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Flexible metathesis-based approaches to highly functionalised furans and pyrroles

Timothy J. Donohoe [a,*], Neil M. Kershaw [a], Allan J. Orr [a], Katherine M.P. Wheelhouse (nee Gosby) [a], Lisa P. Fishlock [a], Adam R. Lacy [a], Matilda Bingham [b], Panayiotis A. Procopiou [c]

[a] *Department of Chemistry, University of Oxford, Chemistry Research Laboratory, Mansfield Road, Oxford OX1 3TA, UK*
[b] *Department of Medicinal Chemistry, Organon Laboratories Ltd, Newhouse, Lanarkshire ML1 5SH, Scotland, UK*
[c] *GlaxoSmithKline Research and Development Limited, Medicines Research Centre, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY, UK*

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Abstract

A range of differentially functionalised furans and pyrroles have been synthesised in short order by the judicious use of a ring-closing metathesis/aromatisation strategy. Two contrasting approaches are described exploiting a palladium-catalysed union of allylic alcohols and sulfonamides in one case, and a titanium mediated methylenation of homoallylic esters in another. A number of groups that are difficult to install via traditional methods were incorporated successfully.

Keywords: Ring-closing metathesis; Furan; Pyrrole; Arenes; Catalysis

1. Introduction

In recent years, the metathesis reaction has become regarded as one of the most important C–C bond forming processes and has been utilised extensively in total synthesis.[1] The advent of well defined catalyst systems combining excellent activity and broad functional group compatibility has been the major factor in popularising this reaction.[2] Ruthenium carbenoids **1**–**4** represent a selection of an increasing number of commercially available metathesis catalysts, which are widely used because of their relative insensitivity to oxygen, moisture and minor impurities in reaction solvents (Fig. 1).

One of the most powerful tactics for the synthesis of carbocyclic and heterocyclic frameworks is ring-closing metathesis (RCM).[3] However, in the context of *aromatic* and *heteroaromatic* ring formation, rationally designed RCM strategies have only recently been highlighted in the literature.[4] Indeed,

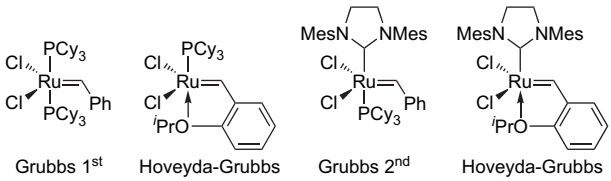

Figure 1. A selection of commercially available metathesis catalysts.

many early examples of the synthesis of aromatic compounds by RCM were viewed as unwanted degradation reactions.[5] As heteroaromatic compounds are prevalent in biologically active compounds, both as natural products and in medicinal chemistry, the development of a flexible, novel approach to aromatic compounds utilising RCM as a key step was undertaken.

In the first instance, it was decided to concentrate efforts on the synthesis of five-membered heterocycles and furans in particular. Two plausible disconnections (A and B) utilising RCM as a key bond forming process were considered (Scheme 1).

* Corresponding author. Tel.: +44 1865 275 649; fax: +44 1865 275 708.
E-mail address: timothy.donohoe@chem.ox.ac.uk (T.J. Donohoe).

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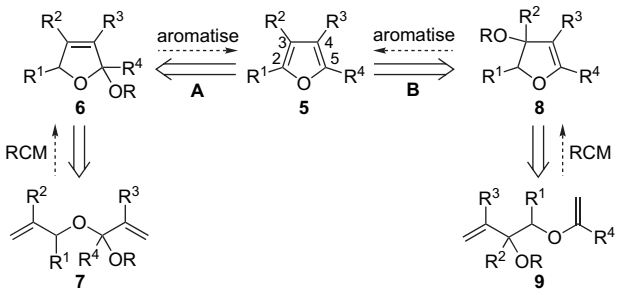
- Disconnection A, in which a leaving group is present at C-5, reveals allylic mixed acetal **7**.
- Disconnection B, in which a leaving group is present at C-3, reveals enol ether **9**.



Scheme 1.

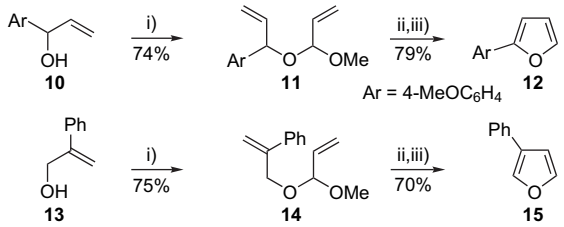
Acyclic dienes **7/9**, bearing groups R^1, R^2, R^3 and R^4, would be expected to form dihydrofurans **6/8** upon RCM. Critically, **6** and **8** are at the correct oxidation level to furnish the aromatic furan **5** upon elimination of the alcohol leaving group.[6] The possibility of achieving the RCM and subsequent aromatisation in 'one-pot' made this a very attractive proposal. It was anticipated that this approach would allow access to a wide variety of differentially substituted furans and, by analogy, pyrroles.

2. Results and discussion

The successful synthesis of a range of furans and pyrroles based on these two disconnections was recently communicated.[7,8] Herein, a full account of these studies is detailed, contrasting the scope of the two strategies outlined in Scheme 1.

2.1. Mixed acetal route to furans and pyrroles

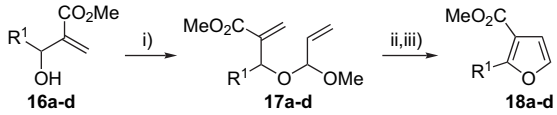
A robust method was required for the formation of *O*,*O*- and *N*,*O*-acetals and it was noted that such transformations had been achieved via the reaction of methoxyallene[9] with alcohols and sulfonamides under palladium(II) catalysis.[5b,10] Initially, allylic alcohols **10**[11] and **13**[12] were synthesised, establishing functionality at R^1 and R^2, respectively, via single step literature procedures. These were then converted to the corresponding mixed acetals in good yield (Scheme 2).



Scheme 2. *Reagents and conditions*: (i) methoxyallene, 5% $Pd(OAc)_2$, 5% dppp, Et_3N, MeCN, reflux; (ii) 10 mol % **3**, CH_2Cl_2, reflux; (iii) 0.6 equiv TFA, CH_2Cl_2, rt.

Treatment of mixed acetals **11** and **14** with 10 mol % of Grubbs second generation catalyst **3** smoothly effected ring closure to the corresponding dihydrofurans. Aromatisation to the desired furans **12** and **15** on exposure to acid proceeded in excellent overall yield. A problem frequently encountered during the purification of metathesis reactions is contamination of the relatively nonpolar products with (nonpolar) phosphine residues from the catalyst. Although the RCM/aromatisation could be performed in a single operation and in high yield (e.g., **11**→**12**; 90% for a one-pot protocol), it was generally found to be advantageous to purify rapidly the more polar dihydrofuran prior to the aromatisation step. This circumvented any unwanted contamination of the less polar furans with phosphine residues.

Having successfully generated monosubstituted furans, the synthesis of a range of disubstituted furans was attempted. Accordingly, known Baylis–Hillman adducts **16a–d**[13] were readily transformed into mixed acetals **17a–d** using the previously described conditions; RCM and aromatisation furnished 2,3-disubstituted furans **18a–d** in moderate to excellent yield (Scheme 3).



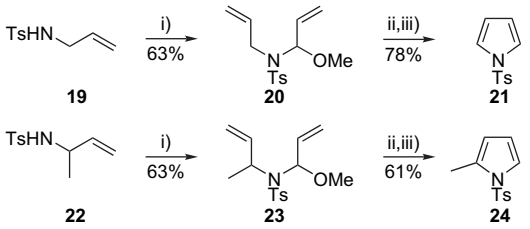
Scheme 3. *Reagents and conditions*: (i) methoxyallene, 5% $Pd(OAc)_2$, 5% dppp, Et_3N, MeCN, reflux; (ii) 10 mol % **3**, CH_2Cl_2, reflux; (iii) 0.6 equiv TFA, CH_2Cl_2, rt.

In addition to the methyl ester at R^2 (see **5**, Scheme 1), both alkyl and a range of substituted aryl groups were readily installed at R^1 via this sequence and yields were generally good (Table 1). Moreover, it seems feasible that additional functionality could be introduced at R^4 by exploiting the reactivity of the furan nucleus in electrophilic substitution reactions or through α-metallation followed by a range of palladium-catalysed couplings or electrophilic quenches.

Table 1
Yields for the sequence depicted in Scheme 3

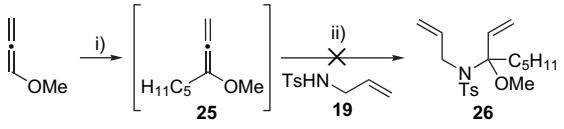
Entry	R^1	Yield (%)	
		(i)	(ii,iii)
1 (a)	Me	91	79
2 (b)	3-MeC_6H_4	73	70
3 (c)	3-$CF_3C_6H_4$	58	59
4 (d)	4-$NO_2C_6H_4$	58	81

Encouraged by this initial success, attention was turned to the synthesis of *N*-protected pyrroles. The required allylic sulfonamides **19** and **22** were prepared in short order from commercially available starting materials and converted to the corresponding *N*,*O*-acetals in an analogous fashion to that described above. Then RCM and aromatisation proceeded smoothly, forming the desired *N*-protected pyrroles **21** and **24** in good yield after purification (Scheme 4).



Scheme 4. *Reagents and conditions*: (i) methoxyallene, 5% $Pd(OAc)_2$, 5% dppp, Et_3N, MeCN, reflux; (ii) 10 mol % **3**, CH_2Cl_2, reflux; (iii) 0.6 equiv TFA, CH_2Cl_2, rt.

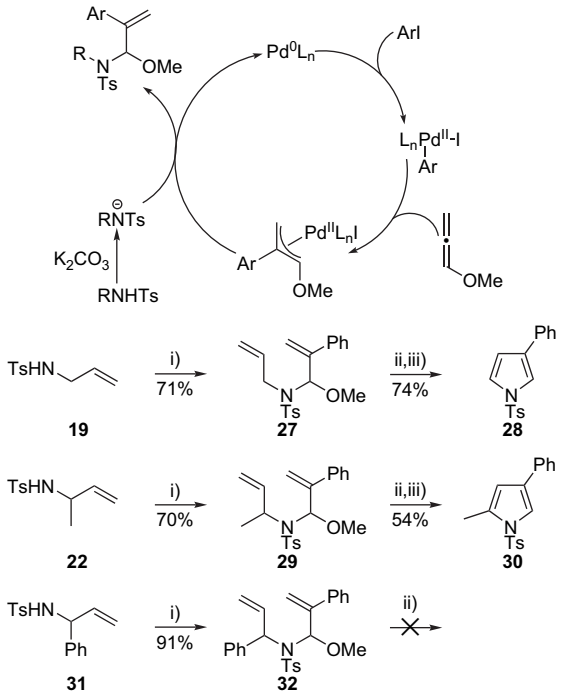
Although the preparation of functionalised allylic alcohols and sulfonamides had been achieved, we were mindful that the portion of the heterocycle derived from methoxyallene remained unsubstituted. Metallation of alkoxyallenes adjacent to the alkoxy group followed by quenching with an appropriate electrophile had been reported in the literature.[14] It was anticipated that this reaction would allow access to more highly substituted heterocycles without the need for further manipulation after RCM and aromatisation. Unfortunately, although the functionalised methoxyallene derivative **25** could be prepared (albeit without purification)[15] the subsequent palladium coupling failed to yield any of the desired *N*,*O*-acetal **26**, with rearrangement and hydrolysis of the allene being the major processes (Scheme 5).



Scheme 5. *Reagents and conditions*: (i) *n*-BuLi, THF, −40 °C then *n*-pentyl bromide; (ii) 5% $Pd(OAc)_2$, 5% dppp, Et_3N, MeCN, reflux.

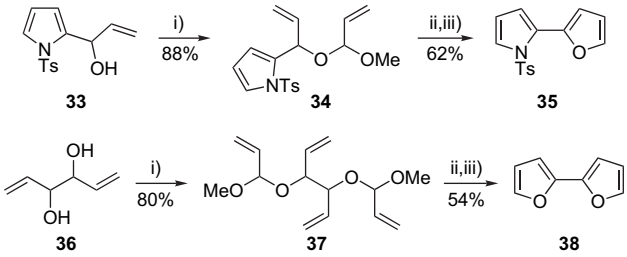
Undeterred, functionalisation at the central carbon of the allene was attempted via a palladium(0)-catalysed coupling of an aryl halide, an allylic sulfonamide and methoxyallene.[16] Presumably, the mechanism involves oxidative addition to the aryl halide to form a palladium(II) species followed by carbopalladation of methoxyallene to yield a π-allyl system. Subsequent attack by the sulfonamide at the most electron deficient end of the π-allyl system would yield the *N*,*O*-acetal and regenerate the palladium(0) catalyst (Scheme 6).[16,17]

To our delight, the three component coupling proceeded smoothly furnishing *N*,*O*-acetals **27**, **29** and **32** in excellent yield. Subsequent RCM and aromatisation was high yielding for the formation of monosubstituted pyrrole **28**, thus installing functionality at R^3. The yield of pyrrole **30**, with substituents at R^1 and R^3, was significantly lower although still very efficient given the brevity of the overall sequence. This reduction in yield was attributed to the increased steric hindrance of *N*,*O*-acetal **29** resulting in a less efficient ring closure. The inability of *N*,*O*-acetal **32** to undergo RCM was disappointing, although not surprising given this hypothesis. More powerful catalysts, which are capable of forming tetrasubstituted double bonds were recently described by Grubbs and co-workers.[18] Reinvestigation of substrates **29** and **32** using these catalysts would be expected to yield more fruitful results, thus enhancing the appeal of this approach.



Scheme 6. *Reagents and conditions*: (i) methoxyallene, 5% $Pd(PPh_3)_2$, PhI, K_2CO_3, toluene, rt; (ii) 10 mol % **3**, CH_2Cl_2, reflux; (iii) 0.6 equiv TFA, CH_2Cl_2, rt.

As an extension to this methodology, a range of biaryl systems were then targeted. Biaryl motifs are present in a range of natural products such as roseophilin[19] and are also of some importance in material science.[20] Accordingly, known pyrrole **33**[21] was converted to allylic acetal **34** in excellent yield. RCM and aromatisation proceeded in good overall yield providing furan-pyrrole **35**. In addition, the tandem cyclisation of bis-allylic acetal **37**, obtained from commercially available diol **36**, furnished bis-furan **38** in a pleasing 54% yield. The expediency of this synthesis, facilitated by the tandem RCM, provides many interesting opportunities for total synthesis and for the generation of polyaromatic arrays (Scheme 7).



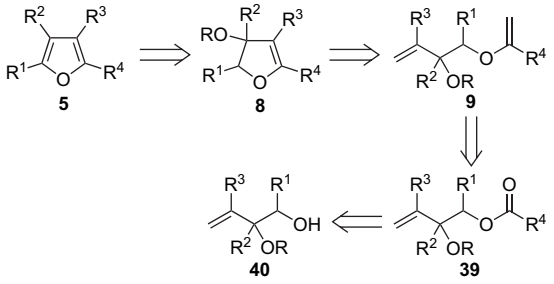
Scheme 7. *Reagents and conditions*: (i) methoxyallene, 5% $Pd(OAc)_2$, 5% dppp, Et_3N, MeCN, reflux; (ii) 10 mol % **3**, CH_2Cl_2, reflux; (iii) 0.6 equiv TFA, CH_2Cl_2, rt.

In summary, monosubstituted furans with groups R^1 and R^2 at C-2 and C-3, respectively, as well as disubstituted examples can be accessed using this strategy. The opportunity to introduce additional functionality after aromatisation by a variety of methods further enhances the appeal of this method. The tolerance of carbonyl, alkyl and a range of electron donating and

withdrawing aryl groups is also significant. *N*-protected pyrroles are also readily synthesised. Although metallation of methoxyallene was ultimately unsuccessful in increasing substitution, the use of a palladium(0)-catalysed three component coupling protocol provided a straightforward route to disubstituted pyrroles containing groups at either, or both, R^1 and R^3.

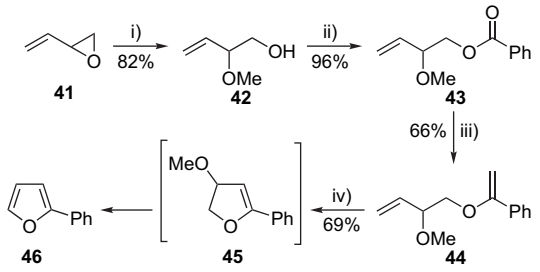
2.2. Enol ether route to furans

As part of our continuing interest in developing novel syntheses of aromatic heterocycles via metathesis strategies, disconnection B outlined in Scheme 1 was then investigated. Clearly, this approach required a flexible synthesis of a range of enol ethers **9**; the enol ether moiety was to be installed by methylenation of the corresponding ester **39**, derived from acylation of a homoallylic alcohol **40** (Scheme 8).



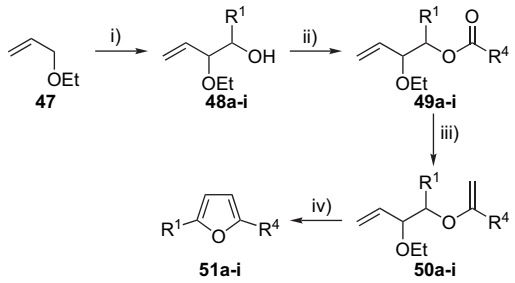
Scheme 8.

Schrock's molybdenum catalyst had been reported to be an effective catalyst for enol ether-olefin RCM reactions.[22] However, poor activity was frequently observed when using Grubbs' first generation catalyst **1**.[22b,23] This has been attributed to the formation of Fisher-type carbenes,[24] which have been shown to be relatively inactive in the metathetic processes required for RCM.[25] Recently, several groups have reported the use of the more active second generation catalyst **3** in enol ether-olefin RCM, generating cyclic enol ethers in high yields in many cases.[26] Encouraged by these results the synthesis of a simple, monosubstituted furan was attempted. Acid-catalysed ring opening of butadiene monoxide **41** with methanol afforded the requisite homoallylic alcohol **42**.[27] Reaction with benzoyl chloride then furnished ester **43** in excellent overall yield. Initially, methylenation using the Petasis reagent was attempted.[28] Unfortunately, poor conversion was observed, as judged by ^{1}H NMR analysis, even after long reaction times or by increasing the amount of Petasis reagent. An additional problem was that enol ether **44** was unstable to flash column chromatography on silica gel (triethylamine doped) and neutral or basic alumina. Eventually, it was discovered that the Takai–Utimoto protocol[29] effected complete conversion to enol ether **44**, which was sufficiently pure to be used without further purification. It had been reported that ring closure of enol ethers with appropriately placed pendant alkenes could occur in situ using the Takai–Utimoto procedure and the related Tebbe reagent.[30,31] However, this was not observed in any of the methylenation reactions performed in this study. Pleasingly, on exposure to catalyst **3**, followed by treatment of the intermediate dihydrofuran with catalytic acid in situ, furan **46** was isolated in a 69% yield over the two steps (Scheme 9).



Scheme 9. *Reagents and conditions*: (i) MeOH, 5% concd aq H_2SO_4, reflux; (ii) PhCOCl, Et_3N, CH_2Cl_2; (iii) $TiCl_4$, TMEDA, Zn, $PbCl_2$ (cat.), CH_2Br_2, CH_2Cl_2, THF; (iv) 10 mol % **3**, PhMe, 40 °C then 0.6 equiv TFA.

Buoyed by this initial success, it was decided to investigate the synthesis of 2,5-disubstituted furans. Araki and co-workers had reported the addition of γ-methoxyallylindium reagents to aldehydes with complete regioselectivity at the γ-position.[32] With this in mind a synthetic scheme was devised allowing elaboration of both R^1 and R^4. Accordingly, the formation of a range of homoallylic alcohols **48a–i** was achieved from the commercially available allyl ethyl ether **47** utilising this procedure. These were then esterified by reaction with the appropriate acid chloride or anhydride and methylenated in good yields. RCM followed by aromatisation successfully generated a range of 2,5-disubstituted furans **51a–i** (Scheme 10).



Scheme 10. *Reagents and conditions*: (i) *s*-BuLi, $InCl_3$, R^1CHO, THF, −78 °C; (ii) R^4COCl or $(R^4CO)_2O$, Et_3N, CH_2Cl_2; (iii) $TiCl_4$, TMEDA, Zn, $PbCl_2$ (cat.), CH_2Br_2, CH_2Cl_2, THF; (iv) 10 mol % **3**, PhMe, 60 °C then 0.6 equiv TFA.

The results of this study are summarised in Table 2 and demonstrate that the R^1 substituent tolerated a range of aliphatic (Table 2, entry 3), aromatic (Table 2, entry 1, 4–7), heteroaromatic (Table 2, entry 2) and fluorinated (Table 2, entry 9) groups. Whilst aromatic (Table 2, entry 1, 2), primary aliphatic (Table 2, entry 4) and secondary aliphatic (Table 2, entry 3, 5 and 9) groups were tolerated at R^4, the tertiary aliphatic derivative failed to undergo methylenation, presumably due to steric constraints (Table 2, entry 7). This difficulty was overcome by introducing the *tert*-butyl group at R^1, although the yields for methylenation and the RCM/aromatisation were lower than for the other examples (Table 2, entry 8). The RCM of trifluoromethyl enol ether successfully generated the corresponding

Table 2
Yields for the sequence depicted in Scheme 10

Entry	R^1	R^4	Yield (%)			
			(i)	(ii)	(iii)	(iv)
1 (a)	4-BrC_6H_4	Ph	70	93	72	58
2 (b)	2-Furyl	Ph	75	82	71	50[a]
3 (c)	Cyclopropyl	*i*-Pr	91	99	79	54
4 (d)	Ph	Me	90	95	82	51
5 (e)	Ph	*i*-Pr	90	86	79	52
6 (f)	Ph	CF_3	90	77	62	0
7 (g)	Ph	*t*-Bu	90	70	0	—
8 (h)	*t*-Bu	Ph	65	84	50	41[b]
9 (i)	C_6F_5	*i*-Pr	83	80	63	64[c]

[a] Furan **51b** was unstable, and decomposition was observed within hours after purification by column chromatography.
[b] Contaminated with ca. 5% phosphine ligand that could not be removed by column chromatography.
[c] Aromatisation carried out by heating the metathesis reaction mixture at 60 °C with 1 equiv of PPTS until TLC analysis showed complete consumption of starting material.

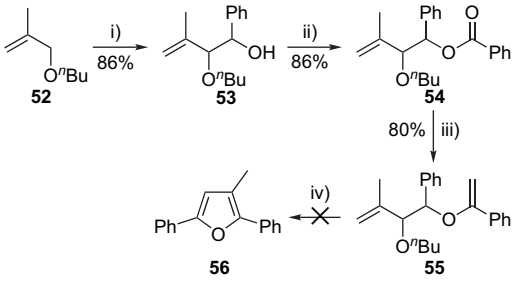
dihydrofuran, however, aromatisation could not be achieved under standard conditions (Table 2, entry 6). Even heating at reflux was unsuccessful, with eventual decomposition of the dihydrofuran being the only observable process. This was attributed to the electron withdrawing effect of the trifluoromethyl group destabilising the cation formed during an E1 elimination of ethanol. As a result, the aromatisation was attempted under basic conditions using DBU but unfortunately, no reaction was observed. Recently, phosphine free catalyst **4**, developed by Hoveyda and co-workers,[2b] became commercially available. Although rarely used in enol ether-olefin RCM[33] it was decided to attempt the cyclisation using this catalyst. Gratifyingly, yields were comparable to those using catalyst **3** and in the case of aliphatic enol ethers much higher yields were obtained. In addition, shorter reaction times were frequently observed. Although similar increases in yield were not observed for the aromatic enol ethers, purification was simplified due to the absence of phosphine ligands in the reaction (Table 3).

Table 3
Yields for the RCM/aromatisation sequence of aliphatic enol ethers using catalyst **4**

Entry	R^1	R^4	Yield (%)
1 (c)	Cyclopropyl	*i*-Pr	60
2 (d)	Ph	Me	56
3 (e)	Ph	*i*-Pr	72
4 (i)	C_6F_5	*i*-Pr	75[a]

[a] Aromatisation carried out by heating the metathesis reaction mixture at 60 °C with 1 equiv of PPTS until TLC analysis showed complete consumption of starting material.

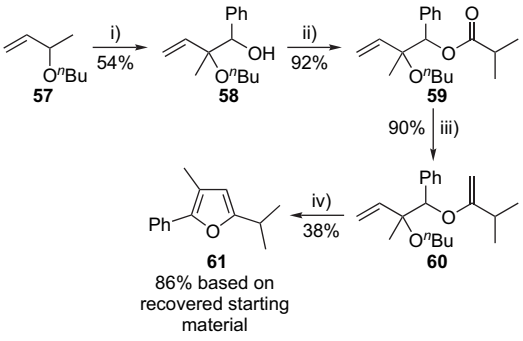
In order to synthesise trisubstituted furans, an additional substituent was required on the allyl ether starting material. Accordingly, allyl ether **52**, bearing a methyl group at R^3, was metallated and then reacted with benzaldehyde using the previously described indium methodology. Esterification, followed by methylenation furnished the metathesis precursor **55** in good overall yield. Unfortunately, this substrate failed to undergo RCM under a variety of conditions, returning only starting material in each case. It was thought that the catalyst was unable to initiate on the 1,1-disubstituted alkene due to an increased steric bulk (Scheme 11).



Scheme 11. *Reagents and conditions*: (i) *s*-BuLi, $InCl_3$, PhCHO, THF, −78 °C; (ii) PhCOCl, Et_3N, CH_2Cl_2; (iii) $TiCl_4$, TMEDA, Zn, $PbCl_2$ (cat.), CH_2Br_2, CH_2Cl_2, THF; (iv) 10 mol % **3**, PhMe, reflux then 0.6 equiv TFA.

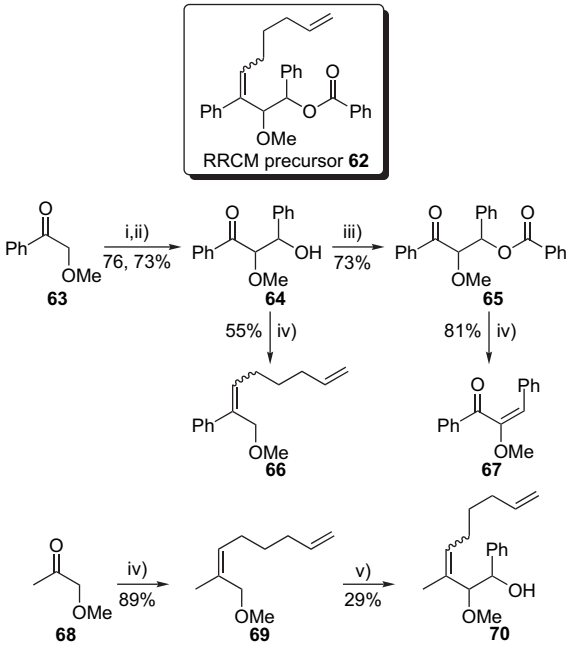
In order to circumvent this problem, the extra substituent was moved to R^2 and a similar sequence was repeated using allyl ether **57**. Addition of the γ-alkoxyallylindium reagent to benzaldehyde furnished homoallylic alcohol **58** in moderate yield. Esterification and methylenation then proceeded in excellent overall yield. The RCM/aromatisation sequence afforded trisubstituted furan **61** in a 38% yield. Interestingly, homoallylic alcohol **58** was also isolated in a 56% yield, presumably from hydrolysis of enol ether **60**, meaning the yield based on recovered starting material was 86%. It is likely that this deleterious side reaction is a result of hydrolysis of unreacted enol ether **60** during the aromatisation as a result of the slower RCM reaction. Unfortunately, increasing catalyst loading and/or reaction time did not lead to an increase in the yield. Catalyst **4** was also successful in the RCM but did not lead to any enhancement of the yield. It seems likely that the steric hindrance is not too severe to prevent RCM completely but may result in some unwanted initiation on the enol ether to give a Fisher-type carbene, which is unreactive to RCM, thus effectively sequestering the catalyst (Scheme 12).

A novel strategy for promoting RCM of unreactive substrates was recently communicated by Hoye and co-workers and referred to as relay ring-closing metathesis (RRCM).[1f,34] A sacrificial tether containing a sterically unencumbered



Scheme 12. *Reagents and conditions*: (i) *s*-BuLi, $InCl_3$, PhCHO, THF, −78 °C; (ii) *i*-PrCOCl, Et_3N, CH_2Cl_2; (iii) $TiCl_4$, TMEDA, Zn, $PbCl_2$ (cat.), CH_2Br_2, CH_2Cl_2, THF; (iv) 10 mol % **3**, PhMe, reflux then 0.6 equiv TFA.

alkene on which the catalyst can initiate delivers the ruthenium carbene onto a sterically hindered or electron poor position by intramolecular cyclisation and extrusion of cyclopentene. It seemed feasible that this method could be used to improve the yield for trisubstituted furans and allow access to tetrasubstituted furans. A route to the requisite RRCM precursor **62** (Scheme 13) was devised and relied on a Wittig olefination to install the diene moiety. Whilst the Mukaiyama aldol[35] and acylation of methoxyacetophenone **63** proceeded uneventfully, subsequent Wittig reaction of **65** with hex-5-enyltriphenylphosphonium iodide failed to yield any of the expected diene **62**. Instead, elimination occurred, furnishing enone **67** in 81% yield. Wittig reaction of alcohol **64** using 2 equiv of ylide, perhaps unsurprisingly, simply promoted *retro* aldol followed by olefination. Reaction of alcohol **64** and ester **65** under Takai–Utimoto conditions using 1,1-dibromohex-5-ene were also unsuccessful. Finally, Wittig reaction of **68** was followed by reaction with benzaldehyde under the γ-alkoxyallylindium metallation conditions described previously. Although this route was successful in producing **70**, unfortunately, the reaction was low yielding. Subsequent esterification and methylenation were also too low yielding to allow significant quantities of material to be produced in order to complete the synthesis (Scheme 13).



Scheme 13. *Reagents and conditions*: (i) TMSCl, Et_3N, NaI, MeCN; (ii) PhCHO, $TiCl_4$, CH_2Cl_2; (iii) PhCOCl, Et_3N, pyridine, CH_2Cl_2; (iv) hex-5-enyltriphenylphosphonium iodide, KHMDS, THF; (v) *s*-BuLi, $InCl_3$, PhCHO, THF, −78 °C.

In spite of the difficulties encountered during the attempted synthesis of the RRCM precursor the general strategy had been highly successful in the synthesis of monosubstituted and 2,5-disubstituted furans. It is particularly noteworthy that the aldehyde and carboxylic acid equivalents used in the synthesis of the 2,5-disubstituted furans are ultimately manifested as groups R^1 and R^4, thus allowing great flexibility. In addition a number of groups that are difficult to install by conventional methods (e.g., cyclopropyl, *i*-Pr, *t*-Bu) were readily incorporated. Trisubstituted furans were also accessible via this methodology, albeit in slightly lower yield. These studies demonstrate the usefulness of the currently available catalysts in RCM but also highlight limitations such as intolerance to sterically encumbered substrates. Recent developments in this respect by Grubbs and co-workers[18] are expected to further enhance the synthetic utility of this approach by facilitating the synthesis of tri- and tetrasubstituted furans.

3. Conclusions

Two contrasting strategies have been developed, which allow access to a wide variety of functionalised furans and pyrroles. The functional group tolerance and access to otherwise difficult substitution patterns is particularly significant. It seems likely that as novel metathesis catalysts are developed with increased activity, wider functional group tolerance and decreased sensitivity to steric constraints,[18] substrates such as **60** or **55**, which are currently less reactive or even unreactive will become viable. This will undoubtedly increase the usefulness of this methodology and provides excellent opportunity for future investigations. Thus, the scope of the RCM reaction has been expanded from the formation of isolated alkenes to allow the rapid synthesis of intermediates at the correct oxidation level to prepare fully aromatic arrays. The further development of this concept and applications to total synthesis are currently underway in our laboratories and will be reported in due course.

4. Experimental

4.1. General procedures and methods

Unless otherwise specified, all reactions were carried out under an atmosphere of argon. Tetrahydrofuran (THF) was purified by filtration through two columns of activated alumina (grade DD-2) as supplied by Alcoa, employing the method of Grubbs.[36] Acetonitrile, dichloromethane and toluene were dried by passing through activated alumina columns (activated basic aluminium oxide, Brockmann I, standard grade, ~150 mesh, 58 Å) as supplied by Aldrich. Methanol was purified by distillation over calcium hydride, and stored over molecular sieves (4 Å). Other solvents were used as supplied without further purification. Reactions were monitored by thin-layer chromatography (TLC) carried out on aluminium plates precoated with Merck silica gel 60 F_{254}. Flash column chromatography was performed using Merck silica gel 60 (4.3–6.3 μm). Melting points were recorded using a Leica VMTG heated-stage microscope and are uncorrected. Infrared spectra were recorded on a Bruker Tensor 27 Fourier Transform spectrometer, as a thin film between NaCl plates or as a KBr disc. Proton (^1H) and carbon (^{13}C) NMR were recorded using a Bruker AV400 (400 MHz and 100 MHz). Mass spectra (*m*/*z*) and accurate mass (HRMS) were recorded on an Agilent

6890 Series GC system for chemical ionisation (CI) and on a Fisons Platform II for electrospray ionisation (ESI).

4.1.1. Procedure A: oxy- and amidopalladation of methoxyallene

Triethylamine (1.5 equiv), $Pd(OAc)_2$ (5 mol %), dppp (5 mol %) and methoxyallene (3 equiv) were added to a solution of the appropriate sulfonamide or alcohol in acetonitrile (0.3 M). The reaction mixture was heated at reflux for 16 h then cooled to room temperature. Triethylamine (1 mL/mmol) was added and the reaction was quenched with water (10 mL/mmol). The product was extracted with diethyl ether (3×10 mL/mmol). The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The resulting crude products were purified by flash column chromatography as indicated.

4.1.2. Procedure B: amidopalladation of methoxyallene with in situ trapping of iodobenzene

Iodobenzene (1 equiv), $Pd(PPh_3)_4$ (5 mol %), K_2CO_3 (2 equiv) and methoxyallene (3 equiv) were added to a solution of the appropriate sulfonamide in toluene (0.3 M). The reaction mixture was heated at reflux for 16 h then cooled to room temperature. Triethylamine (1 mL/mmol) was added and the reaction was quenched with water (10 mL/mmol). The product was extracted with diethyl ether (3×10 mL/mmol). The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The resultant crude products were purified by flash column chromatography as indicated.

4.1.3. Procedure C: ring-closing metathesis

The acyclic diene starting materials were dissolved in deoxygenated (sparged with argon for 30 min) dichloromethane or toluene (ca. 0.01–0.02 M). The mixture was heated at reflux for the indicated time then cooled to room temperature. The resulting cyclised product could either be isolated by concentrating in vacuo and purifying by flash column chromatography or subjected directly to general method D.

4.1.4. Procedure D: aromatisation

Trifluoroacetic acid (0.6 equiv) was added to a solution of RCM product in dichloromethane or toluene (ca. 0.01–0.02 M) and the reaction mixture was stirred at room temperature until TLC indicated complete consumption of starting material. Diethyl ether (10 mL/mmol) was then added. The reaction mixture was washed with saturated aqueous $NaHCO_3$ (10 mL/mmol) and the organic layer was separated, dried over $MgSO_4$, and concentrated in vacuo. The resulting aromatic products were then purified by flash column chromatography as indicated.

4.1.5. Procedure E: formation of alcohols via allyl indium reagents

s-Butyl lithium (1.0 M solution in hexanes, 3.0 equiv) was added to a solution of allyl ethyl ether (3.0 equiv) in THF (0.1 M) at −78 °C. After stirring for 1 h, a solution of $InCl_3$ (1.0 equiv) in THF (0.2 M) was added. Stirring was continued for a further 30 min before addition of the corresponding aldehyde (1.0 equiv). After 1 h, the reaction mixture was allowed to warm to room temperature before addition of 1.0 M aqueous hydrochloric acid solution (5 mL/mmol). The aqueous layer was extracted with diethyl ether (3×10 mL/mmol) and the combined organic layers were washed with water (10 mL/mmol) and saturated aqueous sodium chloride solution (10 mL/mmol) then dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash column chromatography to give the corresponding alcohol as an inconsequential mixture of diastereoisomers, which were not separated.

4.1.6. Procedure F: ester formation

The appropriate acid chloride or anhydride (1.2 equiv) was added dropwise to a stirred solution of the corresponding alcohol (1.0 equiv) and triethylamine (1.2 equiv) in CH_2Cl_2 (5 mL/mmol) at room temperature. The reaction mixture was stirred at room temperature until TLC analysis indicated complete consumption of starting material. The reaction mixture was diluted with diethyl ether (10 mL/mmol), washed with 1.0 M aqueous hydrochloric acid solution (5 mL/mmol) and 32% aqueous ammonia solution (5 mL/mmol), then dried over $MgSO_4$. The solvent was removed in vacuo and the crude product was purified by flash column chromatography as indicated.

4.1.7. Procedure G: Takai–Utimoto olefination

$TiCl_4$ (1.0 M solution in CH_2Cl_2, 8.5 equiv) and TMEDA (16.5 equiv) were slowly added to THF (5 mL/mmol) with stirring at 0 °C. After stirring at this temperature for 20 min, Zn dust (18.5 equiv) and $PbCl_2$ (0.1 equiv) were added to the solution. The resulting slurry was warmed to room temperature and stirred for 30 min. A solution of the appropriate ester (1.0 equiv) and dibromomethane (4.7 equiv) in THF (5 mL/mmol) was added at room temperature and the slurry was stirred for 16 h. The mixture was cooled to 0 °C and saturated aqueous K_2CO_3 solution (5 mL/mmol) was added. The reaction mixture was passed through a thin pad of basic aluminium oxide and washed with a solution of triethylamine in ether (ether/triethylamine; 200:1, 250 mL). The mixture was concentrated in vacuo; if a white solid appeared at this point the filtration was repeated until the solid was removed, and the product was used without further purification.

4.1.8. Procedure H: Wittig olefination

KHMDS (0.5 M in toluene, 2.2 equiv) was added dropwise to a stirred solution of hex-5-enyltriphenylphosphonium iodide (2.2 equiv) (which was dried under vacuum at 60 °C for 12 h prior to use) in THF (0.1 M) at −78 °C. The orange slurry was allowed to warm to room temperature and stirred at room temperature for 90 min. The reaction mixture was cooled to −78 °C and a solution of the appropriate ketone (1 equiv) in THF (0.1 M) was then added dropwise. The reaction mixture was stirred at room temperature until TLC indicated complete consumption of starting material, then concentrated in vacuo onto silica gel and purified by flash column chromatography.

4.2. Methods

The experimental details for compounds **12**,[7] **15**,[37] **18a**,[38] **18d**,[7] **19**,[39] **21**,**22**,[40,41] **24**,[42] **28**,[7] **31**,[43] **35**,[7] **38**,[7] **46**,[44] **48–51a–g**,**i**,[8] **52–61**,[8] **64**[45] and **67**[46] have been published previously.

4.2.1. 1-Methoxy-4-(1-(1-methoxyallyloxy)allyl)benzene (*11*)

Allylic alcohol **10** (750 mg, 4.60 mmol) was subjected to general procedure A. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 9:1+1% Et_3N) yielded **11** as a yellow oil (799 mg, 74%) and as a 1:1 mixture of diastereomers, which were not separated; ν_{max} (film)/cm^{-1} 3080, 2834, 1641, 1611; δ_H (400 MHz; C_6D_6) 7.45–7.42 (1H, m, Ar*H*), 7.37–7.34 (1H, m, Ar*H*), 6.93–6.85 (2H, m, 2×Ar*H*), 6.22–6.14 (0.5H, m, CH_2=C*H*CHAr), 6.04–5.92 (1.5H, m, CH_2=C*H*CHAr, CH_2=C*H*CHOCH$_3$), 5.56–5.43 (2H, m, C*H*$_2$=CHCHAr), 5.40–5.13 (3.5H, m, C*H*$_2$=CHCHOCH$_3$, C*H*Ar, C*H*OCH$_3$), 5.08–5.06 (0.5H, m, C*H*OCH$_3$), 3.41, 3.39 (3H, 2×s, ArOC*H*$_3$), 3.28, 3.25 (3H, 2×s, OC*H*$_3$); δ_C (100 MHz; C_6D_6) 160.0, 159.8, 140.2, 139.3, 136.1, 136.0, 134.0, 133.2, 129.2, 128.7, 128.5, 118.3, 116.2, 114.8, 114.4, 114.3, 100.1, 99.5, 78.2, 77.8, 54.93, 54.91, 51.5, 51.2; *m/z* (ESI) 257 (10%, $[M+Na]^+$), 163 (7), 147 (100); HRMS (ESI) $C_{14}H_{18}O_3Na$ ($[M+Na]^+$) requires 257.1154, found 257.1158.

4.2.2. (1-(1-Methoxyallyloxymethyl)vinyl)benzene (*14*)

Allylic alcohol **13** (314 mg, 2.30 mmol) was subjected to general procedure A. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 95:5+1% Et_3N) yielded **14** as a colourless oil (350 mg, 75%); ν_{max} (film)/cm^{-1} 3083, 2829, 1632; δ_H (400 MHz; C_6D_6) 7.50–7.42 (2H, m, 2×Ar*H*), 7.26–7.17 (3H, m, 3×Ar*H*), 5.96–5.87 (1H, m, C*H*=CH$_2$), 5.55–5.51 (2H, m, CH=C*H*$_2$), 5.50–5.49 (1H, m, PhC=C*H*H), 5.47–5.45 (1H, m, PhC=CH*H*), 5.03–5.00 (1H, m, C*H*OCH$_3$), 4.58 (1H, d, J_{AB} 13.1, one of OC*H*$_2$), 4.44 (1H, d, J_{AB} 13.1, one of OC*H*$_2$), 3.24 (3H, s, OC*H*$_3$); δ_C (100 MHz; C_6D_6) 145.2, 139.6, 135.7, 128.7, 128.0, 126.6, 118.6, 113.8, 101.6, 67.1, 52.3; *m/z* (CI) 205 (4%, $[M+H]^+$), 174 (20), 134 (35); HRMS (CI) $C_{13}H_{17}O_2$ ($[M+H]^+$) requires 205.1229, found 205.1226.

4.2.3. 2-(1-(1-Methoxyallyloxy)ethyl)acrylic acid methyl ester (*17a*)

Allylic alcohol **16a** (500 mg, 3.80 mmol) was subjected to general procedure A. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 9:1+1% Et_3N) yielded **17a** as a pale yellow oil (691 mg, 91%) and as a 1:1 mixture of diastereomers; ν_{max} (film)/cm^{-1} 3071, 2954, 2800, 1720, 1631, 1439, 1349; δ_H (400 MHz; C_6D_6) 6.36–6.33 (1H, m, C*H*H=CCO$_2$Me), 6.05–6.04 (0.5H, m, CH*H*=CCO$_2$Me), 5.95–5.86 (1.5H, m, CH*H*=CCO$_2$Me), 5.46–5.44, 5.42–5.40 (2H, m, C*H*$_2$=CH), 5.05 (0.5H, q, *J* 6.4, C*H*CH$_3$), 4.97–4.91 (1.5H, m, C*H*CH$_3$, C*H*OCH$_3$), 3.45, 3.44 (3H, s, OC*H*$_3$), 3.23, 3.21 (3H, s, OC*H*$_3$), 1.53, 1.43 (3H, d, *J* 6.4, C*H*$_3$); δ_C (100 MHz; C_6D_6) 166.4, 144.3, 143.6, 136.1, 135.9, 128.5, 124.3, 118.3, 101.7, 100.9, 70.4, 69.6, 52.7, 51.4, 51.2, 22.7, 22.0; *m/z* (ESI) 259 (35%, $([M+MeCN+NH_4]^+)$), 223 (100, $[M+Na]^+$); HRMS (ESI) $C_{10}H_{16}O_4Na$ ($[M+Na]^+$) requires 223.0937, found 223.0946.

4.2.4. 2-((1-Methoxyallyloxy)-m-tolylmethyl)acrylic acid methyl ester (*17b*)

Allylic alcohol **16b** (800 mg, 3.88 mmol) was subjected to general procedure A. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 8:2+1% Et_3N) yielded **17b** as a pale yellow oil (812 mg, 70%) and as a 1:1 mixture of diastereomers; ν_{max} (film)/cm^{-1} 1725, 1632, 1622, 1588, 1261, 1147, 1034; δ_H (400 MHz; C_6D_6) 7.39–7.33 (2H, m, 2×Ar*H*), 7.13–7.06 (1H, m, Ar*H*), 6.89 (1H, t, *J* 8.0, Ar*H*), 6.35 and 6.32 (1H, 2×apparent dd, *J* 1.5, 1.1, C=C*H*H), 6.12 and 6.01 (1H, 2×apparent t, *J* 1.5, C=C*H*H), 5.99 and 5.88 (1H, 2×br s, C*H*Ar), 5.83 and 5.78 (1H, 2×ddd, *J* 17.4, 10.6, 4.8, and 17.4, 10.6, 4.8, *H*C=CH$_2$), 5.35 and 5.31 (1H, 2×apparent dt, *J* 17.4, 1.5, *trans*-HC=C*H*H), 5.07 and 5.04 (1H, 2×apparent dt, *J* 10.4, 1.5, *cis*-HC=C*H*H), 4.99 and 4.97 (1H, 2×dt, *J* 4.7, 1.2, C*H*(OCH$_3$)), 3.20 (3H, 2×s, OC*H*$_3$), 3.14 and 3.07 (3H, 2×s, OC*H*$_3$), 2.06 and 2.04 (3H, 2×s, C*H*$_3$); δ_C (100 MHz; C_6D_6) 166.0, 165.9, 142.7, 142.2, 140.7, 140.0, 138.1, 138.0, 135.5, 135.4, 129.2, 129.0, 128.9, 128.8, 128.6, 128.5, 125.7, 125.4, 124.4, 124.3, 118.4, 118.3, 101.5, 99.5, 75.6, 74.6, 52.0, 51.3, 51.2, 21.4, 21.3; *m/z* (ESI) 299 (100%, $[M+Na]^+$); HRMS (ESI) $C_{16}H_{20}O_4Na$ ($[M+Na]^+$) requires 299.1259, found 299.1256.

4.2.5. 2-((1-Methoxyallyloxy)-3-trifluoromethylphenyl methyl)acrylic acid methyl ester (*17c*)

Allylic alcohol **16c** (500 mg, 1.92 mmol) was subjected to general procedure A. Flash chromatography (SiO_2; petroleum ether/ethyl acetate 96:4+1% Et_3N) yielded **17c** as a pale yellow oil (366 mg, 58%) and as a 1:1 mixture of diastereomers; ν_{max} (film)/cm^{-1} 1724, 1662, 1632, 1602, 1529, 1330, 1265, 1176, 1129, 1079; δ_H (400 MHz; C_6D_6) 7.94 and 7.90 (1H, 2×s, Ar*H*), 7.50 and 7.46 (1H, 2×d, *J* 7.6, Ar*H*), 7.24 (1H, t, *J* 7.4, Ar*H*), 6.95–6.88 (1H, m, Ar*H*), 6.25 and 6.22 (1H, 2×s, C=C*H*H), 5.96 and 5.84 (1H, 2×d, *J* 1.0, C=C*H*H), 5.86 and 5.79 (1H, 2×s, C*H*Ar), 5.70 (1H, ddd, *J* 17.4, 10.5, 4.6, *H*C=CHH), 5.28 and 5.23 (1H, 2×dd, *J* 17.4, 1.1, *trans*-HC=C*H*H), 5.03 and 5.00 (1H, 2×dd, *J* 10.5, 1.1, *cis*-HC=C*H*H), 4.87 and 4.77 (1H, 2×d, *J* 4.7 and 4.6, C*H*(OCH$_3$)), 3.17 (3H, 2×s, OC*H*$_3$), 3.01 and 2.95 (3H, 2×s, OC*H*$_3$); δ_C (100 MHz; C_6D_6) 165.6, 165.5, 142.4, 142.3, 141.9, 141.4, 135.1, 135.0, 131.6, 131.3, 129.2, 129.1, 129.0, 128.5, 125.3, 125.1, 125.0, 124.9, 124.8, 124.7, 124.6, 124.5, 118.7, 118.6, 101.6, 100.3, 74.7, 73.9, 52.1, 51.9, 51.4, 51.3; *m/z* (ESI) 394 (100%, $([M+MeCN+Na]^+)$) 353 (60, $[M+Na]^+$); HRMS (ESI) $C_{18}H_{17}NO_4F_3Na$ requires 394.1242, found 394.1231.

4.2.6. 2-((1-Methoxyallyloxy)4-nitrophenylmethyl) acrylic acid methyl ester (*17d*)

Allylic alcohol **16d** (500 mg, 2.1 mmol) was subjected to general procedure A. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 75:25+1% Et_3N) yielded **17d** as a yellow oil (370 mg, 58%) and as a 1:1 mixture of

diastereomers, which were not separated; ν_{max} (film)/cm^{-1} 3081, 2832, 1721, 1632, 1608, 1523, 1349; δ_H (400 MHz; $CDCl_3$) 8.21–8.17 (2H, m, 2×Ar*H*), 7.61–7.56 (2H, m, 2×Ar*H*), 6.44, 6.42 (1H, s, C*H*=C), 6.18, 6.10 (1H, s, CH*H*=C), 5.84–5.75 (1H, m, C*H*=CH_2), 5.70, 5.67 (1H, s, C*H*Ar), 5.47–5.42 (1H, m, C*H*=CH), 5.38–5.30 (1H, m, C*H*=CH), 4.96, 4.83 (1H, d, *J* 5.0, 4.7, C*H*OCH_3), 3.70, 3.69 (3H, s, CO_2CH_3), 3.24, 3.19 (3H, s, OCH_3); δ_C (100 MHz; $CDCl_3$) 134.1, 128.6, 128.2, 126.4, 126.1, 123.53, 123.51, 119.4, 119.3, 101.5, 101.4, 74.1, 73.1, 52.4, 52.3, 51.99, 51.95; *m/z* (CI) 308 (5%, $[M+H]^+$); HRMS (CI) $C_{15}H_{18}NO_6$ ($[M+H]^+$) requires 308.1132, found 308.1134.

4.2.7. 2-m-Tolylfuran-3-carboxylic acid methyl ester (*18b*)

Mixed acetal **17b** (211 mg, 0.85 mmol) was subjected to general procedure C for 16 h in dichloromethane, then general procedure D. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 97:3) yielded **18b** as a colourless oil (129 mg, 70%); ν_{max} (film)/cm^{-1} 1723, 1610, 1573, 1515, 1487, 1439, 1297, 1254, 1196, 1149, 1068; δ_H (400 MHz; $CDCl_3$) 7.79–7.77 (2H, m, 2×Ar*H*), 7.42 (1H, d, *J* 1.9, C(5)*H*), 7.35–7.31 (1H, m, Ar*H*), 7.22 (1H, d, *J* 7.5, Ar*H*), 6.83 (1H, d, *J* 1.9, C(4)*H*), 3.83 (3H, s, CO_2CH_3), 2.42 (3H, s, CH_3); δ_C (100 MHz; $CDCl_3$) 164.0, 157.8, 141.1, 137.7, 130.2, 129.6, 128.8, 128.0, 125.6, 113.4, 112.9, 51.6, 21.5; *m/z* (CI) 234 (20%, $[M+NH_4]^+$), 217 (100, $[M+H]^+$), 216 (40, $[M]^+$); HRMS (CI) $C_{13}H_{13}O_3$ ($[M+H]^+$) requires 217.0865, found 217.0863.

4.2.8. 2-(3-Trifluoromethylphenyl)furan-3-carboxylic acid methyl ester (*18c*)

Mixed acetal **17c** (127 mg, 0.42 mmol) was subjected to general procedure C for 2 days in dichloromethane, then general procedure D. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 98:2) yielded **18c** as a colourless oil (67 mg, 59%); ν_{max} (film)/cm^{-1} 1724, 1604, 1578, 1516, 1479, 1440, 1331, 1298, 1201, 1127, 1103, 1083; δ_H (400 MHz; $CDCl_3$) 8.30 (1H, s, Ar*H*), 8.23 (1H, d, *J* 7.7, Ar*H*), 7.65 (1H, d, *J* 7.6, Ar*H*), 7.56 (1H, t, *J* 7.8, Ar*H*), 7.48 (1H, d, *J* 1.9, C(5)*H*), 6.87 (1H, d, *J* 1.9, C(4)*H*), 3.85 (3H, s, CO_2CH_3); δ_C (100 MHz; $CDCl_3$) 163.7, 155.6, 141.8, 131.4, 131.0, 130.3, 128.6, 125.8, 125.2, 122.6, 114.7, 113.2, 51.8; *m/z* (CI) 270 (100%, $[M]^+$); HRMS (CI) $C_{13}H_9F_3O_3$ ($[M]^+$) requires 270.0504, found 270.0497.

4.2.9. N-(1-Methoxyallyl)-N-(1-methylallyl)-4-methyl benzenesulfonamide (*23*)

Allylic sulfonamide **22** (305 mg, 1.40 mmol) was subjected to general procedure A. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 95:5+1% Et_3N) yielded **23** as a colourless oil (259 mg, 63%) and as a 1:1 mixture of diastereoisomers; ν_{max} (film)/cm^{-1} 2936, 2785, 1598, 1495, 1450, 1160; δ_H (400 MHz; C_6D_6) 7.87–7.84 (2H, m, 2×Ar*H*) 6.88–6.86 (2H, m, 2×Ar*H*), 6.50–6.41, 6.27–6.18 (1H, m, CH(CH_3)C*H*=CH_2), 5.81–5.69 (1H, m, CH_2=C*H*CH(OCH_3)), 5.55–5.52, 5.50–5.48, 5.46–5.44 (2H, m, CH_2=CHCH(OCH_3)), 5.13–4.98 (3H, m, CH_2=CHCH(CH_3), C*H*OCH_3) 4.27–4.20 (1H, m, C*H*CH_3), 3.34, 3.28 (3H, s, OCH_3), 2.00 (3H, s, ArCH_3), 1.65, 1.49 (3H, d, *J* 6.8, CHCH_3); δ_C (100 MHz; C_6D_6) 142.74, 142.71, 141.4, 141.8, 139.9, 135.63, 135.60, 129.6, 129.5, 128.7, 128.4, 118.3, 118.1, 116.0, 115.3, 89.4, 89.0, 55.8, 55.7, 54.6, 21.3, 21.2, 20.2; *m/z* (ESI) 318 (10%, $[M+Na]^+$), 354 (100, $[M+MeCN+NH_4]^+$); HRMS (ESI) $C_{15}H_{21}NO_3NaS$ ($[M+Na]^+$) requires 318.1140, found 318.1151.

4.2.10. N-Allyl-N-(1-methoxy-2-phenylallyl)-4-methyl benzenesulfonamide (*27*)

Allylic sulfonamide **19** (500 mg, 2.40 mmol) was subjected to general procedure B. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 9:1+1% Et_3N) yielded **27** as an off white solid (643 mg, 71%); mp 69–71 °C; ν_{max} (KBr disc)/cm^{-1} 3087, 2834, 1630, 1597, 1496, 1340, 1332, 1163, 1075, 1026; δ_H (400 MHz; C_6D_6) 7.42–7.29 (7H, m, 5×Ph*H*, 2×Ar*H*), 7.06 (2H, d, *J* 8.2, 2×Ar*H*), 6.15 (1H, s, C*H*OCH_3), 5.58 (1H, s, C*H*H=CPh), 5.56 (1H, s, CH*H*=CPh), 5.54–5.46 (1H, m, C*H*=CH_2), 4.92 (1H, dd, *J* 17.1, 1.3, *trans*-C*H*H=CH_2), 4.86 (1H, dd, *J* 10.1, 1.3, *cis*-CH*H*=CH), 3.72–3.60 (2H, m, CH_2CH=CH_2), 3.50 (3H, s, OCH_3), 2.05 (3H, s, ArCH_3); δ_C (100 MHz; C_6D_6) 144.1, 143.1, 138.7, 137.0, 134.8, 129.1, 128.5, 128.0, 127.8, 127.2, 117.0, 116.8, 87.9, 56.1, 45.0, 21.5; *m/z* (CI) 358 (100%, $[M+H]^+$); HRMS (CI) $C_{20}H_{24}NO_3S$ ($[M+H]^+$) requires 358.1477, found 358.1480.

4.2.11. N-(1-Methoxy-2-phenylallyl)-N-(1-methylallyl)-4-methylbenzenesulfonamide (*29*)

Allylic sulfonamide **22** (400 mg, 2.40 mmol) was subjected to general procedure B. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 9:1+1% Et_3N) yielded **29** as a yellow oil (464 mg, 70%) and as a 1:1 mixture of diastereoisomers; ν_{max} (film)/cm^{-1} 3064, 2984, 2934, 1639, 1598, 1495, 1445, 1380, 1336, 1196, 1159, 1094, 1074; δ_H (400 MHz; C_6D_6) 7.63–6.69 (9H, m, 5×Ph*H*, 4×Ar*H*), 6.44 (1H, br s, C*H*OCH_3), 6.37 (0.5H, ddd, *J* 17.3, 10.4, 6.1, C*H*=CH_2), 5.91 (0.5H, ddd, *J* 17.3, 10.4, 6.1, C*H*=CH_2), 5.74–5.71 (1H, m, C*H*H=CPh), 5.45–5.43 (1H, m, CH*H*=CPh), 5.07, 4.96 (1H, apparent dt, *J* 17.4, 1.5, *trans*-C*H*H=CH), 5.01, 4.82 (1H, apparent dt, *J* 10.4, 1.5, *cis*-CH*H*=CH), 4.49–4.40 (1H, m, C*H*CH_3), 3.54, 3.47 (3H, s, OCH_3), 1.96 (3H, s, ArCH_3), 1.68, 1.33 (3H, dd, *J* 6.9, 7.1, CHCH_3); δ_C (100 MHz; C_6D_6) 145.8, 145.4, 142.44, 143.28, 141.1, 140.3, 140.1, 139.9, 139.5, 139.4, 137.7, 130.3, 129.1, 129.0, 128.62, 128.59, 126.8, 126.6, 117.6, 117.4, 114.83, 114.8, 89.8, 89.6, 56.4, 56.3, 53.8, 53.7, 21.1, 20.1, 19.4, 17.5; *m/z* (ESI) 394 (5%, $[M+Na]^+$) 430 (100, $[M+MeCN+NH_4]^+$); HRMS (ESI) $C_{21}H_{25}NO_3SNa$ ($[M+Na]^+$) requires 394.1447, found 394.1449.

4.2.12. 1-(4-Methylbenzenesulfonyl)-2-methyl-4-phenyl-1H-pyrrole (*30*)

Mixed acetal **29** (200 mg, 0.54 mmol) was subjected to general procedure C for 24 h in toluene, then general procedure D. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 85:15) yielded **30** as a viscous yellow oil (93 mg, 54%);

ν_{max} (film)/cm^{-1} 3142, 3061, 2927, 1596, 1533, 1447, 1363, 1305, 1264, 1174, 1153, 1100, 1045, 990, 919; δ_H (400 MHz; $CDCl_3$) 7.72 (2H, d, *J* 8.4, 2×Ar*H*), 7.58 (1H, d, *J* 2.0, C(5)*H*), 7.51–7.23 (7H, m, 2×Ar*H*, 5×Ph*H*), 6.30 (1H, s, C(3)*H*), 2.42 (3H, s, ArCH_3), 2.35 (3H, s, pyrrole-CH_3); δ_C (100 MHz; $CDCl_3$) 144.9, 136.1, 133.6, 131.8, 130.0, 128.8, 126.9, 126.82, 126.78, 125.4, 117.5, 111.8, 21.6, 13.7; *m/z* (CI) 312 (100%, $[M+H]^+$); HRMS (CI) $C_{18}H_{18}NO_2S$ ($[M+H]^+$) requires 312.1058, found 312.1064.

4.2.13. N-(1-Methoxy-2-phenylallyl)-N-(1-phenylallyl)-4-methylbenzenesulfonamide (32)

Allylic sulfonamide **31** (300 mg, 1.00 mmol) was subjected to general procedure B. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 4:1+1% Et_3N) yielded **32** as a yellow solid (395 mg, 91%) and as a 1:1 mixture of diastereoisomers; mp 90–92 °C; ν_{max} (KBr disc)/cm^{-1} 3083, 2832, 1630, 1598, 1493, 1346, 1330, 1162, 1073; δ_H (400 MHz; $CDCl_3$) 7.42–7.37, 7.34–7.25, 7.19–7.06, 7.02–6.96, 6.95–6.89, 6.78–6.69 (14H, m, 10×Ph*H*, 4×Ar*H*), 6.80–6.67 (0.5H, m, C*H*=CH_2), 6.36 (0.5H, ddd, *J* 17.2, 10.3, 8.1, C*H*=CH_2) 6.21, 6.14 (1H, s, one of CH_2=CPh), 5.71, 5.65 (1H, s, one of CH_2=CPh), 5.61, 5.59 (1H, s, C*H*OCH_3), 5.36 (0.5H, d, *J* 8.1, C*H*Ph) 5.31 (0.5H, d, *J* 8.6, C*H*Ph), 5.27 (0.5H, dt, *J* 10.3, 1.1, *cis*-CH_2=CHCHPh) 5.17 (0.5H, dt, *J* 17.2, 1.1, *trans*-CH_2=CHPh), 5.12 (0.5H, dt, *J* 10.3, 1.1, *cis*-CH*H*=CH_2) 4.84 (0.5H, dt, *J* 17.2, 1.1, *trans*-CH*H*=CH_2) 3.51, 3.33 (3H, s, OCH_3), 2.35, 2.26 (3H, s, ArCH_3); δ_C (100 MHz; $CDCl_3$) 145.1, 143.0, 142.3, 142.0, 139.0, 138.8, 138.7, 138.5, 137.9, 136.5, 129.8, 129.0, 128.6, 128.4, 128.1, 128.0, 127.8, 127.5, 127.34, 127.29, 127.2, 127.0, 126.9, 126.8, 118.0, 117.9, 117.7, 117.2, 89.6, 89.2, 61.5, 60.9, 56.6, 21.4, 21.3; *m/z* (ESI) 456 (10%, $[M+Na]^+$) 451 (10, $[M+NH_4]^+$); HRMS (ESI) $C_{26}H_{31}N_2O_3S$ ($[M+NH_4]^+$) requires 451.2055, found 451.2066.

4.2.14. 2-(1-(1-Methoxyallyloxy)allyl)-1-(4-methyl benzenesulfonamide)-1H-pyrrole (34)

Pyrrole **33** (250 mg, 0.90 mmol) was subjected to general procedure A. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 9:1+1% Et_3N) yielded **34** as a colourless oil (276 mg, 88%) and as a 1:1 mixture of diastereomers; ν_{max} (film)/cm^{-1} 1647, 1603, 1597, 1498, 1485, 1370, 1216, 1176, 1129, 1088, 1029; δ_H (400 MHz; C_6D_6) 7.65 (2H, d, *J* 8.4, 2×Ar*H*), 7.32, 7.30 (1H, 2×apparent dd, *J* 3.3, 1.8, C(5)*H*), 6.62 (2H, d, *J* 8.4, 2×Ar*H*), 6.40, 6.35 (1H, 2×dd, *J* 3.3, 1.7, C(4)*H*), 6.11, 5.91 (1H, 2×ddd, *J* 16.9, 10.2, 6.7, CH(pyrrolyl)C*H*=CH_2), 6.09–6.00 (1H, m, C*H*(pyrrolyl)), 6.03–6.00 (1H, m, C(3)*H*), 5.80–5.70 (1H, m, CH(OCH_3)C*H*=CH_2), 5.35–5.25 (2H, m, 2×*trans*-CH=CH_2), 5.05–4.97 (2H, m, 2×*cis*-CH=CH_2), 5.02–4.85 (1H, m, C*H*(OCH_3)), 3.10, 3.08 (3H, 2×s, OCH_3), 1.74 (3H, s, CH_3); δ_C (100 MHz; C_6D_6) 144.6, 144.4, 138.3, 137.4, 137.3, 137.1, 135.9, 135.7, 135.5, 135.3, 129.9, 129.8, 127.2, 127.1, 123.5, 123.4, 118.3, 118.2, 116.9, 115.6, 114.4, 114.0, 112.4, 112.2, 100.5, 100.0, 70.9, 70.7, 52.24, 52.17, 21.1; *m/z* (ESI) 370 (100%, $[M+Na]^+$); HRMS (ESI) $C_{18}H_{21}NO_4NaS$ ($[M+Na]^+$) requires 370.1089, found 370.1086.

4.2.15. 3,4-Bis-(1-methoxyallyloxy)hexa-1,5-diene (37)

Diol **36** (1.0 g, 8.80 mmol) was subjected to general procedure A. Flash column chromatography (SiO_2; petroleum ether/ethyl acetate; 95:5+1% Et_3N) yielded **37** as a colourless oil (1.79 g, 80%) and as a mixture of diastereoisomers; ν_{max} (film)/cm^{-1} 3080, 2830, 1645; δ_H (400 MHz; $CDCl_3$) 5.94–5.68 (4H, m, 4×C*H*=CH_2), 5.45–5.23 (8H, m, 4×CH_2=CH), 5.04–4.93 (2H, m, 2×C*H*OCH_3), 4.26–4.08 (2H, m, 2×C*H*OCHOCH_3) 3.34–3.28 (6H, m, 2×OCH_3); δ_C (100 MHz; $CDCl_3$) 135.6, 135.3, 135.2, 135.0, 134.94, 134.91, 134.8, 134.75, 134.5, 134.4, 134.3, 119.4, 119.2, 119.1, 118.9, 118.6, 118.53, 118.50, 118.4, 118.0, 117.8, 117.7, 117.6, 102.5, 102.4, 102.2, 102.0, 99.1, 99.0, 79.5, 79.1, 78.9, 78.8, 78.5, 78.45, 78.2, 52.97, 52.91, 52.83, 52.76, 51.21, 51.17, 51.1, 51.0; *m/z* (ESI) 227 (100%, $[M+Na]^+$), 272 (25, $[M+NH_4]^+$); HRMS (ESI) $C_{14}H_{22}O_4Na$ ($[M+Na]^+$) requires 277.1416, found 277.1415.

4.2.16. 2-Methoxybut-3-enyl benzoate (43)

Alcohol **42** (50 mg, 0.49 mmol) was subjected to general procedure F. Flash column chromatography (SiO_2; petroleum ether/diethylether; 10:1) yielded **43** as a colourless oil (84 mg, 90%); ν_{max} (film)/cm^{-1} 3071, 2985, 2940, 2825, 1723, 1602, 1585, 1452, 1315, 1275, 1177, 1111, 1027, 993, 935, 712; δ_H (400 MHz, $CDCl_3$) 8.08–8.04 (2H, m, 2×Ph*H*), 7.59–7.54 (1H, m, Ph*H*), 7.47–7.41 (2H, m, 2×Ph*H*), 5.78 (1H, ddd, *J* 17.5, 10.0, 7.0, C(3)*H*), 5.41 (1H, d, *J* 17.5, C(4)*H*), 5.35 (1H, d, *J* 10.0, C(4)*H*), 4.39 (1H, dd, *J* 11.5, 4.5, C(1)*H*), 4.33 (1H, dd, *J* 11.5, 6.5, C(1)*H*), 4.02–3.96 (1H, m, C(2)*H*), 3.39 (3H, s, OCH_3); δ_C (100 MHz, $CDCl_3$) 166.4, 134.6, 133.0, 130.1, 129.7, 128.3, 119.3, 80.5, 66.5, 56.8; *m/z* (CI) 224 (100%, $[M+NH_4]^+$), 206 (20, $[M+H]^+$); HRMS (CI) $C_{12}H_{15}O_3$ ($[M+H]^+$) requires 207.1021, found 207.1020.

4.2.17. 1-(1-(2-Methoxybut-3-enyloxy)vinylbenzene (44)

Ester **43** (250 mg, 1.20 mmol) was subjected to general procedure G to give **44** as a yellow oil (195 mg, 66%), which was used without further purification; ν_{max} (film)/cm^{-1} 2928, 1642, 1601, 1574, 1494, 1447, 1286, 1196, 1128, 929, 803, 771, 701; δ_H (400 MHz, $CDCl_3$) 7.67–7.64 (2H, m, 2×Ph*H*), 7.38–7.32 (3H, m, 3×Ph*H*), 5.88 (1H, ddd, *J* 17.0, 10.0, 7.0, C*H*=CH_2), 5.44 (1H, ddd, *J* 17.0, 1.5, 1.0, one of CH=CH_2), 5.37 (1H, ddd, *J* 10.0, 1.5, 1.0, one of CH=CH_2), 4.70 (1H, d, *J* 3.0, one of CH_2=CPh), 4.23 (1H, d, *J* 3.0, one of CH_2=CPh), 4.09–4.03 (1H, m, $CH_2CH(OCH_3)CH=CH_2$), 3.98 (1H, dd, *J* 10.0, 6.0, one of CH_2CH(OCH_3)), 3.90 (1H, dd, *J* 10.0, 4.0, one of CH_2CH(OCH_3)), 3.44 (3H, s, OCH_3); δ_C (100 MHz, $CDCl_3$) 159.8, 136.3, 135.4, 128.5, 128.1, 125.4, 118.8, 82.7, 80.9, 70.2, 56.9; *m/z* (ESI) 227 (100%, $[M+Na]^+$); HRMS (ESI) $C_{13}H_{16}NaO_2$ ($[M+Na]^+$) requires 227.1043, found 277.1040.

4.2.18. 4-Ethoxy-2,2-dimethylhex-5-en-3-ol (48h)

Freshly distilled trimethylacetaldehyde (327 μL, 3.00 mmol) was subjected to general procedure E. Flash column chromatography (SiO_2; petroleum ether/diethyl ether; 20:1) yielded **48h** as a colourless oil (336 mg, 65%) and a mixture of diastereoisomers (ca. 2:1 from ^{1}H NMR), which were not separated.

The ^{1}H and ^{13}C NMR data provided is for the major diastereoisomer; ν_{max} (film)/cm^{-1} 3508, 3077, 2957, 2872, 1481, 1339, 1364, 1244, 1079, 996, 925; δ_H (400 MHz, $CDCl_3$) 5.76–5.91 (1H, m, C*H*=CH$_2$), 5.16–5.32 (2H, m, CH=C*H*$_2$), 3.68–3.72 (1H, m, C*H*CH=CH$_2$), 3.50–3.62 (1H, m, one of OC*H*$_2$CH$_3$), 3.44 (1H, d, *J* 4.0, C*H*OH), 3.24–3.33 (1H, m, one of OC*H*$_2$CH$_3$), 3.09 (1H, br s, O*H*), 1.13–1.21 (3H, m, OCH$_2$C*H*$_3$), 0.93 (9H, s, C(C*H*$_3$)$_3$); δ_C (100 MHz, $CDCl_3$) 137.5, 117.3, 80.5, 80.0, 63.4, 34.7, 26.6, 15.1; *m/z* (ESI) 195 (100%, [M+Na]$^+$); HRMS (ESI) $C_{10}H_{20}NaO_2$ ([M+Na]$^+$) requires 195.1356, found 195.1358.

4.2.19. 4-Ethoxy-2,2-dimethylhex-5-en-3-yl benzoate (*49h*)

Alcohol **48h** (259 mg, 1.51 mmol) was subjected to general procedure F. Flash column chromatography (SiO_2; petroleum ether/diethyl ether; 25:1) yielded **49h** as a colourless oil (375 mg, 84%) and as a mixture of diastereoisomers (ca. 2:1 from ^{1}H NMR), which were not separated. The ^{1}H and ^{13}C NMR data provided is for the major diastereoisomer; ν_{max} (film)/cm^{-1} 2972, 2871, 1723, 1602, 1481, 1451, 1398, 1366, 1337, 1314, 1111, 994; δ_H (400 MHz, $CDCl_3$) 8.14–7.41 (5H, m, 5×Ph*H*), 5.74 (1H, ddd, *J* 17.5, 10.5, 7.0, C*H*=CH$_2$), 5.28–5.15 (2H, m, CH=C*H*$_2$), 4.97 (1H, d, *J* 3.5, C*H*OC(O)Ph), 4.01 (1H, dd, *J* 7.0, 3.5, C*H*CH=CH$_2$), 3.61–3.50 (1H, m, one of OC*H*$_2$CH$_3$), 3.38–3.25 (1H, m, one of OC*H*$_2$CH$_3$), 1.16 (3H, t, *J* 7.0, OCH$_2$C*H*$_3$), 1.09 (9H, s, C(C*H*$_3$)$_3$); δ_C (100 MHz, $CDCl_3$) 166.3, 136.2, 132.7, 130.6, 129.8, 128.3, 117.3, 81.2, 80.5, 64.2, 35.1, 27.2, 15.2; *m/z* (ESI) 335 (100%, [M+MeCN+NH$_4$]$^+$), 299 (80, [M+Na]$^+$), 277 (20), 237 (10); HRMS (ESI) $C_{17}H_{24}NaO_3$ ([M+Na]$^+$) requires 299.1618, found 299.1612.

4.2.20. 1-(1-(4-Ethoxy-2,2-dimethylhex-5-en-3-yloxy)-vinyl)benzene (*50h*)

Ester **49h** (200 mg, 0.72 mmol) was subjected to general procedure G to give the **50h** as a yellow oil (99 mg, 50%) and a mixture of diastereoisomers, which were not separated (ca. 2:1 from ^{1}H NMR) and used without further purification. The ^{1}H and ^{13}C NMR data provided is for the major diastereoisomer; ν_{max} (film)/cm^{-1} 2961, 1446, 1365, 1283, 1120, 1032, 771, 701; δ_H (400 MHz, $CDCl_3$) 7.71–7.20 (5H, m, 5×Ph*H*), 5.89 (1H, ddd, *J* 17.5, 10.5, 7.5, C*H*=CH$_2$), 5.22–5.13 (2H, m, CH=C*H*$_2$), 4.74 (1H, d, *J* 3.0, one of C*H*$_2$=CPh), 4.28 (1H, d, *J* 3.0, one of C*H*$_2$=CPh), 4.01–3.98 (2H, m, C*H*CH=CH$_2$ and C*H*OC(=CH$_2$)Ph), 3.62–3.50 (1H, m, one of OC*H*$_2$CH$_3$), 3.37–3.25 (1H, m, one of OC*H*$_2$CH$_3$), 1.17 (3H, t, *J* 7.0, OCH$_2$C*H*$_3$), 1.06 (9H, s, C(C*H*$_3$)$_3$); δ_C (100 MHz, $CDCl_3$) 160.4, 137.4, 132.7, 128.2, 128.0, 125.4, 116.7, 83.1, 85.4, 81.6, 64.2, 36.2, 27.4, 15.3; *m/z* (ESI) 275 (10%, [M+H]$^+$), 261 (100), 260 (30), 259 (10); HRMS (ESI) $C_{18}H_{27}O_2$ ([M+H]$^+$) requires 275.2011, found 275.2020.

4.2.21. 2-tert-Butyl-5-phenylfuran (*51h*)

Enol ether **50h** (40 mg, 146 μmol) was subjected to general procedure C in toluene then general procedure D. Flash column chromatography (SiO_2; petroleum ether) yielding **51h** as a colourless oil (11 mg, 41%) contaminated with ca. 5% phosphine ligand, which could not be removed by further purification; ν_{max} (film)/cm^{-1} 2946, 1596, 1549, 1487, 1447, 1380, 1250, 1204, 1070, 1022, 957, 921; δ_H (400 MHz, $CDCl_3$) 7.66–7.63 (2H, m, 2×Ph*H*), 7.39–7.34 (2H, m, 2×Ph*H*), 7.25–7.20 (1H, m, Ph*H*), 6.54 (1H, d, *J* 3.5, C(4)*H*), 6.05 (1H, d, *J* 3.5, C(3)*H*), 1.35 (9H, s, C(C*H*$_3$)$_3$); δ_C (100 MHz, $CDCl_3$) 164.0, 151.8, 131.3, 128.6, 126.7, 123.3, 105.3, 104.0, 32.8, 29.1; *m/z* (CI) 201 (100%, [M+H]$^+$); HRMS (CI) $C_{14}H_{17}O$ ([M+H]$^+$) requires 201.1279, found 201.1279.

4.2.22. 2-Methoxy-3-oxo-1,3-diphenylpropyl benzoate (*65*)

Alcohol **64** (942 mg, 3.70 mmol) was subjected to general procedure F. Flash column chromatography (SiO_2; petroleum ether/diethyl ether; 3:1) yielded **65** as a viscous yellow oil (967 mg, 73%) and as a mixture of diastereoisomers, which were not separated. The ^{1}H and ^{13}C NMR data provided is for the major diastereoisomer; ν_{max} (film)/cm^{-1} 3430, 3064, 2598, 2340, 2251, 1969, 1817, 1714, 1694, 1682, 1598, 1583, 1495, 1453, 1109, 1001; δ_H (400 MHz, $CDCl_3$) 8.14–8.03 (15H, m, 15×Ph*H*), 6.38 (1H, d, *J* 6.5, C*H*OC(O)Ph), 5.02 (1H, d, *J* 6.5, C*H*OCH$_3$),3.39 (3H, s, OC*H*$_3$); δ_C (100 MHz, $CDCl_3$) 197.7, 165.4, 136.1, 136.0, 135.9, 133.6, 133.2, 129.7, 128.9, 128.8, 128.8, 128.7, 128.4, 128.4, 86.3, 76.0, 58.8; *m/z* (ESI) 419 (100%, [M+MeCN+NH$_4$]$^+$); HRMS (ESI) $C_{23}H_{20}NaO_4$ ([M+Na]$^+$) requires 383.1254, found 383.1254.

4.2.23. (*E*) and (*Z*)-1-(1-Methoxyocta-2,7-dien-2-yl) benzene (*66*)

Ketone **64** (190 mg, 0.74 mmol) was subjected to general procedure H. Flash column chromatography (SiO_2; petroleum ether/diethyl ether; 40:1) yielded **66** as a yellow oil (88 mg, 55%) and as a mixture of isomers (ca. 3:1 from ^{1}H NMR), which were not separated. The ^{1}H and ^{13}C NMR data provided is for the major isomer; ν_{max} (film)/cm^{-1} 3078, 2978, 2925, 1640, 1600, 1494, 1443, 1352, 1190, 1101, 993, 912, 762; δ_H (400 MHz, $CDCl_3$) 7.48–7.23 (5H, m, 5×Ph*H*), 5.92–5.72 (2H, m, PhC=C*H* and C*H*=CH$_2$), 5.01–4.91 (2H, m, CH=C*H*$_2$), 4.15 (2H, s, C*H*$_2$OCH$_3$), 3.36 (3H, s, OC*H*$_3$), 2.12–2.00 (4H, m, C*H*$_2$CH=CPh and C*H*$_2$CH=CH$_2$),1.50 (2H, apparent quintet, *J* 8.0, C*H*$_2$CH$_2$CH=CPh); δ_C (100 MHz, $CDCl_3$) 139.0, 138.6, 137.4, 133.7, 130.6, 128.1, 126.9, 114.5, 77.7, 57.7, 29.1, 33.3, 28.1; *m/z* (ESI) 239 (100%, [M+Na]$^+$); HRMS (ESI) $C_{15}H_{20}NaO$ ([M+Na]$^+$) requires 239.1406, found 239.1400.

4.2.24. (*E*) and (*Z*)-8-Methoxy-7-methylocta-1,6-diene (*69*)

Methoxyacetone **68** (184 μL, 0.74 mmol) was subjected to general procedure H. Flash column chromatography (SiO_2; petroleum ether) yielded **69** as a colourless oil (275 mg, 89%) and a mixture of isomers (ca. 10:1, (*Z*)/(*E*) from ^{1}H NMR and ^{1}H NOE experiments). The ^{1}H and ^{13}C NMR data provided is for the major (*Z*)-isomer; ν_{max} (film)/cm^{-1} 3078, 2966, 1641, 1608, 1490, 1447, 1350, 1201, 952; δ_H (400 MHz, $CDCl_3$) 5.81 (1H, ddt, *J* 17.0, 10.5, 6.5, C*H*=CH$_2$), 5.38 (1H, t, *J* 6.5, CH$_3$C=C*H*), 5.01 (1H, ddd, *J* 17.0, 2.0, 3.0, one of CH=C*H*$_2$), 4.98–4.94 (1H, m, one of CH=C*H*$_2$), 3.92 (2H,

s, CH_2OCH_3), 3.29 (3H, s, OCH_3), 2.11–2.03 (4H, m, $CH_2CH{=}CCH_3$ and $CH_2CH{=}CH_2$), 1.76–1.74 (3H, m, CH_3), 1.70–1.40 (2H, m, $CH_2CH_2CH{=}CCH_3$); δ_C (100 MHz, $CDCl_3$) 138.7, 132.1, 129.3, 114.5, 70.8, 57.6, 29.1, 33.3, 27.1, 21.5; *m/z* (CI) 172 (50%, $[M+NH_4]^+$), 140 (10), 123 (100), 107 (20), 85 (20), 81 (20); HRMS (CI) $C_{10}H_{22}NO$ ($[M+NH_4]^+$) requires 172.1701, found 172.1699.

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References and notes

1. (a) For reviews see: Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4490–4527; (b) *Handbook of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH: Weinheim, 2003; Vols. 1–3, p 1234; (c) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012–3043; (d) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450; (e) Gradillas, A.; Perez-Castells, Jr. *Angew. Chem., Int. Ed.* **2006**, *45*, 6086–6101; (f) Wallace, D. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 1912–1915.
2. (a) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 4035–4037; (b) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179; (c) Scholl, M.; Ding, S.; Choon, W. L.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956; (d) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791–799; (e) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2039–2041.
3. (a) Michaut, A.; Rodriguez, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 5740–5750; (b) Martin, S. F.; Deiters, A. *Chem. Rev.* **2004**, *104*, 2199–2238; (c) Hanson, P. R.; McReynolds, M. D.; Dougherty, J. M. *Chem. Rev.* **2004**, *104*, 2239–2258.
4. Donohoe, T. J.; Orr, A. J.; Bingham, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 2664–2670 and references cited therein.
5. (a) Bassindale, M. J.; Hamley, P.; Leitner, A.; Harrity, J. P. A. *Tetrahedron Lett.* **1999**, *40*, 3247–3250; (b) Kinderman, S. S.; Doodeman, R.; van Beijma, J. W.; Russcher, J. C.; Tjen, K. C. M. F.; Kooistra, T. M.; Mohaselzadeh, H.; van Maarseveen, J. H.; Hiemstra, H.; Schoemaker, H. E.; Rutjes, F. P. J. T. *Adv. Synth. Catal.* **2002**, *344*, 736–748.
6. Similar tactics have been utilised in a number of recent reports of the formation of aromatic compounds by RCM: (a) Chen, Y. Z.; Dias, H. V. R.; Lovely, C. J. *Tetrahedron Lett.* **2003**, *44*, 1379–1382; (b) Declerck, V.; Ribiere, P.; Martinez, J.; Lamaty, F. *J. Org. Chem.* **2004**, *69*, 8372–8381; (c) Huang, K. S.; Wang, E. C. *Tetrahedron Lett.* **2001**, *42*, 6155–6157; (d) Yoshida, K.; Kawagoe, F.; Iwadate, N.; Takahashi, H.; Imamoto, T. *Chem. Asian J.* **2006**, *1*, 611–613.
7. Donohoe, T. J.; Orr, A. J.; Gosby, K.; Bingham, M. *Eur. J. Org. Chem.* **2005**, 1969–1971.
8. Donohoe, T. J.; Fishlock, L. P.; Lacy, A. R.; Procopiou, P. A. *Org. Lett.* **2007**, *9*, 953–956.
9. For review and preparation see: Zimmer, R. *Synthesis* **1993**, 165–178.
10. (a) Rutjes, F. P. J. T.; Kooistra, T. M.; Hiemstra, H.; Schoemaker, H. E. *Synlett* **1998**, 192–194; (b) Kinderman, S. S.; de Gelder, R.; van Maarseveen, J. H.; Hiemstra, H.; Schoemaker, H. E.; Rutjes, F. P. J. T. *J. Am. Chem. Soc.* **2004**, *126*, 4100–4101.
11. Murakami, A.; Toyota, K.; Ohura, S.; Koshimizu, K.; Ohigashi, H. *J. Agric. Food Chem.* **2000**, *48*, 1518–1523.
12. Barluenga, J.; Fernandez-Simon, J. L.; Concellon, J. M.; Yus, M. *J. Chem. Soc., Perkin Trans. 1* **1989**, 77–80.
13. (a) Cai, J.; Zhou, Z.; Zhao, G.; Tang, C. *Org. Lett.* **2002**, *4*, 4723–4725; (b) Chengzhi, Y.; Bin, L.; Longqin, H. *J. Org. Chem.* **2001**, *66*, 5413–5418.
14. (a) Derguini, F.; Linstrumelle, G. *Tetrahedron Lett.* **1984**, *25*, 5763–5766; (b) Hoff, S.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 916–924.
15. Methoxyallene derivative **25** proved unstable to flash column chromatography using silica gel (triethylamine doped) or either neutral or basic alumina. Distillation also failed to achieve satisfactory results.
16. Desurbre, E.; Merour, J.-Y. *Tetrahedron Lett.* **1996**, *37*, 43–46.
17. Larock, R. C.; Berrios-Peiia, N. G.; Fried, C. A. *J. Org. Chem.* **1991**, *56*, 2615–2617.
18. Stewart, I. C.; Ung, T.; Pletnev, A. A.; Berlin, J. M.; Grubbs, R. H.; Schrodi, Y. *Org. Lett.* **2007**, *9*, 1589–1592.
19. Hayakawa, Y.; Kawakami, K.; Seto, H.; Furihata, K. *Tetrahedron Lett.* **1992**, *33*, 2701–2704.
20. (a) Deits, W.; Cukor, P.; Rubner, M.; Jopson, H. *J. Electron. Mater.* **1981**, *10*, 683–702; (b) Joshi, M. V.; Hemler, C.; Cava, M. P.; Cain, J. L.; Bakker, M. G.; Mckinley, A. J.; Metzger, R. M. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1081–1086; (c) Ferraris, J. P.; Skiles, G. D. *Polymer* **1987**, *28*, 179–182.
21. Abell, A. D.; Nabbs, B. K.; Battersby, A. R. *J. Org. Chem.* **1998**, *63*, 8163–8169.
22. (a) Fujimura, O.; Fu, G. C.; Grubbs, R. H. *J. Org. Chem.* **1994**, *59*, 4029–4031; (b) Clark, J. S.; Kettle, J. G. *Tetrahedron Lett.* **1997**, *38*, 123–126.
23. Hekking, K. F. W.; van Delft, F. L.; Rutjes, P. J. T. *Tetrahedron* **2003**, *59*, 6751–6758.
24. Louie, J.; Grubbs, R. H. *Organometallics* **2002**, *21*, 2153–2164.
25. Wu, Z.; Nguyen, S. T.; Grubbs, R. H.; Zillers, J. W. *J. Am. Chem. Soc.* **1995**, *117*, 5503–5511.
26. (a) Aggarwal, V. K.; Daly, A. M. *Chem. Commun.* **2002**, 2490–2491; (b) Rainier, J. D.; Cox, J. M.; Allwein, S. P. *Tetrahedron Lett.* **2001**, *42*, 179–181; (c) Okada, A.; Ohshima, T.; Shibasaki, M. *Tetrahedron Lett.* **2001**, *42*, 8023–8027; (d) Arisawa, M.; Theeraladanon, C.; Nishida, A.; Nakagawa, M. *Tetrahedron Lett.* **2001**, *42*, 8029–8033.
27. Kenworthy, M. N.; Taylor, R. J. K. *Org. Biomol. Chem.* **2005**, *3*, 603–611.
28. Petasis, N. A.; Bzowej, E. I. *J. Am. Chem. Soc.* **1990**, *112*, 6392–6394.
29. (a) Takai, K.; Kataoka, Y.; Kahiuchi, T.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 2668–2670; (b) Takai, K.; Okazoe, T.; Oshima, K.; Utimoto, K. *J. Org. Chem.* **1987**, *52*, 4410–4412.
30. (a) Allwein, S. P.; Cox, J. M.; Howard, B. E.; Johnson, H. W. B.; Rainier, J. D. *Tetrahedron* **2002**, *58*, 1997–2009; (b) Majunder, U.; Rainier, J. D. *Tetrahedron Lett.* **2005**, *46*, 7209–7211.
31. (a) Nicolaou, K. C.; Postema, M. H. D.; Claiborne, C. F. *J. Am. Chem. Soc.* **1996**, *118*, 1565–1566; (b) Nicolaou, K. C.; Postema, M. H. D.; Yue, E. W.; Nadin, A. *J. Am. Chem. Soc.* **1996**, *118*, 10335–10336.
32. Hirashita, T.; Kamei, T.; Horie, T.; Yamamura, H.; Kawai, M.; Araki, S. *J. Org. Chem.* **1999**, *64*, 172–177.
33. Lee, A.-L.; Malcolmson, S. J.; Puglisi, A.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128*, 5153–5157.
34. Hoye, T. R.; Jeffery, C. S.; Tennakoon, M. A.; Wang, J.; Zhao, H. *J. Am. Chem. Soc.* **2004**, *126*, 10210–10211.
35. Mukaiyama, T. *Pure Appl. Chem.* **1983**, *55*, 1749–1758.
36. Pangbon, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.
37. Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302–4314.
38. Padwa, A.; Zhi, L.; Fryxell, G. E. *J. Org. Chem.* **1991**, *56*, 1077–1083.
39. Bates, D. K.; Li, X.; Jog, P. V. *J. Org. Chem.* **2004**, *69*, 2750–2754.
40. Zonta, C.; Fabris, F.; De Lucchi, O. *Org. Lett.* **2005**, *7*, 1003–1006.
41. Lorne, R.; Julia, S. A. *Bull. Soc. Chim. Fr.* **1986**, 317–324.
42. Lautens, M.; Fillian, E. *J. Org. Chem.* **1997**, *62*, 4418–4427.
43. Chopade, P. R.; Davis, T. A.; Prasad, E.; Flowers, R. A. *Org. Lett.* **2004**, *6*, 2685–2688.
44. Pridgen, L. N.; Jones, S. S. *J. Org. Chem.* **1982**, *47*, 1590–1592.
45. Swiss, K. A.; Choi, W. B.; Liotta, D. C.; Abdel-Magid, A. F.; Maryanoff, C. A. *J. Org. Chem.* **1991**, *56*, 5978–5980.
46. Arnould, J. C.; Enger, A.; Feigenbaum, A.; Pete, J. P. *Tetrahedron* **1979**, *35*, 2501–2512.