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The Diels-Alder reaction of 1,4-quinones in hexafluoroisopropanol

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We dedicate this work to Professor Léon Ghosez, an inspiring mentor, in recognition of his important contributions to organic synthesis

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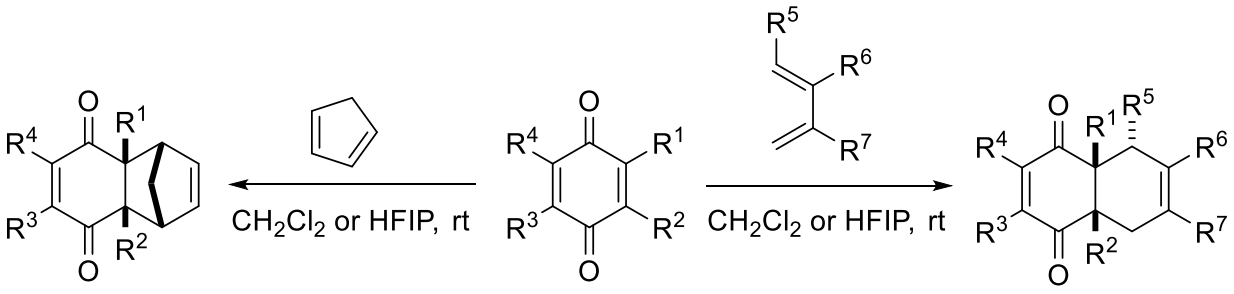
Abstract

The Diels-Alder reaction of quinones is both of historical and current importance, and numerous asymmetric and catalytic versions have been described. Herein we describe the dramatic rate enhancement observed in the Diels-Alder reactions of a large variety of quinones with moderately activated dienes when hexafluoroisopropanol is used as a solvent, even allowing reactions that are not observed in dichloromethane. When chiral sulfinylquinones are used, hexafluoroisopropanol has a marked effect on stereoselectivity. Since the Diels-Alder reactions of sulfinylquinones are known to be an entry into several classes of natural products, and many other quinone cycloadditions have found wide-spread use in synthesis, the findings described will further facilitate their application.



Keywords: Diels-Alder reaction, quinones, hexafluoroisopropanol, sulfinylquinones, asymmetric synthesis.

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Introduction

The ability of the Diels-Alder [4+2]-cycloaddition to generate molecular complexity rapidly *via* the simultaneous formation of two carbon-carbon bonds in chemo-, regio- and stereoselective manner is almost unrivalled, and is illustrated by the numerous reported applications of this reaction for the preparation of six-membered rings, including natural products. Historically, the use of quinones as dienophiles is highly significant, being the very first example investigated by Diels and Alder.[1] 1,4-Benzoquinone and various quinone derivatives have been used in numerous well-known syntheses of natural products.[1,2] In addition to their electron-deficient nature, which leads them to react with electron-rich or electron-neutral dienes, 1,4-quinones incorporate functional groups which can be transformed after the Diels–Alder reaction,[2] and therefore facilitate the synthesis of complex molecules.[3-8] Controlling the regioselectivity of cycloadditions with quinones is an essential task *en route* to the synthesis of these targets.[1] Lewis[3] and Brønsted[8] acid catalysts are known to improve the regioselectivity of cycloadditions with unsymmetrical quinones by coordination (or protonation) with the least sterically hindered or the most basic carbonyl group of the quinones.[7] Some asymmetric catalysts have been reported to promote highly enantio- and regioselective reactions with quinones.[9-11] The regioselectivity of the Diels–Alder reaction can also be controlled by remote substituents in benzo-, naphtho- and 1,4-phenanthrenequinones.[5,8,12,13] In those cases, Lewis acid catalysts are also used to improve the regioselectivity. The introduction of Cl or Br atoms (X) at the quinone's dienophilic double bond has been used with the double aim of controlling regioselectivity and recovering the quinone skeleton after the cycloaddition by elimination of HX.[14] Sulfoxides[15,16] and boronic acids[8] have also been used to this end. With enantiomerically pure sulfinylquinones, we have reached excellent regio- and stereochemical control in the cycloadditions, *en route* to salvinorin A.[17,18] The group of C. Carreño successfully applied this strategy to the synthesis of a number of complex molecules.[19-21]

Solvents play a crucial role in Diels-Alder reactions. They greatly influence the reaction rates, the regioselectivity as well as the *endo/exo* selectivity of cycloadditions.[22-25] Solvents with a high hydrogen-bond-donating (HBD) ability, namely fluorinated alcohols, lead to selectivities that are comparable to those obtained when Lewis acids are used as catalysts.[26] In fact, 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) is widely used as a reaction medium since it is a strong hydrogen bonding donor, but a weak acceptor and nucleophile. It has been shown to accelerate a variety of transformations,[27-31] and has emerged as a remarkable solvent for [4 + 2] cycloaddition reactions.[23,32-34]

To our knowledge, only few examples have been reported in which HFIP facilitates a cycloaddition using 1,4-quinones,[32,35] among which one describes exclusive *endo*- and very high regioselectivity.[32,36]

Results and Discussion

In the context of a total synthesis, we set out to explore the reactivity of sulfinylquinone **1a**, which had already been shown to be a convenient chiral starting material for the enantioselective synthesis of terpene natural products, towards moderately reactive dienes (Figure 1).[18]

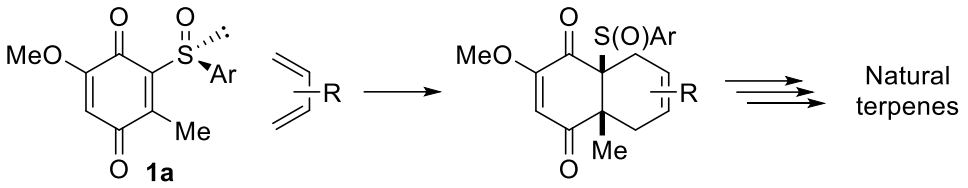
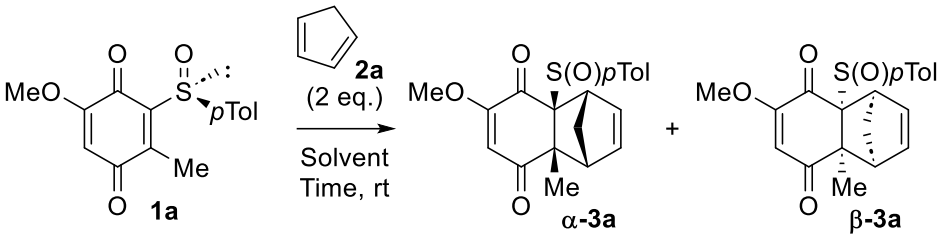


Figure 1. General strategy towards the synthesis of natural products.

We screened a variety of solvents in order to determine the optimal conditions in terms of reaction rate and stereoselectivity (Table 1). This screening is similar to the one performed by Carreño's group on a less substituted sulfinylquinone.[37]

Table 1. Time, conversions, yields and products ratios for the Diels-Alder reaction between sulfinylquinone **1a** and cyclopentadiene **2a** in different solvents at room temperature



Entry	Solvent	Time	Conversion[a] (%)	α:β[b]	Isolated Yield (%)
1	Benzene	10d	80	21:79	—
2	$CHCl_3$	5d	Quant.	32:68	74
3	CH_2Cl_2	5d	Quant.	35:65	78
4	THF	18h	Quant.	—	—
5	Acetone	5d	Quant.	28:72	69
6	DMF	26h	Quant.	—	—
7	MeCN	5d	Quant.	30:70	70
8	DMSO	10h	Quant.	—	—
9	AcOH	2d	Quant.	64:36	75
10	HFIP	35 min	Quant.	88:12	66
11	EtOH	3d	Quant.	42:58	85
12	H_2O	5d	Quant.	93:7	86

[a]Based on the ^{1}H NMR ratio of the starting material and the products. [b]Based on the ^{1}H NMR ratio of the products.

The first trials were run in aprotic solvents and the major cycloadduct was **β-3a**, corresponding to an approach of the diene **2a** on the C3-*Si* face of the sulfinylquinone. The best stereoselectivity was observed in benzene (entry 1). More polar aprotic solvents gave less good stereoselectivities (entries 2, 3, 5 and 7).

On the other hand, when protic solvents were used (entries 9-12), the major isomer was the α-adduct (with the exception of ethanol, entry 11). This inversion of selectivity was also accompanied by a decrease of the reaction time. This phenomenon had been described in Carreño's work.[37] Although they insisted on the

importance of the solvent polarity, we hypothesized that the hydrogen bond between the solvent and the dienophile best explains this change of selectivity. The stronger a hydrogen bond donor the solvent is, the better the selectivity towards **α-3a** and the lower the reaction times. Among those results, we noticed that HFIP and water gave the highest diastereoselectivities (entries 10 and 12). Even though water gave the best selectivity, HFIP offered both a good selectivity and a very high reaction rate compared to the other solvents.

Among the screened solvents, THF, DMF, and DMSO (entries 4, 6, and 8) did not afford the expected cycloadducts but gave rise to the formation of addition products whose structure is so far elusive.

Given the remarkable results obtained in HFIP, we decided to further study its use as a solvent in Diels-Alder reaction of other quinones.

Study of the influence of HFIP as solvent on the reaction rate and selectivity of Diels-Alder reactions

In order to assess the effect of HFIP in those cycloadditions, differently substituted quinones (Figure 2) were engaged in Diels-Alder reactions.

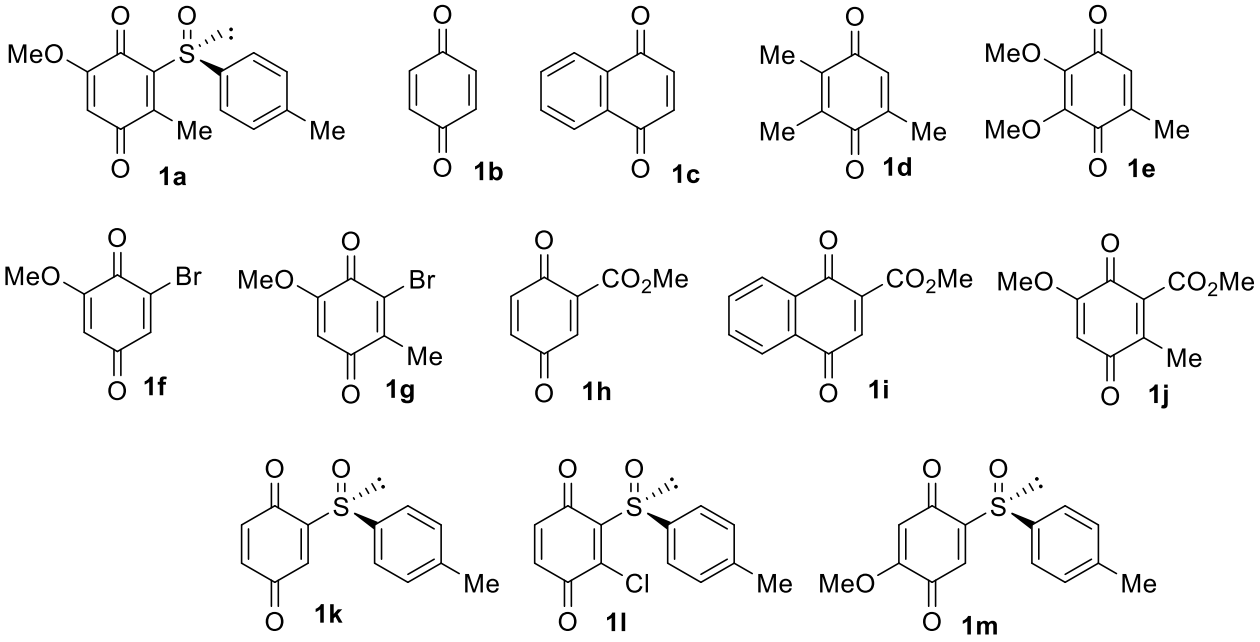
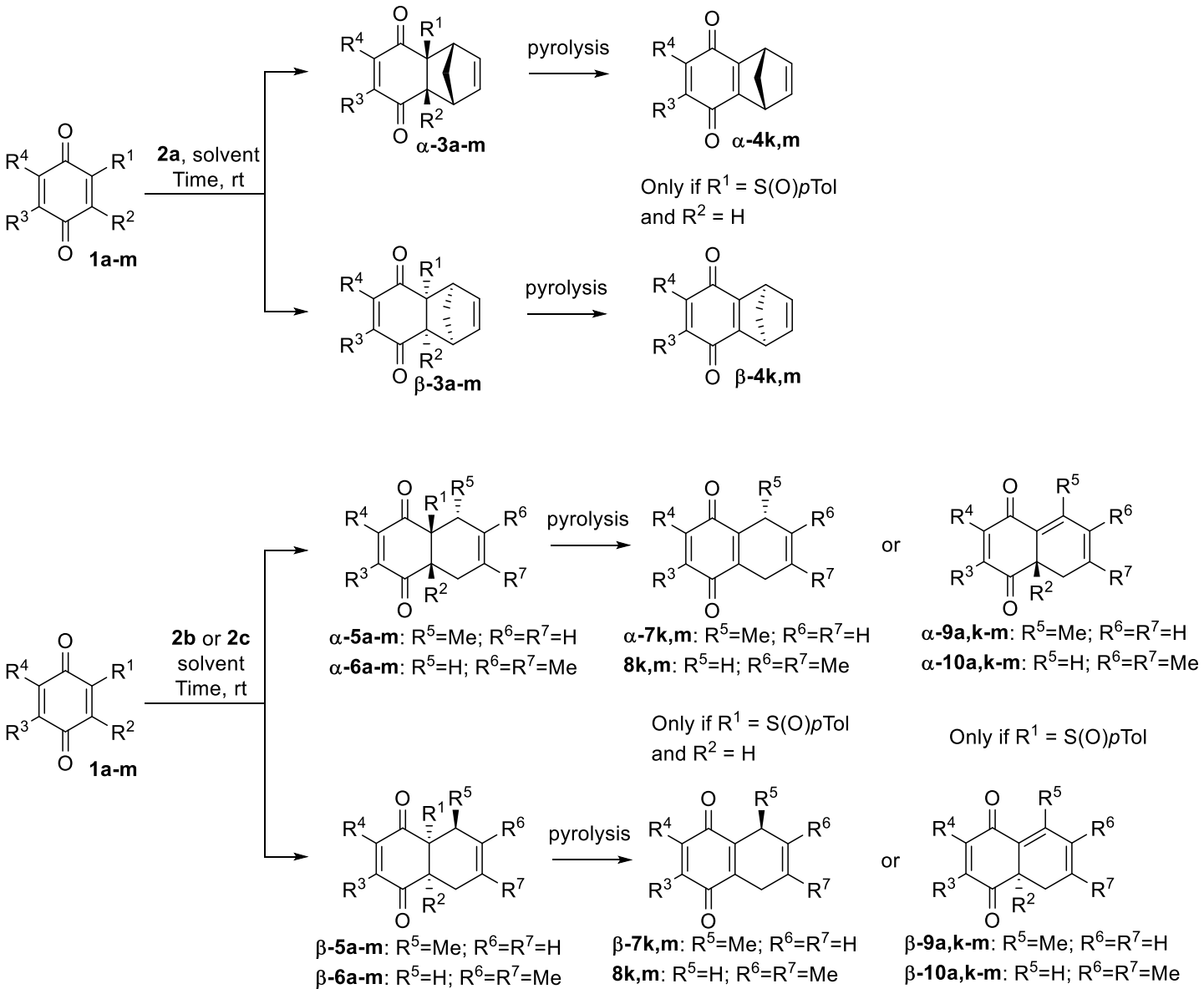


Figure 2. Structures of the quinones studied in this work.

We planned to make these quinones react with three different model dienes (cyclopentadiene **2a**, piperylene (penta-1,3-diene) **2b**, and 2,3-dimethybutadiene **2c**) in both dichloromethane and HFIP. The different expected products are presented in Scheme 1.



Scheme 1. Diels-Alder reactions between quinones **1a-l** and dienes **2a-c** and cycloadducts thereof. Presentation of the possible products with sulfinylquinones **1a,k-m**.

In the case of the quinones **1b-j**, standard *endo*-selective Diels-Alder reactions are expected. However, when a sulfoxide is present in R^1 (**1a,k-m**), a sulfoxide elimination can occur after the cycloaddition. Indeed, some of the sulfinyl-containing cycloadducts are not stable at room temperature and may undergo a β-*syn* elimination if a hydrogen atom is properly placed on the same face as the sulfoxide moiety. The results obtained with quinones **1b-g** are presented in Table 2.

At first glance, it can be noted that the use of HFIP greatly decreased the reaction time for every reaction compared to the ones run in dichloromethane (from days to hours or minutes in some of the cases). The use of HFIP allowed for rather hindered quinones to reach a total conversion, as opposed to partial conversions (entries 11, 13, 15, 21, and 29) or total absence of reaction (entries 17, 23, and 27) observed in dichloromethane. However, the reaction of quinone **1g** with diene **2c** (entry 32), two very hindered partners, never reached completion, even in HFIP.

Table 2. Reaction times, products, conversions and yields for the Diels-Alder reactions between quinones **1b-g** and dienes **2a-c** (equivalents of diene in parentheses) in dichloromethane and HFIP at room temperature

Entry	Quinone	Diene (eq.)	Solvent	Time	Products	Conversion[a] (%)	Isolated yield (%)
1	**1b**	**2a** (2)	CH_2Cl_2	30 min	**3b**	Quant.	94
2	**1b**	**2a** (1)	HFIP	< 1 min	**3b**	Quant.	>98
3	**1b**	**2b** (2)	CH_2Cl_2	6 d	**5b**	Quant.	92
4	**1b**	**2b** (2)	HFIP	< 1 min	**5b**	Quant.	97
5	**1b**	**2c** (2)	CH_2Cl_2	8 d	**6b**	Quant.	80
6	**1b**	**2c** (2)	HFIP	5 min	**6b**	Quant.	96
7	**1c**	**2a** (2)	CH_2Cl_2	3h	**3c**	Quant.	93
8	**1c**	**2a** (2)	HFIP	< 1 min	**3c**	Quant.	>98
9	**1c**	**2b** (2)	CH_2Cl_2	14 d	**5c**	Quant.	>98
10	**1c**	**2b** (2)	HFIP	30 min	**5c**	Quant.	>98
11	**1c**	**2c** (2)	CH_2Cl_2	>15 d	**6c**	68	59
12	**1c**	**2c** (2)	HFIP	40 min	**6c**	Quant.	95
13	**1d**	**2a** (2)	CH_2Cl_2	>15 d	**3d**	68	60
14	**1d**	**2a** (2)	HFIP	2 h	**3d**	Quant.	>98
15	**1d**	**2b** (2)	CH_2Cl_2	>15 d	**5d**	40	31
16	**1d**	**2b** (2)	HFIP	31 h	**5d**	Quant.	>98
17	**1d**	**2c** (2)	CH_2Cl_2	>15 d	—	0	—
18	**1d**	**2c** (2)	HFIP	35h	**6d**	Quant.	>98
19	**1e**	**2a** (2)	CH_2Cl_2	10 d	**3e**	Quant.	98
20	**1e**	**2a** (2)	HFIP	1 h	**3e**	Quant.	>98
21	**1e**	**2b** (2)	CH_2Cl_2	>15 d	**5e**	35	23
22	**1e**	**2b** (2)	HFIP	19h	**5e**	Quant.	95
23	**1e**	**2c** (2)	CH_2Cl_2	>15d	—	0	—
24	**1e**	**2c** (2)	HFIP	24h	**6e**	Quant.	70
25	**1f**	**2a** (2)	CH_2Cl_2	2h	**3f**	Quant.	>98
26	**1f**	**2a** (2)	HFIP	< 1min	**3f**	Quant.	>98
27	**1g**	**2a** (2)	CH_2Cl_2	>15 d	—	0	—
28	**1g**	**2a** (2)	HFIP	22h	**3g**	Quant.	>98
29	**1g**	**2b** (2)	CH_2Cl_2	>15 d	**5g**	13	—
30	**1g**	**2b** (2)	HFIP	20h	**5g**	Quant.	>98
31	**1g**	**2c** (2)	CH_2Cl_2	>15d	—	0	—
32	**1g**	**2c** (2)	HFIP	>15d	**6g**	55	36

[a]Based on the ^{1}H NMR ratio of the starting material and the products in the crude mixture.

Unsurprisingly, the substituents on the quinone substrates greatly influence their reactivity. Compared to 1,4-benzoquinone **1b**, the addition of methyl or methoxy groups (**1d**-**g**) decreases the reaction rate due to both their electron-donating character and steric hindrance. Both are known to be major factors in Diels-Alder reactions.

On the other hand, when electron withdrawing groups are added (**1h-j**), the reactivity of the quinone is generally strongly increased (Table 3). For example, when quinone **1h** reacts with cyclopentadiene, the reaction is complete within a minute, even in dichloromethane.

Table 3. Reaction times, products, conversions and yields for the Diels-Alder reactions between quinones **1h-j** and dienes **2a-c** (equivalents of diene in parentheses) in dichloromethane and HFIP at room temperature

Entry	Quinone	Diene (eq.)	Solvent	Time	Products	Conversion[a] (%)	Isolated yield (%)
1	**1h**	**2a** (2)	CH_2Cl_2	<1 min	**3h**	Quant.	88
2	**1h**	**2a** (2)	HFIP	<1 min	**3h**	Quant.	92
3	**1h**	**2b** (2)	CH_2Cl_2	1h	**5h**	Quant.	>98
4	**1h**	**2b** (2)	HFIP	<1 min	**5h**	Quant.	>98
5	**1h**	**2c** (2)	CH_2Cl_2	100 min	**6h**	Quant.	>98
6	**1h**	**2c** (2)	HFIP	<1 min	**6h**	Quant.	98
7	**1i**	**2a** (2)	CH_2Cl_2	10 min	**3i**	Quant.	95
8	**1i**	**2a** (2)	HFIP	<1 min	**3i**	Quant.	97
9	**1i**	**2b** (2)	CH_2Cl_2	6h	**5i**	Quant.	>98
10	**1i**	**2b** (2)	HFIP	<1 min	**5i**	Quant.	>98
11	**1i**	**2c** (2)	CH_2Cl_2	18h	**6i**	Quant.	>98
12	**1i**	**2c** (2)	HFIP	<1 min	**6i**	Quant.	>98
13	**1j**	**2a** (2)	CH_2Cl_2	15 d	**3j**	Quant.	85
14	**1j**	**2a** (2)	HFIP	7h	**3j**	Quant.	82
15	**1j**	**2b** (2)	HFIP	8h	**5j**	Quant.	79
16	**1j**	**2c** (2)	HFIP	14h	**6j**	Quant.	82

[a]Based on the ^{1}H NMR ratio of the starting material and the products in the crude mixture

However, in that series, one example that caught our attention was the reactivity of quinone **1j** (entries 13-16). It is the only case showing different double bond selectivities between the reaction run in dichloromethane and in HFIP with dienes **2b** and **2c**, but gave the same expected cycloadduct with cyclopentadiene (**2a**). Both unexpected products are presented in Table 5 and will be discussed in the next section.

In the case of sulfinylquinones **1a,k-m** (**Table 4**), the relationship between their structure and their reactivity is less obvious as they possess a rather bulky electron-withdrawing group. The main factor in those cases seems to be steric hindrance, as less substituted sulfinylquinones (**1k,l**) react rapidly (less than 24h with every diene) while **1a** needs days to achieve complete conversion in CH_2Cl_2. The reactivity of **1k**, **1l** and **1a** in dichloromethane was already known[37-40] and we compared those results to the ones in HFIP. For the cycloadditions involving quinones **1a** and **1k**, in dichloromethane, the β-adduct (either followed by the sulfoxide elimination or not) was the major one for all three dienes, when the latter reacted on the expected double bond (entries 1, 3, 5, and 7). A model explaining that selectivity with sulfinylquinones (invoking a specific orientation of the sulfinyl moiety, blocking one face or the other) had already been proposed by Carreño's group[41] and supported by Hanquet's group.[17] When the solvent is replaced by HFIP, with cyclopentadiene, the selectivity is inverted towards the α-adduct (entry 2).

Table 4. Reaction times, products, conversions, selectivities and yields for the Diels-Alder reactions between sulfinylquinones **1a,k,m** and dienes **2a-c** (equivalents of diene in parentheses) in dichloromethane and HFIP at room temperature

Entry	Quinone	Diene (eq.)	Solvent	Time	Products	Conv.[a] (%)	α:β ratio	Isolated yield (%)
1	**1a**	**2a** (2)	CH_2Cl_2	5d	**3a**	Quant.	35:65	93
2	**1a**	**2a** (2)	HFIP	35 min	**3a**	Quant.	88:12	66
3[17]	**1a**	**2b** (2)	CH_2Cl_2	10d	**9a**	Quant.	<2:98<	90
4	**1a**	**2b** (2)	HFIP	2h	**9a**	Quant.	<5:95<[b]	79
5[17]	**1a**	**2c** (2)	CH_2Cl_2	12d	**α-10a** + **β-6a**	Quant.	10:90	81
6	**1a**	**2c** (2)	HFIP	24h	**α-10a** + **β-6a**	Quant.	12:88[c]	81
7[39]	**1k**	**2b** (1)	CH_2Cl_2	20h	**7k**	Quant.	<3:97<	71
8	**1k**	**2b** (1)	HFIP	5 min	—	Quant.	—	—[d]
9	**1m**	**2a** (2)	CH_2Cl_2	20 min	**4m**	Quant.	<5:95<[b,e]	36
10	**1m**	**2a** (2)	HFIP	<1 min	**4m**	Quant.	>95:5>[b,e]	46
11	**1m**	**2b** (2)	CH_2Cl_2	16 h	**7m**	Quant.	α << β[e,f]	59
12	**1m**	**2b** (2)	HFIP	3 min	**7m**	Quant.	α < β[e,f]	63

[a]Based on the ^{1}H NMR ratio of the starting material and the products in the crude mixture. [b]Based on the ^{1}H NMR ratio of the adducts still containing the sulfoxide in the crude mixture. [c]Based on the ^{1}H NMR ratio of the α-adduct and the β-adduct (that underwent a sulfoxide elimination) in the crude mixture. [d]No product could be isolated, although the presence of thiosulfinate in the crude mixture suggests the formation of a cycloadduct followed by the sulfoxide elimination. [e]Assignment of the structure based on the selectivity for **1a**. [f]The exact selectivity could not be determined.

We reasoned that a strong hydrogen bond between the solvent molecules and the solute might change the orientation of that sulfinyl group and, therefore, influence the approach of the diene. Surprisingly, acyclic dienes (**2b** and **2c**) did not show the same inversion of selectivity. Instead, the same selectivity as in dichloromethane was observed (entries 4 and 6). Such observations had already been made by Carreño's group by studying the reaction of diverse quinones with cyclopentadiene and piperylene in the presence of Lewis acids.[39] When they used a chelating Lewis acid ($ZnBr_2$), favoring the s-trans conformation and the approach of the diene on the opposite face of the quinone, an inversion of facial selectivity was observed compared to the reaction without catalyst or with a non-chelating Lewis acid (BF_3•OEt_2). However, with acyclic dienes, such as piperylene, the stereoselectivity was the same whether chelating or non-chelating Lewis acids were used. In order to rationalize those different behaviors, they postulated a significant difference in the transition state energies between cyclic and acyclic dienes, leading to the selection of one face or the other with sulfinylquinones in the presence of chelating Lewis acids.

Despite the presence of (*p*-tolyl) 4-methylbenzenesulfinothiolate in the crude mixture, suggesting the formation of the cycloadduct, followed by the sulfoxide elimination, we were not able to isolate and identify any Diels-Alder adduct from the reaction between quinone **1k** and diene **2b**, neither in HFIP nor by reproducing Carreño's procedure,[39] and therefore could not assess the effect of the solvent in this particular case.

Finally, we tested quinone **1m** that was never described in Diels-Alder reactions so far. When it was reacted with diene **2a** (entries 9 and 10), we obtained, after chromatography, product **4m**, in both

dichloromethane and HFIP. The cycloaddition being quite fast in both solvents, we were able to analyze the cycloadducts by ^{1}H NMR before they underwent the sulfoxide elimination. Each one of them possessed a different spectrum with the presence of only one diastereoisomer, leading us to the conclusion that we may have obtained both α- and β-adducts individually depending on the solvent we used. The opposite optical rotations for each sample after the sulfoxide elimination confirmed that hypothesis. We suspected that, as for quinone **1a**, the product formed in dichloromethane is **β-4m** and the one obtained in HFIP is **α-4m**, corresponding to an inversion of selectivity, as observed for quinone **1a** with cyclopentadiene. When the same quinone was reacted with diene **2b** (entries 11 and 12), the cycloadduct **5m** could not be observed, probably due to a rather fast sulfoxide elimination and we isolated **7m** as product of that reaction. Although we did not assess the stereoselectivity obtained from both reactions, we measured the specific optical rotations of both samples; +100.9° for dichloromethane and +85.1° for HFIP. We assumed, for the same reasons as described earlier, that the major adduct obtained in dichloromethane was the β-isomer (possessing a positive optical rotation). The relatively high positive optical rotation measured for the HFIP sample, would indicate that, although the selectivity was slightly decreased, the β-adduct remained the major one, just as observed with quinone **1a**.

Although the involvement of strong hydrogen bonds is consistent with the spectacular acceleration of the reactions, its influence on the diastereoselectivity of the Diels-Alder reactions with sulfinylquinones remains unclear.

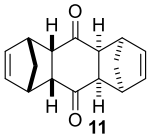
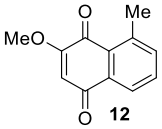
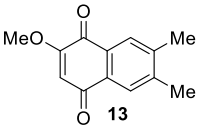
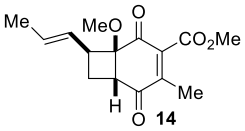
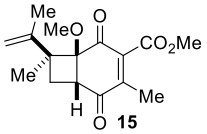
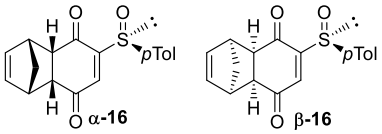
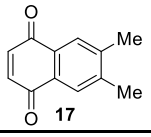
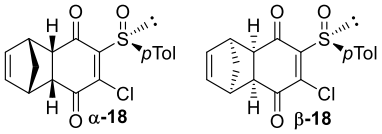
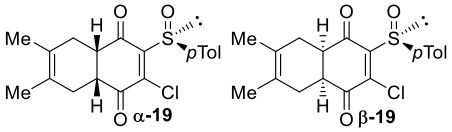
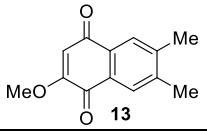
Unexpected outcomes of the Diels-Alder reactions

Some of the cycloadducts and their elimination products (in the case of quinones **1k-m**) are not stable or do not react as expected. The reactions that led to unexpected products are presented in Table 5.

When benzoquinone **1b** was reacted with two equivalents of cyclopentadiene (**2a**) in HFIP at room temperature, the *trans* double cycloaddition was reached in forty minutes (entry 1). In dichloromethane, thirty minutes were needed to reach the mono-cycloaddition. In order to obtain a single addition with **1b** in HFIP, only one equivalent of cyclopentadiene must be used (Table 2, entry 2). Next, when bromoquinone **1f** was used with acyclic dienes **2b** and **2c** (entries 2-5), even though the reactions were much faster in HFIP than in dichloromethane, the cycloaddition products could not be isolated. Any attempt to dry the crude mixture led to the degradation of the products. We identified them as being naphthoquinone derivatives coming from the elimination of bromide followed by oxidative aromatization.

In order to obtain those products more cleanly, we treated the cycloadducts with Et_3N to control the elimination process (HFIP was removed and replaced by dichloromethane for that step). We were then able to isolate naphthoquinones **12** and **13** in acceptable yields. As explained for quinone **1j**, the reactions in dichloromethane and HFIP did not give the same products for dienes **2b** and **2c**. In dichloromethane, not only the reaction did not occur on the expected double bond, but it also gave products which were not Diels-Alder cycloadducts. Through ^{1}H-^{13}C correlation NMR experiments, we determined the structure to be the result of a [2+2]-cycloaddition of the diene on the more electron-rich double bond of the quinone. The relative configurations were determined by a series of Nuclear Overhauser Effect (NOE) experiments (Figure 3).

Table 5. Results for the Diels-Alder reactions that did not lead to the standard cycloadducts and elimination products presented in Scheme 1

Entry	Quin.	Diene (eq.)	Solv.	Time	Products	Conv.[a] (%)	Ratio[b]	Yield (%)
1	**1b**	**2a** (2)	HFIP	40 min	 **11**	Quant.	—	93
2	**1f**	**2b** (2)	CH_2Cl_2	24h	 **12**	Quant.	—	74
3	**1f**	**2b** (2)	HFIP	3 min		Quant.	—	71
4	**1f**	**2c** (2)	CH_2Cl_2	42h	 **13**	Quant.	—	75
5	**1f**	**2c** (2)	HFIP	10 min		Quant.	—	72
6	**1j**	**2b** (2)	CH_2Cl_2	>15 d	 **14**	54	—	50
7	**1j**	**2c** (2)	CH_2Cl_2	>15 d	 **15**	30	—	24
8	**1k**	**2a** (1)	CH_2Cl_2	1h	 α-**16** β-**16**	Quant.	68:32[c]	89
9	**1k**	**2a** (1)	HFIP	<1 min		Quant.	77:23[c]	78
10	**1k**	**2c** (1)	CH_2Cl_2	20h	 **17**	Quant.	—	11
11	**1k**	**2c** (1)	HFIP	5 min		Quant.	—	15
12	**1l**	**2a** (2)	CH_2Cl_2	1h	 α-**18** β-**18**	Quant.	56:44[c]	75
13	**1l**	**2a** (2)	HFIP	<1 min		Quant.	77:23[c]	72
14	**1l**	**2b** (2)	CH_2Cl_2	20h	Complex mixture	Quant.	—	—
15	**1l**	**2b** (2)	HFIP	10 min		Quant.	—	—
16	**1l**	**2c** (2)	CH_2Cl_2	20h	 α-**19** β-**19**	Quant.	79:21[c]	90
17	**1l**	**2c** (2)	HFIP	10 min		Quant.	39:61[c]	82
18	**1m**	**2c** (2)	CH_2Cl_2	22h	 **13**	Quant.	—	53
19	**1m**	**2c** (2)	HFIP	3 min		Quant.	—	56

[a]Based on the ^{1}H NMR ratio of the starting material and the products in the crude mixture. [b]Based on the ^{1}H NMR ratio of the products in the crude mixture. [c]Assignment of the structure as proposed in Carreño's work.

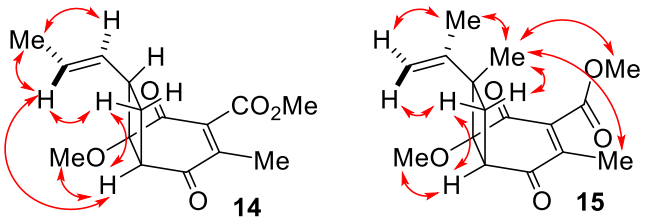


Figure 3. Tridimensional representation of products 14 and 15 and n.O.e correlations.

Even though this quinone presents a strong electron-withdrawing group, and should behave as **1h** and **1i**, it also presents a methoxy group and a methyl group, both of which disfavor the standard Diels-Alder reaction by electron donation and steric hindrance, respectively. As seen in its X-ray structure (Figure 4), the ester moiety of **1j** is 53.98° out of the quinone plane, probably due to an electrostatic repulsion between both oxygen atoms of the quinone carbonyl and the ester group, as well as steric hindrance caused by the methyl group.

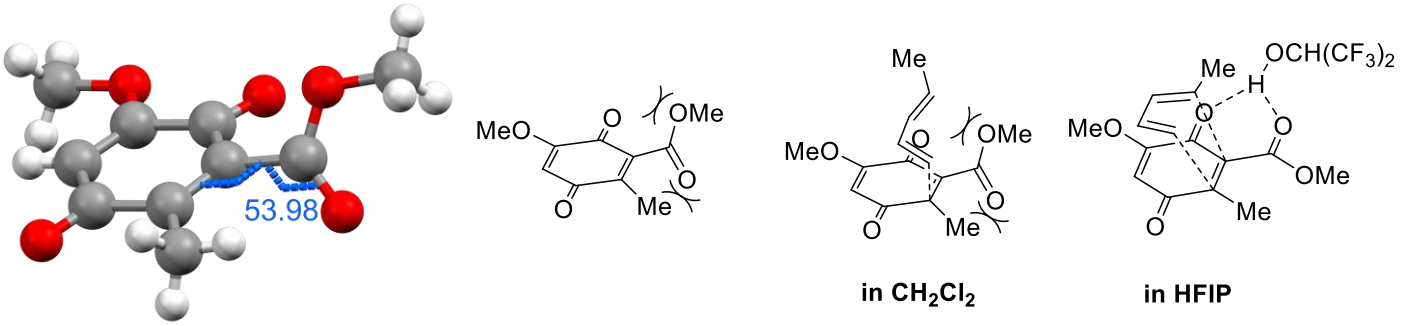


Figure 4. X-ray structure of quinone **1j**, torsion angle between the ester group and the quinone plane, and representation of the supposed approaches of an acyclic diene in dichloromethane and in HFIP.

Assuming the conformation in apolar and aprotic solvent (such as dichloromethane) is similar to the one in the solid state, the out-of-plane conformation of the ester reduces its electron-withdrawing effect, decreasing the reactivity of that double bond in a Diels-Alder reaction. We also supposed that, being almost perpendicular to the quinone plane, the ester group, combined with the methyl group, causes a significant steric hindrance effect, disfavoring the approach of a diene on that double bond (Figure 4). However, as can be seen in Table 3, the expected Diels-Alder reaction with cyclopentadiene (**2a**) (entry 13) took place, albeit very slowly. We supposed that the forced s-*cis* conformation of **2a** increases its reactivity enough to outweigh the steric hindrance.

Due to the strong hydrogen bond donation of HFIP, the ester group could be brought back into the quinone plane (as shown in Figure 4), increasing its electron-withdrawing effect, and decreasing the steric hindrance, thereby increasing the reactivity of the quinone double bond. Indeed, reactions with dienes **2b** and **2c** in HFIP gave the expected cycloadducts and the reactions for all three dienes **2a-c** were complete within hours (Table 3, entries 14-16).

A similar phenomenon was observed with sulfinylquinone **1k** and diene **2c** (entries 10 and 11) as was observed for quinone **1f**. As described by Carreño's group,[39] after formation of the cycloadduct, the latter undergoes sulfoxide elimination followed by aromatization. Unfortunately, the cycloadduct could not be

observed and the stereoselectivity could not be determined as an achiral product (**17**) was formed. Given the poor yields, this product may not be the major one, but no others were isolated.

The same observation was made for quinone **1m** reacting with diene **2c** (entries 18 and 19). After the cycloaddition, the sulfoxide elimination most probably occurred on the ring junction (leading to intermediate **8m**), followed by an oxidative aromatization leading to compound **13** in moderate yields.

Other unusual observations were made with quinone **1k** reacting with diene **2a** (entries 8 and 9), and quinone **1l** reacting with dienes **2a** and **2c** (entries 12, 13, 16 and 17). Counterintuitively, the Diels-Alder reaction occurred on the more electron-rich double bond. This phenomenon was already described in Carreño's work which studied the effect of different parameters on the selectivity of those reactions.[38,40] In the case of quinone **1k**, they observed a preference for the α-adduct that was reinforced when the reaction occurred in protic solvents. When the reaction is run in HFIP, not only the reaction rate, but also the selectivity towards the α-product increases, as was expected.

In the case of the reaction of quinone **1l** with cyclopentadiene (**2a**), a similar selectivity was observed towards the α-adduct and reinforced in HFIP (based on the structural assignment proposed by Carreño's group[40]). When the same quinone was reacted with diene **2c**, one diastereoisomer stood out and was assigned as the α-adduct in Carreño's work, which is in agreement with the stereoselectivities observed so far for those particular examples.[40] When the reaction is run in HFIP, however, an inversion of selectivity, supposedly towards the β-adduct, occurred. These last results confirm that the stereoselectivities observed for sulfinylquinones are far from trivial. Even though the models proposed up to now seem to provide a rational explanation for the observed selectivity in aprotic solvents, the ones proposed for reactions in protic solvents do not apply to every example presented in this work.

Finally, the reaction between quinone **1l** and diene **2b** (entries 14 and 15) was rapidly finished in both dichloromethane (twenty hours) and HFIP (ten minutes), however, complex mixtures of isomers were obtained and we were not able to isolate the different constituents or identify them.

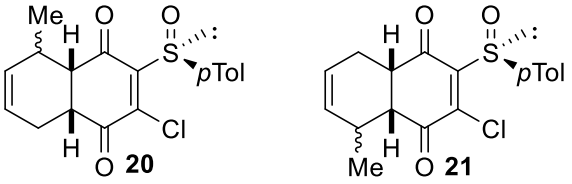


Figure 5. Proposed structures of the products obtained from the reaction between quinone **1l** and diene **2b**.

We supposed that the reaction occurred on the least hindered double bond (as for dienes **2a** and **2c** reacting with **1l**), and that two regioisomers (**20** and **21**, Figure 5) were formed, as the regioselectivity on that bond is poorly controlled. This is supported by the observation of the mass of the expected cycloadducts by HRMS in the crude reaction mixtures (HRMS (ESI+) for $[M+H]^+$ calc.: 349.0660, found: 349.0656).

Limitation of the use of HFIP

Although HFIP showed attractive properties in Diels-Alder reactions with quinones, its use cannot be extended to all dienes. One major limitation comes from its relatively high acidity. We tried to react sulfinylquinone **1a** with oxygenated dienes, such as Danishefsky's diene or 2-trimethylsilyloxybutadiene, but the only reaction which occurred was the cleavage of the silyl enol ether group, leading to the ketone. This does not represent a major drawback, however, since both dienes are quite reactive, even in apolar solvents.

Therefore, the sensitivity of the reactants to acidic media should be taken into account before attempting to use HFIP as solvent.

We also observed that, at a temperature of and above 30°C, a clear precipitate was forming, but the Diels-Alder reaction was not occurring. We suspected a polymerization of the diene. The sensitivity of the reactants to acidic media should then be then taken into account before attempting to use HFIP as solvent.

Conclusions

In summary, we have shown that the use of HFIP as solvent could greatly accelerate Diels-Alder reactions of quinones, thanks to its strong hydrogen bond donating ability. We could reach complete conversion in many cases at room temperature for reactions that otherwise needed higher temperatures and longer reaction times to complete in other solvents. Therefore, reactions that are inconveniently slow (or even not observed at all) in traditional solvents can be run in minutes or hours in HFIP. HFIP also showed the capacity to favor Diels-Alder reactions where other apolar and aprotic solvents gave other unexpected outcomes, such as [2+2]-cycloadducts.

We could also highlight the impact of HFIP on the stereoselectivity observed for sulfinylquinones. Selectivities obtained with cyclopentadiene reacting on the sulfoxide-bearing double bond were inverted between dichloromethane and HFIP, whereas acyclic dienes conserved the same facial selectivity. It was then concluded that the models proposed so far to explain the selectvities obtained in apolar solvents were not sufficient in the case of protic solvents.

Finally, we have also shown that HFIP may change the selectivity between the double bonds of the quinone, restoring the expected reactivity. The above findings establish that HFIP is a solvent of choice to accelerate moderately or very slow Diels-Alder reactions whilst assuring high levels of regio- and diasteroselectivity.

Experimental Section

General. Reagents and solvents were purchased as reagent grade and used without further purification, with the exception of cyclopentadiene **2a**, which is commercially available in its dimer form. The monomer was freshly distilled after the cracking of the dimer. THF and dichloromethane were purified and dried using an MBraun SPS Compact solvent purification system. Column chromatography: silica gel 60 (230-400 mesh, 0.040-0.063 mm). Demetallated silica gel was prepared according to a published procedure.[42] Thin Layer Chromatography (TLC) was performed on aluminum sheets coated with silica gel 60 F_{254} Merck (unless otherwise stated), visualization by UV light, $KMnO_4$ stain, or *p*-anisaldehyde stain followed by heating. NMR spectra (^1H and ^{13}C) were recorded on a Jeol JNM 400 MHz or 500 MHz (^1H NMR at 400 MHz or 500 MHz and ^{13}C NMR at 100 MHz or 125 MHz spectrometer). Chemical shifts are reported in ppm with the solvent resonance at δ 7.26 ppm for $CDCl_3$ and 7.16 ppm for C_6D_6 in ^1H spectra, and relative to the central $CDCl_3$ resonance δ 77.16 ppm for $CDCl_3$ and the central resonance at δ 128.06 ppm for C_6D_6 in ^{13}C spectra, unless stated otherwise. NMR data are reported as (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad; coupling constant(s) in Hz; integration). Optical rotations were measured using a MCP200 Polarimeter (Anton Paar). The solutions were prepared using analytical grade solvents and concentrations (c) are given in g/100 mL.

Synthesis of quinones

(+)-(*S*)-5-Methoxy-2-methyl-3-(*p*-tolylsulfinyl)cyclo-hexa-2,5-diene-1,4-dione (1a). Compound **1a** was synthesized according to the procedure of Hanquet *et al.*[17,18]; R_f (5/5 cyclohex./AcOEt): 0.43; m: 130-132°C; $[\alpha]_D^{20}$ (c = 1.0, CH_2Cl_2): +469.4°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (2H, d, *J* = 8.1 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 7.29 (2H, d, *J* = 8.1 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 5.96 (1H, s, MeOCC<u>H</u>), 3.79 (3H, s, <u>Me</u>O), 2.50 (3H, s, <u>Me</u>^{quinone}), 2.39 (3H, s, Ar<u>Me</u>$^{p\text{-tolyl}}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.37, 179.30, 157.96, 148.23, 144.67, 141.89, 139.48, 130.24, 125.02, 108.06, 56.68, 21.54, 9.55.

2,3,5-Trimethylcyclohexa-2,5-diene-1,4-dione (1d). A solution of CAN (27.9 g, 50.9 mmol) in water (150 mL) was added to solution of 2,3,5-trimethylhydroquinone (3.07 g, 20.2 mmol) in acetonitrile (300 mL). After ten minutes at room temperature, the acetonitrile was evaporated, and the aqueous residue was extracted with dichloromethane. The organic phase was washed with water and brine and dried over $MgSO_4$. It was filtered and the solvents evaporated *in vacuo* to give **1d** (2.00 g, 66%) as a yellow solid which was used without any further purifications; R_f (6/4 cyclohex./AcOEt): 0.64; m_p: 34-36°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.54 (1H, q, *J* = 1.6 Hz, MeCC<u>H</u>), 2.02 (3H, d, *J* = 1.6 Hz, <u>Me</u>CCH), 2.01 (3H, dd, *J* = 2.3, 1.2 Hz, <u>Me</u>CCMe), 1.99 (3H, dd, *J* = 2.3, 1.2 Hz, MeCC<u>Me</u>); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.01, 187.63, 145.45, 141.02, 140.85, 133.19, 16.00, 12.47, 12.17.

2,3-Dimethoxy-5-methyl-cyclohexa-2,5-diene-1,4-dione (1e). A solution of CAN (6.63 g, 12.1 mmol) in water (75 mL) was added to a solution of 1,2,3,4-tetramethoxy-5-methylbenzene (1.01 g, 4.77 mmol) in acetonitrile (75 mL). After twenty minutes at room temperature the acetonitrile was evaporated and the aqueuous residue was extracted with dichloromethane. The organic phase was washed with water and brine and dried over $MgSO_4$. The solution was filtered and the solvents evaporated *in vacuo* to give **1e** (815 mg, 94%) as a red solid which was used without any further purifications; R_f (7/3 cyclohex./AcOEt): 0.56; m_p: 58-60°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.43 (1H, q, *J* = 1.6 Hz, MeCC<u>H</u>), 4.02 (3H, s, <u>Me</u>O), 3.99 (3H, s, <u>Me</u>O), 2.03 (3H, d, *J* = 1.6 Hz, <u>Me</u>CCH); ^{13}C NMR (500 MHz, $CDCl_3$) δ 184.56, 184.34, 145.16, 144.98, 144.19, 131.43, 61.40, 61.33, 15.62.

2-Bromo-6-methoxycyclohexa-2,5-diene-1,4-dione (1f). A solution of CAN (12.7 g, 23.2 mmol) in water (150 mL) was added to a solution of 2-bromo-6-methoxybenzene-1,4-diol[43] (2.01 g, 9.19 mmol) in acetonitrile (150 mL). After one hour at room temperature, the acetonitrile was evaporated and the aqueous residue was extracted with dichloromethane. The organic phase was washed with water and brine and dried over $MgSO_4$. The solution was filtered and the solvent evaporated. The crude was recrystallized in boiling ethanol to give **1f** (1.64 g, 72%) as orange needles; R_f (6/4 cyclohex./AcOEt): 0.37; m_p: 167-169°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (1H, d, *J* = 2.3 Hz, BrCC<u>H</u>), 5.96 (1H, d, *J* = 2.3 Hz, MeOCC<u>H</u>), 3.85 (3H, s, <u>Me</u>O); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.76, 174.67, 158.38, 138.61, 134.39, 107.76, 56.95.

3-Bromo-5-methoxy-2-methylcyclohexa-2,5-diene-1,4-dione (1g). A solution of CAN (26.3 g, 48.2 mmol) in water (250 mL) was added to a solution of 3-bromo-1,2,5-trimethoxy-4-methylbenzene[17] (5.00 g, 19.2 mmol) in acetonitrile (250 mL). After thirty minutes at room temperature, the acetonitrile was evaporated and the aqueous residue was extracted with dichloromethane. The organic phase was washed with water and brine and dried over $MgSO_4$. The solution was filtered and the solvent evaporated. The crude was recrystallized in boiling ethanol to give **1g** (4.06 g, 92%) as yellow needles; R_f (5/5 cyclohex./AcOEt): 0.54; m_p: 101-104°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.96 (1H, s, MeOCC<u>H</u>), 3.84 (3H, s, <u>Me</u>O), 2.23 (3H, s, <u>Me</u>CCBr); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.11, 174.74, 158.42, 146.78, 133.13, 107.39, 56.82, 17.23; HRMS (ESI+): for $[M+H]^+$ calc.: 230.9657, found: 230.9651.

Methyl 3,6-dioxocyclohexa-1,4-diene-1-carboxylate (1h)

Methyl 2,5-dihydroxybenzoate. A solution of 2,5-dihydroxybenzoic acid (10.0, 65.1 mmol) and H_2SO_4 (5 mL) in methanol (70 mL) was refluxed overnight. The methanol was removed and replaced by dichloromethane. The

organic phase was washed with water and a saturated solution of $NaHCO_3$ and dried over Na_2SO_4. The solution was filtered and the solvents evaporated to give methyl 2,5-dihydroxybenzoate (9.70 g, 89%) as a white solid; R_f (7/3 PhMe/AcOEt): 0.60; m_p: 89-92°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (1H, d, *J* = 3.3 Hz, $MeO_2CCC\underline{H}$), 6.99 (1H, dd, *J* = 9.0, 3.3 Hz, middle aromatic $\underline{H}$), 6.84 (1H, d, *J* = 9.0 Hz, third aromatic $\underline{H}$), 3.89 (3H, s, $CO_2\underline{Me}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.37, 155.34, 148.29, 124.26, 118.41, 114.85, 112.24, 52.47.

Methyl 3,6-dioxocyclohexa-1,4-diene-1-carboxylate (1h). A solution of methyl 2,5-dihydroxybenzoate (2.00 g, 11.9 mmol), $MgSO_4$ (4.10 g, 34.1 mmol) and Ag_2O (4.06 g, 17.5 mmol) in diethyl ether (20 mL) was stirred four hours at room temperature. The solution was filtered over Celite® and the solvent evaporated to give **1h** (1.88 g, 95%) as an orange solid which was used without any further purifications; R_f (7/3 PhMe/AcOEt): 0.65; m_p: 51-52°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (1H, dd, *J* = 2.0, 0.5 Hz, $\underline{H}CCH$), 6.83 (1H, d, *J* = 2.0 Hz, $HCC\underline{H}$), 6.82 (1H, d, *J* = 0.5 Hz, $MeO_2CCC\underline{H}$), 3.91 (3H, s, $CO_2\underline{Me}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.95, 183.11, 163.27, 137.14, 137.07, 136.70, 136.28, 53.28.

Methyl 1,4-dioxonaphthalene-2-carboxylate (1i). Compound **1i** was synthesized according to the procedure of Lee *et al.*[44]; R_f (7/3 cyclohex./AcOEt): 0.47; m_p: 88-90°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15-8.08 (1H, m, aromatic $C\underline{H}$), 8.07-8.04 (1H, m, aromatic $C\underline{H}$), 7.83-7.74 (2H, m, 2 × aromatic $C\underline{H}$), 7.26 (1H, s, $MeO_2CCC\underline{H}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.68, 181.24, 163.91, 139.54, 138.45, 134.70, 134.38, 131.88, 131.69, 127.14, 126.42, 53.27.

Methyl 5-methoxy-2-methyl-3,6-dioxocyclohexa-1,4-diene-1-carboxylate (1j)

Methyl 2,3,5-trimethoxy-6-methylbenzoate. A solution of hexyllithium (2.3 M in hexanes, 6.5 mL, 15.0 mmol) was added to a solution of 3-bromo-1,2,5-trimethoxy-4-methylbenzene[17] (3.06 g, 11.7 mmol) in dry THF (100 mL) cooled down to -78°C. After ten minutes, methyl chloroformate (1.2 mL, 15.5 mmol) was added dropwise and the reaction mixture was allowed to warm up to room temperature. After one hour, the mixture was cooled down to 0°C, quenched with distilled water and diluted with diethyl ether. The phases were separated, the organic phase was dried over Na_2SO_4 and the solvents were evaporated. The crude mixture was purified by flash chromatography on silica gel (95/5 cyclohex./AcOEt) to give the title compound (2.33 g, 83%) as a white powder. R_f (8/2 cyclohex./AcOEt): 0.36; m_p: 51-53°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.52 (1H, s, $MeOCC\underline{H}$), 3.92 (3H, s, $CO_2\underline{Me}$), 3.87 (3H, s, $ArO\underline{Me}$), 3.81 (3H, s, $ArO\underline{Me}$), 3.80 (3H, s, $ArO\underline{Me}$), 2.06 (3H, s, $Ar\underline{Me}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.46, 154.20, 151.00, 139.57, 130.39, 115.71, 98.92, 61.84, 56.53, 56.36, 52.39, 12.23.

Methyl 5-methoxy-2-methyl-3,6-dioxocyclohexa-1,4-diene-1-carboxylate (**1j**). A solution of CAN (12.91 g, 23.5 mmol) in water (100 mL) was added to a solution of Methyl 2,3,5-trimethoxy-6-methylbenzoate (2.24 g, 9.33 mmol) in acetonitrile (100 mL). After fifteen minutes, acetonitrile was evaporated and the aqueous phase was extracted with dichloromethane. The organic phase was then dried over Na_2SO_4 and the solvents were evaporated. The crude mixture was dissolved in a minimum of dichloromethane and the product was precipitated by the addition of pentane. The yellow precipitate was filtrated, washed with pentane and dried under vacuum to give the title compound (1.62g, 83%) as a bright yellow powder. R_f (7/3 cyclohex./AcOEt): 0.38; m_p: 98-100°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.98 (1H, s, $MeOCC\underline{H}$), 3.92 (3H, s, $CO_2\underline{Me}$), 3.83 (3H, s, $ArO\underline{Me}$), 2.06 (3H, s, $MeO_2CCC\underline{Me}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.42, 178.65, 164.48, 158.14, 143.44, 135.81, 107.71, 56.58, 53.00, 13.59; HRMS (ESI+): for $[M+Na]^+$ calc.: 233.0420, found: 233.0412. Crystals for quinone **1j** were obtained by slow evaporation from dichloromethane at room temperature.

(+)-(*S*)-2-(*p*-Tolylsulfinyl)cyclohexa-2,5-diene-1,4-dione (1k) was synthesized according to the procedure of Carreño *et al.*[38]; R_f (5/5 cyclohex./AcOEt): 0.63; m_p: 124-126°C; $[\alpha]_D^{20}$ (c = 1.0, $CHCl_3$): +1011°; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (2H, d, *J* = 8.1 Hz, 2 × $C\underline{H}^{p\text{-tolyl}}$), 7.43 (1H, d, *J* = 2.5 Hz, $ArS(O)CC\underline{H}^{quinone}$), 7.29 (2H, d, *J* = 8.1 Hz, 2 × $C\underline{H}^{p\text{-tolyl}}$), 6.79 (1H, dd, *J* = 10.1, 2.5 Hz, $HCC\underline{H}^{quinone}$), 6.71 (1H, d, *J* = 10.1 Hz, $\underline{H}CCH^{quinone}$), 2.39 (3H, s,

ArMe$^{p\text{-tolyl}}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.23, 183.71, 155.46, 143.09, 138.31, 137.53, 136.56, 131.69, 130.39, 125.94, 21.62.

(+)-(*S*)-2-Chloro-3-(*p*-tolylsulfinyl)cyclohexa-2,5-diene-1,4-dione (1l) was synthesized according to the procedure of Carreño *et al.*[40]; R_f (5/5 cyclohex./AcOEt): 0.41; m_p: 138-140°C; $[\alpha]_D^{20}$ (c = 1.0, $CHCl_3$): +638°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (2H, d, *J* = 8.2 Hz, 2 × CH$^{p\text{-tolyl}}$), 7.33 (2H, d, *J* = 8.2 Hz, 2 × CH$^{p\text{-tolyl}}$), 6.91 (1H, d, *J* = 10.1 Hz, CH^{quinone}), 6.78 (1H, d, *J* = 10.1 Hz, CH^{quinone}), 2.40 (3H, s, ArMe$^{p\text{-tolyl}}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.27, 177.91, 146.28, 143.71, 142.61, 138.03, 130.34, 125.17, 21.63.

(+)-(*S*)-2-Methoxy-5-(*p*-tolylsulfinyl)cyclohexa-2,5-diene-1,4-dione (1m)

1-Bromo-2,5-bis(ethoxymethoxy)-4-methoxybenzene. To an ice bath (0°C) cooled down solution of 2-bromo-5-methoxybenzene-1,4-diol[45] (2.50 g, 11.4 mmol) and $BnEt_3NCl$ (267 mg, 1.17 mmol) in dry THF (25 mL) was added NaOH (2.761 g, 69.0 mmol) and ethoxymethyl chloride (4.2 mL, 45.3 mmol). The solution was stirred one hour at 0°C and one hour at room temperature. It was then poured in water (25 mL). After ten minutes, the phases were separated, the organic layer was washed with brine and dried over $MgSO_4$. It was filtered and the solvent was evaporated. The crude was chromatographied on silica gel (9/1 cyclohex./AcOEt) to give the title compound (2.81 g, 73%) as a yellowish oil; R_f (7/3 cyclohex./AcOEt): 0.57; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (1H, s, BrCCH), 6.82 (1H, s, MeOCCH), 5.22 (2H, s, $MeCH_2OCH_2OC$), 5.18 (2H, s, $MeCH_2OCH_2OAr$), 3.84 (3H, s, MeO), 3.84 (2H, q, *J* = 7.1 Hz, $MeCH_2OCH_2O$), 3.80 (2H, q, *J* = 7.1 Hz, $MeCH_2OCH_2O$), 1.24 (3H, t, *J* = 7.1 Hz, $MeCH_2OCH_2O$), 1.23 (3H, t, *J* = 7.1 Hz, $MeCH_2OCH_2O$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.08, 149.57, 142.26, 121.41, 102.72, 102.60, 95.00, 94.92, 64.68, 64.57, 56.27, 15.22, 15.18.

(–)-(S)-1,4-Bis(ethoxymethoxy)-2-methoxy-5-(*p*-tolylsulfinyl)benzene. A solution of Hexyllithium (2.3 M in hexane, 2.7 mL, 6.21 mmol) was added to a solution of 1-bromo-2,5-bis(ethoxymethoxy)-4-methoxybenzene (2.06 g, 6.15 mmol) in dry THF (60 mL) cooled down to -78°C. After thirty minutes at -78°C, the lithium solution was quickly cannulated over a solution of methyl (–)-*S*(S)-*p*-tolylsulfinate[46] (1.88 g, 6.38 mmol) in dry THF (60 mL) cooled down to -78°C. The final mixture was stirred one hour at -78°C, one hour at room temperature and quenched with saturated NH_4Cl. The phases were separated and the organic layer was washed with brine and dried over $MgSO_4$. It was filtered and the solvent was evaporated. The crude was chromatographied over silica gel (8/2 to 6/4 cyclohex./AcOEt) to give the title compound (1.67 g, 69%) as a yellowish oil; R_f (7/3 cyclohex./AcOEt): 0.11; $[\alpha]_D^{20}$ (c = 1.0, $CHCl_3$): -75.2°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (1H, s, ArS(O)CCH), 7.55 (2H, d, *J* = 8.1 Hz, CH$^{p\text{-tolyl}}$), 7.21 (2H, d, *J* = 8.1 Hz, CH$^{p\text{-tolyl}}$), 6.73 (1H, s, MeOCCH), 5.21 (2H, dd, *AB*, J_{AB} = 6.6 Hz, $\Delta\nu_{AB}$ = 10.7 Hz, $MeCH_2OCH_2O$), 5.14 (2H, dd, *A'B'*, $J_{A'B'}$ = 7.1 Hz, $\Delta\nu_{A'B'}$ = 19.2 Hz, $MECH_2OCH_2O$), 3.84 (3H, s, MeO), 3.75 (2H, q, *J* = 7.1 Hz, $MeCH_2OCH_2O$), 3.58 (2H, ddq, *CD*X, J_{CD} = 9.6 Hz, $J_{CX} = J_{DX}$ = 7.1 Hz, $\Delta\nu_{CD}$ = 45.2 Hz, $MeCH_2OCH_2O$), 2.34 (3H, s, ArMe$^{p\text{-tolyl}}$), 1.19 (3H, t, *J* = 7.1 Hz, $MeCH_2OCH_2O$), 1.15 (3H, dd, CD*X*, $J_{CX} = J_{DX}$ = 7.1 Hz, $MeCH_2OCH_2O$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.43, 149.68, 142.09 (two signals at the same shielding), 141.24, 129.74, 125.34 (two signals at the same shielding), 113.73, 100.24, 94.97, 93.95, 64.65, 64.53, 56.31, 21.50, 15.16, 15.13.

(+)-(S)-2-Methoxy-5-(*p*-tolylsulfinyl)cyclohexa-2,5-diene-1,4-dione (1m). A solution of CAN (5.27 g, 9.61 mmol) in water (25 mL) was added to a solution of (–)-(*S*)-1,4-bis(ethoxymethoxy)-2-methoxy-5-(*p*-tolylsulfinyl)benzene (1.50 g, 3.80 mmol) in acetonitrile (50 mL). after thirty minutes, the acetonitrile was evaporated and the aqueous residue was extracted with dichloromethane. The organic layer was washed with brine and dried over $MgSO_4$. The solution was filtered and the sovents evaporated to give **1l** (935 mg, 89%) as an orange powder which was used without any further purifications; R_f (5/5 cyclohax./TBME) 0.20; m_p: 121-123°C; $[\alpha]_D^{20}$ (c = 1.0, $CHCl_3$): +428.8°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (2H, d, *J* = 8.2 Hz, 2 × CH$^{p\text{-tolyl}}$), 7.34 (1H, s, ArS(O)CCH), 7.29 (2H, d, *J* = 8.2 Hz, 2 × CH$^{p\text{-tolyl}}$), 5.85 (1H, s, MeOCCH), 3.91 (3H, s, MeO), 2.38 (3H, s, ArMe$^{p\text{-}}$

^{tolyl}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.65, 179.70, 159.73, 156.54, 149.94, 138.54, 130.35, 129.73, 125.98, 107.64, 56.87, 21.60; HRMS (ESI+): for $[M+H]^+$ calc.: 277.0535, found: 277.0529.

Diels-Alder reactions and derived products

General procedure for the Diels-Alder reaction. The quinone was dissolved in dichloromethane or HFIP (10 mL/mmol of quinone). The diene (1 or 2 equivalents) was then added at room temperature. All reaction mixtures were homogeneous. Once the reaction reached complete or maximum conversion, the solvent was evaporated and the crude purified if necessary (otherwise it was pure enough to be analyzed without any further purification). See Tables 2-5 for times of reactions, equivalents of dienes, conversions and yields.

(-)-(1*R*,4*S*,4a*S*,8a*R*)-6-Methoxy-8a-methyl-4a-((*S*)-*p*-tolylsulfinyl)-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (α-3a). Quinone **1a** (257 mg, 0.885 mmol in CH_2Cl_2; 260 mg, 0.896 mmol in HFIP) and diene **2a** (0.15 mL, 1.78 mmol in CH_2Cl_2; 0.15 mL, 1.78 mmol in HFIP) were reacted following general procedure. The crude product was purified by flash chromatography on silica gel (40/1/0.2 CH_2Cl_2/AcOEt/acetone) to isolate **α-3a** (103 mg, 33% in CH_2Cl_2; 186 mg, 58% in HFIP) in the first fraction as a brown powder; R_f (40/5/1 CH_2Cl_2/AcOEt/acetone): 0.61; m_p: 124-126°C (decomp.); $[\alpha]_D^{20}$ (c = 1.0, $CHCl_3$): -249.6°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (2H, d, *J* = 8.0 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 7.27 (2H, d, *J* = 8.0 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 6.23 (1H, dd, *J* = 5.0, 2.6 Hz, <u>H</u>CCH^{diene}), 6.08 (1H, dd, *J* = 5.0, 2.6 Hz, HCC<u>H</u>^{diene}), 5.48 (1H, s, MeOCC<u>H</u>), 4.07 (1H, s(br), C<u>H</u>^{bridge}), 3.32 (3H, s, <u>Me</u>O), 3.23 (1H, s(br), C<u>H</u>^{bridge}), 2.39 (3H, s, Ar<u>Me</u>$^{p\text{-tolyl}}$), 2.25 (1H, d, *J* = 10.0 Hz, ½ × C<u>H$_2$</u>^{bridge}), 1.85 (3H, s, <u>Me</u>^{angular}), 1.68 (1H, d, *J* = 10.0 Hz, ½ × C<u>H$_2$</u>^{bridge}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.13, 187.01, 164.32, 157.21, 142.69, 140.39, 136.81, 129.79, 126.46, 111.57, 81.25, 58.29, 56.03, 54.46, 49.99, 43.47, 25.78, 21.55. Crystals for compound α-3a were obtained by slow evaporation from dichloromethane at room temperature.

(+)-(1*S*,4*R*,4a*R*,8a*S*)-6-Methoxy-8a-methyl-4a-((*S*)-*p*-tolylsulfinyl)-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (β-3a). The same procedure as **α-3a** was followed to give **β-3a** (189 mg in CH_2Cl_2, 60%; 25 mg, 7.9% in HFIP) in the second fraction as a brown powder; R_f (40/5/1 CH_2Cl_2/AcOEt/acetone): 0.37; m_p: 130-132°C (decomp.); $[\alpha]_D^{20}$ (c = 1.0, $CHCl_3$): +189.6°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (2H, d, *J* = 8.0 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 7.38 (2H, d, *J* = 8.0 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 6.25 (1H, dd, *J* = 5.0, 3.0 Hz, <u>H</u>CCH^{diene}), 5.83 (1H, s, MeOCC<u>H</u>), 5.80 (1H, dd, *J* = 5.0, 3.0 Hz, HCC<u>H</u>^{diene}), 3.77 (3H, s, <u>Me</u>O), 3.27 (1H, s(br), C<u>H</u>^{bridge}), 2.87 (1H, s(br), C<u>H</u>^{bridge}), 2.48 (3H, s, Ar<u>Me</u>$^{p\text{-tolyl}}$), 2.17 (3H, s, <u>Me</u>^{angular}), 2.07 (1H, d, *J* = 9.0 Hz, ½ × C<u>H$_2$</u>^{bridge}), 1.58 (1H, d, *J* = 9.0 Hz, ½ × C<u>H$_2$</u>^{bridge}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.84, 190.57, 164.91, 143.53, 141.18, 136.66, 135.69, 129.57, 126.93, 112.04, 79.35, 59.58, 56.65, 53.24, 51.04, 43.41, 25.04, 21.92.

(-)-(*R*)-2-Methoxy-4a,8-dimethyl-4a,5-dihydronaphthalene-1,4-dione (β-9a). Quinone **1a** (187 mg, 0.645 mmol in HFIP) and diene **2b** (0.13 mL, 1.30 mmol in HFIP) were reacted following the general procedure. Once the cycloaddition was over, HFIP was removed *in vacuo* and replace by CH_2Cl_2 (7 mL) to let the sulfoxide elimination occur overnight. The solvent was evaporated and the crude product purified by flash chromatography on demetallated silica gel (9/1 to 8/2 cyclohex./AcOEt) to give **β-9a** (111 mg, 79% in HFIP) as a yellow oil that crystallizes in the fridge; R_f (2/1 cyclohex./AcOEt): 0.31; m_p : 129-131°C; $[\alpha]_D^{20}$ (c = 0.40, $CHCl_3$): -109.2°; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (1H, ddd, *J* = 9.2, 6.4, 2.4 Hz, H_2CC<u>H</u>CHCMe), 6.08 (1H, dd, *J* = 9.6, 3.2 Hz, H_2CCHC<u>H</u>CMe), 5.87 (1H, s, MeOCC<u>H</u>), 3.81 (3H, s, <u>Me</u>O), 2.62 (1H, dd, *J* = 19.2, 6.0 Hz, ½ × C<u>H$_2$</u>), 2.43 (1H, ddd, *J* = 19.2, 5.0, 2.8 Hz, ½ × C<u>H$_2$</u>), 2.32 (3H, s, $H_2CCHCHC$<u>Me</u>), 1.23 (3H, s, <u>Me</u>^{angular}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.25, 181.42, 164.09, 147.56, 134.07, 131.16, 128.32, 107.71, 56.51, 45.51, 32.48, 26.44, 22.28.

(+)-(*S*)-2-Methoxy-4a,6,7-trimethyl-4a,5-dihydronaphthalene-1,4-dione (α-10a). Quinone **1a** (198 mg, 0.682 mmol in HFIP) and diene **2c** (0.16 mL, 1.41 mmol in HFIP) were reacted following the general procedure. The crude product was purified by flash chromatography on demetallated silica gel (9/1 to 8/2 cyclohex./AcOEt) to

isolate **α-10a** (HFIP: 15 mg, 9.7%) in the first fraction as a yellow oil; R_f (5/5 cyclohex./AcOEt): 0.56; $[\alpha]_D^{20}$ (c = 0.40, $CHCl_3$): +12.8°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (1H, s, MeCC<u>H</u>), 5.94 (1H, s, MeOCC<u>H</u>), 3.84 (3H, s, <u>Me</u>O), 2.56-2.43 (2H, m, C<u>H</u>$_2$), 1.92 (3H, s(br), MeCC<u>Me</u>), 1.89 (3H, s(br), <u>Me</u>CCMe), 1.21 (3H, s, <u>Me</u>^{angular}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.14, 179.79, 163.67, 140.45, 138.82, 131.49, 125.18, 109.48, 56.52, 44.78, 39.42, 26.06, 20.86, 17.16.

(-)-(4a*S*,8a*R*)-2-Methoxy-4a,6,7-trimethyl-8a-((*S*)-*p*-tolylsulfinyl)-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (β-6a). The same procedure as for **α-10a** was followed to isolate **β-6a** (181 mg, 71% in HFIP) as a light orange solid foam; R_f (5/5 cyclohex./AcOEt): 0.49; m_p: 125-126°C; $[\alpha]_D^{20}$ (c = 1.0, CH_2Cl_2): -207.0°; ^{1}H NMR (500 MHz, C_6D_6) δ 7.21 (2H, d, *J* = 7.7 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 6.87 (2H, d, *J* = 7.7 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 6.10 (1H, s, MeOCC<u>H</u>), 2.97 (3H, s, <u>Me</u>O), 2.64 (1H, d, *J* = 17.4 Hz, ½ × ArS(O)CC<u>H</u>$_2$), 2.20 (1H, d, *J* = 17.4 Hz, ½ × ^{angular}MeCC<u>H</u>$_2$), 2.07 (1H, d, *J* = 17.4 Hz, ArS(O)CC<u>H</u>$_2$), 1.89 (3H, s, Ar<u>Me</u>$^{p\text{-tolyl}}$), 1.82 (1H, d, *J* = 17.4 Hz, ^{angular}MeCC<u>H</u>$_2$), 1.78 (3H, s, <u>Me</u>^{angular}), 1.44 (3H, s, <u>Me</u>CCMe), 1.22 (3H, s, MeCC<u>Me</u>); ^{13}C NMR (125 MHz, C_6D_6) δ 197.42, 186.31, 161.67, 142.50, 136.42, 129.94, 122.81, 122.81, 121.93, 113.32, 79.11, 55.27, 49.77, 45.21, 30.10, 21.19, 18.58, 18.50, 16.94.

(1*R*,4*S*,4a*R*,8a*S*)-1,4,4a,8a-Tetrahydro-1,4-methanonaphthalene-5,8-dione (3b): Quinone **1b** (208 mg, 1.92 mmol in CH_2Cl_2; 51 mg, 0.476 mmol in HFIP) and diene **2a** (0.33 mL, 3.92 mmol in CH_2Cl_2; 0.04 mL, 0.476 mmol in HFIP) were reacted following the general procedure to give **1b** (326 mg, 94% in CH_2Cl_2; 83 mg, >98% in HFIP) as a grey powder; R_f (8/2 cyclohex./AcOEt): 0.26; m_p: 66-69°C ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (2H, s, <u>H</u>CC<u>H</u>^{quinone}), 6.06 (2H, dd, AB*X*YZ, J_{AX} = J_{AY} = 1.8 Hz, <u>H</u>CC<u>H</u>^{diene}), 3.54 (2H, m, ABX*Y*Z, 2 × C<u>H</u>^{bridge}), 3.22 (2H, dd, ABXY*Z*, J_{YZ} = 2.3 Hz, J_{BZ} = 1.5 Hz, 2 × C<u>H</u>^{angular}), 1.48 (2H, dddd, *AB*XYZ, J_{AB} = 8.8 Hz, J_{AX} = 1.8 Hz, J_{BZ} = 1.5 Hz, $\Delta\nu_{AB}$ = 55.7 Hz, C<u>H</u>$_2^{bridge}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.62, 142.20, 135.43, 48.91, 48.85, 48.47.

(±)-*rel*-(4a*R*,5*R*,8a*S*)-5-Methyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (5b). Quinone **1b** (217 mg, 2.01 mmol in CH_2Cl_2; 56 mg, 0.516 mmol in HFIP) and diene **2b** (0.40 mL, 4.01 mmol in CH_2Cl_2; 0.10 mL, 1.00 mmol in HFIP) were reacted following general procedure to give **5b** (324 mg, 92% in CH_2Cl_2; 88 mg, 97% in HFIP) as a grey oil; R_f (7/3 cyclohex./AcOEt): 0.50; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.75 (1H, d, *J* = 10.3 Hz, <u>H</u>CCH^{quinone}), 6.69 (1H, d, *J* = 10.3 Hz, HCC<u>H</u>^{quinone}), 5.70-5.59 (2H, m, <u>H</u>CC<u>H</u>^{diene}), 3.34 (1H, dd, *J* = 6.0, 5.9 Hz, MeCHC<u>H</u>^{angular}), 3.24 (1H, ddd, *J* = 7.5, 5.9, 3.9 Hz, CH_2C<u>H</u>^{angular}), 2.57 (1H, m, MeC<u>H</u>), 2.49 (2H, m, C<u>H</u>$_2$), 0.94 (3H, d, <u>Me</u>CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.31, 199.71, 141.21, 140.60, 130.99, 123.48, 50.52, 45.49, 31.86, 22.50, 18.69.

(4a*R*,8a*S*)-6,7-Dimethyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (6b). Quinone **1b** (206 mg, 1.90 mmol in CH_2Cl_2; 56 mg, 0.521 mmol in HFIP) and diene **2c** (0.43 mL, 3.80 mmol in CH_2Cl_2; 0.12 mL, 1.06 mmol in HFIP) were reacted following general procedure to give **6b** (288 mg, 80% in CH_2Cl_2; 95 mg, 96% in HFIP) as a grey powder; R_f (7/3 cyclohex./AcOEt): 0.59; m_p: 120-123°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.65 (2H, s, <u>H</u>CC<u>H</u>^{quinone}), 3.24-3.12 (2H, m, 2 × C<u>H</u>^{angular}), 2.46-1.98 (4H, m, 2 × C<u>H</u>$_2$), 1.62 (6H, s, 2 × <u>Me</u>); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.42, 139.45, 123.41, 47.18, 30.55, 18.97.

(1*R*,4*S*,4a*R*,9a*S*)-1,4,4a,9a-Tetrahydro-1,4-methanoanthracene-9,10-dione (3c). Quinone **1c** (195 mg, 1.23 mmol in CH_2Cl_2; 51 mg, 0.323 mmol in HFIP) and diene **2a** (0.21 mL, 2.50 mmol in CH_2Cl_2; 0.06 mL, 0.714 mmol in HFIP) were reacted following general procedure to give **3c** (257 mg, 93% in CH_2Cl_2; 72 mg, >98% in HFIP) as a grey powder; R_f (8/2 cyclohex./AcOEt): 0.33; m_p: 108-110°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (2H, dd, *J* = 5.9, 3.3 Hz, 2 × C<u>H</u>^{Ar}), 7.69 (2H, dd, *J* = 5.9, 3.3 Hz, 2 × C<u>H</u>^{Ar}), 5.98 (2H, dd, AB*X*YZ, J_{AX} = J_{XY} = 1.8 Hz, <u>H</u>CC<u>H</u>^{diene}), 3.66 (2H, m, ABX*Y*Z, 2 × C<u>H</u>^{bridge}), 3.45 (2H, dd, ABXY*Z*, J_{YZ} = 2.5 Hz, J_{BY} = 1.4 Hz, 2 × C<u>H</u>^{angular}), 1.55 (2H, dddd, *AB*XYZ, J_{AB} = 8.6 Hz, J_{AX} = 1.8 Hz, J_{BZ} = 1.4 Hz, $\Delta\nu_{AB}$ = 17.2 Hz, C<u>H</u>$_2^{bridge}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.97, 135.93, 135.86, 134.24, 126.98, 49.66, 49.63, 49.35.

(±)-*rel*-(1*R*,4a*S*,9a*R*)-1-Methyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione (5c). Quinone **1c** (208 mg, 1.32 mmol in CH_2Cl_2; 66 mg, 0.419 mmol in HFIP) and diene **2b** (0.26 mL, 2.61 mmol in CH_2Cl_2; 0.08 mL, 0.802 mmol in HFIP) were reacted following general procedure to give **5c** (300 mg, >98% in CH_2Cl_2; 96 mg, >98% in HFIP) as

a grey oil; R_f (7/3 cyclohex./AcOEt): 0.81; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09-8.00 (2H, m, 2 × C$\underline{H}^{Ar}$), 7.77-7.71 (2H, m, 2 × C$\underline{H}^{Ar}$), 5.76-5.65 (2H, m, $\underline{H}$CC$\underline{H}^{diene}$), 3.51 (1H, dd, *J* = 5.9, 5.8 Hz, MeCHC$\underline{H}^{angular}$), 3.43-3.38 (1H, m, $CH_2C\underline{H}^{angular}$), 2.85-2.75 (1H, m, ½ × C$\underline{H}_2$), 2.73-2.55 (1H, m, MeC$\underline{H}$), 2.26-2.18 (1H, m, ½ × C$\underline{H}_2$), 0.84 (3H, d, *J* = 7.4 Hz, $\underline{Me}$CH); ^{13}C NMR (125 MHz, $CDCl_3$) 199.14, 198.35, 135.90, 135.43, 134.33, 134.24, 131.29, 126.76, 126.63, 123.65, 50.90, 46.03, 23.09, 18.49.

(4a*R*,9a*S*)-2,3-Dimethyl-1,4,4a,9a-tetrahydroanthracene-9,10-dione (6c). Quinone **1c** (196 mg, 1.24 mmol in CH_2Cl_2; 56 mg, 0.354 mmol in HFIP) and diene **2c** (0.28 mL, 2.47 mmol in CH_2Cl_2; 0.08 mL, 0.707 mmol in HFIP) were reacted following general procedure. The crude product was purified by flash chromatography on silica gel (9/1 cyclohex./AcOEt) to give **6c** (176 mg, 59% in CH_2Cl_2; 81 mg, 95% in HFIP) as a grey powder; R_f (7/3 cyclohex./AcOEt): 0.70; m_p: 146-149°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (2H, dd, *J* = 5.8, 3.3 Hz, 2 × C$\underline{H}^{Ar}$), 7.73 (2H, dd, *J* = 5.8, 3.3 Hz, 2 × C$\underline{H}^{Ar}$), 3.40-3.29 (2H, m, 2 × C$\underline{H}^{angular}$), 2.53-2.05 (4H, m, 2 × C$\underline{H}_2$), 1.64 (6H, s, 2 × $\underline{Me}$); ^{13}C NMR (125 MHz, $CDCl_3$) 198.55, 134.37, 134.22, 126.97, 123.60, 47.48, 30.79, 19.04.

(±)-*rel*-(1*R*,4*S*,4a*R*,8a*S*)-4a,6,7-Trimethyl-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (3d). Quinone **1d** (118 mg, 0.783 mmol in CH_2Cl_2; 52 mg, 0.345 mmol in HFIP) and diene **2a** (0.13 mL, 1.55 mmol in CH_2Cl_2; 0.06 mL, 0.713 mmol in HFIP) were reacted following general procedure. The crude product was purified by flash chromatography on silica gel (95/5 PhMe/AcOEt) to give **3d** (101 mg, 60% in CH_2Cl_2; 75 mg, >98% in HFIP) as a pale yellow oil; R_f (8/2 PhMe/AcOEt): 0.73; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06 (1H, dd, *J* = 5.6, 2.9 Hz, $\underline{H}$CCH^{diene}), 5.92 (1H, dd, *J* = 5.6, 2.8 Hz, HCC$\underline{H}^{diene}$), 3.43-3.36 (1H, m, C$\underline{H}^{bridge}$), 3.09-3.02 (1H, m, C$\underline{H}^{bridge}$), 2.81 (1H, d, *J* = 3.9 Hz, C$\underline{H}^{angular}$), 1.91 (6H, s, $\underline{Me}$CC$\underline{Me}^{quinone}$), 1.54 (2H, dd, *AB*, J_{AB} = 9.0 Hz, $\Delta\nu_{AB}$ = 78.9 Hz, C$\underline{H}_2^{bridge}$), 1.43 (3H, s, $\underline{Me}^{angular}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.48, 199.14, 147.06, 146.82, 138.28, 134.82, 56.96, 53.68, 52.47, 49.09, 46.40, 26.92, 13.50, 13.12; HRMS (ESI+): for $[M+H]^+$ calc.: 235.1329, found: 235.1322.

(±)-*rel*-(4a*R*,8*S*,8a*S*)-2,3,4a,8-Tetramethyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (5d). Quinone **1d** (215 mg, 1.43 mmol in CH_2Cl_2; 86 mg, 0.569 mmol in HFIP) and diene **2b** (0.29 mL, 2.91 mmol in CH_2Cl_2; 0.11 mL, 1.10 mmol in HFIP) were reacted following general procedure. The crude product was purified by flash chromatography on silica gel (8/2/0.1 cyclohex./CH_2Cl_2/acetone) to give **5d** (97 mg, 31% in CH_2Cl_2; 124 mg, >98% in HFIP) as a pale yellow oil; R_f (6/4/0.2 CH_2Cl_2/cyclohex./acetone): 0.70; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.67-5.52 (2H, m, $\underline{H}$CC$\underline{H}^{diene}$), 2.93-2.82 (2H, m, ½ × C$\underline{H}_2$ + C$\underline{H}^{angular}$), 2.16-2.09 (1H, m, MeC$\underline{H}$), 2.09-2.03 (1H, m, ½ × C$\underline{H}_2$), 2.00 (3H, q, *J* = 1.0 Hz, $\underline{Me}$CCMe), 1.98 (3H, q, *J* = 1.0 Hz, MeCC$\underline{Me}$), 1.40 (3H, s, $\underline{Me}^{angular}$), 0.72 (3H, d, *J* = 7.3 Hz, $\underline{Me}$CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.25, 199.43, 146.07, 144.75, 130.17, 122.79, 50.34, 50.02, 39.56, 24.29, 20.93, 19.35, 13.36, 12.80; HRMS (ESI+): for $[M+H]^+$ calc.: 219.1385, found: 219.1380.

(±)-*cis*-2,3,4a,6,7-Pentamethyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (6d). Quinone **1d** (176 mg, 1.17 mmol in HFIP) and diene **2c** (0.26 mL, 2.30 mmol in HFIP) were reacted following general procedure. The crude product was purified by flash chromatography on silica gel (99/1 cyclohex./AcOEt) to give **6d** (269 mg, >98% in HFIP) as a pale yellow oil; R_f (8/2 cyclohex./AcOEt): 0.66; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.81 (1H, t, *J* = 5.9 Hz, C$\underline{H}^{angular}$), 2.52-2.43 (1H, m, ½ × CHC$\underline{H}_2$), 2.40 (1H, d, *J* = 17.2 Hz, ½ × MeCC$\underline{H}_2$), 2.11-2.03 (1H, m, ½ × CHC$\underline{H}_2$), 1.97 (6H, s, $\underline{Me}$CC$\underline{Me}^{quinone}$), 1.66 (1H, d, *J* = 17.2 Hz, ½ × MeCC$\underline{H}_2$), 1.62 (3H, s, $\underline{Me}$CCMe^{diene}), 1.57 (3H, s, MeCC$\underline{Me}^{diene}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.70, 200.20, 143.37, 142.56, 122.97, 122.87, 52.80, 48.16, 39.18, 30.17, 23.39, 19.08, 18.72, 13.26, 13.02; HRMS (ESI+): for $[M++H]^+$ calc.: 233.1542, found: 233.1536.

(±)-*rel*-(1*R*,4*S*,4a*R*,8a*S*)-6,7-Dimethoxy-4a-methyl-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (3e). Quinone **1e** (43 mg, 0.236 mmol in CH_2Cl_2; 50 mg, 0.276 mmol in HFIP) and diene **2a** (0.04 mL, 0.476 mmol in CH_2Cl_2; 0.05 mL, 0.595 mmol in HFIP) were reacted following the general procedure to give **3e** (58 mg, 98% in CH_2Cl_2; 68 mg, >98% in HFIP) as a yellow waxy solid; R_f (7/3 cyclohex./AcOEt): 0.38; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.09 (1H, dd, *J* = 5.7, 2.9 Hz, $\underline{H}$CCH^{diene}), 5.95 (1H, dd, *J* = 5.7, 2.8 Hz, HCC$\underline{H}^{diene}$), 3.88 (3H, s,

MeOCCOMe), 3.87 (3H, s, MeOCCOMe), 3.36 (1H, s(br), angularHCCH^{bridge}), 3.02 (1H, s(br), ^{angular}MeCCH^{bridge}), 2.78 (1H, d, *J* = 3.9 Hz, CH^{angular}), 1.52 (2H, ddd, *AB*XY, J_{AB} = 9.2 Hz, J_{BX} = J_{BY} = 1.7 Hz, $\Delta\nu_{AB}$ = 60.3 Hz, CH$_2^{bridge}$), 1.43 (3H, s, Me^{angular}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.49, 194.89, 150.60, 150.54, 138.15, 134.52, 60.66, 60.64, 57.05, 53.41, 52.56, 48.83, 46.34, 26.51.

(±)-*rel*-(4a*R*,8*S*,8a*S*)-2,3-Dimethoxy-4a,8-dimethyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (5e). Quinone **1e** (150 mg, 0.821 mmol in CH_2Cl_2; 173 mg, 0.947 mmol in HFIP) and diene **2b** (0.13 mL, 1.65 mmol in CH_2Cl_2; 0.15 mL, 1.90 mmol in HFIP) were reacted following general procedure. The crude product was purified by flash chromatography on silica gel (5/5 cyclohex./CH_2Cl_2) to give **5e** (47 mg, 23% in CH_2Cl_2; 225 mg, 95% in HFIP) as a yellow oil; R_f (5/5/0.2 cyclohex./CH_2Cl_2/acetone): 0.46; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.66-5.53 (2H, m, HCCH^{diene}), 3.98 (3H, s, MeO), 3.97 (3H, s, MeO), 2.97-2.86 (1H, m, ½ × CH$_2$), 2.80 (1H, dd, *J* = 7.3, 1.8 Hz, CH^{angular}), 2.21-2.12 (1H, m, MeCH), 2.10-2.02 (1H, m, ½ × CH$_2$), 1.41 (3H, s, Me^{angular}), 0.85 (3H, d, *J* = 7.3 Hz, MeCH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.53, 194.88, 150.42, 148.92, 130.09, 122.48, 60.87, 60.51, 49.54, 49.08, 39.55, 23.99, 20.48, 19.36; HRMS (ESI+): for $[M+H]^+$ calc.: 251.1283, found: 251.1278.

(±)-*cis*-2,3-Dimethoxy-4a,6,7-trimethyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (6e). Quinone **1e** (245 mg, 1.35 mmol in HFIP) and diene **2c** (0.30 mL, 2.65 mmol in HFIP) were reacted following general procedure. The crude product was purified by flash chromatography on silica gel (9/1 cyclohex./AcOEt) to give **6e** (246 mg, 70% in HFIP) as a yellow oil; R_f (5/5 PhMe/AcOEt): 0.78; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.96 (3H, s, MeO), 3.95 (3H, s, MeO), 2.76 (1H, ddd, *J* = 6.1, 5.2, 0.6 Hz, CH^{angular}), 2.56-2.47 (1H, m, ½ × CHCH$_2$), 2.43 (1H, d, *J* = 17.2 Hz, ½ × MeCCH$_2$), 2.16-2.02 (1H, m, ½ × CHCH$_2$), 1.73-1.67 (1H, m, ½ × MeCCH$_2$), 1.63-1.59 (3H, m, MeCCMe), 1.58-1.54 (3H, m, MeCCMe), 1.29 (3H, s, Me^{angular}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.77, 195.94, 147.70, 147.08, 122.84, 122.73, 60.72, 60.62, 51.80, 47.41, 39.13, 29.89, 23.28, 19.06, 18.70; HRMS (ESI+): for $[M+H]^+$ calc.: 265.1440, found: 265.1434.

(±)-*rel*-(1*R*,4*S*,4a*S*,8a*R*)-4a-Bromo-6-methoxy-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (3f). Quinone **1f** (200 mg, 0.923 mmol in CH_2Cl_2; 50 mg, 0.230 mmol in HFIP) and diene **2a** (0.16 mL, 1.90 mmol in CH_2Cl_2; 0.04 mL, 0.476 mmol in HFIP) were reacted following standard procedure to give **3f** (261 mg, >98% in CH_2Cl_2; 65 mg, >98% in HFIP) as a white powder; R_f (8/2 PhMe/AcOEt): 0.45; m_p: 103-105°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.18 (1H, dd, *J* = 5.6, 2.8 Hz, HCCH^{diene}), 6.06 (1H, dd, *J* = 5.6, 3.0 Hz, HCCH^{diene}), 5.97 (1H, s, MeOCCH), 3.79 (3H, s, MeO), 3.75-3.70 (1H, m, BrCCH^{bridge}), 3.67 (1H, d, *J* = 3.9 Hz, CH^{angular}), 3.56-3.48 (1H, m, HCCH^{bridge}), 2.06 (2H, ddd, *AB*X, J_{AX} = 1.3 Hz, J_{BX} = 1.8 Hz, J_{AB} = 9.4 Hz, $\Delta\nu_{AB}$ = 136.6 Hz, CH$_2^{bridge}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.58, 194.98, 171.16, 141.45, 141.42, 137.20, 136.45, 54.26, 53.37, 52.07, 48.33, 48.10; HRMS (ESI+): for $[M+H]^+$ calc.: 282.9964, found: 282.9954. Crystals for compound **3f** were obtained by slow evaporation from dichloromethane at room temperature.

(±)-*rel*-(1*R*,4*S*,4a*S*,8a*R*)-4a-Bromo-6-methoxy-8a-methyl-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (3g). Quinone **1g** (209 mg, 0.903 mmol in HFIP) and diene **2a** (0.15 mL, 1.78 mmol in HFIP) were reacted following general procedure to give **3g** (265 mg, >98% in HFIP) as a grey powder; R_f (7/3 cyclohex./AcOEt): 0.43; m_p: 93-96°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.24 (1H, dd, *J* = 5.5, 2.8 Hz, HCCH^{diene}), 5.96 (1H, dd, *J* = 5.5, 3.1 Hz, HCCH^{diene}), 5.88 (1H, s, MeOCCH), 3.79 (3H, s, MeO), 3.72-3.66 (1H, m, BrCCH^{bridge}), 3.14-3.08 (1H, m, MeCCH^{bridge}), 2.06 (2H, ddd, *AB*XY, J_{AX} = 1.6 Hz, J_{BY} = 1.7 Hz, J_{AB} = 9.7 Hz, $\Delta\nu_{AB}$ = 189.9 Hz, CH$_2^{bridge}$), 1.69 (3H, s, Me^{angular}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.62, 187.17, 162.47, 140.89, 134.63, 113.06, 71.17, 59.25, 56.86, 56.31, 52.84, 44.75, 30.83. HRMS (ESI+): for $[M+H]^+$ calc.: 299.0283, found: 299.0277. Crystals for compounds **3g** were obtained by slow evaporation from dichloromethane at room temperature.

(±)-*rel*-(4a*R*,8*R*,8a*S*)-8a-Bromo-2-methoxy-4a,8-dimethyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (5g). Quinone **1g** (207 mg, 0.895 mmol in CH_2Cl_2; 208 mg, 0.902 mmol in HFIP) and diene **2b** (0.14 mL, 1.77 mmol in CH_2Cl_2; 0.14 mL, 1.77 mmol in HFIP) were reacted following general procedure to give **5g** (268 mg, >98% in

HFIP) as a yellowish oil. The conversion being too low in dichloromethane (13%), we did not try to isolate the adduct; R_f (7/3 cyclohex./AcOEt): 0.64; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.64 (1H, s, MeOC<u>H</u>), 5.63-5.51 (2H, m, <u>H</u>CC<u>H</u>^{diene}), 3.80 (3H, s, <u>Me</u>O), 2.99-2.88 (1H, m, MeC<u>H</u>), 2.54-2.16 (2H, m, C<u>H$_2$</u>), 1.56 (3H, d, *J* = 0.8 Hz, <u>Me</u>^{angular}), 1.53 (3H, d, *J* = 7.4 Hz, <u>Me</u>CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.34, 186.49, 159.87, 130.15, 122.17, 105.96, 74.92, 56.67, 55.05, 38.68, 36.40, 17.31, 16.59; HRMS (ESI+): for $[M+H]^+$ calc.: 299.0283, found: 299.0277.

(±)-*cis*-8a-Bromo-2-methoxy-4a,6,7-trimethyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (6g). Quinone **1g** (106 mg, 0.458 mmol in HFIP) and diene **2c** (0.10 mL, 0.884 mmol in HFIP) were reacted following general procedure. The crude product was purified by flash chromatography on on silica gel (9/1 cyclohex./AcOEt) to give **6g** (52 mg, 36% in HFIP) as a light yellow oil; R_f (7/3 cyclohex./AcOEt): 0.59; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.71 (1H, s, MeOC<u>H</u>), 3.81 (3H, s, <u>Me</u>O), 3.18 (1H, d, *J* = 17.3 Hz, ½ × BrCC<u>H$_2$</u>), 2.67-2.59 (1H, m, ½ × BrCC<u>H$_2$</u>), 2.46 (1H, d, *J* = 17.5 Hz, ½ × ^{angular}MeCC<u>H$_2$</u>), 2.02 (1H, d, *J* = 17.5 Hz, ½ × ^{angular}MeCC<u>H$_2$</u>), 1.67 (3H, s, <u>Me</u>CCMe), 1.51 (3H, s, MeCC<u>Me</u>), 1.49 (3H, s, <u>Me</u>^{angular}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.85, 185.75, 159.26, 124.31, 122.11, 107.26, 69.31, 56.60, 53.21, 42.26, 38.59, 18.50, 18.48, 18.02; HRMS (ESI+): for $[M+H]^+$ calc.: 313.0439, found: 313.0435.

Methyl (±)-*rel*-(1*R*,4*S*,4a*S*,8a*S*)-5,8-dioxo-1,5,8,8a-tetrahydro-1,4-methanonaphthalene-4a(4*H*)-carboxylate (3h). Quinone **1h** (230 mg, 1.38 mmol in CH_2Cl_2; 55 mg, 0.333 mmol in HFIP) and diene **2a** (0.23 mL, 2.74 mmol in CH_2Cl_2; 0.06 mL, 0.712 mmol in HFIP) were reacted following general procedure. The crude product was purified by flash chromatography on silica gel (9/1 cyclohex./AcOEt) to give **3h** (281 mg, 88% in CH_2Cl_2; 71 mg, 92% in HFIP) as a light yellow oil; R_f (7/3 cyclohex./AcOEt): 0.47; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (2H, dd, *AB*, J_{AB} = 10.4 Hz, $\Delta\nu_{AB}$ = 4.6 Hz, <u>H</u>CC<u>H</u>^{quinone}), 6.12 (1H, dd, *J* = 5.6, 2.8 Hz, <u>H</u>CCH^{diene}), 6.09 (1H, dd, *J* = 5.6, 2.9 Hz, HCC<u>H</u>^{diene}), 3.82-3.76 (1H, m, MeO$_2$CCC<u>H</u>^{bridge}), 3.73 (3H, s, CO$_2$<u>Me</u>), 3.52-3.44 (1H, m, C<u>H</u>^{bridge}), 3.38 (1H, d, *J* = 4.0 Hz, C<u>H</u>^{angular}), 1.65 (2H, dddd, *AB*XY, J_{AB} = 9.3 Hz, J_{AX} = J_{AY} = 1.4Hz, J_{BX} = J_{BY} = 1.7 Hz, $\Delta\nu_{AB}$ = 21.9 Hz, C<u>H$_2$</u>^{bridge}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.58, 194.98, 171.16, 141.45, 141.42, 137.20, 136.45, 63.27, 54.26, 53.37, 52.07, 48.33, 48.10.

Methyl (±)-*rel*-(4a*R*,5*S*,8a*R*)-5-methyl-1,4-dioxo-1,5,8,8a-tetrahydronaphthalene-4a(4*H*)-carboxylate (5h). Quinone **1h** (213 mg, 1.29 mmol in CH_2Cl_2; 67 mg, 0.403 mmol in HFIP) and diene **2b** (0.26 mL, 2.61 mmol in CH_2Cl_2; 0.08 mL, 0.802 mmol in HFIP) were reacted following standard procedure to give **5h** (300 mg, >98% in CH_2Cl_2; 94 mg, >98% in HFIP) as a light yellow oil; R_f (7/3 cyclohex./AcOEt): 0.46; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (2H, dd, *AB*, J_{AB} = 10.3 Hz, $\Delta\nu_{AB}$ = 16.6 Hz, <u>H</u>CC<u>H</u>^{quinone}), 5.67-5.54 (2H, m, <u>H</u>CC<u>H</u>^{diene}), 3.78 (3H, s, CO$_2$<u>Me</u>), 3.73 (1H, dd, *J* = 7.3, 4.3 Hz, C<u>H</u>^{angular}), 3.07-2.94 (1H, m, MeC<u>H</u>), 2.70-2.04 (2H, m, C<u>H$_2$</u>), 0.99 (3H, d, *J* = 7.5 Hz, <u>Me</u>CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.74, 196.65, 170.75, 140.29, 140.17, 130.55, 122.65, 63.13, 53.36, 48.20, 34.65, 22.16, 18.42.

Methyl (±)-*cis*-6,7-dimethyl-1,4-dioxo-1,5,8,8a-tetrahydronaphthalene-4a(4*H*)-carboxylate (6h). Quinone **1h** (216 mg, 1.30 mmol in CH_2Cl_2; 52 mg, 0.312 mmol in HFIP) and diene **2c** (0.30 mL, 2.65 mmol in CH_2Cl_2; 0.07 mL, 0.619 mmol in HFIP) were reacted following the general procedure to give **6h** (321 mg, >98% in CH_2Cl_2; 76 mg, 98% in HFIP) as a grey powder; R_f (7/3 cyclohex./AcOEt): 0.46; m_p: 104-107°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.66 (2H, dd, *AB*, J_{AB} = 10.5 Hz, $\Delta\nu_{AB}$ = 4.8 Hz, <u>H</u>CC<u>H</u>^{quinone}), 3.74 (3H, s, CO$_2$<u>Me</u>), 3.54 (1H, dd, *J* = 7.2, 6.5 Hz, C<u>H</u>^{angular}), 2.62-2.54 (1H, m, ½ × MeO$_2$CCC<u>H$_2$</u>), 2.38-2.30 (2H, m, ½ × MeO$_2$CCC<u>H$_2$</u> + ½ × HCC<u>H$_2$</u>), 2.16-2.01 (1H, m, ½ × HCC<u>H$_2$</u>), 1.63 (3H, s(br), <u>Me</u>CCMe), 1.59 (3H, s(br), MeCC<u>Me</u>); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.15, 195.17, 170.65, 139.63, 138.07, 123.08, 122.78, 60.84, 53.32, 49.04, 33.96, 30.21, 18.83, 18.77.

Methyl (±)-*rel*-(1*R*,4*S*,4a*S*,9a*S*)-9,10-dioxo-1,9,9a,10-tetrahydro-1,4-methanoanthracene-4a(4*H*)-carboxylate (3i). Quinone **1i** (205 mg, 0.949 mmol in CH_2Cl_2; 51 mg, 0.237 mmol in HFIP) and diene **2a** (0.16 mL, 1.90 mmol in CH_2Cl_2; 0.04 mL, 0.476 mmol in HFIP) were reacted following general procedure. The crude product was

purified by flash chromatography on silica gel (8/2 cyclohex./AcOEt) to give **3i** (256 mg, 95% in CH_2Cl_2; 65 mg, 97% in HFIP) as a light yellow visquous oil; R_f (7/3 cyclohex./AcOEt): 0.55; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09-8.00 (2H, m, 2 × C$\underline{H}^{Ar}$), 7.75-7.69 (2H, m, 2 × C$\underline{H}^{Ar}$), 6.03 (2H, ddd, *AB*XY, J_{AB} = 14.0 Hz, J_{AX} = 5.6 Hz, J_{BY} = 2.7 Hz, $\Delta\nu_{AB}$ = 13.1 Hz, $\underline{H}CC\underline{H}^{diene}$), 3.95-3.88 (1H, m, $^{angular}HCC\underline{H}$), 3.70 (3H, s, $CO_2\underline{Me}$), 3.63-3.49 (2H, m, C$\underline{H}^{angular}$ + $MeO_2CCC\underline{H}^{bridge}$), 1.68 (2H, dddd, *A'B'*XY, $J_{A'B'}$ = 9.2 Hz, $J_{A'X'} = J_{A'Y} = J_{B'X} = J_{B'Y}$ = 1.5 Hz, $\Delta\nu_{A'B'}$ = 53.5 Hz, $C\underline{H}_2^{bridge}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.92, 193.68, 171.78, 137.39, 136.61, 135.27, 134.99, 134.60, 134.48, 127.49, 127.16, 64.37, 55.29, 53.25, 52.80, 49.05, 48.63; HRMS (ESI+): for $[M+H]^+$ calc.: 283.0965, found: 283.0961.

Methyl (±)-*rel*-(4*R*,4a*S*,9a*S*)-4-methyl-9,10-dioxo-1,9,9a,10-tetrahydroanthracene-4a(4*H*)-carboxylate (5i). Quinone **1i** (205 mg, 0.948 mmol in CH_2Cl_2; 62 mg, 0.286 mmol in HFIP) and diene **2b** (0.15 mL, 1.90 mmol in CH_2Cl_2; 0.06 mL, 0.602 mmol in HFIP) were reacted following general procedure to give **5i** (266 mg, >98% in CH_2Cl_2; 80 mg, >98% in HFIP) as a grey powder; R_f (7/3 cyclohex./AcOEt): 0.71; m_p: 98-101°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10-8.01 (2H, m, 2 × C$\underline{H}^{Ar}$), 7.79-7.72 (2H, m, 2 × C$\underline{H}^{Ar}$), 5.73-5.60 (2H, m, $\underline{H}CC\underline{H}^{diene}$), 3.89 (1H, dd, *J* = 6.8, 4.6 Hz, C$\underline{H}^{angular}$), 3.74 (3H, s, $CO_2\underline{Me}$), 3.16-3.04 (1H, m, MeC$\underline{H}$), 2.80-2.12 (2H, m, $C\underline{H}_2$), 0.89 (3H, d, *J* = 7.5 Hz, $\underline{Me}$CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.34, 194.95, 171.11, 135.01, 134.77, 134.67, 134.54, 130.85, 127.22, 126.64, 122.80, 63.23, 53.24, 48.59, 34.83, 22.64, 18.04. Crystals for compounds **5i** were obtained by slow evaporation from dichloromethane at room temperature.

Methyl (±)-*cis*-2,3-dimethyl-9,10-dioxo-1,9,9a,10-tetrahydroanthracene-4a(4*H*)-carboxylate (6i). Quinone **1i** (217 mg, 1.00 mmol in CH_2Cl_2; 63 mg, 0.291 mmol in HFIP) and diene **2c** (0.23 mL, 2.03 mmol in CH_2Cl_2; 0.07 mL, 0.619 mmol in HFIP) were reacted following general procedure to give **6i** (297 mg, >98% in CH_2Cl_2; 85 mg, >98% in HFIP) as a light yellow oil; R_f (7/3 cyclohex./AcOEt): 0.75; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10-8.00 (2H, m, 2 × C$\underline{H}^{Ar}$), 7.80-7.70 (2H, m, 2 × C$\underline{H}^{Ar}$), 3.69 (3H, s, $CO_2\underline{Me}$), 2.77-2.64 (1H, m, ½ × $MeO_2CCC\underline{H}_2$), 2.47-2.35 (2H, m, ½ × $MeO_2CCC\underline{H}_2$ + ½ × $HCC\underline{H}_2$), 2.23-2.09 (1H, m, ½ × $HCC\underline{H}_2$), 1.66 (3H, s(br), $\underline{Me}$CCMe), 1.61 (3H, s(br), MeCC$\underline{Me}$); ^{13}C NMR (125MHz, $CDCl_3$) 196.35, 193.67, 171.01, 134.88, 134.46, 133.73, 133.19, 127.43, 127.16, 123.18, 123.05, 61.01, 53.22, 49.37, 34.22, 30.66, 18.90, 18.82; HRMS (ESI+): for $[M+H]^+$ calc.: 299.1283, found: 299.1278.

Methyl (±)-*rel*-(1*R*,4*S*,4a*S*,8a*S*)-6-methoxy-8a-methyl-5,8-dioxo1,5,8,8a-tetrahydro-1,4-methanonaphthalene-4a(4*H*)-carboxylate (3j). Quinone **1j** (130 mg, 0.619 mmol in CH_2Cl_2; 118 mg, 0.561 mmol in HFIP) and diene **2a** (0.10 mL, 1.19 mmol in CH_2Cl_2; 0.10 mL, 1.19 mmol in HFIP) were reacted following the general procedure. After evaporation of the solvent, the crude mixture was triturated with diethyl ether, filtered and dried under vacuum to give **3i** (142 mg, 85% in CH_2Cl_2; 125 mg, 82% in HFIP) as a white powder; R_f (7/3 cyclohex./AcOEt): 0.55; m_p: 164-166°C (decomposition); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.18 (1H, dd, *J* = 5.7, 3.0 Hz, $\underline{H}CCH$), 6.02 (1H, dd, *J* = 5.7, 2.9 Hz, $HCC\underline{H}$), 5.88 (1H, s, MeOCC$\underline{H}$), 3.77 (3H, s, HCCO$\underline{Me}$), 3.70 (3H, s, $CO_2\underline{Me}$), 3.67-3.64 (1H, m, C$\underline{H}^{bridge}$), 3.06-3.02 (1H, m, C$\underline{H}^{bridge}$), 2.10 (1H, dt, *J* = 9.7, 1.4 Hz, ½ × $C\underline{H}_2^{bridge}$), 1.60 (1H, dt, *J* = 9.7, 1.7 Hz, ½ × $C\underline{H}_2^{bridge}$), 1.40 (3H, s, $\underline{Me}^{angular}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.20, 191.73, 171.31, 162.42, 140.02, 136.05, 113.10, 66.95, 57.48, 56.62, 54.06, 52.77, 52.61, 45.79, 23.64; HRMS (ESI+): for $[M+Na]^+$ calc.: 299.0890, found: 299.0878.

Methyl(±)-*rel*-(4a*R*,5*S*,8a*R*)-3-methoxy-5,8a-dimethyl-1,4-dioxo-1,5,8,8a-tetrahydronaphthalene-4a(4*H*)-carboxylate (5j). Quinone **1j** (127 mg, 0.605 mmol in HFIP) and diene **2b** (0.12 mL, 1.20 mmol in HFIP) were reacted following the general procedure. After evaporation of the solvent, the crude mixture was triturated with diethyl ether, filtered and dried under vacuum to give **5j** (132 mg, 79% in HFIP) as a white powder; R_f (5/5/0.5 cyclohex./CH_2Cl_2/acetone): 0.47; m_p: 133-134°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68 (1H, s, MeOCC$\underline{H}$), 5.66 (1H, ddt, *J* = 10.1, 2.5, 1.8 Hz, $HCC\underline{H}^{diene}$), 5.52 (1H, ddt, *J* = 10.1, 5.1, 2.6 Hz, $\underline{H}CCH^{diene}$), 3.79 (3H, s, HCCO$\underline{Me}$), 3.69 (3H, s, $CO_2\underline{Me}$), 2.87-2.78 (1H, m, MeC$\underline{H}$), 2.35-2.28 (1H, m, ½ × $C\underline{H}_2$), 1.97 (1H, appearing as a ddt, *J* = 18.4, 4.9, 2.0 Hz, ½ × $C\underline{H}_2$), 1.52 (3H, s, $\underline{Me}^{angular}$), 1.33 (3H, d, *J* = 7.5, $\underline{Me}$CH); ^{13}C NMR (125 MHz, $CDCl_3$)

δ 199.95, 189.79, 170.88, 162.98, 130.52, 121.63, 106.65, 65.19, 56.75, 52.73, 52.61, 37.41, 33.43, 17.01, 16.05; HRMS (ESI+): for $[M+Na]^+$ calc.: 301.1046, found: 301.1037. Crystals for compounds **5j** were obtained by slow evaporation from dichloromethane at room temperature.

Methyl (±)-*cis*-6,7,8a-trimethyl-1,4-dioxo-1,5,8,8a-tetrahydronaphthalene-4a(4*H*)-carboxylate (6j). Quinone **1j** (139 mg, 0.663 mmol in HFIP) and diene **2c** (0.15 mL, 1.33 mmol in HFIP) were reacted following the general procedure. After evaporation of the solvent, the crude mixture was triturated with diethyl ether, filtered and dried under vacuum to give **6j** (159 mg, 82% in HFIP) as a white powder; R_f (5/5/0.5 cyclohex./CH_2Cl_2/acetone): 0.47; m_p: 112-114°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91 (1H, s, MeOCC<u>H</u>), 3.75 (3H, s, HCCO<u>Me</u>), 3.66 (3H, s, CO_2<u>Me</u>), 3.07 (1H, d, *J* = 17.8 Hz, ½ × MeO_2CCC<u>H_2</u>), 2.38-2.24 (2H, m, ½ × MeO_2CCC<u>H_2</u> + ½ × ^{angular}MeCC<u>H_2</u>), 1.79 (1H, d, *J* = 17.7 Hz, ½ × ^{angular}MeCC<u>H_2</u>), 1.69 (3H, s, MeCC<u>Me</u>^{diene}), 1.52 (3H, s, <u>Me</u>CCMe^{diene}), 1.29 (3H, s, <u>Me</u>^{angular}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.59, 188.99, 169.52, 158.97, 122.76, 121.68, 110.55, 65.34, 56.41, 53.34, 50.57, 42.74, 31.66, 18.75, 18.72, 17.62; HRMS (ESI+): for $[M+Na]^+$ calc.: 315.1203, found: 315.1200.

(1*R*,4*S*,4a*S*,8a*R*)-7-Methoxy-4a-((*S*)-*p*-tolylsulfinyl)-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (α-3m). Quinone **1l** (66 mg, 0.238 mmol in HFIP) and diene **2a** (0.04 mL, 0.476 mmol in HFIP) were reacted following the general procedure to give the crude product **α-3l**; R_f (8/2 PhMe/AcOEt): 0.68; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (2H, d, *J* = 8.4 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 7.20 (2H, d, *J* = 8.4 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 6.24 (1H, dd, *J* = 5.5 Hz, 3.0 Hz, <u>H</u>CCH^{diene}), 6.18 (1H, dd, *J* = 5.5, 2.8 Hz, HCC<u>H</u>^{diene}), 5.33 (1H, s, MeOC<u>H</u>), 3.84-3.81 (1H, m, C<u>H</u>^{bridge}), 3.75 (1H, s, C<u>H</u>^{angular}), 3.56-3.53 (1H, m, C<u>H</u>^{bridge}), 3.39 (3H, s, <u>Me</u>O), 2.34 (3H, s, Ar<u>Me</u>$^{p\text{-tolyl}}$), 2.30-2.27 (1H, m, ½ × C<u>H_2</u>^{bridge}), 1.51-1.40 (1H, m, ½ × C<u>H_2</u>^{bridge}).

(+)-(1*S*,4*R*)-6-Methoxy-1,4-dihydro-1,4-methanonaphthalene-5,8-dione (α-4m). HFIP was removed *in vacuo* and replaced by the same volume of CH_2Cl_2 and the adduct **α-3l** was allowed to undergo a sulfoxide elimination overnight. The crude product was purified by flash chromatography on demetallated silica gel (9/1 cyclohex./AcOEt) to give **α-4l** (22 mg, 46% in HFIP) as a light yellow powder; R_f (6/4 cyclohex./AcOEt): 0.12; m_p: 110-113°C (decomposition); $[\alpha]_D^{20}$ (c = 0.50, $CHCl_3$): +3.1°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89-6.80 (2H, m, <u>H</u>CC<u>H</u>), 5.69 (1H, s, MeOCC<u>H</u>), 4.12-4.09 (1H, m, C<u>H</u>^{bridge}), 4.06-4.09 (1H, m, C<u>H</u>^{bridge}), 3.78 (3H, s, <u>Me</u>O), 2.36-2.21 (2H, m, C<u>H_2</u>^{bridge}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.26, 178.31, 162.61, 159.31, 158.37, 142.74, 142.53, 106.03, 73.83, 56.67, 48.65, 48.34. HRMS (ESI+): for $[M+H]^+$ calc.:203.0708, found: 203.0703.

(1*S*,4*R*,4a*R*,8a*S*)-7-Methoxy-4a-((*S*)-*p*-tolylsulfinyl)-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (β-3m). Quinone **1l** (154 mg, 0.558 mmol in CH_2Cl_2) and diene **2a** (0.10 mL, 1.19 mmol in CH_2Cl_2) were reacted following the general procedure to give the crude product **β-3l;** R_f (3/7/0.2 CH_2Cl_2/cyclohex./acetone): 0.27; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (2H, d, *J* = 8.4 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 7.20 (2H, d, *J* = 8.4 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 5.33 (1H, s, MeOCC<u>H</u>), 6.23 (1H, dd, *J* = 5.3, 3.1 Hz, <u>H</u>CCH^{diene}), 6.17 (1H, dd, *J* = 5.3, 3.2 Hz, HCC<u>H</u>^{diene}), 3.84-3.82 (1H, m, C<u>H</u>^{bridge}), 3.77 (1H, d, *J* = 4.4 Hz, C<u>H</u>^{angular}), 3.56-3.53 (1H, m, C<u>H</u>^{bridge}), 3.38 (3H, s, <u>Me</u>O), 2.33 (3H, s, Ar<u>Me</u>$^{p\text{-tolyl}}$), 2.32-2.29 (1H, m, ½ × C<u>H_2</u>^{bridge}), 1.49-4.45 (1H, m, ½ × C<u>H_2</u>^{bridge}).

(-)-(1*R*,4*S*)-6-Methoxy-1,4-dihydro-1,4-methanonaphthalene-5,8-dione (β-4m). Once the cycloaddition was over, the adduct **β-3l** was allowed to undergo the sulfoxide elimination overnight. The solvent was evaporated and the crude product purified by flash chromatography on demetallated silica gel (9/1 cyclohex./AcOEt) to give **β-4l** (41 mg, 36% in CH_2Cl_2) as a light yellow powder; R_f (6/4 cyclohex./AcOEt): 0.12; m_p: 109-111°C (decomposition) $[\alpha]_D^{20}$ (c = 0.50, $CHCl_3$): -3.0°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89-6.80 (2H, m, <u>H</u>CC<u>H</u>), 5.69 (1H, s, MeOCC<u>H</u>), 4.12-4.09 (1H, m, C<u>H</u>^{bridge}), 4.06-4.09 (1H, m, C<u>H</u>^{bridge}), 3.78 (3H, s, <u>Me</u>O), 2.36-2.21 (2H, m, C<u>H_2</u>^{bridge}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.26, 178.31, 162.61, 159.31, 158.37, 142.74, 142.53, 106.03, 73.83, 56.67, 48.65, 48.34. HRMS (ESI+): for $[M+H]^+$ calc.:203.0708, found: 203.0712.

2-Methoxy-5-methyl-5,8-dihydronaphthalene-1,4-dione (α/β-7m). Quinone **1l** (84 mg, 0.304 mmol in CH_2Cl_2; 90 mg, 0.326 mmol in HFIP) and diene **2b** (0.06 mL, 0.602 mmol in CH_2Cl_2; 0.06 mL, 0.602 mmol in HFIP) were

reacted following general procedure. The crude product was purified by flash chromatography on demetallated silica gel (95/5 cyclohex./AcOEt) to give **7l** (33 mg, 53% in CH_2Cl_2; 42 mg, 63% in HFIP) as a waxy orange solid; R_f (7/3 cyclohex./AcOEt): 0.57; $[\alpha]_D^{20}$ (c = 0.50, $CHCl_3$): from CH_2Cl_2: +100.9°; from HFIP: +85.1°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 (1H, s, MeOCC<u>H</u>), 5.83-5.72 (2H, m, <u>H</u>CC<u>H</u>^{diene}), 3.80 (3H, s, <u>Me</u>O), 3.43 (1H, qdd, *J* = 7.0, 3.7, 1.3 Hz, MeC<u>H</u>), 3.21-2.89 (2H, m, C<u>H</u>$_2$), 1.18 (3H, d, *J* = 7.0 Hz, <u>Me</u>CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.84, 182.14, 158.45, 144.76, 137.47, 130.02, 121.29, 107.63, 56.26, 29.13, 24.07, 22.29; HRMS (ESI+): for $[M+H]^+$ calc.: 205.0865, found: 2050860.

(1*R*,4*S*,4a*R*,5*S*,8*R*,8a*S*,9a*S*,10a*R*)-1,4,4a,5,8,8a,9a,10a-Octahydro-1,4:5,8-dimethanoanthracene-9,10-dione (11). Quinone **1b** (57 mg, 0.525 mmol in HFIP) and diene **2a** (0.09 mL, 1.07 mmol in HFIP) were reacted following the standard procedure to give **11** (118 mg, 93% in HFIP) as a white powder; R_f (8/2 cyclohex./AcOEt): 0.33; m_p: 156-158°C (decomp.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.18 (4H, dd, AB*X*YZ, J_{AX} = J_{XY} = 1.8 Hz, 2 × <u>H</u>CC<u>H</u>^{diene}), 3.35-3.32 (4H, m, ABX*Y*Z, 4 × C<u>H</u>^{bridge}), 2.88-2.83 (4H, m, ABXY*Z*, 4 × C<u>H</u>^{angular}), 1.39 (4H, dddd, *AB*XYZ, J_{AX} = J_{AY} = 1.8 Hz, J_{BY} = J_{BZ} = 1.4 Hz, J_{AB} = 8.6 Hz, $\Delta\nu_{AB}$ = 84.6 Hz, 2 × C<u>H</u>$_2^{bridge}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.85, 136.49, 53.34, 49.71, 48.37.

2-Methoxy-8-methylnaphthalene-1,4-dione (12). Quinone **1f** (116 mg, 0.535 mml in CH_2Cl_2; 50 mg, 0.229 mmol in HFIP) and diene **2b** (0.11 mL, 1.10 mmol in CH_2Cl_2; 0.05 mL, 0.501 mmol in HFIP) were reacted following the standard procedure. Once the cycloaddition was over (remove HFIP *in vacuo* and replace by the same volume of CH_2Cl_2), Et_3N (0.15 mL, 1.08 mmol in CH_2Cl_2; 0.07 mL, 0.504 mmol in HFIP) was added and the solution was stirred overnight at room temperature. The solution was washed with a saturated solution of NH_4Cl and brine and dried over Na_2SO_4. The solution was filtered and the solvent evaporated. The crude product was purified by filtration over silica gel (eluent: CH_2Cl_2) to give **12** (80 mg, 74% in CH_2Cl_2; 33 mg, 71% in HFIP) as a light yellow powder; R_f (7/3 cyclohex./AcOEt): 0.54; m_p: 133-135°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04-7.98 (1H, m, <u>H</u>CCHCHCMe), 7.58 (1H, dd, *J* = 7.7, 7.6 Hz, HCC<u>H</u>CHCMe), 7.50-7.47 (1H, m, HCCHC<u>H</u>CMe), 6.12 (1H, s, MeOCC<u>H</u>), 3.89 (3H, s, <u>Me</u>O), 2.75 (3H, s, HCCHCHC<u>Me</u>); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.21, 181.68, 160.99, 142.01, 137.45, 133.67, 133.54, 128.79, 125.16, 108.62, 56.56, 23.00.

2-Methoxy-6,7-dimethylnaphthalene-1,4-dione (13)

From Quinone 1f. Quinone **1f** (102 mg, 0.470 mmol in CH_2Cl_2; 62 mg, 0.288 mmol in HFIP) and diene **2c** (0.11 mL, 0.972 mmol in CH_2Cl_2; 0.07, 0.619 mmol in HFIP) were reacted following the general procedure. Once the cycloaddition is over (remove HFIP *in vacuo* and replace it with the same volume of CH_2Cl_2), Et_3N (0.13 mL, 0.935 mmol in CH_2Cl_2; 0.08 mL, 0.576 mmol in HFIP) was added and the solution was stirred overnight at room temperature. The mixture was washed with a saturated solution of NH_4Cl and brine and dried over Na_2SO_4. The solution was filtered and the solvent evaporated. The crude product was filtered over silica gel (eluent: CH_2Cl_2) to give **13** (76 mg, 75% in CH_2Cl_2; 45 mg, 72% in HFIP) as a light yellow powder.

From Quinone 1m. Quinone **1m** (91 mg, 0.328 mmol in CH_2Cl_2; 90 mg, 0.326 mmol in HFIP) and diene **2c** (0.07 mL, 0.619 mmol in CH_2Cl_2; 0.07 mL, 0.619 mmol in HFIP) were reacted following the general procedure. The crude product was purified by flash chromatography on demetallated silica gel to give **13** (38 mg, 53% in CH_2Cl_2; 39 mg, 56% in HFIP) as a light yellow powder; R_f (7/3 cyclohex./AcOEt): 0.38; m_p:168-169°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (1H, s, MeCC<u>H</u>), 7.82 (1H, s, MeCC<u>H</u>), 6.10 (1H, s, MeOCC<u>H</u>), 3.89 (3H, s, <u>Me</u>O), 2.39(3) (3H, s, <u>Me</u>CCMe), 2.38(6) (3H, s, MeCC<u>Me</u>); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.45, 180.49, 160.53, 144.51, 143.22, 130.16, 129.14, 127.92, 127.42, 109.78, 56.50, 20.44, 20.20.

Methyl (±)-*rel*-(1*R*,6*R*,8*S*)-1-methoxy-4,6-dimethyl-2,5-dioxo-8-((*E*)-prop-1-en-1-yl)bicyclo[4.2.0]oct-3-ene-3-carboxylate (14). Quinone **1j** (80 mg, 0.381 mmol in CH_2Cl_2) and diene **2b** (0.08 mL, 0.802 mmol in CH_2Cl_2) were reacted following the general procedure. After fifteen days, the solvent was evaporated and the crude mixture was purified by flash chromatography (9/1 cyclohex./AcOEt) to give the title compound **14** (53 mg,

50% in CH_2Cl_2) as a yellow oil; R_f (7/3 cyclohex./AcOEt): 0.54; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.66-5.66 (2H, m, HCCH^{alkene}), 3.91 (3H, s, CO_2Me), 3.40 (1H, dd, *J* = 10.9, 6.5 Hz, CH^{quinone}), 3.23-3.19 (4H, s + m, OMe + CH^{diene}), 2.39 (1H, m, ½ × CH_2), 2.16 (1H, ddd, *J* = 11.7, 8.6, 6.5 Hz, ½ × CH_2), 2.04 (3H, s, Me^{quinone}), 1.71 (3H, d, *J* = 5.2 Hz, Me^{diene}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.74, 193.13, 165.02, 147.24, 142.11, 129.76, 126.61, 81.80, 52.97, 52.95, 46.36, 44.00, 27.88, 18.32, 14.43; HRMS (ESI+): for $[M+Na]^+$ calc.: 301.1046, found: 301.1033.

Methyl (±)-*rel*-(1*R*,6*S*,8*R*)-1-methoxy-4,6,8-trimethyl-2,5-dioxo-8-(prop-1-en-2-yl)bicyclo[4.2.0]oct-3-ene-3-carboxylate (15). Quinone **1j** (76 mg, 0.362 mmol in CH_2Cl_2) and diene **2c** (0.08 mL, 0.707 mL in CH_2Cl_2) were reacted following the general method. After fifteen days, the solvent was evaporated and the crude mixture was purified by flash chromatography on silica gel (9/1 cyclohex./AcOEt) to give the title compound **15** (25 mg, 24% in CH_2Cl_2) as a yellow oil; R_f (7/3 cyclohex./AcOEt): 0.62; ^{1}H NMR (500MHz, $CDCl_3$) δ 4.96 (1H, s, ½ × CH$_2^{vinyl}$), 4.79 (1H, s, ½ × CH$_2^{vinyl}$), 3.92 (3H, s, CO_2Me), 3.24 (1H, dd, *J* = 11.3, 5.1 Hz, CH^{quinone}), 3.16 (3H, s, OMe), 2.96 (1H, appearing as t, *J* = 11.3 Hz, ½ × CH$_2^{cyclobut.}$), 2.07 (3H, s, MeO$_2$CCCMe), 2.06-2.03 (1H, m, ½ × CH$_2^{cyclobut.}$), 1.82 (3H, s, Me^{vinyl}), 1.14 (3H, s, Me$^{cyclobut.}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.19, 193.80, 165.04, 147.74, 147.66, 143.97, 110.99, 85.90, 52.97, 52.76, 51.37, 43.90, 34.09, 24.32, 20.46, 14.63; HRMS (ESI+): for $[M+Na]^+$ calc.: 315.1203, found: 315.1189.

(+)-(1*S*,4*R*,4a*S*,8a*R*)-6-((*S*)-*p*-Tolylsulfinyl)-1,4,4a-8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (α-16). Quinone **1k** (151 mg, 0.611 mmol in CH_2Cl_2; 158 mg, 0.640 mmol in HFIP) and diene **2a** (0.06 mL, 0.713 mmol in CH_2Cl_2; 0.06 mL, 0.713 mmol in HFIP) were reacted following standard procedure. The crude product was purified by flash chromatography on demetallated silica gel (100/0 to 100/5 CH_2Cl_2/acetone) to give **α-14** (116 mg, 61% in CH_2Cl_2; 120 mg, 60% in HFIP) in the second fraction as a yellow oil; R_f (10/1 CH_2Cl_2/acetone): 0.48; $[\alpha]_D^{20}$ (c = 1.0, $CHCl_3$): +273.2°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (2H, d, *J* = 8.8 Hz, 2 × CH$^{p\text{-tolyl}}$), 7.27 (2H, d, *J* = 8.8 Hz, 2 × CH$^{p\text{-tolyl}}$), 7.16 (1H, s, ArS(O)CCH), 5.83 (1H, dd, *J* = 6.1, 3.1 Hz, HCCH^{diene}), 4.81 (1H, dd, *J* = 6.1, 2.7 Hz, HCCH^{diene}), 3.47 (1H, s(br), CH^{bridge}), 3.28-3.18 (3H, m, CH^{bridge} + 2 × CH^{angular}), 2.38 (3H, s, ArMe$^{p\text{-tolyl}}$), 1.49-1.23 (2H, m, CH$_2^{bridge}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.74, 196.16, 161.16, 142.81, 139.07, 136.58, 135.34, 134.13, 130.00, 126.10, 50.26, 49.85, 49.74, 49.68, 49.42, 21.60.

(+)-(1*R*,4*S*,4a*R*,8a*S*)-6-((*S*)-*p*-Tolylsulfinyl)-1,4,4a-8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (β-16). The same procedure as **α-16** was followed to give **β-16** (54 mg, 28% in CH_2Cl_2; 36 mg, 18% in HFIP) in the first fraction as a yellow solid; R_f (10/1 CH_2Cl_2/acetone): 0.61; m_p: 162-163°C; $[\alpha]_D^{20}$ (c = 1.0, $CHCl_3$): +471.6°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (2H, d, *J* = 7.7 Hz, 2 × CH$^{p\text{-tolyl}}$), 7.27 (2H, d, *J* = 7.7 Hz, 2 × CH$^{p\text{-tolyl}}$), 7.21 (1H, s, ArS(O)CCH), 6.19-6.14 (2H, m, HCCH^{diene}), 3.59-3.48 (2H, m, 2 × CH^{bridge}), 3.17 (2H, ddd, *AB*XY, J_{AB} = 8.5 Hz, J_{AX} = J_{BY} = 4.0 Hz, $\Delta\nu_{AB}$ = 49.0 Hz, HCCH^{angular}), 2.38 (3H, s, ArMe$^{p\text{-tolyl}}$), 1.63-1.42 (2H, m, CH$_2^{bridge}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.94, 196.03, 160.95, 142.85, 142.65, 137.29, 135.83, 135.43, 130.28, 125.92, 50.45, 49.65, 49.07, 48.87 (two signals at the same shielding), 48.86, 21.67.

6,7-Dimethylnaphthalene-1,4-dione (17): Quinone **1k** (100 mg, 0.406 mmol in CH_2Cl_2; 152 mg, 0.615 mmol in HFIP) and diene **2c** (0.05 mL, 0.442 mmol in CH_2Cl_2; 0.07 mL, 0.619 mmol in HFIP) were reacted following general procedure. In the case of HFIP, once the cycloaddition was over, the solvent was evaporated *in vacuo* and replaced by the same volume of CH_2Cl_2 and the sulfoxide elimination was allowed overnight. The crude product was purified by flash chromatography on demetallated silica gel (7/3 cyclohex./CH_2Cl_2) to give **15** (8 mg, 11% in CH_2Cl_2; 17 mg, 15% in HFIP) as a brown powder; R_f (6/4/0.5 cyclohex./CH_2Cl_2/acetone): 0.54; m_p: 117-119°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (2H, s, 2 × MeCCH), 6.90 (2H, s, HCCH^{quinone}), 2.40 (6H, s, 2 × MeCCH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.50, 143.95, 138.69, 130.05, 127.57, 20.36.

(+)-(1*R*,4*S*,4a*R*,8a*S*)-6-Chloro-7-((*S*)-*p*-tolylsulfinyl)-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (α-18). Quinone **1l** (106 mg, 0.377 mmol in CH_2Cl_2; 104 mg, 0.370 mmol in HFIP) and diene **2a** (0.06 mL, 0.713 mmol in CH_2Cl_2; 0.06 mL, 0.713 mmol in HFIP) were reacted following the general procedure. The crude

product was purified by flash chromatography on demetallated silica gel (100% CH_2Cl_2) to give **α-16** (55 mg, 42% in CH_2Cl_2; 72 mg, 55% in HFIP) in the first fraction as a yellow oil; R_f (20/1 CH_2Cl_2/acetone): 0.62; $[\alpha]_D^{20}$ (c = 0.75, $CHCl_3$): +132.0°; ^{1}H NMR (500 MHz, $CDCl_3$) δ7.67 (2H, d, *J* = 8.1 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 7.30 (2H, d, *J* = 8.1 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 6.00 (1H, dd, *J* = 5.6, 2.8 Hz, <u>H</u>CCH^{diene}), 5.86 (1H, dd, *J* = 5.6, 2.8 Hz, HCC<u>H</u>^{diene}), 3.58-3.52 (1H, m, C<u>H</u>^{bridge}), 3.52-3.46 (1H, m, C<u>H</u>^{bridge}), 3.36 (1H, dd, *J* = 8.5, 3.9 Hz, C<u>H</u>^{angular}), 3.31 (1H, dd, *J* = 8.5, 3.9 Hz, C<u>H</u>^{angular}), 2.39 (3H, s, Ar<u>Me</u>$^{p\text{-tolyl}}$), 1.48 (2H, m, C<u>H$_2$</u>^{bridge}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.44, 190.05, 152.24, 148.35, 142.33, 138.19, 135.83, 135.08, 130.09, 125.29, 50.37, 49.79, 49.41, 48.52, 21.61.

(+)-(1*S*,4*R*,4a*S*,8a*R*)-6-Chloro-7-((*S*)-*p*-tolylsulfinyl)-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (β-18). The same procedure as **α-18** was followed to give **β-18** (43 mg, 33% in CH_2Cl_2; 21 mg, 17% in HFIP) in the second fraction as yellow solid; R_f (20/1 CH_2Cl_2/acetone): 0.53; $[\alpha]_D^{20}$ (c = 0.5, $CHCl_3$): +89.9°; m_p:102-104°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (2H, d, *J* = 8.1 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 7.30 (2H, d, *J* = 8.1 Hz, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 6.04 (1H, dd, *J* = 5.6, 2.9 Hz, <u>H</u>CCH^{diene}), 5.93 (1H, dd, *J* = 5.6, 2.8 Hz, HCC<u>H</u>^{diene}), 3.60-3.53 (1H, m, C<u>H</u>^{bridge}), 3.53-3.46 (1H, m, C<u>H</u>^{bridge}), 3.35 (2H, ddd, *AB*XY, J_{AB} = 8.8 Hz, J_{AX} = J_{BY} = 3.7 Hz, $\Delta\nu_{AB}$ = 13.7 Hz, <u>H</u>CC<u>H</u>^{angular}), 2.40 (3H, s, Ar<u>Me</u>$^{p\text{-tolyl}}$), 1.56-1.40 (2H, m, C<u>H$_2$</u>^{bridge}); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.31, 189.86, 152.26, 148.53, 142.37, 138.22, 136.09, 135.53, 130.13, 125.35, 50.47, 49.21, 49.03, 48.93, 48.89, 21.62.

(4a*S*,8a*R*)-2-Chloro-6,7-dimethyl-3-((*S*)-*p*-tolylsulfinyl)-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (α-19) and (4a*R*,8a*S*)-2-chloro-6,7-dimethyl-3-((*S*)-*p*-tolylsulfinyl)-4a,5,8,8a-tetrahydronaphthalene-1,4-dione (β-19). Quinone **1l** (97 mg, 0.344 mmol in CH_2Cl_2; 30 mg, 0.107 mmol in HFIP) and diene **2c** (0.09 mL, 0.795 mmol in CH_2Cl_2; 0.02 mL, 0.177 mmol in HFIP) were reacted following general procedure to give a mixture of **α-19** and **β-19** (112 mg, 90%, α/β: 79/21 in CH_2Cl_2; 32 mg, 82%, α/β: 39/61 in HFIP) as a light orange solid foam: R_f (20/1 CH_2Cl_2/acetone): 0.67; ^{1}H NMR of the α/β mixture obtained from dichloromethane (400 MHz, C_6D_6) δ 7.90-7.79 (2H, m, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 6.90-6.80 (2H, m, 2 × C<u>H</u>$^{p\text{-tolyl}}$), 2.40-1.95 (2H, m), 1.90 (0.63H, s(br), Ar<u>Me</u>$^{p\text{-tolyl}}$ (**β**)), 1.88 (2.37H, s(br), Ar<u>Me</u>$^{p\text{-tolyl}}$ (**α**)), 1.85-1.33 (4H, m), 1.29 (2.37H, s(br), <u>Me</u>CCMe (**α**)), 1.27 (0.63H, s(br), <u>Me</u>CCMe (**β**)), 1.18 (0.63H, s(br), MeCC<u>Me</u> (**β**)), 1.15 (2.37H, s(br), MeCC<u>Me</u> (**α**)).

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Supplementary Material

Copies of ^{1}H and ^{13}C NMR spectra of synthesized compounds, as well as crystallographic data of compounds **1j**, **α-3a**, **3f**, **3g**, **5i** and **5j** are available in the supplementary material file associated with this paper. References used to compare the data of compounds that were already described in the literature are also cited in the supplementary material file.

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