CHAPTER 3

Synthesis of a series of quinone-terminated oligo(phenylenevinylene) molecular wires

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3.1 Introduction

The cytoplasmic membrane of many organisms is populated with quinones, some of which participate in the aerobic or an alternative respiratory chain, shuttling electrons between often membrane-bound oxidoreductases [1]. Electrochemical research in these enzymes may be performed by using soluble analogues of these quinones, mediating electron transfer between electrode and enzyme. The applicability of mediators may be limited, however, since complex diffusional and kinetic effects complicate data interpretation and reproducibility. Direct, non-mediated electron transfer between electrode and enzyme is only meaningful when the enzyme's active site can directly exchange electrons with the electrode surface, and, additionally, the enzyme is structurally/functionally unaffected by the surface, which is frequently not the case (see chapter 1).

Here, we present a third approach in addition to mediated and direct electron transfer: the application of 'Q-wires'. The quinone moieties are not allowed to freely diffuse, but are instead linked to the electrode surface using molecular wires. These wires, which terminate in a gold-electrode-binding methyl thiol, are composed of a segment of semi-conductive, fully conjugated oligo(phenylenevinylene) (OPV) (see figure 1 for their thioacetate ester analogues). Direct, non-rate-limiting electron transport from the electrode surface to the quinone unit is therefore expected [2, 3], and, when interacting with the active site of an oxidoreductase, direct electron transfer between electrode and enzyme should be established as well.

In this chapter, the synthesis of a series of ubiquinone- and menaquinone-terminated molecular wires – varying in the length of the OPV systems – (figure 1) will be described. From a general perspective, the synthesis of the quinone and OPV parts were performed separately, and both parts were connected in a final synthesis step using Grubbs olefin metathesis [4, 5, 6]. Although ultimately successful, several complications had to be overcome. Besides the formation of byproducts (e.g. homodimers) and, consequently, challenging purifications, it was found that not all combinations of cross

metathesis partners resulted in the desired product. Nevertheless, sufficient amounts of satisfactorily pure products were obtained.

Besides the conjugated wires **U_0**-**U_3** and **M_0**-**M_3** (figure 1), a fully saturated wire **U_{SAT}** was synthesized as well. By comparing the electrochemical properties of both classes of wire (chapter 4), verification of whether the presence of an OPV system indeed enhances electron transfer rates is possible.

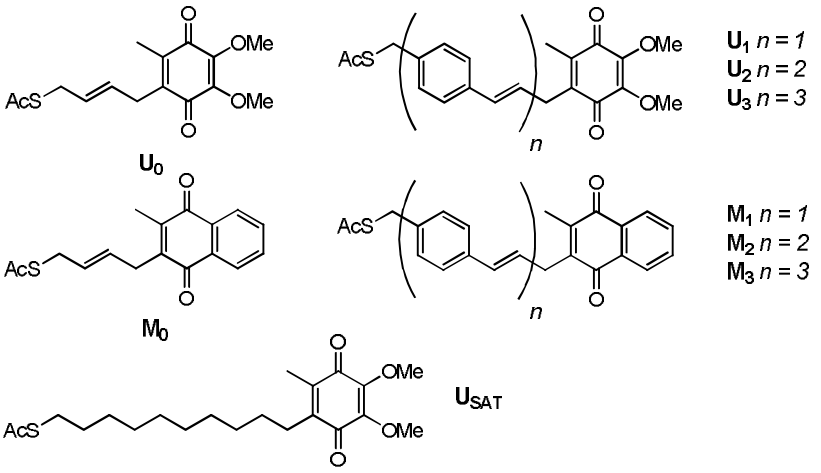


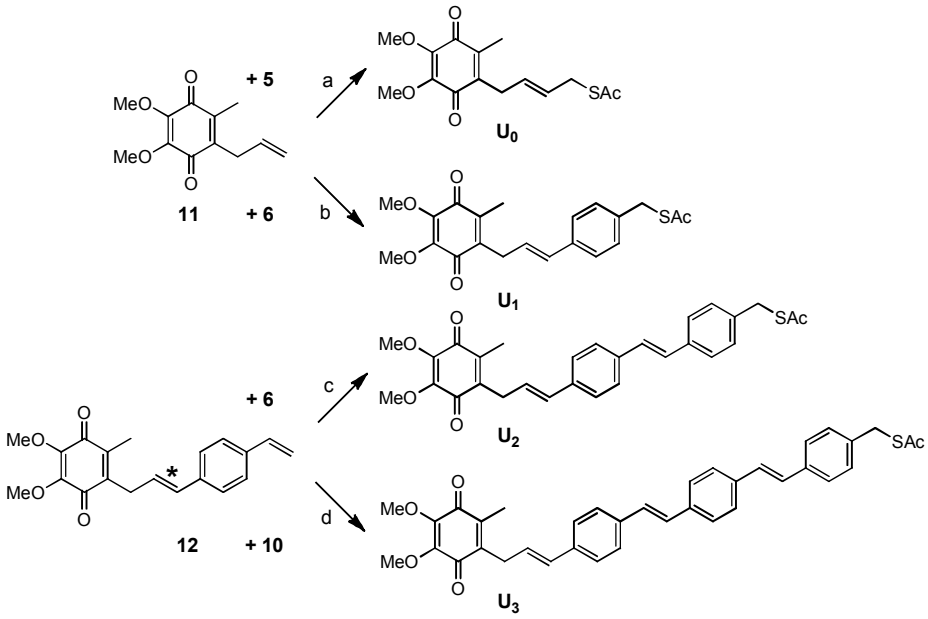
Figure 1 'Q-wires' synthesized in this study

3.2 Results and discussion

As mentioned previously, it was decided to synthesize the quinone moieties and the vinyl-terminated OPV methyl thiol wire separately, and join both parts in a later stage using Grubbs olefin metathesis. This provides a level of flexibility in their composition (i.e. alternative quinone moiety; variation in length of the OPV segment). The Grubbs olefin metathesis reactions performed in this study are depicted in scheme 1 and 2.

Initially, it was expected that the synthesis of 'allyl ubiquinone' (**11**) and 'allyl menaquinone' (**15**) would suffice, and that they could be linked to any length of vinyl-terminated OPV methyl thiol wire. In accordance with the literature [4], the connection between an allyl derivative (**11**) and a styrene (**6**) was indeed achieved to provide compound **U_1**. Curiously, however, the

cross metathesis between compound **10** and **11** proved unsuccessful using 2nd generation Grubbs catalyst. An observation that (substituted) styrenes generally undergo successful cross metathesis inspired an alternative approach to obtain compound $\mathbf{U_2}$. The location where the quinone moiety and the OPV wire were to be connected to provide the desired molecule $\mathbf{U_2}$ was moved, instead envisioning a cross metathesis between compounds **6** and **12** – both of which can be considered substituted styrenes.

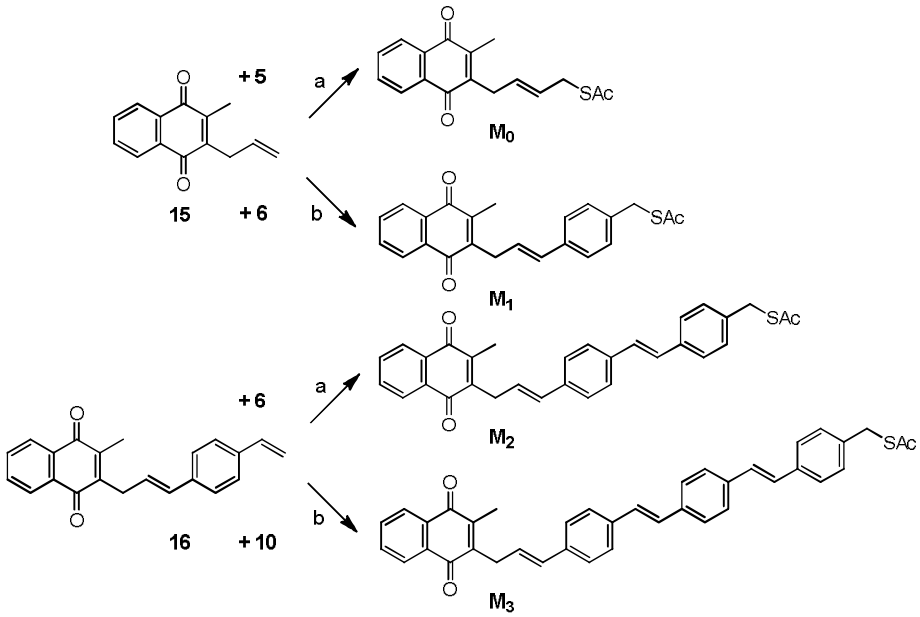


Scheme 1 Synthesis of Q-wires $\mathbf{U_0}$-$\mathbf{U_3}$ by means of Grubbs olefin metathesis: (a-d) 2nd generation Grubbs catalyst, DCM, RT, 18 h; (a) 29%; (b) 16%; (c) 10%; (d) 8%. The asterisk indicates an additional reactive double bond, besides the vinyl group

Indeed, the reaction described above (scheme 1, reaction *c*) provided an acceptable amount of compound $\mathbf{U_2}$. Similarly, by reacting **10** and **12**, compound $\mathbf{U_3}$ could be obtained (scheme 1, reaction *d*). However, besides the anticipated complicating factors such as formation of homodimers and reaction incompleteness, an additional issue was identified. In both cases, not only the expected wires were found, but also wires that were one styrene moiety shorter (i.e. in scheme 1, $\mathbf{U_1}$ was found in reaction *c* and $\mathbf{U_2}$ in reaction *d*). A likely explanation for the presence of these byproducts is the reactivity of another double bound in compound **12**, indicated with an

asterisk in scheme 1. Several rounds of purification were required to isolate the desired products from the complex mixtures, resulting in low yields (typically 5-10%).

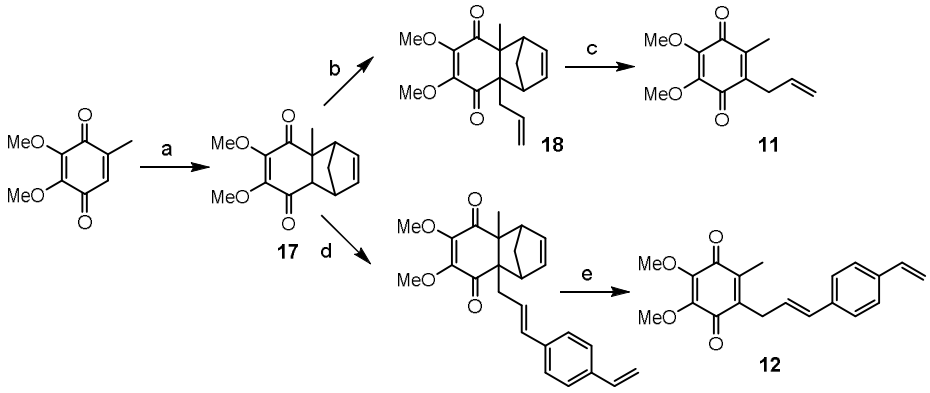
The synthesis of wires **M_0** through **M_3**, depicted in scheme 2, was fully analogous to the synthesis of wires **U_0** through **U_3**, outlined in scheme 1.



Scheme 2 Synthesis of Q-wires **M_0**-**M_3** by means of Grubbs olefin metathesis: (a-d) 2nd generation Grubbs catalyst, DCM, RT, 18 h; (a) 21%; (b) 3%; (c) 10%; (d) 5%

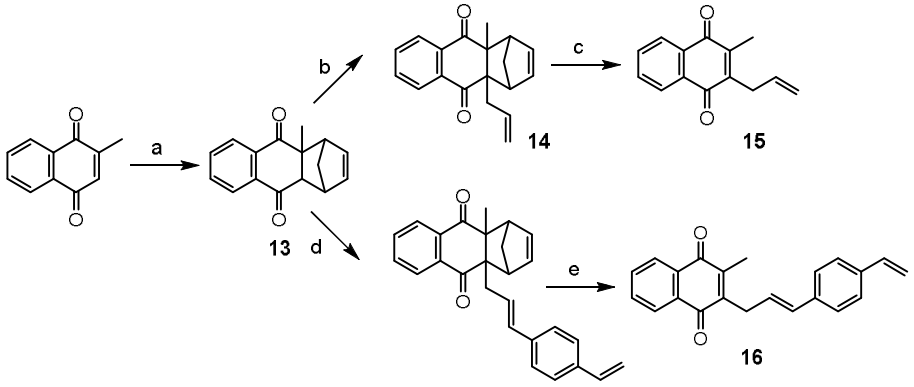
As suggested previously [7], the synthetic strategy to obtain 'allyl ubiquinone' (**11**) from commercially available 5,6-dimethoxy-3-methyl-1,4-benzoquinone, which is summarized in scheme 3 (step *a* through *c*), allows for the introduction of alternative substituents, besides the allyl moiety. After a Diels-Alder reaction [8] between 5,6-dimethoxy-3-methyl-1,4-benzoquinone and cyclopentadiene, compound **17** was obtained. After treatment of **17** with a base (*tert*-butoxide), addition of allyl bromide led to compound **18**. The retro-Diels-Alder reaction that provided 'allyl ubiquinone' (**11**), was achieved by refluxing in toluene for several hours. Similarly, reacting *p*-vinyl cinnamyl bromide (**4**, see scheme 5 for its synthesis), with compound **17**, ultimately provided compound **12**, one of

the starting materials required in the Grubbs cross metathesis reactions described above.



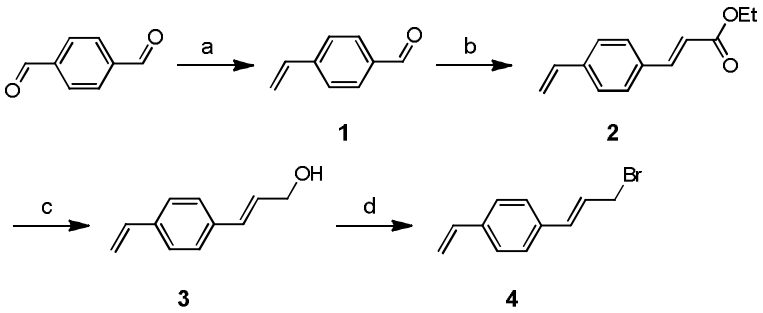
Scheme 3 Synthesis of compounds **11** and **12**: (a) cyclopentadiene, glacial AcOH, RT; (b) 18-crown-6, *t*-BuOK, allyl bromide, THF, 0°C; (c) toluene, reflux; (d) 18-crown-6, *t*-BuOK, *p*-vinyl cinnamyl bromide, THF, 0°C 1 h, then RT 1 h; (e) toluene, reflux, 5 h; (d-e) 18%

The synthetic pathways outlined in scheme 3 proved to be fully compatible with menadione as well, resulting in the fully analogous synthetic strategy depicted in scheme 4.



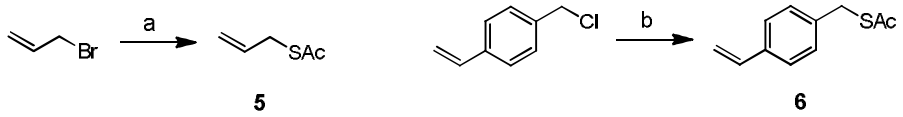
Scheme 4 Synthesis of compounds **15** and **16**: (a) cyclopentadiene, AcOH/$CHCl_3$, RT, 50 h, 32%; (b) *t*-BuOK, allyl bromide, THF, 0°C, 2 h; (c) toluene, reflux, 4 h; (b-c) 45%; (d) 18-crown-6, *t*-BuOK, *p*-vinyl cinnamyl bromide, THF, 0°C 1 h, then RT 1 h; (e) toluene, reflux, 4 h; (d-e) 8%

As can be observed in scheme 3 and 4, the synthesis of compounds **12** and **16** requires *p*-vinyl cinnamyl bromide (**4**), a compound that could not be purchased. A synthetic route to obtain this compound was therefore devised (scheme 5). Starting with an excess of terephthalaldehyde, a Wittig reaction [9] with methyltriphenylphosphonium bromide provided compound **1**. In a Horner-Wadsworth-Emmons reaction [10], this aldehyde was then treated with triethyl phosphonoacetate and base, to provide the α,β-unsaturated ester **2**. Reduction of this ester to the allylic alcohol **3** was achieved by diisobutylaluminium hydride (DIBAL-H), which is particularly suitable for this step, since it does not affect the double bond [11]. Finally, alcohol **3** was converted to *p*-vinyl cinnamyl bromide **4** using phosphorus tribromide [12, 13].



Scheme 5 Synthesis of *p*-vinyl cinnamyl bromide (**4**): (a) PPh_3CH_3Br, *t*-BuOK, THF, 0°C ~10 min, then RT 2.5 h, 31%; (b) triethyl phosphonoacetate, *t*-BuOK, THF, 0°C ~10 min, then RT 18 h, 73%; (c) 1 M DIBAL-H, THF, 0°C ~10 min, then RT 18 h, 73%; (d) PBr_3, Et_2O, 0°C, 20 min, >95%

The cross metathesis partners required for the synthesis of wires $\mathbf{U_0}$-$\mathbf{U_2}$ and $\mathbf{M_0}$-$\mathbf{M_2}$ were obtained as outlined in scheme 6. Curiously, some protocols (e.g. [14]) require high temperatures and troublesome solvents, such as DMF. Other protocols [15, 16], however, describe successful conversion of chlorides and bromides to their thioacetate ester counterparts under mild conditions (e.g. room temperature) and convenient solvents (e.g. acetone). Allyl bromide was reacted with potassium thioacetate to provide **5**, simply by dissolving both in aceton, followed by overnight stirring at room temperature. Compound **6** was obtained in a similar manner.



5 **6**

Scheme 6 Synthesis of compounds **5** and **6**: (a) KSAc, aceton, RT, 18 h, 37%; (b) KSAc, aceton/MeOH, RT, 50 h, 77%

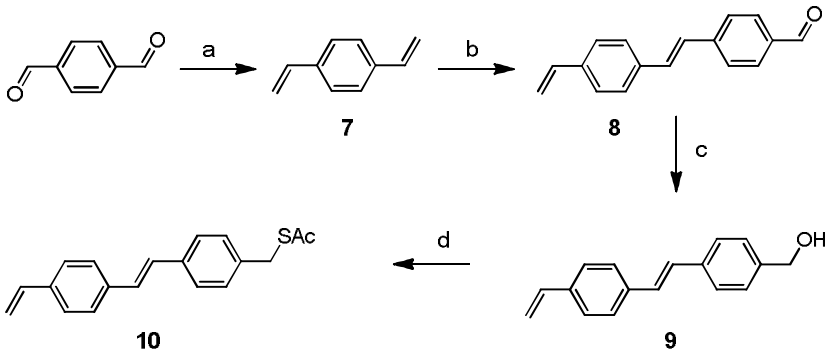
A more involved synthesis route (scheme 7) was necessary to arrive at compound **10**, required in the cross metathesis affording the longest wires $\mathbf{U_3}$ and $\mathbf{M_3}$. A double Wittig reaction with methyltriphenylphosphonium bromide was performed to convert terephthalaldehyde into *p*-divinylbenzene (**7**). A Heck coupling [17] between **7** and *p*-bromobenzaldehyde resulted in compound **8**, which then required reduction.

Curiously, this reduction could only be achieved using the aforementioned reducing agent DIBAL-H. Reduction using different sodium borohydrides was attempted, for example, which often led to formation of byproducts and insignificant amounts of the target product. The successful application of DIBAL-H in this reduction reaction may be related to the reduction of the α,β-unsaturated ester **2** encountered above. Here, DIBAL-H does not reduce the double bond. This may also provide an explanation for the success of the reduction of compound **8**, since the double bonds within the molecules are preserved.

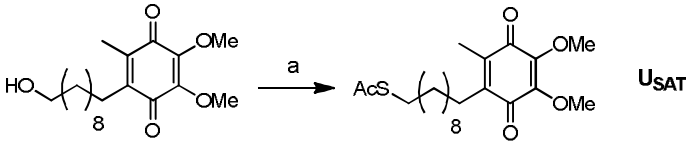
After the reduction of compound **8**, a Mitsunobu reaction [18] was performed to convert alcohol **9** into the corresponding thioacetate ester **10**. Hydrolysis of the thioester bond was performed after the Grubbs cross metathesis reactions, because of the anticipated interference of the unprotected thiol with the catalyst. The deprotection (deacetylation) of the wires and their subsequent binding onto gold electrode surfaces will be described in chapter 4.

In addition to the highly conjugated wires described above, a fully saturated wire ($\mathbf{U_{SAT}}$) was synthesized as well (i.e. a quinone moiety attached to an alkanethiol), similar in length to $\mathbf{U_2}$. This was achieved by reacting commercially available idebenone to its thioacetate ester counterpart

(scheme 8) by means of a Mitsunobu reaction. Electrochemical characterization of both the conjugated wires and $\mathbf{U_{SAT}}$ (chapter 4) will be used to determine whether the OPV section in the conjugated wires indeed improves electron transport rates, compared to the rates obtained from the fully saturated wire.



Scheme 7 Synthesis of compound **10**: (a) PPh_3CH_3Br, *t*-BuOK, THF, 0°C 30 min, then RT 1 h, 69%; (b) *p*-Br-benzaldehyde, Et_3N, $Pd(OAc)_2$, P(*o*-tolyl)$_3$, DMF, 80°C, 24 h, 28%; (c) 1 M DIBAL-H, THF, 0°C ~10 min, then RT 15 min, 79%; (d) DCAD, PPh_3, AcSH, THF, 0°C ~10 min, then RT 18 h, 47%



Scheme 8 Synthesis of $\mathbf{U_{SAT}}$: (a) DCAD, PPh_3, AcSH, THF, 0°C, then RT 18 h, 74%

3.3 Conclusion & Outlook

In this chapter, the synthesis of a series of 'Q-wires' – $\mathbf{U_0}$ through $\mathbf{U_3}$ and $\mathbf{M_0}$ through $\mathbf{M_3}$ – and an additional fully conjugated wire ($\mathbf{U_{SAT}}$) was described. Crucially, the synthesis was performed by separately preparing the quinone-containing part and the OPV-containing part. In a final Grubbs olefin metathesis reaction, these two parts were then joined. However, significant challenges were encountered during this final reaction, leading to low yields and incompletely purified products. Nevertheless, these issues

did not prove to be problematic during the electrochemical experiments performed in the following chapters.

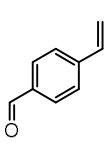
The electrochemical properties of the Q-wires will be explored in the following chapter. There, the influence of the length of the wire on electron transfer rates will be assessed. In addition, the electron transfer rates of the fully saturated $\mathbf{U_{SAT}}$ will be compared to those of $\mathbf{U_2}$, which is similar in length, in order to determine whether the presence of an OPV system indeed enhances said rates.

3.4 Experimental section

General

All chemicals and solvents were purchased from Sigma-Aldrich, except, most notably: 5,6-dimethoxy-3-methyl-1,4-benzoquinone (Alfa Aesar) and idebenone (TCI). THF and diethyl ether were dried over 60% sodium hydride in mineral oil for several hours, prior to distillation under reduced pressure. Dry DCM and DMF were purchased. Flash chromatography was performed on Screening Devices B.V. silica gel 60 (0.040-0.063 mm). NMR spectra were recorded on a Bruker DPX-300 spectrometer (300/75 MHz). A Thermo Finnigan LTQ Orbitrap system was used for HRMS.

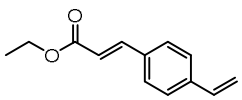
4-vinylbenzaldehyde (1)



To a stirring suspension of methyltriphenylphosphonium bromide (10 g, 28 mmol) and terephthalaldehyde (6 g, 45 mmol) in 75 mL THF under an argon atmosphere at 0°C, potassium *t*-butoxide (3.2 g, 29 mmol) was added in small portions over a period of about 10 minutes. The reaction mixture turned reddish brown. The reaction was allowed to continue for an additional 2.5 hours at room temperature. Afterwards, 100 mL of diethyl ether was added and the mixture was filtered. The solvent was evaporated from the filtrate and the crude product was taken up in $CHCl_3$ and directly applied to a silica gel column (PET), eluting with a gradient of PET/DCM (1:0 to 2:1) to afford 1.13 g of a white solid (31%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.95 (s, 1H), 7.80 (d, J = 8.1 Hz, 2H), 7.50 (d, J = 8.1 Hz, 2H), 6.73 (dd, J_1 = 17.6 Hz, J_2 = 11.0 Hz,

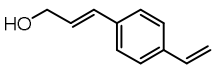
1H), 5.87 (d, *J* = 17.7 Hz, 1H), 5.40 (d, *J* = 10.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.5, 143.3, 135.8, 135.6, 129.9, 126.3, 117.3.

Ethyl (*E*)-3-(4-vinylphenyl)acrylate (2)



In 100 mL THF, 1.13 g (8.6 mmol) of 4-vinylbenzaldehyde (**1**) and 1.9 mL (9.6 mmol) of triethyl phosphonoacetate were dissolved. While stirring at 0°C under an argon atmosphere, potassium *t*-butoxide (1.13 g, 10.1 mmol) was added portionwise. After overnight stirring at room temperature, water was added to the reaction mixture, which was then extracted with several portions of $CHCl_3$. The combined organic phase was dried over anhydrous $MgSO_4$. After filtration and solvent evaporation, 1.27 g (73%) of crude product was obtained, which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 15.9 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 6.69 (dd, J_1 = 17.7 Hz, J_2 = 10.8 Hz, 1H), 6.41 (d, *J* = 15.9 Hz, 1H), 5.79 (dd, J_1 = 17.5 Hz, J_2 = 0.5 Hz, 1H), 5.30 (d, *J* = 11.4 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.0, 144.1, 139.4, 136.1, 133.9, 128.3, 126.7, 118.0, 115.3, 60.5, 14.4. HR-MS m/z: 203.10659 $[M+H]^+$, calcd $[C_{13}H_{15}O_2]^+$: 203.10666, Δ = 0.3 ppm.

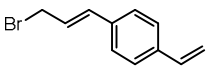
4-vinyl cinnamyl alcohol (3)



A solution of ethyl (*E*)-3-(4-vinylphenyl)acrylate (**2**) (1.27 g, 6.3 mmol) in 15 mL dry, distilled THF was added dropwise to 15 mL of a stirred diisobutylaluminum hydride solution (1 M in THF, 15 mmol) at 0°C under an argon atmosphere. After stirring for an additional 1.5 hours at room temperature, the reaction mixture was again cooled to 0°C and water was carefully added. The resulting suspension was then extracted with several portions of diethyl ether (200 mL in total). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude product was redissolved in DCM and subjected to silica gel column chromatography, using a DCM/ethyl acetate gradient (0% to 1% ethyl acetate) for elution, yielding 430 mg (43%) of a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36

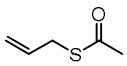
(s, 4H), 6.70 (dd, J_1 = 17.7 Hz, J_2 = 10.8 Hz, 1H), 6.61 (d, J = 18.3 Hz, 1H), 6.37 (dt, J_1 = 15.9 Hz, J_2 = 5.7 Hz, 1H), 5.75 (dd, J_1 = 17.7 Hz, J_2 = 0.6 Hz, 1H), 5.24 (d, J = 10.8 Hz, 1H), 4.34 (dd, J_1 = 5.7 Hz, J_2 = 1.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.0, 136.5, 136.3, 130.7, 128.5, 126.7, 126.5, 113.8, 63.6.

4-vinyl cinnamyl bromide (4)



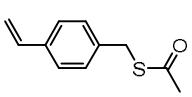
4-vinyl cinnamyl alcohol (**3**) (700 mg, 4.4 mmol) was dissolved in 30 mL of dry, distilled diethyl ether at 0°C under argon. To this, approximately 0.5 mL (5.3 mmol) phosphorus tribromide was added dropwise. After 20 minutes, TLC indicated completion of the reaction, and 10 mL of saturated sodium bicarbonate was added. After a while, additional water was added and the mixture was extracted with DCM several times. The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and the solvents were evaporated, giving approximately 980 mg (> 95%) of a white crystal, which required no further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 8.7 Hz, 2H), 6.63 (d, J = 13.8 Hz, 1H), 6.37 (dd, J_1 = 16.5 Hz, J_2 = 9.9 Hz, 1H), 6.34-6.44 (m, 1H), 5.76 (d, J = 17.7 Hz, 1H), 5.26 (d, J = 10.8 Hz, 1H), 4.17 (d, J = 8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.7, 136.4, 135.3, 134.2, 127.0, 126.6, 125.2, 114.3, 33.7.

***S*-allyl thioacetate (5)**



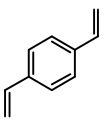
Allyl bromide (0.71 mL, 8.3 mmol) and potassium thioacetate (0.97 g, 8.5 mmol) were added to 50 mL of distilled aceton. The mixture was stirred overnight at room temperature, after which water was added. The aqueous phase was then extracted twice with $CHCl_3$. The combined organic phase was washed once with water and then dried over anhydrous $MgSO_4$. After filtration, removal of the solvents afforded 360 mg (37%) of a yellow oil, which required no purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.74-5.87 (m, 1H), 5.23 (d, J = 20.7 Hz, 1H), 5.10 (d, J = 10.8 Hz, 1H), 3.54 (d, J = 6.9 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.0, 133.1, 117.8, 32.0, 30.5.

_S_-(4-vinylbenzyl) thioacetate (6)



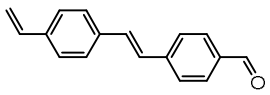
In a mixture of 25 mL aceton and 10 mL methanol, 2.5 mL (17.5 mmol) of 4-vinylbenzyl chloride and 2.6 g (23 mmol) potassium thioacetate were dissolved. The suspension was allowed to stir for approximately 50 hours at room temperature, after which the solvents were removed. The residue was redissolved in 50 mL DCM, which was then filtered. The filtrate was washed once with water and once with brine, prior to drying over anhydrous $MgSO_4$. After filtration, the DCM was evaporated off to yield 2.6 g (77%) of a reddish oil. Although not strictly necessary, the crude product was purified by performing silica gel column chromatography, using PET/DCM (1:1) as eluent, to afford 1.23 g (36%) of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32 (d, J = 6.3 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 6.67 (dd, J_1 = 17.6 Hz, J_2 = 10.9 Hz, 1H), 5.71 (dd, J_1 = 17.6 Hz, J_2 = 0.7 Hz, 1H), 5.21 (dd, J_1 = 11.0 Hz, J_2 = 0.7 Hz, 1H), 4.09 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.1, 137.2, 136.7, 136.4, 129.1, 126.5, 114.0, 33.3, 30.4.

1,4-divinylbenzene (7)



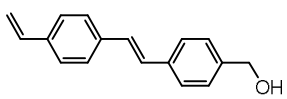
A stirring suspension of methyltriphenylphosphonium bromide (12.2 g, 34 mmol) and terephthalaldehyde (2 g, 15 mmol) in 50 mL THF under argon was cooled to 0°C, after which potassium *t*-butoxide (3.9 g, 35 mmol) was added in small portions. After 30 minutes at 0°C, the reaction mixture was stirred for an additional 1 hour at room temperature. The solvent was subsequently removed *in vacuo* and DCM and silica powder were added to the residue to form a slurry. After drying to the air for several hours, the powder-like substance was poured on top of a silica gel column (PET), and the product – 1.33 g (69%) of a colorless oil – was eluted with PET. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34 (s, 4H), 6.67 (dd, J_1 = 17.7 Hz, J_2 = 10.8 Hz, 2H), 5.72 (dd, J_1 = 17.6 Hz, J_2 = 0.7 Hz, 2H), 5.21 (dd, J_1 = 10.9 Hz, J_2 = 0.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.2, 136.6, 126.5, 113.8.

(*E*)-4-(4-vinylstyryl)benzaldehyde (8)



p-bromobenzaldehyde (2.25 g, 12 mmol), 1,4-divinylbenze (**7**) (1.5 g, 11.5 mmol) and triethylamine (2.5 g, 25 mmol) were added to a round-bottom flask containing 50 mL of dry DMF. The flask was then purged with argon, after which palladium (II) acetate (180 mg, 0.8 mmol) and tri(*o*-tolyl)phosphine (500 mg, 1.6 mmol) were added. The reaction mixture was heated to 80°C and stirred for 24 hours, after which the solvent was removed under reduced pressure and elevated temperature. The residue was again solubilized in DCM, washed with water twice, and directly applied to a silica gel column, eluting with DCM/methanol. The volume of the combined fractions containing the product was reduced, prior to the addition of silica powder. The resulting slurry was dried overnight in a 70°C stove, after which the powder-like substance was poured on top of a silica gel column (PET). A gradient from 100% PET to 100% DCM was used as eluent, providing (*E*)-4-(4-vinylstyryl)benzaldehyde as a light yellow solid (750 mg, 28% - further purification of impure fractions may improve yields). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.98 (s, 1H), 7.88 (d, *J* = 8.1 Hz, 2H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 17.4 Hz, 1H), 7.14 (d, *J* = 16.2 Hz, 1H), 6.73 (dd, J_1 = 17.6 Hz, J_2 = 10.9 Hz, 1H), 5.80 (d, *J* = 17.7 Hz, 1H), 5.29 (d, *J* = 11.1 Hz, 1H). HR-MS m/z: 235.11178 $[M+H]^+$, calcd $[C_{17}H_{15}O]^+$: 235.11174, Δ = 0.2 ppm.

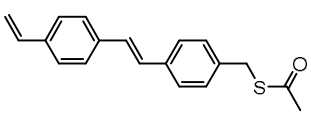
(*E*)-(4-(4-vinylstyryl)phenyl)methanol (9)



(*E*)-4-(4-vinylstyryl)benzaldehyde (**8**) (159 mg, 0.68 mmol) was dissolved in 7.5 mL of dry, distilled THF at 0°C while stirring under an argon atmosphere. A 1 M solution of diisobutylaluminium hydride in THF (1.25 mL, 1.25 mmol) was added dropwise using a syringe. After this addition, the reaction mixture was allowed to warm up to room temperature. After approximately 15 minutes, TLC indicated completion of the reaction, and water was carefully added to the reaction mixture. The aqueous phase was then extracted with DCM several times. The combined DCM layers were dried over $MgSO_4$, filtered and evaporated to provide a (mostly) white solid

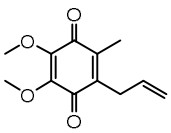
(127 mg, 79%), which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35-7.53 (overlapping m, 8H), 7.09 (s, 2H), 6.72 (dd, J_1 = 17.7 Hz, J_2 = 10.8 Hz, 1H), 5.77 (d, J = 17.4 Hz, 1H), 5.26 (d, J = 10.8 Hz, 1H), 4.71 (s, 2H).

(*E*)-*S*-(4-(4-vinylstyryl)benzyl) thioacetate (10)



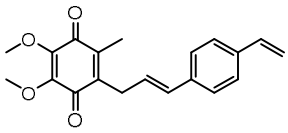
To 10 mL of dry, distilled THF, stirring at 0°C under an argon atmosphere, triphenylphosphine (186 mg, 0.7 mmol) and di-(4-chlorobenzyl)-azodicarboxylate (258 mg, 0.7 mmol) were added. Thioacetic acid (51 µl, 0.72 mmol) and (*E*)-(4-(4-vinylstyryl)phenyl)methanol (**9**) (127 mg, 0.54 mmol) were together dissolved in 5 mL of dry THF and added to the former solution in dropwise fashion. The reaction mixture was stirred at room temperature overnight. Prior to silica gel column chromatography, the precipitate was removed from the reaction mixture by filtration, after which the solvent was evaporated. The crude product was redissolved in $CHCl_3$ and applied to the column (PET). A PET/DCM gradient (1:0 to 1:1) was used to elute the product as a white solid (74 mg, 47%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36-7.45 (overlapping m, 6H), 7.25 (d, J = 8.1 Hz, 2H), 7.04 (s, 2H), 6.69 (dd, J_1 = 17.6 Hz, J_2 = 10.9 Hz, 1H), 5.74 (d, J = 17.7 Hz, 1H), 5.23 (d, J = 11.1 Hz, 1H), 4.10 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.1, 137.1, 137.0, 136.8, 136.5, 136.47, 129.3, 128.4, 128.1, 126.8, 126.75, 126.6, 113.8, 33.3, 30.4. HR-MS m/z: 295.11477 $[M+H]^+$, calcd $[C_{19}H_{19}OS]^+$: 295.11511, Δ = 1.1 ppm.

2-allyl-5,6-dimethoxy-3-methyl-1,4-benzoquinone (11)



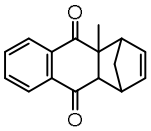
The title compound was prepared according to a 3-step literature procedure [7], except for a slight modification during the allylation reaction: an equimolar amount of 18-crown-6 was added to the reaction mixture as well. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.68-5.81 (m, 1H), 5.06-5.08 (m, 1H), 5.01-5.04 (m, 1H), 4.00 (s, 3H), 3.99 (s, 3H), 3.24 (d, J = 6.0 Hz, 2H), 2.03 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 184.3, 183.5, 144.3, 144.2, 139.7, 133.0, 116.5, 61.0, 30.1, 11.7.

(*E*)-2,3-dimethoxy-5-methyl-6-(3-(4-vinylphenyl)allyl)-1,4-benzoquinone (12)



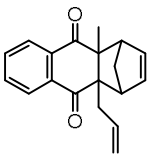
The cycloaddition of cyclopentadiene to 2,3-dimethoxy-5-methyl-1,4-benzoquinone was performed according to a previously described protocol [7]. However, an additional purification step was performed (silica gel column, PET/DCM gradient (3:1 to 1:1)). The resulting Diels-Alder adduct (275 mg, 1.1 mmol) was dissolved in 3 mL dry, distilled THF, together with 18-crown-6 (290 mg, 1.1 mmol), after which the solution was purged with argon and cooled to 0°C. While stirring, potassium *t*-butoxide (185 mg, 1.7 mmol) was added in small portions. A solution of 4-vinyl cinnamyl bromide (**4**) (306 mg, 1.4 mmol) in 3 mL dry THF was added dropwise to the reaction mixture, which was then stirred for 1 hour at 0°C. After stirring for an additional hour at room temperature, water was added. The aqueous phase was then extracted with chloroform several times (150 mL in total). The combined organic layers were dried over $MgSO_4$, filtered and concentrated. The crude product was roughly purified by performing silica gel column chromatography, using a PET/DCM/EtOAc gradient (1:0:0 to 0:1:0 to 0:9:1) to elute the main product (still containing some impurities). After removal of the eluent, the residue was dissolved in 5 mL toluene and stirred for 5 hours at reflux temperature. The crude product was subjected to another round of purification (silica gel column, 100% DCM as eluent) to provide at least 63 mg (18% after 2 steps) of the title compound as a thick orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 6.67 (dd, J_1 = 17.6 Hz, J_2 = 10.9 Hz, 1H), 6.41 (d, *J* = 15.9 Hz, 1H), 6.10 (dt, J_1 = 15.8 Hz, J_2 = 6.7 Hz, 1H), 5.72 (d, *J* = 17.7 Hz, 1H), 5.21 (d, *J* = 11.1 Hz, 1H), 4.00 (s, 3H), 3.99 (s, 3H), 3.38 (d, *J* = 6.6 Hz, 2H), 2.08 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 184.6, 183.9, 144.5, 140.0, 139.8, 136.8, 136.6, 136.5, 131.8, 126.5, 126.4, 124.8, 113.7, 61.3, 29.7, 12.1. HR-MS m/z: 325.14362 $[M+H]^+$, calcd $[C_{20}H_{21}O_4]^+$: 325.14344, Δ = 0.6 ppm.

4a-methyl-1,4,4a,9a-tetrahydro-1,4-methanoanthracene-9,10-dione (13)



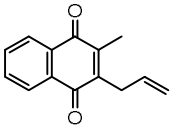
Freshly distilled cyclopentadiene (11 mL, 131 mmol) and menadione (15 g, 87 mmol) were added to a 1:1 mixture of glacial acetic acid and dry chloroform. After 50 hours of stirring at room temperature, 5 M NaOH was added at 0°C until a basic pH was achieved. The mixture was extracted with chloroform several times (250 mL in total). The combined organic phase was washed with water and brine, dried over $MgSO_4$ and concentrated *in vacuo* to provide 16 mL of a yellow oil, 2.5 mL of which was applied to a silica gel column (PET). Elution using a PET/DCM gradient (1:0 to 2:1) afforded the product as a light yellow solid (1.04 g, 32%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02-8.06 (m, 2H), 7.67-7.78 (m, 2H), 6.09-6.12 (m, 1H), 5.90-5.93 (m, 1H), 3.55 (m, 1H), 3.22 (m, 1H), 3.06 (d, *J* = 3.9 Hz, 1H), 1.76-1.79 (m, 1H), 1.56-1.59 (m, 1H), 1.56 (s, 3H).

4a-allyl-9a-methyl-1,4,4a,9a-tetrahydro-1,4-methanoanthracene-9,10-dione (14)



In 3 mL dry, distilled THF, stirring at 0°C under argon, 250 mg of compound **13** (1.05 mmol) was dissolved. Potassium *t*-butoxide (176 mg, 1.6 mmol) was then added in small portions as well, followed by dropwise addition of a solution of allyl bromide (136 µl, 1.6 mmol) in 3 mL dry THF. The reaction mixture was stirred at 0°C for 2 hours. The subsequent workup and (crude) purification were performed as described for compound **12**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88-7.97 (m, 2H), 7.64-7.72 (m, 2H), 6.06-6.07 (m, 2H), 5.60-5.71 (m, 1H), 4.95-5.05 (m, 2H), 3.24-3.26 (m, 1H), 3.15-3.16 (m, 1H), 2.78-2.85 (m, 1H), 2.54-2.62 (m, 1H), 1.88-1.91 (m, 1H), 1.58 (s, 3H), 1.48-1.53 (m, 1H).

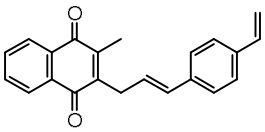
2-allyl-3-methyl-1,4-naphthoquinone (15)



The (crude) compound **14** was dissolved in 3 mL toluene and stirred for 4 hours at reflux temperature. The crude product was purified by silica gel column chromatography,

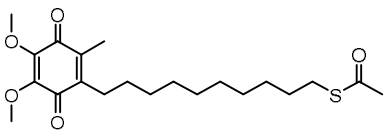
using 100% DCM as eluent, which afforded 100 mg (45% yield over two steps) of the title compound as a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05-8.09 (m, 2H), 7.67-7.73 (m, 2H), 5.77-5.90 (m, 1H), 5.05-5.14 (m, 2H), 3.42 (d, *J* = 6.3 Hz, 2H), 2.20 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 185.3, 184.3, 144.4, 144.3, 133.54, 133.5, 133.3, 132.2, 132.1, 126.5, 126.4, 116.7, 31.0, 12.7. HR-MS m/z: 213.09099 $[M+H]^+$, calcd $[C_{14}H_{13}O_2]^+$: 213.09101, Δ = 0.1 ppm.

(*E*)-2-methyl-3-(3-(4-vinylphenyl)allyl)-1,4-naphthoquinone (16)



The synthesis of compound **16** was performed as described for compound **14** and **15**, using 500 mg of **13** (2.1 mmol), 350 mg potassium *t*-butoxide (3.1 mmol), 500 mg (2.3 mmol) 4-vinyl cinnamyl bromide (**4**) and 420 mg (1.6 mmol) 18-crown-6 in 5 mL dry THF instead. After a crude purification, the retro-Diels-Alder reaction was performed according to **15**, yielding, after another round of purification (silica gel column, 100% DCM as eluent), 53 mg (8% yield over two steps) of an orange/yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04-8.11 (m, 2H), 7.65-7.71 (m, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 14.1 Hz, 2H), 6.65 (dd, J_1 = 17.6 Hz, J_2 = 10.9 Hz, 1H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.18 (dt, J_1 = 15.9 Hz, J_2 = 6.7 Hz, 1H), 5.70 (d, *J* = 17.4 Hz, 1H), 5.19 (d, *J* = 11.1 Hz, 1H), 3.55 (d, *J* = 6.9 Hz, 2H), 2.24 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 185.3, 184.4, 144.3, 144.2, 136.7, 136.6, 136.5, 133.6, 132.2, 132.1, 131.7, 126.5, 126.4, 125.0, 113.7, 30.4. HR-MS m/z: 315.13786 $[M+H]^+$, calcd $[C_{22}H_{19}O_2]^+$: 315.13796, Δ = 0.3 ppm.

***S*-(10-(4,5-dimethoxy-2-methyl-3,6-benzoquinone-1-yl)decyl) thioacetate (U_{SAT})**



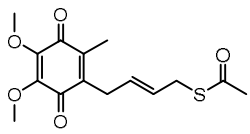
To 10 mL of dry, distilled THF, stirring at 0°C under argon, triphenylphosphine (242 mg, 0.9 mmol) and di-(4-chlorobenzyl)-azodicarboxylate (339 mg, 0.9 mmol) were added. Thioacetic acid (66 µl, 0.9 mmol) and idebenone (250 mg, 0.7 mmol) were together dissolved in 10 mL of dry THF and added

to the former solution in a dropwise fashion. The reaction mixture was stirred at room temperature overnight, after which the solvent was evaporated. The residue was taken up in $CHCl_3$ and directly applied to a silica gel column (PET). A PET/DCM/EtOAc gradient (1:0:0 to 0:1:0 to 0:98:2) was used to elute the product (9) as an orange oil (200 mg, 74%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.00 (s, 3H), 3.99 (s, 3H), 2.86 (t, *J* = 7.3 Hz, 2H), 2.45 (t, *J* = 7.2 Hz, 2H), 2.32 (s, 3H), 2.01 (s, 3H), 1.51-1.61 (m, 2H), 1.28-1.45 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.8, 184.5, 184.0, 144.2, 142.9, 138.5, 61.0, 30.5, 29.7, 29.4, 29.3, 29.2, 29.0, 28,97, 28.7, 28.6, 26.3, 11.8. HR-MS m/z: 397.20387 $[M+H]^+$, calcd $[C_{21}H_{33}O_5S]^+$: 397.20432, Δ = 1.1 ppm.

General procedure for wire synthesis

Compounds **U_0** through **U_3** and **M_0** through **M_3** were synthesized by means of Grubbs olefin cross metathesis. The general procedure was as follows: in 3-5 mL of dry, distilled DCM, stirring under argon at room temperature, the appropriate quinone derivative (**11**, **12**, **15** or **16**) was dissolved, together with the appropriate thioacetate (**5**, **6** or **10**). The reaction mixture was purged with argon for an additional 10 minutes, after which 10 mg of Grubbs catalyst 2nd generation was added. The reaction was stirred under argon at room temperature overnight, after which the mixture was concentrated and subjected to silica gel column chromatography (typically using a PET/DCM gradient, in case of **U_0**-**U_3** a maximum of 2.5% EtOAc was also added to the DCM) at least twice, resulting in relatively low yields.

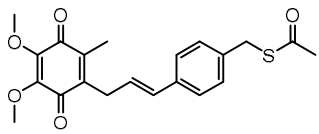
(*E*)-*S*-(4-(4,5-dimethoxy-2-methyl-3,6-benzoquinone-1-yl)but-2-en-1-yl) thioacetate (U_0)



Using the general procedure outlined above, compound **11** (62 mg, 0.3 mmol) and **5** (150 mg, 1.3 mmol) were reacted, providing 25 mg (29%) of **U_0** as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.42-5.57 (m, 2H), 4.00 (s, 3H), 3.99 (s, 3H), 3.47 (d, *J* = 6.3 Hz, 2H), 3.19 (d, *J* = 6.0 Hz, 2H), 2.32 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.3, 184.6, 183.7, 144.5, 144.4, 139.9, 139.8, 128.9, 127.2, 61.4, 31.1, 30.6, 29.0,

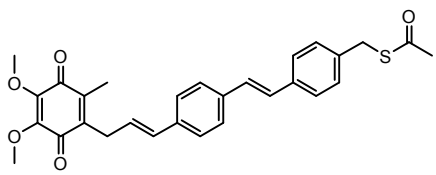
12.0. HR-MS m/z: 311.09432 $[M+H]^+$, calcd $[C_{15}H_{19}O_5S]^+$: 311.09477, Δ = 1.4 ppm.

(*E*)-*S*-(4-(3-(4,5-dimethoxy-2-methyl-3,6-benzoquinone-1-yl)prop-1-en-1-yl)benzyl) thioacetate (U_1)



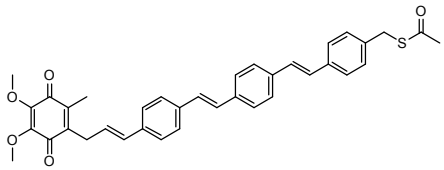
Using the general procedure outlined above, compound **11** (35 mg, 0.16 mmol) and **6** (75 mg, 0.4 mmol) were reacted, providing 10 mg (16%) of $\mathbf{U_1}$ as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.40 (d, *J* = 15.9 Hz, 1H), 6.07 (dt, J_1 = 15.8 Hz, J_2 = 6.8 Hz, 1H), 4.08 (s, 2H), 4.01 (s, 3H), 3.99 (s, 3H), 3.38 (d, *J* = 6.6 Hz, 2H), 2.33 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.3, 184.7, 183.9, 144.53, 144.5, 140.0, 139.8, 136.9, 136.2, 131.7, 129.2, 126.5, 125.0, 61.4, 33.3, 30.5, 29.7, 12.1. HR-MS m/z: 387.12613 $[M+H]^+$, calcd $[C_{21}H_{23}O_5S]^+$: 387.12607, Δ = 0.2 ppm.

***S*-(4-((*E*)-4-((*E*)-3-(4,5-dimethoxy-2-methyl-3,6-benzoquinone-1-yl)prop-1-en-1-yl)styryl)benzyl) thioacetate (U_2)**



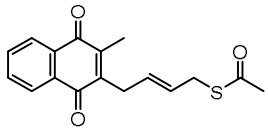
Using the general procedure outlined above, compound **12** (48 mg, 0.15 mmol) and **6** (28 mg, 0.15 mmol) were reacted, providing 7 mg (10%) of $\mathbf{U_2}$ as an orange solid. ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 7.44 (d, *J* = 8.3 Hz, 4H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.07 (s, 2H), 6.42 (d, *J* = 15.9 Hz, 1H), 6.15 (dt, J_1 = 15.8 Hz, J_2 = 6.6 Hz, 1H), 4.11 (s, 2H), 3.98 (s, 3H), 3.96 (s, 3H), 3.39 (d, *J* = 6.6 Hz, 2H), 2.34 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 184.7, 183.9, 140.1, 139.9, 137.1, 136.6, 136.5, 131.9, 129.3, 128.5, 128.1, 126.9, 126.6, 124.9, 61.4, 33.4, 30.5, 29.8, 12.2. HR-MS m/z: 489.17240 $[M+H]^+$, calcd $[C_{29}H_{29}O_5S]^+$: 489.17302, Δ = 1.3 ppm.

***S*-(4-((*E*)-4-((*E*)-4-((*E*)-3-(4,5-dimethoxy-2-methyl-3,6-benzoquinone-1-yl)prop-1-en-1-yl)styryl)styryl)benzyl) thioacetate (U_3)**



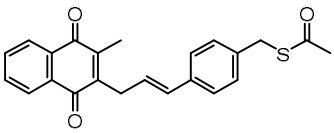
Using the general procedure outlined above, compound **12** (41 mg, 0.13 mmol) and **10** (45 mg, 0.15 mmol) were reacted, providing 6 mg (8%) of $\mathbf{U_3}$ as an orange solid. ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 7.53 (s, 4H), 7.48 (d, *J* = 8.1 Hz, 4H), 7.34 (d, *J* = 8.7 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.12 (s, 4H), 6.43 (d, *J* = 15.9 Hz, 1H), 6.17 (dt, J_1 = 15.8 Hz, J_2 = 6.6 Hz, 1H), 4.13 (s, 2H), 3.99 (s, 3H), 3.97 (s, 3H), 3.40 (d, *J* = 6.3 Hz, 2H), 2.35 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.0, 139.8, 137.2, 136.9, 136.7, 136.6, 136.5, 131.9, 129.4, 128.5, 128.3, 128.2, 127.0, 126.96, 126.88, 126.85, 126.6, 124.9, 61.4, 33.4, 30.5, 29.8, 12.2. HR-MS m/z: 591.21959 $[M+H]^+$, calcd $[C_{37}H_{35}O_5S]^+$: 591.21997, Δ = 0.6 ppm.

(*E*)-*S*-(4-(3-methyl-1,4-naphthoquinone-2-yl)but-2-en-1-yl) thioacetate (M_0)



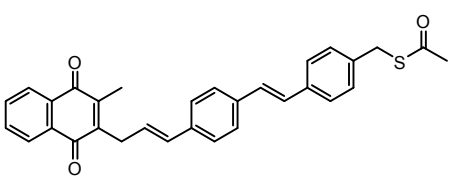
Using the general procedure outlined above, compound **15** (33 mg, 0.16 mmol) and **5** (40 mg, 0.35 mmol) were reacted, providing 10 mg (21%) of $\mathbf{M_0}$ as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09-8.12 (m, 2H), 7.72-7.78 (m, 2H), 5.52-5.75 (m, 2H), 3.52 (d, *J* = 7.2 Hz, 2H), 3.42 (d, *J* = 6.3 Hz, 2H), 2.35 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.3, 185.4, 184.4, 144.4, 144.3, 133.6, 132.3, 132.2, 128.8, 127.3, 126.5, 126.4, 31.2, 30.6, 29.7, 12.8. HR-MS m/z: 301.08927 $[M+H]^+$, calcd $[C_{17}H_{17}O_3S]^+$: 301.08929, Δ = 0.1 ppm.

(*E*)-*S*-(4-(3-(3-methyl-1,4-naphthoquinone-2-yl)prop-1-en-1-yl)benzyl) thioacetate (M_1)



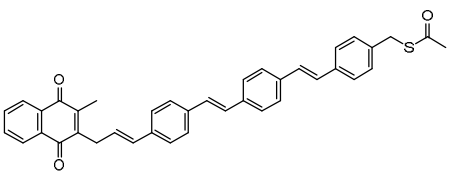
Using the general procedure outlined above, compound **15** (33 mg, 0.16 mmol) and **6** (60 mg, 0.31 mmol) were reacted, providing 2 mg (3%) of $\mathbf{M_1}$ as a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07-8.12 (m, 2H), 7.69-7.74 (m, 2H), 7.25 (d, *J* = 9.3 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.17 (dt, J_1 = 15.8 Hz, J_2 = 6.7 Hz, 1H), 4.07 (s, 2H), 3.56 (d, *J* = 6.6 Hz, 2H), 2.33 (s, 3H), 2.25 (s, 3H). HR-MS m/z: 377.12055 $[M+H]^+$, calcd $[C_{23}H_{21}O_3S]^+$: 377.12059, Δ = 0.1 ppm.

***S*-(4-((*E*)-4-((*E*)-3-(3-methyl-1,4-naphthoquinone-2-yl)prop-1-en-1-yl)styryl)benzyl) thioacetate (M_2)**



Using the general procedure outlined above, compound **16** (20 mg, 0.06 mmol) and **6** (18 mg, 0.09 mmol) were reacted, providing 3 mg (10%) of $\mathbf{M_2}$ as a yellow solid. ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 8.06-8.11 (m, 2H), 7.71-7.74 (m, 2H), 7.44 (d, *J* = 8.3 Hz, 4H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.06 (s, 2H), 6.48 (d, *J* = 15.9 Hz, 1H), 6.25 (dt, J_1 = 15.8 Hz, J_2 = 6.6 Hz, 1H), 4.10 (s, 2H), 3.58 (d, *J* = 6.8 Hz, 2H), 2.34 (s, 3H), 2.25 (s, 3H). HR-MS m/z: 479.16718 $[M+H]^+$, calcd $[C_{31}H_{27}O_3S]^+$: 479.16754, Δ = 0.8 ppm.

***S*-(4-((*E*)-4-((*E*)-4-((*E*)-3-(3-methyl-1,4-naphthoquinone-2-yl)prop-1-en-1-yl)styryl)styryl)benzyl) thioacetate (M_3)**



Using the general procedure outlined above, compound **16** (20 mg, 0.06 mmol) and **10** (20 mg, 0.07 mmol) were reacted, providing at least 2 mg (5%) of $\mathbf{M_3}$ as a yellow solid. ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 8.05-8.12 (m, 2H), 7.70-7.75 (m, 2H), 7.51 (s, 4H), 7.43-7.54 (m, 4H), 7.28-7.34 (m, 4H), 7.11 (s, 4H), 6.49 (d, *J* =

16.8 Hz, 1H), 6.21-6.30 (m, 1H), 4.11 (s, 2H), 3.58 (d, *J* = 6.3 Hz, 2H), 2.34 (s, 3H), 2.25 (s, 3H). HR-MS m/z: 581.21427 $[M+H]^+$, calcd $[C_{39}H_{33}O_3S]^+$: 581.21449, Δ = 0.4 ppm.

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