted in exclusive 7-lithiation, and the geranyl group was incorporated in the standard fashion to give the desired compound (52) in reasonable yield (Scheme 34).

The geranyl substituted derivative (52) was then lithiated under standard conditions and its tin derivative (53) formed. Reaction of (53) with 1,3-bis(triisopropylsiloxy)-5-iodobenzene (19) under palladium catalysis gave the coupled compound (54) in moderate yield, which was desilylated to give mulberrofuran B (Scheme 35).



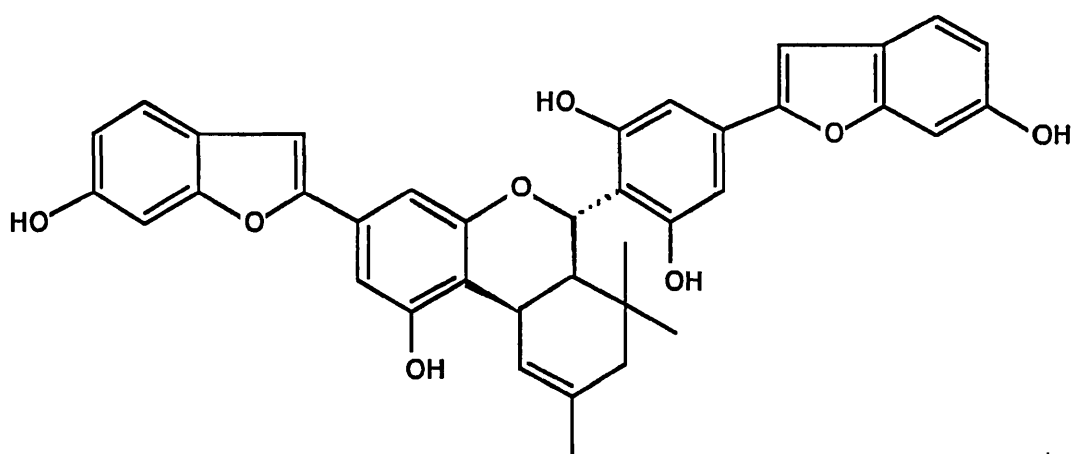
Scheme 34



Scheme 35

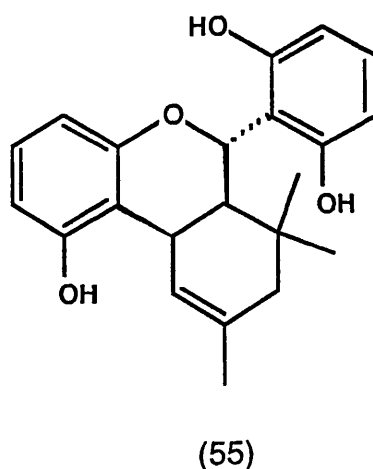
2.4 Routes to dimoracin

Dimoracin (6), is an example of a highly functionalised resorcinyll benzofuran phytoalexin, consisting of two resorcinyll benzofuran units, both substituted on the resorcinyll ring between the oxy substituents, *cf* moracin C, and linked together through a C₁₀ terpenoid moiety.



Having already established that the resorcinyll benzofuran units could be substituted in the relevant positions, it remained to synthesise the C₁₀ unit (57) (Scheme 36) in the required stereoselective manner.

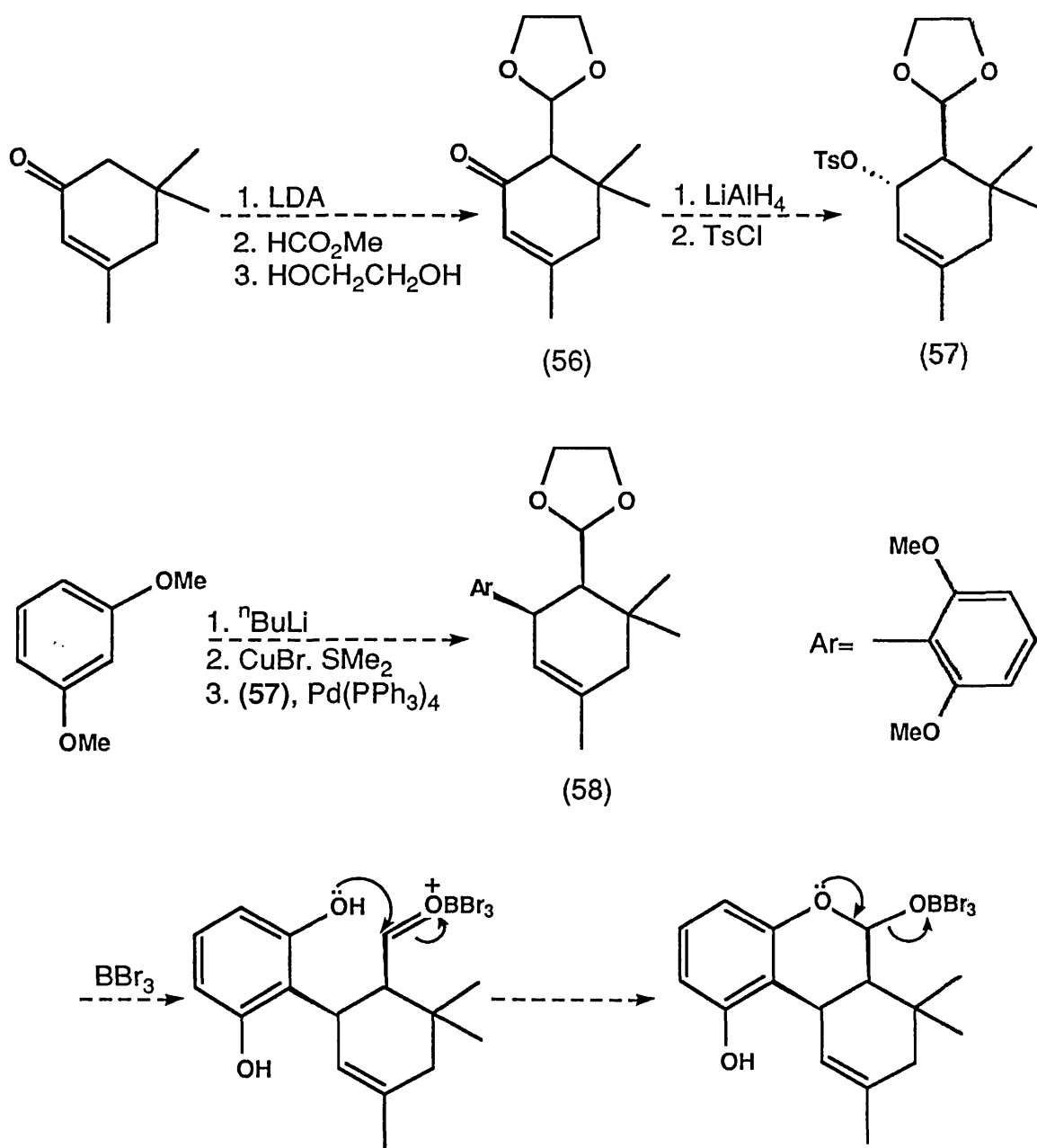
An analogue (55), which incorporated all the major structural features of dimoracin was decided on as an initial target molecule.

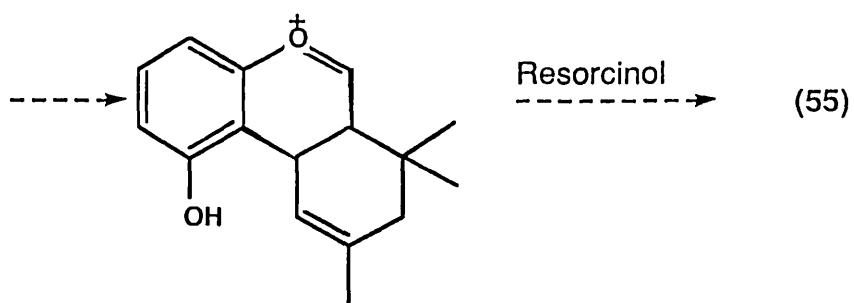


2.4.1 Routes towards the C₁₀ moiety and (55)

Method 1

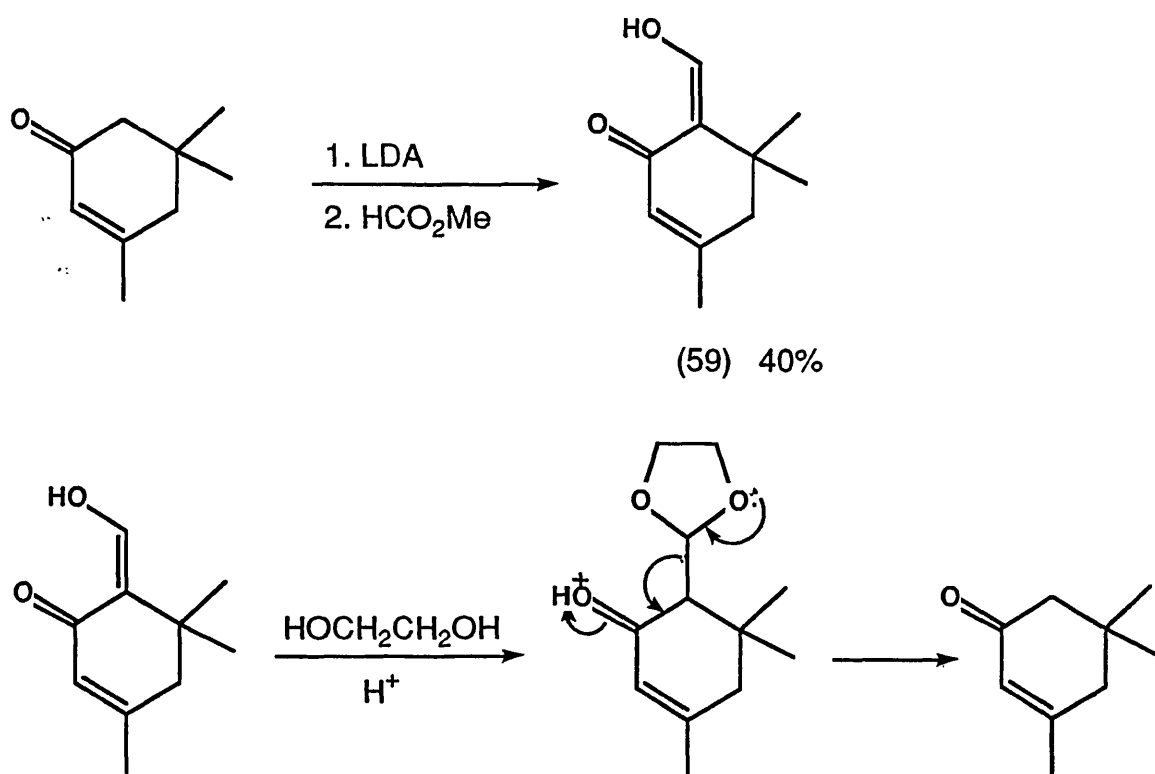
A proposed route to compound (55) via the C₁₀ unit (57) is shown in scheme 36, starting from readily available isophorone.





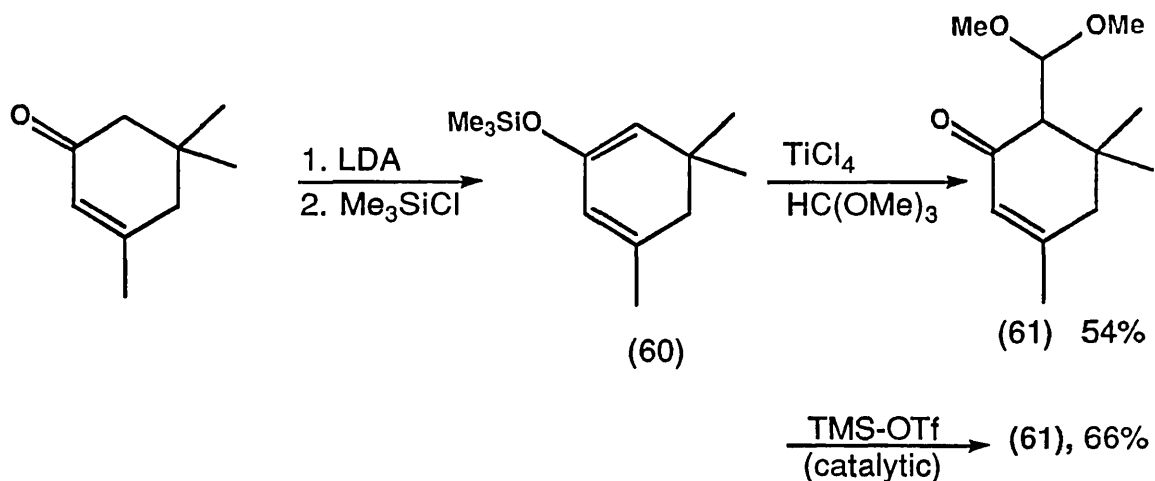
Scheme 36

The enolate formed by LDA reaction with isophorone was quenched with methyl formate, to give the product (59) in moderate yield (Scheme 37). Attempts to form the acetal derivative under standard ethylene glycol/ H^+ conditions failed and led only to deformylation to give isophorone (Scheme 37).



Scheme 37

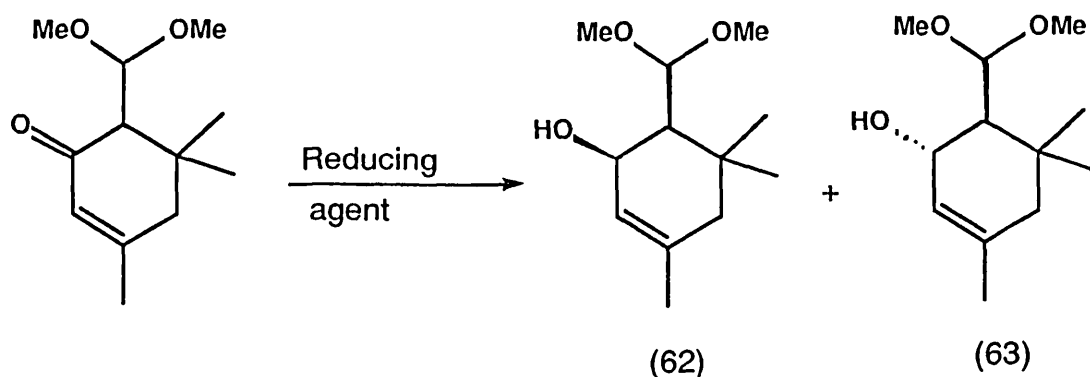
However the dimethyl acetal derivative (61) could be prepared in good yield, from isophorone, by reacting the TMS-enol ether (60) derived from isophorone, with TiCl_4 /trimethylorthoformate¹⁰⁸ or TMS-OTf/trimethylorthoformate¹⁰⁹ (Scheme 38).



Scheme 38

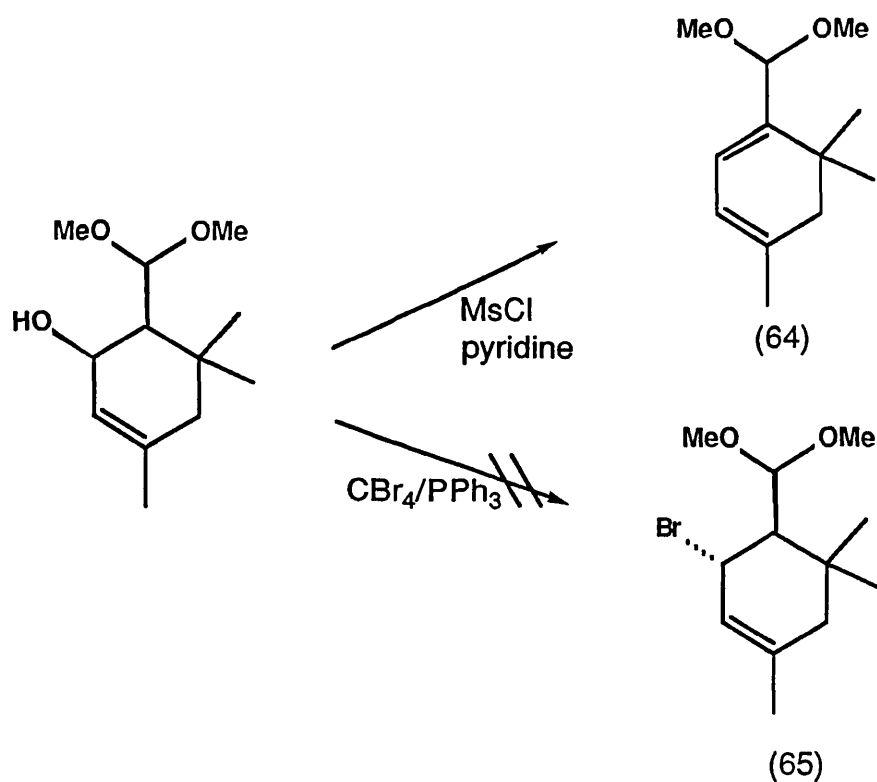
Reduction of this ketone (61) with lithium aluminium hydride gave a mixture of *cis* and *trans* alcohols, whereas DIBAL gave almost exclusively the *cis* product (Scheme 39).

Reducing agent	yield/%	<i>cis:trans</i>	temp/
DIBAL	80	10 : 1	R.T.
LiAlH_4	75	1 : 1	R.T.
LiAlH_4	53	2 : 1	-78°C
NaBH_4	7	<i>cis</i> only	R.T.
$\text{NaBH}_4/\text{CeCl}_3$	14	<i>cis</i> only	R.T.

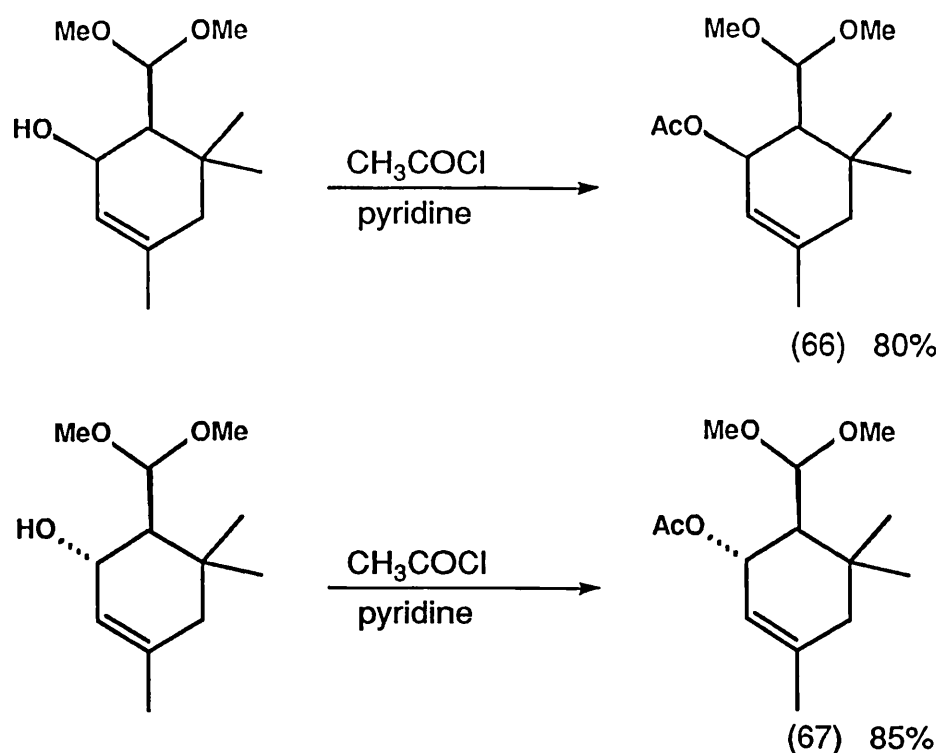


Scheme 39

Attempts to form the tosyl or mesyl derivatives of these alcohols were unsuccessful because of the ready elimination to form the diene (64). The conversion of the *cis*-alcohol to the *trans*-bromo derivative (65) using $\text{CBr}_4/\text{PPh}_3$ ¹¹⁰ was also unsuccessful (Scheme 40). However, the acetate derivatives could be formed in high yield (Scheme 41).



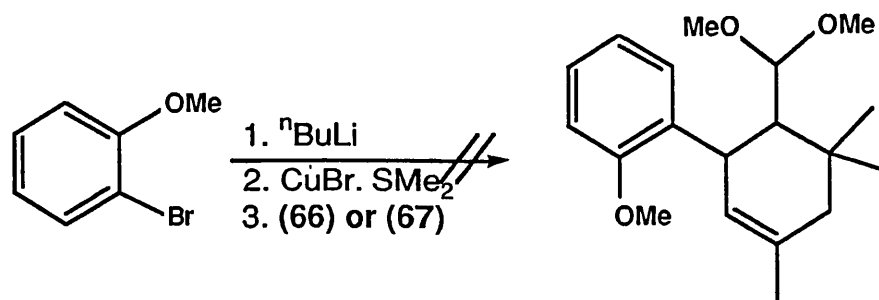
Scheme 40

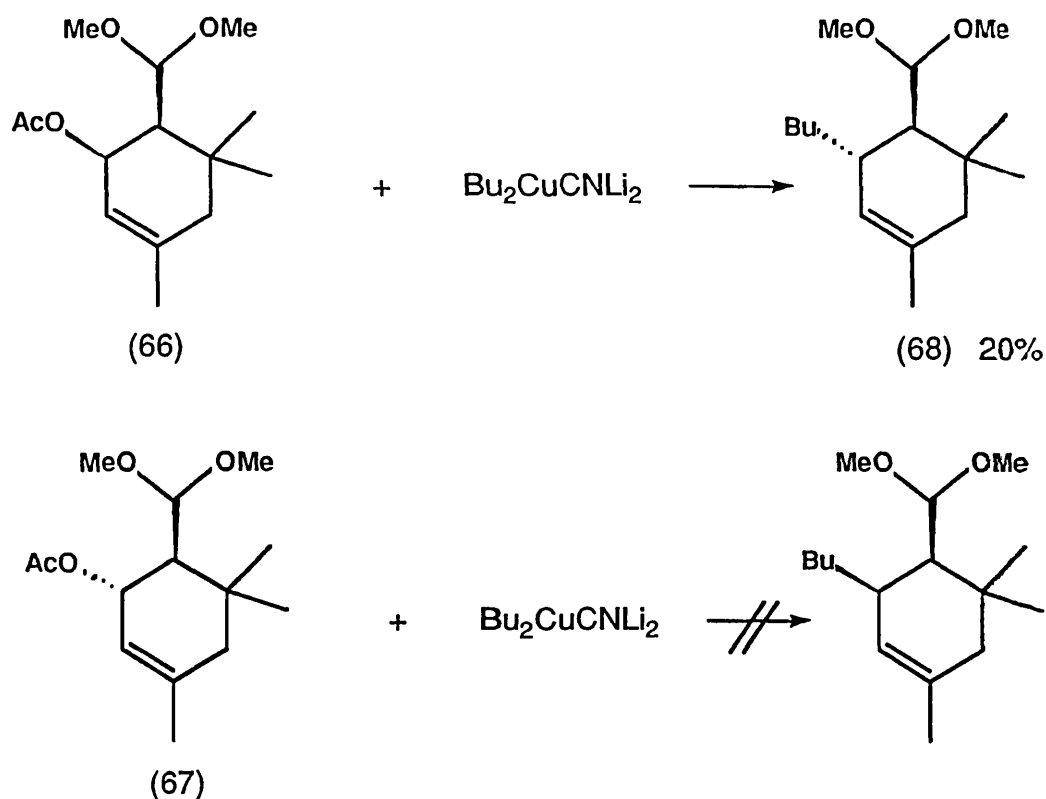


Scheme 41

2.4.2 Displacement and cross coupling reactions of acetates

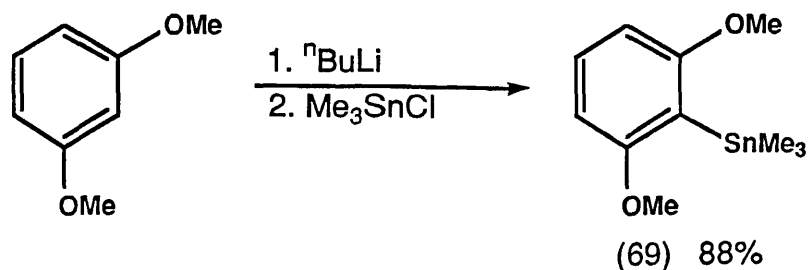
The displacement reactions of the allylic acetates (66) and (67) were initially attempted with organocopper species derived from 2-bromoanisole (Scheme 42), but were not successful. The use of a higher order cuprate¹¹¹ such as $\text{Bu}_2\text{CuCNLi}_2$, was only mildly successful when reacted with the *cis*-acetate (66) to give the *trans* butylated product (68) in very low yield (Scheme 42). The *trans* acetate did not react, because of the steric hindrance caused by the adjacent acetal group.

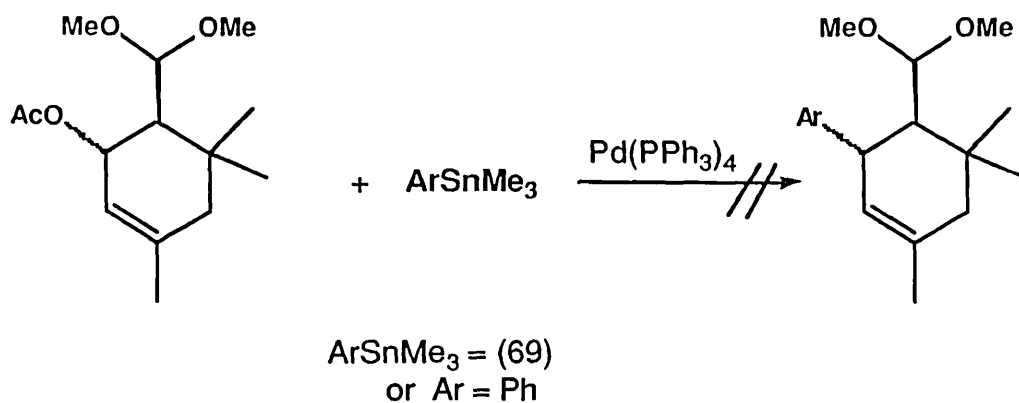




Scheme 42

The palladium cross coupling reactions of organotin compounds with the allylic acetates¹¹² were then attempted (Scheme 43). Again no reaction was found to work, which was perhaps to be expected for the *trans* acetate, where the oxidative addition step is inhibited by the acetal group, although no such problem exists with the *cis* compound.

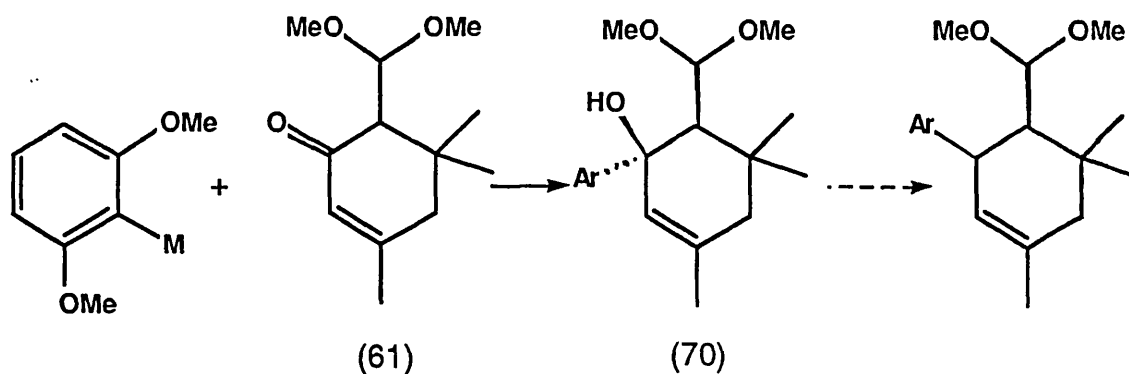




Scheme 43

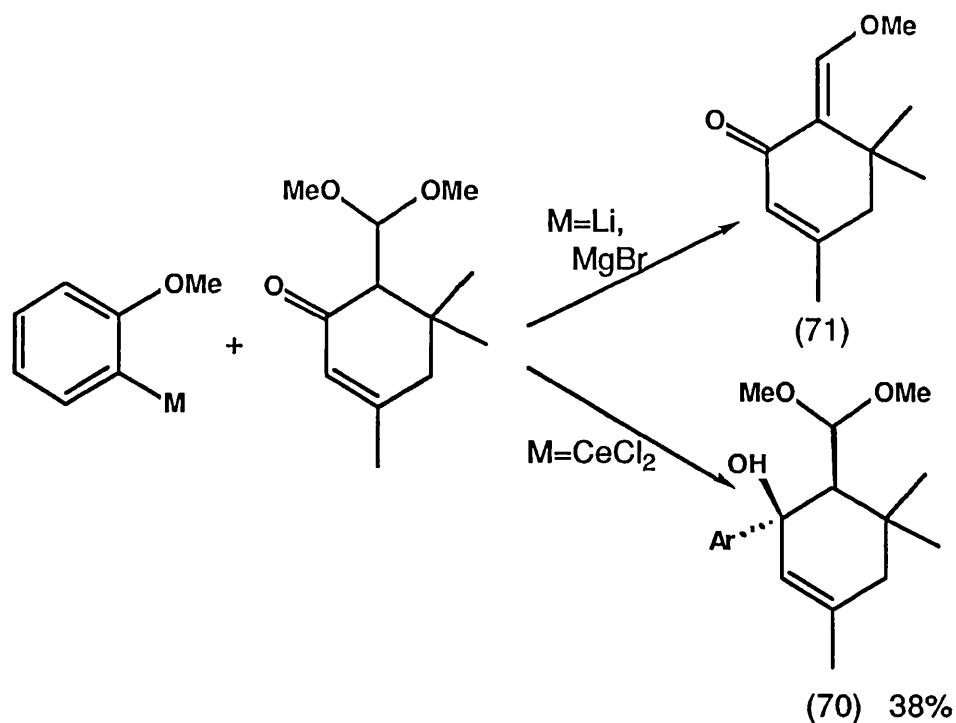
2.4.3 Nucleophilic addition reactions of the enone (61)

Nucleophilic attack of organometals on the enone (61), would lead to the alcohol (70). It was envisaged that the alcohol could be stereoselectively reduced to the *cis* compound as required (Scheme 44).



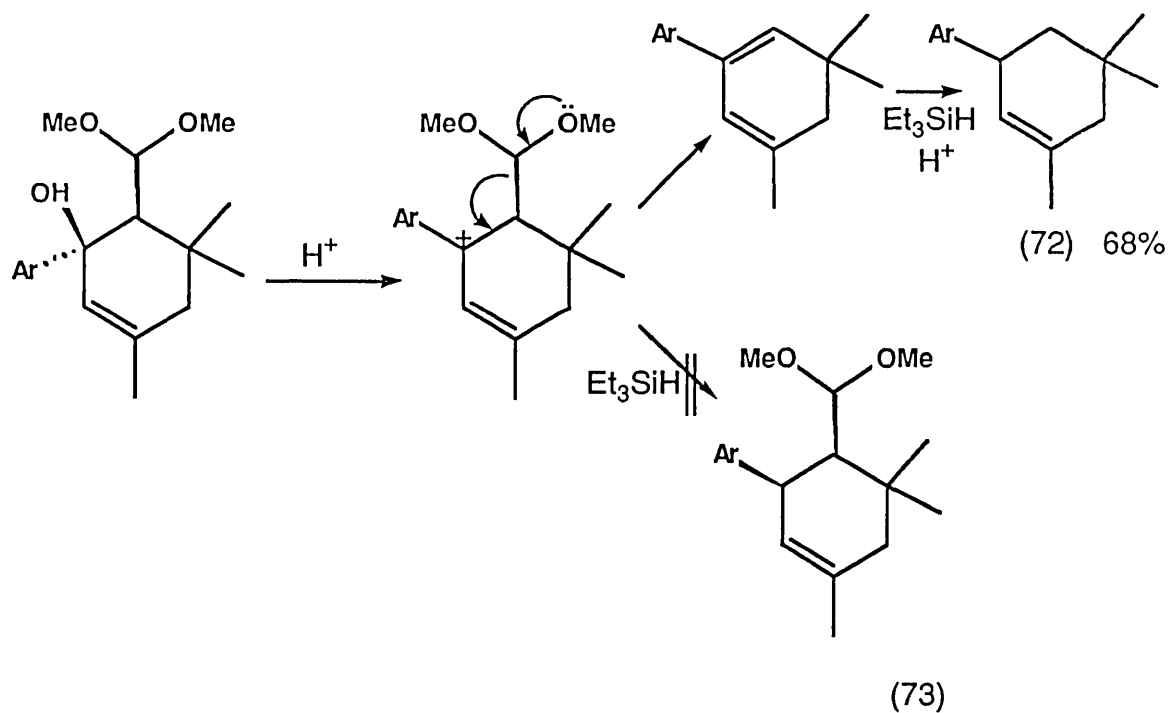
Scheme 44

The reactions of the enone (61) with various 2-metalloanisole derivatives were carried out (Scheme 45). Where M was Li or MgBr, the major product was the result of elimination of methanol to give the dienone (71). However using the highly nucleophilic and non-basic cerium analogue¹¹³, the alcohol (70) was formed in moderate yield (Scheme 45).



Scheme 45

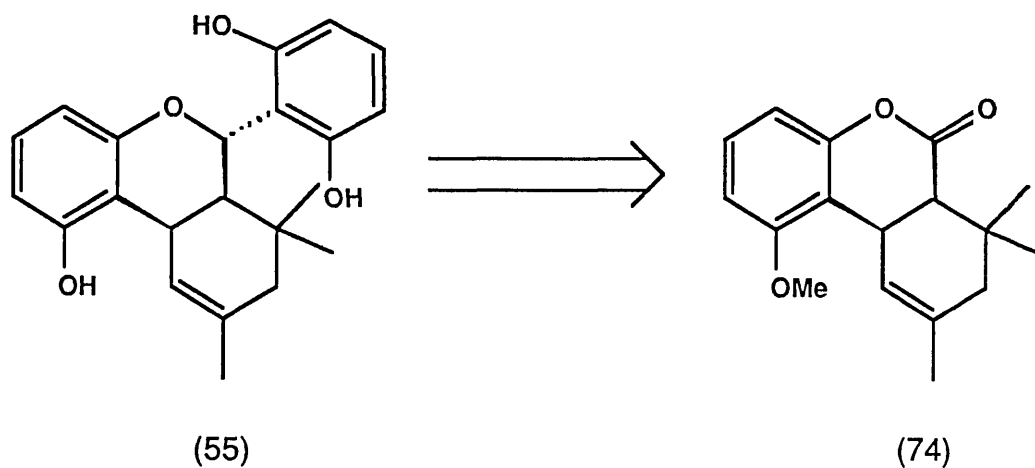
Reduction of this alcohol was attempted using ionic hydrogenation methods, such as trifluoroacetic acid/triethylsilane mixtures¹¹⁴, which proceed via intermediate carbonium ion formation. It was anticipated that the hydride source would then attack from the opposite face to the acetal group leading to *cis* stereochemistry (Scheme 46). However, it was found that all ionic hydrogenation methods, led only to deacetalation via the intermediate carbonium ion (Scheme 46).



Scheme 46

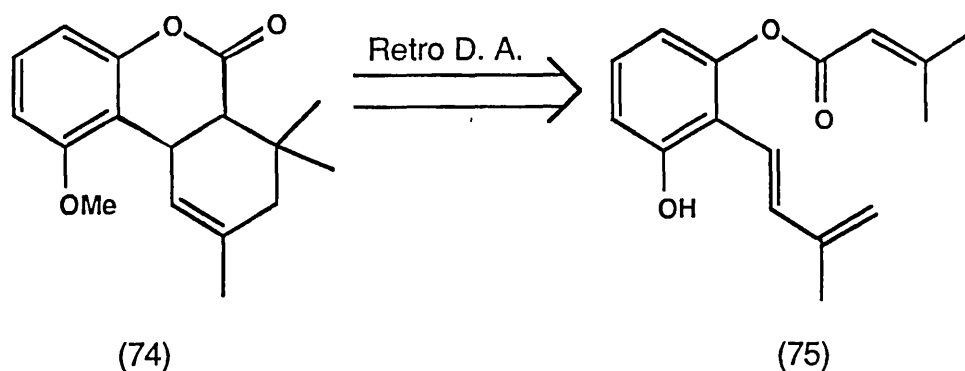
2.4.4 Diels Alder approaches to compound (55)

An alternative approach to the synthesis of (55) was to construct the tricyclic lactone (74), which could be elaborated to the target compound (55) (Scheme 47).



Scheme 47

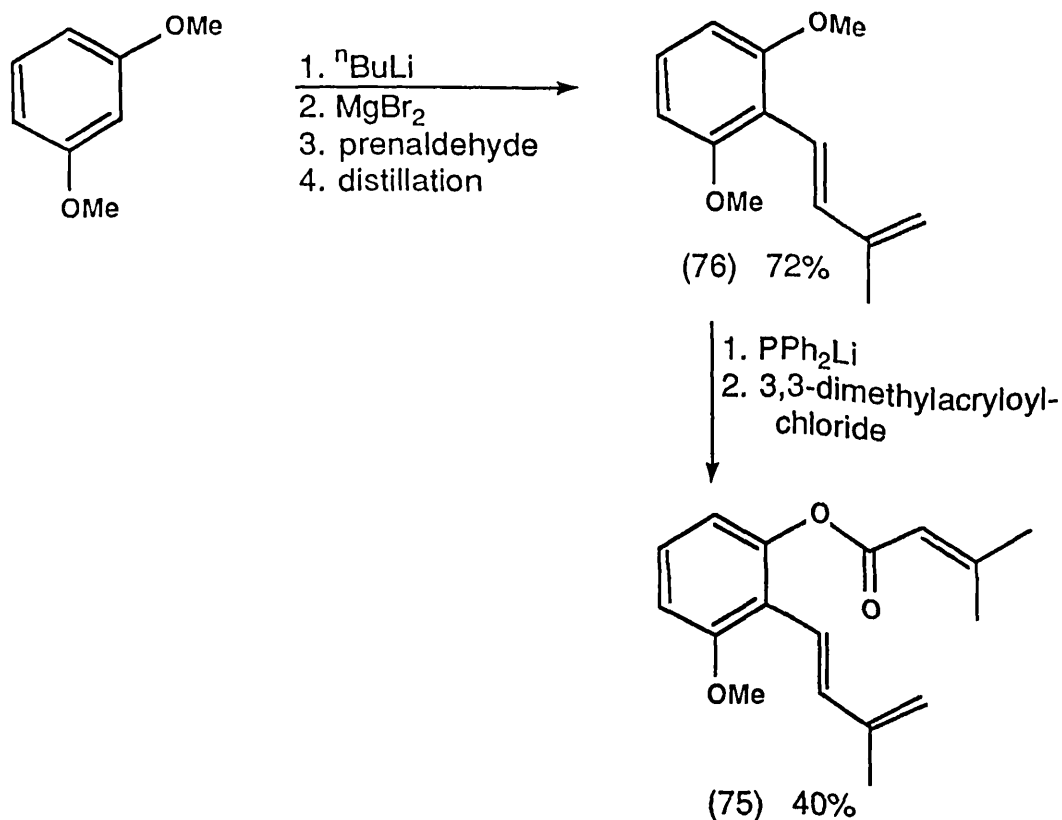
A retro analysis of the lactone (74) leads to the compound (75), which it was envisaged would undergo ring closure in the required *cis endo* fashion to yield the corresponding product (74) (Scheme 48).



Scheme 48

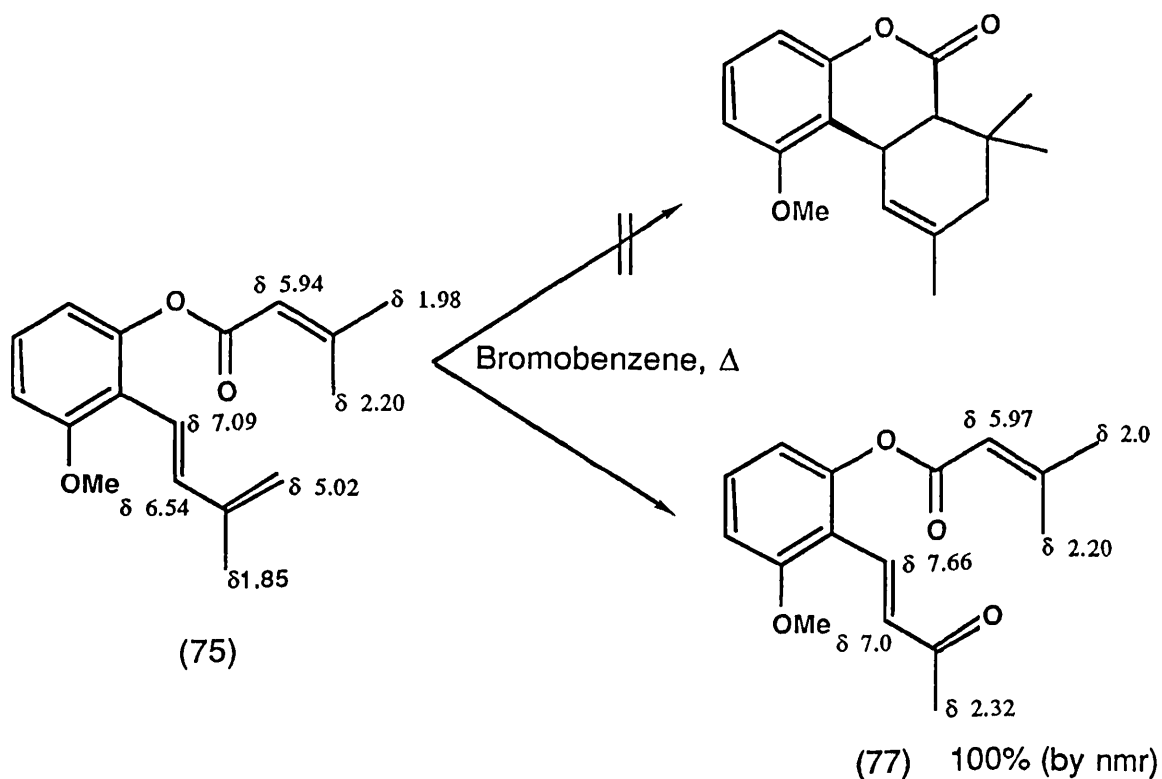
It was synthesised in moderate yield via the procedures documented in Scheme 49. The diene (76) was formed in good yield, from reaction of the Grignard with prenaldehyde. The dienophile fragment was then attached by mono de-methylation of the diene using lithium diphenylphosphide, followed by reaction with 3,3-dimethylacryloylchloride to give (75).

The intramolecular Diels Alder reaction was carried under various conditions of temperature and pressure. Unfortunately, the reaction was not successful, and led in most reactions to clean conversion to a compound which appears to be the result of oxidation to the enone (77) (Scheme 50).



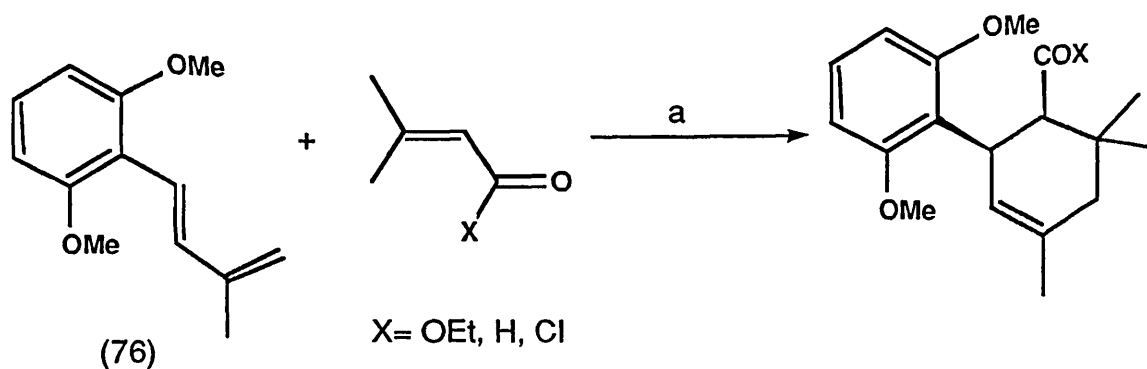
Scheme 49

The spectral data for this compound (77) is consistent with the above assignment. In the proton nmr, the terminal methylene singlet at δ 5.02 in the starting material (75) has disappeared along with the vinyl methyl at δ 1.85, to be replaced only by a sharp singlet at δ 2.32 corresponding to a methyl ketone. Additionally, the signals at 7.0 and 7.66 ppm, corresponding to the *trans* alkenyl protons in the product (77), have been shifted downfield. The ^{13}C nmr is also consistent with this interpretation with two carbonyl signals at 200 and 165 ppm; and the accurate mass is also in accord with the proposed conversion to the enone (77).



Scheme 50

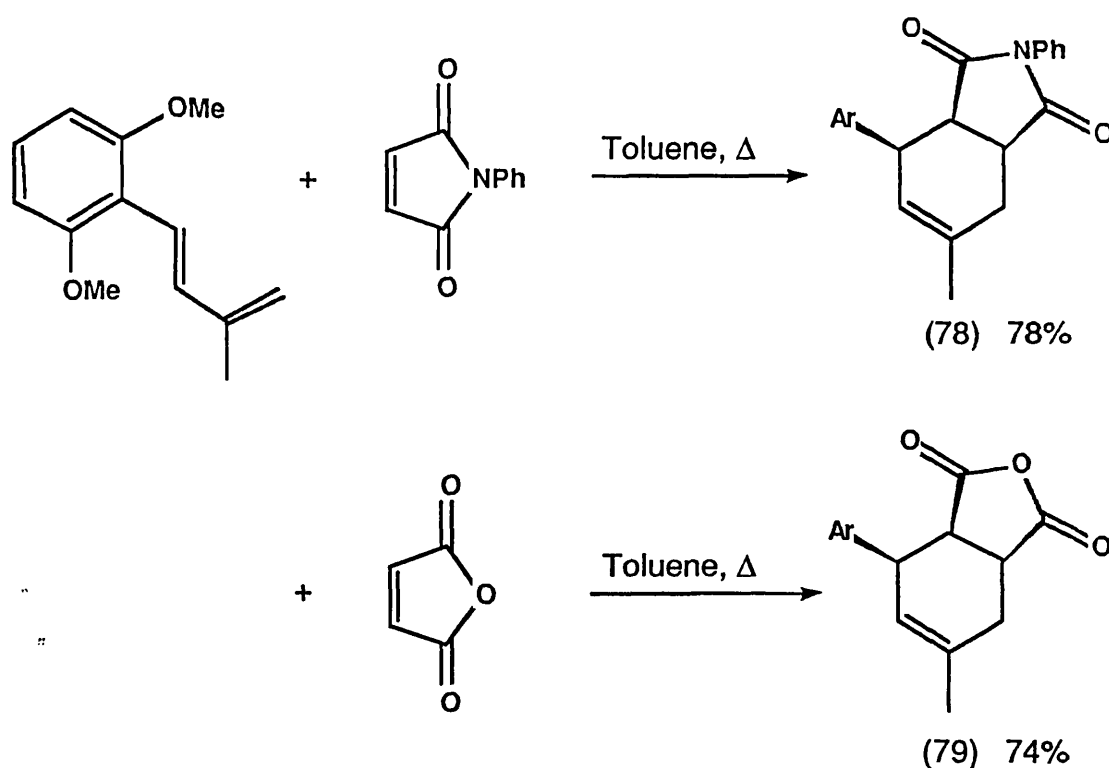
Various intermolecular reactions of the diene (76) with the appropriate dienophiles were also attempted, under different conditions of temperature and pressure, but without success (Scheme 51). The failure of these reactions can probably be attributed to the steric demands imposed by the *gem* dimethyl group present on the dienophile.



a. Bromobenzene Δ , Toluene Δ , Toluene/ Et_2AlCl , 9 Kbar /neat

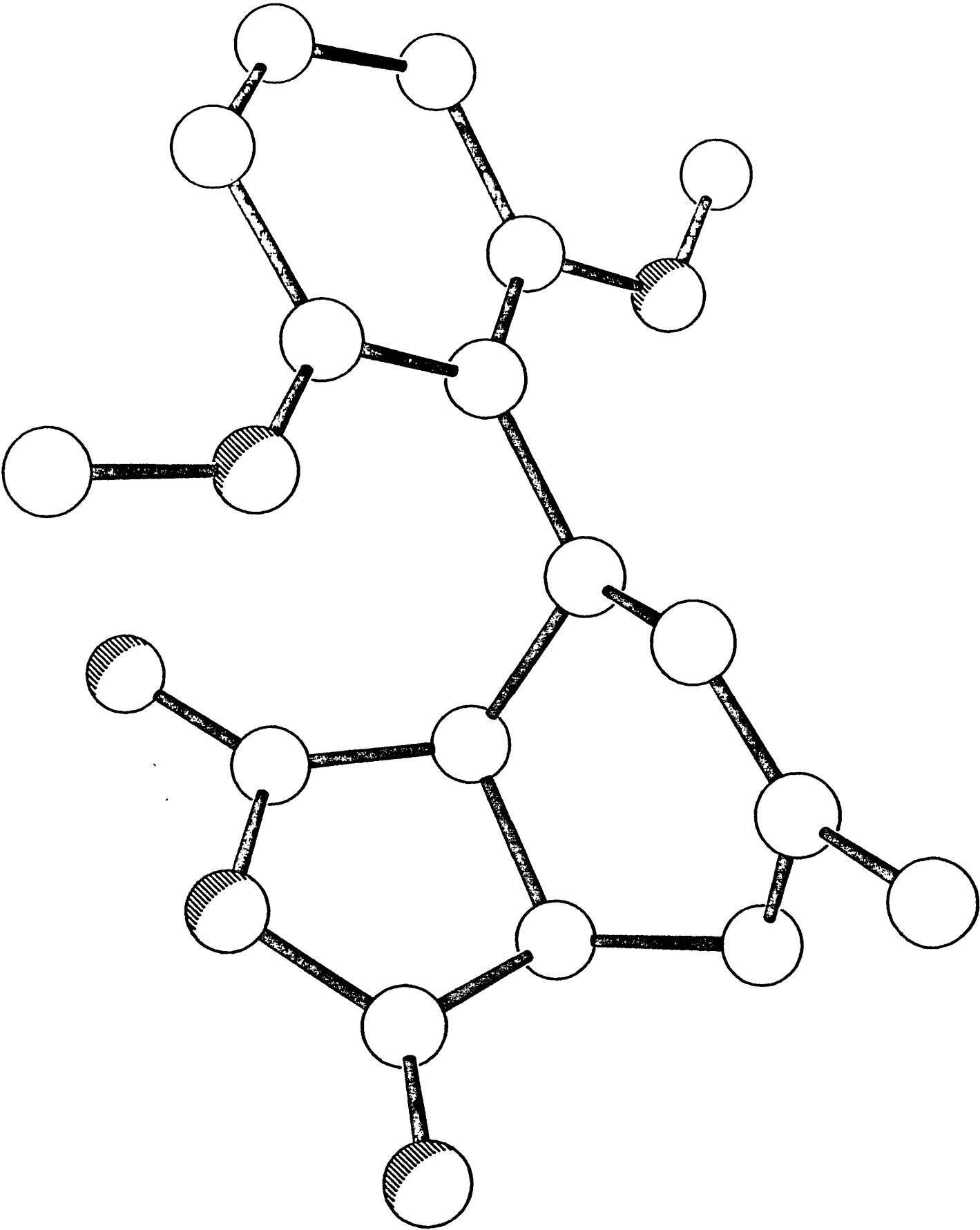
Scheme 51

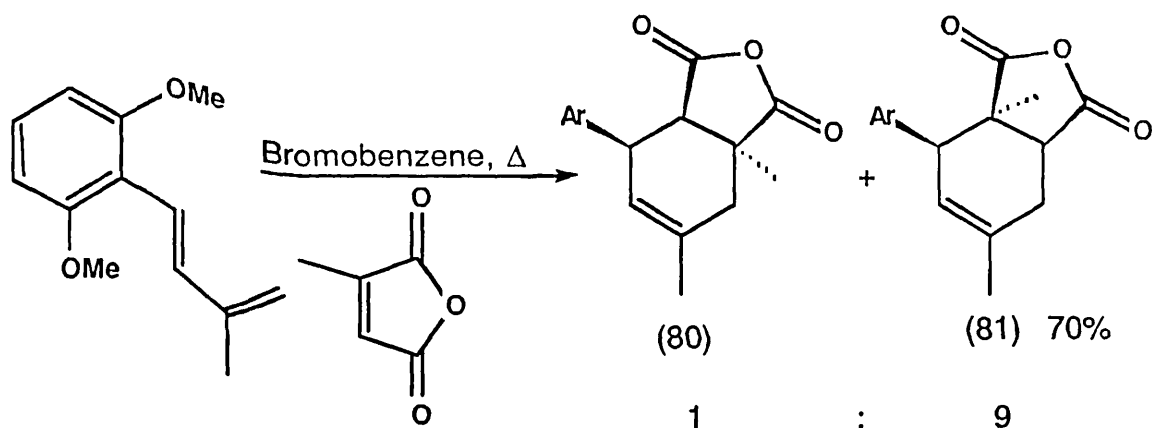
The reactions of the diene (76) with highly activated dienophiles such as N-phenyl maleimide, and maleic anhydride, were found to work very well giving the requisite *cis* stereochemistry, as confirmed by X-ray analysis for the maleic anhydride adduct (79) (Scheme 52). This adduct was one methyl substituent short of the required carbon framework, hence the diene (76) was reacted with citraconic anhydride (Scheme 53).



Scheme 52

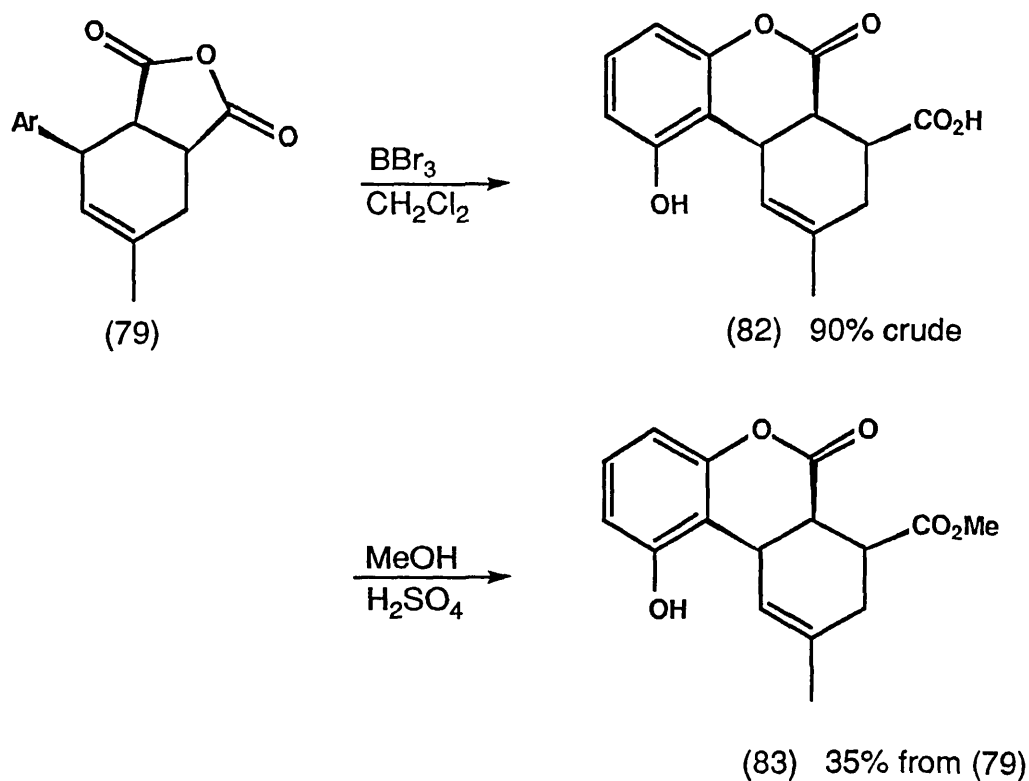
The reaction proceeded well, in high yield, but gave mainly the wrong regioisomer (81). This was not totally unexpected since Diels Alder reactions with citraconic anhydride are well precedented¹¹⁵, and from molecular orbital coefficient considerations, would be expected to go in the direction found.





Scheme 53

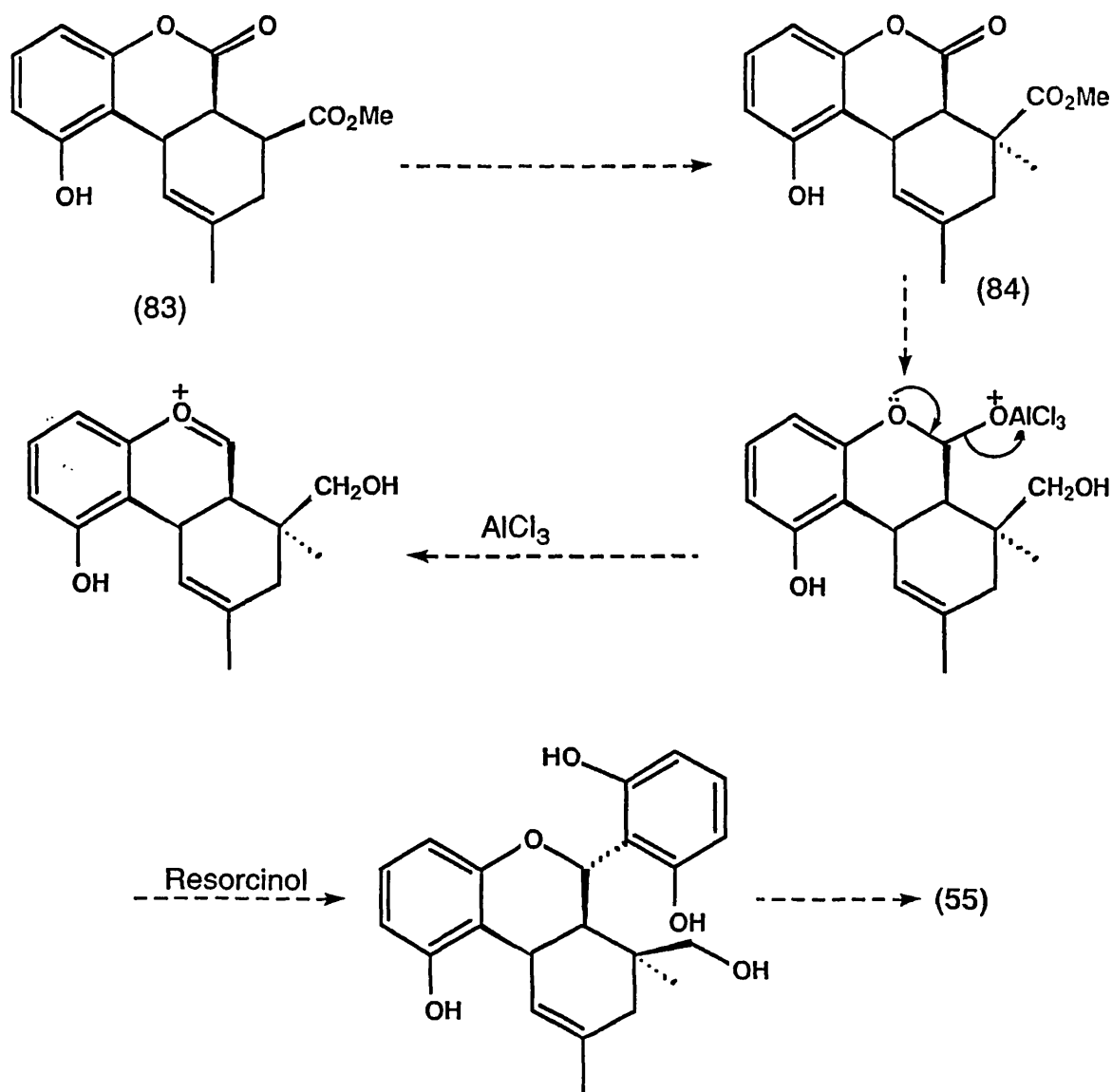
The adduct (79) was further elaborated to form the lactone (82) when treated with boron tribromide solution, and the acid part methylated to give the lactone ester (83) (Scheme 54).



Scheme 54

2.5 Further developments

It is hoped that the lactone ester derivative (83) can be further developed by incorporating the additional methyl and resorcynyl substituents (Scheme 55). It would be more advantageous if the Diels Alder reaction between the diene and citraconic anhydride could be pursued to yield the required regioisomer as the dominant product. The next important step would be to couple this lactone (84) with the resorcynyl unit. Reduction of this lactone with DIBAL would lead to the lactol, which could conceivably be coupled with resorcinol, in the presence of a Lewis acid (AlCl_3).



Scheme 55

2.6 Conclusion

The aim of this project has been to synthesise a variety of resorcinyll benzofuran phytoalexins, of differing substitution patterns and complexity. This has, to a large extent, been achieved.

The initial concept of using chromium tricarbonyl chemistry to iodinate in the 5-position of resorcinol, has largely been superseded by the use of phloroglucinol and its triflate derivatives. Although this was only used in the synthesis of moracin I, it could be just as applicable to the synthesis of the other three natural products.

The synthesis of dimoracin has mainly involved approaches to the stereoselective synthesis of the C₁₀ terpenoid unit and its coupling to the resorcinyll moiety. Of the three methods tried, the Diels Alder approach to the construction of this ring system has been the most successful, although there are constraints on the dienophiles that can be used. Nevertheless, it should be possible, from the present position, to extend the synthesis, using methods previously outlined, to achieve the desired targets.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 298 grating spectrometer or a Perkin-Elmer model 1710 FT spectrometer. ^1H -nmr spectra were recorded at 60 MHz on a Varian EM-360A spectrometer, at 250 MHz on a Brüker WH-250 FT spectrometer, at 270 MHz on a Jeol GSX FT 270 spectrometer, and at 500 MHz on a Brüker 500 FT spectrometer with trimethylsilane as an internal standard. Signals are described as b-broad, s-singlet, d-doublet, t-triplet, q-quartet, and m-multiplet. Apparent coupling constants (J) are given in Hertz. Mass spectra, micro-analyses, and X-ray structure determinations were carried out by the appropriate services at Imperial College.

Solvents were purified as follows: diethyl ether and THF were dried by distillation from sodium-potassium-benzophenone ketyl; di-*n*-butyl ether was distilled from sodium; dry dichloromethane, DMF and acetonitrile were purified according to literature¹¹⁶ methods. Petrol refers to that fraction with b. p. 40-60°C, and is redistilled.

Reactions involving arenetricarbonyl chromium (0) complexes, palladium catalysts, or alkyl lithiums, were performed under an atmosphere of dry, oxygen free nitrogen. Organic phases were dried with magnesium sulphate after extraction. Solvents were removed at reduced pressure on a Büchi rotary evaporator.

Tetrakis(triphenylphosphine)palladium(0) was prepared according to the procedure of Coulson¹¹⁷. Cuprous bromide dimethylsulphide complex was prepared by the method of Keller¹¹⁸ *et al.* *n*-Butyl lithium (Aldrich Chemicals Co.) was standardised regularly by the method of Whitesides¹¹⁹ *et al.* and used as about a 1.6 M solution in hexanes.

Column chromatography was performed using Rose Chemicals silica gel H. Thin layer chromatography was performed using Merck aluminium sheets precoated with silica gel 60 F₂₅₄, layer thickness 0.2mm.

General Procedures

Complexations

A solution of the arene (10mmol) and chromium hexacarbonyl (2.42g, 11mmol) in *n*-butyl ether (85ml) and THF (8ml) was refluxed at 140°C for 24-48 hours. After cooling the solution was filtered through a silica pad and the solvent evaporated. Chromatography was carried out if required, and the complex recrystallized from petrol or petrol/dichloromethane.

Cross coupling of 2-bromozincbenzofurans

To a solution of benzofuran (0.5mmol) in THF (1ml) at -10°C, was added *n*-butyl lithium (0.5mmol). After stirring for 2 hours, zinc bromide (0.75mmol) in THF (10ml) was added and the reaction stirred at room temperature for 1 hour. To this was added a mixture of the iodoarene (0.5mmol) and Pd(PPh₃)₄ (23mg, 4mol%) in THF, and the reaction allowed to stir overnight. Work up using 2.8M ammonium chloride solution and extraction as usual, followed by drying, and evaporation of solvent, gave after chromatography, the required product.

Cross coupling of 2-stannybenzofurans

To a solution of the benzofuran (1-1.5mmol) in ether (2ml) at -78°C, was added *n*-butyl lithium (1-1.5mmol) and the reaction stirred at -10°C for 2.5 hours. To this was added a solution of trimethyltin chloride (1-1.5mmol) in ether, and the reaction stirred for 1 hour at room temperature. This was then transferred under nitrogen to a solution containing the iodoarene (1mmol) and Pd(PPh₃)₄ (4mol%) in THF, or benzene, or toluene (20ml), and the reaction refluxed overnight. Work up was carried out as usual, followed by extraction into ether, drying, removal of solvent, and subsequent chromatography.

Diels Alder reactions

A mixture of the diene (76) (0.204g, 1mmol) and dienophile (1mmol) in toluene or bromobenzene (5ml), was refluxed until completion of reaction. The solvent was evaporated and the compound chromatographed.

2-Iodobenzofuran

To a solution of benzofuran (2.36 g, 2.2 ml, 20 mmol) in dry ether at -78°C, was added *n*-butyl lithium (15.4 ml, 20 mmol). The reaction was then stirred at -10°C for 2 hours, after which iodine (5.18 g, 20 mmol) was added via a solid addition funnel. After stirring for a further 30 minutes, the reaction was allowed to warm to room temperature. Ammonium chloride solution (25 ml of 2.8M) was added and the mixture extracted with ether. The organic extracts were washed with sodium metabisulphite solution, followed by water, dried, and the solvent evaporated to give the *title* compound as a brown oil which was distilled (b. p. 90°C/0.8 mbar) to give the product as a colourless oil in 81% yield.

$\nu_{\max}$ (film) 3132, 3065, 3035, 2683, 2489, 2093, 1614, 1524, 1471, 1441, 1419, 1338, 1302, 1248 cm^{-1} ;

δ_{H} (CDCl_3) 6.8 (1H, d, $J = 0.8$ Hz, H_3), 7.17-7.21 (2H, m, H_4 H_7), 7.44-7.51 (2H, m, H_5 H_6);

m/z 244 (M^+) (100%).

1,3 - Bis(trisopropylsiloxy)benzene (7)

To a mixture of resorcinol (2.2g, 20 mmol) and imidazole (6.8g, 100 mmol) dissolved in dry DMF (6 ml), was added triisopropylsilylchloride (8.47 g, 9.4 ml, 44mmol), and the reaction left to stir for 48 hours. Saturated sodium bicarbonate solution (20 ml) was added and the mixture extracted with petrol. These extracts were washed with 2N sodium hydroxide solution, followed by water. After drying, the solvent was evaporated to leave the *title* product in 99% yield.

$\nu_{\max}$ (film) 2950, 2865, 1590, 1480, 1380, 1300, 1260, 1180, 1150, 1070, 1000, 920, 880, 860, 770, 680 cm^{-1} ;

δ_{H} (CDCl_3) 1.08 (36H, d, $J = 7$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.2 (6H, m, $J = 7$ Hz, $\text{CH}(\text{CH}_3)_2$), 6.43 (1H, t, $J = 2.1$ Hz, H_2), 6.48 (2H, dd, $J = 2.1, 7.9$ Hz, H_4 H_6), 7.03 (1H, t, $J = 7.9$ Hz, H_5).

η^6 -1,3- *Bis(triisopropylsiloxybenzene)tricarbonyl chromium (0)* (8)

Following the general procedure, refluxing a solution of 1,3-bis(triisopropylsiloxybenzene) for 48 hours, gave the *title* compound in 90% yield.

m. p. 88-9°C;

$\nu_{\max}$ (CHCl_3) 1965, 1885 cm^{-1} ;

δ_{H} (CDCl_3) 1.1 (36H, d, $J = 7$ Hz, Me), 1.12 (6H, m, $\text{CH}(\text{Me})_3$), 4.7 (2H, dd, $J = 7, 2$ Hz, H_4 H_6), 5.15 (1H, t, $J = 2$ Hz, H_2), 5.5 (1H, t, $J = 7$ Hz, H_5).

2,2'-*Bis(benzofuran)* (11)

To a solution of η^6 -1,3-bis(triisopropylsiloxybenzene)tricarbonyl chromium (0) (0.139g, 0.25mmol) in THF (10ml) at -78°C, was added *n*-butyl lithium (0.2ml, 0.25mmol) and the reaction stirred for 1 hour. $\text{CuBr} \cdot \text{SMe}_2$ (0.052g, 0.25mmol) was then added and the reaction stirred at -20°C for 1 hour. To this solution was added a mixture of 2-iodobenzofuran (0.061g, 0.25mmol) and $\text{Pd}(\text{PPh}_3)_4$ (2mol%) in THF, and the reaction allowed to stir overnight. Work up and extraction as usual, gave after drying, removal of solvent, and subsequent chromatography the *title* compound in 77% yield.

m. p. 190-2°C (lit⁸⁴ 192.5-5.5°C);

$\nu_{\max}$ (Nujol) 1370, 1340, 1300, 1250, 1210, 1170, 1150, 1140, 1045 cm^{-1} ;

δ_{H} (CDCl_3) 7.16 (2H, d, $J = 0.9$ Hz, H_3), 7.27 (2H, dt, $J = 1.7, 7.2$ Hz, H_5), 7.34 (2H, dt, $J = 1.7, 7.2$ Hz, H_6), 7.55 (2H, bd, $J = 7.2$ Hz, H_4), 7.63 (2H, bd, $J = 7.2$ Hz, H_7);

m/z 234 (M^+) (100%), 205, 176, 117.

*η^6 -Tri-*n*-butylstannylbenzenetricarbonyl chromium (0)*

To a solution of η^6 -benzenetricarbonyl chromium (0) (0.428g, 2mmol) in THF (50ml) at -78°C , was added *n*-butyl lithium (1.6ml, 2mmol), and the reaction stirred for 1 hour. Tri-*n*-butyltin chloride (0.65g, 0.54ml, 2mmol) was then added and the reaction stirred for a further hour. After allowing to warm to room temperature, ammonium chloride solution was added, and the mixture extracted with ether. The ether extracts were washed with 2M potassium fluoride solution, followed by water. After drying, and evaporation of solvent, a yellow oil was obtained, which upon chromatography gave the *title* compound as a yellow oil in 92% yield.

ν_{max} (CHCl_3) 1967, 1893 cm^{-1} ;

δ_{H} (CDCl_3) 0.92 (9H, t, $J = 7.2$ Hz, CH_2CH_3), 1.12 (6H, t, $J = 8.2$ Hz, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$), 1.36 (6H, sext, $J = 7.2$ Hz, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$), 1.55 (6H, m, $J = 7.2$, 8.2 Hz, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$), 5.19 (2H, t, $J = 6.3$ Hz, H_3 H_5), 5.31 (2H, dd, $J = 1.1$, 6.3 Hz, H_2 H_6), 5.44 (1H, tt, $J = 1.1$, 6.3 Hz, H_4);

m/z 504 (M^+), 448, 420;

(Found C, 50.19%; H, 6.59%; $\text{C}_{21}\text{H}_{32}\text{O}_3\text{SnCr}$ requires C, 50.13%; H, 6.41%).

2-[η^6 -Phenyltricarbonyl chromium (0)]benzofuran (12)

To a solution of η^6 -benzenetricarbonyl chromium (0) (0.214g, 1mmol) in THF (35ml) at -78°C , was added *n*-butyl lithium (0.8ml, 1mmol), and the reaction stirred for 1 hour. Zinc bromide (1.5mmol) [made by refluxing a solution of zinc dust and 1,2-dibromoethane in THF (10ml)] was added, and the reaction stirred for 1 hour at -20°C . To this was added a mixture of 2-iodobenzofuran (0.244g, 1mmol) and $\text{Pd}(\text{PPh}_3)_4$ (2mol%) in THF (10ml), and the reaction stirred at room temperature overnight. Work up using ammonium chloride solution, followed by ether extraction, drying, and subsequent removal of the solvent gave, after column chromatography, the *title* compound in 82% yield.

Using 2-bromobenzofuran the *title* compound was obtained in 70% yield.

Using the standard cross coupling procedure for 2-bromozinc benzofurans,

gave the *title* compound in 36% yield.

A mixture of 2-trimethylstannylbenzofuran (0.140g, 0.5mmol), iodobenzene tricarbonyl chromium (0) (0.170g, 0.5mmol), and Pd(PPh₃)₄ (11mg, 4mol%) in THF (20ml) was refluxed for 1.5 hours. The solution was filtered through a silica pad to remove the precipitated palladium metal, and water added. The mixture was extracted with ether, dried, and the solvent removed. Column chromatography of the product gave the *title* compound in 64% yield.

m. p. 148-9°C;

$\nu_{\max}$ (CHCl₃) 1970, 1900 cm⁻¹;

δ_{H} (CDCl₃) 5.36 (1H, tt, J = 1.7, 6.3 Hz, H_{4'}), 5.49 (2H, t, J = 6.3 Hz, H_{3'} H_{5'}), 5.95 (2H, dd, J = 1.7, 6.3 Hz, H_{2'} H_{6'}), 6.94 (1H, d, J = 0.97 Hz, H₃), 7.25 (1H, dt, J = 1.2, 7.2 Hz, H₆), 7.33 (1H, dt, J = 1.5, 8.2 Hz, H₅), 7.50 (1H, dd, J = 1.2, 8.2 Hz, H₄), 7.58 (1H, bd, J = 7.2 Hz, H₇);

m/z 330 (M⁺), 274, 246 (100 %);

(Found C, 61.82%; H, 2.93%; C₁₇H₁₀O₄Cr requires C, 61.83%; H, 3.05%).

1,3-Bis(t-butyldimethylsiloxy)benzene

To a mixture of resorcinol (1.1g, 10mmol) and imidazole (3.4g, 50mmol) in DMF (3ml), was added *t*-butyldimethylsilylchloride (3.32g, 22mmol), and the reaction stirred for 48 hours at room temperature. Work up as before, followed by removal of solvent gave the *title* compound in 74% yield.

$\nu_{\max}$ (film) 2960, 2940, 2880, 2875, 1580, 1460, 1295, 1255 cm⁻¹;

δ_{H} (CDCl₃) 0.18 (12H, s, Si (CH₃)₂), 0.97 (18H, s, ^tBu), 6.34 (1H, t, J = 2 Hz, H₂), 6.45 (2H, dd, J = 2, 8 Hz, H₄ H₆), 7.05 (1H, t, J = 8 Hz, H₅);

m/z 338 (M⁺), 323, 281 (100 %);

(Found C, 64.06%; H, 10.31%; C₁₈H₃₄O₂Si₂ requires C, 63.84%; 10.12%).

η^6 -1,3-Bis(*t*-butyldimethylsiloxy)benzenetricarbonyl chromium (0)

Refluxing a solution of 1,3-bis(*t*-butyldimethylsiloxy)benzene for 48 hours, using the standard procedure, gave the *title* compound in 70% yield.

m. p. 114-5°C;

$\nu_{\max}$ (CHCl₃) 1975, 1890 cm⁻¹;

δ_{H} (CDCl₃) 0.25 (12H, s, Si(CH₃)₂), 0.95 (18H, s, ^tBu), 4.67 (2H, bd, J = 6.3 Hz, H₄ H₆), 4.97 (1H, bs, H₂), 5.48 (1H, t, J = 6.3 Hz, H₅);

m/z 474 (M⁺), 418, 390 (100 %);

(Found C, 53.18%; H, 7.23%; C₂₁H₃₄O₅Si₂Cr requires C, 53.14%; H, 7.22%).

2-Trimethylstannylbenzofuran (14)

To a solution of benzofuran (1.89g, 1.76ml, 16mmol) in ether (16ml) at -78°C, was added *n*-butyl lithium (11.1ml, 16mmol) and the reaction stirred at -10°C for 2.5 hours. To this was added a solution of trimethyltinchloride (3.24g, 16mmol) in ether. After stirring at room temperature overnight, water was added and the mixture extracted with ether. The ether extracts were washed with 2N potassium fluoride solution followed by water. After drying and removal of solvent, distillation of the resulting oil gave the *title* compound in 79% yield.

b. p. 80°C/0.05mbar;

$\nu_{\max}$ (CHCl₃) 3020, 2970, 2900, 1510, 1465, 1435, 1290, 1250, 1150 cm⁻¹;

δ_{H} (CDCl₃) 0.4 (9H, s, Sn(CH₃)₃), 6.93 (1H, d, J = 0.9 Hz, H₃), 7.20 (1H, dd, J = 1.4, 7.2 Hz, H₄), 7.26 (1H, dt, J = 1.4, 7.2 Hz, H₅), 7.48-7.58 (2H, m, H₆ H₇);

m/z 282(M⁺) 267 (100%);

(Found accurate mass 282.0069, C₁₁H₁₄OSn requires 282.0066).

η^6 -1,3-Bis(triisopropylsiloxy)-5-iodobenzenetricarbonyl chromium (0) (15)

To a solution of 1,3-bis(triisopropylsiloxy)benzenetricarbonyl chromium (0) (1.116g, 2mmol), in THF (70ml) at -78°C, was added *n*-butyl lithium (1.8ml, 3mmol, 1.5eq), and the reaction stirred for 1 hour. Iodine (0.762g, 3mmol) was added via a solid addition funnel to the rapidly stirring solution. Stirring was continued for a further hour, before allowing the reaction to warm to room temperature. Sodium metabisulphite solution was immediately added, and the mixture shaken thoroughly. The mixture was extracted with ether, and the

extracts washed with brine and water. After drying, removal of solvent, and subsequent chromatography, the *title* compound was obtained as a yellow oil which solidified on standing. Recrystallisation from petrol gave the compound in 57% yield.

m. p. 66-7°C;

$\nu_{\max}$ (CHCl₃) 1985, 1900 cm⁻¹;

δ_{H} (CDCl₃) 1.1 (36H, d, J = 7 Hz, CH(CH₃)₂), 1.2 (6H, m, J = 7 Hz, CH(CH₃)₂), 5.04 (1H, t, J = 2.2 Hz, H₂), 5.18 (2H, d, J = 2.2 Hz, H₄ H₆);

m/z 684 (M⁺), 628, 600 (100 %);

(Found C, 47.56%; H, 6.69%; C₂₇H₄₅IO₅Si₂Cr requires C, 47.36%; H, 6.62%).

2-[η⁶-3,5-Bis(triisopropylsiloxyphenyl)tricarbonyl chromium (0)]benzofuran
(16)

Following the standard procedure for 2-bromozinc benzofurans the *title* compound was obtained as an orange solid after recrystallization from ethanol, in 22 % yield.

A mixture of 2-trimethylstannylbenzofuran (0.062g, 0.22mmol), 1,3-bis(triisopropylsiloxy)-5-iodobenzenetricarbonyl chromium (0) (0.150g, 0.22mmol), and Pd(PPh₃)₄ (4mol%) in THF (20ml) was refluxed for 20 minutes. The solution was filtered through a silica pad to remove the precipitated palladium metal, and water added. The mixture was extracted with ether, dried, and the solvent removed. Column chromatography of the product gave the *title* compound in 20% yield.

m. p. 68-9°C;

$\nu_{\max}$ (CHCl₃) 1965, 1890 cm⁻¹;

δ_{H} (CDCl₃) 1.15 (36H, d, J = 7 Hz, CH(CH₃)₂), 1.27 (6H, m, J = 7 Hz, CH(CH₃)₂), 5.13 (1H, t, J = 1.8 Hz, H₄'), 5.36 (2H, d, J = 1.8 Hz, H₂' H₆'), 6.95 (1H, d, J = 0.75 Hz, H₃), 7.26 (1H, dd, J = 1.4, 7.3 Hz, H₄), 7.32 (1H, dt, J = 1.4, 7.3 Hz, H₅), 7.56 (1H, bt, J = 7.3 Hz, H₆), 7.58 (1H, bd, J = 7.3 Hz, H₇);

m/z 538 (M⁺-Cr(CO)₃), 495, 422, 379 (100%);

(Found C, 62.32%; H, 7.70%; C₃₅H₅₀O₆Si₂Cr requires C, 62.28%; H, 7.47%).

1,3-Dimethoxy-5-iodobenzene (17)

To 1,3-bis(triisopropylsiloxy)-5-iodobenzenetricarbonyl chromium (0) (2.18g, 3.2mmol) in THF (10ml) was added dimethylsulphate(7ml) followed by TBAF (7ml, 7mmol), and the reaction stirred overnight. The mixture was poured into ammonia solution and ether added. The ether layer was extracted and washed 4 or 5 times with ammonia solution to remove the excess dimethylsulphate, then washed with water. After drying and removal of solvent, the tricarbonyl complex of the *title* compound was obtained in 90% yield. This was decomplexed with iodine, and the resulting material chromatographed to give the *title* compound.

m. p. 72.5-3.5°C;

$\nu_{\max}$ (CHCl₃) 3028, 3009, 2964, 2837, 1597, 1570, 1456, 1434, 1422, 1328, 1314, 1296, 1277, 1220, 1216, 1207, 1158, 1062, 1037 cm⁻¹;

δ_{H} (CDCl₃) 3.76 (6H, s, OCH₃), 6.40 (1H, t, J = 2.2 Hz, H₂), 6.85 (2H, d, J = 2.2 Hz, H₄ H₆);

m/z 264 (M⁺) (100%), 234;

(Found C, 36.32%; H, 3.35%; C₈H₉O₂I requires C, 36.39%; H, 3.44%).

2-[η^6 -3,5-dimethoxyphenyltricarbonyl chromium (0)]benzofuran (18)

The *title* compound was obtained in 31% yield, using the standard cross coupling procedure for 2-bromozinc benzofurans.

A mixture of 2-trimethylstannylbenzofuran (0.07g, 0.25mmol), η^6 -1,3-dimethoxy-5-iodobenzenetricarbonyl chromium (0) (0.098g, 0.25mmol), and Pd(PPh₃)₄ (29mg, 10mol%) in THF (20ml) was refluxed. The solution was filtered through a silica pad to remove the precipitated palladium metal, and water added. The mixture was extracted with ether, dried, and the solvent removed. Column chromatography of the product gave the *title* compound in 46% yield.

m. p. 138°C;

$\nu_{\max}$ (CHCl₃) 1966, 1892 cm⁻¹;

δ_{H} (CDCl₃) 3.85 (3H, s, OCH₃), 5.19 (1H, t, J = 1.9 Hz, H₄'), 5.45 (2H, d, J = 1.9

Hz, H_{2'} H_{6'}) 7.01 (1H, d, J = 0.6 Hz, H₃) 7.2-7.4 (2H, m, H₅ H₆), 7.5-7.6 (2H, m, H₄ H₇).

m/z 390 (M⁺), 334, 306 (100 %);

(Found C, 58.27%; H, 3.56%; C₁₉H₁₄O₆ requires C, 58.47%; H, 3.62%).

2-[3,5-Bis(triisopropylsiloxy)phenyl]benzofuran (20)

A mixture of 2-trimethylstannylbenzofuran (14) (0.059g, 0.21mmol), 1,3-bis(triisopropylsiloxy)-5-iodobenzene (0.106g, 0.19mmol) and Pd(PPh₃)₄ (10mg, 4mol%) in THF (30ml) was refluxed overnight. The solution was filtered through a silica pad to remove the palladium metal. The organic layer was then washed with water, dried, and the solvent evaporated to give a compound, which upon chromatography gave the *title* compound in 73% yield.

*v*_{max} (film) 2945, 2892, 2868, 2360, 2342, 1607, 1592, 1568, 1454, 1432, 1251, 1174 cm⁻¹;

δ_H (CDCl₃) 1.13 (36H, d, J = 7.2 Hz, CH(CH₃)₂), 1.30 (6H, m, J = 7.2 Hz, CH(CH₃)₂), 6.43 (1H, t, J = 2.2 Hz, H_{4'}), 6.94 (1H, d, J = 1.1 Hz, H₃), 7.0 (2H, d, J = 2.2 Hz, H_{2'} H_{6'}), 7.22 (1H, dd, J = 1.6, 7.6 Hz, H₄), 7.27 (1H, dt, J = 1.6, 7.6 Hz, H₅), 7.5-7.6 (2H, m, H₆ H₇);

m/z 538 (M⁺) 495 (100%);

(Found C, 71.12%; H, 9.63%; C₃₂H₅₀O₃Si₂ requires C, 71.32%; H, 9.35%).

2-(4-Anisyl)benzofuran

The reaction was carried out in THF, using the standard cross coupling procedure for 2-trimethylstannylbenzofuran (14), and the *title* compound was obtained in 30% yield.

m. p. 147-8°C;

*v*_{max} (nujol) 1611, 1505, 1464, 1378, 1308, 1249, 1181, 1112 cm⁻¹;

δ_H (CDCl₃) 3.87 (3H, s, OCH₃), 6.88 (1H, d, J = 0.7 Hz, H₃), 6.98 (2H, d, J = 9 Hz, H_{3'} H_{5'}), 7.22 (1H, dd, J = 1.8, 5.2 Hz, H₄), 7.24 (1H, dd, J = 1.8, 5.2 Hz, H₇), 7.47-7.58 (2H, m, H₅ H₆), 7.8 (2H, d, J = 9 Hz, H_{2'} H_{6'});

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%).

2-Trimethylsilyl-6-methoxybenzofuran (a), (23)

and 6-methoxy-7-trimethylsilylbenzofuran (b) (24)

To a solution of 6-methoxybenzofuran (0.296g, 2mmol) in THF (2ml) and ether (1ml), was added *n*-butyl lithium (1.3ml, 2mmol) and the reaction stirred at room temperature for 2 hours. Trimethylsilylchloride (0.5ml) was then added and the reaction stirred for 1 hour. Work up and extraction as usual gave, after drying and removal of solvent, the crude products in a 3.5:1 ratio. These were separated by chromatography to give the *title* compounds in 71% overall yield.

Compound (a):-

$\nu_{\max}$ ($CHCl_3$) 3149, 3116, 3009, 3053, 2899, 2836, 1593, 1538, 1462, 1440, 1398, 1382, 1338, 1308, 1243, 1206, 1151, 1144, 1130, 1075, 1031 cm^{-1} ;

δ_H ($CDCl_3$) 0.30 (9H, s, $Si(CH_3)_3$), 3.85 (3H, s, OCH_3), 6.84 (1H, dd, $J = 2.3, 8.6$ Hz, H_5), 6.88 (1H, d, $J = 0.8$ Hz, H_3), 7.04 (1H, bd, $J = 2.3$ Hz, H_7), 7.42 (1H, d, $J = 8.6$ Hz, H_4);

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%).

Compound (b):-

$\nu_{\max}$ (film) 2956, 2925, 2854, 1619, 1592, 1489, 1462, 1436, 1378, 1349, 1319, 1276, 1252, 1195, 1149, 1126, 1111, 1063, 1029 cm^{-1} ;

δ_H ($CDCl_3$) 0.20 (9H, s, $Si(CH_3)_3$), 3.85 (3H, s, OCH_3), 6.66 (1H, d, $J = 2.2$ Hz, H_3), 6.85 (1H, d, $J = 8.4$ Hz, H_5), 7.52 (1H, d, $J = 8.4$ Hz, H_4), 7.55 (1H, d, $J = 2.2$ Hz, H_2);

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-(*t*-Butyldiphenylsiloxy)benzofuran (25)*

To a solution of 6-hydroxybenzofuran (0.86g, 6.42mmol), and imidazole (1.1g, 16mmol) in DMF (5ml) was added *t*-butyldiphenylsilylchloride (1.9ml, 7.1mmol) and the reaction stirred at 50°C for 16 hours. Saturated sodium bicarbonate solution was added, and the mixture extracted with petrol. After drying, and evaporation of solvent, the resultant oil was distilled to give the *title* compound in 90% yield, which solidified on standing.

b. p. 210°C/0.15mmHg; m. p. 68°C;

$\nu_{\max}$ (nujol) 3071, 2926, 2856, 1621, 1485, 1467, 1429, 1290, 1199, 1155, 1114 cm^{-1} ;

δ_{H} (CDCl_3) 0.85 (9H, s, *t*Bu), 6.35 (1H, dd, $J = 1.1, 2.2$ Hz, H_3), 6.50 (1H, dd, $J = 2.3, 8.8$ Hz, H_5), 6.63 (1H, bd, $J = 2.3$ Hz, H_7), 7.02 (1H, d, $J = 8.8$ Hz, H_4), 7.20 (1H, d, $J = 2.2$ Hz, H_2), 7.05-7.18 (6H,m, Ph), 7.45-7.50 (4H,m, Ph);

m/z 372 (M^+), 315 (100 %);

(Found C, 77.12%; H, 6.45%; $\text{C}_{24}\text{H}_{24}\text{O}_2\text{Si}$ requires C, 77.38%; H, 6.49%).

*2-[η^6 -Phenyltricarbonyl chromium (0)]-6-*t*-butyldiphenylsiloxybenzofuran*

The *title* compound was obtained in 28% yield, using the standard cross coupling procedure for 2-bromozinc benzofurans.

m. p. 162-4°C;

$\nu_{\max}$ (CHCl_3) 1975, 1905 cm^{-1} ;

δ_{H} (CDCl_3) 1.10 (9H, s, *t*Bu), 5.30 (1H, t, $J = 6.2$ Hz, H_4'), 5.44 (2H, t, $J = 6.2$ Hz, H_3' H_5'), 5.83 (2H, d, $J = 6.2$ Hz, H_2' H_6'), 6.75 (1H, bd, $J = 8.4$ Hz, H_5), 6.80 (1H, s, H_3), 6.87 (1H, bs, H_7), 7.24 (1H, d, $J = 8.4$ Hz, H_4), 7.40 (6H, m, Ph), 7.74 (4H, m, Ph).

m/z 584 (M^+), 500 (100 %);

(Found accurate mass 584.1121, $\text{C}_{33}\text{H}_{28}\text{O}_5\text{SiCr}$ requires 584.1111).

2-[3,5-Bis(triisopropylsiloxy)phenyl]-6-t-butylidiphenylsiloxybenzofuran (27)

The reaction was carried out in THF using the standard procedure for 2-stannylbenzofurans, giving the *title* compound in 90% yield as a colourless oil.

$\nu_{\max}$ (CHCl₃) 3135, 3072, 3051, 3017, 2946, 2892, 2867, 1621, 1592, 1567, 1489, 1467, 1428, 1390, 1357, 1337, 1296, 1282, 1250, 1227, 1201, 1171, 1114, 1066, 1031, 1015, 1000 cm⁻¹;

δ_{H} (CDCl₃) 1.05-1.15 (45H, m, ^tBu₂CH(CH₃)₂), 1.2-1.4 (6H, m, CH(CH₃)₂), 6.37 (1H, t, J = 2.0 Hz, H_{4'}), 6.72 (1H, dd, J = 2.4, 8.1 Hz, H₅), 6.80 (1H, d, J = 0.8 Hz, H₃), 6.88 (2H, d, J = 2.0 Hz, H_{2'} H_{6'}), 6.94 (1H, bd, J = 2.4 Hz, H₇), 7.23 (1H, d, J = 8.1 Hz, H₄), 7.3-7.5 (10H, m, Ph);

m/z 749 (M⁺-iPr), 735 (100%);

(Found C, 72.77%; H, 8.65%; C₄₈H₆₈O₄Si₃ requires C, 72.67%; H, 8.64%).

Moracin M

To a solution of compound (27) (0.207g, 0.26mmol) in THF (10ml) was added a solution of tetrabutylammonium fluoride (0.8ml, 0.8mmol) and the reaction stirred overnight. Evaporation of solvent was followed by addition of aqueous acetic acid, and extraction with ethyl acetate. After drying, and removal of solvent, the compound was chromatographed to give the *title* compound in 86% yield.

m. p. 259-62°C (lit⁸⁵ 262°C);

$\nu_{\max}$ (nujol) 3274, 2925, 2854, 1614, 1579, 1464, 1378, 1294, 1143, 1123 cm⁻¹;

δ_{H} (d⁶-acetone, 500MHz) 3.5 (1H, bs, OH), 6.38 (1H, t, J = 2.4 Hz, H_{4'}), 6.81 (1H, dd, J = 2.1, 8.3 Hz, H₅), 6.87 (2H, d, J = 2.4 Hz, H_{2'} H_{6'}), 6.98 (1H, bd, J = 2.1 Hz, H₇), 7.02 (1H, d, J = 0.9 Hz, H₃), 7.40 (1H, d, J = 8.3 Hz, H₄), 8.50 (2H, bs, OH);

m/z 242 (M⁺) (100%).

2-(4-Anisyl)-6-hydroxybenzofuran

The reaction was carried in THF, using the standard cross coupling procedure for 2-trimethylstannylbenzofurans. This was followed by addition of TBAF to remove the silicon protecting group. Work up and extraction as usual gave the *title* compound in 40% yield.

m. p. 205-7°C ;

$\nu_{\max}$ (Nujol) 3293, 3027, 3009, 1622, 1507, 1489, 1465, 1442, 1420, 1358, 1303, 1272, 1251, 1212, 1177, 1148, 1113, 1040, 1024, 1008 cm^{-1} ;

δ_{H} (CDCl_3) 3.86 (3H, s, OCH_3), 4.82 (1H, bs, OH), 6.76 (1H, dd, $J = 2.2, 8.5$ Hz, H_5), 6.80 (1H, d, $J = 0.8$ Hz, H_3), 6.96 (2H, d, $J = 9.0$ Hz, H_3' H_5'), 7.00 (1H, bd, $J = 2.2$ Hz, H_7), 7.37 (1H, d, $J = 8.5$ Hz, H_4), 7.74 (2H, d, $J = 9$ Hz, H_2' H_6');

m/z 240 (M^+), 225.

*2-[η^6 -3,5-Dimethoxyphenyltricarbonyl chromium (0)]6-*t*-butyldiphenylsiloxy benzofuran (28)*

The reaction was carried out using the standard cross coupling procedure for 2-stannylbenzofurans, in refluxing benzene to give the *title* compound in 54% yield.

m. p. 163°C;

$\nu_{\max}$ (CHCl_3) 1965, 1891 cm^{-1} ;

δ_{H} (CDCl_3) 1.12 (9H, s, tBu), 3.82 (6H, s, OCH_3), 5.11 (1H, t, $J = 1.8$ Hz, H_2'), 5.31 (2H, d, $J = 1.8$ Hz, H_4' H_6'), 6.75 (1H, dd, $J = 2.0, 8.5$ Hz, H_5), 6.83 (1H, d, $J = 1.0$ Hz, H_3), 6.87 (1H, bd, $J = 2.0$ Hz, H_7), 7.26 (1H, d, $J = 8.5$ Hz, H_4), 7.3-7.8 (10H, m, Ph);

m/z 560 ($\text{M}^+ - 3\text{CO}$), 508;

(Found C, 65.23%; H, 5.00%; $\text{C}_{35}\text{H}_{32}\text{O}_7\text{SiCr}$ requires C, 65.20%; H, 5.00%).

*2-(3,5-Dimethoxyphenyl)-6-*t*-butyldiphenylsiloxybenzofuran*

The reaction was carried out using the standard cross coupling procedure for 2-stannylbenzofurans, in refluxing benzene to give the *title* compound in 70% yield.

m. p. 126-7°C;

$\nu_{\max}$ (CHCl₃) 3074, 3009, 2962, 2934, 2860, 1601, 1573, 1488, 1475, 1430, 1393, 1352, 1331, 1311, 1297, 1280, 1258, 1223, 1220, 1216, 1213, 1207, 1156, 1114, 1066, 1036 cm⁻¹;

δ_{H} (CDCl₃) 1.10 (9H, s, ^{*t*}Bu), 3.82 (6H, s, OCH₃), 6.41 (1H, t, J = 2.2 Hz, H_{4'}), 6.68 (1H, dd, J = 2.2, 8.0 Hz, H₅), 6.83 (1H, d, J = 0.7 Hz, H₃), 6.85 (3H, d, J = 2.2 Hz, H_{2'} H_{6'} H₇), 7.24 (1H, d, J = 8.0 Hz, H₄), 7.3-7.5 (6H, m, Ph), 7.7-7.8 (4H, m, Ph);

m/z 508 (M⁺), 451 (100%);

(Found C, 75.42%; H, 6.46%; C₃₂H₃₂O₄Si requires C, 75.56%; H, 6.34%).

η^6 -1,3-Dimethoxybenzenetricarbonyl chromium (0)

Refluxing a solution of 1,3-dimethoxybenzene for 48 hours, using the standard complexation procedure, gave the *title* compound in 50% yield.

m. p. 120-1°C;

$\nu_{\max}$ (CHCl₃) 1965, 1880 cm⁻¹;

δ_{H} (CDCl₃) 3.73 (6H, s, OCH₃), 4.83 (2H, dd, J = 2.1, 7.1 Hz, H₄ H₆), 5.14 (1H, t, J = 2.1 Hz, H₂), 5.59 (1H, t, J = 7.1 Hz, H₅);

m/z 274(M⁺), 218, 190 (100%);

(Found C, 48.28%; H, 3.59%; C₁₁H₁₀O₅Cr requires C, 48.19%; H, 3.68%).

η^6 -1,3-Dimethoxy-2-trimethylsilylbenzenetricarbonyl chromium (0)

To a solution of η^6 -1,3-dimethoxybenzenetricarbonyl chromium (0) (0.274g, 1mmol) in THF (35ml) at -78°C, was added *n*-butyl lithium (1.1mmol) and the reaction stirred for 1 hour. Trimethylsilylchloride (0.2ml) was then added, and

the reaction stirred for 10 minutes, before allowing to warm to room temperature. Work up and extraction as usual, gave after drying, removal of solvent and subsequent chromatography, the *title* compound in 70% yield.

m. p. 139°C;

$\nu_{\max}$ (CHCl₃) 1960, 1875 cm⁻¹;

δ_{H} (CDCl₃) 0.32 (9H, s, Si(CH₃)₃), 3.68 (6H, s, OCH₃), 4.70 (2H, d, J = 7.2 Hz, H₄ H₆), 5.72 (1H, t, J = 7.2 Hz, H₅);

m/z 346(M⁺), 290, 262 (100 %);

(Found C, 48.48%; H, 5.25%; C₁₄H₁₈O₅SiCr requires C, 48.55%; H, 5.24%).

η^6 -1,3-Dimethoxy-2-prenylbenzenetricarbonyl chromium (0)

η^6 -1,3-Dimethoxybenzenetricarbonyl chromium (0) (0.274g, 1mmol) was lithiated as before. CuBr. SMe₂ (0.206g, 1mmol) was added and the reaction stirred at -20°C for 1 hour. Prenyl bromide (0.2ml) was then added and the reaction stirred at -20°C for a further 2 hours, and then at room temperature overnight. Work up and extraction as usual, followed by removal of solvent, drying, and subsequent chromatography, gave the *title* compound in 32% yield.

m. p. 103°C;

$\nu_{\max}$ (CHCl₃) 1960, 1880 cm⁻¹;

δ_{H} (CDCl₃, 90MHz) 1.70 (6H, bs, CH₃), 3.23 (2H,d, J = 8 Hz, ArCH₂CH), 3.80 (6H, s, OCH₃), 4.80 (2H, d, J = 7 Hz, H₄ H₆), 5.18 (1H, bt, J = 8 Hz, ArCH₂CH), 5.54 (1H, t, J = 7 Hz, H₅);

m/z 342(M⁺), 286, 258 (100 %);

(Found C, 55.96%; H, 5.30%; C₁₆H₁₈O₅Cr requires C, 56.14%; H, 5.35%).

2-[η^6 -3,5-Dimethoxy-4-trimethylsilylphenyltricarbonyl chromium (0)]6-*t*-butyldiphenylsiloxybenzofuran (29)

To a solution of complex (28) (0.644g, 1mmol) in THF (35ml) at -78°C, was added *n*-butyl lithium (0.7ml, 1mmol), and the reaction stirred for 1 hour.

Trimethylsilylchloride (0.5ml) was then added, and the reaction stirred for a further hour. After allowing to warm to room temperature, work up and extraction was carried out as usual. After drying, and removal of solvent, the compound was chromatographed to give the *title* compound in 80% yield.

m. p. 184-5°C (decomposes);

$\nu_{\max}$ (CHCl₃) 1960, 1887 cm⁻¹;

δ_{H} (CDCl₃) 0.35 (9H, s, Si(CH₃)₃), 1.10 (9H, s, ^tBu), 3.75 (6H, s, OCH₃), 5.20 (2H, s, H_{2'} H_{6'}), 6.76 (1H, dd, J = 2.3, 8.5 Hz, H₅), 6.86 (1H, bs, H₃), 6.89 (1H, bd, J = 2.3 Hz, H₇), 7.26 (1H, d, J = 8.5 Hz, H₄), 7.3-7.8 (10H, m, Ph);

m/z 716 (M⁺), 632 (100%);

(Found C, 63.45%; H, 5.63%; C₃₈H₄₀O₇Si₂Cr requires C, 63.67%; H, 5.62%).

*2-[η^6 -3,5-Dimethoxy-4-prenylphenyltricarboxylchromium(0)]-6-*t*-butyldiphenylsiloxybenzofuran (30)*

To a solution of the complex (28) (0.322g, 0.5mmol) in THF (20ml) at -78°C, was added *n*-butyl lithium (0.3ml, 0.5mmol) and the reaction stirred for 1 hour. CuBr. SMe₂ (0.103, 0.5mmol) was added, and the reaction stirred at -20°C for 1 hour. Prenyl bromide (0.1ml), was then added and the reaction stirred at -20°C for a further 2 hours, after which the reaction was allowed to warm to room temperature and stir overnight. Work up and extraction as usual, followed by drying and removal of solvent, gave after chromatography, the *title* compound in 60% yield.

m. p. 166-7°C;

$\nu_{\max}$ (CHCl₃) 1959, 1886 cm⁻¹;

δ_{H} (CDCl₃) 1.12 (9H, s, ^tBu), 1.70 (3H, s, CH₃), 1.75 (3H, s, CH₃), 3.25 (2H, d, J = 8 Hz, ArCH₂), 3.91 (6H, s, OCH₃), 5.15 (1H, t, J = 8 Hz, CH), 5.29 (2H, s, H_{2'} H_{6'}), 6.78 (1H, dd, J = 2.2, 8.4 Hz, H₅), 6.86 (1H, bs, H₃), 6.90 (1H, bd, J = 2.2 Hz, H₇), 7.28 (1H, d, J = 8.4 Hz, H₄), 7.35-7.76 (10H, m, Ph);

m/z 712 (M⁺), 628, 576 (100%);

(Found C, 67.43%; H, 5.76%; C₄₀H₄₀O₇SiCr requires C, 67.40%; H, 5.66%).

2-[3,5-Dimethoxy-4-prenylphenyl]-6-t-butylidiphenylsiloxybenzofuran (31)

A solution of the complex (30) in dichloromethane was shaken with excess iodine for a few minutes. Sodium metabisulphite solution was then added to remove excess iodine. The dichloromethane layer was separated, dried, and the solvent removed, to give an oil which was chromatographed. The resulting oil on addition of petrol caused crystallization, to give a white solid of the *title* compound.

m. p. 135-7°C;

$\nu_{\max}$ (CHCl₃) 3071, 2955, 2925, 2855, 1622, 1596, 1570, 1486, 1455, 1428, 1412, 1377, 1348, 1322, 1297, 1278, 1249, 1228, 1207 cm⁻¹;

δ_{H} (CDCl₃) 1.10 (9H, s, ^tBu), 1.64 (3H, s, CH₃), 1.75 (3H, s, CH₃), 3.33 (2H, d, J = 7.7 Hz, ArCH₂); 3.86 (6H, s, OCH₃), 5.15 (1H, t, J = 7.7 Hz, CH), 6.74 (1H, dd, J = 2.25, 8.5 Hz, H₅), 6.83 (1H, d, J = 1 Hz, H₃), 6.90 (3H, bs, H₇ H₂' H₆'), 7.24 (1H, d, J = 8.5 Hz, H₄), 7.3-7.8 (10H, m, Ph);

m/z 576 (M⁺);

(Found C, 76.92%; H, 7.08%; C₃₇H₄₀O₄Si requires C, 77.05%; H, 6.99%).

Moracin C

To a solution of diphenylphosphine (0.186g, 0.17ml, 1mmol) in THF (3ml) at 0°C, was added *n*-butyl lithium, and the reaction stirred at room temperature for 1 hour. To the resulting red solution was added the moracin C derivative (31) (0.100g, 0.17mmol), and the reaction refluxed overnight. 10% Sodium hydroxide solution was added, and the mixture extracted with ether. To the sodium hydroxide extracts was added 2N hydrochloric acid, until the solution was just acidic. The aqueous layer was then extracted with ethyl acetate, the extracts dried, and the solvent removed to give a mixture of silylated and desilylated compounds. This mixture was dissolved in THF, and TBAF (1ml, 1mmol) added, and the reaction stirred overnight. Addition of acetic acid, followed by extraction into ethyl acetate, gave after removal of solvent and chromatography, the *title* compound in 50% yield.

m. p. 197-9°C (lit⁸⁶ 199°C);

$\nu_{\max}$ (Nujol) 3235, 2927, 2727, 1621, 1602, 1580, 1550, 1514, 1502, 1301, 1288, 1226, 1201, 1162, 1145, 1117 cm^{-1} ;

δ_{H} (d^6 -acetone, 500 MHz) 1.63 (3H, s, CH_3), 1.76 (3H, s, CH_3), 3.37 (2H, d, $J = 7$ Hz, ArCH_2), 5.30 (1H, t, $J = 7$ Hz, CH), 6.78 (1H, dd, $J = 2.0, 8.5$ Hz, H_5), 6.88 (1H, d, $J = 0.7$ Hz, H_3), 6.90 (2H, s, H_2' H_6'), 6.94 (1H, bd, $J = 2.0$ Hz, H_7), 7.37 (1H, d, $J = 8.5$ Hz, H_4), 8.3 (2H, s, OH), 8.5 (1H, s, OH);

m/z 310 (M^+) (100%), 295, 255.

2-(3,5-Dimethoxyphenyl)-3-geranyl-6-hydroxybenzofuran (32)

To a solution of complex (29) (0.358g, 0.5mmol), in THF (20ml), at -78°C , was added *n*-butyl lithium (0.35ml, 1.1eq), and the reaction stirred for 1 hour. $\text{CuBr} \cdot \text{SMe}_2$ (0.103g, 0.5mmol) was then added and the reaction stirred at -20°C for 1 hour. Geranyl bromide (0.2ml) was added, and the reaction stirred for a further 2 hours at -20°C before allowing to warm to room temperature and stirred overnight. Work up and extraction as usual gave, after drying, and evaporation of solvent, an orange oil. This oil was taken up in THF (5ml), and tetrabutylammonium fluoride (2 eq) added, and the reaction left to stir overnight. Work up and extraction with dichloromethane was carried out. The dichloromethane extracts were left exposed to air until decomplexation had occurred, and the resulting solution was filtered through a silica pad. The solvent was evaporated to give an oil, which upon preparative thin layer chromatography gave the *title* compound in 67% overall yield.

$\nu_{\max}$ (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, CH_3), 1.63 (3H, s, CH_3), 1.71 (2H, m, CH_2), 1.8 (3H, s, CH_3), 2.0 (2H, m, CH_2), 3.57 (2H, d, $J = 7.7$ Hz, ArCH_2), 5.06 (1H, bt, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 5.29 (1H, bt, $J = 7.7$ Hz, ArCH_2CH), 6.46 (1H, t, $J = 2.25$ Hz, H_4'), 6.77 (1H, dd, $J = 2.0, 8.0$ Hz, H_5), 6.88 (2H, d, $J = 2.25$ Hz, H_2' H_6'), 6.97 (1H, d, $J = 2.0$ Hz, H_7), 7.35 (1H, d, $J = 8.0$ Hz, H_4);

m/z 406 (M^+);

(Found accurate mass, 406.2153; $\text{C}_{26}\text{H}_{30}\text{O}_4$ requires 406.2144).

1-Trisopropylsiloxy-3-methoxybenzene (34)

To a solution of 3-methoxyphenol (2.48g, 20mmol) and imidazole (3.4g, 50mmol) in DMF (5ml), was added triisopropylsilylchloride (4.23g, 4.7ml, 22mmol), and the reaction stirred overnight. Saturated sodium bicarbonate solution was added and the mixture extracted with petrol. The petrol extracts were washed successively with 2M NaOH and water. After drying and removal of solvent, the resulting oil was distilled to give the *title* compound in 90% yield.

b. p. 92°C/0.06mbar;

$\nu_{\max}$ (film) 2947, 2893, 2868, 1601, 1493 cm^{-1} ;

δ_{H} (CDCl_3) 1.10 (18H, d, $J = 7 \text{ Hz}$, $\text{CH}(\text{CH}_3)_2$), 1.25 (3H, m, $J = 7 \text{ Hz}$, $\text{CH}(\text{CH}_3)_2$), 3.77 (3H, s, OCH_3), 6.45 (1H, t, $J = 2.2 \text{ Hz}$, H_2), 6.49 (2H, m, $J = 2.2, 7.8 \text{ Hz}$, H_4 , H_6), 7.11 (1H, t, $J = 7.8 \text{ Hz}$, H_5);

m/z 280 (M^+), 237 (100%);

(Found C, 68.61%; H, 10.35%; $\text{C}_{16}\text{H}_{28}\text{O}_2\text{Si}$ requires C, 68.52%; H, 10.06%).

η^6 -1-Trisopropylsiloxy-3-methoxybenzenetricarbonyl chromium (0) (35)

The *title* compound was made from the corresponding arene, using the standard complexation procedure, in 90% yield.

m. p. 82-3°C;

$\nu_{\max}$ (CHCl_3) 1967, 1889 cm^{-1} ;

δ_{H} (CDCl_3) 1.07 (18H, d, $J = 7.5 \text{ Hz}$, CH_3), 1.13-1.30 (3H, m, $J = 7.5 \text{ Hz}$, CH), 3.71 (3H, s, OCH_3), 4.74 (1H, ddd, $J = 0.75, 1.88, 6.75 \text{ Hz}$, H_6), 4.79 (1H, ddd, $J = 0.75, 1.88, 6.75 \text{ Hz}$, H_4), 5.15 (1H, t, $J = 1.88 \text{ Hz}$, H_2), 5.52 (1H, t, $J = 6.75 \text{ Hz}$, H_5);

m/z 416 (M^+), 360, 332 (100%);

(Found C, 54.93%; H, 6.77%; $\text{C}_{19}\text{H}_{28}\text{O}_5\text{SiCr}$ requires C, 54.79%; H, 6.78%).

η^6 -1-Prenyloxy-2-triisopropylsilyl-3-methoxybenzenetricarbonyl chromium (0)
(37)

To a solution of η^6 -1-triisopropylsiloxy-3-methoxybenzenetricarbonyl chromium (0) (0.832g, 2mmol) in THF (50ml) at -78°C , was added *n*-butyl lithium (1.2ml, 2mmol) and the reaction stirred for 1 hour. CuBr. SMe₂ (0.412, 2mmol) was then added and the reaction stirred at -20°C for 1 hour. Prenyl bromide (0.4ml) was added and the reaction stirred for a further 2 hours at -20°C , before allowing to warm to room temperature and stirred overnight. Work up and extraction as usual, gave after chromatography the *title* compound in 30% yield.

m. p. $123-7^\circ\text{C}$;

ν_{max} (CHCl₃) 1958, 1880 cm^{-1} ;

δ_{H} (CDCl₃) 1.10 (9H, d, $J = 7.8$ Hz, CH₃), 1.20 (9H, d, $J = 7.8$ Hz, CH₃), 1.50 (3H, s, CH₃), 1.55 (3H, s, CH₃), 1.57 (3H, m, $J = 7.8$ Hz, CH), 3.62 (3H, s, OCH₃), 4.66 (1H, d, $J = 6.8$ Hz, H₄), 5.04 (1H, d, $J = 6.8$ Hz, H₆) 5.19 (1H, d, $J = 18$ Hz, OCH₂), 5.21 (1H, d, $J = 11$ Hz, OCH₂), 5.68 (1H, t, $J = 6.8$ Hz, H₅), 6.27 (1H, dd, $J = 11, 18$ Hz, CH);

m/z 484 (M⁺), 400, 288, 237 (100%);

(Found C, 59.18%; H, 7.52%; C₂₄H₃₆O₅Si Cr requires C, 59.48%; H, 7.49%).

η^6 -1-Prenyloxy-2-triisopropylsilyl-3-methoxy-4-iodobenzenetricarbonyl chromium(0)

To a solution of η^6 -1-prenyloxy-2-triisopropylsilyl-3-methoxybenzene tricarbonyl chromium (0) (0.242g, 0.5mmol) in THF (20ml) at -78°C , was added *n*-butyl lithium (0.6ml, 1mmol), and the reaction stirred for 1 hour. Iodine (0.254g, 1mmol) was then added and the reaction stirred for 1 hour before allowing to warm to room temperature. Sodium metabisulphite solution was immediately added, and the mixture extracted with ether. The ether extracts were washed with water, dried, and the solvent evaporated to give the crude compound, which upon chromatography gave the *title* compound in 76% yield.

m. p. $128-30^\circ\text{C}$ (decomposes);

ν_{max} (CHCl₃) 1964, 1892 cm^{-1} ;

δ_{H} (CDCl_3) 1.2 (9H, d, $J = 7.5$ Hz), 1.24 (9H, d, $J = 7.5$ Hz), 1.6 (3H, s), 1.65 (3H, s), 1.66 (3H, m, $J = 7.5$ Hz), 3.97 (3H, s) 5.0 (1H, d, $J = 7.2$ Hz), 5.22 (1H, d, $J = 18.8$ Hz), 5.24 (1H, d, $J = 11.3$ Hz), 6.02 (1H, d, $J = 7.2$ Hz), 6.14 (1H, dd, $J = 11.3, 18.8$ Hz);

m/z 610 (M^+);

(Found C, 47.06%; H, 5.78%; $\text{C}_{24}\text{H}_{35}\text{O}_5\text{SiCr}$ requires C, 47.22%; H, 5.78%).

η^6 -1-triisopropylsiloxy-2-triisopropylsilyl-3-methoxybenzenetricarbonyl chromium (0) (39)

To a solution of η^6 -1-triisopropylsiloxy-3-methoxytricarbonyl chromium (0) (0.416g, 1mmol) in THF (35ml) at -78°C , was added *n*-butyl lithium (0.7ml, 1.1mmol) and the reaction stirred for 1 hour. Triisopropylsilylchloride (0.43ml, 2mmol) was then added and the reaction stirred at -78°C for a 1 hour, and then a further hour at room temperature. Work up and extraction as usual, followed by removal of solvent and subsequent chromatography, gave the *title* compound in 78% yield.

m. p. $155-7^\circ\text{C}$ (decomposes);

ν_{max} (CHCl_3) 1959, 1883 cm^{-1} ;

δ_{H} (CDCl_3) 1.1-1.4 (39H, m, iPr_3), 1.57 (3H, m, CH), 3.66 (3H, s, OCH_3), 4.71 (1H, d, $J = 6.6$ Hz, H_6), 4.73 (1H, d, $J = 6.6$ Hz, H_4), 5.7 (1H, t, $J = 6.6$ Hz, H_5).

m/z 572 (M^+), 488, 446 (100%);

(Found C, 58.61%; H, 8.64%; $\text{C}_{28}\text{H}_{48}\text{O}_5\text{Si}_2\text{Cr}$ requires C, 58.71%; H, 8.45%).

η^6 -1-triisopropylsiloxy-2-triisopropylsilyl-3-methoxy-4-prenylbenzene tricarbonyl chromium (0) (40)

To a solution of η^6 -1-triisopropylsiloxy-3-methoxytricarbonyl chromium (0) (0.416g, 1mmol) in THF (35ml) at -78°C , was added *n*-butyl lithium (0.7ml, 1mmol), and the reaction stirred for 1 hour. Triisopropylsilylchloride (0.23ml, 1mmol) was then added and the reaction stirred at -78°C for 1 hour, and then at room temperature for a further hour. The reaction was recooled to -78°C , and

n-butyl lithium (0.7ml, 1mmol) was added. After stirring for 1 hour, CuBr. SMe₂ (0.206g, 1mmol) was added, and the reaction stirred at -20°C for 1 hour. Prenyl bromide (0.3ml) was added, and the reaction stirred for 2 hours at this temperature, and then at room temperature overnight. Work up and extraction as usual, followed by drying, removal of solvent, and chromatography gave the *title* compound in 51% yield.

m. p. 144°C;

$\nu_{\max}$ (CHCl₃) 1958, 1882 cm⁻¹;

δ_{H} (CDCl₃) 1.1-1.35 (39H, m, ⁱPr₃), 1.6 (3H, m, CH), 1.72 (3H, s, CH₃), 1.82 (3H, s, CH₃), 3.04 (1H, dd, J = 6.9, 16 Hz, ArCH₂), 3.20 (1H, dd, J = 7.5, 16 Hz, ArCH₂), 3.84 (3H, s, OCH₃), 4.74 (1H, d, J = 6.8 Hz, H₆), 5.24 (1H, bt, J = 7 Hz, CH), 5.57 (1H, d, J = 6.8 Hz, H₅);

m/z 640 (M⁺), 556, 514 (100%);

(Found C, 61.71%; H, 8.91%; C₃₃H₅₆O₅Si₂Cr requires C, 61.84%; H, 8.81%).

1-Trimethylsiloxy-3-methoxybenzene

To a solution of 3-methoxyphenol (2.48g, 20mmol) and imidazole (3.4g, 50mmol) in DMF (5ml) at 0°C, was added trimethylsilylchloride (2.4g, 2.8ml, 20mmol) and the reaction stirred overnight. Work up and extraction as before, followed by drying, and removal of solvent gave the *title* compound in 90% yield.

$\nu_{\max}$ (film) 1603, 1490, 1289, 1196, 1153, 1044, 959, 866 cm⁻¹;

δ_{H} (CDCl₃) 0.24 (9H, s, SiMe₃), 3.75 (3H, s, OCH₃), 6.43 (1H, t, J = 2.4 Hz, H₂), 6.47 (1H, ddd, J = 0.8, 2.4, 8.9 Hz, H₆), 6.55 (1H, ddd, J = 0.8, 2.4, 8.9 Hz, H₄), 7.13 (1H, t, J = 8.9 Hz, H₅);

m/z 196 (M⁺), 181 (100%);

(Found C, 61.18%; H, 8.21%; C₁₀H₁₆O₂Si requires C, 60.96%; H, 8.31%).

1-t-Butyldimethylsiloxy-3,5-dimethoxy-4-prenylbenzene (45)

To a solution of 1,3-dimethoxy-5-*t*-butyldimethylsiloxybenzene (1.072g, 4mmol) in THF (4ml) and ether (2ml) at 0°C, was added *n*-butyl lithium (2.5ml, 4mmol), and the reaction stirred at room temperature for 3 hours. After recooling to 0°C, CuBr. SMe₂ (0.824g, 4mmol) was added and the reaction stirred for 1 hour. To the resulting black solution was added prenyl bromide (0.5ml, 4mmol) and the reaction stirred at 0°C for 2 hours, then at room temperature overnight. Work up and extraction as usual, gave after drying and removal of solvent, the crude material, which was chromatographed to give the *title* compound in 76% yield.

m. p. 64-6°C;

$\nu_{\max}$ (CHCl₃) 2926, 2855, 1587, 1492, 1460, 1413, 1377, 1362, 1337, 1254, 1219, 1200, 1184, 1164, 1117, 1098, 1047, 1017, 1007 cm⁻¹;

δ_{H} (CDCl₃) 0.20 (6H, s, Si(CH₃)₂), 0.98 (9H, s, ^tBu), 1.65 (3H, s, CH₃), 1.75 (3H, s, CH₃), 3.25 (2H, bd, J = 6.8 Hz, ArCH₂), 3.74 (6H, s, OCH₃), 5.15 (1H, bt, J = 6.8 Hz, ArCH₂CH), 6.05 (2H, s, H₂ H₆);

m/z 336 (M⁺), 321 (100%), 279, 268;

(Found C, 67.83%; H, 9.63%; C₁₉H₃₂O₃Si requires C, 67.81%; H, 9.58%).

1-t-Butyldimethylsiloxy-3-methoxy-4-prenyl-5-hydroxybenzene (46)

To a solution of diphenylphosphine (0.36ml, 2mmol) in THF (10ml) at 0°C, was added *n*-butyl lithium (1.25ml, 2mmol), and the reaction stirred at room temperature for 1 hour. 1-*t*-butyldimethylsiloxy-3,5-dimethoxy-4-prenylbenzene (0.672g, 2mmol) in THF was then added, and the reaction refluxed overnight. Work up and extraction as usual gave, after drying, removal of solvent and chromatography, the *title* compound in 50% yield.

m. p. 53-4°C;

$\nu_{\max}$ (CHCl₃) 3408, 3007, 2959, 2932, 2859, 1618, 1588, 1499, 1465, 1452, 1354, 1256, 1220, 1216, 1212, 1154, 1094, 1026, 970, 904 cm⁻¹;

δ_{H} (CDCl₃) 0.20 (6H, s, Si(CH₃)₂), 0.98 (9H, s, ^tBu), 1.73 (3H, bs, CH₃), 1.79 (3H,

bs, CH₃), 3.32 (2H, bd, J = 7.1 Hz, ArCH₂), 3.75 (3H, s, OCH₃), 5.22 (1H, bt, J = 7.1 Hz, ArCH₂CH), 6.00 (2H, s, H₂ H₆);
m/z 322 (M⁺) (100%), 307, 265, 254;
(Found C, 67.18%; H, 9.39%; C₁₈H₃₀O₃Si requires C, 67.03%; H, 9.38%).

1-t-Butyldimethylsiloxy-3-methoxy-4-prenyl-5-trifluoromethanesulphonyloxybenzene (47)

To a solution of 1-t-butyldimethylsiloxy-3-methoxy-4-prenyl-5-hydroxybenzene (46) (0.281g, 0.87mmol) in pyridine (3ml) at 0°C, was added triflic anhydride (0.16ml, 0.96mmol) and the reaction stirred at 0°C for 5 minutes, before allowing to warm to room temperature and stirred overnight. Saturated sodium bicarbonate solution was added, and the mixture extracted with ether. After drying, removal of solvent, and subsequent chromatography, the *title* compound was obtained in 96% yield.

ν_{max} (film) 2959, 2933, 2861, 2359, 1620, 1579, 1495, 1455, 1420, 1364, 1336, 1290, 1247, 1213, 1168, 1143, 1100, 1062, 1024 cm⁻¹;
 δ_{H} (CDCl₃) 0.21 (6H, s, Si(CH₃)₂), 0.97 (9H, s, ^tBu), 1.67 (3H, bs, CH₃), 1.73 (3H, bs, CH₃), 3.30 (2H, d, J = 7.1 Hz, ArCH₂), 3.80 (3H, s, OCH₃), 5.09 (1H, bt, J = 7.1 Hz, ArCH₂CH), 6.35 (1H, d, J = 2.2 Hz, H₂), 6.37 (1H, d, J = 2.2 Hz, H₆);
m/z 454 (M⁺) (100%), 439, 397, 383;
(Found C, 50.40%; H, 6.46%; C₁₉H₂₉O₅F₃SSi requires C, 50.20%; H, 6.43%).

2-(3-t-Butyldimethylsiloxy-5-methoxy-6-prenylphenyl)benzofuran (48)

To a mixture of the aryl triflate (47) (0.109g, 0.24mmol), lithium chloride (0.03g, 0.72mmol), and Pd(PPh₃)₄ (0.011g, 4mol%) in dioxan (3ml) was added a solution of 2-trimethylstannylbenzofuran (14) (0.073g, 0.26mmol) in dioxan, and the mixture refluxed overnight. Saturated sodium bicarbonate solution was added and the mixture extracted with ether. After drying, removal of solvent, and subsequent chromatography, the *title* compound was obtained in 91% yield.

ν_{max} (CHCl₃) 3056, 2957, 2932, 1891, 1603, 1577, 1456, 1408, 1375, 1351,

1337, 1304, 1250, 1192, 1162, 1117, 1097, 1047, 1002 cm⁻¹;

δ_{H} (CDCl₃) 0.15 (6H, s, Si(CH₃)₂), 0.93 (9H, s, ^tBu), 1.60 (6H, bs, CH₃), 3.42 (2H, bd, J = 7.1 Hz, ArCH₂), 3.75 (3H, s, OCH₃), 5.12 (1H, bt, J = 7.1 Hz, ArCH₂CH), 6.38 (1H, d, J = 2.2 Hz, H₄'), 6.74 (1H, d, J = 0.9 Hz, H₃), 6.75 (1H, d, J = 2.2 Hz, H₂'), 7.15-7.27 (2H, m), 7.41-7.53 (2H, m);

m/z 422 (M⁺) (100%), 407, 379, 365;

(Found accurate mass, 422.2283; C₂₆H₃₄O₃Si requires 422.2277).

*2-(3-*t*-Butyldimethylsiloxy-5-methoxy-6-prenylphenyl)-6-*t*-butyldiphenylsiloxybenzofuran (49)*

To a solution of 6-*t*-butyldiphenylsiloxybenzofuran (0.58g, 1.56mmol) in ether (2ml) at -10°C, was added *n*-butyl lithium (0.95ml, 1.6mmol), and the reaction stirred for 2 hours. Trimethyltinchloride (0.32g, 1.6mmol) in ether was then added and the reaction stirred at room temperature for 1 hour. This was then added to a mixture of the aryl triflate (47) (0.354g, 0.78mmol), lithium chloride (0.066g, 1.56mmol), and Pd(PPh₃)₄ (0.03g, 4mol%). The ether was removed by blowing nitrogen through the solution, and dioxan (10ml) added. The solution was then refluxed overnight. Work up and extraction as usual, followed by drying, removal of solvent, and subsequent chromatography, gave the *title* compound in 84% yield.

m. p. 109-10°C;

ν_{max} (Nujol) 2955, 2926, 2855, 1622, 1607, 1580, 1488, 1462, 1428, 1378, 1358, 1336, 1291, 1280, 1249, 1199, 1158, 1125, 1114, 1048, 1003 cm⁻¹;

δ_{H} (CDCl₃) 0.20 (6H, s, Si(CH₃)₂), 0.98 (9H, s, ^tBu), 1.12 (9H, s, ^tBu), 1.60 (3H, s, CH₃), 1.68 (3H, s, CH₃), 3.43 (2H, bd, J = 5.4 Hz, ArCH₂), 3.78 (3H, s, OCH₃), 5.14 (1H, bt, J = 5.4 Hz, ArCH₂CH), 6.39 (1H, d, J = 2.4 Hz, H₄'), 6.66 (1H, d, J = 0.8 Hz, H₃), 6.73 (1H, d, J = 2.4 Hz, H₂'), 6.74 (1H, dd, J = 2.1, 8.3 Hz, H₅), 6.90 (1H, bd, J = 2.1 Hz, H₇), 7.26 (1H, d, J = 8.3 Hz, H₄), 7.35-7.45 (6H, m, Ph), 7.73-7.77 (4H, m, Ph);

m/z 676 (M⁺) (100%), 661, 619, 563;

(Found C, 74.60%; H, 7.87%; C₄₂H₅₂O₄Si₂ requires C, 74.51%; H, 7.74%).

Moracin I

To a solution of 2-(3-*t*-butyldimethylsiloxy-5-methoxy-6-prenylphenyl)-6-*t*-butyldiphenylsiloxybenzofuran (49) (0.39g, 0.58mmol) in THF (10ml) was added a solution of TBAF (1.5ml, 1.5mmol), and the reaction left to stir overnight. Ammonium chloride solution was added and the mixture extracted with ethyl acetate. After drying and removal of solvent, a waxy oil was obtained. Addition of toluene induced crystallisation, to afford the *title* compound in 96% yield.

m. p. 139-40°C;

$\nu_{\max}$ (Nujol) 3304, 2925, 2854, 1620, 1590, 1487, 1462, 1378, 1283, 1206, 1181, 1154, 1117, 1041, 984 cm^{-1} ;

δ (d^6 -acetone, 500 MHz) 1.64 (3H, s, CH_3), 1.68 (3H, s, CH_3), 3.47 (2H, d, $J = 6.5$ Hz, ArCH_2), 3.84 (3H, s, OCH_3), 5.14 (1H, bt, $J = 6.5$ Hz, ArCH_2CH), 6.54 (1H, d, $J = 2.2$ Hz, H_4'), 6.80 (1H, s, H_3), 6.81 (1H, d, $J = 2.2$ Hz, H_2'), 6.83 (1H, dd, $J = 2.0, 8.0$ Hz, H_5), 6.98 (1H, bd, $J = 2.0$ Hz, H_7), 7.44 (1H, d, $J = 8.0$ Hz, H_4); m/z 324 (M^+), 309, 281, 202, 92, 91 (100%).

η^6 -6-Methoxybenzofurantricarbonyl chromium (0) (50)

Refluxing a solution of 6-methoxybenzofuran for 24 hours, using the standard complexation procedure, gave the *title* compound in 20% yield.

m. p. 143-5°C;

$\nu_{\max}$ (CHCl_3) 1967, 1891 cm^{-1} ;

δ_{H} (CDCl_3 , 60 MHz) 3.75 (3H, s, OCH_3), 4.95 (1H, dd, $J = 2, 7$ Hz, H_5), 6.04 (1H, m, $J = 2$ Hz, H_7), 6.23 (1H, d, $J = 7$ Hz, H_4), 6.55 (1H, m, $J = 3$ Hz, H_3), 7.45 (1H, d, $J = 3$ Hz, H_2);

m/z 284 (M^+) 228, 200 (100%);

(Found C, 50.98%; H, 2.68%; $\text{C}_{12}\text{H}_8\text{O}_5\text{Cr}$ requires C, 50.72%; H, 2.84%).

η^6 -6-Methoxy-7-trimethylsilylbenzofurantricarboxyl chromium (0) (51)

To a solution of η^6 -6-methoxybenzofurantricarboxyl chromium (0) (0.142g, 0.5mmol) in THF (20ml) at -78°C , was added *n*-butyl lithium (0.3ml, 0.5mmol), and the reaction stirred for 1 hour. Trimethylsilylchloride (0.3ml) was then added and the reaction stirred for 30 minutes before allowing to warm to room temperature. Work up and extraction as usual, followed by drying, and removal of solvent gave an oil which was chromatographed to give the *title* compound in 67% yield.

m. p. $128-9^\circ\text{C}$ (decomposes);

ν_{max} (CHCl_3) 1962, 1888 cm^{-1} ;

δ_{H} (CDCl_3) 0.5 (9H, s, $\text{Si}(\text{CH}_3)_3$), 3.67 (3H, s, OCH_3), 4.75 (1H, d, $J = 7 \text{ Hz}$, H_5), 6.30 (1H, d, $J = 7 \text{ Hz}$, H_4), 6.45 (1H, d, $J = 3 \text{ Hz}$, H_3), 7.40 (1H, d, $J = 3 \text{ Hz}$, H_2);

m/z 356 (M^+), 300, 272 (100%);

(Found C, 50.58%; H, 4.59%; $\text{C}_{15}\text{H}_{16}\text{O}_5\text{SiCr}$ requires C, 50.56%; H, 4.53%).

6-Methoxy-7-geranylbenzofuran (52)

To a solution of η^6 -6-methoxybenzofurantricarboxyl chromium (0) (0.426g, 1.5mmol) in THF (50ml) at -78°C , was added *n*-butyl lithium (0.9ml, 1.5mmol) and the reaction stirred for 1 hour. $\text{CuBr} \cdot \text{SMe}_2$ (0.309g, 1.5mmol) was then added, and the reaction stirred at -20°C for 1 hour. Geranyl bromide (0.65g, 0.6ml, 3mmol) was added and the reaction stirred for 2 hours at -20°C , after which it was stirred at room temperature overnight. Work up and extraction as usual, followed by drying and removal of solvent gave an orange oil. This was taken up in dichloromethane and allowed to stand in air to decomplex it. The solution was then filtered through a silica pad, and the solvent removed. After chromatography the *title* compound was obtained in 60% yield as a colourless oil.

ν_{max} (film) 3147, 3113, 2911, 2728, 1625, 1601, 1541, 1490, 1462, 1422, 1377, 1363, 1323, 1273, 1249 cm^{-1} ;

δ_{H} (CDCl_3) 1.52 (3H, s, CH_3), 1.60 (3H, s, CH_3), 1.6-1.7 (4H, m, $(\text{CH}_2)_2$), 1.80 (3H, s, CH_3), 3.60 (2H, d, $J = 6.5 \text{ Hz}$, ArCH_2CH), 3.88 (3H, s, OCH_3), 5.07 (1H, bt, $J =$

5.4 Hz, (CH₂)₂CH), 5.34 (1H, bt, J = 6.5 Hz, ArCH₂CH), 6.68 (1H, d, J = 2.5 Hz, H₃), 6.88 (1H, d, J = 9 Hz, H₅), 7.35 (1H, d, J = 9 Hz, H₄), 7.52 (1H, d, J = 2.5 Hz, H₂);

m/z 284 (M⁺), 215, 201, 161 (100%);

(Found C, 80.21%; H, 8.66%; C₁₉H₂₄O₂ requires C, 80.24%; H, 8.51%).

Mulberrofuran B

Following the same cross coupling and desilylation procedures for the synthesis of *moracin M*, gave the *title* compound in 40% yield.

m. p. 59-61°C (lit⁸⁸ 68-70°C);

*v*_{max} 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 (d⁶-acetone, 500Mz) 1.48 (3H, s, CH₃), 1.54 (3H, s, CH₃), 1.88 (3H, s, CH₃), 1.9-2.0 (4H, m, CH₂CH₂), 3.63 (2H, d, J = 7.5 Hz, ArCH₂), 3.89 (3H, s, OCH₃), 5.03 (1H, bt, J = 7.0 Hz, CH), 5.38 (1H, bt, J = 7.5 Hz, ArCH₂CH), 6.37 (1H, t, J = 2.0 Hz, H₄'), 6.90 (2H, d, J = 2.0 Hz, H₂' H₆'), 6.96 (1H, d, J = 8.0 Hz, H₅), 7.05 (1H, s, H₃) 7.37 (1H, d, J = 8.0 Hz, H₄);

m/z 392 (M⁺) (100%), 323, 269.

α-Formylisophorone (59)

To a solution of diisopropylamine (1.11g, 1.54ml, 11mmol) in THF (50ml) at -78°C, was added *n*-butyl lithium. After stirring for 1 hour at 0°C, the LDA solution was recooled to -78°C, and isophorone (1.38g, 1.5ml, 10mmol) was added dropwise. After 1.5 hours stirring methyl formate (0.6g, 1.03ml, 11mmol) was added, and the reaction stirred for a further 1 hour, before allowing to warm to room temperature, and left to stir overnight. Addition of 2N HCl was followed by ether extraction. After drying, and removal of solvent, the crude material was chromatographed to give the *title* compound in 40% yield.

*v*_{max} (film) 2963, 1646, 1627, 1574, 1467, 1407, 1365, 1310, 1273, 1204, 1186, 1134 cm⁻¹;

δ_{H} (CDCl_3 , 60 MHz) 1.10 (6H, s, CH_3), 1.87 (3H, bs, CH_3), 2.10 (2H, s, CH_2), 5.85 (1H, bs, CH), 7.50 (1H, d, $J = 9.8$ Hz, CHOH), 14.6 (1H, d, $J = 9.8$ Hz, CHOH);

m/z 166 (M^+), 151, 123 (100%);

(Found C, 72.40%; H, 8.59%; $\text{C}_{10}\text{H}_{14}\text{O}_2$ requires C, 72.26%, H, 8.49%).

1-Methyl-3-trimethylsiloxy-5,5-dimethylcyclohexadiene (60)

To a solution of diisopropylamine (1.11g, 1.54ml, 11mmol) in THF (50ml) at -78°C , was added *n*-butyl lithium (6.9ml, 11mmol). After stirring for 1 hour at 0°C , isophorone (1.38g, 1.5ml, 10mmol) was added dropwise to the LDA solution which had been recooled to -78°C . After 1.5 hours stirring, trimethylsilylchloride (2.2g, 2.5ml, 20mmol) was added, and the reaction stirred for 1 hour. After allowing to warm to room temperature, the mixture was poured into cold saturated sodium bicarbonate solution (100ml), and the mixture extracted with ether. The ether extracts were washed with cold water, dried, and the solvent removed to give a brown oil, which upon distillation gave the *title* compound in 87% yield.

b. p. $50^\circ\text{C}/1\text{mbar}$;

ν_{max} (film) 3040, 2960, 2900, 2860, 2800, 1660, 1600, 1440, 1360, 1240, 1150, 1120, 1020, 1000 cm^{-1} ;

δ_{H} (d^6 -acetone) 0.16 (9H, s, $\text{Si}(\text{CH}_3)_3$), 1.00 (6H, s, $(\text{CH}_3)_2$), 1.78 (3H, bs, CH_3), 1.96 (2H, s, CH_2), 4.52 (1H, bs, CH), 5.42 (1H, m, CH);

m/z 210 (M^+), 195;

(Found C, 68.31%; H, 10.79%; $\text{C}_{12}\text{H}_{22}\text{OSi}$ requires C, 68.51%; H, 10.54%).

α -(Dimethylacetal)isophorone (61)

Method 1:-

To a solution of TiCl_4 (0.494g, 0.3ml, 2.6mmol) in dichloromethane (5ml) at -78°C , was added a solution of trimethylorthoformate (0.265g, 0.3ml, 2.5mmol) in dichloromethane (5ml). To the resulting slurry was immediately added the TMS-

enol ether (60) (0.53g, 2.5mmol) in dichloromethane (5ml), and the reaction stirred at -78°C for 2 hours. Work up with cold saturated sodium bicarbonate solution (careful), and extraction with dichloromethane, gave after drying and removal of solvent, an oil which was distilled to give the *title* compound in 54% yield.

b. p. 110°C/0.5mbar;

$\nu_{\max}$ (film) 2960, 2834, 1669, 1584, 1441, 1380, 1317, 1243, 1194, 1115, 1059 cm^{-1} ;

δ_{H} (CDCl_3) 1.00 (3H, s, CH_3), 1.12 (3H, s, CH_3), 1.90 (3H, s, CH_3), 1.92 (1H, d, $J = 18 \text{ Hz}$, CH_2), 2.35 (1H, d, $J = 5 \text{ Hz}$, $\text{CHCH}(\text{OCH}_3)_2$), 2.45 (1H, d, $J = 18 \text{ Hz}$, CH_2), 3.30 (1H, s, OCH_3), 3.35 (3H, s, OCH_3), 4.55 (1H, d, $J = 5 \text{ Hz}$, $\text{CH}(\text{OCH}_3)_2$), 5.85 (1H, bs, CH);

m/z 212 (M^+), 197, 181, 75 (100%);

(Found C, 67.91%; H, 9.73%; $\text{C}_{12}\text{H}_{20}\text{O}_3$ requires C, 67.89%; H, 9.50%).

Method 2

To a solution of the TMS-enol ether (60) (1.05g, 5mmol) in dichloromethane (15ml) at -78°C, was added trimethylorthoformate (1.06g, 10mmol) followed by TMS-triflate (0.25mmol, 0.05ml, 5mol%), and the reaction stirred for 8 hours at -78°C. Work up and extraction as in method 1 afforded the *title* compound in 66% yield.

Cis-1-methyl-3-hydroxy-4-dimethylacetal-5,5-dimethylcyclohexene (62)

To a solution of the enone (61) (0.106g, 0.5mmol) in ether (2ml) was added a solution of DIBAL (1ml, 1mmol), and the reaction stirred at room temperature for 24 hours. Ammonium chloride solution was added and the mixture extracted with ether. The ether extracts were dried, and the solvent removed to give the crude compound, which upon HPLC gave the *title* compound in 80% yield.

$\nu_{\max}$ (film) 3500, 2932, 2829, 1683, 1446, 1368, 1246, 1189, 1126, 1073 cm^{-1} ;

δ_{H} (CDCl_3) 1.00 (3H, s, CH_3), 1.10 (3H, s, CH_3), 1.66 (3H, s, CH_3), 1.69 (1H, d, $J = 18 \text{ Hz}$, CH_2), 1.70 (1H, dd, $J = 4.0, 5.5 \text{ Hz}$, $\text{CHCH}(\text{OCH}_3)_2$), 1.85 (1H, bd, $J = 18$

Hz, CH₂), 3.18 (1H, d, J = 5.5 Hz, OH), 3.40 (3H, s, OCH₃), 3.45 (3H, s, OCH₃), 4.42 (1H, bs, CH(OH)), 4.62 (1H, d, J = 5.5 Hz, CH(OCH₃)₂), 5.55 (1H, bs, CH); decouple @ 5.55: δ_H (D₂O) 4.42 (1H, d, J = 4.0 Hz);
 m/z 197 (M⁺-17), 182 (M⁺-MeOH);
 (Found C, 67.43%; H, 10.38%; C₁₂H₂₂O₃ requires C, 67.26%; H, 10.35%).

Trans-1-methyl-3-hydroxy-4-dimethylacetal-5,5-dimethylcyclohexene (63)

To a solution of the enone (61) (0.212g, 1mmol) in ether (3ml) at room temperature, was added LiAlH₄ (43mg), and the reaction allowed to stir for 1 hour. Ammonium chloride was added, and the mixture extracted with ether. The ether extracts were dried, and the solvent removed to give the crude compound, which upon HPLC gave the *title* compound in 34% yield.

ν_{max} (film) 3525, 2927, 1452, 1369, 1190, 1125, 1072 cm⁻¹;
 δ_H (CDCl₃) 0.87 (3H, s, CH₃), 1.00 (3H, s, CH₃), 1.52 (1H, d, J = 16.9 Hz, CH₂), 1.62 (1H, dd, J = 3.4, 8.5 Hz, CHCH(OMe)₂), 1.63 (3H, bs, CH₃), 2.03 (1H, bd, J = 16.9 Hz, CH₂), 3.36 (3H, s, OCH₃), 3.50 (3H, s, OCH₃), 3.82 (1H, bs, OH), 4.36 (1H, bd, J = 8.5 Hz, CHOH), 4.53 (1H, d, J = 3.4 Hz, CHCH(OMe)₂), 5.37 (1H, bs, CHCH(OH));
 m/z 182 (M⁺-MeOH), 167, 75 (100%);
 (Found C, 67.17%; H, 10.42%; C₁₂H₂₂O₃ requires C, 67.26%; H, 10.35%).

Cis-1-methyl-3-acetoxy-4-dimethylacetal-5,5-dimethylcyclohexene (66)

To a solution of the *cis*-alcohol (62) (0.107g, 0.5mmol) in dichloromethane (2ml), was added pyridine (0.119g, 0.12ml, 1.5mmol), followed by acetyl chloride (0.07g, 1mmol), and the reaction stirred for 2 hours. Saturated sodium bicarbonate solution was added, and the mixture extracted with ether. After drying, and removal of solvent, the resultant oil was chromatographed to afford the *title* compound in 80% yield.

ν_{max} (film) 2933, 2830, 1737, 1684, 1443, 1372, 1246, 1190, 1125, 1065, 1015 cm⁻¹;

δ_{H} (CDCl_3) 1.05 (3H, s, CH_3), 1.07 (3H, s, CH_3), 1.69 (3H, s, CH_3), 1.70 (2H, d, $J = 16.8$ Hz, CH_2), 1.89 (1H, dd, $J = 4.4, 8.2$ Hz, $\text{CHCHCH}(\text{OMe})_2$), 2.0 (3H, s, OCOCH_3), 3.30 (3H, s, OCH_3), 3.32 (3H, s, OCH_3), 4.55 (1H, d, $J = 8.2$ Hz, $\text{CHCHCH}(\text{OMe})_2$), 5.38 (1H, t, $J = 4.4$ Hz, $\text{CHCHCH}(\text{OMe})_2$), 5.55 (1H, bs, $\text{CHCH}(\text{OAc})$);

m/z 224 ($\text{M}^+ - \text{MeOH}$), 185, 161;

(Found accurate mass 224.1412; $\text{C}_{13}\text{H}_{20}\text{O}_3$ requires 224.1419).

Trans-1-methyl-3-acetoxy-4-dimethylacetal-5,5-dimethylcyclohexene (67)

By employing the same procedure used for the *cis*-acetate, the *title* compound was obtained in 85% yield.

ν_{max} (film) 2957, 2831, 1734, 1684, 1445, 1374, 1245, 1126, 1078, 1019 cm^{-1} ;

δ_{H} (CDCl_3) 0.96 (3H, s, CH_3), 1.06 (3H, s, CH_3), 1.67 (3H, bs, CH_3), 1.68 (1H, d, $J = 16.2$ Hz, CH_2), 1.82 (1H, dd, $J = 3.5, 7.3$ Hz, $\text{CHCHCH}(\text{OMe})_2$), 1.92 (1H, bd, $J = 16.2$ Hz, CH_2), 2.03 (3H, s, OCOCH_3), 3.32 (3H, s, OCH_3), 3.36 (3H, s, OCH_3), 4.34 (1H, d, $J = 3.5$ Hz, $\text{CHCHCH}(\text{OMe})_2$), 5.32 (1H, bs, $\text{CHCH}(\text{OAc})$), 5.44 (1H, bd, $J = 7.3$ Hz, $\text{CHCHCH}(\text{OMe})_2$);

m/z 256 (M^+), 224 ($\text{M}^+ - \text{MeOH}$);

(Found accurate mass 224.1412; $\text{C}_{13}\text{H}_{20}\text{O}_3$ requires 224.1419).

Trans-1-methyl-3-butyl-4-dimethylacetal-5,5-dimethylcyclohexene (68)

To a suspension of CuCN (0.045g, 0.5mmol) in THF (10ml) at -78°C , was added *n*-butyl lithium (0.6ml, 1mmol), and the reaction stirred for 1 hour. The *cis*-acetate (66) (0.256g, 1mmol) was then added, and the reaction stirred for 3 hours, before allowing to warm to room temperature. The resulting black solution was extracted with ether. After drying, and removal of solvent, the resulting oil was chromatographed to afford the *title* compound in 20% yield.

δ_{H} (CDCl_3) 0.86 (3H, s, CH_3), 0.87 (3H, t, $J = 5.4$ Hz, $\text{CH}_3(\text{CH}_2)_3$), 1.00 (3H, s, CH_3), 1.2-1.35 (6H, m, $\text{CH}_3(\text{CH}_2)_3$), 1.38 (1H, dd, $J = 1.6, 8.3$ Hz, $\text{CHCH}(\text{OMe})_2$),

1.60 (1H, bd, $J = 16.5$ Hz, CH_2), 1.62 (3H, s, CH_3), 1.80 (1H, bd, $J = 16.5$ Hz, CH_2), 2.32 (1H, m, $\text{CHCHCH}(\text{OMe})_2$), 3.34 (3H, s, OCH_3), 3.41 (3H, s, OCH_3), 4.33 (1H, d, $J = 1.6$ Hz, $\text{CHCH}(\text{OMe})_2$), 5.27 (1H, bs, CH).

1,3-Dimethoxy-2-trimethylstannylbenzene (69)

To a solution of 1,3-dimethoxybenzene (1.38g, 1.3ml, 10mmol) in THF (10ml) and Et_2O (5ml) at 0°C , was added *n*-butyl lithium (9.4ml, 15mmol) and the reaction stirred at room temperature for 3 hours. This solution was transferred under nitrogen to a flask containing trimethyltin chloride (3g, 15mmol), and the reaction allowed to stir for 2 hours. Addition of water, followed by ether extraction, gave after drying, and removal of solvent, an oil which was distilled to give the *title* compound in 88% yield.

b. p. $80^\circ\text{C}/0.04\text{mbar}$

ν_{max} (film) 3081, 2994, 2938, 2915, 2834, 2499, 2349, 2137, 1578, 1461, 1429, 1303, 1237, 1171, 1152, 1105, 1042 cm^{-1} ;

δ_{H} (CDCl_3) 0.27 (9H, s, SnMe_3), 3.75 (6H, s, OCH_3), 6.47 (2H, d, $J = 6$ Hz, H_4 , H_6), 7.24 (1H, t, $J = 6$ Hz, H_5);

m/z 302 (M^+), 287 (100%);

(Found accurate mass 302.0322, $\text{C}_{11}\text{H}_{18}\text{O}_2\text{Sn}$ requires 302.0328).

1-(2-Methoxyphenyl)-2-(dimethylacetal)isophorol (70)

To a solution of 2-bromoanisole (0.12ml, 1mmol) in THF (3ml) at -20°C , was added *n*-butyl lithium (0.63ml, 1mmol). After stirring for 1 hour, this was transferred to a suspension of dry CeCl_3^* (0.271g, 1.1mmol) in THF (5ml) at -78°C . After stirring for 1 hour, the enone (61) (0.212g, 1mmol) in THF was added, and the reaction allowed to stir at -40°C overnight. Work up and extraction as usual, gave after drying and removal of solvent, the crude compound, which upon chromatography afforded the *title* compound in 38% yield.

* CeCl_3 was dried by heating at 150°C under high vacuum for 2 hours, and then

allowed to cool under nitrogen.

$\nu_{\max}$ (film) 3489, 2934, 2832, 2031, 1667, 1597, 1582, 1484, 1466 cm^{-1} ;

δ_{H} (CDCl_3) 1.10 (3H, s, CH_3), 1.25 (3H, s, CH_3), 1.62 (1H, d, $J = 16.3$ Hz, CH_2), 1.67 (3H, bs, CH_3), 2.12 (1H, bd, $J = 16.3$ Hz, CH_2), 2.73 (1H, d, $J = 2.3$ Hz, $\text{CHCH}(\text{OCH}_3)_2$), 3.05 (3H, s, OCH_3), 3.10 (3H, s, OCH_3), 3.73 (3H, s, ArOCH_3), 4.20 (1H, s, OH), 4.38 (1H, d, $J = 2.3$ Hz, $\text{CH}(\text{OCH}_3)_2$), 5.16 (1H, bs, CH), 6.84 (1H, d, $J = 7.9$ Hz, H_6), 6.97 (1H, t, $J = 7.0$ Hz, H_4), 7.20 (1H, dd, $J = 7.0, 7.9$ Hz, H_5), 7.70 (1H, d, $J = 7.9$ Hz, H_3);

m/z 302 ($\text{M}^+ - \text{H}_2\text{O}$), 288;

(Found C, 71.38%; H, 8.67%; $\text{C}_{19}\text{H}_{28}\text{O}_4$ requires C, 71.22%; H, 8.81%).

1-(2-Anisyl)-3-methyl-5,5-dimethylcyclohexene (72)

To a solution of the alcohol (70) (0.045g, 0.14mmol) and triethylsilane (0.04ml, 0.24mmol) in dichloromethane, was added trifluoroacetic acid (0.03ml, 0.36mmol) and the reaction stirred for 1 hour. Saturated sodium bicarbonate solution was then added, and the mixture extracted with ether. After drying and removal of solvent, the compound was chromatographed to give the *title* compound in 68% yield.

$\nu_{\max}$ (film) 2952, 2903, 2867, 2837, 1598, 1579, 1490, 1456, 1435, 1383, 1363, 1330, 1293, 1278, 1250, 1226, 1181, 1161, 1116, 1054 cm^{-1} ;

δ_{H} (CDCl_3) 0.96 (3H, s, CH_3), 0.98 (3H, s, CH_3), 1.05 (3H, d, $J = 7.9$ Hz, CH_3), 1.46 (1H, bd, $J = 13$ Hz, ArCCH_2), 1.48 (1H, bd, $J = 13$ Hz, ArCCH_2), 1.98 (1H, bd, $J = 17$ Hz, CH_2), 2.21 (1H, dt, $J = 3.2, 17$ Hz, CH_2), 2.35 (1H, vbs, CH_3CHCH_2), 5.54 (1H, bs, CH), 6.85 (1H, d, $J = 7.2$ Hz, H_6), 6.90 (1H, t, $J = 7.2$ Hz, H_4), 7.12 (1H, t, $J = 7.2$ Hz, H_3), 7.20 (1H, t, $J = 7.2$ Hz, H_5);

m/z 230 (M^+) (100%), 215;

(Found C, 83.62%; H, 9.67%; $\text{C}_{16}\text{H}_{22}\text{O}$ requires C, 83.43; H, 9.63%).

2-Methyl-4-hydroxy-4-(2,6-dimethoxyphenyl)but-2-ene

To a solution of 1,3-dimethoxybenzene (0.26ml, 2mmol) in THF (2ml) and ether (1ml) at 0°C, was added *n*-butyl lithium (1.25ml, 2mmol), and the reaction stirred at room temperature for 3 hours. This was then cathetered into a solution of MgBr₂ (2mmol) in THF (10ml), which had been prepared by the reaction of magnesium with 1,2-dibromoethane, and the reaction stirred for 1 hour. After cooling to 0°C, prenaldehyde (0.84g, 0.95ml, 10mmol) was added, and the reaction allowed to warm to room temperature and stirred overnight. Ammonium chloride solution was added, and the mixture extracted with ether. After drying and removal of solvent, the *title* compound was obtained in 80% yield.

δ_{H} (CDCl₃) 1.70 (3H, s, CH₃), 1.82 (3H, s, CH₃), 3.85 (6H, s), 4.74 (1H, d, J = 11.9 Hz, OH), 5.65 (1H, bd, J = 9.1 Hz, CHC(CH₃)₂), 5.90 (1H, dd, J = 9.1, 11.9 Hz, ArCH(OH)), 6.56 (2H, d, J = 8.3 Hz, H₃ H₅), 7.16 (1H, t, J = 8.3 Hz, H₄);
m/z 222 (M⁺), 207, 204, 154 (100%).

1-(2,6-Dimethoxyphenyl)-3-methylbutadiene (76)

To a solution of 2-methyl-4-hydroxy-4-(2,6-dimethoxyphenyl)but-2-ene (0.100g, 0.45mmol) in dichloromethane (3ml) was added pyridine (0.1ml, 1mmol) and then methanesulphonylchloride (0.04ml, 0.5mmol), and the reaction stirred at room temperature for 2 hours. Saturated sodium bicarbonate solution was added, and the mixture extracted with dichloromethane. After drying and removal of solvent, the compound was chromatographed to give the *title* compound in 50% yield.

Alternatively, upon distillation of the alcohol, the *title* compound was obtained in 72% yield overall.

ν_{max} (film) 3080, 3000, 2941, 2837, 2366, 2183, 2135, 1672, 1592, 1473, 1435, 1377, 1270, 1245, 1203, 1180, 1153, 1110, 1037 cm⁻¹ ;
 δ_{H} (CDCl₃) 2.00 (3H, bs, CH₃), 3.88 (6H, s, OCH₃), 5.05 (1H, bs, CH₂), 5.10 (1H, bs, CH₂), 6.56 (2H, d, J = 7.2 Hz, H₃ H₅), 6.86 (1H, d, J = 16.2 Hz, ArCHCH), 7.13 (1H, t, J = 7.2 Hz, H₄), 7.34 (1H, d, J = 16.2 Hz, ArCH);

m/z 204 (M^+) (100%), 189, 173;

(Found accurate mass, 204.1144; $C_{13}H_{16}O_2$ requires 204.1150).

1-[2-Methoxy-6-(3,3-dimethylacryloyloxy)phenyl]3-methylbutadiene (75)

To a solution of diphenylphosphine (0.223g, 0.21ml, 1.2mmol) in THF (4ml) at room temperature was added *n*-butyl lithium (0.75ml, 1.2 mmol), and the reaction stirred for 1 hour. To the resulting orange solution was added a solution of the diene (76) (0.204g, 1mmol) in THF, and the reaction refluxed until the orange colour disappeared. After cooling to room temperature, 3,3-dimethylacryloylchloride (0.26g, 2.4mmol) was added, and the reaction stirred overnight. Saturated sodium bicarbonate solution was added, and the mixture extracted with ether. After drying and removal of solvent, chromatography on alumina afforded the *title* compound in 28% yield.

$\nu_{\max}$ ($CHCl_3$) 3080, 2939, 2839, 1739, 1647, 1598, 1577, 1469, 1439, 1379, 1351, 1316, 1259, 1217, 1190, 1122, 1074 cm^{-1} ;

δ_H ($CDCl_3$) 1.85 (3H, s, CH_3), 1.98 (3H, s, CH_3), 2.20 (3H, s, CH_3), 3.88 (3H, s, OCH_3), 5.02 (2H, bs, CH_2), 5.94 (1H, m, $OC(O)CH$), 6.54 (1H, d, $J = 16.7$ Hz, $ArCHCH$), 6.70 (1H, dd, $J = 0.8, 8.1$ Hz, H_3), 6.77 (1H, dd, $J = 0.8, 8.1$ Hz, H_5), 7.09 (1H, d, $J = 16.7$ Hz, $ArCH$), 7.18 (1H, t, $J = 8.1$ Hz, H_4);

m/z 272 (M^+), 206 (100%);

(Found accurate mass, 272.1419; $C_{17}H_{20}O_3$ requires 272.1412).

4-[2-Methoxy-(3,3-dimethylacryloyloxy)phenyl]butenone (77)

A solution of the butadiene (75) (0.132g, 0.49mmol) in bromobenzene (10ml) was refluxed for 24 hours. The solvent was then removed on a rotary evaporator to afford the *title* compound only, in 100%(by nmr) yield.

$\nu_{\max}$ ($CHCl_3$) 3013, 2942, 2841, 1734, 1691, 1648, 1604, 1578, 1471, 1439, 1379, 1353, 1260, 1228, 1183, 1124, 1087 cm^{-1} ;

δ_H ($CDCl_3$) 2.0 (3H, bs, CH_3), 2.20 (3H, bs, CH_3), 2.32 (3H, s, $COCH_3$), 3.90 (3H, s, OCH_3), 5.97 (1H, m, $OCOCH$), 6.75 (1H, d, $J = 8.1$ Hz, H_3), 6.82 (1H, d, $J = 8.1$

Hz, H₅), 7.0 (1H, d, J = 16.6 Hz, ArCHCHCOMe), 7.34 (1H, t, J = 8.1 Hz, H₄), 7.66 (1H, d, J = 16.6 Hz, ArCHCHCOMe);
 δ_{C} (CDCl₃) 21, 27, 28, 56, 108, 115, 117, 118, 131, 132, 134, 152, 160, 163, 165, 200;
 m/z 274 (M⁺), 243, 231, 206 (100%);
(Found accurate mass, 274.1200; C₁₆H₁₈O₄ requires 274.1205).

N-phenylmaleimide adduct (78)

The *title* compound was obtained by refluxing the diene (76) with *N*-phenylmaleimide in toluene, according to the general procedure.

m. p. 141-2°C;

ν_{max} (CHCl₃) 3025, 3010, 2939, 2841, 1776, 1708, 1595, 1501, 1475, 1385, 1330, 1276, 1247, 1219, 1198, 1172, 1109, 1039 cm⁻¹;

δ_{H} (CDCl₃) 1.80 (3H, s, CH₃), 2.32 (1H, bd, J = 15.6 Hz, CH₂), 2.76 (1H, bd, J = 15.6 Hz, CH₂), 3.30 (2H, m, ArCHCH(CO)CH(CO)), 3.60 (3H, vbs, OCH₃), 4.44 (1H, m, ArCH), 5.66 (1H, m, ArCHCH), 6.49 (2H, bd, J = 7.8 Hz, H₄ H₆), 7.1-7.4 (6H, m, H₅ Ph);

m/z 377 (M⁺) (100%), 362, 346;

(Found C, 73.15%; H, 6.22%; N, 3.76%; C₂₃H₂₃NO₄ requires C, 73.19%; H, 6.14%; N, 3.71%).

Maleic anhydride adduct (79)

The *title* compound was obtained by refluxing the diene with maleic anhydride in toluene, according to the general procedure.

m. p. 178-80°C;

ν_{max} (CHCl₃) 3030, 3009, 2938, 2841, 1844, 1776, 1596, 1476, 1438, 1350, 1250, 1208, 1111, 1060, 1029 cm⁻¹;

δ_{H} (CDCl₃) 1.80 (3H, bs, CH₃), 2.28 (1H, bd, J = 15.5 Hz, CH₂), 2.65 (1H, dd, J = 2.9, 15.5 Hz, CH₂), 3.34 (1H, t, J = 9.6 Hz, ArCHCH(CO)), 3.48 (1H, ddd, J = 2.9, 6.0, 9.6 Hz, ArCHCH(CO)CH(CO)), 3.76 (6H, s, OCH₃), 4.33 (1H, m, J = 9.6 Hz, ArCH), 5.62 (1H, bs, ArCHCH), 6.57 (2H, d, J = 9.0 Hz, H₃ H₅), 7.22 (1H, t, J =

9.0 Hz, H₄);

m/z 302 (M⁺), 274, 204, 173 (100%);

(Found C, 67.54%; H, 5.98%; C₁₇H₁₈O₅ requires C, 67.54%; H, 6.00%).

Citraconic anhydride adduct (81)

The *title* compound was obtained in 70% yield, on refluxing a solution of the diene (76) with citraconic anhydride in bromobenzene, according to the general procedure.

m. p. 142-4°C;

ν_{max} (CHCl₃) 3031, 3009, 2938, 2841, 1841, 1773, 1596, 1476, 1437, 1383, 1346, 1288, 1250, 1220, 1216, 1212, 1140, 1106, 1041, 1017 cm⁻¹;

δ_{H} (CDCl₃) 1.40 (3H, s, CH₃), 1.80 (3H, bs, CH₃), 2.26 (1H, bd, J = 15.8 Hz, CH₂), 2.66 (1H, dd, J = 2.7, 15.8 Hz, CH₂), 3.08 (1H, dd, J = 2.7, 4.7 Hz, CH₂CH(CO)), 3.63 (3H, s, OCH₃), 3.82 (3H, s, OCH₃), 4.00 (1H, q, J = 2.4 Hz, ArCH), 5.50 (1H, bs, CHC(CH₃)), 6.52 (1H, d, J = 7.8 Hz, H₃), 6.59 (1H, d, J = 7.8 Hz, H₅), 7.23 (1H, t, J = 7.8 Hz, H₄);

m/z 316 (M⁺), 288, 244, 204 (100%);

(Found C, 68.57%; H, 6.35%; C₁₈H₂₀O₅ requires C, 68.34%; H, 6.37%).

Compound (82)

To a solution of (79) (1.51g, 5mmol) in dichloromethane (10ml) at 0°C, was added BBr₃ (40ml of 1M, 40mmol), and the reaction stirred at room temperature for 3 hours. Water was added, and the mixture extracted with ethyl acetate. After drying and removal of solvent, the crude acid was obtained in 80% yield. Chromatography yielded only a small amount of the *title* compound, due to decomposition on silica.

m. p. 286-90°C;

ν_{max} (Nujol) 3372, 3175, 2969, 2947, 2888, 2845, 1732, 1704, 1621, 1604, 1466, 1400, 1377, 1352, 1293, 1271, 1239, 1179, 1171, 1158, 1119, 1034 cm⁻¹;

δ_{H} (d⁵-DMSO) 1.63 (3H, s, CH₃), 2.2-2.3 (2H, m, CH₂), 2.95 (1H, ddd, J = 3.1,

5.9, 12.2 Hz, CHCO_2H), 3.49 (1H, dd, $J = 3.1, 5.9$ Hz, ArCHCH), 4.0 (1H, m, $J = 3.1$ Hz, ArCH), 5.20 (1H, bs, CH), 6.50 (1H, d, $J = 6.7$ Hz, H_3), 6.70 (1H, d, $J = 6.7$ Hz, H_5), 7.20 (1H, t, $J = 6.7$ Hz, H_4);

m/z 274 (M^+), 256, 228, 213 (100%);

(Found C, 65.63%; H, 5.33%; $\text{C}_{15}\text{H}_{14}\text{O}_5$ requires C, 65.69%; H, 5.15%).

Compound (83)

To a solution of the crude acid (82) (1.3g, 5mmol) in methanol (20ml) was added concentrated sulphuric acid (2ml), and the reaction refluxed overnight. Water was added and the mixture extracted with ethyl acetate. After drying, removal of solvent, and subsequent chromatography, the *title* compound was obtained in 35% overall yield.

m. p. 224-5°C;

ν_{max} (Nujol) 3343, 2927, 2855, 1757, 1723, 1668, 1643, 1614, 1600, 1555, 1536, 1504, 1466, 1442, 1378, 1362, 1347, 1292, 1275, 1242, 1223, 1181 cm^{-1} ;

δ_{H} (CDCl_3) 1.60 (3H, bs, CH_3), 2.26 (1H, dd, $J = 6.3, 19$ Hz, CH_2), 2.42 (1H, dd, $J = 11.3, 19$ Hz, CH_2), 2.92 (1H, ddd, $J = 3.3, 6.3, 11.3$ Hz, $\text{CH}_2\text{CHCO}_2\text{CH}_3$), 3.58 (1H, dd, $J = 3.3, 6.6$ Hz, $\text{ArCHCHCHCO}_2\text{CH}_3$), 3.66 (3H, s, CO_2CH_3), 4.08 (1H, m, $J = 6.6$ Hz, ArCHCH), 5.25 (1H, bs, ArCHCH), 6.45 (1H, d, $J = 7.1$ Hz, H_3), 6.70 (1H, d, $J = 7.1$ Hz, H_5), 7.08 (1H, t, $J = 7.1$ Hz, H_4), 8.85 (1H, bs, OH);

m/z 288 (M^+), 256, 228 (100%);

(Found C, 66.70%; H, 5.74%; $\text{C}_{16}\text{H}_{16}\text{O}_5$ requires C, 66.66%; H, 5.59%).

Appendix

X-ray data:-

Crystal data: $C_{17}H_{18}O_5$, $M = 302.3$, monoclinic, $a = 12.760(7)$, $b = 8.163(4)$, $c = 14.500(5)$ Å, $\beta = 91.26(4)^\circ$, $U = 1510$ Å³, space group $P2_1/n$, $Z = 4$, $D_c = 1.33$ gcm⁻³, Cu radiation, $\lambda = 1.54178$ Å, $\mu(\text{Cu-K}\alpha) = 8\text{cm}^{-1}$, $F(000) = 640$. Data were measured on a Nicolet R3m diffractometer with Cu-K α radiation (graphite monochromator) using ω scans. 2034 Independent reflections were measured ($20 \leq 116^\circ$), of which 1895 had $|F_o| > 3\sigma(|F_o|)$ and were considered to be observed. The data were corrected for Lorentz and polarisation factors; no absorption correction was applied. The structure was solved by direct methods. The non-hydrogen atoms were refined anisotropically. The leading proton on the methyl group on the sp² centres, C (10), was located from a ΔF map. The positions of the remaining hydrogen atoms were idealised, C-H = 0.96 Å, assigned isotropic thermal parameters, $U(H) = 1.2 U_{eq}(C)$, and allowed to ride on their parent carbon atoms. The methyl groups were refined as rigid bodies. Refinement was by block-cascade, full-matrix least-squares to $R = 0.068$, $R_w = 0.081$ [$w^{-1} = \sigma^2(F) + 0.00200F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.28 and 0.33 eÅ⁻³ respectively. The mean and maximum shift/error in the final refinement were 0.018 and 0.117 respectively.

REFERENCES

1. P. Cagniant and D. Cagniant, *Adv. Het. Chem.*, 1975, 18, 337.
2. A. Mustapha, 'The Chemistry of Heterocyclic Compounds', Vol 29, A. Weissberger and E. C. Taylor, eds., p. 4911, Wiley, New York.
3. A. Hercouet and M. Le Corre, *Tetrahedron*, 1981, 37, 2867.
4. K. B. Becker, *Tetrahedron*, 1980, 36, 1717.
5. J. M. Burke and R. Stevenson, *J. Chem. Research (S)*, 1985, 34.
6. J. M. Burke and R. Stevenson, *J. Chem. Research (S)*, 1987, 179.
7. B. A. McKittrick and R. Stevenson, *J. Chem. Soc. P1*, 1983, 475.
8. B. A. McKittrick and R. Stevenson, *J. Chem. Soc. P1*, 1984, 709.
9. B. A. McKittrick, R. T. Scannell and R. Stevenson, *J. Chem. Soc. P1*, 1982, 3017.
10. W. Sahm, E. Schinzel and P. Jürges, *Ann. Der Chemie*, 1974, 4, 523.
11. S. Akiyama, H. Akimoto, S. Nakatsuji and K. Nakashima, *Bull. Chem. Soc. Jpn.*, 1985, 58, 2192.
12. O. Dann, H. Char and H. Greißmeier, *Ann. Der Chemie*, 1982, 1836.
13. H. Singh and P. Nand, *CA85(3):20983f*.
14. W. T. Brady and Y. F. Giang, *J. Org. Chem.*, 1986, 51, 2145.
15. W.T. Brady, A. P. Marchand Y.F. Giang and A. H. Wu, *Synthesis*, 1987, 395.
16. M. Mukaiyama and M. Hashimoto, *Chem. Lett.*, 1975, 1045.
17. W. T. Brady, A. P. Marchand Y.F. Giang and A. H. Wu, *J. Org. Chem.*, 1987, 52, 3457.
18. J. Freeman and R. C. Grabiak, *J. Org. Chem.*, 1976, 41, 2531.
19. J. Grimshaw and N. Thompson, *J. Chem. Soc., Chem. Commun.*, 1987, 240.
20. G. M. Brooke, W. K. R. Musgrave and T. R. Thomas, *J. Chem. Soc. (C)*, 1971, 3956.
21. M. Jawdosiuik, I. K. Skarzynska and E. Czarnecka, *Pol. J. Chem.*, 1978, 52, 1837.
22. J. C. Sheehan, R. M. Wilson and A. W. Oxford, *J. Am. Chem. Soc.*, 1971, 93, 7222.
23. R. S. Givens and B. Matuzewski, *J. Am. Chem. Soc.*, 1984, 106, 6860.

24. K. Okamoto, I. Nitta and H. Shingu,
Bull. Chem. Soc. Jpn., 1969, **42**, 1464.
25. K. Okamoto, K. Takeuchi and T. Kitagawa,
J. Chem. Soc., Chem. Commun., 1983, 7.
26. R. J. Cremllyn, O. O. Shode and F. J. Swinbourne,
J. Chem. Soc. P1, 1988, 2181.
27. R. J. Cremllyn, O. O. Shode, F. J. Swinbourne and J. Lynch,
J. Het. Chem, 1987, **24**, 117.
28. A. Guy and J. P. Guette, *Synthesis*, 1980, 222.
29. C. Katamna, *Bull. Soc. Chim. Fr.*, 1970, 2309.
30. C. Katamna, M. A. Auger and J. Chopin, *Bull. Soc. Chim. Fr.*, 1970, 4024.
31. G. Capozzi and G. Modena, *J. Chem. Soc. P1*, 1972, 216.
32. J. R. Collier, M. K. M. Dirania and J. Hill, *J. Chem. Soc. (C)*, 1970, 155.
33. T. Sheradsky, *Tetrahedron Lett.*, 1966, 5225.
34. A. Mooradian and P. E. Dupont, *J. Het. Chem.*, 1967, **4**, 441.
35. M. Kira, M. O. A. Raman and Z. M. Nofal, *Egypt. J. Chem.*, 1978, **19**, 109.
36. L. Jurd, *J. Org. Chem.*, 1964, **29**, 2602.
37. L. Jurd, *Tetrahedron*, 1966, **22**, 2913.
38. L. Jurd, *Tetrahedron Lett.*, 1963, **18**, 1151.
39. L. Jurd, *J. Am. Chem. Soc.*, 1964, **29**, 3036.
40. L. Jurd, A. L. Livingston, E. M. Bickoff and R. E. Lundin,
Tetrahedron, 1964, **20**, 1963.
41. B. C. B. Bedouidenhoudt, E. V. Brandt and D. Ferreira,
J. Chem. Soc. P1, 1987, 1081.
42. H. Ishibashi, M. Okada, H. Nakatani, M. Ikeda and Y. Tamara,
J. Chem. Soc. P1, 1986, 1763.
43. C. E. Castro and R. D. Stephens, *J. Org. Chem.*, 1963, **28**, 2163.
44. C. E. Castro and R. D. Stephens, *J. Org. Chem.*, 1963, **28**, 3313.
45. C. E. Castro, E. J. Gaughan and D. C. Owsley,
J. Org. Chem., 1966, **31**, 4071.
46. R. P. Duffley and R. Stevenson, *J. Chem. Soc. P1*, 1977, 802.
47. R. T. Scannell and R. Stevenson, *J. Het. Chem.*, 1982, **19**, 299.

48. T. Biftu, G. E. Schneiders and R. Stevenson,
J. Chem. Res. (S), 1982, 270.
49. R. T. Scannell and R. Stevenson, *J. Het. Chem.*, 1980, 17, 1727.
50. G. E. Schneiders and R. Stevenson, *J. Org. Chem.*, 1979, 44, 4711.
51. F. G. Schreiber and R. Stevenson, *J. Chem. Soc. P1*, 1976, 1514.
52. F. G. Schreiber and R. Stevenson, *Chem. Lett.*, 1975, 1257.
53. D. R. Buckle and C. J. M. Rockell, *J. Chem. Soc. P1*, 1985, 2443.
54. R. C. Larock and L. W. J. Harrison, *J. Am. Chem. Soc.*, 1984, 106, 4218.
55. S. Cacchi, A. Arcadi and F. Marinelli, *Synthesis*, 1986, 749.
56. G. Manecke and D. Zerpner, *Chem. Ber.*, 1972, 105, 1943.
57. R. A. Aitken and G. Burns, *Tetrahedron Lett.*, 1987, 28, 3717.
58. H. W. Moore, K. F. West, U. Wriede, K. Chow, M. Fernandez and N. V. Nguyen, *J. Org. Chem.*, 1987, 52, 2537.
59. K. Kurosawa and K. Nogami, *Bull. Chem. Soc. Jpn.*, 1974, 47, 505.
60. S. K. Talapatra, P. Chaudhuri and B. Talapatra,
Heterocycles, 1980, 14, 1279.
61. B. Cardillo, M. Cornia and L. Merlini, *Gazz. Chim. Ital.*, 1975, 105, 1151.
62. K. Schofield, R. S. Ward and A. M. Choudhury,
J. Chem. Soc. (C), 1971, 2834.
63. W. D. Ollis, K. L. Ormand and I. O. Sutherland,
J. Chem. Soc. (C), 1970, 119.
64. S. Antus, F. Boross and M. Nogradi, *Liebigs Ann. Chem.*, 1978, 107.
65. J. L. Ingham and P. M. Dewick, *Phytochem.*, 1978, 17, 534.
66. B. Vu, G. M. Vandor and M. Nogradi, *Liebigs Ann. Chem.*, 1984, 734.
67. T. Suzuki, T. Kitamura, T. Sonoda, S. Kobayashi and H. Taniguchi,
J. Org. Chem., 1981, 46, 5324.
68. T. Suzuki, T. Sonoda, S. Kobayashi and H. Taniguchi,
J. Chem. Soc., Chem. Commun., 1976, 180.
69. T. Sonoda, M. Kawakanu, T. Ikeda, S. Kobayashi and H. Taniguchi,
J. Chem. Soc., Chem. Commun., 1976, 612.
70. T. Sonoda, S. Kobayashi and H. Taniguchi,
Bull. Chem. Soc. Jpn, 1976, 49, 2560.
71. H. Ohba, T. Ikeda. S. Kobayashi and H. Taniguchi,
J. Chem. Soc., Chem. Commun., 1980, 988.

72. T. Ikeda, S. Kobayashi and H. Taniguchi, *Chem. Lett.*, 1982, 391.
73. T. Ikeda, S. Kobayashi and H. Taniguchi, *Synthesis*, 1982, 393.
74. H. L. McPherson and B. W. Ponder, *J. Het. Chem.*, 1976, 13, 909.
75. R. Adams and L. Whitaker, *J. Am. Chem. Soc.*, 1956, 78, 658.
76. T. Mukaiyama, Y. Sagawa and S. Kobayashi, *Chem. Lett.*, 1987, 2169.
77. B. R. Brown, G. A. Somerfield and P. D. J. Wietzman,
J. Chem. Soc., 1958, 4305.
78. P. Yates, *J. Am. Chem. Soc.*, 1952, 74, 5376.
79. E. Bisagni and C. Rivalle, *Bull. Soc. Chim. Fr.*, 1969, 3111.
80. B. Ledoussal, A. Gorgues and A. Le Coq,
J. Chem. Soc., Chem. Commun., 1986, 171.
81. P. D. Seemuth and H. Zimmer, *J. Org. Chem.*, 1978, 43, 3063.
82. R. E. Koenigkramer and H. Zimmer, *J. Org. Chem.*, 1980, 45, 3994.
83. B. D. Dean and W. E. Truce, *J. Org. Chem.*, 1981, 46, 3575.
84. A. Kasahara, T. Izumi, M. Yodono, R. Saito, T. Takedo and T. Sugawara,
Bull. Chem. Soc. Jpn., 1973, 46, 1220.
85. V. H. Deshpande, R. Srinivasan and A. V. Rama Rao,
Ind. J. Chem., 1975, 13, 453.
86. M. Takasugi, S. Nagao, S. Ueno, T. Masamune, A. Shirata and K.
Takahashi, *Chem. Lett.*, 1978, 1239.
87. CA92(19):160540d.
88. T. Nomura and T. Fukai, *Planta Med.*, 1981, 42, 197.
T. Nomura, T. Fukai, T. Fujimoto and Y. Hano, *Heterocycles*, 1984, 22,
2805.
89. M. Takasugi, S. Ishikawa and T. Masamune, *Chem. Lett.*, 1982, 1221.
90. M. Takasugi, S. Nagao and T. Masamune, *Chem. Lett.*, 1982, 1217.
91. For a comprehensive account, see R. F. Heck, '*Palladium Reagents in
Organic Synthesis*', Academic Press 1985.
92. M. Cugnon de Sevracourt and M. Robba, *Bull. Soc. Chim. Fr.*, 1977, 142.
93. N. F. Masters and D. A. Widdowson,
J. Chem. Soc., Chem. Commun., 1983, 995.
94. P. J. Beswick, *PhD Thesis*, University of London, 1985.
95. E. Negishi, F. T. Lao, R. Frisbee and H. Matsuhita,
Heterocycles, 1982, 18, 117.

96. D. A. Widdowson and Y. Z. Zhang, *Tetrahedron*, 1986, 42, 2111.
97. D. Milstein, *J. Chem. Soc., Chem. Commun.*, 1986, 817.
98. T. R. Bailey, *Tetrahedron Lett.*, 1986, 27, 4407.
99. Computer molecular modelling was carried out on ICI's CLASH program.
100. L. Rene and R. Royer, *Bull. Soc. Chim. Fr.*, 1973, 2355.
101. G. I. Fentrill and R. N. Mirrington, *Aust. J. Chem.*, 1972, 25, 1719, 1731.
102. S. Hannessian and P. Lavallee, *Canad. J. Chem.*, 1975, 53, 2975.
103. See ref. 94.
104. R. E. Ireland and D. M. Walba, *Organic Syntheses*, 56, 44.
105. G. Nechvatal, *PhD Thesis*, University of London, 1982.
106. J. K. Stille and A. M. Echavarren, *J. Am. Chem. Soc.*, 1987, 109, 5478.
107. B. M. Trost and M. G. Saulmer, *Tetrahedron Lett.*, 1985, 26, 123.
108. T. Mukaiyama and M. Hayashi, *Chem. Lett.*, 1974, 15.
T. Mukaiyama, M. Osaki and K. Saigo, *Chem. Lett.*, 1976, 769.
109. S. Murata, M. Suzuki and R. Noyori, *J. Am. Chem. Soc.*, 1980, 102, 3248.
110. L. Gruber, J. Tomoskozi and L. Radics, *Synthesis*, 1975, 708.
111. G. H. Posner, '*An Introduction to Syntheses using Organocopper Reagents*', Wiley, 1980.
112. P. Beletskaya, *J. Organomet. Chem.*, 1983, 250, 551.
113. H. B. Kagan and J. L. Namy, *Tetrahedron*, 1986, 42, 6573.
114. D. N. Kursanov, Z. N. Parnes and N. M. Loirn, *Synthesis*, 1974, 633.
115. I. Fleming, '*Frontier Orbitals and Organic Chemical Reactions*', Wiley, 1985.
116. D. D. Perrin, W. L. F. Armarego and D. R. Perrin, '*Purification of Laboratory Chemicals*, 2nd Ed., Pergamon Press, 1980.
117. D. Coulson, *Inorg. Synth.*, 13, 121.
118. R. N. Keller and H. D. Wycoff, *Inorg. Synth.*, 1946, 2, 1.
119. G. M. Whitesides, C. P. Casey and J. R. Kreiger, *J. Am. Chem. Soc.*, 1971, 93, 1386.