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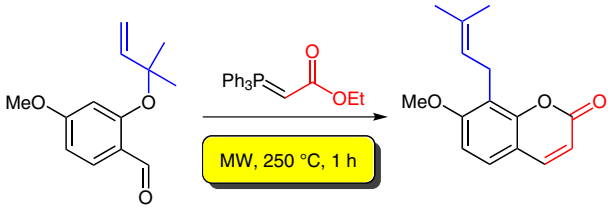
# Synthesis of Allyl- and Prenylcoumarins via Microwave-Promoted Tandem Claisen Rearrangement/Wittig Olefination

**Bernd Schmidt***
**Martin Riemer**

Universitaet Potsdam, Institut fuer Chemie,
Karl-Liebknecht-Strasse 24-25, 14476 Potsdam-Golm,
Germany
bernd.schmidt@uni-potsdam.de

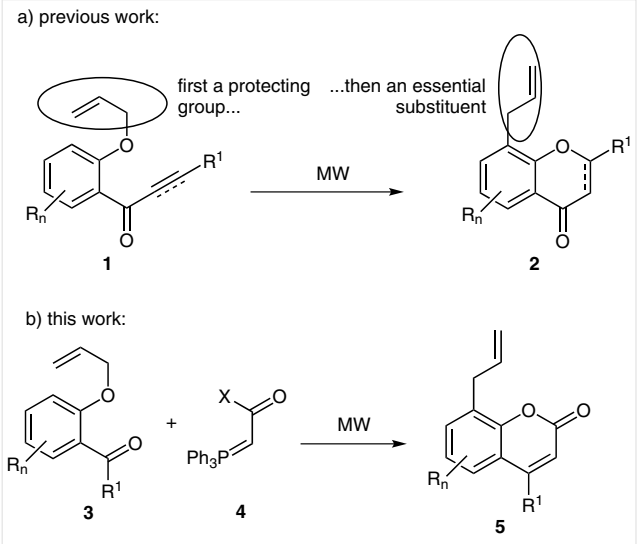



Received: 18.08.2015
Accepted after revision: 22.09.2015
Published online: 20.10.2015
DOI: 10.1055/s-0035-1560501; Art ID: ss-2015-z0490-op

**Abstract** Allyl, dimethylallyl, crotyl, and prenyl ethers of various aromatic *ortho*-hydroxy carbonyl compounds undergo a tandem sequence of Claisen rearrangement, carbonyl olefination, and cyclization upon microwave irradiation in the presence of a stabilized ylide. The products are multiply substituted 6- or 8-allylated or prenylated coumarins (2*H*-chromen-2-ones).

**Key words** aldehydes, coumarins, ketones, microwave irradiation, olefination, tandem reaction, ylides

We have very recently developed a synthesis of 6- and 8-allyl-substituted 4*H*-chromen-4-one derivatives **2** from alkenyl or alkynyl ketones **1**.[1,2] This approach, which relies on a microwave-promoted tandem Claisen rearrangement/6-*endo*-cyclization sequence, makes dual use of the allyl ether moiety in the starting material. During the synthesis of the tandem precursors, the allyl ether serves as a protecting group for the acidic and oxidation sensitive phenol. Upon its cleavage by Claisen rearrangement, the nucleophilic phenol required for the 6-*endo*-cyclization is liberated, and the allyl (or prenyl) substituent is transferred to the 6- or 8-position as an essential part of the target structure (Scheme 1). With a view to translating this scheme to the use of allyl ethers in a microwave-promoted synthesis of isomeric 6- or 8-allyl-substituted 2*H*-chromen-2-ones (coumarins), we reinvestigated an approach that was pioneered by Harwood et al.[3,4] and Mali et al.[5–8] Harwood and co-workers reported that O-prenylated or allylated (*E*)-coumarates [(*E*)-3-phenylprop-2-enoates] react upon heating in refluxing *N*,*N*-diethylaniline to give 6- or 8-allyl- or -prenylcoumarins. This sequence involves one or two sigmatropic rearrangements, *E*/*Z*-isomerization of the double bond[9] of the coumarate, and cyclization to the final products.[3,4] Mali et al. and others extended this sequence by starting from O-allylated or O-prenylated salicylaldehydes, which were heated in the presence of a stabilized ylide to 200 °C for 4–12 hours in *N*,*N*-dimethylaniline or without solvent.[5–8,10] Under these conditions, the (*E*)-coumarates are formed initially in a Wittig olefination and react then via Claisen rearrangement, *E*/*Z*-isomerization, and cyclization to the prenyl- or allylcoumarins.




**Scheme 1** Microwave-promoted tandem Claisen rearrangement/cyclization and tandem Claisen rearrangement/olefination/cyclization approaches to 4*H*-chromen-4-ones and 2*H*-chromen-2-ones

Typically, yields of ca. 50% of prenylated or allylated coumarins are obtained under these conditions. Later, others investigated Mali's tandem sequence in refluxing diphe-

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nyl ether (bp 258 °C), but no substantial improvement was reported with regard to selectivity, yield, and reaction time.[11,12]

In particular for reactions with very high activation barriers, microwave irradiation has been found to be a useful alternative form of energy supply. Reaction times can normally be substantially reduced, leading to smaller amounts of decomposition products and hence improved yields. In addition, dedicated microwave reactors have power, temperature, and pressure control mechanisms that ensure reproducibility and a high degree of safety even if the reaction mixture is heated beyond its boiling point in a closed vessel.[13–16] These considerations, and the indisputable biomedicinal relevance of naturally occurring coumarins,[17–23] prompted us to investigate the tandem sequence leading directly from O-allylated aldehydes or ketones **3** and stabilized ylides **4** to substituted coumarins **5** under microwave conditions (Scheme 1). We were particularly interested to investigate whether microwave conditions would allow an expansion of the substrate scope to benzo- or acetophenones ($R^1$ = aryl or methyl in structure **3**), which would react to 4-aryl- or 4-alkylcoumarins bearing an allyl or prenyl substituent at C6 or C8. There has been an increased interest in these special substitution patterns over the past two decades, because they have been discovered in numerous natural products isolated from plants of the family Clusiaceae.[24–27] A representative example is mammea A/AA (**6**), which was isolated from the seeds of the tree *Mammea americana*, and found to be cytotoxic against a range of human colon cancer cell lines and display high anti-oxidant activity.[26] On the other hand, non-natural 4-alkyl- or 4-arylcoumarins have been synthesized and tested in various biological assays to gain insight into structure-activity relationships.[20,28–34] In this regard, coumarins with a bulky and hydrophobic aryl substituent at C4 were found to be better inhibitors of P-glycoprotein, a transmembrane drug transporter responsible for pumping cytotoxic drugs out of cancer cells, which has been identified as a major mechanism for multidrug resistance in chemotherapy.[29] An example of a coumarin that has been used to study and identify the inhibitor binding site of hepatitis C virus non-structural protein 5B (a potential antiviral target) is compound **7** (Figure 1).[33]

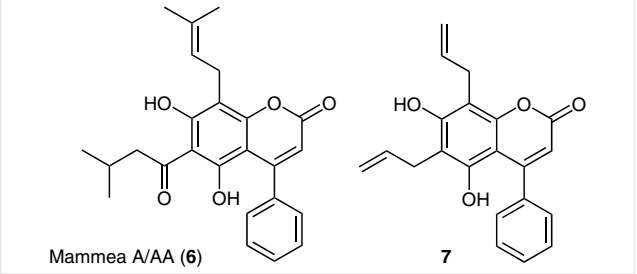
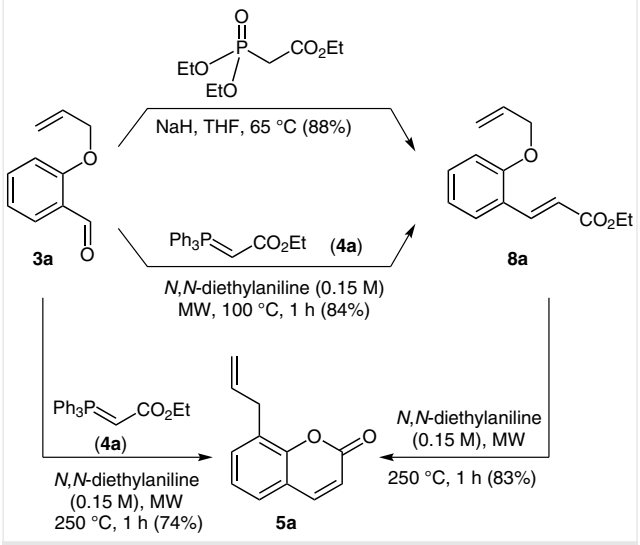



**Figure 1** Representative examples for a natural **6** and synthetic **7** allylated or prenylated 4-arylcoumarins

At the outset we investigated the steps of the tandem sequence, olefination, and Claisen rearrangement with subsequent isomerization/cyclization, separately. To this end, coumarate **8a** was synthesized from *o*-(allyloxy)benzaldehyde (**3a**) via Horner–Wadsworth–Emmons olefination and then subjected to the conditions previously established by us for the Claisen rearrangement/6-*endo*-cyclization, i.e. microwave irradiation at 250 °C for one hour in *N*,*N*-diethylaniline.[1,2] This resulted in a full conversion of the starting material into 8-allylcoumarin **5a**, which was isolated in 83% yield. This result shows that the standard microwave conditions can efficiently promote the Claisen rearrangement and the *E*/*Z*-isomerization of the coumarate. Next, we investigated the first step of the sequence, the Wittig olefination, by subjecting a mixture of **3a** and [(ethoxycarbonyl)methylene]triphenylphosphorane (**4a**) to microwave irradiation in *N*,*N*-diethylaniline. By choosing a temperature of 100 °C, we ensured that the olefination reaction proceeded cleanly and quantitatively, without any Claisen rearrangement or *E*/*Z*-isomerization, to furnish coumarate **8a** in 84% yield. Eventually, **3a** and **4a** were irradiated at 250 °C for one hour, resulting in the formation of 8-allylcoumarin **5a** in 74% yield, which corresponds well with the theoretical yield of 70% for the two-step synthesis (Scheme 2).




**Scheme 2** Tandem olefination/Claisen rearrangement/isomerization/cyclization sequence vs. two-step procedure

A variety of allyl aryl ethers **3a**–**k** were then subjected to the optimized conditions (Table 1). In almost all cases the expected 8-allylcoumarins **5a**–**k** were isolated in synthetically useful yields (≥70%), with the exception of 7-methoxy-substituted coumarin **5c**, which was reproducibly obtained in a yield of 40% (entry 3).

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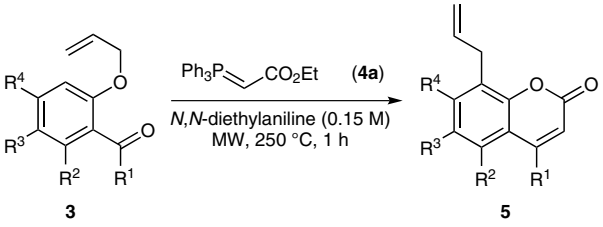
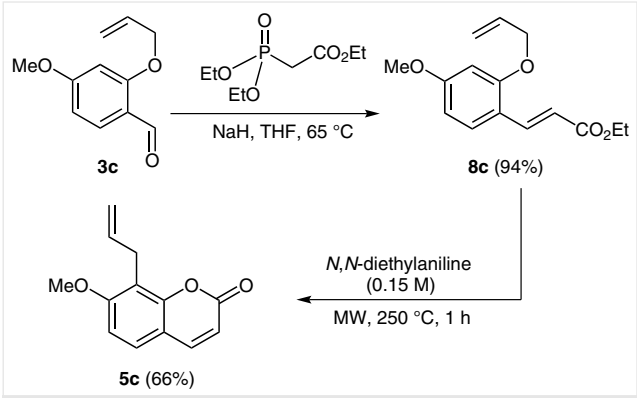
**Table 1** Scope of the Tandem Sequence for Allyl Ethers



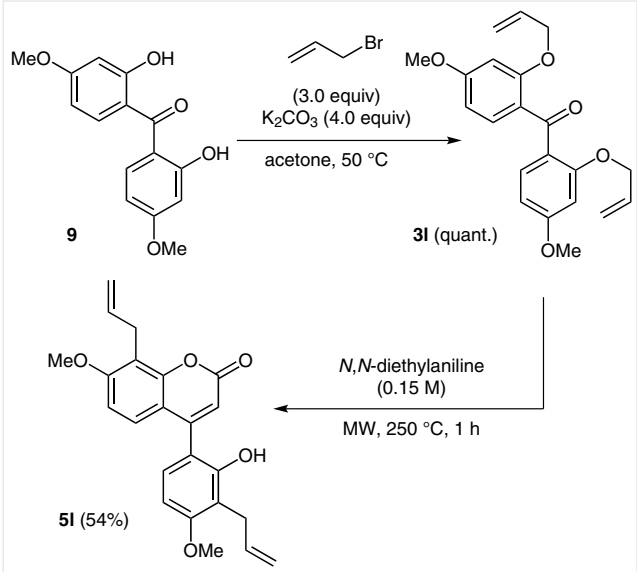

3 5

| Entry | 3 | $R^1$ | $R^2$ | $R^3$ | $R^4$ | Product | Yield (%) |
|---|---|---|---|---|---|---|---|
| 1 | **3a** | H | H | H | H | **5a** | 74 |
| 2 | **3b** | H | OMe | H | OMe | **5b** | 62 |
| 3 | **3c** | H | H | H | OMe | **5c** | 40 |
| 4 | **3d** | H | H | Br | H | **5d** | 77 |
| 5 | **3e** | H | H | 2-$MeOC_6H_4$ | H | **5e** | 76 |
| 6 | **3f** | Me | H | H | H | **5f** | 80 |
| 7 | **3g** | Me | H | OMe | H | **5g** | 78 |
| 8 | **3h** | Me | H | Cl | H | **5h** | 74 |
| 9 | **3i** | Me | H | Br | H | **5i** | quant. |
| 10 | **3j** | Ph | H | H | H | **5j** | 73 |
| 11 | **3k** | Ph | H | H | OMe | **5k** | 67 |

Interestingly, the yields were substantially higher for the 5,7-dimethoxycoumarin **5b** (entry 2) and the 7-methoxy-4-phenyl derivative **5k** (entry 11). The corresponding precursors **3b**,**c**,**k** have in common that an electron-donating substituent is located *ortho* or *para* to the carbonyl group, which might affect the olefination as well as the *E*/*Z* isomerization. We investigated the Claisen rearrangement/cyclization steps for the outlier **5c** separately by synthesizing **8c** independently via Horner–Wadsworth–Emmons olefination of **3c**. Coumarate **8c** was then subjected to microwave irradiation under the standard conditions, resulting in the formation of **5c** in 66% yield. Although this yield is significantly lower than that observed for the unsubstituted derivative **5a** (83%, see Scheme 2), we can not conclude that the Claisen rearrangement/isomerization part of the tandem sequence is solely responsible for the comparatively low yield under tandem conditions (Scheme 3). We concluded this part of the investigation into the tandem sequence with the bis(allyloxy)benzophenone **3l**. This substrate was expected to be comparatively challenging, because in order to obtain a useful yield for the tandem sequence, two Claisen rearrangements had to proceed simultaneously and selectively in high yield, and the Wittig olefination step might be impeded by the bulky 2,4-disubstituted aryl substituents. We thought, however, that this substrate should be interesting because its reaction in the tandem sequence would reduce the molecular symmetry from $C_{2v}$ in the precursor to $C_s$ in the product, or even to $C_1$ if the rotation barrier around the C4-aryl bond is sufficiently high to result in the formation of atropisomers. The precursor **3l** was synthesized from commercial benzophenone **9** in quantitative yield and irradiated under standard conditions, resulting in the formation of **5l**, which was isolated in a fair yield of 54% (Scheme 4).




**Scheme 3** Microwave irradiation of coumarate **8c**




**Scheme 4** Symmetry-reducing dual Claisen rearrangement/Wittig olefination/cyclization sequence

In biaryl compounds, a di-*ortho*-substitution pattern will normally only induce atropisomerism if both substituents are sterically demanding, but other substituents in the *meta*- and *para*-positions will also affect the rotational barrier through steric or electronic effects.[35] Axial chirality and atropisomerization in 4-arylcoumarins have previously been investigated using NMR, HPLC, and DFT methods, with the result that 6-isopropyl-4-(*o*-tolyl)coumarin is configurationally stable at ambient temperature, and that the barrier for atropisomerization is further increased by an additional substituent in the *meta*-position of the 4-aryl sub-

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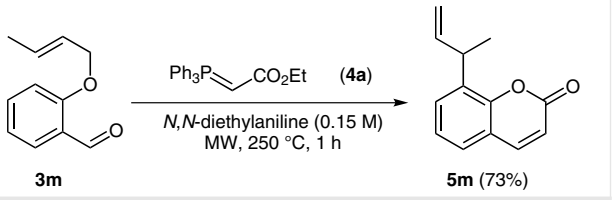
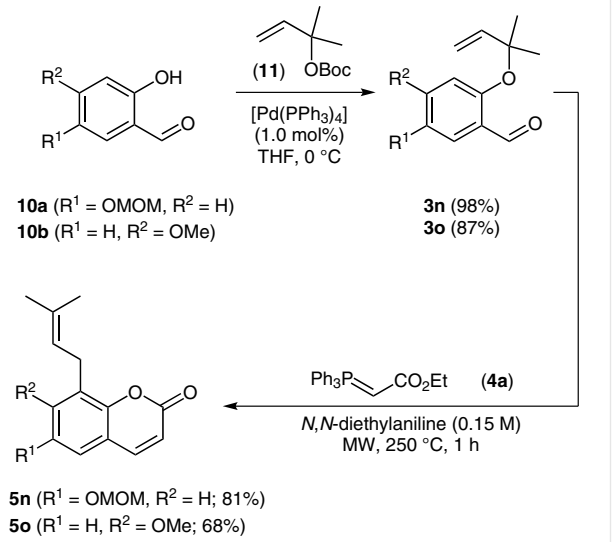
stituent.[36] For compound **5l**, all attempts to separate atropisomers via HPLC on chiral stationary phases (Chiralcel ODH and ADH) failed, even if the temperature was reduced to 12 °C. It is currently unclear whether this failure must be attributed to an insufficient resolution on the chiral stationary phases or to fast atropisomerization due to a very low rotational barrier.

In addition to the allyl ethers **3a**–**l** studied so far, we investigated a crotyl ether **3m**[2] and two 1,1-dimethylallyl ethers **3n** and **3o** in the tandem sequence. The crotyl ether **3m** reacted under standard conditions to the coumarin **5m**, with a but-3-en-2-yl side chain at C8, the substitution pattern expected for a single Claisen rearrangement. Gratifyingly, no positional isomers resulting from a subsequent Cope rearrangement (which have been observed for some thermal Claisen rearrangements of crotyl ethers)[37–39] were detected in this case (Scheme 5).




**Scheme 5** Tandem Claisen rearrangement/Wittig olefination sequence for a crotyl ether **3m**

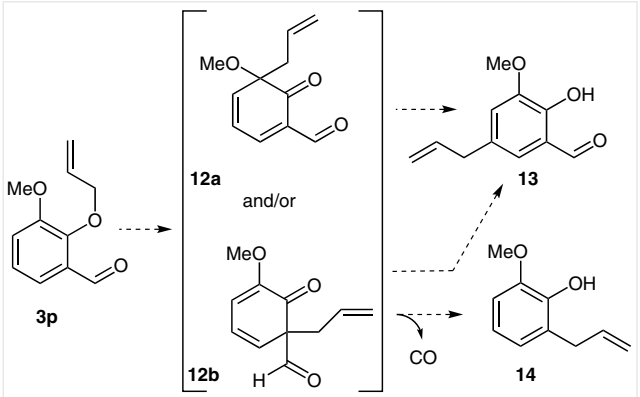
The 1,1-dimethylallyl ethers **3n**[2] and **3o** were synthesized from *o*-hydroxybenzaldehydes **10a** and **10b**, respectively, via palladium-catalyzed allylation with 1,1-dimethylallyl carbonate **11**.[40,41] Under standard conditions, **3n** and **3o** were converted into the 8-prenylcoumarins **5n** and **5o** in 81% and 68% yield, respectively. As for **3m**, no products resulting from other sigmatropic rearrangements, e.g. a subsequent Cope rearrangement, were detected (Scheme 6).




**Scheme 6** Synthesis of 8-prenylcoumarins **5n** and osthole (**5o**)

The prenylated coumarin **5o** is a natural product known as osthole. It was first isolated from the roots of *Angelica archangelica*[42] and later from numerous other plants.[43–45] It has been reported to show numerous interesting bioactivities,[46] inter alia anti-inflammatory activity[44] and activity as a $Ca^{2+}$-channel antagonist.[47]

In the next step we investigated whether the tandem conditions would be compatible with a substitution pattern predestined for a *para*-Claisen rearrangement. Migration of the allyl moiety to the *para*-position occurs regularly when both *ortho*-positions of the allyl ether are blocked, as for example in **3p**. The *para*-Claisen rearrangement is a cascade of Claisen rearrangement, Cope rearrangement, and eventually enolization, which would accordingly give **13** via **12a** or **12b**.[48] In our particular case, one *ortho*-substituent has to be a formyl group, which might result in a highly undesirable decarbonylation to **14** if the initial Claisen rearrangement proceeds via **12b**. This decarbonylation has indeed been reported to occur upon heating **3p** to 200 °C, giving **14** in synthetically useful yields (Scheme 7).[49]




**Scheme 7** Possible pathways for 2-allyloxy-3-substituted benzaldehydes under Claisen rearrangement conditions

To test whether the danger of decarbonylation can be averted under tandem conditions, we synthesized the known allyl, crotyl, and prenyl ethers **3p**–**r**[50] via Williamson etherification. These starting materials were then subjected to the standard conditions. Gratifyingly, for all three examples the 6-substituted coumarins **5p**–**r**, the products expected for a *para*-Claisen rearrangement pathway, were isolated (Scheme 8).

We could not detect any decarbonylation products, most likely because olefination of the aldehyde is too fast for any sigmatropic rearrangement to compete (compare conditions for the microwave-promoted two-step reaction shown in Scheme 2).

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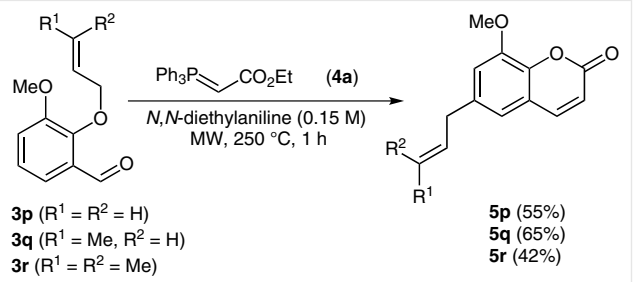
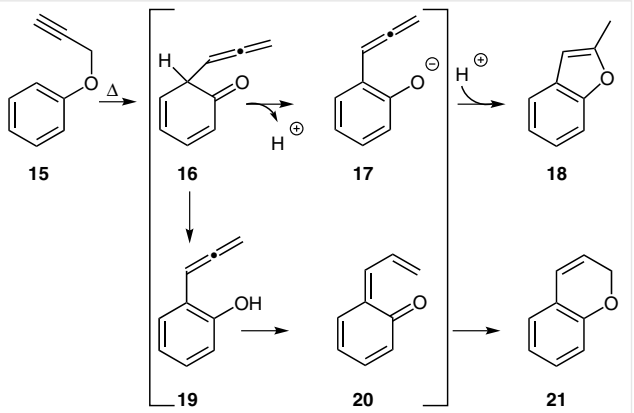


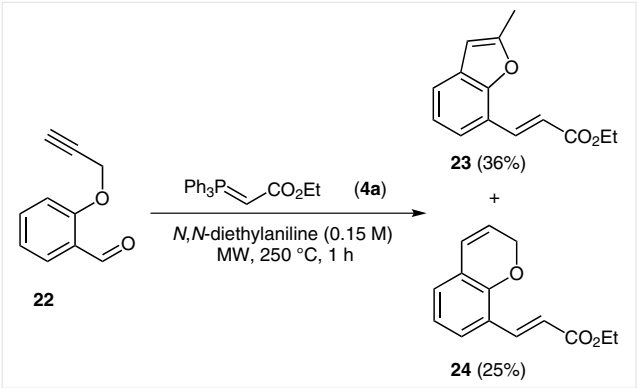

**Scheme 8** 6-Substituted coumarins via *para*-Claisen rearrangement/Wittig olefination

Finally, we investigated the compatibility of the tandem sequence with a propargyl Claisen rearrangement.[51–53] This transformation was originally discovered for aryl propargyl ethers, which react at high temperatures to give benzopyran derivatives.[54] Compared to the allyl Claisen rearrangement, its propargyl variant has found few applications.[55–57] The mechanism proposed for this reaction proceeds via sigmatropic rearrangement of an aryl propargyl ether such as **15** to an allenyl ketone **16**. A sequence of enolization to **19** and 1,5-H-shift to **20** sets the stage for a final electrocyclic ring closure, leading to the isolated product **21**.[56,58,59] Substantial amounts of *endo*-cyclization products, such as benzofuran **18**, have only been reported when the propargyl Claisen rearrangement was conducted in the presence of a base, because this leads to a deprotonation of **16** to phenolate **17**, which undergoes cyclization and reprotonation to the 2-methylbenzofuran (**18**) (Scheme 9).[58,60]




**Scheme 9** Mechanistic rationale for the formation of benzofurans and benzopyrans from aryl propargyl ethers

We investigated the reaction of propargyl ether **22** and phosphorane **4a** in the tandem Claisen rearrangement/Wittig olefination/cyclization sequence (Scheme 10). This starting material could react to give an 8-allenylcoumarin, in analogy to the allyl aryl ethers investigated so far. Alternatively, a benzopyran or benzofuran product might result, if a cyclization involving the allenyl substituent as outlined above is faster than the *E*/*Z*-isomerization step required for coumarin formation. The experimental results clearly show that the latter scenario is preferred, because we could not detect any coumarin product in the reaction mixture, but isolated benzofuran **23** and benzopyran **24** in a combined yield of ca. 60%. In light of the literature precedence on propargyl Claisen rearrangements discussed above, the rather high proportion of *endo*-cyclization product is quite intriguing. Presumably, the ylide **4a** (which is used in excess) reacts as a base and catalyzes the formation of a phenolate analogous to **17** (see Scheme 9), which would pave the way for the *endo*-cyclization product **23**.




**Scheme 10** Tandem propargyl Claisen/cyclization/Wittig olefination sequence

In summary, we describe conditions for a microwave-promoted tandem sequence leading from *ortho*-allyloxy-substituted aromatic aldehydes or ketones to allyl-, crotyl-, or prenyl-substituted coumarins. The sequence involves Wittig olefination, Claisen rearrangement, and thermally induced *E*/*Z*-isomerization, and is terminated by lactonization. The advantages of our conditions over conventional heating conditions used previously are: reduced reaction times, improved yields, and a broader substrate scope. This makes the method potentially highly useful for the synthesis of numerous naturally occurring coumarins, inter alia those with an alkyl or aryl substituent at the 4-position.

All experiments were conducted in dry reaction vessels under an atmosphere of dry $N_2$. Solvents were purified by standard procedures. $^1$H NMR spectra were obtained at 300 MHz with a Bruker ARX-300 spectrometer in $CDCl_3$ with $CHCl_3$ ($\delta$ = 7.26) as an internal standard, or in $C_6D_6$ with $C_6D_5H$ ($\delta$ = 7.18) as an internal standard. $^{13}$C NMR spectra were recorded at 75 MHz with a Bruker ARX-300 in $CDCl_3$ with $CDCl_3$ ($\delta$ = 77.0) as an internal standard or in $C_6D_6$ with $C_6D_6$ ($\delta$ = 128.0) as an internal standard. IR spectra were recorded as ATR-FTIR spectra on a Perkin-Elmer UART-two spectrophotometer. LRMS and HRMS were obtained by EI-TOF (Micromass Manchester Waters Inc.) or ESI-TOF (Micromass Manchester Waters Inc.). Microanalyses were obtained with an Elementar-Vario EL-III apparatus. Microwave

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reactions were carried out in an Anton-Paar-monowave-300 reactor at 250 °C (monowave, maximum power 850 W, temperature control via IR-sensor, vial volume 20 mL).

### 8-Allyl-2*H*-chromen-2-ones 5 by Microwave-Promoted Tandem Wittig Reaction/Isomerization/Cyclization; General Procedure

A solution of the appropriate aldehyde or ketone **3** (0.50 mmol) and [(ethoxycarbonyl)methylene]triphenylphosphorane (**4a**, 261 mg, 0.75 mmol) in *N*,*N*-diethylaniline (5 mL) was placed in a vessel suited for irradiation in a dedicated microwave reactor. The vessel was sealed and irradiated at 250 °C for 1 h. It was then cooled to r.t., the mixture was diluted with EtOAc (50 mL) and washed 1 M HCl (3 × 30 mL). The organic extract was dried ($MgSO_4$), filtered, and evaporated. The residue was chromatographed (silica gel, hexane–MTBE), to furnish the coumarins **5**.

### 8-Allyl-2*H*-chromen-2-one (5a)[9]

Following the general procedure, **3a** (121 mg, 0.75 mmol) was converted into **5a** (103 mg, 0.55 mmol, 74%); colorless oil.

IR (ATR): 1717 (s), 1601 (m), 1176 (m), 1116 (m), 829 $cm^{-1}$ (m).

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 9.5 Hz, 1 H), 7.36 (dd, *J* = 7.5, 1.3 Hz, 1 H), 7.32 (dd, *J* = 7.8, 1.5 Hz, 1 H), 7.19 (d, *J* = 7.6 Hz, 1 H), 6.37 (d, *J* = 9.5 Hz, 1 H), 5.97 (ddt, *J* = 16.8, 10.1, 6.7 Hz, 1 H), 5.11 (dm, *J* = 17.0 Hz, 1 H), 5.08 (dm, *J* = 10.1 Hz, 1 H), 3.57 (d, *J* = 6.6 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 160.7, 151.8, 143.8, 135.3, 132.4, 128.3, 126.1, 124.2, 118.7, 116.8, 116.3, 33.2.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_{10}O_2$: 186.0681; found: 186.0686.

### 8-Allyl-5,7-dimethoxy-2*H*-chromen-2-one (5b)[6]

Following the general procedure, **3b** (111 mg, 0.50 mmol) was converted into **5b** (76 mg, 0.31 mmol, 62%); colorless oil.

IR (ATR): 1711 (m), 1602 (s), 1433 (m), 1329 (m), 1116 $cm^{-1}$ (s).

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 9.6 Hz, 1 H), 6.28 (s, 1 H), 6.06 (d, *J* = 9.6 Hz, 1 H), 5.89 (ddt, *J* = 16.3, 10.0, 6.2 Hz, 1 H), 4.98 (dm, *J* = 17.1 Hz, 1 H), 4.91 (dm, *J* = 10.0 Hz, 1 H), 3.89 (s, 3 H), 3.88 (s, 3 H), 3.44 (d, *J* = 6.2 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 161.7, 161.1, 155.6, 153.6, 138.9, 135.7, 114.8, 110.5, 108.0, 103.6, 90.3, 56.1, 55.9, 26.3.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{14}O_4$: 246.0892; found: 246.0880.

### 8-Allyl-7-methoxy-2*H*-chromen-2-one (5c)[61]

Following the general procedure, **3c** (96 mg, 0.50 mmol) was converted into **5c** (43 mg, 0.20 mmol, 40%); colorless solid; mp 137–138 °C.

IR (ATR): 1715 (m), 1602 (s), 1249 (s), 1117 (s), 836 $cm^{-1}$ (m).

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 9.5 Hz, 1 H), 7.30 (d, *J* = 8.6 Hz, 1 H), 6.82 (d, *J* = 8.6 Hz, 1 H), 6.18 (d, *J* = 9.4 Hz, 1 H), 5.92 (ddt, *J* = 16.4, 10.0, 6.3 Hz, 1 H), 5.03 (dm, *J* = 17.1 Hz, 1 H), 4.94 (dm, *J* = 10.0 Hz, 1 H), 3.88 (s, 3 H), 3.55 (d, *J* = 6.3 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 161.3, 160.3, 152.9, 143.8, 135.1, 126.7, 116.0, 115.3, 112.9, 112.9, 107.4, 56.1, 26.8.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{12}O_3$: 216.0786; found: 216.0779.

### 8-Allyl-6-bromo-2*H*-chromen-2-one (5d)

Following the general procedure, **3d** (121 mg, 0.50 mmol) was converted into **5d** (102 mg, 0.38 mmol, 77%); colorless oil.

IR (ATR): 1722 (s), 1565 (m), 1168 (m), 1119 (m), 856 $cm^{-1}$ (m).

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 9.6 Hz, 1 H), 7.48 (s, 2 H), 6.44 (d, *J* = 9.6 Hz, 1 H), 5.96 (ddt, *J* = 17.3, 10.3, 6.7 Hz, 1 H), 5.20–5.11 (m, 2 H), 3.57 (d, *J* = 6.6 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 160.1, 150.9, 142.6, 134.9, 134.5, 130.8, 128.4, 120.3, 117.8, 117.7, 116.9, 33.1.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{12}H_9O_2{}^{79}Br$: 263.9786; found: 273.9769.

### 8-Allyl-6-(2-methoxyphenyl)-2*H*-chromen-2-one (5e)

Following the general procedure, **3e** (118 mg, 0.44 mmol) was converted into **5e** (98 mg, 0.34 mmol, 76%); colorless oil.

IR (ATR): 1721 (s), 1579 (m), 1465 (m), 1240 (s), 1165 $cm^{-1}$ (s).

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 9.5 Hz, 1 H), 7.58 (d, *J* = 1.9 Hz, 1 H), 7.52 (d, *J* = 2.0 Hz, 1 H), 7.40–7.28 (m, 2 H), 7.05 (dd, *J* = 7.4, 7.4, 1.7 Hz, 1 H), 7.01 (d, *J* = 8.3 Hz, 1 H), 6.43 (d, *J* = 9.5 Hz, 1 H), 6.06 (ddt, *J* = 16.8, 10.0, 6.7 Hz, 1 H), 5.19 (dm, *J* = 17.0 Hz, 1 H), 5.12 (dm, *J* = 10.4 Hz, 1 H), 3.83 (s, 3 H), 3.67 (d, *J* = 6.7 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 161.0, 156.4, 150.9, 144.2, 135.4, 134.8, 133.9, 130.7, 129.3, 129.0, 127.9, 126.9, 121.1, 118.5, 116.9, 116.4, 111.4, 55.7, 33.3.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{16}O_3$: 292.1074; found: 292.1099.

### 8-Allyl-4-methyl-2*H*-chromen-2-one (5f)

Following the general procedure, **3f** (88 mg, 0.50 mmol) was converted into **5f** (80 mg, 0.40 mmol, 80%); colorless oil.

IR (ATR): 1716 (s), 1383 (m), 1449 (w), 1173 (m), 855 $cm^{-1}$ (m).

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 7.8 Hz, 1 H), 7.36 (d, *J* = 7.3 Hz, 1 H), 7.20 (t, *J* = 7.7 Hz, 1 H), 6.24 (s, 1 H), 5.98 (ddt, *J* = 16.8, 10.1, 6.7 Hz, 1 H), 5.09 (d, *J* = 17.2 Hz, 1 H), 5.07 (d, *J* = 10.1 Hz, 1 H), 3.57 (d, *J* = 6.6 Hz, 2 H), 2.40 (d, *J* = 0.9 Hz, 3 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 160.7, 152.7, 151.3, 135.5, 132.3, 128.4, 123.9, 122.8, 119.8, 116.7, 114.9, 33.4, 18.9.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{12}O_2$: 200.0837; found: 200.0840.

### 8-Allyl-6-methoxy-4-methyl-2*H*-chromen-2-one (5g)

Following the general procedure, **3g** (60 mg, 0.29 mmol) was converted into **5g** (52 mg, 0.23 mmol, 78%); colorless solid; mp 70–71 °C.

IR (ATR): 1707 (s), 1583 (s), 1462 (m), 1160 (s), 1052 $cm^{-1}$ (m).

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 6.96 (d, *J* = 2.7 Hz, 1 H), 6.86 (d, *J* = 2.8 Hz, 1 H), 6.25 (s, 1 H), 5.97 (ddt, *J* = 16.8, 10.1, 6.7 Hz, 1 H), 5.11 (dm, *J* = 16.5 Hz, 1 H), 5.08 (dm, *J* = 10.1 Hz, 1 H), 3.82 (s, 3 H), 3.56 (d, *J* = 6.6 Hz, 2 H), 2.39 (s, 3 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 160.9, 155.6, 152.4, 145.9, 135.3, 129.8, 120.4, 119.4, 117.0, 115.4, 105.6, 55.8, 33.6, 19.0.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{14}O_3$: 230.0943; found: 230.0945.

### 8-Allyl-6-chloro-4-methyl-2*H*-chromen-2-one (5h)

Following the general procedure, **3h** (75 mg, 0.36 mmol) was converted into **5h** (62 mg, 0.26 mmol, 74%); colorless solid; mp 65–67 °C.

IR (ATR): 1715 (s), 1574 (m), 1421 (m), 1361 (m), 866 $cm^{-1}$ (s).

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 2.1 Hz, 1 H), 7.33 (d, *J* = 2.1 Hz, 1 H), 6.30 (s, 1 H), 5.95 (ddt, *J* = 17.2, 10.0, 6.7 Hz, 1 H), 5.22–5.00 (m, 2 H), 3.56 (d, *J* = 6.6 Hz, 2 H), 2.40 (s, 3 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 160.0, 151.7, 149.8, 134.6, 131.9, 130.5, 129.3, 122.3, 121.0, 117.6, 116.0, 33.3, 18.9.

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HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{11}O_2{}^{35}Cl$: 234.0448; found: 234.0439.

**8-Allyl-6-bromo-4-methyl-2*H*-chromen-2-one (5i)**

Following the general procedure, **3i** (128 mg, 0.50 mmol) was converted into **5i** (139 mg, 0.50 mmol, quant.); colorless oil.

IR (ATR): 1729 (s), 1359 (m), 1137 (m), 920 (m), 852 cm$^{-1}$ (s).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 1.7 Hz, 1 H), 7.42 (d, *J* = 1.8 Hz, 1 H), 6.24 (s, 1 H), 5.91 (ddt, *J* = 17.1, 10.1, 6.7 Hz, 1 H), 5.16–5.06 (m, 2 H), 3.51 (d, *J* = 6.6 Hz, 2 H), 2.35 (d, *J* = 1.1 Hz, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 159.7, 151.5, 150.2, 134.6, 134.5, 130.7, 125.2, 121.4, 117.6, 116.7, 115.8, 33.2, 18.8.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{11}O_2{}^{79}Br$: 277.9942; found: 277.9921.

**8-Allyl-4-phenyl-2*H*-chromen-2-one (5j)**

Following the general procedure, **3j** (119 mg, 0.50 mmol) was converted into **5j** (95 mg, 0.36 mmol, 73%); yellow solid; mp 110–113 °C.

IR (ATR): 1710 (s), 1595 (m), 1367 (m), 1248 (m), 1165 cm$^{-1}$ (m).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.56–7.50 (m, 3 H), 7.47–7.42 (m, 3 H), 7.36 (dd, *J* = 8.1, 1.2 Hz, 1 H), 7.17 (t, *J* = 7.7 Hz, 1 H), 6.37 (s, 1 H), 6.07 (ddt, *J* = 16.8, 10.0, 6.7 Hz, 1 H), 5.18 (dm, *J* = 16.8 Hz, 1 H), 5.15 (dm, *J* = 10.1 Hz, 1 H), 3.68 (d, *J* = 6.6 Hz, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 160.6, 156.0, 152.0, 135.5, 135.5, 132.5, 129.6, 128.8, 128.7, 128.5, 125.3, 123.9, 118.9, 116.8, 115.0, 33.6.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{14}O_2$: 262.0994; found: 262.1010.

**8-Allyl-7-methoxy-4-phenyl-2*H*-chromen-2-one (5k)**

Following the general procedure, **3k** (134 mg, 0.50 mmol) was converted into **5k** (98 mg, 0.34 mmol, 67%); colorless oil.

IR (ATR): 1716 (s), 1596 (s), 1371 (s), 1277 (s), 1077 cm$^{-1}$ (m).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.44 (m, 3 H), 7.44–7.36 (m, 2 H), 7.31 (d, *J* = 8.9 Hz, 1 H), 6.79 (d, *J* = 8.9 Hz, 1 H), 6.17 (s, 1 H), 5.98 (ddt, *J* = 17.1, 10.0, 6.3 Hz, 1 H), 5.09 (dm, *J* = 17.1 Hz, 1 H), 4.99 (dm, *J* = 10.0 Hz, 1 H), 3.89 (s, 3 H), 3.63 (d, *J* = 6.2 Hz, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 161.3, 160.3, 156.1, 153.0, 135.8, 135.2, 129.5, 128.8, 128.4, 126.0, 116.2, 115.4, 112.9, 111.9, 107.1, 56.1, 27.0.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{19}H_{16}O_3$: 292.1099; found: 292.1078.

**8-Allyl-4-(3-allyl-2-hydroxy-4-methoxyphenyl)-7-methoxy-2*H*-chromen-2-one (5l)**

Following the general procedure, **3l** (172 mg, 0.50 mmol) was converted into **5l** (103 mg, 0.27 mmol, 54%); colorless solid; mp 183 °C.

IR (ATR): 3284 (br w), 1699 (m), 1598 (s), 1375 (m), 1270 cm$^{-1}$ (s).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.18 (d, *J* = 8.8 Hz, 1 H), 7.06 (d, *J* = 8.5 Hz, 1 H), 6.78 (d, *J* = 8.9 Hz, 1 H), 6.62 (d, *J* = 8.5 Hz, 1 H), 6.21 (s, 1 H), 6.07–5.89 (m, 2 H), 5.42 (s, 1 H), 5.15 (dm, *J* = 17.3 Hz, 1 H), 5.09 (dm, *J* = 10.1 Hz, 1 H), 5.03 (dm, *J* = 17.3 Hz, 1 H), 4.98 (dm, *J* = 10.1 Hz, 1 H), 3.89 (s, 3 H), 3.88 (s, 3 H), 3.61 (d, *J* = 6.3 Hz, 2 H), 3.54 (d, *J* = 6.2 Hz, 2 H)

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 161.6, 160.5, 159.3, 153.4, 152.9, 152.1, 136.0, 135.3, 128.3, 126.3, 116.3, 116.0, 115.9, 115.5, 114.8, 113.3, 113.2, 107.3, 103.6, 56.2, 56.0, 27.7, 27.1.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{23}H_{22}O_5$: 378.1467; found: 378.1434.

**8-(But-3-en-2-yl)-2*H*-chromen-2-one (5m)**

Following the general procedure, **3m** (132 mg, 0.75 mmol) was converted into **5m** (109 mg, 0.55 mmol, 73%); colorless oil.

IR (ATR): 1720 (s), 1598 (m), 1116 (m), 833 (m), 751 cm$^{-1}$ (m).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 9.5 Hz, 1 H), 7.37 (dd, *J* = 7.5, 1.4 Hz, 1 H), 7.30 (dd, *J* = 7.7, 1.5 Hz, 1 H), 7.19 (t, *J* = 7.6 Hz, 1 H), 6.36 (d, *J* = 9.5 Hz, 1 H), 6.01 (ddd, *J* = 17.3, 10.3, 6.2 Hz, 1 H), 5.09 (dm, *J* = 17.2 Hz, 1 H), 5.06 (dm, *J* = 10.0 Hz, 1 H), 4.15 (pent., *J* = 7.0 Hz, 1 H), 1.35 (d, *J* = 7.0 Hz, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 160.7, 151.2, 144.0, 141.2, 133.6, 130.2, 126.0, 124.3, 118.8, 116.2, 114.2, 35.1, 19.6.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{12}O_2$: 200.0837; found: 200.0858.

**6-(Methoxymethoxy)-8-(3-methylbut-2-enyl)-2*H*-chromen-2-one (5n)**

Following the general procedure, **3n** (125 mg, 0.50 mmol) was converted into **5n** (111 mg, 0.41 mmol, 81%); colorless solid; mp 72–74 °C.

IR (ATR): 1720 (s), 1580 (m), 1448 (m), 1150 (s), 1016 cm$^{-1}$ (s).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 9.5 Hz, 1 H), 7.01 (d, *J* = 2.5 Hz, 1 H), 6.93 (d, *J* = 2.5 Hz, 1 H), 6.33 (d, *J* = 9.5 Hz, 1 H), 5.26 (tm, *J* = 6.0 Hz, 1 H), 5.12 (s, 2 H), 3.48–3.41 (m, 5 H), 1.69 (s, 6 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 160.9, 153.3, 147.1, 143.7, 134.3, 131.2, 121.4, 120.5, 119.0, 116.6, 110.7, 94.8, 56.0, 27.6, 25.7, 17.8.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{18}O_4$: 274.1205; found: 274.1234.

**7-Methoxy-8-(3-methylbut-2-enyl)-2*H*-chromen-2-one (Osthole, 5o)**[62]

Following the general procedure, **3o** (110 mg, 0.50 mmol) was converted into **5o** (83 mg, 0.34 mmol, 68%); colorless solid; mp 65–67 °C.

IR (ATR): 1717 (s), 1603 (s), 1278 (m), 1249 (s), 1116 cm$^{-1}$ (s).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 9.4 Hz, 1 H), 7.25 (d, *J* = 8.5 Hz, 1 H), 6.79 (d, *J* = 8.6 Hz, 1 H), 6.17 (d, *J* = 9.4 Hz, 1 H), 5.19 (t, *J* = 7.1 Hz, 1 H), 3.88 (s, 3 H), 3.49 (d, *J* = 7.2 Hz, 2 H), 1.80 (s, 3 H), 1.63 (s, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 161.4, 160.2, 152.8, 143.8, 132.6, 126.3, 121.2, 117.8, 113.0, 112.9, 107.4, 56.1, 25.8, 21.9, 17.9.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{15}H_{16}O_3$: 244.1099; found: 244.1085.

**6-Allyl-8-methoxy-2*H*-chromen-2-one (5p)**

Following the general procedure, **3p** (150 mg, 0.78 mmol) was converted into **5p** (92 mg, 0.43 mmol, 55%); colorless solid; mp 87–89 °C.

IR (ATR): 1724 (s), 1580 (m), 1395 (w), 1257 (w), 1155 cm$^{-1}$ (w).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 9.5 Hz, 1 H), 6.87 (d, *J* = 1.5 Hz, 1 H), 6.83 (d, *J* = 1.3 Hz, 1 H), 6.36 (d, *J* = 9.5 Hz, 1 H), 5.92 (ddt, *J* = 16.1, 10.8, 6.7 Hz, 1 H), 5.16–4.98 (m, 2 H), 3.90 (s, 3 H), 3.37 (d, *J* = 6.6 Hz, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 160.3, 147.1, 143.7, 142.3, 136.5, 136.5, 119.2, 118.7, 116.8, 116.7, 114.5, 56.2, 39.8.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{12}O_3$: 216.0786; found: 216.0777.

**(*E*)-6-(But-2-enyl)-8-methoxy-2*H*-chromen-2-one (5q)**

Following the general procedure, **3q** (145 mg, 0.70 mmol) was converted into **5q** (104 mg, 0.45 mmol, 65%); colorless solid; mp 78–79 °C.

IR (ATR): 1717 (s), 1578 (s), 1394 (m), 1154 (m), 1085 cm$^{-1}$ (s).

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$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 9.5 Hz, 1 H), 6.86 (d, *J* = 1.0 Hz, 1 H), 6.81 (d, *J* = 1.2 Hz, 1 H), 6.35 (d, *J* = 9.5 Hz, 1 H), 5.61–5.48 (m, 2 H), 3.90 (s, 3 H), 3.30 (d, *J* = 3.8 Hz, 2 H), 1.67 (d, *J* = 3.7 Hz, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 160.4, 147.0, 143.7, 142.1, 137.6, 129.2, 127.3, 119.2, 118.5, 116.7, 114.4, 56.2, 38.6, 17.9.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{14}O_3$: 230.0943; found: 230.0965.

**8-Methoxy-6-(3-methylbut-2-enyl)-2*H*-chromen-2-one (5r)**

Following the general procedure, **3r** (85 mg, 0.39 mmol) was converted into **5r** (40 mg, 0.16 mmol, 42%); colorless oil.

IR (ATR): 2920 (w), 1718 (s), 1578 (m), 1463 (m), 1086 $cm^{-1}$ (s).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 9.5 Hz, 1 H), 6.89 (d, *J* = 1.5 Hz, 1 H), 6.83 (d, *J* = 1.5 Hz, 1 H), 6.39 (d, *J* = 9.5 Hz, 1 H), 5.30 (t, *J* = 7.3 Hz, 1 H), 3.94 (s, 3 H), 3.36 (d, *J* = 7.2 Hz, 2 H), 1.77 (s, 3 H), 1.72 (s, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 160.4, 147.1, 143.6, 138.3, 133.7, 122.2, 119.2, 118.2, 116.8, 116.4, 114.4, 56.3, 34.0, 25.7, 17.9.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{15}H_{16}O_3$: 244.1094; found: 244.1095.

**Ethyl (*E*)-3-(2-Methylbenzofuran-7-yl)acrylate (23) and Ethyl (*E*)-3-(2*H*-Chromen-8-yl)acrylate (24)**

Following the general procedure, **22** (120 mg, 0.75 mmol) was converted into a separable mixture of **23** (63 mg, 0.27 mmol, 36%) and **24** (42 mg, 0.18 mmol, 25%).

**Ethyl (*E*)-3-(2-Methylbenzofuran-7-yl)acrylate (23)**

Colorless oil; yield: 63 mg (0.27 mmol, 36%).

IR (ATR): 1706 (s), 1632 (m), 1426 (m), 1267 (m), 1161 $cm^{-1}$ (s).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 16.1 Hz, 1 H), 7.50 (d, *J* = 7.6 Hz, 1 H), 7.32 (d, *J* = 7.3 Hz, 1 H), 7.20 (t, *J* = 7.6 Hz, 1 H), 6.99 (d, *J* = 16.1 Hz, 1 H), 6.42 (s, 1 H), 4.33 (q, *J* = 7.1 Hz, 2 H), 2.52 (s, 3 H), 1.39 (t, *J* = 7.1 Hz, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 167.5, 156.1, 152.9, 140.0, 130.0, 125.1, 122.9, 122.2, 121.0, 118.8, 102.8, 60.6, 14.5, 14.2.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{14}O_3$: 230.0943; found: 230.0961.

**Ethyl (*E*)-3-(2*H*-Chromen-8-yl)acrylate (24)**

Colorless oil; yield: 42 mg (0.18 mmol, 25%).

IR (ATR): 1704 (m), 1630 (m), 1446 (m), 1161 (s), 802 $cm^{-1}$ (m).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 16.2 Hz, 1 H), 7.33 (dd, *J* = 7.8, 1.1 Hz, 1 H), 6.97 (dd, *J* = 7.5, 1.5 Hz, 1 H), 6.86 (t, *J* = 7.5 Hz, 1 H), 6.51 (d, *J* = 16.2 Hz, 1 H), 6.42 (dt, *J* = 9.9, 1.8 Hz, 1 H), 5.82 (dt, *J* = 9.9, 3.5 Hz, 1 H), 4.92 (dd, *J* = 3.5, 1.8 Hz, 2 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 1.35 (t, *J* = 7.1 Hz, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 167.5, 153.2, 139.4, 128.5, 128.3, 124.4, 122.9, 122.3, 122.2, 121.2, 119.0, 65.9, 60.4, 14.5.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{14}O_3$: 230.0943; found: 230.0933.

## Acknowledgment

We thank Evonik for generous donations of solvents. Support from the equal opportunities fund of the Faculty of Science is gratefully acknowledged. We thank Prof. Pablo Wessig, University of Potsdam, for dynamic enantioselective HPLC measurements.

## Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560501.

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