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Synthesis of Tetrahydropyran-4-ones and Thiopyran-4-ones from Donor-Substituted α-Bromostyrene Derivatives

Anna Rosiak,[a,b] Wolfgang Frey,[b] and Jens Christoffers*[a]

In memoriam Michael Brommer

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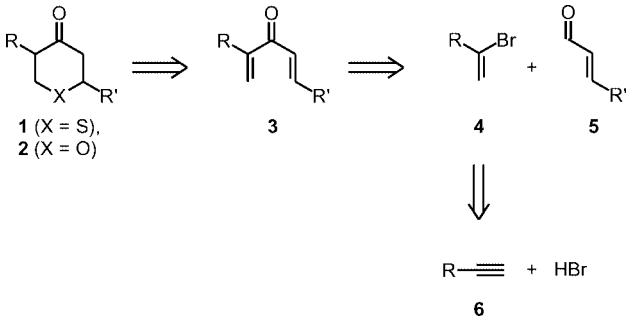
Tetrahydropyran-4-one and tetrahydrothiopyran-4-one derivatives with a 3-aryl substituent were synthesized by double-conjugate addition of water or H_2S to divinyl ketones. These starting materials were prepared in two steps by conversion of lithiated α-bromostyrene derivatives with acrolein or cinnamaldehyde and subsequent oxidation of the divinyl alcohols with MnO_2. The electron-rich α-bromostyrene building blocks were prepared by addition of HBr to the respective alkyne under strictly anhydrous conditions, which works reliably on a multigram scale. Two routes to arylacetylenes with a specific substitution pattern have been explored; however, on a larger scale only the Corey–Fuchs sequence turned out to be feasible.

Introduction

Successful drug development is often dependent on the availability of heterocyclic building blocks with a specific substitution pattern. Of particular importance are compounds with aromatic and heteroaromatic side chains with the need for a broad variety of substituents. Moreover, in late stages of optimization and screening processes a scalable access to these intermediates is required. In the course of a search program in a medicinal chemistry context tetrahydrothiopyran-4-ones **1** and tetrahydropyran-4-ones **2** were required as building blocks (Scheme 1). Of course, many procedures[1] have been reported to access tetrahydropyran-4-one derivatives[2] and their sulfur analogs;[3] however, our requirement for an electron-rich aromatic substituent in the 3-position has not been addressed in the literature so far. The obvious first approach to our target structures **1** and **2** is the α-arylation of the unsubstituted heterocyclic ketone, which failed, however, due to the decomposition by E1cb elimination of the respective enolates. Therefore, we envisioned to build up the heterocycle by double-conjugate addition of water (X = O) or sulfane (X = S) to a divinyl ketone **3**[4] with the accurate substitution pattern in the aromatic ring. Furthermore, we decided to prepare the divinyl ketones **3** by addition of the lithiated α-bromostyrene derivatives **4** to the α,β-unsaturated aldehydes **5** followed by oxidation of the secondary alcohol function. Although the parent compound α-bromostyrene **4e** itself is a commercially available material, substituted congeners, in particular 3,4-dialkoxy-substituted ones, are mostly unknown and moreover, common routes to these building blocks utilize a bromination/dehydrobromination sequence,[5] which results in low yields and low purity of the respective bromo olefin **4**. Therefore, we envisioned the addition of hydrogen bromide to an alkyne **6** under anhydrous conditions[6] to be the best alternative for the preparation of our target α-bromostyrenes **4** on a multigram scale. An advantage of this route might clearly be the availability of various phenylacetylene derivatives, which should guarantee access to a broad spectrum of these building blocks. Never-



Scheme 1. Strategy for the preparation of 3-aryl-substituted tetrahydrothiopyran-4-ones **1** and tetrahydropyran-4-ones **2** by double-conjugate addition. Retrosynthesis of the divinyl ketones **3** by α-bromostyrene derivatives **4** to alkynes **6**. R = electron-rich aryl, R′ = H, Ph.

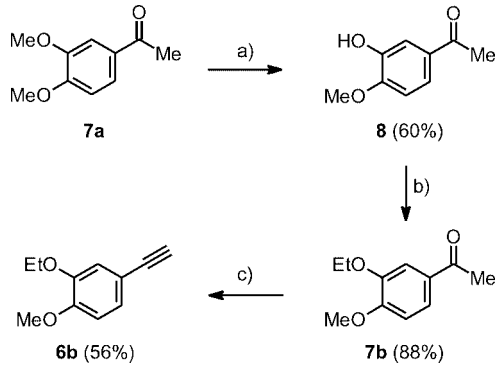
[a] Institut für Reine und Angewandte Chemie, Carl von Ossietzky-Universität Oldenburg, 26111 Oldenburg, Germany
Fax: +49-441-798-3873
E-mail: jens.christoffers@uni-oldenburg.de
[b] Institut für Organische Chemie, Universität Stuttgart, Pfaffenwaldring 55, 70569 Stuttgart, Germany

theless, alkynes with a 3,4-dialkyoxyphenyl residue, which was in the focus of our efforts, required some synthetic developments, as pointed out below.

Results and Discussion

Route to an Alkyne via an Enol Phosphate

As a first approach to an arylacetylene **6** we investigated the elimination of an enol phosphate generated in situ from a corresponding acetophenone derivative **7** (Scheme 2).[7] In order to have direct access to one of our particular target compounds, we decided to establish the 3-ethoxy-4-methoxyphenyl substitution pattern by a dealkylation/alkylation sequence starting from veratrophenone (**7a**).[8] Ether cleavage was regioselectively achieved at the more basic *meta*-methoxy group with concd. sulfuric acid to give the phenol derivative **8** (60%), which was subsequently alkylated in an S_N2 reaction to give the ketone **7b** (88%). At this stage, the regiochemistry was undoubtedly established by single-crystal X-ray analysis[9] (Figure 1). The ketone **7b** was deprotonated (LDA) and the enolate esterified with $(EtO)_2P(O)Cl$ to give the enol phosphate, which was eliminated with an excess of LDA to give the alkyne **6b** in moderate yield (56%). However, the reproducibility of this one-pot sequence was limited. In some cases yields were as low as 20%. For this reason and because the total yield over three steps was even in optimal cases only 30%, the decision was made to establish the alkyne moiety by the most reliable literature procedure for alkyne synthesis, the Corey–Fuchs[10] sequence.



Scheme 2. From veratrophenone (**7a**) to alkyne **6b** by dealkylation, alkylation, and elimination. Reagents and conditions: a) H_2SO_4 (concd.), 65 °C, 46 h; 60% (**8**). b) EtBr, K_2CO_3, DMF, 100 °C, 6 h; 88% (**7b**). c) 1. LDA, THF, –78 °C, 1 h; 2. $(EtO)_2P(O)Cl$, 23 °C, 3 h; 3. LDA, –78 °C, 23 °C, 3 h; 56% (**6b**).

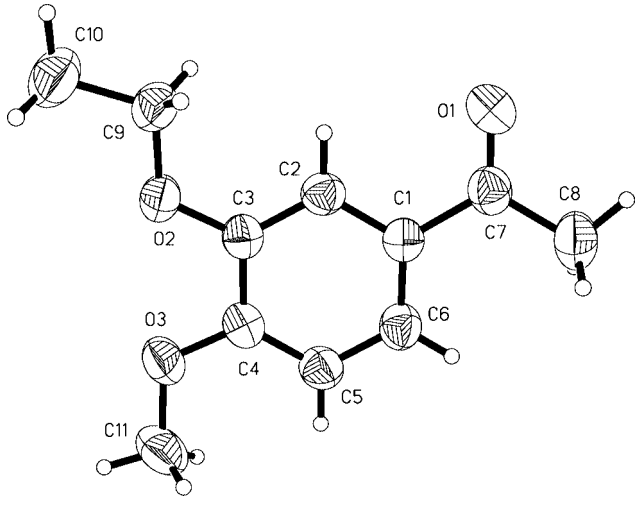
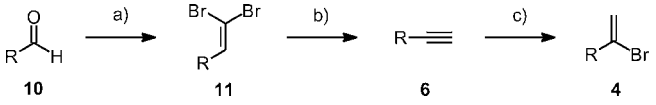


Figure 1. ORTEP representation of the structure of compound **7b** in the solid state.

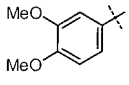
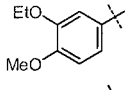
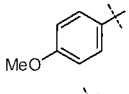
Corey–Fuchs Sequence to Alkynes and HBr Addition

Four commercially available, electron-rich aromatic aldehydes **10** – including a thiophene derivative **10d** as a heterocyclic example – were converted with PPh_3 and CBr_4 into the corresponding dibromovinyl derivatives **11** in high yields (86–99%, Scheme 3). Products **11a** and **11b** are new; yields for compounds **11c**[11] and **11d**[12] have been significantly improved compared to literature reports. For compounds **11a** and **11b** the preparation was executed on a 40-g scale, which made the chromatographic separation of the product from phosphane oxide a little tedious. From one of these materials single crystals could be grown and the constitution of compound **11b** was undoubtedly proven by X-ray crystallography[9] (Figure 2).



Scheme 3. Synthesis of α-bromostyrene derivatives **4** from aromatic aldehydes **10** via arylacetylenes **6** (Corey–Fuchs sequence). Reagents and conditions: a) PPh_3, CBr_4, CH_2Cl_2, 5 °C, 40 min (for **10a**–**10c**), 2 h (for **10d**). b) *n*BuLi, THF, –78 °C, 1.5 h; 23 °C, 1.5 h. c) HBr, AcOH, 23 °C, 20 min. For yields and substituents see Table 1.

Table 1. Synthesis of electron-rich α-bromostyrene derivatives **4** from aromatic aldehydes.

Ar	Starting material	Dibromo compound	Arylacetylene	α-Bromostyrene
	**10a**	**11a**, 92%	**6a**, 92%	**4a**, 87%
	**10b**	**11b**, 95%	**6b**, 99%	**4b**, 94%
	**10c**	**11c**, 86%	**6c**, 82%	**4c**, 68%
	**10d**	**11d**, 99%	**6d**, 69%	**4d**, 72%

Elimination with 2 equiv. of *n*BuLi and rearrangement gave the respective alkynes **6** in 82–99% yield, for compound **6a**,[13] and **6b** (previously unknown) on scales up to 80 g. In contrast to alkynes **6c**,[14] and **6d**,[15] which behave

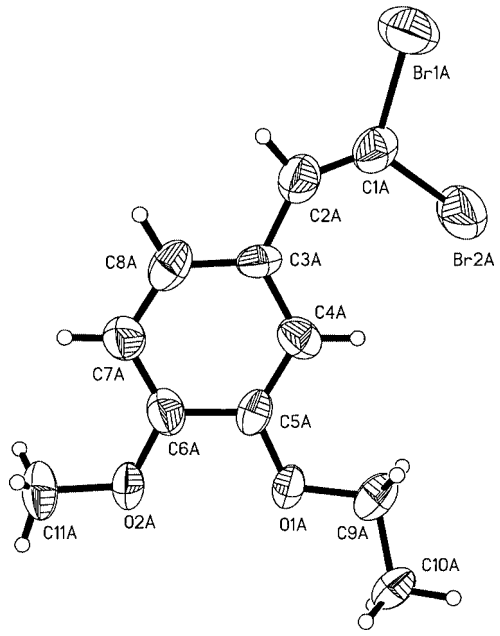


Figure 2. ORTEP representation of the structure of compound **11b** in the solid state.

indifferent under ambient conditions, the dialkoxy congeners **6a** and **6b** turned surprisingly out to be hygroscopic. The latter is an important aspect with regard to the next step of the synthesis of α-bromostyrenes **4**, which is highly sensitive to traces of moisture, yielding acetophenones as byproducts or even major products under the reaction conditions. The addition of HBr to the alkynes **6a**–**6d** has therefore to be performed under strictly anhydrous conditions. A suitable solution of HBr in glacial acetic acid is fortunately commercially available. Starting material **6b** has to be thoroughly dried by lyophilization in high vacuum prior to use. The α-bromostyrene derivatives **4a**, **4b**, **4c**,[6,16] **4d** are obtained in 68–94% yield as light-sensitive compounds, which are not stable under ambient conditions. For compounds **4a** and **4b**, the preparation works reliable in scales up to 20 g.

Synthesis of Divinyl Ketones

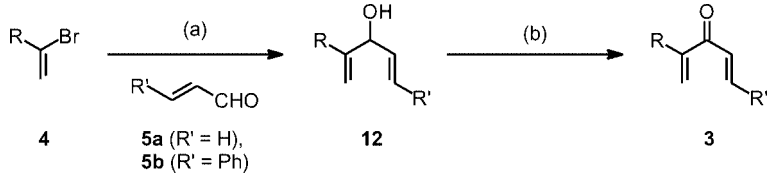
The dienones **3** were prepared in two steps from α-bromostyrene derivatives **4** (Scheme 4). The parent compound **4e** (R = Ph) is commercially available. Lithium/bromine exchange of compounds **4a**–**c** and **4e** with *n*BuLi proceeded smoothly at –78 °C. The reaction mixtures were treated with freshly distilled acrolein (**5a**) or cinnamaldehyde (**5b**) to yield the divinyl alcohols **12a**–**12f** after chromatographic purification. Thiophene derivative **4d** led to unspecific decomposition when treated with *n*BuLi. Therefore, no thienyl substituents are found in further intermediates and the target structures. The alcohols **12d**–**12f** derived from aldehyde **5b** are obtained as single diastereoisomers with the double-bond configuration being (*E*) as seen from the olefinic ^3J(H,H) coupling constant. Oxidation to the ketones **3** was achieved with MnO_2 of commercial activity. The oxidant was added portionwise to a suspension in CH_2Cl_2 until almost no starting materials **12** were detectable by TLC, which normally took 20–30 equiv. of MnO_2 and about 1 h. The products are generally pure by ^{1}H NMR spectroscopy without further chromatography, and are again obtained exclusively with (*E*) double-bond configuration in cases with R′ = Ph. If the conversion in this step is not complete, the remaining starting material **12** might be hardly separable from the cyclization product of the next step (**1** or **2**). On the other hand, prolonged reaction times result in an over-oxidation to an epoxide. Therefore, monitoring of the reaction progress by TLC is an important issue. The divinyl ketones **3a**–**c**, which derive from acrolein (**5a**), are highly reactive and neither stable at ambient conditions nor at low temperatures (Table 2). They even decompose significantly upon chromatography on SiO_2. Therefore, these materials were directly converted further after filtration from MnO_2 into the heterocyclic products **1** and **2**.

Table 2. Yields and substituents R and R′ in the synthesis of divinyl ketones **3**.

Starting materials	R	R′	Yield of **12**	Yield of **3**
4e, **5a**	Ph	H	**12a** (78%)	**3a** (95%)
4a, **5a**	3,4-$(MeO)_2C_6H_3$	H	**12b** (62%)	**3b** (56%)
4b, **5a**	3-EtO-4-$MeOC_6H_3$	H	**12c** (64%)	**3c** (74%)
4a, **5b**	3,4-$(MeO)_2C_6H_3$	Ph	**12d** (63%)	**3d** (70%)
4b, **5b**	3-EtO-4-$MeOC_6H_3$	Ph	**12e** (48%)	**3e** (64%)
4c, **5b**	4-$MeOC_6H_4$	Ph	**12f** (74%)	**3f** (83%)

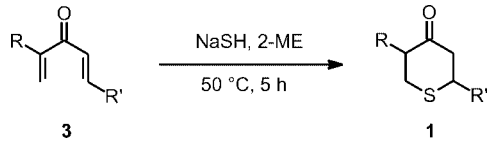
Double-Conjugate Addition of Sulfide

First of all, the reaction conditions of the ring closure were optimized with model compound **3a** (R = Ph, R′ = H), because it was prepared from commercially available α-bromostyrene **4e**. Although sulfides, as soft nucleophiles, are expected to cleanly undergo conjugate additions, yields turned out to be highly dependent on the reaction condi-



Scheme 4. Synthesis of divinyl ketones **3** from α-bromostyrenes **4**. Reagents and conditions: (a) 1. *n*BuLi, THF, 1.5 h, –78 °C; 2. aldehyde **5**, 1.5 h, –78 °C; (b) excess MnO_2, CH_2Cl_2, 60 min, 23 °C.

tions applied, particularly on the solvent used. Best results were achieved with NaHS in 2-methoxyethanol (2-ME, Scheme 5) or Na_2S in THF/H_2O (1:1) at moderate temperatures (45–55 °C). Yields for products **1a**–**1f** are presented in Table 3. Compounds **1b** and **1c** were of particular interest and batchwise prepared in amounts of 20 and 50 g, respectively.



3 **1**

Scheme 5. Synthesis of 3-aryl-substituted tetrahydrothiopyran-4-ones **1** by double-conjugate addition. For yields and substituents see Table 3.

Table 3. Yields and substituents R and R′ in the synthesis of tetrahydrothiopyran-4-ones **1** (X = S).

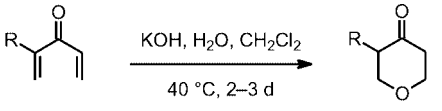
Dienone	R	R′	Product	Yield
3a	Ph	H	**1a**	70%
3b	3,4-$(MeO)_2C_6H_3$	H	**1b**	67%
3c	3-EtO-4-$MeOC_6H_3$	H	**1c**	59%
3d	3,4-$(MeO)_2C_6H_3$	Ph	**1d**	60% (*dr* 4:1)[a]
3e	3-EtO-4-$MeOC_6H_3$	Ph	**1e**	48% (*dr* 9:1)[a]
3f	4-$MeOC_6H_4$	Ph	**1f**	57% (*dr* 3:1)[a]

[a] The *trans* isomer is the major diastereoisomer in all three cases.

All compounds were of course obtained as racemates. The molecular constitution of dimethoxyphenyl derivative **1b** was established by an X-ray single-crystal structure analysis. An ORTEP representation of the solid-state structure is given in Figure 3.[9] For products **1d**–**1f** mixtures of two diastereoisomers were obtained with moderate stereoselectivity. The relative configuration was assigned based on ^3J(H,H) coupling constants.

Double-Conjugate Addition of Water

For the pyranone series, various acidic and basic reaction conditions with different solvent/water mixtures, even with phase-transfer catalysis have been investigated with the dienone **3a** as starting material. Surprisingly, only with the system KOH/H_2O/CH_2Cl_2 at 50 °C the racemic pyranones **2a** and **2b** were formed, although yields are not fully satisfying (Scheme 6). They are dependent on the purity of the respective divinyl ketone **3**. Actually, the low stability of these dienones **3** might be the major reason for the moderate yields in these cases. Nevertheless, the product of specific interest **2b** was batchwise prepared in total amounts of 20 g by using the conditions depicted in Scheme 6.



3a, R = Ph
3c, R = 3-EtO-4-$MeOC_6H_3$

2a, 50%,
2b, 25%

Scheme 6. Synthesis of 3-aryl-substituted tetrahydropyran-4-ones **2** by double conjugate addition.

Conclusions

A simple access to electron-rich α-bromostyrene derivatives has been developed by hydrobromination of donor-substituted arylacetylenes under strictly anhydrous conditions. The respective alkynes were prepared by the Corey–Fuchs procedure in a straightforward manner from aromatic aldehydes. The latter are available in a broad variety that assures a convenient access to a large number of α-bromostyrenes. Particular emphasis was put on the 3,4-dialkoxyphenyl derivatives, which were prepared in three steps from the corresponding benzaldehydes in 73% (**4a**) and 88% (**4b**) overall yields, respectively, and on multigram scales. The α-bromostyrenes are further converted by lithium/bromine exchange and subsequent treatment with α,β-unsaturated aldehydes **5** to give the divinyl alcohols **12**,

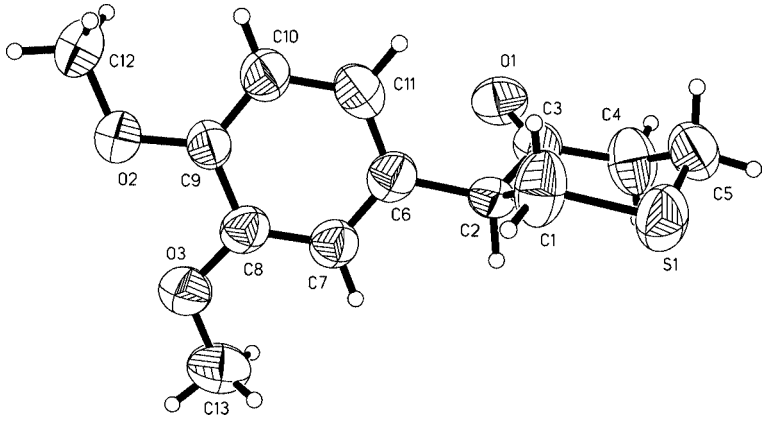


Figure 3. ORTEP representation of the structure of compound **1b** in the solid state.

which are further oxidized to the divinyl ketones **3**. These compounds are the relevant starting materials for tetrahydrothiopyran-4-ones **1** with an aromatic substituent in the 3-position, which are accessed by double-conjugate addition of the sulfide to the dienones **3**. The respective oxacycles **2** can be similarly prepared from compounds **3** and water, however in lower yields. Overall yields allow for the preparation of final products on multigram scales.

Experimental Section

General Methods: Procedures using *n*BuLi, LDA, CBr_4, and HBr were performed in flame-dried glassware and with absolute solvents under nitrogen. Acrolein was freshly distilled prior to use. Column chromatography was carried out using Merck SiO_2 60 with hexanes (PE, b.p. 40–60 °C), ethyl acetate (EA), and CH_2Cl_2 as eluents. ^1H NMR spectra were recorded with a Bruker ARX 500 (500 MHz), a Bruker ARX 300 (300 MHz), or a Bruker AC 250 (250 MHz) spectrometer. ^{13}C NMR spectra were recorded with a Bruker ARX 500 (125 MHz), a Bruker ARX 300 (75 MHz), or a Bruker AC 250 (62 MHz) spectrometer. Multiplicities were determined with DEPT experiments. Melting points were measured with a Büchi 510 apparatus and are uncorrected. All starting materials were commercially available. *n*BuLi (2 mol dm^{-3} solution in pentane), CBr_4, and HBr (33% solution in glacial acetic acid) were purchased from Aldrich Chemical Company. NaSH hydrate (72 wt.-% NaSH; Aldrich) is in accordance with the formula $NaHS{\cdot}1.2H_2O$.

3-Phenyltetrahydrothiopyran-4-one (1a): $NaHS{\cdot}1.2H_2O$ (138 mg, 1.78 mmol) was added to a solution of divinyl ketone **3a** (50 mg, 0.32 mmol) in 2-ME (3 mL). The resulting mixture was stirred at 50 °C for 5 h, then water (15 mL) and EA (20 mL) were added and the layers separated. The aqueous layer was extracted with EA (3 × 20 mL) and the combined organic phases were washed with water (10 mL), dried ($MgSO_4$), and concentrated after filtration. The residue was chromatographed on SiO_2 (PE/EA, 5:1; R_f = 0.27) to give the title compound **1a** (42 mg, 0.22 mmol, 70%) as a light yellow oil, which solidified after a while at ambient temperature, m.p. 64–66 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.84–2.87 (m, 2 H, CH_2), 2.99–3.15 (m, 3 H, CH_2), 3.28 (dd, J = 14.5 Hz, J = 10.9 Hz, 1 H, CH_2), 3.97 (dd, J = 10.9 Hz, J = 4.8 Hz, 1 H, CH), 7.16–7.28 (m, 5 H, Ph) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 30.8 (CH_2), 36.7 (CH_2), 44.3 (CH_2), 59.5 (CH), 127.5 (CH), 128.5 (2 CH), 128.6 (2 CH), 137.4 (C), 207.3 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1707 (vs), 1494 (m), 1448 (m), 1315 (m), 1287 (m), 1003 (m), 759 (m), 730 (m), 695 (vs), 674 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 192 (22) [M$^+$], 135 (5), 104 (100). HRMS (EI, 70 eV): calcd. 192.0609 ($C_{11}H_{12}OS$); found 192.0608 [M$^+$].

3-(3,4-Dimethoxyphenyl)tetrahydrothiopyran-4-one (1b): According to the procedure given for compound **1a**, divinyl ketone **3b** (40 mg, 0.18 mmol) was converted with $NaHS{\cdot}1.2H_2O$ (78 mg, 1.00 mmol) to give the title compound **1b** (30 mg, 0.12 mmol, 67%) after chromatography (SiO_2; PE/EA, 2:1; R_f = 0.26) as a colorless solid, m.p. 114–118 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.83–2.88 (m, 2 H, CH_2), 3.03–3.13 (m, 3 H), 3.25 (dd, J = 13.5 Hz, J = 10.7 Hz, 1 H), 3.87 (br. s, 6 H, 2 OCH_3), 3.92 (dd, J = 10.6 Hz, J = 4.8 Hz, 1 H, CH), 6.69–6.77 (m, 2 H, Ar-H), 6.83–6.87 (m, 1 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (62 MHz, $CDCl_3$): δ = 30.8 (CH_2), 36.7 (CH_2), 44.3 (CH_2), 55.9 (2 OCH_3), 59.0 (CH), 111.2 (CH), 111.8 (CH), 120.6 (CH), 130.0 (C), 148.4 (C), 148.9 (C), 207.7 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1701 (s), 1587 (m), 1516 (s), 1439 (m), 1258 (s), 1221 (m), 1138 (s), 1022 (s), 865 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 252 (39) [M$^+$], 164 (100). $C_{13}H_{16}O_3S$ (252.33): calcd. C 61.88, H 6.39; found C 61.76, H 6.47.

3-(3-Ethoxy-4-methoxyphenyl)tetrahydrothiopyran-4-one (1c): According to the procedure given for compound **1a**, divinyl ketone **3c** (1.9 g, 8.2 mmol) was converted with $NaHS{\cdot}1.2H_2O$ (2.7 g, 34.8 mmol) to give the title compound **1c** (1.24 g, 4.66 mmol, 57%) after chromatography (SiO_2; PE/EA, 2:1; R_f = 0.31) as colorless crystals, m.p. 103–104 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.46 (t, J = 7.0 Hz, 3 H, CH_3), 2.76–2.92 (m, 2 H), 2.98–3.17 (m, 3 H), 3.24 (dd, J = 13.6 Hz, J = 10.6 Hz, 1 H), 3.86 (s, 3 H), 3.90 (dd, J = 10.6 Hz, J = 4.8 Hz, 1 H), 4.04–4.13 (m, 2 H), 6.71 (d, J = 1.9 Hz, 1 H, Ar-H), 6.74 (dd, J = 8.2 Hz, J = 2.0 Hz, 1 H, Ar-H), 6.85 (d, J = 8.2 Hz, 1 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 14.8 (CH_3), 30.8 (CH_2), 36.7 (CH_2), 44.2 (CH_2), 55.9 (OCH_3), 58.9 (CH), 64.4 (OCH_2), 111.5 (CH), 113.3 (CH), 120.6 (CH), 129.9 (C), 148.2 (C), 148.6 (C), 207.7 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1703 (vs), 1588 (m), 1514 (s), 1444 (m), 1422 (m), 1344 (m), 1306 (m), 1243 (vs), 1182 (m), 1155 (m), 1137 (s), 1111 (m), 1042 (m), 1019 (s), 980 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 266 (53) [M$^+$], 178 (100), 150 (26). $C_{14}H_{18}O_3S$ (266.35): calcd. C 63.13, H 6.81; found C 62.81, H 6.89.

5-(3,4-Dimethoxyphenyl)-2-phenyltetrahydrothiopyran-4-one (1d): According to the procedure given for compound **1a**, divinyl ketone **3d** (180 mg, 0.61 mmol) was converted with $NaHS{\cdot}1.2H_2O$ (264 mg, 3.40 mmol) to give the title compound **1d** (120 mg, 0.37 mmol, 60%) after chromatography (SiO_2; PE/EA, 2:1; R_f = 0.33) as a light brown solid, m.p. 160–162 °C. Two signal sets are observed in the ^1H NMR spectrum (ratio 4:1), which can be assigned to the *trans* (major) and *cis* (minor) isomer. The signals of the *cis* isomer are partly hidden by the *trans* isomer in the ^1H NMR spectrum. They cannot be doubtlessly assigned in the ^{13}C NMR spectrum. ^1H NMR (250 MHz, $CDCl_3$), *trans* isomer: δ = 3.06 (dd, ^2J = 13.1 Hz, $^3J_{eq,ax}$ = 3.0 Hz, 1 H, 6-H_{eq}), 3.10 (dd, ^2J = 13.7 Hz, $^3J_{eq,ax}$ = 5.0 Hz, 1 H, 2-H_{eq}), 3.19 (t, ^2J = $^3J_{ax,ax}$ = 12.8 Hz, 1 H, 6-H_{ax}), 3.36 (dd, ^2J = 13.7 Hz, $^3J_{ax,ax}$ = 12.1 Hz, 1 H, 2-H_{ax}), 3.88 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.00 (dd, $^3J_{ax,ax}$ = 11.5 Hz, $^3J_{ax,eq}$ = 4.8 Hz, 1 H, 2-H_{ax}), 4.41 (dd, $^3J_{ax,ax}$ = 12.4 Hz, $^3J_{ax,eq}$ = 3.0 Hz, 1 H, 5-H_{ax}), 6.70 (d, J = 2.0 Hz, 1 H, Ar-H), 6.75 (dd, J = 8.1 Hz, J = 2.0 Hz, 1 H, Ar-H), 6.88 (d, J = 8.1 Hz, 1 H, Ar-H), 7.27–7.43 (m, 5 H, Ar-H) ppm; *cis* isomer: δ = 2.96 (dd, J = 14.2 Hz, J = 3.9 Hz, 1 H), 3.87 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 4.46 (dd, J = 9.1 Hz, J = 3.9 Hz, 1 H), 6.83 (d, J = 2.0 Hz, 1 H, Ar-H), 6.92 (dd, J = 8.3 Hz, J = 2.0 Hz, 1 H, Ar-H), 6.98 (d, J = 8.6 Hz, 1 H, Ar-H), 7.27–7.43 (m, 5 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$), *trans* isomer: δ = 37.0 (CH_2), 49.8 (CH), 52.2 (CH_2), 55.6 (OCH_3), 55.9 (OCH_3), 58.7 (CH), 111.2 (CH), 111.9 (CH), 120.8 (CH), 127.0 (2 CH), 128.2 (CH), 129.0 (2 CH), 139.7 (C) 148.4 (C), 148.9 (C), 179.8 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1704 (s), 1591 (m), 1515 (s), 1491 (m), 1456 (m), 1417 (m), 1256 (s), 1238 (s), 1213 (m), 1147 (m), 1024 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 328 (38) [M$^+$], 178 (3), 164 (100), 103 (3). $C_{19}H_{20}O_3S$ (328.43): calcd. C 69.49, H 6.14; found C 69.45, H 6.21.

5-(3-Ethoxy-4-methoxyphenyl)-2-phenyltetrahydrothiopyran-4-on (1e): According to the procedure given for compound **1a**, divinyl ketone **3e** (200 mg, 0.65 mmol) was converted with $NaHS{\cdot}1.2H_2O$ (280 mg, 3.60 mmol) to give the title compound **1e** (105 mg, 0.31 mmol, 48%) after chromatography (SiO_2; PE/EA, 2:1; R_f = 0.47) as colorless crystals, m.p. 141–142 °C. Two signal sets are observed in the ^1H NMR spectrum (ratio 9:1), which can be assigned to the *trans* (major) and *cis* (minor) isomer. The signals of the *cis* isomer are partly hidden by those of the *trans* isomer in the ^1H NMR spectrum. They cannot be doubtlessly assigned in the ^{13}C

NMR spectrum. ^{1}H NMR (500 MHz, $CDCl_3$), *trans* isomer: δ = 1.47 (t, J = 7.0 Hz, 3 H, CH_3), 3.05 (dd, ^2J = 13.2 Hz, $^3J_{eq,ax}$ = 3.0 Hz, 1 H, 6-H_{eq}), 3.10 (dd, ^2J = 13.7 Hz, $^3J_{eq,ax}$ = 4.9 Hz, 1 H, 2-H_{eq}), 3.17 (t, ^2J = $^3J_{ax,ax}$ = 12.7 Hz, 1 H, 6-H_{ax}), 3.34 (dd, ^2J = 13.6 Hz, $^3J_{ax,ax}$ = 12.7 Hz, 1 H, 2-H_{ax}), 3.87 (s, 3 H, OCH_3), 3.97 (dd, $^3J_{ax,ax}$ = 12.0 Hz, $^3J_{ax,eq}$ = 4.9 Hz, 1 H, 2-H_{ax}), 4.40 (dd, $^3J_{ax,ax}$ = 12.3 Hz, $^3J_{ax,eq}$ = 2.9 Hz, 1 H, 5-H_{ax}), 6.71 (d, J = 1.8 Hz, 1 H, Ar-H), 6.74 (dd, J = 8.2 Hz, J = 1.8 Hz, 1 H, Ar-H), 6.88 (d, J = 8.1 Hz, 1 H, Ar-H), 7.30–7.42 (m, 5 H, Ar-H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$), *trans* isomer: δ = 14.9 (CH_3), 37.0 (CH_2), 49.8 (CH), 52.2 (CH_2), 56.0 (OCH_3), 58.7 (CH), 64.4 (OCH_2), 111.6 (CH), 113.6 (CH), 120.8 (CH), 127.1 (2 CH), 128.2 (CH), 129.0 (2 CH), 129.7 (C), 139.7 (C), 148.2 (C), 148.8 (C), 207.0 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1705 (m), 1590 (m), 1514 (m), 1255 (s), 1211 (m), 1134 (m), 1022 (m), 696 (s), 589 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 342 (37) [M$^+$], 178 (100), 150 (14), 103 (4). $C_{20}H_{22}O_3S$ (342.45): calcd. C 70.14, H 6.48; found C 69.69, H 6.48.

5-(4-Methoxyphenyl)-2-phenyltetrahydrothiopyran-4-one (1f): According to the procedure given for compound **1a**, divinyl ketone **3f** (130 mg, 0.49 mmol) was converted with NaHS·1.2H_2O (212 mg, 2.73 mmol) to give the title compound **1f** (85 mg, 0.28 mmol, 57%) after chromatography (SiO_2; PE/EA, 2:1; R_f = 0.50) as a light yellow solid, m.p. 125–127 °C. Two signal sets are observed in the ^{1}H NMR spectrum (ratio 3:1), which can be assigned to the *trans* (major) and *cis* (minor) isomer. The signals of the *cis* isomer are hidden by those of the *trans* isomer in the ^{1}H NMR spectrum. They cannot be doubtlessly assigned in the ^{13}C NMR spectrum. ^{1}H NMR (500 MHz, $CDCl_3$), *trans* isomer: δ = 3.06 (m, 2 H, 2-H_{eq}, 6-H_{eq}), 3.18 (t, ^2J = $^3J_{ax,ax}$ = 12.6 Hz, 1 H, 6-H_{ax}), 3.33 (dd, ^2J = 13.4 Hz, $^3J_{ax,ax}$ = 12.1 Hz, 1 H, 2-H_{ax}), 3.81 (s, OCH_3), 3.99 (dd, $^3J_{ax,ax}$ = 12.1 Hz, $^3J_{ax,eq}$ = 4.9 Hz, 1 H, 2-H_{ax}), 4.40 (dd, $^3J_{ax,ax}$ = 12.4 Hz, $^3J_{ax,eq}$ = 2.9 Hz, 1 H, 5-H_{ax}), 6.91–6.93 (m, 2 H, Ar-H), 7.10–7.12 (m, 2 H, Ar-H), 7.22–7.41 (5 H, Ar-H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$), *trans* isomer: δ = 37.0 (CH_2), 49.8 (CH), 52.1 (CH_2), 55.3 (OCH_3), 58.3 (CH), 114.0 (2 CH), 127.1 (2 CH), 128.1 (CH), 128.9 (2 CH), 129.3 (C), 129.7 (2 CH), 139.7 (C), 158.9 (C), 207.0 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1702 (vs), 1610 (m), 1583 (m), 1511 (s), 1453 (m), 1305 (m), 1246 (s), 1229 (m), 1179 (m), 1103 (m), 1027 (m), 823 (s), 749 (m), 695 (vs) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 298 (17) [M$^+$], 134 (100). $C_{18}H_{18}O_2S$ (298.39): calcd. C 72.45, H 6.08; found C 72.57, H 6.14.

3-Phenyltetrahydropyran-4-one (2a): KOH (130 mg, 2.30 mmol) was added to a mixture of divinyl ketone **3a** (250 mg, 1.58 mmol), CH_2Cl_2 (6 mL) and water (12 mL), and the mixture was stirred at 35 °C for 28 h. Water was added, the layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were dried ($MgSO_4$), filtered, and the solvents evaporated. Chromatography (PE/EA, 5:1; R_f = 0.16) gave the title compound **2a** (142 mg, 0.80 mmol, 51%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.54–2.73 (m, 2 H, CH_2), 3.79 (dd, J = 8.7 Hz, J = 5.9 Hz, 1 H), 3.94–4.04 (m, 2 H), 4.20–4.29 (m, 2 H), 7.22–7.39 (m, 5 H, Ph) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 42.3 (CH_2), 58.4 (CH), 68.9 (CH_2), 73.5 (CH_2), 128.0 (CH), 129.1 (2 CH), 129.5 (2 CH), 135.3 (C), 206.1 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 2965 (m), 2854 (m), 1714 (vs), 1206 (s), 1146 (s), 1096 (m), 971 (m), 761 (m), 699 (s), 634 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 176 (10) [M$^+$], 104 (100). $C_{11}H_{12}O_2$ (176.21): calcd. C 74.98, H 6.86; found C 75.01, H 6.78.

3-(3-Ethoxy-4-methoxyphenyl)tetrahydropyran-4-one (2b): KOH (4.34 g, 77.5 mmol) was added to a mixture of divinyl ketone **3c** (4.50 g, 19.40 mmol), CH_2Cl_2 (100 mL), and water (100 mL), and the mixture was vigorously stirred at 40 °C for 50 h, then poured into a mixture of water (100 mL) and an aqueous solution of citric acid (c = 20%, 25 mL). The resulting mixture was extracted with CH_2Cl_2 (2 × 80 mL). The combined organic layers were washed with water (80 mL) and dried ($MgSO_4$). After filtration and removal of all volatile materials in vacuo, the residue was chromatographed on SiO_2 (PE/EA, 2:1; R_f = 0.23) to give a title compound **2b** (1.21 g, 4.83 mmol, 25%) as a light yellow oil, which solidified after 1 d, m.p. 65–67 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.45 (t, J = 7.0 Hz, 3 H, CH_3), 2.59–2.65 (m, 2 H, CH_2), 3.71 (dd, J = 8.2 Hz, J = 5.9 Hz, 1 H, CH), 3.85 (s, 3 H, OCH_3), 3.93–4.13 (m, 4 H, 2 CH_2), 4.16–4.25 (m, 2 H, CH_2), 6.76–6.87 (m, 3 H, Ar-H) ppm. ^{13}C{^{1}H} NMR (62 MHz, $CDCl_3$): δ = 14.8 (CH_3), 41.8 (CH_2), 55.9 (OCH_3), 57.5 (CH), 64.4 (OCH_2), 68.5 (CH_2), 73.2 (CH_2), 111.6 (CH), 113.6 (CH), 121.0 (CH), 127.4 (C), 148.3 (C), 148.8 (C), 206.1 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 2973 (m), 1715 (vs), 1589 (m), 1517 (vs), 1433 (m), 1389 (m), 1251 (vs), 1167 (m), 1094 (m), 1045 (m), 1020 (s), 969 (m), 924 (m), 887 (m), 851 (m), 822 (m), 693 (s) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 250 (100) [M$^+$], 222 (4), 178 (72), 150 (34), 107 (6). $C_{14}H_{18}O_4$ (250.29): calcd. C 67.18, H 7.25; found C 67.09, H 7.29.

2-Phenyl-1,4-pentadien-3-one (3a): MnO_2 (3.41 g, 39.3 mmol) was added portionwise to a solution of **12a** (300 mg, 1.87 mmol) in CH_2Cl_2 (10 mL) at ambient temperature. The progress of the reaction was monitored by TLC [product **3a**: R_f(SiO_2; PE/EA, 5:1) = 0.44]. After being stirred at 23 °C for 60 min, the reaction mixture was filtered with vacuum through SiO_2 to separate MnO_2, the residue was washed several times with EA (total ca. 100 mL). The filtrate was concentrated under vacuum to give **3a** as a yellow oil (280 mg, 1.77 mmol, 95%), which decomposed under ambient conditions. It could not even be stored at –5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.87 [dd, J = 10.4 Hz, J = 1.5 Hz, 1 H, (*E*)-5-H], 5.96 (s, 1 H, 1-H), 5.98 (s, 1 H, 1-H), 6.35 [dd, J = 17.3 Hz, J = 1.6 Hz, 1 H, (*Z*)-5-H], 6.75 (dd, J = 17.3 Hz, J = 10.4 Hz, 1 H, 4-H), 7.34–7.36 (m, 5 H, Ph) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 123.4 (CH_2), 127.9 (2 CH), 128.4 (CH), 128.4 (2 CH), 130.4 (CH_2), 134.3 (CH), 136.9 (C), 148.8 (C), 193.5 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1665 (vs), 1604 (vs), 1575 (m), 1493 (s), 1445 (m), 1400 (s), 1327 (m), 1307 (m), 1278 (m), 1192 (m), 1137 (m), 1037 (m), 1026 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 158 (46) [M$^+$], 130 (19) [M$^+$ – C_2H_4], 115 (5), 103 (100), 77 (39). HR-MS (EI, 70 eV): calcd. 158.0732 ($C_{11}H_{10}O$), found 158.0731 [M$^+$]. $C_{11}H_{10}O$ (158.20): calcd. C 83.52, H 6.37; found C 82.99, H 6.65.

2-(3,4-Dimethoxyphenyl)-1,4-pentadien-3-one (3b): According to the procedure reported for ketone **3a**, divinyl alcohol **12b** (220 mg, 0.99 mmol) was oxidized with MnO_2 (1.81 g, 20.8 mmol) to give the title compound **3b** (122 mg, 0.56 mmol, 56%) as a yellow oil, which could not be stored neither under ambient conditions nor at low temperatures due to decomposition processes. R_f(SiO_2; PE/EA, 2:1) = 0.37. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 5.88 (dd, J = 10.5 Hz, J = 1.6 Hz, 1 H, 5-H), 5.90 (s, 1 H, 1-H), 5.92 (s, 1 H, 1-H), 6.35 (dd, J = 17.2 Hz, J = 1.5 Hz, 1 H, 5-H), 6.75 (dd, J = 17.3 Hz, J = 10.5 Hz, 1 H, 4-H), 6.84–6.95 (m, 3 H, Ar-H) ppm. ^{13}C{^{1}H} NMR (62 MHz, $CDCl_3$): δ = 55.9 (2 OCH_3), 110.97 (CH), 111.01 (CH), 120.6 (CH), 122.1 (CH_2), 129.5 (C), 130.4 (CH_2), 134.4 (CH), 148.3 (C), 148.8 (C), 149.4 (C), 193.9 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1670 (m), 1605 (m), 1516 (s), 1463 (m), 1403 (m), 1256 (s), 1027 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 218 (92) [M$^+$], 203 (19), 163 (100), 148 (27), 132 (17), 119 (19). HR-MS (EI, 70 eV): calcd. 218.0943 ($C_{13}H_{14}O_3$), found 218.0942 [M$^+$].

2-(3-Ethoxy-4-methoxyphenyl)-1,4-pentadien-3-one (3c): MnO_2 (25.0 g, 287 mmol) was added portionwise to a solution of **12c**

(2.00 g, 8.55 mmol) in CH_2Cl_2 (60 mL) at ambient temperature. The progress of the reaction was monitored by TLC [product **3c**: $R_f(SiO_2$; PE/EA, 2:1) = 0.45]. After being stirred at 23 °C for 60 min, the reaction mixture was filtered with vacuum through SiO_2 to separate MnO_2, the residue was washed several times with EA (total ca. 600 mL). The filtrate was concentrated under vacuum to give **3c** as a yellow oil (1.47 g, 6.33 mmol, 74%) with 90–95% purity by ^1H NMR spectroscopy. The product decomposed under ambient conditions. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.46 (t, J = 7.0 Hz, 3 H, CH_3), 3.88 (s, 3 H, OCH_3), 4.10 (q, J = 7.0 Hz, 2 H, OCH_2), 5.87 [dd, J = 10.5 Hz, J = 1.5 Hz, 1 H, (*E*)-5-H], 5.87 (s, 1 H, 1-H), 5.89 (s, 1 H, 1-H), 6.34 [dd, J = 17.4 Hz, J = 1.6 Hz, 1 H, (*Z*)-5-H], 6.73 (dd, J = 17.3 Hz, J = 10.5 Hz, 1 H, 4-H), 6.84–6.93 (m, 3 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 14.8 (CH_3), 56.0 (OCH_3), 64.4 (OCH_2), 111.3 (CH), 112.4 (CH), 120.5 (CH), 121.9 (CH_2), 129.4 (C), 130.4 (CH_2), 134.5 (CH), 148.0 (C), 148.3 (C), 149.6 (C), 194.0 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 2932 (m, br.), 1671 (m), 1604 (m), 1514 (s), 1255 (s), 1141 (m), 1028 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 232 (100) [M^+], 177 (89), 149 (43), 117 (5), 89 (8). HR-MS (EI, 70 eV): calcd. 232.1099 ($C_{14}H_{16}O_3$); found 232.1099 [M^+].

(*E*)-4-(3,4-Dimethoxyphenyl)-1-phenyl-1,4-pentadien-3-one (3d): According to the procedure reported for ketone **3a**, divinyl alcohol **12d** (400 mg, 1.35 mmol) was oxidized with MnO_2 (3.50 g, 40.5 mmol) to give the title compound **3d** (280 g, 0.95 mmol, 70%) as a yellow oil, which was not stable under ambient conditions, but could be stored at lower temperature. $R_f(SiO_2$; PE/EA, 2:1) = 0.31. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.89 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 5.89 (s, 1 H, 5-H), 5.93 (s, 1 H, 5-H), 6.87 (d, J = 8.2 Hz, 1 H, Ar-H), 6.95 (d, J = 2.0 Hz, 1 H, Ar-H), 6.96 (dd, J = 8.2 Hz, J = 2.0 Hz, 1 H, Ar-H), 7.07 (d, J = 15.9 Hz, 1 H, 2-H), 7.38–7.40 (m, 3 H, Ar-H), 7.53–7.55 (m, 2 H, Ar-H), 7.71 (d, J = 15.9 Hz, 1 H, 1-H) ppm. $^{13}C\{^1H\}$ NMR (62 MHz, $CDCl_3$): δ = 55.9 (2 OCH_3), 110.9 (CH), 111.0 (CH), 120.6 (CH), 121.0 (CH_2), 124.5 (CH), 128.5 (2 CH), 129.0 (2 CH), 130.6 (CH), 134.6 (C), 145.0 (CH), 148.8 (C), 149.1 (C), 149.3 (C), 162.4 (C), 193.7 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1732 (m), 1682 (m), 1595 (m), 1511 (s), 1447 (m), 1411 (m), 1250 (s), 1137 (s), 1099 (m), 1022 (s) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 294 (63) [M^+], 235 (23), 163 (100), 131 (28), 77 (25). HR-MS (EI, 70 eV): calcd. 294.1256 ($C_{19}H_{18}O_3$), found 294.1255 [M^+].

(*E*)-4-(3-Ethoxy-4-methoxyphenyl)-1-phenyl-1,4-pentadien-3-one (3e): According to the procedure reported for ketone **3a**, divinyl alcohol **12e** (0.80 g, 2.6 mmol) was oxidized with MnO_2 (6.7 g, 77 mmol) to give the title compound **3e** (0.52 g, 1.69 mmol, 65%) as a yellow oil, which was not stable under ambient conditions, but could be stored at lower temperature. $R_f(SiO_2$; PE/EA, 2:1) = 0.34. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.45 (t, J = 7.0 Hz, 3 H, CH_3), 3.89 (s, 3 H, OCH_3), 4.10 (q, J = 7.0 Hz, 2 H, OCH_2), 5.87 (s, 1 H, C*H*H), 5.91 (s, 1 H, CH*H*), 6.87 (d, J = 8.9 Hz, 1 H, Ar-H), 6.95 (br. s, 1 H, Ar-H), 6.96 (dd, J = 8.9 Hz, J = 1.9 Hz, 1 H, Ar-H), 7.06 (d, J = 15.8 Hz, 1 H, 4-H), 7.36–7.39 (m, 3 H, Ph), 7.52–7.54 (m, 2 H, Ph), 7.70 (d, J = 15.9 Hz, 1 H, 5-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.8 (CH_3), 56.0 (OCH_3), 64.4 (OCH_2), 111.3 (CH), 112.4 (CH), 120.5 (CH), 120.8 (CH_2), 124.5 (CH), 128.5 (2 CH), 128.7 (CH), 128.9 (2 CH), 130.6 (CH), 134.7 (C), 144.9 (CH), 148.1 (C), 149.2 (C), 149.7 (C), 193.7 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1664 (m, br.), 1598 (s), 1575 (m), 1511 (s), 1448 (m), 1329 (m), 1251 (s), 1140 (m), 1027 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 308 (97) [M^+], 177 (100), 149 (8), 131 (17), 103 (10). HR-MS (EI, 70 eV): calcd. 308.1412 ($C_{20}H_{20}O_3$), found 308.1412 [M^+].

(*E*)-4-(4-Methoxyphenyl)-1-phenyl-1,4-pentadien-3-one (3f): According to the procedure reported for ketone **3a**, divinyl alcohol **12f** (220 mg, 0.83 mmol) was oxidized with MnO_2 (1.3 g, 15 mmol) to give the title compound **3e** (180 mg, 0.68 mmol, 83%) as green crystals, m.p. 104–106 °C, which was not stable under ambient conditions, but could be stored at lower temperature. $R_f(SiO_2$; PE/EA, 2:1) = 0.56. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 5.88 (s, 1 H, 5-H), 5.91 (s, 1 H, 5-H), 6.89–6.92 (m, 2 H, Ar-H), 7.06 (d, J = 15.9 Hz, 1 H, 2-H), 7.33–7.40 (m, 5 H, Ar-H), 7.53–7.55 (m, 2 H, Ar-H), 7.70 (d, J = 15.9 Hz, 1 H, 5-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 55.32 (OCH_3), 113.9 (2 CH), 120.7 (CH_2), 124.5 (CH), 128.5 (2 CH), 128.9 (2 CH), 129.1 (2 CH), 129.4 (C), 130.6 (CH), 134.7 (C), 144.9 (CH), 148.9 (C), 159.8 (C), 193.8 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1654 (s), 1594 (vs), 1572 (m), 1509 (s), 1447 (m), 1344 (m), 1293 (m), 1246 (s), 1180 (m), 1132 (m), 1031 (s), 984 (m), 939 (m), 871 (m), 851 (s), 781 (m), 686 (s) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 264 (31) [M^+], 236 (7), 133 (100), 103 (14), 77 (13). $C_{18}H_{16}O_2$ (264.32): calcd. C 81.79, H 6.10; found C 81.41; H 6.44.

1-Bromo-1-(3,4-dimethoxyphenyl)ethene (4a): Starting material **6a** is hygroscopic and must be carefully dried by lyophilization prior to use. Under strict exclusion of moisture, HBr (24.7 mmol, 4.4 mL of a 33% solution in acetic acid) was added dropwise with cooling (ice/water bath) to arylacetylene **6a** (4.00 g, 24.7 mmol). After being stirring at room temperature for 25 min, water (40 mL) and CH_2Cl_2 (25 mL) were added to the dark blue reaction mixture. This mixture was vigorously shaken until the color changed from blue to yellow-green, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ (2 × 25 mL), water (25 mL) and dried ($MgSO_4$). After filtration and removal of all volatile materials in vacuo (rotary evaporator), the residue was chromatographed on SiO_2 (PE/EA, 5:1; R_f = 0.41) to give the title compound **4a** (5.23 g, 21.5 mmol, 87%) as a light brown oil, which solidified upon storage at –15 °C. The product decomposed under ambient conditions. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 5.68 (d, J = 1.9 Hz, 1 H, C*H*H), 6.01 (d, J = 1.9 Hz, 1 H, CH*H*), 6.81 (d, J = 8.4 Hz, 1 H, Ar-H), 7.10 (d, J = 2.1 Hz, 1 H, Ar-H), 7.14 (dd, J = 8.3 Hz, J = 2.0 Hz, 1 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (62 MHz, $CDCl_3$): δ = 55.8 (OCH_3), 55.9 (OCH_3), 110.4 (CH), 110.4 (CH), 116.1 (CH_2), 120.2 (CH), 130.7 (C), 131.3 (C), 148.3 (C), 149.7 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1601 (m), 1515 (s), 1460 (m), 1269 (s), 1143 (m), 1026 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 242 (28) [M^+], 180 (14), 163 (100). $C_{10}H_{11}BrO_2$ (243.10): calcd. C 49.41, H 4.56; found C 49.29, H 4.59.

1-Bromo-1-(3-ethoxy-4-methoxyphenyl)ethene (4b): Starting material **6b** is hygroscopic and must be carefully dried by lyophilization prior to use. According to the procedure reported for compound **4a**, acetylene **6b** (15.0 g, 85.2 mmol) was converted with HBr (85.2 mmol, 15.4 mL of a 33% solution in acetic acid) to give the title compound **4b** (19.5 g, 75.8 mmol, 89%) after chromatography on SiO_2 (PE/EA, 2:1; R_f = 0.56) as a light brown solid, m.p. 32–34 °C. The product decomposed under ambient conditions. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.48 (t, J = 7.0 Hz, 3 H, CH_3), 3.88 (s, 3 H, OCH_3), 4.08–4.17 (m, 2 H, OCH_2), 5.68 (d, J = 2.0 Hz, 1 H, C*H*H), 6.01 (d, J = 2.0 Hz, 1 H, CH*H*), 6.82 (d, J = 8.4 Hz, 1 H, Ar-H), 7.11 (d, J = 2.2 Hz, 1 H, Ar-H), 7.17 (dd, J = 8.4 Hz, J = 2.2 Hz, 1 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.7 (CH_3), 56.0 (OCH_3), 64.5 (OCH_2), 110.7 (CH), 112.1 (CH), 116.0 (CH_2), 120.2 (CH), 130.8 (C), 131.4 (C), 147.7 (C), 150.2 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1670 (m), 1586 (m), 1510 (s), 1425 (m), 1258 (s), 1137 (s), 1019 (s), 810 (m), 775 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 256 (21) [M^+], 177 (100), 149 (29), 117 (11). $C_{11}H_{13}BrO_2$ (257.13): calcd. C 51.38, H 5.10; found C 51.28, H 5.16.

1-Bromo-1-(4-methoxyphenyl)ethene (4c): According to the procedure reported for compound **4a**, acetylene **6c** (1.58 g, 11.9 mmol) was converted with HBr (11.9 mmol, 2.14 mL of a 33% solution in acetic acid) to give the title compound **4c** (1.73 g, 8.12 mmol, 68%) after chromatography on SiO_2 (PE/EA, 2:1; R_f = 0.59) as a light brown solid, m.p. 35–36 °C. The product decomposed under ambient conditions. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 5.67 (d, J = 1.9 Hz, 1 H, C*H*H), 6.00 (d, J = 1.9 Hz, 1 H, CH*H*), 6.84–6.87 (m, 2 H, Ar-H), 7.52–7.55 (m, 2 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 113.5 (2 CH), 115.9 (CH_2), 128.7 (2 CH), 130.7 (C), 131.1 (C), 160.2 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1600 (s), 1569 (m), 1504 (s), 1456 (m), 1437 (m), 1410 (m), 1303 (s), 1246 (br. s), 1177 (m), 1058 (s), 1022 (s), 876 (s), 825 (vs) cm^{-1}. MS (EI, 70 eV): m/z (%) = 212 (22) [M^+], 133 (100), 118 (8), 89 (9). C_9H_9BrO (213.07): calcd. C 50.73, H 4.26; found C 50.88, H 4.30.

1-Bromo-1-(2-thienyl)ethene (4d): According to the procedure reported for compound **4a**, acetylene **6d** (1.28 g, 11.9 mmol) was converted with HBr (11.9 mmol, 2.1 mL of a 33% solution in acetic acid) to give the title compound **4d** (1.63 g, 8.62 mmol, 72%) after chromatography on SiO_2 (PE/EA, 2:1; R_f = 0.68) as a brown oil, which decomposed under ambient conditions. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.85 (d, J = 2.4 Hz, 1 H, C*H*H), 6.08 (d, J = 2.4 Hz, 1 H, CH*H*), 6.97 (dd, J = 5.1 Hz, J = 3.7 Hz, 1 H, Ar-H), 7.21–7.29 (m, 2 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (62 MHz, $CDCl_3$): δ = 115.8 (CH_2), 122.3 (C), 126.7 (CH), 127.3 (CH), 128.4 (CH), 142.0 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2917 (s), 2849 (m), 1743 (m), 1534 (m), 1501 (m), 1335 (s), 1118 (m), 743 (m) cm^{-1}. MS (CI, CH_4): m/z (%) = 189 (100) [$M + H^+$], 110 (88). C_6H_5BrS (189.07): calcd. C 38.12, H 2.67; found C 38.36, H 2.97.

3,4-Dimethoxyphenylacetylene (6a): *n*BuLi (162 mmol, 81 mL of a 2 mol·dm^{-3} solution in pentane) was added to a solution of dibromo compound **11a** (24.7 g, 76.7 mmol) in THF (300 mL) at –78 °C over a period of 45 min. Stirring was continued at –78 °C for 1.5 h, then the reaction mixture, while being stirred, was warmed to 23 °C over a period of 1.5 h. After dilution with saturated aqueous NH_4Cl solution (300 mL) and extraction with CH_2Cl_2 (2 × 80 mL), the combined organic layers were dried ($MgSO_4$), filtered, and the solvents evaporated. The residue was chromatographed on SiO_2 (PE/EA, 2:1; R_f = 0.35) to yield the title compound **6a** (11.6 g, 71.5 mmol, 93%) as colorless crystals, m.p. 71–72 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 3.02 (s, 1 H, CH), 3.85 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 6.78 (d, J = 8.3 Hz, 1 H, Ar-H), 6.98 (d, J = 1.9 Hz, 1 H, Ar-H), 7.09 (dd, J = 8.3 Hz, J = 1.9 Hz, 1 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (62 MHz, $CDCl_3$): δ = 55.8 (2 OCH_3), 75.8 (CH), 83.8 (C), 110.9 (CH), 114.2 (C), 114.7 (CH), 125.5 (CH), 149.6 (C), 149.8 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3248 (m), 1578 (m), 1507 (m), 1444 (m), 1406 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 162 (100) [M^+], 147 (29). $C_{10}H_{10}O_2$ (162.19): calcd. C 74.06, H 6.21; found C 73.97, H 6.30.

3-Ethoxy-4-methoxyphenylacetylene (6b). a) Corey–Fuchs Protocol: According to the procedure reported for **6a**, dibromo compound **11b** (32.0 g, 95.2 mmol) was converted with *n*BuLi (210 mmol, 105 mL of a 2 mol·dm^{-3} solution in pentane) to yield the title compound **6b** (16.60 g, 94.25 mmol, 99%) after chromatography on SiO_2 (PE/EA, 2:1; R_f = 0.54) as a colorless, hygroscopic solid. **b) Via Enol Phosphate:** A solution of ketone **7b** (2.60 g, 13.4 mmol) in THF (7 mL) was slowly added to LDA (14.1 mmol, 7.05 mL of a 2 mol·dm^{-3} solution in ethylbenzene/THF/heptane) in THF (10 mL) at –78 °C, and the reaction mixture was further stirred at –78 °C for 1 h. Then diethyl chlorophosphate (2.51 g, 14.1 mmol) was added, and the reaction mixture was warmed and stirred at ambient temperature for 3 h. LDA (30.2 mmol, 15.1 mL of a 2 mol·dm^{-3} solution) was added dropwise at –78 °C over 30 min, and the reaction mixture was then warmed and stirred at ambient temperature for 3 h. Water (10 mL) was added at 0 °C, and the reaction mixture stirred at 0 °C for 20 min. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined extracts were washed with hydrochloric acid (40 mL, 1 mol·dm^{-3}), water (3 × 100 mL) and dried ($MgSO_4$). After filtration, the solvent was removed in vacuo, and the residue chromatographed on SiO_2 (PE/EA, 5:1; R_f = 0.31) to give the compound **6b** as a colorless solid (1.33 g, 7.60 mmol, 56%), m.p. 95–96 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.46 (t, J = 7.0 Hz, 3 H, CH_3), 2.99 (s, 1 H, CH), 3.87 (s, 3 H, OCH_3), 4.09 (q, J = 7.0 Hz, 2 H, OCH_2), 6.80 (d, J = 8.3 Hz, 1 H, Ar-H), 6.99 (d, J = 1.8 Hz, 1 H, Ar-H), 7.09 (dd, J = 8.3 Hz, J = 1.8 Hz, 1 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.7 (CH_3), 55.9 (OCH_3), 64.3 (OCH_2), 75.5 (CH), 83.8 (C), 111.2 (CH), 114.1 (C), 116.1 (CH), 125.4 (CH), 147.9 (C), 150.1 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3258 (m), 1509 (m), 1458 (m), 1442 (m), 1412 (m), 1319 (m), 1233 (s), 1152 (m), 1129 (s), 1044 (m), 1018 (s) cm^{-1}. MS (EI, 70 eV): m/z (%) = 176 (100) [M^+], 148 (57), 133 (79), 105 (22), 91 (10). $C_{11}H_{12}O_2$ (176.12): calcd. C 74.93, H 6.85; found C 74.98, H 6.86.

4-Methoxyphenylacetylene (6c): According to the procedure reported for **6a**, dibromo compound **11c** (10.0 g, 34.3 mmol) was converted with *n*BuLi (72 mmol, 36 mL of a 2 mol·dm^{-3} solution in pentane) to yield the title compound **6c** (3.7 g, 28 mmol, 82%) after chromatography on SiO_2 (PE/EA, 5:1; R_f = 0.44) as a colorless solid, m.p. 25 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.00 (s, 1 H, CH), 3.81 (s, 3 H, OCH_3), 6.83–6.85 (m, 2 H, Ar-H), 7.42–7.44 (m, 2 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 75.8 (CH), 83.7 (C), 113.9 (2 CH), 114.1 (C), 133.6 (2 CH), 159.9 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3255 (m), 1604 (s), 1504 (vs), 1465 (m), 1442 (m), 1289 (s), 1243 (vs), 1170 (s), 1109 (m), 1026 (vs), 833 (vs), 639 (br. s) cm^{-1}. MS (EI, 70 eV): m/z (%) = 132 (100) [M^+], 117 (24), 89 (28), 63 (9). C_9H_8O (132.16): calcd. C 81.79, H 6.10; found C 81.86, H 6.00.

2-Ethynylthiophene (6d): According to the procedure reported for **6a**, the dibromo compound **11d** (4.00 g, 14.9 mmol) was converted with *n*BuLi (30 mmol, 15 mL of a 2 mol·dm^{-3} solution in pentane) to yield the title compound **6d** (1.1 g, 10 mmol, 68%) after distillation (b.p. 31–34 °C/13 mbar) as a colorless liquid. R_f(SiO_2; PE/EA, 2:1) = 0.72. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.33 (s, 1 H, CH), 6.93 (dd, J = 5.1 Hz, J = 3.8 Hz, 1 H, Ar-H), 7.22 (dd, J = 5.1 Hz, J = 1.1 Hz, 1 H, Ar-H), 7.25 (dd, J = 3.8 Hz, J = 1.0 Hz, 1 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 77.0 (CH), 81.2 (C), 122.1 (C), 126.9 (CH), 127.5 (CH), 133.1 (CH) ppm. IR (ATR): $\tilde{\nu}$ = 3298 (s), 2957 (s), 2926 (s), 2870 (m), 1239 (m), 928 (m), 852 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 108 (100) [M^+], 82 (17).

3-Ethoxy-4-methoxyacetophenone (7b): A suspension of phenol **8** (4.00 g, 24.1 mmol) and K_2CO_3 (4.77 g, 48.1 mmol) in DMF (20 mL) was heated at 100 °C for 30 min and then cooled to ambient temperature. Ethyl bromide (5.25 g, 48.14 mmol) was slowly added dropwise, and the reaction mixture heated at 100 °C for 6 h. After cooling to ambient temperature and removal of the solvent, the residue was dissolved in water (40 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined extracts were dried ($MgSO_4$), filtered and concentrated. The crude product was recrystallized from 2-propanol (25 mL) to give ketone **7b** as fine colorless needles (4.09 g, 21.1 mmol, 88%), m.p. 66–67 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.48 (t, J = 7.0 Hz, 3 H, CH_3), 2.56 (s, 3 H, CH_3), 3.94 (s, 3 H, OCH_3), 4.16 (q, J = 7.0 Hz, 2 H, OCH_2), 6.88 (d, J =

8.4 Hz, 1 H, Ar-H), 7.52 (d, J = 1.9 Hz, 1 H, Ar-H), 7.57 (dd, J = 8.4 Hz, J = 1.9 Hz, 1 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.7 (CH_3), 26.2 (CH_3), 56.1 (OCH_3), 64.4 (OCH_2), 110.2 (CH), 111.4 (CH), 123.1 (CH), 130.5 (C), 148.3 (C), 153.6 (C), 196.8 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1668 (vs), 1583 (vs), 1508 (vs), 1469 (m), 1422 (s), 1396 (m), 1355 (m), 1341 (m), 1290 (m), 1257 (m, br.), 1213 (br. s), 1180 (m), 1105 (m), 1081 (m), 1042 (s), 1012 (vs) cm^{-1}. MS (EI, 70 eV): m/z (%) = 194 (62) [M^+], 179 (45), 151 (100). $C_{11}H_{14}O_3$ (194.23): calcd. C 68.02, H 7.26; found C 67.90, H 7.36.

3-Hydroxy-4-methoxyacetophenone (8): A solution of ketone **7a** (15 g, 83 mmol) in concd. H_2SO_4 (75 mL) was stirred at 65 °C for 46 h. After cooling to ambient temperature, the reaction mixture was poured on ice (300 g) and the mixture stirred for 1 h. The precipitate was filtered off, washed with water, and redissolved in NaOH (0.19 mol, 190 mL of a 1 mol·dm^{-3} solution in water). The mixture was extracted with CH_2Cl_2 (80 mL). The aqueous layer was acidified (cooling with ice/water bath) with concd. hydrochloric acid (30 mL), stirred for 1.5 h, and the precipitate filtered off to give phenol **8** as a light brown solid (8.291 g, 49.89 mmol, 60%), m.p. 88–90 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.55 (s, 3 H, CH_3), 3.93 (s, 3 H, OCH_3), 5.94 (s, 1 H, OH), 6.90–6.92 (m, 1 H, Ar-H), 7.56–7.57 (m, 2 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (62 MHz, $CDCl_3$): δ = 26.7 (CH_3), 56.5 (OCH_3), 110.3 (CH), 114.9 (CH), 122.2 (CH), 131.4 (C), 145.8 (C), 151.2 (C), 197.4 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3169 (m, br.), 1665 (m), 1574 (m), 1509 (m), 1361 (m), 1272 (m, br.), 1204 (s), 1122 (m), 1017 (m), 820 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 166 (45) [M^+], 151 (100), 123 (19). $C_9H_{10}O_3$ (166.18): calcd. C 65.05, H 6.07; found C 64.70, H 6.08.

1,1-Dibromo-2-(3,4-dimethoxyphenyl)ethene (11a): Ph_3P (31.6 g, 120 mmol) was added to a cooled (ice/water bath) and well-stirred solution of CBr_4 (20.0 g, 60.2 mmol) in abs. CH_2Cl_2 (150 mL). The mixture was stirred with cooling for further 5 min, then aldehyde **10a** (10.0 g, 60.0 mmol) was added portionwise (exothermic reaction). The resulting solution was stirred for 30 min, then extracted with water (250 mL). The organic layer was separated and dried with $MgSO_4$. After filtration, the solvent was stripped off and the residue chromatographed on SiO_2 (CH_2Cl_2; R_f = 0.55) to give the title compound **11a** in the first fraction as a light yellow oil (17.9 g, 55.6 mmol, 92%). ^1H NMR (250 MHz, $CDCl_3$): δ = 3.87 (s, 6 H, 2 OCH_3), 6.82 (d, J = 8.4 Hz, 1 H, Ar-H), 7.09 (dd, J = 8.4 Hz, J = 1.7 Hz, 1 H, Ar-H), 7.17 (d, J = 1.7 Hz, 1 H, Ar-H), 7.39 (s, 1 H, 2-H) ppm. $^{13}C\{^1H\}$ NMR (62 MHz, $CDCl_3$): δ = 55.89 (OCH_3), 55.92 (OCH_3), 87.4 (C), 110.8 (CH), 111.1 (CH), 121.9 (CH), 127.9 (C), 136.4 (CH), 148.6 (C), 149.3 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1600 (m), 1515 (s), 1462 (m), 1269 (s), 1142 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 320 (100) [M^+], 305 (20), 198 (10), 162 (19), 118 (30). $C_{10}H_{10}Br_2O_2$ (322.00): calcd. C 37.30, H 3.13; found 37.05, H 3.15.

1,1-Dibromo-2-(3-ethoxy-4-methoxyphenyl)ethene (11b): According to the procedure reported for compound **11a**, the aldehyde **10b** (24.0 g, 133 mmol), PPh_3 (69.6 g, 266 mmol) and CBr_4 (44.4 g, 133 mmol) were converted to yield title compound **11b** (42.8 g, 127 mmol, 96%) after chromatography on SiO_2 (CH_2Cl_2; R_f = 0.55) as a pale yellow solid, m.p. 41–42 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.46 (t, J = 7.0 Hz, 3 H, CH_3), 3.86 (s, 3 H, OCH_3), 4.08 (q, J = 7.0 Hz, 2 H, OCH_2), 6.83 (d, J = 8.4 Hz, 1 H, Ar-H), 7.10 (dd, J = 8.4 Hz, J = 2.0 Hz, 1 H, Ar-H), 7.18 (d, J = 2.0 Hz, 1 H, Ar-H), 7.38 (s, 1 H, 2-H) ppm. $^{13}C\{^1H\}$ NMR (62 MHz, $CDCl_3$): δ = 14.8 (CH_3), 55.9 (OCH_3), 64.4 (OCH_2), 87.1 (C), 110.9 (CH), 112.5 (CH), 121.9 (CH), 127.8 (C), 136.4 (CH), 147.8 (C), 149.5 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1596 (m), 1511 (s), 1428 (m), 1387 (m), 1302 (m), 1262 (s), 1236 (s), 1145 (s), 1045 (m), 1021 (m), 991 (m), 868 (s), 815 (m), 795 (s), 721 (m), 628 (m), 612 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 334 (100) [M^+], 306 (41), 291 (53), 263 (9), 176 (11), 148 (21), 133 (27), 105 (21), 76 (14). $C_{11}H_{12}Br_2O_2$ (336.02): calcd. C 39.32, H 3.60; found C 39.32, H 3.62.

1,1-Dibromo-2-(4-methoxyphenyl)ethene (11c): According to the procedure reported for compound **11a**, the aldehyde **10c** (3.0 g, 22 mmol), PPh_3 (11.6 g, 44.2 mmol) and CBr_4 (7.3 g, 22 mmol) were converted to yield title compound **11c** (5.54 g, 19.0 mmol, 86%) after chromatography (SiO_2; CH_2Cl_2; R_f = 0.74) as a yellow solid, m.p. 34–36 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, OCH_3), 6.88 (d, J = 8.9 Hz, 2 H, Ar-H), 7.39 (s, 1 H, 2-H), 7.49 (d, J = 8.7 Hz, 2 H, Ar-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 87.2 (C), 113.8 (2 CH), 127.8 (C), 129.9 (2 CH), 136.3 (CH), 159.7 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1602 (m), 1565 (m), 1506 (m), 1454 (m), 1329 (m), 1305 (m), 1253 (m), 1176 (m), 1025 (s), 862 (s), 802 (s), 730 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 290 (100) [M^+], 276 (16), 132 (30). $C_9H_8Br_2O$ (291.80): calcd. C 37.02, H 2.76; found C 37.12, H 2.78.

1,1-Dibromo-2-(2-thienyl)ethene (11d): According to the procedure reported for compound **11a**, the aldehyde **10d** (4.00 g, 35.7 mmol), PPh_3 (23.4 g, 89.2 mmol) and CBr_4 (14.8 g, 44.6 mmol) were converted to yield title compound **11d** (9.50 g, 35.4 mmol, 99%) after chromatography on SiO_2 (CH_2Cl_2; R_f = 0.78) as light brown crystals, m.p. 55–56 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.03 (dd, J = 5.0 Hz, J = 3.8 Hz, 1 H, Ar-H), 7.25 (d, J = 4.3 Hz, 1 H, Ar-H), 7.38 (d, J = 5.0 Hz, 1 H, Ar-H), 7.65 (s, 1 H, 2-H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 86.9 (C), 126.5 (CH), 127.1 (CH), 130.0 (CH), 130.9 (CH), 138.1 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1420 (m), 1346 (m), 1208 (s), 1077 (m), 1050 (m), 855 (s), 816 (s) 741 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 266 (100) [M^+], 189 (10), 108 (67). $C_6H_4Br_2S$ (268.00): calcd. C 26.89, H 1.51; found C 27.10, H 1.61.

2-Phenyl-1,4-pentadien-3-ol (12a): Under N_2, nBuLi (68.30 mmol, 40.2 mL of a 1.7 mol·dm^{-3} solution in pentane) was added dropwise at –78 °C to a solution of the bromo olefin **4e** (5.00 g, 27.3 mmol) in abs. THF (100 mL) over a period of 30 min. The reaction mixture was further stirred at –78 °C for 1.5 h. Then freshly distilled acrolein **5a** (4.59 g, 81.9 mmol) was added dropwise over a period of 10 min. After being stirred at –78 °C for a further 1.5 h, the reaction mixture was warmed to room temperature and washed with saturated aqueous NH_4Cl (150 mL) and water (50 mL). The layers were separated, and the combined aqueous layers were extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried with $MgSO_4$. After filtration and removal of solvent, the residue was chromatographed on SiO_2 (PE/EA, 5:1; R_f = 0.35) to give **12a** (3.40 g, 21.2 mmol, 78%) as a light yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.0 (br. s, 1 H, OH), 5.06 (d, br., $J \approx$ 6 Hz, 1 H, 3-H), 5.09 [dt, J = 10.3 Hz, J = 1.4 Hz, 1 H, (*E*)-5-H], 5.26 [dt, J = 17.2 Hz, J = 1.4 Hz, 1 H, (*Z*)-5-H], 5.34–5.36 (m, br., 1 H, 1-H), 5.37 (t, J = 1.1 Hz, 1 H, 1-H), 5.90 (ddd, J = 17.2 Hz, J = 10.3 Hz, J = 5.8 Hz, 1 H, 4-H), 7.19–7.32 (m, 3 H, Ph), 7.36–7.41 (m, 2 H, Ph) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 75.0 (CH), 114.0 (CH_2), 116.3 (CH_2), 127.4 (2 CH), 128.1 (CH), 128.7 (2 CH), 139.4 (CH), 139.8 (C), 150.4 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3390 (br. s), 3110 (m), 3100 (m), 2957 (m), 1501 (m), 1489 (m), 1018 (s), 951 (s) cm^{-1}. MS (EI, 70 eV): m/z (%) = 160 (30) [M^+], 142 (24), 103 (100), 77 (39). HRMS (EI, 70 eV): calcd. 160.0888 ($C_{11}H_{12}O$); found 160.0889 [M^+].

2-(3,4-Dimethoxyphenyl)-1,4-pentadien-3-ol (12b): According to the procedure reported for compound **12a**, nBuLi (8.65 mmol, 4.3 mL of a 2 mol·dm^{-3} solution in pentane), bromo olefin **4a** (1.00 g, 4.12 mmol), and acrolein **5a** (685 mg, 12.3 mmol) were converted to give the title compound **12b** (560 mg, 2.54 mmol, 62%) after

chromatography [SiO_2; PE/EA, 5:1; R_f(PE/EA, 2:1) = 0.21] as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.95 (br. s, 1 H, OH), 3.88 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 5.10 (d, J = 5.5 Hz, 1 H, 3-H), 5.19 [dt, J = 10.4 Hz, J = 1.2 Hz, 1 H, (*E*)-5-H], 5.34 (s, 1 H, 1-H), 5.35 (s, 1 H, 1-H), 5.35 (dt, J = 18.1 Hz, J = 1.2 Hz, 1 H, 5-H), 5.97 (ddd, J = 17.1 Hz, J = 10.3 Hz, J = 5.7 Hz, 1 H, 4-H), 6.82–6.84 (m, 1 H, Ar-H), 7.00–7.02 (m, 2 H, Ar-H) ppm. ^{13}C{^{1}H} NMR (62 MHz, $CDCl_3$): δ = 55.85 (2 OCH_3), 74.7 (CH), 110.4 (CH), 110.9 (CH), 112.6 (CH_2), 115.7 (CH_2), 119.3 (CH), 132.1 (C), 139.2 (CH), 148.7 (C), 148.8 (C), 149.5 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1516 (m), 1256 (m), 1025 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 220 (34) [M$^+$], 163 (100), 148 (4), 91 (6). $C_{13}H_{16}O_3$ (220.26): calcd. C 70.89, H 7.32; found C 70.73, H 7.56.

2-(3-Ethoxy-4-methoxyphenyl)-1,4-pentadien-3-ol (12c): According to the procedure reported for compound **12a**, *n*BuLi (154 mmol, 77.0 mL of a 2 mol·dm^{-3} solution in pentane), bromo olefin **4b** (18.0 g, 70.0 mmol), and acrolein **5a** (10.5 g, 187 mmol) were converted to give the title compound **12c** (10.5 g, 44.8 mmol, 64%) after chromatography [SiO_2; PE/EA, 5:1; R_f(PE/EA, 2:1) = 0.31] as a colorless solid, m.p. 30–32 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45 (t, J = 7.0 Hz, 3 H, CH_3), 2.18 (d, br., J = 3.5 Hz, 1 H, OH), 3.87 (s, 3 H, OCH_3), 4.06–4.15 (m, 2 H, OCH_2), 5.08 (br. s, 1 H, 3-H), 5.17 [dt, J = 10.3 Hz, J = 1.4 Hz, 1 H, (*E*)-5-H], 5.32 (t, br., J = 1.0 Hz, 1 H, 1-H), 5.33 (br. s, 1 H, 1-H), 5.34 [dt, J = 17.2 Hz, J = 1.4 Hz, 1 H, (*Z*)-5-H], 5.96 (ddd, J = 17.2 Hz, J = 10.4 Hz, J = 5.6 Hz, 1 H, 4-H), 6.81–6.84 (m, 1 H, Ar-H), 6.98–7.01 (m, 2 H, Ar-H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.8 (CH_3), 55.9 (OCH_3), 64.35 (OCH_2), 74.8 (CH), 111.3 (CH), 112.0 (CH), 112.5 (CH_2), 115.7 (CH_2), 119.4 (CH), 132.0 (C), 139.2 (CH), 148.0 (C), 149.2 (C), 149.6 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3435 (m, br.), 1511 (s), 1249 (s), 1211 (m), 1137 (m), 1025 (s) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 234 (48) [M$^+$], 177 (100), 149 (14), 117 (7). $C_{14}H_{18}O_3$ (234.29): calcd. C 71.77, H 7.74; found C 71.44, H 8.09.

(*E*)-4-(3,4-Dimethoxyphenyl)-1-phenyl-1,4-pentadien-3-ol (12d): According to the procedure reported for compound **12a**, *n*BuLi (16.0 mmol, 8.0 mL of a 2 mol·dm^{-3} solution in pentane), bromo olefin **4a** (1.60 g, 6.58 mmol), and aldehyde **5b** (1.33 mL, 10.5 mmol) were converted to give the title compound **12d** (1.20 g, 4.10 mmol, 63%) after chromatography (SiO_2; PE/EA, 2:1; R_f = 0.23) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.15 (br. s, 1 H, OH), 3.85 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 5.25 (d, br., J = 6.0 Hz, 1 H, 3-H), 5.38 [br. s, 1 H, (*Z*)-5-H], 5.40 [br. s, 1 H, (*E*)-5-H], 6.33 (dd, J = 16.0 Hz, J = 6.0 Hz, 1 H, 2-H), 6.67 (dd, J = 16.0 Hz, J = 1.0 Hz, 1 H, 1-H), 6.81 (d, J = 8.9 Hz, 1 H, Ar-H), 7.00–7.07 (m, 2 H, Ar-H), 7.19–7.40 (m, 5 H, Ar-H) ppm. ^{13}C{^{1}H} NMR (62 MHz, $CDCl_3$): δ = 55.8 (OCH_3), 55.9 (OCH_3), 74.5 (CH), 110.4 (CH), 110.9 (CH), 112.7 (CH_2), 119.4 (CH), 126.5 (2 CH), 127.7 (CH), 128.6 (2 CH), 130.5 (CH), 131.1 (CH), 132.0 (C), 136.6 (C), 148.7 (C), 148.8 (C), 149.7 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1513 (s), 1462 (m), 1250 (s), 1174 (m), 1143 (m), 1025 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 296 (45) [M$^+$], 192 (12), 163 (100), 148 (7), 133 (10). $C_{19}H_{20}O_3$ (296.37): calcd. C 77.00, H 6.80; found C 76.93, H 7.03.

(*E*)-4-(3-Ethoxy-4-methoxyphenyl)-1-phenyl-1,4-pentadien-3-ol (12e): According to the procedure reported for compound **12a**, *n*BuLi (13 mmol, 6.5 mL of a 2 mol·dm^{-3} solution in pentane), bromo olefin **4b** (1.67 g, 6.49 mmol), and aldehyde **5b** (1.2 mL, 9.75 mmol) were converted to give the title compound **12e** (968 mg, 3.12 mmol, 48%) after chromatography (SiO_2; PE/EA, 2:1; R_f = 0.44) as a yellow solid, m.p. 73–76 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.43 (t, J = 7.0 Hz, 3 H, CH_3), 2.10 (br. s, 1 H, OH), 3.86 (s, 3 H, OCH_3), 4.07 (q, J = 7.0 Hz, 2 H, OCH_2), 5.24 (d, J = 6.2 Hz, 1 H, 3-H), 5.37 (s, 1 H, 5-H), 5.38 (s, 1 H, 5-H), 6.31 (dd, J = 16.0 Hz, J = 6.2 Hz, 1 H, 2-H), 6.67 (d, J = 16.5 Hz, 1 H, 1-H), 6.82 (d, J = 8.2 Hz, 1 H, Ar-H), 7.01 (d, J = 1.9 Hz, 1 H, Ar-H), 7.03–7.04 (m, 1 H, Ar-H), 7.22–7.36 (m, 5 H, Ph) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.5 (CH_3), 55.9 (OCH_3), 64.3 (OCH_2), 74.5 (CH), 111.2 (CH), 112.0 (CH), 112.6 (CH_2), 119.4 (CH), 126.5 (2 CH), 127.7 (CH), 128.6 (2 CH), 130.5 (CH), 131.1 (CH), 132.0 (C), 136.6 (C), 148.0 (C), 149.2 (C), 149.7 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3344 (m, br.), 1578 (m), 1515 (m), 1465 (m), 1392 (m), 1331 (m), 1254 (s), 1216 (s), 1180 (m), 1145 (s), 1124 (m), 1098 (m), 1020 (s), 959 (s), 898 (m), 755 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 310 (47) [M$^+$], 206 (7), 177 (100), 149 (8), 91 (8). HRMS (EI, 70 eV): calcd. 310.1569 ($C_{20}H_{22}O_3$), found 310.1568 [M$^+$].

(*E*)-4-(4-Methoxyphenyl)-1-phenyl-1,4-pentadien-3-ol (12f): According to the procedure reported for compound **12a**, *n*BuLi (3.10 mmol, 1.55 mL of a 2 mol·dm^{-3} solution in pentane), bromo olefin **4c** (550 g, 2.58 mmol), and aldehyde **5b** (400 mg, 3.03 mmol) were converted to give the title compound **12f** (511 g, 1.92 mmol, 74%) after chromatography (SiO_2; PE/EA, 2:1; R_f = 0.37) as a yellow oil, which slowly solidified at ambient temperature, m.p. 56–58 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.00 (br. s, 1 H, OH), 3.79 (s, 3 H, OCH_3), 5.25 (d, br. J = 5.4 Hz, 1 H, 3-H), 5.37 [s, 1 H, (*Z*)-5-H], 5.38 [s, 1 H, (*E*)-5-H], 6.31 (dd, J = 16.1 Hz, J = 6.2 Hz, 1 H, 2-H), 6.65 (d, J = 15.8 Hz, 1 H, 1-H), 6.84–6.87 (m, 2 H, Ar-H), 7.20–7.24 (m, 1 H, Ar-H), 7.27–7.30 (m, 2 H, Ar-H), 7.34–7.36 (m, 2 H, Ar-H), 7.39–7.42 (m, 2 H, Ar-H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 74.4 (CH), 112.4 (CH_2), 113.8 (2 CH), 126.6 (2 CH), 127.7 (CH), 128.1 (2 CH), 128.5 (2 CH), 130.4 (CH), 131.2 (CH), 131.6 (C), 136.6 (C), 149.4 (C), 159.3 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3327 (m, br.), 1605 (s), 1574 (m), 1513 (s), 1448 (m), 1290 (m), 1246 (vs), 1184 (s), 1068 (m), 1030 (s), 970 (m), 906 (m), 832 (s), 727 (m), 691 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 266 (35) [M$^+$], 162 (8), 133 (100). $C_{18}H_{18}O_2$ (266.32): calcd. C 81.17, H 6.81; found C 81.08, H 6.74.

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