The 'Mikami'-Catalyst in Enantioselective Diels–Alder Reactions of Juglone-Based Dienophiles with Different 1-Oxygenated Dienes: An Investigation on the Substitution Pattern Dependent Regioselectivity

Dietrich Böse,[a] Wolfgang Frey,[b] Jörg Pietruszka*[a,c]

[a] Institut für Bioorganische Chemie, Heinrich-Heine-Universität Düsseldorf, Forschungszentrum Jülich, 52426 Jülich, Germany

[b] Institut für Organische Chemie, Universität Stuttgart, 70569 Stuttgart, Germany

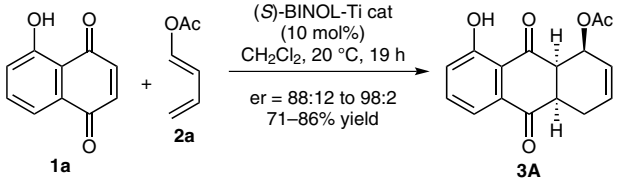
[c] Institut für Bio- und Geowissenschaften (IBG-1: Biotechnologie), Forschungszentrum Jülich, 52428 Jülich, Germany
Fax +49(2461)611669; E-mail: j.pietruszka@fz-juelich.de

Received: 09.04.2014; Accepted after revision: 06.05.2014

Abstract: A mechanistic study investigating the substitution pattern depending regioselectivity of enantioselective BINOL-Ti-catalyzed Diels–Alder reactions of juglone-based dienophiles with 1-oxygenated dienes is reported. The different influences of residues both on the diene as well as on the dienophiles are investigated giving a detailed picture of their role on the regioselectivity.

Key words: catalysis, Diels–Alder reaction, Lewis acids, regioselectivity, enantioselectivity

Enantioselective Diels–Alder (D–A)[1] reactions are one of the most powerful transformations in organic chemistry.[2] The formation of two new σ-bonds and up to four stereogenic centers allows a fast construction of molecular complexity. In particular, the Lewis acid catalyzed asymmetric D–A reaction is of enormous interest to synthetic chemists and a large number of catalysts have been developed for this purpose.[2,3] In 1990, Mikami and coworkers reported a BINOL-Ti-derived catalyst ('Mikami'-catalyst)[4] which was applied in enantioselective (hetero)-Diels–Alder reactions.[5] In spite of the fact that the exact catalyst structure is still unknown, many studies applying the 'Mikami-catalyst' were presented.[5,6] Of particular interest was the finding that the BINOL-Ti complex could catalyse a D–A reaction of 5-hydroxy-1,4-naphthoquinone (juglone, **1a**) with 1-acetoxybuta-1,3-diene (**2a**) with very high regio- and high enantioselectivities to form 1-acetoxy-8-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (**3A**) (Scheme 1).[7]



Scheme 1 (*S*)-BINOL-Ti-catalyzed D–A reaction of Juglone (**1a**) with 1-acetoxybuta-1,3-diene (**2a**)

SYNTHESIS 2014, 46, 2524–2532
Advanced online publication: 25.06.2014
DOI: 10.1055/s-0034-1378230; Art ID: ss-2014-t0233-op

The so formed structural motif can be found within a large number of bioactive natural products, for example, in the polyketide family of altersolanols, shown in Figure 1.[8]

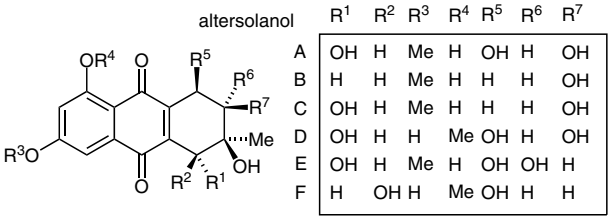


Figure 1 Structures of altersolanol A–F

Some of the related targets have been addressed in total synthesis by means of similar D–A reactions, but mostly in a racemic or diastereoselective manner.[9] However, there are only few examples of nonracemic total syntheses of natural compounds applying a BINOL-Ti-catalyzed enantioselective D–A reaction as the key step.[6a,b,10] A possible reason for this lack of application is the inherent regioselectivity problem with unsymmetrically substituted 1,4-naphthoquinones as the dienophiles. This arises from the double activation of the C=C bond by the two carbonyl groups present in the molecules. Several groups have studied the influence of dienophiles, dienes, and of simple Lewis acids, such as $Et_2O{\cdot}BF_3$, $AlCl_3$, $B(OAc)_3$, and MgI_2, on the orientation of the diene in the transition state and therefore on the regiochemical outcome of the reaction.[11] It was found that significantly polarized, electron rich dienes, with a strong electron-donating group at the 1-position give the highest regioselectivities.[11f] Furthermore, it was reasoned that the intramolecular hydrogen bond leads to a polarization of the C=C bond and thus enables an orientation of the diene as shown in Figure 2.

The Corey group has devised a set of rules for a very similar system, which predict the coordination of a Lewis acid catalyst at the most basic carbonyl group in the molecule. They also state that: '…the more nucleophilic end of the diene, will attach to the carbon β to the carbonyl group that coordinates with the catalyst, i.e., the more electrophilic carbon.'[12] The basicity of the two carbonyl groups is also remotely influenced by electron-withdrawing or electron-donating groups attached to the aromatic back-

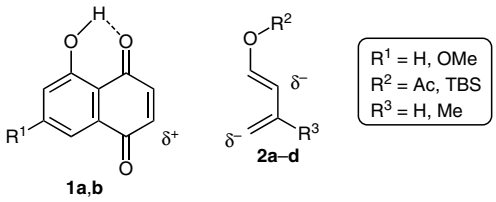
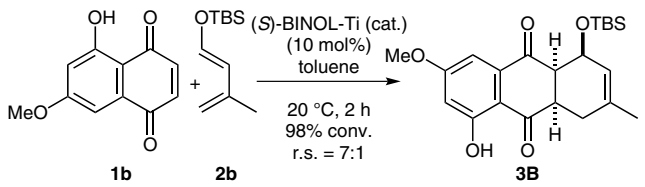


Figure 2 Polarization of 5-hydroxy-1,4-naphthoquinone and 1-oxygenated dienes influenced by the residues attached to them

bone of the 1,4-naphthoquinones **1a** and **1b** (Figure 2) as shown by Corey and Kelly.[11a,12] The Kelly group found during their investigations that the Lewis acid MgI_2 shows, in contrast to all the other tested Lewis acids, a completely inverted regioselectivity.[11c]

During our investigations towards the total synthesis of altersolanols, the synthetic potential of chiral 'Mikami'-catalyzed D–A reactions was investigated. However, 5-hydroxy-7-methoxy-1,4-naphthoquinone (**1b**) and 1-[(*tert*-butyldimethylsilyl)oxy]-3-methylbuta-1,3-diene (**2b**) were chosen as the dienophile and diene, respectively (Scheme 2). To our surprise, a reversed regioselectivity was observed by applying the original 'Mikami'-catalyst in the above D–A reaction, very similar to the one published by Mikami.



Scheme 2 Unexpected formation of the undesired regioisomer **3B**

Therefore, we decided to investigate the regiochemical outcome of a cycloaddition between 5-hydroxy-1,4-naphthoquinone derivatives **1** and different 1-oxygenated dienes **2a**–**d**. The aim of this study was to elucidate the influence of the three different groups (R^1, R^2, and R^3) to the regioselectivity. Juglone (**1a**, R^1 = H), which was commercially available and 5-hydroxy-7-methoxy-1,4-naphthoquinone (**1b**, R^1 = OMe), which has an additional methoxy group in the 7-position installed, thus showing the same substitution pattern as the altersolanol compounds, were chosen as model substrates. First we wanted to analyze the inherent regioselectivity of the racemic, uncatalyzed reaction.

The results presented in Table 1 clearly show the independent influences of the three residues. One can see that a change of an acetyl group to a TBS group (R^2) leads to a slightly increased regioselectivity (Table 1, entry 2 vs. 3, 4 vs. 5, 6 vs. 7, and 8 vs. 9), a result which is consistent with the aforementioned findings of Boeckman et al.[11f] Introducing a methyl group in the 3-position of the diene (R^3 = Me) also leads to a better selectivity towards the regioisomer **A** (entry 2 vs. 4, 3 vs. 5), which can be explained in the same way. Surprisingly with 7-methoxylated dienophile **1b** a strong decrease of the orientation control and – in one case (entry 8) – even the complete loss of regioselectivity is observed. At this point, it is worth mentioning that in all cases full *endo*-selectivity was achieved, none of the *exo*-product could be observed at all.

Table 1 Investigation on the Influence of the Substituents to the Regioselectivity of the Racemic, Uncatalyzed D–A Reaction

Entry	R^1	R^2	R^3	**A**:**B** (*rac*)[a]	Yield (%)[b] (*rac*)
1[c]	H	Ac	H (**2a**)	80:20 (**3**)	quant
2	H	Ac	H (**2a**)	80:20 (**3**)	99
3	H	TBS	H (**2d**)	81:19 (**4**)	60
4	H	Ac	Me (**2c**)	88:12 (**5**)	97
5	H	TBS	Me (**2b**)	90:10 (**6**)	97
6	OMe	Ac	H (**2a**)	57:43 (**7**)	78
7	OMe	TBS	H (**2d**)	60:40 (**8**)	85
8	OMe	Ac	Me (**2c**)	50:50 (**9**)	83
9	OMe	TBS	Me (**2b**)	66:34 (**10**)	89
10[d]	OMe	TBS	Me (**2b**)	66:34 (**10**)	86

[a] Regioselectivities were determined by ^{1}H NMR analysis of the crude reaction mixture.
[b] Isolated yield after column chromatography.
[c] According to literature.[7]
[d] Reaction performed in toluene.

For the assignment of the individual isomers, an isolation, purification, and most difficult, a separation of the two isomers was necessary. However, during standard purification (chromatography on silica gel) a fast aromatization was observed, which is well documented.[7,11a,c,f,h] Nevertheless, careful exclusion of air and acidic conditions, enabled the isolation of analytically pure compounds **3**–**10**. The stereochemical analysis was performed using one- and two-dimensional NMR studies as shown in Figure 3.

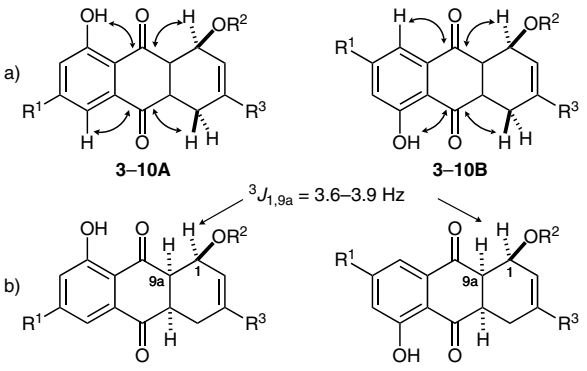


Figure 3 a) Selected HMBC-correlations and b) $^3J_{1,9a}$ coupling constants showing the relative regio- and stereochemistry in **3**–**10**

In all cases, a small coupling constant between 1-H and 9a-H ($^3J_{1,9a}$ = 3.6–3.9 Hz) was observed, indicating the *endo*-stereochemistry. A distinct assignment of the two regioisomers was done using HMBC correlations. The ^{1}H NMR spectra of the two regioisomers **3–10 A** and **3–10 B** were found to be almost identical only differing in the chemical shifts of the phenolic OH group. Here a clear trend could be observed showing a shift of the OH group belonging to regioisomers **A** of 0.24 to 0.60 ppm downfield relative to the signal of regioisomers **B** (see Table 2).

Table 2 Chemical Shifts (ppm) of OH Groups Belonging to the Two Different Regioisomers

Entry	R^1	R^2	R^3	δ **A**	δ **B**	Δδ
1	H	Ac	H	11.99	11.75	0.24
2	H	TBS	H	12.21	11.64	0.57
3	H	Ac	Me	12.01	11.75	0.26
4	H	TBS	Me	12.22	11.65	0.57
5	OMe	Ac	H	12.32	12.03	0.29
6	OMe	TBS	H	12.52	11.93	0.59
7	OMe	Ac	Me	12.35	12.03	0.33
8	OMe	TBS	Me	12.53	11.93	0.60

The OH signals shown in Table 2 were used for the determination of the regioselectivity of the D–A reactions via NMR analysis of the crude reaction mixtures and for the assignment of the two regioisomers of products **7** and **8**, which could not be separated by MPLC, in case the assignment by HMBC correlation was not possible. Additionally, the assignments (*endo*-selectivity and regioselectivity) were proven by X-ray crystal structure of adduct **6A** (Figure 4).[13]

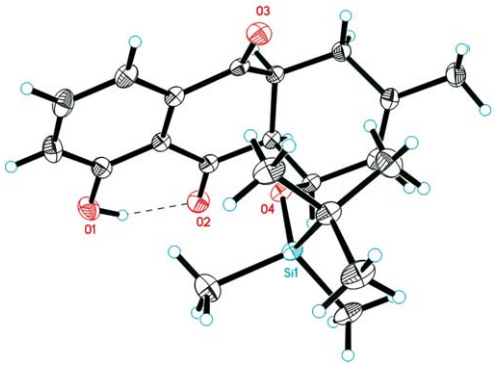


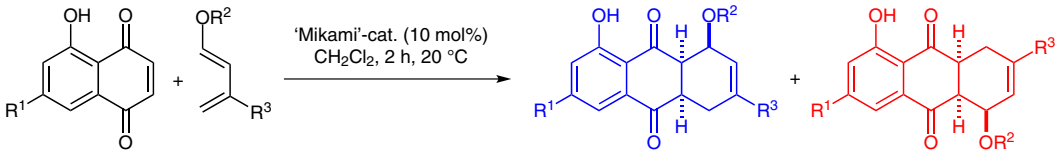
Figure 4 Single crystal structure of **6A**[13]

For the investigation towards the 'Mikami'-catalyzed D–A reaction, "molecular sieves-free" catalyst was prepared as described by Mikami and Posner.[7,10a] In order to be able to compare relative reaction rates, the experiments were stopped after 2 hours and the conversions were analyzed by ^{1}H NMR spectrosocpy. The experiment was repeated as described by Mikami,[7] and to our surprise it was found that the reported regioselectivity could not be reproduced (Table 3, entries 1 and 2). In our case, the regioisomer **B** was formed as the major isomer in very good enantioselectivity (er 97:3) and regioisomer **A** was formed as the minor product with only moderate enantioselectivity (er 76:23). However, it is commonly known that the preparation process (i.e., source of the MS, water content of MS) of the catalyst plays an essential role on the stereochemical outcome, particularly on the enantiomeric ratio. But such a dramatic change in the regioisomer preference has never been reported. When the same reaction was repeated in toluene instead of dichloromethane as a solvent (entry 3), the ratio changed back to isomer **A** being the major product, but still not to the same extent as shown by Mikami. The reaction proceeded considerably slower (19% vs 37% conv.) and with a lower er for isomer **B** (82:18 vs 97:03) and basically unchanged er for isomer **A**.

From Table 3 one can see that while cycloadditions with juglone (**1a**) gave mixed results regarding the regioselectivity, reactions with 7-methoxyjuglone (**1b**) gave products with good (17:83, entry 8) to very good (1:99, entry 9 and 10) regioselectivities, an observation which is in agreement with the result in Table 1. The enantiomeric ratios of all the products were found to be moderate (60:40, entry 4, to 77:23, entry 7) for regioisomers **A** but good to excellent (97:03 to 99:1) for regioisomers **B**. This observation can be understood taking into account that the uncatalyzed background reaction is faster for the regioisomers **A**. In cases where TBS was used as protecting group, decomposition of the diene was observed during the reaction leading to lower conversions compared to the reactions with the acetate protecting group. The decomposition of TBS-protected dienes can be avoided when toluene is used as a solvent (Scheme 2) instead of dichloromethane. Unfortunately, this leads also to a decreased enantiomeric purity of the product. However, the reaction with 1-acetoxy-3-methylbuta-1,3-diene (**2c**) and 5-hydroxy-7-methoxy-1,4-naphthoquinone (**1b**) (entry 9) proceeds with excellent conversion and perfect regio- and enantioselectivities.

In conclusion, we could show that a surprising and very strong remote influence of the methoxy group in 7-position is responsible for the change of regioselectivity of a juglone-like dienophile **1b** in the reaction shown in Scheme 2 (Table 3, entries 2–6 vs entries 7–10). In addition to that electronic effect, a less strong steric effect of a methyl group in 3-position of the dienes (R^3) was disclosed. The methyl group also shifts the product distribution towards regioisomer **B** (Table 3, entries 7 and 8 vs entries 9 and 10). A mixture of electronic and steric effects leads to mixed results when the acetyl group in 1-position was changed to a TBS group – a TBS group is a more electron-donating and at the same time a sterically more hindered group compared to an acetyl group. While in one case use of a TBS group leads to a preferred formation of regioisomer **B** (Table 3, entry 5 vs entry 6) in other cases an opposite effect is observed (Table 3, entry 2 vs

Table 3 Investigation on the Influence of the Substituents to the Regioselectivity of the D–A Reaction Applying the Chiral 'Mikami' Catalyst



1a,b **2a–d** (2.5 equiv) **3–10A** both *endo* **3–10B**

Entry (Prod)	R^1	R^2	R^3	Conv. after 2 h (%)[a]	**A**:**B** (cat.)[a]	er (%) **A**[b]	er (%) **B**[b]
1[c] (**3**)	H	Ac	H	–	99:01	88:12–98:2	–
2 (**3**)	H	Ac	H	37	28:72	76:23	97:03
3[d] (**3**)	H	Ac	H	19	66:34	73:27	82:18
4 (**4**)	H	TBS	H	18	78:22	60:40	99:01
5 (**5**)	H	Ac	Me	74	26:74	70:30	97:03
6 (**6**)	H	TBS	Me	26	01:99	–	99:01
7 (**7**)	OMe	Ac	H	41	10:90	77:23	96:04
8 (**8**)	OMe	TBS	H	15	17:83	n.d.	n.d.
9 (**9**)	OMe	Ac	Me	93	01:99	–	99:01
10 (**10**)	OMe	TBS	Me	29	01:99	–	99:01

[a] Conversions and regioselectivities were determined by ^{1}H NMR analysis of the crude reaction mixture.
[b] The er values were determined by HPLC analysis. n.d.: not detected.
[c] According to literature.7
[d] Reaction performed in toluene.

entry 4 and entry 7 vs entry 8). A number of studies towards the structure of the 'Mikami'-catalyst and towards optimal preparation conditions, with focus on the role of molecular sieves and the nature of the catalytically active species, have been published.[4,10a,14] Reports, claiming dichlorotitanium 3,3′-dimethylbinaphthoxide (BINOL-Ti-Cl_2) being the catalytically active species, have been disproved, as, for example, by a strong positive nonlinear effect.[7,14b] However, any attempts on disclosing the real nature of the 'Mikami'-catalyst as well as any attempts in synthesizing structurally defined active BINOL-Ti-complexes is still elusive, thus making it impossible to propose a structure for the transition state of the cycloaddition. Nevertheless, with the studies shown, prediction of the regioselectivity outcome of similar chiral Lewis acid catalyzed D–A reactions should be facilitated.

Unless otherwise specified, all reactions were carried out using standard Schlenk techniques under dry N_2 with magnetic stirring. Glassware was oven dried at 120 °C overnight. Solvents were dried and purified by conventional methods prior to use. All reagents were used as purchased from commercial suppliers without further purification. Common solvents for chromatography [petroleum ether (PE) (bp 40–60 °C), EtOAc] were distilled prior to use. Flash column chromatography was performed on silica gel 60, 0.040–0.063 mm (230–400 mesh). Preparative medium pressure liquid chromatography (MPLC) was performed with a packed column (25 × 300 mm or 40 × 475 mm; Si 60, 15–25 µm) and a UV detector (205 nm). TLC (monitoring the course of the reaction) was performed on precoated plastic sheets with detection by UV (254 nm) and/or by coloration with cerium molybdenum solution. [phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot H_2O$ (10 g), concd H_2SO_4 (60 mL), H_2O (940 mL)]. IR spectra were recorded on a FT-IR-Perkin Elmer (SpectrumOne), fitted with an ATR sampling accessory. ^{1}H and ^{13}C NMR spectra were recorded at r.t. in $CDCl_3$ on a Bruker Avance/DRX 600 NMR spectrometer at 600 and 151 MHz, respectively, relative to internal standard TMS (^{1}H: δ TMS = 0.00) or relative to the resonance of the solvent [^{13}C: δ ($CDCl_3$) = 77.0]. Higher order δ and *J* values are not corrected. ^{13}C signals were assigned by means of C, H, COSY, and HSQC, or HMBC spectroscopy. Enantiomeric ratios were determined by HPLC analysis using Dionex (UltiMate® 3000) equipped with Chiralpak IC, Chrialpak IA, Chiralpak AS, Chiracel OB, and Chiracel OD-H columns. Optical rotations were measured on a Perkin-Elmer Model 341 polarimeter using a quartz cell with 1 mL capacity and a 10 cm path length. Melting points are uncorrected. Chiral Ti-BINOL based catalyst was prepared according to literature procedure and dissolved in anhydrous toluene in order to obtain a stock solution (0.03 mg/mL); a detailed description is given in the Supporting Information.[7,10a]

Racemic Diels–Alder Reactions; General Procedure A (GP A)
In a Schlenk-tube, equipped with a magnetic stirring bar, dienophile **1a** or **1b** was dissolved in anhydrous CH_2Cl_2 (4 mL/mmol). Diene **1a**, **1b**, **1c**, or **1d** (3 equiv) was added via a syringe in one portion and the reaction mixture was stirred at 20 °C for the allotted time. After full conversion (TLC, eluent: PE–EtOAc, 90:10) a small sample was taken and analyzed by ^{1}H NMR spectroscopy in order to determine the regioselectivity of the reaction. The reaction mixture was directly submitted to a short column chromatography to afford the cycloaddition products **3**–**10** as a mixture of two regioisomers. If applicable the two regioisomers were separated by means of MPLC.

1-Acetoxy-8-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (3A) and 1-Acetoxy-5-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (3B)
Juglone (**1a**; 196 mg, 1.13 mmol) was reacted with (*E*)-1-acetoxybuta-1,3-diene (**2a**; 401 mg, 3.58 mmol, 3.17 equiv) according to GP A. The was reaction stopped after 2 d and the adduct **3** was isolated after column chromatography (PE–EtOAc, 85:15) as a 4:1 (**A**:**B**) mixture of regioisomers (318 mg, 99%). Regioisomers **3A** and **3B** were separated using MPLC (PE–EtOAc, 85:15) yielding pure regioisomer **A** and a 1:3 (**A**:**B**) mixture of the two isomers as pale yellow solids; R_f = 0.1 (PE–EtOAc, 90:10).

MS (ESI, +): *m*/*z* = 304.1 [100, $(M + NH_4)^+$], 309.0 [100, $(M + Na)^+$], 325.1 [30, $(M + K)^+$].

Anal. Calcd for $C_{16}H_{14}O_5$: C, 67.13; H, 4.93. Found: C, 66.94 ± 0.10; H, 4.92 ± 0.01.

Regioisomer A; 1-Acetoxy-8-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (3A)
Mp 132 °C.

FT-IR (Diamond-ATR, neat): 3040, 1740, 1702, 1642, 1454, 1369, 1246, 1221, 1162, 1017, 824, 714 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.38 (s, 3 H, $COCH_3$), 2.24 (dddd, *J* = 19.2, 7.1, 2.7, 2.3 Hz, 1 H, 4-H_a), 3.25 (ddd, *J* = 19.2, 4.8, 2.0 Hz, 1 H, 4-H_b), 3.42 (dd, *J* = 7.1, 6.0 Hz, 1 H, 4a-H), 3.47 (dd, *J* = 6.0, 4.0 Hz, 1 H, 9a-H), 5.47 (dd, *J* = 5.1, 4.0 Hz, 1 H, 1-H), 5.93 (dddd, *J* = 10.1, 5.1, 2.3, 2.0 Hz, 1 H, 2-H), 6.09 (ddd, *J* = 10.1, 4.8, 2.7 Hz, 1 H, 3-H), 7.23 (dd, *J* = 8.4, 1.2 Hz, 1 H, 7-H), 7.56 (dd, *J* = 7.5, 1.2 Hz, 1 H, 5-H), 7.64 (dd, *J* = 8.4, 7.5 Hz, 1 H, 6-H), 11.99 (s, 1 H, 8-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 20.0 ($CO\mathit{C}H_3$), 21.9 (C-4), 42.4 (C-4a), 50.7 (C-9a), 65.8 (C-1), 117.3 (C-5), 118.4 (C-8a), 122.8 (C-2), 123.0 (C-7), 131.8 (C-3), 136.8 (C-10a), 136.9 (C-6), 161.7 (C-8), 169.2 (C=O), 194.8 (C-10), 203.0 (C-9).

Regioisomer 3B; 1-Acetoxy-5-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (3B)
Mp 120 °C.

FT-IR (Diamond-ATR, neat): 3041, 1740, 1695, 1650, 1455, 1369, 1266, 1224, 1163, 1016, 824, 716 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.39 (s, 3 H, $COCH_3$), 2.20–2.29 (m, 1 H, 4-H_a), 3.20–3.30 (m, 1 H, 4-H_b), 3.40–3.53 (m, 2 H, 9a-H, 4a-H), 5.47 (dd, *J* = 4.9, 4.0 Hz, 1 H, 1-H), 5.93 (dddd, *J* = 10.2, 4.9, 2.3, 2.3 Hz, 1 H, 2-H), 6.08 (ddd, *J* = 10.2, 4.8, 2.7 Hz, 1 H, 3-H), 7.26 (dd, *J* = 8.1, 1.5 Hz, 1 H, 6-H), 7.58 (dd, *J* = 7.4, 1.5 Hz, 1 H, 8-H), 7.61 (dd, *J* = 8.1, 7.4 Hz, 1 H, 7-H), 11.75 (s, 1 H, 5-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 20.0 ($CO\mathit{C}H_3$), 21.6 (C-4), 42.3 (C-4a), 50.3 (C-9a), 65.7 (C-1), 118.2 (C-8), 118.8 (C-10a), 123.5 (C-2), 123.8 (C-6), 131.1 (C-3), 135.7 (C-8a), 136.0 (C-7), 160.2 (C-5), 169.1 (C=O), 195.4 (C-9), 202.3 (C-10).

1-[(*tert*-Butyldimethylsilyl)oxy]-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (4A) and 1-[(*tert*-Butyldimethylsilyl)oxy]-5-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (4B)
Juglone (**1a**; 299 mg, 1.15 mmol) was reacted with (*E*)-1-(*tert*-butyldimethylsilyl)oxybuta-1,3-diene (**2d**; 635 mg, 3.45 mmol, 3.00 equiv) according to GP A. The reaction was stopped after 21 h and the adducts **4A** and **4B** were isolated after column chromatography (PE–EtOAc, 90:10) as a 7:1 (**A**:**B**) mixture of regioisomers (250 mg, 61%). Regioisomers **4A** and **4B** were separated using MPLC (PE–EtOAc, 90:10) yielding pure regioisomers **A** and **B** as pale yellow solids; R_f = 0.3 (PE–EtOAc, 90:10).

MS (ESI, +): *m*/*z* (%) = 381.2 [100, $(M + NH_4)^+$], 358.8 [40, $(M + H)^+$].

Anal. Calcd for $C_{20}H_{26}O_4Si$: C, 67.00; H, 7.31. Found: C, 66.96 ± <0.1; H, 7.39 ± 0.02.

Regioisomer A; 1-[(*tert*-Butyldimethylsilyl)oxy]-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (4A)
Mp 160 °C.

FT-IR (Diamond-ATR, neat): 2951, 2930, 2876, 2858, 1698, 1637, 1452, 1327, 1246, 1158, 1107, 1040, 950, 896, 824, 776, 698 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = –0.35, –0.13 [2 s, 2 × 3 H, $Si(CH_3)_2$], 0.44 [s, 9 H, $SiC(CH_3)_3$], 2.19 (dddd, *J* = 19.1, 7.0, 2.7, 2.7 Hz, 1 H, 4-H_a), 3.19 (dddd, *J* = 19.1, 4.7, 2.0, 0.9 Hz, 1 H, 4-H_b), 3.29–3.34 (m, 2 H, 4a-H, 9a-H), 4.45 (ddd, *J* = 5.0, 3.8, 1.4 Hz, 1 H, 1-H), 5.80 (dddd, *J* = 10.2, 5.0, 2.7, 2.0 Hz, 1 H, 2-H), 5.92 (ddd, *J* = 10.2, 4.7, 2.7 Hz, 1 H, 3-H), 7.16 (dd, *J* = 8.4, 1.2 Hz, 1 H, 7-H), 7.48 (dd, *J* = 7.5, 1.2 Hz, 1 H, 5-H), 7.56 (dd, *J* = 8.4, 7.5 Hz, 1 H, 6-H), 12.20 (s, 1 H, 8-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = –5.7, –4.9 [$Si(CH_3)_2$], 17.5 (SiC), 21.8 (C-4), 25.1 [$SiC(\mathit{C}H_3)_3$], 42.4 (C-4a), 53.3 (C-9a), 65.5 (C-1), 117.3 (C-5), 119.4 (C-8a), 122.4 (C-7), 126.9 (C-2), 128.8 (C-3), 136.4 (C-6), 137.8 (C-10a), 161.6 (C-8), 195.2 (C-10), 205.5 (C-9).

Regioisomer B; 1-[(*tert*-Butyldimethylsilyl)oxy]-5-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (4B)
Mp 138 °C.

FT-IR (Diamond-ATR, neat): 2955, 2883, 2929, 2857, 1690, 1651, 1455, 1331, 1298, 1263, 11207, 1161, 1046, 953, 894, 836, 777, 716 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = –0.39, –0,13 [2 s, 2 × 3 H, $Si(CH_3)_2$], 0.46 [s, 9 H, $SiC(CH_3)_3$], 2.16 (dddd, *J* = 19.2, 7.5, 2.6, 2.6 Hz, 1 H, 4-H_a), 3.23 (ddd, *J* = 19.2, 4.7, 1.2 Hz, 1 H, 4-H_b), 3.28 (dd, *J* = 6.0, 3.8 Hz, 1 H, 9a-H), 3.42 (dd, *J* = 7.5, 6.0 Hz, 1 H, 4a-H), 4.45 (ddd, *J* = 4.8, 3.8, 1.2 Hz, 1 H, 1-H), 5.82 (ddd, *J* = 10.2, 4.8, 2.7 Hz, 1 H, 2-H), 5.90 (dddd, *J* = 10.2, 4.7, 2.6, 1.2 Hz, 1 H, 3-H), 7.19 (dd, *J* = 8.3, 1.2 Hz, 1 H, 6-H), 7.54 (dd, *J* = 8.3, 7.6 Hz, 1 H, 7-H), 7.61 (dd, *J* = 7.6, 1.2 Hz, 1 H, 8-H), 11.64 (s, 1 H, 5-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = –5.6, –4.9 [$Si(CH_3)_2$], 17.5 (SiC), 21.2 (C-4), 25.1 [$SiC(\mathit{C}H_3)_3$], 42.0 (C-4a), 52.8 (C-9a), 65.5 (C-1), 118.0 (C-8), 119.9 (C-10a), 123.4 (C-6), 127.5 (C-2), 128.3 (C-3), 135.2 (C-7), 136.2 (C-8a), 159.9 (C-5), 197.7 (C-9), 202.8 (C-10).

1-Acetoxy-3-methyl-8-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (5A) and Acetoxy-3-methyl-5-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (5B)
Juglone (**1a**; 155 mg, 0.89 mmol) was reacted with (*E*)-1-acetoxy-3-methylbuta-1,3-diene (**2c**; 336 mg, 2.66 mmol, 2.99 equiv) according to GP A. The reaction was stopped after 18 h and the adduct **5** was isolated after column chromatography (PE–EtOAc, 85:15) as a 4.4:1 (**A**:**B**) mixture of regioisomers (259 mg, 97%). Regioisomers **5A** and **5B** were separated using MPLC (PE–EtOAc, 85:15) yielding pure regioisomer **A** and a 1:2.3 (**A**:**B**) mixture of the two isomers as pale yellow solids; R_f = 0.1 (PE–EtOAc, 90:10).

Regioisomer A; 1-Acetoxy-3-methyl-8-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (5A)
Mp 141 °C.

FT-IR (Diamond-ATR, neat): 2916, 1739, 1702, 1642, 1454, 1368, 1346, 1240, 1219, 1159, 1014, 925, 901, 826, 770, 729 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, $COCH_3$), 1.84 (s, 3 H, 3-CH_3), 2.15 (ddd, *J* = 18.7, 7.3, 3.0 Hz, 1 H, 4-H_a), 3.12 (d, *J* = 18.7 Hz, 1 H, 4-H_b), 3.38 (dd, *J* = 6.0, 4.0 Hz, 1 H, 9a-H), 3.43 (dd, *J* = 7.3, 6.0 Hz, 1 H, 4a-H), 5.45 (dd, *J* = 5.5, 4.0 Hz, 1 H, 1-H), 5.67 (dd, *J* = 5.5, 3.0 Hz, 1 H, 2-H), 7.22 (dd, *J* = 8.4, 1.2 Hz, 1 H, 7-H), 7.55 (dd, *J* = 7.6, 1.2 Hz, 1 H, 5-H), 7.63 (dd, *J* = 8.4, 7.6 Hz, 1 H, 6-H), 12.00 (s, 1 H, 8-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 20.0 ($CO\mathit{C}H_3$), 23.5 (3-CH_3), 26.9 (C-4), 43.1 (C-4a), 50.5 (C-9a), 67.0 (C-1), 117.2 (C-5), 117.7 (C-2), 118.4 (C-8a), 123.0 (C-7), 136.8 (C-6), 136.8 (C-10a), 140.5 (C-3), 161.6 (C-8), 169.3 (C=O), 194.9 (C-10), 203.3 (C-9).

MS (ESI, +): *m*/*z* (%) = 317.9 [100, $(M + NH_4)^+$], 323.2 [90, $(M + Na)^+$].

Anal. Calcd for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 67.80 ± 0.15; H, 5.34 ± 0.03.

Regioisomer B; 1-Acetoxy-3-methyl-5-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (5B)
Mp 110 °C.

FT-IR (Diamond-ATR, neat): 2916, 1740, 1695, 1650, 1455, 1369, 1266, 1224, 1163, 1013, 909, 723 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.37 (s, 3 H, $COCH_3$), 1.86 (s, 3 H, 3-CH_3), 2.18 (dd, *J* = 18.6, 7.5 Hz, 1 H, 4-H_a), 3.14 (d, *J* = 18.6 Hz, 1 H, 4-H_b), 3.41 (dd, *J* = 5.9, 4.2 Hz, 1 H, 9a-H), 3.53 (ddd, *J* = 7.5, 5.9, 1.6 Hz, 1 H, 4a-H), 5.44–5.49 (m, 1 H, 1-H), 5.68 (dd, *J* = 5.3, 1.6 Hz, 1 H, 2-H), 7.26 (dd, *J* = 7.8, 1.7 Hz, 1 H, 6-H), 7.58 (dd, *J* = 7.8, 7.5 Hz, 1 H, 8-H), 7.60 (dd, *J* = 7.5, 1.7 Hz, 1 H, 7-H), 11.76 (s, 1 H, 5-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 20.0 ($CO\mathit{C}H_3$), 23.5 (3-CH_3), 26.2 (C-4), 42.9 (C-4a), 50.1 (C-9a), 66.9 (C-1), 118.2 (C-2), 118.2 (C-8), 118.8 (C-10a), 123.8 (C-6), 135.8 (C-8a), 135.9 (C-3), 139.8 (C-3), 160.2 (C-5), 169.2 (C=O), 195.7 (C-9), 202.3 (C-10).

MS (ESI, +): *m*/*z* (%) = 323.2 [100, $(M + Na)^+$], 317.9 [60, $(M + NH_4)^+$].

Anal. Calcd for $C_{17}H_{16}O_5$: C 67.99, H 5.37. Found: C, 67.86 ± <0.1; H, 5.37 ± 0.01.

1-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (6A) and 1-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-5-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (6B)
Juglone (**1a**; 146 mg, 0.84 mmol) was reacted with (*E*)-1-(*tert*-butyldimethylsilyl)oxy-3-methylbuta-1,3-diene (**2b**; 500 mg, 2.52 mmol, 3.00 equiv) according to GP A. The reaction was stopped after 2 h and the adducts **6A** and **6B** were isolated after column chromatography (PE–EtOAc, 95:5) as a 9:1 (**A**:**B**) mixture of regioisomers (304 mg, 97%). Regioisomers **6A** and **6B** were separated using MPLC (PE–EtOAc, 95:5) yielding pure regioisomers **A** and **B** as pale yellow solids; R_f = 0.5 (PE–EtOAc, 90:10).

MS (ESI, +): *m*/*z* (%) = 395.3 [100, $(M + Na)^+$], 390.0 [50, $(M + NH_4)^+$].

Anal. Calcd for $C_{21}H_{28}O_4Si$: C, 67.71; H, 7.58. Found: C, 67.41 ± 0.06; H, 7.62 ± 0.04.

Regioisomer A; 1-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (6A)
Mp 123 °C.

FT-IR (Diamond-ATR, neat): 2928, 2884, 2857, 1706, 1640, 1454, 1334, 1247, 1044, 953, 828, 768, 699 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = –0.35, –0.15 [2 s, 2 × 3 H, $Si(CH_3)_2$], 0.44 [s, 9 H, $SiC(CH_3)_3$], 1.80 (s, 3 H, 3-CH_3), 2.06 (dd, *J* = 18.6, 7.5 Hz, 1 H, 4-H_a), 3.07 (d, *J* = 18.6 Hz, 1 H, 4-H_b), 3.22 (dd, *J* = 6.0, 3.8 Hz, 1 H, 9a-H), 3.32 (dd, *J* = 7.5 Hz, 6.0 Hz, 1 H, 4a-H), 4.44 (dd, *J* = 5.2, 3.5 Hz, 1 H, 1-H), 5.53 (d, *J* = 5.2 Hz, 1 H, 2-H), 7.16 (dd, *J* = 8.4, 1.2 Hz, 1 H, 7-H), 7.47 (dd, *J* = 7.5, 1.2 Hz, 1 H, 5-H), 7.55 (dd, *J* = 8.4, 7.5 Hz, 1 H, 6-H), 12.22 (s, 1 H, 8-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = –5.6, –4.8 [$Si(CH_3)_2$], 17.5 (SiC), 23.5 (3-$\mathit{C}H_3$), 25.1 [$SiC(\mathit{C}H_3)_3$], 43.0 (C-4a), 53.1 (C-9a), 66.5 (C-1), 117.3 (C-5), 119.4 (C-8a), 121.9 (C-2), 122.3 (C-7), 136.3 (C-6), 136.9 (C-3), 137.7 (C-10a), 161.6 (C-8), 195.2 (C-10), 205.9 (C-9).

Regioisomer B; 1-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-5-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (6B)
Mp 122 °C.

FT-IR (Diamond-ATR, neat): 2955, 2883, 2929, 2857, 1690, 1651, 1455, 1331, 1298, 1263, 11207, 1161, 1046, 953, 894, 836, 777, 716 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = –0.39, –0,13 [2 s, 2 × 3 H, $Si(CH_3)_2$], 0.46 [s, 9 H, $SiC(CH_3)_3$], 2.16 (dddd, *J* = 19.2, 7.5, 2.6, 2.6 Hz, 1 H, 4-H_a), 3.23 (ddd, *J* = 19.2, 4.7, 1.2 Hz, 1 H, 4-H_b), 3.28 (dd, *J* = 6.0, 3.8 Hz, 1 H, 9a-H), 3.42 (dd, *J* = 7.5, 6.0 Hz, 1 H, 4a-H), 4.45 (ddd, *J* = 4.8, 3.8, 1.2 Hz, 1 H, 1-H), 5.82 (ddd, *J* = 10.2, 4.8, 2.7 Hz, 1 H, 2-H), 5.90 (dddd, *J* = 10.2, 4.7, 2.6, 1.2 Hz, 1 H, 3-H), 7.19 (dd, *J* = 8.3, 1.2 Hz, 1 H, 6-H), 7.54 (dd, *J* = 8.3, 7.6 Hz, 1 H, 7-H), 7.61 (dd, *J* = 7.6, 1.2 Hz, 1 H, 8-H), 11.64 (s, 1 H, 5-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = –5.6, –4.9 [$Si(CH_3)_2$], 17.5 (SiC), 21.2 (C-4), 25.1 [$SiC(\mathit{C}H_3)_3$)], 42.0 (C-4a), 52.8 (C-9a), 65.5 (C-1), 118.0 (C-8), 119.9 (C-10a), 123.4 (C-6), 127.5 (C-2), 128.3 (C-3), 135.2 (C-7), 136.2 (C-8a), 159.9 (C-5), 197.7 (C-9), 202.8 (C-10).

1-Acetoxy-8-hydroxy-6-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (7A) and 1-Acetoxy-5-hydroxy-7-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (7B)
5-Hydroxy-7-methoxy-1,4-naphthoquinone (**1b**; 168 mg, 0.82 mmol) was reacted with (*E*)-1-acetoxybuta-1,3-diene (**2a**; 330 mg, 2.94 mmol, 3.59 equiv) according to GP A. The reaction was stopped after 2 d and the adduct **7** was isolated after column chromatography (PE–EtOAc, 80:20) as a 1.3:1 (**A**:**B**) mixture of regioisomers (203 mg, 78%). Regioisomers **7A** and **7B** were purified using MPLC (PE–EtOAc, 85:15) yielding a 1.1:1 (**A**:**B**) mixture of the two isomers as a pale yellow solid; mp 134 °C; R_f = 0.4 (PE–EtOAc, 90:10).

FT-IR (Diamond-ATR, neat): 2943, 1740, 1699, 1632, 1613, 1574, 1443, 1370, 12194, 1219, 1161, 1128, 1011, 970, 932, 909, 846, 782, 723 cm^{-1}.

MS (ESI, +): *m*/*z* (%) = 339.1 [100, $(M + Na)^+$], 334.0 [70, $(M + NH_4)^+$].

Anal. Calcd for $C_{17}H_{16}O_6$: C 64.55, H 5.10. Found: C, 64.32 ± 0.18; H, 5.12 ± 0.01.

Regioisomer A; 1-Acetoxy-8-hydroxy-6-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (7A)
^1H NMR (600 MHz, $CDCl_3$): δ = 1.44 (s, 3 H, $COCH_3$), 2.19–2.26 (m, 1 H, 4-H_a), 3.17–3.25 (m, 1 H, 4-H_b), 3.35–3.48 (m, 2 H, 4a-H, 9a-H), 3.90 (s, 3 H, OCH_3), 5.45 (dd, *J* = 5.0, 4.0 Hz, 1 H, 1-H), 5.88–5.95 (m, 1 H, 2-H), 6.02–6.09 (m, 1 H, 3-H), 6.63 (d, *J* = 1.5 Hz, 1 H, 7-H), 7.08 (d, *J* = 1.5 Hz, 1 H, 5-H), 12.32 (s, 1 H, 8-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 20.2 ($CO\mathit{C}H_3$), 21.6 (C-4), 41.7 (C-4a), 50.4 (C-9a), 65.8 (C-1), 56.0 (OCH_3), 105.1 (C-7), 105.3 (C-5), 113.0 (C-8a), 122.9 (C-3), 130.9 (C-2), 137.3 (C-10a), 163.0 (C-8), 166.3 (C-6), 169.1 (C=O), 195.4 (C-10), 200.6 (C-9).

Regioisomer B; 1-Acetoxy-5-hydroxy-7-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (7B)
FT-IR (Diamond-ATR, neat): 3041, 1740, 1695, 1650, 1455, 1369, 1266, 1224, 1163, 1016, 824, 716 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.39 (s, 3 H, $COCH_3$), 2.20–2.29 (m, 1 H, 4-H_a), 3.20–3.30 (m, 1 H, 4-H_b), 3.40–3.53 (m, 2 H, 9a-H, 4a-H), 5.47 (dd, *J* = 4.9, 4.0 Hz, 1 H, 1-H), 5.93 (dddd, *J* = 10.2, 4.9, 2.3, 2.3 Hz, 1 H, 2-H), 6.08 (ddd, *J* = 10.2, 4.8, 2.7 Hz, 1 H, 3-H), 7.26 (dd, *J* = 8.1, 1.5 Hz, 1 H, 6-H), 7.58 (dd, *J* = 7.4, 1.5 Hz, 1 H, 8-H), 7.61 (dd, *J* = 8.1, 7.4 Hz, 1 H, 7-H), 11.75 (s, 1 H, 5-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 20.0 ($CO\mathit{C}H_3$), 21.6 (C-4), 42.3 (C-4a), 50.3 (C-9a), 65.7 (C-1), 118.2 (C-8), 118.8 (C-10a), 123.5 (C-2), 123.8 (C-6), 131.1 (C-3), 135.7 (C-8a), 136.0 (C-7), 160.2 (C-5), 169.1 (C=O), 195.4 (C-9), 202.3 (C-10).

1-[(*tert*-Butyldimethylsilyl)oxy]-6-methoxy-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (8A) and 1-[(*tert*-Butyldimethylsilyl)oxy]-5-hydroxy-7-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (8B)
5-Hydroxy-7-methoxy-1,4-naphthoquinone (**1b**; 226 mg, 1.11 mmol) was reacted with (*E*)-1-(*tert*-butyldimethylsilyl)oxybuta-1,3-diene (**2d**; 541 mg, 2.94 mmol, 2.65 equiv) according to GP A. The reac-

tion was stopped after 1 d and the adducts **8A** and **8B** were isolated after column chromatography (PE–EtOAc, 93:7) as a 1.5:1 (**A**:**B**) mixture of regioisomers (366 mg, 85%) as a pale yellow solid. Regioisomers **8A** and **8B** could not be separated using MPLC; mp 89 °C; R_f = 0.5 (PE–EtOAc, 90:10).

FT-IR (Diamond-ATR, neat): 2929, 2886, 2856, 1709, 1632, 1577, 1463, 1443, 1379, 1302, 1253, 1206, 1161, 1120, 1046, 952, 898, 838, 826, 776 cm^{-1}.

HRMS (FT-ICR-MS, +): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{29}O_5Si$: 389.17843; found: 389.17795.

Anal. Calcd for $C_{21}H_{28}O_5Si$: C, 65.32; H, 6.75. Found: C, 64.73 ± 0.10; H, 7.27 ± 0.01.

Regioisomer A; 1-[(*tert*-Butyldimethylsilyl)oxy]-6-methoxy-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (8A)

^{1}H NMR (600 MHz, $CDCl_3$): δ = –0.33, –0.12 [2 s, 2 × 3 H, $Si(CH_3)_2$], 0.48 [s, 9 H, $SiC(CH_3)_3$], 2.09–2.17 (m, 1 H, 4-H_a), 3.18 (ddd, *J* = 19.0, 4.8, 2.1 Hz, 1 H, 4-H_b), 3.24 (m_c, 1 H, 9a-H), 3.27 (m_c, 1 H, 4a-H), 3.87 (s, 3 H, OCH_3), 4.43 (m_c, 1 H, 1-H), 5.78–5.92 (m, 2 H, 2-H, 3-H), 6.59 (d, *J* = 2.5 Hz, 1 H, 7-H), 7.03 (d, *J* = 2.5 Hz, 1 H, 5-H), 12.51 (s, 1 H, 8-OH).

^{13}C NMR (151 MHz, $CDCl_3$) δ = –5.7, –4.9 [$Si(CH_3)_2$], 17.5 (SiC), 21.8 (C-4), 25.1 [$SiC(CH_3)_3$], 42.6 (C-4a), 53.1 (C-9a), 56.0 (OCH_3), 63.3 (C-1), 105.0 (C-5), 105.1 (C-7), 114.2 (C-8a), 128.6, 127.0 (C-2, C-3), 139.5 (C-10a), 164.5 (C-8), 166.1 (C-6), 195.2 (C-10), 203.9 (C-9).

Regioisomer B; 1-[(*tert*-Butyldimethylsilyl)oxy]-5-hydroxy-7-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (8B)

^{1}H NMR (600 MHz, $CDCl_3$): δ = –0.35, –0,13 [2 s, 2 × 3 H, $Si(CH_3)_2$], 0.48 [s, 9 H, $SiC(CH_3)_3$], 2.09–2.17 (m, 1 H, 4-H_a), 3.23 (ddd, *J* = 19.0, 4.7, 2.2 Hz, 1 H, 4-H_b), 3.25 (m_c, 1 H, 9a-H), 3.36 (dd, *J* = 7.3, 6.0 Hz, 1 H, 4a-H), 3.87 (s, 3 H, OCH_3), 4.43 (m_c, 1 H, 1-H), 5.78–5.92 (m, 1 H, 2-H, 3-H), 6.63 (d, *J* = 2.5 Hz, 1 H, 6-H), 7.13 (d, 1 H, 8-H), 11.92 (s, 1 H, 5-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = –5.6, –4.8 [$Si(CH_3)_2$], 17.5 (SiC), 21.1 (C-4), 25.1 [$SiC(CH_3)_3$], 41.3 (C-4a), 52.6 (C-9a), 55.9 (OCH_3), 65.5 (C-1), 104.7 (C-8), 106.6 (C-6), 114.6 (C-10a), 127.5, 128.3 (C-2, C-3), 137.7 (C-8a), 162.5 (C-5), 165.1 (C-7), 197.8 (C-9), 201.1 (C-10).

1-Acetoxy-3-methyl-8-hydroxy-6-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (9A) and 1-Acetoxy-3-methyl-5-hydroxy-7-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (9B)

5-Hydroxy-7-methoxy-1,4-naphthoquinone (**1b**; 140 mg, 0.68 mmol) was reacted with (*E*)-1-acetoxy-3-methylbuta-1,3-diene (**2c**; 320 mg, 2.54 mmol, 3.74 equiv) according to GP A. The reaction was stopped after 12 h and the adduct **9** was isolated after column chromatography (PE–EtOAc, 80:20) as a 1:1 (**A**:**B**) mixture of regioisomers (193 mg, 85%). Regioisomers **9A** and **9B** were purified using MPLC (PE–EtOAc, 85:15) yielding a 1:1 (**A**:**B**) mixture of the two isomers as a pale yellow solid; mp 104 °C; R_f = 0.4 (PE–EtOAc, 90:10).

FT-IR (Diamond-ATR, neat): 2940, 1740, 1693, 1639, 1613, 1575, 1491, 1441, 1377, 1300, 1223, 1159, 1129, 1013, 927 cm^{-1}.

MS (ESI, +): *m*/*z* (%) = 348.0 [100, $(M + NH_4)^+$], 353.1 [30, $(M + Na)^+$].

Anal. Calcd for $C_{18}H_{18}O_6$: C, 65.45; H, 5.49. Found: C, 65.25 ± 0.16; H, 5.46 ± 0.01.

Regioisomer A; 1-Acetoxy-3-methyl-8-hydroxy-6-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (9A)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.43 (s, 3 H, $COCH_3$), 1.83 (m_c, 3 H, 3-CH_3), 2.10–2.17 (m, 1 H, 4-H_a), 3.10 (d, *J* = 18.5 Hz, 1 H, 4-H_b), 3.32 (dd, *J* = 6.0, 3.9 Hz, 1 H, 9a-H), 3.36–3.39 (m, 1 H, 4a-H), 3.38 (s, 3 H, OCH_3), 5.44 (dd, *J* = 5.3, 4.3 Hz, 1 H, 1-H), 5.68 (dq, *J* = 5.3, 1.6 Hz, 1 H, 2-H), 6.62 (d, *J* = 2.5 Hz, 1 H, 7-H), 7.07 (d, *J* = 2.5 Hz, 1 H, 5-H), 12.34 (s, 1 H, 8-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 20.3 ($COCH_3$), 23.5 (3-CH_3), 26.5 (C-4), 42.3 (C-4a), 50.2 (C-9a), 55.9 (6-OCH_3), 66.9 (C-1), 105.2 (C-5), 105.3 (C-7), 113.1 (C-8a), 117.8 (C-2), 134.4 (C-10a), 140.2 (C-3), 164.6 (C-8), 166.2 (C-6), 169.3 (C=O), 195.0 (C-10), 201.1 (C-9).

Regioisomer B; 1-Acetoxy-3-methyl-5-hydroxy-7-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (9B)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.44 (s, 3 H, $COCH_3$), 1.83 (d, *J* = 1.6 Hz, 3 H, 3-CH_3), 2.14 (dd, *J* = 18.6, 7.5 Hz, 1 H, 4-H_a), 3.10 (d, *J* = 18.6 Hz, 1 H, 4-H_b), 3.38 (dd, *J* = 5.8, 4.3 Hz, 1 H, 9a-H), 3.46 (dd, *J* = 7.5, 5.8 Hz, 1 H, 4a-H), 3.89 (s, 3 H, OCH_3), 5.45 (dd, *J* = 5.3, 4.3 Hz, 1 H, 1-H), 5.66 (dq, *J* = 5.3, 1.6 Hz, 1 H, 2-H), 6.68 (d, *J* = 2.5 Hz, 1 H, 6-H), 7.10 (d, *J* = 2.5 Hz, 1 H, 8-H), 12.00 (s, 1 H, 5-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 20.3 ($COCH_3$), 23.6 (3-CH_3), 26.3 (C-4), 42.4 (C-4a), 50.0 (C-9a), 55.9 (7-OCH_3), 66.9 (C-1), 105.1 (C-8), 106.8 (C-6), 113.4 (C-10a), 118.3 (C-2), 137.4 (C-8a), 139.7 (C-3), 162.9 (C-2), 165.6 (C-7), 169.4 (C=O), 195.8 (C-9), 200.8 (C-10).

1-[(*tert*-Butyldimethylsilyl)oxy]-3methyl-6-methoxy-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (10A) and 1-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-5-hydroxy-7-methoxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (10B)

5-Hydroxy-7-methoxy-1,4-naphthoquinone (**1b**; 100 mg, 0.49 mmol) was reacted with (*E*)-1-(*tert*-butyldimethylsilyl)oxy-3-methylbuta-1,3-diene (**2b**; 243 mg, 1.22 mmol, 2.49 equiv) according to GP A. The reaction was stopped after 8 h and adducts **10A** and **10B** were isolated after column chromatography (PE–EtOAc, 90:10) as a 2:1 (**A**:**B**) mixture of regioisomers (173 mg, 89%) as a pale yellow solid. Regioisomers **10A** and **10B** were separated using MPLC; mp 102 °C; R_f = 0.3 (PE–EtOAc, 90:10).

HRMS (FT-ICR-MS, +): *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{30}O_5Si + Na$: 425.17602; found: 425.17586.

Anal. Calcd for $C_{22}H_{30}O_5Si$: C, 65.64; H, 7.51. Found: C, 65.22 ± 0.21; H, 7.54 ± 0.04.

Regioisomer A; 1-[(*tert*-Butyldimethylsilyl)oxy]-3methyl-6-methoxy-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (10A)

FT-IR (Diamond-ATR, neat): 2929, 2884, 2857, 1707, 1627, 1557, 1443, 1380, 1295, 1258, 1204, 1160, 1128, 1045, 1021, 995, 952, 896, 826, 775, 699 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = –0.34, –0,14 [2 s, 2 × 3 H, $Si(CH_3)_2$], 0.47 [s, 9 H, $SiC(CH_3)_3$], 1.80 (s, 3 H, 3-CH_3), 2.04 (m_c, 1 H, 4-H_a), 3.05 (m_c, 1 H, 4-H_b), 3.16 (dd, *J* = 6.0, 3.6 Hz, 1 H, 9a-H), 3.26 (dd, *J* = 7.6, 6.0 Hz, 1 H, 4a-H), 3.87 (s, 3 H, OCH_3), 4.41 (dd, *J* = 5.4, 3.6 Hz, 1 H, 1-H), 5.53 (m_c, 1 H, 2-H), 6.61 (d, *J* = 2.5 Hz, 1 H, 7-H), 7.13 (d, *J* = 2.5 Hz, 1 H, 5-H), 12.53 (s, 1 H, 8-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = –5.6, –4.8 [$Si(CH_3)_2$], 17.5 (SiC), 23.4 (C-3), 25.2 [$SiC(CH_3)_3$], 26.5 (C-4), 43.2 (C-4a), 53.0 (C-9a), 55.9 (OCH_3), 66.3 (C-1), 105.0 (C-5), 105.0 (C-7), 114.2 (C-8a), 122.0 (C-2), 136.7 (C-3), 139.4 (C-10a), 164.4 (C-8), 166.0 (C-6), 199.2 (C-10), 203.6 (C-9).

Regioisomer B; 1-[(*tert*-Butyldimethylsilyl)oxy]-5-hydroxy-7-methoxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (10B)

FT-IR (Diamond-ATR, neat): 2929, 2857, 1692, 1643, 1613, 1577, 1441, 1379, 1305, 1253, 1220, 1159, 1127, 1047, 954, 828, 776 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = –0.36, –0,15 [2 s, 2 × 3 H, $Si(CH_3)_2$)], 0.47 [s, 9 H, $SiC(CH_3)_3$], 1.79 (s, 3 H, 3-CH_3), 2.04 (m_c, 1 H, 4-H_a), 3.10 (m_c, 1 H, 4-H_b), 3.16 (dd, *J* = 6.1, 4.0 Hz, 1 H, 9a-H), 3.37 (dd, *J* = 7.8, 6.1 Hz, 1 H, 4a-H), 3.86 (s, 3 H, OCH_3), 4.42 (dd, *J* = 5.1, 4.0 Hz, 1 H, 1-H), 5.53 (m_c, 1 H, 2-H), 6.62 (d, *J* =

2.6 Hz, 1 H, 6-H), 7.13 (d, *J* = 2.6 Hz, 1 H, 8-H), 11.90 (s, 1 H, 5-OH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = –5.5, –4.8 [Si(CH_3)$_2$], 17.6 (SiC), 23.4 (3-CH_3), 25.2 [SiC(CH_3)$_3$], 25.8 (C-4), 41.9 (C-4a), 52.4 (C-9a), 55.9 (OCH_3), 65.6 (C-1), 104.6 (C-8), 106.6 (C-6), 114.5 (C-10a), 122.4 (C-2a), 136.4 (C-3), 137.8 (C-8a), 162.5 (C-5), 165.0 (C-7), 198.1 (C-9), 201.2 (C-10).

Ti-BINOL-Catalysed, Enantioselective Diels–Alder Reactions; General Procedure B (GP B)

In a Schlenk tube, equipped with a magnetic stirring bar, dienophile **1a** or **1b** was dissolved in anhydrous CH_2Cl_2 (4 mL/mmol) before 10 mol% of the Ti-catalyst stock solution (0.03 mg/mL, 0.10 equiv) were added via a syringe. Diene **2a**, **2b**, **2c**, or **2d** (3 equiv) was added via a syringe in one portion and the reaction mixture was stirred for 2 h at 20 °C. The crude mixture was analyzed by ^{1}H NMR spectroscopy in order to investigate the conversion of the reaction and the regioselectivity distribution. The reaction mixture was directly submitted to a short column chromatography and the product containing fractions were analyzed by means of HPLC (see Supporting Information for copies of chromatograms).

1-Acetoxy-8-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (3A) and 1-Acetoxy-5-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (3B) (Table 3, entry 2)

Juglone (**1a**; 30 mg, 0.17 mmol) was reacted with (*E*)-1-acetoxybuta-1,3-diene (**2a**; 48 mg, 0.43 mmol, 2.53 equiv) according to GP B. The was reaction stopped after 2 h, analysed by ^{1}H NMR spectroscopy, and filtered over a short column of silica gel (PE–EtOAc, 85:15). Enantiomeric ratios were determined using HPLC.

Conversion: 37%; **A**/**B** = 28:72, er (**3A**) = 76:23, er (**3B**) = 97:03 (Chiralpak IC, flow rate 0.5 mL/min, 20% *i*-PrOH–80% heptane).

1-Acetoxy-8-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (3A) and 1-Acetoxy-5-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (3B) (Table 3, entry 3)

Juglone (**1a**; 30 mg, 0.17 mmol) was reacted with (*E*)-1-acetoxybuta-1,3-diene (**2a**; 48 mg, 0.43 mmol, 2.53 equiv) in toluene (1.7 mL) according to GP B. The was reaction stopped after 2 h, analysed by ^{1}H NMR spectroscopy, and filtered over a short column of silica gel (PE–EtOAc, 85:15). Enantiomeric ratios were determined using HPLC.

Conversion: 19%; **A**/**B** = 66:34, er (**3A**) = 73:27, er (**3B**) = 82:18 (Chiralpak IC, flow rate 0.5 mL/min, 20% *i*-PrOH–80% heptane).

1-[(*tert*-Butyldimethylsilyl)oxy]-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (4A) and 1-[(*tert*-Butyldimethylsilyl)oxy]-5-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (4B) (Table 3, entry 4)

Juglone (**1a**; 30 mg, 0.17 mmol) was reacted with (*E*)-1-(*tert*-butyldimethylsilyl)oxybuta-1,3-diene (**2d**; 79 mg, 0.43 mmol, 2.53 equiv) according to GP B. The was reaction stopped after 2 h, analysed by ^{1}H NMR spectroscopy, and filtered over a short column of silica gel (PE–EtOAc, 90:10). Enantiomeric ratios were determined using HPLC.

Conversion: 18%; **A**/**B** = 78:22, er (**4A**) = 60:40, er (**4B**) = 99:01 (Chiracel OD-H, flow rate 0.5 mL/min, 0.2% *i*-PrOH–99.8% heptane).

1-Acetoxy-3-methyl-8-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (5A) and 1-Acetoxy-3-methyl-5-hydroxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (5B) (Table 3, entry 5)

Juglone (**1a**; 30 mg, 0.17 mmol) was reacted with (*E*)-1-acetoxy-3-methylbuta-1,3-diene (**2c**; 49 mg, 0.39 mmol, 2.29 equiv) according to GP B. The was reaction stopped after 2 h, analysed by ^{1}H NMR spectroscopy, and filtered over a short column of silica gel (PE–EtOAc, 80:20). Enantiomeric ratios were determined using HPLC.

Conversion: 74%; **A**/**B** = 26:74, er (**5A**) = 70:30, er (**5B**) = 97:03 (Chiralpak IC, flow rate 0.5 mL/min, 20% *i*-PrOH–80% heptane).

1-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (6A) and 1-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-5-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (6B) (Table 3, entry 6)

Juglone (**1a**; 30 mg, 0.17 mmol) was reacted with (*E*)-1-(*tert*-butyldimethylsilyl)oxy-3-methylbuta-1,3-diene (**2b**; 85 mg, 0.43 mmol, 2.53 equiv) according to GP B. The was reaction stopped after 2 h, analysed by ^{1}H NMR spectroscopy, and filtered over a short column of silica gel (PE–EtOAc, 95:5). Enantiomeric ratios were determined using HPLC.

Conversion: 26%; **A**/**B** = 01:99, er (**6A**) = n.d., er (**6B**) = 99:01 (Chiralpak IC, flow rate 0.5 mL/min, 0.2% *i*-PrOH–99.8% heptane).

1-Acetoxy-8-hydroxy-6-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (7A) and 1-Acetoxy-5-hydroxy-7-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (7B) (Table 3, entry 7)

5-Hydroxy-7-methoxy-1,4-naphthoquinone (**1b**; 30 mg, 0.15 mmol) was reacted with (*E*)-1-acetoxybuta-1,3-diene (**2a**; 41 mg, 0.37 mmol, 2.47 equiv) according to GP B. The reaction was stopped after 2 h, analysed by ^{1}H NMR spectroscopy, and filtered over a short column of silica gel (PE–EtOAc, 85:15). Enantiomeric ratios were determined using HPLC.

Conversion: 41%; **A**/**B** = 10:90, er (**7A**) = 77:23, er (**7B**) = 96:04 (Chiralpak IC, flow rate 0.5 mL/min, 20% *i*-PrOH–80% heptane).

1-[(*tert*-Butyldimethylsilyl)oxy]-6-methoxy-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (8A) and 1-[(*tert*-Butyldimethylsilyl)oxy]-5-hydroxy-7-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (8B) (Table 3, entry 8)

5-Hydroxy-7-methoxy-1,4-naphthoquinone (**1b**; 30 mg, 0.15 mmol) was reacted with (*E*)-1-(*tert*-butyldimethylsilyl)oxybuta-1,3-diene (**2d**; 46 mg, 0.37 mmol, 2.47 equiv) according to GP B. The reaction was stopped after 2 h, analysed by ^{1}H NMR spectroscopy, and filtered over a short column of silica gel (PE–EtOAc, 93:7). For this compound no separation on HPLC using different column and solvents could be achieved.

Conversion: 15%; **A**/**B** = 17:83, er (**8A**) = n.d, er (**8B**) = n.d.

1-Acetoxy-3-methyl-8-hydroxy-6-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (9A) and 1-Acetoxy-3-methyl-5-hydroxy-7-methoxy-9,10-dioxo-1,4,4a,9,9a,10-hexahydroanthracene (9B) (Table 3, entry 9)

5-Hydroxy-7-methoxy-1,4-naphthoquinone (**1b**; 30 mg, 0.15 mmol) was reacted with (*E*)-1-acetoxy-3-methylbuta-1,3-diene (**2c**; 46 mg, 0.37 mmol, 2.47 equiv) according to GP B. The reaction was stopped after 2 h, analysed by ^{1}H NMR spectroscopy, and filtered over a short column of silica gel (PE–EtOAc, 85:15); mp 111 °C; $[\alpha]_D^{20}$ +420.7 (*c* 0.27, $CHCl_3$). Enantiomeric ratios were determined using HPLC.

Conversion: 93%; **A**/**B** = 01:99, er (**9A**) = n.d., er (**9B**) = 99:01 (Chiralpak IC, flow rate 0.5 mL/min, 20% *i*-PrOH–80% heptane).

1-[(*tert*-Butyldimethylsilyl)oxy]-3methyl-6-methoxy-8-hydroxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (10A) and 1-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-5-hydroxy-7-methoxy-9,10-dioxo-1,4,4a,9a-tetrahydroanthracene (10B) (Table 3, entry 10)

5-Hydroxy-7-methoxy-1,4-naphthoquinone (**1b**; 30 mg, 0.15 mmol) was reacted with (*E*)-1-(*tert*-butyldimethylsilyl)oxy-3-methylbuta-1,3-diene (**2b**; 73 mg, 0.37 mmol, 2.47 equiv) according to GP B. The was reaction stopped after 2 h, analysed by ^{1}H NMR spectroscopy, and filtered over a short column of silica gel (PE–EtOAc, 90:10). Enantiomeric ratios were determined using HPLC.

Conversion: 29%; **A**/**B** = 01:99, er (**10A**) = n.d., er (**10B**) = 99:01 (Chiralpak IC, flow rate 0.5 mL/min, 0.2% *i*-PrOH–99.8% heptane).

Acknowledgment

We gratefully acknowledge the Fonds der Chemischen Industrie (scholarship to D.B.), the Ministry of Innovation, Science, and Research of the German federal state of North Rhine-Westphalia, the Heinrich-Heine-Universität Düsseldorf, and the Forschungszentrum Jülich GmbH for their generous support of our projects. Furthermore, we thank the analytical departments of the Forschungszentrum Jülich as well as Marvin Lübcke, Monika Gehsing, Rainer Goldbaum, Birgit Henßen, Erik Kranz, Vera Ophoven, and Bea Paschold for their ongoing support.

Supporting Information for this article is available online at http://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00000084.

References

(1) Diels, O.; Alder, K. *Justus Liebigs Ann. Chem.* **1928**, *460*, 98.

(2) (a) Oppolzer, W. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, **1991**, 315–399. (b) Evans, D. A.; Johnson, J. S. In *Comprehensive Asymmetric Catalysis I–III*; Vol. 3; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: New York, **1999**, 1177–1235.

(3) (a) Du, H.; Ding, K. In *Handbook of Cyclization Reactions*; Vol. 1; Ma, S., Ed.; Wiley-VCH: Weinheim, **2010**, 1–57. (b) Reymond, S. B.; Cossy, J. *Chem. Rev.* **2008**, *108*, 5359. (c) Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007. (d) Corey, E. J. *Angew. Chem. Int. Ed.* **2002**, *41*, 1650. (e) Sauer, J. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 211. (f) Sauer, J. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 16. (g) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779. (h) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem. Int. Ed.* **2002**, *41*, 1668. (i) Maddaluno, J. *Synlett* **2006**, 2534. (j) Funel, J.-A.; Abele, S. *Angew. Chem. Int. Ed.* **2013**, *52*, 3822. (k) Nawrat, C. C.; Moody, C. J. *Angew. Chem. Int. Ed.* **2014**, *53*, 2056.

(4) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1990**, *112*, 3949.

(5) Mikami, K.; Terada, M.; Motoyama, Y.; Nakai, T. *Tetrahedron: Asymmetry* **1991**, *2*, 643.

(6) (a) White, J. D.; Choi, Y. *Org. Lett.* **2000**, *2*, 2373. (b) White, J. D.; Choi, Y. *Helv. Chim. Acta* **2002**, *85*, 4306. (c) Breuning, M.; Corey, E. J. *Org. Lett.* **2001**, *3*, 1559. (d) Motoyama, Y.; Terada, M.; Mikami, K. *Synlett* **1995**, 967. (e) Quitschalle, M.; Christmann, M.; Bhatt, U.; Kalesse, M. *Tetrahedron Lett.* **2001**, *42*, 1263.

(7) Mikami, K.; Motoyama, Y.; Terada, M. *J. Am. Chem. Soc.* **1994**, *116*, 2812.

(8) (a) Holenstein, J. E.; Stoessl, A. *J. Phytopathol.* **1983**, *108*, 143. (b) Suemitsu, R.; Horiuchi, K.; Kubota, M.; Okamatsu, T. *Phytochemistry* **1990**, *29*, 1509. (c) Okamura, N.; Haraguchi, H.; Hashimoto, K.; Yagi, A. *Phytochemistry* **1993**, *34*, 1005. (d) Haraguchi, H.; Abo, T.; Fukuda, A.; Okamura, N.; Yagi, A. *Phytochemistry* **1996**, *43*, 989. (e) Zheng, C.-J.; Shao, C.-L.; Guo, Z.-Y.; Chen, J.-F.; Deng, D.-S.; Yang, K.-L.; Chen, Y.-Y.; Fu, X.-M.; She, Z.-G.; Lin, Y.-C.; Wang, C.-Y. *J. Nat. Prod.* **2012**, *75*, 189. (f) Debbab, A.; Aly, A. H.; Edrada-Ebel, R.; Wray, V.; Pretsch, A.; Pescitelli, G.; Kurtan, T.; Proksch, P. *Eur. J. Org. Chem.* **2012**, 1351. (g) Kanamaru, S.; Honma, M.; Murakami, T.; Tsushima, T.; Kudo, S.; Tanaka, K.; Nihei, K.-I.; Nehira, T.; Hashimoto, M. *Chirality* **2012**, *24*, 137. (h) Stoessl, A. *Can. J. Chem.* **1969**, *47*, 777. (i) Pretsch, A.; Proksch, P.; Debbab, A. WO2010135759 A1, **2010**.

(9) (a) Foulgoc, L.; Sissouma, D.; Evain, M.; Collet, S.; Guingant, A. *Synlett* **2012**, *23*, 768. (b) Krohn, K.; Tolkiehn, K.; Lehne, V.; Schmalle, H. W.; Grutzmacher, H. F. *Liebigs Ann. Chem.* **1985**, 1311. (c) Krohn, K.; Markus, H.; Kraemer, H. P.; Frank, W. *Liebigs Ann. Chem.* **1988**, 1033. (d) Kelly, T. R.; Montury, M. *Tetrahedron Lett.* **1978**, 4309.

(10) (a) Posner, G. H.; Dai, H.; Bull, D. S.; Lee, J.-K.; Eydoux, F.; Ishihara, Y.; Welsh, W.; Pryor, N.; Petr, S. *J. Org. Chem.* **1996**, *61*, 671. (b) Nicolaou, K. C.; Vassilikogiannakis, G.; Mägerlein, W.; Kranich, R. *Chem. Eur. J.* **2001**, *7*, 5359. (c) Nicolaou, K. C.; Vassilikogiannakis, G.; Mägerlein, W.; Kranich, R. *Angew. Chem. Int. Ed.* **2001**, *40*, 2482.

(11) (a) Kelly, T. R. *Tetrahedron Lett.* **1978**, 1387. (b) Trost, B. M.; Ippen, J.; Vladuchick, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 8116. (c) Kelly, T. R.; Montury, M. *Tetrahedron Lett.* **1978**, 4311. (d) Nicolaou, K. C.; Becker, J.; Lim, Y. H.; Lemire, A.; Neubauer, T.; Montero, A. *J. Am. Chem. Soc.* **2009**, *131*, 14812. (e) Kelly, T. R.; Whiting, A.; Chandrakumar, N. S. *J. Am. Chem. Soc.* **1986**, *108*, 3510. (f) Boeckman, R. K.; Dolak, T. M.; Culos, K. O. *J. Am. Chem. Soc.* **1978**, *100*, 7098. (g) Hayden, A. E.; Paton, R. S.; Becker, J.; Lim, Y. H.; Nicolaou, K. C.; Houk, K. N. *J. Org. Chem.* **2010**, *75*, 922. (h) Boisvert, L.; Brassard, P. *J. Org. Chem.* **1988**, *53*, 4052. (i) Tietze, L. F.; Güntner, C.; Gericke, K. M.; Schuberth, I.; Bunkoczi, G. *Eur. J. Org. Chem.* **2005**, 2459.

(12) Ryu, D. H.; Zhou, G.; Corey, E. J. *J. Am. Chem. Soc.* **2004**, *126*, 4800.

(13) CCDC 1000648 contains the crystallographic data for **6A**. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44(1223)336033; E-mail: deposit@ccdc.cam.ac.uk.

(14) (a) Mikami, K.; Terada, M.; Matsumoto, Y.; Tanaka, M.; Nakamura, Y. *Micropor. Mesopor. Mater.* **1998**, *21*, 461. (b) Terada, M.; Matsumoto, Y.; Nakamura, Y.; Mikami, K. *Inorg. Chim. Acta* **1999**, *296*, 267.

