A Novel Palladium-Catalyzed Domino Tsuji–Trost–Heck Process for the Synthesis of Tetrahydroanthracenes

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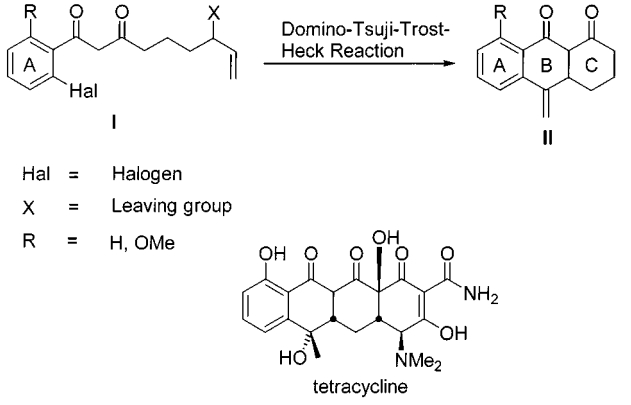
Dedicated to Professor Barry M. Trost on the occasion of his 60th birthday

Keywords: Heck reaction / Tsuji–Trost reaction / Palladium / Domino reactions / Tetracyclines

A novel type of palladium-catalyzed domino reaction is described combining Tsuji–Trost and Heck reactions. This method allows efficient access to tetrahydroanthracene derivatives **1** in up to 89% isolated yield in a one-pot process starting from the diketone **3**. The tetrahydroanthracene structural motif is found in many natural products, such as in the antibiotic tetracycline.

Introduction

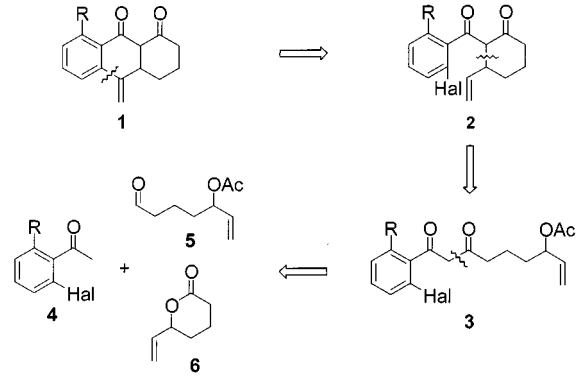
Domino reactions[1,2] represent one of the most efficient and elegant ways of forming highly diversified scaffolds of all-carbon and heterocyclic compounds; in the past few years this concept has also extended into the field of transition metal catalysis. Here, the palladium-catalyzed Heck reaction[3–6] and the Tsuji–Trost reaction[7–9] have found wide application and have been exploited in the synthesis of natural products.[10–16] We have recently used a combination of these two reactions for the first enantioselective total synthesis of the antileukemic pentacyclic alkaloid cephalotaxin.[17–20] Herein, we describe the preparation of the tetrahydroanthracene skeleton **II** from **I** in a domino process using a Tsuji–Trost reaction followed by a Heck reaction. The tetrahydroanthracene structural motif is found in many natural products, for instance in the antibiotic tetracycline (Scheme 1).[21]



Scheme 1. Concept for the synthesis of tetracyclines

One of the major problems associated with the combination of two Pd-catalyzed reactions[22] is the differentiation of the reacting functional groups; thus, a fine adjustment of their reactivity is necessary. In the Heck reaction, aryl iodides, bromides, and triflates are usually used; in our investigations we employed aryl iodides as well as bromides. For the Tsuji–Trost reaction, allyl halides, carbonates, acetates, and even ethers are suitable; since allyl halides are rather unstable and allyl ethers are too unreactive, we decided to use allyl acetates, which are usually more easily accessible than the carbonates.

Thus, we set out to use a substrate such as **3**, containing an allyl acetate moiety that could give an allylpalladium complex on treatment with Pd^0 and a 1,3-dicarbonyl moiety that could act as a nucleophile. In the Tsuji–Trost reaction, compound **2**, with a new ring bearing a vinyl group would be formed, which should undergo a Heck reaction under the same reaction conditions to give the desired tetrahydroanthracene **1** (Scheme 2).



Scheme 2. Retrosynthetic analysis of **1**

Results and Discussion

The starting material **3** for the domino reaction can be prepared either by an aldol reaction of an acetophenone **4**

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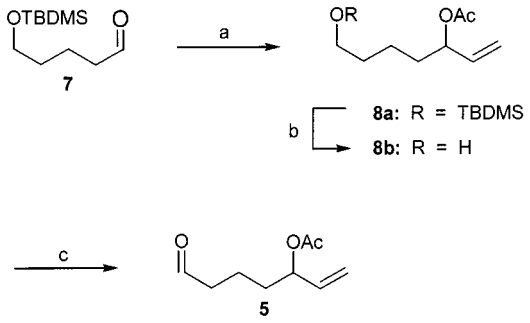
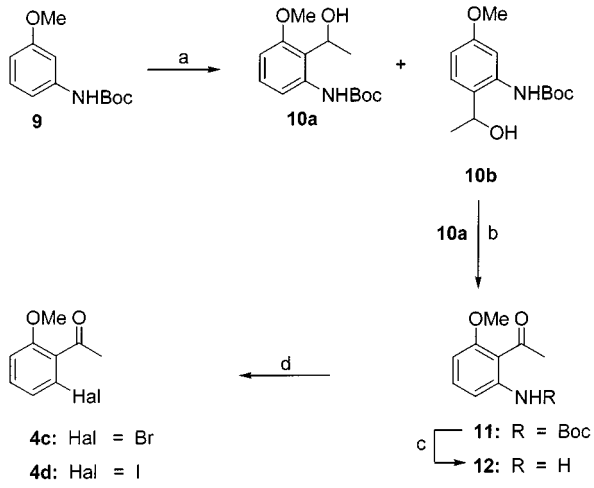
with an aldehyde **5** followed by oxidation, or by Claisen condensation of **4** with the lactone **6** followed by in situ acetylation. In practice, however, the latter reaction proved unreliable and hence we used the first approach. To make the synthesis as efficient as possible, we introduced the allyl acetate moiety required for the Tsuji–Trost reaction at the beginning. Fortunately, the allyl acetate survived the aldol reaction as well as the oxidation step. For the synthesis of **5**, the known TBDMS-protected 5-hydroxypentanal **7**[23] was treated with vinylmagnesium bromide in THF at −78 °C and the resulting adduct was acetylated in situ to give **8a**. Cleavage of the silyl ether in **8a** to form **8b** followed by oxidation led to the desired aldehyde **5** in 44% overall yield over the four steps (Scheme 3).

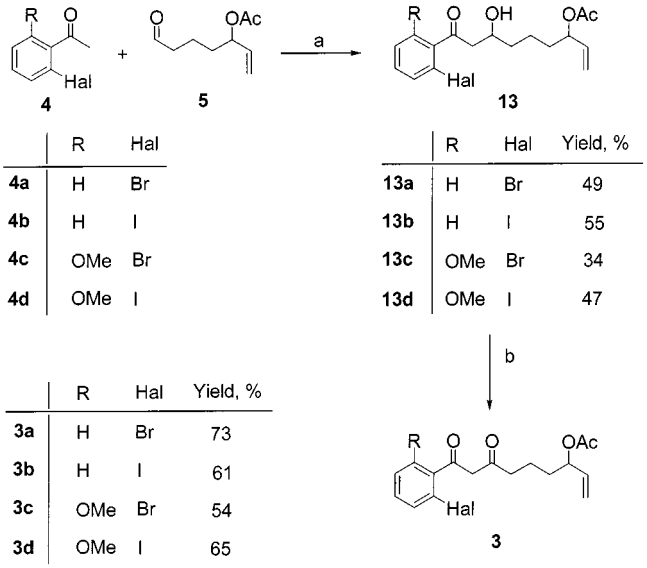


Scheme 3. Synthesis of aldehyde **5**: (a) vinylMgBr, THF, −78 °C, 15 min; then Ac_2O, room temp., 30 min; (b) camphorsulfonic acid (0.2 equiv.), MeOH/CH_2Cl_2 (1:1), 0 °C, 2 h, 46% over two steps; (c) ClCOCOCl, Me_2SO, CH_2Cl_2, −78 °C, 30 min, 96%

As the second component in the aldol reactions, we used the halogenated acetophenones **4a–d**. Compound **4a** is commercially available,[24] while **4b** was prepared according to the literature.[25] Additionally, **4c** and **4d** were incorporated in our investigations, since many tetrahydroanthracene-containing natural products, such as the tetracyclines, bear a hydroxy or a methoxy group on ring A. Compounds **4c** and **4d** were prepared starting from *N*-(*tert*-butyloxycarbonyl)anisidine (**9**)[26] using an *ortho*-lithiation[27] as the key step. The *tert*-butyloxycarbonyl group and the methoxy substituent were prerequisites for lithiation at C-2 in **9**, since both groups direct lithiation to their *ortho*-positions. However, reaction of **9** with *t*BuLi at −78 °C in THF followed by addition of ethanal led to the alcohol **10a** in only a moderate yield of 41%. In addition, 11% of the regioisomer **10b** was isolated and 23% of the starting material was recovered, which could easily be separated by chromatography. Thus, the reaction was not as selective as anticipated. Oxidation of **10a** with Dess–Martin periodinane[28–30] provided the corresponding ketone **11** in 66% yield. Treatment of **11** with 3 M HCl in dioxane resulted in clean formation of amine **12** in 94% yield, which was converted into **4c** and **4d** by means of Sandmeyer reactions in 62% and 88% yield, respectively (Scheme 4). Aldol reactions of the acetophenones **4a–d** with **5** using lithium diisopropylamide as the base gave the desired β-hydroxy ketones **13a–d** in 34–55% yield, which were oxidized to the corresponding 1,3-diketones **3a–d** using Dess–Martin periodinane[28–30] in 54–73% yield (Scheme 5).



Scheme 4. Synthesis of the acetophenones **4c** and **4d**: (a) *t*BuLi, ethanal, THF, −78 °C → −20 °C, 2 h, 41%; (b) Dess–Martin periodinane, CH_2Cl_2, 0 °C, 4 h, 66%; (c) 3 M HCl/dioxane, room temp., 2 h 30 min, 94%; (d) Hal = Br: CuBr, $NaNO_2$, H_2SO_4, acetic acid, 60 °C, 30 min, 62%; Hal = I: KI, $NaNO_2$, HCl, acetic acid, 60 °C, 1 h, 88%



	R	Hal
4a	H	Br
4b	H	I
4c	OMe	Br
4d	OMe	I

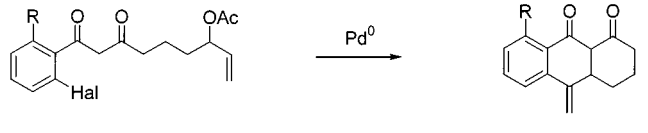
	R	Hal	Yield, %
13a	H	Br	49
13b	H	I	55
13c	OMe	Br	34
13d	OMe	I	47

	R	Hal	Yield, %
3a	H	Br	73
3b	H	I	61
3c	OMe	Br	54
3d	OMe	I	65

Scheme 5. Synthesis of the 1,3-diketones **3a–d**: (a) LDA, THF, −78 °C, 30 min, 34–55%; (b) Dess–Martin periodinane, CH_2Cl_2, 0 °C, 4 h, 54–73%

The moderate yields of the aldol reaction and the oxidation can be attributed to the instability of the aldehyde, the β-hydroxy ketone, and the 1,3-diketone. Thus, none of the compounds should be stored for longer than necessary and the best yields of **3a–d** are obtained using freshly prepared hydroxy ketones **13**. For the palladium-catalyzed domino process, we carefully chose our catalyst system such that the two different transformations would be possible under the same reaction conditions. Preliminary experiments revealed that the Tsuji–Trost reaction in the case of **3a** takes place

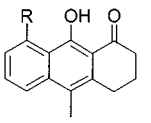
smoothly within 1.5 h at 20 °C using 10 mol % palladium acetate, 20 mol % triphenylphosphane, and 2.2 equiv. of triethylamine in acetonitrile/water (10:1). The Heck reaction did not take place under these conditions, since, as expected, a higher temperature is necessary. However, heating **3a** at 80 °C for 22 h using the aforementioned catalyst system resulted in the clean formation of **1a** in 49% yield together with 16% of its aromatized isomer **14a** (Scheme 6) as the only detectable compounds. Encouraged by this result, the same reaction conditions were applied to **3b**, **c**, and **d**. Substrate **3b** gave the cyclization product **1a** in only 23% yield together with 6% of the aromatized by-product **14a** in a somewhat sluggish reaction. Compound **3c** gave **1b** in 77% yield accompanied by less than 5% of the aromatized by-product **14b**. The best results were obtained with **3d**, which led to **1b** in 89% yield with almost no formation of the undesired naphthalene derivative **14b**. Furthermore, we have also shown that the amount of catalyst can be reduced, although a slight reduction in the yield may result. It is important that freshly prepared 1,3-diketones **3** are used for the domino process since they decompose on storage. The good results obtained using the 1,3-diketones **3c** and **3d** bearing a methoxy group at the arene moiety might be explained by their lower reactivity in the oxidative addition due to the presence of the electron-donating group. This leads to a better discrimination of the two functionalities that are able to react with Pd^0. The differentiation in the Tsuji−Trost and Heck reactions would clearly be highest for **3c** bearing a methoxy group and a bromo substituent. However, the corresponding intermediate of type **2** formed from **3c** is less reactive in the Heck reaction (Scheme 2) and hence **3d** gives the best results.



3 **1a**: R = H **1b**: R = OMe

	R	Hal
3a	H	Br
3b	H	I
3c	OMe	Br
3d	OMe	I

Substrate	Product	Yield, %
3a	**1a**	49
3b	**1a**	23
3c	**1b**	77
3d	**1b**	89



14a: R = H **14b**: R = OMe

Scheme 6. Domino reactions of **3a**−**d**: 10 mol % $Pd(OAc)_2$, 20 mol % PPh_3, 2.2 equiv. NEt_3, CH_3CN/H_2O (10:1), 80 °C, 23−89%

The structures of the newly formed compounds have mainly been determined by NMR spectroscopy. The ^1H NMR spectra of **3a**−**d** all show a broad singlet at δ = 16.07−16.30 and a singlet due to one proton at δ = 5.50−5.76, clearly indicating that under the conditions of the NMR experiments the diketones exist exclusively in their proton chelate form. The hydrogen atoms at the terminal double bond give rise to three multiplets at δ = 4.96−4.98, δ = 5.12−5.15, and δ = 5.58−5.63. In the ^1H NMR spectra of **1a** and **1b**, broad singlets are observed at δ = 15.14 for **1a** and at δ = 17.45 for **1b**. The two hydrogen atoms of the *exo* double bond give rise to two doublets at δ = 4.88 and δ = 5.18 with J = 2.7 Hz for **1a**, and at δ = 4.87 and δ = 5.25 with J = 2.1 Hz for **1b**.

Conclusion

The conceptually new domino process using a Tsuji−Trost and a Heck reaction described herein represents a powerful and flexible tool for the synthesis of substituted tetrahydroanthracenes. The approach will now be extended to modifications in C-ring size and to different substitution patterns on rings A and C.

Experimental Section

General: All reactions were performed under nitrogen or argon in flame-dried flasks; reactants were introduced by means of syringes. All solvents were dried by standard methods. Solvents used in Pd-catalyzed reactions were degassed by pump and freeze methodology. All reagents obtained from commercial sources were used without further purification. − Thin-layer chromatography (TLC) was performed on precoated silica gel SIL G/UV_{254} plates (Macherey−Nagel GmbH & Co. KG). Silica gel 32−63 (0.032−0.063 mm) (Macherey−Nagel GmbH & Co. KG) was used for column chromatography. Deactivated silica gel was prepared by dispersing it in a phosphate buffer solution (pH = 7.4) and then concentrating in vacuo to complete dryness. − UV/Vis spectra (λ_{max} [nm], log ε) were recorded with samples in CH_3CN using a Mettler Lambda 2 spectrophotometer. − IR spectra were recorded with samples in KBr pellets or as films using Bruker IFS 25 or Vector 22 spectrometers. − ^1H and ^{13}C NMR spectra were recorded with Varian XL 200, VXR 200, and VXR 500 spectrometers or with a Bruker AM-300 instrument, with tetramethylsilane (TMS) as an internal standard in [D]chloroform or [D_6]benzene solution. Multiplicities of ^{13}C NMR peaks were determined with the APT pulse sequence. In the ^{13}C NMR spectra of several aromatic ketones, signals attributable to the carbonyl groups were absent. Mass spectra were measured at 70 eV with a Varian MAT 311A instrument. − High-resolution mass spectra were recorded with a Varian MAT 731 instrument. − Melting points were measured with a Mettler FP 61 apparatus.

5-Acetoxyhept-6-en-1-ol (8b): To a solution of **7** (5.15 g, 23.8 mmol) in dry THF (50 mL), vinylmagnesium bromide in THF (60 mL, 60.0 mmol, 1.0 M) was added at −78 °C and the reaction mixture was stirred for 15 min. Acetic anhydride (5.6 mL, 59.5 mmol) was then added and the resulting mixture was allowed to warm to room temperature and stirred for 30 min. The solvent was then evaporated in vacuo and the residue was treated with a mixture of water and diethyl ether (1:1, 200 mL). The organic layer was washed with saturated aqueous K_2CO_3 (100 mL) and brine, dried with $MgSO_4$, and the solvents were evaporated in vacuo. Crude **8a** was then dissolved in $MeOH/CH_2Cl_2$ (1:1, 100 mL), camphorsulfonic acid (663 mg, 2.90 mmol) was added at 0 °C, and the mixture was stirred at this temp. for 2 h. It was then diluted with water (100 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated in vacuo, and the residue was purified by column chromatography (250 g SiO_2; pentane/EtOAc, 2:1) to

give **8b** (1.91 g, 11.1 mmol, 46%) as a yellow liquid; R_f = 0.16 (pentane/EtOAc, 2:1). − UV (CH_3CN): no absorption. − IR (film): $\tilde{\nu}$ = 3410, 3088, 2940, 2866, 1737, 1647, 1428, 1374, 1243, 1023, 933 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 1.18−1.79 (m, 6 H, 2-H_2, 3-H_2, 4-H_2), 2.07 (s, 3 H, CH_3), 3.65 (t, J = 6.1 Hz, 2 H, 1-H_2), 5.12−5.31 (m, 3 H, 5-H, 7-H), 5.78 (m_c, 1 H, 6-H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 21.2 (CH_3), 21.3 (C-3), 32.2, 33.9 (C-2, C-4), 62.5 (C-1), 74.6 (C-5), 116.6 (C-7), 136.3 (C-6), 170.4 (CO). − MS (DCI): *m/z* (%) = 362 (2) $[2 \times M + NH_4]^+$, 207 (14) $[M + NH_3 + NH_4]^+$, 190 (100) $[M + NH_4]^+$. − $C_9H_{16}O_3$ (172.1): calcd. C 62.77, H 9.36; found C 62.76, H 9.13.

5-Acetoxyhept-6-enal (5): To a solution of oxalyl chloride (673 µL, 7.83 mmol) in CH_2Cl_2 (15 mL), a solution of Me_2SO (1.1 mL, 15.6 mmol) in CH_2Cl_2 (2 mL) was added dropwise at −78 °C. The reaction mixture was stirred for 5 min at this temp. and then a solution of **8b** (900 mg, 5.23 mmol) in CH_2Cl_2 (4 mL) was added dropwise. After stirring for a further 30 min at −78 °C, triethylamine (3.6 mL, 26.1 mmol) was added and the mixture was allowed to warm to room temperature. It was washed with water (2 × 20 mL) and brine, dried with $MgSO_4$, and the volatiles were evaporated in vacuo. Chromatographic purification (20 g SiO_2; pentane/EtOAc, 2:1) of the residue afforded **5** (852 mg, 5.01 mmol, 96%) as a yellow liquid; R_f = 0.60 (pentane/EtOAc, 1:1). − UV (CH_3CN): no absorption. − IR (film): $\tilde{\nu}$ = 3419, 3088, 2941, 2727, 1737, 1650, 1427, 1373, 1242, 1111, 1075, 1022, 935 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 1.62−1.73 (m, 4 H, 3-H_2, 4-H_2), 2.07 (s, 3 H, CH_3), 2.41−2.55 (m, 2 H, 2-H_2), 5.14−5.34 (m, 3 H, 5-H, 7-H_2), 5.67−5.88 (m_c, 1 H, 6-H), 9.78 (s, 1 H, CHO). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 17.6 (CH_3), 21.2 (C-3), 33.4 (C-4), 43.3 (C-2), 74.2 (C-5), 117.0 (C-7), 136.0 (C-6), 170.3 (CO), 201.8 (C-1). − MS (DCI): *m/z* (%) = 358 (10) $[2 \times M + NH_4]^+$, 205 (27) $[M + NH_3 + NH_4]^+$, 188 (100) $[M + NH_4]^+$.

1-[2-(*tert*-Butyloxycarbonylamino)-6-methoxyphenyl]ethanol (10a): To a solution of **9** (1.00 g, 4.48 mmol) in dry THF (5 mL), a solution of *t*BuLi (6.4 mL, 10.8 mmol, 1.7 M in pentane) was added dropwise at −78 °C. The resulting mixture was stirred for 15 min at −78 °C and then for 2 h at −20 °C. A solution of ethanal (330 µL, 5.84 mmol) in dry THF (2 mL) was added and the resulting mixture was stirred for 2 h 30 min at −20 °C. It was then diluted with water/diethyl ether (1:1) and extracted with diethyl ether (3 × 25 mL). The combined extracts were washed with brine, dried with $MgSO_4$, and the solvent was evaporated in vacuo. Column chromatography (100 g SiO_2; pentane/EtOAc, 5:1) of the residue gave pure **10a** (371 mg, 1.39 mmol, 41%) as a yellow oil. The regioisomer **10b** (136 mg, 509 µmol) [R_f = 0.36 (pentane/EtOAc, 5:1)] and starting material **9** (231 mg, 1.03 mmol) could be separated by virtue of their different R_f values. R_f(**10a**) = 0.43 (pentane/EtOAc, 5:1). − UV (CH_3CN): λ_{max} (lg ε) = 285.5 (3.254), 279.5 (3.261), 241.0 (4.000), 212.5 (4.586). − IR (film): $\tilde{\nu}$ = 3444, 3322, 2976, 1705, 1598, 1531, 1476, 1431, 1367, 1255, 1163, 1049, 895, 785 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 1.48 (d, J = 6.9 Hz, 3 H, CH_3), 1.51 [s, 9 H, $OC(CH_3)_3$], 2.57 (br. s, 1 H, OH), 3.77 (s, 3 H, OCH_3), 5.60 (q, J = 6.9 Hz, 1 H, 1-H), 6.54 (d, J = 8.1 Hz, 1 H, 5-H), 7.16 (t, J = 8.1 Hz, 1 H, 4-H), 7.62 (d, J = 8.1 Hz, 1 H, 3-H), 8.65 (br. s, 1 H, NH). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 21.7 (C-2), 26.9 [$OC(CH_3)_3$], 55.6 (OCH_3), 64.5 (C-1), 79.9 [$OC(CH_3)_3$], 105.2 (Ar-C-5), 113.9 (Ar-C-2), 120.3 (Ar-C-1), 128.3 (Ar-C-4), 138.5 (Ar-C-3), 153.5 (NHCO), 156.0 (Ar-C-6). − MS (70 eV): *m/z* (%) = 267 (70) $[M]^+$, 166 (9) $[M - C_4H_9 - CO_2]^+$, 149 (78) $[M - C_4H_9 - CO_2 - OH]^+$, 57 (100) $[C_4H_9]^+$. − $C_{14}H_{21}NO_4$ (267.1): calcd. C 62.90, H 7.92; found C 63.19, H 8.13.

1-[2-(*tert*-Butyloxycarbonylamino)-6-methoxyphenyl]ethanone (11): To a solution of **10a** (300 mg, 1.12 mmol) in CH_2Cl_2 (15 mL), Dess−Martin periodinane (620 mg, 1.46 mmol) was added at 0 °C. The reaction mixture was stirred at this temp. for 1 h, then extracted with cold 1 N NaOH (2 × 10 mL), washed with brine, dried with $MgSO_4$, and concentrated to dryness in vacuo. Column chromatography (5 g SiO_2; pentane/EtOAc, 10:1) of the residue afforded **11** as an orange oil (195 mg, 735 µmol, 66%), which crystallized upon storage in a freezer; m.p. 63 °C; R_f = 0.34 (pentane/EtOAc, 10:1). − UV (CH_3CN): λ_{max} (lg ε) = 327.0 (3.565), 274.5 (3.749), 229.5 (4.333), 202.0 (4.409). − IR (KBr): $\tilde{\nu}$ = 3309, 3010, 2977, 2846, 1728, 1649, 1591, 1522, 1474, 1412, 1368, 1272, 1158, 1046, 1025, 881, 780, 602 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 1.51 [s, 9 H, $OC(CH_3)_3$], 2.59 (s, 3 H, CH_3), 3.89 (s, 3 H, OCH_3), 6.60 (d, J = 8.5 Hz, 1 H, 5-H), 7.36 (dd, J = 8.5, 8.5 Hz, 1 H, 4-H), 7.88 (d, J = 8.5 Hz, 1 H, 3-H), 9.67 (br. s, 1 H, NH). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 28.3 [$OC(CH_3)_3$], 33.5 (CH_3), 55.6 (OCH_3), 80.4 [$OC(CH_3)_3$], 104.8 (C-5), 112.4 (C-3), 116.2 (C-1), 133.4 (C-4), 140.1 (C-2), 153.0 (NHCO), 159.9 (C-6). − MS (70 eV): *m/z* (%) = 265 (17) $[M]^+$, 192 (7) $[M - C_4H_9O]^+$, 57 (100) $[C_4H_9]^+$. − $C_{14}H_{19}NO_4$ (265.1): calcd. C 63.38, H 7.22; found C 63.64, H 7.04.

1-(2-Amino-6-methoxyphenyl)ethanone (12): A solution of **11** (970 mg, 3.66 mmol) in 3 M HCl/dioxane (20 mL) was stirred for 2 h 30 min at room temperature. It was then neutralized with aqueous NaOH (10%, 40 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated in vacuo to give **12** (570 mg, 3.45 mmol, 94%) as yellow needles; m.p. 41 °C; R_f = 0.44 (pentane/EtOAc, 3:1). − UV (CH_3CN): λ_{max} (lg ε) = 352.0 (3.527), 275.0 (3.727), 237.0 (4.133), 202.0 (4.430). − IR (KBr): $\tilde{\nu}$ = 3478, 3368, 2939, 1610, 1466, 1356, 1277, 1138, 1101, 784, 735, 615 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 2.57 (s, 3 H, CH_3), 3.86 (s, 3 H, OCH_3), 5.86 (br. s, 2 H, NH_2), 6.19, 6.25 (d, J = 8.1 Hz, 1 H, 3-H, 5-H), 7.12 (t, J = 8.1 Hz, 1 H, 4-H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 33.8 (CH_3), 55.3 (OCH_3), 98.7 (C-5), 109.8 (C-3), 111.6 (C-1), 133.5 (C-4), 150.7 (C-2), 161.6 (C-6). − MS (70 eV): *m/z* (%) = 165 (64) $[M]^+$, 150 (100) $[M - CH_3]^+$, 135 (17) $[M - 2 \times CH_3]^+$. − $C_9H_{11}NO_2$ (165.1): calcd. 165.0789; found 165.0789 (HRMS).

1-(2-Bromo-6-methoxyphenyl)ethanone (4c): To prepare the Sandmeyer catalyst, $CuSO_4$ (720 mg, 4.51 mmol) was dissolved in water (4 mL), NaBr (700 mg, 6.80 mmol) was added, and then a solution of Na_2SO_3 (160 mg, 1.55 mmol) in water (1 mL) was added dropwise. The precipitate formed was washed with water and dissolved in concentrated HBr (2 mL). To generate the diazonium salt, a solution of $NaNO_2$ (270 mg, 3.91 mmol) in concentrated H_2SO_4 (2 mL) was added dropwise at 15 °C to a solution of **12** (560 mg, 3.39 mmol) in glacial acetic acid (8 mL). The mixture was stirred for 5 min at room temperature and subsequently added to the solution of the Sandmeyer catalyst at 15 °C. The reaction mixture was warmed to 60 °C for 30 min, cooled to room temperature, and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and the solvents were evaporated in vacuo. Column chromatography (50 g SiO_2; pentane/EtOAc, 3:1) of the residue afforded **4c** (483 mg, 2.12 mmol, 62%) as a yellow oil that crystallized on standing; m.p. 35 °C; R_f = 0.42 (pentane/EtOAc, 5:1). − UV (CH_3CN): λ_{max} (lg ε) = 345.5 (2.473), 281.0 (3.404), 197.5 (4.540). − IR (film): $\tilde{\nu}$ = 3400, 2943, 1713, 1589, 1462, 1430, 1353, 1261, 1184, 1152, 1095, 1032, 829, 776, 735 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 2.52 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 6.19 (dd, J = 2.0, 7.1 Hz, 1 H, 5-H), 7.11−7.24 (m,

2 H, 3-H, 4-H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 31.5 (CH_3), 56.0 (OCH_3), 109.9 (C-5), 117.8 (C-2), 124.8 (C-3), 130.7 (C-4), 132.8 (C-1), 156.6 (C-6), 202.3 (CO). − MS (70 eV): *m/z* (%) = 228 (26) $[M]^+$, 213 (100) $[M - CH_3]^+$, 198 (4) $[M - 2 \times CH_3]^+$, 170 (10) $[M - CH_3 - COCH_3]^+$. − $C_9H_9BrO_2$ (228.0): calcd. 227.9786; found 227.9786 (HRMS).

1-(2-Iodo-6-methoxyphenyl)ethanone (4d): A suspension of **12** (600 mg, 3.63 mmol) in water (4 mL), concentrated HCl (1 mL), and glacial acetic acid (4 mL) was warmed until the solid had fully dissolved. A solution of $NaNO_2$ (262 mg, 3.80 mmol) in water (1 mL) was then added at 0 °C and stirring was continued for 5 min. A solution of KI (631 mg, 3.80 mmol) in water (1 mL) was added and the resulting mixture was heated to 60 °C for 1 h and then cooled to room temperature. $NaHSO_3$ was added to destroy the excess iodine. The reaction mixture was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with aqueous $NaHCO_3$ and brine and dried with $MgSO_4$. Column chromatography (50 g SiO_2; pentane/EtOAc, 3:1) afforded **4b** (885 mg, 3.21 mmol, 88%) as yellow crystals; m.p. 41 °C; R_f = 0.42 (pentane/EtOAc, 10:1). − UV (CH_3CN): λ_{max} (lg ε) = 284.5 (3.392), 204.5 (4.410). − IR (KBr): $\tilde{\nu}$ = 3385, 2957, 1702, 1582, 1563, 1459, 1427, 1352, 1242, 1017, 817, 770, 732, 604 cm^{-1}. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.52 (s, 3 H, CH_3), 3.81 (s, 3 H, OCH_3), 6.89 (d, *J* = 8.1 Hz, 1 H, Ar-5-H), 7.03 (t, *J* = 8.1 Hz, 1 H, Ar-4-H), 7.40 (d, *J* = 8.1 Hz, 1 H, Ar-3-H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 30.9 (CH_3), 55.8 (OCH_3), 90.3 (Ar-C-2), 110.6 (Ar-C-5), 131.1 (Ar-C-3, Ar-C-4), 136.6 (Ar-C-1), 156.0 (Ar-C-6). − MS (70 eV): *m/z* (%) = 276 (52) $[M]^+$, 261 (100) $[M - CH_3]^+$, 246 (3) $[M - OCH_3]^+$, 218 (5) $[M - CH_3 - COCH_3]^+$, 203 (5) $[M - OCH_3 - COCH_3]^+$. − $C_9H_9IO_2$ (276.0): calcd. C 39.16, H 3.29; found C 38.90, H 3.45.

General Procedure I. − Synthesis of the β-Hydroxy Ketones 13a−d by Aldol Reactions of 4a−d with 5: To a stirred solution of diisopropylamine (1.2 equiv.) in dry THF (2 mL/mmol), *n*BuLi was added at 0 °C and the resulting mixture was stirred for 30 min at this temp. Thereafter, a solution of the appropriate ketone **4** (1.0 equiv.) in dry THF (1 mL/mmol) was added, the mixture was stirred for 30 min, then cooled to −78 °C, whereupon a solution of the aldehyde **5** (1.0 equiv.) in dry THF (1 mL/mmol) was added. The reaction mixture was stirred at −78 °C for 30 min, then quenched with saturated aqueous $NaHCO_3$ (1 mL/mmol) and extracted with CH_2Cl_2 (3 × 5 mL/mmol). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography.

7-Acetoxy-1-(2-bromophenyl)-3-hydroxynon-8-en-1-one (13a): According to General Procedure I, 2-bromoacetophenone (**4a**)[24] (746 mg, 3.75 mmol) was treated with aldehyde **5** (640 mg, 3.76 mmol). Column chromatography (50 g SiO_2; pentane/EtOAc, 2:1) afforded **13a** (673 mg, 1.83 mmol, 49%) as a yellow oil; R_f = 0.23 (pentane/EtOAc, 2:1). − UV (CH_3CN): λ_{max} (lg ε) = 280.5 (2.920), 206.5 (4.303). − IR (film): $\tilde{\nu}$ = 3459, 3086, 2941, 2866, 1732, 1587, 1465, 1429, 1372, 1244, 1023, 759 cm^{-1}. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.29−1.76 (m, 6 H, 4-H_2, 5-H_2, 6-H_2), 2.07 (s, 3 H, CH_3), 2.92−3.22 (m, 2 H, 2-H_2), 4.21 (m_c, 1 H, 3-H), 5.12−5.32 (m, 3 H, 7-H, 9-H), 5.78 (m_c, 1 H, 8-H), 7.27−7.44 (m, 3 H, Ar-3-H, Ar-4-H, Ar-5-H), 7.62 (d, *J* = 8.1 Hz, 1 H, Ar-6-H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 21.1 (C-5), 21.3 (CH_3), 34.0, 36.2 (C-4, C-6), 49.3 (C-2), 67.7 (C-3), 74.6 (C-7), 116.8 (C-9), 118.7 (Ar-C-2), 127.5, 128.6, 132.0, 133.8 (Ar-C-3, Ar-C-4, Ar-C-5, Ar-C-6), 136.4 (C-8), 141.0 (C-1), 170.4 (CO), 204.6 (C-1). − MS (DCI): *m/z* (%) = 754 (6) $[2 \times M + NH_4]^+$, 386 (98) $[M + NH_4]^+$. − $C_{17}H_{21}BrO_4$ (368.1): calcd. C 55.30, H 5.73; found C 55.60, H 5.83.

7-Acetoxy-3-hydroxy-1-(2-iodophenyl)non-8-en-1-one (13b): According to General Procedure I, 2-iodoacetophenone (**4b**) (1.25 g, 5.06 mmol) was treated with aldehyde **5** (861 mg, 5.06 mmol). Column chromatography (100 g SiO_2; pentane/EtOAc, 2:1) afforded **13b** (1.15 g, 2.76 mmol, 55%) as a yellow oil; R_f = 0.26 (pentane/EtOAc, 2:1). − UV (CH_3CN): λ_{max} (lg ε) = 290.0 (3.023), 218.0 (4.207). − IR (film): $\tilde{\nu}$ = 3459, 3083, 2941, 1733, 1696, 1581, 1461, 1426, 1372, 1244, 1019, 758, 722 cm^{-1}. − ^{1}H NMR (200 MHz, C_6D_6): δ = 1.13−1.60 (m, 6 H, 4-H_2, 5-H_2, 6-H_2), 1.71 (s, 3 H, CH_3), 2.53−2.61 (m, 2 H, 2-H_2), 4.06 (m_c, 1 H, 3-H), 5.02 (td, *J* = 1.4, 10.5 Hz, 1 H, 9-H_{cis}), 5.22 (td, *J* = 1.4, 17.2 Hz, 1 H, 9-H_{trans}), 5.42 (q, *J* = 6.9 Hz, 1 H, 7-H), 5.70 (ddd, *J* = 1.1, 10.5, 17.2 Hz, 1 H, 8-H), 6.46, 6.78 (dt, *J* = 1.6, 7.8 Hz, Ar-4-H, Ar-5-H), 6.89, 7.57 (dd, *J* = 1.6, 7.8 Hz, Ar-3-H, Ar-6-H). − ^{13}C NMR (50.3 MHz, C_6D_6): δ = 20.7 (CH_3), 21.3 (C-5), 34.3, 36.5 (C-4, C-6), 48.8 (C-2), 67.6 (C-3), 74.4 (C-7), 91.2 (Ar-C-2), 116.4 (C-9), 127.7, 128.1, 131.4, 137.0 (Ar-C-3, Ar-C-4, Ar-C-5, Ar-C-6), 140.6 (C-8), 144.4 (Ar-C-1), 169.4 (CO), 204.0 (C-1). − MS (DCI): *m/z* (%) = 850 (7) $[2 \times M + NH_4]^+$, 434 (100) $[M + NH_4]^+$. − $C_{17}H_{21}IO_4$ (416.0): calcd. C 49.05, H 5.09; found C 49.39, H 5.08.

7-Acetoxy-1-(2-bromo-6-methoxyphenyl)-3-hydroxynon-8-en-1-one (13c): According to General Procedure I, ketone **4c** (520 mg, 2.28 mmol) was treated with aldehyde **5** (350 mg, 2.06 mmol). Column chromatography (25 g SiO_2; pentane/EtOAc, 2:1) afforded **13c** (312 mg, 784 μmol, 34%) as a yellow oil; R_f = 0.40 (pentane/EtOAc, 2:1). − UV (CH_3CN): λ_{max} (lg ε) = 282.0 (3.264), 198.0 (4.421). − IR (film): $\tilde{\nu}$ = 3459, 3087, 2943, 2868, 1735, 1646, 1588, 1570, 1462, 1432, 1373, 1244, 1031, 828, 777, 736 cm^{-1}. − ^{1}H NMR (200 MHz, C_6D_6): δ = 1.17−1.60 (m, 6 H, 4-H_2, 5-H_2, 6-H_2), 1.69 (s, 3 H, CH_3), 2.79 (d, *J* = 5.7 Hz, 2 H, 2-H_2), 2.99 (s, 3 H, OCH_3), 4.27 (m_c, 1 H, 3-H), 4.99 (d, *J* = 10.7 Hz, 1 H, 9-H_{cis}), 5.19 (d, *J* = 17.3 Hz, 1 H, 9-H_{trans}), 5.40 (m_c, 1 H, 7-H), 5.68 (m_c, 1 H, 8-H), 6.13 (d, *J* = 8.3 Hz, 1 H, Ar-5-H), 6.60 (t, *J* = 8.3 Hz, 1 H, Ar-4-H), 6.91 (d, *J* = 8.3 Hz, 1 H, Ar-3-H). − ^{13}C NMR (50.3 MHz, C_6D_6): δ = 20.8 (CH_3), 21.5 (C-5), 34.5, 36.4 (C-4, C-6), 51.2 (C-2), 55.4 (OCH_3), 67.4 (C-3), 74.6 (C-7), 110.1 (Ar-C-5), 116.4 (C-9), 118.4 (Ar-C-2), 124.9 (Ar-C-1), 128.3, 130.8 (Ar-C-3, Ar-C-4), 137.2 (C-8), 156.8 (Ar-C-6), 169.5 (CO), 204.1 (C-1). − MS (DCI): *m/z* (%) = 416 (89) $[M + NH_4]^+$, 336 (100) $[M + NH_4 - Br]^+$. − $C_{18}H_{23}BrO_5$ (398.1): calcd. C 54.15, H 5.81; found C 54.02, H 5.71.

7-Acetoxy-1-(2-iodo-6-methoxyphenyl)-3-hydroxynon-8-en-1-one (13d): According to General Procedure I, ketone **4d** (558 mg, 2.02 mmol) was treated with aldehyde **5** (350 mg, 2.06 mmol). Column chromatography (35 g SiO_2; pentane/EtOAc, 2:1) afforded **13d** (421 mg, 944 μmol, 47%) as a colourless oil; R_f = 0.39 (pentane/EtOAc, 2:1). − UV (CH_3CN): λ_{max} (lg ε) = 285.0 (3.430), 205.0 (4.435). − IR (film): $\tilde{\nu}$ = 3640, 3084, 2942, 2866, 1733, 1582, 1565, 1459, 1429, 1372, 1245, 1026, 818, 775, 736 cm^{-1}. − ^{1}H NMR (300 MHz, C_6D_6): δ = 1.25−1.63 (m, 6 H, 4-H_2, 5-H_2, 6-H_2), 1.69 (s, 3 H, CH_3), 2.78 (d, *J* = 5.9 Hz, 2 H, 2-H_2), 2.97 (s, 3 H, OCH_3), 4.29 (m_c, 1 H, 3-H), 4.99 (d, *J* = 10.2 Hz, 1 H, 9-H_{cis}), 5.19 (d, *J* = 17.2 Hz, 1 H, 9-H_{trans}), 5.41 (m_c, 1 H, 7-H), 5.69 (m_c, 1 H, 8-H), 6.15 (d, *J* = 8.1 Hz, 1 H, Ar-5-H), 6.45 (t, *J* = 8.1 Hz, 1 H, Ar-4-H), 7.18 (d, *J* = 8.1 Hz, 1 H, Ar-3-H). − ^{13}C NMR (50.3 MHz, C_6D_6): δ = 20.8 (CH_3), 21.5 (C-5), 34.5, 36.4 (C-4, C-6), 50.7 (C-2), 55.3 (OCH_3), 67.4 (C-3), 74.5 (C-7), 91.1 (Ar-C-2), 110.8 (Ar-C-5), 116.4 (C-9), 131.1, 131.4 (Ar-C-3, Ar-C-4), 136.6 (Ar-C-1), 137.2 (C-8), 156.3 (Ar-C-6), 169.5 (CO), 205.9 (C-1). −

MS (DCI): *m/z* (%) = 464 (35) $[M + NH_4]^+$. − $C_{18}H_{23}IO_5$ (446.1): calcd. C 48.44, H 5.19; found C 48.37, H 5.08.

General Procedure II. − Synthesis of 1,3-Diketones 3a−d from β-Hydroxy Ketones 13a−d: To a solution of the freshly prepared β-hydroxy ketone **13**, Dess−Martin periodinane[28−30] was added at 0 °C. The resulting mixture was stirred for 4 h at 0 °C, concentrated in vacuo, and purified by chromatography on deactivated silica gel.

7-Acetoxy-1-(2-bromophenyl)non-8-ene-1,3-dione (3a): According to General Procedure II, β-hydroxy ketone **13a** (250 mg, 679 μmol) was oxidized with Dess−Martin periodinane (318 mg, 74.7 μmol). Column chromatography (5 g of deactivated SiO_2; pentane/EtOAc, 4:1) afforded **3a** (181 mg, 494 μmol, 73%) as a yellow oil; R_f = 0.37 (pentane/EtOAc, 4:1). − UV (CH_3CN): λ_{max} (lg ε) = 292.0 (4.063), 206.0 (4.133). − IR (film): $\tilde{\nu}$ = 3445, 3087, 2941, 1737, 1607, 1431, 1372, 1242, 1096, 1026, 964, 933, 767 cm^{-1}. − ^1H NMR (300 MHz, C_6D_6): δ = 1.33−1.60 (m, 4 H, 5-H_2, 6-H_2), 1.68 (s, 3 H, CH_3), 2.01 (t, *J* = 7.6 Hz, 2 H, 4-H_2), 4.98 (td, *J* = 1.4, 10.4 Hz, 1 H, 9-H_{cis}), 5.15 (td, *J* = 1.4, 17.1 Hz, 1 H, 9-H_{trans}), 5.34 (q, *J* = 6.2 Hz, 1 H, 7-H), 5.63 (m_c, 1 H, 8-H), 5.76 (s, 1 H, 2-H), 6.67, 6.82 (dt, *J* = 1.3, 8.1 Hz, 2 H, Ar-4-H, Ar-5-H), 7.27 (dd, *J* = 1.3, 8.1 Hz, 2 H, Ar-3-H, Ar-6-H), 16.30 (br. s, 1 H, OH). − ^{13}C NMR (75.5 MHz, C_6D_6): δ = 21.1 (CH_3), 21.2 (C-5), 33.5 (C-6), 38.2 (C-4), 74.2 (C-7), 101.2 (C-2), 117.0 (C-9), 120.1 (Ar-C-2), 127.4, 129.9, 131.6, 133.9 (Ar-C-3, Ar-C-4, Ar-C-5, Ar-C-6), 136.1 (C-8), 137.8 (Ar-C-1), 170.3 (CO), 186.2, 194.6 (C-1, C-3). − MS (70 eV): *m/z* (%) = 366 (17) $[M]^+$, 307 (22) $[M - CO_2CH_3]^+$, 227 (100) $[M - CO_2CH_3 - Br]^+$. − $C_{17}H_{19}BrO_4$ (366.0): calcd. C 55.60, H 5.21; found C 55.88, H 5.04.

7-Acetoxy-1-(2-iodophenyl)non-8-ene-1,3-dione (3b): According to General Procedure II, β-hydroxy ketone **13b** (1.00 g, 2.40 mmol) was oxidized with Dess−Martin periodinane[28−30] (1.54 g, 3.62 mmol). Column chromatography (100 g of deactivated SiO_2; pentane/EtOAc, 10:1) afforded **3b** (608 mg, 1.47 mmol, 61%) as a colourless oil; R_f = 0.27 (pentane/EtOAc, 10:1). − UV (CH_3CN): λ_{max} (lg ε) = 292.5 (4.074), 222.5 (4.058). − IR (film): $\tilde{\nu}$ = 3445, 3085, 2940, 1736, 1606, 1428, 1371, 1242, 1093, 1016, 964, 932, 767 cm^{-1}. − ^1H NMR (200 MHz, C_6D_6): δ = 1.28−1.60 (m, 4 H, 5-H_2, 6-H_2), 1.67 (s, 3 H, CH_3), 2.00 (t, *J* = 7.3 Hz, 2 H, 4-H_2), 4.98 (dd, *J* = 1.3, 10.3 Hz, 1 H, 9-H_{cis}), 5.15 (td, *J* = 1.3, 17.1 Hz, 1 H, 9-H_{trans}), 5.32 (q, *J* = 5.9 Hz, 1 H, 7-H), 5.51 (s, 1 H, 2-H), 5.61 (m_c, 1 H, 8-H), 6.48, 6.82 (dt, *J* = 1.6, 7.8 Hz, 2 H, Ar-4-H, Ar-5-H), 7.13, 7.61 (dd, *J* = 1.6, 7.8 Hz, 2 H, Ar-3-H, Ar-6-H), 16.24 (br. s, 1 H, OH). − ^{13}C NMR (50.3 MHz, C_6D_6): δ = 20.7 (CH_3), 21.3 (C-5), 33.8 (C-6), 38.1 (C-4), 74.0 (C-7), 93.4 (Ar-C-2), 100.9 (C-2), 116.7 (C-9), 128.3, 129.3, 131.4, 136.8 (Ar-C-3, Ar-C-4, Ar-C-5, Ar-C-6), 140.7 (C-8), 142.1 (Ar-C-1), 169.4 (CO), 188.5, 194.9 (C-1, C-3). − MS (DCI): *m/z* (%) = 846 (8) $[2 \times M + NH_4]^+$, 432 (100) $[M + NH_4]^+$. − $C_{17}H_{19}IO_4$ (414.0): calcd. C 49.29, H 4.62; found C 49.56, H 4.54.

7-Acetoxy-1-(2-bromo-6-methoxyphenyl)non-8-ene-1,3-dione (3c): According to General Procedure II, β-hydroxy ketone **13c** (228 mg, 573 μmol) was oxidized with Dess−Martin periodinane (366 mg, 860 μmol). Column chromatography (50 g of deactivated SiO_2; pentane/EtOAc, 5:1) afforded **3c** (123 mg, 311 μmol, 54%) as a yellow oil; R_f = 0.32 (pentane/EtOAc, 4:1). − UV (CH_3CN): λ_{max} (lg ε) = 284.5 (3.816), 198.5 (4.344). − IR (film): $\tilde{\nu}$ = 3444, 3089, 2943, 1736, 1590, 1571, 1462, 1432, 1372, 1242, 1032, 836, 780, 742 cm^{-1}. − ^1H NMR (200 MHz, C_6D_6): δ = 1.25−1.58 (m, 4 H, 5-H_2, 6-H_2), 1.65 (s, 3 H, CH_3), 1.95 (t, *J* = 7.2 Hz, 2 H, 4-H_2), 3.08 (s, 3 H, OCH_3), 4.96 (td, *J* = 1.1, 10.5 Hz, 1 H, 9-H_{cis}), 5.12 (td, *J* = 1.1, 17.1 Hz, 1 H, 9-H_{trans}), 5.28 (q, *J* = 5.9 Hz, 1 H, 7-H), 5.54 (s, 1 H, 2-H), 5.58 (m_c, 1 H, 8-H), 6.21 (d, *J* = 8.2 Hz, 1 H, Ar-5-H), 6.65 (t, *J* = 8.2 Hz, 1 H, Ar-4-H), 7.02 (d, *J* = 8.2 Hz, 1 H, Ar-3-H), 16.08 (br. s, 1 H, OH). − ^{13}C NMR (50.3 MHz, C_6D_6): δ = 20.4 (CH_3), 20.9 (C-5), 33.4 (C-6), 37.3 (C-4), 55.2 (OCH_3), 73.7 (C-7), 102.6 (C-2), 109.9 (Ar-C-5), 116.3 (C-9), 124.7 (Ar-C-2), 128.0 (Ar-C-1), 129.2, 130.7 (Ar-C-3, Ar-C-4), 136.5 (C-8), 157.5 (Ar-C-6), 169.0 (CO), 187.0, 192.8 (C-1, C-3). − MS (DCI): *m/z* (%) = 416 (100) $[M + NH_3 + NH_4]^+$. − $C_{18}H_{21}IO_4$ (396.0): calcd. C 54.42, H 5.33; found C 54.24, H 5.20.

7-Acetoxy-1-(2-iodo-6-methoxyphenyl)non-8-ene-1,3-dione (3d): According to General Procedure II, β-hydroxy ketone **13d** (343 mg, 769 μmol) was oxidized with Dess−Martin periodinane (491 mg, 1.15 mmol). Column chromatography (50 g of deactivated SiO_2; pentane/EtOAc, 5:1) afforded **3d** (222 mg, 500 μmol, 65%) as a yellow oil; R_f = 0.32 (pentane/EtOAc, 4:1). − UV (CH_3CN): λ_{max} (lg ε) = 287.0 (4.060), 206.0 (4.446). − IR (film): $\tilde{\nu}$ = 3444, 3087, 2941, 1735, 1612, 1565, 1459, 1429, 1372, 1243, 1027, 821, 778, 743 cm^{-1}. − ^1H NMR (200 MHz, C_6D_6): δ = 1.25−1.59 (m, 4 H, 5-H_2, 6-H_2), 1.66 (s, 3 H, CH_3), 1.97 (t, *J* = 7.3 Hz, 2 H, 4-H_2), 3.07 (s, 3 H, OCH_3), 4.96 (dd, *J* = 1.4, 10.3 Hz, 1 H, 9-H_{cis}), 5.13 (dd, *J* = 1.4, 17.3 Hz, 1 H, 9-H_{trans}), 5.30 (q, *J* = 6.0 Hz, 1 H, 7-H), 5.50 (s, 1 H, 2-H), 5.59 (m_c, 1 H, 8-H), 6.24 (d, *J* = 8.3 Hz, 1 H, Ar-5-H), 6.51 (t, *J* = 8.3 Hz, 1 H, Ar-4-H), 7.30 (d, *J* = 8.3 Hz, 1 H, Ar-3-H), 16.07 (br. s, 1 H, OH). − ^{13}C NMR (50.3 MHz, C_6D_6): δ = 20.7 (CH_3), 21.3 (C-5), 33.7 (C-6), 37.7 (C-4), 55.4 (OCH_3), 74.3 (C-7), 95.0 (Ar-C-2), 102.5 (C-2), 111.0 (Ar-C-5), 116.6 (C-9), 128.3 (Ar-C-1), 131.4, 133.2 (Ar-C-3, Ar-C-4), 136.8 (C-8), 157.1 (Ar-C-6), 169.3 (CO), 189.3, 193.3 (C-1, C-3). − MS (DCI): *m/z* (%) = 906 (7) $[2 \times M + NH_4]^+$, 462 (96) $[M + NH_4]^+$. − $C_{18}H_{21}IO_5$ (444.0): calcd. C 48.66, H 4.76; found C 48.35, H 4.49.

General Procedure III. − Domino Reaction of 3: A solution of the respective freshly prepared 1,3-diketone **3**, PPh_3 (20 mol %), and NEt_3 (2.2 equiv.) in CH_3CN/H_2O (10:1, 10 mL/mmol) was thoroughly degassed. $Pd(OAc)_2$ (10 mol %) was added and the reaction mixture was heated to 80 °C for the indicated time. After cooling to room temperature, it was concentrated in vacuo and purified by chromatography on deactivated silica gel.

10-Methylene-3,4,4a,10-tetrahydro-2*H*,9a*H*-anthracene-1,9-dione (1a). − A: According to General Procedure III, the 1,3-diketone **3a** (1.18 g, 3.22 mmol) was treated with $Pd(OAc)_2$ (75.3 mg, 335 μmol), PPh_3 (173 mg, 660 μmol), and NEt_3 (1.0 mL, 7.22 mmol) in CH_3CN/H_2O (10:1; 30 mL) for 22 h. Column chromatography (50 g of deactivated SiO_2; pentane/EtOAc, 30:1) afforded **1a** (359 mg, 1.59 mmol, 49%) together with its aromatized isomer **14a** (119 mg, 526 μmol, 16%). − **B:** According to General Procedure III, the 1,3-diketone **3b** (223 mg, 539 μmol) was treated with $Pd(OAc)_2$ (12.1 mg, 53.9 μmol), PPh_3 (28.3 mg, 108 μmol), and NEt_3 (165 μL, 1.19 mmol) in CH_3CN/H_2O (10:1; 5 mL) for 19 h. Column chromatography (10 g of deactivated SiO_2, pentane/EtOAc, 30:1) afforded **1a** (28 mg, 124 μmol, 23%) together with its aromatized isomer **14a** (7.23 mg, 32.0 μmol, 6%).

1a: R_f = 0.25 (pentane/EtOAc, 30:1). − UV (CH_3CN): λ_{max} (lg ε) = 346.0 (3.890), 317.5 (3.832), 262.0 (4.145), 223.5 (4.130). − IR (KBr): $\tilde{\nu}$ = 3456, 3062, 2945, 1611, 1408, 1317, 1110, 961, 911, 820, 772, 696, 578, 545 cm^{-1}. − ^1H NMR (200 MHz, C_6D_6): δ = 1.06−1.54 (m, 4 H, 3-H_2, 4-H_2), 1.59−1.76 (m, 1 H, 2-H), 1.97−2.15 (m, 1 H, 2-H), 3.02 (m_c, 1 H, 4a-H), 4.88, 5.18 (d, *J* = 2.7 Hz, 2 H, CH_2), 7.04−7.12 (m, 2 H, 6-H, 7-H), 7.25−7.32 (m, 1 H, 5-H), 8.19−8.28 (m, 1 H, 8-H), 15.14 (br. s, 1 H, OH). − ^{13}C NMR (50.3 MHz, C_6D_6): δ = 20.5 (C-3), 26.0 (C-4), 32.2 (C-4a), 38.1 (C-2), 107.3 (CH_2), 110.0 (C-9a), 124.8, 126.3, 129.0, 132.7

(C-5, C-6, C-7, C-8), 137.5 (C-10a), 140.9 (C-8a), 145.6 (C-10), 182.3, 187.5 (C-1, C-9). − MS (70 eV): *m/z* (%) = 226 (100) $[M]^+$, 198 (26) $[M - 2 \times CH_2]^+$, 170 (42) $[M - 4 \times CH_2]^+$. − $C_{15}H_{14}O_2$ (226.1): calcd. 226.0994; found 226.0993 (HRMS).

14a: M.p. 131 °C; R_f = 0.55 (pentane/EtOAc, 4:1). − UV (CH_3CN): λ_{max} (lg ε) = 382.0 (3.537), 300.0 (3.580), 290.5 (3.654), 271.0 (4.365), 263.0 (4.337), 220.5 (4.357). − IR (KBr): $\tilde{\nu}$ = 3424, 2926, 1613, 1392, 1241, 1185, 876, 764, 546 cm^{-1}. − ^1H NMR (200 MHz, C_6D_6): δ = 1.47 (tt, *J* = 5.9, 5.9 Hz, 2 H, 3-H_2), 2.17 (s, 3 H, CH_3), 2.29 (t, *J* = 5.9 Hz, 2 H, 2-H_2), 2.41 (t, *J* = 5.9 Hz, 2 H, 4-H_2), 7.28, 7.41 (dd, *J* = 8.1 Hz, 2 H, 6-H, 7-H), 7.75, 8.85 (d, *J* = 8.1 Hz, 1 H, 5-H, 8-H). − ^{13}C NMR (75.5 MHz, C_6D_6): δ = 13.6 (CH_3), 22.1, 27.2 (C-3, C-4), 38.4 (C-2), 119.8 (C-9a), 124.5 (C-10), 123.8, 124.8, 125.2, 130.3 (C-5, C-6, C-7, C-8), 134.9, 137.3 (C-4a, C-10a), 162.6 (C-9), 205.3 (C-1). − MS (70 eV): *m/z* (%) = 226 (100) $[M]^+$, 211 (12) $[M - CH_3]^+$, 198 (6) $[M - 2 \times CH_2]^+$. − $C_{15}H_{14}O_2$ (226.1): calcd. 226.0994; found 226.0994 (HRMS).

8-Methoxy-10-methylene-3,4,4a,10-tetrahydro-2*H*,9a*H*-anthracene-1,9-dione (1b). − A: According to General Procedure III, the 1,3-diketone **3c** (74.3 mg, 188 μmol) was treated with $Pd(OAc)_2$ (4.31 mg, 19.2 μmol), PPh_3 (10.4 mg, 39.6 μmol), and NEt_3 (58 μL, 418 μmol) in CH_3CN/H_2O (10:1; 4 mL) for 19 h. Column chromatography (10 g of deactivated SiO_2; pentane/EtOAc, 5:1) afforded **1b** (37 mg, 144 μmol, 77%) as yellow crystals. − **B:** According to General Procedure III, the 1,3-diketone **3d** (161 mg, 363 μmol) was treated with $Pd(OAc)_2$ (8.23 mg, 36.7 μmol), PPh_3 (19.3 mg, 73.6 μmol), and NEt_3 (112 μL, 808 μmol) in CH_3CN/H_2O (10:1, 4 mL) for 20 h. Column chromatography (20 g of deactivated SiO_2; pentane/EtOAc, 5:1) afforded **1b** (83.3 mg, 325 μmol, 89%) as a yellow oil that crystallized immediately. − M.p. 124 °C; R_f = 0.41 (pentane/EtOAc, 5:1). − UV (CH_3CN): λ_{max} (lg ε) = 339.5 (4.040), 228.0 (4.115), 203.5 (4.265). − IR (KBr): $\tilde{\nu}$ = 3424, 2953, 1587, 1469, 1440, 1395, 1335, 1320, 1294, 1260, 1053, 896, 820, 758 cm^{-1}. − ^1H NMR (300 MHz, C_6D_6): δ = 1.03−1.26 (m, 2 H, 3-H_2), 1.36 (m_c, 1 H, 4-H), 1.63 (m_c, 1 H, 4-H), 2.00−2.14 (m, 2 H, 2-H_2), 2.97 (m_c, 1 H, 4a-H), 3.39 (s, 3 H, OCH_3), 4.87, 5.25 (d, *J* = 2.1 Hz, 1 H, CH_2), 6.47 (d, *J* = 7.8 Hz, 1 H, 7-H), 6.96 (d, *J* = 7.8 Hz, 1 H, 5-H), 7.06 (d, *J* = 7.8 Hz, 1 H, 6-H), 17.45 (br. s, 1 H, OH). − ^{13}C NMR (50.3 MHz, C_6D_6): δ = 20.5 (C-3), 25.9 (C-4), 31.8 (C-2), 37.9 (C-4a), 55.7 (OCH_3), 107.8 (CH_2), 109.6 (C-9a), 112.4 (C-7), 117.5 (C-5), 120.4 (C-8a), 133.5 (C-6), 144.1 (C-10a), 147.1 (C-10), 160.3 (C-8), 183.9, 185.6 (C-1, C-9). − MS (70 eV): *m/z* (%) = 256 (100) $[M]^+$, 228 (27) $[M - 2 \times CH_3]^+$, 213 (11) $[M - 2 \times CH_2 - CH_3]^+$, 200 (28) $[M - 4 \times CH_2]^+$, 185 (11) $[M - 4 \times CH_2 - CH_3]^+$. − $C_{16}H_{16}O_3$ (256.1): calcd. 256.1099; found 256.1099 (HRMS).

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