Intramolecular Heck Reactions for the Synthesis of the Novel Antibiotic Mensacarcin: Investigation of Catalytic, Electronic and Conjugative Effects in the Preparation of the Hexahydroanthracene Core

Lutz F. Tietze,*[a] Scott G. Stewart,[a] and Marta E. Polomska[a]

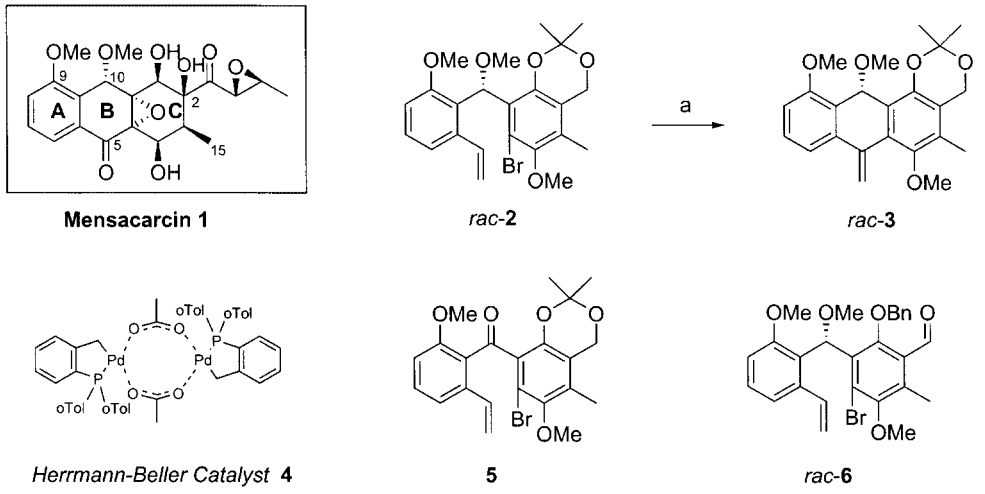
Keywords: Anthracenes / Antibiotics / Aromatic substitution / Heck reaction / Palladium

The intramolecular Heck reaction of the three complex diphenyl substrates *rac*-**2**, **5** and *rac*-**6**, containing substituents with different electronic and conjugative properties, were examined. The Pd compounds $[Pd_2(dba)_3]/[(tBu)_3PH]BF_4$, $[Pd_2(OAc)_2\{P(o\text{-}Tol)_3\}_2]$ (**4**), $[PdCl_2(PPh_3)_2]$ and $Pd(OAc)_2$ were used as catalysts.

Introduction

Mensacarcin (**1**) is a novel polyfunctionalised hexahydroanthracene isolated from a strain of *Streptomyces* (Gö C4/4) which shows cytostatic and cytotoxic activity comparable to doxorubicin, another anticancer agent currently used in the treatment of malignant lymphomas and leukemias.[1] In our investigations towards the synthesis of this novel anticancer agent we wanted to use an intramolecular Heck transformation of an appropriately substituted diphenylcarbinol. Thus, for the synthesis of the core structure of **1** we employed a Pd^0-catalysed transformation of *rac*-**2** as the key step with the Herrmann–Beller catalyst **4**. Unfortunately, this reaction led to the tricycle *rac*-**3** in only 24% yield (Scheme 1).

The Heck reaction has been utilized in the synthesis of a wide variety of natural products and analogues.[2] This coupling reaction, first observed in 1968, has recently advanced with the discovery of novel catalysts and catalytic systems.[3] Exploring the potential of these systems is an important aspect in the refining of synthetic organic processes. Previous studies of both inter- and intramolecular Heck reactions have revealed that matching the appropriate catalytic conditions with the electronic properties of the aryl or vinyl halide substrate is essential. Initial development of new catalysts and catalytic methodology by the



Scheme 1. Mensacarcin (**1**), synthesis of tetrahydroanthracene *rac*-**3** and structures of substrates *rac*-**2**, **5** and *rac*-**6**: (a) nBu_4NOAc, DMF/CH_3CN/H_2O, 60 °C then HB cat **4**, 120 °C, 4 h, 24%.

[a] Institut für Organische und Biomolekulare Chemie, Georg-August Universität,
Tammannstraße 2, 37077 Göttingen
E-mail: ltietze@gwdg.de
Fax: +49-551-399-476

  DOI: 10.1002/ejoc.200400786

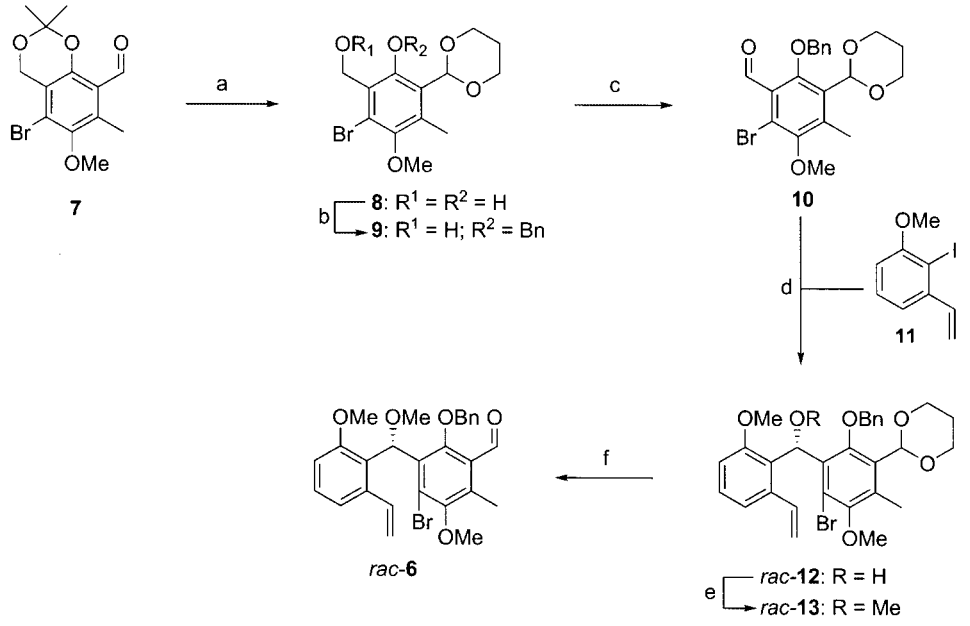
groups of Milstein (bulky, electron-rich chelating bisphosphanes),[4] Herrmann and Beller (palladacycles),[5] Reetz (tetraphenylphosphonium salts)[6] and Beller (phosphites)[7] has provided a variety of conditions for carrying out high yielding Heck transformations. Generally, from these studies, electron-poor aryl halides were considered essential for the oxidative addition to the Pd^0 species. More recently, Fu et al. have developed systems {$[Pd_2(dba)_3]$, $[(tBu)_3PH]BF_4$ and Cy_2NMe} that catalyse Heck couplings using less-reactive electron-rich aryl chlorides and bromides as substrates.[8] Furthermore, the group of Lautens has reported on intramolecular Heck reactions involving dihydronaphthalene substrates with a variety of electronically diverse aryl bromides.[9]

Here we describe our investigations on the importance of matching certain catalytic parameters with the electronic nature of the aryl bromide being employed as starting material. With the intention of optimising a synthesis of tetrahydroanthracene compounds[10] we prepared three substrates − *rac*-**2**, **5** and *rac*-**6**. Importantly, each of these compounds contains a contrasting substitution pattern which was tested in a Pd^0-catalysed transformation using four different types of catalysts.

Results and Discussion

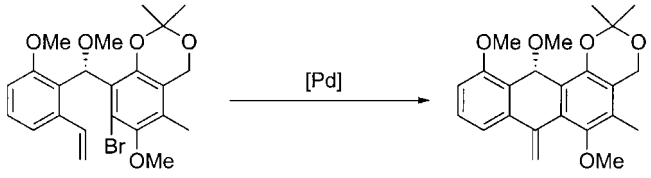
The substrates *rac*-**2** and **5** were synthesised using the procedures reported previously,[1] whereas *rac*-**6** was prepared as shown in Scheme 2 from **7**, which was treated with acetic acid to remove the acetonide group and then with propanediol in order to protect the aldehyde moiety. The resulting acetal **8** was subsequently benzylated at the phenolic position to give **9,** and the remaining hydroxyl group oxidised to furnish compound **10** in 65% yield over two steps. For the attachment of the left fragment aryl ring, the iodobenzene **11** was treated with *n*BuLi to generate the corresponding aryllithium species, followed by addition of the aldehyde **10** to give the diphenylcarbinol *rac*-**12** in a moderate yield of 39%. Additional treatment of this latter compound with KH and MeI afforded the methyl ether *rac*-**13** in 91% yield. The desired substrate for the Heck reaction *rac*-**6** was obtained in 71% yield by deprotection of the acetal moiety in *rac*-**13** using PPTS in acetone/water.

With the three substrates *rac*-**2**, **5** and *rac*-**6** in hand, a variety of palladium catalysts and reaction conditions were investigated to provide their corresponding anthracene-type compounds. Substrate *rac*-**2**, which contains a highly electron-rich aryl bromide moiety, was initially tested with the two first-generation catalysts $Pd(OAc)_2$ and $[PdCl_2(PPh_3)_2]$.[11] After 5 h at 90 °C both reactions afforded the product tetrahydroanthracene (*rac*-**3**), although only in poor yields (11% and 6%, respectively; entries 1 and 2, Table 1). Interestingly, large amounts of starting material remained, which prompted the screening of second-generation catalysts that can withstand higher temperatures and/or give better TONs. Thus, we next performed Heck reactions using the palladacycle developed by Herrmann and Beller. However, even a catalyst loading of 20 mol-% $[Pd_2(OAc)_2\{P(o\text{-Tol})_3\}_2]$ (**4**) furnished only a low yield (27%) of *rac*-**3** after 5 h at 120 °C, with 42% of starting material remaining (entry 3, Table 1). Longer reaction times



Scheme 2. Synthesis of diphenylcarbinol *rac*-**6**: (a) i) AcOH, 60 °C, 4 h, 66%; ii) 1,3-propanediol, Amberlyst 15 H^+, C_6H_6, reflux, 5 h, 98%; (b) BnBr, K_2CO_3, $CHCl_3$/MeOH, 40 °C, 12 h, 80%; (c) Dess–Martin periodinane, CH_2Cl_2, 1 h, 81%; (d) iodobenzene **11**, *n*BuLi, THF, –78 °C, 20 min then **10**, THF, –78 °C, 20 min, 20 °C, 39%; (e) KH, THF, 0 °C, 40 min then MeI, 20 °C, 1 h, 91%; (f) PPTS, H_2O/acetone, reflux, 12 h, 71%.

Table 1. Intramolecular Heck reaction with *rac*-**2**.



rac-**2** *rac*-**3**

Entry	Catalyst/phosphane	Base	Solvent	Reaction time [h]	Temp. [°C]	Yield of *rac*-3 (recovered substrate) [%]
1	10 mol-% $[PdCl_2(PPh_3)_2]$	NaOAc	MeCN	5	90	6 (58)
2[a]	10 mol-% $Pd(OAc)_2$	nBu$_4$NOAc K_2CO_3	DMF	5	90	11 (40)
3	20 mol-% HB cat[b]	nBu$_4$NOAc	DMF/MeCN/H_2O	5	120	27 (42)
4	20 mol-% HB cat[b]	nBu$_4$NOAc	DMF/MeCN/H_2O	20	120	33 (18)
5	3 mol-% $[Pd_2(dba)_3]$/ 6 mol-% P(tBu)$_3$	Cy_2NMe	dioxane	5	120	94 (5)
6	3 mol-% $[Pd_2(dba)_3]$/ 6 mol-% HP(tBu)$_3$BF$_4$	Cy_2NMe	dioxane	5	120	92 (5)
7	3 mol-% $[Pd_2(dba)_3]$/ 6 mol-% HP(tBu)$_3$BF$_4$	Cy_2NMe	dioxane	20	120	78 (2)

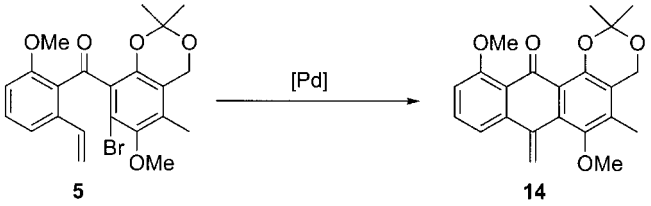
[a] The Jeffery system requires K_2CO_3 and no phosphane.[13] [b] Herrmann–Beller catalyst *trans*-{di(μ-acetato)bis[*ortho*-(di-*ortho*-tolylphosphanyl)benzyl]dipalladium(II)} (**4**).

(entry 4, Table 1) led to decomposition of both the starting material and the product. On switching to the more electron-rich palladium complex $[Pd_2(dba)_3]$/P(tBu)$_3$ we discovered that this system is very effective for the similarly electron-rich substrate *rac*-**2**, especially in the presence of the bulky tertiary amine Cy_2NMe.[12] Using a moderate catalyst loading (3 mol-% Pd) and 6 mol-% of phosphane [1:1 ratio of Pd to P(tBu)$_3$], with Cy_2NMe as the base, led to the desired product *rac*-**3** in an excellent 94% yield (entry 5, Table 1). The more stable and practical trialkylphosphonium salt [(tBu)$_3$PH]BF$_4$ gave a similar yield of 92%. The optimised temperature for this reaction was 110–120 °C and, as in the papers of Fu et al., dioxane was the solvent of choice. Longer reaction times once again resulted in decomposition of the tricyclic product (entry 7, Table 1), while at ambient temperature the catalytic system is completely unreactive.

The second olefin examined, compound **5**, contains a carbonyl group *ortho* to the bromine atom, which lowers the electron-rich nature of the aromatic ring and flattens the molecule through conjugation. We found that the carbonyl functionality causes a noticeable alteration of the yield in the Heck reaction. The yield of the transformation when using $Pd(OAc)_2$ and K_2CO_3 as a base at 90 °C increased to 22%, although prolongation of the reaction time resulted in decomposition of both starting material and product (entries 2 and 3, Table 2). Reaction with the Herrmann–Beller palladacycle **4** at 90 °C over 5 h gave a 59% yield of the anthracenone **14** (entry 4, Table 2), which is more than double that obtained for the cyclisation of *rac*-**2**. However, to complete the reaction a high catalyst loading (40 mol-% Pd) was still necessary. A further improvement of the yield to 73% was obtained when the reaction was carried out at 120 °C (entry 5, Table 2). As previously, longer reaction times resulted in decomposition of both product and starting material. Using $Pd_2(dba)_3$ in the presence of the electron rich phosphane ligand tBu$_3$P resulted in a still slightly higher yield (78%) of **14** than when using catalyst **4**, but more importantly this yield was slightly lower when compared with compound *rac*-**2** (entry 7, Table 2). This result suggested that the oxidative addition in **5** occurs less rapidly with an electron rich palladium complex. Extended reaction times at these temperatures again resulted in a decomposition of substrate and product and at ambient temperature no reaction occurred (entry 8, Table 2).

The final substrate, *rac*-**6**, which contains a *para*-aldehyde moiety, was considered to contain the least electron-rich aryl ring of the three substrates. The introduction of the aldehyde moiety led to an increased reactivity for $Pd(OAc)_2$ and the Herrmann–Beller catalyst (entries 1–4, Table 3). The best result (entry 3, Table 3) was obtained with the HB catalyst **4** at 120 °C for 5 h, and afforded the desired tricyclic product *rac*-**15** in 82% yield. The Heck reaction of substrate *rac*-**6** in the presence of the electron-rich tBu$_3$P ligand also led to *rac*-**15** in a reasonable but slightly lower yield than with the substrates *rac*-**2** and **5**. These new sets of results substantiate the theory that the electronic properties of the substrate must be compatible with the catalyst, although the electron-rich system Pd^0/tBu$_3$P still works quite well with electron-poor substrates.

Table 2. Intramolecular Heck reaction with **5**.

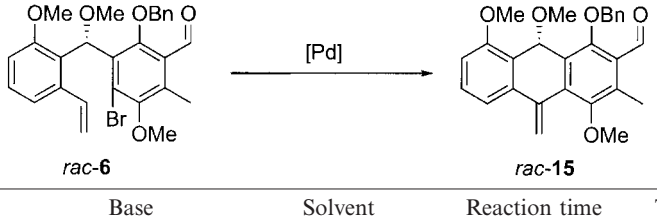


5 **14**

Entry	Catalyst/phosphane	Base	Solvent	Reaction time [h]	Temp. [°C]	Yield of **14** (recovered substrate) [%]
1	10 mol-% $[PdCl_2(PPh_3)_2]$	NaOAc	MeCN	5	90	7 (70)
2[a]	10 mol-% $Pd(OAc)_2$	nBu_4NOAc/K_2CO_3	DMF	5	90	22 (61)
3[a]	10 mol-% $Pd(OAc)_2$	nBu_4NOAc/K_2CO_3	DMF	20	90	0 (25)
4	20 mol-% HB cat[b]	nBu_4NOAc	$DMF/MeCN/H_2O$	5	90	59 (20)
5	20 mol-% HB cat[b]	nBu_4NOAc	$DMF/MeCN/H_2O$	5	120	73 (6)
6	20 mol-% HB cat[b]	nBu_4NOAc	$DMF/MeCN/H_2O$	20	120	31 (6)
7	3 mol-% $[Pd_2(dba)_3]$/ 6 mol-% $HP(tBu)_3BF_4$	Cy_2NMe	dioxane	5	120	78 (5)
8	3 mol-% $[Pd_2(dba)_3]$/ 6 mol-% $HP(tBu)_3BF_4$	Cy_2NMe	dioxane	5	20	0 (93)

[a] The Jeffery system requires K_2CO_3 and no phosphane. [b] Herrmann–Beller catalyst *trans*-{di(μ-acetato)bis[*ortho*-(di-*ortho*-tolylphosphanyl)benzyl}dipalladium(II)] (**4**).

Table 3. Intramolecular Heck reaction with *rac*-**6**.



rac-**6** *rac*-**15**

Entry	Catalyst/phosphane	Base	Solvent	Reaction time [h]	Temp. [°C]	Yield of *rac*-**15** (recovered substrate) [%]
1	10 mol-% $[PdCl_2(PPh_3)_2]$	NaOAc	MeCN	5	90	12 (48)
2[a]	10 mol-% $Pd(OAc)_2$	$nBu_4NOAc\ K_2CO_3$	DMF	5	90	34 (52)
3	20 mol-% HB cat[b]	nBu_4NOAc	$DMF/MeCN/H_2O$	5	120	82 (3)
4	20 mol-% HB cat[b]	nBu_4NOAc	$DMF/MeCN/H_2O$	20	120	64 (—)
5	3 mol-% $[Pd_2(dba)_3]$/ 6 mol-% $HP(tBu)_3BF_4$	Cy_2NMe	dioxane	5	120	77 (18)
6	3 mol-% $[Pd_2(dba)_3]$/ 6 mol-% $HP(tBu)_3BF_4$	Cy_2NMe	dioxane	20	120	67 (4)

[a] The Jeffery system requires K_2CO_3 and no phosphane. [b] Herrmann–Beller catalyst *trans*-{di(μ-acetato)-bis[*ortho*-(di-*ortho*-tolylphosphanyl)benzyl]dipalladium(II)} (**4**).

Conclusions

In summary, we have developed efficient pathways to dihydroanthracenes through an intramolecular Heck approach. When carrying out the transformation with *rac*-**2** the combination $[Pd_2(dba)_3]/P(tBu)_3/Cy_2NMe$ has been shown to be most effective by providing the desired product *rac*-**3** in an excellent yield of 94%. In contrast, $Pd(OAc)_2$ and the Herrmann–Beller catalyst led to *rac*-**13** in only 11% and 33% yield, respectively. Introducing a carbonyl moiety into the substrate, as in olefin **5**, increased the conversion to the anthracene-type compound when using the so-called first-generation catalysts, and 73% with the Herrmann–Beller catalyst **4**. Employing the catalyst $[Pd_2(dba)_3]/P(tBu)_3/Cy_2NMe$ in the reactions of substrates **5** and *rac*-**6** resulted in a decrease of overall yield when compared to the reaction of the more electron-rich *rac*-**2**. Hence, this work demonstrates how a modification of a substrate by changing the

electronic nature of the substituents influences the Heck reaction. Furthermore, we observed that there is a pattern evolving between matching the electronic nature of the catalytic system and substrate.

Experimental Section

General: All reactions were performed in flame-dried glassware under an argon atmosphere. Solvents were dried and purified according to the method defined by Perin and Armarego.[14] TLC chromatography was performed on precoated aluminium silica gel SIL G/UV254 plates (Macherey, Nagel Co.), and silica gel 32–63 (0.032–0.064 mm; Macherey, Nagel Co.) was used for column chromatography. Melting points: Mettler FP61. IR: Bruker IFS25. UV/Vis: Perkin–Elmer Lambda 9. NMR: Varian VXR-200 (200 MHz, ^{1}H), Bruker AM-300 (300 MHz, 75 MHz, for ^{1}H and ^{13}C, respectively). For ^{1}H and ^{13}C, $CDCl_3$ and C_6D_6 were used as solvents. Chemical shift are reported on a δ scale. MS: Varian MAT 731. HRMS was performed using a modified peak matching technique, error ± 2 ppm, with a resolution of about 10 000. Elemental analysis: Mikroanalytisches Labor des Institutes für Organische und Biomolekulare Chemie der Universität Göttingen.

3-Bromo-6-(1,3-dioxan-2-yl)-2-hydroxymethyl-4-methoxy-5-methylphenol (8). 4-Bromo-2-hydroxy-3-hydroxymethyl-5-methoxy-6-methylbenzaldehyde: A magnetically stirred solution of aldehyde **7** (1.4 g, 4.44 mmol) in acetic acid (60 mL of 40% solution) was heated to 60 °C for 4 h. The resulting mixture was cooled to 20 °C, diluted with Et_2O (200 mL), washed with $NaHCO_3$ (5 × 30 mL saturated solution), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a yellow solid. Subjection of this material to flash chromatography (9:1 pentane/EtOAc) and concentration of the appropriate fractions afforded the desired product (803 mg, 2.92 mmol, 66%) as a colourless solid; m.p. 131 °C (recrystallised from hexane/EtOAc); R_f = 0.4. UV/Vis (CH_3CN): λ_{max} (lg ε) = 194.5 nm (4.2829), 277.0 (4.1471), 355.5 (3.6208). IR (KBr): $\tilde{\nu}$ = 1646 cm^{-1}, 1404. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.22 (s, 1 H, OH), 2.59 (s, 3 H, CH_3), 3.77 (s, 3 H, OCH_3), 4.95 (s, 2 H, CH_2OH), 10.34 (s, 1 H, CHO) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 11.2, 59.9, 60.4, 117.6, 128.1, 119.6, 130.9, 134.5, 158.2, 195.2 ppm. MS (EI, 70 eV): *m*/*z* (%) = 276.1 (60), 274.1 (58) $[M]^+$, 258.0 (100), 256.0 (98) $[M - H_2O]^+$. $C_{10}H_{11}BrO_4$ (275.11). HRMS: calcd. 273.9841; found 273.9841. **3-Bromo-6-(1,3-dioxan-2-yl)-2-hydroxymethyl-4-methoxy-5-methylphenol (8):** A magnetically stirred solution of the benzaldehyde described above (800 mg, 2.90 mmol) and 1,3-propanediol (634 μL, 8.76 mmol) in benzene (80 mL) was treated in one portion with Amberlyst 15™ (cat.) at 20 °C. The resulting mixture was heated to reflux for 5 h in a Dean–Stark apparatus. After cooling, the mixture was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting white solid was recrystallised (EtOAc/hexane) to afford acetal **8** (955 mg, 2.86 mmol, 98%) as a colourless solid; m.p. 128 °C (recrystallised from hexane/EtOAc); R_f = 0.2 (9:1 pentane/EtOAc). UV/Vis (CH_3CN): λ_{max} (lg ε) = 204.5 nm (4.5580), 286.0 (3.1993). IR (KBr): $\tilde{\nu}$ = 3528 cm^{-1}, 2873, 1449. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.18–1.48 (m, 1 H, 5-H), 2.16–2.27 (m, 1 H, 5-H), 2.84 (br. s, 1 H, OH), 2.22 (s, 3 H, CH_3), 3.90 (s, 3 H, OCH_3), 3.84–3.97 (m, 4 H, 4-H/6-H), 4.19–4.27 (m, 1 H, 2-H), 4.81 (s, 2 H, CH_2); 5.93 (s, 1 H, 2-H), 9.01 (s, 1 H, OH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.7, 25.7, 60.4, 66.0, 67.7, 98.8, 122.5, 127.6, 128.2, 128.6, 134.7, 136.9, 152.9 ppm. MS (EI, 70 eV): *m*/*z* (%) = 333.1 (5) $[M]^+$, 316.1 (20) $[M - OH]^+$, 91.1 (100). $C_{13}H_{17}BrO_5$ (333.18). HRMS: calcd. 333.1751; found 333.1751.

(2-Benzyloxy-6-bromo-3-(1,3-dioxan-2-yl)-5-methoxy-4-methylphenyl)methanol (9): A magnetically stirred solution of acetal **8** (1.10 g, 3.30 mmol) and K_2CO_3 (1.83 g, 13.20 mmol) in $CHCl_3$/MeOH (30:15 mL) was heated to 40 °C for 10 min. The resulting mixture was then treated with benzyl bromide (470 μL, 3.96 mmol) and stirring continued at this temperature for a further 12 h. After cooling to 20 °C, the mixture was diluted with CH_2Cl_2 (60 mL), washed with H_2O (2 × 10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting white solid was recrystallised (EtOAc/hexane) to afford alcohol **9** (1.12 g, 2.64 mmol, 80%) as a white solid; m.p. 148 °C (recrystallised from hexane/EtOAc); R_f = 0.4 (9:1 pentane/EtOAc). UV/Vis (CH_3CN): λ_{max} (lg ε) = 205.0 nm (4.7277), 286.8 (3.3296). IR (KBr): $\tilde{\nu}$ = 3489 cm^{-1}, 2852, 1448. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20–1.24 (m, 1 H, 5-H), 2.16–2.27 (m, 1 H, 5-H), 2.25 (s, 3 H, CH_3), 3.85 (s, 3 H, OCH_3), 3.89–4.17 (m, 4 H, 4-H/6-H), 4.81 (s, 2 H, CH_2OH), 4.97 (s, 2 H, CH_2OPh), 5.93 (s, 1 H, 2-H), 7.41–7.55 (m, 5 H, Ph) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.7, 25.8, 60.2, 60.5, 67.8, 79.1, 98.8, 121.3, 127.7, 128.0, 128.4, 128.5, 128.7, 130.6, 132.6, 134.4, 136.6, 152.4, 153.0 ppm. MS (EI, 70 eV): *m*/*z* (%) = 424.1 (24), 422.1 (25) $[M]^+$, 394.1 (5), 392.1 (7) $[M - CH_2O]^+$, 318.1 (57), 316.1 (40) $[M - HOCH_2Ph]^+$. $C_{20}H_{23}BrO_5$ (423.30). HRMS: calcd. 422.0729; found 422.0729.

2-Benzyloxy-6-bromo-3-(1,3-dioxan-2-yl)-5-methoxy-4-methylbenzaldehyde (10): A magnetically stirred solution of alcohol **9** (625 mg, 1.48 mmol) in CH_2Cl_2 (60 mL) at 20 °C was treated with Dess–Martin periodinane (941 mg, 2.22 mmol). The resulting mixture was stirred for 1.5 h before being treated with $NaHCO_3$ (1 × 25 mL of a saturated solution) and $Na_2S_2O_3$ (1 × 25 mL of a 1 M solution). Stirring was continued until the cloudy solution became clear (ca. 1 h). The resulting mixture was transferred to a separating funnel and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic fractions were subjected to flash chromatography (9:1 pentane/EtOAc) and concentration of the appropriate fractions afforded benzaldehyde **10** (505 mg, 1.20 mmol, 81%) as a white solid; m.p. 123 °C (recrystallised from hexane/EtOAc); R_f = 0.7. UV/Vis (CH_3CN): λ_{max} (lg ε) = 209.0 nm (4.4501), 264.0 (3.8917). IR (KBr): $\tilde{\nu}$ = 2947 cm^{-1}, 2846, 1703, 1573. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.18–1.34 (m, 1 H, 5-H), 2.16–2.27 (m, 1 H, 5-H), 2.57 (s, 3 H, CH_3), 3.73 (s, 3 H, OCH_3), 3.66–3.78 (m, 4 H, 4-H/6-H), 4.85 (s, 2 H, CH_2OPh), 5.93 (s, 1 H, 2-H), 7.31–7.45 (m, 5 H, Ph), 10.24 (s, 1 H, CHO) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 14.4, 25.7, 60.3, 60.9, 67.8, 79.8, 98.0, 109.3, 121.1, 126.8, 129.0, 130.2, 131.7, 132.5, 136.1, 140.9, 146.2, 153.4, 154.8, 190.3 ppm. MS (EI, 70 eV): *m*/*z* (%) = 422.0 (15), 420.0 (13) $[M]^+$, 394.1 (10), 392.1 (9) $[M - CH_2O]^+$, 316.1 (65), 314.1 (58) $[M - HOCH_2Ph]^+$. $C_{20}H_{21}BrO_5$ (421.28). HRMS: calcd. 420.0572; found 420.0572.

{2-Benzyloxy-6-bromo-3-(1,3-dioxan-2-yl)-5-methoxy-4-methylphenyl}-(2-methoxy-6-vinylphenyl)methanol (12): A magnetically stirred solution of iodobenzene **11** (251 mg, 0.97 mmol) in THF (10 mL) at –78 °C was treated dropwise with *n*BuLi (425 μL, 1.06 mmol, 2.5 M solution in hexane, 1.01 mmol). The resulting mixture was stirred at this temperature for 20 min before being treated with aldehyde **10** (277 mg, 0.88 mmol) in THF (5 mL). Stirring was continued at this temperature for 20 min, the solution warmed to 20 °C and quenched immediately with NH_4Cl (4 mL of a saturated aqueous solution). The resulting mixture was extracted with diethyl ether (3 × 10 mL), washed with brine (1 × 2 mL) and the combined organic fractions dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a clear yellow oil. Subjection of the resulting crude oil to flash chromatography (9:1 pentane/EtOAc) and concentration of the appropriate fractions afforded diphenylcarbinol **12** (190 mg, 0.34 mmol, 39%) as a colour-

less solid; R_f = 0.4. IR (KBr): $\tilde{\nu}$ = 3560 cm^{-1}, 2838, 1572. UV (CH_3CN): λ_{max} (lg ε) = 203.5 nm (4.6397), 292.0 (3.5932). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.20–1.24 (m, 1 H, 5′-H), 1.29–1.37 (m, 1 H, 5′-H), 2.60 (s, 3 H, CH_3), 3.52 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 3.62–3.82 (m, 2 H, 4′-H/6′-H), 4.01–4.21 (m, 2 H, 4′-H/6′-H), 4.41 (d, J = 12.0 Hz, 1 H, CH_2Ph), 4.81 (d, J = 12.0 Hz, 1 H, CH_2Ph), 5.15 (dd, J = 12.7, 1.6 Hz, 1 H, 2′′-H), 5.21 (dd, J = 12.7, 1.6 Hz, 1 H, 2′′-H), 5.45 (d, J = 7.2 Hz, 1 H, 1′-H), 5.93 (s, 1 H, 2′-H), 6.54 (d, J = 9.2 Hz, 1 H, 1′′-H), 6.64 (d, J = 8.2 Hz, 1 H, Ar-H), 6.95–7.09 (m, 3 H, Ar-H), 7.25–7.37 (m, 4 H, Ar-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 12.5, 14.1, 20.9, 25.8, 55.5, 55.8, 60.3, 67.4, 67.8, 99.1, 110.4, 111.4, 116.7, 119.9, 127.1, 127.6, 127.8, 127.9, 128.2, 128.3, 128.4, 130.6, 133.5, 135.2, 137.6, 138.6, 148.6, 154.6, 157.4 ppm. MS (EI, 70 eV): m/z (%) = 556.1 (5), 554.1 (4) $[M]^+$, 465.1 (43), 463.1 (42) $[M - C_7H_7]^+$, 417.1 (11), 415.1 (10). $C_{29}H_{31}BrO_6$ (555.46) HRMS: calcd. 554.1304; found 554.1304.

2-{(2-Benzyloxy-4-bromo-5-methoxy)-(3*RS*)-[methoxy-(2-methoxy-6-vinylphenyl)methyl]-6-methylphenyl}-1,3-dioxane (*rac*-13): A magnetically stirred solution of diphenylcarbinol **12** (150 mg, 0.27 mmol) in THF (5 mL) was treated in one portion with KH (22 mg, 0.54 mmol) at 0 °C. Stirring was continued for 40 min before the reaction mixture was treated dropwise with MeI (34 μL, 0.54 mmol). The ensuing solution was warmed to 20 °C and stirred for a further 1 h before being treated with water (2 mL) and extracted with diethyl ether (3 × 5 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a colourless solid. Subjection of this material to flash chromatography (19:1 pentane/EtOAc) and concentration of the appropriate fractions afforded methyl ether **13** (148 mg, 0.26 mmol, 91%) as a colourless oil; R_f = 0.2. IR (KBr): $\tilde{\nu}$ = 3543 cm^{-1}, 2812, 1589. UV (CH_3CN): λ_{max} (lg ε) = 209.0 nm (4.7395), 294.5 (3.4654). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.20–1.24 (m, 1 H, 5′-H), 1.29–1.37 (m, 1 H, 5′-H), 2.60 (s, 3 H, CH_3), 3.32 (s, 3 H, OCH_3), 3.59 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 3.62–3.82 (m, 2 H, 4′-H/6′-H), 4.01- 4.21 (m, 2 H, 4′-H/6′-H), 4.41 (d, J = 12.4 Hz, 1 H, CH_2Ph), 4.81 (d, J = 12.4 Hz, 1 H, CH_2Ph), 5.15 (dd, J = 12.4, 1.6 Hz, 1 H, 2′′-H), 5.21 (dd, J = 12.4, 1.6 Hz, 1 H, 2′′-H), 5.74 (s, 1 H, 2′-H), 6.25 (s, 1 H, 1′-H) 6.54 (d, J = 9.2 Hz, 1 H, 1′′-H), 6.64 (d, J = 8.2 Hz, 1 H, Ar-H), 6.95–7.09 (m, 3 H, Ar-H), 7.25–7.37 (m, 4 H, Ar-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.7, 25.7, 55.4, 55.8, 57.4, 60.0, 67.62, 67.64, 80.2, 80.79, 80.80, 98.8, 109.6, 113.4, 120.8, 126.1, 126.2, 127.1, 127.6, 127.9, 130.6, 131.2, 132.6, 133.6, 137.9, 138.6, 139.9, 152.8, 153.1, 157.2 ppm. MS (EI, 70 eV): m/z (%) = 570.3 (20), 568.2 (19) $[M]^+$, 479.2 (30), 477.2 (28), $[M - CH_2Ph]^+$, 447.2 (25), 445.2 (26), 91 (100). $C_{30}H_{33}BrO_6$ (569.48) HRMS: calcd. 568.1461; found 568.1461.

2-Benzyloxy-4-bromo-5-methoxy-(3*RS*)-[methoxy-(2-methoxy-6-vinylphenyl)methyl]-6-methylbenzaldehyde (*rac*-6): A magnetically stirred solution of acetal **13** (100 mg, 0.18 mmol) in a water/acetone mixture (2.5:5 mL) was treated in one portion with a few crystals of pyridinium *p*-toluenesulfonate at 20 °C. The resulting suspension was heated at reflux for 12 h before being extracted with diethyl ether (3 × 15 mL). The combined organic fractions were washed with brine (1 × 2 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a crude solid. Subjection of this material to flash chromatography (19:1 pentane/EtOAc) and concentration of the appropriate fractions afforded the corresponding aldehyde **6** (65 mg, 0.13 mmol, 71%) as a colourless solid; R_f = 0.3. IR (KBr): $\tilde{\nu}$ = 2941 cm^{-1}, 1710, 1597. UV (CH_3CN): λ_{max} (lg ε) = 205.0 nm (4.6429), 292.0 (4.0995). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.63 (s, 3 H, CH_3), 3.34 (s, 3 H, OCH_3), 3.56 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 4.03 (d, J = 11.2 Hz, 1 H, CH_2Ph), 4.55 (d, J = 11.2 Hz, 1 H, CH_2Ph), 5.16 (dd, J = 12.4, 1.6 Hz, 1 H, 2′′-H), 5.41 (dd, J = 12.4, 1.6 Hz, 1 H, 2′′-H), 6.25 (s, 1 H, 1′-H), 6.89 (d, J = 8.2 Hz, 1 H, Ar-H), 7.10–7.25 (m, 3 H, Ar-H), 7.25–7.37 (m, 4 H, Ar-H), 7.66 (d, J = 9.2 Hz, 1 H, 1′′-H), 10.16 (s, 1 H, CHO) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.1, 55.3, 55.8, 59.2, 65.0, 80.4, 109.7, 118.6, 119.7, 124.2, 127.6, 128.6, 128.9, 129.1, 129.5, 129.9, 130.1, 130.2, 130.4, 136.4, 136.6, 137.8, 141.3, 152.3, 158.5, 158.2, 194.1 ppm. MS (EI, 70 eV): m/z (%) = 512.2 (38), 510.2 (42) $[M]^+$, 433.1 (12) $[M - Br]^+$. $C_{27}H_{27}BrO_5$ (511.40). HRMS: calcd. 510.1042; found 510.1042.

6,11,12-Trimethoxy-2,2,5-trimethyl-7-methylene-7,12-dihydro-4*H*-1,3-dioxabenzo[*a*]anthracene (*rac*-3). Procedure I: A magnetically stirred solution of *rac*-**2** (70 mg, 0.15 mmol) and nBu$_4$NOAc (46 mg, 0.15 mmol), in a degassed mixture of DMF/CH_3CN/H_2O (2 mL of a 5:5:1 solution) at 60 °C was treated in one portion with *trans*-{di(μ-acetato)-bis[*ortho*-(di-*ortho*-tolylphosphanyl)benzyl]dipalladium(II)} (**4**; 14 mg, 0.015 mmol). The resulting suspension was heated to 120 °C for 4 h with stirring. The ensuing brown mixture was cooled, diluted with diethyl ether (20 mL) and washed with water (3 × 3 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a crude brown solid. Subjection of this material to flash chromatography (19:1 pentane/EtOAc) and concentration of the appropriate fractions afforded the dihydroanthracene *rac*-**3** (14 mg, 0.004 mmol, 24%) as a yellow solid along with starting material *rac*-**2** (40 mg, 0.086 mmol, 57%). R_f = 0.2. UV/Vis: λ_{max} (lg ε) = 201.5 (4.4756), 290.5 (4.5398), 306.0 (3.5456) nm. IR (KBr): $\tilde{\nu}$ = 2929, 1456 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.57 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 2.11 (s, 3 H, CH_3), 3.30 (s, 3 H, OCH_3), 3.57 (s, 3 H, OCH_3), 9.92 (s, 3 H, OCH_3), 4.77 (s, 2 H, 4-H), 5.95 (d, J = 1.2 Hz, 1 H, 1′-H), 6.16 (s, 1 H, 12-H), 6.34 (d, J = 1.2 Hz, 1 H, 1′-H), 6.85–6.89 (m, 1 H, Ar-H), 7.26–7.30 (m, 2 H, Ar-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.7, 24.5, 25.0, 55.7, 56.3, 59.7, 60.2, 64.0, 98.9, 109.5, 116.6, 117.2, 117.8, 122.2, 123.4, 127.0, 128.8, 129.2, 137.9, 140.8, 145.1, 148.9, 157.0 ppm. MS (EI, 70 eV): m/z (%) = 382 (32) $[M^+]$, 324 (100) $[M - C_3H_6O]^+$, 293 (86) $[M - C_3H_6O - CH_3O]^+$, 278 (65) $[M - C_3H_6O - CH_3O - CH_3]^+$, 265 (29). HRMS: calcd. for $C_{23}H_{26}O_5$: 382.1780; found 382.1780. **Procedure II:** Cy_2NMe (12.5 μL, 59.3 μmol) in degassed dioxane (0.5 mL) and P(tBu)$_3$ (5.2 μL, 2.58 μmol of a 0.5 M solution in hexane) were added, in a glovebox, to a magnetically stirred mixture of [Pd_2(dba)$_3$] (1.18 mg, 1.29 μmol) and *rac*-**2** (20 mg, 43.0 μmol) at 20 °C. The resulting suspension was heated to 120 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (19:1 pentane/EtOAc) of the crude product afforded dihydroanthracene *rac*-**3** (15.5 mg, 40.5 μmol, 94%) as a yellow solid along with starting material *rac*-**2** (1.1 mg, 2.4 μmol, 5%). **Procedure III:** [Pd_2(dba)$_3$] (1.45 mg, 1.62 μmol) and HP(tBu)$_3$$BF_4$ (0.94 mg, 3.23 μmol) were transferred into a flask containing a magnetic stirrer bar, which was then evacuated and refilled with argon. A solution of *rac*-**2** (25 mg, 53.9 μmol) and Cy_2NMe (12.5 μL, 59.3 μmol) in degassed dioxane (0.5 mL) was then added in one portion at 20 °C. The resulting suspension was heated to 120 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (19:1 pentane/EtOAc) of the crude product afforded dihydroanthracene *rac*-**3** (18.8 mg, 49.3 μmol, 92%) as a yellow solid along with starting material *rac*-**2** (1.5 mg, 3.2 μmol, 6%). **Procedure IV:** A magnetically stirred solution of *rac*-**2** (25 mg, 53.9 μmol), nBu$_4$NOAc (29.5 mg, 107.8 μmol) and K_2CO_3 (14.9 mg, 107.8 μmol) in degassed DMF (0.5 mL) at 20 °C was treated with $Pd(OAc)_2$ (1.21 mg, 5.39 μmol). The resulting suspension was heated to 90 °C for 5 h with stirring.

Work up was performed as described previously. Flash chromatography (19:1 pentane/EtOAc) of the crude product afforded dihydroanthracene *rac*-**3** (2.3 mg, 5.9 μmol, 11%) as a yellow solid along with starting material *rac*-**2** (10 mg, 21.6 μmol, 40%). **Procedure V:** A magnetically stirred solution of *rac*-**2** (25 mg, 53.9 μmol) and NaOAc (9.0 mg, 107.8 μmol) in degassed CH_3CN (0.5 mL) at 20 °C was treated with $[PdCl_2(PPh_3)_2]$ (4.48 mg, 5.39 μmol). The resulting suspension was heated to 90 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (19:1 pentane/EtOAc) of the crude product afforded dihydroanthracene *rac*-**3** (1.2 mg, 3.23 μmol, 6%) as a yellow solid along with starting material *rac*-**2** (14.5 mg, 31.3 μmol, 58%).

6,11-Dimethoxy-2,2,5-trimethyl-7-methylene-4,7-dihydro-1,3-dioxabenzo[*a*]anthracen-12-one (14). Procedure I: A magnetically stirred solution of benzophenone (**5**; 25 mg, 55.9 μmol) and nBu$_4$NOAc (34 mg, 111.8 μmol) in a degassed mixture of DMF/CH_3CN/H_2O (0.5 mL of a 5:5:1 solution) at 60 °C was treated with **4** (10.4 mg, 11.2 μmol). The resulting suspension was heated at 110 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (19:1 pentane/EtOAc) of the crude product afforded anthracenone **14** (15 mg, 40.8 μmol, 73%) along with starting material **3** (1.5 mg, 3.6 μmol, 6%) as a yellow solid. R_f = 0.3. UV/Vis λ_{max} (lg ε) = 194.0 nm (4.6834), 229.0 (4.6089). IR (KBr): $\tilde{\nu}$ = 1672 cm^{-1}, 1456, 1273. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60 (s, 6 H, 2×CH_3), 2.14 (s, 3 H, CH_3), 3.61 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 4.77 (s, 2 H, CH_2), 6.07 (s, 1 H, 1′-H), 6.53 (s, 1 H, 1′-H), 6.95 (d, J = 8.2 Hz, 1 H, Ar-H), 7.31–7.44 (m, 2 H, Ar-H) ppm. ^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 11.3, 24.7, 56.2, 59.8, 60.1, 67.0, 99.2, 111.2, 116.0, 119.3, 120.0, 121.7, 122.4, 129.3, 131.9, 132.5, 136.2, 141.1, 146.6, 147.9, 158.3, 183.5 ppm. MS (EI, 70 eV): m/z (%) = 366.2 (10) $[M]^+$, 308.1 (23) $[M - C_3H_6O]^+$, 293.1 (100) $[M - C_3H_6O - CH_3]^+$, 265.1 (6). $C_{22}H_{22}O_5$ (366.41). HRMS: calcd. 366.1467; found 366.1467. **Procedure II:** $[Pd_2(dba)_3]$ (1.53 mg, 1.68 μmol) and HP(tBu)$_3$BF$_4$ (0.97 mg, 3.35 μmol) were transferred into a flask containing a magnetic stirrer bar, which was then evacuated and refilled with argon. A solution of compound **5** (25 mg, 55.9 μmol) and Cy_2NMe (13.0 μL, 61.0 μmol) in degassed dioxane (0.5 mL) was then added in one portion at 20 °C. The resulting suspension was heated to 120 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (19:1 pentane/EtOAc) of the crude product afforded anthracenone **14** (15.9 mg, 43.6 μmol, 78%) as a yellow solid along with starting material **5** (1.2 mg, 2.7 μmol, 5%). **Procedure III:** A magnetically stirred solution of **5** (25 mg, 55.9 μmol), nBu$_4$NOAc (31.0 mg, 111.8 μmol) and K_2CO_3 (15.0 mg, 111.8 μmol) in degassed DMF (0.5 mL) at 20 °C was treated with $Pd(OAc)_2$ (1.25 mg, 5.59 μmol). The resulting suspension was heated to 90 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (19:1 pentane/EtOAc) of the crude product afforded anthracenone **14** (4.2 mg, 11.5 μmol, 22%) as a yellow solid along with starting material **5** (15.3 mg, 34.2 μmol, 61%). **Procedure IV:** A magnetically stirred solution of **5** (25 mg, 55.9 μmol) and NaOAc (9.1 mg, 111.8 μmol) in degassed CH_3CN (0.5 mL) at 20 °C was treated with $[PdCl_2(PPh_3)_2]$ (4.60 mg, 5.59 μmol). The resulting suspension was heated to 90 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (19:1 pentane/EtOAc) of the crude product afforded anthracenone **14** (1.4 mg, 4.17 μmol, 7%) as a yellow solid along with starting material **5** (17.4 mg, 38.9 μmol, 70%).

1-Benzyloxy-4,8,9-trimethoxy-3-methyl-10-methylene-9,10-dihydroanthracene-2-carbaldehyde (*rac*-15). Procedure I: A magnetically stirred solution of aldehyde *rac*-**6** (20 mg, 39.1 μmol) and nBu$_4$NOAc (23.6 mg, 78.2 μmol) in a degassed mixture of DMF/CH_3CN/H_2O (2 mL of a 5:5:1 solution) at 60 °C was treated in one portion with **4** (7.3 mg, 7.82 μmol). The resulting suspension was heated at 120 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (9:1 pentane/EtOAc) of the crude product afforded dihydroanthracene *rac*-**15** (13.8 mg, 32.1 μmol, 82%) as a yellow solid along with starting material *rac*-**6** (5.9 mg, 1.17 μmol, 3%). R_f = 0.8 (9:1 pentane/EtOAc). IR (KBr): $\tilde{\nu}$ = 2932 cm^{-1}, 1687, 1584. UV (CH_3CN): λ_{max} (lg ε) = 206.5 nm (4.6564), 283.0 (4.0785). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.53 (s, 3 H, CH_3), 3.21 (s, 3 H, OCH_3), 3.61 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.92 (d, J = 10.8 Hz, 1 H, CH_2Ph), 5.20 (d, J = 10.8 Hz, 1 H, CH_2Ph), 6.08 (s, 1 H, 1′-H), 6.31 (s, 1 H, 9-H), 6.46 (s, 1 H, 1′-H), 6.89 (dd, J = 9 Hz, 1.2 Hz, 1 H, Ar-H), 7.24–7.53 (m, 6 H, Ar-H), 7.55 (d, J = 1.5 Hz, 1 H, Ar-H), 10.50 (s, 1 H, CHO) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.0, 55.7, 55.8, 59.7, 64.6, 80.1, 109.6, 117.6, 118.9, 122.2, 127.2, 127.7, 128.4, 128.5, 128.5, 128.6, 128.7, 128.8, 129.0, 129.5, 136.3, 136.6, 137.8, 140.5, 152.7, 157.2, 192.2 ppm. MS (EI, 70 eV): m/z (%) = 430.2 (20) $[M]^+$, 308.1 (58), 280.1 (100). $C_{27}H_{26}O_5$ (430.49) HRMS: calcd. 430.1780; found 430.1780. **Procedure II:** $[Pd_2(dba)_3]$ (1.00 mg, 1.17 μmol) and HP(tBu)$_3$BF$_4$ (0.68 mg, 2.34 μmol) were transferred to a flask containing a magnetic stirrer bar, which was evacuated and then refilled with argon. A solution of compound *rac*-**6** (20 mg, 39.1 μmol) and Cy_2NMe (9.0 μL, 43.0 μmol) in degassed dioxane (0.5 mL) was then added in one portion at 20 °C. The resulting suspension was heated to 120 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (9:1 pentane/EtOAc) of the crude product afforded dihydroanthracene *rac*-**15** (13 mg, 30.2 μmol, 77%) as a yellow solid along with starting material *rac*-**6** (3.5 mg, 6.8 μmol, 18%). **Procedure III:** A magnetically stirred solution of *rac*-**6** (20 mg, 39.1 μmol), nBu$_4$NOAc (22 mg, 78.2 μmol) and K_2CO_3 (10.5 mg, 78.2 μmol) in degassed DMF (0.5 mL) at 20 °C was treated with $Pd(OAc)_2$ (1.2 mg, 5.4 μmol). The resulting suspension was heated to 90 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (9:1 pentane/EtOAc) of the crude product afforded dihydroanthracene *rac*-**15** (5.7 mg, 13.3 μmol, 34%) as a yellow solid along with starting material *rac*-**6** (10.5 mg, 20.4 μmol, 52%). **Procedure IV:** A magnetically stirred solution of *rac*-**6** (20 mg, 31.1 μmol) and NaOAc (6.4 mg, 78.2 μmol) in degassed CH_3CN (0.5 mL) at 20 °C was treated with $[PdCl_2(PPh_3)_2]$ (4.4 mg, 5.40 μmol). The resulting suspension was heated to 90 °C for 5 h with stirring. Work up was performed as described previously. Flash chromatography (9:1 pentane/EtOAc) of the crude product afforded dihydroanthracene *rac*-**15** (1.6 mg, 4.73 μmol, 12%) as a yellow solid along with starting material *rac*-**6** (13.4 mg, 26.4 μmol, 84%).

[1] a) W. Maison, J. V. Frangioni, *Angew. Chem.* **2003**, *115*, 4874; *Angew. Chem. Int. Ed.* **2003**, *42*, 4726; b) D. Farquhar, A. Cherif, E. Bakina, J. A. Nelson, *J. Med. Chem.* **1998**, *41*, 965; c) F. Arcamone, *Doxorubicin. Anticancer Antibiotics*, Academic Press, New York, **1981**.

[2] For application of the Heck reaction in natural product synthesis, see: a) L. F. Tietze, K. M. Sommer, J. Zinngrebe, F. Stecker, *Angew. Chem.* **2005**, in press; b) R. A. Britton, P. Edward, O. Brian, *J. Org. Chem.* **2004**, *69*, 3068; c) P.-H. Liang, J.-P. Liu, L.-W. Hsin, C.-Y. Cheng, *Tetrahedron* **2004**, *60*, 11655; d) L. F. Tietze, J. M. Wiegand C. A. Vock, *Eur. J. Org. Chem.* **2004**, 4107; e) S. Luo, C. A. Zificsak, R. P. Hsung, *Org. Lett.* **2003**, *5*, 4709; f) J. Zhao, X. Yang, X. Jia, S. Luo, H. Zhai, *Tetrahedron* **2003**, *59*, 9379; g) G. Mehta, H. M. Shinde, *Tetrahedron Lett.* **2003**, *44*, 7049; h) H.-J. Knölker, S. Filali, *Synlett* **2003**, 11,1752; i) G. D. Artman, III, S. M. Weinreb, *Org. Lett.* **2003**,

5, 1523; j) M. Kalesse, K. P. Chary, M. Quitschalle, A. Burzlaff, C. Kasper, T. Scheper, *Chem. Eur. J.* **2003**, *9*, 1129; k) L. F. Tietze, J. M. Wiegand, C. A. Vock, *J. Organomet. Chem.* **2003**, *9*, 2155; l) A. D. Lebsack, J. T. Link, L. E. Overman, B. A. Stearns, *J. Am. Chem. Soc.* **2002**, *124*, 9008; m) M. Mori, M. Nakanishi, D. Kajishima, Y. Sato, *J. Am. Chem. Soc.* **2003**, *125*, 9801; n) L. F. Tietze, W.-R. Krahnert, *Chem. Eur. J.* **2002**, *8*, 2116; o) B. M. Trost, O. R. Thiel, H.-C. Tsui, *J. Am. Chem. Soc.* **2002**, *124*, 11 616; p) A. Fürstner, O. R. Thiel, N. Kindler, B. Bartkowska, *J. Org. Chem.* **2000**, *65*, 7990; q) L. F. Tietze, S. Petersen, *Eur. J. Org. Chem.* **2000**, *9*, 1827; r) L. F. Tietze, H. Schirok, *J. Am. Chem. Soc.* **1999**, *121*, 10 264; s) M. E. Fox, C. Li, J. P. Marino Jr, L. E. Overman, *J. Am. Chem. Soc.* **1999**, *121*, 5467; t) L. F. Tietze, T. Nöbel, M. Spescha, *J. Am. Chem. Soc.* **1998**, *120*, 8971.

[3] For reviews see: a) L. F. Tietze, I. Hiriyakkanavar, H. P. Bell, *Chem. Rev.* **2004**, *104*, 3453; b) M. Shibasaki, F. Miyazaki, in *Handbook of Organopalladium Chemistry for Organic Synthesis* (Ed.: E. Negishi), John Wiley & Sons, Hoboken, NJ, **2002**; vol. 1, chapter IV, p. 1283; c) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009; d) Y. Donde, L. E. Overman, in *Catalytic Asymmetric Synthesis*, 2nd ed. (Ed.: I. Ojima.), John Wiley & Sons, New York, **2000**; chapter 8G; e) J. T. Link, L. E. Overman, in *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: F. Diedrich, P. J. Stang), Wiley-VCH, New York, **1998**; f) G. T. Crisp, *Chem. Soc. Rev.* **1998**, *27*, 42; g) A. de Meijere, F. E. Meyer, *Angew. Chem.* **1994**, *106*, 2373; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2379; h) R. F. Heck, *Org. React.* **1982**, *27*, 345.

[4] M. Portnoy, Y. Ben-David, I. Rousso, D. Milstein, *Organometallics* **1994**, *13*, 3465.

[5] W. A. Herrmann, C. B. Broßmer, K. Öfele, C.-P. Reisinger, T. Priermeier, M. Beller, H. Fisher, *Angew. Chem.* **1995**, *107*, 1989; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1844.

[6] M. T. Reetz, G. Lohmer, R. Schwickardi, *Angew. Chem. Int. Ed.* **1998**, *37*, 481.

[7] M. Beller, H. Fisher, W. A. Herrmann, K. Öfele, C. Broßmer, *Angew. Chem.* **1995**, *107*, 1992; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1848.

[8] a) M. R. Netherton, G. C. Fu, *Org. Lett.* **2001**, *3*, 4295; b) A. F. Littke, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 6989.

[9] M. Lautens, Y.-Q. Fang, *Org. Lett.* **2003**, *5*, 3679.

[10] L. F. Tietze, S. G. Stewart, M. E. Polomska, A. Modi, A. Zeeck, *Chem. Eur. J.* **2004**, *10*, 5233.

[11] For example see: a) D. W. Old, J. P. Wolfe, S. L. Buchwald, *J. Am. Chem. Soc.* **1998**, *120*, 9722; b) W. Shen, *Tetrahedron Lett.* **1997**, *38*, 5575; c) Y. Ben-David, M. Portnoy, D. Milstein, *J. Am. Chem. Soc.* **1989**, *111*, 8742.

[12] a) C. Gürtler, S. L. Buchwald, *Chem. Eur. J.* **1999**, *5*, 3107; b) A. F. Littke, G. C. Fu, *J. Org. Chem.* **1999**, *64*, 10.

[13] a) T. Jeffery, *Tetrahedron Lett.* **1985**, *26*, 2667; b) T. Jeffery, *Synthesis* **1987**, *1*, 70.

[14] D. D. Perrin, W. L. F. Armarego, *Purification of Laboratory Chemicals*, Pentagon Press, Oxford; **1988**, 3rd ed..

Received: November 2, 2004

