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Asymmetric organocatalytic anthrone additions to activated alkenes

Alex Zea [a], Andrea-Nekane R. Alba [a], Natalia Bravo [a], Albert Moyano [a,*], Ramon Rios [a,b,*]

[a] Departament de Química Orgànica, Universitat de Barcelona, Facultat de Química, C. Martí i Franquès 1-11, 08028 Barcelona, Spain
[b] ICREA, Pg. Lluís Companys 23, 08019 Barcelona, Spain

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Dedicated to Professor Carmen Nájera on the occasion of her 60th birthday

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ABSTRACT

Asymmetric organocatalytic additions of anthrones to activated alkenes are discussed. The reaction between anthrone or dithranol and α,β-unsaturated aldehydes is catalyzed by diphenylprolinol trimethylsilyl ether in toluene at −40 °C, giving the Michael adducts with good yields and enantioselectivities. Bifunctional amino-thioureas efficiently catalyze the additions of anthrones to both nitroalkenes and maleimides, and high enantioselectivities can be achieved in both instances at room temperature. In the case of nitroalkenes, a Michael addition takes exclusively place. Anthrone generally gives Diels–Alder cycloadducts in the reaction with maleimides, while dithranol affords the Michael adducts. Transition state working models in which the bifunctional catalyst binds simultaneously to the alkene and to the anthrone enolate account for the stereochemical outcome of these additions.

1. Introduction

The chemistry of anthrone and its derivatives is an important topic in modern organic chemistry.[1] The parent anthrone (9-[10*H*]-anthracenone, **1a**) has been classically used as a reagent for the analytical determination of sugars. Dithranol (1,8-dihydroxy-9-[10*H*]-anthracenone, **1b**) is a synthetic compound, that is, widely used in the treatment of psoriasis. Anthrones and their enol tautomers, 9-anthrols, play a central role in the chemistry of anthracenes, because by oxidation of the central ring they afford 9,10-anthraquinones; the reduction of anthrones provides anthracenes, useful in the preparation of dyestuffs and of optoelectronic materials.[2] On the other hand, natural derivatives of anthrone are isolated, either in free form or as *O*- or *C*-glycosides, from a wide variety of vegetal sources (plants, shrubs), such as rhubarb, cassia, and 'cáscara sagrada' bark, among others.[3] Many of these compounds have interesting biological properties, and are being used either as antimicrobial, laxative, antipsoriatic or as androgen-receptor and telomerase inhibitors.[4] Recently, it has been shown that some anthrone- or anthraquinone-based natural products display potent and selective antitumor activity.[5]

The development of efficient methods for the asymmetric synthesis of anthrones appears therefore as a worthy objective. However, only a few examples of asymmetric reactions of anthrone or its derivatives have been reported, most of them dealing with its base-catalyzed Diels–Alder reactions. In the light of these precedents, and given our interest on the development of new methodology for asymmetric organocatalysis,[6] we undertook a study of the chiral amine-catalyzed enantioselective reactions of anthrones with electron-deficient alkenes such as α,β-unsaturated aldehydes, nitrostyrenes, and maleimides. We present herein a full account of our results in this topic.

2. Results and discussion

2.1. Anthrones as nucleophiles in Michael additions

Although the most common reaction of anthrone with electron-poor alkenes is the Diels–Alder cycloaddition,[7] the anthracenolate ion generated from the deprotonation of anthrone by strong bases like sodium alkoxides usually undergoes a double Michael addition at C10 when reacted with α,β-unsaturated esters.[8] Therefore, we decided to study the amine-catalyzed reaction between anthrones and enals,[9] in order to see whether we obtained the Diels–Alder or the Michael adduct (Fig. 1).

We found out that when anthrone **1a** was added to cinnamaldehyde (**2a**) in toluene using different proline or prolinol derivatives as catalysts, only the single Michael addition product **3a** was observed (Table 1).

Proline (**I**, entry 1 in Table 1) was a rather inefficient catalyst for the reaction, leading to the racemic adduct **3a** with low conversion.

* Corresponding authors. Fax: +34 933397878; e-mail addresses: amoyano@ub.edu (A. Moyano), rios.ramon@icrea.cat (R. Rios).

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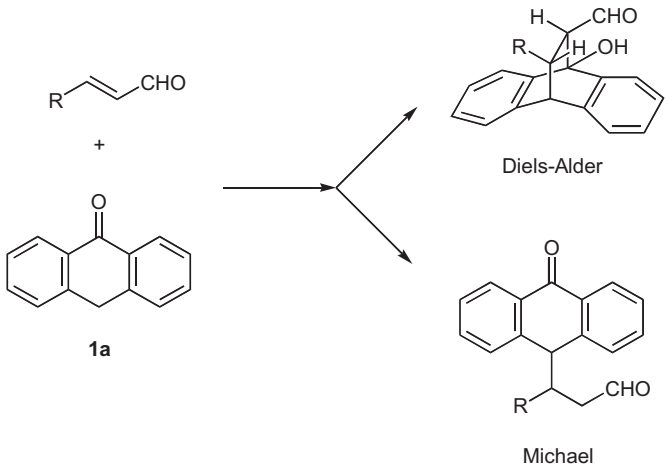


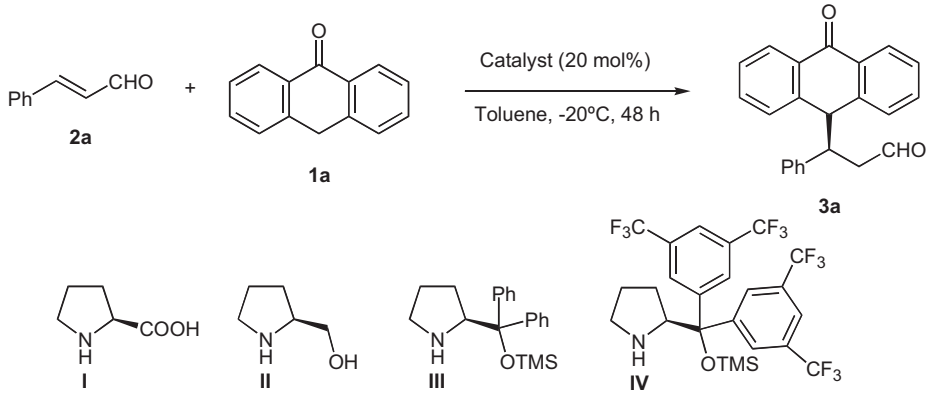
Fig. 1. Possible products of the addition of anthrone to enals.

entry 7), that clearly enhanced the reaction rates at −40 °C, did not bring about any positive effect in terms of enantioselectivity.

Using the most suitable reaction conditions for the enantioselective addition of anthrone to cinnamaldehyde (diphenylprolinol trimethylsilyl ether **III** as the catalyst, toluene, −40 °C), we studied the scope of the reaction with other α,β-unsaturated aldehydes **2b**–**g**, as shown in Table 3.

Gratifyingly, in most instances the anthrone addition took place with good yields, albeit with prolonged reaction times (5–36 days). Enantioselectivities ranged from good to excellent for 4-substituted cinnamaldehyde derivatives. For example, when 4-nitrocinnamaldehyde **2c** was used, the addition product **3c** was obtained with 75% yield and 78% ee after 36 days at −40 °C (entry 3). In the case of 4-cyanocinnamaldehyde **2b**, the reaction proceeded extremely well, obtaining the final adduct **3b** in 85% yield and 99% ee after only 5 days at −40 °C (entry 2). On the other hand, 2-substituted cinnamaldehydes **2d** and **2e** gave very low yields and enantioselectivities, even after very prolonged reaction times

Table 1
Catalyst screening in the reaction between anthrone (**1a**) and cinnamaldehyde (**2a**)[a]



Entry	Catalyst	Conversion (%)[b]	ee[c]
1	**I**	8	0%
2	**II**	23	0%
3	**III**	76	48%
4	**IV**	<5	n.d.[d]

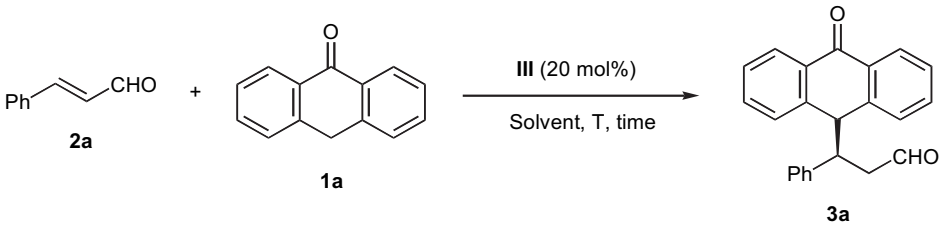
[a] Experimental conditions: A mixture of **1a** (0.30 mmol), **2a** (0.25 mmol), and the catalyst (0.05 mmol) in toluene (1 mL) was stirred at −20 °C during 48 h.
[b] Determined by ^{1}H NMR analysis of the reaction mixture.
[c] Determined by HPLC analysis.
[d] Not determined.

Prolinol **II** (entry 2) also gave racemic **3a**. Best results were obtained with diphenylprolinol trimethylsilyl ether **III**, that afforded promising conversion and enantioselectivity (entry 3). Jérgensen–Hayashi catalyst **IV**, on the other hand, showed a very low catalytic activity (entry 4).

We decided next to optimize the reaction conditions in order to achieve higher yields and enantioselectivities. In an initial screening (Table 2), we found that amine **III** efficiently catalyzed the reaction in toluene at room temperature, although no significant enantioselective induction was observed (entry 1; Table 2). For this reason, we performed the reaction at lower temperatures. At −30 °C, the reaction exhibited a reasonable rate in dichloromethane, but the enantiomeric excess of the product was much lower than in toluene (entries 3 and 4, Table 2). We were pleased to find that in toluene at −40 °C the enantiomeric excess of the product was increased to 80% (entry 5; Table 2), although the reaction rate was rather low. Furthermore, the use of different additives, such as acids (benzoic acid; entry 6) or hydrogen-bond donors (Schreiner's thiourea;[10] (entries 4 and 5). When aliphatic enals **2f**–**i** were used, the reaction took place with high yields and enantioselectivities after 10 days at −40 °C (entries 6–9). Further studies showed that the final adducts racemize very fast at room temperature, probably due to a retro-Michael process, especially when aromatic aldehydes are used. This could account for the better enantioselectivities obtained with aliphatic aldehydes, as well as for the poor results afforded by *ortho*-substituted cinnamaldehydes, that react very slowly.

Spurred on by these results, we tried next to expand this methodology to dithranol **1b**. It is well known that anthranols are more nucleophilic than anthrones, so that normally only 1,4-addition is observed. For example, Tan and co-workers reported that while anthrones reacted with maleimides affording the expected Diels–Alder adducts, dithranol only gave the 1,4-Michael addition.[11] When we performed the amine-catalyzed reaction of dithranol with cinnamaldehyde derivatives, we obtained however very complex reaction mixtures, from which we could not isolate the expected addition products. We were therefore delighted to

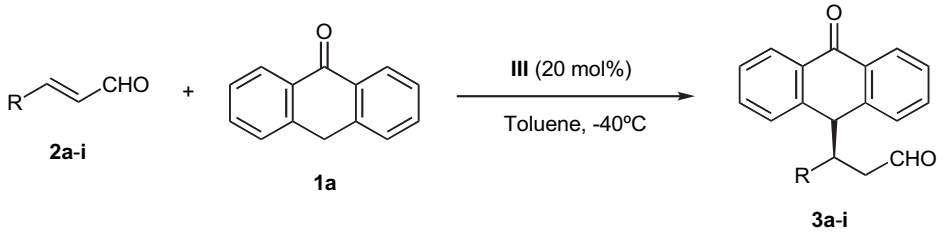
Table 2
Solvent and temperature screening in the reaction between anthrone (**1a**) and cinnamaldehyde (**2a**) catalyzed by **III**[a]



Entry	Solvent	*T*	Time	Conversion (%)[b]	ee (%)[c]
1	Toluene	rt	3 h	100	4
2	Toluene	−20 °C	48 h	76	48
3	CH_2Cl_2	−30 °C	24 h	43	14
4	Toluene	−30 °C	72 h	48	63
5	Toluene	−40 °C	10 days	23	80
6[d]	Toluene	−40 °C	48 h	33	54
7[e]	Toluene	−40 °C	48 h	23	60

[a] Experimental conditions: A mixture of **1a** (0.30 mmol), **2a** (0.25 mmol), and catalyst **III** (0.05 mmol) in toluene or dichloromethane (1 mL) was stirred at the temperature specified in the table.
[b] Determined by ^{1}H NMR analysis of the reaction mixture.
[c] Determined by HPLC analysis.
[d] Benzoic acid (0.2 mmol) was present in the reaction mixture.
[e] Schreiner's thiourea (0.2 mmol) was present in the reaction mixture.

Table 3
Scope of the reaction between anthrone (**1a**) and α,β-unsaturated aldehydes (**2a**-**i**) catalyzed by **III**[a]



Entry	Aldehyde (R)	Product	Time	Yield (%)[b]	ee (%)[c]
1	**2a** (Ph)	**3a**	36 days	88	80
2	**2b** (4-CNPh)	**3b**	5 days	85	99
3	**2c** (4-NO_2Ph)	**3c**	36 days	75	78
4	**2d** (2-BrPh)	**3d**	53 days	32[d]	3
	2e (2-NO_2Ph)	**3e**	53 days	35[d]	7
4	**2f** (Me)	**3f**	10 days	95	94
5	**2g** (Et)	**3g**	10 days	82	96
6	**2h** (*n*-Pr)	**3h**	10 days	84	96
7	**2i** (*n*-Bu)	**3i**	10 days	92	86

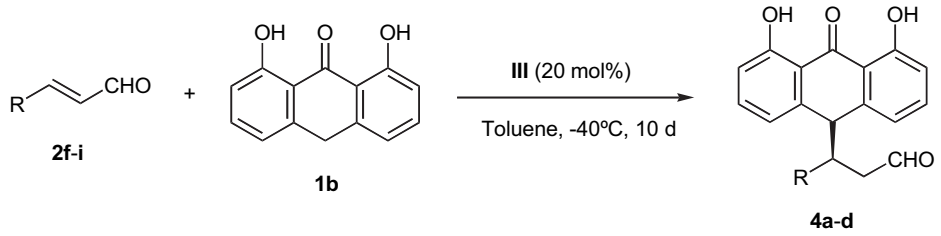
[a] Experimental conditions: A mixture of **1a** (0.30 mmol), **2a**–**i** (0.25 mmol), and catalyst **III** (0.06 mmol) in toluene (2 mL) was stirred at −40 °C for the time necessary to achieve full conversion, as determined by ^{1}H NMR analysis of the reaction mixture.
[b] Yield of isolated product after chromatographic purification.
[c] Determined by HPLC analysis of the reaction mixture.
[d] Conversion was not complete.

find that when dithranol was used in our reaction with aliphatic α,β-unsaturated aldehydes, the products of single Michael addition **4a**–**d** were isolated with good yields and with very high enantioselectivities after 10 days at −40 °C (Table 4).

In order to determine the absolute configuration of our compounds, we took advantage of the fact that, after the publication of our preliminary results on the addition of anthrones to enals,[9] Ye coworkers reported the reaction of anthrones with β-aryl-α,β-unsaturated ketones catalyzed by *Cinchona*-alkaloid derived tertiary amino-thioureas, the corresponding Michael adducts being obtained with good yields and enantioselectivities.[12] Moreover, the authors were able to ascertain the absolute configuration of their products from the anomalous X-ray diffraction analysis of a halogenated adduct. Therefore, the Michael adduct **3a** (80% ee), resulting from the reaction between anthrone **1a** and cinnamaldehyde **2a**, was treated with methylmagnesium bromide, affording the corresponding diastereomeric mixture of alcohols **5a** and **5a**′. Next, the oxidation of this mixture with pyridinium chlorochromate (PCC) gave the corresponding ketone **6a** (Scheme 1). Comparison of its specific rotation with the literature data[12] revealed that the absolute configuration of this compound, and accordingly that of **3a**, is (3*R*): $[\alpha]_D^{25}$ −1.8 (*c* 2.7, CH_2Cl_2), (3*S*)-**6a**, lit.: $[\alpha]_D^{25}$ +2.88 (*c* 1.0, CH_2Cl_2)].

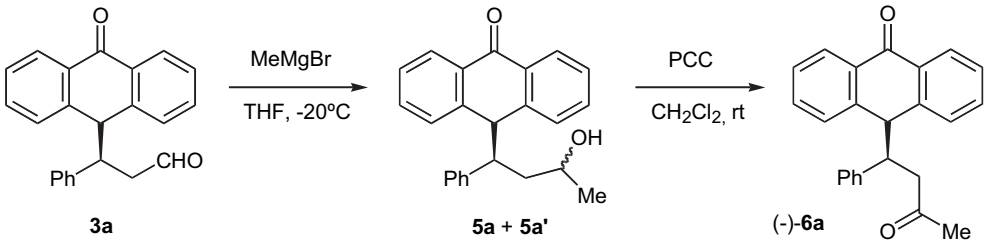
This stereochemical outcome can be easily rationalized within the mechanistic model proposed for other chiral secondary amine-catalyzed reactions between nucleophiles and enals,[13] as exemplified in Scheme 2. Thus, efficient shielding of the *Re*-face of the chiral iminium intermediate **7** by the bulky aryl groups of the chiral pyrrolidine **III** leads to stereoselective *Si*-facial nucleophilic conjugate attack on the β-carbon of **7**. Hydrolysis of the resulting enamine intermediate **8** would regenerate the catalyst and release the

Table 4
Scope of the reaction between dithranol (**1b**) and aliphatic α,β-unsaturated aldehydes (**2f**–**i**) catalyzed by **III**[a]



Entry	Aldehyde (R)	Product	Yield (%)[b]	ee (%)[c]
1	**2f** (Me)	**4a**	88	97
2	**2g** (Et)	**4b**	95	99
3	**2h** (*n*-Pr)	**4c**	93	99
4	**2i** (*n*-Bu)	**4d**	92	99

[a] Experimental conditions: A mixture of **1b** (0.25 mmol), **2f**–**i** (0.37 mmol), and catalyst **III** (0.05 mmol) in toluene (2 mL) was stirred at −40 °C during 10 days.
[b] Yield of isolated product after chromatographic purification.
[c] Determined by HPLC analysis.



Scheme 1. Determination of the absolute configuration of **3a**.

(3*R*)-Michael adduct. A mechanism involving the intermediacy of the Diels–Alder cycloadduct **9**, that by a retro-aldol reaction would lead to **8**, can also be envisaged.

In 2007, Shi and co-workers described a highly efficient addition of anthrone to nitroalkenes catalyzed by *Cinchona* alkaloids and some of their derivatives.[14] When using *O*-benzoylcupreine as a chiral catalyst, the Michael addition of anthrone **1a** to nitroalkenes took place with excellent yields and enantioselectivities, but the reaction had to be performed at low temperature (−40 °C) in chlorinated solvents. This methodology was not suitable moreover for the addition of dithranol **1b**, since in a single example described by the authors, the enantiomeric excess of the adduct was very low (9% ee).

In the past few years, bifunctional amino-thioureas have emerged as an important class of enantioselective organocatalysts,[15] and in particular they have demonstrated their usefulness in asymmetric Michael additions to nitroolefins.[16] We hypothesized that bifunctional organocatalysts would also lead to good results in the addition of anthrones to nitroalkenes, due to their ability to bring together the two reactants in the transition state by hydrogen-bonding. In order to test this hypothesis, we investigated the reaction between anthrone **1a** and *trans*-β-nitrostyrene **10a**, using as a catalyst the commercially available thiourea (*R*,*R*)-**V** described by Takemoto[17] in different solvents at room temperature (Table 5). Independently of the solvent used, conversion was excellent after 14 h. However, the enantioselectivity decreased from a maximum of 89% ee using toluene (entry 1 in Table 5) down to nearly racemic when the reaction was run in dimethylsulfoxide (entry 6) or in ethanol (entry 5), probably due to the fact that their interaction with the catalyst disrupts the hydrogen-bond network in the transition state.

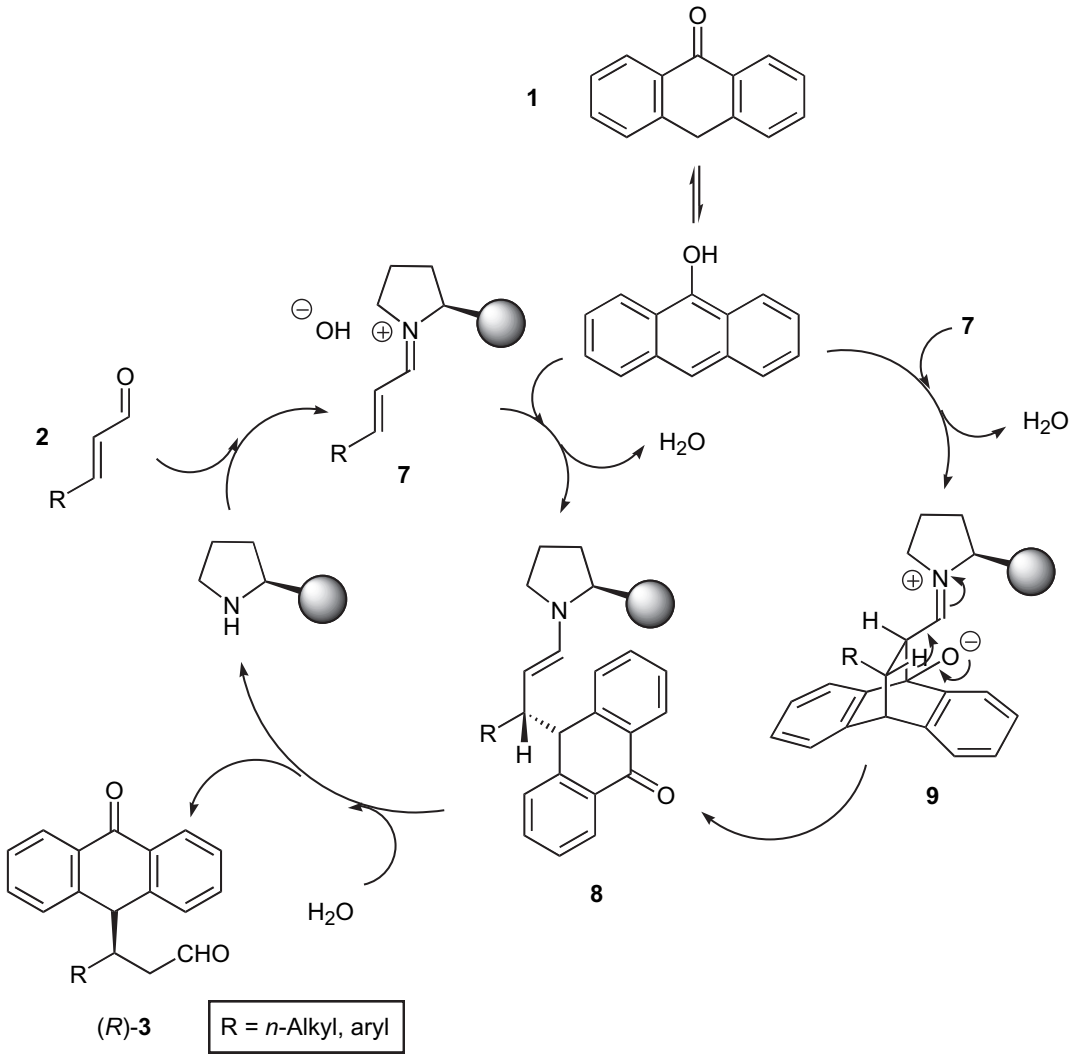
We compared next the behavior of **V** with that of other bifunctional catalysts bearing a thiourea and a tertiary amine (Table 6). Either with the quinine-derived thiourea catalyst **VI** or with the quinidine-derived thiourea catalyst **VII**, the enantiomeric purities of the adduct **11a** were lower than with Takemoto's thiourea catalyst **V**. As expected, quasienantiomeric catalysts **VI** and **VII** preferently rendered opposite enantiomers of **11a** in the reaction, with total conversion after 14 h at room temperature in toluene. It is interesting to note that both (*R*,*R*)-**V** and **VII** (that also has an (*R*) absolute configuration at the thiourea stereogenic center) show the same sense of asymmetric induction.

Having selected the most suitable reaction conditions for the enantioselective addition of anthrone to nitrostyrene at room temperature (toluene, Takemoto's thiourea **V** as the catalyst), we studied the scope of the reaction with different *trans*-β-nitrostyrene derivatives, as shown in Table 7.

Conversion was completed in all instances after 14 h at room temperature, and the adducts **11a**–**e** were isolated in excellent yields (91–95%) after chromatographic purification. Enantiomeric purities were also uniformly high (85–92% ee), although electron-withdrawing *para*-substituents gave slightly lower enantioselectivities than electron-donating ones (compare entries 4 and 5 in Table 7).

As it could be inferred from the precedent reported by Shi,[14] the addition of dithranol (**1b**) to β-nitrostyrenes was much more challenging (Table 8).

At room temperature, the reaction between **1b** and *trans*-β-nitrostyrene **10a** was completed after 14 h, but the Michael addition product **12a** was racemic (entry 1 in Table 8). Fortunately, we could go down to −40 °C maintaining a reasonable reaction rate, achieving a 36% ee for this product (entry 3 in Table 8). Under these conditions, electron-rich styrenes **10c** and **10d** afforded the corresponding adducts **12c** and **12d** with somewhat higher enantioselectivities (38 and 40% ee, respectively; entries 5 and 6). On the other hand, under these conditions both *trans*-β-nitro(2-fluorostyrene) **10b** (entry 4)



Scheme 2. Mechanistic proposal for the enantioselective addition of anthrones to enals.

and *trans*-β-nitro(4-nitrostyrene) **10d** (entry 7) afforded lower enantioselectivities (21% and 13% ee, respectively). These results suggest that the hydroxyl groups of dithranol **1b** might interfere with the hydrogen-bond network between the catalyst and nitrostyrene, resulting in a loss of stereoselectivity. Even if the bifunctional catalyst (*R*,*R*)-**V** affords much better results than *O*-benzoylcupreine,[14] the high nucleophilic reactivity of dithranol renders its asymmetric addition to highly reactive Michael acceptors such as nitrostyrenes very hard to control.

The absolute (*R*)-configuration of our compounds was easily ascertained by chemical correlation with those previously described by Shi.[14] Thus, for instance, we determined a specific rotation $[\alpha]_D^{25}$ −22.8 (*c* 0.9, $CHCl_3$) for adduct **11a**, whose dextrorotatory enantiomer had been shown to have an (*S*)-configuration.

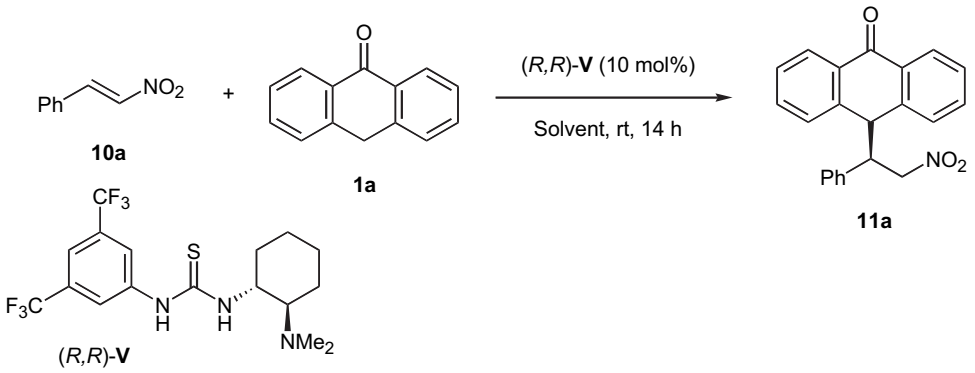
This stereochemical result can be accommodated either by a qualitative model related to that proposed by Takemoto for the addition of malonates to β-nitrostyrenes[17] (transition state **A** in Fig. 2, in which the thiourea binds the nitro group), or by another related to the one forwarded by Pápai and co-workers[18] (transition state **B** in Fig. 2, in which the thiourea binds the anthrone enolate oxygen). As before, the initial formation of a Diels–Alder adduct **C** (being produced either by transition states **A** or **B**) that leads to the Michael product by a retro-Henry reaction is also possible.

While this work was in progress, Yuan and co-workers reported on the use of tertiary amines bearing a thiourea moiety as catalysts for the addition of **1a** to nitroalkenes, with similar results.[19]

2.2. Anthrones in Diels–Alder reactions

Asymmetric Diels–Alder cycloadditions of anthrones were first disclosed more than twenty years ago. Kinetic studies performed by Koerner and Rickborn[20] on the reaction between anthrone and *N*-methylmaleimide showed that this cycloaddition was efficiently catalyzed by tertiary amines, probably due to the high reactivity of the anthrone enolate as a diene. Building upon these results, Riant and Kagan investigated the effect of chiral bases in the same reaction,[21] finding that quinidine and prolinol were the most enantioselective catalysts (up to 61% ee was achieved with a 10 mol % of quinidine in chloroform at −50 °C). More recently, Fache and Piva used perfluoroalkylated *Cinchona*-alkaloid derivatives for the same purpose, obtaining up to 40% ee in trifluorotoluene at room temperature.[22] Later on, Yamamoto and co-workers[23] described the asymmetric cycloaddition of anthrone and maleimides catalyzed by C_2-chiral 2,5-bis(hydroxymethyl)pyrrolidines, obtaining variable enantioselectivities (47–87% ee). The enantioselective Diels–Alder cycloaddition of substituted anthrones with

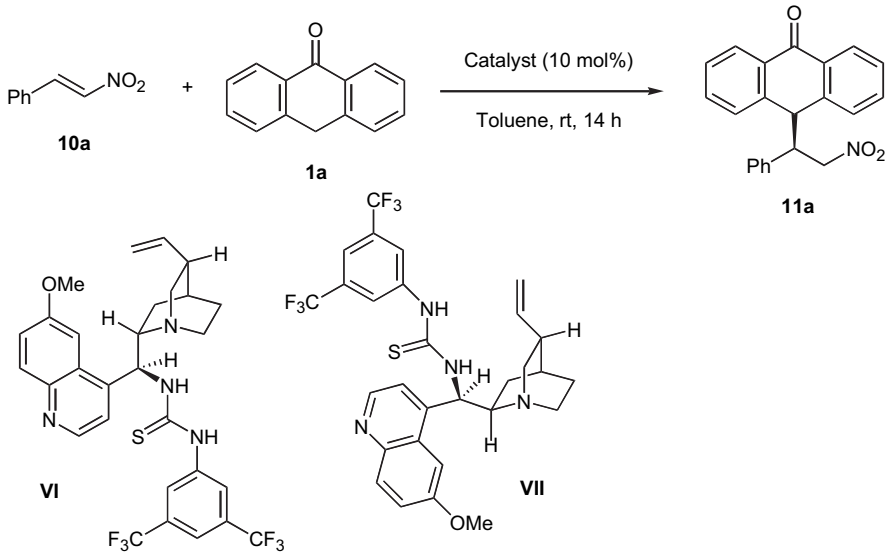
Table 5
Solvent screening in the reaction between anthrone (**1a**) and *trans*-β-nitrostyrene (**10a**) catalyzed by **V**[a]



Entry	Solvent	Conversion (%)[b]	ee (%)[c]
1	Toluene	100	89
2	$CHCl_3$	100	76
3	CH_2Cl_2	100	46
4	AcOEt	100	64
5	DMSO	100	0
6	EtOH	100	7

[a] Experimental conditions: A mixture of **1a** (0.25 mmol), **10a** (0.28 mmol), and the catalyst (*R*,*R*)-**V** (0.025 mmol) in the solvent specified in the table (1 mL) was stirred at rt during 14 h.
[b] Determined by ^{1}H NMR analysis of the reaction mixture.
[c] Determined by HPLC analysis.

Table 6
Catalyst screening in the reaction between anthrone (**1a**) and *trans*-β-nitrostyrene (**10a**) in toluene[a]

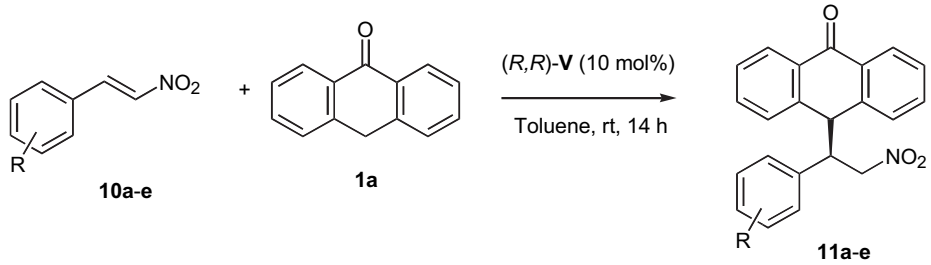


Entry	Catalyst	Conversion (%)[b]	ee (%)[c]
1	(*R*,*R*)-**V**	100	89
2	**VI**	100	−58[d]
3	**VII**	100	63

[a] Experimental conditions: A mixture of **1a** (0.25 mmol), **10a** (0.28 mmol), and the catalyst (0.025 mmol) in toluene (1 mL) was stirred at rt during 14 h.
[b] Determined by ^{1}H NMR analysis of the reaction mixture.
[c] Determined by HPLC analysis.
[d] Preferential formation of *ent*-**11a**.

maleimides catalyzed by chiral bicyclic guanidines, which takes place with excellent yields and enantioselectivities (85–99% ee) when run in dichloromethane solution at −20 °C, was reported in 2006 by Tan and co-workers.[11] This reaction showed however a very strong temperature dependence, and the enantiomeric purities of the Diels–Alder products were much lower when it was performed at room temperature. Very recently, the same research group has reported on the use of an adduct of anthrone and *N*-acetoxyphthalimide, obtained in 92% ee, as a precursor of catalysts for the asymmetric aerobic oxidation of organic compounds.[24] In 2008, Göbel and co-workers developed an addition of anthrones to maleimides catalyzed by metal-free bis(oxazolines), with

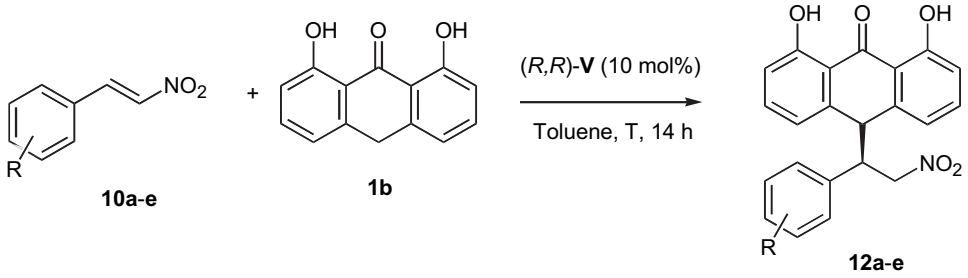
Table 7
Scope of the addition of anthrone (**1a**) to nitrostyrenes (**10a–e**) catalyzed by **V**[a]



Entry	Nitrostyrene (R)	Product	Yield (%)[b]	ee (%)[c]
1	**10a** (H)	**11a**	92	89
2	**10b** (2-F)	**11b**	95	92
3	**10c** (4-Me)	**11c**	92	90
4	**10d** (4-MeO)	**11d**	94	90
5	**10e** (4-NO_2)	**11e**	91	85

[a] Experimental conditions: A mixture of **1a** (0.25 mmol), the nitroolefin (0.28 mmol), and the catalyst (*R,R*)-**V** (0.025 mmol) in toluene (1 mL) was stirred at rt during 14 h.
[b] Yield of isolated product after chromatographic purification.
[c] Determined by HPLC analysis.

Table 8
Scope of the addition of dithranol (**1b**) to nitrostyrenes (**10a-e**) catalyzed by **V**[a]



Entry	Nitrostyrene (R)	Product	*T*	Yield[b]	ee (%)[c]
1	**10a** (H)	**12a**	rt	n.d.[d]	0
2	**10a** (H)	**12a**	−20 °C	n.d.[d]	26
3	**10a** (H)	**12a**	−40 °C	77%	36
4	**10b** (2-F)	**12b**	−40 °C	89%	21
5	**10c** (4-Me)	**12c**	−40 °C	85%	38
6	**10d** (4-MeO)	**12d**	−40 °C	70%	40
7	**10e** (4-NO_2)	**12e**	−40 °C	87%	13

[a] Experimental conditions: A mixture of **1b** (0.25 mmol), the nitroolefin (0.28 mmol), and the catalyst (*R,R*)-**V** (0.025 mmol) in toluene (1 mL) was stirred at the temperature specified in the table during 14 h.
[b] Yield of isolated product after chromatographic purification.
[c] Determined by HPLC analysis.
[d] Not determined; 100% conversion by ^{1}H NMR.

moderate enantioselectivities (39–70% ee).[25] Similar results were achieved through the use of chiral bisamidines as catalysts.[26] Finally, a chiral ionic liquid derived from lactic acid has been lately used as an asymmetric inducer in Diels–Alder reactions between anthrone and several maleimides, with moderate success (up to 37% ee).[27]

Given the good performance of bifunctional amino-thiourea catalysts in the addition of anthrones to nitroalkenes, we decided to assess their usefulness in the Diels–Alder cycloaddition of anthrones with maleimides.[28] the reaction of anthrone **1a** with *N*-phenylmaleimide **13a** as the benchmark process, we studied the effect of the catalyst and of the solvent (Table 9).

Takemoto's thiourea **V** was an efficient catalyst for this reaction, and complete conversion of anthrone to the expected cycloadduct **14a** was obtained after 14 h at room temperature in relatively non-polar solvents (entries 1–3 in Table 9). Toluene (entry 1) provided the best enantioselectivity. Not surprisingly, the use of dimethylsulfoxide as a solvent inhibited the catalytic activity of **V** (entry 4). The *Cinchona*-alkaloid derived thioureas **VI** and **VII** also catalyzed the cycloaddition, but with lower enantioselectivities (entries 5 and 6). The positive effect of the thiourea moiety is evinced by the fact that quinidine (**VIII**) was a less enantioselective catalyst than **VII** (compare entries 6 and 7). The fact that with quinidine **VIII** the major product was *ent*-**14a**[21,23b] also allowed us to conclude that the absolute configuration of **14a** was (*R,R*), an assumption that was also supported by comparison of its specific rotation with that previously described in the literature.[11]

The reaction of **1a** with other maleimides was then performed using the conditions of entry 1 in Table 9 (Table 10). The yields of the reaction were uniformly high (90–94% after direct purification of the reaction crude by column chromatography in silica gel). *N*-arylmaleimides, with the sole exception of the 4-bromophenyl derivative **13f** (entry 6 in Table 10), afforded the corresponding Diels–Alder adducts with excellent enantioselectivities (90–97%

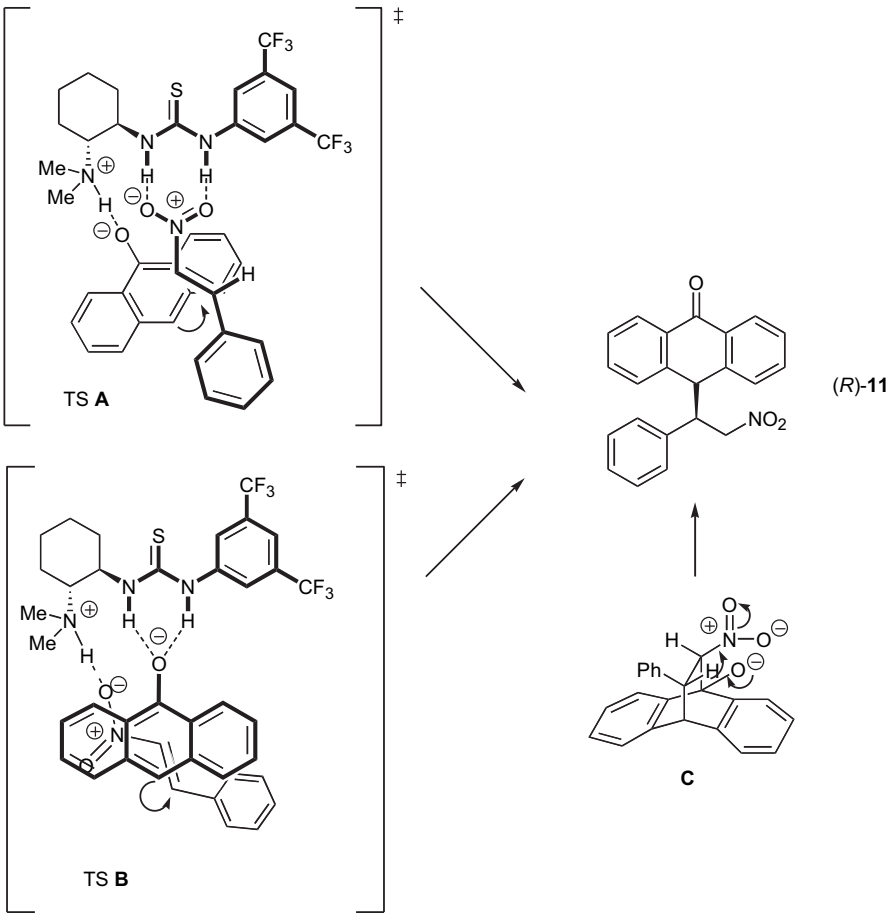


Fig. 2. Transition state working models for the Michael addition of anthrones to nitroalkenes catalyzed by (*R*,*R*)-**V**.

ee, entries 1, 3–5 in Table 10). For these substrates, therefore, Takemoto's thiourea **V** is a much better catalyst at room temperature than the bicyclic guanidine employed by Tan, that afforded *ent*-**14a** in only 12% ee.[11]

We were surprised to find that the reaction of anthrone with *N*-(4-(trifluoromethyl)phenyl)maleimide **13e** furnished the Michael adduct **14′e** (94% yield, 97% ee; entry 5 in Table 10) instead of the Diels–Alder product **14e**, that had been previously obtained by Yamamoto with low enantioselectivity (up to 50% ee) using either **VIII** or C_2-chiral pyrrolidines as catalysts in chloroform at room temperature.[23b] Since it is known that the anthrone/maleimide Diels–Alder cycloadducts readily isomerize to the 'open' Michael products upon treatment with base,[11,23] we assume that the initially formed adduct **14e** undergoes a base-promoted retro-aldol ring-opening reaction to give the thermodynamically more stable product **14′e**. This process is probably facilitated by the strongly electron-withdrawing trifluoromethyl substituent.

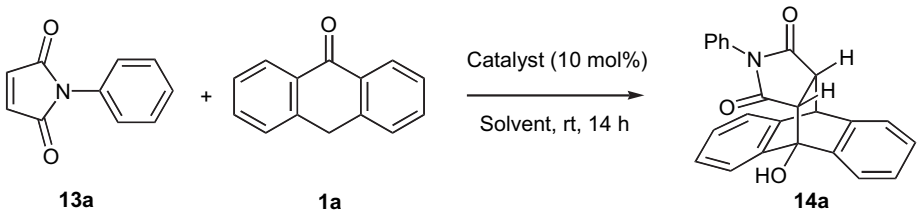
While *N*-benzylmaleimide **13b** gave the cycloadduct **14b** with good enantioselectivity (85% ee; entry 2 in Table 10), *N*-benzhydrylmaleimide **13g** afforded **14g** with good yield but with a much lower enantiomeric purity (33% ee; entry 7 in Table 10).

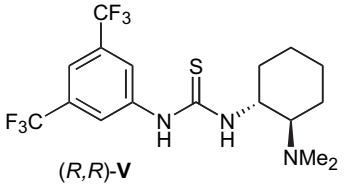
The deletereous effect of α-branching in *N*-benzylmaleimides for the stereoselectivity of the reaction was also evinced when (*R*)-*N*-(1-phenylethyl)maleimide **13h** was reacted with anthrone (Scheme 3). Under catalysis by DABCO, cycloadduct **14h** was obtained in 85% yield as a 1:1.40 mixture of the (*R*,*R*)- and (*S*,*S*)-diastereomers (determined by ^{1}H NMR of the crude reaction mixture), a result that closely matched that previously reported by Yamamoto co-workers with (*S*)-**13h** and with pyrrolidine as the catalyst[23a] By using (*R*,*R*)-**V** as the catalyst, a 2.56:1 mixture of the same diastereomers was obtained in 80% yield. We can estimate an inthrinsic diastereomeric ratio[29] of 3.58:1 (i.e., a 78% de) for catalyst **V** in the reaction of anthrone with *N*-(1-phenylethyl)maleimide. The stereoselectivity of the cycloaddition therefore decreases with increasing bulkiness of the α-substituent.

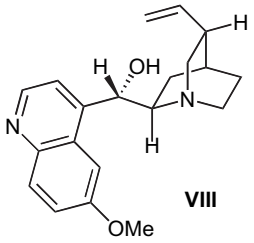
In line with the previous results of Tan,[11] we found that dithranol **1b** afforded exclusively the Michael adducts **15** in its reaction with maleimides (Table 11). We were pleased to find that, contrary to what happened in the reaction of **1b** with nitroalkenes, the Michael adducts were obtained not only with high yields, but generally with good enantioselectivities (entries 1-3 and 5 in Table 11). Contrary to what happened in the case of anthrone, maleimide **13f** reacted with excellent enantioselectivity (entry 5). However, the presence of a chlorine atom at the *meta*-position of the phenyl ring in maleimide **13c** resulted in a low enantiomeric purity of the corresponding adduct **15c** (22% ee, entry 3). The reaction between **1b** and *N*-benzhydrylmaleimide **13g** (entry 6) gave the corresponding adduct **15g** in good yield, but unfortunately we were not able to find suitable HPLC conditions for the determination of its enantiomeric excess.

An absolute (*S*) configuration was assigned to the predominant enantiomers of these adducts under the assumption that they arise from the retro-aldol ring-opening of an initially formed (*R*,*R*)-cycloadduct. On the other hand, the specific rotations of compounds **15a** and **15b** match (both in sign and in magnitude) those previously reported by Tan.[11] We propose that the in the case of the dithranol-maleimide derivatives the stability of the Michael adduct with respect to the kinetic Diels–Alder product is enhanced by hydrogen-bonding of the anthrone carbonyl with the neighboring hydroxyls (Fig. 3).

Table 9
Catalyst and solvent screening in the Diels–Alder cycloaddition between anthrone (**1a**) and *N*-phenylmaleimide (**13a**)[a]



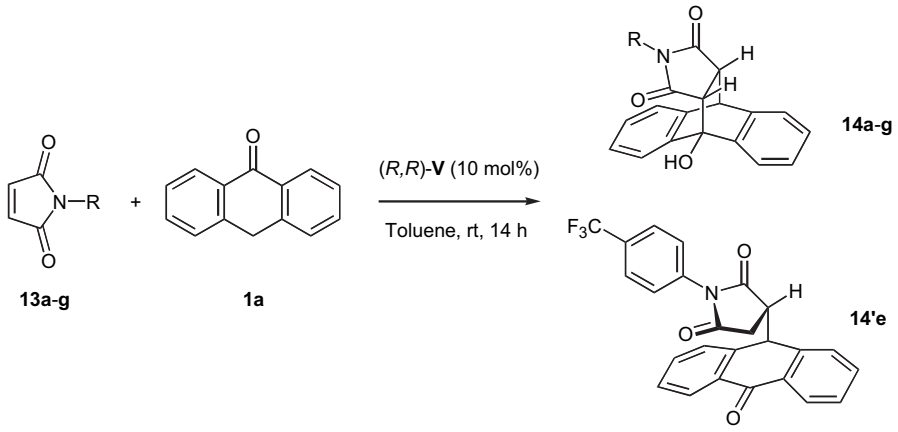




Entry	Catalyst	Solvent	Conversion (%)[b]	ee[c]
1	(*R*,*R*)-**V**	Toluene	100	90%
2	(*R*,*R*)-**V**	CH_2Cl_2	100	73%
3	(*R*,*R*)-**V**	$CHCl_3$	100	71%
4	(*R*,*R*)-**V**	DMSO	0	—
5	**VI**	Toluene	100	75%
6	**VII**	Toluene	100	−51%[d]
7	**VIII**	Toluene	100	−34%[d]

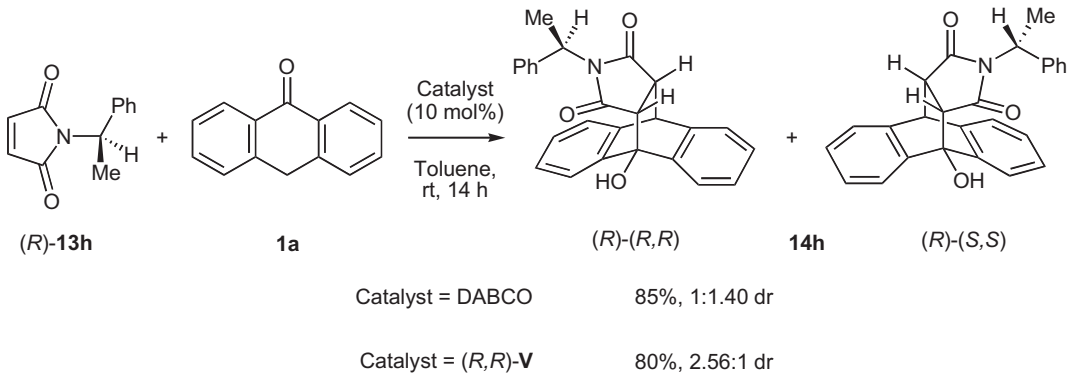
[a] Experimental conditions: A mixture of **1a** (0.25 mmol), **13a** (0.30 mmol), and the catalyst (0.025 mmol) in the solvent specified in the table (1 mL) was stirred at rt during 14 h. See Table 6 for the structures of catalysts **VI** and **VII**.
[b] Determined by ^{1}H NMR analysis of the reaction mixture.
[c] Determined by HPLC analysis.
[d] Preferential formation of *ent*-**14a**.

Table 10
Scope of the Diels–Alder cycloaddition between anthrone (**1a**) and maleimides (**13a**–**e**) catalyzed by **V**[a]



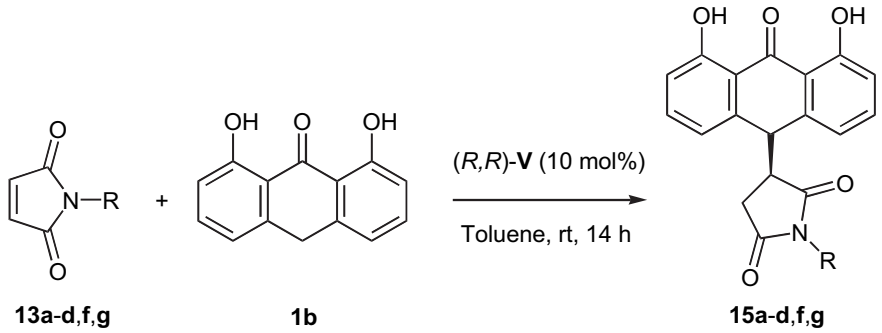
Entry	Maleimide (R)	Product	Yield[b]	ee[c]
1	**13a** (Ph)	**14a**	91%	90%
2	**13b** (CH_2Ph)	**14b**	92%	85%
3	**13c** (3-ClPh)	**14c**	92%	90%
4	**13d** (4-MeOPh)	**14d**	90%	97%
5	**13e** (4-CF_3Ph)	**14′e**[d]	94%	97%
6	**13f** (4-BrPh)	**14f**	94%	29%
7	**13 g** ($CHPh_2$)	**14 g**	86%	33%

[a] Experimental conditions: Maleimides **13a**–**g** (0.30 mmol) were added to a solution of **1a** (0.25 mmol) and of catalyst (*R*,*R*)-**V** (0.025 mmol) in toluene (1 mL) and the resulting mixture was stirred at rt for 14 h.
[b] Yield of isolated product after chromatographic purification.
[c] Determined by HPLC analysis.
[d] Only the Michael adduct **14′e** was isolated.



Scheme 3. Amine-catalyzed Diels–Alder cycloaddition between anthrone (**1a**) and (*R*)-*N*-(1-phenylethyl)maleimide **13h**.

Table 11
Scope of the reaction between dithranol (**1b**) and maleimides (**13a-d**,**f**,**g**) catalyzed by **V**[a]



Entry	Maleimide (R)	Product	Yield (%)[b]	ee[c]
1	**13a** (Ph)	**15a**	93	99%
2	**13b** (CH_2Ph)	**15b**	92	85%
3	**13c** (3-ClPh)	**15c**	92	22%
4	**13d** (4-MeOPh)	**15d**	94	97%
5	**13f** (4-BrPh)	**15e**	91	96%
6	**13g** ($CHPh_2$)	**15g**	78	n.d.[d]

[a] Experimental conditions: Maleimides **13a-d**,**f**,**g** (0.30 mmol) were added to a solution of **1b** (0.25 mmol) and of catalyst (*R*,*R*)-**V** (0.025 mmol) in toluene (1 mL) and the resulting mixture was stirred at rt for 14 h.
[b] Yield of isolated product after chromatographic purification.
[c] Determined by HPLC analysis.
[d] Not determined.

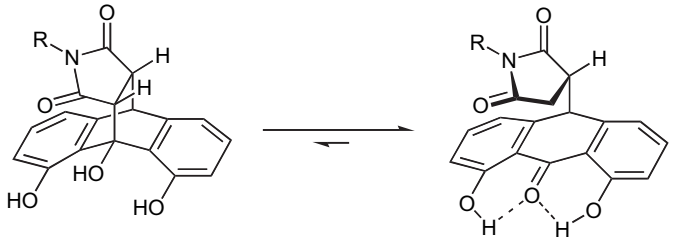


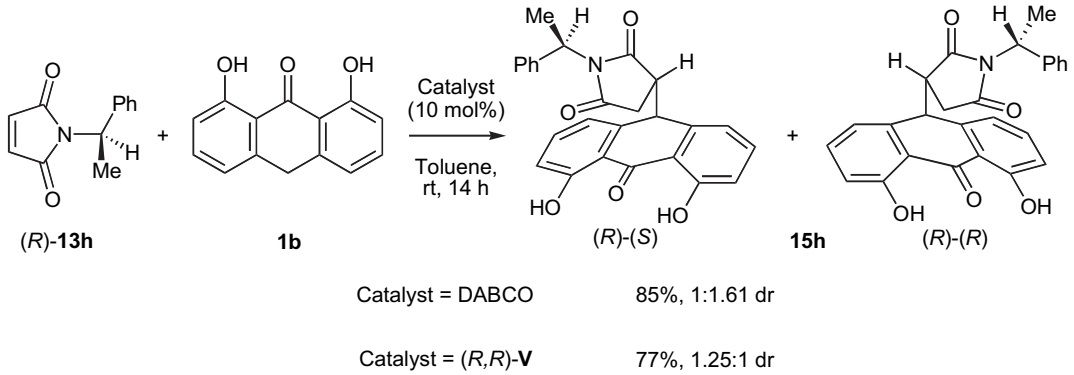
Fig. 3. Rationalization of the enhanced thermodynamic stability of the Michael product in front of the Diels–Alder dithranol-maleimide cycloadducts.

On the other hand, the reaction of dithranol with (*R*)-*N*-(1-phenylethyl)maleimide **13h** gave the Michael adduct **15h** as a diastereomeric mixture (Scheme 4). While catalysis with DABCO afforded a 1:1.61 diastereomer ratio, when using (*R*,*R*)-**V** as a catalyst the diastereomer ratio changed to 1.25:1. The calculated inthrinsic diastereomeric ratio for **V** (2.01:1)[29] therefore lower than in the case of anthrone.

The stereochemical outcome of the anthrone/maleimide Diels–Alder reaction (preferential formation of the (*R*,*R*)-cycloadducts when (*R*,*R*)-**V** was used as a catalyst) can be accounted for by the transition state working model depicted in Fig. 4. In this transition state, the thiourea moiety binds to a carbonyl of the maleimide, while the anthrone enolate interacts, also by hydrogen bonding, with the protonated amine. Molecular modeling of this transition state (Fig. 5) suggests that π-stacking interactions between the *N*-aryl substituent of the maleimide and the 3,5-bis(trifluoromethyl)phenyl moiety of the catalyst may also play a role in the preferred orientation of the maleimide. The fact that *N*-(α-branched) benzylmaleimides give low stereoselectivities with Takemoto's catalyst **V** gives support to this hypothesis.

3. Conclusions

In summary, we have presented full details of three different organocatalytic asymmetric additions of anthrones to activated alkenes. The reaction between anthrone (**1a**) or dithranol (**1b**) and α,β-unsaturated aromatic or aliphatic aldehydes is catalyzed by diphenylprolinol trimethylsilyl ether **III**, giving the Michael adducts with good yields and enantioselectivities when low reaction temperatures were used. The absolute configuration of the products, determined by chemical correlation, can be accounted for within



Scheme 4. Amine-catalyzed Michael addition between dithranol (**1b**) and (*R*)-*N*-(1-phenylethyl)maleimide **13e**.

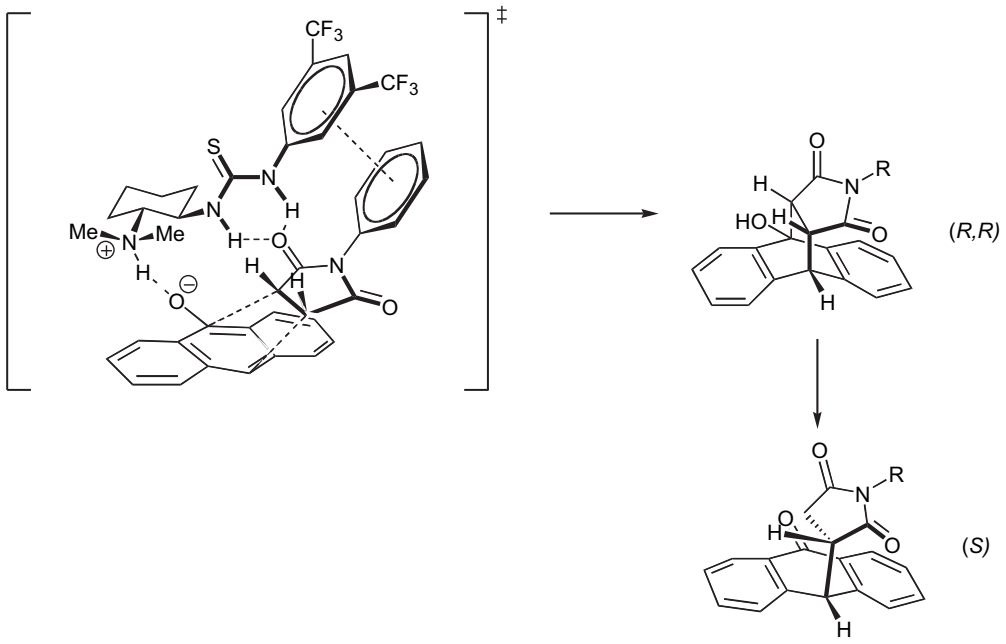


Fig. 4. Transition state working model for the Diels–Alder cycloaddition between anthrones and maleimides catalyzed by (*R*,*R*)-**V**.

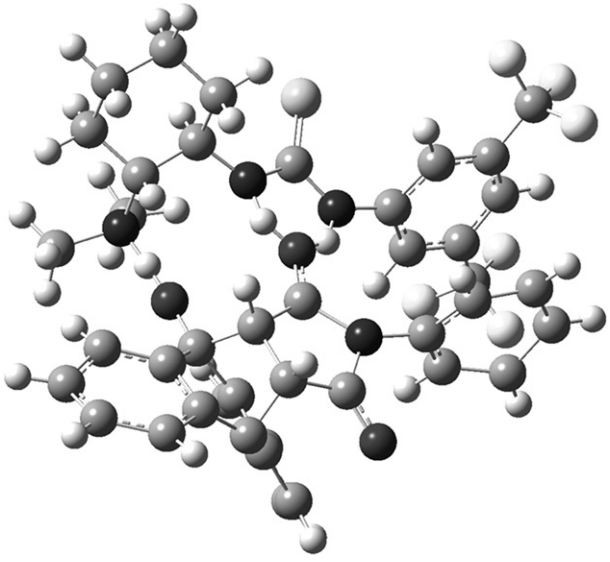


Fig. 5. Ball-and-stick representation of the proposed transition state for the Diels–Alder cycloaddition between anthrones and maleimides catalyzed by (*R*,*R*)-**V**.

the mechanistic framework commonly accepted for chiral secondary amine-catalyzed Michael additions to enals. On the other hand, bifunctional amino-thioureas, especially Takemoto's thiourea **V**, have been shown to be extremely preactical organocatalysts for the additions of anthrones to both nitroalkenes and maleimides, since high enantioselectivities can be achieved in both instances at room temperature in non-halogenated solvents (toluene). In the case of nitroalkenes, the reaction goes exclusively through a Michael addition. Anthrone generally gives Diels–Alder cycloadducts in the reaction with maleimides (except for *N*-(4-trifluoromethyl) phenylmaleimide), while dithranol affords the Michael adducts. Transition state working models in which the bifunctional catalyst binds simultaneously to the alkene and to the anthrone enolate rationalize the stereochemical outcome of these processes.

4. Experimental section

4.1. General materials and methods

Melting points were taken on a Gallenkamp apparatus and are uncorrected. Specific rotations were measured at room temperature in a Perkin–Elmer 241 MC polarimeter, using a sodium lamp

(λ=589 nm) and a 1 dm-long 1 mL cell. NMR spectra were recorded in $CDCl_3$ solution. ^1H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) were obtained on a Varian Unity 300 or on a Unity-Innova 300 spectrometer; ^1H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) were obtained on a Mercury 400 spectrometer. Chemical shifts (δ) are quoted in parts per million and referenced to internal TMS for ^1H NMR and to $CDCl_3$ (δ 77.0) for ^{13}C NMR; data are reported as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad; coupling constants (*J*) are quoted in hertz. High resolution mass spectra (HRMS) were obtained with the ESI (+or −) technique at the 'Unitat d' Espectrometria de Masses' of the Barcelona University. Enantiomeric purities were determined by HPLC using Daicel Chiralpak® IA, IB or IC columns in a Shimadzu LC-20AD instrument with UV detection. Reactions were generally run with magnetic stirring in loosely stoppered glass vials under air. Commercially available reagents, catalysts and solvents were used as received. Aldehydes **2b**,**c**[30] and maleimides **13c**–**f**[23a,31] were prepared according to literature procedures. Catalysts **VI** and **VII** were obtained from quinine and from quinidine, respectively, by the method described by Jérgensen and co-workers.[32] Silica gel (0.063–0.200 mm) was used for chromatographic purifications.

4.2. General experimental procedure for the addition of anthrones to α,β-unsaturated aldehydes

To a stirred solution of catalyst (*S*)-**III** (20 mg, 0.06 mmol) in toluene (2 mL) were added the α,β-unsaturated aldehyde (0.25 mmol) and the anthrone (**1a** or **1b**, 0.30 mmol). The reaction crude was vigorously stirred at −40 °C until the starting anthrone was not detected by ^1H NMR. After warming up the reaction flask to room temperature, the reaction crude was directly purified by column chromatography on silica gel (hexane/ethyl acetate mixtures) to afford the Michael adduct. Racemic products were obtained from the corresponding substrates by catalysis with an artificially constructed racemic mixture of **III** in toluene at room temperature during 5 days. Enantiomeric purities were directly determined from the crude reaction mixture immediately after complete conversion, because racemization took place at room temperature. This fact precluded in most instances the reliable determination of specific rotations for adducts **3** and **4**.

*4.2.1. (R)-3-(10-Oxo-9,10-dihydro-anthracen-9-yl)-3-phenyl-propanal (**3a**).* Obtained in 88% yield and 80% ee from **2a** and **1a**. Colorless oil. ^1H NMR (400 MHz) δ 2.70 (ddd, *J*=17.4, 8.6, 1.8 Hz, 1H), 2.82 (ddd, *J*=17.4, 6.8, 1.4 Hz, 1H), 3.76–3.83 (m, 1H), 4.52 (d, *J*=4.0 Hz, 1H), 6.28–6.32 (m, 2H), 6.99–7.04 (m, 2H), 7.12–7.21 (m, 2H), 7.38–7.53 (m, 4H), 7.59 (dt, *J*=7.5, 1.4 Hz, 1H), 8.00 (dd, *J*=7.7, 1.4 Hz, 1H), 8.06 (dd, *J*=7.7, 1.4 Hz, 1H), 9.61 (t, *J*=1.5 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 45.0, 48.7, 49.5, 126.6, 127.0, 127.4, 127.6, 127.8, 128.5, 128.7, 132.2, 133.3, 133.9, 134.1, 137.4, 139.8, 141.1, 142.4, 183.9, 200.6. HRMS (ESI) calcd from $C_{46}H_{36}O_4Na$ $(2M+Na)^+$: 675.2505; found: 675.2505. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=44.4 min, t_{minor}=39.2 min.

*4.2.2. (R)-3-(4-Cyanophenyl)-3-(10-oxo-9,10-dihydro-anthracen-9-yl)-propanal (**3b**).* Obtained in 85% yield and 99% ee from **2b** and **1a**. Colorless oil. ^1H NMR (400 MHz) δ 2.76 (ddd, *J*=18.0, 8.2 Hz, 1H), 2.97 (dd, *J*=18.0, 6.9 Hz, 1H), 3.83–3.89 (m, 1H), 4.55 (d, *J*=4.0 Hz, 1H), 6.36 (d, *J*=8.3 Hz, 2H), 7.25–7.30 (m, 2H), 7.40–7.70 (m, 6H), 8.02–8.12 (m, 2H), 9.67 (m, 1H). ^{13}C NMR (100.6 MHz) δ 45.2, 48.1, 49.3, 118.5, 127.0, 127.4, 127.8, 128.1, 128.3, 128.5, 129.4, 131.6, 132.3, 132.6, 140.2, 141.9, 143.3, 172.3, 199.3. HRMS (ESI) calcd from $C_{24}H_{17}NO_2Na$ $(M+Na)^+$: 374.1151; found: 374.1153. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=60.8 min, t_{minor}=37.0 min.

*4.2.3. (R)-3-(4-Nitrophenyl)-3-(10-oxo-9,10-dihydro-anthracen-9-yl)-propanal (**3c**).* Obtained in 75% yield and 78% ee from **2c** and **1a**. Yellowish oil. ^1H NMR (400 MHz) δ 3.17 (ddd, *J*=18.0, 8.0, 1.2 Hz, 1H), 3.38 (ddd, *J*=18.0, 8.0, 1.2 Hz, 1H), 4.94 (d, *J*=4.0 Hz, 1H), 6.77 (m, 2H), 7.63–8.23 (m, 8H), 8.41 (dd, *J*=7.6, 1.6 Hz, 1H), 8.46 (dd, *J*=7.6, 1.6 Hz, 1H), 10.05 (m, 1H). ^{13}C NMR (100.6 MHz) δ 46.0, 48.6, 49.7, 123.5, 127.6, 128.0, 128.5, 128.7, 128.9, 129.1, 130.1, 132.9, 133.3, 140.7, 142.5, 146.0, 163.1, 184.2, 199.8. HRMS (ESI) calcd from $C_{23}H_{18}NO_4$ $(M+H)^+$: 372.1233; found: 372.1230. HPLC conditions: Daicel Chiralpak® IA column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=55.16 min, t_{minor}=50.29 min.

*4.2.4. (R)-3-(2-Bromophenyl)-3-(10-oxo-9,10-dihydro-anthracen-9-yl)-propanal (**3d**).* Obtained in 32% yield and 3% ee from **2d** and **1a**. Colorless oil. ^1H NMR (400 MHz) δ 2.41 (dd, *J*=17.6, 5.6 Hz, 1H), 2.51 (ddd, *J*=17.2, 10.4, 2.0 Hz, 1H), 4.49 (q, *J*=4.8 Hz, 1H), 4.82 (d, *J*=4.0 Hz, 1H), 6.40 (dd, *J*=7.6, 1.6 Hz, 1H), 6.50 (d, *J*=7.6 Hz, 1H), 7.19–7.79 (m, 8H), 8.34 (d, *J*=1.2 Hz, 1H), 8.36 (d, *J*=1.2 Hz, 1H), 9.39 (m, 1H). ^{13}C NMR (100.6 MHz) δ 45.4, 49.0, 49.4, 121.9, 130.8, 131.5, 132.7, 132.8, 133.7, 134.3, 137.4, 141.4, 142.5, 184.3, 200.4. HRMS (ESI) calcd from $C_{23}H_{18}BrO_2$ $(M+H)^+$: 405.0487; found: 405.0484. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=68.5 min, t_{minor}=76.5 min.

*4.2.5. (R)-3-(2-Nitrophenyl)-3-(10-oxo-9,10-dihydro-anthracen-9-yl)-propanal (**3e**).* Obtained in 35% yield and 7% ee from **2e** and **1a**. Yellowish oil. ^1H NMR (400 MHz) δ 2.72 (m, 2H), 4.81 (m, 1H), 4.92 (d, *J*=4.0 Hz, 1H), 6.42 (dd, *J*=8.0, 1.2 Hz, 1H), 6.87 (d, *J*=7.2 Hz, 1H), 7.42–7.98 (m, 8H), 8.32 (d, *J*=1.2 Hz, 1H), 8.34 (d, *J*=1.2 Hz, 1H), 9.57 (t, *J*=1.6 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 43.2, 44.1, 47.8, 125.5, 127.8, 128.0, 128.7, 128.8, 129.0, 129.2, 130.5, 130.9, 132.5, 132.6, 133.6, 140.5, 142.4, 185.1, 199.7. HRMS (ESI) calcd from $C_{23}H_{18}NO_4$ $(M+H)^+$: 372.1233; found: 372.1230. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=24.0 min, t_{minor}=28.0 min.

*4.2.6. (R)-3-(10-Oxo-9,10-dihydro-anthracen-9-yl)-butanal (**3f**).* Obtained in 95% yield and 94% ee from **2f** and **1a**. Colorless oil. ^1H NMR (400 MHz) δ 0.70 (d, *J*=6.8 Hz, 3H), 2.03 (ddd, *J*=17.0, 8.6, 1.6 Hz, 1H), 2.42 (ddd, *J*=17.3, 5.8, 1.1 Hz, 1H), 2.62–2.72 (m, 1H), 4.28 (d, *J*=3.1 Hz, 1H), 7.39–7.52 (m, 4H), 7.56–7.61 (m, 2H), 8.26 (dt, *J*=7.7, 1.6 Hz, 2H), 9.65 (t, *J*=1.8 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 17.0, 38.4, 47.9, 48.0, 127.7, 127.9, 128.0, 128.1, 129.2, 129.3, 133.1, 133.2, 142.7, 143.6, 185.8, 201.9. HRMS (ESI) calcd from $C_{18}H_{17}NO_2$ $(M+H)^+$: 265.1223; found: 265.1222. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 8:92, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=38.0 min, t_{minor}=32.2 min.

*4.2.7. (R)-3-(10-Oxo-9,10-dihydro-anthracen-9-yl)-pentanal (**3g**).* Obtained in 82% yield and 96% ee from **2g** and **1a**. Colorless oil. ^1H NMR (400 MHz) δ 0.91–1.10 (m, 5H), 1.99 (ddd, *J*=17.6, 7.3, 1.5 Hz, 1H), 2.22 (ddd, *J*=17.6, 6.4, 1.5 Hz, 1H), 2.40–2.50 (m, 1H), 4.42 (d, *J*=2.9 Hz, 1H), 7.40–7.50 (m, 4H), 7.56–7.62 (m, 2H), 8.24–8.29 (m, 2H), 9.56 (t, *J*=1.5 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 12.8, 24.2, 45.0, 45.1, 45.5, 127.9, 128.0, 128.1, 129.2, 129.3, 133.1, 133.4, 143.1, 143.8, 185.7, 202.1. HRMS (ESI) calcd from $C_{19}H_{19}NO_2$ $(M+H)^+$: 279.1380; found: 279.1377. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 8:92, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=42.1 min, t_{minor}=35.3 min.

*4.2.8. (R)-3-(10-Oxo-9,10-dihydro-anthracen-9-yl)-hexanal (**3h**).* Obtained in 84% yield and 96% ee from **2h** and **1a**. Colorless

oil. ^{1}H NMR (400 MHz) δ 0.85 (t, J=7.0 Hz, 3H), 0.91–1.00 (m, 1H), 1.24–1.40 (m, 3H), 1.96 (ddd, J=17.4, 7.1, 1.8 Hz, 1H), 2.21 (ddd, J=17.6, 6.3, 1.5 Hz, 1H), 2.51–2.59 (m, 1H), 4.41 (d, J=2.9 Hz, 1H), 7.41–7.49 (m, 4H), 7.57–7.61 (m, 2H), 8.24–8.29 (m, 2H), 9.54 (t, J=1.4 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 14.5, 21.1, 33.6, 45.0, 43.3, 45.3, 127.8, 128.0, 129.2, 129.3, 133.1, 133.3, 143.0, 143.8, 185.6, 202.0. HRMS (ESI) calcd from $C_{20}H_{219}NO_2$ $(M+H)^+$: 293.1536; found: 293.1535. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 8:92, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=44.7 min, t_{minor}=32.7 min.

*4.2.9. (R)-3-(10-Oxo-9,10-dihydro-anthracen-9-yl)-heptanal (**3i**).* Obtained in 92% yield and 86% ee from **2i** and **1a**. Colorless oil. $[\alpha]_D^{25}$ −3.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz) δ 0.83 (t, J=7.1 Hz, 3H), 1.20–1.36 (m, 6H), 1.95 (ddd, J=17.4, 7.2, 1.8 Hz, 1H), 2.20 (ddd, J=17.4, 6.3, 1.6 Hz, 1H), 2.49–2.57 (m, 1H), 4.41 (d, J=2.9 Hz, 1H), 7.40–7.50 (m, 4H), 7.56–7.62 (m, 2H), 8.23–8.30 (m, 2H), 9.53 (t, J=1.6 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 13.9, 22.5, 29.6, 30.5, 42.9, 44.6, 44.7, 127.1, 127.2, 127.3, 127.4, 128.6, 128.7, 132.5, 132.7, 133.3, 133.4, 142.4, 143.3, 185.0, 201.4. HRMS (ESI) calcd from $C_{21}H_{22}O_2Na$ $(M+Na)^+$: 329.1512; found: 329.1511. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 8:92, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=38.0 min, t_{minor}=25.2 min.

*4.2.10. (R)-3-(4,5-Dihydroxy-10-oxo-9,10-dihydro-anthracen-9-yl)-butanal (**4a**).* Obtained in 88% yield and 97% ee from **2f** and **1b**. Yellowish oil. ^{1}H NMR (300 MHz) δ 0.72 (d, J=6.7 Hz, 3H), 2.09 (ddd, J=17.0, 7.9, 1.8 Hz, 1H), 2.40–2.65 (m, 2H), 4.21 (d, J=3.2 Hz, 1H), 6.79–6.83 (m, 1H), 6.91–6.97 (m, 3H), 7.45–7.53 (m, 2H), 9.67 (t, J=1.5 Hz, 1H), 12.07 (s, 1H, O*H*), 12.11 (s, 1H, O*H*). ^{13}C NMR (100.6 MHz) δ 16.3, 38.9, 47.4, 47.7, 116.3, 116.5, 119.6, 135.9, 136.2, 143.7, 144.8, 162.5, 162.7, 193.8, 201.1. HRMS (ESI) calcd from $C_{18}H_{17}O_4$ $(M+H)^+$: 297.1121; found: 297.1121. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=23.7 min, t_{minor}=17.0 min.

*4.2.11. (R)-3-(4,5-Dihydroxy-10-oxo-9,10-dihydro-anthracen-9-yl)-pentanal (**4b**).* Obtained in 95% yield and 99% ee from **2g** and **1b**. Yellowish oil. ^{1}H NMR (400 MHz) δ 0.92 (t, J=7.0 Hz, 3H), 0.97–1.30 (m, 1H), 1.33–1.41 (m, 1H), 2.07 (ddd, J=16.9, 6.3, 1.6 Hz, 1H), 2.26–2.38 (m, 2H), 4.35 (d, J=2.7 Hz, 1H), 6.82–6.85 (m, 1H), 6.90–6.95 (m, 3H), 7.46–7.52 (m, 2H), 9.59 (t, J=1.5 Hz, 1H), 12.10–12.12 (m, 2H, O*H*). ^{13}C NMR (100.6 MHz) δ 12.1, 23.2, 44.3, 44.9, 46.3, 116.4, 119.5, 119.6, 128.5, 132.0, 132.1, 136.1, 136.2, 144.3, 144.8, 162.6, 193.8, 201.3. HRMS (ESI) calcd from $C_{19}H_{19}O_4$ $(M+H)^+$: 311.1278; found: 311.1280. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=27.8 min, t_{minor}=19.0 min.

*4.2.12. (R)-3-(4,5-Dihydroxy-10-oxo-9,10-dihydro-anthracen-9-yl)-hexanal (**4c**).* Obtained in 93% yield and 99% ee from **2h** and **1b**. Yellowish oil. $[\alpha]_D^{20}$ −5.7 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz) δ 0.86 (t, J=7.1 Hz, 3H), 1.20–1.38 (m, 4H), 2.03 (ddd, J=17.4, 6.9, 1.8 Hz, 1H), 2.29 (ddd, J=17.4, 6.6, 1.6 Hz, 1H), 2.41–2.50 (m, 1H), 4.33 (d, J=3.1 Hz, 1H), 6.82–6.85 (m, 1H), 6.90–6.95 (m, 3H), 7.46–7.52 (m, 2H), 9.56 (t, J=1.6 Hz, 1H), 12.11 (s, 1H, O*H*), 12.13 (s, 1H, O*H*). ^{13}C NMR (100.6 MHz) δ 13.9, 20.5, 32.5, 44.1, 44.6, 45.1, 116.3, 116.4, 116.5, 119.5, 119.6, 136.1, 136.2, 144.2, 144.9, 162.6, 193.8, 201.3. HRMS (ESI) calcd from $C_{20}H_{20}NaO_4$ $(M+Na)^+$: 347.1254; found: 347.1255. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=27.1 min, t_{minor}=17.9 min.

*4.2.13. (R)-3-(4,5-Dihydroxy-10-oxo-9,10-dihydro-anthracen-9-yl)-heptanal (**4d**).* Obtained in 92% yield and 99% ee from **2i** and **1b**. Yellowish oil. ^{1}H NMR (400 MHz) δ 0.88 (t, J=7.1 Hz, 3H), 0.90–1.43 (m, 6H), 2.00–2.32 (m, 2H), 2.40–2.51 (m, 1H), 4.34 (d, J=3.1 Hz, 1H), 6.83–6.86 (m, 1H), 6.89–6.94 (m, 3H), 7.46–7.51 (m, 2H), 9.55 (t, J=1.5 Hz, 1H), 12.11–12.13 (m, 2H, O*H*). ^{13}C NMR (100.6 MHz) δ 14.0, 19.8, 31.3, 33.0, 43.9, 44.3, 45.0, 116.3, 116.5, 119.5, 119.6, 131.9, 132.1, 136.0, 136.2, 144.1, 144.9, 162.6, 193.8, 201.3. HRMS (ESI) calcd from $C_{21}H_{25}O_4$ $(M+H)^+$: 341.1747; found: 341.1751. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=25.7 min, t_{minor}=18.7 min.

4.3. Determination of the absolute configuration of 3a

In an oven-dried, 25 mL round-bottomed flask, 300 mg of anthrone **1a** (1.54 mmol, 1 equiv) were dissolved in 9 mL of dry toluene. The solution was cooled to −20 °C under an atmosphere of pre-purified nitrogen and 204 mg of cinnamaldehyde **2a** (1.54 mmol, 1 equiv) and 101 mg of (*S*)-diphenylprolinol trimethylsilyl ether **III** (0.31 mmol, 0.2 equiv) were added sequentially via syringe. After 4 days of stirring at this temperature, 0.46 mL of methylmagnesium bromide solution (3.0 M in diethyl ether, 1.39 mmol, 0.9 equiv) was added. The reaction mixture was allowed to slowly reach room temperature and was quenched with a saturated aqueous solution of NH_4Cl, extracted three times with dichloromethane and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure and the crude was purified by flash chromatography using mixtures of hexane/ethyl acetate as eluent, affording 123 mg of the diastereomeric alcohols **5a**, **5a′** as a 1:1 mixture (33% yield).

^{1}H NMR (400 MHz): δ 1.10 (d, J=6.1 Hz, 3H), 1.11 (d, J=6.1 Hz, 3H), 1.80–2.04 (m, 4H), 3.16–3.74 (m, 4H), 4.46–4.49 (m, 2H), 6.16–6.20 (m, 4H), 6.69–8.38 (m, 22H).

This alcohol mixture (0.36 mmol, 1 equiv) was dissolved in 1 mL of dichloromethane in a 5 mL round-bottomed flask, equipped with magnetic stirring, and 116 mg of pyridinium chlorochromate (0.54 mmol, 1.5 equiv) was added in one portion. After consumption of starting material (monitored by TLC), diethyl ether (5 mL) was added and the mixture was filtered through Celite®. Purification by column chromatography gave 55 mg of ketone (−)-**6a** (45% yield), whose spectroscopic data matched those previously reported in the literature for (*S*)-(+)-**6a**.[12] $[\alpha]_D^{20}$ −1.8 (*c* 2.7, CH_2Cl_2).

4.4. General experimental procedure for the addition of anthrones to *trans*-β-nitrostyrenes

To a stirred solution of catalyst (*R*,*R*)-**V** (10 mg, 0.025 mmol) in toluene (1 mL) were added the nitrostyrene (0.30 mmol) and the anthrone (**1a** or **1b**, 0.25 mmol). The reaction crude was vigorously stirred at room temperature (anthrone **1a**) or at −40 °C (dithranol **1b**) during 14 h. After warming up the reaction flask to room temperature, the crude product was directly purified by column chromatography on silica gel (hexane/ethyl acetate mixtures) to afford the Michael adduct. Racemic products were obtained from the corresponding substrates by catalysis with DABCO in toluene at room temperature.

*4.4.1. (R)-(−)-10-(2-Nitro-1-phenyl-ethyl)-10H-anthracen-9-one (**11a**)[14,19].* Obtained in 92% yield and 89% ee from **10a** and **1a**. Colorless solid. Mp 147–148 °C. $[\alpha]_D^{25}$ −22.8 (*c* 0.9, $CHCl_3$). ^{1}H NMR (300 MHz) δ 4.05 (m, 1H), 4.55 (d, J=3.5 Hz, 1H), 4.57–4.62 (dd, J=13.0, 7.0 Hz, 1H), 4.86–4.92 (dd, J=13.0, 9.0 Hz, 1H), 6.04–6.06 (d. J=7.0 Hz, 2H), 6.93–6.97 (t, J=8.0 Hz, 2H), 7.13–7.17 (t, J=8.0 Hz, 1H), 7.48–7.66 (m, 6H), 7.97–7.99 (d, J=7.0 Hz, 1H), 8.05–8.07 (d. J=6.5 Hz, 1H), 8.17–8.19 (d, J=6.5 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 46.4, 53.5, 73.4126.7, 127.2, 127.3, 127.4, 127.5, 127.9, 128.1, 128.2, 128.7, 129.1, 132.3, 133.0, 133.5, 133.6, 139.5, 140.7, 142.2, 183.5. HPLC conditions: Daicel Chiralpak® IA column, *i*-PrOH/hexane 10:90,

flow rate 1 mL/min, UV detection at 254 nm, t_{major}=10.7 min, t_{minor}=10.0 min.

*4.4.2. (−)-10-[1-(2-Fluorophenyl)-2-nitroethyl]-10H-anthracen-9-one (**11b**).* Obtained in 95% yield and 92% ee from **10b** and **1a**. Colorless waxy solid. $[\alpha]_D^{25}$ −17.8 (*c* 0.9, $CHCl_3$). ^{1}H NMR (300 MHz) δ 4.38 (m, 1H), 4.50–4.56 (dd, *J*=12.0, 6.0 Hz, 1H), 4.60 (d, *J*=3.0 Hz, 1H), 4.71–4.77 (dd, *J*=9.0, 6.0 Hz, 1H), 6.04–6.08 (t, *J*=6.0 Hz, 1H), 6.78–6.82 (t, *J*=6.0 Hz, 1H), 6.84–6.88 (t, *J*=6.0 Hz, 1H), 7.09–7.66 (m, 7H), 8.06–8.08 (d, *J*=6.0 Hz, 1H), 8.12–8.14 (d, *J*=6.0 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 45.9, 47.2, 75.6, 115.8, 116.1, 121.7, 121.8, 123.9, 127.3, 127.6, 128.3, 128.9, 129.8, 130.3, 132.9, 133.2, 134.0, 140.1, 141.1, 159.5, 162.8, 183.7. HRMS (ESI) calcd from $C_{22}H_{16}FNNaO_3$ $(M+Na)^+$: 384.1006; found: 384.1003. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 5:95, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=68.5 min, t_{minor}=40.5 min.

*4.4.3. (−)-10-(2-Nitro-1-p-tolyl-ethyl)-10H-anhtracen-9-one (**11c**)[14,19].* Obtained in 92% yield and 90% ee from **10c** and **1a**. Colorless solid. Mp 157–159 °C. $[\alpha]_D^{20}$ −17.8 (*c* 0.8, $CHCl_3$). ^{1}H NMR (300 MHz) δ 2.35 (s, 3H), 4.03 (m, 1H), 4.52 (d, *J*=3.0 Hz, 1H), 4.53–4.58 (dd, *J*=12.0, 6.0 Hz, 1H), 4.87 (dd, *J*=9.0, 6.0 Hz, 1H), 5.95–5.97 (d, *J*=6.0 Hz, 2H), 6.75–6.77 (d, *J*=6.0 Hz, 2H), 7–26–7.65 (m, 4H), 8.01–7.99 (d, *J*=6.0 Hz, 1H), 8.07–8.09 (d, *J*=6.0 Hz, 1H), 8.20 (m, 2H). ^{13}C NMR (100.6 MHz) δ 21.3, 46.4, 53.2, 76.8, 127.0, 127.5, 127.9, 128.3, 128.4, 128.6, 128.9, 130.4, 132.5, 132.9, 133.5, 134.1, 138.2, 139.7, 142.2, 185.4. HPLC conditions: Daicel Chiralpak® IA column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=7.0 min, t_{minor}=7.6 min.

*4.4.4. (−)-10-[1-(4-Methoxyphenyl)-2-nitroethyl]-10H-anthracen-9-one (**11d**)[14,19].* Obtained in 94% yield and 90% ee from **10d** and **1a**. Colorless solid. Mp 122–123 °C. $[\alpha]_D^{20}$ −18.9 (*c* 0.8, $CHCl_3$). ^{1}H NMR (300 MHz) δ 3.75 (s, 3H), 4.01 (m, 1H), 4.51 (d, *J*=3.5 Hz, 1H), 4.52–4.57 (dd, *J*=12.0, 6.0 Hz, 1H), 4.81–4.86 (dd, *J*=9.0, 6.0 Hz, 1H), 5.95–5.97 (d, *J*=7.0 Hz, 2H), 6.47–6.49 (d, *J*=7.0 Hz, 2H), 7.40–7.43 (m, 2H), 7.45–7.52 (m, 2H), 7.61–7.65 (m, 2H), 8.00 (d, *J*=7.0 Hz, 1H), 8.02 (d, *J*=7.0 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 46.5, 52.9, 55.4, 76.8, 113.7, 125.1, 126.8, 127.0, 127.5, 127.9, 128.3, 128.4, 128.7, 129.9, 132.4, 132.5, 132.9, 133.5, 134.5, 139.6, 142.3, 159.6, 183.4. HPLC conditions: Daicel Chiralpak® IA column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=11.9 min, t_{minor}=11.2 min.

*4.4.5. (−)-10-[2-Nitro-1-(4-nitrophenyl)ethyl]-10H-anthracen-9-one (**11e**)[14,19].* Obtained in 91% yield and 85% ee from **10e** and **1a**. Colorless solid. Mp 195–196 °C. $[\alpha]_D^{20}$ −20.1 (*c* 0.9, $CHCl_3$). ^{1}H NMR (300 MHz) δ 4.19 (m, 1H), 4.60 (d, *J*=3.0 Hz, 1H), 4.61–4.66 (dd, *J*=12.0, 9.0 Hz, 1H), 4.93–4.98 (dd, *J*=12.0, 5.0 Hz, 1H), 6.25–6.27 (d, *J*=6.0 Hz, 2H), 7.45–7.84 (m, 7H), 8.00–8.02 (d, *J*=6.0 Hz, 1H), 8.09–8.11 (d, *J*=6.0 Hz, 1H), 8.32–8.34 (dd, *J*=6.0, 3.0 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 46.2, 53.2, 76.5, 123.3, 127.4, 127.9, 128.2, 128.5, 128.6, 128.9, 129.7, 132.9, 133.3, 133.4, 134.3, 138.6, 140.9, 141.3, 147.4, 184.8. HPLC conditions: Daicel Chiralpak® IA column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=25.2 min, t_{minor}=24.8 min.

*4.4.6. 1,8-Dihydroxy-10-(1-phenyl-2-nitroethyl)anthracen-9(10H)-one (**12a**).* Obtained in 77% yield and 35% ee from **10a** and **1b**. Yellow solid. ^{1}H NMR (300 MHz) δ 3.95 (m, 1H), 4.47 (d. *J*=3.0 Hz, 1H), 4.55–4.61 (dd, *J*=12.0, 6.0 Hz, 1H), 4.91–4.99 (dd, *J*=12.0, 9.0 Hz, 1H), 6.06–6.09 (d, *J*=9.0 Hz, 2H), 6.89–7.04 (m, 5H), 7.16–7.18 (t, *J*=6.0 Hz, 2H), 7.57 (m, 2H). ^{13}C NMR (100.6 MHz) δ 46.7, 54.3, 76.5, 116.9, 117.5, 119.1, 119.6, 128.0, 128.1, 128.7, 128.8, 129.2, 133.2, 135.9, 136.6, 140.8, 144.1, 162.2, 162.7, 192.5. HRMS (ESI) calcd from $C_{22}H_{16}NO_5$ $(M-H)^-$: 374.1034; found: 374.1031. HPLC conditions: Daicel IB column, *i*-PrOH/hexane 5:95, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=18.5 min, t_{minor}=19.5 min.

*4.4.7. 1,8-Dihydroxy-10-(1-(2-fluorophenyl)-2-nitroethyl)anthracen-9(10H)-one (**12b**).* Obtained in 89% yield and 21% ee from **10b** and **1b**. Yellow solid. ^{1}H NMR (300 MHz) δ 4.11 (m, 1H), 4.53 (d, *J*=3.0 Hz, 1H), 4.56–4.65 (dd, *J*=12.0, 9.0 Hz, 1H), 4.89–4.95 (dd, *J*=12.0, 9.0 Hz, 1H), 6.55–6.59 (t, *J*=6.0 Hz, 1H), 6.82–6.99 (m, 7H), 7.25–7.27 (d, *J*=6.0 Hz, 1H), 7.30–7.32 (d, *J*=6.0 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 46.4, 48.3, 75.4, 115.8, 116.0, 116.8, 117.3, 117.7, 119.8, 121.4, 121.6, 123.9, 130.0, 130.5, 130.6, 136.2, 136.5, 141.3, 142.8, 159.9, 162.5, 162.8, 192.6. HRMS (ESI) calcd from $C_{22}H_{17}FNO_5$ $(M+H)^+$: 394.1085; found: 394.1088. HPLC conditions: Daicel Chiralpak® IB column, *i*-PrOH/hexane 5:95, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=13.7 min, t_{minor}=15.7 min.

*4.4.8. 1,8-Dihydroxy-10-(2-nitro-1-p-tolylethyl)anthracen-9(10H)-one (**12c**).* Obtained in 85% yield and 38% ee from **10c** and **1b**. Yellow solid. ^{1}H NMR (300 MHz) δ 2.34 (s, 3H), 3.91 (m, 1H), 4.45 (d, *J*=3.0 Hz, 1H), 4.52–4.58 (dd, *J*=12.0, 6.0 Hz, 1H), 4.88–4.95 (dd, *J*=12.0, 9.0 Hz, 1H), 5.97 (d, *J*=6.0 Hz, 2H), 6.82 (d, *J*=9.0, 2H), 6.92–6.97 (m, 4H), 7.50–7.57 (dd, *J*=9.0, 6.0 Hz, 2H). ^{13}C NMR (100.6 MHz) δ 21.2, 46.8, 54.1, 76.6, 116.8, 117.4, 119.2, 119.6, 128.6, 128.8, 130.0, 135.9, 136.5, 138.5, 141.0, 144.2, 162.2, 162.6, 192.5. HRMS (ESI) calcd from $C_{23}H_{18}NO_5$ $(M-H)^-$: 388.1190; found: 388.1193. HPLC conditions: Daicel Chiralpak® IB column, *i*-PrOH/hexane 5:95, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=18.2 min, t_{minor}=24.2 min.

*4.4.9. 1,8-Dihydroxy-10-(1-(4-methoxyphenyl)-2-nitroethyl)anthracen-9(10H)-one (**12d**).* Obtained in 70% yield and 40% ee from **10d** and **1b**. Yellow solid. ^{1}H NMR (300 MHz) δ 3.72 (s, 3H), 3.88 (m, 1H), 4.43 (d, *J*=6.0 Hz, 1H), 4.50–4.57 (dd, *J*=12.0, 6.0 Hz, 1H), 4.87–4.94 (dd, *J*=12.0, 9.0 Hz, 1H), 5.96–5.99 (d, *J*=9.0 Hz, 2H), 6.53–6.56 (d, *J*=9.0 Hz, 2H), 6.88–6.98 (m, 4H), 7.51–7.57 (m, 2H). ^{13}C NMR (100.6 MHz) δ 46.8, 53.8, 55.5, 76.8, 113.6, 116.8, 116.9, 117.5, 117.6, 119.1, 119.6, 124.8, 129.9, 135.8, 136.5, 140.9, 144.3, 159.9, 162.2, 162.6, 192.4. HRMS (ESI) calcd from $C_{23}H_{18}NO_6$ $(M-H)^-$: 404.1140; found: 404.1139. HPLC conditions: Daicel Chiralpak® IB column, *i*-PrOH/hexane 5:95, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=24.0 min, t_{minor}=34.9 min.

4.4.10. 1,8-Dihydroxy-10-[2-nitro-1-(4-nitrophenyl)ethyl]-10H-anthracen-9-one (12e). Obtained in 87% yield and 13% ee from **10e** and **1b**. Yellow solid. ^{1}H NMR (300 MHz) δ 4.09 (m, 1H), 4.51 (d. *J*=3.0 Hz, 1H), 4.58–4.67 (dd, *J*=12.0, 9.0 Hz, 1H), 4.93–4.99 (dd, *J*=12.0, 9.0 Hz, 1H), 6.34–6.37 (d, *J*=9.0 Hz, 2H), 6.89–6.96 (m, 2H), 7.00–7.03 (d, *J*=9.0 Hz, 2H), 7.55–7.61 (t, *J*=9.0 Hz, 2H), 7.90–7.93 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (100.6 MHz) δ 46.6, 54.0, 76.1, 117.7, 118.2, 119.2, 119.6, 123.2, 129.7, 136.4, 136.9, 141.0, 204.8. HRMS (ESI) calcd from $C_{22}H_{15}N_2O_7$ $(M-H)^-$: 419.0885; found: 419.0888. HPLC conditions: Daicel Chiralpak® IB column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=24.8 min, t_{minor}=28.6 min.

4.5. General experimental procedure for the addition of anthrones to maleimides

To a stirred solution of catalyst (*R*,*R*)-**V** (10 mg, 0.025 mmol) in toluene (1 mL) were added the maleimide (0.30 mmol) and the anthrone (**1a** or **1b**, 0.25 mmol). The reaction mixture was vigorously stirred at room temperature during 14 h, and the crude product was directly purified by column chromatography on silica gel (hexane/ethyl acetate mixtures) to afford the Diels–Alder or the Michael adduct. Racemic products were obtained from the

corresponding substrates by catalysis with DABCO in toluene at room temperature.

*4.5.1. (R,R)-(−)-4-Hydroxy-2-phenyl-3a,4,9,9a-tetrahydro-4, 9-[1′,2′]-benzeno-1H-benz[f]isoindole-1,3(2H)-dione (**14a**)*[11,23b,25]. Obtained in 91% yield and 90% ee from **13a** and **1a**. Colorless solid. Mp 209–210 °C. $[\alpha]_D^{20}$ −17.8 (*c* 0.9, $CHCl_3$). ^1H NMR (300 MHz) *δ* 3.26–3.29 (d, *J*=9.0 Hz, 1H), 3.47–3.51 (dd, *J*=9.0, 3.0 Hz, 1H), 4.54 (s, 1H, O*H*), 4.84 (d, *J*=3.0 Hz, 1H), 6.47–7.36 (m, 10H), 7.40–7.42 (d, *J*=6.0 Hz, 1H), 7.55–7.57 (d, *J*=6.0 Hz, 1H), 7.66–7.68 (d, *J*=6.0 Hz, 1H). ^{13}C NMR (100.6 MHz) *δ* 45.1, 47.9, 51.1, 77.7, 121.2, 121.4, 124.0, 125.0, 126.5, 127.1, 127.5, 127.6, 129.2, 129.4, 131.1, 136.9, 139.1, 141.2, 142.6, 176.5, 177.4. HRMS (ESI) calcd from $C_{24}H_{18}NO_3$ $(M+H)^+$: 368.1281; found: 368.1279. HPLC conditions: Daicel Chiralpak® IA column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=47.1 min, t_{minor}=37.5 min.

*4.5.2. (R,R)-(−)-4-Hydroxy-2-benzyl-3a,4,9,9a-tetrahydro-4,9-[1′,2′]-benzeno-1H-benz[f]isoindole-1,3(2H)-dione (**14b**)*[23b,25]. Obtained in 92% yield and 95% ee from **13a** and **1a**. Colorless solid. Mp 213–214 °C. $[\alpha]_D^{20}$ −36.8 (*c* 0.9, $CHCl_3$). ^1H NMR (300 MHz) *δ* 3.12–3.15 (d. *J*=9.0 Hz, 1H), 3.32–3.35 (dd, *J*=9.0, 3.0 Hz, 1H), 4.27 (s, 2H), 4.40 (s, 1H, O*H*), 4.70 (d, *J*=3.0 Hz, 1H), 6.70–6.72 (d, *J*=6.0 Hz, 2H), 6.97–7.01 (t, *J*=6.0 Hz, 1H), 7.05–7.09 (t, *J*=6.0 Hz, 1H), 7.13–7.27 (m, 6H), 7.34–7.36 (d, *J*=6.0 Hz, 1H), 7.38–7.40 (d, *J*=6.0 Hz, 1H), 7.66–7.68 (d, *J*=6.0 Hz, 1H). ^{13}C NMR (100.6 MHz) *δ* 42.5, 44.6, 47.8, 50.8, 121.0, 123.9, 124.6, 126.9, 127.0, 127.4, 127.5, 127.7, 128.1, 128.7, 134.8, 136.6, 139.5, 140.9, 143.0, 176.3, 177.8. HRMS (ESI) calcd from $C_{25}H_{20}NO_3$ $(M+H)^+$: 382.1438; found: 382.1426. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=59.7 min, t_{minor}=63.8 min.

*4.5.3. (−)-4-Hydroxy-2-(3-chlorophenyl)-3a,4,9,9a-tetrahydro-4, 9-[1′,2′]-benzeno-1H-benz[f]isoindole-1,3(2H)-dione (**14c**)*[28]. Obtained in 92% yield and 90% ee from **13c** and **1a**. Colorless solid. $[\alpha]_D^{20}$ −9.3 (*c* 0.9, $CHCl_3$). ^1H NMR (300 MHz) *δ* 3.26–3.29 (d, *J*=9.0 Hz, 1H), 3.47–3.51 (dd, *J*=9.0, 3.0 Hz, 1H), 4.49 (s, 1H, O*H*), 4.83 (d, *J*=3.0 Hz, 1H), 7.23–7.40 (m, 10H), 7.55–7.57 (d, *J*=6.0 Hz, 1H), 7.65–7.67 (d, *J*=6.0 Hz, 1H). ^{13}C NMR (100.6 MHz) *δ* 45.1, 48.0, 51.1, 121.2, 121.4, 123.7, 124.0, 124.8, 125.0, 126.9, 127.2, 127.3, 127.6, 127.7, 129.5, 130.3, 175.4, 177.2. HRMS (ESI) calcd from $C_{24}H_{17}ClNO_3$ $(M+H)^+$: 402.0891; found: 402.0888. HPLC conditions: Daicel Chiralpak® IA column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=38.1 min, t_{minor}=29.0 min.

4.5.4. (−)-4-Hydroxy-2-(4-methoxyphenyl)-3a,4,9,9a-tetrahydro-4, 9-[1′,2′]-benzeno-1H-benz[f]isoindole-1,3(2H)-dione (14d)[23b,25]. Obtained in 90% yield and 97% ee from **13d** and **1a**. Colorless solid. Mp 207–209 °C. $[\alpha]_D^{20}$ −14.7 (*c* 0.9, $CHCl_3$). ^1H NMR (300 MHz) *δ* 3.24–3.27 (d, *J*=9.0 Hz, 1H), 3.45–3.49 (dd, *J*=9.0, 3.0 Hz, 1H), 3.75 (s, 3H), 4.55 (s, 1H, O*H*), 4.83 (d, *J*=3.0 Hz, 1H), 6.37–6.39 (d, *J*=6.0 Hz, 2H), 6.79–6.81 (d, *J*=6.0 Hz, 2H), 7.22–7.32 (m, 5H), 7.40–7.42 (d, *J*=6.0 Hz, 1H), 7.54–7.56 (d, *J*=6.0 Hz, 1H), 7.66–7.68 (d, *J*=6.0 Hz, 1H). ^{13}C NMR (100.6 MHz) *δ* 45.1, 47.9, 51.0, 55.7, 76.9, 114.7, 121.1, 121.4, 123.7, 124.0, 125.0, 127.1, 127.2, 127.5, 127.6, 127.7, 137.0, 139.1, 141.3, 142.6, 160.0, 176.2, 177.6. HRMS (ESI) calcd from $C_{25}H_{20}NO_4$ $(M+H)^+$: 398.1387; found: 398.1371. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=18.5 min, t_{minor}=19.9 min.

*4.5.5. (−)-4-Hydroxy-2-(4-bromophenyl)-3a,4,9,9a-tetrahydro-4,9-[1′,2′]-benzeno-1H-benz[f]isoindole-1,3(2H)-dione (**14f**)*[25]. Obtained in 94% yield and 29% ee from **13f** and **1a**. Colorless solid. $[\alpha]_D^{20}$ −12.7 (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz) *δ* 3.25–3.28 (d, *J*=9.0 Hz, 1H), 3.46–3.50 (dd, *J*=9.0, 3.0 Hz, 1H), 4.49 (s, 1H, O*H*), 4.83 (d, *J*=3.0 Hz, 1H), 6.38–6.40 (d, *J*=6.0 Hz, 2H), 7.23–7.44 (m, 8H), 7.54–7.56 (d, *J*=6.0 Hz, 1H), 7.65–7.67 (d, *J*=6.0 Hz, 1H). ^{13}C NMR (100.6 MHz) *δ* 45.1, 47.9, 51.1, 76.9, 121.2, 121.3, 123.2, 124.0, 125.0, 127.2, 127.3, 127.5, 127.6, 128.1, 128.4, 130.1, 132.6, 132.7, 136.8, 139.0, 141.2, 142.4, 175.5, 177.0. HRMS (ESI) calcd from $C_{24}H_{17}BrNO_3$ $(M+H)^+$: 446.0386; found: 446.0384. HPLC conditions: Daicel Chiralpak® IC column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=46.1 min, t_{minor}=47.8 min.

*4.5.6. 4-Hydroxy-2-(diphenylmethyl)-3a,4,9,9a-tetrahydro-4,9-[1′,2′]-benzeno-1H-benz[f]isoindole-1,3(2H)-dione (**14g**).* Obtained in 86% yield and 33% ee from **13g** and **1a**. Colorless solid. ^1H NMR (300 MHz) *δ* 3.12 (d, *J*=9.0 Hz, 1H), 3.33 (dd, *J*=9.0, 3.6 Hz, 1H), 4.44 (s, 1H), 4.74 (d, *J*=3.6 Hz, 1H), 6.16 (s, 1H, O*H*), 6.57 (d, *J*=6.0 Hz, 2H), 6.82 (d, *J*=6.0 Hz, 2H), 7.14–7.23 (m, 12H), 7.52 (d, *J*=7.2 Hz, 1H), 7.66 (d, *J*=7.2 Hz, 1H). HPLC conditions: Daicel Chiralpak® IA column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=27.3 min, t_{minor}=23.0 min.

*4.5.7. (+)-3-(10-Oxo-9,10-dihydro-anthracen-9-yl)-1-(4-trifluoromethyl-phenyl)-pyrrolidine-2,5-dione (**14′e**)*[28]. Obtained in 94% yield and 97% ee from **13e** and **1a**. Colorless oil. $[\alpha]_D^{20}$ +54.7 (*c* 0.4, $CHCl_3$). ^1H NMR (300 MHz) *δ* 2.11 (dd, *J*=18.9, 4.8 Hz, 1H), 2.44 (dd, *J*=18.9, 9.6 Hz, 1H), 3.65–3.75 (m, 1H), 5.24 (d, *J*=2.3 Hz, 1H), 7.25–7.28 (m, 2H), 7.43–7.75 (m, 8H), 8.30–8.42 (m, 2H). ^{13}C NMR (100.6 MHz) *δ* 29.5, 42.3, 50.1, 126.50, 126.55, 126.60, 126.65, 126.8, 128.1, 128.2, 128.3, 128.4, 128.5, 129.1, 132.7, 133.5, 133.8, 134.1, 136.2, 142.2, 173.6, 176.7, 183.9. ^{19}F NMR (376 MHz, $CDCl_3$): *δ* −63.2-(-64.1) (br s). HRMS (ESI) calcd from $C_{25}H_{16}F_3NNaO_3$ $(M+Na)^+$: 458.0974; found: 458.0970. HPLC conditions: Daicel Chiralpak® IB column, *i*-PrOH/hexane 20:80, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=34.7 min, t_{minor}=24.1 min.

*4.5.8. 4-Hydroxy-2-(R)-1-phenylethyl-3a,4,9,9a-tetrahydro-4,9-[1′,2′]-benzeno-1H-benz[f]isoindole-1,3(2H)-dione (**14h**)*[23a]. Obtained in 80% yield as a 2.56:1 mixture of the (*R*,*R*,*R*)- and (*R*,*S*,*S*)-diastereomers from (*R*)-**13h** and **1a**. ^1H NMR (300 MHz) *δ* 1.15–1.18 (d, *J*=7.5 Hz, 3H, major diastereomer), 1.25–1.27 (d, *J*=7.2 Hz, 3H, minor diastereomer), 2.99–3.02 (d, *J*=8.7 Hz, 1H, major diastereomer), 3.04–3.07 (d, *J*=8.7 Hz, 1H, minor diastereomer), 3.21–3.26 (dd, *J*=9.6, 3.6 Hz, 1H, minor diastereomer), 3.25–3.29 (dd, *J*=8.7, 3.6 Hz, 1H, major diastereomer), 4.47 (s, 1H, minor diastereomer), 4.51 (s, 1H, major diastereomer), 4.69–4.70 (d, *J*=3.3 Hz, 1H, major diastereomer), 4.70–4.71 (d, *J*=3.3 Hz, 1H, minor diastereomer), 5.93–5.00 (q, *J*=7.2 Hz, both diastereomers), 6.91–7.67 (m, 13H, both diastereomers). ^{13}C NMR (75.5 MHz, diastereomer mixture) *δ* 16.0, 16.1, 44.7, 44.8, 47.3 47.4, 50.1, 50.3, 50.4, 76.8, 120.9, 121.0, 121.2, 121.3, 123.8, 124.8, 126.9, 127.0, 127.2, 127.3, 127.4, 127.5, 127.7, 127.8, 128.5, 136.8, 138.5, 139.4, 141.2, 142.9, 176.3, 178.0. HRMS (ESI) calcd from $C_{26}H_{22}NO_3$ $(M+H)^+$: 396.1594; found: 396.1590.

*4.5.9. (+)-3-(4,5-Dihydroxy-10-oxo-9,10-dihydro-anthracen-9-yl)-1-phenyl-pyrrolidine-2,5-dione (**15a**)*[28]. Obtained in 93% yield and 99% ee from **13a** and **1b**. Yellow solid. $[\alpha]_D^{20}$ +40.2 (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz) *δ* 2.18–2.26 (dd, *J*=18.0, 6.0 Hz, 1H), 2.48–2.57 (dd, *J*=18.0, 9.0 Hz, 1H), 3.52 (m, 1H), 5.20 (d, *J*=3.0 Hz, 1H), 7.07–6.94 (m, 3H), 7.10 (d, *J*=6.0 Hz, 2H), 7.48–7.40 (m, 5H), 7.61 (t, *J*=6.0 Hz, 1H). ^{13}C NMR (100.6 MHz) *δ* 29.8, 42.5, 51.3, 116.0, 116.7, 117.3, 118.3, 118.9, 119.3, 126.5, 129.1, 129.5, 131.7, 136.9, 137.5, 139.9, 144.1, 163.3, 163.5, 174.2, 176.6, 193.4. HRMS (ESI) calcd from $C_{24}H_{16}NO_5$ $(M-H)^-$: 398.1034; found: 398.1024. HPLC conditions: Daicel Chiralpak® IB column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=41.5 min, t_{minor}=47.1 min.

*4.5.10. (+)-1-Benzyl-3-(4,5-dihydroxy-10-oxo-9,10-dihydro-anthracen-9-yl)-pyrrolidine-2,5-dione (**15b**)*[28]. Obtained in 92% yield and 85% ee from **13b** and **1b**. Yellow solid. $[\alpha]_D^{20}$ +38.5 (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz) δ 1.98–2.05 (dd, *J*=15.0, 6.0 Hz, 1H), 2.30–2.38 (dd, *J*=15.0, 9.0 Hz, 1H), 3.31 (m, 1H), 4.56 (s, 1H), 4.58 (s, 1H), 5.08 (d, *J*=3.0 Hz, 1H), 6.59–6.56 (d, *J*=9.0 Hz, 1H), 6.84–6.81 (d, *J*=9.0 Hz, 1H), 6.93–6.96 (d, *J*=9.0 Hz, 1H), 7.00–7.03 (d, *J*=9.0 Hz, 1H), 7.26–7.33 (m, 6H), 7.51–7.57 (t, *J*=9.0 Hz, 1H). ^{13}C NMR (100.6 MHz) δ 29.4, 42.0, 42.8, 51.1, 115.8, 116.4, 117.1, 117.8, 118.9, 119.1, 128.3, 128.8, 129.2, 135.5, 137.0, 137.4, 139.6, 144.3, 163.1, 163.3, 174.9, 177.3, 193.3. HRMS (ESI) calcd from $C_{25}H_{20}NO_5$ $(M+H)^+$: 414.1336; found: 414.1337. Daicel Chiralpak® IB column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=30.2 min, t_{minor}=36.8 min.

*4.5.11. (+)-1-(3-Chlorophenyl)-3-(4,5-dihydroxy-10-oxo-9,10-dihydro-anthracen-9-yl)-pyrrolidine-2,5-dione (**15c**).* Obtained in 92% yield and 22% ee from **13c** and **1b**. Yellow solid. $[\alpha]_D^{20}$ +11.6 (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz) δ 2.47–2.52 (dd, *J*=9.0, 6.0 Hz, 1H), 2.53–2.58 (dd, *J*=9.0, 6.0 Hz, 1H), 3.52 (m, 1H), 5.18 (d, *J*=3.0 Hz, 1H), 7.59–6.91 (m, 10H). ^{13}C NMR (100.6 MHz) δ 32.4, 45.2, 53.9, 118.6, 119.3, 120.0, 121.1, 121.6, 121.8, 127.4, 129.5, 132.0, 133.1, 135.3, 137.7, 139.6, 140.2, 142.4, 146.5, 165.9, 166.2, 176.4, 178.9, 196.0. HRMS (ESI) calcd from $C_{24}H_{15}ClNO_5$ $(M-H)^-$: 432.0644; found: 432.0638. HPLC conditions: Daicel Chiralpak® IB column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=33.3 min, t_{minor}=40.8 min.

*4.5.12. (+)-3-(4,5-Dihydroxy-10-oxo-9,10-dihydro-anthracen-9-yl)-1-(4-methoxyphenyl)-pyrrolidine-2,5-dione (**15d**)*[28]. Obtained in 94% yield and 97% ee from **13d** and **1b**. Yellow solid. $[\alpha]_D^{20}$ +74.9 (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz) δ 2.16–2.23 (dd, *J*=15.0, 6.0 Hz, 1H), 2.47–2.54 (dd, *J*=15.0, 6.0 Hz, 1H), 3.49 (m, 1H), 3.83 (s, 3H), 5.19 (d, *J*=3.0 Hz, 1H), 6.94–7.02 (m, 5H), 7.09 (d, *J*=6.0 Hz, 1H), 7.46–7.48 (d, *J*=6.0 Hz, 1H), 7.49–7.51 (d, *J*=6.0 Hz, 1H), 7.57–7.61 (t, *J*=6.0 Hz, 2H). ^{13}C NMR (100.6 MHz) δ 29.7, 42.5, 51.2, 55.7, 114.8, 116.7, 117.3, 118.2, 118.9, 119.3, 124.2, 127.7, 136.9, 137.5, 139.9, 144.1, 159.9, 163.2, 163.5, 174.5, 176.9, 193.4. HRMS (ESI) calcd from $C_{25}H_{20}NO_6$ $(M+H)^+$: 430.1285; found: 430.1288. HPLC conditions: Daicel Chiralpak® IB column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=31.7 min, t_{minor}=38.8 min.

*4.5.13. (+)-1-(4-Bromophenyl)-3-(4,5-dihydroxy-10-oxo-9,10-dihydro-anthracen-9-yl)-pyrrolidine-2,5-dione (**15f**)*[28]. Obtained in 91% yield and 96% ee from **13f** and **1b**. Yellow solid. $[\alpha]_D^{20}$ +35.8 (*c* 0.9, $CHCl_3$). ^1H NMR (300 MHz) δ 2.17–2.25 (dd, *J*=18.0, 6.0 Hz, 1H), 2.48–2.57 (dd, *J*=18.0, 9.0 Hz, 1H), 3.47–3.52 (m, 1H), 5.17 (d, *J*=3.0 Hz, 1H), 6.89–6.92 (d, *J*=9.0 Hz, 1H), 6.98–7.02 (m, 4H), 7.06–7.08 (d, *J*=6.0 Hz, 1H), 7.44–7.48 (t, *J*=6.0 Hz, 1H), 7.56–7.61 (m, 3H). ^{13}C NMR (100.6 MHz) δ 29.8, 42.6, 51.3, 116.0, 116.7, 117.4, 118.4, 118.9, 119.1, 123.1, 128.0, 130.6, 132.7, 136.9, 137.6, 139.8, 143.8, 163.3, 163.6, 173.8, 176.3, 193.4. HRMS (ESI) calcd from $C_{24}H_{15}BrNO_5$ $(M-H)^-$: 476.0139; found: 476.0129. HPLC conditions: Daicel Chiralpak® IB column, *i*-PrOH/hexane 10:90, flow rate 1 mL/min, UV detection at 254 nm, t_{major}=37.3 min, t_{minor}=56.3 min.

*4.5.14. 3-(4,5-Dihydroxy-10-oxo-9,10-dihydro-anthracen-9-yl)-1-((R)-1-phenylethyl)-pyrrolidine-2,5-dione (**15h**).* Obtained in 77% yield as a 1.25:1 mixture of the (*R*,*S*)- and (*R*,*R*)-diastereomers from (*R*)-**13h** and **1b**. ^1H NMR (300 MHz) δ 1.70–1.73 (d, *J*=7.2 Hz, 3H, minor diastereomer), 1.72–1.74 (d, *J*=7.2 Hz, 3H, major diastereomer), 1.91–1.94 (dd, *J*=5.1, 2.4 Hz, 1H, minor diastereomer), 1.97–2.00 (dd, *J*=5.4, 2.4 Hz, 1H, major diastereomer), 2.24–2.29 (dd, *J*=9.6, 3.9 Hz, 1H, major diastereomer), 2.30–2.35 (dd, *J*=9.3, 3.9 Hz, 1H, minor diastereomer), 3.22–3.29 (m, 1H, both diastereomers), 5.03–5.04 (d, *J*=3.0 Hz, 1H, minor diastereomer), 5.07–5.08 (d, *J*=3.0 Hz, 1H, major diastereomer), 5.28–5.37 (m, 1H, both diastereomers), 6.48–6.50 (d, *J*=7.5 Hz, 1H, minor diastereomer), 6.77–6.80 (d, *J*=7.5 Hz, 1H, major diastereomer), 6.84–7.36 (m, 12H, both diastereomers), 7.50–7.55 (t, *J*=7.5 Hz, 1H, both diastereomers). ^{13}C NMR (100.6 MHz) δ 29.8, 42.6, 51.3, 116.0, 116.7, 117.4, 118.4, 118.9, 119.1, 123.1, 128.0, 130.6, 132.7, 136.9, 137.6, 139.8, 143.8, 163.3, 163.6, 173.8, 176.3, 193.4. HRMS (ESI) calcd from $C_{26}H_{20}NO_5$ $(M-H)^-$: 426.1347; found: 426.1346.

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